Implementation of the CYP Index for the design of selective tryptophan-2,3-dioxygenase (TDO) inhibitors

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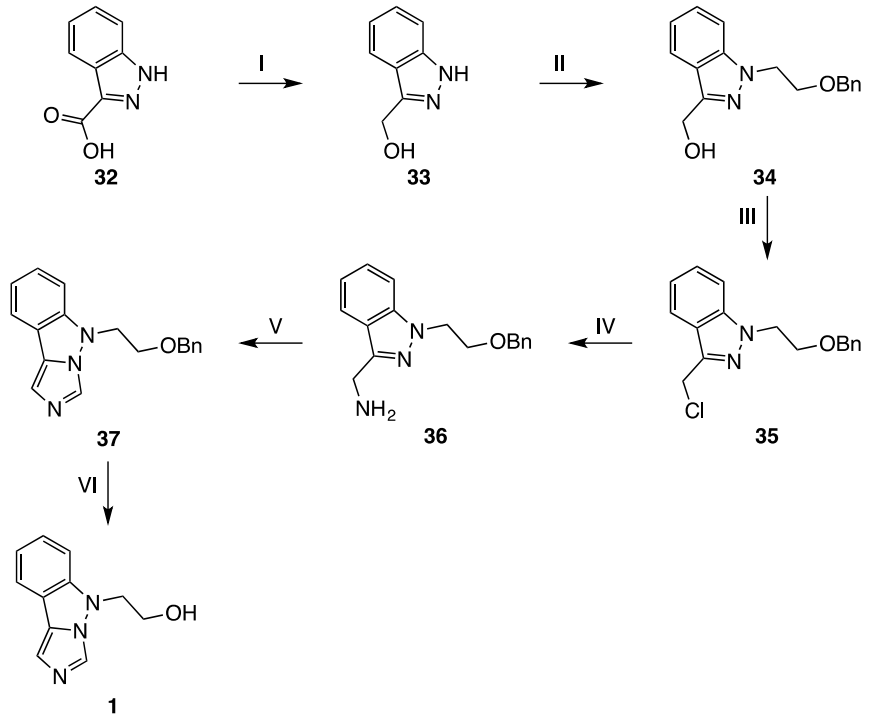
General Information

All solvents and commercial reagents were used as received unless otherwise stated. Where products were purified by chromatography on silica gel this was carried out using either a glass column manually packed with silica gel (Kieselgel 60, 220-440 mesh, 35-75 μm) or an Isolute SPE Si II cartridge. 'Isolute SPE Si cartridge' refers to a pre-packed polypropylene column containing unbonded activated silica with irregular particles with average size of 50 μm and nominal 60 Å porosity. Where an Isolute ® SCX2 cartridge was used, 'Isolute ® SCX-2 cartridge' refers to a pre-packed polypropylene column containing a non-end-capped propylsulphonic acid functionalized silica strong cation exchange sorbent. ^{1}H NMR spectra were obtained at ambient temperature, unless otherwise indicated, in deuterated $CDCl_3$, DMSO-d_6 or methanol-d_4 solvent solutions (reported in ppm) using trimethylsilane (TMS) or residual non-deuterated solvent peaks as the reference standard. When peak multiplicities are reported, the following abbreviates are used: app (apparent), s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad), dd (doublet of doublets), dt (doublet of triplets). Coupling constants, when determined, are reported in Hz (Hertz). LC-MS analysis was performed on a Shimadzu LCMS-202 instrument equipped with Waters Acquity BEH C18-reverse-phase column (50 mm × 2.1 mm × 1.7 μm), eluting with water (+ 0.1% formic acid, 0.05% trifluoroacetic acid or 0.1% ammonium hydroxide)–acetonitrile. Compounds **2**,[1] **7**,[1] **8**,[2] **9**,[3] **11–18**,[3] **20–24**,[3] **26–31**,[3] **38**,[4] **45**,[5] **52**[1] and **65**[1] were prepared according to published procedures.

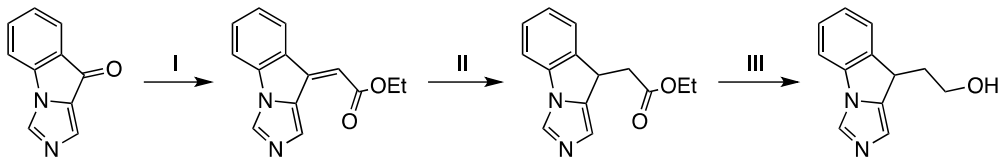
Computational Methods

The ability of each tricyclic core (*e.g.* **1–6**) to coordinate with a heme iron was estimated through a calculation of the partial charge of the iron-binding nitrogen using quantum mechanical calculations with Schrodinger's Jaguar[6] version 8.7 at a B3LYP/6-31G** level of theory. Following a geometry optimization of each three-ring core, partial charges at the nitrogen atom were derived from the electrostatic potential.

Synthetic Schemes

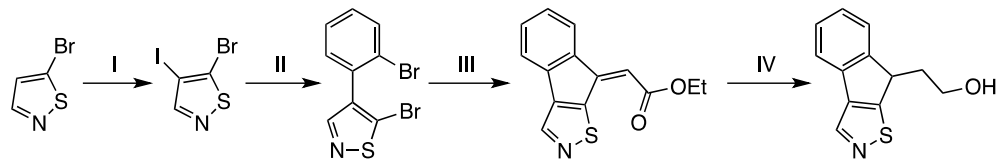


Scheme S1. Reagents and conditions: (I) lithium aluminum hydride, tetrahydrofuran, 25 °C; (II) ((2-bromoethoxy)methyl)benzene, potassium *tert*-butoxide, *N*,*N*-dimethylformamide, 25 °C; (III) thionyl chloride, toluene, 60 °C; (IV) ammonium hydroxide, *N*,*N*-dimethylformamide, 1,4-dioxane, 50 °C; (V) formic acid, acetic anhydride, 60 °C then phosphoryl chloride, toluene, 100 °C; (VI) palladium-on-carbon, hydrogen (1 atm), acetic acid, methanol, 25 °C.

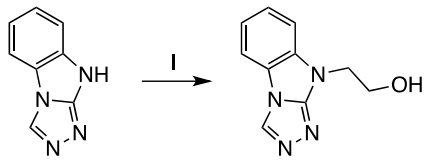


38 **39** **40** **3**

Scheme S2. Reagents and conditions: (I) ethyl 2-(diethoxyphosphoryl)acetate, sodium hydride, tetrahydrofuran, 0–25 °C; (II) palladium-on-carbon, hydrogen (10 atm), ethyl acetate, 25 °C; (III) lithium aluminum hydride, tetrahydrofuran, 0 °C.

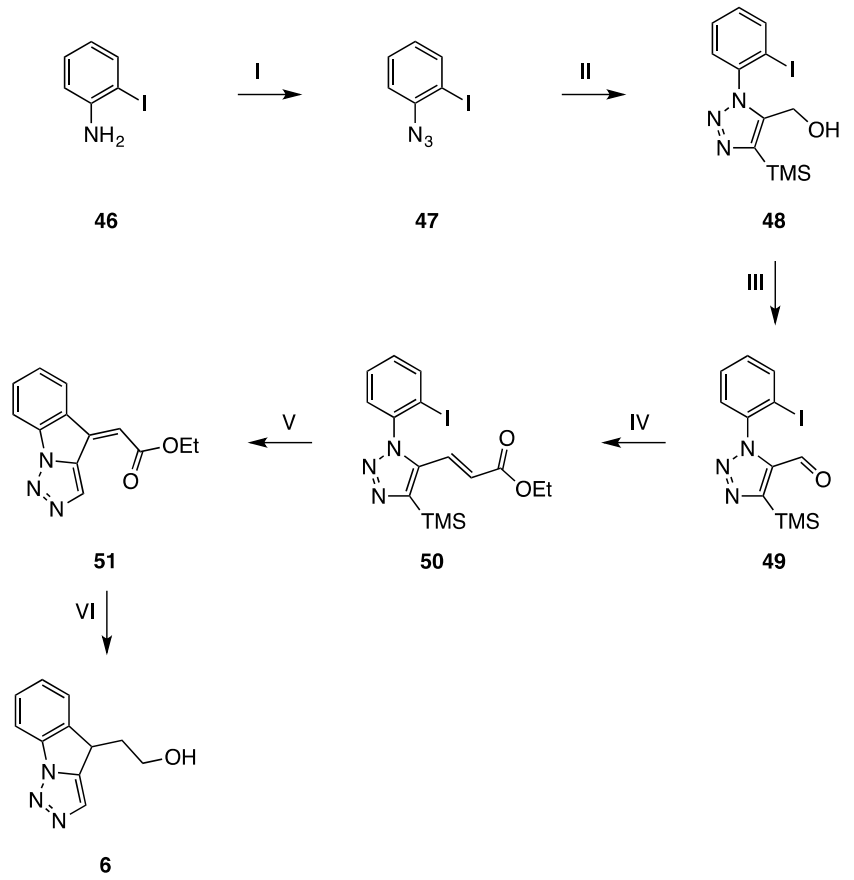


Scheme S3. Reagents and conditions: (I) *N*-iodosuccinimide, trifluoroacetic acid, 80 °C; (II) (2-bromophenyl)boronic acid, bis(triphenylphosphine)palladium(II) dichloride, sodium bicarbonate, 1,4-dioxane, water, 100 °C; (III) ethyl propenoate, palladium(II) acetate, tris(*o*-tolyl)phosphine, potassium acetate, *N*,*N*-dimethylformamide, 100 °C; (IV) sodium borohydride, methanol, 25 °C.

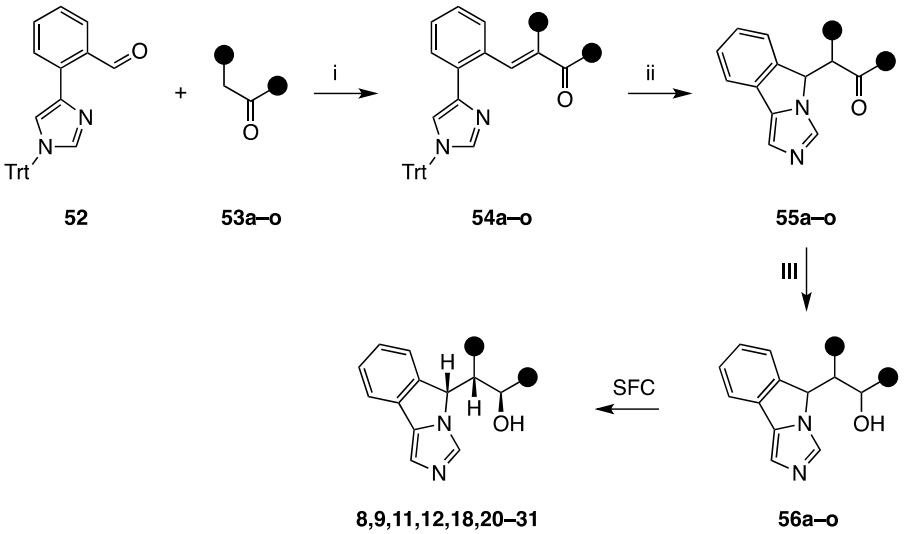


45 **5**

Scheme S4. Reagents and conditions: (I) 2-bromoethan-1-ol, potassium hydroxide, *N*,*N*-dimethylformamide, 25 °C.

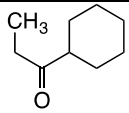
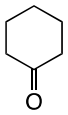
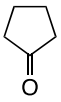
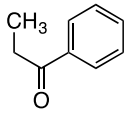
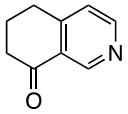
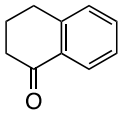
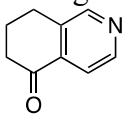
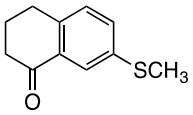
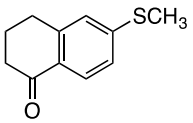
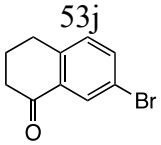


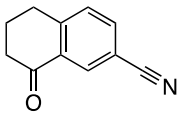
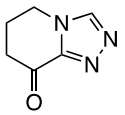
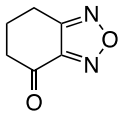
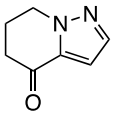
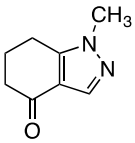
Scheme S5. Reagents and conditions: (I) sodium nitrate, sodium azide, hydrogen chloride, water, 0 °C; (II) 3-(trimethylsilyl)prop-2-yn-1-ol, toluene, 110 °C; (III) Dess-Martin periodinane, dichloromethane, 25 °C; (IV) ethyl (triphenylphosphoranylidene)acetate, tetrahydrofuran, 25 °C; (V) palladium(II) acetate, tris(*o*-tolyl)phosphine, potassium acetate, *N*,*N*-dimethylformamide, 100 °C; (VI) sodium borohydride, methanol, 25 °C.

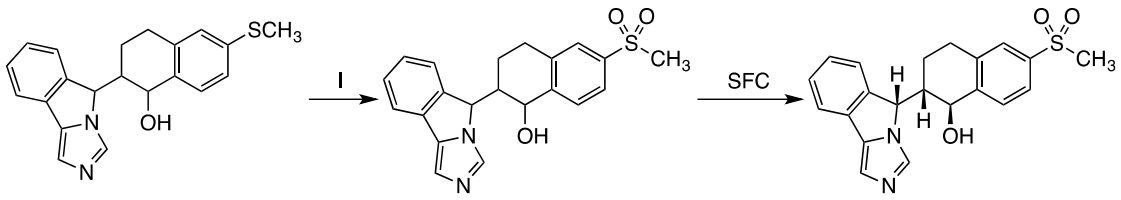


Scheme S6. Reagents and conditions: (I) See Table S1; (II) acetic acid, methanol, 70 °C; (III) sodium borohydride, methanol, 25 °C.

Table S1. Reaction conditions for Step I aldol condensation

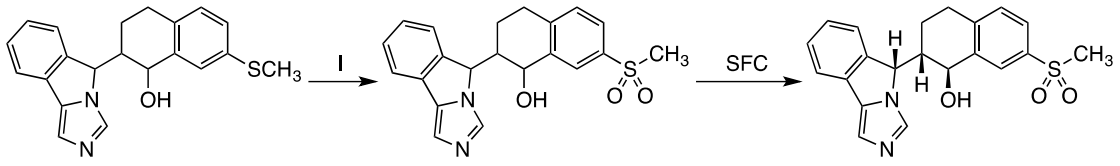
Ketone 53	Reagents & Conditions
 53a	sodium hydroxide ethanol, 50 °C
 53b	pyrrolidine methanol, 50 °C
 53c	pyrrolidine methanol, 50 °C
 53d	sodium hydroxide ethanol, 50 °C
 53e	sodium methoxide tetrahydrofuran, 50 °C
 53f	sodium hydroxide tetrahydrofuran, 25 °C
 53g	sodium ethoxide ethanol, 80 °C
 53h	sodium hydroxide tetrahydrofuran, 25 °C
 53i	sodium ethoxide methanol, 70 °C
 53j	sodium hydroxide ethanol, 50 °C
 53k	sodium hydroxide ethanol, 50 °C

 53l	sodium ethoxide methanol, 70 °C
 53m	lithium hydroxide tetrahydrofuran/water, 25 °C
 53n	pyrrolidine methanol, 70 °C
 53o	sodium hydroxide ethanol, 50 °C
 53p	sodium hydroxide ethanol, 50 °C



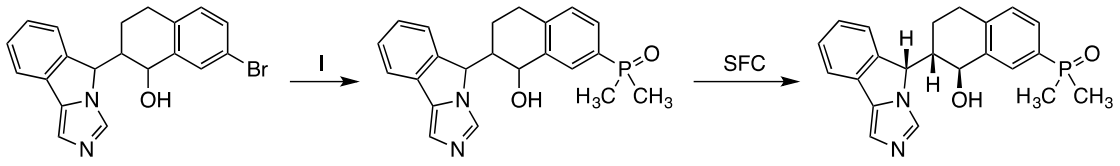
56i **57** **23**

Scheme S7. Reagents and conditions: (I) hydrogen peroxide (30% aqueous solution), acetic acid, 25 °C.



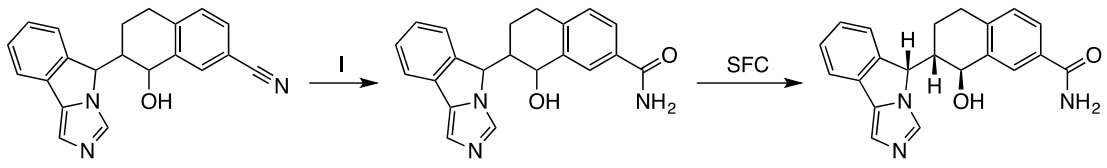
56j **58** **24**

Scheme S8. Reagents and conditions: (I) hydrogen peroxide (30% aqueous solution), acetic acid, 25 °C.



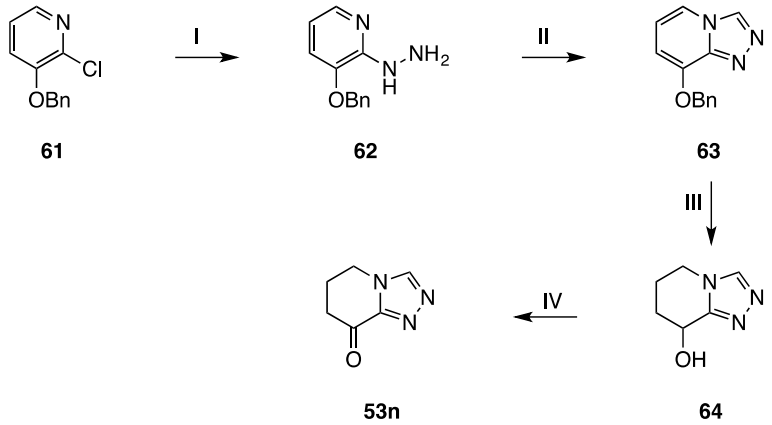
56k **59** **25**

Scheme S9. Reagents and conditions: (I) dimethylphosphine oxide, palladium(II) acetate, 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene, potassium phosphate, *N*,*N*-dimethylformamide, 140 °C.

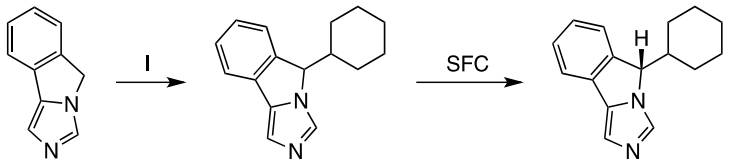


56l **60** **27**

Scheme S10. Reagents and conditions: (I) sodium hydroxide, sodium peroxide (30% aqueous solution), methanol, 25 °C.

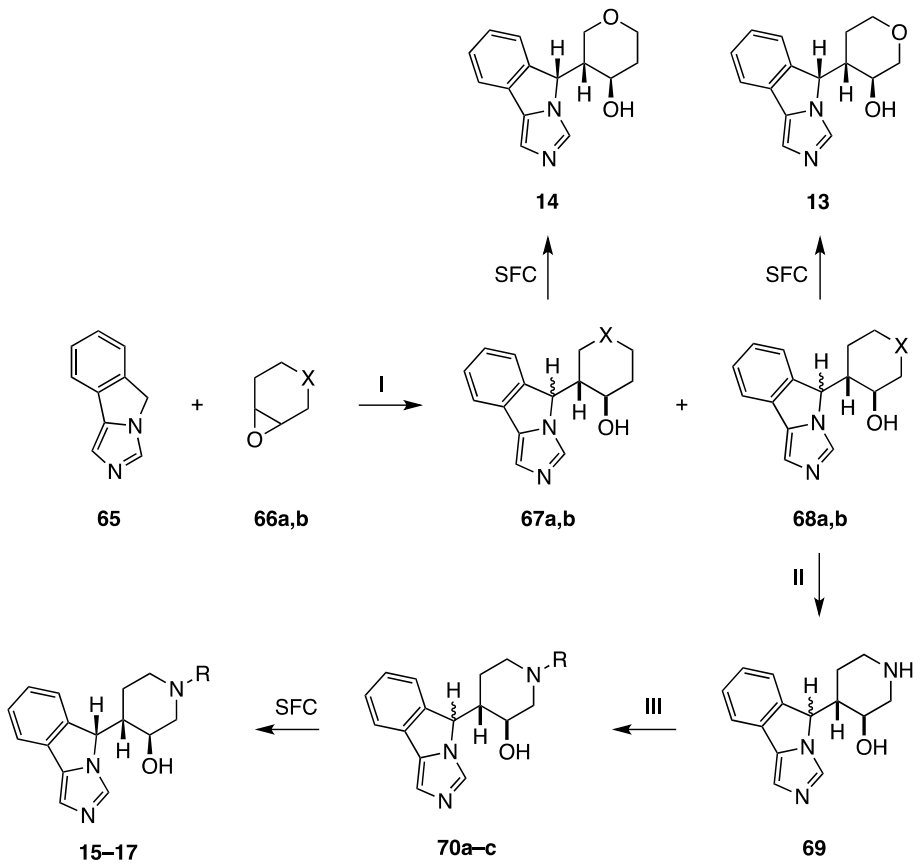


Scheme S11. Reagents and conditions: (I) hydrazine, potassium carbonate, isopropanol, 100 °C; (II) triethyl orthoformate, 160 °C; (III) palladium-on-carbon, hydrogen (1 atm), methanol, 25 °C; (IV) Dess-Martin periodinane, dichloromethane, 25 °C.



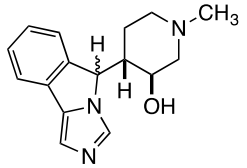
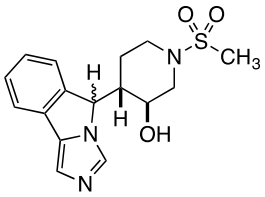
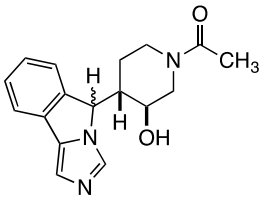
65 ***rac*-10** **10**

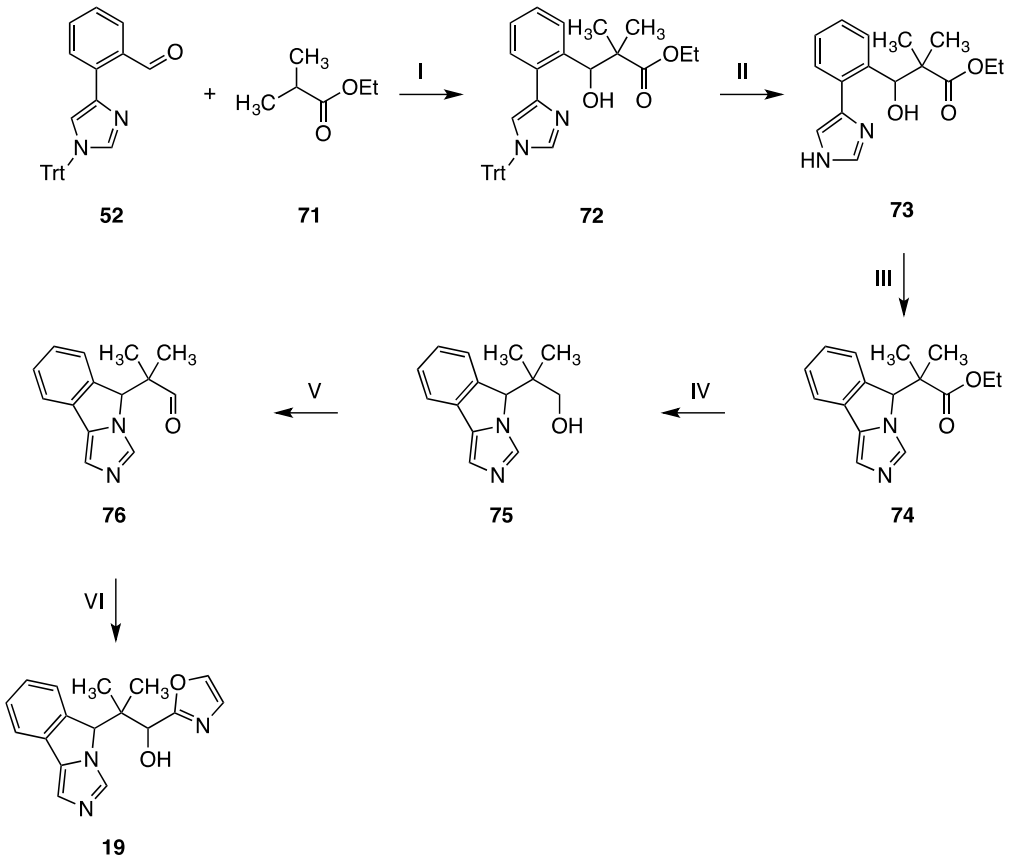
Scheme S12. Reagents and conditions: (I) *n*-butyllithium, bromocyclohexane, tetrahydrofuran, -78–25 °C.



Scheme S13. Reagents and conditions: (I) **39a**, X = O, **39b**, X = *N*-Boc, *n*-butyllithium, tetrahydrofuran, -78–25 °C; (II) **68b**, trifluoroacetic acid, dichloromethane, 25 °C; (III) See Table S2.

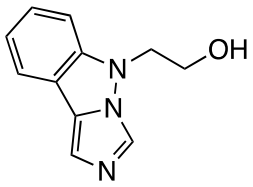
Table S2. Reaction conditions for Step III *N*-substitution

***N*-Substitution Product 70**	**Reagents & Conditions**
 70a	formalin, sodium cyanborohydride acetic acid, water, 25 °C
 70b	methanesulfonyl chloride, triethylamine dichloromethane, 25 °C
 70c	acetyl chloride, triethylamine dichloromethane, 25 °C

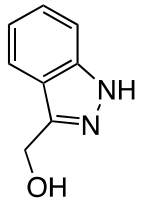


Scheme S14. Reagents and conditions: (I) *N*,*N*-diisopropylamine, *n*-butyllithium, tetrahydrofuran, -40 °C; (II) acetic acid, methanol, 70 °C; (III) cyanomethylene trimethyphosphorane, tetrahydrofuran, 25 °C; (IV) diisobutylaluminum hydride, toluene, 0–25 °C; (V) Dess-Martin periodinane, sodium bicarbonate, dichloromethane, 25 °C; (VI) oxazole, *n*-butyllithium, tetrahydrofuran, -78–25 °C.

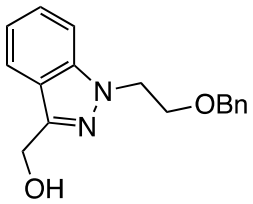
Characterization Data



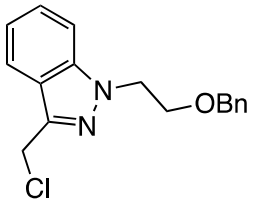
2-(5*H*-imidazo[1,5-*b*]indazol-5-yl)ethan-1-ol (1).



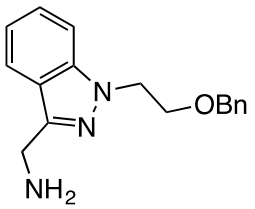
(1*H*-indazol-3-yl)methanol (**33**): To a solution of lithium aluminum hydride (4.7 g, 120 mmol) in tetrahydrofuran (500 mL) was added 1*H*-indazole-3-carboxylic acid (**32**, 10 g, 62 mmol). The resulting solution was stirred for 5 h at 0 °C. The reaction was then quenched with water and 15% sodium hydroxide. The solids were filtered out. The filtrate was concentrated under vacuum. Purification by silica gel flash chromatography eluting with 40% dichloromethane–ethyl acetate afforded the title compound (2.6 g, 28%) as a light yellow solid. LCMS-ESI (m/z): $[M+H]^+$ calcd for $C_8H_9N_2O$, 149.2; found 149.3.



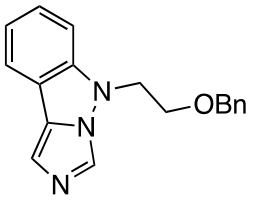
(1-(2-(benzyloxy)ethyl)-1*H*-indazol-3-yl)methanol (**34**): To a solution of 1*H*-indazol-3-ylmethanol (**33**, 2.6 g, 17.6 mmol) in *N*,*N*-dimethylformamide (120 mL) was added potassium *tert*-butoxide (3.94 g, 35 mmol) and ((2-bromoethoxy)methyl)benzene (5.67 g, 26 mmol). The resulting solution was stirred for 2 h at ambient temperature. The resulting solution was diluted with water and extracted with ethyl acetate. The organic layers were combined and concentrated under vacuum. Purification by silica gel flash chromatography eluting with 50% ethyl acetate–petroleum ether afforded the title compound (3.5 g, 71%) as a yellow oil. LCMS-ESI (m/z): $[M+H]^+$ calcd for $C_{17}H_{19}N_2O_2$, 283.3; found 283.1.



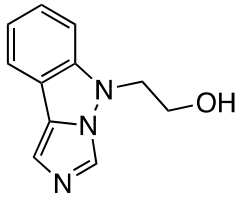
1-(2-(benzyloxy)ethyl)-3-(chloromethyl)-1*H*-indazole (**35**): To a solution of (1-(2-(benzyloxy)ethyl)-1*H*-indazol-3-yl)methanol (**34**, 2.5 g, 8.9 mmol) in toluene (20 mL) was added thionyl chloride (10 mL, 138 mmol). The resulting solution was stirred for 1.5 h at 65 °C in an oil bath. The resulting mixture was concentrated under vacuum to afford the title compound (2.5 g, crude) as a yellow oil. LCMS-ESI (m/z): $[M+H]^+$ calcd for $C_{17}H_{18}{}^{35}ClN_2O$, 301.8; found 301.2.



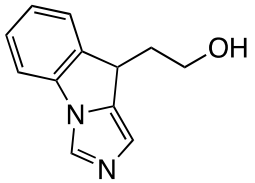
(1-(2-(benzyloxy)ethyl)-1*H*-indazol-3-yl)methanamine (**36**): To ammonia (90 mL) was added a solution of 1-(2-(benzyloxy)ethyl)-3-(chloromethyl)-1*H*-indazole (**35**, 2.5 g, 8.3 mmol) in 1,4-dioxane (10 mL) and *N*,*N*-dimethylformamide (5 mL). The resulting solution was stirred for 2 h at 50 °C in an oil bath. The reaction mixture was concentrated under vacuum. Purification by silica gel flash chromatography eluting with 0.1% ammonia–10% dichloromethane–methanol afforded the title compound (1.3 g, 56%) as a yellow oil. LCMS-ESI (m/z): $[M+H]^+$ calcd for $C_{17}H_{20}N_3O$, 282.4; found 282.2.



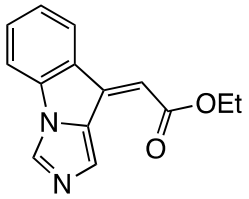
5-(2-(benzyloxy)ethyl)-5*H*-imidazo[1,5-*b*]indazole (**37**): A mixture of (1-(2-(benzyloxy)ethyl)-1*H*-indazol-3-yl)methanamine (**36**, 500 mg, 1.8 mmol) in acetic anhydride (10 mL) and formic acid (5 mL) was stirred for 2 h at 60 °C in an oil bath. The mixture was concentrated under vacuum, and resuspended in toluene (10 mL) and phosphorus oxychloride (3 mL). The resulting solution was stirred for 1 h at 100 °C in an oil bath. The reaction mixture was concentrated under vacuum. Purification by preparative HPLC afforded the title compound (85 mg, 16%) as a yellow oil. LCMS-ESI (m/z): $[M+H]^+$ calcd for $C_{18}H_{18}N_3O$, 292.4; found 292.2.



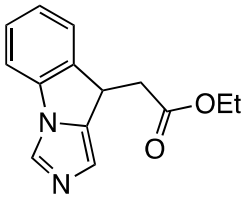
2-(5*H*-imidazo[1,5-*b*]indazol-5-yl)ethan-1-ol (**1**): 5-(2-(benzyloxy)ethyl)-5*H*-imidazo[1,5-b]indazole (**37**, 620 mg, 2.1 mmol), acetic acid (25 mg, 0.42 mmol) and 10% Pd/C (45 mg) were combined in methanol (25 mL) under an atmosphere of hydrogen and stirred for 2 h at ambient temperature. The solids were removed by filtration. The filtrate was concentrated under vacuum. Purification by preparative HPLC afforded the title compound (24 mg, 5%) as a pale yellow solid. LCMS-ESI (m/z): $[M+H]^+$ calcd for $C_{11}H_{12}N_3O$, 202.2; found 202.1. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.18 (s, 1H), 7.74 (d, J = 7.7 Hz, 1H), 7.43 (d, J = 8.2 Hz, 1H), 7.41 – 7.32 (m, 1H), 7.22 – 7.13 (m, 2H), 4.96 (t, J = 5.1 Hz, 1H), 4.21 (t, J = 5.4 Hz, 2H), 3.79 – 3.62 (m, 2H).



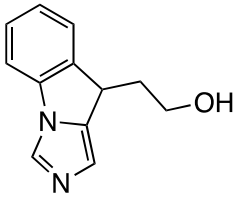
2-(9*H*-imidazo[1,5-*a*]indol-9-yl)ethan-1-ol (3).



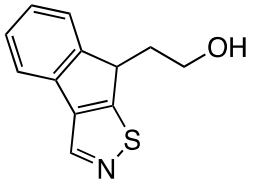
ethyl (*Z*)-2-(9*H*-imidazo[1,5-*a*]indol-9-ylidene)acetate (**39**): To a solution of ethyl 2-(diethoxyphosphoryl)acetate (263 mg, 1.2 mmol) in tetrahydrofuran (2 mL) was added sodium hydride (30 mg, 1.2 mmol) at 0 °C. After 5 min, a tetrahydrofuran (1 mL) solution of 9*H*-Imidazo[1,5-*a*]indol-9-one (**38**, 100 mg, 0.59 mmol) was added to the reaction vessel. The reaction was allowed to warm to ambient temperature for 1 h. The crude mixture was concentrated under vacuum. The residue was partitioned between ethyl acetate and water. The organic layer was washed with water and dried over anhydrous sodium sulfate. The solvent was removed under vacuum. Purification by silica gel flash chromatography eluting with 1–10% methanol–dichloromethane afforded the title compound (120 mg, 85%) as a yellow solid. LCMS-ESI (m/z): $[M+H]^+$ calcd for $C_{14}H_{13}N_2O_2$, 241.3; found 241.0.



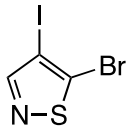
ethyl 2-(9*H*-imidazo[1,5-*a*]indol-9-yl)acetate (**40**): A suspension of ethyl (*Z*)-2-(9*H*-imidazo[1,5-*a*]indol-9-ylidene)acetate (**39**, 200 mg, 0.83 mmol) and palladium-on-carbon (100 mg) in ethyl acetate (4 mL) was stirred under hydrogen (10 atm) for 2 h at room temperature. The reaction mixture was filtered. The solvent was removed under vacuum to afford the title compound (175mg, 85%) as a pale yellow solid. LCMS-ESI (m/z): $[M+H]^+$ calcd for $C_{14}H_{15}N_2O_2$, 243.3; found 243.1.



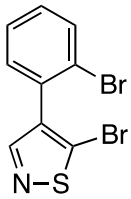
2-(9*H*-imidazo[1,5-*a*]indol-9-yl)ethan-1-ol (**3**): To a solution of ethyl 2-(9*H*-imidazo[1,5-*a*]indol-9-yl)acetate (**40**, 120 mg, 0.50 mmol) in tetrahydrofuran (5 mL) was added lithium aluminum hydride (56 mg, 1.5 mmol) at 0 °C. The resulting suspension was allowed to warm to ambient temperature for 2 h. The reaction was quenched with water and extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous sodium sulfate. The solvent was removed under vacuum. Purification by silica gel flash chromatography eluting with 1–10% methanol–dichloromethane afforded the title compound (6 mg, 4%) as a pale yellow solid. LCMS-ESI (m/z): $[M+H]^+$ calcd for $C_{12}H_{13}N_2O$, 201.3; found 201.1. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.22 (s, 1H), 7.68 (d, *J* = 7.8 Hz, 1H), 7.54 (dq, *J* = 7.5, 1.0 Hz, 1H), 7.39 (tt, *J* = 7.8, 1.0 Hz, 1H), 7.24 (td, *J* = 7.6, 1.1 Hz, 1H), 6.91 (d, *J* = 1.4 Hz, 1H), 4.62 (t, *J* = 5.1 Hz, 1H), 4.19 (dd, *J* = 9.8, 5.1 Hz, 1H), 3.66 (dt, *J* = 7.3, 5.7 Hz, 3H), 2.17 (dtd, *J* = 12.7, 7.4, 5.1 Hz, 1H), 1.60 (ddt, *J* = 13.3, 9.7, 5.8 Hz, 1H).



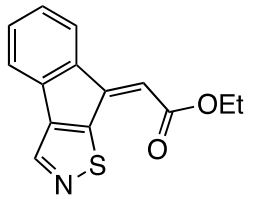
2-(8*H*-indeno[1,2-*d*]isothiazol-8-yl)ethan-1-ol (4).



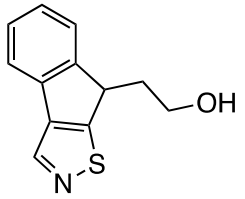
5-bromo-4-iodo-1,2-thiazole (**42**): To a solution of 5-bromo-1,2-thiazole (**41**, 500 mg, 3.0 mmol) in trifluoroacetic acid (50 mL) was added *N*-iodosuccinimide (1.6 g, 7.1 mmol). The resulting solution was stirred for 12 h at 80 °C. The reaction was quenched with water and extracted with ethyl acetate. The solvent was removed under vacuum. Purification by silica gel flash chromatography eluting with 5% ethyl acetate–petroleum ether afforded the title compound (600 mg, 68%) as a yellow solid. LCMS-ESI (m/z): $[M+H]^+$ calcd for $C_3H_2{}^{79}BrINS$, 289.9; found 289.8.



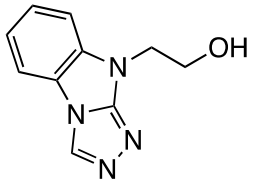
5-bromo-4-(2-bromophenyl)-1,2-thiazole (**43**): To a solution of 5-bromo-4-iodo-1,2-thiazole (**42**, 500 mg, 1.7 mmol) in dioxane (10 mL) and water (2 mL) was added (2-bromophenyl)boronic acid (345 mg, 1.7 mmol), bis(triphenylphosphine)palladium(II) dichloride (120 mg, 0.17 mmol) and sodium bicarbonate (540 mg, 6.4 mmol). The resulting solution was stirred for 15 min at 120 °C. The reaction mixture was concentrated under vacuum. Purification by silica gel flash chromatography eluting with 10% ethyl acetate–petroleum ether afforded the title compound (300 mg, 55%) as yellow oil. LCMS-ESI (m/z): $[M+H]^+$ calcd for $C_9H_6{}^{79}Br_2NS$, 317.9; found 318.1.



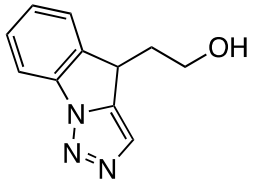
ethyl (*Z*)-2-(8*H*-indeno[1,2-*d*]isothiazol-8-ylidene)acetate (**44**): To a solution of 5-bromo-4-(2-bromophenyl)-1,2-thiazole (**43**, 500 mg, 1.6 mmol) in *N*,*N*-dimethylformamide (10 mL) was added ethyl prop-2-enoate (1.0 g, 10 mmol), palladium(II) acetate (20 mg, 0.09 mmol), potassium acetate (387 mg, 15 mmol) and tris(*o*-tolyl)phosphine (20 mg, 0.07 mmol). The resulting solution was stirred for 12 h at 100 °C. The reaction was quenched with water and extracted with ethyl acetate. The solvent was removed under vacuum. Purification by silica gel flash chromatography eluting with 10% ethyl acetate–petroleum ether afforded the title compound (150 mg, 40%) as yellow oil. LCMS-ESI (m/z): $[M+H]^+$ calcd for $C_{14}H_{12}NO_2S$, 258.1; found 258.1.



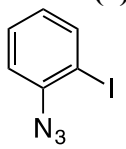
2-(8*H*-indeno[1,2-*d*]isothiazol-8-yl)ethan-1-ol (**4**): To a solution of ethyl (*Z*)-2-(8*H*-indeno[1,2-*d*]isothiazol-8-ylidene)acetate (**44**, 300 mg, 1.2 mmol) in methanol (20 mL) was added sodium borohydride(1.2 g, 32 mmol). The resulting solution was stirred for 3 h at ambient temperature. The reaction was then quenched with water and extracted with ethyl acetate. The organic layers were combined and concentrated under vacuum. Purification by silica gel flash chromatography eluting with 50% ethyl acetate–petroleum ether afforded the title compound (25 mg, 10%) as yellow oil. LCMS-ESI (m/z): $[M+H]^+$ calcd for $C_{12}H_{12}NOS$, 218.1; found 218.1. ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.87 (s, 1H), 7.73 (d, *J* = 7.4 Hz, 1H), 7.57 (d, *J* = 7.5 Hz, 1H), 7.36 (t, *J* = 7.4 Hz, 1H), 7.31 – 7.24 (m, 1H), 4.99 (t, *J* = 4.8 Hz, 1H), 4.25 (dd, *J* = 10.5, 4.2 Hz, 1H), 3.81 – 3.68 (m, 2H), 2.44 – 2.27 (m, 1H), 1.63 – 1.43 (m, 1H).



2-(9*H*-benzo[4,5]imidazo[2,1-*c*][1,2,4]triazol-9-yl)ethan-1-ol (5). To a solution of 9*H*-benzo[4,5]imidazo[2,1-*c*][1,2,4]triazole (**45**, 54 mg, 0.34 mmol) in *N*,*N*-dimethylformamide (1 mL) was added cesium carbonate (156 mg, 0.48 mmol) and 2-bromoethanol (0.060 mL, 0.80 mmol). The resulting suspension was stirred for 4 d at ambient temperature. The mixture was dilute with ethyl acetate and filtered. The solvent was removed under vacuum. Purification by reverse phase HPLC on C18 with water (0.1% ammonium hydroxide)–acetonitrile afforded the title compound (2 mg, 3%) as a tan solid. LCMS-ESI (m/z): $[M+H]^+$ calcd for $C_{10}H_{11}N_4O$, 203.1; found 203.1. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.99 (s, 1H), 7.87 (d, *J* = 7.9 Hz, 1H), 7.57 (d, *J* = 8.2 Hz, 1H), 7.39 (ddd, *J* = 8.3, 7.4, 1.2 Hz, 1H), 7.23 (app td, *J* = 7.8, 1.1 Hz, 1H), 4.85 (t, *J* = 5.6 Hz, 1H), 4.22 (t, *J* = 5.5 Hz, 2H), 3.87 (app q, *J* = 5.5 Hz, 2H).

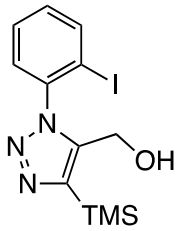


2-(4*H*-[1,2,3]triazolo[1,5-*a*]indol-4-yl)ethan-1-ol (6).

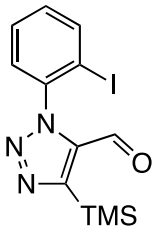


1-azido-2-iodobenzene (**47**): To a solution of 2-iodoaniline (**46**, 1.0 g, 4.6 mmol) in aqueous hydrogen chloride (6 N) was added a solution of sodium nitrite (380 mg, 5.5 mmol) in water (5 mL). The resulting solution was stirred for 40 min at 0 °C. Then a solution of sodium azide (590 mg, 9.1 mmol) in water (5 mL) was added. The resulting solution was stirred for 1.5 h at 0 °C.

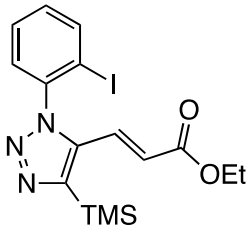
The aqueous solution was extracted with ethyl acetate and the organic layers were combined. The organic layer was concentrated under vacuum to afford the title compound (569 mg, 51%) as a brown oil. LCMS-ESI (m/z): $[M+H]^+$ calcd for $C_6H_5IN_3$, 246.0; found 246.1. ^1H NMR (300 MHz, DMSO-d_6) δ 7.85 – 7.82 (m, 1H), 7.57 – 7.46 (m, 1H), 7.45 – 7.33 (m, 1H), 6.98 – 6.95 (m, 1H).



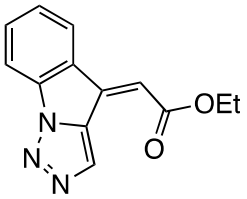
(1-(2-iodophenyl)-4-(trimethylsilyl)-1*H*-1,2,3-triazol-5-yl)methanol (**48**): To a solution of 1-azido-2-iodobenzene (**47**, 5.0 g, 20 mmol) in toluene (150 mL) was added 3-(trimethylsilyl)prop-2-yn-1-ol (5.0 g, 39 mmol). The resulting solution was stirred for 24 h at 120 °C in an oil bath. The reaction mixture was concentrated under vacuum. Purification by silica gel flashed column eluting with 50% ethyl acetate–petroleum ether afforded the title compound (3.0 g, 39%) as a pale yellow solid. LCMS-ESI (m/z): $[M+H]^+$ calcd for $C_{12}H_{17}IN_3OSi$, 374.0; found 374.0.



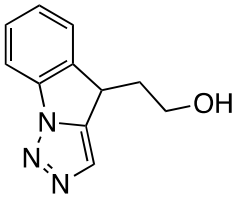
1-(2-iodophenyl)-4-(trimethylsilyl)-1*H*-1,2,3-triazole-5-carbaldehyde (**49**): To a solution of (1-(2-iodophenyl)-4-(trimethylsilyl)-1*H*-1,2,3-triazol-5-yl)methanol (**48**, 2.0 g, 5.4 mmol) in dichloromethane (100 mL) was added (1,1,1-triacetoxy)-1,1-dihydro-1,2-benziodoxol-3(1*H*)-one (4.5 g, 11 mmol). The resulting solution was stirred for 3 h at ambient temperature. The resulting solution was diluted with ethyl acetate. The solids were removed by filtration. The resulting mixture was concentrated under vacuum to afford the title compound (2.5 g, crude) as a pale red solid. LCMS-ESI (m/z): $[M+H]^+$ calcd for $C_{12}H_{15}IN_3OSi$, 372.0; found 372.1.



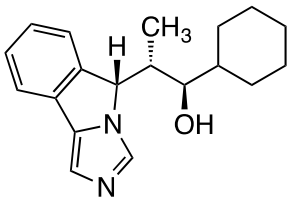
ethyl (2*E*)-3-[1-(2-iodophenyl)-4-(trimethylsilyl)-1*H*-1,2,3-triazol-5-yl]prop-2-enoate (**50**): To a solution of 1-(2-iodophenyl)-4-(trimethylsilyl)-1*H*-1,2,3-triazole-5-carbaldehyde (**49**, 2.5 g, 6.7 mmol) in tetrahydrofuran (150 mL) was added ethyl 2-(triphenylphosphoranylidene)acetate (2.3 g, 6.6 mmol). The resulting solution was stirred for 3 h at ambient. The solids were removed by filtration. The filtrate was concentrated under vacuum. Purification by silica gel flash chromatography eluting with 20% ethyl acetate–petroleum ether afforded the title compound (1.4 g, 47%) as a pale yellow solid. LCMS-ESI (m/z): $[M+H]^+$ calcd for $C_{16}H_{21}IN_3O_2Si$, 442.0; found 442.1.



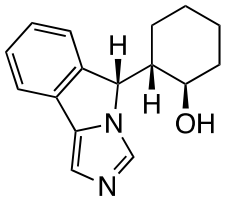
ethyl (*Z*)-2-(4*H*-[1,2,3]triazolo[1,5-*a*]indol-4-ylidene)acetate (**51**): To a solution of ethyl (2*E*)-3-[1-(2-iodophenyl)-4-(trimethylsilyl)-1*H*-1,2,3-triazol-5-yl]prop-2-enoate (**50**, 300 mg, 0.68 mmol) in *N,N*-dimethylformamide (15 mL) was added palladium(II) acetate (30 mg, 0.13 mmol), tri(2-methylphenyl)phosphine (50 mg, 0.16 mmol) and potassium acetate (200 mg, 2.0 mmol). The resulting solution was stirred for 3 h at 100 °C in an oil bath. The reaction mixture was concentrated under vacuum. Purification by silica gel flash chromatography eluting with 25% ethyl acetate–petroleum ether afforded the title compound (135 mg, 82%) as a yellow solid. LCMS-ESI (m/z): $[M+H]^+$ calcd for $C_{13}H_{12}N_3O_2$, 242.1; found 242.2.



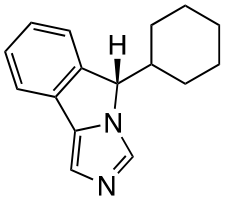
2-[4*H*-[1,2,3]triazolo[1,5-*a*]indol-4-yl]ethan-1-ol (**6**): To a solution of ethyl 2-[(4*Z*)-4*H*-[1,2,3]triazolo[1,5-*a*]indol-4-ylidene]acetate (**51**, 200 mg, 0.83 mmol) in methanol (20 mL) was added sodium borohydride (1.5 g, 40 mmol). The resulting solution was stirred for 2 h at ambient temperature. The reaction was then quenched by the addition of water. The resulting mixture was extracted with ethyl acetate and the organic layers were combined. The organic solution was concentrated. under vacuum. Purification by silica gel flash chromatography eluting with 50% dichloromethane–ethyl acetate afforded the title compound (30 mg, 18%) as a yellow solid. LCMS-ESI (m/z): $[M+H]^+$ calcd for $C_{11}H_{12}N_3O$, 202.1; found 202.1. ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.91 – 7.83 (m, 2H), 7.72 (d, J = 7.5 Hz, 1H), 7.53 (t, J = 7.6 Hz, 1H), 7.48 – 7.39 (m, 1H), 4.83 (t, J = 5.1 Hz, 1H), 4.37 (dd, J = 10.0, 5.0 Hz, 1H), 3.79 – 3.47 (m, 2H), 2.39 – 2.15 (m, 1H), 1.74 – 1.50 (m, 1H).



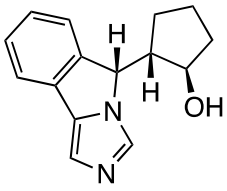
(1*R*,2*S*)-1-cyclohexyl-2-((*S*)-5*H*-imidazo[5,1-*a*]isoindol-5-yl)propan-1-ol (8). LCMS-ESI (m/z): $[M+H]^+$ calcd for $C_{19}H_{25}N_2O$, 297.2; found 297.1. ^{1}H NMR (300 MHz, methanol-d_4) δ 9.15 (s, 1H), 7.86 (d, J = 7.2 Hz, 1H), 7.80 – 7.64 (m, 2H), 7.59 – 7.46 (m, 2H), 6.12 (s, 1H), 3.66 (d, J = 10.3 Hz, 1H), 2.71 (d, J = 6.4 Hz, 1H), 1.94 – 1.44 (m, 7H), 1.39 – 1.11 (m, 5H), 0.28 (d, J = 6.8 Hz, 3H). Chiral HPLC: t_R = 7.412 min, Chiral ADH, 15% hexanes (0.1% diethanolamine)–isopropyl acetate.



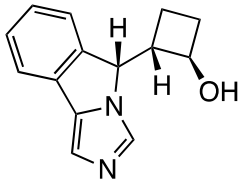
(1*R*,2*S*)-2-((*S*)-5*H*-imidazo[5,1-*a*]isoindol-5-yl)cyclohexan-1-ol (9). LCMS-ESI (m/z): $[M+H]^+$ calcd for $C_{16}H_{19}N_2O$, 255.2; found 255.1. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.88 (s, 1H), 7.66 (d, J = 7.5 Hz, 1H), 7.58 (d, J = 7.5 Hz, 1H), 7.40 – 7.32 (m, 1H), 7.27 – 7.18 (m, 1H), 7.10 (s, 1H), 5.16 (d, J = 5.4 Hz, 1H), 4.69 (d, J = 4.0 Hz, 1H), 4.09 – 4.04 (m, 1H), 1.82 – 1.30 (m, 7H), 1.18 – 1.10 (m, 1H). Chiral SFC: t_R = 1.739 min, Chiral Art, 10% methanol (0.1% ammonium hydroxide)–carbon dioxide.



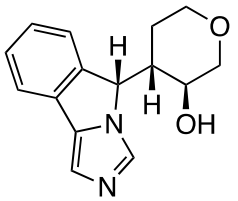
(*S*)-5-cyclohexyl-5*H*-imidazo[5,1-*a*]isoindole (10). To a solution of 5*H*-imidazo[5,1-*a*]isoindole (**65**, 502 mg, 3.2 mmol) in tetrahydrofuran (21 mL) at –78 °C was added *s*-butyllithium (1.4 M in cyclohexane, 2.5 mL, 3.5 mmol) over 5 min. The solution was stirred for 1 h at –78 °C. A solution of bromocyclohexane (524 mg, 3.2 mmol) in tetrahydrofuran (3 mL) was added down the side of the flask. The reaction was stirred for 1 h at –78 °C and allowed to warm to ambient temperature for 2 h. The reaction was quenched by addition of saturated aqueous ammonium chloride solution. The biphasic mixture was extracted with dichloromethane. The organic layer was dried over anhydrous sodium sulfate. The solvent was removed under vacuum. Purification by silica gel flash chromatography with 0–5% methanol–dichloromethane afforded the title compound as a tan solid (306 mg, 49%). LCMS-ESI (m/z): $[M+H]^+$ calcd for $C_{16}H_{19}N_2$, 239.2; found 239.1. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.88 (s, 1H), 7.58 (d, J = 7.4 Hz, 1H), 7.49 (dd, J = 7.7, 1.1 Hz, 1H), 7.37 (td, J = 7.4, 1.4 Hz, 1H), 7.27 (td, J = 7.5, 1.2 Hz, 1H), 7.12 (s, 1H), 5.25 (d, J = 2.8 Hz, 1H), 2.12 (tdd, J = 15.3, 7.7, 4.7 Hz, 1H), 1.71 (dq, J = 12.0, 2.8 Hz, 1H), 1.58 (td, J = 11.2, 4.9 Hz, 2H), 1.34 – 0.93 (m, 3H), 0.66 (qd, J = 12.3, 3.3 Hz, 1H). Chiral SFC: t_R = 1.154 min, Trefoil Amy-1, 10% methanol (0.1% ammonium hydroxide)–carbon dioxide.



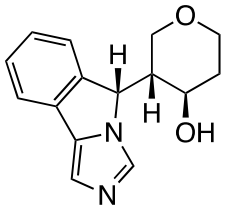
(1*R*,2*S*)-2-((*S*)-5*H*-imidazo[5,1-*a*]isoindol-5-yl)cyclopentan-1-ol (11). LCMS-ESI (m/z): $[M+H]^+$ calcd for $C_{15}H_{17}N_2O$, 241.1; found 241.1. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.90 (s, 1H), 7.61 (dd, J = 22.5, 7.6 Hz, 2H), 7.37 (t, J = 7.5 Hz, 1H), 7.31 – 7.23 (m, 1H), 5.39 (d, J = 6.8 Hz, 1H), 5.16 (d, J = 3.8 Hz, 1H), 4.37 (q, J = 4.7 Hz, 1H), 2.14 – 2.01 (m, 1H), 1.84 – 1.39 (m, 7H). Chiral SFC: t_R = 0.458 min, Chiralpak AD, 20% methanol (0.1% ammonium hydroxide)–carbon dioxide.



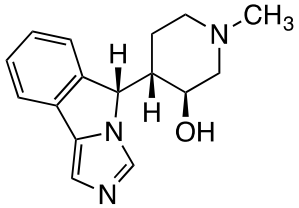
(1*R*,2*S*)-2-((*S*)-5*H*-imidazo[5,1-*a*]isoindol-5-yl)cyclobutan-1-ol (12). LCMS-ESI (m/z): $[M+H]^+$ calcd for $C_{14}H_{15}N_2O$, 227.1; found 227.1. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.84 (s, 1H), 7.61 – 7.54 (m, 2H), 7.36 (t, *J* = 7.6 Hz, 1H), 7.31 – 7.21 (m, 1H), 7.13 (s, 1H), 5.34 (dd, *J* = 15.4, 6.8 Hz, 2H), 4.25 (p, *J* = 7.5 Hz, 1H), 3.39 – 3.30 (m, 1H), 2.41 (dq, *J* = 9.6, 7.7 Hz, 1H), 2.15 – 2.03 (m, 1H), 1.73 – 1.50 (m, 2H), 1.12 (qd, *J* = 10.2, 8.1 Hz, 1H). Chiral SFC: t_R = 0.627 min, Chiralpak AD, 20% methanol (0.1% ammonium hydroxide)–carbon dioxide.



(3*S*,4*S*)-4-((*S*)-5*H*-imidazo[5,1-*a*]isoindol-5-yl)tetrahydro-2*H*-pyran-3-ol (13). LCMS-ESI (m/z): $[M+H]^+$ calcd for $C_{15}H_{17}N_2O_2$, 257.1; found 257.1. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.55 – 7.53 (m, 1H), 7.40 – 7.28 (m, 3H), 7.20 (s, 1H), 5.85 (d, *J* = 2.1 Hz, 1H), 4.16 – 4.11(m, 1H), 4.07 – 3.97 (m, 1H), 3.75 – 3.69 (m, 1H), 3.27 – 3.12 (m, 2H), 2.40 – 2.30 (m, 1H), 0.92 – 0.72 (m, 2H). Chiral HPLC: t_R = 3.201 min, Chiralcel OJ-3, 85% hexanes (0.1% diethanolamine)–ethanol.

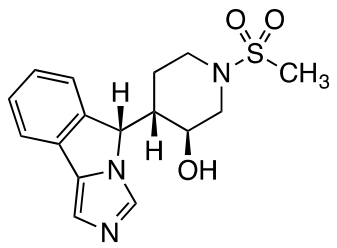


(3*R*,4*R*)-3-((*S*)-5*H*-imidazo[5,1-*a*]isoindol-5-yl)tetrahydro-2*H*-pyran-4-ol (14). LCMS-ESI (m/z): $[M+H]^+$ calcd for $C_{15}H_{17}N_2O_2$, 257.1; found 257.1. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.80 (s, 1H), 7.53 – 7.50 (m, 1H), 7.39 – 7.24 (m, 3H), 7.17 (s, 1H), 5.82 (d, *J* = 2.1 Hz, 1H), 4.14 – 4.06 (m, 1H), 3.94 – 3.89 (m, 1H), 3.31 – 3.21 (m, 2H), 2.57 – 2.49 (m, 1H), 2.42 – 2.33 (m, 1H), 2.11 – 2.05 (m, 1H), 1.90 – 1.77 (m, 1H). Chiral HPLC: t_R = 4.958 min, Chiralpak OJ-3, 85% hexanes (0.1% diethanolamine)–ethanol.

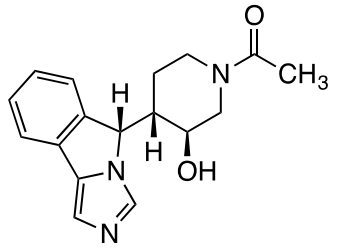


(3*S*,4*S*)-4-((*S*)-5*H*-imidazo[5,1-*a*]isoindol-5-yl)-1-methylpiperidin-3-ol (15). LCMS-ESI (m/z): $[M+H]^+$ calcd for $C_{16}H_{20}N_3O$, 270.2; found 270.1. ^{1}H NMR (300 MHz, CD_3OD): δ 7.92 (s, 1H), 7.63 (d, *J* = 7.5 Hz, 1H), 7.47 (d, *J* = 7.5 Hz, 1H), 7.42 – 7.33 (m, 2H), 7.19 (s, 1H), 5.80 (d, *J* = 3.3 Hz, 1H), 3.97 – 3.90 (m, 1H), 3.18 – 3.13 (m, 1H), 2.70 – 2.62 (m, 1H), 2.63 (s, 3H),

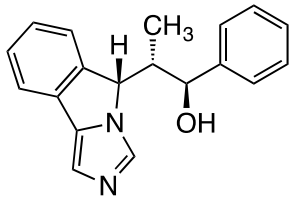
2.06 – 1.83 (m, 3H), 0.91 – 0.86 (m, 1H), 0.72 – 0.64 (m, 1H).). Chiral HPLC: t_R = 5.153 min, Chiralpak AD-H, 60% hexanes (0.1% diethanolamine)–ethanol.



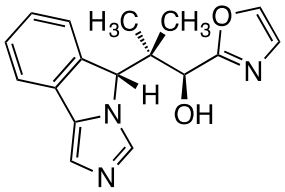
(3*S*,4*S*)-4-((*S*)-5*H*-imidazo[5,1-*a*]isoindol-5-yl)-1-(methylsulfonyl)piperidin-3-ol (16). LCMS-ESI (m/z): $[M+H]^+$ calcd for $C_{16}H_{20}N_3O_3S$, 334.1; found 334.1. ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.92 (s, 1H), 7.63 (d, *J* = 7.8 Hz, 1H), 7.52 (d, *J* = 7.8 Hz, 1H), 7.44 – 7.27 (m, 2H), 7.15 (s, 1H), 5.81 (d, *J* = 3.6 Hz, 1H), 5.79 (d, *J* = 3.6 Hz, 1H), 3.84 – 3.71 (m, 2H), 3.34 – 3.29 (m, 1H), 2.84 (s, 3H), 2.55 – 2.51 (m, 1H), 2.49 – 2.48 (m, 2H), 2.34 – 2.21 (m, 1H), 0.71 – 0.66 (m, 1H), 0.55 – 0.54 (m, 1H). Chiral HPLC: t_R = 2.022 min, Chiralpak IC-3, 50% hexanes (0.1% diethanolamine)–ethanol.



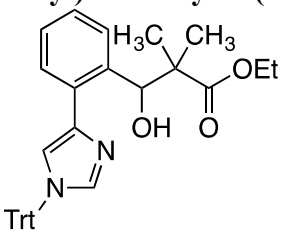
1-((3*S*,4*S*)-3-hydroxy-4-((*S*)-5*H*-imidazo[5,1-*a*]isoindol-5-yl)piperidin-1-yl)ethan-1-one (17). LCMS-ESI (m/z): $[M+H]^+$ calcd for $C_{17}H_{20}N_3O_2$, 298.2; found 298.2. ^{1}H NMR (300 MHz, CD_3OD): δ 7.95 – 7.90 (m, 1H), 7.64 – 7.62 (m, 1H), 7.52 – 7.36 (m, 3H), 7.20 (s, 1H), 5.84 – 5.83 (m, 1H), 4.88 – 4.78 (m, 1H), 4.34 – 4.08 (m, 1H), 3.83 – 3.67 (m, 2H), 3.06 – 2.85 (m, 1H), 2.55 – 2.28 (m, 2H), 2.14 – 1.98 (m, 3H), 1.00 – 0.85 (m, 1H), 0.59 – 0.58 (m, 1H). Chiral HPLC: t_R = 10.807 min, Chiralpak OD-3, 93% hexanes (0.1% diethanolamine)–ethanol.



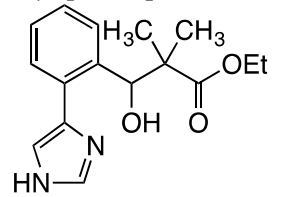
(1*S*,2*S*)-2-((*S*)-5*H*-imidazo[5,1-*a*]isoindol-5-yl)-1-phenylpropan-1-ol (18). LCMS-ESI (m/z): $[M+H]^+$ calcd for $C_{19}H_{19}N_2O$, 291.2; found 291.1. ^{1}H NMR (DMSO-d_6): δ 7.74 (s, 1H), 7.61 – 7.46 (m, 4H), 7.38 (dt, *J* = 15.0, 7.5 Hz, 3H), 7.33 – 7.21 (m, 2H), 7.10 (s, 1H), 5.69 (d, *J* = 4.3 Hz, 1H), 5.20 (s, 1H), 5.02 (t, *J* = 4.9 Hz, 1H), 2.57 (ddd, *J* = 7.2, 5.6, 1.7 Hz, 1H), 0.30 (d, *J* = 6.9 Hz, 3H). Chiral SFC: t_R = 3.167 min, Trefoil Cel-1, 22% methanol (0.1% ammonium hydroxide)–carbon dioxide.



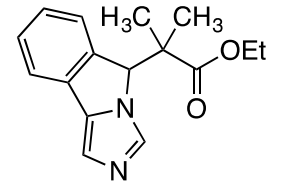
(*S*)-2-((*R*)-5*H*-imidazo[5,1-*a*]isoindol-5-yl)-2-methyl-1-(oxazol-2-yl)propan-1-ol (19).



ethyl 3-hydroxy-2,2-dimethyl-3-(2-(1-trityl-1*H*-imidazol-4-yl)phenyl)propanoate (**72**): A solution of *n*-butyllithium (2.5 M, 2.3 mL, 5.8 mmol) in hexanes was added to a stirred solution of *N*,*N*-diisopropylamine (0.88 mL, 6.3 mmol) in tetrahydrofuran (20 mL) at 0 °C. The mixture was stirred for 20 min at 0 °C. A solution of ethyl 2-methylpropanoate (0.78 mL, 5.8 mmol) in tetrahydrofuran (2 mL) was added to the reaction vessel at -78 °C. The mixture was stirred for 40 min at -78 °C. A solution of 2-(1-trityl-1*H*-imidazol-4-yl)benzaldehyde (**52**, 1.00 g, 2.4 mmol) in tetrahydrofuran (7 mL) was added to the reaction vessel at -40 °C. The mixture was stirred for 1 h at -40 °C. The reaction was quenched by addition of saturated aqueous ammonium chloride solution. The quenched mixture was partitioned between water and ethyl acetate. The organic layer was washed with water and dried over anhydrous sodium sulfate. Purification by silica gel flash chromatography with 25–50% ethyl acetate–heptane afforded the title compound (1.1 g, 86%) as a yellow solid. LCMS-ESI (m/z): $[M+H]^+$ calcd for $C_{35}H_{35}N_2O_3$, 531.3; found 531.5.

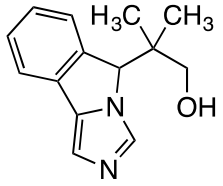


ethyl 3-(2-(1*H*-imidazol-4-yl)phenyl)-3-hydroxy-2,2-dimethylpropanoate (**73**): Acetic acid (15 mL) was added to a stirred solution of ethyl 3-hydroxy-2,2-dimethyl-3-(2-(1-trityl-1*H*-imidazol-4-yl)phenyl)propanoate (**72**, 5.50 g, 10 mmol) in methanol (35 mL). The reaction was stirred for 5 h at 80 °C. The mixture was concentrated under vacuum. The residue was partitioned between water and ethyl acetate. The organic layer was washed with water and dried over anhydrous sodium sulfate. Purification by silica gel flash chromatography with 1–15% methanol–dichloromethane afforded the title compound (3.0 g, >99%) as a yellow solid. LCMS-ESI (m/z): $[M+H]^+$ calcd for $C_{16}H_{21}N_2O_3$, 289.2; found 289.2.

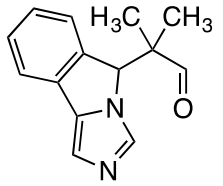


ethyl 2-(5*H*-imidazo[5,1-*a*]isoindol-5-yl)-2-methylpropanoate (**74**): Ethyl 3-(2-(1*H*-imidazol-4-yl)phenyl)-3-hydroxy-2,2-dimethylpropanoate (**73**, 525 mg 1.8 mmol) was added to a stirred solution of cyanomethylene trimethylphosphorane (0.5 M, 10 mL, 5 mmol) in tetrahydrofuran. The reaction was stirred for 12 h at ambient temperature. The mixture was partitioned between

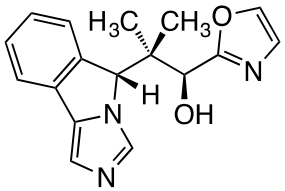
water and ethyl acetate. The organic layer was washed with water and dried over anhydrous sodium sulfate. Purification by silica gel flash chromatography with 1–15% methanol–dichloromethane afforded the title compound (410 mg, 83%) as a yellow solid. LCMS-ESI (m/z): $[M+H]^+$ calcd for $C_{14}H_{19}N_2O_2$, 271.1; found 271.3.



2-(5*H*-imidazo[5,1-*a*]isoindol-5-yl)-2-methylpropan-1-ol (**75**): A solution of diisobutylaluminum hydride (1 M, 22 mL, 22 mmol) in toluene was added to a stirred solution of ethyl 2-(5*H*-imidazo[5,1-*a*]isoindol-5-yl)-2-methylpropanoate (**74**, 1.20 g, 4.4 mmol) in tetrahydrofuran (10 mL) at 0 °C. The mixture was allowed to warm to ambient temperature for 2 h. The reaction was quenched by addition of saturated aqueous ammonium chloride solution. The biphasic mixture was partitioned between water and ethyl acetate. The organic layer was washed with water and dried over anhydrous sodium sulfate. The solvent was removed under vacuum. Purification by silica gel flash chromatography with 1–15% methanol–dichloromethane afforded the title compound (700 mg, 69%) as a pale yellow solid. LCMS-ESI (m/z): $[M+H]^+$ calcd for $C_{14}H_{17}N_2O$, 229.1; found 229.1.

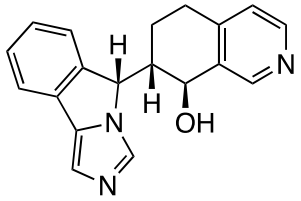


2-(5*H*-imidazo[5,1-*a*]isoindol-5-yl)-2-methylpropanal (**76**): A solution of Dess-Martin periodinane (19.0 g, 44 mmol) in dichloromethane (50 mL) was added to a stirred solution of 2-(5*H*-imidazo[5,1-*a*]isoindol-5-yl)-2-methylpropan-1-ol (**75**, 5.00 g, 22 mmol) in dichloromethane (50 mL). Following addition, sodium bicarbonate (5.80 g, 66 mmol) was added. The suspension was stirred for 3 h at ambient temperature. The reaction mixture was concentrated under vacuum. The residue was partitioned between water and ethyl acetate. The organic layer was washed with water and dried over anhydrous sodium sulfate. The solvent was removed under vacuum. Purification by silica gel flash chromatography with 1–15% methanol–dichloromethane afforded the title compound (4.1 g, 83%) as a yellow solid. LCMS-ESI (m/z): $[M+H]^+$ calcd for $C_{14}H_{15}N_2O$, 227.1; found 227.1.

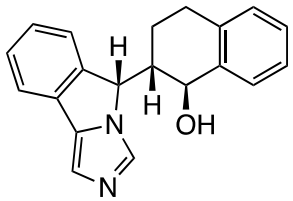


(*S*)-2-((*R*)-5*H*-imidazo[5,1-*a*]isoindol-5-yl)-2-methyl-1-(oxazol-2-yl)propan-1-ol (**19**): A solution of oxazole (95 mg, 1.4 mmol) and borane–tetrahydrofuran complex (1 M in tetrahydrofuran, 1.4 mL, 1.4 mmol) in tetrahydrofuran (0.50 mL) was stirred for 30 min at ambient temperature. The solution was cooled to –78 °C. *n*-Butyllithium (2.5 M in hexanes, 0.54 mL, 1.4 mmol) was added. The mixture was stirred for 30 min at –78 °C. A solution of 2-(5*H*-imidazo[5,1-*a*]isoindol-5-yl)-2-methylpropanal (**76**, 77 mg, 0.34 mmol) in tetrahydrofuran (0.20 mL) was added. The reaction was then stirred for 1 h at -40 °C. The reaction was quenched with

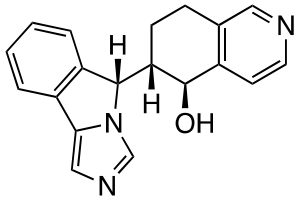
water and extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous sodium sulfate. The solvent was removed under vacuum. Purification by silica gel flash chromatography with 1–10% methanol–dichloromethane afforded the title compound (30 mg, 29%) as a mixture of diastereomers. LCMS-ESI (m/z): $[M+H]^+$ calcd for $C_{17}H_{18}N_3O_2$, 296.1; found 296.1. ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.46 – 7.36 (m, 1H), 7.31 – 7.21 (m, 2H), 7.17 (s, 1H), 6.35 (d, 4.7 Hz, 1H), 1.10 (s, 3H), 0.32 (s, 3H). Chiral SFC: t_R = 0.858 min, Trefoil Cel-4, 25% methanol (0.1% ammonium hydroxide)–carbon dioxide.



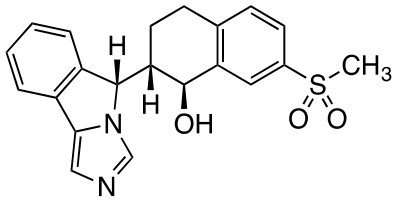
(7*S*,8*S*)-7-((*S*)-5*H*-imidazo[5,1-*a*]isoindol-5-yl)-5,6,7,8-tetrahydroisoquinolin-8-ol (20). LCMS-ESI (m/z): $[M+H]^+$ calcd for $C_{19}H_{18}N_3O$, 304.1; found 304.1. ^{1}H NMR (300 MHz, CD_3OD): δ 8.79 (s, 1H), 8.27 (d, *J* = 5.1 Hz, 1H), 7.99 (s, 1H), 7.66 – 7.64 (m, 1H), 7.50 – 7.32 (m, 3H), 7.20 (s, 1H), 7.18 (d, *J* = 5.1 Hz, 1H), 5.89 (d, *J* = 3.0 Hz, 1H), 5.10 (d, *J* = 10.5 Hz, 1H), 2.70 – 2.68 (m, 2H), 2.50 – 2.42 (m, 1H), 1.14 – 0.98 (m, 2H). Chiral SFC: t_R = 1.182 min, Trefoil Amy-4, 25% methanol (0.1% ammonium hydroxide)–carbon dioxide.



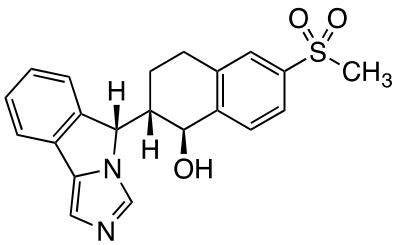
(1*S*,2*S*)-2-((*S*)-5*H*-imidazo[5,1-*a*]isoindol-5-yl)-1,2,3,4-tetrahydronaphthalen-1-ol (21). LCMS-ESI (m/z): $[M+H]^+$ calcd for $C_{20}H_{19}N_2O$, 303.2; found 303.1. ^{1}HNMR (400 MHz, DMSO-d_6): 7.96 (s, 1H), 7.66 (d, *J* = 7.7 Hz, 1H), 7.63 (d, *J* = 7.4 Hz, 1H), 7.50 – 7.46 (m, 1H), 7.41 (t, *J* = 7.4 Hz, 1H), 7.31 (td, *J* = 7.5, 1.2 Hz, 1H), 7.23 (td, *J* = 7.5, 1.2 Hz, 1H), 7.18 (s, 1H), 7.14 (td, *J* = 7.4, 1.4 Hz, 1H), 7.00 (dd, *J* = 7.5, 1.3 Hz, 1H), 5.97 (d, *J* = 7.7 Hz, 1H), 5.84 – 5.78 (m, 1H), 4.93 (dd, *J* = 10.6, 7.8 Hz), 2.56 (s, 3H), 2.38 (tt, *J* = 11.2, 2.9 Hz, 1H), 0.95 – 0.73 (m, 2H). Chiral HPLC: t_R = 7.284 min, Daicel OZ-H, 90% hexanes (0.1% diethanolamine)–ethanol.



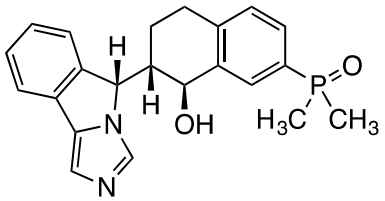
(5*S*,6*S*)-6-((*S*)-5*H*-imidazo[5,1-*a*]isoindol-5-yl)-5,6,7,8-tetrahydroisoquinolin-5-ol (22). LCMS-ESI (m/z): $[M+H]^+$ calcd for $C_{19}H_{18}N_3O$, 304.1; found 304.2. ^{1}H NMR (300 MHz, CD_3OD): δ 8.39 – 8.37 (m, 1H), 8.23 (s, 1H), 8.04 (s, 1H), 7.72 – 7.66 (m, 2H), 7.51 – 7.35 (m, 3H), 7.24 (s, 1H), 5.91 (s, 1H), 5.04 (d, *J* = 5.4 Hz, 1H), 2.71 – 2.68 (m, 2H), 2.53 – 2.46 (m, 1H), 1.20 – 1.17 (m, 1H), 1.08 – 0.94 (m, 1H). Chiral SFC: t_R = 1.397 min, Chiralpak AS-3, 10–50% methanol (0.1% ammonium hydroxide)–carbon dioxide.



(1*S*,2*S*)-2-((*S*)-5*H*-imidazo[5,1-*a*]isoindol-5-yl)-7-(methylsulfonyl)-1,2,3,4-tetrahydronaphthalen-1-ol (23). LCMS-ESI (m/z): $[M+H]^+$ calcd for $C_{21}H_{21}N_2O_3S$, 381.1; found 381.1. ^{1}HNMR (500 MHz, DMSO-d_6): δ 8.29 (s, 1H), 8.18 (dd, *J* = 2.2, 0.9 Hz, 1H), 7.73 – 7.68 (m, 2H), 7.53 (dq, *J* = 7.7, 1.0 Hz, 1H), 7.46 (tt, *J* = 7.6, 0.8 Hz, 1H), 7.37 (td, *J* = 7.5, 1.1 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 1H), 6.27 (d, *J* = 7.7 Hz, 1H), 5.90 (s, 1H), 4.99 – 4.92 (m, 1H), 3.18 (s, 3H), 2.70 (d, *J* = 4.2 Hz, 2H), 1.05 – 0.83 (m, 2H). Chiral SFC: t_R = 1.948 min, Lux Cell-3, 10–50% methanol (0.1% ammonium hydroxide)–carbon dioxide.

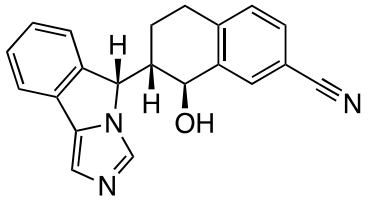


(1*S*,2*S*)-2-((*S*)-5*H*-imidazo[5,1-*a*]isoindol-5-yl)-6-(methylsulfonyl)-1,2,3,4-tetrahydronaphthalen-1-ol (24). LCMS-ESI (m/z): $[M+H]^+$ calcd for $C_{21}H_{21}N_2O_3S$, 381.1; found 381.2. ^{1}HNMR (500 MHz, $CDCl_3$): δ 7.92 (d, *J* = 8.2 Hz, 1H), 7.79 (d, *J* = 8.3 Hz, 1H), 7.68 (s, 1H), 7.54 – 7.62 (m, 2H), 7.40 (t, *J* = 7.5 Hz, 1H), 7.31 (app dd, *J* = 20.3, 7.6 Hz, 2H), 7.19 (s, 1H), 5.86 (s, 1H), 4.98 (d, *J* = 10.7 Hz, 1H), 3.04 (d,J = 2.0 Hz, 3H), 2.69 – 2.80 (m, 2H), 2.42 (t, *J* = 11.6 Hz, 1H), 1.25 (d, *J* = 14.1 Hz, 1H), 1.04 (dd, *J* = 12.4, 6.9 Hz, 1H). Chiral SFC: t_R = 1.160 min, Chiralpak AS-3, 20% methanol (0.1% isopropylamine)–carbon dioxide.

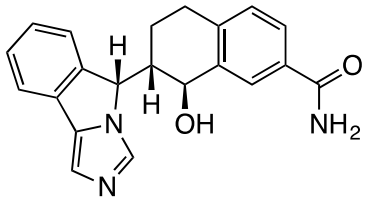


((7*S*,8*S*)-8-hydroxy-7-((*S*)-5*H*-imidazo[5,1-*a*]isoindol-5-yl)-5,6,7,8-tetrahydronaphthalen-2-yl)dimethylphosphine oxide (25). A suspension of 7-bromo-2-(5*H*-imidazo[5,1-*a*]isoindol-5-yl)-1,2,3,4-tetrahydronaphthalen-1-ol (**56k**, 1.27 g, 3.3 mmol), dimethylphosphine oxide (516 mg, 6.5 mmol), palladium(II) acetate (163 mg, 0.73 mmol), 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene (1.00 g, 1.7 mmol) and potassium phosphate (2.32 g, 11 mmol) in *N*,*N*-dimethylformamide (11 mL) were heated in a microwave reactor at 140 °C for 30 min. The reaction mixture was diluted with dichloromethane (100 mL) and filtered. The solvent was removed under vacuum. The filtrate was suspended in ethyl acetate–dichloromethane (1:1, 100 mL) and sonicated. The suspension was filtered. The filtrate was concentrated under vacuum. Purification by silica gel flash chromatography with 0–25% methanol–dichloromethane afforded the title compound (1.1 g, 85%) as a mixture of diastereomers. LCMS-ESI (m/z): $[M+H]^+$ calcd for $C_{22}H_{24}N_2O_2P$, 379.2; found 379.2. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.08 (dd, *J* = 12.2, 1.4

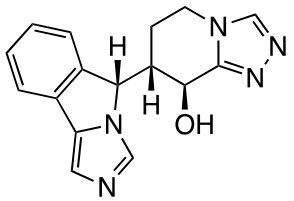
Hz, 1H), 7.97 (s, 1H), 7.64 (dt, *J* = 7.6, 0.9 Hz, 1H), 7.55 – 7.45 (m, 2H), 7.41 (tt, *J* = 7.5, 0.9 Hz, 1H), 7.31 (td, *J* = 7.5, 1.1 Hz, 1H), 7.18 (s, 1H), 7.15 (dd, *J* = 7.8, 2.9 Hz, 1H), 6.14 (d, *J* = 7.7 Hz, 1H), 5.84 – 5.78 (m, 1H), 4.96 (dd, *J* = 10.7, 7.7 Hz, 1H), 2.65 – 2.56 (m, 2H), 2.46 – 2.36 (m, 1H), 1.64 (dd, *J* = 13.3, 2.5 Hz, 6H), 0.98 – 0.75 (m, 2H). Chiral SFC: t_R = 0.790 min, Chiralcel OX, 40% methanol (0.1% isopropylamine)–carbon dioxide.



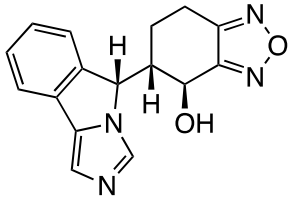
(7*S*,8*S*)-8-hydroxy-7-((*S*)-5*H*-imidazo[5,1-*a*]isoindol-5-yl)-5,6,7,8-tetrahydronaphthalene-2-carbonitrile (26). LCMS-ESI (m/z): $[M+H]^+$ calcd for $C_{21}H_{18}N_3O$, 328.1; found 328.1. ^1H NMR (400 MHz, DMSO-d_6): δ 8.04 – 7.93 (m, 2H), 7.69 – 7.56 (m, 2H), 7.52 – 7.45 (m, 1H), 7.41 (ddd, *J* = 8.2, 7.2, 1.0 Hz, 1H), 7.31 (td, *J* = 7.6, 1.1 Hz, 1H), 7.23 (d, *J* = 8.0 Hz, 1H), 7.18 (s, 1H), 6.30 (d, *J* = 7.4 Hz, 1H), 5.81 (d, *J* = 1.8 Hz, 1H), 4.95 (dd, *J* = 10.6, 7.3 Hz, 1H), 2.66 (dd, *J* = 8.7, 4.4 Hz, 2H), 2.45 – 2.31 (m, 1H), 0.98 – 0.90 (m, 1H), 0.85 (dd, *J* = 8.1, 3.9 Hz, 1H). Chiral SFC: t_R = 1.530 min, Chiralpak OX-H, 50% methanol (0.1% isopropylamine)–carbon dioxide.



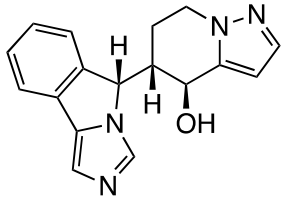
(7*S*,8*S*)-8-hydroxy-7-((*S*)-5*H*-imidazo[5,1-*a*]isoindol-5-yl)-5,6,7,8-tetrahydronaphthalene-2-carboxamide (27). LCMS-ESI (m/z): $[M+H]^+$ calcd for $C_{21}H_{20}N_3O_2$, 346.2; found 346.1. ^1H NMR (400 MHz, DMSO-d_6): δ 8.22 (dd, *J* = 1.9, 0.9 Hz, 1H), 7.95 (t, *J* = 0.6 Hz, 1H), 7.90 (s, 1H), 7.69 – 7.61 (m, 2H), 7.48 (dq, *J* = 7.6, 0.9 Hz, 1H), 7.46 – 7.37 (m, 1H), 7.31 (td, *J* = 7.5, 1.1 Hz, 1H), 7.24 (s, 1H), 7.18 (s, 1H), 7.06 (d, *J* = 7.9 Hz, 1H), 6.06 (d, *J* = 7.8 Hz, 1H), 5.83 (d, *J* = 1.9 Hz, 1H), 5.04 – 4.85 (m, 1H), 3.51 – 3.39 (m, 1H), 2.65 – 2.56 (m, 2H), 2.45 – 2.32 (m, 1H), 1.30 – 1.19 (m, 1H). Chiral SFC: t_R = 0.8491 min, Chiralpak OX-H, 40% methanol (0.1% isopropylamine)–carbon dioxide.



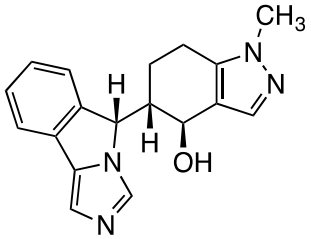
(7*S*,8*S*)-7-((*S*)-5*H*-imidazo[5,1-*a*]isoindol-5-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-*a*]pyridin-8-ol (28). LCMS-ESI (m/z): $[M+H]^+$ calcd for $C_{16}H_{16}N_5O$, 394.1; found 294.1. ^1H NMR (300 MHz, CD_3OD): δ 8.41 (s, 1H), 8.13 (s, 1H), 7.69 – 7.56 (m, 2H), 7.50 – 7.29 (m, 2H), 7.17 (s, 1H), 5.68 (s, 1H), 5.47 (d, *J* = 3.5 Hz, 1H), 4.25 – 4.12 (m, 1H), 3.79 – 3.61 (m, 1H), 2.88 – 2.75 (m, 1H), 1.95 – 1.89 (m, 1H), 1.24 (d, *J* = 13.9 Hz, 1H). Chiral HPLC: t_R = 3.827 min, Chiralpak AD-H, 50% hexanes (0.1% diethanolamine)–ethanol.



(4*S*,5*S*)-5-((*S*)-5*H*-imidazo[5,1-*a*]isoindol-5-yl)-4,5,6,7-tetrahydrobenzo[*c*][1,2,5]oxadiazol-4-ol (29). LCMS-ESI (m/z): $[M+H]^+$ calcd for $C_{16}H_{15}N_4O_2$, 295.1; found 295.4. ^{1}HNMR (500 MHz, DMSO-d_6): δ 7.99 (s, 1H), 7.64 (dt, *J* = 7.7, 1.0 Hz, 1H), 7.52 – 7.46 (m, 1H), 7.43 (tt, *J* = 7.6, 0.9 Hz, 1H), 7.33 (td, *J* = 7.6, 1.1 Hz, 1H), 7.19 (s, 1H), 6.69 (d, *J* = 7.2 Hz, 1H), 5.80 – 5.71 (m, 1H), 5.26 (dd, *J* = 11.0, 7.3 Hz, 1H), 2.78 (dt, *J* = 17.3, 3.8 Hz, 1H), 2.65 – 2.53 (m, 2H), 0.96 (dtd, *J* = 11.2, 6.4, 3.9 Hz, 2H). Chiral SFC: t_R = 0.990 min, Chiralpak OX-H, 45% ethanol (0.1% isopropylamine)–carbon dioxide.



(4*S*,5*S*)-5-((*S*)-5*H*-imidazo[5,1-*a*]isoindol-5-yl)-4,5,6,7-tetrahydropyrazolo[1,5-*a*]pyridin-4-ol (30). LCMS-ESI (m/z): $[M+H]^+$ calcd for $C_{17}H_{17}N_4O$, 293.1; found 293.5. ^{1}HNMR (500 MHz, DMSO-d_6): δ 7.98 (s, 1H), 7.64 (dt, *J* = 7.6, 0.9 Hz, 1H), 7.51 (dd, *J* = 7.6, 1.0 Hz, 1H), 7.46 – 7.38 (m, 2H), 7.34 (dd, *J* = 7.5, 1.1 Hz, 1H), 7.19 (s, 1H), 6.31 (dd, *J* = 1.9, 0.8 Hz, 1H), 6.18 (d, *J* = 7.2 Hz, 1H), 5.76 (d, *J* = 1.9 Hz, 1H), 5.03 (dd, *J* = 10.5, 7.2 Hz, 1H), 4.01 – 3.93 (m, 1H), 3.84 – 3.73 (m, 1H), 2.59 – 2.51 (m, 1H), 1.16 – 1.01 (m, 2H). SFC: t_R = 1.238 min, Chiralpak OX-H, 30% methanol (0.1% isopropylamine)–carbon dioxide.



(4*S*,5*S*)-5-((*S*)-5*H*-imidazo[5,1-*a*]isoindol-5-yl)-1-methyl-4,5,6,7-tetrahydro-1*H*-indazol-4-ol (31). LCMS-ESI (m/z): $[M+H]^+$ calcd for $C_{18}H_{19}N_4O$, 307.2; found 307.1. ^{1}HNMR (500 MHz, DMSO-d_6): δ 7.92 (s, 1H), 7.63 (d, *J* = 7.5 Hz, 1H), 7.45 (d, *J* = 7.6 Hz, 1H), 7.43 – 7.29 (m, 3H), 7.17 (s, 1H), 5.76 (s, 1H), 5.62 (d, *J* = 7.1 Hz, 1H), 4.92 (d, *J* = 8.0 Hz, 1H), 3.58 (s, 3H), 2.44 (dd, *J* = 16.2, 5.4 Hz, 1H), 2.36 – 2.25 (m, 1H), 2.20 (td, *J* = 11.9, 2.5 Hz, 1H), 0.96 – 0.79 (m, 2H). SFC: t_R = 1.345 min, Chiralpak OX-H, 45% methanol (0.1% isopropylamine)–carbon dioxide.

Pharmacological Assays

TDO (1.13.11.11) Biochemical Assay

Test compound is added to duplicate wells of a 384 well v-bottom polypropylene microplate (Greiner) as 100 nL of DMSO solution for a final concentration of 3 nM to 25 μM in the enzyme reaction. 10 μL human recombinant TDO enzyme (NTRC) is added at 50 nM in assay buffer (50 mM sodium phosphate pH 7.0, 0.01% Tween-20) with 2 mM tris(2-carboxyethyl)phosphine (TCEP, Sigma) and 100 μM sodium-L-ascorbate (Sigma). Enzyme is not added to low control wells. After 5 minutes pre-incubation at ambient temperature, the reaction is initiated by the addition of 10 μL L-tryptophan (Calbiochem) at 400 μM in assay buffer. The final tryptophan concentration of 200 μM is slightly higher than the apparent hTDO K_m for tryptophan measured as 160 μM. After 15 minutes reaction at ambient temperature, the reaction is stopped by a 20 μL addition of 1% formic acid (Thermo). 60 μL 0.1% formic acid (Burdick and Jackson) is added to dilute the reaction mixture. Tryptophan and NFK concentrations are measured using a RapidFire (Biocius) coupled to an ABSciex 5500 QTrap mass spectrometer. Briefly, samples are loaded onto a phenyl cartridge (Agilent) and eluted with 0.1% formic acid in 80% acetonitrile followed by ionization, m/z selection, and identification by fragmentation. Analyst and RapidFire Integrator software (Biocius) are used to identify substrate and product peaks and calculate area under the curve (AUC). The normalized ratio of AUCNFK divided by (AUCtryptophan + AUCNFK) is calculated for each well to minimize the effect of injection variability. Signal is further normalized to % inhibition relative to DMSO treatment as 0% inhibition and low control wells as 100% inhibition. IC_{50} values are determined using a four-parameter fit of percent inhibition versus compound concentration using Genedata Analyst software (Genedata).

IDO and TDO Cell Assays

The NFK GreenScreen™ (NTRC, Netherlands) uses a specific chemical probe that binds to *N*-Formylkynurenine (NFK), a product of tryptophan catabolism facilitated by IDO1 or TDO and causes fluorescence at 510 nm when excited at 410 nm. The assay is used to assess compound inhibition of TDO and IDO1 leading to decreased levels of NFK in SW48 cells (high TDO expressing cells) and to determine whether compounds are selective against A172+IFNγ cells (high IDO expressing cells) or are dual inhibitors in cells. The assay is multiplexed with Cell Titer-Glo® (Promega) to determine if compounds are cytotoxic. Briefly, SW48 or A172 cells are harvested in growth media, RPMI 1640 with 10% FBS, 2 mM L-glutamine, and 1× pen/strep. Cells are re-suspended in assay media, tryptophan-free RPMI 1640 supplemented with 2% dialyzed FBS, 2 mM L-glutamine, and 1× pen/strep. Cells are counted on a Vi-Cell (Beckman Coulter). SW48 cells are diluted to 1×10^6 cells/ml in assay media. A172 cells are diluted to 0.24×10^6 cells/mL in assay media. 25 μL of cells are dispensed with a Multi-Flo (Bio-Tek) dispenser to a 384 well greiner μclear plate (Greiner, 781091) with 14 compounds in duplicate. Compounds are dispensed into plates with an Echo® (Labcyte) starting at the highest concentration of 25 μM and are diluted approximately 3× in a 10-point titration. 5 μL of assay media containing 1.2 mM tryptophan are added to the SW48 cells for a final concentration of 200 μM tryptophan in each well. 5 μL of assay media containing 600 μM tryptophan and 600

ng/mL IFNγ are added to the A172 cells for a final concentration of 100 μM tryptophan and 100 ng/mL IFNγ in each well. The final DMSO concentration is 0.5%. Cell plates are placed at room temperature in a closed TC hood with the blower off to allow cells to settle for approximately 30 min. Plates are then moved to an incubator set at 37 °C, 5% CO_2 for 24 hours. After the 24 hour compound incubation, 8 μL of NFK green reagent is added to each well with a Multidrop™ Combi dispenser (Thermo Scientific). Plates are sealed and incubated at 37 °C, 5% CO_2 for 5 hours, then read on a PHERAstar®(BMG labtech). Data are analyzed by normalizing to DMSO and high inhibitor controls. After the plates have been read for NFK green, 25 μL of Cell Titer-Glo® (Promega) are added to each well, incubated for 15 minutes at room temperature, and read on the Envision (Perkin Elmer). Cell Titer-Glo data are analyzed by normalizing to the DMSO controls. Four parameter curve fitting is used and EC_{50} data are reported to the database.

TDO2 Expression, Purification and Crystallization

C-terminal FLAG-tagged TDO2 L18-F388 was expressed in insect cells in the presence of 4 uM hemin and 0.4 mM 5-aminolevulinic acid (5-ALA). After the first 4 hours of infection, 100 uM tryptophan was added. The cells were harvested then lysed in a buffer of 50 mM HEPES pH 7.5, 1.0 M sodium chloride, 10 mM tryptophan, 200 ug/mL sodium nitroprusside (SNP), 5% glycerol, 50 uM E-64 protease inhibitor, 0.5 ug/mL leupeptin, 1 mM phenylmethane sulfonyl fluoride (PMSF) and Calbiochem protease inhibitor cocktail set III, EDTA-free. The protein was purified using equilibrated anti-FLAG M2 affinity agarose gel (Sigma) by gravity flow and then eluted with 150 ug/mL FLAG peptide. The pooled FLAG-tagged protein was concentrated and purified over an equilibrated S75 16/60 gel filtration column in a buffer of 20 mM HEPES pH 7.5, 1.0M sodium chloride, 5% glycerol, 200 uM tryptophan, 200 ug/mL SNP. The BCA assay was used to measure TDO2 protein concentration. The protein was concentrated to 20 mg/mL and flash frozen in liquid nitrogen. Heme incorporation was determined by measuring the ratio of A406/A280, with a value of 2.2 representing 100% heme incorporation.[7] TDO2 protein samples purified for crystallography were measured to have a 406:280 ratio of 1.1 or above. TDO2 samples were also measured via ICP-MS and confirmed to have >67% heme incorporation.

After adding 1 mM of the compound to the TDO2-heme protein, single crystals of TDO2-heme were grown in a 1:1 ratio of protein:well solution of 100 mM MES, pH 6.0, 16%-19% PEG 6000, 0.2M calcium chloride and 3% ethylene glycol. Red rod-shaped crystals appeared about 6 days after setup at 4^{o}C. The crystals were then harvested in a cryo-protectant solution of 8%-10% ethylene glycol and 2% sucrose, flash frozen in liquid nitrogen for data collection.

Data were collected at the Stanford Synchrotron Radiation Lightsource (SSRL) beamline 12-2. The structure was determined by molecular replacement using PHASER[8] and search model 4PW8, subsequently refined with iterative cycles of manual model building (COOT[9]) and refinement (BUSTER[10]). The final statistics on data reduction and refinement are shown in supplemental Table X. Coordinates and structure factors are deposited under accession code 6VBN.

Table S3. Data collection and refinement statistics.

	6VBN
Wavelength	0.9795
Resolution range	39.27 - 3.18 (3.294 - 3.18)
Space group	P 21 21 21
Unit cell	78.475 143.044 147.236 90 90 90
Total reflections	376599 (38816)
Unique reflections	28519 (2802)
Multiplicity	13.2 (13.9)
Completeness (%)	99.71 (99.82)
Mean I/sigma(I)	17.58 (2.22)

Wilson B-factor	93.23
R-merge	0.1371 (1.634)
R-meas	0.1427 (1.696)
R-pim	0.0391 (0.4499)
CC1/2	0.999 (0.82)
CC*	1 (0.949)
Reflections used in refinement	28510 (2801)
Reflections used for R-free	1383 (150)
R-work	0.2102 (0.3188)
R-free	0.2496 (0.3704)
CC(work)	0.958 (0.806)
CC(free)	0.963 (0.799)
Number of non-hydrogen atoms	11873
macromolecules	11589
ligands	248
solvent	36
Protein residues	1375
RMS(bonds)	0.014
RMS(angles)	1.62
Ramachandran favored (%)	95.98
Ramachandran allowed (%)	3.66
Ramachandran outliers (%)	0.37
Rotamer outliers (%)	4.66
Clashscore	2.56
Average B-factor	110.85
macromolecules	111.01
ligands	108.83
solvent	71.34

Statistics for the highest-resolution shell are shown in parentheses

Small Molecule X-ray Crystallography

Experimental data for SC-XRD on Compound 7

X-ray quality crystals were grown from a saturated toluene/ethanol/methanol solution followed by the slow vapor diffusion of diisopropyl ether to deposit the crystal diffracted. A colorless rod 0.050 x 0.020 x 0.020 mm in size was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 100(2) K using phi and omega scans. Crystal-to-detector distance was 60 mm and exposure time was 10 seconds per frame using a scan width of 2.0°. Data collection was 100.0% complete to 67.000° in theta. A total of 44320 reflections were collected covering the indices, -19<=*h*<=19, -5<=*k*<=5, -23<=*l*<=22. 5518 reflections were found to be symmetry independent, with an R_{int} of 0.0513. Indexing and unit cell refinement indicated a primitive, monoclinic lattice. The space group was found to be P 21 (No. 4). The data were integrated using the Bruker SAINT software program and scaled using the SADABS software program. Solution by iterative methods (SHELXT) produced a complete heavy-atom phasing model consistent with the proposed structure. All non-hydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-2014). All hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-2014. Absolute stereochemistry was unambiguously determined to be *S* at C1, C12, C19, and C30, respectively.

Table 1. Crystal data and structure refinement for Compound 7.

X-ray ID	Compound 7
Sample/notebook ID	Compound 7
Empirical formula	C18 H22 N2 O
Formula weight	282.37
Temperature	100(2) K
Wavelength	1.54178 Å
Crystal system	Monoclinic
Space group	P 21
Unit cell dimensions	a = 16.3071(3) Å alpha = 90°.
	b = 4.73520(10) Å beta = 97.8660(10)°.
	c = 19.7305(4) Å gamma = 90°.
Volume	1509.20(5) Å3
Z	4
Density (calculated)	1.243 Mg/m3
Absorption coefficient	0.605 mm-1
F(000)	608
Crystal size	0.050 x 0.020 x 0.020 mm3
Theta range for data collection	2.260 to 68.425°.
Index ranges	-19<=h<=19, -5<=k<=5, -23<=l<=22
Reflections collected	44320
Independent reflections	5518 [R(int) = 0.0513]
Completeness to theta = 67.000°	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.929 and 0.815
Refinement method	Full-matrix least-squares on F2
Data / restraints / parameters	5518 / 1 / 381
Goodness-of-fit on F2	1.048
Final R indices [I>2sigma(I)]	R1 = 0.0299, wR2 = 0.0738
R indices (all data)	R1 = 0.0323, wR2 = 0.0753
Absolute structure parameter	0.00(9)
Extinction coefficient	n/a
Largest diff. peak and hole	0.164 and -0.165 e.Å-3

Table 2. Atomic coordinates (x 104) and equivalent isotropic displacement parameters (Å2x 103)
for Compound 7. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
C(1)	7535(1)	9506(4)	9157(1)	20(1)
C(2)	8077(1)	8628(4)	9814(1)	21(1)
C(3)	8016(1)	9489(5)	10477(1)	26(1)
C(4)	8553(1)	8307(5)	11008(1)	29(1)
C(5)	9128(1)	6275(5)	10882(1)	27(1)
C(6)	9197(1)	5428(5)	10219(1)	25(1)
C(7)	8671(1)	6645(5)	9683(1)	21(1)
C(8)	8599(1)	6286(4)	8943(1)	21(1)
C(9)	8922(1)	5085(5)	8406(1)	25(1)
C(10)	7910(1)	7729(4)	7970(1)	22(1)
C(11)	6632(1)	8638(4)	9164(1)	21(1)
C(12)	6061(1)	9229(4)	8502(1)	19(1)
C(13)	5151(1)	8499(4)	8560(1)	20(1)
C(14)	4809(1)	9916(5)	9159(1)	24(1)
C(15)	3904(1)	9099(5)	9179(1)	28(1)
C(16)	3359(1)	9828(5)	8510(1)	29(1)
C(17)	3689(1)	8450(5)	7908(1)	29(1)
C(18)	4598(1)	9209(5)	7888(1)	25(1)
C(19)	7428(1)	2719(4)	5467(1)	18(1)
C(20)	6936(1)	1229(4)	4861(1)	19(1)
C(21)	7063(1)	1278(5)	4183(1)	24(1)
C(22)	6554(1)	-364(5)	3713(1)	27(1)
C(23)	5930(1)	-2014(5)	3921(1)	29(1)
C(24)	5801(1)	-2091(5)	4602(1)	25(1)
C(25)	6307(1)	-450(4)	5070(1)	20(1)
C(26)	6319(1)	-8(4)	5802(1)	20(1)
C(27)	5943(1)	-547(5)	6370(1)	23(1)
C(28)	6900(1)	2548(5)	6670(1)	22(1)
C(29)	8318(1)	1593(4)	5602(1)	19(1)
C(30)	8784(1)	2305(4)	6301(1)	18(1)
C(31)	9683(1)	1286(4)	6373(1)	18(1)
C(32)	10223(1)	2829(4)	5912(1)	20(1)
C(33)	11097(1)	1604(5)	5990(1)	25(1)
C(34)	11506(1)	1669(5)	6735(1)	26(1)
C(35)	10971(1)	164(5)	7197(1)	25(1)
C(36)	10097(1)	1395(4)	7119(1)	21(1)
N(1)	8488(1)	6013(4)	7799(1)	25(1)
N(2)	7951(1)	7937(4)	8653(1)	19(1)

N(3)	6307(1)	1083(4)	6909(1)	23(1)
N(4)	6931(1)	1937(4)	6010(1)	19(1)
O(1)	6163(1)	12098(3)	8313(1)	22(1)
O(2)	8718(1)	5268(3)	6415(1)	19(1)

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Table 3. Bond lengths [Å] and angles [°] for Compound 7.

C(1)-N(2)	1.479(2)	C(18)-H(18B)	0.9900
C(1)-C(2)	1.523(3)	C(19)-N(4)	1.476(2)
C(1)-C(11)	1.530(3)	C(19)-C(20)	1.519(3)
C(1)-H(1)	1.0000	C(19)-C(29)	1.535(2)
C(2)-C(3)	1.386(3)	C(19)-H(19)	1.0000
C(2)-C(7)	1.399(3)	C(20)-C(21)	1.382(3)
C(3)-C(4)	1.388(3)	C(20)-C(25)	1.403(3)
C(3)-H(3)	0.9500	C(21)-C(22)	1.393(3)
C(4)-C(5)	1.389(3)	C(21)-H(21)	0.9500
C(4)-H(4)	0.9500	C(22)-C(23)	1.387(3)
C(5)-C(6)	1.387(3)	C(22)-H(22)	0.9500
C(5)-H(5)	0.9500	C(23)-C(24)	1.390(3)
C(6)-C(7)	1.392(3)	C(23)-H(23)	0.9500
C(6)-H(6)	0.9500	C(24)-C(25)	1.389(3)
C(7)-C(8)	1.459(3)	C(24)-H(24)	0.9500
C(8)-C(9)	1.370(3)	C(25)-C(26)	1.458(3)
C(8)-N(2)	1.374(2)	C(26)-C(27)	1.373(3)
C(9)-N(1)	1.378(3)	C(26)-N(4)	1.378(3)
C(9)-H(9)	0.9500	C(27)-N(3)	1.381(3)
C(10)-N(1)	1.323(3)	C(27)-H(27)	0.9500
C(10)-N(2)	1.344(2)	C(28)-N(3)	1.327(3)
C(10)-H(10)	0.9500	C(28)-N(4)	1.341(2)
C(11)-C(12)	1.523(3)	C(28)-H(28)	0.9500
C(11)-H(11A)	0.9900	C(29)-C(30)	1.520(2)
C(11)-H(11B)	0.9900	C(29)-H(29A)	0.9900
C(12)-O(1)	1.425(2)	C(29)-H(29B)	0.9900
C(12)-C(13)	1.542(3)	C(30)-O(2)	1.427(2)
C(12)-H(12)	1.0000	C(30)-C(31)	1.531(2)
C(13)-C(14)	1.531(3)	C(30)-H(30)	1.0000
C(13)-C(18)	1.535(3)	C(31)-C(32)	1.534(2)
C(13)-H(13)	1.0000	C(31)-C(36)	1.535(2)
C(14)-C(15)	1.531(3)	C(31)-H(31)	1.0000
C(14)-H(14A)	0.9900	C(32)-C(33)	1.528(3)
C(14)-H(14B)	0.9900	C(32)-H(32A)	0.9900
C(15)-C(16)	1.526(3)	C(32)-H(32B)	0.9900
C(15)-H(15A)	0.9900	C(33)-C(34)	1.529(3)
C(15)-H(15B)	0.9900	C(33)-H(33A)	0.9900
C(16)-C(17)	1.517(3)	C(33)-H(33B)	0.9900
C(16)-H(16A)	0.9900	C(34)-C(35)	1.523(3)
C(16)-H(16B)	0.9900	C(34)-H(34A)	0.9900
C(17)-C(18)	1.531(3)	C(34)-H(34B)	0.9900
C(17)-H(17A)	0.9900	C(35)-C(36)	1.527(3)
C(17)-H(17B)	0.9900	C(35)-H(35A)	0.9900
C(18)-H(18A)	0.9900	C(35)-H(35B)	0.9900

C(36)-H(36A)	0.9900
C(36)-H(36B)	0.9900

O(1)-H(1A)	0.8400
O(2)-H(2)	0.8400

N(2)-C(1)-C(2)	99.73(15)
N(2)-C(1)-C(11)	113.69(16)
C(2)-C(1)-C(11)	111.47(15)
N(2)-C(1)-H(1)	110.5
C(2)-C(1)-H(1)	110.5
C(11)-C(1)-H(1)	110.5
C(3)-C(2)-C(7)	120.82(19)
C(3)-C(2)-C(1)	127.92(18)
C(7)-C(2)-C(1)	111.23(16)
C(2)-C(3)-C(4)	118.3(2)
C(2)-C(3)-H(3)	120.8
C(4)-C(3)-H(3)	120.8
C(3)-C(4)-C(5)	121.05(19)
C(3)-C(4)-H(4)	119.5
C(5)-C(4)-H(4)	119.5
C(6)-C(5)-C(4)	120.82(19)
C(6)-C(5)-H(5)	119.6
C(4)-C(5)-H(5)	119.6
C(5)-C(6)-C(7)	118.4(2)
C(5)-C(6)-H(6)	120.8
C(7)-C(6)-H(6)	120.8
C(6)-C(7)-C(2)	120.52(18)
C(6)-C(7)-C(8)	132.03(19)
C(2)-C(7)-C(8)	107.45(17)
C(9)-C(8)-N(2)	105.63(17)
C(9)-C(8)-C(7)	146.67(19)
N(2)-C(8)-C(7)	107.62(16)
C(8)-C(9)-N(1)	109.46(18)
C(8)-C(9)-H(9)	125.3
N(1)-C(9)-H(9)	125.3
N(1)-C(10)-N(2)	111.16(17)
N(1)-C(10)-H(10)	124.4
N(2)-C(10)-H(10)	124.4
C(12)-C(11)-C(1)	114.83(15)
C(12)-C(11)-H(11A)	108.6
C(1)-C(11)-H(11A)	108.6
C(12)-C(11)-H(11B)	108.6
C(1)-C(11)-H(11B)	108.6
H(11A)-C(11)-H(11B)	107.5
O(1)-C(12)-C(11)	108.68(16)
O(1)-C(12)-C(13)	112.39(16)
C(11)-C(12)-C(13)	112.22(15)
O(1)-C(12)-H(12)	107.8
C(11)-C(12)-H(12)	107.8
C(13)-C(12)-H(12)	107.8
C(14)-C(13)-C(18)	109.76(16)
C(14)-C(13)-C(12)	114.50(16)
C(18)-C(13)-C(12)	110.20(15)
C(14)-C(13)-H(13)	107.4
C(18)-C(13)-H(13)	107.4
C(12)-C(13)-H(13)	107.4
C(13)-C(14)-C(15)	111.30(17)
C(13)-C(14)-H(14A)	109.4
C(15)-C(14)-H(14A)	109.4
C(13)-C(14)-H(14B)	109.4
C(15)-C(14)-H(14B)	109.4
H(14A)-C(14)-H(14B)	108.0
C(16)-C(15)-C(14)	111.71(17)
C(16)-C(15)-H(15A)	109.3
C(14)-C(15)-H(15A)	109.3
C(16)-C(15)-H(15B)	109.3
C(14)-C(15)-H(15B)	109.3
H(15A)-C(15)-H(15B)	107.9
C(17)-C(16)-C(15)	110.67(17)
C(17)-C(16)-H(16A)	109.5
C(15)-C(16)-H(16A)	109.5
C(17)-C(16)-H(16B)	109.5
C(15)-C(16)-H(16B)	109.5
H(16A)-C(16)-H(16B)	108.1
C(16)-C(17)-C(18)	111.57(18)
C(16)-C(17)-H(17A)	109.3
C(18)-C(17)-H(17A)	109.3
C(16)-C(17)-H(17B)	109.3
C(18)-C(17)-H(17B)	109.3
H(17A)-C(17)-H(17B)	108.0
C(17)-C(18)-C(13)	112.53(16)
C(17)-C(18)-H(18A)	109.1
C(13)-C(18)-H(18A)	109.1
C(17)-C(18)-H(18B)	109.1
C(13)-C(18)-H(18B)	109.1
H(18A)-C(18)-H(18B)	107.8
N(4)-C(19)-C(20)	99.89(14)
N(4)-C(19)-C(29)	112.79(15)
C(20)-C(19)-C(29)	111.06(15)
N(4)-C(19)-H(19)	110.9
C(20)-C(19)-H(19)	110.9

C(29)-C(19)-H(19) 110.9
C(21)-C(20)-C(25) 120.35(18)
C(21)-C(20)-C(19) 128.47(17)
C(25)-C(20)-C(19) 111.13(16)
C(20)-C(21)-C(22) 118.71(19)
C(20)-C(21)-H(21) 120.6
C(22)-C(21)-H(21) 120.6
C(23)-C(22)-C(21) 120.81(18)
C(23)-C(22)-H(22) 119.6
C(21)-C(22)-H(22) 119.6
C(22)-C(23)-C(24) 120.96(19)
C(22)-C(23)-H(23) 119.5
C(24)-C(23)-H(23) 119.5
C(25)-C(24)-C(23) 118.19(19)
C(25)-C(24)-H(24) 120.9
C(23)-C(24)-H(24) 120.9
C(24)-C(25)-C(20) 120.99(17)
C(24)-C(25)-C(26) 131.64(18)
C(20)-C(25)-C(26) 107.36(17)
C(27)-C(26)-N(4) 105.50(17)
C(27)-C(26)-C(25) 146.69(19)
N(4)-C(26)-C(25) 107.57(16)
C(26)-C(27)-N(3) 109.35(17)
C(26)-C(27)-H(27) 125.3
N(3)-C(27)-H(27) 125.3
N(3)-C(28)-N(4) 111.01(18)
N(3)-C(28)-H(28) 124.5
N(4)-C(28)-H(28) 124.5
C(30)-C(29)-C(19) 115.07(15)
C(30)-C(29)-H(29A) 108.5
C(19)-C(29)-H(29A) 108.5
C(30)-C(29)-H(29B) 108.5
C(19)-C(29)-H(29B) 108.5
H(29A)-C(29)-H(29B) 107.5
O(2)-C(30)-C(29) 108.78(15)
O(2)-C(30)-C(31) 112.82(15)
C(29)-C(30)-C(31) 111.53(15)
O(2)-C(30)-H(30) 107.8
C(29)-C(30)-H(30) 107.8
C(31)-C(30)-H(30) 107.8
C(30)-C(31)-C(32) 114.53(15)
C(30)-C(31)-C(36) 111.57(15)
C(32)-C(31)-C(36) 109.85(15)
C(30)-C(31)-H(31) 106.8
C(32)-C(31)-H(31) 106.8
C(36)-C(31)-H(31) 106.8
C(33)-C(32)-C(31) 111.27(16)
C(33)-C(32)-H(32A) 109.4
C(31)-C(32)-H(32A) 109.4
C(33)-C(32)-H(32B) 109.4
C(31)-C(32)-H(32B) 109.4
H(32A)-C(32)-H(32B) 108.0
C(32)-C(33)-C(34) 111.56(16)
C(32)-C(33)-H(33A) 109.3
C(34)-C(33)-H(33A) 109.3
C(32)-C(33)-H(33B) 109.3
C(34)-C(33)-H(33B) 109.3
H(33A)-C(33)-H(33B) 108.0
C(35)-C(34)-C(33) 110.85(16)
C(35)-C(34)-H(34A) 109.5
C(33)-C(34)-H(34A) 109.5
C(35)-C(34)-H(34B) 109.5
C(33)-C(34)-H(34B) 109.5
H(34A)-C(34)-H(34B) 108.1
C(34)-C(35)-C(36) 111.33(17)
C(34)-C(35)-H(35A) 109.4
C(36)-C(35)-H(35A) 109.4
C(34)-C(35)-H(35B) 109.4
C(36)-C(35)-H(35B) 109.4
H(35A)-C(35)-H(35B) 108.0
C(35)-C(36)-C(31) 111.49(15)
C(35)-C(36)-H(36A) 109.3
C(31)-C(36)-H(36A) 109.3
C(35)-C(36)-H(36B) 109.3
C(31)-C(36)-H(36B) 109.3
H(36A)-C(36)-H(36B) 108.0
C(10)-N(1)-C(9) 105.91(16)
C(10)-N(2)-C(8) 107.83(16)
C(10)-N(2)-C(1) 138.30(17)
C(8)-N(2)-C(1) 113.78(15)
C(28)-N(3)-C(27) 106.00(16)
C(28)-N(4)-C(26) 108.12(16)
C(28)-N(4)-C(19) 138.39(17)
C(26)-N(4)-C(19) 113.48(15)
C(12)-O(1)-H(1A) 109.5
C(30)-O(2)-H(2) 109.5

Table 4. Anisotropic displacement parameters (Å2x 103)for Compound 7. The anisotropic displacement factor exponent takes the form: -2□2[h2a*2U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
C(1)	23(1)	21(1)	16(1)	-1(1)	5(1)	1(1)
C(2)	20(1)	22(1)	20(1)	0(1)	4(1)	-4(1)
C(3)	28(1)	28(1)	23(1)	-4(1)	6(1)	-2(1)
C(4)	31(1)	37(1)	18(1)	-3(1)	3(1)	-7(1)
C(5)	24(1)	35(1)	20(1)	6(1)	-3(1)	-7(1)
C(6)	19(1)	32(1)	24(1)	2(1)	1(1)	-1(1)
C(7)	19(1)	24(1)	20(1)	-1(1)	4(1)	-4(1)
C(8)	19(1)	23(1)	20(1)	2(1)	3(1)	0(1)
C(9)	24(1)	30(1)	22(1)	0(1)	5(1)	6(1)
C(10)	23(1)	26(1)	17(1)	1(1)	5(1)	1(1)
C(11)	22(1)	25(1)	18(1)	0(1)	7(1)	1(1)
C(12)	24(1)	19(1)	16(1)	1(1)	7(1)	1(1)
C(13)	23(1)	21(1)	17(1)	2(1)	5(1)	2(1)
C(14)	25(1)	28(1)	19(1)	-2(1)	7(1)	0(1)
C(15)	25(1)	36(1)	23(1)	-1(1)	10(1)	-2(1)
C(16)	23(1)	35(1)	32(1)	3(1)	7(1)	2(1)
C(17)	24(1)	37(1)	23(1)	4(1)	0(1)	-1(1)
C(18)	26(1)	34(1)	17(1)	3(1)	5(1)	1(1)
C(19)	20(1)	20(1)	15(1)	3(1)	5(1)	-1(1)
C(20)	18(1)	20(1)	18(1)	2(1)	1(1)	3(1)
C(21)	23(1)	30(1)	20(1)	4(1)	4(1)	1(1)
C(22)	26(1)	40(1)	15(1)	0(1)	3(1)	2(1)
C(23)	23(1)	40(1)	22(1)	-6(1)	-1(1)	-1(1)
C(24)	19(1)	32(1)	25(1)	-1(1)	3(1)	-3(1)
C(25)	17(1)	24(1)	17(1)	3(1)	3(1)	4(1)
C(26)	17(1)	22(1)	20(1)	2(1)	1(1)	2(1)
C(27)	19(1)	29(1)	20(1)	4(1)	4(1)	1(1)
C(28)	20(1)	28(1)	17(1)	-1(1)	2(1)	4(1)
C(29)	19(1)	22(1)	17(1)	0(1)	4(1)	-2(1)
C(30)	21(1)	17(1)	16(1)	1(1)	7(1)	-2(1)
C(31)	20(1)	18(1)	16(1)	-1(1)	2(1)	-1(1)
C(32)	20(1)	23(1)	20(1)	0(1)	5(1)	-1(1)
C(33)	20(1)	31(1)	24(1)	-4(1)	7(1)	1(1)
C(34)	17(1)	31(1)	29(1)	-7(1)	2(1)	2(1)
C(35)	24(1)	31(1)	19(1)	-4(1)	-1(1)	4(1)
C(36)	22(1)	25(1)	17(1)	-2(1)	4(1)	-1(1)
N(1)	25(1)	31(1)	21(1)	-1(1)	6(1)	3(1)
N(2)	19(1)	22(1)	16(1)	0(1)	5(1)	1(1)
N(3)	21(1)	32(1)	16(1)	3(1)	5(1)	3(1)
N(4)	17(1)	23(1)	17(1)	2(1)	3(1)	1(1)
O(1)	29(1)	21(1)	17(1)	1(1)	6(1)	0(1)

O(2) 25(1) 18(1) 16(1) -1(1) 5(1) 0(1)

Table 5. Hydrogen coordinates (x 104) and isotropic displacement parameters (Å2x 103) for Compound 7.

	x	y	z	U(eq)
H(1)	7576	11587	9083	24
H(3)	7617	10854	10565	31
H(4)	8526	8897	11465	34
H(5)	9478	5455	11255	32
H(6)	9593	4050	10133	30
H(9)	9376	3811	8446	30
H(10)	7517	8690	7651	26
H(11A)		6615	6591	9263	25
H(11B)		6417	9648	9542	25
H(12)	6242	8008	8137	23
H(13)	5120	6411	8628	24
H(14A)		4851	11992	9116	28
H(14B)		5145	9345	9594	28
H(15A)		3869	7046	9265	33
H(15B)		3695	10104	9561	33
H(16A)		2787	9171	8530	35
H(16B)		3345	11903	8447	35
H(17A)		3354	9072	7477	34
H(17B)		3635	6374	7941	34
H(18A)		4640	11254	7795	30
H(18B)		4800	8169	7508	30
H(19)	7424	4810	5396	22
H(21)	7488	2409	4040	29
H(22)	6635	-355	3246	33
H(23)	5587	-3107	3592	35
H(24)	5377	-3235	4744	31
H(27)	5501	-1839	6389	27
H(28)	7255	3855	6931	26
H(29A)		8302	-487	5550	23
H(29B)		8631	2361	5247	23
H(30)	8506	1301	6653	21
H(31)	9667	-745	6232	21
H(32A)		9967	2662	5429	24
H(32B)		10251	4859	6033	24
H(33A)		11438	2704	5705	30
H(33B)		11073	-370	5824	30
H(34A)		12055	741	6773	31
H(34B)		11592	3654	6886	31

H(35A)		11229	346	7680	30
H(35B)		10940	-1871	7081	30
H(36A)		10124	3380	7278	26
H(36B)		9759	318	7409	26
H(1A)	6182	12193	7890	33	
H(2)	8697	5566	6832	29	

Experimental data for SC-XRD on Compound 8

X-ray quality crystals were grown from a saturated 1,2-dichloroethane/ethanol/methanol solution followed by the slow vapor diffusion of diethyl ether to deposit the crystal diffracted. A colorless rod 0.080 x 0.050 x 0.050 mm in size was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 90(2) K using phi and omega scans. Crystal-to-detector distance was 40 mm and exposure time was 0.05 seconds per frame using a scan width of 0.5°. Data collection was 99.9% complete to 67.000° in theta. A total of 17678 reflections were collected covering the indices, -8<=*h*<=8, -11<=*k*<=11, -18<=*l*<=18. 6643 reflections were found to be symmetry independent, with an R_{int} of 0.0255. Indexing and unit cell refinement indicated a primitive, triclinic lattice. The space group was found to be P 1 (No. 1). The data were integrated and scaled using CrysAlisPro 1.171.40.35a. Solution by iterative methods (SHELXT-2014) produced a complete heavy-atom phasing model. All non-hydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-2018). All hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-2018. Absolute stereochemistry was unambiguously determined to be *R* at C11 and C30, and *S* at C1, C13, C20, and C32, respectively.

Table 1. Crystal data and structure refinement for Compound 8.

X-ray ID	Compound 8
Sample/notebook ID	Compound 8
Empirical formula	C38 H55 Cl N4 O5
Formula weight	683.31
Temperature	90(2) K
Wavelength	1.54184 Å
Crystal system	Triclinic
Space group	P 1
Unit cell dimensions	a = 6.81630(10) Å alpha = 73.148(2)°.
	b = 9.5313(2) Å beta = 77.8340(10)°.
	c = 15.3468(2) Å gamma = 89.575(2)°.
Volume	931.27(3) Å3
Z	1
Density (calculated)	1.218 Mg/m3
Absorption coefficient	1.278 mm-1
F(000)	368
Crystal size	0.080 x 0.050 x 0.050 mm3
Theta range for data collection	3.083 to 75.128°.
Index ranges	-8<=h<=8, -11<=k<=11, -18<=l<=18
Reflections collected	17678
Independent reflections	6643 [R(int) = 0.0255]
Completeness to theta = 67.000°	99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.00000 and 0.83098
Refinement method	Full-matrix least-squares on F2
Data / restraints / parameters	6643 / 3 / 437
Goodness-of-fit on F2	1.053
Final R indices [I>2sigma(I)]	R1 = 0.0420, wR2 = 0.1122
R indices (all data)	R1 = 0.0429, wR2 = 0.1136
Absolute structure parameter	0.050(7)
Extinction coefficient	n/a
Largest diff. peak and hole	0.476 and -0.486 e.Å-3

Table 2. Atomic coordinates (x 104) and equivalent isotropic displacement parameters (Å2x 103)
for Compound 8. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
C(1)	10695(4)	2562(3)	6744(2)	24(1)
C(2)	11901(4)	1210(3)	6988(2)	24(1)
C(3)	13464(4)	981(4)	7459(2)	27(1)
C(4)	14362(5)	-362(4)	7594(2)	31(1)
C(5)	13764(5)	-1440(4)	7247(2)	31(1)
C(6)	12200(5)	-1220(4)	6769(2)	29(1)
C(7)	11279(4)	99(3)	6656(2)	25(1)
C(8)	9665(4)	651(3)	6183(2)	24(1)
C(9)	8311(4)	361(4)	5702(2)	27(1)
C(10)	7932(4)	2609(4)	5769(2)	26(1)
C(11)	9384(4)	3008(3)	7562(2)	24(1)
C(12)	8280(5)	1670(4)	8321(2)	28(1)
C(13)	10625(4)	3935(3)	7944(2)	24(1)
C(14)	9380(4)	4494(3)	8724(2)	24(1)
C(15)	7691(5)	5457(4)	8416(2)	28(1)
C(16)	6549(5)	6049(4)	9192(2)	34(1)
C(17)	7963(5)	6908(4)	9522(2)	36(1)
C(18)	9613(5)	5942(4)	9858(2)	35(1)
C(19)	10759(5)	5320(4)	9099(2)	30(1)
C(20)	951(4)	4488(3)	3249(2)	24(1)
C(21)	-306(4)	3412(3)	2995(2)	24(1)
C(22)	-1855(5)	3678(4)	2514(2)	28(1)
C(23)	-2779(5)	2498(4)	2367(2)	32(1)
C(24)	-2243(5)	1067(4)	2714(2)	32(1)
C(25)	-727(5)	788(4)	3206(2)	29(1)
C(26)	246(4)	1966(4)	3326(2)	25(1)
C(27)	1875(4)	2005(3)	3805(2)	25(1)
C(28)	3172(5)	1196(4)	4284(2)	28(1)
C(29)	3709(4)	3509(4)	4209(2)	27(1)
C(30)	2288(4)	5682(3)	2436(2)	26(1)
C(31)	3301(5)	5063(4)	1653(2)	30(1)
C(32)	1087(4)	7018(3)	2087(2)	26(1)
C(33)	2310(4)	8268(4)	1285(2)	26(1)
C(34)	4039(5)	8940(4)	1566(2)	30(1)
C(35)	5139(5)	10255(4)	779(2)	34(1)
C(36)	3701(6)	11424(4)	470(2)	36(1)
C(37)	2024(6)	10786(4)	151(2)	36(1)
C(38)	909(5)	9465(4)	920(2)	31(1)

N(1)	7260(4)	1609(3)	5449(2)	27(1)
N(2)	9390(4)	2067(3)	6222(2)	24(1)
N(3)	4287(4)	2162(3)	4530(2)	27(1)
N(4)	2238(4)	3445(3)	3765(2)	24(1)
O(1)	11712(3)	5124(2)	7208(2)	30(1)
O(2)	286(4)	7600(3)	2838(2)	37(1)
O(3)	1980(5)	7781(4)	4272(3)	64(1)
O(4)	-594(5)	6502(4)	5929(2)	68(1)
O(5)	-4382(4)	5505(4)	6107(2)	57(1)
Cl(1)	-3796(1)	6703(1)	3944(1)	58(1)

Table 3. Bond lengths [Å] and angles [°] for Compound 8.

C(1)-N(2)	1.477(4)	C(18)-H(18A)	0.9900
C(1)-C(2)	1.520(4)	C(18)-H(18B)	0.9900
C(1)-C(11)	1.544(4)	C(19)-H(19A)	0.9900
C(1)-H(1)	1.0000	C(19)-H(19B)	0.9900
C(2)-C(3)	1.392(4)	C(20)-N(4)	1.486(4)
C(2)-C(7)	1.403(4)	C(20)-C(21)	1.525(4)
C(3)-C(4)	1.394(5)	C(20)-C(30)	1.547(4)
C(3)-H(3)	0.9500	C(20)-H(20)	1.0000
C(4)-C(5)	1.386(5)	C(21)-C(22)	1.392(4)
C(4)-H(4)	0.9500	C(21)-C(26)	1.402(4)
C(5)-C(6)	1.399(4)	C(22)-C(23)	1.389(5)
C(5)-H(5)	0.9500	C(22)-H(22)	0.9500
C(6)-C(7)	1.384(4)	C(23)-C(24)	1.390(5)
C(6)-H(6)	0.9500	C(23)-H(23)	0.9500
C(7)-C(8)	1.456(4)	C(24)-C(25)	1.385(4)
C(8)-C(9)	1.372(4)	C(24)-H(24)	0.9500
C(8)-N(2)	1.378(4)	C(25)-C(26)	1.385(4)
C(9)-N(1)	1.384(4)	C(25)-H(25)	0.9500
C(9)-H(9)	0.9500	C(26)-C(27)	1.460(4)
C(10)-N(1)	1.316(4)	C(27)-C(28)	1.360(4)
C(10)-N(2)	1.347(4)	C(27)-N(4)	1.378(4)
C(10)-H(10)	0.9500	C(28)-N(3)	1.379(4)
C(11)-C(12)	1.527(4)	C(28)-H(28)	0.9500
C(11)-C(13)	1.536(4)	C(29)-N(3)	1.325(4)
C(11)-H(11)	1.0000	C(29)-N(4)	1.337(4)
C(12)-H(12A)	0.9800	C(29)-H(29)	0.9500
C(12)-H(12B)	0.9800	C(30)-C(31)	1.525(4)
C(12)-H(12C)	0.9800	C(30)-C(32)	1.534(4)
C(13)-O(1)	1.423(4)	C(30)-H(30)	1.0000
C(13)-C(14)	1.541(4)	C(31)-H(31A)	0.9800
C(13)-H(13)	1.0000	C(31)-H(31B)	0.9800
C(14)-C(19)	1.528(4)	C(31)-H(31C)	0.9800
C(14)-C(15)	1.534(4)	C(32)-O(2)	1.426(3)
C(14)-H(14)	1.0000	C(32)-C(33)	1.537(4)
C(15)-C(16)	1.528(4)	C(32)-H(32)	1.0000
C(15)-H(15A)	0.9900	C(33)-C(38)	1.538(4)
C(15)-H(15B)	0.9900	C(33)-C(34)	1.539(4)
C(16)-C(17)	1.522(5)	C(33)-H(33)	1.0000
C(16)-H(16A)	0.9900	C(34)-C(35)	1.531(5)
C(16)-H(16B)	0.9900	C(34)-H(34A)	0.9900
C(17)-C(18)	1.527(5)	C(34)-H(34B)	0.9900
C(17)-H(17A)	0.9900	C(35)-C(36)	1.517(5)
C(17)-H(17B)	0.9900	C(35)-H(35A)	0.9900
C(18)-C(19)	1.526(4)	C(35)-H(35B)	0.9900

C(36)-C(37)	1.528(5)
C(36)-H(36A)	0.9900
C(36)-H(36B)	0.9900
C(37)-C(38)	1.526(5)
C(37)-H(37A)	0.9900
C(37)-H(37B)	0.9900
C(38)-H(38A)	0.9900
C(38)-H(38B)	0.9900
N(3)-H(3A)	0.8800
O(1)-H(1A)	0.8400
O(2)-H(2)	0.8400
O(3)-H(3X)	0.8501
O(3)-H(3Y)	0.8500
O(4)-H(4X)	0.8411
O(4)-H(4Y)	0.8444
O(5)-H(5X)	0.8500
O(5)-H(5Y)	0.8501

N(2)-C(1)-C(2)	99.7(2)
N(2)-C(1)-C(11)	109.6(2)
C(2)-C(1)-C(11)	117.3(2)
N(2)-C(1)-H(1)	109.9
C(2)-C(1)-H(1)	109.9
C(11)-C(1)-H(1)	109.9
C(3)-C(2)-C(7)	119.6(3)
C(3)-C(2)-C(1)	129.0(3)
C(7)-C(2)-C(1)	111.4(2)
C(2)-C(3)-C(4)	118.6(3)
C(2)-C(3)-H(3)	120.7
C(4)-C(3)-H(3)	120.7
C(5)-C(4)-C(3)	121.3(3)
C(5)-C(4)-H(4)	119.4
C(3)-C(4)-H(4)	119.4
C(4)-C(5)-C(6)	120.6(3)
C(4)-C(5)-H(5)	119.7
C(6)-C(5)-H(5)	119.7
C(7)-C(6)-C(5)	117.9(3)
C(7)-C(6)-H(6)	121.0
C(5)-C(6)-H(6)	121.0
C(6)-C(7)-C(2)	121.9(3)
C(6)-C(7)-C(8)	130.5(3)
C(2)-C(7)-C(8)	107.5(3)
C(9)-C(8)-N(2)	106.2(3)
C(9)-C(8)-C(7)	146.4(3)
N(2)-C(8)-C(7)	107.4(2)
C(8)-C(9)-N(1)	107.7(3)
C(8)-C(9)-H(9)	126.2
N(1)-C(9)-H(9)	126.2
N(1)-C(10)-N(2)	109.7(3)
N(1)-C(10)-H(10)	125.2
N(2)-C(10)-H(10)	125.2
C(12)-C(11)-C(13)	112.5(2)
C(12)-C(11)-C(1)	111.4(2)
C(13)-C(11)-C(1)	111.2(2)
C(12)-C(11)-H(11)	107.2
C(13)-C(11)-H(11)	107.2
C(1)-C(11)-H(11)	107.2
C(11)-C(12)-H(12A)	109.5
C(11)-C(12)-H(12B)	109.5
H(12A)-C(12)-H(12B)	109.5
C(11)-C(12)-H(12C)	109.5
H(12A)-C(12)-H(12C)	109.5
H(12B)-C(12)-H(12C)	109.5
O(1)-C(13)-C(11)	110.7(2)
O(1)-C(13)-C(14)	110.7(2)
C(11)-C(13)-C(14)	113.9(2)
O(1)-C(13)-H(13)	107.1
C(11)-C(13)-H(13)	107.1
C(14)-C(13)-H(13)	107.1
C(19)-C(14)-C(15)	110.5(2)
C(19)-C(14)-C(13)	110.0(2)
C(15)-C(14)-C(13)	113.1(2)
C(19)-C(14)-H(14)	107.7
C(15)-C(14)-H(14)	107.7
C(13)-C(14)-H(14)	107.7
C(16)-C(15)-C(14)	111.7(2)
C(16)-C(15)-H(15A)	109.3
C(14)-C(15)-H(15A)	109.3
C(16)-C(15)-H(15B)	109.3
C(14)-C(15)-H(15B)	109.3
H(15A)-C(15)-H(15B)	107.9
C(17)-C(16)-C(15)	111.2(3)
C(17)-C(16)-H(16A)	109.4
C(15)-C(16)-H(16A)	109.4
C(17)-C(16)-H(16B)	109.4
C(15)-C(16)-H(16B)	109.4
H(16A)-C(16)-H(16B)	108.0
C(16)-C(17)-C(18)	110.2(3)
C(16)-C(17)-H(17A)	109.6
C(18)-C(17)-H(17A)	109.6

C(16)-C(17)-H(17B) 109.6
C(18)-C(17)-H(17B) 109.6
H(17A)-C(17)-H(17B) 108.1
C(19)-C(18)-C(17) 111.3(3)
C(19)-C(18)-H(18A) 109.4
C(17)-C(18)-H(18A) 109.4
C(19)-C(18)-H(18B) 109.4
C(17)-C(18)-H(18B) 109.4
H(18A)-C(18)-H(18B) 108.0
C(18)-C(19)-C(14) 112.8(3)
C(18)-C(19)-H(19A) 109.0
C(14)-C(19)-H(19A) 109.0
C(18)-C(19)-H(19B) 109.0
C(14)-C(19)-H(19B) 109.0
H(19A)-C(19)-H(19B) 107.8
N(4)-C(20)-C(21) 99.7(2)
N(4)-C(20)-C(30) 109.8(2)
C(21)-C(20)-C(30) 117.3(2)
N(4)-C(20)-H(20) 109.9
C(21)-C(20)-H(20) 109.9
C(30)-C(20)-H(20) 109.9
C(22)-C(21)-C(26) 119.1(3)
C(22)-C(21)-C(20) 129.5(3)
C(26)-C(21)-C(20) 111.4(2)
C(23)-C(22)-C(21) 118.6(3)
C(23)-C(22)-H(22) 120.7
C(21)-C(22)-H(22) 120.7
C(22)-C(23)-C(24) 121.7(3)
C(22)-C(23)-H(23) 119.1
C(24)-C(23)-H(23) 119.1
C(25)-C(24)-C(23) 120.1(3)
C(25)-C(24)-H(24) 120.0
C(23)-C(24)-H(24) 120.0
C(26)-C(25)-C(24) 118.4(3)
C(26)-C(25)-H(25) 120.8
C(24)-C(25)-H(25) 120.8
C(25)-C(26)-C(21) 122.0(3)
C(25)-C(26)-C(27) 130.4(3)
C(21)-C(26)-C(27) 107.6(3)
C(28)-C(27)-N(4) 106.8(3)
C(28)-C(27)-C(26) 145.6(3)
N(4)-C(27)-C(26) 107.5(3)
C(27)-C(28)-N(3) 106.8(3)
C(27)-C(28)-H(28) 126.6
N(3)-C(28)-H(28) 126.6
N(3)-C(29)-N(4) 108.4(3)
N(3)-C(29)-H(29) 125.8
N(4)-C(29)-H(29) 125.8
C(31)-C(30)-C(32) 112.3(2)
C(31)-C(30)-C(20) 111.5(3)
C(32)-C(30)-C(20) 111.0(2)
C(31)-C(30)-H(30) 107.3
C(32)-C(30)-H(30) 107.3
C(20)-C(30)-H(30) 107.3
C(30)-C(31)-H(31A) 109.5
C(30)-C(31)-H(31B) 109.5
H(31A)-C(31)-H(31B) 109.5
C(30)-C(31)-H(31C) 109.5
H(31A)-C(31)-H(31C) 109.5
H(31B)-C(31)-H(31C) 109.5
O(2)-C(32)-C(30) 109.5(2)
O(2)-C(32)-C(33) 107.8(2)
C(30)-C(32)-C(33) 114.4(2)
O(2)-C(32)-H(32) 108.3
C(30)-C(32)-H(32) 108.3
C(33)-C(32)-H(32) 108.3
C(32)-C(33)-C(38) 109.8(2)
C(32)-C(33)-C(34) 112.9(2)
C(38)-C(33)-C(34) 110.2(3)
C(32)-C(33)-H(33) 107.9
C(38)-C(33)-H(33) 107.9
C(34)-C(33)-H(33) 107.9
C(35)-C(34)-C(33) 112.0(3)
C(35)-C(34)-H(34A) 109.2
C(33)-C(34)-H(34A) 109.2
C(35)-C(34)-H(34B) 109.2
C(33)-C(34)-H(34B) 109.2
H(34A)-C(34)-H(34B) 107.9
C(36)-C(35)-C(34) 111.3(3)
C(36)-C(35)-H(35A) 109.4
C(34)-C(35)-H(35A) 109.4
C(36)-C(35)-H(35B) 109.4
C(34)-C(35)-H(35B) 109.4
H(35A)-C(35)-H(35B) 108.0
C(35)-C(36)-C(37) 110.4(3)
C(35)-C(36)-H(36A) 109.6
C(37)-C(36)-H(36A) 109.6
C(35)-C(36)-H(36B) 109.6
C(37)-C(36)-H(36B) 109.6
H(36A)-C(36)-H(36B) 108.1
C(38)-C(37)-C(36) 111.0(3)
C(38)-C(37)-H(37A) 109.4

C(36)-C(37)-H(37A)	109.4	C(8)-N(2)-C(1)	114.0(2)
C(38)-C(37)-H(37B)	109.4	C(29)-N(3)-C(28)	109.2(3)
C(36)-C(37)-H(37B)	109.4	C(29)-N(3)-H(3A)	125.4
H(37A)-C(37)-H(37B)	108.0	C(28)-N(3)-H(3A)	125.4
C(37)-C(38)-C(33)	113.1(3)	C(29)-N(4)-C(27)	108.8(3)
C(37)-C(38)-H(38A)	109.0	C(29)-N(4)-C(20)	137.4(3)
C(33)-C(38)-H(38A)	109.0	C(27)-N(4)-C(20)	113.8(2)
C(37)-C(38)-H(38B)	109.0	C(13)-O(1)-H(1A)	109.5
C(33)-C(38)-H(38B)	109.0	C(32)-O(2)-H(2)	109.5
H(38A)-C(38)-H(38B)	107.8	H(3X)-O(3)-H(3Y)	107.7
C(10)-N(1)-C(9)	108.1(2)	H(4X)-O(4)-H(4Y)	109.3
C(10)-N(2)-C(8)	108.3(2)	H(5X)-O(5)-H(5Y)	107.7
C(10)-N(2)-C(1)	137.7(3)		

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters (Å2x 103)for G03081798.1-1. The anisotropic displacement factor exponent takes the form: -2□2[h2a*2U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
C(1)	24(1)	28(2)	21(1)	-6(1)	-6(1)	-2(1)
C(2)	21(1)	29(2)	20(1)	-5(1)	-2(1)	-2(1)
C(3)	24(1)	32(2)	26(2)	-8(1)	-5(1)	-3(1)
C(4)	24(1)	37(2)	31(2)	-5(1)	-9(1)	0(1)
C(5)	26(2)	29(2)	33(2)	-3(1)	-7(1)	2(1)
C(6)	29(2)	27(2)	29(2)	-5(1)	-6(1)	-1(1)
C(7)	22(1)	30(2)	20(1)	-5(1)	-5(1)	-2(1)
C(8)	23(1)	26(2)	22(1)	-7(1)	-4(1)	0(1)
C(9)	26(1)	30(2)	25(2)	-9(1)	-5(1)	0(1)
C(10)	25(1)	33(2)	19(1)	-6(1)	-4(1)	2(1)
C(11)	25(1)	27(2)	22(1)	-8(1)	-5(1)	0(1)
C(12)	27(1)	33(2)	24(1)	-10(1)	0(1)	-7(1)
C(13)	24(1)	26(2)	22(1)	-6(1)	-5(1)	-2(1)
C(14)	29(2)	26(2)	20(1)	-7(1)	-8(1)	0(1)
C(15)	30(2)	33(2)	23(2)	-9(1)	-7(1)	4(1)
C(16)	34(2)	38(2)	31(2)	-14(2)	-4(1)	4(1)
C(17)	44(2)	34(2)	30(2)	-14(2)	-4(1)	0(2)
C(18)	45(2)	35(2)	28(2)	-12(2)	-11(1)	-2(2)
C(19)	36(2)	32(2)	27(2)	-10(1)	-13(1)	0(1)
C(20)	23(1)	27(2)	22(1)	-7(1)	-5(1)	6(1)
C(21)	20(1)	33(2)	19(1)	-8(1)	-3(1)	3(1)
C(22)	24(1)	36(2)	26(2)	-9(1)	-7(1)	9(1)
C(23)	24(2)	42(2)	32(2)	-14(2)	-10(1)	8(1)
C(24)	28(2)	42(2)	33(2)	-21(2)	-8(1)	5(1)
C(25)	28(2)	33(2)	31(2)	-14(1)	-9(1)	7(1)
C(26)	23(1)	31(2)	20(1)	-8(1)	-3(1)	4(1)
C(27)	24(1)	27(2)	20(1)	-4(1)	-3(1)	1(1)
C(28)	26(1)	31(2)	24(2)	-5(1)	-6(1)	1(1)
C(29)	26(1)	33(2)	22(1)	-7(1)	-6(1)	0(1)
C(30)	25(1)	29(2)	21(1)	-6(1)	-3(1)	4(1)
C(31)	29(2)	29(2)	27(2)	-4(1)	2(1)	11(1)
C(32)	27(1)	30(2)	21(1)	-9(1)	-4(1)	7(1)
C(33)	27(2)	31(2)	19(1)	-6(1)	-5(1)	6(1)
C(34)	31(2)	32(2)	25(2)	-4(1)	-5(1)	0(1)
C(35)	34(2)	36(2)	28(2)	-5(1)	-2(1)	-3(1)
C(36)	43(2)	29(2)	30(2)	-5(1)	0(1)	2(1)
C(37)	46(2)	33(2)	27(2)	-5(1)	-11(1)	11(2)
C(38)	33(2)	32(2)	30(2)	-8(1)	-9(1)	7(1)
N(1)	25(1)	33(1)	24(1)	-7(1)	-7(1)	2(1)
N(2)	24(1)	29(1)	21(1)	-8(1)	-6(1)	0(1)
N(3)	24(1)	34(2)	23(1)	-5(1)	-7(1)	0(1)

N(4)	25(1)	28(1)	19(1)	-5(1)	-5(1)	2(1)
O(1)	30(1)	30(1)	27(1)	-8(1)	-2(1)	-7(1)
O(2)	48(1)	31(1)	28(1)	-12(1)	6(1)	8(1)
O(3)	56(2)	75(2)	75(2)	-39(2)	-18(2)	10(2)
O(4)	43(2)	59(2)	62(2)	31(2)	7(1)	-11(1)
O(5)	34(1)	60(2)	66(2)	-13(2)	4(1)	9(1)
Cl(1)	38(1)	68(1)	69(1)	-31(1)	2(1)	-8(1)

Table 5. Hydrogen coordinates (x 104) and isotropic displacement parameters (Å2x 103) for Compound 8.

	x	y	z	U(eq)
H(1)	11603	3417	6320	29
H(3)	13910	1724	7684	33
H(4)	15405	-541	7931	37
H(5)	14422	-2336	7335	37
H(6)	11784	-1954	6529	35
H(9)	8128	-534	5566	32
H(10)	7459	3569	5692	31
H(11)	8338	3642	7308	29
H(12A)		9213	1157	8695 42
H(12B)		7755	1006	8031 42
H(12C)		7164	1989	8723 42
H(13)	11638	3289	8218	29
H(14)	8743	3617	9247	29
H(15A)		8272	6290	7863 34
H(15B)		6741	4872	8233 34
H(16A)		5512	6696	8959 41
H(16B)		5861	5221	9723 41
H(17A)		7196	7251	10038 43
H(17B)		8576	7781	9005 43
H(18A)		10561	6529	10040 41
H(18B)		9005	5124	10415 41
H(19A)		11747	4645	9355 36
H(19B)		11514	6135	8577 36
H(20)	70	4956	3681	29
H(22)	-2271	4645	2292	34
H(23)	-3803	2675	2020	38
H(24)	-2918	278	2613	38
H(25)	-364	-187	3455	35
H(28)	3287	165	4422	33
H(29)	4249	4374	4282	32
H(30)	3376	6020	2687	31
H(31A)		2332	4971	1280 46
H(31B)		3781	4094	1921 46
H(31C)		4442	5725	1254 46
H(32)	-60	6686	1868	31
H(33)	2909	7855	766	31
H(34A)		3493	9259	2124 36
H(34B)		5007	8182	1732 36

H(35A)	6196	10680	997	41
H(35B)	5800	9919	241	41
H(36A)	4445	12247	-49	43
H(36B)	3111	11813	994	43
H(37A)	1066	11549	-20	43
H(37B)	2607	10482	-409	43
H(38A)	-99	9035	676	38
H(38B)	178	9802	1445	38
H(3A)	5233	1921	4850	33
H(1A)	10958	5519	6849	45
H(2)	-893	7246	3087	56
H(3X)	1691	7720	3771	77
H(3Y)	3246	7742	4209	77
H(4X)	-1575	6110	5816	82
H(4Y)	272	6849	5428	82
H(5X)	-5520	5496	6466	68
H(5Y)	-4232	6299	5662	68

Experimental data for SC-XRD on Compound 9

X-ray quality crystals were grown from a saturated 1,2-dichloroethane/ethanol/methanol solution followed by the slow vapor diffusion of heptane to deposit the crystal diffracted. A colorless rod 0.070 x 0.030 x 0.030 mm in size was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 90(2) K using phi and omega scans. Crystal-to-detector distance was 40 mm and exposure time was 0.05 seconds per frame using a scan width of 0.5°. Data collection was 100.0% complete to 67.000° in theta. A total of 13517 reflections were collected covering the indices, -13<=*h*<=13, -5<=*k*<=5, -17<=*l*<=17. 2595 reflections were found to be symmetry independent, with an R_{int} of 0.0389. Indexing and unit cell refinement indicated a primitive, monoclinic lattice. The space group was found to be P 21 (No. 4). The data were integrated and scaled using CrysAlisPro 1.171.40.35a. Solution by iterative methods (SHELXT-2014) produced a complete heavy-atom phasing model. All non-hydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-2018). All hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-2018. Absolute stereochemistry was unambiguously determined to be *R* at C11 and C12, and *S* at C1, respectively.

Table 1. Crystal data and structure refinement for Compound 9.

X-ray ID	Compound 9
Sample/notebook ID	Compound 9
Empirical formula	C16 H18 N2 O
Formula weight	254.32
Temperature	90(2) K
Wavelength	1.54184 Å
Crystal system	Monoclinic
Space group	P 21
Unit cell dimensions	a = 10.7972(5) Å alpha = 90°.
	b = 4.73210(10) Å beta = 111.019(5)°.
	c = 13.9575(6) Å gamma = 90°.
Volume	665.69(5) Å3
Z	2
Density (calculated)	1.269 Mg/m3
Absorption coefficient	0.631 mm-1
F(000)	272
Crystal size	0.070 x 0.030 x 0.030 mm3
Theta range for data collection	3.392 to 74.741°.
Index ranges	-13<=h<=13, -5<=k<=5, -17<=l<=17
Reflections collected	13517
Independent reflections	2595 [R(int) = 0.0389]
Completeness to theta = 67.000°	100.0 %
Absorption correction	Gaussian
Max. and min. transmission	1.000 and 0.626
Refinement method	Full-matrix least-squares on F2
Data / restraints / parameters	2595 / 1 / 174
Goodness-of-fit on F2	1.061
Final R indices [I>2sigma(I)]	R1 = 0.0285, wR2 = 0.0773
R indices (all data)	R1 = 0.0289, wR2 = 0.0777
Absolute structure parameter	-0.12(13)
Extinction coefficient	0.0134(16)
Largest diff. peak and hole	0.189 and -0.144 e.Å-3

Table 2. Atomic coordinates (x 104) and equivalent isotropic displacement parameters (Å2x 103)
for Compound 9. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
C(1)	6466(2)	3958(4)	2951(1)	16(1)
C(2)	7645(2)	5334(3)	2776(1)	17(1)
C(3)	8123(2)	4925(4)	1990(1)	20(1)
C(4)	9233(2)	6446(4)	1996(1)	24(1)
C(5)	9862(2)	8336(4)	2782(1)	26(1)
C(6)	9407(2)	8725(4)	3586(1)	22(1)
C(7)	8306(2)	7202(4)	3581(1)	17(1)
C(8)	7688(2)	6954(4)	4349(1)	17(1)
C(9)	7746(2)	7692(4)	5315(1)	19(1)
C(10)	6236(2)	4447(4)	4766(1)	18(1)
C(11)	5099(2)	4986(4)	2199(1)	15(1)
C(12)	3981(2)	4199(3)	2586(1)	16(1)
C(13)	2617(2)	4988(4)	1819(1)	19(1)
C(14)	2362(2)	3777(4)	748(1)	21(1)
C(15)	3465(2)	4720(4)	372(1)	20(1)
C(16)	4825(2)	3804(4)	1118(1)	18(1)
N(1)	6839(1)	6092(3)	5569(1)	20(1)
N(2)	6713(1)	4925(3)	4011(1)	16(1)
O(1)	4075(1)	1245(3)	2802(1)	19(1)

Table 3. Bond lengths [Å] and angles [°] for Compound 9.

C(1)-N(2)	1.4785(19)	C(10)-N(2)	1.348(2)
C(1)-C(2)	1.525(2)	C(10)-H(10)	0.9500
C(1)-C(11)	1.551(2)	C(11)-C(12)	1.534(2)
C(1)-H(1)	1.0000	C(11)-C(16)	1.535(2)
C(2)-C(3)	1.384(2)	C(11)-H(11)	1.0000
C(2)-C(7)	1.407(2)	C(12)-O(1)	1.426(2)
C(3)-C(4)	1.395(2)	C(12)-C(13)	1.524(2)
C(3)-H(3)	0.9500	C(12)-H(12)	1.0000
C(4)-C(5)	1.389(3)	C(13)-C(14)	1.530(2)
C(4)-H(4)	0.9500	C(13)-H(13A)	0.9900
C(5)-C(6)	1.391(3)	C(13)-H(13B)	0.9900
C(5)-H(5)	0.9500	C(14)-C(15)	1.530(2)
C(6)-C(7)	1.388(3)	C(14)-H(14A)	0.9900
C(6)-H(6)	0.9500	C(14)-H(14B)	0.9900
C(7)-C(8)	1.456(2)	C(15)-C(16)	1.528(2)
C(8)-C(9)	1.372(2)	C(15)-H(15A)	0.9900
C(8)-N(2)	1.377(2)	C(15)-H(15B)	0.9900
C(9)-N(1)	1.381(2)	C(16)-H(16A)	0.9900
C(9)-H(9)	0.9500	C(16)-H(16B)	0.9900
C(10)-N(1)	1.328(2)	O(1)-H(1A)	0.8400

N(2)-C(1)-C(2)	99.61(12)	C(2)-C(7)-C(8)	107.59(14)
N(2)-C(1)-C(11)	111.45(13)	C(9)-C(8)-N(2)	105.92(14)
C(2)-C(1)-C(11)	113.86(13)	C(9)-C(8)-C(7)	146.20(16)
N(2)-C(1)-H(1)	110.5	N(2)-C(8)-C(7)	107.43(13)
C(2)-C(1)-H(1)	110.5	C(8)-C(9)-N(1)	109.03(15)
C(11)-C(1)-H(1)	110.5	C(8)-C(9)-H(9)	125.5
C(3)-C(2)-C(7)	119.67(15)	N(1)-C(9)-H(9)	125.5
C(3)-C(2)-C(1)	129.59(15)	N(1)-C(10)-N(2)	110.67(14)
C(7)-C(2)-C(1)	110.71(14)	N(1)-C(10)-H(10)	124.7
C(2)-C(3)-C(4)	119.14(16)	N(2)-C(10)-H(10)	124.7
C(2)-C(3)-H(3)	120.4	C(12)-C(11)-C(16)	110.99(13)
C(4)-C(3)-H(3)	120.4	C(12)-C(11)-C(1)	111.36(12)
C(5)-C(4)-C(3)	120.83(16)	C(16)-C(11)-C(1)	110.58(13)
C(5)-C(4)-H(4)	119.6	C(12)-C(11)-H(11)	107.9
C(3)-C(4)-H(4)	119.6	C(16)-C(11)-H(11)	107.9
C(4)-C(5)-C(6)	120.57(17)	C(1)-C(11)-H(11)	107.9
C(4)-C(5)-H(5)	119.7	O(1)-C(12)-C(13)	111.45(14)
C(6)-C(5)-H(5)	119.7	O(1)-C(12)-C(11)	107.93(13)
C(7)-C(6)-C(5)	118.51(17)	C(13)-C(12)-C(11)	112.22(13)
C(7)-C(6)-H(6)	120.7	O(1)-C(12)-H(12)	108.4
C(5)-C(6)-H(6)	120.7	C(13)-C(12)-H(12)	108.4
C(6)-C(7)-C(2)	121.25(16)	C(11)-C(12)-H(12)	108.4
C(6)-C(7)-C(8)	130.97(16)	C(12)-C(13)-C(14)	112.58(14)

C(12)-C(13)-H(13A)	109.1	C(16)-C(15)-H(15B)	109.4
C(14)-C(13)-H(13A)	109.1	C(14)-C(15)-H(15B)	109.4
C(12)-C(13)-H(13B)	109.1	H(15A)-C(15)-H(15B)	108.0
C(14)-C(13)-H(13B)	109.1	C(15)-C(16)-C(11)	111.48(13)
H(13A)-C(13)-H(13B)	107.8	C(15)-C(16)-H(16A)	109.3
C(15)-C(14)-C(13)	109.67(14)	C(11)-C(16)-H(16A)	109.3
C(15)-C(14)-H(14A)	109.7	C(15)-C(16)-H(16B)	109.3
C(13)-C(14)-H(14A)	109.7	C(11)-C(16)-H(16B)	109.3
C(15)-C(14)-H(14B)	109.7	H(16A)-C(16)-H(16B)	108.0
C(13)-C(14)-H(14B)	109.7	C(10)-N(1)-C(9)	106.41(13)
H(14A)-C(14)-H(14B)	108.2	C(10)-N(2)-C(8)	107.94(13)
C(16)-C(15)-C(14)	111.04(13)	C(10)-N(2)-C(1)	138.46(14)
C(16)-C(15)-H(15A)	109.4	C(8)-N(2)-C(1)	113.58(13)
C(14)-C(15)-H(15A)	109.4	C(12)-O(1)-H(1A)	109.5

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters (Å2x 103)for Compound 9. The anisotropic displacement factor exponent takes the form: -2□2[h2a*2U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
C(1)	18(1)	15(1)	13(1)	-2(1)	6(1)	0(1)
C(2)	15(1)	17(1)	18(1)	4(1)	4(1)	3(1)
C(3)	17(1)	24(1)	18(1)	2(1)	5(1)	4(1)
C(4)	18(1)	35(1)	20(1)	7(1)	8(1)	7(1)
C(5)	16(1)	32(1)	29(1)	7(1)	8(1)	0(1)
C(6)	17(1)	23(1)	24(1)	0(1)	4(1)	-1(1)
C(7)	14(1)	18(1)	18(1)	2(1)	4(1)	4(1)
C(8)	14(1)	16(1)	18(1)	0(1)	3(1)	2(1)
C(9)	17(1)	20(1)	18(1)	-4(1)	3(1)	1(1)
C(10)	18(1)	21(1)	17(1)	2(1)	6(1)	3(1)
C(11)	16(1)	14(1)	15(1)	0(1)	6(1)	1(1)
C(12)	19(1)	14(1)	15(1)	-1(1)	7(1)	0(1)
C(13)	17(1)	20(1)	21(1)	0(1)	7(1)	1(1)
C(14)	18(1)	24(1)	18(1)	0(1)	2(1)	-2(1)
C(15)	22(1)	23(1)	15(1)	0(1)	5(1)	-1(1)
C(16)	19(1)	20(1)	15(1)	-1(1)	7(1)	0(1)
N(1)	18(1)	24(1)	17(1)	-2(1)	6(1)	3(1)
N(2)	17(1)	16(1)	14(1)	-1(1)	5(1)	1(1)
O(1)	24(1)	15(1)	19(1)	2(1)	10(1)	-2(1)

Table 5. Hydrogen coordinates (x 104) and isotropic displacement parameters (Å2x 103) for Compound 9.

	x	y	z	U(eq)	
H(1)	6529	1853	2928	19	
H(3)	7701	3627	1452	24	
H(4)	9563	6186	1456	29	
H(5)	10610	9372	2769	31	
H(6)	9839	10005	4128	26	
H(9)	8318	9080	5741	23	
H(10)	5562	3117	4729	22	
H(11)	5130	7094	2160	18	
H(12)	4126	5245	3240	19	
H(13A)		2541	7072	1772	23
H(13B)		1928	4278	2072	23
H(14A)		2337	1688	773	25
H(14B)		1493	4448	267	25
H(15A)		3310	3887	-312	24
H(15B)		3444	6803	300	24
H(16A)		5520	4476	864	21
H(16B)		4867	1714	1150	21
H(1A)	3749	899	3253	28	

Experimental data for SC-XRD on Compound ent-12

X-ray quality crystals were grown from a saturated 1,2-dichloroethane/ethanol/methanol solution followed by the slow vapor diffusion of diisopropyl ether to deposit the crystal diffracted. A colorless prism 0.070 x 0.060 x 0.050 mm in size was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 100(2) K using and scans. Crystal-to-detector distance was 60 mm and exposure time was 1 seconds per frame using a scan width of 2.0°. Data collection was 99.4% complete to 67.000° in theta. A total of 10940 reflections were collected covering the indices, -6<=*h*<=6, -7<=*k*<=8, -35<=*l*<=35. 2032 reflections were found to be symmetry independent, with an R_{int} of 0.0552. Indexing and unit cell refinement indicated a primitive, orthorhombic lattice. The space group was found to be P 21 21 21 (No. 19). The data were integrated using the Bruker SAINT software program and scaled using the SADABS software program. Solution by iterative methods (SHELXT-2014) produced a complete heavy-atom phasing model consistent with the proposed structure. All non-hydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-2014). All hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-2014. Absolute stereochemistry was unambiguously determined to be *R* at C1 and C11, and *S* at C12, respectively.

Table 1. Crystal data and structure refinement for Compound ent-12.

X-ray ID	Compound ent-12
Sample/notebook ID	Compound ent-12
Empirical formula	C14 H14 N2 O
Formula weight	226.27
Temperature	100(2) K
Wavelength	1.54178 Å
Crystal system	Orthorhombic
Space group	P 21 21 21
Unit cell dimensions	a = 5.7576(3) Å alpha = 90°.
	b = 6.6825(4) Å beta = 90°.
	c = 29.3671(16) Å gamma = 90°.
Volume	1129.90(11) Å3
Z	4
Density (calculated)	1.330 Mg/m3
Absorption coefficient	0.679 mm-1
F(000)	480
Crystal size	0.070 x 0.060 x 0.050 mm3
Theta range for data collection	3.009 to 68.154°.
Index ranges	-6<=h<=6, -7<=k<=8, -35<=l<=35
Reflections collected	10940
Independent reflections	2032 [R(int) = 0.0552]
Completeness to theta = 67.000°	99.4 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.929 and 0.825
Refinement method	Full-matrix least-squares on F2
Data / restraints / parameters	2032 / 0 / 155
Goodness-of-fit on F2	1.050
Final R indices [I>2sigma(I)]	R1 = 0.0331, wR2 = 0.0821
R indices (all data)	R1 = 0.0339, wR2 = 0.0825
Absolute structure parameter	0.01(14)
Extinction coefficient	n/a
Largest diff. peak and hole	0.180 and -0.191 e.Å-3

Table 2. Atomic coordinates (x 104) and equivalent isotropic displacement parameters (Å2x 103)
for Compound ent-12. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
C(1)	2015(4)	6641(3)	3695(1)	18(1)
C(2)	3751(3)	6491(3)	4085(1)	19(1)
C(3)	5351(4)	7902(3)	4229(1)	21(1)
C(4)	6920(4)	7381(3)	4571(1)	23(1)
C(5)	6887(4)	5463(3)	4760(1)	24(1)
C(6)	5269(4)	4052(3)	4622(1)	23(1)
C(7)	3680(4)	4579(3)	4286(1)	19(1)
C(8)	1795(3)	3469(3)	4070(1)	19(1)
C(9)	533(4)	1739(3)	4055(1)	23(1)
C(10)	-890(3)	3678(3)	3538(1)	23(1)
C(11)	3212(3)	6863(3)	3234(1)	19(1)
C(12)	4403(3)	8876(3)	3123(1)	21(1)
C(13)	3512(4)	8680(3)	2629(1)	22(1)
C(14)	1732(4)	7109(3)	2796(1)	22(1)
N(1)	-1146(3)	1876(3)	3721(1)	25(1)
N(2)	856(3)	4687(2)	3739(1)	19(1)
O(1)	6829(2)	8937(2)	3176(1)	26(1)

Table 3. Bond lengths [Å] and angles [°] for Compound ent-12.

C(1)-N(2)	1.472(2)	C(9)-N(1)	1.381(3)
C(1)-C(2)	1.523(3)	C(9)-H(9)	0.9500
C(1)-C(11)	1.528(2)	C(10)-N(1)	1.327(3)
C(1)-H(1)	1.0000	C(10)-N(2)	1.347(2)
C(2)-C(3)	1.385(3)	C(10)-H(10)	0.9500
C(2)-C(7)	1.408(3)	C(11)-C(12)	1.545(3)
C(3)-C(4)	1.394(3)	C(11)-C(14)	1.551(2)
C(3)-H(3)	0.9500	C(11)-H(11)	1.0000
C(4)-C(5)	1.398(3)	C(12)-O(1)	1.406(2)
C(4)-H(4)	0.9500	C(12)-C(13)	1.545(2)
C(5)-C(6)	1.387(3)	C(12)-H(12)	1.0000
C(5)-H(5)	0.9500	C(13)-C(14)	1.547(3)
C(6)-C(7)	1.390(3)	C(13)-H(13A)	0.9900
C(6)-H(6)	0.9500	C(13)-H(13B)	0.9900
C(7)-C(8)	1.460(3)	C(14)-H(14A)	0.9900
C(8)-C(9)	1.366(3)	C(14)-H(14B)	0.9900
C(8)-N(2)	1.377(2)	O(1)-H(1A)	0.8400

N(2)-C(1)-C(2)	99.96(14)	N(2)-C(8)-C(7)	107.37(16)
N(2)-C(1)-C(11)	111.59(15)	C(8)-C(9)-N(1)	109.78(17)
C(2)-C(1)-C(11)	112.15(16)	C(8)-C(9)-H(9)	125.1
N(2)-C(1)-H(1)	110.9	N(1)-C(9)-H(9)	125.1
C(2)-C(1)-H(1)	110.9	N(1)-C(10)-N(2)	111.05(17)
C(11)-C(1)-H(1)	110.9	N(1)-C(10)-H(10)	124.5
C(3)-C(2)-C(7)	120.57(18)	N(2)-C(10)-H(10)	124.5
C(3)-C(2)-C(1)	128.43(17)	C(1)-C(11)-C(12)	118.06(15)
C(7)-C(2)-C(1)	110.89(16)	C(1)-C(11)-C(14)	119.87(16)
C(2)-C(3)-C(4)	118.77(18)	C(12)-C(11)-C(14)	88.73(14)
C(2)-C(3)-H(3)	120.6	C(1)-C(11)-H(11)	109.5
C(4)-C(3)-H(3)	120.6	C(12)-C(11)-H(11)	109.5
C(3)-C(4)-C(5)	120.45(19)	C(14)-C(11)-H(11)	109.5
C(3)-C(4)-H(4)	119.8	O(1)-C(12)-C(11)	116.32(18)
C(5)-C(4)-H(4)	119.8	O(1)-C(12)-C(13)	115.81(16)
C(6)-C(5)-C(4)	121.08(19)	C(11)-C(12)-C(13)	88.59(15)
C(6)-C(5)-H(5)	119.5	O(1)-C(12)-H(12)	111.4
C(4)-C(5)-H(5)	119.5	C(11)-C(12)-H(12)	111.4
C(5)-C(6)-C(7)	118.53(19)	C(13)-C(12)-H(12)	111.4
C(5)-C(6)-H(6)	120.7	C(12)-C(13)-C(14)	88.88(14)
C(7)-C(6)-H(6)	120.7	C(12)-C(13)-H(13A)	113.8
C(6)-C(7)-C(2)	120.57(18)	C(14)-C(13)-H(13A)	113.8
C(6)-C(7)-C(8)	131.98(18)	C(12)-C(13)-H(13B)	113.8
C(2)-C(7)-C(8)	107.43(17)	C(14)-C(13)-H(13B)	113.8
C(9)-C(8)-N(2)	105.61(17)	H(13A)-C(13)-H(13B)	111.1
C(9)-C(8)-C(7)	147.02(19)	C(13)-C(14)-C(11)	88.30(14)

C(13)-C(14)-H(14A)	113.9	C(10)-N(1)-C(9)	105.70(17)
C(11)-C(14)-H(14A)	113.9	C(10)-N(2)-C(8)	107.85(16)
C(13)-C(14)-H(14B)	113.9	C(10)-N(2)-C(1)	138.07(17)
C(11)-C(14)-H(14B)	113.9	C(8)-N(2)-C(1)	114.07(15)
H(14A)-C(14)-H(14B)	111.1	C(12)-O(1)-H(1A)	109.5

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters (Å2x 103)for Compound ent-12. The anisotropic displacement factor exponent takes the form: -2□2[h2a*2U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
C(1)	19(1)	17(1)	20(1)	-2(1)	1(1)	-2(1)
C(2)	19(1)	21(1)	16(1)	-2(1)	3(1)	0(1)
C(3)	23(1)	21(1)	17(1)	-3(1)	3(1)	-4(1)
C(4)	21(1)	30(1)	18(1)	-5(1)	1(1)	-5(1)
C(5)	23(1)	32(1)	16(1)	-2(1)	-2(1)	1(1)
C(6)	26(1)	24(1)	18(1)	1(1)	0(1)	2(1)
C(7)	22(1)	21(1)	16(1)	-4(1)	2(1)	0(1)
C(8)	21(1)	21(1)	16(1)	-2(1)	1(1)	1(1)
C(9)	25(1)	23(1)	20(1)	0(1)	2(1)	-2(1)
C(10)	20(1)	28(1)	20(1)	-1(1)	-2(1)	-3(1)
C(11)	18(1)	21(1)	17(1)	-2(1)	-1(1)	1(1)
C(12)	18(1)	23(1)	20(1)	-2(1)	0(1)	-1(1)
C(13)	23(1)	24(1)	19(1)	2(1)	-1(1)	0(1)
C(14)	20(1)	29(1)	17(1)	-1(1)	-2(1)	-1(1)
N(1)	24(1)	27(1)	23(1)	-3(1)	0(1)	-6(1)
N(2)	19(1)	21(1)	17(1)	-1(1)	0(1)	-1(1)
O(1)	20(1)	34(1)	26(1)	-7(1)	1(1)	-6(1)

Table 5. Hydrogen coordinates (x 104) and isotropic displacement parameters (Å2x 103) for Compound ent-12.

	x	y	z	U(eq)	
H(1)	893	7760	3748	22	
H(3)	5379	9201	4098	25	
H(4)	8018	8337	4676	28	
H(5)	7992	5120	4988	28	
H(6)	5246	2753	4753	27	
H(9)	775	611	4246	27	
H(10)	-1815	4188	3296	27	
H(11)	4347	5745	3191	23	
H(12)	3635	10013	3286	25	
H(13A)		4679	8141	2414	27
H(13B)		2794	9918	2509	27
H(14A)		1663	5890	2604	26
H(14B)		160	7658	2851	26
H(1A)	7183	9839	3363	40	

Experimental data for SC-XRD on Compound ent-13

X-ray quality crystals were grown from a saturated 1,2-dichloroethane/ethanol/methanol solution followed by the slow vapor diffusion of heptane to deposit the crystal diffracted. A colorless prism 0.120 x 0.100 x 0.100 mm in size was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 100(2) K using and scans. Crystal-to-detector distance was 60 mm and exposure time was 1 seconds per frame using a scan width of 2.0°. Data collection was 99.4% complete to 67.000° in theta. A total of 13431 reflections were collected covering the indices, -6<=*h*<=6, -11<=*k*<=11, -28<=*l*<=25. 2340 reflections were found to be symmetry independent, with an R_{int} of 0.0385. Indexing and unit cell refinement indicated a primitive, orthorhombic lattice. The space group was found to be P 21 21 21 (No. 19). The data were integrated using the Bruker SAINT software program and scaled using the SADABS software program. Solution by iterative methods (SHELXT-2014) produced a complete heavy-atom phasing model consistent with the proposed structure. All non-hydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-2014). All hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-2014. Absolute stereochemistry was unambiguously determined to be *R* at C1, C11, and C12, respectively.

Table 1. Crystal data and structure refinement for Compound ent-13.

X-ray ID	Compound ent-13
Sample/notebook ID	Compound ent-13
Empirical formula	C15 H16 N2 O2
Formula weight	256.30
Temperature	100(2) K
Wavelength	1.54178 Å
Crystal system	Orthorhombic
Space group	P 21 21 21
Unit cell dimensions	a = 5.7224(3) Å alpha = 90°.
	b = 9.4414(5) Å beta = 90°.
	c = 23.8273(12) Å gamma = 90°.
Volume	1287.33(12) Å3
Z	4
Density (calculated)	1.322 Mg/m3
Absorption coefficient	0.719 mm-1
F(000)	544
Crystal size	0.120 x 0.100 x 0.100 mm3
Theta range for data collection	5.039 to 68.456°.
Index ranges	-6<=h<=6, -11<=k<=11, -28<=l<=25
Reflections collected	13431
Independent reflections	2340 [R(int) = 0.0385]
Completeness to theta = 67.000°	99.4 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.929 and 0.802
Refinement method	Full-matrix least-squares on F2
Data / restraints / parameters	2340 / 0 / 173
Goodness-of-fit on F2	1.086
Final R indices [I>2sigma(I)]	R1 = 0.0304, wR2 = 0.0778
R indices (all data)	R1 = 0.0306, wR2 = 0.0780
Absolute structure parameter	0.05(7)
Extinction coefficient	n/a
Largest diff. peak and hole	0.183 and -0.198 e.Å-3

Table 2. Atomic coordinates (x 104) and equivalent isotropic displacement parameters (Å2x 103)
for Compound ent-13. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
C(1)	4134(3)	4455(2)	4020(1)	16(1)
C(2)	2873(3)	3063(2)	3921(1)	16(1)
C(3)	3435(3)	2008(2)	3543(1)	18(1)
C(4)	1978(4)	822(2)	3503(1)	21(1)
C(5)	-11(4)	718(2)	3836(1)	21(1)
C(6)	-590(3)	1784(2)	4217(1)	19(1)
C(7)	864(3)	2953(2)	4258(1)	16(1)
C(8)	794(3)	4207(2)	4619(1)	15(1)
C(9)	-214(3)	4848(2)	5073(1)	18(1)
C(10)	2805(4)	6107(2)	4849(1)	19(1)
C(11)	4231(3)	5402(2)	3494(1)	16(1)
C(12)	5024(3)	6915(2)	3619(1)	17(1)
C(13)	5354(4)	7695(2)	3064(1)	21(1)
C(14)	2298(4)	6397(2)	2642(1)	23(1)
C(15)	1922(3)	5517(2)	3168(1)	19(1)
N(1)	1073(3)	6038(2)	5215(1)	19(1)
N(2)	2696(3)	5031(2)	4480(1)	16(1)
O(1)	3222(3)	7777(1)	2757(1)	23(1)
O(2)	7136(2)	6934(1)	3930(1)	21(1)

Table 3. Bond lengths [Å] and angles [°] for Compound ent-13.

C(1)-N(2)	1.474(2)	C(10)-N(1)	1.322(2)
C(1)-C(2)	1.518(2)	C(10)-N(2)	1.346(2)
C(1)-C(11)	1.540(2)	C(10)-H(10)	0.9500
C(1)-H(1)	1.0000	C(11)-C(12)	1.529(2)
C(2)-C(3)	1.381(3)	C(11)-C(15)	1.537(2)
C(2)-C(7)	1.406(2)	C(11)-H(11)	1.0000
C(3)-C(4)	1.399(3)	C(12)-O(2)	1.418(2)
C(3)-H(3)	0.9500	C(12)-C(13)	1.526(3)
C(4)-C(5)	1.391(3)	C(12)-H(12)	1.0000
C(4)-H(4)	0.9500	C(13)-O(1)	1.424(2)
C(5)-C(6)	1.395(3)	C(13)-H(13A)	0.9900
C(5)-H(5)	0.9500	C(13)-H(13B)	0.9900
C(6)-C(7)	1.386(3)	C(14)-O(1)	1.432(2)
C(6)-H(6)	0.9500	C(14)-C(15)	1.520(3)
C(7)-C(8)	1.464(3)	C(14)-H(14A)	0.9900
C(8)-C(9)	1.368(3)	C(14)-H(14B)	0.9900
C(8)-N(2)	1.378(2)	C(15)-H(15A)	0.9900
C(9)-N(1)	1.385(3)	C(15)-H(15B)	0.9900
C(9)-H(9)	0.9500	O(2)-H(2)	0.8400

N(2)-C(1)-C(2)	99.79(14)	C(9)-C(8)-N(2)	105.87(16)
N(2)-C(1)-C(11)	114.26(14)	C(9)-C(8)-C(7)	146.53(18)
C(2)-C(1)-C(11)	113.09(14)	N(2)-C(8)-C(7)	107.10(15)
N(2)-C(1)-H(1)	109.8	C(8)-C(9)-N(1)	109.15(16)
C(2)-C(1)-H(1)	109.8	C(8)-C(9)-H(9)	125.4
C(11)-C(1)-H(1)	109.8	N(1)-C(9)-H(9)	125.4
C(3)-C(2)-C(7)	120.64(17)	N(1)-C(10)-N(2)	111.05(17)
C(3)-C(2)-C(1)	128.02(16)	N(1)-C(10)-H(10)	124.5
C(7)-C(2)-C(1)	111.29(15)	N(2)-C(10)-H(10)	124.5
C(2)-C(3)-C(4)	118.88(17)	C(12)-C(11)-C(15)	106.69(14)
C(2)-C(3)-H(3)	120.6	C(12)-C(11)-C(1)	113.28(14)
C(4)-C(3)-H(3)	120.6	C(15)-C(11)-C(1)	114.95(14)
C(5)-C(4)-C(3)	120.34(17)	C(12)-C(11)-H(11)	107.2
C(5)-C(4)-H(4)	119.8	C(15)-C(11)-H(11)	107.2
C(3)-C(4)-H(4)	119.8	C(1)-C(11)-H(11)	107.2
C(4)-C(5)-C(6)	120.97(17)	O(2)-C(12)-C(13)	109.98(15)
C(4)-C(5)-H(5)	119.5	O(2)-C(12)-C(11)	111.47(15)
C(6)-C(5)-H(5)	119.5	C(13)-C(12)-C(11)	108.65(15)
C(7)-C(6)-C(5)	118.55(18)	O(2)-C(12)-H(12)	108.9
C(7)-C(6)-H(6)	120.7	C(13)-C(12)-H(12)	108.9
C(5)-C(6)-H(6)	120.7	C(11)-C(12)-H(12)	108.9
C(6)-C(7)-C(2)	120.61(17)	O(1)-C(13)-C(12)	111.39(15)
C(6)-C(7)-C(8)	132.02(17)	O(1)-C(13)-H(13A)	109.3
C(2)-C(7)-C(8)	107.34(16)	C(12)-C(13)-H(13A)	109.3

O(1)-C(13)-H(13B)	109.3	C(11)-C(15)-H(15A)	109.8
C(12)-C(13)-H(13B)	109.3	C(14)-C(15)-H(15B)	109.8
H(13A)-C(13)-H(13B)	108.0	C(11)-C(15)-H(15B)	109.8
O(1)-C(14)-C(15)	113.06(15)	H(15A)-C(15)-H(15B)	108.2
O(1)-C(14)-H(14A)	109.0	C(10)-N(1)-C(9)	106.10(15)
C(15)-C(14)-H(14A)	109.0	C(10)-N(2)-C(8)	107.82(15)
O(1)-C(14)-H(14B)	109.0	C(10)-N(2)-C(1)	137.60(16)
C(15)-C(14)-H(14B)	109.0	C(8)-N(2)-C(1)	114.28(15)
H(14A)-C(14)-H(14B)	107.8	C(13)-O(1)-C(14)	111.43(14)
C(14)-C(15)-C(11)	109.55(15)	C(12)-O(2)-H(2)	109.5
C(14)-C(15)-H(15A)	109.8		

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters (Å2x 103)for Compound ent-13. The anisotropic displacement factor exponent takes the form: -2□2[h2a*2U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
C(1)	15(1)	17(1)	15(1)	-3(1)	2(1)	0(1)
C(2)	17(1)	16(1)	15(1)	1(1)	-1(1)	1(1)
C(3)	18(1)	19(1)	18(1)	-1(1)	0(1)	2(1)
C(4)	28(1)	17(1)	19(1)	-2(1)	-5(1)	3(1)
C(5)	25(1)	18(1)	20(1)	2(1)	-7(1)	-4(1)
C(6)	18(1)	21(1)	19(1)	4(1)	-3(1)	-2(1)
C(7)	16(1)	16(1)	15(1)	2(1)	-2(1)	3(1)
C(8)	15(1)	17(1)	14(1)	3(1)	-1(1)	0(1)
C(9)	17(1)	19(1)	17(1)	3(1)	3(1)	2(1)
C(10)	23(1)	17(1)	17(1)	-1(1)	1(1)	-1(1)
C(11)	16(1)	17(1)	14(1)	-2(1)	3(1)	-1(1)
C(12)	17(1)	18(1)	16(1)	-2(1)	1(1)	-1(1)
C(13)	24(1)	19(1)	22(1)	0(1)	0(1)	-3(1)
C(14)	28(1)	23(1)	18(1)	0(1)	-2(1)	-4(1)
C(15)	19(1)	22(1)	17(1)	-1(1)	-1(1)	-4(1)
N(1)	24(1)	17(1)	16(1)	0(1)	3(1)	3(1)
N(2)	17(1)	16(1)	14(1)	-1(1)	2(1)	-1(1)
O(1)	29(1)	19(1)	21(1)	1(1)	-4(1)	0(1)
O(2)	20(1)	22(1)	21(1)	-4(1)	-3(1)	-4(1)

Table 5. Hydrogen coordinates (x 104) and isotropic displacement parameters (Å2x 103) for Compound ent-13.

	x	y	z	U(eq)	
H(1)	5754	4267	4159	19	
H(3)	4789	2085	3314	22	
H(4)	2348	85	3246	25	
H(5)	-988	-92	3804	25	
H(6)	-1952	1710	4443	23	
H(9)	-1580	4528	5261	21	
H(10)	3973	6822	4847	23	
H(11)	5410	4976	3234	19	
H(12)	3781	7405	3841	20	
H(13A)		5937	8664	3139	26
H(13B)		6541	7195	2835	26
H(14A)		3386	5889	2389	27
H(14B)		789	6500	2443	27
H(15A)		1367	4559	3064	23
H(15B)		717	5967	3407	23
H(2)	7047	7548	4184	31	

Experimental data for SC-XRD on Compound ent-14

X-ray quality crystals were grown from a saturated 1,2-dichloroethane/ethanol/methanol solution followed by the slow vapor diffusion of heptane to deposit the crystal diffracted. A colorless plate 0.080 x 0.050 x 0.020 mm in size was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 100(2) K using and scans. Crystal-to-detector distance was 60 mm and exposure time was 4 seconds per frame using a scan width of 2.0°. Data collection was 98.3% complete to 67.000° in theta. A total of 7624 reflections were collected covering the indices, -12<=*h*<=11, -5<=*k*<=6, -15<=*l*<=15. 2136 reflections were found to be symmetry independent, with an R_{int} of 0.0768. Indexing and unit cell refinement indicated a primitive, monoclinic lattice. The space group was found to be P 21 (No. 4). The data were integrated using the Bruker SAINT software program and scaled using the SADABS software program. Solution by iterative methods (SHELXT-2014) produced a complete heavy-atom phasing model consistent with the proposed structure. All non-hydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-2014). All hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-2014. Absolute stereochemistry was unambiguously determined to be *R* at C1 and *S* at C11, and C12, respectively.

Table 1. Crystal data and structure refinement for Compound ent-14.

X-ray ID	Compound ent-14
Sample/notebook ID	Compound ent-14
Empirical formula	C15 H16 N2 O2
Formula weight	256.30
Temperature	100(2) K
Wavelength	1.54178 Å
Crystal system	Monoclinic
Space group	P 21
Unit cell dimensions	a = 9.9840(9) Å alpha = 90°.
	b = 5.4028(3) Å beta = 111.475(6)°.
	c = 12.6101(10) Å gamma = 90°.
Volume	632.99(9) Å3
Z	2
Density (calculated)	1.345 Mg/m3
Absorption coefficient	0.731 mm-1
F(000)	272
Crystal size	0.080 x 0.050 x 0.020 mm3
Theta range for data collection	3.767 to 68.373°.
Index ranges	-12<=h<=11, -5<=k<=6, -15<=l<=15
Reflections collected	7624
Independent reflections	2136 [R(int) = 0.0768]
Completeness to theta = 67.000°	98.3 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.929 and 0.753
Refinement method	Full-matrix least-squares on F2
Data / restraints / parameters	2136 / 1 / 173
Goodness-of-fit on F2	1.036
Final R indices [I>2sigma(I)]	R1 = 0.0417, wR2 = 0.0984
R indices (all data)	R1 = 0.0490, wR2 = 0.1019
Absolute structure parameter	0.1(3)
Extinction coefficient	n/a
Largest diff. peak and hole	0.245 and -0.208 e.Å-3

Table 2. Atomic coordinates (x 104) and equivalent isotropic displacement parameters (Å2x 103)
for Compound ent-14. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
C(1)	6156(3)	4049(5)	2954(2)	15(1)
C(2)	4750(3)	5393(5)	2755(2)	16(1)
C(3)	3405(3)	4891(5)	1948(2)	19(1)
C(4)	2255(3)	6421(6)	1897(2)	22(1)
C(5)	2456(3)	8427(6)	2634(3)	24(1)
C(6)	3808(3)	8942(5)	3437(3)	21(1)
C(7)	4955(3)	7421(5)	3497(2)	16(1)
C(8)	6466(3)	7433(5)	4243(2)	17(1)
C(9)	7480(3)	8427(5)	5207(2)	19(1)
C(10)	8470(3)	5302(5)	4696(2)	19(1)
C(11)	6606(3)	3997(5)	1905(2)	15(1)
C(12)	8191(3)	3341(5)	2216(2)	16(1)
C(13)	8525(3)	3201(5)	1131(2)	20(1)
C(14)	8135(3)	5664(6)	498(3)	23(1)
C(15)	6306(3)	6429(5)	1232(2)	20(1)
N(1)	8737(3)	7062(5)	5484(2)	20(1)
N(2)	7128(3)	5478(4)	3931(2)	16(1)
O(1)	6651(2)	6211(4)	227(2)	23(1)
O(2)	8513(2)	1082(4)	2836(2)	20(1)

Table 3. Bond lengths [Å] and angles [°] for Compound ent-14.

C(1)-N(2)	1.477(3)	C(10)-N(1)	1.330(4)
C(1)-C(2)	1.517(4)	C(10)-N(2)	1.337(4)
C(1)-C(11)	1.546(4)	C(10)-H(10)	0.9500
C(1)-H(1)	1.0000	C(11)-C(12)	1.526(3)
C(2)-C(3)	1.383(4)	C(11)-C(15)	1.533(4)
C(2)-C(7)	1.406(4)	C(11)-H(11)	1.0000
C(3)-C(4)	1.397(4)	C(12)-O(2)	1.421(3)
C(3)-H(3)	0.9500	C(12)-C(13)	1.525(4)
C(4)-C(5)	1.394(4)	C(12)-H(12)	1.0000
C(4)-H(4)	0.9500	C(13)-C(14)	1.527(4)
C(5)-C(6)	1.387(4)	C(13)-H(13A)	0.9900
C(5)-H(5)	0.9500	C(13)-H(13B)	0.9900
C(6)-C(7)	1.388(4)	C(14)-O(1)	1.424(3)
C(6)-H(6)	0.9500	C(14)-H(14A)	0.9900
C(7)-C(8)	1.457(4)	C(14)-H(14B)	0.9900
C(8)-C(9)	1.374(4)	C(15)-O(1)	1.435(3)
C(8)-N(2)	1.378(3)	C(15)-H(15A)	0.9900
C(9)-N(1)	1.385(4)	C(15)-H(15B)	0.9900
C(9)-H(9)	0.9500	O(2)-H(2)	0.8400

N(2)-C(1)-C(2)	100.0(2)	C(9)-C(8)-N(2)	106.1(3)
N(2)-C(1)-C(11)	114.5(2)	C(9)-C(8)-C(7)	145.7(3)
C(2)-C(1)-C(11)	114.1(2)	N(2)-C(8)-C(7)	107.7(2)
N(2)-C(1)-H(1)	109.3	C(8)-C(9)-N(1)	108.7(3)
C(2)-C(1)-H(1)	109.3	C(8)-C(9)-H(9)	125.6
C(11)-C(1)-H(1)	109.3	N(1)-C(9)-H(9)	125.6
C(3)-C(2)-C(7)	120.5(3)	N(1)-C(10)-N(2)	111.2(3)
C(3)-C(2)-C(1)	128.2(3)	N(1)-C(10)-H(10)	124.4
C(7)-C(2)-C(1)	111.3(2)	N(2)-C(10)-H(10)	124.4
C(2)-C(3)-C(4)	118.5(3)	C(12)-C(11)-C(15)	108.4(2)
C(2)-C(3)-H(3)	120.7	C(12)-C(11)-C(1)	112.5(2)
C(4)-C(3)-H(3)	120.7	C(15)-C(11)-C(1)	113.5(2)
C(5)-C(4)-C(3)	121.0(3)	C(12)-C(11)-H(11)	107.4
C(5)-C(4)-H(4)	119.5	C(15)-C(11)-H(11)	107.4
C(3)-C(4)-H(4)	119.5	C(1)-C(11)-H(11)	107.4
C(6)-C(5)-C(4)	120.4(3)	O(2)-C(12)-C(13)	111.8(2)
C(6)-C(5)-H(5)	119.8	O(2)-C(12)-C(11)	110.2(2)
C(4)-C(5)-H(5)	119.8	C(13)-C(12)-C(11)	109.1(2)
C(5)-C(6)-C(7)	118.9(3)	O(2)-C(12)-H(12)	108.6
C(5)-C(6)-H(6)	120.5	C(13)-C(12)-H(12)	108.6
C(7)-C(6)-H(6)	120.5	C(11)-C(12)-H(12)	108.6
C(6)-C(7)-C(2)	120.6(3)	C(12)-C(13)-C(14)	109.1(2)
C(6)-C(7)-C(8)	132.1(3)	C(12)-C(13)-H(13A)	109.9
C(2)-C(7)-C(8)	107.3(2)	C(14)-C(13)-H(13A)	109.9

C(12)-C(13)-H(13B) 109.9
C(14)-C(13)-H(13B) 109.9
H(13A)-C(13)-H(13B) 108.3
O(1)-C(14)-C(13) 110.5(2)
O(1)-C(14)-H(14A) 109.5
C(13)-C(14)-H(14A) 109.5
O(1)-C(14)-H(14B) 109.5
C(13)-C(14)-H(14B) 109.5
H(14A)-C(14)-H(14B) 108.1
O(1)-C(15)-C(11) 110.9(2)
O(1)-C(15)-H(15A) 109.5
C(11)-C(15)-H(15A) 109.5
O(1)-C(15)-H(15B) 109.5
C(11)-C(15)-H(15B) 109.5
H(15A)-C(15)-H(15B) 108.1
C(10)-N(1)-C(9) 106.1(2)
C(10)-N(2)-C(8) 107.9(2)
C(10)-N(2)-C(1) 138.0(2)
C(8)-N(2)-C(1) 113.7(2)
C(14)-O(1)-C(15) 111.7(2)
C(12)-O(2)-H(2) 109.5

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters (Å2x 103)for Compound ent-14. The anisotropic displacement factor exponent takes the form: -2□2[h2a*2U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
C(1)	13(1)	17(1)	15(1)	-1(1)	3(1)	-1(1)
C(2)	17(1)	15(1)	18(1)	2(1)	9(1)	0(1)
C(3)	15(1)	22(2)	18(1)	1(1)	3(1)	-2(1)
C(4)	15(1)	29(2)	22(1)	5(1)	6(1)	-2(1)
C(5)	22(2)	29(2)	24(1)	9(1)	13(1)	8(1)
C(6)	26(2)	20(2)	22(1)	1(1)	14(1)	3(1)
C(7)	18(1)	16(1)	16(1)	3(1)	9(1)	-2(1)
C(8)	22(2)	14(1)	18(1)	3(1)	11(1)	2(1)
C(9)	22(1)	18(1)	18(1)	-4(1)	10(1)	-4(1)
C(10)	18(1)	23(2)	18(1)	0(1)	7(1)	0(1)
C(11)	17(1)	14(1)	15(1)	-3(1)	6(1)	0(1)
C(12)	16(1)	14(1)	16(1)	0(1)	4(1)	0(1)
C(13)	19(1)	19(1)	20(1)	2(1)	7(1)	4(1)
C(14)	22(1)	26(2)	24(1)	7(1)	11(1)	6(1)
C(15)	19(1)	20(2)	20(1)	2(1)	8(1)	4(1)
N(1)	15(1)	27(1)	17(1)	-2(1)	4(1)	-3(1)
N(2)	17(1)	16(1)	15(1)	-2(1)	6(1)	0(1)
O(1)	21(1)	31(1)	19(1)	6(1)	9(1)	7(1)
O(2)	20(1)	18(1)	20(1)	3(1)	4(1)	2(1)

Table 5. Hydrogen coordinates (x 104) and isotropic displacement parameters (Å2x 103) for Compound ent-14.

	x	y	z	U(eq)	
H(1)	6081	2314	3203	18	
H(3)	3266	3534	1439	23	
H(4)	1323	6089	1352	27	
H(5)	1661	9448	2586	28	
H(6)	3947	10314	3937	25	
H(9)	7342	9820	5615	22	
H(10)	9144	4078	4679	23	
H(11)	6027	2675	1382	18	
H(12)	8790	4686	2710	19	
H(13A)		7964	1846	639	23
H(13B)		9561	2850	1325	23
H(14A)		8730	7002	980	28
H(14B)		8341	5581	-211	28
H(15A)		5277	6869	1013	24
H(15B)		6887	7773	1720	24
H(2)	9344	1160	3338	30	

Experimental data for SC-XRD on Compound 20

X-ray quality crystals were grown from a saturated 1,2-dichloroethane/ethanol/methanol solution followed by the slow vapor diffusion of diisopropyl ether to deposit the crystal diffracted. A colorless needle 0.040 x 0.010 x 0.010 mm in size was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 100(2) K using and scans. Crystal-to-detector distance was 60 mm and exposure time was 30 seconds per frame using a scan width of 2.0°. Data collection was 98.1% complete to 50.000° in theta. A total of 9062 reflections were collected covering the indices, -13<=*h*<=13, -4<=*k*<=4, -15<=*l*<=15. 2151 reflections were found to be symmetry independent, with an R_{int} of 0.0871. Indexing and unit cell refinement indicated a primitive, monoclinic lattice. The space group was found to be P 21 (No. 4). The data were integrated using the Bruker SAINT software program and scaled using the SADABS software program. Solution by iterative methods (SHELXT-2014) produced a complete heavy-atom phasing model consistent with the proposed structure. All non-hydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-2014). All hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-2014.

Table 1. Crystal data and structure refinement for Compound 20.

X-ray ID	Compound 20
Sample/notebook ID	Compound 20
Empirical formula	C27 H25 N3 O4
Formula weight	455.50
Temperature	100(2) K
Wavelength	1.54178 Å
Crystal system	Monoclinic
Space group	P 21
Unit cell dimensions	a = 13.777(6) Å alpha = 90°.
	b = 5.073(2) Å beta = 103.272(7)°.
	c = 15.860(6) Å gamma = 90°.
Volume	1078.9(8) Å3
Z	2
Density (calculated)	1.402 Mg/m3
Absorption coefficient	0.775 mm-1
F(000)	480
Crystal size	0.040 x 0.010 x 0.010 mm3
Theta range for data collection	2.862 to 50.420°.
Index ranges	-13<=h<=13, -4<=k<=4, -15<=l<=15
Reflections collected	9062
Independent reflections	2151 [R(int) = 0.0871]
Completeness to theta = 50.000°	98.1 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.929 and 0.784
Refinement method	Full-matrix least-squares on F2
Data / restraints / parameters	2151 / 1 / 309
Goodness-of-fit on F2	1.024
Final R indices [I>2sigma(I)]	R1 = 0.0394, wR2 = 0.0774
R indices (all data)	R1 = 0.0650, wR2 = 0.0875
Absolute structure parameter	0.3(4)
Extinction coefficient	n/a
Largest diff. peak and hole	0.190 and -0.194 e.Å-3

Table 2. Atomic coordinates (x 104) and equivalent isotropic displacement parameters (Å2x 103)
for Compound 20. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
C(1)	2654(4)	6225(15)	2139(3)	19(2)
C(2)	2090(5)	8453(15)	1593(4)	23(2)
C(3)	1124(4)	9357(15)	1561(4)	26(2)
C(4)	745(4)	11403(16)	985(4)	28(2)
C(5)	1309(5)	12477(14)	451(4)	27(2)
C(6)	2262(4)	11530(15)	473(4)	24(2)
C(7)	2637(4)	9533(15)	1040(4)	22(2)
C(8)	3571(5)	8079(15)	1164(4)	25(2)
C(9)	4436(5)	7757(16)	906(4)	28(2)
C(10)	4380(5)	4698(15)	1889(4)	24(2)
C(11)	2895(4)	6567(14)	3133(3)	21(2)
C(12)	3333(4)	9244(15)	3459(4)	24(2)
C(13)	3474(4)	9450(14)	4443(4)	20(2)
C(14)	4154(4)	11261(15)	4907(4)	23(2)
C(15)	3792(5)	10135(15)	6192(4)	26(2)
C(16)	3124(4)	8233(15)	5804(4)	26(2)
C(17)	2942(4)	7880(14)	4903(4)	21(2)
C(18)	2192(4)	5826(14)	4460(3)	22(2)
C(19)	1950(4)	6083(16)	3472(3)	25(2)
C(20)	8454(4)	-129(15)	2478(4)	23(2)
C(21)	9264(4)	1504(15)	2781(4)	27(2)
C(22)	9867(4)	1103(16)	3616(4)	29(2)
C(23)	9661(5)	-858(14)	4130(4)	27(2)
C(24)	8853(5)	-2516(14)	3829(4)	31(2)
C(25)	8258(5)	-2156(14)	3007(4)	26(2)
C(26)	7762(4)	280(14)	1602(4)	26(2)
C(27)	6821(4)	1830(16)	1674(4)	26(2)
N(1)	4920(4)	5649(11)	1365(3)	24(2)
N(2)	3554(4)	6141(12)	1776(3)	21(1)
N(3)	4318(3)	11627(12)	5768(3)	25(2)
O(1)	4218(3)	9906(10)	3193(2)	26(1)
O(2)	8254(3)	1604(11)	1024(2)	35(1)
O(3)	6635(3)	3913(10)	1200(3)	32(1)
O(4)	6311(3)	1015(11)	2168(3)	35(1)

Table 3. Bond lengths [Å] and angles [°] for Compound 20.

C(1)-N(2)	1.483(7)	C(15)-N(3)	1.333(8)
C(1)-C(2)	1.524(9)	C(15)-C(16)	1.378(9)
C(1)-C(11)	1.545(8)	C(15)-H(15)	0.9500
C(1)-H(1)	1.0000	C(16)-C(17)	1.404(8)
C(2)-C(7)	1.393(9)	C(16)-H(16)	0.9500
C(2)-C(3)	1.397(8)	C(17)-C(18)	1.521(9)
C(3)-C(4)	1.401(9)	C(18)-C(19)	1.532(8)
C(3)-H(3)	0.9500	C(18)-H(18A)	0.9900
C(4)-C(5)	1.386(9)	C(18)-H(18B)	0.9900
C(4)-H(4)	0.9500	C(19)-H(19A)	0.9900
C(5)-C(6)	1.391(8)	C(19)-H(19B)	0.9900
C(5)-H(5)	0.9500	C(20)-C(21)	1.385(8)
C(6)-C(7)	1.374(9)	C(20)-C(25)	1.393(9)
C(6)-H(6)	0.9500	C(20)-C(26)	1.508(8)
C(7)-C(8)	1.457(9)	C(21)-C(22)	1.408(8)
C(8)-C(9)	1.356(8)	C(21)-H(21)	0.9500
C(8)-N(2)	1.386(8)	C(22)-C(23)	1.357(9)
C(9)-N(1)	1.376(8)	C(22)-H(22)	0.9500
C(9)-H(9)	0.9500	C(23)-C(24)	1.389(9)
C(10)-N(1)	1.328(7)	C(23)-H(23)	0.9500
C(10)-N(2)	1.330(8)	C(24)-C(25)	1.384(8)
C(10)-H(10)	0.9500	C(24)-H(24)	0.9500
C(11)-C(12)	1.527(9)	C(25)-H(25)	0.9500
C(11)-C(19)	1.537(8)	C(26)-O(2)	1.428(7)
C(11)-H(11)	1.0000	C(26)-C(27)	1.542(9)
C(12)-O(1)	1.420(7)	C(26)-H(26)	1.0000
C(12)-C(13)	1.531(8)	C(27)-O(4)	1.237(8)
C(12)-H(12)	1.0000	C(27)-O(3)	1.288(8)
C(13)-C(14)	1.396(8)	N(1)-H(1A)	0.8800
C(13)-C(17)	1.396(9)	O(1)-H(1A)	0.8400
C(14)-N(3)	1.344(7)	O(2)-H(2)	0.8400
C(14)-H(14)	0.9500		

N(2)-C(1)-C(2)	99.4(5)	C(4)-C(3)-H(3)	120.8
N(2)-C(1)-C(11)	113.4(4)	C(5)-C(4)-C(3)	120.8(6)
C(2)-C(1)-C(11)	117.3(6)	C(5)-C(4)-H(4)	119.6
N(2)-C(1)-H(1)	108.7	C(3)-C(4)-H(4)	119.6
C(2)-C(1)-H(1)	108.7	C(4)-C(5)-C(6)	120.4(7)
C(11)-C(1)-H(1)	108.7	C(4)-C(5)-H(5)	119.8
C(7)-C(2)-C(3)	119.7(6)	C(6)-C(5)-H(5)	119.8
C(7)-C(2)-C(1)	111.7(6)	C(7)-C(6)-C(5)	118.8(6)
C(3)-C(2)-C(1)	128.4(6)	C(7)-C(6)-H(6)	120.6
C(2)-C(3)-C(4)	118.4(6)	C(5)-C(6)-H(6)	120.6
C(2)-C(3)-H(3)	120.8	C(6)-C(7)-C(2)	121.7(6)

C(6)-C(7)-C(8)	130.5(6)	H(18A)-C(18)-H(18B)	107.9
C(2)-C(7)-C(8)	107.7(6)	C(18)-C(19)-C(11)	111.6(5)
C(9)-C(8)-N(2)	106.5(6)	C(18)-C(19)-H(19A)	109.3
C(9)-C(8)-C(7)	146.2(7)	C(11)-C(19)-H(19A)	109.3
N(2)-C(8)-C(7)	107.3(6)	C(18)-C(19)-H(19B)	109.3
C(8)-C(9)-N(1)	106.7(6)	C(11)-C(19)-H(19B)	109.3
C(8)-C(9)-H(9)	126.7	H(19A)-C(19)-H(19B)	108.0
N(1)-C(9)-H(9)	126.7	C(21)-C(20)-C(25)	119.0(5)
N(1)-C(10)-N(2)	107.5(6)	C(21)-C(20)-C(26)	121.8(6)
N(1)-C(10)-H(10)	126.3	C(25)-C(20)-C(26)	119.2(6)
N(2)-C(10)-H(10)	126.3	C(20)-C(21)-C(22)	119.6(6)
C(12)-C(11)-C(19)	108.9(5)	C(20)-C(21)-H(21)	120.2
C(12)-C(11)-C(1)	114.9(5)	C(22)-C(21)-H(21)	120.2
C(19)-C(11)-C(1)	109.7(4)	C(23)-C(22)-C(21)	120.8(7)
C(12)-C(11)-H(11)	107.7	C(23)-C(22)-H(22)	119.6
C(19)-C(11)-H(11)	107.7	C(21)-C(22)-H(22)	119.6
C(1)-C(11)-H(11)	107.7	C(22)-C(23)-C(24)	119.9(6)
O(1)-C(12)-C(11)	114.2(5)	C(22)-C(23)-H(23)	120.1
O(1)-C(12)-C(13)	111.8(5)	C(24)-C(23)-H(23)	120.1
C(11)-C(12)-C(13)	110.7(5)	C(25)-C(24)-C(23)	119.9(6)
O(1)-C(12)-H(12)	106.6	C(25)-C(24)-H(24)	120.0
C(11)-C(12)-H(12)	106.6	C(23)-C(24)-H(24)	120.0
C(13)-C(12)-H(12)	106.6	C(24)-C(25)-C(20)	120.7(6)
C(14)-C(13)-C(17)	118.0(5)	C(24)-C(25)-H(25)	119.7
C(14)-C(13)-C(12)	119.7(6)	C(20)-C(25)-H(25)	119.7
C(17)-C(13)-C(12)	122.3(6)	O(2)-C(26)-C(20)	111.3(5)
N(3)-C(14)-C(13)	124.2(6)	O(2)-C(26)-C(27)	109.8(6)
N(3)-C(14)-H(14)	117.9	C(20)-C(26)-C(27)	111.5(5)
C(13)-C(14)-H(14)	117.9	O(2)-C(26)-H(26)	108.0
N(3)-C(15)-C(16)	123.8(6)	C(20)-C(26)-H(26)	108.0
N(3)-C(15)-H(15)	118.1	C(27)-C(26)-H(26)	108.0
C(16)-C(15)-H(15)	118.1	O(4)-C(27)-O(3)	125.3(6)
C(15)-C(16)-C(17)	119.3(6)	O(4)-C(27)-C(26)	119.0(7)
C(15)-C(16)-H(16)	120.3	O(3)-C(27)-C(26)	115.6(6)
C(17)-C(16)-H(16)	120.3	C(10)-N(1)-C(9)	109.9(5)
C(13)-C(17)-C(16)	117.8(6)	C(10)-N(1)-H(1A)	125.1
C(13)-C(17)-C(18)	122.2(5)	C(9)-N(1)-H(1A)	125.1
C(16)-C(17)-C(18)	120.0(6)	C(10)-N(2)-C(8)	109.5(5)
C(17)-C(18)-C(19)	112.3(5)	C(10)-N(2)-C(1)	136.8(6)
C(17)-C(18)-H(18A)	109.1	C(8)-N(2)-C(1)	113.7(5)
C(19)-C(18)-H(18A)	109.1	C(15)-N(3)-C(14)	116.8(6)
C(17)-C(18)-H(18B)	109.1	C(12)-O(1)-H(1A)	109.5
C(19)-C(18)-H(18B)	109.1	C(26)-O(2)-H(2)	109.5

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters (Å2x 103)for Compound 20. The anisotropic displacement factor exponent takes the form: -2□2[h2a*2U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
C(1)	16(3)	19(5)	21(3)	0(3)	1(3)	2(4)
C(2)	21(4)	29(5)	17(4)	-5(3)	-3(3)	-2(4)
C(3)	22(4)	34(6)	20(4)	-4(4)	0(3)	-5(4)
C(4)	14(3)	41(6)	23(4)	-5(4)	-7(3)	5(4)
C(5)	29(4)	29(6)	20(4)	-8(3)	-2(3)	4(4)
C(6)	21(4)	33(5)	17(4)	-9(4)	2(3)	2(4)
C(7)	19(4)	27(5)	16(4)	-2(4)	-1(3)	5(4)
C(8)	30(5)	32(5)	9(4)	-1(4)	-4(3)	2(4)
C(9)	19(4)	45(6)	18(4)	-1(4)	4(3)	3(4)
C(10)	24(4)	28(5)	16(4)	-4(4)	-1(3)	-5(4)
C(11)	17(3)	25(5)	20(4)	3(4)	3(3)	-1(4)
C(12)	18(4)	31(6)	22(4)	-3(4)	2(3)	-10(4)
C(13)	16(4)	20(5)	21(4)	-1(4)	1(3)	4(4)
C(14)	19(4)	23(5)	25(4)	2(4)	0(3)	0(4)
C(15)	20(4)	38(6)	18(4)	-2(4)	1(3)	7(4)
C(16)	21(4)	33(5)	22(4)	6(4)	2(3)	4(4)
C(17)	12(3)	26(5)	22(4)	-1(4)	0(3)	7(4)
C(18)	19(4)	20(5)	27(4)	2(3)	7(3)	-1(3)
C(19)	26(4)	25(5)	22(4)	-8(4)	3(3)	-1(4)
C(20)	18(4)	29(5)	21(4)	-4(4)	1(3)	3(4)
C(21)	28(4)	30(5)	26(4)	2(4)	11(3)	6(4)
C(22)	22(4)	39(6)	28(4)	-1(4)	7(3)	-6(4)
C(23)	21(4)	35(6)	23(4)	-3(4)	1(3)	-2(4)
C(24)	36(4)	34(6)	23(4)	3(4)	4(3)	-1(4)
C(25)	26(4)	24(5)	25(4)	-4(4)	-1(3)	-2(4)
C(26)	25(4)	32(6)	23(4)	1(3)	9(3)	1(4)
C(27)	17(4)	37(6)	23(4)	-15(4)	0(3)	-8(4)
N(1)	16(3)	33(5)	23(3)	0(3)	1(3)	6(3)
N(2)	15(3)	30(4)	17(3)	-5(3)	1(2)	4(3)
N(3)	19(3)	35(4)	18(3)	0(3)	-2(2)	2(3)
O(1)	20(2)	34(4)	21(2)	6(2)	0(2)	-6(2)
O(2)	32(3)	46(4)	27(3)	9(3)	6(2)	12(3)
O(3)	28(3)	35(4)	30(3)	8(3)	3(2)	6(3)
O(4)	24(3)	50(4)	31(3)	4(3)	8(2)	5(3)

Table 5. Hydrogen coordinates (x 104) and isotropic displacement parameters (Å2x 103) for Compound 20.

	x	y	z	U(eq)	
H(1)	2272	4549	1986	23	
H(3)	733	8603	1920	31	
H(4)	94	12062	961	33	
H(5)	1042	13870	67	33	
H(6)	2646	12252	103	29	
H(9)	4665	8787	490	33	
H(10)	4552	3251	2275	28	
H(11)	3393	5187	3390	25	
H(12)	2823	10596	3200	29	
H(14)	4525	12303	4595	28	
H(15)	3882	10399	6799	31	
H(16)	2790	7170	6141	31	
H(18A)		1569	6019	4666	26
H(18B)		2463	4045	4625	26
H(19A)		1479	7563	3294	29
H(19B)		1620	4449	3209	29
H(21)	9412	2889	2427	32	
H(22)	10425	2218	3823	35	
H(23)	10069	-1097	4695	33	
H(24)	8710	-3895	4187	38	
H(25)	7710	-3304	2802	31	
H(26)	7546	-1492	1352	31	
H(1A)	5501	5024	1317	29	
H(1A)	4700	9057	3491	38	
H(2)	7897	2857	783	53	

Experimental data for SC-XRD on Compound ent-21

X-ray quality crystals were grown from a saturated 1,2-dichloroethane/ethanol/methanol solution followed by the slow vapor diffusion of diisopropyl ether to deposit the crystal diffracted. A colorless blade 0.050 x 0.030 x 0.020 mm in size was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 100(2) K using and scans. Crystal-to-detector distance was 60 mm and exposure time was 10 seconds per frame using a scan width of 2.0°. Data collection was 100.0% complete to 67.000° in theta. A total of 22900 reflections were collected covering the indices, -11<=*h*<=11, -6<=*k*<=6, -16<=*l*<=16. 2697 reflections were found to be symmetry independent, with an R_{int} of 0.0457. Indexing and unit cell refinement indicated a primitive, monoclinic lattice. The space group was found to be P 21 (No. 4). The data were integrated using the Bruker SAINT software program and scaled using the SADABS software program. Solution by iterative methods (SHELXT-2014) produced a complete heavy-atom phasing model consistent with the proposed structure. All non-hydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-2014). All hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-2014. Absolute stereochemistry was unambiguously determined to be *R* at all chiral centers.

Table 1. Crystal data and structure refinement for Compound ent-21.

X-ray ID	Compound ent-21
Sample/notebook ID	Compound ent-21
Empirical formula	C20 H18 N2 O
Formula weight	302.36
Temperature	100(2) K
Wavelength	1.54178 Å
Crystal system	Monoclinic
Space group	P 21
Unit cell dimensions	a = 9.8446(8) Å alpha = 90°.
	b = 5.8701(5) Å beta = 101.772(6)°.
	c = 13.6268(11) Å gamma = 90°.
Volume	770.91(11) Å3
Z	2
Density (calculated)	1.303 Mg/m3
Absorption coefficient	0.638 mm-1
F(000)	320
Crystal size	0.050 x 0.030 x 0.020 mm3
Theta range for data collection	3.313 to 68.234°.
Index ranges	-11<=h<=11, -6<=k<=6, -16<=l<=16
Reflections collected	22900
Independent reflections	2697 [R(int) = 0.0457]
Completeness to theta = 67.000°	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.929 and 0.797
Refinement method	Full-matrix least-squares on F2
Data / restraints / parameters	2697 / 1 / 209
Goodness-of-fit on F2	1.050
Final R indices [I>2sigma(I)]	R1 = 0.0313, wR2 = 0.0656
R indices (all data)	R1 = 0.0373, wR2 = 0.0690
Absolute structure parameter	0.03(16)
Extinction coefficient	n/a
Largest diff. peak and hole	0.150 and -0.110 e.Å-3

Table 2. Atomic coordinates (x 104) and equivalent isotropic displacement parameters (Å2x 103)
for Compound ent-21. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
C(1)	7356(2)	-72(4)	3246(2)	28(1)
C(2)	8695(2)	-1194(5)	3105(2)	28(1)
C(3)	9499(2)	-694(5)	2406(2)	33(1)
C(4)	10627(2)	-2083(5)	2359(2)	37(1)
C(5)	10950(3)	-3927(5)	2994(2)	39(1)
C(6)	10155(2)	-4441(5)	3702(2)	36(1)
C(7)	9033(2)	-3058(5)	3755(2)	29(1)
C(8)	8034(2)	-3113(5)	4409(2)	28(1)
C(9)	7684(2)	-4058(5)	5244(2)	33(1)
C(10)	6286(2)	-1220(5)	4799(2)	31(1)
C(11)	6169(2)	-441(4)	2330(2)	26(1)
C(12)	4757(2)	361(4)	2507(2)	27(1)
C(13)	3700(2)	262(4)	1522(2)	28(1)
C(14)	2676(2)	1913(5)	1274(2)	34(1)
C(15)	1687(2)	1784(5)	393(2)	38(1)
C(16)	1695(2)	-47(5)	-244(2)	35(1)
C(17)	2714(2)	-1686(5)	-8(2)	32(1)
C(18)	3750(2)	-1536(5)	855(2)	27(1)
C(19)	4955(2)	-3172(5)	1002(2)	32(1)
C(20)	6004(2)	-2915(5)	1988(2)	30(1)
N(1)	6586(2)	-2858(4)	5481(1)	33(1)
N(2)	7130(2)	-1331(4)	4137(1)	28(1)
O(1)	4849(2)	2542(3)	2953(1)	33(1)

Table 3. Bond lengths [Å] and angles [°] for Compound ent-21.

C(1)-N(2)	1.477(3)	C(11)-C(12)	1.533(3)
C(1)-C(2)	1.521(3)	C(11)-H(11)	1.0000
C(1)-C(11)	1.542(3)	C(12)-O(1)	1.412(3)
C(1)-H(1A)	1.0000	C(12)-C(13)	1.523(3)
C(2)-C(3)	1.388(3)	C(12)-H(12)	1.0000
C(2)-C(7)	1.404(3)	C(13)-C(14)	1.389(3)
C(3)-C(4)	1.390(4)	C(13)-C(18)	1.400(3)
C(3)-H(3)	0.9500	C(14)-C(15)	1.385(3)
C(4)-C(5)	1.381(4)	C(14)-H(14)	0.9500
C(4)-H(4)	0.9500	C(15)-C(16)	1.383(4)
C(5)-C(6)	1.395(3)	C(15)-H(15)	0.9500
C(5)-H(5)	0.9500	C(16)-C(17)	1.380(4)
C(6)-C(7)	1.384(3)	C(16)-H(16)	0.9500
C(6)-H(6)	0.9500	C(17)-C(18)	1.394(3)
C(7)-C(8)	1.456(3)	C(17)-H(17)	0.9500
C(8)-C(9)	1.371(3)	C(18)-C(19)	1.508(3)
C(8)-N(2)	1.374(3)	C(19)-C(20)	1.525(3)
C(9)-N(1)	1.383(3)	C(19)-H(19A)	0.9900
C(9)-H(9)	0.9500	C(19)-H(19B)	0.9900
C(10)-N(1)	1.328(3)	C(20)-H(20A)	0.9900
C(10)-N(2)	1.347(3)	C(20)-H(20B)	0.9900
C(10)-H(10)	0.9500	O(1)-H(1)	0.8400
C(11)-C(20)	1.524(4)		

N(2)-C(1)-C(2)	99.62(18)	C(5)-C(6)-H(6)	120.8
N(2)-C(1)-C(11)	112.26(19)	C(6)-C(7)-C(2)	120.9(2)
C(2)-C(1)-C(11)	111.73(18)	C(6)-C(7)-C(8)	131.6(2)
N(2)-C(1)-H(1A)	110.9	C(2)-C(7)-C(8)	107.5(2)
C(2)-C(1)-H(1A)	110.9	C(9)-C(8)-N(2)	105.9(2)
C(11)-C(1)-H(1A)	110.9	C(9)-C(8)-C(7)	146.3(2)
C(3)-C(2)-C(7)	120.2(2)	N(2)-C(8)-C(7)	107.4(2)
C(3)-C(2)-C(1)	128.7(2)	C(8)-C(9)-N(1)	109.2(2)
C(7)-C(2)-C(1)	110.96(19)	C(8)-C(9)-H(9)	125.4
C(2)-C(3)-C(4)	118.7(2)	N(1)-C(9)-H(9)	125.4
C(2)-C(3)-H(3)	120.6	N(1)-C(10)-N(2)	110.7(2)
C(4)-C(3)-H(3)	120.6	N(1)-C(10)-H(10)	124.6
C(5)-C(4)-C(3)	121.0(2)	N(2)-C(10)-H(10)	124.6
C(5)-C(4)-H(4)	119.5	C(20)-C(11)-C(12)	107.32(18)
C(3)-C(4)-H(4)	119.5	C(20)-C(11)-C(1)	113.4(2)
C(4)-C(5)-C(6)	120.9(3)	C(12)-C(11)-C(1)	113.05(18)
C(4)-C(5)-H(5)	119.6	C(20)-C(11)-H(11)	107.6
C(6)-C(5)-H(5)	119.6	C(12)-C(11)-H(11)	107.6
C(7)-C(6)-C(5)	118.4(3)	C(1)-C(11)-H(11)	107.6
C(7)-C(6)-H(6)	120.8	O(1)-C(12)-C(13)	112.7(2)

O(1)-C(12)-C(11)	111.46(19)	C(17)-C(18)-C(13)	118.6(2)
C(13)-C(12)-C(11)	109.14(17)	C(17)-C(18)-C(19)	119.5(2)
O(1)-C(12)-H(12)	107.8	C(13)-C(18)-C(19)	121.7(2)
C(13)-C(12)-H(12)	107.8	C(18)-C(19)-C(20)	115.2(2)
C(11)-C(12)-H(12)	107.8	C(18)-C(19)-H(19A)	108.5
C(14)-C(13)-C(18)	119.2(2)	C(20)-C(19)-H(19A)	108.5
C(14)-C(13)-C(12)	121.2(2)	C(18)-C(19)-H(19B)	108.5
C(18)-C(13)-C(12)	119.5(2)	C(20)-C(19)-H(19B)	108.5
C(15)-C(14)-C(13)	121.3(2)	H(19A)-C(19)-H(19B)	107.5
C(15)-C(14)-H(14)	119.4	C(11)-C(20)-C(19)	112.0(2)
C(13)-C(14)-H(14)	119.4	C(11)-C(20)-H(20A)	109.2
C(16)-C(15)-C(14)	119.6(2)	C(19)-C(20)-H(20A)	109.2
C(16)-C(15)-H(15)	120.2	C(11)-C(20)-H(20B)	109.2
C(14)-C(15)-H(15)	120.2	C(19)-C(20)-H(20B)	109.2
C(17)-C(16)-C(15)	119.5(2)	H(20A)-C(20)-H(20B)	107.9
C(17)-C(16)-H(16)	120.2	C(10)-N(1)-C(9)	106.13(19)
C(15)-C(16)-H(16)	120.2	C(10)-N(2)-C(8)	108.1(2)
C(16)-C(17)-C(18)	121.6(2)	C(10)-N(2)-C(1)	138.0(2)
C(16)-C(17)-H(17)	119.2	C(8)-N(2)-C(1)	113.88(18)
C(18)-C(17)-H(17)	119.2	C(12)-O(1)-H(1)	109.5

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters (Å2x 103)for Compound ent-21. The anisotropic displacement factor exponent takes the form: -2□2[h2a*2U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
C(1)	31(1)	31(2)	22(1)	3(1)	6(1)	-2(1)
C(2)	27(1)	35(2)	22(1)	-2(1)	4(1)	-4(1)
C(3)	29(1)	44(2)	25(1)	-1(1)	5(1)	-6(1)
C(4)	29(1)	55(2)	26(1)	-6(1)	7(1)	-7(1)
C(5)	31(1)	53(2)	32(1)	-10(1)	4(1)	6(1)
C(6)	34(1)	45(2)	27(1)	-2(1)	2(1)	5(1)
C(7)	27(1)	36(2)	22(1)	-4(1)	3(1)	-2(1)
C(8)	29(1)	32(1)	23(1)	0(1)	3(1)	-1(1)
C(9)	34(1)	38(2)	26(1)	3(1)	3(1)	-1(1)
C(10)	30(1)	39(2)	24(1)	1(1)	7(1)	0(1)
C(11)	29(1)	31(1)	20(1)	3(1)	7(1)	1(1)
C(12)	31(1)	28(1)	24(1)	1(1)	12(1)	-1(1)
C(13)	27(1)	34(2)	24(1)	4(1)	10(1)	-2(1)
C(14)	32(1)	39(2)	33(1)	0(1)	12(1)	6(1)
C(15)	28(1)	46(2)	40(1)	9(1)	8(1)	10(1)
C(16)	26(1)	53(2)	28(1)	6(1)	6(1)	-2(1)
C(17)	30(1)	41(2)	25(1)	0(1)	8(1)	-5(1)
C(18)	26(1)	34(1)	23(1)	3(1)	8(1)	-2(1)
C(19)	32(1)	35(2)	29(1)	-4(1)	6(1)	0(1)
C(20)	30(1)	33(2)	27(1)	0(1)	5(1)	2(1)
N(1)	32(1)	43(1)	24(1)	5(1)	7(1)	-2(1)
N(2)	29(1)	36(1)	21(1)	3(1)	7(1)	0(1)
O(1)	38(1)	32(1)	30(1)	-5(1)	13(1)	-1(1)

Table 5. Hydrogen coordinates (x 104) and isotropic displacement parameters (Å2x 103) for Compound ent-21.

	x	y	z	U(eq)	
H(1A)	7501	1588	3398	33	
H(3)	9282	573	1969	39	
H(4)	11185	-1759	1883	44	
H(5)	11724	-4857	2946	46	
H(6)	10378	-5709	4138	43	
H(9)	8126	-5334	5602	40	
H(10)	5573	-120	4781	37	
H(11)	6388	475	1763	31	
H(12)	4453	-733	2982	32	
H(14)	2653	3153	1718	41	
H(15)	1008	2947	228	45	
H(16)	1004	-175	-840	42	
H(17)	2709	-2949	-445	38	
H(19A)		5447	-2970	443	39
H(19B)		4585	-4745	962	39
H(20A)		5697	-3836	2511	36
H(20B)		6914	-3509	1903	36
H(1)	4415	2546	3424	49	

Experimental data for SC-XRD on Compound ent-22

X-ray quality crystals were grown from a saturated 1,2-dichloroethane/ethanol/methanol solution followed by the slow vapor diffusion of diisopropyl ether to deposit the crystal diffracted. A yellow plate 0.090 x 0.070 x 0.050 mm in size was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 100(2) K using and scans. Crystal-to-detector distance was 60 mm and exposure time was 1 seconds per frame using a scan width of 2.0°. Data collection was 99.6% complete to 67.000° in theta. A total of 20046 reflections were collected covering the indices, -6<=*h*<=6, -11<=*k*<=12, -32<=*l*<=32. 2772 reflections were found to be symmetry independent, with an R_{int} of 0.0482. Indexing and unit cell refinement indicated a primitive, orthorhombic lattice. The space group was found to be P 21 21 21 (No. 19). The data were integrated using the Bruker SAINT software program and scaled using the SADABS software program. Solution by iterative methods (SHELXT-2014) produced a complete heavy-atom phasing model consistent with the proposed structure. All non-hydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-2014). All hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-2014. Absolute stereochemistry was unambiguously determined to be *R* at C1, C11, and C12, respectively.

Table 1. Crystal data and structure refinement for Compound ent-22.

X-ray ID	Compound ent-22
Sample/notebook ID	Compound ent-22
Empirical formula	C19 H17 N3 O
Formula weight	303.35
Temperature	100(2) K
Wavelength	1.54178 Å
Crystal system	Orthorhombic
Space group	P 21 21 21
Unit cell dimensions	a = 5.3519(2) Å alpha = 90°.
	b = 10.5670(4) Å beta = 90°.
	c = 26.7767(11) Å gamma = 90°.
Volume	1514.32(10) Å3
Z	4
Density (calculated)	1.331 Mg/m3
Absorption coefficient	0.672 mm-1
F(000)	640
Crystal size	0.090 x 0.070 x 0.050 mm3
Theta range for data collection	3.301 to 68.304°.
Index ranges	-6<=h<=6, -11<=k<=12, -32<=l<=32
Reflections collected	20046
Independent reflections	2772 [R(int) = 0.0482]
Completeness to theta = 67.000°	99.6 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.929 and 0.845
Refinement method	Full-matrix least-squares on F2
Data / restraints / parameters	2772 / 0 / 209
Goodness-of-fit on F2	1.079
Final R indices [I>2sigma(I)]	R1 = 0.0408, wR2 = 0.0951
R indices (all data)	R1 = 0.0424, wR2 = 0.0961
Absolute structure parameter	-0.09(9)
Extinction coefficient	n/a
Largest diff. peak and hole	0.251 and -0.258 e.Å-3

Table 2. Atomic coordinates (x 104) and equivalent isotropic displacement parameters (Å2x 103)
for Compound ent-22. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
C(1)	1682(5)	4753(2)	5888(1)	23(1)
C(2)	2901(5)	3468(2)	5964(1)	25(1)
C(3)	2359(6)	2559(2)	6321(1)	32(1)
C(4)	3843(7)	1479(3)	6340(1)	40(1)
C(5)	5828(6)	1313(3)	6010(1)	41(1)
C(6)	6374(5)	2215(3)	5651(1)	34(1)
C(7)	4891(5)	3291(2)	5629(1)	25(1)
C(8)	4965(5)	4383(2)	5298(1)	24(1)
C(9)	5967(5)	4906(3)	4873(1)	28(1)
C(10)	2959(5)	6137(2)	5109(1)	25(1)
C(11)	1996(5)	5636(2)	6344(1)	23(1)
C(12)	1425(5)	7014(2)	6215(1)	24(1)
C(13)	1388(5)	7778(2)	6697(1)	30(1)
C(14)	-237(10)	8752(3)	6773(1)	74(2)
C(15)	-238(11)	9386(4)	7226(1)	87(2)
C(16)	2810(5)	8150(3)	7526(1)	33(1)
C(17)	3011(5)	7470(3)	7082(1)	29(1)
C(18)	4863(7)	6417(4)	7031(1)	70(1)
C(19)	4615(5)	5587(3)	6575(1)	27(1)
N(1)	4704(4)	6001(2)	4760(1)	28(1)
N(2)	3072(4)	5189(2)	5442(1)	22(1)
N(3)	1238(6)	9092(2)	7608(1)	49(1)
O(1)	-849(3)	7120(2)	5949(1)	29(1)

Table 3. Bond lengths [Å] and angles [°] for Compound ent-22.

C(1)-N(2)	1.481(3)	C(11)-C(12)	1.528(3)
C(1)-C(2)	1.520(3)	C(11)-C(19)	1.533(3)
C(1)-C(11)	1.544(3)	C(11)-H(11)	1.0000
C(1)-H(1)	1.0000	C(12)-O(1)	1.415(3)
C(2)-C(3)	1.387(4)	C(12)-C(13)	1.521(3)
C(2)-C(7)	1.404(4)	C(12)-H(12)	1.0000
C(3)-C(4)	1.392(4)	C(13)-C(14)	1.363(5)
C(3)-H(3)	0.9500	C(13)-C(17)	1.387(4)
C(4)-C(5)	1.393(5)	C(14)-C(15)	1.386(4)
C(4)-H(4)	0.9500	C(14)-H(14)	0.9500
C(5)-C(6)	1.384(4)	C(15)-N(3)	1.329(5)
C(5)-H(5)	0.9500	C(15)-H(15)	0.9500
C(6)-C(7)	1.387(4)	C(16)-N(3)	1.322(4)
C(6)-H(6)	0.9500	C(16)-C(17)	1.393(3)
C(7)-C(8)	1.456(3)	C(16)-H(16)	0.9500
C(8)-C(9)	1.373(3)	C(17)-C(18)	1.496(4)
C(8)-N(2)	1.379(3)	C(18)-C(19)	1.510(4)
C(9)-N(1)	1.374(4)	C(18)-H(18A)	0.9900
C(9)-H(9)	0.9500	C(18)-H(18B)	0.9900
C(10)-N(1)	1.329(3)	C(19)-H(19A)	0.9900
C(10)-N(2)	1.343(3)	C(19)-H(19B)	0.9900
C(10)-H(10)	0.9500	O(1)-H(1A)	0.8400

N(2)-C(1)-C(2)	99.72(18)	C(6)-C(7)-C(2)	121.1(2)
N(2)-C(1)-C(11)	113.25(19)	C(6)-C(7)-C(8)	131.2(2)
C(2)-C(1)-C(11)	112.82(19)	C(2)-C(7)-C(8)	107.7(2)
N(2)-C(1)-H(1)	110.2	C(9)-C(8)-N(2)	105.7(2)
C(2)-C(1)-H(1)	110.2	C(9)-C(8)-C(7)	146.5(2)
C(11)-C(1)-H(1)	110.2	N(2)-C(8)-C(7)	107.4(2)
C(3)-C(2)-C(7)	120.4(2)	C(8)-C(9)-N(1)	109.2(2)
C(3)-C(2)-C(1)	128.3(2)	C(8)-C(9)-H(9)	125.4
C(7)-C(2)-C(1)	111.1(2)	N(1)-C(9)-H(9)	125.4
C(2)-C(3)-C(4)	118.2(3)	N(1)-C(10)-N(2)	110.8(2)
C(2)-C(3)-H(3)	120.9	N(1)-C(10)-H(10)	124.6
C(4)-C(3)-H(3)	120.9	N(2)-C(10)-H(10)	124.6
C(3)-C(4)-C(5)	121.1(3)	C(12)-C(11)-C(19)	107.8(2)
C(3)-C(4)-H(4)	119.5	C(12)-C(11)-C(1)	112.10(18)
C(5)-C(4)-H(4)	119.5	C(19)-C(11)-C(1)	113.5(2)
C(6)-C(5)-C(4)	120.9(3)	C(12)-C(11)-H(11)	107.7
C(6)-C(5)-H(5)	119.5	C(19)-C(11)-H(11)	107.7
C(4)-C(5)-H(5)	119.5	C(1)-C(11)-H(11)	107.7
C(5)-C(6)-C(7)	118.2(3)	O(1)-C(12)-C(13)	112.0(2)
C(5)-C(6)-H(6)	120.9	O(1)-C(12)-C(11)	111.2(2)
C(7)-C(6)-H(6)	120.9	C(13)-C(12)-C(11)	108.52(18)

O(1)-C(12)-H(12)	108.4	C(17)-C(18)-C(19)	116.6(3)
C(13)-C(12)-H(12)	108.4	C(17)-C(18)-H(18A)	108.2
C(11)-C(12)-H(12)	108.4	C(19)-C(18)-H(18A)	108.2
C(14)-C(13)-C(17)	117.8(2)	C(17)-C(18)-H(18B)	108.2
C(14)-C(13)-C(12)	122.3(2)	C(19)-C(18)-H(18B)	108.2
C(17)-C(13)-C(12)	119.8(2)	H(18A)-C(18)-H(18B)	107.3
C(13)-C(14)-C(15)	119.7(3)	C(18)-C(19)-C(11)	112.8(2)
C(13)-C(14)-H(14)	120.1	C(18)-C(19)-H(19A)	109.0
C(15)-C(14)-H(14)	120.1	C(11)-C(19)-H(19A)	109.0
N(3)-C(15)-C(14)	124.1(4)	C(18)-C(19)-H(19B)	109.0
N(3)-C(15)-H(15)	118.0	C(11)-C(19)-H(19B)	109.0
C(14)-C(15)-H(15)	118.0	H(19A)-C(19)-H(19B)	107.8
N(3)-C(16)-C(17)	125.4(3)	C(10)-N(1)-C(9)	106.4(2)
N(3)-C(16)-H(16)	117.3	C(10)-N(2)-C(8)	107.9(2)
C(17)-C(16)-H(16)	117.3	C(10)-N(2)-C(1)	138.2(2)
C(13)-C(17)-C(16)	117.7(3)	C(8)-N(2)-C(1)	113.80(19)
C(13)-C(17)-C(18)	121.5(2)	C(16)-N(3)-C(15)	115.2(3)
C(16)-C(17)-C(18)	120.8(3)	C(12)-O(1)-H(1A)	109.5

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters (Å2x 103)for Compound ent-22. The anisotropic displacement factor exponent takes the form: -2□2[h2a*2U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
C(1)	23(1)	24(1)	21(1)	2(1)	2(1)	-3(1)
C(2)	29(1)	22(1)	24(1)	0(1)	-5(1)	-5(1)
C(3)	45(2)	25(1)	26(1)	2(1)	-8(1)	-7(1)
C(4)	68(2)	23(1)	30(1)	2(1)	-18(1)	-7(1)
C(5)	60(2)	23(2)	39(2)	-6(1)	-23(2)	10(1)
C(6)	40(2)	28(2)	35(1)	-8(1)	-11(1)	8(1)
C(7)	26(1)	23(1)	26(1)	-3(1)	-7(1)	-3(1)
C(8)	22(1)	25(1)	25(1)	-6(1)	-1(1)	0(1)
C(9)	26(1)	30(1)	27(1)	-6(1)	5(1)	-2(1)
C(10)	30(1)	24(1)	21(1)	1(1)	1(1)	-1(1)
C(11)	26(1)	25(1)	18(1)	2(1)	2(1)	-3(1)
C(12)	25(1)	26(1)	19(1)	3(1)	2(1)	-2(1)
C(13)	45(2)	21(1)	23(1)	4(1)	3(1)	-8(1)
C(14)	142(4)	43(2)	37(2)	-11(1)	-30(2)	50(2)
C(15)	155(5)	57(2)	50(2)	-24(2)	-34(3)	64(3)
C(16)	37(2)	35(2)	27(1)	-4(1)	2(1)	-7(1)
C(17)	25(1)	33(1)	29(1)	-5(1)	4(1)	-7(1)
C(18)	39(2)	103(3)	68(2)	-58(2)	-24(2)	28(2)
C(19)	30(1)	28(1)	24(1)	0(1)	-2(1)	-1(1)
N(1)	32(1)	26(1)	25(1)	-1(1)	5(1)	-3(1)
N(2)	23(1)	23(1)	20(1)	0(1)	1(1)	-1(1)
N(3)	74(2)	39(2)	33(1)	-10(1)	-2(1)	13(2)
O(1)	27(1)	31(1)	29(1)	3(1)	-1(1)	2(1)

Table 5. Hydrogen coordinates (x 104) and isotropic displacement parameters (Å2x 103) for Compound ent-22.

	x	y	z	U(eq)	
H(1)	-130	4647	5807	27	
H(3)	1010	2671	6547	38	
H(4)	3497	845	6581	48	
H(5)	6820	569	6031	49	
H(6)	7729	2102	5426	41	
H(9)	7321	4565	4687	33	
H(10)	1792	6814	5122	30	
H(11)	777	5359	6605	28	
H(12)	2803	7344	5999	28	
H(14)	-1364	8995	6516	89	
H(15)	-1365	10073	7266	105	
H(16)	3892	7918	7792	40	
H(18A)		4731	5872	7331	84
H(18B)		6560	6790	7031	84
H(19A)		5005	4702	6668	33
H(19B)		5853	5859	6322	33
H(1A)	-742	7715	5742	44	

Experimental data for SC-XRD on Compound ent-30

X-ray quality crystals were grown from a saturated 1,2-dichloroethane/ethanol/methanol solution followed by the slow vapor diffusion of diisopropyl ether to deposit the crystal diffracted. A colorless plate 0.080 x 0.050 x 0.020 mm in size was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 100(2) K using and scans. Crystal-to-detector distance was 60 mm and exposure time was 5 seconds per frame using a scan width of 2.0°. Data collection was 99.5% complete to 67.000° in theta. A total of 26837 reflections were collected covering the indices, -11<=*h*<=11, -5<=*k*<=6, -15<=*l*<=15. 2520 reflections were found to be symmetry independent, with an R_{int} of 0.0415. Indexing and unit cell refinement indicated a primitive, monoclinic lattice. The space group was found to be P 21 (No. 4). The data were integrated using the Bruker SAINT software program and scaled using the SADABS software program. Solution by iterative methods (SHELXT-2014) produced a complete heavy-atom phasing model consistent with the proposed structure. All non-hydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-2014). All hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-2014. Absolute stereochemistry was unambiguously determined to be *R* at all chiral centers.

Table 1. Crystal data and structure refinement for Compound ent-30.

X-ray ID	Compound ent-30
Sample/notebook ID	Compound ent-30
Empirical formula	C17 H16 N4 O
Formula weight	292.34
Temperature	100(2) K
Wavelength	1.54178 Å
Crystal system	Monoclinic
Space group	P 21
Unit cell dimensions	a = 9.6081(4) Å alpha = 90°.
	b = 5.9379(2) Å beta = 102.380(2)°.
	c = 13.0825(5) Å gamma = 90°.
Volume	729.03(5) Å3
Z	2
Density (calculated)	1.332 Mg/m3
Absorption coefficient	0.695 mm-1
F(000)	308
Crystal size	0.080 x 0.050 x 0.020 mm3
Theta range for data collection	3.459 to 68.313°.
Index ranges	-11<=h<=11, -5<=k<=6, -15<=l<=15
Reflections collected	26837
Independent reflections	2520 [R(int) = 0.0415]
Completeness to theta = 67.000°	99.5 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.929 and 0.809
Refinement method	Full-matrix least-squares on F2
Data / restraints / parameters	2520 / 1 / 200
Goodness-of-fit on F2	1.040
Final R indices [I>2sigma(I)]	R1 = 0.0261, wR2 = 0.0663
R indices (all data)	R1 = 0.0273, wR2 = 0.0674
Absolute structure parameter	0.15(10)
Extinction coefficient	n/a
Largest diff. peak and hole	0.136 and -0.137 e.Å-3

Table 2. Atomic coordinates (x 104) and equivalent isotropic displacement parameters (Å2x 103)
for Compound ent-30. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
C(1)	-2341(2)	6147(3)	6833(1)	23(1)
C(2)	-3695(2)	4982(3)	6983(1)	23(1)
C(3)	-4497(2)	5426(4)	7725(1)	27(1)
C(4)	-5639(2)	3996(4)	7767(1)	31(1)
C(5)	-5958(2)	2179(4)	7101(2)	32(1)
C(6)	-5156(2)	1725(4)	6353(1)	29(1)
C(7)	-4024(2)	3143(4)	6302(1)	24(1)
C(8)	-3017(2)	3138(3)	5612(1)	23(1)
C(9)	-2665(2)	2247(3)	4737(1)	26(1)
C(10)	-1269(2)	5098(4)	5198(1)	26(1)
C(11)	-1105(2)	5811(3)	7791(1)	21(1)
C(12)	329(2)	6647(3)	7601(1)	22(1)
C(13)	1412(2)	6415(3)	8616(1)	23(1)
C(14)	2575(2)	7671(4)	9091(2)	29(1)
C(15)	3152(2)	6496(4)	10010(2)	33(1)
C(16)	179(2)	3032(3)	9154(1)	25(1)
C(17)	-895(2)	3342(3)	8118(1)	25(1)
N(1)	-1572(2)	3486(3)	4486(1)	27(1)
N(2)	-2112(2)	4935(3)	5895(1)	23(1)
N(3)	2416(2)	4656(3)	10122(1)	31(1)
N(4)	1355(2)	4634(3)	9247(1)	24(1)
O(1)	270(2)	8871(2)	7224(1)	27(1)

Table 3. Bond lengths [Å] and angles [°] for Compound ent-30.

C(1)-N(2)	1.479(2)	C(10)-H(10)	0.9500
C(1)-C(2)	1.523(2)	C(11)-C(17)	1.528(3)
C(1)-C(11)	1.544(2)	C(11)-C(12)	1.534(2)
C(1)-H(1)	1.0000	C(11)-H(11)	1.0000
C(2)-C(3)	1.388(2)	C(12)-O(1)	1.407(2)
C(2)-C(7)	1.402(3)	C(12)-C(13)	1.507(2)
C(3)-C(4)	1.398(3)	C(12)-H(12)	1.0000
C(3)-H(3)	0.9500	C(13)-N(4)	1.350(3)
C(4)-C(5)	1.380(3)	C(13)-C(14)	1.376(3)
C(4)-H(4)	0.9500	C(14)-C(15)	1.398(3)
C(5)-C(6)	1.395(3)	C(14)-H(14)	0.9500
C(5)-H(5)	0.9500	C(15)-N(3)	1.327(3)
C(6)-C(7)	1.387(3)	C(15)-H(15)	0.9500
C(6)-H(6)	0.9500	C(16)-N(4)	1.461(2)
C(7)-C(8)	1.458(2)	C(16)-C(17)	1.529(2)
C(8)-C(9)	1.368(2)	C(16)-H(16A)	0.9900
C(8)-N(2)	1.376(2)	C(16)-H(16B)	0.9900
C(9)-N(1)	1.378(3)	C(17)-H(17A)	0.9900
C(9)-H(9)	0.9500	C(17)-H(17B)	0.9900
C(10)-N(1)	1.324(3)	N(3)-N(4)	1.360(2)
C(10)-N(2)	1.346(2)	O(1)-H(1A)	0.8400

N(2)-C(1)-C(2)	99.75(14)	C(6)-C(7)-C(8)	131.24(18)
N(2)-C(1)-C(11)	112.67(14)	C(2)-C(7)-C(8)	107.79(16)
C(2)-C(1)-C(11)	111.47(14)	C(9)-C(8)-N(2)	105.65(16)
N(2)-C(1)-H(1)	110.8	C(9)-C(8)-C(7)	146.59(19)
C(2)-C(1)-H(1)	110.8	N(2)-C(8)-C(7)	107.28(16)
C(11)-C(1)-H(1)	110.8	C(8)-C(9)-N(1)	109.31(17)
C(3)-C(2)-C(7)	120.62(17)	C(8)-C(9)-H(9)	125.3
C(3)-C(2)-C(1)	128.42(17)	N(1)-C(9)-H(9)	125.3
C(7)-C(2)-C(1)	110.76(15)	N(1)-C(10)-N(2)	110.59(17)
C(2)-C(3)-C(4)	118.02(18)	N(1)-C(10)-H(10)	124.7
C(2)-C(3)-H(3)	121.0	N(2)-C(10)-H(10)	124.7
C(4)-C(3)-H(3)	121.0	C(17)-C(11)-C(12)	106.62(15)
C(5)-C(4)-C(3)	121.34(18)	C(17)-C(11)-C(1)	112.56(15)
C(5)-C(4)-H(4)	119.3	C(12)-C(11)-C(1)	112.83(14)
C(3)-C(4)-H(4)	119.3	C(17)-C(11)-H(11)	108.2
C(4)-C(5)-C(6)	120.9(2)	C(12)-C(11)-H(11)	108.2
C(4)-C(5)-H(5)	119.6	C(1)-C(11)-H(11)	108.2
C(6)-C(5)-H(5)	119.6	O(1)-C(12)-C(13)	111.29(15)
C(7)-C(6)-C(5)	118.2(2)	O(1)-C(12)-C(11)	113.02(15)
C(7)-C(6)-H(6)	120.9	C(13)-C(12)-C(11)	107.62(13)
C(5)-C(6)-H(6)	120.9	O(1)-C(12)-H(12)	108.3
C(6)-C(7)-C(2)	120.96(17)	C(13)-C(12)-H(12)	108.3

C(11)-C(12)-H(12)	108.3
N(4)-C(13)-C(14)	106.53(16)
N(4)-C(13)-C(12)	119.92(16)
C(14)-C(13)-C(12)	133.53(18)
C(13)-C(14)-C(15)	104.59(19)
C(13)-C(14)-H(14)	127.7
C(15)-C(14)-H(14)	127.7
N(3)-C(15)-C(14)	112.52(18)
N(3)-C(15)-H(15)	123.7
C(14)-C(15)-H(15)	123.7
N(4)-C(16)-C(17)	110.97(15)
N(4)-C(16)-H(16A)	109.4
C(17)-C(16)-H(16A)	109.4
N(4)-C(16)-H(16B)	109.4
C(17)-C(16)-H(16B)	109.4
H(16A)-C(16)-H(16B)	108.0
C(11)-C(17)-C(16)	112.78(16)
C(11)-C(17)-H(17A)	109.0
C(16)-C(17)-H(17A)	109.0
C(11)-C(17)-H(17B)	109.0
C(16)-C(17)-H(17B)	109.0
H(17A)-C(17)-H(17B)	107.8
C(10)-N(1)-C(9)	106.35(15)
C(10)-N(2)-C(8)	108.08(15)
C(10)-N(2)-C(1)	138.16(17)
C(8)-N(2)-C(1)	113.74(14)
C(15)-N(3)-N(4)	103.69(16)
C(13)-N(4)-N(3)	112.67(16)
C(13)-N(4)-C(16)	126.26(15)
N(3)-N(4)-C(16)	120.18(15)
C(12)-O(1)-H(1A)	109.5

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters (Å2x 103)for Compound ent-30. The anisotropic displacement factor exponent takes the form: -2□2[h2a*2U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
C(1)	28(1)	24(1)	17(1)	-2(1)	5(1)	2(1)
C(2)	24(1)	26(1)	20(1)	2(1)	3(1)	5(1)
C(3)	28(1)	32(1)	21(1)	1(1)	4(1)	7(1)
C(4)	24(1)	44(1)	23(1)	6(1)	6(1)	7(1)
C(5)	26(1)	43(1)	26(1)	7(1)	3(1)	-2(1)
C(6)	29(1)	34(1)	23(1)	-1(1)	2(1)	-3(1)
C(7)	24(1)	29(1)	18(1)	1(1)	1(1)	4(1)
C(8)	24(1)	24(1)	20(1)	-1(1)	1(1)	1(1)
C(9)	28(1)	29(1)	20(1)	-4(1)	3(1)	0(1)
C(10)	26(1)	33(1)	19(1)	-1(1)	6(1)	1(1)
C(11)	28(1)	22(1)	15(1)	-2(1)	5(1)	0(1)
C(12)	28(1)	20(1)	18(1)	-2(1)	8(1)	1(1)
C(13)	27(1)	24(1)	20(1)	-3(1)	10(1)	2(1)
C(14)	30(1)	33(1)	26(1)	-6(1)	9(1)	-5(1)
C(15)	28(1)	43(1)	26(1)	-8(1)	2(1)	-4(1)
C(16)	32(1)	23(1)	21(1)	2(1)	6(1)	-1(1)
C(17)	28(1)	24(1)	21(1)	-2(1)	3(1)	-1(1)
N(1)	28(1)	33(1)	19(1)	-3(1)	5(1)	2(1)
N(2)	26(1)	26(1)	16(1)	-2(1)	5(1)	0(1)
N(3)	30(1)	40(1)	19(1)	-3(1)	0(1)	2(1)
N(4)	26(1)	28(1)	19(1)	0(1)	3(1)	2(1)
O(1)	36(1)	22(1)	26(1)	2(1)	13(1)	0(1)

Table 5. Hydrogen coordinates (x 104) and isotropic displacement parameters (Å2x 103) for Compound ent-30.

	x	y	z	U(eq)	
H(1)	-2517	7785	6680	27	
H(3)	-4275	6665	8191	32	
H(4)	-6208	4281	8264	37	
H(5)	-6733	1224	7152	38	
H(6)	-5378	479	5891	35	
H(9)	-3104	974	4361	31	
H(10)	-556	6214	5215	31	
H(11)	-1330	6678	8391	26	
H(12)	620	5641	7071	26	
H(14)	2912	9032	8848	35	
H(15)	3980	6964	10500	39	
H(16A)		-305	3253	9742	30
H(16B)		560	1477	9196	30
H(17A)		-562	2496	7563	30
H(17B)		-1822	2699	8183	30
H(1A)	709	8953	6734	40	

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