Electronic Supplementary Information

Piezoactive Amino Acid Derivatives Containing Fragments of Planar-Chiral *ortho*-Carboranes

Dmitry A. Gruzdev,[*, a, b] Alla S. Nuraeva,[c] Pavel A. Slepukhin,[a,b] Galina L. Levit,[a, b] Pavel S. Zelenovskiy,[c] Vladimir Ya. Shur,[c] and Victor P. Krasnov [a, b]

[a] *Postovsky Institute of Organic Synthesis, Russian Academy of Sciences (Ural Branch), 22/20 S. Kovalevskoy/Akademicheskaya St., Ekaterinburg, 620990 Russia*

[b] *Institute of Chemical Engineering, Ural Federal University, 19 Mira St., Ekaterinburg, 620002 Russia*

[c] *School of Natural Sciences and Mathematics, Ural Federal University, 51 Lenin Ave., Ekaterinburg, 620000 Russia*

* Corresponding author: gruzdev-da@ios.uran.ru (Dmitry A. Gruzdev)

Contents

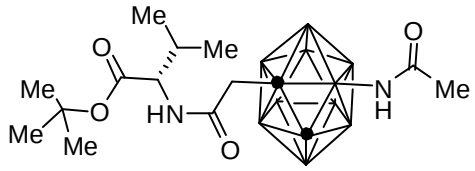
1. Chemistry

1.1. General

tert-Butyl (*S*)-valinate hydroacetate,[S1] *tert*-butyl (*S*)-*tert*-leucinate,[S2] *tert*-butyl (*S*)-leucinate,[S3] (3-acetamido-1,2-dicarba-*closo*-dodecaboran-1-yl)acetic acid[S4] and (3-formamido-1,2-dicarba-*closo*-dodecaboran-1yl)acetic acid[S4] were obtained according to known procedures. *tert*-Butyl (*S*)-valinate (yield 79%) was isolated from its salt with acetic acid on treatment with a $CHCl_3$–5% aqueous Na_2CO_3 mixture. Other reagents were commercially available. Solvents were purified according to traditional methods[S5] and used freshly distilled. Melting points were obtained on a SMP3 apparatus (Barloworld Scientific, UK). Optical rotations were measured on a Perkin Elmer 341 polarimeter. The ^1H and ^{13}C NMR spectra were recorded on Bruker Avance 500 (500, and 125 MHz, respectively) spectrometer at 298 K using DMSO-d_6 as a solvent and tetramethylsilane as an internal reference. Microanalyses were performed using a Perkin Elmer 2400 II automatic analyzer. Analytical TLC was performed using Sorbfil plates (Imid, Russia). Flash column chromatography was performed using Silica gel 60 (230–400 mesh) (Alfa Aesar, UK). Analytical chiral HPLC of compounds **3a-f** was performed on a Knauer Smartline-1100 instrument using a Chiralcel OD-H column (250×4.6 mm, 5 μm), detection at 210 nm, 1 mL/min flow rate. Preparative HPLC was performed on a Shimadzu LC-20 Prominence instrument using a Chiralcel OD-H column (250×20 mm, 5 μm), detection at 210 nm, 10 mL/min flow rate. The high-resolution mass spectra were obtained on a Bruker maXis Impact HD mass spectrometer, electrospray ionization with direct sample inlet (4 L/min flow rate).

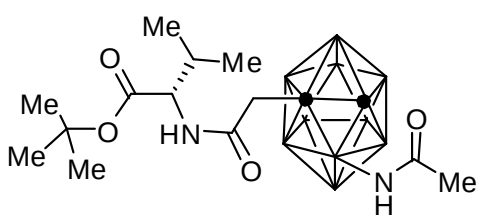
1.2. Synthetic Procedures and Compounds Characterization

Compounds 3a-d. General Procedure. TBTU (0.43 g, 1.35 mmol) was added to a solution of compound **1a** (or **1b**) (1.35 mmol), compound **2a** (**2b-d**) (1.35 mmol), and TEA (0.56 mL, 4.05 mmol) in dichloromethane (18 mL) under stirring. The reaction mixture was stirred for 70 h at room temperature, then washed consequently with 10% aqueous citric acid (3×20 mL), saturated NaCl (20 mL), 5% aqueous $NaHCO_3$ (3×20 mL), and water (2×20 mL). Organic layer was dried ($MgSO_4$) and evaporated to dryness under reduced pressure The residue was recrystallized, or subjected to flash column chromatography or preparative HPLC to afford individual (S,S_P)- and (S,R_P)-amides **3a-d**.



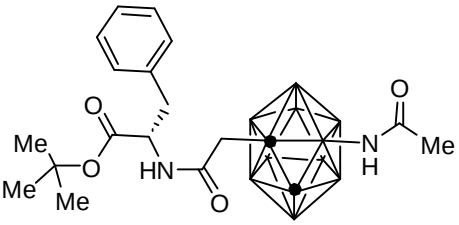
● denotes carbon atom and CH group,
other vertices are boron atoms and BH groups

(S,S_P)-*tert*-Butyl *N*-(3-acetamido-1,2-dicarba-*closo*-dodecaboran-1-yl)acetyl-valinate [(S,S_P)-3a]. Yield 0.076 g (13.6%) after two crystallizations from hexane–acetone 1:1. Colorless needles, mp 228-229 °C. *De* > 98%. HPLC (hexane–*i*PrOH 10:1): τ 6.51 min. $[\alpha]_D^{20}$ +22.5 (*c* 0.26, CH_2Cl_2). ^{1}H NMR: δ 0.879 (d, J = 6.8 Hz, 3H, *i*Pr), 0.885 (d, J = 6.8 Hz, 3H, *i*Pr), 1.42 (s, 9 H, O*t*Bu), 1.98 (s, 3H, Ac), 1.97–2.03 (m, 1H, *i*Pr), 2.96 (d, J = 14.7 Hz, 1H, H-2'B), 3.11 (d, J = 14.7 Hz, 1H, H-2'A), 1.4–3.1 (br. s, 9H, 9×BH), 3.99 (dd, J = 8.3, 6.2 Hz, 1H, H-2), 5.20 (s, 1H, CH-carborane), 8.39 (s, 1H, NHAc), 8.40 (d, J = 8.3 Hz, 1H, NH-Val). ^{13}C NMR: δ 18.05, 18.86, 24.43, 27.58 (3C), 29.85, 38.58, 58.18, 59.85, 71.41, 80.82, 166.03, 170.18, 173.86. HRMS (ESI) *m*/*z* calcd. for $C_{15}H_{35}{}^{10}B_2{}^{11}B_8N_2O_4$ $[M + H]^+$ 415.3595; found 415.3605. Anal. Calcd. for $C_{15}H_{34}B_{10}N_2O_4$: C 43.46, H 8.27, N 6.76. Found: C 43.52, H 8.40, N 6.67.

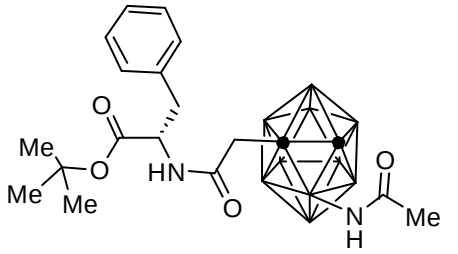


(S,R_P)-*tert*-Butyl *N*-(3-acetamido-1,2-dicarba-*closo*-dodecaboran-1-yl)acetyl-valinate [(S,R_P)-3a]. Yield 0.127 g (22.7%) after flash column chromatography on silica gel (eluent hexane–acetone from 9:1 to 75:25). Colorless needles, mp 220-222 °C. *De* > 98%. HPLC (hexane–*i*PrOH 10:1): τ 7.94 min. $[\alpha]_D^{20}$ −2.1 (*c* 0.64, CH_2Cl_2). ^{1}H NMR: δ 0.88 (d, J = 6.8 Hz, 6H, *i*Pr), 1.41 (s, 9H, O*t*Bu), 1.98 (s, 3H, Ac), 1.96–2.06 (m, 1H, *i*Pr), 2.94 (d, J = 14.8 Hz, 1H, H-2'B), 3.14 (d, J = 14.8 Hz, 1H, H-2'A), 1.5–2.9 (br. s, 9H, 9×BH), 4.03 (dd, J = 8.4, 6.0 Hz,

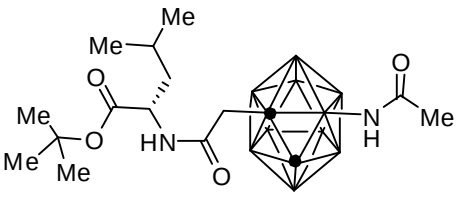
1H, H-2), 5.22 (s, 1H, CH-carborane), 8.36 (d, *J* = 8.4 Hz, 1H, NH-Val), 8.39 (s, 1H, NHAc). ^{13}C NMR: *δ* 17.94, 18.87, 24.43, 27.59 (3C), 29.96, 38.64, 57.97, 59.74, 71.36, 80.87, 166.00, 170.16, 173.93. Anal. Calcd. for $C_{15}H_{34}B_{10}N_2O_4$: C 43.46, H 8.27, N 6.76, B 26.08. Found: C 43.44, H 8.14, N 6.78, B 26.04.



(*S*,*S*$_P$)-*tert*-Butyl *N*-(3-acetamido-1,2-dicarba-*closo*-dodecaboran-1-yl)acetyl-phenylalaninate [(*S*,*S*$_P$)-3b]. Yield 0.076 g (28.2%) after preparative HPLC (hexane–*i*PrOH 10:1, τ 12-18 min). Colorless solid, mp 166–168 °C. $[\alpha]_D^{20}$ +32.9 (*c* 0.42, CH_2Cl_2). *De* > 99%. HPLC (hexane–*i*PrOH 10:1): τ 13.85 min. ^{1}H NMR: *δ* 1.33 (s, 9H, O*t*Bu), 1.95 (s, 3H, Ac), 1.4–2.7 (br. s, 9H, 9×BH), 2.84 (d, *J* = 14.8 Hz, 1H, H-2'B), 2.86 (dd, *J* = 13.8, 8.8 Hz, 1H, H-3B), 2.96 (dd, *J* = 13.8, 6.5 Hz, 1H, H-3A), 3.01 (d, *J* = 14.8 Hz, 1H, H-2'A), 4.32–4.37 (m, 1H, H-2), 5.13 (s, 1H, CH-carborane), 7.20–7.23 (m, 3H, Ph), 7.27–7.30 (m, 2H, Ph), 8.35 (s, 1H, NHAc), 8.67 (d, *J* = 7.9 Hz, 1H, NH-Phe). ^{13}C NMR: *δ* 24.40, 27.44 (3C), 36.86, 38.52, 54.28, 59.60, 71.18, 80.91, 126.57, 128.19 (2C), 129.11 (2C), 136.79, 165.66, 170.12, 173.81. Anal. Calcd. for $C_{19}H_{34}B_{10}N_2O_4$: C 49.33, H 7.41, N 6.06, B 23.37. Found: C 49.03, H 7.70, N 6.00, B 23.52.

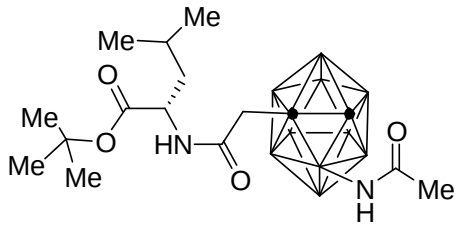


(*S*,*R*$_P$)-*tert*-Butyl *N*-(3-acetamido-1,2-dicarba-*closo*-dodecaboran-1-yl)acetyl-phenylalaninate [(*S*,*R*$_P$)-3b]. Yield 0.076 g (25.1%) after preparative HPLC (hexane–*i*PrOH 10:1, τ 21-30 min). Colorless solid, mp 121–122 °C. $[\alpha]_D^{20}$ +10.4 (*c* 0.58, CH_2Cl_2). *De* > 97.4%. HPLC (hexane–*i*PrOH 10:1): τ 22.08 min. ^{1}H NMR: *δ* 1.34 (s, 9H, O*t*Bu), 1.97 (s, 3H, Ac), 1.5–2.5 (br. s, 9H, 9×BH), 2.85 (dd, *J* = 13.6, 9.3 Hz, 1H, H-3B), 2.87 (d, *J* = 14.8 Hz, 1H, H-2'B), 2.98 (dd, *J* = 13.6, 6.3 Hz, 1H, H-3A), 3.00 (d, *J* = 14.8 Hz, 1H, H-2'A), 4.36–4.41 (m, 1H, H-2), 5.12 (s, 1H, CH-carborane), 7.21–7.30 (m, 5H, Ph), 8.37 (s, 1H, NHAc), 8.63 (d, *J* = 7.9 Hz, 1H, NH-Phe). ^{13}C NMR: *δ* 24.36, 27.45 (3C), 36.95, 38.54, 54.02, 59.50, 71.72, 80.97, 126.53, 128.15 (2C), 129.11 (2C), 136.73, 165.59, 170.04, 173.81. HRMS (ESI) *m*/*z* calcd. for $C_{19}H_{35}{}^{10}B_2{}^{11}B_8N_2O_4$ $[M + H]^+$ 463.3595; found 463.3600.

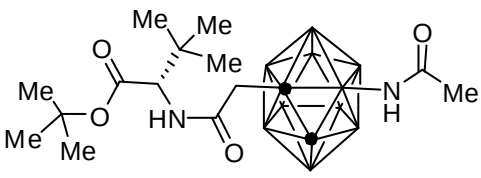


(*S*,*S*$_P$)-*tert*-Butyl *N*-(3-acetamido-1,2-dicarba-*closo*-dodecaboran-1-yl)acetyl-leucinate [(*S*,*S*$_P$)-3c]. Yield

0.089 g (32.5%) after preparative HPLC (hexane–*i*PrOH 11:1, τ 10-16 min) followed by crystallization from hexane–CH_2Cl_2 (5:2). Colorless needles, mp 210 °C (hexane–CH_2Cl_2). $[\alpha]_D^{20}$ +7.1 (*c* 0.27, C_6H_6). *De* > 99%. HPLC (hexane–*i*PrOH 10:1): τ 15.50 min. ^{1}H NMR: *δ* 0.84 (d, *J* = 6.5 Hz, 3H, *i*Pr), 0.90 (d, *J* = 6.6 Hz, 3H, *i*Pr), 1.40 (s, 9H, *t*Bu), 1.44–1.49 (m, 2H, 2×H-3), 1.55–1.67 (m, 1H, *i*Pr), 1.97 (s, 3H, Ac), 1.4–2.8 (br. s, 9H, 9×BH), 2.90 (d, *J* = 14.8 Hz, 1H, H-2'B), 3.03 (d, *J* = 14.8 Hz, 1H, H-2'A), 4.06–4.11 (m, 1H, H-2), 5.19 (s, 1H, CH-carborane), 8.38 (s, 1H, NHAc), 8.54 (d, *J* = 7.6 Hz, 1H, NH-Leu). ^{13}C NMR: *δ* 21.35, 22.59, 24.17 (2C), 24.42, 27.53 (3C), 38.62, 51.29, 59.72, 71.29, 80.69, 165.76, 171.19, 173.84. Anal. Calcd. for $C_{16}H_{36}B_{10}N_2O_4$: C 44.84, H 8.47, N 6.54. Found: C 44.88, H 8.68, N 6.43.

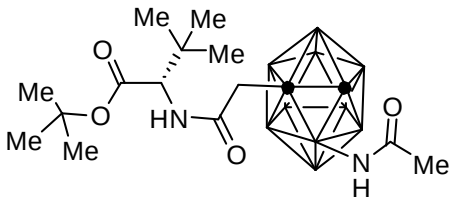


(*S*,*R*$_P$)-*tert*-Butyl *N*-(3-acetamido-1,2-dicarba-*closo*-dodecaboran-1-yl)acetyl-leucinate [(*S*,*R*$_P$)-3c]. Yield 0.075 g (27.5%) after flash column chromatography on silica gel (eluent hexane–acetone 9:1) followed by preparative HPLC (hexane–*i*PrOH 11:1, τ 18-24 min). Colorless solid, mp 178–179 °C. $[\alpha]_D^{20}$ −24.9 (*c* 0.56, C_6H_6). *De* > 99%. HPLC (hexane–*i*PrOH 10:1): τ 15.50 min. ^{1}H NMR: *δ* 0.85 (d, *J* = 6.5 Hz, 3H, *i*Pr), 0.91 (d, *J* = 6.6 Hz, 3H, *i*Pr), 1.40 (s, 9H, *t*Bu), 1.45–1.49 (m, 2H, 2×H-3), 1.58–1.68 (m, 1H, *i*Pr), 1.98 (s, 3H, Ac), 1.5–2.7 (br. s, 9H, 9×BH), 2.89 (d, *J* = 14.7 Hz, 1H, H-2'B), 3.04 (d, *J* = 14.7 Hz, 1H, H-2'A), 4.08–4.15 (m, 1H, H-2), 5.19 (s, 1H, CH-carborane), 8.39 (s, 1H, NHAc), 8.51 (d, *J* = 7.6 Hz, 1H, NH-Leu). ^{13}C NMR: *δ* 21.21, 22.63, 24.20 (2C), 24.40, 27.53 (3C), 38.75, 51.14, 59.79, 71.24, 80.72, 165.70, 171.17, 173.89. HRMS (ESI) *m*/*z* calcd. for $C_{16}H_{37}{}^{10}B_2{}^{11}B_8N_2O_4$ $[M + H]^+$ 429.3751; found 429.3754.



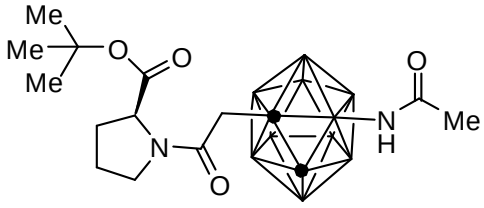
(*S*,*S*$_P$)-*tert*-Butyl *N*-(3-acetamido-1,2-dicarba-*closo*-dodecaboran-1-yl)acetyl-*tert*-leucinate [(*S*,*S*$_P$)-3d]. Yield 0.024 g (8.7%) after flash column chromatography on silica gel (eluent benzene–EtOAc 8:2). Colorless crystals, mp 222–225 °C (CH_2Cl_2–MeOH). $[\alpha]_D^{20}$ +10.2 (*c* 0.56, CH_2Cl_2). *De* > 99%. HPLC (hexane–*i*PrOH–MeOH 20:0.8:0.2): τ 15.45 min. ^{1}H NMR: *δ* 0.94 (s, 9H, *t*Bu), 1.42 (s, 9H, O*t*Bu), 1.6–2.7 (br. s, 9H, 9×BH), 1.98 (s, 3H, Ac), 2.97 (d, *J* = 14.7 Hz, 1H, H-2'B), 3.19 (d, *J* = 14.7 Hz, 1H, H-2'A), 3.97 (d, *J* = 8.7 Hz, 1H, H-2), 5.18 (s, 1H, CH-carborane), 8.28 (d, *J* = 8.7 Hz, 1H, NH-Tle), 8.40 (s, 1H, NHAc). ^{13}C NMR: *δ* 24.39, 26.50 (3C), 27.57 (3C), 33.39,

38.48, 59.86, 61.21, 71.46, 80.80, 166.05, 169.54, 173.83. HRMS (ESI) *m*/*z* calcd. for $C_{16}H_{37}{}^{10}B_2{}^{11}B_8N_2O_4$ $[M + H]^+$ 429.3751; found 429.3757.



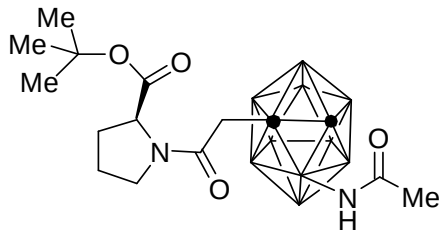
(*S*,*R*$_P$)-*tert*-Butyl *N*-(3-acetamido-1,2-dicarba-*closo*-dodecaboran-1-yl)acetyl-*tert*-leucinate [(*S*,*R*$_P$)-3d]. Yield 0.040 g (14.6%) after flash column chromatography on silica gel (eluent benzene–EtOAc) followed by preparative HPLC (hexane–*i*PrOH–MeOH 20:0.8:0.2, τ 26-36 min). Colorless solid, mp 228–229 °C (hexane–*i*PrOH). $[\alpha]_D^{20}$ −2.6 (*c* 0.5, CH_2Cl_2). *De* > 99%. HPLC (hexane–*i*PrOH–MeOH 20:0.8:0.2): τ 26.50 min. ^{1}H NMR: *δ* 0.95 (s, 9H, *t*Bu), 1.42 (s, 9H, O*t*Bu), 1.6–2.7 (br. s, 9H, 9×BH), 1.98 (s, 3H, Ac), 3.00 (d, *J* = 14.7 Hz, 1H, H-2'B), 3.16 (d, *J* = 14.7 Hz, 1H, H-2'A), 4.00 (d, *J* = 8.8 Hz, 1H, H-2), 5.22 (s, 1H, CH-carborane), 8.24 (d, *J* = 8.8 Hz, 1H, NH-Tle), 8.41 (s, 1H, N<u>H</u>Ac). ^{13}C NMR: *δ* 24.42, 26.54 (3C), 27.63 (3C), 33.53, 38.68, 59.86, 61.06, 71.42, 80.89, 165.95, 169.56, 173.97. Anal. Calcd. for $C_{16}H_{36}B_{10}N_2O_4$: C 44.84, H 8.47, N 6.54. Found: C 44.71, H 8.64, N 6.69.

Compounds 3e,f. General Procedure. Ethyl chloroformate (0.061 g, 0.64 mmol) was added to a solution of compound **1a** (or **1b**) (0.64 mmol) and *N*-methylmorpholine (0.070 mL, 0.64 mmol) in THF (2 mL) under stirring at −10 °C. The reaction mixture was stirred at −10 °C for 20 min; then compound **2e** (or **2f**) (0.64 mmol) and a solution of DIPEA (0.223 mL, 1.28 mmol) in THF (4 mL) was added. The reaction mixture was stirred at −10 °C for 30 min and at +20 °C for a day, and evaporated to dryness under reduced pressure. The residue was purified by flash column chromatography on silica gel (eluent hexane–acetone from 9:1 to 7:3 for compound **3e**, or benzene–ethyl acetate from 9:1 to 75:25 for compound **3f**). The resulting mixture of diastereomeric amides was subjected to preparative HPLC to afford individual (*S*,*S*$_P$)- and (*S*,*R*$_P$)-amides **3e,fd**.

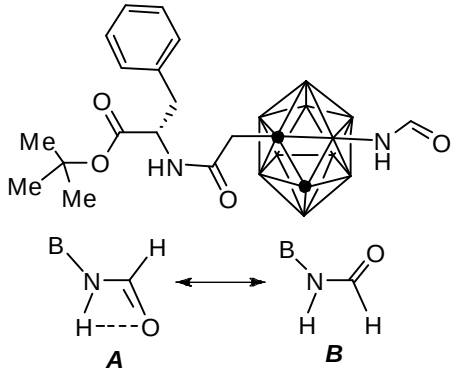


(*S*,*S*$_P$)-*tert*-Butyl *N*-(3-acetamido-1,2-dicarba-*closo*-dodecaboran-1-yl)acetyl-prolinate [(*S*,*S*$_P$)-3e]. Yield 0.039 g (14.8%) after preparative HPLC (hexane–*i*PrOH–MeOH 20:0.8:0.2, τ 20-30 min). Colorless solid, mp 187–188 °C. $[\alpha]_D^{20}$ −34.7 (*c* 0.66, MeOH). *De* > 99%. HPLC (hexane–*i*PrOH–MeOH 20:0.8:0.2): τ 18.15 min. ^{1}H NMR (rotamers ***A*** and ***B*** are observable, ***A*** / ***B*** 8 : 2): *δ* 1.39 (s, 7.2H, *t*Bu (***A***)), 1.42 (s, 1.8H, *t*Bu (***B***)), 1.78–1.84 (m, 1H,

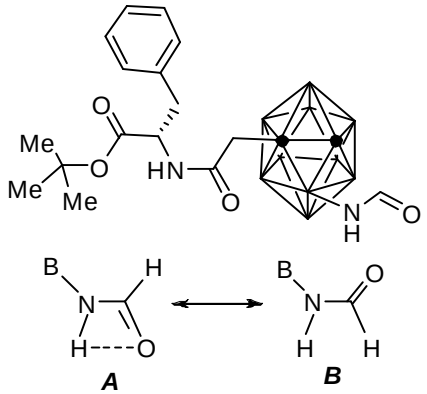
H-3B), 1.88–1.93 (m, 2H, 2×H-4), 1.96 (s, 2.4H, Ac (***A***)); 1.97 (s, 0.6H, Ac (***B***)); 2.02–2.16 (m, 1H, H-3A), 1.4–2.7 (br. s, 9H, 9×BH); 2.84 (d, *J* = 15.9 Hz, 0.2H, H-2'B (***B***)); 3.08 (d, *J* = 15.6 Hz, 0.8H, H-2'B (***A***)); 3.20 (d, *J* = 15.9 Hz, 0.2H, H-2'A (***B***)); 3.29 (d, *J* = 15.6 Hz, 0.8H, H-2'A (***A***)); 4.10 (dd, *J* = 8.7, 4.0 Hz, 0.8H, H-2 (***A***)); 4.50–4.53 (m, 0.2H, H-2 (***B***)); 5.33 (s, 0.8H, CH-carborane (***A***)); 5.43 (s, 0.2H, CH-carborane (***B***)); 8.44 (s, 0.8H, NHAc (***A***)); 8.49 (s, 0.2H, NHAc (***B***)). ^{13}C NMR (rotamers ***A*** and ***B*** are observable, ***A*** / ***B*** 8 : 2): *δ* 21.88 (***B***), 24.18 (***A***), 24.25 (***B***), 24.28 (***A***), 27.43 (3C) (***B***), 27.48 (3C) (***A***), 28.76 (***A***), 30.51 (***B***), 36.29 (***B***), 36.51 (***A***), 46.10 (***B***), 47.35 (***A***), 59.33 (***B***), 59.37 (***A***), 59.48 (***A***), 59.74 (***B***), 71.11 (***A*** and ***B***), 80.48 (***A***), 81.84 (***B***), 164.49 (***A***), 164.73 (***B***), 170.52 (***A***), 170.61 (***B***), 173.60 (***B***), 173.64 (***A***). Anal. Calcd. for $C_{15}H_{32}B_{10}N_2O_4$: C 43.67, H 7.82, N 6.89. Found: C 43.79, H 7.70, N 6.49.



(*S*,*R*$_P$)-*tert*-Butyl *N*-(3-acetamido-1,2-dicarba-*closo*-dodecaboran-1-yl)acetyl-prolinate [(*S*,*R*$_P$)-3e]. Yield 0.023 g (8.7%) after preparative HPLC (hexane–*i*PrOH–MeOH 20:0.8:0.2, τ 32-46 min). Colorless solid, mp 167–169 °C. $[\alpha]_D^{20}$ −46.2 (*c* 0.67, CH_2Cl_2). *De* > 99%. HPLC (hexane–*i*PrOH–MeOH 20:0.8:0.2): τ 26-28 min (broad peak). ^{1}H NMR (rotamers ***A*** and ***B*** are observable, ***A*** / ***B*** 8 : 2): *δ* 1.38 (s, 7.2H, *t*Bu (***A***)), 1.43 (s, 1.8H, *t*Bu (***B***)), 1.77–1.85 (m, 1H, H-3B), 1.87–1.93 (m, 2H, 2×H-4), 1.94 (s, 0.6H, Ac (***B***)), 1.98 (s, 2.4H, Ac (***A***)), 2.11–2.18 (m, 1H, H-3A), 1.7–2.8 (br. s, 9H, 9×BH), 2.92 (d, *J* = 15.8 Hz, 0.2H, H-2'B (***B***)), 3.08 (d, *J* = 15.6 Hz, 0.8H, H-2'B (***A***)), 3.11 (d, *J* = 15.8 Hz, 0.2H, H-2'A (***B***)), 3.28 (d, *J* = 15.6 Hz, 0.8H, H-2'A (***A***)), 4.14 (dd, *J* = 8.7, 4.0 Hz, 0.8H, H-2 (***A***)), 4.59–4.62 (m, 0.2H, H-2 (***B***)), 5.35 (s, 0.8H, CH-carborane (***A***)), 5.59 (s, 0.2H, CH-carborane (***B***)), 8.43 (s, 1H, NHAc). ^{13}C NMR (rotamers ***A*** and ***B*** are observable, ***A*** / ***B*** 8 : 2): *δ* 21.86 (***B***), 24.16 (***A***), 24.24 (***B***), 24.31 (***A***), 27.45 (3C) (***B***), 27.50 (3C) (***A***), 28.76 (***A***), 30.65 (***B***), 36.50 (***B***), 36.70 (***A***), 46.13 (***B***), 47.39 (***A***), 59.33 (***A***), 59.42 (***B***), 59.69 (***B***), 60.00 (***A***), 71.03 (***B***), 71.13 (***A***), 80.43 (***A***), 81.79 (***B***), 164.49 (***A***), 164.82 (***B***), 170.55 (***A***), 170.69 (***B***), 173.52 (***B***), 173.71 (***A***). Anal. Calcd. for $C_{15}H_{32}B_{10}N_2O_4$: C 43.67, H 7.82, N 6.89. Found: C 43.57, H 7.86, N 6.74.



(*S*,*S*$_P$)-*tert*-Butyl *N*-(3-formamido-1,2-dicarba-*closo*-dodecaboran-1-yl)acetyl-phenylalaninate [(*S*,*S*$_P$)-3f]. Yield 0.091 g (31.6%) after preparative HPLC (hexane–*i*PrOH 8:1, τ 34-42 min). Colorless solid, mp 146–149 °C. $[\alpha]_D^{20}$ +30.0 (*c* 0.45, CH_2Cl_2). *De* > 98%. HPLC (hexane–*i*PrOH 10:1): τ 24.92 min. ^{1}H NMR (rotamers ***A*** and ***B*** are observable, ***A*** / ***B*** 1 : 1): *δ* 1.34 (s, 9H, *t*Bu), 1.4–2.6 (br. s, 9H, 9×BH), 2.83–2.89 (m, 1H, H-3B), 2.87 (d, *J* = 14.7 Hz, 0.5H, H-2'B (***A***)), 2.94 (d, *J* = 14.8 Hz, 0.5H, H-2'B (***B***)), 2.95–3.00 (m, 1H, H-3A), 3.05 (d, *J* = 14.8 Hz, 0.5H, H-2'A (***B***)), 3.12 (d, *J* = 14.7 Hz, 0.5H, H-2'A (***A***)), 4.32–4.40 (m, 1H, H-2), 4.97 (s, 0.5H, CH-carborane (***A***)), 5.13 (s, 0.5H, CH-carborane (***B***)), 8.24 (d, 0.5H, *J* = 1.8 Hz, NHCHO (***A***)), 8.32–8.37 (m, 1H, NHCHO (***B***)), 8.55 (br. s, 0.5H, NHCHO (***A***)), 8.69 (d, 0.5H, *J* = 7.7 Hz, NH-Phe (***A***)), 8.76 (d, 0.5H, *J* = 7.8 Hz, NH-Phe (***B***)). ^{13}C NMR (rotamers ***A*** and ***B*** are observable, ***A*** / ***B*** 1 : 1): *δ* 27.45 (3C), 36.82 (***A*** and ***B***), 38.48 (***A*** and ***B***), 54.26 (***A*** and ***B***), 59.90 (***A***), 60.78 (***B***), 71.02 (***A***), 71.25 (***B***), 80.95 (***A***), 80.99 (***B***), 126.57 (***A*** and ***B***), 128.19 (2C), 129.11 (2C), 136.80 (***A*** and ***B***), 165.28 (***A***), 165.58 (***A***), 165.59 (***B***), 166.60 (***B***), 170.04 (***A***), 170.10 (***B***). HRMS (ESI) *m*/*z* calcd. for $C_{18}H_{33}{}^{10}B_2{}^{11}B_8N_2O_4$ $[M + H]^+$ 449.3438; found 449.3443.



(*S*,*R*$_P$)-*tert*-Butyl *N*-(3-formamido-1,2-dicarba-*closo*-dodecaboran-1-yl)acetyl-phenylalaninate [(*S*,*R*$_P$)-3f]. Yield 0.080 g (27.7%) after preparative HPLC (hexane–*i*PrOH 8:1, τ 24-30 min). Colorless solid, mp 127–130 °C. $[\alpha]_D^{20}$ +21.8 (*c* 0.42, CH_2Cl_2). *De* > 98%. HPLC (hexane–*i*PrOH 10:1): τ 17.47 min. ^{1}H NMR (rotamers ***A*** and ***B*** are observable, ***A*** / ***B*** 1 : 1): *δ* 1.34 (s, 9 H, *t*Bu), 1.5–2.6 (br. s, 9 H, 9×BH); 2.83–3.02 (m, 3 H, 2×H-3 and H-2'B), 3.02 (d, 0.5 H, *J* = 14.7 Hz, H-2'A (***A***)), 3.10 (d, 0.5 H, *J* = 14.7 Hz, H-2'A (***B***)), 4.36–4.42 (m, 1 H, H-2); 4.93 (s, 0.5 H, CH-carborane (***A***)), 5.12 (s, 0.5 H, CH-carborane (***B***)), 8.26 (br. s, 0.5 H, NHCHO (***A***)), 8.32–8.37 (m, 1 H, NHCHO (***B***)), 8.56 (br. s, 0.5 H, NHCHO (***A***)), 8.66 (d, 0.5 H, *J* = 7.8 Hz, NH-Phe (***A***)), 8.74 (d, 0.5 H, *J* = 7.7 Hz, NH-Phe (***B***)). ^{13}C NMR (rotamers ***A*** and ***B*** are observable, ***A*** / ***B*** 1 : 1): *δ* 27.47 (3C), 36.85 (***A***), 36.92 (***B***), 38.52 (***A*** and ***B***), 54.02 (***A***), 54.07 (***B***), 59.86 (***A***), 60.87 (***B***), 71.00 (***A***), 71.21 (***B***), 81.00 (***A***), 81.03 (***B***), 126.57 (***A*** and

B), 128.19 (2C), 129.14 (2C), 136.75, 165.30 (***A***), 165.53, 166.63 (***B***), 170.06. HRMS (ESI) *m*/*z* calcd. for $C_{18}H_{33}{}^{10}B_2{}^{11}B_8N_2O_4$ $[M + H]^+$ 449.3438; found 449.3444.

2. Copies of NMR spectra

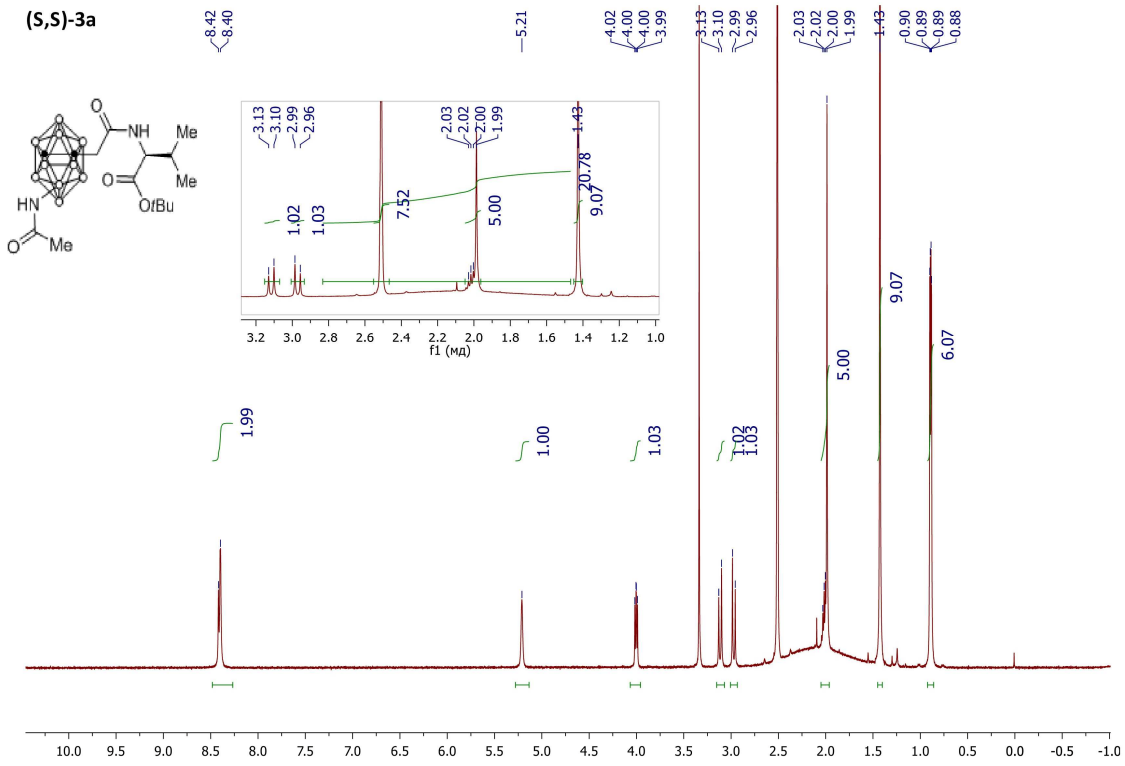


Figure S1. ^{1}H NMR spectrum of compound (S,S_P)-**3a** (DMSO-d_6, 25 °C, 500 MHz)

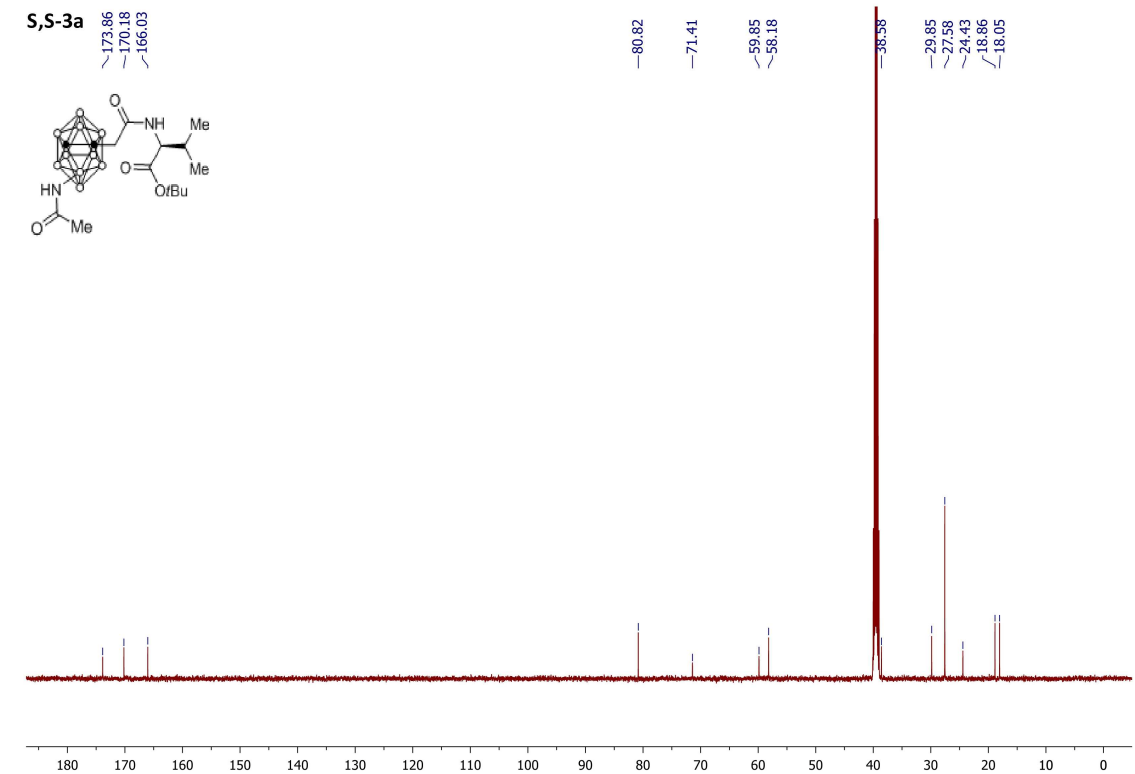


Figure S2. ^{13}C NMR spectrum of compound (S,S_P)-**3a** (DMSO-d_6, 25 °C, 125 MHz)

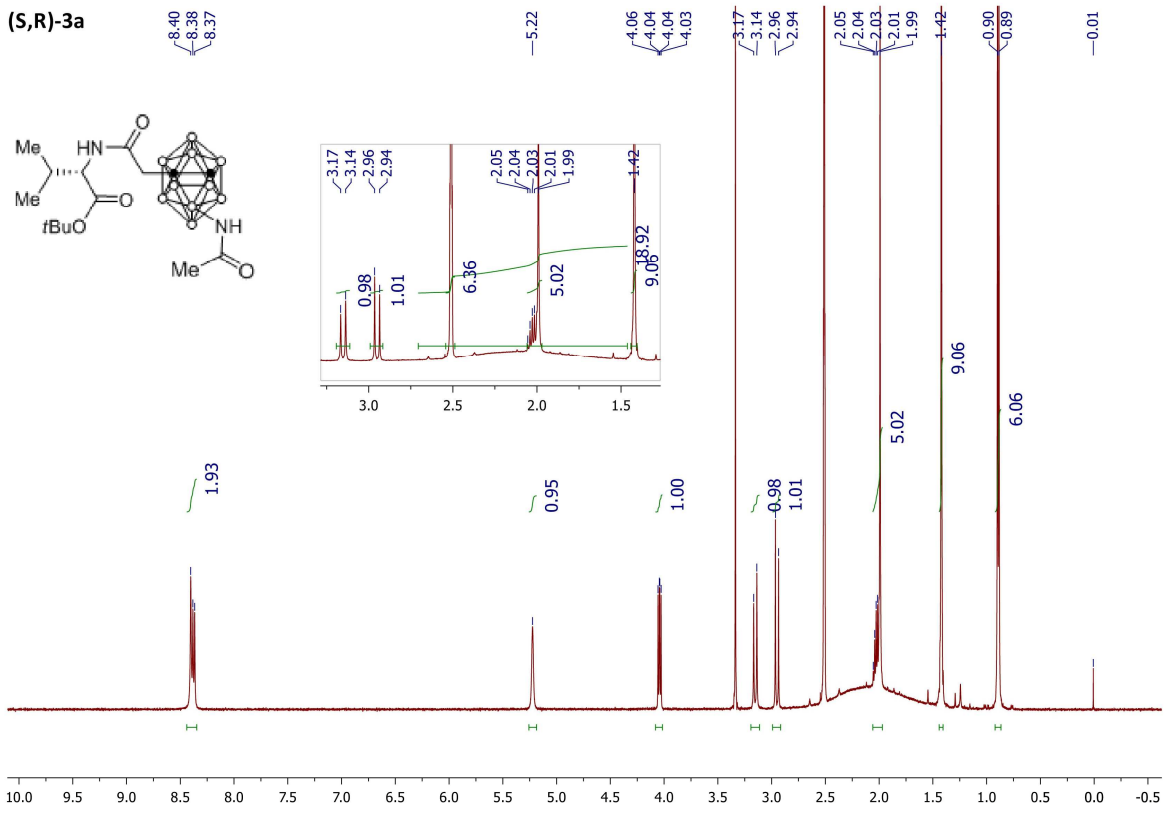


Figure S3. ^{1}H NMR spectrum of compound (S,R_P)-**3a** (DMSO-d_6, 25 °C, 500 MHz)

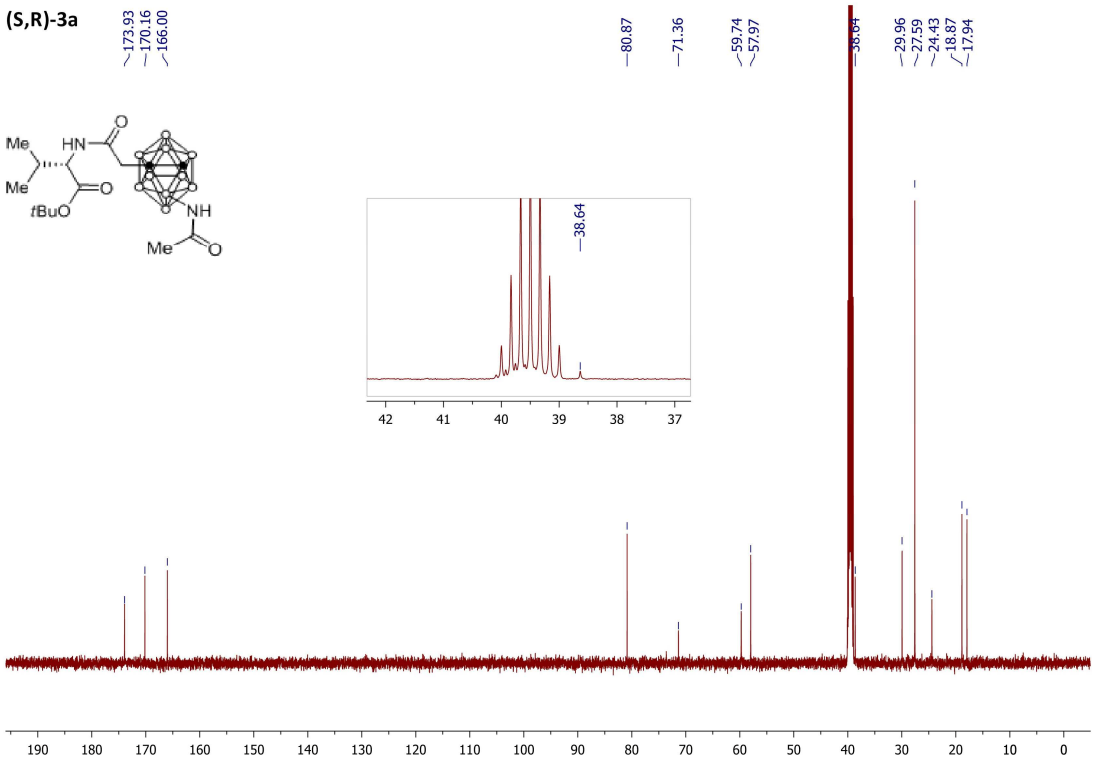


Figure S4. ^{13}C NMR spectrum of compound (S,R_P)-**3a** (DMSO-d_6, 25 °C, 125 MHz)

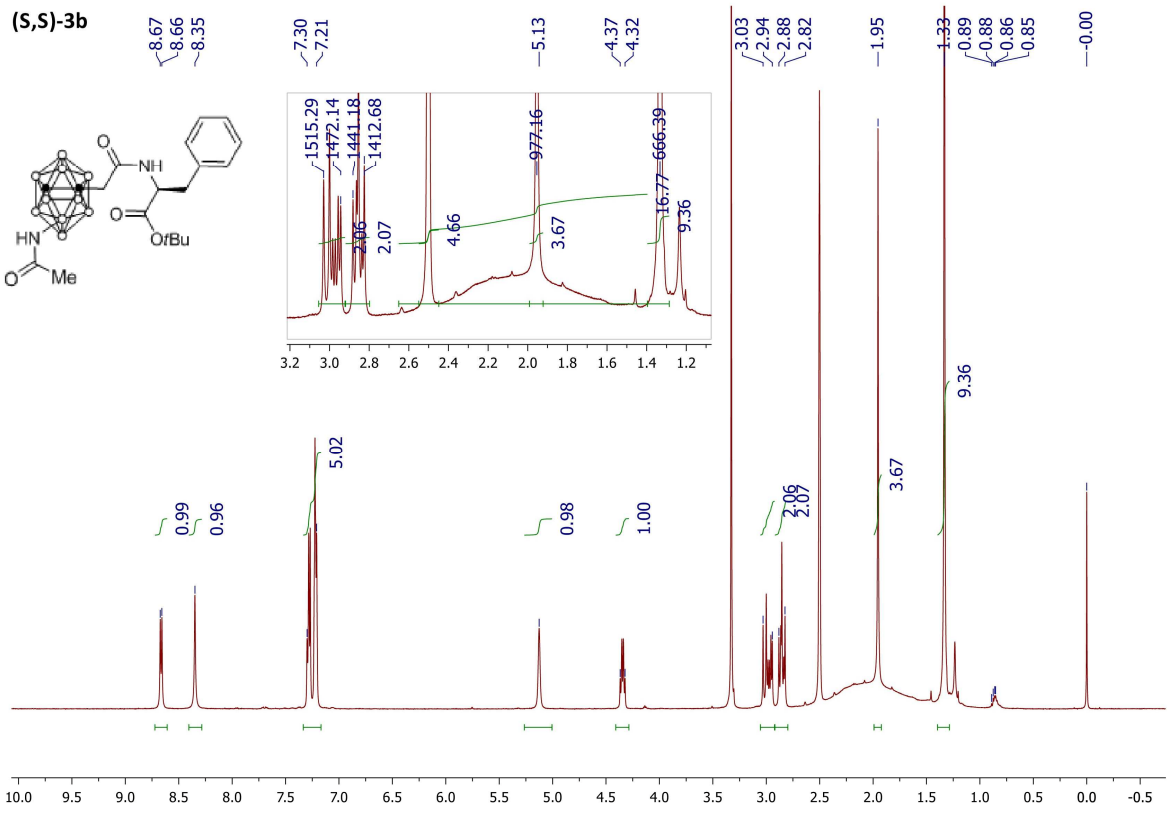


Figure S5. ^{1}H NMR spectrum of compound (S,S_P)-**3b** (DMSO-d_6, 25 °C, 500 MHz)

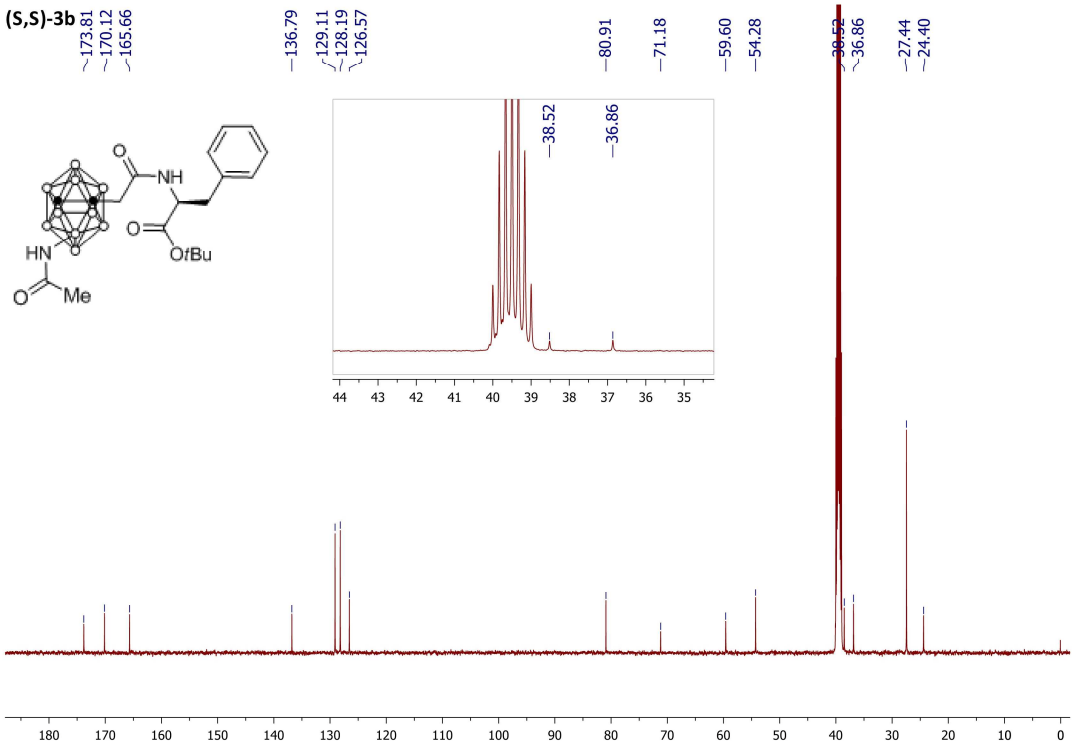


Figure S6. ^{13}C NMR spectrum of compound (S,S_P)-**3b** (DMSO-d_6, 25 °C, 125 MHz)

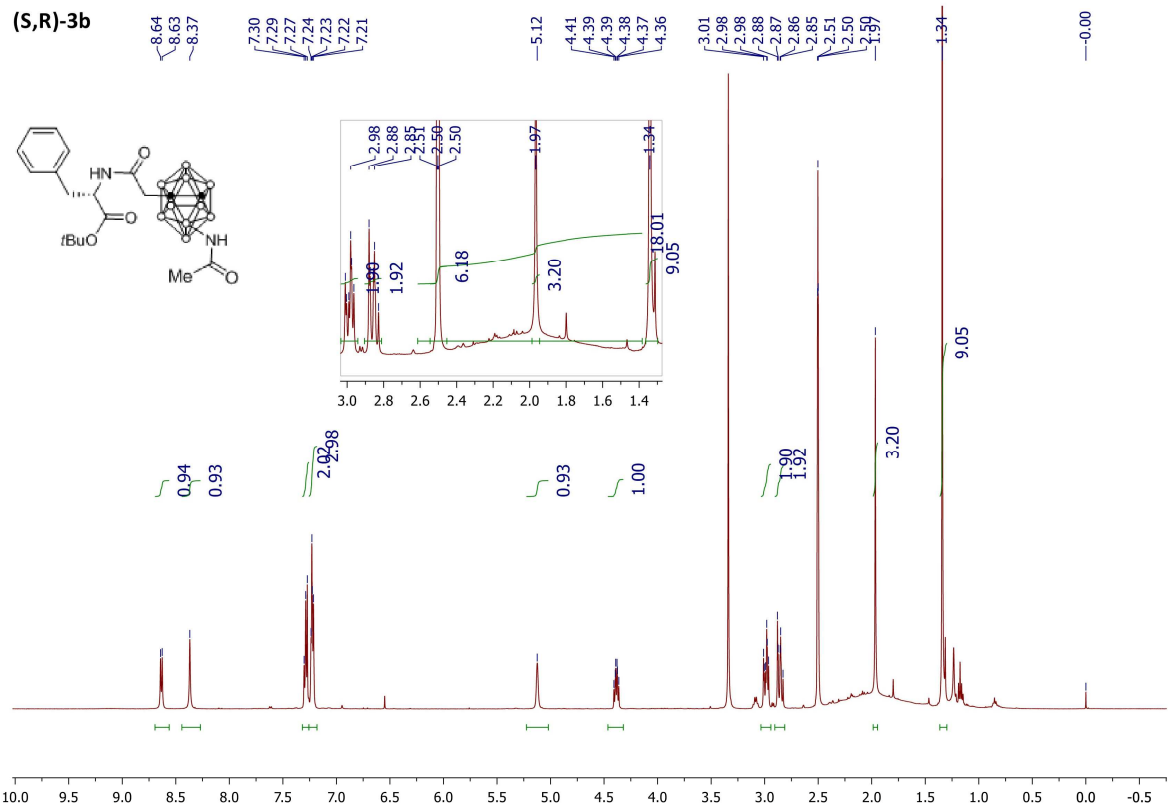


Figure S7. ^{1}H NMR spectrum of compound (S,R_P)-**3b** (DMSO-d_6, 25 °C, 500 MHz)

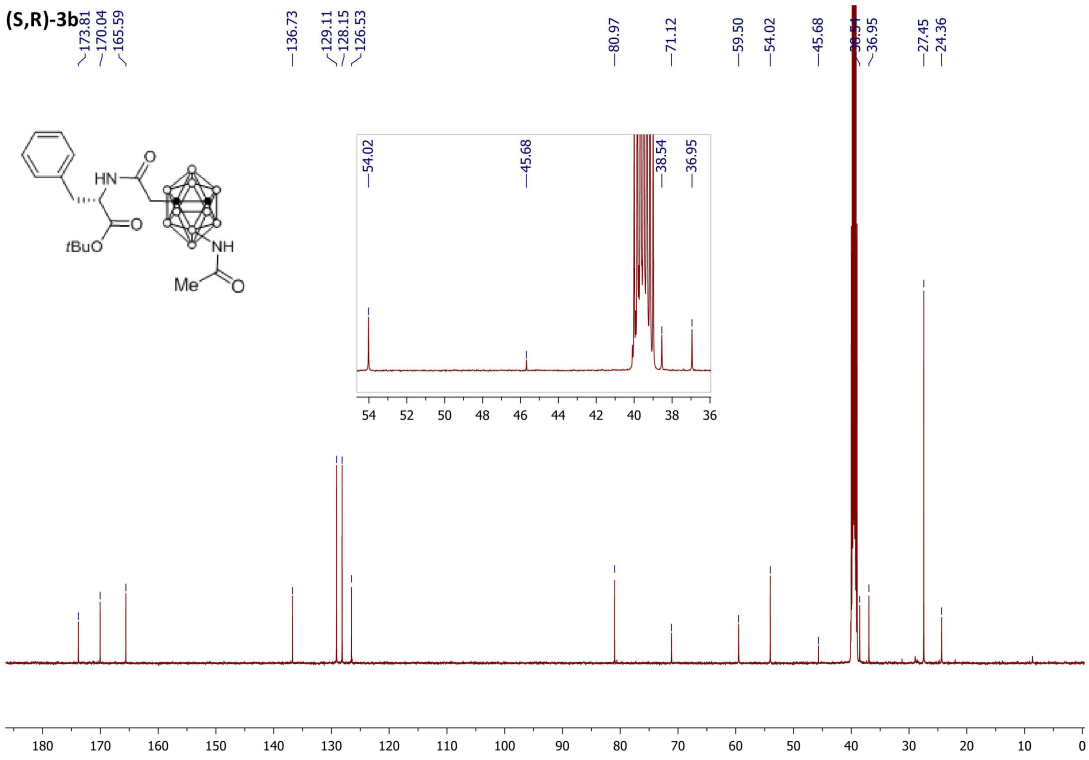


Figure S8. ^{13}C NMR spectrum of compound (S,R_P)-**3b** (DMSO-d_6, 25 °C, 125 MHz)

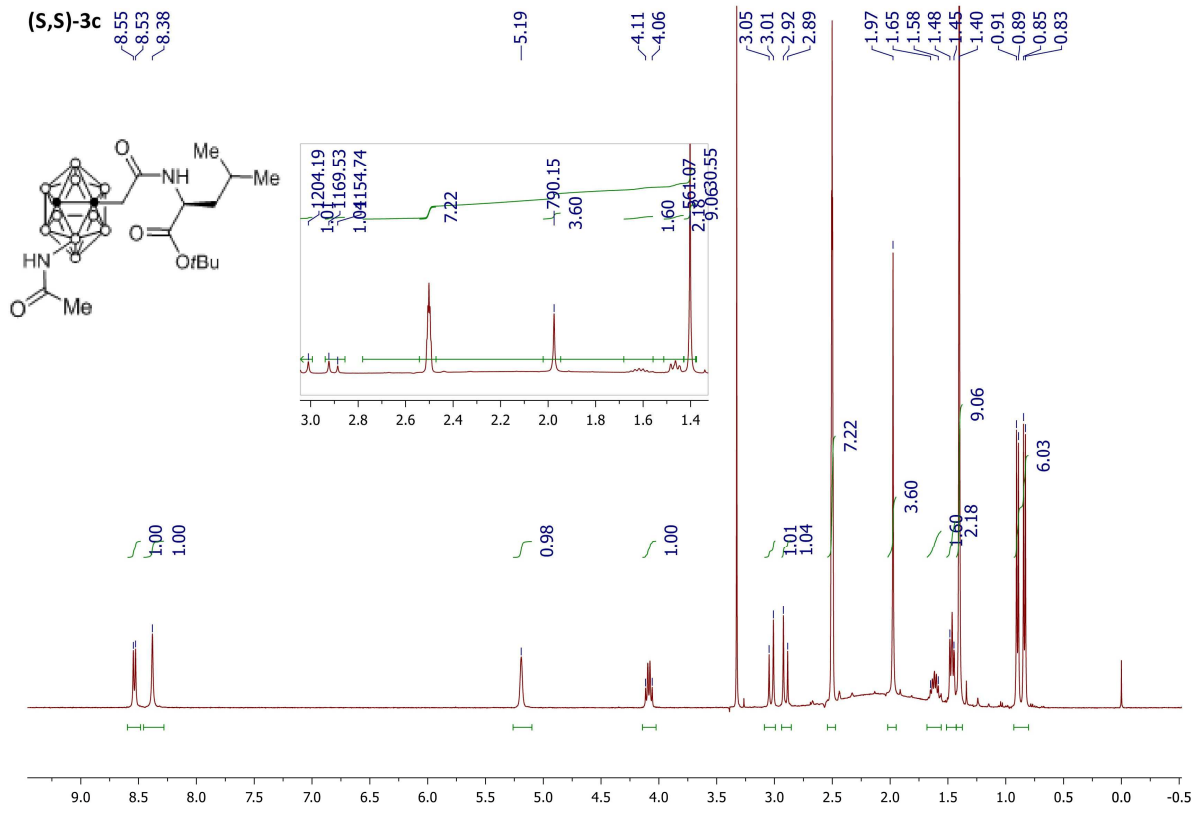


Figure S9. ^{1}H NMR spectrum of compound (S,S_P)-**3c** (DMSO-d_6, 25 °C, 500 MHz)

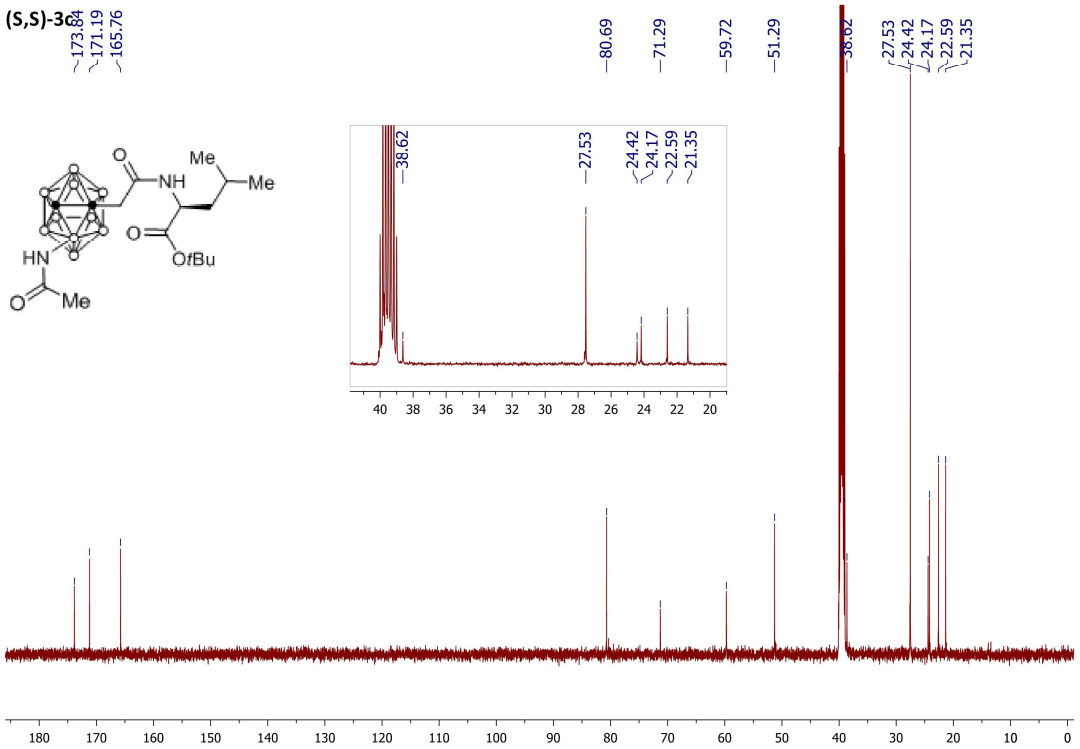


Figure S10. ^{13}C NMR spectrum of compound (S,S_P)-**3c** (DMSO-d_6, 25 °C, 125 MHz)

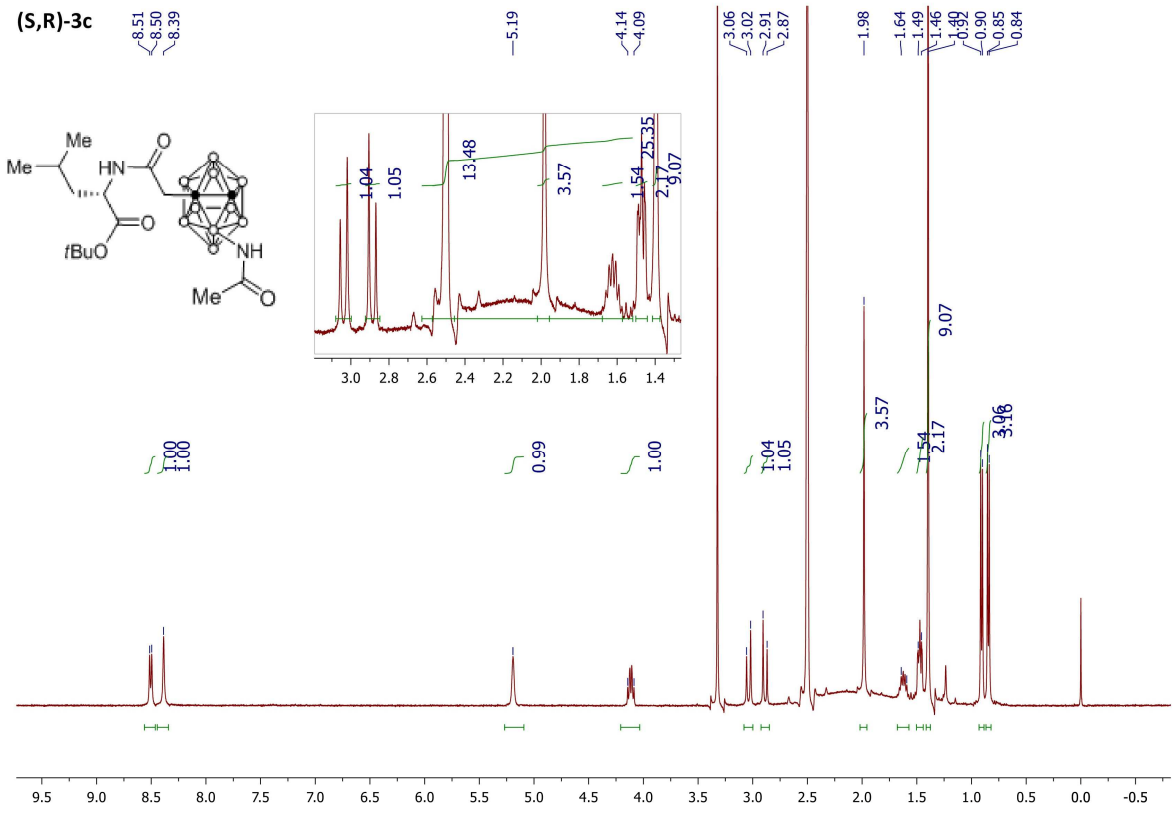


Figure S11. ^{1}H NMR spectrum of compound (S,R_P)-**3c** (DMSO-d_6, 25 °C, 500 MHz)

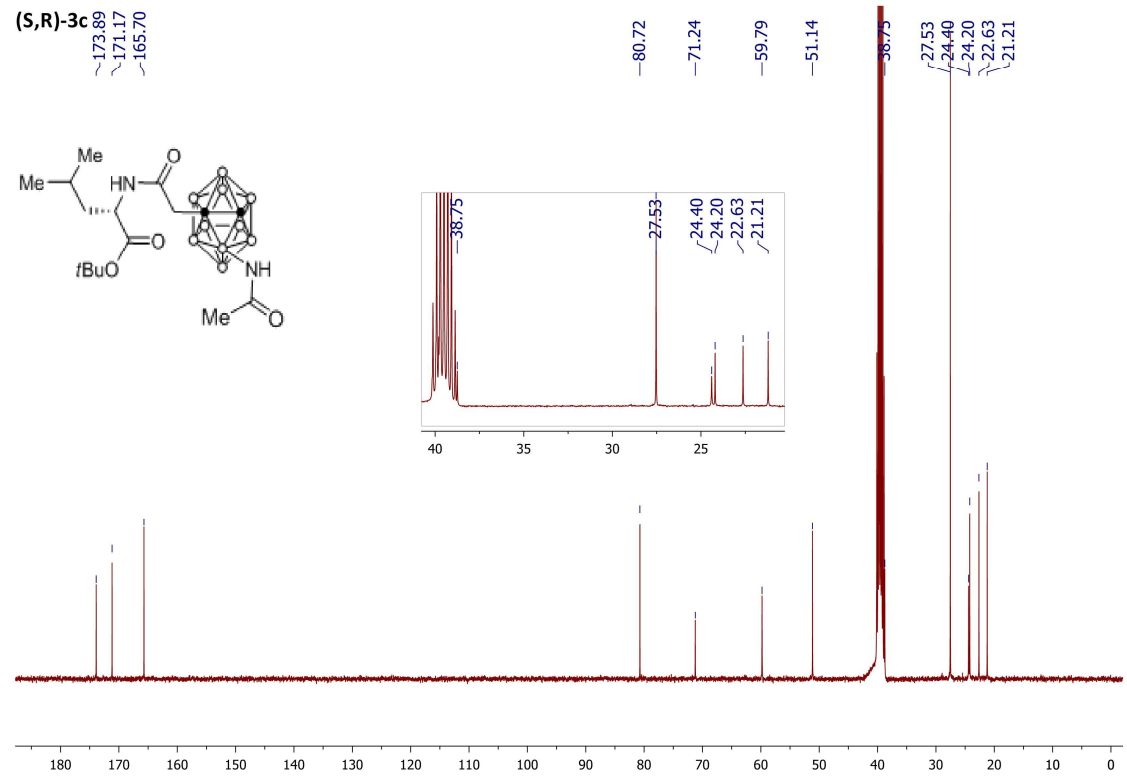


Figure S12. ^{13}C NMR spectrum of compound (*S*,*R*$_P$)-**3c** (DMSO-*d*$_6$, 25 °C, 125 MHz)

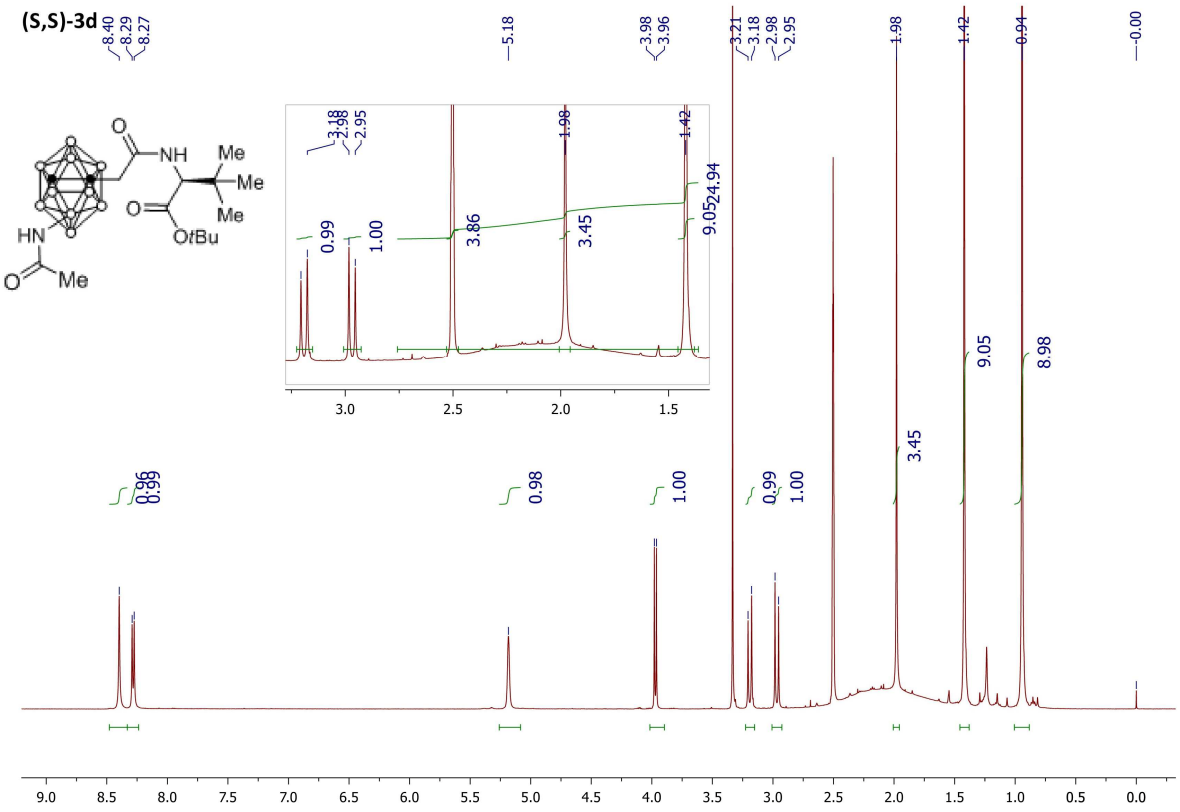


Figure S13. ^{1}H NMR spectrum of compound (*S*,*S*$_P$)-**3d** (DMSO-*d*$_6$, 25 °C, 500 MHz)

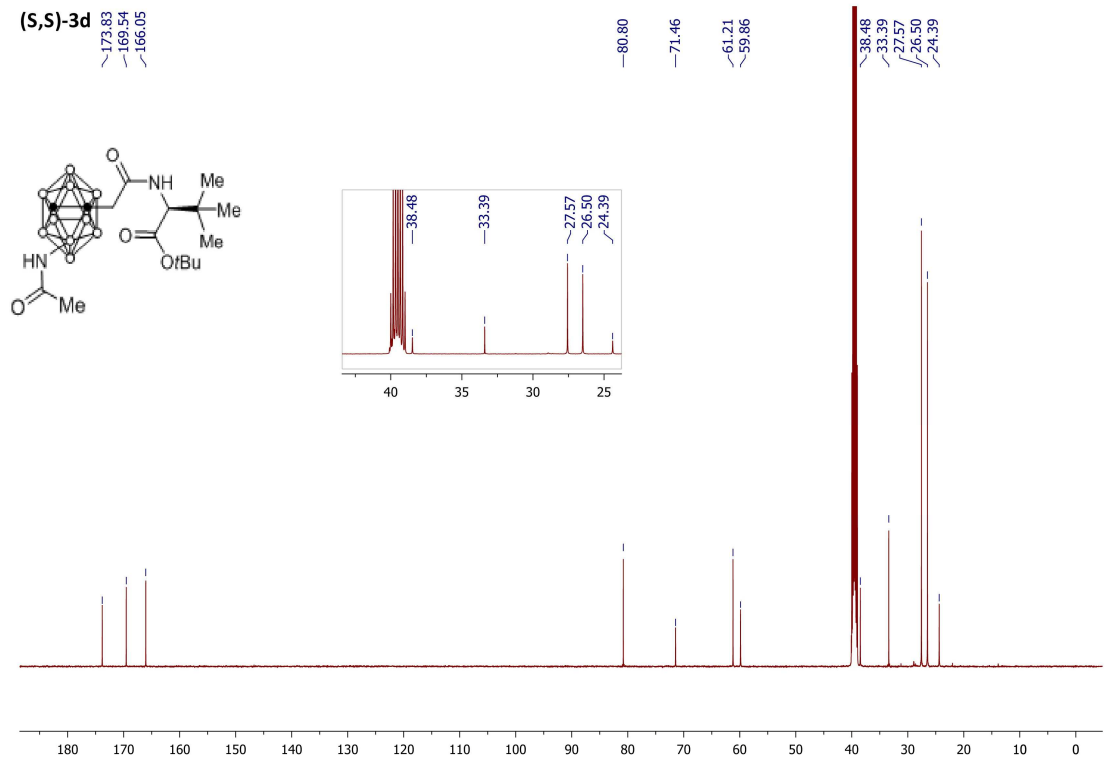


Figure S14. ^{13}C NMR spectrum of compound (*S*,*S*$_P$)-**3d** (DMSO-*d*$_6$, 25 °C, 125 MHz)

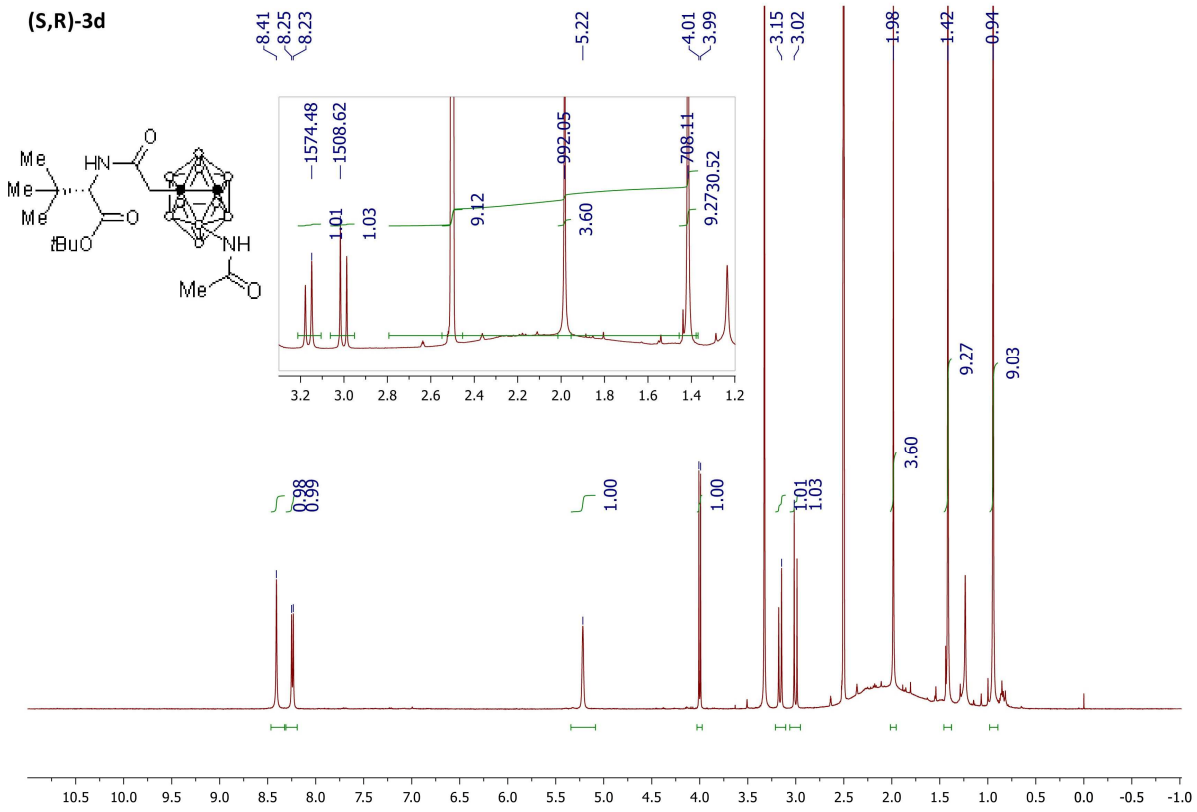


Figure S15. ^{1}H NMR spectrum of compound (*S*,*R*$_P$)-**3d** (DMSO-*d*$_6$, 25 °C, 500 MHz)

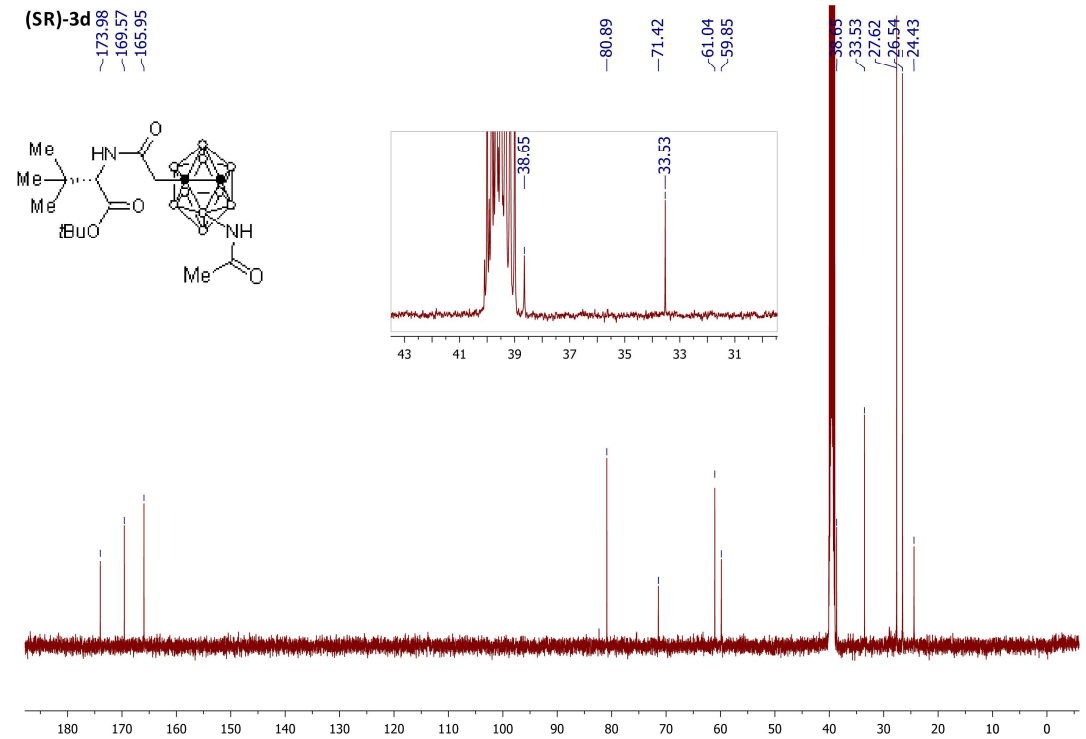


Figure S16. ^{13}C NMR spectrum of compound (*S*,*R*$_P$)-**3d** (DMSO-*d*$_6$, 25 °C, 125 MHz)

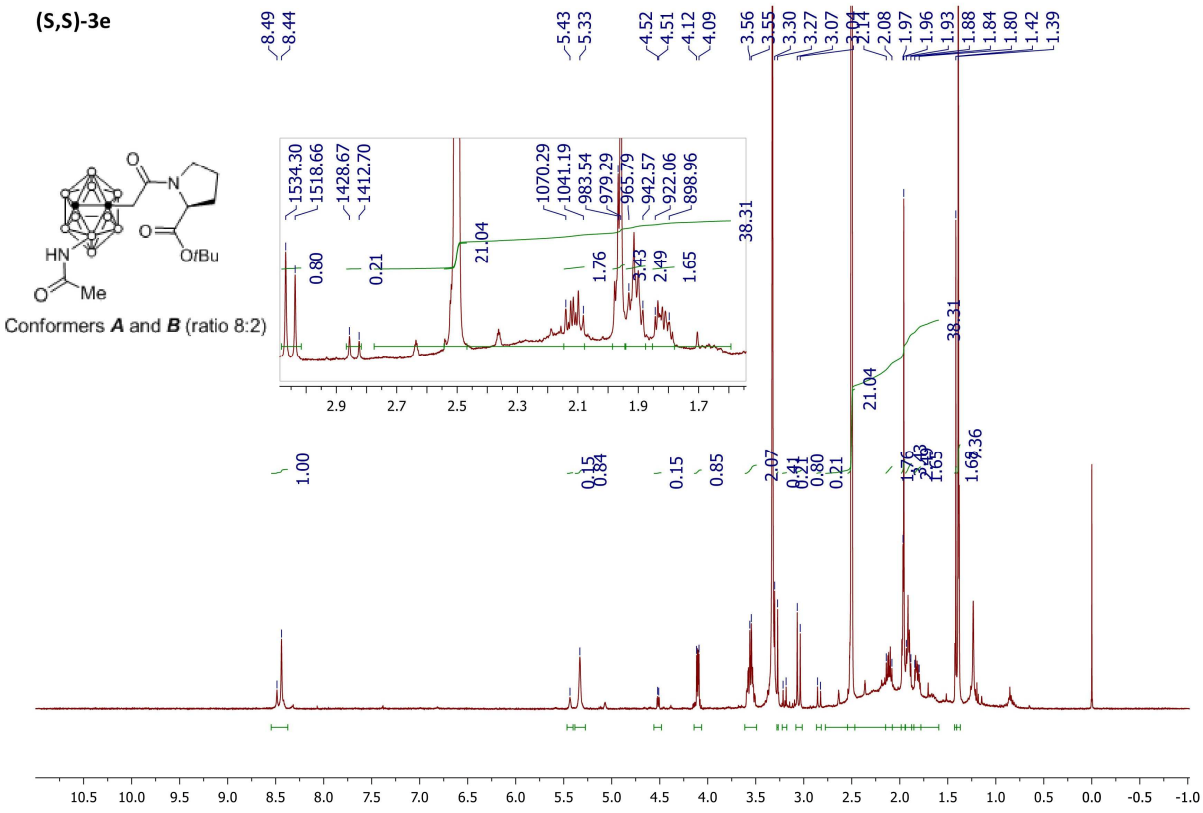


Figure S17. ^{1}H NMR spectrum of compound (S,S_P)-**3e** (DMSO-d_6, 25 °C, 500 MHz)

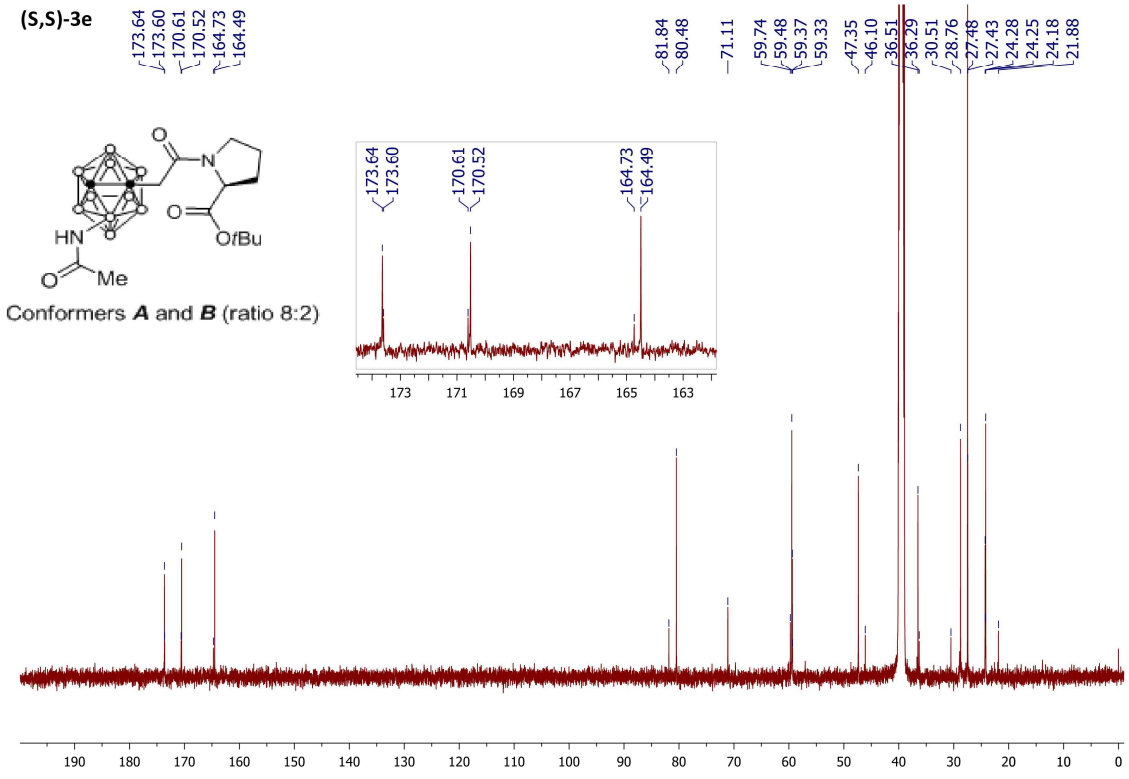


Figure S18. ^{13}C NMR spectrum of compound (S,S_P)-**3e** (DMSO-d_6, 25 °C, 125 MHz)

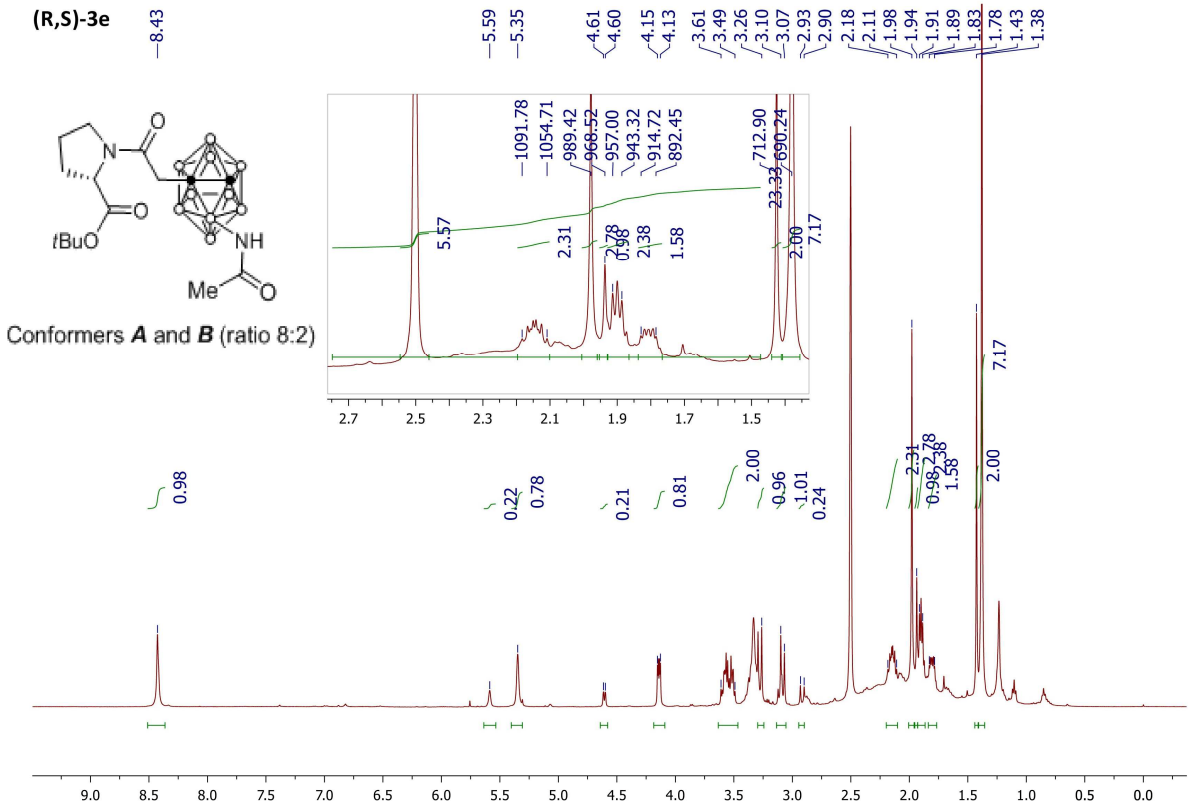


Figure S19. ^{1}H NMR spectrum of compound (S,R_P)-**3e** (DMSO-d_6, 25 °C, 500 MHz)

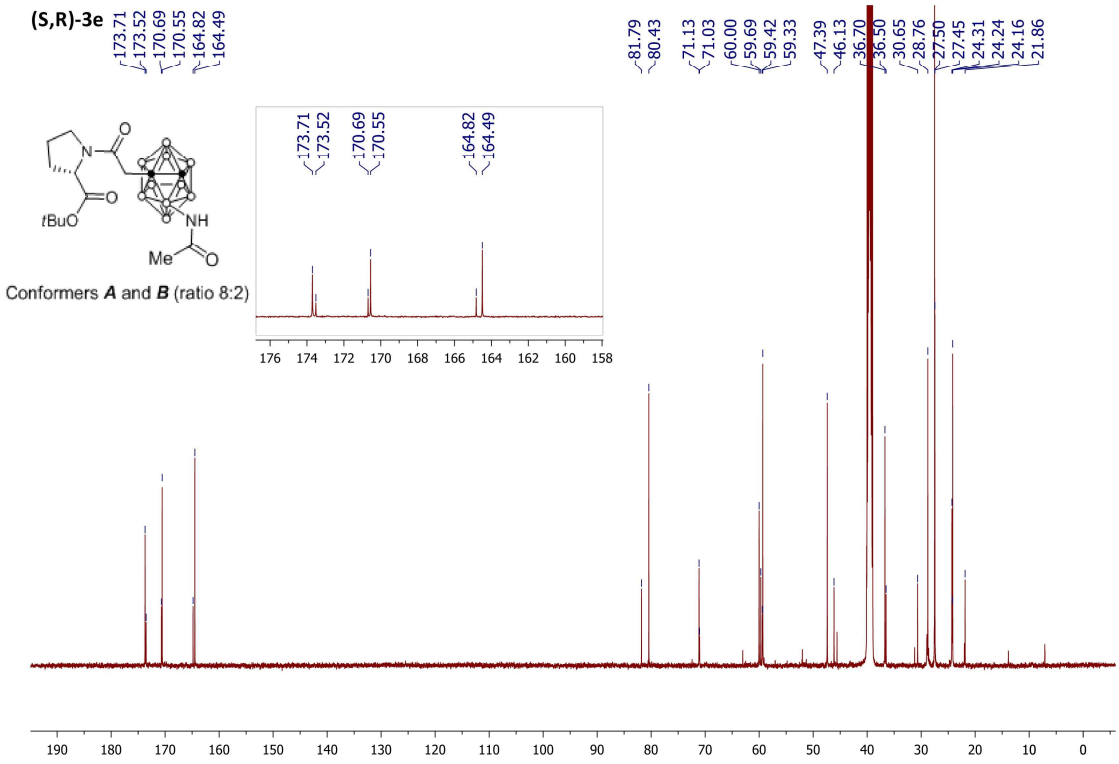


Figure S20. ^{13}C NMR spectrum of compound (S,R_P)-**3e** (DMSO-d_6, 25 °C, 125 MHz)

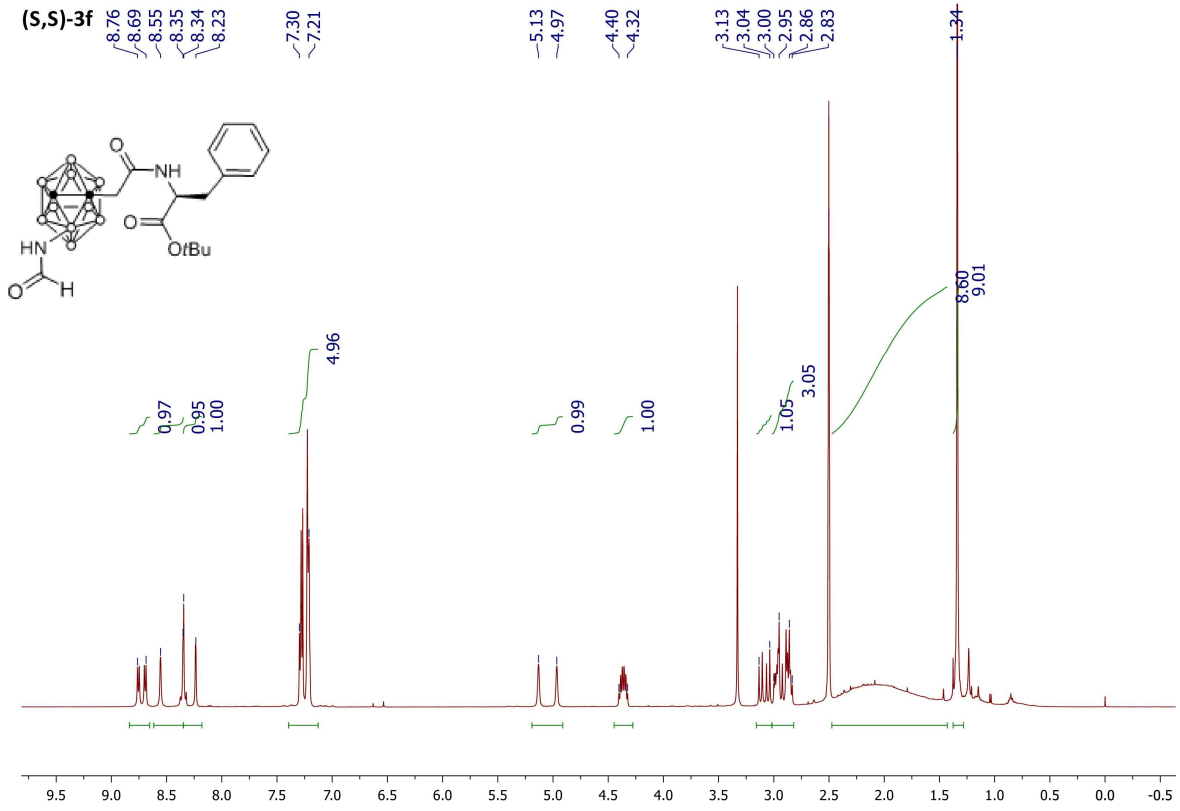


Figure S21. ^{1}H NMR spectrum of compound (S,S_P)-**3f** (DMSO-d_6, 25 °C, 500 MHz)

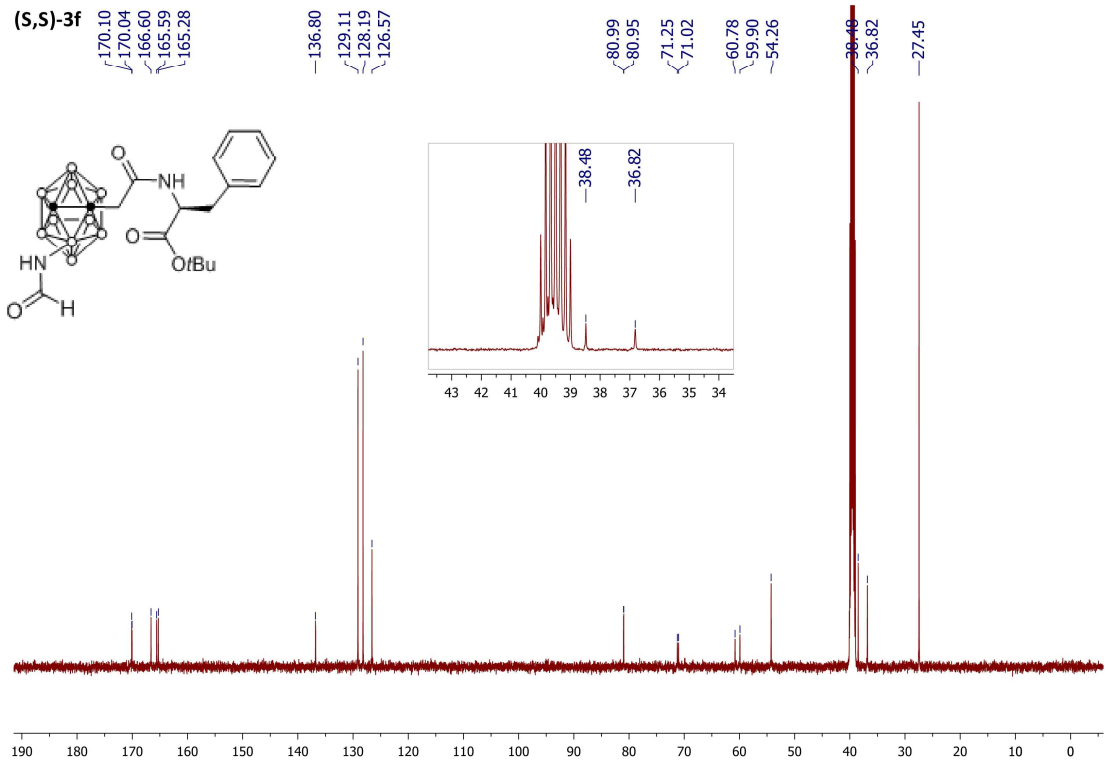


Figure S22. ^{13}C NMR spectrum of compound (S,S_P)-**3f** (DMSO-d_6, 25 °C, 125 MHz)

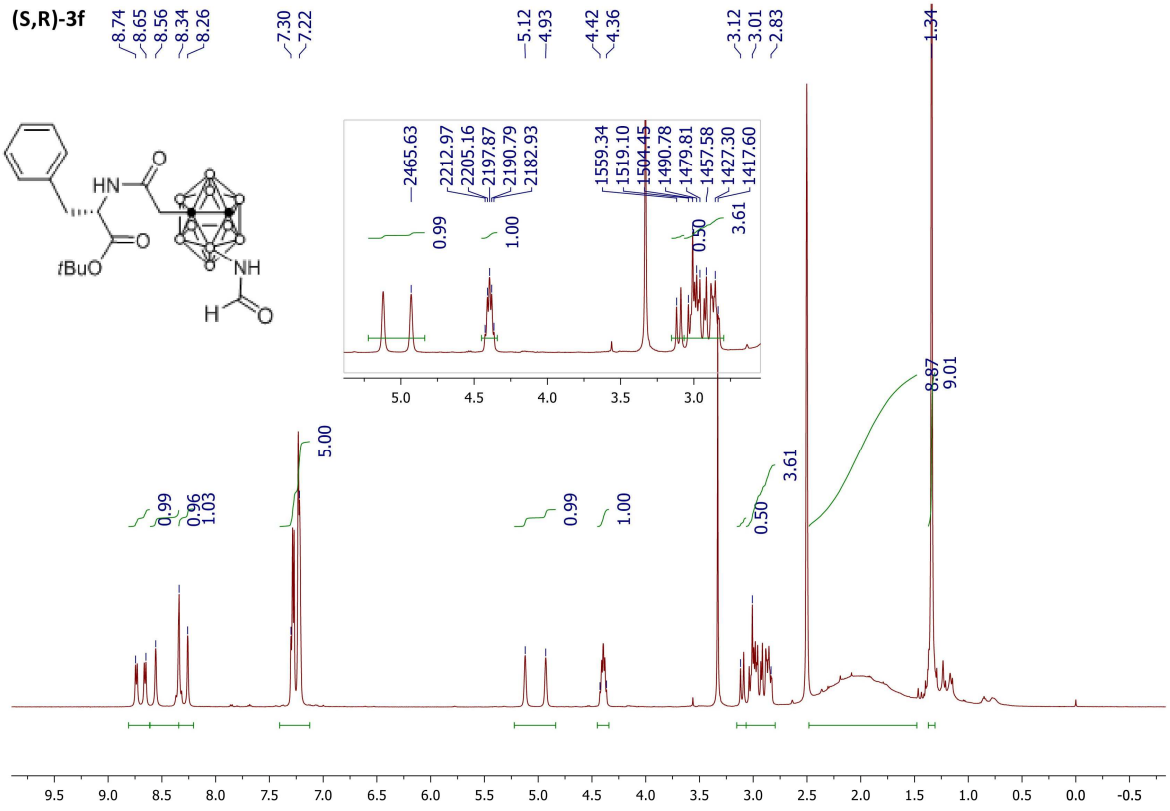


Figure S23. ^{1}H NMR spectrum of compound (S,R_P)-**3f** (DMSO-d_6, 25 °C, 500 MHz)

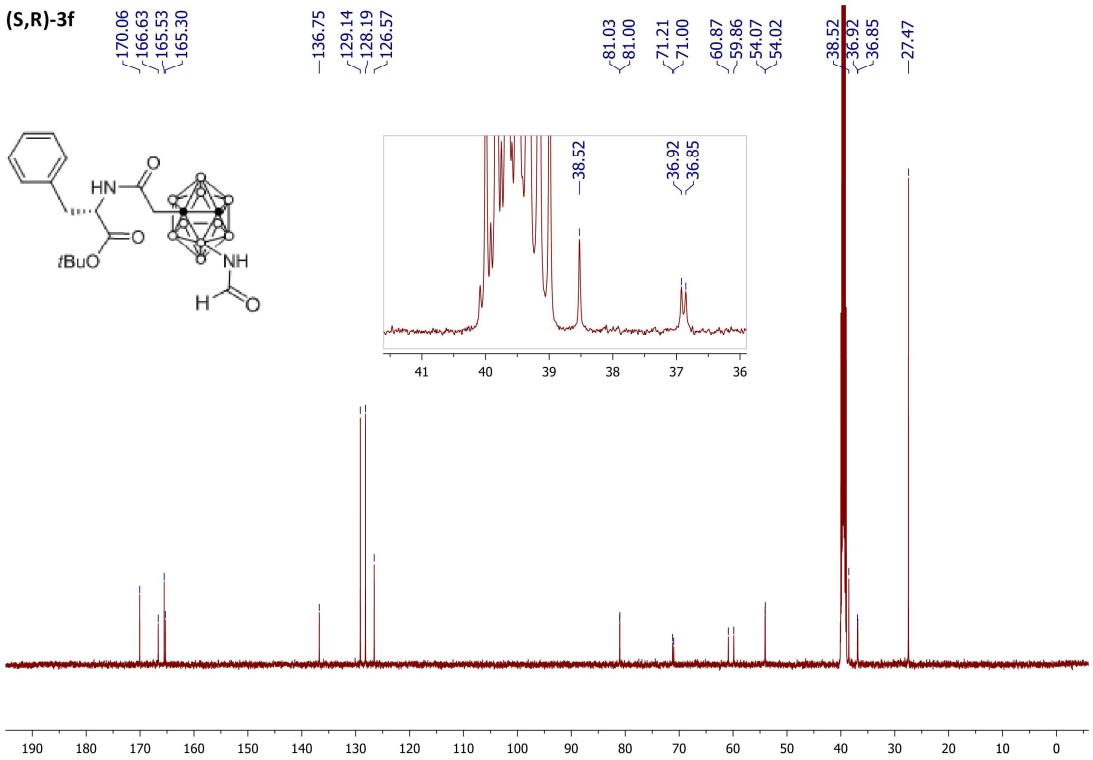


Figure S24. ^{13}C NMR spectrum of compound (S,R_P)-**3f** (DMSO-d_6, 25 °C, 125 MHz)

3. Crystallographic Data and Optical Microscopy

X-Ray Diffraction Study of Compounds 3a-f was performed on an Xcalibur-3 X-ray diffractometer with a CCD detector according to the standard procedure (Cu*K*α radiation, graphite monochromator, ω-scanning). Single crystals of compounds **3a-f** were obtained by spontaneous crystallization from water–methanol or benzene–acetone mixtures. An empirical absorption correction was applied. The structures were solved by direct method in the SHELXS program and refined by full-matrix least-squares on F^2 in the SHELXL program.[S6] All non-hydrogen atoms were refined in anisotropic approximation (isotropically for hydrogen atoms). The hydrogen atom positions were partially solved and refined independently, and partially included in the refinement according to the "rider" model with dependent thermal parameters. The general crystal data and results of the refinements are presented in Tables S1 and S2. The X-ray structural analysis data were deposited with the Cambridge Crystallographic Data Centre (CCDC Nos. 661110 [(*R*,R_P)-**3a**], 1839003 [(*S*,R_P)-**3a**], 1839004 [(*S*,R_P)-**3b**], 1839005 [(*S*,R_P)-**3d**], 1839006 [(*S*,S_P)-**3b**], 1839007 [(*S*,S_P)-**3c**], 1839008 [(*S*,S_P)-**3d**], 1839009 [(*S*,S_P)-**3e**], and 1839010 [(*S*,S_P)-**3f**]). Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44(0) 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].

Molecular structures of the selected compounds are shown in Figure 25.

We visualized crystals of compounds **3a-f** by an Olympus BX-61 optical microscope (Japan) using reflected light mode with objective 5X.

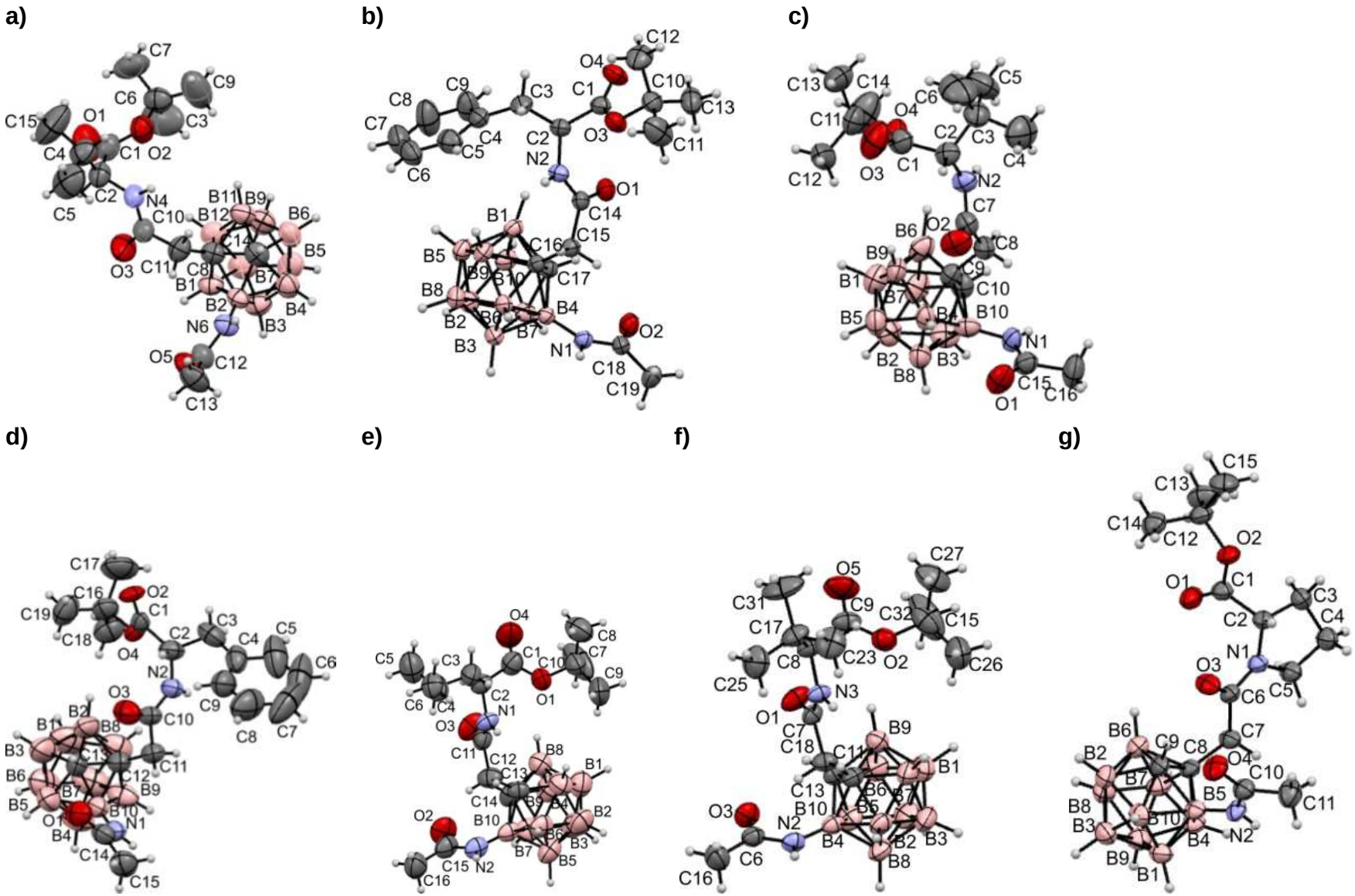


Figure 25. Structures of compounds (**a**) (*S*,*R*$_P$)-**3a**, (**b**) (*S*,*R*$_P$)-**3b**, (**c**) (*S*,*R*$_P$)-**3d**, (**d**) (*S*,*S*$_P$)-**3b**, (**e**) (*S*,*S*$_P$)-**3c**, (**f**) (*S*,*S*$_P$)-**3d**, and (**g**) (*S*,*R*$_P$)-**3e** (thermal ellipsoids of 50% probability).

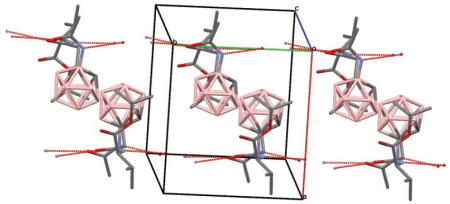
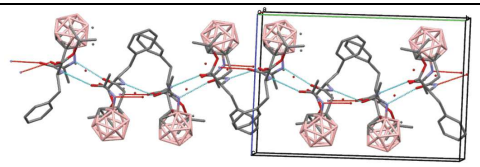
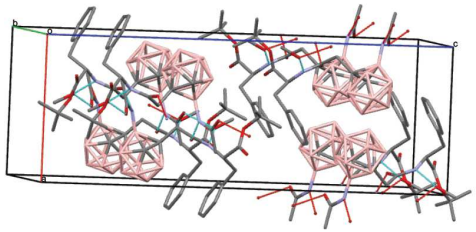
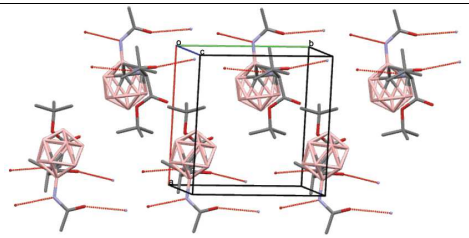
Table S1. Crystallographic parameters of single crystals of monoclinic system

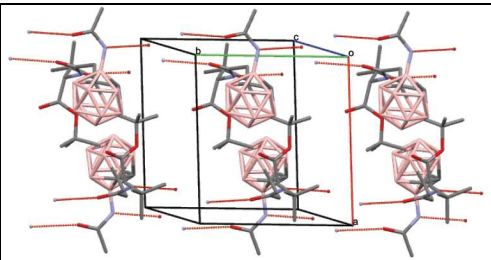
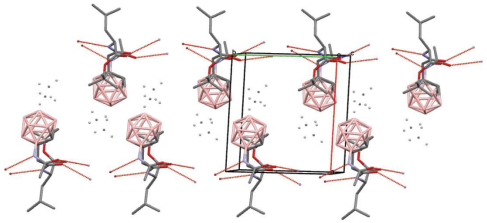
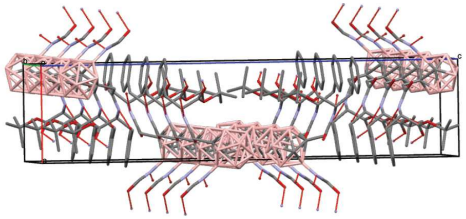
	(*S*,R_P)-**3a**	(*S*,S_P)-**3b**	(*S*,S_P)-**3c**	(*S*,S_P)-**3d**	(*S*,R_P)-**3d**
Solvent for crystallization	C_6H_{14}–Me_2CO 85:15	MeOH–H_2O 1:3	MeOH–H_2O 5:1	MeOH–H_2O 4:1	MeOH
Crystal size, mm	0.25×0.20×0.15	0.48×0.22×0.04	0.41×0.27×0.04	0.40×0.30×0.20	0.40×0.30×0.20
Space group	$P2_1$	$P2_1$	$P2_1$	$P2_1$	$P2_1$
Empirical formula	$C_{15}H_{34}B_{10}N_2O_4$	$C_{19}H_{34}B_{10}N_2O_4$	$C_{16}H_{36}B_{10}N_2O_4$	$C_{16}H_{36}B_{10}N_2O_4$	$C_{16}H_{36}B_{10}N_2O_4$
Formula weight	414.54	462.58	428.57	428.57	428.57
Unit cell dimensions					
a, Å	10.325(10)	12.565(11)	11.118(7)	10.388(11)	10.440(4)
b, Å	9.558(6)	17.879(6)	9.389(4)	9.372(10)	9.605(5)
c, Å	12.703(8)	13.048(5)	13.347(7)	13.622(10)	13.592(8)
α, ^{o}	90.00	90.00	90.00	90.00	90.00
β, ^{o}	90.73(7)	112.99(6)	109.56(5)	107.01(8)	102.89(4)
γ, ^{o}	90.00	90.00	90.00	90.00	90.00
Volume, Å^3; Z	1253.5(16); 2	2698(3); 4	1313.0(12); 2	1268(2); 2	1328.7(12); 2
D_{calc}, g/cm^3	1.098	1.139	1.084	1.122	1.071
Absorption coefficient μ, mm^{-1}	0.534	0.550	0.524	0.542	0.518
F(000)	440	976	456	456	456
Θ range for data collection	3.48 to 65.95 ^{o}	3.68 to 67.74^o	3.51 to 65.80^o	3.39 to 67.12^o	3.34 to 65.68^o
Limiting indices	-12 < h < 12, -10 < k < 10, -15 < l < 12	−14 < h < 13, −21 < k < 21, −15 < l < 15	−12 < h < 13, −11 < k < 9, −15 < l < 15	−12 < h < 11, −11 < k < 9, −14 < l < 16	−12 < h < 12, −10 < k < 11, −15 < l < 16
Reflections collected	11070	25355	10209	16531	16411
Independent reflections	2208 (R_{int} = 0.0982)	4870 (R_{int} = 0.0776)	2354 (R_{int}= 0.0648)	3928 (R_{int}= 0.0605)	2440 (R_{int}= 0.0978)
Completeness (to θ)	94.8% (65.95°)	96.3 % (67.74^o)	96.9 % (65.80^o)	99.1 % (67.12^o)	99.7 % (65.68^o)
Data / restraints / parameters	2208 / 1 / 86	4870 / 121 / 720	2354 / 31 / 362	3928 / 1 / 338	2440 / 1 / 345
Goodness-of-fit on F^2	1.005	1.003	1.002	1.003	1.001
Final R indices [$I > 2\sigma(I)$]		R_1 = 0.0512, wR_2 = 0.1033	R_1 = 0.0583, wR_2 = 0.1254	R_1 = 0.0402, wR_2 = 0.0990	R_1 = 0.0529, wR_2 = 0.1020
R indices (all data)	R_1 = 0.1223, wR_2 = 0.1196	R_1 = 0.0979, wR_2 = 0.1117	R_1 = 0.0995, wR_2 = 0.1345	R_1 = 0.0464, wR_2 = 0.1008	R_1 = 0.0879, wR_2 = 0.1064
Absolute structure parameter	0	0	0	0.22(19)	0
Largest diff. peak and hole, ēÅ^{-3}	0.182 / −0.190	0.126 / −0.169	0.184 / −0.200	0.135 / −0.138	0.141 / −0.225

Table S2. Crystallographic parameters of single crystals of orthorhombic system

	(*S*,*R*$_P$)-**3b**	(*S*,*S*$_P$)-**3e**	(*S*,*S*$_P$)-**3f**
Solvent for crystallization	MeOH–H_2O 1:3	MeOH–H_2O 20:1	MeOH–H_2O 6:1
Crystal size, mm	0.48×0.39×0.27	0.25×0.20×0.15	0.28×0.13×0.04
Space group	$P2_12_12_1$	$P2_12_12_1$	$P22_12_1$
Empirical formula	$C_{20}H_{38}B_{10}N_2O_5$	$C_{15}H_{32}B_{10}N_2O_4$	$C_{18}H_{32}B_{10}N_2O_4$
Formula weight	494.62	412.53	448.71
Unit cell dimensions			
a, Å	9.797(5)	9.994(6)	7.376(3)
b, Å	10.754(4)	10.816(4)	11.388(3)
c, Å	27.432(13)	21.367(15)	31.773(17)
α, ^{o}	90	90.00	90
β, ^{o}	90	90.00	90
γ, ^{o}	90	90.00	90
Volume, Å^3; Z	2890(2); 4	2310(2); 4	2669(2); 4
D_{calc}, g/cm^3	1.137	1.186	1.1162
Absorption coefficient μ, mm^{-1}	0.568	0.580	0.542
F(000)	1048	872	943.8
Θ range for data collection	3.22 to 65.43^o	4.14 to 66.37^o	2.78 to 68.14
Limiting indices	−11 < h < 11, −11 < k < 12, −32 < l < 31	−11 < h < 11, −10 < k < 12, −25 < l < 25	−8 ≤ h ≤ 7, −13 ≤ k ≤ 12, −30 ≤ l ≤ 38
Reflections collected	22714	17713	10617
Independent reflections	4884 (R_{int}= 0.0515)	3937 (R_{int}= 0.0662)	2637 (R_{int}= 0.0643)
Completeness (to θ)	99.7 % (65.43^o)	96.9 % (65.80^o)	95.4 % (66.0^o)
Data / restraints / parameters	4884 / 0 / 389	3937 / 0 / 324	2637/0/309
Goodness-of-fit on F^2	1.007	1.005	1.037
Final *R* indices [$I > 2\sigma(I)$]	R_1 = 0.0428, wR_2 = 0.0973	R_1 = 0.0404, wR_2 = 0.0839	R_1 = 0.0396, wR_2 = 0.0734
R indices (all data)	R_1 = 0.0469, wR_2 = 0.0987	R_1 = 0.0525, wR_2 = 0.0857	R_1 = 0.0895, wR_2 = 0.0775
Absolute structure parameter	0.06(16)	−0.2(2)	0
Largest diff. peak and hole, ēÅ^{-3}	0.176 / −0.206	0.148 / −0.223	0.25 / −0.32

Table S3. Order of elemental lattice and parameters of intermolecular hydrogen bonds of single crystals of compounds 3a-d,f

Compound	General view of the unit cell	Parameters of intermolecular hydrogen bonds					
		Donor of hydrogen bond (D)	Acceptor of hydrogen bond (A)	Interatomic distances, Å			DHA angle, degrees
				D–H	H···A	D···A	
(*S*,R_P)-**3a**		N2-H2A	O4 [−x, y−½, −z]	0.860	2.016	2.825	156.50
		N1-H1A	O5 [−x, y−½, −z]	0.860	2.035	2.878	166.22
(*S*,S_P)-**3b**		N1-H1A	O3A [−x, y+½, −z−1]	0.860	2.017	2.858	165.63
		N2-H2B	O1A [−x−1, y+½, −z−1]	0.902	1.943	2.823	164.53
(*S*,R_P)-**3b**		N2-H2	O1S [−x, y+½, −z−½]	0.843	2.037	2.873	171.10
		N1-H1A	O1 [−x, y−½, −z−½]	0.814	2.134	2.921	162.66
(*S*,S_P)-**3c**		N3-H1A	O3 [−x+2, y−½, −z+1]	0.870	2.075	2.908	159.,92
		N2-H6A	O1 [−x+2, y−½, −z+1]	0.909	1.954	2.844	166.15

(R,S_P)-**3c**		N2-H2A	O1 [−x+2, y−½, −z+2]	0.796	2.148	2.916	162.27
		N1-H1C	O2 [−x+2, y−½, −z+2]	0.712	2.193	2.871	159.70
(S,S_P)-**3d**		N1-H1A	O2 [−x+2, y+½, −z]	0.854	2.060	2.871	158.22
		N2-H2A	O3 [−x+2, y+½, −z]	0.970	1.901	2.867	172.84
(S,S_P)-**3f**		N7-H7	O5 [x−1, y, z]	0.860	2.105	2.930	160.5
		N1-H1	O3 [x+1, y, z]	0.859	2.014	2.843	161.7

4. Piezoelectric Measurements

Piezoelectric characterizations were performed by Piezoresponse Force Microscopy (PFM) using a MFP-3D scanning probe microscope (Asylum Research, USA). We placed studied crystals on conductive Cu tape used as a bottom electrode. Conductive tips covered by Ti/Pt with resonant frequency 60-90 kHz and force constant 1.2-5.5 N/m were used as top point electrode. To obtain the voltage dependence of crystal piezoelectric response we discretely increased the modulating voltage on a tip. Voltage dependencies of piezoelectric response of some investigated crystals are shown in Figure S26.

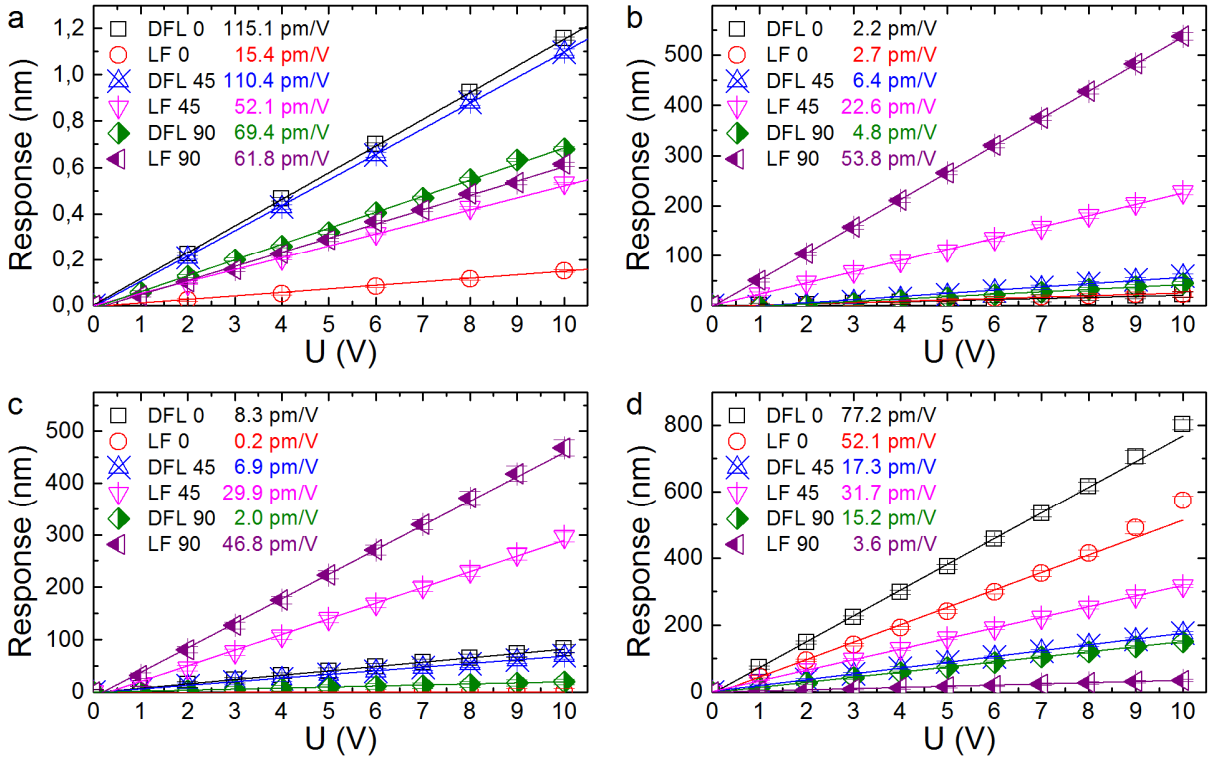


Figure S26. Voltage dependencies of piezoelectric response of (a) (*S*,S_P)-**3a** crystals, (b) (*S*,S_P)-**3b** crystals, (c) (*S*,S_P)-**3d** crystals, and (d) (*S*,S_P)-**3f** crystals.

5. References

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