Expanded therapeutic potential in activity space of next-generation 5-nitroimidazole antimicrobials with broad structural diversity

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Supplemental Materials and Methods

1. Synthesis and structural characterization

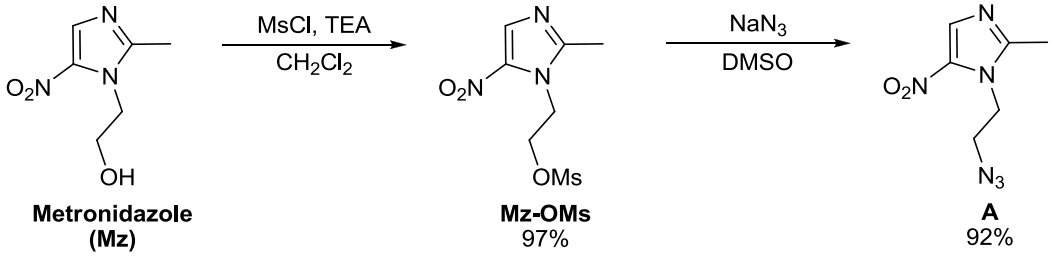
1.1. General

All chemical reagents and solvents were purchased from commercial suppliers and used without further purifications. ^{1}H, ^{13}C NMR spectra were obtained on Varian Inova 400 MHz or Bruker 500 MHz spectrometers. The chemical shifts (δ) were expressed in parts per million (ppm) relative to residual: $CHCl_3$ (δH 7.26 ppm), $CDCl_3$ (δC 77.0 ppm), CH_3SOCH_3 (δH 2.50 ppm) and CD_3SOCD_3 (δC 39.43 ppm). NMR acquisitions were performed at 295 K unless otherwise noted. Abbreviations are: s, singlet; d, doublet; t, triplet; q, quartet, brs, broad singlet. High resolution mass spectrometry was performed on an Agilent ES-TOF instrument at The Scripps Center for Metabolomics and Mass Spectrometry. Reactions were monitored by LCMS analysis (Hewlett-Packard Series 1100, ESI MS) eluting with 0.1% trifluoroacetic acid in H_2O and 0.05% trifluoroacetic acid in CH_3CN and/or TLC chromatography using Merck TLC Silica Gel 60 F254 plates and visualized by staining with cerium molybdate (Hanessian's Stain) or by

absorbance of UV light at 254 nm. Crude reaction mixtures were purified by column chromatography using Merck Silica Gel 60 as stationary phase. The purity of all synthesized alkynes was ≥90% based on the LCMS analysis. The purity and conversion of all "Click chemistry" reaction mixtures were ≥80% based on the LCMS analysis. Selected products for in-vivo studies were prepared in pure form and characterized by ^{1}H, ^{13}C NMR and HRMS (ESI TOF).

1.2. Synthesis of azides (A-F)

1.2.1. Synthesis of azide A

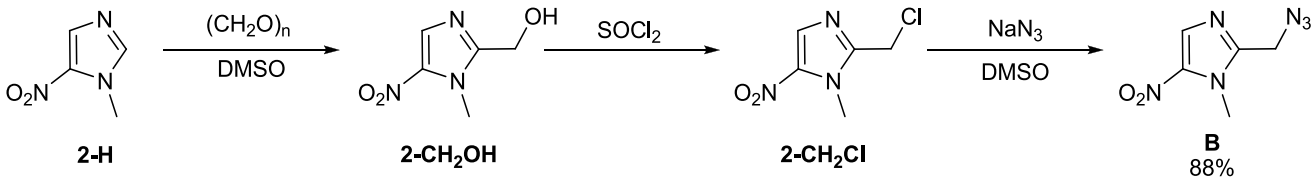


Scheme 1. Synthesis of azide **A**.

2-(2-Methyl-5-nitro-1*H*-imidazol-1-yl)ethyl methanesulfonate (Mz-OMs). A solution of methanesulfonyl chloride (27.0 mL, 40.0 g, 349 mmol, 1.2 equiv.) in CH_2Cl_2 (50 mL) was added dropwise into stirred, cooled (~10°C) suspension of metronidazole (50 g, 292 mmol), TEA (61 mL, 44.3 g, 439 mmol, 1.5 equiv.) in CH_2Cl_2 (250 mL) (1, 2). After addition the reaction was stirred at r.t. for 4 h then evaporated. The solid residue was washed with H_2O and dried on vacuum to give white solid (71 g, 97%). ^{1}H NMR (400 MHz, d_6-DMSO) δ= 8.06 (s, 1H), 4.65 (t, *J*=5.0 Hz, 2H), 4.55 (t, *J*=5.0 Hz, 2H), 3.15 (s, 3H), 2.46 (s, 3H). ^{13}C NMR (100 MHz, d_6-DMSO) δ= 151.6, 138.3, 133.0, 68.4, 45.0, 36.6, 13.9.

1-(2-Azidoethyl)-2-methyl-5-nitro-1*H*-imidazole (A). A suspension of **Mz-OMs** (71 g, 285 mmol) and NaN_3 (22.2 g, 341 mmol, 1.2 equiv.) in DMSO (600 mL) was stirred at 70°C for 4 h. Subsequently, the mixture was cooled, diluted with H_2O (1 L) and brine (2 L) and extracted using $CHCl_3$ (4×300 mL). Combined organic layers were washed with H_2O (2×500 mL), dried over $MgSO_4$, filtered and evaporated to give white solid of **A** (51.7g, 92%). ^{1}H NMR (400 MHz, $CDCl_3$) δ= 7.95 (s, 1H), 4.41 (t, *J*=5.6 Hz, 2H), 3.75 (t, *J*=5.6 Hz, 2H), 2.52 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ= 151.2, 138.1, 133.3, 50.8, 45.4, 14.4.

1.2.2. **Synthesis of azide B**



Scheme 2. Synthesis of azide **B**.

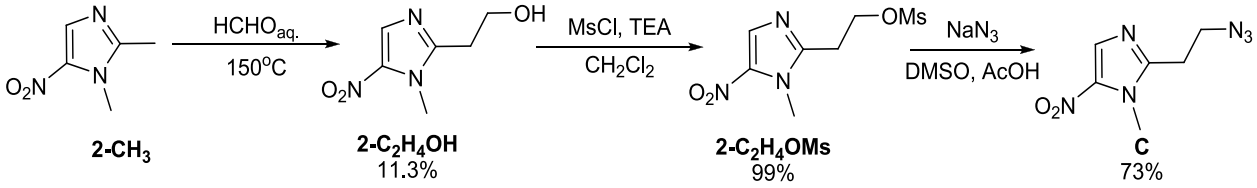
(1-Methyl-5-nitro-1*H*-imidazol-2-yl)methanol (2-CH_2OH). The title compound was prepared according to the literature procedure (3). ^{1}H NMR (400 MHz, d_6-DMSO) δ= 8.00 (s, 1H), 5.67 (t, *J*=6.0 Hz, 1H), 4.58 (d, *J*=6.0 Hz, 2H), 3.92 (s, 3H). ^{13}C NMR (100 MHz, d_6-DMSO) δ= 152.3, 139.2, 131.4, 56.0, 33.2. ESI MS (MeOH) for $[M+H]^+$ = 158.2 Da.

2-(Chloromethyl)-1-methyl-5-nitro-1*H*-imidazole (2-CH_2Cl). The title compound was prepared according to the literature procedure (4). ^{1}H NMR (400 MHz, $CDCl_3$) δ= 7.93 (s, 1H), 4.67 (s, 2H), 4.03 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ= 147.1, 139.6, 131.7, 36.1, 33.8. ESI MS (MeOH) for $[M+H]^+$ = 176.2 Da.

2-(Azidomethyl)-1-methyl-5-nitro-1*H*-imidazole (B). A mixture of **2-CH_2Cl** (3 g, 17.1 mmol), NaN_3 (1.22 g, 18.8 mmol, 1.1 equiv.) in DMSO (20 mL) was stirred at r.t. overnight.

Subsequently, the mixture was diluted with EtOAc (150 mL) and washed with brine (5×25 mL). The organic layer was passed through short silica-gel pad and evaporated to give **B** as a brown oil (2.76 g, 88%). ^{1}H NMR (400 MHz, $CDCl_3$) δ= 7.94 (s, 1H), 4.49 (s, 2H), 3.98 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ= 146.6, 139.7, 131.8, 46.7, 33.6.

1.2.3. Synthesis of azide C



Scheme 3. Synthesis of azide **C**.

2-(1-Methyl-5-nitro-1*H*-imidazol-2-yl)ethanol (2-C_2H_4OH). A mixture of **2-CH_3** (40 g, 283 mmol) and 37% formaldehyde solution in H_2O (140 mL, 1.86 mol, 6.6 equiv.) in high-pressure resistant sealed glass tube was heated at 150°C for 12 h, then cooled down and carefully opened. The brown solution was stirred with EtOAc (1 L) at 60°C for 15 min. The organic layer was separated and evaporated. The residue was purified by column chromatography (silica-gel, EtOAc→5% MeOH in EtOAc) to give a yellowish solid that was additionally purified by crystallization from CH_3CN (20 mL) (5.5 g, 11.3%). H NMR (400 MHz, d_6-DMSO) δ= 8.02 (s, 1H), 4.84 (t, *J*=5.4 Hz, 1H, -OH), 3.85 (s, 3H, N-Me), 3.77-3.73 (m, 2H), 2.91 (t, *J*=6.0 Hz, 2H). ^{13}C NMR (100 MHz, d_6-DMSO) δ= 152.4, 138.7, 132.4, 58.8, 33.1, 30.6.

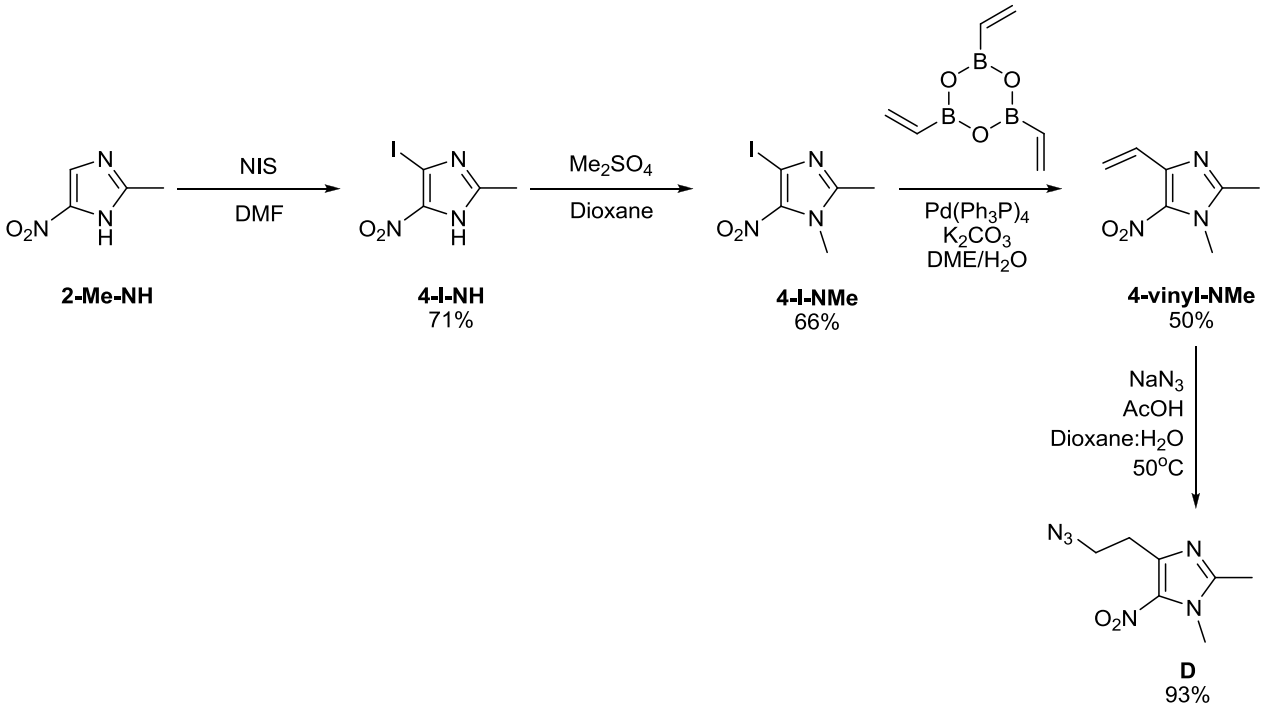
2-(1-Methyl-5-nitro-1*H*-imidazol-2-yl)ethyl methanesulfonate (2-C_2H_4OMs). To a suspension of **2-C_2H_4OH** (2 g, 11.7 mmol) and TEA (1.8 mL, 1.3 g, 12.9 mmol, 1.1 equiv.) in anhydrous CH_2Cl_2 (30 mL), methanesulfonyl chloride (1 mL, 1.48 g, 12.9 mmol, 1.1 equiv.) was

added. The mixture was stirred at r.t. for 1 h and H_2O (30 mL) was added. The organic layer was dried over $MgSO_4$, filtered and evaporated to give a yellow solid (2.9 g, 99%). The crude product was used in the next step without purification. ESI MS (MeOH) for $[M+H]^+$ = 250.1 Da.

2-(2-Azidoethyl)-1-methyl-5-nitro-1*H*-imidazole (C). To a mixture of **2-C_2H_4OMs** (7 g, 28 mmol) and AcOH (8 mL, 8.4 g, 140 mmol, 5 equiv.) in DMSO (60 mL), NaN_3 (5.5 g, 84 mmol, 3 equiv.) was added. The mixture was stirred at r.t. for 1 day, and then diluted with H_2O (30 mL) and EtOAc (100 mL). The organic layer was washed with brine (5×25 mL), dried over $MgSO_4$, filtered and evaporated. The residue was purified by column chromatography (silica-gel, EtOAc) to give an orange solid (4 g, 73%). ^{1}H NMR (400 MHz, $CDCl_3$) δ= 7.97 (s, 1H), 3.94 (s, 3H), 3.83 (t, *J*=6.6 Hz, 2H), 2.96 (t, *J*=6.6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ= 149.9, 132.4, 125.6, 48.6, 33.2, 27.4. ESI MS (MeOH) for $[M+H]^+$ = 197.4 Da.

- Elimination of the methanesulfonic acid takes place and 1-Methyl-5-nitro-2-vinyl-1*H*-imidazole is a major side product. Addition of AcOH reduces amount of the vinyl side-product.
- *CAUTION!* Any experiments that may result in the formation of hydrazoic acid (HN_3) should be performed in a well-ventilated fume hood and behind a blast shield. Sodium azide should not be mixed with strong acids.

1.2.4. Synthesis of azide D



Scheme 4. Synthesis of azide **D**.

4-Iodo-2-methyl-5-nitro-1*H*-imidazole (4-I-NH). The title compound was prepared using a similar literature procedure as for the bromination reaction (5). To a stirred warm (55°C) solution of **2-Me-NH** (45 g, 354 mmol) in anhydrous DMF (150 mL), NIS (87.5 g, 389 mmol, 1.1 equiv.) was added in one portion. After addition, the temperature was increased to 80°C and the reaction was carried out for 4 h. Subsequently, the reaction was cooled and poured into H_2O (2 L). A yellow solid was filtered, washed with 10% $Na_2S_2O_3$ solution, H_2O and dried on high vacuum (63.5 g, 71%). ESI MS (MeOH) for $[M+H]^+$ = 254.1 Da.

4-Iodo-1,2-dimethyl-5-nitro-1*H*-imidazole (4-I-NMe). A mixture of **4-I-NH** (63.5 g, 251 mmol) and Me_2SO_4 (31.6 g, 23.7 mL, 251 mmol) in 1,4-dioxane (600 mL) was stirred under reflux for 3 h and then evaporated. The resulting yellow oil was dissolved in H_2O (330 mL) and neutralized with saturated $NaHCO_{3(aq)}$. Yellow solid was filtered and washed with 1 M NaOH to

give the product as a yellow solid (44 g, 66%). ^{1}H NMR (400 MHz, d_6-DMSO) δ= 3.80 (s, 3H), 2.40 (s, 3H). ^{13}C NMR (100 MHz, d_6-DMSO) δ= 152.0, 139.5, 92.6, 34.4, 13.5. ESI MS (MeOH) for $[M+H]^+$ = 268.2 Da. The product contains approx. 15% of the 5-iodo-1,2-dimethyl-4-nitro-1*H*-imidazole isomer. The structure of **4-I-NH** was confirmed by comparison with the literature NMR spectra (6).

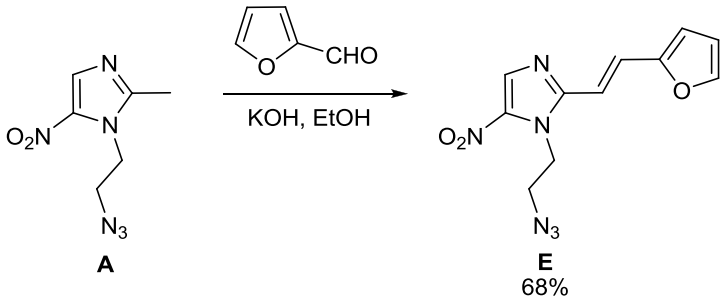
1,2-Dimethyl-5-nitro-4-vinyl-1*H*-imidazole (4-vinyl-NMe). The title compound was prepared using a similar literature procedure (7). To a mixture of **4-I-NMe** (17.7 g, 66.4 mmol) in degassed DME (520 mL), $Pd(PPh_3)_4$ (7.67 g, 6.6 mmol, 10% mol.) was added and the reaction was stirred under N_2 at r.t. for 20 min. Subsequently, K_2CO_3 (9.15 g, 66.4 mmol), H_2O (160 mL) and vinylboronic anhydride pyridine complex (16 g, 66.4 mmol) were added. The reaction was stirred under reflux under N_2 for overnight, then evaporated to the final volume (~100 mL) and extracted using Et_2O (2×300 mL). The combined organic layers were washed with 1 M HCl (4×50 mL). The aqueous layers were filtered, saturated with solid NaCl and neutralized with 2 M NaOH, and the aqueous mixture was transferred to separatory funnel and extracted using Et_2O (5×100 mL). The organic layers were dried over $MgSO_4$ and filtered. The product crystallized from Et_2O, yellowish solid (5.5 g, 50%). ^{1}H NMR (400 MHz, $CDCl_3$) δ= 7.33-7.25 (m, 1H), 6.31 (dd, *J*=17.2, 1.6 Hz, 1H), 5.57 (dd, *J*=17.2, 1.6 Hz, 1H), 3.84 (s, 3H), 2.44 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ= 148.8, 141.6, 126.6, 121.8, 33.8, 14.1. ESI MS (MeOH) for $[M+H]^+$ = 168.4 Da.

4-(2-Azidoethyl)-1,2-dimethyl-5-nitro-1H-imidazole (D). To a mixture of **4-vinyl-NMe** (2 g, 12 mmol), NaN_3 (2.34 g, 36 mmol, 3 equiv.) in 1,4-dioxane:H_2O (3:1, 80 mL), TEA (5.05 mL, 3.64 g, 36 mmol, 3 equiv.) and AcOH (6.86 mL, 7.2 g, 120 mmol, 10 equiv.) were added. The mixture was stirred at 50°C for 2 days and then cooled. The reaction was neutralized with solid

$NaHCO_3$ and evaporated to the final volume of ~20 mL. The remaining solution was diluted with H_2O (100 mL) and extracted using EtOAc (2×100 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and evaporated to give a red oil (2.35 g, 93%). ^{1}H NMR (400 MHz, $CDCl_3$) δ= 3.85 (s, 3H), 3.65 (t, *J*=6.8 Hz, 2H), 3.21 (t, *J*=6.8 Hz, 2H), 2.43 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ= 148.3, 143.7, 49.0, 33.9, 29.1, 14.0. ESI MS (MeOH) for $[M+H]^+$ = 211.2 Da.

- *CAUTION!* Any experiments that may result in the formation of hydrazoic acid (HN_3) should be performed in a well-ventilated fume hood and behind a blast shield. Sodium azide should not be mixed with strong acids.
- The product slowly decomposes at r.t. and should be stored at +4°C.

1.2.5. Synthesis of azide E

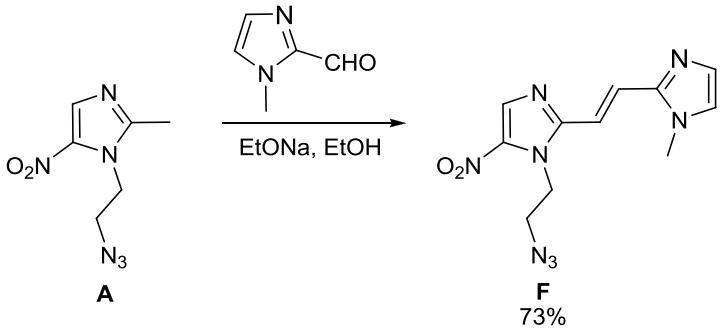


Scheme 5. Synthesis of azide **E**.

(E)-1-(2-Azidoethyl)-2-(2-(furan-2-yl)vinyl)-5-nitro-1*H*-imidazole (E). A mixture of **A** (4 g, 20.4 mmol), 2-furaldehyde (2.35 g, 24.5 mmol, 1.2 equiv.) and KOH (85%, 1.3 g, 20.4 mmol) in EtOH (20 mL) was stirred at 60°C for one day. After cooling, the mixture was diluted with H_2O (200 mL) and a brown-yellow solid was filtered. Crude product was dissolved in EtOAc, passed through a short silica-gel pad and evaporated to give a yellow-red solid (3.8 g, 68%). ^{1}H NMR

(400 MHz, $CDCl_3$) δ= 8.10 (s, 1H), 7.64 (d, *J*=15.6 Hz, 1H), 7.48 (s, 1H), 6.82 (d, *J*=15.6 Hz, 1H), 6.58 (d, *J*=3.2 Hz, 1H), 6.49-6.47 (m, 1H), 4.58 (t, *J*=5.6 Hz, 2H), 3.77 (t, *J*=5.6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ= 151.5, 150.6, 144.3, 138.2, 135.1, 126.6, 114.1, 112.5, 109.0, 50.8, 44.6. ESI MS (MeOH) for $[M+H]^+$ = 275.2 Da.

1.2.6. Synthesis of azide F



Scheme 6. Synthesis of azide **F**.

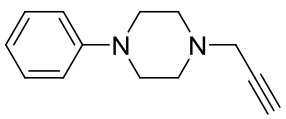
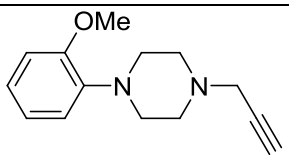
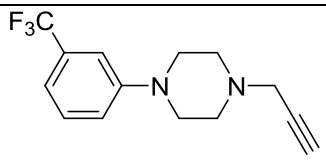
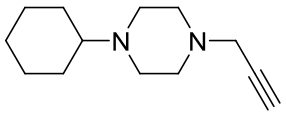
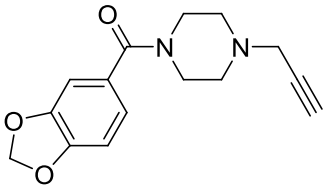
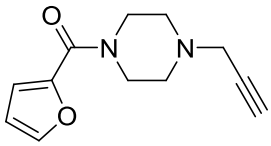
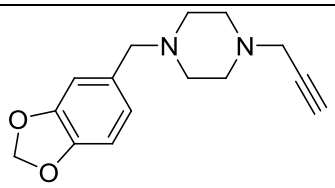
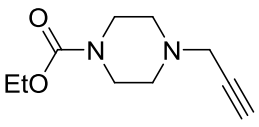
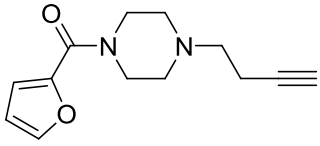
(E)-1-(2-Azidoethyl)-2-(2-(1-methyl-1*H*-imidazol-2-yl)vinyl)-5-nitro-1*H*-imidazole (F). To a solution of **A** (2.97 g, 15.1 mmol) in EtOH (15 mL), EtONa (2.55 g, 37.5 mmol, 2.5 equiv.) was added. The mixture was stirred at r.t. for 10 min and 1-methyl-1*H*-imidazole-2-carbaldehyde (2 g, 18.2 mmol, 1.2 equiv.) was added. The reaction was carried out at 60°C for 2 h and then cooled and diluted with H_2O (100 mL). The mixture was extracted using EtOAc (2×100 mL) and the combined organic layers were dried over $MgSO_4$, filtered and evaporated. The residue was purified by column chromatography (silica-gel, EtOAc→10% MeOH in $CHCl_3$) to give an orange solid that was additionally purified by crystallization from EtOAc (3.2 g, 73%). ^1H NMR (400 MHz, d_6-DMSO) δ= 8.28 (s, 1H), 7.69 (d, *J*=15.2 Hz, 1H), 7.39 (d, *J*=15.0 Hz, 1H), 7.31 (s, 1H), 7.07 (s, 1H), 4.69 (t, *J*=5.4 Hz, 2H), 3.82 (t, *J*=5.4 Hz, 2H), 3.79 (s, 3H). ^{13}C NMR (100

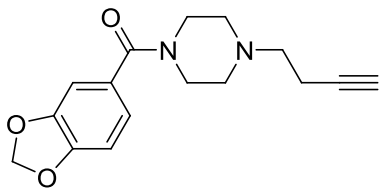
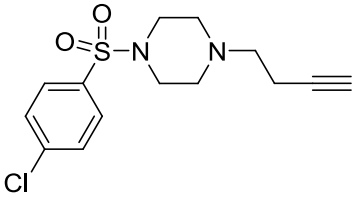
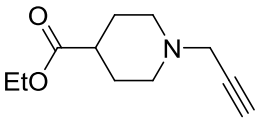
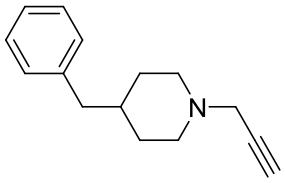
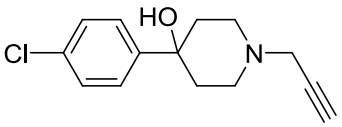
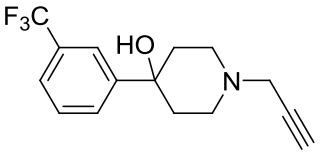
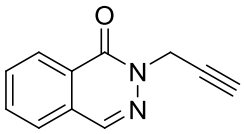
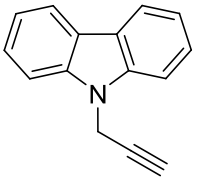
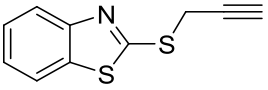
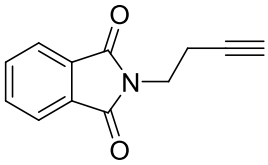
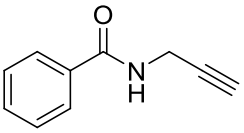
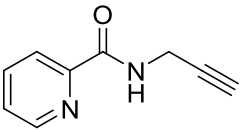
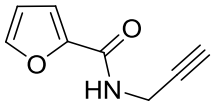
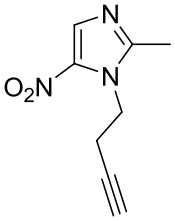
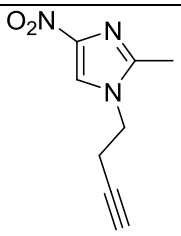
MHz, d_6-DMSO) δ= 149.9, 143.5, 138.6, 135.0, 129.3, 124.2, 123.5, 113.7, 50.4, 44.5, 32.5. ESI MS (MeOH) for $[M+H]^+$ = 289.2 Da.

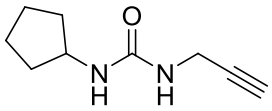
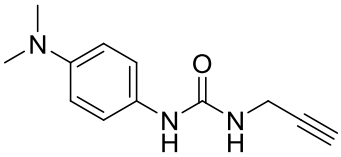
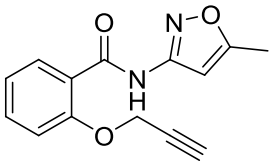
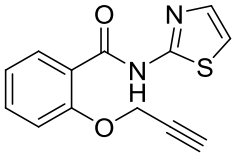
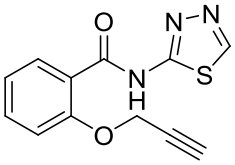
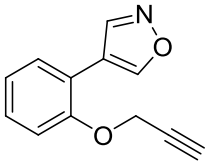
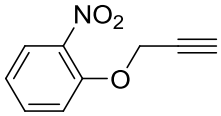
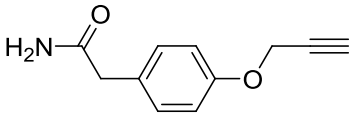
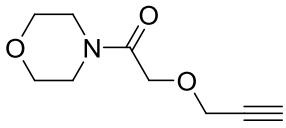
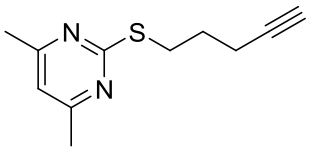
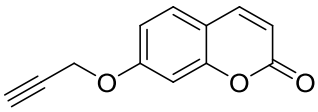
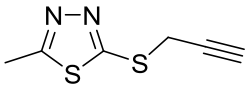
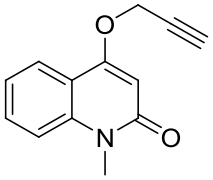
1.3. List and synthesis of alkynes for training set compounds

1.3.1. List of alkynes 101-163

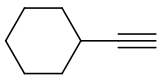
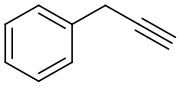
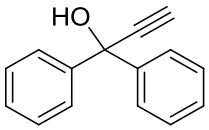
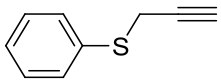
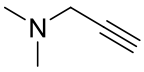
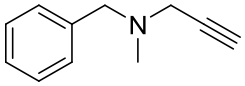
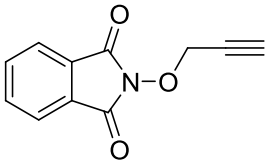
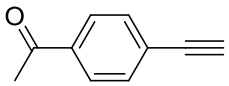
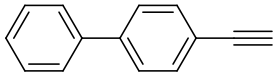
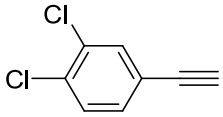
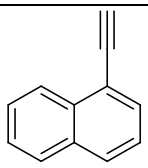
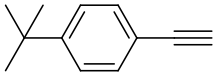
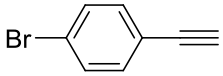
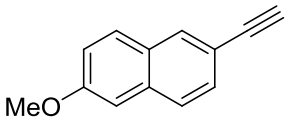
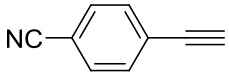
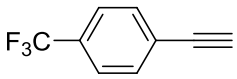
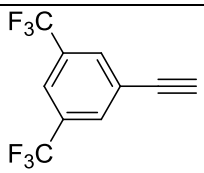
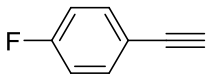
The following alkynes were used to synthesize triazole compounds for the training set. Of these, alkynes **101-137** were newly synthesized, while alkynes **138-163** were obtained from commercial sources.

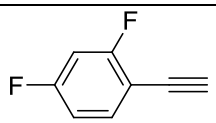
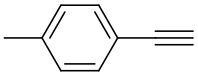
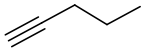
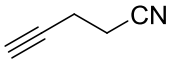
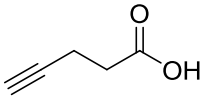
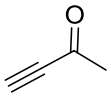
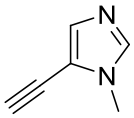
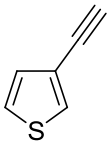
Synthesized Alkynes (101-137)		
 **101**	 **102**	 **103**
 **104**	 **105**	 **106**
 **107**	 **108**	 **109**

 **110**	 **111**	 **112**
 **113**	 **114**	 **115**
 **116**	 **117**	 **118**
 **119**	 **120**	 **121**
 **122**	 **123**	 **124**

 **125**	 **126**	 **127**
 **128**	 **129**	 **130**
 **131**	 **132**	 **133**
 **134**	 **135**	 **136**
 **137**		

Commercially available alkynes (138-163)

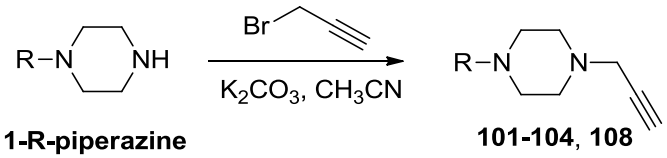
 **138**	 **139**	 **140**
 **141**	 **142**	 **143**
 **144**	 **145**	 **146**
 **147**	 **148**	 **149**
 **150**	 **151**	 **152**
 **153**	 **154**	 **155**

 **156**	 **157**	 **158**
 **159**	 **160**	 **161**
 **162**	 **163**	

1.3.2. Synthesis of alkynes 101-137

Compounds **117** (8), **118** (9), **119** (10), **120** (11), **122** (11), **131** (12), **135** (13), **137** (14) were prepared according to published procedures. Alkynes **102**, **103**, **107**, **116**, **121**, **133** were described before but without general synthetic procedures (15).

Synthesis of alkynes 101-104, 108

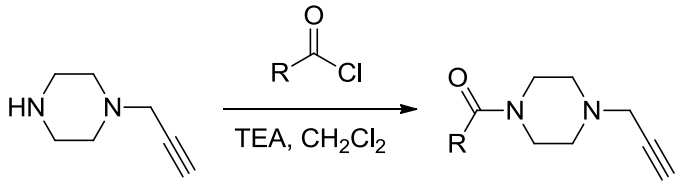


Scheme 7. General procedure for the synthesis of alkynes **101-104, 108.**

General procedure: To a mixture of an appropriate *N*-substituted piperazine (32 mmol) and anhydrous K_2CO_3 (4.4 g, 32 mmol) in anhydrous CH_3CN (50 mL), propargyl bromide (80%

solution in toluene, 3.6 mL, 4.8 g, 32 mmol) was added. The mixture was stirred overnight under reflux, and then filtered and evaporated. The residue was purified by column chromatography (Hexanes:EtOAc).

Synthesis of alkynes 105-106

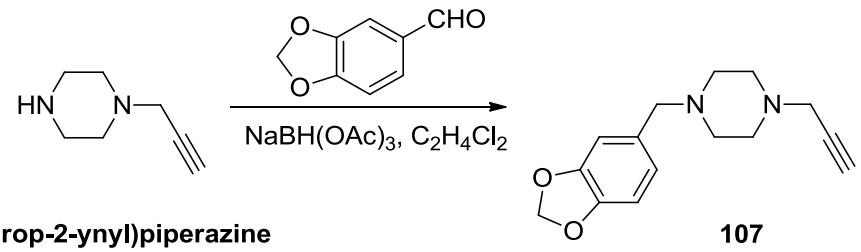


1-(Prop-2-ynyl)piperazine **105-106**

Scheme 8. General procedure for the synthesis of alkynes **105-106**.

General procedure: To a mixture of 1-(prop-2-ynyl)piperazine (16) (1.25 g, 10.1 mmol) and TEA (1.4 mL, 1.0 g, 10.1 mmol) in anhydrous CH_2Cl_2 (30 mL), an appropriate acid chloride (10.1 mmol) was added. The mixture was stirred at r.t. overnight and then diluted with H_2O (30 mL). The organic layer was dried over $MgSO_4$, filtered and evaporated. The product was used without further purification.

Synthesis of alkyne 107

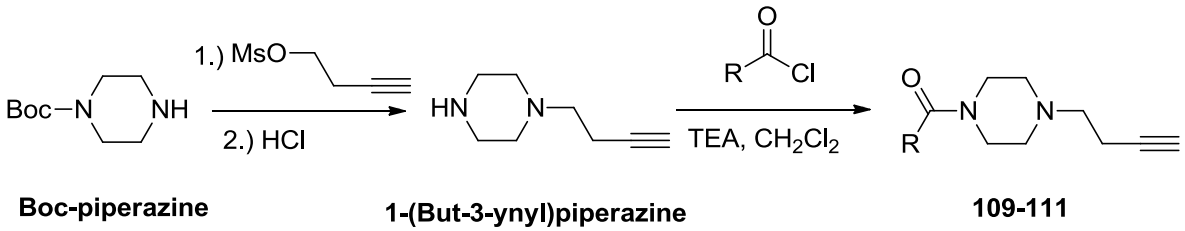


1-(Prop-2-ynyl)piperazine **107**

Scheme 9. Synthesis of alkyne **107**.

1-(Benzo[d][1,3]dioxol-5-ylmethyl)-4-(prop-2-ynyl)piperazine (**107**): To a mixture of 1-(prop-2-ynyl)piperazine(16) (1.25 g, 10.1 mmol) and the aldehyde (1.51 g, 10.1 mmol) in anhydrous CH_2Cl_2 (30 mL) and AcOH (12 mg, 0.2 mmol, 2% mol.), $NaBH_3CN$ (0.95 g, 15.1 mmol, 1.5 equiv.) was added. The mixture was stirred at r.t. for one day and then diluted with H_2O (30 mL) and saturated $NaHCO_3$ (30 mL). The organic layer was dried over $MgSO_4$, filtered and evaporated. The residue was purified by column chromatography (silica-gel, hexanes:EtOAc, 4:6) to give a yellow solid (1.5 g, 57%).

Synthesis of alkynes 109-111



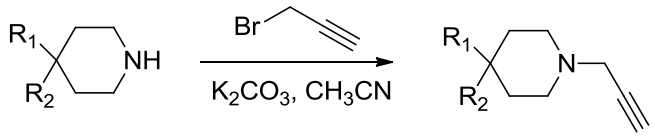
Scheme 10. General procedure for the synthesis of alkynes **109-111**.

1-(But-3-ynyl)piperazine: To a mixture of Boc-piperazine (11.6 g, 62.8 mmol) and but-3-ynyl methanesulfonate (17) (9.3 g, 62.8 mmol) in CH_3CN (130 mL), DIPEA (11.4 mL, 8.9 g, 69 mmol, 1.1 equiv.) was added. The mixture was stirred under reflux overnight and then evaporated. The yellow oil was dissolved in hexanes:EtOAc (1:1), passed through short silica-gel pad and evaporated. The residue was dissolved in $HCl_{conc.}$:H_2O (20 mL:50 mL), stirred at r.t. for 30 min, and then evaporated to give a white solid of 1-(but-3-ynyl)piperazine dihydrochloride (10.5 g, 80%).

General procedure for the synthesis of alkynes 109-111: To a mixture of 1-(but-3-ynyl)piperazine dihydrochloride (2 g, 9.5 mmol) and TEA (4.4 mL, 3.2 g, 31.3 mmol, 3.3 equiv.)

in anhydrous CH_2Cl_2 (20 mL), an appropriate acid chloride (9.5 mmol) was added. The mixture was stirred at r.t. overnight and then diluted with H_2O (30 mL). The organic layer was dried over $MgSO_4$, filtered and evaporated, and the product was used without further purification.

Synthesis of alkynes 112-115

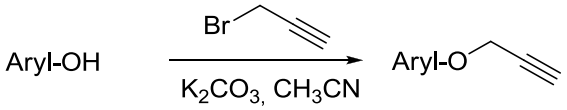


4,4-R_1,R_2-piperidine **112-115**

Scheme 11. General procedure for the synthesis of alkynes **112-115**.

General procedure: To a mixture of an appropriate R_1,R_2-substituted piperidine (26 mmol) and DIPEA (4.7 mL, 3.7 g, 28.6 mmol, 1.1 equiv.) in CH_2Cl_2 (100 mL), propargyl bromide (80% solution in toluene, 3.1 mL, 4.2 g, 28.6 mmol, 1.1 equiv.) was added dropwise. The mixture was stirred at r.t. overnight and evaporated. The residue was purified by column chromatography (hexanes:EtOAc).

Synthesis of alkynes 130, 132



130, 132

Scheme 12. General procedure for the synthesis of alkynes **130** and **132**.

General procedure: A mixture of an appropriate phenol (31.7 mmol) and anhydrous K_2CO_3 (4.4 g, 31.7 mmol) in anhydrous CH_3CN (100 mL) was stirred at 50°C for 15 min, and propargyl

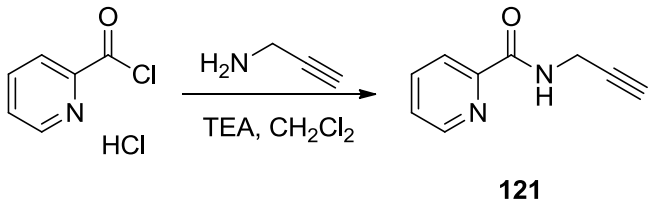
bromide (80% solution in toluene, 3.4 mL, 4.7 g, 31.7 mmol) was added. The mixture was stirred at 50°C for one day, filtered and evaporated. The residue was purified by column chromatography (hexanes:EtOAc or $CHCl_3$:MeOH).

Synthesis of alkyne 116

Scheme 13. General procedure for the synthesis of alkyne **116**.

General procedure: To a mixture of phthalazone in anhydrous DMF (270 mL), NaOEt (21% w/w solution in EtOH, 51 mL, 137 mmol) was added. After 15 min, propargyl bromide (80% solution in toluene, 14.8 mL, 20.4 g, 137 mmol) was added and the reaction mixture was stirred at r.t. for 2 days. After evaporation, the residue was stirred with hot H_2O (3 L), cooled down and the product was filtered (51%).

Synthesis of alkyne 121



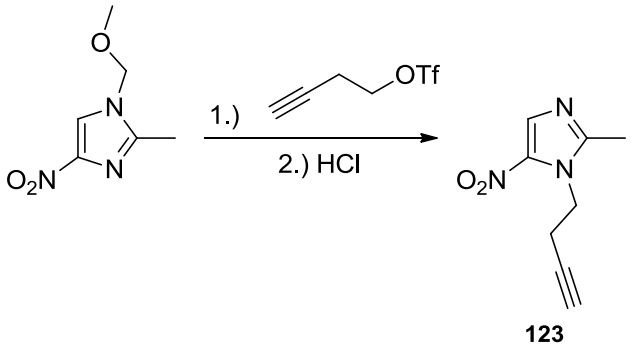
121

Scheme 14 . Synthesis of alkyne **121**.

***N*-(Prop-2-ynyl)picolinamide (121).** To a cold (0°C) solution of the acid chloride (5.8 g, 32.6 mmol) in CH_2Cl_2 (50 mL), a mixture of propargyl amine (1.79 g, 32.6 mmol) and TEA (10.0

mL, 7.24 g, 71.7 mmol, 2.2 equiv.) in CH_2Cl_2 (20 mL) was added dropwise. After addition the reaction was stirred at r.t. overnight and washed with H_2O (100 mL). The organic layer was separated, dried over $MgSO_4$, filtered and evaporated. The residue was dissolved in Et_2O, filtered and the solution was evaporated to the final volume of ~50 mL. The product was filtered (3 g, 57%).

Synthesis of alkyne 123



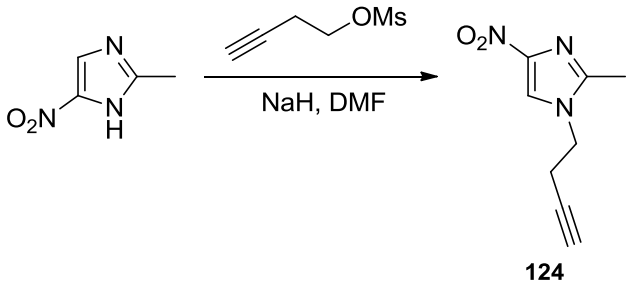
123

Scheme 15. Synthesis of alkyne **123**.

1-(But-3-ynyl)-2-methyl-5-nitro-1*H*-imidazole (123). 1-(Methoxymethyl)-2-methyl-4-nitro-1*H*-imidazole was obtained using the literature procedure for the similar compound (18). ^{1}H NMR (400 MHz, $CDCl_3$) δ= 7.78 (s, 1H), 5.23 (s, 2H), 3.35 (s, 3H), 2.48 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ= 145.4, 119.7, 77.8, 56.6, 13.0. ESI MS (MeOH) for $[M+Na]^+$ = 194.4 Da. To a solution of but-3-ynyl trifluoromethanesulfonate (19) 15.6 g, 77.2 mmol, 1.1 equiv.) in CH_3NO_2 (50 mL) a mixture of 1-(methoxymethyl)-2-methyl-4-nitro-1*H*-imidazole (12 g, 70.2 mmol) in CH_3NO_2 (50 mL) was added. The mixture was stirred at 70°C for overnight and then evaporated. The residue was dissolved in 1 M HCl (110 mL) and stirred at 70°C for 3 h and then cooled to r.t. The reaction mixture was neutralized with 2 M NaOH and extracted using EtOAc. The

organic layer was dried over $MgSO_4$, filtered and evaporated. The residue was purified by column chromatography (silica-gel, Et_2O:MeOH, 95:5) to give **38** (5.2 g, 56%) and then unreacted 1-(methoxymethyl)-2-methyl-4-nitro-1*H*-imidazole (3.2 g). ^{1}H NMR (400 MHz, $CDCl_3$) δ= 7.92 (s, 1H), 4.44 (t, *J*=6.4 Hz, 2H), 2.73-2.69 (m, 2H), 2.54 (s, 3H), 2.01-1.99 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ= 150.9, 138.2, 133.1, 79.0, 71.7, 44.4, 19.9, 14.6. ESI MS (MeOH) for $[M+H]^+$ = 180.4 Da.

Synthesis of the alkyne 124



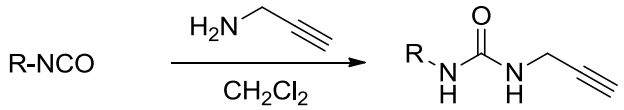
124

Scheme 16. Synthesis of alkyne **124**.

1-(But-3-ynyl)-2-methyl-4-nitro-1*H*-imidazole (124). To a mixture of NaH (95%, 1.6 g, 66.9 mmol, 1.1 equiv.) in anhydrous DMF (60 mL) a solution of 2-methyl-5-nitro-1*H*-imidazole (7.7 g, 60.8 mmol) in anhydrous DMF (60 mL) was added dropwise at r.t. After addition, the mixture was stirred at 90°C for 1 h, then cooled and but-3-ynyl methanesulfonate (17) (9 g, 60.8 mmol) was added. The reaction was stirred at 90°C overnight and then evaporated. The residue was diluted with brine (200 mL) and H_2O (100 mL) and extracted using EtOAc (2×150 mL). The combined organic layers were dried over $MgSO_4$, filtered and evaporated. The crude product was dissolved in warm (60°C) EtOAc (50 mL) and filtered. Et_2O (100 mL) was carefully added (on the top of the EtOAc solution to form biphasic system) and the mixture was kept at r.t. overnight.

Crystals of **39** were separated (3.4 g, 31%). ^{1}H NMR (400 MHz, d_6-DMSO) δ= 8.34-8.33 (m, 1H), 4.17-4.12 (m, 2H), 2.95-2.93 (m, 1H), 2.75-2.70 (m, 2H), 2.40-2.39 (m, 3H). ^{13}C NMR (100 MHz, d_6-DMSO) δ= 145.2, 145.1, 122.0, 80.4, 73.5, 44.7, 19.5, 12.6. ESI MS (MeOH) for $[M+Na]^+$ = 180.3 Da.

Synthesis of alkynes 125-126

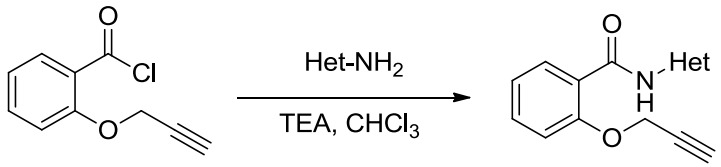


125-126

Scheme 17. General procedure for the synthesis of alkynes **125-126**.

General procedure: To a cooled (-25°C) solution of an appropriate isocyanate (6.2 mmol) in anhydrous CH_2Cl_2 (20 mL), propargylamine (0.39 mL, 340 mg, 6.2 mmol) in anhydrous CH_2Cl_2 (20 mL) was added dropwise. The reaction mixture was stirred at r.t. for 30 min and the product was filtered off, washed with small amount of CH_2Cl_2 and Et_2O.

Synthesis of alkynes 127-129

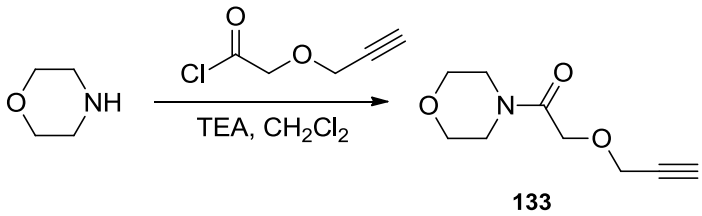


127-129

Scheme 18. General procedure for the synthesis of alkynes **127-129**.

General procedure: To a cooled (0°C) mixture of an appropriate Het-NH_2 (77 mmol) in $CHCl_3$ (100 mL), the acid chloride (20) (15 g, 77 mmol) in $CHCl_3$ (50 mL) was added. The reaction was stirred under reflux for one day and then cooled down and washed with H_2O (200 mL). The organic layer was dried over $MgSO_4$, filtered and evaporated, and the residue was purified by column chromatography (silica-gel, EtOAc).

Synthesis of alkyne 133

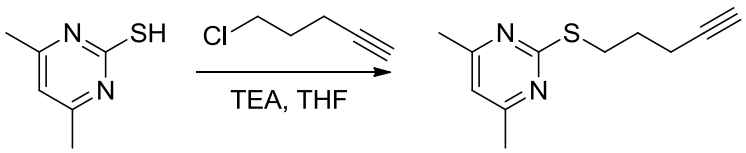


133

Scheme 19. Synthesis of alkyne **133**.

1-Morpholino-2-(prop-2-ynyloxy)ethanone (133). The title compound was obtained using the acid chloride (21) and general procedure as for alkynes **105-106**.

Synthesis of alkyne 134

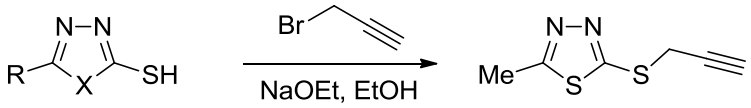


134

Scheme 20. Synthesis of alkyne **134**.

4,6-Dimethyl-2-(pent-4-ynylthio)pyrimidine (134). The title compound was obtained using literature conditions for a similar compound (22).

Synthesis of alkyne 136



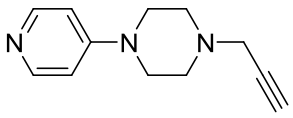
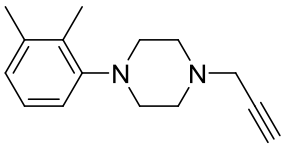
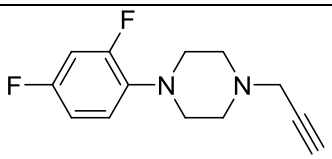
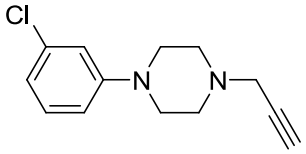
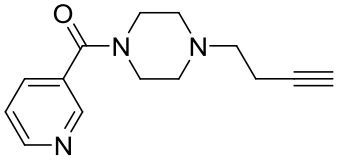
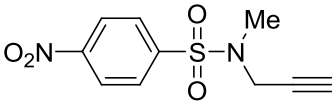
Scheme 21. General procedure for the synthesis of alkyne **136**.

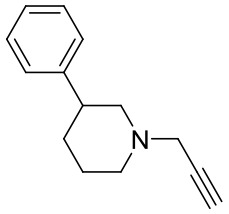
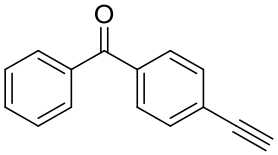
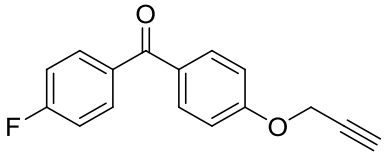
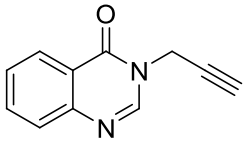
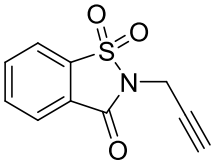
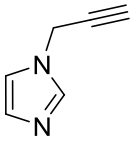
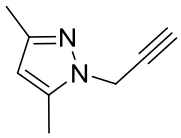
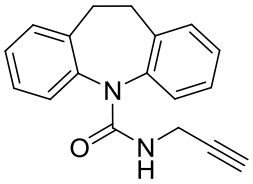
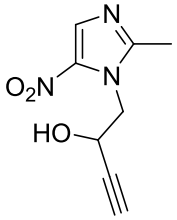
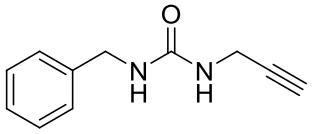
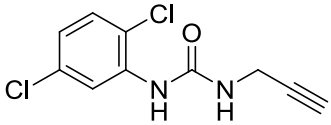
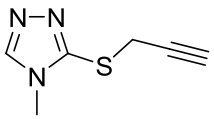
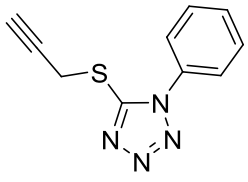
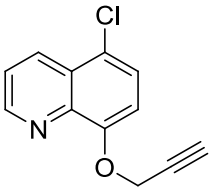
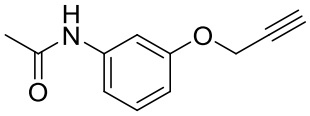
General procedure: Alkyne **136** was obtained using literature conditions for a similar compound (23).

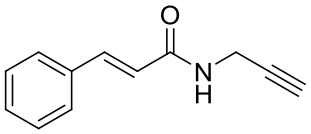
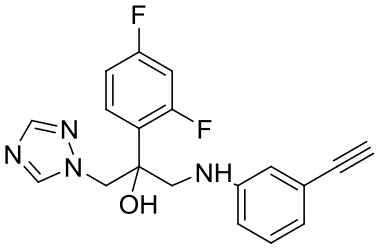
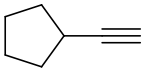
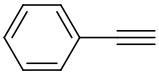
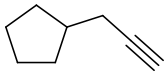
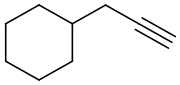
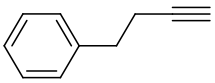
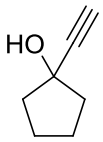
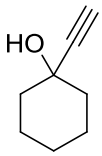
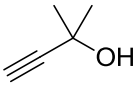
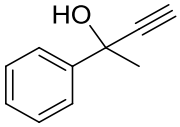
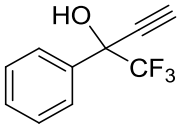
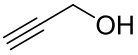
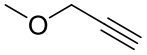
1.4 List and synthesis of alkynes for triazole compounds in test set

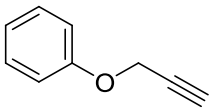
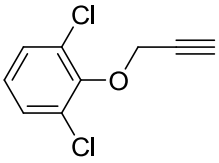
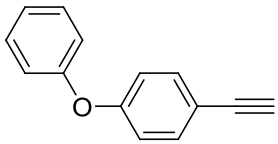
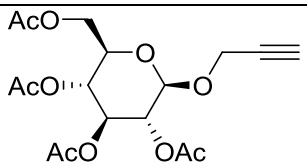
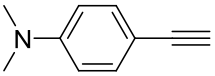
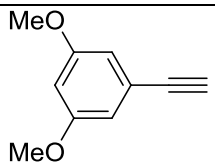
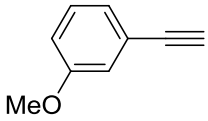
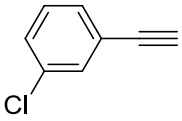
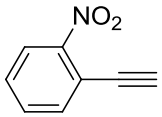
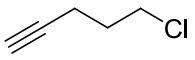
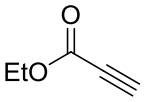
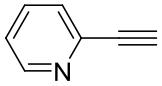
1.4.1. List of alkynes 201-247

The following alkynes were used to synthesize test set compounds. Of these, alkynes **201-223** were newly synthesized, while alkynes **224-247** were obtained commercially.

Synthesized Alkynes (201-223)		
 **201**	 **202**	 **203**
 **204**	 **205**	 **206**

 **207**	 **208**	 **209**
 **210**	 **211**	 **212**
 **213**	 **214**	 **215**
 **216**	 **217**	 **218**
 **219**	 **220**	 **221**

 **222**	 **223**	
Commercially available alkynes (224-247)		
 **224**	 **225**	 **226**
 **227**	 **228**	 **229**
 **230**	 **231**	 **232**
 **233**	 **234**	 **235**

 **236**	 **237**	 **238**
 **239**	 **240**	 **241**
 **242**	 **243**	 **244**
 **245**	 **246**	 **247**

1.4.2. Synthesis of alkynes 201-223

Alkynes **206** (24), **208** (25), **211** (26), **212** (27), **213** (28), **219** (29), and **222** (11) were synthesized according to literature procedures. Alkynes **210** and **220** were described before but without general synthetic procedures (15).

Synthesis of alkynes 201-204. The compounds were obtained using **Scheme 7** and the general procedure as for alkynes **101-104, 108**.

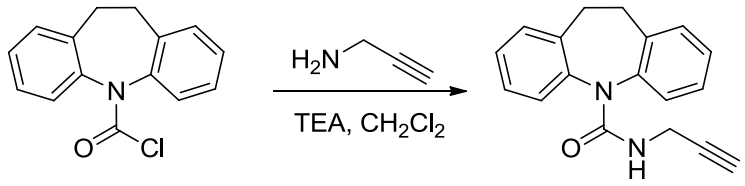
Synthesis of alkyne 205. The compound was obtained using **Scheme 10** and the general procedure as for alkynes **109-111**.

Synthesis of alkyne 207. The compound was obtained using **Scheme 11** and the general procedure as for alkynes **112-115**.

Synthesis of alkynes 209, 220-221. The compounds were obtained using **Scheme 12** and the general procedure as for alkynes **130, 132**.

Synthesis of alkyne 210. The compounds were obtained using **Scheme 13** (X=CH, Y=N)**.** To 4-hydroxyquinazoline (20 g, 137 mmol) in anhydrous DMF (270 mL), NaOEt (21% w/w solution in EtOH, 51 mL, 137 mmol) was added. After 15 min, propargyl bromide (80% solution in toluene, 14.8 mL, 20.4 g, 137 mmol) was added and the reaction mixture was stirred at r.t. for 2 days. After evaporation, the residue was stirred with hot H_2O (3 L), cooled and the product was filtered (87%).

Synthesis of alkyne 214

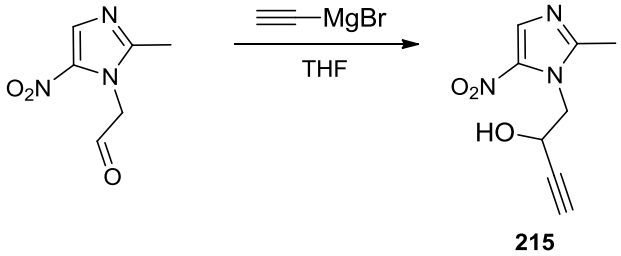


214

Scheme 22. Synthesis of alkyne **214**.

***N*-(Prop-2-ynyl)-10,11-dihydro-5*H*-dibenzo[b,f]azepine-5-carboxamide (214).** To a cold (0°C) solution of the acid chloride (5 g, 19.4 mmol) in CH_2Cl_2 (100 mL), a mixture of propargyl amine (1.07 g, 19.4 mmol) and TEA (2.7 mL, 1.96 g, 19.4 mmol) in CH_2Cl_2 (50 mL) was added dropwise. After addition the reaction was stirred under reflux for one1 day, cooled and washed with H_2O (100 mL). The organic layer was separated, dried over $MgSO_4$, filtered and evaporated. The residue was washed with Et_2O and then hexanes (4.1 g, 76%).

Synthesis of alkyne 215



215

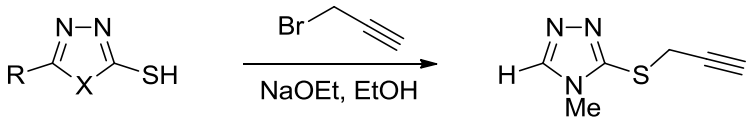
Scheme 23. The synthesis of alkyne **215**.

1-(2-Methyl-5-nitro-1*H*-imidazol-1-yl)but-3-yn-2-ol (215). A mixture of the aldehyde (30) (3.7 g, 21.9 mmol) in anhydrous THF (150 mL) was cooled to −70°C. A solution of ethynylmagnesium bromide (0.5 M in THF, 109 mL, 54,5 mmol, 2.5 equiv.) was added dropwise while maintaining the reaction temperature at −60°C (the aldehyde was obtained in the hydrate form, and therefore an excess of ethynylmagnesium bromide was used). After addition, the reaction was stirred at −60°C for 1.5 h and then slowly warmed up to r.t. and stirred for 2 h. The reaction was quenched with brine+H_2O (100+50 mL), filtered through Celite and washed with EtOAc. The filtrate was transferred to separatory funnel and the organic layer was collected. The aqueous layer was extracted using EtOAc (100 mL). The combined organic fractions were dried

over $MgSO_4$, filtered and evaporated. The residue was purified by column chromatography (silica-gel, EtOAc) (2.7 g, 63%). ^{1}H NMR (400 MHz, $CDCl_3$) δ= 7.76 (s, 1H), 4.70-4.66 (m, 1H), 4.57-4.52 (m, 1H), 4.41-4.36 (m, 1H), 2.53 (d, *J*=2.0 Hz, 1H), 2.47 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ= 151.8, 138.2, 131.8, 81.2, 75.0, 60.3, 50.9, 14.4. ESI MS (MeOH) for $[M+H]^+$ = 196.2 Da.

Synthesis of alkynes 216-217 The compounds were obtained using **Scheme 19** and the general procedure as for alkynes **125-126**.

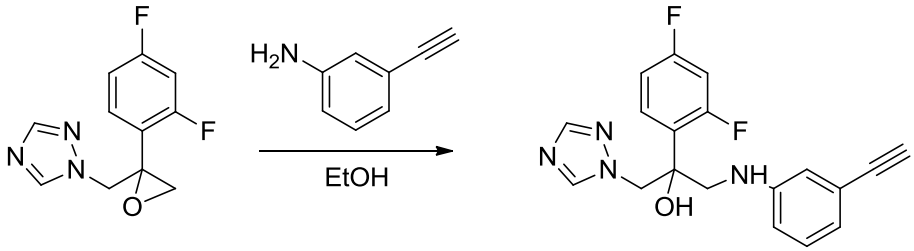
Synthesis of alkyne 218



Scheme 24 General procedure for the synthesis of alkyne **218**.

General procedure: Alkyne **218** was obtained using literature conditions for a similar compound (23).

Synthesis of alkyne 223

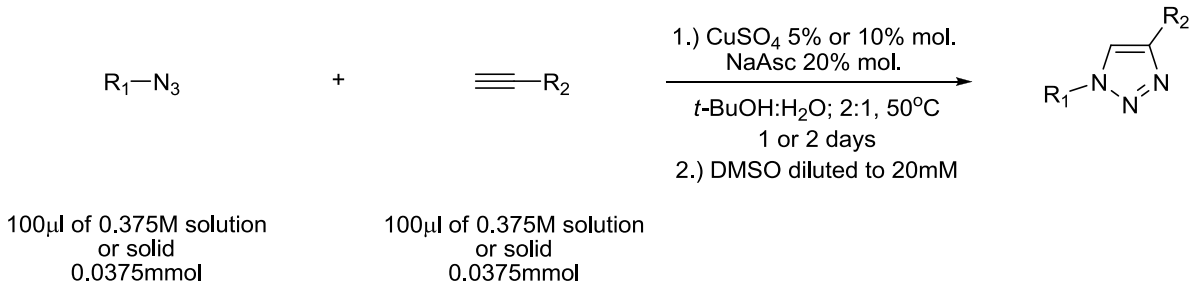


223

Scheme 25. Synthesis of alkyne **223**.

2-(2,4-Difluorophenyl)-1-(3-ethynylphenylamino)-3-(1*H*-1,2,4-triazol-1-yl)propan-2-ol (223). The title compound was obtained using the literature conditions for a similar compound (31).

1.5. "Click Chemistry" reaction

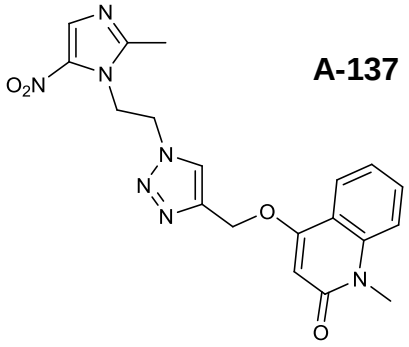


Scheme 26. General procedure for the click chemistry-mediated synthesis of 5-NI compounds.

General procedure: A 4 mL vial containing a stirring bar was charged with the azide (100 µL of 0.375M) and alkyne (100 µL of 0.375M). Solutions were made in *t*-BuOH : H_2O; 2:1. In case the azide was not-soluble in the solvent system, solid substrate was added followed by 100 µl of *t*-BuOH : H_2O; 2:1. If the alkyne was not-soluble in the solvent system, solid substrate was added followed by 100 µl of *t*-BuOH : H_2O; 2:1. Subsequently, sodium ascorbate (156 µL of 0.048 M) and $CuSO_4$ (19 µL or 38 µL of 0.1 M in H_2O) were added, giving concentrations of 100 mM each for azide and alkyne, 20 mM sodium ascorbate, 5 or 10 mM $CuSO_4$, 63.3% *t*-BuOH, and 36.7% H_2O. The reaction was carried out at 50°C for 1-2 days. If alkynes reacted slower, the reaction was carried out for 2 days at 50°C using twice the amount of $CuSO_4$ (38 µl of 0.1 M in H_2O). The reaction mixture was diluted with DMSO (1.5 mL) and used directly in the biological assays. Final concentrations in reaction mixtures: 20 mM 1,2,3-triazole product, 4 mM sodium ascorbate, 1 or 2 mM $CuSO_4$, 80% DMSO, 12.7% *t*-BuOH, and 7.3% H_2O.

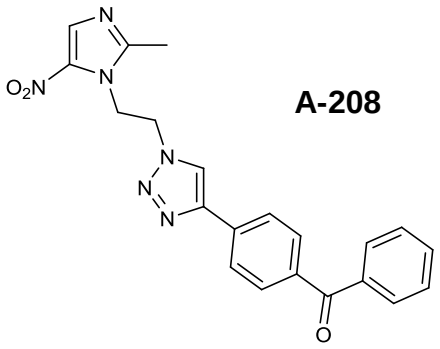
1.6. Synthesis of compounds for in vivo testing

General procedure: To a mixture of azide (2 mmol) and alkyne (2 mmol) in *t*-BuOH:H_2O (2:1, 10 mL), sodium ascorbate (158 mg, 0.8 mmol, 40% mol.) was added and the mixture was stirred at r.t. for 5 min. A 1 M solution of $CuSO_4$ (200 µL, 0.2 mmol, 10% mol.) was added and the reaction was carried out at 60°C for 1-3 days. After evaporation, the residue was purified by column chromatography (silica-gel, EtOAc or $CHCl_3$:MeOH, 9:1 or EtOAc:MeOH, 9:1).



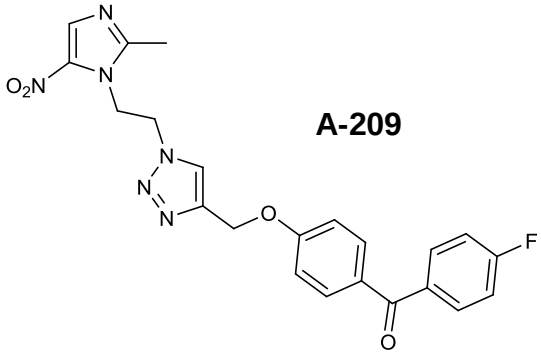
A-137

1-Methyl-4-((1-(2-(2-methyl-5-nitro-1*H*-imidazol-1-yl)ethyl)-1*H*-1,2,3-triazol-4-yl)methoxy)quinolin-2(1*H*)-one (A-137). The title compound was prepared according to the general procedure (1 day) and purified by column chromatography (silica-gel, $CHCl_3$:MeOH, 9:1) to give a white solid (93%), m.p. 212-213°C. ^{1}H NMR (500 MHz, d_6-DMSO) δ= 8.22 (s, 1H), 8.03 (s, 1H), 7.79 (d, *J*=7.9 Hz, 1H), 7.64 (t, *J*=7.8 Hz, 1H), 7.50 (d, *J*=8.6 Hz, 1H), 7.24 (t, *J*=7.5 Hz, 1H), 6.23 (s, 1H), 5.30 (s, 2H), 4.89 (t, *J*=5.3 Hz, 2H), 4.74 (t, *J*=5.2 Hz, 2H), 3.56 (s, 3H), 1.85 (s, 3H). ^{13}C NMR (125 MHz, d_6-DMSO) δ= 162.2, 160.3, 151.2, 142.0, 139.5, 138.4, 133.2, 131.5, 125.8, 122.6, 121.5, 115.4, 114.6, 97.5, 61.7, 48.9, 46.2, 28.6, 12.8. HRMS calcd for $C_{19}H_{20}N_7O_4$ *m/z* 410.1571, meas 410.1571. IR (cm^{-1}): 3130 (m), 1639 (s), 1459 (s), 1236 (s), 763 (s).



A-208

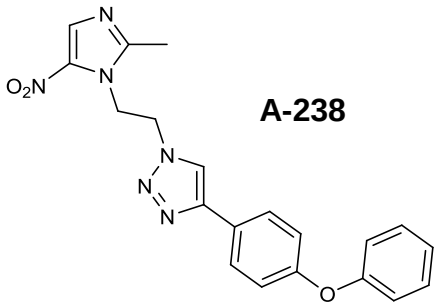
(4-(1-(2-(2-Methyl-5-nitro-1*H*-imidazol-1-yl)ethyl)-1*H*-1,2,3-triazol-4-yl)phenyl)(phenyl)methanone (A-208). The title compound was prepared according to the general procedure (2 days) and purified by column chromatography (silica-gel, EtOAc) to give a white solid (75%), m.p. 174-176°C. ^{1}H NMR (500 MHz, d_6-DMSO) δ= 8.63 (s, 1H), 8.07 (s, 1H), 7.96 (d, *J*=8.0 Hz, 2H), 7.83 (d, *J*=8.0 Hz, 2H), 7.77 (d, *J*=8.0 Hz, 2H), 7.69 (t, *J*=7.4 Hz, 1H), 7.58 (t, *J*=7.5 Hz, 2H), 4.92 (t, *J*=5.3 Hz, 2H), 4.79 (t, *J*=5.3 Hz, 2H), 1.95 (s, 3H). ^{13}C NMR (125 MHz, d_6-DMSO) δ= 195.1, 151.2, 145.6, 138.4, 137.1, 136.2, 134.3, 133.3, 132.6, 130.6, 129.5, 128.6, 125.0, 123.5, 49.0, 46.0, 12.9. HRMS calcd for $C_{21}H_{19}N_6O_3$ *m/z* 403.1513, meas 403.1515. IR (cm^{-1}): 3120 (m), 2925 (m), 2852 (m), 1661 (s), 1611 (m), 1452 (s), 1358 (s), 1257 (s), 1200 (s), 1147 (s), 823 (s), 700 (s).



A-209

(4-Fluorophenyl)(4-((1-(2-(2-methyl-5-nitro-1*H*-imidazol-1-yl)ethyl)-1*H*-1,2,3-triazol-4-yl)methoxy)phenyl)methanone (A-209). The title compound was prepared according to the

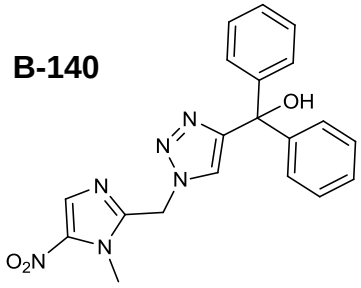
general procedure (2 days) and purified by column chromatography (silica-gel, EtOAc) to give a white solid (78%), m.p. 146-148°C. ^{1}H NMR (500 MHz, d_6-DMSO) δ= 8.16 (s, 1H), 8.04 (s, 1H), 7.79 (dd, *J*=8.5, 5.6 Hz, 2H), 7.73 (d, *J*=8.8 Hz, 2H), 7.38 (t, *J*=8.9 Hz, 2H), 7.16 (d, *J*=8.6 Hz, 2H), 5.27 (s, 2H), 4.86 (t, *J*=5.3 Hz, 2H), 4.72 (t, *J*=5.4 Hz, 2H), 1.79 (s, 3H). ^{13}C NMR (125 MHz, d_6-DMSO) δ= 193.1, 164.3 (*J*=250.5 Hz), 161.5, 151.2, 142.5, 138.3, 134.2 (*J*=2.9 Hz), 133.2, 132.2 (*J*=9.0 Hz), 132.0, 129.6, 125.6, 115.5 (*J*=22.0 Hz), 114.7, 61.1, 48.8, 46.1, 12.7. HRMS calcd for $C_{22}H_{20}FN_6O_4$ *m/z* 451.1525, meas 451.1545. IR (cm^{-1}): 3131 (m), 1641 (s), 1601 (s), 1458 (s), 1248 (s), 1148 (s), 730 (s).



A-238

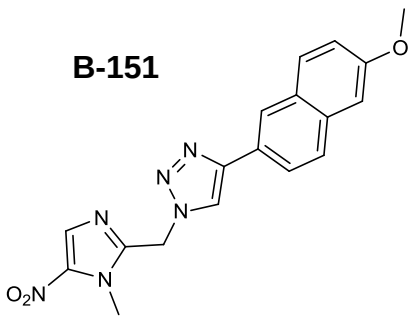
1-(2-(2-Methyl-5-nitro-1*H*-imidazol-1-yl)ethyl)-4-(4-phenoxyphenyl)-1*H*-1,2,3-triazole (A-238). The title compound was prepared according to the general procedure (2 days) and purified by column chromatography (silica-gel, EtOAc) to give a yellowish solid (90%), m.p. 178-179°C. ^{1}H NMR (500 MHz, d_6-DMSO) δ= 8.39 (s, 1H), 8.06 (s, 1H), 7.76 (d, *J*=8.1 Hz, 2H), 7.41 (t, *J*=7.7 Hz, 2H), 7.16 (t, *J*=7.5 Hz, 1H), 7.06 (t, *J*=7.0 Hz, 4H), 4.88 (t, *J*=5.5 Hz, 2H), 4.77 (t, *J*=5.4, 2H), 1.92 (s, 3H). ^{13}C NMR (125 MHz, d_6-DMSO) δ= 156.5, 156.4, 151.2, 146.1, 138.4, 133.3, 130.1, 126.9, 125.7, 123.6, 121.8, 118.9, 118.8, 48.9, 46.1, 12.9. HRMS calcd for $C_{21}H_{18}N_6O_3$ *m/z* 391.1513, meas 391.1501. IR (cm^{-1}): 3148 (m), 3070 (m), 1589 (m), 1558 (w), 1526 (m), 1460 (s), 1365 (s), 1260 (s), 1185 (s), 749 (s).

B-140



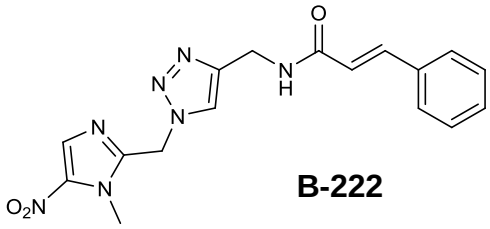
(1-((1-Methyl-5-nitro-1*H*-imidazol-2-yl)methyl)-1*H*-1,2,3-triazol-4-yl)diphenylmethanol (B-140). The title compound was prepared according to the general procedure (1 day) and purified by column chromatography (silica-gel, EtOAc:MeOH, 9:1) to give a white solid (87%), m.p. 189-191°C. ^{1}H NMR (500 MHz, d_6-DMSO) δ= 8.06 (s, 1H), 7.93 (s, 1H), 7.37 (d, *J*=7.9 Hz, 4H), 7.29 (t, *J*=7.6 Hz, 4H), 7.22 (t, *J*=7.3 Hz, 2H), 6.60 (s, 1H), 5.90 (s, 2H), 3.96 (s, 3H). ^{13}C NMR (125 MHz, d_6-DMSO) δ= 154.1, 146.9, 139.5, 131.9, 127.5, 127.0, 126.7, 124.1, 75.6, 45.3, 33.5. HRMS calcd for $C_{20}H_{19}N_6O_3$ *m/z* 391.1513, meas 391.1531. IR (cm^{-1}): 3277 (m), 3157 (m), 2984 (w), 2941 (w), 1597 (w), 1527 (w), 1467 (s), 1371 (s), 1180 (s), 1050 (s), 743 (s).

B-151



4-(6-Methoxynaphthalen-2-yl)-1-((1-methyl-5-nitro-1*H*-imidazol-2-yl)methyl)-1*H*-1,2,3-triazole (B-151). The title compound was prepared according to the general procedure (1 day) and purified by column chromatography (silica-gel, $CHCl_3$:MeOH, 9:1) to give a yellowish solid (58%), m.p. 188-189°C. ^{1}H NMR (500 MHz, d_6-DMSO) δ= 8.66 (s, 1H), 8.34 (s, 1H), 8.10 (s, 1H), 7.96 (dd, *J*=8.5, 1.2 Hz, 1H), 7.88 (d, *J*=9.1 Hz, 2H), 7.34 (d, *J*=2.3 Hz, 1H), 7.19 (dd,

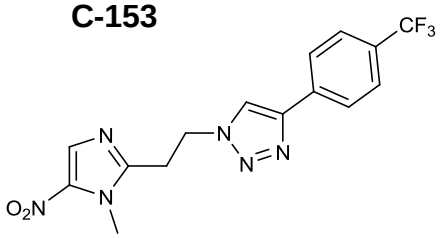
J=8.9, 2.4 Hz, 1H), 5.99 (s, 2H), 4.01 (s, 3H), 3.88 (s, 3H). ^{13}C NMR (125 MHz, d_6-DMSO) δ= 157.5, 146.9, 146.7, 139.6, 133.9, 131.9, 129.5, 128.5, 127.4, 125.6, 124.1, 123.6, 122.0, 119.1, 106.0, 55.2, 45.8, 33.6. HRMS calcd for $C_{18}H_{17}N_6O_3$ *m/z* 365.1357, meas 365.1364. IR (cm^{-1}): 3106 (m), 2971 (m), 2843 (m), 1610 (w), 1529 (s), 1468 (s), 1370 (s), 1261 (s), 1218 (s), 1021 (s), 862 (s), 827 (s).



B-222

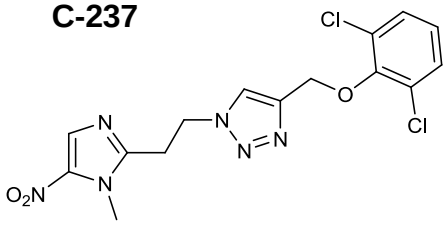
***N*-((1-((1-Methyl-5-nitro-1*H*-imidazol-2-yl)methyl)-1*H*-1,2,3-triazol-4-yl)methyl)cinnamamide (B-222).** The title compound was prepared according to the general procedure (2 days) and purified by column chromatography (silica-gel, EtOAc:MeOH, 9:1) to give a white solid (71%), m.p. 160-162°C ^{1}H NMR (500 MHz, d_6-DMSO) δ= 8.64 (t, *J*=5.6 Hz, 1H), 8.05 (s, 2H), 7.55 (d, *J*=7.7 Hz, 2H), 7.50-7.31 (m, 3H), 6.67 (d, *J*=15.7 Hz, 1H), 5.89 (s, 2H), 4.44 (d, *J*=5.8 Hz, 2H), 3.96 (s, 3H), NH broadened and missing in DMSO. ^{13}C NMR (125 MHz, d_6-DMSO) δ= 165.0, 147.0, 145.0, 139.5, 139.0, 134.8, 131.8, 129.5, 128.9, 127.5, 123.8, 121.8, 45.4, 34.2, 33.5. HRMS calcd for $C_{17}H_{18}N_7O_3$ *m/z* 368.1466, meas 368.1455. IR (cm^{-1}): 3231 (m), 3140 (m), 3046 (m), 2961 (m), 1650 (s), 1535 (s), 1445 (s), 1372 (s), 1052 (s), 825 (s).

C-153



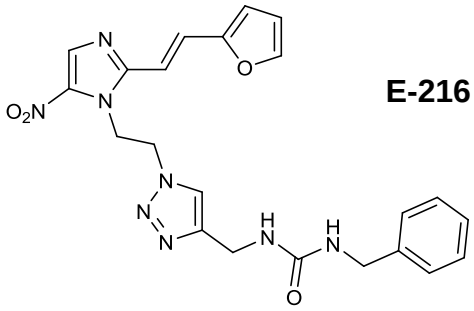
1-(2-(1-methyl-5-nitro-1*H*-imidazol-2-yl)ethyl)-4-(4-(trifluoromethyl)phenyl)-1*H*-1,2,3-triazole (C-153). The title compound was prepared according to the general procedure (1 day) and purified by column chromatography (silica-gel, EtOAc) to give a gray solid (70%), m.p. 137-141°C. ^{1}H NMR (500 MHz, d_6-DMSO) δ= 8.76 (s, 1H), 8.04 (d, *J*=7.2 Hz, 3H), 7.81 (d, *J*=8.3, 2H), 4.88 (t, *J*=6.8 Hz, 2H), 3.83 (s, 3H), 3.46 (t, *J*=6.9 Hz, 2H). ^{13}C NMR (125 MHz, d_6-DMSO) δ= 151.1, 145.7, 140.0, 135.5, 133.0, 129.0 (*J*=3.9 Hz), 126.8 (*J*=3.8 Hz), 126.5, 125.1 (*J*=271.9 Hz), 124.0, 47.5, 33.8, 28.3. HRMS calcd for $C_{15}H_{14}F_3N_6O_2$ *m/z* 367.1125, meas 367.1131. IR (cm^{-1}): 3135 (m), 1621 (m), 1527 (m), 1465 (m), 1326 (s), 1264 (s), 1185 (s), 1159 (s), 1115 (s), 1064 (s), 812 (s).

C-237



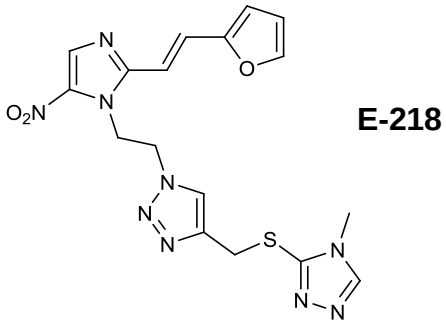
4-((2,6-Dichlorophenoxy)methyl)-1-(2-(1-methyl-5-nitro-1*H*-imidazol-2-yl)ethyl)-1*H*-1,2,3-triazole (C-237). The title compound was prepared according to the general procedure (1 day) and purified by column chromatography (silica-gel, $CHCl_3$:MeOH, 9:1) to give a white solid (82%), m.p. 125-126°C. ^{1}H NMR (500 MHz, d_6-DMSO) δ= 8.30 (s, 1H), 8.04 (s, 1H), 7.48 (d, *J*=8.0 Hz, 2H), 7.19 (t, *J*=8.4 Hz, 1H), 5.20 (s, 2H), 4.83 (t, *J*=7.0 Hz, 2H), 3.79 (s, 3H), 3.42 (t, *J*=7.0 Hz, 2H). ^{13}C NMR (125 MHz, d_6-DMSO) δ= 150.3, 150.1, 141.9, 139.1, 132.1, 129.3,

128.8, 126.3, 125.4, 66.0, 46.5, 32.9, 27.5. HRMS calcd for $C_{15}H_{14}Cl_2N_6O_3$ *m/z* 397.0577, meas 397.0560. IR (cm^{-1}): 3135 (m), 3080 (m), 2952 (m), 1566 (w), 1528 (s), 1465 (s), 1446 (s), 1438(s), 1373 (s), 1186 (s), 968 (s).



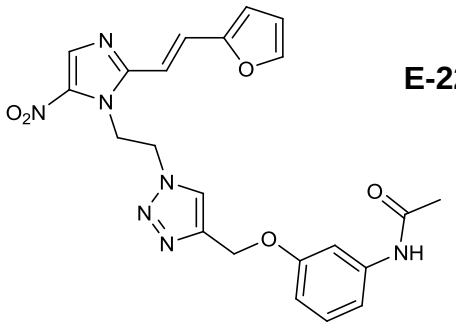
E-216

(*E*)-1-Benzyl-3-((1-(2-(2-(2-(furan-2-yl)vinyl)-5-nitro-1*H*-imidazol-1-yl)ethyl)-1*H*-1,2,3-triazol-4-yl)methyl)urea (E-216). The title compound was prepared according to the general procedure (1 day) and purified by column chromatography (silica-gel, $CHCl_3$:MeOH, 9:1) to give an orange solid (75%), m.p. 153-156°C. ^{1}H NMR (500 MHz, d_6-DMSO) δ= 8.22 (s, 1H), 7.88 (s, 1H), 7.82 (s, 1H), 7.40 (d, *J*=15.4 Hz, 1H), 7.30 (t, *J*=7.6 Hz, 2H), 7.25-7.19 (m, 3H), 6.82 (d, *J*=3.4 Hz, 1H), 6.62 (dd, *J*=3.4, 1.7 Hz, 1H), 6.39 (t, *J*=5.9 Hz, 1H), 6.35 (d, *J*=15.4 Hz, 1H), 6.26 (t, *J*=5.7 Hz, 1H), 4.91 (t, *J*=5.6 Hz, 2H), 4.79 (t, *J*=5.3 Hz, 2H), 4.19 (d, *J*=5.8 Hz, 2H), 4.05 (d, *J*=5.7 Hz, 2H). ^{13}C NMR (125 MHz, d_6-DMSO) δ= 157.7, 151.3, 150.0, 146.2, 145.0, 140.7, 138.5, 135.1, 128.2, 127.0, 126.5, 125.2, 123.3, 113.7, 112.7, 109.3, 48.9, 45.2, 42.9, 34.8. HRMS calcd for $C_{22}H_{23}N_8O_4$ *m/z* 463.1837, meas 463.1858. IR (cm^{-1}): 3091 (m), 3029 (m), 1629 (m), 1367 (s), 1200 (s), 741 (s).



E-218

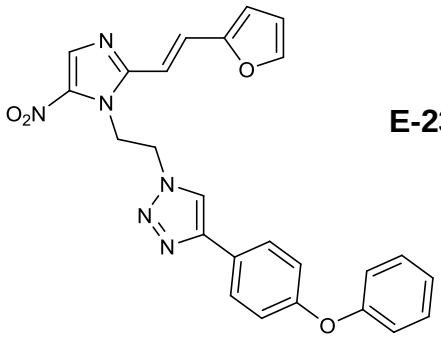
(*E*)-1-(2-(2-(2-(Furan-2-yl)vinyl)-5-nitro-1*H*-imidazol-1-yl)ethyl)-4-((4-methyl-4*H*-1,2,4-triazol-3-ylthio)methyl)-1*H*-1,2,3-triazole (E-218). The title compound was prepared according to the general procedure (1 day) and purified by column chromatography (silica-gel, $CHCl_3$:MeOH, 9:1) to give an orange solid (74%), m.p. 184-186°C. ^{1}H NMR (500 MHz, d_6-DMSO) δ= 8.52 (s, 1H), 8.19 (s, 1H), 7.94 (s, 1H), 7.81 (s, 1H), 7.37 (d, *J*=15.5 Hz, 1H), 6.81 (d, *J*=3.3 Hz, 1H), 6.62 (dd, *J*=3.3, 1.7 Hz, 1H), 6.31 (d, *J*=15.6 Hz, 1H), 4.89 (t, *J*=5.3 Hz, 2H), 4.79 (t, *J*=5.3 Hz, 2H), 4.29 (s, 2H), 3.42 (s, 3H). ^{13}C NMR (125 MHz, d_6-DMSO) δ= 151.4, 150.0, 148.5, 146.1, 144.9, 142.8, 138.4, 135.1, 125.2, 124.4, 113.7, 112.7, 109.1, 49.0, 45.2, 30.6, 27.2. HRMS calcd for $C_{17}H_{18}N_9O_3S$ *m/z* 428.1248, meas 428.1264. IR (cm^{-1}): 3091 (m), 3028 (m), 1629 (m), 1420 (s), 1367 (s), 1256 (s), 1190 (s), 931 (s), 741 (s).



E-221

(*E*)-*N*-(3-((1-(2-(2-(2-(Furan-2-yl)vinyl)-5-nitro-1*H*-imidazol-1-yl)ethyl)-1*H*-1,2,3-triazol-4-yl)methoxy)phenyl)acetamide (E-221). The title compound was prepared according to the

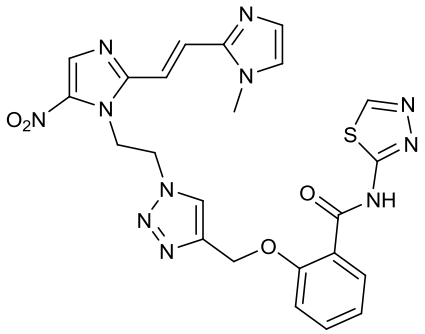
general procedure (1 day) and purified by column chromatography (silica-gel, $CHCl_3$:MeOH, 9:1) to give a yellow solid (77%), m.p. 151-153°C. ^{1}H NMR (500 MHz, d_6-DMSO) δ= 9.89 (s, 1H), 8.22 (s, 1H), 8.14 (s, 1H), 7.80 (s, 1H), 7.37 (d, *J*=15.4 Hz, 1H), 7.29 (s, 1H), 7.16 (t, *J*=8.1 Hz, 1H), 7.08 (d, *J*=8.0 Hz, 1H), 6.81 (d, *J*=3.3 Hz, 1H), 6.62-6.57 (m, 2 H), 6.35 (d, *J*=15.2 Hz, 1H), 4.94 (t, *J*=5.3 Hz, 2H), 4.85 (s, 2H), 4.84 (t, *J*=5.2 Hz, 2H), 2.03 (s, 3H). ^{13}C NMR (125 MHz, d_6-DMSO) δ= 158.1, 151.3, 150.1, 144.9, 143.0, 140.4, 138.4, 135.1, 129.4, 125.2, 125.1, 113.7, 112.7, 111.7, 109.2, 108.7, 105.8, 99.1, 60.8, 49.1, 45.2, 24.0. HRMS calcd for $C_{22}H_{22}N_7O_5$ *m/z* 464.1677, meas 464.1680. IR (cm^{-1}): 3587 (m), 3302 (m), 3242 (m), 3109 (m), 1666 (s), 1600 (s), 1371 (s), 1260 (s), 1193 (s), 723 (s).



E-238

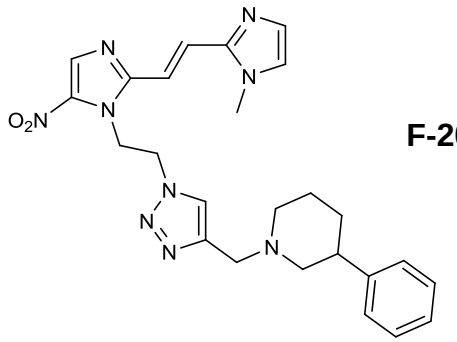
(*E*)-1-(2-(2-(2-(Furan-2-yl)vinyl)-5-nitro-1*H*-imidazol-1-yl)ethyl)-4-(4-phenoxyphenyl)-1*H*-1,2,3-triazole (E-238). The title compound was prepared according to the general procedure (3 days) and purified by column chromatography (silica-gel, $CHCl_3$:MeOH, 9:1) to give a yellow solid (75%), m.p. 221-223°C. ^{1}H NMR (500 MHz, d_6-DMSO) δ= 8.45 (s, 1H), 8.23 (s, 1H), 7.69 (s, 1H), 7.60 (d, *J*=8.2 Hz, 2H), 7.41 (t, *J*=7.6 Hz, 2H), 7.32 (d, *J*=15.4 Hz, 1H), 7.16 (t, *J*=7.4 Hz, 1H), 7.02 (d, *J*=8.0 Hz, 2H), 6.96 (d, *J*=8.0 Hz, 2H), 3.32 (d, *J*=3.2 Hz, 1H), 6.53 (d, *J*=1.6 Hz, 1H), 6.36 (d, *J*=15.4 Hz, 1H), 4.98 (t, *J*=5.0 Hz, 2H), 4.67 (t, *J*=5.0 Hz, 2H). ^{13}C NMR (125 MHz, d_6-DMSO) δ= 156.5, 156.2, 151.2, 150.1, 146.2, 144.8, 138.5, 135.3, 130.1,

126.8, 125.9, 125.2, 123.5, 121.8, 118.9, 118.6, 113.7, 112.5, 109.0, 49.3, 45.3. HRMS calcd for $C_{25}H_{21}N_6O_4$ *m/z* 469.1619, meas 469.1628. IR (cm^{-1}): 3119 (m), 3096 (m), 1617 (m), 1522 (s), 1487 (s), 1447 (s), 1400 (s), 1294 (s), 1196 (s), 745 (s).



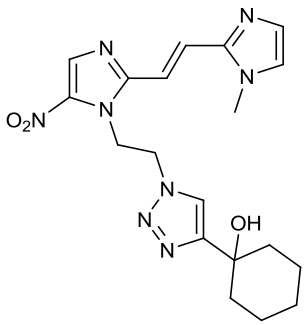
F-129

(*E*)-2-((1-(2-(2-(2-(1-Methyl-1*H*-imidazol-2-yl)vinyl)-5-nitro-1*H*-imidazol-1-yl)ethyl)-1*H*-1,2,3-triazol-4-yl)methoxy)-*N*-(1,3,4-thiadiazol-2-yl)benzamide (F-129). The title compound was prepared according to the general procedure (1 day) and purified by column chromatography (silica-gel, $CHCl_3$:MeOH, 9:1) to give a yellow solid (86%), m.p. 214-216°C. ^{1}H NMR (500 MHz, d_6-DMSO) δ= 9.24 (s, 1H), 8.25 (s, 1H), 8.23 (s, 1H), 7.80 (d, *J*=7.8 Hz, 1H), 7.58 (d, *J*=7.8 Hz, 1H), 7.41 (d, *J*=15.0 Hz, 1H), 7.25 (d, *J*=8.4 Hz, 1H), 7.12-7.21 (m, 2H), 6.91 (d, *J*=15.1 Hz, 1H), 6.41 (s, 1H), 5.06 (s, 2H), 5.02 (s, 2H), 4.83 (s, 2H), 3.68 (s, 3H), missing NH. ^{13}C NMR (125 MHz, d_6-DMSO) δ= 164.2, 156.0, 150.1, 149.1, 143.8, 143.2, 138.5, 135.1, 133.8, 130.6, 128.5, 124.2, 123.9, 122.8, 121.8, 121.3, 113.5, 113.2, 63.0, 49.5, 48.6, 45.5, 32.6. HRMS calcd for $C_{23}H_{21}N_{11}O_4S$ *m/z* 548.1571, meas 548.1582. IR (cm^{-1}): 3141 (m), 1664 (m), 1555 (m), 1451 (m), 1438 (m), 1421 (m), 1259 (s), 1195 (s), 1025 (s), 821 (s), 731 (s).



F-207

(*E*)-1-((1-(2-(2-(2-(1-Methyl-1*H*-imidazol-2-yl)vinyl)-5-nitro-1*H*-imidazol-1-yl)ethyl)-1*H*-1,2,3-triazol-4-yl)methyl)-3-phenylpiperidine (F-207). The title compound was prepared according to the general procedure (1 day) and purified by column chromatography (silica-gel, $CHCl_3$:MeOH, 9:1) to give a yellow solid (69%), m.p. broadened decomposition. ^{1}H NMR (500 MHz, d_6-DMSO) δ= 8.21 (s, 1H), 7.88 (s, 1H), 7.47 (d, *J*=15.1 Hz, 1H), 7.31-7.24 (m, 3H), 7.22-7.14 (m, 3H), 7.05 (d, *J*=7.0 Hz, 1H), 6.79 (d, *J*=15.1 Hz, 1H), 4.94 (t, *J*=4.8 Hz, 2H), 4.80 (t, *J*=5.0 Hz, 2H), 3.71 (s, 3H), 3.45-3.37 (m, 2H), 2.74 (d, *J*=10.3 Hz, 1H), 2.69-2.59 (m, 2H), 1.90 (t, *J*=10.8 Hz, 1H), 1.76 (t, *J*=10.9 Hz, 1H), 1.71 (d, *J*=12.3 Hz, 1H), 1.56-1.38 (m, 2H), 1.26 (ddd, *J*=12.3, 12.3, 4.0 Hz, 1H). ^{13}C NMR (125 MHz, d_6-DMSO) δ= 149.8, 144.5, 143.3, 143.2, 138.6, 135.0, 129.3, 128.2, 127.1, 126.1, 124.4, 124.2, 123.8, 112.6, 59.9, 52.6, 52.0, 48.9, 45.3, 42.2, 32.6, 30.9, 25.1. HRMS calcd for $C_{25}H_{30}N_9O_2$ *m/z* 488.2517, meas 488.2506. IR (cm^{-1}): 3131 (m), 2929 (s), 1631 (m), 1519 (m), 1450 (s), 1400 (s), 1260 (s), 731 (s).



F-230

(*E*)-1-(1-(2-(2-(2-(1-Methyl-1*H*-imidazol-2-yl)vinyl)-5-nitro-1*H*-imidazol-1-yl)ethyl)-1*H*-1,2,3-triazol-4-yl)cyclohexanol (F-230). The title compound was prepared according to the general procedure (1 day) and purified by column chromatography (silica-gel, $CHCl_3$:MeOH, 9:1) to give a yellow solid (63%), m.p. 229-230°C. ^{1}H NMR (500 MHz, d_6-DMSO) δ= 8.24 (s, 1H), 7.87 (s, 1H), 7.47 (d, *J*=15.1 Hz, 1H), 7.28 (s, 1H), 7.04 (s, 1H), 6.64 (d, *J*=15.0 Hz, 1H), 4.91 (t, *J*=5.0 Hz, 2H), 4.82-4.77 (m, 3H), 3.71 (s, 3H), 1.67-1.35 (m, 7H), 1.31-1.18 (m, 2H), 1.15-1.00 (m, 1H). ^{13}C NMR (500 MHz, d_6-DMSO) δ= 156.1, 149.8, 138.6, 135.0, 129.2, 124.2, 124.1, 123.6, 121.6, 112.7, 67.7, 48.8, 45.6, 37.4, 32.6, 25.1, 21.5. HRMS calcd for $C_{19}H_{25}N_8O_3$ *m/z* 413.2044, meas 413.2041. IR (cm^{-1}): 3240 (m), 3119 (m), 3098 (m), 2924 (m), 2852 (m), 1635 (m), 1518 (m), 1462 (s), 1369 (s), 1264 (s), 1194 (s), 1178 (s), 979 (s), 740 (s).

2. Biological methods and data analysis

2.1. Microbial strains

The following three Mz-sensitive isolates of *G. lamblia* were used: BRIS/87/HEPU/713 (713) (32), BRIS/83/HEPU/106 (106) (33), and GS/M (ATCC 50580). The Mz-resistant syngeneic lines, 713-M3 and 106-2ID10, were derived in the laboratory from isolates 713 and 106, respectively (32, 33). These lines show a stable 10- to 25-fold increase in EC50 for Mz

compared to the parental lines (34). For *T. vaginalis*, we used the two Mz-sensitive clinical isolates, G3 (ATCC PRA-98) and BRIS/92/STDL/F1623 (F1623) (35), and the two Mz-resistant clinical isolates, LA/03/CDC/1 (LA1) (36) and BRIS/92/STDL/B7268 (B7268) (37). *Giardia* lines were grown in TYI-S-33 medium supplemented with 10% bovine serum and 1 mg/mL bovine bile (Sigma). *Trichomonas* lines were grown in TYM complete media (38). The *H. pylori* isolates SS1 and S. Africa R7 (CS22), and the *ΔfrxAΔrdxA* double-mutant strain of SS1 were described before (39, 40). *C. difficile* isolate (ATCC 9689) and *B. fragilis* (ATCC 25285) were obtained from ATCC. The bacterial strains were grown in BHI medium supplemented with 10% bovine fetal serum.

2.2. Antimicrobial assays

Antimicrobial assays were done as described before (34). Briefly, stocks of the test compounds (10 mM in DMSO) were diluted in PBS to 75 μM, and 1:3 serial dilutions were made. Trophozoites were added to the wells in a 96-well plates. *Giardia* cultures were grown for two days and *Trichomonas* cultures for one day at 37°C under anaerobic conditions (AnaeroPack-Anaero system, Remel). For protozoa, cell growth and viability after incubation were determined with an ATP assay by adding BacTiter-Glo microbial cell viability assay reagent (Promega) and measuring ATP-dependent luminescence in a microplate reader. Bacterial cultures were grown for 1 day at 37°C under anaerobic conditions (AnaeroPack-Anaero system, Remel). Cell growth and viability were determined by optical density measurements at 600 nm. The 50% effective concentration (EC50) was derived from the concentration-response curves using BioAssay software (Cambridge soft). In preliminary studies, we confirmed that EC50 values showed good correlations with minimal inhibitory concentrations (MIC), as determined

microscopically with serial dilutions of test compounds and *Giardia* as a target microbe. However, activity data are reported as EC50 in this study, because the values are more precise and allow better quantitative comparisons.

2.3. Cytotoxicity assay in mammalian cells

The human epithelial cell line, HeLa (ATCC CCL-2), was used to determine drug cytotoxicity in human cells (34). Compounds were serially diluted (1:3) and added to HeLa cell cultures in 96-well plates. Cells were grown for 2 days, and viable cell numbers were determined using AlamarBlue reagent (Invitrogen). The 50% cytotoxic concentration (CC50) was derived from the concentration-response curves using BioAssay software (Cambridge soft).

2.4. Analysis of Quantitative Structure-Activity Relationship (QSAR)

E-dragon 1.0 from Virtual Computational Chemistry Laboratory was used to calculate 1,666 chemical descriptors for each compound (41). Measured EC50 and chemical descriptor values were used as input attributes for Service Vector Machine calculations and decision tree analyses in WEKA machine learning software (42). To eliminate chemical descriptor redundancy, we used Selected Classifier (Evaluator: CfssubsetEval and search: BestFirst) function with SMO or J48 as classifiers in WEKA. The models were evaluated for significance by Chi-square test. Selected attributes were employed to generate chemical landscapes by Principal Component Analysis (XL-STAT). Graph-R software (version 2.29) was used to generate 3D contour graphs.

2.5. Murine *Giardia* infection model

Adult C57BL/6 mice (Jackson Laboratory) were infected orally with 10^7 trophozoites of *G. lamblia* GS/M. After 2 days, mice were given five doses of test compound in 0.1% Hypromellose in PBS by oral gavage over a 3-day period. Controls received only 0.1 % Hypromellose/PBS. On day 5, the small intestine was removed, opened in 5 ml PBS, and chilled and shaken to release attached trophozoites. Live trophozoites were enumerated in a counting chamber. All animal studies were reviewed and approved by the UCSD Institutional Animal Care and Use Committee.

2.6. Assays of plasma drug levels

Mice were given a single 30 mg/kg dose of test compound by oral gavage in 0.1% Hypromellose in PBS. After 2 h, blood samples were taken and centrifuged to collect plasma. A 200 µl volume of plasma was mixed with 1 ml acetone, the mixture was centrifuged, and the supernatant was collected and dried at 50°C. After resuspension in 20 µL complete TYI-SS-33 medium, the plasma concentration of active drug was determined by in vitro antimicrobial assay using *G. lamblia* 713. As a standard curve, pooled plasma from untreated mice was spiked with different concentrations of test compound, and the samples were processed in parallel with the test samples.

2.7. Determination of water solubility

Compounds were dissolved in DMSO at 10 mM and serially diluted 1:3 in DMSO. Two µl of each DMSO solution was tranfered into 98 µl PBS and shaken for 90 min at room

temparature. Crystal formation was assessed by microscopy and the highest compound concentration without crystal formation was used to estimate water solubility.

2.8. In vitro micronucleus assays

Micronucleus assays were carried out with CHO-K1 cell line as described before (43). Cells were cultured in 12-well plates for 24 h, and then exposed to tested compounds at 100 µM concentrations for 24 h. The known mutagen, methyl methanesulfonate (MMS), was used as a positive control. Solvent alone (DMSO) was the negative control. Cells were rinsed with PBS, re-suspended in media, and spread onto pre-cleaned glass slides. After air drying, slides were fixed with 1% glutaraldehyde in PBS for 10 min and stained with Hoechst 33342 (Life technology) and Cell Mask™ deep red plasma membrane stain (Life technology) in PBS for 3 min. For the assessment of micronucleus frequency, at least 1,000 cells with well-preserved cytoplasm were scored using 200 × magnification following established criteria (44). At least three independent experiments were performed for each test compound.

2.9. Assessment of in vivo toxicity

Adult C57BL/6 mice (Jackson Laboratory) were given five doses of 100 mg/kg of 5-NI compounds orally over a 3-day period. On day 4, blood, small intestine, colon, liver, spleen and kidneys were removed and fixed, and paraffin sections were prepared and stained with hematoxylin and eosin. Standard hematological analysis and determination of plasma levels of albumin, alkaline phosphatase, ALT, AST, bilirubin, creatinine, glucose, and electrolytes were performed in the UCSD Murine Hematology and Coagulation Core Laboratory.

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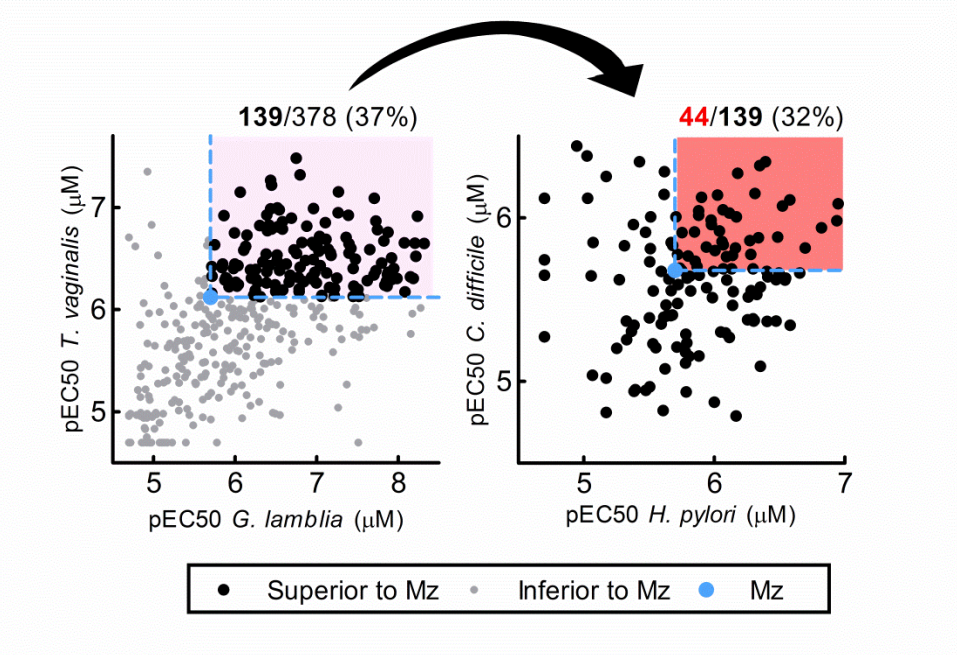


Figure S1. Expanded antimicrobial activity range of new 5-NI compounds. The activities of 378 new 5-NI compounds were tested against *G. lamblia* (strain 713), *T. vaginalis* (strain G3), *H. pylori* (strain SS1) and *C. difficile* (ATCC 9689) in 24-48 h growth assays, using ATP content or OD600 as read-outs. Each data point represents the mean value for one compound, with Mz shown in blue for comparison. The graphs depict relationships between activities of individual compounds against the four target pathogens. The left panel shows correlations for antiprotozoan activities. The region with compounds that exceeded the activity of Mz for both protozoa is shaded light red. These superior compounds (black circles) were then analyzed for their activities against the two bacteria (right panel). The region containing compounds with superior activity against all four pathogens is shaded in dark red.

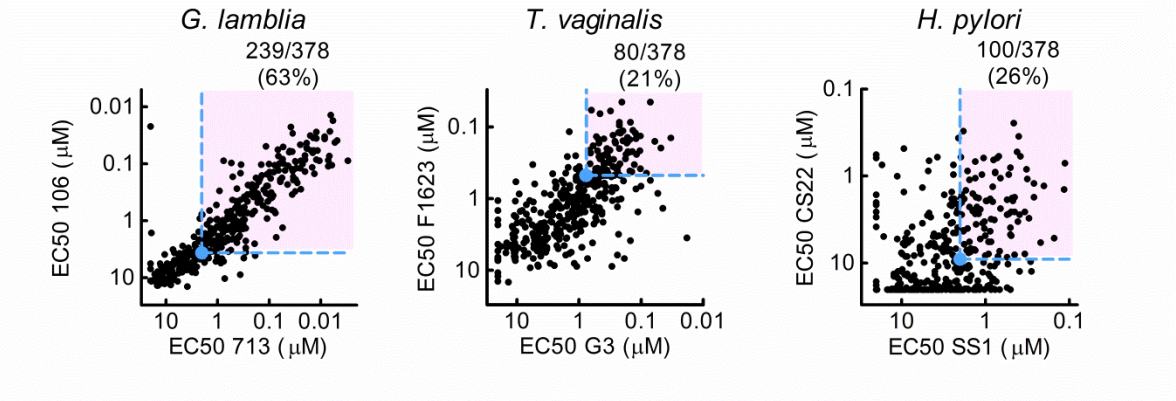


Figure S2. Relationship of compound activities between clinical isolates. The 5-NI library was tested for activity against two different clinical Mz-sensitive (MzS) isolates of *G. lamblia* (strains 713 and 106), *T. vaginalis* (strains G3 and F1623), and *H. pylori* (strains SS1 and CS22). Compounds with greater activity than Mz (light blue point) against both of the respective Mz-sensitive isolates are highlighted by light red shading (and their numbers and percentages of all tested compounds are given above the region).

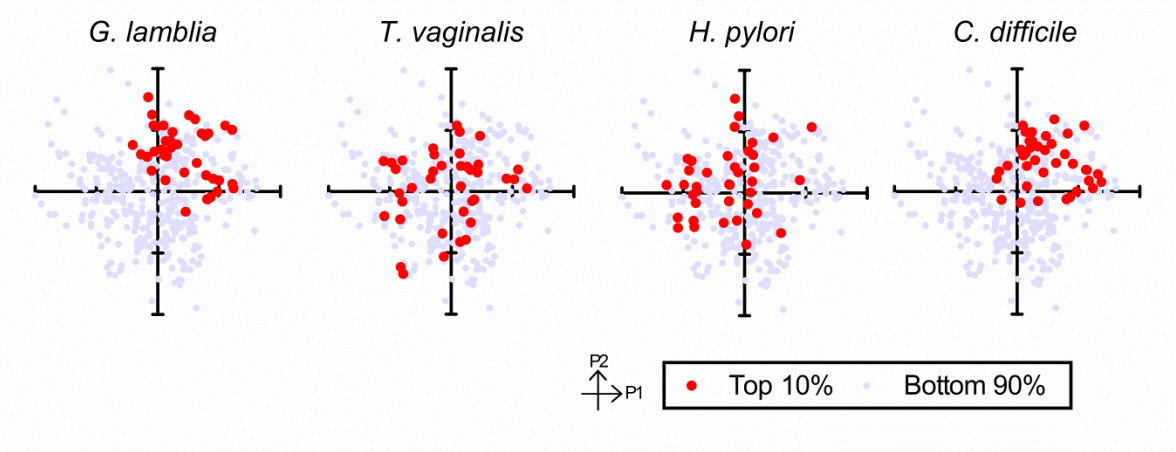


Figure S3. Distribution of active 5-NI compounds in chemical space. A structural space was generated by principal component analysis using activity data of all 378 compounds in the 5-NI library against the four target microbes, and the individual compounds were plotted in the resulting space. The top 10% most potent compounds are shown in red for activity against Mz-sensitive (MzS) isolates of each of the indicated pathogens. All other compounds are shown in light gray.

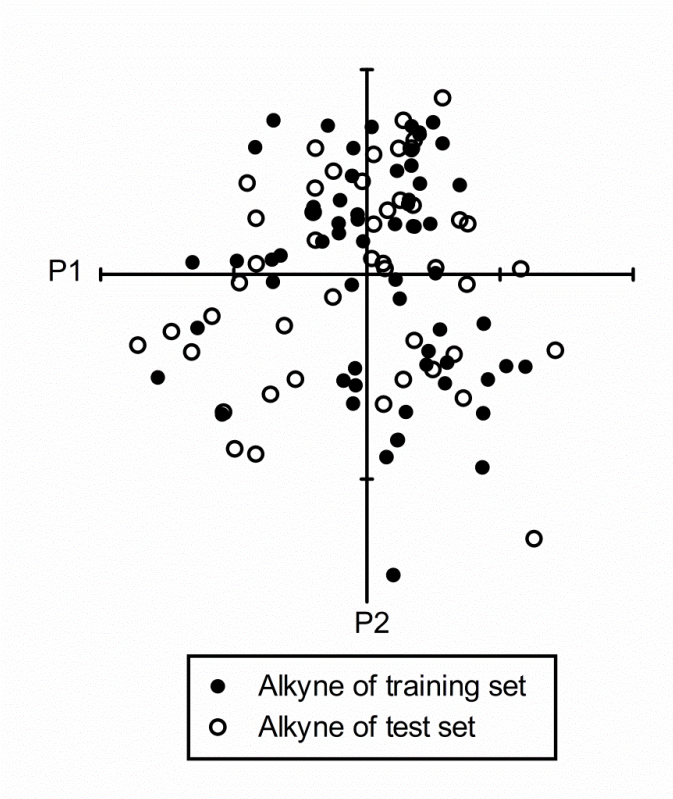


Figure S4. Structural analysis of alkyne sets used in library generation. Alkynes used for synthesizing the training triazole compounds (closed circles) or test triazole compounds (open circles) were analyzed by principal component analysis for their distribution in a common structural space.

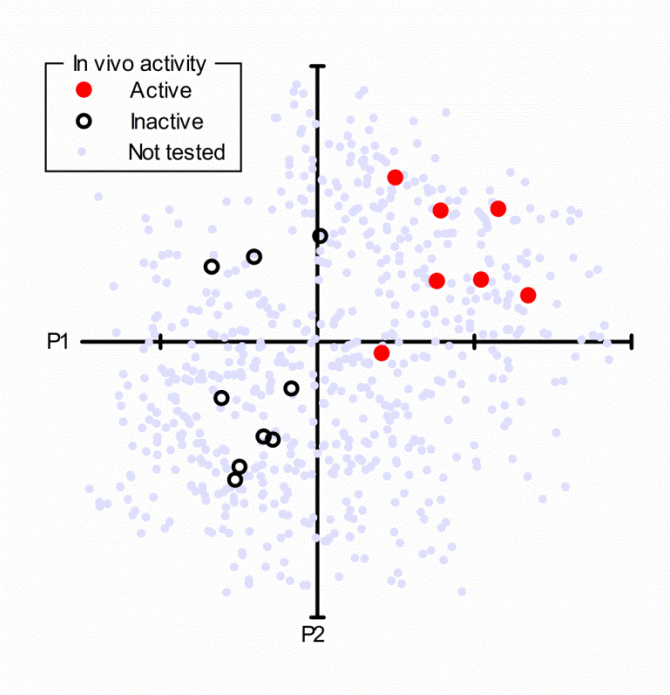


Figure S5. Structural analysis of in vivo active 5-NI compounds. A structural space was generated by principal component analysis for all 659 compounds in the total 5-NI library. Compounds that were efficacious in the mouse giardiasis model are shown as red dots. Compounds not active in vivo are shown as black open circles, while the small gray dots represent all other 5-NI compounds in the library not tested in vivo.

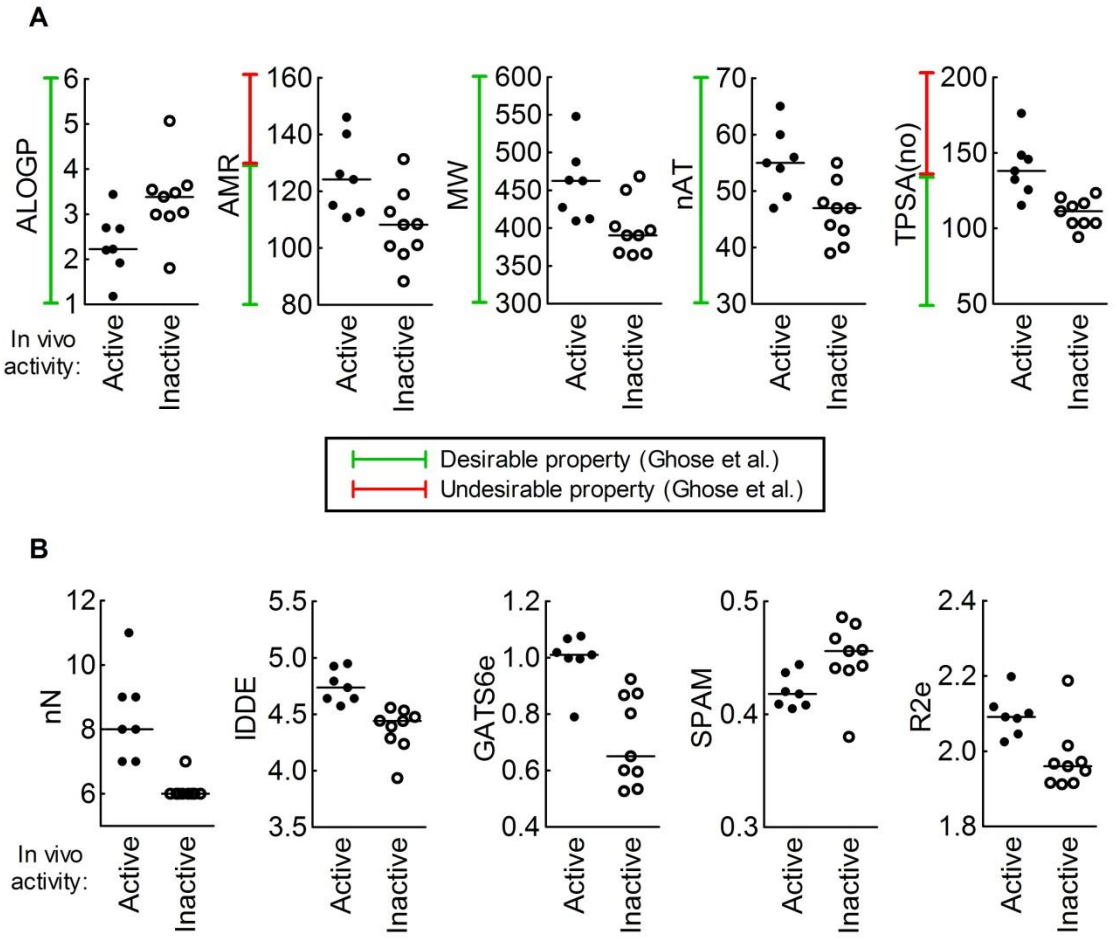


Figure S6. Chemical descriptors for prediction of in vivo activity. A. Comparison of five chemical descriptors by Lipinski's profiling tool. Each data point shows the value of the indicated chemical descriptor for compounds tested in vivo. Active compounds (closed circles) cleared *Giardia* infection in mice, while inactive compounds (open circles) did not (see Fig. 6). Means are shown as horizontal lines for each group. Vertical lines on the left of each panel indicate the preferred range for drug likeness as characterized by Ghose et al. (21); green, preferable; red, not preferable. B. Comparison of five alternative chemical descriptors for prediction of in vivo activity, as selected by a machine learning algorithm trained by data from the in vivo studies. These descriptors were used for the principal component analysis shown in Fig. S5.Explanations: nN, Number of nitrogen atoms; IDDE, Mean information content on the distance degree equality; GATS6e, Geary autocorrelation of lag 6 weighted by Sanderson electronegativity; SPAM, Average span R geometrical descriptors; R2e, R autocorrelation of lag 2 weighted by Sanderson electronegativity.

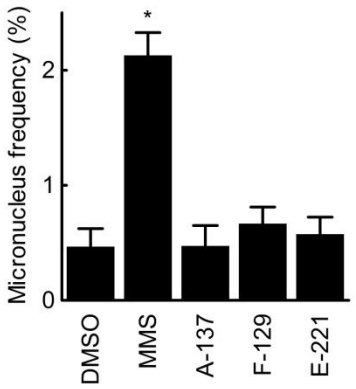


Figure S7. Micronucleus assays for genotoxicity evaluation. CHO-K1 cells were exposed to the indicated test compounds for 24 h, fixed, and stained with a DNA dye (Hoechst 33342) and a cellular counterstain (Cell Mask™ membrane stain). The mutagen, methyl methanesulfonate (MMS), was used as a positive control. Micronuclei were microscopically counted in at least 1,000 cells per sample, and are expressed as percentage of all cells. Bars represent mean + SE of the data from 3-5 independent experiments. *$p < 0.001$ (t-test) vs. DMSO controls

Table S1a. Structures of core A-C training compounds

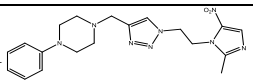
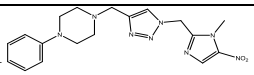
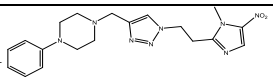
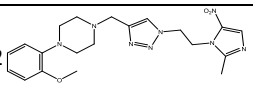
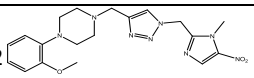
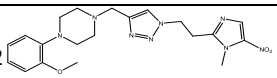
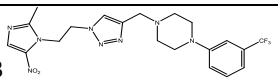
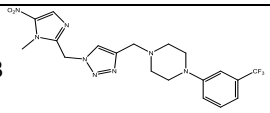
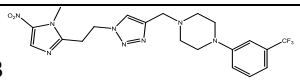
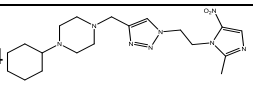
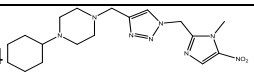
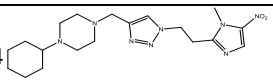
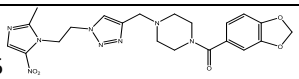
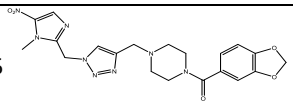
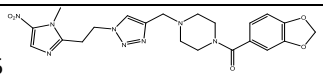
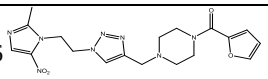
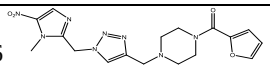
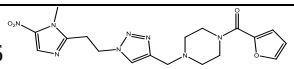
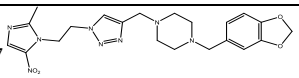
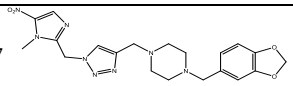
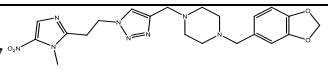
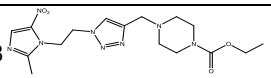
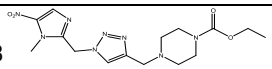
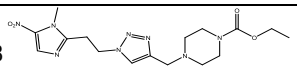
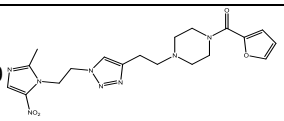
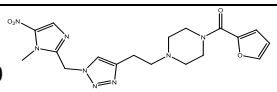
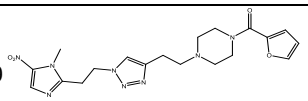
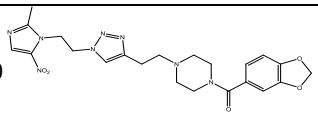
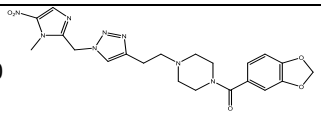
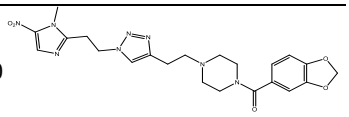
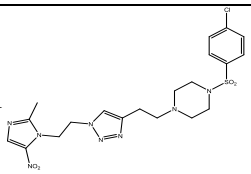
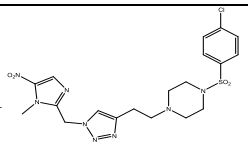
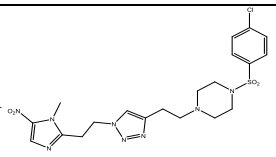
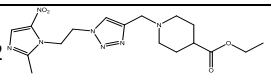
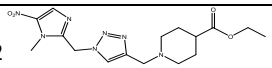
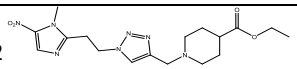
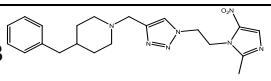
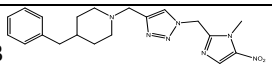
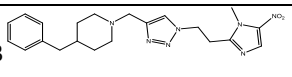
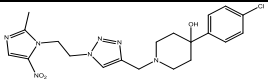
	Core **A**		Core **B**		Core **C**	
Alkyne	Name	Structure	Name	Structure	Name	Structure
101	A-101		B-101		C-101	
102	A-102		B-102		C-102	
103	A-103		B-103		C-103	
104	A-104		B-104		C-104	
105	A-105		B-105		C-105	
106	A-106		B-106		C-106	
107	A-107		B-107		C-107	
108	A-108		B-108		C-108	
109	A-109		B-109		C-109	
110	A-110		B-110		C-110	
111	A-111		B-111		C-111	
112	A-112		B-112		C-112	
113	A-113		B-113		C-113	
114	A-114		B-114		C-114	
115	A-115		B-115		C-115	

Table S1a. Structures of core A-C training compounds

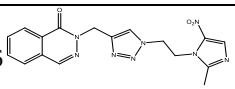
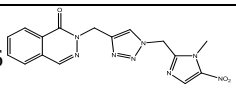
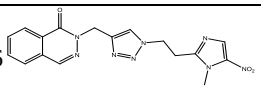
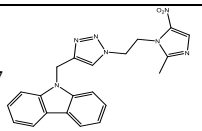
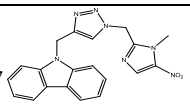
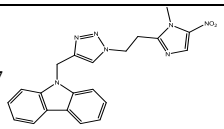
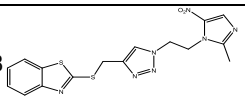
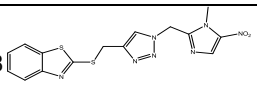
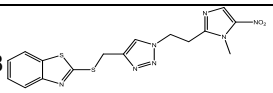
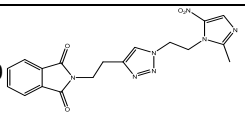
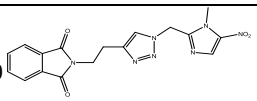
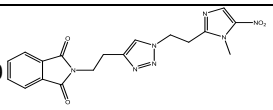
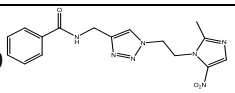
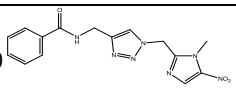
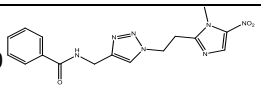
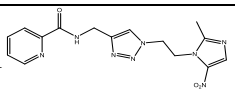
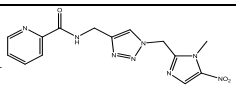
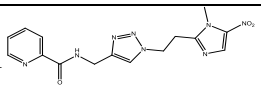
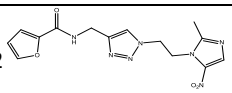
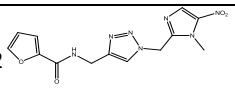
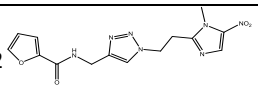
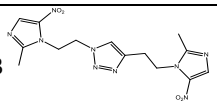
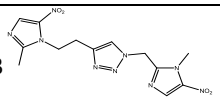
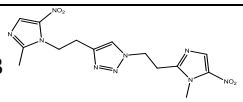
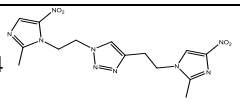
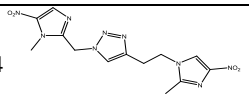
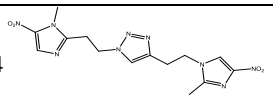
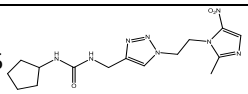
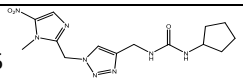
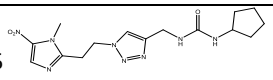
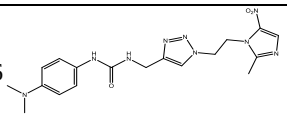
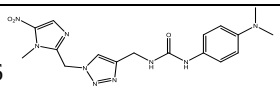
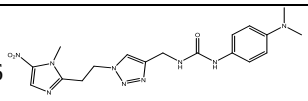
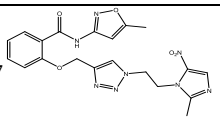
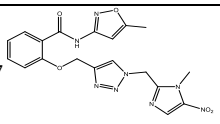
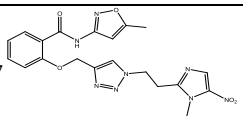
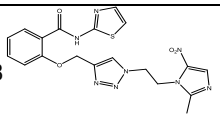
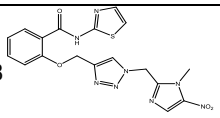
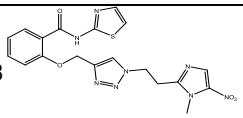
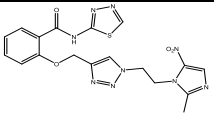
	Core **A**		Core **B**		Core **C**	
Alkyne	Name	Structure	Name	Structure	Name	Structure
116	A-116		B-116		C-116	
117	A-117		B-117		C-117	
118	A-118		B-118		C-118	
119	A-119		B-119		C-119	
120	A-120		B-120		C-120	
121	A-121		B-121		C-121	
122	A-122		B-122		C-122	
123	A-123		B-123		C-123	
124	A-124		B-124		C-124	
125	A-125		B-125		C-125	
126	A-126		B-126		C-126	
127	A-127		B-127		C-127	
128	A-128		B-128		C-128	
129	A-129		B-129		C-129	

Table S1a. Structures of core A-C training compounds

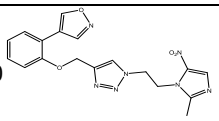
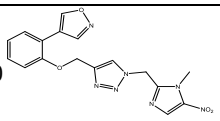
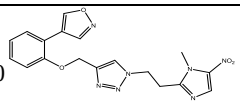
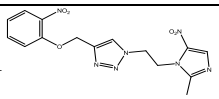
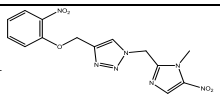
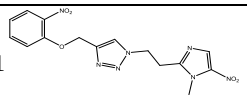
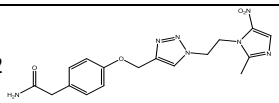
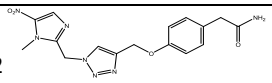
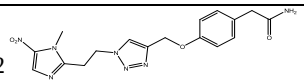
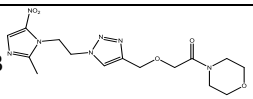
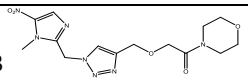
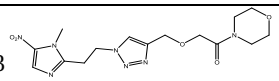
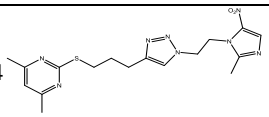
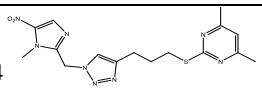
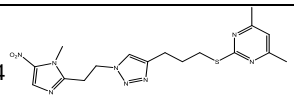
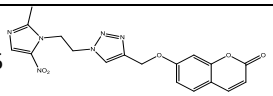
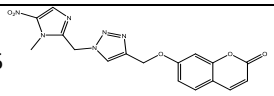
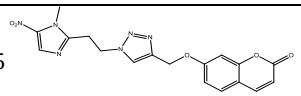
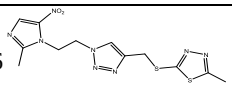
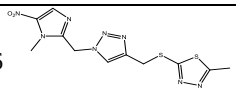
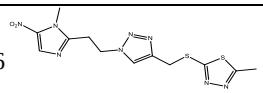
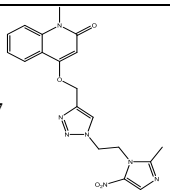
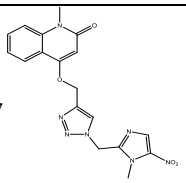
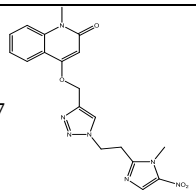
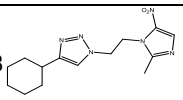
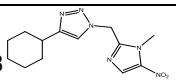
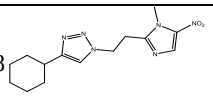
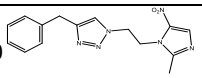
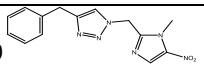
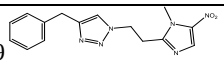
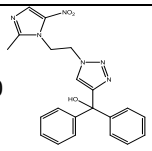
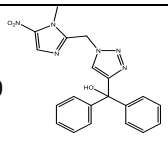
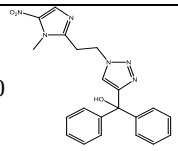
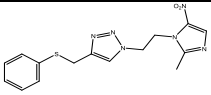
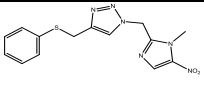
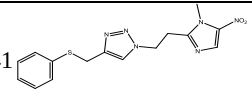
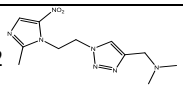
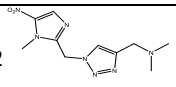
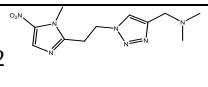
	Core **A**		Core **B**		Core **C**	
Alkyne	Name	Structure	Name	Structure	Name	Structure
130	A-130		B-130		C-130	
131	A-131		B-131		C-131	
132	A-132		B-132		C-132	
133	A-133		B-133		C-133	
134	A-134		B-134		C-134	
135	A-135		B-135		C-135	
136	A-136		B-136		C-136	
137	A-137		B-137		C-137	
138	A-138		B-138		C-138	
139	A-139		B-139		C-139	
140	A-140		B-140		C-140	
141	A-141		B-141		C-141	
142	A-142		B-142		C-142	

Table S1a. Structures of core A-C training compounds

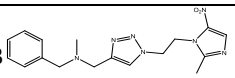
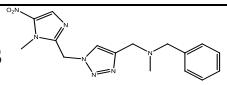
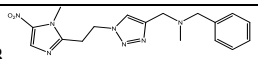
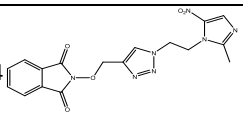
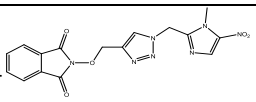
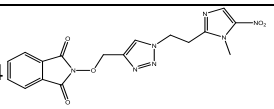
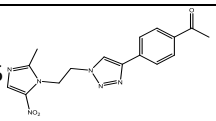
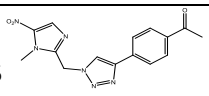
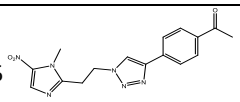
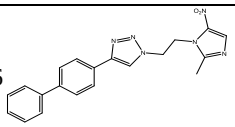
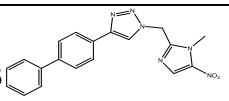
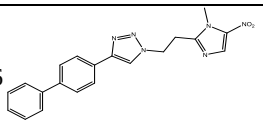
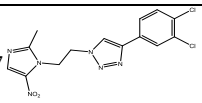
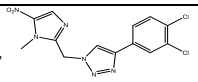
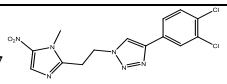
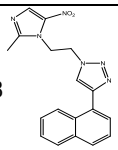
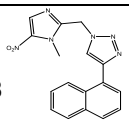
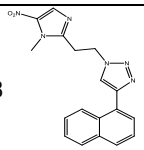
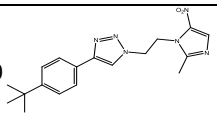
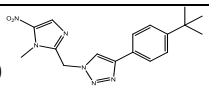
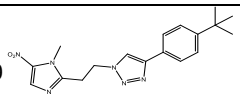
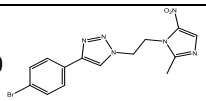
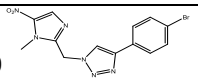
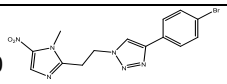
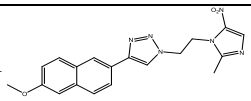
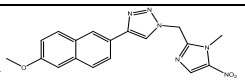
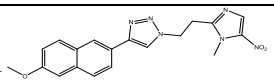
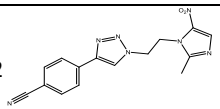
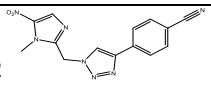
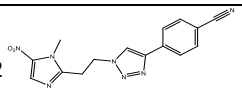
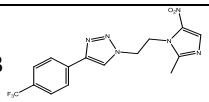
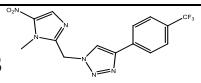
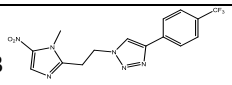
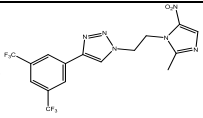
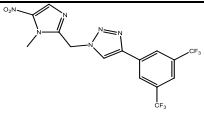
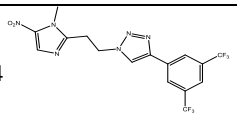
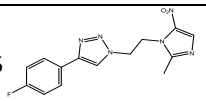
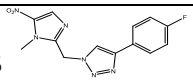
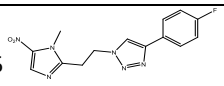
	Core **A**		Core **B**		Core **C**	
Alkyne	Name	Structure	Name	Structure	Name	Structure
143	A-143		B-143		C-143	
144	A-144		B-144		C-144	
145	A-145		B-145		C-145	
146	A-146		B-146		C-146	
147	A-147		B-147		C-147	
148	A-148		B-148		C-148	
149	A-149		B-149		C-149	
150	A-150		B-150		C-150	
151	A-151		B-151		C-151	
152	A-152		B-152		C-152	
153	A-153		B-153		C-153	
154	A-154		B-154		C-154	
155	A-155		B-155		C-155	

Table S1a. Structures of core A-C training compounds

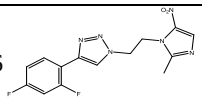
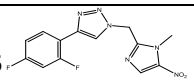
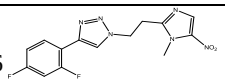
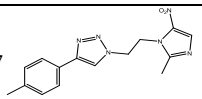
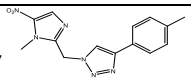
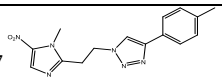
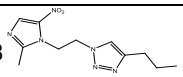
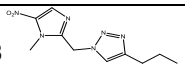
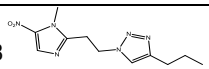
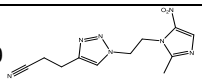
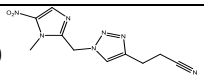
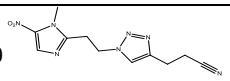
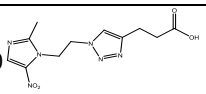
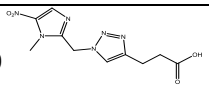
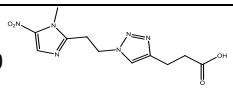
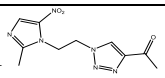
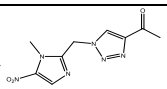
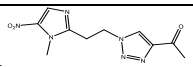
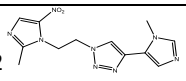
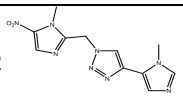
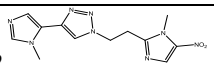
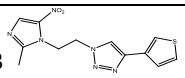
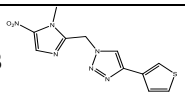
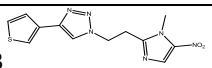
	Core **A**		Core **B**		Core **C**	
Alkyne	Name	Structure	Name	Structure	Name	Structure
156	A-156		B-156		C-156	
157	A-157		B-157		C-157	
158	A-158		B-158		C-158	
159	A-159		B-159		C-159	
160	A-160		B-160		C-160	
161	A-161		B-161		C-161	
162	A-162		B-162		C-162	
163	A-163		B-163		C-163	

Table S1b. Structures of core D-F training compounds

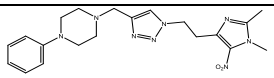
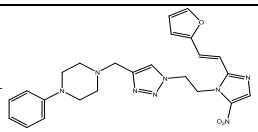
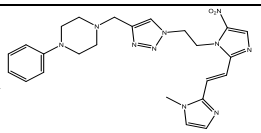
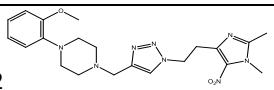
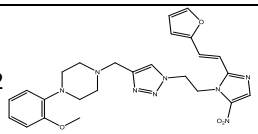
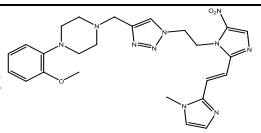
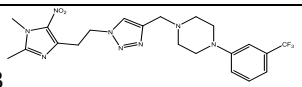
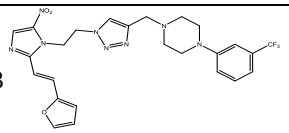
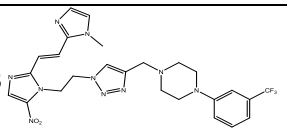
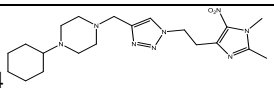
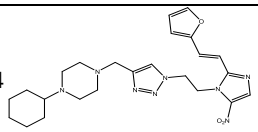
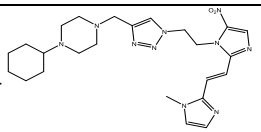
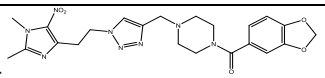
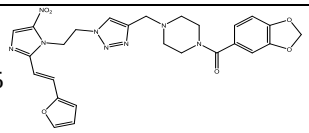
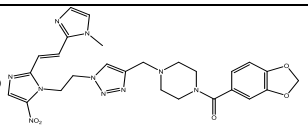
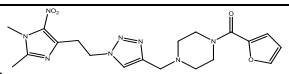
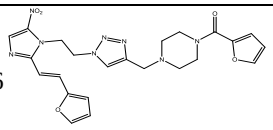
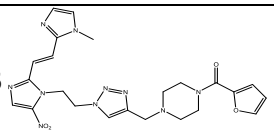
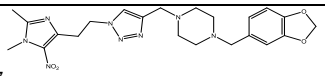
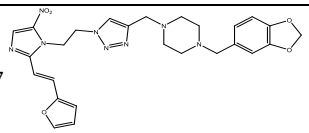
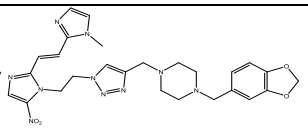
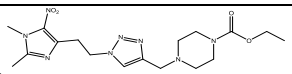
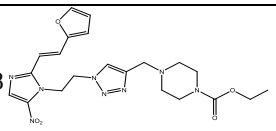
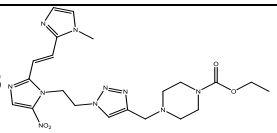
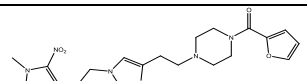
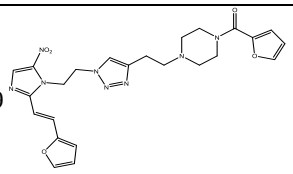
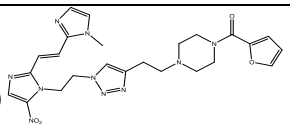
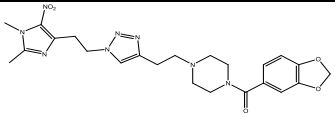
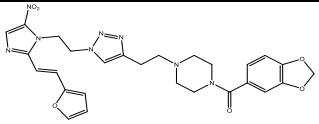
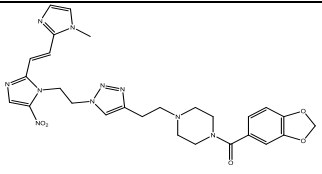
	Core **D**		Core **E**		Core **F**	
Alkyne	Name	Structure	Name	Structure	Name	Structure
101	D-101		E-101		F-101	
102	D-102		E-102		F-102	
103	D-103		E-103		F-103	
104	D-104		E-104		F-104	
105	D-105		E-105		F-105	
106	D-106		E-106		F-106	
107	D-107		E-107		F-107	
108	D-108		E-108		F-108	
109	D-109		E-109		F-109	
110	D-110		E-110		F-110	

Table S1b. Structures of core D-F training compounds

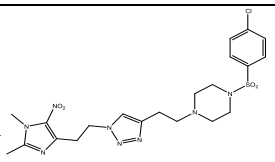
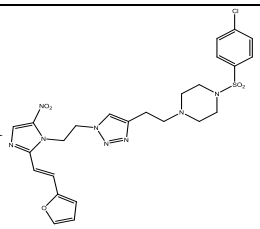
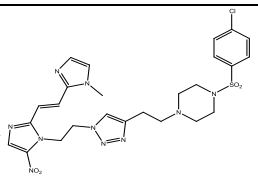
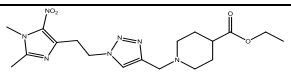
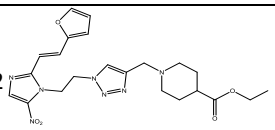
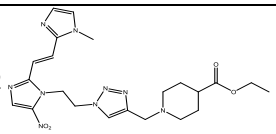
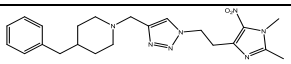
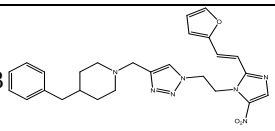
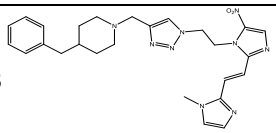
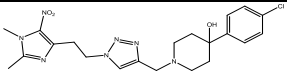
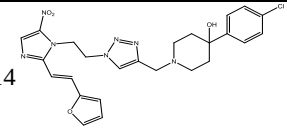
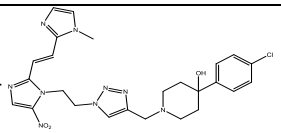
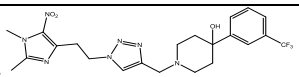
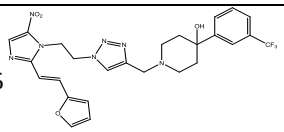
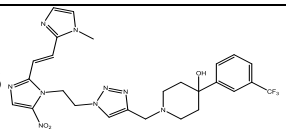
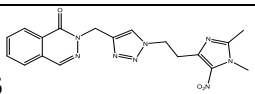
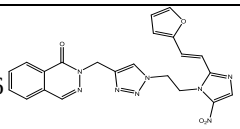
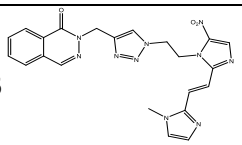
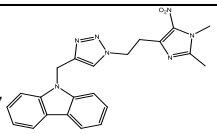
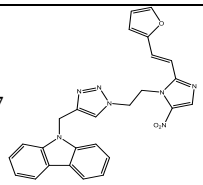
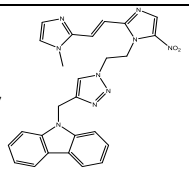
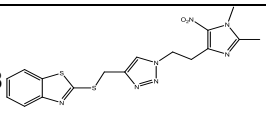
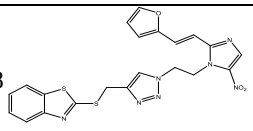
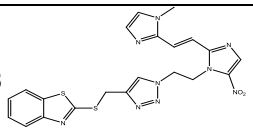
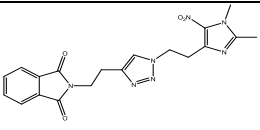
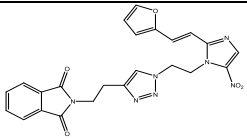
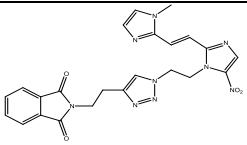
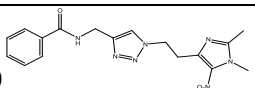
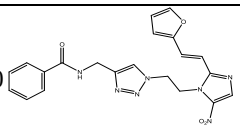
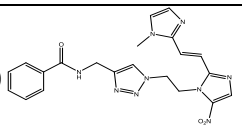
	Core **D**		Core **E**		Core **F**	
Alkyne	Name	Structure	Name	Structure	Name	Structure
111	D-111		E-111		F-111	
112	D-112		E-112		F-112	
113	D-113		E-113		F-113	
114	D-114		E-114		F-114	
115	D-115		E-115		F-115	
116	D-116		E-116		F-116	
117	D-117		E-117		F-117	
118	D-118		E-118		F-118	
119	D-119		E-119		F-119	
120	D-120		E-120		F-120	

Table S1b. Structures of core D-F training compounds

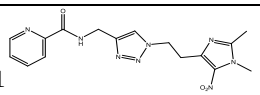
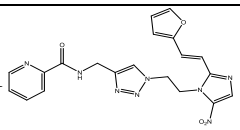
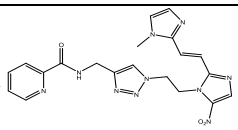
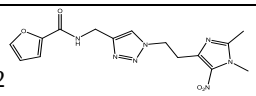
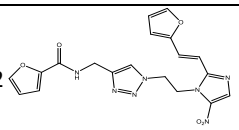
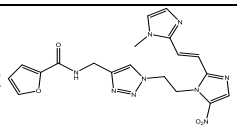
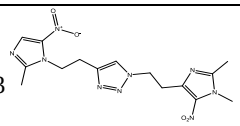
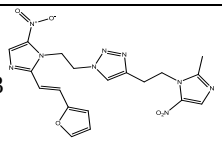
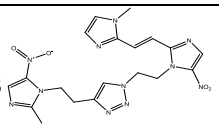
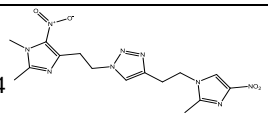
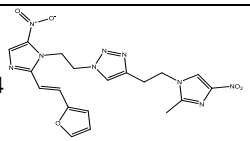
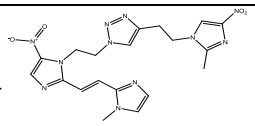
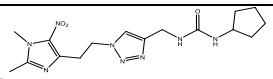
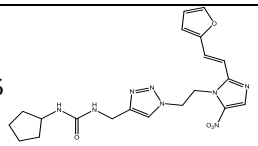
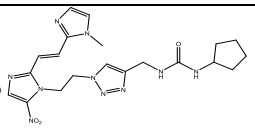
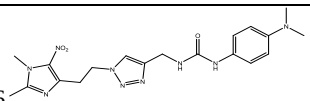
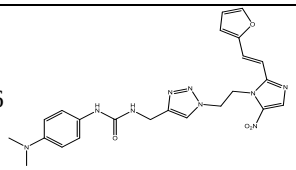
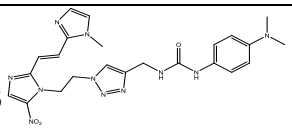
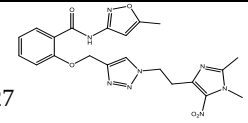
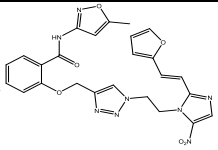
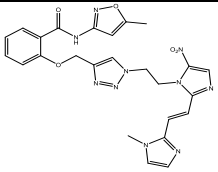
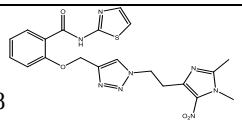
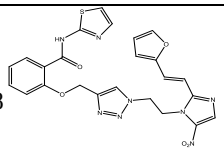
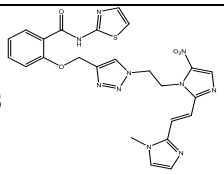
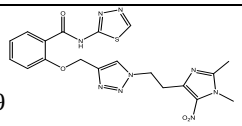
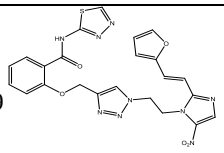
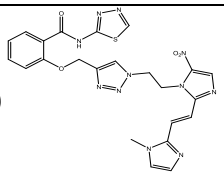
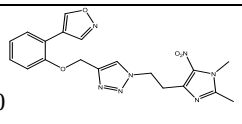
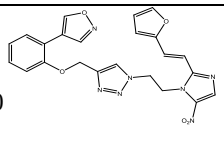
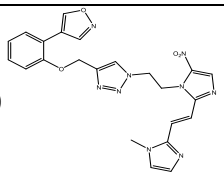
	Core **D**		Core **E**		Core **F**	
Alkyne	Name	Structure	Name	Structure	Name	Structure
121	D-121		E-121		F-121	
122	D-122		E-122		F-122	
123	D-123		E-123		F-123	
124	D-124		E-124		F-124	
125	D-125		E-125		F-125	
126	D-126		E-126		F-126	
127	D-127		E-127		F-127	
128	D-128		E-128		F-128	
129	D-129		E-129		F-129	
130	D-130		E-130		F-130	

Table S1b. Structures of core D-F training compounds

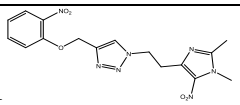
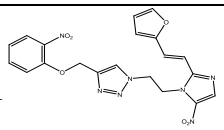
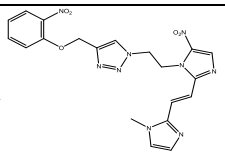
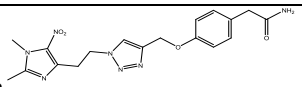
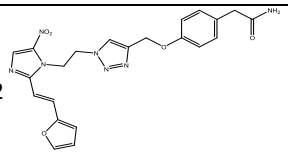
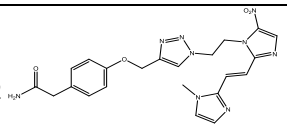
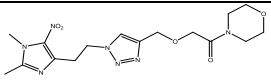
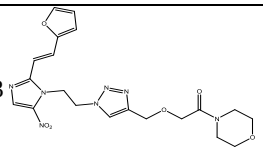
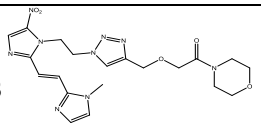
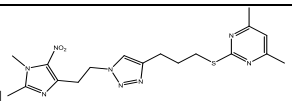
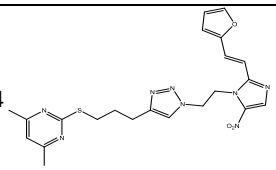
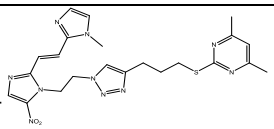
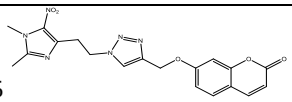
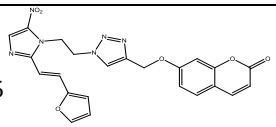
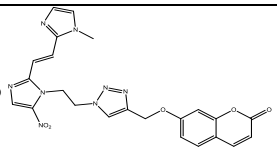
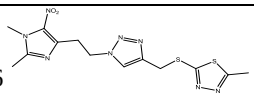
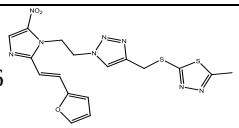
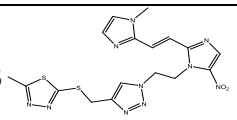
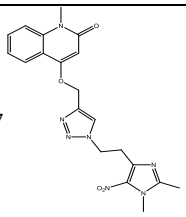
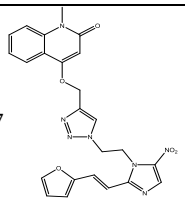
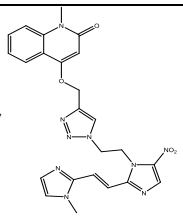
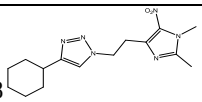
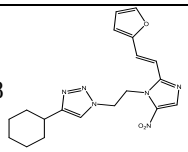
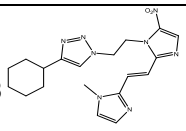
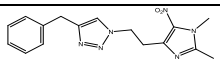
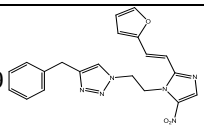
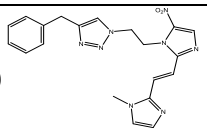
	Core **D**		Core **E**		Core **F**	
Alkyne	Name	Structure	Name	Structure	Name	Structure
131	D-131		E-131		F-131	
132	D-132		E-132		F-132	
133	D-133		E-133		F-133	
134	D-134		E-134		F-134	
135	D-135		E-135		F-135	
136	D-136		E-136		F-136	
137	D-137		E-137		F-137	
138	D-138		E-138		F-138	
139	D-139		E-139		F-139	

Table S1b. Structures of core D-F training compounds

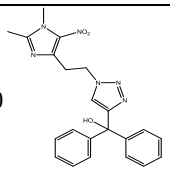
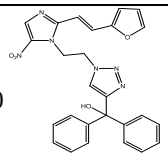
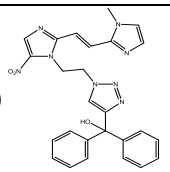
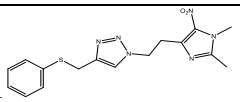
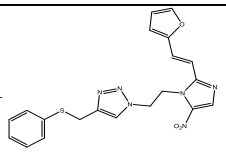
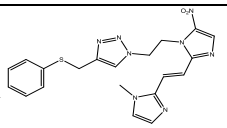
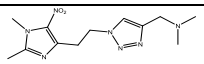
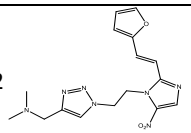
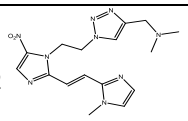
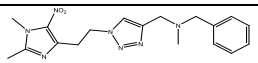
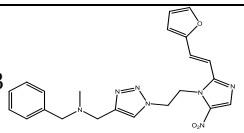
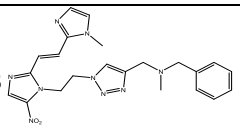
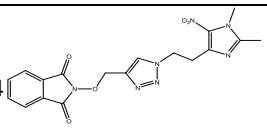
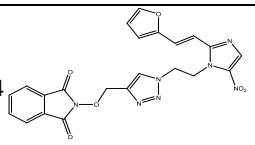
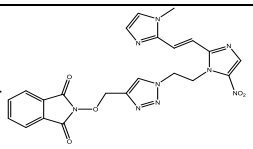
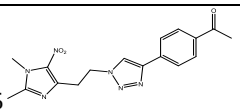
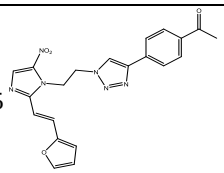
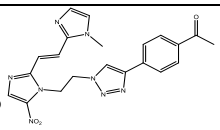
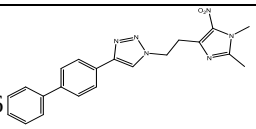
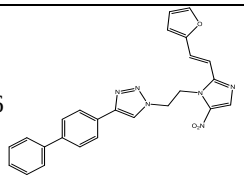
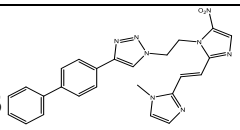
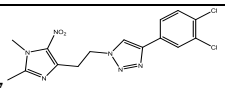
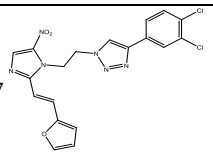
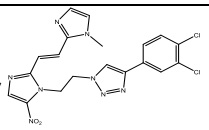
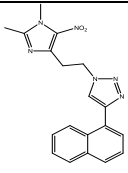
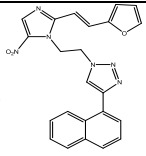
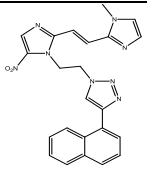
	Core **D**		Core **E**		Core **F**	
Alkyne	Name	Structure	Name	Structure	Name	Structure
140	D-140		E-140		F-140	
141	D-141		E-141		F-141	
142	D-142		E-142		F-142	
143	D-143		E-143		F-143	
144	D-144		E-144		F-144	
145	D-145		E-145		F-145	
146	D-146		E-146		F-146	
147	D-147		E-147		F-147	
148	D-148		E-148		F-148	

Table S1b. Structures of core D-F training compounds

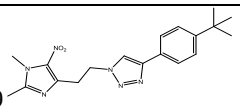
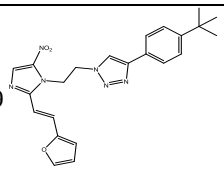
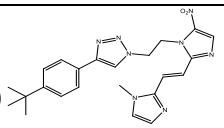
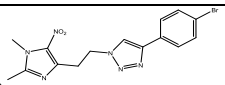
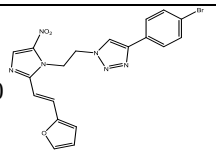
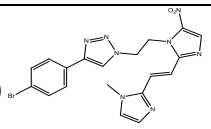
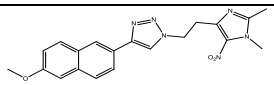
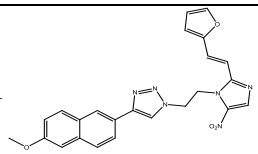
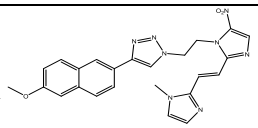
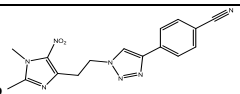
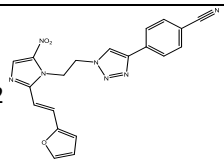
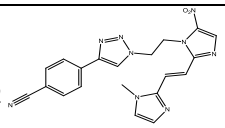
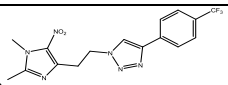
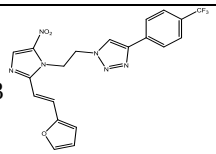
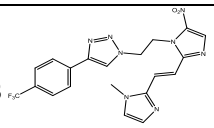
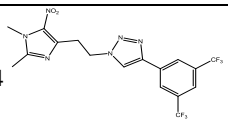
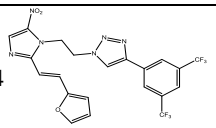
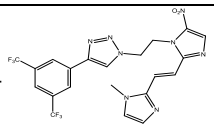
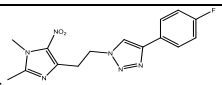
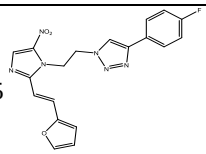
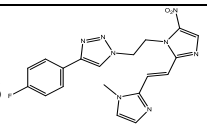
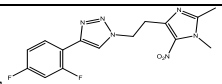
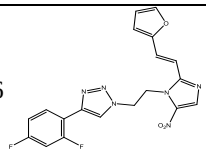
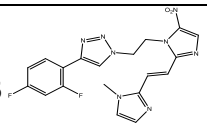
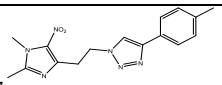
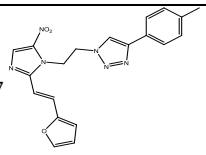
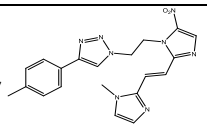
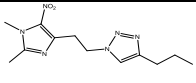
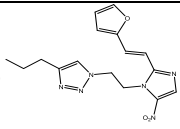
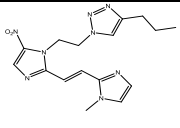
	Core **D**		Core **E**		Core **F**	
Alkyne	Name	Structure	Name	Structure	Name	Structure
149	D-149		E-149		F-149	
150	D-150		E-150		F-150	
151	D-151		E-151		F-151	
152	D-152		E-152		F-152	
153	D-153		E-153		F-153	
154	D-154		E-154		F-154	
155	D-155		E-155		F-155	
156	D-156		E-156		F-156	
157	D-157		E-157		F-157	
158	D-158		E-158		F-158	

Table S1b. Structures of core D-F training compounds

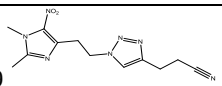
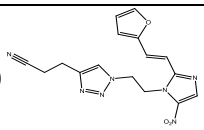
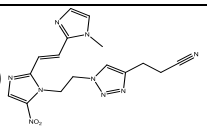
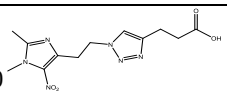
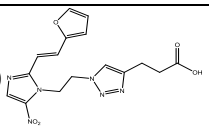
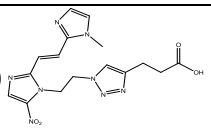
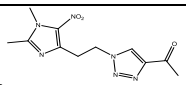
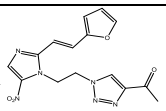
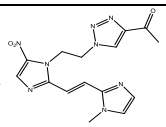
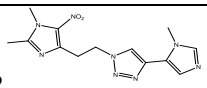
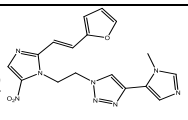
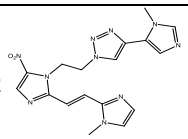
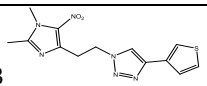
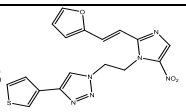
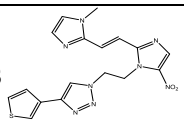
	Core **D**		Core **E**		Core **F**	
Alkyne	Name	Structure	Name	Structure	Name	Structure
159	D-159		E-159		F-159	
160	D-160		E-160		F-160	
161	D-161		E-161		F-161	
162	D-162		E-162		F-162	
163	D-163		E-163		F-163	

Table S2. Activity of 5-NI compounds against *Giardia lamblia*

	G. lamblia 713				*G. lamblia* 106			
	MzS		MzR		MzS		MzR	
Compound	EC50 (μM)	pEC50	EC50 (μM)	pEC50	EC50 (μM)	pEC50	EC50 (μM)	pEC50
Mz	1.995	5.70 ± 0.01	50.119	4.30 ± 0.02	3.631	5.44 ± 0.01	77.625	4.11 ± 0.02
A-101	1.056	5.98 ± 0.02	10.041	5.00 ± 0.04	0.962	6.02 ± 0.14	5.943	5.23 ± 0.12
A-102	1.791	5.75 ± 0.02	13.392	4.87 ± 0.04	2.171	5.66 ± 0.14	7.727	5.11 ± 0.14
A-103	0.212	6.67 ± 0.02	2.248	5.65 ± 0.12	0.227	6.64 ± 0.19	1.445	5.84 ± 0.15
A-104	3.961	5.40 ± 0.06	18.261	4.74 ± 0.04	4.677	5.33 ± 0.25	9.404	5.03 ± 0.12
A-105	4.636	5.33 ± 0.13	10.928	4.96 ± 0.25	2.754	5.56 ± 0.25	8.643	5.06 ± 0.12
A-106	5.401	5.27 ± 0.06	11.150	4.95 ± 0.18	3.715	5.43 ± 0.27	10.077	5.00 ± 0.10
A-107	2.487	5.60 ± 0.04	11.658	4.93 ± 0.12	2.997	5.52 ± 0.18	10.000	5.00 ± 0.09
A-108	3.665	5.44 ± 0.02	14.385	4.84 ± 0.10	2.929	5.53 ± 0.19	7.989	5.10 ± 0.21
A-109	3.545	5.45 ± 0.04	10.648	4.97 ± 0.20	3.831	5.42 ± 0.15	9.829	5.01 ± 0.16
A-110	3.468	5.46 ± 0.04	9.737	5.01 ± 0.29	3.951	5.40 ± 0.23	11.614	4.94 ± 0.13
A-111	0.951	6.02 ± 0.11	4.806	5.32 ± 0.15	2.188	5.66 ± 0.08	8.366	5.08 ± 0.16
A-112	2.686	5.57 ± 0.04	13.853	4.86 ± 0.08	2.570	5.59 ± 0.12	10.174	4.99 ± 0.14
A-113	0.633	6.20 ± 0.04	8.326	5.08 ± 0.08	0.832	6.08 ± 0.15	5.821	5.24 ± 0.14
A-114	3.874	5.41 ± 0.02	15.476	4.81 ± 0.07	4.433	5.35 ± 0.32	9.226	5.04 ± 0.08
A-115	3.625	5.44 ± 0.01	12.963	4.89 ± 0.03	3.467	5.46 ± 0.24	11.285	4.95 ± 0.11
A-116	0.551	6.26 ± 0.04	7.622	5.12 ± 0.06	0.676	6.17 ± 0.21	3.090	5.51 ± 0.12
A-117	0.077	7.11 ± 0.11	1.621	5.79 ± 0.18	0.106	6.98 ± 0.18	1.230	5.91 ± 0.39
A-118	0.079	7.10 ± 0.28	0.761	6.12 ± 0.24	0.671	6.17 ± 0.35	6.202	5.21 ± 0.20
A-119	0.491	6.31 ± 0.05	10.163	4.99 ± 0.05	0.992	6.00 ± 0.12	8.777	5.06 ± 0.12
A-120	4.233	5.37 ± 0.03	15.474	4.81 ± 0.06	3.715	5.43 ± 0.20	8.254	5.08 ± 0.14
A-121	2.308	5.64 ± 0.04	13.254	4.88 ± 0.09	2.154	5.67 ± 0.24	7.470	5.13 ± 0.12
A-122	6.740	5.17 ± 0.03	>20	<4.70	4.898	5.31 ± 0.22	12.589	4.90 ± 0.11
A-123	2.790	5.55 ± 0.01	13.109	4.88 ± 0.09	1.920	5.72 ± 0.20	6.213	5.21 ± 0.13
A-124	12.812	4.89 ± 0.03	18.881	4.72 ± 0.02	5.580	5.25 ± 0.24	12.882	4.89 ± 0.10
A-125	>20	<4.70	>20	<4.70	6.918	5.16 ± 0.15	14.454	4.84 ± 0.08
A-126	5.282	5.28 ± 0.06	23.805	4.62 ± 0.08	5.799	5.24 ± 0.07	14.454	4.84 ± 0.07
A-127	0.034	7.47 ± 0.08	2.013	5.70 ± 0.05	0.168	6.78 ± 0.67	7.189	5.14 ± 0.11
A-128	0.280	6.55 ± 0.23	2.494	5.60 ± 0.12	2.239	5.65 ± 0.09	10.715	4.97 ± 0.03
A-129	0.132	6.88 ± 0.12	0.712	6.15 ± 0.32	0.540	6.27 ± 0.15	3.187	5.50 ± 0.36
A-130	0.040	7.40 ± 0.07	1.472	5.83 ± 0.09	0.059	7.23 ± 0.18	2.531	5.60 ± 0.17
A-131	0.110	6.96 ± 0.05	5.567	5.25 ± 0.18	0.151	6.82 ± 0.14	3.890	5.41 ± 0.39
A-132	19.088	4.72 ± 0.02	>20	<4.70	1.641	5.79 ± 0.74	14.905	4.83 ± 0.07
A-133	2.905	5.54 ± 0.04	17.477	4.76 ± 0.06	3.494	5.46 ± 0.06	14.017	4.85 ± 0.08
A-134	0.205	6.69 ± 0.02	3.767	5.42 ± 0.06	0.295	6.53 ± 0.13	2.291	5.64 ± 0.14
A-135	0.092	7.03 ± 0.04	1.510	5.82 ± 0.13	0.178	6.75 ± 0.14	1.328	5.88 ± 0.14
A-136	1.263	5.90 ± 0.03	11.733	4.93 ± 0.03	1.549	5.81 ± 0.08	11.548	4.94 ± 0.09
A-137	0.285	6.55 ± 0.19	2.137	5.67 ± 0.15	1.339	5.87 ± 0.29	4.597	5.34 ± 0.25
A-138	0.307	6.51 ± 0.07	7.630	5.12 ± 0.11	1.259	5.90 ± 0.29	11.548	4.94 ± 0.09
A-139	0.385	6.41 ± 0.04	5.168	5.29 ± 0.09	0.708	6.15 ± 0.18	6.060	5.22 ± 0.12
A-140	0.177	6.75 ± 0.05	4.164	5.38 ± 0.11	0.240	6.62 ± 0.15	2.630	5.58 ± 0.09
A-141	0.116	6.94 ± 0.02	3.396	5.47 ± 0.08	0.049	7.31 ± 0.59	1.698	5.77 ± 0.14
A-142	14.312	4.84 ± 0.03	17.477	4.76 ± 0.06	9.624	5.02 ± 0.05	16.596	4.78 ± 0.08
A-143	0.910	6.04 ± 0.00	9.302	5.03 ± 0.03	0.295	6.53 ± 0.49	5.158	5.29 ± 0.07
A-144	14.312	4.84 ± 0.02	17.671	4.75 ± 0.05	7.822	5.11 ± 0.06	18.302	4.74 ± 0.04
A-145	1.008	6.00 ± 0.10	9.510	5.02 ± 0.05	4.241	5.37 ± 0.13	15.578	4.81 ± 0.06
A-146	0.082	7.09 ± 0.12	0.286	6.54 ± 0.18	0.138	6.86 ± 0.38	1.923	5.72 ± 0.53
A-147	0.314	6.50 ± 0.09	0.573	6.24 ± 0.13	1.393	5.86 ± 0.17	12.647	4.90 ± 0.05
A-148	0.013	7.88 ± 0.11	0.391	6.41 ± 0.11	0.150	6.83 ± 0.24	3.020	5.52 ± 0.08

Table S2. Activity of 5-NI compounds against *Giardia lamblia*

	G. lamblia 713				*G. lamblia* 106			
	MzS		MzR		MzS		MzR	
Compound	EC50 (μM)	pEC50	EC50 (μM)	pEC50	EC50 (μM)	pEC50	EC50 (μM)	pEC50
A-149	0.143	6.84 ± 0.16	0.363	6.44 ± 0.02	0.431	6.37 ± 0.18	2.333	5.63 ± 0.19
A-150	0.306	6.51 ± 0.21	1.388	5.86 ± 0.07	4.487	5.35 ± 0.18	11.912	4.92 ± 0.06
A-151	0.109	6.96 ± 0.10	1.330	5.88 ± 0.18	0.613	6.21 ± 0.49	3.266	5.49 ± 0.37
A-152	1.188	5.93 ± 0.10	10.980	4.96 ± 0.03	2.309	5.64 ± 0.11	12.882	4.89 ± 0.07
A-153	0.283	6.55 ± 0.13	2.615	5.58 ± 0.22	2.934	5.53 ± 0.16	7.039	5.15 ± 0.12
A-154	0.411	6.39 ± 0.34	9.404	5.03 ± 0.05	1.370	5.86 ± 0.03	7.120	5.15 ± 0.10
A-155	0.303	6.52 ± 0.02	6.109	5.21 ± 0.08	0.571	6.24 ± 0.05	5.041	5.30 ± 0.11
A-156	0.366	6.44 ± 0.02	6.901	5.16 ± 0.10	0.737	6.13 ± 0.09	7.161	5.15 ± 0.05
A-157	0.525	6.28 ± 0.04	8.006	5.10 ± 0.16	2.101	5.68 ± 0.09	10.965	4.96 ± 0.01
A-158	1.444	5.84 ± 0.03	13.656	4.86 ± 0.08	1.644	5.78 ± 0.07	11.049	4.96 ± 0.04
A-159	5.053	5.30 ± 0.02	18.265	4.74 ± 0.04	5.781	5.24 ± 0.09	16.218	4.79 ± 0.05
A-160	6.306	5.20 ± 0.04	14.221	4.85 ± 0.07	5.105	5.29 ± 0.16	18.197	4.74 ± 0.03
A-161	1.867	5.73 ± 0.03	14.325	4.84 ± 0.07	2.477	5.61 ± 0.08	12.303	4.91 ± 0.04
A-162	4.233	5.37 ± 0.03	15.309	4.82 ± 0.12	4.332	5.36 ± 0.10	13.412	4.87 ± 0.06
A-163	0.235	6.63 ± 0.01	6.906	5.16 ± 0.15	0.341	6.47 ± 0.06	4.704	5.33 ± 0.22
B-101	1.183	5.93 ± 0.04	8.046	5.09 ± 0.08	1.585	5.80 ± 0.03	9.661	5.02 ± 0.03
B-102	1.563	5.81 ± 0.04	7.698	5.11 ± 0.10	3.802	5.42 ± 0.01	10.902	4.96 ± 0.01
B-103	0.402	6.40 ± 0.09	2.496	5.60 ± 0.06	0.533	6.27 ± 0.09	4.121	5.39 ± 0.16
B-104	3.104	5.51 ± 0.06	13.086	4.88 ± 0.07	5.412	5.27 ± 0.15	12.662	4.90 ± 0.07
B-105	5.522	5.26 ± 0.10	14.633	4.83 ± 0.08	7.079	5.15 ± 0.17	13.032	4.89 ± 0.06
B-106	4.524	5.34 ± 0.11	13.099	4.88 ± 0.09	5.754	5.24 ± 0.17	12.882	4.89 ± 0.06
B-107	1.648	5.78 ± 0.05	11.440	4.94 ± 0.09	1.891	5.72 ± 0.04	7.371	5.13 ± 0.11
B-108	2.328	5.63 ± 0.13	9.606	5.02 ± 0.06	4.433	5.35 ± 0.09	10.233	4.99 ± 0.01
B-109	3.874	5.41 ± 0.06	13.099	4.88 ± 0.09	7.189	5.14 ± 0.11	12.589	4.90 ± 0.03
B-110	2.178	5.66 ± 0.03	12.531	4.90 ± 0.07	4.713	5.33 ± 0.10	12.209	4.91 ± 0.02
B-111	0.921	6.04 ± 0.02	4.625	5.33 ± 0.04	2.399	5.62 ± 0.04	9.190	5.04 ± 0.06
B-112	1.976	5.70 ± 0.03	13.999	4.85 ± 0.08	3.890	5.41 ± 0.10	10.965	4.96 ± 0.02
B-113	0.592	6.23 ± 0.07	5.901	5.23 ± 0.16	0.905	6.04 ± 0.01	6.072	5.22 ± 0.15
B-114	2.130	5.67 ± 0.03	13.099	4.88 ± 0.09	4.571	5.34 ± 0.05	10.715	4.97 ± 0.02
B-115	3.104	5.51 ± 0.05	13.392	4.87 ± 0.09	7.943	5.10 ± 0.07	10.881	4.96 ± 0.03
B-116	0.723	6.14 ± 0.13	6.033	5.22 ± 0.13	2.362	5.63 ± 0.05	8.577	5.07 ± 0.12
B-117	0.258	6.59 ± 0.16	0.502	6.30 ± 0.28	0.234	6.63 ± 0.05	1.622	5.79 ± 0.44
B-118	1.046	5.98 ± 0.24	5.463	5.26 ± 0.10	0.529	6.28 ± 0.11	1.905	5.72 ± 0.25
B-119	1.191	5.92 ± 0.05	8.792	5.06 ± 0.26	2.222	5.65 ± 0.06	7.328	5.14 ± 0.17
B-120	2.408	5.62 ± 0.03	11.083	4.96 ± 0.26	3.114	5.51 ± 0.08	8.913	5.05 ± 0.12
B-121	2.249	5.65 ± 0.02	6.131	5.21 ± 0.25	3.861	5.41 ± 0.05	11.049	4.96 ± 0.01
B-122	4.140	5.38 ± 0.01	9.381	5.03 ± 0.26	5.329	5.27 ± 0.01	9.924	5.00 ± 0.04
B-123	0.925	6.03 ± 0.04	5.395	5.27 ± 0.27	1.240	5.91 ± 0.04	3.744	5.43 ± 0.12
B-124	1.731	5.76 ± 0.03	8.154	5.09 ± 0.28	1.672	5.78 ± 0.05	10.312	4.99 ± 0.02
B-125	13.999	4.85 ± 0.09	11.347	4.95 ± 0.17	13.386	4.87 ± 0.09	17.512	4.76 ± 0.04
B-126	4.834	5.32 ± 0.03	15.298	4.82 ± 0.09	7.943	5.10 ± 0.08	16.469	4.78 ± 0.05
B-127	0.315	6.50 ± 0.12	2.602	5.58 ± 0.22	1.148	5.94 ± 0.05	4.365	5.36 ± 0.26
B-128	0.192	6.72 ± 0.04	3.342	5.48 ± 0.11	0.676	6.17 ± 0.08	7.762	5.11 ± 0.25
B-129	0.159	6.80 ± 0.06	0.454	6.34 ± 0.08	0.383	6.42 ± 0.08	1.502	5.82 ± 0.29
B-130	0.109	6.96 ± 0.11	1.447	5.84 ± 0.29	0.242	6.62 ± 0.33	1.380	5.86 ± 0.19
B-131	0.167	6.78 ± 0.10	1.749	5.76 ± 0.11	0.331	6.48 ± 0.11	1.725	5.76 ± 0.15
B-132	8.792	5.06 ± 0.15	10.045	5.00 ± 0.23	7.586	5.12 ± 0.14	13.490	4.87 ± 0.09
B-133	2.074	5.68 ± 0.08	9.094	5.04 ± 0.23	3.337	5.48 ± 0.08	10.391	4.98 ± 0.00
B-134	0.217	6.66 ± 0.09	1.636	5.79 ± 0.11	0.251	6.60 ± 0.12	1.920	5.72 ± 0.10

Table S2. Activity of 5-NI compounds against *Giardia lamblia*

	G. lamblia 713				*G. lamblia* 106			
	MzS		MzR		MzS		MzR	
Compound	EC50 (μM)	pEC50	EC50 (μM)	pEC50	EC50 (μM)	pEC50	EC50 (μM)	pEC50
B-135	0.306	6.51 ± 0.08	2.530	5.60 ± 0.17	0.607	6.22 ± 0.08	1.920	5.72 ± 0.14
B-136	1.119	5.95 ± 0.08	5.089	5.29 ± 0.10	1.380	5.86 ± 0.10	1.920	5.72 ± 0.27
B-137	1.680	5.77 ± 0.06	4.380	5.36 ± 0.17	2.733	5.56 ± 0.08	11.659	4.93 ± 0.04
B-138	0.164	6.78 ± 0.07	2.994	5.52 ± 0.07	0.482	6.32 ± 0.05	1.806	5.74 ± 0.11
B-139	0.318	6.50 ± 0.10	3.743	5.43 ± 0.05	0.747	6.13 ± 0.11	3.286	5.48 ± 0.15
B-140	2.015	5.70 ± 0.05	1.344	5.87 ± 0.40	0.759	6.12 ± 0.30	6.918	5.16 ± 0.20
B-141	0.562	6.25 ± 0.12	2.554	5.59 ± 0.13	1.266	5.90 ± 0.05	4.713	5.33 ± 0.21
B-142	8.411	5.08 ± 0.02	11.217	4.95 ± 0.01	5.991	5.22 ± 0.14	14.125	4.85 ± 0.08
B-143	0.869	6.06 ± 0.07	6.448	5.19 ± 0.03	1.357	5.87 ± 0.03	10.798	4.97 ± 0.13
B-144	4.834	5.32 ± 0.03	13.999	4.85 ± 0.06	4.721	5.33 ± 0.17	17.113	4.77 ± 0.06
B-145	0.345	6.46 ± 0.09	2.500	5.60 ± 0.03	0.102	6.99 ± 0.00	5.559	5.26 ± 0.28
B-146	0.513	6.29 ± 0.14	3.014	5.52 ± 0.09	0.432	6.37 ± 0.34	3.913	5.41 ± 0.39
B-147	1.059	5.98 ± 0.11	1.755	5.76 ± 0.12	3.020	5.52 ± 0.21	11.156	4.95 ± 0.17
B-148	0.076	7.12 ± 0.09	1.692	5.77 ± 0.18	0.733	6.14 ± 0.04	4.266	5.37 ± 0.28
B-149	0.618	6.21 ± 0.10	3.241	5.49 ± 0.15	3.508	5.46 ± 0.21	7.456	5.13 ± 0.19
B-150	0.321	6.49 ± 0.35	3.365	5.47 ± 0.29	0.977	6.01 ± 0.67	8.511	5.07 ± 0.16
B-151	0.858	6.07 ± 0.32	3.448	5.46 ± 0.16	5.559	5.26 ± 0.33	2.630	5.58 ± 0.34
B-152	0.137	6.86 ± 0.07	4.284	5.37 ± 0.09	0.158	6.80 ± 0.33	1.928	5.72 ± 0.40
B-153	0.488	6.31 ± 0.45	4.913	5.31 ± 0.10	2.042	5.69 ± 0.70	12.162	4.92 ± 0.08
B-154	0.822	6.09 ± 0.21	10.266	4.99 ± 0.05	4.571	5.34 ± 0.27	11.817	4.93 ± 0.10
B-155	0.114	6.95 ± 0.10	4.326	5.36 ± 0.04	0.240	6.62 ± 0.28	1.496	5.83 ± 0.39
B-156	0.105	6.98 ± 0.17	5.454	5.26 ± 0.16	0.462	6.34 ± 0.16	3.311	5.48 ± 0.31
B-157	0.533	6.27 ± 0.19	6.448	5.19 ± 0.12	0.097	7.02 ± 0.61	3.780	5.42 ± 0.33
B-158	0.549	6.26 ± 0.07	7.045	5.15 ± 0.09	0.750	6.13 ± 0.04	6.060	5.22 ± 0.17
B-159	2.305	5.64 ± 0.04	11.217	4.95 ± 0.02	2.291	5.64 ± 0.04	11.482	4.94 ± 0.09
B-160	12.531	4.90 ± 0.10	14.633	4.83 ± 0.08	6.026	5.22 ± 0.24	12.957	4.89 ± 0.08
B-161	0.783	6.11 ± 0.03	8.046	5.09 ± 0.09	0.977	6.01 ± 0.01	8.561	5.07 ± 0.13
B-162	2.489	5.60 ± 0.06	10.275	4.99 ± 0.02	3.273	5.49 ± 0.08	10.116	5.00 ± 0.12
B-163	0.151	6.82 ± 0.14	3.034	5.52 ± 0.23	0.184	6.74 ± 0.00	2.113	5.68 ± 0.37
C-101	0.782	6.11 ± 0.08	10.266	4.99 ± 0.07	1.600	5.80 ± 0.08	11.324	4.95 ± 0.10
C-102	1.300	5.89 ± 0.09	10.972	4.96 ± 0.05	1.711	5.77 ± 0.10	8.750	5.06 ± 0.09
C-103	0.262	6.58 ± 0.04	2.320	5.63 ± 0.02	0.457	6.34 ± 0.05	4.966	5.30 ± 0.13
C-104	1.159	5.94 ± 0.10	13.999	4.85 ± 0.08	2.256	5.65 ± 0.05	13.490	4.87 ± 0.07
C-105	2.709	5.57 ± 0.04	13.099	4.88 ± 0.03	4.936	5.31 ± 0.14	14.791	4.83 ± 0.06
C-106	3.674	5.43 ± 0.07	11.469	4.94 ± 0.03	3.773	5.42 ± 0.10	14.454	4.84 ± 0.06
C-107	1.226	5.91 ± 0.03	5.053	5.30 ± 0.15	1.561	5.81 ± 0.09	9.333	5.03 ± 0.03
C-108	2.676	5.57 ± 0.03	10.972	4.96 ± 0.03	2.775	5.56 ± 0.20	10.233	4.99 ± 0.06
C-109	2.799	5.55 ± 0.02	13.999	4.85 ± 0.08	4.201	5.38 ± 0.12	11.482	4.94 ± 0.03
C-110	1.933	5.71 ± 0.09	10.972	4.96 ± 0.03	3.067	5.51 ± 0.07	10.881	4.96 ± 0.04
C-111	1.019	5.99 ± 0.06	10.041	5.00 ± 0.07	1.269	5.90 ± 0.06	8.710	5.06 ± 0.07
C-112	1.005	6.00 ± 0.09	7.045	5.15 ± 0.12	0.926	6.03 ± 0.15	7.703	5.11 ± 0.08
C-113	0.411	6.39 ± 0.04	4.325	5.36 ± 0.16	0.509	6.29 ± 0.06	4.266	5.37 ± 0.06
C-114	0.955	6.02 ± 0.08	10.496	4.98 ± 0.08	1.876	5.73 ± 0.05	9.550	5.02 ± 0.06
C-115	1.267	5.90 ± 0.06	8.411	5.08 ± 0.07	2.551	5.59 ± 0.04	9.924	5.00 ± 0.04
C-116	0.592	6.23 ± 0.04	9.396	5.03 ± 0.07	0.825	6.08 ± 0.09	8.777	5.06 ± 0.08
C-117	0.072	7.14 ± 0.09	1.661	5.78 ± 0.09	1.950	5.71 ± 0.11	10.965	4.96 ± 0.04
C-118	0.106	6.97 ± 0.03	10.731	4.97 ± 0.09	0.240	6.62 ± 0.11	1.413	5.85 ± 0.18
C-119	0.647	6.19 ± 0.08	10.731	4.97 ± 0.09	0.926	6.03 ± 0.09	9.772	5.01 ± 0.06
C-120	1.795	5.75 ± 0.13	12.257	4.91 ± 0.08	2.951	5.53 ± 0.03	13.568	4.87 ± 0.06

Table S2. Activity of 5-NI compounds against *Giardia lamblia*

	G. lamblia 713				*G. lamblia* 106			
	MzS		MzR		MzS		MzR	
Compound	EC50 (μM)	pEC50	EC50 (μM)	pEC50	EC50 (μM)	pEC50	EC50 (μM)	pEC50
C-121	1.337	5.87 ± 0.02	11.725	4.93 ± 0.11	1.359	5.87 ± 0.05	12.445	4.91 ± 0.07
C-122	1.875	5.73 ± 0.08	6.306	5.20 ± 0.23	2.840	5.55 ± 0.20	11.049	4.96 ± 0.00
C-123	0.565	6.25 ± 0.04	10.266	4.99 ± 0.22	0.697	6.16 ± 0.07	5.754	5.24 ± 0.15
C-124	2.123	5.67 ± 0.07	9.821	5.01 ± 0.12	2.089	5.68 ± 0.10	11.049	4.96 ± 0.00
C-125	4.081	5.39 ± 0.10	11.469	4.94 ± 0.01	4.201	5.38 ± 0.11	13.698	4.86 ± 0.08
C-126	2.210	5.66 ± 0.04	14.633	4.83 ± 0.08	0.917	6.04 ± 0.11	12.115	4.92 ± 0.04
C-127	0.165	6.78 ± 0.06	6.168	5.21 ± 0.14	0.414	6.38 ± 0.38	6.761	5.17 ± 0.18
C-128	0.986	6.01 ± 0.02	5.167	5.29 ± 0.14	2.317	5.64 ± 0.08	13.284	4.88 ± 0.04
C-129	0.366	6.44 ± 0.08	7.870	5.10 ± 0.21	1.404	5.85 ± 0.13	10.715	4.97 ± 0.01
C-130	0.054	7.27 ± 0.10	1.843	5.73 ± 0.10	0.051	7.30 ± 0.14	0.898	6.05 ± 0.04
C-131	0.178	6.75 ± 0.05	3.514	5.45 ± 0.11	0.176	6.76 ± 0.15	2.493	5.60 ± 0.06
C-132	4.313	5.37 ± 0.10	8.792	5.06 ± 0.26	3.569	5.45 ± 0.08	11.134	4.95 ± 0.00
C-133	1.369	5.86 ± 0.04	12.531	4.90 ± 0.10	0.970	6.01 ± 0.10	11.817	4.93 ± 0.08
C-134	0.286	6.54 ± 0.08	6.448	5.19 ± 0.16	0.407	6.39 ± 0.13	6.998	5.16 ± 0.10
C-135	0.359	6.45 ± 0.07	5.522	5.26 ± 0.16	0.427	6.37 ± 0.13	4.365	5.36 ± 0.14
C-136	0.866	6.06 ± 0.07	10.041	5.00 ± 0.11	1.175	5.93 ± 0.08	8.861	5.05 ± 0.13
C-137	0.160	6.80 ± 0.06	2.466	5.61 ± 0.17	0.206	6.69 ± 0.31	2.974	5.53 ± 0.07
C-138	0.264	6.58 ± 0.14	8.912	5.05 ± 0.05	0.733	6.14 ± 0.04	8.861	5.05 ± 0.14
C-139	0.368	6.43 ± 0.17	10.972	4.96 ± 0.11	1.834	5.74 ± 0.52	7.718	5.11 ± 0.18
C-140	0.441	6.36 ± 0.17	7.203	5.14 ± 0.13	0.447	6.35 ± 0.04	8.241	5.08 ± 0.20
C-141	0.190	6.72 ± 0.03	6.741	5.17 ± 0.05	0.304	6.52 ± 0.06	5.129	5.29 ± 0.19
C-142	0.860	6.07 ± 0.05	10.972	4.96 ± 0.04	2.018	5.70 ± 0.09	12.209	4.91 ± 0.06
C-143	1.428	5.85 ± 0.10	11.217	4.95 ± 0.03	0.665	6.18 ± 0.08	6.166	5.21 ± 0.04
C-144	0.555	6.26 ± 0.04	11.708	4.93 ± 0.19	3.236	5.49 ± 0.07	13.804	4.86 ± 0.08
C-145	0.646	6.19 ± 0.11	5.096	5.29 ± 0.21	0.697	6.16 ± 0.08	7.447	5.13 ± 0.13
C-146	0.598	6.22 ± 0.32	10.812	4.97 ± 0.01	1.370	5.86 ± 0.26	12.589	4.90 ± 0.05
C-147	0.323	6.49 ± 0.22	7.533	5.12 ± 0.12	1.189	5.93 ± 0.18	10.593	4.98 ± 0.11
C-148	0.499	6.30 ± 0.13	4.325	5.36 ± 0.12	0.167	6.78 ± 0.18	3.532	5.45 ± 0.19
C-149	0.454	6.34 ± 0.30	9.912	5.00 ± 0.06	1.413	5.85 ± 0.09	9.661	5.02 ± 0.11
C-150	0.281	6.55 ± 0.38	7.698	5.11 ± 0.02	3.548	5.45 ± 0.14	11.695	4.93 ± 0.09
C-151	0.751	6.12 ± 0.30	5.645	5.25 ± 0.14	0.088	7.06 ± 0.59	3.487	5.46 ± 0.40
C-152	1.930	5.71 ± 0.13	6.592	5.18 ± 0.18	0.776	6.11 ± 0.18	8.318	5.08 ± 0.15
C-153	2.309	5.64 ± 0.03	3.961	5.40 ± 0.35	1.567	5.81 ± 0.02	8.643	5.06 ± 0.04
C-154	1.980	5.70 ± 0.07	9.821	5.01 ± 0.08	3.187	5.50 ± 0.04	11.749	4.93 ± 0.04
C-155	0.359	6.45 ± 0.01	5.019	5.30 ± 0.11	0.145	6.84 ± 0.05	1.514	5.82 ± 0.19
C-156	0.416	6.38 ± 0.07	8.411	5.08 ± 0.09	0.267	6.57 ± 0.07	4.365	5.36 ± 0.21
C-157	0.414	6.38 ± 0.06	5.734	5.24 ± 0.14	1.012	6.00 ± 0.02	8.643	5.06 ± 0.09
C-158	0.109	6.96 ± 0.05	5.772	5.24 ± 0.29	0.919	6.04 ± 0.08	8.191	5.09 ± 0.06
C-159	1.473	5.83 ± 0.15	11.315	4.95 ± 0.05	1.950	5.71 ± 0.05	9.624	5.02 ± 0.04
C-160	7.328	5.14 ± 0.20	14.312	4.84 ± 0.06	3.138	5.50 ± 0.09	11.570	4.94 ± 0.04
C-161	0.741	6.13 ± 0.07	11.988	4.92 ± 0.01	1.166	5.93 ± 0.01	8.066	5.09 ± 0.10
C-162	1.916	5.72 ± 0.08	12.257	4.91 ± 0.11	2.570	5.59 ± 0.02	13.996	4.85 ± 0.06
C-163	0.302	6.52 ± 0.07	5.901	5.23 ± 0.01	0.368	6.43 ± 0.15	5.781	5.24 ± 0.19
D-101	15.565	4.81 ± 0.11	14.199	4.85 ± 0.08	11.659	4.93 ± 0.13	11.885	4.93 ± 0.01
D-102	16.089	4.79 ± 0.09	12.850	4.89 ± 0.10	10.312	4.99 ± 0.17	12.882	4.89 ± 0.06
D-103	9.620	5.02 ± 0.06	>20	<4.70	7.528	5.12 ± 0.09	16.724	4.78 ± 0.03
D-104	12.142	4.92 ± 0.22	14.171	4.85 ± 0.08	9.190	5.04 ± 0.22	11.049	4.96 ± 0.01
D-105	19.091	4.72 ± 0.02	15.825	4.80 ± 0.05	11.570	4.94 ± 0.13	12.589	4.90 ± 0.02
D-106	>20	<4.70	17.096	4.77 ± 0.06	11.307	4.95 ± 0.14	12.686	4.90 ± 0.02

Table S2. Activity of 5-NI compounds against *Giardia lamblia*

	G. lamblia 713				*G. lamblia* 106			
	MzS		MzR		MzS		MzR	
Compound	EC50 (µM)	pEC50	EC50 (µM)	pEC50	EC50 (µM)	pEC50	EC50 (µM)	pEC50
D-107	12.683	4.90 ± 0.02	13.410	4.87 ± 0.09	10.155	4.99 ± 0.18	11.570	4.94 ± 0.03
D-108	12.826	4.89 ± 0.03	11.364	4.94 ± 0.14	8.511	5.07 ± 0.13	10.312	4.99 ± 0.03
D-109	13.257	4.88 ± 0.04	13.709	4.86 ± 0.08	10.532	4.98 ± 0.12	11.885	4.93 ± 0.02
D-110	12.135	4.92 ± 0.01	13.861	4.86 ± 0.08	10.058	5.00 ± 0.14	12.809	4.89 ± 0.06
D-111	5.911	5.23 ± 0.21	12.413	4.91 ± 0.10	11.416	4.94 ± 0.09	12.209	4.91 ± 0.01
D-112	10.166	4.99 ± 0.04	12.551	4.90 ± 0.10	10.715	4.97 ± 0.11	11.885	4.93 ± 0.02
D-113	4.884	5.31 ± 0.16	12.795	4.89 ± 0.10	7.470	5.13 ± 0.10	15.136	4.82 ± 0.06
D-114	10.626	4.97 ± 0.04	13.861	4.86 ± 0.08	12.023	4.92 ± 0.07	17.113	4.77 ± 0.07
D-115	10.861	4.96 ± 0.10	12.973	4.89 ± 0.09	11.092	4.96 ± 0.10	12.686	4.90 ± 0.01
D-116	12.135	4.92 ± 0.03	14.688	4.83 ± 0.05	10.593	4.98 ± 0.11	12.784	4.89 ± 0.04
D-117	9.201	5.04 ± 0.09	17.585	4.75 ± 0.03	11.134	4.95 ± 0.15	12.882	4.89 ± 0.04
D-118	7.306	5.14 ± 0.04	18.829	4.73 ± 0.03	5.980	5.22 ± 0.13	18.197	4.74 ± 0.04
D-119	10.393	4.98 ± 0.05	12.866	4.89 ± 0.08	12.686	4.90 ± 0.10	14.791	4.83 ± 0.05
D-120	11.870	4.93 ± 0.00	>20	<4.70	8.710	5.06 ± 0.23	7.852	5.11 ± 0.09
D-121	8.805	5.06 ± 0.07	14.567	4.84 ± 0.14	10.715	4.97 ± 0.01	4.416	5.36 ± 0.03
D-122	11.109	4.95 ± 0.02	17.769	4.75 ± 0.05	10.233	4.99 ± 0.18	10.471	4.98 ± 0.04
D-123	1.098	5.96 ± 0.12	6.587	5.18 ± 0.08	2.493	5.60 ± 0.09	4.898	5.31 ± 0.06
D-124	12.005	4.92 ± 0.06	17.477	4.76 ± 0.06	9.050	5.04 ± 0.21	9.120	5.04 ± 0.06
D-125	13.263	4.88 ± 0.09	15.058	4.82 ± 0.08	9.404	5.03 ± 0.22	10.552	4.98 ± 0.01
D-126	16.722	4.78 ± 0.07	16.908	4.77 ± 0.06	8.511	5.07 ± 0.26	11.839	4.93 ± 0.07
D-127	6.776	5.17 ± 0.09	13.977	4.85 ± 0.09	10.798	4.97 ± 0.15	11.220	4.95 ± 0.02
D-128	7.136	5.15 ± 0.15	17.049	4.77 ± 0.07	10.552	4.98 ± 0.18	12.303	4.91 ± 0.06
D-129	14.328	4.84 ± 0.08	15.183	4.82 ± 0.12	11.839	4.93 ± 0.23	13.183	4.88 ± 0.09
D-130	3.836	5.42 ± 0.13	14.688	4.83 ± 0.08	14.125	4.85 ± 0.09	17.783	4.75 ± 0.05
D-131	4.838	5.32 ± 0.17	15.694	4.80 ± 0.06	6.119	5.21 ± 0.04	12.493	4.90 ± 0.10
D-132	14.487	4.84 ± 0.08	16.539	4.78 ± 0.08	11.134	4.95 ± 0.15	11.134	4.95 ± 0.02
D-133	14.487	4.84 ± 0.08	16.357	4.79 ± 0.09	13.183	4.88 ± 0.09	11.749	4.93 ± 0.03
D-134	13.268	4.88 ± 0.06	>20	<4.70	10.312	4.99 ± 0.12	14.622	4.84 ± 0.14
D-135	2.401	5.62 ± 0.12	16.539	4.78 ± 0.07	4.169	5.38 ± 0.04	11.350	4.95 ± 0.02
D-136	14.642	4.83 ± 0.07	18.266	4.74 ± 0.04	13.386	4.87 ± 0.08	11.659	4.93 ± 0.02
D-137	8.435	5.07 ± 0.04	>20	<4.70	9.226	5.04 ± 0.07	14.706	4.83 ± 0.05
D-138	11.482	4.94 ± 0.02	17.477	4.76 ± 0.06	9.624	5.02 ± 0.09	11.614	4.94 ± 0.01
D-139	11.484	4.94 ± 0.02	17.671	4.75 ± 0.05	12.397	4.91 ± 0.05	10.965	4.96 ± 0.01
D-140	5.655	5.25 ± 0.12	>20	<4.70	8.318	5.08 ± 0.10	13.490	4.87 ± 0.09
D-141	7.498	5.13 ± 0.07	16.908	4.77 ± 0.07	5.667	5.25 ± 0.11	9.550	5.02 ± 0.03
D-142	6.760	5.17 ± 0.20	17.096	4.77 ± 0.07	3.631	5.44 ± 0.24	5.289	5.28 ± 0.17
D-143	10.512	4.98 ± 0.01	17.096	4.77 ± 0.07	3.861	5.41 ± 0.29	6.506	5.19 ± 0.13
D-144	11.232	4.95 ± 0.01	15.825	4.80 ± 0.07	8.066	5.09 ± 0.17	15.136	4.82 ± 0.05
D-145	1.786	5.75 ± 0.10	14.810	4.83 ± 0.02	5.412	5.27 ± 0.08	12.589	4.90 ± 0.07
D-146	5.929	5.23 ± 0.19	17.477	4.76 ± 0.06	5.667	5.25 ± 0.28	6.658	5.18 ± 0.21
D-147	2.386	5.62 ± 0.30	15.651	4.81 ± 0.08	3.521	5.45 ± 0.27	11.659	4.93 ± 0.13
D-148	7.625	5.12 ± 0.11	>20	<4.70	7.413	5.13 ± 0.17	12.303	4.91 ± 0.13
D-149	7.794	5.11 ± 0.14	>20	<4.70	7.079	5.15 ± 0.17	12.023	4.92 ± 0.07
D-150	3.265	5.49 ± 0.16	18.674	4.73 ± 0.03	5.934	5.23 ± 0.25	10.633	4.97 ± 0.02
D-151	9.732	5.01 ± 0.07	18.469	4.73 ± 0.03	6.865	5.16 ± 0.21	10.312	4.99 ± 0.01
D-152	5.202	5.28 ± 0.24	17.285	4.76 ± 0.03	6.761	5.17 ± 0.20	10.965	4.96 ± 0.02
D-153	4.014	5.40 ± 0.16	17.671	4.75 ± 0.05	5.623	5.25 ± 0.28	8.004	5.10 ± 0.22
D-154	8.429	5.07 ± 0.09	19.517	4.71 ± 0.01	7.134	5.15 ± 0.19	10.965	4.96 ± 0.15
D-155	5.488	5.26 ± 0.06	19.091	4.72 ± 0.02	4.233	5.37 ± 0.17	10.000	5.00 ± 0.06

Table S2. Activity of 5-NI compounds against *Giardia lamblia*

	G. lamblia 713				*G. lamblia* 106			
	MzS		MzR		MzS		MzR	
Compound	EC50 (μM)	pEC50	EC50 (μM)	pEC50	EC50 (μM)	pEC50	EC50 (μM)	pEC50
D-156	7.259	5.14 ± 0.09	>20	<4.70	5.934	5.23 ± 0.18	10.233	4.99 ± 0.05
D-157	3.663	5.44 ± 0.04	>20	<4.70	3.603	5.44 ± 0.15	3.715	5.43 ± 0.28
D-158	11.872	4.93 ± 0.04	>20	<4.70	6.358	5.20 ± 0.22	10.000	5.00 ± 0.08
D-159	11.358	4.94 ± 0.02	>20	<4.70	7.943	5.10 ± 0.14	9.261	5.03 ± 0.10
D-160	11.354	4.94 ± 0.04	>20	<4.70	6.761	5.17 ± 0.20	6.972	5.16 ± 0.14
D-161	9.409	5.03 ± 0.06	16.722	4.78 ± 0.08	5.667	5.25 ± 0.18	9.050	5.04 ± 0.08
D-162	7.969	5.10 ± 0.13	17.671	4.75 ± 0.05	13.183	4.88 ± 0.09	10.666	4.97 ± 0.12
D-163	>20	<4.70	>20	<4.70	5.580	5.25 ± 0.14	14.723	4.83 ± 0.06
E-101	0.012	7.92 ± 0.37	0.293	6.53 ± 0.10	0.028	7.56 ± 0.03	0.401	6.40 ± 0.20
E-102	0.016	7.80 ± 0.24	0.209	6.68 ± 0.06	0.032	7.50 ± 0.11	0.300	6.52 ± 0.07
E-103	0.043	7.36 ± 0.10	0.926	6.03 ± 0.10	0.231	6.64 ± 0.17	0.440	6.36 ± 0.05
E-104	0.063	7.20 ± 0.02	1.585	5.80 ± 0.08	0.097	7.01 ± 0.11	2.934	5.53 ± 0.28
E-105	0.101	7.00 ± 0.06	0.912	6.04 ± 0.17	0.101	7.00 ± 0.16	3.073	5.51 ± 0.23
E-106	0.098	7.01 ± 0.18	1.980	5.70 ± 0.13	0.137	6.86 ± 0.08	2.985	5.53 ± 0.21
E-107	0.018	7.74 ± 0.16	0.404	6.39 ± 0.04	0.054	7.27 ± 0.09	1.245	5.91 ± 0.41
E-108	0.067	7.18 ± 0.12	0.708	6.15 ± 0.07	0.072	7.14 ± 0.09	1.531	5.82 ± 0.27
E-109	0.070	7.16 ± 0.22	1.175	5.93 ± 0.07	0.110	6.96 ± 0.12	2.126	5.67 ± 0.20
E-110	0.068	7.17 ± 0.23	0.819	6.09 ± 0.11	0.057	7.25 ± 0.04	1.047	5.98 ± 0.19
E-111	0.091	7.04 ± 0.19	0.719	6.14 ± 0.13	0.334	6.48 ± 0.08	1.421	5.85 ± 0.12
E-112	0.019	7.73 ± 0.10	0.641	6.19 ± 0.05	0.043	7.37 ± 0.15	0.439	6.36 ± 0.17
E-113	0.014	7.85 ± 0.14	0.200	6.70 ± 0.12	0.064	7.20 ± 0.18	0.501	6.30 ± 0.13
E-114	0.034	7.47 ± 0.12	0.440	6.36 ± 0.03	0.191	6.72 ± 0.15	0.661	6.18 ± 0.08
E-115	0.061	7.22 ± 0.09	0.386	6.41 ± 0.08	0.185	6.73 ± 0.01	0.733	6.14 ± 0.07
E-116	0.005	8.28 ± 0.28	0.207	6.68 ± 0.14	0.041	7.38 ± 0.09	0.992	6.00 ± 0.12
E-117	0.035	7.45 ± 0.33	5.077	5.29 ± 0.46	0.340	6.47 ± 0.25	0.661	6.18 ± 0.07
E-118	0.024	7.61 ± 0.07	0.340	6.47 ± 0.19	0.046	7.34 ± 0.21	1.221	5.91 ± 0.21
E-119	0.030	7.52 ± 0.13	1.063	5.97 ± 0.13	0.187	6.73 ± 0.17	2.570	5.59 ± 0.17
E-120	0.011	7.94 ± 0.18	0.193	6.71 ± 0.13	0.058	7.24 ± 0.10	0.321	6.49 ± 0.16
E-121	0.007	8.15 ± 0.08	0.631	6.20 ± 0.00	0.086	7.07 ± 0.18	0.307	6.51 ± 0.17
E-122	0.020	7.70 ± 0.08	1.000	6.00 ± 0.00	0.135	6.87 ± 0.13	0.651	6.19 ± 0.09
E-123	0.013	7.87 ± 0.11	0.275	6.56 ± 0.00	0.059	7.23 ± 0.12	0.227	6.64 ± 0.09
E-124	0.447	6.35 ± 0.20	3.467	5.46 ± 0.00	0.596	6.23 ± 0.05	3.920	5.41 ± 0.12
E-125	0.024	7.61 ± 0.10	0.440	6.36 ± 0.12	0.117	6.93 ± 0.17	1.505	5.82 ± 0.13
E-126	0.049	7.31 ± 0.27	0.759	6.12 ± 0.38	0.130	6.89 ± 0.16	1.326	5.88 ± 0.16
E-127	0.143	6.85 ± 0.29	1.271	5.90 ± 0.30	0.104	6.99 ± 0.27	0.977	6.01 ± 0.22
E-128	0.012	7.92 ± 0.14	0.374	6.43 ± 0.24	0.035	7.45 ± 0.04	0.084	7.07 ± 0.27
E-129	0.031	7.51 ± 0.07	0.813	6.09 ± 0.30	0.090	7.05 ± 0.05	0.770	6.11 ± 0.10
E-130	0.024	7.62 ± 0.25	0.893	6.05 ± 0.18	0.279	6.56 ± 0.12	1.193	5.92 ± 0.24
E-131	0.038	7.42 ± 0.23	1.277	5.89 ± 0.45	0.022	7.65 ± 0.21	0.259	6.59 ± 0.10
E-132	0.420	6.38 ± 0.06	1.995	5.70 ± 0.31	2.380	5.62 ± 0.04	2.163	5.67 ± 0.28
E-133	0.035	7.46 ± 0.16	0.482	6.32 ± 0.28	0.132	6.88 ± 0.09	1.372	5.86 ± 0.24
E-134	0.008	8.08 ± 0.25	0.258	6.59 ± 0.34	0.033	7.48 ± 0.30	0.109	6.96 ± 0.12
E-135	>20	<4.70	9.848	5.01 ± 0.31	0.022	7.66 ± 0.02	0.193	6.71 ± 0.25
E-136	0.007	8.18 ± 0.09	0.169	6.77 ± 0.20	0.027	7.57 ± 0.07	0.132	6.88 ± 0.17
E-137	0.053	7.28 ± 0.30	0.603	6.22 ± 0.12	0.098	7.01 ± 0.12	1.522	5.82 ± 0.32
E-138	0.015	7.82 ± 0.02	0.430	6.37 ± 0.43	0.058	7.24 ± 0.21	0.923	6.04 ± 0.37
E-139	0.010	7.98 ± 0.07	0.547	6.26 ± 0.39	0.088	7.06 ± 0.26	1.457	5.84 ± 0.26
E-140	0.066	7.18 ± 0.06	3.039	5.52 ± 0.14	0.130	6.89 ± 0.26	0.567	6.25 ± 0.48
E-141	0.012	7.92 ± 0.14	0.131	6.88 ± 0.32	0.084	7.08 ± 0.23	0.414	6.38 ± 0.22

Table S2. Activity of 5-NI compounds against *Giardia lamblia*

	G. lamblia 713				*G. lamblia* 106			
	MzS		MzR		MzS		MzR	
Compound	EC50 (μM)	pEC50	EC50 (μM)	pEC50	EC50 (μM)	pEC50	EC50 (μM)	pEC50
E-142	0.127	6.90 ± 0.14	0.819	6.09 ± 0.11	0.280	6.55 ± 0.11	1.573	5.80 ± 0.09
E-143	0.006	8.24 ± 0.10	0.124	6.91 ± 0.06	0.018	7.76 ± 0.24	0.213	6.67 ± 0.19
E-144	0.386	6.41 ± 0.27	5.741	5.24 ± 0.19	1.941	5.71 ± 0.11	10.654	4.97 ± 0.11
E-145	0.003	8.53 ± 0.18	0.186	6.73 ± 0.18	0.088	7.06 ± 0.30	0.251	6.60 ± 0.15
E-146	0.024	7.62 ± 0.09	1.618	5.79 ± 0.55	0.088	7.06 ± 0.37	0.822	6.09 ± 0.50
E-147	0.054	7.26 ± 0.04	0.196	6.71 ± 0.24	1.306	5.88 ± 0.09	9.829	5.01 ± 0.07
E-148	0.015	7.84 ± 0.25	1.088	5.96 ± 0.21	0.115	6.94 ± 0.15	2.469	5.61 ± 0.26
E-149	0.014	7.86 ± 0.16	0.551	6.26 ± 0.23	0.035	7.46 ± 0.29	0.708	6.15 ± 0.52
E-150	0.007	8.15 ± 0.04	0.346	6.46 ± 0.22	0.110	6.96 ± 0.15	1.437	5.84 ± 0.29
E-151	0.043	7.37 ± 0.18	0.951	6.02 ± 0.14	0.108	6.97 ± 0.16	0.703	6.15 ± 0.22
E-152	0.201	6.70 ± 0.33	4.137	5.38 ± 0.27	0.695	6.16 ± 0.12	4.870	5.31 ± 0.20
E-153	0.030	7.52 ± 0.16	2.400	5.62 ± 0.20	0.092	7.04 ± 0.05	2.493	5.60 ± 0.18
E-154	0.035	7.46 ± 0.26	3.352	5.47 ± 0.14	0.029	7.54 ± 0.24	0.457	6.34 ± 0.47
E-155	0.006	8.22 ± 0.09	0.667	6.18 ± 0.27	0.105	6.98 ± 0.13	0.858	6.07 ± 0.30
E-156	0.008	8.08 ± 0.11	0.774	6.11 ± 0.32	0.037	7.44 ± 0.13	0.713	6.15 ± 0.10
E-157	0.006	8.20 ± 0.28	0.157	6.80 ± 0.08	0.014	7.86 ± 0.10	0.084	7.07 ± 0.08
E-158	0.005	8.32 ± 0.08	0.244	6.61 ± 0.12	0.039	7.41 ± 0.14	0.248	6.61 ± 0.14
E-159	0.014	7.87 ± 0.15	0.251	6.60 ± 0.20	0.058	7.24 ± 0.08	0.465	6.33 ± 0.12
E-160	0.083	7.08 ± 0.06	1.163	5.93 ± 0.14	0.353	6.45 ± 0.16	3.162	5.50 ± 0.17
E-161	0.007	8.17 ± 0.16	0.461	6.34 ± 0.14	0.073	7.14 ± 0.16	0.519	6.29 ± 0.13
E-162	0.028	7.55 ± 0.22	0.401	6.40 ± 0.17	0.213	6.67 ± 0.14	1.895	5.72 ± 0.11
E-163	0.036	7.45 ± 0.08	0.401	6.40 ± 0.23	0.061	7.22 ± 0.11	1.088	5.96 ± 0.12
F-101	0.651	6.19 ± 0.05	2.604	5.58 ± 0.13	1.404	5.85 ± 0.08	6.972	5.16 ± 0.10
F-102	0.501	6.30 ± 0.09	2.929	5.53 ± 0.14	1.245	5.91 ± 0.09	6.166	5.21 ± 0.15
F-103	0.087	7.06 ± 0.23	1.548	5.81 ± 0.08	0.385	6.41 ± 0.10	2.042	5.69 ± 0.03
F-104	0.947	6.02 ± 0.22	3.687	5.43 ± 0.16	2.380	5.62 ± 0.03	10.292	4.99 ± 0.03
F-105	0.736	6.13 ± 0.12	2.203	5.66 ± 0.10	1.491	5.83 ± 0.06	8.270	5.08 ± 0.10
F-106	1.015	5.99 ± 0.15	2.727	5.56 ± 0.11	3.548	5.45 ± 0.06	9.495	5.02 ± 0.06
F-107	0.593	6.23 ± 0.16	3.420	5.47 ± 0.09	1.328	5.88 ± 0.13	7.079	5.15 ± 0.09
F-108	0.407	6.39 ± 0.24	0.955	6.02 ± 0.07	1.980	5.70 ± 0.16	8.175	5.09 ± 0.10
F-109	0.482	6.32 ± 0.14	1.426	5.85 ± 0.08	0.846	6.07 ± 0.07	4.217	5.38 ± 0.09
F-110	0.215	6.67 ± 0.28	1.751	5.76 ± 0.12	0.753	6.12 ± 0.12	3.737	5.43 ± 0.06
F-111	3.022	5.52 ± 0.10	5.208	5.28 ± 0.06	6.865	5.16 ± 0.13	11.092	4.96 ± 0.02
F-112	0.261	6.58 ± 0.55	1.023	5.99 ± 0.16	0.339	6.47 ± 0.08	3.020	5.52 ± 0.06
F-113	0.351	6.45 ± 0.40	1.725	5.76 ± 0.08	0.617	6.21 ± 0.10	3.255	5.49 ± 0.10
F-114	3.020	5.52 ± 0.13	7.586	5.12 ± 0.00	7.762	5.11 ± 0.12	12.303	4.91 ± 0.07
F-115	0.919	6.04 ± 0.06	4.739	5.32 ± 0.06	2.512	5.60 ± 0.09	10.471	4.98 ± 0.01
F-116	1.493	5.83 ± 0.04	3.316	5.48 ± 0.01	4.467	5.35 ± 0.05	3.861	5.41 ± 0.14
F-117	0.030	7.53 ± 0.22	1.138	5.94 ± 0.22	0.117	6.93 ± 0.28	0.268	6.57 ± 0.08
F-118	0.036	7.45 ± 0.09	1.025	5.99 ± 0.17	0.123	6.91 ± 0.11	0.516	6.29 ± 0.04
F-119	0.724	6.14 ± 0.11	5.382	5.27 ± 0.20	2.291	5.64 ± 0.16	4.814	5.32 ± 0.12
F-120	3.034	5.52 ± 0.06	6.105	5.21 ± 0.04	5.710	5.24 ± 0.20	4.169	5.38 ± 0.19
F-121	1.327	5.88 ± 0.07	4.677	5.33 ± 0.00	3.494	5.46 ± 0.10	1.221	5.91 ± 0.40
F-122	6.607	5.18 ± 0.04	3.020	5.52 ± 0.00	8.643	5.06 ± 0.10	6.556	5.18 ± 0.11
F-123	0.362	6.44 ± 0.18	0.759	6.12 ± 0.00	8.643	5.06 ± 0.07	5.843	5.23 ± 0.15
F-124	0.719	6.14 ± 0.19	0.575	6.24 ± 0.00	10.155	4.99 ± 0.03	5.538	5.26 ± 0.16
F-125	2.485	5.60 ± 0.06	3.802	5.42 ± 0.19	6.261	5.20 ± 0.13	7.025	5.15 ± 0.11
F-126	0.898	6.05 ± 0.06	3.162	5.50 ± 0.09	2.138	5.67 ± 0.23	6.026	5.22 ± 0.11
F-127	0.087	7.06 ± 0.15	1.568	5.80 ± 0.12	0.646	6.19 ± 0.10	0.569	6.25 ± 0.44

Table S2. Activity of 5-NI compounds against *Giardia lamblia*

	G. lamblia 713				*G. lamblia* 106			
	MzS		MzR		MzS		MzR	
Compound	EC50 (µM)	pEC50	EC50 (µM)	pEC50	EC50 (µM)	pEC50	EC50 (µM)	pEC50
F-128	1.387	5.86 ± 0.25	13.067	4.88 ± 0.13	3.311	5.48 ± 0.28	14.706	4.83 ± 0.08
F-129	0.764	6.12 ± 0.17	2.479	5.61 ± 0.08	5.129	5.29 ± 0.14	8.222	5.09 ± 0.14
F-130	1.071	5.97 ± 0.21	8.993	5.05 ± 0.15	5.176	5.29 ± 0.11	13.032	4.89 ± 0.03
F-131	0.192	6.72 ± 0.11	0.701	6.15 ± 0.32	2.541	5.60 ± 0.30	0.808	6.09 ± 0.26
F-132	2.604	5.58 ± 0.09	4.868	5.31 ± 0.10	8.128	5.09 ± 0.06	8.913	5.05 ± 0.10
F-133	0.646	6.19 ± 0.02	1.980	5.70 ± 0.11	2.011	5.70 ± 0.14	6.658	5.18 ± 0.26
F-134	0.202	6.70 ± 0.18	2.165	5.66 ± 0.07	0.378	6.42 ± 0.41	2.163	5.67 ± 0.08
F-135	1.585	5.80 ± 0.12	4.520	5.34 ± 0.13	1.138	5.94 ± 0.17	3.508	5.46 ± 0.22
F-136	0.509	6.29 ± 0.02	2.862	5.54 ± 0.08	1.597	5.80 ± 0.19	2.712	5.57 ± 0.29
F-137	0.627	6.20 ± 0.17	6.905	5.16 ± 0.16	2.213	5.66 ± 0.25	6.645	5.18 ± 0.09
F-138	0.116	6.94 ± 0.20	2.263	5.65 ± 0.16	0.322	6.49 ± 0.31	4.004	5.40 ± 0.18
F-139	0.060	7.22 ± 0.05	1.444	5.84 ± 0.08	0.203	6.69 ± 0.05	0.589	6.23 ± 0.20
F-140	4.480	5.35 ± 0.11	10.862	4.96 ± 0.06	5.433	5.27 ± 0.14	8.318	5.08 ± 0.11
F-141	0.041	7.39 ± 0.15	0.669	6.17 ± 0.03	0.062	7.21 ± 0.19	0.355	6.45 ± 0.16
F-142	1.122	5.95 ± 0.11	4.550	5.34 ± 0.08	2.256	5.65 ± 0.23	4.266	5.37 ± 0.20
F-143	0.101	7.00 ± 0.14	1.259	5.90 ± 0.09	0.347	6.46 ± 0.05	0.529	6.28 ± 0.40
F-144	1.391	5.86 ± 0.05	5.050	5.30 ± 0.13	2.455	5.61 ± 0.18	2.154	5.67 ± 0.41
F-145	0.825	6.08 ± 0.11	3.978	5.40 ± 0.10	2.906	5.54 ± 0.18	2.380	5.62 ± 0.48
F-146	0.020	7.70 ± 0.09	0.215	6.67 ± 0.20	0.071	7.15 ± 0.34	0.316	6.50 ± 0.17
F-147	0.188	6.73 ± 0.43	1.599	5.80 ± 0.28	4.097	5.39 ± 0.14	6.310	5.20 ± 0.27
F-148	0.022	7.65 ± 0.05	0.576	6.24 ± 0.15	0.100	7.00 ± 0.34	0.713	6.15 ± 0.14
F-149	0.020	7.70 ± 0.05	0.621	6.21 ± 0.15	0.084	7.08 ± 0.26	0.440	6.36 ± 0.04
F-150	0.091	7.04 ± 0.08	1.422	5.85 ± 0.12	0.398	6.40 ± 0.10	3.441	5.46 ± 0.08
F-151	0.381	6.42 ± 0.11	3.476	5.46 ± 0.09	1.157	5.94 ± 0.09	5.329	5.27 ± 0.12
F-152	0.497	6.30 ± 0.13	3.342	5.48 ± 0.21	1.468	5.83 ± 0.29	1.080	5.97 ± 0.27
F-153	0.031	7.51 ± 0.13	0.732	6.14 ± 0.19	0.302	6.52 ± 0.05	1.491	5.83 ± 0.09
F-154	0.057	7.25 ± 0.13	0.913	6.04 ± 0.18	0.174	6.76 ± 0.51	0.651	6.19 ± 0.55
F-155	0.054	7.26 ± 0.14	1.145	5.94 ± 0.08	0.081	7.09 ± 0.11	0.636	6.20 ± 0.05
F-156	0.019	7.73 ± 0.13	0.327	6.49 ± 0.15	0.051	7.29 ± 0.20	0.411	6.39 ± 0.02
F-157	0.040	7.40 ± 0.14	1.425	5.85 ± 0.12	0.060	7.22 ± 0.08	0.759	6.12 ± 0.16
F-158	0.091	7.04 ± 0.06	1.080	5.97 ± 0.02	0.319	6.50 ± 0.08	0.324	6.49 ± 0.40
F-159	1.991	5.70 ± 0.02	4.560	5.34 ± 0.08	4.137	5.38 ± 0.19	5.129	5.29 ± 0.18
F-160	2.491	5.60 ± 0.06	8.676	5.06 ± 0.18	3.715	5.43 ± 0.22	3.890	5.41 ± 0.22
F-161	0.293	6.53 ± 0.09	5.667	5.25 ± 0.28	0.948	6.02 ± 0.03	6.131	5.21 ± 0.13
F-162	1.157	5.94 ± 0.03	6.617	5.18 ± 0.11	3.388	5.47 ± 0.18	10.839	4.97 ± 0.02
F-163	0.094	7.03 ± 0.23	1.387	5.86 ± 0.18	0.178	6.75 ± 0.15	1.148	5.94 ± 0.04

Activity against two Mz-sensitive (MzS) isolates of *G. lamblia* , 713 and 106, and their syngeneic Mz-resistant (MzR) derivative lines, was determined as EC50 (in µM; geometric mean, n=3-6 experiments), the compound concentration that inhibits parasite growth by 50%, and is also shown as negative log10 value of the EC50 (pEC50; mean ± SE, n=3-6 experiments).

Table S3. Activity of 5-NI compounds against *Trichomonas vaginalis*

	MzS				MzR			
	T. vaginalis G3		*T. vaginalis* F1623		*T. vaginalis* B7268		*T. vaginalis* LA1	
Compound	EC50 (μM)	pEC50	EC50 (μM)	pEC50	EC50 (μM)	pEC50	EC50 (μM)	pEC50
Mz	0.759	6.12 ± 0.02	0.468	6.33 ± 0.01	5.623	5.25 ± 0.02	3.631	5.44 ± 0.02
A-101	0.977	6.01 ± 0.15	0.846	6.07 ± 0.13	4.606	5.34 ± 0.00	4.493	5.35 ± 0.14
A-102	1.479	5.83 ± 0.00	1.122	5.95 ± 0.12	4.074	5.39 ± 0.15	3.981	5.40 ± 0.29
A-103	0.461	6.34 ± 0.46	0.065	7.19 ± 0.21	2.022	5.69 ± 0.07	2.390	5.62 ± 0.18
A-104	2.280	5.64 ± 0.31	1.090	5.96 ± 0.26	13.335	4.88 ± 0.18	2.645	5.58 ± 0.45
A-105	1.556	5.81 ± 0.17	1.266	5.90 ± 0.08	3.020	5.52 ± 0.30	1.466	5.83 ± 0.26
A-106	2.469	5.61 ± 0.21	3.073	5.51 ± 0.13	6.506	5.19 ± 0.20	3.831	5.42 ± 0.39
A-107	1.370	5.86 ± 0.27	2.615	5.58 ± 0.09	2.312	5.64 ± 0.34	10.839	4.97 ± 0.27
A-108	2.723	5.57 ± 0.27	1.303	5.89 ± 0.16	3.114	5.51 ± 0.47	2.371	5.63 ± 0.35
A-109	2.934	5.53 ± 0.22	1.576	5.80 ± 0.08	4.105	5.39 ± 0.34	5.495	5.26 ± 0.56
A-110	1.995	5.70 ± 0.27	1.365	5.87 ± 0.18	5.089	5.29 ± 0.19	4.233	5.37 ± 0.39
A-111	0.589	6.23 ± 0.56	1.421	5.85 ± 0.11	1.337	5.87 ± 0.25	7.762	5.11 ± 0.41
A-112	0.729	6.14 ± 0.19	1.059	5.98 ± 0.11	1.078	5.97 ± 0.39	0.759	6.12 ± 0.40
A-113	0.490	6.31 ± 0.09	0.546	6.26 ± 0.12	1.928	5.72 ± 0.10	2.884	5.54 ± 0.12
A-114	9.333	5.03 ± 0.02	4.786	5.32 ± 0.33	10.471	4.98 ± 0.02	11.749	4.93 ± 0.23
A-115	10.715	4.97 ± 0.00	5.721	5.24 ± 0.11	3.548	5.45 ± 0.25	12.882	4.89 ± 0.19
A-116	0.788	6.10 ± 0.28	1.245	5.91 ± 0.32	2.723	5.57 ± 0.23	12.735	4.90 ± 0.20
A-117	0.205	6.69 ± 0.20	0.045	7.35 ± 0.27	0.494	6.31 ± 0.19	0.682	6.17 ± 0.18
A-118	0.141	6.85 ± 0.17	0.414	6.38 ± 0.38	1.017	5.99 ± 0.19	2.469	5.61 ± 0.34
A-119	0.746	6.13 ± 0.36	0.638	6.20 ± 0.17	3.217	5.49 ± 0.11	1.905	5.72 ± 0.43
A-120	3.181	5.50 ± 0.24	3.508	5.46 ± 0.19	6.346	5.20 ± 0.18	4.898	5.31 ± 0.00
A-121	0.994	6.00 ± 0.17	1.349	5.87 ± 0.10	1.705	5.77 ± 0.16	2.712	5.57 ± 0.25
A-122	2.331	5.63 ± 0.25	0.716	6.15 ± 0.43	3.758	5.43 ± 0.26	5.129	5.29 ± 0.00
A-123	2.265	5.65 ± 0.26	2.661	5.58 ± 0.13	3.913	5.41 ± 0.21	1.259	5.90 ± 0.22
A-124	3.408	5.47 ± 0.18	3.758	5.43 ± 0.13	3.003	5.52 ± 0.41	0.302	6.52 ± 0.49
A-125	10.965	4.96 ± 0.00	5.580	5.25 ± 0.05	>20	<4.70	>20	<4.70
A-126	1.349	5.87 ± 0.57	1.730	5.76 ± 0.09	2.145	5.67 ± 0.19	4.713	5.33 ± 0.49
A-127	0.320	6.50 ± 0.17	0.211	6.68 ± 0.17	1.075	5.97 ± 0.10	3.090	5.51 ± 0.15
A-128	5.453	5.26 ± 0.33	0.331	6.48 ± 0.18	1.751	5.76 ± 0.27	5.991	5.22 ± 0.31
A-129	0.153	6.82 ± 0.41	0.406	6.39 ± 0.23	1.802	5.74 ± 0.08	2.831	5.55 ± 0.30
A-130	0.279	6.55 ± 0.31	0.130	6.89 ± 0.25	1.113	5.95 ± 0.09	0.885	6.05 ± 0.32
A-131	0.324	6.49 ± 0.19	0.283	6.55 ± 0.14	0.851	6.07 ± 0.10	1.142	5.94 ± 0.16
A-132	10.471	4.98 ± 0.01	5.339	5.27 ± 0.28	>20	<4.70	>20	<4.70
A-133	0.949	6.02 ± 0.18	0.409	6.39 ± 0.12	1.714	5.77 ± 0.07	1.437	5.84 ± 0.27
A-134	0.128	6.89 ± 0.28	0.335	6.48 ± 0.09	1.118	5.95 ± 0.10	1.429	5.85 ± 0.26
A-135	0.193	6.72 ± 0.30	0.562	6.25 ± 0.16	0.794	6.10 ± 0.10	1.496	5.83 ± 0.11
A-136	2.385	5.62 ± 0.16	0.573	6.24 ± 0.17	3.337	5.48 ± 0.10	>20	<4.70
A-137	0.412	6.39 ± 0.16	2.109	5.68 ± 0.30	2.704	5.57 ± 0.10	>20	<4.70
A-138	0.333	6.48 ± 0.15	0.309	6.51 ± 0.09	1.318	5.88 ± 0.08	0.525	6.28 ± 0.46
A-139	0.150	6.83 ± 0.22	0.086	7.07 ± 0.07	0.955	6.02 ± 0.11	0.763	6.12 ± 0.15
A-140	0.282	6.55 ± 0.29	0.357	6.45 ± 0.20	1.468	5.83 ± 0.05	1.738	5.76 ± 0.42
A-141	0.482	6.32 ± 0.50	0.165	6.78 ± 0.24	1.101	5.96 ± 0.19	1.845	5.73 ± 0.26
A-142	10.233	4.99 ± 0.00	2.831	5.55 ± 0.30	6.457	5.19 ± 0.30	>20	<4.70
A-143	0.569	6.25 ± 0.31	1.328	5.88 ± 0.22	5.089	5.29 ± 0.12	3.363	5.47 ± 0.03
A-144	4.467	5.35 ± 0.37	3.388	5.47 ± 0.10	10.965	4.96 ± 0.00	>20	<4.70
A-145	2.109	5.68 ± 0.19	3.090	5.51 ± 0.20	8.610	5.07 ± 0.17	2.222	5.65 ± 0.32
A-146	1.549	5.81 ± 0.33	3.494	5.46 ± 0.14	15.607	4.81 ± 0.11	12.784	4.89 ± 0.10

Table S3. Activity of 5-NI compounds against *Trichomonas vaginalis*

	MzS				MzR			
	T. vaginalis G3		*T. vaginalis* F1623		*T. vaginalis* B7268		*T. vaginalis* LA1	
Compound	EC50 (μM)	pEC50	EC50 (μM)	pEC50	EC50 (μM)	pEC50	EC50 (μM)	pEC50
A-147	0.608	6.22 ± 0.38	4.111	5.39 ± 0.11	2.168	5.66 ± 0.44	1.629	5.79 ± 0.37
A-148	0.175	6.76 ± 0.17	0.241	6.62 ± 0.17	0.360	6.44 ± 0.27	1.540	5.81 ± 0.17
A-149	0.532	6.27 ± 0.17	1.297	5.89 ± 0.15	2.158	5.67 ± 0.33	1.562	5.81 ± 0.18
A-150	0.902	6.05 ± 0.36	4.704	5.33 ± 0.11	1.961	5.71 ± 0.76	4.677	5.33 ± 0.29
A-151	1.189	5.93 ± 0.36	7.898	5.10 ± 0.05	2.906	5.54 ± 0.35	5.248	5.28 ± 0.13
A-152	0.955	6.02 ± 0.16	2.447	5.61 ± 0.17	2.427	5.62 ± 0.43	2.901	5.54 ± 0.13
A-153	10.715	4.97 ± 0.00	4.074	5.39 ± 0.13	0.782	6.11 ± 0.51	4.105	5.39 ± 0.18
A-154	0.424	6.37 ± 0.25	1.613	5.79 ± 0.10	3.181	5.50 ± 0.20	6.972	5.16 ± 0.28
A-155	0.101	7.00 ± 0.42	0.665	6.18 ± 0.05	1.830	5.74 ± 0.24	0.649	6.19 ± 0.44
A-156	0.832	6.08 ± 0.00	0.754	6.12 ± 0.15	0.776	6.11 ± 0.35	0.875	6.06 ± 0.18
A-157	1.259	5.90 ± 0.24	1.462	5.84 ± 0.11	1.274	5.90 ± 0.51	2.089	5.68 ± 0.19
A-158	0.387	6.41 ± 0.33	0.468	6.33 ± 0.16	0.936	6.03 ± 0.23	0.695	6.16 ± 0.16
A-159	2.026	5.69 ± 0.47	3.673	5.44 ± 0.11	7.762	5.11 ± 0.41	4.217	5.38 ± 0.24
A-160	2.138	5.67 ± 0.40	2.851	5.55 ± 0.26	3.528	5.45 ± 0.31	5.129	5.29 ± 0.30
A-161	2.630	5.58 ± 0.18	1.660	5.78 ± 0.06	1.023	5.99 ± 0.65	4.233	5.37 ± 0.12
A-162	2.034	5.69 ± 0.21	1.730	5.76 ± 0.14	2.556	5.59 ± 0.15	3.311	5.48 ± 0.22
A-163	0.358	6.45 ± 0.11	0.399	6.40 ± 0.15	1.748	5.76 ± 0.09	1.479	5.83 ± 0.10
B-101	0.598	6.22 ± 0.34	0.635	6.20 ± 0.11	0.423	6.37 ± 0.71	1.109	5.96 ± 0.45
B-102	1.349	5.87 ± 0.43	1.090	5.96 ± 0.13	0.626	6.20 ± 0.27	4.786	5.32 ± 0.12
B-103	0.169	6.77 ± 0.17	0.167	6.78 ± 0.21	0.610	6.22 ± 0.15	0.813	6.09 ± 0.17
B-104	1.421	5.85 ± 0.52	5.710	5.24 ± 0.03	8.446	5.07 ± 0.19	3.090	5.51 ± 0.43
B-105	2.222	5.65 ± 0.42	4.519	5.35 ± 0.05	1.057	5.98 ± 0.44	8.810	5.06 ± 0.36
B-106	2.917	5.54 ± 0.18	7.989	5.10 ± 0.07	2.818	5.55 ± 0.36	14.289	4.85 ± 0.14
B-107	1.096	5.96 ± 0.34	2.226	5.65 ± 0.05	2.606	5.58 ± 0.18	2.385	5.62 ± 0.23
B-108	3.266	5.49 ± 0.24	4.966	5.30 ± 0.06	1.895	5.72 ± 0.47	6.166	5.21 ± 0.30
B-109	4.169	5.38 ± 0.32	5.445	5.26 ± 0.08	4.145	5.38 ± 0.35	14.454	4.84 ± 0.14
B-110	1.665	5.78 ± 0.23	2.421	5.62 ± 0.08	1.306	5.88 ± 0.27	3.090	5.51 ± 0.31
B-111	1.164	5.93 ± 0.23	1.052	5.98 ± 0.15	1.131	5.95 ± 0.21	2.585	5.59 ± 0.25
B-112	6.506	5.19 ± 0.18	5.788	5.24 ± 0.06	4.571	5.34 ± 0.25	4.983	5.30 ± 0.35
B-113	0.464	6.33 ± 0.21	0.419	6.38 ± 0.17	3.750	5.43 ± 0.20	1.057	5.98 ± 0.25
B-114	6.998	5.16 ± 0.28	3.780	5.42 ± 0.07	5.370	5.27 ± 0.15	1.603	5.80 ± 0.07
B-115	5.188	5.29 ± 0.16	3.737	5.43 ± 0.07	2.630	5.58 ± 0.45	3.589	5.45 ± 0.36
B-116	2.304	5.64 ± 0.40	3.350	5.48 ± 0.13	5.922	5.23 ± 0.23	1.905	5.72 ± 0.55
B-117	1.631	5.79 ± 0.23	0.439	6.36 ± 0.15	2.906	5.54 ± 0.14	0.248	6.61 ± 0.46
B-118	0.396	6.40 ± 0.38	0.143	6.84 ± 0.26	0.324	6.49 ± 0.53	1.496	5.83 ± 0.47
B-119	2.497	5.60 ± 0.46	1.288	5.89 ± 0.40	2.278	5.64 ± 0.41	11.350	4.95 ± 0.24
B-120	1.708	5.77 ± 0.32	4.467	5.35 ± 0.12	2.512	5.60 ± 0.16	2.818	5.55 ± 0.30
B-121	1.471	5.83 ± 0.28	2.432	5.61 ± 0.20	1.995	5.70 ± 0.14	0.631	6.20 ± 0.41
B-122	4.571	5.34 ± 0.26	8.318	5.08 ± 0.05	2.109	5.68 ± 0.35	6.683	5.18 ± 0.47
B-123	0.372	6.43 ± 0.34	0.794	6.10 ± 0.09	1.225	5.91 ± 0.13	0.670	6.17 ± 0.22
B-124	3.447	5.46 ± 0.47	2.640	5.58 ± 0.28	6.346	5.20 ± 0.50	2.512	5.60 ± 0.25
B-125	>20	<4.70	6.506	5.19 ± 0.16	9.120	5.04 ± 0.34	>20	<4.70
B-126	3.589	5.45 ± 0.38	3.575	5.45 ± 0.16	2.371	5.63 ± 0.17	1.380	5.86 ± 0.38
B-127	1.413	5.85 ± 0.40	0.114	6.94 ± 0.35	0.769	6.11 ± 0.26	0.622	6.21 ± 0.36
B-128	0.968	6.01 ± 0.30	0.450	6.35 ± 0.15	1.237	5.91 ± 0.15	0.670	6.17 ± 0.27
B-129	0.385	6.41 ± 0.30	0.610	6.22 ± 0.09	2.065	5.69 ± 0.13	1.862	5.73 ± 0.35
B-130	0.509	6.29 ± 0.38	0.506	6.30 ± 0.39	1.851	5.73 ± 0.09	6.607	5.18 ± 0.24

Table S3. Activity of 5-NI compounds against *Trichomonas vaginalis*

	MzS				MzR			
	T. vaginalis G3		*T. vaginalis* F1623		*T. vaginalis* B7268		*T. vaginalis* LA1	
Compound	EC50 (μM)	pEC50	EC50 (μM)	pEC50	EC50 (μM)	pEC50	EC50 (μM)	pEC50
B-131	0.484	6.32 ± 0.18	0.258	6.59 ± 0.12	3.508	5.46 ± 0.45	2.742	5.56 ± 0.27
B-132	0.295	6.53 ± 0.00	8.710	5.06 ± 0.00	6.213	5.21 ± 0.37	3.090	5.51 ± 0.00
B-133	1.126	5.95 ± 0.18	1.033	5.99 ± 0.11	1.472	5.83 ± 0.18	1.738	5.76 ± 0.11
B-134	0.537	6.27 ± 0.35	0.377	6.42 ± 0.16	1.406	5.85 ± 0.28	4.027	5.40 ± 0.21
B-135	0.292	6.53 ± 0.18	0.696	6.16 ± 0.08	1.330	5.88 ± 0.07	2.692	5.57 ± 0.10
B-136	2.278	5.64 ± 0.22	0.650	6.19 ± 0.07	0.666	6.18 ± 0.07	1.514	5.82 ± 0.16
B-137	>20	<4.70	1.445	5.84 ± 0.49	1.531	5.82 ± 0.31	9.016	5.05 ± 0.04
B-138	0.664	6.18 ± 0.19	0.324	6.49 ± 0.13	1.179	5.93 ± 0.18	2.997	5.52 ± 0.07
B-139	0.664	6.18 ± 0.21	0.546	6.26 ± 0.08	0.474	6.32 ± 0.19	0.917	6.04 ± 0.47
B-140	0.663	6.18 ± 0.14	0.325	6.49 ± 0.21	1.072	5.97 ± 0.19	1.654	5.78 ± 0.14
B-141	0.405	6.39 ± 0.20	0.415	6.38 ± 0.33	0.845	6.07 ± 0.33	3.737	5.43 ± 0.16
B-142	12.764	4.89 ± 0.13	4.365	5.36 ± 0.37	19.953	4.70 ± 0.00	13.107	4.88 ± 0.11
B-143	1.190	5.92 ± 0.37	1.828	5.74 ± 0.33	0.933	6.03 ± 0.57	2.906	5.54 ± 0.50
B-144	5.208	5.28 ± 0.58	4.266	5.37 ± 0.22	13.594	4.87 ± 0.17	19.953	4.70 ± 0.00
B-145	10.233	4.99 ± 0.29	0.582	6.24 ± 0.21	2.333	5.63 ± 0.09	4.365	5.36 ± 0.34
B-146	1.462	5.84 ± 0.06	0.920	6.04 ± 0.42	>20	<4.70	5.370	5.27 ± 0.22
B-147	1.105	5.96 ± 0.55	0.518	6.29 ± 0.27	2.600	5.59 ± 0.10	3.715	5.43 ± 0.16
B-148	0.437	6.36 ± 0.33	0.479	6.32 ± 0.33	0.355	6.45 ± 0.21	1.135	5.95 ± 0.33
B-149	0.986	6.01 ± 0.52	1.303	5.89 ± 0.25	4.290	5.37 ± 0.07	5.329	5.27 ± 0.14
B-150	10.471	4.98 ± 0.00	1.076	5.97 ± 0.31	2.531	5.60 ± 0.29	4.519	5.35 ± 0.34
B-151	0.990	6.00 ± 0.29	0.692	6.16 ± 0.12	1.135	5.95 ± 0.36	1.811	5.74 ± 0.23
B-152	0.331	6.48 ± 0.11	0.295	6.53 ± 0.29	12.686	4.90 ± 0.20	1.609	5.79 ± 0.26
B-153	4.074	5.39 ± 0.56	6.310	5.20 ± 0.13	5.453	5.26 ± 0.08	5.934	5.23 ± 0.39
B-154	11.570	4.94 ± 0.13	2.417	5.62 ± 0.50	5.099	5.29 ± 0.14	14.791	4.83 ± 0.13
B-155	0.220	6.66 ± 0.15	0.468	6.33 ± 0.30	0.251	6.60 ± 0.14	0.479	6.32 ± 0.22
B-156	0.432	6.37 ± 0.17	1.514	5.82 ± 0.29	5.649	5.25 ± 0.34	2.265	5.65 ± 0.48
B-157	0.539	6.27 ± 0.22	1.451	5.84 ± 0.13	0.490	6.31 ± 0.35	1.531	5.82 ± 0.09
B-158	0.507	6.30 ± 0.08	0.442	6.36 ± 0.10	0.721	6.14 ± 0.18	0.982	6.01 ± 0.11
B-159	4.201	5.38 ± 0.16	4.111	5.39 ± 0.12	1.334	5.88 ± 0.43	6.531	5.19 ± 0.18
B-160	6.026	5.22 ± 0.52	9.226	5.04 ± 0.25	6.839	5.17 ± 0.10	>20	<4.70
B-161	1.023	5.99 ± 0.09	1.042	5.98 ± 0.11	2.291	5.64 ± 0.22	2.535	5.60 ± 0.08
B-162	3.311	5.48 ± 0.38	4.898	5.31 ± 0.09	>20	<4.70	2.951	5.53 ± 0.00
B-163	0.220	6.66 ± 0.13	0.322	6.49 ± 0.17	3.090	5.51 ± 0.41	0.657	6.18 ± 0.21
C-101	0.263	6.58 ± 0.11	0.363	6.44 ± 0.21	2.247	5.65 ± 0.30	0.671	6.17 ± 0.58
C-102	0.487	6.31 ± 0.26	0.646	6.19 ± 0.13	1.884	5.73 ± 0.17	8.128	5.09 ± 0.11
C-103	0.138	6.86 ± 0.54	0.218	6.66 ± 0.29	0.283	6.55 ± 0.17	0.208	6.68 ± 0.38
C-104	0.804	6.10 ± 0.30	0.933	6.03 ± 0.21	1.326	5.88 ± 0.13	5.370	5.27 ± 0.09
C-105	0.933	6.03 ± 0.55	1.549	5.81 ± 0.23	1.059	5.98 ± 0.34	>20	<4.70
C-106	0.813	6.09 ± 0.26	0.994	6.00 ± 0.22	1.698	5.77 ± 0.32	8.382	5.08 ± 0.19
C-107	1.609	5.79 ± 0.38	0.929	6.03 ± 0.14	1.274	5.90 ± 0.06	1.015	5.99 ± 0.36
C-108	0.881	6.06 ± 0.29	1.300	5.89 ± 0.05	2.934	5.53 ± 0.24	1.502	5.82 ± 0.49
C-109	0.521	6.28 ± 0.38	1.507	5.82 ± 0.16	1.792	5.75 ± 0.31	3.715	5.43 ± 0.45
C-110	0.380	6.42 ± 0.46	0.973	6.01 ± 0.09	3.144	5.50 ± 0.30	1.139	5.94 ± 0.58
C-111	0.178	6.75 ± 0.33	0.277	6.56 ± 0.11	0.937	6.03 ± 0.16	0.700	6.16 ± 0.48
C-112	0.358	6.45 ± 0.24	0.471	6.33 ± 0.10	0.560	6.25 ± 0.27	6.026	5.22 ± 0.31
C-113	0.118	6.93 ± 0.36	0.242	6.62 ± 0.09	0.776	6.11 ± 0.17	1.288	5.89 ± 0.16
C-114	1.122	5.95 ± 0.21	1.209	5.92 ± 0.13	0.335	6.48 ± 0.31	0.782	6.11 ± 0.68

Table S3. Activity of 5-NI compounds against *Trichomonas vaginalis*

	MzS				MzR			
	T. vaginalis G3		*T. vaginalis* F1623		*T. vaginalis* B7268		*T. vaginalis* LA1	
Compound	EC50 (μM)	pEC50	EC50 (μM)	pEC50	EC50 (μM)	pEC50	EC50 (μM)	pEC50
C-115	0.500	6.30 ± 0.29	0.601	6.22 ± 0.23	1.728	5.76 ± 0.12	5.395	5.27 ± 0.13
C-116	1.105	5.96 ± 0.23	0.553	6.26 ± 0.20	2.570	5.59 ± 0.28	2.362	5.63 ± 0.29
C-117	0.257	6.59 ± 0.41	0.688	6.16 ± 0.26	1.660	5.78 ± 0.24	4.074	5.39 ± 0.24
C-118	0.234	6.63 ± 0.43	0.357	6.45 ± 0.27	1.288	5.89 ± 0.13	0.575	6.24 ± 0.30
C-119	0.407	6.39 ± 0.36	0.617	6.21 ± 0.20	0.451	6.35 ± 0.37	0.461	6.34 ± 0.54
C-120	1.841	5.74 ± 0.34	0.972	6.01 ± 0.07	0.173	6.76 ± 0.28	2.541	5.60 ± 0.22
C-121	0.513	6.29 ± 0.34	0.569	6.25 ± 0.05	0.501	6.30 ± 0.26	1.778	5.75 ± 0.19
C-122	1.249	5.90 ± 0.27	0.950	6.02 ± 0.08	1.353	5.87 ± 0.31	4.043	5.39 ± 0.07
C-123	0.646	6.19 ± 0.41	0.525	6.28 ± 0.22	0.659	6.18 ± 0.16	1.549	5.81 ± 0.03
C-124	0.209	6.68 ± 0.17	0.994	6.00 ± 0.12	1.144	5.94 ± 0.25	1.688	5.77 ± 0.44
C-125	2.862	5.54 ± 0.51	1.708	5.77 ± 0.10	2.388	5.62 ± 0.20	6.918	5.16 ± 0.03
C-126	0.234	6.63 ± 0.16	1.035	5.99 ± 0.11	2.985	5.53 ± 0.25	2.113	5.68 ± 0.10
C-127	0.626	6.20 ± 0.28	0.592	6.23 ± 0.35	1.434	5.84 ± 0.32	1.298	5.89 ± 0.34
C-128	0.541	6.27 ± 0.12	1.841	5.74 ± 0.33	1.413	5.85 ± 0.36	3.428	5.47 ± 0.25
C-129	0.054	7.27 ± 0.04	0.827	6.08 ± 0.31	0.676	6.17 ± 0.35	1.055	5.98 ± 0.40
C-130	0.071	7.15 ± 0.24	0.045	7.35 ± 0.19	0.444	6.35 ± 0.16	0.694	6.16 ± 0.27
C-131	0.033	7.48 ± 0.21	0.141	6.85 ± 0.14	0.557	6.25 ± 0.18	0.168	6.78 ± 0.30
C-132	1.109	5.96 ± 0.60	3.187	5.50 ± 0.18	4.823	5.32 ± 0.14	0.808	6.09 ± 0.39
C-133	0.120	6.92 ± 0.29	0.733	6.14 ± 0.21	0.819	6.09 ± 0.17	1.230	5.91 ± 0.19
C-134	0.106	6.98 ± 0.34	0.213	6.67 ± 0.27	0.327	6.49 ± 0.37	1.274	5.90 ± 0.27
C-135	0.060	7.22 ± 0.28	0.158	6.80 ± 0.42	0.438	6.36 ± 0.19	0.150	6.83 ± 0.25
C-136	0.071	7.15 ± 0.47	0.545	6.26 ± 0.11	0.579	6.24 ± 0.15	0.531	6.28 ± 0.38
C-137	0.048	7.32 ± 0.39	0.196	6.71 ± 0.27	0.335	6.48 ± 0.25	0.827	6.08 ± 0.60
C-138	0.162	6.79 ± 0.17	0.220	6.66 ± 0.09	0.532	6.27 ± 0.17	0.401	6.40 ± 0.20
C-139	0.103	6.99 ± 0.16	0.131	6.88 ± 0.10	0.452	6.35 ± 0.08	0.210	6.68 ± 0.22
C-140	0.977	6.01 ± 0.26	0.355	6.45 ± 0.34	1.820	5.74 ± 0.05	3.187	5.50 ± 0.20
C-141	0.261	6.58 ± 0.05	0.160	6.80 ± 0.25	1.023	5.99 ± 0.34	1.189	5.93 ± 0.14
C-142	1.820	5.74 ± 0.18	1.995	5.70 ± 0.13	5.689	5.25 ± 0.13	3.388	5.47 ± 0.20
C-143	0.358	6.45 ± 0.08	0.200	6.70 ± 0.11	1.288	5.89 ± 0.24	0.885	6.05 ± 0.10
C-144	0.797	6.10 ± 0.19	1.514	5.82 ± 0.09	4.732	5.33 ± 0.06	2.317	5.64 ± 0.17
C-145	0.968	6.01 ± 0.34	0.497	6.30 ± 0.21	1.365	5.87 ± 0.23	0.319	6.50 ± 0.35
C-146	4.416	5.36 ± 0.14	2.985	5.53 ± 0.23	5.559	5.26 ± 0.16	1.641	5.79 ± 0.71
C-147	0.572	6.24 ± 0.10	0.485	6.31 ± 0.27	1.834	5.74 ± 0.09	3.715	5.43 ± 0.12
C-148	0.150	6.82 ± 0.11	0.147	6.83 ± 0.15	0.430	6.37 ± 0.20	0.253	6.60 ± 0.34
C-149	0.339	6.47 ± 0.14	0.441	6.36 ± 0.15	1.009	6.00 ± 0.32	0.948	6.02 ± 0.53
C-150	1.939	5.71 ± 0.11	3.126	5.51 ± 0.07	6.607	5.18 ± 0.12	0.955	6.02 ± 0.43
C-151	1.223	5.91 ± 0.17	1.770	5.75 ± 0.10	3.494	5.46 ± 0.08	1.980	5.70 ± 0.23
C-152	0.692	6.16 ± 0.10	1.197	5.92 ± 0.17	3.236	5.49 ± 0.40	5.370	5.27 ± 0.30
C-153	0.498	6.30 ± 0.16	0.597	6.22 ± 0.19	1.029	5.99 ± 0.69	0.505	6.30 ± 0.46
C-154	1.175	5.93 ± 0.23	2.158	5.67 ± 0.10	9.261	5.03 ± 0.17	3.020	5.52 ± 0.30
C-155	0.163	6.79 ± 0.10	0.160	6.80 ± 0.29	1.413	5.85 ± 0.49	0.556	6.26 ± 0.45
C-156	0.287	6.54 ± 0.13	1.047	5.98 ± 0.22	1.862	5.73 ± 0.22	0.804	6.10 ± 0.14
C-157	0.550	6.26 ± 0.09	0.676	6.17 ± 0.13	0.617	6.21 ± 0.42	0.475	6.32 ± 0.33
C-158	0.102	6.99 ± 0.25	0.380	6.42 ± 0.21	2.385	5.62 ± 0.34	0.933	6.03 ± 0.48
C-159	0.891	6.05 ± 0.23	0.839	6.08 ± 0.21	1.920	5.72 ± 0.21	1.718	5.77 ± 0.39
C-160	0.585	6.23 ± 0.16	1.038	5.98 ± 0.15	3.337	5.48 ± 0.07	1.834	5.74 ± 0.44
C-161	0.240	6.62 ± 0.16	0.406	6.39 ± 0.11	1.122	5.95 ± 0.14	0.401	6.40 ± 0.35

Table S3. Activity of 5-NI compounds against *Trichomonas vaginalis*

	MzS				MzR			
	T. vaginalis G3		*T. vaginalis* F1623		*T. vaginalis* B7268		*T. vaginalis* LA1	
Compound	EC50 (μM)	pEC50	EC50 (μM)	pEC50	EC50 (μM)	pEC50	EC50 (μM)	pEC50
C-162	0.470	6.33 ± 0.31	1.308	5.88 ± 0.21	3.133	5.50 ± 0.23	1.738	5.76 ± 0.66
C-163	0.155	6.81 ± 0.25	0.223	6.65 ± 0.20	0.752	6.12 ± 0.25	2.417	5.62 ± 0.35
D-101	6.131	5.21 ± 0.16	1.052	5.98 ± 0.40	>20	<4.70	>20	<4.70
D-102	10.715	4.97 ± 0.16	6.839	5.17 ± 0.07	>20	<4.70	>20	<4.70
D-103	2.261	5.65 ± 0.32	2.371	5.63 ± 0.16	9.190	5.04 ± 0.20	>20	<4.70
D-104	17.701	4.75 ± 0.04	4.613	5.34 ± 0.36	>20	<4.70	>20	<4.70
D-105	>20	<4.70	7.189	5.14 ± 0.10	11.749	4.93 ± 0.23	>20	<4.70
D-106	>20	<4.70	7.126	5.15 ± 0.20	10.312	4.99 ± 0.29	>20	<4.70
D-107	14.791	4.83 ± 0.13	5.623	5.25 ± 0.11	8.981	5.05 ± 0.18	>20	<4.70
D-108	14.344	4.84 ± 0.14	4.677	5.33 ± 0.20	2.985	5.53 ± 0.48	>20	<4.70
D-109	11.482	4.94 ± 0.24	3.108	5.51 ± 0.33	13.259	4.88 ± 0.10	>20	<4.70
D-110	11.482	4.94 ± 0.24	2.526	5.60 ± 0.37	5.433	5.27 ± 0.33	>20	<4.70
D-111	8.175	5.09 ± 0.08	2.061	5.69 ± 0.44	12.092	4.92 ± 0.14	>20	<4.70
D-112	10.902	4.96 ± 0.18	6.346	5.20 ± 0.23	9.441	5.03 ± 0.23	>20	<4.70
D-113	9.698	5.01 ± 0.19	2.158	5.67 ± 0.42	12.882	4.89 ± 0.19	>20	<4.70
D-114	>20	<4.70	6.918	5.16 ± 0.00	15.971	4.80 ± 0.10	>20	<4.70
D-115	>20	<4.70	6.658	5.18 ± 0.06	>20	<4.70	>20	<4.70
D-116	>20	<4.70	2.317	5.64 ± 0.06	10.593	4.98 ± 0.02	>20	<4.70
D-117	10.593	4.98 ± 0.01	4.467	5.35 ± 0.13	>20	<4.70	>20	<4.70
D-118	1.393	5.86 ± 0.38	0.646	6.19 ± 0.23	6.658	5.18 ± 0.20	>20	<4.70
D-119	11.220	4.95 ± 0.00	4.974	5.30 ± 0.06	>20	<4.70	>20	<4.70
D-120	2.138	5.67 ± 0.47	4.898	5.31 ± 0.09	>20	<4.70	>20	<4.70
D-121	5.309	5.28 ± 0.30	4.823	5.32 ± 0.12	>20	<4.70	>20	<4.70
D-122	7.674	5.12 ± 0.14	6.358	5.20 ± 0.09	>20	<4.70	>20	<4.70
D-123	1.193	5.92 ± 0.33	0.933	6.03 ± 0.11	4.074	5.39 ± 0.13	3.487	5.46 ± 0.27
D-124	10.471	4.98 ± 0.00	7.244	5.14 ± 0.16	>20	<4.70	>20	<4.70
D-125	>20	<4.70	10.633	4.97 ± 0.14	>20	<4.70	7.528	5.12 ± 0.42
D-126	0.240	6.62 ± 0.00	6.095	5.22 ± 0.03	8.660	5.06 ± 0.36	>20	<4.70
D-127	4.955	5.31 ± 0.32	2.500	5.60 ± 0.14	1.950	5.71 ± 0.43	13.032	4.89 ± 0.19
D-128	3.908	5.41 ± 0.16	4.768	5.32 ± 0.09	>20	<4.70	6.310	5.20 ± 0.42
D-129	3.715	5.43 ± 0.20	4.137	5.38 ± 0.12	7.528	5.12 ± 0.42	16.218	4.79 ± 0.09
D-130	1.995	5.70 ± 0.69	2.738	5.56 ± 0.30	13.490	4.87 ± 0.17	>20	<4.70
D-131	8.066	5.09 ± 0.26	1.452	5.84 ± 0.15	5.623	5.25 ± 0.22	5.129	5.29 ± 0.59
D-132	7.161	5.15 ± 0.45	3.569	5.45 ± 0.37	>20	<4.70	>20	<4.70
D-133	10.965	4.96 ± 0.00	1.683	5.77 ± 0.43	>20	<4.70	>20	<4.70
D-134	0.861	6.07 ± 0.32	1.038	5.98 ± 0.14	10.471	4.98 ± 0.14	>20	<4.70
D-135	0.575	6.24 ± 0.36	2.249	5.65 ± 0.14	7.943	5.10 ± 0.08	0.720	6.14 ± 0.54
D-136	1.413	5.85 ± 0.48	1.650	5.78 ± 0.13	>20	<4.70	13.183	4.88 ± 0.18
D-137	1.059	5.98 ± 0.20	1.613	5.79 ± 0.44	4.114	5.39 ± 0.17	3.330	5.48 ± 0.42
D-138	3.589	5.45 ± 0.75	2.150	5.67 ± 0.08	10.233	4.99 ± 0.00	>20	<4.70
D-139	6.998	5.16 ± 0.19	1.202	5.92 ± 0.38	>20	<4.70	>20	<4.70
D-140	0.921	6.04 ± 0.41	0.468	6.33 ± 0.33	6.839	5.17 ± 0.18	5.129	5.29 ± 0.59
D-141	5.188	5.29 ± 0.59	0.622	6.21 ± 0.41	7.943	5.10 ± 0.20	>20	<4.70
D-142	>20	<4.70	4.266	5.37 ± 0.36	14.566	4.84 ± 0.14	>20	<4.70
D-143	0.148	6.83 ± 0.08	3.802	5.42 ± 0.09	14.234	4.85 ± 0.15	>20	<4.70
D-144	>20	<4.70	1.950	5.71 ± 0.00	>20	<4.70	>20	<4.70
D-145	0.232	6.64 ± 0.50	3.114	5.51 ± 0.30	14.017	4.85 ± 0.15	>20	<4.70

Table S3. Activity of 5-NI compounds against *Trichomonas vaginalis*

	MzS				MzR			
	T. vaginalis G3		*T. vaginalis* F1623		*T. vaginalis* B7268		*T. vaginalis* LA1	
Compound	EC50 (µM)	pEC50	EC50 (µM)	pEC50	EC50 (µM)	pEC50	EC50 (µM)	pEC50
D-146	>20	<4.70	6.658	5.18 ± 0.34	>20	<4.70	>20	<4.70
D-147	4.519	5.35 ± 0.64	8.710	5.06 ± 0.12	>20	<4.70	>20	<4.70
D-148	10.471	4.98 ± 0.00	6.457	5.19 ± 0.37	>20	<4.70	>20	<4.70
D-149	>20	<4.70	14.289	4.85 ± 0.14	>20	<4.70	>20	<4.70
D-150	13.490	4.87 ± 0.17	14.454	4.84 ± 0.14	>20	<4.70	>20	<4.70
D-151	14.622	4.84 ± 0.14	4.074	5.39 ± 0.69	15.971	4.80 ± 0.10	>20	<4.70
D-152	4.467	5.35 ± 0.00	4.493	5.35 ± 0.32	16.218	4.79 ± 0.09	>20	<4.70
D-153	>20	<4.70	14.017	4.85 ± 0.15	>20	<4.70	>20	<4.70
D-154	>20	<4.70	12.162	4.92 ± 0.14	>20	<4.70	>20	<4.70
D-155	7.674	5.12 ± 0.42	4.036	5.39 ± 0.11	7.762	5.11 ± 0.23	>20	<4.70
D-156	>20	<4.70	6.722	5.17 ± 0.12	7.178	5.14 ± 0.38	>20	<4.70
D-157	2.723	5.57 ± 0.01	2.103	5.68 ± 0.10	7.703	5.11 ± 0.21	>20	<4.70
D-158	0.045	7.35 ± 0.00	1.345	5.87 ± 0.26	>20	<4.70	>20	<4.70
D-159	1.084	5.97 ± 0.06	8.710	5.06 ± 0.25	>20	<4.70	16.469	4.78 ± 0.08
D-160	0.018	7.74 ± 0.00	3.499	5.46 ± 0.43	>20	<4.70	>20	<4.70
D-161	10.233	4.99 ± 0.00	1.770	5.75 ± 0.42	>20	<4.70	>20	<4.70
D-162	>20	<4.70	5.248	5.28 ± 0.14	>20	<4.70	>20	<4.70
D-163	10.715	4.97 ± 0.00	3.373	5.47 ± 0.00	>20	<4.70	>20	<4.70
E-101	0.311	6.51 ± 0.12	0.059	7.23 ± 0.32	0.871	6.06 ± 0.12	0.888	6.05 ± 0.24
E-102	0.349	6.46 ± 0.08	0.251	6.60 ± 0.11	0.839	6.08 ± 0.10	1.622	5.79 ± 0.15
E-103	0.196	6.71 ± 0.38	0.112	6.95 ± 0.43	0.820	6.09 ± 0.24	1.738	5.76 ± 0.50
E-104	2.615	5.58 ± 0.36	0.452	6.35 ± 0.24	1.786	5.75 ± 0.05	14.125	4.85 ± 0.15
E-105	0.550	6.26 ± 0.10	0.450	6.35 ± 0.28	1.669	5.78 ± 0.09	13.490	4.87 ± 0.17
E-106	0.241	6.62 ± 0.48	1.298	5.89 ± 0.27	10.233	4.99 ± 0.00	14.791	4.83 ± 0.13
E-107	0.165	6.78 ± 0.15	0.139	6.86 ± 0.30	0.724	6.14 ± 0.30	10.351	4.99 ± 0.29
E-108	0.295	6.53 ± 0.33	0.804	6.10 ± 0.11	1.746	5.76 ± 0.15	4.732	5.33 ± 0.32
E-109	0.606	6.22 ± 0.36	0.501	6.30 ± 0.50	1.195	5.92 ± 0.26	0.876	6.06 ± 0.55
E-110	0.279	6.56 ± 0.21	0.282	6.55 ± 0.17	1.607	5.79 ± 0.28	6.531	5.19 ± 0.18
E-111	0.955	6.02 ± 0.29	0.400	6.40 ± 0.23	2.455	5.61 ± 0.11	1.525	5.82 ± 0.35
E-112	0.417	6.38 ± 0.25	0.871	6.06 ± 0.02	2.252	5.65 ± 0.11	2.951	5.53 ± 0.22
E-113	0.529	6.28 ± 0.15	0.136	6.87 ± 0.18	0.265	6.58 ± 0.29	0.398	6.40 ± 0.17
E-114	0.952	6.02 ± 0.25	0.884	6.05 ± 0.13	0.933	6.03 ± 0.09	1.873	5.73 ± 0.11
E-115	0.732	6.14 ± 0.29	0.636	6.20 ± 0.17	1.000	6.00 ± 0.10	0.444	6.35 ± 0.34
E-116	0.963	6.02 ± 0.22	0.571	6.24 ± 0.20	1.078	5.97 ± 0.33	7.536	5.12 ± 0.13
E-117	1.031	5.99 ± 0.59	0.851	6.07 ± 0.87	0.700	6.16 ± 0.39	>20	<4.70
E-118	0.770	6.11 ± 0.15	1.023	5.99 ± 0.23	3.404	5.47 ± 0.09	4.713	5.33 ± 0.40
E-119	0.744	6.13 ± 0.09	0.585	6.23 ± 0.12	1.057	5.98 ± 0.27	3.337	5.48 ± 0.27
E-120	0.397	6.40 ± 0.32	0.358	6.45 ± 0.22	0.989	6.01 ± 0.13	3.060	5.51 ± 0.18
E-121	0.479	6.32 ± 0.36	0.905	6.04 ± 0.34	2.884	5.54 ± 0.04	>20	<4.70
E-122	1.493	5.83 ± 0.41	1.609	5.79 ± 0.16	1.928	5.72 ± 0.23	4.624	5.34 ± 0.63
E-123	0.432	6.37 ± 0.12	0.252	6.60 ± 0.29	1.344	5.87 ± 0.19	0.540	6.27 ± 0.16
E-124	3.350	5.48 ± 0.50	2.531	5.60 ± 0.19	0.923	6.04 ± 0.21	0.781	6.11 ± 0.41
E-125	1.585	5.80 ± 0.12	0.832	6.08 ± 0.30	4.169	5.38 ± 0.24	6.761	5.17 ± 0.13
E-126	1.950	5.71 ± 0.12	0.827	6.08 ± 0.26	1.380	5.86 ± 0.34	5.580	5.25 ± 0.23
E-127	0.804	6.10 ± 0.32	2.252	5.65 ± 0.17	10.174	4.99 ± 0.17	8.643	5.06 ± 0.36
E-128	0.507	6.30 ± 0.37	0.213	6.67 ± 0.29	1.109	5.96 ± 0.21	1.450	5.84 ± 0.31
E-129	>20	<4.70	1.047	5.98 ± 0.39	1.318	5.88 ± 0.04	0.972	6.01 ± 0.60

Table S3. Activity of 5-NI compounds against *Trichomonas vaginalis*

	MzS				MzR			
	T. vaginalis G3		*T. vaginalis* F1623		*T. vaginalis* B7268		*T. vaginalis* LA1	
Compound	EC50 (μM)	pEC50	EC50 (μM)	pEC50	EC50 (μM)	pEC50	EC50 (μM)	pEC50
E-130	0.521	6.28 ± 0.21	0.515	6.29 ± 0.11	3.715	5.43 ± 0.01	5.318	5.27 ± 0.23
E-131	0.251	6.60 ± 0.10	0.708	6.15 ± 0.27	4.732	5.33 ± 0.20	4.545	5.34 ± 0.24
E-132	3.388	5.47 ± 0.49	5.517	5.26 ± 0.12	14.125	4.85 ± 0.15	19.679	4.71 ± 0.01
E-133	1.765	5.75 ± 0.12	0.966	6.02 ± 0.22	2.399	5.62 ± 0.37	8.318	5.08 ± 0.09
E-134	0.222	6.65 ± 0.20	0.202	6.70 ± 0.17	2.421	5.62 ± 0.04	1.589	5.80 ± 0.28
E-135	0.196	6.71 ± 0.15	0.155	6.81 ± 0.27	1.683	5.77 ± 0.21	4.188	5.38 ± 0.32
E-136	0.496	6.30 ± 0.09	0.374	6.43 ± 0.33	9.333	5.03 ± 0.33	2.018	5.70 ± 0.25
E-137	1.531	5.82 ± 0.28	0.257	6.59 ± 0.34	1.247	5.90 ± 0.24	3.363	5.47 ± 0.28
E-138	0.213	6.67 ± 0.20	0.121	6.92 ± 0.16	0.679	6.17 ± 0.11	0.962	6.02 ± 0.28
E-139	0.494	6.31 ± 0.12	0.146	6.84 ± 0.14	0.896	6.05 ± 0.19	0.669	6.17 ± 0.27
E-140	0.767	6.12 ± 0.26	0.414	6.38 ± 0.17	1.521	5.82 ± 0.10	2.840	5.55 ± 0.28
E-141	0.433	6.36 ± 0.18	0.277	6.56 ± 0.16	1.105	5.96 ± 0.08	2.466	5.61 ± 0.20
E-142	2.050	5.69 ± 0.39	2.175	5.66 ± 0.23	2.723	5.57 ± 0.18	4.266	5.37 ± 0.13
E-143	0.122	6.91 ± 0.16	0.121	6.92 ± 0.25	0.698	6.16 ± 0.10	0.410	6.39 ± 0.14
E-144	1.318	5.88 ± 0.00	5.495	5.26 ± 0.16	>20	<4.70	>20	<4.70
E-145	3.951	5.40 ± 0.15	2.809	5.55 ± 0.18	>20	<4.70	9.261	5.03 ± 0.26
E-146	0.522	6.28 ± 0.32	1.977	5.70 ± 0.18	3.078	5.51 ± 0.21	10.798	4.97 ± 0.16
E-147	9.120	5.04 ± 0.34	0.846	6.07 ± 0.44	2.309	5.64 ± 0.35	7.025	5.15 ± 0.33
E-148	0.577	6.24 ± 0.13	0.447	6.35 ± 0.18	0.959	6.02 ± 0.15	1.148	5.94 ± 0.34
E-149	0.589	6.23 ± 0.06	0.460	6.34 ± 0.16	2.466	5.61 ± 0.08	0.944	6.03 ± 0.23
E-150	1.728	5.76 ± 0.27	0.747	6.13 ± 0.33	1.076	5.97 ± 0.20	2.089	5.68 ± 0.58
E-151	5.412	5.27 ± 0.44	1.103	5.96 ± 0.26	5.580	5.25 ± 0.14	>20	<4.70
E-152	2.474	5.61 ± 0.32	8.511	5.07 ± 0.24	>20	<4.70	10.471	4.98 ± 0.28
E-153	1.856	5.73 ± 0.13	0.552	6.26 ± 0.32	1.462	5.84 ± 0.27	5.559	5.26 ± 0.20
E-154	0.589	6.23 ± 0.39	0.181	6.74 ± 0.35	1.675	5.78 ± 0.25	1.357	5.87 ± 0.40
E-155	0.300	6.52 ± 0.07	0.490	6.31 ± 0.13	2.344	5.63 ± 0.08	1.972	5.71 ± 0.59
E-156	0.671	6.17 ± 0.31	0.209	6.68 ± 0.08	1.344	5.87 ± 0.26	0.437	6.36 ± 0.16
E-157	0.223	6.65 ± 0.14	0.085	7.07 ± 0.10	1.000	6.00 ± 0.14	0.442	6.35 ± 0.27
E-158	0.226	6.65 ± 0.18	0.093	7.03 ± 0.34	1.318	5.88 ± 0.06	0.858	6.07 ± 0.06
E-159	0.455	6.34 ± 0.28	0.845	6.07 ± 0.27	2.371	5.63 ± 0.17	2.775	5.56 ± 0.18
E-160	1.182	5.93 ± 0.33	2.474	5.61 ± 0.09	11.092	4.96 ± 0.25	3.508	5.46 ± 0.12
E-161	1.096	5.96 ± 0.16	0.383	6.42 ± 0.26	1.237	5.91 ± 0.14	1.376	5.86 ± 0.15
E-162	1.573	5.80 ± 0.24	3.548	5.45 ± 0.20	10.715	4.97 ± 0.00	2.455	5.61 ± 0.00
E-163	0.395	6.40 ± 0.23	0.315	6.50 ± 0.13	0.406	6.39 ± 0.31	2.391	5.62 ± 0.21
F-101	8.710	5.06 ± 0.00	1.472	5.83 ± 0.13	2.344	5.63 ± 0.36	10.116	5.00 ± 0.30
F-102	1.184	5.93 ± 0.43	1.252	5.90 ± 0.09	4.936	5.31 ± 0.15	6.119	5.21 ± 0.29
F-103	0.724	6.14 ± 0.26	0.437	6.36 ± 0.26	0.258	6.59 ± 0.18	0.372	6.43 ± 0.25
F-104	2.512	5.60 ± 0.31	1.370	5.86 ± 0.12	4.169	5.38 ± 0.28	>20	<4.70
F-105	2.835	5.55 ± 0.18	0.878	6.06 ± 0.16	1.834	5.74 ± 0.30	4.624	5.34 ± 0.35
F-106	5.642	5.25 ± 0.15	2.273	5.64 ± 0.06	5.934	5.23 ± 0.34	12.589	4.90 ± 0.20
F-107	0.719	6.14 ± 0.36	1.139	5.94 ± 0.11	4.704	5.33 ± 0.14	8.035	5.10 ± 0.17
F-108	1.514	5.82 ± 0.34	1.905	5.72 ± 0.08	14.289	4.85 ± 0.14	>20	<4.70
F-109	1.941	5.71 ± 0.15	0.898	6.05 ± 0.21	4.390	5.36 ± 0.14	14.289	4.85 ± 0.14
F-110	0.958	6.02 ± 0.23	0.567	6.25 ± 0.20	2.427	5.62 ± 0.17	3.454	5.46 ± 0.18
F-111	5.297	5.28 ± 0.23	3.408	5.47 ± 0.05	3.784	5.42 ± 0.28	1.023	5.99 ± 0.50
F-112	0.644	6.19 ± 0.19	0.232	6.64 ± 0.30	1.386	5.86 ± 0.12	2.312	5.64 ± 0.20
F-113	1.387	5.86 ± 0.28	0.703	6.15 ± 0.27	2.335	5.63 ± 0.09	2.477	5.61 ± 0.19

Table S3. Activity of 5-NI compounds against *Trichomonas vaginalis*

	MzS				MzR			
	T. vaginalis G3		*T. vaginalis* F1623		*T. vaginalis* B7268		*T. vaginalis* LA1	
Compound	EC50 (µM)	pEC50	EC50 (µM)	pEC50	EC50 (µM)	pEC50	EC50 (µM)	pEC50
F-114	0.933	6.03 ± 0.00	2.818	5.55 ± 0.43	5.012	5.30 ± 0.39	19.953	4.70 ± 0.00
F-115	4.043	5.39 ± 0.32	1.561	5.81 ± 0.25	3.032	5.52 ± 0.18	3.373	5.47 ± 0.32
F-116	5.265	5.28 ± 0.20	1.402	5.85 ± 0.28	9.550	5.02 ± 0.05	15.252	4.82 ± 0.12
F-117	1.122	5.95 ± 0.24	0.251	6.60 ± 0.10	0.579	6.24 ± 0.07	0.700	6.16 ± 0.30
F-118	0.741	6.13 ± 0.39	0.427	6.37 ± 0.04	0.507	6.30 ± 0.14	0.340	6.47 ± 0.27
F-119	6.865	5.16 ± 0.13	1.634	5.79 ± 0.14	1.950	5.71 ± 0.33	>20	<4.70
F-120	5.370	5.27 ± 0.25	6.792	5.17 ± 0.09	0.531	6.28 ± 0.47	>20	<4.70
F-121	3.447	5.46 ± 0.17	2.867	5.54 ± 0.07	14.371	4.84 ± 0.08	14.791	4.83 ± 0.13
F-122	0.724	6.14 ± 0.00	6.813	5.17 ± 0.18	>20	<4.70	>20	<4.70
F-123	3.251	5.49 ± 0.21	4.677	5.33 ± 0.04	1.274	5.90 ± 0.30	14.454	4.84 ± 0.14
F-124	0.186	6.73 ± 0.13	6.761	5.17 ± 0.06	>20	<4.70	>20	<4.70
F-125	7.586	5.12 ± 0.00	5.188	5.29 ± 0.16	8.414	5.08 ± 0.38	7.943	5.10 ± 0.40
F-126	2.551	5.59 ± 0.28	1.259	5.90 ± 0.06	1.380	5.86 ± 0.30	4.786	5.32 ± 0.28
F-127	0.741	6.13 ± 0.27	0.928	6.03 ± 0.32	0.856	6.07 ± 0.22	1.023	5.99 ± 0.45
F-128	4.642	5.33 ± 0.50	5.309	5.28 ± 0.17	7.328	5.14 ± 0.44	5.888	5.23 ± 0.53
F-129	1.641	5.79 ± 0.43	6.095	5.22 ± 0.35	1.669	5.78 ± 0.64	4.677	5.33 ± 0.63
F-130	3.528	5.45 ± 0.34	0.837	6.08 ± 0.25	0.580	6.24 ± 0.40	2.929	5.53 ± 0.46
F-131	1.093	5.96 ± 0.17	0.485	6.31 ± 0.17	1.308	5.88 ± 0.14	1.622	5.79 ± 0.23
F-132	4.571	5.34 ± 0.00	2.399	5.62 ± 0.39	>20	<4.70	4.050	5.39 ± 0.43
F-133	1.876	5.73 ± 0.36	1.311	5.88 ± 0.09	1.454	5.84 ± 0.44	7.385	5.13 ± 0.12
F-134	1.738	5.76 ± 0.11	0.600	6.22 ± 0.18	2.531	5.60 ± 0.20	1.437	5.84 ± 0.24
F-135	7.244	5.14 ± 0.14	2.469	5.61 ± 0.11	4.027	5.40 ± 0.32	>20	<4.70
F-136	8.004	5.10 ± 0.10	2.188	5.66 ± 0.10	10.715	4.97 ± 0.01	3.020	5.52 ± 0.44
F-137	0.884	6.05 ± 0.34	2.057	5.69 ± 0.40	7.413	5.13 ± 0.00	13.490	4.87 ± 0.17
F-138	0.928	6.03 ± 0.18	0.631	6.20 ± 0.22	0.917	6.04 ± 0.26	0.188	6.73 ± 0.39
F-139	0.619	6.21 ± 0.41	0.570	6.24 ± 0.25	2.333	5.63 ± 0.13	2.385	5.62 ± 0.36
F-140	3.802	5.42 ± 0.00	4.012	5.40 ± 0.22	6.358	5.20 ± 0.31	>20	<4.70
F-141	0.120	6.92 ± 0.19	0.146	6.84 ± 0.33	0.861	6.07 ± 0.38	0.667	6.18 ± 0.30
F-142	6.358	5.20 ± 0.08	1.950	5.71 ± 0.13	1.000	6.00 ± 0.44	5.866	5.23 ± 0.33
F-143	1.031	5.99 ± 0.37	0.845	6.07 ± 0.26	2.793	5.55 ± 0.36	0.724	6.14 ± 0.53
F-144	4.047	5.39 ± 0.37	2.205	5.66 ± 0.12	>20	<4.70	2.897	5.54 ± 0.53
F-145	5.470	5.26 ± 0.23	3.020	5.52 ± 0.15	>20	<4.70	0.774	6.11 ± 0.43
F-146	0.457	6.34 ± 0.20	0.277	6.56 ± 0.39	0.252	6.60 ± 0.06	1.122	5.95 ± 0.38
F-147	2.089	5.68 ± 0.39	1.208	5.92 ± 0.43	6.879	5.16 ± 0.36	2.512	5.60 ± 0.34
F-148	0.258	6.59 ± 0.20	0.166	6.78 ± 0.18	0.439	6.36 ± 0.16	0.799	6.10 ± 0.17
F-149	0.081	7.09 ± 0.43	0.441	6.36 ± 0.33	0.832	6.08 ± 0.24	0.805	6.09 ± 0.21
F-150	0.372	6.43 ± 0.24	0.240	6.62 ± 0.10	0.525	6.28 ± 0.17	1.851	5.73 ± 0.26
F-151	0.369	6.43 ± 0.57	0.665	6.18 ± 0.25	1.298	5.89 ± 0.27	7.943	5.10 ± 0.24
F-152	2.797	5.55 ± 0.35	2.023	5.69 ± 0.08	19.953	4.70 ± 0.00	2.767	5.56 ± 0.34
F-153	0.631	6.20 ± 0.51	0.058	7.24 ± 0.44	0.337	6.47 ± 0.20	1.281	5.89 ± 0.41
F-154	0.490	6.31 ± 0.37	0.552	6.26 ± 0.32	0.283	6.55 ± 0.32	0.798	6.10 ± 0.39
F-155	0.112	6.95 ± 0.34	1.514	5.82 ± 0.52	0.828	6.08 ± 0.38	1.148	5.94 ± 0.43
F-156	0.136	6.87 ± 0.34	0.110	6.96 ± 0.30	0.578	6.24 ± 0.41	0.562	6.25 ± 0.27
F-157	0.227	6.64 ± 0.19	0.116	6.93 ± 0.20	0.447	6.35 ± 0.34	0.646	6.19 ± 0.23
F-158	1.472	5.83 ± 0.12	0.363	6.44 ± 0.02	3.311	5.48 ± 0.25	1.023	5.99 ± 0.12
F-159	11.858	4.93 ± 0.02	2.388	5.62 ± 0.14	>20	<4.70	4.130	5.38 ± 0.45
F-160	11.307	4.95 ± 0.14	3.548	5.45 ± 0.16	>20	<4.70	6.531	5.19 ± 0.16

Table S3. Activity of 5-NI compounds against *Trichomonas vaginalis*

	MzS				MzR			
	T. vaginalis G3		*T. vaginalis* F1623		*T. vaginalis* B7268		*T. vaginalis* LA1	
Compound	EC50 (µM)	pEC50	EC50 (µM)	pEC50	EC50 (µM)	pEC50	EC50 (µM)	pEC50
F-161	3.192	5.50 ± 0.25	1.679	5.78 ± 0.03	2.007	5.70 ± 0.21	4.416	5.36 ± 0.19
F-162	3.831	5.42 ± 0.23	2.651	5.58 ± 0.02	9.441	5.03 ± 0.03	4.624	5.34 ± 0.28
F-163	0.268	6.57 ± 0.32	0.473	6.33 ± 0.23	0.764	6.12 ± 0.17	7.189	5.14 ± 0.28

Activity against two Mz-sensitive (MzS) and two Mz-resistant (MzR) isolates of *T. vaginalis* was determined as EC50 (in µM; geometric mean, n=3-6 experiments), the compound concentration that inhibits parasite growth by 50%, and is also shown as negative log10 value of the EC50 (pEC50; mean ± SE, n=3-6 experiments).

Table S4. Activity of 5-NI compounds against anaerobic bacteria

	H. pylori SS1		*H. pylori* CS22		*H. pylori* Δ*frxA* Δ*rdxA*		*C. difficile* ATCC9689		*B. fragilis* ATCC25285	
Compound	EC50 (μM)	pEC50	EC50 (μM)	pEC50	EC50 (μM)	pEC50	EC50 (μM)	pEC50	EC50 (μM)	pEC50
Mz	2.00	5.70 ± 0.01	8.91	5.05 ± 0.02	169.82	3.77 ± 0.05	2.09	5.68 ± 0.01	14.10	4.85 ± 0.01
A-101	4.86	5.31 ± 0.08	15.85	4.80 ± 0.09	> 20	< 4.70	7.59	5.12 ± 0.13	> 20	< 4.70
A-102	0.55	6.26 ± 0.11	1.85	5.73 ± 0.31	> 20	< 4.70	4.68	5.33 ± 0.17	> 20	< 4.70
A-103	2.15	5.67 ± 0.14	3.89	5.41 ± 0.28	> 20	< 4.70	3.95	5.40 ± 0.19	> 20	< 4.70
A-104	5.62	5.25 ± 0.05	3.49	5.46 ± 0.23	> 20	< 4.70	11.39	4.94 ± 0.02	> 20	< 4.70
A-105	1.54	5.81 ± 0.15	2.24	5.65 ± 0.19	> 20	< 4.70	7.19	5.14 ± 0.18	> 20	< 4.70
A-106	1.83	5.74 ± 0.12	4.14	5.38 ± 0.09	> 20	< 4.70	7.30	5.14 ± 0.19	> 20	< 4.70
A-107	2.24	5.65 ± 0.04	6.76	5.17 ± 0.16	> 20	< 4.70	6.92	5.16 ± 0.18	> 20	< 4.70
A-108	2.03	5.69 ± 0.16	2.12	5.67 ± 0.36	> 20	< 4.70	7.59	5.12 ± 0.18	> 20	< 4.70
A-109	1.40	5.85 ± 0.18	2.51	5.60 ± 0.23	> 20	< 4.70	11.66	4.93 ± 0.01	> 20	< 4.70
A-110	1.21	5.92 ± 0.20	2.44	5.61 ± 0.30	> 20	< 4.70	11.84	4.93 ± 0.01	> 20	< 4.70
A-111	4.30	5.37 ± 0.20	16.98	4.77 ± 0.10	> 20	< 4.70	4.94	5.31 ± 0.20	> 20	< 4.70
A-112	0.51	6.30 ± 0.17	0.79	6.10 ± 0.14	> 20	< 4.70	7.64	5.12 ± 0.17	> 20	< 4.70
A-113	4.71	5.33 ± 0.21	2.63	5.58 ± 0.20	> 20	< 4.70	4.27	5.37 ± 0.21	> 20	< 4.70
A-114	> 20	< 4.70	17.67	4.75 ± 0.14	> 20	< 4.70	6.31	5.20 ± 0.17	> 20	< 4.70
A-115	> 20	< 4.70	16.38	4.79 ± 0.23	> 20	< 4.70	4.43	5.35 ± 0.20	> 20	< 4.70
A-116	3.69	5.43 ± 0.05	18.44	4.73 ± 0.09	> 20	< 4.70	4.40	5.36 ± 0.19	> 20	< 4.70
A-117	3.14	5.50 ± 0.08	7.36	5.13 ± 0.43	> 20	< 4.70	4.07	5.39 ± 0.23	18.91	4.72 ± 0.02
A-118	4.11	5.39 ± 0.05	5.89	5.23 ± 0.22	> 20	< 4.70	4.54	5.34 ± 0.20	14.91	4.83 ± 0.08
A-119	1.66	5.78 ± 0.18	7.12	5.15 ± 0.19	> 20	< 4.70	6.61	5.18 ± 0.20	> 20	< 4.70
A-120	2.80	5.55 ± 0.11	10.72	4.97 ± 0.43	> 20	< 4.70	9.70	5.01 ± 0.05	> 20	< 4.70
A-121	0.77	6.11 ± 0.25	3.14	5.50 ± 0.29	> 20	< 4.70	4.50	5.35 ± 0.19	> 20	< 4.70
A-122	1.48	5.83 ± 0.16	6.71	5.17 ± 0.16	> 20	< 4.70	10.47	4.98 ± 0.03	> 20	< 4.70
A-123	2.95	5.53 ± 0.09	9.70	5.01 ± 0.15	> 20	< 4.70	2.47	5.61 ± 0.02	> 20	< 4.70
A-124	3.60	5.44 ± 0.14	10.67	4.97 ± 0.43	> 20	< 4.70	11.13	4.95 ± 0.02	> 20	< 4.70
A-125	12.78	4.89 ± 0.05	19.68	4.71 ± 0.01	> 20	< 4.70	12.30	4.91 ± 0.21	> 20	< 4.70
A-126	2.24	5.65 ± 0.22	4.47	5.35 ± 0.14	> 20	< 4.70	11.22	4.95 ± 0.02	> 20	< 4.70
A-127	0.71	6.15 ± 0.15	8.25	5.08 ± 0.25	> 20	< 4.70	2.82	5.55 ± 0.06	> 20	< 4.70
A-128	2.17	5.66 ± 0.20	> 20	< 4.70	> 20	< 4.70	2.67	5.57 ± 0.05	> 20	< 4.70
A-129	2.14	5.67 ± 0.17	> 20	< 4.70	> 20	< 4.70	2.78	5.56 ± 0.35	> 20	< 4.70
A-130	0.85	6.07 ± 0.18	> 20	< 4.70	> 20	< 4.70	1.46	5.84 ± 0.16	> 20	< 4.70
A-131	5.33	5.27 ± 0.20	9.82	5.01 ± 0.37	> 20	< 4.70	2.38	5.62 ± 0.40	> 20	< 4.70
A-132	11.31	4.95 ± 0.04	14.45	4.84 ± 0.04	> 20	< 4.70	5.67	5.25 ± 0.37	> 20	< 4.70
A-133	1.93	5.71 ± 0.23	1.79	5.75 ± 0.09	> 20	< 4.70	5.17	5.29 ± 0.35	> 20	< 4.70
A-134	1.51	5.82 ± 0.11	7.36	5.13 ± 0.03	> 20	< 4.70	2.80	5.55 ± 0.37	> 20	< 4.70
A-135	0.94	6.03 ± 0.11	18.06	4.74 ± 0.01	> 20	< 4.70	0.72	6.14 ± 0.23	8.51	5.07 ± 0.22
A-136	1.85	5.73 ± 0.18	11.57	4.94 ± 0.08	> 20	< 4.70	4.27	5.37 ± 0.23	> 20	< 4.70
A-137	0.89	6.05 ± 0.06	17.78	4.75 ± 0.09	> 20	< 4.70	4.97	5.30 ± 0.19	15.14	4.82 ± 0.11
A-138	0.34	6.47 ± 0.19	2.55	5.59 ± 0.16	> 20	< 4.70	4.27	5.37 ± 0.23	> 20	< 4.70
A-139	0.26	6.58 ± 0.19	1.19	5.92 ± 0.09	> 20	< 4.70	4.54	5.34 ± 0.21	> 20	< 4.70
A-140	0.50	6.30 ± 0.13	3.89	5.41 ± 0.04	> 20	< 4.70	4.27	5.37 ± 0.20	> 20	< 4.70
A-141	0.44	6.35 ± 0.19	7.99	5.10 ± 0.10	> 20	< 4.70	2.65	5.58 ± 0.04	> 20	< 4.70
A-142	0.99	6.00 ± 0.12	8.22	5.09 ± 0.36	> 20	< 4.70	10.80	4.97 ± 0.02	> 20	< 4.70
A-143	0.52	6.28 ± 0.18	2.71	5.57 ± 0.36	> 20	< 4.70	2.78	5.56 ± 0.03	> 20	< 4.70
A-144	3.00	5.52 ± 0.15	19.57	4.71 ± 0.02	> 20	< 4.70	7.13	5.15 ± 0.19	> 20	< 4.70
A-145	9.12	5.04 ± 0.10	13.39	4.87 ± 0.25	> 20	< 4.70	9.05	5.04 ± 0.08	> 20	< 4.70
A-146	7.08	5.15 ± 0.12	8.22	5.09 ± 0.17	> 20	< 4.70	3.98	5.40 ± 0.22	> 20	< 4.70
A-147	1.00	6.00 ± 0.25	4.79	5.32 ± 0.26	> 20	< 4.70	13.39	4.87 ± 0.09	> 20	< 4.70
A-148	0.47	6.33 ± 0.14	1.92	5.72 ± 0.21	> 20	< 4.70	2.93	5.53 ± 0.24	> 20	< 4.70
A-149	0.44	6.35 ± 0.18	2.60	5.59 ± 0.11	> 20	< 4.70	8.07	5.09 ± 0.27	> 20	< 4.70
A-150	2.22	5.65 ± 0.22	9.72	5.01 ± 0.11	> 20	< 4.70	5.67	5.25 ± 0.28	> 20	< 4.70
A-151	6.07	5.22 ± 0.15	6.49	5.19 ± 0.31	> 20	< 4.70	3.98	5.40 ± 0.22	> 20	< 4.70
A-152	11.05	4.96 ± 0.03	12.40	4.91 ± 0.36	> 20	< 4.70	10.63	4.97 ± 0.01	> 20	< 4.70
A-153	2.12	5.67 ± 0.28	2.65	5.58 ± 0.39	> 20	< 4.70	11.05	4.96 ± 0.00	> 20	< 4.70
A-154	0.39	6.41 ± 0.14	2.77	5.56 ± 0.25	> 20	< 4.70	4.30	5.37 ± 0.20	> 20	< 4.70
A-155	0.49	6.31 ± 0.28	2.57	5.59 ± 0.13	> 20	< 4.70	4.23	5.37 ± 0.22	> 20	< 4.70

Table S4. Activity of 5-NI compounds against anaerobic bacteria

	H. pylori SS1		*H. pylori* CS22		*H. pylori* Δ*frxA* Δ*rdxA*		*C. difficile* ATCC9689		*B. fragilis* ATCC25285	
Compound	EC50 (μM)	pEC50	EC50 (μM)	pEC50	EC50 (μM)	pEC50	EC50 (μM)	pEC50	EC50 (μM)	pEC50
A-156	0.55	6.26 ± 0.17	2.78	5.56 ± 0.23	> 20	< 4.70	5.25	5.28 ± 0.17	> 20	< 4.70
A-157	0.67	6.18 ± 0.21	1.05	5.98 ± 0.50	> 20	< 4.70	9.77	5.01 ± 0.03	> 20	< 4.70
A-158	0.32	6.50 ± 0.21	1.08	5.97 ± 0.23	> 20	< 4.70	2.17	5.66 ± 0.05	> 20	< 4.70
A-159	0.96	6.02 ± 0.18	1.89	5.72 ± 0.32	> 20	< 4.70	2.22	5.65 ± 0.02	> 20	< 4.70
A-160	0.87	6.06 ± 0.22	4.23	5.37 ± 0.07	> 20	< 4.70	11.05	4.96 ± 0.00	> 20	< 4.70
A-161	1.61	5.79 ± 0.16	19.50	4.71 ± 0.02	> 20	< 4.70	1.56	5.81 ± 0.11	> 20	< 4.70
A-162	1.21	5.92 ± 0.20	2.69	5.57 ± 0.02	> 20	< 4.70	4.23	5.37 ± 0.20	> 20	< 4.70
A-163	1.15	5.94 ± 0.23	2.41	5.62 ± 0.08	> 20	< 4.70	1.50	5.82 ± 0.17	> 20	< 4.70
B-101	1.65	5.78 ± 0.22	15.25	4.82 ± 0.19	> 20	< 4.70	5.13	5.29 ± 0.28	> 20	< 4.70
B-102	4.30	5.37 ± 0.11	> 20	< 4.70	> 20	< 4.70	5.32	5.27 ± 0.21	> 20	< 4.70
B-103	0.51	6.30 ± 0.22	> 20	< 4.70	> 20	< 4.70	4.14	5.38 ± 0.25	> 20	< 4.70
B-104	2.71	5.57 ± 0.02	16.50	4.78 ± 0.16	> 20	< 4.70	9.23	5.04 ± 0.08	> 20	< 4.70
B-105	3.98	5.40 ± 0.06	17.89	4.75 ± 0.07	> 20	< 4.70	9.94	5.00 ± 0.05	> 20	< 4.70
B-106	4.20	5.38 ± 0.04	19.39	4.71 ± 0.02	> 20	< 4.70	7.76	5.11 ± 0.16	> 20	< 4.70
B-107	3.02	5.52 ± 0.02	17.99	4.75 ± 0.08	> 20	< 4.70	3.35	5.48 ± 0.23	> 20	< 4.70
B-108	7.47	5.13 ± 0.15	19.57	4.71 ± 0.02	> 20	< 4.70	4.20	5.38 ± 0.21	> 20	< 4.70
B-109	8.00	5.10 ± 0.05	> 20	< 4.70	> 20	< 4.70	10.88	4.96 ± 0.03	> 20	< 4.70
B-110	4.37	5.36 ± 0.12	17.05	4.77 ± 0.12	> 20	< 4.70	11.31	4.95 ± 0.02	> 20	< 4.70
B-111	4.01	5.40 ± 0.13	13.57	4.87 ± 0.15	> 20	< 4.70	7.64	5.12 ± 0.19	> 20	< 4.70
B-112	6.66	5.18 ± 0.01	16.88	4.77 ± 0.14	> 20	< 4.70	12.21	4.91 ± 0.05	> 20	< 4.70
B-113	3.11	5.51 ± 0.03	6.24	5.21 ± 0.27	> 20	< 4.70	10.80	4.97 ± 0.01	> 20	< 4.70
B-114	11.05	4.96 ± 0.01	17.62	4.75 ± 0.12	> 20	< 4.70	6.17	5.21 ± 0.18	> 20	< 4.70
B-115	11.22	4.95 ± 0.01	19.77	4.70 ± 0.01	> 20	< 4.70	4.14	5.38 ± 0.23	> 20	< 4.70
B-116	1.27	5.90 ± 0.01	18.09	4.74 ± 0.09	> 20	< 4.70	6.56	5.18 ± 0.22	> 20	< 4.70
B-117	2.33	5.63 ± 0.04	9.62	5.02 ± 0.35	> 20	< 4.70	13.49	4.87 ± 0.09	> 20	< 4.70
B-118	0.68	6.17 ± 0.13	> 20	< 4.70	> 20	< 4.70	16.22	4.79 ± 0.09	> 20	< 4.70
B-119	8.07	5.09 ± 0.11	> 20	< 4.70	> 20	< 4.70	10.88	4.96 ± 0.02	> 20	< 4.70
B-120	2.29	5.64 ± 0.14	11.42	4.94 ± 0.25	> 20	< 4.70	3.63	5.44 ± 0.20	> 20	< 4.70
B-121	4.37	5.36 ± 0.11	16.85	4.77 ± 0.18	> 20	< 4.70	3.74	5.43 ± 0.19	> 20	< 4.70
B-122	1.33	5.88 ± 0.07	7.08	5.15 ± 0.24	> 20	< 4.70	10.39	4.98 ± 0.03	> 20	< 4.70
B-123	0.26	6.58 ± 0.13	1.73	5.76 ± 0.33	> 20	< 4.70	0.78	6.11 ± 0.02	> 20	< 4.70
B-124	0.91	6.04 ± 0.07	5.62	5.25 ± 0.39	> 20	< 4.70	10.55	4.98 ± 0.02	> 20	< 4.70
B-125	5.25	5.28 ± 0.10	16.72	4.78 ± 0.11	> 20	< 4.70	13.08	4.88 ± 0.09	> 20	< 4.70
B-126	2.95	5.53 ± 0.05	15.00	4.82 ± 0.20	> 20	< 4.70	10.23	4.99 ± 0.01	> 20	< 4.70
B-127	0.48	6.32 ± 0.09	1.78	5.75 ± 0.15	> 20	< 4.70	10.00	5.00 ± 0.03	> 20	< 4.70
B-128	0.76	6.12 ± 0.08	> 20	< 4.70	> 20	< 4.70	8.45	5.07 ± 0.06	> 20	< 4.70
B-129	2.43	5.62 ± 0.15	4.47	5.35 ± 0.35	> 20	< 4.70	4.04	5.39 ± 0.17	14.96	4.83 ± 0.13
B-130	0.74	6.13 ± 0.18	16.22	4.79 ± 0.12	> 20	< 4.70	2.04	5.69 ± 0.39	> 20	< 4.70
B-131	0.55	6.26 ± 0.13	19.16	4.72 ± 0.03	> 20	< 4.70	3.04	5.52 ± 0.04	> 20	< 4.70
B-132	6.03	5.22 ± 0.15	6.92	5.16 ± 0.26	> 20	< 4.70	7.82	5.11 ± 0.13	> 20	< 4.70
B-133	2.06	5.69 ± 0.21	11.28	4.95 ± 0.26	> 20	< 4.70	6.81	5.17 ± 0.20	> 20	< 4.70
B-134	1.63	5.79 ± 0.14	11.48	4.94 ± 0.32	> 20	< 4.70	11.57	4.94 ± 0.02	> 20	< 4.70
B-135	0.82	6.09 ± 0.17	1.97	5.71 ± 0.28	> 20	< 4.70	5.05	5.30 ± 0.20	15.67	4.81 ± 0.11
B-136	0.91	6.04 ± 0.05	13.06	4.88 ± 0.27	> 20	< 4.70	1.23	5.91 ± 0.31	> 20	< 4.70
B-137	1.18	5.93 ± 0.13	18.84	4.73 ± 0.05	> 20	< 4.70	4.61	5.34 ± 0.19	> 20	< 4.70
B-138	3.34	5.48 ± 0.07	> 20	< 4.70	> 20	< 4.70	11.31	4.95 ± 0.02	> 20	< 4.70
B-139	1.56	5.81 ± 0.11	10.96	4.96 ± 0.29	> 20	< 4.70	7.03	5.15 ± 0.10	> 20	< 4.70
B-140	6.81	5.17 ± 0.21	> 20	< 4.70	> 20	< 4.70	12.30	4.91 ± 0.03	> 20	< 4.70
B-141	4.01	5.40 ± 0.21	12.40	4.91 ± 0.18	> 20	< 4.70	11.22	4.95 ± 0.00	> 20	< 4.70
B-142	2.80	5.55 ± 0.08	19.23	4.72 ± 0.04	> 20	< 4.70	10.15	4.99 ± 0.04	> 20	< 4.70
B-143	3.02	5.52 ± 0.06	17.48	4.76 ± 0.12	> 20	< 4.70	11.31	4.95 ± 0.02	> 20	< 4.70
B-144	5.93	5.23 ± 0.05	16.72	4.78 ± 0.13	> 20	< 4.70	10.55	4.98 ± 0.01	> 20	< 4.70
B-145	9.77	5.01 ± 0.09	> 20	< 4.70	> 20	< 4.70	14.02	4.85 ± 0.08	> 20	< 4.70
B-146	0.87	6.06 ± 0.11	14.07	4.85 ± 0.37	> 20	< 4.70	16.98	4.77 ± 0.06	> 20	< 4.70
B-147	10.84	4.97 ± 0.05	15.31	4.82 ± 0.20	> 20	< 4.70	17.11	4.77 ± 0.07	> 20	< 4.70
B-148	2.45	5.61 ± 0.26	3.36	5.47 ± 0.70	> 20	< 4.70	15.02	4.82 ± 0.07	> 20	< 4.70

Table S4. Activity of 5-NI compounds against anaerobic bacteria

	H. pylori SS1		*H. pylori* CS22		*H. pylori* Δ*frxA* Δ*rdxA*		*C. difficile* ATCC9689		*B. fragilis* ATCC25285	
Compound	EC50 (μM)	pEC50	EC50 (μM)	pEC50	EC50 (μM)	pEC50	EC50 (μM)	pEC50	EC50 (μM)	pEC50
B-149	8.61	5.07 ± 0.02	13.11	4.88 ± 0.23	> 20	< 4.70	17.25	4.76 ± 0.06	> 20	< 4.70
B-150	10.12	5.00 ± 0.06	> 20	< 4.70	> 20	< 4.70	> 20	< 4.70	> 20	< 4.70
B-151	1.08	5.97 ± 0.00	3.49	5.46 ± 0.42	14.45	4.84 ± 0.12	10.39	4.98 ± 0.04	> 20	< 4.70
B-152	1.93	5.71 ± 0.07	> 20	< 4.70	> 20	< 4.70	6.17	5.21 ± 0.13	> 20	< 4.70
B-153	10.55	4.98 ± 0.03	> 20	< 4.70	> 20	< 4.70	> 20	< 4.70	> 20	< 4.70
B-154	1.93	5.71 ± 0.11	11.61	4.94 ± 0.27	> 20	< 4.70	> 20	< 4.70	> 20	< 4.70
B-155	2.38	5.62 ± 0.32	8.22	5.09 ± 0.27	> 20	< 4.70	8.38	5.08 ± 0.14	> 20	< 4.70
B-156	4.12	5.39 ± 0.44	9.33	5.03 ± 0.16	> 20	< 4.70	11.48	4.94 ± 0.01	> 20	< 4.70
B-157	6.71	5.17 ± 0.17	> 20	< 4.70	> 20	< 4.70	15.49	4.81 ± 0.06	> 20	< 4.70
B-158	1.66	5.78 ± 0.19	7.12	5.15 ± 0.48	> 20	< 4.70	7.70	5.11 ± 0.16	> 20	< 4.70
B-159	2.04	5.69 ± 0.04	> 20	< 4.70	> 20	< 4.70	4.75	5.32 ± 0.19	> 20	< 4.70
B-160	> 20	< 4.70	> 20	< 4.70	> 20	< 4.70	17.11	4.77 ± 0.07	> 20	< 4.70
B-161	3.52	5.45 ± 0.17	18.68	4.73 ± 0.08	> 20	< 4.70	6.71	5.17 ± 0.17	> 20	< 4.70
B-162	1.22	5.91 ± 0.16	15.85	4.80 ± 0.17	> 20	< 4.70	5.37	5.27 ± 0.21	19.50	4.71 ± 0.01
B-163	1.31	5.88 ± 0.20	> 20	< 4.70	> 20	< 4.70	6.97	5.16 ± 0.20	> 20	< 4.70
C-101	0.80	6.10 ± 0.19	19.69	4.71 ± 0.02	> 20	< 4.70	2.40	5.62 ± 0.03	> 20	< 4.70
C-102	2.55	5.59 ± 0.03	> 20	< 4.70	> 20	< 4.70	2.12	5.67 ± 0.04	> 20	< 4.70
C-103	1.78	5.75 ± 0.09	6.07	5.22 ± 0.21	> 20	< 4.70	2.09	5.68 ± 0.06	15.73	4.80 ± 0.09
C-104	1.51	5.82 ± 0.05	6.71	5.17 ± 0.26	> 20	< 4.70	2.44	5.61 ± 0.10	> 20	< 4.70
C-105	1.95	5.71 ± 0.07	> 20	< 4.70	> 20	< 4.70	6.07	5.22 ± 0.19	> 20	< 4.70
C-106	1.72	5.76 ± 0.10	19.31	4.71 ± 0.04	> 20	< 4.70	2.67	5.57 ± 0.02	> 20	< 4.70
C-107	2.53	5.60 ± 0.03	> 20	< 4.70	> 20	< 4.70	1.89	5.72 ± 0.05	> 20	< 4.70
C-108	2.78	5.56 ± 0.01	19.35	4.71 ± 0.02	> 20	< 4.70	1.79	5.75 ± 0.05	> 20	< 4.70
C-109	1.55	5.81 ± 0.07	15.37	4.81 ± 0.10	> 20	< 4.70	1.89	5.72 ± 0.07	> 20	< 4.70
C-110	1.83	5.74 ± 0.01	11.05	4.96 ± 0.16	> 20	< 4.70	2.03	5.69 ± 0.06	> 20	< 4.70
C-111	0.68	6.17 ± 0.08	7.19	5.14 ± 0.18	> 20	< 4.70	0.98	6.01 ± 0.09	> 20	< 4.70
C-112	0.85	6.07 ± 0.02	5.62	5.25 ± 0.30	> 20	< 4.70	2.04	5.69 ± 0.07	> 20	< 4.70
C-113	1.14	5.94 ± 0.05	5.25	5.28 ± 0.28	> 20	< 4.70	2.67	5.57 ± 0.34	16.47	4.78 ± 0.08
C-114	2.19	5.66 ± 0.04	15.85	4.80 ± 0.09	> 20	< 4.70	2.04	5.69 ± 0.08	> 20	< 4.70
C-115	2.22	5.65 ± 0.06	19.50	4.71 ± 0.02	> 20	< 4.70	2.36	5.63 ± 0.17	16.60	4.78 ± 0.08
C-116	1.17	5.93 ± 0.01	> 20	< 4.70	> 20	< 4.70	1.79	5.75 ± 0.10	18.62	4.73 ± 0.03
C-117	2.93	5.53 ± 0.03	> 20	< 4.70	> 20	< 4.70	2.79	5.55 ± 0.14	15.67	4.81 ± 0.11
C-118	0.53	6.27 ± 0.12	10.23	4.99 ± 0.07	> 20	< 4.70	1.37	5.86 ± 0.10	19.20	4.72 ± 0.02
C-119	2.55	5.59 ± 0.05	19.24	4.72 ± 0.04	> 20	< 4.70	4.45	5.35 ± 0.15	> 20	< 4.70
C-120	1.07	5.97 ± 0.13	12.69	4.90 ± 0.08	> 20	< 4.70	1.85	5.73 ± 0.09	> 20	< 4.70
C-121	0.72	6.14 ± 0.09	9.70	5.01 ± 0.14	> 20	< 4.70	1.69	5.77 ± 0.09	> 20	< 4.70
C-122	1.39	5.86 ± 0.06	> 20	< 4.70	> 20	< 4.70	1.77	5.75 ± 0.09	> 20	< 4.70
C-123	0.49	6.31 ± 0.05	4.79	5.32 ± 0.25	> 20	< 4.70	0.71	6.15 ± 0.09	> 20	< 4.70
C-124	0.78	6.11 ± 0.05	10.72	4.97 ± 0.05	> 20	< 4.70	3.89	5.41 ± 0.15	> 20	< 4.70
C-125	1.98	5.70 ± 0.16	12.53	4.90 ± 0.28	> 20	< 4.70	4.02	5.40 ± 0.15	> 20	< 4.70
C-126	1.03	5.99 ± 0.05	> 20	< 4.70	> 20	< 4.70	3.77	5.42 ± 0.23	> 20	< 4.70
C-127	2.31	5.64 ± 0.04	16.16	4.79 ± 0.24	> 20	< 4.70	3.98	5.40 ± 0.25	16.60	4.78 ± 0.08
C-128	2.95	5.53 ± 0.06	> 20	< 4.70	> 20	< 4.70	5.89	5.23 ± 0.21	17.25	4.76 ± 0.06
C-129	1.91	5.72 ± 0.03	> 20	< 4.70	> 20	< 4.70	3.34	5.48 ± 0.14	13.18	4.88 ± 0.18
C-130	0.30	6.52 ± 0.02	3.02	5.52 ± 0.34	> 20	< 4.70	0.84	6.07 ± 0.32	1.25	5.90 ± 0.12
C-131	0.86	6.07 ± 0.09	3.07	5.51 ± 0.31	> 20	< 4.70	0.89	6.05 ± 0.31	6.17	5.21 ± 0.14
C-132	1.37	5.86 ± 0.05	19.80	4.70 ± 0.01	> 20	< 4.70	2.47	5.61 ± 0.03	19.65	4.71 ± 0.01
C-133	1.02	5.99 ± 0.04	3.98	5.40 ± 0.44	> 20	< 4.70	2.12	5.67 ± 0.23	> 20	< 4.70
C-134	1.58	5.80 ± 0.08	7.59	5.12 ± 0.19	> 20	< 4.70	1.71	5.77 ± 0.19	17.65	4.75 ± 0.05
C-135	0.40	6.39 ± 0.42	3.29	5.48 ± 0.37	> 20	< 4.70	0.45	6.34 ± 0.29	5.67	5.25 ± 0.15
C-136	0.81	6.09 ± 0.02	15.73	4.80 ± 0.07	> 20	< 4.70	1.72	5.76 ± 0.20	12.88	4.89 ± 0.14
C-137	1.06	5.98 ± 0.03	9.68	5.01 ± 0.30	> 20	< 4.70	1.03	5.99 ± 0.07	16.72	4.78 ± 0.04
C-138	0.22	6.66 ± 0.24	5.75	5.24 ± 0.17	> 20	< 4.70	2.17	5.66 ± 0.05	> 20	< 4.70
C-139	0.29	6.54 ± 0.12	9.61	5.02 ± 0.13	> 20	< 4.70	2.40	5.62 ± 0.07	> 20	< 4.70
C-140	1.32	5.88 ± 0.14	19.14	4.72 ± 0.04	> 20	< 4.70	1.83	5.74 ± 0.12	> 20	< 4.70
C-141	0.51	6.30 ± 0.13	4.64	5.33 ± 0.28	> 20	< 4.70	2.04	5.69 ± 0.08	> 20	< 4.70

Table S4. Activity of 5-NI compounds against anaerobic bacteria

	H. pylori SS1		*H. pylori* CS22		*H. pylori* Δ*frxA* Δ*rdxA*		*C. difficile* ATCC9689		*B. fragilis* ATCC25285	
Compound	EC50 (μM)	pEC50	EC50 (μM)	pEC50	EC50 (μM)	pEC50	EC50 (μM)	pEC50	EC50 (μM)	pEC50
C-142	2.14	5.67 ± 0.08	12.53	4.90 ± 0.13	> 20	< 4.70	2.59	5.59 ± 0.16	18.62	4.73 ± 0.03
C-143	1.35	5.87 ± 0.04	6.92	5.16 ± 0.13	> 20	< 4.70	1.98	5.70 ± 0.20	> 20	< 4.70
C-144	1.57	5.80 ± 0.00	> 20	< 4.70	> 20	< 4.70	3.16	5.50 ± 0.33	> 20	< 4.70
C-145	2.69	5.57 ± 0.05	18.87	4.72 ± 0.03	> 20	< 4.70	2.33	5.63 ± 0.01	11.84	4.93 ± 0.23
C-146	4.43	5.35 ± 0.06	> 20	< 4.70	> 20	< 4.70	10.88	4.96 ± 0.01	> 20	< 4.70
C-147	2.80	5.55 ± 0.03	7.19	5.14 ± 0.34	> 20	< 4.70	6.21	5.21 ± 0.21	> 20	< 4.70
C-148	1.03	5.99 ± 0.13	3.34	5.48 ± 0.38	> 20	< 4.70	3.07	5.51 ± 0.17	18.62	4.73 ± 0.03
C-149	0.55	6.26 ± 0.08	8.45	5.07 ± 0.11	> 20	< 4.70	4.20	5.38 ± 0.21	> 20	< 4.70
C-150	4.33	5.36 ± 0.08	> 20	< 4.70	> 20	< 4.70	6.61	5.18 ± 0.21	> 20	< 4.70
C-151	1.58	5.80 ± 0.10	10.55	4.98 ± 0.28	> 20	< 4.70	7.30	5.14 ± 0.19	18.20	4.74 ± 0.04
C-152	8.78	5.06 ± 0.04	19.23	4.72 ± 0.04	> 20	< 4.70	2.26	5.65 ± 0.01	> 20	< 4.70
C-153	1.83	5.74 ± 0.11	4.27	5.37 ± 0.14	> 20	< 4.70	3.31	5.48 ± 0.13	> 20	< 4.70
C-154	5.41	5.27 ± 0.06	> 20	< 4.70	> 20	< 4.70	5.75	5.24 ± 0.20	> 20	< 4.70
C-155	1.30	5.89 ± 0.07	3.55	5.45 ± 0.28	> 20	< 4.70	2.24	5.65 ± 0.10	> 20	< 4.70
C-156	2.09	5.68 ± 0.08	18.20	4.74 ± 0.09	> 20	< 4.70	3.92	5.41 ± 0.21	> 20	< 4.70
C-157	1.89	5.72 ± 0.29	8.38	5.08 ± 0.11	> 20	< 4.70	2.55	5.59 ± 0.05	> 20	< 4.70
C-158	0.34	6.47 ± 0.03	7.76	5.11 ± 0.19	> 20	< 4.70	2.38	5.62 ± 0.02	> 20	< 4.70
C-159	0.80	6.10 ± 0.11	15.02	4.82 ± 0.11	> 20	< 4.70	1.95	5.71 ± 0.09	> 20	< 4.70
C-160	1.56	5.81 ± 0.13	15.92	4.80 ± 0.15	> 20	< 4.70	3.63	5.44 ± 0.13	> 20	< 4.70
C-161	0.28	6.55 ± 0.19	12.30	4.91 ± 0.18	> 20	< 4.70	2.33	5.63 ± 0.05	> 20	< 4.70
C-162	0.39	6.41 ± 0.10	12.21	4.91 ± 0.20	> 20	< 4.70	2.29	5.64 ± 0.03	17.11	4.77 ± 0.07
C-163	0.87	6.06 ± 0.15	10.72	4.97 ± 0.14	> 20	< 4.70	1.39	5.86 ± 0.13	> 20	< 4.70
D-101	9.26	5.03 ± 0.02	> 20	< 4.70	> 20	< 4.70	9.55	5.02 ± 0.02	> 20	< 4.70
D-102	14.91	4.83 ± 0.04	> 20	< 4.70	> 20	< 4.70	9.85	5.01 ± 0.01	> 20	< 4.70
D-103	10.47	4.98 ± 0.02	> 20	< 4.70	> 20	< 4.70	9.48	5.02 ± 0.03	> 20	< 4.70
D-104	11.57	4.94 ± 0.01	> 20	< 4.70	> 20	< 4.70	9.92	5.00 ± 0.04	> 20	< 4.70
D-105	9.48	5.02 ± 0.07	> 20	< 4.70	> 20	< 4.70	10.88	4.96 ± 0.09	> 20	< 4.70
D-106	8.91	5.05 ± 0.08	> 20	< 4.70	> 20	< 4.70	9.48	5.02 ± 0.01	> 20	< 4.70
D-107	8.84	5.05 ± 0.08	> 20	< 4.70	> 20	< 4.70	9.40	5.03 ± 0.02	> 20	< 4.70
D-108	10.72	4.97 ± 0.05	> 20	< 4.70	> 20	< 4.70	9.48	5.02 ± 0.02	> 20	< 4.70
D-109	13.59	4.87 ± 0.05	> 20	< 4.70	> 20	< 4.70	9.40	5.03 ± 0.01	> 20	< 4.70
D-110	8.00	5.10 ± 0.03	> 20	< 4.70	> 20	< 4.70	9.40	5.03 ± 0.01	> 20	< 4.70
D-111	11.57	4.94 ± 0.02	> 20	< 4.70	> 20	< 4.70	9.85	5.01 ± 0.02	> 20	< 4.70
D-112	4.82	5.32 ± 0.04	> 20	< 4.70	> 20	< 4.70	5.80	5.24 ± 0.19	> 20	< 4.70
D-113	14.34	4.84 ± 0.07	> 20	< 4.70	> 20	< 4.70	9.33	5.03 ± 0.01	> 20	< 4.70
D-114	10.80	4.97 ± 0.04	> 20	< 4.70	> 20	< 4.70	9.19	5.04 ± 0.02	> 20	< 4.70
D-115	8.98	5.05 ± 0.03	> 20	< 4.70	> 20	< 4.70	9.55	5.02 ± 0.01	> 20	< 4.70
D-116	10.15	4.99 ± 0.04	> 20	< 4.70	> 20	< 4.70	9.33	5.03 ± 0.01	> 20	< 4.70
D-117	19.50	4.71 ± 0.01	> 20	< 4.70	> 20	< 4.70	9.19	5.04 ± 0.03	> 20	< 4.70
D-118	1.29	5.89 ± 0.10	> 20	< 4.70	> 20	< 4.70	7.47	5.13 ± 0.08	> 20	< 4.70
D-119	8.13	5.09 ± 0.08	> 20	< 4.70	> 20	< 4.70	9.55	5.02 ± 0.01	> 20	< 4.70
D-120	10.39	4.98 ± 0.05	> 20	< 4.70	> 20	< 4.70	9.92	5.00 ± 0.02	> 20	< 4.70
D-121	13.91	4.86 ± 0.02	> 20	< 4.70	> 20	< 4.70	9.92	5.00 ± 0.02	> 20	< 4.70
D-122	11.93	4.92 ± 0.03	> 20	< 4.70	> 20	< 4.70	9.92	5.00 ± 0.02	> 20	< 4.70
D-123	1.48	5.83 ± 0.11	> 20	< 4.70	> 20	< 4.70	1.86	5.73 ± 0.26	> 20	< 4.70
D-124	10.72	4.97 ± 0.02	> 20	< 4.70	> 20	< 4.70	10.23	4.99 ± 0.02	> 20	< 4.70
D-125	8.13	5.09 ± 0.04	> 20	< 4.70	> 20	< 4.70	10.63	4.97 ± 0.03	> 20	< 4.70
D-126	5.21	5.28 ± 0.03	> 20	< 4.70	> 20	< 4.70	10.08	5.00 ± 0.03	> 20	< 4.70
D-127	1.58	5.80 ± 0.20	> 20	< 4.70	> 20	< 4.70	10.08	5.00 ± 0.03	> 20	< 4.70
D-128	1.81	5.74 ± 0.14	> 20	< 4.70	> 20	< 4.70	10.63	4.97 ± 0.03	> 20	< 4.70
D-129	4.17	5.38 ± 0.06	> 20	< 4.70	> 20	< 4.70	10.00	5.00 ± 0.02	16.47	4.78 ± 0.08
D-130	2.61	5.58 ± 0.09	> 20	< 4.70	> 20	< 4.70	10.00	5.00 ± 0.03	> 20	< 4.70
D-131	9.12	5.04 ± 0.05	> 20	< 4.70	> 20	< 4.70	8.58	5.07 ± 0.03	> 20	< 4.70
D-132	9.92	5.00 ± 0.03	> 20	< 4.70	> 20	< 4.70	9.40	5.03 ± 0.05	> 20	< 4.70
D-133	5.45	5.26 ± 0.10	> 20	< 4.70	> 20	< 4.70	9.77	5.01 ± 0.05	> 20	< 4.70
D-134	7.53	5.12 ± 0.12	> 20	< 4.70	> 20	< 4.70	9.77	5.01 ± 0.05	> 20	< 4.70

Table S4. Activity of 5-NI compounds against anaerobic bacteria

	H. pylori SS1		*H. pylori* CS22		*H. pylori* Δ*frxA* Δ*rdxA*		*C. difficile* ATCC9689		*B. fragilis* ATCC25285	
Compound	EC50 (μM)	pEC50	EC50 (μM)	pEC50	EC50 (μM)	pEC50	EC50 (μM)	pEC50	EC50 (μM)	pEC50
D-135	7.88	5.10 ± 0.06	> 20	< 4.70	> 20	< 4.70	2.09	5.68 ± 0.05	> 20	< 4.70
D-136	8.19	5.09 ± 0.05	> 20	< 4.70	> 20	< 4.70	9.26	5.03 ± 0.02	> 20	< 4.70
D-137	4.86	5.31 ± 0.16	> 20	< 4.70	> 20	< 4.70	2.29	5.64 ± 0.01	> 20	< 4.70
D-138	7.19	5.14 ± 0.14	> 20	< 4.70	> 20	< 4.70	10.00	5.00 ± 0.03	> 20	< 4.70
D-139	6.36	5.20 ± 0.13	> 20	< 4.70	> 20	< 4.70	9.92	5.00 ± 0.02	> 20	< 4.70
D-140	10.00	5.00 ± 0.10	> 20	< 4.70	> 20	< 4.70	9.77	5.01 ± 0.03	> 20	< 4.70
D-141	9.05	5.04 ± 0.09	> 20	< 4.70	> 20	< 4.70	8.91	5.05 ± 0.04	> 20	< 4.70
D-142	12.02	4.92 ± 0.01	> 20	< 4.70	> 20	< 4.70	10.00	5.00 ± 0.03	> 20	< 4.70
D-143	11.13	4.95 ± 0.03	> 20	< 4.70	> 20	< 4.70	10.31	4.99 ± 0.03	> 20	< 4.70
D-144	11.93	4.92 ± 0.02	19.69	4.71 ± 0.02	> 20	< 4.70	10.55	4.98 ± 0.02	> 20	< 4.70
D-145	6.71	5.17 ± 0.05	18.06	4.74 ± 0.07	> 20	< 4.70	9.55	5.02 ± 0.03	> 20	< 4.70
D-146	12.02	4.92 ± 0.02	> 20	< 4.70	> 20	< 4.70	9.85	5.01 ± 0.03	> 20	< 4.70
D-147	12.88	4.89 ± 0.04	> 20	< 4.70	> 20	< 4.70	8.32	5.08 ± 0.04	> 20	< 4.70
D-148	3.60	5.44 ± 0.12	> 20	< 4.70	> 20	< 4.70	3.49	5.46 ± 0.20	> 20	< 4.70
D-149	10.23	4.99 ± 0.04	16.82	4.77 ± 0.11	> 20	< 4.70	10.15	4.99 ± 0.03	> 20	< 4.70
D-150	6.41	5.19 ± 0.13	> 20	< 4.70	> 20	< 4.70	6.03	5.22 ± 0.20	> 20	< 4.70
D-151	3.83	5.42 ± 0.07	> 20	< 4.70	> 20	< 4.70	10.00	5.00 ± 0.03	> 20	< 4.70
D-152	7.82	5.11 ± 0.10	> 20	< 4.70	> 20	< 4.70	9.70	5.01 ± 0.03	> 20	< 4.70
D-153	10.08	5.00 ± 0.03	> 20	< 4.70	> 20	< 4.70	9.55	5.02 ± 0.03	> 20	< 4.70
D-154	10.47	4.98 ± 0.04	19.61	4.71 ± 0.02	> 20	< 4.70	9.40	5.03 ± 0.03	> 20	< 4.70
D-155	5.80	5.24 ± 0.08	> 20	< 4.70	> 20	< 4.70	9.40	5.03 ± 0.02	> 20	< 4.70
D-156	6.26	5.20 ± 0.24	> 20	< 4.70	> 20	< 4.70	9.40	5.03 ± 0.03	> 20	< 4.70
D-157	2.33	5.63 ± 0.05	> 20	< 4.70	> 20	< 4.70	7.88	5.10 ± 0.06	> 20	< 4.70
D-158	11.57	4.94 ± 0.02	> 20	< 4.70	> 20	< 4.70	8.64	5.06 ± 0.03	> 20	< 4.70
D-159	9.12	5.04 ± 0.07	> 20	< 4.70	> 20	< 4.70	5.33	5.27 ± 0.21	> 20	< 4.70
D-160	11.13	4.95 ± 0.04	> 20	< 4.70	> 20	< 4.70	12.12	4.92 ± 0.11	> 20	< 4.70
D-161	7.13	5.15 ± 0.13	> 20	< 4.70	> 20	< 4.70	11.31	4.95 ± 0.12	> 20	< 4.70
D-162	8.84	5.05 ± 0.04	> 20	< 4.70	> 20	< 4.70	8.45	5.07 ± 0.02	> 20	< 4.70
D-163	2.20	5.66 ± 0.20	> 20	< 4.70	> 20	< 4.70	5.37	5.27 ± 0.22	> 20	< 4.70
E-101	0.91	6.04 ± 0.12	7.70	5.11 ± 0.19	> 20	< 4.70	1.20	5.92 ± 0.09	4.94	5.31 ± 0.15
E-102	0.98	6.01 ± 0.08	1.92	5.72 ± 0.20	> 20	< 4.70	1.58	5.80 ± 0.16	3.14	5.50 ± 0.20
E-103	1.54	5.81 ± 0.15	1.10	5.96 ± 0.21	> 20	< 4.70	2.27	5.64 ± 0.08	8.91	5.05 ± 0.08
E-104	1.41	5.85 ± 0.06	2.53	5.60 ± 0.21	> 20	< 4.70	1.65	5.78 ± 0.18	5.75	5.24 ± 0.11
E-105	0.76	6.12 ± 0.04	0.89	6.05 ± 0.27	> 20	< 4.70	0.93	6.03 ± 0.08	12.98	4.89 ± 0.07
E-106	1.40	5.85 ± 0.09	2.47	5.61 ± 0.18	> 20	< 4.70	1.83	5.74 ± 0.22	15.14	4.82 ± 0.07
E-107	1.32	5.88 ± 0.02	0.67	6.17 ± 0.18	> 20	< 4.70	0.91	6.04 ± 0.08	4.20	5.38 ± 0.10
E-108	3.09	5.51 ± 0.04	1.63	5.79 ± 0.27	> 20	< 4.70	1.54	5.81 ± 0.13	12.49	4.90 ± 0.10
E-109	2.14	5.67 ± 0.05	2.47	5.61 ± 0.24	> 20	< 4.70	1.41	5.85 ± 0.19	13.39	4.87 ± 0.09
E-110	1.05	5.98 ± 0.08	0.62	6.21 ± 0.21	> 20	< 4.70	1.10	5.96 ± 0.09	12.02	4.92 ± 0.12
E-111	2.47	5.61 ± 0.09	7.87	5.10 ± 0.30	> 20	< 4.70	0.62	6.21 ± 0.06	8.32	5.08 ± 0.19
E-112	9.33	5.03 ± 0.33	0.48	6.32 ± 0.21	> 20	< 4.70	0.76	6.12 ± 0.09	7.19	5.14 ± 0.28
E-113	9.40	5.03 ± 0.05	1.53	5.82 ± 0.31	> 20	< 4.70	0.42	6.38 ± 0.14	1.42	5.85 ± 0.03
E-114	12.40	4.91 ± 0.03	13.12	4.88 ± 0.37	> 20	< 4.70	0.65	6.19 ± 0.09	4.33	5.36 ± 0.11
E-115	6.71	5.17 ± 0.03	15.97	4.80 ± 0.17	> 20	< 4.70	0.56	6.25 ± 0.14	6.36	5.20 ± 0.25
E-116	3.92	5.41 ± 0.08	6.52	5.19 ± 0.31	> 20	< 4.70	0.75	6.13 ± 0.01	4.86	5.31 ± 0.10
E-117	> 20	< 4.70	2.15	5.67 ± 0.24	> 20	< 4.70	3.98	5.40 ± 0.20	> 20	< 4.70
E-118	0.80	6.10 ± 0.04	0.65	6.19 ± 0.35	> 20	< 4.70	2.47	5.61 ± 0.25	12.59	4.90 ± 0.15
E-119	1.61	5.79 ± 0.14	0.86	6.06 ± 0.07	> 20	< 4.70	2.33	5.63 ± 0.21	18.91	4.72 ± 0.02
E-120	2.40	5.62 ± 0.07	0.74	6.13 ± 0.12	> 20	< 4.70	0.52	6.28 ± 0.19	2.57	5.59 ± 0.13
E-121	3.74	5.43 ± 0.03	15.14	4.82 ± 0.12	> 20	< 4.70	0.45	6.34 ± 0.15	4.97	5.30 ± 0.13
E-122	2.91	5.54 ± 0.03	2.82	5.55 ± 0.11	> 20	< 4.70	1.33	5.88 ± 0.18	4.54	5.34 ± 0.14
E-123	> 20	< 4.70	1.61	5.79 ± 0.23	> 20	< 4.70	0.76	6.12 ± 0.02	6.17	5.21 ± 0.26
E-124	> 20	< 4.70	3.77	5.42 ± 0.05	> 20	< 4.70	1.95	5.71 ± 0.10	14.79	4.83 ± 0.08
E-125	17.11	4.77 ± 0.07	0.74	6.13 ± 0.02	> 20	< 4.70	1.96	5.71 ± 0.06	5.62	5.25 ± 0.16
E-126	4.82	5.32 ± 0.09	0.86	6.06 ± 0.11	> 20	< 4.70	1.46	5.84 ± 0.20	5.98	5.22 ± 0.18
E-127	2.93	5.53 ± 0.02	4.17	5.38 ± 0.13	> 20	< 4.70	2.44	5.61 ± 0.01	19.65	4.71 ± 0.01

Table S4. Activity of 5-NI compounds against anaerobic bacteria

	H. pylori SS1		*H. pylori* CS22		*H. pylori* Δ*frxA* Δ*rdxA*		*C. difficile* ATCC9689		*B. fragilis* ATCC25285	
Compound	EC50 (μM)	pEC50	EC50 (μM)	pEC50	EC50 (μM)	pEC50	EC50 (μM)	pEC50	EC50 (μM)	pEC50
E-128	0.11	6.94 ± 0.04	1.40	5.85 ± 0.17	> 20	< 4.70	1.04	5.98 ± 0.12	11.75	4.93 ± 0.12
E-129	3.58	5.45 ± 0.02	> 20	< 4.70	> 20	< 4.70	3.63	5.44 ± 0.26	> 20	< 4.70
E-130	1.25	5.90 ± 0.07	2.22	5.65 ± 0.32	> 20	< 4.70	0.75	6.13 ± 0.31	11.22	4.95 ± 0.10
E-131	0.76	6.12 ± 0.11	0.91	6.04 ± 0.17	> 20	< 4.70	5.37	5.27 ± 0.19	12.88	4.89 ± 0.07
E-132	9.62	5.02 ± 0.03	5.84	5.23 ± 0.22	> 20	< 4.70	2.31	5.64 ± 0.03	8.13	5.09 ± 0.12
E-133	3.74	5.43 ± 0.20	0.60	6.22 ± 0.03	> 20	< 4.70	2.40	5.62 ± 0.16	8.71	5.06 ± 0.23
E-134	1.96	5.71 ± 0.11	0.60	6.22 ± 0.34	> 20	< 4.70	0.98	6.01 ± 0.21	9.85	5.01 ± 0.06
E-135	0.41	6.38 ± 0.08	0.52	6.28 ± 0.46	> 20	< 4.70	0.81	6.09 ± 0.20	0.66	6.18 ± 0.37
E-136	4.86	5.31 ± 0.07	2.82	5.55 ± 0.19	> 20	< 4.70	1.48	5.83 ± 0.12	7.94	5.10 ± 0.10
E-137	1.71	5.77 ± 0.11	1.45	5.84 ± 0.24	> 20	< 4.70	0.81	6.09 ± 0.17	11.48	4.94 ± 0.24
E-138	0.46	6.34 ± 0.05	0.24	6.61 ± 0.13	> 20	< 4.70	1.32	5.88 ± 0.25	9.33	5.03 ± 0.20
E-139	0.69	6.16 ± 0.14	0.59	6.23 ± 0.16	> 20	< 4.70	1.53	5.82 ± 0.18	9.66	5.02 ± 0.31
E-140	2.51	5.60 ± 0.10	1.51	5.82 ± 0.29	> 20	< 4.70	1.19	5.92 ± 0.11	> 20	< 4.70
E-141	0.11	6.95 ± 0.07	0.70	6.15 ± 0.24	10.72	4.97 ± 0.05	0.82	6.09 ± 0.31	17.78	4.75 ± 0.05
E-142	2.33	5.63 ± 0.08	1.81	5.74 ± 0.22	> 20	< 4.70	1.51	5.82 ± 0.11	2.51	5.60 ± 0.17
E-143	0.66	6.18 ± 0.19	2.33	5.63 ± 0.47	> 20	< 4.70	0.53	6.27 ± 0.06	2.01	5.70 ± 0.12
E-144	9.85	5.01 ± 0.08	11.86	4.93 ± 0.40	> 20	< 4.70	11.31	4.95 ± 0.03	> 20	< 4.70
E-145	9.19	5.04 ± 0.07	6.12	5.21 ± 0.45	> 20	< 4.70	5.29	5.28 ± 0.16	14.57	4.84 ± 0.14
E-146	4.68	5.33 ± 0.11	0.66	6.18 ± 0.19	> 20	< 4.70	5.54	5.26 ± 0.30	> 20	< 4.70
E-147	1.81	5.74 ± 0.07	0.30	6.52 ± 0.30	> 20	< 4.70	10.80	4.97 ± 0.00	19.35	4.71 ± 0.01
E-148	> 20	< 4.70	0.62	6.21 ± 0.33	> 20	< 4.70	5.33	5.27 ± 0.28	15.97	4.80 ± 0.10
E-149	> 20	< 4.70	0.57	6.25 ± 0.32	> 20	< 4.70	2.24	5.65 ± 0.12	> 20	< 4.70
E-150	0.38	6.42 ± 0.25	0.59	6.23 ± 0.22	> 20	< 4.70	2.73	5.56 ± 0.19	> 20	< 4.70
E-151	1.91	5.72 ± 0.14	2.73	5.56 ± 0.25	> 20	< 4.70	3.19	5.50 ± 0.25	> 20	< 4.70
E-152	> 20	< 4.70	16.34	4.79 ± 0.13	> 20	< 4.70	12.88	4.89 ± 0.10	> 20	< 4.70
E-153	2.20	5.66 ± 0.18	2.61	5.58 ± 0.37	> 20	< 4.70	2.15	5.67 ± 0.10	> 20	< 4.70
E-154	5.58	5.25 ± 0.07	1.35	5.87 ± 0.47	> 20	< 4.70	6.26	5.20 ± 0.21	> 20	< 4.70
E-155	2.07	5.68 ± 0.08	0.37	6.44 ± 0.17	> 20	< 4.70	1.47	5.83 ± 0.28	17.65	4.75 ± 0.05
E-156	0.40	6.40 ± 0.21	0.35	6.46 ± 0.07	> 20	< 4.70	2.12	5.67 ± 0.07	10.88	4.96 ± 0.13
E-157	0.20	6.70 ± 0.10	1.30	5.89 ± 0.19	> 20	< 4.70	1.53	5.82 ± 0.17	> 20	< 4.70
E-158	0.33	6.49 ± 0.01	0.83	6.08 ± 0.33	> 20	< 4.70	1.31	5.88 ± 0.03	1.92	5.72 ± 0.08
E-159	1.76	5.75 ± 0.03	1.82	5.74 ± 0.06	> 20	< 4.70	1.23	5.91 ± 0.11	2.78	5.56 ± 0.03
E-160	2.34	5.63 ± 0.19	2.01	5.70 ± 0.22	> 20	< 4.70	3.55	5.45 ± 0.07	> 20	< 4.70
E-161	1.10	5.96 ± 0.03	0.96	6.02 ± 0.25	> 20	< 4.70	3.92	5.41 ± 0.22	2.78	5.56 ± 0.03
E-162	> 20	< 4.70	2.00	5.70 ± 0.25	> 20	< 4.70	1.12	5.95 ± 0.11	4.33	5.36 ± 0.01
E-163	0.52	6.28 ± 0.11	0.95	6.02 ± 0.09	> 20	< 4.70	1.67	5.78 ± 0.16	14.23	4.85 ± 0.09
F-101	3.52	5.45 ± 0.06	4.82	5.32 ± 0.27	> 20	< 4.70	2.21	5.66 ± 0.21	18.48	4.73 ± 0.02
F-102	2.49	5.60 ± 0.05	2.19	5.66 ± 0.18	> 20	< 4.70	3.24	5.49 ± 0.14	16.34	4.79 ± 0.05
F-103	3.11	5.51 ± 0.13	4.32	5.37 ± 0.30	> 20	< 4.70	1.85	5.73 ± 0.11	10.39	4.98 ± 0.06
F-104	7.59	5.12 ± 0.05	5.37	5.27 ± 0.16	> 20	< 4.70	8.37	5.08 ± 0.10	> 20	< 4.70
F-105	2.53	5.60 ± 0.01	1.83	5.74 ± 0.20	> 20	< 4.70	5.72	5.24 ± 0.25	19.65	4.71 ± 0.01
F-106	4.79	5.32 ± 0.15	6.27	5.20 ± 0.16	> 20	< 4.70	10.41	4.98 ± 0.21	> 20	< 4.70
F-107	2.34	5.63 ± 0.08	2.05	5.69 ± 0.10	> 20	< 4.70	3.41	5.47 ± 0.21	16.47	4.78 ± 0.06
F-108	2.12	5.67 ± 0.18	2.11	5.68 ± 0.10	> 20	< 4.70	7.46	5.13 ± 0.15	19.35	4.71 ± 0.01
F-109	0.87	6.06 ± 0.18	1.81	5.74 ± 0.05	> 20	< 4.70	4.90	5.31 ± 0.12	15.37	4.81 ± 0.06
F-110	1.32	5.88 ± 0.17	1.04	5.98 ± 0.09	> 20	< 4.70	2.71	5.57 ± 0.21	15.73	4.80 ± 0.07
F-111	7.88	5.10 ± 0.11	> 20	< 4.70	> 20	< 4.70	3.63	5.44 ± 0.14	17.78	4.75 ± 0.03
F-112	0.72	6.14 ± 0.20	0.62	6.21 ± 0.02	> 20	< 4.70	3.43	5.47 ± 0.15	11.75	4.93 ± 0.12
F-113	1.89	5.72 ± 0.17	1.62	5.79 ± 0.03	> 20	< 4.70	1.22	5.91 ± 0.18	5.13	5.29 ± 0.11
F-114	7.64	5.12 ± 0.13	15.37	4.81 ± 0.11	> 20	< 4.70	3.98	5.40 ± 0.25	> 20	< 4.70
F-115	4.04	5.39 ± 0.16	6.31	5.20 ± 0.11	> 20	< 4.70	2.65	5.58 ± 0.20	18.62	4.73 ± 0.02
F-116	5.89	5.23 ± 0.08	7.76	5.11 ± 0.12	> 20	< 4.70	1.97	5.71 ± 0.24	> 20	< 4.70
F-117	8.25	5.08 ± 0.08	14.29	4.85 ± 0.25	> 20	< 4.70	1.28	5.89 ± 0.08	13.39	4.87 ± 0.15
F-118	> 20	< 4.70	2.56	5.59 ± 0.33	> 20	< 4.70	1.81	5.74 ± 0.18	3.77	5.42 ± 0.28
F-119	3.80	5.42 ± 0.02	17.99	4.75 ± 0.05	> 20	< 4.70	4.07	5.39 ± 0.21	15.61	4.81 ± 0.05
F-120	8.38	5.08 ± 0.07	5.75	5.24 ± 0.12	> 20	< 4.70	6.20	5.21 ± 0.13	> 20	< 4.70

Table S4. Activity of 5-NI compounds against anaerobic bacteria

	H. pylori SS1		*H. pylori* CS22		*H. pylori* Δ*frxA* Δ*rdxA*		*C. difficile* ATCC9689		*B. fragilis* ATCC25285	
Compound	EC50 (μM)	pEC50	EC50 (μM)	pEC50	EC50 (μM)	pEC50	EC50 (μM)	pEC50	EC50 (μM)	pEC50
F-121	7.47	5.13 ± 0.08	3.77	5.42 ± 0.16	> 20	< 4.70	5.37	5.27 ± 0.16	19.50	4.71 ± 0.01
F-122	10.00	5.00 ± 0.03	7.54	5.12 ± 0.26	> 20	< 4.70	9.07	5.04 ± 0.18	> 20	< 4.70
F-123	1.55	5.81 ± 0.15	5.67	5.25 ± 0.09	> 20	< 4.70	0.94	6.03 ± 0.19	16.60	4.78 ± 0.08
F-124	8.58	5.07 ± 0.11	4.43	5.35 ± 0.38	> 20	< 4.70	9.17	5.04 ± 0.17	> 20	< 4.70
F-125	8.00	5.10 ± 0.07	10.08	5.00 ± 0.36	> 20	< 4.70	12.52	4.90 ± 0.07	> 20	< 4.70
F-126	4.47	5.35 ± 0.09	2.97	5.53 ± 0.16	> 20	< 4.70	5.62	5.25 ± 0.26	19.35	4.71 ± 0.01
F-127	8.45	5.07 ± 0.07	8.41	5.08 ± 0.34	> 20	< 4.70	1.41	5.85 ± 0.13	15.02	4.82 ± 0.07
F-128	12.21	4.91 ± 0.05	14.18	4.85 ± 0.36	> 20	< 4.70	6.87	5.16 ± 0.21	> 20	< 4.70
F-129	2.61	5.58 ± 0.08	6.96	5.16 ± 0.42	> 20	< 4.70	2.11	5.68 ± 0.08	13.80	4.86 ± 0.08
F-130	7.13	5.15 ± 0.05	13.72	4.86 ± 0.32	> 20	< 4.70	3.29	5.48 ± 0.24	9.48	5.02 ± 0.18
F-131	> 20	< 4.70	2.93	5.53 ± 0.36	> 20	< 4.70	0.83	6.08 ± 0.17	3.83	5.42 ± 0.33
F-132	9.85	5.01 ± 0.02	7.76	5.11 ± 0.44	> 20	< 4.70	9.17	5.04 ± 0.19	> 20	< 4.70
F-133	2.65	5.58 ± 0.08	2.12	5.67 ± 0.40	> 20	< 4.70	6.35	5.20 ± 0.25	18.91	4.72 ± 0.02
F-134	3.83	5.42 ± 0.09	8.32	5.08 ± 0.32	> 20	< 4.70	1.25	5.90 ± 0.25	9.19	5.04 ± 0.13
F-135	2.97	5.53 ± 0.04	6.17	5.21 ± 0.51	> 20	< 4.70	3.41	5.47 ± 0.23	1.88	5.73 ± 0.18
F-136	4.11	5.39 ± 0.10	4.57	5.34 ± 0.20	> 20	< 4.70	5.50	5.26 ± 0.17	17.65	4.75 ± 0.05
F-137	2.73	5.56 ± 0.08	5.50	5.26 ± 0.49	> 20	< 4.70	4.17	5.38 ± 0.19	4.75	5.32 ± 0.33
F-138	2.88	5.54 ± 0.07	5.47	5.26 ± 0.34	> 20	< 4.70	1.31	5.88 ± 0.15	4.68	5.33 ± 0.11
F-139	1.32	5.88 ± 0.12	2.67	5.57 ± 0.05	> 20	< 4.70	0.96	6.02 ± 0.20	6.03	5.22 ± 0.06
F-140	16.22	4.79 ± 0.08	4.90	5.31 ± 0.25	> 20	< 4.70	2.04	5.69 ± 0.25	16.09	4.79 ± 0.09
F-141	0.45	6.35 ± 0.08	1.74	5.76 ± 0.10	> 20	< 4.70	0.48	6.32 ± 0.25	1.72	5.76 ± 0.11
F-142	3.07	5.51 ± 0.08	4.94	5.31 ± 0.39	> 20	< 4.70	9.12	5.04 ± 0.23	19.05	4.72 ± 0.02
F-143	3.00	5.52 ± 0.16	6.17	5.21 ± 0.22	> 20	< 4.70	1.35	5.87 ± 0.12	10.96	4.96 ± 0.13
F-144	8.91	5.05 ± 0.05	8.38	5.08 ± 0.17	> 20	< 4.70	13.11	4.88 ± 0.06	> 20	< 4.70
F-145	8.98	5.05 ± 0.06	5.09	5.29 ± 0.23	> 20	< 4.70	6.35	5.20 ± 0.24	3.02	5.52 ± 0.41
F-146	1.62	5.79 ± 0.14	4.01	5.40 ± 0.16	> 20	< 4.70	5.80	5.24 ± 0.22	10.88	4.96 ± 0.13
F-147	4.50	5.35 ± 0.04	5.92	5.23 ± 0.50	> 20	< 4.70	12.59	4.90 ± 0.10	13.39	4.87 ± 0.06
F-148	1.21	5.92 ± 0.04	1.79	5.75 ± 0.17	16.98	4.77 ± 0.89	0.26	6.58 ± 0.40	1.06	5.98 ± 0.09
F-149	0.15	6.82 ± 0.21	5.09	5.29 ± 0.16	> 20	< 4.70	1.15	5.94 ± 0.14	5.33	5.27 ± 0.03
F-150	1.91	5.72 ± 0.13	2.01	5.70 ± 0.23	> 20	< 4.70	1.67	5.78 ± 0.11	7.41	5.13 ± 0.12
F-151	3.36	5.47 ± 0.02	6.81	5.17 ± 0.19	> 20	< 4.70	1.22	5.91 ± 0.04	10.96	4.96 ± 0.11
F-152	10.12	5.00 ± 0.15	12.36	4.91 ± 0.20	> 20	< 4.70	4.54	5.34 ± 0.22	7.88	5.10 ± 0.20
F-153	3.07	5.51 ± 0.04	6.26	5.20 ± 0.39	> 20	< 4.70	0.98	6.01 ± 0.08	15.02	4.82 ± 0.07
F-154	11.31	4.95 ± 0.02	1.00	6.00 ± 0.43	> 20	< 4.70	0.36	6.44 ± 0.31	12.02	4.92 ± 0.09
F-155	4.17	5.38 ± 0.14	4.90	5.31 ± 0.21	> 20	< 4.70	1.10	5.96 ± 0.16	9.05	5.04 ± 0.24
F-156	0.81	6.09 ± 0.07	1.31	5.88 ± 0.19	18.20	4.74 ± 0.04	0.26	6.59 ± 0.15	7.13	5.15 ± 0.05
F-157	2.42	5.62 ± 0.09	0.96	6.02 ± 0.25	18.62	4.73 ± 0.05	0.72	6.15 ± 0.23	1.96	5.71 ± 0.11
F-158	2.55	5.59 ± 0.07	3.49	5.46 ± 0.19	> 20	< 4.70	2.25	5.65 ± 0.19	10.80	4.97 ± 0.14
F-159	11.31	4.95 ± 0.02	5.21	5.28 ± 0.22	> 20	< 4.70	11.35	4.95 ± 0.03	> 20	< 4.70
F-160	6.51	5.19 ± 0.11	17.65	4.75 ± 0.09	> 20	< 4.70	13.72	4.86 ± 0.06	> 20	< 4.70
F-161	1.29	5.89 ± 0.05	1.74	5.76 ± 0.18	> 20	< 4.70	2.63	5.58 ± 0.07	14.34	4.84 ± 0.08
F-162	3.77	5.42 ± 0.08	4.90	5.31 ± 0.11	> 20	< 4.70	10.39	4.98 ± 0.02	> 20	< 4.70
F-163	1.41	5.85 ± 0.10	1.58	5.80 ± 0.15	> 20	< 4.70	1.22	5.92 ± 0.38	4.61	5.34 ± 0.06

Activity against the indicated bacteria was determined as EC50 (in μM; geometric mean, n=3-6 experiments), the compound concentration that inhibits bacterial growth by 50%, and is also shown as negative log10 value of the EC50 (pEC50; mean ± SE, n=3-6 experiments).

Table S5. Cytotoxicity in human cells and therapeutic ratio of 5-NI compounds

	HeLa		MzS *G. lamblia*	Therapeutic ratio
Compound	CC50 (μM)	pCC50	EC50 (μM)	CC50/EC50
Mz	> 50	< 4.30	2.00	> 25
A-101	> 50	< 4.30	1.06	> 47
A-102	> 50	< 4.30	1.79	> 28
A-103	> 50	< 4.30	0.21	> 235
A-104	> 50	< 4.30	3.96	> 13
A-105	> 50	< 4.30	4.64	> 11
A-106	> 50	< 4.30	5.40	> 9
A-107	> 50	< 4.30	2.49	> 20
A-108	> 50	< 4.30	3.66	> 14
A-109	> 50	< 4.30	3.55	> 14
A-110	> 50	< 4.30	3.47	> 14
A-111	> 50	< 4.30	0.95	> 53
A-112	> 50	< 4.30	2.69	> 19
A-113	> 50	< 4.30	0.63	> 79
A-114	> 50	< 4.30	3.87	> 13
A-115	> 50	< 4.30	3.62	> 14
A-116	> 50	< 4.30	0.55	> 91
A-117	> 50	< 4.30	0.08	> 651
A-118	> 50	< 4.30	0.08	> 636
A-119	> 50	< 4.30	0.49	> 102
A-120	> 50	< 4.30	4.23	> 12
A-121	> 50	< 4.30	2.31	> 22
A-122	> 50	< 4.30	6.74	> 7
A-123	> 50	< 4.30	2.79	> 18
A-124	> 50	< 4.30	12.81	> 4
A-125	> 50	< 4.30	> 20	N/A
A-126	> 50	< 4.30	5.28	> 9
A-127	> 50	< 4.30	0.03	> 1488
A-128	> 50	< 4.30	0.28	> 179
A-129	> 50	< 4.30	0.13	> 380
A-130	> 50	< 4.30	0.04	> 1244
A-131	> 50	< 4.30	0.11	> 454
A-132	> 50	< 4.30	19.09	> 3
A-133	> 50	< 4.30	2.90	> 17
A-134	> 50	< 4.30	0.20	> 244
A-135	> 50	< 4.30	0.09	> 542
A-136	> 50	< 4.30	1.26	> 40
A-137	> 50	< 4.30	0.28	> 176
A-138	> 50	< 4.30	0.31	> 163
A-139	> 50	< 4.30	0.38	> 130
A-140	> 50	< 4.30	0.18	> 282
A-141	> 50	< 4.30	0.12	> 431
A-142	> 50	< 4.30	14.31	> 3
A-143	> 50	< 4.30	0.91	> 55
A-144	> 50	< 4.30	14.31	> 3
A-145	> 50	< 4.30	1.01	> 50
A-146	> 50	< 4.30	0.08	> 609
A-147	> 50	< 4.30	0.31	> 159

Table S5. Cytotoxicity in human cells and therapeutic ratio of 5-NI compounds

	HeLa		MzS *G. lamblia*	Therapeutic ratio
Compound	CC50 (μM)	pCC50	EC50 (μM)	CC50/EC50
A-148	> 50	< 4.30	0.01	> 3752
A-149	> 50	< 4.30	0.14	> 349
A-150	> 50	< 4.30	0.31	> 163
A-151	5.36	5.27 ± 0.06	0.11	49
A-152	> 50	< 4.30	1.19	> 42
A-153	> 50	< 4.30	0.28	> 177
A-154	> 50	< 4.30	0.41	> 122
A-155	> 50	< 4.30	0.30	> 165
A-156	> 50	< 4.30	0.37	> 136
A-157	> 50	< 4.30	0.52	> 95
A-158	> 50	< 4.30	1.44	> 35
A-159	> 50	< 4.30	5.05	> 10
A-160	> 50	< 4.30	6.31	> 8
A-161	> 50	< 4.30	1.87	> 27
A-162	> 50	< 4.30	4.23	> 12
A-163	> 50	< 4.30	0.24	> 212
B-101	> 50	< 4.30	1.18	> 42
B-102	> 50	< 4.30	1.56	> 32
B-103	> 50	< 4.30	0.40	> 124
B-104	> 50	< 4.30	3.10	> 16
B-105	> 50	< 4.30	5.52	> 9
B-106	> 50	< 4.30	4.52	> 11
B-107	> 50	< 4.30	1.65	> 30
B-108	> 50	< 4.30	2.33	> 21
B-109	> 50	< 4.30	3.87	> 13
B-110	> 50	< 4.30	2.18	> 23
B-111	> 50	< 4.30	0.92	> 54
B-112	> 50	< 4.30	1.98	> 25
B-113	> 50	< 4.30	0.59	> 84
B-114	> 50	< 4.30	2.13	> 23
B-115	> 50	< 4.30	3.10	> 16
B-116	> 50	< 4.30	0.72	> 69
B-117	> 50	< 4.30	0.26	> 194
B-118	> 50	< 4.30	1.05	> 48
B-119	> 50	< 4.30	1.19	> 42
B-120	> 50	< 4.30	2.41	> 21
B-121	> 50	< 4.30	2.25	> 22
B-122	> 50	< 4.30	4.14	> 12
B-123	> 50	< 4.30	0.92	> 54
B-124	> 50	< 4.30	1.73	> 29
B-125	> 50	< 4.30	14.00	> 4
B-126	> 50	< 4.30	4.83	> 10
B-127	> 50	< 4.30	0.31	> 159
B-128	> 50	< 4.30	0.19	> 260
B-129	> 50	< 4.30	0.16	> 314
B-130	49.12	4.31 ± 0.29	0.11	449
B-131	> 50	< 4.30	0.17	> 300
B-132	> 50	< 4.30	8.79	> 6

Table S5. Cytotoxicity in human cells and therapeutic ratio of 5-NI compounds

	HeLa		MzS *G. lamblia*	Therapeutic ratio
Compound	CC50 (μM)	pCC50	EC50 (μM)	CC50/EC50
B-133	> 50	< 4.30	2.07	> 24
B-134	> 50	< 4.30	0.22	> 230
B-135	> 50	< 4.30	0.31	> 163
B-136	> 50	< 4.30	1.12	> 45
B-137	> 50	< 4.30	1.68	> 30
B-138	> 50	< 4.30	0.16	> 304
B-139	> 50	< 4.30	0.32	> 157
B-140	> 50	< 4.30	2.02	> 25
B-141	> 50	< 4.30	0.56	> 89
B-142	> 50	< 4.30	8.41	> 6
B-143	> 50	< 4.30	0.87	> 58
B-144	> 50	< 4.30	4.83	> 10
B-145	> 50	< 4.30	0.35	> 145
B-146	> 50	< 4.30	0.51	> 97
B-147	> 50	< 4.30	1.06	> 47
B-148	> 50	< 4.30	0.08	> 662
B-149	> 50	< 4.30	0.62	> 81
B-150	> 50	< 4.30	0.32	> 156
B-151	> 50	< 4.30	0.86	> 58
B-152	> 50	< 4.30	0.14	> 366
B-153	> 50	< 4.30	0.49	> 102
B-154	> 50	< 4.30	0.82	> 61
B-155	> 50	< 4.30	0.11	> 441
B-156	> 50	< 4.30	0.11	> 475
B-157	> 50	< 4.30	0.53	> 94
B-158	> 50	< 4.30	0.55	> 91
B-159	> 50	< 4.30	2.30	> 22
B-160	> 50	< 4.30	12.53	> 4
B-161	> 50	< 4.30	0.78	> 64
B-162	> 50	< 4.30	2.49	> 20
B-163	> 50	< 4.30	0.15	> 331
C-101	> 50	< 4.30	0.78	> 64
C-102	> 50	< 4.30	1.30	> 38
C-103	> 50	< 4.30	0.26	> 191
C-104	> 50	< 4.30	1.16	> 43
C-105	> 50	< 4.30	2.71	> 18
C-106	> 50	< 4.30	3.67	> 14
C-107	> 50	< 4.30	1.23	> 41
C-108	> 50	< 4.30	2.68	> 19
C-109	> 50	< 4.30	2.80	> 18
C-110	> 50	< 4.30	1.93	> 26
C-111	> 50	< 4.30	1.02	> 49
C-112	> 50	< 4.30	1.00	> 50
C-113	> 50	< 4.30	0.41	> 122
C-114	> 50	< 4.30	0.95	> 52
C-115	> 50	< 4.30	1.27	> 39
C-116	> 50	< 4.30	0.59	> 84
C-117	> 50	< 4.30	0.07	> 691

Table S5. Cytotoxicity in human cells and therapeutic ratio of 5-NI compounds

	HeLa		MzS *G. lamblia*	Therapeutic ratio
Compound	CC50 (μM)	pCC50	EC50 (μM)	CC50/EC50
C-118	> 50	< 4.30	0.11	> 470
C-119	> 50	< 4.30	0.65	> 77
C-120	> 50	< 4.30	1.79	> 28
C-121	> 50	< 4.30	1.34	> 37
C-122	> 50	< 4.30	1.87	> 27
C-123	> 50	< 4.30	0.56	> 89
C-124	> 50	< 4.30	2.12	> 24
C-125	> 50	< 4.30	4.08	> 12
C-126	> 50	< 4.30	2.21	> 23
C-127	> 50	< 4.30	0.16	> 304
C-128	> 50	< 4.30	0.99	> 51
C-129	> 50	< 4.30	0.37	> 137
C-130	> 50	< 4.30	0.05	> 921
C-131	> 50	< 4.30	0.18	> 282
C-132	> 50	< 4.30	4.31	> 12
C-133	43.88	4.36 ± 0.15	1.37	32
C-134	> 50	< 4.30	0.29	> 175
C-135	> 50	< 4.30	0.36	> 139
C-136	> 50	< 4.30	0.87	> 58
C-137	> 50	< 4.30	0.16	> 312
C-138	> 50	< 4.30	0.26	> 190
C-139	> 50	< 4.30	0.37	> 136
C-140	> 50	< 4.30	0.44	> 113
C-141	> 50	< 4.30	0.19	> 263
C-142	> 50	< 4.30	0.86	> 58
C-143	> 50	< 4.30	1.43	> 35
C-144	> 50	< 4.30	0.56	> 90
C-145	> 50	< 4.30	0.65	> 77
C-146	> 50	< 4.30	0.60	> 84
C-147	> 50	< 4.30	0.32	> 155
C-148	> 50	< 4.30	0.50	> 100
C-149	> 50	< 4.30	0.45	> 110
C-150	> 50	< 4.30	0.28	> 178
C-151	40.17	4.40 ± 0.14	0.75	53
C-152	> 50	< 4.30	1.93	> 26
C-153	> 50	< 4.30	2.31	> 22
C-154	> 50	< 4.30	1.98	> 25
C-155	> 50	< 4.30	0.36	> 139
C-156	> 50	< 4.30	0.42	> 120
C-157	> 50	< 4.30	0.41	> 121
C-158	> 50	< 4.30	0.11	> 459
C-159	> 50	< 4.30	1.47	> 34
C-160	> 50	< 4.30	7.33	> 7
C-161	> 50	< 4.30	0.74	> 68
C-162	> 50	< 4.30	1.92	> 26
C-163	> 50	< 4.30	0.30	> 165
D-101	> 50	< 4.30	15.56	> 3
D-102	> 50	< 4.30	16.09	> 3

Table S5. Cytotoxicity in human cells and therapeutic ratio of 5-NI compounds

	HeLa		MzS *G. lamblia*	Therapeutic ratio
Compound	CC50 (μM)	pCC50	EC50 (μM)	CC50/EC50
D-103	> 50	< 4.30	9.62	> 5
D-104	> 50	< 4.30	12.14	> 4
D-105	> 50	< 4.30	19.09	> 3
D-106	> 50	< 4.30	> 20	N/A
D-107	> 50	< 4.30	12.68	> 4
D-108	> 50	< 4.30	12.83	> 4
D-109	> 50	< 4.30	13.26	> 4
D-110	> 50	< 4.30	12.14	> 4
D-111	> 50	< 4.30	5.91	> 8
D-112	> 50	< 4.30	10.17	> 5
D-113	> 50	< 4.30	4.88	> 10
D-114	> 50	< 4.30	10.63	> 5
D-115	> 50	< 4.30	10.86	> 5
D-116	> 50	< 4.30	12.14	> 4
D-117	> 50	< 4.30	9.20	> 5
D-118	> 50	< 4.30	7.31	> 7
D-119	> 50	< 4.30	10.39	> 5
D-120	> 50	< 4.30	11.87	> 4
D-121	> 50	< 4.30	8.80	> 6
D-122	> 50	< 4.30	11.11	> 5
D-123	> 50	< 4.30	1.10	> 46
D-124	> 50	< 4.30	12.00	> 4
D-125	> 50	< 4.30	13.26	> 4
D-126	> 50	< 4.30	16.72	> 3
D-127	> 50	< 4.30	6.78	> 7
D-128	> 50	< 4.30	7.14	> 7
D-129	> 50	< 4.30	14.33	> 3
D-130	> 50	< 4.30	3.84	> 13
D-131	> 50	< 4.30	4.84	> 10
D-132	> 50	< 4.30	14.49	> 3
D-133	> 50	< 4.30	14.49	> 3
D-134	> 50	< 4.30	13.27	> 4
D-135	> 50	< 4.30	2.40	> 21
D-136	> 50	< 4.30	14.64	> 3
D-137	> 50	< 4.30	8.44	> 6
D-138	> 50	< 4.30	11.48	> 4
D-139	> 50	< 4.30	11.48	> 4
D-140	> 50	< 4.30	5.65	> 9
D-141	> 50	< 4.30	7.50	> 7
D-142	> 50	< 4.30	6.76	> 7
D-143	> 50	< 4.30	10.51	> 5
D-144	> 50	< 4.30	11.23	> 4
D-145	> 50	< 4.30	1.79	> 28
D-146	> 50	< 4.30	5.93	> 8
D-147	> 50	< 4.30	2.39	> 21
D-148	> 50	< 4.30	7.62	> 7
D-149	> 50	< 4.30	7.79	> 6
D-150	> 50	< 4.30	3.27	> 15

Table S5. Cytotoxicity in human cells and therapeutic ratio of 5-NI compounds

	HeLa		MzS *G. lamblia*	Therapeutic ratio
Compound	CC50 (μM)	pCC50	EC50 (μM)	CC50/EC50
D-151	> 50	< 4.30	9.73	> 5
D-152	> 50	< 4.30	5.20	> 10
D-153	> 50	< 4.30	4.01	> 12
D-154	> 50	< 4.30	8.43	> 6
D-155	> 50	< 4.30	5.49	> 9
D-156	> 50	< 4.30	7.26	> 7
D-157	> 50	< 4.30	3.66	> 14
D-158	> 50	< 4.30	11.87	> 4
D-159	> 50	< 4.30	11.36	> 4
D-160	> 50	< 4.30	11.35	> 4
D-161	> 50	< 4.30	9.41	> 5
D-162	> 50	< 4.30	7.97	> 6
D-163	> 50	< 4.30	> 20	N/A
E-101	> 50	< 4.30	0.01	> 4149
E-102	> 50	< 4.30	0.02	> 3135
E-103	> 50	< 4.30	0.04	> 1152
E-104	> 50	< 4.30	0.06	> 792
E-105	> 50	< 4.30	0.10	> 496
E-106	> 50	< 4.30	0.10	> 508
E-107	> 50	< 4.30	0.02	> 2769
E-108	> 50	< 4.30	0.07	> 751
E-109	> 50	< 4.30	0.07	> 717
E-110	> 50	< 4.30	0.07	> 740
E-111	40.74	4.39 ± 0.04	0.09	447
E-112	> 50	< 4.30	0.02	> 2665
E-113	23.07	4.64 ± 0.03	0.01	1646
E-114	37.24	4.43 ± 0.06	0.03	> 1107
E-115	30.20	4.52 ± 0.07	0.06	> 497
E-116	> 50	< 4.30	0.01	> 9447
E-117	> 50	< 4.30	0.04	> 1421
E-118	> 50	< 4.30	0.02	> 2048
E-119	> 50	< 4.30	0.03	> 1652
E-120	> 50	< 4.30	0.01	> 4402
E-121	> 50	< 4.30	0.01	> 7068
E-122	> 50	< 4.30	0.02	> 2525
E-123	> 50	< 4.30	0.01	> 3735
E-124	> 50	< 4.30	0.45	> 112
E-125	> 50	< 4.30	0.02	> 2053
E-126	> 50	< 4.30	0.05	> 1012
E-127	> 50	< 4.30	0.14	> 350
E-128	> 50	< 4.30	0.01	> 4172
E-129	> 50	< 4.30	0.03	> 1615
E-130	> 50	< 4.30	0.02	> 2076
E-131	> 50	< 4.30	0.04	> 1317
E-132	> 50	< 4.30	0.42	> 119
E-133	> 50	< 4.30	0.03	> 1435
E-134	> 50	< 4.30	0.01	> 5956
E-135	> 50	< 4.30	> 20	N/A

Table S5. Cytotoxicity in human cells and therapeutic ratio of 5-NI compounds

	HeLa		MzS *G. lamblia*	Therapeutic ratio
Compound	CC50 (μM)	pCC50	EC50 (μM)	CC50/EC50
E-136	> 50	< 4.30	0.01	> 7626
E-137	> 50	< 4.30	0.05	> 951
E-138	40.77	4.39 ± 0.39	0.01	> 2721
E-139	> 50	< 4.30	0.01	> 4823
E-140	40.77	4.39 ± 0.39	0.07	> 618
E-141	> 50	< 4.30	0.01	> 4124
E-142	> 50	< 4.30	0.13	> 394
E-143	> 50	< 4.30	0.01	> 8603
E-144	> 50	< 4.30	0.39	> 130
E-145	> 50	< 4.30	0.00	> 16774
E-146	> 50	< 4.30	0.02	> 2086
E-147	> 50	< 4.30	0.05	> 920
E-148	45.64	4.34 ± 0.34	0.01	> 3131
E-149	> 50	< 4.30	0.01	> 3656
E-150	> 50	< 4.30	0.01	> 7117
E-151	40.97	4.39 ± 0.39	0.04	> 955
E-152	> 50	< 4.30	0.20	> 249
E-153	> 50	< 4.30	0.03	> 1668
E-154	> 50	< 4.30	0.03	> 1429
E-155	> 50	< 4.30	0.01	> 8215
E-156	> 50	< 4.30	0.01	> 6048
E-157	> 50	< 4.30	0.01	> 7989
E-158	> 50	< 4.30	0.00	> 10383
E-159	> 50	< 4.30	0.01	> 3690
E-160	> 50	< 4.30	0.08	> 606
E-161	> 50	< 4.30	0.01	> 7435
E-162	> 50	< 4.30	0.03	> 1774
E-163	> 50	< 4.30	0.04	> 1398
F-101	> 50	< 4.30	0.65	> 77
F-102	> 50	< 4.30	0.50	> 100
F-103	> 50	< 4.30	0.09	> 575
F-104	> 50	< 4.30	0.95	> 53
F-105	> 50	< 4.30	0.74	> 68
F-106	> 50	< 4.30	1.01	> 49
F-107	> 50	< 4.30	0.59	> 84
F-108	> 50	< 4.30	0.41	> 123
F-109	> 50	< 4.30	0.48	> 104
F-110	> 50	< 4.30	0.22	> 232
F-111	> 50	< 4.30	3.02	> 17
F-112	> 50	< 4.30	0.26	> 191
F-113	> 50	< 4.30	0.35	> 142
F-114	> 50	< 4.30	3.02	> 17
F-115	> 50	< 4.30	0.92	> 54
F-116	> 50	< 4.30	1.49	> 33
F-117	> 50	< 4.30	0.03	> 1677
F-118	44.86	4.35 ± 0.09	0.04	> 1255
F-119	> 50	< 4.30	0.72	> 69
F-120	> 50	< 4.30	3.03	> 16

Table S5. Cytotoxicity in human cells and therapeutic ratio of 5-NI compounds

	HeLa		MzS *G. lamblia*	Therapeutic ratio
Compound	CC50 (µM)	pCC50	EC50 (µM)	CC50/EC50
F-121	> 50	< 4.30	1.33	> 38
F-122	> 50	< 4.30	6.61	> 8
F-123	> 50	< 4.30	0.36	> 138
F-124	> 50	< 4.30	0.72	> 70
F-125	> 50	< 4.30	2.49	> 20
F-126	> 50	< 4.30	0.90	> 56
F-127	> 50	< 4.30	0.09	> 574
F-128	> 50	< 4.30	1.39	> 36
F-129	> 50	< 4.30	0.76	> 65
F-130	> 50	< 4.30	1.07	> 47
F-131	> 50	< 4.30	0.19	> 261
F-132	> 50	< 4.30	2.60	> 19
F-133	> 50	< 4.30	0.65	> 77
F-134	> 50	< 4.30	0.20	> 248
F-135	> 50	< 4.30	1.59	> 32
F-136	> 50	< 4.30	0.51	> 98
F-137	18.18	4.74 ± 0.66	0.63	> 29
F-138	> 50	< 4.30	0.12	> 431
F-139	> 50	< 4.30	0.06	> 828
F-140	> 50	< 4.30	4.48	> 11
F-141	> 50	< 4.30	0.04	> 1227
F-142	> 50	< 4.30	1.12	> 45
F-143	> 50	< 4.30	0.10	> 496
F-144	> 50	< 4.30	1.39	> 36
F-145	> 50	< 4.30	0.83	> 61
F-146	> 50	< 4.30	0.02	> 2510
F-147	> 50	< 4.30	0.19	> 265
F-148	> 50	< 4.30	0.02	> 2247
F-149	43.88	4.36 ± 0.03	0.02	> 2220
F-150	> 50	< 4.30	0.09	> 551
F-151	> 50	< 4.30	0.38	> 131
F-152	> 50	< 4.30	0.50	> 101
F-153	> 50	< 4.30	0.03	> 1608
F-154	> 50	< 4.30	0.06	> 883
F-155	> 50	< 4.30	0.05	> 918
F-156	> 50	< 4.30	0.02	> 2659
F-157	10.85	4.96 ± 0.01	0.04	> 271
F-158	> 50	< 4.30	0.09	> 548
F-159	> 50	< 4.30	1.99	> 25
F-160	> 50	< 4.30	2.49	> 20
F-161	> 50	< 4.30	0.29	> 171
F-162	> 50	< 4.30	1.16	> 43
F-163	> 50	< 4.30	0.09	> 532

Toxicity against the human HeLa cells was determined as CC50 (in µM; geometric mean, n=3-6 experiments), the compound concentration that kills 50% of HeLa cells in a cytotoxicity assay, is also shown as negative log10 value of the CC50 (pCC50; mean ± SE, n=3-6 experiments). Therapeutic ratio, the ratio of CC50 in HeLa cells to EC50 of *G. lamblia* (strain 713), reflects the relative selectivity of compound potency against *Giardia* compared to cytotoxicity in HeLa cells, with higher ratios indicating greater selectivity for the parasite.

Table S6a. Structures of core A-C test compounds

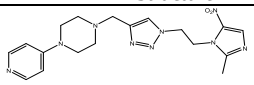
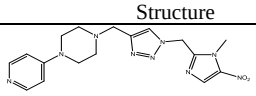
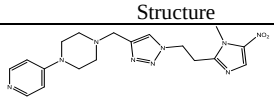
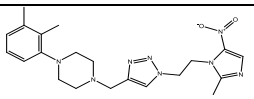
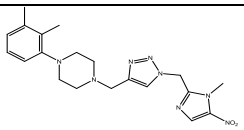
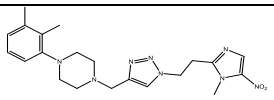
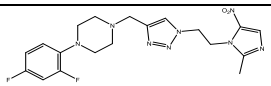
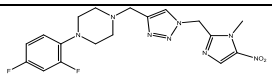
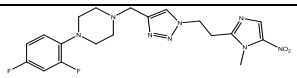
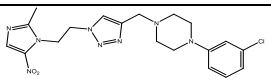
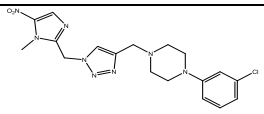
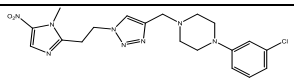
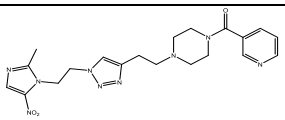
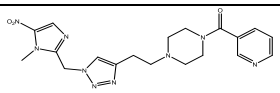
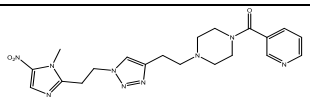
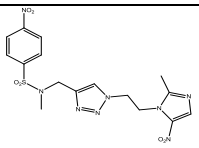
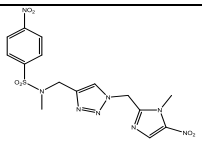
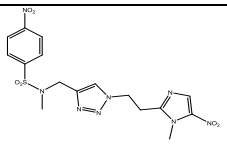
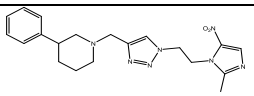
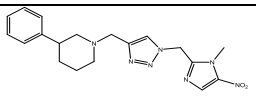
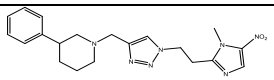
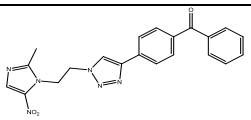
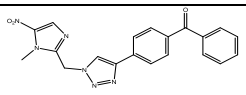
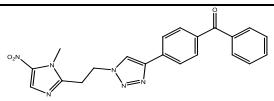
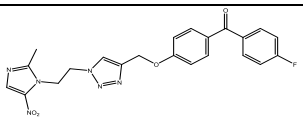
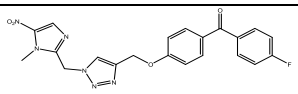
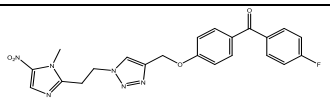
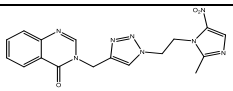
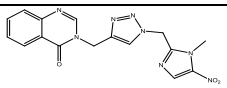
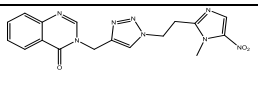
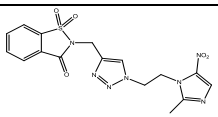
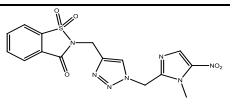
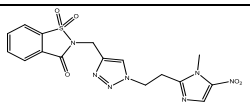
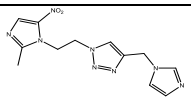
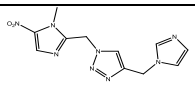
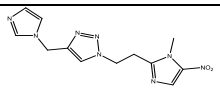
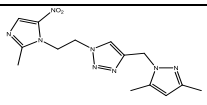
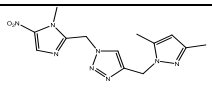
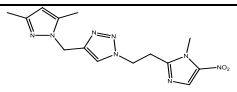
	Core **A**		Core **B**		Core **C**	
Alkyne	Name	Structure	Name	Structure	Name	Structure
201	A-201		B-201		C-201	
202	A-202		B-202		C-202	
203	A-203		B-203		C-203	
204	A-204		B-204		C-204	
205	A-205		B-205		C-205	
206	A-206		B-206		C-206	
207	A-207		B-207		C-207	
208	A-208		B-208		C-208	
209	A-209		B-209		C-209	
210	A-210		B-210		C-210	
211	A-211		B-211		C-211	
212	A-212		B-212		C-212	
213	A-213		B-213		C-213	

Table S6a. Structures of core A-C test compounds

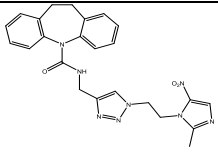
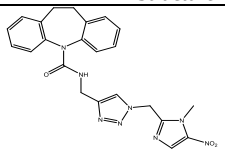
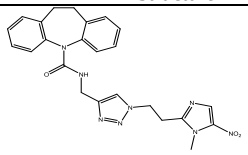
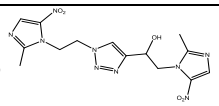
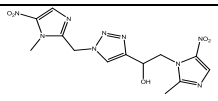
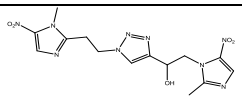
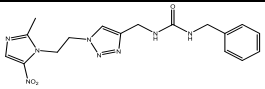
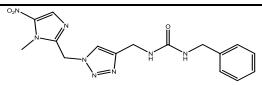
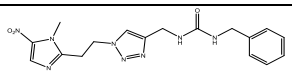
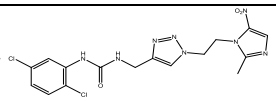
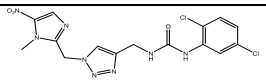
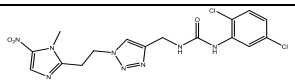
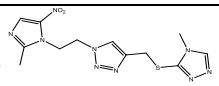
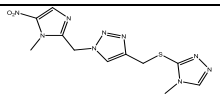
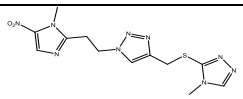
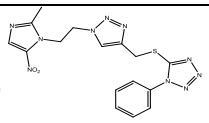
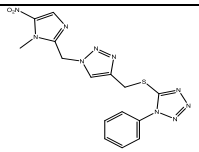
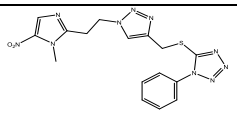
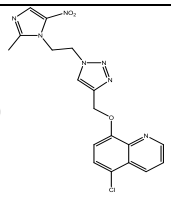
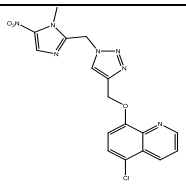
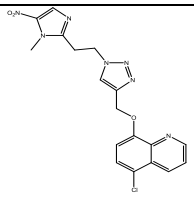
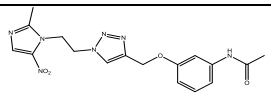
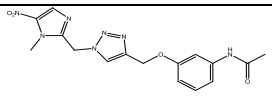
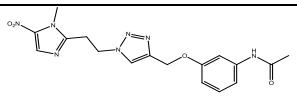
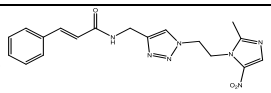
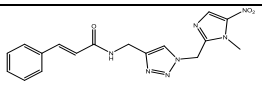
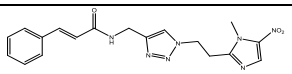
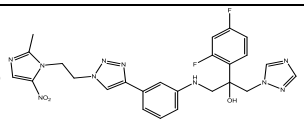
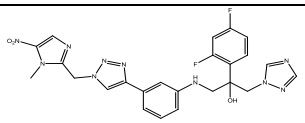
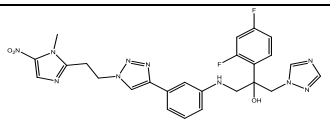
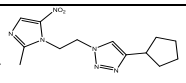
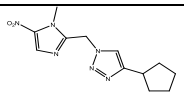
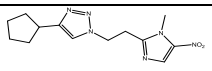
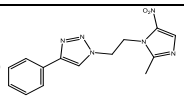
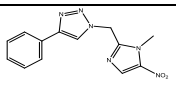
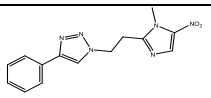
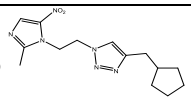
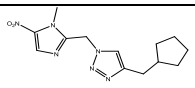
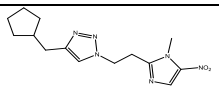
	Core **A**		Core **B**		Core **C**	
Alkyne	Name	Structure	Name	Structure	Name	Structure
214	A-214		B-214		C-214	
215	A-215		B-215		C-215	
216	A-216		B-216		C-216	
217	A-217		B-217		C-217	
218	A-218		B-218		C-218	
219	A-219		B-219		C-219	
220	A-220		B-220		C-220	
221	A-221		B-221		C-221	
222	A-222		B-222		C-222	
223	A-223		B-223		C-223	
224	A-224		B-224		C-224	
225	A-225		B-225		C-225	
226	A-226		B-226		C-226	

Table S6a. Structures of core A-C test compounds

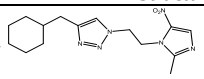
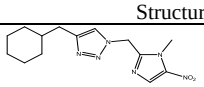
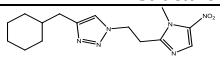
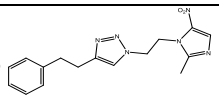
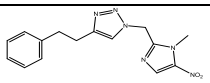
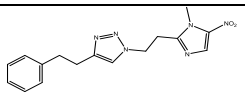
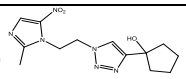
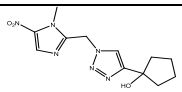
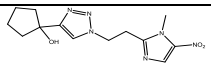
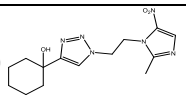
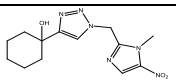
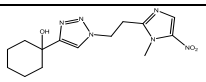
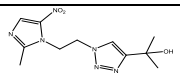
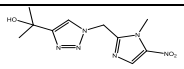
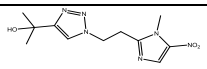
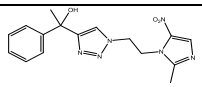
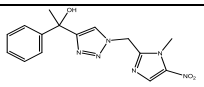
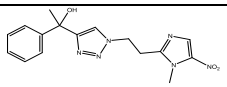
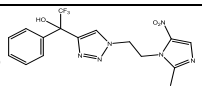
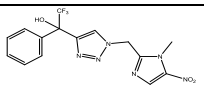
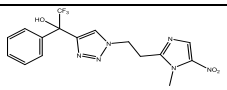
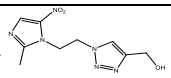
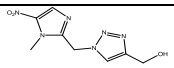
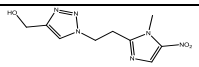
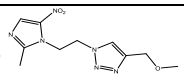
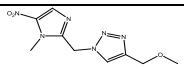
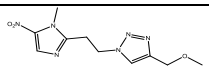
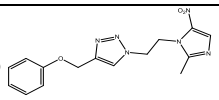
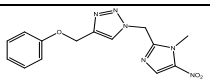
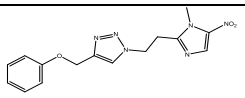
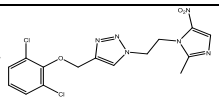
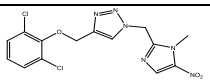
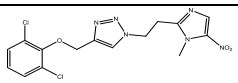
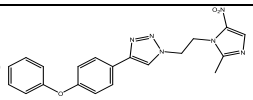
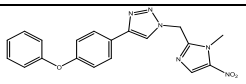
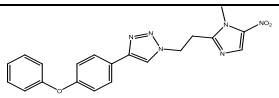
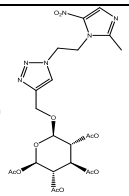
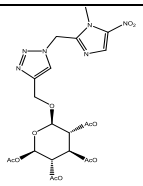
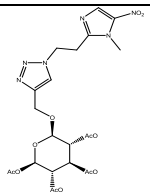
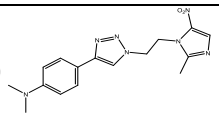
	Core **A**		Core **B**		Core **C**	
Alkyne	Name	Structure	Name	Structure	Name	Structure
227	A-227		B-227		C-227	
228	A-228		B-228		C-228	
229	A-229		B-229		C-229	
230	A-230		B-230		C-230	
231	A-231		B-231		C-231	
232	A-232		B-232		C-232	
233	A-233		B-233		C-233	
234	A-234		B-234		C-234	
235	A-235		B-235		C-235	
236	A-236		B-236		C-236	
237	A-237		B-237		C-237	
238	A-238		B-238		C-238	
239	A-239		B-239		C-239	
240	A-240		B-240		C-240	

Table S6a. Structures of core A-C test compounds

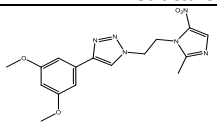
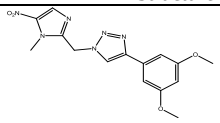
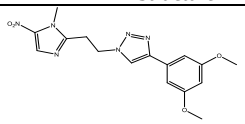
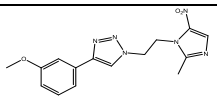
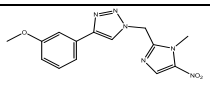
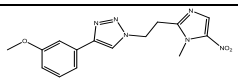
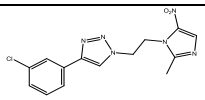
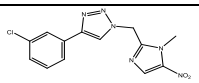
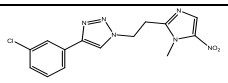
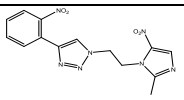
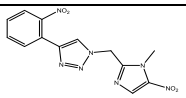
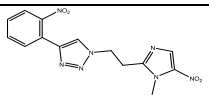
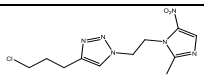
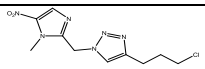
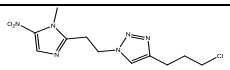
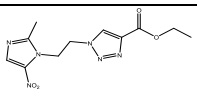
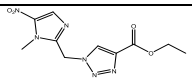
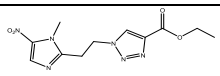
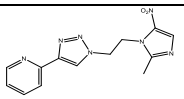
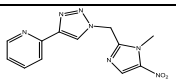
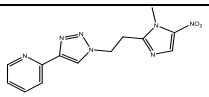
	Core **A**		Core **B**		Core **C**	
Alkyne	Name	Structure	Name	Structure	Name	Structure
241	A-241		B-241		C-241	
242	A-242		B-242		C-242	
243	A-243		B-243		C-243	
244	A-244		B-244		C-244	
245	A-245		B-245		C-245	
246	A-246		B-246		C-246	
247	A-247		B-247		C-247	

Table S6b. Structures of core D-F test compounds

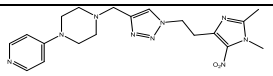
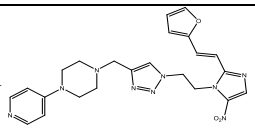
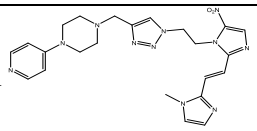
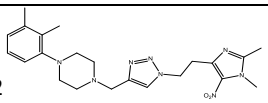
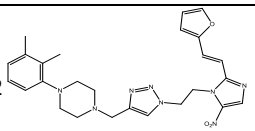
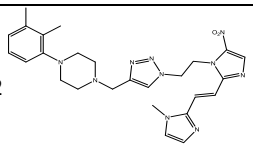
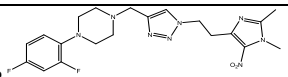
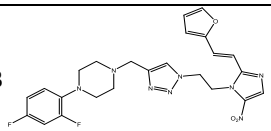
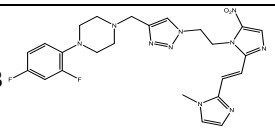
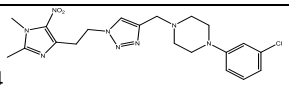
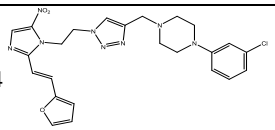
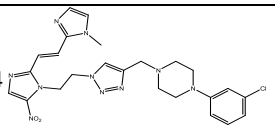
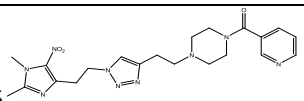
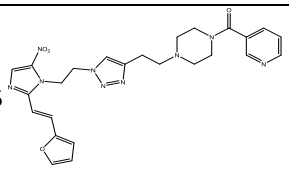
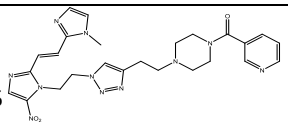
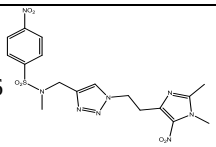
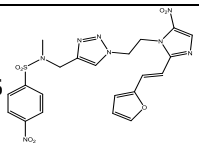
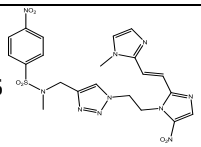
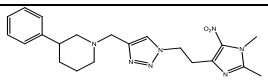
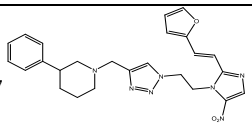
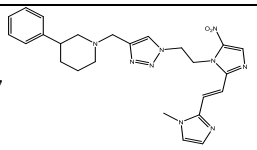
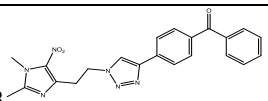
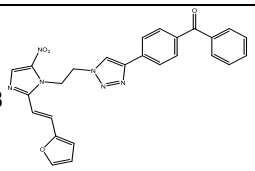
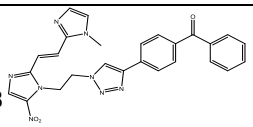
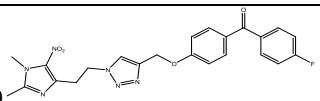
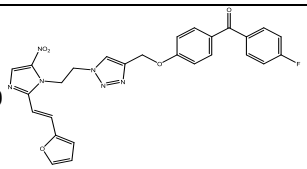
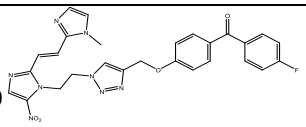
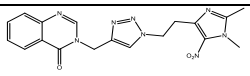
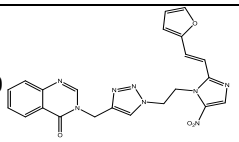
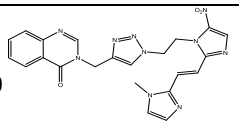
Alkynes	Core **D** Name	Core **D** Structure	Core **E** Name	Core **E** Structure	Core **F** Name	Core **F** Structure
201	D-201		E-201		F-201	
202	D-202		E-202		F-202	
203	D-203		E-203		F-203	
204	D-204		E-204		F-204	
205	D-205		E-205		F-205	
206	D-206		E-206		F-206	
207	D-207		E-207		F-207	
208	D-208		E-208		F-208	
209	D-209		E-209		F-209	
210	D-210		E-210		F-210	

Table S6b. Structures of core D-F test compounds

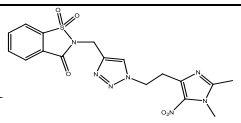
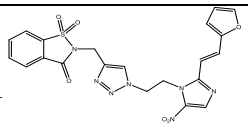
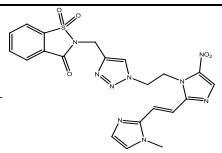
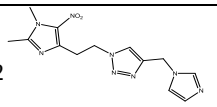
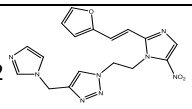
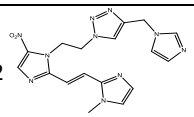
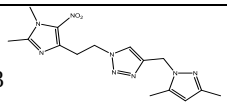
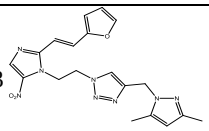
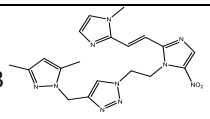
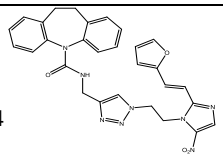
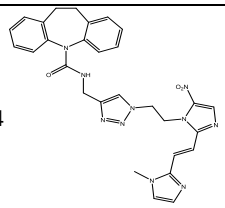
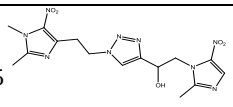
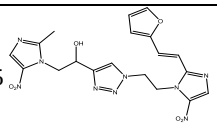
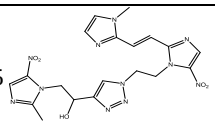
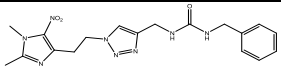
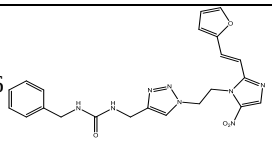
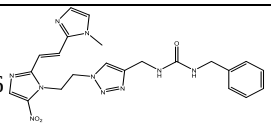
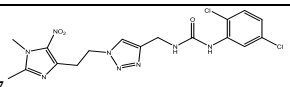
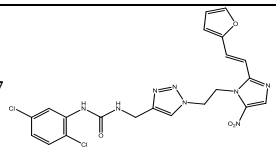
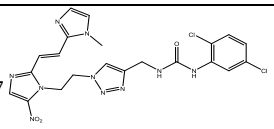
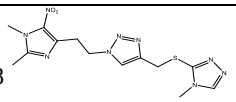
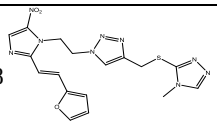
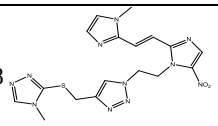
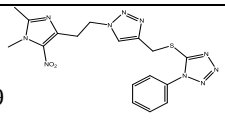
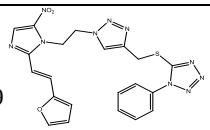
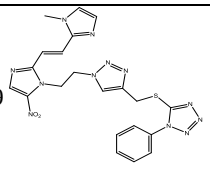
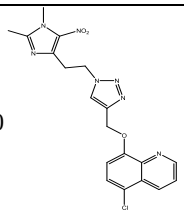
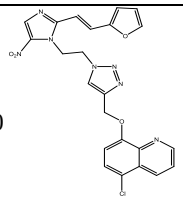
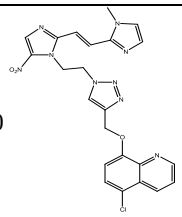
Alkynes	Core **D**		Core **E**		Core **F**	
	Name	Structure	Name	Structure	Name	Structure
211	D-211		E-211		F-211	
212	D-212		E-212		F-212	
213	D-213		E-213		F-213	
214			E-214		F-214	
215	D-215		E-215		F-215	
216	D-216		E-216		F-216	
217	D-217		E-217		F-217	
218	D-218		E-218		F-218	
219	D-219		E-219		F-219	
220	D-220		E-220		F-220	

Table S6b. Structures of core D-F test compounds

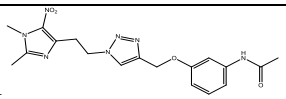
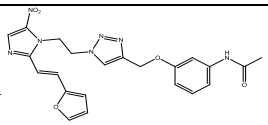
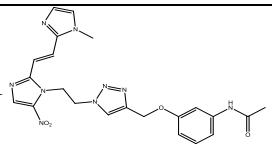
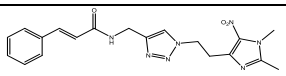
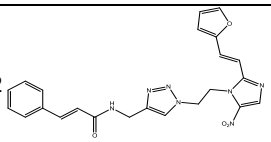
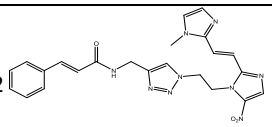
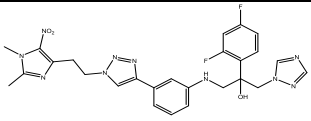
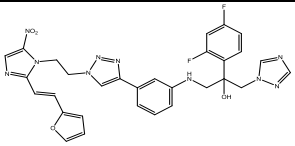
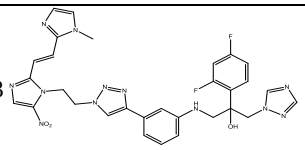
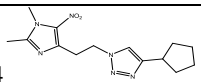
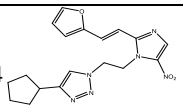
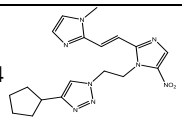
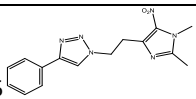
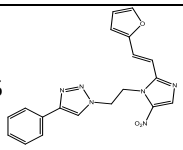
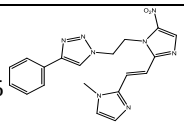
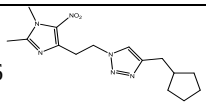
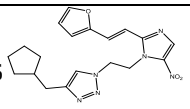
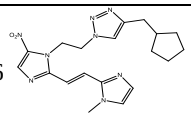
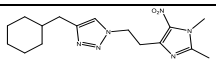
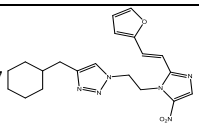
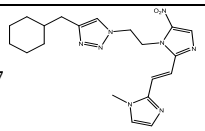
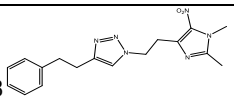
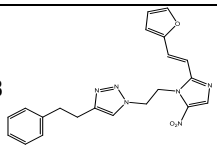
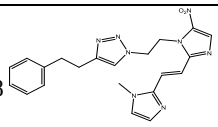
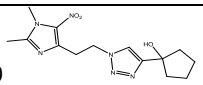
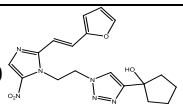
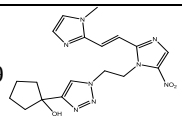
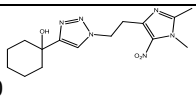
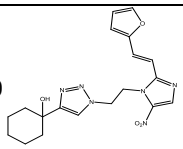
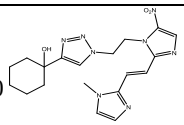
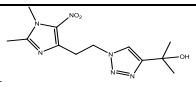
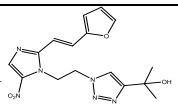
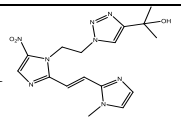
Alkynes	Core **D**		Core **E**		Core **F**	
	Name	Structure	Name	Structure	Name	Structure
221	D-221		E-221		F-221	
222	D-222		E-222		F-222	
223	D-223		E-223		F-223	
224	D-224		E-224		F-224	
225	D-225		E-225		F-225	
226	D-226		E-226		F-226	
227	D-227		E-227		F-227	
228	D-228		E-228		F-228	
229	D-229		E-229		F-229	
230	D-230		E-230		F-230	
231	D-231		E-231		F-231	

Table S6b. Structures of core D-F test compounds

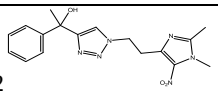
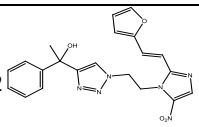
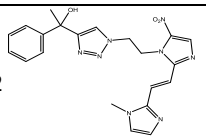
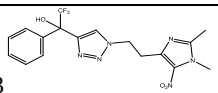
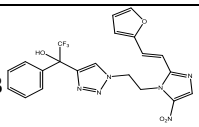
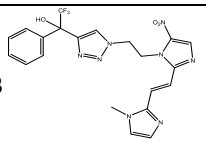
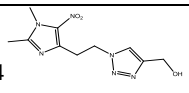
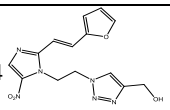
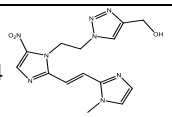
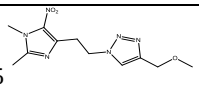
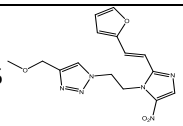
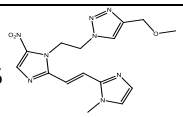
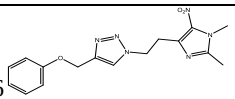
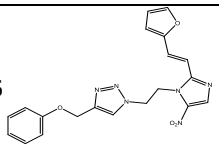
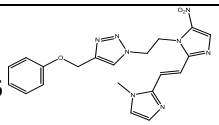
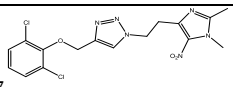
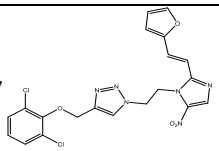
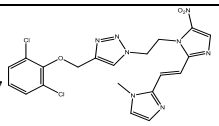
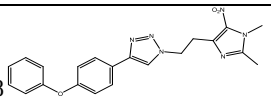
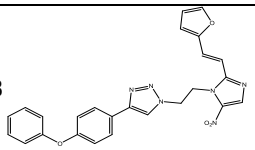
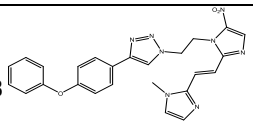
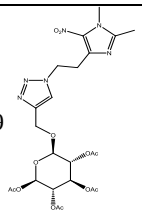
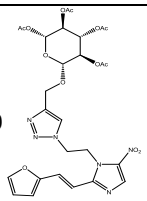
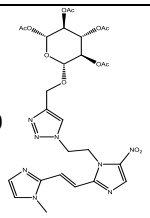
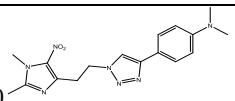
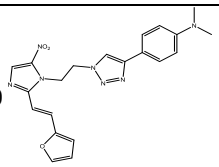
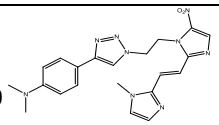
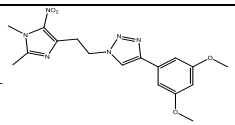
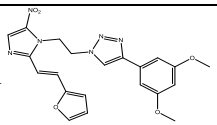
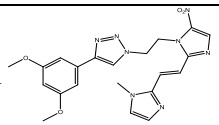
Alkynes	Core **D** Name	Core **D** Structure	Core **E** Name	Core **E** Structure	Core **F** Name	Core **F** Structure
232	D-232		E-232		F-232	
233	D-233		E-233		F-233	
234	D-234		E-234		F-234	
235	D-235		E-235		F-235	
236	D-236		E-236		F-236	
237	D-237		E-237		F-237	
238	D-238		E-238		F-238	
239	D-239		E-239		F-239	
240	D-240		E-240		F-240	
241	D-241		E-241		F-241	

Table S6b. Structures of core D-F test compounds

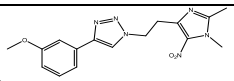
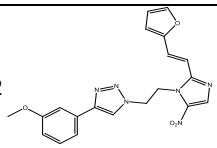
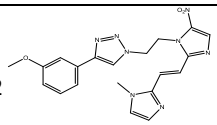
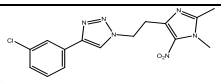
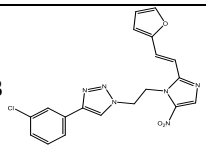
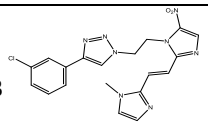
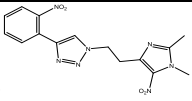
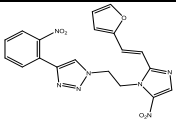
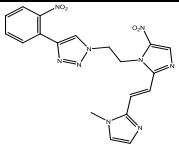
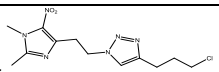
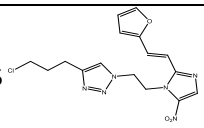
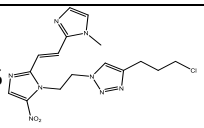
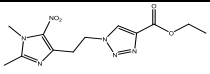
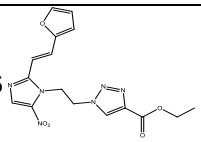
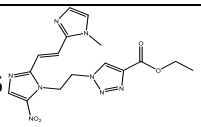
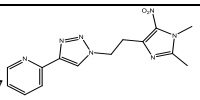
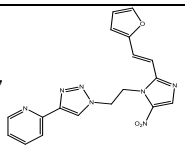
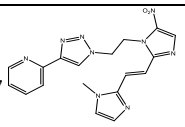
Alkynes	Core **D** Name	Core **D** Structure	Core **E** Name	Core **E** Structure	Core **F** Name	Core **F** Structure
242	D-242		E-242		F-242	
243	D-243		E-243		F-243	
244	D-244		E-244		F-244	
245	D-245		E-245		F-245	
246	D-246		E-246		F-246	
247	D-247		E-247		F-247	

Table S7. Activity of 5-NI test compounds against *Giarda lamblia*

	G. lamblia 713				*G. lamblia* 106			
	MzS		MzR		MzS		MzR	
Compound	EC50 (μM)	pEC50	EC50 (μM)	pEC50	EC50 (μM)	pEC50	EC50 (μM)	pEC50
Mz	1.995	5.70 ± 0.01	50.119	4.30 ± 0.02	3.631	5.44 ± 0.01	77.625	4.11 ± 0.02
A-201	12.531	4.90 ± 0.02	17.470	4.76 ± 0.06	2.610	5.58 ± 0.19	9.772	5.01 ± 0.12
A-202	0.161	6.79 ± 0.04	1.271	5.90 ± 0.16	0.220	6.66 ± 0.13	2.466	5.61 ± 0.11
A-203	0.438	6.36 ± 0.03	6.166	5.21 ± 0.08	0.666	6.18 ± 0.18	3.162	5.50 ± 0.10
A-204	0.179	6.75 ± 0.01	2.349	5.63 ± 0.13	0.278	6.56 ± 0.22	1.622	5.79 ± 0.07
A-205	2.970	5.53 ± 0.04	10.859	4.96 ± 0.18	3.090	5.51 ± 0.21	10.715	4.97 ± 0.14
A-206	1.076	5.97 ± 0.09	8.707	5.06 ± 0.10	2.630	5.58 ± 0.42	11.394	4.94 ± 0.13
A-207	0.456	6.34 ± 0.02	6.442	5.19 ± 0.06	0.457	6.34 ± 0.09	2.265	5.65 ± 0.19
A-208	0.299	6.52 ± 0.20	0.972	6.01 ± 0.27	0.154	6.81 ± 0.46	0.452	6.35 ± 0.28
A-209	0.070	7.16 ± 0.21	0.248	6.61 ± 0.39	0.142	6.85 ± 0.35	0.631	6.20 ± 0.23
A-210	1.061	5.97 ± 0.02	7.291	5.14 ± 0.08	1.122	5.95 ± 0.08	7.703	5.11 ± 0.14
A-211	1.253	5.90 ± 0.05	15.993	4.80 ± 0.05	1.685	5.77 ± 0.12	6.556	5.18 ± 0.13
A-212	2.600	5.59 ± 0.04	18.066	4.74 ± 0.04	3.067	5.51 ± 0.22	10.965	4.96 ± 0.10
A-213	2.273	5.64 ± 0.04	15.647	4.81 ± 0.07	2.326	5.63 ± 0.11	7.244	5.14 ± 0.13
A-214	1.662	5.78 ± 0.03	5.348	5.27 ± 0.05	1.806	5.74 ± 0.10	7.413	5.13 ± 0.18
A-215	7.529	5.12 ± 0.08	> 20	< 4.70	5.089	5.29 ± 0.18	12.397	4.91 ± 0.13
A-216	18.670	4.73 ± 0.03	18.674	4.73 ± 0.03	6.407	5.19 ± 0.13	13.804	4.86 ± 0.08
A-217	0.858	6.07 ± 0.06	3.914	5.41 ± 0.12	2.065	5.69 ± 0.43	17.378	4.76 ± 0.06
A-218	> 20	< 4.70	12.532	4.90 ± 0.19	4.241	5.37 ± 0.34	14.905	4.83 ± 0.07
A-219	0.225	6.65 ± 0.02	5.473	5.26 ± 0.17	0.363	6.44 ± 0.12	2.818	5.55 ± 0.17
A-220	0.038	7.42 ± 0.07	0.701	6.15 ± 0.23	0.052	7.28 ± 0.20	1.006	6.00 ± 0.26
A-221	12.439	4.91 ± 0.14	15.825	4.80 ± 0.10	5.721	5.24 ± 0.16	14.962	4.83 ± 0.07
A-222	1.607	5.79 ± 0.06	15.305	4.82 ± 0.07	1.806	5.74 ± 0.10	15.668	4.81 ± 0.08
A-223	2.558	5.59 ± 0.02	11.604	4.94 ± 0.03	5.623	5.25 ± 0.10	16.312	4.79 ± 0.06
A-224	0.419	6.38 ± 0.07	10.984	4.96 ± 0.10	0.794	6.10 ± 0.13	3.487	5.46 ± 0.26
A-225	0.164	6.78 ± 0.05	5.292	5.28 ± 0.09	0.263	6.58 ± 0.12	3.868	5.41 ± 0.10
A-226	0.393	6.41 ± 0.03	5.912	5.23 ± 0.10	0.838	6.08 ± 0.12	6.569	5.18 ± 0.12
A-227	0.198	6.70 ± 0.06	1.901	5.72 ± 0.15	0.285	6.55 ± 0.14	5.070	5.30 ± 0.22
A-228	0.183	6.74 ± 0.02	3.331	5.48 ± 0.10	0.360	6.44 ± 0.16	3.428	5.47 ± 0.16
A-229	3.359	5.47 ± 0.09	13.254	4.88 ± 0.09	4.169	5.38 ± 0.17	14.791	4.83 ± 0.06
A-230	1.700	5.77 ± 0.04	11.869	4.93 ± 0.12	2.138	5.67 ± 0.10	15.049	4.82 ± 0.07
A-231	1.916	5.72 ± 0.02	12.403	4.91 ± 0.08	2.754	5.56 ± 0.10	15.668	4.81 ± 0.06
A-232	1.139	5.94 ± 0.02	10.163	4.99 ± 0.04	1.288	5.89 ± 0.12	12.023	4.92 ± 0.08
A-233	0.196	6.71 ± 0.03	2.590	5.59 ± 0.16	0.398	6.40 ± 0.09	3.369	5.47 ± 0.12
A-234	8.226	5.08 ± 0.03	17.671	4.75 ± 0.05	6.761	5.17 ± 0.03	14.706	4.83 ± 0.05
A-235	2.487	5.60 ± 0.03	13.401	4.87 ± 0.09	4.233	5.37 ± 0.14	14.234	4.85 ± 0.07
A-236	0.124	6.91 ± 0.05	2.349	5.63 ± 0.12	0.339	6.47 ± 0.26	10.000	5.00 ± 0.05
A-237	0.033	7.48 ± 0.04	0.486	6.31 ± 0.29	0.137	6.86 ± 0.10	2.188	5.66 ± 0.29
A-238	0.667	6.18 ± 0.21	0.533	6.27 ± 0.12	0.028	7.56 ± 0.97	0.567	6.25 ± 0.44
A-239	12.812	4.89 ± 0.01	19.517	4.71 ± 0.01	9.261	5.03 ± 0.06	17.378	4.76 ± 0.06
A-240	0.141	6.85 ± 0.03	5.216	5.28 ± 0.10	0.713	6.15 ± 0.22	4.898	5.31 ± 0.14
A-241	0.049	7.31 ± 0.05	1.296	5.89 ± 0.15	0.035	7.45 ± 0.03	3.273	5.49 ± 0.06
A-242	0.112	6.95 ± 0.02	1.830	5.74 ± 0.13	0.161	6.79 ± 0.07	5.129	5.29 ± 0.08
A-243	0.057	7.25 ± 0.06	1.385	5.86 ± 0.18	0.140	6.85 ± 0.07	1.116	5.95 ± 0.15
A-244	0.165	6.78 ± 0.10	1.468	5.83 ± 0.28	0.617	6.21 ± 0.40	2.997	5.52 ± 0.34
A-245	0.902	6.04 ± 0.03	9.944	5.00 ± 0.01	1.318	5.88 ± 0.06	9.477	5.02 ± 0.02

Table S7. Activity of 5-NI test compounds against *Giarda lamblia*

	G. lamblia 713				*G. lamblia* 106			
	MzS		MzR		MzS		MzR	
Compound	EC50 (µM)	pEC50	EC50 (µM)	pEC50	EC50 (µM)	pEC50	EC50 (µM)	pEC50
A-246	1.986	5.70 ± 0.01	13.163	4.88 ± 0.09	2.399	5.62 ± 0.03	7.630	5.12 ± 0.15
A-247	0.352	6.45 ± 0.02	13.906	4.86 ± 0.01	0.558	6.25 ± 0.10	4.493	5.35 ± 0.08
B-201	5.053	5.30 ± 0.08	13.999	4.85 ± 0.05	5.799	5.24 ± 0.11	14.289	4.85 ± 0.05
B-202	0.352	6.45 ± 0.15	1.892	5.72 ± 0.10	0.531	6.28 ± 0.11	6.683	5.18 ± 0.08
B-203	0.578	6.24 ± 0.08	5.522	5.26 ± 0.08	0.671	6.17 ± 0.06	7.718	5.11 ± 0.10
B-204	0.345	6.46 ± 0.11	3.961	5.40 ± 0.10	0.263	6.58 ± 0.09	3.037	5.52 ± 0.11
B-205	6.448	5.19 ± 0.19	13.392	4.87 ± 0.09	8.318	5.08 ± 0.14	11.482	4.94 ± 0.02
B-206	1.963	5.71 ± 0.02	4.242	5.37 ± 0.03	2.733	5.56 ± 0.22	3.467	5.46 ± 0.20
B-207	0.236	6.63 ± 0.06	3.685	5.43 ± 0.09	0.307	6.51 ± 0.04	3.415	5.47 ± 0.18
B-208	0.346	6.46 ± 0.17	2.094	5.68 ± 0.36	0.261	6.58 ± 0.45	5.168	5.29 ± 0.16
B-209	0.210	6.68 ± 0.07	2.142	5.67 ± 0.31	4.713	5.33 ± 0.15	10.839	4.97 ± 0.02
B-210	0.844	6.07 ± 0.04	9.606	5.02 ± 0.26	0.955	6.02 ± 0.04	9.772	5.01 ± 0.12
B-211	1.064	5.97 ± 0.03	13.099	4.88 ± 0.17	1.935	5.71 ± 0.06	10.000	5.00 ± 0.08
B-212	3.625	5.44 ± 0.01	10.972	4.96 ± 0.18	5.934	5.23 ± 0.04	11.220	4.95 ± 0.01
B-213	1.388	5.86 ± 0.07	7.529	5.12 ± 0.15	1.935	5.71 ± 0.07	5.799	5.24 ± 0.13
B-214	1.834	5.74 ± 0.04	7.552	5.12 ± 0.30	7.052	5.15 ± 0.20	16.982	4.77 ± 0.04
B-215	13.392	4.87 ± 0.09	9.396	5.03 ± 0.33	11.570	4.94 ± 0.09	12.303	4.91 ± 0.03
B-216	9.190	5.04 ± 0.08	10.699	4.97 ± 0.27	12.784	4.89 ± 0.08	14.344	4.84 ± 0.08
B-217	0.860	6.07 ± 0.08	3.538	5.45 ± 0.38	1.862	5.73 ± 0.05	9.624	5.02 ± 0.21
B-218	8.599	5.07 ± 0.16	9.827	5.01 ± 0.20	6.358	5.20 ± 0.13	13.490	4.87 ± 0.09
B-219	0.278	6.56 ± 0.08	2.001	5.70 ± 0.20	1.072	5.97 ± 0.01	4.823	5.32 ± 0.10
B-220	0.101	6.99 ± 0.13	0.999	6.00 ± 0.20	0.533	6.27 ± 0.08	5.710	5.24 ± 0.12
B-221	2.622	5.58 ± 0.05	7.535	5.12 ± 0.13	3.415	5.47 ± 0.12	8.511	5.07 ± 0.02
B-222	1.806	5.74 ± 0.08	7.820	5.11 ± 0.17	4.606	5.34 ± 0.10	11.749	4.93 ± 0.08
B-223	1.621	5.79 ± 0.03	6.456	5.19 ± 0.13	2.455	5.61 ± 0.09	10.233	4.99 ± 0.06
B-224	0.247	6.61 ± 0.04	2.808	5.55 ± 0.08	0.440	6.36 ± 0.11	2.026	5.69 ± 0.17
B-225	0.099	7.01 ± 0.09	3.688	5.43 ± 0.12	0.185	6.73 ± 0.17	0.933	6.03 ± 0.18
B-226	0.291	6.54 ± 0.09	3.961	5.40 ± 0.05	0.636	6.20 ± 0.10	2.436	5.61 ± 0.11
B-227	0.285	6.55 ± 0.16	2.520	5.60 ± 0.03	0.681	6.17 ± 0.05	2.326	5.63 ± 0.12
B-228	0.322	6.49 ± 0.09	4.834	5.32 ± 0.05	0.832	6.08 ± 0.06	2.754	5.56 ± 0.11
B-229	1.081	5.97 ± 0.06	5.901	5.23 ± 0.13	1.660	5.78 ± 0.11	5.248	5.28 ± 0.16
B-230	1.993	5.70 ± 0.24	5.522	5.26 ± 0.12	1.031	5.99 ± 0.10	4.332	5.36 ± 0.10
B-231	5.984	5.22 ± 0.05	7.045	5.15 ± 0.16	4.974	5.30 ± 0.08	11.749	4.93 ± 0.06
B-232	0.841	6.08 ± 0.03	4.686	5.33 ± 0.08	1.308	5.88 ± 0.09	4.823	5.32 ± 0.12
B-233	0.207	6.69 ± 0.06	3.313	5.48 ± 0.07	0.450	6.35 ± 0.04	1.402	5.85 ± 0.17
B-234	6.448	5.19 ± 0.07	14.313	4.84 ± 0.09	6.658	5.18 ± 0.14	13.594	4.87 ± 0.08
B-235	1.681	5.77 ± 0.07	10.976	4.96 ± 0.07	1.457	5.84 ± 0.08	7.762	5.11 ± 0.13
B-236	0.310	6.51 ± 0.09	1.913	5.72 ± 0.28	0.676	6.17 ± 0.05	2.493	5.60 ± 0.15
B-237	0.113	6.95 ± 0.09	0.659	6.18 ± 0.38	0.404	6.39 ± 0.04	2.273	5.64 ± 0.38
B-238	3.574	5.45 ± 0.16	10.266	4.99 ± 0.00	5.799	5.24 ± 0.14	14.566	4.84 ± 0.07
B-239	15.296	4.82 ± 0.09	11.988	4.92 ± 0.05	7.413	5.13 ± 0.14	16.853	4.77 ± 0.07
B-240	0.938	6.03 ± 0.08	10.041	5.00 ± 0.03	2.556	5.59 ± 0.23	11.134	4.95 ± 0.05
B-241	0.050	7.30 ± 0.12	0.646	6.19 ± 0.09	0.291	6.54 ± 0.41	2.862	5.54 ± 0.31
B-242	0.066	7.18 ± 0.09	1.728	5.76 ± 0.10	0.105	6.98 ± 0.21	1.613	5.79 ± 0.38
B-243	0.101	7.00 ± 0.21	2.305	5.64 ± 0.19	0.238	6.62 ± 0.19	1.783	5.75 ± 0.25
B-244	0.110	6.96 ± 0.05	1.580	5.80 ± 0.23	0.170	6.76 ± 0.14	0.540	6.26 ± 0.14
B-245	0.442	6.35 ± 0.05	6.472	5.19 ± 0.08	0.759	6.12 ± 0.15	6.839	5.17 ± 0.16

Table S7. Activity of 5-NI test compounds against *Giarda lamblia*

	G. lamblia 713				*G. lamblia* 106			
	MzS		MzR		MzS		MzR	
Compound	EC50 (µM)	pEC50	EC50 (µM)	pEC50	EC50 (µM)	pEC50	EC50 (µM)	pEC50
B-246	0.878	6.06 ± 0.03	9.396	5.03 ± 0.05	0.944	6.03 ± 0.17	7.630	5.12 ± 0.18
B-247	0.177	6.75 ± 0.03	2.924	5.53 ± 0.06	0.339	6.47 ± 0.16	3.126	5.51 ± 0.28
C-201	1.257	5.90 ± 0.15	12.812	4.89 ± 0.07	2.291	5.64 ± 0.04	14.191	4.85 ± 0.06
C-202	0.180	6.74 ± 0.06	1.497	5.82 ± 0.03	0.161	6.79 ± 0.14	2.793	5.55 ± 0.27
C-203	0.486	6.31 ± 0.05	3.930	5.41 ± 0.09	0.851	6.07 ± 0.03	10.046	5.00 ± 0.12
C-204	> 20	< 4.70	> 20	< 4.70	0.329	6.48 ± 0.06	4.385	5.36 ± 0.19
C-205	3.226	5.49 ± 0.05	13.692	4.86 ± 0.06	3.575	5.45 ± 0.11	11.570	4.94 ± 0.03
C-206	1.838	5.74 ± 0.05	7.529	5.12 ± 0.05	1.660	5.78 ± 0.15	10.312	4.99 ± 0.02
C-207	0.366	6.44 ± 0.04	5.487	5.26 ± 0.14	0.486	6.31 ± 0.11	3.162	5.50 ± 0.11
C-208	0.439	6.36 ± 0.13	7.045	5.15 ± 0.18	2.326	5.63 ± 0.14	11.307	4.95 ± 0.03
C-209	0.212	6.67 ± 0.08	3.109	5.51 ± 0.08	1.965	5.71 ± 0.13	9.848	5.01 ± 0.06
C-210	0.544	6.26 ± 0.06	6.891	5.16 ± 0.10	1.175	5.93 ± 0.07	7.762	5.11 ± 0.07
C-211	0.831	6.08 ± 0.05	8.989	5.05 ± 0.06	2.291	5.64 ± 0.10	10.391	4.98 ± 0.05
C-212	2.917	5.54 ± 0.02	10.164	4.99 ± 0.06	3.415	5.47 ± 0.10	9.333	5.03 ± 0.15
C-213	2.044	5.69 ± 0.02	11.988	4.92 ± 0.03	1.920	5.72 ± 0.02	10.391	4.98 ± 0.02
C-214	1.181	5.93 ± 0.04	7.727	5.11 ± 0.03	1.765	5.75 ± 0.05	12.092	4.92 ± 0.07
C-215	3.696	5.43 ± 0.05	7.203	5.14 ± 0.21	4.571	5.34 ± 0.13	11.839	4.93 ± 0.02
C-216	3.297	5.48 ± 0.07	9.035	5.04 ± 0.06	4.169	5.38 ± 0.04	11.659	4.93 ± 0.03
C-217	2.209	5.66 ± 0.03	6.322	5.20 ± 0.15	1.792	5.75 ± 0.07	12.686	4.90 ± 0.04
C-218	3.961	5.40 ± 0.09	11.469	4.94 ± 0.14	3.773	5.42 ± 0.18	12.957	4.89 ± 0.06
C-219	0.357	6.45 ± 0.03	4.029	5.39 ± 0.11	0.380	6.42 ± 0.04	5.689	5.25 ± 0.08
C-220	0.075	7.13 ± 0.07	0.996	6.00 ± 0.17	0.098	7.01 ± 0.13	2.929	5.53 ± 0.25
C-221	2.733	5.56 ± 0.04	13.099	4.88 ± 0.09	2.309	5.64 ± 0.10	11.220	4.95 ± 0.02
C-222	0.436	6.36 ± 0.04	10.273	4.99 ± 0.14	0.347	6.46 ± 0.14	4.332	5.36 ± 0.08
C-223	1.676	5.78 ± 0.09	8.989	5.05 ± 0.21	2.436	5.61 ± 0.07	14.566	4.84 ± 0.08
C-224	0.136	6.87 ± 0.05	12.812	4.89 ± 0.10	0.776	6.11 ± 0.01	9.441	5.03 ± 0.13
C-225	2.546	5.59 ± 0.07	8.226	5.08 ± 0.19	0.412	6.39 ± 0.00	7.328	5.14 ± 0.20
C-226	0.067	7.18 ± 0.02	8.046	5.09 ± 0.20	0.519	6.29 ± 0.09	4.241	5.37 ± 0.24
C-227	0.039	7.40 ± 0.07	6.891	5.16 ± 0.06	1.647	5.78 ± 0.54	7.630	5.12 ± 0.18
C-228	0.449	6.35 ± 0.20	12.257	4.91 ± 0.11	1.765	5.75 ± 0.53	5.991	5.22 ± 0.20
C-229	0.256	6.59 ± 0.04	12.812	4.89 ± 0.10	4.137	5.38 ± 0.34	9.550	5.02 ± 0.12
C-230	0.139	6.86 ± 0.17	8.037	5.09 ± 0.16	3.773	5.42 ± 0.36	9.016	5.05 ± 0.12
C-231	0.251	6.60 ± 0.18	5.884	5.23 ± 0.31	4.898	5.31 ± 0.31	7.079	5.15 ± 0.24
C-232	1.053	5.98 ± 0.26	9.453	5.02 ± 0.05	4.105	5.39 ± 0.34	7.718	5.11 ± 0.17
C-233	0.178	6.75 ± 0.06	6.485	5.19 ± 0.21	1.090	5.96 ± 0.42	6.109	5.21 ± 0.11
C-234	0.142	6.85 ± 0.01	6.839	5.17 ± 0.26	2.138	5.67 ± 0.09	12.764	4.89 ± 0.05
C-235	0.081	7.09 ± 0.10	5.772	5.24 ± 0.29	1.107	5.96 ± 0.08	12.417	4.91 ± 0.09
C-236	0.264	6.58 ± 0.08	6.741	5.17 ± 0.15	0.583	6.23 ± 0.02	5.572	5.25 ± 0.08
C-237	1.208	5.92 ± 0.09	4.682	5.33 ± 0.18	0.191	6.72 ± 0.09	3.020	5.52 ± 0.21
C-238	1.744	5.76 ± 0.08	11.469	4.94 ± 0.04	2.205	5.66 ± 0.06	10.391	4.98 ± 0.02
C-239	3.990	5.40 ± 0.06	14.960	4.83 ± 0.06	3.388	5.47 ± 0.12	13.490	4.87 ± 0.09
C-240	1.220	5.91 ± 0.10	7.189	5.14 ± 0.09	0.961	6.02 ± 0.12	4.898	5.31 ± 0.05
C-241	0.455	6.34 ± 0.40	5.632	5.25 ± 0.15	0.087	7.06 ± 0.24	0.730	6.14 ± 0.34
C-242	3.162	5.50 ± 0.03	9.396	5.03 ± 0.11	0.094	7.03 ± 0.06	2.222	5.65 ± 0.27
C-243	1.533	5.81 ± 0.09	5.030	5.30 ± 0.23	0.098	7.01 ± 0.10	1.298	5.89 ± 0.15
C-244	0.443	6.35 ± 0.01	4.642	5.33 ± 0.03	0.214	6.67 ± 0.10	6.709	5.17 ± 0.22
C-245	1.983	5.70 ± 0.11	11.469	4.94 ± 0.08	0.713	6.15 ± 0.03	5.580	5.25 ± 0.15

Table S7. Activity of 5-NI test compounds against *Giarda lamblia*

	G. lamblia 713				*G. lamblia* 106			
	MzS		MzR		MzS		MzR	
Compound	EC50 (µM)	pEC50	EC50 (µM)	pEC50	EC50 (µM)	pEC50	EC50 (µM)	pEC50
C-246	0.540	6.27 ± 0.17	6.448	5.19 ± 0.14	2.358	5.63 ± 0.31	7.278	5.14 ± 0.23
C-247	3.549	5.45 ± 0.12	11.217	4.95 ± 0.07	0.556	6.26 ± 0.18	8.954	5.05 ± 0.20
D-201	17.769	4.75 ± 0.05	13.117	4.88 ± 0.09	10.881	4.96 ± 0.15	11.682	4.93 ± 0.03
D-202	1.750	5.76 ± 0.12	12.008	4.92 ± 0.12	5.453	5.26 ± 0.04	10.715	4.97 ± 0.03
D-203	15.689	4.80 ± 0.04	16.000	4.80 ± 0.05	10.233	4.99 ± 0.10	17.920	4.75 ± 0.05
D-204	12.482	4.90 ± 0.11	15.651	4.81 ± 0.06	7.356	5.13 ± 0.15	11.931	4.92 ± 0.02
D-205	14.328	4.84 ± 0.07	12.413	4.91 ± 0.10	10.174	4.99 ± 0.13	11.954	4.92 ± 0.02
D-206	9.620	5.02 ± 0.03	13.861	4.86 ± 0.08	11.156	4.95 ± 0.09	15.488	4.81 ± 0.06
D-207	8.148	5.09 ± 0.09	12.831	4.89 ± 0.10	10.000	5.00 ± 0.04	14.678	4.83 ± 0.07
D-208	5.474	5.26 ± 0.15	11.641	4.93 ± 0.12	9.829	5.01 ± 0.03	> 20	< 4.70
D-209	4.596	5.34 ± 0.15	12.551	4.90 ± 0.10	11.416	4.94 ± 0.06	16.982	4.77 ± 0.03
D-210	14.803	4.83 ± 0.06	> 20	< 4.70	7.189	5.14 ± 0.31	16.218	4.79 ± 0.05
D-211	14.482	4.84 ± 0.06	15.233	4.82 ± 0.07	12.209	4.91 ± 0.11	14.791	4.83 ± 0.06
D-212	12.405	4.91 ± 0.03	13.747	4.86 ± 0.06	10.155	4.99 ± 0.18	12.303	4.91 ± 0.03
D-213	14.804	4.83 ± 0.07	18.986	4.72 ± 0.02	11.749	4.93 ± 0.13	12.809	4.89 ± 0.04
D-215	13.117	4.88 ± 0.09	> 20	< 4.70	8.577	5.07 ± 0.21	9.441	5.03 ± 0.04
D-216	13.410	4.87 ± 0.09	> 20	< 4.70	9.050	5.04 ± 0.22	8.810	5.06 ± 0.07
D-217	5.982	5.22 ± 0.05	> 20	< 4.70	9.261	5.03 ± 0.21	10.715	4.97 ± 0.08
D-218	13.861	4.86 ± 0.08	16.539	4.78 ± 0.08	9.550	5.02 ± 0.21	9.698	5.01 ± 0.04
D-219	8.190	5.09 ± 0.16	16.178	4.79 ± 0.09	9.441	5.03 ± 0.05	13.107	4.88 ± 0.04
D-220	2.883	5.54 ± 0.40	16.218	4.79 ± 0.09	6.958	5.16 ± 0.30	9.716	5.01 ± 0.12
D-221	12.827	4.89 ± 0.04	14.810	4.83 ± 0.07	6.346	5.20 ± 0.20	10.654	4.97 ± 0.11
D-222	19.303	4.71 ± 0.01	> 20	< 4.70	14.791	4.83 ± 0.08	14.706	4.83 ± 0.06
D-223	> 20	< 4.70	> 20	< 4.70	16.032	4.80 ± 0.07	18.478	4.73 ± 0.03
D-224	10.987	4.96 ± 0.02	17.477	4.76 ± 0.06	8.175	5.09 ± 0.09	11.614	4.94 ± 0.08
D-225	4.402	5.36 ± 0.06	16.539	4.78 ± 0.05	3.236	5.49 ± 0.27	10.715	4.97 ± 0.01
D-226	8.151	5.09 ± 0.05	16.178	4.79 ± 0.06	10.798	4.97 ± 0.03	6.683	5.18 ± 0.20
D-227	10.987	4.96 ± 0.02	17.477	4.76 ± 0.06	6.556	5.18 ± 0.30	8.810	5.06 ± 0.08
D-228	8.906	5.05 ± 0.02	17.096	4.77 ± 0.07	8.777	5.06 ± 0.03	12.445	4.91 ± 0.04
D-229	16.178	4.79 ± 0.05	17.477	4.76 ± 0.06	10.155	4.99 ± 0.19	10.881	4.96 ± 0.03
D-230	12.544	4.90 ± 0.02	16.722	4.78 ± 0.08	13.284	4.88 ± 0.09	10.881	4.96 ± 0.00
D-231	13.109	4.88 ± 0.07	16.908	4.77 ± 0.07	13.082	4.88 ± 0.09	11.394	4.94 ± 0.04
D-232	12.969	4.89 ± 0.04	16.908	4.77 ± 0.07	13.698	4.86 ± 0.10	13.284	4.88 ± 0.09
D-233	8.903	5.05 ± 0.06	18.066	4.74 ± 0.04	9.333	5.03 ± 0.06	13.594	4.87 ± 0.08
D-234	11.166	4.95 ± 0.01	17.477	4.76 ± 0.06	12.303	4.91 ± 0.13	10.312	4.99 ± 0.02
D-235	11.543	4.94 ± 0.01	15.651	4.81 ± 0.07	9.550	5.02 ± 0.11	12.023	4.92 ± 0.11
D-236	8.705	5.06 ± 0.07	16.722	4.78 ± 0.08	3.744	5.43 ± 0.14	4.043	5.39 ± 0.30
D-237	2.068	5.68 ± 0.05	14.171	4.85 ± 0.10	3.211	5.49 ± 0.12	10.965	4.96 ± 0.09
D-238	14.810	4.83 ± 0.13	18.266	4.74 ± 0.04	7.244	5.14 ± 0.13	13.082	4.88 ± 0.09
D-239	16.357	4.79 ± 0.09	17.285	4.76 ± 0.06	7.943	5.10 ± 0.13	12.115	4.92 ± 0.05
D-240	2.095	5.68 ± 0.15	16.539	4.78 ± 0.05	2.951	5.53 ± 0.03	12.256	4.91 ± 0.07
D-241	0.696	6.16 ± 0.31	12.690	4.90 ± 0.04	2.205	5.66 ± 0.35	11.526	4.94 ± 0.12
D-242	4.019	5.40 ± 0.02	> 20	< 4.70	3.744	5.43 ± 0.12	11.482	4.94 ± 0.05
D-243	3.756	5.43 ± 0.03	19.734	4.70 ± 0.00	3.575	5.45 ± 0.04	11.220	4.95 ± 0.05
D-244	8.065	5.09 ± 0.08	19.303	4.71 ± 0.01	6.658	5.18 ± 0.16	11.570	4.94 ± 0.05
D-245	10.167	4.99 ± 0.03	> 20	< 4.70	7.300	5.14 ± 0.19	7.762	5.11 ± 0.08
D-246	8.804	5.06 ± 0.08	17.477	4.76 ± 0.06	7.413	5.13 ± 0.17	7.943	5.10 ± 0.13

Table S7. Activity of 5-NI test compounds against *Giarda lamblia*

	G. lamblia 713				*G. lamblia* 106			
	MzS		MzR		MzS		MzR	
Compound	EC50 (µM)	pEC50	EC50 (µM)	pEC50	EC50 (µM)	pEC50	EC50 (µM)	pEC50
D-247	3.519	5.45 ± 0.04	15.141	4.82 ± 0.06	8.382	5.08 ± 0.05	11.482	4.94 ± 0.10
E-201	0.103	6.99 ± 0.03	1.862	5.73 ± 0.10	0.118	6.93 ± 0.03	2.154	5.67 ± 0.09
E-202	0.039	7.41 ± 0.27	0.596	6.22 ± 0.09	0.034	7.47 ± 0.12	0.182	6.74 ± 0.13
E-203	0.011	7.97 ± 0.19	0.241	6.62 ± 0.12	0.040	7.39 ± 0.16	0.201	6.70 ± 0.16
E-204	0.023	7.63 ± 0.15	0.728	6.14 ± 0.10	0.023	7.64 ± 0.19	0.316	6.50 ± 0.09
E-205	0.075	7.12 ± 0.17	1.639	5.79 ± 0.16	0.263	6.58 ± 0.06	3.126	5.51 ± 0.43
E-206	0.165	6.78 ± 0.28	1.479	5.83 ± 0.13	0.165	6.78 ± 0.32	2.884	5.54 ± 0.13
E-207	0.019	7.73 ± 0.29	0.334	6.48 ± 0.06	0.047	7.33 ± 0.10	0.468	6.33 ± 0.14
E-208	0.016	7.81 ± 0.30	0.453	6.34 ± 0.10	0.272	6.57 ± 0.19	0.940	6.03 ± 0.25
E-209	0.358	6.45 ± 0.15	6.077	5.22 ± 0.27	1.028	5.99 ± 0.13	8.446	5.07 ± 0.12
E-210	0.006	8.22 ± 0.09	0.188	6.73 ± 0.14	0.054	7.27 ± 0.06	0.231	6.64 ± 0.12
E-211	0.043	7.37 ± 0.22	1.288	5.89 ± 0.06	0.363	6.44 ± 0.07	2.906	5.54 ± 0.16
E-212	0.161	6.79 ± 0.13	2.309	5.64 ± 0.25	0.449	6.35 ± 0.11	1.660	5.78 ± 0.16
E-213	0.014	7.87 ± 0.06	0.293	6.53 ± 0.04	0.073	7.13 ± 0.05	0.475	6.32 ± 0.10
E-214	0.042	7.38 ± 0.08	0.215	6.67 ± 0.10	0.257	6.59 ± 0.12	1.047	5.98 ± 0.16
E-215	0.039	7.41 ± 0.50	6.166	5.21 ± 0.00	0.412	6.39 ± 0.05	3.687	5.43 ± 0.10
E-216	0.209	6.68 ± 0.17	1.047	5.98 ± 0.00	0.100	7.00 ± 0.17	2.362	5.63 ± 0.09
E-217	0.156	6.81 ± 0.34	0.240	6.62 ± 0.00	0.229	6.64 ± 0.42	0.336	6.47 ± 0.29
E-218	1.684	5.77 ± 0.02	5.204	5.28 ± 0.16	1.916	5.72 ± 0.07	9.120	5.04 ± 0.04
E-219	0.014	7.84 ± 0.19	0.801	6.10 ± 0.34	0.037	7.44 ± 0.03	0.203	6.69 ± 0.24
E-220	0.016	7.80 ± 0.24	1.008	6.00 ± 0.46	0.086	7.07 ± 0.38	0.203	6.69 ± 0.61
E-221	0.044	7.36 ± 0.08	0.453	6.34 ± 0.24	0.147	6.83 ± 0.18	0.427	6.37 ± 0.12
E-222	0.008	8.09 ± 0.06	0.179	6.75 ± 0.29	0.045	7.35 ± 0.12	0.804	6.10 ± 0.22
E-223	0.020	7.69 ± 0.31	0.302	6.52 ± 0.19	0.123	6.91 ± 0.14	0.272	6.57 ± 0.11
E-224	0.010	7.99 ± 0.10	0.576	6.24 ± 0.21	0.023	7.64 ± 0.16	0.550	6.26 ± 0.25
E-225	0.012	7.92 ± 0.09	0.186	6.73 ± 0.48	0.066	7.18 ± 0.26	0.507	6.30 ± 0.71
E-226	0.008	8.08 ± 0.03	0.397	6.40 ± 0.25	0.026	7.58 ± 0.16	1.035	5.99 ± 0.35
E-227	0.026	7.59 ± 0.08	0.437	6.36 ± 0.57	0.053	7.27 ± 0.11	1.380	5.86 ± 0.35
E-228	0.011	7.96 ± 0.26	0.118	6.93 ± 0.26	0.046	7.34 ± 0.27	0.238	6.62 ± 0.53
E-229	0.021	7.67 ± 0.22	0.261	6.58 ± 0.15	0.056	7.26 ± 0.12	0.309	6.51 ± 0.19
E-230	0.005	8.31 ± 0.07	0.227	6.64 ± 0.16	0.028	7.56 ± 0.16	0.195	6.71 ± 0.25
E-231	0.036	7.44 ± 0.05	0.610	6.21 ± 0.10	0.169	6.77 ± 0.13	1.148	5.94 ± 0.52
E-232	0.010	8.02 ± 0.09	0.151	6.82 ± 0.21	0.028	7.56 ± 0.06	0.224	6.65 ± 0.03
E-233	0.123	6.91 ± 0.10	1.482	5.83 ± 0.31	0.510	6.29 ± 0.23	8.128	5.09 ± 0.05
E-234	0.049	7.31 ± 0.06	0.764	6.12 ± 0.27	0.170	6.77 ± 0.11	0.933	6.03 ± 0.08
E-235	0.018	7.74 ± 0.12	0.282	6.55 ± 0.11	0.104	6.98 ± 0.24	0.764	6.12 ± 0.03
E-236	0.009	8.04 ± 0.04	0.238	6.62 ± 0.13	0.034	7.47 ± 0.01	0.314	6.50 ± 0.04
E-237	0.019	7.71 ± 0.25	0.055	7.26 ± 0.09	0.084	7.08 ± 0.12	0.970	6.01 ± 0.06
E-238	0.012	7.91 ± 0.32	0.122	6.91 ± 0.37	0.045	7.35 ± 0.16	0.236	6.63 ± 0.27
E-239	0.284	6.55 ± 0.05	1.479	5.83 ± 0.21	0.631	6.20 ± 0.08	6.506	5.19 ± 0.13
E-240	0.013	7.90 ± 0.14	0.464	6.33 ± 0.06	0.142	6.85 ± 0.28	0.510	6.29 ± 0.29
E-241	0.020	7.71 ± 0.08	0.439	6.36 ± 0.11	0.102	6.99 ± 0.21	1.148	5.94 ± 0.31
E-242	0.013	7.88 ± 0.06	1.205	5.92 ± 0.09	0.031	7.51 ± 0.10	0.884	6.05 ± 0.23
E-243	0.034	7.47 ± 0.06	1.700	5.77 ± 0.15	0.080	7.10 ± 0.25	1.080	5.97 ± 0.16
E-244	0.025	7.61 ± 0.12	0.553	6.26 ± 0.16	0.071	7.15 ± 0.08	3.603	5.44 ± 0.29
E-245	0.003	8.59 ± 0.21	0.157	6.80 ± 0.11	0.083	7.08 ± 0.23	0.118	6.93 ± 0.20
E-246	0.003	8.52 ± 0.11	0.122	6.91 ± 0.25	0.033	7.48 ± 0.11	0.265	6.58 ± 0.20

Table S7. Activity of 5-NI test compounds against *Giarda lamblia*

	G. lamblia 713				*G. lamblia* 106			
	MzS		MzR		MzS		MzR	
Compound	EC50 (µM)	pEC50	EC50 (µM)	pEC50	EC50 (µM)	pEC50	EC50 (µM)	pEC50
E-247	0.005	8.29 ± 0.29	0.261	6.58 ± 0.08	0.040	7.40 ± 0.22	0.562	6.25 ± 0.29
F-201	0.788	6.10 ± 0.04	3.586	5.45 ± 0.16	2.291	5.64 ± 0.07	10.715	4.97 ± 0.02
F-202	0.088	7.06 ± 0.29	0.874	6.06 ± 0.15	0.269	6.57 ± 0.08	1.096	5.96 ± 0.09
F-203	0.343	6.47 ± 0.33	4.633	5.33 ± 0.18	0.859	6.07 ± 0.11	4.145	5.38 ± 0.08
F-204	0.148	6.83 ± 0.19	1.553	5.81 ± 0.13	0.369	6.43 ± 0.06	1.995	5.70 ± 0.10
F-205	1.975	5.70 ± 0.37	3.112	5.51 ± 0.12	1.549	5.81 ± 0.04	6.879	5.16 ± 0.11
F-206	1.094	5.96 ± 0.24	1.359	5.87 ± 0.02	8.643	5.06 ± 0.16	12.589	4.90 ± 0.07
F-207	0.521	6.28 ± 0.57	3.008	5.52 ± 0.28	0.884	6.05 ± 0.10	2.441	5.61 ± 0.19
F-208	0.341	6.47 ± 0.14	5.095	5.29 ± 0.20	1.905	5.72 ± 0.11	5.991	5.22 ± 0.15
F-209	0.184	6.74 ± 0.24	1.744	5.76 ± 0.28	2.692	5.57 ± 0.12	10.233	4.99 ± 0.05
F-210	1.259	5.90 ± 0.08	6.653	5.18 ± 0.14	3.548	5.45 ± 0.08	4.332	5.36 ± 0.13
F-211	1.898	5.72 ± 0.03	3.659	5.44 ± 0.09	6.865	5.16 ± 0.20	7.244	5.14 ± 0.11
F-212	0.471	6.33 ± 0.10	2.406	5.62 ± 0.12	2.512	5.60 ± 0.11	4.713	5.33 ± 0.16
F-213	0.697	6.16 ± 0.04	4.550	5.34 ± 0.08	2.818	5.55 ± 0.13	4.860	5.31 ± 0.17
F-214	2.166	5.66 ± 0.08	4.768	5.32 ± 0.05	6.813	5.17 ± 0.06	4.606	5.34 ± 0.20
F-215	1.019	5.99 ± 0.08	1.774	5.75 ± 0.00	6.213	5.21 ± 0.04	4.332	5.36 ± 0.17
F-216	1.820	5.74 ± 0.03	2.818	5.55 ± 0.00	5.329	5.27 ± 0.05	4.137	5.38 ± 0.21
F-217	1.072	5.97 ± 0.03	0.065	7.19 ± 0.00	5.089	5.29 ± 0.37	6.407	5.19 ± 0.11
F-218	0.524	6.28 ± 0.28	1.367	5.86 ± 0.28	3.802	5.42 ± 0.26	2.929	5.53 ± 0.31
F-219	0.290	6.54 ± 0.17	2.956	5.53 ± 0.17	0.839	6.08 ± 0.13	3.199	5.50 ± 0.06
F-220	0.431	6.37 ± 0.14	2.691	5.57 ± 0.14	1.698	5.77 ± 0.34	3.055	5.52 ± 0.60
F-221	2.710	5.57 ± 0.29	3.420	5.47 ± 0.20	4.898	5.31 ± 0.29	5.843	5.23 ± 0.15
F-222	0.195	6.71 ± 0.05	1.445	5.84 ± 0.06	0.259	6.59 ± 0.23	1.479	5.83 ± 0.05
F-223	3.499	5.46 ± 0.03	14.256	4.85 ± 0.11	3.802	5.42 ± 0.32	4.299	5.37 ± 0.20
F-224	0.110	6.96 ± 0.13	1.393	5.86 ± 0.07	0.168	6.78 ± 0.16	0.912	6.04 ± 0.19
F-225	0.057	7.24 ± 0.18	0.776	6.11 ± 0.09	0.293	6.53 ± 0.55	0.318	6.50 ± 0.18
F-226	0.054	7.27 ± 0.11	0.744	6.13 ± 0.07	0.089	7.05 ± 0.18	0.351	6.46 ± 0.19
F-227	0.053	7.27 ± 0.07	3.258	5.49 ± 0.24	0.053	7.28 ± 0.10	0.372	6.43 ± 0.18
F-228	0.056	7.25 ± 0.13	1.600	5.80 ± 0.12	0.080	7.10 ± 0.11	1.820	5.74 ± 0.12
F-229	1.063	5.97 ± 0.10	4.596	5.34 ± 0.08	2.138	5.67 ± 0.26	4.299	5.37 ± 0.17
F-230	0.724	6.14 ± 0.12	3.718	5.43 ± 0.08	2.171	5.66 ± 0.20	3.890	5.41 ± 0.16
F-231	2.679	5.57 ± 0.13	7.786	5.11 ± 0.20	4.365	5.36 ± 0.26	2.951	5.53 ± 0.31
F-232	0.404	6.39 ± 0.08	3.499	5.46 ± 0.04	1.113	5.95 ± 0.22	2.380	5.62 ± 0.19
F-233	0.978	6.01 ± 0.09	8.825	5.05 ± 0.20	0.427	6.37 ± 0.05	7.025	5.15 ± 0.19
F-234	2.046	5.69 ± 0.06	5.563	5.25 ± 0.06	2.862	5.54 ± 0.34	4.043	5.39 ± 0.21
F-235	0.029	7.54 ± 0.22	0.565	6.25 ± 0.09	0.077	7.11 ± 0.13	0.464	6.33 ± 0.09
F-236	0.319	6.50 ± 0.01	3.631	5.44 ± 0.04	0.533	6.27 ± 0.24	1.725	5.76 ± 0.15
F-237	0.056	7.25 ± 0.13	0.409	6.39 ± 0.19	0.224	6.65 ± 0.19	0.116	6.94 ± 0.03
F-238	0.070	7.15 ± 0.33	0.955	6.02 ± 0.18	0.525	6.28 ± 0.27	2.344	5.63 ± 0.20
F-239	2.215	5.65 ± 0.06	7.786	5.11 ± 0.08	3.388	5.47 ± 0.29	5.168	5.29 ± 0.16
F-240	0.088	7.06 ± 0.22	0.760	6.12 ± 0.09	0.110	6.96 ± 0.13	1.965	5.71 ± 0.37
F-241	0.676	6.17 ± 0.16	9.201	5.04 ± 0.09	0.730	6.14 ± 0.27	9.477	5.02 ± 0.05
F-242	0.066	7.18 ± 0.24	1.198	5.92 ± 0.15	0.263	6.58 ± 0.14	1.193	5.92 ± 0.01
F-243	0.092	7.03 ± 0.10	3.565	5.45 ± 0.08	0.113	6.95 ± 0.20	1.175	5.93 ± 0.15
F-244	6.673	5.18 ± 0.23	19.649	4.71 ± 0.01	8.191	5.09 ± 0.14	10.077	5.00 ± 0.02
F-245	0.129	6.89 ± 0.12	3.388	5.47 ± 0.39	0.336	6.47 ± 0.04	4.545	5.34 ± 0.18
F-246	0.490	6.31 ± 0.01	5.204	5.28 ± 0.11	2.089	5.68 ± 0.10	8.861	5.05 ± 0.06

Table S7. Activity of 5-NI test compounds against *Giarda lamblia*

	G. lamblia 713				*G. lamblia* 106			
	MzS		MzR		MzS		MzR	
Compound	EC50 (µM)	pEC50	EC50 (µM)	pEC50	EC50 (µM)	pEC50	EC50 (µM)	pEC50
F-247	0.340	6.47 ± 0.11	8.861	5.05 ± 0.08	0.905	6.04 ± 0.09	3.920	5.41 ± 0.07

Activity against two Mz-sensitive (MzS) isolates of *G. lamblia* , 713 and 106, and their syngeneic Mz-resistant (MzR) derivative lines, was determined as EC50 (in µM; geometric mean, n=3-6 experiments), the compound concentration that inhibits parasite growth by 50%, and is also shown as negative log10 value of the EC50 (pEC50; mean ± SE, n=3-6 experiments).

Table S8. Cytotoxicity in human cells and therapeutic ratio of 5-NI compounds

	HeLa		MzS *G. lamblia*	Therapeutic ratio
Compound	CC50 (μM)	pCC50	EC50 (μM)	CC50/EC50
Mz	> 50	< 4.30	1.995	> 25
A-201	> 50	< 4.30	12.531	> 4
A-202	> 50	< 4.30	0.161	> 311
A-203	> 50	< 4.30	0.438	> 114
A-204	> 50	< 4.30	0.179	> 279
A-205	> 50	< 4.30	2.970	> 17
A-206	26.48	4.58 ± 0.58	1.076	25
A-207	> 50	< 4.30	0.456	> 110
A-208	> 50	< 4.30	0.299	> 167
A-209	> 50	< 4.30	0.070	> 719
A-210	> 50	< 4.30	1.061	> 47
A-211	> 50	< 4.30	1.253	> 40
A-212	> 50	< 4.30	2.600	> 19
A-213	> 50	< 4.30	2.273	> 22
A-214	> 50	< 4.30	1.662	> 30
A-215	> 50	< 4.30	7.529	> 7
A-216	> 50	< 4.30	18.670	> 3
A-217	> 50	< 4.30	0.858	> 58
A-218	> 50	< 4.30	> 20	N/A
A-219	> 50	< 4.30	0.225	> 222
A-220	37.69	4.42 ± 0.47	0.038	994
A-221	> 50	< 4.30	12.439	> 4
A-222	> 50	< 4.30	1.607	> 31
A-223	> 50	< 4.30	2.558	> 20
A-224	> 50	< 4.30	0.419	> 119
A-225	> 50	< 4.30	0.164	> 304
A-226	> 50	< 4.30	0.393	> 127
A-227	> 50	< 4.30	0.198	> 253
A-228	> 50	< 4.30	0.183	> 273
A-229	> 50	< 4.30	3.359	> 15
A-230	> 50	< 4.30	1.700	> 29
A-231	> 50	< 4.30	1.916	> 26
A-232	> 50	< 4.30	1.139	> 44
A-233	> 50	< 4.30	0.196	> 255
A-234	> 50	< 4.30	8.226	> 6
A-235	> 50	< 4.30	2.487	> 20
A-236	> 50	< 4.30	0.124	> 404
A-237	> 50	< 4.30	0.033	> 1508
A-238	> 50	< 4.30	0.667	> 75
A-239	> 50	< 4.30	12.812	> 4
A-240	> 50	< 4.30	0.141	> 355
A-241	> 50	< 4.30	0.049	> 1023
A-242	> 50	< 4.30	0.112	> 445

Table S8. Cytotoxicity in human cells and therapeutic ratio of 5-NI compounds

	HeLa		MzS *G. lamblia*	Therapeutic ratio
Compound	CC50 (μM)	pCC50	EC50 (μM)	CC50/EC50
A-243	> 50	< 4.30	0.057	> 880
A-244	> 50	< 4.30	0.165	> 303
A-245	> 50	< 4.30	0.902	> 55
A-246	> 50	< 4.30	1.986	> 25
A-247	> 50	< 4.30	0.352	> 142
B-201	> 50	< 4.30	5.053	> 10
B-202	> 50	< 4.30	0.352	> 142
B-203	> 50	< 4.30	0.578	> 86
B-204	> 50	< 4.30	0.345	> 145
B-205	> 50	< 4.30	6.448	> 8
B-206	> 50	< 4.30	1.963	> 25
B-207	> 50	< 4.30	0.236	> 212
B-208	> 50	< 4.30	0.346	> 144
B-209	13.14	4.88 ± 0.44	0.210	62
B-210	> 50	< 4.30	0.844	> 59
B-211	> 50	< 4.30	1.064	> 47
B-212	> 50	< 4.30	3.625	> 14
B-213	> 50	< 4.30	1.388	> 36
B-214	> 50	< 4.30	1.834	> 27
B-215	> 50	< 4.30	13.392	> 4
B-216	> 50	< 4.30	9.190	> 5
B-217	> 50	< 4.30	0.860	> 58
B-218	> 50	< 4.30	8.599	> 6
B-219	> 50	< 4.30	0.278	> 180
B-220	> 50	< 4.30	0.101	> 493
B-221	> 50	< 4.30	2.622	> 19
B-222	> 50	< 4.30	1.806	> 28
B-223	43.24	4.36 ± 0.19	1.621	27
B-224	> 50	< 4.30	0.247	> 203
B-225	> 50	< 4.30	0.099	> 506
B-226	> 50	< 4.30	0.291	> 172
B-227	> 50	< 4.30	0.285	> 176
B-228	> 50	< 4.30	0.322	> 155
B-229	> 50	< 4.30	1.081	> 46
B-230	> 50	< 4.30	1.993	> 25
B-231	> 50	< 4.30	5.984	> 8
B-232	> 50	< 4.30	0.841	> 59
B-233	> 50	< 4.30	0.207	> 242
B-234	> 50	< 4.30	6.448	> 8
B-235	> 50	< 4.30	1.681	> 30
B-236	> 50	< 4.30	0.310	> 161
B-237	> 50	< 4.30	0.113	> 441
B-238	> 50	< 4.30	3.574	> 14

Table S8. Cytotoxicity in human cells and therapeutic ratio of 5-NI compounds

	HeLa		MzS *G. lamblia*	Therapeutic ratio
Compound	CC50 (μM)	pCC50	EC50 (μM)	CC50/EC50
B-239	> 50	< 4.30	15.296	> 3
B-240	> 50	< 4.30	0.938	> 53
B-241	> 50	< 4.30	0.050	> 1008
B-242	> 50	< 4.30	0.066	> 763
B-243	> 50	< 4.30	0.101	> 495
B-244	> 50	< 4.30	0.110	> 455
B-245	> 50	< 4.30	0.442	> 113
B-246	> 50	< 4.30	0.878	> 57
B-247	> 50	< 4.30	0.177	> 282
C-201	> 50	< 4.30	1.257	> 40
C-202	> 50	< 4.30	0.180	> 277
C-203	> 50	< 4.30	0.486	> 103
C-204	> 50	< 4.30	> 20	N/A
C-205	> 50	< 4.30	3.226	> 15
C-206	> 50	< 4.30	1.838	> 27
C-207	> 50	< 4.30	0.366	> 137
C-208	> 50	< 4.30	0.439	> 114
C-209	27.41	4.56 ± 0.32	0.212	129
C-210	> 50	< 4.30	0.544	> 92
C-211	> 50	< 4.30	0.831	> 60
C-212	> 50	< 4.30	2.917	> 17
C-213	> 50	< 4.30	2.044	> 24
C-214	> 50	< 4.30	1.181	> 42
C-215	> 50	< 4.30	3.696	> 14
C-216	> 50	< 4.30	3.297	> 15
C-217	> 50	< 4.30	2.209	> 23
C-218	> 50	< 4.30	3.961	> 13
C-219	> 50	< 4.30	0.357	> 140
C-220	41.37	4.38 ± 0.04	0.075	555
C-221	> 50	< 4.30	2.733	> 18
C-222	> 50	< 4.30	0.436	> 115
C-223	> 50	< 4.30	1.676	> 30
C-224	> 50	< 4.30	0.136	> 368
C-225	> 50	< 4.30	2.546	> 20
C-226	> 50	< 4.30	0.067	> 752
C-227	> 50	< 4.30	0.039	> 1270
C-228	> 50	< 4.30	0.449	> 111
C-229	> 50	< 4.30	0.256	> 195
C-230	> 50	< 4.30	0.139	> 359
C-231	> 50	< 4.30	0.251	> 199
C-232	> 50	< 4.30	1.053	> 47
C-233	> 50	< 4.30	0.178	> 281
C-234	> 50	< 4.30	0.142	> 351

Table S8. Cytotoxicity in human cells and therapeutic ratio of 5-NI compounds

	HeLa		MzS *G. lamblia*	Therapeutic ratio
Compound	CC50 (μM)	pCC50	EC50 (μM)	CC50/EC50
C-235	> 50	< 4.30	0.081	> 621
C-236	> 50	< 4.30	0.264	> 190
C-237	> 50	< 4.30	1.208	> 41
C-238	> 50	< 4.30	1.744	> 29
C-239	> 50	< 4.30	3.990	> 13
C-240	> 50	< 4.30	1.220	> 41
C-241	> 50	< 4.30	0.455	> 110
C-242	> 50	< 4.30	3.162	> 16
C-243	> 50	< 4.30	1.533	> 33
C-244	> 50	< 4.30	0.443	> 113
C-245	> 50	< 4.30	1.983	> 25
C-246	> 50	< 4.30	0.540	> 93
C-247	> 50	< 4.30	3.549	> 14
D-201	> 50	< 4.30	17.769	> 3
D-202	> 50	< 4.30	1.750	> 29
D-203	> 50	< 4.30	15.689	> 3
D-204	> 50	< 4.30	12.482	> 4
D-205	> 50	< 4.30	14.328	> 3
D-206	> 50	< 4.30	9.620	> 5
D-207	> 50	< 4.30	8.148	> 6
D-208	49.36	4.31 ± 0.11	5.474	9
D-209	> 50	< 4.30	4.596	> 11
D-210	> 50	< 4.30	14.803	> 3
D-211	> 50	< 4.30	14.482	> 3
D-212	> 50	< 4.30	12.405	> 4
D-213	> 50	< 4.30	14.804	> 3
D-215	> 50	< 4.30	13.117	> 4
D-216	> 50	< 4.30	13.410	> 4
D-217	> 50	< 4.30	5.982	> 8
D-218	> 50	< 4.30	13.861	> 4
D-219	> 50	< 4.30	8.190	> 6
D-220	48.28	4.32 ± 0.00	2.883	17
D-221	> 50	< 4.30	12.827	> 4
D-222	43.56	4.36 ± 0.36	19.303	2
D-223	> 50	< 4.30	> 20	N/A
D-224	> 50	< 4.30	10.987	> 5
D-225	> 50	< 4.30	4.402	> 11
D-226	> 50	< 4.30	8.151	> 6
D-227	> 50	< 4.30	10.987	> 5
D-228	> 50	< 4.30	8.906	> 6
D-229	> 50	< 4.30	16.178	> 3
D-230	> 50	< 4.30	12.544	> 4
D-231	> 50	< 4.30	13.109	> 4

Table S8. Cytotoxicity in human cells and therapeutic ratio of 5-NI compounds

	HeLa		MzS *G. lamblia*	Therapeutic ratio
Compound	CC50 (μM)	pCC50	EC50 (μM)	CC50/EC50
D-232	> 50	< 4.30	12.969	> 4
D-233	> 50	< 4.30	8.903	> 6
D-234	> 50	< 4.30	11.166	> 4
D-235	> 50	< 4.30	11.543	> 4
D-236	> 50	< 4.30	8.705	> 6
D-237	> 50	< 4.30	2.068	> 24
D-238	> 50	< 4.30	14.810	> 3
D-239	> 50	< 4.30	16.357	> 3
D-240	> 50	< 4.30	2.095	> 24
D-241	> 50	< 4.30	0.696	> 72
D-242	> 50	< 4.30	4.019	> 12
D-243	> 50	< 4.30	3.756	> 13
D-244	> 50	< 4.30	8.065	> 6
D-245	> 50	< 4.30	10.167	> 5
D-246	> 50	< 4.30	8.804	> 6
D-247	> 50	< 4.30	3.519	> 14
E-201	> 50	< 4.30	0.103	> 487
E-202	> 50	< 4.30	0.039	> 1272
E-203	> 50	< 4.30	0.011	> 4663
E-204	> 50	< 4.30	0.023	> 2130
E-205	> 50	< 4.30	0.075	> 664
E-206	48.75	4.31 ± 0.26	0.165	296
E-207	39.20	4.41 ± 0.13	0.019	2099
E-208	37.51	4.43 ± 0.43	0.016	2411
E-209	> 50	< 4.30	0.358	> 140
E-210	> 50	< 4.30	0.006	> 8362
E-211	> 50	< 4.30	0.043	> 1172
E-212	> 50	< 4.30	0.161	> 311
E-213	> 50	< 4.30	0.014	> 3678
E-214	> 50	< 4.30	0.042	> 1199
E-215	> 50	< 4.30	0.039	> 1275
E-216	> 50	< 4.30	0.209	> 239
E-217	30.20	4.52 ± 0.03	0.156	193
E-218	> 50	< 4.30	1.684	> 30
E-219	> 50	< 4.30	0.014	> 3457
E-220	> 50	< 4.30	0.016	> 3140
E-221	> 50	< 4.30	0.044	> 1145
E-222	> 50	< 4.30	0.008	> 6184
E-223	36.14	4.44 ± 0.06	0.020	1784
E-224	> 50	< 4.30	0.010	> 4879
E-225	> 50	< 4.30	0.012	> 4181
E-226	> 50	< 4.30	0.008	> 6058
E-227	47.46	4.32 ± 0.32	0.026	1851

Table S8. Cytotoxicity in human cells and therapeutic ratio of 5-NI compounds

	HeLa		MzS *G. lamblia*	Therapeutic ratio
Compound	CC50 (μM)	pCC50	EC50 (μM)	CC50/EC50
E-228	36.78	4.43 ± 0.43	0.011	3339
E-229	> 50	< 4.30	0.021	> 2346
E-230	> 50	< 4.30	0.005	> 10264
E-231	> 50	< 4.30	0.036	> 1377
E-232	> 50	< 4.30	0.010	> 5244
E-233	> 50	< 4.30	0.123	> 406
E-234	> 50	< 4.30	0.049	> 1013
E-235	> 50	< 4.30	0.018	> 2723
E-236	> 50	< 4.30	0.009	> 5440
E-237	> 50	< 4.30	0.019	> 2590
E-238	> 50	< 4.30	0.012	> 4024
E-239	> 50	< 4.30	0.284	> 176
E-240	> 50	< 4.30	0.013	> 3944
E-241	> 50	< 4.30	0.020	> 2537
E-242	> 50	< 4.30	0.013	> 3822
E-243	> 50	< 4.30	0.034	> 1479
E-244	> 50	< 4.30	0.025	> 2015
E-245	> 50	< 4.30	0.003	> 19304
E-246	> 50	< 4.30	0.003	> 16430
E-247	> 50	< 4.30	0.005	> 9785
F-201	> 50	< 4.30	0.788	> 63
F-202	> 50	< 4.30	0.088	> 568
F-203	> 50	< 4.30	0.343	> 146
F-204	> 50	< 4.30	0.148	> 339
F-205	> 50	< 4.30	1.975	> 25
F-206	> 50	< 4.30	1.094	> 46
F-207	> 50	< 4.30	0.521	> 96
F-208	> 50	< 4.30	0.341	> 147
F-209	41.99	4.38 ± 0.07	0.184	228
F-210	> 50	< 4.30	1.259	> 40
F-211	> 50	< 4.30	1.898	> 26
F-212	> 50	< 4.30	0.471	> 106
F-213	> 50	< 4.30	0.697	> 72
F-214	> 50	< 4.30	2.166	> 23
F-215	> 50	< 4.30	1.019	> 49
F-216	> 50	< 4.30	1.820	> 27
F-217	> 50	< 4.30	1.072	> 47
F-218	> 50	< 4.30	0.524	> 95
F-219	> 50	< 4.30	0.290	> 173
F-220	46.54	4.33 ± 0.03	0.431	108
F-221	> 50	< 4.30	2.710	> 18
F-222	> 50	< 4.30	0.195	> 256
F-223	> 50	< 4.30	3.499	> 14

Table S8. Cytotoxicity in human cells and therapeutic ratio of 5-NI compounds

	HeLa		MzS *G. lamblia*	Therapeutic ratio
Compound	CC50 (μM)	pCC50	EC50 (μM)	CC50/EC50
F-224	> 50	< 4.30	0.110	> 455
F-225	> 50	< 4.30	0.057	> 874
F-226	> 50	< 4.30	0.054	> 924
F-227	> 50	< 4.30	0.053	> 940
F-228	> 50	< 4.30	0.056	> 897
F-229	> 50	< 4.30	1.063	> 47
F-230	> 50	< 4.30	0.724	> 69
F-231	> 50	< 4.30	2.679	> 19
F-232	> 50	< 4.30	0.404	> 124
F-233	> 50	< 4.30	0.978	> 51
F-234	> 50	< 4.30	2.046	> 24
F-235	> 50	< 4.30	0.029	> 1751
F-236	> 50	< 4.30	0.319	> 157
F-237	> 50	< 4.30	0.056	> 897
F-238	> 50	< 4.30	0.070	> 712
F-239	> 50	< 4.30	2.215	> 23
F-240	> 50	< 4.30	0.088	> 571
F-241	> 50	< 4.30	0.676	> 74
F-242	> 50	< 4.30	0.066	> 757
F-243	> 50	< 4.30	0.092	> 541
F-244	> 50	< 4.30	6.673	> 7
F-245	> 50	< 4.30	0.129	> 388
F-246	> 50	< 4.30	0.490	> 102
F-247	45.19	4.34 ± 0.00	0.340	133

Toxicity against the human HeLa cells was determined as CC50 (in μM; geometric mean, n=3-6 experiments), the compound concentration that kills 50% of HeLa cells in a cytotoxicity assay, is also shown as negative log10 value of the CC50 (pCC50; mean ± SE, n=3-6 experiments). Therapeutic ratio, the ratio of CC50 in HeLa cells to EC50 of *G. lamblia* (strain 713), reflects the relative selectivity of compound potency against *Giardia* compared to cytotoxicity in HeLa cells, with higher ratios indicating greater selectivity for the parasite.