Expanding Dynamic Kinetic Protocols: Transaminase-Catalyzed Synthesis of α-Substituted β-Amino Ester Derivatives

Aníbal Cuetos, Iván Lavandera, and Vicente Gotor

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1. General

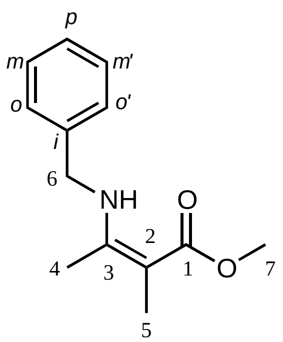
β-Keto esters **1a**, **1c**, **1e**, **1f**, **1j** and **1k** and β-amino ester **2a** were purchased from commercial sources. Codex® Transaminase Screening Kit (ATASK-000250), PLP, lactate dehydrogenase and glucose dehydrogenase were purchased from Codexis. One unit (U) of transaminase (see SI) transforms 1.0 μmol of ethyl acetoaceate **1a** to ethyl 3-aminobutyrate **2a** per minute in phosphate buffer 100 mM at pH 7.5 and 30 ºC in the presence of PLP with isopropylamine (1 M). All other reagents and solvents were of the highest quality available. Methyl (±)-2-methyl-3-oxobutanoate **1b** was obtained by esterification of **1e** employing MeOH under reflux and catalytic HCl (77% yield). Flash chromatography was performed using silica gel 60 (230-400 mesh). Ultrasound reactions were performed using a J.P. Selecta ultrasonic bath (150 W). IR spectra were recorded on a Perkin-Elmer 1720-X infrared Fourier transform spectrophotometer on NaCl pellets. ^{1}H-, ^{13}C-NMR, and DEPT were obtained using a Bruker DPX-300 (^{1}H, 300.13 MHz and ^{13}C, 75.5 MHz) spectrometer for routine experiments. The chemical shifts (δ) are given in ppm and the coupling constants (*J*) in Hertz (Hz). ESI^{+} mode was used to record mass spectra (MS) and ESI-TOF for HRMS. Gas chromatography (GC) analyses were performed on a Hewlett Packard 6890 Series II chromatograph. HPLC analyses were performed with Hewlett Packard 1100 LC liquid chromatograph. Optical rotations were measured using a Perkin-Elmer 241 polarimeter and are quoted in units of 10^{-1} deg cm^{2} g^{-1}.

2. Protocols and compound characterization list

*2.1. General procedure for the synthesis of (Z)-α-alkyl-β-*N*-benzylated enamino esters **4b-k***[1]

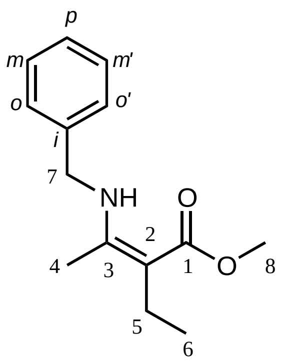
A mixture of (±)-α-alkyl-β-keto esters **1b-k** (3 mmol), benzylamine (4.5 mmol, 1.5 equiv.) and acetic acid (0.6 mmol, 0.2 equiv.) was placed in an ultrasound bath [150 W, (the temperature never exceeding 30 ºC)] for 0.5-1 hour. At the end of the reaction, CH_2Cl_2 (5 mL) was added, and the formed solution was dried (Na_2SO_4), filtered and concentrated in vacuo to give the pure product. Compounds (*Z*)-**4e**,[2] (*Z*)-**4f**,[3] (*Z*)-**4j**[4] and (*Z*)-**4k**[5] exhibited physical and spectral properties in accordance with those reported.

Methyl (*Z*)-3-(benzylamino)-2-methylbut-2-enoate 4b



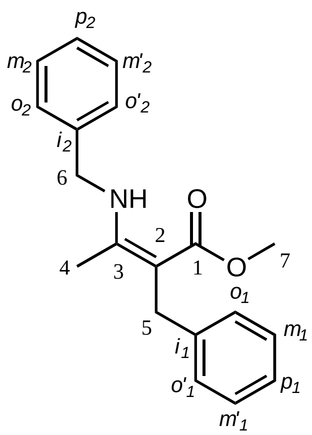
White solid. m.p.: 50-52ºC. IR (KBr) ν 3265, 2948, 3020, 2986, 2948, 1643, 1599, 1492, 1438, 1284, 1255, 1185, 1064 1107 and 781 cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.80 (*s*, 3H, H_5), 1.91 (*s*, 3H, H_4), 3.68 (*s*, 3H, H_7), 4.43 (*ap d*, $|^2J_{HH}|$ 6.1 Hz, 2H, H_6), 5.45 (*br s*, 1H, NH), 7.25-7.36 (*m*, 5H, H_{ar}). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 12.8 (CH_3, C_5), 15.4 (CH_3, C_4), 47.2 (CH_2, C_6), 50.5 (CH_3, C_7), 87.6 (C, C_2), 126.8 (2CH, C_{ar}), 127.2 (CH, C_p), 128.8 (2CH, C_{ar}), 139.5 (C, C_i), 159.7 (C, C_3), 171.5 (C, C_1). MS (ESI^+, *m/z*): 220 [$(M+H)^+$, 100%]. HRMS (ESI^+) calcd for $C_{13}H_{18}NO_2$ $(M+H)^+$: 220.1342; found: 220.1332. Yield: 92%.

Methyl (*Z*)-3-(benzylamino)-2-ethyl-but-2-enoate 4c



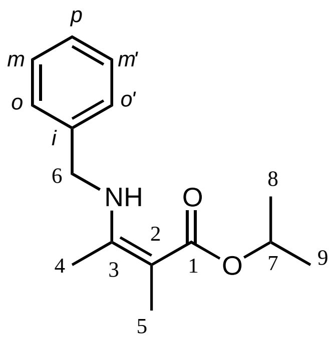
White solid. m.p.: 48-50ºC. IR (KBr) ν 3265, 3028, 2959, 2868, 1736, 1644, 1595, 1495, 1452, 1342, 1283, 1234, 1188, 1106, 1069, 1028, 1002, 945 and 872 cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.96 (*t*, $^{3}J_{HH}$ 7.3 Hz, 3H, H_6), 1.91 (*s*, 3H, H_4), 2.30 (*q*, $^{3}J_{HH}$ 7.2 Hz, 3H, H_5), 3.69 (*s*, 3H, H_8), 4.43 (*ap d*, $|^{2}J_{HH}|$ 6.2 Hz, 2H, H_7), 7.25-7.36 (*m*, 5H, H_{ar}), 9.6 (*br s*, 1H, NH). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 14.5 (CH_3, C_6), 15.2 (CH_3, C_4), 20.4 (CH_2, C_5), 47.0 (CH_2, C_7), 50.2 (CH_3, C_8), 94.7 (C, C_2), 126.6 (2CH, C_{ar}), 127.0 (CH, C_p), 128.6 (2CH, C_{ar}), 139.2 (C, C_i), 159.3 (C, C_3), 171.3 (C, C_1). MS (ESI^+, *m/z*): 234 [$(M+H)^+$, 100%]. HRMS (ESI^+) calcd for $C_{14}H_{20}NO_2$ $(M+H)^+$: 234.1496; found: 234.1489. Yield: 88%.

Methyl (*Z*)-2-benzyl-3-(benzylamino)but-2-enoate 4d



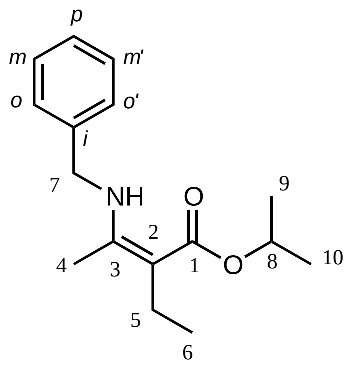
White solid. m.p.: 65-67ºC. IR (KBr) ν 3251, 3024, 2946, 1643, 1595, 1493, 1349, 1265, 1242, 1207, 1187, 1088, 1027, 1002, 949 and 765cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.91 (*s*, 3H, H_4), 3.66 (*s*, 3H, H_7), 3.69 (*s*, 2H, H_5), 4.46 (*ap d*, $|^{2}J_{HH}|$ 6.1 Hz, 2H, H_6), 7.15-7.36 (*m*, 10H, H_{ar}). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 15.3 (CH_3, C_4), 32.6 (CH_2, C_5), 47.1 (CH_2, C_6), 50.4 (CH_3, C_7), 91.2 (C, C_2), 125.3 (CH, C_{ar}), 126.7 (2CH, C_{ar}), 127.1 (CH, C_{ar}), 127.5 (2CH, C_{ar}), 128.0 (2CH, C_{ar}), 128.6 (2CH, C_{ar}), 138.9 (C, C_{ar}), 142.6 (C, C_{ar}), 161.3 (C, C_3), 171.6 (C, C_1). MS (ESI$^+$, *m/z*): 296 [$(M+H)^+$, 100%]. HRMS (ESI$^+$) calcd for $C_{19}H_{22}NO_2$ $(M+H)^+$: 296.1633; found: 296.1645. Yield: 93%.

Isopropyl (*Z*)-3-(benzylamino)-2-methylbut-2-enoate 4g



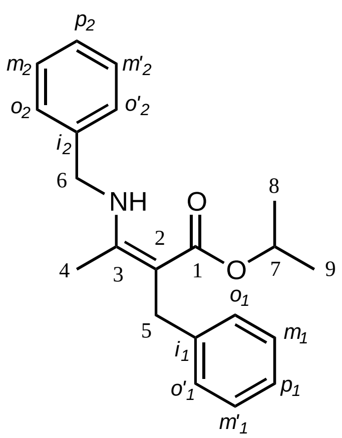
Yellow oil. IR (KBr) ν 3258, 3062, 2979, 2929, 1720, 1639, 1601, 1494, 1453, 1375, 1261, 1208, 1179, 1105, 1028, 1001, 911 and 840 cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.26 (*d*, $^{3}J_{HH}$ 6.2 Hz, 6H, H_8+H_9), 1.79 (*s*, 3H, H_5), 1.92 (*s*, 3H, H_4), 4.42 (*ap d*, $|^{2}J_{HH}|$ 6.1 Hz, 2H, H_6), 5.01 (*hept*, $^{3}J_{HH}$ 6.2 Hz, 1H, H_7), 7.24-7.35 (*m*, 5H, H_{ar}), 9.64 (*br s*, 1H, NH). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 12.7 (CH_3, C_5), 15.2 (CH_3, C_4), 22.2 (2CH_3, C_8+C_9), 47.0 (CH_2, C_6), 65.4 (CH, C_7), 88.0 (C, C_2), 126.6 (2CH, C_{ar}), 127.0 (CH, C_p), 128.5 (2CH, C_{ar}), 139.0 (C, C_i), 159.0 (C, C_3), 170.0 (C, C_1). MS (ESI$^+$, *m/z*): 248 [$(M+H)^+$, 100%]. HRMS (ESI$^+$) calcd for $C_{15}H_{22}NO_2$ $(M+H)^+$: 248.1633; found: 248.1645. Yield: 89%.

Isopropyl (*Z*)-3-(benzylamino)-2-ethylbut-2-enoate 4h



Yellow oil. IR (KBr) ν 3230, 2979, 2936, 2879, 1720, 1659, 1642, 1598, 1496, 1453, 1375, 1244, 1156, 1103, 1028, 1001, 986, and 920 cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.95 (*t*, $^3J_{HH}$ 7.1 Hz, 3H, H_6), 1.25 (*d*, $^3J_{HH}$ 6.1 Hz, 6H, H_9+H_{10}), 1.95 (*s*, 3H, H_4), 2.24 (*q*, $^3J_{HH}$ 7.2 Hz, 2H, H_5), 4.42 (*ap d*, $|^2J_{HH}|$ 6.2 Hz, 2H, H_7), 5.02 (*hept*, $^3J_{HH}$ 6.2 Hz, 1H, H_8), 7.24-7.35 (*m*, 5H, H_{ar}), 9.64 (*br s*, 1H, NH). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 14.5 (CH_3, C_6), 15.2 (CH_3, C_4), 20.5 (CH_2, C_5), 22.2 (2CH_3, C_9+C_{10}), 47.0 (CH_2, C_7), 65.2 (CH, C_8), 88.0 (C, C_2), 126.7 (2CH, C_{ar}), 127.0 (CH, C_p), 128.5 (2CH, C_{ar}), 139.4 (C, C_i), 158.8 (C, C_3), 170.5 (C, C_1). MS (ESI^+, *m/z*): 262 [$(M+H)^+$, 100%]. HRMS (ESI^+) calcd for $C_{16}H_{24}NO_2$ $(M+H)^+$: 262.1775; found: 262.1802. Yield: 91%.

Isopropyl (*Z*)-2-benzyl-3-(benzylamino)but-2-enoate 4i

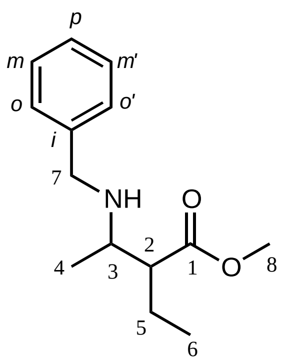


Yellow oil. IR (KBr) ν 3284, 3047, 2948, 2937, 1720, 1639, 1598, 1495, 1454, 1408, 1335, 1274, 1179, 1144, 1105, 1028, 989, 921, and 799 cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.21 (*d*, $^3J_{HH}$ 6.2 Hz, 6H, H_8+H_9), 1.96 (*s*, 3H, H_4), 3.70 (*s*, 2H, H_5), 4.48 (ap *d*, $|^2J_{HH}|$ 6.1 Hz, 2H, H_6), 5.05 (*hept*, $^3J_{HH}$ 6.2 Hz, 1H, H_7), 7.17-7.40 (*m*, 10H, H_{ar}), 9.94 (*br s*, 1H, NH). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 15.3 (CH_3, C_4), 22.1 (2CH_3, C_8+C_9), 32.8 (CH_2, C_5), 47.1 (CH_2, C_6), 65.6 (CH, C_7), 92.3 (C, C_2), 125.1 (CH, C_{ar}), 126.7 (2CH, C_{ar}), 127.1 (CH, C_{ar}), 127.7 (2CH, C_{ar}), 127.9 (2CH, C_{ar}), 128.6 (2CH, C_{ar}), 139.1 (C, C_{ar}), 143.1 (C, C_{ar}), 160.7 (C, C_3), 170.6 (C, C_1). MS (ESI^+, *m/z*): 324 [$(M+H)^+$, 100%]. HRMS (ESI^+) calcd for $C_{21}H_{26}NO_2$ $(M+H)^+$: 324.1954; found: 324.1958. Yield: 95%.

*2.2. General procedure for the synthesis of (±)-α-alkyl-β-*N*-benzylamino esters* syn-***5b-k*** *and* anti-***6b-k***[6,7]

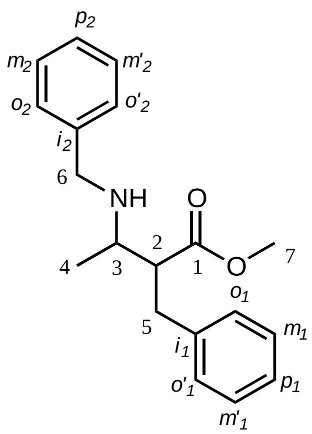
A solution of $NaBH(OAc)_3$ was prepared by adding $NaBH_4$ (0.34 g, 9.0 mmol) to glacial acetic acid (5 mL) while keeping the temperature between 10 and 20 °C. After the H_2 evolution ceased (1 h), the solution was cooled to 0 °C. Then, **4b-k** (3.0 mmol) was added in one portion and the reaction was stirred for 4-12 h at 0 °C. Acetic acid was evaporated under vacuo at 50 °C and the residue was extracted with CH_2Cl_2 and washed with a saturated aqueous solution of Na_2CO_3. The organic layers were combined and dried over Na_2SO_4. The solvent was concentrated under vacuo and the residue subjected to column chromatography (hexanes/ethyl acetate 4:1) furnishing a diastereomeric mixture of **5b-k** and **6b-k** (see SI for ratios). Compounds **5b-6b**[8] and **5k-6k**[7] exhibited physical and spectral properties in accordance with those reported.

Methyl (±)-3-(benzylamino)-2-ethylbutanoate *syn*-5c and *anti*-6c



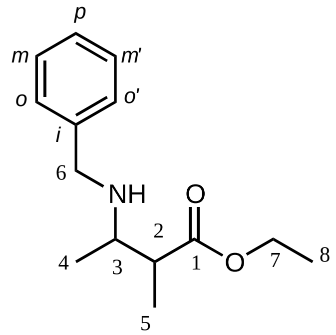
Colourless oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.90 (*m*, 3H, H_6), 1.10 (*d*, $^3J_{HH}$ 6.5 Hz 3H, H_4), 1.65 (*m*, 2H, H_5), 2.34 (*ddd*, $^3J_{HH}$ 9.4, 7.2, 5.2 Hz, 1H, $H_{2,anti}$), 2.47 (*ddd*, $^3J_{HH}$ 10.2, 5.9, 4.6 Hz, 1H, $H_{2,syn}$), 2.90 (*m*, 1H, H_3), 3.68 (*s*, 3H, H_8), 3.81 (*m*, 2H, H_7), 7.23-7.37 (*m*, 5H, H_{ar}). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 12.3 (CH_3, $C_{6,syn}$), 12.4 (CH_3, $C_{6,anti}$), 17.5 (CH_3, $C_{4,syn}$), 17.8 (CH_3, $C_{4,anti}$), 21.4 (CH_2, $C_{5,anti}$), 21.9 (CH_2, $C_{5,syn}$), 50.9 (CH_2, C_7), 51.1 (CH, C_2), 52.3 (CH, C_3), 53.8 (CH_3, $C_{8,anti}$), 53.9 (CH_3, $C_{8,syn}$), 126.8 (CH, C_p), 128.0 (2CH, C_{ar}), 128.2 (2CH, C_{ar}), 140.5 (C, C_i), 175.0 (C, $C_{1,syn}$), 175.5 (C, $C_{1,anti}$). MS (ESI$^+$, *m/z*): 236 [$(M+H)^+$, 100%]. Yield: 78% (obtained as a diastereomeric mixture *syn*/*anti*, 2:1).

Methyl (±)-2-benzyl-3-(benzylamino)butanoate *syn*-5d and *anti*-6d



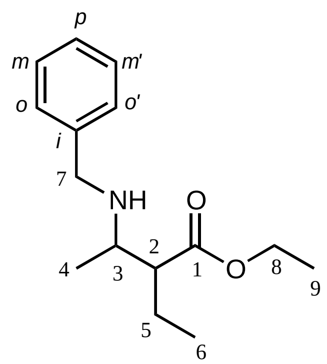
Colourless oil. ^{1}H-NMR (300 MHz, $CDCl_3$) ***syn*-5d**: δ 1.19 (*d*, $^3J_{HH}$ 6.3 Hz, 3H, H_4), 2.89-3.02 (*m*, 4H, H_2+H_3+H_5), 3.60 (s, 3H, H_7), 3.82 (*s*, 2H, H_6), 7.17-7.38 (*m*, 10H, H_{ar}).^{13}C-NMR (75 MHz, $CDCl_3$) δ 17.5 (CH_3, C_4), 34.9 (CH_2, C_5), 50.9 (CH_2, C_6), 51.2 (CH_3, C_7), 52.4 (CH, C_3), 53.8 (CH, C_2), 126.1 (CH, C_{ar}), 126.8 (CH, C_{ar}), 128.0 (2CH, C_{ar}), 128.2 (2CH, C_{ar}), 128.3 (2CH, C_{ar}), 128.6 (2CH, C_{ar}), 139.6 (C, C_{ar}), 140.3 (C, C_{ar}), 174.3 (C, C_1). ***anti*-6d**: δ 1.19 (*d*, $^3J_{HH}$ 6.4 Hz, 3H, H_4), 2.79 (*ddd*, $^3J_{HH}$ 8.0, 6.8, 5.8 Hz, 1H, H_2), 2.97 (*m*, 3H, H_3+H_5), 3.58 (s, 3H, H_7), 3.74 (*d*, $|^2J_{HH}|$ 13.2 Hz, 1H, H_6), 3.90 (*d*, $|^2J_{HH}|$ 13.2 Hz, 1H, H_6), 7.14-7.39 (*m*, 10H, H_{ar}). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 17.9 (CH_3, C_4), 34.0 (CH_2, C_5), 51.0 (CH_2, C_6), 51.3 (CH_3, C_7), 53.5 (CH, C_3), 53.6 (CH, C_2), 126.1 (CH, C_{ar}), 126.8 (CH, C_{ar}), 128.1 (2CH, C_{ar}), 128.2 (2CH, C_{ar}), 128.3 (2CH, C_{ar}), 128.7 (2CH, C_{ar}), 139.9 (C, C_{ar}), 140.4 (C, C_{ar}), 174.5 (C, C_1). MS (ESI^+, *m/z*): 298 $[(M+H)^+$, 100%]. Yield: 84% (obtained as a diastereomeric mixture *syn*/*anti*, 2:1).

Ethyl (±)-3-(benzylamino)-2-methylbutanoate *syn*-5e and *anti*-6e



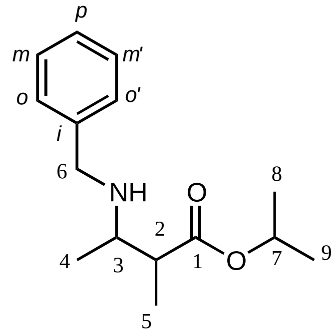
Colourless oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.12 (*m*, 6H, H_4+H_5), 1.24 (*t*, $^3J_{HH}$ 6.9 Hz, 3H, H_8), 2.58 (*m*, 1H, H_2), 2.95 (*m*, 1H, H_3), 3.79 (*m*, 2H, H_6), 4.13 (*q*, $^3J_{HH}$ 7.1 Hz, 2H, H_7), 7.23-7.36 (*m*, 5H, H_{ar}). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 12.6 (CH_3, $C_{5,anti}$), 12.7 (CH_3, $C_{5,syn}$), 14.1 (CH_3, C_4), 17.3 (CH_3, $C_{8,anti}$), 17.4 (CH_3, $C_{8,syn}$), 44.2 (CH, $C_{2,syn}$), 44.3 (CH, $C_{2,anti}$), 50.9 (CH_2, C_6), 54.3 (CH, $C_{3,anti}$), 54.4 (CH, $C_{3,syn}$), 60.2 (CH_2, C_7), 126.7 (CH, C_p), 128.0 (2CH, C_{ar}), 128.2 (2CH, C_{ar}), 140.5 (C, C_i), 175.2 (C, $C_{1,syn}$), 175.3 (C, $C_{1,anti}$). MS (ESI$^+$, *m/z*): 236 [$(M+H)^+$, 100%]. Yield: 75% (obtained as a diastereomeric mixture *syn*/*anti*, 4:1).

Ethyl (±)-3-(benzylamino)-2-ethylbutanoate *syn*-5f and *anti*-6f



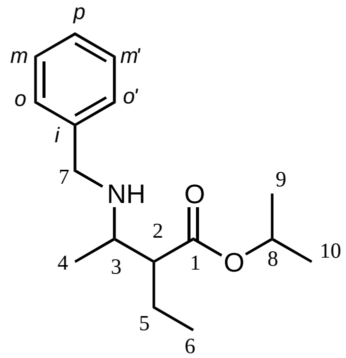
Colourless oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.90 (*t*, $^3J_{HH}$ 6.5 Hz, 3H, H_6), 1.11 (*d*, $^3J_{HH}$ 6.5 Hz, 3H, H_4), 1.25 (*t*, $^3J_{HH}$ 7.1 Hz, 3H, H_9), 1.63 (*m*, 3H, H_5+H_{NH}), 2.32 (*ddd*, $^3J_{HH}$ 9.4, 7.1, 5.1 Hz, 1H, $H_{2,anti}$), 2.44 (*ddd*, $^3J_{HH}$ 10.2, 5.8, 4.5 Hz, 1H, $H_{2,syn}$), 2.88 (*m*, 1H, H_3), 3.79 (*m*, 2H, H_7), 4.15 (*q*, $^3J_{HH}$ 7.1 Hz 2H, H_8), 7.26-7.32 (*m*, 5H, H_{ar}). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 12.2 (CH_3, C_6), 14.3 (CH_3, C_4), 17.5 (CH_3, C_9), 21.9 (CH_2, C_5), 50.9 (CH_2, C_7), 52.3 (CH, C_2), 54.0 (CH, C_3), 60.0 (CH_2, C_8), 126.8 (CH, C_p), 128.0 (2CH, C_{ar}), 128.3 (2CH, C_{ar}), 140.5 (C, C_i), 174.6.2 (C, C_1). MS (ESI$^+$, *m/z*): 250 [$(M+H)^+$, 100%]. Yield: 79% (obtained as a diastereomeric mixture *syn*/*anti*, 4:1).

Isopropyl (±)-3-(benzylamino)-2-methylbutanoate *syn*-5g and *anti*-6g



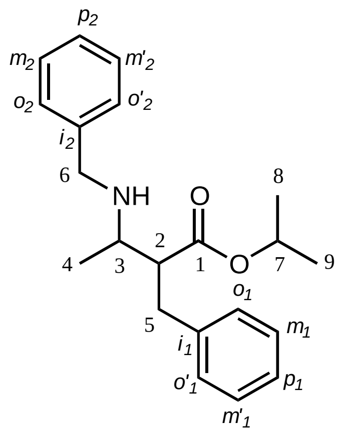
Colourless oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.10-1.25 (*m*, 12H, H_4+H_5+H_8+H_9), 2.56 (*m*, 1H, H_2), 2.96 (*m*, 1H, H_3), 3.81 (*m*, 2H, H_6), 5.02 (*hept*, $^{3}J_{HH}$ 6.2 Hz, 1H, H_7), 7.23-7.36 (*m*, 5H, H_{ar}). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 12.1 (CH_3, $C_{5,anti}$), 12.2 (CH_3, $C_{5,syn}$), 16.7 (CH_3, $C_{4,anti}$), 16.8 (CH_3, $C_{4,syn}$), 21.7 ($2CH_3$, C_8+C_9), 44.2 (CH, $C_{2,syn}$), 44.3 (CH, $C_{2,anti}$), 51.0 (CH_2, C_6), 54.4 (CH, C_3), 67.3 (CH, C_7), 126.7 (CH, C_p), 128.0 (2CH, C_{ar}), 128.2 (2CH, C_{ar}), 140.4 (C, C_i), 174.7 (C, $C_{1,syn}$), 174.8 (C, $C_{1,anti}$). MS (ESI^+, *m/z*): 250 [$(M+H)^+$, 100%]. Yield: 72% (obtained as a diastereomeric mixture *syn*/*anti*, 2:1).

Isopropyl (±)-3-(benzylamino)-2-ethylbutanoate *syn*-5h and *anti*-6h



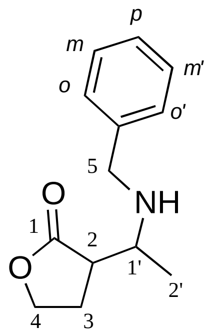
Colourless oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.91 (*m*, 3H, H_6), 1.11 (*m*, 3H, H_4), 1.23 (*m*, 6H, H_9+H_{10}), 1.67 (*m*, 2H, H_5), 2.28 (*ddd*, $^{3}J_{HH}$ 9.6, 7.1, 4.6 Hz, 1H, $H_{2,anti}$), 2.40 (*ddd*, $^{3}J_{HH}$ 10.2, 5.9, 4.6 Hz, 1H, $H_{2,syn}$), 2.89 (*m*, 1H, H_3), 3.80 (*m*, 2H, H_7), 5.06 (*m*, 1H, H_8), 7.23-7.36 (*m*, 5H, H_{ar}). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 12.0 (CH_3, $C_{6,anti}$), 12.1 (CH_3, $C_{6,syn}$), 17.6 (CH_3, C_4), 21.5 (CH_2, $C_{5,anti}$), 21.8 (2CH_3, C_8+C_9), 22.0 (CH_2, $C_{5,syn}$), 50.9 (CH_2, C_7), 52.4 (CH, C_2), 54.0 (CH, $C_{3,anti}$), 54.1 (CH, $C_{3,syn}$), 67.2 (CH, C_8), 126.7 (CH, C_p), 128.0 (2CH, C_{ar}), 128.2 (2CH, C_{ar}), 140.5 (C, C_i), 174.1 (C, C_1). MS (ESI^+, *m/z*): 264 $[(M+H)^+$, 100%]. Yield: 82% (obtained as a diastereomeric mixture *syn*/*anti*, 8:1).

Isopropyl (±)-2-benzyl-3-(benzylamino)butanoate *syn*-5i and *anti*-6i



Colourless oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.04 (*d*, $^3J_{HH}$ 6.3 Hz, 3H, H_4), 1.17 (*m*, 6H, H_8+H_9), 2.79 (*m*, 1H, H_2), 2.94 (*m*, 3H, H_3+H_5), 3.82 (*m*, 2H, H_6), 4.92 (*hept*, $^3J_{HH}$ 6.4 Hz, 1H, H_7), 7.16-7.36 (*m*, 10H, H_{ar}). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 17.6 (CH_3, $C_{4,syn}$), 17.7 (CH_3, $C_{4,anti}$) 21.6 (2CH_3, C_8+C_9), 34.1 (CH_2, $C_{5,anti}$), 35.0 (CH_2, $C_{5,syn}$), 51.0 (CH_2, $C_{6,syn}$), 51.1 (CH_2, $C_{6,anti}$), 52.5 (CH, C_2), 53.5 (CH, $C_{3,anti}$), 54.0 (CH, $C_{3,syn}$), 67.4 (CH, C_7), 126.0 (CH, C_{ar}), 126.7 (CH, C_{ar}), 128.1 (2CH, C_{ar}), 128.2 (2CH, C_{ar}), 128.3 (2CH, C_{ar}), 128.7 (2CH, C_{ar}), 139.7 (C, C_{ar}), 140.5 (C, C_{ar}), 174.4 (C, $C_{1,syn}$), 174.5 (C, $C_{1,anti}$). MS (ESI^+, *m/z*): 326 $[(M+H)^+$, 100%]. Yield: 85% (obtained as a diastereomeric mixture *syn*/*anti*, 9:1).

(±)-3-[1-(Benzylamino)ethyl]dihydrofuran-2(3*H*)-one *syn*-5j and *anti*-6j

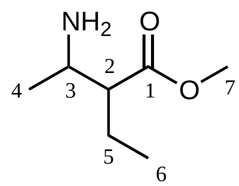


Colourless oil. ***syn*-5j**: ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.17 (*d*, $^3J_{HH}$ 6.5 Hz, 3H, $H_{2'}$), 1.46 (*br s*, 1H, NH), 2.27 (*m*, 2H, H_3), 2.67 (*td*, $^3J_{HH}$ 9.5, 3.7 Hz, 1H, H_2), 3.24 (*qd*, $^3J_{HH}$ 6.7, 3.7 Hz, 1H, $H_{1'}$), 3.74 (*d*, $|^2J_{HH}|$ 13.0 Hz, 1H, H_5), 3.84 (*d*, $|^2J_{HH}|$ 13.0 Hz, 1H, $H_{5'}$), 4.21 (*td*, $^3J_{HH}$ 7.6 Hz, $|^2J_{HH}|$ 8.8 Hz, 1H, H_4), 4.36 (*td*, $^3J_{HH}$ 4.4 Hz, $|^2J_{HH}|$ 8.8 Hz, 1H, H_4). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 18.4 (CH_3, $C_{2'}$), 23.4 (CH_2, C_3), 45.0 (CH, C_2), 51.5 (CH_2, C_5), 51.6 (CH, $C_{1'}$), 66.8 (CH_2, C_4), 126.8 (CH, C_{ar}), 127.9 (CH, C_{ar}), 128.2 (CH, C_{ar}), 140.0 (C, C_{ar}), 178.4 (C, C_1). ***anti*-5j**: ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.18 (*d*, $^3J_{HH}$ 6.4 Hz, 3H, $H_{2'}$), 2.05 (*br s*, 1H, NH), 2.22 (*m*, 2H, H_3), 2.72 (*ddd*, $^3J_{HH}$ 10.2, 9.1, 6.2 Hz, 1H, H_2), 3.08 (*q*, $^3J_{HH}$ 6.3 Hz, 1H, $H_{1'}$), 3.75 (*d*, $|^2J_{HH}|$ 13.2 Hz, 1H, H_5), 3.91 (*d*, $|^2J_{HH}|$ 13.2 Hz, 1H, $H_{5'}$), 4.20 (*td*, $^3J_{HH}$ 7.2 Hz, $|^2J_{HH}|$ 9.2 Hz, 1H, H_4), 4.36 (*td*, $^3J_{HH}$ 3.1 Hz, $|^2J_{HH}|$ 8.9 Hz, 1H, H_4). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 17.1 (CH_3, $C_{2'}$), 24.8 (CH_2, C_3), 43.8 (CH, C_2), 51.1 (CH_2, C_5), 52.7 (CH, $C_{1'}$), 66.6 (CH_2, C_4), 126.9 (CH, C_{ar}), 128.0 (CH, C_{ar}), 128.3 (CH, C_{ar}), 139.9 (C, C_{ar}), 174.4 (C, C_1). MS (ESI$^+$, *m/z*): 220 [$(M+H)^+$, 100%]. Yield: 77% (obtained as a diastereomeric mixture *syn*/*anti*, 2:1).

2.3. General procedure for the synthesis of (±)-α-alkyl-β-amino esters syn-***2b-k*** *and* anti-***3b-k***

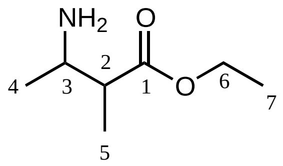
To a solution of the diastereomeric mixture of **5b-k** and **6b-k** (2 mmol) in deoxygenated EtOAc (20 mL), Pd/C on charcoal (10% w w^{-1}, 20 mg) was carefully added and the reaction was stirred for 15 h and room temperature under H_2 pressure (balloon). Then the reaction was filtered over celite and washed with EtOAc. The solvent was concentrated under vacuo and the residue subjected to column chromatography (methanol/ethyl acetate 1:1) furnishing a diastereomeric mixture of **2b-k** and **3b-k**. Compounds **2b-3b**,[3] **2d-3d**,[9] **2j-3j**[6] and **2k-3k**[10] exhibited physical and spectral properties in accordance with those reported.

Methyl (±)**-3-amino-2-ethylbutanoate *syn*-2c and *anti*-3c**



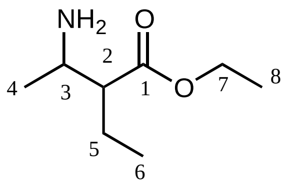
Colourless oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.88 (*t*, $^3J_{HH}$ 7.4 Hz, 3H, H_6), 1.07 (*d*, $^3J_{HH}$ 6.5 Hz, 3H, H_4), 1.59 (*m*, 2H, H_5), 2.01 (*br s*, 2H, NH_2), 2.19 (*m*, 1H, H_2), 3.08 (*m*, 1H, H_3), 3.67 (*s*, 3H, H_7). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 11.7 (CH_3, $C_{6,anti}$), 12.0 (CH_3, $C_{6,syn}$), 20.9 (CH_3, $C_{4,syn}$), 21.4 (CH_2, $C_{5,syn}$), 21.5 (CH_3, $C_{4,anti}$), 22.5 (CH_2, $C_{5,anti}$), 48.2 (CH, $C_{2,anti}$), 48.4 (CH, $C_{2,syn}$), 51.2 (CH_3, C_3), 55.1 (CH, $C_{7,syn}$), 55.3 (CH, $C_{7,anti}$), 175.1 (C, $C_{1,syn}$), 175.4 (C, $C_{1,anti}$). MS (ESI$^+$, *m/z*): 146 [$(M+H)^+$, 100%]. Yield: 62%.

Ethyl (±)-3-amino-2-methylbutanoate *syn*-2e and *anti*-2e



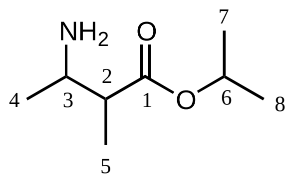
Colourless oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.05 (*d*, $^{3}J_{HH}$ 6.5 Hz, 3H, H_4), 1.11 (*d*, $^{3}J_{HH}$ 7.1 Hz, 3H, H_5), 1.23 (*t*, $^{3}J_{HH}$ 7.1 Hz, 3H, H_7), 1.62 (*br s*, 2H, NH), 2.32 (*m*, 1H, H_2), 3.11 (*m*, 1H, H_3), 4.11 (*q*, $^{3}J_{HH}$ 7.1 Hz, 2H, H_6). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 11.8 (CH_3, C_5), 14.3 (CH_3, C_7), 21.0 (CH_3, C_4), 46.7 (CH, $C_{2,\ syn}$), 47.7 (CH, $C_{2,\ anti}$), 48.7 (CH, $C_{3,syn}$) 49.3 (CH, $C_{3,\ anti}$), 60.1 (CH_2, C_6), 175.3 (C, $C_{1,\ syn}$), 175.5 (C, $C_{1,\ anti}$). MS (ESI^+, *m/z*): 146 $[(M+H)^+$, 100%]. Yield: 68%.

Ethyl (±)-3-amino-2-ethylbutanoate *syn*-2f and *anti*-3f



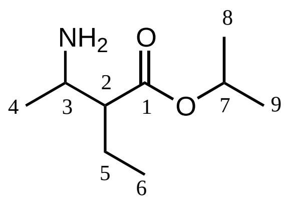
Colourless oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.88 (*t* $^{3}J_{HH}$ 7.3 Hz 3H, H_6), 1.06 (ap *t*, $^{3}J_{HH}$ 6.5 Hz 3H, H_4), 1.24 (*t*, $^{3}J_{HH}$ 7.1 Hz 3H, H_8), 1.62 (*m*, 2H, H_5), 2.13 (*m*, 1H, H_2), 3.05 (*m*, 1H, H_3), 4.13 (*q*, $^{3}J_{HH}$ 7.1 Hz, 2H, H_7). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 11.8 (CH_3, $C_{6,\ anti}$), 12.0 (CH_3, $C_{6,\ syn}$), 14.3 (CH_3, C_8), 21.3 (CH_3, $C_{4,\ syn}$), 21.4 (CH_2, $C_{5,\ syn}$), 21.7 (CH_3, $C_{4,\ anti}$), 22.5 (CH_2, $C_{5,\ anti}$), 48.3 (CH, $C_{2,\ anti}$), 48.5 (CH, $C_{2,\ syn}$), 55.4 (CH, $C_{3,\ syn}$), 55.6 (CH, $C_{3,\ anti}$), 60.1 (CH_2, C_7), 175.3 (C, $C_{1,\ syn}$), 175.4 (C, $C_{1,\ anti}$). MS (ESI^+, *m/z*): 160 $[(M+H)^+$, 100%]. Yield: 76%.

Isopropyl (±)-3-amino-2-methylbutanoate *syn*-2g and *anti*-3g



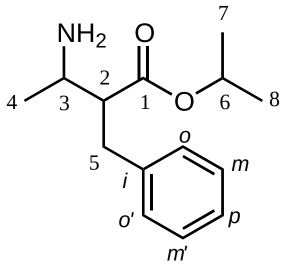
Colourless oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.10 (*d*, $^3J_{HH}$ 6.6 Hz, 3H, H_5), 1.14 (*d*, $^3J_{HH}$ 7.1 Hz, 3H, H_4), 1.23 (*d*, $^3J_{HH}$ 6.3 Hz, 6H, H_7+H_8), 2.19 (*br s*, 2H, NH_2), 2.38 (*m*, 1H, H_2), 3.18 (*m*, 1H, H_3), 5.02 (*hept*, $^3J_{HH}$ 6.4 Hz, 1H, H_6). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 12.0 (CH_3, $C_{5,syn}$), 20.7 (CH_3, C_4), 21.7 ($2CH_3$, C_7+C_8), 46.7 (CH_3, C_2), 48.8 (CH, C_3), 67.4 (CH, C_6), 174.8 (C, C_1). MS (ESI$^+$, *m/z*): 160 [(M+H)$^+$, 100%]. Yield: 73%.

Isopropyl (±)-3-amino-2-ethylbutanoate *syn*-2h and *anti*-3h



Colourless oil. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.89 (*t*, $^3J_{HH}$ 7.4 Hz, 3H, H_6), 1.07 (*m*, 3H, H_4), 1.22 (*d*, $^3J_{HH}$ 6.2 Hz, 6H, H_8+H_9), 1.61 (*m*, 4H, H_5+NH_2), 2.10 (*m*, 1H, H_2), 3.04 (*m*, 1H, H_3), 5.03 (*hept*, $^3J_{HH}$ 6.3 Hz, 1H, H_7). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 11.7 (CH_3, $C_{6,anti}$), 11.9 (CH_3, $C_{6,syn}$), 21.3 (CH_3, $C_{4,syn}$), 21.6 (CH_2, $C_{5,syn}$), 21.7 (CH_3, $C_{4,anti}$), 21.9 ($2CH_3$, C_8+C_9), 22.7 (CH_2, $C_{5,anti}$), 48.3 (CH, $C_{2,anti}$), 48.5 (CH, $C_{2,syn}$), 55.7 (CH, C_3), 67.2 (CH, $C_{7,syn}$), 69.4 (CH, $C_{7,anti}$), 174.2 (C, C_1). MS (ESI$^+$, *m/z*): 174 [(M+H)$^+$, 100%]. Yield: 82%.

Isopropyl (±)-3-amino-2-benzylbutanoate *syn*-2i and *anti*-3i



Colourless oil. ^{1}H-NMR (300 MHz, CDCl$_3$) δ 0.96 (*d*, $^3J_{HH}$ 6.3 Hz, 3H, H$_7$), 1.14 (*d*, $^3J_{HH}$ 6.4 Hz, 3H, H$_8$), 1.29 (*d*, $^3J_{HH}$ 6.6 Hz, 3H, H$_4$,), 2.90 (*m*, 3H, H$_2$+H$_5$), 3.36 (*ap q*, $^3J_{HH}$ 6.5 Hz, 1H, H$_3$), 4.89 (*hept*, $^3J_{HH}$ 6.3 Hz, 1H, H$_6$), 5.32 (*br s*, 2H, NH$_2$), 7.16-7.22 (*m*, 5H, H$_{ar}$). ^{13}C-NMR (75 MHz, CDCl$_3$) δ 18.8 (CH$_3$, C$_{4,syn}$), 18.9 (CH$_3$, C$_{4,anti}$), 21.3 (CH$_3$, C$_7$), 21.5 (CH$_3$, C$_8$), 34.8 (CH$_2$, C$_{5,syn}$), 34.9 (CH$_2$, C$_{5,anti}$), 48.5 (CH, C$_{2,anti}$), 48.7 (CH, C$_{2,syn}$), 53.3 (CH, C$_3$), 67.9 (CH, C$_6$), 126.2 (CH, C$_p$), 128.1 (2CH, C$_{ar}$), 128.7 (2CH, C$_{ar}$), 139.8 (C$_i$), 172.3 (C$_{1,syn}$), 172.8 (C$_{1,anti}$). MS (ESI$^+$, *m/z*): 236 [(M+H)$^+$, 100%]. Yield: 87%.

3. Enzymatic protocols

3.1. Transaminase-catalyzed reaction using alanine as amino donor

In a 1.5 mL Eppendorf tube, transaminase (2 mg, 0.8-3 U), L- or D-alanine (2.5 mg), PRM-102 (15 mg, containing the lactate dehydrogenase, NAD^+, glucose and glucose dehydrogenase neccessary to achieve this transformation), β-keto ester **1a** (25 mM), and DMSO (12.5 μL) were added in phosphate buffer 100 mM pH 8 (500 μL, 1 mM PLP). The reaction was shaken at 30 ºC and 250 rpm for 24 h and stopped by addition of a saturated solution of Na_2CO_3 (400 μL) and extraction with ethyl acetate (2 × 500 μL). The organic layers were separated by centrifugation (90 sec, 13000 rpm), combined and dried over Na_2SO_4. Conversion and *ee* of amine **2a** were determined by GC. The acetylation (K_2CO_3, acetic anhydride) of the sample was necessary to measure the enantioselectivities.

3.2. Transaminase-catalyzed reaction using isopropylamine as amino donor

In a 1.5 mL Eppendorf tube, transaminase (2 mg, 0.8-3 U) and β-keto ester (**1a-k**, 25 mM) were added in phosphate buffer 100 mM pH 7.5 (500 μL, 1 mM PLP, 1 M isopropylamine), and DMSO (12.5 μL). The reaction was shaken at 30 ºC and 250 rpm for 24 h and stopped by addition of a saturated solution of Na_2CO_3 (400 μL). Then the mixture was extracted with ethyl acetate (2 × 500 μL), the organic layers separated by centrifugation (90 sec, 13000 rpm), combined and finally dried over Na_2SO_4. Conversion, *ee* and *de* of amines **2a-k** were determined by GC or HPLC. The acetylation (K_2CO_3, acetic anhydride) of the sample was necessary to measure the stereoselectivities.

4. Enzymatic activities

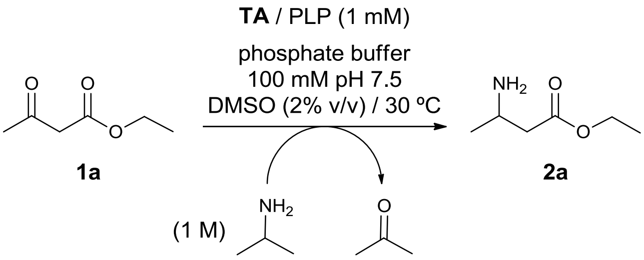


Table S1. Enzymatic activities of commercial TAs with **1a** using isopropylamine as amino donor

Entry	Enzyme	U (μmol 1a converted min^{-1} mg TA^{-1})^{a}
1	ATA-103	0.5
2	ATA-113	1.5
3	ATA-217	0.6
4	ATA-224	0.5
5	ATA-231	0.6
6	ATA-234	0.6
7	TA-P1-A01	0.5
8	TA-P1-A06	0.4
9	TA-P1-F03	0.4
10	TA-P1-F12	0.6
11	TA-P1-G05	0.5
12	TA-P1-G06	0.7
13	ATA-117	0.5
14	ATA-007	0.4
15	ATA-009	0.4
16	ATA-012	0.5
17	ATA-013	0.6
18	ATA-015	0.6
19	ATA-016	0.6
20	ATA-024	0.7
21	ATA-025	0.8
22	ATA-033	0.5
23	ATA-301	0.8
24	TA-P2-A07	0.6

^{a} Measured by GC.

5. Enzymatic screenings

Ethyl 3-oxobutanoate, 1a (with alanine)

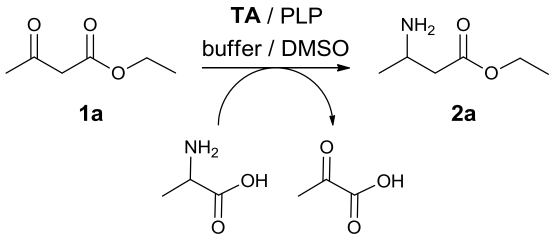


Table S2. TA-catalyzed reaction with **1a** using alanine as amino donor

Entry	Enzyme	*c* (%)[a]	*ee* (%)[b]
1	ATA-103	>99	32 (*S*)
2	ATA-113	99	94 (*S*)
3	ATA-217	13	84 (*S*)
4	ATA-224	<1	n.d.
5	ATA-231	<1	n.d.
6	ATA-234	<1	n.d.
7	TA-P1-A01	>99	90 (*S*)
8	TA-P1-A06	>99	99 (*S*)
9	TA-P1-F03	>99	98 (*S*)
10	TA-P1-F12	99	98 (*S*)
11	TA-P1-G05	>99	99 (*S*)
12	TA-P1-G06	>99	99 (*S*)
13	ATA-117	82	94 (*R*)
14	ATA-007	<1	n.d.
15	ATA-009	<1	n.d.
16	ATA-012	<1	n.d.
17	ATA-013	<1	n.d.
18	ATA-015	<1	n.d.
19	ATA-016	<1	n.d.
20	ATA-024	10	12 (*R*)
21	ATA-025	<1	n.d.
22	ATA-033	<1	n.d.
23	ATA-301	<1	n.d.
24	TA-P2-A07	73	99 (*R*)

[a] Measured by GC. [b] Measured by chiral GC. n.d. not determined.

Ethyl 3-oxobutanoate, 1a (with isopropylamine)

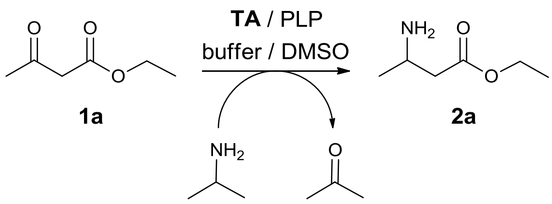


Table S3. TA-catalyzed reaction with **1a** using isopropylamine as amino donor

Entry	Enzyme	*c* (%)[a]	*ee* (%)[b]
1	ATA-103	>99	98 (*S*)
2	ATA-113	>99	98 (*S*)
3	ATA-217	75	86 (*S*)
4	ATA-224	>99	86 (*S*)
5	ATA-231	>99	92 (*S*)
6	ATA-234	>99	87 (*S*)
7	TA-P1-A01	>99	96 (*S*)
8	TA-P1-A06	>99	99 (*S*)
9	TA-P1-F03	>99	98 (*S*)
10	TA-P1-F12	>99	>99 (*S*)
11	TA-P1-G05	>99	>99 (*S*)
12	TA-P1-G06	>99	99 (*S*)
13	ATA-117	43	90 (*R*)
14	ATA-007	12	54 (*R*)
15	ATA-009	18	62 (*R*)
16	ATA-012	86	78 (*R*)
17	ATA-013	96	54 (*R*)
18	ATA-015	>99	68 (*R*)
19	ATA-016	>99	50 (*R*)
20	ATA-024	>99	64 (*R*)
21	ATA-025	>99	64 (*R*)
22	ATA-033	>99	60 (*R*)
23	ATA-301	15	88 (*R*)
24	TA-P2-A07	99	92 (*R*)

[a] Measured by GC. [b] Measured by chiral GC.

pH effect in the transamination of β-keto ester 1c

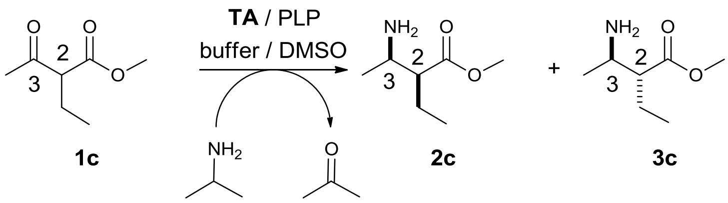


Table S4. TA-catalyzed reaction with **1c** using isopropylamine as amino donor at different pHs

Entry	Enzyme	pH	*c* (%)[a]	Ratio 2c/3c	*ee* 2c (%)[b]	*ee* 2c (%)[b]
1	ATA-103	7.5	45	15/85	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
2	ATA-103	9	21	15/85	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
3	TA-P1-A01	7.5	81	22/78	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
4	TA-P1-A01[c]	7.5	64	18/82	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
5	TA-P1-A01	9	79	21/79	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
6	TA-P1-A06	7	73	22/78	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
7	TA-P1-A06	7.5	87	16/84	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
8	TA-P1-A06[d]	7.5	79	18/82	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
9	TA-P1-A06	8	83	19/81	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
10	TA-P1-A06	9	87	15/85	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
11	TA-P1-G06	7.5	88	20/80	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
12	TA-P1-G06[d]	7.5	81	21/79	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
13	TA-P1-G06	9	88	18/82	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
14	ATA-025	7.5	93	52/48	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
15	ATA-025	9	93	52/48	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
16	ATA-301	7	17	23/77	n.d.	99 (2*R*,3*R*)
17	ATA-301	7.5	21	20/80	n.d.	98 (2*R*,3*R*)
18	ATA-301	8	21	19/81	n.d.	99 (2*R*,3*R*)
19	ATA-301	9	23	17/83	n.d.	>99 (2*R*,3*R*)
20	TA-P2-A07	7.5	47	62/38	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
21	TA-P2-A07	9	87	59/41	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)

[a] Measured by GC. [b] Measured by chiral GC. [c] 1 mg (0.5 U) of the transaminase used. [d] 10 mg of basic resin Dowex MWX-1 was added in the reaction media. n.d. not determined.

Temperature effect in the transamination of β-keto ester 1c

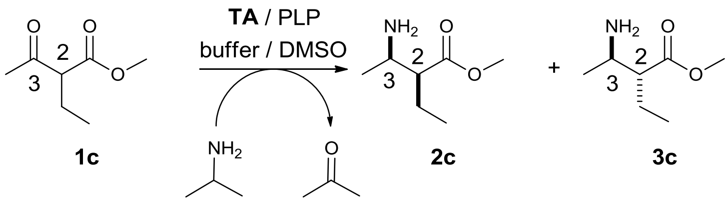


Table S5. TA-catalyzed reaction with **1c** using isopropylamine as amino donor at different temperatures

Entry	Enzyme	T (ºC)	t (h)	*c* (%)[a]	Ratio 2/3	*ee* 2c (%)[b]	*ee* 2c (%)[b]
1	TA-P1-A01	37	24	78	28/72	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
2	TA-P1-A01	30	24	81	22/78	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
3	TA-P1-A01	15	72	65	21/79	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
4	TA-P1-A01	4	72	24	12/88	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
5	TA-P1-A06	37	24	75	21/79	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
6	TA-P1-A06	30	24	87	16/84	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
7	TA-P1-A06	15	72	70	20/80	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
8	TA-P1-A06	4	72	30	9/91	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
9	TA-P1-G06	37	24	79	24/76	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
10	TA-P1-G06	30	24	88	20/80	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
11	TA-P1-G06	15	72	53	13/87	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
12	TA-P1-G06	4	72	35	8/92	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
13	ATA-025	37	24	81	52/48	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
14	ATA-025	30	24	93	52/48	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
15	ATA-025	15	24	86	52/48	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
16	ATA-025	4	72	83	52/48	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)

[a] Measured by GC. [b] Measured by chiral GC.

Methyl 2-methyl-3-oxobutanoate, 1b

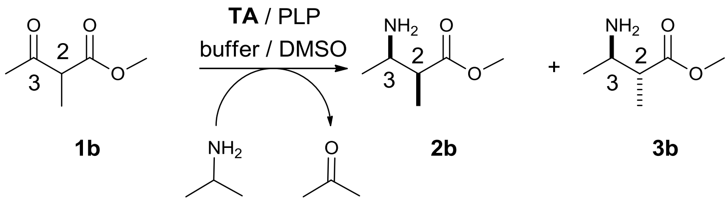


Table S6. TA-catalyzed reaction with **1b** using isopropylamine as amino donor

Entry	Enzyme	*c* (%)[a]	Ratio 2b/3b	*ee* 2b (%)[b]	*ee* 3b (%)[b]
1	ATA-103	53	29/71	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
2	ATA-113	89	57/43	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
3	ATA-217	44	55/45	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
4	ATA-224	79	57/43	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
5	ATA-231	69	56/44	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
6	ATA-234	78	56/44	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
7	TA-P1-A01	85	45/55	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
8	TA-P1-A06	88	34/66	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
9	TA-P1-F03	81	52/48	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
10	TA-P1-F12	86	56/44	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
11	TA-P1-G05	77	57/43	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
12	TA-P1-G06	87	36/64	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
13	ATA-117	7	55/45	n.d.	n.d.
14	ATA-007	9	39/61	n.d.	44 (2*R*,3*R*)
15	ATA-009	31	54/46	62 (2*S*,3*R*)	74 (2*R*,3*R*)
16	ATA-012	70	53/47	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
17	ATA-013	77	53/47	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
18	ATA-015	88	53/47	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
19	ATA-016	93	53/47	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
20	ATA-024	93	52/48	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
21	ATA-025	93	53/47	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
22	ATA-033	93	53/47	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
23	ATA-301	25	17/83	n.d.	>99 (2*R*,3*R*)
24	TA-P2-A07	61	58/42	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)

[a] Measured by GC. [b] Measured by chiral GC. n.d. not determined.

Methyl 2-ethyl-3-oxobutanoate, 1c

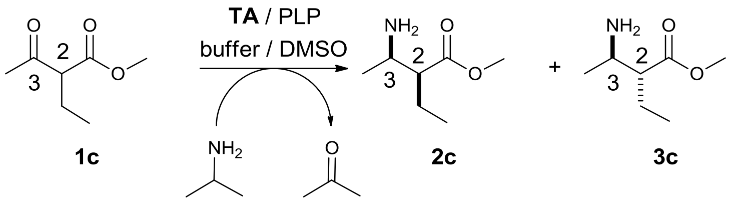


Table S7. TA-catalyzed reaction with **1c** using isopropylamine as amino donor

Entry	Enzyme	*c* (%)[a]	Ratio 2c/3c	*ee* 2c (%)[b]	*ee* 3c (%)[b]
1	ATA-103	45	15/85	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
2	ATA-113	92	52/48	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
3	ATA-217	61	51/49	99 2*R*,3*S*)	95 (2*S*,3*S*)
4	ATA-224	82	55/45	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
5	ATA-231	88	54/46	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
6	ATA-234	87	54/46	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
7	TA-P1-A01	81	22/78	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
8	TA-P1-A06	87	16/84	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
9	TA-P1-F03	86	48/52	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
10	TA-P1-F12	66	44/56	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
11	TA-P1-G05	83	50/50	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
12	TA-P1-G06	88	20/80	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
13	ATA-117	6	58/42	n.d.	n.d.
14	ATA-007	11	48/52	78 (2*S*,3*R*)	74 (2*R*,3*R*)
15	ATA-009	10	48/52	90 (2*S*,3*R*)	77 (2*R*,3*R*)
16	ATA-012	77	50/50	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
17	ATA-013	88	51/49	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
18	ATA-015	93	52/48	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
19	ATA-016	92	52/48	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
20	ATA-024	93	52/48	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
21	ATA-025	93	52/48	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
22	ATA-033	93	52/48	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
23	ATA-301	21	20/80	n.d.	98 (2*R*,3*R*)
24	TA-P2-A07	47	62/38	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)

[a] Measured by GC. [b] Measured by chiral GC. n.d. not determined.

Methyl 2-benzyl-3-oxobutanoate, 1d

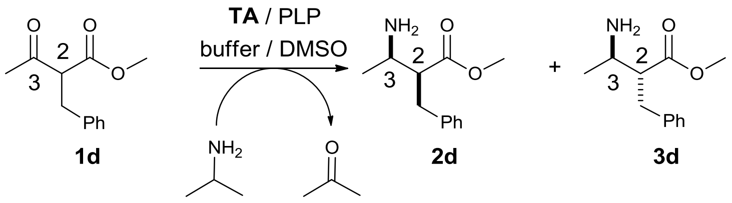


Table S8. TA-catalyzed reaction with **1d** using isopropylamine as amino donor

Entry	Enzyme	*c* (%)[a]	Ratio 2d/3d	*ee* 2d (%)[b]	*ee* 3d (%)[b]
1	ATA-103	76	54/46	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
2	ATA-113	97	56/44	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
3	ATA-217	84	54/46	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
4	ATA-224	98	55/45	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
5	ATA-231	98	55/45	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
6	ATA-234	96	53/47	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
7	TA-P1-A01	93	50/50	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
8	TA-P1-A06	98	58/42	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
9	TA-P1-F03	98	53/47	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
10	TA-P1-F12	95	54/46	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
11	TA-P1-G05	97	56/44	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
12	TA-P1-G06	98	56/44	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
13	ATA-117	29	59/41	59 (2*S*,3*R*)	51 (2*R*,3*R*)
14	ATA-007	10	44/56	n.d.	50 (2*R*,3*R*)
15	ATA-009	55	48/52	69 (2*S*,3*R*)	38 (2*R*,3*R*)
16	ATA-012	97	53/47	99 (2*S*,3*R*)	91 (2*R*,3*R*)
17	ATA-013	98	54/46	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
18	ATA-015	99	56/44	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
19	ATA-016	99	55/45	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
20	ATA-024	>99	56/44	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
21	ATA-025	99	56/44	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
22	ATA-033	>99	55/45	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
23	ATA-301	43	56/44	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
24	TA-P2-A07	90	55/45	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)

[a] Measured by GC. [b] Measured by chiral HPLC. n.d. not determined.

Ethyl 2-methyl-3-oxobutanoate, 1e

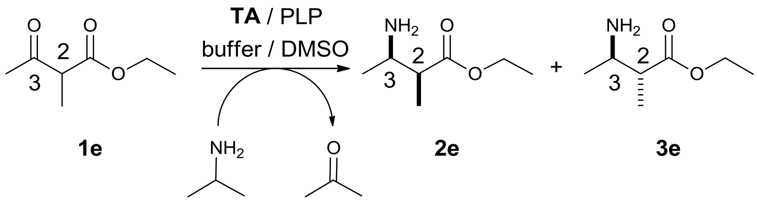


Table S9. TA-catalyzed reaction with **1e** using isopropylamine as amino donor

Entry	Enzyme	*c* (%)[a]	Ratio 2e/3e	*ee* 2e (%)[b]	*ee* 3e (%)[b]
1	ATA-103	89	49/51	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
2	ATA-113	92	54/46	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
3	ATA-217	70	54/46	96 (2*R*,3*S*)	96 (2*S*,3*S*)
4	ATA-224	90	55/45	97 (2*R*,3*S*)	96 (2*S*,3*S*)
5	ATA-231	91	56/44	98 (2*R*,3*S*)	98 (2*S*,3*S*)
6	ATA-234	89	55/45	97 (2*R*,3*S*)	98 (2*S*,3*S*)
7	TA-P1-A01	92	55/45	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
8	TA-P1-A06	92	53/47	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
9	TA-P1-F03	93	54/46	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
10	TA-P1-F12	92	55/45	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
11	TA-P1-G05	88	56/44	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
12	TA-P1-G06	93	54/46	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
13	ATA-117	14	53/47	72 (2*S*,3*R*)	69 (2*R*,3*R*)
14	ATA-007	13	44/56	64 (2*S*,3*R*)	25 (2*R*,3*R*)
15	ATA-009	24	49/51	66 (2*S*,3*R*)	43(2*R*,3*R*)
16	ATA-012	82	54/46	98 (2*S*,3*R*)	96 (2*R*,3*R*)
17	ATA-013	84	54/46	99 (2*S*,3*R*)	99 (2*R*,3*R*)
18	ATA-015	90	54/46	99 (2*S*,3*R*)	99 (2*R*,3*R*)
19	ATA-016	91	54/46	99 (2*S*,3*R*)	99 (2*R*,3*R*)
20	ATA-024	93	54/46	97 (2*S*,3*R*)	99 (2*R*,3*R*)
21	ATA-025	91	54/46	98 (2*S*,3*R*)	99(2*R*,3*R*)
22	ATA-033	91	54/46	97 (2*S*,3*R*)	99 (2*R*,3*R*)
23	ATA-301	39	36/64	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
24	TA-P2-A07	79	55/45	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)

[a] Measured by GC. [b] Measured by chiral GC.

Ethyl 2-ethyl-3-oxobutanoate, 1f

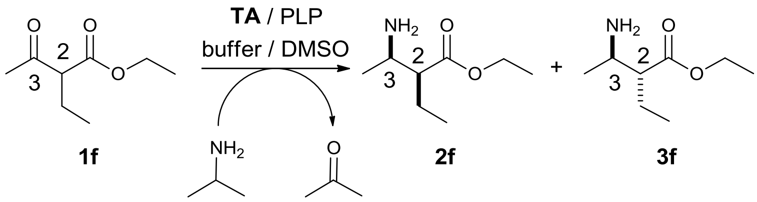


Table S10. TA-catalyzed reaction with **1f** using isopropylamine as amino donor

Entry	Enzyme	*c* (%)[a]	Ratio 2f/3f	*ee* 2f (%)[b]	*ee* 3f (%)[b]
1	ATA-103	77	25/75	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
2	ATA-113	94	51/49	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
3	ATA-217	82	51/49	96 (2*R*,3*S*)	83 (2*S*,3*S*)
4	ATA-224	93	55/45	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
5	ATA-231	93	54/46	>99 (2*S*,3*S*)	>99 (2*S*,3*S*)
6	ATA-234	93	58/42	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
7	TA-P1-A01	94	41/59	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
8	TA-P1-A06	93	29/71	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
9	TA-P1-F03	93	50/50	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
10	TA-P1-F12	86	50/50	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
11	TA-P1-G05	90	49/51	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
12	TA-P1-G06	93	31/69	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
13	ATA-117	5	55/45	n.d.	n.d.
14	ATA-007	19	48/52	75 (2*S*,3*R*)	74 (2*R*,3*R*)
15	ATA-009	29	51/49	89 (2*S*,3*R*)	91 (2*R*,3*R*)
16	ATA-012	92	51/49	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
17	ATA-013	93	51/49	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
18	ATA-015	94	51/49	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
19	ATA-016	95	51/49	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
20	ATA-024	95	51/49	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
21	ATA-025	95	52/48	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
22	ATA-033	95	51/49	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
23	ATA-301	41	32/68	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
24	TA-P2-A07	50	58/42	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)

[a] Measured by GC. [b] Measured by chiral GC. n.d. not determined.

Isopropyl 2-methyl-3-oxobutanoate, 1g

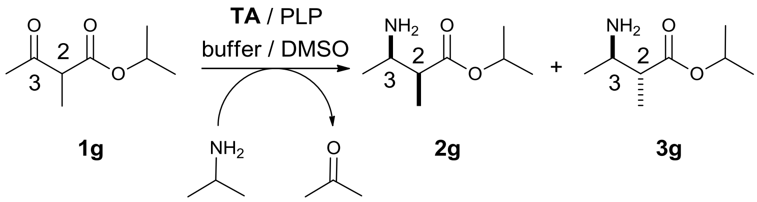


Table S11. TA-catalyzed reaction with **1g** using isopropylamine as amino donor

Entry	Enzyme	*c* (%)[a]	Ratio 2g/3g	*ee* 2g (%)[b]	*ee* 3g (%)[b]
1	ATA-103	79	53/47	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
2	ATA-113	96	55/45	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
3	ATA-217	94	54/46	97 (2*R*,3*S*)	98 (2*S*,3*S*)
4	ATA-224	95	55/45	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
5	ATA-231	95	55/45	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
6	ATA-234	95	55/45	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
7	TA-P1-A01	96	53/47	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
8	TA-P1-A06	92	51/49	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
9	TA-P1-F03	95	54/46	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
10	TA-P1-F12	93	55/45	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
11	TA-P1-G05	94	57/43	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
12	TA-P1-G06	93	48/52	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
13	ATA-117	9	46/54	n.d.	67 (2*R*,3*R*)
14	ATA-007	19	44/56	77 (2*S*,3*R*)	45 (2*R*,3*R*)
15	ATA-009	33	52/48	76 (2*S*,3*R*)	78 (2*R*,3*R*)
16	ATA-012	92	53/47	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
17	ATA-013	93	53/47	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
18	ATA-015	96	53/47	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
19	ATA-016	96	53/47	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
20	ATA-024	97	53/47	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
21	ATA-025	95	54/46	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
22	ATA-033	97	53/47	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
23	ATA-301	47	32/68	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
24	TA-P2-A07	92	53/47	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)

[a] Measured by GC. [b] Measured by chiral GC. n.d. not determined.

Isopropyl 2-ethyl-3-oxobutanoate, 1h

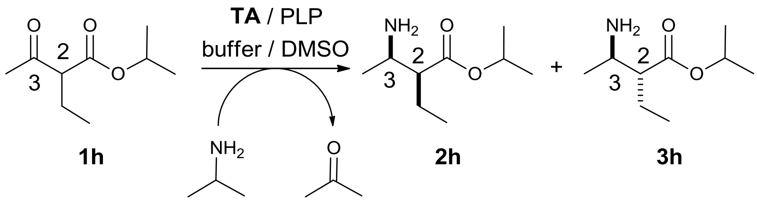


Table S12. TA-catalyzed reaction with **1h** using isopropylamine as amino donor

Entry	Enzyme	*c* (%)[a]	Ratio 2h/3h	*ee* 2h (%)[b]	*ee* 3h (%)[b]
1	ATA-103	88	54/46	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
2	ATA-113	92	52/48	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
3	ATA-217	77	58/42	96 (2*R*,3*S*)	25 (2*S*,3*S*)
4	ATA-224	89	53/47	>99 (2*R*,3*S*)	88 (2*S*,3*S*)
5	ATA-231	90	52/48	>99 (2*R*,3*S*)	93 (2*S*,3*S*)
6	ATA-234	91	51/49	>99 (2*R*,3*S*)	80 (2*S*,3*S*)
7	TA-P1-A01	92	51/49	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
8	TA-P1-A06	91	50/50	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
9	TA-P1-F03	87	54/46	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
10	TA-P1-F12	90	52/48	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
11	TA-P1-G05	88	53/47	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
12	TA-P1-G06	96	50/50	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
13	ATA-117	4	n.d.	n.d.	n.d.
14	ATA-007	21	51/49	78 (2*S*,3*R*)	92 (2*R*,3*R*)
15	ATA-009	31	51/49	83 (2*S*,3*R*)	97 (2*R*,3*R*)
16	ATA-012	86	51/49	99 (2*S*,3*R*)	>99 (2*R*,3*R*)
17	ATA-013	89	52/48	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
18	ATA-015	92	52/48	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
19	ATA-016	92	53/47	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
20	ATA-024	92	52/48	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
21	ATA-025	92	52/48	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
22	ATA-033	92	53/47	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
23	ATA-301	35	38/62	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
24	TA-P2-A07	53	54/46	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)

[a] Measured by GC. [b] Measured by chiral GC. n.d. not determined.

Isopropyl 2-benzyl-3-oxobutanoate, 1i

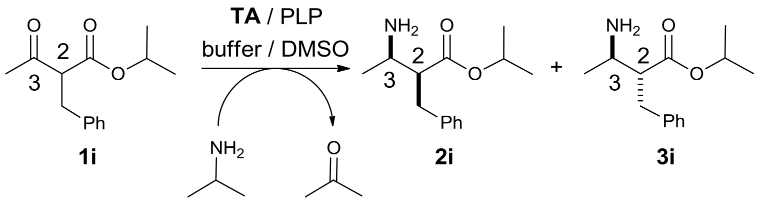


Table S13. TA-catalyzed reaction with **1i** using isopropylamine as amino donor

Entry	Enzyme	*c* (%)[a]	Ratio 2i/3i	*ee* 2i (%)[b]	*ee* 3i (%)[b]
1	ATA-103	94	23/77	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
2	ATA-113	99	42/58	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
3	ATA-217	97	55/45	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
4	ATA-224	99	55/45	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
5	ATA-231	99	53/47	>99 (2*S*,3*S*)	>99 (2*S*,3*S*)
6	ATA-234	98	53/47	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
7	TA-P1-A01	98	31/69	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
8	TA-P1-A06	98	27/73	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
9	TA-P1-F03	98	53/47	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
10	TA-P1-F12	98	58/42	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
11	TA-P1-G05	98	53/47	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
12	TA-P1-G06	96	35/65	>99 (2*R*,3*S*)	>99 (2*S*,3*S*)
13	ATA-117	65	53/47	32 (2*S*,3*R*)	44 (2*R*,3*R*)
14	ATA-007	66	59/41	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
15	ATA-009	70	55/45	99 (2*S*,3*R*)	98 (2*R*,3*R*)
16	ATA-012	97	55/45	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
17	ATA-013	99	55/45	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
18	ATA-015	99	55/45	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
19	ATA-016	99	57/43	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
20	ATA-024	>99	56/44	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
21	ATA-025	>99	53/47	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
22	ATA-033	>99	58/42	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
23	ATA-301	89	59/41	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)
24	TA-P2-A07	98	53/47	>99 (2*S*,3*R*)	>99 (2*R*,3*R*)

[a] Measured by GC. [b] Measured by chiral HPLC.

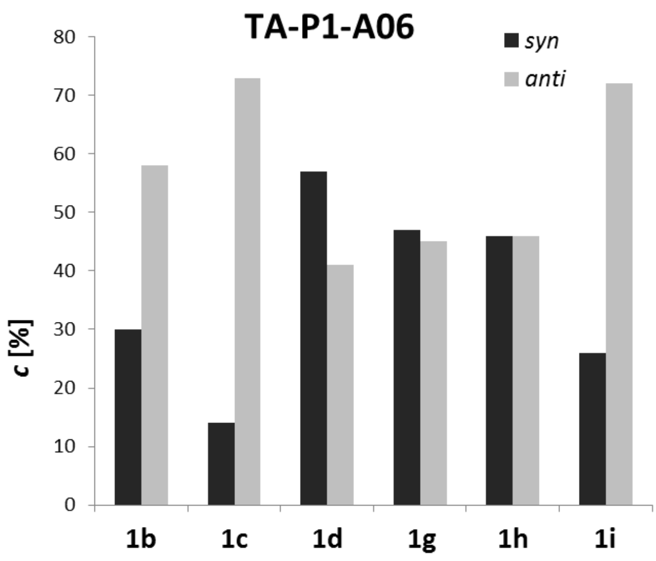


Figure S1. Effect of the alkyl group at α-position in the transaminations catalyzed by TA-P1-A06. In all cases, *ee* of both diastereoisomers were higher than 99%.

For some TAs, *e.g.* TA-P1-A06 and ATA-103, it remained clear that the presence of a benzyl moiety at α-position could largely influence the diastereoselectivity of the process (Figure S1). Thus, while the transamination with α-methylated **1b** or α-ethylated keto ester **1c** favored the formation of the *anti*-(2*S*,3*S*) isomers, α-benzylated **1d** preferentially afforded *syn*-(2*R*,3*S*). On the other hand, for isopropyl esters an opposite effect was observed, getting mainly *anti*-(2*S*,3*S*)-**3i** (R^2= benzyl) whereas no selectivity was achieved for keto esters **1g** (R^2= methyl) and **1h** (R^2= ethyl). These results obviously pointed out to a different substrate disposition within the active centre site of the transaminases.

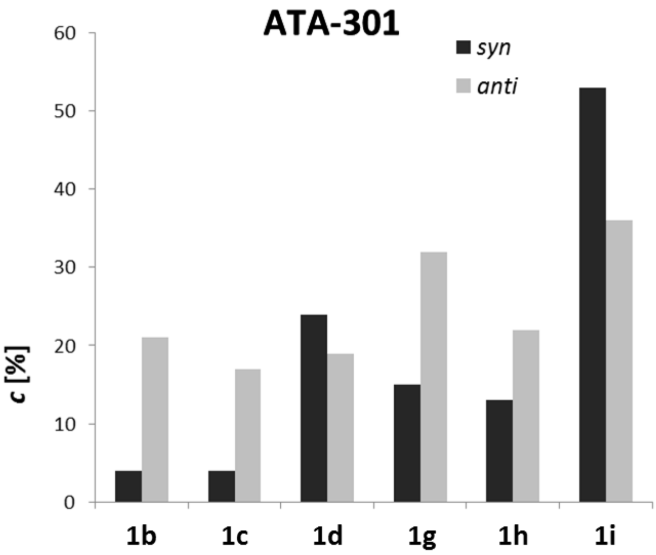


Figure S2. Effect of the alkyl group at α-position in the ATA-301-catalyzed aminations. In all cases, *ee* of both diastereoisomers were higher than 98%.

For ATA-301 (Figure S2), a remarkable effect due to the substituent at α position was observed, changing from *anti* to *syn* preference when a bulky benzyl group was present (**1d** and **1i**).

α-Acetylbutyrolactone, 1j

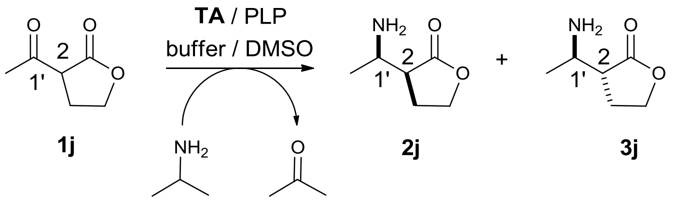


Table S14. TA-catalyzed reaction with **1j** using isopropylamine as amino donor

Entry	Enzyme	*c* (%)[a]	Ratio 2j/3j	*ee* 2j (%)[b]	*ee* 3j (%)[b]
1	ATA-103	21	10/90	n.d.	>99 (2*S*,1'*S*)
2	ATA-113	31	26/74	>99 (2*R*,1'*S*)	>99 (2*S*,1'*S*)
3	ATA-217	14	21/79	n.d.	45 (2*S*,1'*S*)
4	ATA-224	21	14/86	n.d.	81 (2*S*,1'*S*)
5	ATA-231	16	19/81	n.d.	75 (1*S*,2*S*)
6	ATA-234	19	21/79	n.d.	52 (2*S*,1'*S*)
7	TA-P1-A01	41	22/78	>99 (2*R*,1'*S*)	>99 (2*S*,1'*S*)
8	TA-P1-A06	38	18/82	>99 (2*R*,1'*S*)	>99 (2*S*,1'*S*)
9	TA-P1-F03	15	20/80	n.d.	>99 (2*S*,1'*S*)
10	TA-P1-F12	16	15/75	n.d.	>99 (2*S*,1'*S*)
11	TA-P1-G05	29	21/79	>99 (2*R*,1'*S*)	>99 (2*S*,1'*S*)
12	TA-P1-G06	37	19/81	>99 (2*R*,1'*S*)	>99 (2*S*,1'*S*)
13	ATA-117	3	n.d.	n.d.	n.d.
14	ATA-007	3	n.d.	n.d.	n.d.
15	ATA-009	3	n.d.	n.d.	n.d.
16	ATA-012	6	50/50	n.d.	n.d.
17	ATA-013	10	50/50	>99 (2*S*,1'*R*)	>99 (2*R*,1'*R*)
18	ATA-015	12	41/59	>99 (2*S*,1'*R*)	>99 (2*R*,1'*R*)
19	ATA-016	10	50/50	>99 (2*S*,1'*R*)	>99 (2*R*,1'*R*)
20	ATA-024	25	40/60	>99 (2*S*,1'*R*)	>99 (2*R*,1'*R*)
21	ATA-025	21	43/57	>99 (2*S*,1'*R*)	>99 (2*R*,1'*R*)
22	ATA-033	28	44/56	>99 (2*S*,1'*R*)	>99 (2*R*,1'*R*)
23	ATA-301	2	n.d.	n.d.	n.d.
24	TA-P2-A07	4	n.d.	n.d.	n.d.

[a] Measured by GC. [b] Measured by chiral HPLC. n.d. not determined.

Ethyl 2-oxocyclopentanecarboxylate, 1k

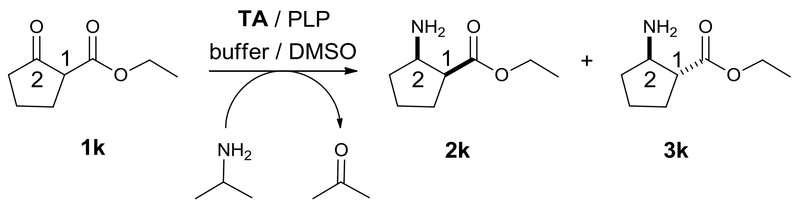


Table S15. TA-catalyzed reaction with **1k** using isopropylamine as amino donor

Entry	Enzyme	*c* (%)[a]	Ratio 2k/3k	*ee* 2k (%)[b]	*ee* 3k (%)[b]
1	ATA-103	28	4/96	n.d.	>99 (1*S*,2*S*)
2	ATA-113	99	3/97	n.d.	>99 (1*S*,2*S*)
3	ATA-217	54	7/93	n.d.	>99 (1*S*,2*S*)
4	ATA-224	92	12/88	61 (1*R*,2*S*)	>99 (1*S*,2*S*)
5	ATA-231	68	13/87	73 (1*R*,2*S*)	>99 (1*S*,2*S*)
6	ATA-234	88	10/90	83 (1*R*,2*S*)	>99 (1*S*,2*S*)
7	TA-P1-A01	72	4/96	n.d.	>99 (1*S*,2*S*)
8	TA-P1-A06	31	2/98	n.d.	>99 (1*S*,2*S*)
9	TA-P1-F03	21	1/99	n.d.	>99 (1*S*,2*S*)
10	TA-P1-F12	88	9/91	78 (1*R*,2*S*)	>99 (1*S*,2*S*)
11	TA-P1-G05	85	2/98	n.d.	>99 (1*S*,2*S*)
12	TA-P1-G06	19	4/96	n.d.	>99 (1*S*,2*S*)
13	ATA-117	<1	n.d.	n.d.	n.d.
14	ATA-007	<1	n.d.	n.d.	n.d.
15	ATA-009	<1	n.d.	n.d.	n.d.
16	ATA-012	3	n.d.	n.d.	n.d.
17	ATA-013	<1	n.d.	n.d.	n.d.
18	ATA-015	7	43/57	n.d.	n.d.
19	ATA-016	8	50/50	n.d.	n.d.
20	ATA-024	13	46/54	>99 (1*S*,2*R*)	>99 (1*R*,2*R*)
21	ATA-025	4	n.d.	n.d.	n.d.
22	ATA-033	5	66/33	n.d.	n.d.
23	ATA-301	<1	n.d.	n.d.	n.d.
24	TA-P2-A07	3	n.d.	n.d.	n.d.

[a] Measured by GC. [b] Measured by chiral HPLC. n.d. not determined.

Transaminase-catalyzed synthesis of anti-*(1*S*,2*S*)-**3k***

In a 15 mL Falcon tube, TA-P1-G05 (12.5 U) and β-keto ester (**1k**, 50 mg, 25 mM) were added in phosphate buffer 100 mM pH 7.5 (5 mL, 1 mM PLP, 1 M isopropylamine), and EtOH (125 μL, 2.5% v v^{-1}). The reaction was shaken at 30 ºC and 250 rpm for 24 h and then the reaction was acidified with HCl 1 M (5 mL) and extracted with EtOAc (2 × 10 mL). Then the aqueous phase was basified with a saturated solution of K_2CO_3 until pH 10-11 and then extracted with ethyl acetate (3 × 10 mL). The organic layers were dried over Na_2SO_4 and the solvent was evaporated under reduced pressure obtaining *anti*-(1*S*,2*S*)-**3k** (58% yield, >99% *ee*, 98% *de*) with excellent purity, so no further purification was neccessary. $[\alpha]_D^{20}$ = +69.0 (c 1.0, EtOH); experimentally described: $[\alpha]_D^{20}$ = +61.8 (c 1.0, EtOH).[11]

6. Analytical data

6.1. GC analyses for determination of conversions and enantiomeric excess

The following column was used: Varian Chirasil Dex CB (25 m x 0.25 mm x 0.25 µm, 12.2 psi N_2).

Table S16. Determination of conversion values by GC

compound	program[a]	retention time (min)	
		1	**2**
a	60/0/5/120/0/30/180/2	7.6	8.5

[a] Program: initial temp. (°C)/ time (min)/ slope (°C/min)/ temp. (°C)/ time (min)/ slope (°C/min)/ temp. (°C)/ time (min).

Table S17. Determination of enantiomeric excess values by GC

compound	program[a]	retention time (min)	
		2	
a	60/0/5/120/0/30/180/2	17.9 (*R*)	19.2 (*S*)

[a] Program: initial temp. (°C)/ time (min)/ slope (°C/min)/ temp. (°C)/ time (min)/ slope (°C/min)/ temp. (°C)/ time (min).

6.2. GC Analyses for determination of conversions of α-substituted amino esters

The following column was used: Varian Chirasil Dex CB (25 m x 0.25 mm x 0.25 µm, 12.2 psi N_2).

Table S18. Determination of conversion values by GC

compound	program[a]	retention time (min)		
		1	*syn*-**2**	*anti*-**3**
b	60/0/5/120/0/30/180/2	7.2	9.2	
c	60/0/5/120/0/30/180/2	9.0	10.5	10.2
d	80/0/10/160/0/20/180/5	10.7	11.5	11.3
e	60/0/5/120/0/30/180/2	8.7	10.1	9.9
f	60/0/5/120/0/30/180/2	10.1	11.5	11.2
g	60/0/5/120/0/30/180/2	8.5	10.1	9.9
h	60/0/5/120/0/30/180/2	10.1	11.8	11.3
i	80/0/10/160/0/20/180/5	11.8	12.7	12.5
j	60/0/5/120/0/30/180/2	13.4	15.0	14.8
k	100/3/2/130/0/3/140/0/20/180/2	12.1	13.8	13.1

[a] Program: initial temp. (°C)/ time (min)/ slope (°C/min)/ temp. (°C)/ time (min)/ slope (°C/min)/ temp. (°C)/ time (min).

6.3. GC analyses for determination of ee *and* de *of α-substituted amino esters*

The following chiral GC columns were used: Varian Chirasil Dex CB (25 m x 0.25 mm x 0.25 µm, 12.2 psi N_2).

Table S19. Determination of *ee* and *de* values by GC.

compound[a]	program[b]	retention time (min)			
		syn-**2**		*anti*-**3**	
		(2*R*,3*S*)	(2*S*,3*R*)	(2*S*,3*S*)	(2*R*,3*R*)
b	100/3/2/130/0/3/140/0/20/180/2	16.4	17.0	14.0	15.1
c	100/3/2/130/0/3/140/0/20/180/2	18.9	19.5	15.1	16.8
e	100/3/2/130/0/3/140/0/20/180/2	18.8	19.4	16.3	17.3
f	100/3/2/130/0/3/140/0/20/180/2	21.0	21.4	17.7	19.1
g	100/3/2/130/0/3/140/0/20/180/2	19.4	19.8	16.9	17.5
h	80/0/1/140/0/20/180/2	44.5	45.0	38.0	39.7
j	130/0/1/160/0/20/180/2	(2*R*,1'*S*) 22.8	(2*S*,1'*R*) 23.7	(2*S*,1'*S*) 20.9	(2*R*,1'*R*) 22.3
k	90/0/1/145/0/20/180/2	(1*R*,2*S*) 46.2	(1*S*,2*R*) 47.3	(1*S*,2*S*) 56.0	(1*R*,2*R*) 56.3

[a] Determined as the corresponding *N*-acetylated derivatives. [b] Program: initial temp. (°C)/ time (min)/ slope (°C/min)/ temp. (°C)/ time (min)/ slope (°C/min)/ temp. (°C)/ time (min).

6.4. HPLC analyses for determination of ee *and* de

The following HPLC conditions were used: **A**: column Chiralpak OD (0.46 cm x 25 cm, Daicel Chemical Ind. Ltd.); isocratic eluent: *n*-hexane / *i*-propanol (95:5), 30°C, flow 0.8 mL min^{-1}. **B**: column Chiralpak OD (0.46 cm x 25 cm, Daicel Chemical Ind. Ltd.); isocratic eluent: *n*-hexane / *i*-propanol (97:3), 30°C, flow 0.8 mL min^{-1}.

Table S20. Determination of *ee* and *de* values by HPLC.

compound[a]	conditions	retention time (min)			
		syn-**2**		*anti*-**3**	
		(2*R*,3*S*)	(2*S*,3*R*)	(2*S*,3*S*)	(2*R*,3*R*)
d	**A**	36.5	24.9	20.4	15.9
i	**B**	44.5	32.6	19.5	17.6

[a] Determined as the corresponding *N*-acetylated derivatives.

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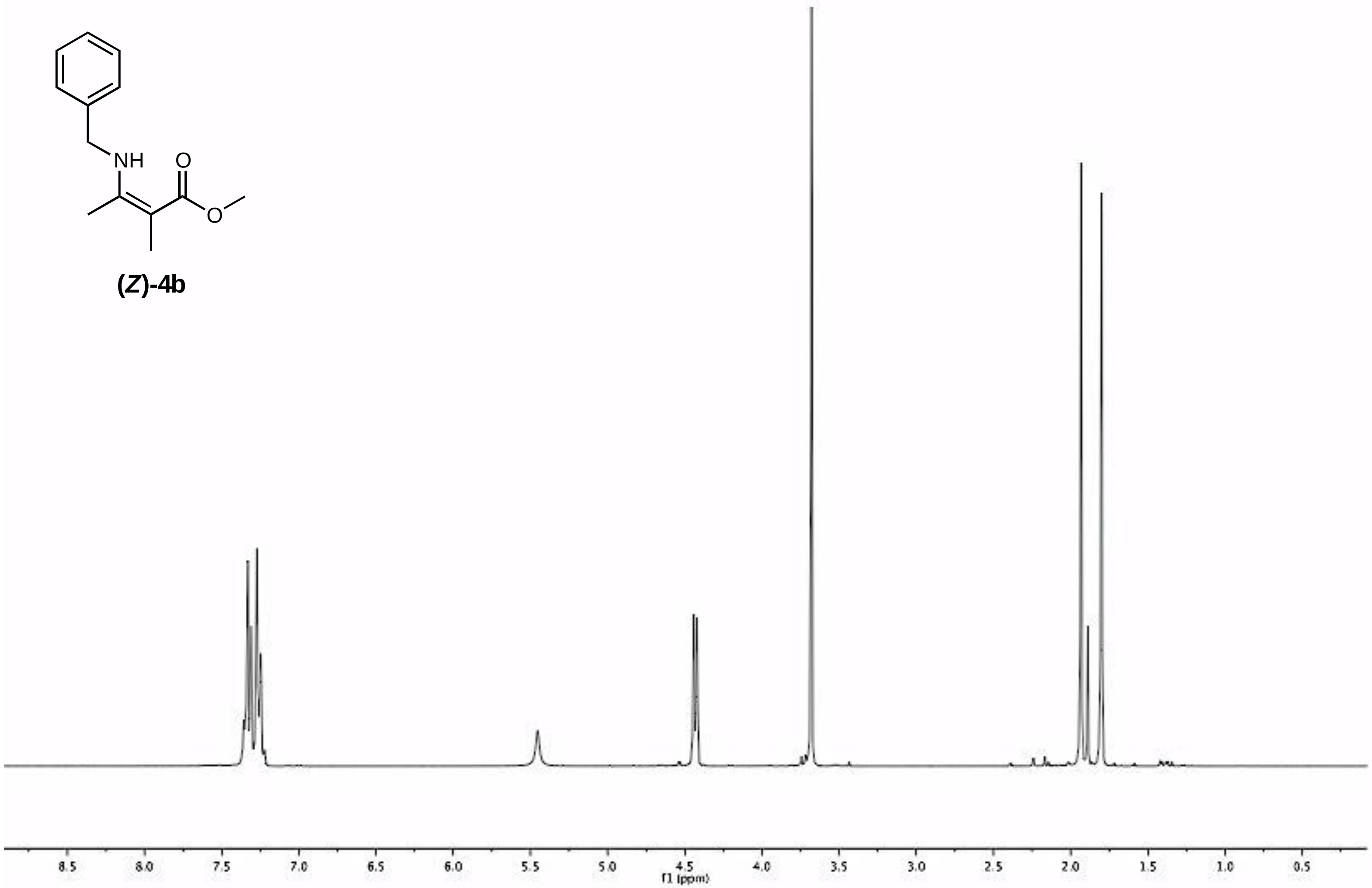
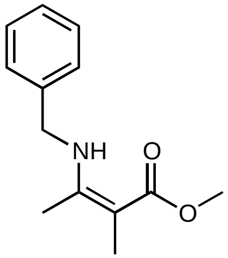
8. Compound NMR spectra

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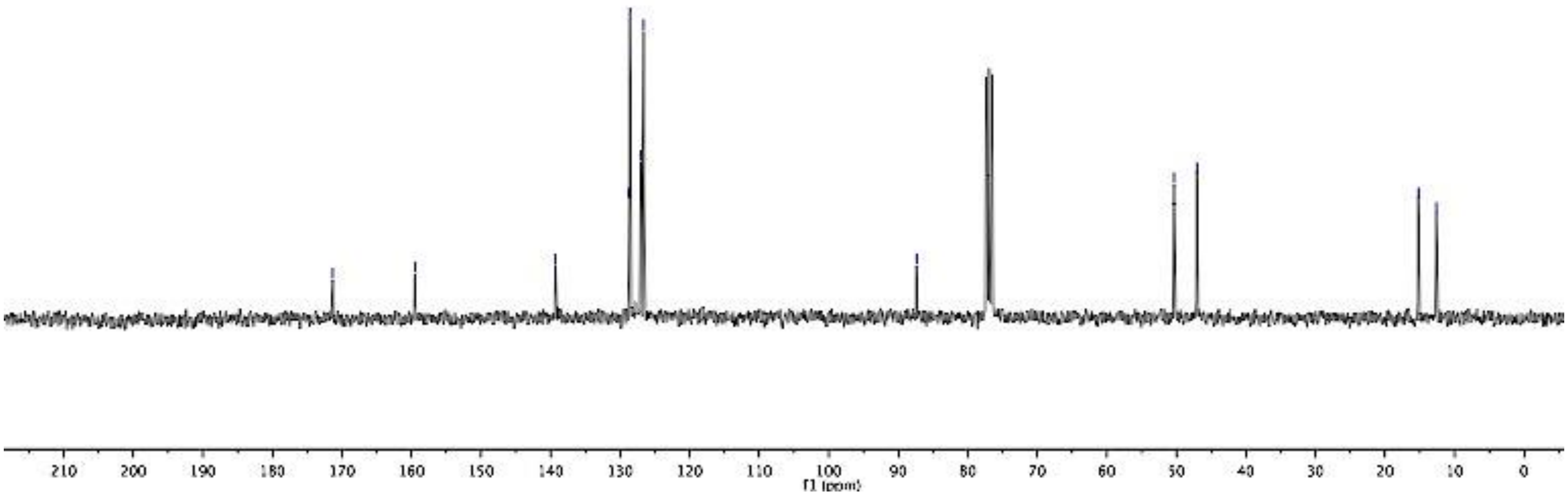
(*Z*)-4b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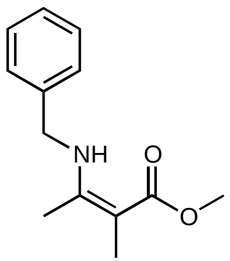
f1 (ppm)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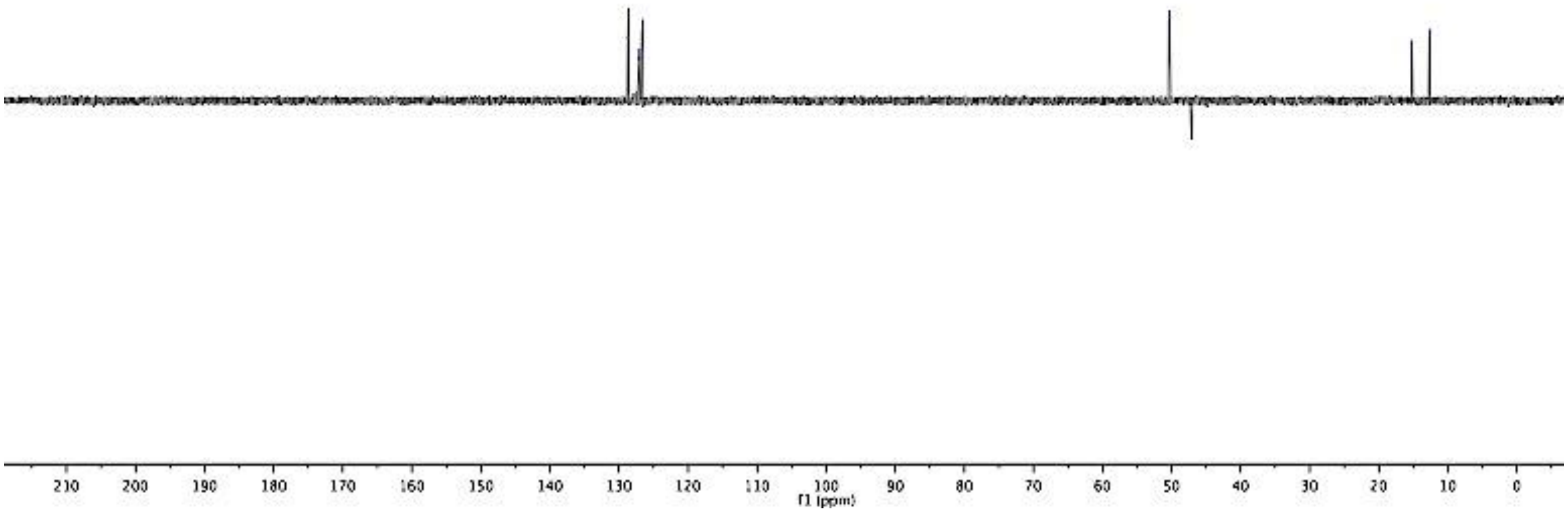
O
O

(*Z*)-4b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70
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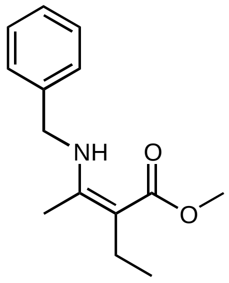
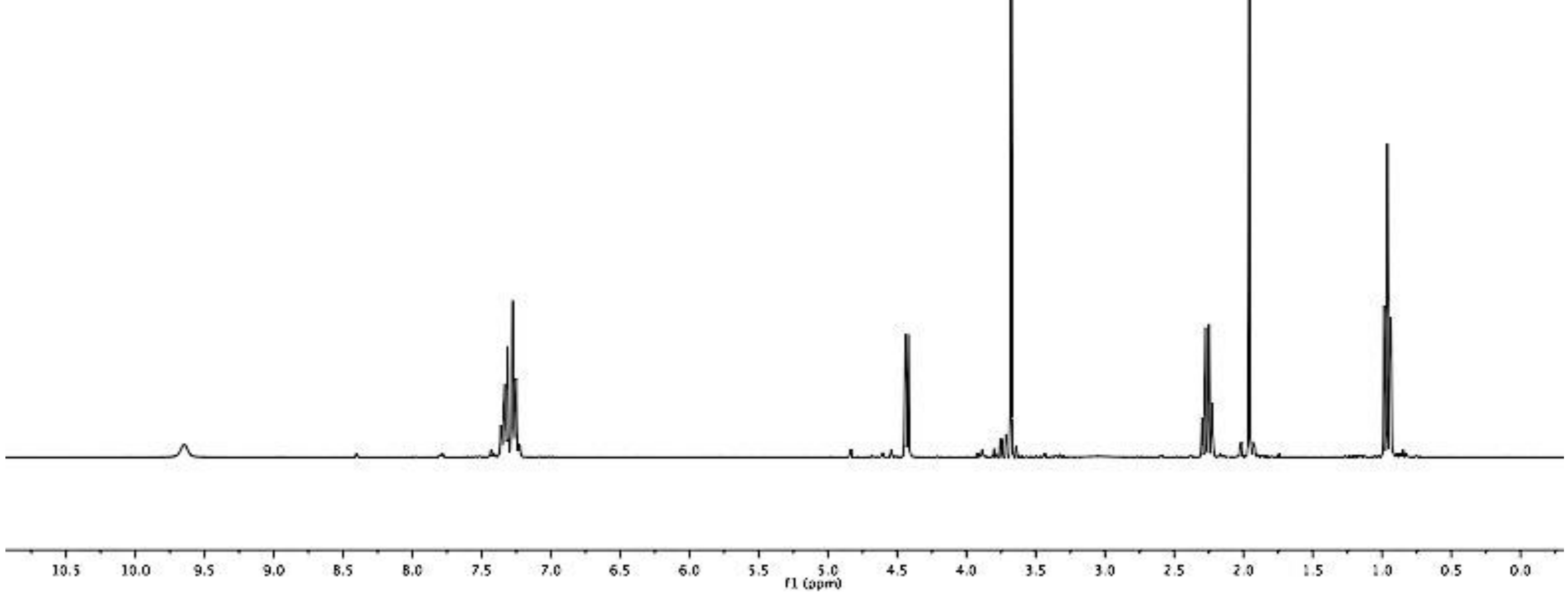
30
20
10
0



(*Z*)-4c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6.0
5.5
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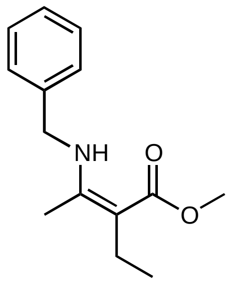
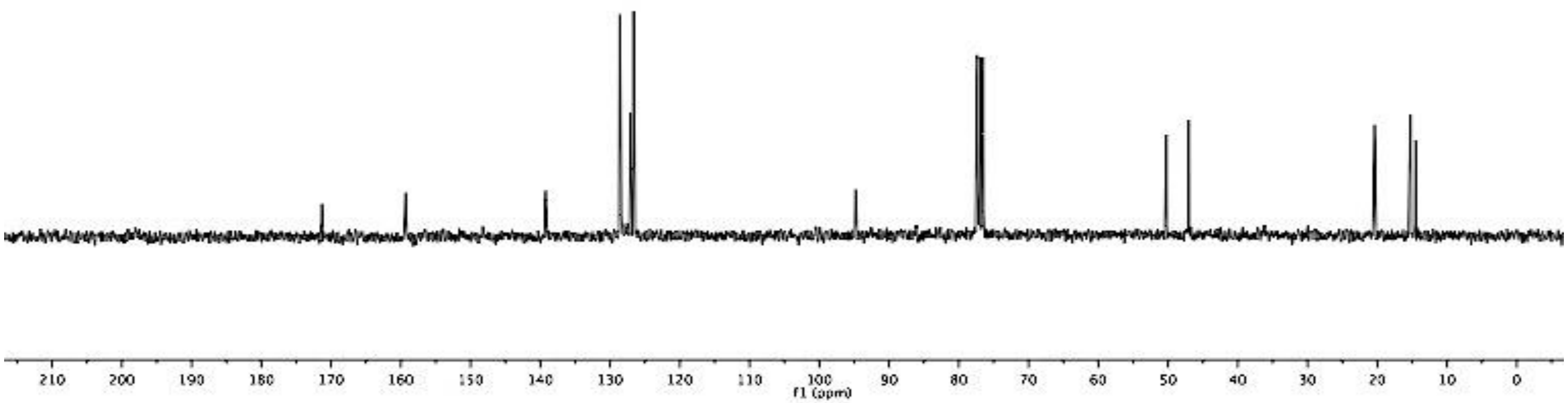
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0



(*Z*)-4c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f1 (ppm)
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10
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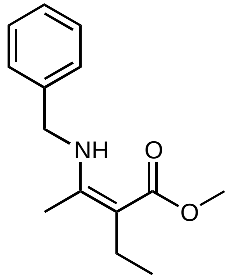

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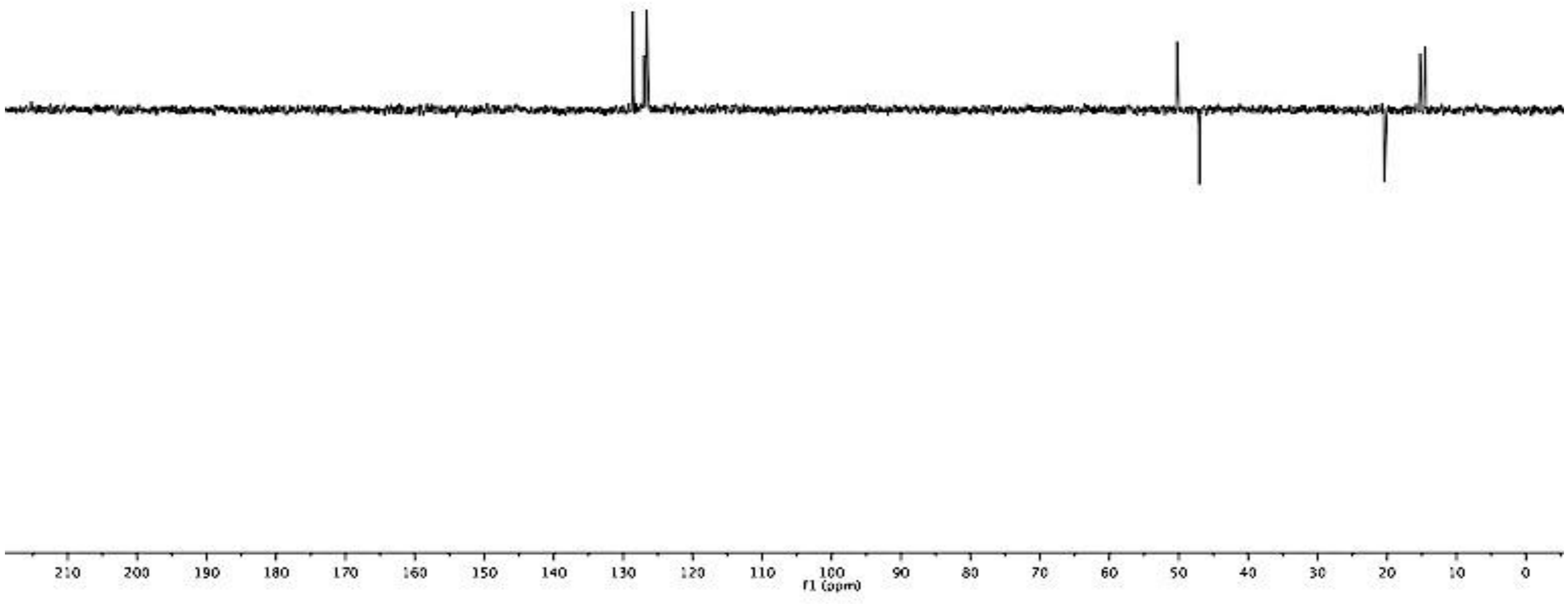
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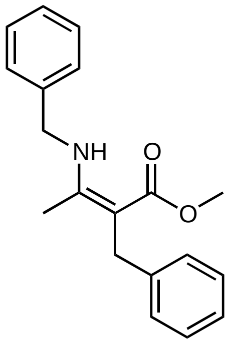
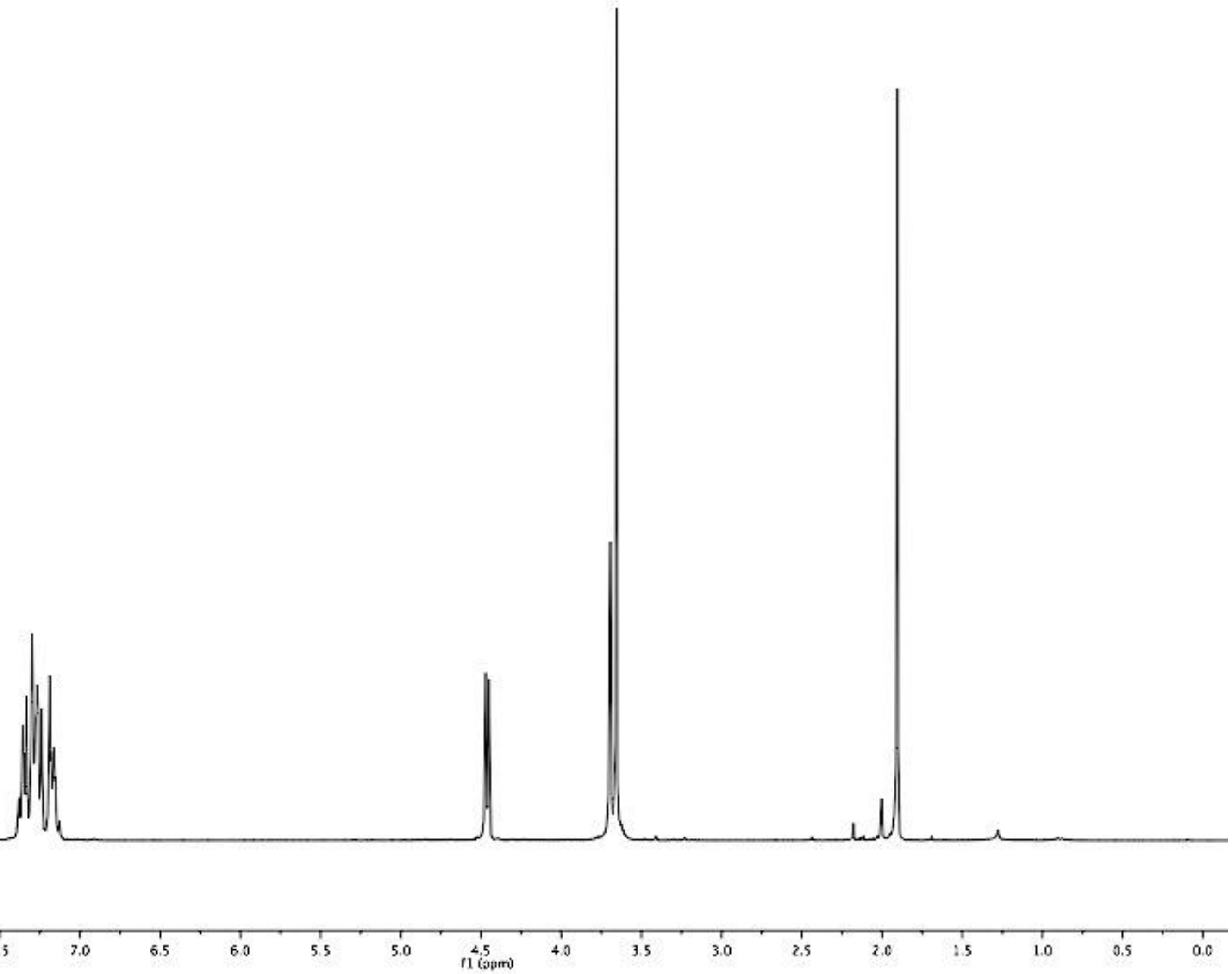
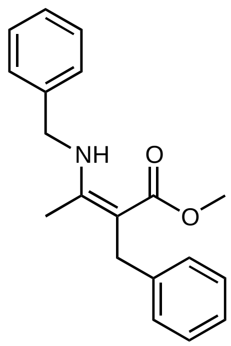
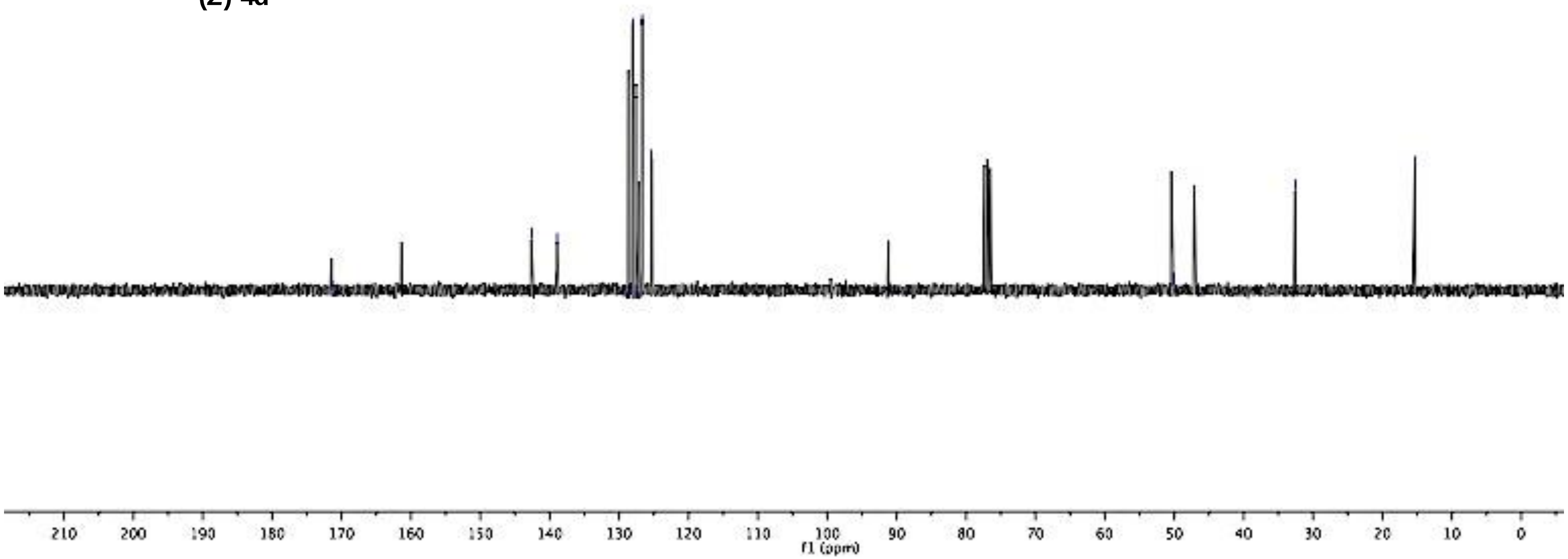


(*Z*)-4d




NH
O
O

(*Z*)-4d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f1 (ppm)
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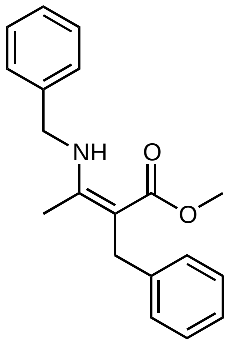
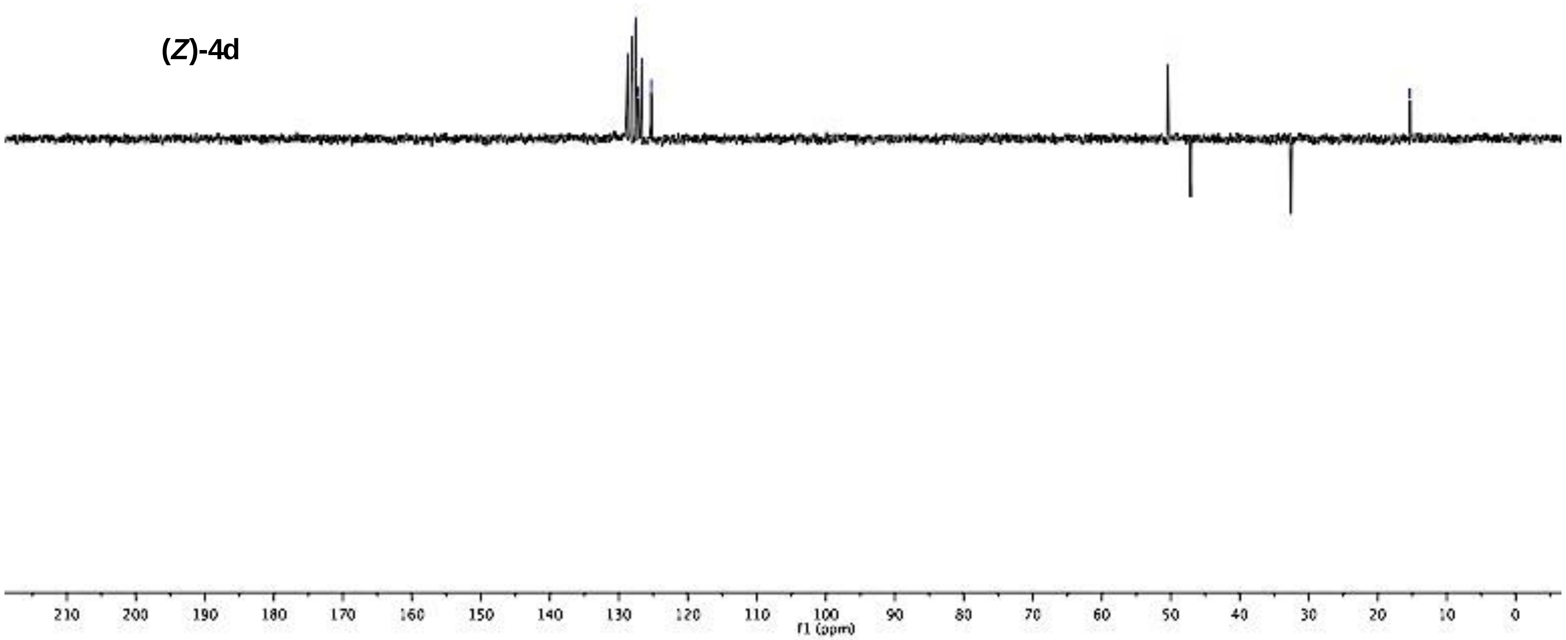

NH
O
O

(*Z*)-4d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f1 (ppm)
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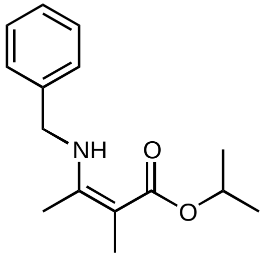
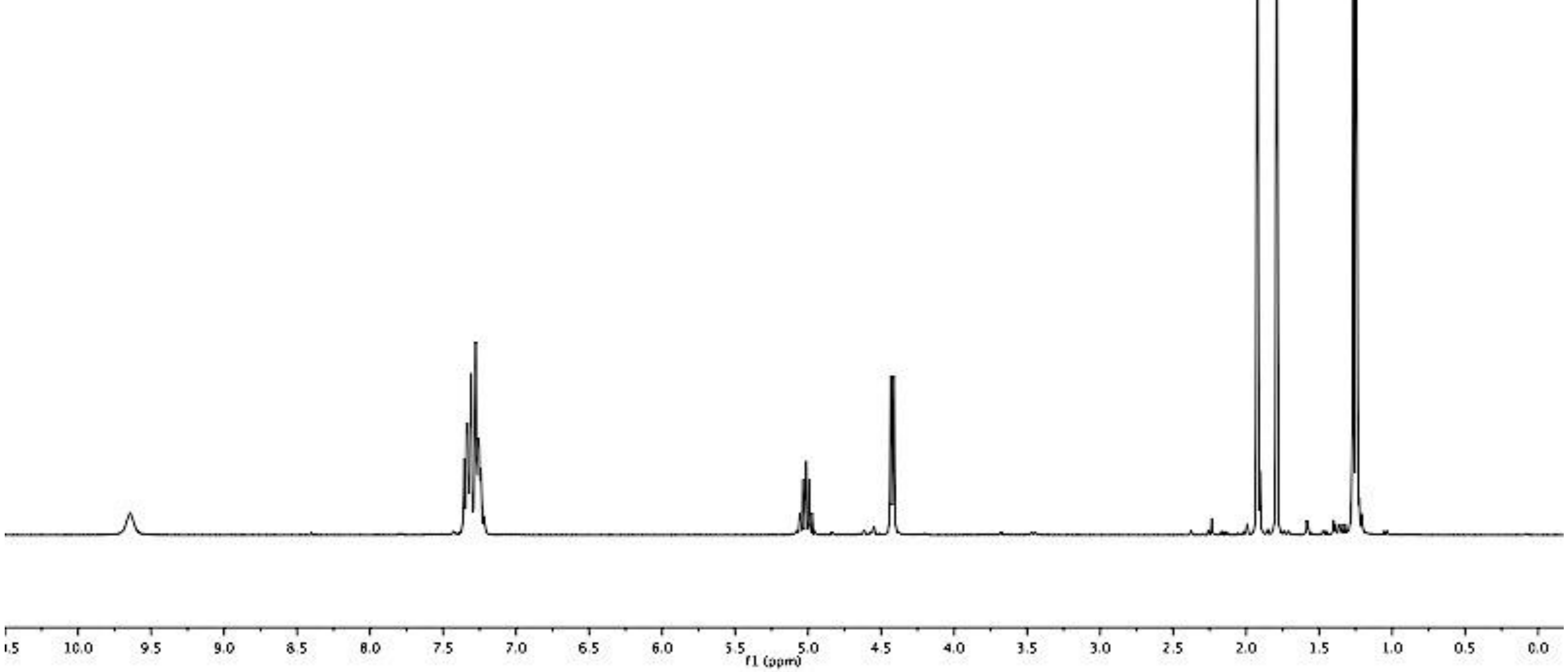
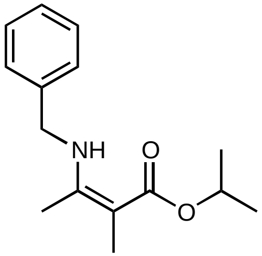
10
0

Electronic Supplementary Material (ESI) for Chemical Communications

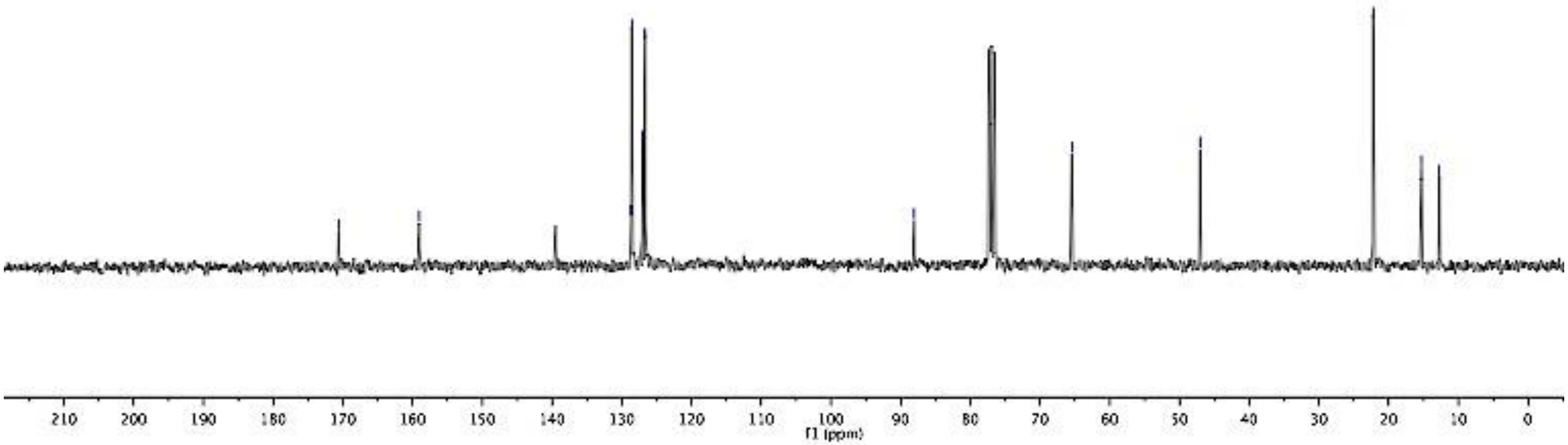


(*Z*)-4g




NH
O
O

(*Z*)-4g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f1 (ppm)
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30
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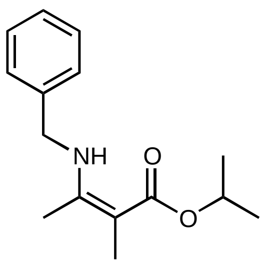
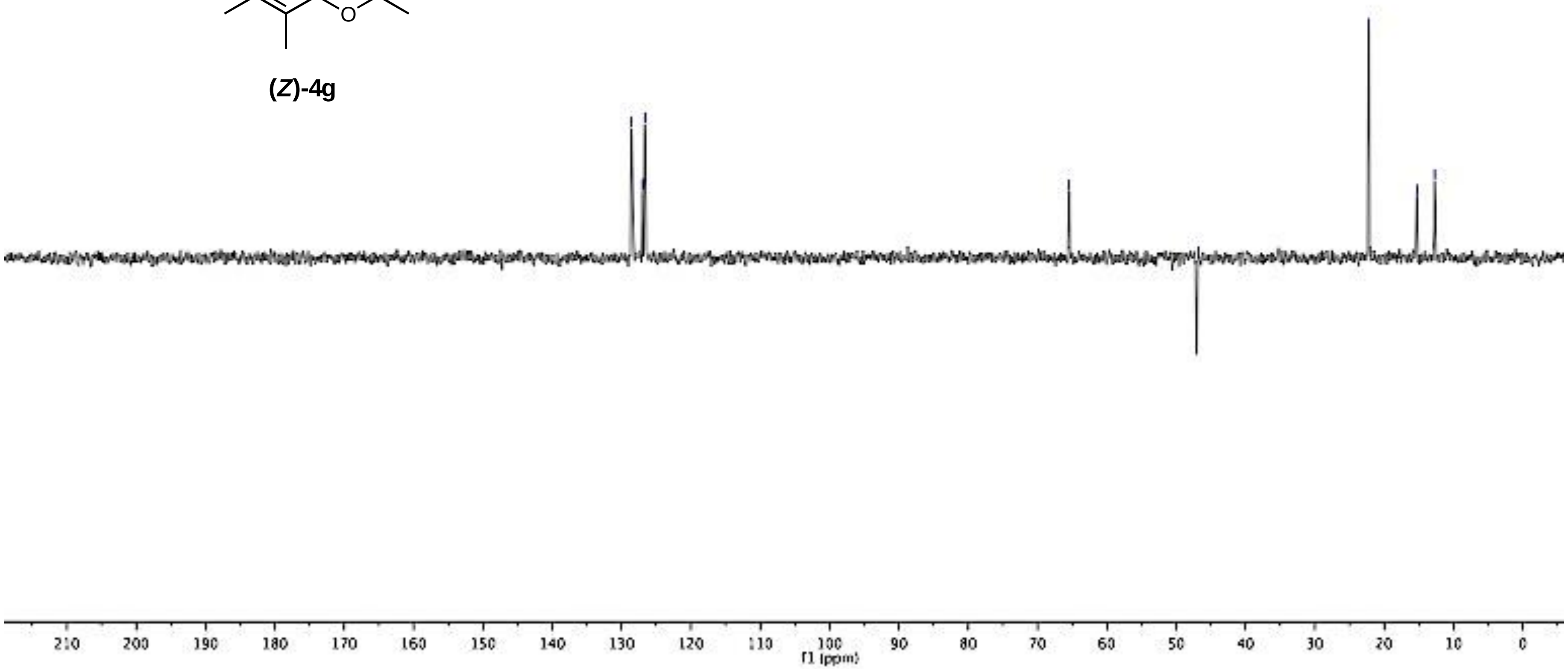
10
0



(*Z*)-4g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f1 (ppm)
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30
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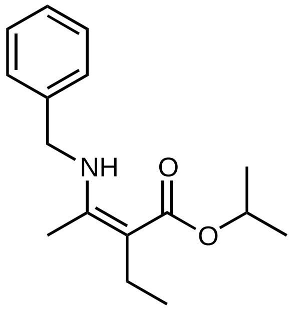
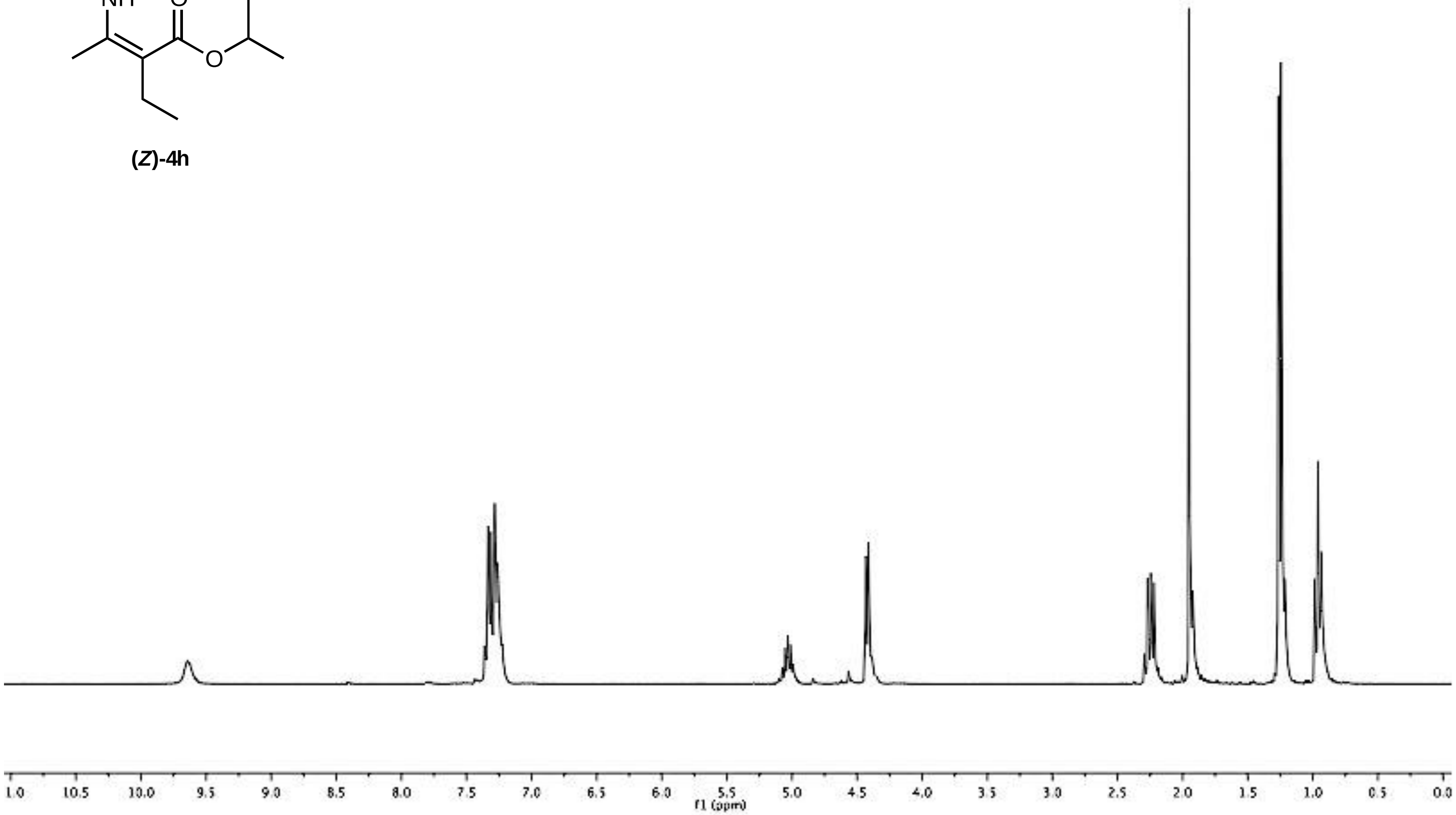
10
0


NH
O
O

(*Z*)-4h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6.0
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5.0
4.5
4.0
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2.5
2.0
1.5
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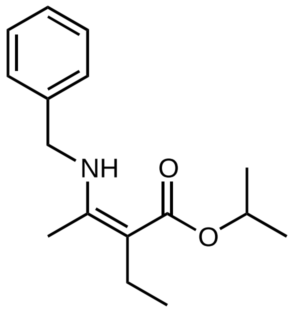
0.5
0.0
f1 (ppm)

Electronic Supplementary Material (ESI) for Chemical Communications



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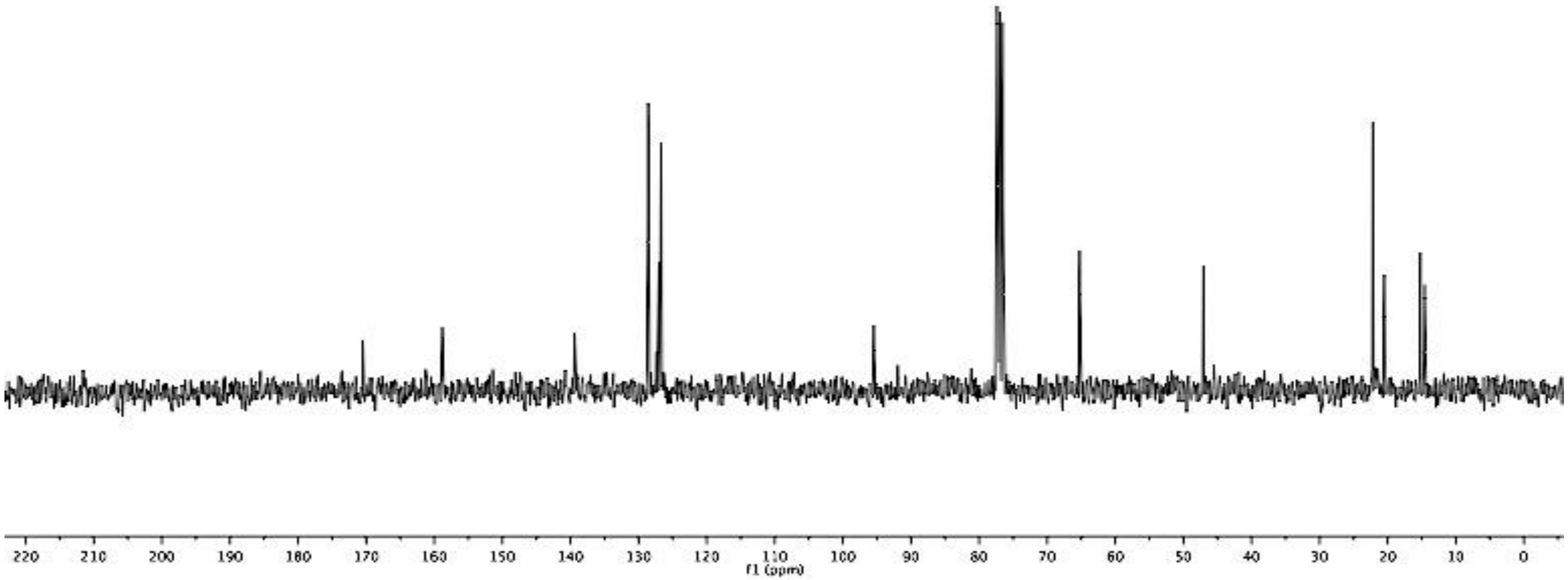
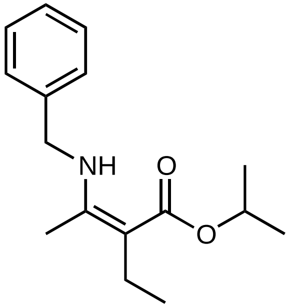
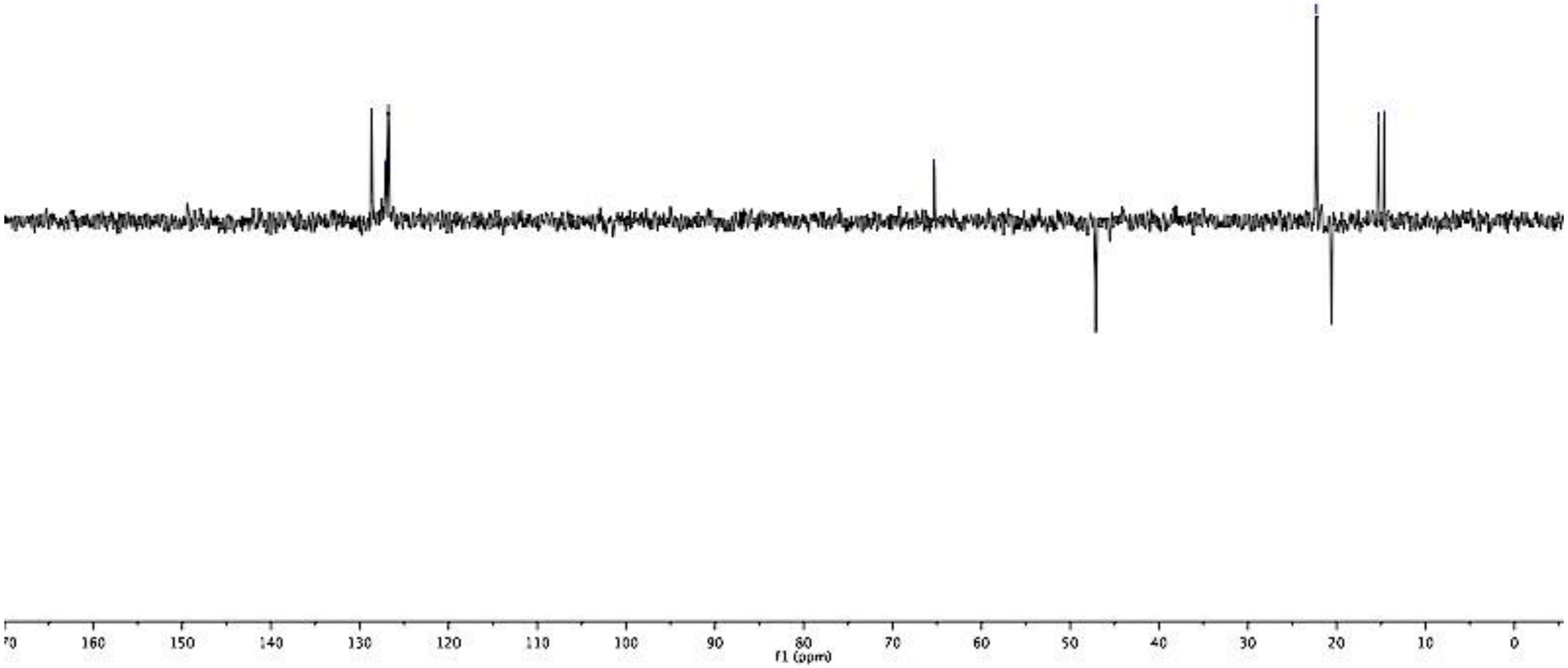
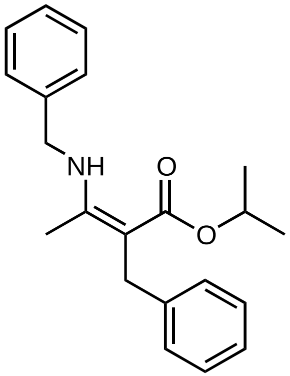


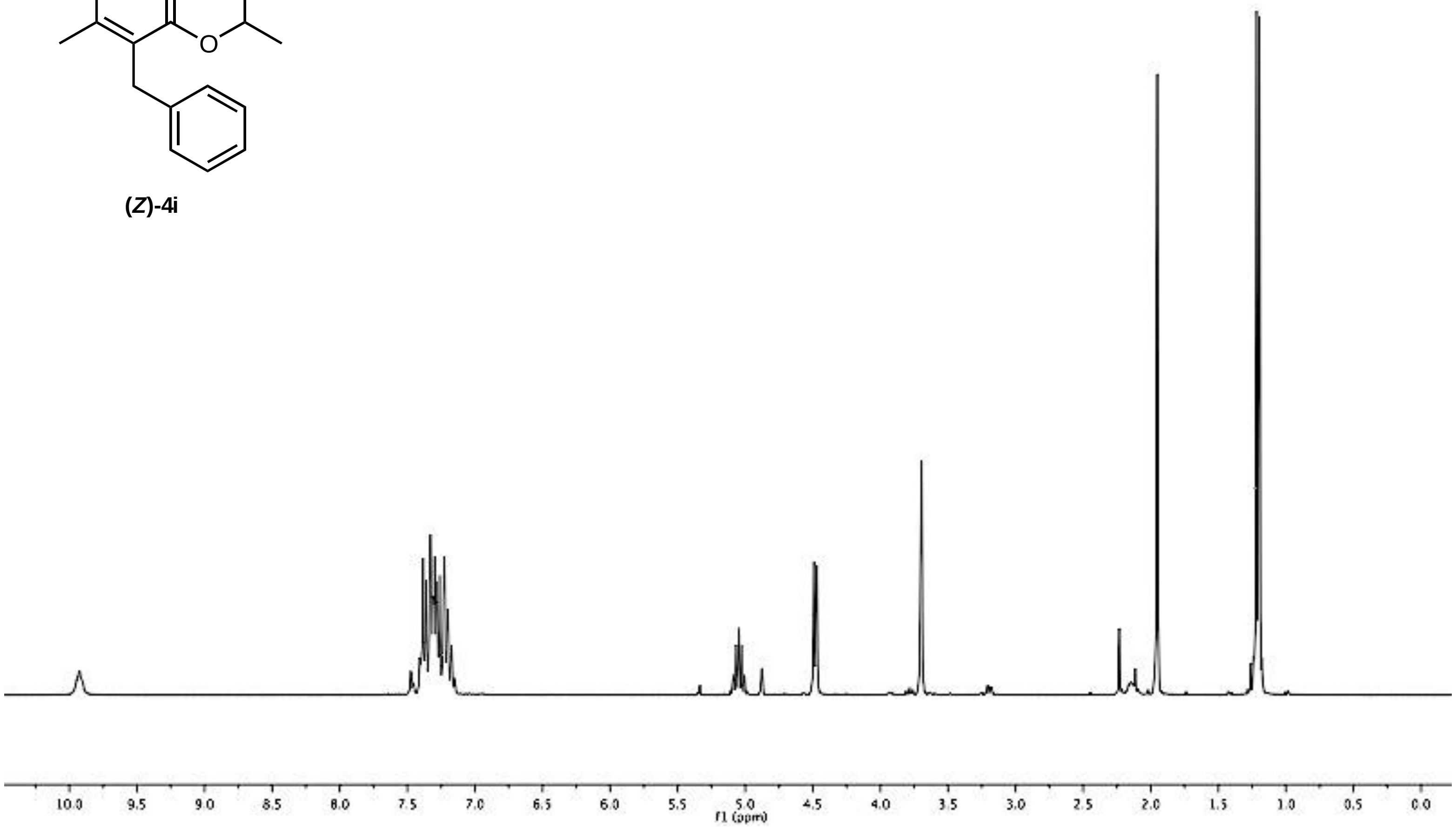


(*Z*)-4h




NH
O
O

(*Z*)-4i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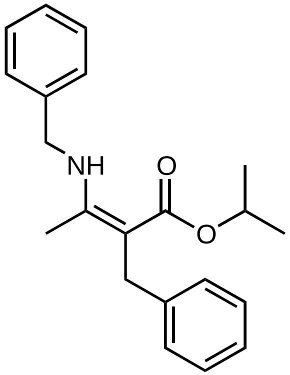
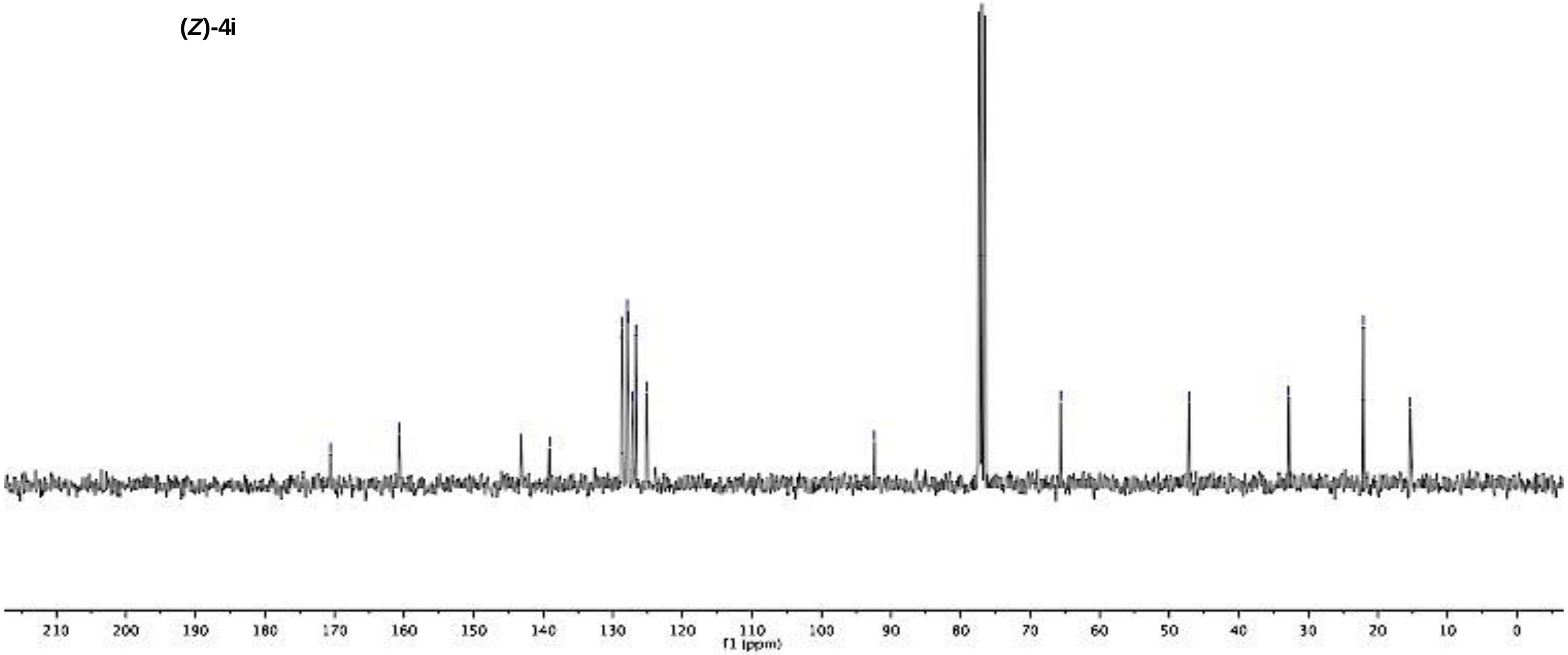
0.0
f1 (ppm)


NH
O
O

(*Z*)-4i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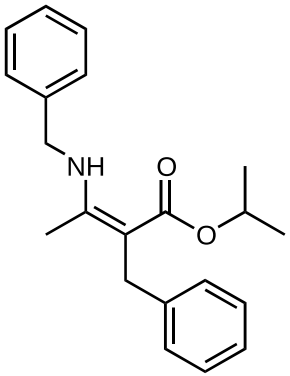
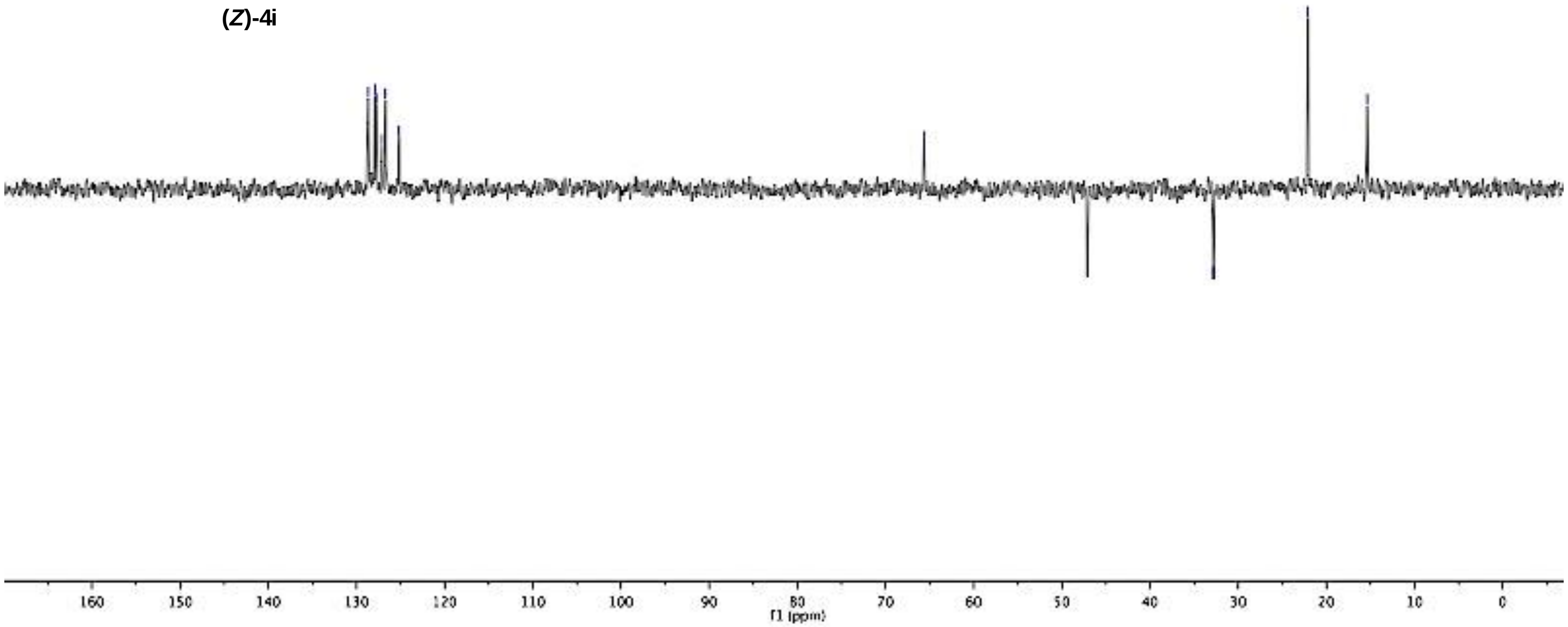
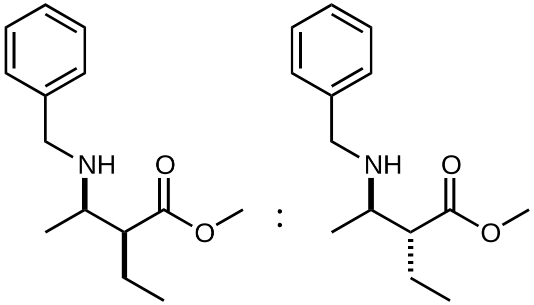
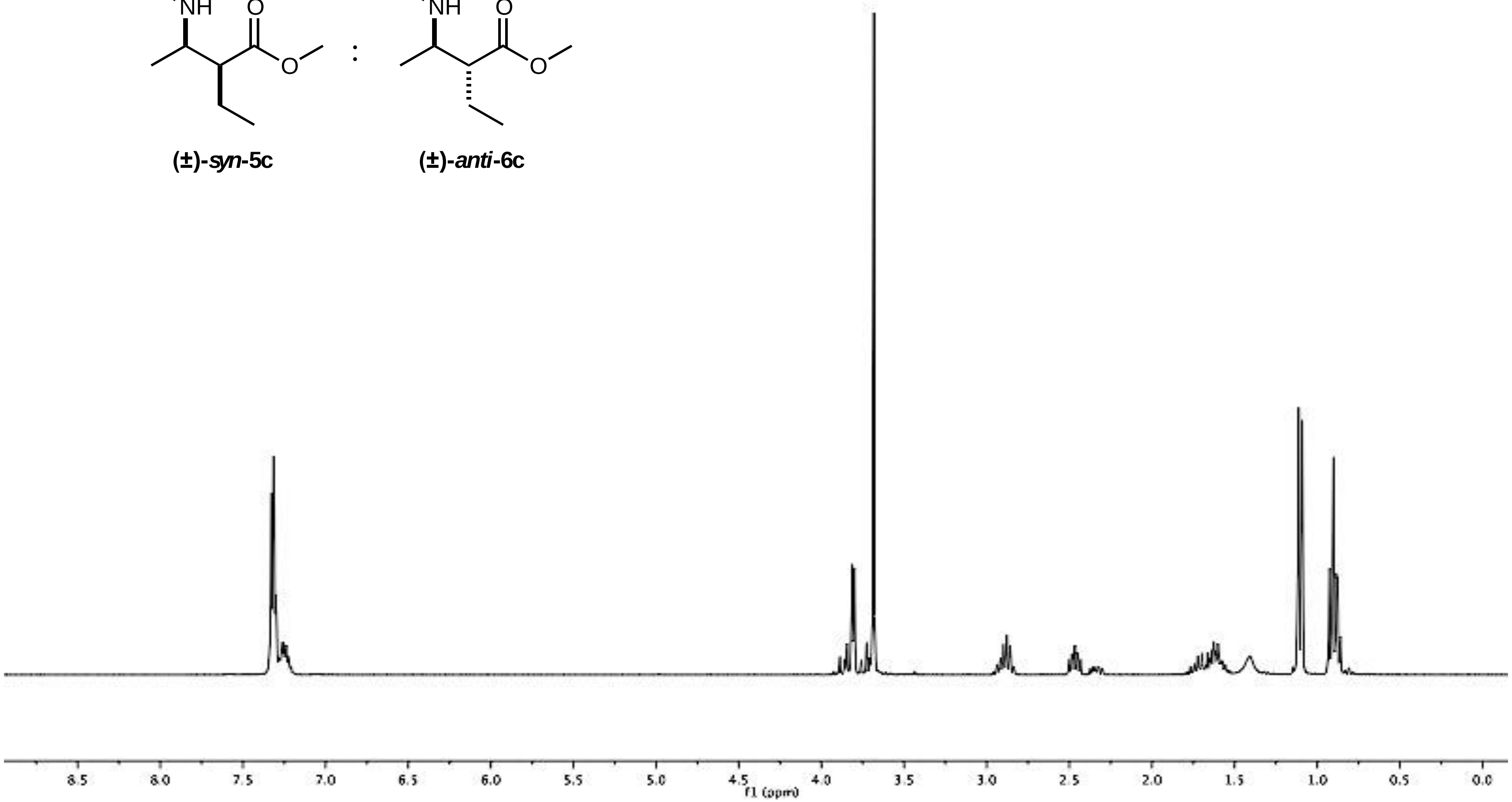


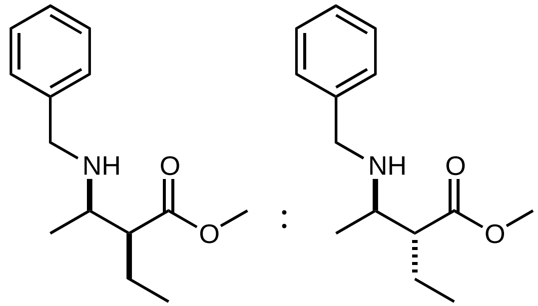
(*Z*)-4i



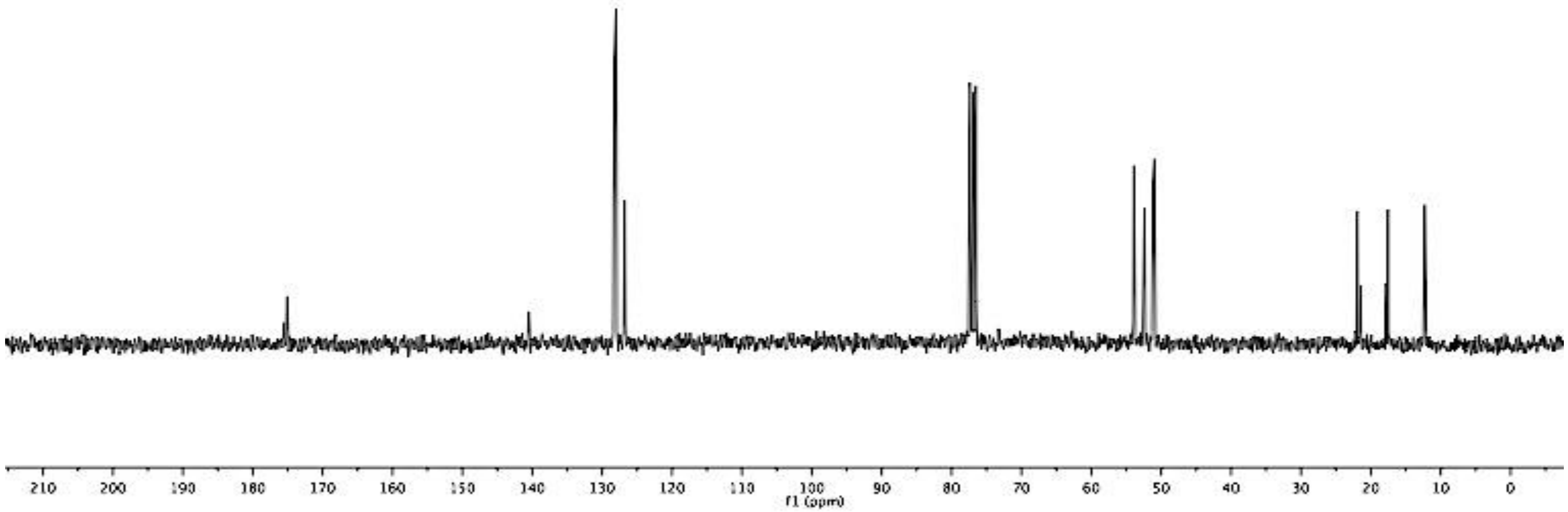


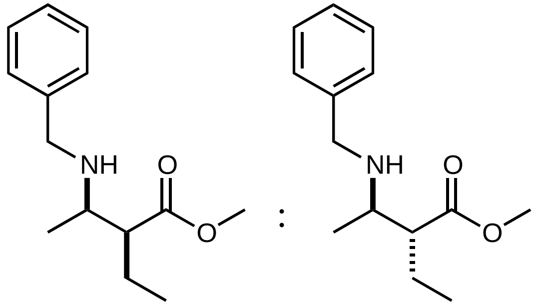
(±)-*syn*-5c **(±)-*anti*-6c**



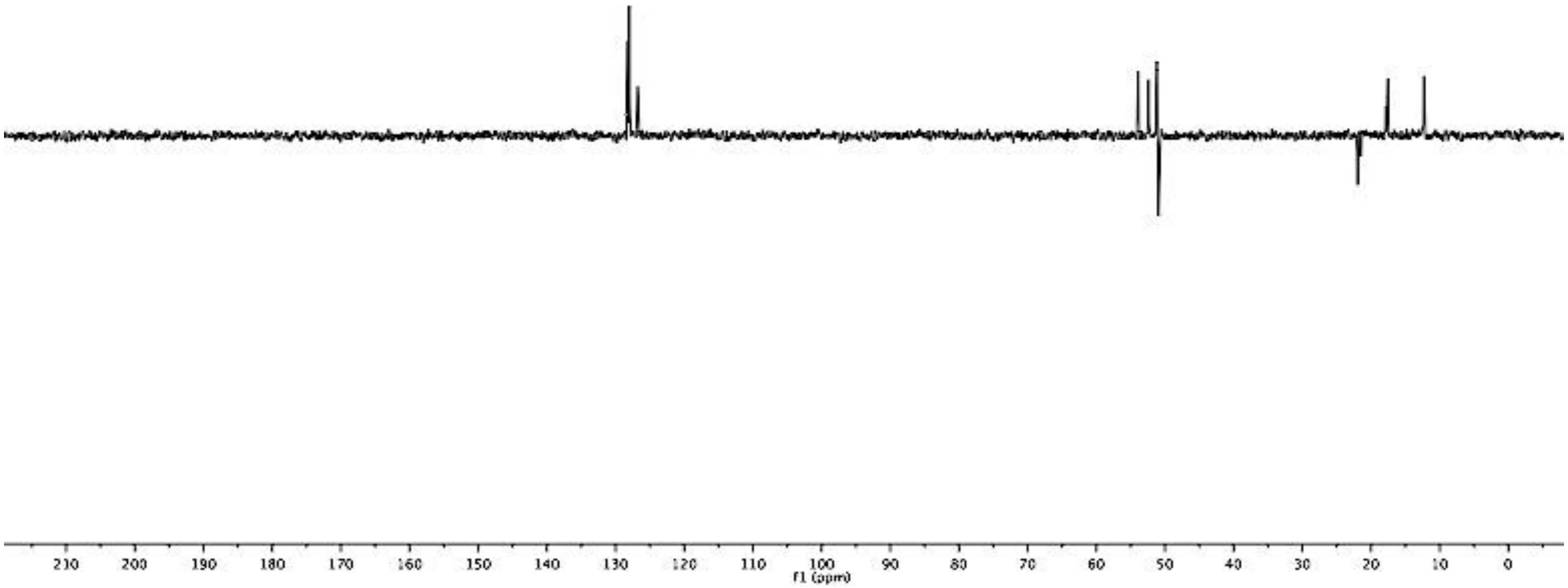


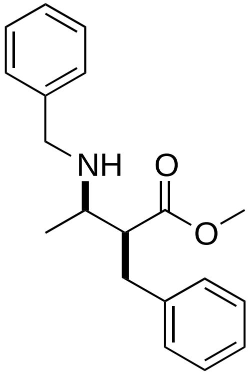
(±)-*syn*-5c **(±)-*anti*-6c**



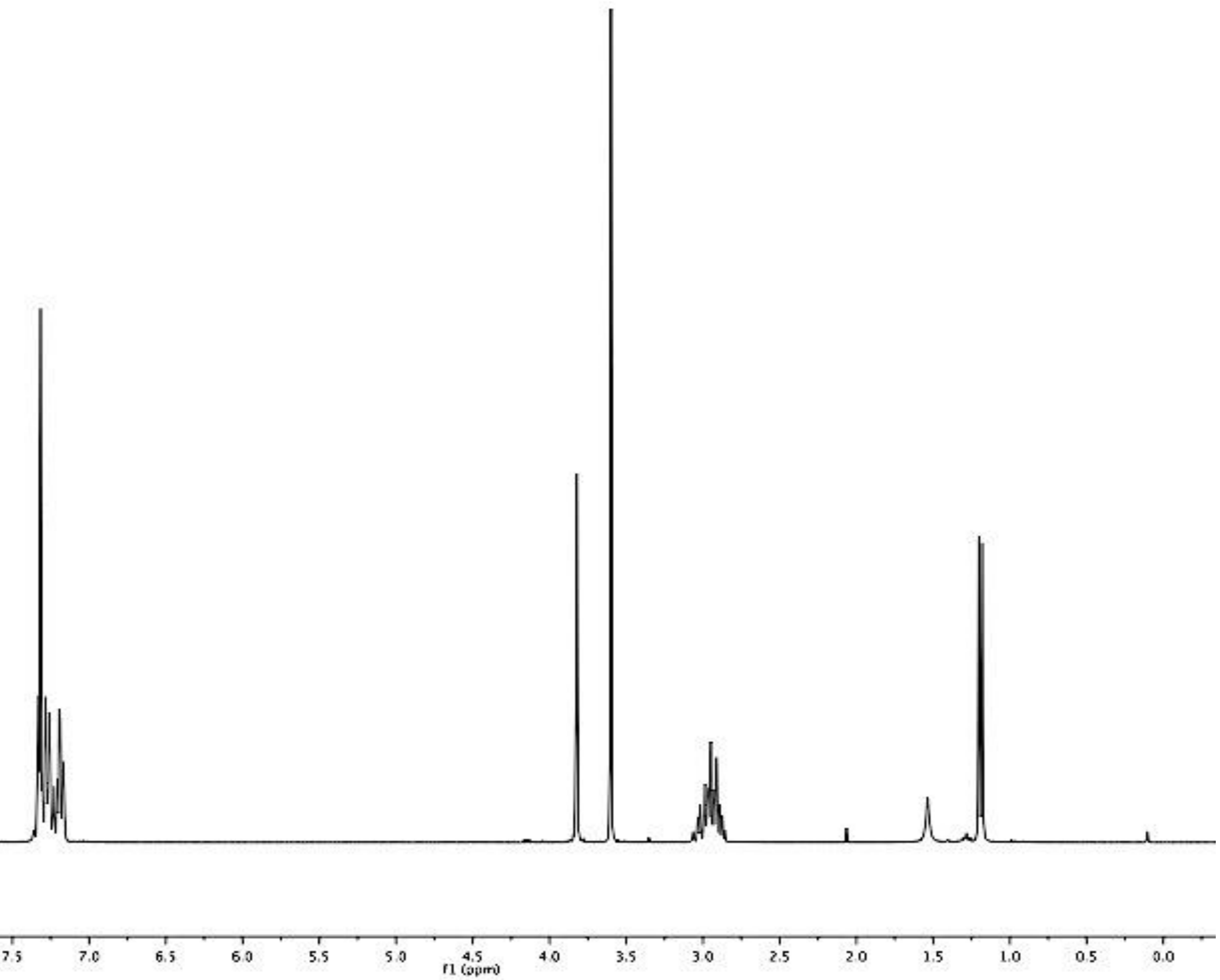


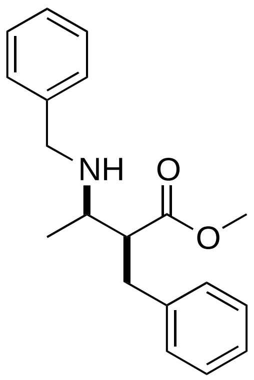
(±)-*syn*-5c (±)-*anti*-6c



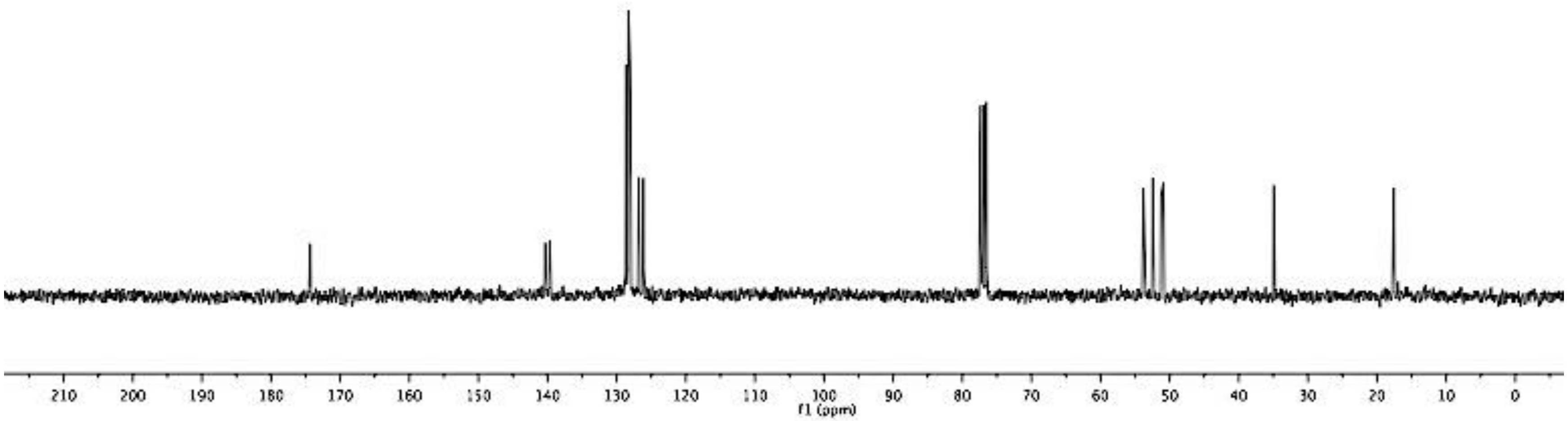


(±)-*syn*-5d




NH
O
O

(±)-*syn*-5d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f1 (ppm)
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10
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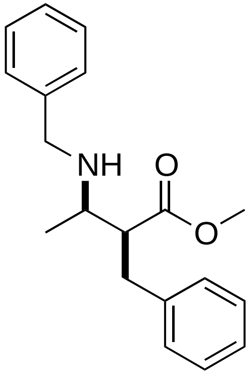
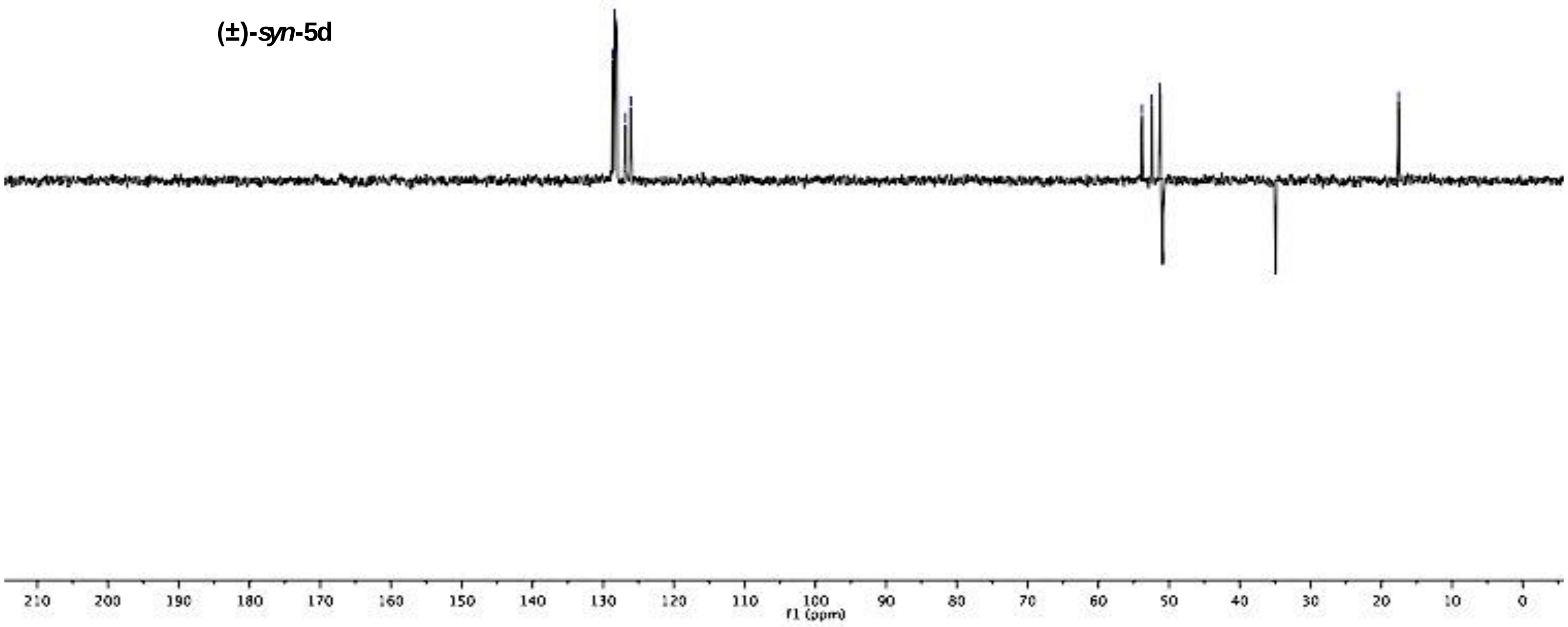

NH
O
O

(±)-*syn*-5d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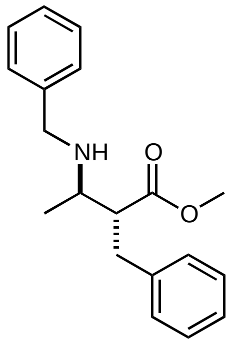
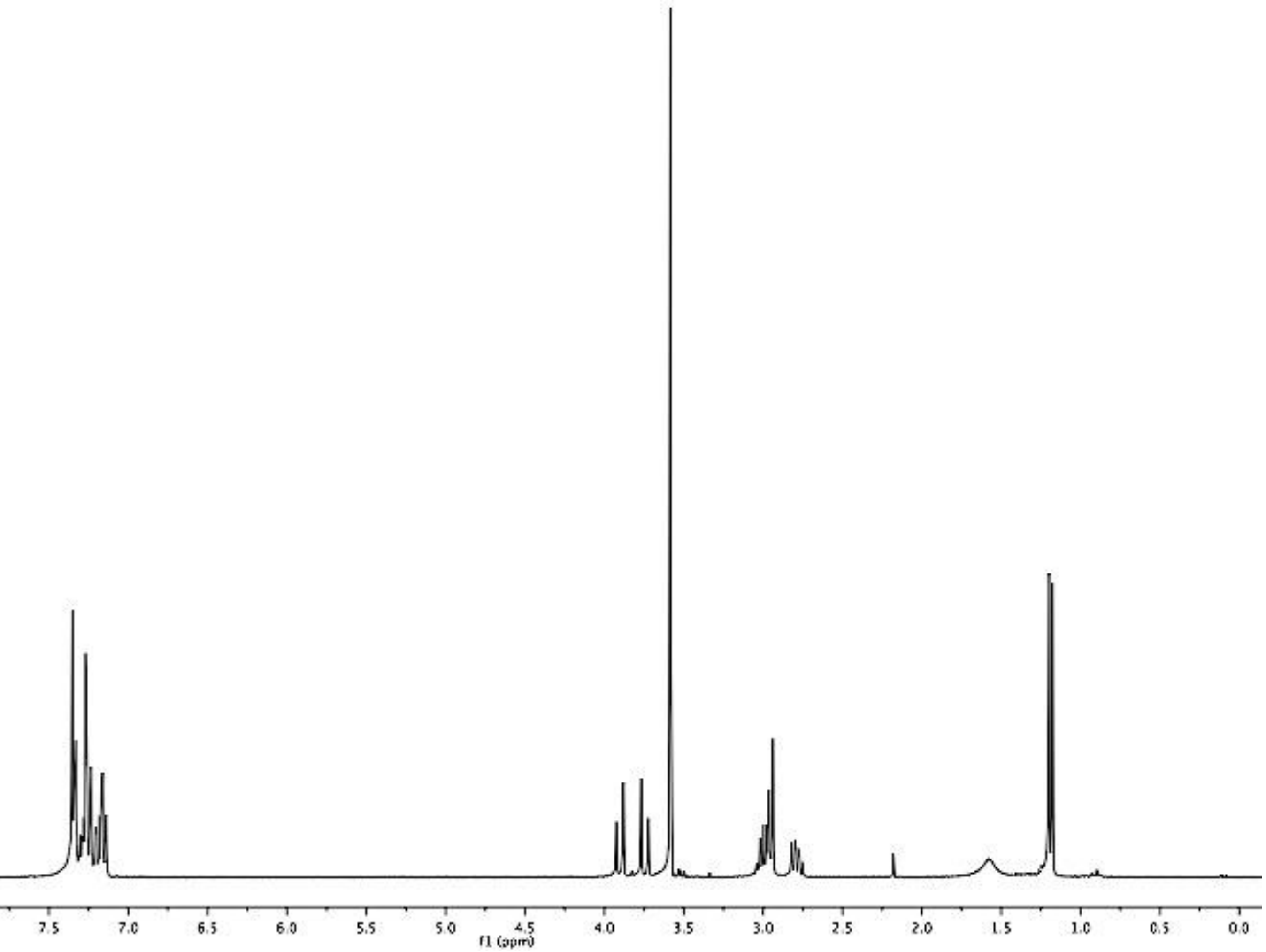
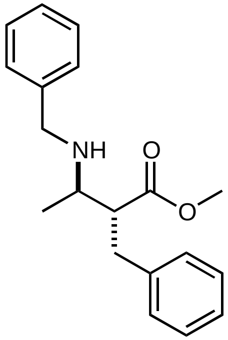
f1 (ppm)

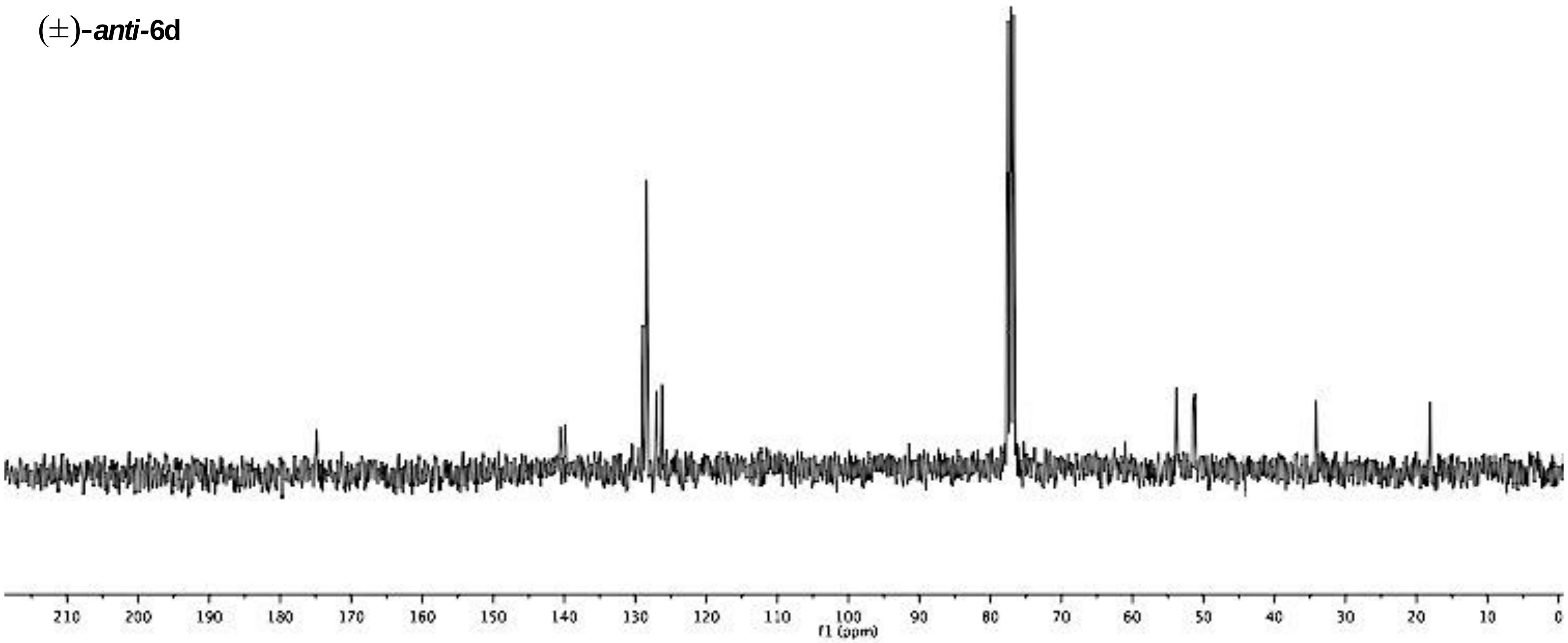


(±)-***anti*-6d**




NH
O
O

(±)-***anti*-6d**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f1 (ppm)
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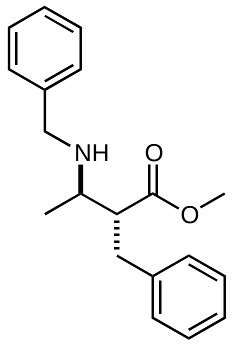
NH
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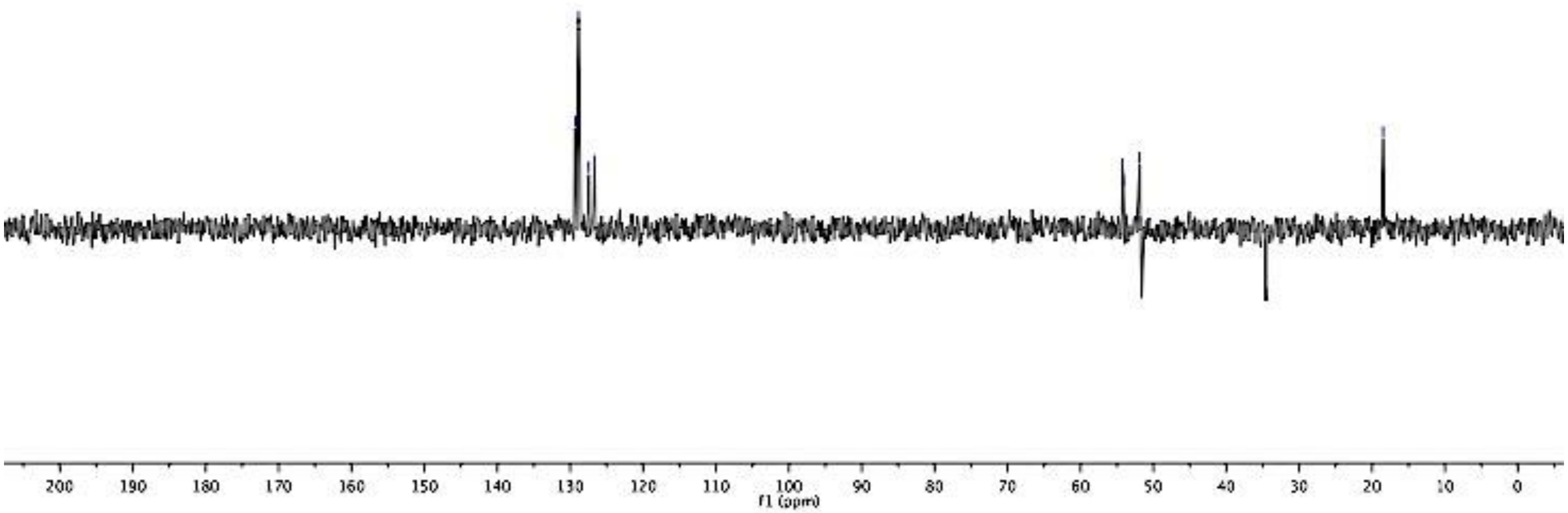
(±)-***anti*-6d**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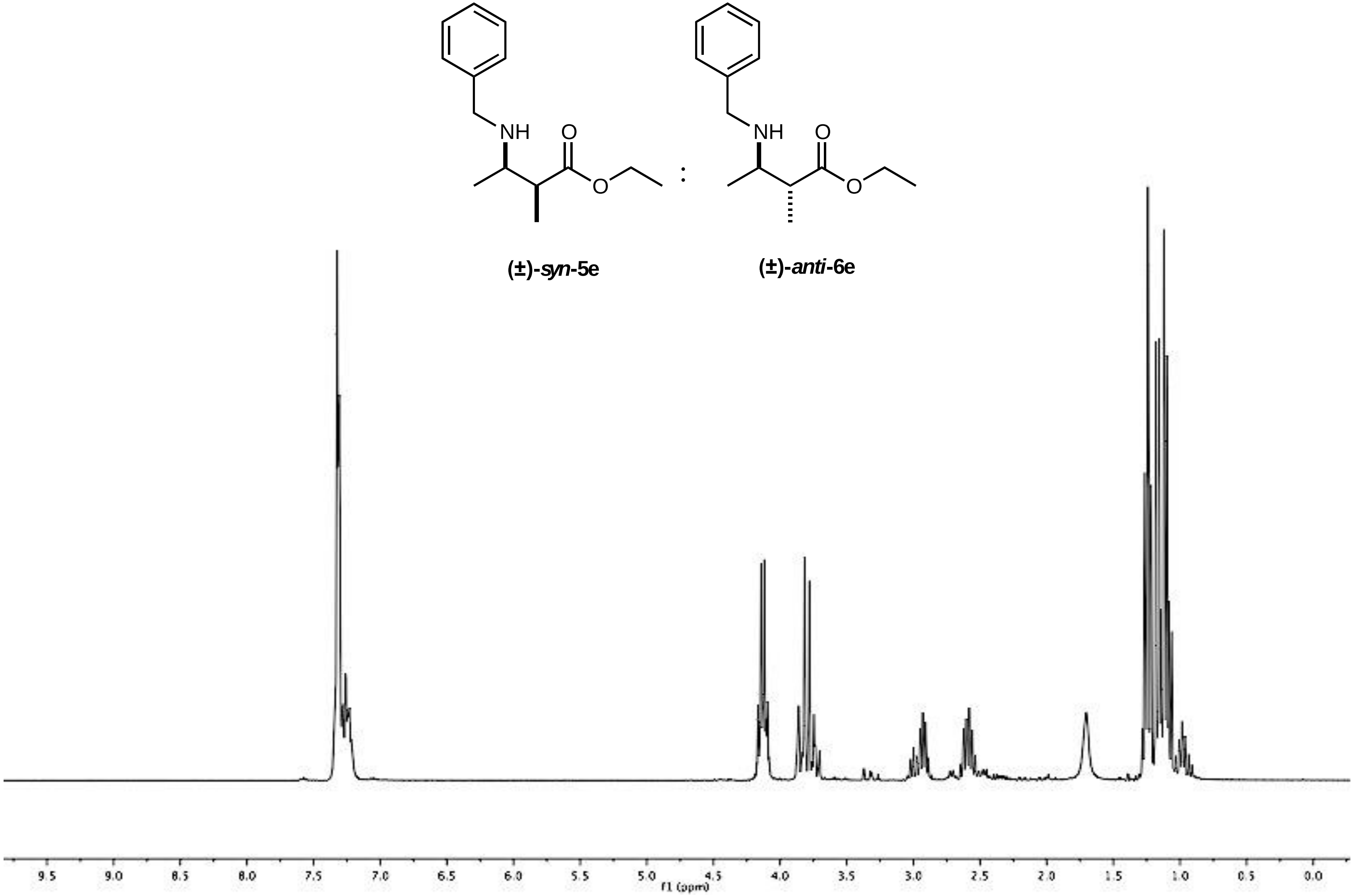
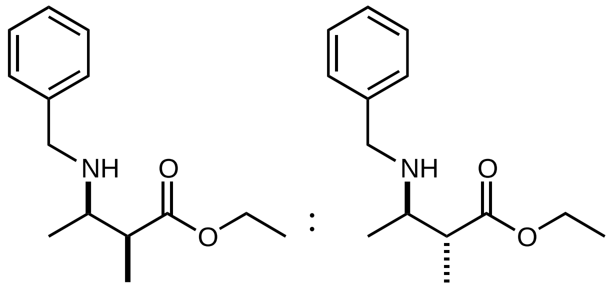
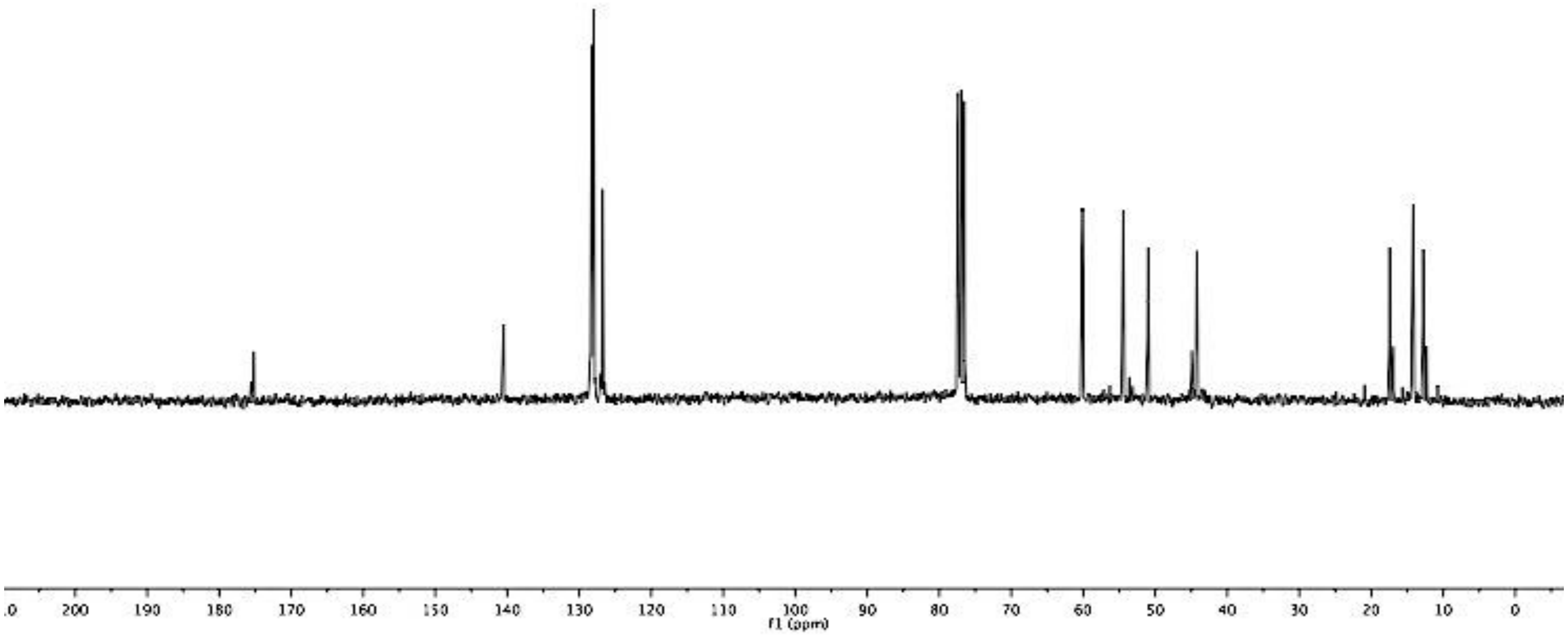
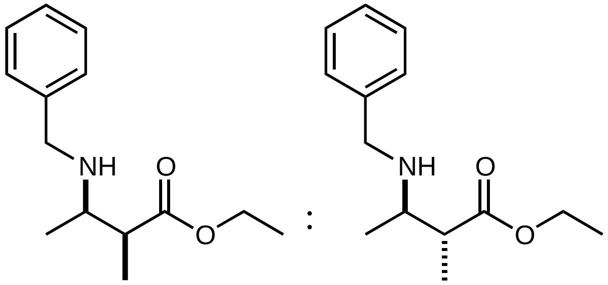

NH
O
O
(±)-*syn*-5e
(±)-*anti*-6e
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

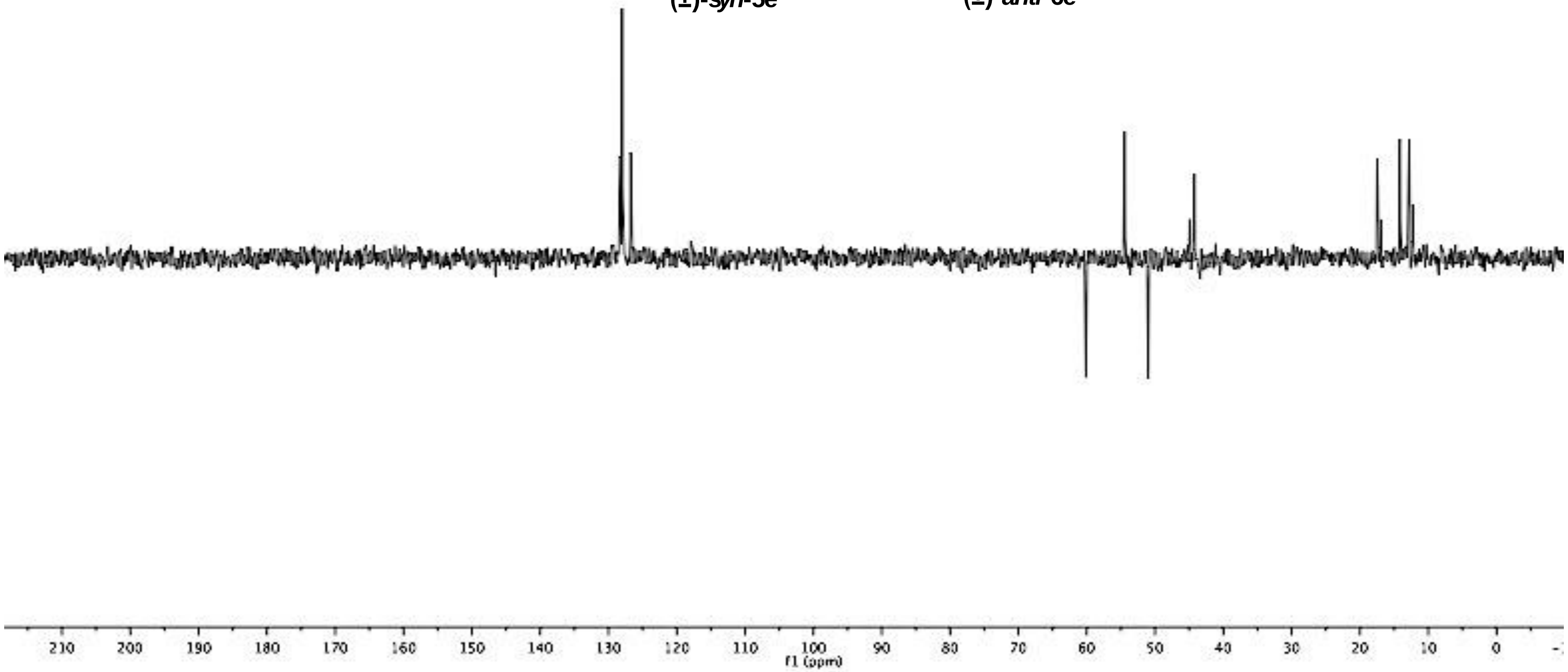


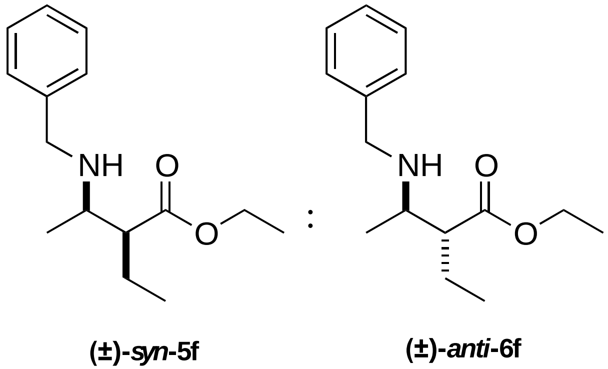
(±)-*syn*-5e **(±)-*anti*-6e**

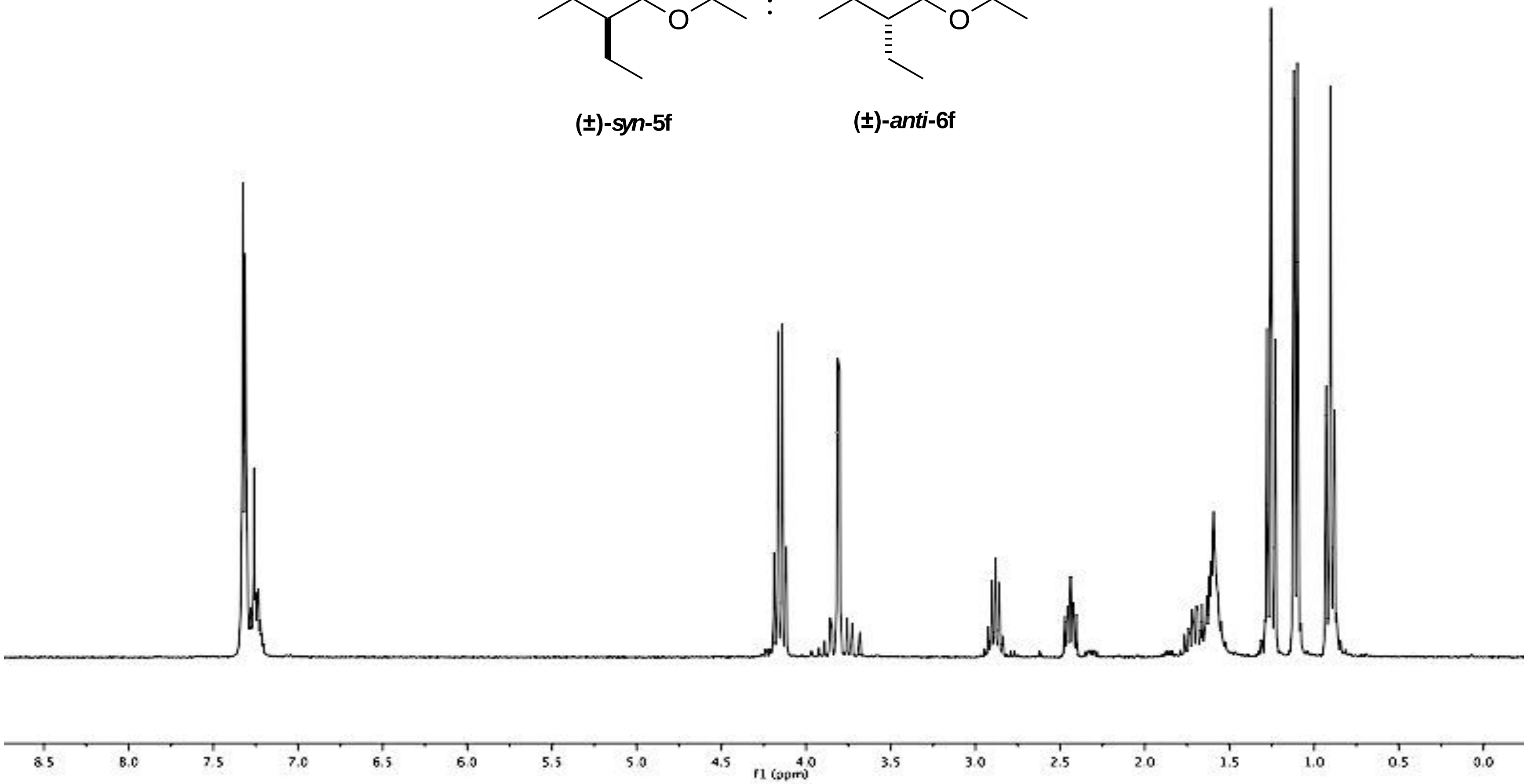




(±)-*syn*-5e : **(±)-*anti*-6e**




NH
O
O
:
NH
O
O
(±)-syn-5f
(±)-anti-6f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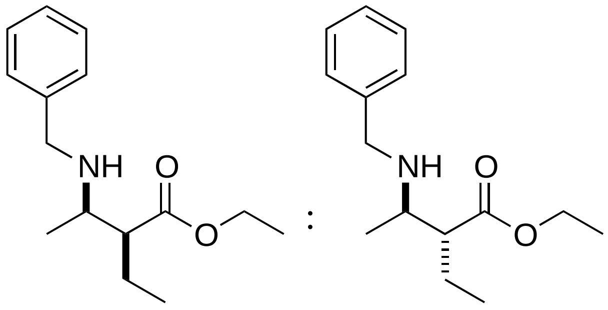
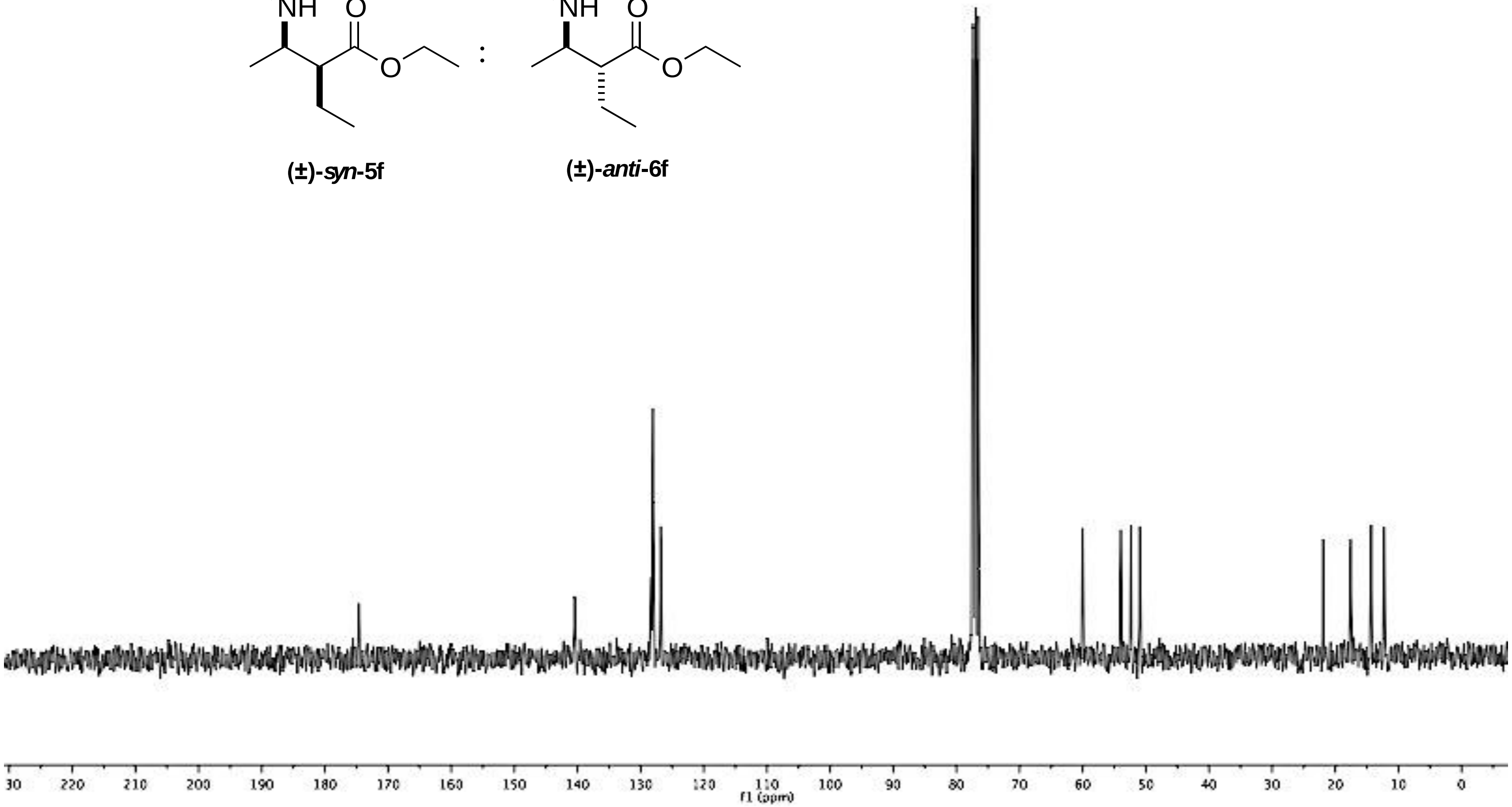
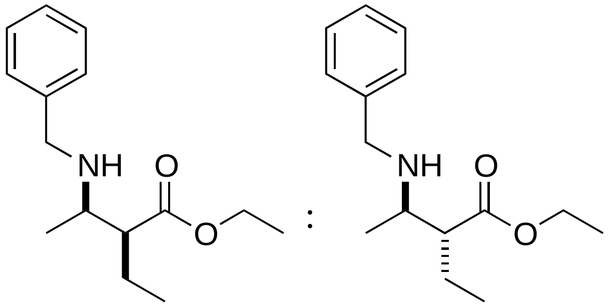
1.0
0.5
0.0
f1 (ppm)



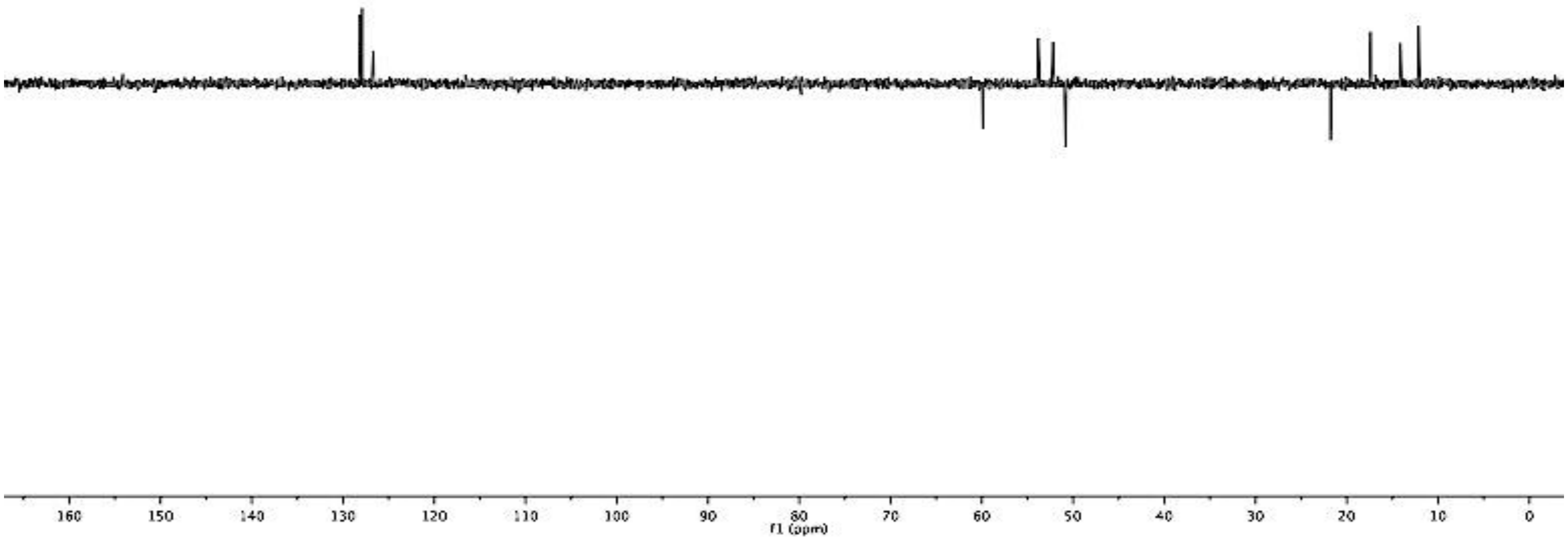
(±)-*syn*-5f (±)-*anti*-6f

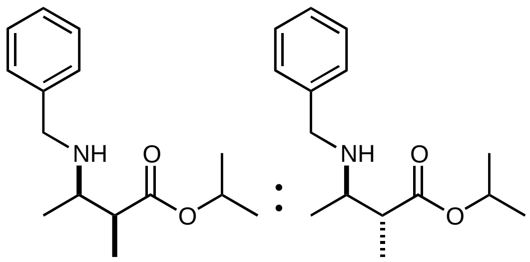


Electronic Supplementary Material (ESI) for Chemical Communications

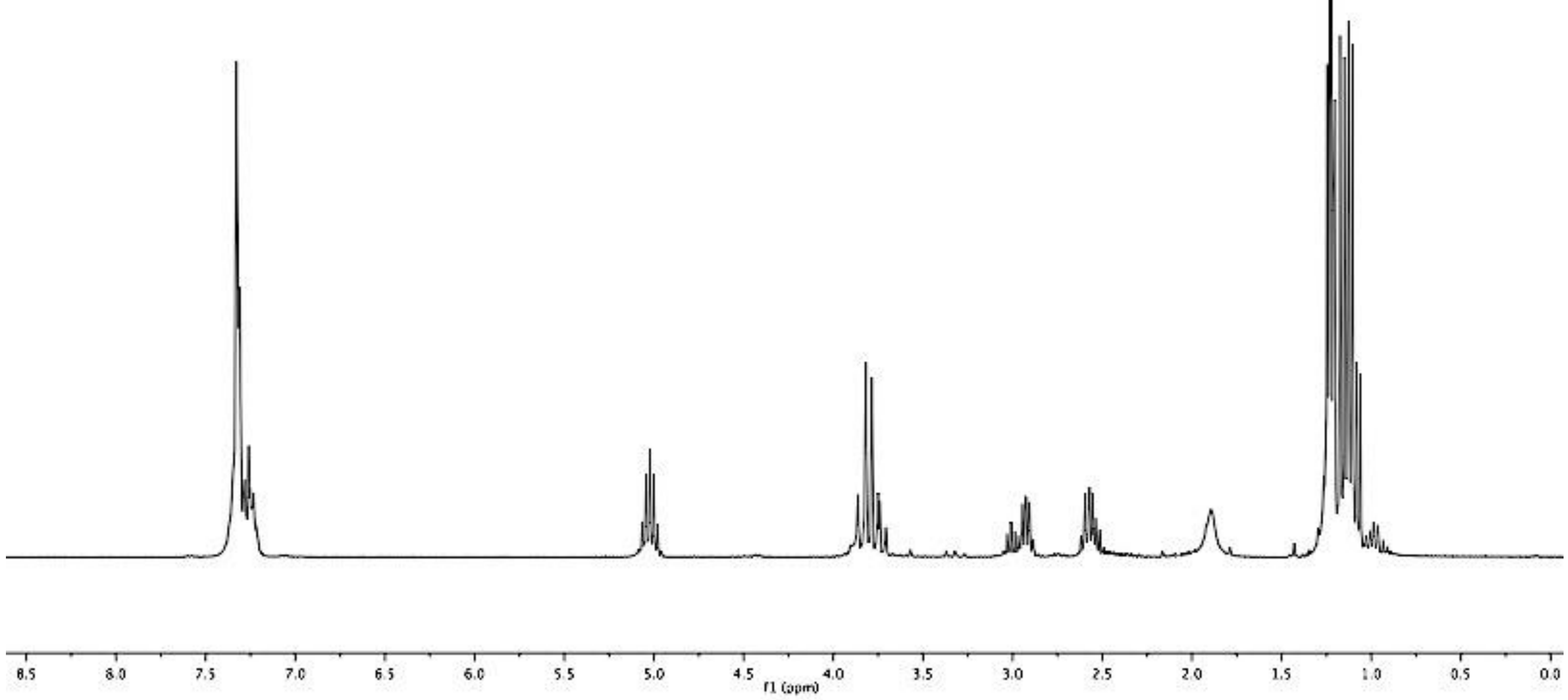


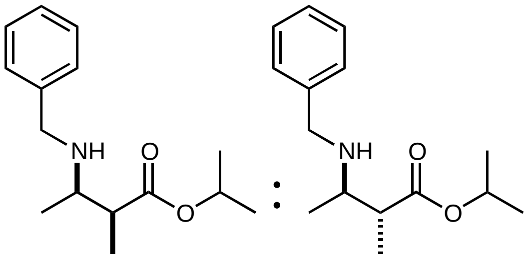
(±)-*syn*-5f (±)-*anti*-6f



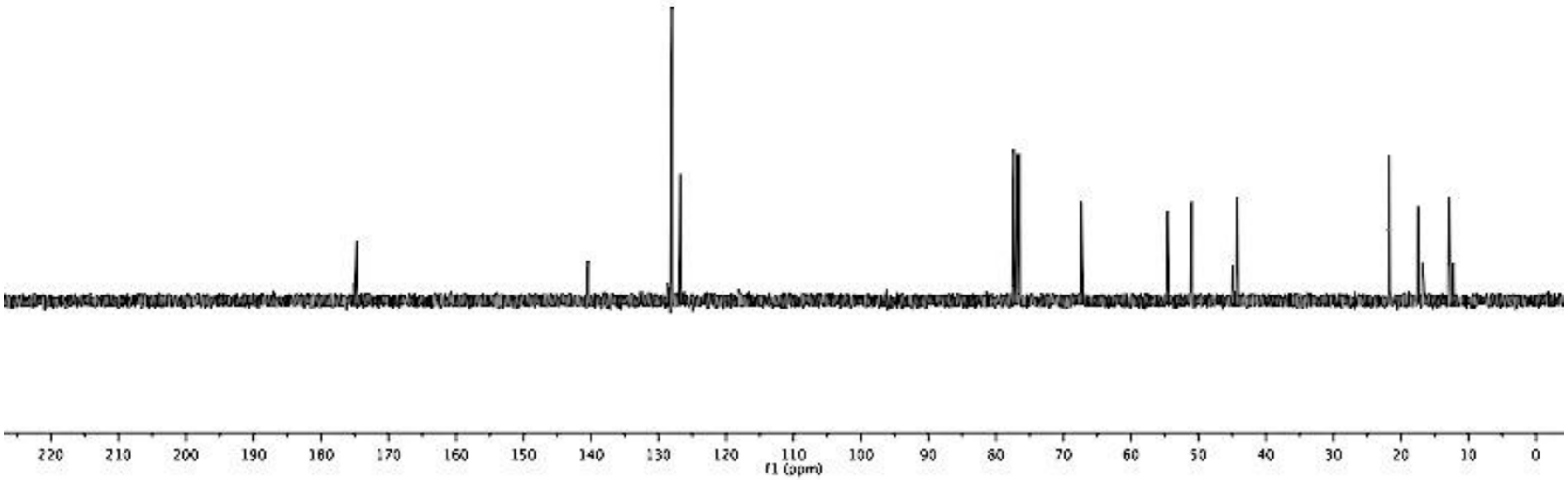


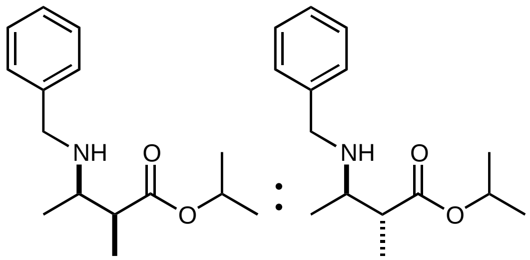
(±)-***syn*-5g**   (±)-***anti*-6g**



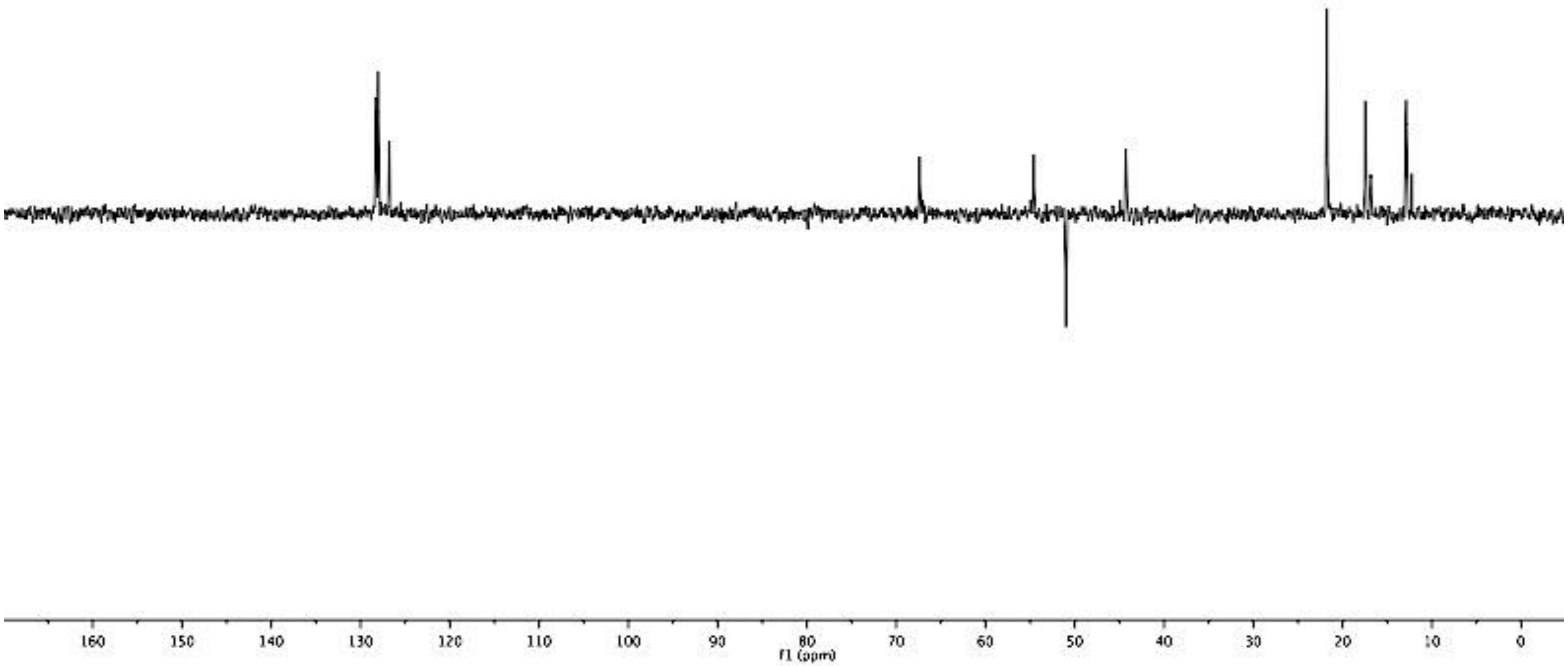


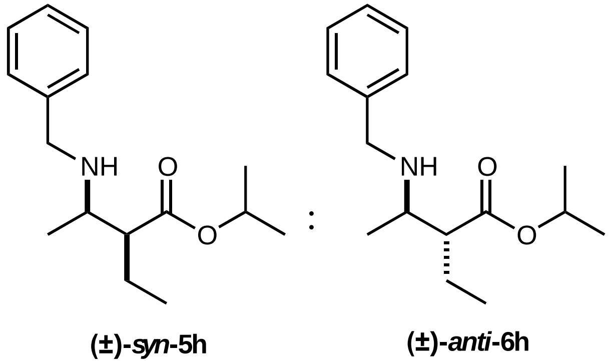
(±)-***syn*-5g** : (±)-***anti*-6g**

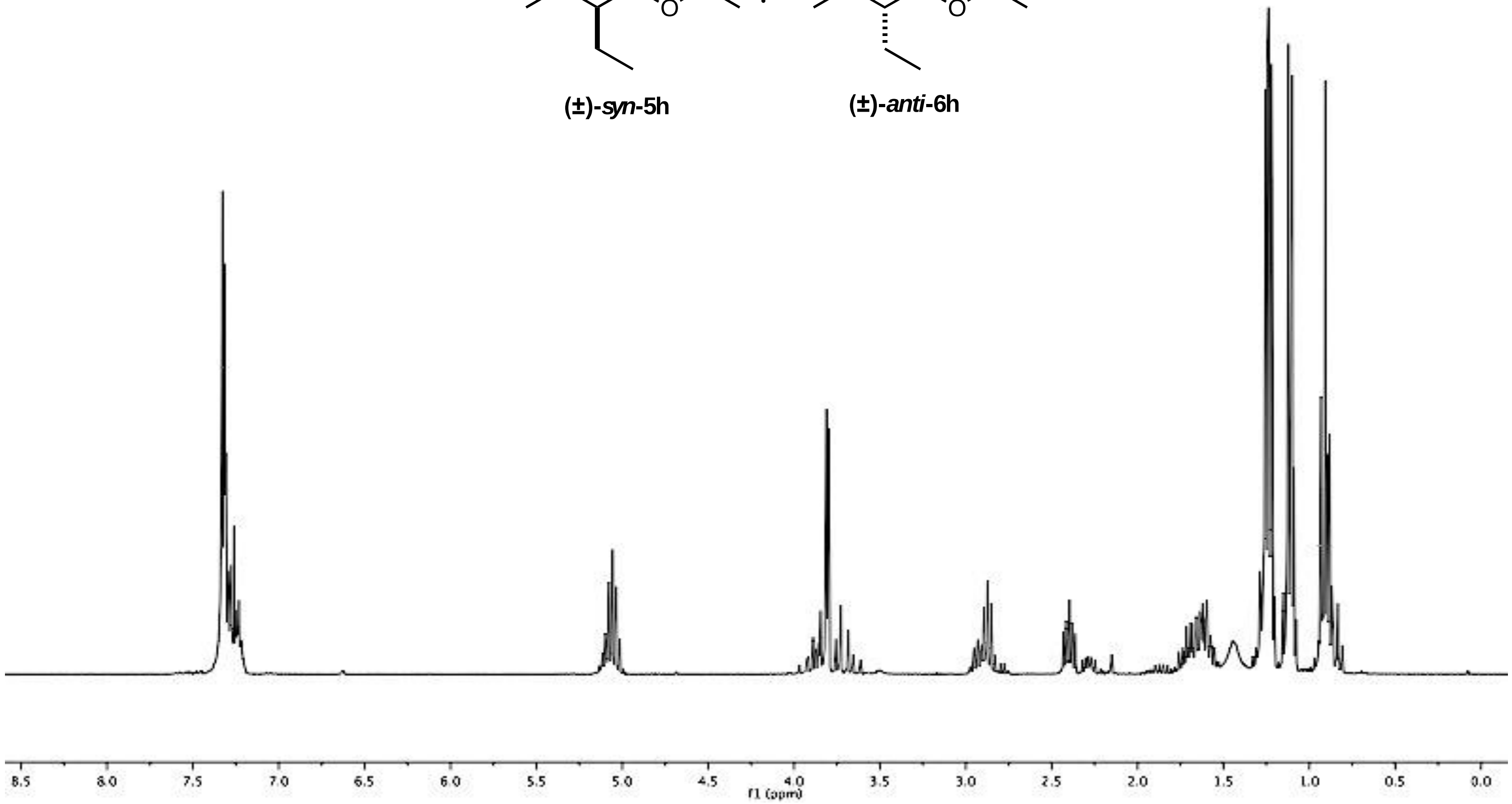


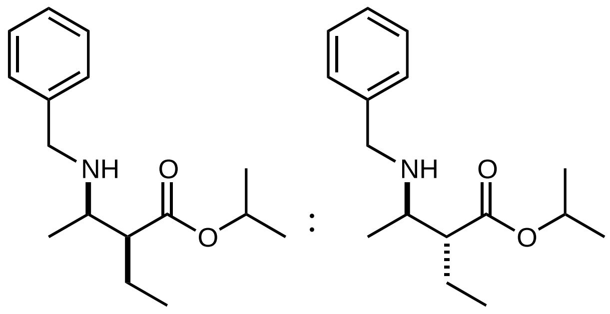


(±)-*syn*-**5g** : (±)-*anti*-**6g**

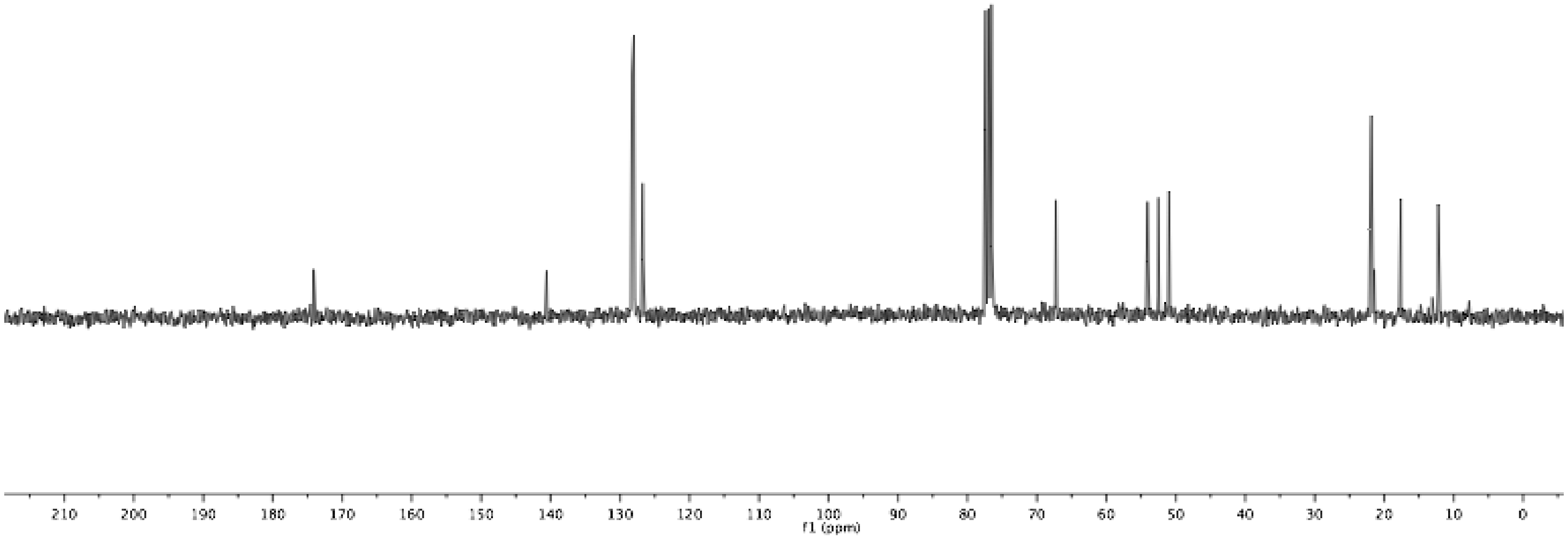


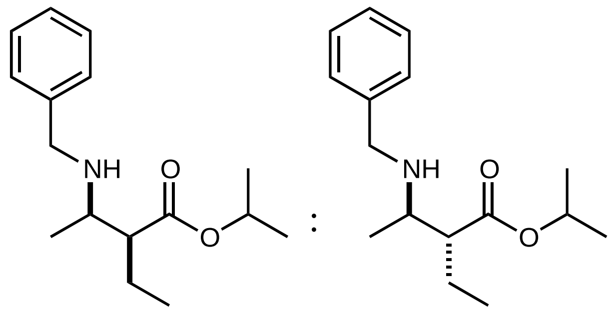

NH
O
O
(±)-*syn*-5h
:
NH
O
O
(±)-*anti*-6h


8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

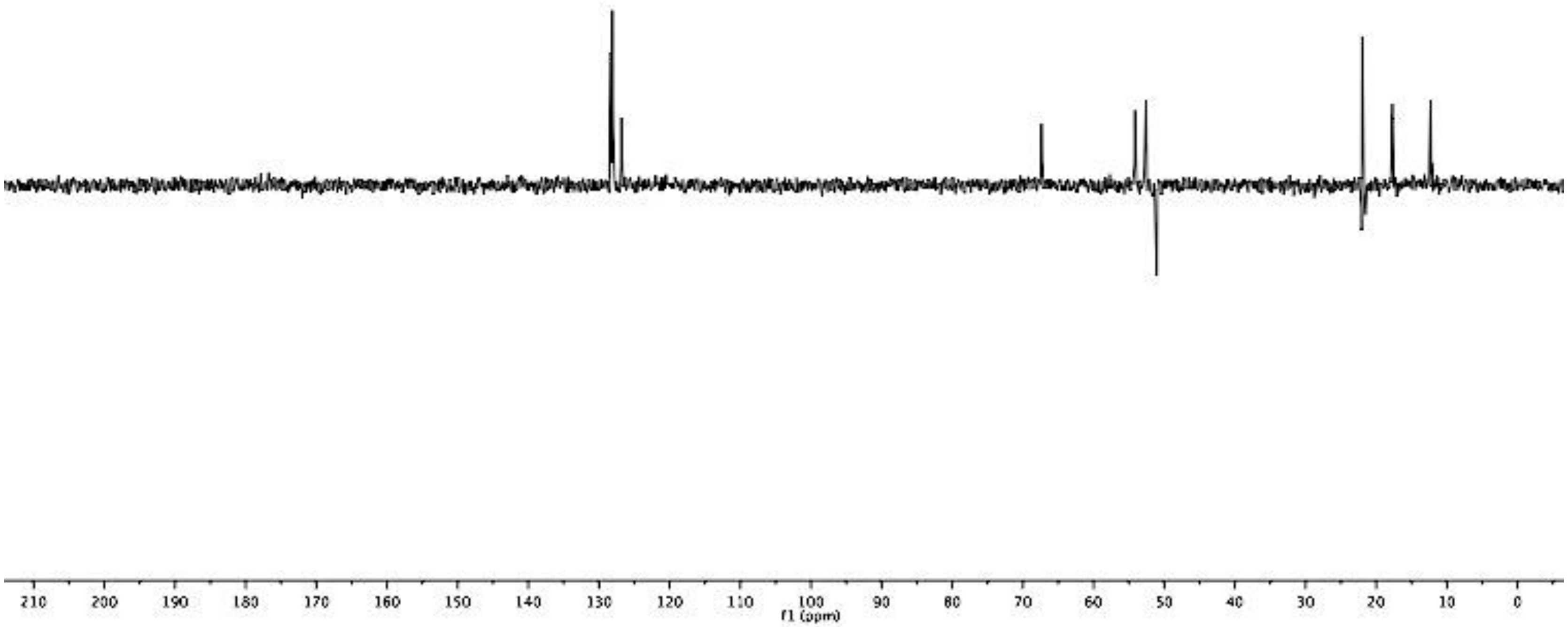


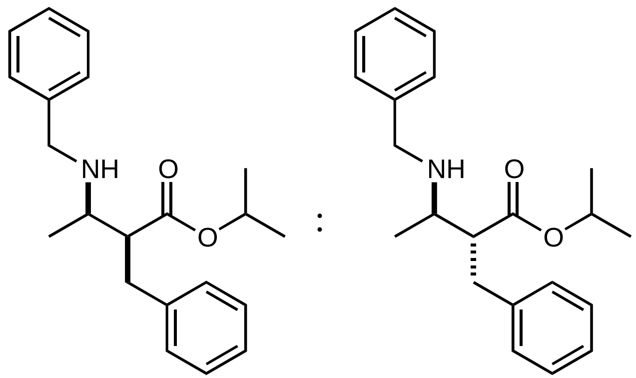
(±)-*syn*-5h **(±)-*anti*-6h**



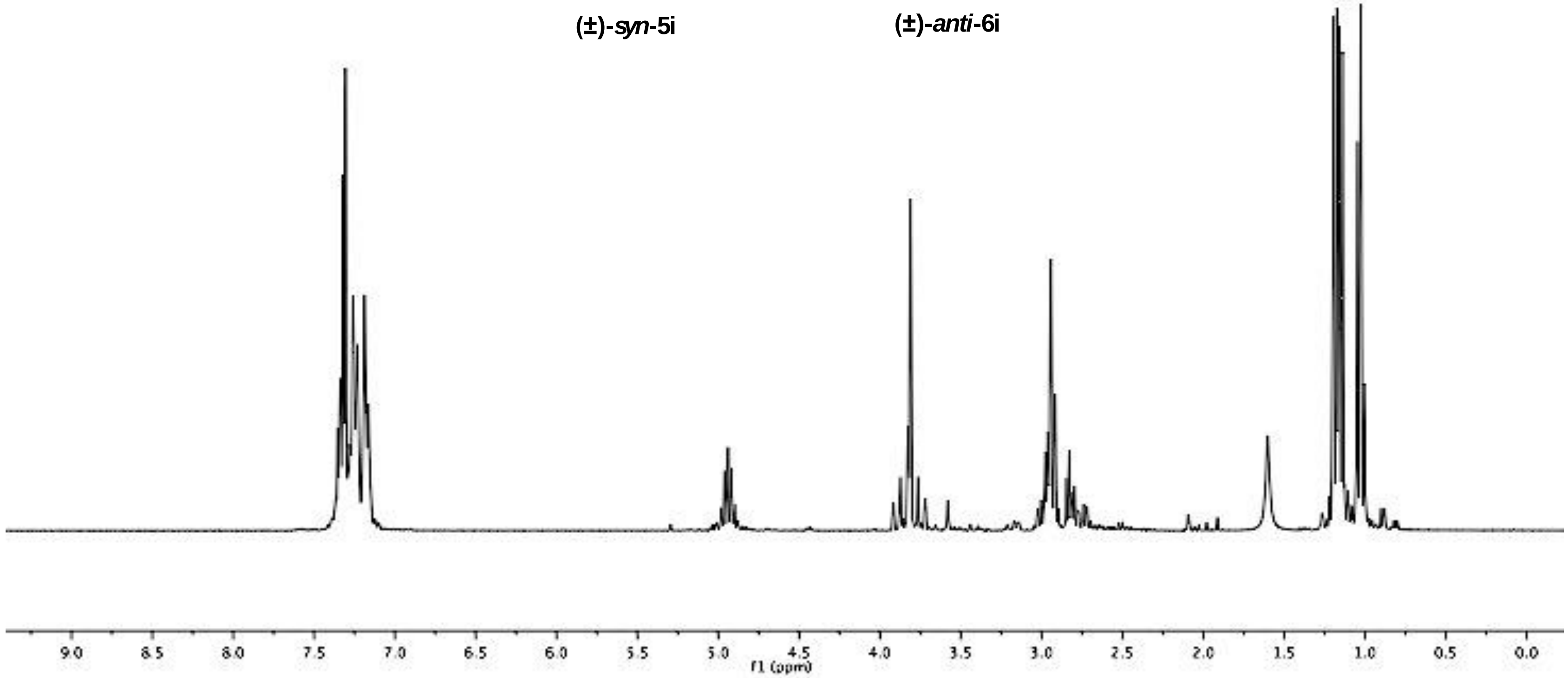


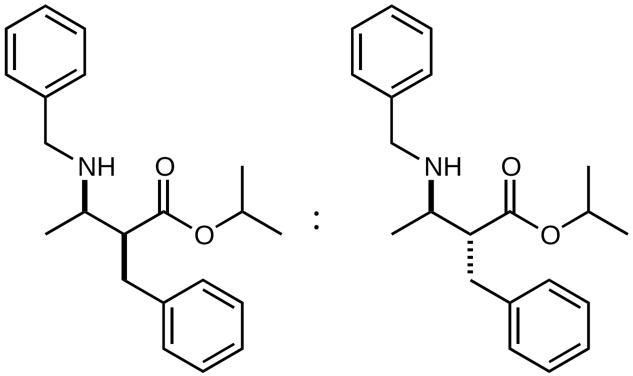
(±)-*syn*-5h (±)-*anti*-6h



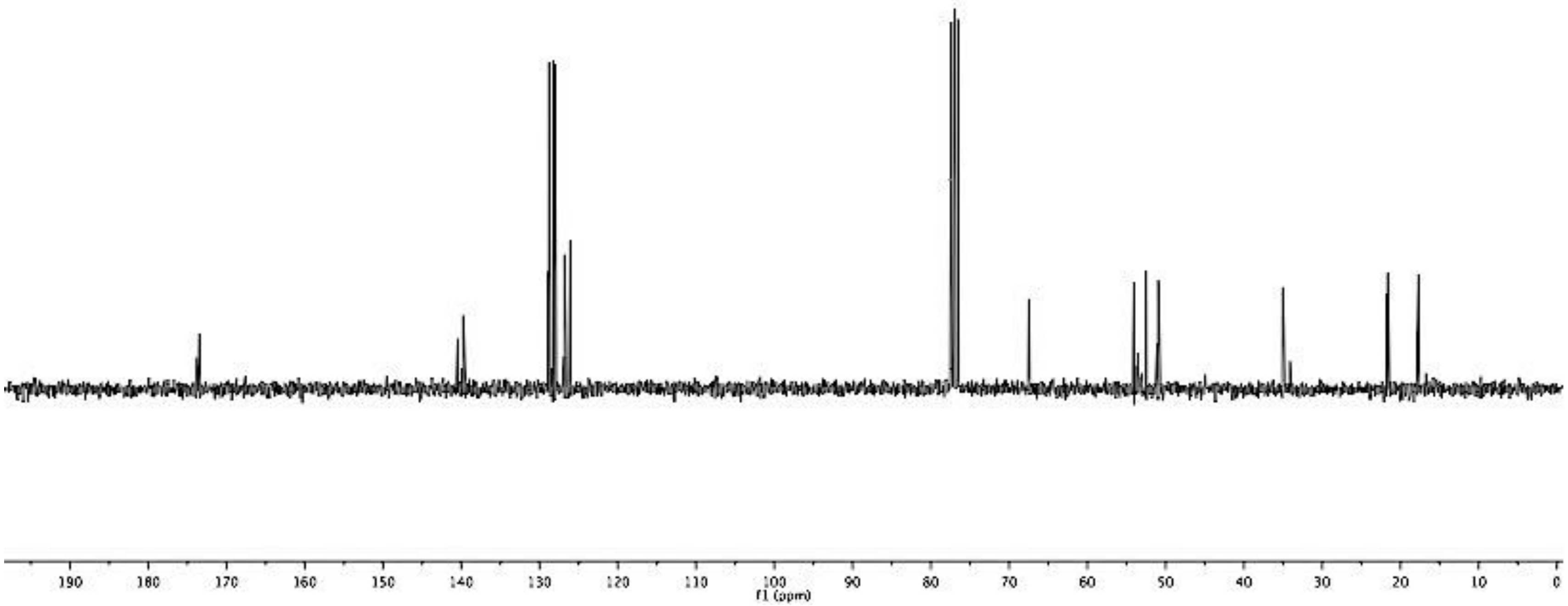


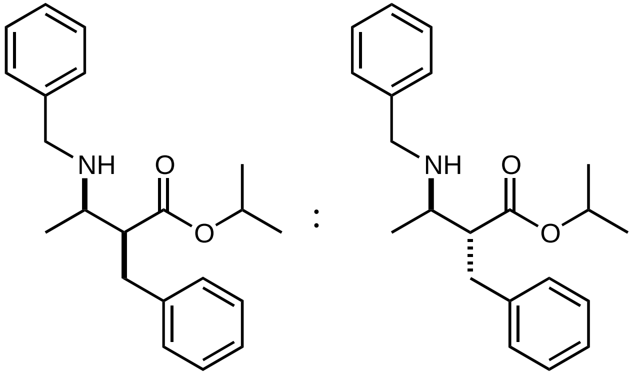
(±)-*syn*-5i **(±)-*anti*-6i**



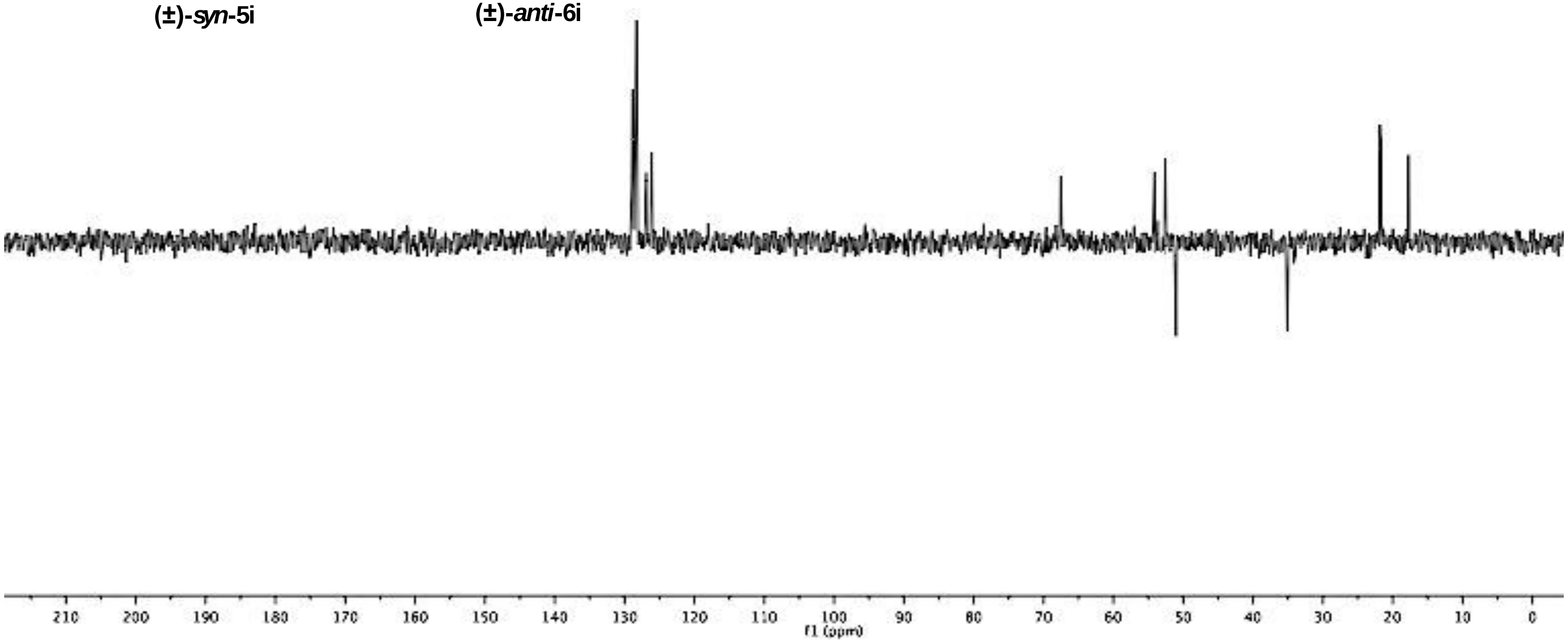


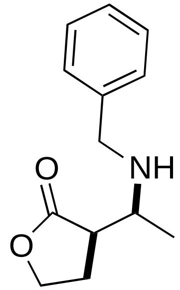
(±)-*syn*-5i **(±)-*anti*-6i**



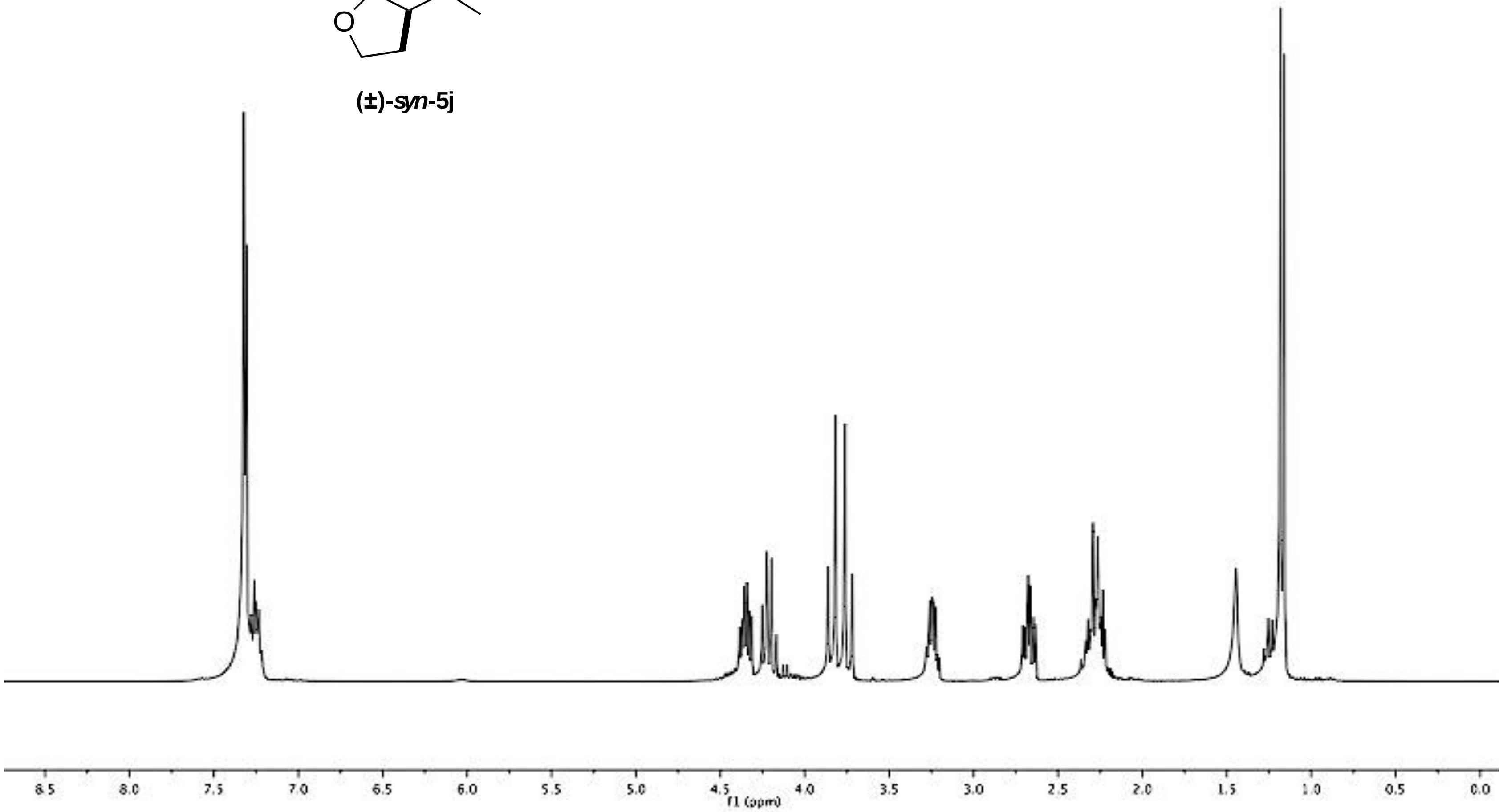


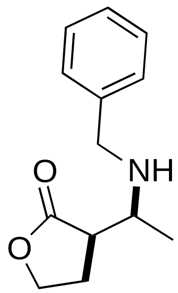
(±)-*syn*-5i **(±)-*anti*-6i**



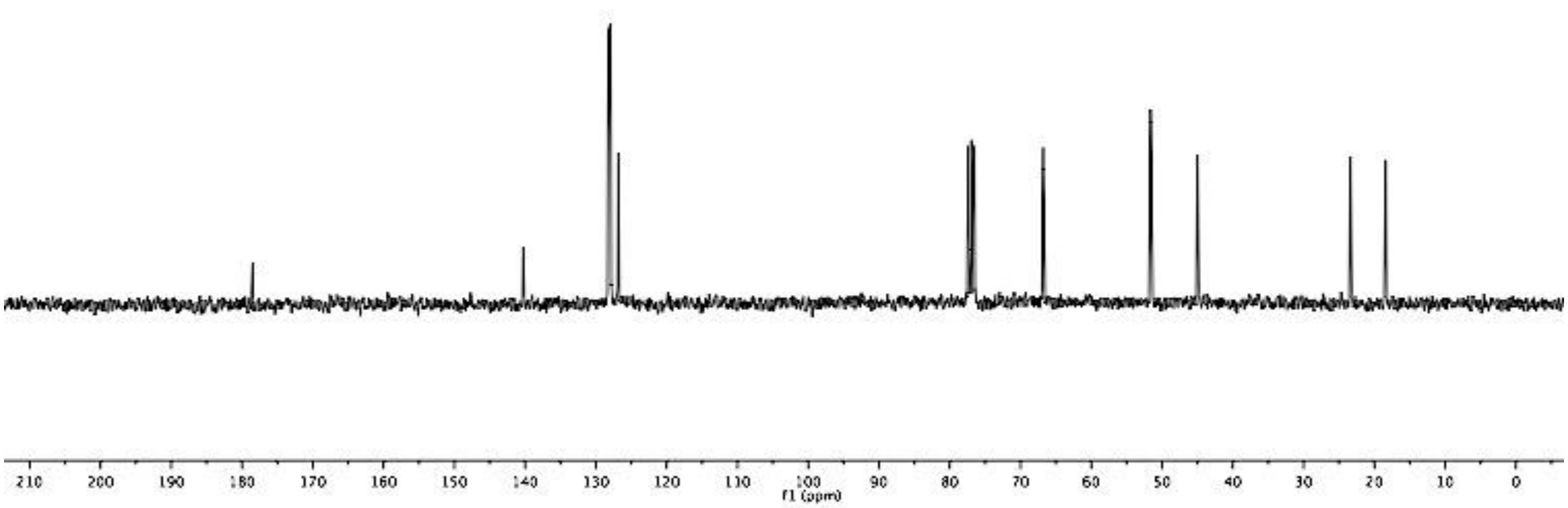


(±)-*syn*-5j




O
NH
O

(±)-*syn*-5j


210
200
190
180
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160
150
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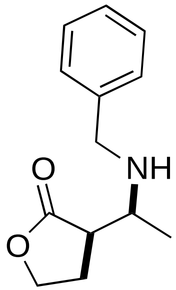
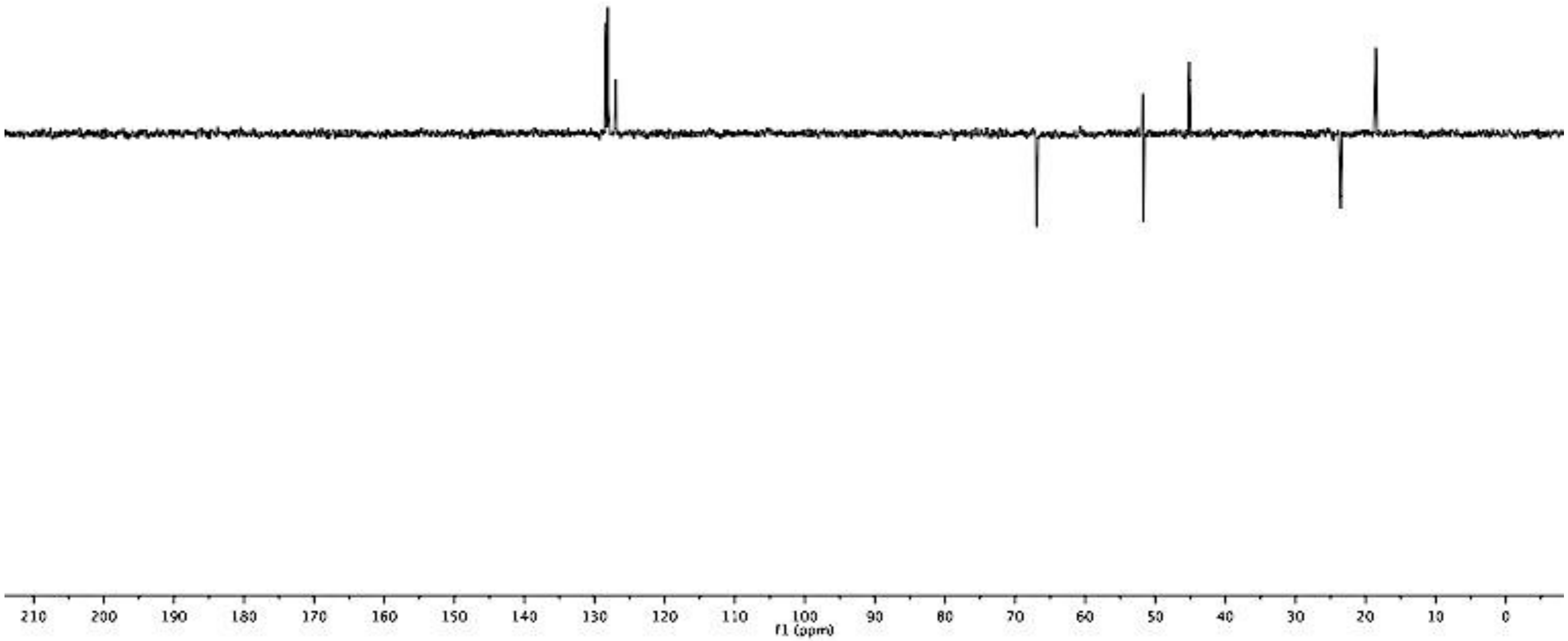
130
120
110
100
f1 (ppm)
90
80
70
60
50
40
30
20
10
0


O
NH
O

(±)-*syn*-5j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110
100
f1 (ppm)
90
80
70
60
50
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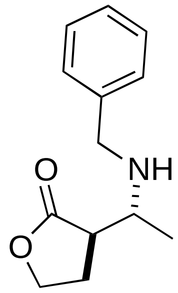
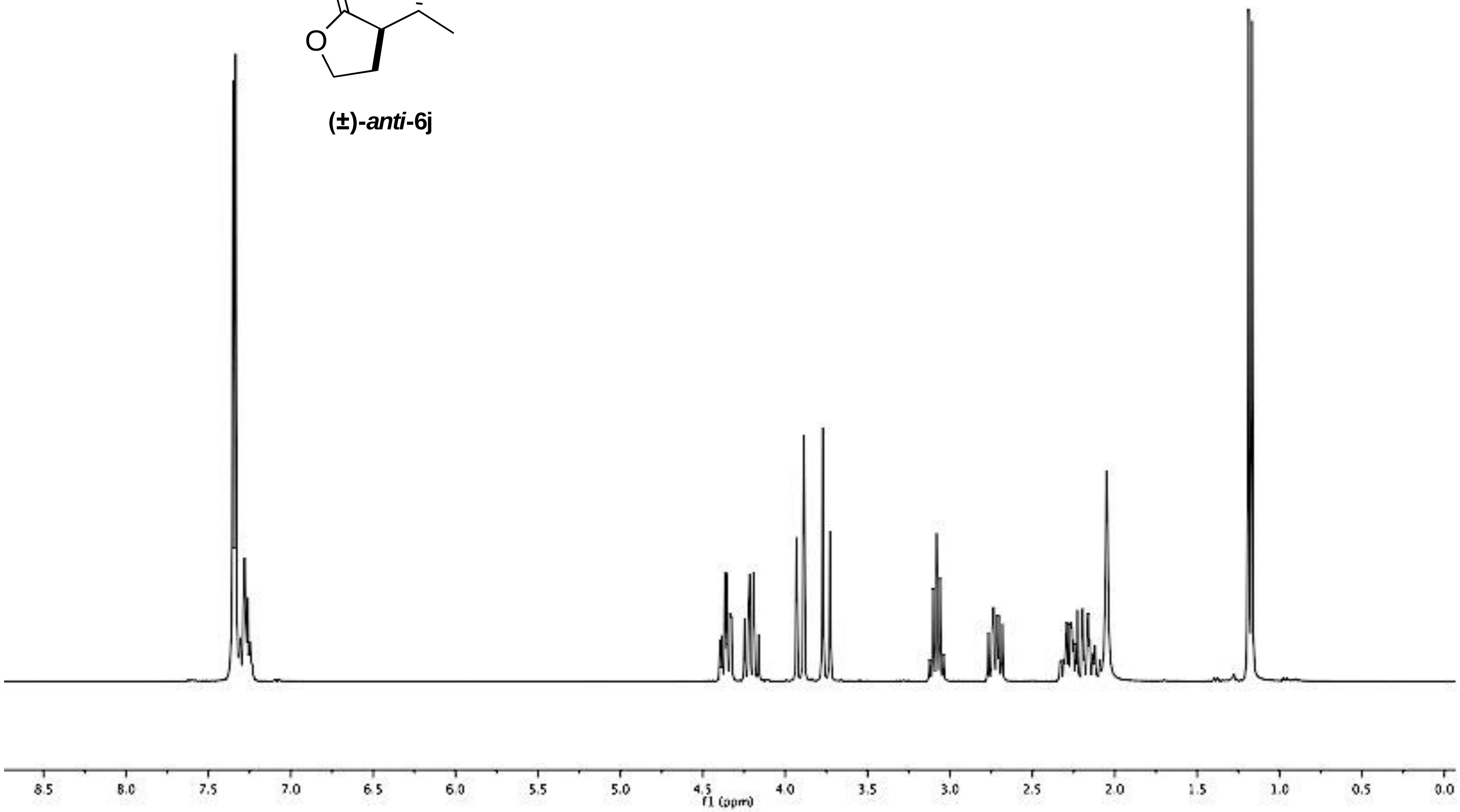
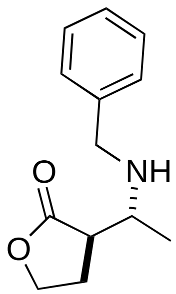
30
20
10
0

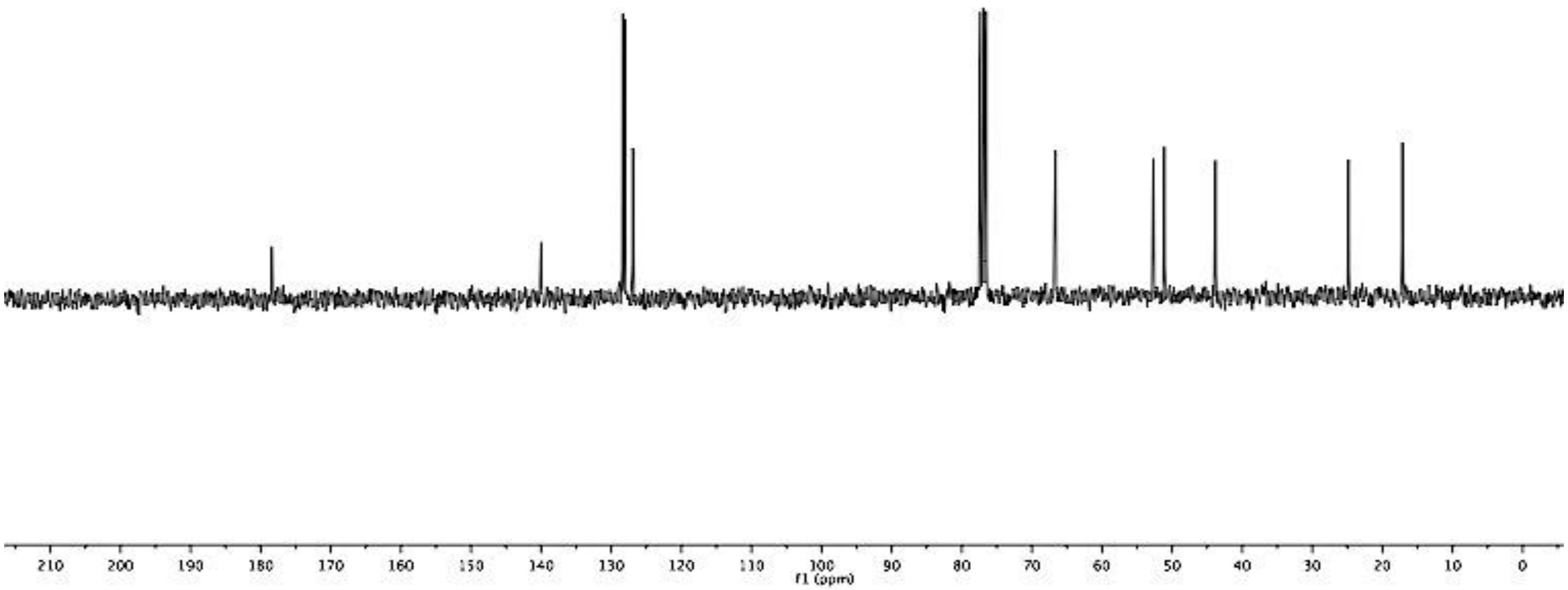


(±)-*anti*-6j




O
NH
O

(±)-*anti*-6j


210
200
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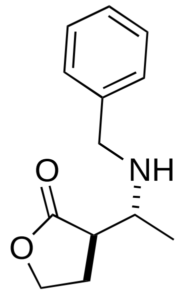
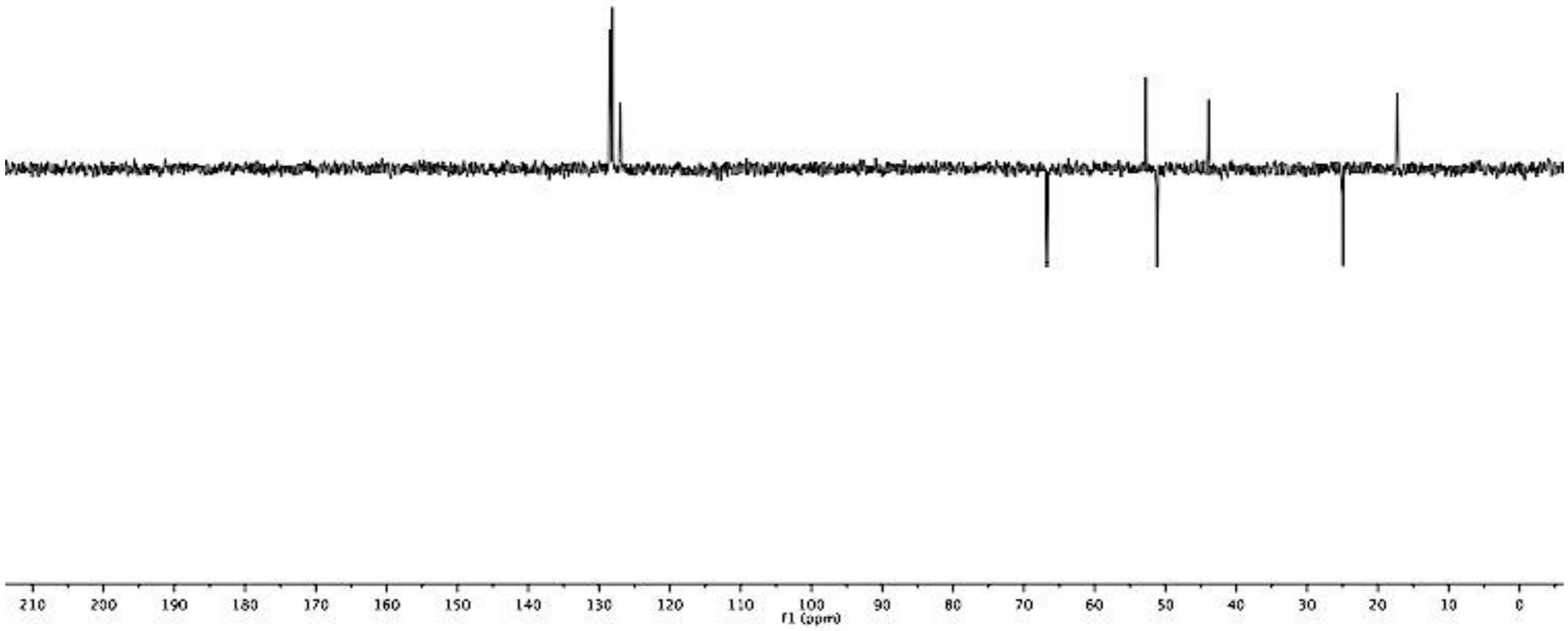
130
120
110
100
f1 (ppm)
90
80
70
60
50
40
30
20
10
0


O
NH
O

(±)-*anti*-6j


210
200
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f1 (ppm)
90
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30
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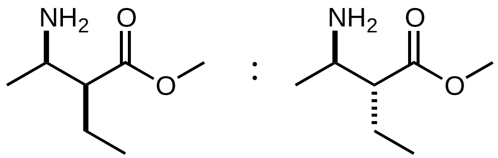
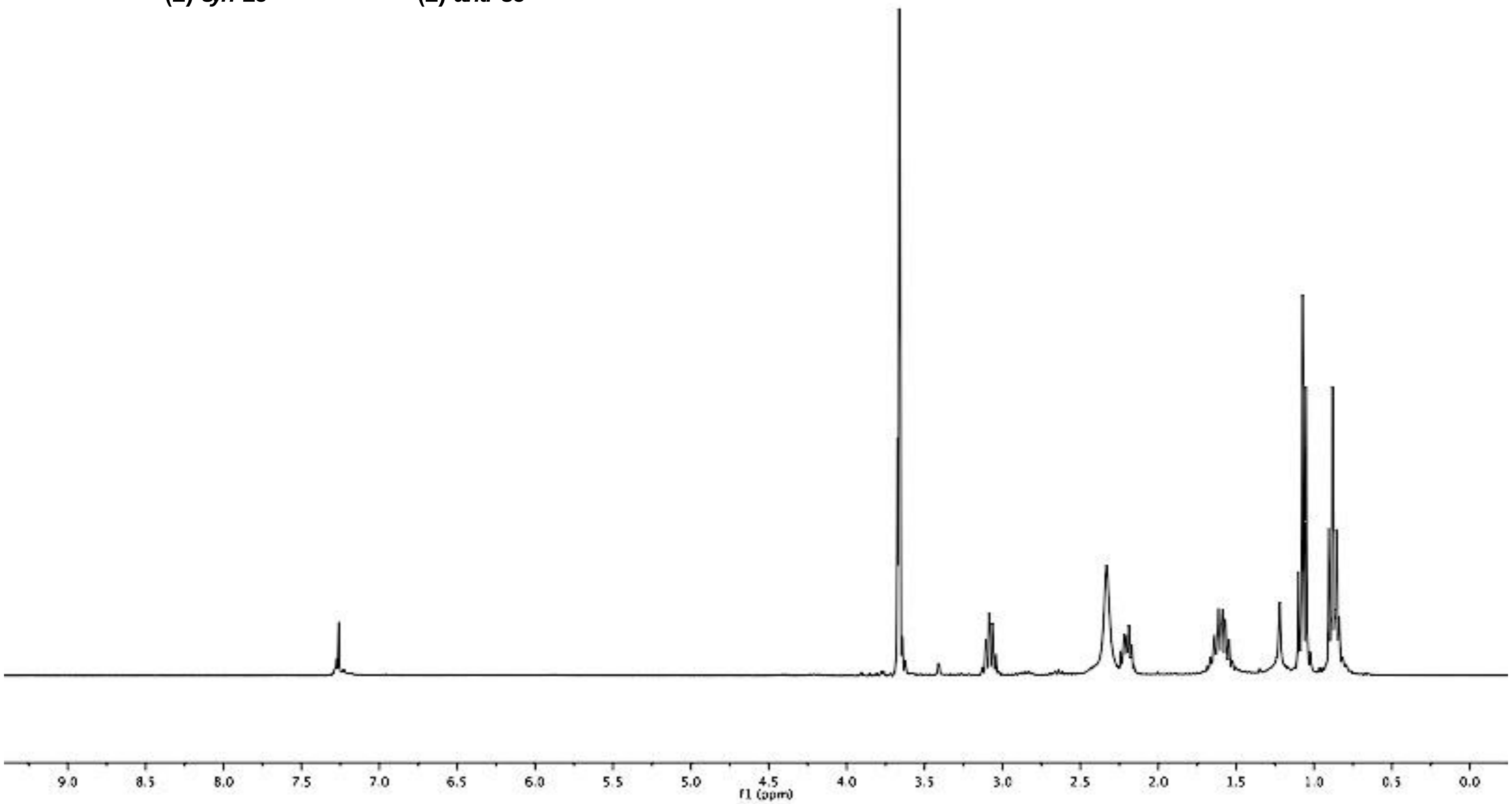
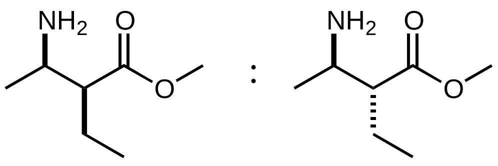
10
0

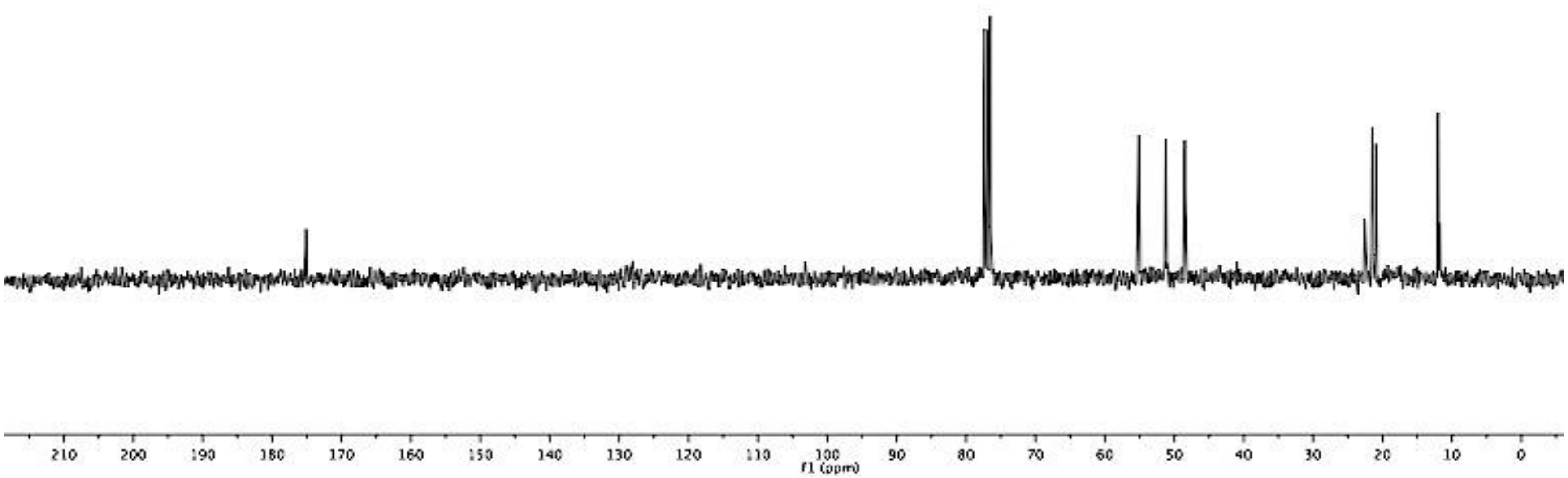


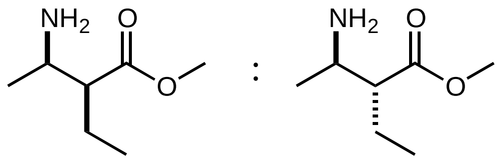
(±)-*syn*-2c **(±)-*anti*-3c**



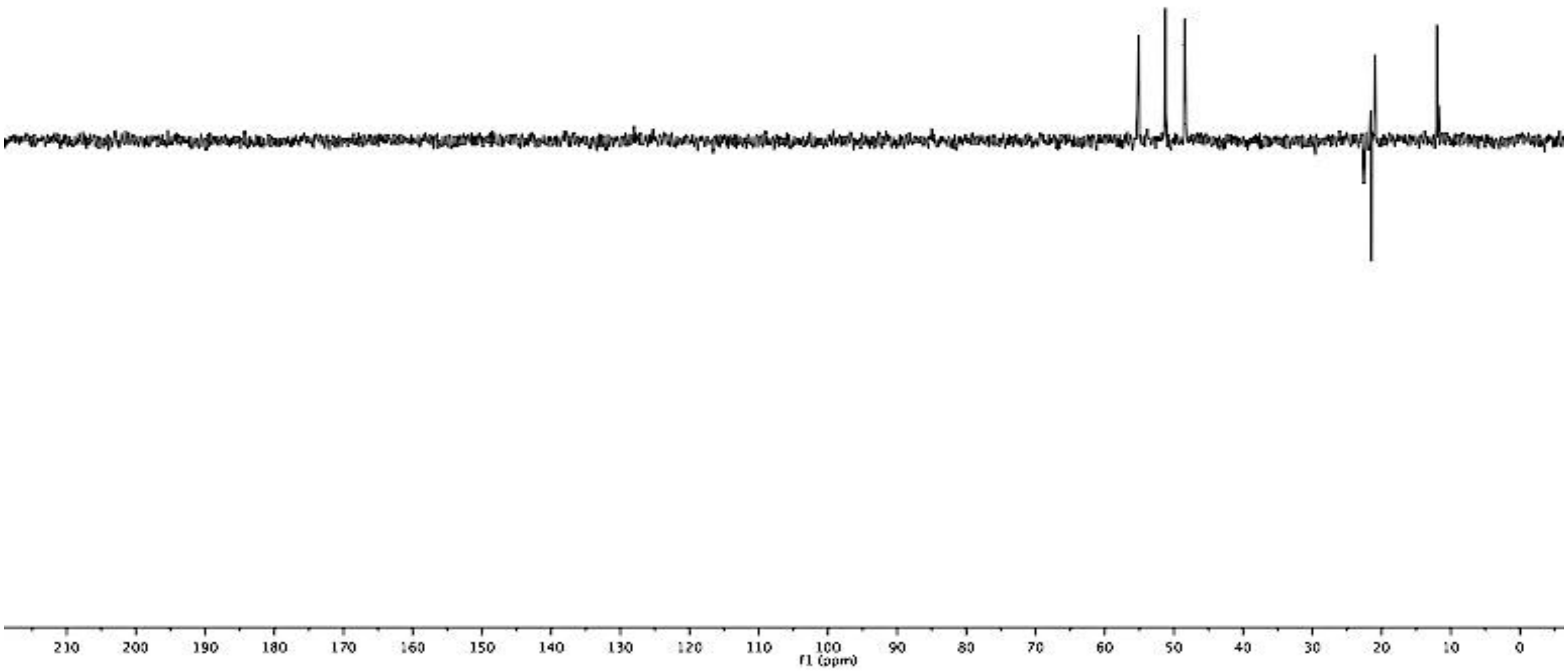


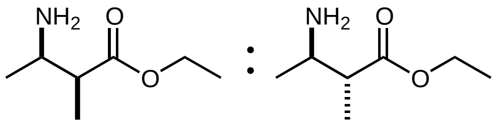
(±)-*syn*-2c : **(±)-*anti*-3c**



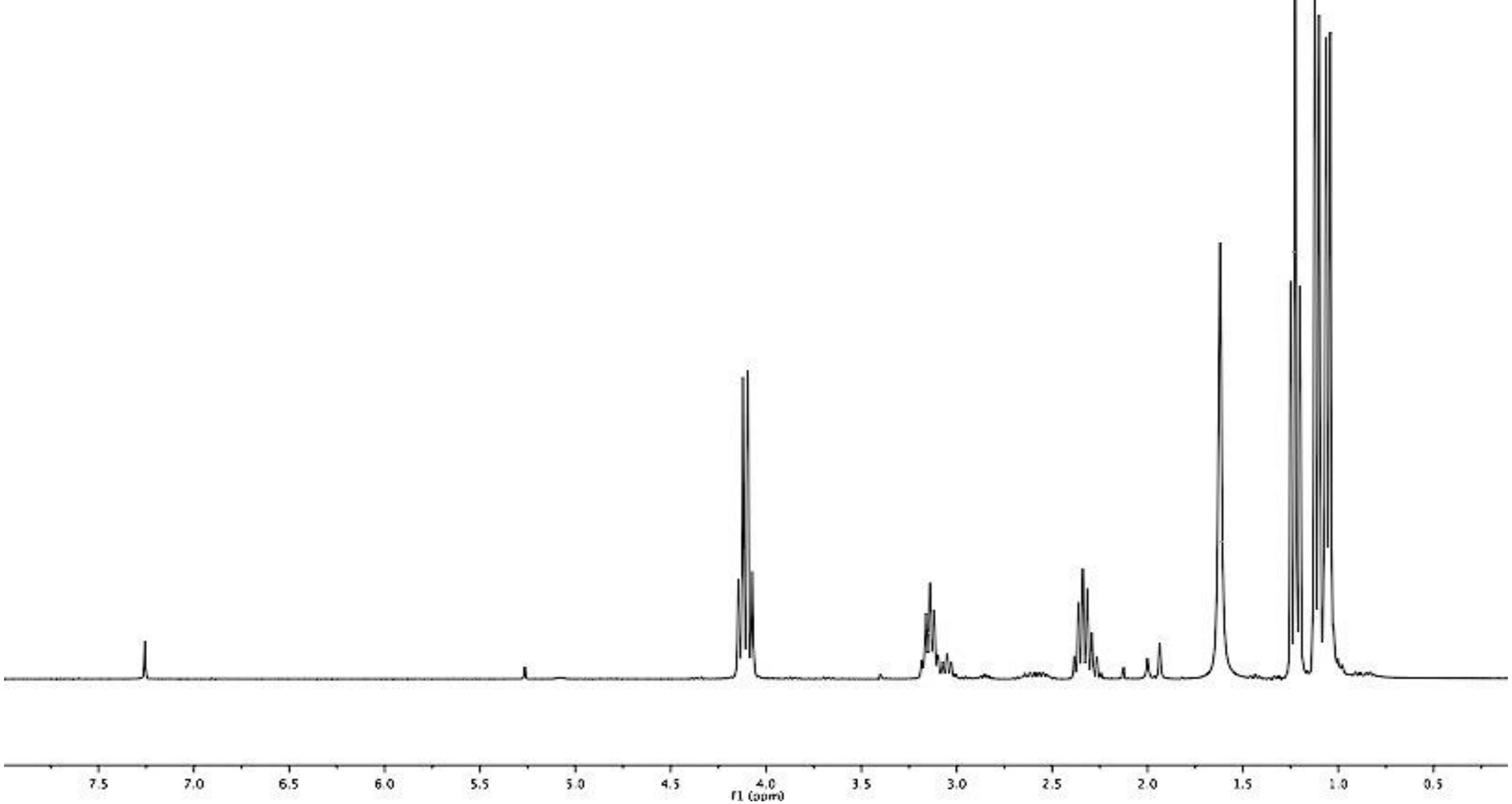


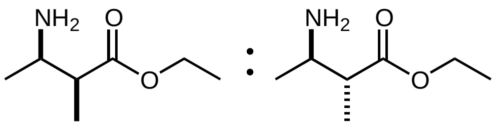
(±)-*syn*-2c **(±)-*anti*-3c**



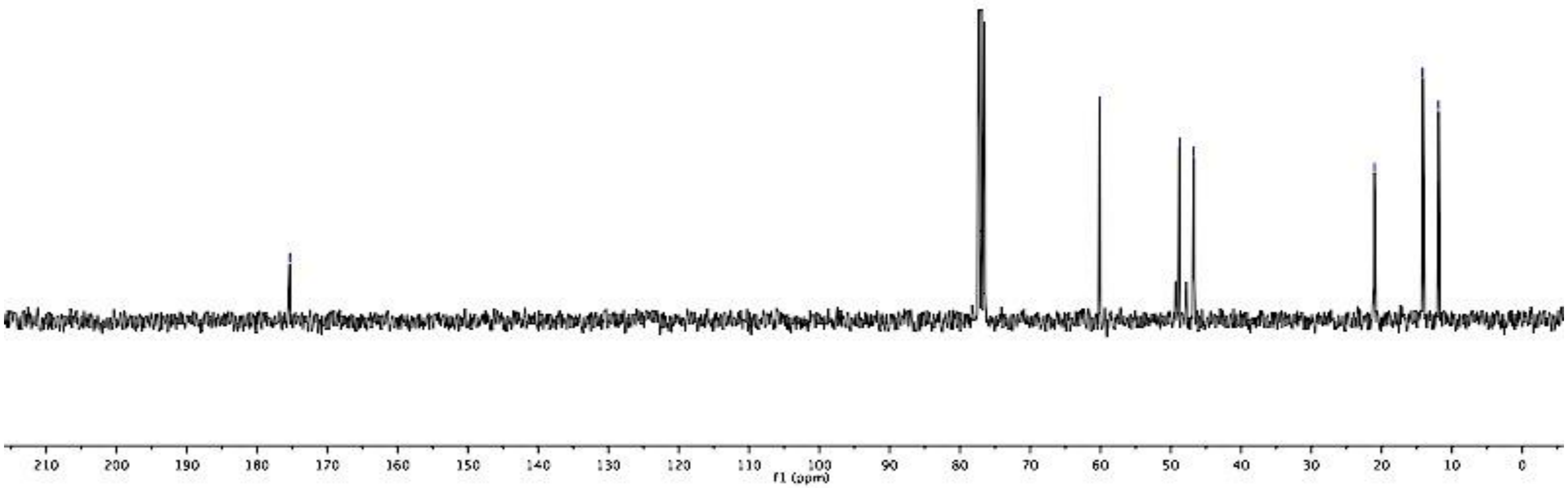


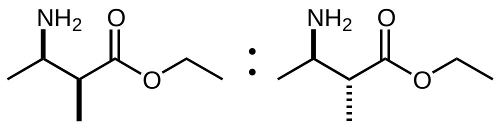
(±)-***syn*-2e** (±)-***anti*-3e**



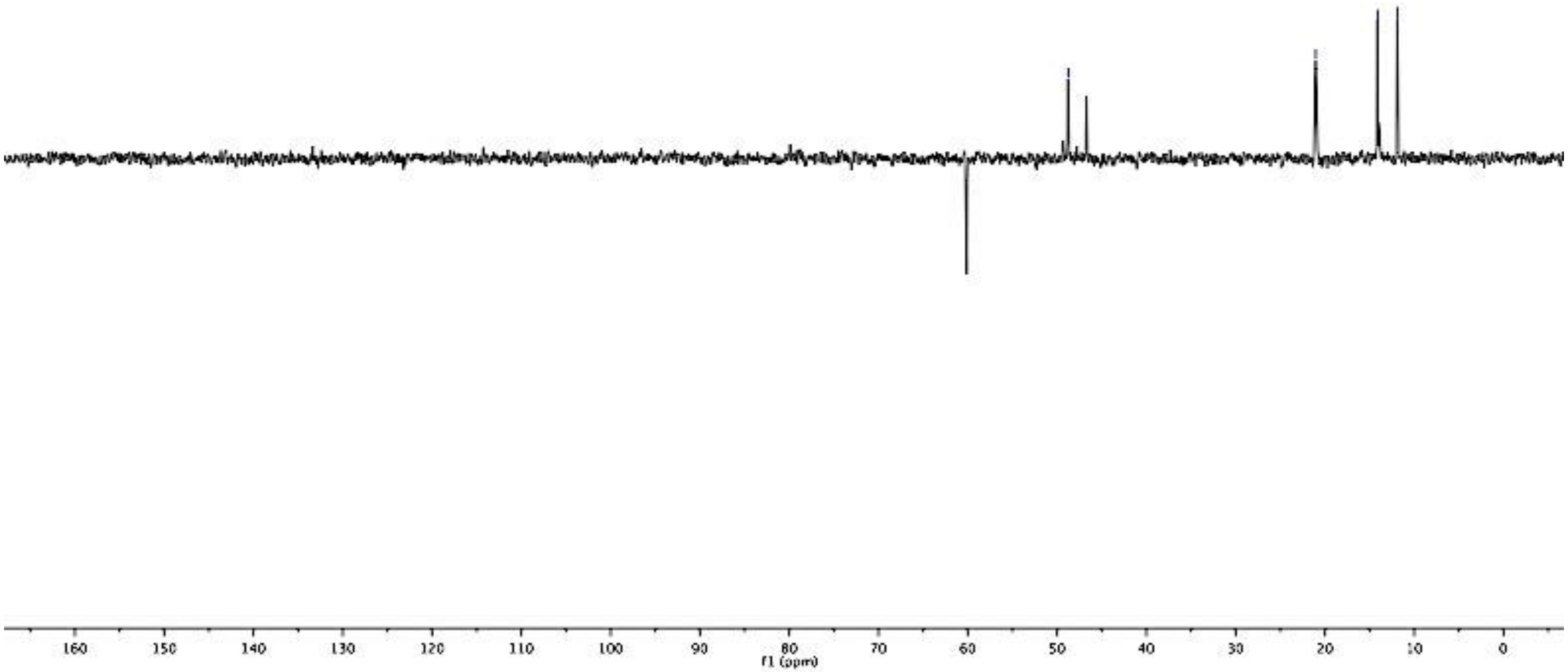


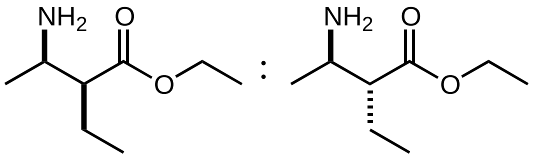
(±)-*syn*-**2e** (±)-*anti*-**3e**



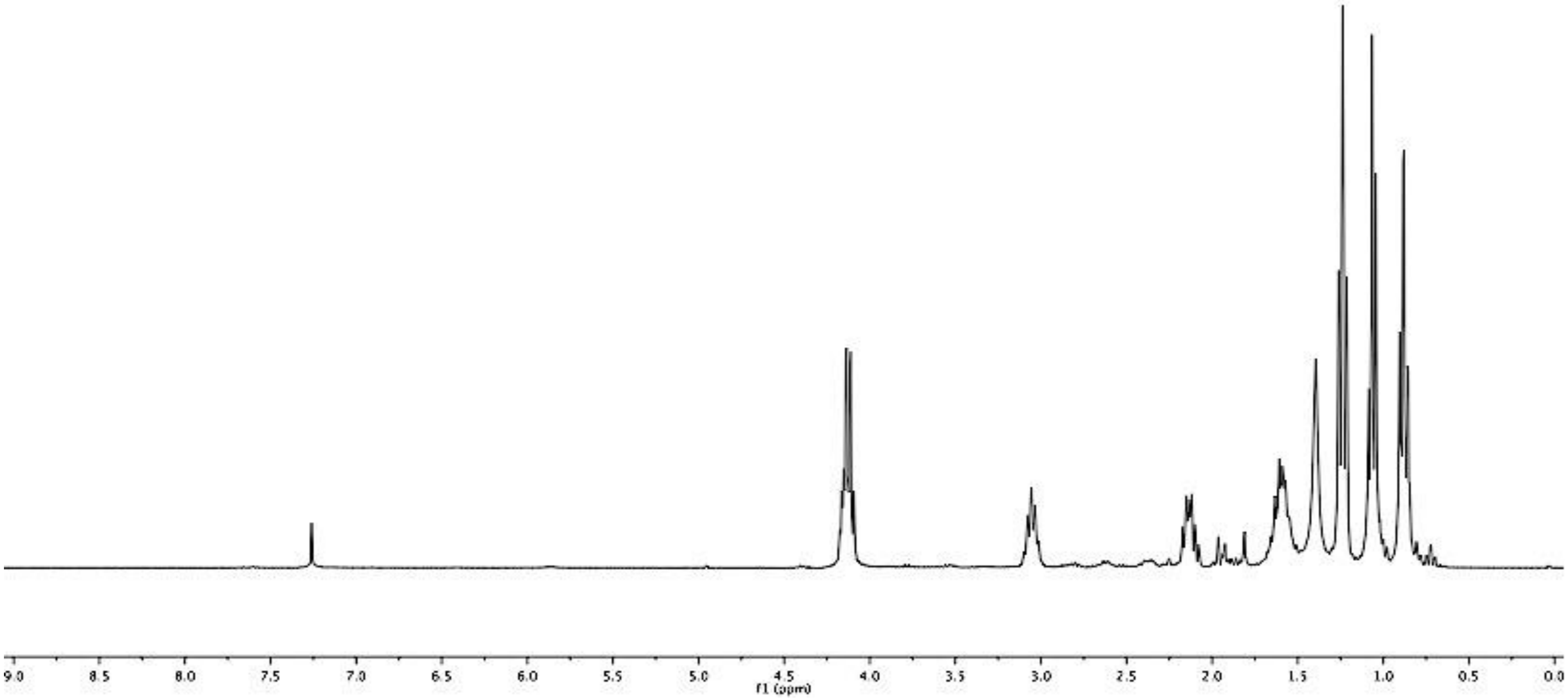


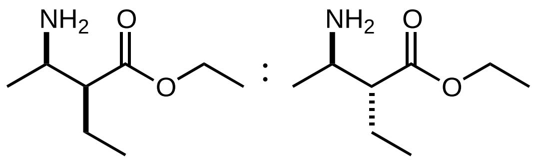
(±)-***syn*-2e**   (±)-***anti*-3e**



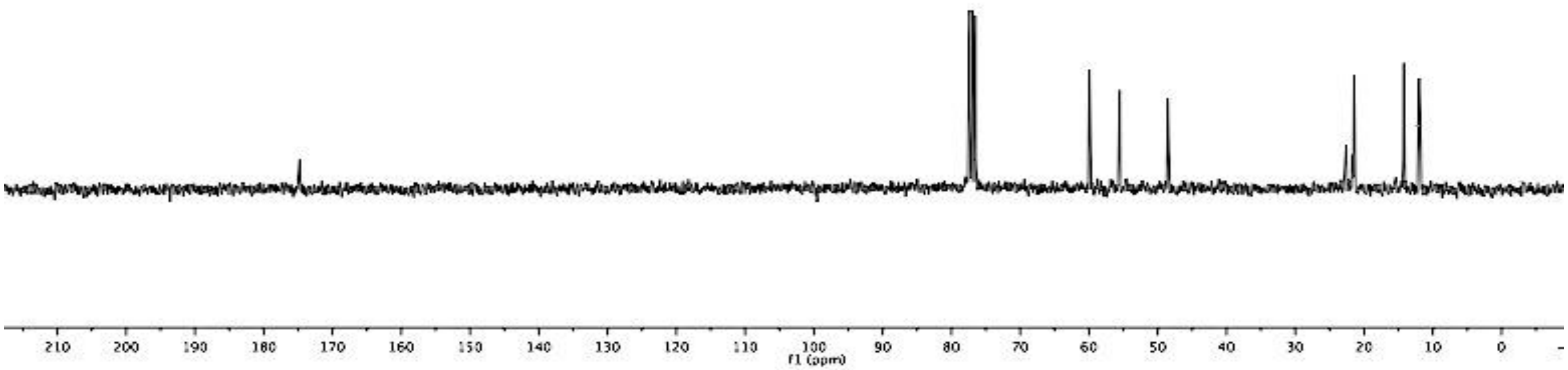


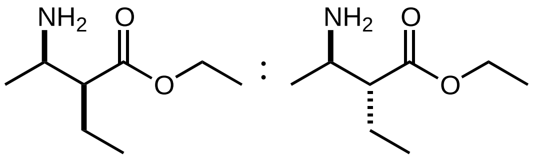
(±)-*syn*-2f **(±)-*anti*-3f**



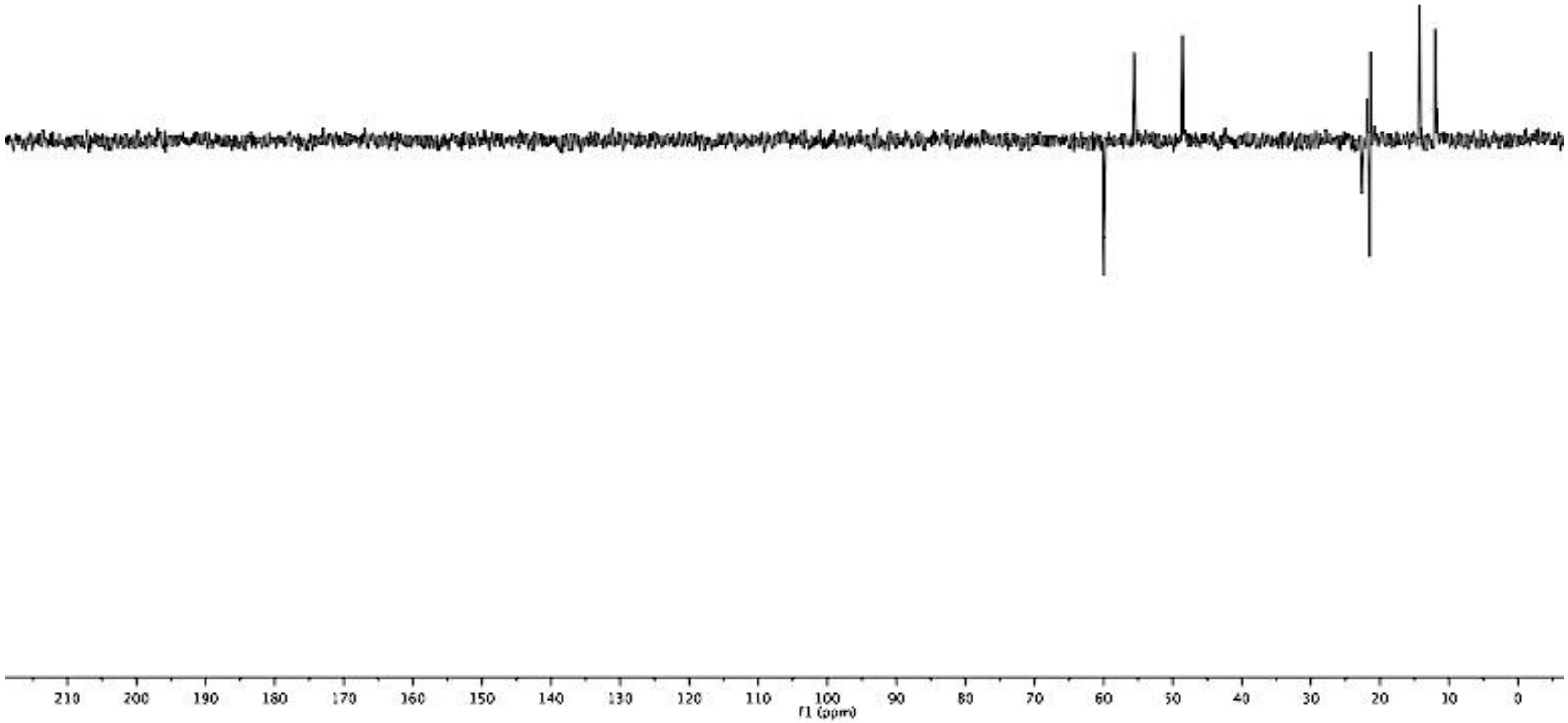


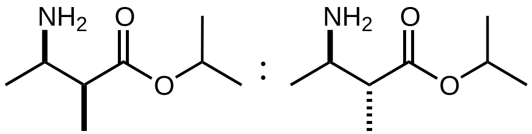
(±)-*syn*-2f **(±)-*anti*-3f**



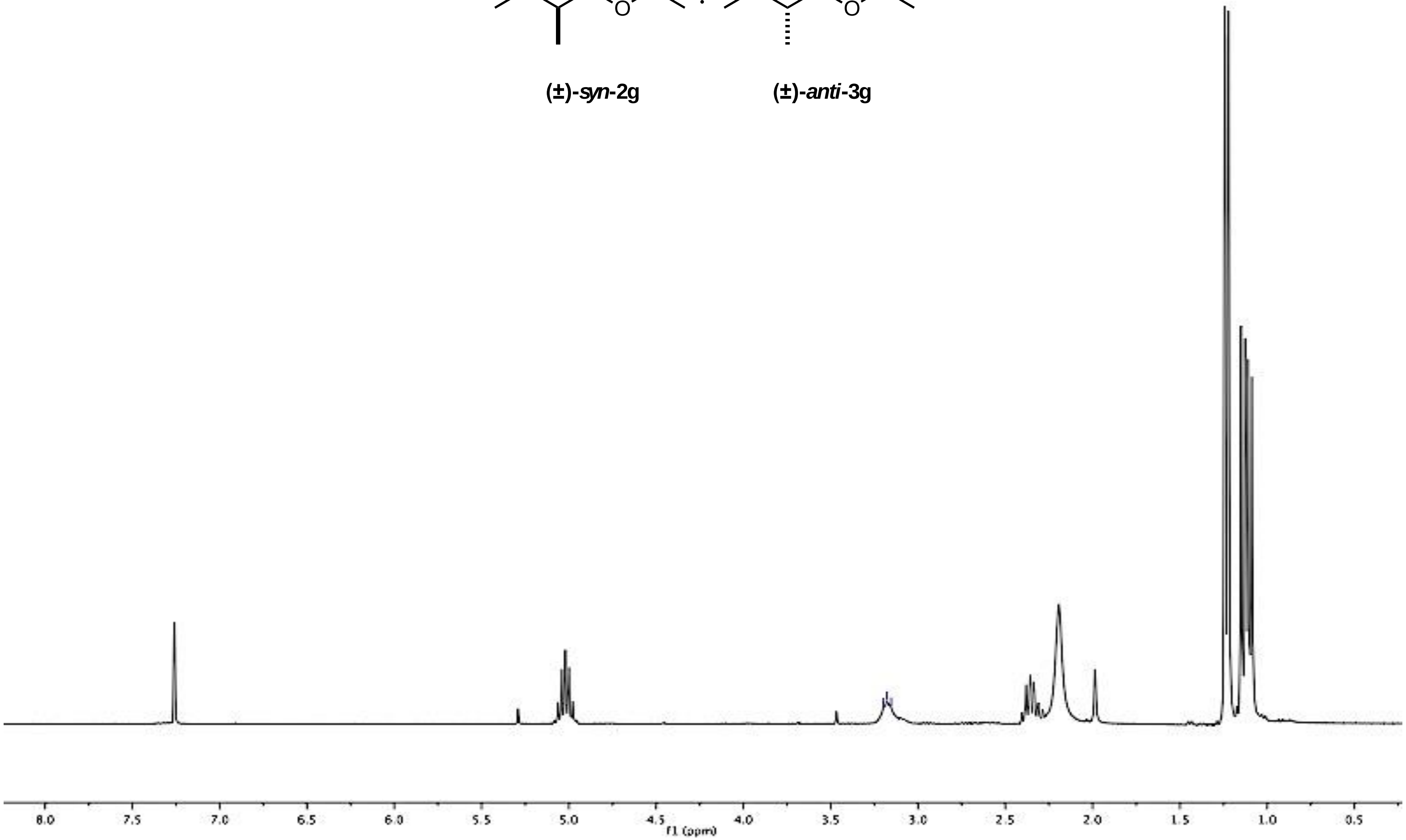


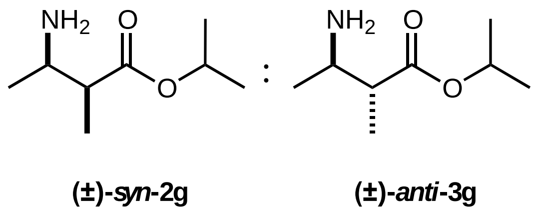
(±)-*syn*-2f : **(±)-*anti*-3f**

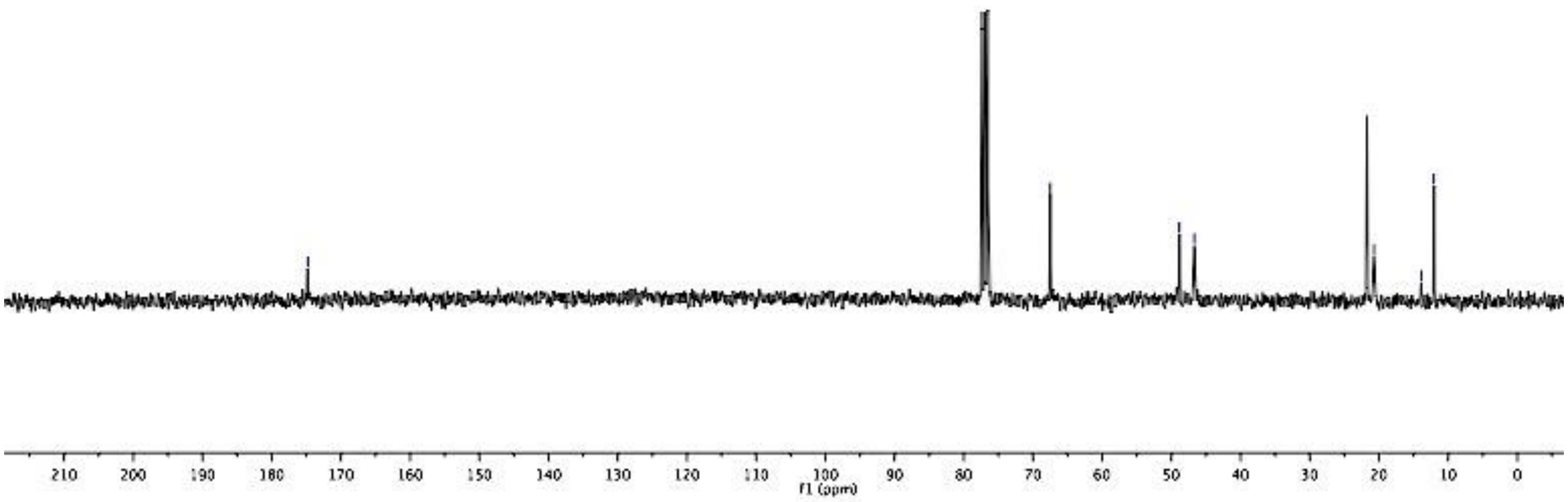




(±)-*syn*-2g (±)-*anti*-3g




NH2
O
O
:
(±)-syn-2g
(±)-anti-3g


210
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f1 (ppm)
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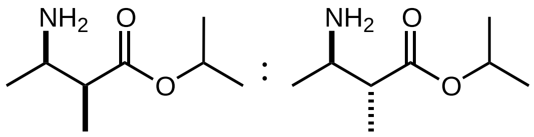
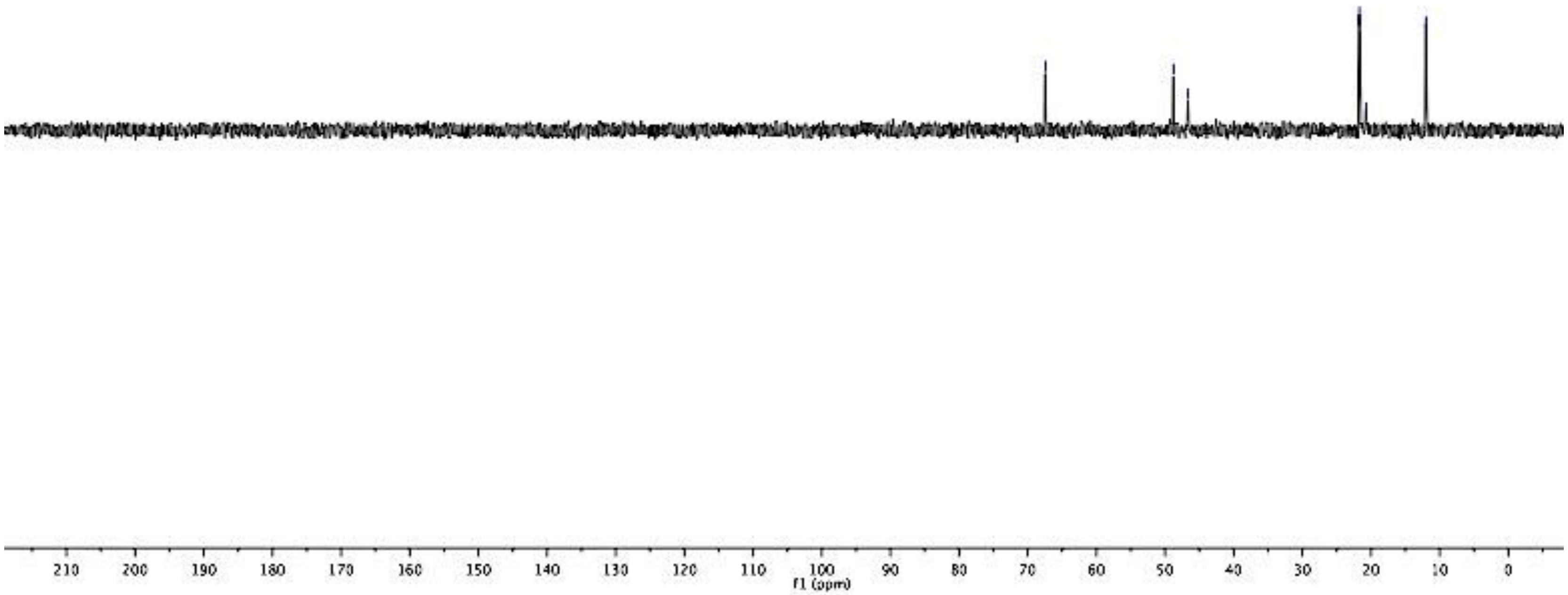
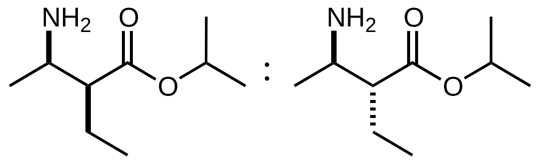
0

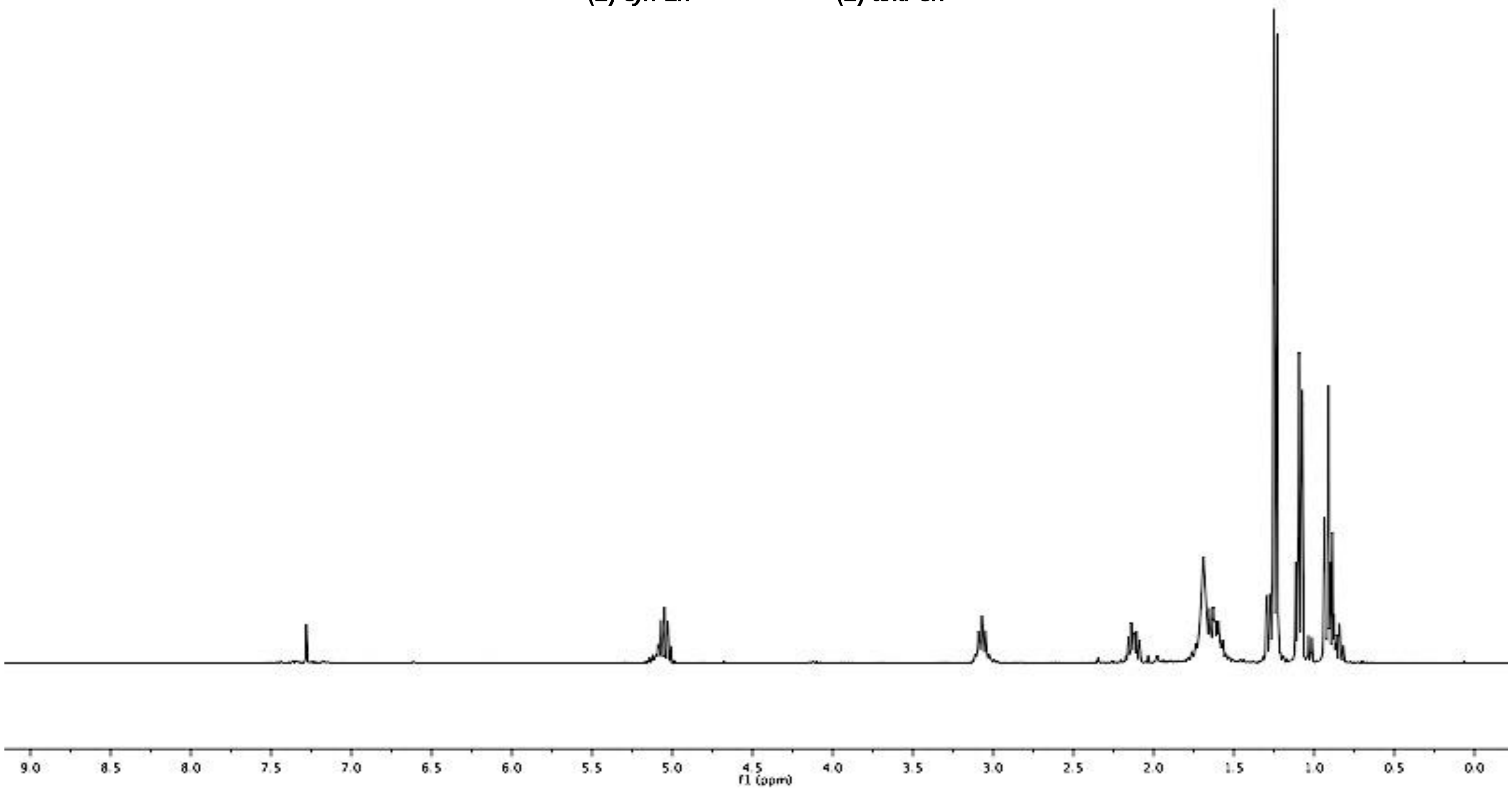


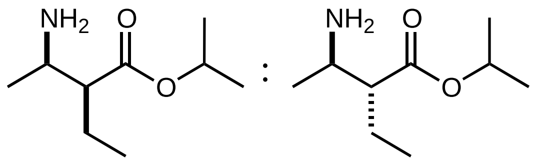
(±)-*syn*-**2g** (±)-*anti*-**3g**



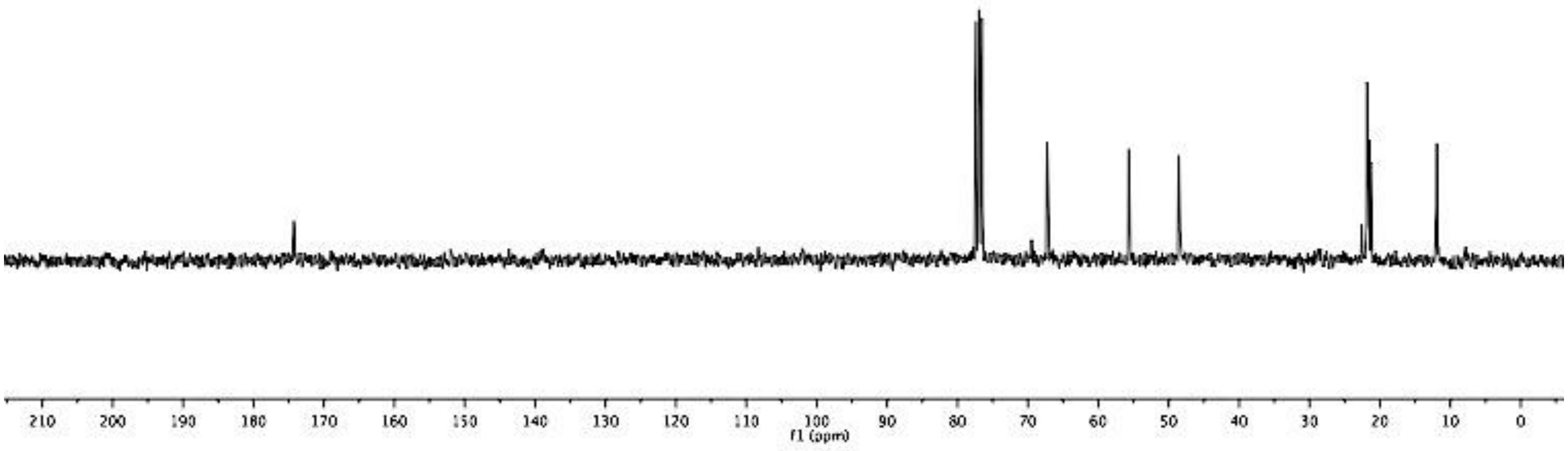


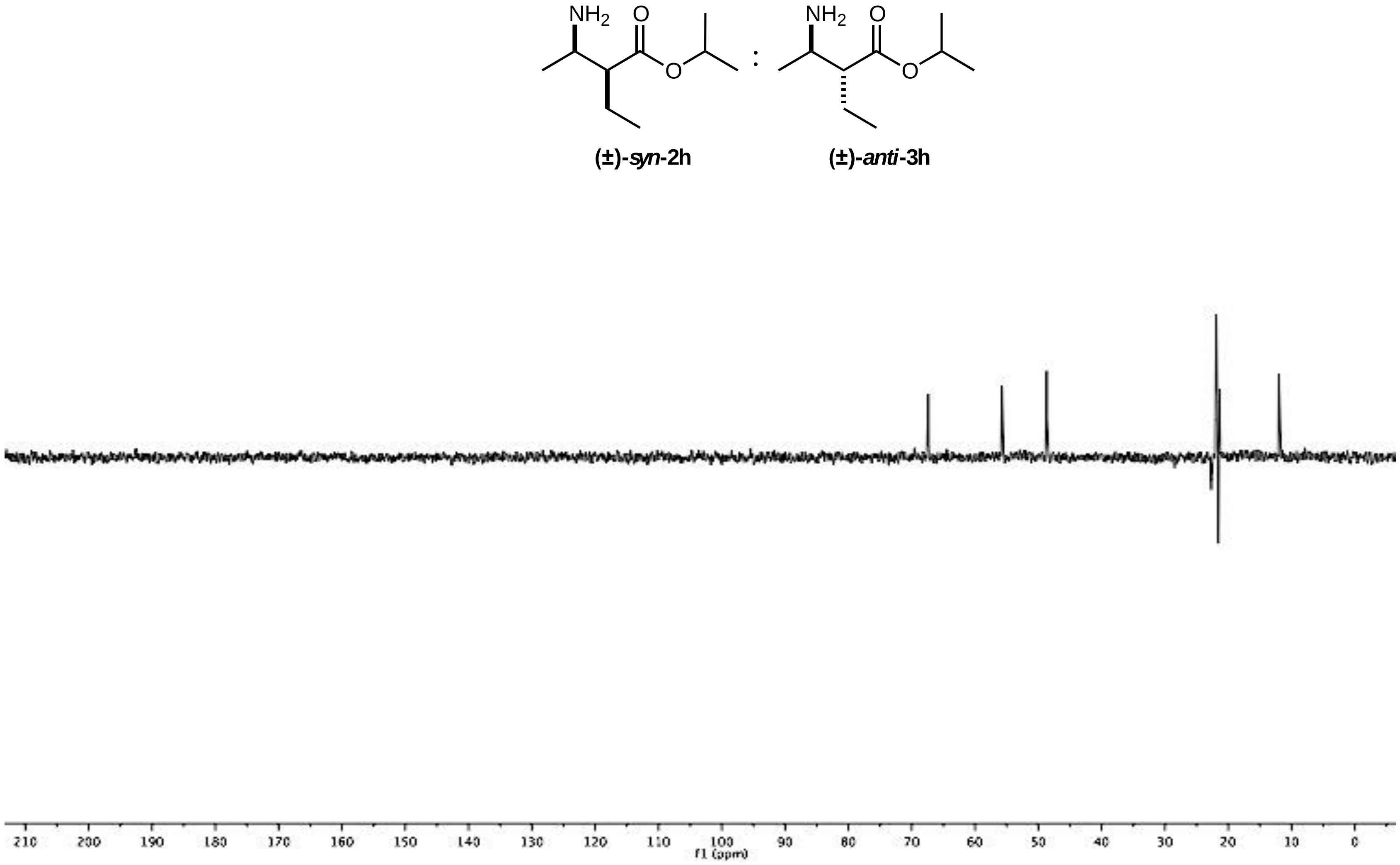
(±)-*syn*-2h **(±)-*anti*-3h**

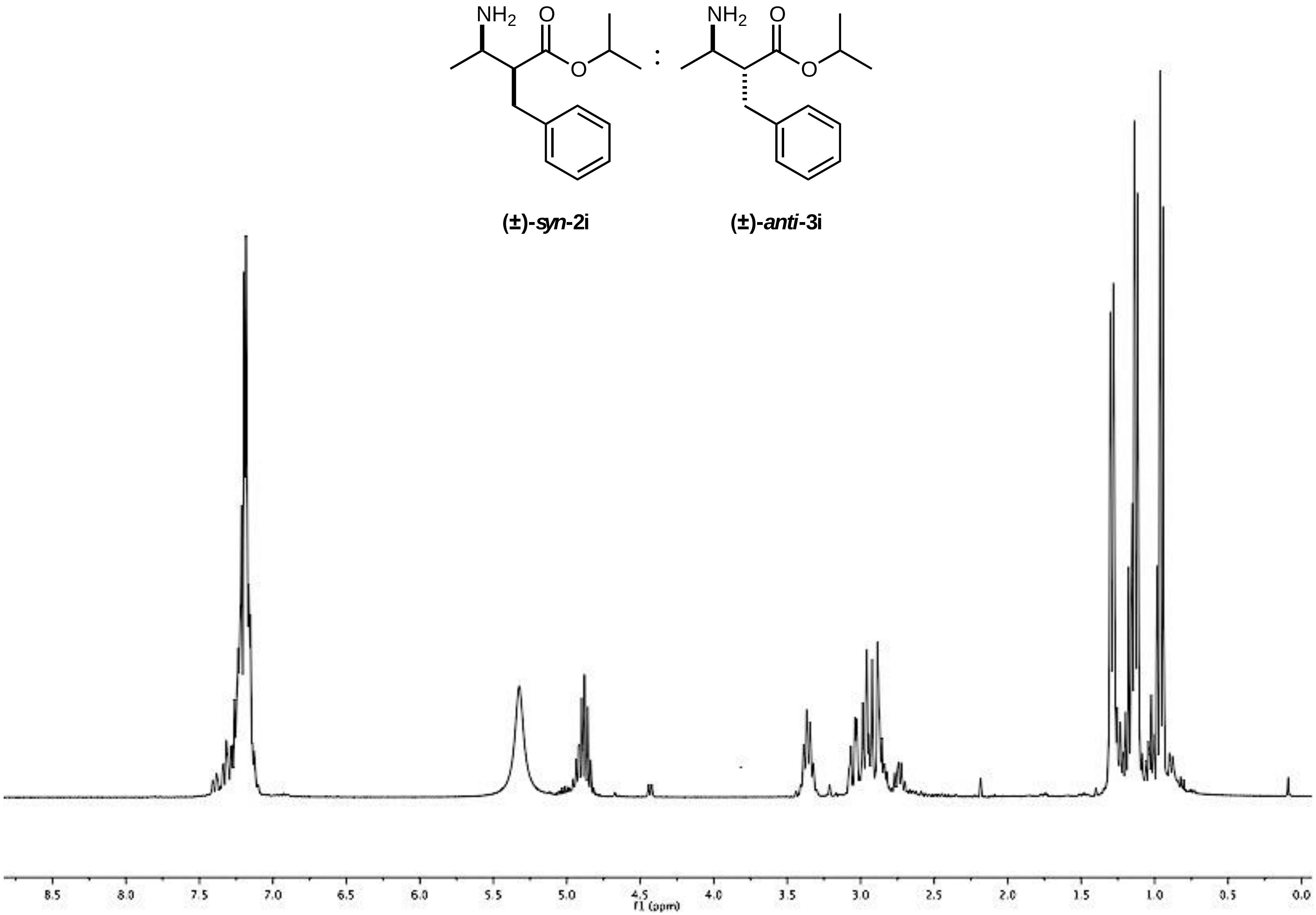




(±)-*syn*-2h (±)-*anti*-3h

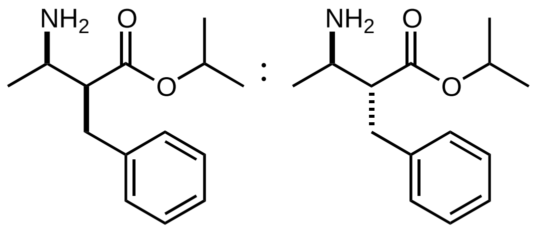



NH2
O
O
:
(±)-syn-2h
(±)-anti-3h
f1 (ppm)

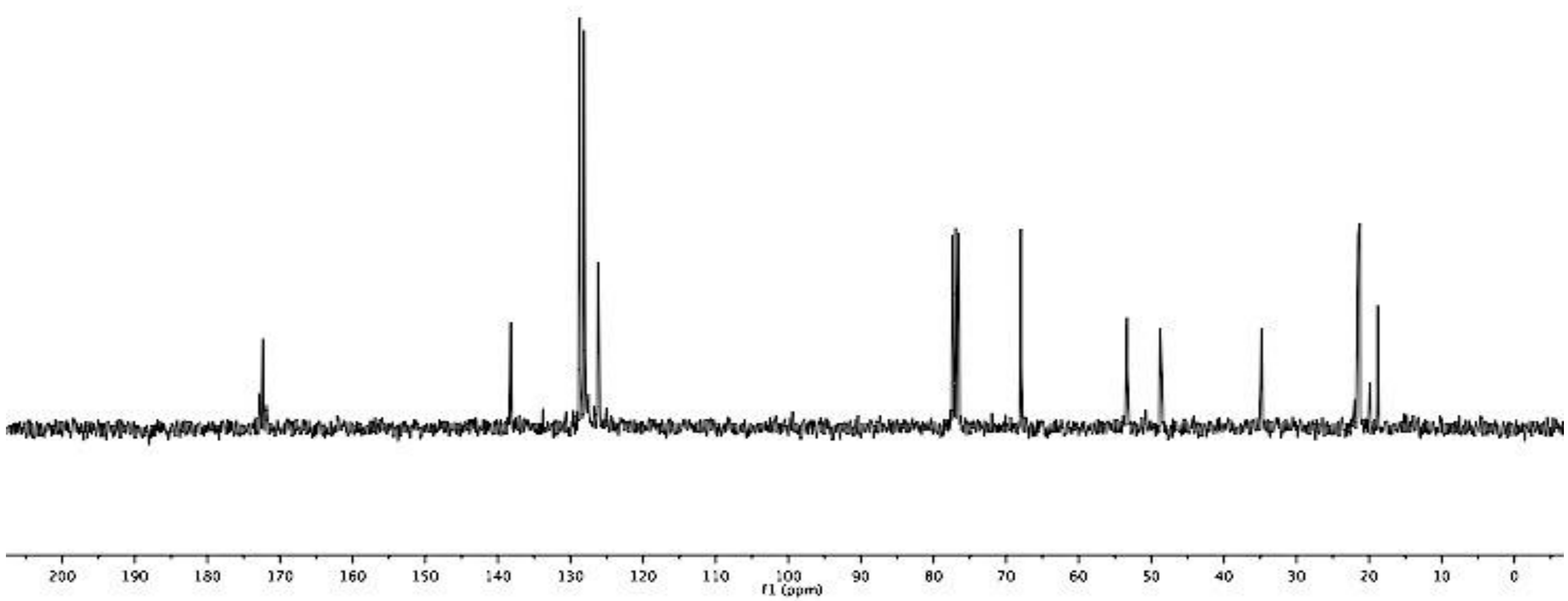


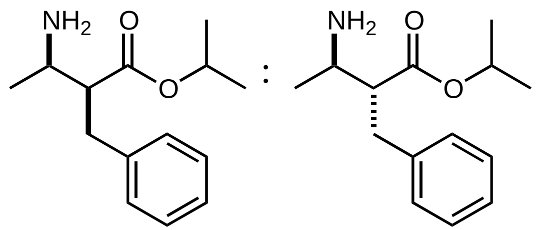
(±)-*syn*-2i **(±)-*anti*-3i**

Electronic Supplementary Material (ESI) for Chemical Communications



(±)-*syn*-2i **(±)-*anti*-3i**





(±)-*syn*-2i **(±)-*anti*-3i**