Supporting Information

Synthesis, antiplasmodial and antimycobacterial evaluation of new nitroimidazole and nitroimidazooxazine derivatives

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Table of Contents

1. Synthesis and characterization of compounds 8-16

• 1.1 General

Chemical reagents used were supplied by either Sigma-Aldrich® or Merck and were used without further purification. The (*S*)-2-nitro-6,7-dihydro-5H-imidazo[2,1-*b*][1,3]oxazin-6-ol (**6**) was purchased from AAT Pharmaceuticals, New Jersey, USA. Unless otherwise stated, all the solvents used were anhydrous and were purchased from Sigma-Aldrich, with the exception of THF and diethyl ether which were dried by appropriate techniques. Chromatographic solvents such as Ethyl acetate, dichloromethane and Hexane were purchased from Kimix or Protea Chemicals and were distilled prior to use. Column chromatography was carried out using Merck Kieselgel 60: particle size 70– 230 mesh as a stationary phase. Analytical TLC was carried out using Merck PF_{254} aluminium-backed pre-coated silica gel plates and visualized under UV light or iodine vapour. Melting points were determined on a Reichert-Jung Thermovar hot-stage microscope and are uncorrected. Low-resolution mass spectra were obtained by flow-injection (5 mM NH_4 formate pH3 in H_2O:ACN, no column used) on a AB SCIEX 4000 QTRAP Hybrid triple quadrupole linear ion trap mass spectrometer, coupled with an Agilent 1200 Rapid Resolution (600 bar) HPLC system consisting of a binary pump, degasser, auto sampler and temperature controlled column compartment. Infra-red spectra were recorded on a PerkinElmer Spectrum 100 FT-IR spectrometer in the 4000 – 450 cm^{-1} range, with samples either as dichloromethane solution or as KBr discs. NMR spectra were recorded on Bruker 400 MHz or Varian Unity 400 MHz and/or Varian Mercury 300 MHz spectrometers, all chemical shifts are reported in ppm and were referenced using solvent signals (2.50 and 39.4 ppm for DMSO-d_6 and 7.26 and 77.0 ppm for $CDCl_3$). Chemical shifts (δ) are recorded in parts per million (ppm). Coupling constants, *J*, are measured in Hertz (Hz) and rounded off to one decimal place. Abbreviations used in the assignment of the ^1H NMR spectra are as follows: br (broad), d (doublet), dd (doublet of doublets), m (multiplets), s (singlet) and t (triplet). ^{13}C NMR chemical shifts are listed without assignment to specific carbon atoms. Purity was determined by HPLC, and all compounds were confirmed to have purity >95%. Sample solutions for purification were prepared at *ca.* 100 mg/mL in 50% methanol. Injection volumes ranged between 50 □L and 1 mL, the mobile phase flow rate was 20 mL/min for all purifications and the

column heater was set at 30°C. A mobile phase gradient was used, where mobile phase A, an aqueous solution of 0.1% formic acid, was mixed on-line with mobile phase B, a 0.1% formic acid solution in methanol.

1.2 General procedure[1] for the synthesis of compounds 8a-b

At 0 °C, under N_2 atmosphere, NaH (60% mineral oil, 1.3 eq) was added to the stirred solution of *p*, *m* and *o*-(bromomethyl)benzaldehydes (1.2 eq) (**7a-c**) and (*S*)-2-nitro-6,7-dihydro-5H-imidazo[2,1-*b*][1,3]oxazin-6-ol (**6**) (1.0 eq) in anhydrous DMF (5 ml). The resultant mixture was maintained at this temperature for 30 minutes, allowed to warm to room temperature and stirred further for 12 hrs. On completion of the reaction as seen on the TLC, the solvent was removed in *vacuo* by azeotropic distillation of toluene to afford crude products **8a-b** (*m*- and *p*-based products). The *o*-(bromomethyl)benzaldehyde reaction did not work as evidence by the recovery of starting materials. The crude products were then purified by column chromatography (on silica gel; elution with DCM: MeOH; 95:05).

4-{[(*S*)-6,7-*dihydro*-2-*nitro*-5H-*imidazo*[2,1-*b*][1,3]*oxazin*-6-*yloxy*]*methyl*}*benzaldehyde* (**8a**)

Yield (91 mg) 46%; m. p. 145- 148 °C, R_f (DCM: MeOH, 95: 05%) 0.27; IR ν_{max} (DCM)/cm^{-1} 1699 (C=O), 1579 (Ar C=C), 1548 (NO_2), 1266 (C-O Ether); δ_H (400 MHz; DMSO-*d6*) 9.99 (1H, s, C*H*O), 8.02 (1H, s, H1), 7.89 (2H, d, *J* 8.1 Hz, 2 x H7), 7.52 (2H, d, *J* 8.1 Hz, 2 x H6), 4.77 (2H, d, *J* 3.2 Hz, H5), 4.49 (1H, dt, *J* 2.6 and 12.1 Hz, H3), 4.48 (1H, d, *J* 11.9 Hz, H*4a*), 4.28 (3H, m, H2 and H*4b*); δ_C (101 MHz; DMSO-*d6*) 193.1, 147.6, 145.2, 136.0, 130.0 (2C), 128.2 (2C), 127.1, 118.4, 69.6, 68.4, 62.9 and 47.2; MS (ESI) *m*/*z* 304.1 (M^++H), HPLC purity: 98.9%; $t_{r'}$=6.98 min.

4-{[(*S*)-6,7-*dihydro*-2-*nitro*-5H-*imidazo*[2,1-*b*][1,3]*oxazin*-6-*yloxy*]*methyl*}*benzaldehyde* (**8b**)

Yield (131 mg) 78%; m. p. 129- 132 °C, R_f (DCM: MeOH, 95: 05%) 0.22; IR ν_{max} (DCM)/cm^{-1} 1685 (C=O), 1569 (Ar C=C), 1538 (NO_2), 1245 (C-O Ether); δ_H (400 MHz; DMSO-*d6*) 10.01 (1H, s, C*H*O), 7.99 (1H, s, H1), 7.83 (2H, m, H8 and H9), 7.65 (1H, t, *J* 7.7 Hz, H7), 7.60 (1H, d, *J* 7.7 Hz, H6), 4.76 (2H, d, *J* 1.9 Hz, H5), 4.66 (1H, dt, *J* 4.7 and 11.9 Hz, H3), 4.49 (1H, d, *J* 11.6 Hz, H3*a*), 4.28 (3H, m, H2 and H3*b*); δ_C (101 MHz; DMSO-*d6*) 192.8, 148.3, 143.2, 138.3, 135.9, 133.3, 129.0, 128.8, 127.9, 117.7, 68.9, 67.7, 66.5 and 46.5; MS (ESI) *m*/*z* 304.2 (M^++H), HPLC purity: 93.6%; t_r=7.29 min.

1.3 General procedure[2] for the synthesis of compounds 9a-h

The nitroimidazo-oxazine aldehyde **8a-b** (0.099 mmol) and various amine (including 4-amino-7chloroquinoline diamines)[§] (0.207 mmol) were stirred in anhydrous methanol as a suspension at 26 °C for 5 minutes. Thereafter, $TMSN_3$ (0.207 mmol) was added, followed by the addition of *tert*-butyl isocyanide (0.207 mmol) and the resulting mixture was then further stirred at 40 °C for 12 hrs. Thereafter, the solvent was removed in *vacuo* to afford the crude tetrazoles which were purified by column chromatography (on silica gel; elution with DCM: MeOH; 95:05) and/or HPLC to give the desired products, **9a-h**, in modest to excellent yields.

(4-{[(*S*)-6,7-*dihydro*-2-*nitro*-5H-*imidazo*[2,1-*b*][1,3]*oxazin*-6-*yloxy*]*methyl*}*phenyl*)(1-tert-*butyl*-1H-*tetrazol*-5-*yl*)-N,N-*dimethylmethanamine* (**9a**)

Yield (25 mg) 46%; m. p. 68- 72 °C, R_f (DCM: MeOH, 95: 05%) 0.32; IR ν_{max} (DCM)/cm^{-1} 1588 (Ar C=C), 1566 (NO_2), 1368 (N=N), 1340 (C=N), 1284 (C-O Ether); δ_H (400 MHz; $CDCl_3$) 7.42 (2H, d, *J* 8.0 Hz, 2 x H7), 7.37 (1H, d, *J* 12.9 Hz, H1), 7.27 (2H, d, *J* 8.0 Hz, 2 x H6), 5.19 (1H, s, H8), 4.72 (1H, m, H3), 4.59 (2H, m, H5), 4.35 (1H, d, *J* 12.1 Hz, H4*a*), 4.17

§ HCl protected amines were neutralized by addition of the base, diisopropyl ethylamine (2 eq)

(3H, m, H2 and H*4b*), 2.29 (6H, s, 2 x H9), 1.69 (9H, s, 3 x H10); δ_C (101 MHz; $CDCl_3$) 154.3, 147.2, 136.9, 136.0, 130.1 (2C), 127.6 (2C), 127.0, 115.0, 70.7, 67.4, 66.7, 65.0, 63.2, 47.5; 42.4 (2C) and 30.2 (3C); MS (ESI) *m*/*z* 457.3 (M^+), HPLC purity: 97.5%; t_r=8.30 min.

N-(4-{[((*S*)-6,7-*dihydro*-2-*nitro*-5H-*imidazo*[2,1-*b*][1,3]*oxazin*-6-*yloxy*)*methyl*]*pheny*}(1-tert-*butyl*-1H-*tetrazol*-5-*yl*)*methyl*)-N-*dimethylmethanamine* (**9b**)

Yield (30.2 mg, 63%); m. p. 48- 50 °C, R_f (DCM: MeOH, 95: 05%) 0.46; IR ν_{max} (DCM)/cm^{-1} 1601 (Ar C=C), 1536 (NO_2), 1378 (N=N), 1340 (C=N), 1260 (C-O Ether); δ_H (400 MHz; $CDCl_3$) 7.37 (1H, d, *J* 15.0 Hz, H1), 7.25 (4H,m, 2 x H6 and 2 x H7), 5.61 (1H, s, H8), 4.72 (1H, m, H3), 4.59 (2H, m, H5), 4.34 (1H, d, *J* 12.3 Hz, H*4a*), 4.16 (3H, m, H2 and H*4b*), 2.78 (2H, q, *J* 7.1 Hz, H*9a*), 2.65 (2H, q, *J* 7.1 Hz, H*9b*), 1.66 (9H, s, 3 x H11), 0.95 (6H, t, *J* 7.1 Hz, 2 x H10); δ_C (101 MHz; $CDCl_3$) 154.7, 147.1, 138.0, 136.4, 136.3, 129.7 (2C), 127.5 (2C), 127.4, 114.9, 70.8, 67.4, 67.3, 60.6, 47.5; 44.8 (2C), 30.3 (3C) and 14.1 (2C); MS (ESI) *m*/*z* 485.4 (M^++H), HPLC purity: 98.9%; t_r=8.06 min.

(*S*)-6-{4-[(1-tert-*butyl*-1H-*tetrazol*-5-*yl*)(*pyrrolidin*-1-*yl*)*methyl]benzyloxy*}-6,7-*dihydro*-2-*nitro*-5H-*imidazo*[2,1-*b*][1,3]*oxazine*, (**9c**)

Yield (21 mg) 44%; m. p. 58- 61 °C, R_f (DCM: MeOH, 95: 05%) 0.39; IR ν_{max} (DCM)/cm^{-1} 1604 (Ar C=C), 1520 (NO_2), 1380 (N=N), 1360 (C=N), 1263 (C-O Ether); δ_H (300 MHz; $CDCl_3$) 7.50 (2H, d, *J* 8.1 Hz, 2 x H7), 7.37 (1H, d, *J* 6.7 Hz, H1), 7.26 (2H, d, *J* 8.1 Hz, 2 x H6), 5.20 (1H, s, H8), 4.72 (1H, m, H3), 4.62 (2H, m, H5), 4.34 (1H, d, *J* 12.1 Hz, H*4a*), 4.17 (3H, m, H2 and H*4b*), 2.59 (2H, m, H*9a*), 2.49 (2H, m, H*9b*), 1.79 (4H, m, 2 x H10), 1.68 (9H, s, 3 x H11); δ_C (75 MHz; $CDCl_3$) 155.5, 147.2, 136.1, 127.4, 123.1, 121.9 (2C), 119.2 (2C), 118.3, 79.9, 67.4, 63.2, 53.0, 52.2, 52.1, 41.2 (2C), 30.2 (3C) and 24.6 (2C); MS (ESI) *m*/*z* 483.4 (M^++H), HPLC purity: 99.6%; t_r=7.68 min.

N-{2-[(4-{[((*S*)-6,7-*dihydro*-2-*nitro*-5H-*imidazo*[2,1-*b*][1,3]*oxazin*-6-*yloxy*)*methyl*]*pheny*}(1-tert-*butyl*-1H-*tetrazol*-5-*yl*)*methylamino*)*ethyl*]}-7-*chloroquinolin-4-amine*, (**9d**)

Yield (27 mg) 65%; m. p. 87- 89 °C, R_f (DCM: MeOH, NH_4OH, 94: 5.5: 0.5%) 0.16; IR ν_{max} (DCM)/cm^{-1} 1610 (Ar C=C), 1550 (NO_2), 1390 (N=N), 1369 (C=N), 1250 (C-O Ether); δ_H (400 MHz; DMSO-*d6*) 8.35 (1H, d, *J* 5.4 Hz, H2'), 8.20 (1H, d, *J* 9.1 Hz, H5'), 7.99 (1H, d, *J* 4.3 Hz, H1), 7.77 (1H, d, *J* 2.2 Hz, H8'), 7.43 (3H, m, 2 x H7 and H6'), 7.26 (2H, d, *J* 8.1 Hz, 2 x H6), 7.18 (1H, t, *J* 5.3 Hz, NH), 6.43 (1H, d, *J* 5.4 Hz, H3'), 5.53 (1H, s, H8), 4.63 (3H, m, H3 and H5), 4.46 (1H, d, *J* 11.9 Hz, H*4a*), 4.23 (3H, m, H2 and H*4b*), 3.35 (2H, m, H9), 4.30 (1H, br m, NH), 2.78 (2H, m, H10), 1.62 (9H, s, 3 x H11); δ_C (101 MHz; DMSO-*d6*) 158.2, 155.8, 151.7 (2C), 149.9, 148.9, 146.5, 138.6, 137.1, 133.2, 128.1 (2C), 127.5 (2C), 127.4 (2C), 123.9, 123.8, 117.8, 98.6, 69.2, 67.7, 66.3, 55.8 46.6, 45.1; 42.5 and 29.2 (3C); MS (ESI) *m/z* 633.5 (M^+), HPLC purity: 96.2%; $t_{r'}$=8.44 min.

N-{3-[(4-{[((*S*)-6,7-*dihydro*-2-*nitro*-5H-*imidazo*[2,1-*b*][1,3]*oxazin*-6-*yloxy*)*methyl*]*pheny*}(1-tert-*butyl*-1H-*tetrazol*-5-*yl*)*methylamino*)*propyl*]}-7-*chloroquinolin-4-amine*, (**9e**)

Yield (20 mg) 47%; m. p. 95- 99 °C, R_f (DCM: MeOH, NH_4OH, 94: 5.5: 0.5%) 0.35; IR ν_{max} (DCM)/cm^{-1} 1613 (Ar C=C), 1576 (NO_2), 1369 (N=N), 1387 (C=N), 1265 (C-O Ether); δ_H (400 MHz; $CDCl_3$) 8.45 (1H, d, *J* 5.3 Hz, H2'), 7.86 (1H, d, *J* 2.2 Hz, H8'), 7.27 (6H, m, 2 x H7, 2 x H6, H1 and H5'), 7.15 (1H, br s, NH), 6.95 (1H, dd, *J* 9.0 and 2.2 Hz, H6'), 6.29 (1H, d, *J* 5.3 Hz, H3'), 5.30 (1H, s, H8), 4.73 (1H, m, H3), 4.63 (2H, dd, *J* 12.1 and 3.5Hz, H5), 4.36 (1H, d, *J* 12.1 Hz, H*4a*), 4.18 (3H, m, H2 and H*4b*), 3.41 (2H, m, H9), 2.88 (1H, m, H*11a*), 2.79 (1H, m, H*11b*), 1.92 (2H, m, H10), 1.53 (9H, s, 3 x H12); δ_C (101 MHz; $CDCl_3$) 156.7, 155.2, 152.0 (2C), 150.2, 149.0, 147.0, 144.1, 143.7, 138.3, 137.4, 134.4, 128.4 (2C), 128.3, 128.2, 124.8, 122.1, 117.4, 98.4, 70.5, 67.2, 67.1, 61.6, 59.0, 47.8, 47.4; 43.5 and 29.8 (3C); MS (ESI) *m/z* 647.4 (M^+), HPLC purity: 99.2%; $t_{r'}$=8.61 min.

N-{4-[(4-{[((*S*)-6,7-*dihydro*-2-*nitro*-5H-*imidazo*[2,1-*b*][1,3]*oxazin*-6-*yloxy*)*methyl*]*pheny*}(1-tert-*butyl*-1H-*tetrazol*-5-*yl*)*methylamino*)*butyl*]}-7-*chloroquinolin-4-amine*, (**9f**)

Yield (37 mg) 85%; m. p. 82- 86 °C, R_f (DCM: MeOH, NH_4OH, 94: 5.5: 0.5%) 0.32; IR ν_{max} (DCM)/cm^{-1} 1619 (Ar C=C), 1555 (NO_2), 1388 (N=N), 1360 (C=N), 1248 (C-O Ether); δ_H (400 MHz; $CDCl_3$) 8.48 (1H, d, *J* 5.4 Hz, H2'), 7.92 (1H, d, *J* 2.0 Hz, H8'), 7.57 (1H, dd, *J* 9.2 and 2.0 Hz, H6'), 7.33 (1H, d, *J* 6.5 Hz, H1), 7.24 (5H, m, 2 x H7, 2 x H6 and H5'), 6.37 (1H, d, *J* 5.4 Hz, H3'), 5.48 (1H, m, NH), 5.27 (1H, s, H8), 4.67 (1H, m, H3), 4.60 (2H, m, H5), 4.32 (1H, d, *J* 11.7 Hz, H4*a*), 4.12 (3H, m, H2 and H4*b*), 3.32 (2H, m, H12), 2.62 (2H, m, H9), 1.83 (2H, m, H11), 1.69 (2H, m, H10), 1.61 (9H, s, 3 x H13); δ_C (101 MHz; $CDCl_3$) 157.4, 155.5, 151.9 (2C), 149.9, 149.8, 138.9, 137.1, 137.0, 128.6, 128.5, 128.3 (2C), 128.1, 128.0, 125.1, 121.2, 115.0, 99.0, 70.6, 67.3, 67.2, 66.9, 66.8, 58.8, 47.5, 42.9, 30.1 (3C), 27.4 and 26.3; MS (ESI) *m*/*z* 661.5 (M^+), HPLC purity: 96.9%; $t_{r'}$=8.66 min.

N-{5-[(4-{[((*S*)-6,7-*dihydro*-2-*nitro*-5H-*imidazo*[2,1-*b*][1,3]*oxazin*-6-*yloxy*)*methyl*]*pheny*}(1-tert-*butyl*-1H-*tetrazol*-5-*yl*)*methylamino*)*pentan*-2-*yl*]}-6-*methoxyquinolin-8-amine* (**9g**)

Yield (55 mg) 83% (1:1 diastereomeric mixture); R_f (DCM: MeOH, 95: 05%) 0.48; IR ν_{max} (DCM)/cm^{-1} 1601 (Ar C=C), 1539 (NO_2), 1388 (N=N), 1338 (C=N), 1238 (C-O Ester); δ_H (300 MHz; $CDCl_3$) 8.59 (1H, s, H1), 8.50 (1H, dd, *J* 4.2 and 1.6 Hz, H2'), 7.91 (1H, dd, *J* 8.3 and 1.6 Hz, H4'), 7.36 (1H, dd, *J* 8.7 and 4.4 Hz, H3'), 7.31 (2H, m, H7), 7.22 (2H, m, H6), 6.32 (1H, d, *J* 2.5 Hz, H7'), 6.24 (1H, t, *J* 2.8 Hz, H5'), 6.01 (1H, br m, NH), 5.24-5.26 (1H, 2 x s, H8), 4.68 (1H, d, *J* 12.2 Hz, H3), 4.57 (2H, m, H5), 4.31 (1H, d, *J* 12.4 Hz, H4*a*), 4.12 (3H, m, H2 and H4*b*), 3.88 (3H, s, OCH_3), 3.57 (1H, m, H12), 2.56 (2H, m, H9), 1.64 (4H, m, H10 and H11), 1.59-1.60 (9H, 2 x s, 3 x H14), 1.27 (3H, d, *J* 6.3 Hz, H13); δ_C (75 MHz; $CDCl_3$) 159.5, 155.6, 145.0, 144.3, 143.8, 139.7, 136.6, 134.8, 129.9, 128.5 (2C), 128.2, 128.1 (2C), 127.4, 121.8, 114.9, 96.6, 91.6, 70.6, 67.3, 67.2, 66.4, 58.5, 55.2, 47.9; 47.5, 47.4, 34.2, 29.8 (3C), 26.5 and 20.6; MS (ESI) *m*/*z* 671.6 (M^++H), HPLC purity: 98.7%; $t_{r'}$=8.52 min.

N-{5-[(3-{[((*S*)-6,7-*dihydro*-2-*nitro*-5H-*imidazo*[2,1-*b*][1,3]*oxazin*-6-*yloxy*)*methyl*]*pheny*}(1-tert-*butyl*-1H-*tetrazol*-5-*yl*)*methylamino*)*pentan*-2-*yl*]}-6-*methoxyquinolin-8-amine* (**9h**)

Yield (140 mg) 79% (1:1 diastereomeric mixture); R_f (DCM: MeOH, 95: 05%) 0.52; IR ν_{max} (DCM)/cm^{-1} 1610 (Ar C=C), 1545 (NO_2), 1390 (N=N), 1340 (C=N), 1228 (C-O Ester); δ_H (400 MHz; $CDCl_3$) 8.50 (1H, s, H1), 8.49 (1H, dd, *J* 4.2 and 1.7 Hz, H2'), 7.90 (1H, dd, *J* 8.3 and 1.6 Hz, H4'), 7.32 (1H, s, H9), 7.31 (2H, m, H3' and H8), 7.20 (2H, m, H6 and H7), 6.32 (1H, d, *J* 2.5 Hz, H7'), 6.24 (1H, dd, *J* 6.8 and 2.7 Hz, H5'), 5.99 (1H, br m, NH), 5.25-5.27 (1H, 2 x s, H10), 4.66 (1H, m, H3), 4.54 (2H, m, H5), 4.26 (1H, m, H*4a*), 4.09 (3H, m, H2 and H*4b*), 3.86-3.87 (3H, 2 x s, OCH_3), 3.59 (1H, m, H14), 2.55 (2H, m, H11), 1.72 (9H, s, 3 x H16), 1.66 (4H, m, H12 and H13), 1.27-1.29 (3H, 2 x d, *J* 5.9 and 6.3 Hz, H15); δ_C (101 MHz; $CDCl_3$) 159.5, 155.7, 145.0, 144.2, 139.7, 137.5, 135.3, 134.8, 129.9, 129.2, 128.1, 127.6, 127.5, 127.0, 121.9, 115.1, 96.7, 91.6, 70.9, 67.7, 66.5, 66.4, 58.6, 55.2, 47.9; 47.8, 47.4, 34.3, 29.9 (3C), 26.5 and 20.6; MS (ESI) *m/z* 671.9 (M^++H); HPLC purity: 95.6%; $t_{r'}$=8.55 min.

1.4 General procedure for the synthesis of compounds 11a-b

To a suspension of **10a/10b** (2.1 mmol) in anhydrous THF (10 ml) under inert nitrogen atmosphere was added TEA (4.2 mmol) and the resulting mixture cooled to below 0°C. Methanesulfonyl chloride (2.2 mmol) was then added slowly while keeping the temperature below 5°C. On complete addition of methanesulfonyl chloride the reaction was stirred in an ice bath for 45 minutes. Upon complete consumption of the alcohol, as evidence by TLC, the reaction mixture was diluted with saturated $NaHCO_3$ solution and extracted with ether (3 x 30 ml). The organic extracts were then dried over $MgSO_4$, filtered, and evaporated to give **11a-b** in reasonable purity and good yields.

*2-((7-Chloroquinolin-4-yl)amino)ethyl methanesulfonate (**11a**)*

Yield (430 mg) 65%; m. p. 134-135 ^{o}C; R_f (DCM: MeOH, 9:1%) 0.58; δ_H (400 MHz; $CDCl_3$): 8.46 (1H, d, *J* 5.4 Hz, H2), 7.91 (1H, d, *J* 9 Hz, H5), 7.73 (1H, d, *J* 2.2 Hz, H8), 7.33 (1H, dd, *J* 2.2 and 9 Hz, H6), 6.35 (1H ,d, *J* 5.4 Hz, H3), 5.83 (1H, bs, NH), 4.53 (2H, t, *J* 5.9 Hz, 2 x H2'), 3.66 (2H, t, *J* 5.9 Hz, 2 x H1'), 3.08 (3H, s, SO_2Me).

*3-((7-Chloroquinolin-4-yl)amino)propyl methanesulfonate (**11b**)*

Yield (0.4 g) 60%; m. p. 128-129 ^{o}C; R_f (DCM: MeOH, 9:1%) 0.52; δ_H (400 MHz; $CDCl_3$): 8.55 (1H, d, *J* 5.3 Hz, H2), 7.97 (1H, d, *J* 8.9 Hz, H5), 7.70 (1H, d, *J* 2.1 Hz, H8), 7.40 (1H, dd, *J* 2.1 and 8.9 Hz, H6), 6.43 (1H ,d, *J* 5.3 Hz, H3), 5.44(1H, bs, NH), 4.41 (2H, t, *J* 5.7 Hz, 2 x H3'), 3.59 (2H, m, 2 x H1'), 3.05 (3H, s, SO_2Me), 2.18 (2H, m, 2 x H2').

1.5 General procedure for the synthesis of compounds 12a-b

Intermediate **11a/11b** (1.66 mmol) was cooled to 0^{o}C and *N*-methyl ethanolamine (33.2 mmol) added drop-wise over a period of 10-15 minutes at this temperature. On complete addition of *N*-methyl ethanolamine, TEA (11.25 mmol) was added drop wise to the mixture. The reaction was allowed to warm to room temperature and stirred for one hour. Then the reaction temperature was raised to 45-55^{o}C and further stirred for 4 hours. On completion of the reaction, H_2O(50 ml) was added and the reaction extracted with ethyl acetate(3 x 50 ml).The organic layers were combined, washed with brine, dried over $MgSO_4$, filtered and evaporation in *vacuo* to afford **12a/b**.

*2[{2-[(7-Chloroquinolin-4-yl)amino]ethyl}-(methyl)amino]ethanol (**12a**)*

Yield (0.372 g) 80%; m. p. 106-107 ^{o}C; R_f (DCM: MeOH, 9:1%) 0.14; δ_H (400 MHz; CD_3OD): 8.34 (1H, d, *J* 5.6 Hz, H2), 8.06 (1H, d, *J* 9 Hz, H5), 7.77 (1H, d, *J* 2.1 Hz, H8), 7.40 (1H, dd, *J* 2.1 and 9 Hz, H6), 6.43 (1H, d, *J* 5.6 Hz, H3), 5.44 (1H, bs, NH), 3.67 (2H, t, *J* 5.7 Hz, 2 x H4'), 3.44 (2H, t, *J* 6.4 Hz, 2 x H1'), 2.78-2.61 (4H, m, 2 x H2' and H3'),

2.36(3H, s, NCH_3); δ_c (100 MHz; CD_3OD): 151.1, 151, 148.1, 134.9, 126.1, 124.6, 122.8, 117.3, 98.3, 58.9, 58.8, 55.1, 41.2 and 40.1; MS (ESI) *m/z* 279.1(M^+); HPLC purity: 98.6%; $t_{r'}$=13.4 min.

*2[{3-[(7-Chloroquinolin-4-yl)amino]propyl}-(methyl)amino]ethanol (**12b**)*

Yield (0.349 g) 75%; m. p. 115-116 ^oC; R_f (DCM: MeOH, 9:1%) 0.12; δ_H (400 MHz; CD3OD): 8.34 (1H, d, *J* 5.6 Hz, H2), 8.06 (1H, d, *J* 9Hz, H5), 7.77 (1H, d, *J* 2.1 Hz, H8), 7.40 (1H, dd, *J* 2.1 and 9 Hz, H6), 6.43 (1H, d, *J* 5.6 Hz, H3), 5.44 (1H, bs, NH), 3.67 (2H, t, *J* 5.9 Hz, 2 x H5'), 3.41 (2H, t, *J* 6.7 Hz, 2 x H1'), 2.80-2.61 (4H, m, 2 x H3' and H4'), 2.32 (3H, s, NCH_3), 2.18 (2H, m, 2 x H2'); δ_c (100 MHz; CD_3OD): 151.3, 151, 148.2, 134.9, 126.1, 124.5, 122.9, 117.4, 98.1, 59, 58.9, 55.7, 41.3(2C), and 25.4; MS(ESI) *m/z* 294.2(M^++H); HPLC purity: 96.8%; $t_{r'}$=11.33 min.

1.6 General procedure for the synthesis of compounds 13a-b

To the suspension of intermediate **12a/12b**(0.852 mmol) in dry toluene (3 ml) and dry DMF(0.3 ml) at 0^oC was added $SOCl_2$ solution (8.8 mmol) in dry toluene(3 ml) drop-wise in 15 minutes. The temperature of the resultant was raised to reflux for 14 hours. On reaction completion, the solvent was evaporated in *vacuo*, H_2O (5 ml) added and pH of the resulting mixture adjusted to 7-8 by addition of saturated sodium bicarbonate. The mixture was extracted with ethyl acetate (3 x 50 ml), washed with brine, dried over $MgSO_4$ and concentrated to give **13a-b.**

*2[{2-[(7-Chloroquinolin-4-yl)amino]ethyl}-(methyl)amino]ethylchloride (**13a**)*

Yield (0.191g) 60%; m. p. 100-101 ^oC; R_f (DCM: MeOH, 8:2%) 0.4; δ_H (400 MHz; CD_3OD): 8.34 (1H, d, *J* 5.6 Hz, H2), 8.02 (1H, d, *J* 9 Hz, H5), 7.75 (1H, d, *J* 2.1 Hz, H8), 7.40 (1H, dd, *J* 2.1 and 9 Hz, H6), 6.44 (1H, d, *J* 5.6 Hz, H3), 5.42 (1H, bs, NH), 3.56 (2H,

t, *J* 5.7 Hz, 2 x H4'), 3.42 (2H, t, *J* 6.4 Hz, 2 x H1'), 2.78-2.56 (4H, m, 2 x H2' and H3'), 2.36 (3H, s, NCH_3); δ_c (100 MHz; CD_3OD): 151.1, 151, 148.1, 134.9, 126.1, 124.6, 122.8, 117.3, 98.3, 58.8, 55.1, 41.2, 40.1 and 39.8; MS(ESI) m/z 298.2(M^++H).

*2[{3-[(7-Chloroquinolin-4-yl)amino]propyl}-(methyl)amino]ethylchloride (**13b**)*

Yield (0.213g) 67%; m. p. 105-106 ^oC; R_f (DCM: MeOH, 8:2%) 0.44; δ_H (400 MHz; CD_3OD): 8.33 (1H, d, *J* 5.6 Hz, H2), 8.01 (1H, d, *J* 9 Hz, H5), 7.76 (1H, d, *J* 2.1 Hz, H8), 7.38 (1H, dd, *J* 2.1 and 9 Hz, H6), 6.50 (1H, d, *J* 5.6 Hz, H3), 5.44 (1H, bs, NH), 3.65 (2H, t, *J* 6.5 Hz, 2 x H5'), 3.42 (2H, t, *J* 6.7 Hz, 2 x H1'), 2.80-2.61 (4H, m, 2 x H3' and H4'), 2.32 (3H, s, NCH_3), 1.90 (2H, m, 2 x H2'); δ_c (100 MHz; CD_3OD): 151.3, 150.8, 148, 134.8, 126, 124.4, 122.7, 117.2, 98.1, 58.7, 55.3, 41.2, 40.9, 40.8 and 25.4; MS(ESI) m/z 312.1(M^++H).

1.7 General procedure for the synthesis of compounds 14a-b

To the solution of 2-methyl-4/5-nitroimidazole (0.385 mmol) and **13a/13b** (0.385 mmol) in dry DMF(20ml) at room temperature was added anhydrous K_2CO_3(1.15 mmol). The reaction mass was then stirred for 6 hours at 100-110 ^oC. On completion, DMF was evaporated and the crude dissolved in MeOH: EtOAc mixture (1:8 ratio), dried over $MgSO_4$, and concentrated. The obtained crude was then purified by column chromatography, eluting with 15-20% MeOH in EtOAc, to afford compounds **14a-b** as regioisomeric mixture.

*2[{2-[(7-Chloroquinolin-4-yl)amino]ethyl}-(methyl)amino]ethyl[2-(2-methyl-4/5-nitroimidazole-1-yl (**14a**)*

Yield (72mg) 60%; R_f (DCM: MeOH, 8:2) 0.38; δ_H (400 MHz; DMSO): 8.34(1H, d, *J* 5.4 Hz, H2), 8.27 (1H, s, H5'), 8.19 (1H, d, *J* 9 Hz, H5), 7.74 (1H, d, *J* 2.2 Hz, H8), 7.39 (1H, dd, *J* 2.1 and 9 Hz, H6), 6.30 (1H, d, *J* 5.6 Hz, H3), 4.07 (2H, t, *J* 6 Hz, 2 x H4'), 3.12 (2H,

t, *J* 6.5 Hz, 2 x H1'), 2.66 (2H, t, *J* 6.1 Hz, 2 x H4'), 2.43 (2H, t, *J* 6.7 Hz, 2 x H3'), 2.34 (3H, s, NCH_3), 2.23 (3H, s, CH_3); δ_c (100 MHz; DMSO): 152.3, 150.5, 149.5, 145.5, 133.8, 129.3, 128.5, 127.9, 124.5, 124.4, 122.9, 117.9, 98.9, 56.9, 55.3, 44.8, 42.2 and 11.4; MS(ESI) m/z 389.2(M^++H); HPLC purity: 93.8%; t_r'=8.26 min.

*2[{3-[(7-Chloroquinolin-4-yl)amino]propyl}-(methyl)amino]ethyl[2-(2-methyl-4/5-nitroimidazole-1-yl (**14b**)*

Yield (0.080g) 51%; R_f (DCM: MeOH, 8:2%) 0.32; δ_H (400 MHz; CD_3OD): 8.33(1H, d, *J* 5.6 Hz, H2), 8.03(1H, s, H6'), 7.98 (1H, d, *J* 9 Hz, H5), 7.73 (1H, d, *J* 2.1 Hz, H8), 7.34 (1H, dd, *J* 2.1 and 9 Hz, H6), 6.37 (1H, d, *J* 5.6 Hz, H3), 5.44 (1H, bs, NH), 4.08(2H, t, *J* 6 Hz, 2 x H5'), 3.22 (2H, t, *J* 6.9 Hz, 2 x H1'), 2.74 (2H, t, *J* 6 Hz, 2 x H4'), 2.54 (2H, *J* 6.7 Hz, 2 x H3'), 2.36 (3H, s, NCH_3), 2.32 (3H, s, CH_3), 1.80 (2H, m, 2 x H2'); δ_c (100 MHz; CD_3OD): 151.4, 150.7, 147.8, 145.5, 135, 125.9, 124.6, 122.8, 122.7, 121, 117.2, 98.1, 56.7, 55.2, 44.6, 40.9, 40.7, 25.6 and 11.4; MS(ESI) m/z 403.1(M^++H); HPLC purity: 98.4%; t_r'=8.48 min.

1.8 General procedure for the synthesis of compounds 15a-b

Following the synthetic protocol used in synthesizing **14a/14b**, intermediate **11a/11b** (0.498 was used in synthesizing regioisomeric mixture of compound **15a-b**.

*(7-Chloroquinolon-4-yl)-[2-(2-methyl-4/5-nitroimidazol-1-yl)-ethyl]-amine (**15a**)*

Yield (0.115 g) 70%; R_f (DCM: MeOH, 8:2%) 0.34; δ_H (300 MHz; CD_3OD): 8.40 (1H, d, *J* 5.7 Hz, H2), 8.06 (1H, s, H3'), 8.02 (1H, d, *J* 9 Hz, H5), 7.83 (1H, d, *J* 2.1 Hz, H8), 7.48 (1H, dd, *J* 2.1 and 9 Hz, H6), 6.65 (1H ,d, *J* 5.7 Hz, H3), 4.37 (2H, t, *J* 7.1 Hz, 2 x H2'), 3.38 (2H, t, *J* 6.6 Hz, 2 x H1'), 2.29 (3H, s, CH3); δ_c (100 MHz; DMSO): 153.5, 150.2, 149.1, 145.9, 145.6, 134.9, 127.8, 125, 124.2, 122.9, 117.8, 100.1, 47.3, 43.4 and 13.6; MS(EI) m/z 331.2(M^+); HPLC purity: 94.2%; t_r'=9.6 min.

(7-Chloroquinolon-4-yl)-[3-(2-methyl-4/5-nitroimidazol-1-yl)-propyl]-amine (***15b***)

Yield (0.158 g) 72%; R_f (DCM: MeOH, 8:2%) 0.30; δ_H (400 MHz; CD_3OD): 8.36 (1H, d, *J* 5.7 Hz,H2), 8.09 (1H, s, H4'), 8.06 (1H, d, *J* 8.9 Hz, H5), 7.79 (1H, d, *J* 2.1 Hz, H8), 7.41 (1H, dd, *J* 2.1 and 8.9 Hz, H6), 6.54(1H ,d, *J* 5.7 Hz, H3), 4.17 (2H, t, *J* 7.1 Hz, 2 x H3'), 3.48 (2H, t, *J* 6.6 Hz, 2 x H1'), 2.37 (3H, s, CH3), 2.26 (2H, m, 2 x H2'); δ_c (100 MHz; CD_3OD): 151, 150.8, 149.9, 145.2, 135, 131.2, 126, 124.7, 122.6, 120.3, 117.2, 98.3, 44.5, 39.4, 28 and 11.2; MS(EI) m/z 345.1(M^+); HPLC purity: 97.3%; t_r=8.43 min.

1.9 General procedure for the synthesis of compound 16

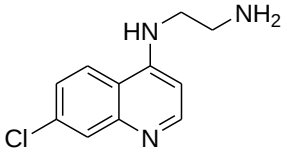
The solution of 2-nitroimidazooxazine alcohol (0.174 mmol) in dry DMF (5 ml) under N_2 was cool to -50^{o}C, NaH (0.174 mmol) was added slowly, and the reaction mass stirred for 15-20 minutes at this temperature. Intermediate **11b** (0.159 mmol) was then added, the temperature of the resultant mass raised to room temperature and further stirred overnight. On completion, DMF was removed in *vacuo*, and the crude diluted with H_2O (10 ml) followed by extraction with EtOAc(3 x 20m l). The combined organic extract was washed with brine, dried over $MgSO_4$ and concentrated. The resultant crude was purified by column chromatography, eluting with 35% MeOH in DCM, to give the title compound **16** as yellow solid.

*(6S)-2-Nitro-6[(7-chloroquinolon-4-aminopropyl)oxy]-6,7-dihydro-5H-imidazo[2,1-b][1,3]oxazine (**16**)*

Yield (0.015g) 27%; m. p. 115-116 ^{o}C; R_f (DCM: MeOH, 8:2%) 0.45; δ_H (300 MHz; CD_3OD): 8.28(1H, d, *J* 6 Hz, H2), 8.02 (1H, d, *J* 9 Hz, H5), 7.74 (1H, d, *J* 2.1 Hz, H8), 7.66 (1H, s, H7'), 7.40 (1H, dd, *J* 2.1 and 9 Hz, H6), 6.49 (1H ,d, *J* 6 Hz, H3), 5.44 (bs, 1H, NH), 4.65 (1H, dt, *J* 2.3 and 2.4 Hz, H4'), 4.42 (1H, d, *J* 12 Hz, H5a'), 4.26-4.10 (3H, m, H5'a, H6'), 3.77 (2H, m, 2 x H3'), 3.43 (2H, t, *J* 6.8 Hz, 2 x H1'), 2.04 (2H, m, 2 x H2'); δ_c

(100 MHz; CD_3OD): 152.2, 148.9, 147.7, 145.9, 136, 125.2, 124.5, 123, 116.8, 116.2, 98.1, 67.9(2C), 67.5, 66.4, 46.7, 40.1 and 28.2; MS(EI) m/z 403.1(M^+); HPLC purity: 98.1%; t_r=10.12 min.

1.10 Structures of quinoline diamines 17a-c



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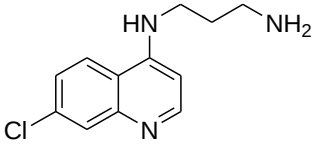

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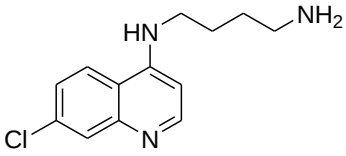

17c

2. *In vitro* assays

2.1 Antimalarial assays[3]

In vitro activity against erythrocytic stages of *P. falciparum* was determined using a ^{3}H-hypoxanthine incorporation assay, using the chloroquine and pyrimethamine resistant K1 strain that originate from Thailand and the standard drug chloroquine (Sigma C6628). Compounds were dissolved in DMSO at 10 mg/mL and added to parasite cultures incubated in RPMI 1640 medium without hypoxanthine, supplemented with HEPES (5.94 g/l), $NaHCO_3$ (2.1 g/l), neomycin (100 U/mL), Albumax^R (5 g/l) and washed human red cells A^+ at 2.5% haematocrit (0.3% parasitaemia). Serial drug dilutions of eleven three-fold dilution steps covering a range from 100 to 0.002 µg/ml were prepared. The 96-well plates were incubated in a humidified atmosphere at 37 C; 4% CO_2, 3% O_2, 93% N_2. After 48 h 50 µl of ^{3}H-hypoxanthine (=0.5 µCi) was added to each well of the plate. The plates were incubated for a further 24 h under the same conditions. The plates were then harvested with a Betaplate™ cell harvester (Wallac, Zurich, Switzerland), and the red blood cells transferred onto a glass fibre filter then washed with distilled water. The dried filters were inserted into a plastic foil with 10

mL of scintillation fluid, and counted in a Betaplate™ liquid scintillation counter (Wallac, Zurich, Switzerland). IC_{50} values were calculated from sigmoidal inhibition curves by linear regression using Microsoft Excel.

2.2 Antimycobacterial assays

Culture preparation of the mycobacterium

Mycobacterial tuberculosis H_{37}Rv drug-sensitive strain was grown on Middlebrook 7H10 (Merck) supplemented with 0.5% glycerol and 10% Middlebrook Oleic acid Dextros catalase (OADC) enrichment (Merck) for five days at 37 °C, without shaking. To prepare the suspension for inoculation, the cultures were vortexed, left for 45 seconds to allow heavy particles to settle, and followed by dilution.

Broth microdilution method assay

All minimum inhibitory concentrations (MICs) were determined by the broth microdilution method.[4] A stock culture of Mtb H37RvMA[5] was grown to OD_{600} 0.6 - 0.7 in Middlebrook 7H9 broth (Difco) supplemented with 0.05% Tween-80, 0.2% glycerol, and albumin/NaCl/ glucose (ADC) complex. The culture was diluted 1:500 in 7H9-based medium before aliquoting 50 μL into each well of a 96-well plate (Rows 2-12). The compounds were dissolved in DMSO to make stock solutions of 12.8 mM and were diluted in 7H9-based medium to a final concentration of 640 µM. 100 μL of each compound was added to the first row of wells of the 96-well plate. After pipet mixing and use of a multichannel pipet, 50 μL was removed from each well in the first row and added to the second row. 2-Fold dilution in this manner was carried out to give ten dilutions of each compound assayed (160-0.078 μM). Rifampicin and kanamycin were used as positive controls, while 5% DMSO and 7H9-based medium were

employed as negative controls. The plates were incubated for 2 weeks at 37 °C, and the MIC_{99} values were read macroscopically using an inverted plate reader at Day 7 and Day 14 post inoculation. MIC_{99} values were recorded as the lowest concentration of compound that resulted in inhibition of growth of more than 99% of the bacterial population at Day 7.

2.3 Cytotoxicity assays[6]

Assays were performed in 96-well microtiter plates, each well containing 100 µl of RPMI 1640 medium supplemented with 1% L-glutamine (200mM) and 10% fetal bovine serum, and 4000 L-6 cells (a primary cell line derived from rat skeletal myoblasts). Serial drug dilutions of eleven three-fold dilution steps covering a range from 100 to 0.002 µg/mL were prepared. After 70hours of incubation the plates were inspected under an inverted microscope to assure growth of the controls and sterile conditions. 10µl of Alamar Blue was then added to each well and the plates incubated for another 2 hours. Then the plates were read with a Spectramax Gemini XS microplate fluorometer (Molecular Devices Cooperation, Sunnyvale, CA, USA) using an excitation wave length of 536 nm and an emission wave length of 588 nm. The IC50 values were calculated by linear regression (Huber 1993) from the sigmoidal dose inhibition curves using SoftmaxPro software (Molecular Devices Cooperation, Sunnyvale, CA, USA).

3 References

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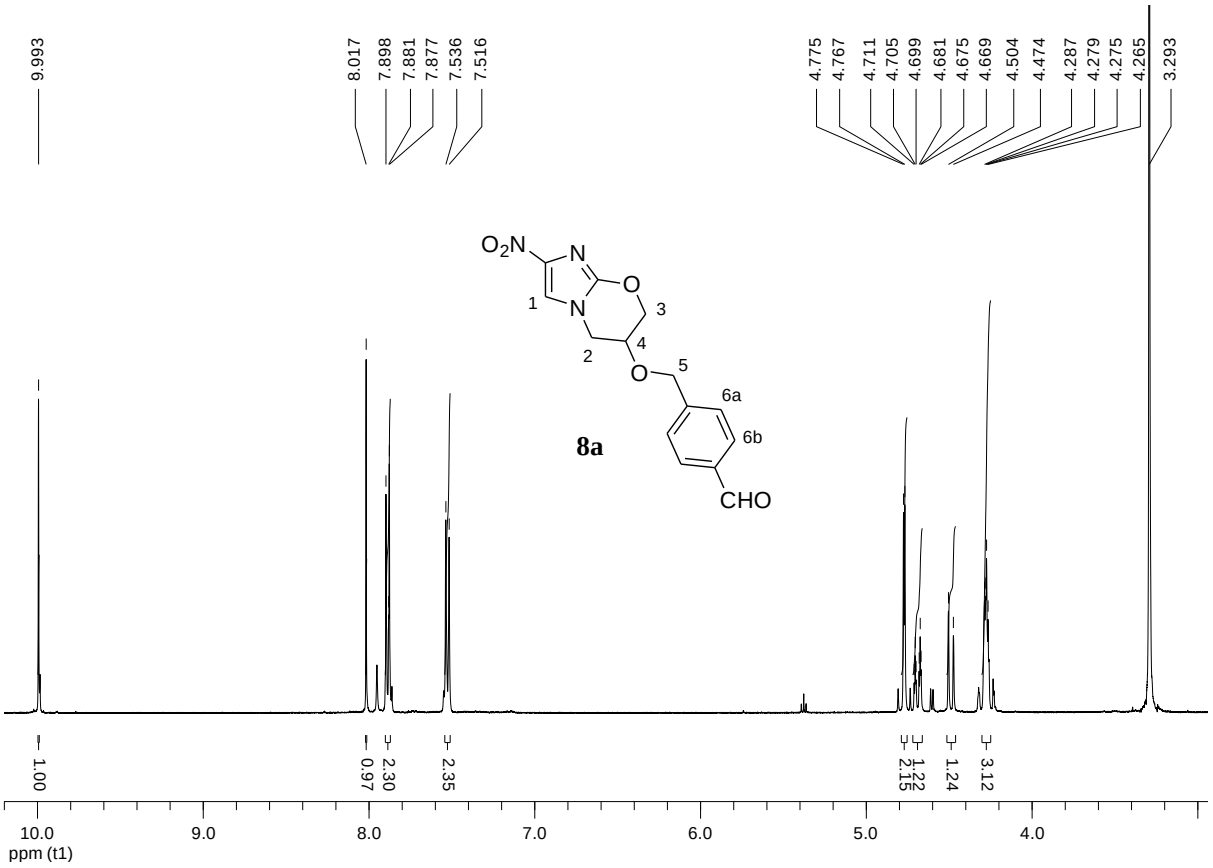
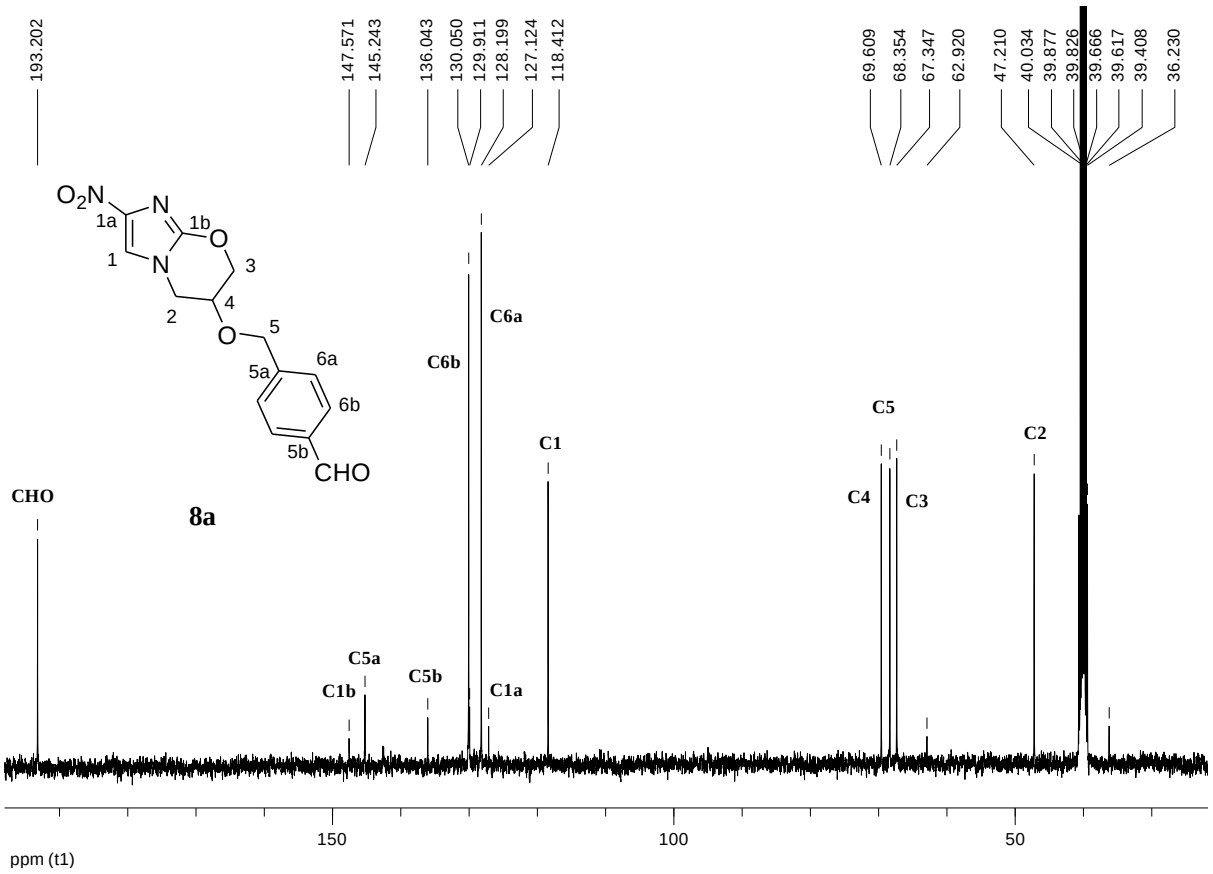
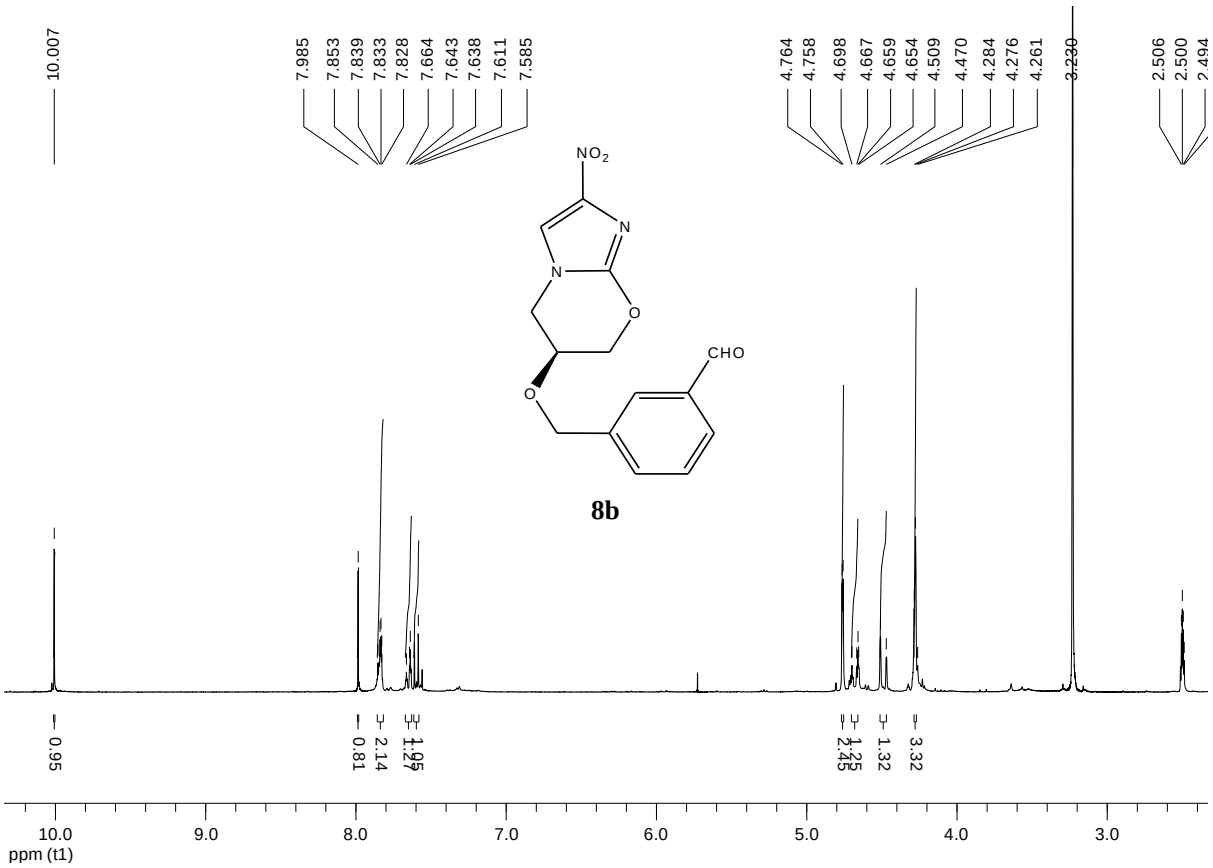
4. NMR spectra for compounds 8-16



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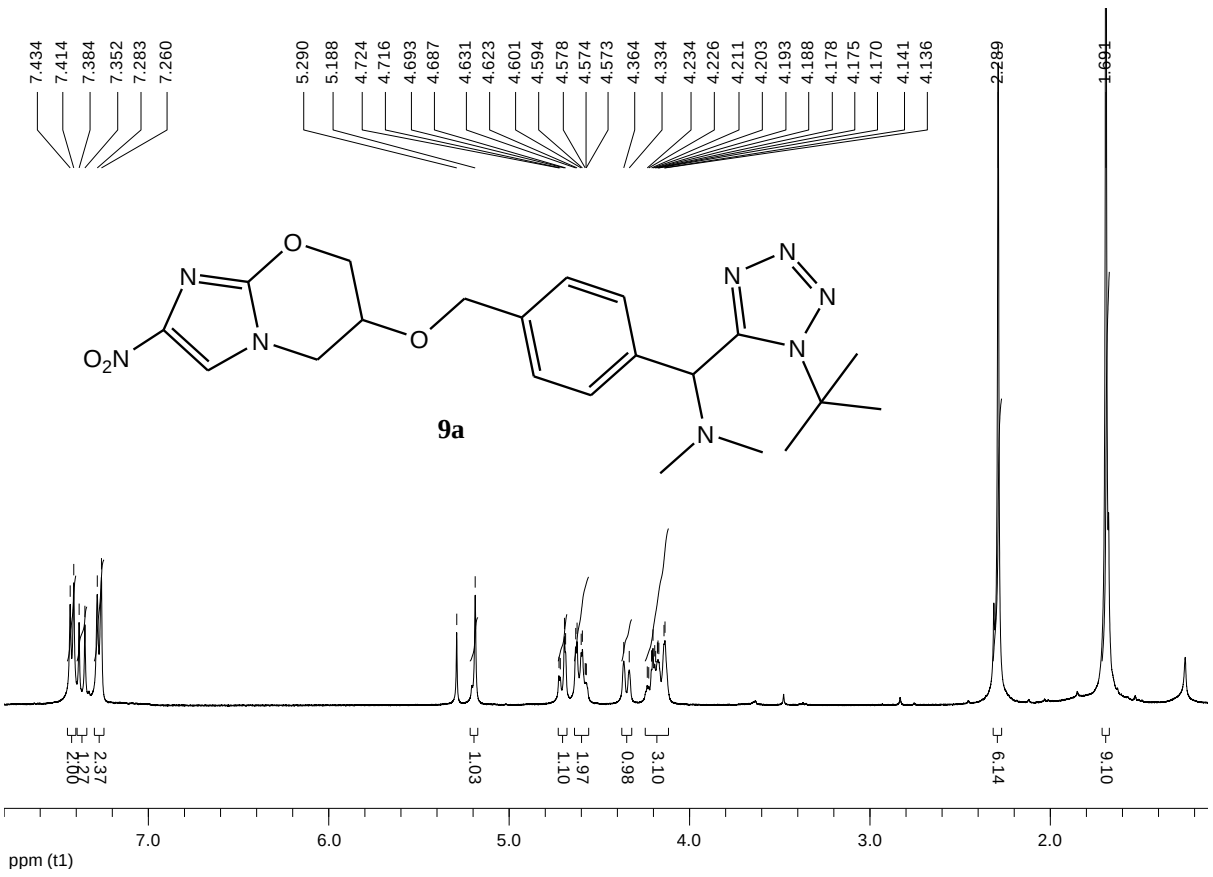
ppm (t1)

8b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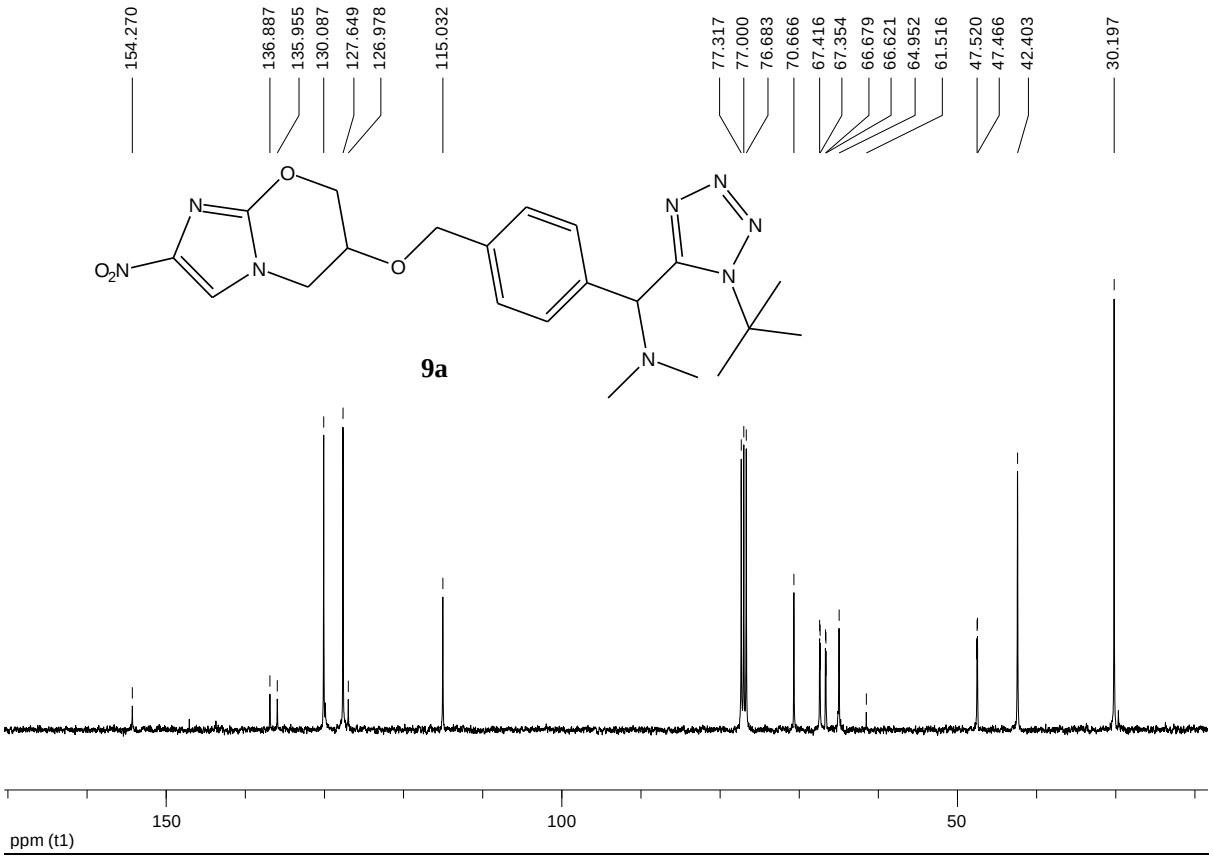
ppm (t1)

9a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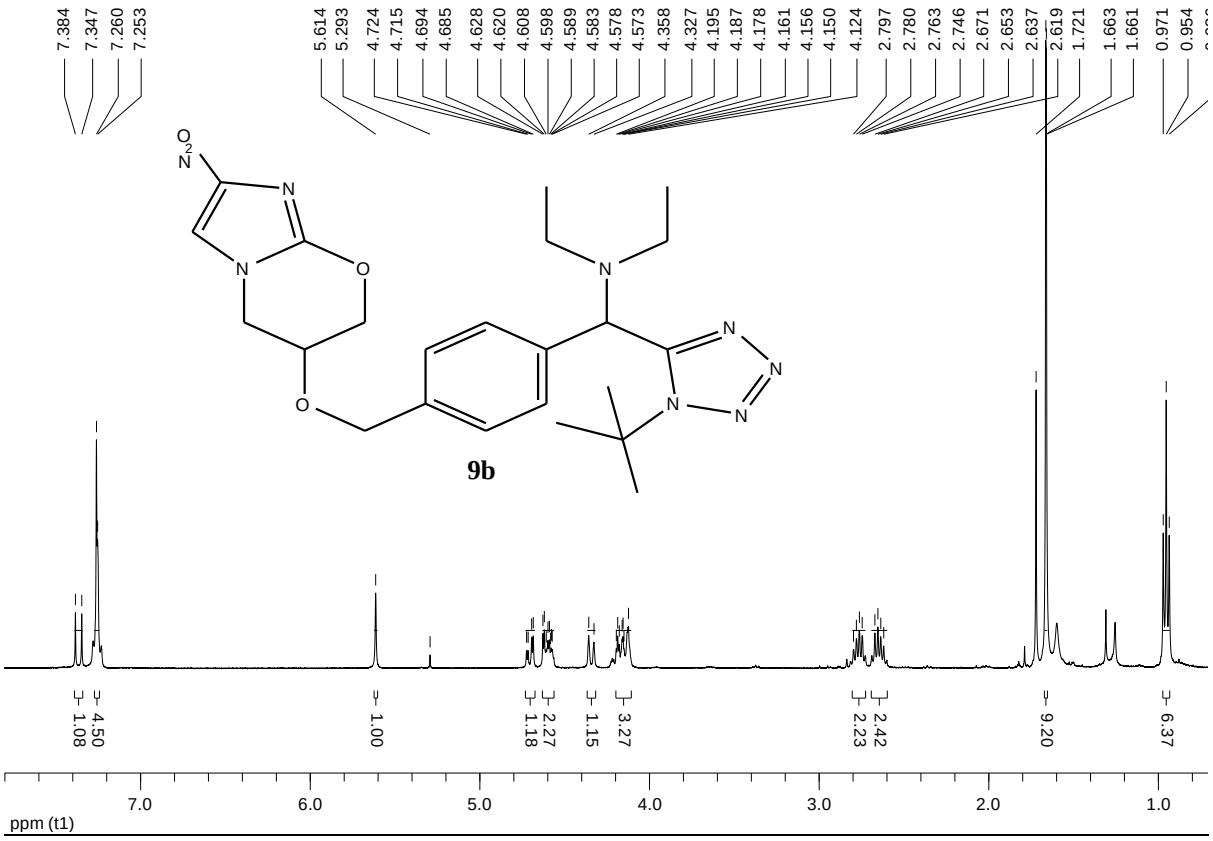
ppm (t1)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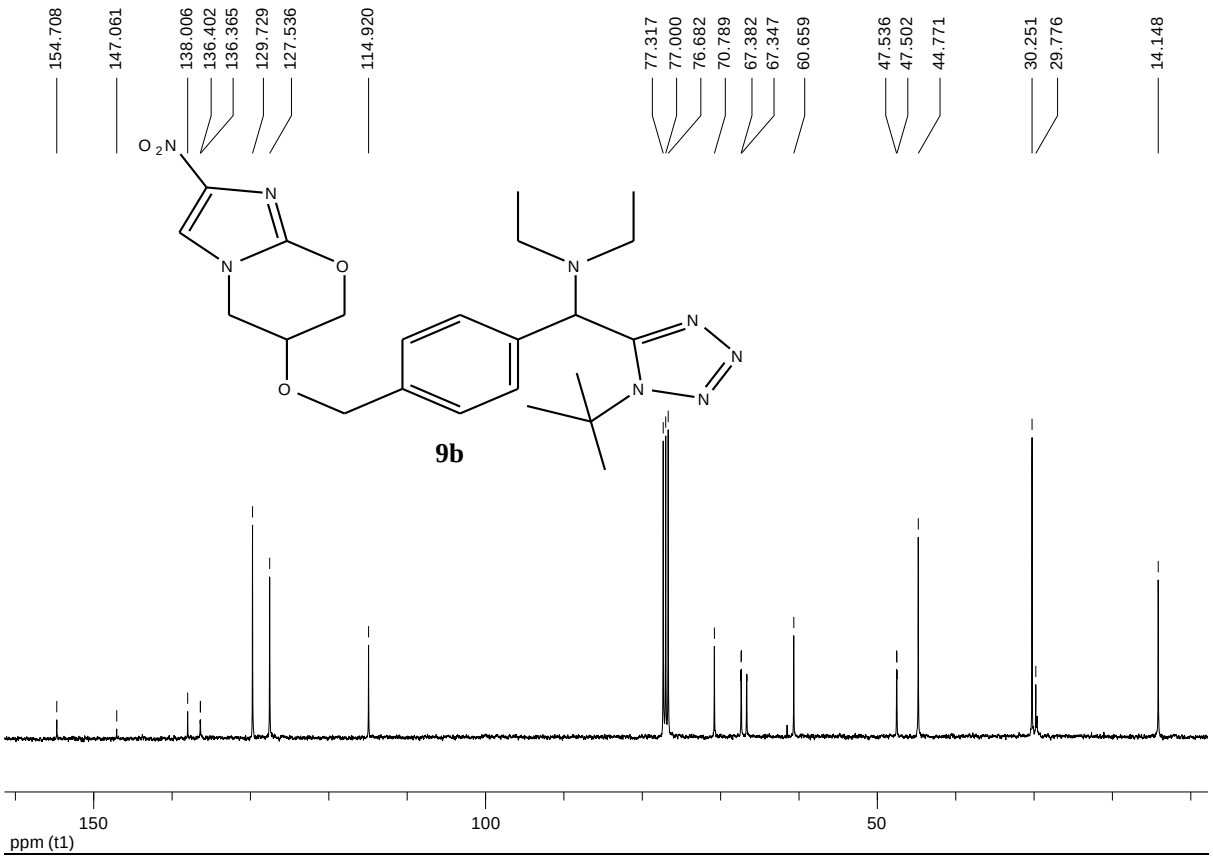
7.347
7.260
7.253
5.614
5.293
4.724
4.715
4.694
4.685
4.628
4.620
4.608
4.598
4.589
4.583
4.578
4.573
4.358
4.327
4.195
4.187
4.178
4.161
4.156
4.150
4.124
2.797
2.780
2.763
2.746
2.671
2.653
2.637
2.619
1.721
1.663
1.661
0.971
0.954
9b
1.08
4.50
1.00
1.18
2.27
1.15
3.27
2.23
2.42
9.20
6.37
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)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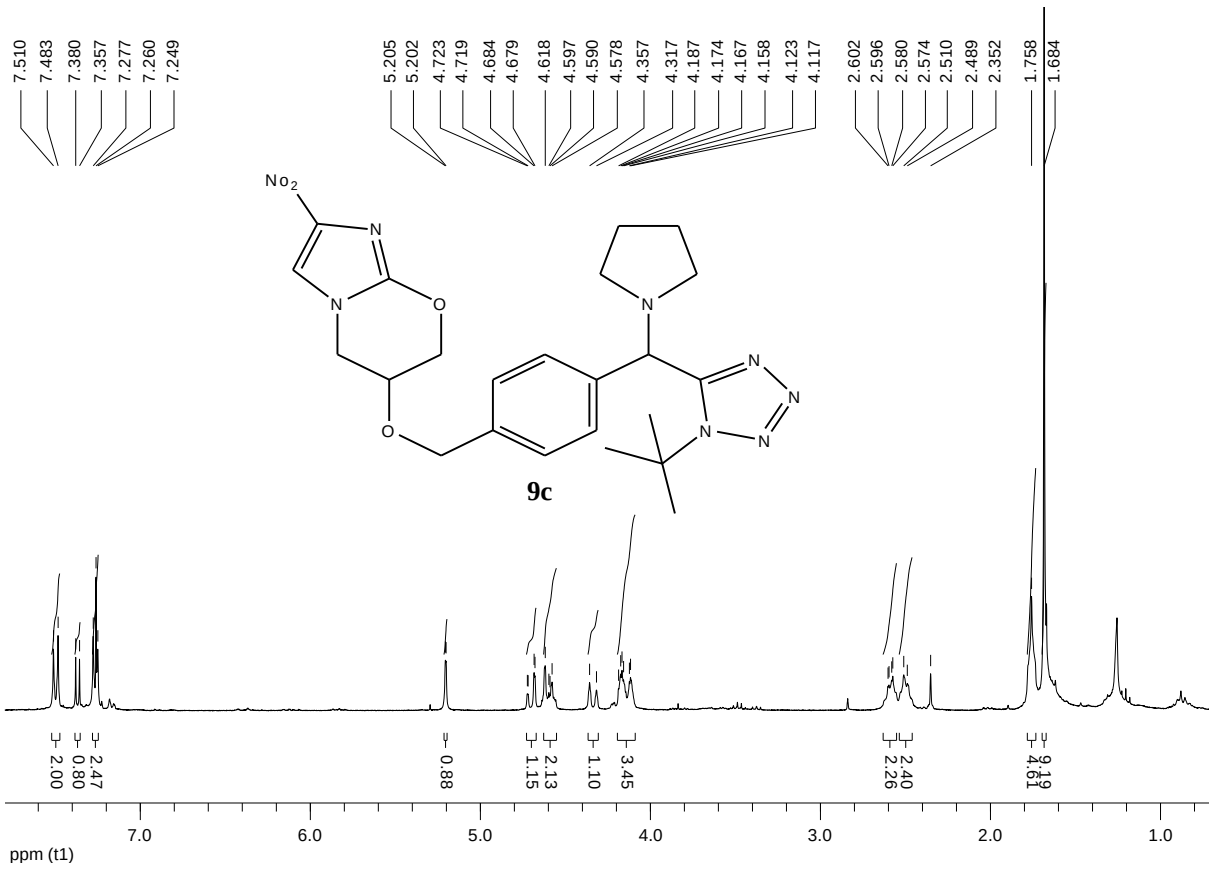
136.365
129.729
127.536
114.920
77.317
77.000
76.682
70.789
67.382
67.347
60.659
47.536
47.502
44.771
30.251
29.776
14.148
O2N
9b
150
100
50
ppm (t1)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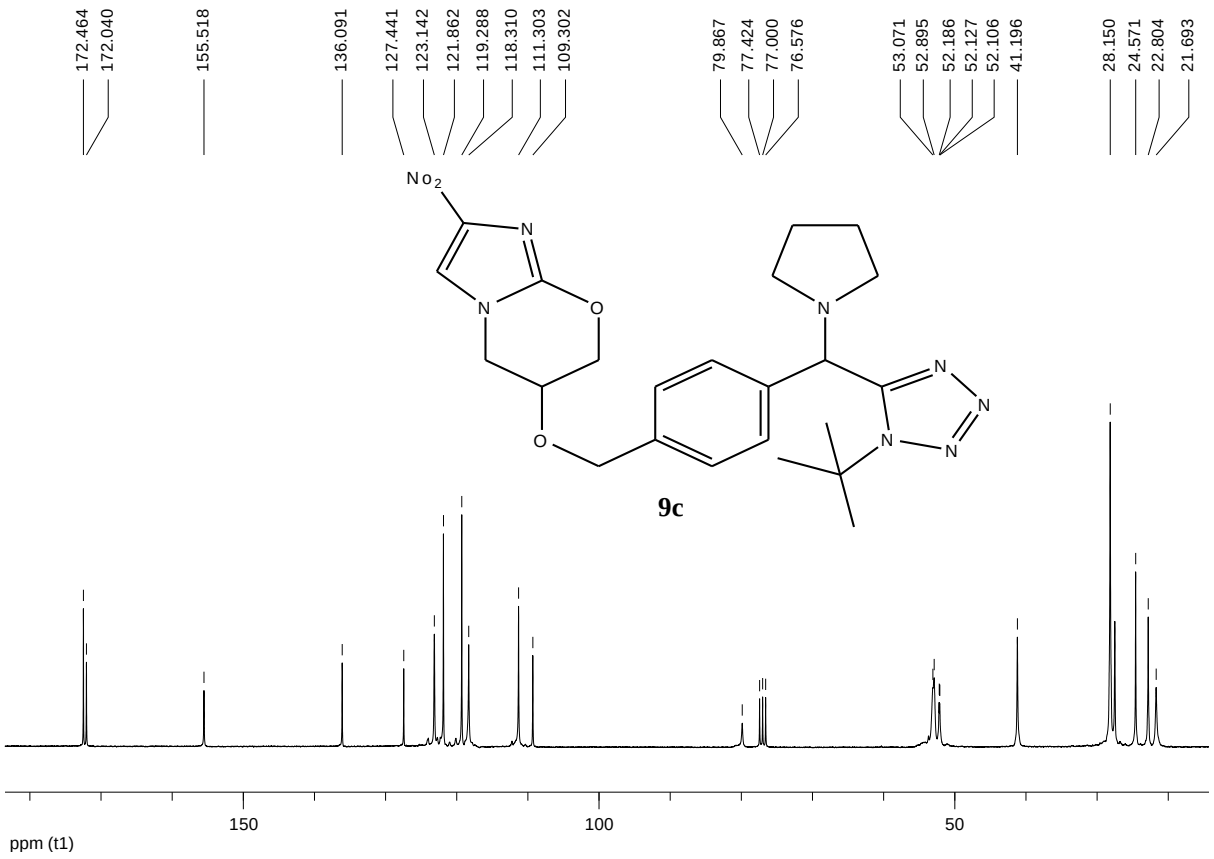
7.483
7.380
7.357
7.277
7.260
7.249
5.205
5.202
4.723
4.719
4.684
4.679
4.618
4.597
4.590
4.578
4.357
4.317
4.187
4.174
4.167
4.158
4.123
4.117
2.602
2.596
2.580
2.574
2.510
2.489
2.352
1.758
1.684
No2
9c
2.00
0.80
2.47
0.88
1.15
2.13
1.10
3.45
2.26
2.40
4.61
9.19
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)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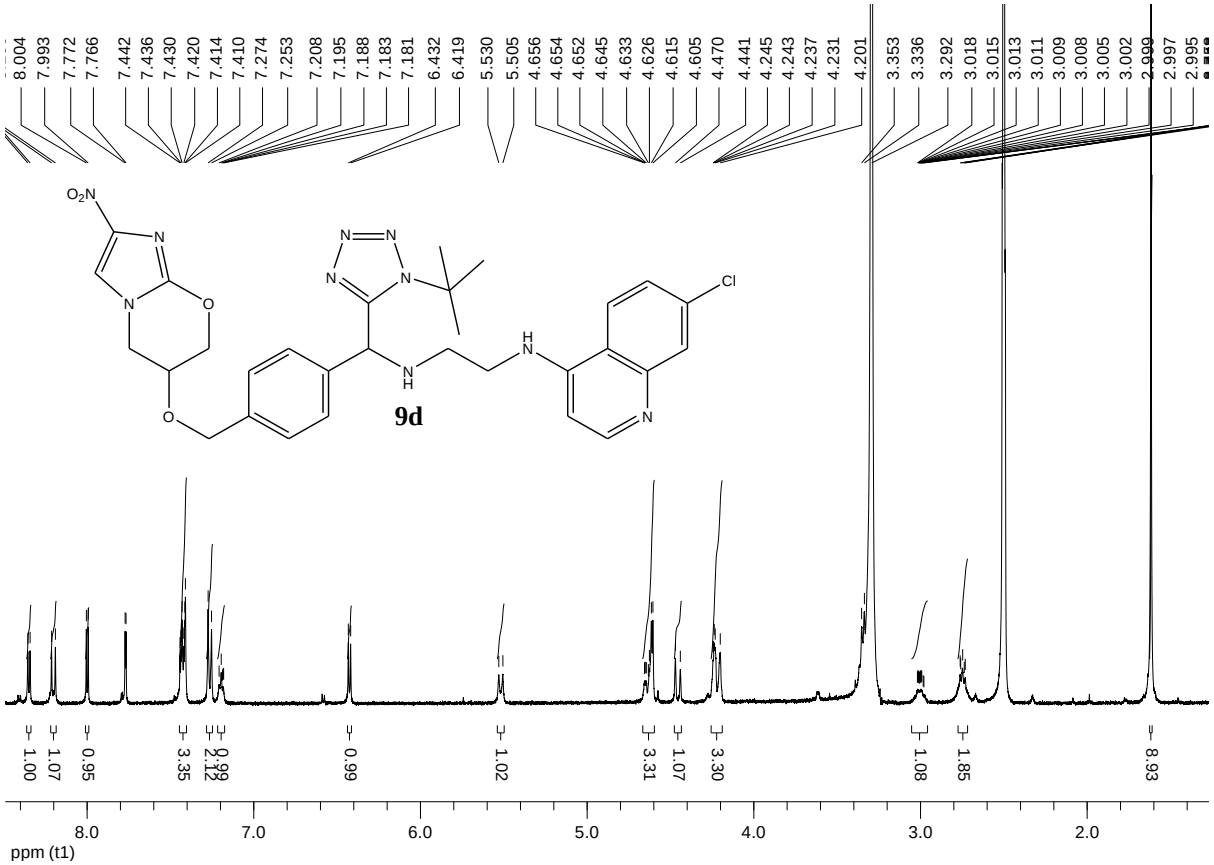
119.288
118.310
111.303
109.302
79.867
77.424
77.000
76.576
53.071
52.895
52.186
52.127
52.106
41.196
28.150
24.571
22.804
21.693
NO2
9c
150
100
50
ppm (t1)


8.004
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7.772
7.766
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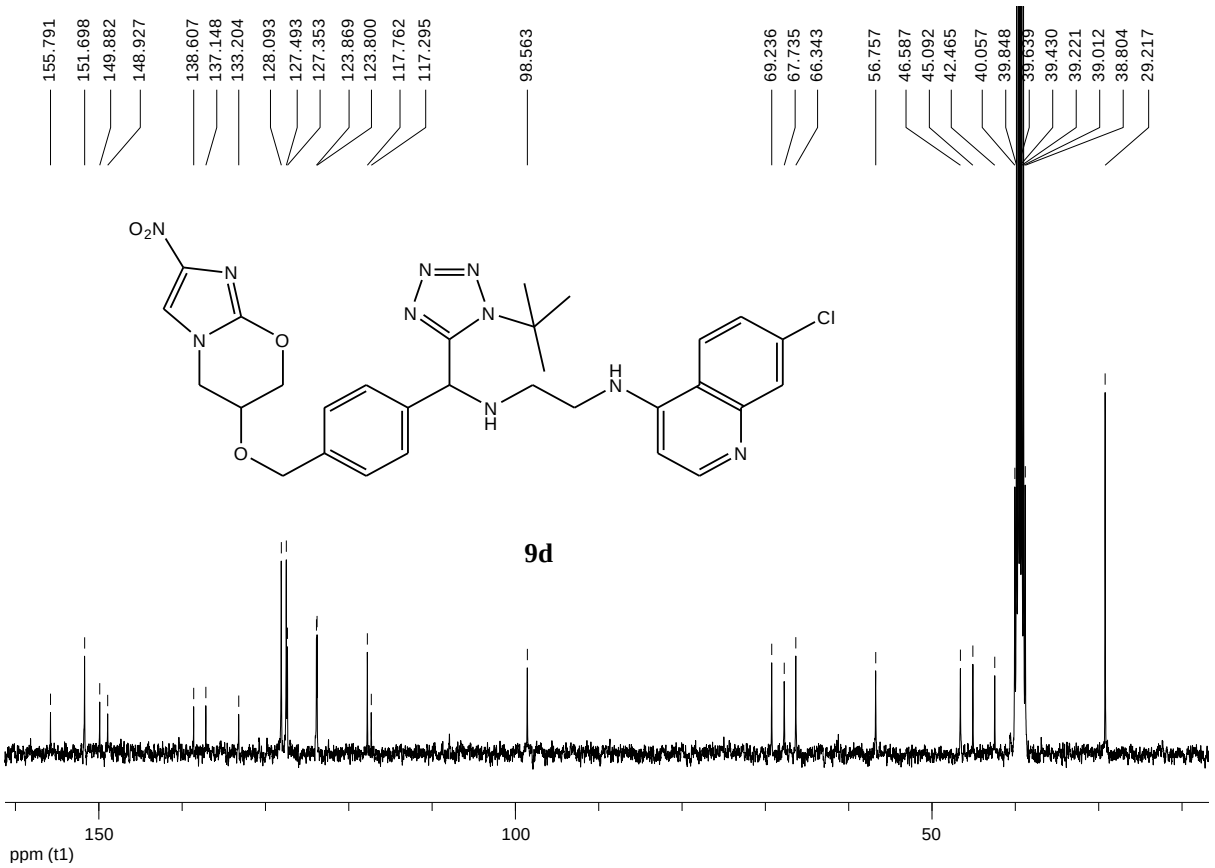
7.436
7.430
7.420
7.414
7.410
7.274
7.253
7.208
7.195
7.188
7.183
7.181
6.432
6.419
5.530
5.505
4.656
4.654
4.652
4.645
4.633
4.626
4.615
4.605
4.470
4.441
4.245
4.243
4.237
4.231
4.201
3.353
3.336
3.292
3.018
3.015
3.013
3.011
3.009
3.008
3.005
3.002
2.990
2.997
2.995
O2N
Cl
9d
1.00
1.07
0.95
3.35
2.12
0.99
0.99
1.02
3.31
1.07
3.30
1.08
1.85
8.93
8.0
7.0
6.0
5.0
4.0
3.0
2.0
ppm (t1)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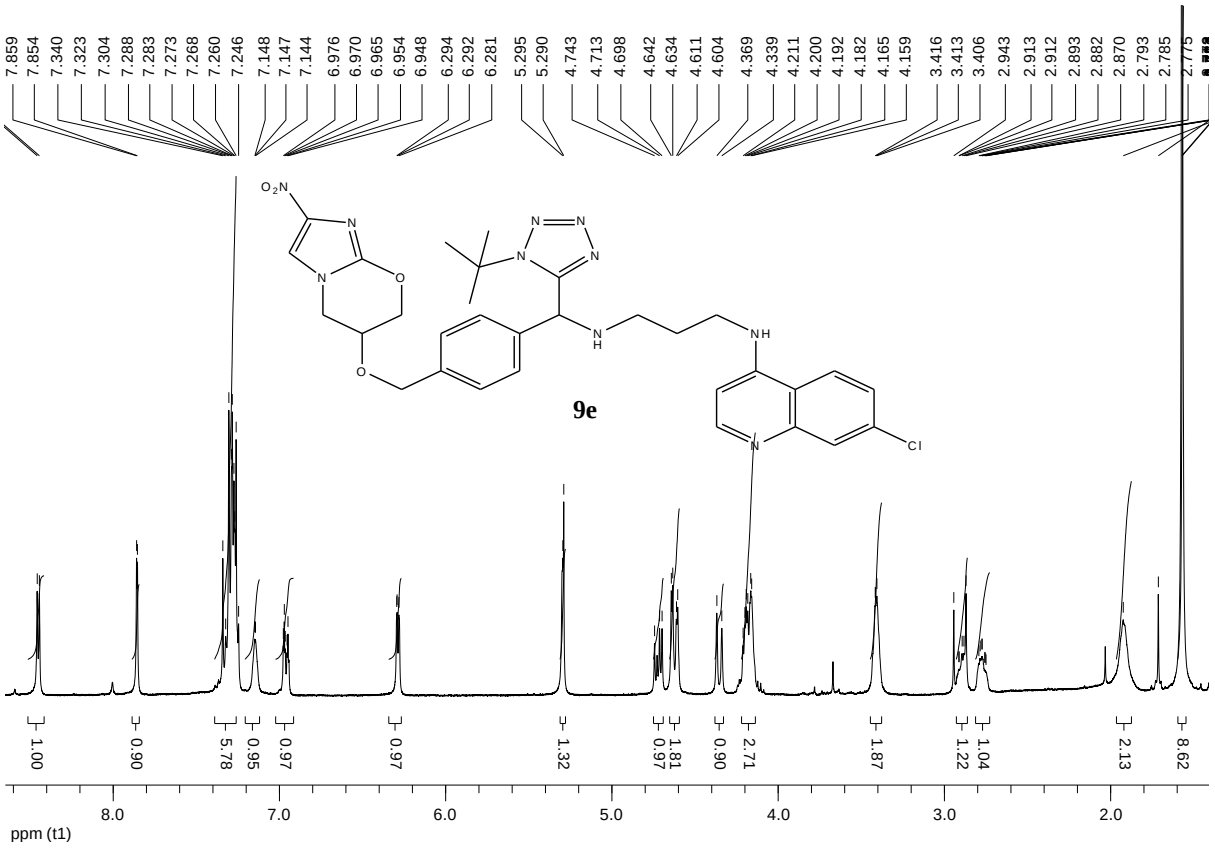
137.148
133.204
128.093
127.493
127.353
123.869
123.800
117.762
117.295
98.563
69.236
67.735
66.343
56.757
46.587
45.092
42.465
40.057
39.848
39.639
39.430
39.221
39.012
38.804
29.217
O2N
Cl
9d
150
100
50
ppm (t1)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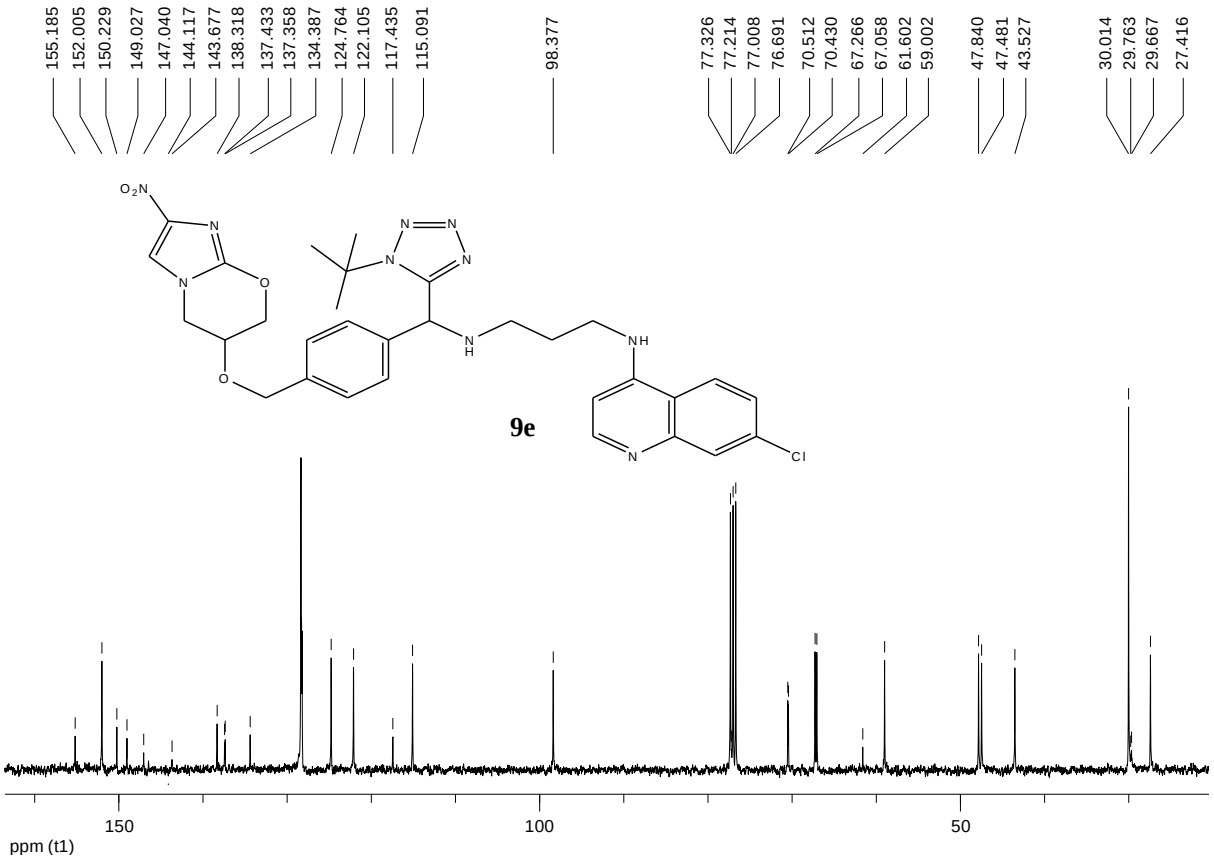
7.340
7.323
7.304
7.288
7.283
7.273
7.268
7.260
7.246
7.148
7.147
7.144
6.976
6.970
6.965
6.954
6.948
6.294
6.292
6.281
5.295
5.290
4.743
4.713
4.698
4.642
4.634
4.611
4.604
4.369
4.339
4.211
4.200
4.192
4.182
4.165
4.159
3.416
3.413
3.406
2.943
2.913
2.912
2.893
2.882
2.870
2.793
2.785
2.775
O2N
Cl
9e
1.00
0.90
5.78
0.95
0.97
0.97
1.32
0.97
1.81
0.90
2.71
1.87
1.22
1.04
2.13
8.62
8.0
7.0
6.0
5.0
4.0
3.0
2.0
ppm (t1)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144.117
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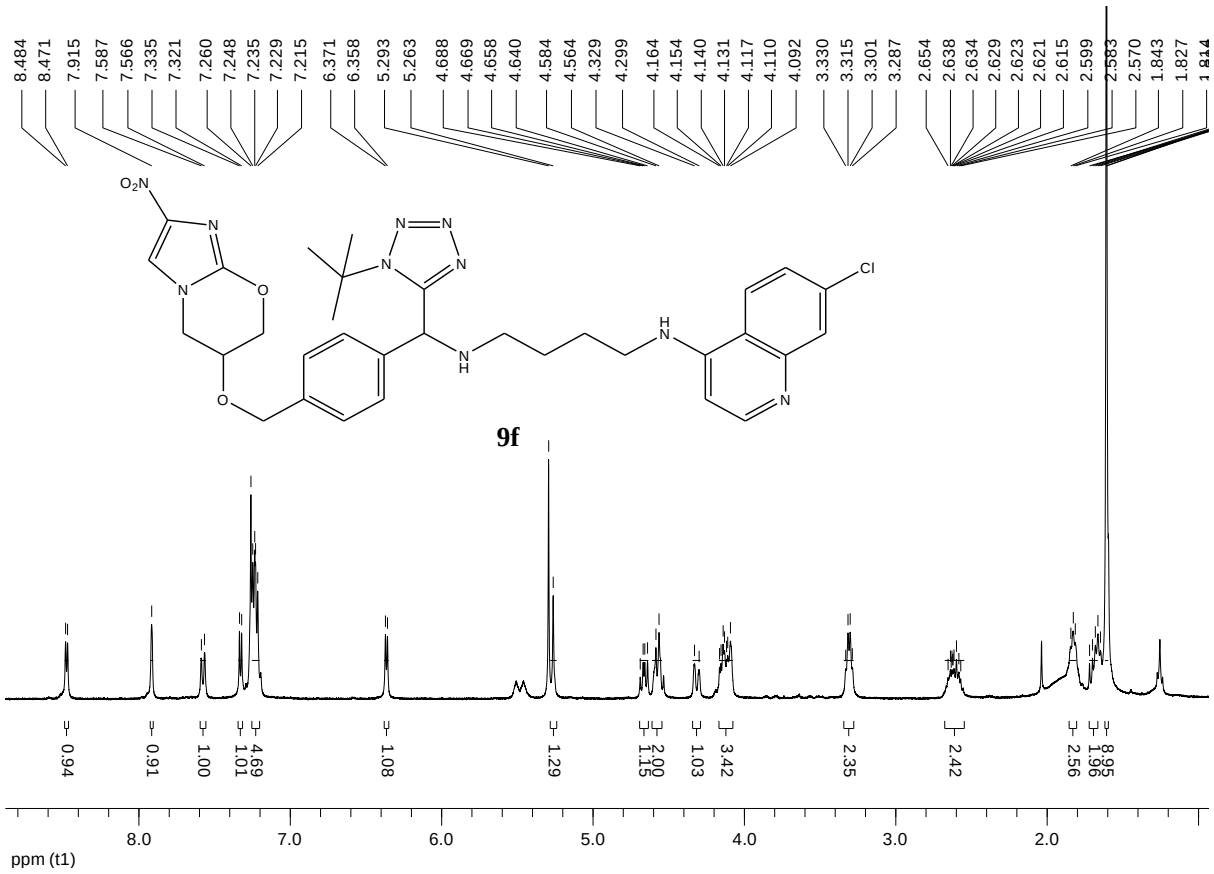
138.318
137.433
137.358
134.387
124.764
122.105
117.435
115.091
98.377
77.326
77.214
77.008
76.691
70.512
70.430
67.266
67.058
61.602
59.002
47.840
47.481
43.527
30.014
29.763
29.667
27.416
9e
150
100
50
ppm (t1)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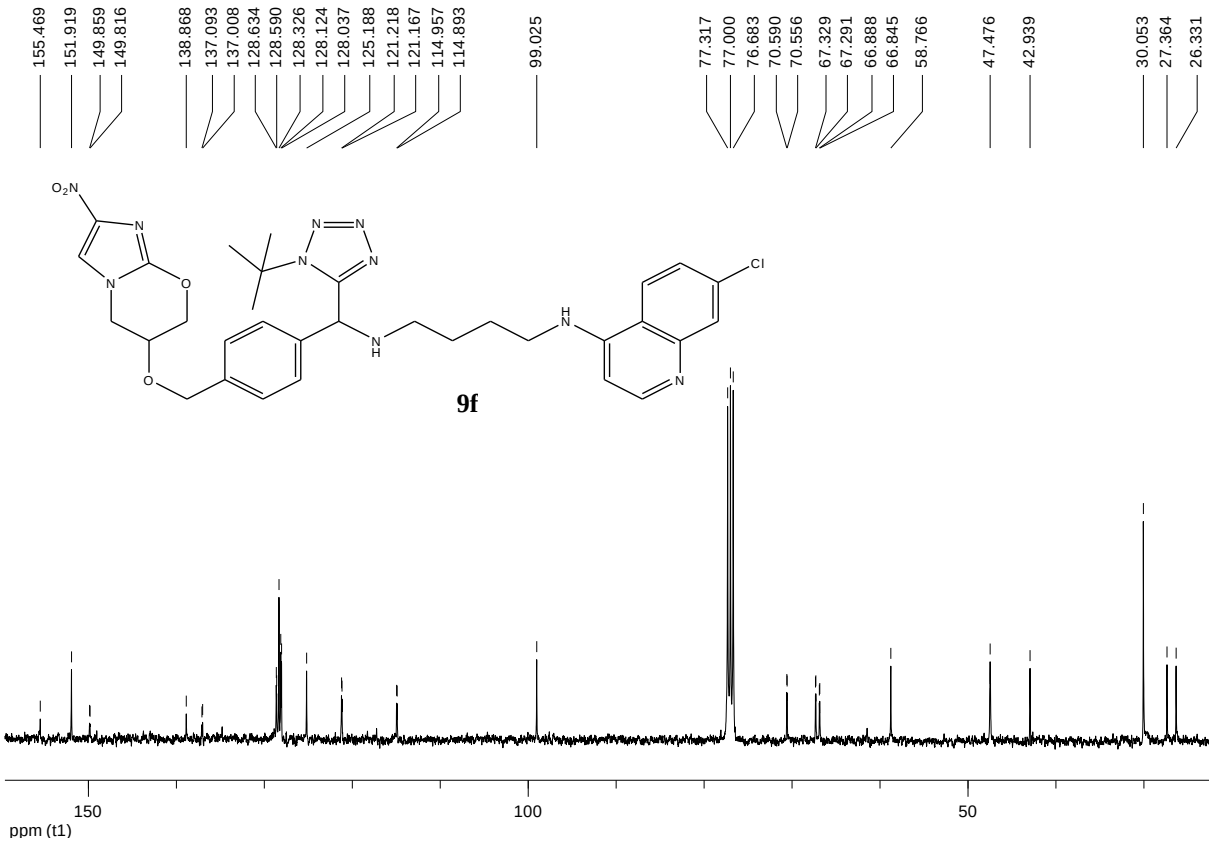
7.587
7.566
7.335
7.321
7.260
7.248
7.235
7.229
7.215
6.371
6.358
5.293
5.263
4.688
4.669
4.658
4.640
4.584
4.564
4.329
4.299
4.164
4.154
4.140
4.131
4.117
4.110
4.092
3.330
3.315
3.301
3.287
2.654
2.638
2.634
2.629
2.623
2.621
2.615
2.599
2.583
2.570
1.843
1.827
0.94
0.91
1.00
1.01
4.69
1.08
1.29
1.15
2.00
1.03
3.42
2.35
2.42
2.56
1.96
8.95
9f
8.0
7.0
6.0
5.0
4.0
3.0
2.0
ppm (t1)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151.919
149.859
149.816
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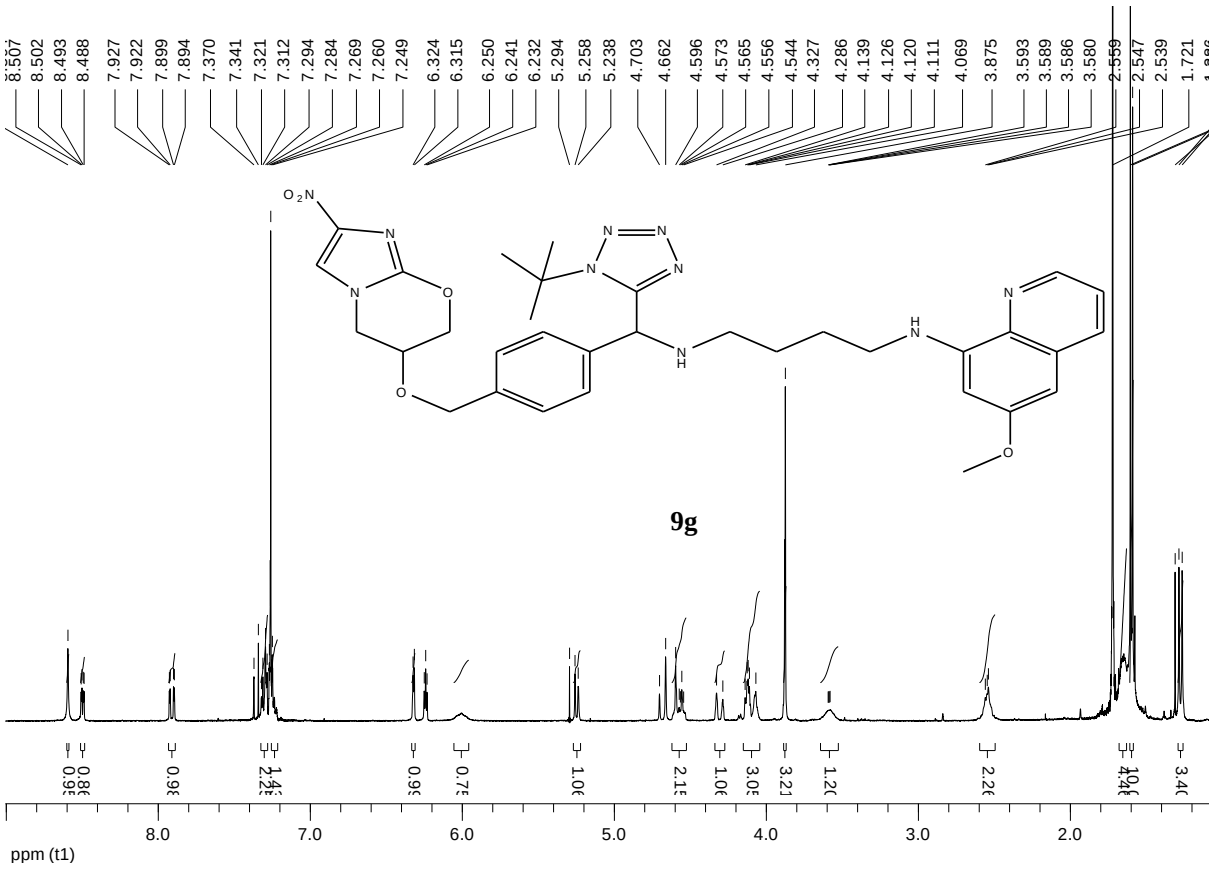
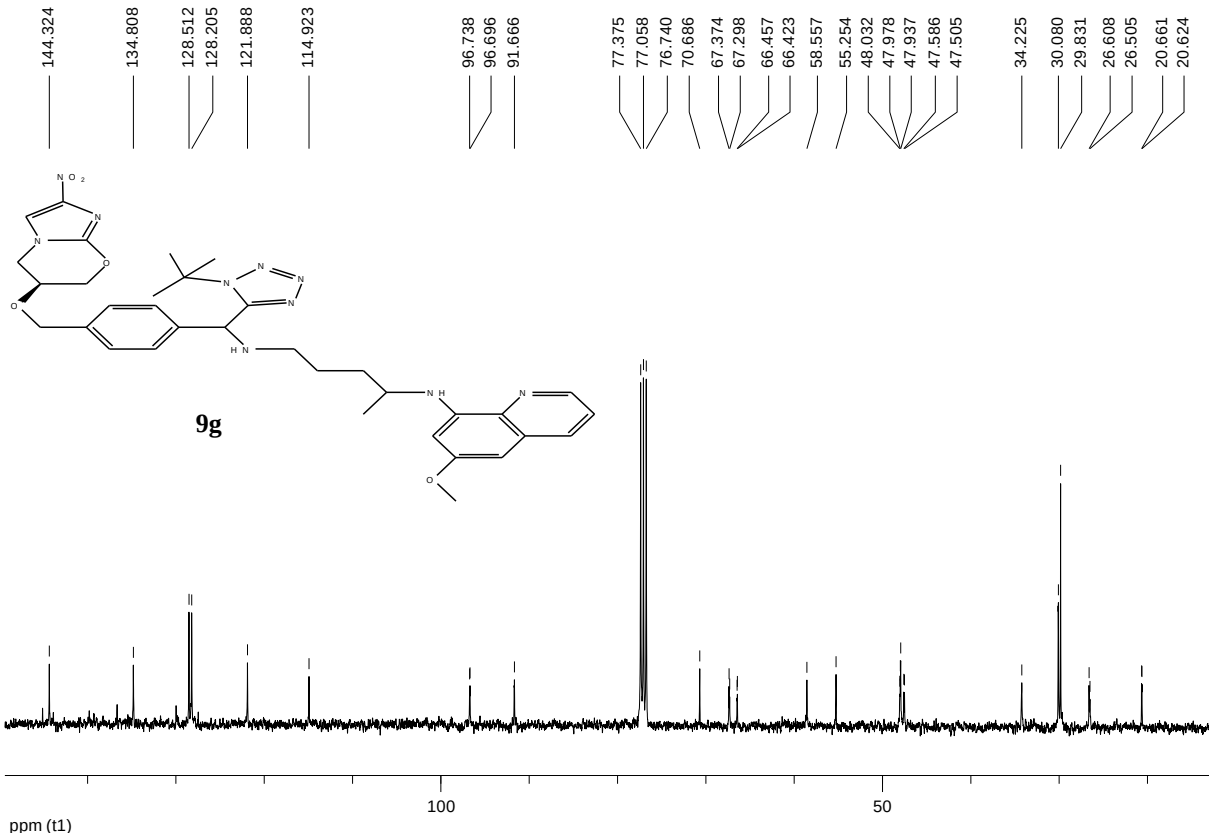
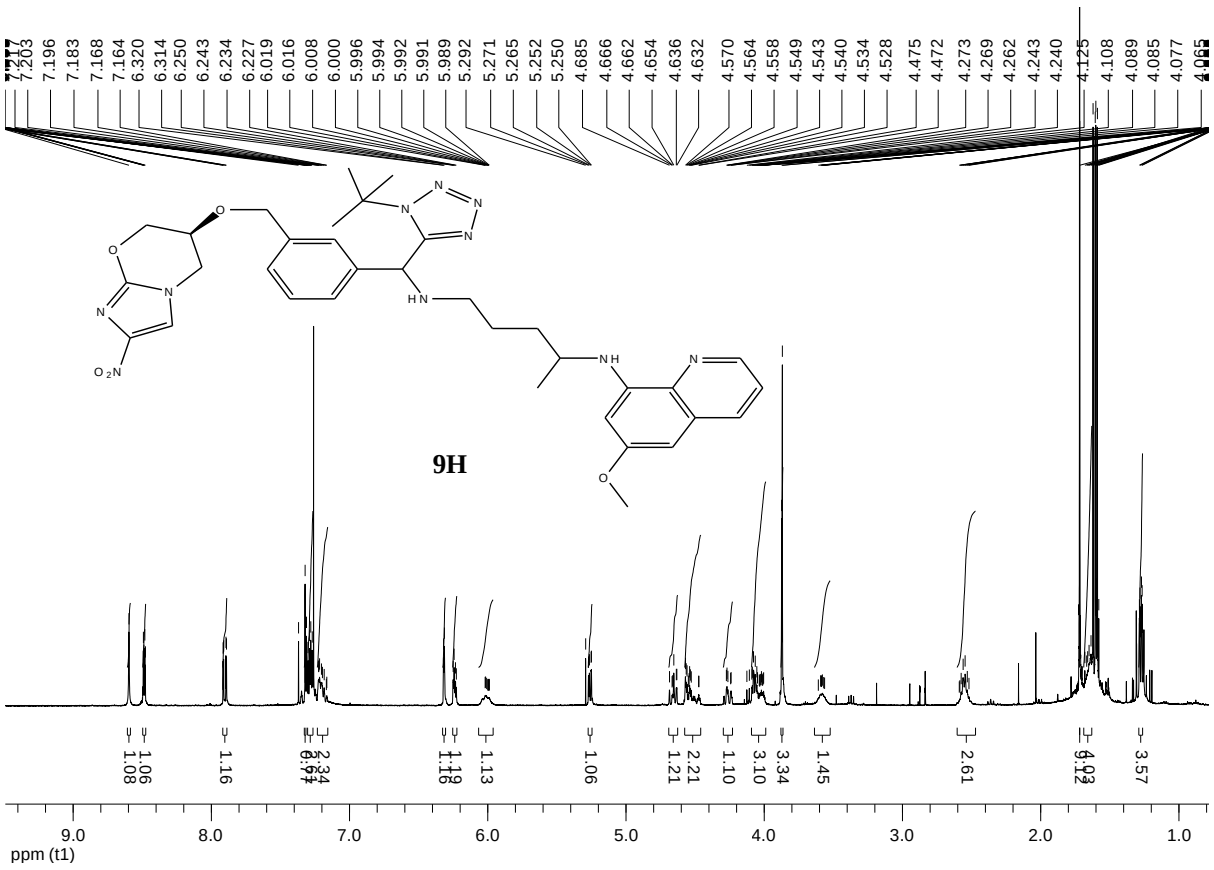
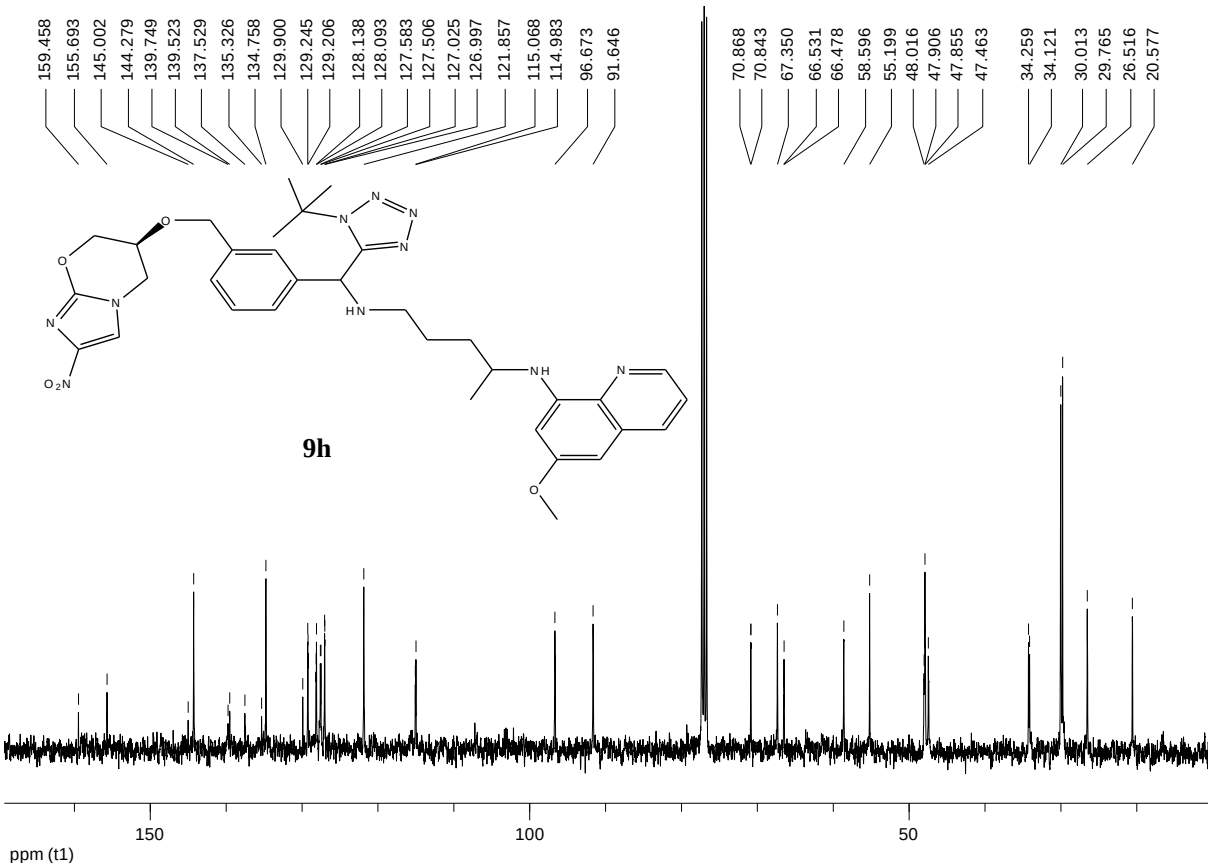
137.008
128.634
128.590
128.326
128.124
128.037
125.188
121.218
121.167
114.957
114.893
99.025
77.317
77.000
76.683
70.590
70.556
67.329
67.291
66.888
66.845
58.766
47.476
42.939
30.053
27.364
26.331
9f
150
100
50
ppm (t1)


8.507
8.502
8.493
8.488
7.927
7.922
7.899
7.894
7.370
7.341
7.321
7.312
7.294
7.284
7.269
7.260
7.249
6.324
6.315
6.250
6.241
6.232
5.294
5.258
5.238
4.703
4.662
4.596
4.573
4.565
4.556
4.544
4.327
4.286
4.139
4.126
4.120
4.111
4.069
3.875
3.593
3.589
3.586
3.580
2.559
2.547
2.539
1.721
9g
8.0
7.0
6.0
5.0
4.0
3.0
2.0
ppm (t1)


144.324
134.808
128.512
128.205
121.888
114.923
96.738
96.696
91.666
77.375
77.058
76.740
70.686
67.374
67.298
66.457
66.423
58.557
55.254
48.032
47.978
47.937
47.586
47.505
34.225
30.080
29.831
26.608
26.505
20.661
20.624
9g
100
50
ppm (t1)


9H
1.08
1.06
1.16
2.34
6.97
1.19
1.13
1.06
1.21
2.21
1.10
3.10
3.34
1.45
2.61
3.57
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)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144.279
139.749
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137.529
135.326
134.758
129.900
129.245
129.206
128.138
128.093
127.583
127.506
127.025
126.997
121.857
115.068
114.983
96.673
91.646
70.868
70.843
67.350
66.531
66.478
58.596
55.199
48.016
47.906
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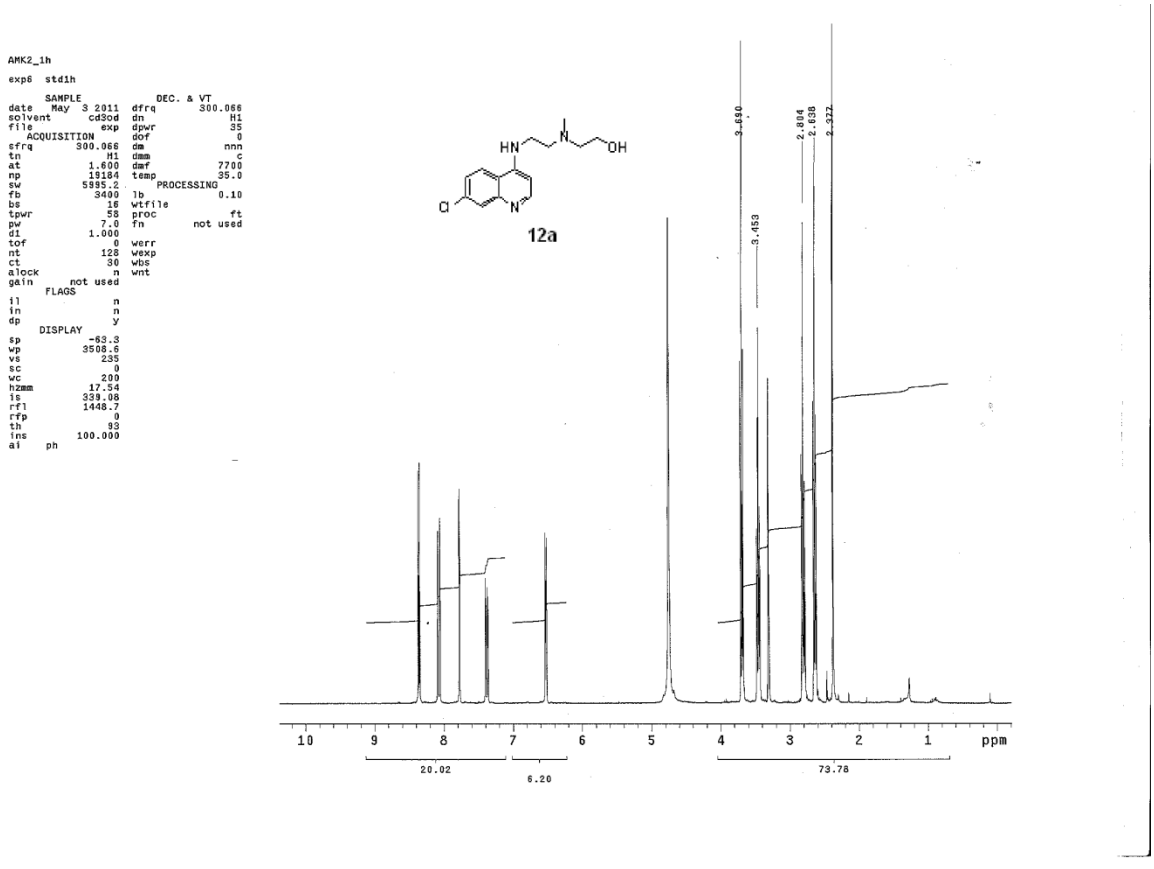
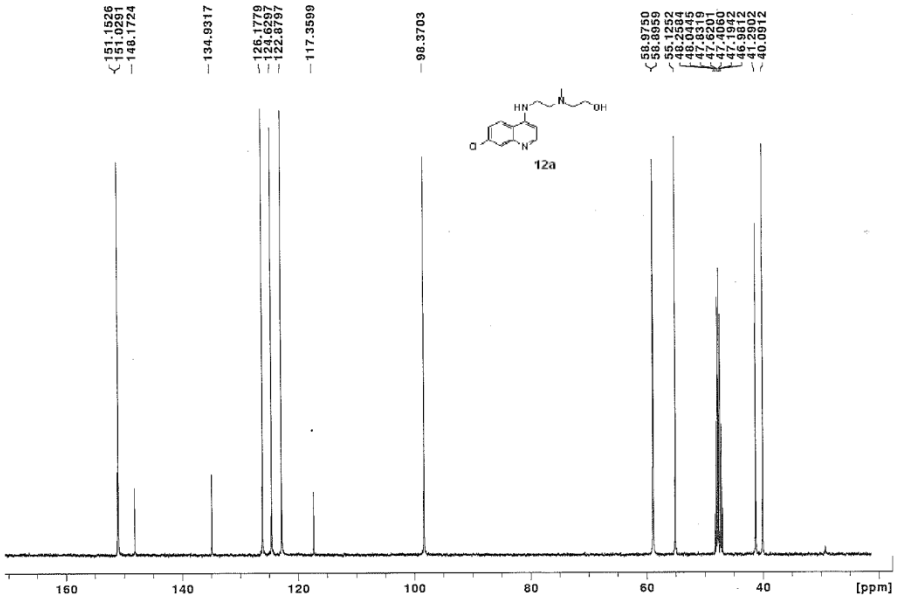
34.121
30.013
29.765
26.516
20.577
9h
150
100
50
ppm (t1)


AMK2_1h
exp6 std1h
SAMPLE
date May 3 2011
solvent cd3od
file exp
ACQUISITION
sfrq 300.066
tn H1
at 1.600
np 19184
sw 5995.2
fb 3400
bs 16
tpwr 58
pw 7.0
dl 1.000
tof 0
nt 128
ct 30
alock n
gain not used
FLAGS
il n
in n
dp y
DISPLAY
sp -63.3
wp 3508.6
vs 235
sc 0
wc 200
hzmm 17.54
is 339.08
rfl 1448.7
rfp 0
th 93
ins 100.000
ai ph
DEC. & VT
dfrq 300.066
dn H1
dpwr 35
dof 0
dm nnn
dmm c
dmf 7700
temp 35.0
PROCESSING
lb 0.10
wtfile
proc ft
fn not used
werr
wexp
wbs
wnt
12a
3.650
3.459
2.804
2.638
2.372
10
9
8
7
6
5
4
3
2
1
ppm
20.02
6.20
73.78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126.1779
124.6297
122.8797
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98.3703
58.8750
58.6855
55.1252
48.2584
48.0445
47.8201
47.6319
47.4060
47.1942
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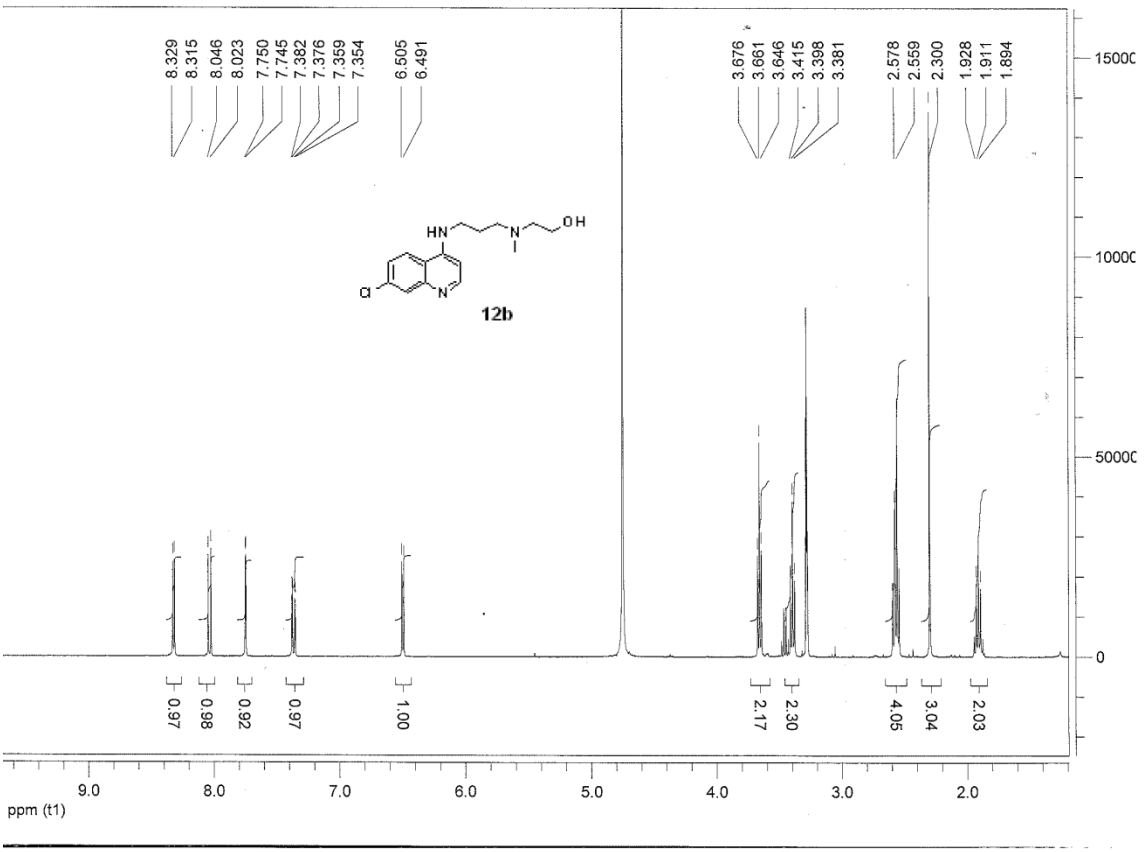
40.0912
HN
OH
N
Cl
12a
160
140
120
100
80
60
40
[ppm]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8.023
7.750
7.745
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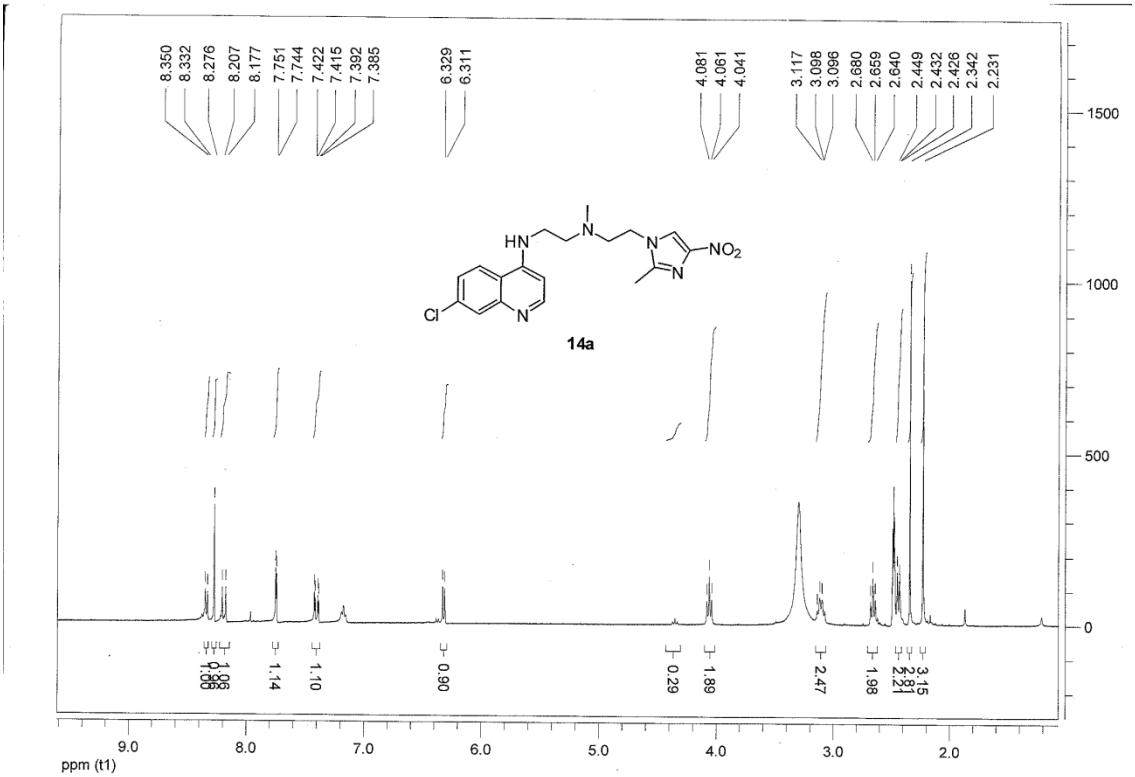
7.376
7.359
7.354
6.505
6.491
3.676
3.661
3.646
3.415
3.398
3.381
2.578
2.559
2.300
1.928
1.911
1.894
HN
OH
N
Cl
12b
0.97
0.98
0.92
0.97
1.00
2.17
2.30
4.05
3.04
2.03
15000
10000
5000
0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
ppm (t1)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8.276
8.207
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7.744
7.422
7.415
7.392
7.385
6.329
6.311
4.081
4.061
4.041
3.117
3.098
3.096
2.680
2.659
2.640
2.449
2.432
2.426
2.342
2.231
HN
N
N
NO2
N
Cl
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1.10
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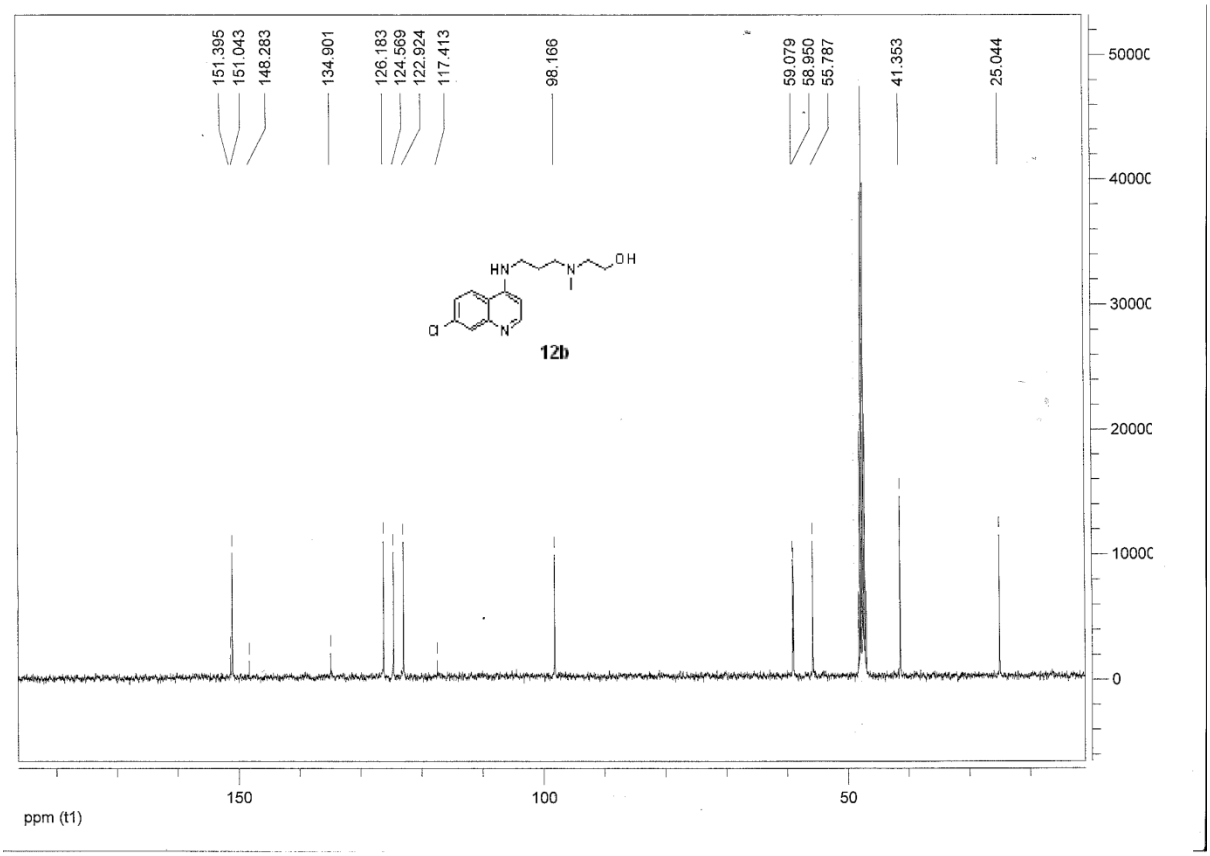
0.29
1.89
2.47
1.98
3.15
ppm (t1)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124.569
122.924
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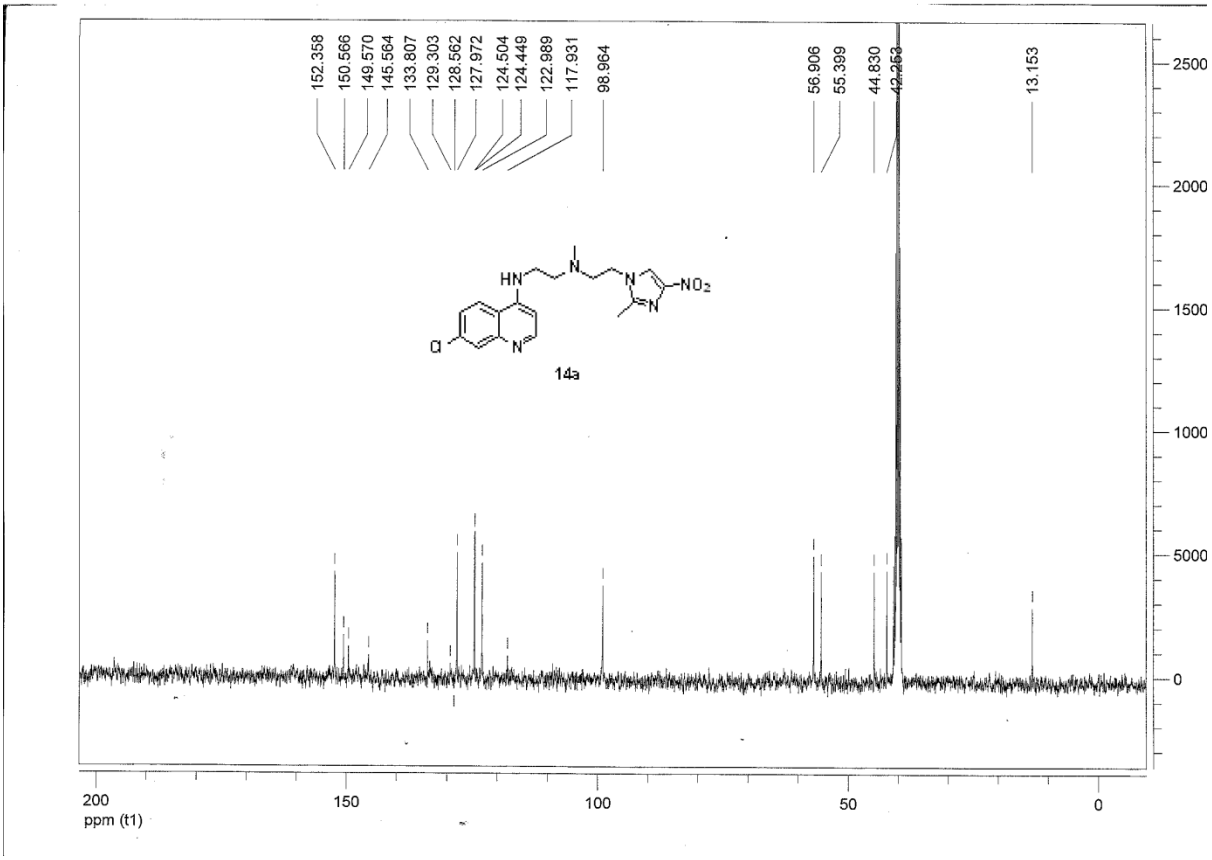
58.950
55.787
41.353
25.044
HN
N
OH
Cl
N
12b
ppm (t1)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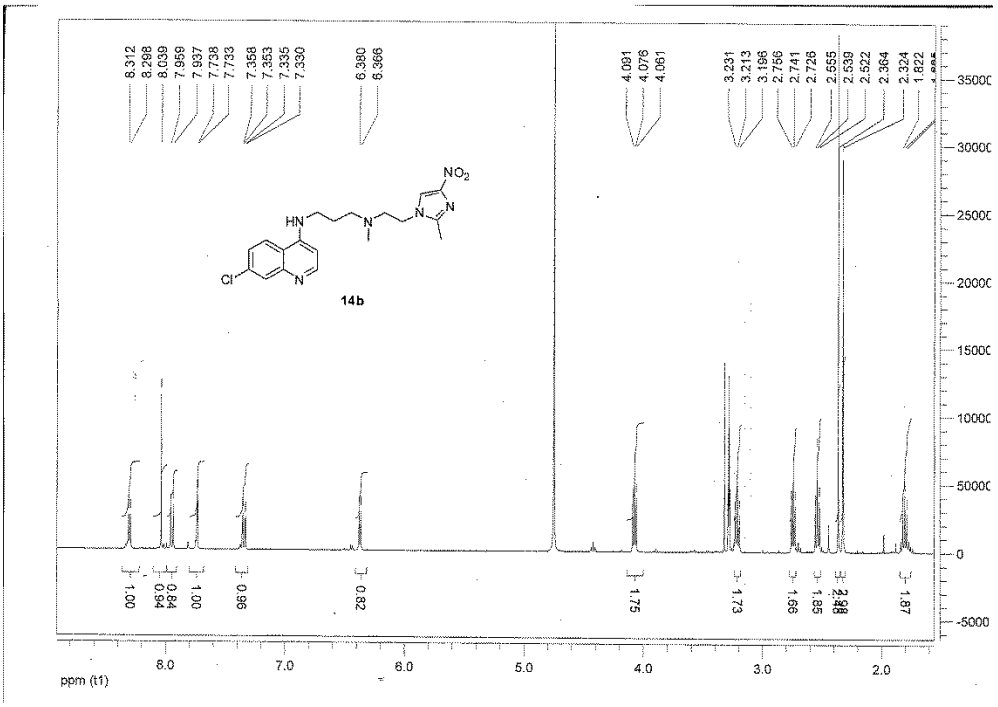
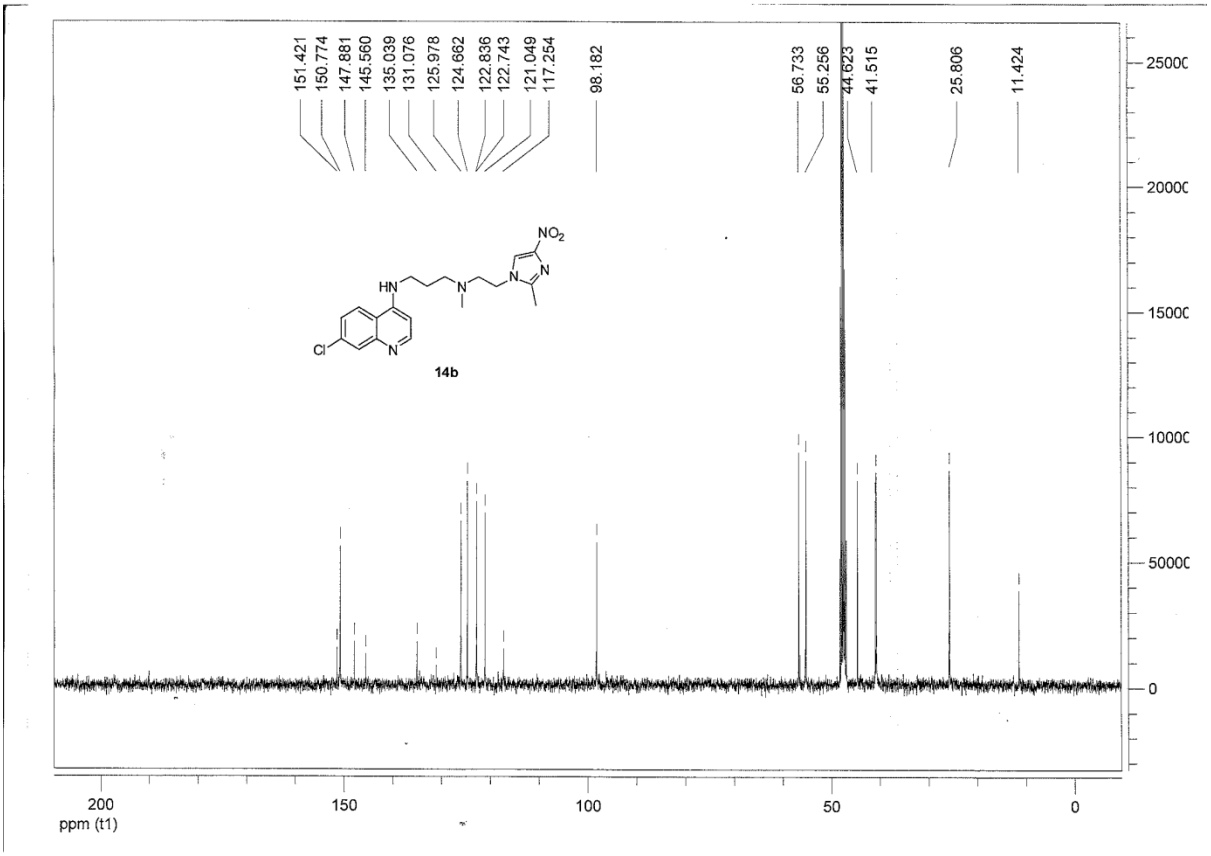
128.562
127.972
124.504
124.449
122.989
117.931
98.964
56.906
55.399
44.830
42.263
13.153
HN
N
N
N
NO2
Cl
N
14a
2500
2000
1500
1000
5000
0
200
150
100
50
0
ppm (t1)


8.312
8.298
8.039
7.959
7.937
7.738
7.733
7.358
7.353
7.335
7.330
6.380
6.366
4.081
4.076
4.061
3.231
3.213
3.196
2.756
2.741
2.728
2.555
2.539
2.522
2.364
2.324
1.822
NO2
HN
N
N
N
Cl
N
14b
1.00
0.84
0.84
1.00
0.96
0.82
1.75
1.73
1.98
1.95
2.38
2.38
1.87
35000
30000
25000
20000
15000
10000
5000
0
-5000
8.0
7.0
6.0
5.0
4.0
3.0
2.0
ppm (t1)


151.421
150.774
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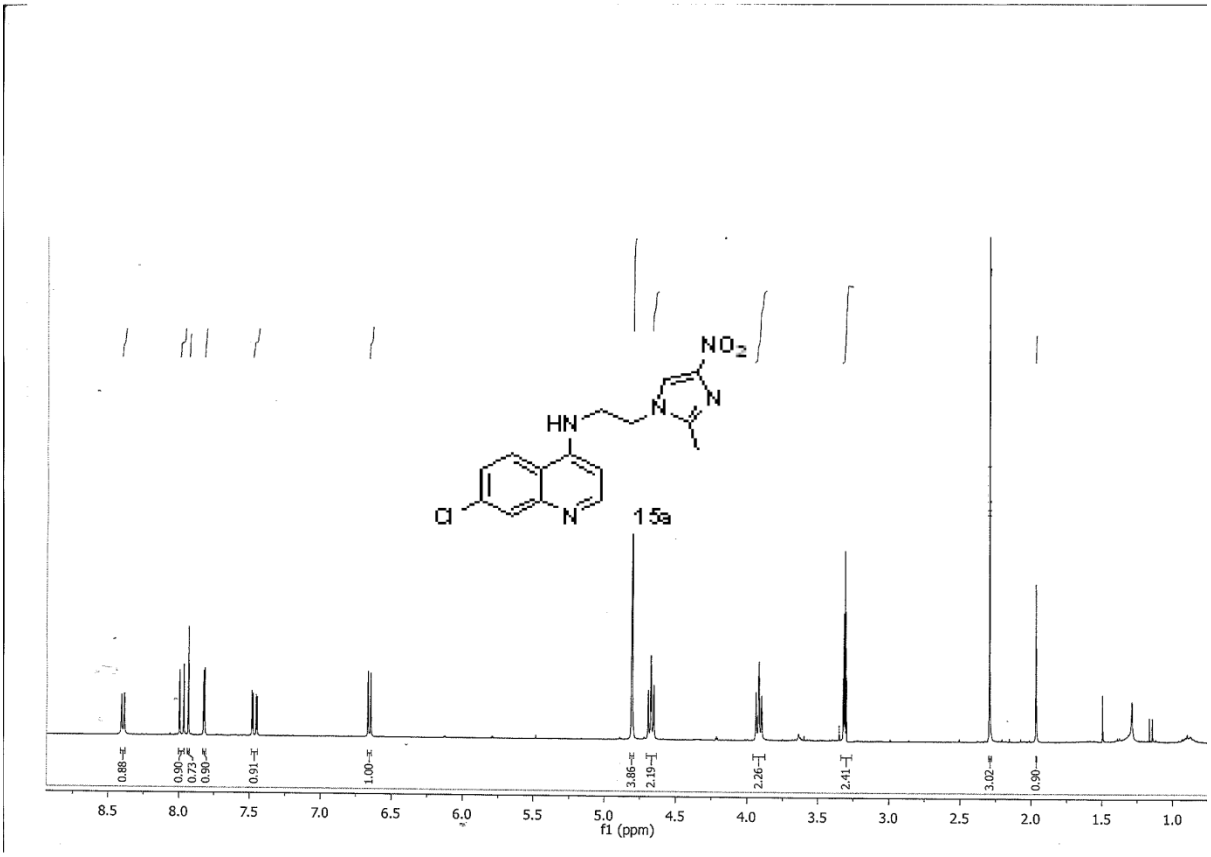
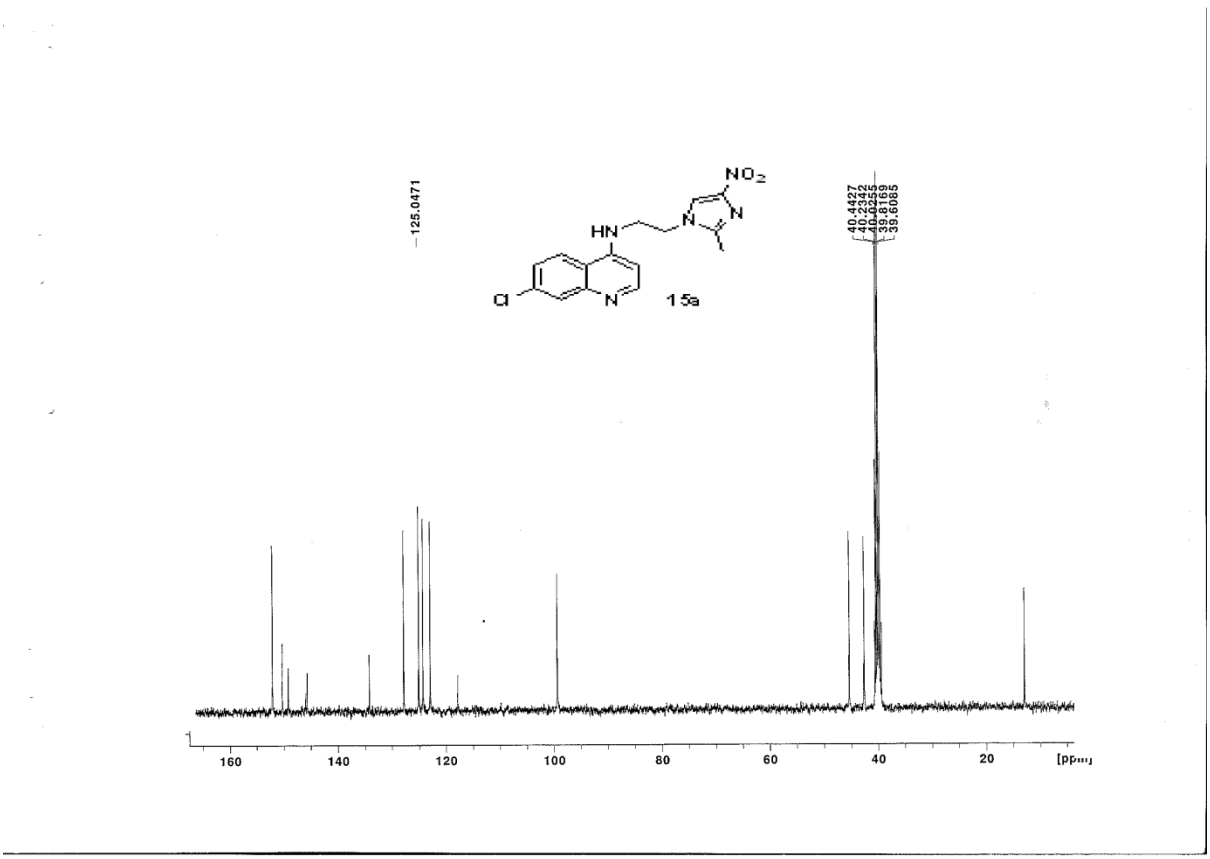
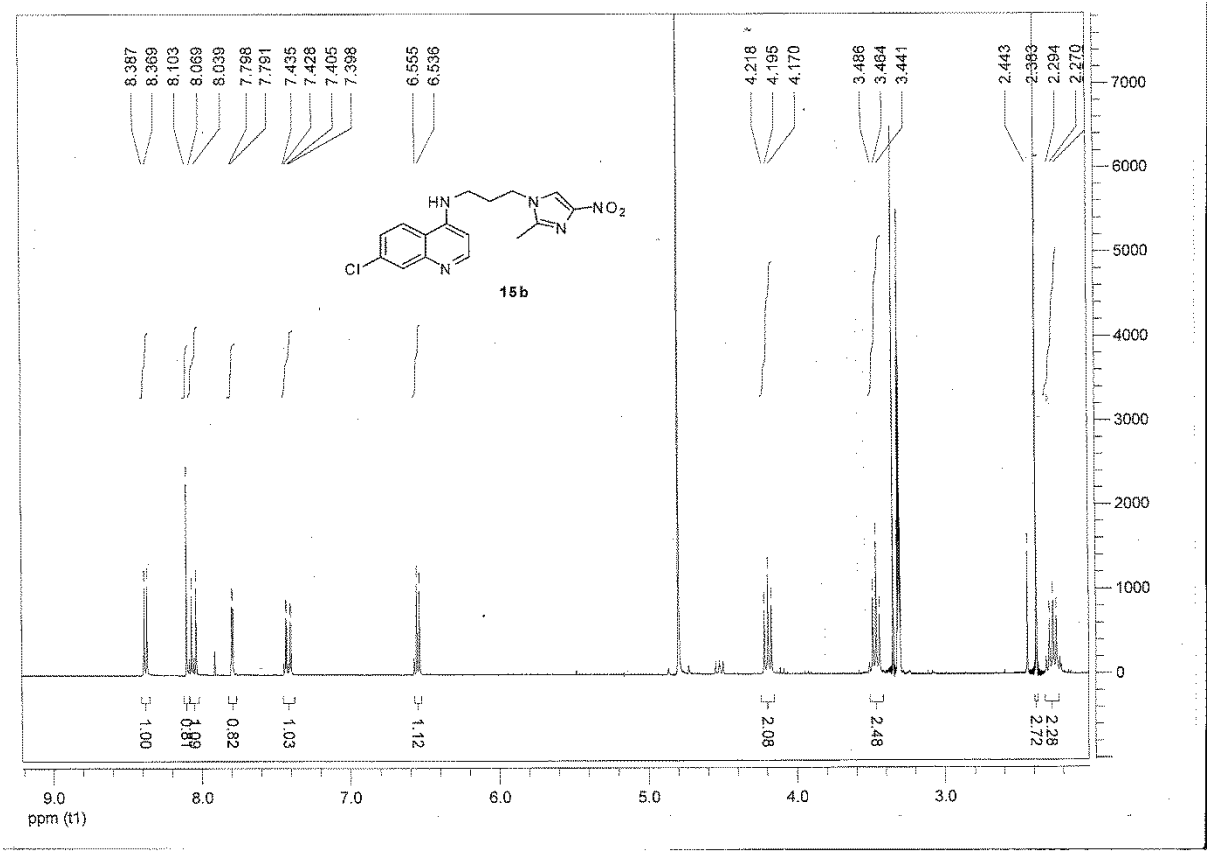
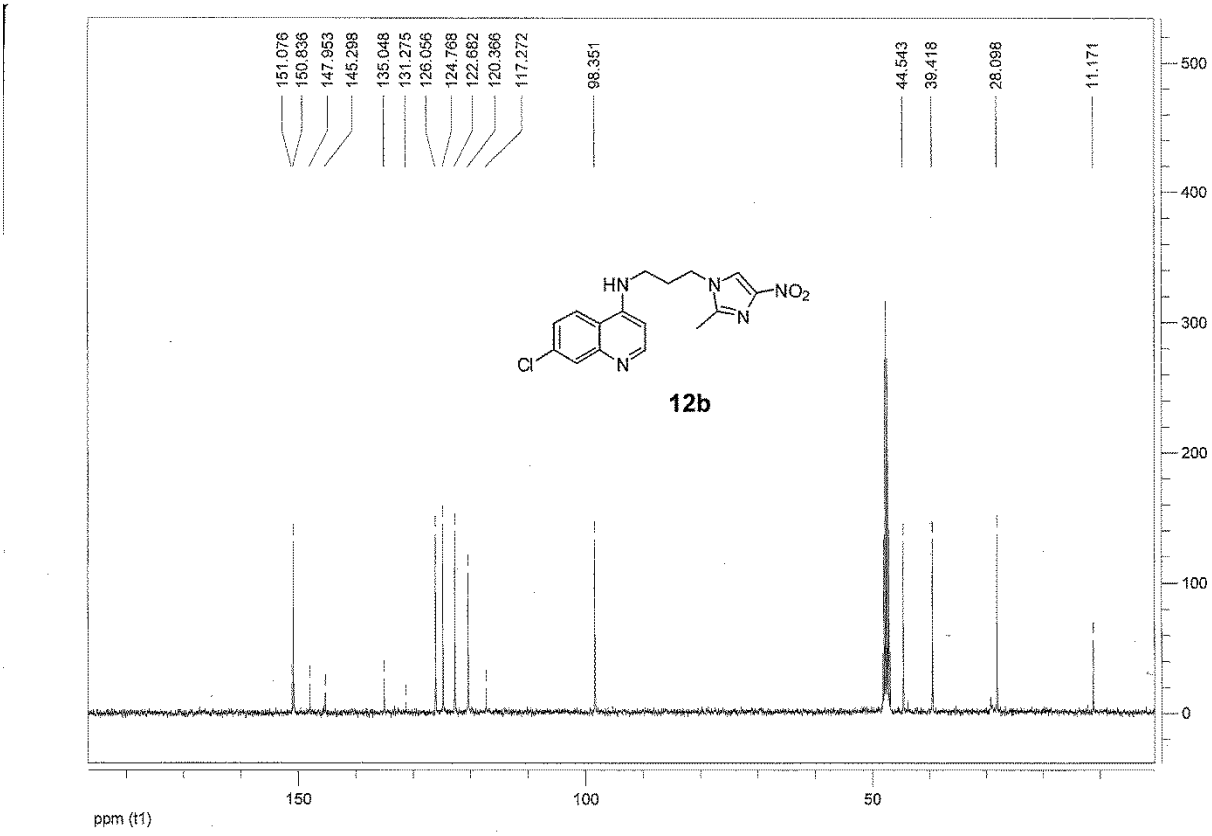
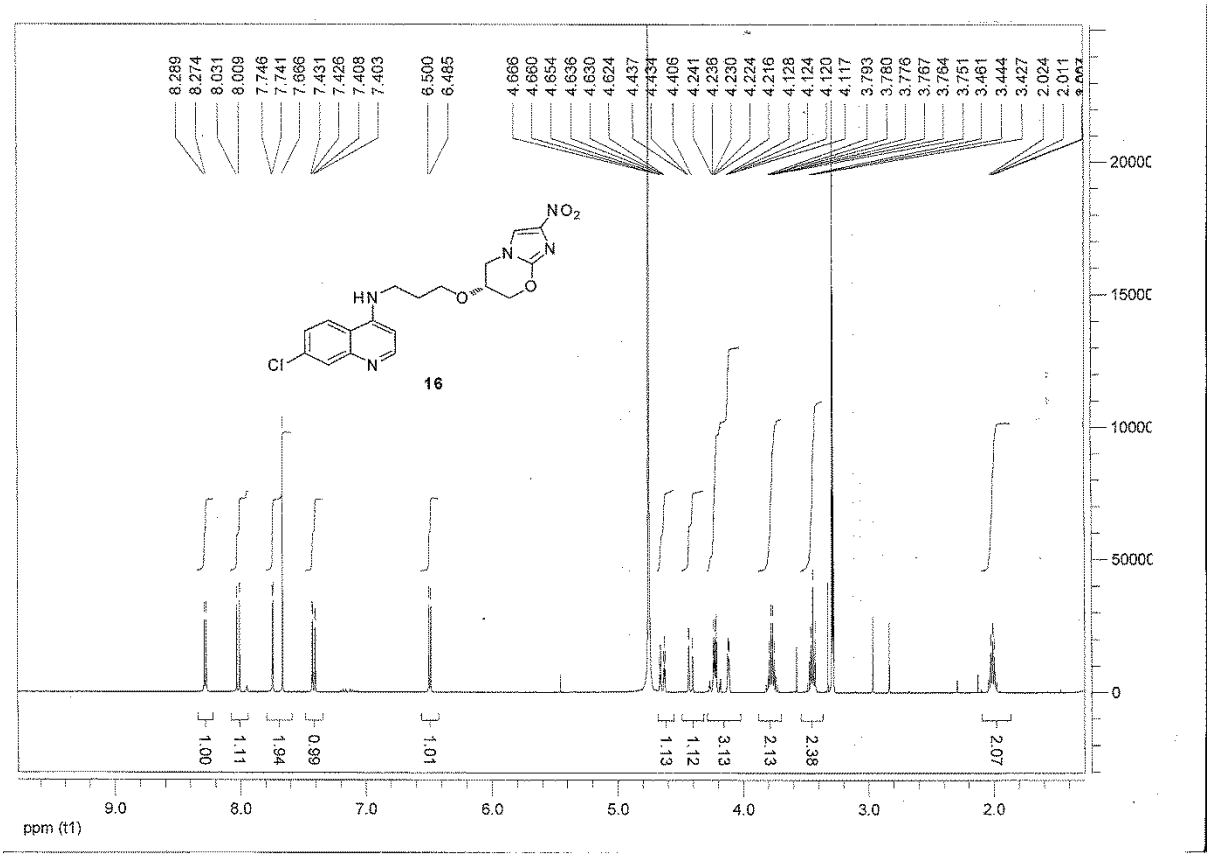
135.039
131.076
125.978
124.662
122.836
122.743
121.049
117.254
98.182
56.733
55.256
44.623
41.515
25.806
11.424
NO2
HN
N
N
Cl
N
14b
2500
2000
1500
1000
5000
0
200
150
100
50
0
ppm (t1)

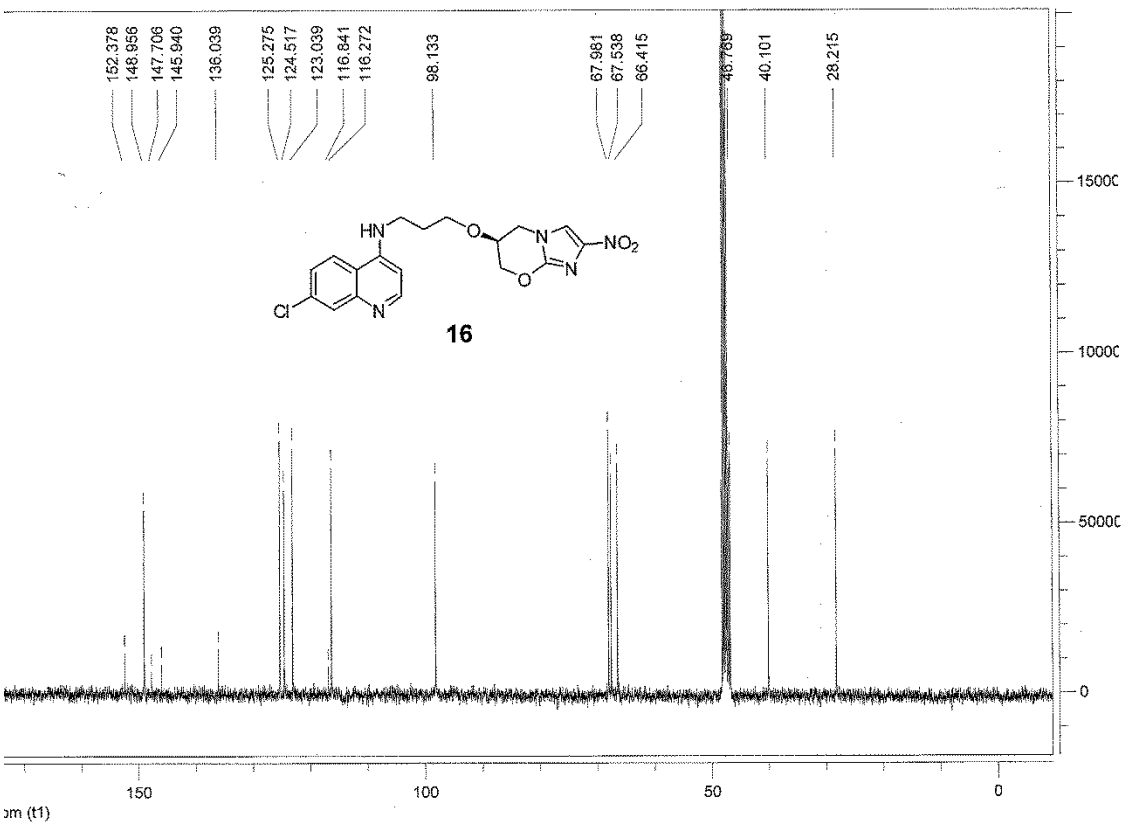

NO2
HN
N
N
Cl
N
15a
0.88
0.90
0.73
0.90
0.91
1.00
3.86
2.19
2.26
2.41
3.02
0.90
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)


125.0471
40.4427
40.2342
40.0258
39.8175
39.6085
NO2
HN
N
N
Cl
N
15a
160
140
120
100
80
60
40
20
[ppm]


8.387
8.369
8.103
8.069
8.039
7.798
7.791
7.435
7.428
7.405
7.398
6.555
6.536
4.218
4.195
4.170
3.486
3.464
3.441
2.443
2.383
2.294
2.270
HN
NO2
N
N
Cl
N
15b
1.00
0.91
0.82
1.03
1.12
2.08
2.48
2.72
2.28
7000
6000
5000
4000
3000
2000
1000
0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
ppm (t1)


151.076
150.836
147.953
145.298
135.048
131.275
126.056
124.768
122.682
120.366
117.272
98.351
44.543
39.418
28.098
11.171
HN
N
NO2
N
Cl
N
12b
ppm (t1)


8.289
8.274
8.031
8.009
7.746
7.741
7.686
7.431
7.426
7.408
7.403
6.500
6.485
4.666
4.660
4.654
4.636
4.630
4.624
4.437
4.434
4.406
4.241
4.236
4.230
4.224
4.216
4.128
4.124
4.120
4.117
3.793
3.780
3.776
3.767
3.764
3.751
3.481
3.444
3.427
2.024
2.011
NO2
N
N
HN
O
O
Cl
N
16
1.00
1.11
1.94
0.99
1.01
1.13
1.12
3.13
2.13
2.38
2.07
ppm (t1)


152.378
148.956
147.706
145.940
136.039
125.275
124.517
123.039
116.841
116.272
98.133
67.981
67.538
66.415
46.789
40.101
28.215
HN
O
N
NO2
O
N
Cl
N
16
15000
10000
5000
0
150
100
50
0
pm (t1)