Electronic Supplementary Information

Desymmetrizing Asymmetric Ring Expansion: Stereoselective Synthesis of 7-Membered Cyclic β-Keto Carbonyl Compounds with an α-Hydrogen

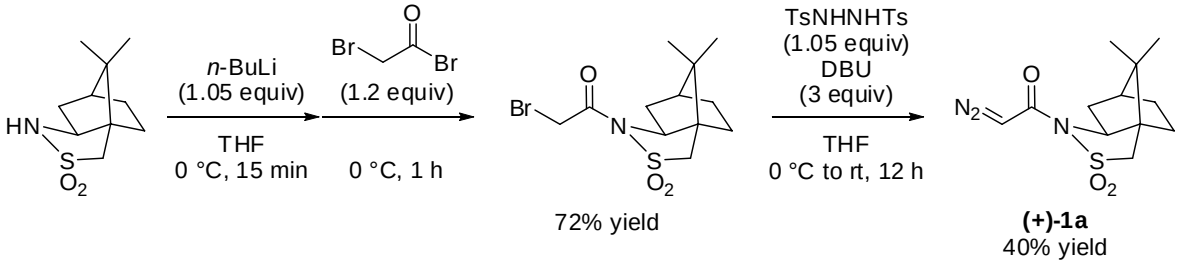
Takuya Hashimoto, Yuki Naganawa, and Keiji Maruoka*

Department of Chemistry, Graduate School of Science, Kyoto University
Sakyo, Kyoto 606-8502, Japan

General Information. Infrared (IR) spectra were recorded on a Shimadzu IRPrestige-21 spectrometer. ^{1}H NMR spectra were measured on a JEOL JNM-FX400 (400 MHz) spectrometer. Data were reported as follows: chemical shifts in ppm from tetramethylsilane as an internal standard, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = double-doublet, ddd= double-double-doublet, dt=double-triplet, m = multiplet, br = broad, and app = apparent), coupling constants (Hz), and assignment. ^{13}C NMR spectra were measured on a JEOL JNM-FX400 (100 MHz) spectrometer with complete proton decoupling. Chemical shifts were reported in ppm from the residual solvent as an internal standard. High-resolution mass spectra (HRMS) were performed on Brucker microTOF. Optical rotations were measured on a JASCO DIP-1000 digital polarimeter. For thin layer chromatography (TLC) analysis throughout this work, Merck precoated TLC plates (silica gel 60 GF_{254}, 0.25 mm) were used. The products were purified by flash column chromatography on silica gel 60 (Merck, 230-400 mesh). High performance liquid chromatography (HPLC) was performed on Shimadzu 10A instruments at 254 nm using 4.6 mm x 25 cm Daicel Chiral columns.

In experiments requiring dry solvent, dichloromethane was purchased from Kanto Chemical Co. Inc. as “Dehydrated” and further purified by passing through neutral alumina under nitrogen atmosphere. $BF_3{\cdot}OEt_2$ was purchased from Tokyo Chemical Industry Co., Ltd. and distilled from CaH_2. Simple cyclic ketones were purchased and used after distillation or column chromatography on silica gel.

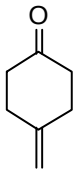
Preparation of *N*-(2-diazo)acetyl (+)-camphorsultam ((+)-1a) using the procedure of Fukuyama et al.[1]



To a stirred solution of (+)-camphorsultam (6.67 g, 31 mmol) in THF (40 mL), *n*-BuLi (1.6 M hexane solution, 20 mL, 32.5 mmol) was added dropwise at 0 °C under Ar atmosphere. After 15 min, bromoacetyl bromide (3.26 mL, 37 mmol) was added dropwise, and the mixture was stirred at the same temperature for 1 h. The resulting mixture was quenched with saturated aqueous NH_4Cl and extracted with ethyl acetate. The combined organic layers were dried over Na_2SO_4 and evaporated. The residue was purified by flash column chromatography (eluting with hexane/ethyl acetate = 7:1) to afford *N*-bromoacetyl (+)-camphorsultam (7.83 g, 22.2 mmol). Spectral data of this compound was reported in the literature.[2]

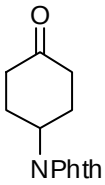
To a stirred solution of thus-obtained *N*-bromoacetyl (+)-camphorsultam (7.83 g, 22.2 mmol) and *N,N*'-ditosylhydrazine (9.07 g, 26.6 mmol) in THF (50 mL) was added DBU (9.7 mL, 66.6 mmol) at 0 °C. The reaction mixture was then allowed to warm to room temperature. After stirring for 12 h, the resulting mixture was quenched with saturated aqueous NH_4Cl, and extracted with ethyl acetate. The combined organic layers were washed with brine, and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure, and the residue was purified by flash column chromatography (eluting with hexane/ethyl acetate = 8:1) to give the title compound (2.54 g, 9.0 mmol) as a pale yellow solid. Spectral data of this compound was reported in the literature.[3]

Preparation of functionalized cyclohexanones.



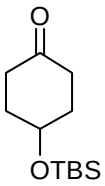
4-Methylenecyclohexanone.

Prepared according to the literature.[4a]



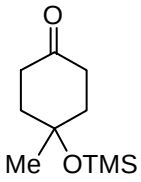
4-(*N*-Phthaloylamino)cyclohexanone (4d).

Prepared according to the literature.[4b]



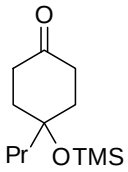
4-(*tert*-Butyldimethylsilyloxy)cyclohexanone (4e).

Prepared according to the literature.[4c]



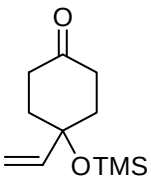
4-Methyl-4-(trimethylsilyloxy)cyclohexanone (4f).

Prepared according to the literature.[4d]



4-Propyl-4-(trimethylsilyloxy)cyclohexanone (4g).

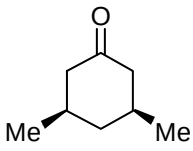
Prepared according to the literature.[4d]



4-(Trimethylsilyloxy)-4-vinylcyclohexanone (4h).

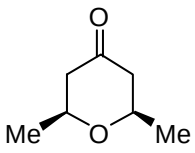
Prepared according to the literature.[4d]

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.07 (1H, dd, *J* = 18.0, 11.2 Hz), 5.20 (1H, dd, *J* = 18.0, 0.8 Hz), 5.15 (1H, dd, 11.2, 0.8 Hz), 2.70 (2H, dt, *J* = 13.6, 6.0 Hz), 2.25 (2H, m), 2.07 (2H, m), 1.85 (2H, dt, *J* = 13.2, 4.8 Hz), 0.15 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.9, 143.8, 113.7, 72.7, 37.2, 37.0, 2.3; IR (neat) 2955, 1719, 1418, 1250, 1217, 1113, 1045, 999 cm^{-1}; HRMS (ESI) exact mass calcd. for $C_{11}H_{20}O_2Si$: *m/z* 235.1125 ($[M + Na]^+$), found: *m/z* 235.1122 ($[M + Na]^+$)

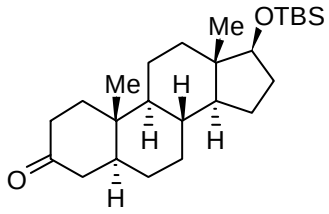


***cis*-3,5-Dimethylcyclohexanone (4i).**

Prepared according to the literarure.[4e]

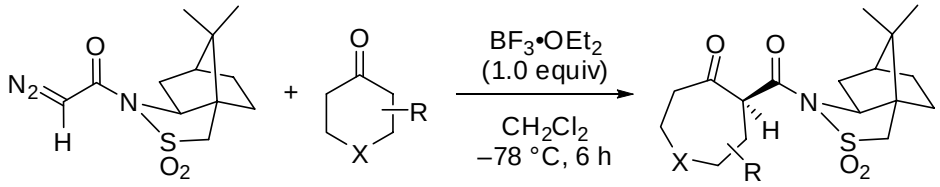


***cis*-2,6-Dimethyltetrahydropyran-4-one (4j).**
Prepared according to the literarure.[4f]

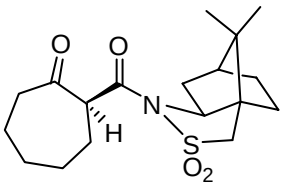


TBSO-Dihydrotestosterone (8).
Prepared according to the literarure.[4g]

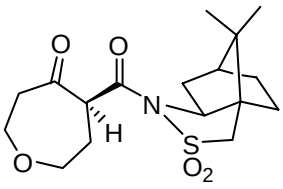
General procedure for the stereoselective ring expansion of functionalized cyclic ketones with (+)-1a.



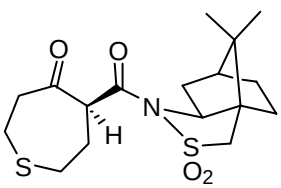
To a stirred solution of *N*-(2-diazo)acetyl (+)-camphorsultam (56.7 mg, 0.20 mmol) and cyclic ketones (0.21 mmol) in dichloromethane (1.0 mL) was added $BF_3{\cdot}OEt_2$ (25.3 μL, 0.20 mmol) at –78 °C under Ar atmosphere. The reaction mixture was stirred at the same temperature for 6 h. The mixture was quenched with H_2O and extracted with ethyl acetate. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by column chromatography on silica gel (eluting with hexane/ethyl acetate = 8:1~4:1) to give the corresponding cyclic β-keto carbonyl compound.



***N*-[(2*S*)-1-oxocycloheptan-2-carbonyl] (+)-camphorsultam (3a).** ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.28 (1H, dd, *J* = 10.5, 3.2 Hz), 3.95 (1H, dd, *J* = 7.8, 5.4 Hz), 3.49 (1H, d, *J* = 13.9 Hz), 3.43 (1H, d, *J* = 13.9 Hz), 2.78 (1H, m), 2.54 (1H, ddd, *J* = 15.6, 11.7, 3.9 Hz), 2.01-2.22 (3H, m), 1.76-2.00 (7H, m), 1.66 (1H, m), 1.52 (1H, m), 1.23-1.44 (3H, m), 1.16 (3H, s), 0.98 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.6, 169.1, 65.6, 57.7, 52.9, 48.4, 47.7, 44.8, 43.4, 38.6, 32.9, 29.0, 28.9, 28.5, 26.3, 23.6, 21.1, 19.8; IR (neat) 2938, 1719, 1684, 1327, 1269, 1236, 1211, 1165, 1136, 1113 cm^{-1}; HRMS (ESI) exact mass calcd. for $C_{18}H_{27}NO_4S$: *m/z* 376.1553 ([M + Na]$^+$), found: *m/z* 376.1561 ([M + Na]$^+$); $[\alpha]_D^{23}$ = +111.0 (*c* = 1.0, $CHCl_3$). [72% yield]

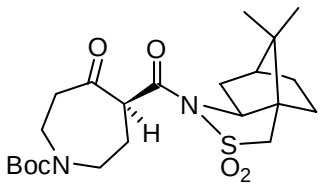


***N*-[(2*S*)-1-oxo-5-oxepan-2-carbonyl] (+)-camphorsultam (3b).** ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.49 (1H, dd, *J* = 11.0, 3.4 Hz), 4.07 (2H, m), 3.98 (1H, dd, *J* = 8.0, 5.4 Hz), 3.75 (1H, ddd, *J* = 13.6, 8.8, 5.4 Hz), 3.66 (1H, ddd, *J* = 13.0, 11.0, 2.4 Hz), 3.51 (1H, d, *J* = 14.2 Hz), 3.44 (1H, d, *J* = 14.2 Hz), 2.80-2.88 (2H, m), 1.84-2.24 (7H, m), 1.24-1.55 (2H, m), 1.16 (3H, s), 0.98 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.3, 167.9, 71.4, 66.3, 65.7, 57.0, 52.9, 48.5, 47.7, 45.8, 44.8, 38.6, 33.0, 30.4, 26.2, 21.2, 19.9; IR (neat) 2959, 1724, 1692, 1325, 1292, 1236, 1219, 1167, 1152, 1134 cm^{-1}; HRMS (ESI) exact mass calcd. for $C_{17}H_{25}NO_5S$: *m/z* 378.1346 ([M + Na]$^+$), found: *m/z* 378.1348 ([M + Na]$^+$); $[\alpha]_D^{24}$ = +94.4 (*c* = 1.0, $CHCl_3$). [75% yield]



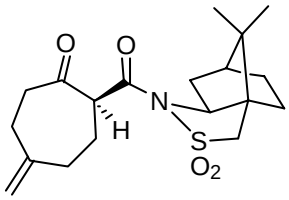
***N*-[(2*S*)-1-oxo-5-thiepan-2-carbonyl] (+)-camphorsultam (3c).** ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.47 (1H, dd, *J* = 10.5, 3.2 Hz), 3.93 (1H, dd, *J* = 7.6, 5.1 Hz), 3.50 (1H, d, *J* = 14.0 Hz), 3.42 (1H, d, *J*

= 14.0 Hz), 3.29(1H, m), 2.74-2.94 (5H, m), 2.07-2.36 (4H, m),1.82-1.97 (3H, m),1.23-1.45 (2H, m), 1.15 (3H, s), 0.98 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.0, 167.1, 65.8, 56.4, 53.0, 48.5, 47.7, 46.9, 44.8, 38.6, 32.94, 32.85, 32.7, 26.7, 26.3, 21.1, 19.8; IR (neat) 2961, 1722, 1690, 1323, 1267, 1236, 1165, 1134, 1117, 1065 cm^{-1}; HRMS (ESI) exact mass calcd. for $C_{17}H_{25}NO_4S_2$: *m/z* 394.1117 ([M + Na]$^+$), found: *m/z* 394.1105 ([M + Na]$^+$); $[\alpha]_D^{21}$ = +57.1 (*c* = 1.0, $CHCl_3$). [65% yield]



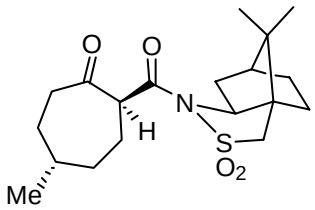
***N*-[(2*S*)-1-oxo-5-(*N*-Boc)azepan-2-carbonyl] (+)-camphorsultam (3d).**

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.47 (1H, dd, *J* = 10.8, 3.2 Hz), 3.80-4.16 (2H, m), 3.96 (1H, dd, *J* = 7.6, 5.2 Hz), 3.50 (1H, d, *J* = 14.0 Hz), 3.42 (1H, d, *J* = 14.0 Hz), 3.28 (1H, m), 3.09 (1H, m), 2.71-2.94 (2H, m), 0.71-2.25 (9H, m), 1.44 (9H, s), 1.16 (3H, s), 0.98 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$, 50 °C) δ 205.6, 167.4, 154.2, 80.2, 77.2, 65.1, 57.2, 52.9, 48.8, 45.0, 44.6, 42.7, 37.8, 29.7, 28.3, 26.6, 20.1, 19.9; IR (neat) 2961, 2928, 1724, 1690, 1366, 1325, 1236, 1219, 1165, 1136 cm^{-1}; HRMS (ESI) exact mass calcd. for $C_{22}H_{34}N_2O_6S$: *m/z* 477.2030 ([M + Na]$^+$), found: *m/z* 477.2029 ([M + Na]$^+$); $[\alpha]_D^{29}$ = +53.4 (*c* = 1.0, $CHCl_3$). [41% yield]



***N*-[(2*S*)-1-oxo-5-methylenecycloheptan-2-carbonyl] (+)-camphorsultam (3e).**

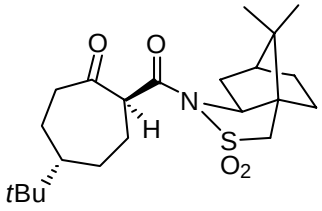
^{1}H NMR (400 MHz, $CDCl_3$) δ 4.83 (1H, m), 4.80 (1H, m), 4.39 (1H, dd, *J* = 10.7, 3.6 Hz), 3.95 (1H, dd, *J* = 8.0, 5.4 Hz), 3.49 (1H, d, *J* = 13.9 Hz), 3.43 (1H, d, *J* = 13.9 Hz), 2.82 (1H, dt, *J* = 15.6, 5.1 Hz), 2.35-2.61 (4H, m), 2.29 (1H, m), 2.03-2.23 (3H, m), 1.81-2.00(4H, m), 1.23-1.45(2H, m), 1.16 (3H, s), 0.98 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.4, 168.5, 147.5, 113.5, 65.7, 57.2, 52.9, 48.4, 47.7, 44.8, 43.0, 38.6, 36.0, 33.0, 31.0, 28.7, 26.3, 21.1, 19.9; IR (neat) 2953, 1721, 1692, 1325, 1267, 1238, 1211, 1167, 1134, 1119 cm^{-1}; HRMS (ESI) exact mass calcd. for $C_{19}H_{27}NO_4S$: *m/z* 388.1553 ([M + Na]$^+$), found: *m/z* 388.1558 ([M + Na]$^+$); $[\alpha]_D^{27}$ = +97.2 (*c* = 1.0, $CHCl_3$). [80% yield]



***N*-[(2*S*,5*S*)-1-oxo-5-methylcycloheptan-2-carbonyl] (+)-camphorsultam (5a).**

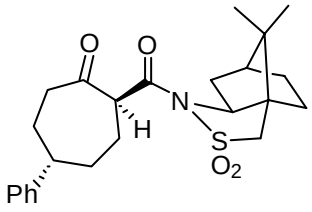
^{1}H NMR (400 MHz, $CDCl_3$) δ 4.24 (1H, dd, *J* = 11.5, 2.7 Hz), 3.94 (1H, dd, *J* = 7.8, 5.4 Hz), 3.49 (1H, d, *J* = 14.0 Hz), 3.43 (1H, d, *J* = 14.0 Hz), 2.74 (1H, m), 2.60 (1H, m), 2.02-2.23 (3H, m), 1.70-1.99 (6H, m), 1.18-1.57 (5H, m), 1.15 (3H, s), 0.98 (3H, d, *J* = 6.1 Hz), 0.97 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.5, 169.1, 65.5, 57.9, 52.9, 48.4, 47.7, 44.8, 42.3, 38.5, 37.3, 35.6, 32.9, 31.8, 28.7, 26.3, 23.8, 21.1, 19.8; IR (neat) 2953, 1719, 1682, 1327, 1269, 1234, 1213, 1165, 1136, 1113 cm^{-1}; HRMS (ESI) exact mass calcd. for $C_{19}H_{29}NO_4S$:

m/z 390.1710 ([M + Na]$^+$), found: *m/z* 390.1708 ([M + Na]$^+$); $[\alpha]_D^{23}$ = +121.3 (*c* = 1.0, $CHCl_3$). [81% yield]



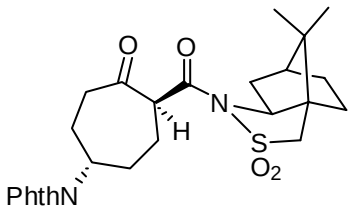
_N_-[(2_S_,5_S_)-1-oxo-5-_tert_-butylcycloheptan-2-carbonyl] (+)-camphorsultam (5b).

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.28 (1H, dd, *J* = 11.7, 2.0 Hz), 3.94 (1H, dd, *J* = 7.3, 5.8 Hz), 3.49 (1H, d, *J* = 13.9 Hz), 3.42 (1H, d, *J* = 13.9 Hz), 2.81 (1H, dt, *J* = 16.1, 3.6 Hz), 2.50 (1H, m), 1.73-2.24 (9H, m), 1.17-1.50 (4H, m), 1.16 (3H, s), 0.97 (3H, s), 0.94 (1H, m), 0.87 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.8, 169.0, 65.6, 57.6, 52.9, 50.8, 48.4, 47.7, 44.8, 42.8, 38.6, 33.6, 32.9, 29.9, 29.6, 27.4, 26.3, 25.3, 21.1, 19.8; IR (neat) 2959, 1721, 1684, 1329, 1269, 1234, 1215, 1167, 1138, 1113 cm^{-1}; HRMS (ESI) exact mass calcd. for $C_{22}H_{35}NO_4S$: *m/z* 432.2179 ([M + Na]$^+$), found: *m/z* 432.2186 ([M + Na]$^+$); $[\alpha]_D^{22}$ = +99.1 (*c* = 1.0, $CHCl_3$). [80% yield]



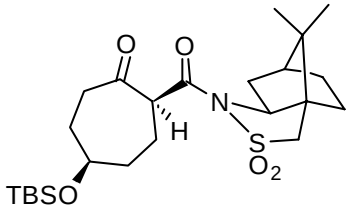
_N_-[(2_S_,5_S_)-1-oxo-5-phenylcycloheptan-2-carbonyl] (+)-camphorsultam (5c).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.13-7.34 (5H, m), 4.38 (1H, dd, *J* = 11.7, 3.0 Hz), 3.97 (1H, dd, *J* = 7.8, 5.1 Hz), 3.51 (1H, d, *J* = 13.9 Hz), 3.45 (1H, d, *J* = 13.9 Hz), 2.88 (1H, dt, *J* = 16.4, 4.4 Hz), 2.76 (1H, m), 2.57 (1H, m), 1.69-2.30 (11H, m), 1.23-1.46 (2H, m), 1.17 (3H, s), 0.98 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.2, 168.9, 147.4, 128.6, 126.4, 126.3, 65.6, 57.8, 52.9, 48.4, 47.7, 47.3, 44.8, 42.6, 38.5, 37.2, 33.0, 31.3, 29.1, 26.3, 21.1, 19.9; IR (neat) 2934, 1721, 1682, 1327, 1236, 1217, 1136, 1065 cm^{-1}; HRMS (ESI) exact mass calcd. for $C_{24}H_{31}NO_4S$: *m/z* 452.1866 ([M + Na]$^+$), found: *m/z* 452.1865 ([M + Na]$^+$); $[\alpha]_D^{19}$ = +87.9 (*c* = 1.0, $CHCl_3$). [78% yield]



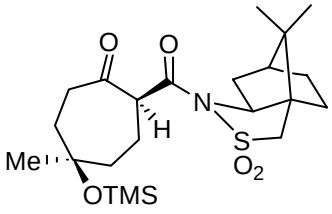
_N_-[(2_S_,5_S_)-1-oxo-5-(_N_-phthaloylamino)cycloheptan-2-carbonyl] (+)-camphorsultam (5d).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (2H, m), 7.71 (2H, m), 4.39 (1H, dd, *J* = 12.0, 3.2 Hz), 4.12 (1H, m), 3.96 (1H, dd, *J* = 8.1, 5.6 Hz), 3.51 (1H, d, *J* = 13.9 Hz), 3.44 (1H, d, *J* = 13.9 Hz), 0.86-2.76 (15H, m), 1.17 (3H, s), 0.98 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.1, 168.6, 167.7, 134.0, 131.8, 123.3, 65.6, 57.5, 52.9, 52.2, 48.5, 47.7, 44.8, 40.6, 38.5, 32.9, 32.6, 28.2, 27.3, 26.3, 21.1, 19.9; IR (neat) 2959, 1707, 1395, 1373, 1329, 1236, 1213, 1167, 1138 cm^{-1}; HRMS (ESI) exact mass calcd. for $C_{26}H_{30}N_2O_6S$: *m/z* 521.1717 ([M + Na]$^+$), found: *m/z* 521.1709 ([M + Na]$^+$); $[\alpha]_D^{21}$ = +85.8 (*c* = 1.0, $CHCl_3$). [40% yield]



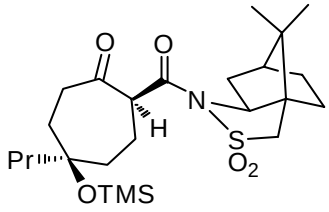
_N_-[(2_S_,5_R_)-1-oxo-5-(_tert_-butyldimethylsiloxy)cycloheptan-2-carbonyl] (+)-camphorsultam (5e).

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.16 (1H, m), 4.13 (1H, dd, *J* = 11.2, 2.7 Hz), 3.95 (1H, dd, *J* = 7.8, 5.2 Hz), 3.49 (1H, d, *J* = 13.9 Hz), 3.43 (1H, d, *J* = 13.9 Hz), 2.93 (1H, m), 2.48 (1H, m), 2.02-2.31 (3H, m), 1.75-2.02 (7H, m), 1.62 (1H, m), 1.23-1.44 (2H, m), 1.15 (3H, s), 0.97 (3H, s), 0.87 (9H, s), 0.04 (3H, s), 0.03 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.2, 169.4, 67.6, 65.5, 58.2, 52.9, 48.3, 47.7, 44.8, 38.5, 36.6, 36.4, 32.9, 30.6, 26.3, 25.7, 22.2, 21.1, 19.9, 18.0, –4.9, –5.0; IR (neat) 2953, 1721, 1688, 1327, 1252, 1217, 1209, 1136, 1082, 1067 cm^{-1}; HRMS (ESI) exact mass calcd. for $C_{24}H_{41}NO_5SSi$: *m/z* 506.2367 ([M + Na]$^+$), found: *m/z* 506.2377 ([M + Na]$^+$); $[\alpha]_D^{22}$ = +86.7 (*c* = 1.0, $CHCl_3$). [81% yield]



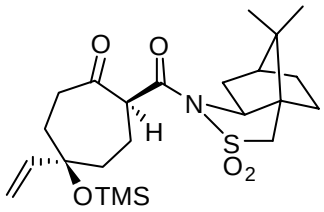
_N_-[(2_S_,5_R_)-1-oxo-5-methyl-5-trimethylsiloxycycloheptan-2-carbonyl] (+)-camphorsultam (5f).

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.12 (1H, dd, *J* = 11.5, 2.5 Hz), 3.95 (1H, dd, *J* = 7.8, 5.1 Hz), 3.49 (1H, d, *J* = 13.9 Hz), 3.43 (1H, d, *J* = 13.9 Hz), 2.90 (1H, ddd, *J* = 16.4, 11.7, 4.6 Hz), 2.45 (1H, m), 2.04-2.25 (3H, m), 1.71-1.98 (7H, m), 1.24-1.62 (3H, m), 1.33 (3H, s), 1.15 (3H, s), 0.97 (3H, s), 0.11 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.3, 169.4, 73.6, 65.5, 58.2, 52.3, 48.3, 47.7, 44.8, 42.8, 38.5, 37.8, 37.0, 32.9, 31.9, 26.3, 23.8, 21.1, 19.9, 2.3; IR (neat) 2961, 1721, 1686, 1327, 1250, 1215, 1167, 1134, 1094 cm^{-1}; HRMS (ESI) exact mass calcd. for $C_{22}H_{37}NO_5SSi$: *m/z* 478.2054 ([M + Na]$^+$), found: *m/z* 478.2055 ([M + Na]$^+$); $[\alpha]_D^{22}$ = +98.4 (*c* = 1.0, $CHCl_3$). [76% yield]



_N_-[(2_S_,5_R_)-1-oxo-5-trimethylsiloxy-5-propylcycloheptan-2-carbonyl] (+)-camphorsultam (5g).

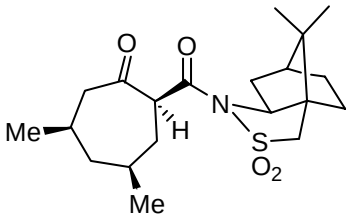
^{1}H NMR (400 MHz, $CDCl_3$) δ 4.10 (1H, dd, *J* = 11.0, 2.7 Hz), 3.95 (1H, dd, *J* = 7.8, 5.1 Hz), 3.49 (1H, d, *J* = 13.9 Hz), 3.44 (1H, d, *J* = 13.9 Hz), 2.88 (1H, ddd, *J* = 16.4, 11.0, 5.4 Hz), 2.47 (1H, m), 2.04-2.25 (3H, m), 1.71-1.98 (7H, m), 1.47-1.65 (3H, m), 1.22-1.45 (4H, m), 1.15 (3H, s), 0.97 (3H, s), 0.91 (3H, t, *J* = 7.3 Hz), 0.11 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.4, 169.4, 76.4, 65.5, 58.0, 52.9, 48.4, 47.7, 47.6, 44.8, 40.0, 38.5, 37.8, 34.7, 32.9, 26.3, 23.6, 21.1, 19.9, 17.4, 14.7, 2.4; IR (neat) 2957, 1684, 1721, 1329, 1250, 1238, 1213, 1167, 1134, 1084 cm^{-1}; HRMS (ESI) exact mass calcd. for $C_{24}H_{41}NO_5SSi$: *m/z* 506.2367 ([M + Na]$^+$), found: *m/z* 506.2361 ([M + Na]$^+$); $[\alpha]_D^{21}$ = +73.9 (*c* = 1.0, $CHCl_3$). [68% yield]



_N_-[(2_S_,5_R_)-1-oxo-5-trimethylsiloxy-5-vinylcycloheptan-2-carbonyl] (+)-camphorsultam (5g).

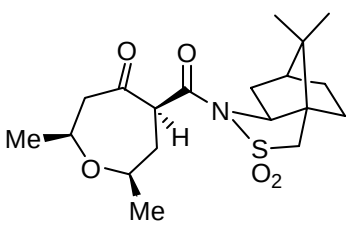
^{1}H NMR (400 MHz, $CDCl_3$) δ 5.99 (1H, dd, *J* = 18.0, 11.2 Hz), 5.14 (1H, dd, *J* = 18.0, 0.8 Hz), 5.08 (1H, dd, *J* = 11.2, 0.8 Hz), 4.13 (1H, dd, *J* = 11.6, 3.2 Hz), 3.96 (1H, dd, *J* = 8.0, 5.2 Hz), 3.49 (1H, d, *J* = 14.0 Hz), 3.44 (1H, d, *J* = 14.0 Hz), 2.94 (1H, ddd, *J* = 16.0, 12.4, 3.2 Hz), 2.51 (1H, ddd, *J* = 16.4, 5.2, 3.2 Hz), 1.25-2.26 (13H, m), 1.15 (3H, s), 0.98 (3H, s), 0.09

(9H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.2, 169.4, 146.0, 112.7, 75.0, 65.5, 58.1, 52.9, 48.4, 47.7, 44.8, 39.9, 38.5, 37.4, 34.6, 32.9, 26.3, 23.2, 21.1, 19.9, 2.3; IR (neat) 2957, 1721, 1686, 1329, 1250, 1213, 1136, 1084, 1065, 1047 cm^{-1}; HRMS (ESI) exact mass calcd. for $C_{23}H_{37}NO_5SSi$: *m/z* 490.2054 ([M + Na]$^+$), found: *m/z* 490.2072 ([M + Na]$^+$); $[\alpha]_D^{29}$ = +86.5 (*c* = 1.0, $CHCl_3$). [41% yield]



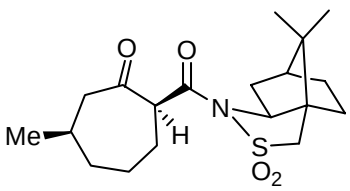
***N*-[(2*S*,4*S*,6*R*)-1-oxo-4,6-dimethylcycloheptan-2-carbonyl] (+)-camphorsultam (5i).**

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.34 (1H, dd, *J* = 11.7, 2.4 Hz), 3.94 (1H, dd, *J* = 7.8, 5.2 Hz), 3.49 (1H, d, *J* = 13.9 Hz), 3.42 (1H, d, *J* = 13.9 Hz), 2.78 (1H, ddd, *J* = 16.4, 3.6, 1.7 Hz), 2.31 (1H, dd, *J* = 16.6, 11.7 Hz), 1.98-2.23 (4H, m), 1.52-1.96 (7H, m), 1.23-1.46 (2H, m), 1.16 (3H, s), 1.00 (3H, d, *J* = 6.6 Hz), 0.97 (3H, s), 0.96 (3H, d, *J* = 6.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.8, 168.8, 65.7, 56.9, 52.9, 51.7, 48.4, 47.7, 46.5, 44.8, 38.6, 37.4, 34.9, 33.0, 29.9, 26.3, 23.8, 23.7, 21.1, 19.9; IR (neat) 2957, 1719, 1686, 1327, 1288, 1238, 1213, 1165, 1134, 1113 cm^{-1}; HRMS (ESI) exact mass calcd. for $C_{20}H_{31}NO_4S$: *m/z* 404.1866 ([M + Na]$^+$), found: *m/z* 404.1866 ([M + Na]$^+$); $[\alpha]_D^{20}$ = +118.0 (*c* = 1.0, $CHCl_3$). [73% yield]



***N*-[(2*S*,4*R*,6*S*)-1-oxo-4,6-dimethyl-5-oxepan-2-carbonyl] (+)-camphorsultam (5j).**

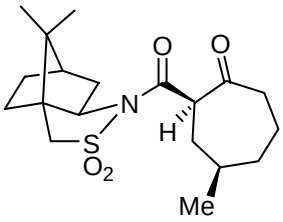
^{1}H NMR (400 MHz, $CDCl_3$) δ 4.57 (1H, dd, *J* = 10.8, 3.9 Hz), 4.04 (1H, m), 3.97 (1H, dd, *J* = 8.1, 5.1 Hz), 3.79 (1H, m), 3.50 (1H, d, *J* = 13.9 Hz), 3.43 (1H, d, *J* = 13.9 Hz), 2.90 (1H, dd, *J* = 17.1, 3.2 Hz), 2.63 (1H, dd, *J* = 17.1, 11.0 Hz), 2.21 (1H, m), 2.12 (1H, dd, *J* = 14.2, 8.0 Hz), 1.83-2.00 (5H, m), 1.30-1.45 (2H, m), 1.24 (3H, d, *J* = 6.4 Hz), 1.23 (3H, d, *J* = 6.3 Hz), 1.16 (3H, s), 0.97 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.8, 167.6, 77.2, 72.1, 65.8, 56.2, 52.9, 52.8, 48.5, 47.7, 44.9, 38.6, 37.9, 33.0, 26.2, 22.5, 22.4, 21.2, 19.8; IR (neat) 2941, 1719, 1692, 1323, 1287, 1223, 1167, 1134, 1121, 1053 cm^{-1}; HRMS (ESI) exact mass calcd. for $C_{19}H_{29}NO_5S$: *m/z* 406.1659 ([M + Na]$^+$), found: *m/z* 406.1659 ([M + Na]$^+$); $[\alpha]_D^{17}$ = +113.8 (*c* = 1.0, $CHCl_3$). [86% yield]



***N*-[(2*S*,6*R*)-1-oxo-6-methylcycloheptan-2-carbonyl] (+)-camphorsultam (7a).**

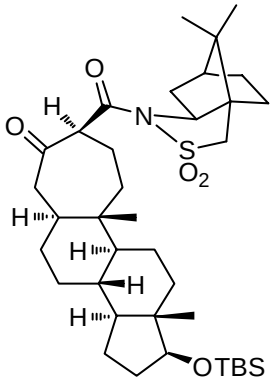
^{1}H NMR (400 MHz, $CDCl_3$) δ 4.22 (1H, dd, *J* = 11.2, 3.2 Hz), 3.93 (1H, dd, *J* = 7.4, 5.2 Hz), 3.49 (1H, d, *J* = 14.2 Hz), 3.43 (1H, d, *J* = 14.2 Hz), 2.73 (1H, dd, *J* = 15.4, 11.5 Hz), 2.49 (1H, ddd, *J* = 17.1, 12.4, 4.2 Hz), 2.02-2.23 (3H, m), 1.68-2.01 (7H, m), 1.08-1.63 (4H, m), 1.15 (3H, s), 1.01 (3H, d, *J* = 6.6 Hz), 0.97 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.9, 169.1, 65.5, 58.2, 52.9, 51.5, 48.4, 47.7, 44.8, 38.5, 37.9, 32.9, 30.9, 29.7, 27.8, 26.3, 23.6,

21.1, 19.8; IR (neat) 2955, 1717, 1682, 1456, 1375, 1329, 1269, 1240, 1213, 1113 cm^{-1}; HRMS (ESI) exact mass calcd. for $C_{19}H_{29}NO_4S$: *m/z* 390.1710 ($[M + Na]^+$), found: *m/z* 390.1720 ($[M + Na]^+$); $[\alpha]_D^{28} = +98.7$ (*c* = 1.0, $CHCl_3$). [72% yield]



***N*-[(2*R*,4R)-1-oxo-4-methylcycloheptan-2-carbonyl] (–)-camphorsultam (7b).**

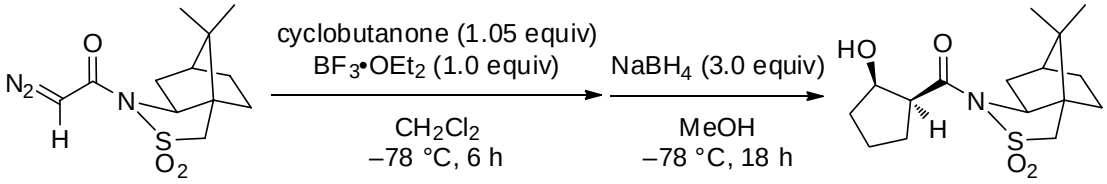
^1H NMR (400 MHz, $CDCl_3$) δ 4.38 (1H, dd, *J* = 11.7, 2.2 Hz), 3.95 (1H, dd, *J* = 7.8, 5.1 Hz), 3.49 (1H, d, *J* = 13.9 Hz), 3.42 (1H, d, *J* = 13.9 Hz), 2.82 (1H, ddt, *J* = 17.1, 4.4, 1.7 Hz), 2.49 (1H, ddd, *J* = 17.1, 12.4, 4.2 Hz), 2.20 (1H, m), 2.11 (1H, dd, *J* = 13.9, 8.4 Hz), 2.02 (1H, m), 1.82-1.97 (5H, m), 1.64-1.82 (2H, m), 1.56 (1H, m), 1.30-1.44 (2H, m), 1.16 (3H, s), 1.02 (1H, m), 0.98 (3H, d, *J* = 6.6 Hz), 0.98 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.5, 168.8, 65.7, 56.5, 52.9, 48.4, 47.7, 44.9, 43.4, 38.6, 37.2, 37.1, 35.9, 33.0, 26.3, 23.5, 22.7, 21.2, 19.9; IR (neat) 2953, 1721, 1690, 1325, 1289, 1236, 1211, 1167, 1138, 1113 cm^{-1}; HRMS (ESI) exact mass calcd. for $C_{19}H_{29}NO_4S$: *m/z* 390.1710 ($[M + Na]^+$), found: *m/z* 390.1719 ($[M + Na]^+$); $[\alpha]_D^{27} = -107.5$ (*c* = 1.0, $CHCl_3$). [62% yield]



Compound 9.

^1H NMR (400 MHz, $CDCl_3$) δ 4.11 (1H, dd, *J* = 9.8, 4.4 Hz), 3.95 (1H, dd, *J* = 7.8, 5.1 Hz), 3.53 (1H, t, *J* = 8.1 Hz), 3.49 (1H, d, *J* = 14.2 Hz), 3.44 (1H, d, *J* = 14.2 Hz), 2.67 (1H, dd, *J* = 16.4, 11.7 Hz), 2.32 (1H, dd, *J* = 16.4, 2.7 Hz), 0.64-2.21 (27H, m), 1.15 (3H, s), 0.97 (3H, s), 0.87 (9H, s), 0.81 (3H, s), 0.68 (3H, s), 0.003 (3H, s), -0.003 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.0, 169.5, 81.7, 65.5, 57.9, 53.6, 52.9, 50.7, 48.4, 48.0, 47.7, 44.8, 43.00, 42.97, 40.8, 39.0, 38.5, 37.3, 35.3, 32.9, 31.4, 31.0, 30.7, 26.3, 25.8, 24.0, 23.5, 21.3, 21.1, 19.9, 18.1, 12.3, 11.3, -4.5, -4.8; IR (neat) 2953, 2928, 1717, 1682, 1331, 1250, 1167, 1136, 1117, 1094 cm^{-1}; HRMS (ESI) exact mass calcd. for $C_{37}H_{61}NO_5SSi$: *m/z* 682.3932 ($[M + Na]^+$), found: *m/z* 682.3929 ($[M + Na]^+$); $[\alpha]_D^{22} = +80.1$ (*c* = 1.0, $CHCl_3$). [70% yield]

***N*-[(1*R*,2*S*)-1-hydroxycyclopentan-2-carbonyl] (+)-camphorsultam (10).**

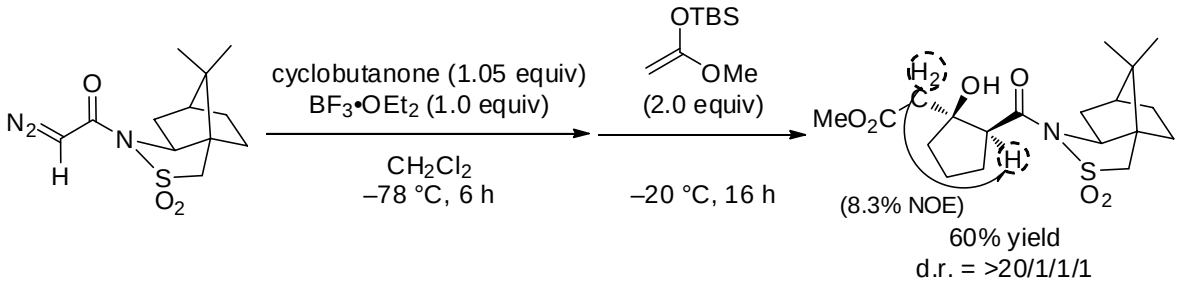


To a stirred solution of *N*-(2-diazo)acetyl (+)-camphorsultam (56.7 mg, 0.20 mmol) and cyclobutanone (15.7 μL, 0.21 mmol) in dichloromethane (1.0 mL) was added $BF_3 \cdot OEt_2$

(25.3 μL, 0.20 mmol) at –78 °C under Ar atmosphere. After stirring for 6 h, $NaBH_4$ (0.3 M methanol solution, 2.0 mL, 0.6 mmol) was added to a stirred solution dropwise at –78 °C. The reaction mixture was then stirred at the same temperature for additional 18 h. The mixture was quenched with 1N HCl and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography on silica gel (eluting with hexane/ethyl acetate = 5:1) to give the title product (28.8 mg, 0.088 mmol).

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.51 (1H, m), 3.92 (1H, dd, *J* = 6.8, 6.1 Hz), 3.78 (1H, m), 3.53 (1H, d, *J* = 13.9 Hz), 3.46 (1H, d, *J* = 13.9 Hz), 3.21 (1H, ddd, *J* = 9.8, 8.5, 4.6 Hz), 1.56-2.24 (11H, m), 1.29-1.50 (2H, m), 1.15 (3H, s), 0.98 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.9, 74.3, 65.2, 53.1, 49.0, 48.3, 47.8, 44.6, 38.5, 34.2, 32.8, 28.6, 26.4, 22.1, 20.8, 19.9; IR (neat) 3497(br), 2959, 1668, 1395, 1329, 1269, 1236, 1217, 1167, 1134 cm^{-1}; HRMS (ESI) exact mass calcd. for $C_{16}H_{25}NO_4S$: *m/z* 350.1397 ([M + Na]$^+$), found: *m/z* 350.1395 ([M + Na]$^+$); $[\alpha]_D^{24}$ = +99.4 (*c* = 1.0, $CHCl_3$).

_N_-[(1_S_,2_S_)-1-hydroxy-1-(2-methoxy-2-oxoethyl)cyclopentan-2-carbonyl] (+)-camphorsultam (11).

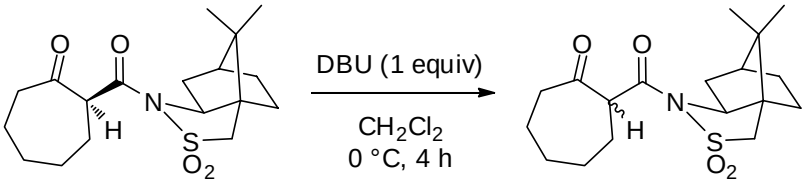


To a stirred solution of *N*-(2-diazo)acetyl (+)-camphorsultam (56.7 mg, 0.20 mmol) and cyclobutanone (15.7 μL, 0.21 mmol) in dichloromethane (1.0 mL) was added $BF_3{\cdot}OEt_2$ (25.3 μL, 0.20 mmol) at –78 °C under Ar atmosphere. After stirring for 6 h, 1-(*tert*-butyldimethylsiloxy)-1-methoxyethene (87.3 μL, 0.40 mmol) was added to the solution dropwise at –78 °C. The reaction mixture was then warmed up to –20 °C and stirred at the same temperature for additional 16 h. The mixture was quenched with aq $NaHCO_3$ and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography on silica gel (eluting with hexane/ethyl acetate = 5:1) to give the title product (47.9 mg, 0.12 mmol).

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.79 (1H, m), 3.93 (1H, app t, *J* = 6.6 Hz), 3.66 (3H, s), 3.51 (1H, d, *J* = 13.9 Hz), 3.45 (1H, d, *J* = 13.9 Hz), 3.18 (1H, t, *J* = 9.0 Hz), 2.68 (2H, s), 2.25 (1H, m), 1.83-2.15 (8H, m), 1.67-1.82 (2H, m), 1.30-1.47 (2H, m), 1.13 (3H, s), 0.98 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.3, 171.2, 80.6, 65.1, 53.0, 51.5, 51.1, 48.3, 47.8, 44.6, 44.1, 38.9, 38.3, 32.8, 29.9, 26.4, 21.3, 20.8, 19.8; IR (neat) 3447(br), 2955, 1736, 1663, 1404, 1333, 1271, 1238, 1221, 1136 cm^{-1}; HRMS (ESI) exact mass calcd. for

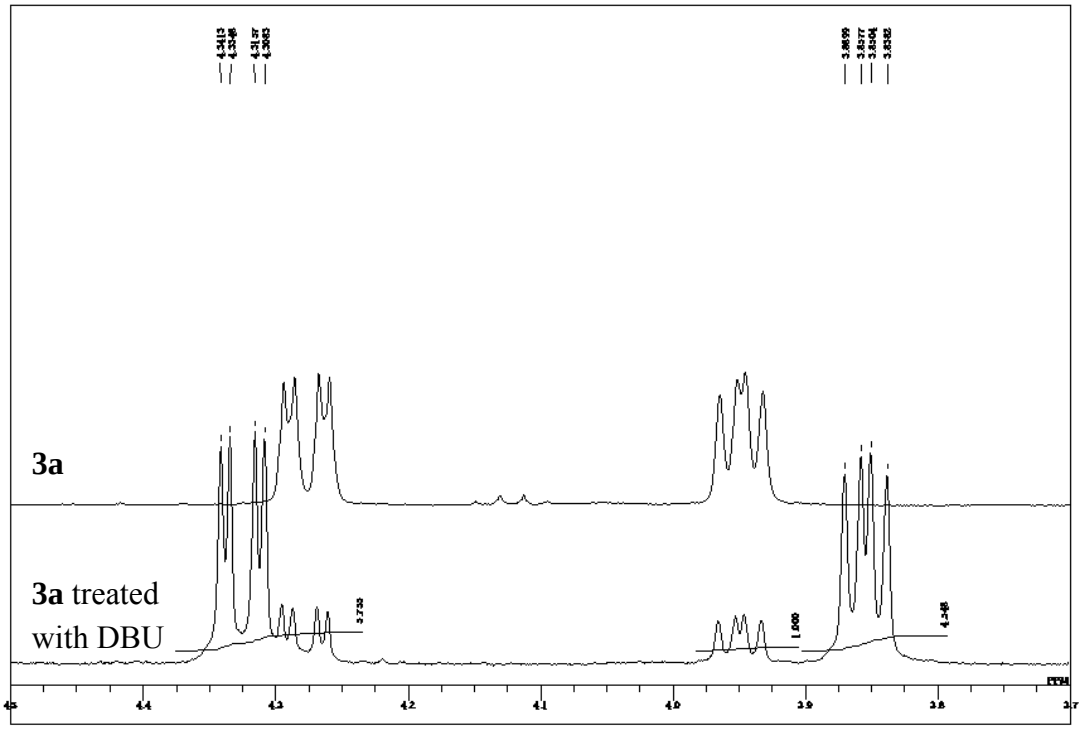
$C_{19}H_{29}NO_6S$: *m/z* 422.1608 ($[M + Na]^+$), found: *m/z* 422.1598 ($[M + Na]^+$); $[\alpha]_D^{20}$ = +82.1 (*c* = 1.0, $CHCl_3$).

Epimerization experiment of 3a with DBU (ref 8).

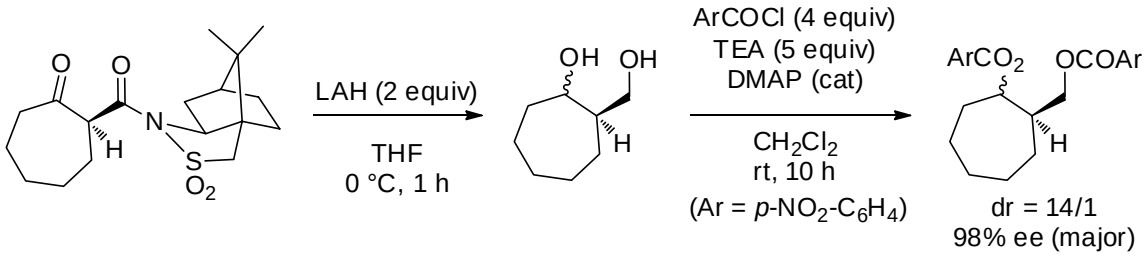


3a, dr = >20/1

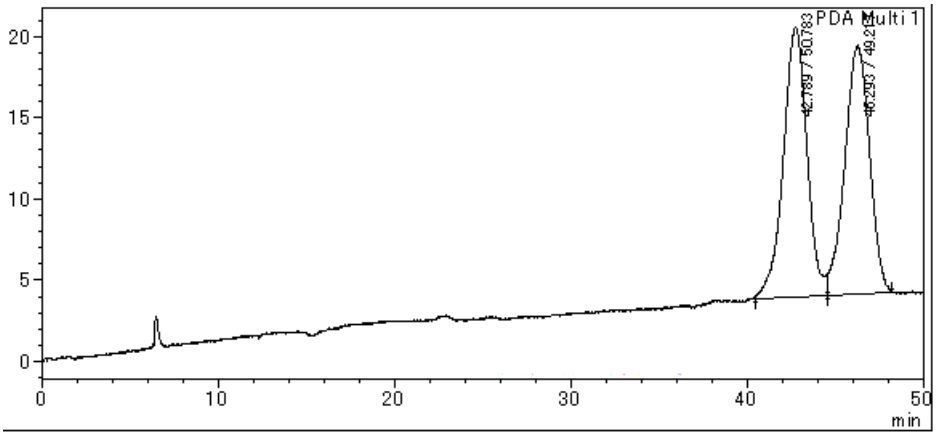
dr = 1/4.6

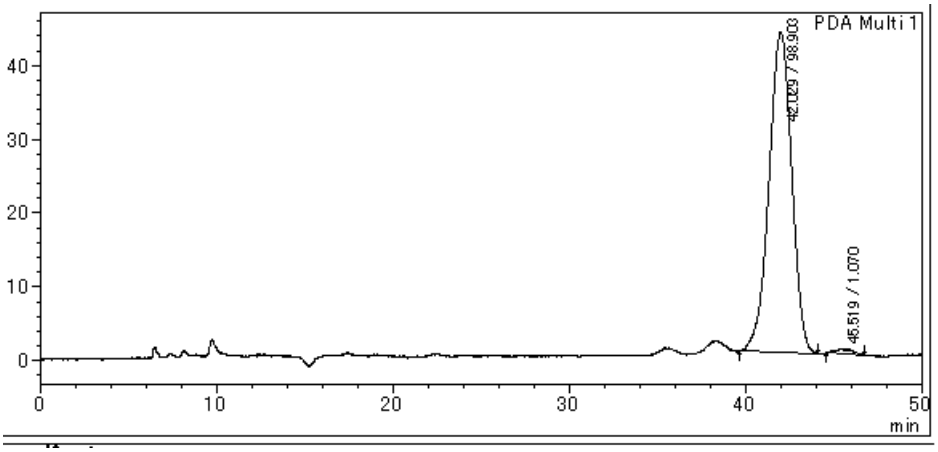


Determination of the ee value after the reductive detachment of the chiral auxiliary (ref 9).

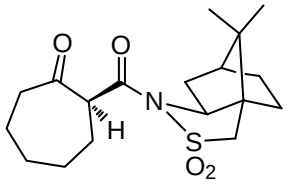


The enantiomeric purity was determined by HPLC analysis (Daicel CHIRALPAK OD-H, hexane/isopropanol = 9:1, flow rate = 0.5 mL/min, retention time; 42.0 min (major), 45.5 (minor)).





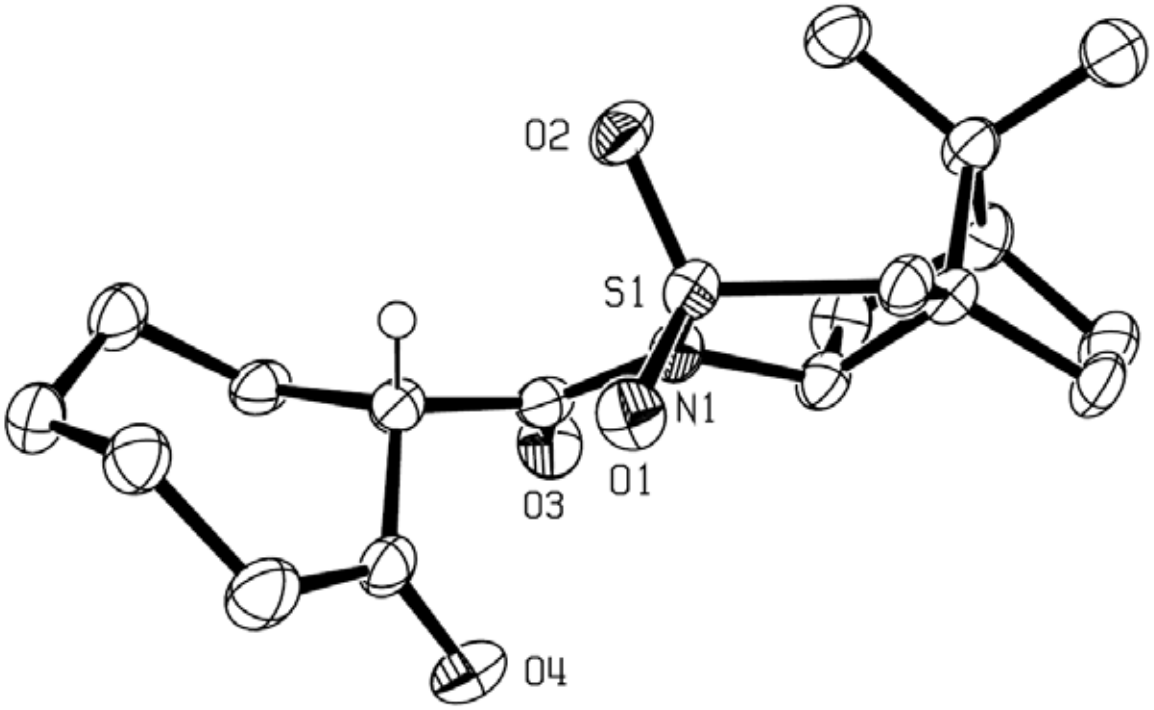
X-ray crystallographic analysis of *N*-[(2*S*)-1-oxocycloheptan-2-carbonyl] (+)-camphorsultam (3a).



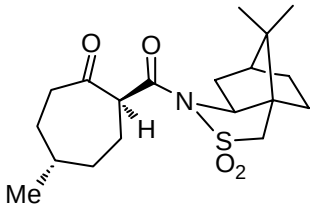
The product was recrystallized from hexane/CH_2Cl_2. The single crystal was mounted on a MicroMesh™ (MiTeGen). Data of X-ray diffraction were collected by a Rigaku RAXIS-RAPID Imaging Plate two-dimensional area detector using graphite-monochromated CuKa (λ = 1.54187 Å) to a maximam 2θ value of 136.5°. The crystal structure was solved by the direct methods and refined by the full-matrix least squares using the program SHELXL-97.[5] All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined by using the riding model. The crystallographic data were summarized in the following table.

empirical formula	$C_{18}H_{27}NO_4S$
formula weight	353.48
crystal system	orthorhombic
space group	$P2_12_12_1$ (#19)
a, Å	10.9574(2)
b, Å	11.6430(2)
c, Å	13.8557(3)
V , Å^3	1767.66(6)
Z	4
D_{calc}, g/cm^3	1.328
T, °C	–150
μ (CuKα), cm^{-1}	18.099
no. of reflns meased	18246
no. of reflns obsd	3221
no. of reflns variable	218
R (All reflections)	0.0380
R_w (All reflections)	0.0901
Goodness of Fit	1.078

The crystal structure has been deposited at the Cambridge Crystallographic Data Centre (CCDC 772682). The data can be obtained free of charge via the Internet at www.ccdc.cam.ac.uk/conts/retrieving.html.


O2
S1
N1
O1
O3
O4

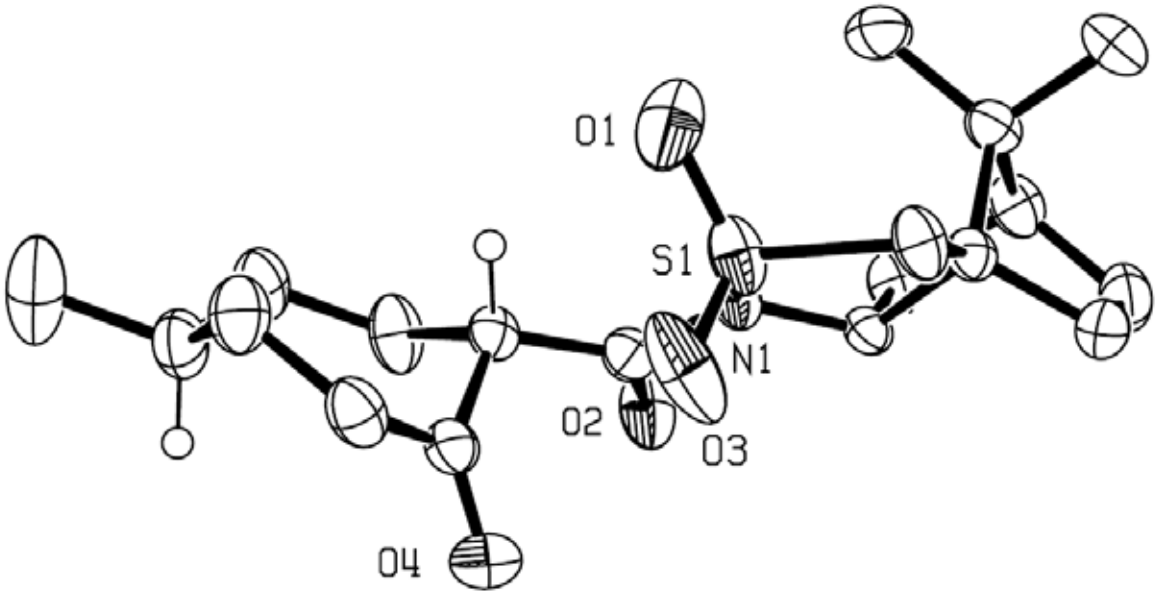
X-ray crystallographic analysis of *N*-[(2*S*,5*S*)-1-oxo-5-methylcycloheptan-2-carbonyl] (+)-camphorsultam (5a).



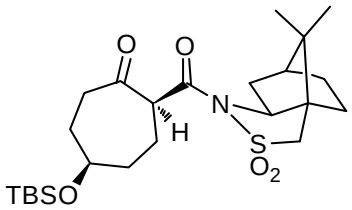
The product was recrystallized from hexane/CH_2Cl_2. The single crystal was mounted on a MicroMesh™ (MiTeGen). Data of X-ray diffraction were collected by a Rigaku RAXIS-RAPID Imaging Plate two-dimensional area detector using graphite-monochromated CuKa (λ = 1.54187 Å) to a maximam 2θ value of 136.5°. The crystal structure was solved by the direct methods and refined by the full-matrix least squares using the program SHELXL-97.[5] All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined by using the riding model. The crystallographic data were summarized in the following table.

empirical formula	$C_{19}H_{29}NO_4S$
formula weight	367.50
crystal system	monoclinic
space group	$P2_1$ (#4)
a, Å	7.8197(2)
b, Å	12.3340(4)
c, Å	10.2203(4)
β, °	97.015(2)
V, Å^3	978.36(5)
Z	2
D_{calc}, g/cm^3	1.247
T, °C	–150
μ (CuKα), cm^{-1}	16.537
no. of reflns meased	10503
no. of reflns obsd	3210
no. of reflns variable	228
R (All reflections)	0.0404
R_w (All reflections)	0.0883
Goodness of Fit	1.070

The crystal structure has been deposited at the Cambridge Crystallographic Data Centre (CCDC 772683). The data can be obtained free of charge via the Internet at www.ccdc.cam.ac.uk/conts/retrieving.html.


O1
S1
N1
O2
O3
O4

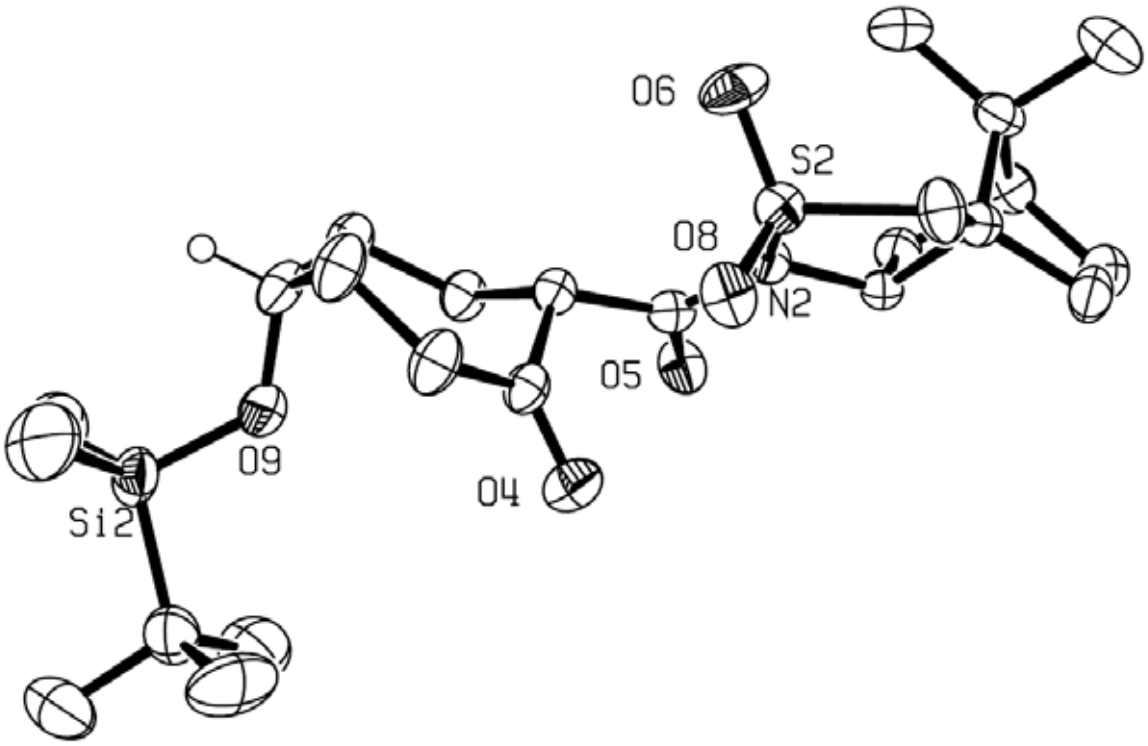
X-ray crystallographic analysis of *N*-[(2*S*,5*R*)-1-oxo-5-(*tert*-butyldimethylsiloxy)-cycloheptan-2-carbonyl] (+)-camphorsultam (5e).



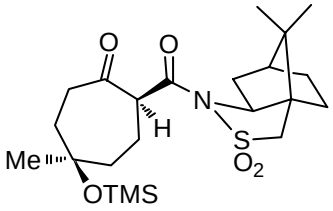
The product was recrystallized from hexane/CH_2Cl_2. The single crystal was mounted on a MicroMesh™ (MiTeGen). Data of X-ray diffraction were collected by a Rigaku RAXIS-RAPID Imaging Plate two-dimensional area detector using graphite-monochromated CuKa (λ = 1.54187 Å) to a maximam 2θ value of 136.5°. The crystal structure was solved by the direct methods and refined by the full-matrix least squares using the program SHELXL-97.[5] All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined by using the riding model. The crystallographic data were summarized in the following table.

empirical formula	$C_{24}H_{41}NO_5SSi$
formula weight	483.74
crystal system	orthorhombic
space group	$P2_12_12_1$ (#19)
a, Å	11.9185(2)
b, Å	16.6964(3)
c, Å	26.4700(5)
V , Å^3	5267.42(17)
Z	8
D_{calc}, g/cm^3	1.220
T, °C	–150
μ (CuKα), cm^{-1}	17.957
no. of reflns meased	56765
no. of reflns obsd	9633
no. of reflns variable	578
R (All reflections)	0.0501
R_w (All reflections)	0.1081
Goodness of Fit	1.090

The crystal structure has been deposited at the Cambridge Crystallographic Data Centre (CCDC 772684). The data can be obtained free of charge via the Internet at www.ccdc.cam.ac.uk/conts/retrieving.html.


O6
S2
O8
N2
O5
O9
O4
Si2

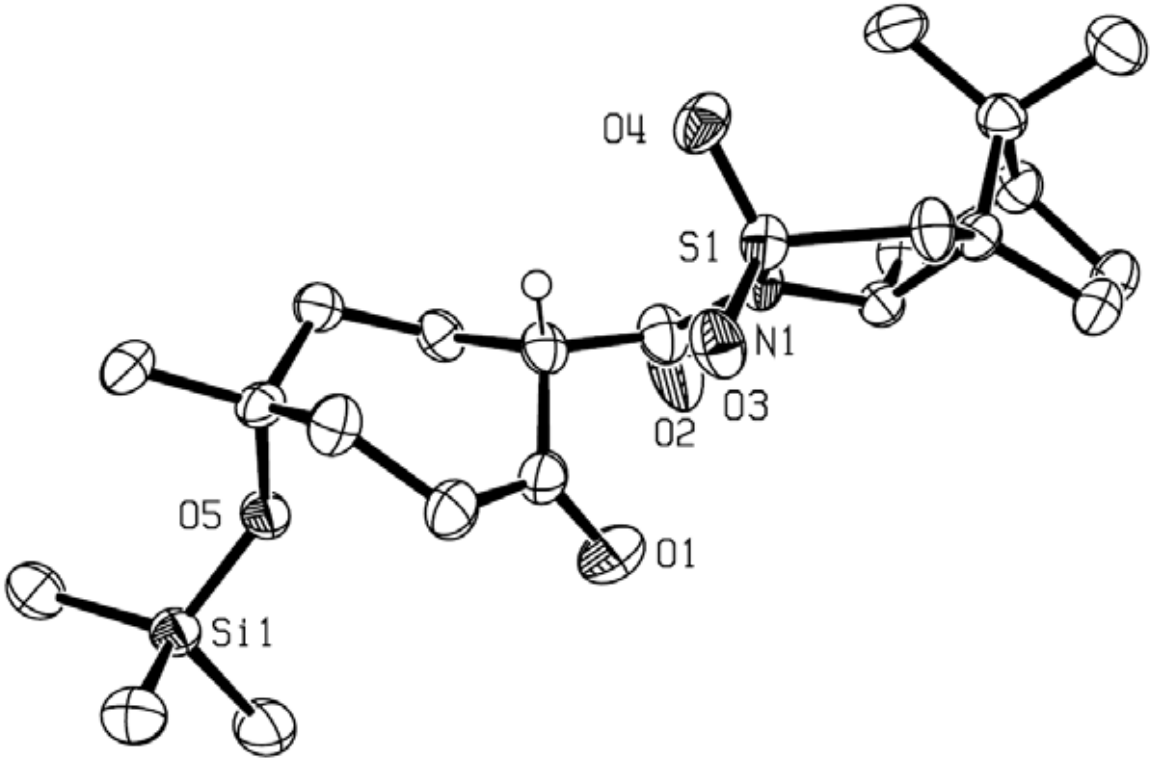
X-ray crystallographic analysis of *N*-[(2*S*,5*R*)-1-oxo-5-methyl-5-trimethylsiloxy-cycloheptan-2-carbonyl] (+)-camphorsultam (5f).



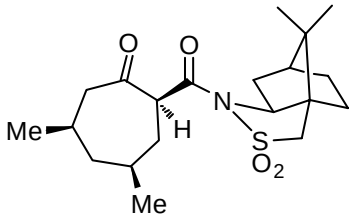
The product was recrystallized from hexane/CH_2Cl_2. The single crystal was mounted on a MicroMesh™ (MiTeGen). Data of X-ray diffraction were collected by a Rigaku RAXIS-RAPID Imaging Plate two-dimensional area detector using graphite-monochromated CuKa (λ = 1.54187 Å) to a maximam 2θ value of 136.5°. The crystal structure was solved by the direct methods and refined by the full-matrix least squares using the program SHELXL-97.[5] All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined by using the riding model. The crystallographic data were summarized in the following table.

empirical formula	$C_{22}H_{37}NO_5SSi$
formula weight	455.68
crystal system	monoclinic
space group	$P2_1$ (#4)
a, Å	9.7818(2)
b, Å	11.7037(2)
c, Å	10.7979(2)
β, °	102.0685(12)
V, Å^3	1208.85(4)
Z	2
D_{calc}, g/cm^3	1.252
T, °C	–150
μ (CuKα), cm^{-1}	19.259
no. of reflns meased	12589
no. of reflns obsd	4260
no. of reflns variable	272
R (All reflections)	0.0465
R_w (All reflections)	0.0927
Goodness of Fit	1.009

The crystal structure has been deposited at the Cambridge Crystallographic Data Centre (CCDC 772685). The data can be obtained free of charge via the Internet at www.ccdc.cam.ac.uk/conts/retrieving.html.


O4
S1
N1
O3
O2
O5
O1
Si1

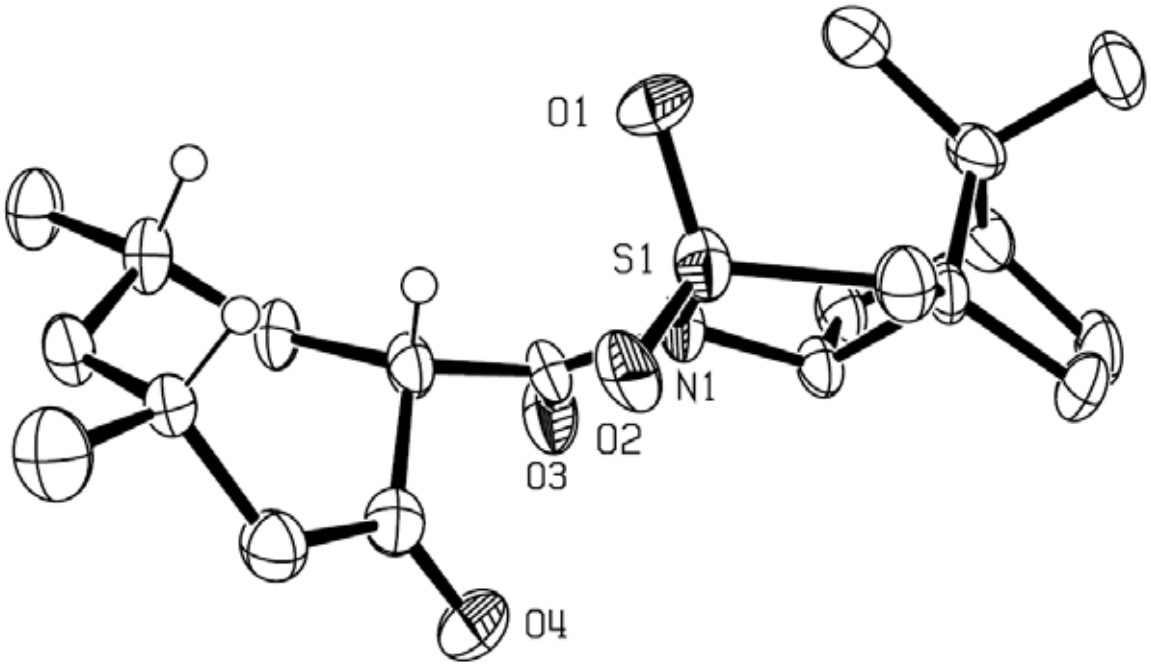
X-ray crystallographic analysis of *N*-[(2*S*,4*S*,6*R*)-1-oxo-4,6-dimethylcycloheptan-2-carbonyl] (+)-camphorsultam (5h).



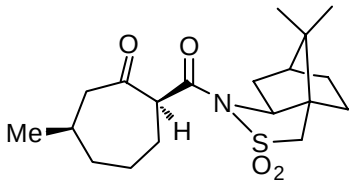
The product was recrystallized from hexane/CH_2Cl_2. The single crystal was mounted on a MicroMesh™ (MiTeGen). Data of X-ray diffraction were collected by a Rigaku RAXIS-RAPID Imaging Plate two-dimensional area detector using graphite-monochromated CuKa (λ = 1.54187 Å) to a maximam 2θ value of 136.5°. The crystal structure was solved by the direct methods and refined by the full-matrix least squares using the program SHELXL-97.[5] All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined by using the riding model. The crystallographic data were summarized in the following table.

empirical formula	$C_{20}H_{31}NO_4S$
formula weight	381.53
crystal system	orthorhombic
space group	$P2_12_12_1$ (#19)
a, Å	11.1745(2)
b, Å	12.9656(2)
c, Å	13.4284(3)
V , Å^3	1945.57(6)
Z	4
D_{calc}, g/cm^3	1.302
T, °C	–150
μ (CuKα), cm^{-1}	16.819
no. of reflns meased	20344
no. of reflns obsd	3543
no. of reflns variable	236
R (All reflections)	0.1266
R_w (All reflections)	0.1956
Goodness of Fit	1.188

The crystal structure has been deposited at the Cambridge Crystallographic Data Centre (CCDC 772686). The data can be obtained free of charge via the Internet at www.ccdc.cam.ac.uk/conts/retrieving.html.


O1
S1
N1
O2
O3
O4

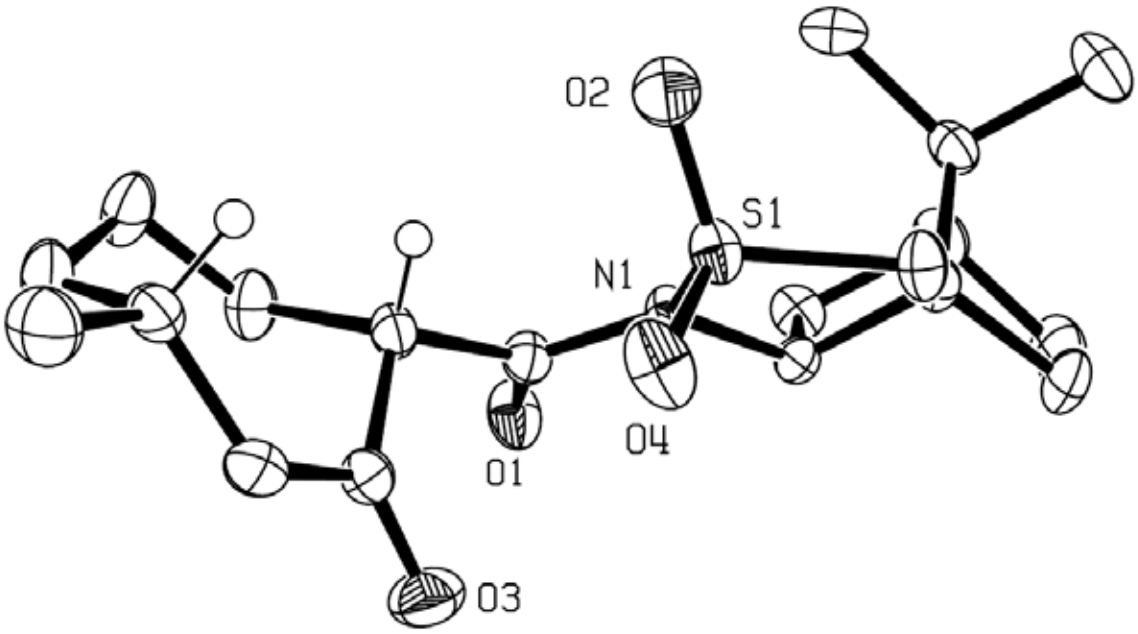
X-ray crystallographic analysis of *N*-[(2*S*,6*R*)-1-oxo-6-methylcycloheptan-2-carbonyl] (+)-camphorsultam (7a).



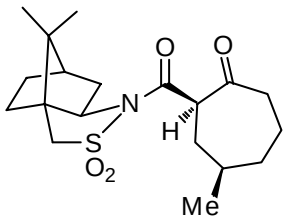
The product was recrystallized from hexane/CH_2Cl_2. The single crystal was mounted on a MicroMesh™ (MiTeGen). Data of X-ray diffraction were collected by a Rigaku RAXIS-RAPID Imaging Plate two-dimensional area detector using graphite-monochromated CuKa (λ = 1.54187 Å) to a maximam 2θ value of 136.5°. The crystal structure was solved by the direct methods and refined by the full-matrix least squares using the program SHELXL-97.[5] All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined by using the riding model. The crystallographic data were summarized in the following table.

empirical formula	$C_{19}H_{29}NO_4S$
formula weight	367.50
crystal system	orthorhombic
space group	$P2_12_12_1$ (#19)
a, Å	12.6668(2)
b, Å	13.3989(2)
c, Å	11.1466(2)
V , Å^3	1891.83(5)
Z	4
D_{calc}, g/cm^3	1.290
T, °C	–150
μ (CuKα), cm^{-1}	17.104
no. of reflns meased	19346
no. of reflns obsd	3423
no. of reflns variable	227
R (All reflections)	0.0344
R_w (All reflections)	0.0852
Goodness of Fit	1.138

The crystal structure has been deposited at the Cambridge Crystallographic Data Centre (CCDC 772688). The data can be obtained free of charge via the Internet at www.ccdc.cam.ac.uk/conts/retrieving.html.


O2
S1
N1
O4
O1
O3

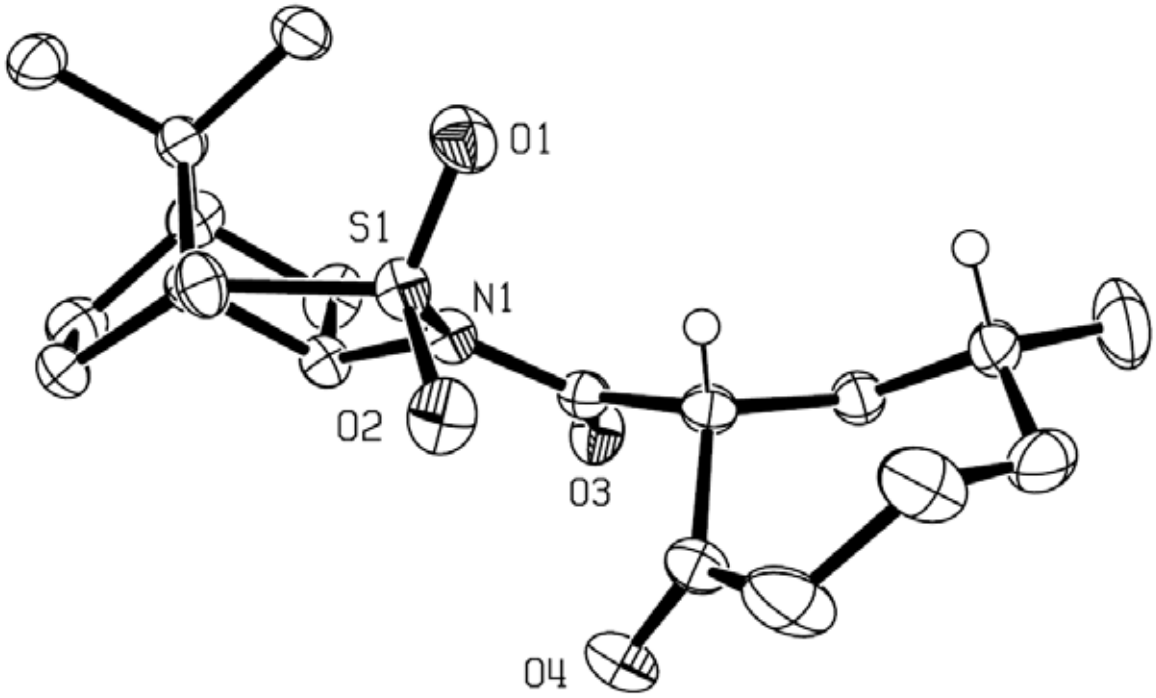
X-ray crystallographic analysis of *N*-[(2*R*,4R)-1-oxo-4-methylcycloheptan-2-carbonyl] (–)-camphorsultam (7b).



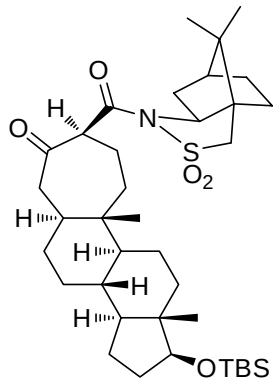
The product was recrystallized from hexane/CH_2Cl_2. The single crystal was mounted on a MicroMesh™ (MiTeGen). Data of X-ray diffraction were collected by a Rigaku RAXIS-RAPID Imaging Plate two-dimensional area detector using graphite-monochromated CuKa (λ = 1.54187 Å) to a maximam 2θ value of 136.5°. The crystal structure was solved by the direct methods and refined by the full-matrix least squares using the program SHELXL-97.[5] All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined by using the riding model. The crystallographic data were summarized in the following table.

empirical formula	$C_{19}H_{29}NO_4S$
formula weight	367.50
crystal system	orthorhombic
space group	$P2_12_12_1$ (#19)
a, Å	8.22600(15)
b, Å	11.6586(2)
c, Å	19.6399(4)
V , Å^3	1883.54(6)
Z	4
D_{calc}, g/cm^3	1.296
T, °C	–150
μ (CuKα), cm^{-1}	17.180
no. of reflns meased	19045
no. of reflns obsd	3425
no. of reflns variable	227
R (All reflections)	0.0365
R_w (All reflections)	0.0864
Goodness of Fit	1.132

The crystal structure has been deposited at the Cambridge Crystallographic Data Centre (CCDC 772687). The data can be obtained free of charge via the Internet at www.ccdc.cam.ac.uk/conts/retrieving.html.


O1
S1
N1
O2
O3
O4

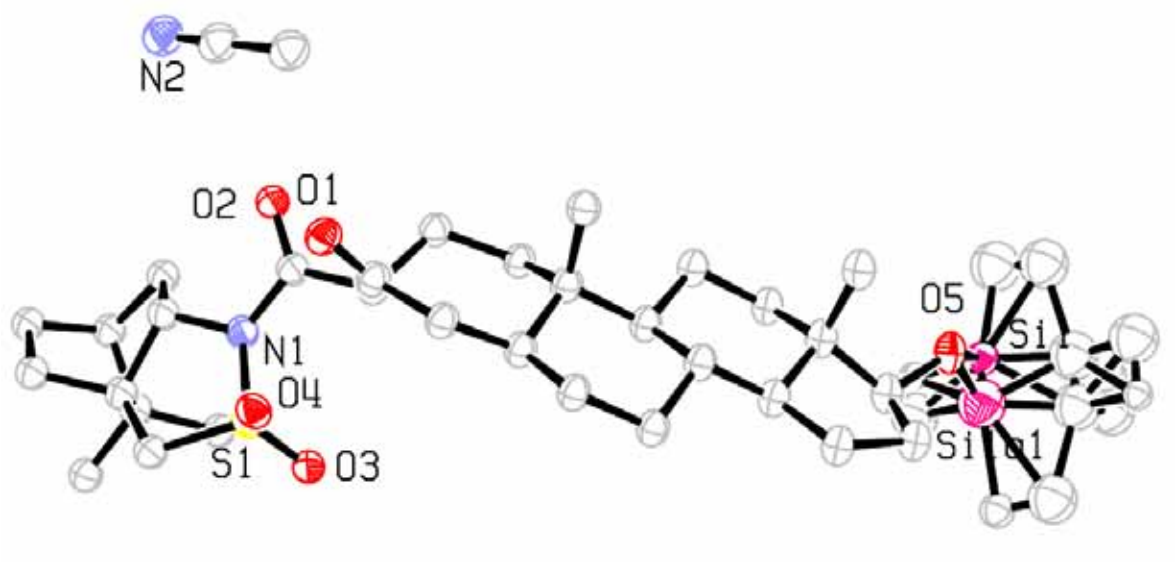
X-ray crystallographic analysis of 9·CH_3CN.



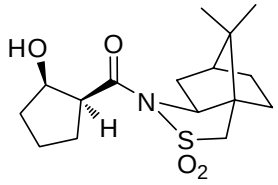
The product was recrystallized from CH_3CN/CH_2Cl_2. The single crystal was mounted on a MicroMesh™ (MiTeGen). Data of X-ray diffraction were collected by a Rigaku RAXIS-RAPID Imaging Plate two-dimensional area detector using graphite-monochromated CuKa (λ = 1.54187 Å) to a maximam 2θ value of 136.5°. The crystal structure was solved by the direct methods and refined by the full-matrix least squares using the program SHELXL-97.[5] All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined by using the riding model. The crystallographic data were summarized in the following table.

empirical formula	$C_{39}H_{64}N_2O_5SSi$
formula weight	701.09
crystal system	orthorhombic
space group	$P2_12_12_1$ (#19)
a, Å	7.49798(16)
b, Å	12.6702(3)
c, Å	41.5163(9)
V , Å^3	3944.09(15)
Z	4
D_{calc}, g/cm^3	1.181
T, °C	–150
μ (CuKα), cm^{-1}	13.550
no. of reflns obsd	7143
no. of reflns variable	395
R (All reflections)	0.0820
R_w (All reflections)	0.2257
Goodness of Fit	1.107

The crystal structure has been deposited at the Cambridge Crystallographic Data Centre (CCDC 772689). The data can be obtained free of charge via the Internet at www.ccdc.cam.ac.uk/conts/retrieving.html.


N2
O2
O1
N1
O4
S1
O3
O5
Si
Si
O1

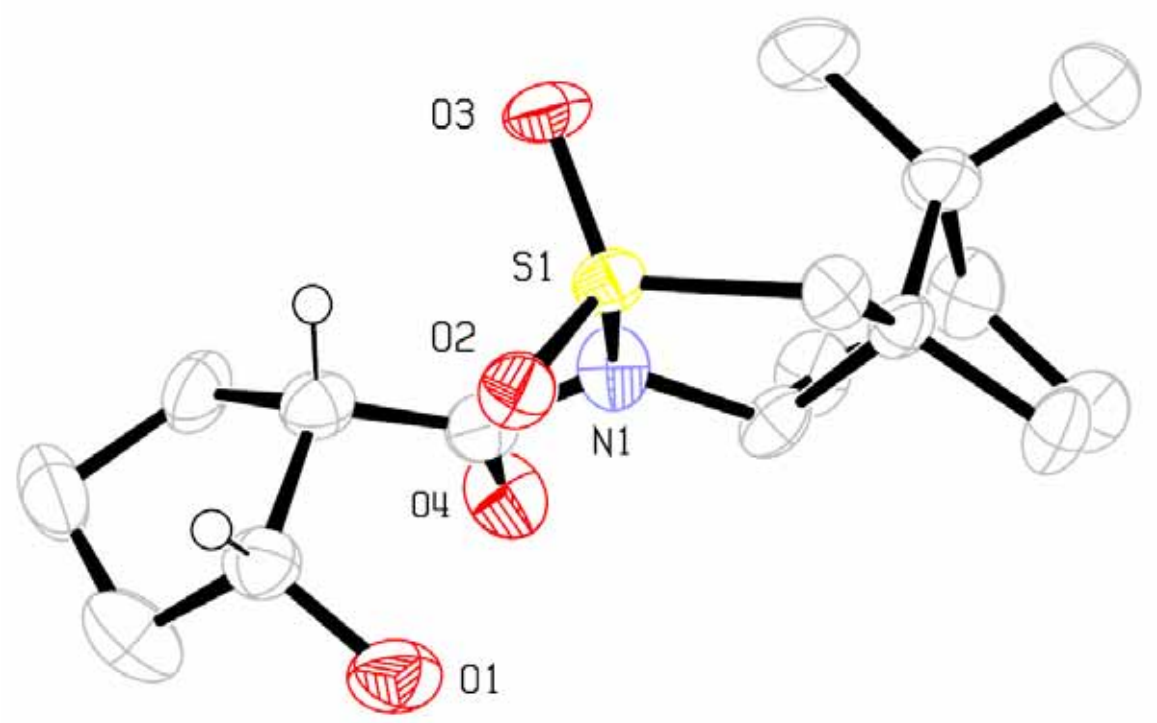
X-ray crystallographic analysis of *N*-[(1*R*,2*S*)-1-hydroxycyclopentan-2-carbonyl] (+)-camphorsultam (10).



The product was recrystallized from hexane/CH_2Cl_2. The single crystal was mounted on a MicroMesh™ (MiTeGen). Data of X-ray diffraction were collected by a Rigaku RAXIS-RAPID Imaging Plate two-dimensional area detector using graphite-monochromated CuKa (λ = 1.54187 Å) to a maximam 2θ value of 136.5°. The crystal structure was solved by the direct methods and refined by the full-matrix least squares using the program SHELXL-97.[5] All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined by using the riding model. The crystallographic data were summarized in the following table.

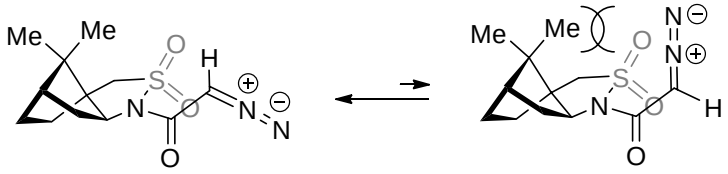
empirical formula	$C_{16}H_{25}NO_4S$
formula weight	327.44
crystal system	monoclinic
space group	$P2_1$ (#4)
a, Å	7.7300(2)
b, Å	21.7617(6)
c, Å	9.9870(3)
β, °	90.343(2)
V , Å^3	1679.97(9)
Z	4
D_{calc}, g/cm^3	18.613
T, °C	–150
μ (CuKα), cm^{-1}	18.613
no. of reflns meased	17491
no. of reflns obsd	5765
no. of reflns variable	399
R (All reflections)	0.1270
R_w (All reflections)	0.3501
Goodness of Fit	1.451

The crystal structure has been deposited at the Cambridge Crystallographic Data Centre (CCDC 772690). The data can be obtained free of charge via the Internet at www.ccdc.cam.ac.uk/conts/retrieving.html.

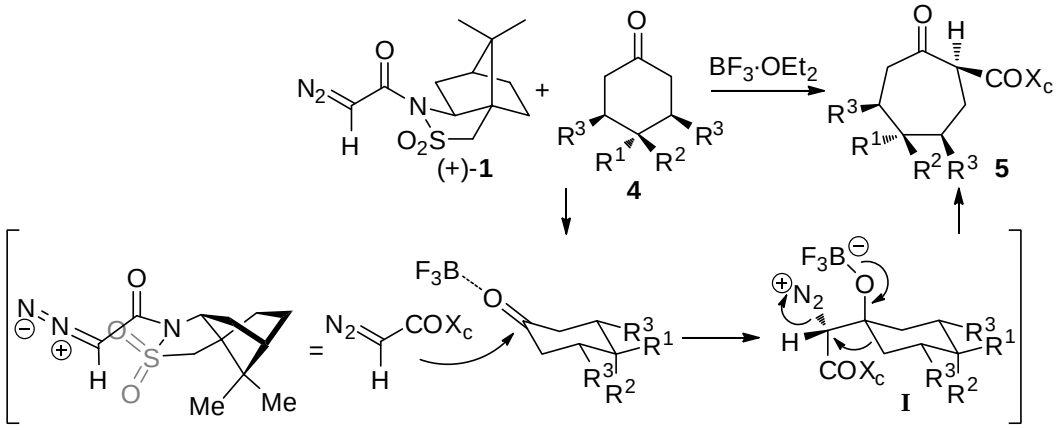

O3
S1
O2
N1
O4
O1

Discussion on the mechanism of the enantiodiscrimination by camphorsultam.

In our previous report on the use of *N*-α-acyl camphorsultam (*J. Am. Chem. Soc.,* 2009, **131**, 11280.), we hypothesized the SO_2 moiety of camphorsultam shields one enantiotopic face. In the case of the *N*-α-diazoacetyl camphorsultam (+)-**1** bearing an α-hydrogen atom, the O=C–C=N bond would preferentially form s-*cis* conformation to minimize the steric repulsion of the diazo moiety and camphorsultam.



To (+)-**1** in the s-*cis* conformation, the Lewis acid-activated cyclohexanone approaches from the less hindered side of the diazo carbon (from the top in the description below) to give the diazonium intermediate **I**. The migration of the carbon atom from this intermediate would proceed via the inversion of the configuration to generate the ring expanded product **5** with the stereochemistry actually observed in this research.



References.

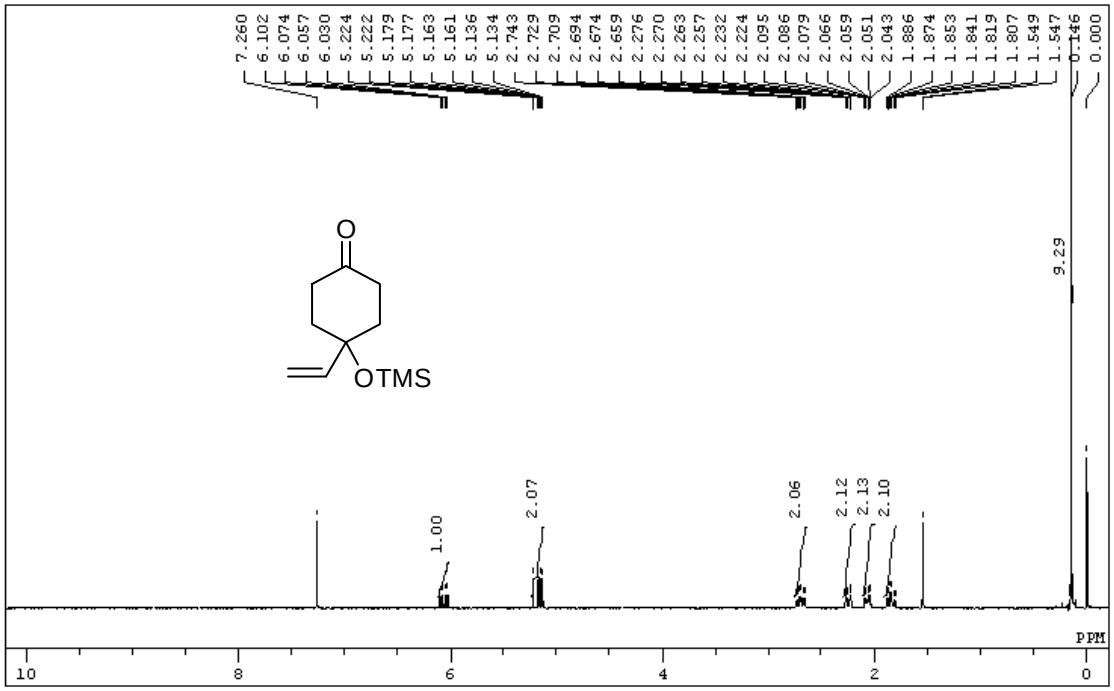
(1) T. Toma, J. Shimokawa, and T. Fukuyama, *Org. Lett*., 2007, **9**, 3195.

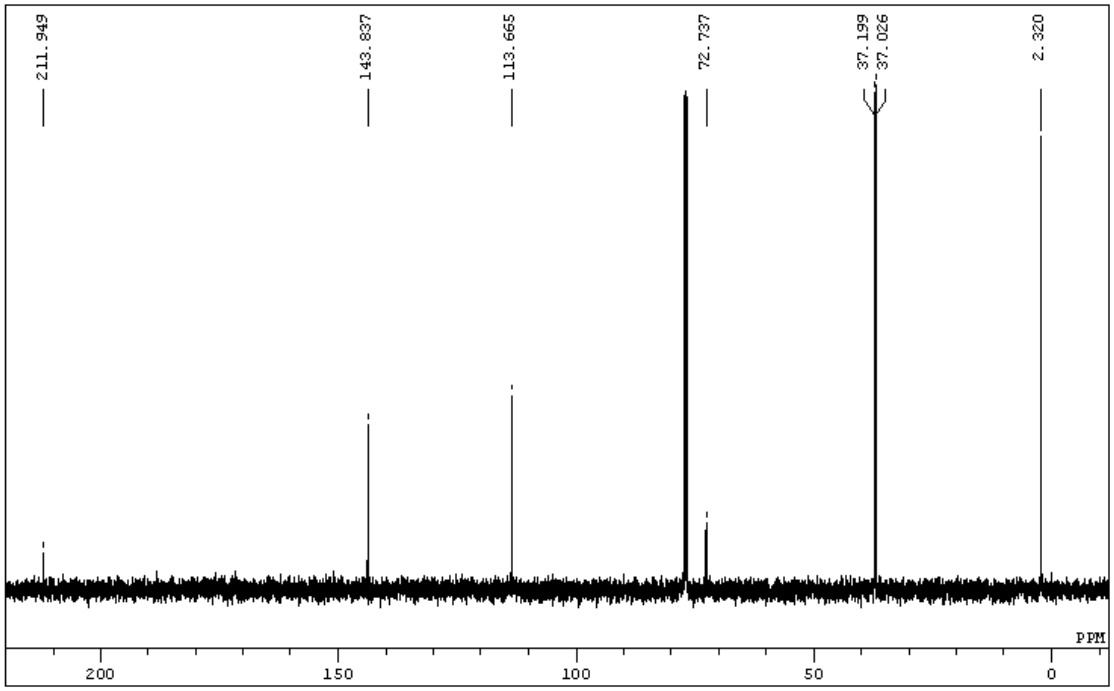
(2) J. B. Sweeney, A. A. Cantrill, A. B. McLaren, and S. Thobhani, *Tetrahedron*, 2006, **62**, 3681.

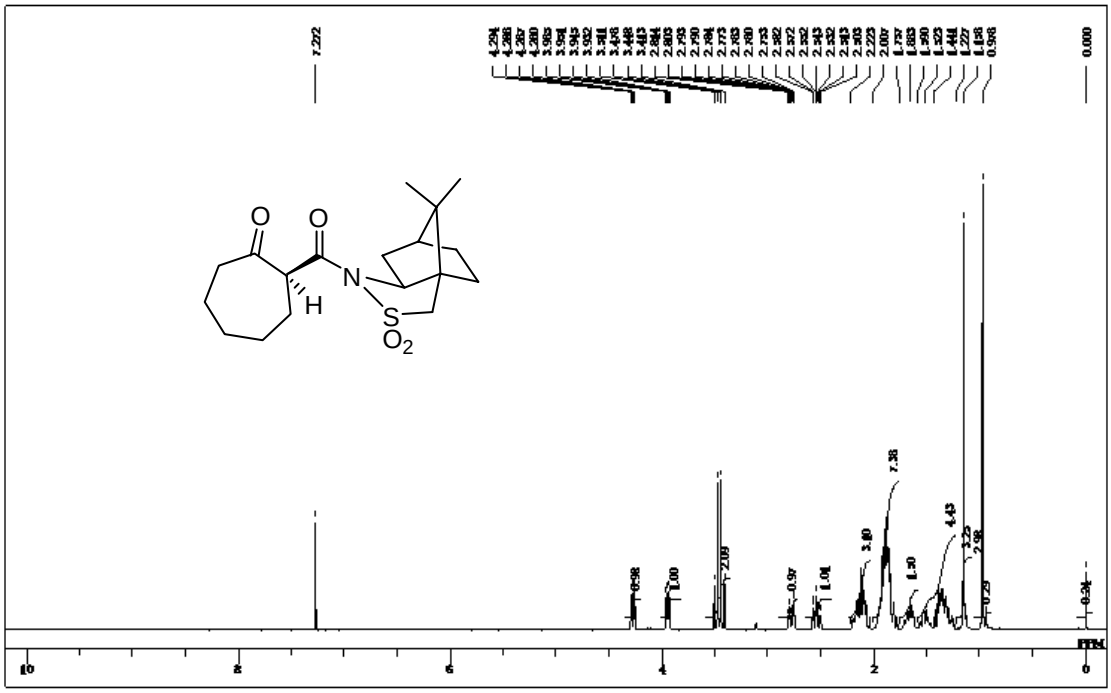
(3) M. Ma, L. Peng, C. Li, X. Zhang, and J. Wang, *J. Am. Chem. Soc*., 2005, **127**, 15016.

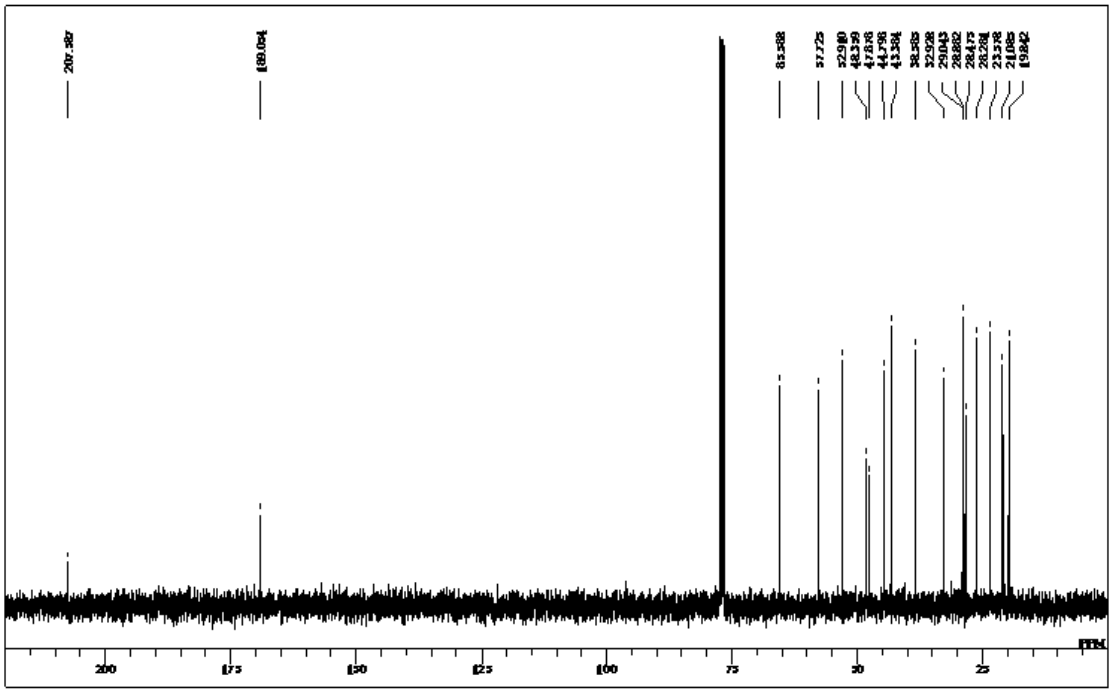
(4) (*a*) A. J. Frontier, S. J. Danishefsky, G. A. Koppel, and D. Meng, *Tetrahedron*, 1998, **54**, 12721; (*b*) R. A. Glennon, S.-s. Hong, M. Bondarev, H. Law, M. Dukat, S. Rakhit, P. Power, E. Fan, D. Kinneau, R. Kamboj, M. Teitler, K. Herrick-Davis, and C. Smith, *J. Med. Chem*., 1996, **36**, 314; (*c*) A. Malapelle, A. Coslovi, G. Doisneau, and J.-m. Beau, *J. Org. Chem*., 2007, **72**, 3145; (*d*) T. Hashimoto, Y. Naganawa, and K. Maruoka, *J. Am. Chem. Soc*., 2009, **131**, 6614; (*e*) C. A. G. M. Weijers, P. M. Könst, M. C. R. Franssen, and E. J. R. Sudhölter, *Org. Biomol. Chem*., 2007, **5**, 3106; (*f*) D. S. Ressy, D. V. Velde, and J. Aubé, *J. Org. Chem*., 2004, **69**, 1716; (*g*) C. H. Heathcock, and S. C. Smith, *J. Org. Chem*., 1994, **59**, 6828.

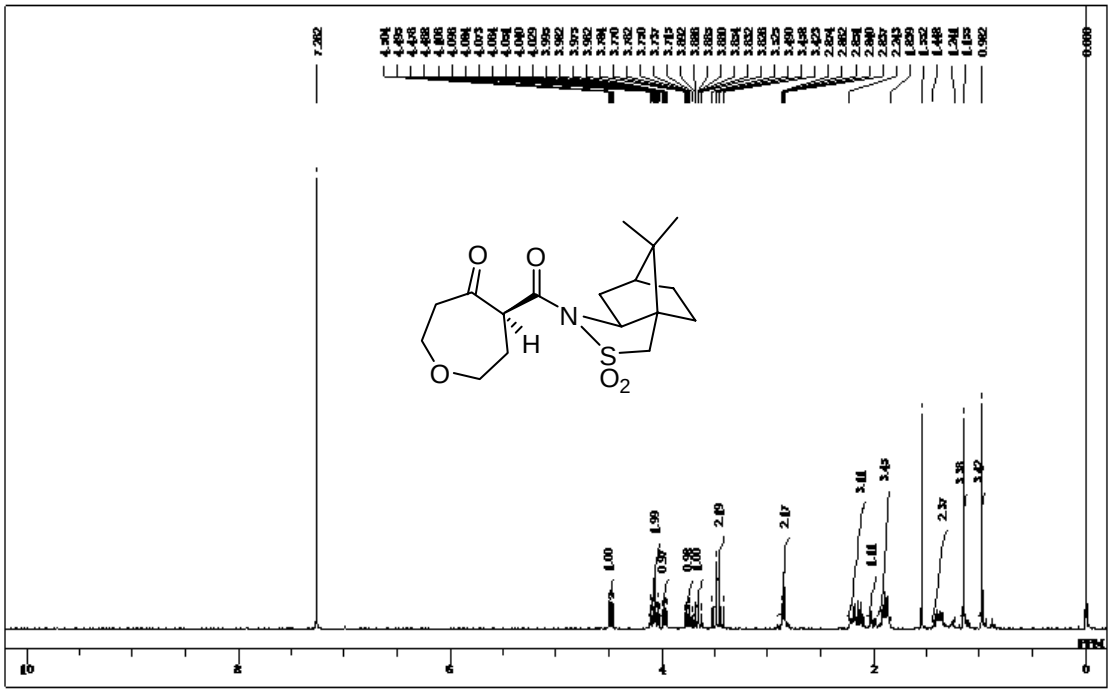
(5) G. M. Sheldrick, SHELX-97: Program for Crystal Structure Refinement, University of Gottingen, Germany, 1997.

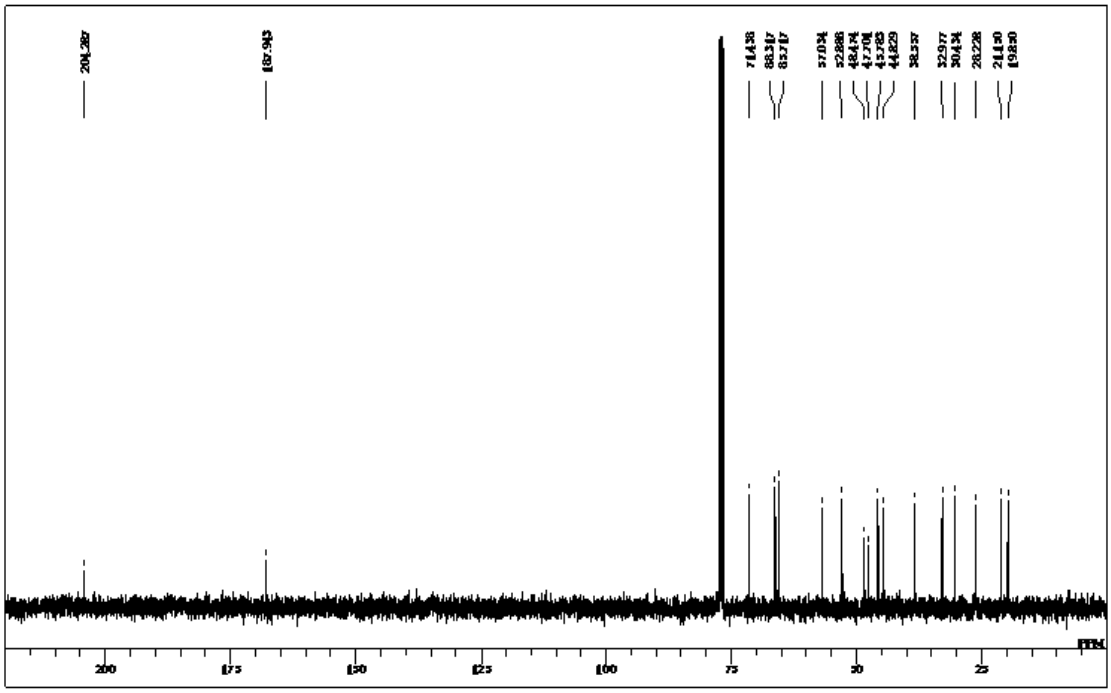

7.260
6.102
6.074
6.057
6.030
5.224
5.222
5.179
5.177
5.163
5.161
5.136
5.134
2.743
2.729
2.709
2.694
2.674
2.659
2.276
2.270
2.263
2.257
2.232
2.224
2.095
2.086
2.079
2.066
2.059
2.051
2.043
1.886
1.874
1.853
1.841
1.819
1.807
1.549
1.547
0.146
0.000
O
OTMS
9.29
1.00
2.07
2.06
2.12
2.13
2.10
PPM
10
8
6
4
2
0

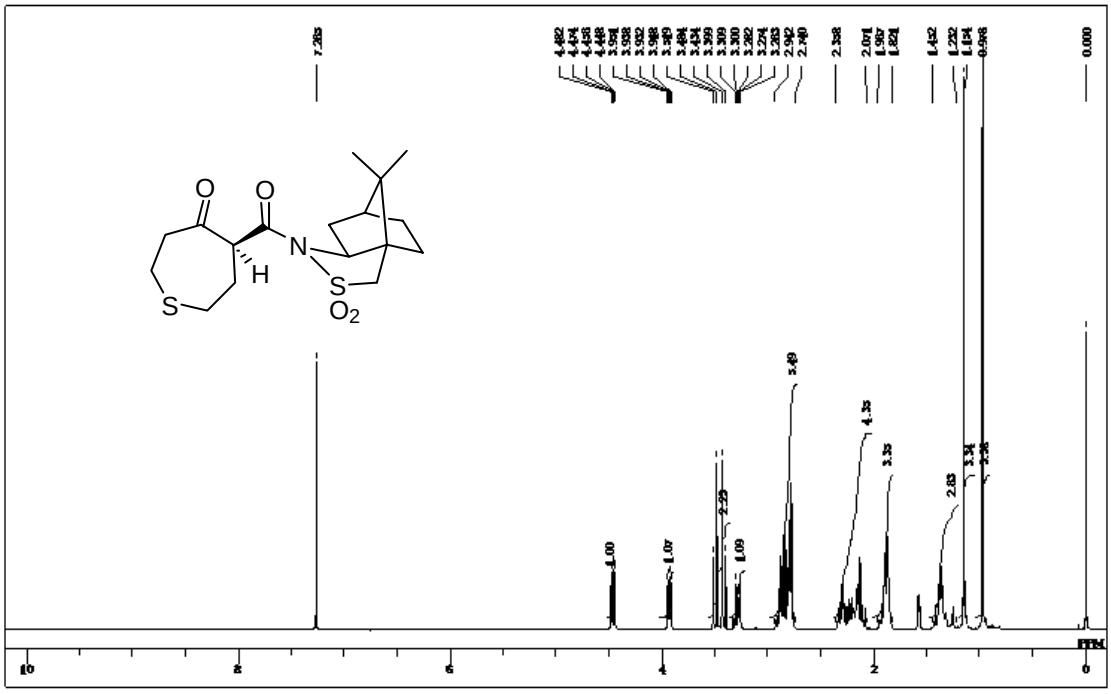

211.949
143.837
113.665
72.737
37.199
37.026
2.320
PPM
200
150
100
50
0

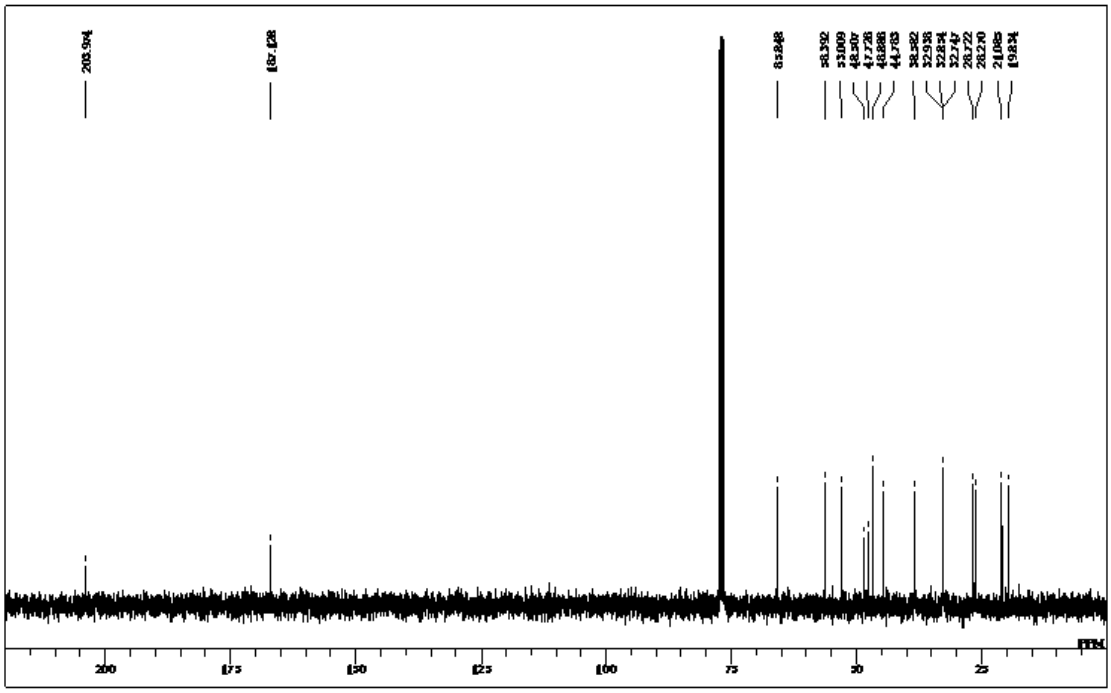

O
O
N
H
S
O2

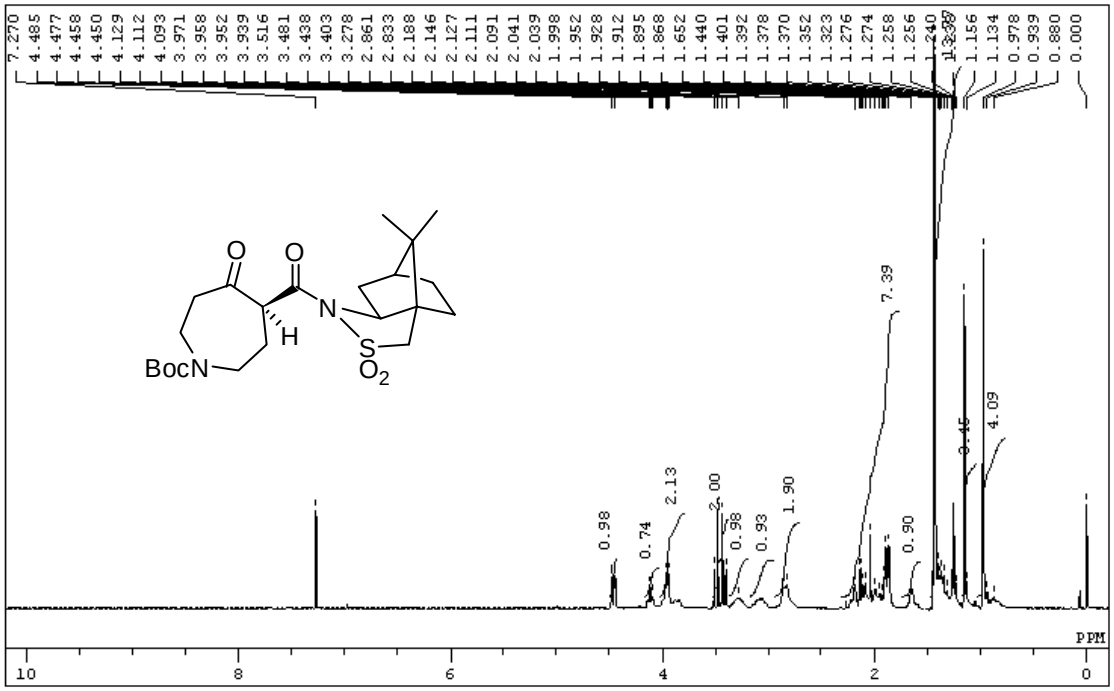


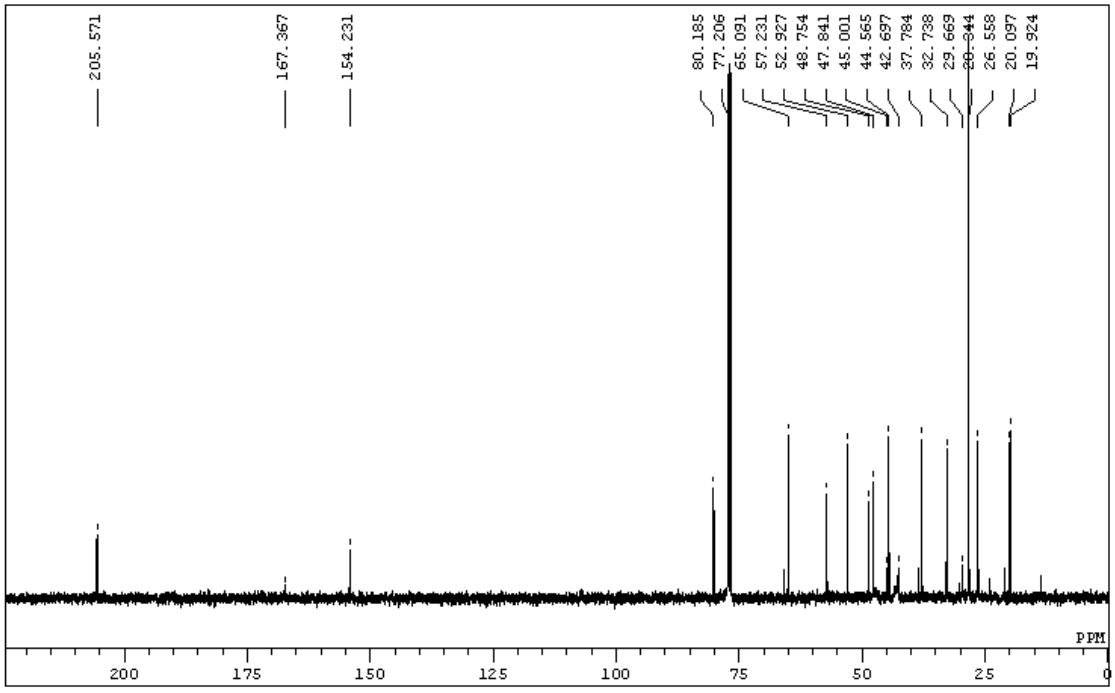

7.282
0.000
O
O
N
H
O
S
O2
1.00
1.99
0.97
0.98
1.00
2.09
2.17
3.41
1.41
3.45
2.37
3.38
3.42
10
8
6
4
2
0
PPM

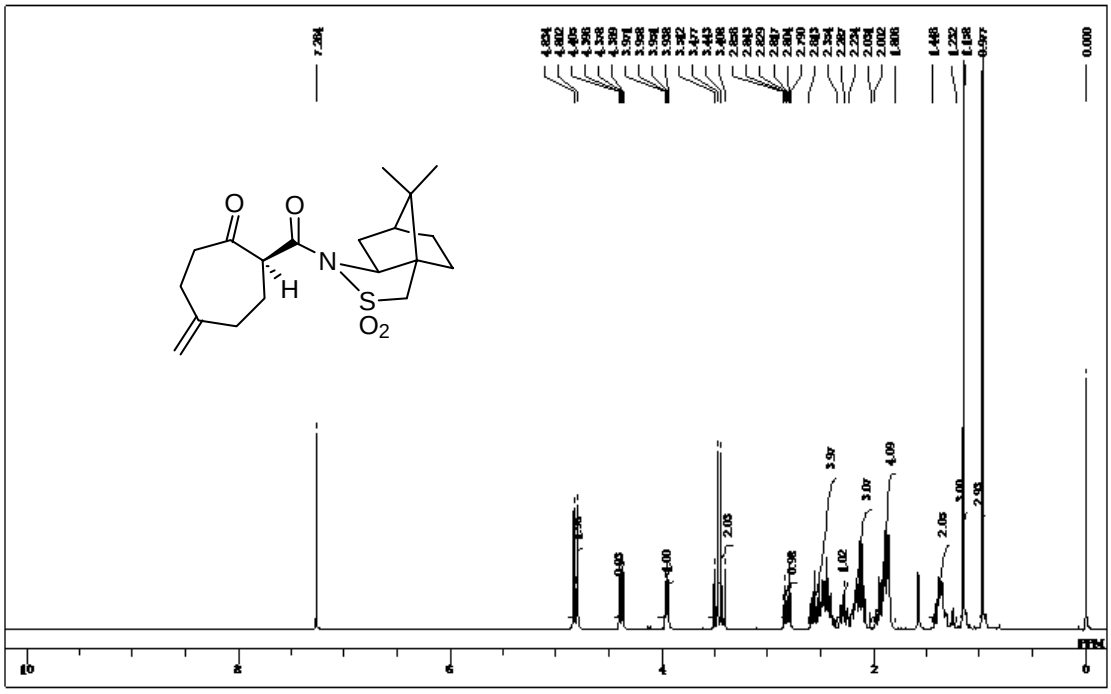

204.287
187.943
71.438
88.317
83.717
57.034
52.886
48.434
47.704
45.783
44.829
38.557
32.977
30.434
28.228
21.430
19.830
200
175
150
125
100
75
50
25
PPM

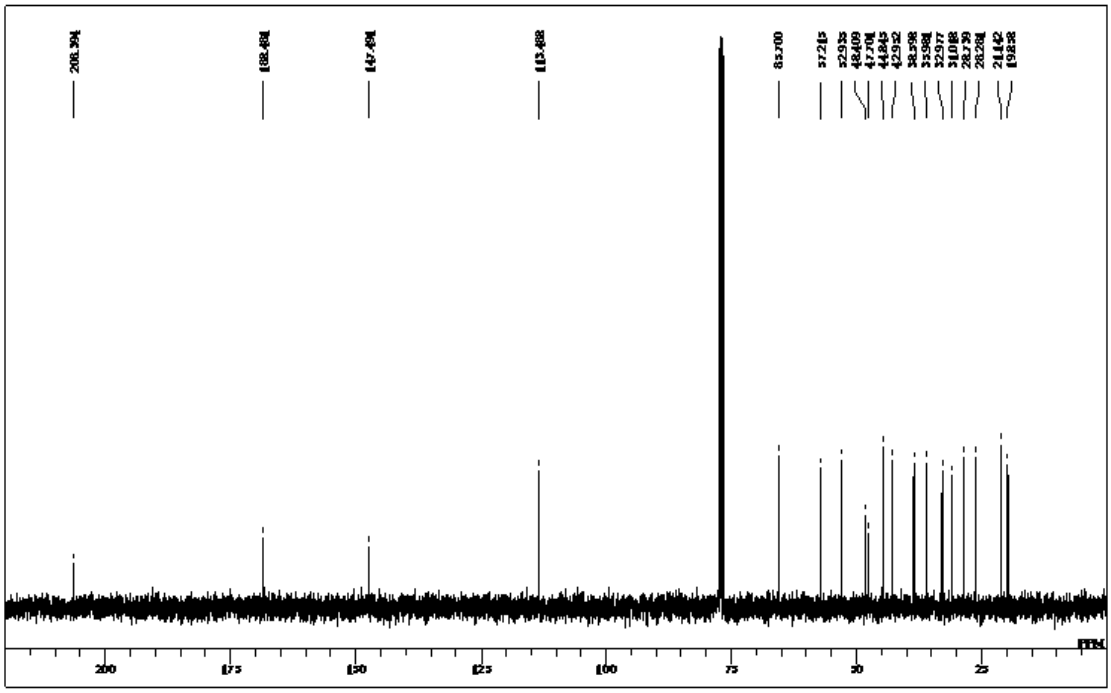

O
O
N
H
S
S
O2

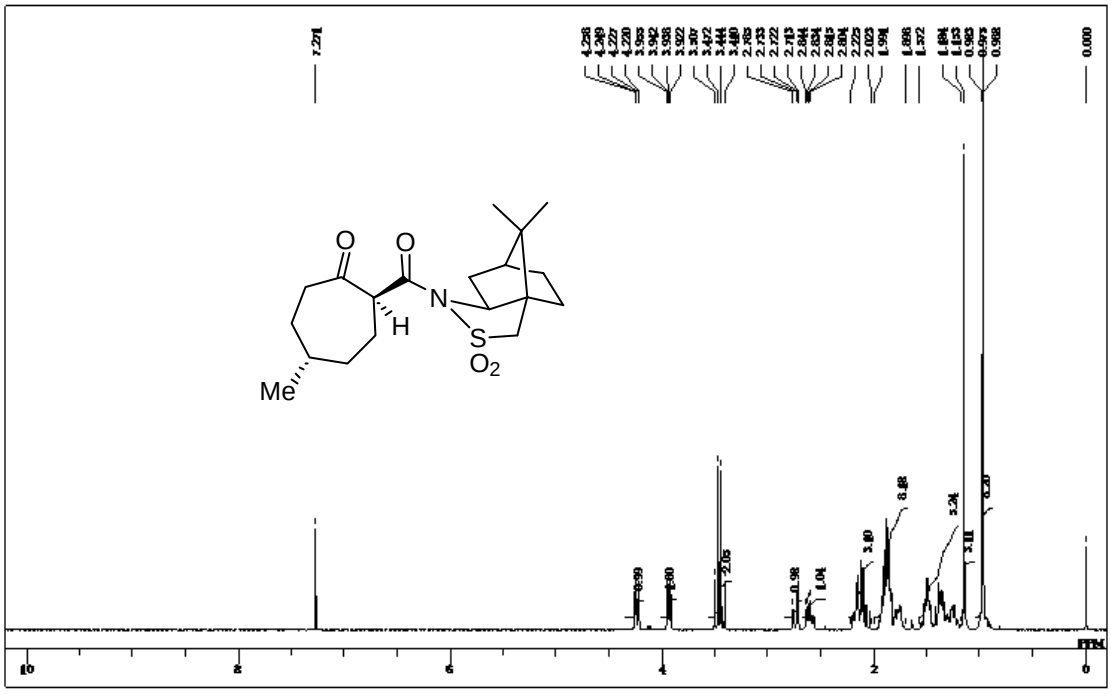


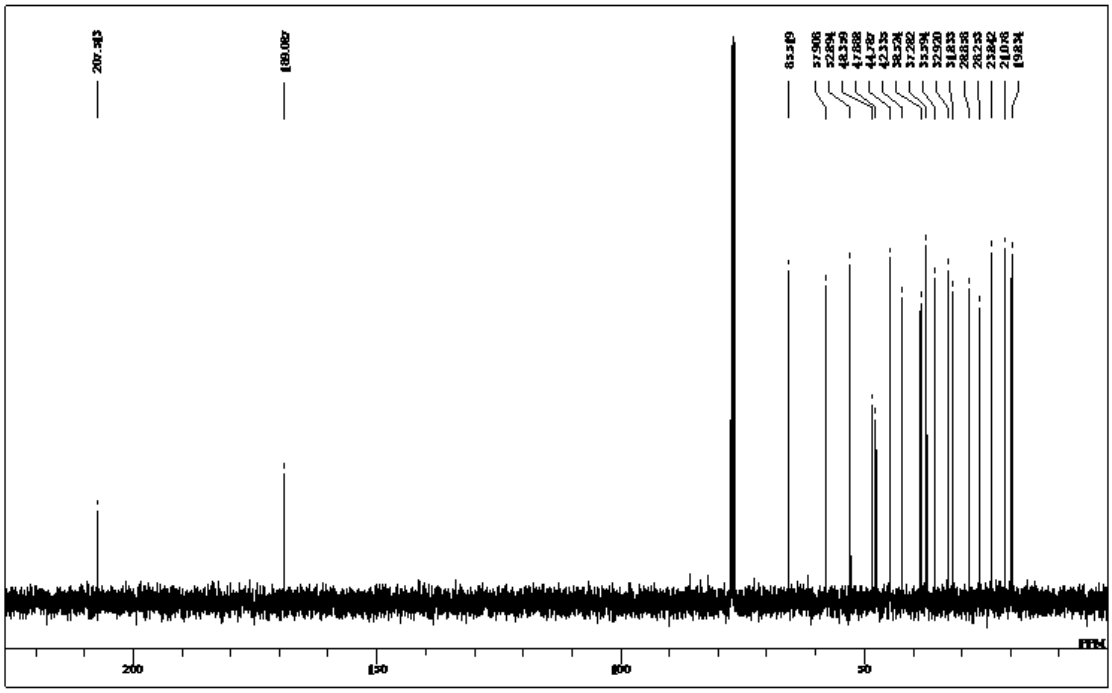

7.270
4.485
4.477
4.458
4.450
4.129
4.112
4.093
3.971
3.958
3.952
3.939
3.516
3.481
3.438
3.403
3.278
2.861
2.833
2.188
2.146
2.127
2.111
2.091
2.041
2.039
1.998
1.952
1.928
1.912
1.895
1.868
1.652
1.440
1.401
1.392
1.378
1.370
1.352
1.323
1.276
1.274
1.258
1.256
1.240
1.156
1.134
0.978
0.939
0.880
0.000
O
O
N
H
S
O2
BocN
7.39
4.09
0.45
2.13
2.00
1.90
0.98
0.74
0.98
0.93
0.90
PPM
10
8
6
4
2
0

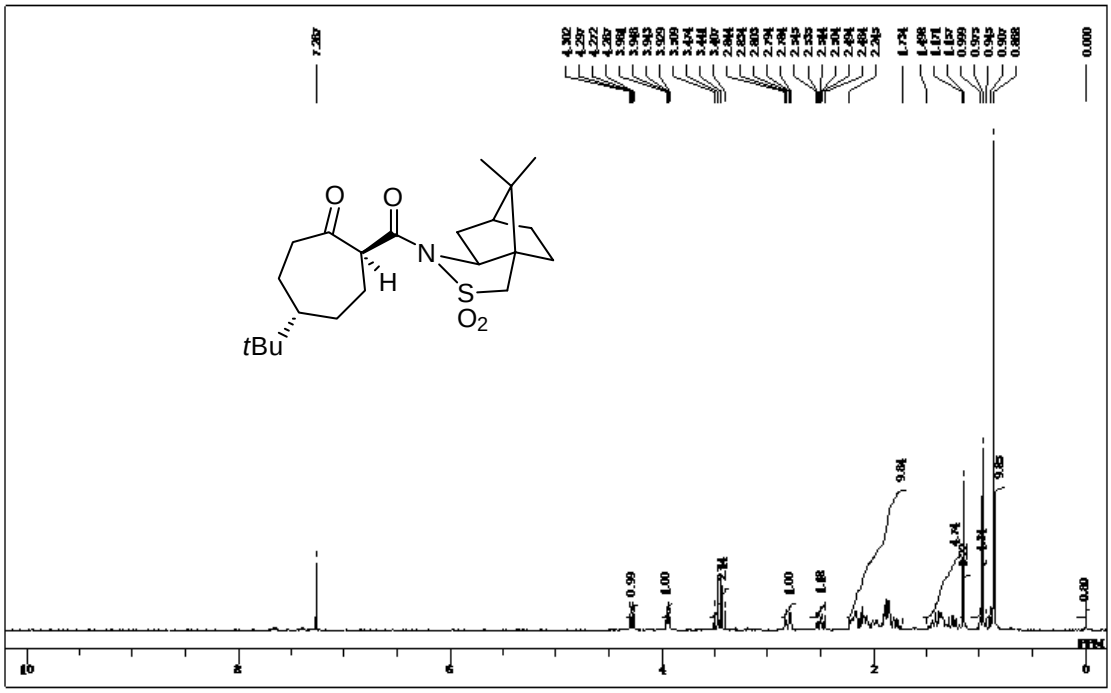

205.571
167.367
154.231
80.185
77.206
65.091
57.231
52.927
48.754
47.841
45.001
44.565
42.697
37.784
32.738
29.669
26.558
20.097
19.924
PPM
200
175
150
125
100
75
50
25
0

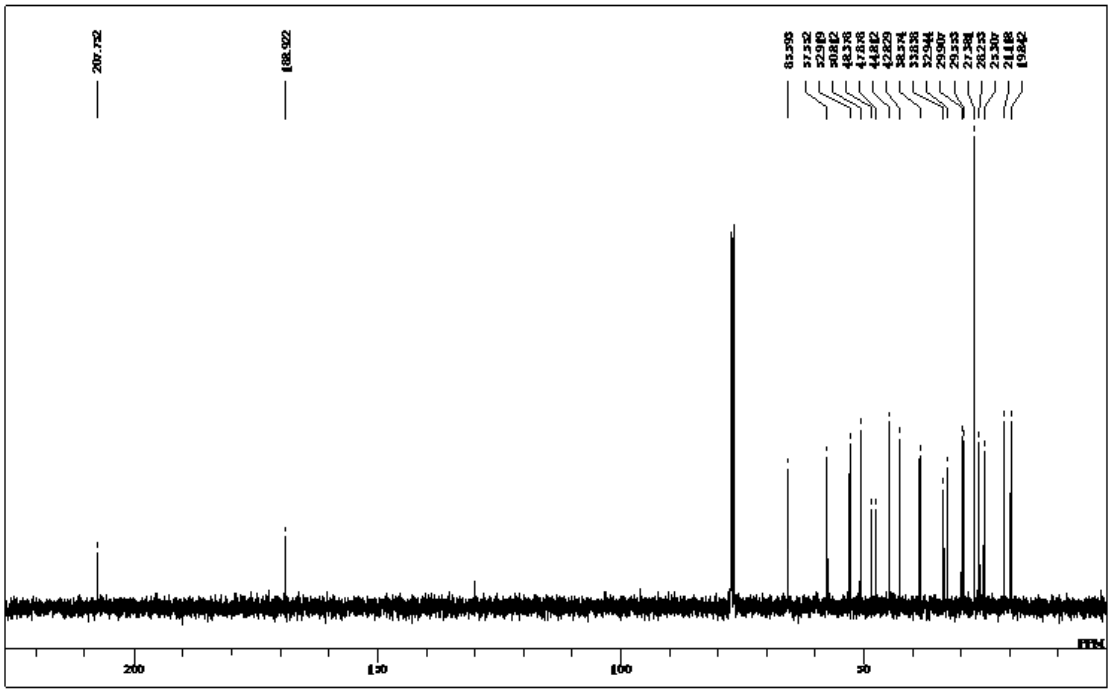

O
O
N
H
S
O2

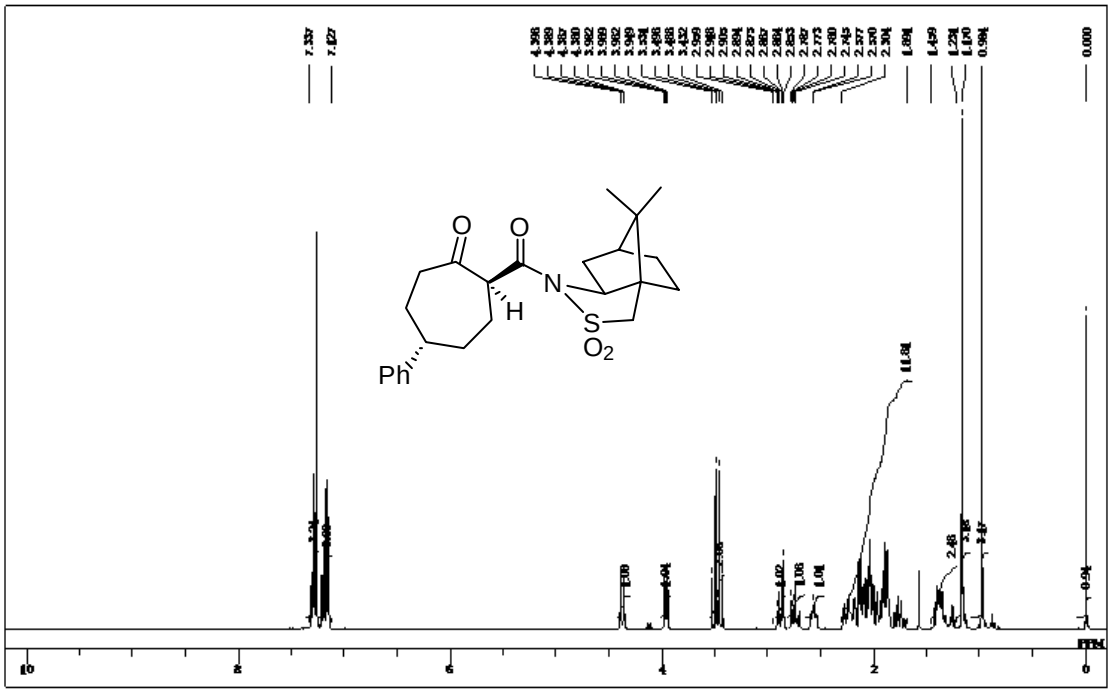


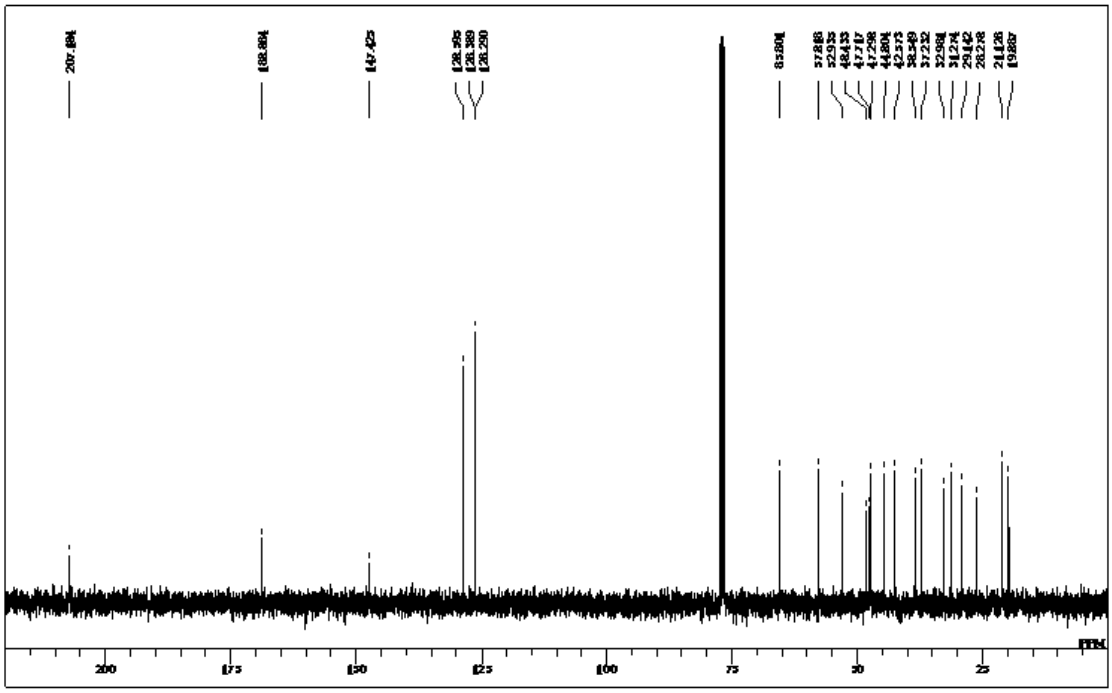

O
O
N
H
S
O2
Me

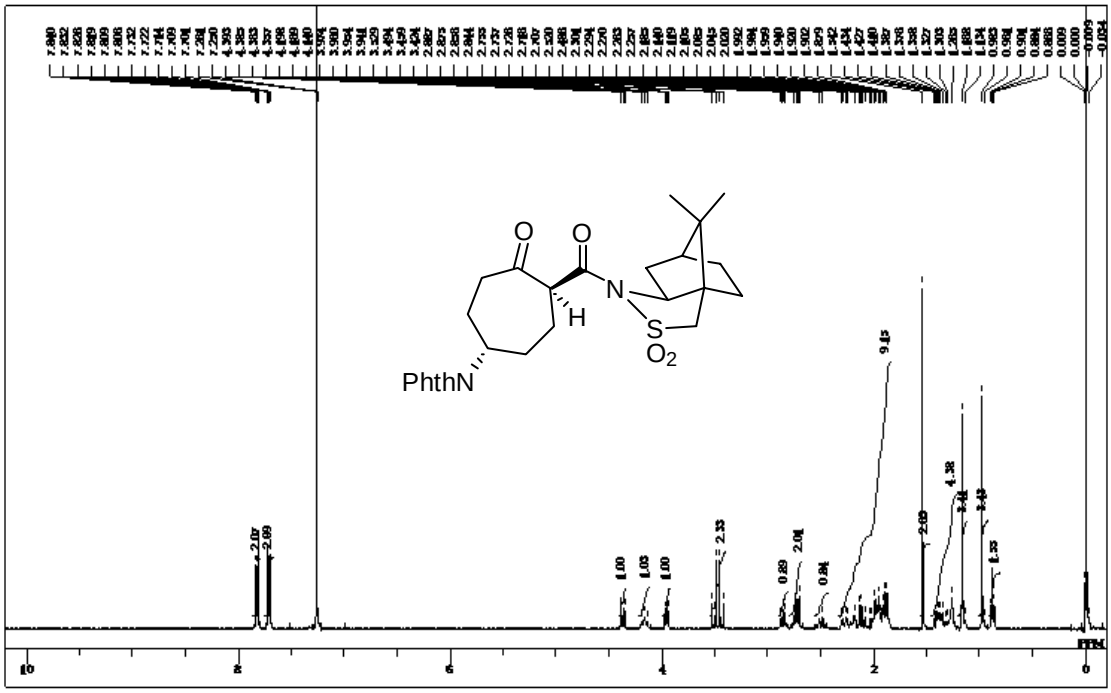


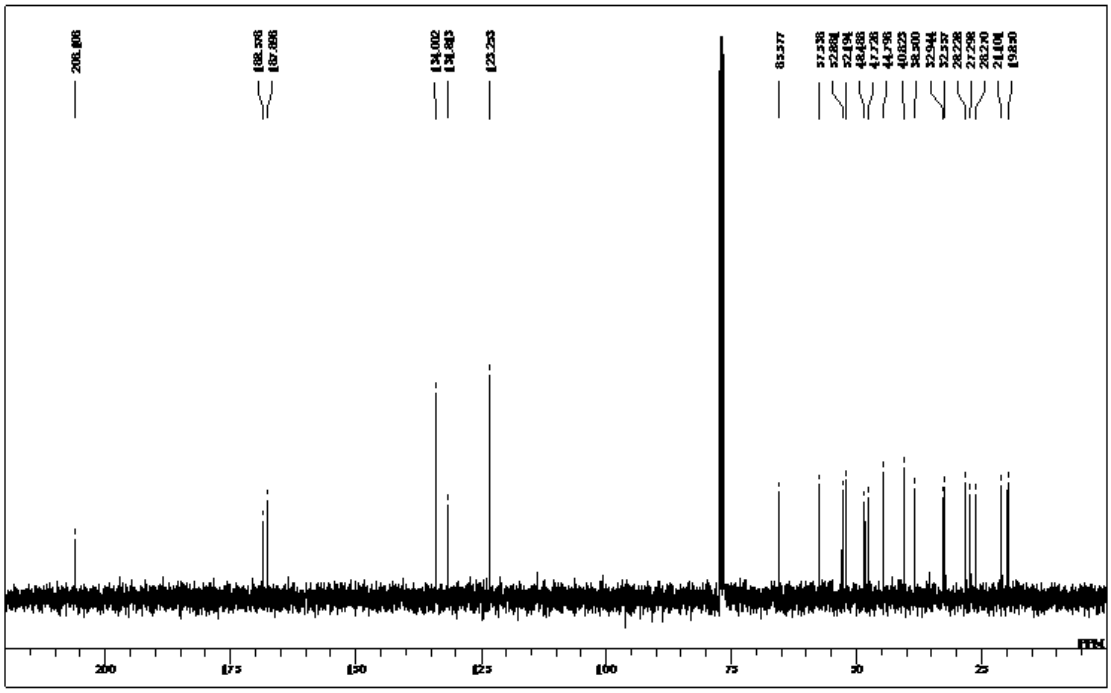

O
O
N
H
S
O2
tBu

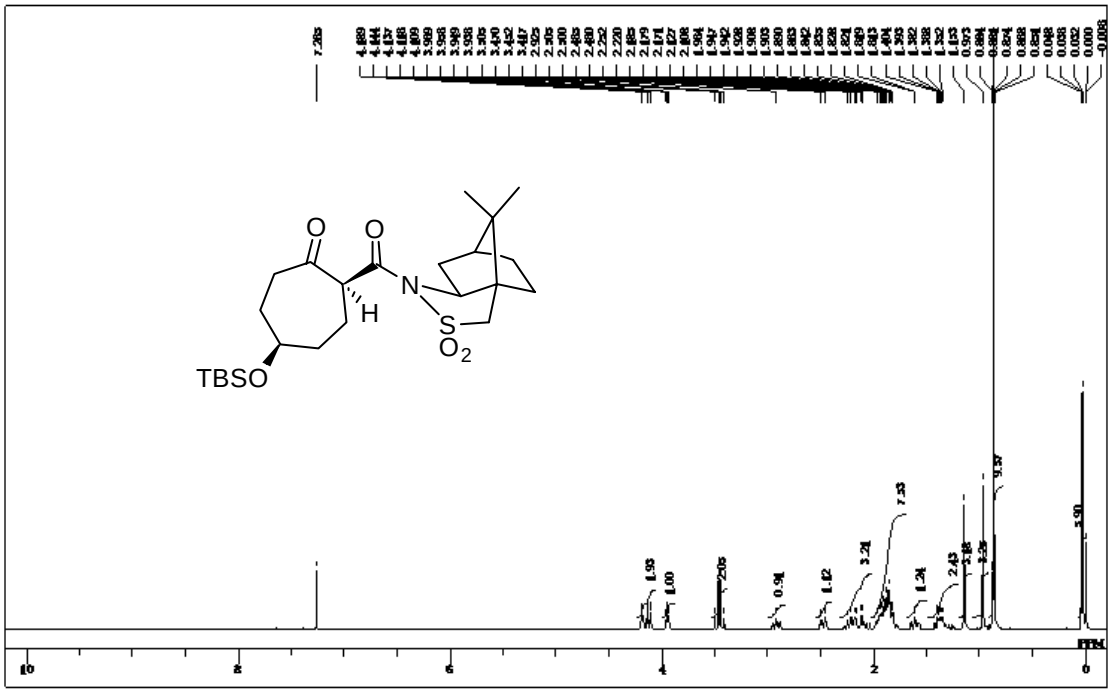


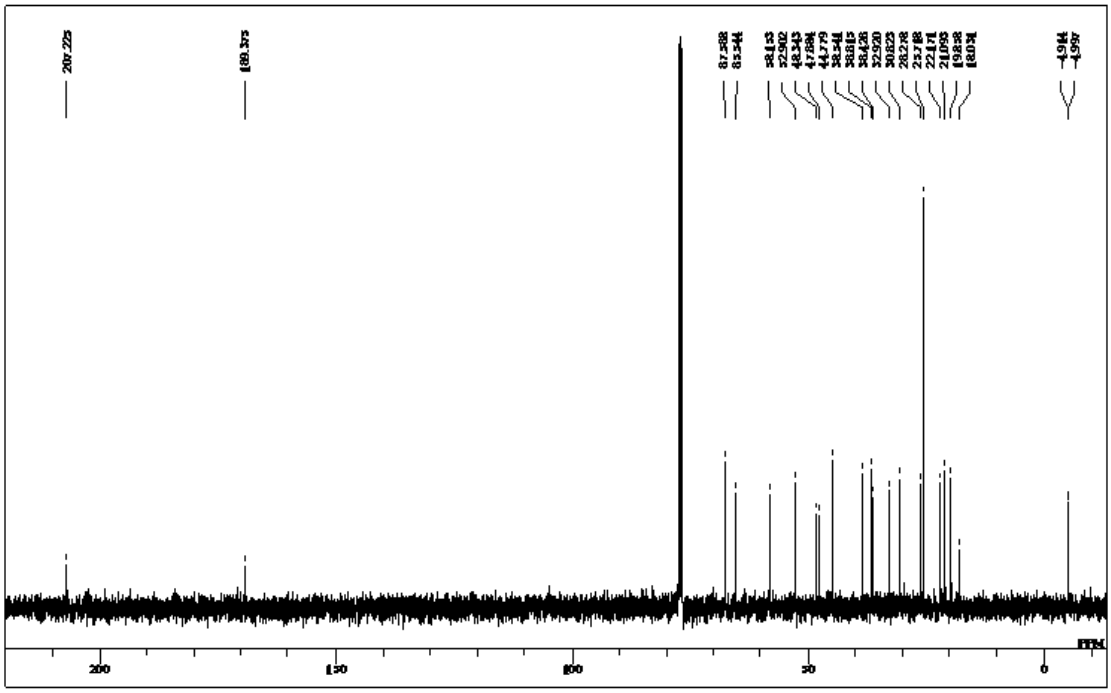

O
O
N
H
S
O2
Ph

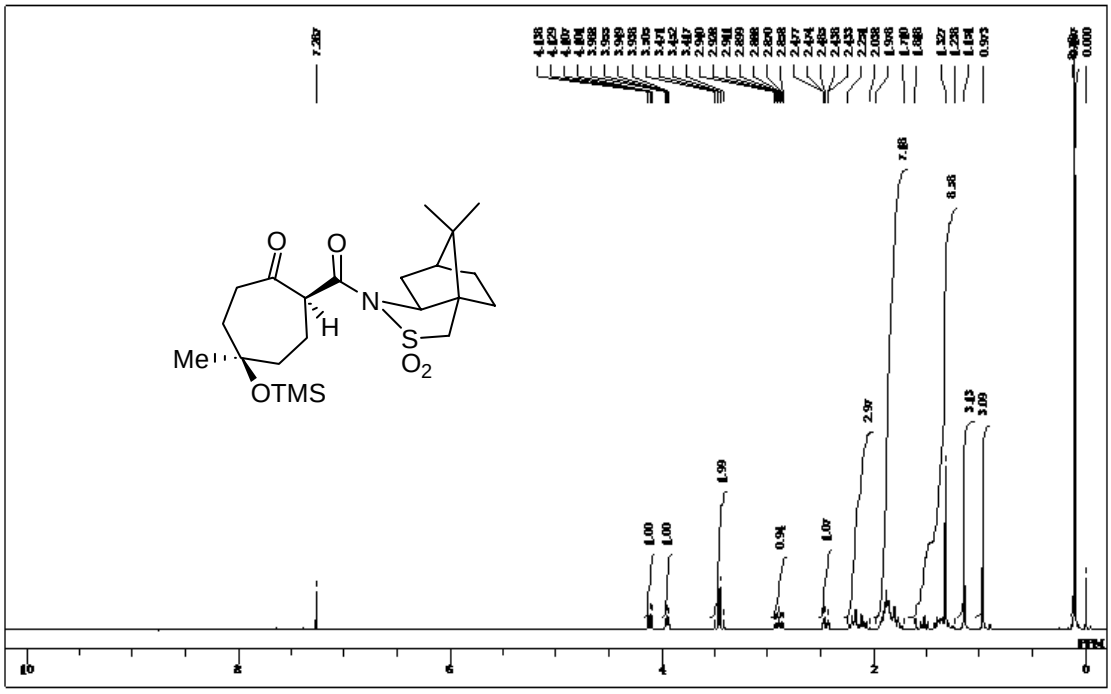


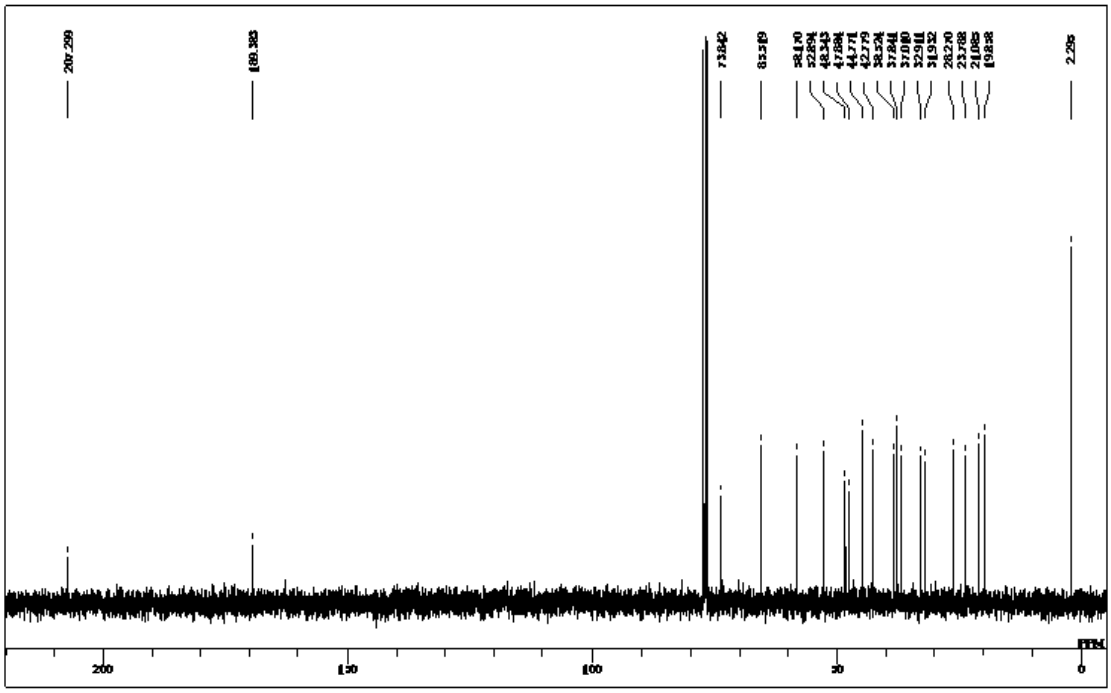

O
O
N
H
S
O2
PhthN

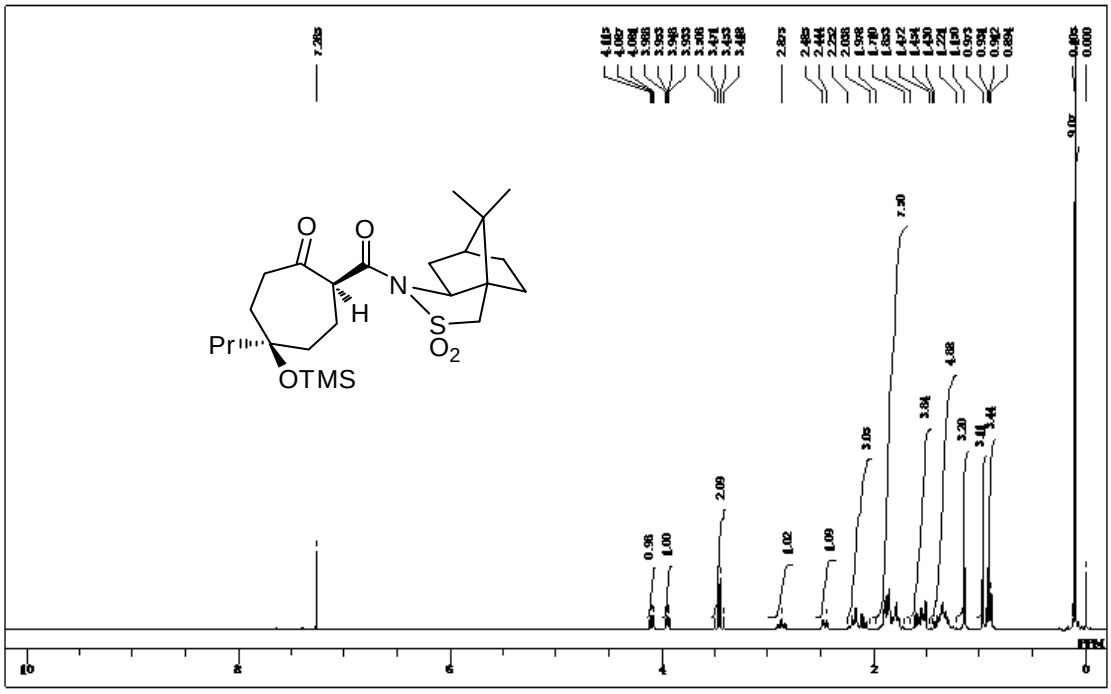


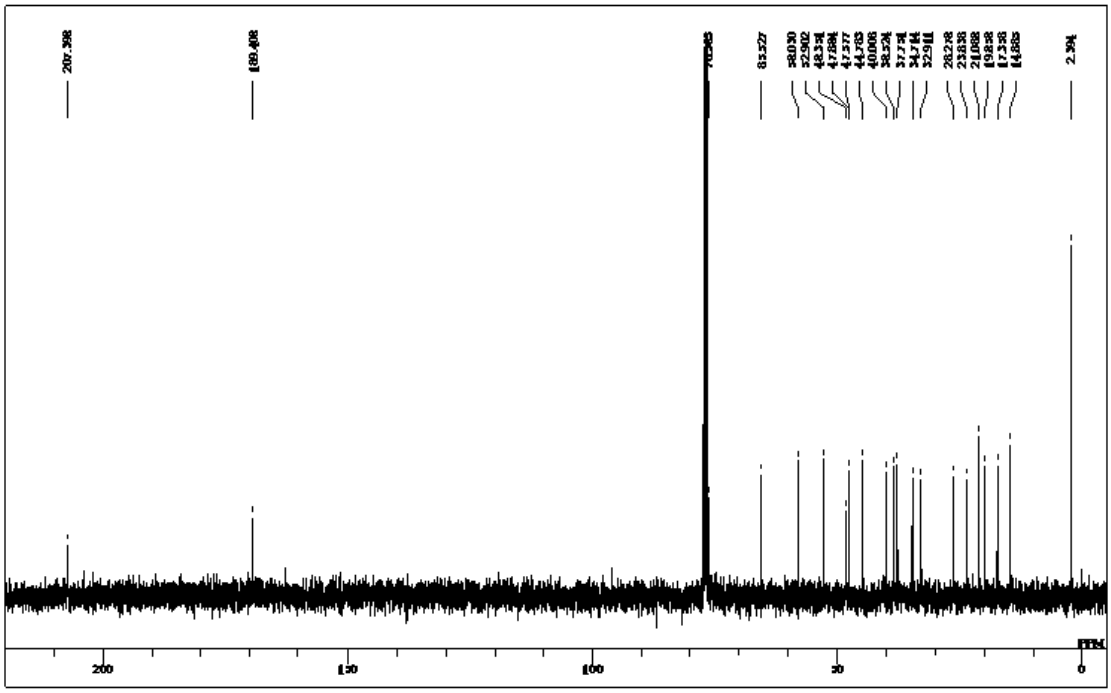

O
O
N
H
S
O2
TBSO

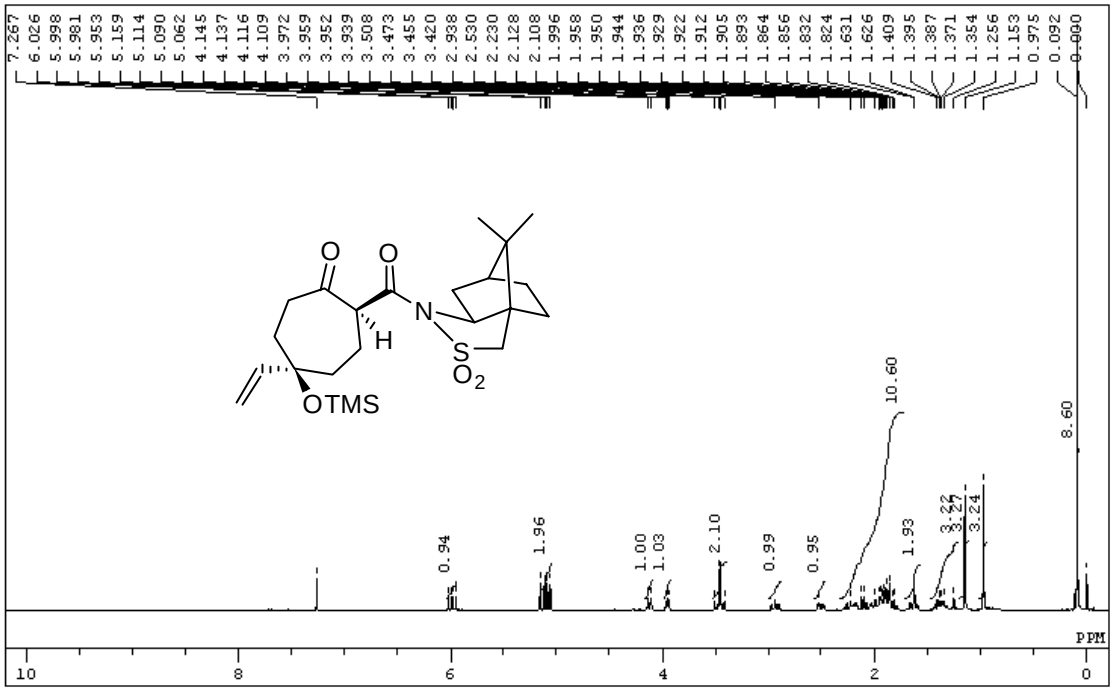


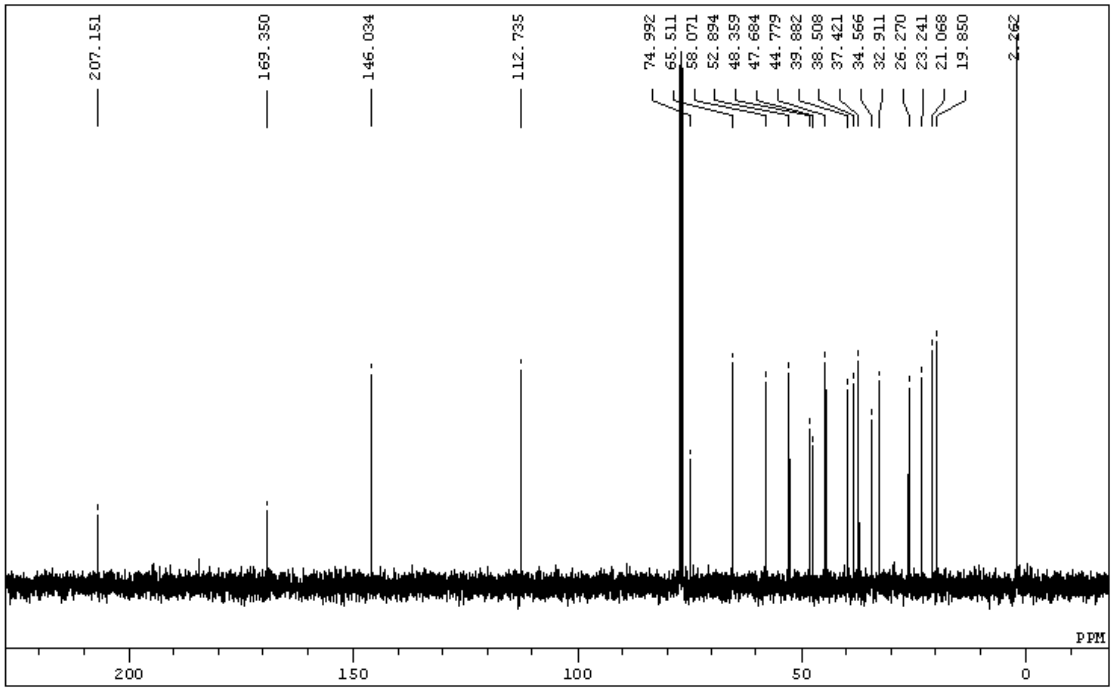

O
O
N
H
S
O2
Me
OTMS

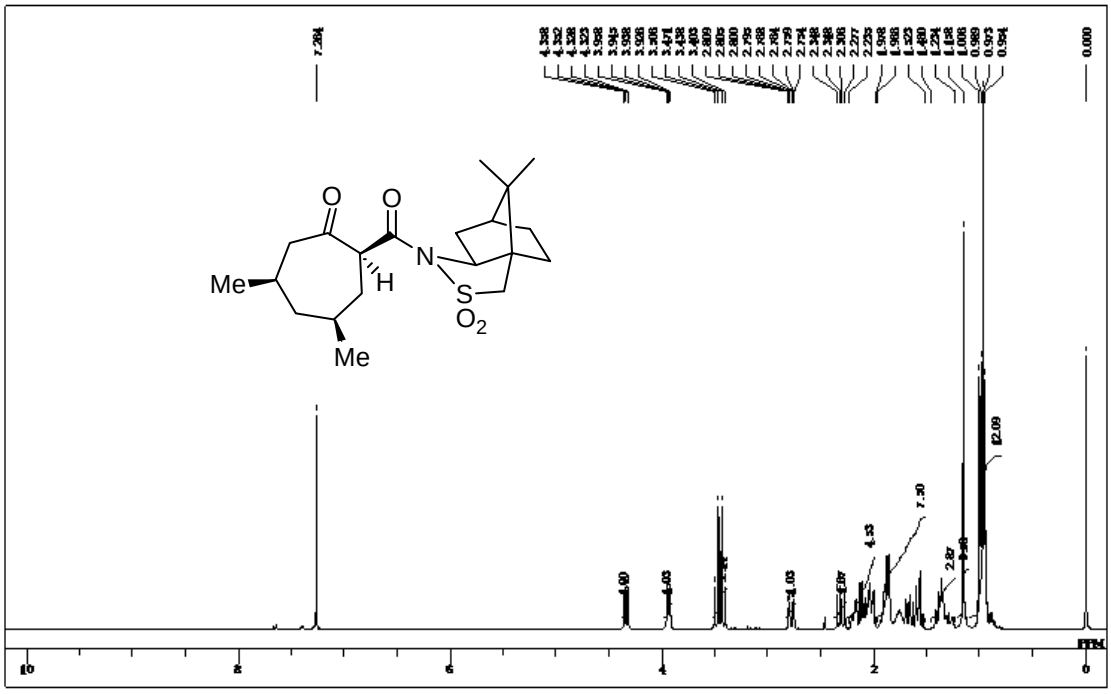


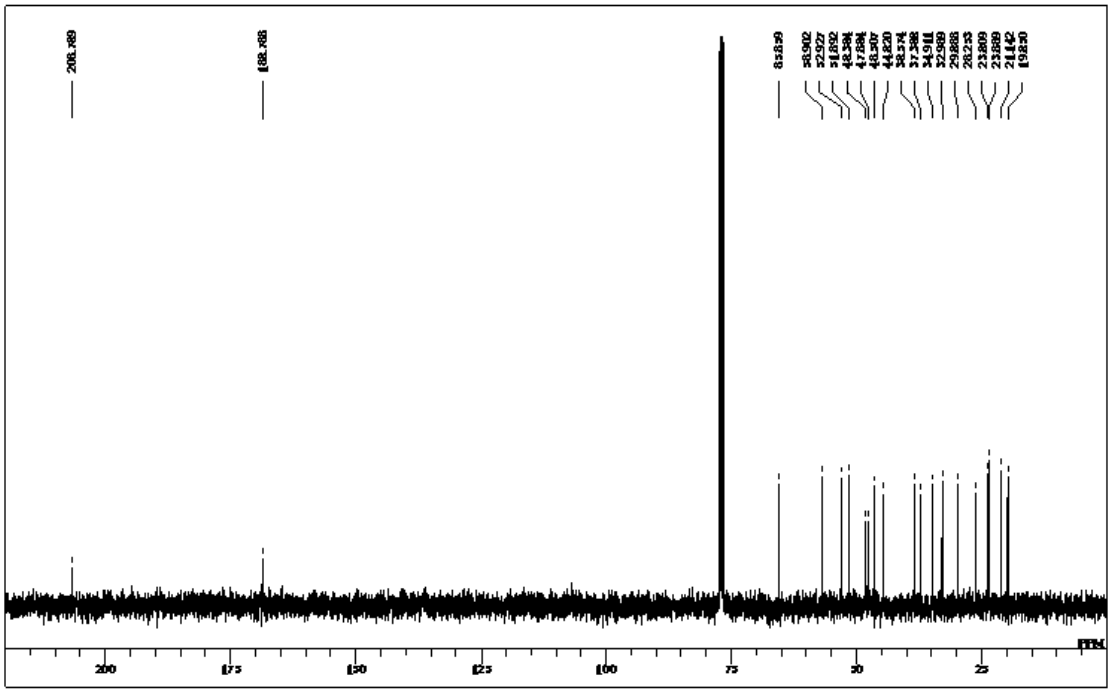

O
O
N
H
S
O2
Pr
OTMS

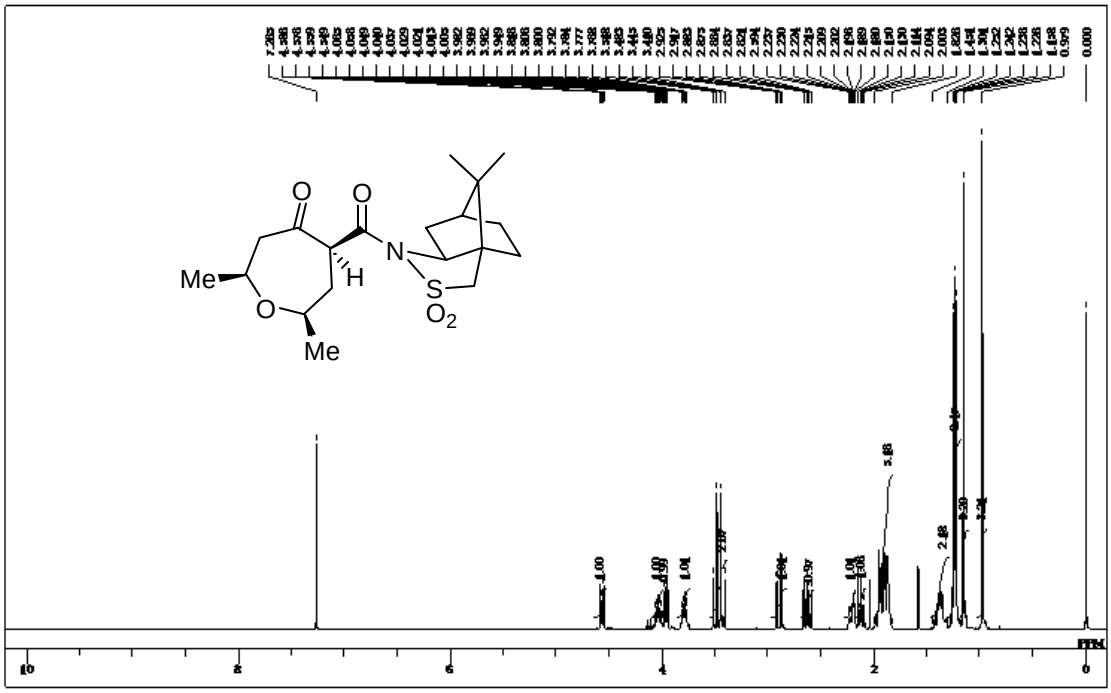


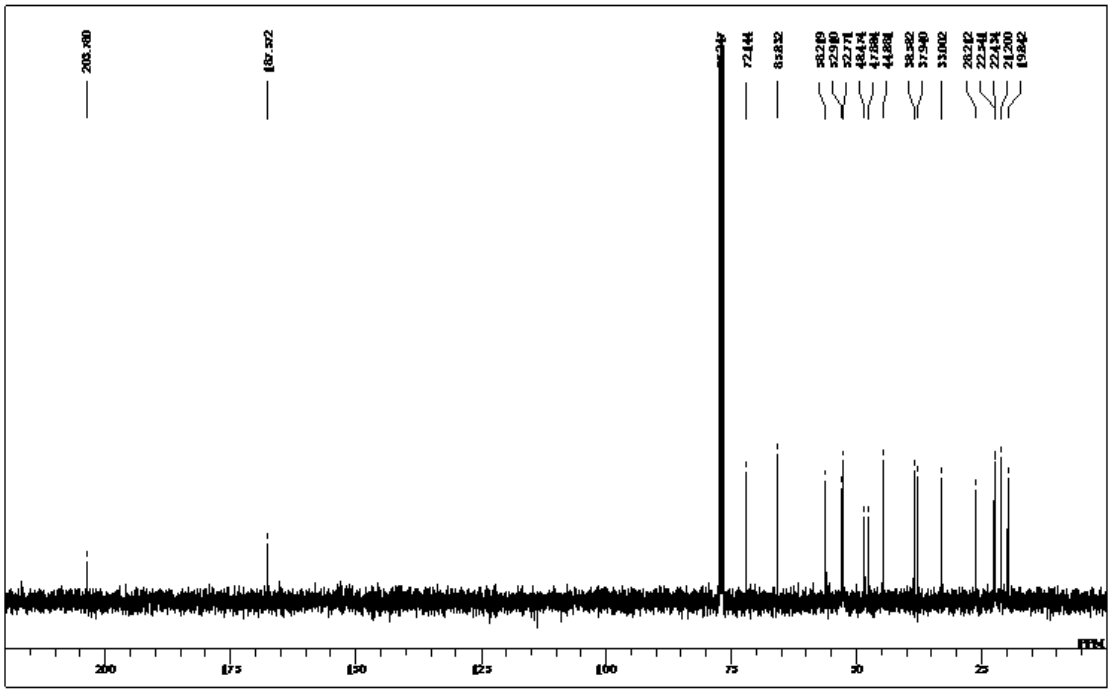

7.267
6.026
5.998
5.981
5.953
5.159
5.114
5.090
5.062
4.145
4.137
4.116
4.109
3.972
3.959
3.952
3.939
3.508
3.473
3.455
3.420
2.938
2.530
2.230
2.128
2.108
1.996
1.958
1.950
1.944
1.936
1.929
1.922
1.912
1.905
1.893
1.864
1.856
1.832
1.824
1.631
1.626
1.409
1.395
1.387
1.371
1.354
1.256
1.153
0.975
0.092
0.000
O
O
N
H
S
O2
OTMS
10.60
8.60
0.94
1.96
1.00
1.03
2.10
0.99
0.95
1.93
3.27
3.24
PPM
10
8
6
4
2
0

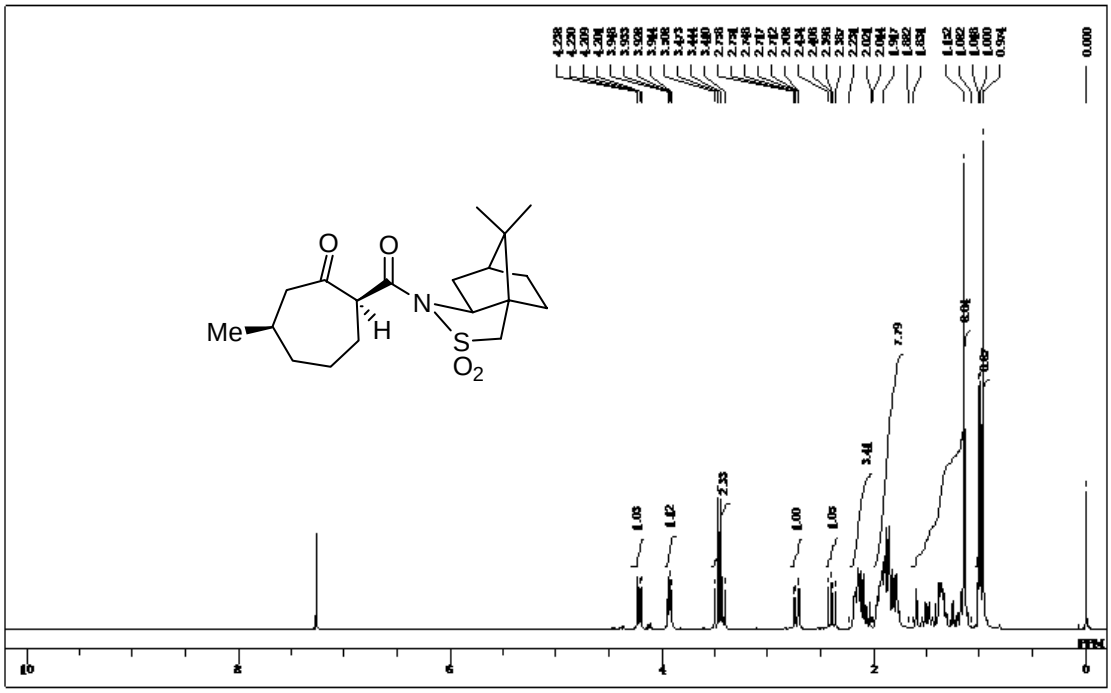

207.151
169.350
146.034
112.735
74.992
65.511
58.071
52.894
48.359
47.684
44.779
39.882
38.508
37.421
34.566
32.911
26.270
23.241
21.068
19.850
2.262
PPM
200
150
100
50
0

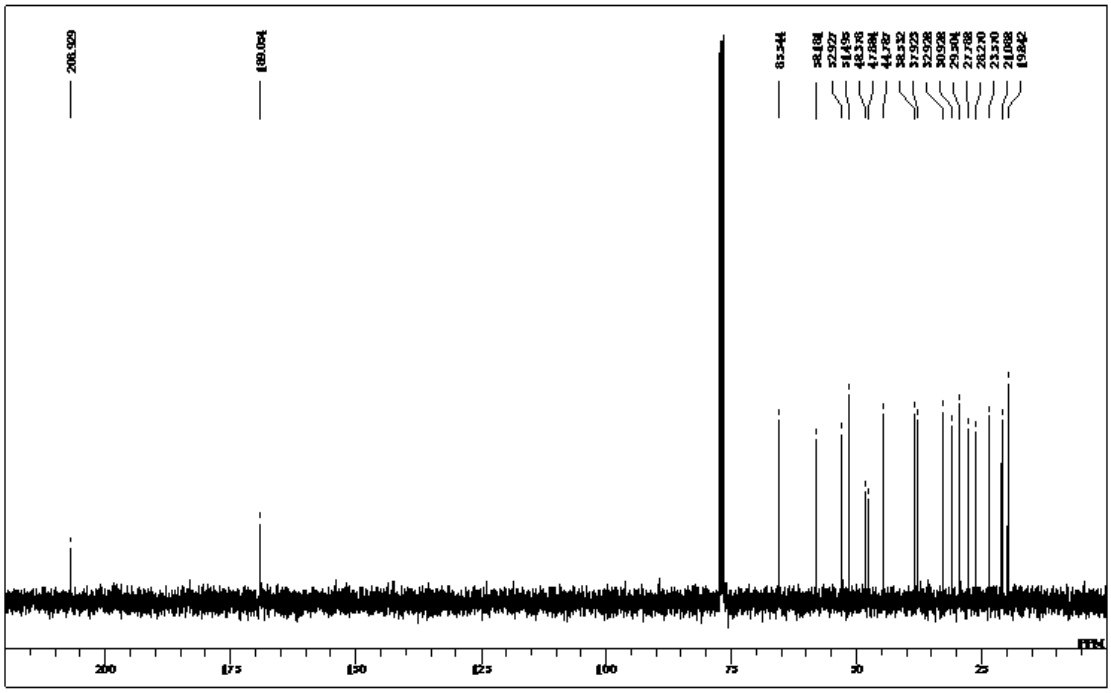

O
O
N
S
O2
Me
H
Me

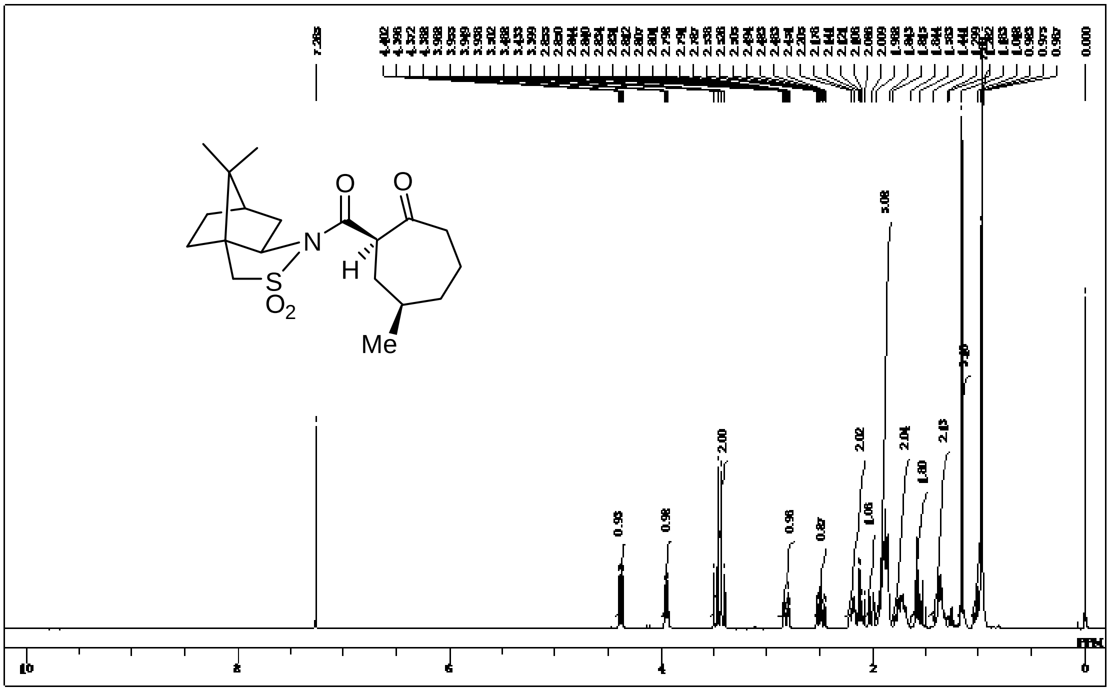


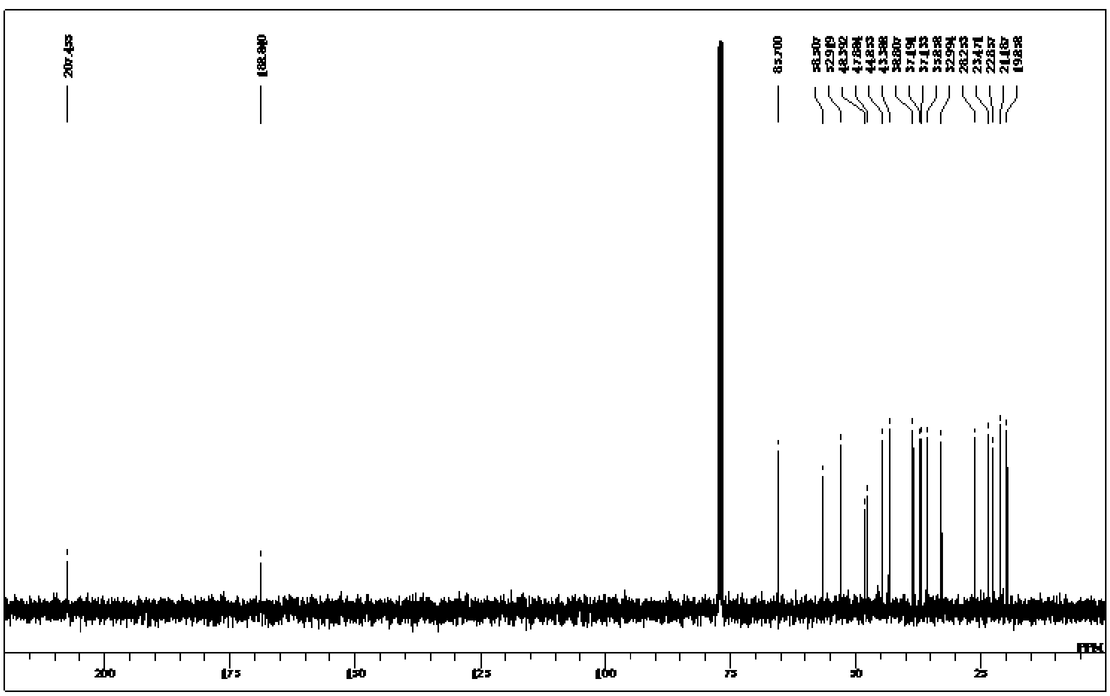

O
O
N
H
Me
O
Me
S
O2

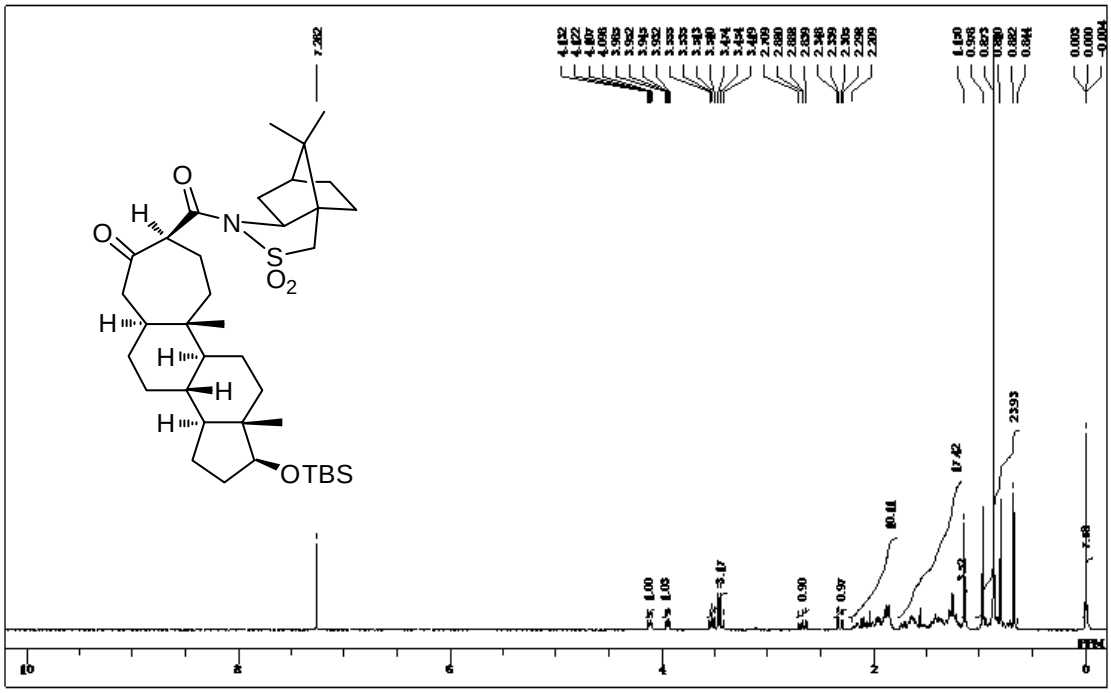


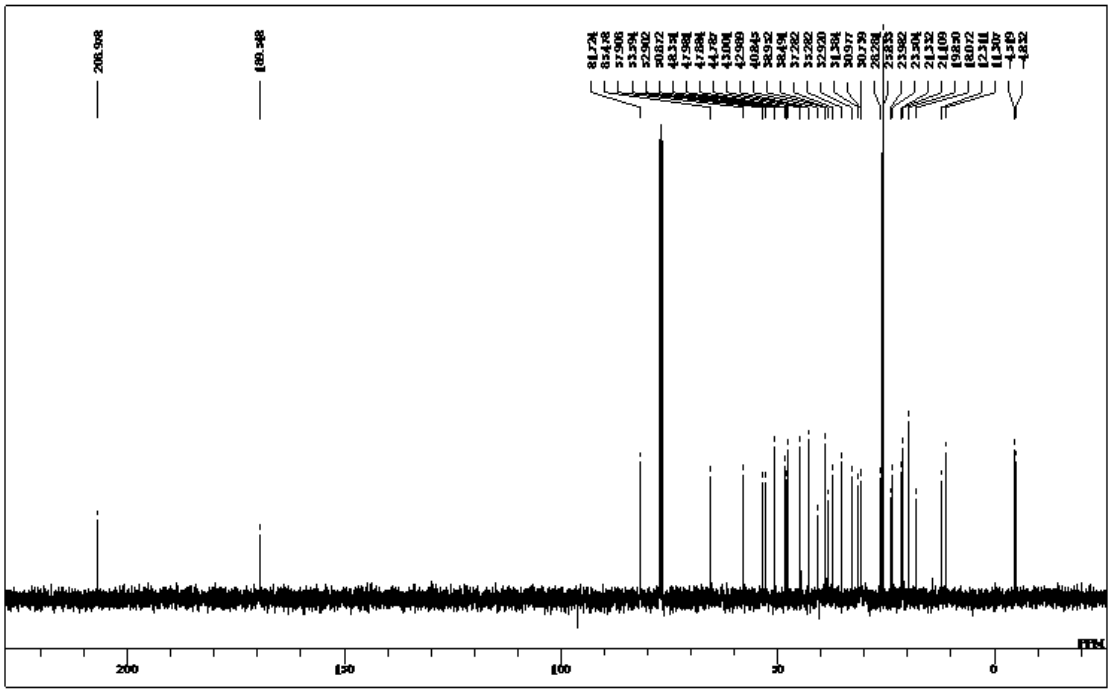

O
O
N
Me
H
S
O2

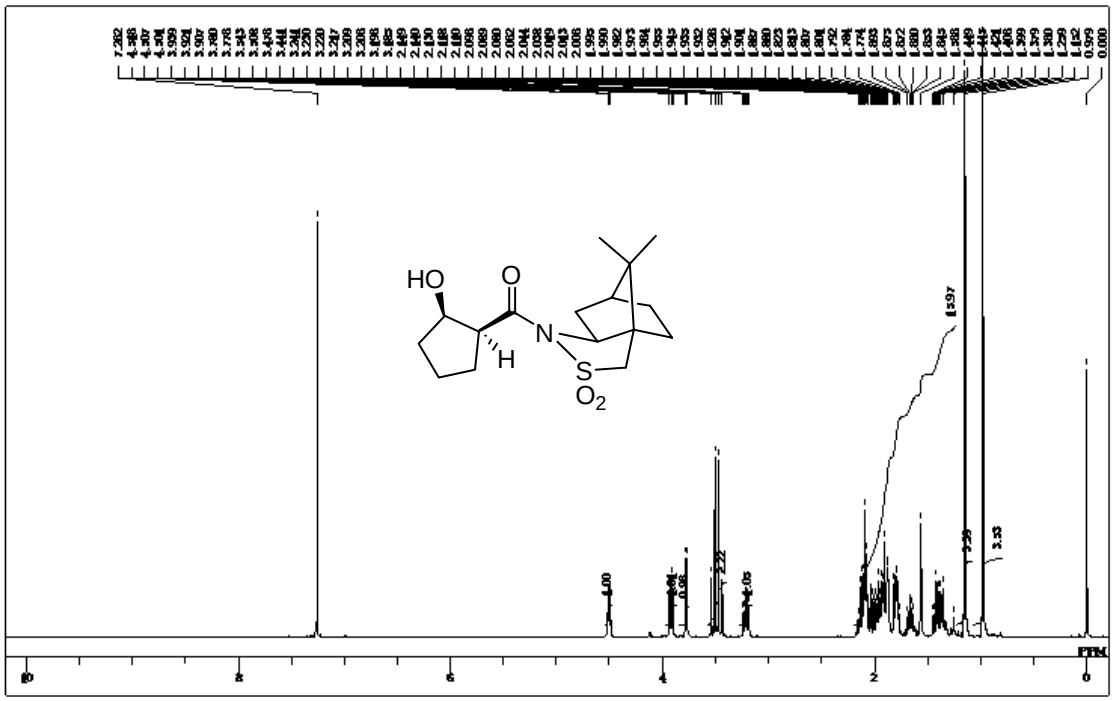


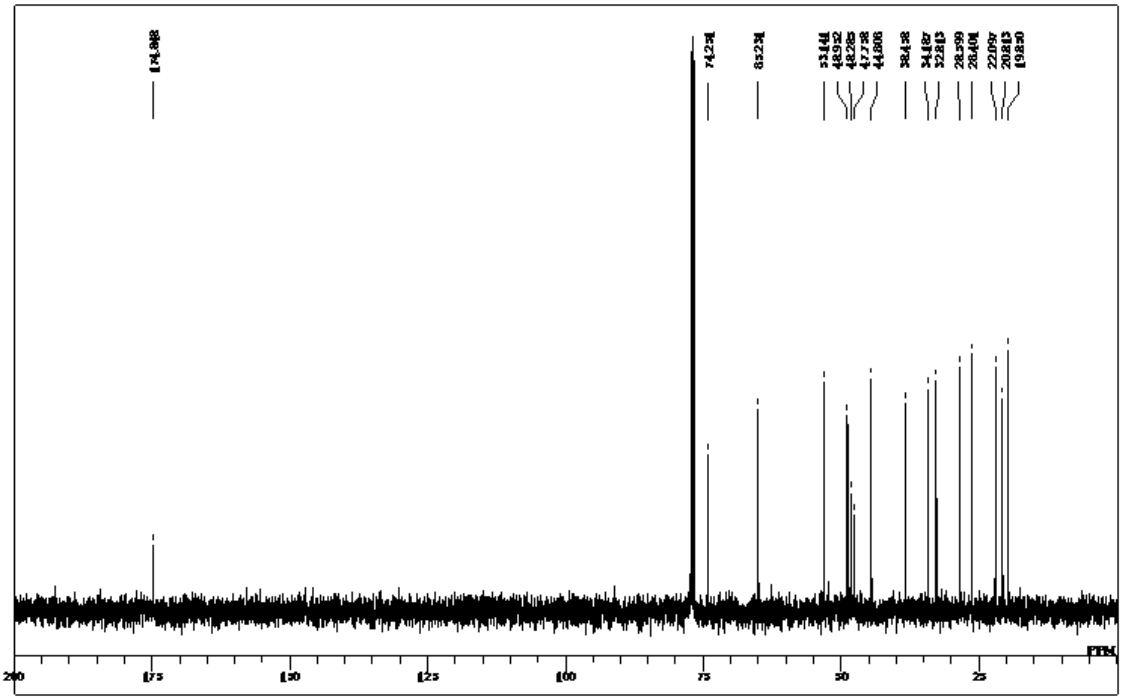

O
O
N
H
S
O2
Me

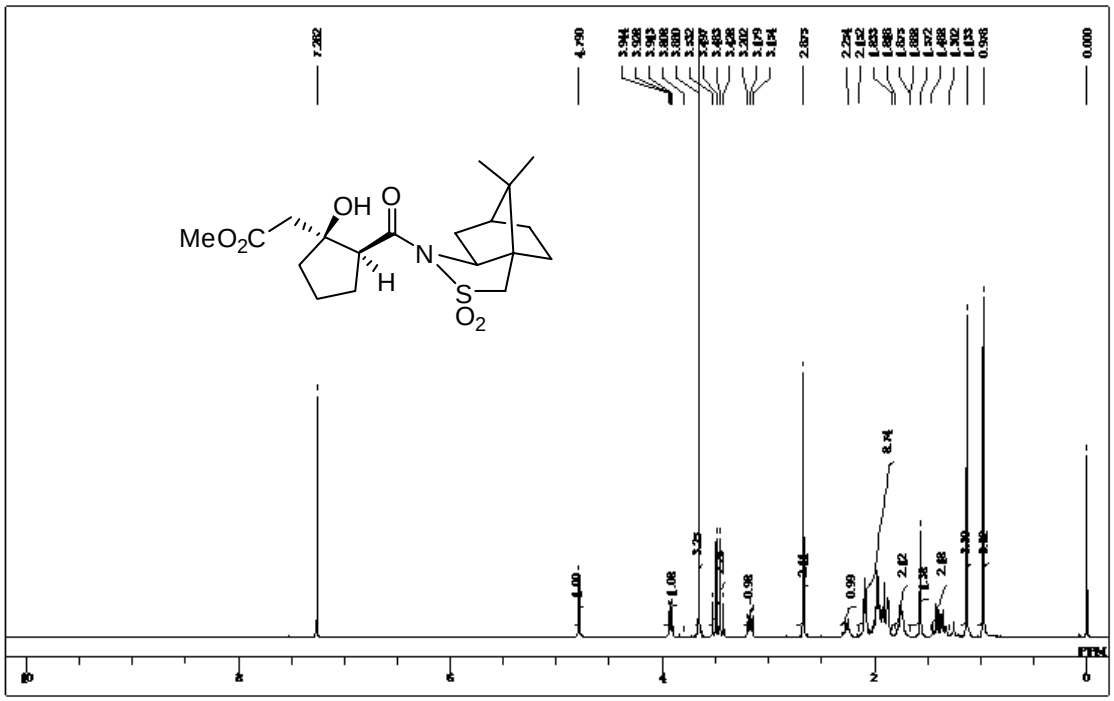



O
H
O
N
S
O2
H
H
H
H
OTBS




HO
O
N
S
O2
H
1.00
0.96
2.22
4.05
7.29
3.33
1.97


174.988
74.234
85.234
53.144
48.932
48.428
47.738
44.806
38.458
34.487
32.813
28.599
28.404
22.097
20.813
19.850


OH
O
MeO2C
N
H
S
O2