SUPPORTING INFORMATION

Organocatalytic Conjugate Addition of Formaldehyde *N,N*-Dialkylhydrazones to β,γ-Unsaturated α-Keto Esters

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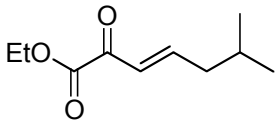
General Methods. Purification of reaction products were carried out by flash chromatography on silica-gel (0.040-0.063 mm or 0.015-0.040 mm). Analytical tlc was performed on 0.25 mm silica gel 60-F plates. ^{1}H NMR spectra were recorded at 300 MHz, 400 MHz or 500 MHz; ^{13}C NMR spectra were recorded at 75 MHz, 100 MHz and 125 MHz in CD_3COCD_3 or $CDCl_3$ as the solvent. Chemical shifts were reported in the δ scale relative to residual CH_3COCH_3 (2.05 ppm) or $CDCl_3$ (7.26 ppm) for ^{1}H NMR and to the central line of CD_3COCD_3 (29.84 ppm) or $CDCl_3$ (77 ppm) for ^{13}C NMR. The enantiomeric excess (ee) of the products was determined by HPLC on chiral stationary phases (Daicel Chiralpak AD or AD-H). Racemic samples were obtained using as catalyst bis[3,5-bis(trifluoromethyl)phenyl]thiourea.

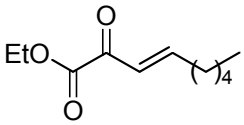
Materials. All commercially available solvents and reagents were used as received. The β,γ-unsaturated α-keto esters **5a-f** were obtained following literature procedures.[1] ^{1}H and ^{13}C NMR spectra for compounds **5a**[1], **5b**[2] and **5f**[2] were consistent with values previously reported in the literature.

(*E*)-Ethyl 6-methyl-2-oxohept-3-enoate (5c)



Following the general procedure, compound **5c** was obtained as an orange oil in 42% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.20-7.10 (m, 1H), 6.62 (d, J = 16.0 Hz, 1H), 4.33 (q, J = 7.2 Hz, 2H), 2.18 (t, J = 7.7 Hz, 2H), 1.86-1.77 (m, 1H), 1.36 (t, J = 7.0 Hz, 3H), 0.93 (d, J = 6.6 Hz, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 183.8, 162.5, 160.4, 122.5, 62.3, 31.7, 21.2, 20.9, 14.1. HRMS (EI) *m/z* calcd. for $C_{10}H_{17}O_3$: 185.1178; found 185.1187.

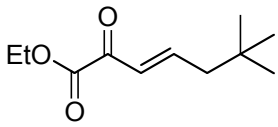
(*E*)-Ethyl 2-oxohex-3-enoate (5d)



Following the general procedure, compound **5d** was obtained as an orange oil in 20% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.17 (dt, J = 15.9, 6.9 Hz, 1H), 6.62 (d, J = 15.9 Hz, 1H), 4.32 (q, J = 7.1 Hz, 2H), 2.32-2.25 (m, 2H), 1.51-1.23 (m, 9H), 0.88 (t, J = 6.3 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 183.7, 162.7, 154.7, 125.1, 62.3, 33.1, 31.0, 27.4, 22.4, 14.0, 13.9. HRMS (EI) *m/z* calcd. for $C_{11}H_{19}O_3$: 199.1334; found 199.1329.

(1) Jensen, K. B.; Thourhaunge, J., Hazell, R. G., Jørgensen, K. A. *Angew. Chem. Int. Ed.* **2001**, *40*, 160.
(2) Sugimura, H.; Miura, M.; Yamada, N. *Tetrahedron: Asymmetry* **1997**, *8*, 4089.

(*E*)-Ethyl 6,6-dimethyl-2-oxohept-3-enoate (5e).



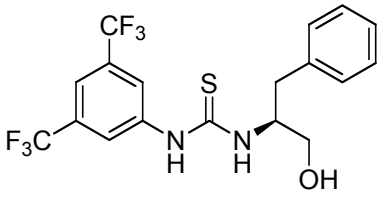
Following the general procedure, compound **5e** was obtained as orange oil in 30% yield. ^{1}H NMR (300 MHz, CD_3COCD_3): δ 7.19-7.08 (m, 1H), 6.53 (d, J = 15.9 Hz, 1H), 4.34 (q, J = 7.2 Hz, 2H), 2.27 (d, J = 8.1 Hz, 2H), 1.34 (t, J = 7.1 Hz, 3H), 0.98 (s, 9H). ^{13}C NMR (75 MHz, CD_3COCD_3): δ 185.4, 164.2, 153.3, 129.0, 62.9, 48.0, 32.6, 29.7, 14.7. HRMS (EI) *m/z* calcd. for $C_{11}H_{19}O_3$: 199.1334; found 199.1341

General procedure for the preparation of catalysts 14a-g and 15.

To a stirred solution of 3,5-bis(trifluoromethyl)phenyl isothiocyanate (5 mmol) in CH_2Cl_2 (10 mL), commercially available chiral amine (5 mmol) was added in one portion. After stirring the resulting solution at room temperature overnight, the solvent was evaporated under reduced pressure and the white solid purified by crystallisation (*n*-hexane/acetone).

The ^{1}H and ^{13}C NMR spectra for catalysts **14a**,[3] **14c**[4] and **14d**[5] are consistent with values previously reported in the literature.

1-[3,5-Bis(trifluoromethyl)phenyl]-3-[(*S*)-1-hydroxy-3-phenylpropan-2-yl]thiourea (14b)

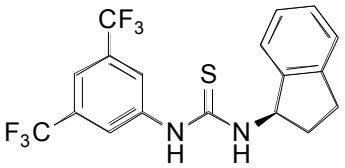


Following the general procedure, compound **14b** was obtained as a white solid in 90% yield. Mp 97-99 °C. ^{1}H NMR (300 MHz, CD_3COCD_3): δ 9.47 (br s, 1H), 8.35 (s, 2H), 7.69 (s, 1H), 7.63 (br s, 1H), 7.40-7-16 (m, 5H), 4.72 (br s, 1H), 4.35-4.02 (m, 1H), 3.80-3.55 (m, 2H), 3.11 (dd, J = 13.5, 6.0 Hz, 1H), 2.97 (dd, J = 13.5, 8.4 Hz, 1H). ^{13}C NMR (75

(3) Sohtome, Y.; Tanatani, A.; Hashimoto, Y.; Nagasawa, K. *Tetrahedron Lett.* **2004**, *45*, 5589.
(4) Munslow, I. J.; Wade, A. R.; Deeth, R. J.; Scott, P. *Chem. Commun*. **2004**, 2596.
(5) Herrera, R. P.; Sgarzani, V.; Bernardi, L.; Ricci, A. *Angew. Chem. Int. Ed*. **2005**, *44*, 6576.

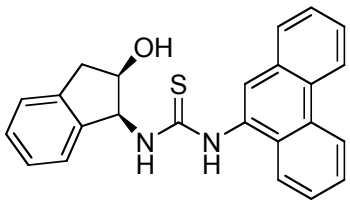
MHz, CD_3COCD_3): δ 181.8, 144.9, 143.0, 132.0 (q, J = 132.0 Hz, $C$$CF_3$), 130.2, 129.2 127.2, 124.4 (q, J = 270.0 Hz, CF_3), 123.2, 117.4, 62.1, 58.2, 37.0. HRMS (EI) *m/z* calcd. for $C_{18}H_{17}F_6N_2OS$: 423.0966; found 423.0954. $[\alpha]^{22}_D$ –54 (*c* 0.3, $CHCl_3$).

1-[3,5-Bis(trifluoromethyl)phenyl]-3-[(*R*)-2,3-dihydro-1*H*-inden-1-yl]thiourea (14e)



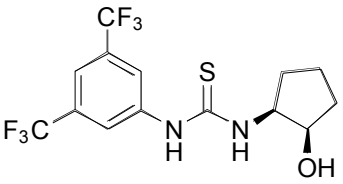
Following the general procedure, compound **14e** was obtained as a white solid in 90% yield. Mp 136-138 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.50 (br s, 1H), 7.79 (s, 2H), 7.70 (s, 1H), 7.37 (d, J = 6.9 Hz, 1H), 7.27-7.19 (m, 3H), 6.41 (br s, 1H), 5.94 (br s, 1H), 3.05-2.72 (m, 3H), 1.97-1.85 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 180.3, 143.5, 141.5, 138.7, 133.5 (q, J = 33.8 Hz, $C$$CF_3$), 128.6, 127.0, 125.2, 124.0, 123.9, 122.7 (q, J = 271.5 Hz, CF_3), 119.6, 60.7, 33.4, 30.1. HRMS (EI) *m/z* calcd. for $C_{18}H_{14}F_6N_2S$: 404.0782; found 404.0777. $[\alpha]^{22}_D$ +34 (*c* 2.1, CH_3COCH_3).

1-[(1*S*,2*R*)-2,3-Dihydro-2-hydroxy-1*H*-inden-1-yl]-3-(phenanthren-9-yl)thiourea (14f)



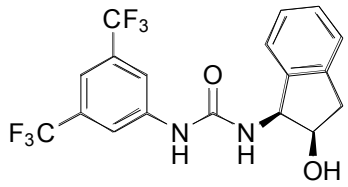
Following the general procedure, compound **14f** was obtained as a white solid in 75% yield. Mp 112-116 °C. ^{1}H NMR (300 MHz, CD_3COCD_3): δ 9.27 (s, 1H), 8.88-8.78 (m, 2H), 8.28-8.23 (m, 1H), 7.97 (s, 1H), 7.95 (d, J = 1.5 Hz, 1H), 7.79-7.60 (m, 4H), 7.41-7.38 (m, 1H), 7.23 (d, J = 8.1 Hz, 1H), 7.15-7.09 (m, 3H), 6.04 (dd, J = 8.1, 5.1 Hz, 1H), 4.63 (dt, J = 5.0, 0.9 Hz, 1H), 4.18 (br s, 1H), 3.12 (dd, J = 16.5, 4.8 Hz, 1H), 2.81 (d, J = 16.5 Hz, 1H). ^{13}C NMR (75 MHz, CD_3COCD_3): δ 184.2, 142.8, 141.5, 133.4, 132.7, 132.5, 130.8, 130.5, 129.7, 128.5, 128.4, 128.3, 128.2, 127.3, 127.0, 126.0, 125.6, 124.8, 124.2, 123.8, 73.6, 63.7, 41.0. HRMS (EI) *m/z* calcd. for $C_{25}H_{20}N_2OS$: 385.1375; found 385.1377. $[\alpha]^{22}_D$ –56 (*c* 0.5, CH_3COCH_3).

1-[3,5-Bis(trifluoromethyl)phenyl]-3-[(1*S*,2*R*)-2-hydroxycyclopentyl]thiourea (14g)



Following the general procedure, compound **14g** was obtained as a white solid in 85% yield. Mp 139-142 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.60 (br s, 1H), 7.82 (s, 2H), 7.66 (s, 1H), 7.06 (d, J = 7.5 Hz, 1H), 4.46 (br s, 1H), 4.39-4.35 (m, 1H), 2.26-1.54 (m, 7H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 179.9, 144.8, 132.9 (q, J = 33.8 Hz, *C*CF_3), 123.2, 122.8 (q, J = 271.5 Hz, CF_3), 118.9, 73.0, 59.2, 33.3, 29.0, 20.41. HRMS (EI) *m/z* calcd. for $C_{14}H_{14}F_6N_2OS$: 372.0731; found 372.0706. $[\alpha]^{22}_D$ –10 (*c* 2, CH_3COCH_3).

1-(3,5-bis(trifluoromethyl)phenyl)-3-((1*S*,2*R*)-2,3-dihydro-2-hydroxy-1*H*-inden-1-yl)urea (15)

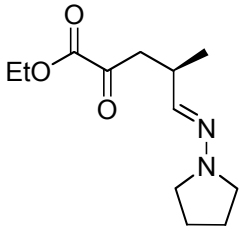


Following the general procedure, compound **15** was obtained as a white solid in 90% yield. Mp 222-225 °C. ^{1}H NMR (300 MHz, CD_3COCD_3): δ 8.90 (br s, 1H), 8.20 (s, 2H), 7.55 (s, 1H), 7.37-7.29 (m, 1H), 7.27-7.15 (m, 3H), 6.40 (br s, 1H), 5.29 (dd, J = 8.4, 5.1 Hz, 1H), 4.66-4.61 (m, 1H), 4.38-4.37 (m, 1H), 3.15 (dd, J = 16.5, 4.8 Hz, 1H), 2.91 (d, J = 16.2, 1H). ^{13}C NMR (75 MHz, CD_3COCD_3): δ 155.9, 143.7, 143.4, 141.5, 133.5 (q, J = 32.3 Hz, *C*CF_3), 128.4, 127.4, 125.8, 125.2, 124.5 (q, J = 270.0 Hz, CF_3), 118.4, 114.8, 73.6, 58.8, 40.7. HRMS (EI) *m/z* calcd. for $C_{18}H_{14}F_6N_2O_2$: 404.0959; found 404.0963. $[\alpha]^{22}_D$ +36 (*c* 2.0, CH_3COCH_3).

General procedure for the organocatalytic enantioselective formylation of *β,γ*-unsaturated *α*-keto esters with hydrazone 4. In a test tube, to a solution of the β,γ-unsaturated α-keto ester **5** (0.25 mmol) and catalyst **14d** (10.5 mg, 0.025 mmol) in CH_2Cl_2 (2.5 mL) cooled to -45 or -60 °C,

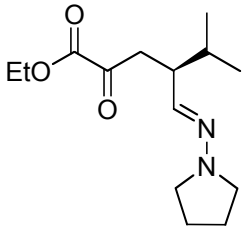
hydrazone **4** (0.3 mmol) was added in one portion. The test tube was placed in a freezer at –45 or -60 °C for 72 h, then the product **8a** was obtained by flash chromathography on silica gel treated with Et_3N (*n*-hexane-AcOEt mixtures).

(*R*,*E*)-Ethyl 4-methyl-2-oxo-5-(pyrrolidin-1-ylimino)pentanoate (8a)



Following the general procedure, compound **8a** was obtained as an orange oil in 60% yield. The ee of the product was determined by HPLC using a Daicel Chiralpak AD column (*n*-hexane/*i*-PrOH = 99:1, flow rate 1 mL/min, τ_{major} = 25.0 min, τ_{minor} = 14.0 min). ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.44 (d, J = 3.5 Hz, 1H), 4.25 (q, J = 6.9 Hz, 2H), 3.10 (dd, J = 15.5, 8.6 Hz, 1H), 3.02-2.85 (m, 5H), 2.56 (dd, J = 15.5, 5.5 Hz, 1H), 1.82-1.77 (m, 4H), 1.30 (t, J = 7.0 Hz, 3H), 1.10 (d, J = 7.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 193.6, 161.5, 138.6, 62.1, 51.4, 51.2, 42.7, 34.3, 23.0, 22.9, 18.9, 14.0. HRMS (EI) *m/z* calcd. for $C_{12}H_{19}N_2O_3$: 239.1396; found 239.1393. $[\alpha]^{25}_D$ –5.4 (*c* 0.7, CH_3COCH_3), 80% ee.

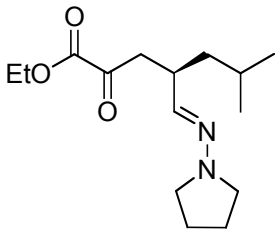
(*S*,*E*)-Ethyl 5-methyl-2-oxo-4-[(pyrrolidin-1-ylimino)methyl]hexanoate (8b)



Following the general procedure, compound **8b** was obtained as an orange oil in 80% yield. The ee of the product was determined by HPLC using a Daicel Chiralpak AD-H column (*n*-hexane/*i*-PrOH = 99:1, flow rate 1 mL/min, τ_{major} = 29.8 min, τ_{minor} = 15.3 min). ^{1}H NMR (300 MHz, CD_3COCD_3): δ 6.48 (d, J = 3.6 Hz, 1H), 4.26 (q, J = 7.1 Hz, 2H), 3.22 (dd, J = 15.3, 10.5 Hz, 1H), 3.06-2.97 (m, 4H), 2.85-2.78 (m, 1H), 2.48 (dd, J = 15.3, 3.9 Hz, 1H), 1.94-1.76 (m, 5H), 1.31 (t, J = 7.1 Hz, 3H), 0.95 (d, J = 6.3 Hz, 3H), 0.93 (d, J = 6.6 Hz, 3H). ^{13}C NMR (75 MHz, CD_3COCD_3): δ 194.4, 162.8, 137.0,

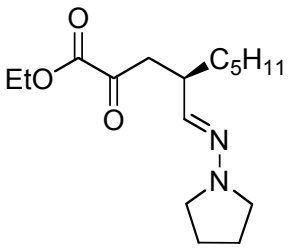
62.4, 52.1, 46.5, 38.2, 31.7, 23.8, 20.1, 20.0, 14.5. HRMS (EI) *m/z* calcd. for $C_{14}H_{23}N_2O_3$: 267.1709; found 267.1695. $[\alpha]^{25}_D$ –13.8 (*c* 1.9, CH_3COCH_3), 78% ee.

(*R,E*)-Ethyl 6-methyl-2-oxo-4-[(pyrrolidin-1-ylimino)methyl]heptanoate (8c)



Following the general procedure, compound **8c** was obtained as an orange oil in 75% yield. The ee of the product was determined by HPLC using a Daicel Chiralpak AD-H column (*n*-hexane/*i*-PrOH = 99:1, flow rate 1 mL/min, τ_{major} = 15.5 min, τ_{minor} = 10.8 min). ^{1}H NMR (500 MHz, CD_3COCD_3): δ 6.42 (d, J = 4.5 Hz, 1H), 4.24 (q, J = 14.0, 7.0 Hz, 2H), 3.02 (dd, J = 15.5, 9.0 Hz, 1H), 2.98-2.88 (m, 5H), 2.61 (dd, J = 15.3, 4.8 Hz, 1H), 1.81-1.77 (m, 4H), 1.74-1.66 (m, 1H), 1.43-1.37 (m, 1H), 1.35-1.22 (m, 4H), 1.11 (d, J = 7.0 Hz, 3H), 1.06 (d, J = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, CD_3COCD_3): δ 194.1, 162.5, 138.2, 62.4, 51.9, 43.9, 42.2, 38.3, 26.3, 23.7, 23.2, 23.0, 22.7, 14.3. HRMS (EI) *m/z* calcd. for $C_{15}H_{25}N_2O_3$: 281.1865; found 281.1854. $[\alpha]^{20}_D$ –4.5 (*c* 1.0, CH_3COCH_3), 78% ee.

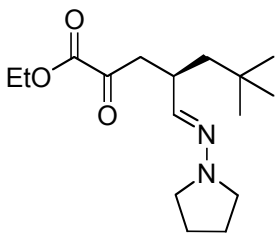
(*R,E*)-Ethyl 2-oxo-4-[(pyrrolidin-1-ylimino)methyl]nonanoate (8d)



Following the general procedure, compound **8d** was obtained as an orange oil in 61% yield. The ee of the product was determined by HPLC using a Daicel Chiralpak AD column (*n*-hexane/*i*-PrOH = 99:1, flow rate 1 mL/min, τ_{major} = 32.2 min, τ_{minor} = 19.0 min). ^{1}H NMR (300 MHz, CD_3COCD_3): δ 6.47 (d, J = 3.9 Hz, 1H), 4.26 (q, J = 7.2 Hz, 2H), 3.10 (dd, J = 15.6, 9.3 Hz, 1H), 3.01-2.97 (m, 4H), 2.88-2.85 (m, 1H), 2.62 (dd, J = 15.3, 4.8 Hz, 1H), 1.85-1.78 (m, 4H), 1.60-1.22 (m, 11H), 0.89 (t, J = 6.9 Hz, 3H). ^{13}C NMR (75 MHz, CD_3COCD_3): δ 194.0, 162.0, 138.0,

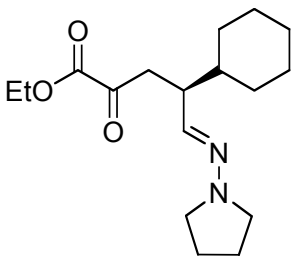
62.3, 51.8, 41.5, 40.2, 34.3, 32.6, 31.4, 28.7. 28.2, 27.8, 27.3, 23.6, 23.0, 14.3. HRMS (EI) *m/z* calcd. for $C_{16}H_{27}N_2O_3$: 295.2022; found 295.2034. $[\alpha]^{20}_D$ –0.7 (*c* 0.9, CH_3COCH_3), 70% ee.

(*R,E*)-Ethyl 6,6-dimethyl-2-oxo-4-[(pyrrolidin-1-ylimino)methyl]heptanoate (8e)



Following the general procedure, compound **8e** was obtained as an orange oil in 64% yield. The ee of the product was determined by HPLC using a Daicel Chiralpak AD-H column (*n*-hexane/*i*-PrOH = 99:1, 1 mL/min, τ_{major} = 25.4 min, τ_{minor} = 14.3 min). ^{1}H NMR (500 MHz, CD_3COCD_3): δ 6.46 (d, *J* = 4.5 Hz, 1H), 4.26 (q, *J* = 7.2 Hz, 2H), 3.09-2.96 (m, 6H), 2.68 (dd, *J* = 14.7, 4.5 Hz, 1H), 1.83-1.78 (m, 4H), 1.54 (dd, *J* = 14.1, 6.9 Hz, 1H), 1.36-1.28 (m, 1H), 1.31 (t, J = 6.9 Hz, 3H), 0.95 (s, 9H). ^{13}C NMR (75 MHz, CD_3COCD_3): δ 193.7, 162.4, 139.9, 62.3, 51.8, 48.0, 44.6, 36.9, 31.7, 29.3, 23.6, 14.3. HRMN calcd. for $C_{16}H_{29}N_2O_3$: 297.2178, found: 297.2175. $[\alpha]^{20}_D$ –2.1 (*c* 0.5, CH_3COCH_3), 58% ee.

(*S,E*)-Ethyl 4-cyclohexyl-2-oxo-5-(pyrrolidin-1-ylimino)pentanoate (8f)

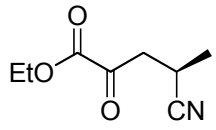


Following the general procedure, compound **8f** was obtained as an orange oil in 82% yield. The ee of the product was determined by HPLC using a Daicel Chiralpak AD-H column (*n*-hexane/*i*-PrOH = 99:1, flow rate 1 mL/min, τ_{major} = 25.9 min, τ_{minor} = 23.7 min). ^{1}H NMR (300 MHz, CD_3COCD_3): δ 6.49 (d, *J* = 3.9 Hz, 1H), 4.26 (q, *J* = 7.2 Hz, 2H), 3.22 (dd, *J* = 15.3, 10.4 Hz, 1H), 3.01-2.97 (m, 4H), 2.84-2.76 (m, 1H), 2.51 (dd, *J* = 15.3, 3.9 Hz, 1H), 1.85-1.50 (m, 9H), 1.31 (t, *J* = 7.0 Hz, 3H), 1.26-1.03 (m, 6H). ^{13}C NMR (125 MHz, CD_3COCD_3): δ 194.2, 162.5, 137.1, 62.2, 51.9, 41.9, 38.2, 31.0, 30.8, 27.3, 27.3, 27.2, 26.1, 23.6, 14.3. HRMS (EI) *m/z* calcd. for $C_{17}H_{27}N_2O_3$: 307.2021; found 307.2014. $[\alpha]^{20}_D$ –3.6 (*c* 1.3, CH_3COCH_3), 72% ee.

General procedure for the synthesis of nitrile derivatives 16a and 16b.

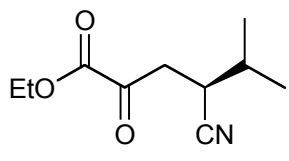
In a test tube, to a solution of product **8a,b** (0.25 mmol) in MeOH (2 mL), cooled to -25 °C, a suspension of MMPP (0.18mmol) in MeOH (1 mL) was added dropwise. The mixture was stirred for 18h and then poured into a mixture of CH_2Cl_2 (5 mL) and water (10 mL). The organic layer was separated, washed with brine (10 mL) and water (10 mL) and dried over Na_2SO_4. The solvent was removed and the residue purified by column chromatography to afford pure compounds **16a** and **16b**.

(*R*)-Ethyl 4-cyano-2-oxopentanoate (16a)



Following the general procedure, compound **16a** was obtained as an orange oil in 74% yield. The ee of the product was determined by chiral GC using a γ-TA column (150 °C, $t_r(S)$ = 15.4 min, $t_r(R)$ = 18.5 min).^{1}H NMR (300 MHz, CD_3COCD_3): δ 4.29 (q, J = 7.0 Hz, 2H), 3.42-3.11 (m, 3H), 1.36 (d, J = 7.2 Hz, 3H), 1.31 (t, J = 7.0 Hz, 3H). ^{13}C NMR (75 MHz, CD_3COCD_3): δ 190.1, 159.4, 121.5, 63.1, 42.9, 19.9, 17.6, 13.9. HRMS (EI) *m/z* calcd. for $C_8H_{11}NO_3$: 169.0739; found 169.0735. $[\alpha]^{20}_D$ –8.5 (*c* 0.5, $CHCl_3$), 76% ee.

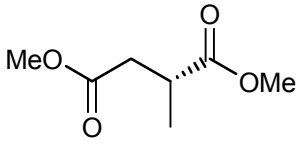
(*S*)-Ethyl 4-cyano-5-methyl-2-oxohexanoate (16b)



Following the general procedure, compound 1**6b** was obtained as orange oil in 88% yield. The ee of the product was determined by chiral GC using a γ-TA column (130 °C, $t_r(R)$ = 55.2 min, $t_r(S)$ = 57.4 min).^{1}H NMR (300 MHz, CD_3COCD_3): δ 4.37 (q, J = 7.2 Hz, 2H), 3.35-3.25 (m, 1H), 3.12-3.01 (m, 2H), 1.94-

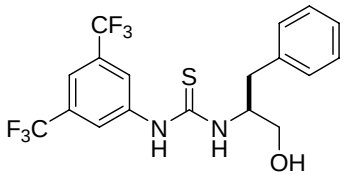
1.89 (m, 1H), 1.40 (t, J = 7.0 Hz, 3H), 1.12 (d, J = 6.5 Hz, 3H), 1.07 (d, J = 6.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 190.2, 160.1, 119.7, 63.2, 39.7, 32.7, 29.8, 20.8, 18.4, 14.0. HRMS (EI) *m/z* calcd. for $C_{10}H_{16}NO_3$: 198.1130; found 198.1126. $[\alpha]^{20}_D$ –11.3 (*c* 0.8, $CHCl_3$), 68% ee

(*R*)-Dimethyl 2-methylsuccinate (17)[6]



Dry ozone was bubbled through a solution of hydrazone **8a** (0.4 mmol) in MeOH (3 mL) at –78 °C until permanent blue colour. The solution was allowed to warm until room temperature. The solvent was removed under reduced pressure and the crude was treated with a mixture of aqueous solution of HCOOH (90%, 0.6 mL, 15 mmol) and H_2O_2 (30%, 0.6 mL, 6.9 mmol). The mixture was stirred for 14 h at room temperature and then the solvent was removed under reduced pressure. The remaining crude in MeOH (2 mL) was treated with $SOCl_2$ (0.09 mL, 1.2 mmol) and stirred at 70 °C for 20 h. The solvent was removed under reduced pressure, and the residue was purified by column chromatography to give pure **17** in 56% yield. The ee of the product was determined by chiral GC using a γ-TA column (100 °C, τ_{major} (*R*) = 13.4 min, τ_{minor} (*S*) = 13.1 min).^{1}H NMR (300 MHz, $CDCl_3$): δ 3.71 (s, 3H), 3.69 (s, 3H), 3.01-2.88 (m, 1H), 2.76 (dd, J = 16.5, 8.1 Hz, 1H), 2.42 (dd, J = 16.4, 10.0 Hz, 1H) 1.24 (d, J = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 175.7, 172.3, 51.9, 51.7, 37.4, 35.7, 17.0. HRMS (EI) *m/z* calcd. for $C_6H_9O_3$: 129.0552; found 129.0548. $[\alpha]^{20}_D$ +3.1 (*c* 0.7, $CHCl_3$), 73% ee.

(6) Guibé-Jampel, E.; Rousseau, G.; Salaün, J. *J. Chem. Soc., Chem. Commun*. **1987**, 1080.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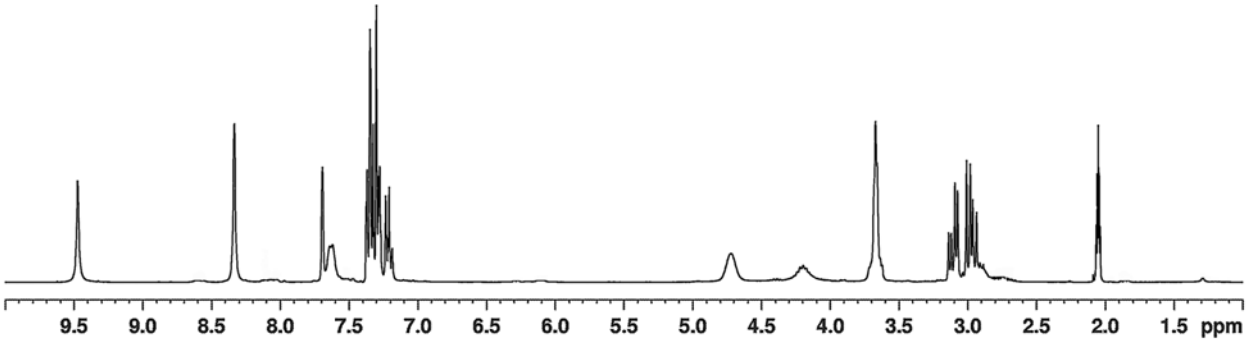
OH

14b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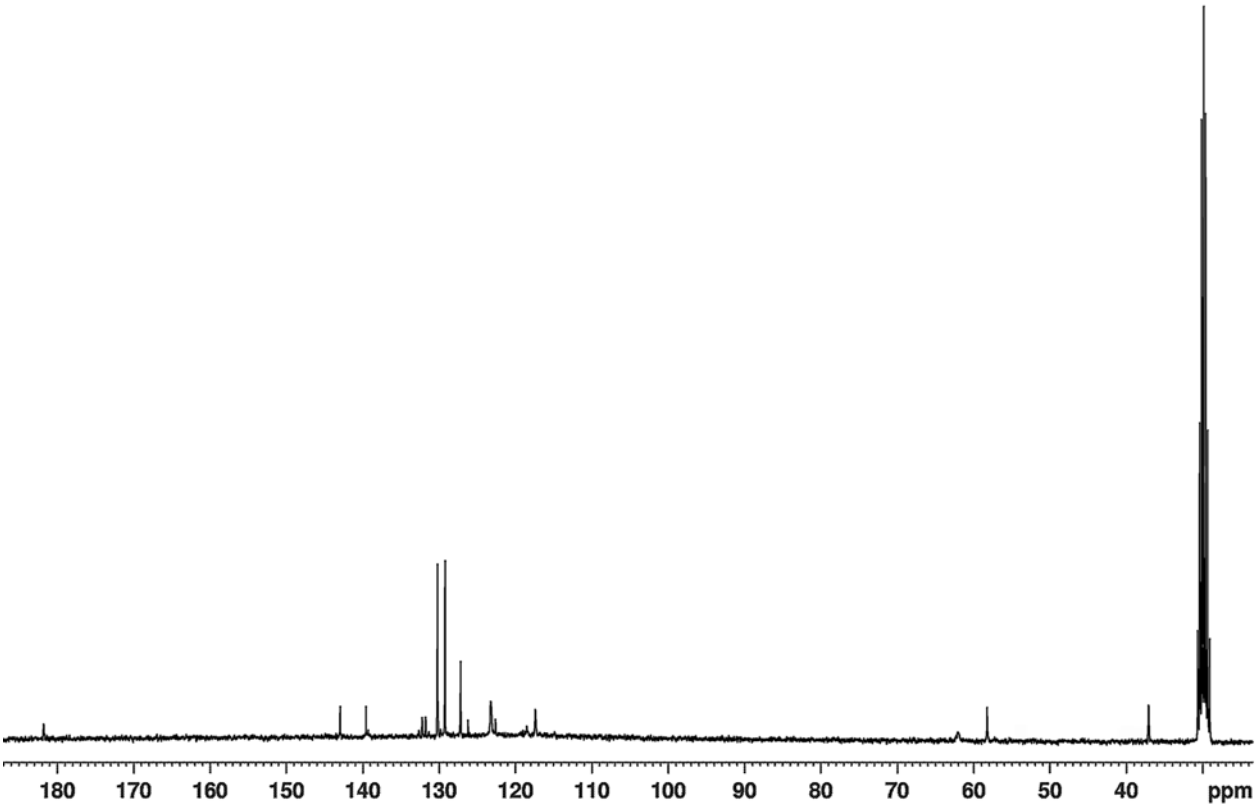
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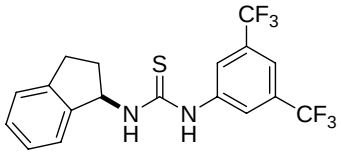
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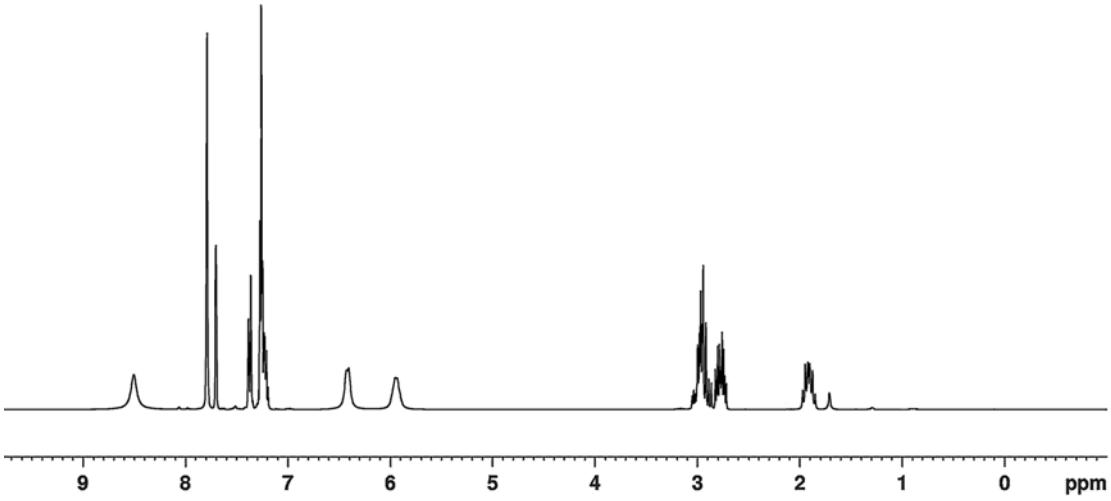
14e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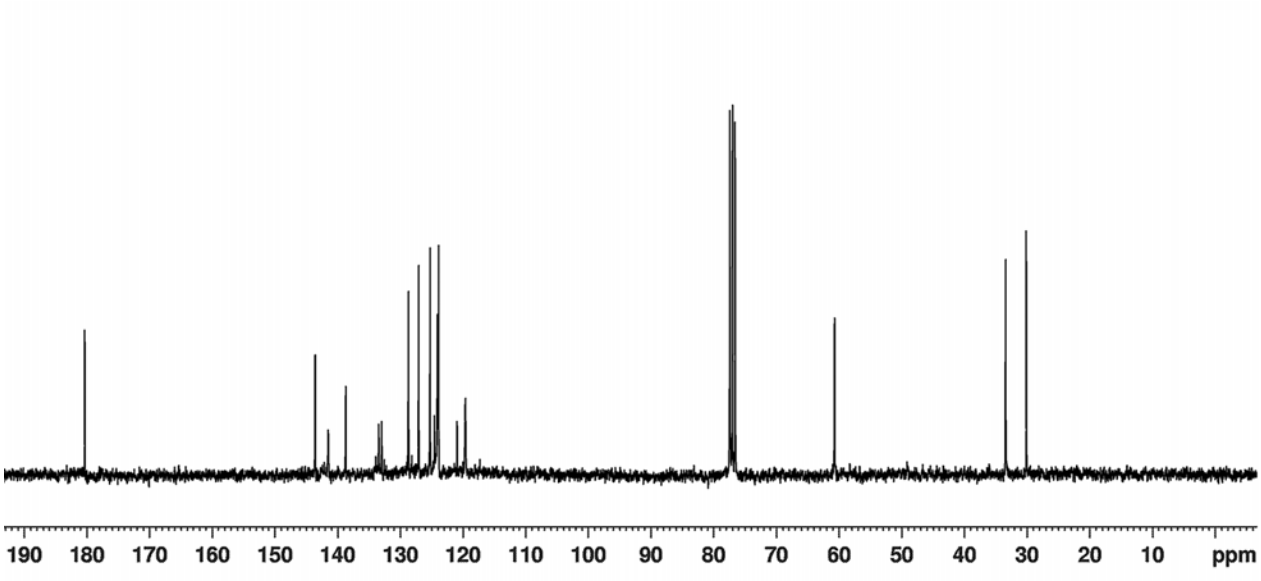
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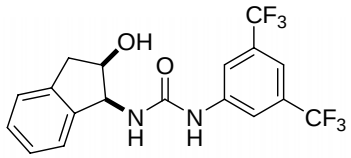
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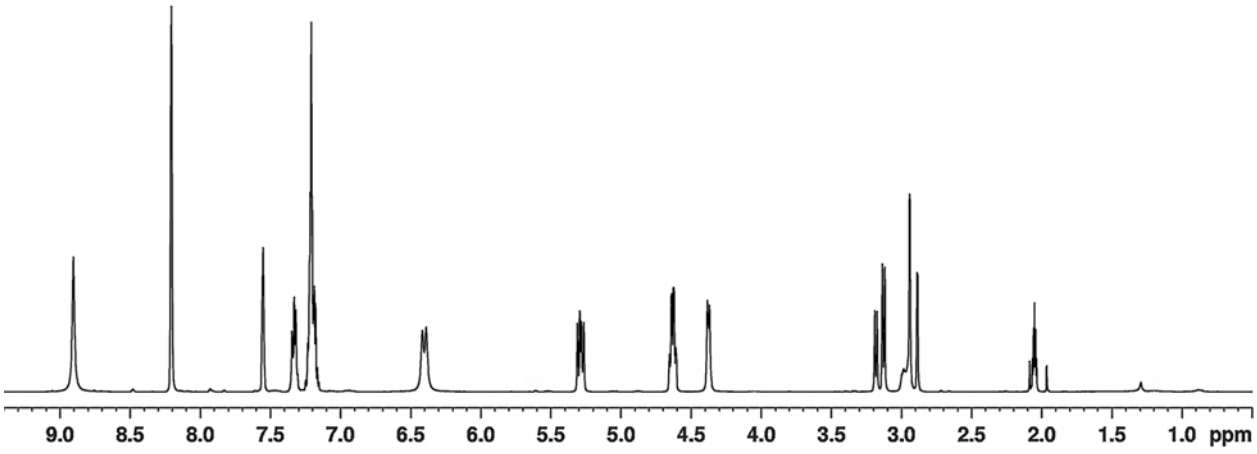
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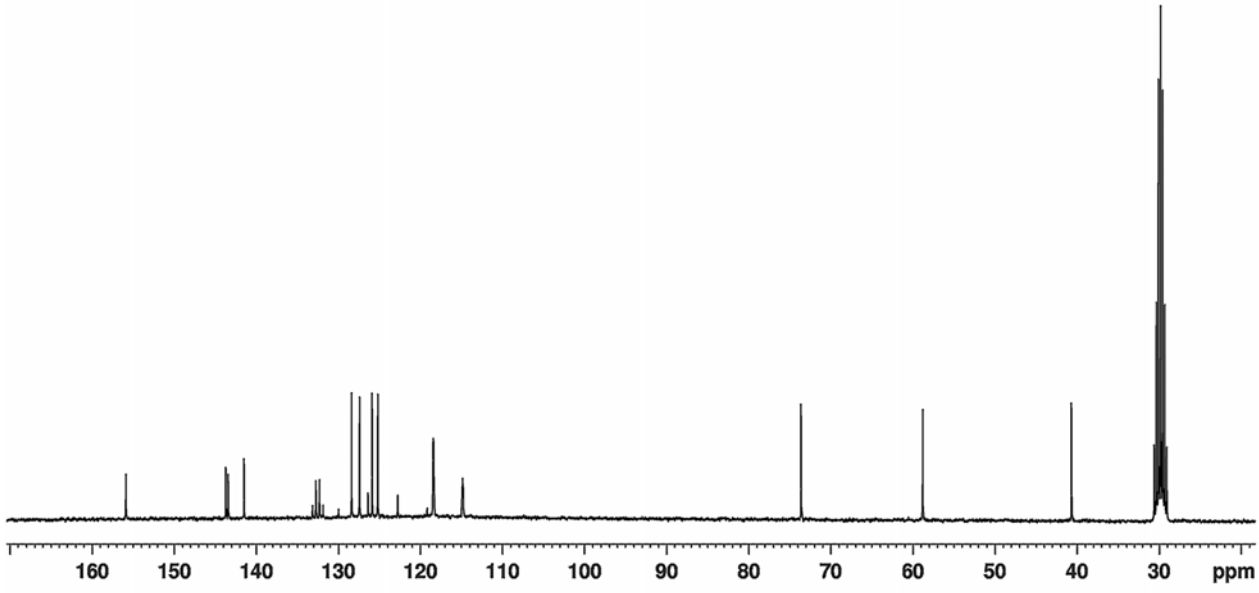
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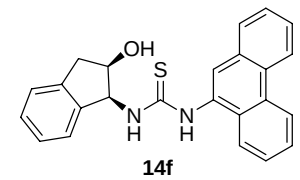
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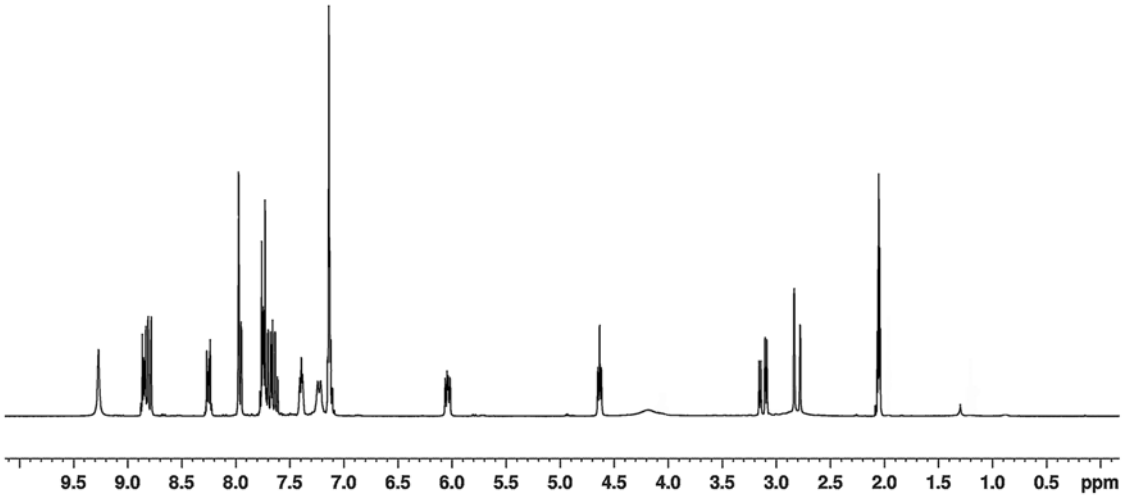
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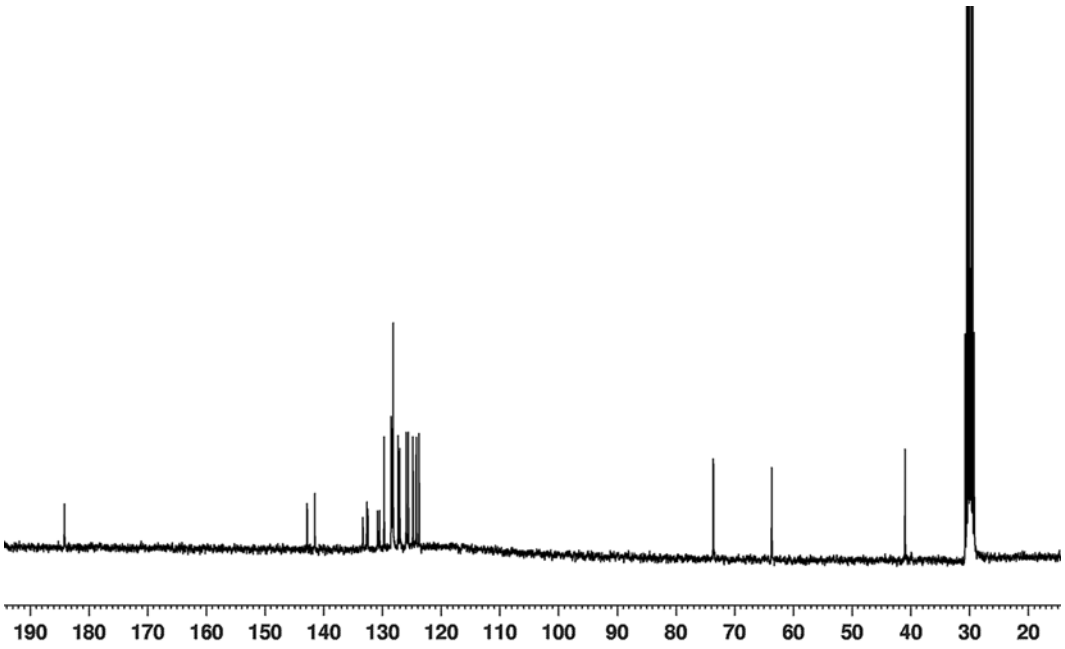
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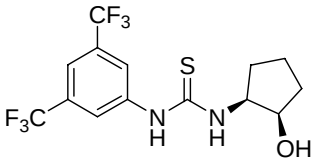
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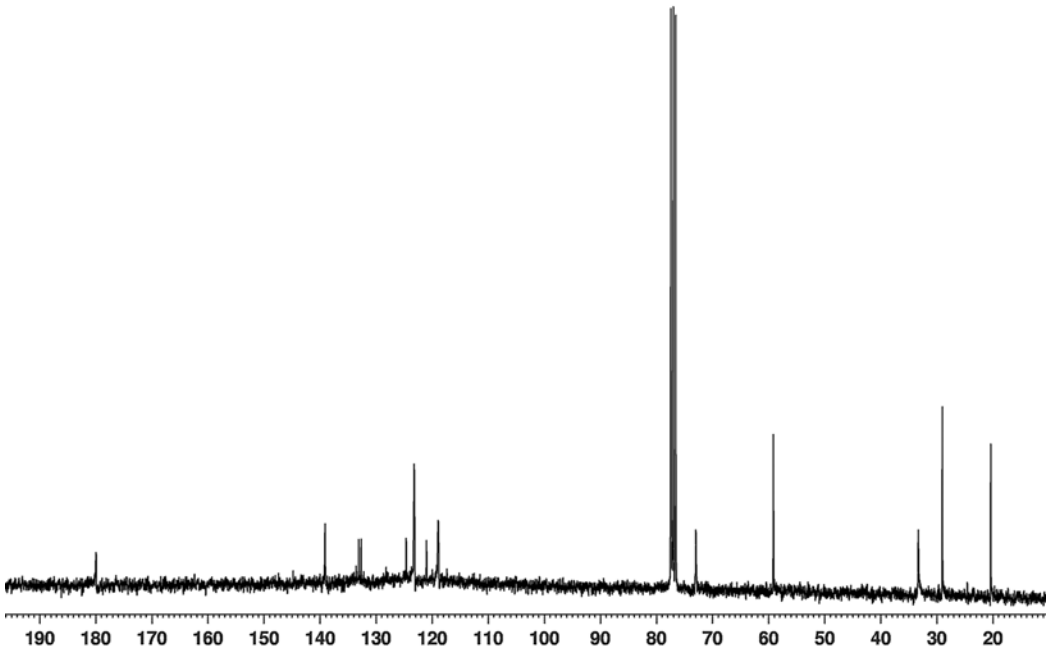
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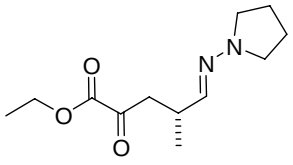

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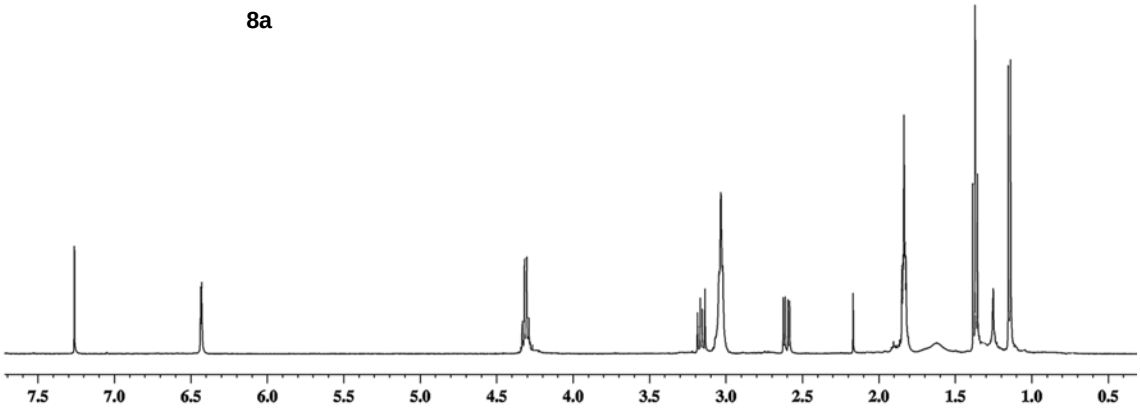
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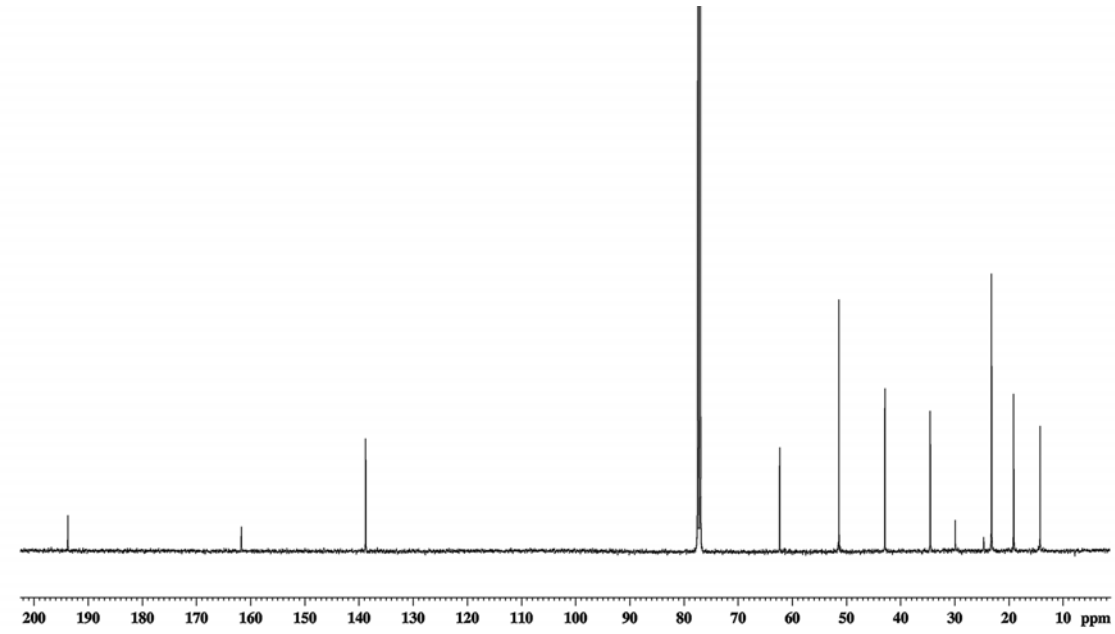
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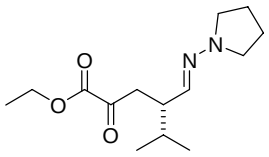

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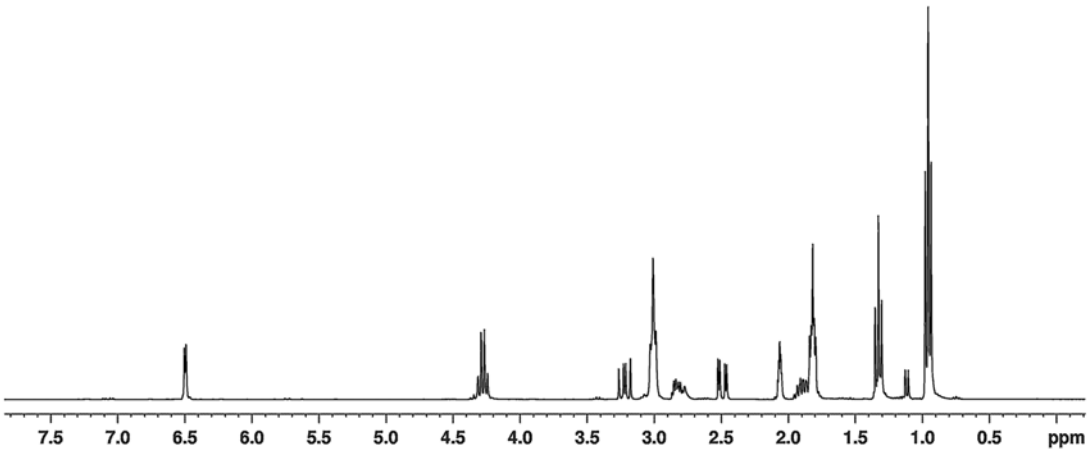
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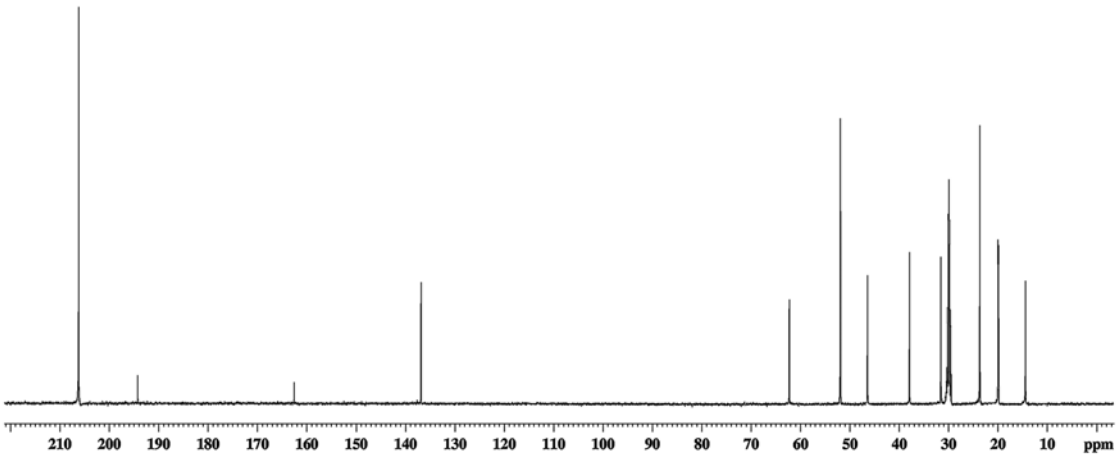
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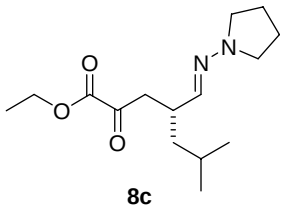
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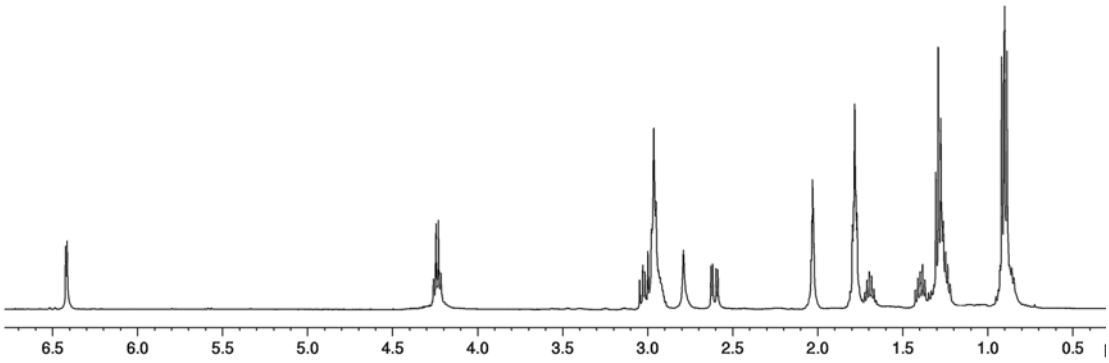
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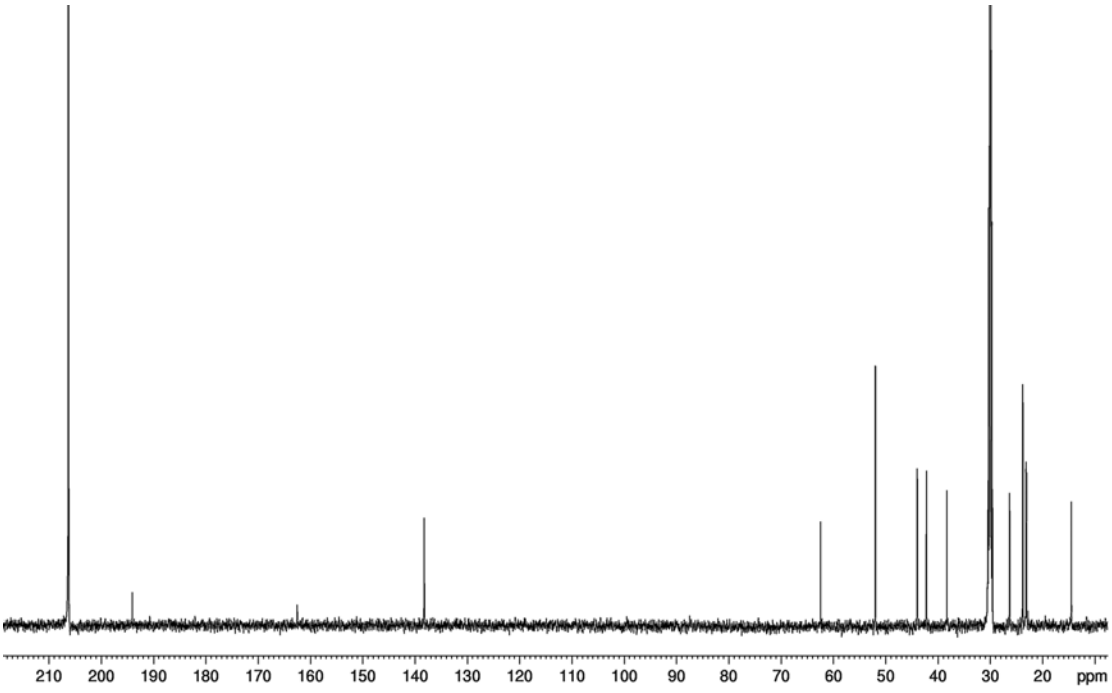
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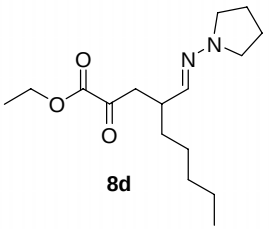
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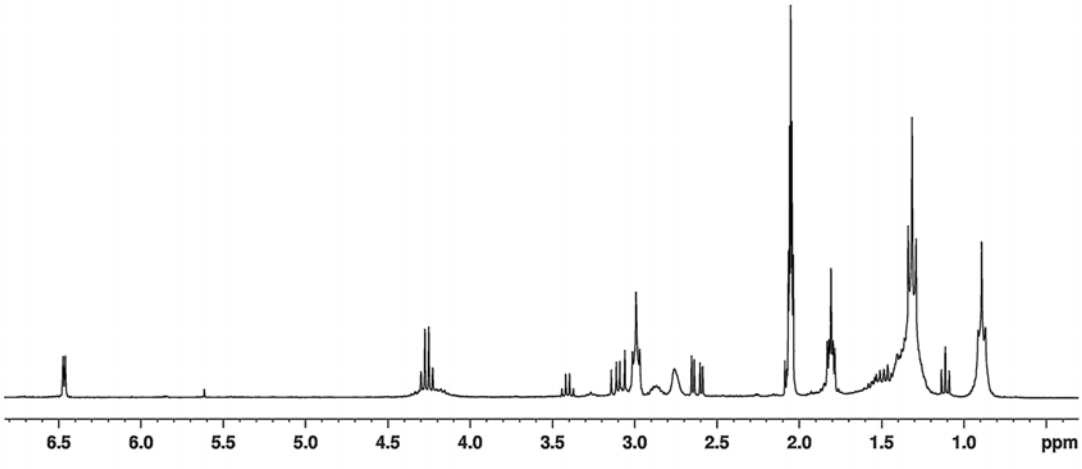
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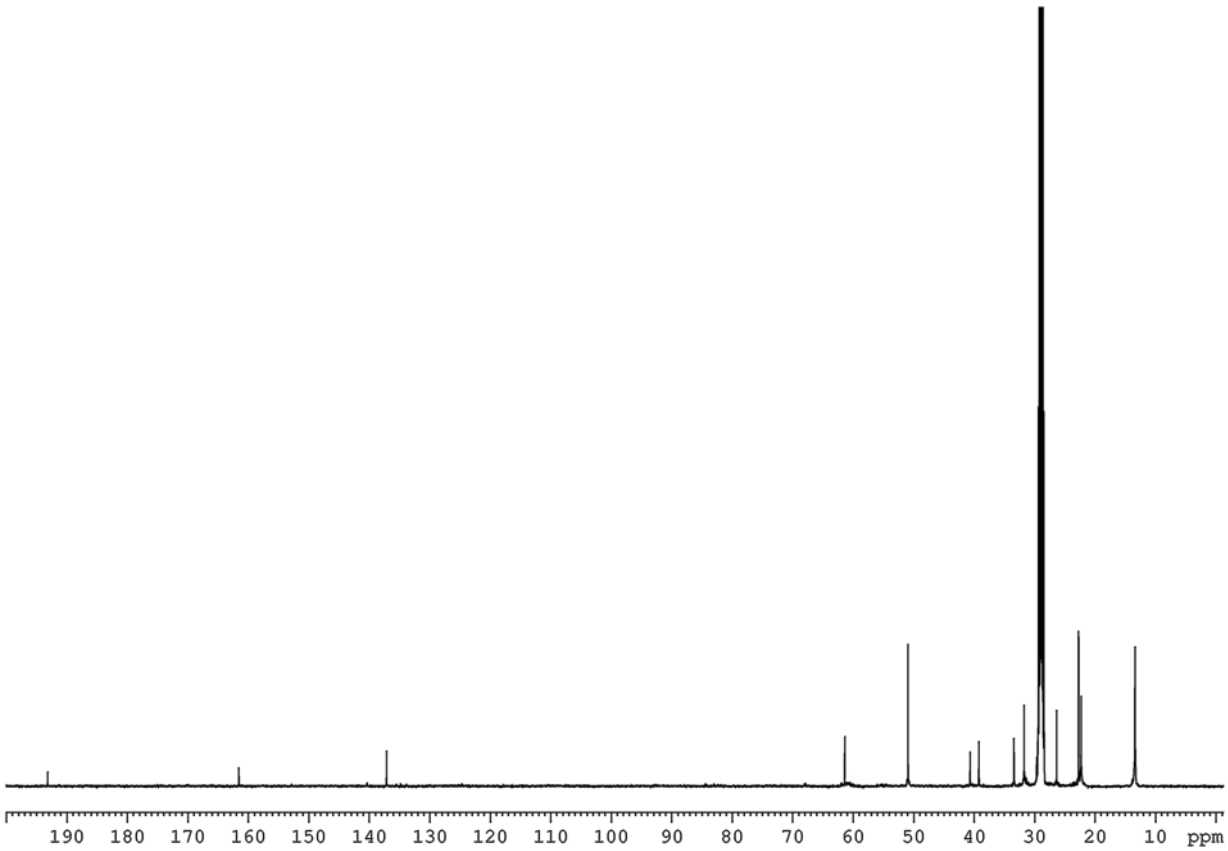
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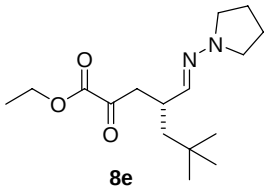

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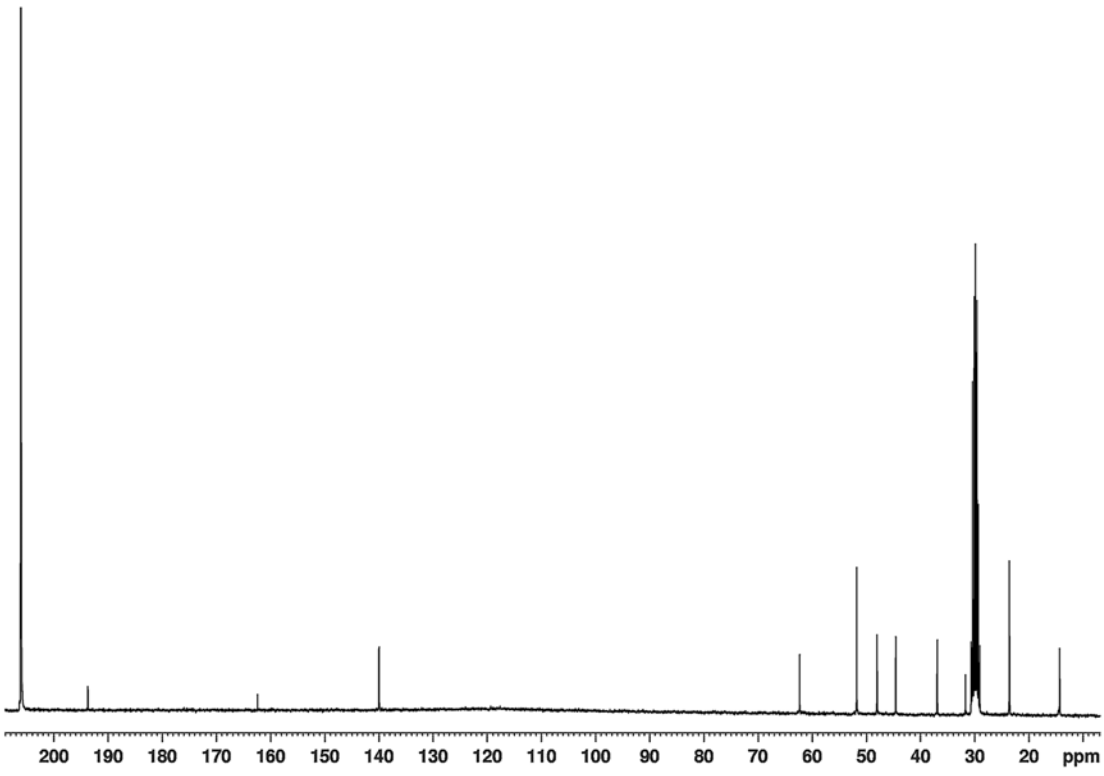
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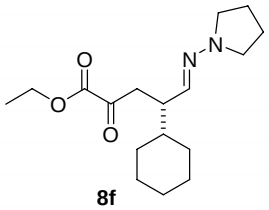
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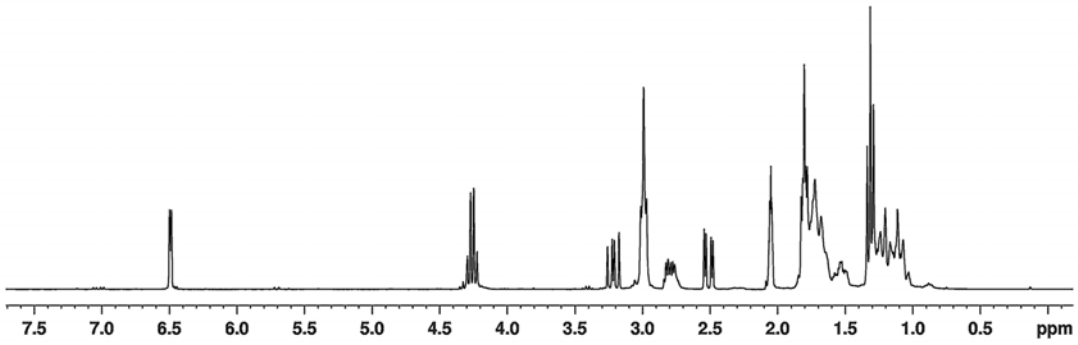
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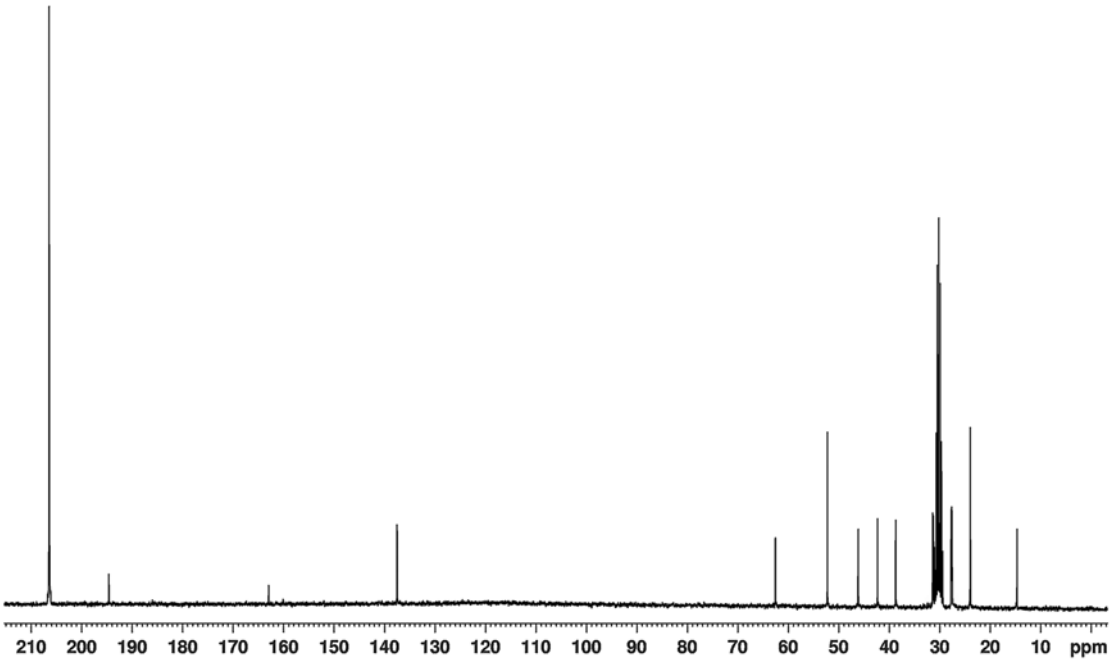
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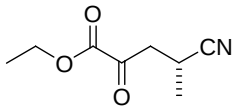
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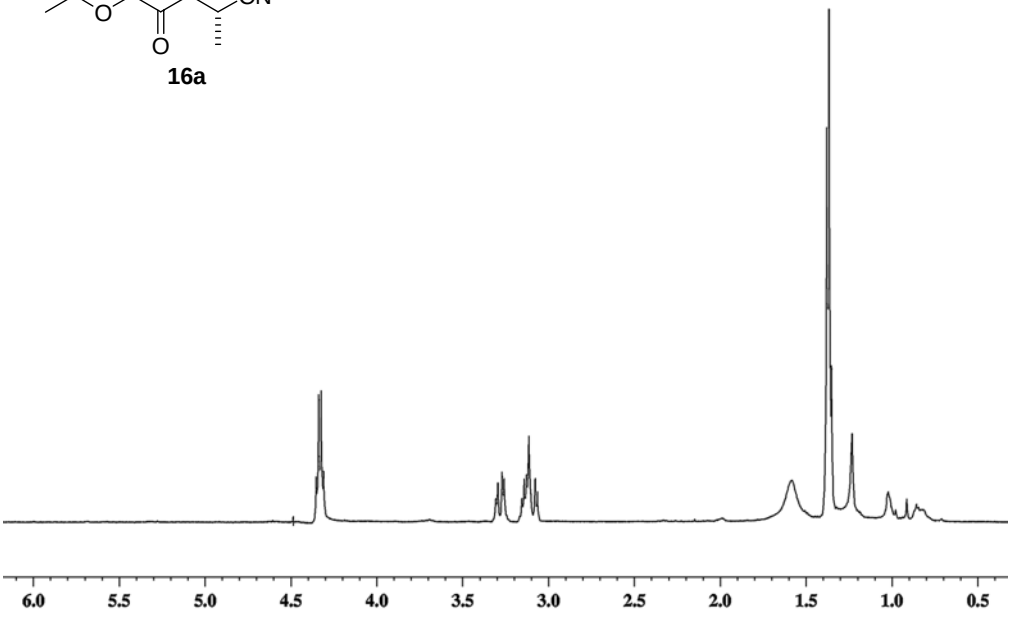
CN

16a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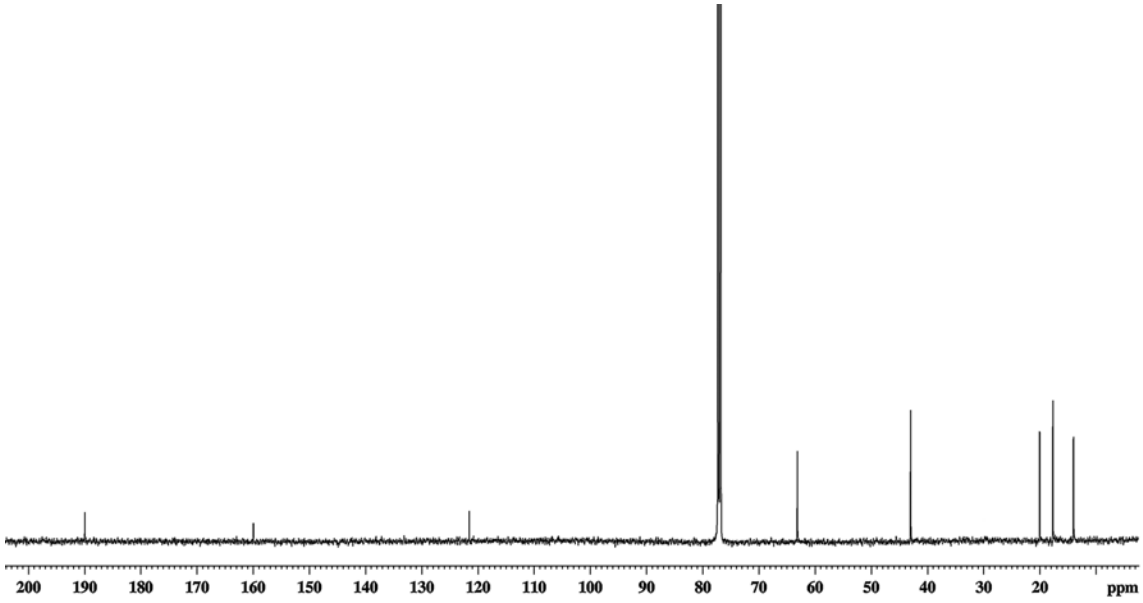
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5


200
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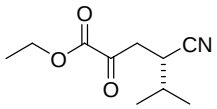
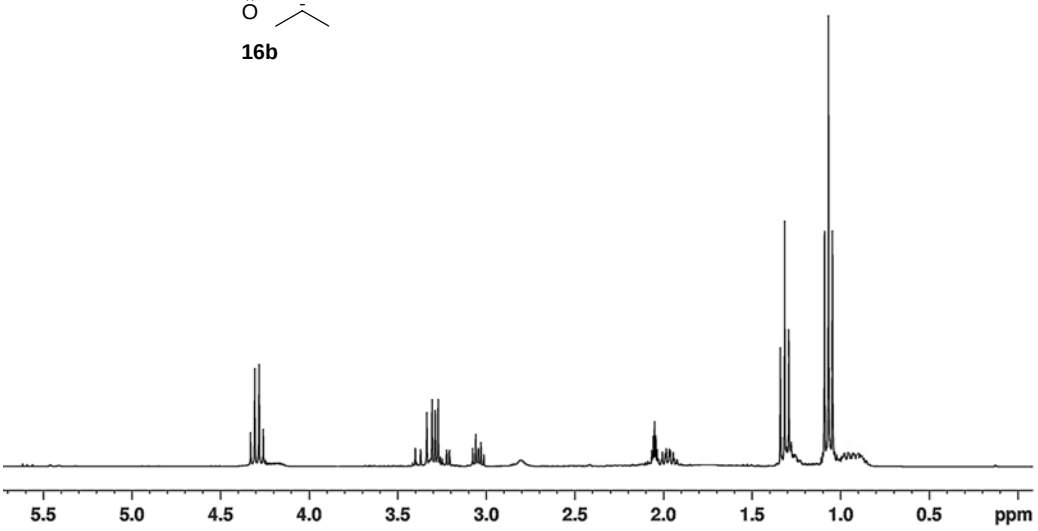
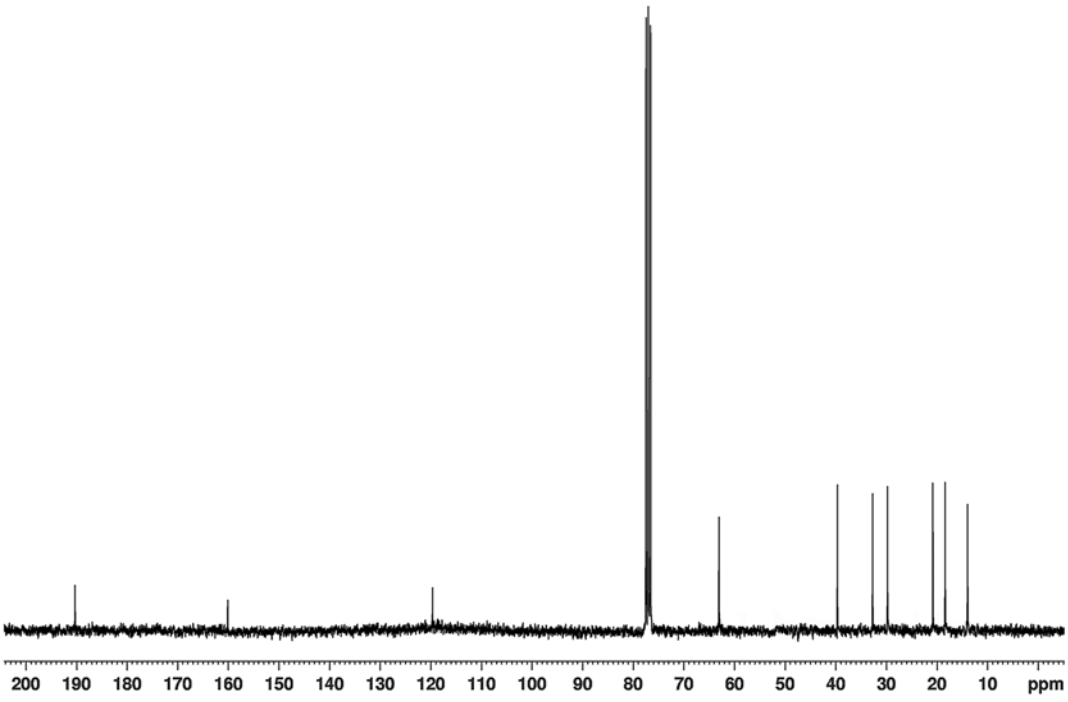
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

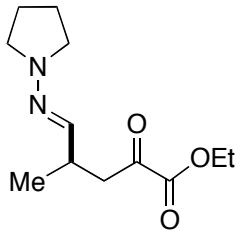

O
O
O
CN

16b

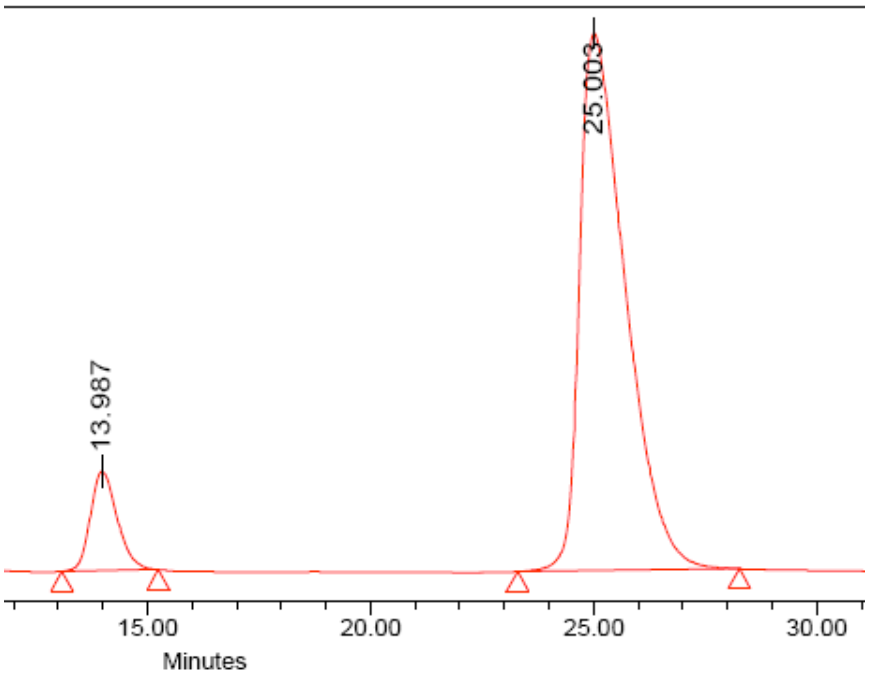

5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm


200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

HPLC data for **8a:** Daicel Chiralpak AD column (*n*-hexane/*i*-PrOH = 99:1, flow rate 1 mL/min)



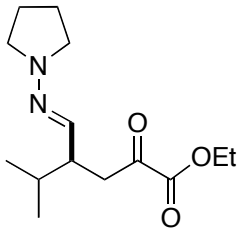
8a



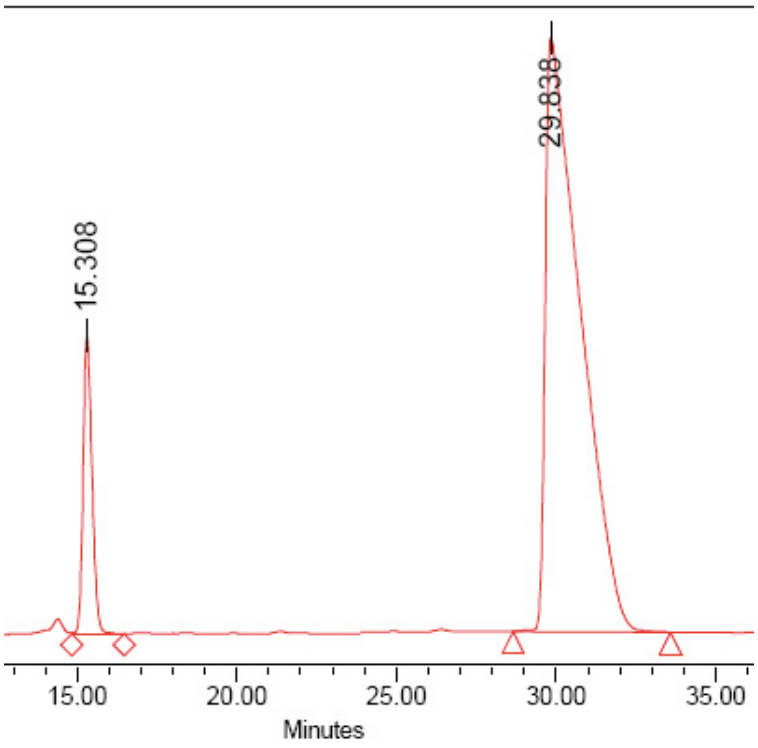
Processed Channel: PDA 243.8 nm

	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 243.8 nm	13.987	11794168	9.76	282285
2	PDA 243.8 nm	25.003	109031499	90.24	1530035

HPLC data for **8b:** Daicel Chiralpak AD-H column (*n*-hexane/*i*-PrOH = 99:1, flow rate 1 mL/min)



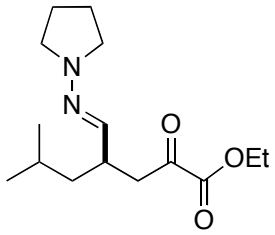
8b



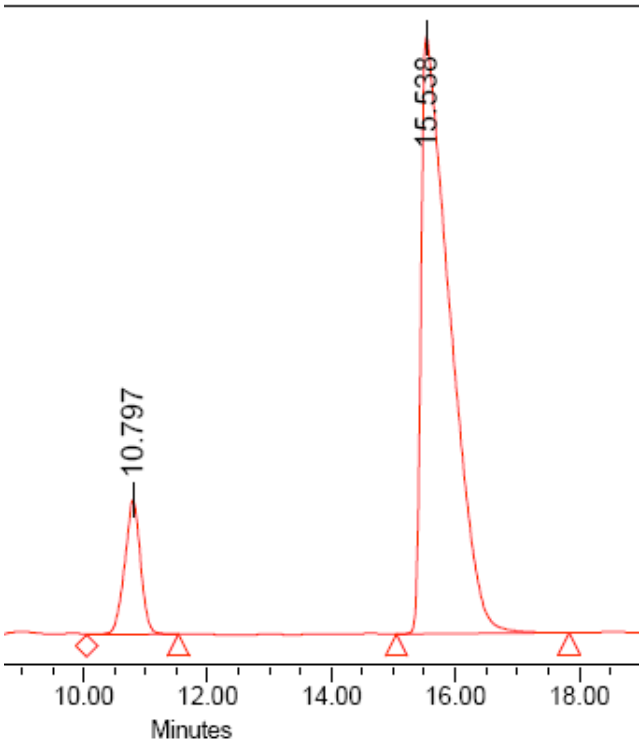
Processed Channel: PDA 235.6 nm

	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 235.6 nm	15.308	17628472	11.35	913453
2	PDA 235.6 nm	29.838	137720913	88.65	1810067

HPLC data for **8c:** Daicel Chiralpak AD-H column (*n*-hexane/*i*-PrOH = 99:1, flow rate 1 mL/min)



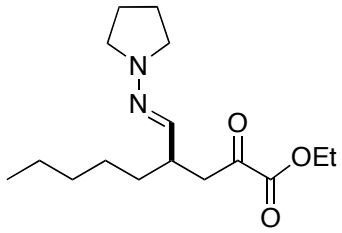
8c



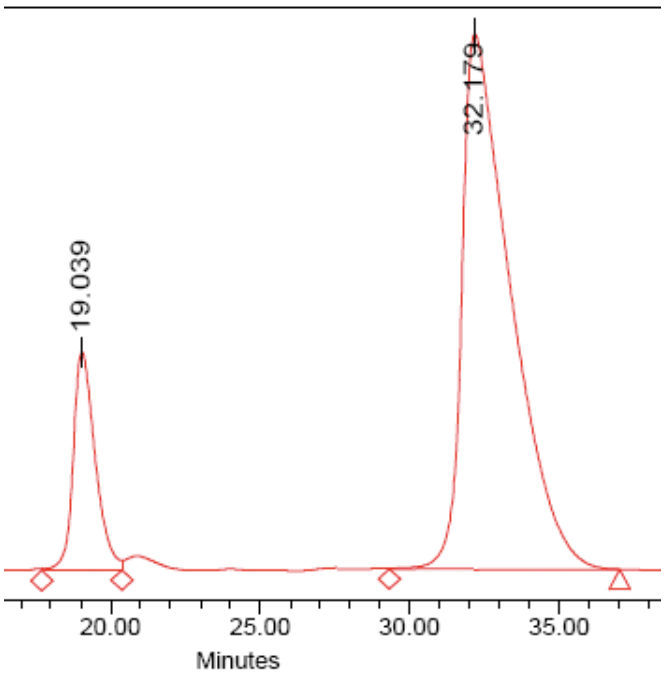
Processed Channel: PDA 215.1 nm

	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 215.1 nm	10.797	5861229	11.03	328235
2	PDA 215.1 nm	15.538	47268004	88.97	1454151

HPLC data for **8d:** Daicel Chiralpak AD column (*n*-hexane/*i*-PrOH = 99:1, flow rate 1 mL/min)



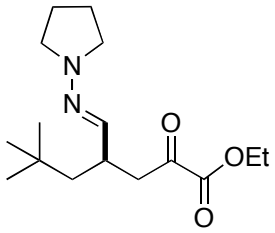
8d



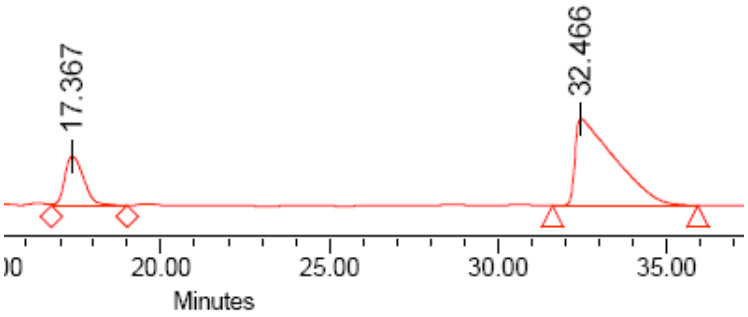
Processed Channel: PDA 244.2 nm

	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 244.2 nm	19.039	23454238	15.02	456658
2	PDA 244.2 nm	32.179	132706055	84.98	1120009

HPLC data for **8e:** Daicel Chiralpak AD-H column (*n*-hexane/*i*-PrOH = 99:1, Flow rate 1 mL/min)



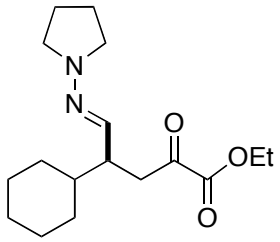
8e



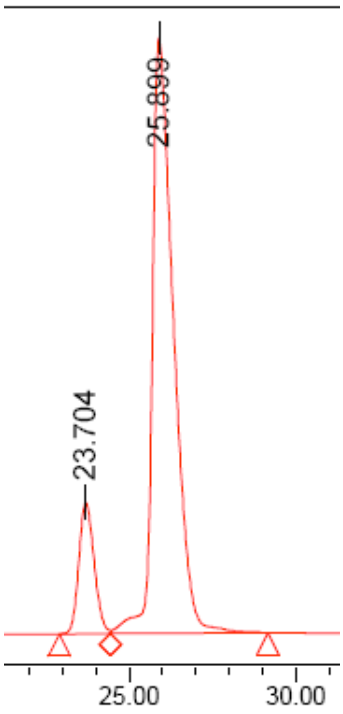
Processed Channel: PDA 229.2 nm

	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 229.2 nm	17.367	7914598	21.44	200453
2	PDA 229.2 nm	32.466	29003373	78.56	352211

HPLC data for **8e:** Daicel Chiralpak AD-H column (*n*-hexane/*i*-PrOH = 99:1, flow rate 1 mL/min)



8f



Processed Channel: PDA 229.3 nm

	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 229.3 nm	23.704	4458919	13.69	140138
2	PDA 229.3 nm	25.899	28108825	86.31	637815