# H-Bond Donor-Directed Switch of Diastereoselectivity in the Michael Addition of α-Azido Ketones to Nitroolefins

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Supporting Information

(Part I)

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## 1. General information:

Unless otherwise noted, all reactions were run in air, and monitored by thin layer chromatography (TLC) using UV light to visualize the course of reaction. Purification of reaction products was carried out by flash chromatography on silica gel. Chemical yields referred to pure isolated substances. The infrared (IR) spectra were obtained using a Bruker tensor 27 infrared spectrometer. Chiral HPLC analysis was performed on a Shimadzu LC-20AD instrument using Daicel Chiracel columns at room temperature and a mixture of HPLC-grade hexane and isopropanol as eluent. Optical rotation was measured using a JASCO P-1030 Polarimeter equipped with a sodium vapor lamp at 589 nm. $^{1}H$, $^{13}C$, $^{19}F$ and $^{31}P$ NMR spectra were obtained using Bruker DPX-500, Bruker DPX-400 or Bruker DPX-300 spectrometer. Chemical shifts were reported in ppm from $CDCl_3$ with the solvent resonance as the internal standard. The following abbreviations were used to designate chemical shift multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, h = heptet, m = multiplet, br = broad.

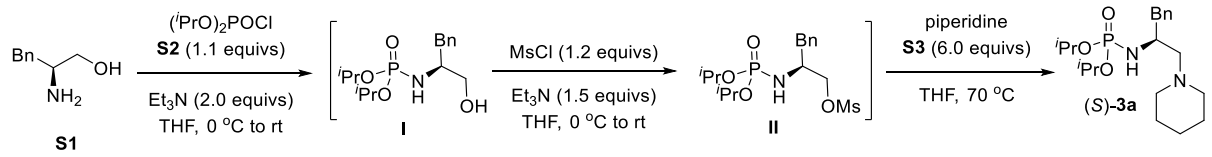
Anhydrous DCE was prepared by first distillation over $P_2O_5$ and then from $CaH_2$. Anhydrous THF and toluene were prepared by distillation over sodium-benzophenone ketyl prior to use. Powered molecular sieves (MS) was purchased from Aldrich and dried under vacuum at 150 $^{o}C$ for 10 h and then stored under nitrogen. All chiral amino alcohols were purchased from shanghai darui finechemical Co., Ltd. and used as received.

**List of abbreviation:**

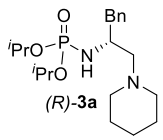
| Entry | Chemical name | Abbreviation |
|---|---|---|
| 1 | Petroleum ether | PE |
| 2 | Ethyl acetate | EtOAc |
| 3 | Tetrahydrofuran | THF |
| 4 | Dichloromethane | DCM |
| 5 | 1,2-Dichloroethane | DCE |
| 6 | Acetonitrile | $CH_3CN$ |
| 7 | 1,3-Diphenylguanidine | DPG |
| 8 | 1,4-Diaza[2.2.2]bicyclooctane | DABCO |

## 2. Materials preparation

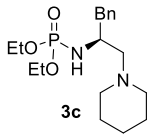
### 2.1 The synthesis of catalysts 3a-f and 4c-d



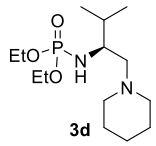

**General procedure**: Under an atmosphere of $N_2$, to a flame-dried 250 mL three-necked flask were added L-phenylalaninol **S1** (7.6 g, 50 mmol) and 80 mL THF. After the mixture was cooled down to 0 °C, $Et_3N$ (14.0 mL, 100 mmol) was added via syringe, followed by the dropwise addition of a solution of freshly distilled diisopropyl chlorophosphate **S2** (11.0 g, 55 mmol) in anhydrous THF (20 mL). The resulting mixture was allowed to warm to room temperature gradually, and kept stirring for 4 h. Then the reaction was cooled down to 0 °C, followed by the successive dropwise addition of $Et_3N$ (11.0 mL, 75 mmol) and a solution of freshly distilled MsCl (4.5 mL, 60 mmol) in anhydrous THF (20 mL). After being stirred at room temperature until full consumption of intermediate **I** by TLC analysis (5 h), piperidine **S3** (15.3 g, 180 mmol) was added. The resulting mixture was stirred at 70 °C for 1.5 days, and cooled down to room temperature. After 50 mL water was added, the mixture was extracted with *n*-hexane (5×20 mL). The combined organic layer was acidified with HCl (2 M), and aqueous phase was washed with *n*-hexane (3×20 mL). Then the aqueous layer was neutralized with sat. $NaHCO_3$ (aq.) until pH = 8-9, and extracted with *n*-hexane (5×30 mL). The combined organic extracts were dried over anhydrous $Na_2SO_4$, filtered, concentrated in *vacuo* to afford pure catalyst (*S*)-**3a** as white solid (7.1 g, 37% overall yield for 3 steps), m.p. = 97-100 °C. $[\alpha]^{20}_D$ = +21.7 (c = 0.8, $CHCl_3$). $^1$H NMR (300 MHz, $CDCl_3$): δ 7.31-7.26 (m, 2H), 7.23-7.17 (m, 3H), 4.65-4.53 (m, 2H), 3.53-3.47 (m, 1H), 3.19 (brs, 1H), 3.13 (ABd, *J* = 13.3 Hz, *J* = 4.2 Hz, 1H ), 2.68 (ABd, *J* = 13.2 Hz, *J* = 7.5 Hz, 1H ), 2.36-2.05 (m, 6H), 1.58-1.50 (m, 4H), 1.43-1.39 (m, 2H), 1.35-1.28 (m, 12H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 138.03, 129.79, 128.14, 126.11, 70.59 (d, $J_{C\text{-}P}$ = 3.9 Hz), 70.54 (d, $J_{C\text{-}P}$ = 3.9 Hz), 62.27 (d, $J_{C\text{-}P}$ = 8.5 Hz), 54.57, 49.80, 40.14 (d, $J_{C\text{-}P}$ = 2.5 Hz), 26.03, 24.34, 23.98, 23.93, 23.87 (d, $J_{C\text{-}P}$ = 1.9 Hz), 23.82 (d, $J_{C\text{-}P}$ = 2.0 Hz); $^{31}$P NMR (121 MHz, $CDCl_3$): δ 7.54 (s, 1P); IR (neat): 3243, 2931, 1649, 1384, 1103, 1004, 901, 742 cm$^{-1}$; HRMS (ESI): Exact mass calcd for $C_{20}H_{36}N_2O_3P$ $[M+H]^+$: 383.2458, found: 383.2455.




Catalyst (*R*)-**3a** was obtained from D-phenylalaninol as white solid (52% overall yield for 3 steps), m.p. = 96-98 °C. $[\alpha]^{20}_D$ = -25.6 (c = 1.1, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$): δ 7.29-7.25 (m, 2H), 7.22-7.18 (m, 3H), 4.63-4.53 (m, 2H), 3.54-3.48 (m, 1H), 3.13-3.09 (m, 2H), 2.71-2.66 (m, 1H), 2.37-2.28 (m, 4H), 2.20-2.07 (m, 2H), 1.57-1.51 (m, 4H), 1.41-1.39 (m, 2H), 1.34-1.28 (m, 12H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 138.09, 129.79, 128.14, 126.11, 70.62 (d, $J_{C-P}$ = 3.8 Hz), 70.56 (d, $J_{C-P}$ = 3.8 Hz), 62.36 (d, $J_{C-P}$ = 8.4 Hz), 54.62, 49.90, 40.24 (d, $J_{C-P}$ = 2.9 Hz), 26.05, 24.36, 23.96, 23.92, 23.85 (d, $J_{C-P}$ = 1.9 Hz), 23.81 (d, $J_{C-P}$ = 1.8 Hz); $^{31}$P NMR (161.7 MHz, $CDCl_3$): δ 7.49 (s, 1P); IR (neat): 2979, 1468, 1383, 1235, 995, 900, 741 $cm^{-1}$. GC-MS: 382 ($M^+$, 4), 281 (17), 201 (66), 110 (12), 98 (100), 91 (7), 84 (6), 70 (5); HRMS (EI): Exact mass calcd for $C_{20}H_{35}N_2O_3P$ $[M]^+$: 382.2385, found: 382.2389.

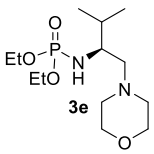



Catalyst **3c** was obtained from L-phenylalaninol as white solid (64% overall yield for 3 steps), m.p. = 87-89 °C. $[\alpha]^{20}_D$ = +17.8 (c = 0.8, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$): δ 7.30-7.26 (m, 2H), 7.22-7.18 (m, 3H), 4.08-3.99 (m, 3H), 3.91-3.85 (m, 1H), 3.53-3.43 (m, 1H), 3.19 (t, *J* = 8.4 Hz, 1H), 3.01 (ABd, *J* = 13.2 Hz, *J* = 5.2 Hz, 1H), 2.73 (ABd, *J* = 13.4 Hz, *J* = 6.8 Hz, 1H), 2.34-2.23 (m, 4H), 2.22-2.10 (m, 2H), 1.57-1.51 (m, 4H), 1.43-1.38 (m, 2H), 1.32 (t, *J* = 7.2 Hz, 3H), 1.27 (t, *J* = 6.8 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 138.03, 129.71, 128.18, 126.16, 62.63 (d, $J_{C-P}$ = 7.6 Hz), 62.11 (d, $J_{C-P}$ = 5.6 Hz), 62.03 (d, $J_{C-P}$ = 5.4 Hz), 54.64, 50.08, 40.45 (d, $J_{C-P}$ = 2.9 Hz), 26.00, 24.29, 16.25 (d, $J_{C-P}$ = 2.7 Hz), 16.18 (d, $J_{C-P}$ = 2.9 Hz); $^{31}$P NMR (121 MHz, $CDCl_3$): δ 9.08 (s, 1P). IR (neat): 3208, 2936, 2796, 1234, 1038, 967, 744, 701 $cm^{-1}$. GC-MS: 354 ($M^+$, 7), 263 (14), 256 (8), 201 (51), 110 (13), 98 (100), 91 (11), 84 (7), 70 (8); HRMS (EI): Exact mass calcd for $C_{18}H_{31}N_2O_3P$ $[M]^+$: 354.2072, found: 354.2074.

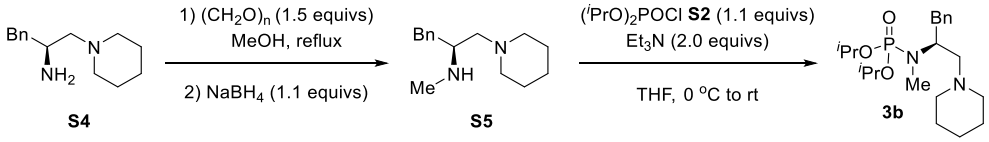



Catalyst **3d** was obtained from L-valinol as white solid (40% overall yield for 3 steps), m.p. = 45-47 °C. $[\alpha]^{20}_D$ = +16.5 (c = 0.5, $CHCl_3$). $^1$H NMR (300 MHz, $CDCl_3$): δ 4.14-4.03 (m, 4H), 3.21-3.12 (m, 1H), 3.07-3.02 (m, 1H), 2.48-2.41 (m, 2H), 2.31-2.15 (m, 4H), 2.08-1.98 (m, 1H), 1.57-1.50 (m, 4H), 1.44-1.39 (m, 2H), 1.34-1.29 (m, 6H), 0.92 (d, *J* = 7.2 Hz, 3H), 0.85 (d, *J* = 6.9 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 62.09 (d, $J_{C-P}$ = 2.1 Hz), 62.03 (d, $J_{C-P}$ = 2.0 Hz), 59.81 (d, $J_{C-P}$ = 7.3 Hz), 54.78, 53.50, 29.81 (d, $J_{C-P}$ = 2.8 Hz), 25.97, 24.32, 17.51, 17.37, 16.22, 16.15; $^{31}$P NMR (121 MHz, $CDCl_3$): δ 9.72 (s, 1P). IR (neat): 3208, 2933, 2777, 1441, 1388, 1232, 1034, 960 $cm^{-1}$; HRMS (ESI): Exact mass calcd for $C_{14}H_{32}N_2O_3P$ $[M+H]^+$: 307.2145,

found: 307.2152.



Catalyst **3e** was obtained from L-valinol as white solid (21% overall yield for 3 steps), m.p. = 51-53 °C. $[\alpha]^{20}_D$ = +9.6 (c = 0.4, $CHCl_3$). $^1$H NMR (300 MHz, $CDCl_3$): δ 4.13-4.02 (m, 4H), 3.68 (t, *J* = 4.8 Hz, 4H), 3.25-3.14 (m, 1H), 2.88-2.80 (m, 1H), 2.56-2.50 (m, 2H), 2.41-2.34 (m, 2H), 2.31-2.22 (m, 2H), 2.06-1.96 (m, 1H), 1.35-1.29 (m, 6H), 0.93 (d, *J* = 6.9 Hz, 3H), 0.86 (d, *J* = 7.2 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 67.0, 62.3 (d, $J_{C\text{-}P}$ = 3.7 Hz), 62.2 (d, $J_{C\text{-}P}$ = 3.6 Hz), 60.1 (d, $J_{C\text{-}P}$ = 6.4 Hz), 53.9, 53.3, 30.0 (d, $J_{C\text{-}P}$ = 3.3 Hz), 17.9, 17.2, 16.3, 16.2; $^{31}$P NMR (121 MHz, $CDCl_3$): δ 9.44 (s, 1P). IR (neat): 3203, 2957, 2806, 1453, 1392, 1223, 1032, 961 cm$^{-1}$. GC-MS: 308 ($M^+$, 0.7), 265 (14), 208 (96), 180 (53), 155 (27), 152 (73), 140 (32), 100 (100), 70 (11), 56 (12); HRMS (EI): Exact mass calcd for $C_{13}H_{29}N_2O_4P$ $[M]^+$: 308.1865, found: 308.1879.

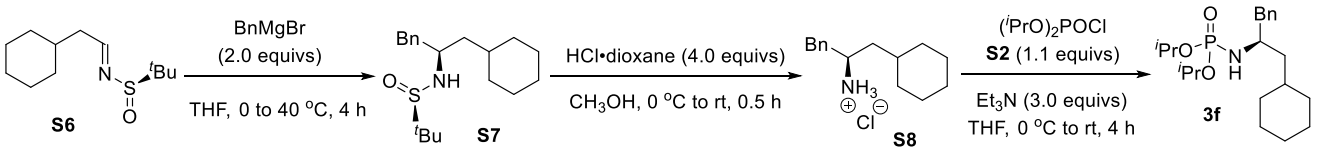



Under an atmosphere of $N_2$, to a flame-dried 25 mL Schlenk tube were added **S4**[1] (0.44 g, 2.0 mmol) and 10 mL absolute MeOH, followed by the addition of paraformaldehyde (0.09 g, 3.0 mmol) in one-portion. The resulting mixture was refluxed for 2 h until full consumption of **S4** by TLC analysis, and then cooled to 0 °C, followed by the slow addition of $NaBH_4$ (0.08 g, 2.2 mmol). The mixture was stirred at room temperature for about 5 h. After 10 mL $H_2O$ was added, the aqueous phase was extracted with DCM (4×20 mL). The combined organic layer was washed with brine, dried over anhydrous $Na_2SO_4$, and concentrated in *vacuo*, the residue was purified by flash silica gel column chromatography using EtOAc:PE (1:1, v/v) as eluent to furnish **S5** as light yellow oil.

Under an atmosphere of $N_2$, to a flame-dried 50 mL three-necked flask were added **S5** (0.12 g, 0.52 mmol) and 3 mL THF. Then the mixture was cooled down to 0 °C, followed by the successive dropwise addition of $Et_3N$ (0.14 mL, 1.0 mmol) and a solution of freshly distilled diisopropyl chlorophosphate **S2** (0.12 g, 0.57 mmol) in anhydrous THF (2 mL). The mixture was stirred at room temperature for about 5 h until full consumption of **S5** by TLC analysis. Then the reaction was quenched by 10 mL $H_2O$, neutralized with saturated $NaHCO_3$ solution (15 mL), and extracted with DCM (4×10 mL). The combined organic layer was washed with brine, dried over anhydrous $Na_2SO_4$,

[1] **S4** and **S12** were prepared following the published procedure: P. Li, Z. Chai, S.-L. Zhao, Y.-Q. Yang, H.-F. Wang, C.-W. Zheng, Y.-P. Cai, G. Zhao and S.-Z. Zhu, *Chem. Commun.*, 2009, **45**, 7369.

and concentrated in *vacuo*, the residue was purified by flash silica gel column chromatography using DCM:MeOH (50:1, v/v) as eluent to furnish **3b** as light yellow oil (0.1 g, 46% yield). $[\alpha]^{20}_{D}$ = -12.2 (c = 1.3, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$): δ 7.28-7.23 (m, 4H), 7.19-7.14 (m, 1H), 4.73-4.62 (m, 1H), 4.28-4.14 (m, 1H), 3.80-3.72 (m, 1H), 2.91-2.86 (m, 1H), 2.74-2.68 (m, 1H), 2.52-2.43 (m, 6H), 2.34 (brs, 2H), 2.23-2.18 (m, 1H), 1.54-1.50 (m, 4H), 1.40-1.37 (m, 2H), 1.27 (d, *J* = 6.0 Hz, 3H), 1.23 (d, *J* = 6.4 Hz, 3H), 1.12 (d, *J* = 6.0 Hz, 3H), 0.96 (d, *J* = 6.4 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 139.45, 129.19, 128.20, 125.89, 69.70 (d, $J_{C\text{-}P}$ = 5.1 Hz), 69.46 (d, $J_{C\text{-}P}$ = 5.1 Hz), 60.82, 54.95, 54.03 (d, $J_{C\text{-}P}$ = 5.0 Hz), 37.60 (d, $J_{C\text{-}P}$ = 3.6 Hz), 26.95, 25.93, 24.41, 23.85, 23.78 (d, $J_{C\text{-}P}$ = 2.8 Hz), 23.72, 23.69; $^{31}$P NMR (161.7 MHz, $CDCl_3$): δ 8.06 (s, 1P). IR (KBr): 3443, 2934, 1765, 1455, 1385, 1237, 1111, 778, 541 $cm^{-1}$; HRMS (ESI): Exact mass calcd for $C_{21}H_{38}N_2O_3P$ $[M+H]^+$: 397.2615, Found: 397.2621.

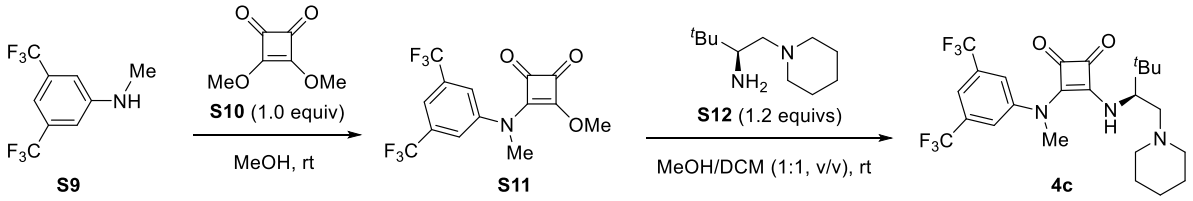



Under an atmosphere of $N_2$, to a flame-dried 100 mL three-necked flask were added **S6**[2] (2.52 g, 11.0 mmol) and 20 mL THF. The mixture was cooled down to 0 °C, followed by the dropwise addition of BnMgBr (22 mL, 22.0 mmol, 1 M in THF). Then the resulting mixture was stirred for 4 h at 40 °C until full consumption of **S6** by TLC analysis. The reaction was quenched by 30 mL saturated $NH_4Cl$. Then aqueous phase was extracted with EtOAc (3×20 mL), and the combined organic layer was washed with brine, dried over anhydrous $Na_2SO_4$, and concentrated in *vacuo*, the residue was purified by flash silica gel column chromatography using EtOAc:PE (1:5 to 1:2, v/v) as eluent. A recrystallization of the thus obtained **S7** in PE improved the diastereoselectivity to over 20:1.

To a 50 mL round-bottom flask were added the pure diastereomer of **S7** (0.18 g, 0.56 mmol) and 1 mL anhydrous MeOH. The mixture was cooled down to 0 °C, followed by the dropwise addition of HCl (0.6 mL, 2.2 mmol, 4 M in dioxane). Then the resulting mixture was stirred at room temperature for about 0.5 h until full consumption of **S7** by TLC analysis. After concentration in *vacuo*, compound **S8**[3] was obtained as white solid. It was used immediately in next step without purification. Under an atmosphere of $N_2$, to a flame-dried 50 mL three-necked flask were added **S8** and 2 mL THF. Then the

[2] **S6** was prepared following the published procedure: K. Brak and J. A. Ellman, *J. Am. Chem. Soc.*, 2009, **131**, 3850.
[3] The absolute configuration of **S8** was determined by optical rotation comparison after neutralization: M. J. Rodig, H. Seo, D. Hirsch-Weil, K. A. Abboud and S. Hong, *Tetrahedron: Asymmetry*, 2011, **22**, 1097.

mixture was cooled down to 0 °C, followed by the successive dropwise addition of $Et_3N$ (0.23 mL, 1.7 mmol) and a solution of freshly distilled diisopropyl chlorophosphate **S2** (0.13 g, 0.62 mmol) in anhydrous THF (1 mL). The resulting mixture was stirred for 4 h at room temperature. After full consumption of **S8** by TLC analysis, the reaction was quenched by 5 mL $H_2O$, and neutralized with saturated $NaHCO_3$ solution (10 mL). Then the aqueous phase was extracted with DCM (3×10 mL), the combined organic layer was washed with brine, dried over anhydrous $Na_2SO_4$, and concentrated in *vacuo*, the residue was purified by flash silica gel column chromatography using EtOAc:PE (1:10 to 1:2, v/v) as eluent to furnish **3f** as white solid (0.14 g, 66% yield), m.p. = 85-87 °C. $[\alpha]^{20}_D$ = +14.0 (c = 0.5, $CHCl_3$). $^1$H NMR (500 MHz, $CDCl_3$): δ 7.30-7.28 (m, 2H), 7.22-7.18 (m, 3H), 4.58-4.48 (m, 2H), 3.53-3.44 (m, 1H), 2.85-2.81 (m, 1H), 2.76-2.72 (m, 1H), 2.17 (t, *J* = 10.0 Hz, 1H), 1.77 (d, *J* = 12.5 Hz, 1H), 1.68-1.65 (m, 2H), 1.61 (brs, 1H), 1.51-1.42 (m, 1H), 1.33-1.30 (m, 6H), 1.29-1.28 (m, 6H), 1.25-1.07 (m, 6H), 0.92-0.84 (m, 1H), 0.78-0.70 (m, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$): see part II; $^{31}$P NMR (202 MHz, $CDCl_3$): δ 6.48 (s, 1P). IR (neat): 2976, 1697, 1339, 1173, 1051, 978, 881, 737 cm$^{-1}$; HRMS (ESI): Exact mass calcd for $C_{21}H_{36}NNaO_3P$ $[M+Na]^+$: 404.2325, Found: 404.2336.

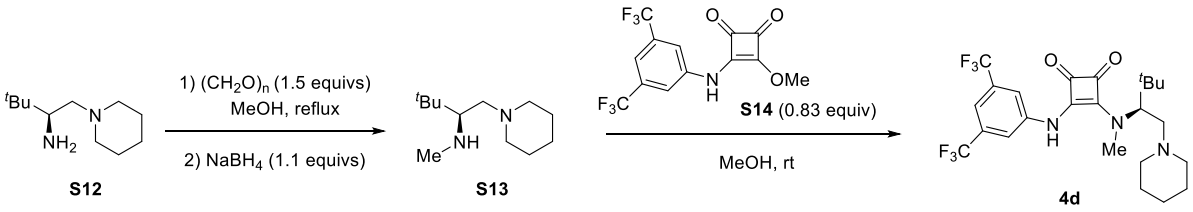



To a 25 mL three-necked flask were added **S10** (0.28 g, 2.0 mmol) and 4 mL MeOH, followed by the addition of **S9**[4] (0.49 g, 2.0 mmol). The mixture was stirred for 1 day at room temperature. Then the formed precipitate was filtered and dried in *vacuo* to give desired product **S11**.

A 25 mL three-necked flask were added **S11** (0.18 g, 0.5 mmol), 2 mL MeOH and 2 mL DCM, followed by the addition of **S12**[1] (0.11 g, 0.6 mmol) in one-portion. The mixture was stirred for 2 days at room temperature. After full consumption of **S11** by TLC analysis, the solvent was removed in *vacuo*, and then the residue was purified by flash silica gel column chromatography using EtOAc:PE (1:4 to 1:2, v/v) as eluent to furnish **4c** as yellow oil (0.12 g, 46% yield). $[\alpha]^{20}_D$ = -69.7 (c = 0.5, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$): δ 7.75 (s, 2H), 7.67 (s, 1H), 4.26 (dd, *J* = 10.8 Hz, *J* = 2.8 Hz, 1H), 3.89 (s, 3H), 2.58 (brs, 2H), 2.51-2.47 (m, 1H), 2.38 (t, *J* = 11.6 Hz, 1H), 2.22 (brs, 2H), 1.56-1.46 (m, 4H), 1.41-1.37 (m, 2H), 1.33-1.29 (m, 1H), 0.96 (s, 9H); $^{13}$C NMR (100 MHz, $CDCl_3$):

[4] **S9** was prepared following the published procedure: G. Jakab, A. Hosseini, H. Hausmann and P. R. Schreiner, *Synthesis*, 2013, **45**, 1635.

δ 183.9, 171.3, 169.3, 142.3, 132.2 (q, $J_{C-F}$ = 33.5 Hz), 127.1, 124.4, 121.6, 121.0, 118.3 (t, $J_{C-F}$ = 3.9 Hz), 61.7, 58.3, 54.6, 37.2 (d, $J_{C-F}$ = 4.2 Hz), 34.0, 26.2, 26.0, 24.2; $^{19}$F NMR (376 MHz, $CDCl_3$): δ -62.96 (s, 6F). IR: 2936, 2114, 1701, 1584, 1373, 1134, 908, 731, 648 cm$^{-1}$; HRMS (ESI): Exact mass calcd for $C_{24}H_{30}F_6N_3O_2$ $[M+H]^+$: 506.2237, Found: 506.2238.

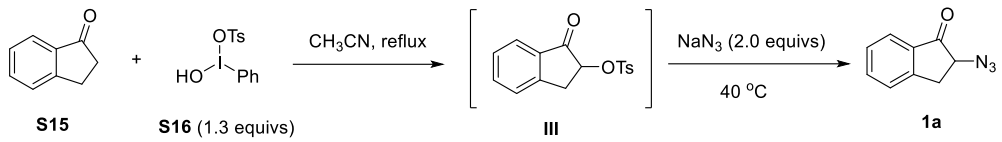



Under an atmosphere of $N_2$, to a 25 mL Schlenk tube were added **S12**[1] (0.66 g, 3.6 mmol) and 20 mL absolute MeOH, followed by the addition of paraformaldehyde (0.16 g, 5.4 mmol). The resulting mixture was refluxed for 2.5 h until full consumption of **S12** by TLC analysis, and then cooled to 0 °C, followed by the slow addition of $NaBH_4$ (0.15 g, 4.0 mmol). Then the mixture was stirred at room temperature for about 5 h, and then 10 mL $H_2O$ was added. After the aqueous phase was extracted with DCM (4×20 mL), the combined organic layer was washed with brine, dried over anhydrous $Na_2SO_4$, and concentrated in *vacuo*, the residue was purified by flash silica gel column chromatography using PE:EtOAc (1:1, v/v) as eluent to furnish **S13** as light yellow oil.

Under an atmosphere of $N_2$, to a flame-dried 50 mL three-necked flask were added **S13** (0.37 g, 1.8 mmol) and 10 mL MeOH, followed by the addition of **S14**[5] (0.51 g, 1.5 mmol) in one-portion. The mixture was then stirred for 4 days at room temperature. After concentration in *vacuo*, the residue was purified by flash silica gel column chromatography using acetone:PE (1:4 to 1:2, v/v) as eluent to furnish **4d** as yellow oil (44 mg, 6% yield). $[\alpha]^{20}_D$ = -72.7 (c = 0.6, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$): δ 7.78-7.69 (m, 2H), 7.48-7.38 (m, 1H), 4.75 (d, $J$ = 11.2 Hz, 0.6H), 3.51 (brs, 0.3H), 3.36-3.25 (m, 3H), 2.66-2.58 (m, 4H), 2.40-2.25 (m, 2H), 1.60-1.38 (m, 6H), 1.05-0.98 (m, 9H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 185.0, 180.9, 172.7, 162.1, 140.1, 131.7 (q, $J_{C-F}$ = 33.2 Hz), 127.2, 124.5, 121.7, 119.9, 119.0, 115.9, 63.8, 54.7, 54.3, 34.8, 33.5, 27.5, 26.0, 24.3; $^{19}$F NMR (376 MHz, $CDCl_3$): δ -63.17 (s, 6F). IR: 2113, 1710, 1558, 1365, 1220, 1070, 974, 557 cm$^{-1}$; HRMS (ESI): Exact mass calcd for $C_{24}H_{30}F_6N_3O_2$ $[M+H]^+$: 506.2237, Found: 506.2246.

[5] **S14** was prepared following the published procedure: E. Badiola, B. Fiser, E. Gómez-Bengoa, A. Mielgo, I. Olaizola, I. Urruzuno, J. M. García, J. M. Odriozola, J. Razkin, M. Oiarbide and C. Palomo, *J. Am. Chem. Soc.*, 2014, **136,** 17869.

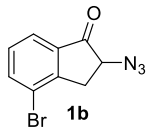
## 2.2 The synthesis of α-azido ketones 1[6]




**S15** **S16** (1.3 equivs) **III** **1a**

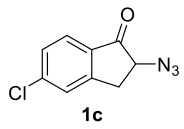
**General procedure**: To a 50 mL three-necked flask were added 1-indanone **S15** (0.13 g, 1 mmol) and 10 mL $CH_3CN$, followed by the addition of **S16**[7] (0.51 g, 1.3 mmol). The mixture was refluxed for 5 h until full consumption of **S15** by TLC analysis. After the mixture was cooled down to 40 °C, $NaN_3$ (0.13 g, 2 mmol) was added. The reaction was kept stirring until full consumption of intermediate **III** by TLC analysis, and then the reaction mixture was cooled down to room temperature. After evaporating solvent, the residue was dissolved in DCM, washed with water (3×10 mL), dried over anhydrous $Na_2SO_4$, and concentrated in *vacuo*. The residue was purified by column chromatography using EtOAc:PE (1:10, v/v) as eluent to furnish **1a** as white solid (0.15 g, 86% yield).[6]

**Substrates 1b-e were prepared according to the above mentioned general procedure:**



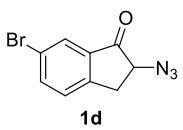

**1b**

White solid, m.p. = 39-40 °C. $^1$H NMR (300 MHz, $CDCl_3$): δ 7.84-7.81 (m, 1H), 7.75 (d, *J* = 7.5 Hz, 1H), 7.37-7.31 (m, 1H), 4.35 (dd, *J* = 8.2 Hz, *J* = 4.5 Hz, 1H), 3.48 (ABd, *J* = 17.7 Hz, *J* = 8.1 Hz, 1H), 2.85 (ABd, *J* = 17.7 Hz, *J* = 4.5 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 201.1, 151.1, 138.7, 136.2, 129.9, 123.5, 122.0, 61.7, 34.0; HRMS (ESI): Exact mass calcd for $C_9H_6BrN_3NaO$ $[M+Na]^+$: 273.9586, found: 273.9597.




**1c**

White solid, m.p. = 82-85 °C. $^1$H NMR (300 MHz, $CDCl_3$): δ 7.72 (d, *J* = 8.1 Hz, 1H), 7.46-7.38 (m, 2H), 4.34 (dd, *J* = 8.2 Hz, *J* = 4.8 Hz, 1H), 3.53-3.44 (m, 1H), 2.95-2.87 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 200.3, 152.6, 142.6, 132.5, 129.0, 126.7, 125.7, 61.8, 32.7; HRMS (DART): Exact mass calcd for $C_9H_{10}ClN_4O$ $[M+NH_4]^+$: 225.0538, found: 225.0537.




**1d**

White solid, m.p. = 88-90 °C. $^1$H NMR (300 MHz, $CDCl_3$): δ 7.92-7.91 (m, 1H), 7.77-7.74 (m, 1H), 7.36-7.33 (m, 1H), 4.35 (dd, *J* = 8.2 Hz, *J* = 4.5 Hz, 1H), 3.51-3.42 (m, 1H), 2.91-2.83 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 200.4, 149.6, 138.8, 135.9, 128.1, 127.5, 122.4, 62.1, 32.7; HRMS (ESI): Exact mass calcd for $C_9H_6BrN_3NaO$ $[M+Na]^+$: 273.9586, found: 273.9593.

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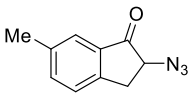
[6] J. C. Lee, S. Kim and W. C. Shin, *Synth. Commun*., 2000, **30**, 4271.

[7] **S16** was prepared according to the corresponding literature method: G. F. Koser and R. H. Wettach, *J. Org. Chem.*, 1977, **42**, 1476.

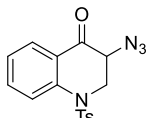


**1e**

White solid, m.p. = 31-33 °C. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.56 (s, 1H), 7.48-7.45 (m, 1H), 7.33 (d, *J* = 8.0 Hz, 1H), 4.30 (dd, *J* = 8.2 Hz, *J* = 4.8 Hz, 1H), 3.45 (ABd, *J* = 17.2 Hz, *J* = 8.0 Hz, 1H), 2.86 (ABd, *J* = 17.0 Hz, *J* = 4.4 Hz, 1H), 2.40 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 201.7, 148.4, 138.2, 137.2, 134.1, 126.1, 124.3, 62.2, 32.5, 21.0; HRMS (ESI): Exact mass calcd for $C_{10}H_9N_3NaO$ $[M+Na]^+$: 210.0638, found: 210.0638.


**General procedure**: To a 25 mL single-necked flask were added $NaN_3$ (0.48 g, 7.4 mmol), 4 mL DMSO and 2 mL acetone at 0 °C, followed by the addition of **S17**[8] (0.97 g, 3.7 mmol). The mixture was stirring for 15 min until full consumption of **S17** by TLC analysis, and then the reaction mixture was poured out to ice water. The mixture was extracted with $Et_2O$ (3×10 mL), washed with brine (3×10 mL), dried over anhydrous $Na_2SO_4$, and concentrated in *vacuo*. The residue was purified by flash silica gel column chromatography using $Et_2O$:PE (1:10, v/v) as eluent to furnish **1f** as white solid (0.39 g, 47% yield), m.p. = 89-91 °C. $^1$H NMR (500 MHz, $CDCl_3$): δ 7.89 (d, *J* = 8.5 Hz, 1H), 7.10 (dd, *J* = 8.5 Hz, *J* = 2.0 Hz, 1H), 7.06 (d, *J* = 2.0 Hz, 1H), 4.54 (ABd, *J* = 11.3 Hz, *J* = 4.5 Hz, 1H), 4.41 (ABd, *J* = 10.5 Hz, *J* = 5.0 Hz, 1H), 4.29 (dd, *J* = 11.2 Hz, *J* = 10.0 Hz, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ 187.6, 161.6, 142.9, 128.9, 123.2, 118.2, 117.9, 69.1, 59.8. HRMS (ESI): Exact mass calcd for $C_9H_6N_3O_2ClNa$ $[M+Na]^+$: 246.0041, found: 246.0036.

**Substrates 1g were prepared according to the above general procedure, 1h and 13 was prepared following the literature procedure[9], 1i-k was prepared following the literature procedure[10]:**



**1g**

**1g** was obtained in 30% yield as white solid, m.p. = 94-96 °C. $^1$H NMR (500 MHz, $CDCl_3$): δ 8.01 (dd, *J* = 8.0 Hz, *J* = 2.0 Hz, 1H), 7.87 (dd, *J* = 8.5 Hz, *J* = 1.0 Hz, 1H), 7.68-7.66 (m, 2H), 7.63-7.60 (m, 1H), 7.32-7.30 (m, 3H), 4.51 (ABd, *J* = 14.0 Hz, *J* = 5.0 Hz, 1H), 4.01 (ABd, *J* = 12.0 Hz, *J* = 5.5 Hz, 1H), 3.80 (dd, *J* = 14.0 Hz, *J* = 11.5 Hz, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ 190.2, 145.1, 142.2, 136.1, 135.6, 130.3, 128.6, 127.0, 125.7, 123.5, 123.4, 59.8, 49.6, 21.7. HRMS (ESI): Exact mass calcd for $C_{16}H_{14}N_4O_3SNa$ $[M+Na]^+$: 365.0679, found: 365.0680.

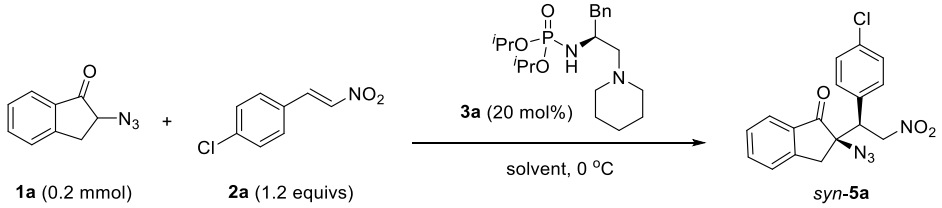
[8] S. H. Wood, S. Etridge, A. R. Kennedy, J. M. Percy and D. J. Nelson, *Chem. Eur. J.*,2019, **25**, 5574.
[9] H. Takeuchi, S. Yanagida, T. Ozaki, S. Hagiwara and S. Eguchi, *J. Org. Chem.*, 1989, **54**, 431.
[10] P. Magnus and L. Barth, *Tetrahedron Lett.*, 1992, **33**, 2777.

## 3. Condition optimization

### 3.1 The *syn*-selective Michael addition

With phosphoramide **3a** as catalyst, the solvent effects were examined at first, and typical results were shown in Table S1. By using DCM, $CH_3CN$ or acetone as solvent, the desired product *syn*-**5a** was obtained in low to moderate enantioselectivity (5-61% ee, entries 1-3). When the reaction was run in EtOAc or THF, *syn*-**5a** could be obtained in 89% and 81% ee respectively, but the yield was poor (entries 4-5). Fortunately, toluene was found to be the optimal solvent, affording *syn*-**5a** in 80% yield, 5.4:1 dr and 88% ee (entry 6).

**Table S1. The effect of solvent**




**1a** (0.2 mmol) **2a** (1.2 equivs) *syn*-**5a**

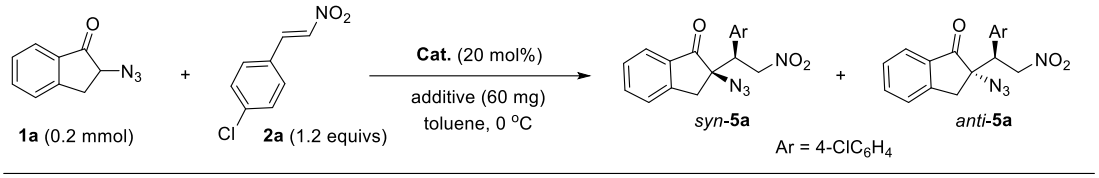
| Entry | Solvent | Time (d) | Yield (%)[a] | *syn:anti*[b] | Ee (%) (major)[c] |
|---|---|---|---|---|---|
| 1 | DCM | 4 | 74 | 1.9:1 | 61 |
| 2 | $CH_3CN$ | 4 | 40 | 1:1.1 | 5 |
| 3 | Acetone | 3 | 69 | 1.8:1 | 36 |
| 4 | EtOAc | 3 | 23 | 1.3:1 | 89 |
| 5 | THF | 4 | 29 | 2.7:1 | 81 |
| 6 | Toluene | 4 | 80 | 5.4:1 | 88 |

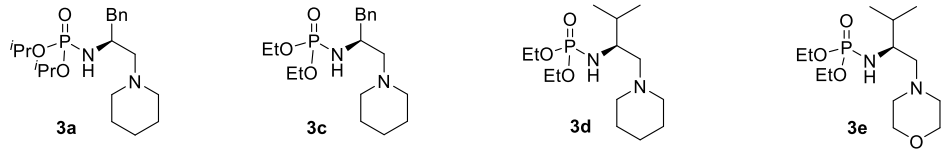
[a] Isolated yield. [b] Determined by $^1H$ NMR analysis of the crude reaction mixtures. [c] Determined by chiral HPLC analysis, for major diastereomer.

Next, chiral phosphoramides **3c-e** bearing different substituents were examined to further improve the reaction outcome. As shown in Table S2, Ethoxy substituted phosphoramide **3c** could give the *syn*-adduct with 6.0:1 dr and 90% ee (entry 2). The L-valinol-derived phosphoramide **3d** and **3e** showed diminished catalytic activity and stereoselectivity (entries 3-4). Then we tried using additive to improve the stereoselectivities. It was found that the addition of 5Å MS to the reaction mediated by **3a** or **3c** slowed down the reaction rate, but resulted in higher dr and ee values (entries 5-6). With the assistance of 5Å MS, phosphoramide **3a** gave *syn*-**5a** in much higher yield and stereoselectivity than that of **3c** (entries 5-6). Other types of powdered MS were also tried, but no better results were

obtained (entries 7-9). Taking into consideration both reactivity and stereoselectivity, we determined that the *syn*-selective Michael addition reaction was carried out in toluene at 0 °C with the addition of 5Å MS, in the presence of 20 mol% of phosphoramide catalyst **3a**.

**Table S2. Condition optimization**



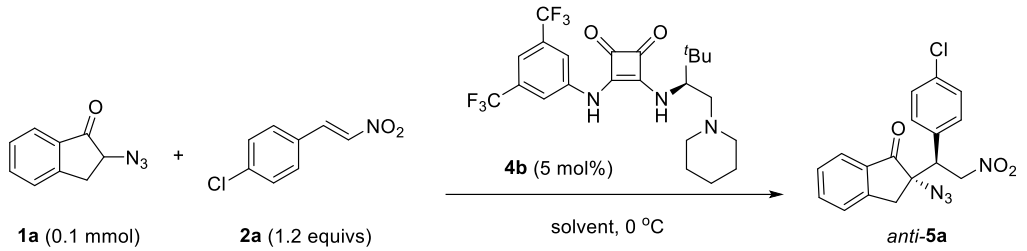

| Entry | **Cat.** | Additive | Time (d) | Yield[a] (%) | *syn*:*anti*[b] | Ee[c] (%) |
|---|---|---|---|---|---|---|
| 1 | **3a** | / | 4 | 80 | 5.4:1 | 88 |
| 2 | **3c** | / | 4 | 87 | 6.0:1 | 90 |
| 3 | **3d** | / | 4 | 78 | 3.7:1 | 86 |
| 4 | **3e** | / | 4 | 10 | 2.6:1 | 70 |
| 5 | **3a** | 5Å MS | 7 | 80 | 8.2:1 | 95 |
| 6 | **3c** | 5Å MS | 7 | 56 | 7.1:1 | 93 |
| 7 | **3a** | 3Å MS | 7 | 82 | 8.0:1 | 94 |
| 8 | **3a** | 4Å MS | 7 | 79 | 7.0:1 | 94 |
| 9 | **3a** | 13X MS | 7 | 57 | 8.1:1 | 94 |

[a] Isolated yield. [b] Determined by $^1$H NMR analysis of the crude mixture. [c] Determined by HPLC analysis.

### 3.2 The *anti*-selective Michael addition

With squaramide **4b** as catalyst, the solvent effects were also examined, and typical results were shown in Table S3. By using DCE or DCM as the solvent, *anti*-**5a** was obtained with 95% ee, but DCE gave a higher 15:1 dr value (entries 1-2). The reaction run in $Et_2O$, THF, acetone or $CH_3CN$ proved to be much slower than that in DCE (entries 3-6 vs 1). Toluene gave much lower yield and stereoslectivity (entry 7). When EtOAc was used, no reaction occurred at all (entry 8). Taking into consideration both reactivity and stereoselectivity, the *anti*-selective Michael addition reaction was determined to be conducted in DCE at 0 °C, in the presence of 5 mol% of catalyst **4b**.

**Table S3. The effect of solvent**

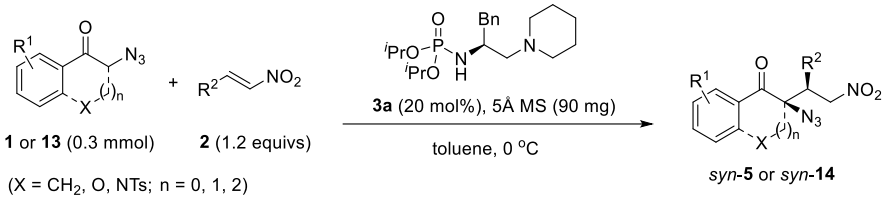



**1a** (0.1 mmol) **2a** (1.2 equivs) *anti*-**5a**

| Entry | Solvent | Time (d) | Yield (%)[a] | *syn*:*anti*[b] | Ee (%) (major)[c] |
|---|---|---|---|---|---|
| 1 | DCE | 2 | 90 | 1:15 | 95 |
| 2 | DCM | 2 | 94 | 1:10 | 95 |
| 3 | $Et_2O$ | 4 | 68 | 1:8 | 87 |
| 4 | THF | 4 | 75 | 1:12 | 92 |
| 5 | Acetone | 4 | 41 | 1:14 | 96 |
| 6 | $CH_3CN$ | 4 | 24 | 1:16 | 95 |
| 7 | Toluene | 4 | 53 | 1:6 | 75 |
| 8 | EtOAc | 4 | NR | / | / |

[a] Isolated yield. [b] Determined by $^1H$ NMR analysis of the crude reaction mixtures. [c] Determined by chiral HPLC analysis, for major diastereomer.

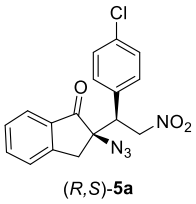
## 4. General procedure for *syn*-selective Michael addition.




**1** or **13** (0.3 mmol) **2** (1.2 equivs) *syn*-**5** or *syn*-**14**

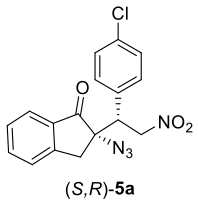
(X = $CH_2$, O, NTs; n = 0, 1, 2)

To a 5.0 mL vial were added bifunctional phosphoramide catalyst **3a** (23.0 mg, 0.06 mmol, 20 mol%), α-azido ketones **1** or **13** (0.3 mmol) and 90.0 mg 5Å MS, followed by the addition of dry toluene (1 mL). The reaction mixture was cooled down to 0 °C and stirred for about 30 min, then nitroolefins **2** (0.36 mmol) was added. After full consumption of α-azido ketones by TLC analysis, the crude reaction mixture was rapidly passed through a short silica gel column chromatography (5 cm), washed with PE:EtOAc (4:1, v/v), and concentrated in *vacuo*. To determine the diastereoselectivity of the product, the residue was first dissolved in $CDCl_3$, and took some samples for $^1$H NMR analysis. Then the sample for analysis and the rest of crude residue were recombined and purified by silica gel column chromatography (PE:$Et_2O$ = 10:1, v/v) to afford the desired products *syn*-**5** or *syn*-**14**.




(*R*,*S*)-**5a**

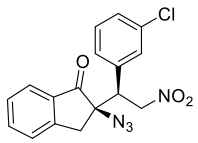
Product (*R*,*S*)-**5a** was obtained in 76% yield as light yellow liquid (7 days). $^1$H NMR analysis revealed that the dr value was 7:1. HPLC analysis [Chiralcel OZ-H, 5% $^i$PrOH/hexane, 1.0 mL/min, 230 nm; major diastereomer: tr (major) = 18.80 min, tr (minor) = 29.47 min, minor diastereomer: tr (major) = 34.04 min, tr (minor) = 25.62 min] gave the isomeric composition of major diastereomer: 93% ee; $[\alpha]^{25}_D$ = -13.6 (c = 0.68, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.78 (d, *J* = 7.6 Hz, 1H), 7.63-7.59 (m, 1H), 7.42 (t, *J* = 7.6 Hz, 1H), 7.30 (d, *J* = 8.0 Hz, 1H), 7.20-7.18 (m, 2H), 7.13-7.11 (m, 2H), 5.14-5.06 (m, 2H), 4.04 (dd, *J* = 9.4 Hz, *J* = 5.2 Hz, 1H), 3.34 (AB, *J* = 18.0 Hz, 1H), 3.24 (AB, *J* = 17.6 Hz, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 200.3, 150.5, 136.9, 134.7, 134.5, 132.4, 130.2, 129.2, 128.7, 126.3, 125.0, 75.7, 70.8, 49.2, 37.6; IR (neat): 2925, 2101, 1709, 1551, 1376, 1093, 978, 692 cm$^{-1}$; HRMS (ESI): Exact mass calcd for $C_{17}H_{17}ClN_5O_3$ $[M+NH_4]^+$: 374.1014, Found: 374.1014.




(*S*,*R*)-**5a**

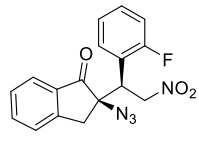
roduct (*S*,*R*)-**5a** was obtained in 89% yield as light yellow liquid by using (*R*)-**3a** as catalyst (7 days). $^1$H NMR analysis revealed that the dr value was 7:1. HPLC analysis [Chiralcel OZ-H, 5% $^i$PrOH/hexane, 1.0 mL/min, 230 nm; major diastereomer: tr (major) = 29.65 min, tr (minor) = 19.02 min, minor diastereomer: tr

(major) = 26.12 min, tr (minor) = 33.88 min] gave the isomeric composition of major diastereomer: 94% ee; $[\alpha]^{25}_D$ = +70.2 (c = 0.65, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.78 (d, *J* = 7.6 Hz, 1H), 7.61 (t, *J* = 7.6 Hz, 1H), 7.42 (t, *J* = 7.2 Hz, 1H), 7.30 (d, *J* = 8.0 Hz, 1H), 7.20-7.17 (m, 2H), 7.14-7.12 (m, 2H), 5.14-5.06 (m, 2H), 4.04 (dd, *J* = 9.6 Hz, *J* = 5.6 Hz, 1H), 3.34 (AB, *J* = 17.6 Hz, 1H), 3.24 (AB, *J* = 18.0 Hz, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 200.3, 150.5, 136.9, 134.7, 134.5, 132.4, 130.2, 129.2, 128.7, 126.3, 125.0, 75.7, 70.8, 49.2, 37.6; IR (neat): 2922, 2102, 1710, 1551, 1377, 1093, 977, 718 cm$^{-1}$; HRMS (ESI): Exact mass calcd for $C_{17}H_{17}ClN_5O_3$ $[M+NH_4]^+$: 374.1014, Found: 374.1011.



*syn*-**5b**

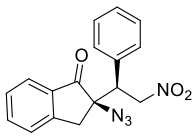
Product *syn*-**5b** was obtained in 79% yield as light yellow liquid (8 days). $^1$H NMR analysis revealed that the dr value was 7:1. HPLC analysis [Chiralcel OZ-H, 5% $^i$PrOH/hexane, 1.0 mL/min, 230 nm; major diastereomer: tr (major) = 16.52 min, tr (minor) = 24.58 min, minor diastereomer: tr (major) = 27.22 min, tr (minor) = 23.35 min] gave the isomeric composition of major diastereomer: 93% ee; $[\alpha]^{25}_D$ = -117.3 (c = 1.80, $CHCl_3$) (dr = 7:1). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.80 (d, *J* = 7.6 Hz, 1H), 7.60 (td, *J* = 7.6 Hz, *J* = 1.2 Hz, 1H), 7.44-7.40 (m, 1H), 7.30 (dt, *J* = 7.6 Hz, *J* = 1.2 Hz, 1H), 7.20-7.12 (m, 3H), 7.07 (dt, *J* = 7.6 Hz, *J* = 1.6 Hz, 1H), 5.12-5.05 (m, 2H), 4.04 (dd, *J* = 8.4 Hz, *J* = 6.4 Hz, 1H), 3.36 (AB, *J* = 17.6 Hz, 1H), 3.25 (AB, *J* = 17.6 Hz, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 200.2, 150.4, 136.8, 135.9, 134.8, 134.6, 130.1, 129.1, 129.0, 128.7, 126.9, 126.3, 125.0, 75.5, 70.8, 49.4, 37.6; IR (neat): 2105, 1712, 1553, 1377, 1155, 903, 739 cm$^{-1}$; HRMS (ESI): Exact mass calcd for $C_{17}H_{17}ClN_5O_3$ $[M+NH_4]^+$: 374.1014, Found: 374.1014.



*syn*-**5c**

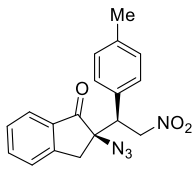
Product *syn*-**5c** was obtained in 73% yield as light yellow liquid (7 days). $^1$H NMR analysis revealed that the dr value was 9:1. HPLC analysis [Chiralcel OZ-H, 5% $^i$PrOH/hexane, 1.0 mL/min, 230 nm; major diastereomer: tr (major) = 14.64 min, tr (minor) = 20.45 min, minor diastereomer: tr (major) = 16.48 min, tr (minor) = 17.60 min] gave the isomeric composition of major diastereomer: 95% ee; $[\alpha]^{25}_D$ = -87.7 (c = 1.10, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.77 (d, *J* = 7.6 Hz, 1H), 7.56 (td, *J* = 7.2 Hz, *J* = 1.2 Hz, 1H), 7.40-7.36 (m, 1H), 7.29-7.26 (m, 1H), 7.21-7.14 (m, 2H), 7.00-6.94 (m, 2H), 5.14 (ABd, *J* = 14.0 Hz, *J* = 10.4 Hz, 1H), 5.08 (ABd, *J* = 13.8 Hz, *J* = 4.8 Hz, 1H), 4.51 (dd, *J* = 10.2 Hz, *J* = 4.8 Hz, 1H), 3.39 (AB, *J* = 18.0 Hz, 1H), 3.26 (AB, *J* = 18.0 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 200.0, 161.0

(d, $J_{C\text{-}F}$ = 245.3 Hz, 1C), 150.5, 136.6, 134.4, 130.4 (d, $J_{C\text{-}F}$ = 8.7 Hz, 1C), 129.5 (d, $J_{C\text{-}F}$ = 3.3 Hz, 1C), 128.5, 126.1, 124.9, 124.6 (d, $J_{C\text{-}F}$ = 2.6 Hz, 1C), 121.1 (d, $J_{C\text{-}F}$ = 13.5 Hz, 1C), 116.0 (d, $J_{C\text{-}F}$ = 22.9 Hz, 1C), 74.7, 71.1, 42.4, 37.6 (d, $J_{C\text{-}F}$ = 2.6 Hz, 1C); $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ -114.61 (s, 1F); IR (neat): 2103, 1710, 1606, 1553, 1467, 1377, 1218, 1014, 719 cm$^{-1}$; HRMS (ESI): Exact mass calcd for $C_{17}H_{17}FN_5O_3$ $[M+NH_4]^+$: 358.1310, Found: 358.1308.



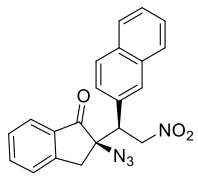
*syn*-**5d**

Product *syn*-**5d** was obtained in 85% yield as light yellow liquid (9 days). $^1$H NMR analysis revealed that the dr value was 9:1. HPLC analysis [Chiralcel OZ-H, 3% $^i$PrOH/hexane, 1.0 mL/min, 230 nm; major diastereomer: tr (major) = 21.14 min, tr (minor) = 33.08 min, minor diastereomer: tr (major) = 36.98 min, tr (minor) = 28.80 min] gave the isomeric composition of major diastereomer: 96% ee; $[\alpha]^{25}_D$ = -125.7 (c = 1.01, $CHCl_3$) (dr = 9:1). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.78 (d, $J$ = 7.6 Hz, 1H), 7.58-7.55 (m, 1H), 7.39 (t, $J$ = 7.6 Hz, 1H), 7.27-7.25 (m, 2H), 7.20-7.16 (m, 4H), 5.17-5.07 (m, 2H), 4.07 (dd, $J$ = 9.8 Hz, $J$ = 4.8 Hz, 1H), 3.39 (AB, $J$ = 17.6 Hz, 1H), 3.23 (AB, $J$ = 17.6 Hz, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 200.56, 150.65, 136.60, 134.72, 133.78, 128.87, 128.86, 128.66, 128.52, 126.23, 124.88, 75.85, 70.94, 49.84, 37.55; IR (neat): 2102, 1710, 1605, 1552, 1376, 1093, 742 cm$^{-1}$; HRMS (ESI): Exact mass calcd for $C_{17}H_{18}N_5O_3$ $[M+NH_4]^+$: 340.1404, Found: 340.1402.



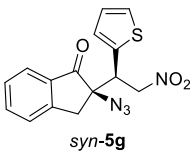
*syn*-**5e**

Product *syn*-**5e** was obtained in 79% yield as light yellow liquid (10 days). $^1$H NMR analysis revealed that the dr value was 9:1. HPLC analysis [Chiralcel OZ-H, 3% $^i$PrOH/hexane, 1.0 mL/min, 230 nm; major diastereomer: tr (major) = 17.62 min, tr (minor) = 27.65 min, minor diastereomer: tr (major) = 30.99 min, tr (minor) = 23.31 min] gave the isomeric composition of major diastereomer: 96% ee; $[\alpha]^{25}_D$ = -138.8 (c = 0.82, $CHCl_3$) (dr = 9:1). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.78 (d, $J$ = 8.0 Hz, 1H), 7.58 (td, $J$ = 7.2 Hz, $J$ = 1.2 Hz, 1H), 7.39 (t, $J$ = 7.6 Hz, 1H), 7.29-7.27 (m, 1H), 7.07-6.99 (m, 4H), 5.14-5.03 (m, 2H), 4.04 (dd, $J$ = 10.4 Hz, $J$ = 4.4 Hz, 1H), 3.39 (AB, $J$ = 17.6 Hz, 1H), 3.20 (AB, $J$ = 17.6 Hz, 1H), 2.22 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 200.6, 150.8, 138.5, 136.6, 134.7, 130.7, 129.6, 128.7, 128.5, 126.3, 124.9, 76.0, 70.9, 49.4, 37.5, 21.0; IR (neat): 2101, 1710, 1606, 1552, 1378, 1218, 747 cm$^{-1}$; HRMS (ESI): Exact mass calcd for $C_{18}H_{20}N_5O_3$ $[M+NH_4]^+$: 354.1561, Found: 354.1559.



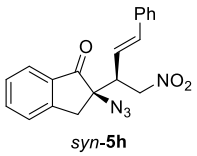
*syn*-**5f**

Product *syn*-**5f** was obtained in 81% yield as white solid (7 days), m.p. = 111-112 °C. $^1$H NMR analysis revealed that the dr value was 8:1. HPLC analysis [Chiralcel OZ-H, 3% $^i$PrOH/hexane, 1.0 mL/min, 230 nm; major diastereomer: tr (major) = 27.38 min, tr (minor) = 46.16 min, minor diastereomer: tr (major) = 48.54 min, tr (minor) = 37.61 min] gave the isomeric composition of major diastereomer: 93% ee; $[\alpha]^{25}_D$ = -102.0 (c = 0.58, $CHCl_3$) (dr = 8:1). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.80 (d, *J* = 7.6 Hz, 1H), 7.75-7.67 (m, 4H), 7.53-7.42 (m, 3H), 7.35 (t, *J* = 7.6 Hz, 1H), 7.27-7.25 (m, 1H), 7.23-7.20 (m, 1H), 5.27 (ABd, *J* = 13.6 Hz, *J* = 10.8 Hz, 1H), 5.20 (ABd, *J* = 13.6 Hz, *J* = 4.0 Hz, 1H), 4.25 (dd, *J* = 10.8 Hz, *J* = 4.0 Hz, 1H), 3.45 (AB, *J* = 17.6 Hz, 1H), 3.25 (AB, *J* = 17.6 Hz, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 200.6, 150.7, 136.6, 134.7, 133.0, 133.0, 131.3, 128.9, 128.8, 128.5, 127.9, 127.6, 126.6, 126.6, 126.3, 125.7, 124.9, 76.0, 71.0, 50.0, 37.6; IR (neat): 2102, 1710, 1605, 1552, 1377, 1093, 719 cm$^{-1}$; HRMS (ESI): Exact mass calcd for $C_{21}H_{20}N_5O_3$ $[M+NH_4]^+$: 390.1561, Found: 390.1560.



*syn*-**5g**

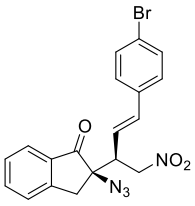
Product *syn*-**5g** was obtained in 85% yield as light yellow liquid (7 days). $^1$H NMR analysis revealed that the dr value was 10:1. HPLC analysis [Chiralcel OZ-H, 5% $^i$PrOH/hexane, 1.0 mL/min, 230 nm; major diastereomer: tr (major) = 17.34 min, tr (minor) = 24.14 min, minor diastereomer: tr (major) = 25.79 min, tr (minor) = 22.00 min] gave the isomeric composition of major diastereomer: 96% ee; $[\alpha]^{25}_D$ = -171.4 (c = 0.72, $CHCl_3$) (dr = 9:1). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.81 (d, *J* = 7.6 Hz, 1H), 7.63 (t, *J* = 7.6 Hz, 1H), 7.43 (t, *J* = 7.6 Hz, 1H), 7.37 (d, *J* = 8.0 Hz, 1H), 7.17 (d, *J* = 5.2 Hz, 1H), 6.94 (d, *J* = 7.6 Hz, 1H), 6.86 (t, *J* = 4.4 Hz, 1H), 5.06-5.00 (m, 1H), 4.47-4.43 (m, 1H), 3.48 (AB, *J* = 17.6 Hz, 1H), 3.27 (AB, *J* = 17.6 Hz, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 200.2, 150.8, 136.7, 135.9, 134.5, 128.6, 128.3, 127.1, 126.4, 126.1, 125.1, 76.8, 70.5, 44.8, 37.7; IR (neat): 2101, 1710, 1606, 1553, 1376, 1217, 803, 702 cm$^{-1}$; HRMS (ESI): Exact mass calcd for $C_{15}H_{16}N_5O_3S$ $[M+NH_4]^+$: 346.0968, Found: 346.0968.



*syn*-**5h**

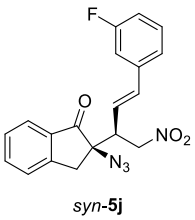
Product *syn*-**5h** was obtained in 76% yield as light yellow liquid (8 days). $^1$H NMR analysis revealed that the dr value is 15:1. HPLC analysis [Chiralcel OZ-H, 5% $^i$PrOH/hexane, 1.0 mL/min, 230 nm; major diastereomer: tr (major) = 16.88 min, tr (minor) = 27.51 min, minor diastereomer: tr (major) = 29.49 min, tr (minor) = 21.28 min] gave the isomeric composition of major diastereomer: 94% ee; $[\alpha]^{25}_D$ = -50.5 (c = 1.01, $CHCl_3$). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.83 (d, *J* = 7.8 Hz, 1H), 7.68-7.63 (m, 1H), 7.48-7.40 (m,

2H), 7.25-7.20 (m, 3H), 7.13-7.10 (m, 2H), 6.63 (d, $J$ = 15.6 Hz, 1H), 5.77-5.68 (m, 1H), 4.82 (ABd, $J$ = 12.6 Hz, $J$ = 3.9 Hz, 1H), 4.68 (ABd, $J$ = 7.8 Hz, $J$ = 1.5 Hz, 1H), 3.64 (td, $J$ = 10.2 Hz, $J$ = 3.9 Hz, 1H), 3.46 (AB, $J$ = 17.7 Hz, 1H), 3.31 (AB, $J$ = 17.7 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 200.3, 150.5, 137.3, 136.9, 135.5, 134.4, 128.7, 128.5, 128.4, 126.6, 126.5, 124.9, 121.2, 75.6, 70.1, 48.3, 37.7; IR (neat): 3028, 2103, 1713, 1607, 1553, 1379, 1242, 969, 745, 694 cm$^{-1}$; HRMS (ESI): Exact mass calcd for $C_{19}H_{20}N_5O_3$ $[M+NH_4]^+$: 366.1561, Found: 366.1559.



*syn*-**5i**

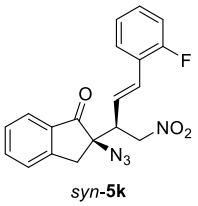
Product *syn*-**5i** was obtained in 70% yield as light yellow liquid (5 days). $^1$H NMR analysis revealed that the dr value was 13:1. HPLC analysis [Chiralcel OZ-H, 5% $^i$PrOH/hexane, 1.0 mL/min, 230 nm; major diastereomer: tr (major) = 20.65 min, tr (minor) = 27.52 min, minor diastereomer: tr (major) = 33.88 min, tr (minor) = 24.68 min] gave the isomeric composition of major diastereomer: 93% ee; $[\alpha]^{25}_D$ = -30.5 (c = 1.34, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.83 (d, $J$ = 7.6 Hz, 1H), 7.67 (t, $J$ = 7.6 Hz, 1H), 7.49-7.26 (m, 4H), 6.99-6.97 (m, 2H), 6.55 (d, $J$ = 15.6 Hz, 1H), 5.76-5.70 (m, 1H), 4.82 (ABd, $J$ = 12.4 Hz, $J$ = 3.6 Hz, 1H), 4.67 (ABd, $J$ = 12.6 Hz, $J$ = 10.4 Hz, 1H), 3.61 (td, $J$ = 10.0 Hz, $J$ = 3.6 Hz, 1H), 3.43 (AB, $J$ = 17.2 Hz, 1H), 3.32 (AB, $J$ = 18.0 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 200.1, 150.4, 136.9, 136.0, 134.4, 134.4, 131.7, 128.8, 128.1, 126.5, 125.0, 122.4, 122.1, 75.5, 70.1, 48.3, 37.7; IR (neat): 2962, 2105, 1713, 1607, 1554, 1434, 1009, 859 cm$^{-1}$; HRMS (ESI): Exact mass calcd for $C_{19}H_{19}BrN_5O_3$ $[M+NH_4]^+$: 444.0666, Found: 444.0662.



*syn*-**5j**

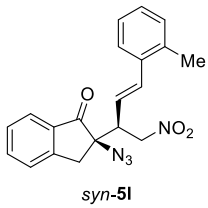
Product *syn*-**5j** was obtained in 68% yield as light yellow liquid (6 days). $^1$H NMR analysis revealed that the dr value was 12:1. HPLC analysis [Chiralcel OZ-H, 5% $^i$PrOH/hexane, 1.0 mL/min, 230 nm; major diastereomer: tr (major) = 17.48 min, tr (minor) = 26.74 min, minor diastereomer: tr (major) = 29.67 min, tr (minor) = 21.52 min] gave the isomeric composition of major diastereomer: 92% ee; $[\alpha]^{25}_D$ = -39.5 (c = 1.1, $CHCl_3$). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.84 (d, $J$ = 7.8 Hz, 1H), 7.68 (d, $J$ = 7.5 Hz, 1H), 7.50-7.42 (m, 2H), 7.23-7.16 (m, 1H), 6.94-6.88 (m, 2H), 6.82-6.78 (m, 1H), 6.59 (d, $J$ = 15.6 Hz, 1H), 5.80-5.72 (m, 1H), 4.81 (ABd, $J$ = 12.6 Hz, $J$ = 3.6 Hz, 1H), 4.68 (ABd, $J$ = 12.8 Hz, $J$ = 10.8 Hz, 1H), 3.63 (td, $J$ = 10.2 Hz, $J$ = 3.6 Hz, 1H), 3.44 (AB, $J$ = 17.4 Hz, 1H), 3.32 (AB, $J$ = 17.7 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 200.1, 162.9 (d, $J_{C\text{-}F}$ = 244.6 Hz, 1C), 150.4, 137.8 (d, $J_{C\text{-}F}$ = 7.7 Hz, 1C), 137.0, 136.1 (d, $J_{C\text{-}F}$ = 2.6 Hz, 1C), 134.4, 130.0 (d, $J_{C\text{-}F}$ = 8.2 Hz, 1C), 128.8, 126.5, 125.0, 122.8,

122.6 (d, $J_{C\text{-}F}$ = 2.9 Hz, 1C), 115.2 (d, $J_{C\text{-}F}$ = 21.2 Hz, 1C), 113.0 (d, $J_{C\text{-}F}$ = 21.9 Hz, 1C), 75.5, 70.1, 48.1, 37.7; $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ -113.11 (s, 1F); IR (neat): 2099, 1703, 1607, 1555, 1437, 1236, 932, 746 cm$^{-1}$; HRMS (ESI): Exact mass calcd for $C_{19}H_{19}FN_5O_3$ $[M+NH_4]^+$: 384.1466, Found: 384.1465.



*syn*-**5k**

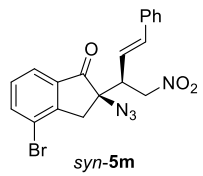
Product *syn*-**5k** was obtained in 81% yield as white solid (8 days), m.p. = 93-95 $^o$C. $^1$H NMR analysis revealed that the dr value was 12:1. HPLC analysis [Chiralcel OZ-H, 5% $^i$PrOH/hexane, 1.0 mL/min, 230 nm; major diastereomer: tr (major) = 16.69 min, tr (minor) = 25.98 min, minor diastereomer: tr (major) = 28.04 min, tr (minor) = 21.03 min] gave the isomeric composition of major diastereomer: 94% ee; $[\alpha]^{25}_D$ = -64.0 (c = 0.48, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.83 (d, $J$ = 8.0 Hz, 1H), 7.69-7.64 (m, 1H), 7.48-7.42 (m, 2H), 7.22-7.16 (m, 1H), 7.12-7.08 (m, 1H), 7.01-6.94 (m, 2H), 6.74 (d, $J$ = 16.0 Hz, 1H), 5.88-5.81 (m, 1H), 4.87-4.82 (m, 1H), 4.73-4.67 (m, 1H), 3.64 (td, $J$ = 10.4 Hz, $J$ = 4.0 Hz, 1H), 3.47 (AB, $J$ = 17.6 Hz, 1H), 3.33 (AB, $J$ = 17.6 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 200.18, 160.22 (d, $J_{C\text{-}F}$ = 249.2 Hz, 1C), 150.49, 136.90, 134.43, 130.04 (d, $J_{C\text{-}F}$ = 3.1 Hz, 1C), 129.77 (d, $J_{C\text{-}F}$ = 8.4 Hz, 1C), 128.72, 127.83 (d, $J_{C\text{-}F}$ = 3.4 Hz, 1C), 126.49, 124.98, 124.10, 124.06 (d, $J_{C\text{-}F}$ = 2.0 Hz, 1C), 123.37 (d, $J_{C\text{-}F}$ = 12.0 Hz, 1C), 115.75 (d, $J_{C\text{-}F}$ = 21.9 Hz, 1C), 75.56, 70.11, 48.74, 37.72; $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ -117.06 (s, 1F); IR (neat): 2098, 1703, 1555, 1378, 1235, 971, 756, 699 cm$^{-1}$; HRMS (ESI): Exact mass calcd for $C_{19}H_{19}FN_5O_3$ $[M+NH_4]^+$: 384.1466, Found: 384.1464.



*syn*-**5l**

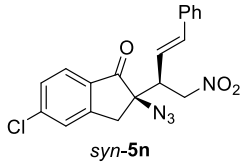
Product *syn*-**5l** was obtained in 80% yield as white solid (9 days), m.p. = 70-71 $^o$C. $^1$H NMR analysis revealed that the dr value was 13:1. HPLC analysis [Chiralcel OZ-H, 5% $^i$PrOH/hexane, 1.0 mL/min, 230 nm; major diastereomer: tr (major) = 13.66 min, tr (minor) = 21.88 min, minor diastereomer: tr (major) = 24.98 min, tr (minor) = 16.40 min] gave the isomeric composition of major diastereomer: 94% ee; $[\alpha]^{25}_D$ = -48.8 (c = 0.56, $CHCl_3$). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.83 (d, $J$ = 7.5 Hz, 1H), 7.68 (t, $J$ = 7.5 Hz, 1H), 7.49-7.42 (m, 2H), 7.15-6.99 (m, 3H), 6.89-6.81 (m, 2H), 5.62-5.53 (m, 1H), 4.85-4.79 (m, 1H), 4.72-4.64 (m, 1H), 3.66 (td, $J$ = 10.5 Hz, $J$ = 3.9 Hz, 1H), 3.47 (AB, $J$ = 17.7 Hz, 1H), 3.33 (AB, $J$ = 17.4 Hz, 1H), 2.23 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 200.30, 150.49, 136.87, 135.74, 135.64, 135.03, 134.48, 130.14, 128.71, 128.22, 126.48, 126.00, 125.98, 124.93, 122.79, 75.71, 70.04, 48.56, 37.73, 19.55, 19.53; GC-MS: 362 ($M^+$, 0.2), 144 (100), 129 (39), 116 (22), 105 (7), 89 (17), 63 (4); IR (neat): 2099, 1704, 1606, 1554, 1377, 1236, 896, 746 cm$^{-1}$; HRMS (EI): Exact mass calcd for

$C_{20}H_{18}N_4O_3$ $[M]^+$: 362.1379, found: 362.1380.



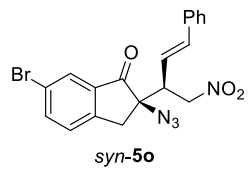
*syn*-**5m**

Product *syn*-**5m** was obtained in 88% yield as light yellow liquid (-20 °C, 4 days). $^1$H NMR analysis revealed that the dr value was 12:1. HPLC analysis [Chiralcel OZ-H, 5% $^i$PrOH/hexane, 1.0 mL/min, 230 nm; major diastereomer: tr (major) = 16.67 min, tr (minor) = 25.86 min, minor diastereomer: tr (major) = 19.70 min, tr (minor) = 18.47 min] gave the isomeric composition of major diastereomer: 90% ee; $[\alpha]^{25}_D$ = -25.6 (c = 1.20, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.82-7.77 (m, 2H), 7.35 (t, *J* = 8.0 Hz, 1H), 7.27-7.22 (m, 3H), 7.21-7.16 (m, 2H), 6.67 (d, *J* = 15.6 Hz, 1H), 5.79-5.73 (m, 1H), 4.77 (ABd, *J* = 12.6 Hz, *J* = 3.6 Hz, 1H), 4.67 (ABd, *J* = 12.6 Hz, *J* = 10.8 Hz, 1H), 3.67 (td, *J* = 10.0 Hz, *J* = 4.0 Hz, 1H), 3.37 (AB, *J* = 18 Hz, 1H), 3.22 (AB, *J* = 18.4 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 199.66, 150.29, 139.40, 137.58, 136.17, 135.33, 130.34, 128.50, 128.46, 126.59, 123.67, 121.83, 120.66, 75.41, 69.96, 47.91, 38.55; IR (neat): 2103, 1718, 1553, 1378, 1266, 1122, 908, 730, 692 cm$^{-1}$; HRMS (DART): Exact mass calcd for $C_{19}H_{19}N_5O_3Br$ $[M+NH_4]^+$: 444.0666, Found: 444.0668.



*syn*-**5n**

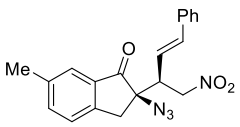
Product *syn*-**5n** was obtained in 79% yield as white solid (2 days), m.p. = 125-127 °C. $^1$H NMR analysis revealed that the dr value was 12:1. HPLC analysis [Chiralcel OZ-H, 10% $^i$PrOH/hexane, 1.0 mL/min, 230 nm; major diastereomer: tr (major) = 13.54 min, tr (minor) = 21.69 min, minor diastereomer: tr (major) = 24.17 min, tr (minor) = 16.04 min] gave the isomeric composition of major diastereomer: 88% ee; $[\alpha]^{25}_D$ = -24.9 (c = 0.9, $CHCl_3$). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.76 (d, *J* = 8.4 Hz, 1H), 7.45-7.41 (m, 2H), 7.28-7.20 (m, 3H), 7.19-7.12 (m, 2H), 6.64 (d, *J* = 15.6 Hz, 1H), 5.72 (dd, *J* = 15.6 Hz, *J* = 9.9 Hz, 1H), 4.82 (ABd, *J* = 12.6 Hz, *J* = 3.9 Hz, 1H), 4.70 (ABd, *J* = 12.6 Hz, *J* = 10.5 Hz, 1H), 3.63 (td, *J* = 10.2 Hz, *J* = 3.9 Hz, 1H), 3.44 (AB, *J* = 18.0 Hz, 1H), 3.28 (AB, *J* = 18.0 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 198.9, 151.9, 143.6, 137.6, 135.3, 132.7, 129.6, 128.6, 128.5, 126.7, 126.6, 126.0, 120.7, 75.5, 70.1, 48.2, 37.4; IR (neat): 2104, 1716, 1599, 1554, 1324, 1242, 969, 745, 694 cm$^{-1}$; HRMS (ESI): Exact mass calcd for $C_{19}H_{19}ClN_5O_3$ $[M+NH_4]^+$: 400.1171, Found: 400.1170.



*syn*-**5o**

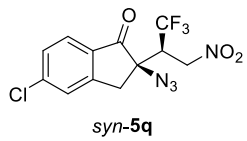
Product *syn*-**5o** was obtained in 72% yield as white solid (-20 °C, 4 days), m.p. = 129-130 °C. $^1$H NMR analysis revealed that the dr value was 13:1. HPLC analysis [Chiralcel OZ-H, 5% $^i$PrOH/hexane, 1.0 mL/min, 230 nm; major diastereomer: tr (major) = 19.05 min, tr (minor) = 29.78 min, minor

diastereomer: tr (major) = 38.31 min, tr (minor) = 23.10 min] gave the isomeric composition of major diastereomer: 93% ee; $[\alpha]^{25}_D$ = -89.1 (c = 0.93, $CHCl_3$). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.96 (d, *J* = 1.8 Hz, 1H), 7.76 (dd, *J* = 8.2 Hz, *J* = 1.8 Hz, 1H), 7.31 (d, *J* = 8.4 Hz, 1H), 7.28-7.22 (m, 3H), 7.17-7.13 (m, 2H), 6.63 (d, *J* = 15.6 Hz, 1H), 5.75-5.67 (m, 1H), 4.83 (ABd, *J* = 12.6 Hz, *J* = 3.9 Hz, 1H), 4.70 (ABd, *J* = 12.6 Hz, *J* = 10.5 Hz, 1H), 3.63 (td, *J* = 9.9 Hz, *J* = 3.6 Hz, 1H), 3.41 (AB, *J* = 18 Hz, 1H), 3.25 (AB, *J* = 17.7 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 199.0, 149.0, 139.6, 137.6, 136.0, 135.3, 128.6, 128.5, 128.0, 127.7, 126.6, 122.8, 120.7, 75.5, 70.3, 48.2, 37.3; IR (neat): 2099, 1725, 1600, 1555, 1374, 1212, 969, 744, 673 cm$^{-1}$; HRMS (DART): Exact mass calcd for $C_{19}H_{19}N_5O_3Br$ $[M+NH_4]^+$: 444.0666, Found: 444.0665.



*syn*-**5p**

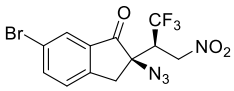
Product *syn*-**5p** was obtained in 69% yield as white solid (8 days), m.p. = 130-132 $^o$C. $^1$H NMR analysis revealed that the dr value was 14:1. HPLC analysis [Chiralcel OZ-H, 5% $^i$PrOH/hexane, 1.0 mL/min, 230 nm; major diastereomer: tr (major) = 14.59 min, tr (minor) = 21.22 min, minor diastereomer: tr (major) = 23.96 min, tr (minor) = 17.80 min] gave the isomeric composition of major diastereomer: 95% ee; $[\alpha]^{25}_D$ = -69.6 (c = 1.44, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.62 (s, 1H), 7.49-7.46 (m, 1H), 7.30 (d, *J* = 7.6 Hz, 1H), 7.26-7.21 (m, 3H), 7.15-7.13 (m, 2H), 6.62 (d, *J* = 15.6 Hz, 1H), 5.74 (dd, *J* = 15.6 Hz, *J* = 10.0 Hz, 1H), 4.81 (ABd, *J* = 12.6 Hz, *J* = 3.6 Hz, 1H), 4.69 (ABd, *J* = 12.6 Hz, *J* = 10.8 Hz, 1H), 3.63 (td, *J* = 10.4 Hz, *J* = 3.6 Hz, 1H), 3.41 (AB, *J* = 17.6 Hz, 1H), 3.25 (AB, *J* = 17.2 Hz, 1H), 2.42 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 200.3, 147.9, 138.9, 138.2, 137.3, 135.5, 134.5, 128.5, 128.4, 126.6, 126.2, 124.7, 121.2, 75.7, 70.4, 48.3, 37.3, 21.1; IR (neat): 2108, 1715, 1555, 1494, 1377, 1285, 969, 752, 695 cm$^{-1}$; HRMS (ESI): Exact mass calcd for $C_{20}H_{22}N_5O_3$ $[M+NH_4]^+$: 380.1717, Found: 380.1715.



*syn*-**5q**

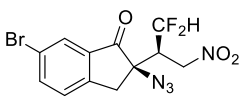
The reaction was conducted with replacing 5Å MS by 20 mol% $K_2HPO_4{\cdot}3H_2O$. Product *syn*-**5q** was obtained in 76% yield as light yellow liquid (3 days). $^1$H NMR analysis revealed that the dr value was 3:1. HPLC analysis [Chiralcel OZ-H, 5% $^i$PrOH/hexane, 1.0 mL/min, 230 nm; major diastereomer: tr (major) = 9.83 min, tr (minor) = 15.06 min, minor diastereomer: tr (major) = 16.55 min, tr (minor) = 13.47 min] gave the isomeric composition of major diastereomer: 90% ee; $[\alpha]^{25}_D$ = -94.6 (c = 0.31, $CHCl_3$). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.81 (d, *J* = 8.1 Hz, 1H), 7.52-7.48 (m, 2H), 4.75-4.67 (m, 1H), 4.49-4.43 (m, 1H), 4.17-4.05 (m, 1H), 3.39 (AB, *J* = 24.4 Hz, 1H), 3.27 (AB, *J* = 24.4 Hz, 1H); $^{13}$C NMR (125 MHz,

$CDCl_3$): $\delta$ 196.08, 151.91, 144.20, 131.25, 130.02, 126.94, 126.90, 125.16 (q, $J_{C\text{-}F}$ = 279.9 Hz, 1C), 70.03 (t, $J_{C\text{-}F}$ = 3.4 Hz, 1C), 66.83, 45.16 (q, $J_{C\text{-}F}$ = 26.6 Hz, 1C), 36.83 (d, $J_{C\text{-}F}$ = 2.4 Hz, 1C); $^{19}$F NMR (282 MHz, $CDCl_3$): $\delta$ -64.86 (d, $J$ = 5.4 Hz, 3F); IR (neat): 2926, 2111, 1719, 1599, 1569, 1379, 1212, 1072, 903, 619 cm$^{-1}$; HRMS (DART): Exact mass calcd for $C_{12}H_9N_4O_3ClF_3$ $[M+H]^+$: 349.0310, Found: 349.0307.



*syn*-**5r**

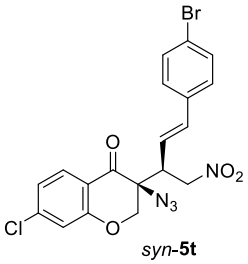
The reaction was conducted with replacing 5Å MS by 20 mol% $K_2HPO_4{\cdot}3H_2O$. Product *syn*-**5r** was obtained in 76% yield as light yellow liquid (2 days). $^1$H NMR analysis revealed that the dr value was 4:1. HPLC analysis [Chiralcel OZ-H, 5% $^i$PrOH/hexane, 1.0 mL/min, 230 nm; major diastereomer: tr (major) = 9.73 min, tr (minor) = 15.67 min, minor diastereomer: tr (major) = 17.66 min, tr (minor) = 16.4 min] gave the isomeric composition of major diastereomer: 92% ee; $[\alpha]^{25}_D$ = -107.9 (c = 1.16, $CHCl_3$) (dr = 4:1). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.01 (d, $J$ = 1.6 Hz, 0.2H) (minor), 7.99 (d, $J$ = 1.6 Hz, 1H) (major), 7.86-7.83 (m, 1H) (major), 7.82 (d, $J$ = 1.6 Hz, 0.1H) (minor), 7.41 (d, $J$ = 8.0 Hz, 1H) (major), 7.38 (s, 0.1H) (minor), 5.06 (ABd, $J$ = 15.2 Hz, $J$ = 4.8 Hz, 0.2H) (minor), 4.78 (ABd, $J$ = 15.2 Hz, $J$ = 5.6 Hz, 0.2H) (minor), 4.74-4.68 (m, 1H) (major), 4.51-4.46 (m, 1H) (major), 4.30 (t, $J$ = 6.8 Hz, 0.2H) (minor), 4.15-4.05 (m, 1H) (major), 3.42 (AB, $J$ = 18.0 Hz, 0.2H) (minor), 3.37 (AB, $J$ = 18.4 Hz, 1H) (major), 3.25 (AB, $J$ = 18 Hz, 1H) (major), 3.09 (AB, $J$ = 18.0 Hz, 0.2H) (minor); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 196.2 (major), 195.9 (minor), 149.0 (major), 148.4 (minor), 140.0 (major), 139.8 (minor), 134.6 (major), 134.5 (minor), 129.8 (q, $J_{C\text{-}F}$ = 207.5 Hz, 1C) (minor), 128.6 (minor), 128.5 (major), 128.1 (major), 128.0 (minor), 125.1 (q, $J_{C\text{-}F}$ = 279.9 Hz, 1C) (major), 123.2 (major), 123.1 (minor), 70.0 (d, $J_{C\text{-}F}$ = 2.7 Hz, 1C) (major), 67.0 (major), 66.7 (minor), 65.5 (minor), 45.2 (q, $J_{C\text{-}F}$ = 26.9 Hz, 1C) (major), 36.8 (d, $J_{C\text{-}F}$ = 2.3 Hz, 1C) (major), 35.7 (d, $J_{C\text{-}F}$ = 2.5 Hz, 1C) (minor); $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ -64.49 (s, 3F) (minor), -64.81 (s, 3F) (major); IR (neat): 2926, 2111, 1719, 1669, 1563, 1467, 1376, 1217, 1019, 612 cm$^{-1}$; HRMS (DART): Exact mass calcd for $C_{12}H_9N_4O_3BrF_3$ $[M+H]^+$: 392.9805, Found: 392.9800.



*syn*-**5s**

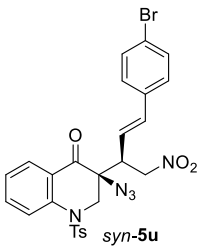
The reaction was conducted with replacing 5Å MS by 20 mol% $K_2HPO_4{\cdot}3H_2O$. Product *syn*-**5s** was obtained in 52% yield as light yellow liquid (6 days). $^1$H NMR analysis revealed that the dr value was 2:1. HPLC analysis [Chiralcel OZ-H, 3% $^i$PrOH/hexane, 1.0 mL/min, 230 nm; major diastereomer: tr (major) = 25.59 min, tr (minor) = 41.71 min, minor diastereomer: tr (major) = 37.49 min, tr (minor) = 34.93 min] gave the isomeric

composition of major diastereomer: 87% ee; $[\alpha]^{25}_{D}$ = -63.1 (c = 1.12, $CHCl_3$) (dr = 2:1). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.98 (t, *J* = 2.4 Hz, 1.5H), 7.85-7.81 (m, 1.5H), 7.42-7.37 (m, 1.5H), 6.46-6.18 (m, 1H) (major), 6.08-5.80 (m, 0.5H) (minor), 4.91 (ABd, *J* = 14.8 Hz, *J* = 4.8 Hz, 0.5H) (minor), 4.82 (ABd, *J* = 14.8Hz, *J* = 6.4 Hz, 0.5H) (minor), 4.74 (ABd, *J* = 14.4 Hz, *J* = 6.8 Hz, 1H) (major), 4.32 (ABd, *J* = 14.4 Hz, *J* = 4.0 Hz, 1H) (major), 3.71-3.62 (m, 1.5H), 3.40 (AB, *J* = 17.6 Hz, 0.5H) (minor), 3.32 (AB, *J* = 18.0 Hz, 1H) (major), 3.18 (AB, *J* = 18.0 Hz, 1H) (major), 3.02 (AB, *J* = 17.6 Hz, 0.5H) (minor); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 197.2 (minor), 196.7 (major), 149.0 (major), 148.9 (minor), 139.9 (major), 139.8 (minor), 134.9 (major), 134.7 (minor), 128.4 (major), 128.4 (minor), 128.1 (major), 123.2 (major), 123.0 (minor), 114.2 (t, $J_{C\text{-}F}$ = 243.2 Hz, 1C) (major), 114.0 (t, $J_{C\text{-}F}$ = 244.4 Hz, 1C) (minor), 69.5 (d, $J_{C\text{-}F}$ = 4.6 Hz, 1C) (minor), 69.1 (major), 67.9 (d, $J_{C\text{-}F}$ = 6.1 Hz, 1C) (major), 67.3 (d, $J_{C\text{-}F}$ = 4.7 Hz, 1C) (minor), 44.5 (t, $J_{C\text{-}F}$ = 20.1 Hz, 1C) (major), 36.7 (d, $J_{C\text{-}F}$ = 2.9 Hz, 1C) (major), 35.9 (t, $J_{C\text{-}F}$ = 2.5 Hz, 1C) (minor); $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ -117.77 (d, $J_{F\text{-}F}$ = 295.5 Hz, 1F) (minor), -120.56 (d, $J_{F\text{-}F}$ = 294.4 Hz, 1F) (major), -122.68 (d, $J_{F\text{-}F}$ = 295.2 Hz, 1F) (minor), -122.93 (d, $J_{F\text{-}F}$ = 294.4 Hz, 1F) (major); IR (neat): 2926, 2111, 1719, 1563, 1467, 1376, 1217, 1019, 612 cm$^{-1}$; HRMS (DART): Exact mass calcd for $C_{12}H_{10}N_2O_3BrF_2$ $[M\text{-}N_2+H]^+$: 346.9837, Found: 346.9837.

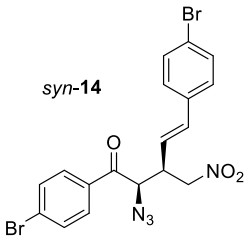


*syn*-**5t**

Product *syn*-**5t** was obtained in 68% yield as light yellow liquid (7 days). $^1$H NMR analysis revealed that the dr value was 9:1. HPLC analysis [Chiralcel AD-H, 10% $^i$PrOH/hexane, 1.0 mL/min, 230 nm; major diastereomer: tr (major) = 25.54 min, tr (minor) = 23.50 min, minor diastereomer: tr (major) = 21.54 min, tr (minor) = 30.51 min] gave the isomeric composition of major diastereomer: 93% ee; $[\alpha]^{25}_{D}$ = +265.4 (c = 1.0, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.85 (d, *J* = 8.4 Hz, 1H), 7.41 (d, *J* = 8.4 Hz, 2H), 7.14-7.11 (m, 3H), 7.08 (d, *J* = 1.6 Hz, 1H), 6.37 (d, *J* = 15.6 Hz, 1H), 6.01 (dd, *J* = 15.8 Hz, *J* = 9.6 Hz, 1H), 4.84-4.82 (m, 2H), 4.53 (AB, *J* = 12.8 Hz, 1H), 4.49 (AB, *J* = 12.8 Hz, 1H), 3.54-3.48 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 186.7, 160.8, 143.6, 136.2, 134.2, 131.8, 129.4, 128.2, 123.9, 122.6, 121.6, 118.3, 118.1, 75.7, 71.6, 65.9, 45.0; IR (neat): 2253, 2118, 1713, 1489, 1364, 1227, 903, 727, 650 cm$^{-1}$; HRMS (ESI): Exact mass calcd for $C_{19}H_{14}N_4O_4ClBrNa$ $[M+Na]^+$: 498.9779, Found: 498.9779.

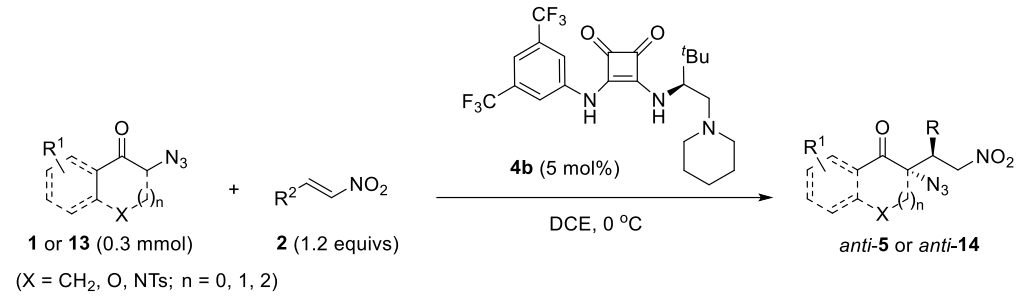



Product *syn*-**5u** was obtained in 53% yield as light yellow liquid (7 days). $^1$H NMR analysis revealed that the dr value was 3:1. HPLC analysis [Chiralcel OZ-H, 30% $^i$PrOH/hexane, 1.0 mL/min, 230 nm; major diastereomer: tr (major) = 39.69 min, tr (minor) = 49.02 min, minor diastereomer: tr (major) = 21.69 min, tr (minor) = 29.41 min] gave the isomeric composition of major diastereomer: 65% ee; $[\alpha]^{25}_D$ = +4.3 (c = 0.2, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.01 (dd, *J* = 8.0 Hz, *J* = 1.5 Hz, 1H), 7.85-7.84 (m, 2H), 7.80 (dd, *J* = 8.0 Hz, *J* = 1.0 Hz, 1H), 7.59-7.56 (m, 1H), 7.44 (d, *J* = 8.5 Hz, 2H), 7.37 (d, *J* = 8.0 Hz, 2H), 7.23-7.19 (m, 1H), 7.18-7.17 (m, 2H), 6.42 (d, *J* = 16.0 Hz, 1H), 6.12-6.07 (m, 1H), 4.93 (ABd, *J* = 12.5 Hz, *J* = 3.5 Hz, 1H), 4.83 (ABd, *J* = 12.5 Hz, *J* = 10.5 Hz, 1H), 4.40 (AB, *J* = 13.5 Hz, 1H), 4.16 (AB, *J* = 14.0 Hz, 1H), 3.77-3.72 (m, 1H), 2.45 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 188.6, 145.3, 141.9, 136.2, 136.1, 135.6, 134.4, 131.7, 130.2, 129.7, 128.3, 127.2, 124.4, 122.5, 121.6, 121.4, 119.2, 75.4, 67.5, 52.1, 44.9, 21.6; IR (neat): 2253, 1713, 1582, 1443, 1364, 1227, 1082, 905, 729, 650 cm$^{-1}$; HRMS (ESI): Exact mass calcd for $C_{26}H_{22}N_5O_5BrSNa$ $[M+Na]^+$: 618.0417, Found: 618.0405.




The reaction was conducted with 30 mol% **3a** at rt. Product *syn*-**14** was obtained in 38% yield as light yellow liquid (7 days). $^1$H NMR analysis revealed that the dr value was 3:1. HPLC analysis [Chiralcel IF, 15% $^i$PrOH/hexane, 1.0 mL/min, 230 nm; major diastereomer: tr (major) = 10.50 min, tr (minor) = 9.53 min, minor diastereomer: tr (major) = 18.13 min, tr (minor) = 12.91 min] gave the isomeric composition of major diastereomer: 81% ee; $[\alpha]^{25}_D$ = +32.2 (c = 0.74, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.81-7.78 (m, 2H), 7.71-7.68 (m, 2H), 7.44-7.41 (m, 2H), 7.14-7.10 (m, 2H), 6.27 (d, *J* = 16 Hz, 1H), 5.96 (dd, *J* = 15.8 Hz, *J* = 9.2 Hz, 1H), 5.15 (d, *J* = 4.4 Hz, 1H), 4.77 (ABd, *J* = 13.6 Hz, *J* = 7.6 Hz, 1H), 4.51 (ABd, *J* = 13.6 Hz, *J* = 6.0 Hz, 1H), 3.70-3.63 (m, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 193.02, 135.21, 134.28, 133.14, 132.65, 131.82, 129.94, 129.88, 128.13, 122.56, 121.07, 75.74, 64.20, 43.48; IR (neat): 2111, 1712, 1608, 1554, 1488, 1219, 1073, 910, 735 cm$^{-1}$; HRMS (DART): Exact mass calcd for $C_{18}H_{15}N_2O_3Br_2$ $[M-N_2+H]^+$: 464.9444, Found: 464.9441.

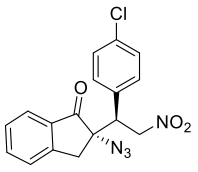
## 5. General procedure for *anti*-selective Michael addition.




**1** or **13** (0.3 mmol) **2** (1.2 equivs) *anti*-**5** or *anti*-**14**

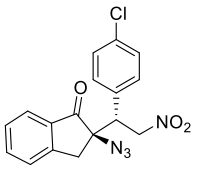
(X = $CH_2$, O, NTs; n = 0, 1, 2)

To a 5.0 mL vial were added bifunctional squaramide catalyst **4b** (7.4 mg, 0.015 mmol, 5.0 mol%) and α-azido ketones **1** or **13** (0.3 mmol, 1.0 equiv), followed by the addition of dry DCE (3.0 mL). The reaction mixture was cooled down to 0 °C and stirred for about 30 min, then nitroolefins **2** (0.36 mmol, 1.2 equivs) was added. After full consumption of α-azido ketones by TLC analysis, the crude reaction mixture was rapidly passed through a short silica gel column chromatography (5 cm), washed with PE:EtOAc (4:1, v/v), and concentrated in *vacuo*. To determine the diastereoselectivity of the product, the residue was first dissolved in $CDCl_3$, and took some samples for $^1H$ NMR analysis. Then the sample for analysis and the rest of crude residue were recombined and purified by silica gel column chromatography (PE:$Et_2O$ = 10:1, v/v) to afford the desired products *anti*-**5** or *anti*-**14**.



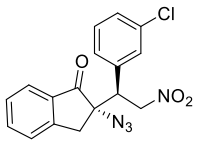

(*S*,*S*)-**5a**

Product (*S*,*S*)-**5a** was obtained in 99% yield as light yellow liquid (2.5 days). $^1H$ NMR analysis revealed that the dr value was 15:1. HPLC analysis [Chiralcel OZ-H, 5% $^i$PrOH/hexane, 1.0 mL/min, 230 nm; major diastereomer: tr (major) = 28.20 min, tr (minor) = 36.94 min, minor diastereomer: tr (major) = 20.03 min, tr (minor) = 32.90 min] gave the isomeric composition of major diastereomer: 95% ee; $[\alpha]^{25}_D$ = +130.5 (c = 0.9, $CHCl_3$). $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.79-7.77 (m, 1H), 7.64 (td, *J* = 7.6 Hz, *J* = 1.2 Hz, 1H), 7.45-7.41 (m, 1H), 7.35 (dt, *J* = 7.6 Hz, *J* = 0.8 Hz, 1H), 7.28-7.26 (m, 4H), 5.43 (ABd, *J* = 14.0 Hz, *J* = 4.2 Hz, 1H), 4.94 (ABd, *J* = 13.8 Hz, *J* = 10.5 Hz, 1H), 3.96 (dd, *J* = 10.8 Hz, *J* = 4.0 Hz, 1H), 3.26 (AB, *J* = 17.6 Hz, 1H), 3.00 (AB, *J* = 17.6 Hz, 1H); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 199.8, 149.9, 136.8, 134.7, 133.4, 133.1, 130.4, 129.2, 128.8, 126.3, 125.5, 75.4, 70.5, 46.7, 37.0; IR (neat): 2104, 1712, 1551, 1466, 1339, 1093, 909, 739, 627 $cm^{-1}$; HRMS (ESI): Exact mass calcd for $C_{17}H_{17}ClN_5O_3$ $[M+NH_4]^+$: 374.1014, Found: 374.1012.



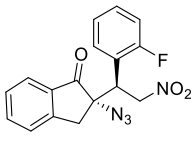
(*R*,*R*)-**5a**

Product (*R*,*R*)-**5a** was obtained in 99% yield as light yellow liquid (2.5 days) by using (*R*)-**4b** as catalyst. $^{1}$H NMR analysis revealed that the dr value was 13:1. HPLC analysis [Chiralcel OZ-H, 5% $^{i}$PrOH/hexane, 1.0 mL/min, 230 nm; major diastereomer: tr (major) = 34.69 min, tr (minor) = 26.46 min, minor diastereomer: tr (major) = 30.60 min, tr (minor) = 19.11 min] gave the isomeric composition of major diastereomer: 95% ee; $[\alpha]^{25}_{D}$ = -113.3 (c = 1.93, $CHCl_3$). $^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.76 (d, *J* = 7.6 Hz, 1H), 7.63 (tt, *J* = 7.6 Hz, *J* = 1.2 Hz, 1H), 7.41 (t, *J* = 7.6 Hz, 1H), 7.35 (d, *J* = 7.6 Hz, 1H), 7.29-7.24 (m, 4H), 5.39 (ABd, *J* = 13.8 Hz, *J* = 4.4 Hz, 1H), 4.95 (ABd, *J* = 13.8 Hz, *J* = 10.4 Hz, 1H), 3.98 (dd, *J* = 10.6 Hz, *J* = 4.4 Hz, 1H), 3.27 (AB, *J* = 18 Hz, 1H), 2.99 (AB, *J* = 17.6 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 199.8, 149.9, 136.7, 134.6, 133.3, 133.0, 130.3, 129.1, 128.7, 126.2, 125.3, 75.3, 70.4, 46.6, 36.8; IR (neat): 2925, 2104, 1712, 1606, 1553, 1377, 1094, 909, 738, 626 cm$^{-1}$; HRMS (ESI): Exact mass calcd for $C_{17}H_{17}ClN_5O_3$ $[M+NH_4]^+$: 374.1014, Found: 374.1010.



*anti*-**5b**

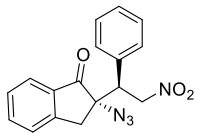
Product *anti*-**5b** was obtained in 99% yield as white solid (2.5 days), m.p. = 117-119 $^{o}$C. $^{1}$H NMR analysis revealed that the dr value was 14:1. HPLC analysis [Chiralcel OZ-H, 3% $^{i}$PrOH/hexane, 1.0 mL/min, 230 nm; major diastereomer: tr (major) = 32.51 min, tr (minor) = 41.57 min, minor diastereomer: tr (major) = 22.95 min, tr (minor) = 35.53 min] gave the isomeric composition of major diastereomer: 95% ee; $[\alpha]^{25}_{D}$ = +88.0 (c = 0.94, $CHCl_3$). $^{1}$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.80 (d, *J* = 7.8 Hz, 1H), 7.66 (td, *J* = 7.5 Hz, *J* = 1.2 Hz, 1H), 7.47-7.42 (m, 1H), 7.39-7.33 (m, 2H), 7.28-7.22 (m, 3H), 5.40 (ABd, *J* = 13.8 Hz, *J* = 4.4 Hz, 1H), 4.94 (ABd, *J* = 13.6 Hz, *J* = 10.8 Hz, 1H), 3.91 (dd, *J* = 10.7 Hz, *J* = 3.9 Hz, 1H), 3.26 (AB, *J* = 17.7 Hz, 1H), 3.02 (AB, *J* = 17.7 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 199.81, 136.84, 136.81, 134.85, 133.40, 130.19, 129.08, 128.96, 128.79, 127.35, 126.30, 125.49, 75.34, 70.57, 47.00, 37.24; IR (neat): 2922, 2106, 1714, 1554, 1466, 1378, 1087, 906, 741 cm$^{-1}$; HRMS (ESI): Exact mass calcd for $C_{17}H_{17}ClN_5O_3$ $[M+NH_4]^+$: 374.1014, Found: 374.1013.



*anti*-**5c**

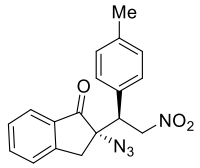
Product *anti*-**5c** was obtained in 95% yield as white solid (3 days), m.p. = 63-64 $^{o}$C. $^{1}$H NMR analysis revealed that the dr value was 8:1. HPLC analysis [Chiralcel OZ-H, 3% $^{i}$PrOH/hexane, 1.0 mL/min, 230 nm; major diastereomer: tr (major) = 24.77 min, tr (minor) = 23.03 min, minor diastereomer: tr (major) = 20.40 min, tr (minor) = 30.12 min] gave the isomeric composition of major diastereomer: 91% ee; $[\alpha]^{25}_{D}$ = +76.6 (c

= 1.5, $CHCl_3$). $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 7.80 (d, $J$ = 7.8 Hz, 1H), 7.66 (td, $J$ = 7.5 Hz, $J$ = 1.2 Hz, 1H), 7.51 (td, $J$ = 7.5 Hz, $J$ = 1.8 Hz, 1H), 7.46-7.38 (m, 2H), 7.33-7.25 (m, 1H), 7.15 (td, $J$ = 7.5 Hz, $J$ = 1.5 Hz, 1H), 7.18-7.01 (m, 1H), 5.50-5.44 (m, 1H), 5.08-5.00 (m, 1H), 4.32 (dd, $J$ = 10.2 Hz, $J$ = 4.5 Hz, 1H), 3.33 (AB, $J$ = 17.7 Hz, 1H), 3.03 (AB, $J$ = 17.7 Hz, 1H); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 199.9, 160.8 (d, $J_{C\text{-}F}$ = 245.0 Hz, 1C), 150.0, 136.7, 133.4, 130.3 (d, $J_{C\text{-}F}$ = 8.6 Hz, 1C), 130.2 (d, $J_{C\text{-}F}$ = 3.2 Hz, 1C), 128.7, 126.3, 125.3, 124.8 (d, $J_{C\text{-}F}$ = 3.5 Hz, 1C), 122.1 (d, $J_{C\text{-}F}$ = 13.3 Hz, 1C), 116.0 (d, $J_{C\text{-}F}$ = 23.1 Hz, 1C), 74.6 (d, $J_{C\text{-}F}$ = 2.7 Hz, 1C), 71.0, 40.5, 37.4 (d, $J_{C\text{-}F}$ = 2.8 Hz, 1C); $^{19}F$ NMR (282 MHz, $CDCl_3$): $\delta$ -115.36 (s, 1F); IR (neat): 2107, 1715, 1555, 1467, 1342, 1233, 909, 760 $cm^{-1}$; HRMS (ESI): Exact mass calcd for $C_{17}H_{17}FN_5O_3$ $[M+NH_4]^+$: 358.1310, Found: 358.1307.



*anti*-**5d**

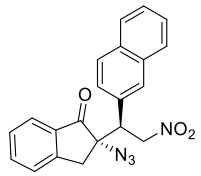
Product *anti*-**5d** was obtained in 90% yield as white solid (5 days), m.p. = 99-101 $^oC$. $^1H$ NMR analysis revealed that the dr value was 20:1. HPLC analysis [Chiralcel OZ-H, 5% $^i$PrOH/hexane, 1.0 mL/min, 230 nm; major diastereomer: tr (major) = 22.08 min, tr (minor) = 27.85 min, minor diastereomer: tr (major) = 16.36 min, tr (minor) = 24.30 min] gave the isomeric composition of major diastereomer: 96% ee; $[\alpha]^{25}_D$ = +124.4 (c = 0.44, $CHCl_3$). $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.77 (d, $J$ = 8.0 Hz, 1H), 7.63 (td, $J$ = 7.2 Hz, $J$ = 1.2 Hz, 1H), 7.41 (t, $J$ = 7.6 Hz, 1H), 7.35-7.24 (m, 6H), 5.40 (ABd, $J$ = 13.6 Hz, $J$ = 4.4 Hz, 1H), 5.00 (ABd, $J$ = 13.6 Hz, $J$ = 10.4 Hz, 1H), 3.99 (dd, $J$ = 10.2 Hz, $J$ = 4.4 Hz, 1H), 3.31 (AB, $J$ = 17.6 Hz, 1H), 2.99 (AB, $J$ = 17.6 Hz, 1H); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 200.1, 150.1, 136.6, 134.5, 133.6, 129.0, 128.9, 128.7, 128.6, 126.2, 125.4, 75.6, 70.7, 47.3, 36.9; IR (neat): 2105, 1712, 1604, 1551, 1422, 1287, 699 $cm^{-1}$; HRMS (ESI): Exact mass calcd for $C_{17}H_{18}N_5O_3$ $[M+NH_4]^+$: 340.1404, Found: 340.1402.



*anti*-**5e**

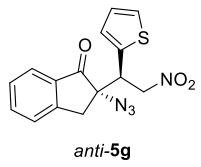
Product *anti*-**5e** was obtained in 91% yield as light yellow liquid (5 days). $^1H$ NMR analysis revealed that the dr value was 25:1. HPLC analysis [Chiralcel OZ-H, 5% $^i$PrOH/hexane, 1.0 mL/min, 230 nm; major diastereomer: tr (major) = 18.29 min, tr (minor) = 24.24 min, minor diastereomer: tr (major) = 13.85 min, tr (minor) = 21.27 min] gave the isomeric composition of major diastereomer: 95% ee; $[\alpha]^{25}_D$ = +142.5 (c = 2.3, $CHCl_3$). $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.77 (d, $J$ = 8.0 Hz, 1H), 7.62 (td, $J$ = 7.6 Hz, $J$ = 1.6 Hz, 1H), 7.43-7.39 (m, 1H), 7.36-7.33 (m, 1H), 7.20-7.18 (m, 2H), 7.09-7.07 (m, 2H), 5.36 (ABd, $J$ = 13.6 Hz, $J$ = 4.4 Hz, 1H), 4.97 (ABd, $J$ = 13.6 Hz, $J$ = 10.4 Hz, 1H), 3.96 (dd, $J$ = 10.6 Hz, $J$ = 4.4 Hz, 1H),

3.32 (AB, $J$ = 17.6 Hz, 1H), 2.98 (AB, $J$ = 17.6 Hz, 1H), 2.27 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 200.1, 150.1, 138.3, 136.5, 133.5, 131.2, 129.5, 128.8, 128.4, 126.2, 125.2, 75.6, 70.7, 46.8, 36.7, 20.9; IR (neat): 2104, 1714, 1554, 1378, 1219, 910, 799, 627 cm$^{-1}$; HRMS (ESI): Exact mass calcd for $C_{18}H_{20}N_5O_3$ $[M+NH_4]^+$: 354.1561, Found: 354.1559.



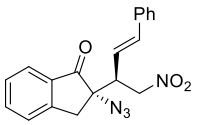
*anti*-**5f**

Product *anti*-**5f** was obtained in 99% yield as white solid (5 days), m.p. = 126-128 $^o$C. $^1$H NMR analysis revealed that the dr value was 22:1. HPLC analysis [Chiralcel OZ-H, 3% $^i$PrOH/hexane, 1.0 mL/min, 230 nm; major diastereomer: tr (major) = 39.89 min, tr (minor) = 51.85 min, minor diastereomer: tr (major) = 28.61 min, tr (minor) = 50.18 min] gave the isomeric composition of major diastereomer: 95% ee; $[\alpha]^{25}_D$ = +129.7 (c = 0.60, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.80-7.75 (m, 5H), 7.59 (t, $J$ = 7.6 Hz, 1H), 7.49-7.46 (m, 3H), 7.38 (t, $J$ = 7.6 Hz, 1H), 7.31 (d, $J$ = 7.6 Hz, 1H), 5.52-5.27 (m, 1H), 5.15-5.08 (m, 1H), 4.17-4.12 (m, 1H), 3.36 (AB, $J$ = 17.6 Hz, 1H), 2.99 (AB, $J$ = 17.6 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 200.03, 150.03, 136.62, 133.46, 133.07, 133.05, 132.15, 128.88, 128.75, 128.64, 127.99, 127.59, 126.64, 126.56, 126.27, 126.11, 125.44, 75.67, 70.90, 47.37, 37.13; GC-MS: 372 ($M^+$, 3), 191 (12), 154 (59), 149 (20), 144 (100), 128 (13), 116 (30), 89 (25), 49 (14); IR (neat): 2099, 1709, 1548, 1467, 1341, 1226, 914, 748, 671 cm$^{-1}$; HRMS (EI): Exact mass calcd for $C_{21}H_{16}N_4O_3$ $[M]^+$: 372.1222, found: 372.1217.



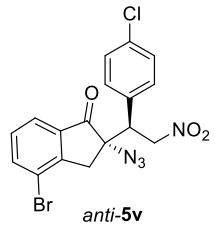
*anti*-**5g**

Product *anti*-**5g** was obtained in 96% yield as white solid (5 days), m.p. = 94-96 $^o$C. $^1$H NMR analysis revealed that the dr value was 20:1. HPLC analysis [Chiralcel OZ-H, 5% $^i$PrOH/hexane, 1.0 mL/min, 230 nm; major diastereomer: tr (major) = 23.33 min, tr (minor) = 27.78 min, minor diastereomer: tr (major) = 18.17 min, tr (minor) = 25.67 min] gave the isomeric composition of major diastereomer: 97% ee; $[\alpha]^{25}_D$ = +163.5 (c = 0.68, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.79 (d, $J$ = 7.6 Hz, 1H), 7.65 (td, $J$ = 7.6 Hz, $J$ = 1.2 Hz, 1H), 7.45-7.38 (m, 2H), 7.21 (dd, $J$ = 5.2 Hz, $J$ = 1.2 Hz, 1H), 6.98 (dd, $J$ = 3.6 Hz, $J$ = 1.2 Hz, 1H), 6.90 (dd, $J$ = 5.2 Hz, $J$ = 3.6 Hz, 1H), 5.37 (ABd, $J$ = 13.6 Hz, $J$ = 4.0 Hz, 1H), 4.86 (ABd, $J$ = 13.6 Hz, $J$ = 10.4 Hz, 1H), 4.38 (dd, $J$ = 10.4 Hz, $J$ = 4.0 Hz, 1H), 3.42 (AB, $J$ = 17.6 Hz, 1H), 3.08 (AB, $J$ = 17.6 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 199.77, 150.24, 136.64, 136.15, 133.50, 128.59, 128.55, 126.80, 126.33, 125.32, 76.65, 70.28, 43.56, 36.91; IR (neat): 2108, 1714, 1556, 1467, 1339, 1156, 911, 709 cm$^{-1}$; HRMS (ESI): Exact mass calcd for $C_{15}H_{16}N_5O_3S$ $[M+NH_4]^+$: 346.0968, Found: 346.0969.



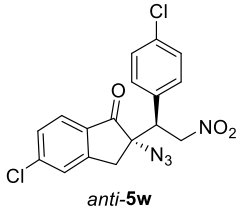
*anti*-**5h**

The reaction was conducted with 10 mol% **4b**. Product *anti*-**5h** was obtained in 78% yield as light yellow liquid (5 days). $^1$H NMR analysis revealed that the dr value was 6:1. HPLC analysis [Chiralcel OZ-H, 5% $^i$PrOH/hexane, 1.0 mL/min, 230 nm; major diastereomer: tr (major) = 19.04 min, tr (minor) = 26.94 min, minor diastereomer: tr (major) = 15.66 min, tr (minor) = 24.04 min] gave the isomeric composition of major diastereomer: 90% ee; $[\alpha]^{25}_D$ = +188.4 (c = 0.67, $CHCl_3$) (dr = 6:1). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.81 (d, *J* = 8.0 Hz, 1H), 7.69 (t, *J* = 8.0 Hz, 1H), 7.45 (t, *J* = 8.4 Hz, 2H), 7.25-7.23 (m, 3H), 7.21-7.19 (m, 2H), 6.58 (d, *J* = 16.0 Hz, 1H), 5.89 (dd, *J* = 15.7 Hz, *J* = 9.2 Hz, 1H), 5.08 (dd, *J* = 12.4 Hz, *J* = 4.0 Hz, 1H), 4.64 (dd, *J* = 12.4 Hz, *J* = 10.4 Hz, 1H), 3.66 (td, *J* = 10.0 Hz, *J* = 4.0 Hz, 1H), 3.42 (AB, *J* = 17.6 Hz, 1H), 3.11 (AB, *J* = 17.6 Hz, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 200.0, 150.3, 137.7, 136.7, 135.6, 133.8, 128.7, 128.6, 128.5, 126.6, 126.4, 125.4, 120.9, 75.7, 69.8, 46.2, 36.5; IR (neat): 2102, 1714, 1606, 1552, 1435, 1378, 1156, 970, 742, 693 cm$^{-1}$; HRMS (DART): Exact mass calcd for $C_{19}H_{20}N_5O_3$ $[M+ NH_4]^+$: 366.1561, Found: 366.1562.



*anti*-**5v**

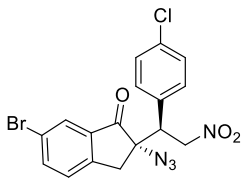
Product *anti*-**5v** was obtained in 89% yield as light yellow liquid (1.5 days). $^1$H NMR analysis revealed that the dr value was 10:1. HPLC analysis [Chiralcel OZ-H, 5% $^i$PrOH/hexane, 1.0 mL/min, 230 nm; major diastereomer: tr (major) = 24.61 min, tr (minor) = 26.47 min, minor diastereomer: tr (major) = 20.70 min, tr (minor) = 32.17 min] gave the isomeric composition of major diastereomer: 93% ee; $[\alpha]^{25}_D$ = +82.4 (c = 1.14, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.79 (dd, *J* = 7.8 Hz, *J* = 0.8 Hz, 1H), 7.70 (d, *J* = 7.6 Hz, 1H), 7.31 (t, *J* = 8.0 Hz, 1H), 7.28-7.23 (m, 4H), 5.34 (ABd, *J* = 13.8 Hz, *J* = 4.0 Hz, 1H), 4.96 (ABd, *J* = 13.6 Hz, *J* = 10.4 Hz, 1H), 4.05 (dd, *J* = 10.4 Hz, *J* = 4.4 Hz, 1H), 3.21 (AB, *J* = 18 Hz, 1H), 2.92 (AB, *J* = 18.4 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 199.3, 149.8, 139.3, 135.4, 134.9, 132.3, 130.4, 130.3, 129.3, 124.1, 121.6, 75.1, 70.4, 46.5, 37.6; IR (neat): 2109, 1721, 1556, 1494, 1379, 1096, 912, 733 cm$^{-1}$; HRMS (ESI): Exact mass calcd for $C_{17}H_{16}BrClN_5O_3$ $[M+NH_4]^+$: 452.0120, Found: 452.0117.



*anti*-**5w**

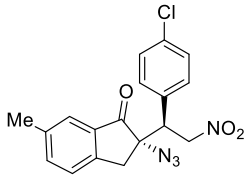
Product *anti*-**5w** was obtained in 86% yield as white solid (3 days), m.p. = 115-116 $^o$C. $^1$H NMR analysis revealed that the dr value was 17:1. HPLC analysis [Chiralcel OZ-H, 10% $^i$PrOH/hexane, 1.0 mL/min, 230 nm; major diastereomer: tr (major) = 19.55 min, tr (minor) = 30.55 min, minor

diastereomer: tr (major) = 14.92 min, tr (minor) = 23.18 min] gave the isomeric composition of major diastereomer: 95% ee; $[\alpha]^{25}_D$ = +143.1 (c = 1.10, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.71 (d, *J* = 8.4 Hz, 1H), 7.42-7.40 (m, 1H), 7.36-7.35 (m, 1H), 7.30-7.24 (m, 4H), 5.36 (ABd, *J* = 13.8 Hz, *J* = 4.4 Hz, 1H), 4.93 (ABd, *J* = 13.6 Hz, *J* = 10.8 Hz, 1H), 3.98 (dd, *J* = 10.6 Hz, *J* = 4.4 Hz, 1H), 3.24 (AB, *J* = 17.6 Hz, 1H), 2.96 (AB, *J* = 18 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 198.4, 151.3, 143.5, 134.8, 132.7, 131.8, 130.3, 129.6, 129.2, 126.5, 126.4, 75.2, 70.5, 46.5, 36.5; IR (neat): 2104, 1715, 1554, 1467, 1378, 1096, 910, 738 cm$^{-1}$; HRMS (DART): Exact mass calcd for $C_{17}H_{16}Cl_2N_5O_3$ $[M+NH_4]^+$: 408.0625, Found: 408.0625.



*anti*-**5x**

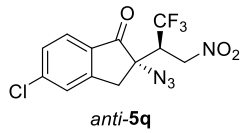
Product *anti*-**5x** was obtained in 91% yield as light yellow liquid (2 days). $^1$H NMR analysis revealed that the dr value was 30:1. HPLC analysis [Chiralcel OZ-H, 10% $^i$PrOH/hexane, 1.0 mL/min, 230 nm; major diastereomer: tr (major) = 20.81 min, tr (minor) = 27.86 min, minor diastereomer: tr (major) = 14.77 min, tr (minor) = 25.27 min] gave the isomeric composition of major diastereomer: 96% ee; $[\alpha]^{25}_D$ = +130.1 (c = 1.39, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.89 (d, *J* = 2.0 Hz, 1H), 7.74 (dd, *J* = 6.2 Hz, *J* = 1.2 Hz, 1H), 7.29-7.24 (m, 5H), 5.35 (ABd, *J* = 13.8 Hz, *J* = 4.0 Hz, 1H), 4.93 (ABd, *J* = 13.6 Hz, *J* = 10.8 Hz, 1H), 3.99 (dd, *J* = 10.6 Hz, *J* = 4.0 Hz, 1H), 3.20 (AB, *J* = 17.6 Hz, 1H), 2.92 (AB, *J* = 17.6 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 198.5, 148.4, 139.5, 135.1, 134.9, 132.6, 130.3, 129.3, 128.2, 127.8, 122.9, 75.2, 70.7, 46.5, 36.5; IR (neat): 2106, 1716, 1553, 1470, 1377, 1095, 980, 731, 652 cm$^{-1}$; HRMS (ESI): Exact mass calcd for $C_{17}H_{16}BrClN_5O_3$ $[M+NH_4]^+$: 452.0120, Found: 452.0116.



*anti*-**5y**

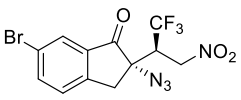
Product *anti*-**5y** was obtained in 99% yield as white solid (4 days), m.p. = 74-76 $^o$C. $^1$H NMR analysis revealed that the dr value was 14:1. HPLC analysis [Chiralcel OZ-H, 3% $^i$PrOH/hexane, 1.0 mL/min, 230 nm; major diastereomer: tr (major) = 34.86 min, tr (minor) = 46.17 min, minor diastereomer: tr (major) = 23.57 min, tr (minor) = 36.79 min] gave the isomeric composition of major diastereomer: 94% ee; $[\alpha]^{25}_D$ = +134.1 (c = 1.24, $CHCl_3$). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.58 (s, 1H), 7.47 (d, *J* = 8.1 Hz, 1H), 7.27-7.23 (m, 5H), 5.39 (ABd, *J* = 13.6 Hz, *J* = 4.2 Hz, 1H), 4.93 (ABd, *J* = 13.8 Hz, *J* = 10.8 Hz, 1H), 3.94 (dd, *J* = 10.8 Hz, *J* = 4.2 Hz, 1H), 3.20 (AB, *J* = 17.4 Hz, 1H), 2.94 (AB, *J* = 17.4 Hz, 1H), 2.41 (m, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 199.8, 147.3, 139.0, 138.1, 134.7, 133.6, 133.2, 130.4, 129.2, 126.0, 125.3, 75.5, 70.9, 46.7, 36.7, 21.1; IR (neat): 2107, 1712,

1554, 1493, 1377, 1095, 982, 734 $cm^{-1}$; HRMS (DART): Exact mass calcd for $C_{18}H_{19}ClN_5O_3$ $[M+NH_4]^+$: 388.1171, Found: 388.1171.



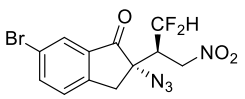
*anti*-**5q**

The reaction was run with **4b** and $K_2HPO_4{\cdot}3H_2O$ (20 mol%, each). Product *anti*-**5q** was obtained in 88% yield as light yellow liquid (3.5 days). $^1H$ NMR analysis revealed that the dr value was 11:1. HPLC analysis [Chiralcel OZ-H, 5% $^i$PrOH/hexane, 1.0 mL/min, 230 nm; major diastereomer: tr (major) = 13.43 min, tr (minor) = 16.55 min, minor diastereomer: tr (major) = 9.85 min, tr (minor) = 15.04 min] gave the isomeric composition of major diastereomer: 94% ee; $[\alpha]^{25}_D$ = +203.9 (c = 0.92, $CHCl_3$). $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.85-7.82 (m, 1H), 7.50-7.48 (m, 2H), 5.06 (ABd, *J* = 15.2 Hz, *J* = 4.8 Hz, 1H), 4.78 (ABd, *J* = 15.4 Hz, *J* = 6.0 Hz, 1H), 4.18-4.09 (m, 1H), 3.46 (AB, *J* = 18.0 Hz, 1H), 3.12 (AB, *J* = 18.0 Hz, 1H); $^{13}C$ NMR (125 MHz, $CDCl_3$): $\delta$ 195.7, 151.2, 143.9, 131.1, 129.9, 126.9, 126.8, 124.5 (q, $J_{C\text{-}F}$ = 280.3 Hz, 1C), 70.1 (q, $J_{C\text{-}F}$ = 2.6 Hz, 1C), 66.5, 45.5 (q, $J_{C\text{-}F}$ = 26.6 Hz, 1C), 35.8 (q, $J_{C\text{-}F}$ = 2.4 Hz, 1C); $^{19}F$ NMR (282 MHz, $CDCl_3$): $\delta$ -64.50 (s, 3F); IR (neat): 2926, 2114, 1723, 1601, 1571, 1462, 1378, 1217, 1074, 668 $cm^{-1}$; HRMS (DART): Exact mass calcd for $C_{12}H_9N_4O_3ClF_3$ $[M+H]^+$: 349.0310, Found: 349.0307.



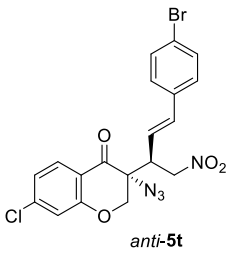
*anti*-**5r**

The reaction was conducted with **4b** and $K_2HPO_4{\cdot}3H_2O$ (10 mol%, each). Product *anti*-**5r** was obtained in 91% yield as light yellow liquid (3.5 days). $^1H$ NMR analysis revealed that the dr value was 19:1. HPLC analysis [Chiralcel OZ-H, 5% $^i$PrOH/hexane, 1.0 mL/min, 230 nm; major diastereomer: tr (major) = 16.89 min, tr (minor) = 18.34 min, minor diastereomer: tr (major) = 10.10 min, tr (minor) = 15.51 min] gave the isomeric composition of major diastereomer: 94% ee; $[\alpha]^{25}_D$ = +98.2 (c = 0.25, $CHCl_3$). $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 8.02 (d, *J* = 1.6 Hz, 1H), 7.84-7.82 (m, 1H), 7.38 (d, *J* = 8.0 Hz, 1H), 5.05 (ABd, *J* = 15.2 Hz, *J* = 4.4 Hz, 1H), 4.77 (ABd, *J* = 15.2 Hz, *J* = 5.6 Hz, 1H), 4.17-4.08 (m, 1H), 3.42 (AB, *J* = 18.0 Hz, 1H), 3.09 (AB, *J* = 17.6 Hz, 1H); $^{13}C$ NMR (125 MHz, $CDCl_3$): $\delta$ 195.9, 148.3, 139.8, 134.5, 128.7, 128.0, 124.5 (q, $J_{C\text{-}F}$ = 224.3 Hz, 1C), 123.1, 70.1 (d, $J_{C\text{-}F}$ = 2.0 Hz, 1C), 66.7, 45.5 (q, $J_{C\text{-}F}$ = 21.4 Hz, 1C), 35.7 (t, $J_{C\text{-}F}$ = 1.8 Hz, 1C); $^{19}F$ NMR (376 MHz, $CDCl_3$): $\delta$ -64.48 (s, 3F); IR (neat): 2113, 1723, 1568, 1467, 1380, 1256, 1199, 1137, 990, 792 $cm^{-1}$; HRMS (DART): Exact mass calcd for $C_{12}H_8N_4O_3BrF_2$ $[M-F]^+$: 372.9742, Found: 372.9736.



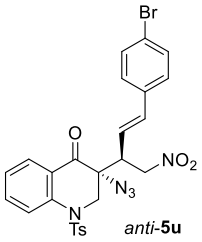
*anti*-**5s**

The reaction was run with **4b** and $K_2HPO_4 \cdot 3H_2O$ (20 mol%, each). Product *anti*-**5s** was obtained in 93% yield as light yellow liquid (3 days). $^1$H NMR analysis revealed that the dr value was 7:1. HPLC analysis [Chiralcel OZ-H, 5% $^i$PrOH/hexane, 1.0 mL/min, 230 nm; major diastereomer: tr (major) = 22.52 min, tr (minor) = 25.04 min, minor diastereomer: tr (major) = 18.03 min, tr (minor) = 26.52 min] gave the isomeric composition of major diastereomer: 94% ee; $[\alpha]^{25}_D$ = +152.6 (c = 0.53, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.01-8.00 (m, 1H), 7.84-7.81 (m, 1H), 7.37 (d, *J* = 8.4 Hz, 1H), 6.08-5.80 (m, 1H), 4.91 (ABd, *J* = 14.8 Hz, *J* = 4.8 Hz, 1H), 4.82 (ABd, *J* = 14.8 Hz, *J* = 6.4 Hz, 1H), 3.76-3.65 (m, 1H), 3.39 (AB, *J* = 17.2 Hz, 1H), 3.01 (AB, *J* = 17.6 Hz, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 197.2, 148.9, 139.8, 134.7, 128.5, 128.1, 123.0, 114.0 (t, $J_{C\text{-}F}$ = 244.1 Hz, 1C), 69.6 (t, $J_{C\text{-}F}$ = 4.5 Hz, 1C), 67.3 (d, $J_{C\text{-}F}$ = 4.5 Hz, 1C), 44.5 (t, $J_{C\text{-}F}$ = 19.6 Hz, 1C), 35.9 (t, $J_{C\text{-}F}$ = 2.6 Hz, 1C); $^{19}$F NMR (282 MHz, $CDCl_3$): $\delta$ -117.08--118.50 (m, 1F), -122.02--123.46 (m, 1F); IR (neat): 2926, 2109, 1719, 1561, 1435, 1378, 1258, 1146, 1071, 822 cm$^{-1}$; HRMS (DART): Exact mass calcd for $C_{12}H_{10}N_2O_3BrF_2$ $[M\text{-}N_2\text{+}H]^+$: 346.9837, Found: 346.9835.



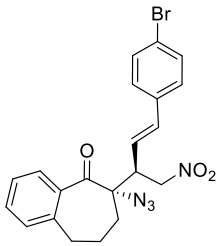
*anti*-**5t**

The reaction was run with 10 mol% **4b**. Product *anti*-**5t** was obtained in 76% yield as light yellow liquid (7 days). $^1$H NMR analysis revealed that the dr value was 18:1. HPLC analysis [Chiralcel AD-H, 10% $^i$PrOH/hexane, 1.0 mL/min, 230 nm; major diastereomer: tr (major) = 30.10 min, tr (minor) = 21.50 min, minor diastereomer: tr (major) = 25.58 min, tr (minor) = 23.44 min] gave the isomeric composition of major diastereomer: 84% ee; $[\alpha]^{25}_D$ = +220.7 (c = 1.0, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.91 (d, *J* = 8.8 Hz, 1H), 7.47-7.44 (m, 2H), 7.25-7.22 (m, 2H), 7.15 (dd, *J* = 8.4 Hz, *J* = 2.0 Hz, 1H), 7.10 (d, *J* = 1.6 Hz, 1H), 6.61 (d, *J* = 15.6 Hz, 1H), 6.03 (dd, *J* = 15.6 Hz, *J* = 9.6 Hz, 1H), 4.63-4.53 (m, 2H), 4.53 (AB, *J* = 11.6 Hz, 1H), 4.33 (AB, *J* = 11.6 Hz, 1H), 3.57 (td, *J* = 9.2 Hz, *J* = 4.8 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 188.2, 161.1, 143.8, 137.3, 134.3, 131.9, 129.6, 128.3, 123.9, 122.7, 121.0, 118.3, 117.5, 75.3, 70.9, 66.7, 43.4; IR (neat): 2253, 2118, 1713, 1443, 1364, 1227, 1082, 905, 727, 650 cm$^{-1}$; HRMS (ESI): Exact mass calcd for $C_{19}H_{14}N_4O_4ClBrNa$ $[M\text{+}Na]^+$: 498.9779, Found: 498.9778.



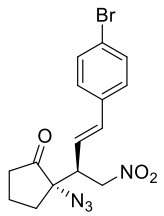
*anti*-**5u**

The reaction was conducted with 20 mol% **4b**. Product *anti*-**5u** was obtained in 58% yield as light yellow liquid (7 days). $^1$H NMR analysis revealed that the dr value was 4:1. HPLC analysis [Chiralcel OZ-H, 30% $^i$PrOH/hexane, 1.0 mL/min, 230 nm; major diastereomer: tr (major) = 29.51 min, tr (minor) = 21.87 min, minor diastereomer: tr (major) = 49.82 min, tr (minor) = 40.50 min] gave the isomeric composition of major diastereomer: 91% ee; $[\alpha]^{25}_D$ = +60.0 (c = 0.1, $CHCl_3$). $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 8.06-8.04 (m, 1H), 7.83 (d, *J* = 9.0 Hz, 1H), 7.78 (d, *J* = 8.0 Hz, 2H), 7.58-7.54 (m, 1H), 7.44 (d, *J* = 8.0 Hz, 2H), 7.34 (d, *J* = 8.5 Hz, 2H), 7.24 (d, *J* = 8.0 Hz, 2H), 7.19 (t, *J* = 7.5 Hz, 1H), 6.70 (d, *J* = 16.0 Hz, 1H), 6.10 (dd, *J* = 16.0 Hz, *J* = 9.5 Hz, 1 H), 4.72-4.71 (m, 2H), 4.62 (AB, *J* = 13.0 Hz, 1H), 3.85 (AB, *J* = 13.0 Hz, 1H), 3.82-3.79 (m, 1H), 2.43 (m, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 189.3, 145.3, 142.0, 138.0, 136.2, 135.1, 134.6, 131.7, 130.2, 129.8, 128.4, 127.3, 124.3, 122.4, 121.0, 120.3, 118.7, 77.2, 75.2, 68.0, 51.5, 43.9, 21.6; IR (neat): 2112, 1711, 1557, 1364, 1215, 1011, 910, 748, 573 cm$^{-1}$; HRMS (ESI): Exact mass calcd for $C_{26}H_{22}N_5O_5BrSNa$ $[M+Na]^+$: 618.0417, Found: 618.0409.



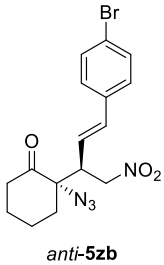
*anti*-**5z**

The reaction was run with **4b** and $K_2HPO_4 \cdot 3H_2O$ (20 mol%, each) at rt. Product *anti*-**5z** was obtained in 70% yield as light yellow liquid (7 days). $^1$H NMR analysis revealed that the dr value was 15:1. HPLC analysis [Chiralcel AD-H, 10% $^i$PrOH/hexane, 1.0 mL/min, 230 nm; major diastereomer: tr (major) = 17.61 min, tr (minor) = 20.11 min, minor diastereomer: tr (major) = 14.59 min, tr (minor) = 19.03 min] gave the isomeric composition of major diastereomer: 95% ee; $[\alpha]^{25}_D$ = +40.9 (c = 0.90, $CHCl_3$). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.49-7.43 (m, 3H), 7.31-7.26 (m, 2H), 7.23 (d, *J* = 7.8 Hz, 1H), 7.18 (d, *J* = 8.4 Hz, 2H), 6.49 (d, *J* = 15.6 Hz, 1H), 5.93 (dd, *J* = 15.8 Hz, *J* = 9.6 Hz, 1H), 4.50 (d, *J* = 6.3 Hz, 2H), 3.69-3.61 (m, 1H), 3.03-2.87 (m, 2H), 2.17-1.93 (m, 4H); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 205.4, 138.4, 137.7, 136.5, 134.6, 132.3, 131.8, 129.4, 128.2, 128.1, 127.3, 122.4, 122.0, 76.2, 73.3, 47.7, 33.4, 32.0, 22.3; IR (neat): 2102, 1715, 1553, 1445, 1225, 1072, 974, 808, 752, 592 cm$^{-1}$; HRMS (ESI): Exact mass calcd for $C_{21}H_{19}N_4O_3BrNa$ $[M+Na]^+$: 477.0533, Found: 477.0530.



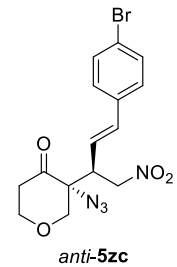
*anti*-**5za**

The reaction was conducted with 0.2 mmol **1i**, 0.1 mmol **2i**, 10 mol% **4b** and 0.1 mL DCE at rt. Product *anti*-**5za** was obtained in 93% yield as light yellow liquid (2 days). $^1$H NMR analysis revealed that the dr value was >50:1. HPLC analysis [Chiralcel OZ-H, 15% $^i$PrOH/hexane, 1.0 mL/min, 230 nm; major diastereomer: tr (major) = 14.55 min, tr (minor) = 26.83 min] gave the isomeric composition of major diastereomer: 98% ee; $[\alpha]^{25}_D$ = +212.50 (c = 0.9, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.45-7.42 (m, 2H), 7.20-7.17 (m, 2H), 6.50 (d, *J* = 15.6 Hz, 1H), 5.91 (dd, *J* = 15.8 Hz, *J* = 9.2 Hz, 1H), 4.87 (ABd, *J* = 12.8 Hz, *J* = 4.0 Hz, 1H), 4.50 (ABd, *J* = 12.6 Hz, *J* = 10.0 Hz, 1H), 3.58-3.52 (m, 1H), 2.52-2.44 (m, 1H), 2.32-2.22 (m, 1H), 2.11-2.05 (m, 1H), 2.02-1.89 (m, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 211.3, 136.5, 134.5, 131.8, 128.1, 122.5, 121.7, 75.5, 69.9, 44.4, 36.7, 31.3, 18.1; IR (neat): 2099, 1740, 1551, 1487, 1402, 1377, 1072, 1009, 970, 810 cm$^{-1}$; HRMS (ESI): Exact mass calcd for $C_{15}H_{15}N_4O_3BrNa$ [M+Na]$^+$: 401.0220, Found: 401.0208.



*anti*-**5zb**

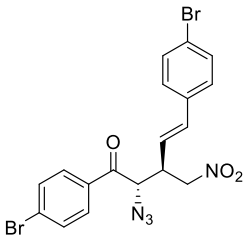
The reaction was conducted with 0.2 mmol **1j**, 0.1 mmol **2i**, 10 mol% **4b** and 0.1 mL DCE at rt. Product *anti*-**5zb** was obtained in 36% yield as light yellow liquid (4 days). $^1$H NMR analysis revealed that the dr value was >50:1. HPLC analysis [Chiralcel OZ-H, 5% $^i$PrOH/hexane, 1.0 mL/min, 230 nm; major diastereomer: tr (major) = 29.52 min, tr (minor) = 34.70 min] gave the isomeric composition of major diastereomer: 91% ee; $[\alpha]^{25}_D$ = +25.5 (c = 0.6, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.47-7.45 (m, 2H), 7.26-7.23 (m, 2H), 6.55 (d, *J* = 16.0 Hz, 1H), 6.01 (dd, *J* = 15.6 Hz, *J* = 9.6 Hz, 1H), 4.47 (ABd, *J* = 12.8 Hz, *J* = 10.4 Hz, 1H), 4.28 (ABd, *J* = 12.8 Hz, *J* = 3.2 Hz, 1H), 3.65 (td, *J* = 9.6 Hz, *J* = 3.2 Hz, 1H), 2.69-2.66 (m, 2H), 2.24-2.19 (m, 1H), 2.15-2.09 (m, 1H), 1.96-1.79 (m, 4H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 206.6, 136.1, 134.5, 131.8, 128.2, 122.5, 122.1, 76.2, 73.3, 45.7, 39.3, 35.7, 27.2, 21.0; IR (neat): 2102, 1715, 1551, 1250, 1190, 1072, 974, 704, 569 cm$^{-1}$; HRMS (ESI): Exact mass calcd for $C_{16}H_{17}N_4O_3BrNa$ [M+Na]$^+$: 415.0376, Found: 415.0374.



*anti*-**5zc**

The reaction was conducted with 0.2 mmol **1k**, 0.1 mmol **2i**, 10 mol% **4b** and 0.1 mL DCE at rt. Product *anti*-**5zc** was obtained in 58% yield as light yellow liquid (2 days). $^1$H NMR analysis revealed that the dr value was >50:1. HPLC analysis [Chiralcel OZ-H, 15% $^i$PrOH/hexane, 1.0 mL/min, 230 nm; major diastereomer: tr (major) = 27.45 min, tr (minor) = 38.08 min] gave the isomeric composition of major

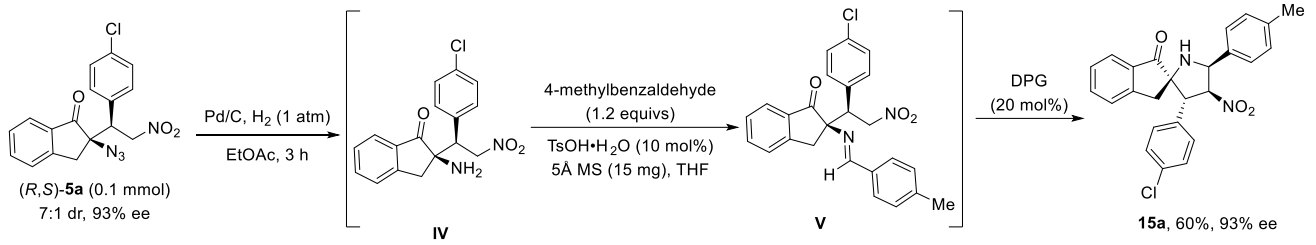
diastereomer: 96% ee; $[\alpha]^{25}_D$ = +56.0 (c = 0.3, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.46 (d, *J* = 8.4 Hz, 2H), 7.24 (d, *J* = 8.4 Hz, 2H), 6.51 (d, *J* = 16.0 Hz, 1H), 5.96 (dd, *J* = 15.8 Hz, *J* = 9.2 Hz, 1H), 4.46 (ABd, *J* = 12.8 Hz, *J* = 10.0 Hz, 1H), 4.34 (ABd, *J* = 12.8 Hz, *J* = 3.6 Hz, 1H), 4.34-4.28 (m, 1H), 4.17 (dd, *J* = 12.0 Hz, *J* = 1.6 Hz, 1H), 3.84 (td, *J* = 11.2 Hz, *J* = 3.6 Hz, 1H), 3.75 (td, *J* = 10.0 Hz, *J* = 4.0 Hz, 1H), 3.60 (d, *J* = 11.6 Hz, 1H), 3.05-2.97 (m, 1H), 2.75-2.69 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 203.0, 137.2, 134.4, 131.8, 128.3, 122.6, 121.1, 75.8, 72.6, 72.3, 68.8, 44.6, 40.7; IR (neat): 2104, 1717, 1551, 1420, 1364, 1223, 1092, 1009, 972, 810 cm$^{-1}$; HRMS (ESI): Exact mass calcd for $C_{15}H_{15}N_4O_4BrNa$ $[M+Na]^+$: 417.0169, Found: 417.0169.



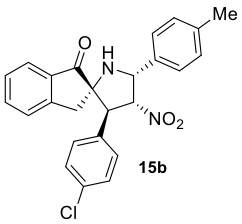
*anti*-**14**

The reaction was conducted with 20 mol% **4b**. Product *anti*-**14** was obtained in 31% yield as white solid (7 days), m.p. = 89-91 $^o$C. $^1$H NMR analysis revealed that the dr value was 5:1. HPLC analysis [Chiralcel IF, 15% $^i$PrOH/hexane, 1.0 mL/min, 230 nm; major diastereomer: tr (major) = 18.82 min, tr (minor) = 13.31 min, minor diastereomer: tr (major) = 10.88 min, tr (minor) = 9.76 min] gave the isomeric composition of major diastereomer: 92% ee; $[\alpha]^{25}_D$ = +129.3 (c = 0.70, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.81-7.78 (m, 2H), 7.71-7.65 (m, 2H), 7.41-7.38 (m, 2H), 7.13-7.06 (m, 2H), 6.48 (d, *J* = 16.0 Hz, 1H), 6.01-5.95 (m, 1H), 4.89-4.87 (m, 1H), 4.73-4.64 (m, 2H), 3.69-3.61 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 193.2, 135.5, 134.3, 133.5, 132.6, 131.8, 130.1, 130.0, 128.0, 122.8, 122.5, 75.8, 63.3, 43.4; IR: 3003, 2924, 2114, 1709, 1556, 1365, 1217, 1072, 1009, 808 cm$^{-1}$; HRMS (DART): Exact mass calcd for $C_{18}H_{18}N_5O_3Br_2$ $[M+NH_4]^+$: 509.9771, Found: 509.9770.

## 6. Synthesis of spiro-pyrrolidines 15

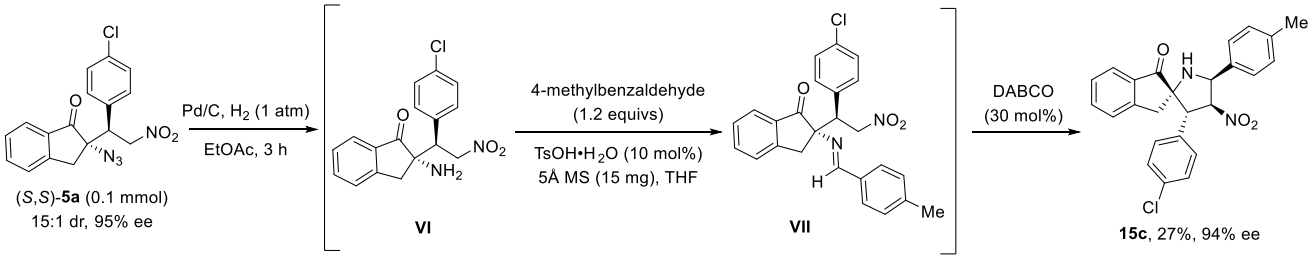



To a 25 mL Schlenk tube were added (*R*,*S*)-**5a** (35.7 mg, 0.1 mmol), 10% Pd/C (10 mg) and 3.5 mL EtOAc. The reaction mixture was purged with $H_2$, and stirred under an atmosphere of $H_2$ (1 atm, $H_2$ balloon) at room temperature for 3 h until full consumption of (*R*,*S*)-**5a** by TLC analysis. Then the mixture was filtered through a pad of Celite, and concentrated in *vacuo*. The residue was dissolved in 1.5 mL THF, followed by the addition of TsOH·$H_2O$ (1.9 mg, 0.01 mmol), 5Å MS (15 mg) and 4-methylbenzaldehyde (13.2 mg, 0.11 mmol). Then the reaction mixture was stirred at 60 $^oC$ for 2 h until full consumption of **IV**. After the mixture was cooled down to room temperature, 1,3-diphenylguanidine (DPG) (4.2 mg, 0.02 mmol) was added and kept stirring for 1.5 days until full consumption of **V**. The crude product was purified by fast column chorography (PE:$Et_2O$ = 8:1 to 4:1) to give **15a** as white solid (60% overall yield for 3 steps), m.p. = 166-168 $^oC$. HPLC analysis [Chiralcel AD-H, 15% $^i$PrOH/hexane, 1.0 mL/min, 230 nm; $t_r$ (major) = 25.83 min, $t_r$ (minor) = 23.25 min] gave the isomeric composition of the product: 93% ee. $[\alpha]^{25}_D$ = -240.5 (c = 0.30, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.58 (d, *J* = 7.6 Hz, 1H), 7.53 (td, *J* = 7.6 Hz, *J* = 1.2 Hz, 1H), 7.37-7.32 (m, 3H), 7.29 (t, *J* = 7.6 Hz, 1H), 7.22-7.20 (m, 2H), 7.15-7.13 (m, 4H), 6.20 (t, *J* = 9.6 Hz, 1H), 5.62 (d, *J* = 9.6 Hz, 1H), 4.38 (d, *J* = 10.0 Hz, 1H), 3.57 (AB, *J* = 17.2 Hz, 1H), 3.40 (AB, *J* = 17.6 Hz, 1H), 2.63 (brs, 1H), 2.32 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 207.4, 151.3, 138.5, 135.9, 134.8, 134.4, 134.1, 131.6, 130.2, 129.0, 128.9, 128.0, 127.6, 126.1, 124.3, 92.9, 73.2, 61.5, 54.5, 38.5, 21.2; IR (neat): 1699, 1556, 1494, 1401, 1095, 967, 815, 621 $cm^{-1}$; HRMS (ESI): Exact mass calcd for $C_{25}H_{22}N_2O_3Cl$ $[M+H]^+$: 433.1313, Found: 433.1309.

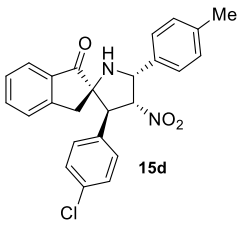



Product **15b** was obtained from (*S*,*R*)-**5a** (7:1 dr, 94% ee) as white solid (52% overall yield for 3 steps), m.p. = 166-167 $^oC$. HPLC analysis [Chiralcel AD-H, 15% $^i$PrOH/hexane, 1.0 mL/min, 230 nm; $t_r$ (major) = 30.02 min, $t_r$ (minor) = 33.91 min] gave the isomeric composition of the product: 94% ee. $[\alpha]^{25}_D$ = +212.7 (c = 0.86, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.57 (d, *J* = 7.6 Hz, 1H), 7.52 (td, *J* = 7.2

Hz, *J* = 1.2 Hz, 1H), 7.37-7.32 (m, 3H), 7.30-7.26 (m, 1H), 7.23-7.19 (m, 2H), 7.18-7.12 (m, 4H), 6.20 (t, *J* = 10.0 Hz, 1H), 5.61 (d, *J* = 9.2 Hz, 1H), 4.38 (d, *J* = 10.0 Hz, 1H), 3.57 (AB, *J* = 17.6 Hz, 1H), 3.40 (AB, *J* = 17.6 Hz, 1H), 2.70 (brs, 1H), 2.32 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 207.4, 151.3, 138.5, 135.9, 134.8, 134.5, 134.1, 131.6, 130.2, 129.0, 128.9, 128.0, 127.6, 126.1, 124.3, 92.9, 73.3, 61.5, 54.5, 38.5, 21.2; IR (neat):1699, 1555, 1494, 1216, 1158, 967, 815, 750, 622 cm$^{-1}$; HRMS (ESI): Exact mass calcd for $C_{25}H_{22}N_2O_3Cl$ $[M+H]^+$: 433.1313, Found: 433.1313.




To a 25 mL Schlenk tube were added (*S,S*)-**5a** (35.7 mg, 0.1 mmol), 10% Pd/C (10 mg) and 3.5 mL EtOAc. The reaction mixture was purged with $H_2$, and stirred under an atmosphere of $H_2$ (1 atm, $H_2$ balloon) at room temperature for 5 h until full consumption of (*S,S*)-**5a** by TLC analysis. Then the mixture was filtered through a pad of Celite, and concentrated in *vacuo*. The residue was dissolved in 1.5 mL THF, followed by the addition of $TsOH{\cdot}H_2O$ (1.9 mg, 0.01 mmol), 5Å MS (15 mg) and 4-methylbenzaldehyde (13.2 mg, 0.11 mmol). Then the reaction mixture was stirred at 60 $^o$C for 2 h until full consumption of **VI**. After the mixture was cooled down to room temperature, DABCO (3.3 mg, 0.03 mmol) was added and kept stirring for 3 days until full consumption of **VII**. The crude product was purified by fast column chorography (PE:$Et_2O$ = 4:1 to 2:1) to give **15c** as white solid (27% overall yield for 3 steps), m.p. = 135-137 $^o$C. HPLC analysis [Chiralcel AD-H, 30% $^i$PrOH/hexane, 1.0 mL/min, 230 nm; $t_r$ (major) = 30.71 min, $t_r$ (minor) = 23.66 min] gave the isomeric composition of the product: 95% ee. $[\alpha]^{25}_D$ = +13.8 (c = 0.65, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.82 (d, *J* = 7.6 Hz, 1H), 7.51 (td, *J* = 7.6 Hz, *J* = 1.2 Hz, 1H), 7.37-7.33 (m, 3H), 7.20-7.17 (m, 3H), 7.14-7.10 (m, 2H), 7.00-6.97 (m, 2H), 5.83 (t, *J* = 8.8 Hz, 1H), 4.99 (d, *J* = 8.4 Hz, 1H), 4.66 (d, *J* = 8.8 Hz, 1H), 3.25 (brs, 1H), 3.15 (AB, *J* = 16.4 Hz, 1H), 3.06 (AB, *J* = 16.4 Hz, 1H), 2.33 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 204.4, 152.1, 138.8, 136.2, 135.1, 133.8, 132.5, 132.0, 129.4, 128.9, 128.8, 128.0, 126.8, 126.4, 124.5, 94.2, 74.0, 65.9, 57.8, 36.6, 21.2; IR (neat): 2926, 2854, 1720, 1695, 1555, 1468, 1375, 1289, 1125, 1017, 744 cm$^{-1}$; HRMS (ESI): Exact mass calcd for $C_{25}H_{22}N_2O_3Cl$ $[M+H]^+$: 433.1313, Found: 433.1312.




Product **15d** was obtained from (*R*,*R*)-**5a** (13:1 dr, 95% ee) as white solid (24% overall yield for 3 steps), m.p. = 135-137 $^{o}$C. HPLC analysis [Chiralcel AD-H, 30% $^{i}$PrOH/hexane, 1.0 mL/min, 230 nm; $t_r$ (major) = 24.39 min, $t_r$ (minor) = 32.83 min] gave the isomeric composition of the product: 94% ee. $[\alpha]^{25}_{D}$ = -15.3 (c = 0.51, $CHCl_3$). $^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.82 (d, *J* = 7.6 Hz, 1H), 7.51 (td, *J* = 7.6 Hz, *J* = 1.6 Hz, 1H), 7.37-7.33 (m, 3H), 7.22-7.17 (m, 3H), 7.15-7.10 (m, 2H), 7.00-6.98 (m, 2H), 5.83 (t, *J* = 8.4 Hz, 1H), 4.99 (d, *J* = 8.4 Hz, 1H), 4.66 (d, *J* = 8.4 Hz, 1H), 3.25 (brs, 1H), 3.15 (AB, *J* = 16.4 Hz, 1H), 3.06 (AB, *J* = 16.8 Hz, 1H), 2.33 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 204.4, 152.1, 138.8, 136.2, 135.1, 133.8, 132.5, 132.0, 129.4, 128.9, 128.8, 128.0, 126.8, 126.4, 124.5, 94.2, 74.0, 65.9, 57.8, 36.6, 21.2; IR (neat): 2923, 2105, 1713, 1607, 1554, 1379, 1217, 1158, 909, 743 cm$^{-1}$; HRMS (ESI): Exact mass calcd for $C_{25}H_{22}N_2O_3Cl$ $[M+H]^+$: 433.1313, Found: 433.1312.

## 7. Mechanistic studies

### 7.1 $^1$H NMR studies

NMR analysis was conducted to investigate the potential H-bonding interaction of the catalyst with α-azido indanone **1a** or nitroolefin **2e**. In case of phosphoramide **3a**, toluene ($d_8$) was distilled from dried 5Å MS before use. Unfortunately, due to its extremely poor solubility in organic solvents other than DMSO or DMF that may interfere the analysis of H-bonding interactions, the NMR analysis of the H-bonding interactions between squaramide **4b** and substrates failed.

To assign the NH signal of phosphoramide **3a**, the H/D exchange experiments were first tried. As shown in Figure S1, when a drop of $D_2O$ was added to a solution of **3a** in toluene-$d_8$, the broad signal at $\delta$ = 3.15 ppm disappeared to a great extent, which should be attributed to the NH signal of **3a**.

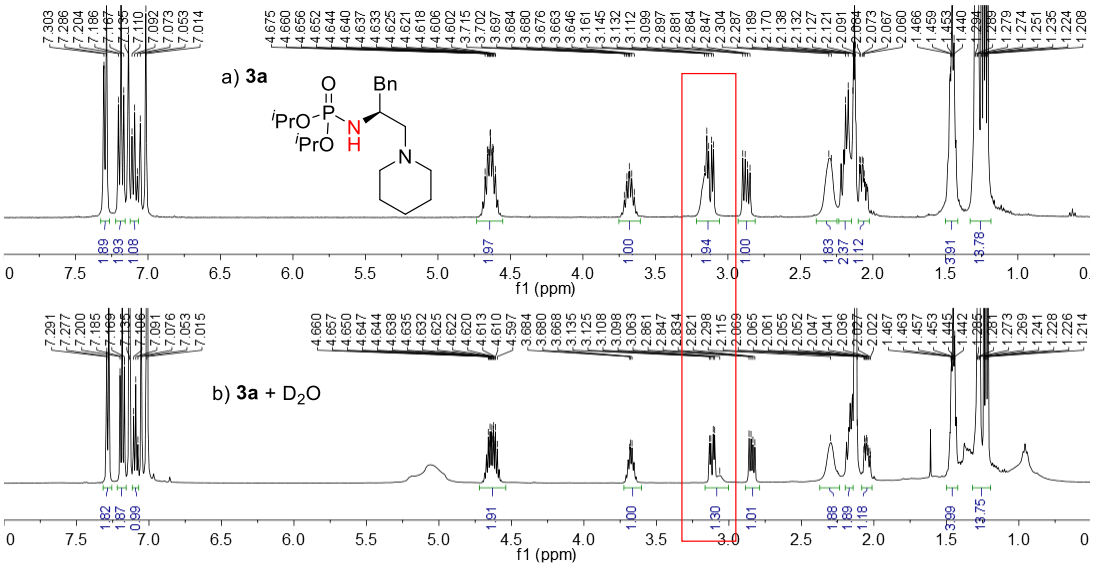



**Figure S1**.Deuteration experiments of phosphoramide **3a** (500 MHz, toluene-*d*8, 25 ºC).

The $^1$H NMR analysis revealed that phosphoramide **3a** could form H-bonding interactions with either α-azido indanone **1a** or nitroolefin **2e**. As shown in Figure S2, when **3a** was mixed with 1.0 equiv of **1a** or **2e** in toluene-$d_8$, its NH signal shifted from 2.945 to ca. 3.025 and 2.977 ppm, respectively (d vs e and f, $\Delta\delta \approx 0.08$ and 0.03 ppm). Notably, when all the three components were mixed together, the NH signal obviously shifted to 3.148 ppm (d vs g, $\Delta\delta = 0.20$ ppm). This change is significantly greater than that observed by mixing either **1a** or **2e** with catalyst **3a** (0.20 vs 0.08 or 0.03), suggesting the catalyst-substrate recognition model in the transition state differed from the binding model of phosphoramide **3a** with either α-azido indanone **1a** or nitroolefin **2e**.

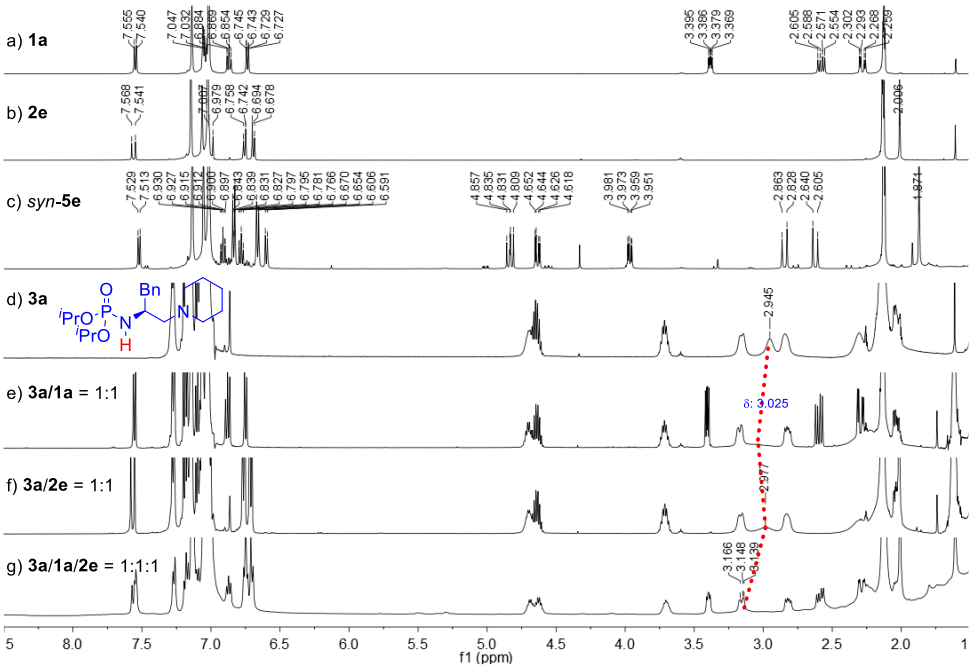



**Figure S2**. Partial $^{1}$H NMR spectra (500 MHz, toluene-$d_8$, 25 $^{o}$C, 5.0 mM).

### 7.2 Results of DFT calculations and discussion

To have a better understanding of the role of H-bond donors in controlling diastereoselectivity in this bifunctional tertiary amine-catalyzed reaction, theoretical calculations were conducted. The most important transition states (TS) of C-C addition step that determined the stereoselectivity of the titled reaction are given below. The details of theoretical studies on the whole reaction and origin of stereoselectivity will be reported later. All DFT calculations were performed with Gaussian 09 program.[11] The Truhlar's M06-2X exchange-correlation functional[12] were utilized with the standard 6-31G(d,p) basis set. The geometries of transition states were fully optimized, followed by vibrational frequency calculations at the same levels of theory to obtain the zero-point energies (ZPE) and verify whether it is a transition state on the potential energy surfaces (PES). To estimate the bulk solvent effects on the reaction, all the structures were optimized in the toluene or $CH_2Cl_2$ with the polarized continuum model using the integral equation formalism variant (IEFPCM). [13] The temperature-dependent enthalpy corrections and the entropy effects were computed at 298 K and 1 atmosphere of pressure. To obtain more accurate energies of TSs, single-point energy calculations

[11] M. J. Frisch et al. *Gaussian 09*, Revision A. 1, Gaussian, Inc., Wallingford, CT, 2009.
[12] Y. Zhao and D. G. Truhlar, *Theor. Chem. Acc.*, 2008, **120**, 215.
[13] (*a*) B. Mennucci and J. Tomasi, *J. Chem. Phys.*, 1997, **106**, 5151; (*b*) B. Mennucci, E. Cances and J. Tomasi, *J. Phys. Chem. B*, 1997, **101**, 10506; (*c*) J. Tomasi, B. Mennucci and E. Cances, *J Mol Struct (THEOCHEM)*, 1999, **464**, 211.

using a larger basis set 6-311++G(d,p) was performed and the D3 dispersion correction of Grimme was included.[14]

For phosphoramide **3a**-catalyzed reaction, four transition states with different hydrogen bonds have been identified and their structures were present in Figure S3. The computed relative Gibbs free energy by the single-point calculations with larger basis set and D3 dispersion correction are close to those at the M06-2X/6-31G(d,p) level. We used the results by single-point calculations for discussion in following section.

All the four TSs lead to the major *syn*-product observed experimentally, but **TSI2A** is the lowest free energy transition state with a total Gibbs free energy barrier of 15.0 kcal/mol. We also identified the TSs leading to minor *anti*-product in experiment. But their Gibbs free energies are higher than that of **TSI2A**. More details and discussions about the result will be reported in our future work. The **TSI2A** is unprecedented in literature reports, and is characterized by two N–O···H–N hydrogen bonds between nitroolefin **2d** with the alkylammonium ion generated in situ and phosphoramide N-H bond. The corresponding hydrogen bond distances are 1.68 and 2.08 Å, respectively, suggesting the former is a strong hydrogen bond and the latter is a relatively weak one. More importantly, the enolate anion in **TSI2A** was stabilized by three nonclassical C–H···O hydrogen bonds. Among the three H-bondings, the $N^+$−CH of the quininium ion interacts with the oxygen of enolate anion to form the $N^+$−C−H···O H−bonding.[15] The corresponding H-bonding distance is 2.29 Å, which is shorter than the sum of van der Waals radii of an oxygen atom (1.5 Å) and a carbon-bonded hydrogen (~1.2 Å).[16] The other two nonclassical C–H···O hydrogen bonds between the oxygen of enolate anion with the C-H bond of the phenyl ring and the α-H of the amide nitrogen have also relative short H···O distances of 2.31 and 2.25 Å, respectively. Notably, this present model, **TSI2A**, is unprecedented in previous reported ion pair-hydrogen bonding model ( type A model) and Brønsted acid-hydrogen bonding model (type B model),[17] because the electrophile interacts with both the H-bond donor and alkylammonium ion while the enolate anion as nucleophile interacts with alkylammonium ion to form the $N^+$−C−H···O hydrogen-bond.

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[14] S. Ehrlich, J. Moellmann, W. Reckien, T. Bredow and S. Grimme, *ChemPhysChem*, 2011, **12**, 3414.

[15] For a review: (*a*) K. Brak and E. N. Jacobsen, *Angew. Chem., Int. Ed.*, 2013, **52**, 534; for selected examples: (*b*) Y. Chen, W. Zhang, Y.-H. Li, X.-S. Xue, X. Li and J.-P. Chen, *J. Org. Chem.*, 2017, **82**, 9321; (*c*) M. T. Reetz, S. Hütte and R. Goddard, *J. Am. Chem. Soc.*, 1993, **115**, 9339; (*d*) C. E. Cannizzaro and K. N. Houk, *J. Am. Chem. Soc.* 2002, **124**, 7163; (*e*) T. Ohshima, T. Shibuguchi, Y. Fukuta and M. Shibasaki, *Tetrahedron*, 2004, **60**, 7743.

[16] (*a*) R. Taylor and O. Kennard, *J. Am. Chem. Soc.*, 1982, **104**, 5063; (*b*) C. E. Cannizzaro and K. N. Houk, *J. Am. Chem. Soc.*, 2002, **124**, 7163.

[17] (*a*) H. Hiemstra and H. Wynberg, *J. Am. Chem. Soc.*, 1981, **103**, 417; (*b*) M. N. Grayson and K. N. Houk, *J. Am. Chem. Soc.*, 2016, **138**, 1170; (*c*) T. Okino, Y. Hoashi, T. Furukawa, X. Xu and Y. Takemoto, *J. Am. Chem. Soc.*, 2005, **127**, 119; (*d*) A. Hamza, G. Schubert, T. Soós and I. Pápai, *J. Am. Chem. Soc.*, 2006, **128**, 13151.

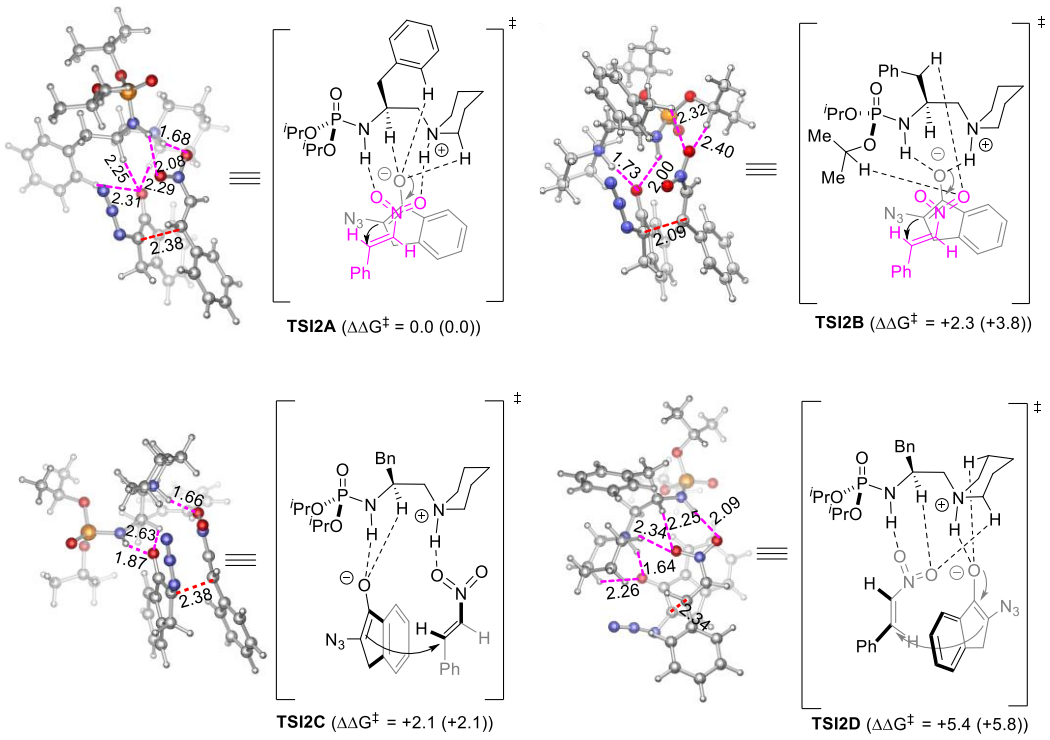


**Figure S3**. The optimized structures for TS modes of phosphoramide **3a**-catalyzed α-azido indanone **1a** and nitroolefin **2d**. The relative Gibbs free energies were calculated at the IEFPCM-M06-2X-D3/6-311++G(d,p)//IEFPCM-M06-2X/6-31G(d,p) level and given in kcal/mol. The relative Gibbs free energies at the IEFPCM-M06-2X/6-31G(d,p) level are given in parameters. The bond distances are given in Å.

The **TSI2B** was higher in free energy by 2.3 kcal/mol, with a reversed catalyst-substrate recognition pattern, because the alkylammonium ion formed in situ and phosphoramide N–H bond of **3a** interact with the indanone **1a** derived enolate. We also identified the corresponding the Brønsted acid-hydrogen bonding model (**TSI2C**) and the ion pair-hydrogen bonding model (**TSI2D**). Although strong hydrogen bonds formed in both transition states, the lowest free energy transition state **TSI2A** is still 2.1 and 5.4 kcal/mol lower than the **TSI2C** and **TSI2D**, respectively. Figure S3 shows that the hydrogen bond interactions in the **TSI2A** lead to the *Re* face nucleophilic addition of the enolate anion to the *Si* face of nitroolefin to afford the final *syn*-adduct. Compared with **TSI2A**, the other three TSs have higher total Gibbs free energy barrier. Thus, the reaction would prefer to proceed via the **TSI2A**. Some weak C–H···O H–bondings have also been observed in **TSI2B**, **TSI2C** and **TSI2D**, but they are weaker than the $N^+$–C–H···O hydrogen-bond in **TSI2A**, which is more important to stabilize the enolate anion in TS.

The three possible transition states for the C-C addition step of squaramide **4b**-catalyzed reaction are shown in Figure S4, with different types of H-bonding interactions being found. The **TSII2A** and

**TSII2B** correspond to the type B and type A model. The **TSII2C** is a new model with the hydrogen bond between azido group and two N-H bonds of **4b**. Among the three TSs, **TSII2A** is the lowest TS leading to the major *anti*-product, in which the enolate derived from **1a** interacts with the two squaramide N–H bonds of **4b** to form two C–O···H–N hydrogen bonds and an N–O···H–N interaction come into being between the nitro group of **2d** and the alkylammonium ion of **4b**. The three strong H-bonding interactions and small intermolecular repulsion in **TSII2A** contribute to a low total Gibbs free energy barrier of 4.6 kcal/mol, which is 6.8 and 14.2 kcal/mol lower than those of **TSII2B** and **TSII2C**, respectively. Figure S4 also shows that the three H-bonding interactions in **TSII2A** lead to the *Si* face nucleophilic addition of the enolate anion to the *Si* face of nitroolefin to yield the final *anti*-adduct.

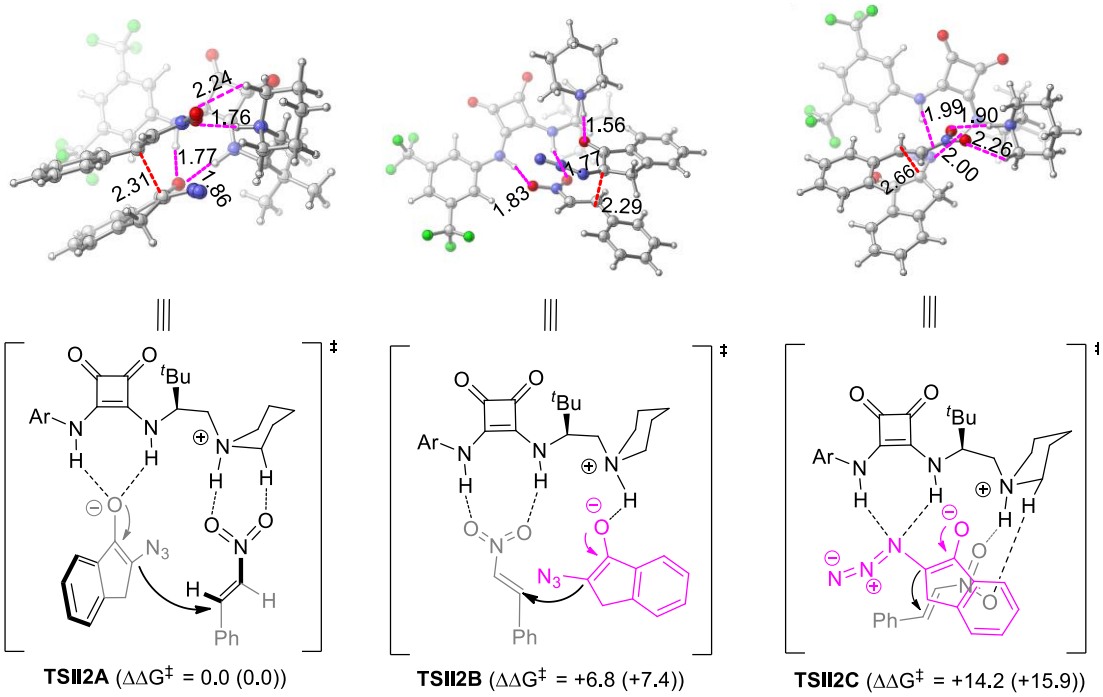


**Figure S4** The optimized structures for TS modes of squaramide **4b**-catalyzed α-azido indanone **1a** and nitroolefin **2d**. The relative Gibbs free energies were calculated at the IEFPCM-M06-2X-D3/6-311++G(d,p)//IEFPCM-M06-2X/6-31G(d,p) level and given in kcal/mol. The relative Gibbs free energies at the IEFPCM-M06-2X/6-31G(d,p) level are given in parameters. The bond distances are given in Å.

Compared with **TSII2A**, **TSII2B** also has three strong hydrogen bonds, but strong intermolecular repulsions between the enolate and nitroolefin lead to a much higher free energy barrier, by 6.8 kcal/mol. We also identified the **TSII2C** with the hydrogen bonds between azido group of **1a** derived enolate and squaramide N–H bond of **4b**. However, the **TSII2C** has quite weak hydrogen bonds as the

hydrogen bond distances in this TS are much longer than those of other two TSs. As a result, it is the highest free energy TS among the three TSs. Figure S5 displayed the obvious different intermolecular repulsions between reactants and **4b** for **TSII2A** and **TSII2B**. In **4b**-catalyzed reaction, it would be the model B rather than the model A involved to form the *anti*-product.

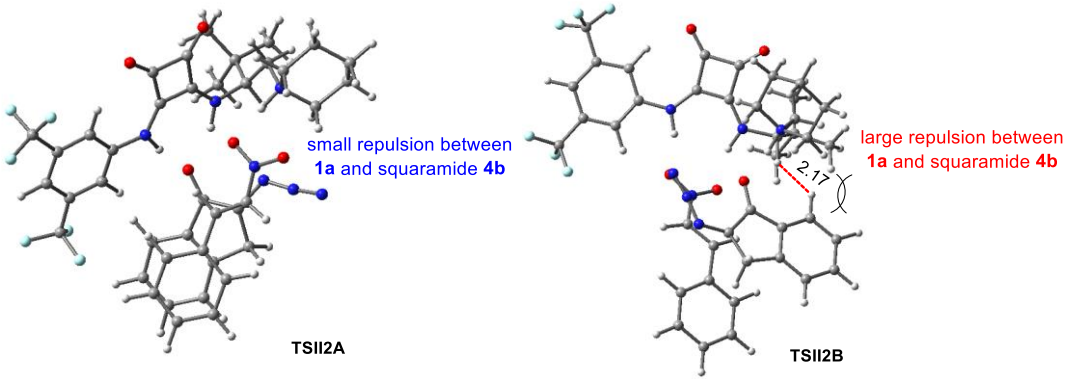


**Figure S5** Different intermolecular repulsions between reactants and squaramide catalyst **4b**. The bond distances are given in Å.

The present calculated results indicate that the different H-bonding modes are involved by using different H-bond donors, and finally enable the *syn*-selective or *anti*-selective Michael addition reaction. In phosphoramide **3a**-catalyzed reaction, the lowest TS, **TSI2A**, prefer to form hydrogen bonds between nitro group of **2d** and the phosphoramide N-H bond and the alkylammonium ion of **3a**. In contrast, the lowest TS for squaramide **4b**-catalyzed reaction, **TSII2A**, prefer to form hydrogen bonds between the enolate and the dual H-bond donor of the squaramide of catalyst **4b**. In addition, **TSII2A** forms stronger hydrogen bonds, so it has a much lower total Gibbs free energy barrier than **TSI2A** (4.6 vs 15.0 kcal/mol). These theoretical results indicate that the reaction catalyzed by **4b** should be faster than that by **3a**, which is in accordance with experimental results.

In conclusion, our theoretical calculations reveal the significant role of the hydrogen bonds in the present catalyst-controlled reactions, highlighting the possibility of varying the H-bond donors of bifunctional tertiary amines to enable different catalyst-substrate binding models for stereodivergent asymmetric catalysis.

Coordinates for the optimized transition states at the IEFPCM-M06-2X/6-31G(d,p) level.

**Table S4. TSI2A** (in toluene solvent)

| Center Number | Atomic Number | Atomic Type | Coordinates (Angstroms) X | Y | Z |
|---|---|---|---|---|---|
| 1 | 7 | 0 | 2.291360 | -0.554604 | 0.884394 |
| 2 | 1 | 0 | 1.555030 | -0.875455 | 1.512067 |
| 3 | 5 | 0 | 3.836434 | -0.932786 | 1.284659 |
| 4 | 8 | 0 | 4.491386 | -1.212002 | -0.155639 |
| 5 | 8 | 0 | 3.930436 | -2.013074 | 2.290466 |
| 6 | 8 | 0 | 4.651138 | 0.404796 | 1.671922 |
| 7 | 6 | 0 | 4.260947 | 1.164657 | 2.840858 |
| 8 | 1 | 0 | 3.162287 | 1.192988 | 2.869118 |
| 9 | 6 | 0 | 4.808722 | 2.564390 | 2.630905 |
| 10 | 1 | 0 | 5.900665 | 2.527625 | 2.572537 |
| 11 | 1 | 0 | 4.425130 | 3.001385 | 1.705835 |
| 12 | 6 | 0 | 4.804335 | 0.509265 | 4.100137 |
| 13 | 1 | 0 | 4.509634 | 1.091130 | 4.977604 |
| 14 | 1 | 0 | 4.427690 | -0.509628 | 4.200428 |
| 15 | 6 | 0 | 5.932518 | -1.304891 | -0.288732 |
| 16 | 1 | 0 | 6.370566 | -1.417908 | 0.709656 |
| 17 | 6 | 0 | 6.432608 | -0.025203 | -0.935065 |
| 18 | 1 | 0 | 7.514194 | -0.073643 | -1.087111 |
| 19 | 1 | 0 | 5.950137 | 0.109717 | -1.908702 |
| 20 | 6 | 0 | 6.214014 | -2.544684 | -1.116147 |
| 21 | 1 | 0 | 7.290408 | -2.671475 | -1.256475 |
| 22 | 6 | 0 | 1.824885 | 0.296707 | -0.208606 |
| 23 | 1 | 0 | 0.786469 | 0.534428 | 0.041456 |
| 24 | 6 | 0 | 1.803525 | -0.446368 | -1.546594 |
| 25 | 1 | 0 | 1.335910 | 0.185739 | -2.303179 |
| 26 | 1 | 0 | 2.816031 | -0.705469 | -1.866959 |
| 27 | 6 | 0 | 2.633996 | 1.592903 | -0.331077 |
| 28 | 1 | 0 | 2.586711 | 2.084107 | 0.647642 |
| 29 | 1 | 0 | 3.686818 | 1.346451 | -0.510139 |
| 30 | 6 | 0 | 2.162770 | 2.557528 | -1.397342 |
| 31 | 6 | 0 | 3.102687 | 3.331773 | -2.083221 |
| 32 | 6 | 0 | 0.806963 | 2.730689 | -1.699083 |
| 33 | 6 | 0 | 2.705931 | 4.266186 | -3.036106 |
| 34 | 1 | 0 | 4.159487 | 3.199752 | -1.862581 |
| 35 | 6 | 0 | 0.409134 | 3.659847 | -2.657659 |
| 36 | 1 | 0 | 0.055388 | 2.119415 | -1.204734 |
| 37 | 6 | 0 | 1.354428 | 4.434206 | -3.325952 |
| 38 | 1 | 0 | 3.453040 | 4.858633 | -3.555044 |
| 39 | 1 | 0 | -0.646737 | 3.776372 | -2.882131 |
| 40 | 1 | 0 | 1.040852 | 5.158525 | -4.070844 |
| 41 | 6 | 0 | 0.012283 | -1.829590 | -2.570045 |
| 42 | 6 | 0 | 1.884406 | -2.928886 | -1.381070 |
| 43 | 6 | 0 | -0.846455 | -3.071883 | -2.382280 |
| 44 | 1 | 0 | 0.587547 | -1.870061 | -3.501998 |
| 45 | 1 | 0 | -0.583510 | -0.915805 | -2.534287 |
| 46 | 6 | 0 | 1.056272 | -4.193922 | -1.202015 |
| 47 | 1 | 0 | 2.454263 | -2.951494 | -2.317399 |
| 48 | 1 | 0 | 2.577002 | -2.767289 | -0.555304 |

| | | | | | |
|---|---|---|---|---|---|
| 49 | 6 | 0 | 0.013256 | -4.334461 | -2.310942 |
| 50 | 1 | 0 | -1.558947 | -3.128067 | -3.211089 |
| 51 | 1 | 0 | -1.419026 | -2.953141 | -1.454089 |
| 52 | 1 | 0 | 1.742706 | -5.045182 | -1.197394 |
| 53 | 1 | 0 | 0.564117 | -4.161923 | -0.225320 |
| 54 | 1 | 0 | -0.614015 | -5.211465 | -2.131690 |
| 55 | 1 | 0 | 0.515996 | -4.487047 | -3.275067 |
| 56 | 7 | 0 | 1.005797 | -1.713760 | -1.454969 |
| 57 | 1 | 0 | 4.526161 | 3.208347 | 3.467250 |
| 58 | 1 | 0 | 5.897002 | 0.476606 | 4.053967 |
| 59 | 1 | 0 | 5.744108 | -2.449436 | -2.100036 |
| 60 | 1 | 0 | 5.815756 | -3.432162 | -0.619682 |
| 61 | 1 | 0 | 6.201706 | 0.833027 | -0.300328 |
| 62 | 1 | 0 | 0.453198 | -1.712053 | -0.554074 |
| 63 | 6 | 0 | -6.142697 | -0.065973 | -2.493116 |
| 64 | 6 | 0 | -5.039891 | -0.823325 | -2.901004 |
| 65 | 6 | 0 | -3.787395 | -0.608668 | -2.329779 |
| 66 | 6 | 0 | -3.669802 | 0.371986 | -1.350523 |
| 67 | 6 | 0 | -4.770606 | 1.125662 | -0.933846 |
| 68 | 6 | 0 | -6.017719 | 0.911805 | -1.504640 |
| 69 | 1 | 0 | -7.111405 | -0.246718 | -2.948435 |
| 70 | 1 | 0 | -5.165884 | -1.582925 | -3.666119 |
| 71 | 1 | 0 | -2.920029 | -1.189199 | -2.629791 |
| 72 | 1 | 0 | -6.884213 | 1.479057 | -1.177196 |
| 73 | 6 | 0 | -2.947136 | 1.628893 | 0.456472 |
| 74 | 6 | 0 | -4.362085 | 2.065384 | 0.174875 |
| 75 | 6 | 0 | -2.469407 | 0.762844 | -0.572306 |
| 76 | 8 | 0 | -1.315528 | 0.314089 | -0.742768 |
| 77 | 1 | 0 | -4.381945 | 3.111800 | -0.155868 |
| 78 | 1 | 0 | -5.026843 | 1.984848 | 1.042707 |
| 79 | 7 | 0 | -2.184076 | 2.477496 | 1.272145 |
| 80 | 7 | 0 | -0.962623 | 2.308554 | 1.367800 |
| 81 | 7 | 0 | 0.149703 | 2.297610 | 1.571132 |
| 82 | 6 | 0 | -3.120880 | -0.312567 | 1.816371 |
| 83 | 6 | 0 | -4.574884 | -0.417124 | 1.959383 |
| 84 | 6 | 0 | -5.364865 | -1.199107 | 1.103320 |
| 85 | 6 | 0 | -5.207918 | 0.306182 | 2.982094 |
| 86 | 6 | 0 | -6.742068 | -1.266045 | 1.279190 |
| 87 | 1 | 0 | -4.904389 | -1.730515 | 0.275108 |
| 88 | 6 | 0 | -6.584730 | 0.235460 | 3.158618 |
| 89 | 6 | 0 | -7.356602 | -0.553695 | 2.307155 |
| 90 | 1 | 0 | -7.338923 | -1.867571 | 0.601124 |
| 91 | 1 | 0 | -7.055739 | 0.796404 | 3.959250 |
| 92 | 6 | 0 | -2.360247 | -1.347905 | 1.288783 |
| 93 | 1 | 0 | -2.741401 | -2.174972 | 0.709393 |
| 94 | 1 | 0 | -2.609902 | 0.339634 | 2.518223 |
| 95 | 7 | 0 | -1.001977 | -1.318749 | 1.387298 |
| 96 | 8 | 0 | -0.408379 | -0.438103 | 2.038360 |
| 97 | 8 | 0 | -0.335382 | -2.248090 | 0.823690 |
| 98 | 1 | 0 | -4.603903 | 0.925492 | 3.640020 |
| 99 | 1 | 0 | -8.432104 | -0.608284 | 2.440919 |

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Sum of electronic and thermal Free Energies = -2558.925462
Imaginary frequency -167.7270 $cm^{-1}$

**Table S5. TSI2B** (in toluene solvent)

| Center Number | Atomic Number | Atomic Type | Coordinates (Angstroms) X | Y | Z |
|---|---|---|---|---|---|
| 1 | 7 | 0 | 1.212412 | 0.854009 | 0.054290 |
| 2 | 1 | 0 | 0.203691 | 0.750151 | 0.133675 |
| 3 | 5 | 0 | 1.801504 | 2.373297 | 0.236566 |
| 4 | 8 | 0 | 3.030720 | 2.148668 | 1.249147 |
| 5 | 8 | 0 | 0.756717 | 3.330007 | 0.668329 |
| 6 | 8 | 0 | 2.612402 | 2.792089 | -1.083166 |
| 7 | 6 | 0 | 1.934393 | 2.791989 | -2.371226 |
| 8 | 1 | 0 | 1.330060 | 1.876910 | -2.428272 |
| 9 | 6 | 0 | 3.033770 | 2.745971 | -3.414824 |
| 10 | 1 | 0 | 3.659056 | 3.641017 | -3.340649 |
| 11 | 1 | 0 | 3.664510 | 1.864772 | -3.275775 |
| 12 | 6 | 0 | 1.057263 | 4.026605 | -2.499275 |
| 13 | 1 | 0 | 0.564904 | 4.027504 | -3.475476 |
| 14 | 1 | 0 | 0.296908 | 4.051031 | -1.716248 |
| 15 | 6 | 0 | 4.021554 | 3.194386 | 1.422672 |
| 16 | 1 | 0 | 3.618915 | 4.129706 | 1.016833 |
| 17 | 6 | 0 | 5.274003 | 2.795329 | 0.663098 |
| 18 | 1 | 0 | 6.054009 | 3.550275 | 0.793339 |
| 19 | 1 | 0 | 5.648787 | 1.839796 | 1.045073 |
| 20 | 6 | 0 | 4.246467 | 3.338675 | 2.915808 |
| 21 | 1 | 0 | 4.992924 | 4.111864 | 3.113978 |
| 22 | 6 | 0 | 1.953883 | -0.392304 | -0.092100 |
| 23 | 1 | 0 | 1.255978 | -1.108918 | -0.536833 |
| 24 | 6 | 0 | 2.410128 | -0.957675 | 1.258286 |
| 25 | 1 | 0 | 2.851210 | -1.944813 | 1.105555 |
| 26 | 1 | 0 | 3.145604 | -0.298526 | 1.727940 |
| 27 | 6 | 0 | 3.157499 | -0.278130 | -1.037972 |
| 28 | 1 | 0 | 2.777672 | 0.143670 | -1.971356 |
| 29 | 1 | 0 | 3.894537 | 0.415337 | -0.616340 |
| 30 | 6 | 0 | 3.786544 | -1.626460 | -1.298055 |
| 31 | 6 | 0 | 5.070289 | -1.923809 | -0.836657 |
| 32 | 6 | 0 | 3.063199 | -2.611495 | -1.982538 |
| 33 | 6 | 0 | 5.631596 | -3.181508 | -1.051974 |
| 34 | 1 | 0 | 5.636289 | -1.159711 | -0.307917 |
| 35 | 6 | 0 | 3.623536 | -3.868065 | -2.192693 |
| 36 | 1 | 0 | 2.064449 | -2.383837 | -2.352899 |
| 37 | 6 | 0 | 4.906823 | -4.157584 | -1.729594 |
| 38 | 1 | 0 | 6.633121 | -3.396169 | -0.691902 |
| 39 | 1 | 0 | 3.055157 | -4.623989 | -2.725525 |
| 40 | 1 | 0 | 5.339888 | -5.138403 | -1.899292 |
| 41 | 6 | 0 | 1.298155 | -2.424759 | 2.943305 |
| 42 | 6 | 0 | 1.157326 | 0.029761 | 3.185240 |
| 43 | 6 | 0 | 0.040294 | -2.593822 | 3.782831 |
| 44 | 1 | 0 | 2.201493 | -2.410721 | 3.562688 |
| 45 | 1 | 0 | 1.392186 | -3.206341 | 2.189010 |
| 46 | 6 | 0 | -0.077543 | -0.108817 | 4.065016 |
| 47 | 1 | 0 | 2.080334 | 0.006586 | 3.775071 |
| 48 | 1 | 0 | 1.140165 | 0.945587 | 2.596177 |

| | | | | | |
|---|---|---|---|---|---|
| 49 | 6 | 0 | -0.102181 | -1.453534 | 4.791089 |
| 50 | 1 | 0 | 0.087099 | -3.564843 | 4.282574 |
| 51 | 1 | 0 | -0.830508 | -2.615828 | 3.113855 |
| 52 | 1 | 0 | -0.077572 | 0.722949 | 4.774685 |
| 53 | 1 | 0 | -0.966956 | -0.003441 | 3.434680 |
| 54 | 1 | 0 | -1.030280 | -1.560937 | 5.357879 |
| 55 | 1 | 0 | 0.724880 | -1.501909 | 5.510835 |
| 56 | 7 | 0 | 1.257785 | -1.115644 | 2.213218 |
| 57 | 1 | 0 | 2.595717 | 2.705826 | -4.414914 |
| 58 | 1 | 0 | 1.670456 | 4.928979 | -2.415735 |
| 59 | 1 | 0 | 4.608541 | 2.392631 | 3.330310 |
| 60 | 1 | 0 | 3.315437 | 3.610322 | 3.417825 |
| 61 | 1 | 0 | 5.053245 | 2.692461 | -0.401428 |
| 62 | 1 | 0 | 0.373076 | -1.090010 | 1.658882 |
| 63 | 6 | 0 | -5.901640 | 1.204575 | 1.868126 |
| 64 | 6 | 0 | -4.718513 | 1.868253 | 2.213346 |
| 65 | 6 | 0 | -3.482380 | 1.292126 | 1.938718 |
| 66 | 6 | 0 | -3.470460 | 0.043080 | 1.323725 |
| 67 | 6 | 0 | -4.649562 | -0.635932 | 0.992682 |
| 68 | 6 | 0 | -5.879369 | -0.048940 | 1.253528 |
| 69 | 1 | 0 | -6.855799 | 1.677506 | 2.078810 |
| 70 | 1 | 0 | -4.770570 | 2.845020 | 2.683089 |
| 71 | 1 | 0 | -2.549535 | 1.803733 | 2.159783 |
| 72 | 1 | 0 | -6.804893 | -0.544983 | 0.977156 |
| 73 | 6 | 0 | -2.840651 | -1.810948 | 0.048676 |
| 74 | 6 | 0 | -4.323728 | -1.951468 | 0.325348 |
| 75 | 6 | 0 | -2.322101 | -0.741651 | 0.850523 |
| 76 | 8 | 0 | -1.111910 | -0.469913 | 1.027138 |
| 77 | 1 | 0 | -4.494307 | -2.792432 | 1.008389 |
| 78 | 1 | 0 | -4.929159 | -2.125846 | -0.568633 |
| 79 | 7 | 0 | -2.136834 | -3.035746 | -0.118790 |
| 80 | 7 | 0 | -0.910386 | -3.040315 | -0.035523 |
| 81 | 7 | 0 | 0.207765 | -3.221318 | 0.012282 |
| 82 | 6 | 0 | -2.631052 | -0.858581 | -1.795125 |
| 83 | 6 | 0 | -3.813073 | 0.032576 | -1.888190 |
| 84 | 6 | 0 | -3.781748 | 1.355924 | -1.423727 |
| 85 | 6 | 0 | -5.002899 | -0.446502 | -2.447741 |
| 86 | 6 | 0 | -4.911438 | 2.159746 | -1.490470 |
| 87 | 1 | 0 | -2.873327 | 1.749350 | -0.976504 |
| 88 | 6 | 0 | -6.136230 | 0.359946 | -2.520793 |
| 89 | 6 | 0 | -6.096120 | 1.662826 | -2.034552 |
| 90 | 1 | 0 | -4.870330 | 3.174615 | -1.108132 |
| 91 | 1 | 0 | -7.048100 | -0.031373 | -2.960571 |
| 92 | 6 | 0 | -1.358205 | -0.283942 | -1.983365 |
| 93 | 1 | 0 | -1.154355 | 0.774514 | -1.928899 |
| 94 | 1 | 0 | -2.749983 | -1.835461 | -2.261677 |
| 95 | 7 | 0 | -0.317498 | -1.011604 | -2.502190 |
| 96 | 8 | 0 | -0.391783 | -2.253277 | -2.609590 |
| 97 | 8 | 0 | 0.712191 | -0.398114 | -2.873194 |
| 98 | 1 | 0 | -5.034181 | -1.460986 | -2.837138 |
| 99 | 1 | 0 | -6.979400 | 2.291505 | -2.083660 |

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Sum of electronic and thermal Free Energies = -2558.919407
Imaginary frequency -165.3223 $cm^{-1}$

**Table S6. TSI2C** (in toluene solvent)

| Center Number | Atomic Number | Atomic Type | Coordinates (Angstroms) X | Y | Z |
|---|---|---|---|---|---|
| 1 | 7 | 0 | 1.618897 | -0.382681 | -0.660365 |
| 2 | 1 | 0 | 0.747908 | -0.202046 | -1.168581 |
| 3 | 15 | 0 | 2.816735 | -1.171164 | -1.456032 |
| 4 | 8 | 0 | 4.129589 | -0.361568 | -1.014053 |
| 5 | 8 | 0 | 2.547774 | -1.316219 | -2.903705 |
| 6 | 8 | 0 | 3.115619 | -2.568403 | -0.706723 |
| 7 | 6 | 0 | 2.231595 | -3.680951 | -0.996277 |
| 8 | 1 | 0 | 1.236497 | -3.283285 | -1.238676 |
| 9 | 6 | 0 | 2.148412 | -4.510459 | 0.270687 |
| 10 | 1 | 0 | 3.142233 | -4.875926 | 0.545027 |
| 11 | 1 | 0 | 1.756401 | -3.917816 | 1.101524 |
| 12 | 6 | 0 | 2.781685 | -4.458517 | -2.178862 |
| 13 | 1 | 0 | 3.779001 | -4.839349 | -1.937652 |
| 14 | 1 | 0 | 2.130756 | -5.306448 | -2.408374 |
| 15 | 6 | 0 | 5.428460 | -0.836511 | -1.457439 |
| 16 | 1 | 0 | 5.373405 | -1.926085 | -1.564543 |
| 17 | 6 | 0 | 6.411668 | -0.479260 | -0.360178 |
| 18 | 1 | 0 | 7.416858 | -0.811077 | -0.631656 |
| 19 | 1 | 0 | 6.431818 | 0.605038 | -0.214965 |
| 20 | 6 | 0 | 5.751451 | -0.191425 | -2.793530 |
| 21 | 1 | 0 | 6.724069 | -0.536505 | -3.154262 |
| 22 | 6 | 0 | 1.651632 | 0.223288 | 0.665685 |
| 23 | 1 | 0 | 0.598826 | 0.414799 | 0.911268 |
| 24 | 6 | 0 | 2.380839 | 1.573822 | 0.698303 |
| 25 | 1 | 0 | 2.513211 | 1.879154 | 1.738378 |
| 26 | 1 | 0 | 3.358810 | 1.501971 | 0.215323 |
| 27 | 6 | 0 | 2.250584 | -0.726368 | 1.712431 |
| 28 | 1 | 0 | 1.718706 | -1.681305 | 1.618916 |
| 29 | 1 | 0 | 3.293505 | -0.939497 | 1.450236 |
| 30 | 6 | 0 | 2.178570 | -0.243759 | 3.145800 |
| 31 | 6 | 0 | 1.118137 | 0.537722 | 3.619594 |
| 32 | 6 | 0 | 3.186805 | -0.613070 | 4.040797 |
| 33 | 6 | 0 | 1.071086 | 0.928750 | 4.956261 |
| 34 | 1 | 0 | 0.330723 | 0.871574 | 2.947530 |
| 35 | 6 | 0 | 3.136482 | -0.229400 | 5.377708 |
| 36 | 1 | 0 | 4.020002 | -1.212251 | 3.681937 |
| 37 | 6 | 0 | 2.075114 | 0.544191 | 5.840851 |
| 38 | 1 | 0 | 0.243946 | 1.539666 | 5.303911 |
| 39 | 1 | 0 | 3.929330 | -0.529880 | 6.055467 |
| 40 | 1 | 0 | 2.034283 | 0.849963 | 6.881255 |
| 41 | 6 | 0 | 1.909975 | 4.004764 | 0.624310 |
| 42 | 6 | 0 | 1.742758 | 2.686317 | -1.458923 |
| 43 | 6 | 0 | 0.977900 | 5.060944 | 0.047181 |
| 44 | 1 | 0 | 2.964151 | 4.214128 | 0.410329 |
| 45 | 1 | 0 | 1.774019 | 3.907158 | 1.703432 |
| 46 | 6 | 0 | 0.807203 | 3.726725 | -2.049563 |
| 47 | 1 | 0 | 2.797607 | 2.907639 | -1.660805 |
| 48 | 1 | 0 | 1.513417 | 1.690223 | -1.829750 |

| | | | | | |
|---|---|---|---|---|---|
| 49 | 6 | 0 | 1.080702 | 5.115420 | -1.476401 |
| 50 | 1 | 0 | 1.225714 | 6.023529 | 0.503164 |
| 51 | 1 | 0 | -0.046606 | 4.798998 | 0.336170 |
| 52 | 1 | 0 | 0.914832 | 3.710143 | -3.137458 |
| 53 | 1 | 0 | -0.219339 | 3.425859 | -1.815979 |
| 54 | 1 | 0 | 0.362024 | 5.835654 | -1.875574 |
| 55 | 1 | 0 | 2.082765 | 5.453782 | -1.772298 |
| 56 | 7 | 0 | 1.598262 | 2.661611 | 0.033443 |
| 57 | 1 | 0 | 1.491087 | -5.369709 | 0.113207 |
| 58 | 1 | 0 | 2.845459 | -3.809751 | -3.053893 |
| 59 | 1 | 0 | 5.786641 | 0.896349 | -2.681371 |
| 60 | 1 | 0 | 4.986001 | -0.446746 | -3.529269 |
| 61 | 1 | 0 | 6.126483 | -0.955473 | 0.580817 |
| 62 | 1 | 0 | 0.589086 | 2.507584 | 0.312062 |
| 63 | 6 | 0 | -2.717079 | -4.087210 | -0.035742 |
| 64 | 6 | 0 | -1.501120 | -3.529738 | 0.370974 |
| 65 | 6 | 0 | -1.147326 | -2.239143 | -0.020233 |
| 66 | 6 | 0 | -2.033459 | -1.525705 | -0.824448 |
| 67 | 6 | 0 | -3.258443 | -2.075108 | -1.216204 |
| 68 | 6 | 0 | -3.607459 | -3.361195 | -0.827799 |
| 69 | 1 | 0 | -2.975621 | -5.093489 | 0.278759 |
| 70 | 1 | 0 | -0.831872 | -4.106697 | 1.002224 |
| 71 | 1 | 0 | -0.203475 | -1.798237 | 0.287035 |
| 72 | 1 | 0 | -4.564085 | -3.787337 | -1.116036 |
| 73 | 6 | 0 | -3.213105 | 0.180735 | -1.855977 |
| 74 | 6 | 0 | -4.052905 | -1.061438 | -2.001440 |
| 75 | 6 | 0 | -1.923503 | -0.135693 | -1.338763 |
| 76 | 8 | 0 | -0.931035 | 0.618962 | -1.218749 |
| 77 | 1 | 0 | -4.135551 | -1.343575 | -3.058892 |
| 78 | 1 | 0 | -5.071324 | -0.952174 | -1.610973 |
| 79 | 7 | 0 | -3.558451 | 1.262502 | -2.677343 |
| 80 | 7 | 0 | -2.770173 | 2.207549 | -2.813574 |
| 81 | 7 | 0 | -2.190849 | 3.146302 | -3.056626 |
| 82 | 6 | 0 | -3.701404 | 1.066816 | 0.292882 |
| 83 | 6 | 0 | -4.741546 | 0.131851 | 0.727472 |
| 84 | 6 | 0 | -4.458944 | -1.014813 | 1.484754 |
| 85 | 6 | 0 | -6.072160 | 0.380062 | 0.356210 |
| 86 | 6 | 0 | -5.481151 | -1.873997 | 1.871442 |
| 87 | 1 | 0 | -3.431120 | -1.254567 | 1.743296 |
| 88 | 6 | 0 | -7.093143 | -0.477945 | 0.747051 |
| 89 | 6 | 0 | -6.800049 | -1.608377 | 1.508838 |
| 90 | 1 | 0 | -5.243051 | -2.762167 | 2.447965 |
| 91 | 1 | 0 | -8.116975 | -0.266377 | 0.456237 |
| 92 | 6 | 0 | -2.544381 | 1.270553 | 1.032664 |
| 93 | 1 | 0 | -2.169157 | 0.616937 | 1.805804 |
| 94 | 1 | 0 | -4.025616 | 1.905311 | -0.316342 |
| 95 | 7 | 0 | -1.720420 | 2.317109 | 0.740693 |
| 96 | 8 | 0 | -2.000892 | 3.162954 | -0.122082 |
| 97 | 8 | 0 | -0.642331 | 2.430024 | 1.422133 |
| 98 | 1 | 0 | -6.295772 | 1.257535 | -0.244800 |
| 99 | 1 | 0 | -7.594975 | -2.281782 | 1.812478 |

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Sum of electronic and thermal Free Energies = -2558.922075
Imaginary frequency -370.0126 $cm^{-1}$

**Table S7. TSI2D** (in toluene solvent)

| Center Number | Atomic Number | Atomic Type | Coordinates (Angstroms) X | Y | Z |
|---|---|---|---|---|---|
| 1 | 7 | 0 | -2.176507 | -0.604466 | -0.951212 |
| 2 | 1 | 0 | -1.346975 | -1.044678 | -1.358368 |
| 3 | 5 | 0 | -3.290360 | -1.648618 | -0.346969 |
| 4 | 8 | 0 | -3.152518 | -1.508939 | 1.249502 |
| 5 | 8 | 0 | -3.167702 | -3.018151 | -0.895237 |
| 6 | 8 | 0 | -4.745166 | -0.980347 | -0.527786 |
| 7 | 6 | 0 | -5.440253 | -1.143920 | -1.791225 |
| 8 | 1 | 0 | -4.698400 | -1.084806 | -2.598968 |
| 9 | 6 | 0 | -6.418021 | 0.012163 | -1.896318 |
| 10 | 1 | 0 | -7.116060 | -0.019756 | -1.054636 |
| 11 | 1 | 0 | -5.903046 | 0.974774 | -1.886156 |
| 12 | 6 | 0 | -6.141184 | -2.492044 | -1.819009 |
| 13 | 1 | 0 | -6.858593 | -2.547951 | -0.994112 |
| 14 | 1 | 0 | -6.685973 | -2.607990 | -2.760017 |
| 15 | 6 | 0 | -4.032772 | -2.265408 | 2.119196 |
| 16 | 1 | 0 | -5.012983 | -2.334436 | 1.631433 |
| 17 | 6 | 0 | -4.148862 | -1.462256 | 3.400155 |
| 18 | 1 | 0 | -4.807505 | -1.971565 | 4.108027 |
| 19 | 1 | 0 | -3.161883 | -1.353805 | 3.860242 |
| 20 | 6 | 0 | -3.447232 | -3.650387 | 2.332746 |
| 21 | 1 | 0 | -4.063886 | -4.216394 | 3.036366 |
| 22 | 6 | 0 | -2.015814 | 0.817410 | -0.654580 |
| 23 | 1 | 0 | -1.197342 | 1.127600 | -1.301225 |
| 24 | 6 | 0 | -1.648252 | 1.115384 | 0.823292 |
| 25 | 1 | 0 | -2.373170 | 1.818877 | 1.241939 |
| 26 | 1 | 0 | -1.702027 | 0.198181 | 1.409966 |
| 27 | 6 | 0 | -3.260051 | 1.635533 | -1.066440 |
| 28 | 1 | 0 | -3.551424 | 1.301201 | -2.067925 |
| 29 | 1 | 0 | -4.093243 | 1.416025 | -0.390793 |
| 30 | 6 | 0 | -2.949961 | 3.111449 | -1.069050 |
| 31 | 6 | 0 | -2.169842 | 3.659226 | -2.092995 |
| 32 | 6 | 0 | -3.345549 | 3.940633 | -0.016462 |
| 33 | 6 | 0 | -1.771178 | 4.991174 | -2.051695 |
| 34 | 1 | 0 | -1.862028 | 3.027517 | -2.923401 |
| 35 | 6 | 0 | -2.946257 | 5.275931 | 0.032164 |
| 36 | 1 | 0 | -3.973083 | 3.536042 | 0.774524 |
| 37 | 6 | 0 | -2.150540 | 5.801912 | -0.981762 |
| 38 | 1 | 0 | -1.162267 | 5.398306 | -2.852704 |
| 39 | 1 | 0 | -3.259647 | 5.903626 | 0.860396 |
| 40 | 1 | 0 | -1.835928 | 6.839850 | -0.945993 |
| 41 | 6 | 0 | 0.177080 | 2.775370 | 0.190830 |
| 42 | 6 | 0 | -0.344110 | 2.241832 | 2.536085 |
| 43 | 6 | 0 | 1.553613 | 3.265250 | 0.619898 |
| 44 | 1 | 0 | -0.564284 | 3.582821 | 0.210975 |
| 45 | 1 | 0 | 0.220771 | 2.343465 | -0.806976 |
| 46 | 6 | 0 | 0.987893 | 2.816719 | 3.001060 |
| 47 | 1 | 0 | -1.125079 | 3.012130 | 2.539288 |
| 48 | 1 | 0 | -0.661641 | 1.410034 | 3.169348 |

| | | | | | |
|---|---|---|---|---|---|
| 49 | 6 | 0 | 1.513327 | 3.864666 | 2.022518 |
| 50 | 1 | 0 | 1.902420 | 3.992580 | -0.118517 |
| 51 | 1 | 0 | 2.246108 | 2.414273 | 0.608899 |
| 52 | 1 | 0 | 0.828807 | 3.248126 | 3.994025 |
| 53 | 1 | 0 | 1.713273 | 2.005545 | 3.095175 |
| 54 | 1 | 0 | 2.511610 | 4.190037 | 2.326399 |
| 55 | 1 | 0 | 0.860696 | 4.748140 | 2.023250 |
| 56 | 7 | 0 | -0.297622 | 1.709995 | 1.127878 |
| 57 | 1 | 0 | -6.989974 | -0.067188 | -2.824198 |
| 58 | 1 | 0 | -5.416988 | -3.301536 | -1.722109 |
| 59 | 1 | 0 | -2.435346 | -3.563830 | 2.741141 |
| 60 | 1 | 0 | -3.398921 | -4.191857 | 1.385919 |
| 61 | 1 | 0 | -4.554220 | -0.468587 | 3.195249 |
| 62 | 1 | 0 | 0.432591 | 0.936061 | 1.158990 |
| 63 | 6 | 0 | 0.752586 | -4.582600 | -0.139320 |
| 64 | 6 | 0 | -0.214924 | -3.673278 | 0.310697 |
| 65 | 6 | 0 | 0.169832 | -2.450968 | 0.846746 |
| 66 | 6 | 0 | 1.530013 | -2.153661 | 0.915849 |
| 67 | 6 | 0 | 2.496838 | -3.071404 | 0.492858 |
| 68 | 6 | 0 | 2.111525 | -4.294573 | -0.046206 |
| 69 | 1 | 0 | 0.432504 | -5.526861 | -0.568888 |
| 70 | 1 | 0 | -1.268793 | -3.907549 | 0.201460 |
| 71 | 1 | 0 | -0.572016 | -1.732563 | 1.185146 |
| 72 | 1 | 0 | 2.853703 | -5.008772 | -0.391905 |
| 73 | 6 | 0 | 3.580587 | -1.091295 | 1.086123 |
| 74 | 6 | 0 | 3.883716 | -2.517036 | 0.720852 |
| 75 | 6 | 0 | 2.198289 | -0.917782 | 1.362328 |
| 76 | 8 | 0 | 1.662411 | 0.106722 | 1.869090 |
| 77 | 1 | 0 | 4.385198 | -3.042002 | 1.544002 |
| 78 | 1 | 0 | 4.526630 | -2.616212 | -0.162361 |
| 79 | 7 | 0 | 4.591352 | -0.309971 | 1.685498 |
| 80 | 7 | 0 | 4.331213 | 0.852354 | 1.998484 |
| 81 | 7 | 0 | 4.266368 | 1.942476 | 2.312041 |
| 82 | 6 | 0 | 3.407818 | -0.217554 | -1.079550 |
| 83 | 6 | 0 | 4.849789 | -0.156118 | -1.348352 |
| 84 | 6 | 0 | 5.528657 | -1.155116 | -2.062774 |
| 85 | 6 | 0 | 5.578305 | 0.949897 | -0.889984 |
| 86 | 6 | 0 | 6.893315 | -1.050663 | -2.301639 |
| 87 | 1 | 0 | 4.987349 | -2.019344 | -2.435967 |
| 88 | 6 | 0 | 6.942253 | 1.056966 | -1.133855 |
| 89 | 6 | 0 | 7.604994 | 0.054719 | -1.838206 |
| 90 | 1 | 0 | 7.403413 | -1.833344 | -2.853775 |
| 91 | 1 | 0 | 7.488101 | 1.923221 | -0.774209 |
| 92 | 6 | 0 | 2.552964 | -0.997618 | -1.838479 |
| 93 | 1 | 0 | 2.824693 | -1.784820 | -2.523370 |
| 94 | 1 | 0 | 2.965922 | 0.658654 | -0.612408 |
| 95 | 7 | 0 | 1.190545 | -0.807506 | -1.721339 |
| 96 | 8 | 0 | 0.758647 | 0.067316 | -0.935823 |
| 97 | 8 | 0 | 0.412119 | -1.496665 | -2.400660 |
| 98 | 1 | 0 | 5.062516 | 1.738459 | -0.346160 |
| 99 | 1 | 0 | 8.670509 | 0.134583 | -2.027593 |

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Sum of electronic and thermal Free Energies = -2558.916137
Imaginary frequency -260.4669 $cm^{-1}$

**Table S8. TSII2A** (in dichloromethane solvent)

| Center Number | Atomic Number | Atomic Type | Coordinates (Angstroms) X | Y | Z |
|---|---|---|---|---|---|
| 1 | 7 | 0 | -2.266019 | 0.908919 | 1.165100 |
| 2 | 1 | 0 | -1.583310 | 0.155220 | 1.310778 |
| 3 | 6 | 0 | -3.617526 | 0.661302 | 1.653969 |
| 4 | 1 | 0 | -3.675520 | -0.430203 | 1.759252 |
| 5 | 6 | 0 | -4.649150 | 1.100511 | 0.617033 |
| 6 | 1 | 0 | -5.658158 | 0.883192 | 0.963707 |
| 7 | 1 | 0 | -4.571887 | 2.170564 | 0.413417 |
| 8 | 6 | 0 | -3.860026 | 1.254813 | 3.070130 |
| 9 | 6 | 0 | -5.107852 | -0.975179 | -0.695723 |
| 10 | 6 | 0 | -4.815394 | 1.188349 | -1.881364 |
| 11 | 6 | 0 | -6.620929 | -0.859624 | -0.830000 |
| 12 | 1 | 0 | -4.677044 | -1.501054 | -1.551072 |
| 13 | 1 | 0 | -4.818593 | -1.492239 | 0.223246 |
| 14 | 6 | 0 | -6.323622 | 1.346621 | -1.988018 |
| 15 | 1 | 0 | -4.301416 | 2.146612 | -1.780623 |
| 16 | 1 | 0 | -4.401172 | 0.643722 | -2.733810 |
| 17 | 6 | 0 | -7.006182 | -0.020316 | -2.049123 |
| 18 | 1 | 0 | -7.060345 | -0.428784 | 0.076849 |
| 19 | 1 | 0 | -7.016721 | -1.875303 | -0.913033 |
| 20 | 1 | 0 | -6.536575 | 1.931408 | -2.886457 |
| 21 | 1 | 0 | -6.703041 | 1.924771 | -1.136514 |
| 22 | 1 | 0 | -8.091563 | 0.095903 | -2.098357 |
| 23 | 1 | 0 | -6.691420 | -0.539975 | -2.962300 |
| 24 | 7 | 0 | -4.434039 | 0.371499 | -0.675336 |
| 25 | 6 | 0 | -1.808039 | 2.014886 | 0.577289 |
| 26 | 6 | 0 | -2.320067 | 3.291216 | 0.019919 |
| 27 | 6 | 0 | -0.493379 | 2.345306 | 0.208803 |
| 28 | 6 | 0 | -0.895121 | 3.640668 | -0.359347 |
| 29 | 8 | 0 | -3.399041 | 3.842680 | -0.099952 |
| 30 | 8 | 0 | -0.364507 | 4.590125 | -0.902945 |
| 31 | 7 | 0 | 0.620092 | 1.620645 | 0.431196 |
| 32 | 1 | 0 | 0.475630 | 0.726846 | 0.916186 |
| 33 | 6 | 0 | 1.949440 | 1.956561 | 0.201502 |
| 34 | 6 | 0 | 2.910088 | 1.065482 | 0.690284 |
| 35 | 6 | 0 | 2.357411 | 3.113210 | -0.470634 |
| 36 | 6 | 0 | 4.259331 | 1.326574 | 0.507843 |
| 37 | 1 | 0 | 2.584818 | 0.171598 | 1.215790 |
| 38 | 6 | 0 | 3.718186 | 3.347125 | -0.633914 |
| 39 | 1 | 0 | 1.624825 | 3.817096 | -0.856264 |
| 40 | 6 | 0 | 4.688055 | 2.470262 | -0.155689 |
| 41 | 1 | 0 | 5.742571 | 2.672443 | -0.297020 |
| 42 | 6 | 0 | 4.150361 | 4.625025 | -1.298651 |
| 43 | 6 | 0 | 5.245660 | 0.312693 | 1.011348 |
| 44 | 9 | 0 | 4.239309 | 5.632313 | -0.414872 |
| 45 | 9 | 0 | 3.284958 | 5.012274 | -2.245213 |
| 46 | 9 | 0 | 5.354883 | 4.504254 | -1.874953 |
| 47 | 9 | 0 | 6.488897 | 0.799600 | 1.073626 |
| 48 | 9 | 0 | 5.282194 | -0.771245 | 0.213823 |

| | | | | | |
|---|---|---|---|---|---|
| 49 | 9 | 0 | 4.918968 | -0.130454 | 2.236981 |
| 50 | 1 | 0 | -3.404994 | 0.197505 | -0.804517 |
| 51 | 6 | 0 | 3.448023 | -4.580102 | 1.733907 |
| 52 | 6 | 0 | 3.603578 | -3.302052 | 2.281139 |
| 53 | 6 | 0 | 2.558752 | -2.383666 | 2.231544 |
| 54 | 6 | 0 | 1.373443 | -2.769290 | 1.610632 |
| 55 | 6 | 0 | 1.205973 | -4.056145 | 1.083534 |
| 56 | 6 | 0 | 2.247417 | -4.970483 | 1.135889 |
| 57 | 1 | 0 | 4.275853 | -5.280956 | 1.775184 |
| 58 | 1 | 0 | 4.546041 | -3.021705 | 2.739950 |
| 59 | 1 | 0 | 2.661315 | -1.394786 | 2.667845 |
| 60 | 1 | 0 | 2.139856 | -5.963581 | 0.710324 |
| 61 | 6 | 0 | -0.657941 | -2.765424 | 0.487667 |
| 62 | 6 | 0 | -0.172062 | -4.196009 | 0.481876 |
| 63 | 6 | 0 | 0.171973 | -1.962620 | 1.324719 |
| 64 | 8 | 0 | -0.018141 | -0.777537 | 1.702539 |
| 65 | 7 | 0 | -2.017121 | -2.422013 | 0.351074 |
| 66 | 7 | 0 | -2.693523 | -3.174839 | -0.363508 |
| 67 | 7 | 0 | -3.428814 | -3.803319 | -0.953825 |
| 68 | 1 | 0 | -0.148065 | -4.655347 | -0.512562 |
| 69 | 1 | 0 | -0.813855 | -4.821906 | 1.116461 |
| 70 | 6 | 0 | 0.230688 | -1.894724 | -1.452220 |
| 71 | 6 | 0 | -0.876807 | -1.992362 | -2.293643 |
| 72 | 6 | 0 | 1.430280 | -2.708423 | -1.685326 |
| 73 | 6 | 0 | 1.376181 | -3.936430 | -2.365714 |
| 74 | 6 | 0 | 2.672558 | -2.268590 | -1.202948 |
| 75 | 6 | 0 | 2.521087 | -4.704956 | -2.537770 |
| 76 | 1 | 0 | 0.432068 | -4.302552 | -2.757595 |
| 77 | 6 | 0 | 3.817783 | -3.034953 | -1.378709 |
| 78 | 1 | 0 | 2.737729 | -1.315277 | -0.685556 |
| 79 | 6 | 0 | 3.744063 | -4.259290 | -2.039898 |
| 80 | 1 | 0 | 2.457549 | -5.653489 | -3.060813 |
| 81 | 1 | 0 | 4.765408 | -2.680532 | -0.990633 |
| 82 | 7 | 0 | -1.889560 | -1.083126 | -2.222390 |
| 83 | 8 | 0 | -1.798175 | -0.076423 | -1.460977 |
| 84 | 8 | 0 | -2.916133 | -1.258650 | -2.918411 |
| 85 | 1 | 0 | 0.372388 | -0.933468 | -0.964162 |
| 86 | 6 | 0 | -5.286964 | 0.923201 | 3.528143 |
| 87 | 1 | 0 | -5.388860 | 1.139209 | 4.595413 |
| 88 | 1 | 0 | -6.038558 | 1.519278 | 3.002190 |
| 89 | 1 | 0 | -5.517109 | -0.138068 | 3.378048 |
| 90 | 6 | 0 | -3.647521 | 2.772293 | 3.089640 |
| 91 | 1 | 0 | -2.601928 | 3.030478 | 2.894333 |
| 92 | 1 | 0 | -4.270916 | 3.290913 | 2.354712 |
| 93 | 1 | 0 | -3.901778 | 3.161160 | 4.080311 |
| 94 | 6 | 0 | -2.864364 | 0.589647 | 4.028676 |
| 95 | 1 | 0 | -2.977014 | 1.006743 | 5.033609 |
| 96 | 1 | 0 | -3.038694 | -0.490340 | 4.087198 |
| 97 | 1 | 0 | -1.831889 | 0.751641 | 3.705514 |
| 98 | 1 | 0 | 4.636877 | -4.862232 | -2.170185 |
| 99 | 1 | 0 | -1.068843 | -2.791749 | -2.992342 |

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Sum of electronic and thermal Free Energies = -2905.461293
Imaginary frequency -252.9204 $cm^{-1}$

**Table S9. TSII2B** (in dichloromethane solvent)

| Center Number | Atomic Number | Atomic Type | Coordinates (Angstroms) X | Y | Z |
|---|---|---|---|---|---|
| 1 | 7 | 0 | -0.013186 | -1.766230 | 0.881633 |
| 2 | 1 | 0 | 0.084422 | -0.755512 | 1.048782 |
| 3 | 6 | 0 | 1.158046 | -2.524414 | 1.318025 |
| 4 | 1 | 0 | 1.957330 | -1.771853 | 1.307124 |
| 5 | 6 | 0 | 1.530667 | -3.605665 | 0.300638 |
| 6 | 1 | 0 | 2.402443 | -4.156687 | 0.655892 |
| 7 | 1 | 0 | 0.713133 | -4.313063 | 0.144729 |
| 8 | 6 | 0 | 1.064949 | -3.027139 | 2.786807 |
| 9 | 6 | 0 | 3.174516 | -3.528084 | -1.589671 |
| 10 | 6 | 0 | 0.814190 | -2.998547 | -2.047260 |
| 11 | 6 | 0 | 2.978959 | -4.948103 | -2.100769 |
| 12 | 1 | 0 | 3.456045 | -2.853697 | -2.404842 |
| 13 | 1 | 0 | 3.940561 | -3.463962 | -0.814072 |
| 14 | 6 | 0 | 0.580026 | -4.398042 | -2.597481 |
| 15 | 1 | 0 | -0.078284 | -2.574156 | -1.588940 |
| 16 | 1 | 0 | 1.144052 | -2.314336 | -2.834886 |
| 17 | 6 | 0 | 1.872956 | -4.993997 | -3.156273 |
| 18 | 1 | 0 | 2.731390 | -5.612947 | -1.264281 |
| 19 | 1 | 0 | 3.930333 | -5.295296 | -2.511593 |
| 20 | 1 | 0 | -0.183908 | -4.322539 | -3.375978 |
| 21 | 1 | 0 | 0.164870 | -5.041316 | -1.813866 |
| 22 | 1 | 0 | 1.704992 | -6.022383 | -3.484854 |
| 23 | 1 | 0 | 2.189506 | -4.419352 | -4.035589 |
| 24 | 7 | 0 | 1.905248 | -2.973577 | -1.011959 |
| 25 | 6 | 0 | -1.222530 | -2.252673 | 0.596139 |
| 26 | 6 | 0 | -1.820998 | -3.564044 | 0.266180 |
| 27 | 6 | 0 | -2.445025 | -1.592647 | 0.379816 |
| 28 | 6 | 0 | -3.155569 | -2.862474 | 0.117768 |
| 29 | 8 | 0 | -1.427685 | -4.708136 | 0.131807 |
| 30 | 8 | 0 | -4.287852 | -3.231737 | -0.122620 |
| 31 | 7 | 0 | -2.689486 | -0.268342 | 0.437734 |
| 32 | 1 | 0 | -1.870554 | 0.347320 | 0.525031 |
| 33 | 6 | 0 | -3.901320 | 0.397857 | 0.254807 |
| 34 | 6 | 0 | -3.868143 | 1.799426 | 0.254583 |
| 35 | 6 | 0 | -5.119620 | -0.266469 | 0.089306 |
| 36 | 6 | 0 | -5.044985 | 2.513536 | 0.090410 |
| 37 | 1 | 0 | -2.919453 | 2.314697 | 0.372070 |
| 38 | 6 | 0 | -6.279986 | 0.482291 | -0.075856 |
| 39 | 1 | 0 | -5.165475 | -1.351277 | 0.083717 |
| 40 | 6 | 0 | -6.268573 | 1.871383 | -0.077603 |
| 41 | 1 | 0 | -7.183438 | 2.437676 | -0.206623 |
| 42 | 6 | 0 | -7.574133 | -0.241237 | -0.322651 |
| 43 | 6 | 0 | -5.013137 | 4.014307 | 0.153302 |
| 44 | 9 | 0 | -7.610652 | -1.427811 | 0.299278 |
| 45 | 9 | 0 | -7.762805 | -0.480817 | -1.630917 |
| 46 | 9 | 0 | -8.630633 | 0.469568 | 0.098746 |
| 47 | 9 | 0 | -5.919868 | 4.562668 | -0.669150 |
| 48 | 9 | 0 | -3.812860 | 4.507269 | -0.180279 |

| | | | | | |
|---|---|---|---|---|---|
| 49 | 9 | 0 | -5.291220 | 4.461765 | 1.389073 |
| 50 | 1 | 0 | 2.091881 | -1.934717 | -0.835104 |
| 51 | 6 | 0 | 7.159240 | -0.335455 | 0.832843 |
| 52 | 6 | 0 | 6.176587 | -1.257445 | 1.205372 |
| 53 | 6 | 0 | 4.882581 | -1.149194 | 0.700979 |
| 54 | 6 | 0 | 4.601044 | -0.111312 | -0.182554 |
| 55 | 6 | 0 | 5.586559 | 0.809700 | -0.565692 |
| 56 | 6 | 0 | 6.871415 | 0.707409 | -0.051130 |
| 57 | 1 | 0 | 8.160271 | -0.430164 | 1.240748 |
| 58 | 1 | 0 | 6.422105 | -2.054179 | 1.899659 |
| 59 | 1 | 0 | 4.108714 | -1.849297 | 1.004193 |
| 60 | 1 | 0 | 7.639024 | 1.423514 | -0.328902 |
| 61 | 6 | 0 | 3.540163 | 1.520914 | -1.452233 |
| 62 | 6 | 0 | 5.013538 | 1.819540 | -1.532797 |
| 63 | 6 | 0 | 3.326818 | 0.253835 | -0.840734 |
| 64 | 8 | 0 | 2.242698 | -0.385378 | -0.849304 |
| 65 | 7 | 0 | 2.694296 | 2.090287 | -2.409711 |
| 66 | 7 | 0 | 1.540063 | 1.634252 | -2.521214 |
| 67 | 7 | 0 | 0.481400 | 1.339627 | -2.782622 |
| 68 | 1 | 0 | 5.281796 | 2.850601 | -1.283950 |
| 69 | 1 | 0 | 5.373081 | 1.624371 | -2.551214 |
| 70 | 6 | 0 | 2.766110 | 2.448431 | 0.492493 |
| 71 | 6 | 0 | 1.408881 | 2.562750 | 0.180555 |
| 72 | 1 | 0 | 0.977772 | 3.305033 | -0.473721 |
| 73 | 6 | 0 | 3.689232 | 3.585245 | 0.463283 |
| 74 | 6 | 0 | 3.467364 | 4.710982 | -0.345749 |
| 75 | 6 | 0 | 4.860306 | 3.522898 | 1.231724 |
| 76 | 6 | 0 | 4.395764 | 5.743260 | -0.380215 |
| 77 | 1 | 0 | 2.577771 | 4.766941 | -0.965044 |
| 78 | 6 | 0 | 5.787604 | 4.560522 | 1.196647 |
| 79 | 1 | 0 | 5.040998 | 2.649776 | 1.853078 |
| 80 | 6 | 0 | 5.558310 | 5.672617 | 0.390371 |
| 81 | 1 | 0 | 4.215624 | 6.607244 | -1.011471 |
| 82 | 1 | 0 | 6.688696 | 4.498715 | 1.798018 |
| 83 | 7 | 0 | 0.518085 | 1.628440 | 0.608243 |
| 84 | 8 | 0 | 0.815108 | 0.792756 | 1.502662 |
| 85 | 8 | 0 | -0.640344 | 1.639278 | 0.114392 |
| 86 | 1 | 0 | 3.009763 | 1.667480 | 1.207316 |
| 87 | 6 | 0 | 2.394258 | -3.687315 | 3.182206 |
| 88 | 1 | 0 | 2.419403 | -3.836474 | 4.265349 |
| 89 | 1 | 0 | 2.526061 | -4.668482 | 2.717176 |
| 90 | 1 | 0 | 3.250592 | -3.056722 | 2.915637 |
| 91 | 6 | 0 | -0.078680 | -4.024572 | 2.995624 |
| 92 | 1 | 0 | -0.034286 | -4.414322 | 4.017308 |
| 93 | 1 | 0 | -1.055423 | -3.546696 | 2.872441 |
| 94 | 1 | 0 | -0.023152 | -4.872397 | 2.306562 |
| 95 | 6 | 0 | 0.841765 | -1.801514 | 3.682234 |
| 96 | 1 | 0 | 0.784655 | -2.112051 | 4.729602 |
| 97 | 1 | 0 | 1.662999 | -1.083798 | 3.579451 |
| 98 | 1 | 0 | -0.089229 | -1.286434 | 3.429212 |
| 99 | 1 | 0 | 6.280019 | 6.482154 | 0.360200 |

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Sum of electronic and thermal Free Energies = -2905.449428
Imaginary frequency -260.0278 $cm^{-1}$

**Table S10. TSII2C** (in dichloromethane solvent)

| Center Number | Atomic Number | Atomic Type | Coordinates (Angstroms) X | Y | Z |
|---|---|---|---|---|---|
| 1 | 7 | 0 | 2.628446 | -0.949341 | 1.050188 |
| 2 | 1 | 0 | 1.915335 | -0.277808 | 1.338669 |
| 3 | 6 | 0 | 4.006905 | -0.608883 | 1.392849 |
| 4 | 1 | 0 | 3.965337 | 0.445927 | 1.693314 |
| 5 | 6 | 0 | 4.900099 | -0.722949 | 0.158508 |
| 6 | 1 | 0 | 5.915613 | -0.404904 | 0.388425 |
| 7 | 1 | 0 | 4.928661 | -1.751438 | -0.208185 |
| 8 | 6 | 0 | 4.537644 | -1.385326 | 2.630394 |
| 9 | 6 | 0 | 4.849580 | 1.576362 | -0.841077 |
| 10 | 6 | 0 | 4.693318 | -0.425372 | -2.315791 |
| 11 | 6 | 0 | 6.325785 | 1.725121 | -1.184695 |
| 12 | 1 | 0 | 4.222337 | 2.138765 | -1.535515 |
| 13 | 1 | 0 | 4.629031 | 1.907053 | 0.176145 |
| 14 | 6 | 0 | 6.176988 | -0.320844 | -2.631030 |
| 15 | 1 | 0 | 4.339995 | -1.458862 | -2.306179 |
| 16 | 1 | 0 | 4.090605 | 0.156588 | -3.016828 |
| 17 | 6 | 0 | 6.640655 | 1.134481 | -2.559739 |
| 18 | 1 | 0 | 6.952031 | 1.252253 | -0.420154 |
| 19 | 1 | 0 | 6.557551 | 2.793014 | -1.155830 |
| 20 | 1 | 0 | 6.334519 | -0.734129 | -3.630305 |
| 21 | 1 | 0 | 6.756287 | -0.941486 | -1.936787 |
| 22 | 1 | 0 | 7.712053 | 1.203863 | -2.761795 |
| 23 | 1 | 0 | 6.124250 | 1.716085 | -3.332937 |
| 24 | 7 | 0 | 4.383550 | 0.144807 | -0.954370 |
| 25 | 6 | 0 | 2.202850 | -1.983582 | 0.317840 |
| 26 | 6 | 0 | 2.775003 | -3.124299 | -0.437210 |
| 27 | 6 | 0 | 0.897238 | -2.349452 | -0.042990 |
| 28 | 6 | 0 | 1.356758 | -3.560648 | -0.751220 |
| 29 | 8 | 0 | 3.882185 | -3.527982 | -0.735783 |
| 30 | 8 | 0 | 0.868456 | -4.503641 | -1.338175 |
| 31 | 7 | 0 | -0.248747 | -1.696552 | 0.246531 |
| 32 | 1 | 0 | -0.120267 | -0.751543 | 0.612627 |
| 33 | 6 | 0 | -1.566396 | -2.140516 | 0.124507 |
| 34 | 6 | 0 | -2.582898 | -1.318492 | 0.634887 |
| 35 | 6 | 0 | -1.885807 | -3.365267 | -0.466325 |
| 36 | 6 | 0 | -3.902926 | -1.738680 | 0.535822 |
| 37 | 1 | 0 | -2.355723 | -0.356705 | 1.101474 |
| 38 | 6 | 0 | -3.218421 | -3.753615 | -0.538990 |
| 39 | 1 | 0 | -1.108703 | -4.003734 | -0.876087 |
| 40 | 6 | 0 | -4.242641 | -2.956965 | -0.045094 |
| 41 | 1 | 0 | -5.277419 | -3.272801 | -0.111712 |
| 42 | 6 | 0 | -3.547220 | -5.102323 | -1.116464 |
| 43 | 6 | 0 | -5.015681 | -0.848571 | 1.013989 |
| 44 | 9 | 0 | -3.521253 | -6.059133 | -0.174567 |
| 45 | 9 | 0 | -2.674187 | -5.465328 | -2.065756 |
| 46 | 9 | 0 | -4.772115 | -5.124332 | -1.661076 |
| 47 | 9 | 0 | -5.971719 | -1.549356 | 1.641674 |
| 48 | 9 | 0 | -5.615609 | -0.233877 | -0.027337 |

| | | | | | |
|---|---|---|---|---|---|
| 49 | 9 | 0 | -4.590760 | 0.104485 | 1.842084 |
| 50 | 1 | 0 | 3.343178 | 0.179706 | -0.899992 |
| 51 | 6 | 0 | -0.779571 | 6.621057 | 0.233561 |
| 52 | 6 | 0 | -2.081118 | 6.278867 | 0.607373 |
| 53 | 6 | 0 | -2.377010 | 4.983684 | 1.032472 |
| 54 | 6 | 0 | -1.345452 | 4.056793 | 1.084503 |
| 55 | 6 | 0 | -0.033947 | 4.397590 | 0.729827 |
| 56 | 6 | 0 | 0.254831 | 5.680050 | 0.286239 |
| 57 | 1 | 0 | -0.566845 | 7.631592 | -0.101376 |
| 58 | 1 | 0 | -2.867418 | 7.025581 | 0.553515 |
| 59 | 1 | 0 | -3.388270 | 4.687789 | 1.296173 |
| 60 | 1 | 0 | 1.264218 | 5.955915 | -0.006771 |
| 61 | 6 | 0 | -0.096605 | 2.123088 | 1.218056 |
| 62 | 6 | 0 | 0.886155 | 3.201359 | 0.890556 |
| 63 | 6 | 0 | -1.402068 | 2.612080 | 1.440117 |
| 64 | 8 | 0 | -2.399187 | 1.963195 | 1.827685 |
| 65 | 7 | 0 | 0.304777 | 0.847645 | 1.722619 |
| 66 | 7 | 0 | -0.312560 | 0.450833 | 2.737606 |
| 67 | 7 | 0 | -0.808280 | -0.040118 | 3.622433 |
| 68 | 1 | 0 | 1.465988 | 3.026890 | -0.027792 |
| 69 | 1 | 0 | 1.611512 | 3.361461 | 1.700253 |
| 70 | 6 | 0 | -0.939390 | 1.767684 | -1.283335 |
| 71 | 6 | 0 | 0.174621 | 2.123215 | -2.001802 |
| 72 | 1 | 0 | 0.234630 | 2.929960 | -2.714988 |
| 73 | 6 | 0 | -2.203232 | 2.479209 | -1.448300 |
| 74 | 6 | 0 | -2.263841 | 3.762270 | -2.021999 |
| 75 | 6 | 0 | -3.394478 | 1.880627 | -1.014845 |
| 76 | 6 | 0 | -3.481799 | 4.402941 | -2.188383 |
| 77 | 1 | 0 | -1.350769 | 4.278307 | -2.302144 |
| 78 | 6 | 0 | -4.614914 | 2.528879 | -1.173684 |
| 79 | 1 | 0 | -3.358625 | 0.897331 | -0.561345 |
| 80 | 6 | 0 | -4.662189 | 3.786882 | -1.767782 |
| 81 | 1 | 0 | -3.511398 | 5.394649 | -2.627720 |
| 82 | 1 | 0 | -5.523373 | 2.046445 | -0.831376 |
| 83 | 7 | 0 | 1.359797 | 1.422433 | -1.884268 |
| 84 | 8 | 0 | 1.485012 | 0.539318 | -1.003489 |
| 85 | 8 | 0 | 2.300545 | 1.701278 | -2.647697 |
| 86 | 1 | 0 | -0.961267 | 0.798342 | -0.796645 |
| 87 | 6 | 0 | 5.964391 | -0.917424 | 2.949014 |
| 88 | 1 | 0 | 6.262410 | -1.295675 | 3.930758 |
| 89 | 1 | 0 | 6.692761 | -1.289679 | 2.222671 |
| 90 | 1 | 0 | 6.028961 | 0.176406 | 2.978013 |
| 91 | 6 | 0 | 4.526288 | -2.899879 | 2.402657 |
| 92 | 1 | 0 | 3.506363 | -3.276136 | 2.273879 |
| 93 | 1 | 0 | 5.113524 | -3.196385 | 1.528912 |
| 94 | 1 | 0 | 4.950906 | -3.398493 | 3.279092 |
| 95 | 6 | 0 | 3.626723 | -1.046150 | 3.816966 |
| 96 | 1 | 0 | 3.970227 | -1.572061 | 4.712187 |
| 97 | 1 | 0 | 3.638423 | 0.028514 | 4.029444 |
| 98 | 1 | 0 | 2.593546 | -1.349515 | 3.623684 |
| 99 | 1 | 0 | -5.613713 | 4.293475 | -1.893758 |

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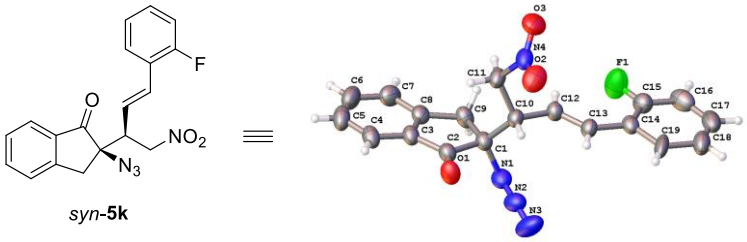
Sum of electronic and thermal Free Energies = -2905.435901
Imaginary frequency -105.0512 $cm^{-1}$

## 8. X-ray crystallographic data of *syn*-5k, *anti*-5g, *anti*-14, 15a and 15c

### 8.1 X-ray crystallographic data of *syn*-5k[18]

Data intensity of *syn*-**5k** was collected using a 'Bruker APEX-II CCD' diffractometer at 296 K. Data collection and reduction were done by using Olex2 and the structure was solved with the ShelXS structure solution program using direct methods and refined by full-matrix least-squares on $F^2$ with anisotropic displacement parameters for non-H atoms using SHELX-97. Hydrogen atoms were added at their geometrically idea positions and refined isotropically. Crystal data for *syn*-**5k**: $C_{19}H_{15}FN_4O_3$, $T$ = 296.15 K, orthorhombic, space group $P2_12_12_1$, $a$ = 10.3148(2) Å, $b$ = 11.9114(3) Å, $c$ = 14.6673(3) Å, $\alpha$ = 90 deg, $\beta$ = 90 deg, $\gamma$ = 90 deg, $V$ = 1802.08(7) Å$^3$. Z = 4, $d_{calc}$ = 1.350 g/cm$^3$. 12680 reflections measured, 3229 [R(int) = 0.0405], $R_1$ = 0.0691, $wR_2$ = 0.2196, ($I > 2\sigma(I)$, final), $R_1$ = 0.0747, $wR_2$ = 0.2314 (all data), GOF = 1.048, and 245 parameters.



*syn*-**5k**

**Table S11.** Crystal data and structure refinement for *syn*-**5k**.

| | | |
|---|---|---|
| Identification code | *syn*-**5k** | |
| Empirical formula | $C_{19}H_{15}FN_4O_3$ | |
| Formula weight | 366.35 | |
| Temperature | 296.15 K | |
| Wavelength | 1.54178 Å | |
| Crystal system | Orthorhombic | |
| Space group | $P2_12_12_1$ | |
| Unit cell dimensions | a = 10.3148(2) Å | a= 90°. |
| | b = 11.9114(3) Å | b= 90°. |
| | c = 14.6673(3) Å | g = 90°. |
| Volume | 1802.08(7) Å$^3$ | |

18 Supplementary crystallographic data have been deposited at the Cambridge Crystallographic Data Center (CCDC number: 1874281).

| | |
|---|---|
| Z | 4 |
| Density (calculated) | 1.350 $Mg/m^3$ |
| Absorption coefficient | 0.848 $mm^{-1}$ |
| F(000) | 760 |
| Crystal size | 0.25 x 0.2 x 0.15 $mm^3$ |
| Theta range for data collection | 4.782 to 68.605°. |
| Index ranges | -12<=h<=12, -14<=k<=9, -17<=l<=16 |
| Reflections collected | 12680 |
| Independent reflections | 3229 [R(int) = 0.0405] |
| Completeness to theta = 67.679° | 99.1 % |
| Absorption correction | Semi-empirical from equivalents |
| Max. and min. transmission | 0.7531 and 0.6639 |
| Refinement method | Full-matrix least-squares on $F^2$ |
| Data / restraints / parameters | 3229 / 0 / 245 |
| Goodness-of-fit on $F^2$ | 1.048 |
| Final R indices [I>2sigma(I)] | $R_1$ = 0.0691, $wR_2$ = 0.2196 |
| R indices (all data) | $R_1$ = 0.0747, $wR_2$ = 0.2314 |
| Absolute structure parameter | 0.06(11) |
| Extinction coefficient | 0.007(2) |
| Largest diff. peak and hole | 0.846 and -0.323 $e.Å^{-3}$ |

**Table S12.** Atomic coordinates ( x $10^4$) and equivalent isotropic displacement parameters ($Å^2$ x $10^3$) for *syn*-**5k**. U(eq) is defined as one third of the trace of the orthogonalized $U^{ij}$ tensor.

| | x | y | z | U(eq) |
|---|---|---|---|---|
| F(1) | 8690(5) | 2750(4) | 4148(4) | 150(2) |
| O(1) | 3852(4) | 6665(3) | 2589(3) | 97(1) |
| O(2) | 7432(5) | 5702(5) | 1188(3) | 120(2) |
| O(3) | 7578(5) | 3984(5) | 854(4) | 133(2) |

| | | | | |
|---|---|---|---|---|
| N(1) | 4770(5) | 5284(5) | 4185(3) | 89(1) |
| N(2) | 5193(6) | 6254(5) | 4263(3) | 102(2) |
| N(3) | 5593(10) | 7108(6) | 4442(5) | 154(3) |
| N(4) | 7063(4) | 4748(5) | 1240(3) | 89(1) |
| C(1) | 4662(4) | 4901(4) | 3232(3) | 68(1) |
| C(2) | 3682(4) | 5672(4) | 2724(3) | 72(1) |
| C(3) | 2580(4) | 4984(4) | 2443(3) | 70(1) |
| C(4) | 1475(5) | 5299(5) | 1951(3) | 89(2) |
| C(5) | 579(5) | 4527(7) | 1749(4) | 106(2) |
| C(6) | 747(6) | 3427(7) | 2043(4) | 111(2) |
| C(7) | 1829(6) | 3103(5) | 2518(5) | 99(2) |
| C(8) | 2767(4) | 3892(4) | 2721(3) | 74(1) |
| C(9) | 4001(4) | 3745(4) | 3244(4) | 80(1) |
| C(10) | 5986(4) | 4978(4) | 2744(2) | 65(1) |
| C(11) | 5864(4) | 4494(5) | 1784(3) | 78(1) |
| C(12) | 7059(4) | 4419(4) | 3259(3) | 66(1) |
| C(13) | 8051(4) | 4980(4) | 3597(3) | 68(1) |
| C(14) | 9205(4) | 4585(4) | 4101(3) | 71(1) |
| C(15) | 9491(6) | 3530(5) | 4349(3) | 87(1) |
| C(16) | 10604(8) | 3202(7) | 4809(4) | 111(2) |
| C(17) | 11471(6) | 4039(9) | 5027(4) | 112(2) |
| C(18) | 11264(6) | 5091(8) | 4802(4) | 110(2) |
| C(19) | 10144(5) | 5449(9) | 4329(4) | 118(3) |

**Table S13.** Bond lengths [Å] and angles [°] for *syn*-**5k**

| | |
|---|---|
| F(1)-C(15) | 1.277(7) |
| O(1)-C(2) | 1.211(6) |
| O(2)-N(4) | 1.201(7) |
| O(3)-N(4) | 1.196(7) |
| N(1)-N(2) | 1.240(8) |

| | |
|---|---|
| N(1)-C(1) | 1.475(6) |
| N(2)-N(3) | 1.128(9) |
| N(4)-C(11) | 1.503(6) |
| C(1)-C(2) | 1.556(6) |
| C(1)-C(9) | 1.537(6) |
| C(1)-C(10) | 1.545(6) |
| C(2)-C(3) | 1.461(6) |
| C(3)-C(4) | 1.401(6) |
| C(3)-C(8) | 1.376(7) |
| C(4)-H(4) | 0.9300 |
| C(4)-C(5) | 1.337(9) |
| C(5)-H(5) | 0.9300 |
| C(5)-C(6) | 1.390(10) |
| C(6)-H(6) | 0.9300 |
| C(6)-C(7) | 1.371(10) |
| C(7)-H(7) | 0.9300 |
| C(7)-C(8) | 1.382(7) |
| C(8)-C(9) | 1.497(7) |
| C(9)-H(9A) | 0.9700 |
| C(9)-H(9B) | 0.9700 |
| C(10)-H(10) | 0.9800 |
| C(10)-C(11) | 1.526(6) |
| C(10)-C(12) | 1.496(6) |
| C(11)-H(11A) | 0.9700 |
| C(11)-H(11B) | 0.9700 |
| C(12)-H(12) | 0.9300 |
| C(12)-C(13) | 1.318(6) |
| C(13)-H(13) | 0.9300 |
| C(13)-C(14) | 1.478(6) |
| C(14)-C(15) | 1.341(7) |
| C(14)-C(19) | 1.453(9) |

| | |
|---|---|
| C(15)-C(16) | 1.388(9) |
| C(16)-H(16) | 0.9300 |
| C(16)-C(17) | 1.377(11) |
| C(17)-H(17) | 0.9300 |
| C(17)-C(18) | 1.313(11) |
| C(18)-H(18) | 0.9300 |
| C(18)-C(19) | 1.414(9) |
| C(19)-H(19) | 0.9300 |
| N(2)-N(1)-C(1) | 113.7(4) |
| N(3)-N(2)-N(1) | 171.7(7) |
| O(2)-N(4)-C(11) | 119.0(5) |
| O(3)-N(4)-O(2) | 123.3(6) |
| O(3)-N(4)-C(11) | 117.7(6) |
| N(1)-C(1)-C(2) | 108.7(4) |
| N(1)-C(1)-C(9) | 107.4(4) |
| N(1)-C(1)-C(10) | 110.8(3) |
| C(9)-C(1)-C(2) | 104.3(3) |
| C(9)-C(1)-C(10) | 116.8(4) |
| C(10)-C(1)-C(2) | 108.5(3) |
| O(1)-C(2)-C(1) | 124.1(4) |
| O(1)-C(2)-C(3) | 127.9(4) |
| C(3)-C(2)-C(1) | 108.0(4) |
| C(4)-C(3)-C(2) | 128.9(5) |
| C(8)-C(3)-C(2) | 109.8(4) |
| C(8)-C(3)-C(4) | 121.3(5) |
| C(3)-C(4)-H(4) | 120.3 |
| C(5)-C(4)-C(3) | 119.5(6) |
| C(5)-C(4)-H(4) | 120.3 |
| C(4)-C(5)-H(5) | 120.2 |
| C(4)-C(5)-C(6) | 119.6(6) |
| C(6)-C(5)-H(5) | 120.2 |

| | |
|---|---|
| C(5)-C(6)-H(6) | 119.2 |
| C(7)-C(6)-C(5) | 121.6(6) |
| C(7)-C(6)-H(6) | 119.2 |
| C(6)-C(7)-H(7) | 120.4 |
| C(6)-C(7)-C(8) | 119.2(6) |
| C(8)-C(7)-H(7) | 120.4 |
| C(3)-C(8)-C(7) | 118.8(5) |
| C(3)-C(8)-C(9) | 112.4(4) |
| C(7)-C(8)-C(9) | 128.8(5) |
| C(1)-C(9)-H(9A) | 110.7 |
| C(1)-C(9)-H(9B) | 110.7 |
| C(8)-C(9)-C(1) | 105.4(4) |
| C(8)-C(9)-H(9A) | 110.7 |
| C(8)-C(9)-H(9B) | 110.7 |
| H(9A)-C(9)-H(9B) | 108.8 |
| C(1)-C(10)-H(10) | 107.7 |
| C(11)-C(10)-C(1) | 109.4(3) |
| C(11)-C(10)-H(10) | 107.7 |
| C(12)-C(10)-C(1) | 113.2(3) |
| C(12)-C(10)-H(10) | 107.7 |
| C(12)-C(10)-C(11) | 111.0(4) |
| N(4)-C(11)-C(10) | 110.2(3) |
| N(4)-C(11)-H(11A) | 109.6 |
| N(4)-C(11)-H(11B) | 109.6 |
| C(10)-C(11)-H(11A) | 109.6 |
| C(10)-C(11)-H(11B) | 109.6 |
| H(11A)-C(11)-H(11B) | 108.1 |
| C(10)-C(12)-H(12) | 118.7 |
| C(13)-C(12)-C(10) | 122.5(4) |
| C(13)-C(12)-H(12) | 118.7 |
| C(12)-C(13)-H(13) | 114.7 |

| | |
|---|---|
| C(12)-C(13)-C(14) | 130.6(4) |
| C(14)-C(13)-H(13) | 114.7 |
| C(15)-C(14)-C(13) | 127.7(5) |
| C(15)-C(14)-C(19) | 117.0(5) |
| C(19)-C(14)-C(13) | 115.3(5) |
| F(1)-C(15)-C(14) | 118.5(5) |
| F(1)-C(15)-C(16) | 116.2(6) |
| C(14)-C(15)-C(16) | 125.3(6) |
| C(15)-C(16)-H(16) | 121.8 |
| C(17)-C(16)-C(15) | 116.5(6) |
| C(17)-C(16)-H(16) | 121.8 |
| C(16)-C(17)-H(17) | 119.1 |
| C(18)-C(17)-C(16) | 121.9(6) |
| C(18)-C(17)-H(17) | 119.1 |
| C(17)-C(18)-H(18) | 118.5 |
| C(17)-C(18)-C(19) | 122.9(8) |
| C(19)-C(18)-H(18) | 118.5 |
| C(14)-C(19)-H(19) | 121.8 |
| C(18)-C(19)-C(14) | 116.4(8) |
| C(18)-C(19)-H(19) | 121.8 |

Symmetry transformations used to generate equivalent atoms:

**Table S14.** Anisotropic displacement parameters ($Å^2$ x $10^3$) for *syn*-**5k**. The anisotropic displacement factor exponent takes the form: $-2p^2[ h^2 a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12} ]$

| | $U^{11}$ | $U^{22}$ | $U^{33}$ | $U^{23}$ | $U^{13}$ | $U^{12}$ |
|---|---|---|---|---|---|---|
| F(1) | 142(4) | 114(3) | 195(5) | 11(3) | -60(4) | 2(3) |
| O(1) | 82(2) | 82(2) | 126(3) | 11(2) | -13(2) | 9(2) |
| O(2) | 115(4) | 154(4) | 92(3) | 16(3) | 11(3) | -33(3) |
| O(3) | 92(3) | 178(5) | 127(4) | -49(4) | 25(3) | 7(3) |

| | | | | | | |
|---|---|---|---|---|---|---|
| N(1) | 85(3) | 121(3) | 61(2) | -8(2) | 2(2) | 15(2) |
| N(2) | 113(4) | 111(4) | 80(3) | -23(3) | -16(3) | 32(3) |
| N(3) | 206(8) | 124(4) | 134(5) | -51(4) | -67(6) | 38(5) |
| N(4) | 65(2) | 139(4) | 63(2) | -8(2) | -7(2) | 0(2) |
| C(1) | 58(2) | 84(2) | 62(2) | 2(2) | -1(2) | 8(2) |
| C(2) | 61(2) | 83(2) | 72(2) | 1(2) | -2(2) | 10(2) |
| C(3) | 53(2) | 99(3) | 60(2) | 4(2) | 4(2) | 4(2) |
| C(4) | 60(2) | 134(4) | 73(3) | 8(3) | 2(2) | 14(3) |
| C(5) | 60(3) | 177(6) | 79(3) | -1(4) | -7(3) | -6(3) |
| C(6) | 71(3) | 162(6) | 102(4) | -28(4) | -3(3) | -24(4) |
| C(7) | 80(3) | 109(3) | 107(4) | -19(3) | 15(3) | -15(3) |
| C(8) | 58(2) | 95(3) | 69(2) | -5(2) | 10(2) | 0(2) |
| C(9) | 61(2) | 87(3) | 94(3) | 9(2) | 2(2) | 9(2) |
| C(10) | 57(2) | 80(2) | 57(2) | -4(2) | -7(2) | 1(2) |
| C(11) | 57(2) | 115(3) | 61(2) | -11(2) | -5(2) | -6(2) |
| C(12) | 57(2) | 75(2) | 67(2) | 2(2) | -5(2) | 3(2) |
| C(13) | 61(2) | 83(2) | 61(2) | -2(2) | -9(2) | 1(2) |
| C(14) | 58(2) | 101(3) | 53(2) | -2(2) | 2(2) | 12(2) |
| C(15) | 87(3) | 96(3) | 78(3) | -3(2) | -10(2) | 14(3) |
| C(16) | 127(5) | 131(5) | 74(3) | 13(3) | 2(3) | 49(4) |
| C(17) | 77(4) | 185(7) | 74(3) | -20(4) | -6(3) | 36(4) |
| C(18) | 64(3) | 184(7) | 83(3) | -16(4) | -11(3) | 4(4) |
| C(19) | 51(2) | 233(8) | 70(3) | -42(4) | -16(2) | -6(4) |

**Table S15.** Hydrogen coordinates ( x $10^4$) and isotropic displacement parameters (Å$^2$ x $10^3$) for *syn*-**5k**.

| | x | y | z | U(eq) |
|---|---|---|---|---|
| H(4) | 1366 | 6040 | 1766 | 107 |
| H(5) | -152 | 4725 | 1414 | 127 |

| | | | | |
|---|---|---|---|---|
| H(6) | 109 | 2899 | 1914 | 134 |
| H(7) | 1930 | 2360 | 2700 | 119 |
| H(9A) | 4549 | 3185 | 2957 | 97 |
| H(9B) | 3822 | 3511 | 3865 | 97 |
| H(10) | 6207 | 5775 | 2685 | 78 |
| H(11A) | 5740 | 3688 | 1819 | 93 |
| H(11B) | 5114 | 4817 | 1484 | 93 |
| H(12) | 7025 | 3646 | 3344 | 80 |
| H(13) | 8018 | 5752 | 3503 | 82 |
| H(16) | 10756 | 2456 | 4963 | 133 |
| H(17) | 12223 | 3854 | 5342 | 134 |
| H(18) | 11883 | 5624 | 4961 | 132 |
| H(19) | 10015 | 6198 | 4174 | 141 |

**Table S16.** Torsion angles [°] for *syn*-**5k**.

| | |
|---|---|
| F(1)-C(15)-C(16)-C(17) | 180.0(6) |
| O(1)-C(2)-C(3)-C(4) | 0.6(8) |
| O(1)-C(2)-C(3)-C(8) | 179.3(5) |
| O(2)-N(4)-C(11)-C(10) | -53.1(6) |
| O(3)-N(4)-C(11)-C(10) | 129.3(5) |
| N(1)-C(1)-C(2)-O(1) | 64.5(6) |
| N(1)-C(1)-C(2)-C(3) | -116.3(4) |
| N(1)-C(1)-C(9)-C(8) | 118.1(4) |
| N(1)-C(1)-C(10)-C(11) | 175.8(4) |
| N(1)-C(1)-C(10)-C(12) | 51.4(5) |
| N(2)-N(1)-C(1)-C(2) | -62.2(6) |
| N(2)-N(1)-C(1)-C(9) | -174.4(4) |
| N(2)-N(1)-C(1)-C(10) | 57.0(6) |
| C(1)-C(2)-C(3)-C(4) | -178.5(4) |
| C(1)-C(2)-C(3)-C(8) | 0.2(5) |

| | |
|---|---|
| C(1)-C(10)-C(11)-N(4) | 169.7(4) |
| C(1)-C(10)-C(12)-C(13) | -115.2(5) |
| C(2)-C(1)-C(9)-C(8) | 2.9(5) |
| C(2)-C(1)-C(10)-C(11) | -65.0(5) |
| C(2)-C(1)-C(10)-C(12) | 170.6(3) |
| C(2)-C(3)-C(4)-C(5) | 178.9(5) |
| C(2)-C(3)-C(8)-C(7) | -179.8(4) |
| C(2)-C(3)-C(8)-C(9) | 1.8(5) |
| C(3)-C(4)-C(5)-C(6) | 1.0(9) |
| C(3)-C(8)-C(9)-C(1) | -3.0(5) |
| C(4)-C(3)-C(8)-C(7) | -1.0(7) |
| C(4)-C(3)-C(8)-C(9) | -179.4(4) |
| C(4)-C(5)-C(6)-C(7) | -1.7(10) |
| C(5)-C(6)-C(7)-C(8) | 1.0(9) |
| C(6)-C(7)-C(8)-C(3) | 0.3(8) |
| C(6)-C(7)-C(8)-C(9) | 178.5(5) |
| C(7)-C(8)-C(9)-C(1) | 178.7(5) |
| C(8)-C(3)-C(4)-C(5) | 0.3(7) |
| C(9)-C(1)-C(2)-O(1) | 178.8(5) |
| C(9)-C(1)-C(2)-C(3) | -2.0(5) |
| C(9)-C(1)-C(10)-C(11) | 52.4(5) |
| C(9)-C(1)-C(10)-C(12) | -72.0(5) |
| C(10)-C(1)-C(2)-O(1) | -56.1(6) |
| C(10)-C(1)-C(2)-C(3) | 123.1(4) |
| C(10)-C(1)-C(9)-C(8) | -116.8(4) |
| C(10)-C(12)-C(13)-C(14) | -178.4(4) |
| C(11)-C(10)-C(12)-C(13) | 121.3(5) |
| C(12)-C(10)-C(11)-N(4) | -64.6(5) |
| C(12)-C(13)-C(14)-C(15) | -1.5(8) |
| C(12)-C(13)-C(14)-C(19) | 176.9(5) |
| C(13)-C(14)-C(15)-F(1) | -0.8(8) |

| | |
|---|---|
| C(13)-C(14)-C(15)-C(16) | 178.8(5) |
| C(13)-C(14)-C(19)-C(18) | -179.3(4) |
| C(14)-C(15)-C(16)-C(17) | 0.3(9) |
| C(15)-C(14)-C(19)-C(18) | -0.7(7) |
| C(15)-C(16)-C(17)-C(18) | -0.8(10) |
| C(16)-C(17)-C(18)-C(19) | 0.5(10) |
| C(17)-C(18)-C(19)-C(14) | 0.2(9) |
| C(19)-C(14)-C(15)-F(1) | -179.3(6) |
| C(19)-C(14)-C(15)-C(16) | 0.4(8) |

Symmetry transformations used to generate equivalent atoms:

### 8.2 X-ray crystallographic data of *anti*-5g[19]

Data intensity of *anti*-**5g** was collected using a 'Bruker APEX-II CCD' diffractometer at 296(2) K. Data collection and reduction were done by using Olex2 and the structure was solved with the ShelXS structure solution program using direct methods and refined by full-matrix least-squares on $F^2$ with anisotropic displacement parameters for non-H atoms using SHELX-97. Hydrogen atoms were added at their geometrically idea positions and refined isotropically. Crystal data for *anti*-**5g**: $C_{15}H_{12}N_4O_3S$, $T$ = 296(2) K, Orthorhombic, P2(1)2(1)2(1), $a$ = 6.4901(2) Å, $b$ = 13.5853(4) Å, $c$ = 17.2054(6) Å, $\alpha$ = 90 deg, $\beta$ = 90 deg, $\gamma$ = 90 deg, $V$ = 1517.00(8) Å$^3$. Z = 4, $d_{calc}$ = 1.438 Mg/m$^3$. 17672 reflections measured, 2673 unique [R(int) = 0.0316], $R_1$ = 0.0332, $wR_2$ = 0.0885 ($I > 2\sigma(I)$, final), $R_1$ = 0.0369, $wR_2$ = 0.0922 (all data), GOF = 1.055, and 208 parameters.

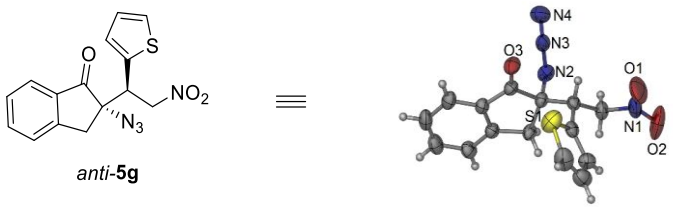



**Table S17.** Crystal data and structure refinement for *anti*-**5g**.

Identification code *anti*-**5g**

19 Supplementary crystallographic data have been deposited at the Cambridge Crystallographic Data Center (CCDC number: 1874277).

| | |
|---|---|
| Empirical formula | $C_{15}H_{12}N_4O_3S$ |
| Formula weight | 328.35 |
| Temperature | 296(2) K |
| Wavelength | 0.71073 Å |
| Crystal system, space group | Orthorhombic, P2(1)2(1)2(1) |
| Unit cell dimensions | a = 6.4901(2) Å alpha = 90 deg. |
| | b = 13.5853(4) Å beta = 90 deg. |
| | c = 17.2054(6) Å gamma = 90 deg. |
| Volume | 1517.00(8) $Å^3$ |
| Z, Calculated density | 4, 1.438 $Mg/m^3$ |
| Absorption coefficient | 0.234 $mm^{-1}$ |
| F(000) | 680 |
| Crystal size | 0.36 x 0.24 x 0.18 mm |
| Theta range for data collection | 1.91 to 25.01 deg. |
| Limiting indices | -7<=h<=7, -14<=k<=16, -20<=l<=20 |
| Reflections collected / unique | 17672 / 2673 [R(int) = 0.0316] |
| Completeness to theta = 25.01 | 100.0 % |
| Absorption correction | Semi-empirical from equivalents |
| Max. and min. transmission | 0.9591 and 0.9205 |
| Refinement method | Full-matrix least-squares on $F^2$ |
| Data / restraints / parameters | 2673 / 0 / 208 |
| Goodness-of-fit on F^2 | 1.055 |
| Final R indices [I>2sigma(I)] | R1 = 0.0332, wR2 = 0.0885 |
| R indices (all data) | R1 = 0.0369, wR2 = 0.0922 |
| Absolute structure parameter | 0.01(9) |
| Largest diff. peak and hole | 0.221 and -0.243 e. $Å^{-3}$ |

**Table S18.** Atomic coordinates ( x $10^4$) and equivalent isotropic displacement parameters ($A^2$ x $10^3$) for *anti*-**5g**. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

| | x | y | z | U(eq) |
|---|---|---|---|---|

| | | | | |
|---|---|---|---|---|
| S(1) | 9720(1) | 4073(1) | 9990(1) | 69(1) |
| O(1) | 11846(4) | 2423(2) | 11872(2) | 104(1) |
| O(2) | 14873(4) | 2708(2) | 12272(1) | 108(1) |
| O(3) | 7033(2) | 5342(1) | 11192(1) | 52(1) |
| N(1) | 13182(4) | 2969(2) | 12065(1) | 60(1) |
| N(2) | 10029(3) | 5549(1) | 12560(1) | 48(1) |
| N(3) | 8274(3) | 5299(1) | 12757(1) | 46(1) |
| N(4) | 6732(4) | 5117(2) | 13022(1) | 68(1) |
| C(1) | 8972(3) | 6847(1) | 11073(1) | 38(1) |
| C(2) | 7593(3) | 7536(2) | 10779(1) | 48(1) |
| C(3) | 8295(4) | 8486(2) | 10665(1) | 56(1) |
| C(4) | 10305(4) | 8728(2) | 10841(1) | 56(1) |
| C(5) | 11672(4) | 8045(2) | 11136(1) | 48(1) |
| C(6) | 10999(3) | 7093(1) | 11250(1) | 38(1) |
| C(7) | 12184(3) | 6210(1) | 11546(1) | 41(1) |
| C(8) | 10520(3) | 5443(1) | 11712(1) | 36(1) |
| C(9) | 8588(3) | 5819(2) | 11277(1) | 38(1) |
| C(10) | 12805(3) | 4054(2) | 12070(1) | 46(1) |
| C(11) | 11057(3) | 4354(1) | 11535(1) | 36(1) |
| C(12) | 11585(3) | 4157(1) | 10695(1) | 38(1) |
| C(13) | 13477(3) | 3959(2) | 10373(1) | 47(1) |
| C(14) | 13370(5) | 3728(2) | 9571(1) | 61(1) |
| C(15) | 11456(5) | 3763(2) | 9298(1) | 70(1) |

**Table S19.** Bond lengths [A] and angles [deg] for *anti*-**5g**.

| | |
|---|---|
| S(1)-C(15) | 1.692(3) |
| S(1)-C(12) | 1.7173(19) |
| O(1)-N(1) | 1.189(3) |
| O(2)-N(1) | 1.207(3) |
| O(3)-C(9) | 1.208(2) |

| | |
|---|---|
| N(1)-C(10) | 1.494(3) |
| N(2)-N(3) | 1.236(3) |
| N(2)-C(8) | 1.500(3) |
| N(3)-N(4) | 1.127(3) |
| C(1)-C(2) | 1.390(3) |
| C(1)-C(6) | 1.391(3) |
| C(1)-C(9) | 1.462(3) |
| C(2)-C(3) | 1.382(3) |
| C(2)-H(2A) | 0.9300 |
| C(3)-C(4) | 1.379(4) |
| C(3)-H(3A) | 0.9300 |
| C(4)-C(5) | 1.381(3) |
| C(4)-H(4A) | 0.9300 |
| C(5)-C(6) | 1.378(3) |
| C(5)-H(5A) | 0.9300 |
| C(6)-C(7) | 1.513(3) |
| C(7)-C(8) | 1.528(3) |
| C(7)-H(7A) | 0.9700 |
| C(7)-H(7B) | 0.9700 |
| C(8)-C(9) | 1.547(3) |
| C(8)-C(11) | 1.550(3) |
| C(10)-C(11) | 1.516(3) |
| C(10)-H(10A) | 0.9700 |
| C(10)-H(10B) | 0.9700 |
| C(11)-C(12) | 1.509(3) |
| C(11)-H(11A) | 0.9800 |
| C(12)-C(13) | 1.374(3) |
| C(13)-C(14) | 1.417(3) |
| C(13)-H(13A) | 0.9300 |
| C(14)-C(15) | 1.329(4) |
| C(14)-H(14A) | 0.9300 |

| | |
|---|---|
| C(15)-H(15B) | 0.9300 |
| C(15)-S(1)-C(12) | 92.53(12) |
| O(1)-N(1)-O(2) | 124.2(2) |
| O(1)-N(1)-C(10) | 119.8(2) |
| O(2)-N(1)-C(10) | 115.9(2) |
| N(3)-N(2)-C(8) | 115.90(17) |
| N(4)-N(3)-N(2) | 171.8(2) |
| C(2)-C(1)-C(6) | 121.80(19) |
| C(2)-C(1)-C(9) | 128.37(19) |
| C(6)-C(1)-C(9) | 109.77(17) |
| C(3)-C(2)-C(1) | 117.9(2) |
| C(3)-C(2)-H(2A) | 121.1 |
| C(1)-C(2)-H(2A) | 121.1 |
| C(4)-C(3)-C(2) | 120.2(2) |
| C(4)-C(3)-H(3A) | 119.9 |
| C(2)-C(3)-H(3A) | 119.9 |
| C(3)-C(4)-C(5) | 121.9(2) |
| C(3)-C(4)-H(4A) | 119.1 |
| C(5)-C(4)-H(4A) | 119.1 |
| C(6)-C(5)-C(4) | 118.6(2) |
| C(6)-C(5)-H(5A) | 120.7 |
| C(4)-C(5)-H(5A) | 120.7 |
| C(5)-C(6)-C(1) | 119.61(19) |
| C(5)-C(6)-C(7) | 129.06(19) |
| C(1)-C(6)-C(7) | 111.33(17) |
| C(6)-C(7)-C(8) | 104.17(15) |
| C(6)-C(7)-H(7A) | 110.9 |
| C(8)-C(7)-H(7A) | 110.9 |
| C(6)-C(7)-H(7B) | 110.9 |
| C(8)-C(7)-H(7B) | 110.9 |
| H(7A)-C(7)-H(7B) | 108.9 |

| | |
|---|---|
| N(2)-C(8)-C(7) | 105.49(16) |
| N(2)-C(8)-C(9) | 105.47(15) |
| C(7)-C(8)-C(9) | 104.88(15) |
| N(2)-C(8)-C(11) | 109.29(15) |
| C(7)-C(8)-C(11) | 117.06(16) |
| C(9)-C(8)-C(11) | 113.75(15) |
| O(3)-C(9)-C(1) | 128.75(18) |
| O(3)-C(9)-C(8) | 123.93(18) |
| C(1)-C(9)-C(8) | 107.09(15) |
| N(1)-C(10)-C(11) | 112.65(18) |
| N(1)-C(10)-H(10A) | 109.1 |
| C(11)-C(10)-H(10A) | 109.1 |
| N(1)-C(10)-H(10B) | 109.1 |
| C(11)-C(10)-H(10B) | 109.1 |
| H(10A)-C(10)-H(10B) | 107.8 |
| C(12)-C(11)-C(10) | 111.31(16) |
| C(12)-C(11)-C(8) | 114.13(15) |
| C(10)-C(11)-C(8) | 107.83(15) |
| C(12)-C(11)-H(11A) | 107.8 |
| C(10)-C(11)-H(11A) | 107.8 |
| C(8)-C(11)-H(11A) | 107.8 |
| C(13)-C(12)-C(11) | 128.60(18) |
| C(13)-C(12)-S(1) | 109.40(15) |
| C(11)-C(12)-S(1) | 121.87(15) |
| C(12)-C(13)-C(14) | 113.1(2) |
| C(12)-C(13)-H(13A) | 123.5 |
| C(14)-C(13)-H(13A) | 123.5 |
| C(15)-C(14)-C(13) | 112.4(2) |
| C(15)-C(14)-H(14A) | 123.8 |
| C(13)-C(14)-H(14A) | 123.8 |
| C(14)-C(15)-S(1) | 112.53(19) |

| | |
|---|---|
| C(14)-C(15)-H(15B) | 123.7 |
| S(1)-C(15)-H(15B) | 123.7 |

Symmetry transformations used to generate equivalent atoms:

**Table S20.** Anisotropic displacement parameters ($A^2$ x $10^3$) for *anti*-**5g**. The anisotropic displacement factor exponent takes the form: $-2\ pi^2\ [h^2\ a^{*2}\ U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

| | U11 | U22 | U33 | U23 | U13 | U12 |
|---|---|---|---|---|---|---|
| S(1) | 61(1) | 91(1) | 55(1) | -18(1) | -19(1) | 9(1) |
| O(1) | 109(2) | 42(1) | 159(2) | 24(1) | -11(2) | -10(1) |
| O(2) | 127(2) | 86(2) | 113(2) | -15(1) | -52(2) | 64(2) |
| O(3) | 36(1) | 50(1) | 70(1) | -2(1) | -9(1) | -4(1) |
| N(1) | 82(2) | 49(1) | 50(1) | 9(1) | -3(1) | 22(1) |
| N(2) | 46(1) | 54(1) | 44(1) | -8(1) | -1(1) | 3(1) |
| N(3) | 57(1) | 39(1) | 44(1) | -1(1) | 6(1) | 9(1) |
| N(4) | 68(1) | 71(1) | 66(1) | 4(1) | 17(1) | -2(1) |
| C(1) | 41(1) | 39(1) | 35(1) | -4(1) | -2(1) | 4(1) |
| C(2) | 48(1) | 52(1) | 43(1) | -3(1) | -8(1) | 12(1) |
| C(3) | 73(2) | 46(1) | 48(1) | 3(1) | -6(1) | 19(1) |
| C(4) | 81(2) | 36(1) | 52(1) | -1(1) | -2(1) | 5(1) |
| C(5) | 54(1) | 39(1) | 53(1) | -2(1) | 0(1) | -3(1) |
| C(6) | 40(1) | 35(1) | 38(1) | -6(1) | -1(1) | 2(1) |
| C(7) | 34(1) | 35(1) | 54(1) | -4(1) | -6(1) | 1(1) |
| C(8) | 35(1) | 34(1) | 39(1) | -2(1) | -5(1) | 2(1) |
| C(9) | 32(1) | 40(1) | 42(1) | -4(1) | -3(1) | 2(1) |
| C(10) | 54(1) | 39(1) | 43(1) | 0(1) | -7(1) | 9(1) |
| C(11) | 36(1) | 32(1) | 40(1) | 2(1) | -2(1) | -2(1) |
| C(12) | 45(1) | 28(1) | 42(1) | -1(1) | -7(1) | -4(1) |
| C(13) | 47(1) | 51(1) | 43(1) | -5(1) | 1(1) | -5(1) |
| C(14) | 77(2) | 56(1) | 50(1) | -6(1) | 15(1) | 0(1) |

| | | | | | | |
|---|---|---|---|---|---|---|
| C(15) | 101(2) | 68(2) | 43(1) | -11(1) | -7(1) | 10(2) |

**Table S21.** Hydrogen coordinates ( x $10^4$) and isotropic displacement parameters ($A^2$ x $10^3$) for *anti*-**5g**.

| | x | y | z | U(eq) |
|---|---|---|---|---|
| H(2A) | 6241 | 7363 | 10662 | 57 |
| H(3A) | 7409 | 8963 | 10469 | 67 |
| H(4A) | 10753 | 9370 | 10758 | 68 |
| H(5A) | 13019 | 8223 | 11256 | 58 |
| H(7A) | 12941 | 6372 | 12015 | 49 |
| H(7B) | 13144 | 5973 | 11156 | 49 |
| H(10A) | 14053 | 4390 | 11911 | 55 |
| H(10B) | 12483 | 4261 | 12596 | 55 |
| H(11A) | 9853 | 3953 | 11668 | 43 |
| H(13A) | 14703 | 3975 | 10653 | 57 |
| H(14A) | 14511 | 3569 | 9269 | 74 |
| H(15B) | 11109 | 3633 | 8784 | 85 |

**Table S22.** Torsion angles [deg] for *anti*-**5g**.

| | |
|---|---|
| C(8)-N(2)-N(3)-N(4) | -172.6(15) |
| C(6)-C(1)-C(2)-C(3) | 0.0(3) |
| C(9)-C(1)-C(2)-C(3) | 176.86(19) |
| C(1)-C(2)-C(3)-C(4) | 0.0(3) |
| C(2)-C(3)-C(4)-C(5) | -0.3(4) |
| C(3)-C(4)-C(5)-C(6) | 0.6(3) |
| C(4)-C(5)-C(6)-C(1) | -0.6(3) |
| C(4)-C(5)-C(6)-C(7) | 178.6(2) |
| C(2)-C(1)-C(6)-C(5) | 0.3(3) |

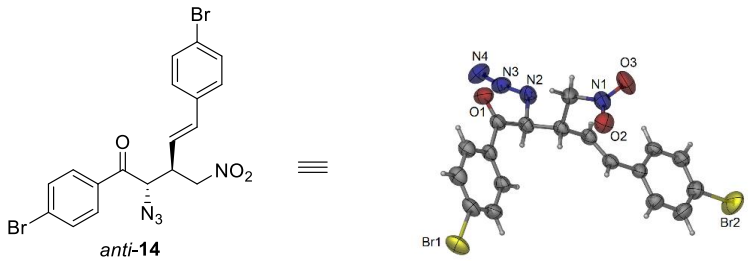
| | |
|---|---|
| C(9)-C(1)-C(6)-C(5) | -177.08(17) |
| C(2)-C(1)-C(6)-C(7) | -178.99(18) |
| C(9)-C(1)-C(6)-C(7) | 3.6(2) |
| C(5)-C(6)-C(7)-C(8) | 167.9(2) |
| C(1)-C(6)-C(7)-C(8) | -12.9(2) |
| N(3)-N(2)-C(8)-C(7) | 153.11(17) |
| N(3)-N(2)-C(8)-C(9) | 42.4(2) |
| N(3)-N(2)-C(8)-C(11) | -80.2(2) |
| C(6)-C(7)-C(8)-N(2) | -94.79(17) |
| C(6)-C(7)-C(8)-C(9) | 16.3(2) |
| C(6)-C(7)-C(8)-C(11) | 143.44(16) |
| C(2)-C(1)-C(9)-O(3) | 4.7(3) |
| C(6)-C(1)-C(9)-O(3) | -178.1(2) |
| C(2)-C(1)-C(9)-C(8) | -169.93(19) |
| C(6)-C(1)-C(9)-C(8) | 7.2(2) |
| N(2)-C(8)-C(9)-O(3) | -78.7(2) |
| C(7)-C(8)-C(9)-O(3) | 170.21(18) |
| C(11)-C(8)-C(9)-O(3) | 41.1(3) |
| N(2)-C(8)-C(9)-C(1) | 96.26(17) |
| C(7)-C(8)-C(9)-C(1) | -14.9(2) |
| C(11)-C(8)-C(9)-C(1) | -143.99(16) |
| O(1)-N(1)-C(10)-C(11) | -22.7(3) |
| O(2)-N(1)-C(10)-C(11) | 158.0(2) |
| N(1)-C(10)-C(11)-C(12) | -65.4(2) |
| N(1)-C(10)-C(11)-C(8) | 168.68(18) |
| N(2)-C(8)-C(11)-C(12) | -179.89(16) |
| C(7)-C(8)-C(11)-C(12) | -60.1(2) |
| C(9)-C(8)-C(11)-C(12) | 62.5(2) |
| N(2)-C(8)-C(11)-C(10) | -55.7(2) |
| C(7)-C(8)-C(11)-C(10) | 64.1(2) |
| C(9)-C(8)-C(11)-C(10) | -173.24(16) |

| | |
|---|---|
| C(10)-C(11)-C(12)-C(13) | -15.0(3) |
| C(8)-C(11)-C(12)-C(13) | 107.3(2) |
| C(10)-C(11)-C(12)-S(1) | 160.51(14) |
| C(8)-C(11)-C(12)-S(1) | -77.2(2) |
| C(15)-S(1)-C(12)-C(13) | 0.88(18) |
| C(15)-S(1)-C(12)-C(11) | -175.42(17) |
| C(11)-C(12)-C(13)-C(14) | 174.90(19) |
| S(1)-C(12)-C(13)-C(14) | -1.1(2) |
| C(12)-C(13)-C(14)-C(15) | 0.8(3) |
| C(13)-C(14)-C(15)-S(1) | -0.1(3) |
| C(12)-S(1)-C(15)-C(14) | -0.5(2) |

Symmetry transformations used to generate equivalent atoms:

### 8.3 Single-Crystal X-ray Crystallography of *anti*-14[20]

Data intensity of *anti*-**14** was collected using a 'Bruker APEX-II CCD' diffractometer at 293(2) K. Data collection and reduction were done by using Olex2 and the structure was solved with the ShelXS structure solution program using direct methods and refined by full-matrix least-squares on $F^2$ with anisotropic displacement parameters for non-H atoms using SHELX-97. Hydrogen atoms were added at their geometrically idea positions and refined isotropically. Crystal data for *anti*-**14**: $C_{18}H_{14}N_4O_3Br_2$, $T$ = 293(2) K, monoclinic, $P2_1$, $a$ = 7.63640(10) Å, $b$ = 11.6851(2) Å, $c$ = 11.5473(2) Å, $\alpha$ = 90 deg, $\beta$ = 104.259(2) deg, $\gamma$ = 90 deg, $V$ = 998.65(3) Å$^3$. Z = 2, $d_{calc}$ = 1.643 g/cm$^3$. 21816 reflections measured, 4011 [$R_{int}$ = 0.0726, $R_{sigma}$ = 0.0335], $R_1$ = 0.0383, $wR_2$ = 0.1042 ($I$ > =2$\sigma$($I$), final), $R_1$ = 0.0402, $wR_2$ = 0.1062 (all data), GOF = 1.059, and 245 parameters.




20 Supplementary crystallographic data have been deposited at the Cambridge Crystallographic Data Center (CCDC number: 1874283).

**Table S23.** Crystal data and structure refinement for *anti*-**14**.

| | |
|---|---|
| Identification code | *anti*-**14** |
| Empirical formula | $C_{18}H_{14}N_4O_3Br_2$ |
| Formula weight | 494.15 |
| Temperature/K | 293(2) |
| Crystal system | Monoclinic |
| Space group | $P2_1$ |
| a/Å | 7.63640(10) |
| b/Å | 11.6851(2) |
| c/Å | 11.5473(2) |
| α/° | 90 |
| β/° | 104.259(2) |
| γ/° | 90 |
| Volume/Å$^3$ | 998.65(3) |
| Z | 2 |
| $\rho_{calc}$g/cm$^3$ | 1.643 |
| μ/mm$^{-1}$ | 5.374 |
| F(000) | 488.0 |
| Crystal size/mm$^3$ | 0.32 × 0.26 × 0.18 |
| Radiation | CuKα (λ = 1.54184) |
| 2Θ range for data collection/° | 7.9 to 148.916 |
| Index ranges | $-9 \leq h \leq 9$, $-14 \leq k \leq 14$, $-14 \leq l \leq 14$ |
| Reflections collected | 21816 |
| Independent reflections | 4011 [$R_{int}$ = 0.0726, $R_{sigma}$ = 0.0335] |
| Data/restraints/parameters | 4011/1/245 |
| Goodness-of-fit on $F^2$ | 1.059 |
| Final R indexes [I>=2σ (I)] | $R_1$ = 0.0383, $wR_2$ = 0.1042 |
| Final R indexes [all data] | $R_1$ = 0.0402, $wR_2$ = 0.1062 |
| Largest diff. peak/hole / e Å$^{-3}$ | 0.56/-0.55 |

Flack parameter -0.015(12)

**Table S24.** Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($Å^2 \times 10^3$) for *anti*-**14**. $U_{eq}$ is defined as 1/3 of of the trace of the orthogonalised $U_{IJ}$tensor.

| **Atom** | ***x*** | ***y*** | ***z*** | **U(eq)** |
|---|---|---|---|---|
| Br1 | 1419.5(9) | 2318.3(8) | -304.8(4) | 87.2(3) |
| Br2 | 3767.4(17) | 9648.1(8) | 9030.8(9) | 115.2(4) |
| O1 | 1169(6) | 340(3) | 5204(4) | 72.0(10) |
| O2 | 6661(6) | 3077(4) | 6254(4) | 76.4(11) |
| O3 | 6852(7) | 2949(6) | 8130(5) | 97.6(16) |
| N1 | 6083(6) | 2766(4) | 7092(4) | 62.9(11) |
| N2 | 683(6) | 1893(5) | 6852(4) | 64.2(11) |
| N3 | -588(6) | 1218(4) | 6746(4) | 62.5(10) |
| N4 | -1720(8) | 608(5) | 6796(6) | 84.7(15) |
| C1 | 1556(6) | 717(5) | 2900(4) | 57.9(11) |
| C2 | 1646(7) | 933(6) | 1743(5) | 64.5(13) |
| C3 | 1401(6) | 2031(6) | 1304(4) | 63.0(13) |
| C4 | 1066(7) | 2925(5) | 2005(5) | 61.4(12) |
| C5 | 986(7) | 2703(5) | 3162(4) | 58.3(12) |
| C6 | 1244(6) | 1609(4) | 3618(4) | 51.3(10) |
| C7 | 1144(6) | 1313(5) | 4864(4) | 53.0(10) |
| C8 | 1056(5) | 2304(5) | 5727(3) | 50.8(9) |
| C9 | 2863(6) | 2949(4) | 6092(4) | 49.2(9) |
| C10 | 2773(6) | 4031(4) | 6764(4) | 50.7(10) |
| C11 | 3391(6) | 5017(4) | 6481(4) | 51.2(10) |
| C12 | 3476(6) | 6111(4) | 7111(4) | 49.7(9) |
| C13 | 3778(7) | 7108(5) | 6544(4) | 60.4(11) |

| | | | | |
|---|---|---|---|---|
| C14 | 3869(9) | 8171(5) | 7099(6) | 70.8(15) |
| C15 | 3691(9) | 8212(5) | 8246(6) | 67.8(14) |
| C16 | 3406(7) | 7234(5) | 8850(4) | 62.8(11) |
| C17 | 3294(7) | 6198(4) | 8288(4) | 55.7(11) |

**Table S25.** Anisotropic Displacement Parameters ($Å^2×10^3$) for *anti*-**14**. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

| **Atom** | **$U_{11}$** | **$U_{22}$** | **$U_{33}$** | **$U_{23}$** | **$U_{13}$** | **$U_{12}$** |
|---|---|---|---|---|---|---|
| Br1 | 103.3(4) | 118.8(6) | 40.7(3) | 2.4(3) | 19.7(2) | 16.7(4) |
| Br2 | 190.9(10) | 57.2(4) | 102.9(6) | -24.6(4) | 46.6(6) | -12.6(5) |
| O1 | 108(3) | 54(2) | 57(2) | -1.9(17) | 24.3(19) | 3(2) |
| O2 | 76(2) | 78(3) | 80(3) | -5(2) | 28(2) | -4(2) |
| O3 | 84(3) | 129(5) | 67(3) | -14(3) | -7(2) | -11(3) |
| N1 | 59(2) | 65(3) | 60(2) | -10.1(19) | 5.6(18) | 7.4(17) |
| N2 | 71(2) | 79(3) | 46(2) | -7.8(19) | 20.0(17) | -14(2) |
| N3 | 79(3) | 57(3) | 57(2) | 3.5(19) | 27(2) | 6(2) |
| N4 | 104(4) | 60(3) | 99(4) | 3(3) | 42(3) | -9(3) |
| C1 | 64(2) | 59(3) | 50(2) | -8(2) | 13.9(19) | 9(2) |
| C2 | 70(3) | 72(3) | 52(3) | -13(2) | 17(2) | 11(2) |
| C3 | 60(2) | 85(4) | 40(2) | -8(2) | 6.6(17) | 8(2) |
| C4 | 75(3) | 61(3) | 46(2) | 5(2) | 11(2) | 6(2) |
| C5 | 72(3) | 58(3) | 42(2) | -7.4(19) | 9.8(19) | 1(2) |
| C6 | 58(2) | 57(3) | 38(2) | -8.5(18) | 10.4(17) | -0.2(19) |
| C7 | 59(2) | 57(3) | 42(2) | -3(2) | 8.7(17) | 1(2) |
| C8 | 56.3(19) | 57(3) | 39.2(17) | -6(2) | 11.5(14) | 1(2) |
| C9 | 56(2) | 53(3) | 38(2) | -5.8(17) | 12.1(16) | 2.6(18) |
| C10 | 58(2) | 56(3) | 39(2) | -6.1(18) | 12.7(17) | 3.3(19) |
| C11 | 62(2) | 51(2) | 38(2) | -2.1(17) | 8.8(17) | 7.1(18) |

| | | | | | | |
|---|---|---|---|---|---|---|
| C12 | 56(2) | 46(2) | 44(2) | -0.2(17) | 7.4(17) | 4.4(17) |
| C13 | 76(3) | 55(3) | 53(2) | 0(2) | 22(2) | -1(2) |
| C14 | 95(4) | 49(3) | 74(4) | 2(3) | 33(3) | -6(3) |
| C15 | 86(4) | 53(3) | 64(3) | -11(2) | 17(3) | -1(3) |
| C16 | 80(3) | 61(3) | 46(2) | -3(2) | 12.9(19) | 0(3) |
| C17 | 73(3) | 54(3) | 40(2) | 3.6(19) | 12.7(19) | 3(2) |
| C18 | 61(2) | 55(3) | 62(2) | 4(2) | 7.7(19) | 0(2) |

**Table S26.** Bond Lengths for *anti*-**14**.

| Atom | Atom | Length/Å | Atom | Atom | Length/Å |
|---|---|---|---|---|---|
| Br1 | C3 | 1.892(5) | C5 | C6 | 1.378(7) |
| Br2 | C15 | 1.902(6) | C6 | C7 | 1.500(6) |
| O1 | C7 | 1.201(7) | C7 | C8 | 1.540(7) |
| O2 | N1 | 1.214(7) | C8 | C9 | 1.537(6) |
| O3 | N1 | 1.217(6) | C9 | C10 | 1.494(6) |
| N1 | C18 | 1.478(7) | C9 | C18 | 1.538(6) |
| N2 | N3 | 1.234(7) | C10 | C11 | 1.317(7) |
| N2 | C8 | 1.477(6) | C11 | C12 | 1.464(7) |
| N3 | N4 | 1.132(7) | C12 | C13 | 1.383(8) |
| C1 | C2 | 1.379(8) | C12 | C17 | 1.404(7) |
| C1 | C6 | 1.388(7) | C13 | C14 | 1.392(9) |
| C2 | C3 | 1.376(9) | C14 | C15 | 1.364(10) |
| C3 | C4 | 1.384(8) | C15 | C16 | 1.383(9) |
| C4 | C5 | 1.377(7) | C16 | C17 | 1.367(8) |

**Table S27.** Bond Angles for *anti*-**14**.

| Atom | Atom | Atom | Angle/° | Atom | Atom | Atom | Angle/° |
|---|---|---|---|---|---|---|---|
| O2 | N1 | O3 | 123.4(5) | N2 | C8 | C9 | 105.8(3) |
| O2 | N1 | C18 | 118.1(4) | C9 | C8 | C7 | 111.5(3) |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| O3 | N1 | C18 | 118.4(5) | C8 | C9 | C18 | 109.9(4) |
| N3 | N2 | C8 | 116.0(4) | C10 | C9 | C8 | 113.8(4) |
| N4 | N3 | N2 | 171.6(6) | C10 | C9 | C18 | 109.7(4) |
| C2 | C1 | C6 | 119.9(5) | C11 | C10 | C9 | 123.1(4) |
| C3 | C2 | C1 | 119.5(5) | C10 | C11 | C12 | 128.0(4) |
| C2 | C3 | Br1 | 119.6(4) | C13 | C12 | C11 | 119.5(4) |
| C2 | C3 | C4 | 121.2(5) | C13 | C12 | C17 | 117.7(4) |
| C4 | C3 | Br1 | 119.2(5) | C17 | C12 | C11 | 122.8(4) |
| C5 | C4 | C3 | 118.9(5) | C12 | C13 | C14 | 121.9(5) |
| C4 | C5 | C6 | 120.7(5) | C15 | C14 | C13 | 118.2(5) |
| C1 | C6 | C7 | 117.2(5) | C14 | C15 | Br2 | 119.6(5) |
| C5 | C6 | C1 | 119.8(4) | C14 | C15 | C16 | 121.8(5) |
| C5 | C6 | C7 | 123.0(4) | C16 | C15 | Br2 | 118.6(5) |
| O1 | C7 | C6 | 122.1(5) | C17 | C16 | C15 | 119.4(5) |
| O1 | C7 | C8 | 120.0(4) | C16 | C17 | C12 | 120.9(5) |
| C6 | C7 | C8 | 117.9(4) | N1 | C18 | C9 | 109.0(4) |
| N2 | C8 | C7 | 111.9(4) | | | | |

**Table S28.** Hydrogen Atom Coordinates (Å×$10^4$) and Isotropic Displacement Parameters (Å$^2$×$10^3$) for *anti*-**14**.

| Atom | x | y | z | U(eq) |
|---|---|---|---|---|
| H1 | 1704.5 | -24.74 | 3199.84 | 69 |
| H2 | 1871.73 | 340.01 | 1261.53 | 77 |
| H4 | 897.16 | 3664.87 | 1700.16 | 74 |
| H5 | 755.97 | 3296.13 | 3640.27 | 70 |
| H8 | 103.32 | 2838.91 | 5337.84 | 61 |
| H9 | 3222.71 | 3150.06 | 5358.99 | 59 |
| H10 | 2256.89 | 4005.88 | 7413.96 | 61 |
| H11 | 3826.52 | 5019.62 | 5796.7 | 61 |

| | | | | |
|---|---|---|---|---|
| H13 | 3925.94 | 7066.34 | 5769.66 | 73 |
| H14 | 4045.52 | 8835.79 | 6699.82 | 85 |
| H16 | 3291.31 | 7282.46 | 9631.66 | 75 |
| H17 | 3095.7 | 5540.57 | 8691.97 | 67 |
| H18A | 4027.46 | 1957.51 | 7575.77 | 73 |
| H18B | 4405.4 | 1463.41 | 6394.06 | 73 |

### 8.4 Single-Crystal X-ray Crystallography of 15a[21]

Data intensity of **15a** was collected using a 'Bruker APEX-II CCD' diffractometer at 296(2) K. Data collection and reduction were done by using Olex2 and the structure was solved with the ShelXS structure solution program using direct methods and refined by full-matrix least-squares on $F^2$ with anisotropic displacement parameters for non-H atoms using SHELX-97. Hydrogen atoms were added at their geometrically idea positions and refined isotropically. Crystal data for **15a**: $C_{25}H_{21}ClN_2O_3$, $T$ = 296(2) K, Orthorhombic, P2(1)2(1)2(1), $a$ = 6.2023(2) Å, $b$ = 15.1707(4) Å, $c$ = 23.3424(7) Å, $\alpha$ = 90 deg, $\beta$ = 90 deg, $\gamma$ = 90 deg, $V$ = 2196.36(11) Å$^3$. Z = 4, $d_{calc}$ = 1.309 Mg/m$^3$. 25874 reflections measured, 3885 unique [R(int) = 0.0399], $R_1$ = 0.0391, $wR_2$ = 0.1005 ($I > 2\sigma(I)$, final), $R_1$ = 0.0508, $wR_2$ = 0.1092 (all data), GOF = 1.046, and 280 parameters.

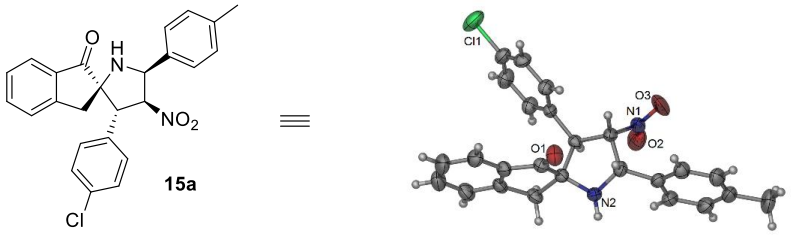



**Table S29.** Crystal data and structure refinement for **15a**.

| | |
|---|---|
| Identification code | **15a** |
| Empirical formula | $C_{25}H_{21}ClN_2O_3$ |
| Formula weight | 432.89 |
| Temperature | 296(2) K |
| Wavelength | 0.71073 Å |

21 Supplementary crystallographic data have been deposited at the Cambridge Crystallographic Data Center (CCDC number: 1874278).

| | |
|---|---|
| Crystal system, space group | Orthorhombic, P2(1)2(1)2(1) |
| Unit cell dimensions | a = 6.2023(2) Å alpha = 90 deg. |
| | b = 15.1707(4) Å beta = 90 deg. |
| | c = 23.3424(7) Å gamma = 90 deg. |
| Volume | 2196.36(11) $Å^3$ |
| Z, Calculated density | 4, 1.309 $Mg/m^3$ |
| Absorption coefficient | 0.203 $mm^{-1}$ |
| F(000) | 904 |
| Crystal size | 0.35 x 0.33 x 0.17 mm |
| Theta range for data collection | 1.60 to 25.01 deg. |
| Limiting indices | -7<=h<=7, -18<=k<=18, -27<=l<=26 |
| Reflections collected / unique | 25874 / 3885 [R(int) = 0.0399] |
| Completeness to theta = 25.01 | 99.9 % |
| Absorption correction | Semi-empirical from equivalents |
| Max. and min. transmission | 0.9663 and 0.9323 |
| Refinement method | Full-matrix least-squares on $F^2$ |
| Data / restraints / parameters | 3885 / 0 / 280 |
| Goodness-of-fit on $F^2$ | 1.046 |
| Final R indices [I>2sigma(I)] | $R_1$ = 0.0391, $wR_2$ = 0.1005 |
| R indices (all data) | $R_1$ = 0.0508, $wR_2$ = 0.1092 |
| Absolute structure parameter | 0.01(9) |
| Largest diff. peak and hole | 0.226 and -0.287 e. $Å^{-3}$ |

**Table S30.** Atomic coordinates ( x $10^4$) and equivalent isotropic displacement parameters ($A^2$ x $10^3$) for **15a**. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

| | x | y | z | U(eq) |
|---|---|---|---|---|
| Cl(1) | 9940(2) | 8404(1) | 8881(1) | 88(1) |
| O(1) | 5563(3) | 4438(1) | 9645(1) | 58(1) |
| O(2) | 12797(4) | 4627(2) | 11007(1) | 84(1) |
| O(3) | 10281(6) | 5206(2) | 11520(1) | 109(1) |

| | | | | |
|---|---|---|---|---|
| N(2) | 9200(3) | 3386(1) | 10118(1) | 45(1) |
| N(1) | 10947(5) | 4883(1) | 11080(1) | 62(1) |
| C(1) | 7688(4) | 4500(2) | 8785(1) | 44(1) |
| C(2) | 6349(5) | 4885(2) | 8373(1) | 58(1) |
| C(3) | 7116(6) | 4975(2) | 7826(1) | 73(1) |
| C(4) | 9184(6) | 4675(2) | 7694(1) | 75(1) |
| C(5) | 10491(5) | 4282(2) | 8094(1) | 60(1) |
| C(6) | 9732(4) | 4195(2) | 8652(1) | 45(1) |
| C(7) | 10778(4) | 3774(2) | 9163(1) | 46(1) |
| C(8) | 9394(3) | 4054(1) | 9672(1) | 37(1) |
| C(9) | 7257(4) | 4345(1) | 9390(1) | 41(1) |
| C(10) | 10195(4) | 5746(1) | 9745(1) | 38(1) |
| C(11) | 8365(4) | 6267(2) | 9775(1) | 47(1) |
| C(12) | 8285(4) | 7079(2) | 9507(1) | 52(1) |
| C(13) | 10034(4) | 7371(2) | 9209(1) | 53(1) |
| C(14) | 11869(4) | 6874(2) | 9166(1) | 60(1) |
| C(15) | 11939(4) | 6066(2) | 9439(1) | 50(1) |
| C(16) | 8298(4) | 3810(1) | 10630(1) | 44(1) |
| C(17) | 9302(4) | 4750(1) | 10607(1) | 45(1) |
| C(18) | 10347(4) | 4840(1) | 10020(1) | 37(1) |
| C(19) | 8652(4) | 3312(1) | 11184(1) | 42(1) |
| C(20) | 10554(5) | 2871(2) | 11298(1) | 53(1) |
| C(21) | 10878(5) | 2499(2) | 11833(1) | 62(1) |
| C(22) | 9358(6) | 2558(2) | 12259(1) | 63(1) |
| C(23) | 7470(5) | 2976(2) | 12136(1) | 61(1) |
| C(24) | 7108(4) | 3351(2) | 11603(1) | 54(1) |
| C(25) | 9764(7) | 2168(2) | 12847(1) | 102(1) |

**Table S31.** Bond lengths [A] and angles [deg] for **15a**.

| | |
|---|---|
| Cl(1)-C(13) | 1.746(2) |
| O(1)-C(9) | 1.217(3) |
| O(2)-N(1) | 1.224(3) |
| O(3)-N(1) | 1.210(3) |
| N(2)-C(8) | 1.457(3) |
| N(2)-C(16) | 1.469(3) |
| N(2)-H(2B) | 0.8600 |
| N(1)-C(17) | 1.515(4) |
| C(1)-C(6) | 1.385(3) |
| C(1)-C(2) | 1.398(3) |
| C(1)-C(9) | 1.455(3) |
| C(2)-C(3) | 1.370(4) |
| C(2)-H(2A) | 0.9300 |
| C(3)-C(4) | 1.396(5) |
| C(3)-H(3A) | 0.9300 |
| C(4)-C(5) | 1.372(4) |
| C(4)-H(4A) | 0.9300 |
| C(5)-C(6) | 1.392(4) |
| C(5)-H(5A) | 0.9300 |
| C(6)-C(7) | 1.500(3) |
| C(7)-C(8) | 1.527(3) |
| C(7)-H(7A) | 0.9700 |
| C(7)-H(7B) | 0.9700 |
| C(8)-C(9) | 1.545(3) |
| C(8)-C(18) | 1.559(3) |
| C(10)-C(15) | 1.384(3) |
| C(10)-C(11) | 1.385(3) |
| C(10)-C(18) | 1.520(3) |
| C(11)-C(12) | 1.381(3) |
| C(11)-H(11A) | 0.9300 |
| C(12)-C(13) | 1.364(4) |

| | |
|---|---|
| C(12)-H(12A) | 0.9300 |
| C(13)-C(14) | 1.368(4) |
| C(14)-C(15) | 1.383(4) |
| C(14)-H(14A) | 0.9300 |
| C(15)-H(15A) | 0.9300 |
| C(16)-C(19) | 1.514(3) |
| C(16)-C(17) | 1.557(3) |
| C(16)-H(16A) | 0.9800 |
| C(17)-C(18) | 1.522(3) |
| C(17)-H(17A) | 0.9800 |
| C(18)-H(18A) | 0.9800 |
| C(19)-C(24) | 1.370(3) |
| C(19)-C(20) | 1.382(4) |
| C(20)-C(21) | 1.385(4) |
| C(20)-H(20A) | 0.9300 |
| C(21)-C(22) | 1.372(4) |
| C(21)-H(21A) | 0.9300 |
| C(22)-C(23) | 1.362(4) |
| C(22)-C(25) | 1.517(4) |
| C(23)-C(24) | 1.387(4) |
| C(23)-H(23A) | 0.9300 |
| C(24)-H(24A) | 0.9300 |
| C(25)-H(25A) | 0.9600 |
| C(25)-H(25B) | 0.9600 |
| C(25)-H(25C) | 0.9600 |
| C(8)-N(2)-C(16) | 107.89(16) |
| C(8)-N(2)-H(2B) | 126.1 |
| C(16)-N(2)-H(2B) | 126.1 |
| O(3)-N(1)-O(2) | 124.5(3) |
| O(3)-N(1)-C(17) | 116.2(3) |
| O(2)-N(1)-C(17) | 119.2(2) |

| | |
|---|---|
| C(6)-C(1)-C(2) | 122.0(2) |
| C(6)-C(1)-C(9) | 109.3(2) |
| C(2)-C(1)-C(9) | 128.7(2) |
| C(3)-C(2)-C(1) | 118.5(3) |
| C(3)-C(2)-H(2A) | 120.8 |
| C(1)-C(2)-H(2A) | 120.8 |
| C(2)-C(3)-C(4) | 119.5(3) |
| C(2)-C(3)-H(3A) | 120.3 |
| C(4)-C(3)-H(3A) | 120.3 |
| C(5)-C(4)-C(3) | 122.4(3) |
| C(5)-C(4)-H(4A) | 118.8 |
| C(3)-C(4)-H(4A) | 118.8 |
| C(4)-C(5)-C(6) | 118.5(3) |
| C(4)-C(5)-H(5A) | 120.7 |
| C(6)-C(5)-H(5A) | 120.7 |
| C(1)-C(6)-C(5) | 119.2(2) |
| C(1)-C(6)-C(7) | 111.1(2) |
| C(5)-C(6)-C(7) | 129.7(2) |
| C(6)-C(7)-C(8) | 104.94(18) |
| C(6)-C(7)-H(7A) | 110.8 |
| C(8)-C(7)-H(7A) | 110.8 |
| C(6)-C(7)-H(7B) | 110.8 |
| C(8)-C(7)-H(7B) | 110.8 |
| H(7A)-C(7)-H(7B) | 108.8 |
| N(2)-C(8)-C(7) | 114.09(18) |
| N(2)-C(8)-C(9) | 115.59(18) |
| C(7)-C(8)-C(9) | 103.23(17) |
| N(2)-C(8)-C(18) | 101.09(16) |
| C(7)-C(8)-C(18) | 113.94(19) |
| C(9)-C(8)-C(18) | 109.26(17) |
| O(1)-C(9)-C(1) | 128.0(2) |

| | |
|---|---|
| O(1)-C(9)-C(8) | 124.4(2) |
| C(1)-C(9)-C(8) | 107.64(19) |
| C(15)-C(10)-C(11) | 117.8(2) |
| C(15)-C(10)-C(18) | 119.13(19) |
| C(11)-C(10)-C(18) | 123.0(2) |
| C(12)-C(11)-C(10) | 121.0(2) |
| C(12)-C(11)-H(11A) | 119.5 |
| C(10)-C(11)-H(11A) | 119.5 |
| C(13)-C(12)-C(11) | 119.5(2) |
| C(13)-C(12)-H(12A) | 120.3 |
| C(11)-C(12)-H(12A) | 120.3 |
| C(12)-C(13)-C(14) | 121.3(2) |
| C(12)-C(13)-Cl(1) | 119.3(2) |
| C(14)-C(13)-Cl(1) | 119.4(2) |
| C(13)-C(14)-C(15) | 118.7(2) |
| C(13)-C(14)-H(14A) | 120.6 |
| C(15)-C(14)-H(14A) | 120.6 |
| C(14)-C(15)-C(10) | 121.6(2) |
| C(14)-C(15)-H(15A) | 119.2 |
| C(10)-C(15)-H(15A) | 119.2 |
| N(2)-C(16)-C(19) | 114.94(18) |
| N(2)-C(16)-C(17) | 102.80(18) |
| C(19)-C(16)-C(17) | 115.32(19) |
| N(2)-C(16)-H(16A) | 107.8 |
| C(19)-C(16)-H(16A) | 107.8 |
| C(17)-C(16)-H(16A) | 107.8 |
| N(1)-C(17)-C(18) | 110.9(2) |
| N(1)-C(17)-C(16) | 111.48(18) |
| C(18)-C(17)-C(16) | 106.40(17) |
| N(1)-C(17)-H(17A) | 109.3 |
| C(18)-C(17)-H(17A) | 109.3 |

| | |
|---|---|
| C(16)-C(17)-H(17A) | 109.3 |
| C(10)-C(18)-C(17) | 115.79(17) |
| C(10)-C(18)-C(8) | 116.63(17) |
| C(17)-C(18)-C(8) | 103.85(18) |
| C(10)-C(18)-H(18A) | 106.6 |
| C(17)-C(18)-H(18A) | 106.6 |
| C(8)-C(18)-H(18A) | 106.6 |
| C(24)-C(19)-C(20) | 118.6(2) |
| C(24)-C(19)-C(16) | 119.2(2) |
| C(20)-C(19)-C(16) | 122.1(2) |
| C(19)-C(20)-C(21) | 119.7(3) |
| C(19)-C(20)-H(20A) | 120.1 |
| C(21)-C(20)-H(20A) | 120.1 |
| C(22)-C(21)-C(20) | 121.8(3) |
| C(22)-C(21)-H(21A) | 119.1 |
| C(20)-C(21)-H(21A) | 119.1 |
| C(23)-C(22)-C(21) | 118.0(2) |
| C(23)-C(22)-C(25) | 121.0(3) |
| C(21)-C(22)-C(25) | 121.1(3) |
| C(22)-C(23)-C(24) | 121.2(3) |
| C(22)-C(23)-H(23A) | 119.4 |
| C(24)-C(23)-H(23A) | 119.4 |
| C(19)-C(24)-C(23) | 120.7(3) |
| C(19)-C(24)-H(24A) | 119.7 |
| C(23)-C(24)-H(24A) | 119.7 |
| C(22)-C(25)-H(25A) | 109.5 |
| C(22)-C(25)-H(25B) | 109.5 |
| H(25A)-C(25)-H(25B) | 109.5 |
| C(22)-C(25)-H(25C) | 109.5 |
| H(25A)-C(25)-H(25C) | 109.5 |
| H(25B)-C(25)-H(25C) | 109.5 |

Symmetry transformations used to generate equivalent atoms:

**Table S32.** Anisotropic displacement parameters ($A^2$ x $10^3$) for **15a**. The anisotropic displacement factor exponent takes the form: -2 $pi^2$ [ $h^2$ $a^{*2}$ U11 + ... + 2 h k a* b* U12 ]

| | U11 | U22 | U33 | U23 | U13 | U12 |
|---|---|---|---|---|---|---|
| Cl(1) | 108(1) | 57(1) | 100(1) | 33(1) | -26(1) | -8(1) |
| O(1) | 36(1) | 82(1) | 54(1) | 5(1) | 2(1) | 9(1) |
| O(2) | 89(2) | 89(2) | 73(2) | 13(1) | -35(1) | -17(1) |
| O(3) | 193(3) | 88(2) | 46(1) | -24(1) | 11(2) | -32(2) |
| N(2) | 56(1) | 36(1) | 42(1) | -1(1) | -3(1) | 5(1) |
| N(1) | 105(2) | 42(1) | 40(1) | -3(1) | -5(1) | -18(1) |
| C(1) | 47(1) | 46(1) | 40(1) | -2(1) | -8(1) | 0(1) |
| C(2) | 64(2) | 57(2) | 52(2) | 3(1) | -13(1) | 5(1) |
| C(3) | 98(3) | 75(2) | 45(2) | 9(1) | -16(2) | 4(2) |
| C(4) | 104(3) | 77(2) | 42(2) | 4(1) | 5(2) | -7(2) |
| C(5) | 67(2) | 65(2) | 49(2) | -9(1) | 8(1) | -1(2) |
| C(6) | 52(1) | 46(1) | 37(1) | -9(1) | -1(1) | -3(1) |
| C(7) | 45(1) | 50(1) | 43(1) | -11(1) | 0(1) | 8(1) |
| C(8) | 36(1) | 38(1) | 38(1) | -1(1) | -3(1) | 6(1) |
| C(9) | 37(1) | 43(1) | 43(1) | -4(1) | -2(1) | 0(1) |
| C(10) | 41(1) | 38(1) | 34(1) | -1(1) | 0(1) | 2(1) |
| C(11) | 43(1) | 48(1) | 49(2) | 2(1) | 4(1) | 5(1) |
| C(12) | 55(2) | 42(1) | 59(2) | 1(1) | -7(1) | 12(1) |
| C(13) | 64(2) | 42(1) | 52(2) | 8(1) | -12(1) | -3(1) |
| C(14) | 58(2) | 65(2) | 58(2) | 17(1) | 3(1) | -8(1) |
| C(15) | 43(1) | 55(1) | 51(2) | 8(1) | 2(1) | 6(1) |
| C(16) | 44(1) | 46(1) | 41(1) | 4(1) | -2(1) | 2(1) |
| C(17) | 58(2) | 38(1) | 38(1) | 0(1) | 4(1) | 10(1) |
| C(18) | 37(1) | 39(1) | 37(1) | -4(1) | -2(1) | 6(1) |

| | | | | | | |
|---|---|---|---|---|---|---|
| C(19) | 47(1) | 36(1) | 44(1) | 3(1) | -4(1) | -3(1) |
| C(20) | 63(2) | 45(1) | 51(2) | 2(1) | 2(1) | 5(1) |
| C(21) | 77(2) | 49(1) | 59(2) | 4(1) | -15(2) | 10(1) |
| C(22) | 97(2) | 44(1) | 47(2) | 5(1) | -8(2) | -8(2) |
| C(23) | 76(2) | 58(2) | 50(2) | 5(1) | 8(2) | -10(2) |
| C(24) | 55(2) | 54(1) | 52(2) | 3(1) | 2(1) | -5(1) |
| C(25) | 156(4) | 100(2) | 50(2) | 25(2) | -17(2) | 6(3) |

**Table S33.** Hydrogen coordinates ( x $10^4$) and isotropic displacement parameters ($A^2$ x $10^3$) for **15a**.

| | x | y | z | U(eq) |
|---|---|---|---|---|
| H(2B) | 9551 | 2840 | 10086 | 54 |
| H(2A) | 4971 | 5076 | 8469 | 69 |
| H(3A) | 6264 | 5234 | 7545 | 87 |
| H(4A) | 9695 | 4744 | 7322 | 89 |
| H(5A) | 11854 | 4077 | 7993 | 73 |
| H(7A) | 12248 | 3980 | 9208 | 55 |
| H(7B) | 10792 | 3137 | 9125 | 55 |
| H(11A) | 7172 | 6068 | 9978 | 56 |
| H(12A) | 7047 | 7423 | 9531 | 62 |
| H(14A) | 13046 | 7077 | 8957 | 73 |
| H(15A) | 13188 | 5729 | 9416 | 60 |
| H(16A) | 6739 | 3870 | 10573 | 52 |
| H(17A) | 8156 | 5191 | 10646 | 54 |
| H(18A) | 11885 | 4716 | 10072 | 45 |
| H(20A) | 11611 | 2825 | 11018 | 63 |
| H(21A) | 12160 | 2202 | 11906 | 74 |
| H(23A) | 6404 | 3011 | 12415 | 73 |
| H(24A) | 5803 | 3631 | 11529 | 64 |
| H(25A) | 8527 | 2266 | 13086 | 153 |

| | | | | |
|---|---|---|---|---|
| H(25B) | 11002 | 2445 | 13016 | 153 |
| H(25C) | 10019 | 1546 | 12812 | 153 |

**Table S34.** Torsion angles [deg] for **15a**.

| | |
|---|---|
| C(6)-C(1)-C(2)-C(3) | -1.2(4) |
| C(9)-C(1)-C(2)-C(3) | 179.1(3) |
| C(1)-C(2)-C(3)-C(4) | 0.6(4) |
| C(2)-C(3)-C(4)-C(5) | 0.6(5) |
| C(3)-C(4)-C(5)-C(6) | -1.2(4) |
| C(2)-C(1)-C(6)-C(5) | 0.6(4) |
| C(9)-C(1)-C(6)-C(5) | -179.6(2) |
| C(2)-C(1)-C(6)-C(7) | -177.3(2) |
| C(9)-C(1)-C(6)-C(7) | 2.5(3) |
| C(4)-C(5)-C(6)-C(1) | 0.5(4) |
| C(4)-C(5)-C(6)-C(7) | 178.0(3) |
| C(1)-C(6)-C(7)-C(8) | -14.0(3) |
| C(5)-C(6)-C(7)-C(8) | 168.4(2) |
| C(16)-N(2)-C(8)-C(7) | 166.53(19) |
| C(16)-N(2)-C(8)-C(9) | -74.0(2) |
| C(16)-N(2)-C(8)-C(18) | 43.8(2) |
| C(6)-C(7)-C(8)-N(2) | 144.96(19) |
| C(6)-C(7)-C(8)-C(9) | 18.7(2) |
| C(6)-C(7)-C(8)-C(18) | -99.6(2) |
| C(6)-C(1)-C(9)-O(1) | -171.5(2) |
| C(2)-C(1)-C(9)-O(1) | 8.2(4) |
| C(6)-C(1)-C(9)-C(8) | 10.0(2) |
| C(2)-C(1)-C(9)-C(8) | -170.2(2) |
| N(2)-C(8)-C(9)-O(1) | 38.3(3) |
| C(7)-C(8)-C(9)-O(1) | 163.6(2) |
| C(18)-C(8)-C(9)-O(1) | -74.8(3) |

| | |
|---|---|
| N(2)-C(8)-C(9)-C(1) | -143.21(18) |
| C(7)-C(8)-C(9)-C(1) | -17.9(2) |
| C(18)-C(8)-C(9)-C(1) | 103.6(2) |
| C(15)-C(10)-C(11)-C(12) | 0.0(4) |
| C(18)-C(10)-C(11)-C(12) | -178.6(2) |
| C(10)-C(11)-C(12)-C(13) | 0.0(4) |
| C(11)-C(12)-C(13)-C(14) | 0.3(4) |
| C(11)-C(12)-C(13)-Cl(1) | -179.0(2) |
| C(12)-C(13)-C(14)-C(15) | -0.8(4) |
| Cl(1)-C(13)-C(14)-C(15) | 178.6(2) |
| C(13)-C(14)-C(15)-C(10) | 0.9(4) |
| C(11)-C(10)-C(15)-C(14) | -0.5(4) |
| C(18)-C(10)-C(15)-C(14) | 178.1(2) |
| C(8)-N(2)-C(16)-C(19) | -160.83(18) |
| C(8)-N(2)-C(16)-C(17) | -34.7(2) |
| O(3)-N(1)-C(17)-C(18) | 148.6(2) |
| O(2)-N(1)-C(17)-C(18) | -34.7(3) |
| O(3)-N(1)-C(17)-C(16) | -93.0(2) |
| O(2)-N(1)-C(17)-C(16) | 83.7(3) |
| N(2)-C(16)-C(17)-N(1) | -110.2(2) |
| C(19)-C(16)-C(17)-N(1) | 15.7(3) |
| N(2)-C(16)-C(17)-C(18) | 10.9(2) |
| C(19)-C(16)-C(17)-C(18) | 136.7(2) |
| C(15)-C(10)-C(18)-C(17) | 141.7(2) |
| C(11)-C(10)-C(18)-C(17) | -39.7(3) |
| C(15)-C(10)-C(18)-C(8) | -95.7(2) |
| C(11)-C(10)-C(18)-C(8) | 82.9(3) |
| N(1)-C(17)-C(18)-C(10) | -95.0(2) |
| C(16)-C(17)-C(18)-C(10) | 143.55(19) |
| N(1)-C(17)-C(18)-C(8) | 135.78(18) |
| C(16)-C(17)-C(18)-C(8) | 14.4(2) |

| | |
|---|---|
| N(2)-C(8)-C(18)-C(10) | -163.10(18) |
| C(7)-C(8)-C(18)-C(10) | 74.1(2) |
| C(9)-C(8)-C(18)-C(10) | -40.8(2) |
| N(2)-C(8)-C(18)-C(17) | -34.4(2) |
| C(7)-C(8)-C(18)-C(17) | -157.26(18) |
| C(9)-C(8)-C(18)-C(17) | 87.9(2) |
| N(2)-C(16)-C(19)-C(24) | -146.5(2) |
| C(17)-C(16)-C(19)-C(24) | 94.1(3) |
| N(2)-C(16)-C(19)-C(20) | 38.3(3) |
| C(17)-C(16)-C(19)-C(20) | -81.1(3) |
| C(24)-C(19)-C(20)-C(21) | -1.5(4) |
| C(16)-C(19)-C(20)-C(21) | 173.7(2) |
| C(19)-C(20)-C(21)-C(22) | -0.2(4) |
| C(20)-C(21)-C(22)-C(23) | 1.7(4) |
| C(20)-C(21)-C(22)-C(25) | -178.3(3) |
| C(21)-C(22)-C(23)-C(24) | -1.5(4) |
| C(25)-C(22)-C(23)-C(24) | 178.6(3) |
| C(20)-C(19)-C(24)-C(23) | 1.8(4) |
| C(16)-C(19)-C(24)-C(23) | -173.6(2) |
| C(22)-C(23)-C(24)-C(19) | -0.3(4) |

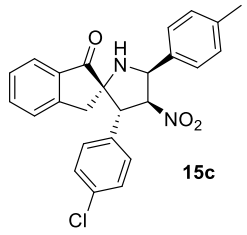
Symmetry transformations used to generate equivalent atoms:

### 8.5 Single-Crystal X-ray Crystallography of 15c[22]

Data intensity of **15c** was collected using a 'Bruker APEX-II CCD' diffractometer at 296(2) K. Data collection and reduction were done by using Olex2 and the structure was solved with the ShelXS structure solution program using direct methods and refined by full-matrix least-squares on $F^2$ with anisotropic displacement parameters for non-H atoms using SHELX-97. Hydrogen atoms were added at their geometrically idea positions and refined isotropically. Crystal data for **15c**: $C_{25}H_{21}ClN_2O_3$, $T$ = 296(2) K, Orthorhombic, P2(1)2(1)2(1), $a$ = 6.6447(5) Å, $b$ = 14.3101(11) Å, $c$ = 22.5008(17) Å, $\alpha$ =

22 Supplementary crystallographic data have been deposited at the Cambridge Crystallographic Data Center (CCDC number: 1874279).

90 deg, $\beta$ = 90 deg, $\gamma$ = 90 deg, $V$ = 2139.5(3) Å$^3$. Z = 4, $d_{calc}$ = 1.344 Mg/m$^3$. 24886 reflections measured, 3762 unique [R(int) = 0.0587], $R_1$ = 0.0430, $wR_2$ = 0.0935 ($I > 2\sigma(I)$, final), $R_1$ = 0.0682, $wR_2$ = 0.1084 (all data), GOF = 0.996, and 280 parameters.




15c

≡

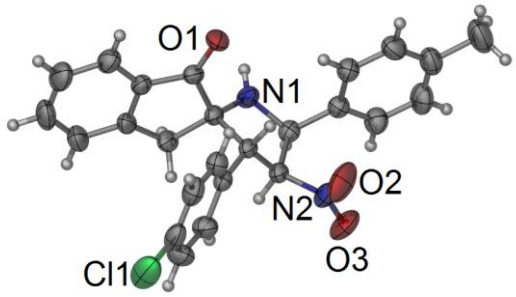



**Table S35.** Crystal data and structure refinement for **15c**.

| | |
|---|---|
| Identification code | **15c** |
| Empirical formula | $C_{25}H_{21}ClN_2O_3$ |
| Formula weight | 432.89 |
| Temperature | 296(2) K |
| Wavelength | 0.71073 Å |
| Crystal system, space group | Orthorhombic, P2(1)2(1)2(1) |
| Unit cell dimensions | a = 6.6447(5) Å alpha = 90 deg. |
| | b = 14.3101(11) Å beta = 90 deg. |
| | c = 22.5008(17) Å gamma = 90 deg. |
| Volume | 2139.5(3) Å$^3$ |
| Z, Calculated density | 4, 1.344 Mg/m$^3$ |
| Absorption coefficient | 0.209 mm$^{-1}$ |
| F(000) | 904 |
| Crystal size | 0.49 x 0.23 x 0.19 mm |
| Theta range for data collection | 1.69 to 25.00 deg. |
| Limiting indices | -7<=h<=7, -17<=k<=17, -26<=l<=23 |
| Reflections collected / unique | 24886 / 3762 [R(int) = 0.0587] |
| Completeness to theta = 25.00 | 99.9 % |
| Absorption correction | Semi-empirical from equivalents |

| | |
|---|---|
| Max. and min. transmission | 0.9615 and 0.9047 |
| Refinement method | Full-matrix least-squares on $F^2$ |
| Data / restraints / parameters | 3762 / 0 / 280 |
| Goodness-of-fit on $F^2$ | 0.996 |
| Final R indices [I>2sigma(I)] | R1 = 0.0430, wR2 = 0.0935 |
| R indices (all data) | R1 = 0.0682, wR2 = 0.1084 |
| Absolute structure parameter | -0.14(10) |
| Largest diff. peak and hole | 0.227 and -0.246 e. $Å^{-3}$ |

**Table S36.** Atomic coordinates ( x $10^4$) and equivalent isotropic displacement parameters ($A^2$ x $10^3$) for **15c**. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

| | x | y | z | U(eq) |
|---|---|---|---|---|
| Cl(1) | 3049(2) | 8332(1) | 8836(1) | 99(1) |
| O(1) | 8832(3) | 4038(2) | 9776(1) | 54(1) |
| O(2) | 3883(5) | 5440(2) | 11283(1) | 98(1) |
| O(3) | 1074(4) | 4738(2) | 11356(1) | 86(1) |
| N(1) | 5146(4) | 3137(2) | 10200(1) | 48(1) |
| N(2) | 2650(4) | 4901(2) | 11105(1) | 54(1) |
| C(1) | 7260(4) | 4055(2) | 9498(1) | 40(1) |
| C(2) | 7007(4) | 4254(2) | 8865(1) | 43(1) |
| C(3) | 8442(5) | 4543(2) | 8455(1) | 58(1) |
| C(4) | 7850(7) | 4656(3) | 7874(2) | 75(1) |
| C(5) | 5875(7) | 4491(3) | 7712(2) | 76(1) |
| C(6) | 4450(6) | 4204(2) | 8118(1) | 64(1) |
| C(7) | 5016(4) | 4084(2) | 8707(1) | 45(1) |
| C(8) | 3808(4) | 3754(2) | 9223(1) | 46(1) |
| C(9) | 5180(4) | 3892(2) | 9768(1) | 37(1) |
| C(10) | 4653(4) | 4757(2) | 10160(1) | 37(1) |
| C(11) | 3040(4) | 4348(2) | 10556(1) | 40(1) |
| C(12) | 3799(4) | 3340(2) | 10706(1) | 42(1) |

| | | | | |
|---|---|---|---|---|
| C(13) | 4801(4) | 3221(2) | 11299(1) | 44(1) |
| C(14) | 3735(5) | 2860(2) | 11773(1) | 58(1) |
| C(15) | 4617(6) | 2732(2) | 12321(2) | 70(1) |
| C(16) | 6622(6) | 2955(2) | 12411(2) | 65(1) |
| C(17) | 7673(5) | 3329(2) | 11942(2) | 62(1) |
| C(18) | 6793(5) | 3459(2) | 11391(1) | 53(1) |
| C(19) | 7602(7) | 2789(3) | 13003(2) | 100(2) |
| C(20) | 4188(4) | 5650(2) | 9834(1) | 39(1) |
| C(21) | 5712(5) | 6286(2) | 9732(1) | 49(1) |
| C(22) | 5384(6) | 7107(2) | 9424(1) | 58(1) |
| C(23) | 3484(6) | 7292(2) | 9215(1) | 62(1) |
| C(24) | 1946(6) | 6687(2) | 9312(2) | 67(1) |
| C(25) | 2286(5) | 5869(2) | 9626(1) | 54(1) |

**Table S37.** Bond lengths [A] and angles [deg] for **15c**.

| | |
|---|---|
| Cl(1)-C(23) | 1.738(3) |
| O(1)-C(1) | 1.218(3) |
| O(2)-N(2) | 1.195(3) |
| O(3)-N(2) | 1.213(3) |
| N(1)-C(9) | 1.454(3) |
| N(1)-C(12) | 1.476(3) |
| N(1)-H(1A) | 0.8600 |
| N(2)-C(11) | 1.489(3) |
| C(1)-C(2) | 1.463(4) |
| C(1)-C(9) | 1.528(4) |
| C(2)-C(3) | 1.389(4) |
| C(2)-C(7) | 1.391(4) |
| C(3)-C(4) | 1.375(5) |
| C(3)-H(3A) | 0.9300 |

| | |
|---|---|
| C(4)-C(5) | 1.382(5) |
| C(4)-H(4A) | 0.9300 |
| C(5)-C(6) | 1.377(5) |
| C(5)-H(5A) | 0.9300 |
| C(6)-C(7) | 1.390(4) |
| C(6)-H(6A) | 0.9300 |
| C(7)-C(8) | 1.487(4) |
| C(8)-C(9) | 1.542(4) |
| C(8)-H(8A) | 0.9700 |
| C(8)-H(8B) | 0.9700 |
| C(9)-C(10) | 1.560(4) |
| C(10)-C(20) | 1.506(4) |
| C(10)-C(11) | 1.511(4) |
| C(10)-H(10A) | 0.9800 |
| C(11)-C(12) | 1.566(4) |
| C(11)-H(11A) | 0.9800 |
| C(12)-C(13) | 1.501(4) |
| C(12)-H(12A) | 0.9800 |
| C(13)-C(14) | 1.381(4) |
| C(13)-C(18) | 1.382(4) |
| C(14)-C(15) | 1.377(5) |
| C(14)-H(14A) | 0.9300 |
| C(15)-C(16) | 1.385(5) |
| C(15)-H(15A) | 0.9300 |
| C(16)-C(17) | 1.373(5) |
| C(16)-C(19) | 1.502(5) |
| C(17)-C(18) | 1.384(4) |
| C(17)-H(17A) | 0.9300 |
| C(18)-H(18A) | 0.9300 |
| C(19)-H(19A) | 0.9600 |
| C(19)-H(19B) | 0.9600 |

| | |
|---|---|
| C(19)-H(19C) | 0.9600 |
| C(20)-C(21) | 1.381(4) |
| C(20)-C(25) | 1.383(4) |
| C(21)-C(22) | 1.382(4) |
| C(21)-H(21A) | 0.9300 |
| C(22)-C(23) | 1.373(5) |
| C(22)-H(22A) | 0.9300 |
| C(23)-C(24) | 1.358(5) |
| C(24)-C(25) | 1.386(4) |
| C(24)-H(24A) | 0.9300 |
| C(25)-H(25A) | 0.9300 |
| C(9)-N(1)-C(12) | 112.3(2) |
| C(9)-N(1)-H(1A) | 123.9 |
| C(12)-N(1)-H(1A) | 123.9 |
| O(2)-N(2)-O(3) | 124.0(3) |
| O(2)-N(2)-C(11) | 120.2(3) |
| O(3)-N(2)-C(11) | 115.8(3) |
| O(1)-C(1)-C(2) | 127.1(3) |
| O(1)-C(1)-C(9) | 124.6(2) |
| C(2)-C(1)-C(9) | 108.3(2) |
| C(3)-C(2)-C(7) | 122.4(3) |
| C(3)-C(2)-C(1) | 128.7(3) |
| C(7)-C(2)-C(1) | 108.8(3) |
| C(4)-C(3)-C(2) | 118.0(3) |
| C(4)-C(3)-H(3A) | 121.0 |
| C(2)-C(3)-H(3A) | 121.0 |
| C(3)-C(4)-C(5) | 120.2(3) |
| C(3)-C(4)-H(4A) | 119.9 |
| C(5)-C(4)-H(4A) | 119.9 |
| C(6)-C(5)-C(4) | 122.0(3) |
| C(6)-C(5)-H(5A) | 119.0 |

| | |
|---|---|
| C(4)-C(5)-H(5A) | 119.0 |
| C(5)-C(6)-C(7) | 118.9(3) |
| C(5)-C(6)-H(6A) | 120.6 |
| C(7)-C(6)-H(6A) | 120.6 |
| C(6)-C(7)-C(2) | 118.6(3) |
| C(6)-C(7)-C(8) | 129.6(3) |
| C(2)-C(7)-C(8) | 111.8(2) |
| C(7)-C(8)-C(9) | 105.1(2) |
| C(7)-C(8)-H(8A) | 110.7 |
| C(9)-C(8)-H(8A) | 110.7 |
| C(7)-C(8)-H(8B) | 110.7 |
| C(9)-C(8)-H(8B) | 110.7 |
| H(8A)-C(8)-H(8B) | 108.8 |
| N(1)-C(9)-C(1) | 113.2(2) |
| N(1)-C(9)-C(8) | 115.4(2) |
| C(1)-C(9)-C(8) | 103.8(2) |
| N(1)-C(9)-C(10) | 102.0(2) |
| C(1)-C(9)-C(10) | 107.8(2) |
| C(8)-C(9)-C(10) | 114.8(2) |
| C(20)-C(10)-C(11) | 118.1(2) |
| C(20)-C(10)-C(9) | 116.4(2) |
| C(11)-C(10)-C(9) | 100.7(2) |
| C(20)-C(10)-H(10A) | 107.0 |
| C(11)-C(10)-H(10A) | 107.0 |
| C(9)-C(10)-H(10A) | 107.0 |
| N(2)-C(11)-C(10) | 114.0(2) |
| N(2)-C(11)-C(12) | 111.5(2) |
| C(10)-C(11)-C(12) | 104.8(2) |
| N(2)-C(11)-H(11A) | 108.8 |
| C(10)-C(11)-H(11A) | 108.8 |
| C(12)-C(11)-H(11A) | 108.8 |

| | |
|---|---|
| N(1)-C(12)-C(13) | 113.2(2) |
| N(1)-C(12)-C(11) | 102.1(2) |
| C(13)-C(12)-C(11) | 116.0(2) |
| N(1)-C(12)-H(12A) | 108.4 |
| C(13)-C(12)-H(12A) | 108.4 |
| C(11)-C(12)-H(12A) | 108.4 |
| C(14)-C(13)-C(18) | 117.9(3) |
| C(14)-C(13)-C(12) | 120.1(3) |
| C(18)-C(13)-C(12) | 122.0(3) |
| C(15)-C(14)-C(13) | 121.5(3) |
| C(15)-C(14)-H(14A) | 119.2 |
| C(13)-C(14)-H(14A) | 119.2 |
| C(14)-C(15)-C(16) | 120.7(3) |
| C(14)-C(15)-H(15A) | 119.7 |
| C(16)-C(15)-H(15A) | 119.7 |
| C(17)-C(16)-C(15) | 117.8(3) |
| C(17)-C(16)-C(19) | 121.5(4) |
| C(15)-C(16)-C(19) | 120.7(4) |
| C(16)-C(17)-C(18) | 121.7(3) |
| C(16)-C(17)-H(17A) | 119.2 |
| C(18)-C(17)-H(17A) | 119.2 |
| C(13)-C(18)-C(17) | 120.4(3) |
| C(13)-C(18)-H(18A) | 119.8 |
| C(17)-C(18)-H(18A) | 119.8 |
| C(16)-C(19)-H(19A) | 109.5 |
| C(16)-C(19)-H(19B) | 109.5 |
| H(19A)-C(19)-H(19B) | 109.5 |
| C(16)-C(19)-H(19C) | 109.5 |
| H(19A)-C(19)-H(19C) | 109.5 |
| H(19B)-C(19)-H(19C) | 109.5 |
| C(21)-C(20)-C(25) | 117.7(3) |

| | |
|---|---|
| C(21)-C(20)-C(10) | 119.3(2) |
| C(25)-C(20)-C(10) | 123.0(2) |
| C(20)-C(21)-C(22) | 121.9(3) |
| C(20)-C(21)-H(21A) | 119.1 |
| C(22)-C(21)-H(21A) | 119.1 |
| C(23)-C(22)-C(21) | 118.8(3) |
| C(23)-C(22)-H(22A) | 120.6 |
| C(21)-C(22)-H(22A) | 120.6 |
| C(24)-C(23)-C(22) | 121.0(3) |
| C(24)-C(23)-Cl(1) | 120.0(3) |
| C(22)-C(23)-Cl(1) | 119.1(3) |
| C(23)-C(24)-C(25) | 119.9(3) |
| C(23)-C(24)-H(24A) | 120.1 |
| C(25)-C(24)-H(24A) | 120.1 |
| C(20)-C(25)-C(24) | 120.8(3) |
| C(20)-C(25)-H(25A) | 119.6 |
| C(24)-C(25)-H(25A) | 119.6 |

Symmetry transformations used to generate equivalent atoms:

**Table S38.** Anisotropic displacement parameters ($A^2$ x $10^3$) for **15c**. The anisotropic displacement factor exponent takes the form: $-2\ pi^2\ [\ h^2\ a^{*2}\ U11 + ... + 2\ h\ k\ a^*\ b^*\ U12\ ]$

| | U11 | U22 | U33 | U23 | U13 | U12 |
|---|---|---|---|---|---|---|
| Cl(1) | 149(1) | 69(1) | 80(1) | 32(1) | 34(1) | 41(1) |
| O(1) | 38(1) | 75(1) | 51(1) | 0(1) | -7(1) | 3(1) |
| O(2) | 116(2) | 98(2) | 80(2) | -46(2) | 30(2) | -40(2) |
| O(3) | 82(2) | 98(2) | 78(2) | -8(2) | 41(2) | 5(2) |
| N(1) | 56(2) | 42(1) | 46(1) | 3(1) | 10(1) | 11(1) |
| N(2) | 62(2) | 53(2) | 46(2) | 0(1) | 17(1) | 4(1) |

| | | | | | | |
|---|---|---|---|---|---|---|
| C(1) | 35(2) | 41(1) | 42(2) | -5(1) | -1(1) | 2(1) |
| C(2) | 46(2) | 43(2) | 40(2) | 0(1) | 4(1) | 8(1) |
| C(3) | 61(2) | 62(2) | 52(2) | 7(2) | 12(2) | 8(2) |
| C(4) | 91(3) | 84(3) | 49(2) | 19(2) | 19(2) | 12(2) |
| C(5) | 107(3) | 83(3) | 37(2) | 6(2) | -7(2) | 18(2) |
| C(6) | 71(2) | 77(2) | 45(2) | -6(2) | -12(2) | 11(2) |
| C(7) | 50(2) | 47(2) | 37(2) | -8(1) | -6(1) | 9(1) |
| C(8) | 39(2) | 56(2) | 44(2) | -11(1) | -5(1) | -2(1) |
| C(9) | 36(1) | 42(1) | 35(2) | -4(1) | -1(1) | -1(1) |
| C(10) | 33(1) | 44(1) | 34(1) | -5(1) | -1(1) | 0(1) |
| C(11) | 37(1) | 46(2) | 37(2) | -4(1) | -1(1) | 1(1) |
| C(12) | 40(2) | 41(2) | 45(2) | -2(1) | 3(1) | -7(1) |
| C(13) | 46(2) | 41(2) | 44(2) | -1(1) | 2(1) | -1(1) |
| C(14) | 62(2) | 61(2) | 52(2) | 8(2) | 7(2) | -7(2) |
| C(15) | 94(3) | 68(2) | 48(2) | 14(2) | 7(2) | -5(2) |
| C(16) | 84(3) | 62(2) | 49(2) | 3(2) | -8(2) | 10(2) |
| C(17) | 59(2) | 66(2) | 61(2) | -6(2) | -10(2) | 7(2) |
| C(18) | 54(2) | 57(2) | 47(2) | 1(2) | 3(2) | 2(2) |
| C(19) | 131(4) | 107(3) | 61(2) | 9(2) | -25(3) | 26(3) |
| C(20) | 42(2) | 42(2) | 34(1) | -4(1) | 3(1) | 0(1) |
| C(21) | 54(2) | 48(2) | 45(2) | -1(1) | 2(2) | -2(1) |
| C(22) | 79(3) | 50(2) | 46(2) | 0(2) | 14(2) | -6(2) |
| C(23) | 90(3) | 52(2) | 43(2) | 6(2) | 20(2) | 17(2) |
| C(24) | 59(2) | 74(2) | 69(2) | 14(2) | -1(2) | 20(2) |
| C(25) | 46(2) | 57(2) | 61(2) | 6(2) | 4(2) | 4(2) |

**Table S39.** Hydrogen coordinates ( x $10^4$) and isotropic displacement parameters ($A^2$ x $10^3$) for **15c**.

| | x | y | z | U(eq) |
|---|---|---|---|---|
| H(1A) | 5833 | 2630 | 10166 | 58 |

| | | | | |
|---|---|---|---|---|
| H(3A) | 9763 | 4657 | 8571 | 70 |
| H(4A) | 8780 | 4844 | 7590 | 90 |
| H(5A) | 5498 | 4576 | 7318 | 91 |
| H(6A) | 3131 | 4092 | 7999 | 77 |
| H(8A) | 3451 | 3101 | 9176 | 55 |
| H(8B) | 2584 | 4118 | 9262 | 55 |
| H(10A) | 5826 | 4880 | 10412 | 44 |
| H(11A) | 1787 | 4300 | 10329 | 48 |
| H(12A) | 2650 | 2912 | 10687 | 50 |
| H(14A) | 2390 | 2700 | 11722 | 70 |
| H(15A) | 3860 | 2494 | 12634 | 84 |
| H(17A) | 9011 | 3500 | 11997 | 74 |
| H(18A) | 7546 | 3708 | 11081 | 63 |
| H(19A) | 8989 | 2975 | 12985 | 149 |
| H(19B) | 7521 | 2137 | 13101 | 149 |
| H(19C) | 6923 | 3148 | 13302 | 149 |
| H(21A) | 6996 | 6158 | 9875 | 59 |
| H(22A) | 6430 | 7527 | 9360 | 70 |
| H(24A) | 666 | 6821 | 9167 | 81 |
| H(25A) | 1222 | 5463 | 9699 | 65 |

**Table S40.** Torsion angles [deg] for **15c**.

| | |
|---|---|
| O(1)-C(1)-C(2)-C(3) | -6.2(5) |
| C(9)-C(1)-C(2)-C(3) | 172.3(3) |
| O(1)-C(1)-C(2)-C(7) | 172.3(3) |
| C(9)-C(1)-C(2)-C(7) | -9.1(3) |
| C(7)-C(2)-C(3)-C(4) | -0.5(5) |
| C(1)-C(2)-C(3)-C(4) | 177.9(3) |
| C(2)-C(3)-C(4)-C(5) | 0.5(5) |
| C(3)-C(4)-C(5)-C(6) | -0.6(6) |

| | |
|---|---|
| C(4)-C(5)-C(6)-C(7) | 0.5(6) |
| C(5)-C(6)-C(7)-C(2) | -0.4(5) |
| C(5)-C(6)-C(7)-C(8) | -177.7(3) |
| C(3)-C(2)-C(7)-C(6) | 0.4(4) |
| C(1)-C(2)-C(7)-C(6) | -178.3(3) |
| C(3)-C(2)-C(7)-C(8) | 178.2(3) |
| C(1)-C(2)-C(7)-C(8) | -0.5(3) |
| C(6)-C(7)-C(8)-C(9) | -172.9(3) |
| C(2)-C(7)-C(8)-C(9) | 9.6(3) |
| C(12)-N(1)-C(9)-C(1) | 142.6(2) |
| C(12)-N(1)-C(9)-C(8) | -98.1(3) |
| C(12)-N(1)-C(9)-C(10) | 27.0(3) |
| O(1)-C(1)-C(9)-N(1) | -41.2(4) |
| C(2)-C(1)-C(9)-N(1) | 140.2(2) |
| O(1)-C(1)-C(9)-C(8) | -167.0(3) |
| C(2)-C(1)-C(9)-C(8) | 14.4(3) |
| O(1)-C(1)-C(9)-C(10) | 70.9(3) |
| C(2)-C(1)-C(9)-C(10) | -107.7(2) |
| C(7)-C(8)-C(9)-N(1) | -138.6(2) |
| C(7)-C(8)-C(9)-C(1) | -14.2(3) |
| C(7)-C(8)-C(9)-C(10) | 103.2(3) |
| N(1)-C(9)-C(10)-C(20) | -169.3(2) |
| C(1)-C(9)-C(10)-C(20) | 71.3(3) |
| C(8)-C(9)-C(10)-C(20) | -43.8(3) |
| N(1)-C(9)-C(10)-C(11) | -40.5(2) |
| C(1)-C(9)-C(10)-C(11) | -159.9(2) |
| C(8)-C(9)-C(10)-C(11) | 85.0(3) |
| O(2)-N(2)-C(11)-C(10) | -20.0(4) |
| O(3)-N(2)-C(11)-C(10) | 162.5(3) |
| O(2)-N(2)-C(11)-C(12) | 98.4(3) |
| O(3)-N(2)-C(11)-C(12) | -79.0(3) |

| | |
|---|---|
| C(20)-C(10)-C(11)-N(2) | -70.2(3) |
| C(9)-C(10)-C(11)-N(2) | 162.1(2) |
| C(20)-C(10)-C(11)-C(12) | 167.6(2) |
| C(9)-C(10)-C(11)-C(12) | 39.9(2) |
| C(9)-N(1)-C(12)-C(13) | -127.9(3) |
| C(9)-N(1)-C(12)-C(11) | -2.4(3) |
| N(2)-C(11)-C(12)-N(1) | -148.1(2) |
| C(10)-C(11)-C(12)-N(1) | -24.3(2) |
| N(2)-C(11)-C(12)-C(13) | -24.4(3) |
| C(10)-C(11)-C(12)-C(13) | 99.4(3) |
| N(1)-C(12)-C(13)-C(14) | -143.0(3) |
| C(11)-C(12)-C(13)-C(14) | 99.3(3) |
| N(1)-C(12)-C(13)-C(18) | 36.6(4) |
| C(11)-C(12)-C(13)-C(18) | -81.0(3) |
| C(18)-C(13)-C(14)-C(15) | -0.5(5) |
| C(12)-C(13)-C(14)-C(15) | 179.2(3) |
| C(13)-C(14)-C(15)-C(16) | -0.7(5) |
| C(14)-C(15)-C(16)-C(17) | 1.8(5) |
| C(14)-C(15)-C(16)-C(19) | -178.2(3) |
| C(15)-C(16)-C(17)-C(18) | -1.8(5) |
| C(19)-C(16)-C(17)-C(18) | 178.2(3) |
| C(14)-C(13)-C(18)-C(17) | 0.5(4) |
| C(12)-C(13)-C(18)-C(17) | -179.2(3) |
| C(16)-C(17)-C(18)-C(13) | 0.7(5) |
| C(11)-C(10)-C(20)-C(21) | 146.6(3) |
| C(9)-C(10)-C(20)-C(21) | -93.5(3) |
| C(11)-C(10)-C(20)-C(25) | -33.5(4) |
| C(9)-C(10)-C(20)-C(25) | 86.4(3) |
| C(25)-C(20)-C(21)-C(22) | -1.3(4) |
| C(10)-C(20)-C(21)-C(22) | 178.6(3) |
| C(20)-C(21)-C(22)-C(23) | 0.0(4) |

| | |
|---|---|
| C(21)-C(22)-C(23)-C(24) | 0.6(5) |
| C(21)-C(22)-C(23)-Cl(1) | 179.1(2) |
| C(22)-C(23)-C(24)-C(25) | 0.0(5) |
| Cl(1)-C(23)-C(24)-C(25) | -178.4(2) |
| C(21)-C(20)-C(25)-C(24) | 1.9(4) |
| C(10)-C(20)-C(25)-C(24) | -177.9(3) |
| C(23)-C(24)-C(25)-C(20) | -1.3(5) |

Symmetry transformations used to generate equivalent atom