SUPPLEMENTARY INFORMATION

Dramatic synergistic effect of a flexible achiral linker on a rigid chiral *cis*-1,2-diamine bifunctional organocatalyst

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Experimental Procedures. Melting points were determined using the Yanaco micro melting point apparatus and are uncorrected. Optical rotations were measured with a JASCO P-1010 polarimeter. ^{1}H NMR spectra were recorded in $CDCl_3$ with tetramethylsilane as an internal standard on a JEOL JNM-AL300 (300 MHz), JEOL JNM-GX400 (400 MHz) and Bruker Avance 600 (600 MHz) spectrometers. ^{13}C NMR spectra were recorded in $CDCl_3$ with tetramethylsilane as an internal standard on a JEOL JNM-AL300 (75 MHz), JEOL JNM-GX400 (100 MHz) and Bruker Avance 600 (150 MHz) spectrometers using broad band proton decoupling. Infrared spectra were measured with a JASCO JIR-6500W FT-IR spectrometer. MS and HRMS (EI or FAB) were obtained with a JEOL JMS-700 mass spectrometer. HPLC analyses were carried out on a JASCO PU-1580 HPLC pump and a JASCO UV-1580 detector, using chiral columns (Daicel; 250 × 4.6 mm).

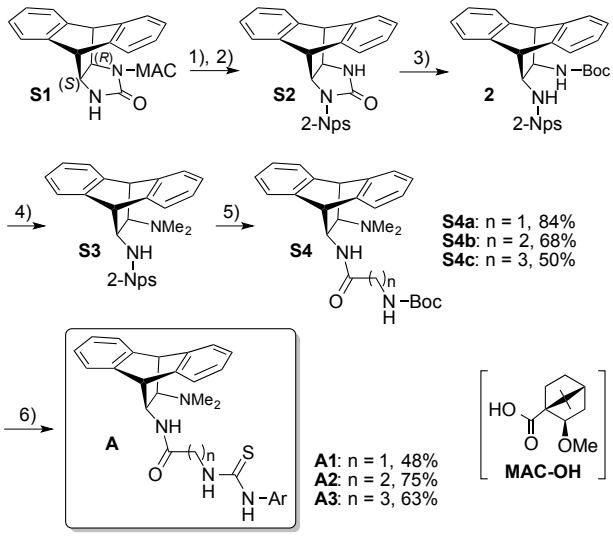
Flash chromatography was performed using Fuji Silysia silica gel PSQ60B. Methylene chloride (dehydrate) and THF (dehydrate) were purchased from Kanto Chemical Co., Inc. Other solvents and reagents were distilled prior to use.

(*E*)-*β*-Aryl nitroolefins (**4**, **7a-7i**),[1] (*E*)-1-nitropent-1-ene (**7j**)[2] and (*E*)-(4-nitrobut-3-en-1-yl)benzene (**7k**)[3] were prepared according to literature procedures.

The preparation of chiral "roofed" *cis*-amine-thiourea organocatalysts A-D :

Planning the synthetic strategy for the preparation of chiral "roofed" amine-thiourea compounds, we started from the optically pure (-)-(2*R*,6*S*)-3-[(1*S*,2*R*)-methoxy-7,7-dimethylbicyclo[2.2.1]-heptane-1-carbonyl] (abbreviated as "MAC") -3,5-diazadibenzo[*h*,*k*]tricyclo[5.2.2.2.^{2,6}]undeca-8,10-dien-4-one (abbreviated as "DHAIm") (**S1**), which is readily available from the thermal [4+2] cycloaddition of 1,3-dihydro-2-imidazolone with anthracene followed by optical resolution using MAC acid (MAC-OH). Thus, *N*'-protection of **S1** with 2-naphthalenesulfonyl (2-Nps) group and subsequent removal of MAC group by $PhCH_2SLi$, followed by ring-opening and *N*-tert-butoxycarbonylation gave *N*,*N*'-diprotected "roofed" *cis*-1,2-diamine **2** as a key intermediate.

Dimethylation of Boc-deprotected amine and subsequent removal of 2-Nps group by lithium naphthalenide followed by the condensation with *N*-Boc amino acids in the presence of diethyl phosphorocyanidate (DEPC) afforded corresponding amides **S4**. Removal of Boc group by TFA followed by the treatment of 3,5-bis(trifluoromethyl)phenyl isothiocyanate gave chiral "roofed" *cis*-amine-thiourea bifunctional compounds with three types of linker between chiral scafford and thiourea moiety (**A1**-**A3**) (Scheme S1).

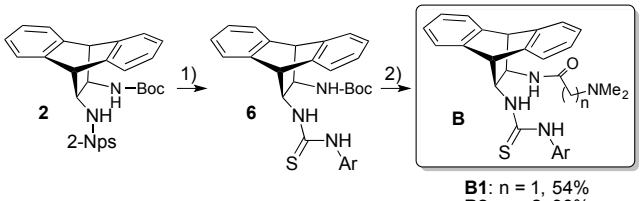


(2-Nps = 2-naphthalenesulfonyl; Ar = 3,5-$(CF_3)_2C_6H_3$)

1) 2-NpsCl, NaH in THF; rt, 1 h (97%); 2) $PhCH_2SLi$ in THF, rt, 1 h (>99%); 3) i) $Ba(OH)_2{\bullet}8H_2O$ in EtOH/H_2O/DMSO (5/1/1), reflux, 24 h, ii) $(Boc)_2O$ in CH_2Cl_2 (84%); 4) i) TFA, ii) MeI, K_2CO_3 in THF, 40 °C, 24 h (81%); 5) i) Na, naphthalene in DME, -30 °C, 1 h, ii) $HO_2C(CH_2)_nNH$-Boc, DEPC, NEt_3 in DMF, rt; 6) i) TFA, ii) 3,5-$(CF_3)_2C_6H_3NCS$, NEt_3 in CH_2Cl_2, rt.

Scheme S1

"Roofed" *cis*-amine-thiourea organocatalysts **B**, with four types of linker between chiral scafford and amine moiety, were also prepared from key intermediate **2**. Thus, the removal of 2-Nps group followed by the treatment with isothiocyanate gave thiourea compound **6**, Boc

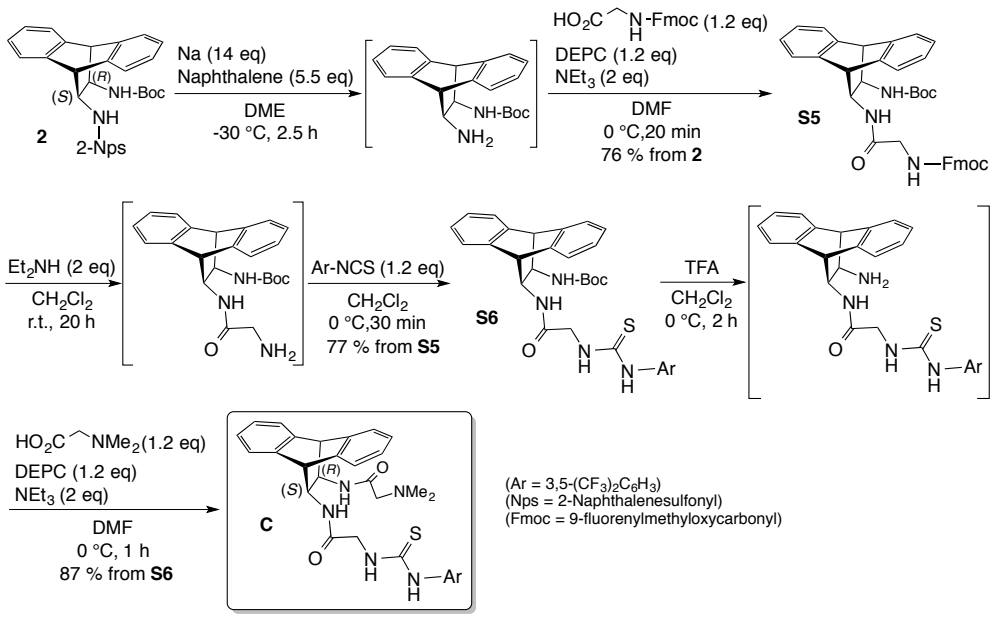


(2-Nps = 2-naphthalenesulfonyl; Ar = 3,5-$(CF_3)_2C_6H_3$)

1) i) Na, naphthalene in DME, -30 °C, 1 h, ii) 3,5-$(CF_3)_2C_6H_3NCS$ in CH_2Cl_2, rt (74%); 2) i) TFA, ii) $HO_2C(CH_2)_nNMe_2$, DEPC, NEt_3 in DMF, rt.

Scheme S2

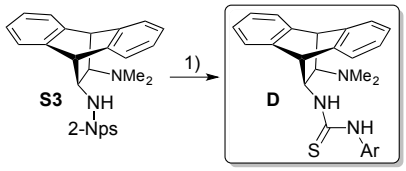
group of which was removed and the corresponding primary amine was condensed with *N*,*N*-dimethylamino acids to afford **B1**-**B4** (Scheme S2).



Scheme S3

"Roofed" *cis*-amine-thiourea organocatalyst with "double-elongated" functional groups using glycine as a linker, **C**, was synthesized from **2** by stepwise deprotection of Boc and 2-Nps groups followed by the condensation of amino groups with glycine moieties, respectively (Scheme S3).

Prototype of "roofed" *cis*-amine-thiourea organocatalysts **D**, without linker, was simply prepared from intermediate **S3** by the removal of 2-Nps group followed by the treatment with isothiocyanate (Scheme S4).

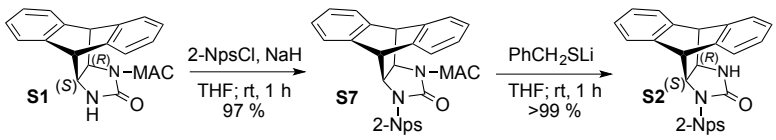


(2-Nps = 2-naphthalenesulfonyl; Ar = 3,5-$(CF_3)_2C_6H_3$)

1) i) Na, naphthalene in DME, -30 °C, 1 h, ii) 3,5-$(CF_3)_2C_6H_3NCS$ in CH_2Cl_2, rt (74%)

Scheme S4

The preparation of compound S2, (+)-(2*S*,6*R*)-3-(2-naphthalenesulfonyl)-3,5-diazadibenzo-[*h*,*k*]tricyclo[5.2.2.2^{2,6}]undeca-8,10-dien-4-one, from S1.



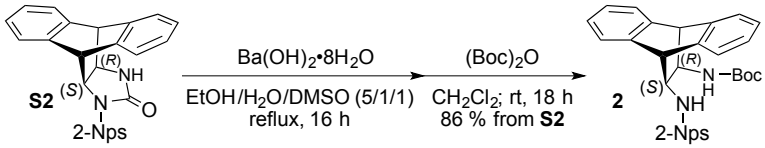
Preparation of S7 from S1: To the solution of **S1**, (+)-(2*R*,6*S*)-3-[*(1S,2R)*-methoxy-7,7-dimethylbicyclo[2.2.1]heptane-1-carbonyl]-3,5-diazadibenzo[*h*,*k*]tricyclo[5.2.2.2^{2,6}]undeca-8,10-dien-4-one (24.88 g, 56.22 mmol), in THF (562 mL) was added NaH (60% in oil; 5.40 g, 134.93 mmol, 2.4 eq) at 0 °C and stirred for 10 minutes. 2-Naphthalenesulfonyl chloride (19.12 g, 84.35

mmol, 1.5 eq) was added to the resulting mixture at 0 °C and the reaction mixture was stirred at room temperature for 1.5 h. The reaction was quenched with sat. NH_4Cl aq. at 0 °C and EtOAc (1200 mL) was added. The reaction solution was washed with brine (200 mL x 3) and dried over anhyd. Na_2SO_4. After the concentration of the organic layer *in vacuo*, the residue was purified by column chromatography on silica gel (CH_2Cl_2/hexane (3:7) to CH_2Cl_2) to afford the *N*-(2-naphthalenesulfonylated) compound **S7** (34.39 g, 54.39 mmol, 97%) as a colorless amorphous solid; $[\alpha]_D^{20}$ +16.6 (*c* 1.26, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.59 (s, 1H), 7.98-7.91 (m, 4H), 7.68-7.60 (m, 2H), 7.40-7.37 (m, 2H), 7.23-7.02 (m, 3H), 7.61 (td, *J* = 7.1, 1.8 Hz, 1H), 6.93-6.85 (m, 2H), 5.03 (d, *J* = 3.3 Hz, 2H), 5.01 (d, *J* = 2.9 Hz, 1H), 4.56 (dd, *J* = 9.7, 3.3 Hz, 1H), 4.44 (dd, *J* = 9.7, 2.9 Hz, 1H), 4.20 (dd, *J* = 7.7, 3.7 Hz, 1H), 2.77 (s, 3H), 1.89-1.72 (m, 2H), 1.62-1.48 (m, 2H), 1.43-1.26 (m, 1H), 1.33 (s, 3H), 1.05 (s, 3H), 0.97-0.86 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 172.8, 149.6, 140.3, 138.9, 137.9, 135.7, 135.3, 131.8, 129.6, 129.4, 129.3, 129.2, 127.9, 127.7, 127.1, 127.0, 126.9, 126.6, 126.5, 125.8, 125.3, 125.2, 122.5, 83.2, 61.9, 57.0, 56.8, 53.4, 50.8, 48.2, 45.6, 45.3, 37.4, 26.9, 26.7, 21.8, 21.3; IR (KBr, cm^{-1}): 3341, 2923, 1764, 1683, 1367, 1070, 750, 659, 626, 576. HRMS (FAB^+): m/z calcd for $C_{38}H_{36}N_2O_5SNa$ $[M+Na]^+$ 655.2243, found 655.2228.

Preparation of S2 from S7: THF (690 mL) solution of benzyl mercaptan (24.3 mL, 206.73 mmol, 3.0 eq) under argon atmosphere was treated with *n*-BuLi (2.6 M in hexane; 66.3 mL, 172.28 mmol, 2.5 eq) at 0 °C and stirred for 10 minutes to form lithium benzylmercaptide. To this solution was added **S7** (43.57 g, 68.91 mmol) in THF (690 mL) dropwise at 0 °C and stirred at rt for 1 hour. The reaction was quenched with sat. NH_4Cl aq. at 0 °C followed by evaporation *in vacuo* to remove THF. EtOAc (600 mL) was added to the residue and the solution was washed with brine (150 mL x 3) and dried over anhyd. Na_2SO_4. After the concentration of the organic layer *in vacuo*, the residue was purified by column chromatography on silica gel (CH_2Cl_2/hexane (3:7) to CH_2Cl_2/EtOAc (7:3)) to yield, in addition to MAC acid thiobenzyl ester (19.62 g, 64.44 mmol, 94%), the deacylated DHAIm **S2** (31.19 g, 68.91 mmol, >99%) as colorless crystals; mp 268-270 °C; $[\alpha]_D^{20}$ +109.3 (*c* 1.32, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.56 (s, 1H), 7.99-7.85 (m, 4H), 7.65-7.54 (m, 2H),

7.43-7.40 (m, 1H), 7.28-7.00 (m, 5H), 6.91-6.86 (m, 2H), 5.95 (br s, 1H), 4.94 (d, J = 3.3 Hz, 1H), 4.56 (dd, J = 9.5, 3.3 Hz, 1H), 4.31, (d, J = 2.9 Hz, 1H), 3.89 (dd, J = 9.5, 2.9 Hz, 1H).; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 155.2, 139.8, 139.2, 138.0, 137.6, 136.3, 135.2, 131.9, 129.4, 129.3, 129.2 (two aromatic carbons were included), 127.8, 127.6, 127.1, 127.0, 126.8, 126.7, 126.2, 126.1, 125.4, 124.8, 122.6, 60.3, 53.1, 48.5, 48.3; IR (KBr, cm^{-1}): 3392, 3342, 3050, 2958, 1739, 1344, 1243, 1164, 1133, 1076, 765, 746, 659, 574. HRMS (FAB^+): m/z calcd for $C_{27}H_{21}N_2O_3S$ $[M+H]^+$ 453.1273, found 453.1270.

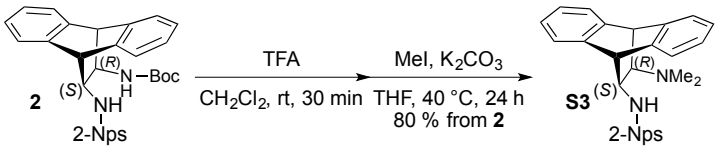
The preparation of 2, *tert*-butyl [(2*R*,3*S*)-3-(2-naphthalenesulfonamido)dibenzo[e,h]bicyclo-[2.2.2]octa-5,7-dien-2-ly]carbamate, from S2.



To the solution of compound **S2** (2.26 g, 5.0 mmol) in EtOH/H_2O/DMSO (5/1/1; 50 mL) was added $Ba(OH)_2$•$8H_2O$ (7.89 g, 25 mmol, 5 eq) and refluxed for 16 hours. The reaction mixture was poured into H_2O (250 mL) at 0 °C and the white precipitate was collecte by filtration and washed by H_2O to yield the mixture of ring-opened crude product and $Ba(OH)_2$•$8H_2O$ as white powder. The crude product was subsequently treated with $(Boc)_2O$ (1.72 mL, 7.5 mmol, 1.5 eq) in CH_2Cl_2 (50 mL) and stirred at rt for 18 hours. The reaction mixture was passed through Celite® pad to remove the precipitate and the pad was washed with CH_2Cl_2. The filtrate was combined and concentrated *in vacuo* followed by column chromatography on silica gel (CH_2Cl_2 to CH_2Cl_2/EtOAc (8:2)) to obtain **2** (2,24 g, 4.25 mmol, 86%) as a colorless amorphous solid; $[\alpha]_D^{20}$ +3.7 (*c* 1.06, $CHCl_3$); ^{1}H NMR ($CDCl_3$+CD_3OD 1 drop, 300 MHz, 50 °C) δ 8.43 (s, 1H), 7.98 (d, J = 8.6 Hz, 2H), 7.92 (dd, J = 8.8, 1.8 Hz, 1H), 7.80 (dd, J = 8.8, 1.8 Hz, 1H), 7.67-7.58 (m, 2H), 7.31-7.18 (m, 5H), 7.11-7.06 (m, 3H), 4.38 (br s, 1H), 4.28 (d, J = 2.4 Hz, 1H), 4.16-4.08 (m, 2H), 3.92 (dd, J = 9.0, 2.4 Hz, 1H), 1.33 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 155.1, 140.5, 139.9, 139.2,138.6, 135.0, 132.3, 129.6, 129.3, 128.9, 128.4, 128.0, 127.6, 127.2, 126.9, 126.7, 126.6, 126.0, 124.4, 122.4, 80.2, 53.4, 51.2,

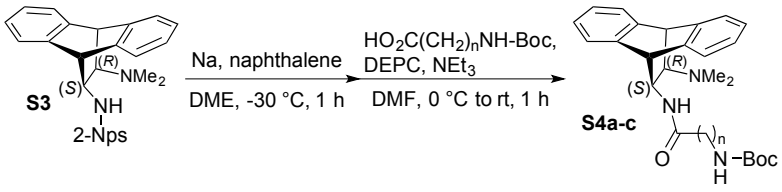
50.0, 49.4, 28.2 (three aromatic carbons were overlapped); IR (KBr, cm^{-1}): 3396, 3361, 3324, 3058, 3025, 2973, 2933, 1710, 1699, 1506, 1483, 1467, 1457, 1392, 1367, 1336, 1243, 1160, 1132, 750, 663. HRMS (FAB^+): m/z calcd for $C_{31}H_{30}N_2O_4SNa$ $[M+Na]^+$ 549.1824, found 549.1801.

The preparation of S3, *N*-[(2*S*,3*R*)-3-(dimethylamino)dibenzo[e,h]bicyclo[2.2.2]octa-5,7-dien-2-ly]2-naphthalenesulfonamide, from 2.



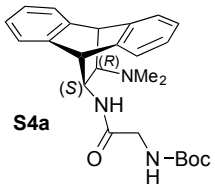
To the solution of compound **2** (790 mg, 1.5 mmol) in CH_2Cl_2 (1.5 mL) was added TFA (7.5 mL) and stirred at rt for 30 minutes to remove Boc group. The reaction mixture was concentrated *in vacuo* and the residue was dissolved in CH_2Cl_2 (100 mL). The solution was washed (i) satd. $NaHCO_3$ aq (20 mL x 3), ii) brine (20 mL x 3)), dried (anhyd. Na_2SO_4) and concentrated *in vacuo*. The residue was dissolved in THF and K_2CO_3 (622 mg, 4.5 mmol, 3 eq) and MeI (0.94 mL, 15 mmol, 10 eq) were subsequently added and stirred at 40 °C for 24 hours. The reaction mixture was passed through Celite® pad to remove the precipitate and the pad was washed with CH_2Cl_2. The filtrate was combined and concentrated *in vacuo* followed by column chromatography on silica gel (hexane/EtOAc (7:3 to 6:4)) to yield **S3** (547 mg, 1.20 mmol, 80%) as a colorless amorphous solid; $[\alpha]_D^{20}$ +69.5 (*c* 0.62, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 8.49 (d, *J* = 1.5 Hz, 1H), 8.00-7.96 (m, 2H), 7.92 (dd, *J* = 6.6, 2.6 Hz, 1H), 7.85 (dd, *J* = 8.8, 1.8 Hz, 1H), 7.67-7.58 (m, 2H), 7.27-7.05 (m, 7H), 6.97 (dd, *J* = 7.0, 1.5 Hz, 1H), 6.12 (br s, 1H), 4.41 (d, *J* = 3.7 Hz, 1H), 4.38 (d, *J* = 1.8 Hz, 1H), 3.75 (dd, *J* = 8.8, 3.7 Hz, 1H), 2.52 (dd, *J* = 8.8, 1.8 Hz), 2.16 (br s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 142.7, 141.0, 140.2, 138.7, 138.4, 134.8, 132.3, 129.2, 129.1, 128.6, 128.1, 127.9, 127.5, 126.7, 126.50, 126.47, 126.2, 126.1, 125.2, 125.0, 123.4, 123.0, 66.6, 52.0, 51.1, 46.7, 44.2 (two carbons were overlapped); IR (KBr, cm^{-1}): 3172, 3043, 2989, 2829, 1375, 1338, 1326, 1160, 1133, 1074, 1029, 821, 755, 661. HRMS (FAB^+): m/z calcd for $C_{28}H_{27}N_2O_2S$ $[M+H]^+$ 455.1793, found 455.1794.

The preparation of S4a-c from S3: General procedure.



To the solution of naphthalene (6 eq) in DME (10 mL / 1 mmol of **S3**) was added small pieces of Na (14 eq) under argon atmosphere and sonicated at 25 °C for 5 minutes to prepare sodium naphthalenide. A solution of **S3** in THF (27 mL / 1 mmol of **S3**) was added dropwise to the solution of sodium naphthalenide at -30 °C and stirred at this temperature until the accomplishment of the reaction (approx. for 30 minutes ~ 2 hours). The reaction mixture was poured into the ice water to quench excess amount of Na metal and the product was extracted (Et_2O, x 3), washed (brine, x 3) and dried (anhyd. Na_2SO_4). The solution was concentrated under reduced pressure and the residue was dissolved in DMF (10 mL / 1 mmol of **S3**) and *N*-Boc-amino acid (1.1 eq) was added. To the solution were subsequently added diethyl cyanophosphonate (DEPC; 1.1 eq) and NEt_3 (2 eq) at 0 °C and stirred at 0 °C and rt for each 30 minutes. EtOAc was added to the reaction mixture and the solution was washed (i) satd. $NaHCO_3$ (x 2), ii) brine (x 3)) and dried (anhyd. Na_2SO_4). After the concentration *in vacuo*, the residue was purified to afford **S4a-c**.

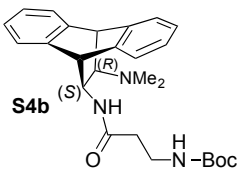
***tert*-butyl [[[(2*S*,3*R*)-3-(dimethylamino)dibenzo[e,h]bicyclo[2.2.2]octa-5,7-dien-2-ly]amino]-2-oxoethyl]carbamate (S4a).**



Product was purified by column chromatography on silica gel (CH_2Cl_2 to CH_2Cl_2/EtOH (19:1) via CH_2Cl_2/EtOAc (9:1)) to afford **S4a** in 84% yield as a colorless amorphous solid; $[\alpha]_D^{23}$ +41.8 (*c* 1.42, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.37-7.09 (m, 8H), 6.71 (br s, 1H), 4.98 (br s, 1H), 4.73 (d, *J* = 3.3 Hz, 1H), 4.46 (d, *J* =1.8 Hz, 1H), 4.21 (ddd, J = 8.4, 6.6, 3.3 Hz, 1H), 3.65 (d, *J* = 2.6 Hz, 1H), 3.63 (d, *J* = 2.6 Hz, 1H), 2.57 (dd, *J* = 8.4, 1.8 Hz, 1H), 2.27 (s, 6H), 1.40 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 168.4, 155.5, 142.4, 141.1, 140.4, 138.7, 126.5, 126.3, 126.2 (two carbons were overlapped), 125.8, 125.1 (two

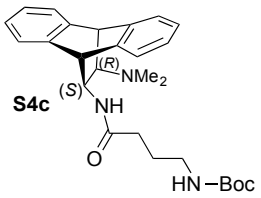
carbons were overlapped), 123.5, 79.6, 66.9, 48.7, 48.3, 47.0, 44.6, 44.0, 28.2; IR (KBr, cm^{-1}): 3299, 3041, 2973, 2946, 2865, 2819, 1691, 1672, 1544, 1521, 1290, 1172, 767. HRMS (FAB^+): m/z calcd for $C_{25}H_{32}N_3O_3$ $[M+H]^+$ 422.2444, found 422.2441.

***tert*-butyl [[[(2*S*,3*R*)-3-(dimethylamino)dibenzo[e,h]bicyclo[2.2.2]octa-5,7-dien-2-ly]amino]-3-oxopropyl]carbamate (S4b).**



Product was purified by column chromatography on silica gel (hexane/EtOAc (8:2) to EtOAc) to afford **S4b** in 68% yield as a pale yellow oil; $[\alpha]_D^{23}$ +42.7 (*c* 2.08, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 7.38-7.31 (m, 2H), 7.26-7.10 (m, 6H), 6.43 (br d, *J* = 6.0 Hz, 1H), 5.15 (br s, 1H), 4.74 (d, *J* = 3.5 Hz, 1H), 4.46 (d, *J* = 1.8 Hz, 1H), 4.20 (ddd, *J* = 8.4, 6.6, 3.5 Hz, 1H), 3.34 (q, *J* = 6.0 Hz, 2H), 2.56 (dd, *J* = 8.4, 1.8 Hz, 1H), 2.27 (s, 6H), 2.24-2.19 (m, 2H), 1.43 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.8, 155.8, 142.3, 141.2, 140.4, 138.7, 126.5, 126.3, 126.19, 126.17, 125.7, 125.2, 125.1, 123.5, 79.0, 66.9, 48.7, 48.3, 47.0, 44.7, 44.6, 36.8, 36.1, 28.4.; IR (KBr, cm^{-1}): 3340, 2975, 2873, 2823, 1700, 1652, 1496, 1172, 757. HRMS (FAB^+): m/z calcd for $C_{26}H_{34}N_3O_3$ $[M+H]^+$ 436.2600, found 436.2587.

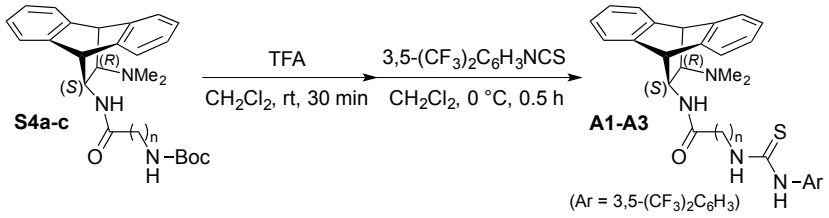
***tert*-butyl [[[(2*S*,3*R*)-3-(dimethylamino)dibenzo[e,h]bicyclo[2.2.2]octa-5,7-dien-2-ly]amino]-4-oxobutyl]carbamate (S4c).**



Product was purified by column chromatography on silica gel (hexane/EtOAc (2:8) to EtOAc) to afford **S4c** in 68% yield as a pale yellow oil; $[\alpha]_D^{20}$ +53.2 (*c* 2.28, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 7.38-7.31 (m, 2H), 7.25-7.18 (m, 2H), 7.16-7.10 (m, 4H), 6.36 (d, *J* = 6.0 Hz, 1H), 4.78 (br s, 1H), 4.72 (d, *J* = 3.3 Hz, 1H), 4.46 (d, *J* = 1.8 Hz, 1H), 4.26-4.19 (m, 1H), 3.18-3.06 (m, 2H), 2.55 (dd, *J* = 6.6, 1.8 Hz, 1H), 2.27 (s, 6H), 2.14-1.99 (m, 2H), 1.74 (quintet, *J* = 7.1 Hz, 2H), 1.44 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz, 50 °C) δ 171.5, 155.9, 142.5, 141.4, 140.6, 138.8, 126.4, 126.2, 126.03, 126.01, 125.8, 125.1, 125.0, 123.4, 78.9, 67.1, 48.7, 48.6, 47.1, 44.6, 40.3 (two carbons were overlapped),

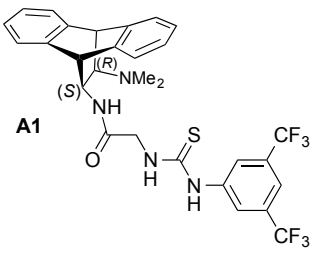
33.9, 28.4, 25.8.; IR (KBr, cm^{-1}): 3349, 3070, 3041, 2973, 2935, 2869, 2827, 2780, 1703, 1657, 1495, 1417, 1365, 1290, 1255, 1172, 1024, 760, 730. HRMS (FAB^+): m/z calcd for $C_{27}H_{36}N_3O_3$ $[M+H]^+$ 450.2757, found 450.2743.

The preparation of catalyst A1-A3 from S4a-c: General procedure



To the solution of compound **S4** in CH_2Cl_2 (5 mL / 1 mmol of **S4**) was added TFA (5 mL / 1 mmol of **S4**) and stirred at rt for 30 minutes to remove Boc group. The reaction mixture was concentrated *in vacuo* and the residue was dissolved in CH_2Cl_2. The solution was washed (i) satd. $NaHCO_3$ aq (x 3), ii) brine (x 3)), dried (anhyd. Na_2SO_4) and concentrated *in vacuo*. The residue was dissolved in CH_2Cl_2 (10 mL / 1 mmol of **S4**) and NEt_3 (4 eq) and 3,5-bis(trifluoromethyl)phenyl isothiocyanate (1.25 eq) was added to the solution at 0 °C and stirred for 30 minutes. The reaction solution was concentrated under reduced pressure and the residue was purified to obtain catslyst **A1-A3**.

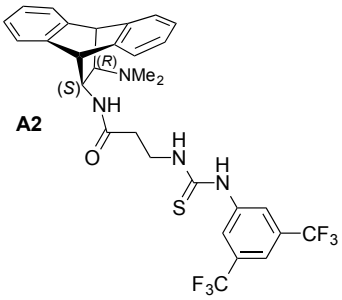
2-[3-[3,5-bis(trifluoromethyl)phenyl]thioureido]-*N*-[(2*S*,3*R*)-3-(dimethylamino)dibenzo[e,h]-bicyclo[2.2.2]octa-5,7-dien-2-ly]acetamide (A1).



Product was purified by column chromatography on silica gel (CH_2Cl_2 to CH_2Cl_2/EtOH (19:1)) to afford **A1** (ca. 81% yield) as a pale yellow amorphous solid, together with slightly amount of inseparable impurities, observed in ^1H NMR. The product was converted to its TFA salt by the addition of TFA and dissolved in MeOH follwed by the addition of slightly amount of Et_2O to obtain the pure TFA salt of **A1** as precipitate. The EtOAc solution of the salt was treated with NEt_3, washed by brine, dried over anhyd. Na_2SO_4 and concentrated *in vacuo* to yield pure **A1** in 48% yield as a pale yellow amorphous solid; $[\alpha]_D^{23}$ +52.9 (*c* 1.82, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz)

δ 9.23 (br s, 1H), 8.43 (br s, 1H), 8.03 (s, 2H), 7.45 (s, 1H), 7.39-7.36 (m, 1H), 7.29-7.18 (m, 4H), 7.16-7.06 (m, 3H), 4.66 (d, *J* = 3.3 Hz, 1H), 4.50 (d, *J* = 1.5 Hz, 1H), 4.38 (dd, *J* = 16.3, 5.1 Hz, 1H), 4.24-4.18 (m, 1H), 4.04 (dd, *J* = 16.3, 5.1Hz, 1H), 2.61 (dd, *J* = 8.2, 1.5 Hz, 1H), 2.04 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz, 50 °C) δ 181.8, 170.2, 142.1, 140.7, 140.3, 139.8, 138.7, 131.3 (q, *J* = 33.6 Hz; two carbons were overlapped), 126.64, 126.61, 126.5, 126.4, 125.9, 125.4, 124.8, 123.8, 123.0 (q, *J* = 272.8 Hz; two carbons were overlapped), 122.54, 122.49, 117.5 (m), 66.7, 49.2, 48.5, 47.4, 47.0, 44.7 (two carbons were overlapped); IR (KBr, cm^{-1}): 3313, 3072, 2957, 2877, 2831, 1652, 1506, 1473, 1384, 1278, 1176, 1133, 951, 887, 760. HRMS (FAB$^+$): m/z calcd for $C_{29}H_{27}F_6N_4OS$ $[M+H]^+$ 593.1809, found 593.1816.

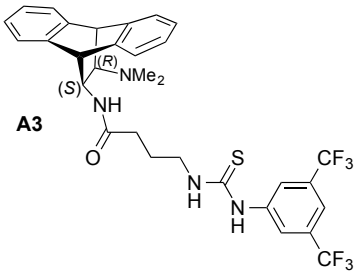
3-[3-[3,5-bis(trifluoromethyl)phenyl]thioureido]-*N*-[(2*S*,3*R*)-3-(dimethylamino)dibenzo[e,h]-bicyclo[2.2.2]octa-5,7-dien-2-ly]propanamide (A2).



Product was purified by column chromatography on silica gel (hexane/EtOAc (1:9)) to afford **A2** (75% yield) as a pale yellow amorphous solid; $[\alpha]_D^{23}$ +56.1 (*c* 1.40, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz, 50 °C) δ 8.06 (br s, 2H), 7.69 and 7.52 (br s, 1H; the peaks of rotational isomers), 7.37-7.09 (m, 10H), 6.62 and 6.47 (br s, 1H; the peaks of rotational isomers), 4.75 and 4.70 (d, *J* = 3.3 Hz, 1H; the peaks of rotational isomers), 4.45 (br s, 1H), 4.21-4.08 (m, 1H), 3.89-3.75 (m, 1.36 H), 3.57 (dd, *J* = 11.3, 5.7 Hz, 0.64 H; one of the peaks of rotational isomers), 2.56 (d, *J* = 8.4 Hz, 1 H), 2.39-2.22 (m, 2H), 2.27 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz, 50 °C; the peaks of rotational isomers were observed) δ 181.3, 171.6, 170.4, 142.5, 142.3, 141.2, 140.9, 140.7, 140.3, 140.1, 138.8, 138.7, 132.3 (q, *J* = 33.6 Hz), 126.71, 126.66, 126.59, 126.54, 126.43, 126.36, 126.30, 125.8, 125.6, 125.4, 125.1, 124.9, 123.7, 123.6, 123.2 (q, *J* = 272.4 Hz), 122.97, 122.93, 118.1 (m), 67.1, 67.0, 49.3, 49.0, 48.5, 48.4, 47.1, 46.2, 44.6, 40.8, 36.0, 35.3, 34.3, 29.7; IR (KBr, cm^{-1}): 3332, 3070, 2956, 2837, 2829, 1722, 1643, 1506, 1473, 1386, 1278, 1174,

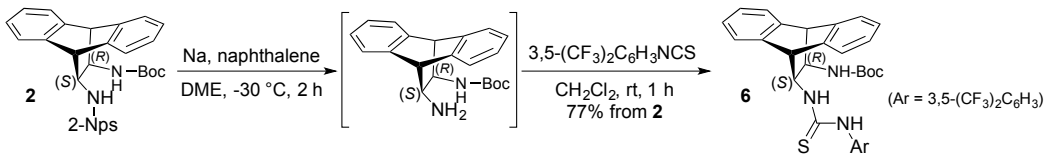
1136, 885, 759, 680. HRMS (FAB$^+$): m/z calcd for $C_{30}H_{29}F_6N_4OS$ $[M+H]^+$ 607.1966, found 607.2000.

4-[3-[3,5-bis(trifluoromethyl)phenyl]thioureido]-*N*-[(2*S*,3*R*)-3-(dimethylamino)dibenzo[e,h]-bicyclo[2.2.2]octa-5,7-dien-2-ly]butanamide (A3).



Product was purified by column chromatography on silica gel (CH_2Cl_2/EtOH (99:1 to 97:3)) to afford **A3** (63% yield) as a pale yellow amorphous solid; $[\alpha]_D^{20}$ +54.0 (*c* 1.46, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz, 50 °C) δ 8.25 (br s, 1H), 7.64 (s, 1H), 7.33-7.09 (m, 10H), 6.58 (br d, *J* = 3.6 Hz, 1H), 4.64 (br s, 1H), 4.45 (br s, 1H), 4.08 (br s, 1H), 3.60 (m, 2H), 2.55 (d, *J* = 8.2 Hz, 1H), 2.27 (br s, 7H), 2.17 (dd, *J* = 7.3, 4.4 Hz, 2H), 1.93-1.81 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz, 50 °C) δ 181.3, 172.7, 142.3, 141.1 (two carbons were overlapped), 140.1, 138.8, 132.0 (q, *J* = 33.6 Hz; two carbons were overlapped), 131.0, 126.7, 126.6, 126.4, 126.3, 125.7, 125.4, 124.9, 123.6 (two carbons were overlapped), 123.3 (q, *J* = 273.2 Hz; two carbons were overlapped), 118.1, 67.1, 49.2, 48.5, 47.1, 44.6 (two carbons were overlapped), 44.2, 33.3, 24.8; IR (KBr, cm^{-1}): 3323, 3091, 3074, 3047, 3025, 2954, 2873, 2829, 2785, 1643, 1506, 1473, 1383, 1330, 1281, 1172, 1133, 1128, 1049, 1024, 978, 950, 885, 848, 759, 730, 702, 680, 647, 638. HRMS (FAB$^+$): m/z calcd for $C_{31}H_{31}F_6N_4OS$ $[M+H]^+$ 621.2123, found 621.2138.

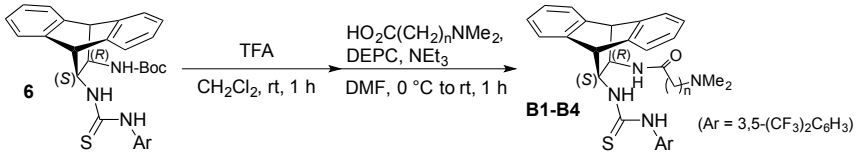
The preparation of 6, *tert*-butyl [(2*R*,3*S*)-3-[3-[3,5-bis(trifluoromethyl)phenyl]thioureido]-dibenzo[e,h]-bicyclo[2.2.2]octa-5,7-dien-2-ly]carbamate, from 2.



To the solution of naphthalene (1.92 g, 15 mmol, 6 eq) in DME (25 mL) was added small pieces of Na (805 mg, 35 mmol, 14 eq) under argon atmosphere and sonicated at 25 °C for 5 minutes to prepare sodium naphthalenide. A solution of **2** in DME (12.5 mL) was added dropwise to the

solution of sodium naphthalenide at -30 °C and stirred at this temperature for 2 hours. The reaction mixture was poured into the ice water to quench excess amount of Na metal and the product was extracted (Et_2O, 50 mL x 3), washed (brine, 25 mL x 3) and dried (anhyd. Na_2SO_4). The solution was concentrated under reduced pressure and the residue was purified by column chromatography on silica gel (CH_2Cl_2/EtOAc (7:3) to EtOAc) to afford desulfonylated amine, which was successively dissolved in CH_2Cl_2 (25 mL) and 3,5-bis(trifluoromethyl)phenyl isothiocyanate (0.47 mL, 2.75 mmol, 1.1 eq) was added to the solution at 0 °C and stirred for 30 minutes. The reaction solution was concentrated *in vacuo* followed by column chromatography on silica gel (hexane/CH_2Cl_2 (5:5) to CH_2Cl_2) to yield **6** (1.169 g, 1.92 mmol, 77%) as a colorless amorphous solid; $[\alpha]_D^{20}$ +2.5 (*c* 1.44, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz, 50 °C) δ 8.28 (br s, 1H), 7.79 (br s, 2H), 7.58 (s, 1H), 7.38-7.16 (m, 8H), 5.81 (br d, *J* = 6.4Hz, 1H), 4.63 (br s, 1H), 4.52 (br s, 1H), 4.29 (m, 2H), 4.09 (br s, 1H), 1.29 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz, 50 °C) δ 181.1, 156.1, 140.2, 139.9 (two carbons were overlapped), 138.9, 138.6, 132.5 (q, *J* = 33.6 Hz; two carbons were overlapped), 127.7, 127.6, 127.1, 127.0, 126.1, 125.9, 124.7, 124.3, 123.1 (two carbons were overlapped), 122.9 (q, *J* = 272.8 Hz; two carbons were overlapped), 118.4, 81.2, 55.4, 51.9, 49.3, 48.7, 28.1 (three carbons were overlapped); IR (KBr, cm^{-1}): 3344, 2979, 1683, 1519, 1469, 1383, 1278, 1176, 1135, 885, 759, 682. HRMS (FAB^+): m/z calcd for $C_{30}H_{27}F_6N_3O_2SNa$ $[M+Na]^+$ 630.1626, found 630.1631.

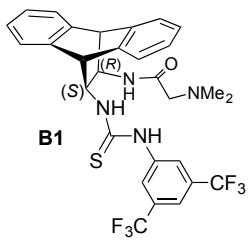
The preparation of catalyst B1-B4 from 6: General procedure



To the solution of compound **6** in CH_2Cl_2 (2 mL / 1 mmol of **6**) was added TFA (5 mL / 1 mmol of **6**) and stirred at rt for 1 hour to remove Boc group. The reaction mixture was concentrated *in vacuo* and azeotroped with toluene for three times to ensure removal of all excess TFA to afford TFA salt of amine as a foam which was used in the next step without further purification. The residue was

dissolved in DMF (10 mL / 1 mmol of **6**) and *N,N*-dimethylamino acid (1.1 eq) was added. To the solution were subsequently added diethyl cyanophosphonate (DEPC; 1.1 eq) and NEt_3 (4.4 eq) at 0 °C and stirred at rt for 1 hour. EtOAc was added to the reaction mixture and the solution was washed (i) satd. $NaHCO_3$ (x 2), ii) brine (x 3)) and dried (anhyd. Na_2SO_4). After the concentration *in vacuo*, the residue was purified to afford **B1-B4**.

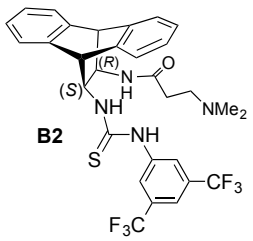
_N_-{(2_R_,3_S_)-3-[3-[3,5-bis(trifluoromethyl)phenyl]thioureido]dibenzo[e,h]-bicyclo[2.2.2]octa-5,7-dien-2-ly}-2-(dimethylamino)acetamide (B1).



Product was purified by column chromatography on silica gel (CH_2Cl_2 to CH_2Cl_2/EtOH (19:1)) to afford **B1** (ca. >99% yield) as a pale yellow amorphous solid, together with slightly amount of inseparable impurities, observed in ^{1}H NMR. The product was dissolved in EtOH and converted to its HCl salt by the addition of HCl solution. After removal of the solvent and excess amount of HCl by azeotrope with toluene, residue was solidified by adding Et_2O, suspended in small amount of Et_2O/EtOH (9/1), collected by filtration and washed (Et_2O/EtOH (9/1)). The collected salt was suspended in EtOAc and NEt_3 was added to convert HCl salt to free amine. The solution was washed (brine, x3), dried (anhyd. Na_2SO_4) and concentrated *in vacuo* to yield pure **B1** in 54% yield as a colorless amorphous solid; $[\alpha]_D^{20}$ -35.3 (*c* 1.00, $CHCl_3$); ^{1}H NMR (DMSO-d_6, 300 MHz) δ 10.4 (s, 1H), 8.21 (s, 2H), 7.75 (s, 1H), 7.49-7.36 (m, 4H), 7.31-7.24 (m, 3H), 7.22-7.15 (m, 2H), 6.66 (d, *J* = 8.6 Hz, 1H), 4.85 (ddd, *J* = 8.6, 8.6, 2.2 Hz, 1H), 4.54 (d, *J* = 2.2 Hz, 1H), 4.42 (d, *J* = 2.7 Hz, 1H), 4.38 (ddd, *J* = 8.6, 8.6, 2.7 Hz, 1H), 2.77 (d, *J* = 15.4 Hz, 1H), 2.70 (d, *J* = 15.4 Hz, 1H), 2.01 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz, 50 °C) δ 182.6, 171.7, 140.3, 139.3, 139.2, 138.3, (other one carbon was overlapped from 140.3 to 138.3), 132.4 (q, *J* = 37.4 Hz; two carbons were overlapped), 127.7, 127.3, 127.2, 125.9, 124.6, 124.5, 124.0, 123.0 (q, *J* = 273.2 Hz; two carbons were overlapped), 118.9 (m), (other three carbons were overlapped from 127.7 to 123.0), 62.8, 56.1, 50.1, 49.3, 49.2, 45.9 (two carbons were overlapped); IR (KBr, cm^{-1}): 3325, 3043, 2950, 2877, 1652,

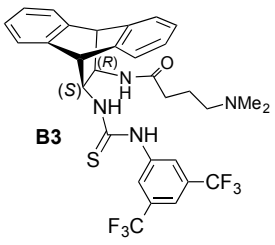
1527, 1471, 1386, 1278, 1176, 1132, 956, 887, 761, 680. HRMS (FAB^+): m/z calcd for $C_{29}H_{27}F_6N_4OS$ $[M+H]^+$ 593.1810, found 593.1818.

***N*-{(2*R*,3*S*)-3-[3-[3,5-bis(trifluoromethyl)phenyl]thioureido]dibenzo[e,h]-bicyclo[2.2.2]octa-5,7-dien-2-ly}-3-(dimethylamino)propanamide (B2).**



Product was purified by column chromatography on silica gel (CH_2Cl_2 to CH_2Cl_2/EtOH (8:2)) to afford **B2** in 38% yield as a pale yellow amorphous solid; $[\alpha]_D^{21}$ -33.7 (*c* 1.04, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz, 50 °C) δ 8.92 (br s, 1H), 8.31 (br s, 1H), 8.04 (s, 2H), 7.56 (s, 1H), 7.52-7.49 (m, 1H), 7.39-7.28 (m, 5H), 7.22-7.15 (m, 2H), 5.71 (br s, 1H), 4.64 (ddd, *J* = 8.6, 8.6, 2.6 Hz, 1H), 4.50 (d, *J* = 2.6 Hz, 1H), 4.34 (br s, 1H), 4.30 (d, *J* = 2.6 Hz, 1H), 2.47-2.35 (m, 3H), 2.24-2.13 (m, 1H), 2.01 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz, 50 °C) δ 182.8, 174.5, 141.4, 140.5, 139.6, 139.3, 138.2, 131.8 (q, *J* = 33.6 Hz; two carbons were overlapped), 127.6, 127.4, 127.3, 127.2, 126.3, 126.0, 124.6, 124.3, 123.54, 123.48, 123.2 (q, *J* = 272.8 Hz; two carbons were overlapped), 118.1 (m), 56.1, 55.0, 51.0, 49.5, 49.1, 44.1 (two carbons were overlapped), 32.3; IR (KBr, cm^{-1}): 3309, 3023, 2948, 2829, 1616, 1558, 1572, 1471, 1384, 1278, 1176, 1133, 960, 887, 761, 680. HRMS (FAB^+): m/z calcd for $C_{30}H_{29}F_6N_4OS$ $[M+H]^+$ 607.1966, found 607.1979.

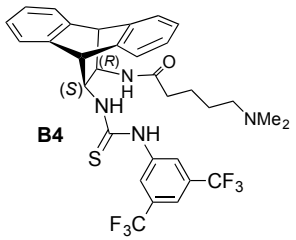
***N*-{(2*R*,3*S*)-3-[3-[3,5-bis(trifluoromethyl)phenyl]thioureido]dibenzo[e,h]-bicyclo[2.2.2]octa-5,7-dien-2-ly}-3-(dimethylamino)propanamide (B3).**



Product was purified by column chromatography on silica gel (CH_2Cl_2 to CH_2Cl_2/EtOH (19:1); contains 0.1% of NEt_3) to afford **B3** (ca. >99% yield) as a pale yellow amorphous solid, together with slightly amount of inseparable impurities, observed in ^{1}H NMR. The product was again purified by column chromatography on Al_2O_3 (CH_2Cl_2 to CH_2Cl_2/MeOH (97:3)) to afford pure **B3** in 74% yield as a colorless amorphous solid; $[\alpha]_D^{23}$ +30.6 (*c* 1.62, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300

MHz, 50 °C) δ 8.01 (s, 2H), 7.58 (s, 1H), 7.50-7.47 (m, 1H), 7.42-7.28 (m, 5H), 7.22-7.15 (m, 2H), 6.40 (br s, 1H), 5.75 (br s, 1H), 4.61 (br t, *J* = 6.0 Hz, 1H), 4.53 (d, *J* = 1.8 Hz, 1H), 4.44 (br s, 1H), 4.29 (d, *J* = 2.2 Hz, 1H), 2.31-2.13 (m, 3H), 2.02 (s, 6H), 1.74-1.52 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz, 50 °C) δ 182.5, 175.0, 141.2, 140.7, 139.4, 139.1, 138.6, 131.8 (q, *J* = 33.6 Hz; two carbons were overlapped), 127.8, 127.7, 127.2, 127.1, 126.4, 126.0, 124.6, 124.2, 123.39, 123.36, 123.2 (q, *J* = 272.8 Hz; two carbons were overlapped), 118.1(m), 58.8, 55.7, 51.2, 49.4, 48.9, 45.0 (two carbons were overlapped), 34.6, 22.7; IR (KBr, cm^{-1}): 3324, 3070, 2952, 2827, 1652, 1521, 1471, 1384, 1278, 1180, 1135, 956, 885, 761, 680. HRMS (FAB$^+$): m/z calcd for $C_{31}H_{31}F_6N_4OS$ $[M+H]^+$ 621.2123, found 621.2133.

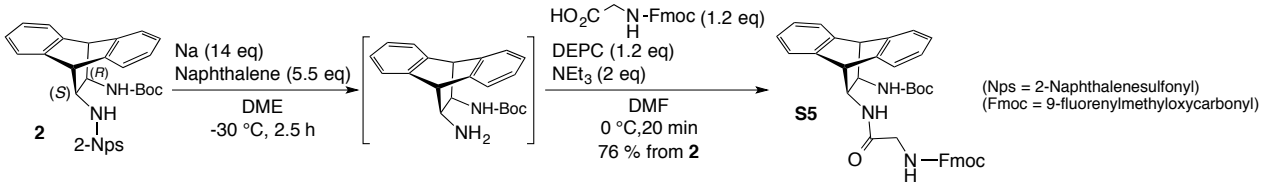
***N*-{(2*R*,3*S*)-3-[3-[3,5-bis(trifluoromethyl)phenyl]thioureido]dibenzo[e,h]-bicyclo[2.2.2]octa-5,7-dien-2-ly}-4-(dimethylamino)butanamide (B4).**



Product was purified by column chromatography on silica gel (CH_2Cl_2 to CH_2Cl_2/EtOH (8:2); contains 0.5% of NEt_3) to afford **B4** in 67% yield as a colorless amorphous solid; $[\alpha]_D^{21}$ +48.2 (*c* 1.11, $CHCl_3$); ^{1}H NMR (DMSO-d_6, 300 MHz) δ 10.0 (br s, 1H), 8.26 (s, 2H), 7.71 (s, 1H), 7.42-7.37 (m, 4H), 7.25-7.21 (m, 2H), 7.19-7.13 (m, 2H), 7.07 (d, *J* = 9.9 Hz, 1H), 6.62 (d, *J* = 8.2 Hz, 1H), 4.89 (br t, *J* = 8.7 Hz, 1H), 4.53 (d, *J* = 2.2 Hz, 1H), 4.36 (br dt, *J* = 8.7, 2.4 Hz, 1H), 4.29 (d, *J* = 2.4 Hz, 1H), 2.04-1.90 (m, 4H), 1.96 (s, 6H), 1.38-1.28 (m, 2H), 1.24-1.15 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz, 50 °C) δ 182.2, 174.1, 141.2, 140.3, 139.7, 139.3, 138.9, 131.8 (q, *J* = 33.6 Hz; two carbons were overlapped), 127.5 (two carbons were overlapped), 127.1 (two carbons were overlapped), 126.4, 125.8, 124.5, 124.3, 123.3 (two carbons were overlapped), 123.2 (q, *J* = 272.8 Hz; two carbons were overlapped), 117.9 (m), 58.8, 55.4, 50.3, 49.2, 49.1, 45.1 (two carbons were overlapped), 35.9, 26.6, 23.1; IR (KBr, cm^{-1}): 3288, 3070, 2952, 2867, 1652, 1538, 1471, 1386, 1278, 1176, 1133, 958, 885, 761, 680. HRMS (FAB$^+$): m/z calcd for $C_{32}H_{33}F_6N_4OS$ $[M+H]^+$ 635.2279, found 635.2291.

The synthesis of catalyst C:

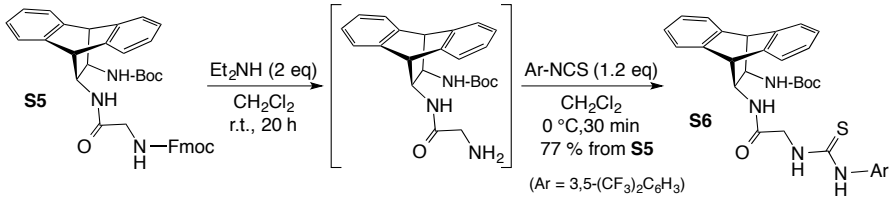
The preparation of S5, *tert*-butyl [(2*R*,3*S*)-3-[2-[(9-fluorenylmethoxycarbonyl)amino]-acetamido]dibenzo[e,h]-bicyclo[2.2.2]octa-5,7-dien-2-ly]carbamate, from 2.



To the solution of naphthalene (1.35 g, 10.55 mmol, 5.3 eq) in DME (20 mL) was added small pieces of Na (644 mg, 28 mmol, 14 eq) under argon atmosphere and sonicated at 25 °C for 5 minutes to prepare sodium naphthalenide. A solution of **2** in DME (10 mL) was added dropwise to the solution of sodium naphthalenide at -30 °C and stirred at this temperature for 2 hours. The reaction mixture was poured into the ice water to quench excess amount of Na metal and the product was extracted (Et_2O, 100 mL x 1, 50 mL x 2), washed (brine, 30 mL x 3) and dried (anhyd. Na_2SO_4). The solution was concentrated under reduced pressure and the residue was dissolved in DMF (10 mL) and Fmoc-glycine (714 mg, 2.4 mmol, 1.2 eq) was added. To the solution were subsequently added diethyl cyanophosphonate (DEPC; 0.36 mL, 2.4 mmol, 1.2 eq) and NEt_3 (0.56 mL, 4.0 mmol, 2 eq) at 0 °C and stirred at this temperature for 30 minutes. EtOAc (100 mL) was added to the reaction mixture and the solution was washed (i) satd. $NaHCO_3$ (20 mL x 2), ii) brine (20 mL x 5)) and dried (anhyd. Na_2SO_4). After the concentration *in vacuo*, the residue was purified by column chromatography on silica gel (hexane/EtOAc (7/3 to 5/5)) to yield **S5** (937 mg, 1.52 mmol, 76%) as a colorless amorphous solid; $[\alpha]_D^{20}$ +16.6 (*c* 1.26, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz, 50 °C) δ 7.77 (d, *J* = 7.3 Hz, 2H), 7.57 (dd, *J* = 7.3, 3.1 Hz, 2H), 7.43-7.23 (m, 8H), 7.17-7.11 (m, 2H), 7.09-7.04 (m, 2H), 5.40 (d, *J* = 9.0 Hz, 1H), 5.31 (br s, 1H), 4.50 (td, *J* = 9.0, 2.4 Hz, 1H), 4.34 (d, *J* = 1.2 Hz, 1H), 4.32 (s, 2H), 4.28-4.12 (br, 1H), 4.27 (d, *J* = 2.4 Hz, 1H), 4.18 (d, *J* = 7.1 Hz, 1H), 4.01 (br s, 1H), 3.73 (d, *J* = 5.3 Hz, 2H), 1.39 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz, 50 °C) δ 168.2, 156.4, 155.2, 143.9, 143.8, 141.4 (two carbons were overlapped), 140.5, 140.3, 139.4, 127.8, 127.1, 127.0, 126.8, 126.7, 126.0, 125.8, 125.10, 125.07, 124.5, 124.2, 120.0, 80.2,

67.5, 51.4, 49.5, 49.4, 49.2, 47.2, 44.7, 28.2 (three carbons were overlapped); IR (KBr, cm^{-1}): 3403, 3325, 3066, 3039, 3018, 2973, 2944, 2931, 2896, 2871, 1712, 1517, 1467, 1450, 1390, 1365, 1243, 1163, 1105, 1047, 759, 740. HRMS (FAB^+): m/z calcd for $C_{38}H_{36}N_2O_5SNa$ $[M+Na]^+$ 655.2243, found 655.2228.

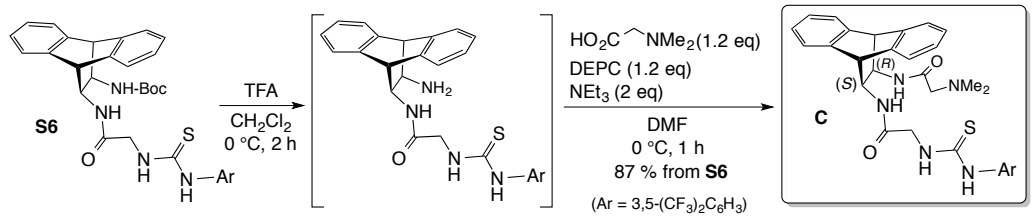
The preparation of S6, *tert*-butyl [(2*R*,3*S*)-3-[2-[3-[3,5-bis(trifluoromethyl)phenyl]thioureido]-acetamido]dibenzo[e,h]-bicyclo[2.2.2]octa-5,7-dien-2-ly]carbamate, from S5.



To the solution of **S5** (145 mg, 0.24 mmol) in CH_2Cl_2 (1 mL) was added diethylamine (50 μL, 0.48 mmol, 2 eq) and stirred at rt for 20 hours. The reaction mixture was acidified with 10% $KHSO_4$ aq. and the Fmoc-removed amine was extracted with 10% $KHSO_4$ aq. (10 mL x 3). Aq. layer combined was alkalined with $NaHCO_3$ and the product was extracted (CH_2Cl_2, 20 mL x 3), washed (brine, 10 mL x 3) and dried (anhyd. Na_2SO_4). The solution was concentrated under reduced pressure and the residue was dissolved in CH_2Cl_2 (2.4 mL), to which was added 3,5-bis(trifluoromethyl)phenyl isothiocyanate (68 μL, 0.36 mmol, 1.5 eq) at 0 °C and stirred at rt for 30 minutes. To the reaction solution was gradually added hexane and the product precipitated, which was collected by filtration to yield **S6** (120 mg, 0.18 mmol, 77%) as a colorless powder; mp 240-241 °C (decomp.); $[\alpha]_D^{20}$ +174.2 (*c* 1.30, THF); ^1H NMR (DMSO-d_6, 300 MHz, 50 °C) δ 10.44 (br s, 1H), 8.33 (s, 2H), 8.11 (br s, 1H), 7.71 (s, 1H), 7.39-7.34 (m, 4H), 7.22-7.14 (m, 5H), 5.52 (br s, 1H), 4.43 (td, *J* = 9.5, 2.6 Hz, 1H), 4.33 (d, *J* = 2.6 Hz, 1H), 4.26 (d, *J* = 2.6 Hz, 1H), 4.13-4.00 (m, 3H), 1.35 (s, 9H); ^{13}C NMR (DMSO-d_6, 100 MHz, 80 °C) δ 181.2, 168.2, 155.5, 142.6, 142.0, 141.8, 140.3, 140.1, 138.0, 130.9 (q, *J* = 32.9 Hz), 126.9, 126.83, 126.77, 126.6, 126.3, 124.6, 124.5, 123.7 (q, *J* = 272.9 Hz), 122.1, 116.6, 78.9, 51.7, 49.8, 49.64, 49.58, 47.7, 28.7; IR (KBr, cm^{-1}): 3384, 3299, 3105, 3076, 3047, 2994, 2972, 2925, 1701, 1655, 1599, 1518, 1471, 1458, 1388, 1367, 1346, 1276, 1176, 1137,

1054, 1024, 991, 970, 960, 883, 756, 700, 680. HRMS (FAB^+): m/z calcd for $C_{32}H_{30}F_6N_4O_3SNa$ $[M+Na]^+$ 687.1841, found 687.1861.

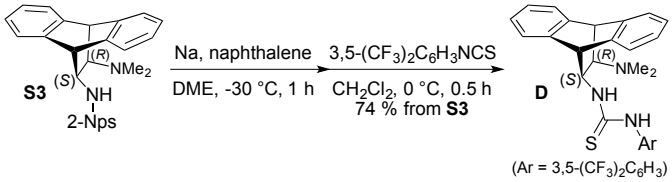
The preparation of catalyst C, 2-[3-[3,5-bis(trifluoromethyl)phenyl]thioureido]-*N*-[(2*S*,3*R*)-3-[2-(dimethylamino)acetamido]dibenzo[e,h]-bicyclo[2.2.2]octa-5,7-dien-2-ly]acetamide, from S6.



To the solution of **S6** (100 mg, 0.15 mmol) in CH_2Cl_2 (1.3 mL) was added TFA (0.2 mL) and stirred at rt for 1.5 hour to remove Boc group. The reaction mixture was alkalined by satd. $NaHCO_3$ aq. and the product was extracted (CH_2Cl_2; 20 mL x 3), washed (brine; 10 mL x 2), dried (anhyd. Na_2SO_4) and concentrated *in vacuo* to afford deprotected amine as a foam which was used in the next step without further purification. The residue was dissolved in DMF (0.5 mL) and *N*,*N*-dimethylglycine (20.8 mg, 0.20 mmol, 1.3 eq) was added. To the solution were subsequently added diethyl cyanophosphonate (DEPC; 30 μL, 0.20 mmol, 1.3 eq) and NEt_3 (45 μL, 0.32 mmol, 2.1 eq) at 0 °C and stirred at this temperature for 1 hour. EtOAc (100 mL) was added to the reaction mixture and the solution was washed (i) satd. $NaHCO_3$ (20 mL x 2), ii) brine (20 mL x 5)) and dried (anhyd. Na_2SO_4). After the concentration *in vacuo*, the residue was purified by column chromatography on silica gel (CH_2Cl_2/EtOH (95/5 to 9/1); contains 0.1% of NEt_3) to yield catalyst **C** (80 mg, 0.13 mmol, 87%) as a colorless amorphous solid; $[\alpha]_D^{22}$ +81.2 (*c* 1.32, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz, 50 °C) δ 9.97 (br s, 1H), 8.12 (s, 2H), 7.93 (br d, *J* = 4.5 Hz, 1H), 7.54 (s, 1H), 7.37-7.06 (m, 8H), 6.83 (d, *J* = 9.2 Hz, 1H), 6.13 (MJ) and 6.09 (MN)* (d, *J* = 8.6 Hz, 1H), 4.54-4.39 (m, 2H), 4.26 (d, *J* = 2.0 Hz, 1H), 4.21 (d, *J* = 2.0 Hz, 1H), 4.30-4.09 (m, 2H), 2.97 (MJ) and 2.99 (MN)* (d, *J* = 16.3 Hz, 1H), 2.67 (MJ) and 2.70 (MN)* (d, *J* = 16.3 Hz, 1H), 2.14 (MJ) and 2.16 (MN)* (s, 6H) (*: the peaks of rotational isomers; MJ = major isomer, MN = minor isomer);

^{13}C NMR ($CDCl_3$, 75 MHz, 50 °C) δ 182.21 (MJ) and 182.17 (MN)*, 171.4, 170.3 (MN) and 170.2 (MJ)*, 141.4, 140.25 (MJ) and 140.22 (MN)*, 140.1 (MJ) and 140.0 (MN)*, 139.0, 138.7, 131.5 (q, *J* = 33.6 Hz), 127.7, 127.5, 127.1, 126.4, 125.7, 124.5, 124.4, 123.4 (q, *J* = 272.8 Hz), 123.04, 123.01, 117.5 (m), 63.1, 51.0 (MJ) and 50.9 (MN)*, 49.7, 49.60 (MJ) and 49.57 (MN)*, 48.9, 48.2 (MJ) and 48.1 (MN)*, 45.81 (MN) and 45.78 (MJ)* (*: the peaks of rotational isomers; MJ = major isomer, MN = minor isomer); IR (KBr, cm^{-1}): 3386, 3301, 3097, 3072, 3047, 3031, 2980, 2950, 2881, 2831, 2786, 1670, 1533, 1471, 1384, 1353, 1278, 1213, 1180, 1133, 1047, 970, 956, 887, 761, 727, 702, 683. HRMS (FAB^+): m/z calcd for $C_{31}H_{30}F_6N_5O_2S$ $[M+H]^+$ 650.2024, found 650.2036.

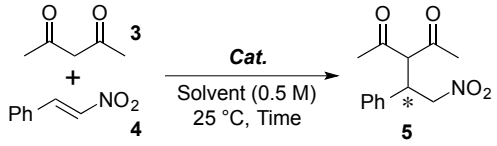
The preparation of catalyst D, 1-(3,5-Bis(trifluoromethyl)phenyl)-3-[(2*S*,3*R*)-3-(dimethylamino)dibenzo[e,h]bicyclo[2.2.2]octa-5,7-dien-2-yl]thiourea, from S3.



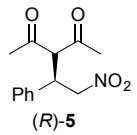
To the solution of naphthalene (231 mg, 1.8 mmol, 6 eq) in DME (3 mL) was added small pieces of Na (97 mg, 4.2 mmol, 14 eq) under argon atmosphere and sonicated at 25 °C for 5 minutes to prepare sodium naphthalenide. A solution of **S3** (136 mg, 0.3 mmol) in THF (8 mL) was added dropwise to the solution of sodium naphthalenide at -30 °C and stirred at this temperature for 40 minutes. The reaction mixture was poured into the ice water to quench excess amount of Na metal and the product was extracted (Et_2O, 40 mL x 3), washed (brine, 20 mL x 3) and dried (anhyd. Na_2SO_4). The solution was concentrated under reduced pressure and the residue was dissolved in CH_2Cl_2 (3 mL). 3,5-Bis(trifluoromethyl)phenyl isothiocyanate (70 μL, 0.38 mmol, 1.25 eq) was added to the solution at 0 °C and stirred for 30 minutes. The reaction solution was directly charged into silica gel column chromatography and purified (hexane/EtOAc (8:2)) to obtain catslyst **D** (119 mg, 0.22 mmol, 74%) as a faint yellowish amorphous solid; $[\alpha]_D^{20}$ +6.6 (*c* 1.20, $CHCl_3$); ^{1}H NMR (DMSO-d_6, 300 MHz) δ 10.7 (s, 1H), 8.34 (s, 2H), 7.70 (s, 1H), 7.49 (dd, J = 6.6, 1.5 Hz, 1H),

7.40-7.33 (m, 3H), 7.25 (dd, J = 6.6, 1.8 Hz, 1H), 7.18-7.09 (m, 4H), 4.84 (d, J = 3.1 Hz, 1H), 4.69 (d, J = 1.7 Hz, 1H), 4.61 (ddd, J = 8.7, 7.1, 3.1 Hz, 1H), 2.58 (dd, J = 8.7, 1.7 Hz, 1H), 2.21 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz, 50 °C) δ 178.3, 142.5, 141.2, 139.9, 138.5, 138.3, 133.1 (q, J = 33.9 Hz; two carbons were overlapped), 126.8, 126.6 (two carbons were overlapped), 126.2, 125.6, 125.5, 125.4, 123.7 (two carbons were overlapped), 123.6, 122.7 (q, J = 271.9 Hz; two carbons were overlapped), 119.1, 67.5, 53.8, 47.3, 47.0, 44.1 (two carbons were overlapped); IR (KBr, cm^{-1}): 3170, 2958, 2873, 1506, 1471, 1382, 1278, 1178, 1137, 893, 756, 683. HRMS (FAB$^+$): m/z calcd for $C_{27}H_{24}F_6N_3S$ $[M+H]^+$ 536.1595, found 536.1592.

Bifunctional "roofed" *cis*-amine-thiourea catalyzed enantioselective Michael addition of nitroolefin and acetylacetone (Table 1 and 2): General procedure



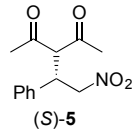
To a solution of *trans*-*β*-nitrostylene (**4**, 29.8 mg, 0.2 mmol) and "roofed" *cis*-amine-thiourea organocatalyst (0.02 mmol, 0.1 eq) in toluene or CH_2Cl_2 (0.4 mL) under argon atmosphere was added acetylacetone (**3**, 41 μL, 0.4 mmol, 2 eq) at 25 °C and stirred at the same temperature. The completion of the reaction was monitored by TLC. The reaction mixture was directly purified by column chromatography on silica gel (hexane/EtOAc (9/1 to 7/3)) to give 3-(2-nitro-1-phenylethyl)pentane-2,4-dione, **5** as a colorless solid; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.34-7.27 (m, 3H), 7.20-7.18 (m, 2H), 4.66 (dd, J = 12.5, 8.0 Hz, 1H), 4.62 (dd, J = 12.5, 4.9 Hz, 1H), 4.37 (d, J = 11.0 Hz, 1H), 4.24 (ddd, J = 11.0, 8.0, 4.9 Hz, 1H), 2.29 (s, 3H), 1.94 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 201.70, 200.94, 135.99, 129.29, 128.50, 127.91, 78.14, 70.68, 42.77, 30.38, 29.52. Spectroscopic data consistent with those previously reported.[4]



(*R*)-**5**

(*R*)-3-(2-nitro-1-phenylethyl)pentane-2,4-dione ((*R*)-5; Table 1, entry 1; 89% ee):

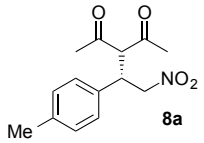
$[\alpha]_D^{29}$ –184.1 (*c* 0.35, $CHCl_3$) (lit.[4] $[\alpha]_D^{21}$ –158.9 (*c* 1.1, $CHCl_3$), 93% ee (*R*)); HPLC analysis: DAICEL CHIRALPAK IE (4.6 x 250 mm, hexane/2-propanol = 85/15, 1.0 mL/min, 210 nm): t_{major} = 16.5 min, t_{minor} = 18.5 min, 89% ee (*R*).



(*S*)-**5**

(*S*)-3-(2-nitro-1-phenylethyl)pentane-2,4-dione ((*S*)-5; Table 1, entry 8; 89% ee):

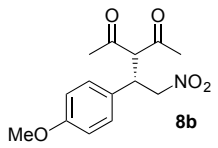
$[\alpha]_D^{29}$ +185.9 (*c* 0.48, $CHCl_3$); HPLC analysis: DAICEL CHIRALPAK IE (4.6 x 250 mm, hexane/2-propanol = 85/15, 1.0 mL/min, 210 nm) : t_{major} = 17.4 min, t_{minor} = 15.9 min, 89% ee (*S*).



8a

(*S*)-3-(2-nitro-1-p-tolylethyl)pentane-2,4-dione (8a; Table 2, entry 2).

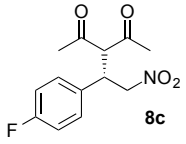
Colorless solid; $[\alpha]_D^{22}$ +197.4 (*c* 2.58, $CHCl_3$) (lit.[4] $[\alpha]_D^{18}$ –177.4 (*c* 0.7, $CHCl_3$), 93% ee (*R*)); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.12 (d, *J* = 8.0 Hz, 2H), 7.06 (d, *J* = 8.0 Hz, 2H), 4.62 (dd, *J* = 12.0, 7.5 Hz, 1H), 4.58 (dd, *J* = 12.0, 5.0 Hz, 1H), 4.35 (d, *J* = 11.0 Hz, 1H), 4.20 (ddd, *J* = 11.0, 7.5, 5.0 Hz, 1H), 2.30 (s, 3H), 2.29 (s, 3H), 1.94 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 201.85, 201.05, 138.35, 132.82, 129.98, 127.77, 78.36, 70.87, 42.47, 30.38, 29.41, 21.05. Spectroscopic data consistent with those previously reported.[4] HPLC analysis: DAICEL CHIRALPAK IC (4.6 x 250 mm, hexane/2-propanol = 85/15, 1.0 mL/min, 210 nm) : t_{major} = 13.7 min, t_{minor} = 20.7 min, 95% ee (*S*).



8b

(*S*)-3-(1-(4-methoxyphenyl)-2-nitroethyl)pentane-2,4-dione (8b; Table 2, entry 3).

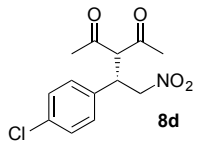
Colorless solid; $[\alpha]_D^{22}$ +194.1 (*c* 2.80, $CHCl_3$) (lit.[4] $[\alpha]_D^{21}$ –192.2 (*c* 1.2, $CHCl_3$), 94% ee (*R*)); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.10 (ddd, *J* = 8.7, 3.0, 2.3 Hz, 2H), 6.84 (ddd, *J* = 8.7, 3.0, 2.3 Hz, 2H), 4.60 (dd, *J* = 12.1, 7.2 Hz, 1H), 4.58 (dd, *J* = 12.1, 5.7 Hz, 1H), 4.33 (d, *J* = 10.9 Hz, 1H), 4.20 (ddd, *J* = 10.9, 7.2, 5.7 Hz, 1H), 3.77 (s, 3H), 2.29 (s, 3H), 1.94 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 201.83, 201.10, 159.51, 129.05, 127.65, 114.68, 78.43, 70.94, 55.21, 42.12, 30.34, 29.41. Spectroscopic data consistent with those previously reported.[4] HPLC analysis: DAICEL CHIRALPAK IE (4.6 x 250 mm, hexane/2-propanol = 85/15, 1.0 mL/min, 210 nm) : t_{major} = 27.3 min, t_{minor} = 25.1 min, 95% ee (*S*).



8c

(*S*)-3-(1-(4-fluorophenyl)-2-nitroethyl)pentane-2,4-dione (8c; Table 2, entry 4).

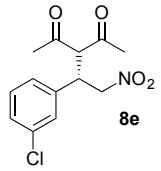
Colorless solid; $[\alpha]_D^{22}$ +175.3 (*c* 2.58, $CHCl_3$) (lit.[5] $[\alpha]_D^{25}$ +12.9 (*c* 1.0, $CHCl_3$), 89% ee (*S*)); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.18 (ddt, *J* = 8.7, 5.3, 3.0 Hz, 2H), 7.03 (tt, *J* = 8.7, 3.0 Hz, 2H), 4.62 (dd, *J* = 12.5, 7.2 Hz, 1H), 4.61 (dd, *J* = 12.5, 5.3 Hz, 1H), 4.33 (d, *J* = 10.6 Hz, 1H), 4.24 (ddd, *J* = 10.6, 7.2, 5.3 Hz, 1H), 2.30 (s, 3H), 1.97 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 201.45, 200.67, 162.50 (d, *J* = 249.1 Hz), 131.76, 129.67 (d, *J* = 7.7 Hz), 116.36 (d, *J* = 21.9 Hz), 78.12, 70.73, 42.05, 30.38, 29.57. Spectroscopic data consistent with those previously reported.[5,6] HPLC analysis: DAICEL CHIRALPAK IE (4.6 x 250 mm, hexane/2-propanol = 85/15, 1.0 mL/min, 210 nm) : t_{major} = 14.9 min, t_{minor} = 13.4 min, 94% ee (*S*).



8d

(*S*)-3-(1-(4-chlorophenyl)-2-nitroethyl)pentane-2,4-dione (8d; Table 2, entry 5).

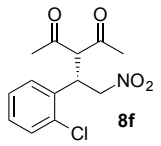
Colorless solid; $[\alpha]_D^{22}$ +173.0 (*c* 1.65, $CHCl_3$) (lit.[4] $[\alpha]_D^{21}$ -149.1 (*c* 1.1, $CHCl_3$), 90% ee (*R*)); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.31 (ddt, *J* = 9.1, 2.7, 1.9 Hz, 2H), 7.14 (ddd, *J* = 9.1, 2.7, 1.9 Hz, 2H), 4.62 (dd, *J* = 12.4, 7.5 Hz, 1H), 4.60 (dd, *J* = 12.4, 5.3 Hz, 1H), 4.33 (d, *J* = 11.0 Hz, 1H), 4.23 (ddd, *J* = 11.0, 7.5, 5.3 Hz, 1H), 2.30 (s, 3H), 1.98 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 201.34, 200.53, 134.55, 134.52, 129.53, 129.30, 76.79, 70.50, 42.13, 30.40, 29.64. Spectroscopic data consistent with those previously reported.[4] HPLC analysis: DAICEL CHIRALPAK AS-H (4.6 x 250 mm, hexane/2-propanol = 7/3, 1.0 mL/min, 210 nm) : t_{major} = 8.9 min, t_{minor} = 15.4 min, 97% ee (*S*).



8e

(*S*)-3-(1-(3-chlorophenyl)-2-nitroethyl)pentane-2,4-dione (8e; Table 2, entry 6).

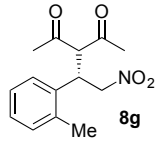
Colorless solid; $[\alpha]_D^{22}$ +167.5 (*c* 1.05, $CHCl_3$) (lit.[7] $[\alpha]_D^{rt}$ +124 (*c* 0.3, $CHCl_3$), 96% ee (*S*)); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.29-7.26 (m, 2H), 7.21-7.20 (m, 1H), 7.09-7.07 (m, 1H), 4.64 (dd, *J* = 12.9, 7.9 Hz, 1H), 4.62 (dd, *J* = 12.9, 4.9 Hz, 1H), 4.35 (d, *J* = 10.6 Hz, 1H), 4.23 (ddd, *J* = 10.6, 7.9, 4.9 Hz, 1H), 2.30 (s, 3H), 2.00 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 201.28, 200.41, 138.21, 135.17, 130.56, 128.83, 128.15, 126.11, 77.72, 70.35, 42.34, 30.46, 29.74. Spectroscopic data consistent with those previously reported.[6,7] HPLC analysis: DAICEL CHIRALPAK IC (4.6 x 250 mm, hexane/2-propanol = 85/15, 1.0 mL/min, 210 nm) : t_{major} = 10.8 min, t_{minor} = 16.3 min, 94% ee (*S*).



8f

(*S*)-3-(1-(2-chlorophenyl)-2-nitroethyl)pentane-2,4-dione (8f; Table 2, entry 8).

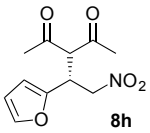
Colorless oil; $[\alpha]_D^{22}$ +248.6 (*c* 2.45, $CHCl_3$) (lit.[7] $[\alpha]_D^{rt}$ +150 (*c* 0.35, $CHCl_3$), >99% ee (*S*)); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.44-7.43 (dd, *J* = 7.2, 1.9 Hz, 1H), 7.28-7.23 (m, 2H), 7.16 (dd, *J* = 7.2, 1.9 Hz, 1H), 4.84 (dd, *J* = 12.4, 6.8 Hz, 1H), 4.75 (ddd, *J* = 10.2, 6.8, 4.1 Hz, 1H), 4.66 (dd, *J* = 12.4, 4.1 Hz, 1H), 4.60 (d, *J* = 10.2 Hz, 1H), 2.30 (s, 3H), 2.04 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 201.85, 200.80, 133.75, 133.43, 130.64, 129.69, 129.03, 127.64, 76.18, 69.00, 38.85, 30.86, 28.42. Spectroscopic data consistent with those previously reported.[7] HPLC analysis: DAICEL CHIRALPAK IE (4.6 x 250 mm, hexane/2-propanol = 85/15, 1.0 mL/min, 210 nm) : t_{major} = 11.6 min, t_{minor} = 13.4 min, 96% ee (*S*).



8g

(*S*)-3-(2-nitro-1-(*o*-tolyl)ethyl)pentane-2,4-dione (8g; Table 2, entry 9).

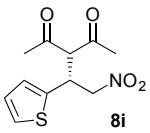
Colorless solid; $[\alpha]_D^{22}$ +158.5 (*c* 2.10, $CHCl_3$) (lit.[4] $[\alpha]_D^{20}$ -122 (*c* 1.1, $CHCl_3$), 90% ee (*R*)); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.18-7.16 (m, 3H), 7.09-7.07 (m, 1H), 4.65-4.54 (m, 3H), 4.41 (d, *J* = 10.2 Hz, 1H), 2.41 (s, 3H), 2.30 (s, 3H), 1.91 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 201.59, 200.92, 136.68, 134.32, 131.59, 128.21, 126.75, 125.97, 77.76, 70.28, 37.69, 30.37, 30.15, 19.50. Spectroscopic data consistent with those previously reported.[4] HPLC analysis: DAICEL CHIRALPAK IC (4.6 x 250 mm, hexane/2-propanol = 85/15, 1.0 mL/min, 210 nm) : t_{major} = 12.6 min, t_{minor} = 21.4 min, 97% ee (*S*).



8h

(*R*)-3-(1-(furan-2-yl)-2-nitroethyl)pentane-2,4-dione (8h; Table 2, entry 10).

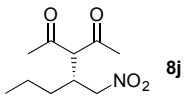
Colorless oil; $[\alpha]_D^{22}$ +152.3 (*c* 1.47, $CHCl_3$) (lit.[8] $[\alpha]_D^{27}$ -162.4 (*c* 1.0, $CHCl_3$), 97% ee (*S*)); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 (d, *J* = 1.8 Hz, 1H), 6.30 (dd, *J* = 3.2, 1.8 Hz, 1H), 6.18 (d, *J* = 3.2 Hz, 1H), 4.67 (d, *J* = 6.0 Hz, 2H), 4.41-4.32 (m, 2H), 2.29 (s, 3H), 2.09 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 201.41, 200.71, 149.43, 142.87, 110.80, 108.83, 75.80, 67.92, 36.57, 30.59, 29.25. Spectroscopic data consistent with those previously reported.[4,8] HPLC analysis: DAICEL CHIRALPAK AS-H (4.6 x 250 mm, hexane/2-propanol = 7/3, 1.0 mL/min, 210 nm) : t_{major} = 11.2 min, t_{minor} = 14.1 min, 93% ee (*R*).



8i

(*R*)-3-(2-nitro-1-(thiophen-2-yl)ethyl)pentane-2,4-dione (8i; Table 2, entry 11).

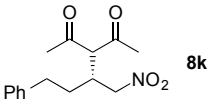
Colorless solid; $[\alpha]_D^{22}$ +178.1 (*c* 1.69, $CHCl_3$) (lit.[4] $[\alpha]_D^{18}$ -155.5 (*c* 1.2, $CHCl_3$), 92% ee (*S*)); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.24 (d, *J* = 5.0 Hz, 1H), 6.94 (dd, *J* = 5.0, 3.6 Hz, 1H), 6.89 (d, *J* = 3.6 Hz, 1H), 4.66 (d, *J* = 5.9 Hz, 2H), 4.58-4.52 (m, 1H), 4.41 (d, *J* = 10.5 Hz, 1H), 2.30 (s, 3H), 2.08 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 201.41, 200.58, 138.44, 127.35, 126.97, 125.70, 78.48, 71.06, 38.23, 30.51, 29.59. Spectroscopic data consistent with those previously reported.[4] HPLC analysis: DAICEL CHIRALPAK AS-H (4.6 x 250 mm, hexane/2-propanol = 7/3, 1.0 mL/min, 210 nm) : t_{major} = 11.6 min, t_{minor} = 14.9 min, 93% ee (*R*).



8j

(*R*)-3-(1-nitropentan-2-yl)pentane-2,4-dione (8j; Table 2, entry 12).

Colorless oil; $[\alpha]_D^{20}$ +141.2 (*c* 0.78, $CHCl_3$) (lit.[7] $[\alpha]_D^{r.t.}$ +106 (*c* 0.22, CH_2Cl_2), >99% ee (*R*)); ^{1}H NMR (600 MHz, $CDCl_3$): δ 4.53 (dd, *J* = 12.5, 4.5 Hz, 1H), 4.49 (dd, *J* = 12.5, 5.3 Hz, 1H), 4.00 (d, *J* = 8.4 Hz, 1H), 2.89-2.83 (m, 1H), 2.28 (s, 3H), 2.27 (s, 3H), 1.51-1.23 (m, 4H), 0.92 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 202.73, 202.31, 75.76, 69.29, 36.73, 31.61, 30.91, 29.83, 19.83, 13.69. Spectroscopic data consistent with those previously reported.[7] HPLC analysis: DAICEL CHIRALPAK AD-H (4.6 x 250 mm, hexane/2-propanol = 98/2, 1.0 mL/min, 210 nm) : t_{major} = 20.3 min, t_{minor} = 22.5 min, 84% ee (*R*).



8k

(*R*)-3-(1-nitro-4-phenylbutan-2-yl)pentane-2,4-dione (8k; Table 2, entry 13).

Colorless oil; $[\alpha]_D^{17}$ +111.5 (*c* 0.82, $CHCl_3$) (lit.[4] $[\alpha]_D^{22}$ -113 (*c* 0.9, $CHCl_3$), 83% ee (*S*)); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.30 (t, *J* = 7.2 Hz, 2H), 7.22 (t, *J* = 7.2 Hz, 1H), 7.14 (d, *J* = 7.2 Hz, 2H), 4.58 (dd, *J* = 12.5, 4.5 Hz, 1H), 4.54 (dd, *J* = 12.5, 4.9 Hz, 1H), 3.97 (d, *J* = 8.3 Hz, 1H), 2.86-2.79 (m, 2H), 2.60 (ddd, *J* = 14.0, 9.1, 7.5 Hz, 1H), 2.21 (s, 3H), 2.14 (s, 3H), 1.79-1.73 (m, 1H), 1.63-1.58 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 202.69, 202.23, 140.08, 128.72, 128.30, 126.50, 75.60, 69.27, 36.23, 32.81, 31.06, 30.81, 29.55. Spectroscopic data consistent with those previously reported.[4] HPLC analysis: DAICEL CHIRALPAK AD-H (4.6 x 250 mm, hexane/2-propanol = 98/2, 1.0 mL/min, 210 nm) : t_{major} = 30.0 min, t_{minor} = 33.3 min, 81% ee (*R*).

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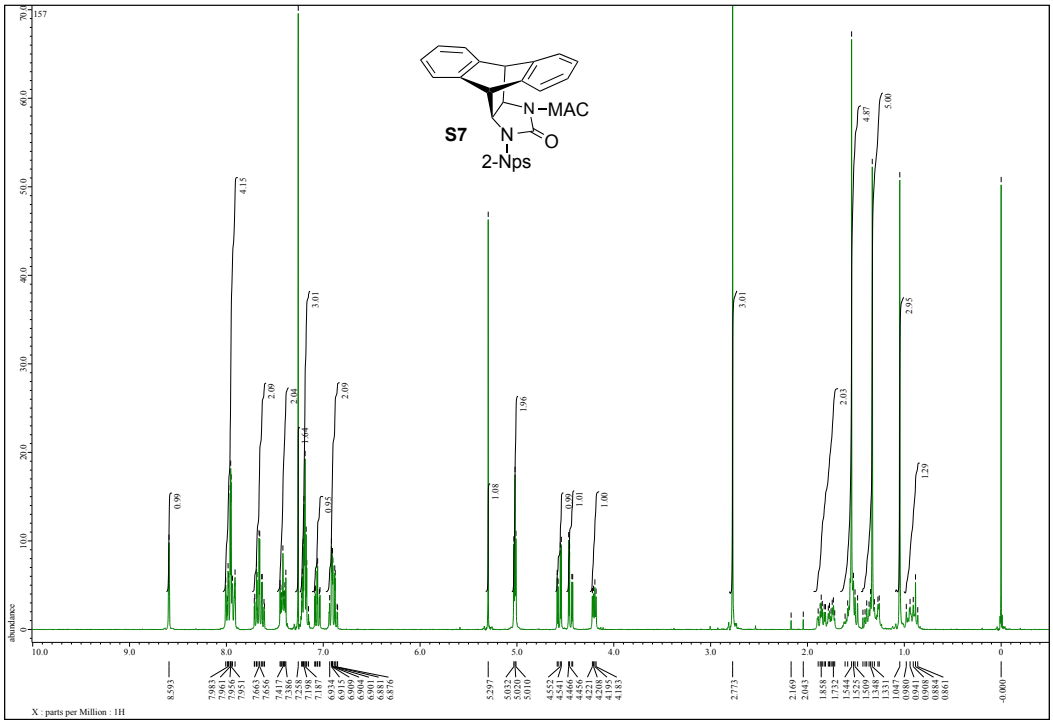
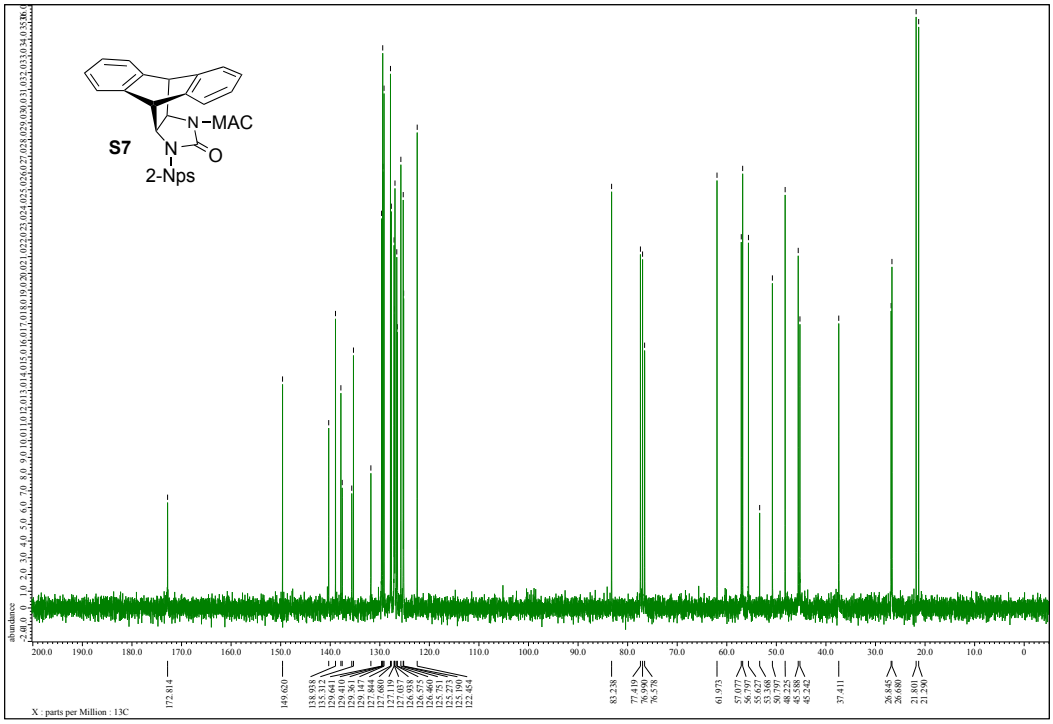
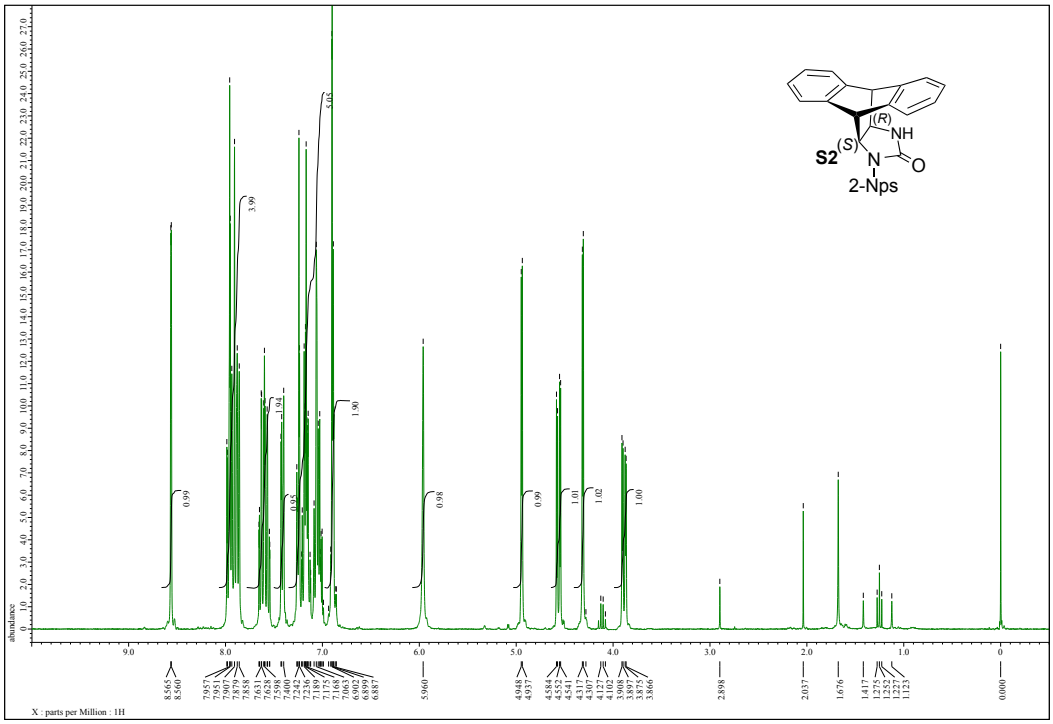
S7: ^{1}H NMR ($CDCl_3$, 300 MHz)



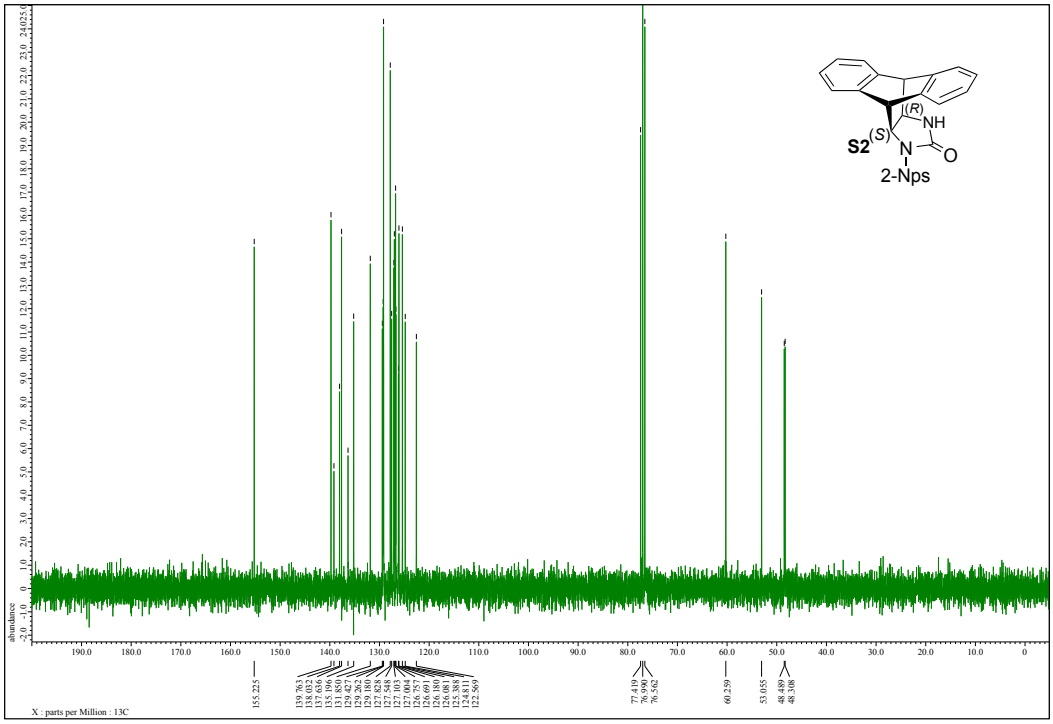
S7: ^{13}C NMR ($CDCl_3$, 75 MHz)



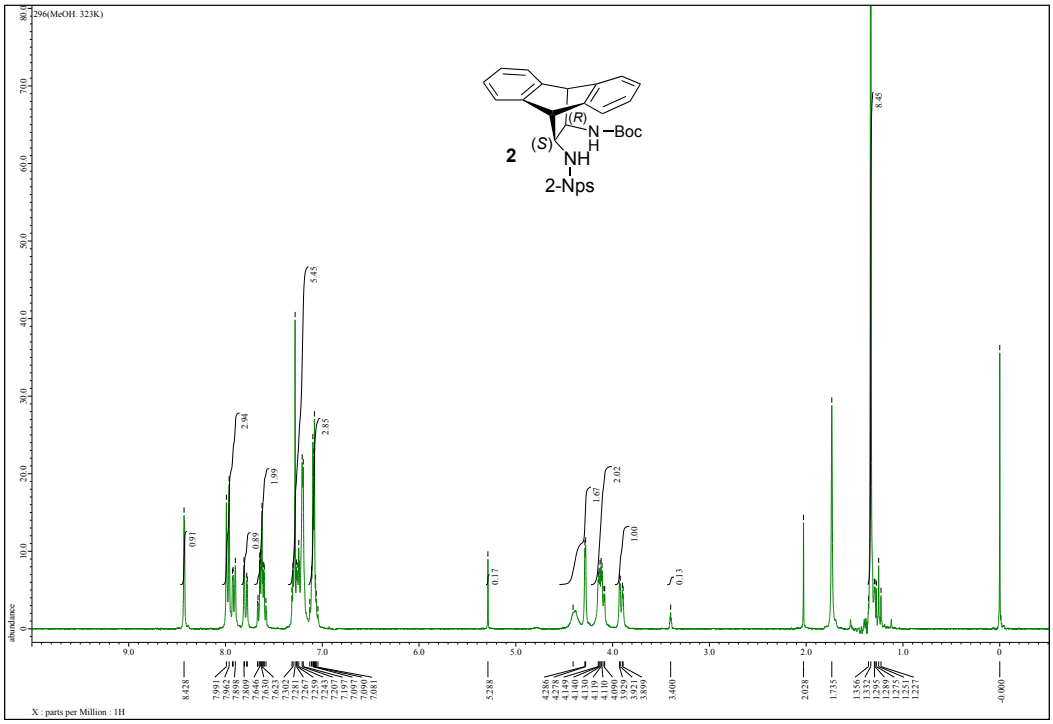
S2: ^{1}H NMR ($CDCl_3$, 300 MHz)



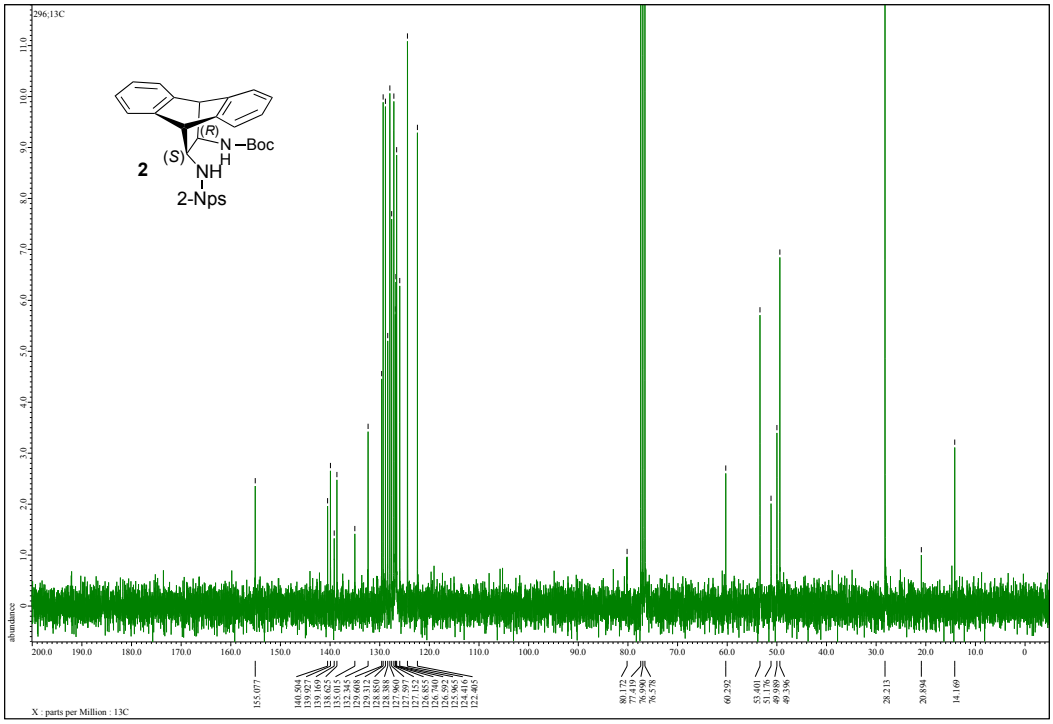
S2: ^{13}C NMR ($CDCl_3$, 75 MHz)



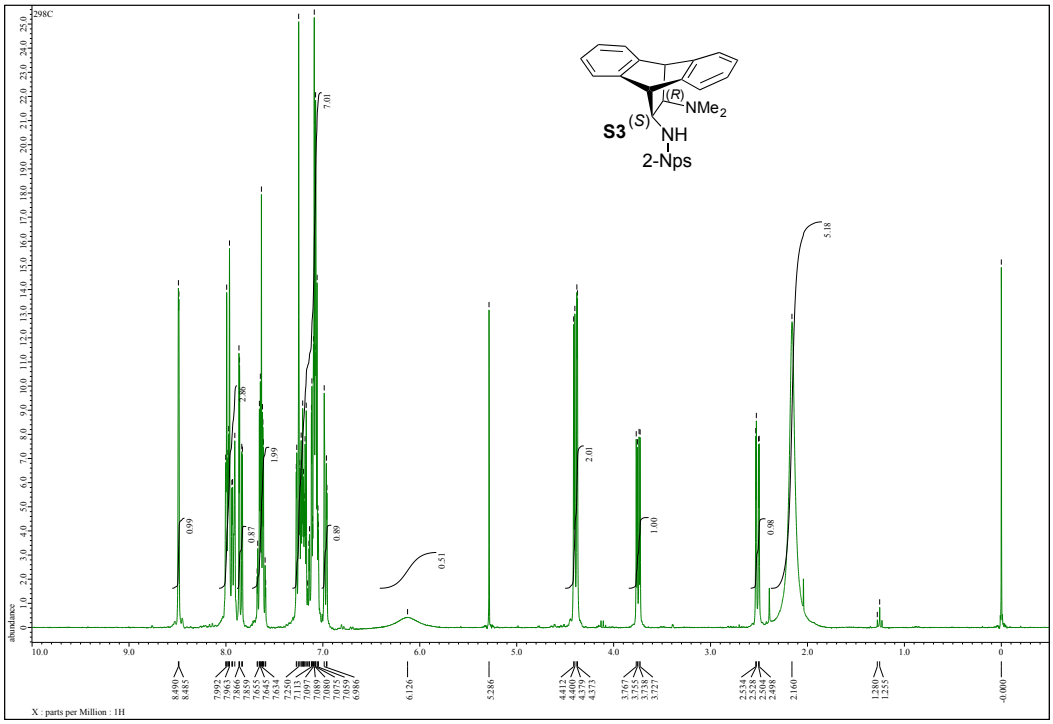
2: ^{1}H NMR ($CDCl_3$+CD_3OD 1 drop, 300 MHz, 50 °C)



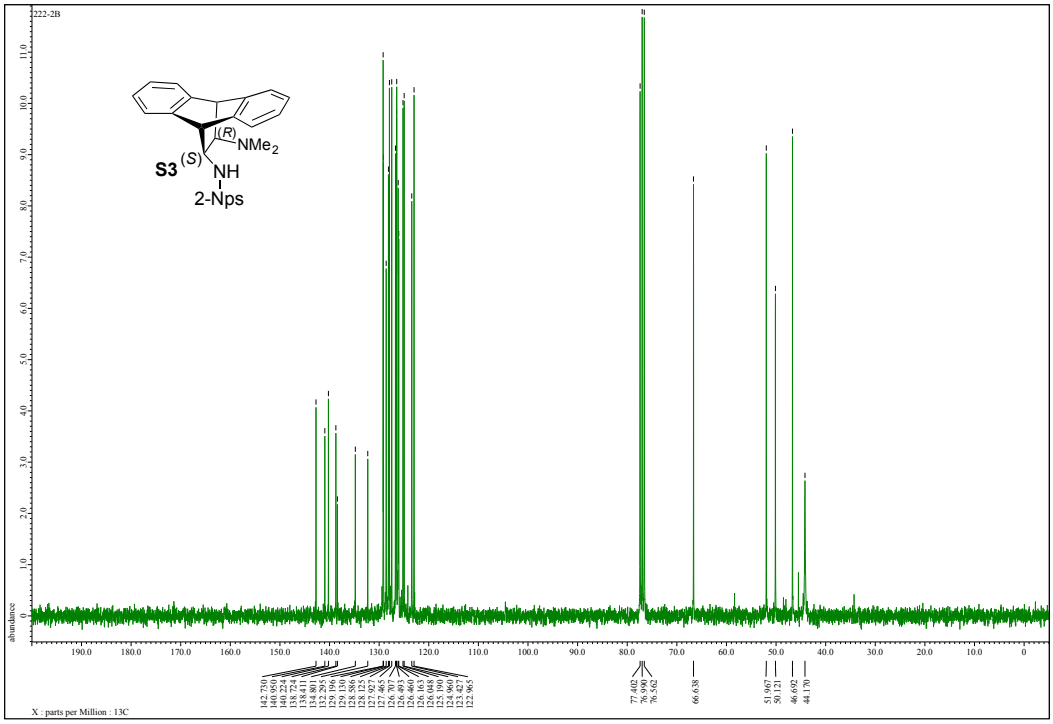
2: ^{13}C NMR ($CDCl_3$, 75 MHz)



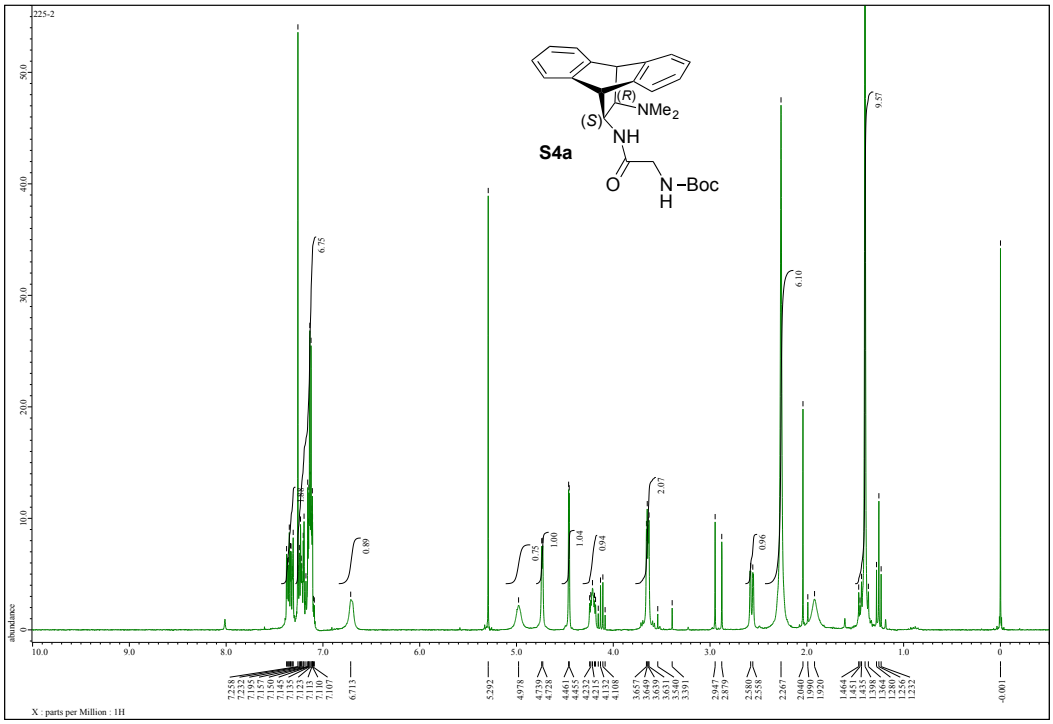
S3: ^{1}H NMR ($CDCl_3$, 300 MHz)



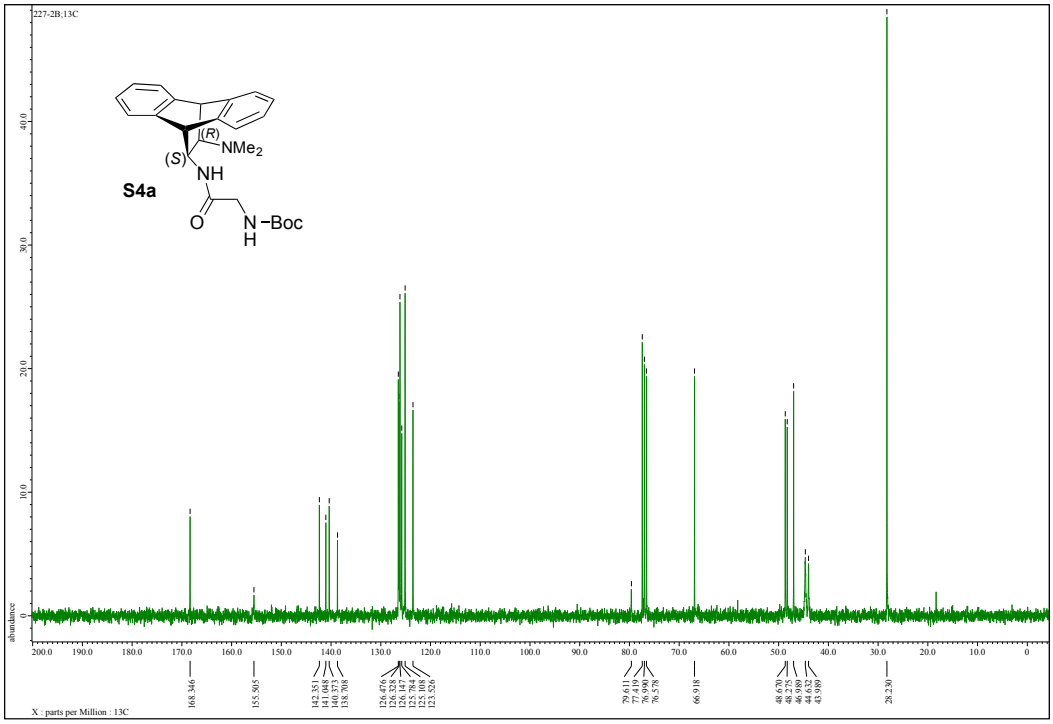
S3: ^{13}C NMR ($CDCl_3$, 75 MHz)



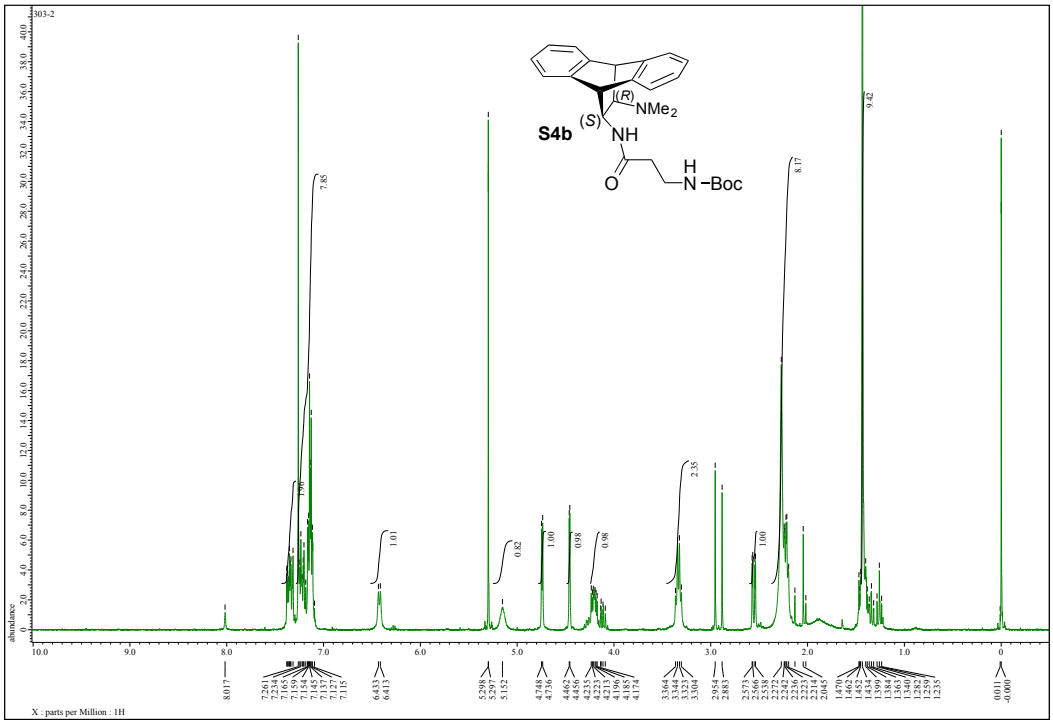
S4a: ^{1}H NMR ($CDCl_3$, 300 MHz)



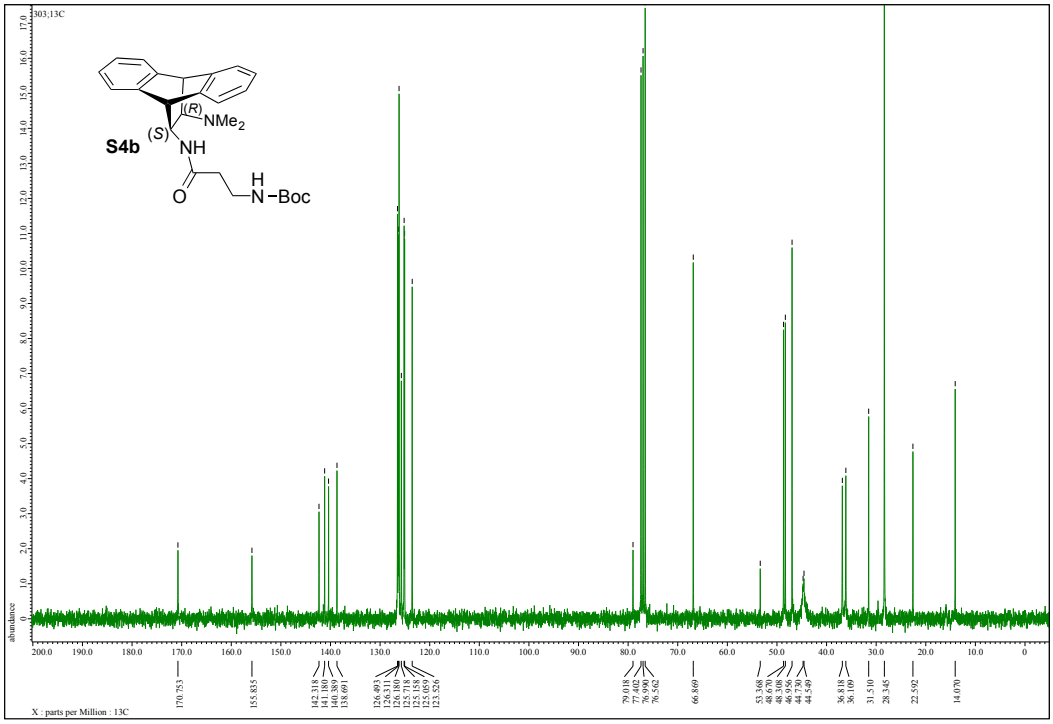
S4a: ^{13}C NMR ($CDCl_3$, 75 MHz)



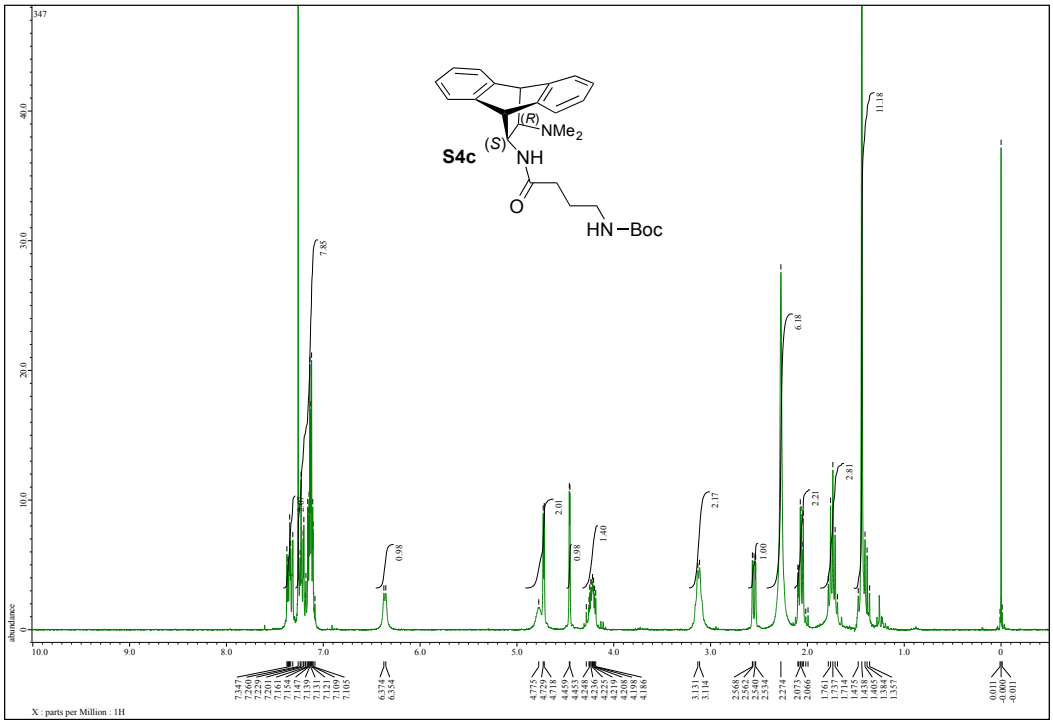
S4b: ^{1}H NMR ($CDCl_3$, 300 MHz)



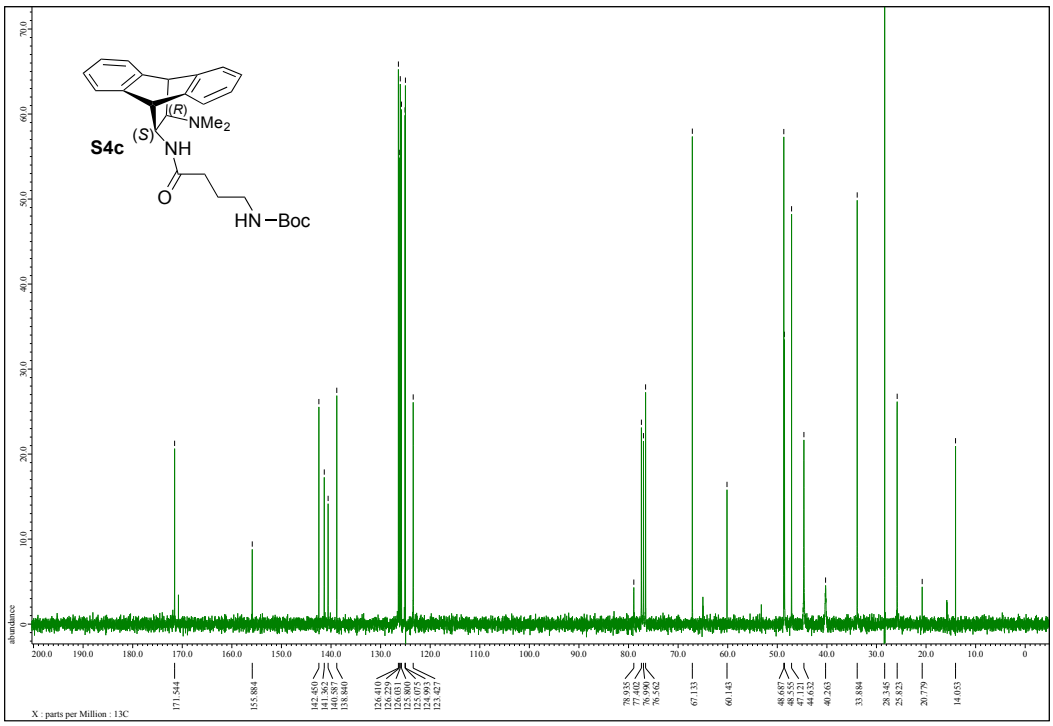
S4b: ^{13}C NMR ($CDCl_3$, 75 MHz)



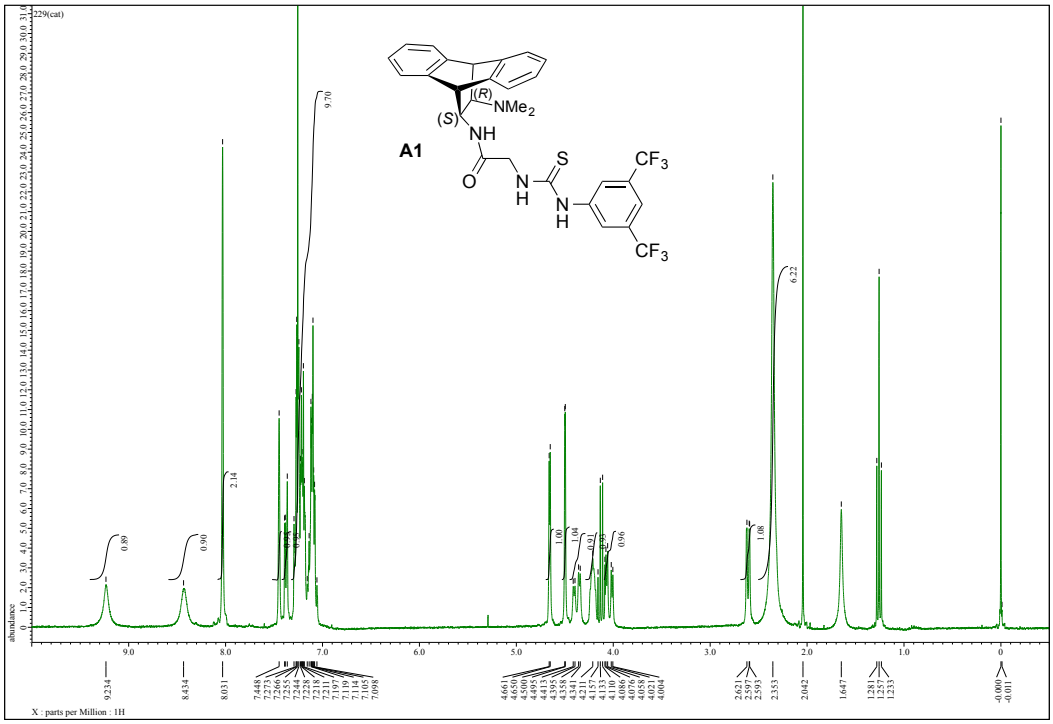
S4c: ^{1}H NMR ($CDCl_3$, 300 MHz)



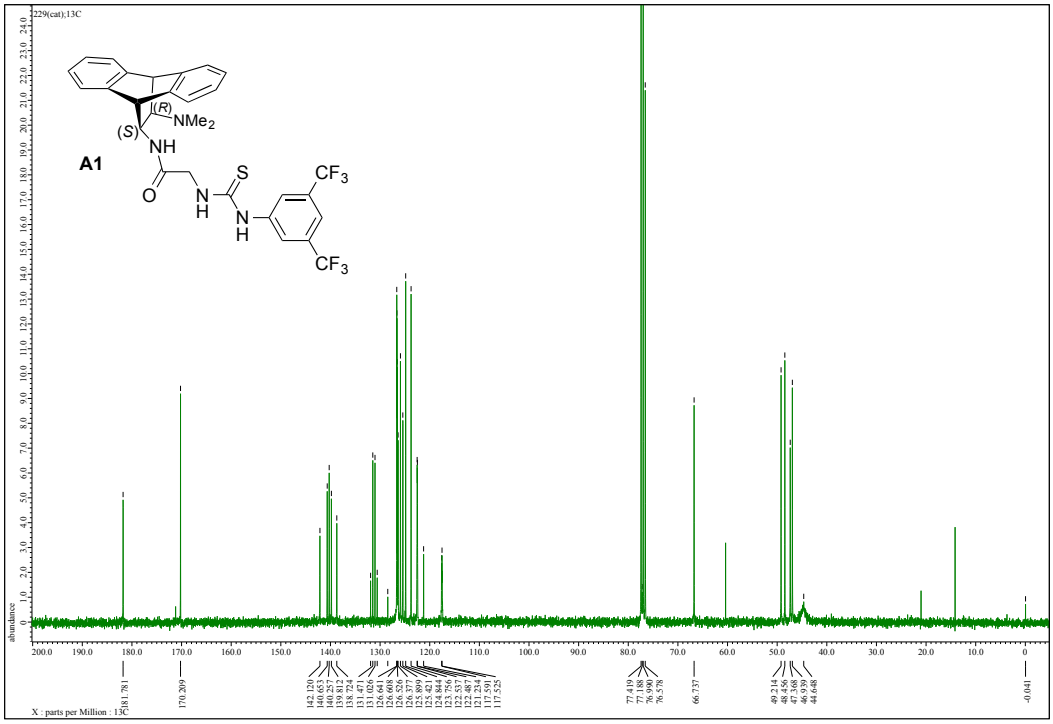
S4c: ^{13}C NMR ($CDCl_3$, 75 MHz, 50 °C)



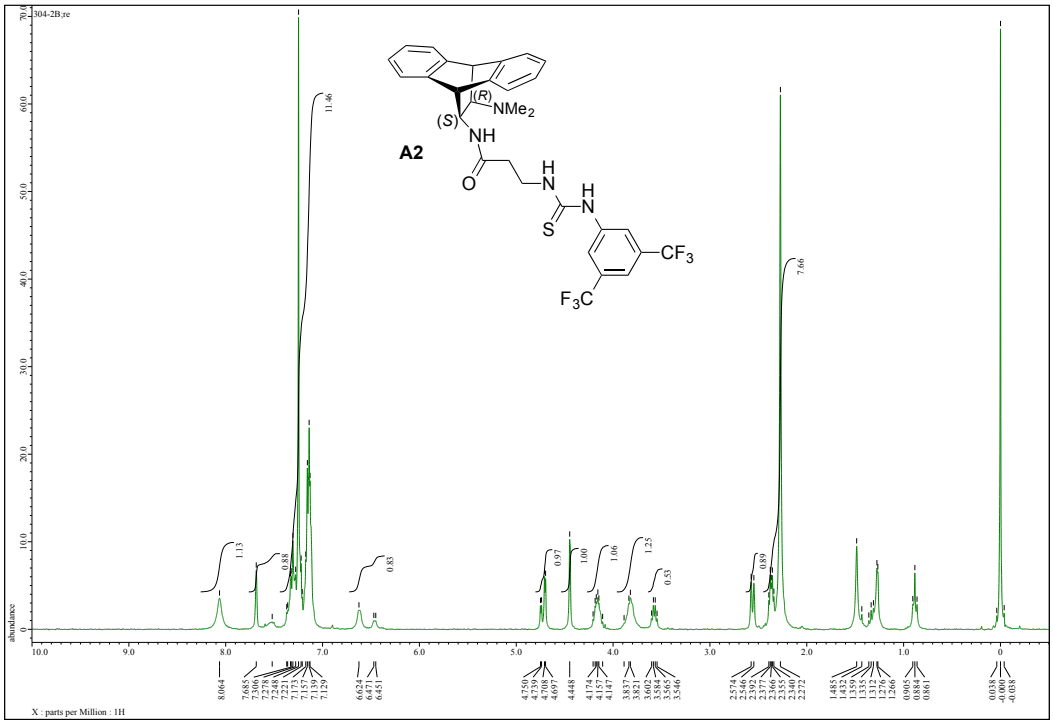
Catalyst A1: ^{1}H NMR ($CDCl_3$, 300 MHz)



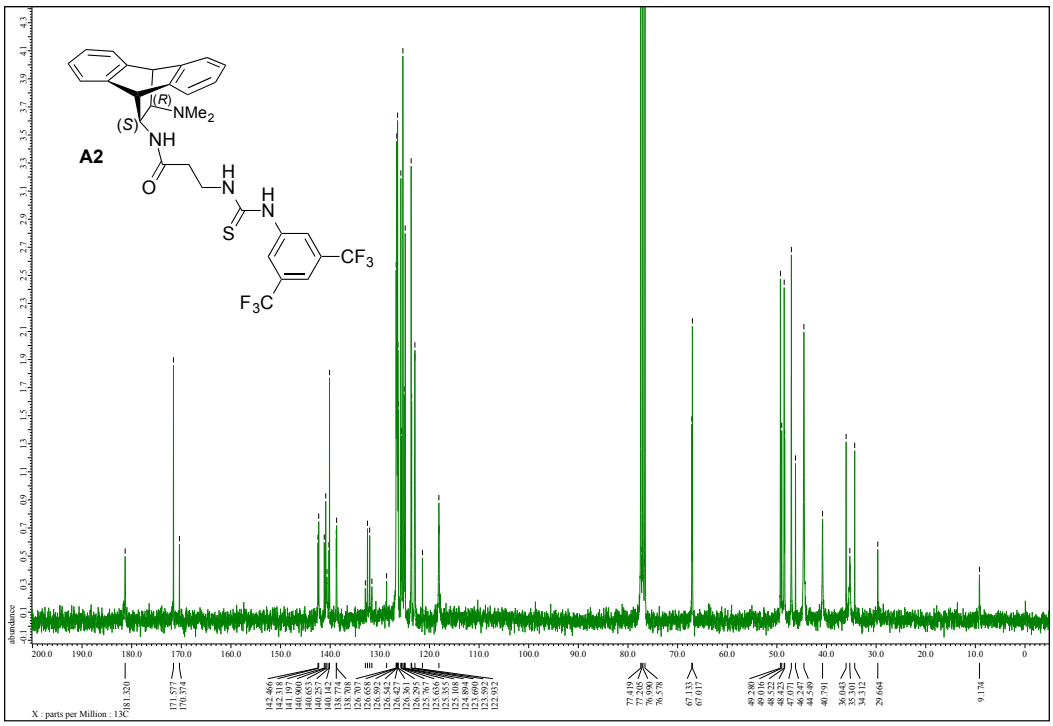
Catalyst A1: ^{13}C NMR ($CDCl_3$, 75 MHz, 50 °C)



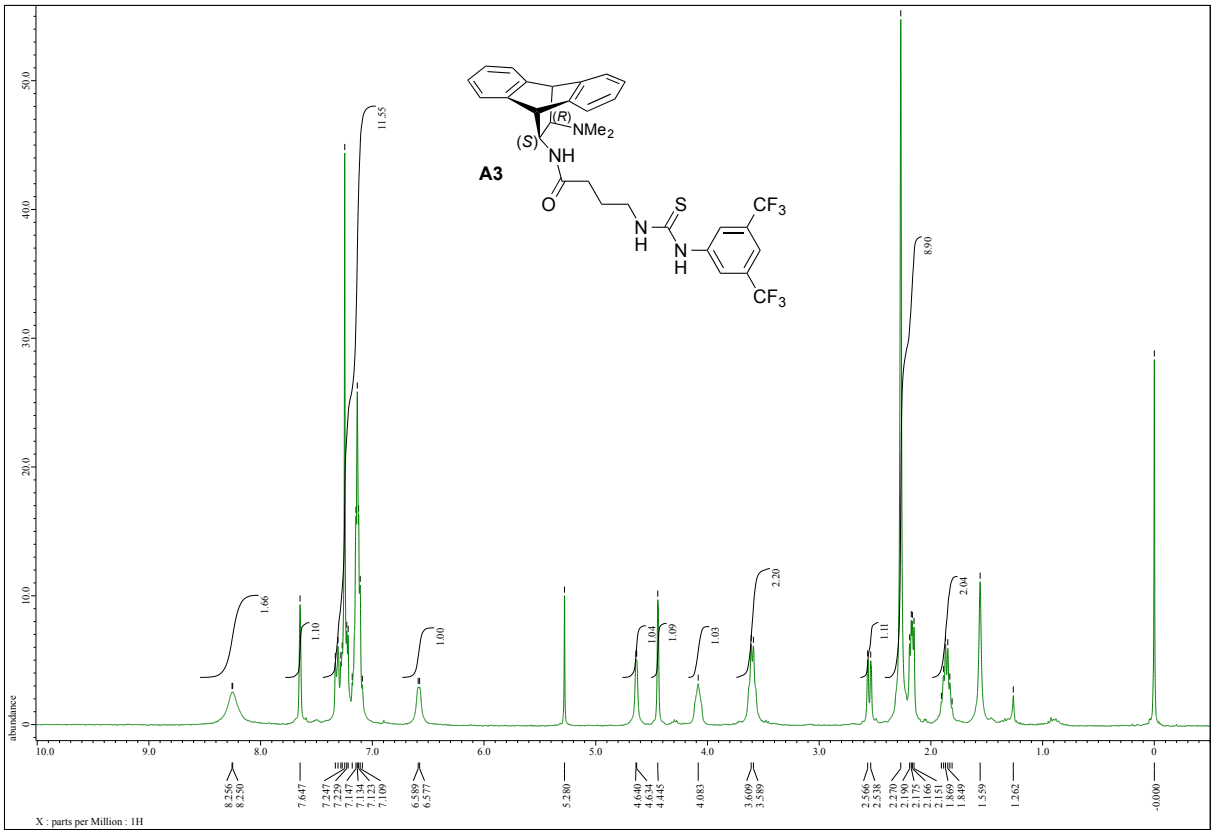
Catalyst A2: ^{1}H NMR ($CDCl_3$, 300 MHz, 50 °C)



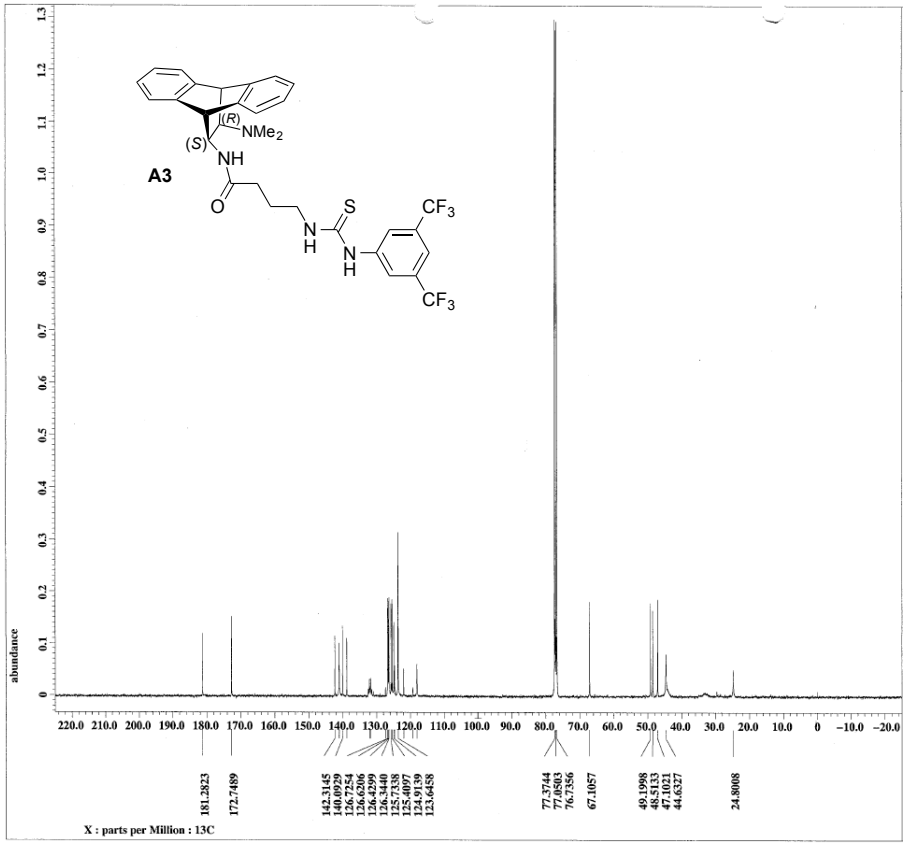
Catalyst A2: ^{13}C NMR ($CDCl_3$, 75 MHz, 50 °C; the peaks of rotational isomers were observed)



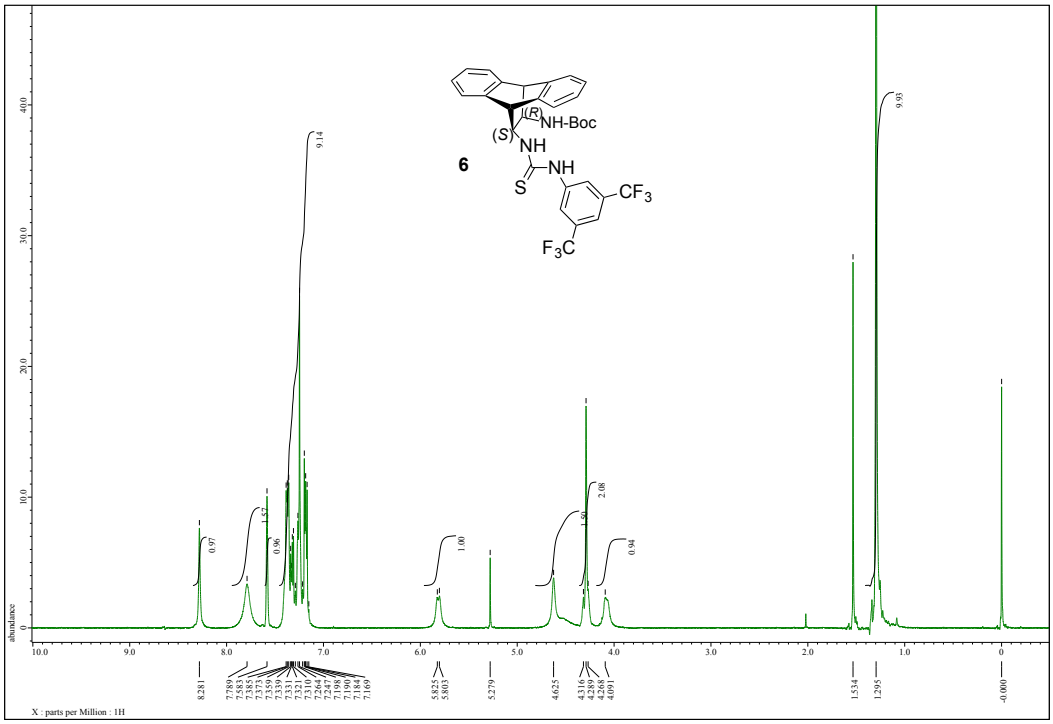
Catalyst A3: ^{1}H NMR ($CDCl_3$, 300 MHz, 50 °C)



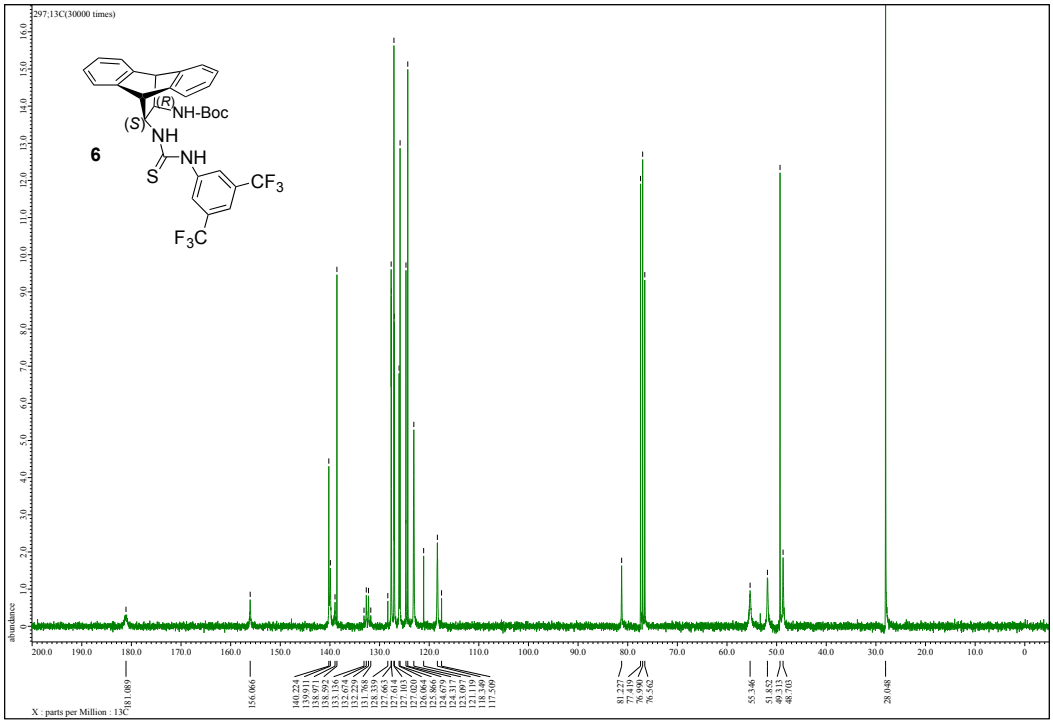
Catalyst A3: ^{13}C NMR ($CDCl_3$, 75 MHz, 50 °C)



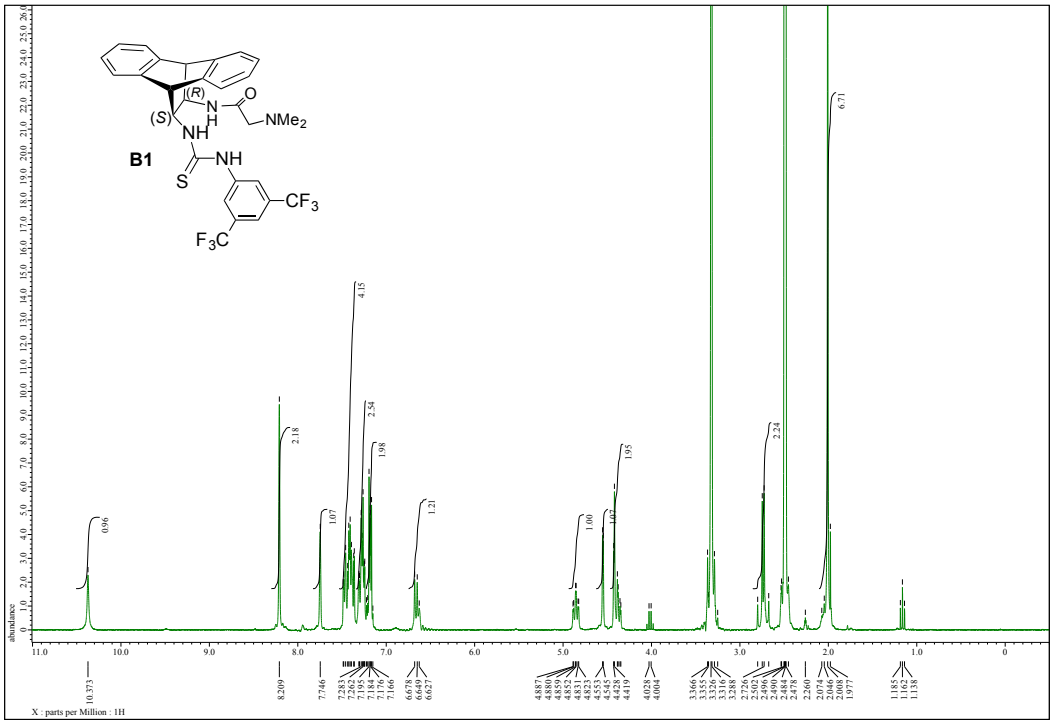
6: ^{1}H NMR ($CDCl_3$, 300 MHz, 50 °C)



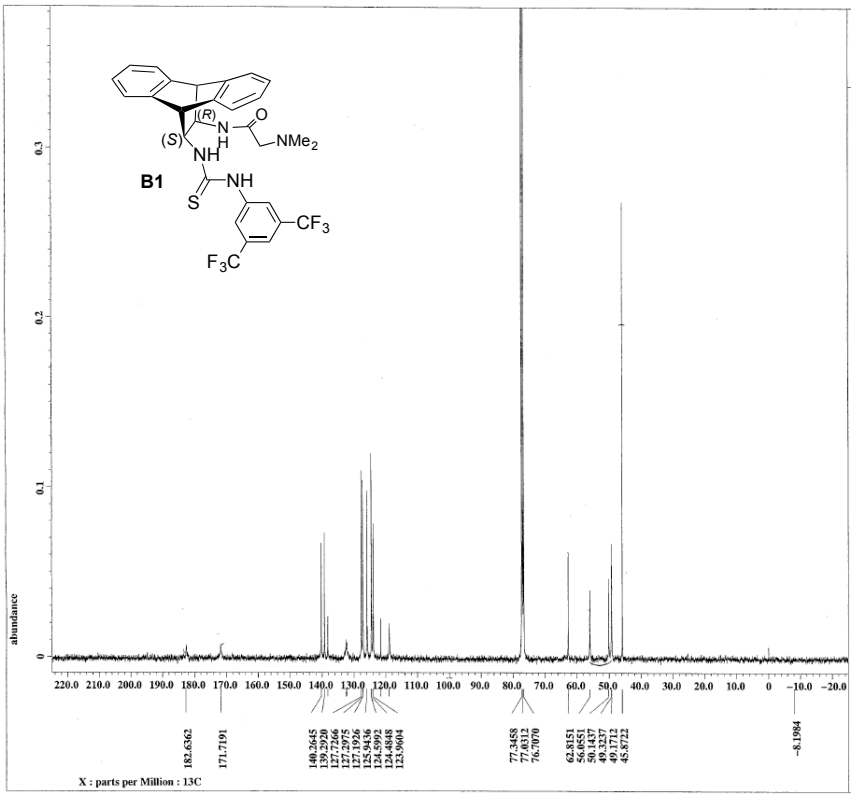
6: ^{13}C NMR ($CDCl_3$, 100 MHz, 50 °C)



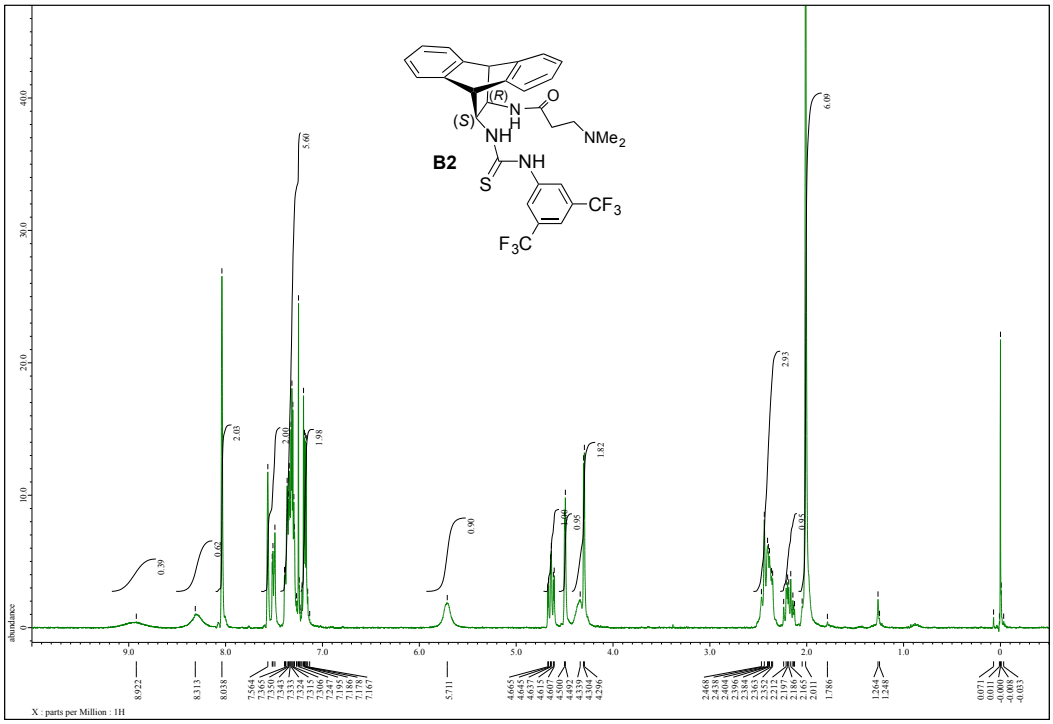
Catalyst B1: ^{1}H NMR (DMSO-d_6, 300 MHz)



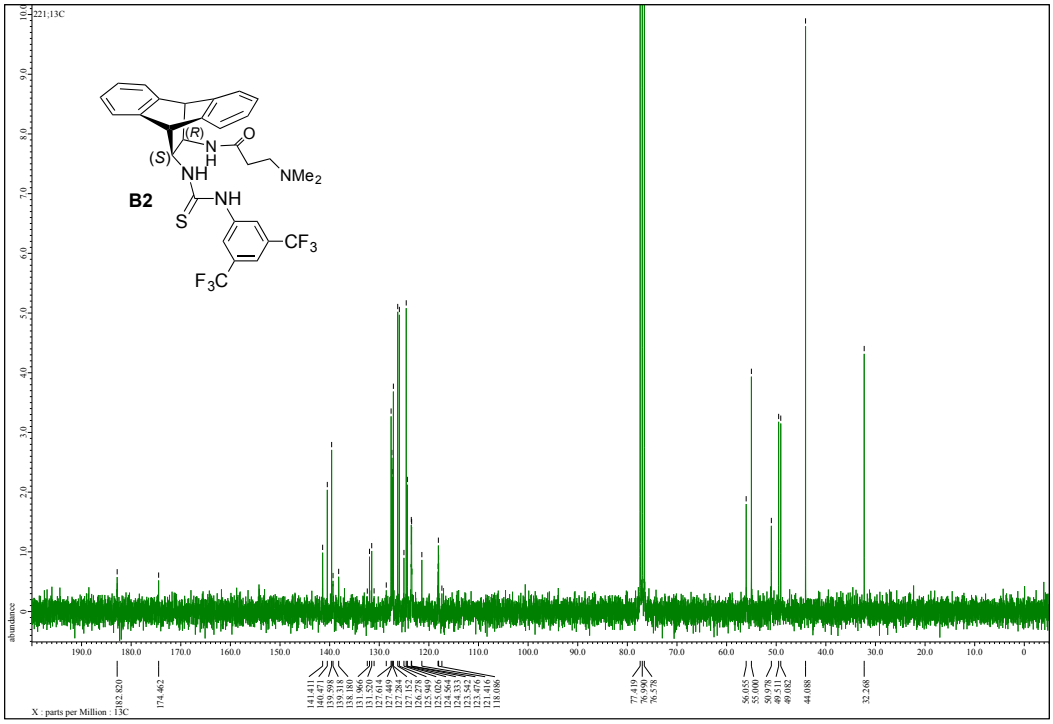
Catalyst B1: ^{13}C NMR ($CDCl_3$, 100 MHz, 50 °C)



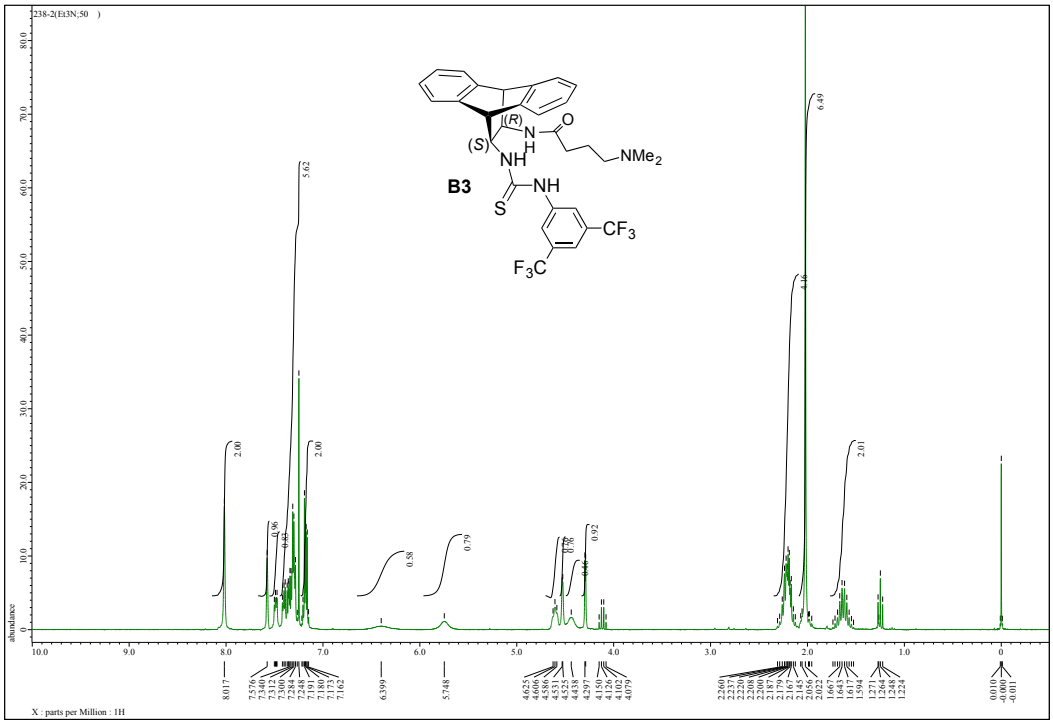
Catalyst B2: ^{1}H NMR ($CDCl_3$, 300 MHz, 50 °C)



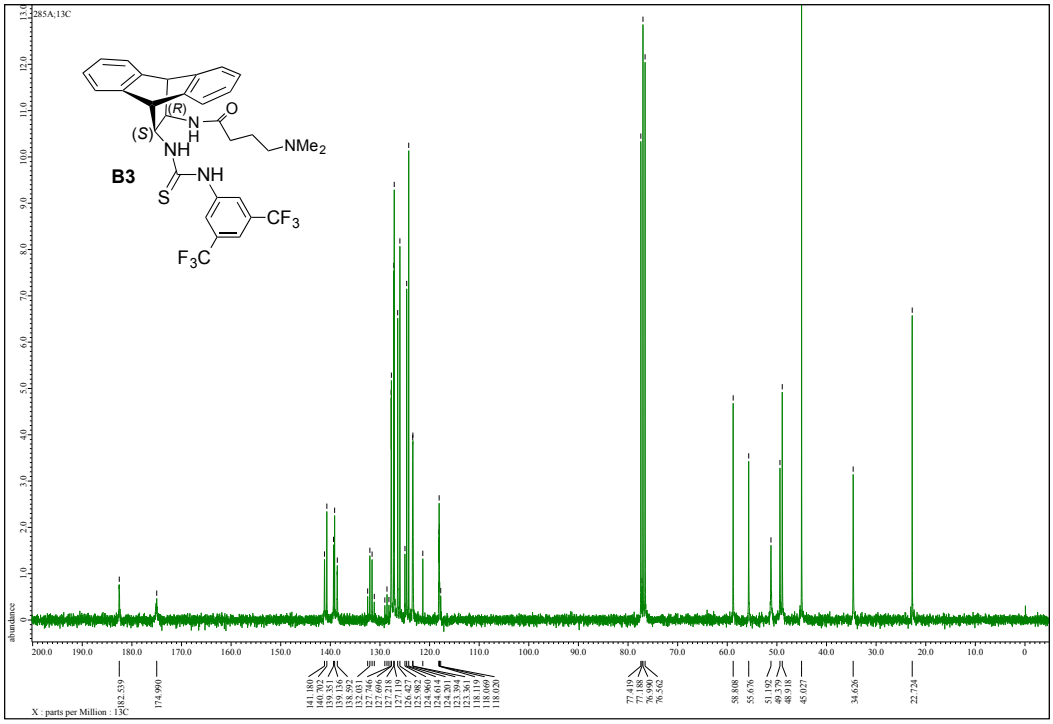
Catalyst B2: ^{13}C NMR ($CDCl_3$, 75 MHz, 50 °C)



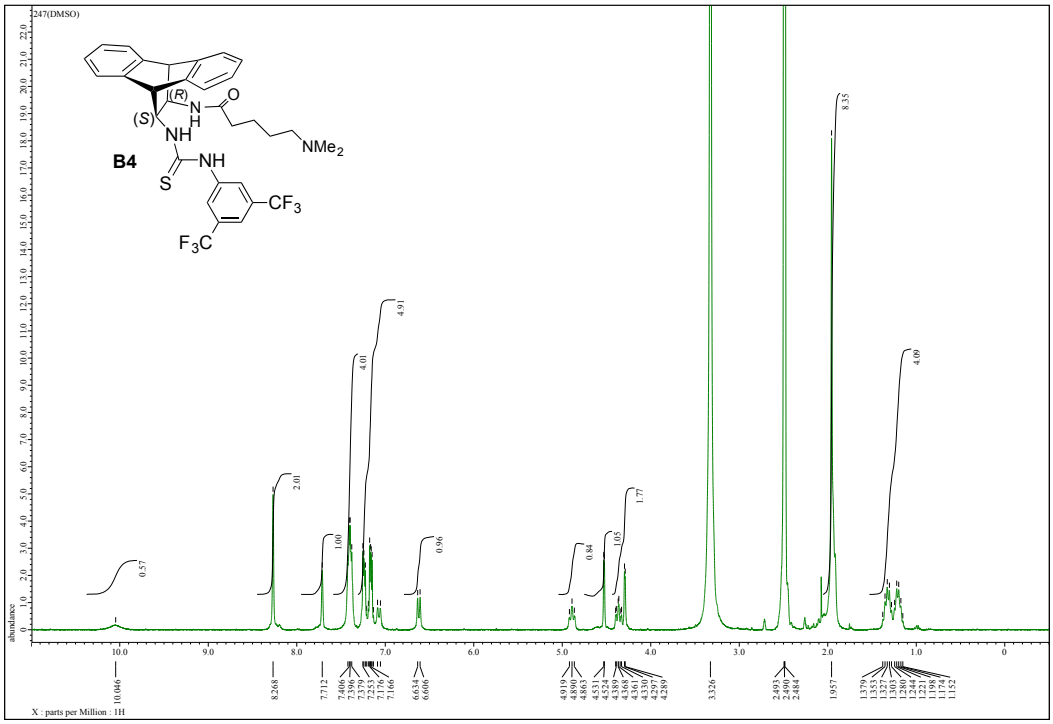
Catalyst B3: ^{1}H NMR ($CDCl_3$, 300 MHz, 50 °C)



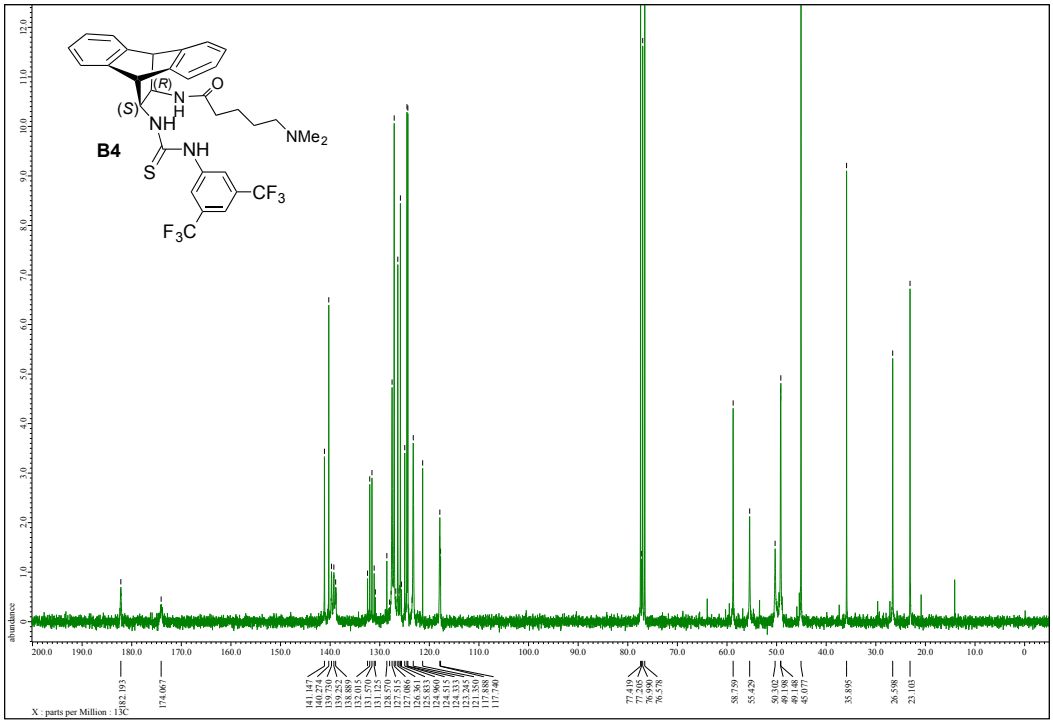
Catalyst B3: ^{13}C NMR ($CDCl_3$, 75 MHz, 50 °C)



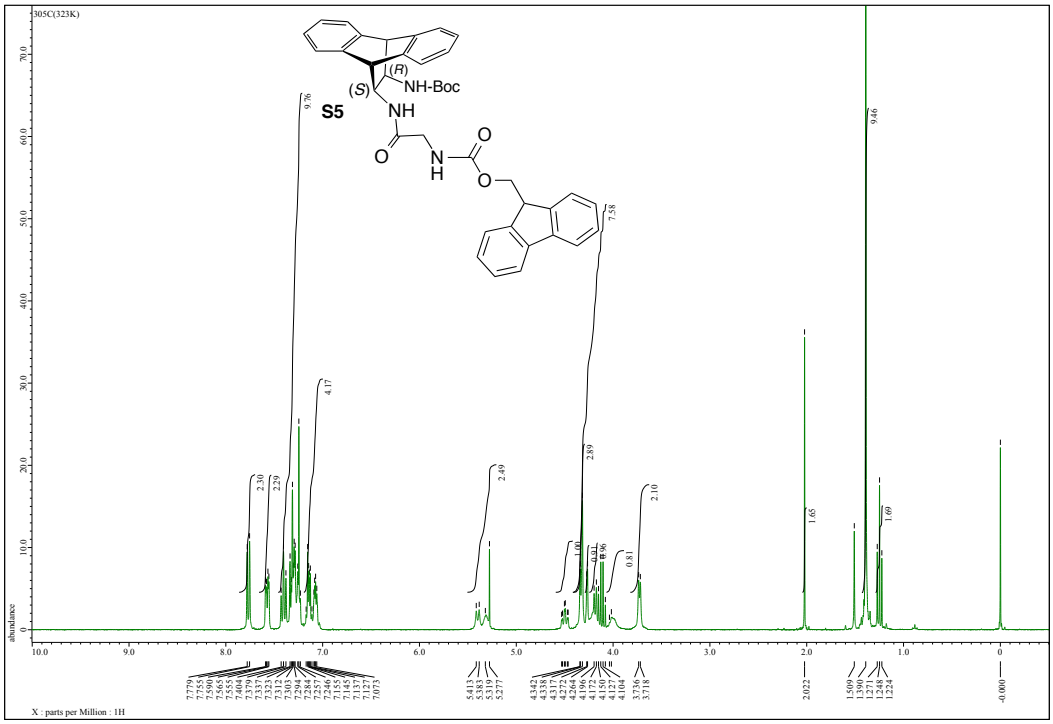
Catalyst B4: ^{1}H NMR (DMSO-d_6, 300 MHz)



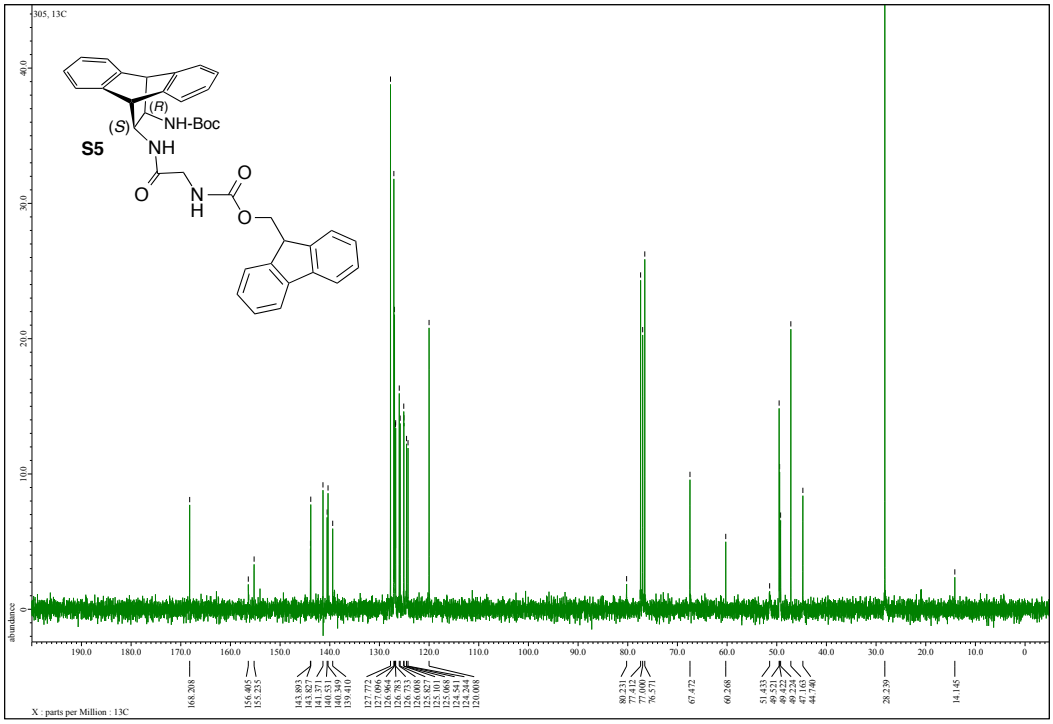
Catalyst B4: ^{13}C NMR ($CDCl_3$, 75 MHz, 50 °C)



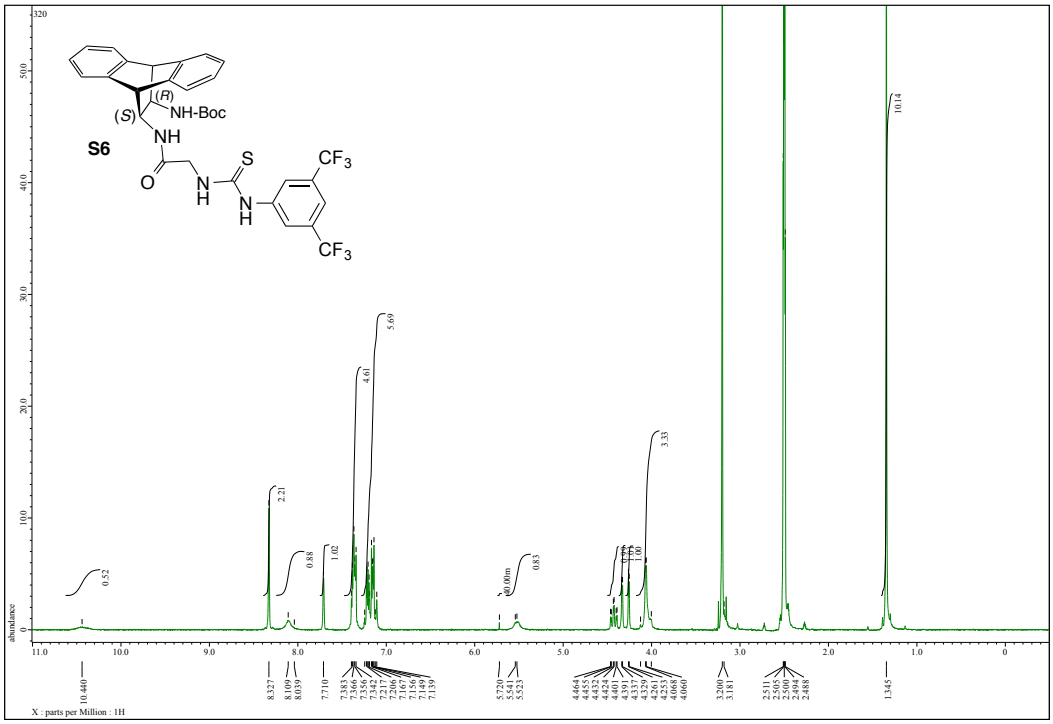
S5: ^{1}H NMR ($CDCl_3$, 300 MHz, 50 °C)



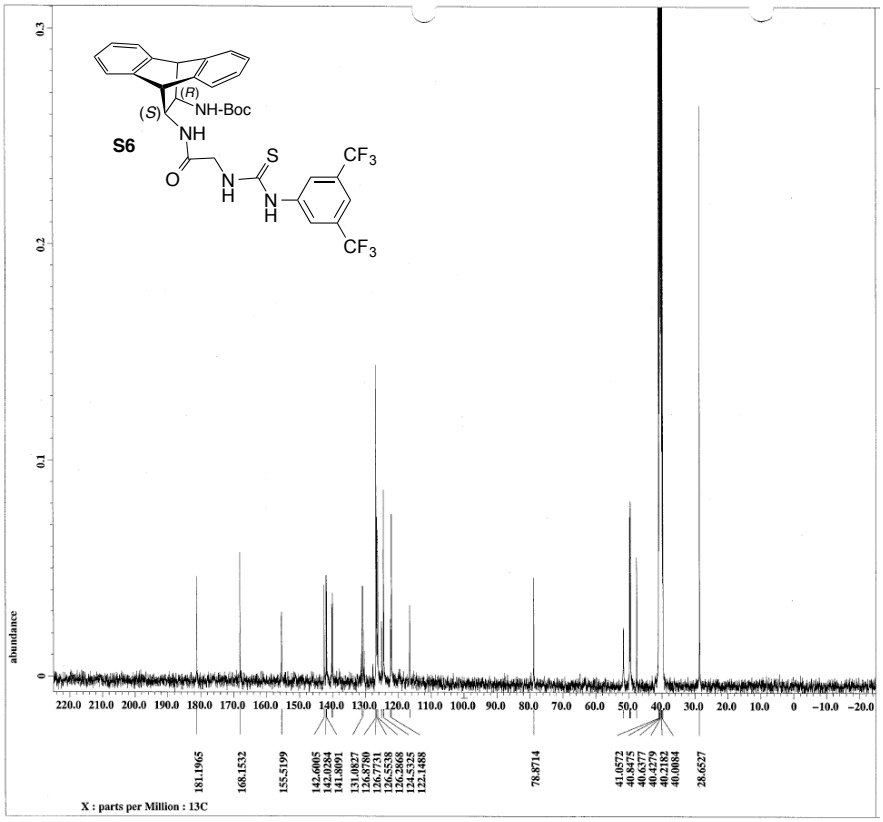
S5: ^{13}C NMR ($CDCl_3$, 75 MHz, 50 °C)



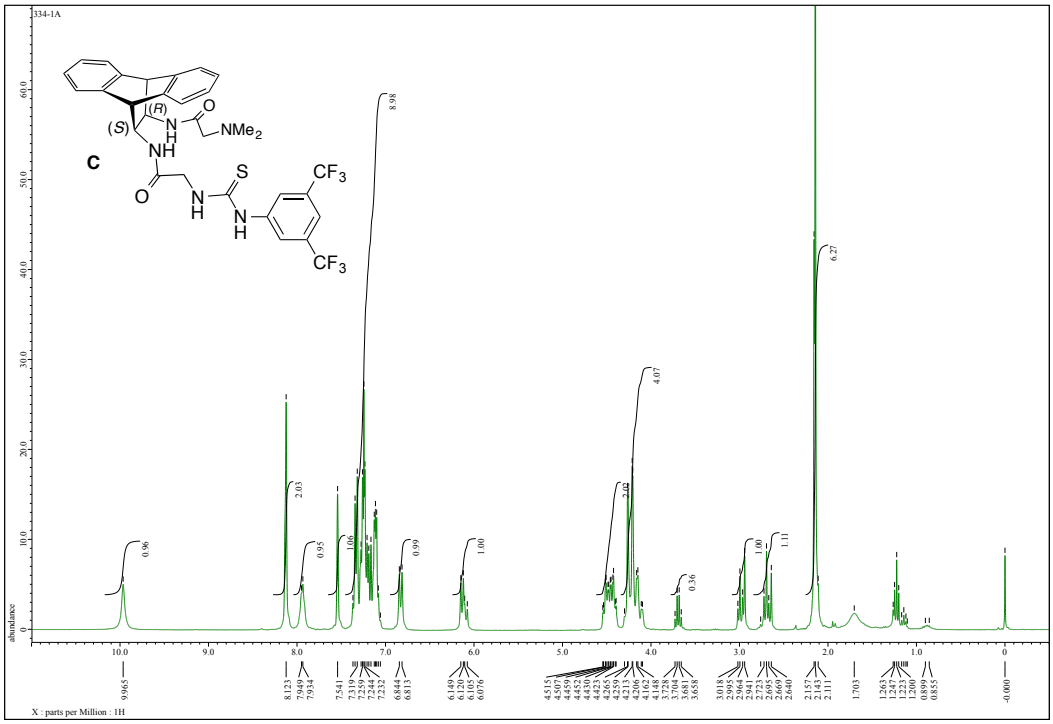
S6: ^{1}H NMR (DMSO-d$_6$, 300 MHz, 50 °C)



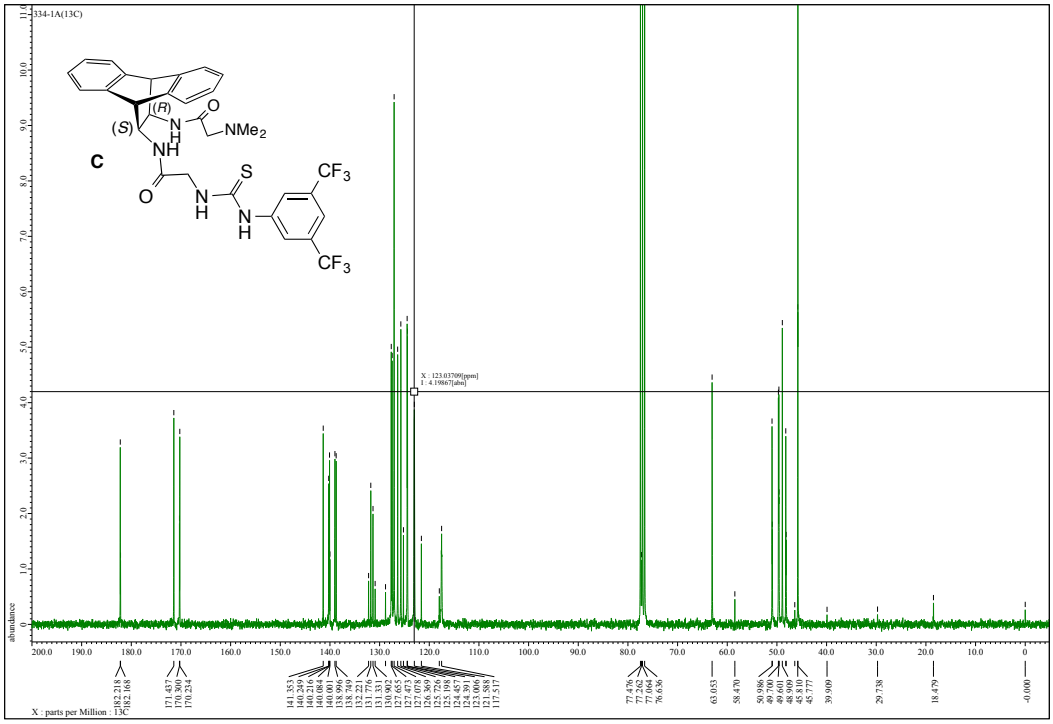
S6: ^{13}C NMR (DMSO-d$_6$, 100 MHz, 80 °C)



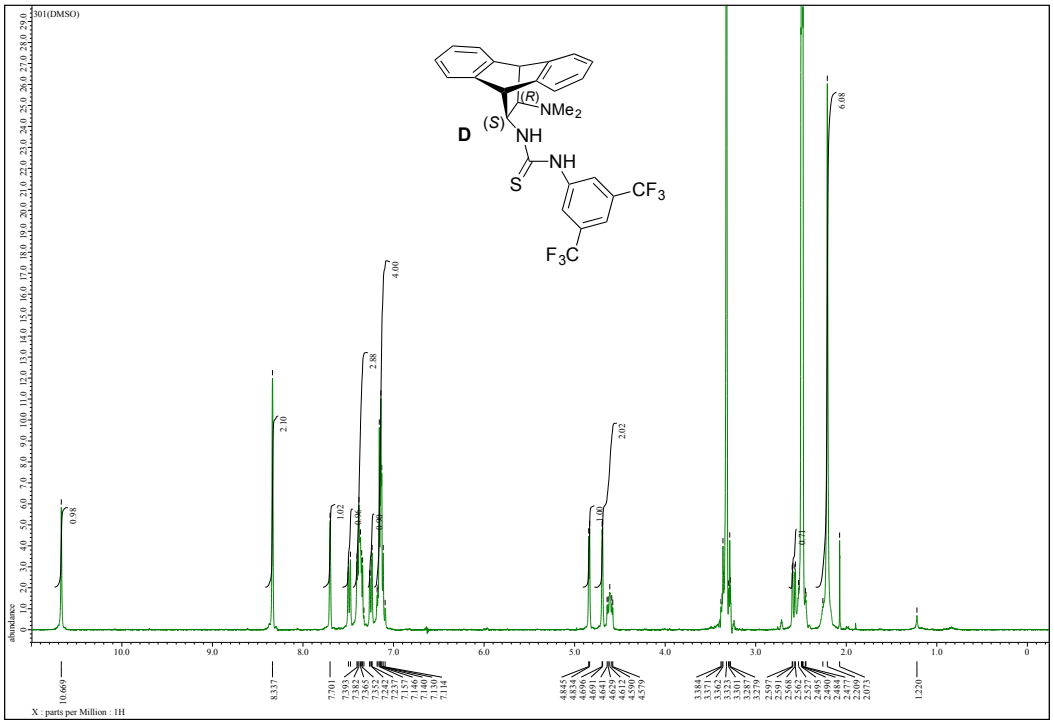
Catalyst C: ^{1}H NMR ($CDCl_3$, 300 MHz, 50 °C)



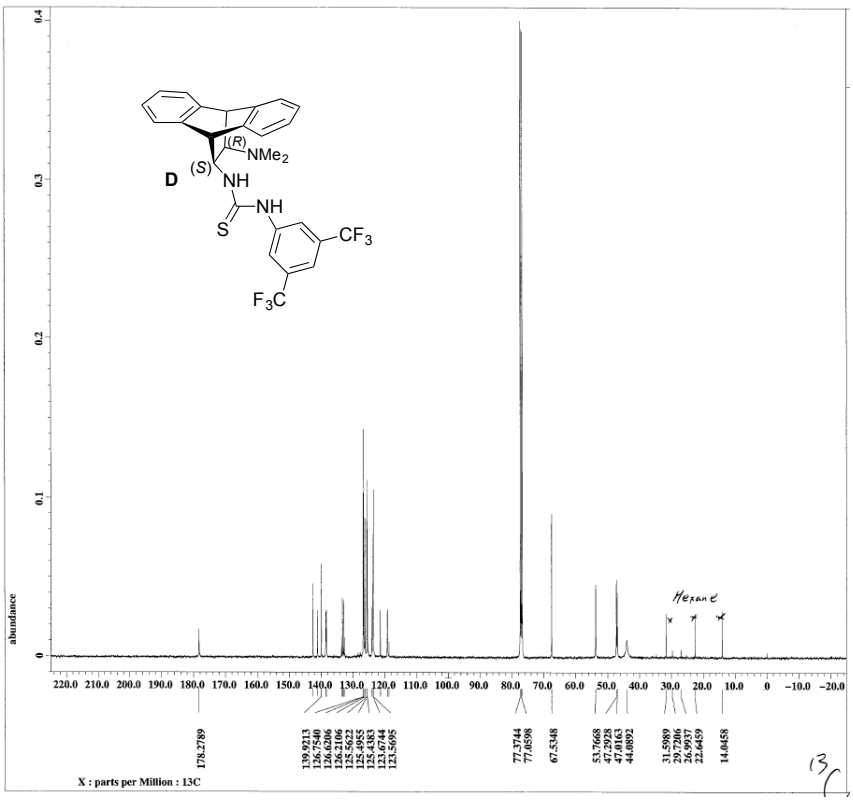
Catalyst C: ^{13}C NMR ($CDCl_3$, 75 MHz, 50 °C)



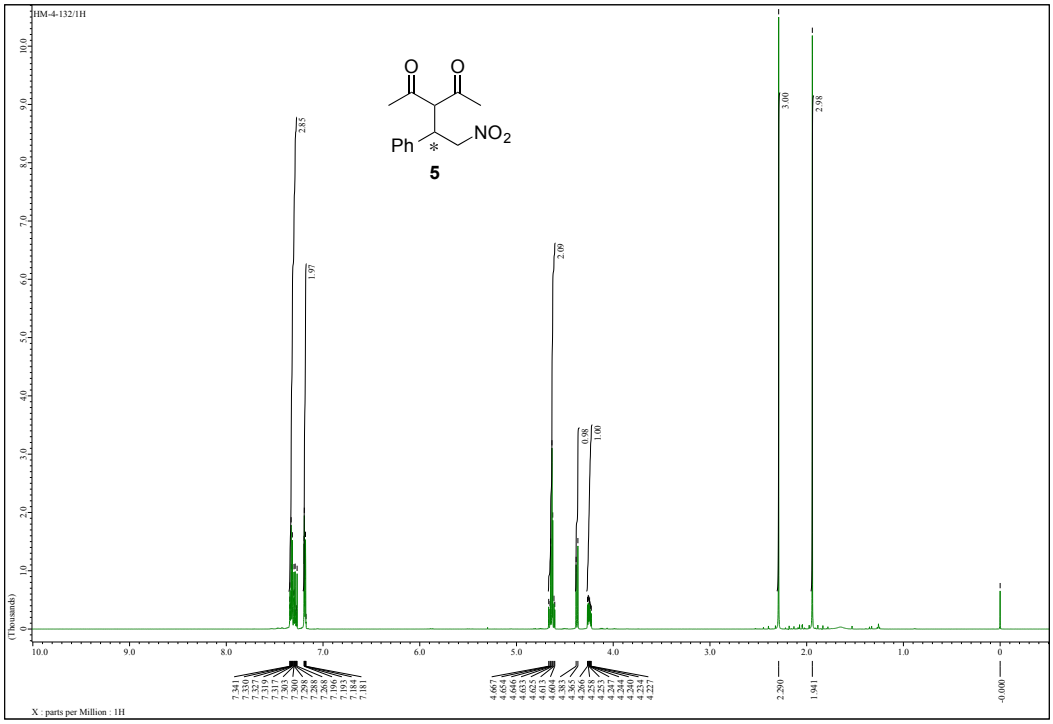
Catalyst D: ^{1}H NMR (DMSO-d_6, 300 MHz)



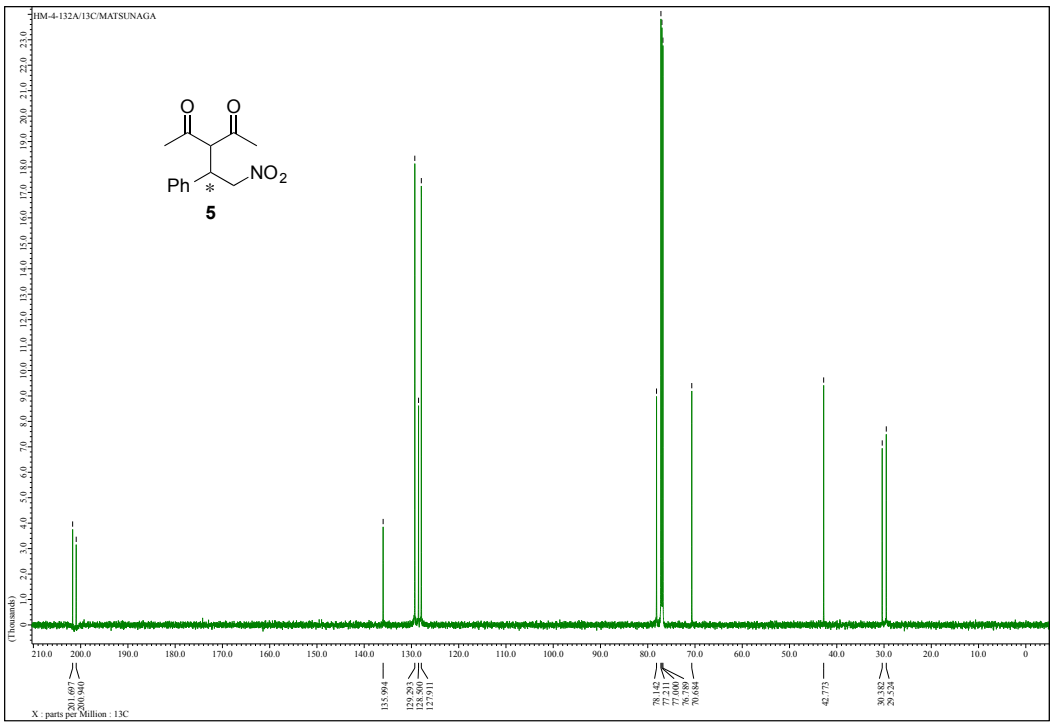
Catalyst D: ^{13}C NMR ($CDCl_3$, 100 MHz, 50 °C)



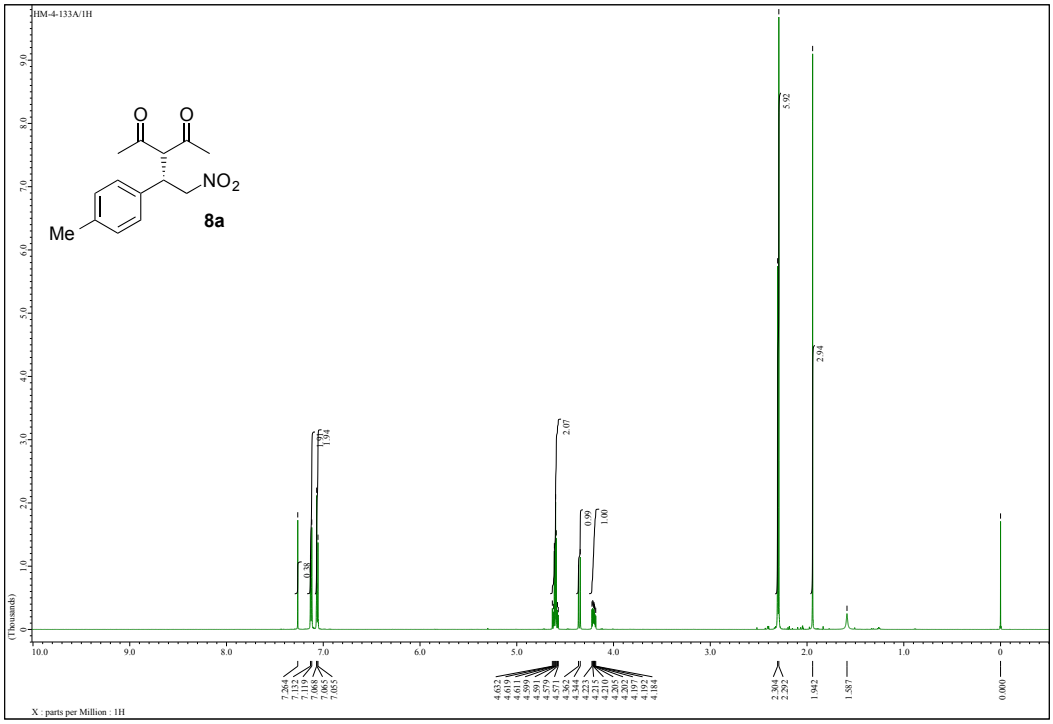
5: ^{1}H NMR (600 MHz, $CDCl_3$)



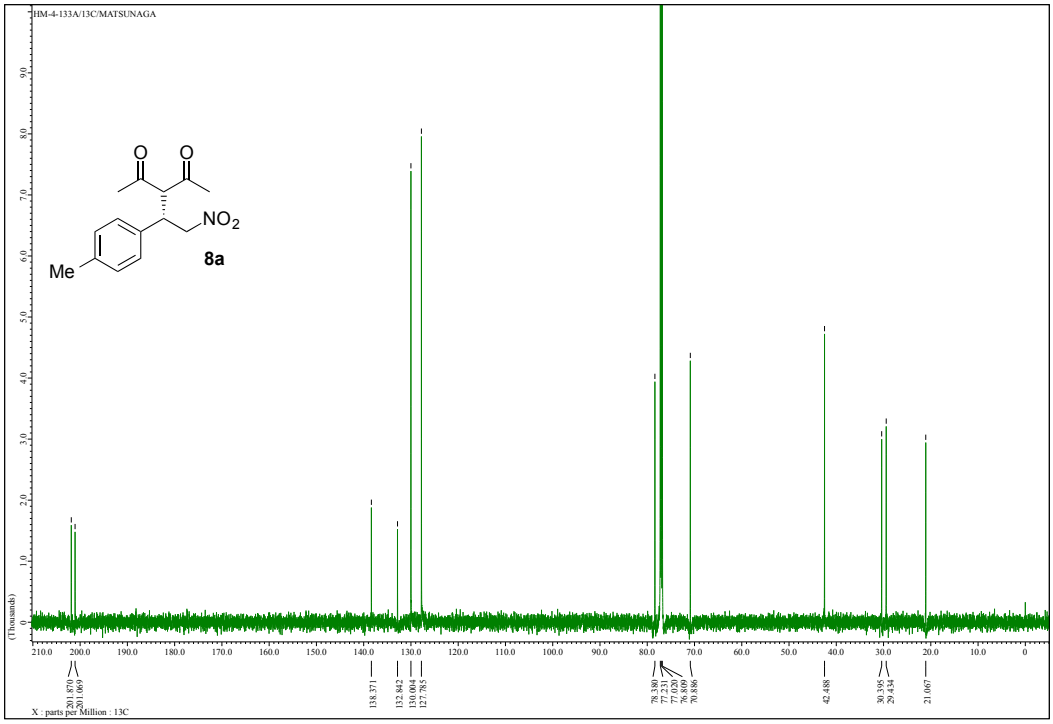
5: ^{13}C NMR (150 MHz, $CDCl_3$)



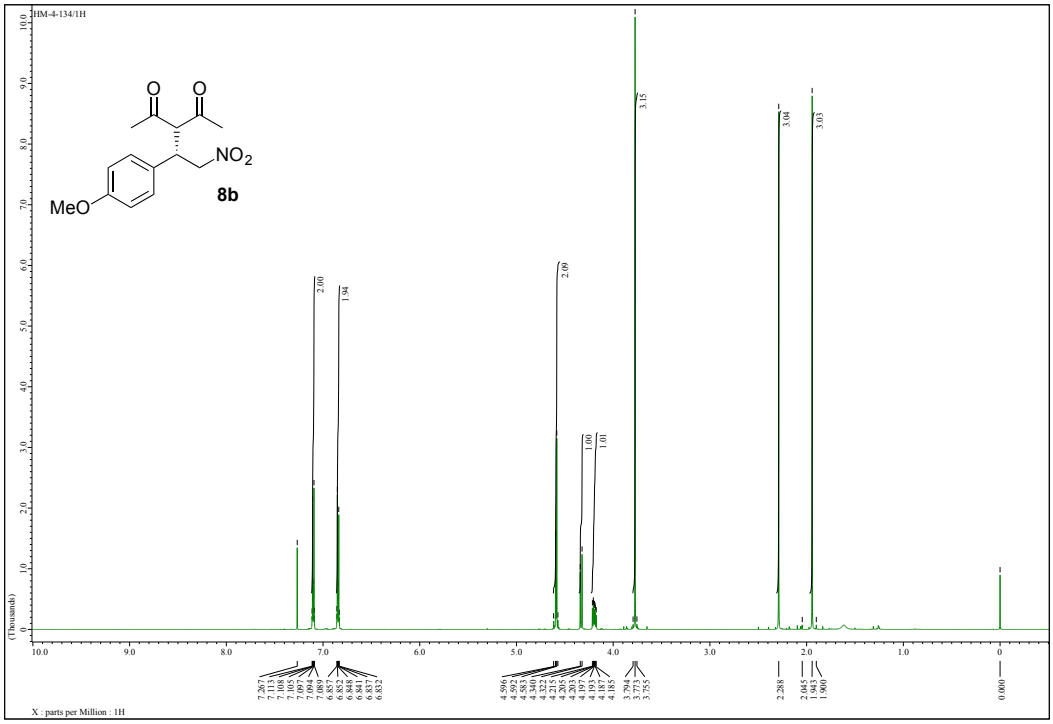
8a: ^{1}H NMR (600 MHz, $CDCl_3$)



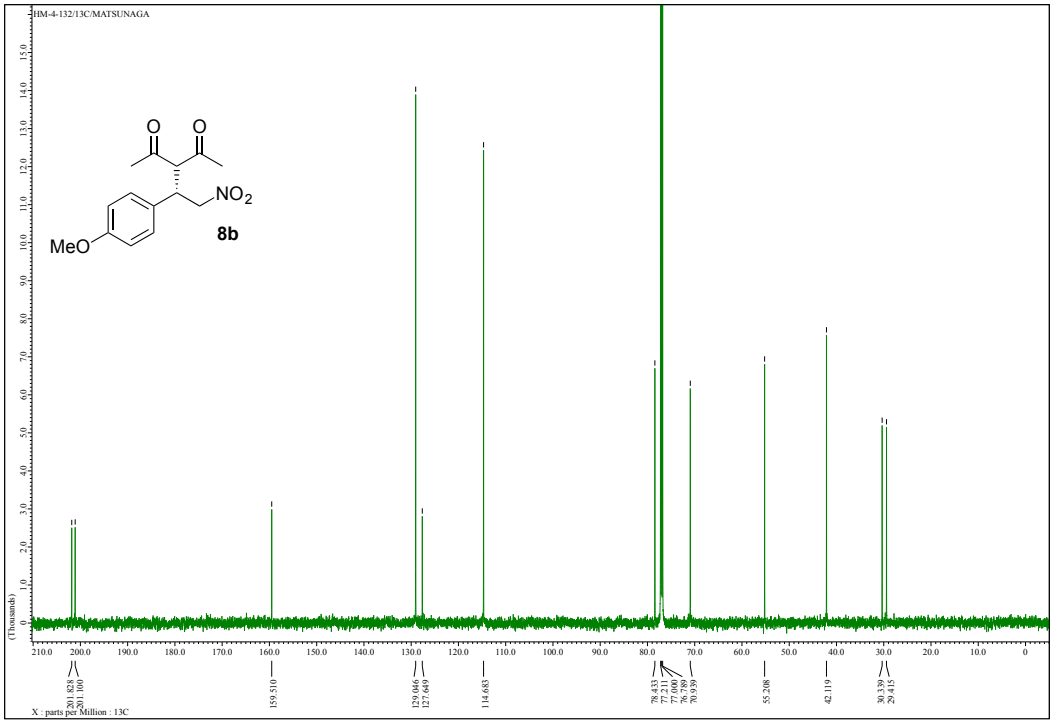
8a: ^{13}C NMR (150 MHz, $CDCl_3$)



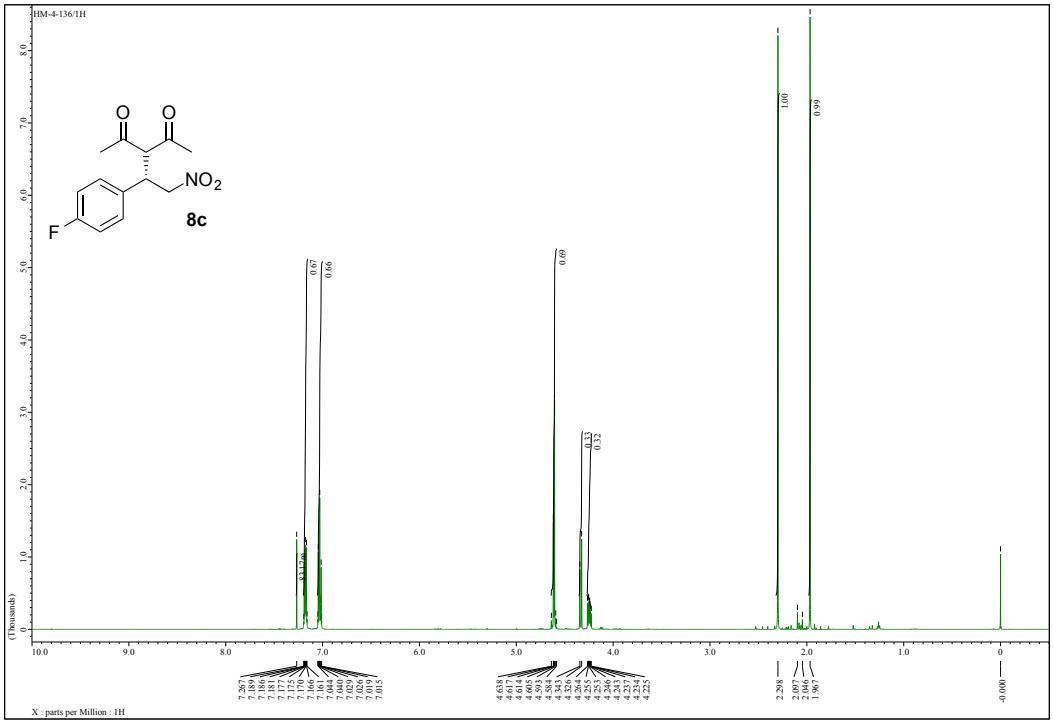
8b: ^{1}H NMR (600 MHz, $CDCl_3$)



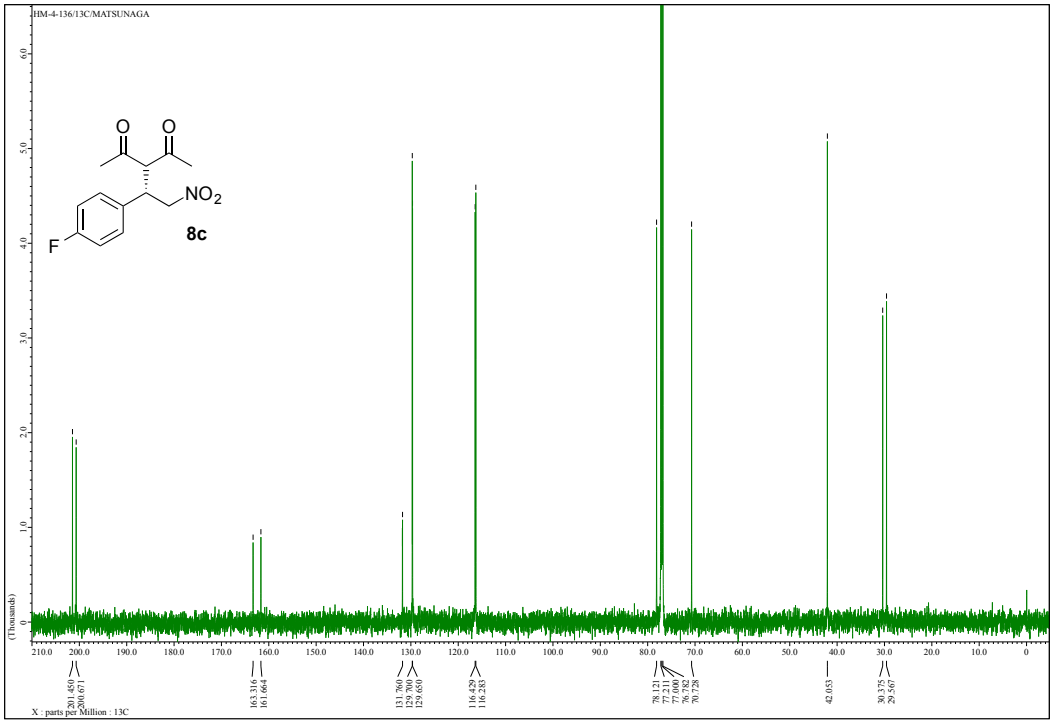
8b: ^{13}C NMR (150 MHz, $CDCl_3$)



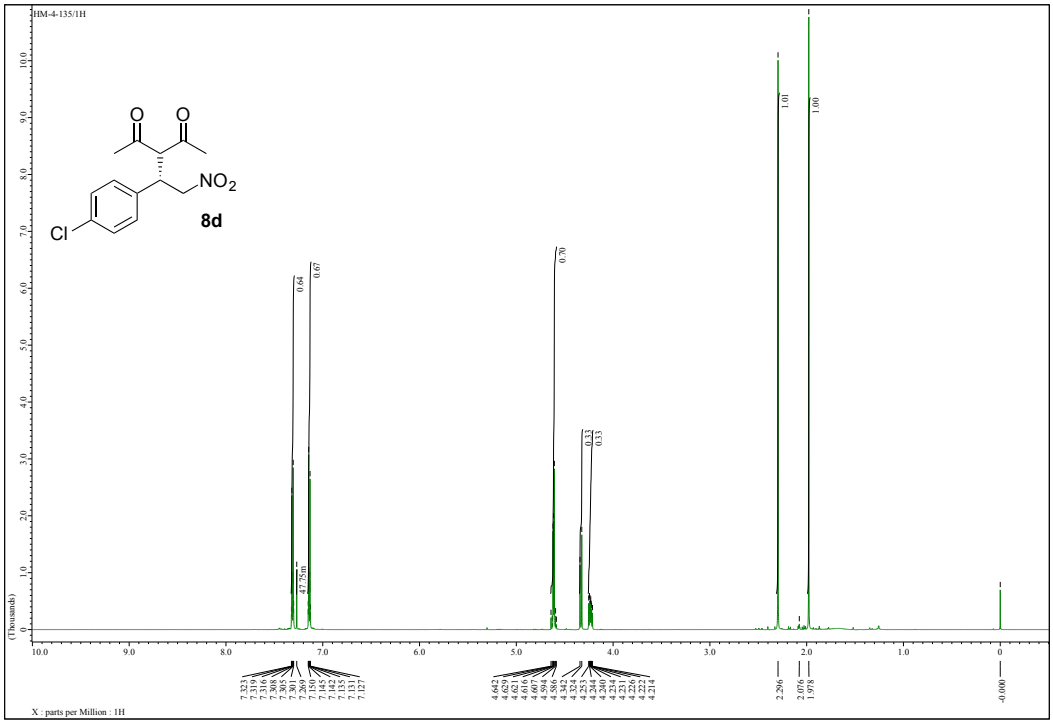
8c: ^{1}H NMR (600 MHz, $CDCl_3$)



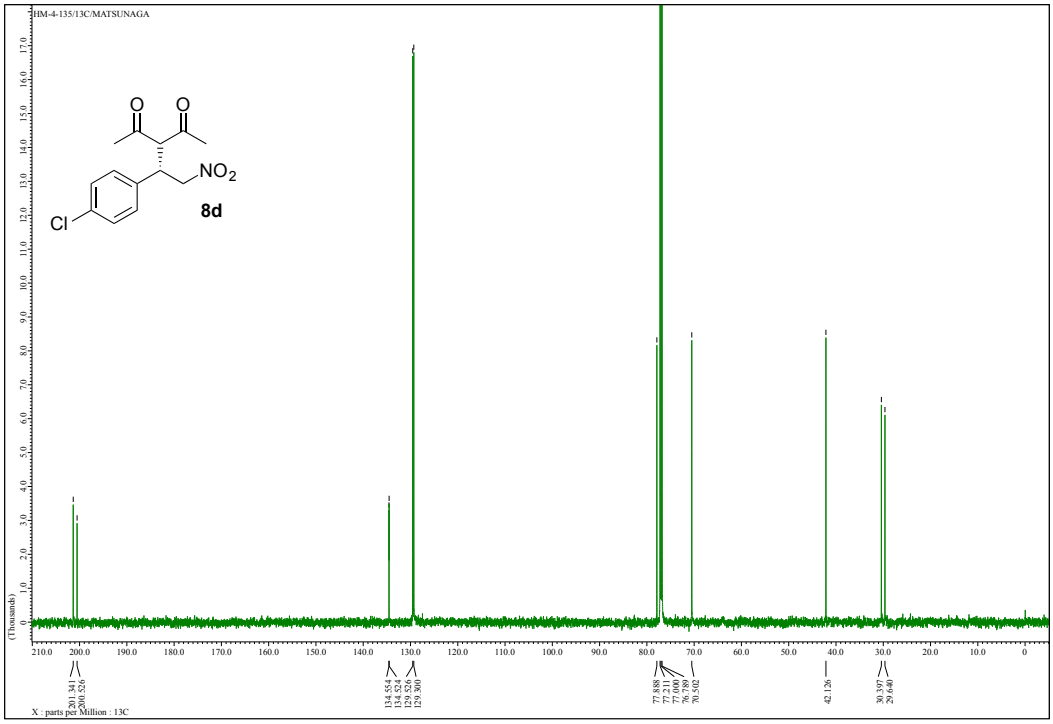
8c: ^{13}C NMR (150 MHz, $CDCl_3$)



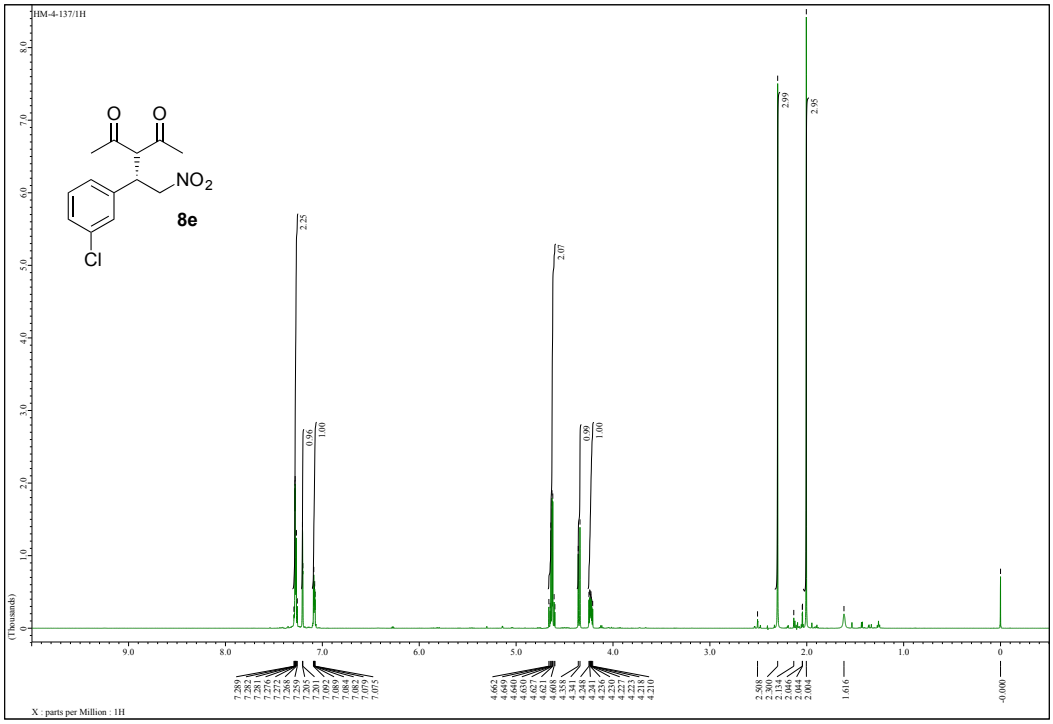
8d: ^{1}H NMR (600 MHz, $CDCl_3$)



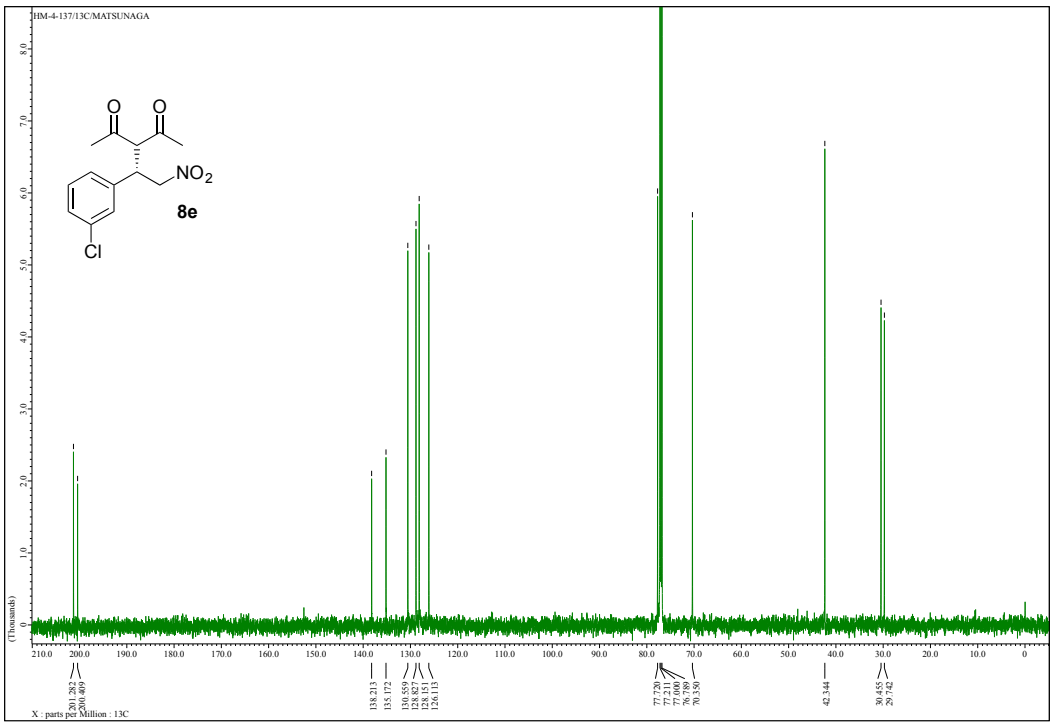
8d: ^{13}C NMR (150 MHz, $CDCl_3$)



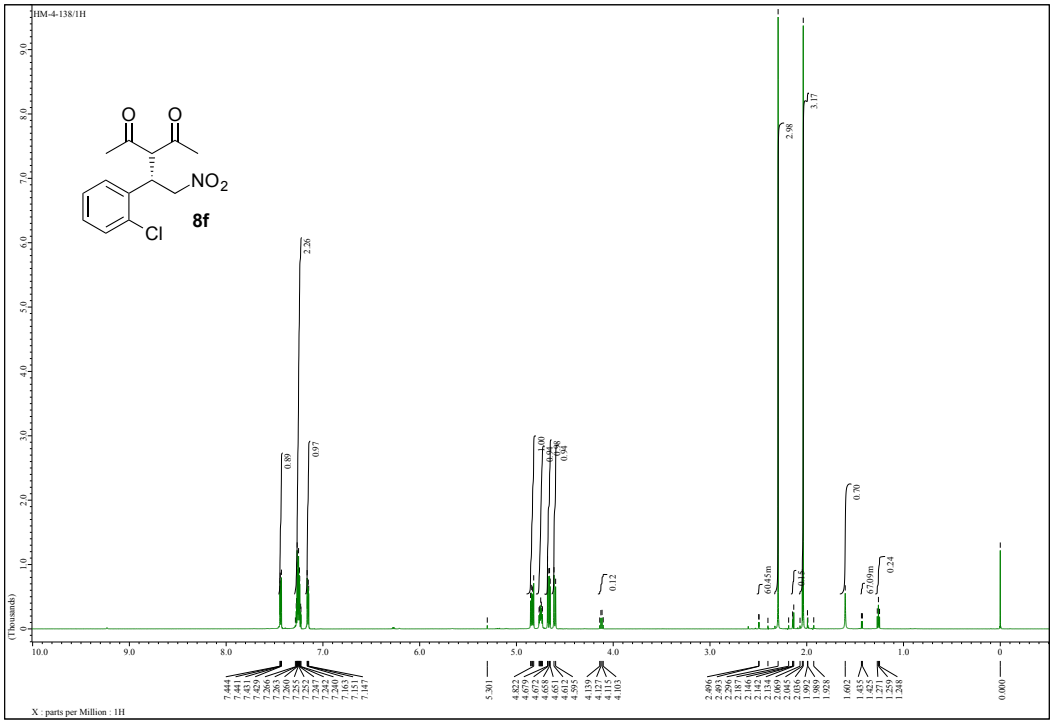
8e: ^{1}H NMR (600 MHz, $CDCl_3$)



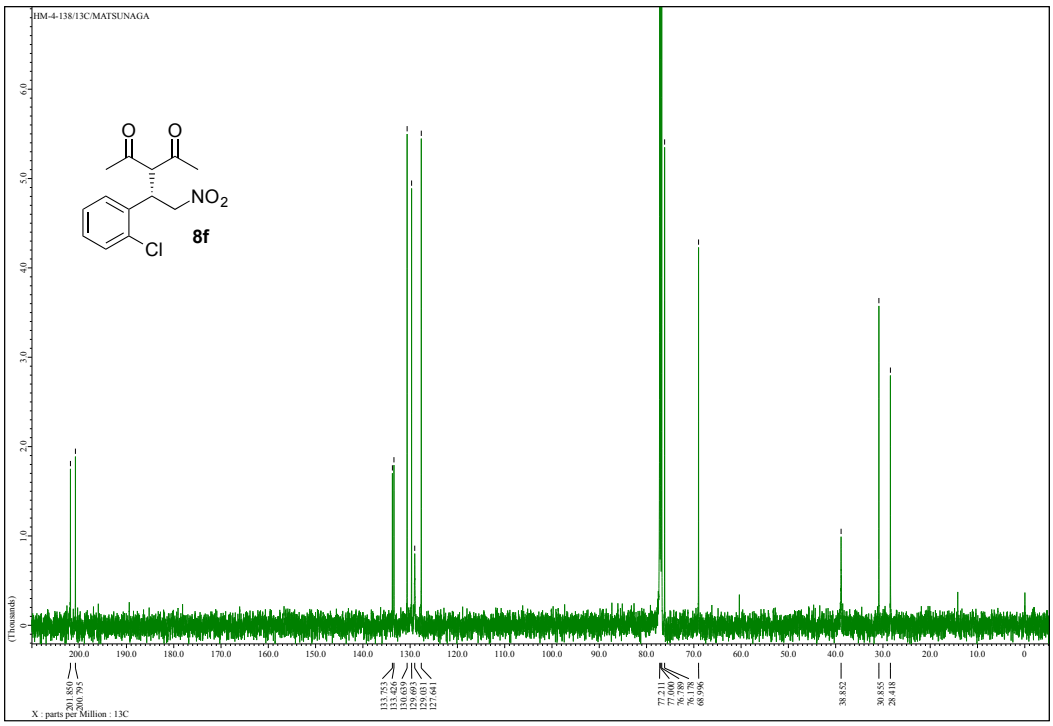
8e: ^{13}C NMR (150 MHz, $CDCl_3$)



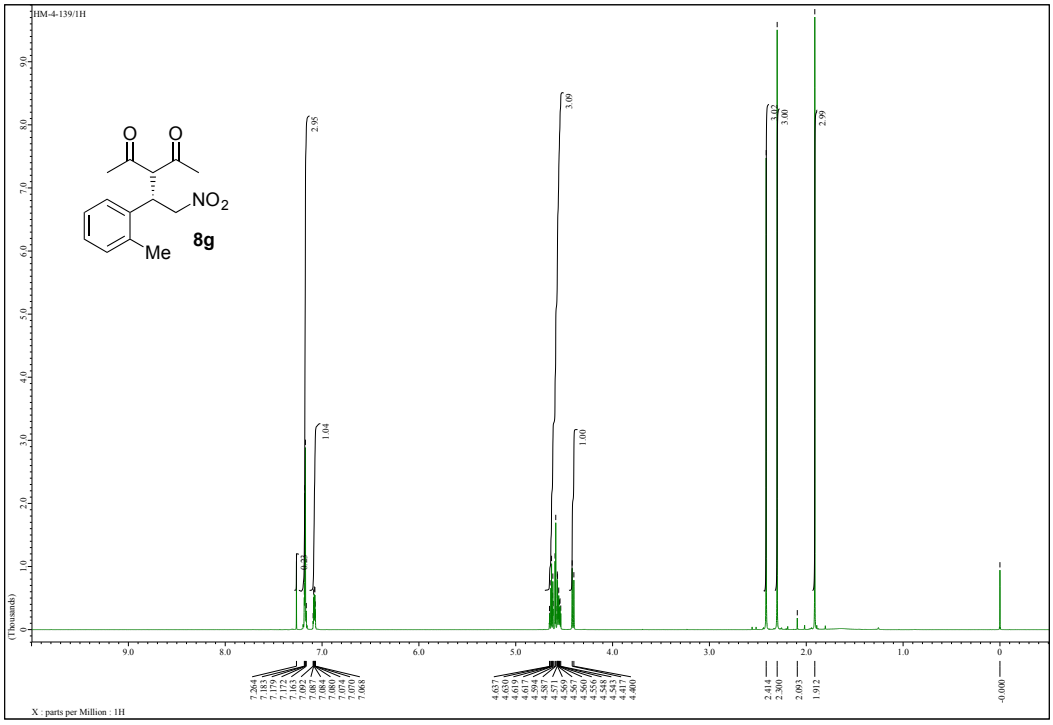
8f: ^{1}H NMR (600 MHz, $CDCl_3$)



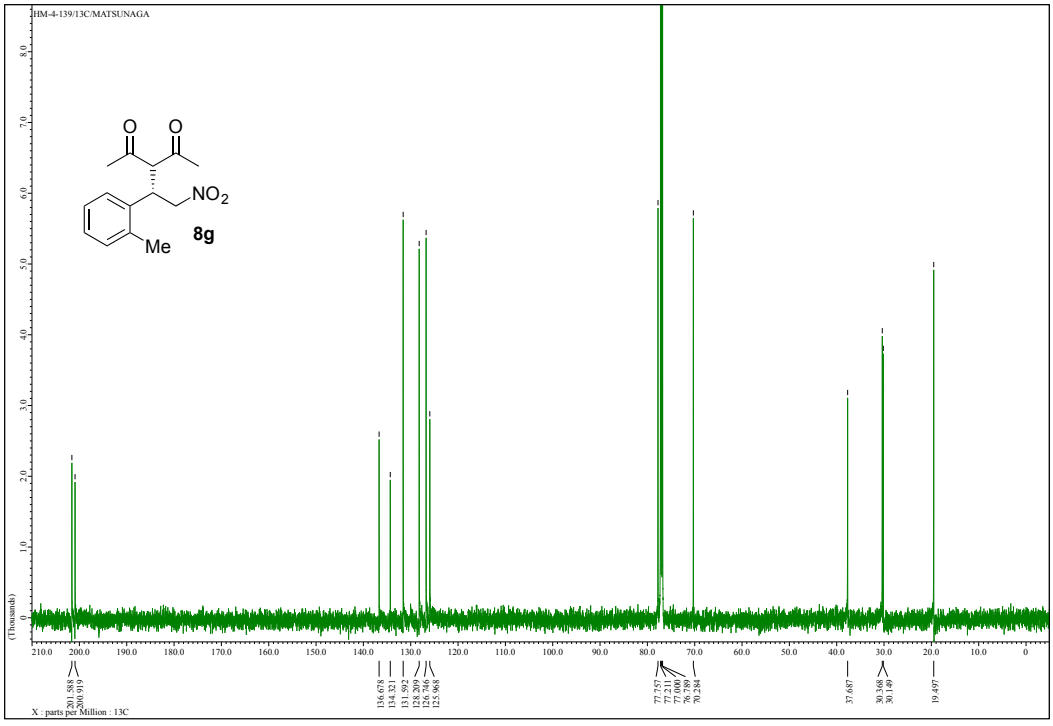
8f: ^{13}C NMR (150 MHz, $CDCl_3$)



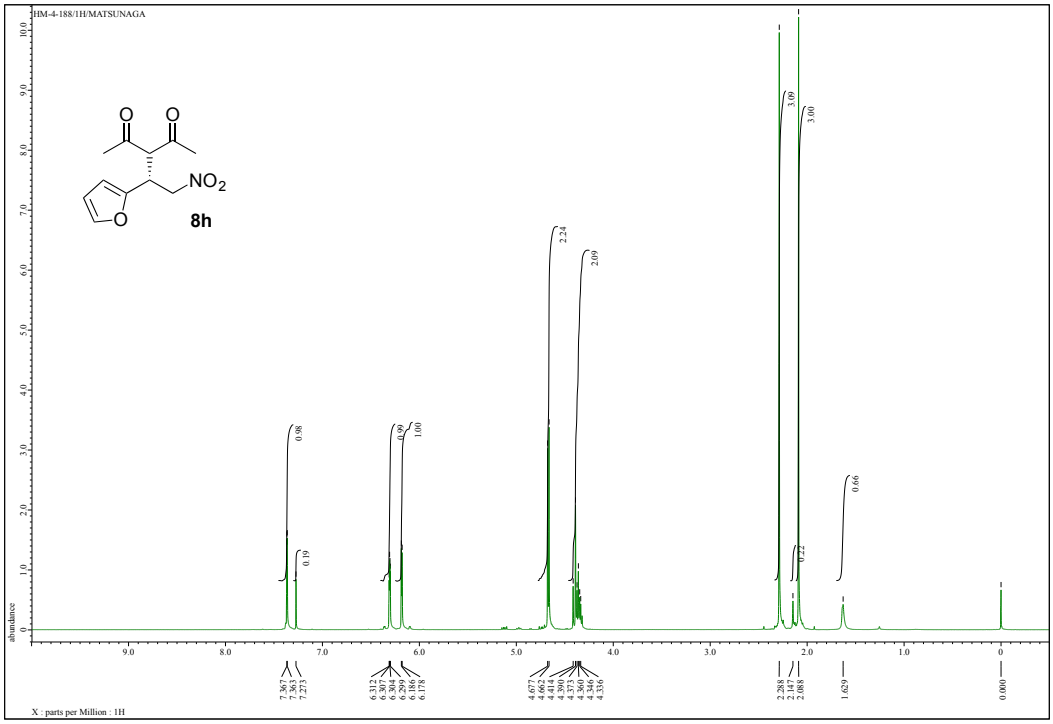
8g: ^{1}H NMR (600 MHz, $CDCl_3$)



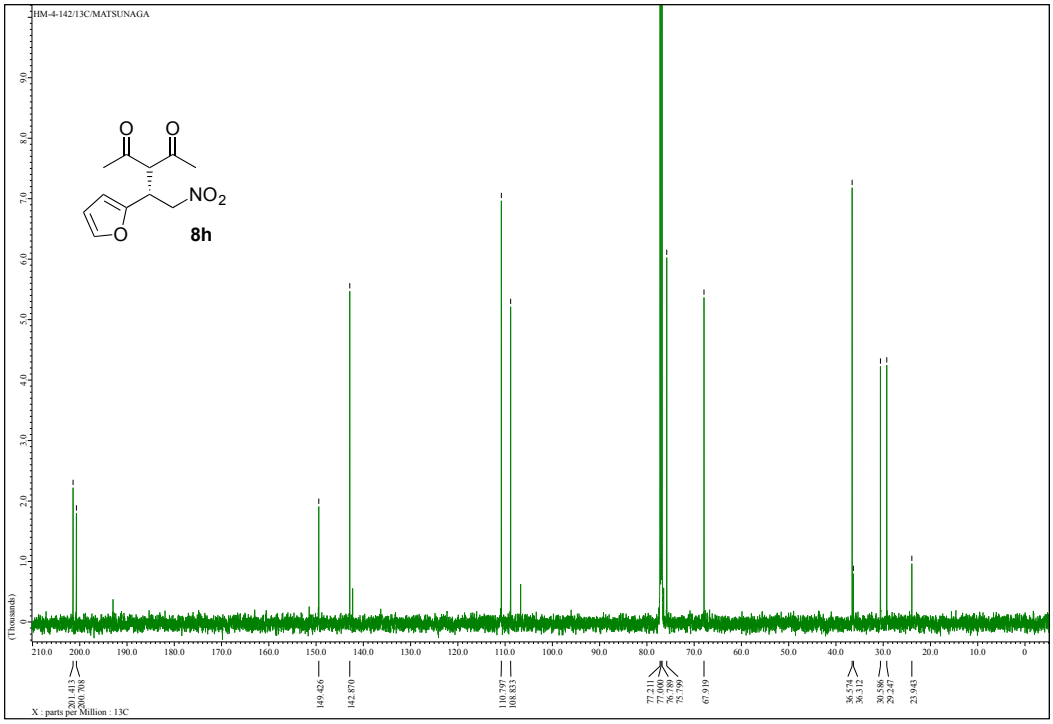
8g: ^{13}C NMR (150 MHz, $CDCl_3$)



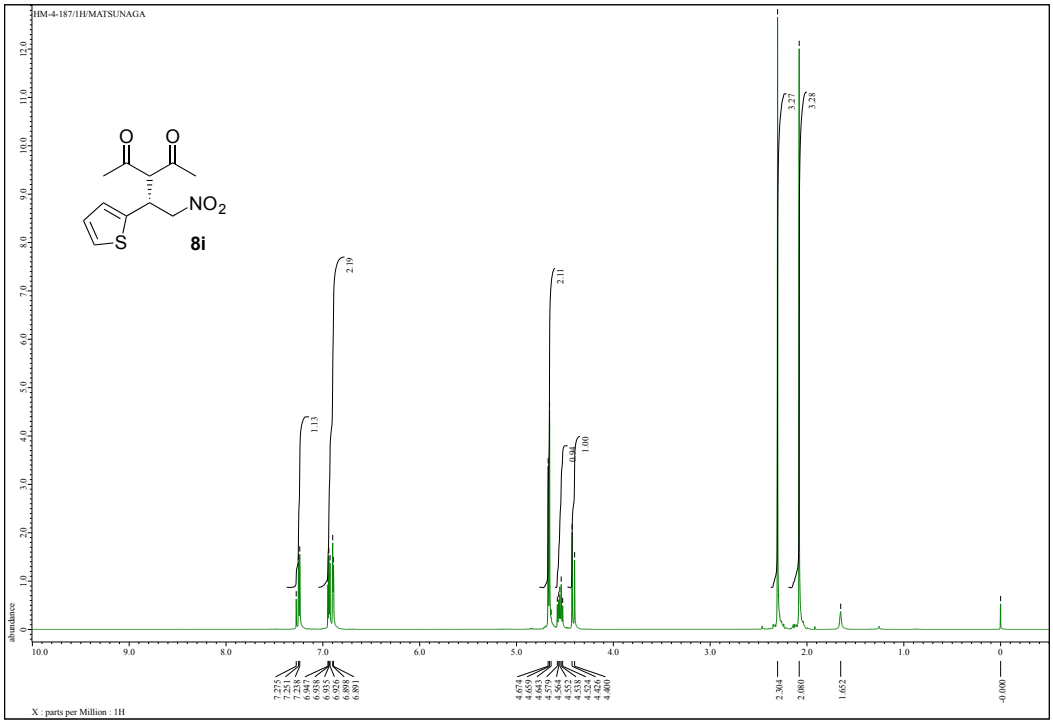
8h: ^{1}H NMR (400 MHz, $CDCl_3$)



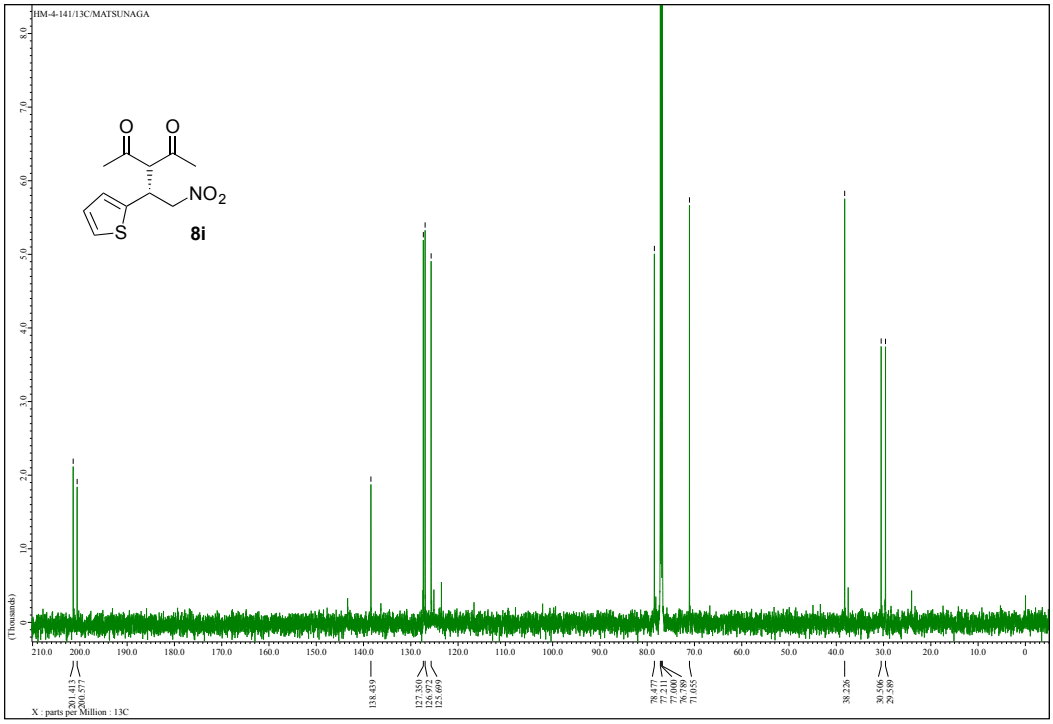
8h: ^{13}C NMR (150 MHz, $CDCl_3$)



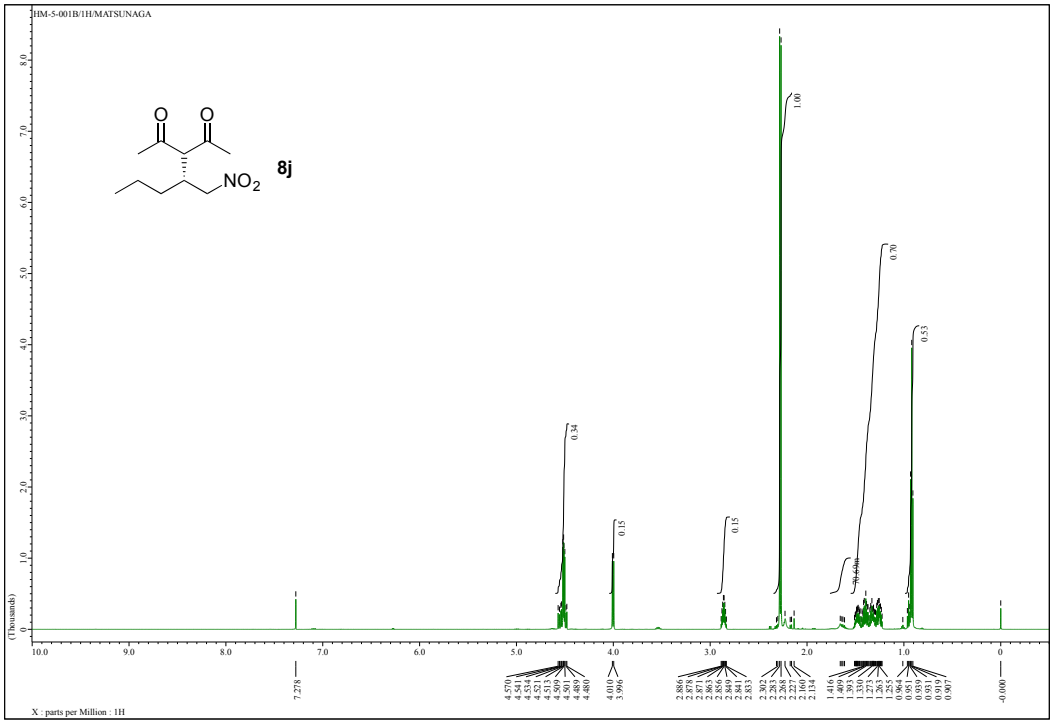
8i: ^{1}H NMR (400 MHz, $CDCl_3$)



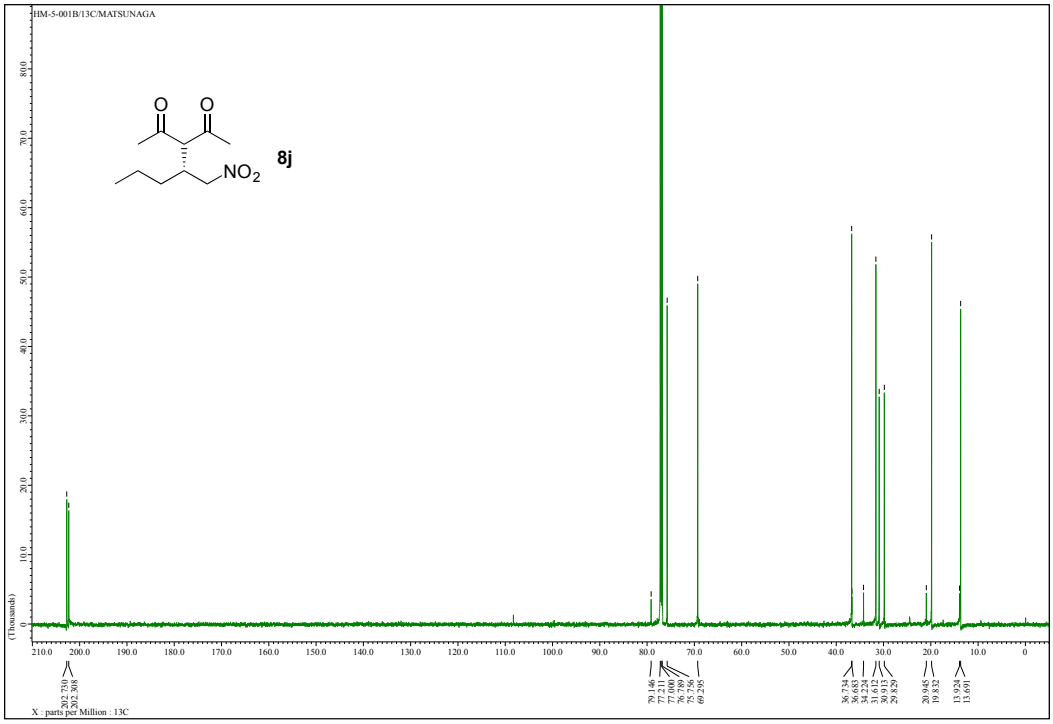
8i: ^{13}C NMR (150 MHz, $CDCl_3$)



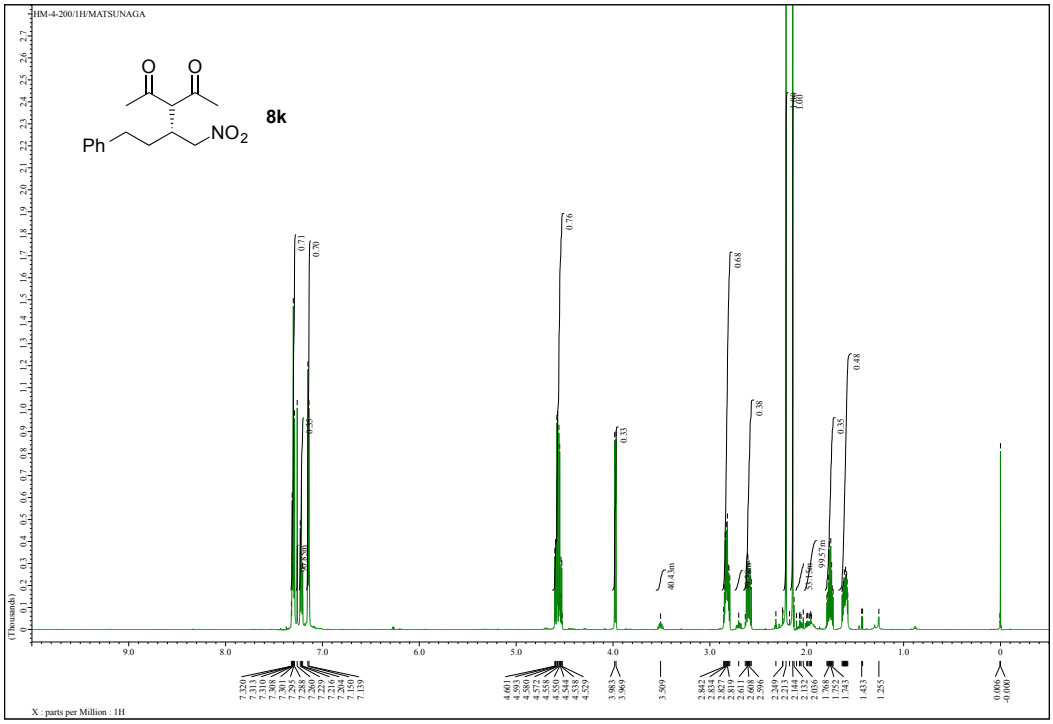
8j: ^{1}H NMR (600 MHz, $CDCl_3$)



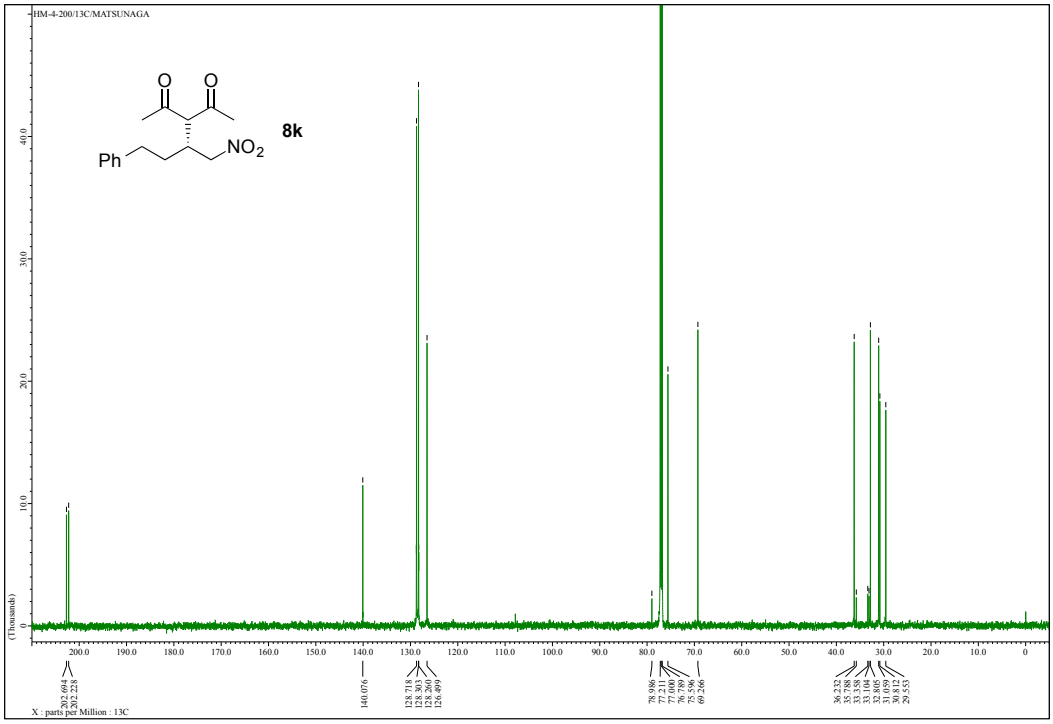
8j: ^{13}C NMR (150 MHz, $CDCl_3$)



8k: ^{1}H NMR (600 MHz, $CDCl_3$)

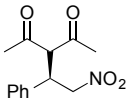


8k: ^{13}C NMR (150 MHz, $CDCl_3$)



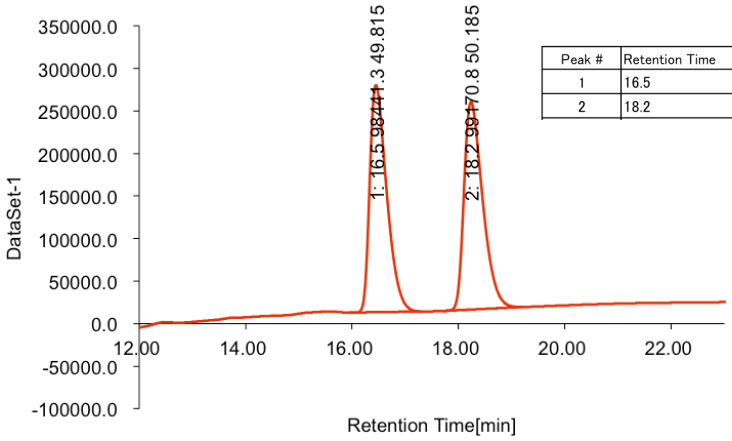
HPLC Spectrum

5: DAICEL CHIRALPAK IE (4.6 x 250 mm, hexane/2-propanol = 85/15, 1.0 mL/min, 210 nm)

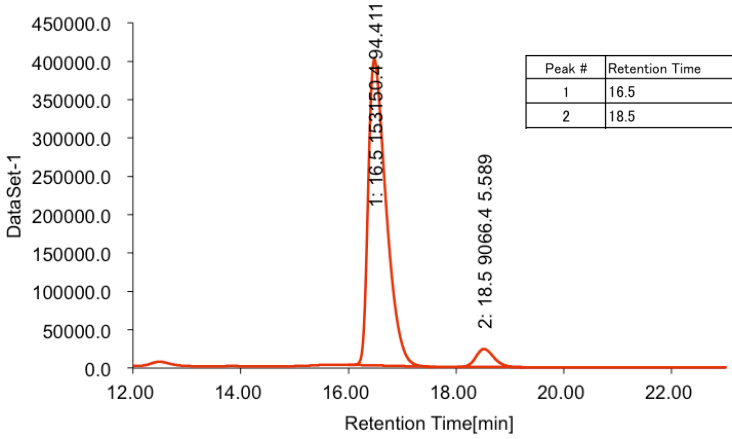


(*R*)-**5**

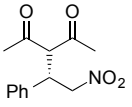
(Prepared in the presence of **A1** (10 mol%) at 25 °C for 48 h (Table 1, entry 1).



Peak #	Retention Time	Area (uV*min)	Area (%)	
1	16.5	98441.3	49.815	(R)
2	18.2	99170.8	50.185	(S)

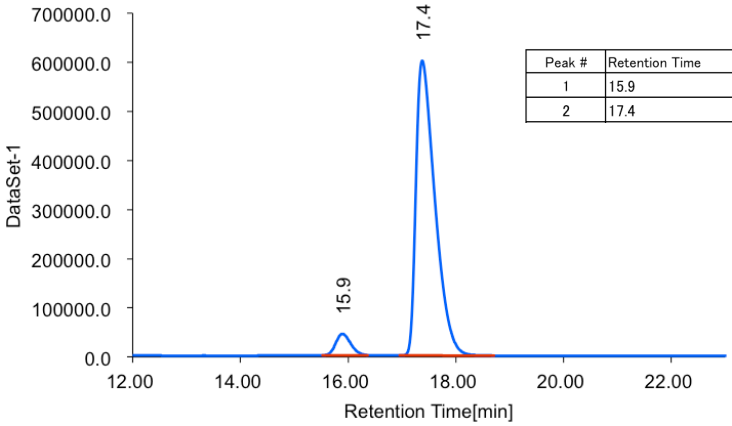


Peak #	Retention Time	Area (uV*min)	Area (%)	%ee(R)
1	16.5	153150.4	94.411	88.822
2	18.5	9066.4	5.589	

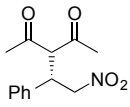


(*S*)-**5**

(Prepared in the presence of **B3** (2.5 mol%) at 25 °C for 30 min (Table 1, entry 12).

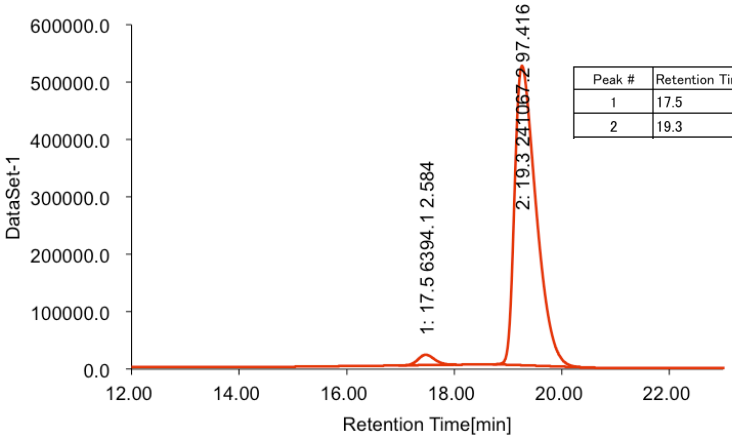


Peak #	Retention Time	Area (uV*min)	Area (%)	%ee(S)
1	15.9	13943.5	5.398	
2	17.4	244357.2	94.602	89.204



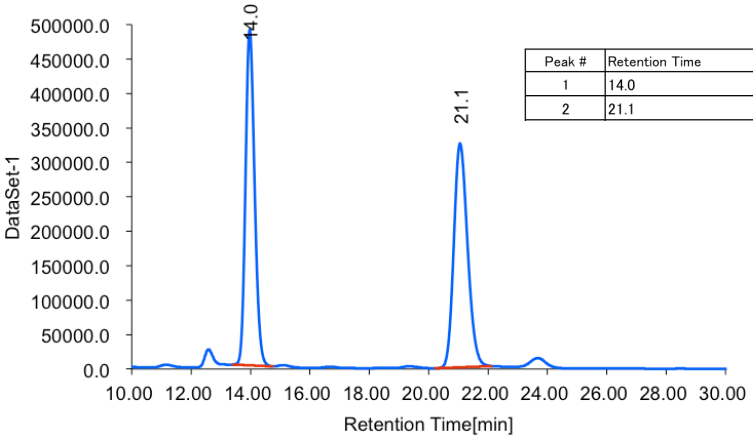
(*S*)-**5**

(Prepared in the presence of **B3** (0.5 mol%) at -30 °C for 24 h (Table 1, entry 22; Table 2, entry 1).

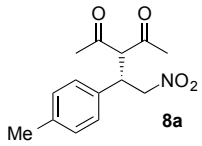


Peak #	Retention Time	Area (uV*min)	Area (%)	%ee (S)
1	17.5	6394.1	2.584	
2	19.3	241067.2	97.416	94.832

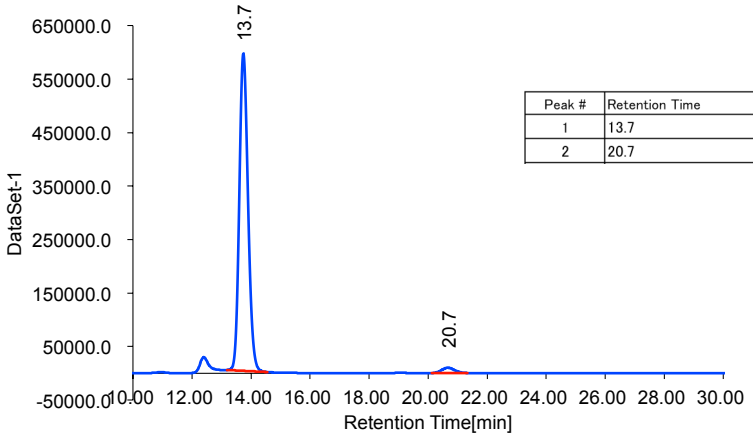
8a: DAICEL CHIRALPAK IC (4.6 x 250 mm, hexane/2-propanol = 85/15, 1.0 mL/min, 210 nm)



Peak #	Retention Time	Area (uV*min)	Area (%)	
1	14.0	172602.4	49.729	(S)
2	21.1	174481.1	50.271	(R)

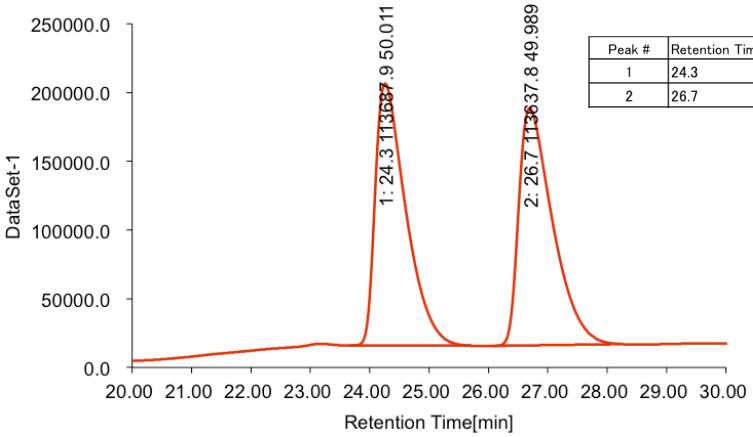


8a

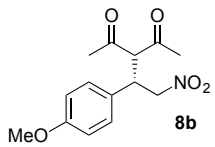


Peak #	Retention Time	Area (uV*min)	Area (%)	%ee (S)
1	13.7	202793.3	97.624	95.248
2	20.7	4935.5	2.376	

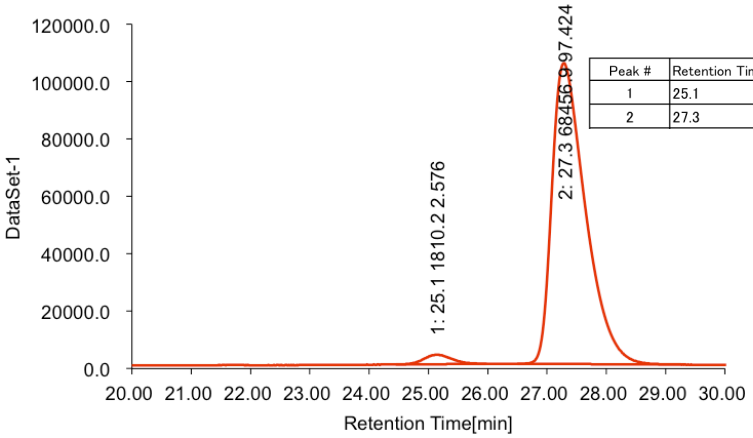
8b: DAICEL CHIRALPAK IE (4.6 x 250 mm, hexane/2-propanol = 85/15, 1.0 mL/min, 210 nm)



Peak #	Retention Time	Area (uV*min)	Area (%)	
1	24.3	113687.9	50.011	(R)
2	26.7	113637.8	49.989	(S)

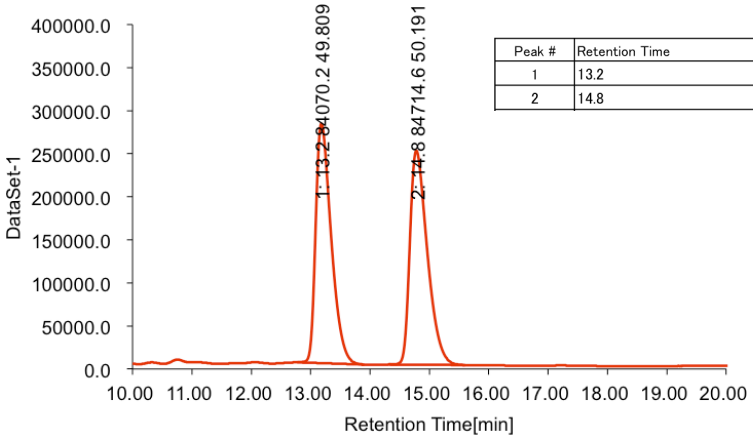


8b

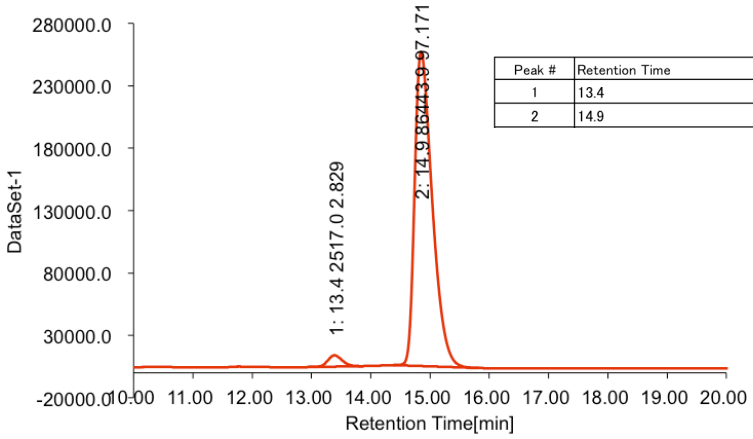


Peak #	Retention Time	Area (uV*min)	Area (%)	%ee (S)
1	25.1	1810.2	2.576	
2	27.3	68456.9	97.424	94.848

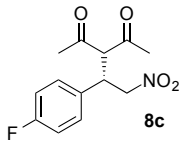
8c: DAICEL CHIRALPAK IE (4.6 x 250 mm, hexane/2-propanol = 85/15, 1.0 mL/min, 210 nm)



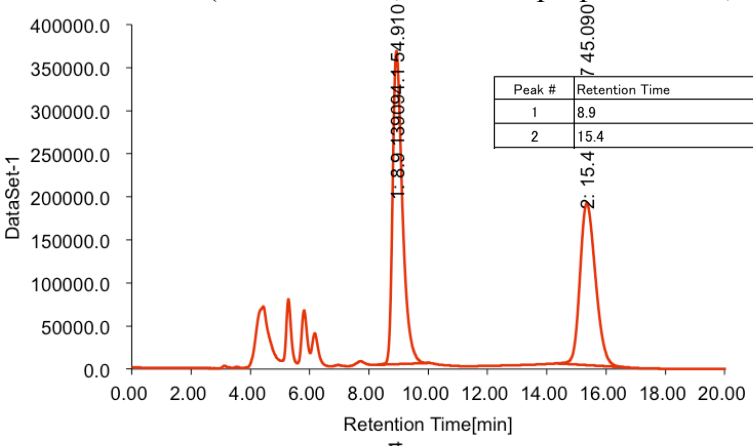
Peak #	Retention Time	Area (uV*min)	Area (%)	
1	13.2	84070.2	49.809	(R)
2	14.8	84714.6	50.191	(S)



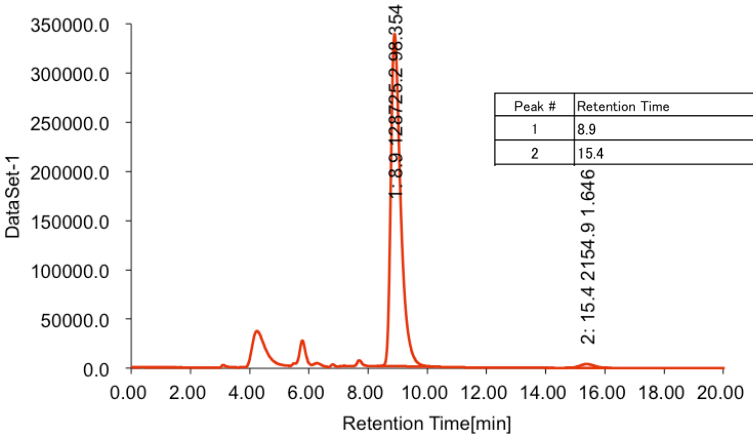
Peak #	Retention Time	Area (uV*min)	Area (%)	%ee (S)
1	13.4	2517.0	2.829	
2	14.9	86443.9	97.171	94.342



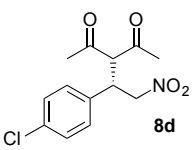
8d: DAICEL CHIRALPAK AS-H (4.6 x 250 mm, hexane/2-propanol = 7/3, 1.0 mL/min, 210 nm)



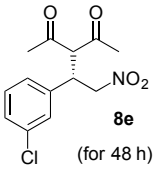
Peak #	Retention Time	Area (uV*min)	Area (%)	
1	8.9	139094.1	54.910	(S)
2	15.4	114220.7	45.090	(R)



Peak #	Retention Time	Area (uV*min)	Area (%)	%ee (S)
1	8.9	128725.2	98.354	96.708
2	15.4	2154.9	1.646	

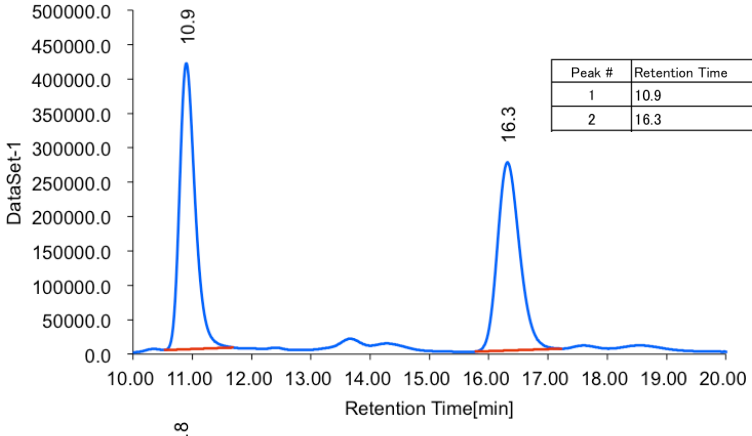


8e: DAICEL CHIRALPAK IC (4.6 x 250 mm, hexane/2-propanol = 85/15, 1.0 mL/min, 210 nm)

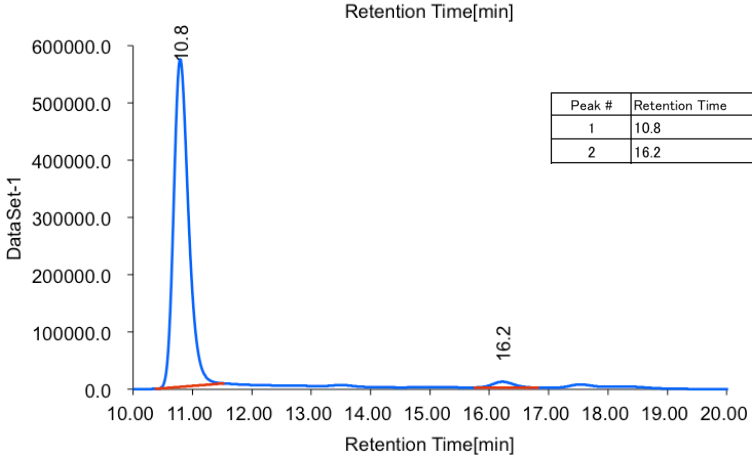


8e

(for 48 h)

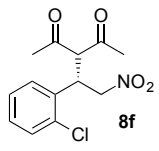


Peak #	Retention Time	Area (uV*min)	Area (%)	
1	10.9	126900.4	51.566	(S)
2	16.3	119191.2	48.434	(R)

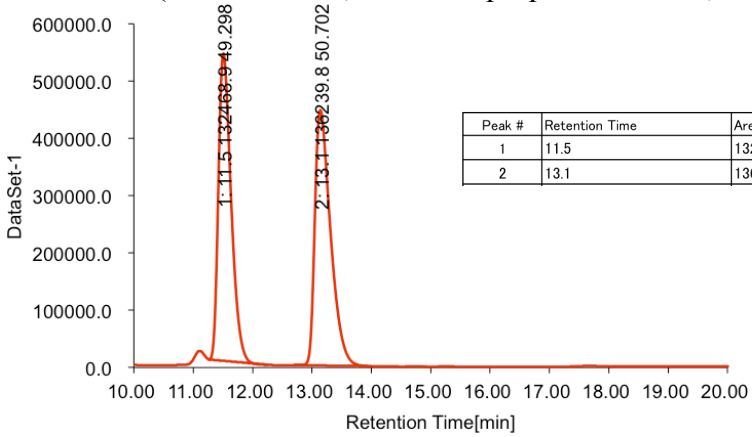


Peak #	Retention Time	Area (uV*min)	Area (%)	%ee (S)
1	10.8	166247.5	97.513	95.026
2	16.2	4239.3	2.487	

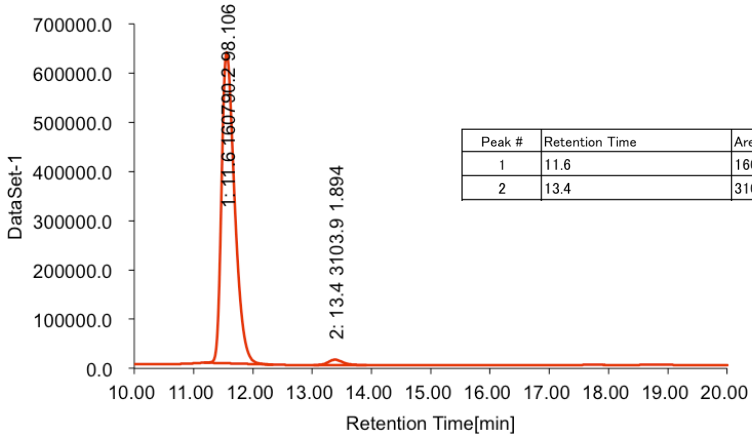
8f: DAICEL CHIRALPAK IE (4.6 x 250 mm, hexane/2-propanol = 85/15, 1.0 mL/min, 210 nm)



8f

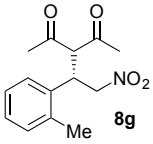


Peak #	Retention Time	Area (uV*min)	Area (%)	
1	11.5	132468.9	49.298	(S)
2	13.1	136239.8	50.702	(R)

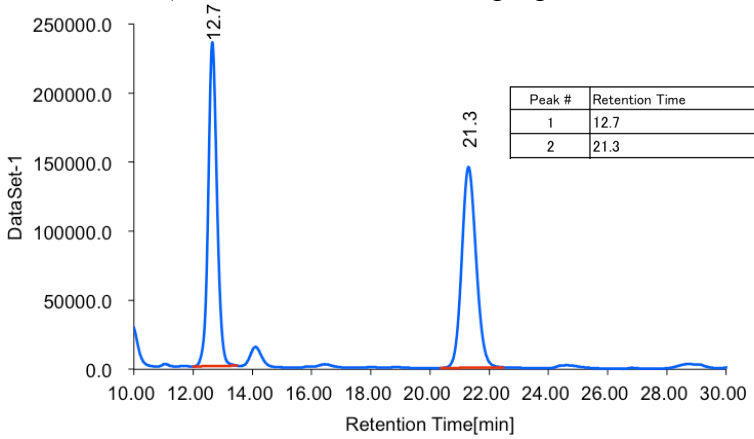


Peak #	Retention Time	Area (uV*min)	Area (%)	%ee (S)
1	11.6	160790.2	98.106	96.212
2	13.4	3103.9	1.894	

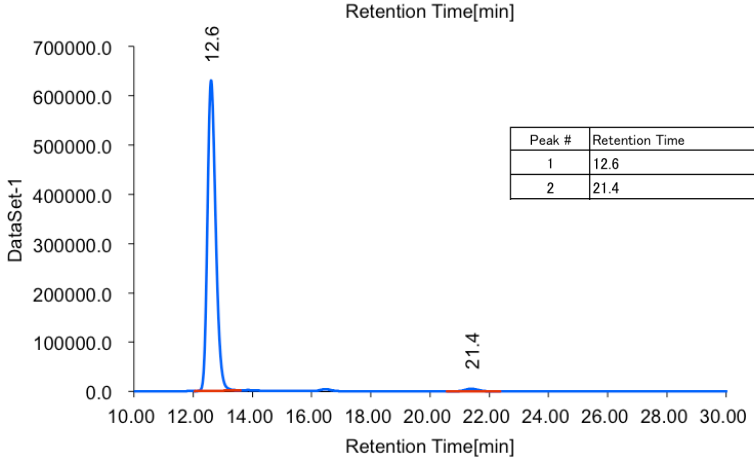
8g: DAICEL CHIRALPAK IC (4.6 x 250 mm, hexane/2-propanol = 85/15, 1.0 mL/min, 210 nm)



8g

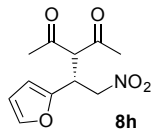


Peak #	Retention Time	Area (uV*min)	Area (%)	
1	12.7	80541.5	49.590	(S)
2	21.3	81872.9	50.410	(R)

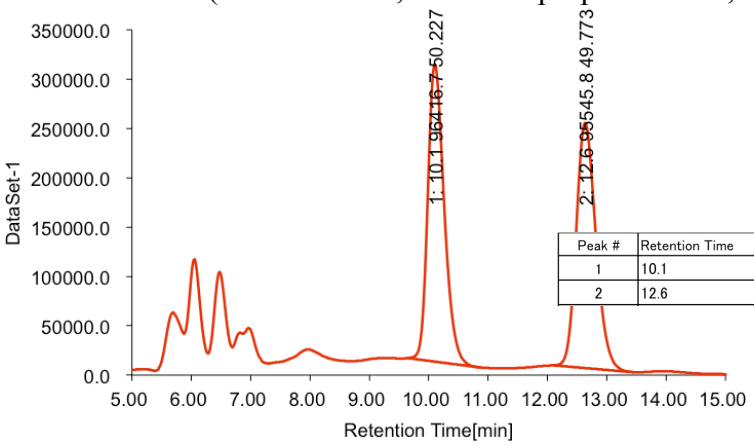


Peak #	Retention Time	Area (uV*min)	Area (%)	%ee (S)
1	12.6	203910.7	98.643	97.286
2	21.4	2806	1.357	

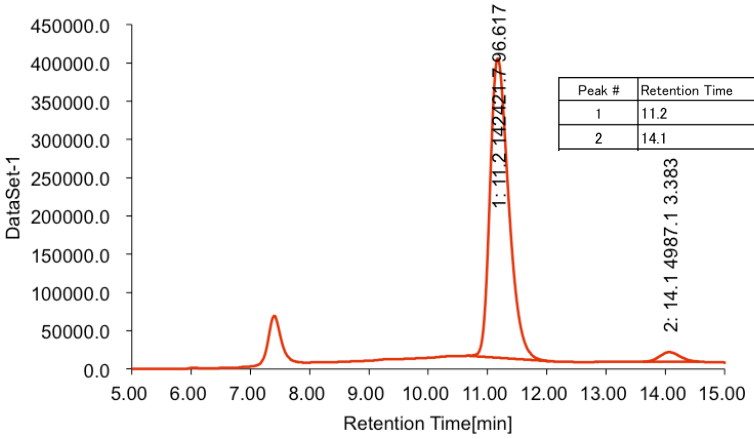
8h: DAICEL CHIRALPAK AS-H (4.6 x 250 mm, hexane/2-propanol = 7/3, 1.0 mL/min, 210 nm)



8h

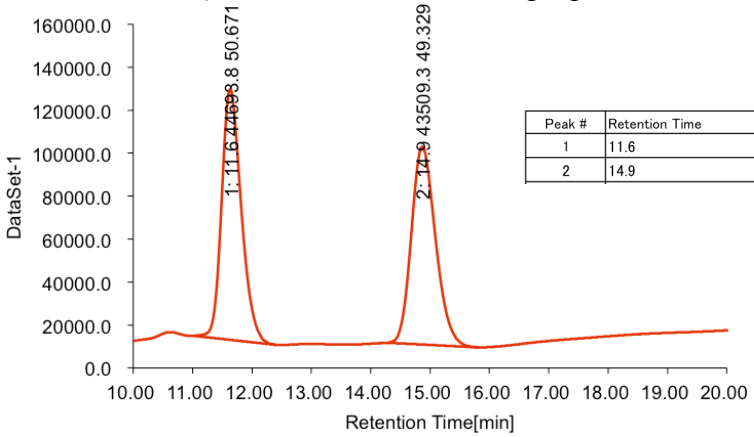


Peak #	Retention Time	Area (uV*min)	Area (%)	
1	10.1	96416.7	50.227	(S)
2	12.6	95545.8	49.773	(R)

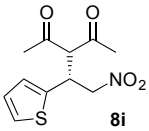


Peak #	Retention Time	Area (uV*min)	Area (%)	%ee (S)
1	11.2	142421.7	96.617	93.234
2	14.1	4987.1	3.383	

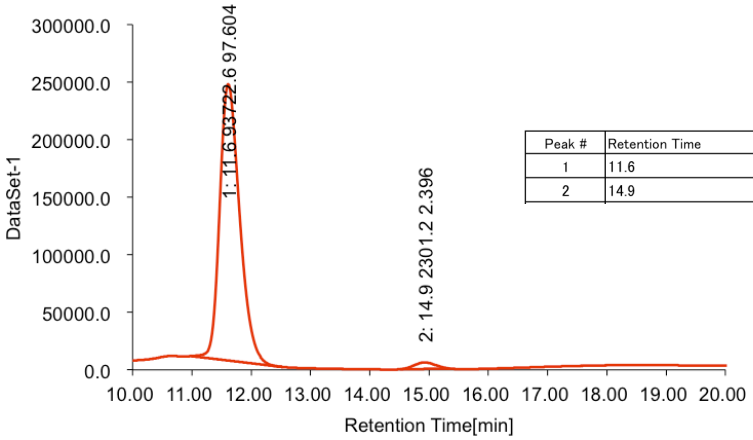
8i: DAICEL CHIRALPAK AS-H (4.6 x 250 mm, hexane/2-propanol = 7/3, 1.0 mL/min, 210 nm)



Peak #	Retention Time	Area (uV*min)	Area (%)	
1	11.6	44693.8	50.671	(S)
2	14.9	43509.3	49.329	(R)

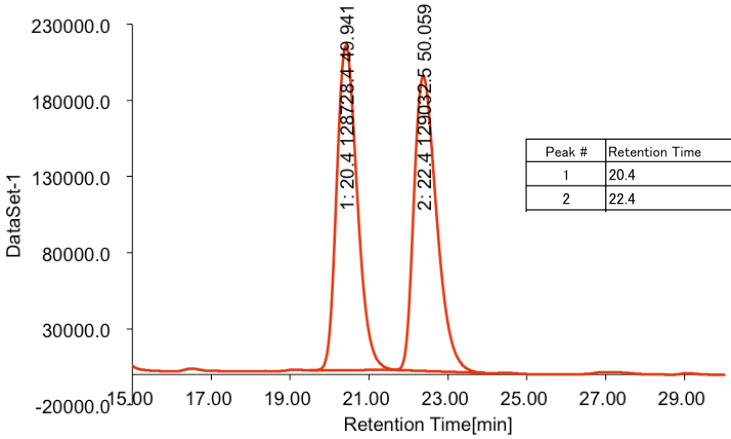


8i

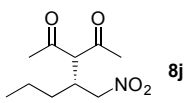


Peak #	Retention Time	Area (uV*min)	Area (%)	%ee (S)
1	11.6	93722.6	97.604	95.208
2	14.9	2301.2	2.396	

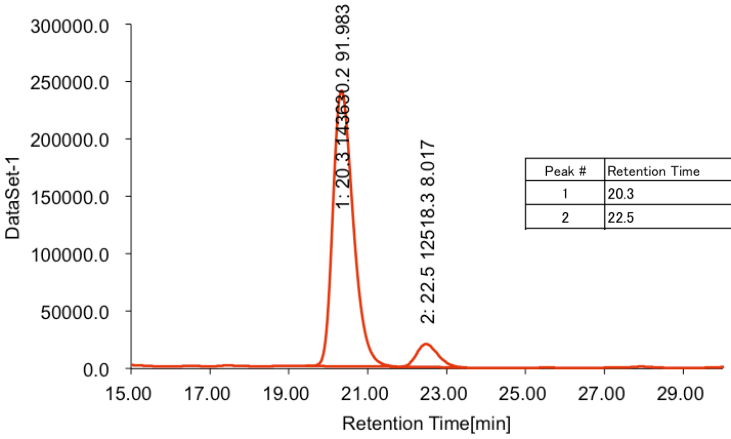
8j: DAICEL CHIRALPAK AD-H (4.6 x 250 mm, hexane/2-propanol = 98/2, 1.0 mL/min, 210 nm)



Peak #	Retention Time	Area (uV*min)	Area (%)	
1	20.4	128728.4	49.941	(R)
2	22.4	129032.5	50.059	(S)

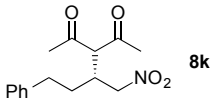


8j

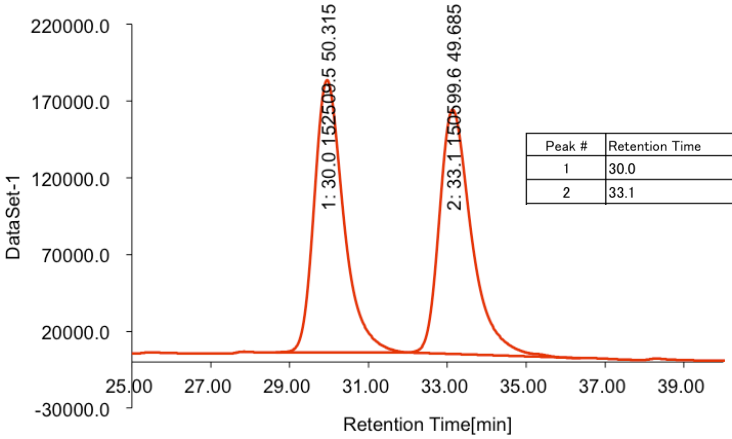


Peak #	Retention Time	Area (uV*min)	Area (%)	%ee(R)
1	20.3	143630.2	91.983	83.966
2	22.5	12518.3	8.017	

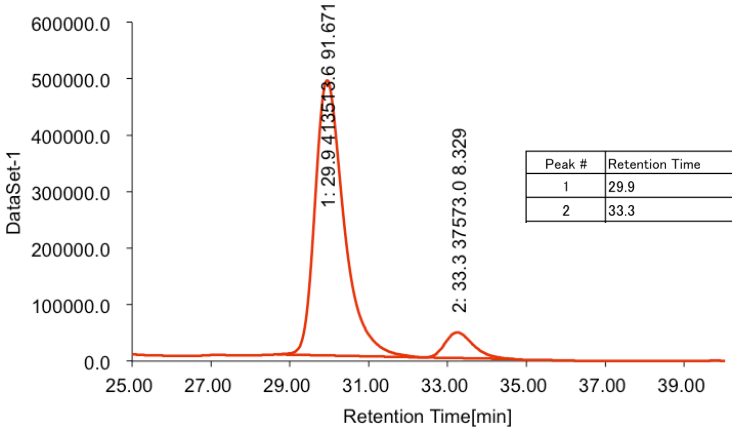
8k: DAICEL CHIRALPAK AD-H (4.6 x 250 mm, hexane/2-propanol = 98/2, 1.0 mL/min, 210 nm)



8k



Peak #	Retention Time	Area (uV*min)	Area (%)	
1	30.0	152509.5	50.315	(R)
2	33.1	150599.6	49.685	(S)



Peak #	Retention Time	Area (uV*min)	Area (%)	%ee(R)
1	29.9	413513.6	91.671	83.342
2	33.3	37573	8.329	