Electronic Supporting Information

The Thio-adduct Facilitated, Enzymatic Kinetic Resolution of 4-Hydroxycyclopentenone and 4-Hydroxycyclohexenone

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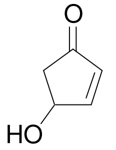
General

Reagents were obtained from commercial suppliers. Dry THF and diethyl ether were distilled from sodium benzophenone ketyl radical and dry CH_2Cl_2 distilled from calcium hydride, under nitrogen. Low reaction temperatures were obtained with an acetone/solid CO_2 bath. Thin-layer chromatography was performed on silica coated aluminium sheets (60 F_{254}) supplied by Merck. Flash column chromatography was performed using flash silica 60 Å (230-400 mesh) 9385 supplied by Merck. ^1H and ^{13}C NMR spectra were recorded using Varian Inova 300 MHz, 400 MHz and 500 MHz instruments. Deuterochloroform was used as the solvent and chemical shifts are given in ppm relative to the standard reference TMS or residual chloroform. Infrared spectra were recorded on a Mattson Instruments Galaxy series FT-IR 3000 spectrometer. Melting points were recorded on a Gallenkamp electrothermal melting point apparatus and are uncorrected. High resolution mass spectra were carried out on a VG analytical 70-E mass spectrometer. The names of compounds provided were generated using the Autonom programme on the Beilstein chemical database. Optical rotation data was obtained using a Perkin Elmer Model 343 polarimeter and values are quoted in units of $10^{-1}degcm^2g^{-1}$.

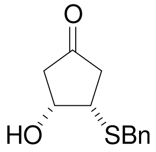
(±)-4-Hydroxycyclopent-2-enone 1:[1]



Furfuryl alcohol **2** (7.35 mL, 85.0 mmol, 1.00 equiv.) and potassium dihydrogen orthophosphate (2.109 g, 15.5 mmol, 0.18 equiv.) were dissolved in water (0.5 L). The solution was degassed with a stream of nitrogen along with stirring for 1 h. The reaction was heated to reflux for 48 h and then cooled to room temperature. The aqueous layer was washed with EtOAc (2 x 100 mL), the combined organic layers were checked for product by NMR and then discarded. The aqueous layer was concentrated almost to dryness (ca. 25 mL) under reduced pressure and the residue was then thoroughly extracted with EtOAc (5 x 20 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent removed under reduced pressure. The title compound **1** was obtained as a brown oil (2.943 g, 30% yield). $R_f = 0.1$ (cyclohexane-EtOAc; 1:1); ν_{max} (neat/cm^{-1}) 3417, 2920, 2704, 1712, 1586, 1405, 1343, 1190, 1154, 1104, 1045, 947, 797; δ_H (400 MHz, $CDCl_3$) 2.25 (1H, dd, *J* = 2.0, 18.5 Hz, CH_2), 2.75 (1H, dd, *J* = 6.0, 18.5 Hz, CH_2), 5.00-5.03 (1H, m, CH), 6.20 (1H, dd, *J* = 1.5, 5.5 Hz, CH), 7.57 (1H, dd, *J* = 2.5, 5.5 Hz, CH); δ_C NMR (100 MHz, $CDCl_3$) 44.2 (CH_2), 70.2 (CH), 134.9 (CH), 163.8 (CH), 207.2 (CO).

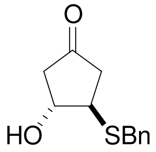
Synthesis of (+)- and (–)-6a

(±)-*cis*-3-Benzylthio-4-hydroxycyclopentanone (±)-4a:



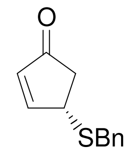
To (±)-4-hydroxycyclopent-2-enone **1** (1.717 g, 17.5 mmol, 1.0 equiv.), dissolved in dichloromethane (40 mL), benzyl mercaptan (1.85 mL, 15.8 mmol, 0.9 equiv.) and triethylamine (0.24 mL, 1.8 mmol, 0.1 equiv.) were added dropwise. The reaction mixture was stirred at room temperature for 24 h. The solvent was removed under reduced pressure and the residue purified by column chromatography (cyclohexane-EtOAc, 4:1) to afford the title compound (±)-**4a** (2.801 g, 80%) as a white solid with data as reported previously.[2] $R_f = 0.1$ (cyclohexane-EtOAc, 4:1).

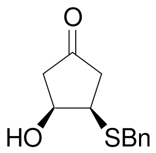
(±)-*trans*-3-Benzylthio-4-hydroxycyclopentanone (±)-*trans*-4a:



To (±)-4-hydroxycyclopent-2-enone **1** (200 mg, 2.04 mmol, 1.0 equiv.), dissolved in ethanol (5 mL), benzyl mercaptan (0.22 mL, 1.83 mmol, 0.9 equiv.) and triethylamine (30 µL, 0.20 mmol, 0.1 equiv.) were added dropwise. The reaction mixture was stirred at room temperature for 24 h. The solvent was removed under reduced pressure and the residue purified by column chromatography (CH_2Cl_2-MeOH, 100:1) to afford (±)-*cis*-**4a** (86 mg, 19 %) as white solid. $R_f = 0.2$ (CH_2Cl_2-MeOH, 100:1). Further elution gave (±)-*trans*-**4a** (231 mg, 51%) as a clear, viscous oil whose data was in accordance with that reported previously. $R_f = 0.1$ (CH_2Cl_2-MeOH, 100:1).[2]

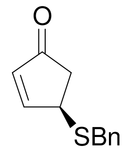
(*S*)-4-(Benzylthio)cyclopent-2-enone (–)-6a and (3*R*,4*S*)-3-(Benzylthio)-4-hydroxycyclopentanone (–)-4a:





To *cis*-3-benzylthio-4-hydroxycyclopentanone (±)-**4a** (2.290 g, 10.3 mmol, 1 equiv.) dissolved in diisopropyl ether (220 mL), vinyl acetate (4.75 mL, 51.5 mmol, 5 equiv.) and *Candida antarctica* Lipase B [2.290 g, 1:1 *w/w* (enzyme:substrate)] were added. The reaction was shaken for 16 h and monitored by ^{1}H NMR spectroscopy. The mixture was filtered, and the enzyme residue washed with diisopropyl ether (2 × 30 mL). The solvent was removed under reduced pressure and the residue was dissolved in THF (50 mL) and cooled to 0 °C. Triethylamine (1.44 mL, 10.3 mmol, 1 equiv.) was added dropwise and the reaction stirred for 30 min. NMR showed that the reaction was complete. The solvent was removed under reduced pressure and the residue purified by column chromatography (cyclohexane-EtOAc, 8:1) to afford (*S*)-4-(benzylthio)cyclopent-2-enone (–)-**6a** (1.013 g, 48%) as a colourless oil. $R_f = 0.1$ (cyclohexane-EtOAc, 8:1); ν_{max} (neat/cm^{-1}) 3061, 3029, 2919, 1953, 1716, 1582, 1495, 1454, 1400, 1341, 1240, 1180, 1096, 1028, 940, 831, 771, 704; δ_H (400 MHz, $CDCl_3$) 2.25 (1H, dd, *J* = 2.0, 19.0 Hz, CH_2), 2.67 (1H, dd, *J* = 6.5, 19.0 Hz, CH_2), 3.71 (1H, d, *J* = 13.5 Hz, CH_2) 3.76 (1H, d, *J* = 13.5 Hz, CH_2), 3.85-3.88 (1H, m, CH), 6.13 (1H, dd, *J* = 1.5, 5.5 Hz, CH), 7.22-7.28 (5H, m, ArH), 7.41 (1H, dd, *J* = 2.5, 5.5 Hz, CH); δ_C (100 MHz, $CDCl_3$) 35.5 (CH_2), 42.5 (CH_2), 43.2 (CH), 127.3 (CH), 128.5 (CH), 128.7 (CH), 134.4 (CH), 137.5 (C), 163.2 (CH), 207.1 (CO); HRMS (CI) cald. for $C_{12}H_{13}OS$ (MH^+) requires 205.06873; found 205.06852; $[\alpha]_D = -163$ (*c* = 0.1, $CHCl_3$); HPLC analysis (ASH) isocratic heptane-EtOH; 50:50, (0.5 mL/min): t_r (*S*): 17.0 min; 84% e.e. Further elution gave (–)-**4a** as a white solid (1.085 g, 47%), $[\alpha]_D = -56$ (*c* = 0.4, $CHCl_3$), with additional data in accord to that reported.[2]

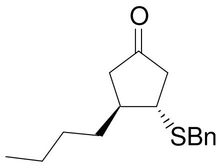
(*R*)-4-(Benzylthio)cyclopent-2-enone (+)-6a:



To (3*R*,4*S*)-3-(benzylthio)-4-hydroxycyclopentanone (–)-**4a** (1.022 g, 4.6 mmol, 1.0 equiv.) dissolved in acetic anhydride (15 mL), pyridine (0.78 mL, 9.7 mmol, 2.1 equiv.) was added dropwise and the reaction stirred for 5 h. The solvent was evaporated under reduced pressure and residue purified by column chromatography (cyclohexane-EtOAc, 8:1) to afford the title compound (+)-**6a** (0.865 g, 92%) as a colourless oil. $[\alpha]_D = +171$ (*c* = 0.1, $CHCl_3$), with spectroscopic data as above. HPLC analysis (ASH) isocratic heptane-EtOH; 50:50, (0.5 mL/min): t_r (*R*): 15.0 min; 77% e.e.

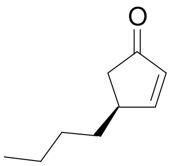
Synthesis of (+)- and (–)-12

(3*S*,4*S*)-3-(Benzylthio)-4-butylcyclopentanone (+)-10:



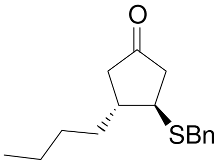
To CuI (19.0 mg, 0.10 mmol, 0.1 equiv.) in diethyl ether (5 mL) under nitrogen at –78 °C, 2 M butylmagnesium chloride in diethyl ether (1.47 mL, 2.94 mmol, 3.0 equiv.) was added dropwise. The reaction was stirred at –78 °C for 1 h. Then (–)-**6a** (200 mg, 0.98 mmol, 1 equiv.) dissolved in diethyl ether (10 mL) was added drop wise and was stirring maintained at –78 °C for 2 h. 1 M HCl (10 mL) and diethyl ether (10 mL) were added and the resultant aqueous layer was further extracted with diethyl ether (2 x 10 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent removed under reduced pressure. Purification by flash column chromatography (cyclohexane-EtOAc; 20:1) afforded the title compound (+)-**10** (164 mg, 64%) as a yellow oil. R_f = 0.7 (cyclohexane-EtOAc; 2:1); ν_{max} (neat/cm^{-1}) 3062, 3029, 2957, 2857, 1746, 1602, 1495, 1454, 1401, 1289, 1239, 1192, 1156, 1071, 1029, 916, 805, 769, 702, 669; δ_H (400 MHz, $CDCl_3$) 0.89 (3H, t, *J* = 7.0 Hz, CH_3), 1.13-1.43 (5H, m, CH_2), 1.69-1.78 (1H, m, CH_2), 1.86 (1H, ddd, *J* = 1.0, 9.0, 18.5 Hz, CH_2), 2.04-2.13 (1H, m, CH), 2.20 (1H, ddd, *J* = 1.0, 8.0, 19.0 Hz, CH_2), 2.51-2.62 (2H, m, 2 x CH_2), 2.87 (1H, dd, *J* = 8.0, 16.0 Hz, CH), 3.76 (1H, d, *J* = 13.5 Hz, CH_2), 3.79 (1H, d, *J* = 13.5 Hz, CH_2), 7.23-7.28 (1H, m, ArH), 7.30-7.34 (4H, m, ArH); δ_C (100 MHz, $CDCl_3$) 13.9 (CH_3), 22.6 (CH_2), 29.8 (CH_2), 33.4 (CH_2), 36.2 (CH_2), 42.4 (CH), 44.0 (CH_2), 45.5 (CH), 46.2 (CH_2), 127.2 (CH), 128.6 (CH),128.7 (CH), 138.0 (C), 216.1 (CO); $[\alpha]_D$ = +54 (*c* = 0.2, $CHCl_3$).

(*S*)-4-Butylcyclopent-2-enone (–)-12:



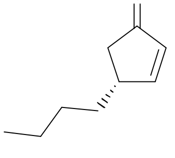
(3*S*,4*S*)-3-(Benzylthio)-4-butylcyclopentanone (+)-**10** (113 mg, 0.43 mmol, 1.0 equiv.) was dissolved in dichloromethane (10 mL) and brought to 0 °C, 77 % *m*-CPBA (202 mg, 0.90 mmol, 2.1 equiv.) was added and the reaction stirred for 1 h. Sodium thiosulfate solution (10 mL) was added and stirring maintained for 30 min. The resultant aqueous layer was extracted with dichloromethane (2 x 10 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent removed under reduced pressure which gave (+)-**11** (125 mg, 99%) as a brown oil {R_f = 0.5 (cyclohexane-EtOAc; 2:1); $[\alpha]_D$ = +50 (*c* = 0.1, $CHCl_3$)}. (+)-**11** (57.0 mg, 0.19 mmol, 1.00 equiv.) was dissolved in dichloromethane (5 mL) and cooled to 0 °C. Triethylamine (30 μL, 0.20 mmol, 1.05 equiv.) was added and the reaction stirred for 1 h. Saturated NH_4Cl (5 mL) and dichloromethane (5 mL) were added and the resultant aqueous layer was further extracted with dichloromethane (2 x 5 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent removed under reduced pressure. Purification by flash column chromatography (cyclohexane-EtOAc; 6:1) afforded the enone (–)-**12** (17.3 mg, 65%) as a yellow oil. R_f = 0.5 (cyclohexane-EtOAc; 2:1); ν_{max} (neat/cm^{-1}) 2958, 2927, 2858, 2250, 1713, 1586, 1505, 1491, 1466, 1446, 1407, 1379, 1350, 1250, 1185, 1097, 1080, 1038, 915, 833, 780, 732, 650; δ_H (400 MHz, $CDCl_3$) 0.91 (3H, t, *J* = 7.0 Hz, CH_3), 1.31-1.43 (5H, m, CH_2), 1.55-1.61 (1H, m, CH_2), 2.00 (1H, dd, *J* = 2.0, 19.0 Hz, CH_2), 2.53 (1H, dd, *J* = 6.5, 19.0 Hz, CH_2), 2.88-2.94 (1H, m, CH), 6.14 (1H, dd, *J* = 2.0, 5.5 Hz, CH), 7.63 (1H, dd, *J* = 2.5, 5.5 Hz, CH); δ_C (100 MHz, $CDCl_3$) 13.9 (CH_3), 22.7 (CH_2), 29.8 (CH_2), 34.4 (CH_2), 41.1 (CH_2) 41.5 (CH), 133.6 (CH), 168.7 (CH), 210.1 (CO); $[\alpha]_D$ = -120 (*c* = 0. 1, $CHCl_3$); {lit. $[\alpha]_D$ = -160.8 (*c* = 1.7, $CHCl_3$), 98% e.e.}.[3]

(3*R*,4*R*)-3-(Benzylthio)-4-butylcyclopentanone (–)-10:



As described above, CuI (19.0 mg, 0.10 mmol, 0.1 equiv.) in diethyl ether (5 mL) was treated with a 2 M solution of butylmagnesium chloride in diethyl ether (1.47 mL, 2.94 mmol, 3.0 equiv.) was added dropwise. The reaction was stirred at –78 °C for 1 h before (+)-**6a** (200 mg, 0.98 mmol, 1.0 equiv.) in diethyl ether (10 mL) was added dropwise. After stirring at –78 °C for 2 h saturated NH_4Cl solution (10 mL) and diethyl ether (10 mL) were added. Work up and purification by flash column chromatography as described afforded (–)-**10** (161 mg, 63%) as a yellow oil. $[\alpha]_D$ = -57 (*c* = 0.1, $CHCl_3$).

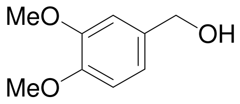
(*R*)-4-Butylcyclopent-2-enone (+)-12:



As described above, (–)-**10** (111 mg, 0.42 mmol, 1.0 equiv.) was dissolved in dichloromethane (10 mL) and brought to 0 °C, 77 % *m*-CPBA (199 mg, 0.89 mmol, 2.1 equiv.) was added and the reaction stirred for 1 h. Saturated sodium thiosulfate solution (10 mL) was added and stirring maintained for 30 min. The resultant aqueous layer was extracted with dichloromethane (2 x 10 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent removed under reduced pressure. Thus, (–)-**11** (120 mg, 97%) was collected as a brown oil and used subsequently without additional purification {$[\alpha]_D$ = -56 (*c* = 0.1, $CHCl_3$)}. (–)-**9** (106 mg, 0.36 mmol, 1.00 equiv.) was dissolved in dichloromethane (10 mL) and brought to 0 °C. Triethylamine (50 µL, 0.38 mmol, 1.05 equiv.) was added and the reaction stirred for 1 h. Saturated NH_4Cl (10 mL) and dichloromethane (10 mL) were added and the resultant aqueous layer was further extracted with dichloromethane (2 x 10 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent removed under reduced pressure. Purification by flash column chromatography (cyclohexane-EtOAc; 6:1) afforded (+)-**12** (31 mg, 62%) as a yellow oil. $[\alpha]_D$ = +121 (*c* = 0.1, $CHCl_3$).

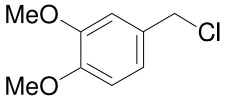
Synthesis of 3,4-Dimethoxybenzyl thiol 8

3,4-Dimethoxybenzylalcohol:[4]



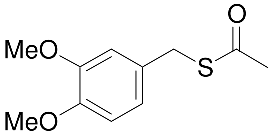
3-4-Dimethoxybenzaldehyde **7** (10.00 g, 60.2 mmol, 1 equiv.) was dissolved in MeOH (300 mL) and cooled to 0 °C. $NaBH_4$ (2.73 g, 72.2 mmol, 1.2 equiv.) was added portionwise and the reaction stirred for 20 min. The reaction was quenched with 1 M HCl (10 mL) until a neutral pH was reached. The solvent was removed under reduced pressure and the residue was extracted with dichloromethane (3 x 50 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent removed under reduced pressure to yield the *title compound* (9.88 g, 98%) as a clear oil. R_f = 0.3 (cyclohexane-EtOAc; 1:1); ν_{max} (neat/cm^{-1}) 3495, 3002, 2938, 2874, 2837, 1594, 1518, 1465, 1420, 1262, 1237, 1138, 1027, 919, 858, 810, 765, 741, 642, 553; δ_H (400 MHz, $CDCl_3$) 2.50 (1H, s, OH), 3.80 (6H, s(br), CH_3), 4.52 (2H, s, CH_2), 6.76-6.82 (3H, m, ArH); δ_C (100 MHz, $CDCl_3$) 55.6 (CH_3), 55.7 (CH_3), 64.8 (CH_2), 110.4 (CH), 111.0 (CH), 119.2 (CH), 133.6 (C), 148.3 (C), 148.9 (C).

3-4-Dimethoxybenzyl chloride:[5]



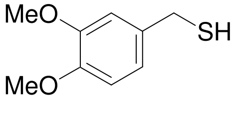
3-4-Dimethoxybenzylalcohol (9.86 g, 58.6 mmol, 1 equiv.) was dissolved in dichloromethane (300 mL) and cooled to 0 °C. Thionyl chloride (8.52 mL, 117.0 mmol, 2 equiv.) was added dropwise followed by dropwise addition of pyridine (4.72 mL, 58.6 mmol, 1 equiv.). The reaction was stirred for 20 min before water (300 mL) was added. The resultant aqueous layer was extracted with dichloromethane (3 x 100 mL) and the combined organic layers were dried over $MgSO_4$. Filteration and the solvent removed under reduced pressure gave the *title compound* (10.83 g, 99%) as a white solid, M.p. = 50-52 °C. R_f = 0.8 (cyclohexane-EtOAc; 1:1); ν_{max} (neat/cm^{-1}) 3002, 2958, 2836, 1607, 1516, 1464, 1419, 1344, 1263, 1238, 1160, 1138, 1099, 1027, 855, 810, 766, 723, 691, 601, 547; δ_H (500 MHz, $CDCl_3$) 3.88 (3H, s, CH_3), 3.90 (3H, s, CH_3), 4.57 (2H, s, CH_2), 6.82 (1H, d, *J* = 8.0 Hz, ArH), 6.92-6.94 (2H, m, ArH); δ_C (75 MHz, $CDCl_3$) 46.7 (CH_2), 55.9 (CH_3), 55.9 (CH_3), 111.0 (CH), 111.7 (CH), 121.1 (CH), 130.0 (C), 149.1 (C), 149.2 (C).

3,4-Dimethoxybenzyl ethanethioate:



3-4-Dimethoxybenzyl chloride (10.94 g, 58.6 mmol, 1 equiv.) was dissolved in DMF (150 mL). To this potassium thioacetate (8.03 g, 70.3 mmol, 1.2 equiv.) was added and the reaction was stirred overnight. Water (200 mL) was added and the mixture was extracted with diethyl ether (4 x 100 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent removed under reduced pressure. Purification by flash column chromatography (cyclohexane-EtOAc; 4:1) afforded the *title compound* (12.60 g, 95%) as a white solid, M.p. = 32-33 °C. R_f = 0.3 (cyclohexane-EtOAc; 4:1); ν_{max} (neat/cm^{-1}) 3000, 2936, 2835, 1689, 1592, 1515, 1465, 1420, 1265, 1231, 1138, 1028, 959, 910, 863, 733, 632, 473; δ_H (400 MHz, $CDCl_3$) 2.33 (3H, s, CH_3), 3.84 (3H, s, CH_3), 3.86 (3H, s, CH_3), 4.08 (2H, s, CH_2), 6.76-6.85 (3H, m, ArH); δ_C (100 MHz, $CDCl_3$) 30.3 (CH_3), 33.4 (CH_2), 55.8 (CH_3), 55.9 (CH_3), 111.2 (CH), 112.0 (CH), 121.0 (CH), 130.1 (C), 148.4 (C), 149.0 (C), 195.2 (CO); Anal. Calcd for $C_{11}H_{14}O_3S$: C, 58.38; H, 6.24; S, 14.17. Found: C, 58.23; H, 6.22; S, 14.54.

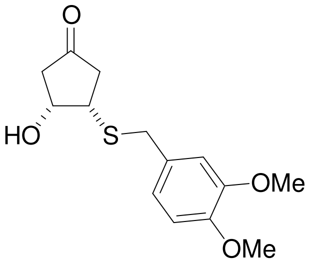
3,4-Dimethoxybenzyl thiol 8:[6]



3,4-Dimethoxybenzyl ethanethioate (3.07 g, 13.6 mmol, 1 equiv.) was dissolved in EtOH (100 mL) and cooled to 0 °C. $NaBH_4$ (0.92 g, 24.4 mmol, 1.8 equiv.) was added portionwise. After 6 h the reaction was quenched with 1 M HCl solution (8 mL) until a neutral pH was reached. EtOH was partially removed under reduced pressure and the residue was extracted with dichloromethane (3 x 30 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent removed under reduced pressure. Purification by flash column chromatography (cyclohexane-EtOAc; 4:1) afforded **8** (2.08 g, 83%) as a clear oil. $R_f = 0.3$ (cyclohexane-EtOAc; 4:1); ν_{max} (neat/cm^{-1}) 2999, 2934, 2834, 2560, 1591, 1514, 1463, 1417, 1334, 1262, 1233, 1138, 1027, 913, 854, 810, 764, 730, 609, 542; δ_H (400 MHz, $CDCl_3$) 1.75 (1H, t, *J* = 7.5 Hz, SH), 3.71 (2H, d, *J* = 7.5 Hz, CH_2), 3.86 (3H, s, CH_3), 3.88 (3H, s, CH_3), 6.78-6.86 (3H, m, ArH); δ_C (100 MHz, $CDCl_3$) 28.8 (CH_2), 55.8 (CH_3), 55.9 (CH_3), 111.2 (CH), 111.3 (CH), 120.0 (CH), 133.6 (C), 148.1 (C), 149.1 (C).

Synthesis of (+)- and (–)-6b

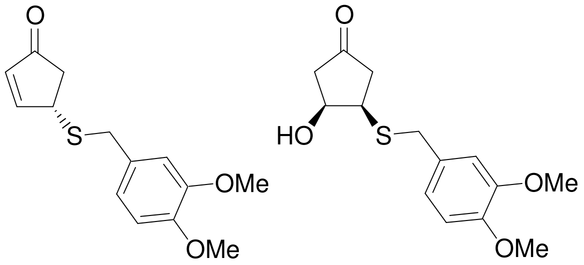
3-(3,4-Dimethoxybenzylthio)-4-hydroxycyclopentanone (±)-4b:



(±)-4-Hydroxycyclopent-2-enone **1** (0.643 g, 6.6 mmol, 1 equiv.) and 3,4-dimethoxybenzyl thiol **8** (1.21 g, 6.6 mmol, 1 equiv.) were dissolved in dichloromethane (70 mL). Triethylamine (90 µL, 0.66 mmol, 0.1 equiv.) was added dropwise and the reaction was stirred for 2 h. The solvent was removed under reduced pressure and the residue purified by column chromatography (cyclohexane-EtOAc, 4:1) to afford the title compound (±)-**4b** (1.61 g, 86%) as a white solid; M.p. = 60-62 °C. R_f = 0.1 (cyclohexane-EtOAc; 4:1); ν_{max} (neat/cm^{-1}) 3448, 3058, 3029, 2951, 2867, 1747, 1686, 1515, 1454, 1396, 1331, 1265, 1153, 1009, 909, 735, 650, 475; δ_H (400 MHz, $CDCl_3$) 2.21 (1H, dd, *J* = 12.0, 18.5 Hz, CH_2), 2.29 (1H, dd, *J* = 4.5, 18.5 Hz, CH_2), 2.42 (1H, dd, *J* = 8.0, 18.5 Hz, CH_2), 2.54 (1H, d, *J* = 18.5 Hz, CH_2), 2.75 (1H, s, OH), 3.30 (1H, ddd, *J* = 3.5, 8.0, 12.0 Hz, CH), 3.74

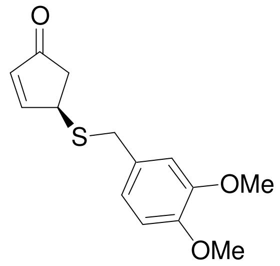
(1H, d, *J* = 13.5 Hz, CH_2), 3.80 (1H, d, *J* = 13.5 Hz, CH_2), 3.88 (3H, s, CH_3), 3.90 (3H, s, CH_3), 4.19-4.21 (1H, m, CH), 6.80-6.87 (2H, m, ArH), 6.91 (1H, d, *J* = 1.5 Hz, ArH); δ_C (125 MHz, $CDCl_3$) 35.3 (CH_2), 40.3 (CH_2), 46.5 (CH_2), 47.0 (CH), 55.9 (CH_3), 56.0 (CH_3), 68.0 (CH), 111.1 (CH), 111.6 (CH), 120.8 (CH), 129.8 (C), 148.6 (C), 149.4 (C), 213.4 (CO). Anal. Calcd for $C_{14}H_{18}O_4S$: C, 59.55; H, 6.43; S, 11.36. Found: C, 59.38; H, 6.38; S, 11.82.

(*S*)-4-(3,4-Dimethoxybenzylthio)cyclopent-2-enone (–)-6b and (3*R*,4*S*)-3-(3,4-dimethoxybenzylthio)-4-hydroxycyclopentanone (–)-4b:



To *cis*-(±)-**4b** (300 mg, 1.06 mmol, 1 equiv.) dissolved in diisopropyl ether (50 mL), vinyl acetate (0.49 mL, 5.31 mmol, 5 equiv.) and *Candida antarctica* Lipase B [300 mg, 1:1 *w/w* (enzyme:substrate)] were added. The reaction was stirred for 16 h. The mixture was filtered, and the enzyme residue washed with diisopropyl ether (2 ×. 30 mL). The solvent was removed under reduced pressure and the residue was dissolved in THF (50 mL) and cooled to 0°C. Triethylamine (0.15 mL, 1.08 mmol, 1.0 equiv.) was added dropwise and the reaction stirred for 1 h. The solvent was removed under reduced pressure and the residue purified by column chromatography (cyclohexane-EtOAc, 4:1) to afford (–)-**6b** (129 mg, 46%) as a colourless oil. R_f = 0.1 (cyclohexane-EtOAc, 4:1); ν_{max} (neat/cm^{-1}) 3060, 3002, 2935, 2836, 1715, 1589, 1515, 1464, 1420, 1341, 1265, 1244, 1139, 1026, 939, 855, 733, 548; δ_H (400 MHz, $CDCl_3$) 2.32 (1H, dd, *J* = 2.0, 19.0 Hz, CH_2), 2.74 (1H, dd, *J* = 6.5, 19.0 Hz, CH_2), 3.72 (1H, d, *J* = 13.5 Hz, CH_2) 3.77 (1H, d, *J* = 13.5 Hz, CH_2), 3.87 (3H, s, CH_3), 3.89 (3H, s, CH_3), 3.90-3.93 (1H, m, CH), 6.18 (1H, dd, *J* = 2.0, 5.5 Hz, CH), 6.78-7.83 (2H, m, ArH), 6.87 (1H, d, *J* = 1.0 Hz, ArH), 7.46 (1H, dd, *J* = 2.5, 5.5 Hz, CH); δ_C (100 MHz, $CDCl_3$) 35.5 (CH_2), 42.6 (CH_2), 43.3 (CH), 55.9 (2 x CH_3), 111.1 (CH), 111.9 (CH), 121.1 (CH), 129.9 (C), 134.4 (CH), 148.5 (C), 149.3 (C), 163.3 (CH), 207.2 (CO); HRMS (EI) cald. for $C_{14}H_{16}O_3S$ (M^+) requires 264.0820; found 264.0818; $[\alpha]_D$ = -97 (*c* = 0.1, $CHCl_3$); HPLC analysis (ASH) isocratic heptane-EtOH; 50:50, (0.6 mL/min): t_r (*S*): 19.5 min, 85% e.e. Further elution gave (–)-**4b** as a white solid (140 mg, 47%); $[\alpha]_D$ = -36 (*c* = 1.0, $CHCl_3$) with data in accord with that reported above. Recrystallisation from dichloromethane gave crystals suitable for X-ray crystallographic analysis.

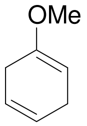
(*R*)-4-(3,4-Dimethoxybenzylthio)cyclopent-2-enone (+)-6b:



To (–)-**4b** (121 mg, 0.43 mmol, 1 equiv.) dissolved in acetic anhydride (2 mL), pyridine (35 μL, 0.43 mmol, 1 equiv.) and triethylamine (60 μL, 0.43 mmol, 1 equiv.) were added dropwise and the reaction stirred for 1 h. The solvent was evaporated under reduced pressure and residue purified by column chromatography (cyclohexane-EtOAc, 3:1) to afford (+)-**6b** (98 mg, 87%) as a colourless oil; $[\alpha]_D$ = + 95 (*c* = 0.1, $CHCl_3$); HPLC analysis (ASH) isocratic heptane-EtOH; 50:50, (0.6 mL/min): t_r (*R*): 17.0 min, 85% e.e. Where additional data was as reported above.

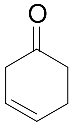
Synthesis of (±)-4-Hydroxycyclohex-2-enone 15

1-Methoxycyclohexa-1,4-diene:[7]



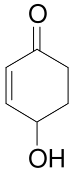
Under nitrogen anisole (21.00 mL, 0.19 mol, 1.0 equiv.) was dissolved in THF (50 mL) and *t*-BuOH (80 mL) and cooled to -78 °C. Liquid ammonia (500 mL approx.) was then introduced. Lithium metal (3.68 g, 0.53 mol, 2.7 equiv.) was added in portions to the mixture. Stirring was continued for 1 h at -33 °C. MeOH (approx. 20 mL) was added until the blue colour disappeared. Water (60 mL) was then gradually added and the reaction allowed warm to room temperature overnight. Extraction was performed with diethyl ether (3 x 80 mL) and the combined organic extracts were washed with water (4 x 50 mL), dried over $MgSO_4$ and the solvent removed under reduced pressure. Thus, the product (19.89 g, 94%) was obtained as a colourless oil. δ_H (300 MHz, $CDCl_3$) 2.68-2.73 (2H, m, CH_2), 2.76-2.84 (2H, m, CH_2), 3.54 (3H, s, CH_3), 4.60-4.63 (1H, m, CH), 5.68-5.72 (2H, m, CH).

Cyclohex-3-enone:[8]



1-Methoxycyclohexa-1,4-diene (19.80 g, 0.18 mol, 1 equiv.) was dissolved in $CHCl_3$ (100 mL) and H_2O (200 mL). To this solution perchloric acid (0.2 mL, 3.3 mmol, 0.02 equiv.) was added and the reaction was stirred overnight. The mixture was concentrated *in vacuo* then re-suspended in Et_2O (100 mL) and sat. NaCl (100 mL). The biphasic mixture was separated and the organic layer washed with H_2O (80 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by column chromatography (*n*-hexane-EtOAc, 19:1), to give the *title compound* (15.09 g, 87%) as a colourless oil. $R_f = 0.30$ (*n*-hexane-EtOAc, 19:1); ν_{max} (neat, cm^{-1}) 3037, 2972, 1720; δ_H (300 MHz, $CDCl_3$) 2.47-2.52 (4H, m, CH_2), 2.86-2.90 (2H, m, CH_2), 5.72-5.78 (1H, m, CH), 5.88-5.91 (1H, m, CH); ^{13}C NMR (100 MHz, $CDCl_3$) 26.0 (CH_2), 39.2 (CH_2), 40.3 (CH_2), 124.7 (CH), 127.4 (CH), 210.4 (CO); HRMS calcd for: $C_6H_{12}ONS$ (CI, MNH_4^+) requires 114.09190: found 114.09225.

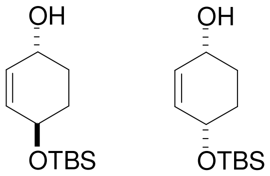
4-Hydroxycyclohex-2-enone:[8]



Cyclohex-3-enone (17.30 g, 0.18 mol, 1.0 equiv.) was dissolved in CH_2Cl_2 (200 mL) and *m*-CPBA 77% (44.37 g, 0.20 mol, 1.1 equiv.) was added over 30 min. The reaction was stirred overnight and sat. sodium bicarbonate solution (100 mL) and sat. sodium thiosulfate solution (100 mL) were added and the reaction stirred for 30 min. The layers were separated and the resulting aqueous layer was extracted with dichloromethane (2 x 80 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent removed under reduced pressure to afford crude epoxide which was dissolved in MeOH-Et_2O (1:1) (200 mL). To this basic Al_2O_3 (20 g) was added and the resultant slurry was stirred at room temperature for 2 h. The mixture was filtered and the solid washed with MeOH-Et_2O (1:1) (100 mL). The filtrate was then concentrated under reduced pressure to dryness and the residue purified by column chromatography (cyclohexane-EtOAc; 1:1) to give the title compound (12.77 g, 63%) as a clear oil. $R_f = 0.1$ (cyclohexane-EtOAc; 4:1); ν_{max} (neat/cm^{-1}) 3396, 2957, 1698, 1417, 1378, 1132, 1065, 970, 943, 862; δ_H (400 MHz, $CDCl_3$) 1.96-2.07 (1H, m, CH_2), 2.32-2.44 (2H, m,CH_2), 2.54-2.63 (1H, m, CH_2), 4.55-4.62 (1H, m, C*H*-OH), 5.97 (1H, d, *J* = 10.0 Hz, CH), 6.91-3.95 (1H, m, CH); δ_C (100 MHz, $CDCl_3$) 32.9 (CH_2), 35.7 (CH_2), 66.7 (CH), 129.7 (CH), 152.8 (CH), 198.9 (CO); HRMS cald for: $C_6H_{12}O_2N$ (Cl, MNH_4^+) requires 130.08681: found 130.08660.

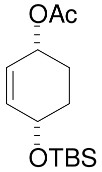
Reduction of (±)-4-(*tert*-Butyldimethylsilyloxy)cyclohex-2-enone 19

cis-4-(*tert*-Butyldimethylsilyloxy)cyclohex-2-enol (±)-*cis*-20 and *trans*-4-(*tert*-butyldimethylsilyloxy)cyclohex-2-enol (±)-*trans*-20:[9,10]



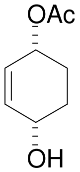
$LiAlH_4$ (10 mg, 0.26 mmol, 1 equiv.) was added to THF (5 mL) and cooled to 0 °C. To this (±)-**19** (58 mg, 0.26 mmol, 1 equiv.) in THF (5 mL) was added dropwise and the reaction stirred at this temperature for 20 min. 0.1 M HCl (10 mL) was added and the resulting aqueous layer was extracted with dichloromethane (3 x 10 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent removed under reduced pressure. Purification by flash column chromatography (cyclohexane-EtOAc; 30:1) afforded (±)-*cis*-**20** (24 mg, 41%) as a clear oil. R_f = 0.65 (cyclohexane-EtOAc; 1:1); δ_H (400 MHz, $CDCl_3$) 0.08 (6H, s, 2 x CH_3), 0.90 (9H, s, CH_3), 1.70-1.74 (2H, m, CH_2), 1.76-1.83 (2H, m, CH_2), 4.07-4.12 (1H, m, CH-OTBS), 4.13-4.16 (1H, m, CH), 5.74 (1H, dd, *J* = 2.0, 10.0 Hz, CH), 5.80 (1H, dd, *J* = 3.0, 10.0 Hz, CH); δ_C (100 MHz, $CDCl_3$) -4.7 (CH_3), -4.6 (CH_3), 18.2 (C), 25.9 (3 x CH_3), 28.2 (CH_2), 28.5 (CH_2), 64.9 (CH), 66.3 (CH), 130.5 (CH), 134.3 (CH). Further elution gave (±)-*trans*-**20** (23 mg, 39%) as a clear oil R_f = 0.60 (cyclohexane-EtOAc; 1:1); δ_H (400 MHz, $CDCl_3$) 0.07 (3H, s, CH_3), 0.08 (3H, s, CH_3), 0.89 (9H, s, CH_3), 1.39-1.59 (2H, m, CH_2), 1.97-2.03 (1H, m, CH_2), 2.10-2.17 (1H, m, CH_2), 4.24-4.28 (2H, m, 2 x CH), 5.70 (1H, d, *J* = 10.5 Hz, CH), 5.73 (1H, d, *J* = 10.5 Hz, CH); δ_C (100 MHz, $CDCl_3$) -4.7 (CH_3), -4.6 (CH_3), 18.2 (C), 25.9 (CH_3), 30.9 (CH_2), 31.0 (CH_2), 66.6 (CH), 67.0 (CH), 131.7 (CH), 133.8 (CH).

cis-4-(*tert*-Butyldimethylsilyloxy)cyclohex-2-enyl acetate:[10]



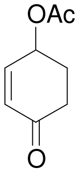
(±)-*cis*-**20** (30 mg, 0.13 mmol, 1 equiv.) was dissolved in acetic anhydride (1 mL), to this pyridine (20 μL, 0.26 mmol, 2 equiv.) was added. The reaction was stirred for 7 h and the solvent was removed under reduced pressure to give the *title compound* (35 mg, 99%) as a clear oil. R_f = 0.7 (cyclohexane-EtOAc; 1:1); δ_H (400 MHz, $CDCl_3$) 0.07 (3H, s, CH_3), 0.08 (3H, s, CH_3), 0.89 (9H, s, CH_3), 1.71-1.83 (3H, m, CH_2), 1.85-1.91 (1H, m, CH_2), 2.03 (3H, s, CH_3), 4.14-4.19 (1H, m, CH), 5.15 (1H, ddd, app. q, *J* = 4.0 Hz, CH), 5.73 (1H, dd, *J* = 3.5, 10.0 Hz, CH), 5.86 (1H, dd, *J* = 2.0, 10.0 Hz, CH); δ_C (100 MHz, $CDCl_3$) -4.7 (CH_3), -4.6 (CH_3), 18.2 (C), 21.3 (CH_3), 25.4 (CH_2), 25.8 (CH_3), 28.4 (CH_2), 66.3 (CH), 67.0 (CH), 126.2 (CH), 136.4 (CH), 170.8 (CO).

cis-4-Hydroxycyclohex-2-enyl acetate 21:[11]



(±)-*cis*-**20** (28 mg, 0.10 mmol, 1 equiv.) was dissolved in THF (2 mL), to this a 1.0 M solution of TBAF in THF (0.21 mL, 0.21 mmol, 2 equiv.) was added and the reaction stirred overnight. The solvent was removed under reduced pressure and the crude product was purified by flash column chromatography (pentane-EtOAc; 1:1) to afford the title compound (±)-*cis*-**21** (12 mg, 74%) as a clear oil. R_f = 0.3 (cyclohexane-EtOAc; 1:1); δ_H (400 MHz, $CDCl_3$) 1.71-1.79 (1H, m, CH_2), 1.82-1.87 (2H, m, CH_2), 1.89-1.94 (1H, m, CH_2), 2.06 (3H, s, CH_3), 4.15-4.22 (1H, m, CH), 5.19 (1H, ddd, app. q, *J* = 4.0, CH), 5.80 (1H, dd, *J* = 3.5, 10.0 Hz, CH), 5.97 (1H, dd, *J* = 2.5, 10.0 Hz, CH); δ_C (100 MHz, $CDCl_3$) 21.3 (CH_3), 24.9 (CH_2), 28.2 (CH_2), 65.4 (CH), 67.2 (CH), 128.0 (CH), 134.7 (CH), 170.7 (CO).

4-(Acetoxy)cyclohex-2-enone (±)-18:[12]

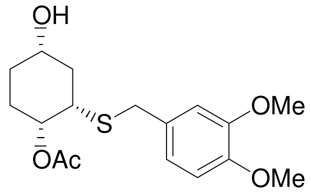


Under nitrogen (±)-*cis*-**21** (10 mg, 0.064 mmol, 1 equiv.) was dissolved in dry dichloromethane (2 mL). Dess-Martin periodinane (33 mg, 0.077 mmol, 1.2 equiv.) was added and the reaction stirred for 30 mins. Sat. sodium bicarbonate solution (3 mL) and sat. sodium thiosulfate solution (3 mL) were added and the reaction stirred for 20 min. The layers were separated and the resulting aqueous layer was extracted with dichloromethane (2 x 5 mL). The combined organic layers were dried over

$MgSO_4$, filtered and the solvent removed under reduced pressure to afford the title compound (±)-**18** (8 mg, 81 %) as a clear oil. $R_f = 0.35$ (pentane-EtOAc; 3:1); ν_{max} (neat/cm^{-1}) 1741, 1686, 1372, 1236, 1037; δ_H (400 MHz, $CDCl_3$) 1.99-2.20 (1H, m, CH_2), 2.12 (3H, s, CH_3), 2.28-2.70 (3H, m, CH_2), 5.55-5.58 (1H, m, CH), 6.06 (1H, ddd, *J* = 1.0, 1.5, 10.0 Hz, CH), 6.84 (1H, ddd, *J* = 1.5, 2.5, 10.0 Hz, CH); δ_C (100 MHz, $CDCl_3$) 21.0 (CH_3), 28.7 (CH_2), 35.0 (CH_2), 67.7 (CH), 130.8 (CH), 147.6 (CH), 170.3 (CO); HRMS (CI) cald. for $C_8H_{14}O_3N$ (MNH_4^+) requires 173.08459; found 173.08510.

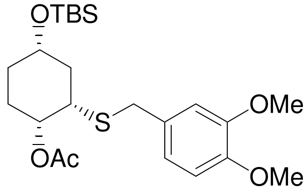
Cope-type sulfoxide elimination for conversion of (–)-17 to (–)-19

(1*R*,2*S*,4*S*)-2-(3,4-Dimethoxybenzylthio)-4-hydroxycyclohexyl acetate (–)-22:



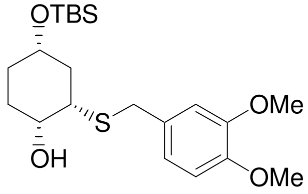
Compound (–)-**17** (2.53 g, 7.48 mmol, 1.0 equiv.) was dissolved in EtOH (80 mL), to this $NaBH_4$ (283 mg, 7.48 mmol, 1.0 equiv.) was added portion wise over 5 min. The reaction was stirred for 20 min. TLC analysis indicated consumption of starting material. The reaction was quenched with 1M HCl (10 mL approx.) until a neutral pH was reached. The solvent was removed under reduced pressure and the residue was extracted with dichloromethane (3 x 50 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent removed under reduced pressure. Purification by flash column chromatography (cyclohexane-EtOAc; 1:1) afforded the title compound (–)-**22** (2.44 g, 96%) as a clear oil. $R_f = 0.1$ (cyclohexane-EtOAc; 1:1); ν_{max} (neat/cm^{-1}) 3487, 2991, 2941, 2861, 1733, 1573, 1513, 1457, 1372, 1336, 1256, 1145, 1103, 1028, 965; δ_H (400 MHz, $CDCl_3$) 1.37-1.82 (4H, m, CH_2), 1.94-2.06 (2H, m, CH_2), 2.12 (3H, s, CH_3), 2.63 (1H, ddd, *J* = 3.0, 3.5, 12.5 Hz, CH), 3.57–3.66 (1H, m, CH), 3.69 (1H, d, *J* = 13.5 Hz, CH_2), 3.74 (1H, d, *J* = 13.5 Hz, CH_2), 3.86 (3H, s, CH_3), 3.88 (3H, s, CH_3), 5.06–5.17 (1H, m, CH), 6.77 (1H, d, *J* = 8.0 Hz, ArH), 6.82 (1H, dd, *J* = 2.0, 8.0 Hz, ArH), 6.88 (1H, d, *J* = 2.0 Hz, ArH); δ_C (100 MHz, $CDCl_3$) 21.1 (CH_3), 27.7 (CH_2), 29.3 (CH_2), 35.1 (CH_2), 36.6 (CH_2), 43.4 (CH), 55.9 (CH_3), 56.0 (CH_3), 68.3 (CH), 69.4 (CH), 110.9 (CH), 111.8 (CH), 121.0 (CH), 130.2 (C), 148.1 (C), 149.1 (C), 170.4 (CO); HRMS (ES^+) cald. for $C_{17}H_{24}O_5NaS$ (MNa^+) requires 363.1242; found 363.1233; $[\alpha]_D = -78.3$ (*c* = 0.25, $CHCl_3$).

(1*R*,2*S*,4*S*)-4-(*tert*-Butyldimethylsilyloxy)-2-(3,4-dimethoxybenzylthio)cyclohexyl acetate:



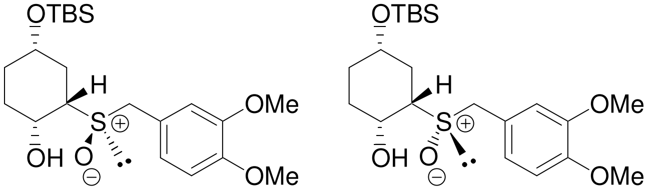
Under nitrogen compound (–)-**22** (0.985 g, 2.89 mmol, 1 equiv.) was dissolved in dry dichloromethane (20 mL). To this TBSCl (0.872 g, 5.79 mmol, 2 equiv.), DBU (1.10 mL, 7.23 mmol, 2.5 equiv.) and catalytic DMAP (5 mg) were added. The reaction was stirred for 18 h. After this time dichloromethane (50 mL) and H_2O (50 mL) were added. The resulting organic layer was further extracted with 0.1 M HCl (2 × 40 ml), sat. sodium bicarbonate (40 mL) and brine (40 mL). The organic layer was dried over $MgSO_4$, filtered and the solvent removed under reduced pressure, purification by flash column chromatography (CH_2Cl_2-Pentane; 9:1) afforded the *title compound* (1.185 g, 90%) as a viscous opaque oil. $R_f = 0.2$ (CH_2Cl_2-Pentane; 9:1); ν_{max} (neat/cm^{-1}) 3053, 2990, 2946, 2857,1737, 1513, 1463, 1372, 1254, 1146, 1113, 1081, 1372, 1254, 1146, 1113, 1081, 1029, 987; δ_H (400 MHz, $CDCl_3$) 0.04 (6H, s, CH_3), 0.87 (9H, s, CH_3), 1.33-1.43 (1H, m, CH_2), 1.49-1.59 (1H, m, CH_2), 1.64-1.74 (2H, m, CH_2), 1.82-1.87 (1H, m, CH_2), 1.98 (1H, ddd, *J* = 3.0, 6.5, 14.0 Hz, CH_2), 2.11 (3H, s, CH_3), 2.58 (1H, ddd, *J* = 3.0, 6.5, 13.0 Hz, CH), 3.50–3.57 (1H, m, CH), 3.69 (1H, d, *J* = 13.5 Hz, CH_2), 3.74 (1 H, d, *J* = 13.5 Hz, CH_2), 3.87 (3H, s, CH_3), 3.89 (3H, s, CH_3), 5.12 (1H, app. q, *J* = 2.5 Hz, CH), 6.77 (1H, d, *J* = 8.0 Hz, ArH), 6.82 (1H, dd, *J* = 2.0, 8.0 Hz, ArH), 6.89 (1H, d, *J* = 2.0 Hz, ArH); δ_C (100 MHz, $CDCl_3$) -4.7 (2 x CH_3), 11.1 (C), 21.2 (CH_3), 25.8 (CH_3), 28.1 (CH_2), 29.6 (CH_2), 35.2 (CH_2), 37.1 (CH_2), 43.6 (CH), 55.8 (CH_3), 55.9 (CH_3), 69.2 (CH), 70.2 (CH), 110.9 (CH), 111.8 (CH), 120.9 (CH), 130.4 (C), 148.1 (C), 149.1 (C), 170.6 (CO); HRMS (ES$^+$) cald. for $C_{23}H_{38}O_5SiSNa$ (MNa$^+$) requires 477.2107; found 477.2127; $[\alpha]_D = -72.7$ (*c* = 1.0, $CHCl_3$).

(1*R*,2*S*,4*S*)-4-(*tert*-Butyldimethylsilyloxy)-2-(3,4-dimethoxybenzylthio)cyclohexanol:



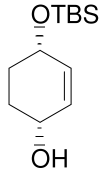
The above acetoxy compound (750 mg, 1.65 mmol, 1 equiv.) was dissolved in MeOH (50 mL), to this potassium carbonate (342 mg, 2.47 mmol, 1.5 equiv.) was added and the reaction was stirred for 18 h. After this time most of the methanol was removed under reduced pressure and dichloromethane (50 mL) and brine (50 mL) were added. The layers were separated and the resulting aqueous layer was extracted with dichloromethane (2 × 30 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent removed under reduced pressure. Purification by flash column chromatography (dichloromethane-MeOH; 100:1) afforded the *title compound* (647 mg, 95%) as a clear oil. $R_f = 0.2$ (dichloromethane-MeOH; 100:1); ν_{max} (neat/cm^{-1}) 3509, 3053, 2993, 2938, 2856, 1593, 1513, 1463, 1423, 1375, 1344, 1258, 1193, 1139, 1110, 1086, 1032, 975; δ_H (400 MHz, $CDCl_3$) 0.02 (6H, s, CH_3), 0.86 (9H, s, CH_3), 1.28-1.35 (1H, m, CH_2), 1.55-1.76 (4H, m, CH_2), 2.04 (1H, ddd, *J* = 3.5, 7.0, 14.5 Hz, CH_2), 2.70 (1H, ddd, *J* = 2.5, 4.0, 13.0 Hz, CH), 3.48-3.56 (1H, m, CH), 3.67 (1H, d, *J* = 13.5 Hz, CH_2), 3.72 (1H, d, *J* = 13.5 Hz, CH_2), 3.77-3.79 (1H, m, CH), 3.87 (3H, s, CH_3), 3.88 (3H, s, CH_3), 6.77-6.82 (2H, m, ArH), 6.87 (1H, d, *J* = 1.5 Hz, ArH); δ_C (100 MHz, $CDCl_3$) -4.7 (CH_3), -4.6 (CH_3), 18.0 (C), 25.8 (CH_3), 28.8 (CH_2), 28.9 (CH_2), 34.5 (CH_2), 35.7 (CH_2), 46.9 (CH), 55.8 (CH_3), 55.9 (CH_3), 64.1 (CH), 70.5 (CH), 110.9 (CH), 111.7 (CH), 120.8 (CH), 130.2 (C), 148.2 (C), 149.1 (C); HRMS (ES$^+$) cald. for $C_{21}H_{37}O_4SiS$ (MH$^+$) requires 413.2182; found 413.2200; $[\alpha]_D = -58.4$ (*c* = 1.0, $CHCl_3$).

(1*R*,2*S*,4*S*)-4-(*tert*-Butyldimethylsilyloxy)-2-(3,4-dimethoxybenzylsulfinyl)cyclo-hexanol (–)-23:



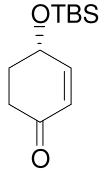
The above secondary alcohol (0.961 g, 2.33 mmol, 1 equiv.) was dissolved in MeOH (30 mL) and the solution was brought to 0 °C. $NaIO_4$ (0.498 mg, 2.33 mmol, 1 equiv.) dissolved in H_2O (30 mL) was added and the reaction was stirred for 45 min at this temperature and then for 4 h at rt. Most of the methanol was removed under reduced pressure and dichloromethane (50 mL) was added. The layers were separated and the resulting aqueous layer was extracted with dichloromethane (2 x 30 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent removed under reduced pressure. Purification by flash column chromatography (cyclohexane-EtOAc; 1:1) afforded **23** (0.779 g, 78%) as an amorphous white solid 3:2 mixture of diastereoisomers, M.p. = 125-128 °C. Data for the major diastereoisomer, M.p. = 162-163 °C. $R_f = 0.05$ (cyclohexane-EtOAc; 1:1); ν_{max} (neat/cm^{-1}) 3303, 3015, 2949, 2855, 1590, 1518, 1464, 1342, 1258, 1214, 1191, 1151, 1108, 1073, 1026, 975; δ_H (400 MHz, $CDCl_3$) 0.04 (6H, s, CH_3), 0.85 (9H, s, CH_3), 1.29-1.36 (1H, m, CH_2), 1.61-1.72 (2H, m, CH_2), 1.76-1.86 (1H, m, CH_2), 1.97 (1H, ddd, *J* = 3.5, 7.5, 14.5 Hz, CH_2), 2.10-2.24 (1H, m, CH_2), 2.36 (1H, ddd, *J* = 2.5, 3.5, 13.5 Hz, CHS), 3.53–3.60 (1H, m, CH), 3.86 (6H, s(br), CH_3), 4.03 (1H, s, OH), 4.05 (2H, s, CH_2), 4.54–4.59 (1H, m, CH), 6.79-6.84 (3H, m, ArH); δ_C (100 MHz, $CDCl_3$) -4.4 (CH_3), -4.3 (CH_3), 18.2 (C), 26.0 (CH_3), 29.3 (CH_2), 30.9 (CH_2), 31.8 (CH_2), 55.6 (CH_2), 56.1 (CH_3), 56.2 (CH_3), 56.8 (CH), 64.2 (CH), 70.3 (CH), 111.7 (CH), 113.0 (CH), 122.3 (C), 122.6 (CH), 149.5 (C), 149.6 (C); HRMS (ES^+) cald. for $C_{21}H_{37}O_5SiS$ (MH^+) requires 429.2131; found 429.2110; $[\alpha]_D$ = -50.0 (*c* = 0.25, $CHCl_3$). Data for both diastereoisomers: M.p. = 125-128 °C. δ_H (400 MHz, $CDCl_3$); 0.04 (6H, s, CH_3^{*}), 0.07 (3H, s, $CH_3^{\wedge}$), 0.08 (3H, s, $CH_3^{\wedge}$), 0.87 (9H, s, CH_3^{*}), 0.89 (9H, s, $CH_3^{\wedge}$), 1.30-1.39 (2H, m, CH_2^{*}, $CH_2^{\wedge}$), 1.62-2.03 (8H, m, 4 × CH_2^{*}, 4 × $CH_2^{\wedge}$), 2.09-2.24 (2H, m, CH_2^{*}, $CH_2^{\wedge}$), 2.36-2.45 (2H, m, CH^{*}-S, $CH^{\wedge}$-S), 3.32 (1H, s, $OH^{\wedge}$), 3.53-3.68 (2H, m, CH^{*}-OTBS, $CH^{\wedge}$-OTBS), 3.87 (12H, s(br), CH_3^{*}, $CH_3^{\wedge}$), 3.96 (1H, d, *J* = 13.0 Hz, $CH_2^{\wedge}$-S), 4.04-4.07 (4H, m, OH^{*}, 2 × CH_2^{*}-S, $CH_2^{\wedge}$-S), 4.28-4.32 (1H, m, C$H^{\wedge}$-OH), 4.55-4.59 (1H, m, CH^{*}-OH), 6.78-6.86 (6H, m, 3 x ArH^{*}, 3 x $ArH^{\wedge}$);δ_C (100 MHz, $CDCl_3$) -4.4 (CH_3^{*}), -4.3 (2 x $CH_3^{\wedge}$), -4.3 (CH_3^{*}), 18.2 (C^{*}), 18.3 ($C^{\wedge}$), 26.0 (CH_3^{*}), 26.0 ($CH_3^{\wedge}$), 29.3 (CH_2^{*}), 29.9 ($CH_2^{\wedge}$), 30.9 (CH_2^{*}), 31.3 ($CH_2^{\wedge}$), 31.8 (CH_2^{*}), 31.9 ($CH_2^{\wedge}$), 54.9 ($CH_2^{\wedge}$), 55.6 (CH_2^{*}), 56.1 (CH_3^{*}, $CH_3^{\wedge}$), 56.2 (CH_3^{*}, $CH_3^{\wedge}$), 57.2 (CH-S^{*}), 57.5 (CH-$S^{\wedge}$), 64.1 (CH-OH^{*}), 66.3 (CH-$OH^{\wedge}$), 70.3 (CH-$OTBS^{*}$), 70.6 (CH-$OTBS^{\wedge}$), 111.7 (CH^{*}), 111.7 ($CH^{\wedge}$), 112.9 ($CH^{\wedge}$), 113.0 (CH^{*}), 122.3 (C^{*}), 122.4 ($CH^{\wedge}$), 122.5 ($C^{\wedge}$), 122.6 (CH^{*}), 149.4 ($C^{\wedge}$), 149.5 (2 x C^{*}, 1 x $C^{\wedge}$).

(1*R*,4*S*)-4-(*tert*-Butyldimethylsilyloxy)cyclohex-2-enol (–)-20:[9,10]



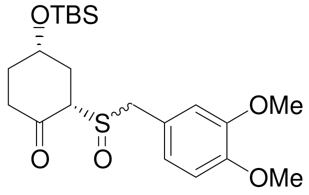
In a sealed tube **23** (70 mg, 0.16 mmol, 1 equiv.) was dissolved in mesitylene (3 mL) and $CaCO_3$ (70 mg, 0.70 mmol, 4.4 equiv.) was added. The reaction was heated under nitrogen at 165 °C for 3 h. The solvent was removed under reduced pressure and the residue was dissolved in CH_2Cl_2 (10 mL) and H_2O (10 mL). The resultant aqueous layer was extracted with CH_2Cl_2 (2 x 10 mL). The combined organic layers were dried over $MgSO_4$. Filtration and removal of the solvent *in vacuo* afforded the crude material which was purified by flash column chromatography (cyclohexane-EtOAc; 15:1) to afford (–)-**20** (5.5 mg, 14%) as a clear oil. R_f = 0.6 (pentane -EtOAc; 1:1); with spectroscopic data as above; $[\alpha]_D$ = -37.6 (*c* = 0.2, $CHCl_3$); {lit. $[\alpha]_D$ = -30 (*c* = 0.4, EtOH)}.[9] Further elution gave **23** (50 mg, 71%) as a single diastereoisomer.

(*S*)-4-(*tert*-Butyldimethylsilyloxy)cyclohex-2-enone (–)-19:[2,13]



Under nitrogen (–)-**20** (8 mg, 0.035 mmol, 1 equiv.) was dissolved in dry dichloromethane (2 mL). Dess-Martin periodinane (18 mg, 0.042 mmol, 1.2 equiv.) was added and the reaction stirred for 30 mins. Sat. sodium bicarbonate solution (3 mL) and sat. sodium thiosulfate solution (3 mL) were added and the reaction stirred for 20 min. The layers were separated and the resulting aqueous layer was extracted with dichloromethane (2 x 5 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent removed under reduced pressure to afford (–)-**19** (7 mg, 88%) as a clear oil. $R_f = 0.15$ (CH_2Cl_2); ν_{max} (neat/cm^{-1}) 3020, 3000, 2942, 2840, 1675, 1377, 1245; δ_H (400 MHz, $CDCl_3$) 0.12 (3H, s, CH_3), 0.13 (3H, s, CH_3), 0.91 (9H, s, CH_3), 1.95-2.05 (1H, m, CH_2), 2.17-2.24 (1H, m, CH_2), 2.30-2.39 (1H, m, CH_2), 2.54-2.60 (1H, m, CH_2), 4.50-4.55 (1H, m, CH), 5.92 (1H, ddd, *J* = 1.0, 2.0, 10.0 Hz, CH), 6.83 (1H, ddd, *J* = 1.5, 2.5, 10.0 Hz, CH); δ_C (100 MHz, $CDCl_3$) -4.8 (CH_3), -4.6 (CH_3), 18.1 (C), 25.7 (CH_3), 32.9 (CH_2), 35.5 (CH_2), 67.0 (CH), 128.7 (CH), 153.9 (CH), 198.8 (CO); HRMS (CI) cald. for $C_{12}H_{26}O_2SiN$ (MNH_4^+) requires 244.17791; found 244.17786; $[\alpha]_D^{20} = +101.0$ (*c* = 1.0, $CHCl_3$); {lit. $[\alpha]_D^{20} = +107.1$ (*c* = 1.3, $CHCl_3$)}.[13]

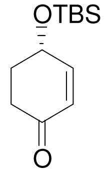
(2*S*,4*S*)-4-(*tert*-Butyldimethylsilyloxy)-2-(3,4-dimethoxybenzylsulfinyl)cyclo-hexanone (–)-24:



Under nitrogen compound (–)-**23** (76 mg, 0.18 mmol, 1.0 equiv.) was dissolved in dry dichloromethane (10 mL), to this Dess-Martin Periodinane (90 mg, 0.21 mmol, 1.2 equiv.) was added and the reaction was stirred for 1 h. Sat. sodium bicarbonate solution (10 mL) and sat. sodium thiosulfate solution (10 mL) were added and the reaction stirred for 15 min. The layers were separated and the resulting aqueous layer was extracted with dichloromethane (2 x 10 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent removed under reduced pressure. Purification by flash column chromatography (pentane-EtOAc; 1:1) afforded the title compound (–)-**24** (44 mg, 58%) as a clear oil. $R_f = 0.1$ (pentane-EtOAc; 1:1); ν_{max} (neat/cm^{-1}) 3015, 2934, 2856, 1734, 1712, 1593, 1514, 1463, 1421, 1370, 1344, 1257, 1149, 1115, 1081, 1028, 957;

δ_H (400 MHz, $CDCl_3$) 0.03 (3H, s, CH_3), 0.06 (3H, s, CH_3), 0.82 (9H, s, CH_3), 1.82-1.93 (1H, m, CH_2), 2.00-2.13 (2H, m, CH_2), 2.30-2.42 (2H, m, CH_2), 2.62-2.73 (1H, m, CH_2), 3.56-3.63 (1H, dd, *J* = 6.5, 12.5 Hz, CH), 3.85 (3H, s, CH_3), 3.86 (3H, s, CH_3), 3.98 (1 H, d, *J* = 13.5 Hz, CH_2), 4.14 (1 H, d, *J* = 13.5 Hz, CH_2), 4.31-4.37 (1H, m, CH), 6.75 (1H, dd, *J* = 2.0, 8.0 Hz, ArH). 6.80-6.83 (2H, m, ArH); δ_C (100 MHz, $CDCl_3$) -5.0 (CH_3), 17.8 (C), 25.6 (CH_3), 33.6 (CH_2), 34.0 (CH_2), 37.0 (CH_2), 55.7 (CH_3), 55.9 (CH_3), 56.0 (CH_2), 61.6 (CH), 64.8 (CH), 111.0 (CH), 112.9 (CH), 122.2 (C), 122.4 (CH), 149.1 (C), 149.2 (C), 207.2 (CO); HRMS (ES^-) cald. for $C_{21}H_{34}O_5SiS$ ($M-H^-$) requires 425.1818; found 425.1822; $[\alpha]_D$ = -10 (*c* = 0.1, $CHCl_3$).

(*S*)-4-(*tert*-Butyldimethylsilyloxy)cyclohex-2-enone (–)-19:[2,13]



In a sealed tube (–)-**24** (25 mg, 0.059 mmol, 1 equiv.) was dissolved in toluene (3 mL) and $CaCO_3$ (25 mg, 0.25 mmol, 4.2 equiv.) was added. The reaction was heated under nitrogen at 110 °C for 1 h. The solvent was removed under reduced pressure and resulting residue and the resulting residue was taken up in CH_2Cl_2 (5 mL). H_2O (5 mL) was added and the resultant aqueous layer was extracted with CH_2Cl_2 (2 x 5 mL). The combined organic layers were dried over $MgSO_4$. Filtration and removal of the solvent *in vacuo* afforded the crude material which was purified by flash column chromatography (pentane-CH_2Cl_2; 1:1) which gave (–)-**19** (10 mg, 75%) as a clear oil. $[\alpha]_D$ = -99 (*c* = 0.3, $CHCl_3$), where additional data was as reported above.

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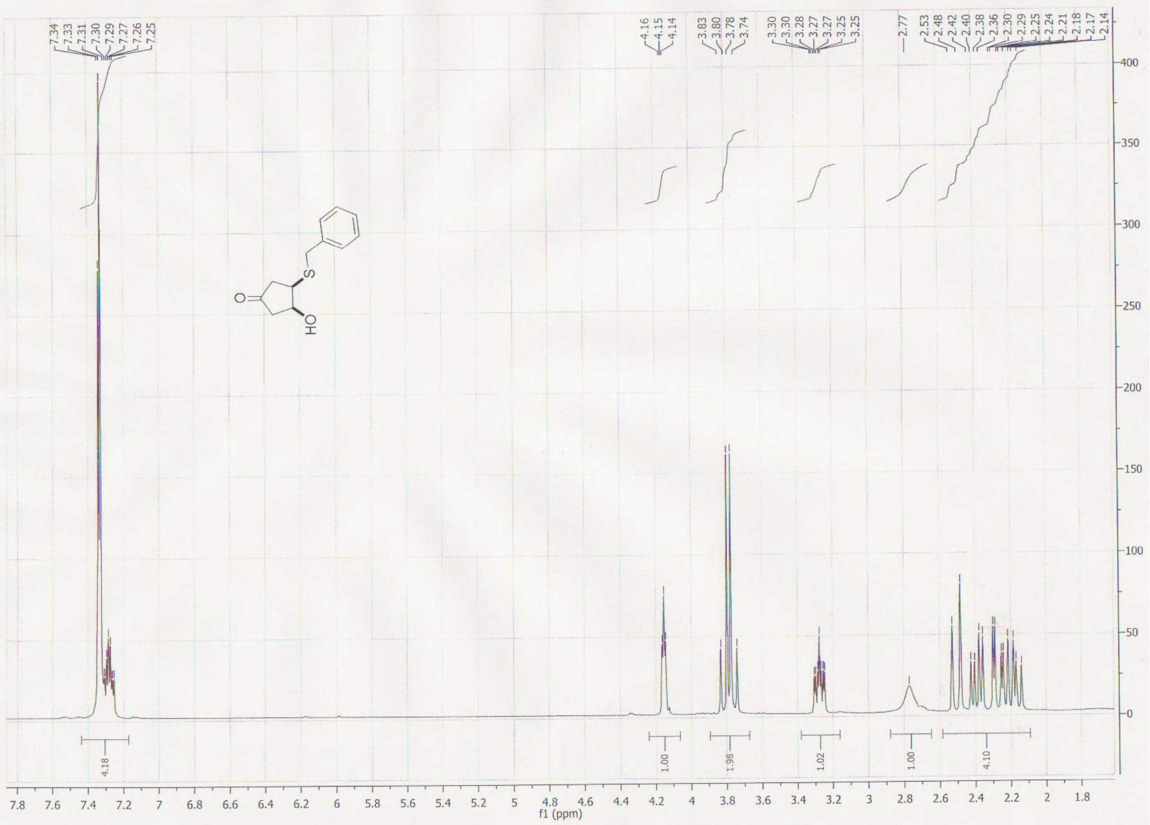
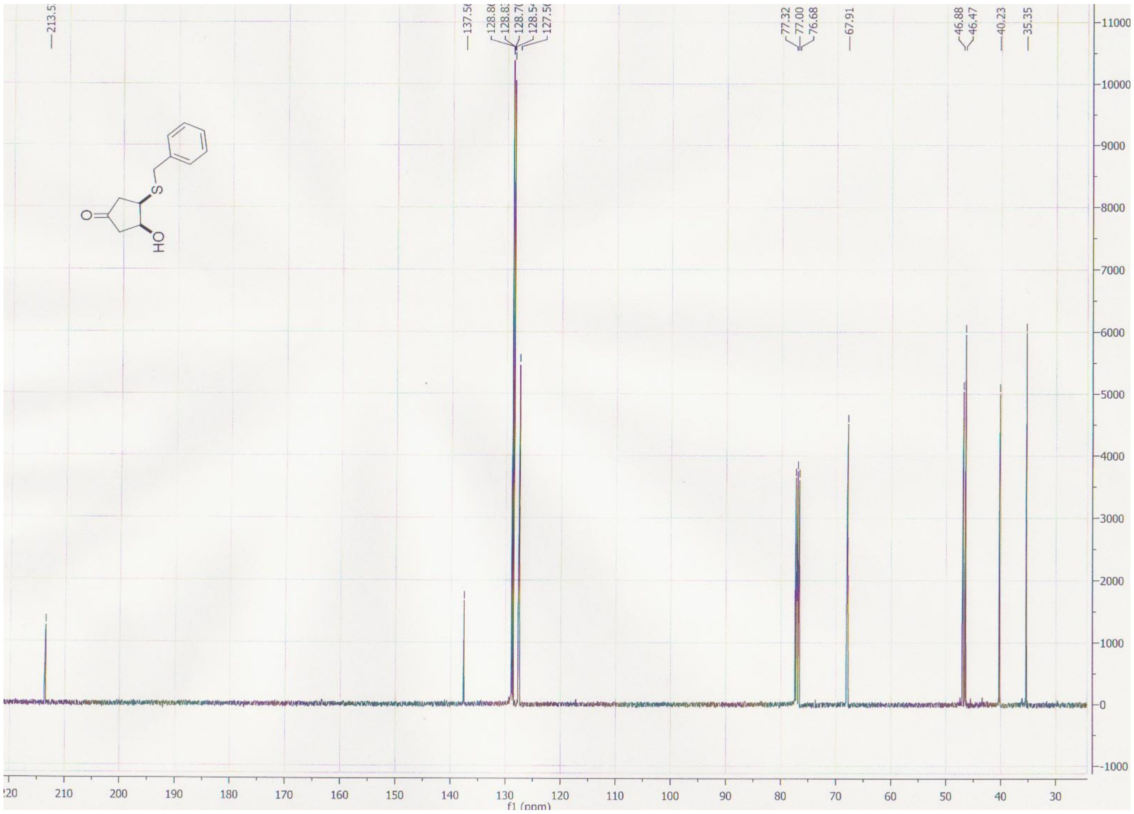
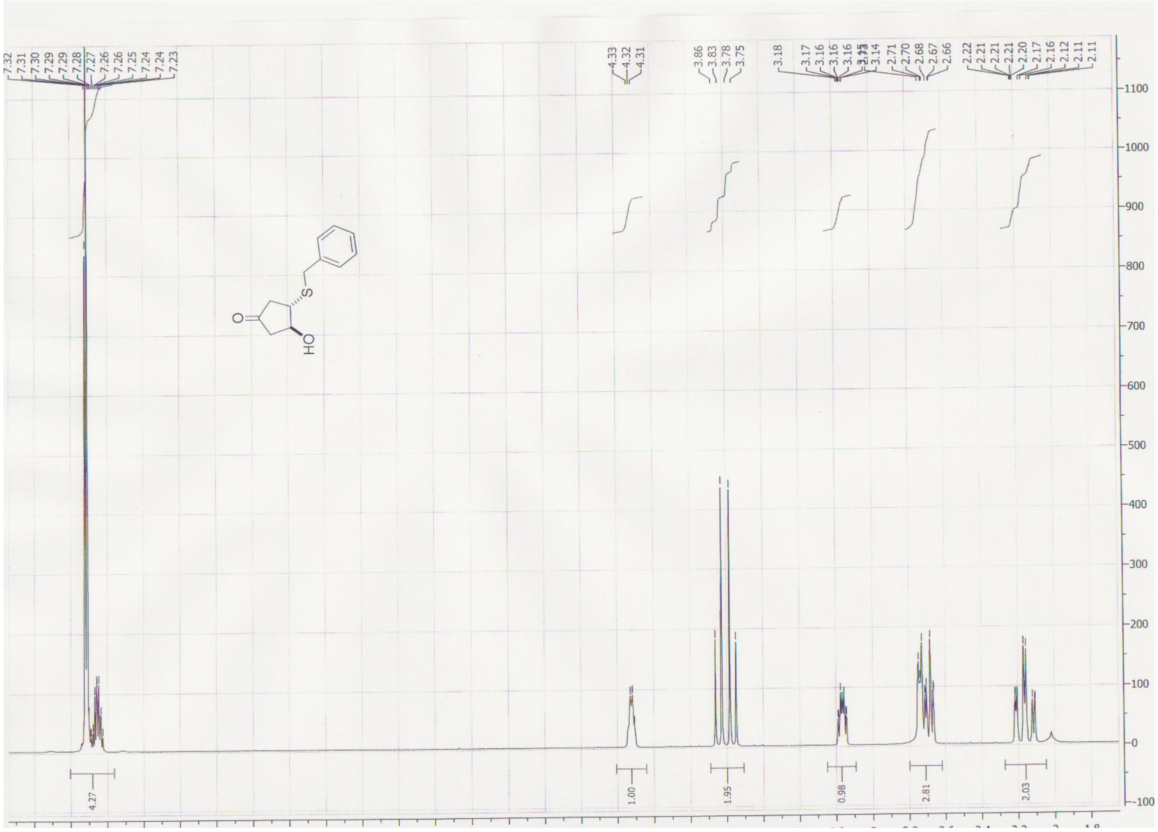
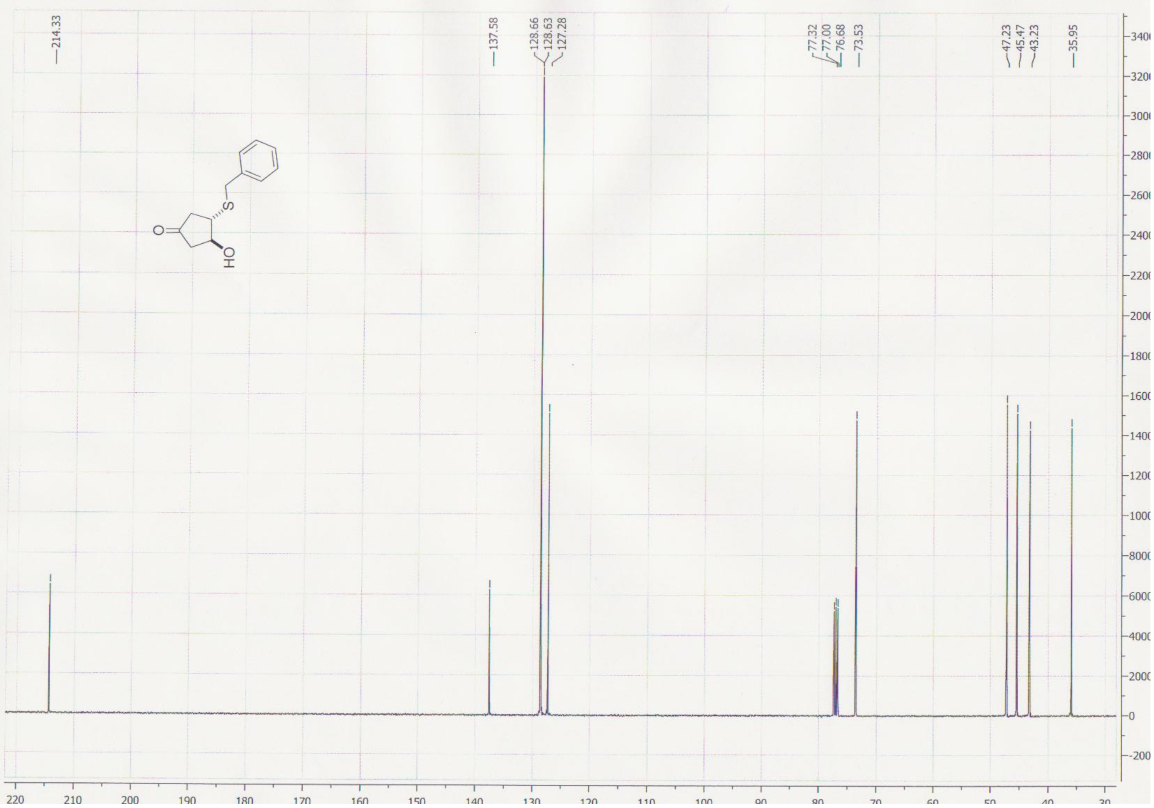
Compound *cis*-**4a**



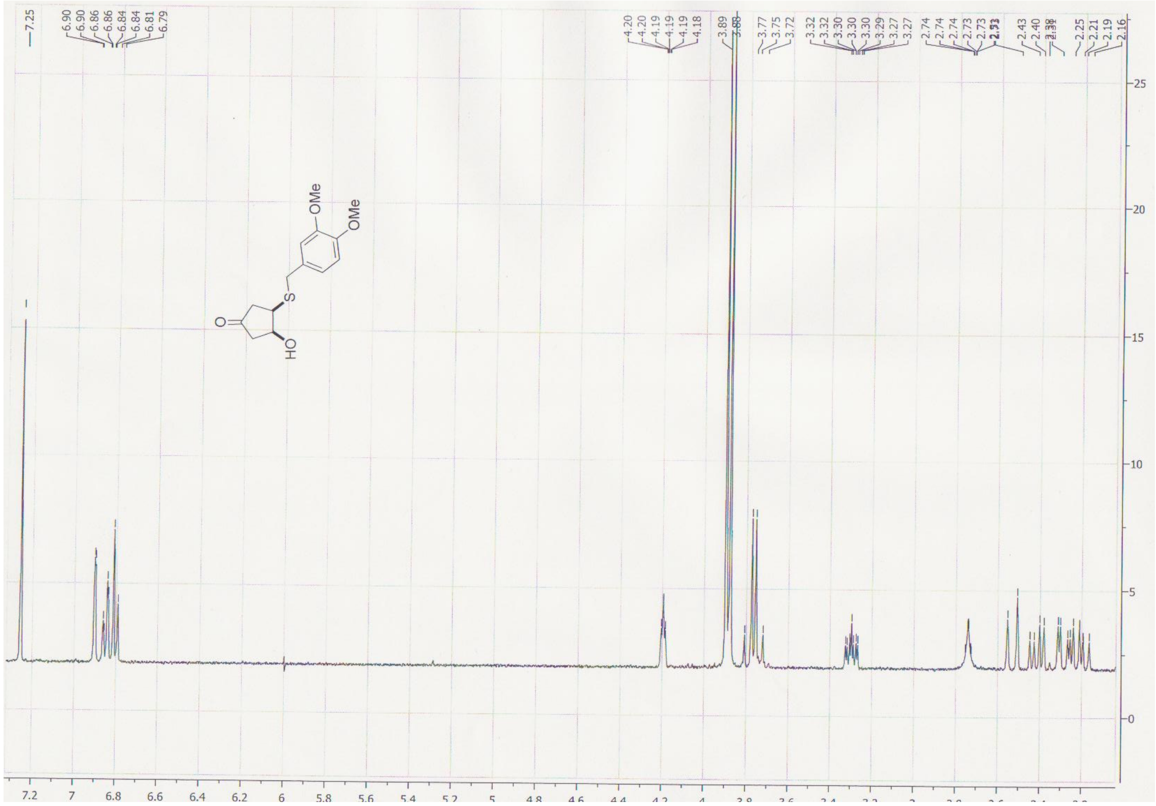


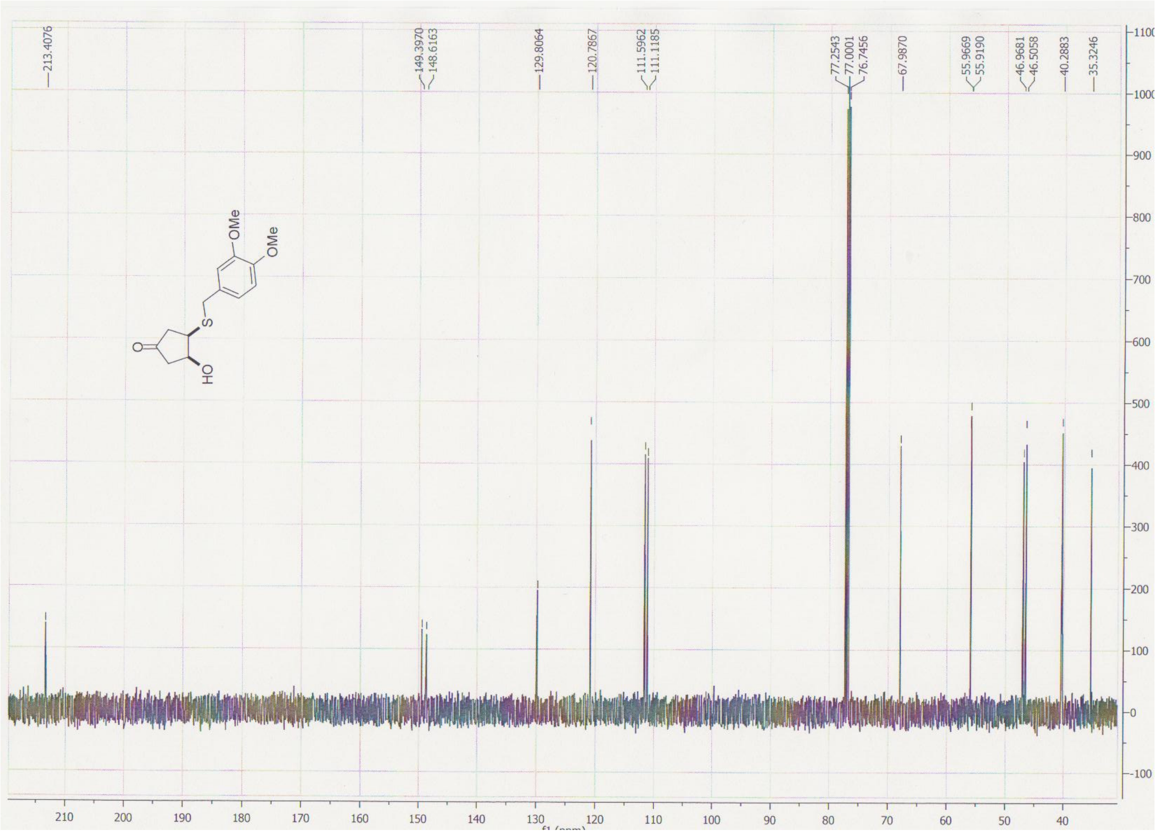
Compound *trans*-**4a**



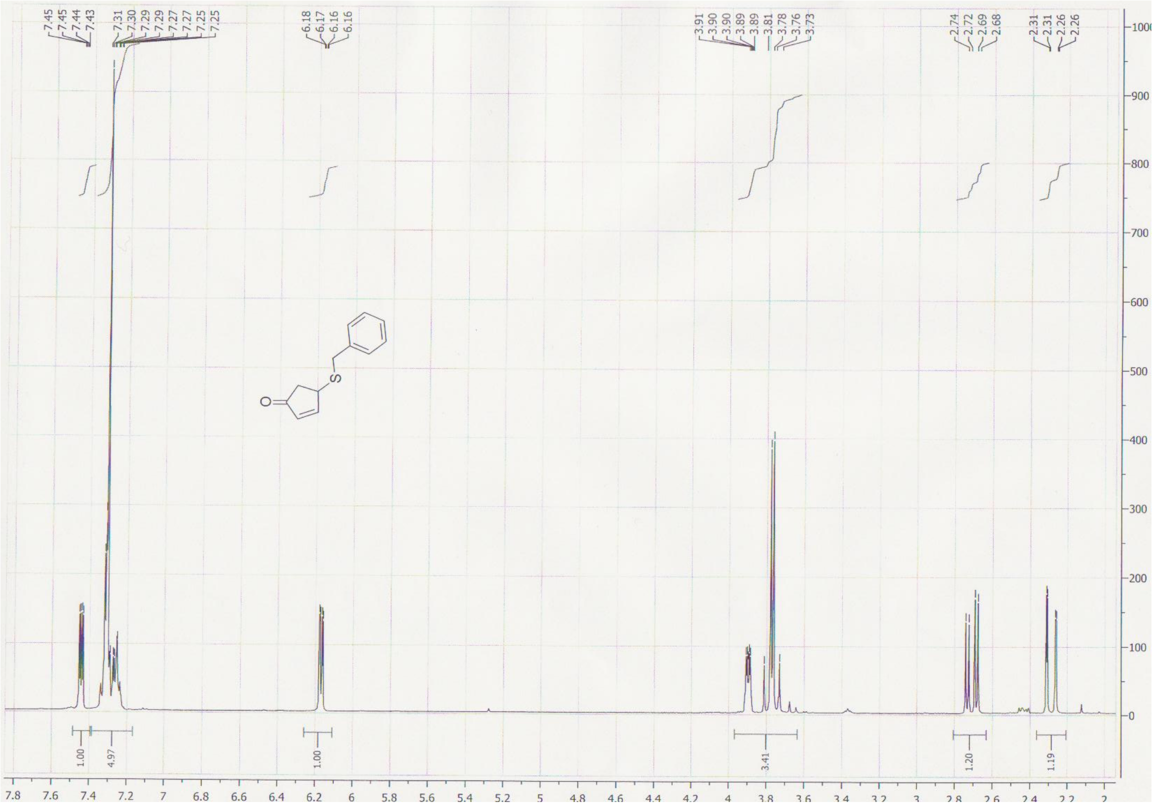


Compound *cis*-**4b**





Compound **6a**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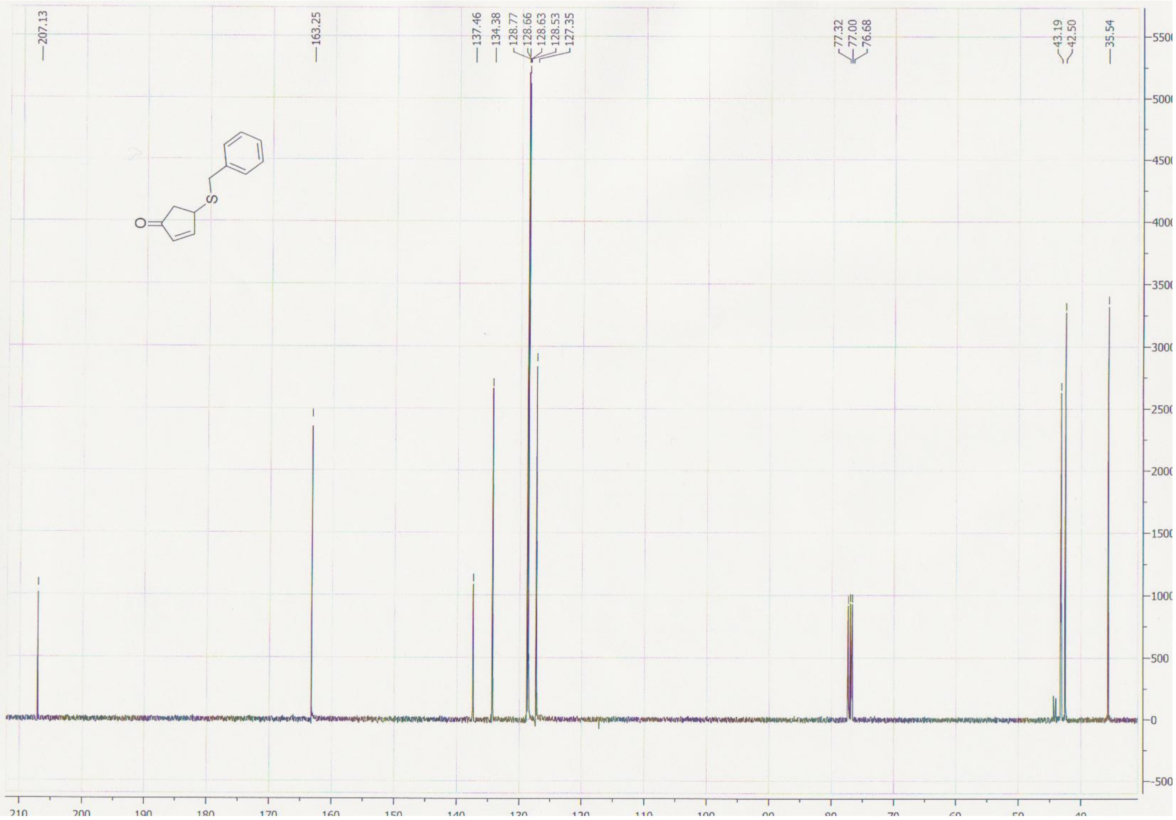
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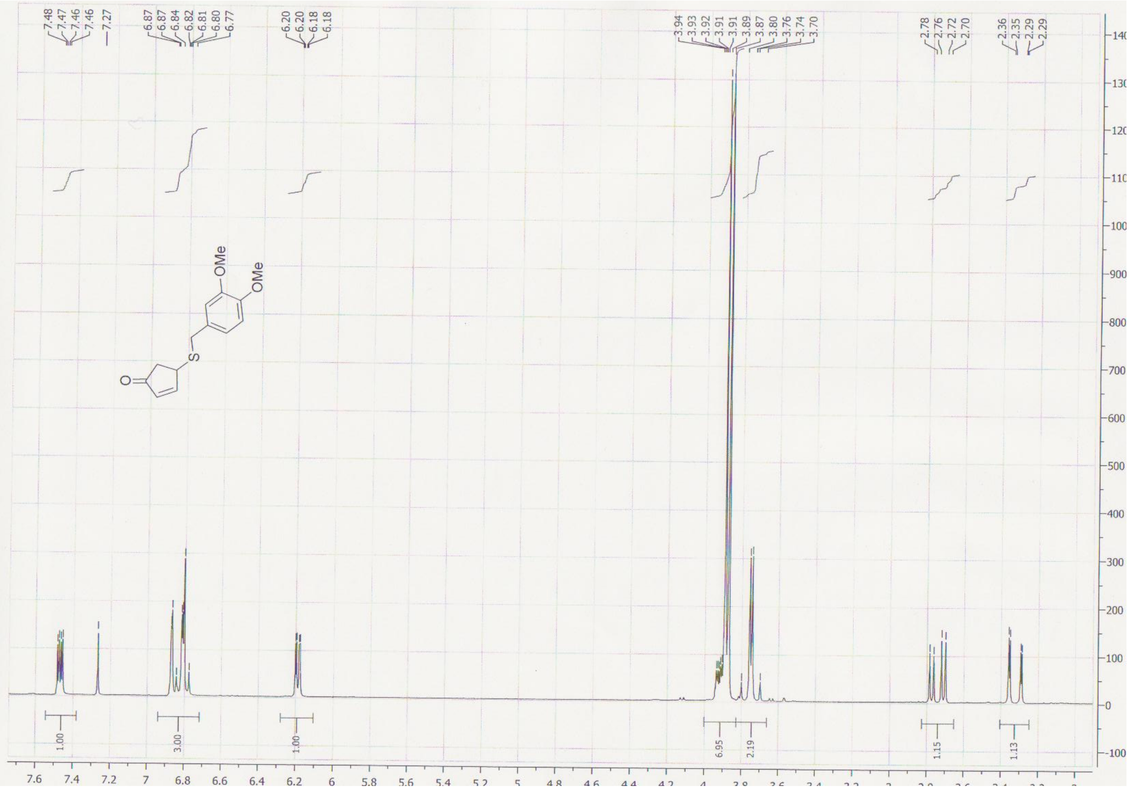
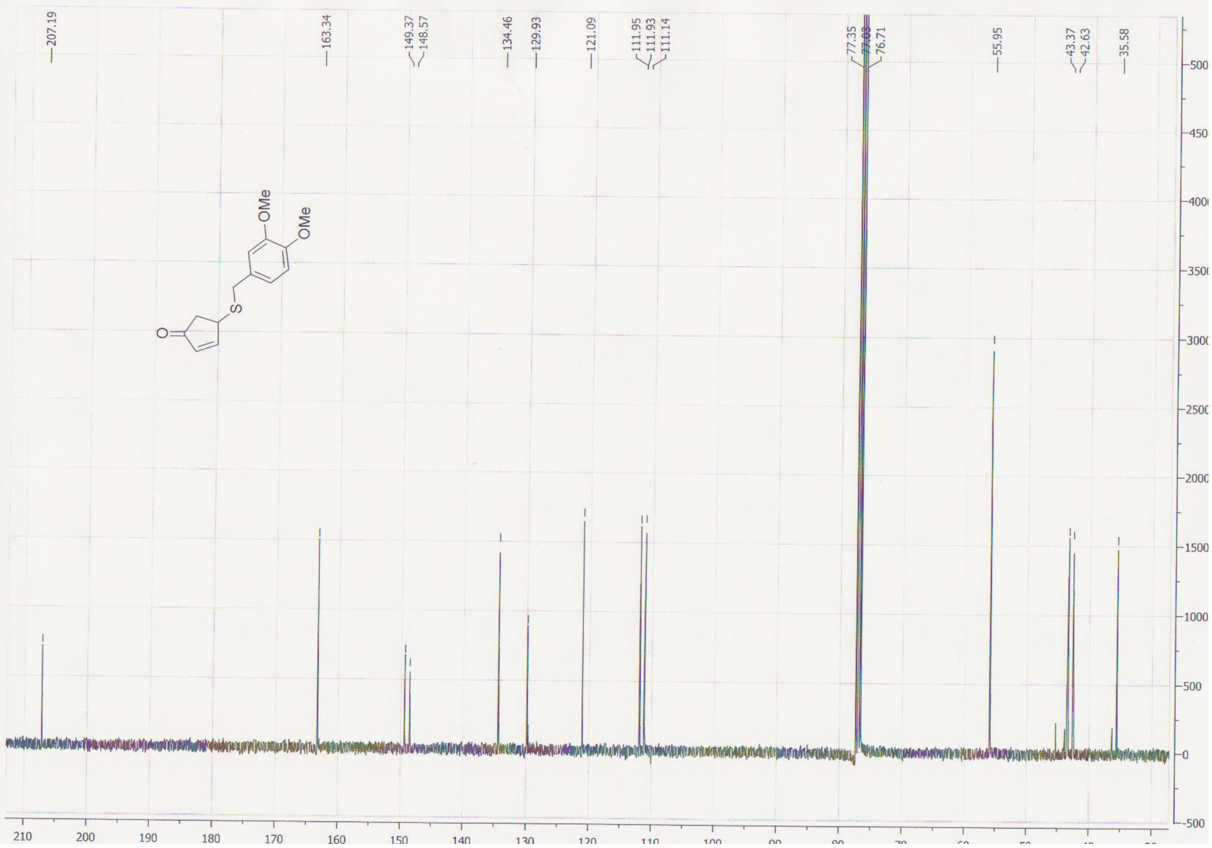
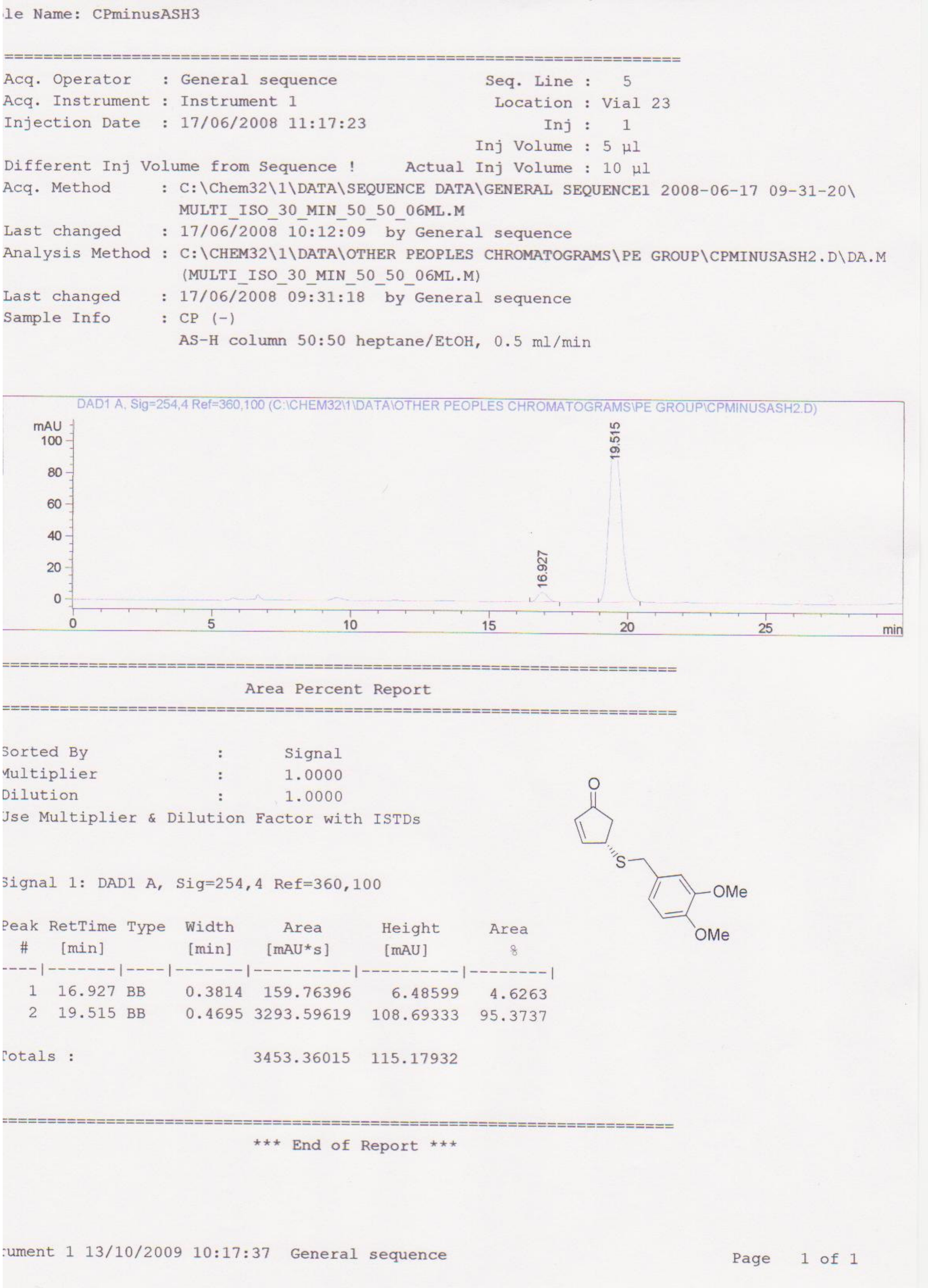
500 0 -500

Compound **6b**


7.48
7.47
7.46
7.46
7.27
6.87
6.87
6.84
6.82
6.81
6.80
6.77
6.20
6.20
6.18
6.18
3.94
3.93
3.92
3.91
3.91
3.89
3.87
3.80
3.76
3.74
3.70
2.78
2.76
2.72
2.70
2.36
2.35
2.29
2.29
OMe
OMe
S
O
1.00
3.00
1.00
6.95
2.19
1.15
1.13
7.6
7.4
7.2
7
6.8
6.6
6.4
6.2
6
5.8
5.6
5.4
5.2
5
4.8
4.6
4.4
4.2
4

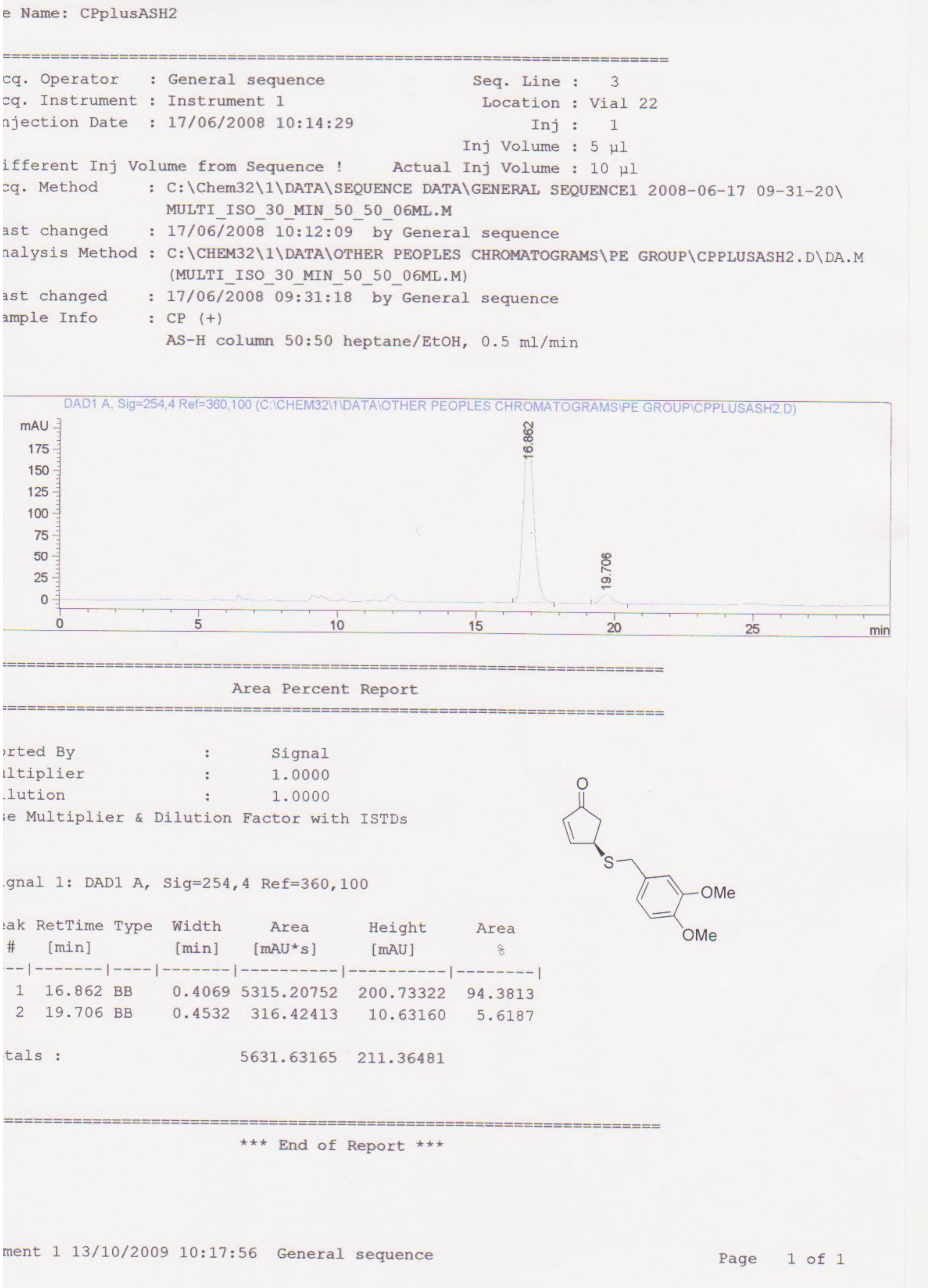

207.19
163.34
149.37
148.57
134.46
129.93
121.09
111.95
111.93
111.14
77.35
77.03
76.71
55.95
43.37
42.63
35.58
OMe
OMe
S
O
500
0
-500
210
200
190
180
170
160
150
140
130
120
110

HPLC Traces (–)- and (+)-**6b**



```
le Name: CPminusASH3

=====================================================================
Acq. Operator   : General sequence               Seq. Line :   5
Acq. Instrument : Instrument 1                    Location : Vial 23
Injection Date  : 17/06/2008 11:17:23                  Inj :   1
                                                Inj Volume : 5 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 10 µl
Acq. Method     : C:\Chem32\1\DATA\SEQUENCE DATA\GENERAL SEQUENCE1 2008-06-17 09-31-20\
                  MULTI_ISO_30_MIN_50_50_06ML.M
Last changed    : 17/06/2008 10:12:09  by General sequence
Analysis Method : C:\CHEM32\1\DATA\OTHER PEOPLES CHROMATOGRAMS\PE GROUP\CPMINUSASH2.D\DA.M
                  (MULTI_ISO_30_MIN_50_50_06ML.M)
Last changed    : 17/06/2008 09:31:18  by General sequence
Sample Info     : CP (-)
                  AS-H column 50:50 heptane/EtOH, 0.5 ml/min
```

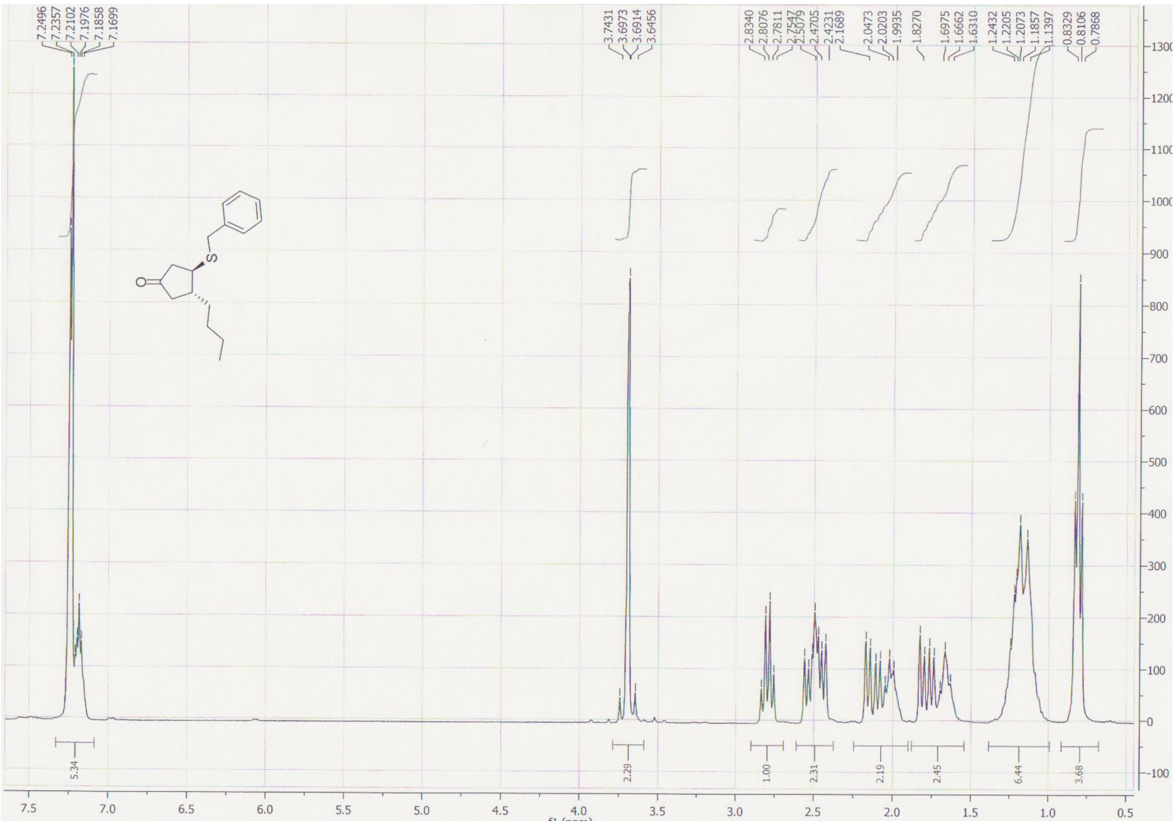
```
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  16.927 BB    0.3814  159.76396    6.48599   4.6263
   2  19.515 BB    0.4695 3293.59619  108.69333  95.3737

Totals :                  3453.36015  115.17932


=====================================================================
                        *** End of Report ***



ument 1 13/10/2009 10:17:37  General sequence               Page    1 of 1
```

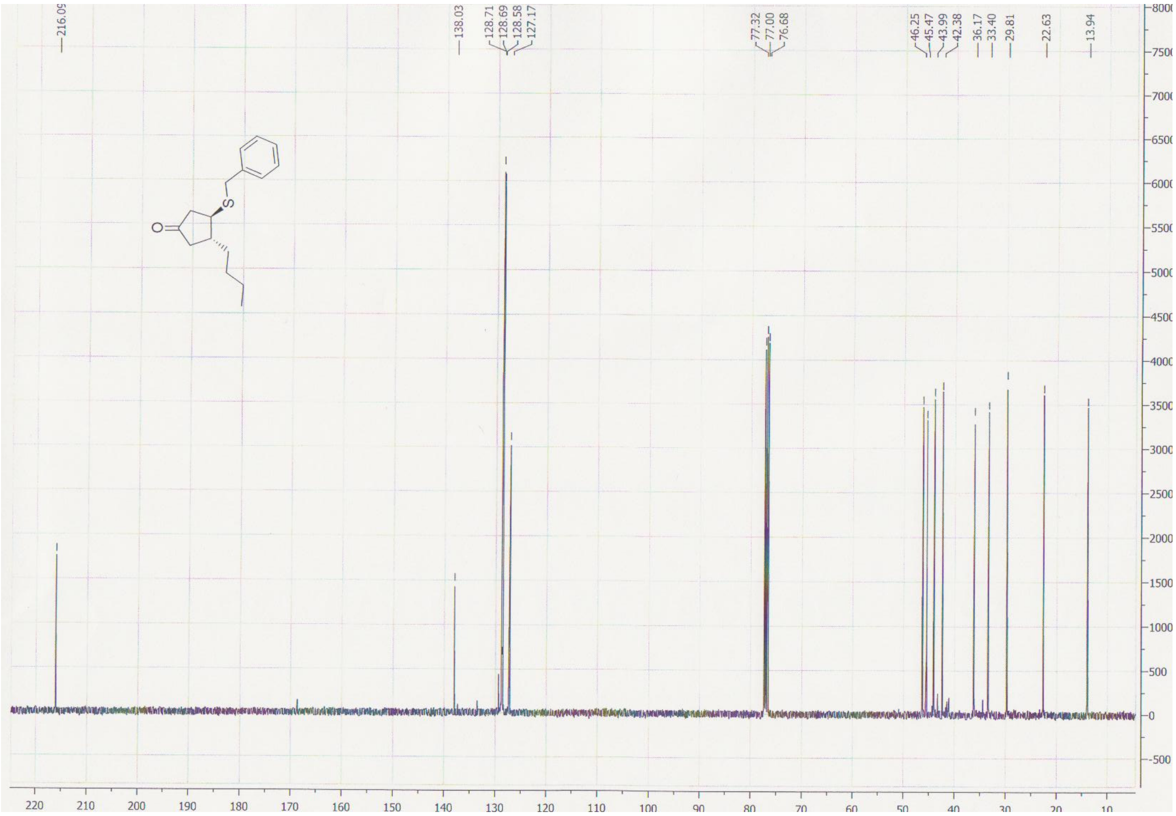


```
e Name: CPplusASH2

=====================================================================
cq. Operator   : General sequence              Seq. Line :   3
cq. Instrument : Instrument 1                   Location : Vial 22
njection Date  : 17/06/2008 10:14:29                 Inj :   1
                                              Inj Volume : 5 µl
ifferent Inj Volume from Sequence !     Actual Inj Volume : 10 µl
cq. Method     : C:\Chem32\1\DATA\SEQUENCE DATA\GENERAL SEQUENCE1 2008-06-17 09-31-20\
                 MULTI_ISO_30_MIN_50_50_06ML.M
ast changed    : 17/06/2008 10:12:09  by General sequence
nalysis Method : C:\CHEM32\1\DATA\OTHER PEOPLES CHROMATOGRAMS\PE GROUP\CPPLUSASH2.D\DA.M
                 (MULTI_ISO_30_MIN_50_50_06ML.M)
ast changed    : 17/06/2008 09:31:18  by General sequence
ample Info     : CP (+)
                 AS-H column 50:50 heptane/EtOH, 0.5 ml/min
```

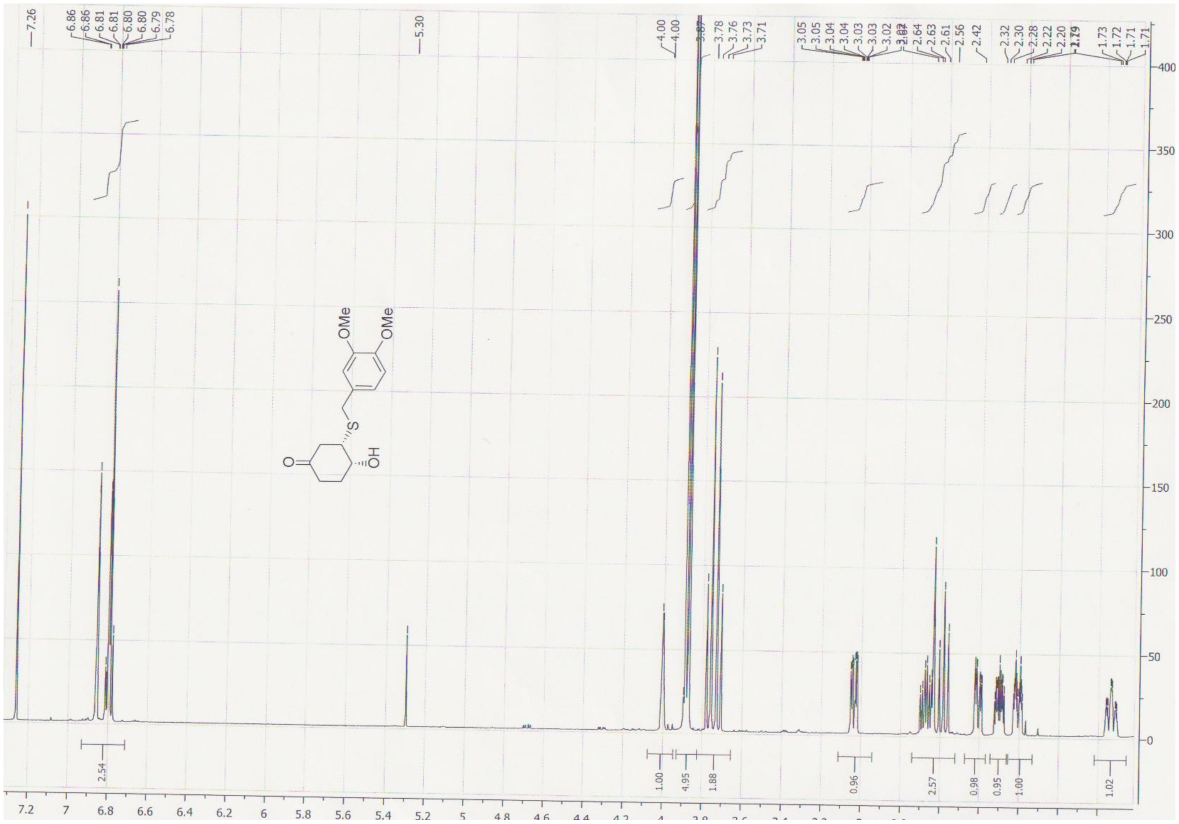
```
=====================================================================
                       Area Percent Report
=====================================================================

orted By             :      Signal
ltiplier             :      1.0000
lution               :      1.0000
se Multiplier & Dilution Factor with ISTDs


gnal 1: DAD1 A, Sig=254,4 Ref=360,100

ak RetTime Type  Width     Area      Height     Area
 #   [min]        [min]   [mAU*s]     [mAU]       %
--|-------|----|-------|----------|----------|--------|
 1  16.862 BB    0.4069 5315.20752  200.73322  94.3813
 2  19.706 BB    0.4532  316.42413   10.63160   5.6187

tals :                  5631.63165  211.36481


=====================================================================
                       *** End of Report ***



ment 1 13/10/2009 10:17:56  General sequence                 Page   1 of 1
```

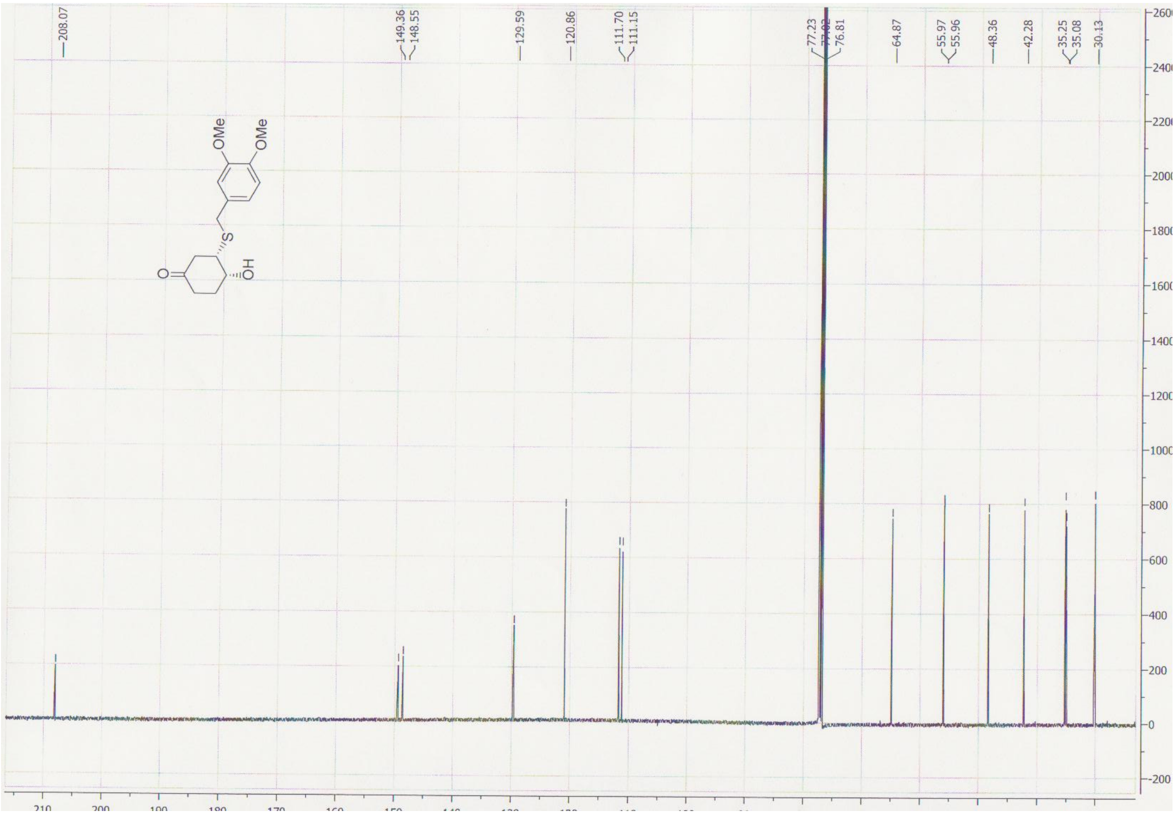
Compound **10**


7.2496
7.2357
7.2102
7.1976
7.1858
7.1699
3.7431
3.6973
3.6914
3.6456
2.8340
2.8076
2.7811
2.7547
2.5079
2.4705
2.4231
2.1689
2.0473
2.0203
1.9935
1.8270
1.6975
1.6662
1.6310
1.2432
1.2205
1.2073
1.1857
1.1397
0.8329
0.8106
0.7868
S
O
5.34
2.29
1.00
2.31
2.19
2.45
6.44
3.68
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100

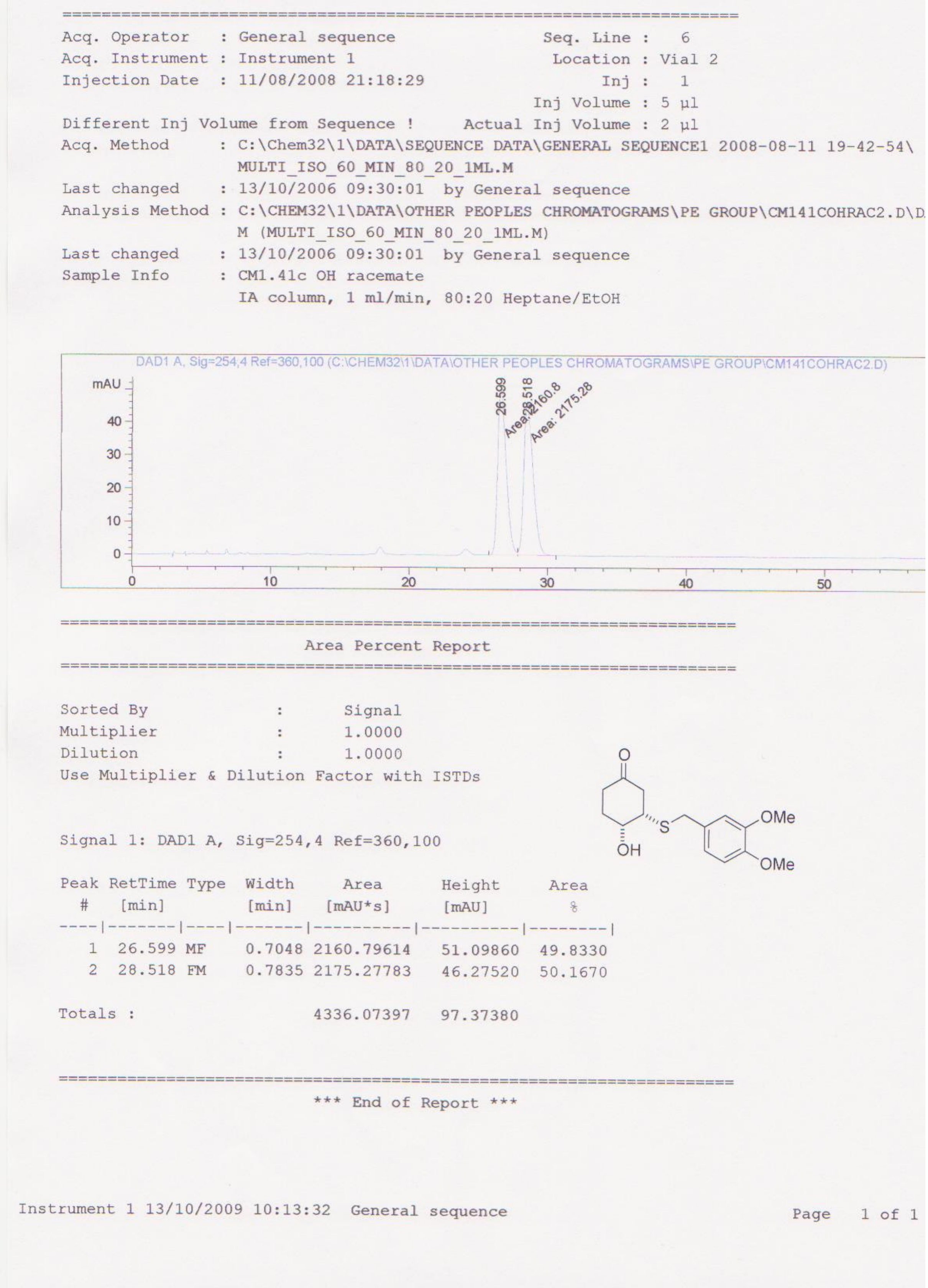

216.09
138.03
128.71
128.69
128.58
127.17
77.32
77.00
76.68
46.25
45.47
43.99
42.38
36.17
33.40
29.81
22.63
13.94
S
O
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
8000
7500
7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500

Compound **16**

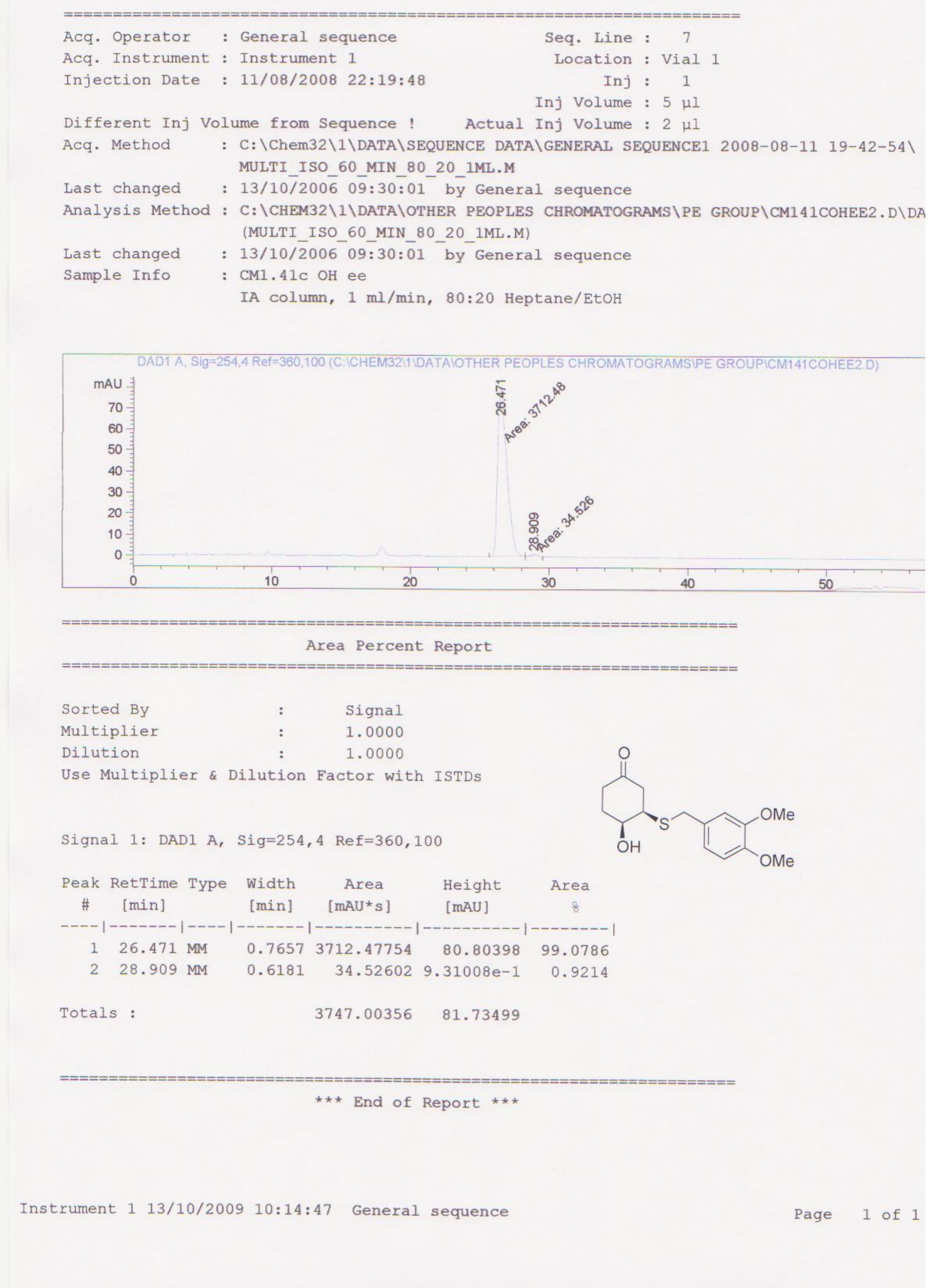

7.26
6.86
6.86
6.81
6.81
6.80
6.80
6.79
6.78
5.30
4.00
4.00
3.87
3.78
3.76
3.73
3.71
3.05
3.05
3.04
3.04
3.03
3.03
3.02
3.02
2.64
2.63
2.61
2.56
2.42
2.32
2.30
2.28
2.22
2.20
2.19
1.73
1.72
1.71
1.71
2.54
1.00
4.95
1.88
0.96
2.57
0.98
0.95
1.00
1.02
OMe
OMe
S
O
OH
400
350
300
250
200
150
100
50
0
7.2
7
6.8
6.6
6.4
6.2
6
5.8
5.6
5.4
5.2
5
4.8
4.6
4.4
4.2
4


208.07
149.36
148.55
129.59
120.86
111.70
111.15
77.23
77.02
76.81
64.87
55.97
55.96
48.36
42.28
35.25
35.08
30.13
OMe
OMe
S
O
OH
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
210
200
190
180
170
160
150
140
130
120
110
100
90

HPLC traces (±)- and (+)-**16**



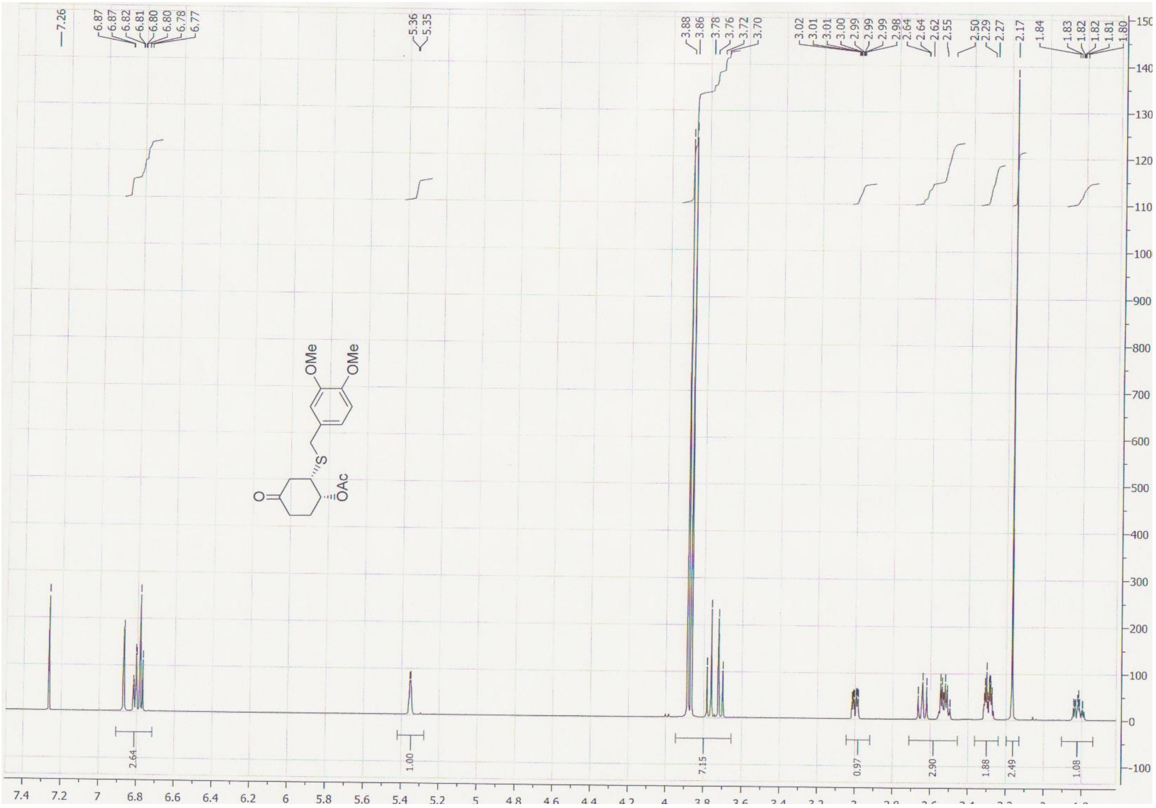
```
=====================================================================
Acq. Operator   : General sequence                Seq. Line :    6
Acq. Instrument : Instrument 1                     Location : Vial 2
Injection Date  : 11/08/2008 21:18:29                   Inj :    1
                                                 Inj Volume : 5 µl
Different Inj Volume from Sequence !      Actual Inj Volume : 2 µl
Acq. Method     : C:\Chem32\1\DATA\SEQUENCE DATA\GENERAL SEQUENCE1 2008-08-11 19-42-54\
                  MULTI_ISO_60_MIN_80_20_1ML.M
Last changed    : 13/10/2006 09:30:01  by General sequence
Analysis Method : C:\CHEM32\1\DATA\OTHER PEOPLES CHROMATOGRAMS\PE GROUP\CM141COHRAC2.D\D
                  M (MULTI_ISO_60_MIN_80_20_1ML.M)
Last changed    : 13/10/2006 09:30:01  by General sequence
Sample Info     : CM1.41c OH racemate
                  IA column, 1 ml/min, 80:20 Heptane/EtOH

=====================================================================
                         Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  26.599 MF    0.7048 2160.79614   51.09860  49.8330
   2  28.518 FM    0.7835 2175.27783   46.27520  50.1670

Totals :                  4336.07397   97.37380


=====================================================================
                         *** End of Report ***



Instrument 1 13/10/2009 10:13:32  General sequence                 Page   1 of 1
```

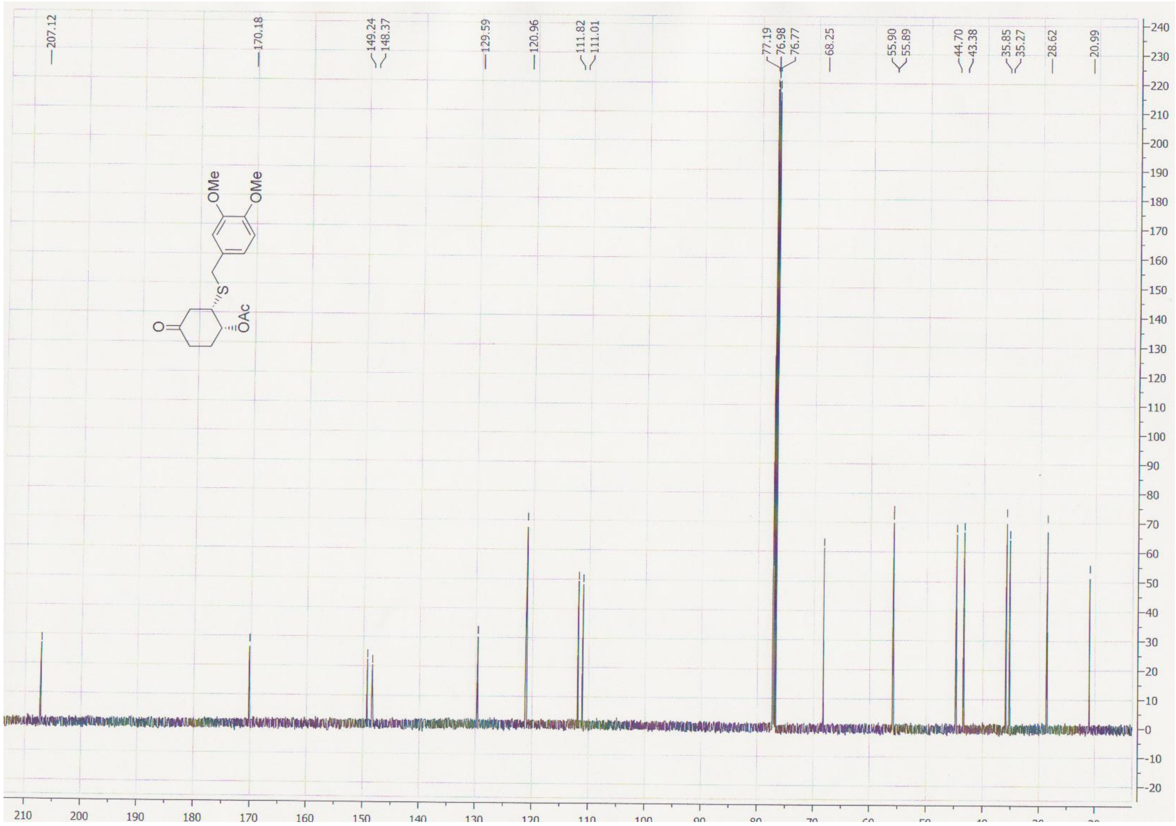


```
=====================================================================
Acq. Operator   : General sequence                Seq. Line :   7
Acq. Instrument : Instrument 1                     Location : Vial 1
Injection Date  : 11/08/2008 22:19:48                   Inj :   1
                                                 Inj Volume : 5 µl
Different Inj Volume from Sequence !      Actual Inj Volume : 2 µl
Acq. Method     : C:\Chem32\1\DATA\SEQUENCE DATA\GENERAL SEQUENCE1 2008-08-11 19-42-54\
                  MULTI_ISO_60_MIN_80_20_1ML.M
Last changed    : 13/10/2006 09:30:01  by General sequence
Analysis Method : C:\CHEM32\1\DATA\OTHER PEOPLES CHROMATOGRAMS\PE GROUP\CM141COHEE2.D\DA
                  (MULTI_ISO_60_MIN_80_20_1ML.M)
Last changed    : 13/10/2006 09:30:01  by General sequence
Sample Info     : CM1.41c OH ee
                  IA column, 1 ml/min, 80:20 Heptane/EtOH
```

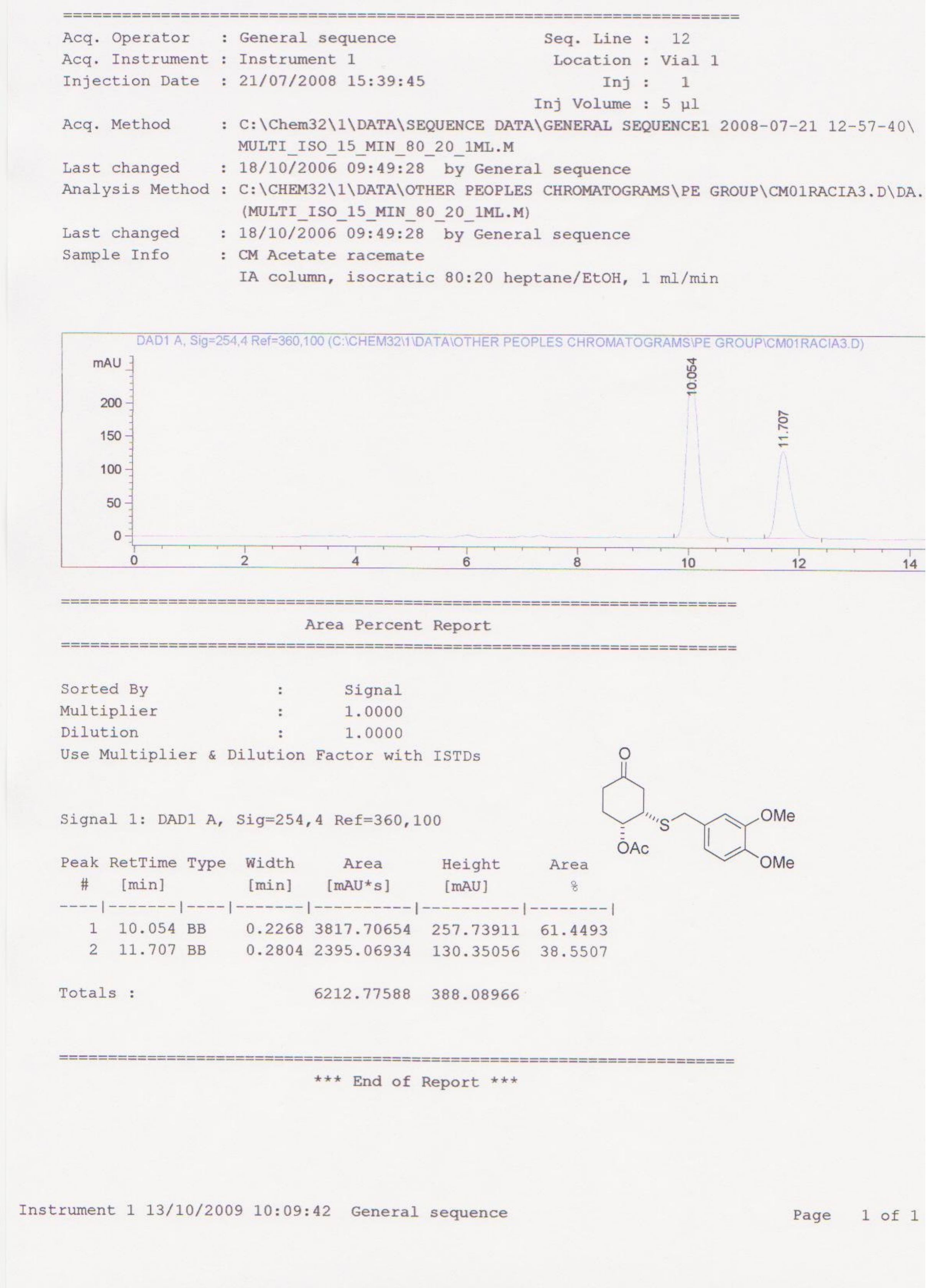
```
=====================================================================
                         Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  26.471 MM    0.7657 3712.47754   80.80398 99.0786
   2  28.909 MM    0.6181   34.52602 9.31008e-1  0.9214

Totals :                  3747.00356   81.73499

=====================================================================
                          *** End of Report ***


Instrument 1 13/10/2009 10:14:47  General sequence               Page    1 of 1
```

Compound **17**

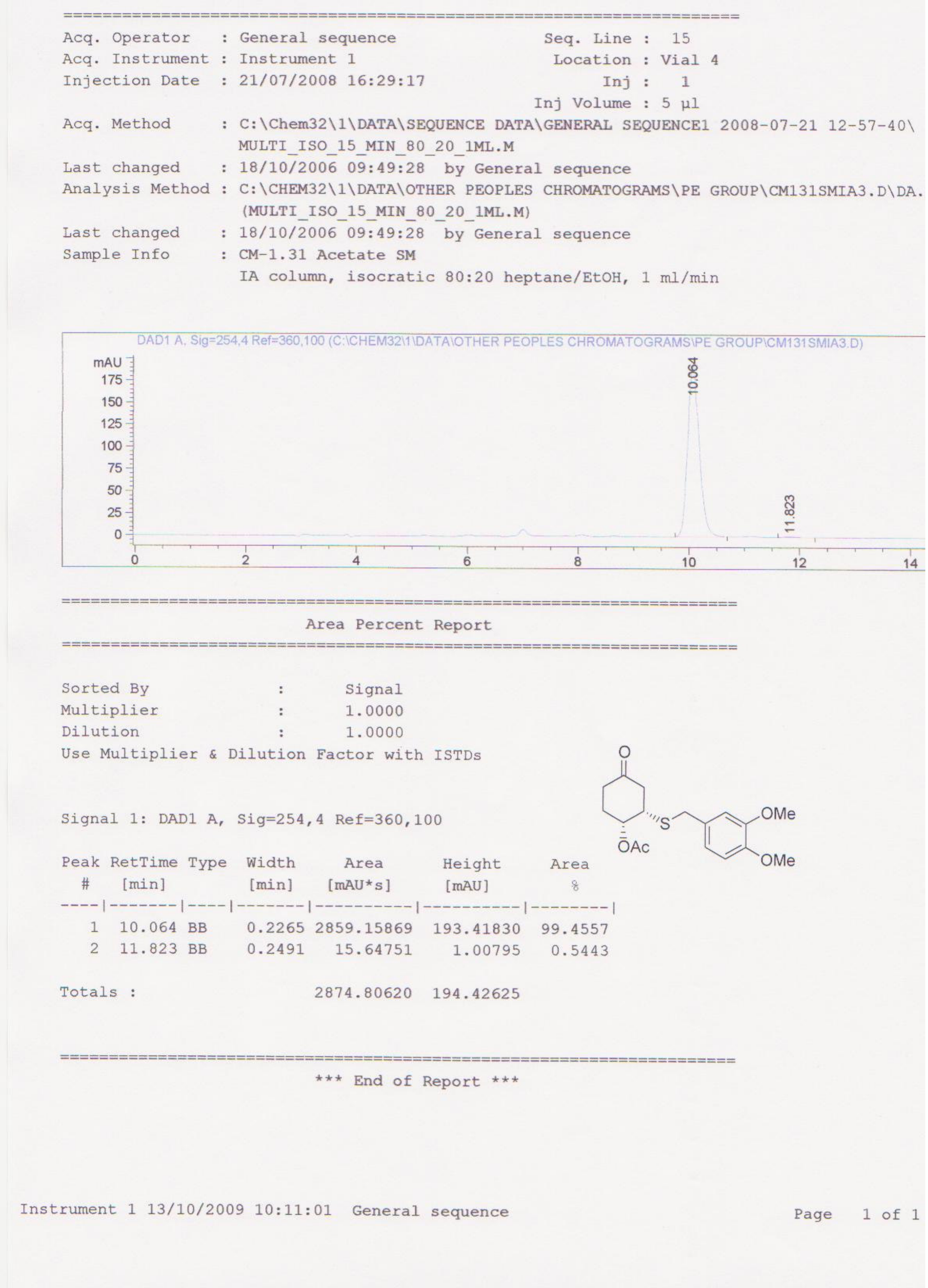

7.26
6.87
6.87
6.82
6.81
6.80
6.80
6.78
6.77
5.36
5.35
3.88
3.86
3.78
3.76
3.72
3.70
3.02
3.01
3.01
3.00
2.99
2.99
2.99
2.98
2.64
2.62
2.55
2.50
2.29
2.27
2.17
1.84
1.83
1.82
1.82
1.81
1.80
O
S
OAc
OMe
OMe
2.64
1.00
7.15
0.97
2.90
1.88
2.49
1.08


207.12
170.18
149.24
148.37
129.59
120.96
111.82
111.01
77.19
76.98
76.77
68.25
55.90
55.89
44.70
43.38
35.85
35.27
28.62
20.99
O
S
OAc
OMe
OMe

HPLC traces *pseudo*-(±)- and (–)-**17**



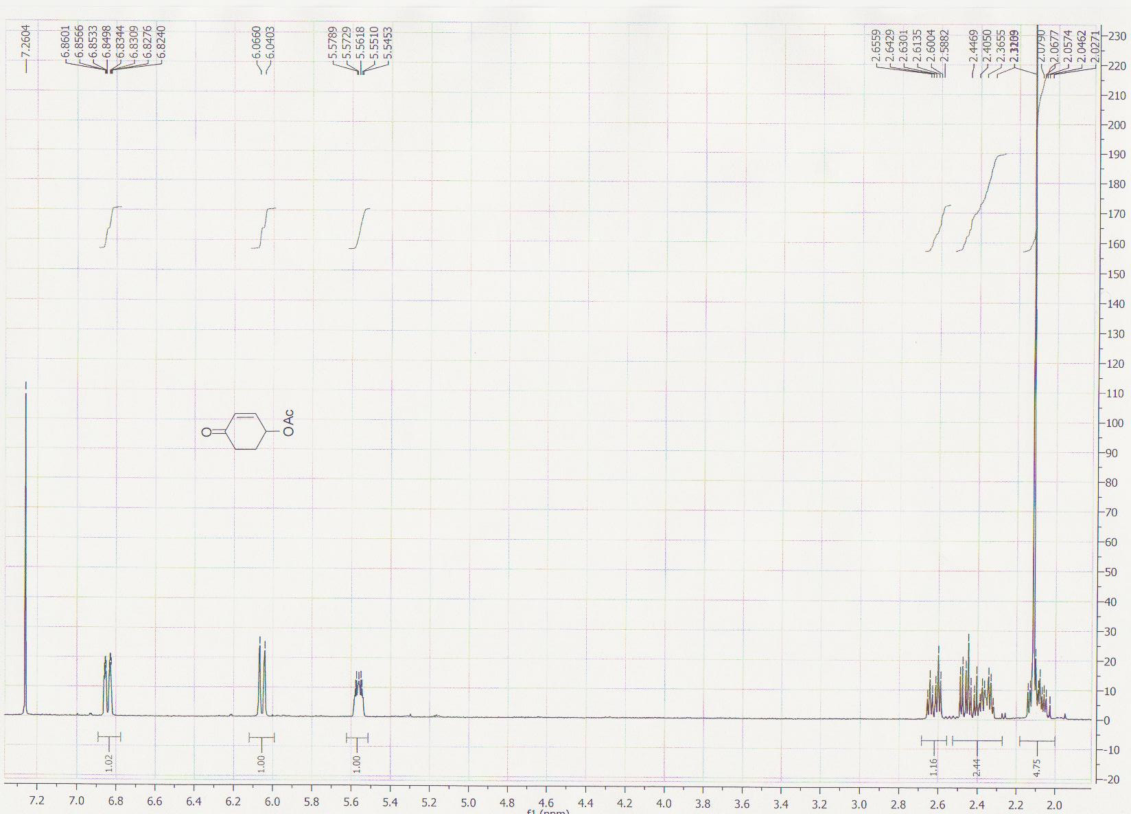
```
=====================================================================
Acq. Operator   : General sequence              Seq. Line :  12
Acq. Instrument : Instrument 1                   Location : Vial 1
Injection Date  : 21/07/2008 15:39:45                 Inj :   1
                                               Inj Volume : 5 µl
Acq. Method     : C:\Chem32\1\DATA\SEQUENCE DATA\GENERAL SEQUENCE1 2008-07-21 12-57-40\
                  MULTI_ISO_15_MIN_80_20_1ML.M
Last changed    : 18/10/2006 09:49:28  by General sequence
Analysis Method : C:\CHEM32\1\DATA\OTHER PEOPLES CHROMATOGRAMS\PE GROUP\CM01RACIA3.D\DA.
                  (MULTI_ISO_15_MIN_80_20_1ML.M)
Last changed    : 18/10/2006 09:49:28  by General sequence
Sample Info     : CM Acetate racemate
                  IA column, isocratic 80:20 heptane/EtOH, 1 ml/min

=====================================================================
                         Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  10.054 BB    0.2268 3817.70654  257.73911  61.4493
   2  11.707 BB    0.2804 2395.06934  130.35056  38.5507

Totals :                  6212.77588  388.08966


=====================================================================
                          *** End of Report ***




Instrument 1 13/10/2009 10:09:42  General sequence                  Page   1 of 1
```

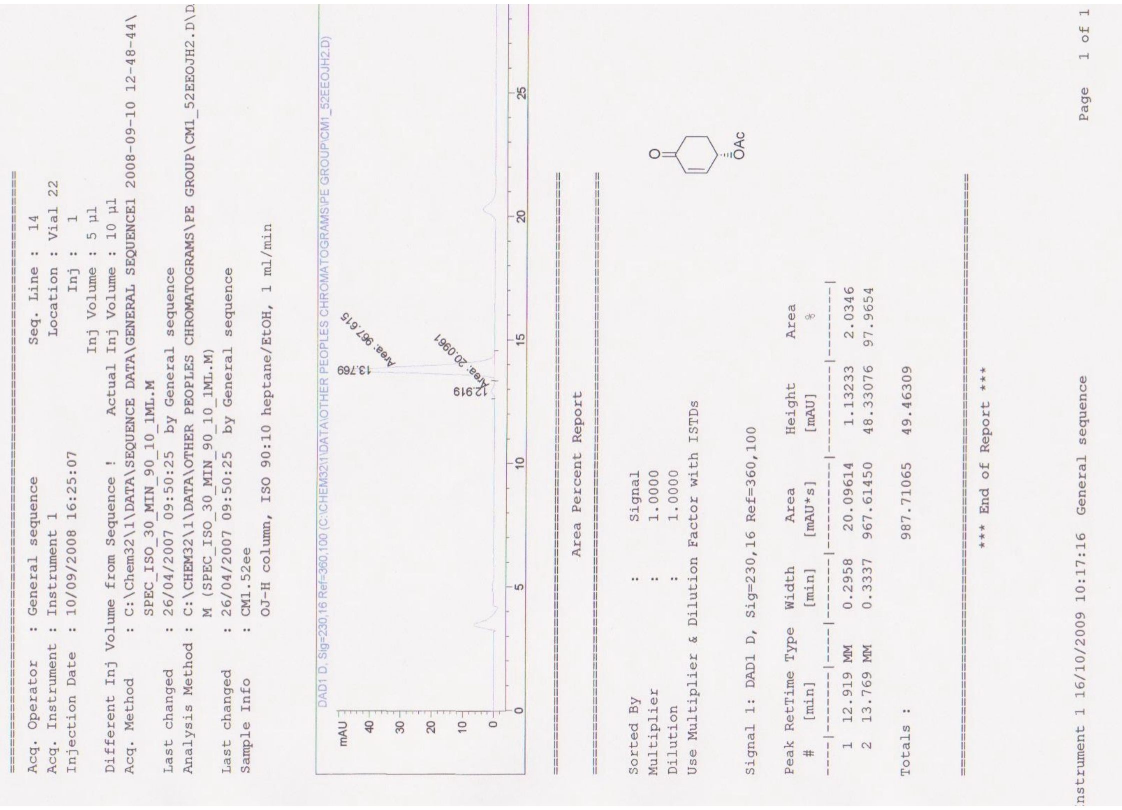


```
=====================================================================
Acq. Operator   : General sequence                Seq. Line :  15
Acq. Instrument : Instrument 1                     Location : Vial 4
Injection Date  : 21/07/2008 16:29:17                   Inj :   1
                                                 Inj Volume : 5 µl
Acq. Method     : C:\Chem32\1\DATA\SEQUENCE DATA\GENERAL SEQUENCE1 2008-07-21 12-57-40\
                  MULTI_ISO_15_MIN_80_20_1ML.M
Last changed    : 18/10/2006 09:49:28  by General sequence
Analysis Method : C:\CHEM32\1\DATA\OTHER PEOPLES CHROMATOGRAMS\PE GROUP\CM131SMIA3.D\DA.
                  (MULTI_ISO_15_MIN_80_20_1ML.M)
Last changed    : 18/10/2006 09:49:28  by General sequence
Sample Info     : CM-1.31 Acetate SM
                  IA column, isocratic 80:20 heptane/EtOH, 1 ml/min
```

```
=====================================================================
                         Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  10.064 BB    0.2265 2859.15869  193.41830  99.4557
   2  11.823 BB    0.2491   15.64751    1.00795   0.5443

Totals :                  2874.80620  194.42625


=====================================================================
                         *** End of Report ***



Instrument 1 13/10/2009 10:11:01  General sequence              Page    1 of 1
```

Compound **18**

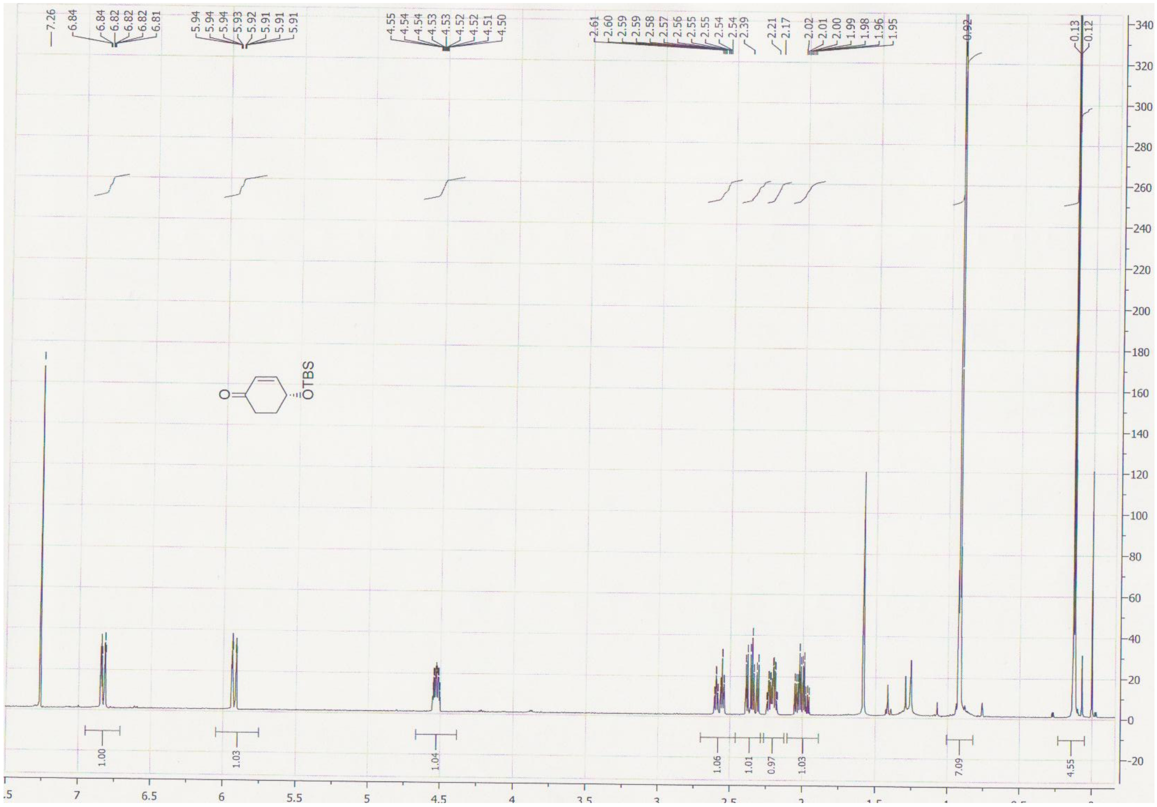


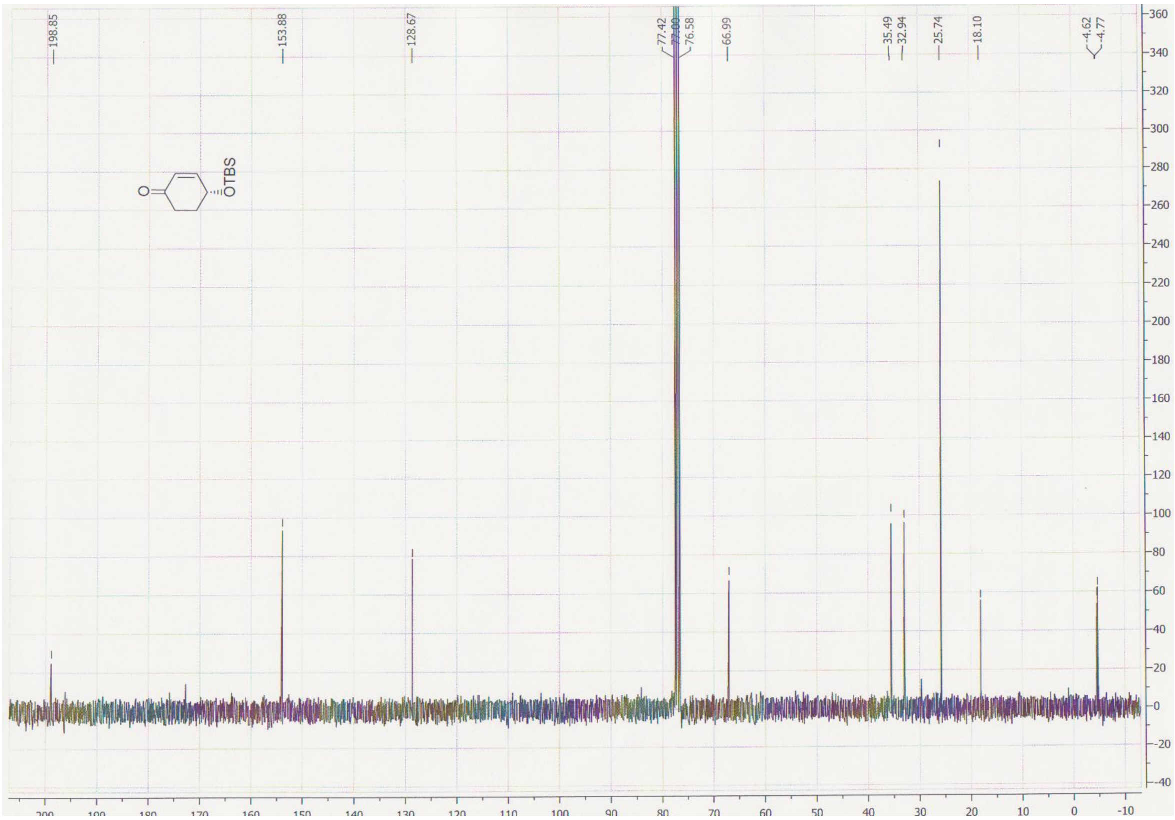


```
=====================================================================
Acq. Operator   : General sequence              Seq. Line :  14
Acq. Instrument : Instrument 1                   Location : Vial 22
Injection Date  : 10/09/2008 16:25:07                 Inj :   1
                                               Inj Volume : 5 µl
Different Inj Volume from Sequence !      Actual Inj Volume : 10 µl
Acq. Method     : C:\Chem32\1\DATA\SEQUENCE DATA\GENERAL SEQUENCE1 2008-09-10 12-48-44\
                  SPEC_ISO_30_MIN_90_10_1ML.M
Last changed    : 26/04/2007 09:50:25  by General sequence
Analysis Method : C:\CHEM32\1\DATA\OTHER PEOPLES CHROMATOGRAMS\PE GROUP\CM1_52EEOJH2.D\D
                  M (SPEC_ISO_30_MIN_90_10_1ML.M)
Last changed    : 26/04/2007 09:50:25  by General sequence
Sample Info     : CM1.52ee
                  OJ-H column, ISO 90:10 heptane/EtOH, 1 ml/min
```

```
=====================================================================
                          Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 D, Sig=230,16 Ref=360,100

Peak RetTime Type  Width     Area       Height     Area
  #   [min]        [min]   [mAU*s]      [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  12.919 MM    0.2958   20.09614    1.13233   2.0346
   2  13.769 MM    0.3337  967.61450   48.33076  97.9654

Totals :                   987.71065   49.46309

=====================================================================
                         *** End of Report ***

nstrument 1 16/10/2009 10:17:16  General sequence                  Page    1 of 1
```

Compound **19**


7.26
6.84
6.84
6.82
6.82
6.82
6.81
5.94
5.94
5.94
5.93
5.92
5.91
5.91
5.91
5.91
4.55
4.54
4.54
4.53
4.53
4.52
4.52
4.51
4.50
2.61
2.60
2.59
2.59
2.58
2.57
2.56
2.55
2.55
2.54
2.54
2.39
2.21
2.17
2.02
2.01
2.00
1.99
1.98
1.96
1.95
0.92
0.13
0.12
O
OTBS
1.00
1.03
1.04
1.06
1.01
0.97
1.03
7.09
4.55
.5
7
6.5
6
5.5
5
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
340
320
300
280
260
240
220
200
180
160
140
120
100
80
60
40
20
0
-20


198.85
153.88
128.67
77.42
77.00
76.58
66.99
35.49
32.94
25.74
18.10
-4.62
-4.77
O
OTBS
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
360
340
320
300
280
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240
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200
180
160
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120
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80
60
40
20
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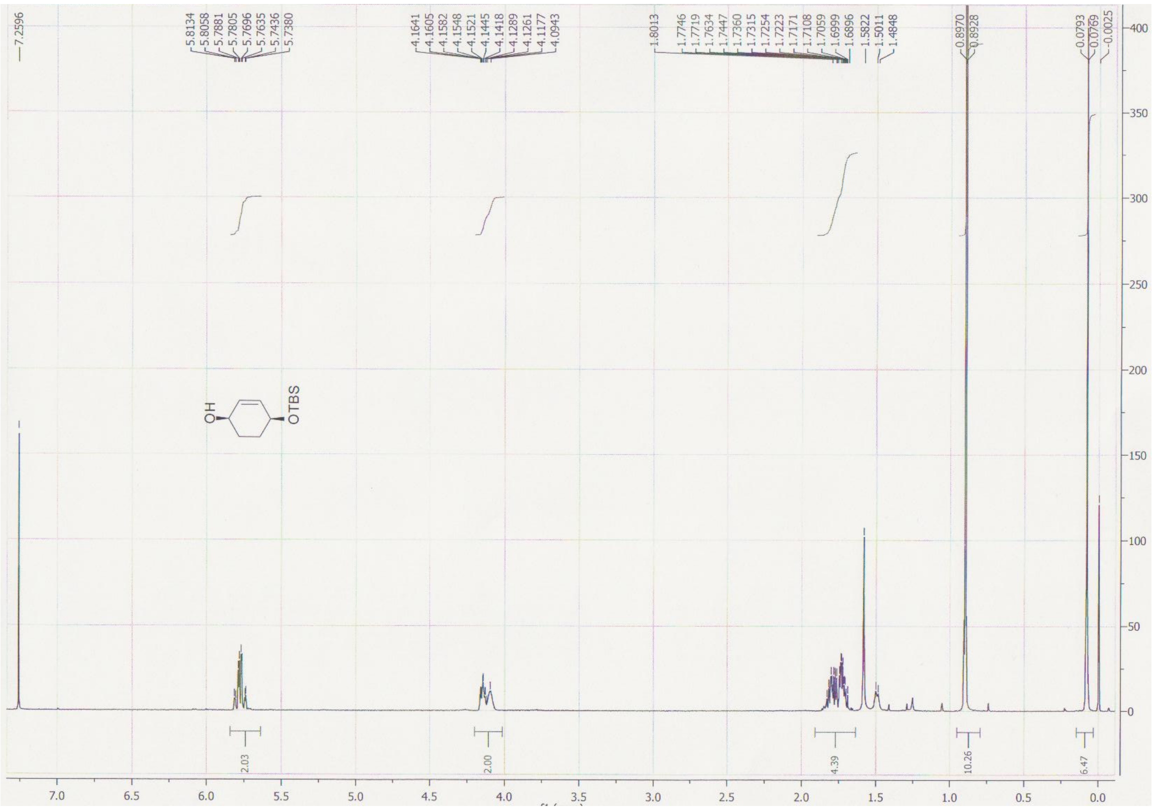
-20
-40

Compound **20**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5.7805
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5.7635
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5.7380
4.1641
4.1605
4.1582
4.1548
4.1521
4.1445
4.1418
4.1289
4.1261
4.1177
4.0943
1.8013
1.7746
1.7719
1.7634
1.7447
1.7360
1.7315
1.7254
1.7223
1.7171
1.7108
1.7059
1.6999
1.6896
1.5822
1.5011
1.4848
0.8970
0.8928
0.0793
0.0769
-0.0025
OH
OTBS
2.03
2.00
4.39
10.26
6.47
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
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250
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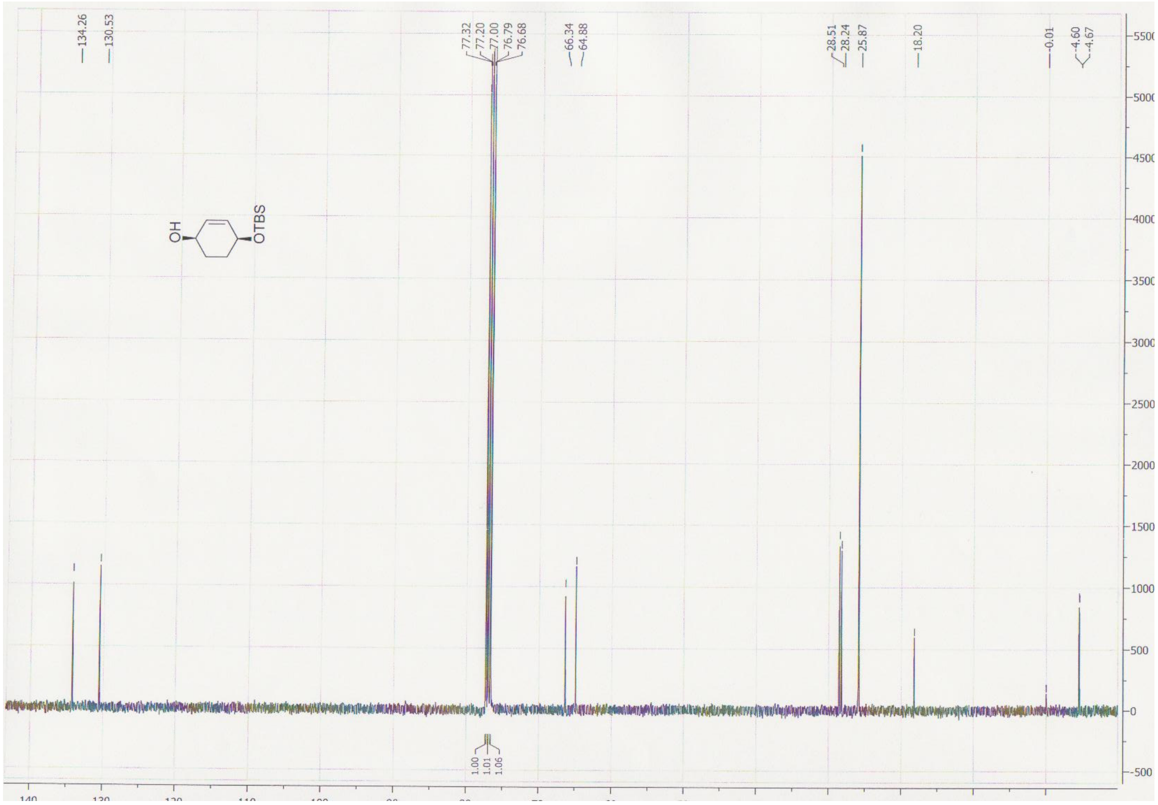
150
100
50
0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77.00
76.79
76.68
66.34
64.88
28.51
28.24
25.87
18.20
-0.01
-4.60
-4.67
OH
OTBS
1.00
1.01
1.06
5500
5000
4500
4000
3500
3000
2500
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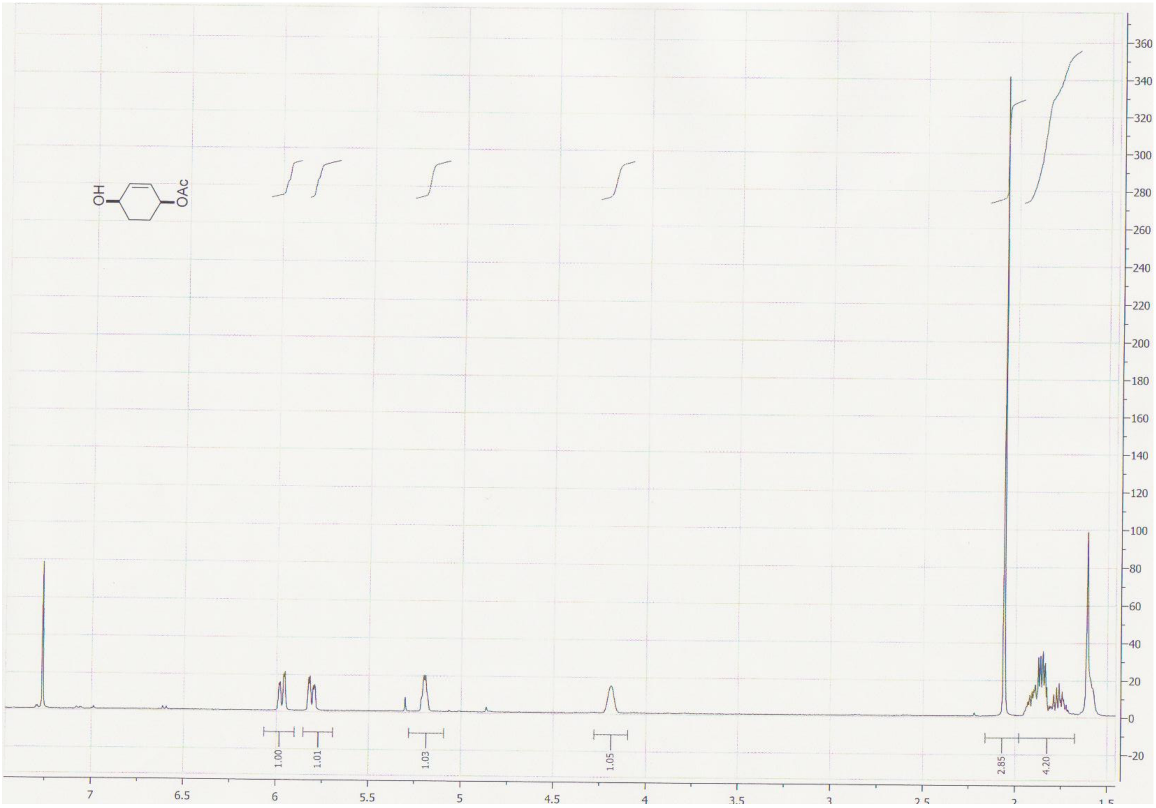
1500
1000
500
0
-500
140

Compound **21**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OAc
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1.01
1.03
1.05
2.85
4.20
7
6.5
6
5.5
5
4.5
4
3.5
3
2.5
2
1.5
360
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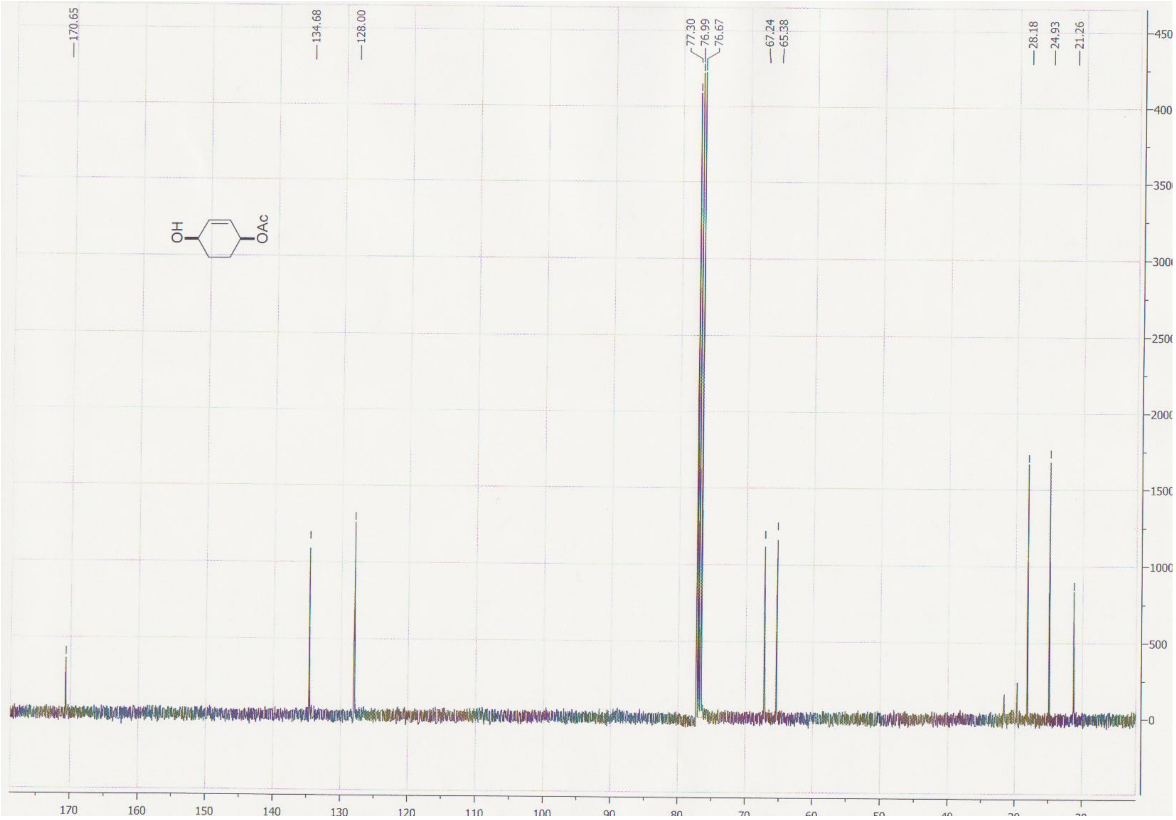
320
300
280
260
240
220
200
180
160
140
120
100
80
60
40
20
0
-20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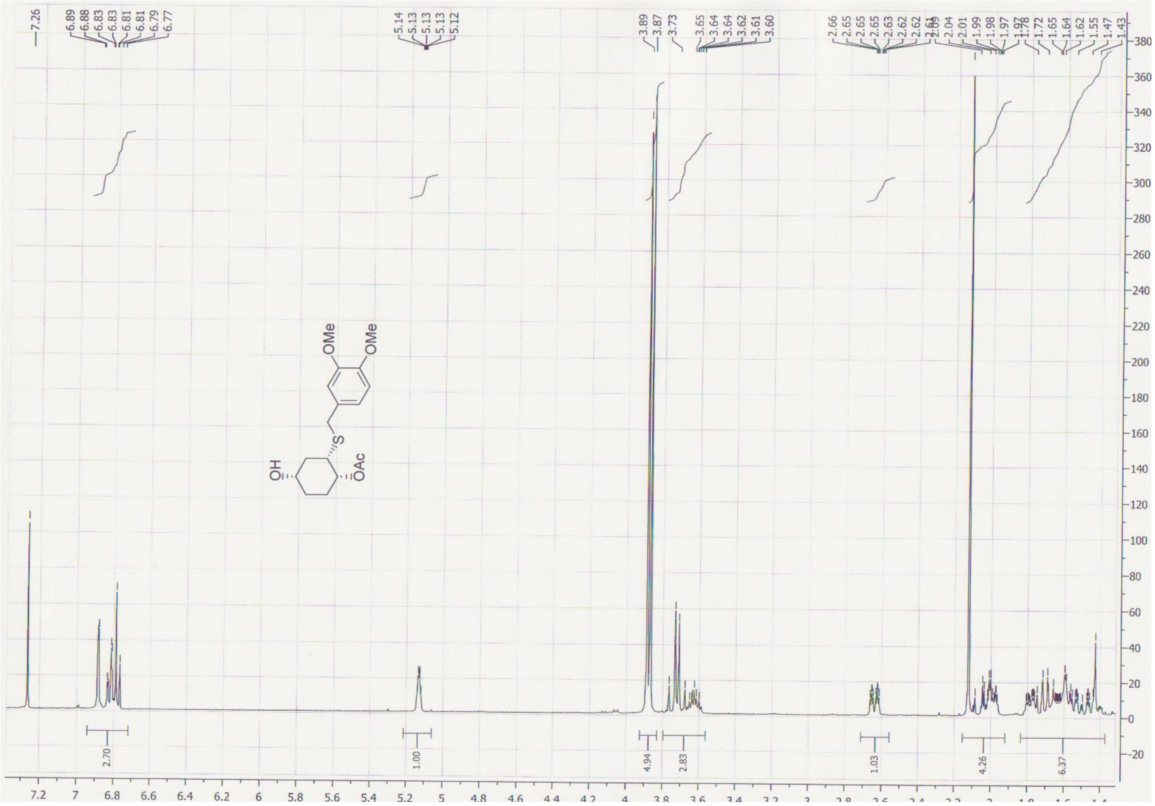
134.68
128.00
77.30
76.99
76.67
67.24
65.38
28.18
24.93
21.26
OH
OAc
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
4500
4000
3500
3000
2500
2000
1500
1000
500
0

Compound **22**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6.83
6.81
6.81
6.79
6.77
5.14
5.13
5.13
5.13
5.12
3.89
3.87
3.73
3.65
3.64
3.64
3.62
3.61
3.60
2.66
2.65
2.65
2.65
2.63
2.62
2.62
2.04
2.01
1.99
1.98
1.97
1.97
1.78
1.72
1.65
1.64
1.62
1.55
1.47
1.43
OH
S
OAc
OMe
OMe
2.70
1.00
4.94
2.83
1.03
4.26
6.37
7.2
7
6.8
6.6
6.4
6.2
6
5.8
5.6
5.4
5.2
5
4.8
4.6
4.4
4.2
4
3.8
3.6
3.4
3.2
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2.8
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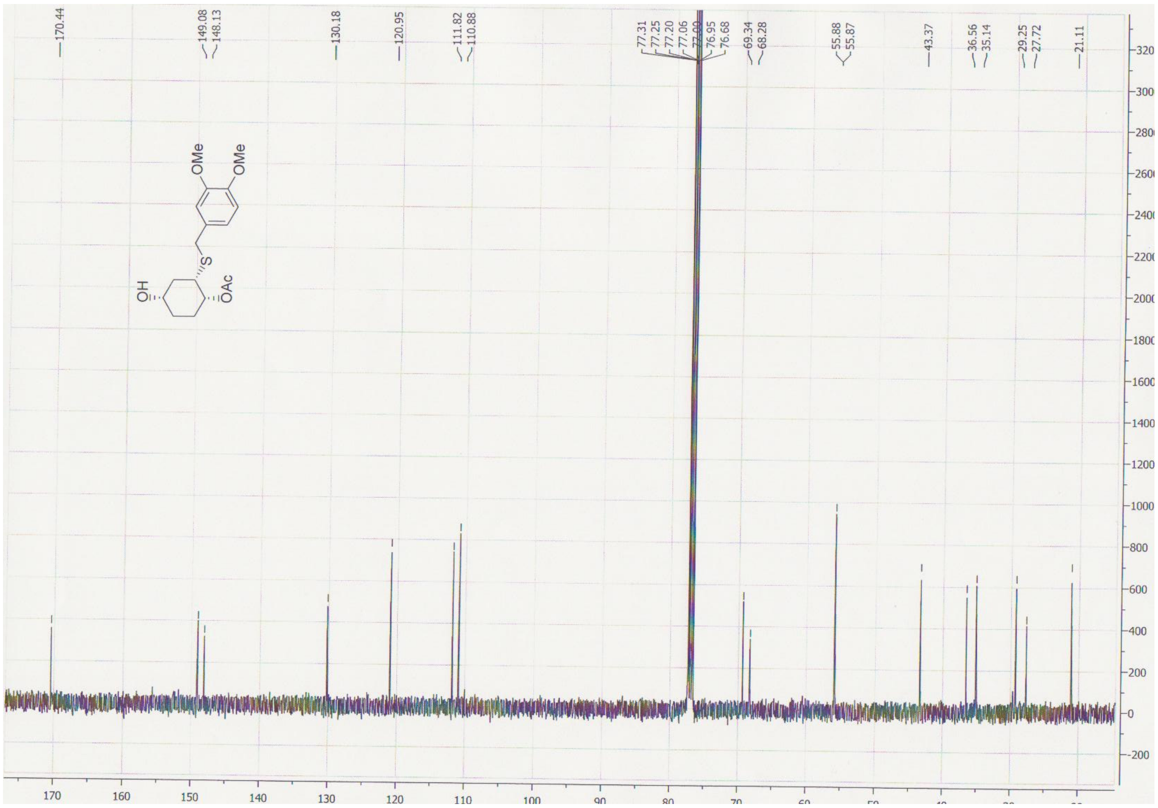
2.4
2.2
2
1.8
1.6
1.4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130.18
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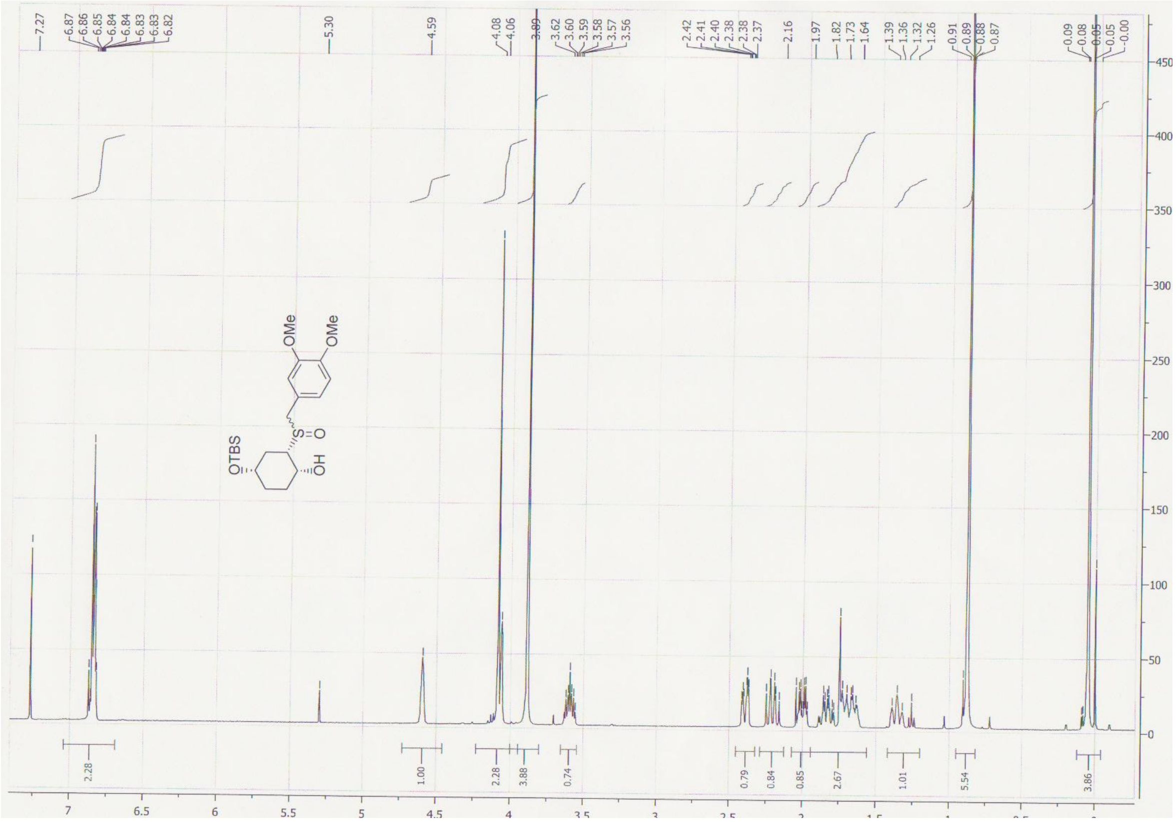
111.82
110.88
77.31
77.25
77.20
77.06
77.00
76.95
76.68
69.34
68.28
55.88
55.87
43.37
36.56
35.14
29.25
27.72
21.11
OH
S
OAc
OMe
OMe
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20

Compound **23**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6.84
6.83
6.83
6.82
5.30
4.59
4.08
4.06
3.89
3.62
3.60
3.59
3.58
3.57
3.56
2.42
2.41
2.40
2.38
2.38
2.37
2.16
1.97
1.82
1.73
1.64
1.39
1.36
1.32
1.26
0.91
0.89
0.88
0.87
0.09
0.08
0.05
0.05
0.00
OTBS
OH
S=O
OMe
OMe
2.28
1.00
2.28
3.88
0.74
0.79
0.84
0.85
2.67
1.01
5.54
3.86
7
6.5
6
5.5
5
4.5
4
3.5
3
2.5
2
1.5
1
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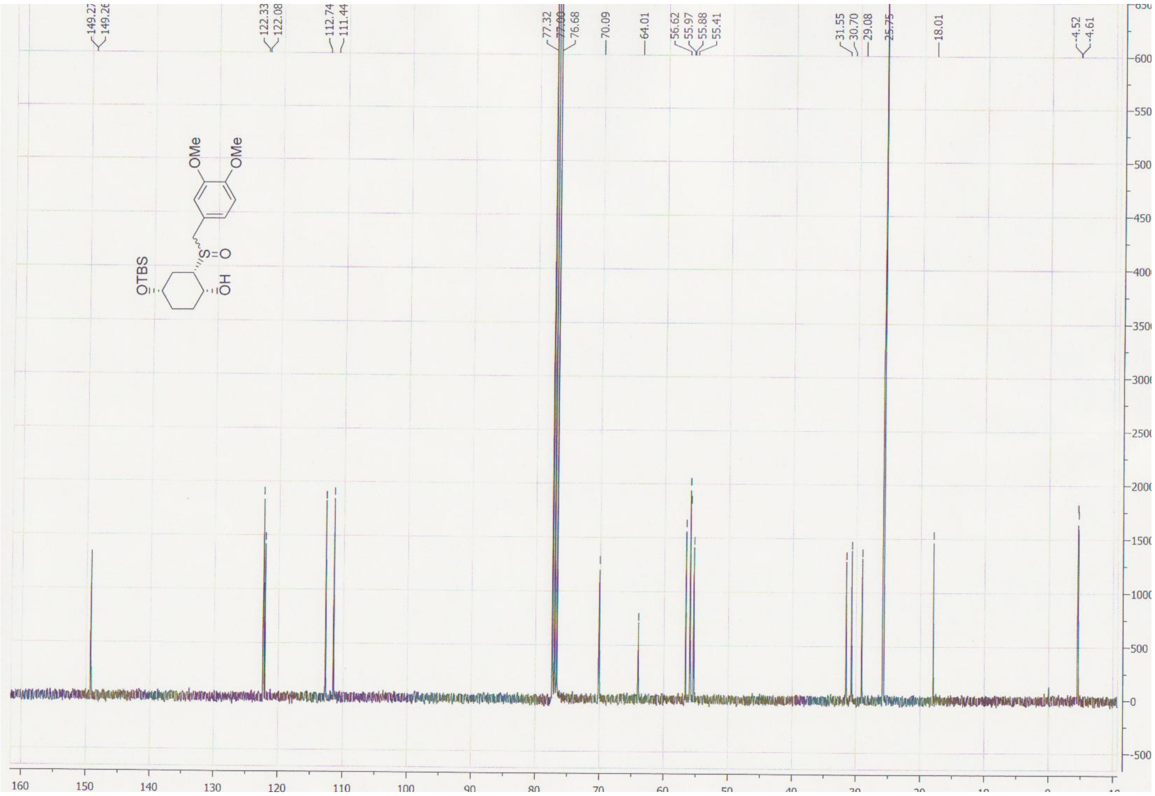
400
350
300
250
200
150
100
50
0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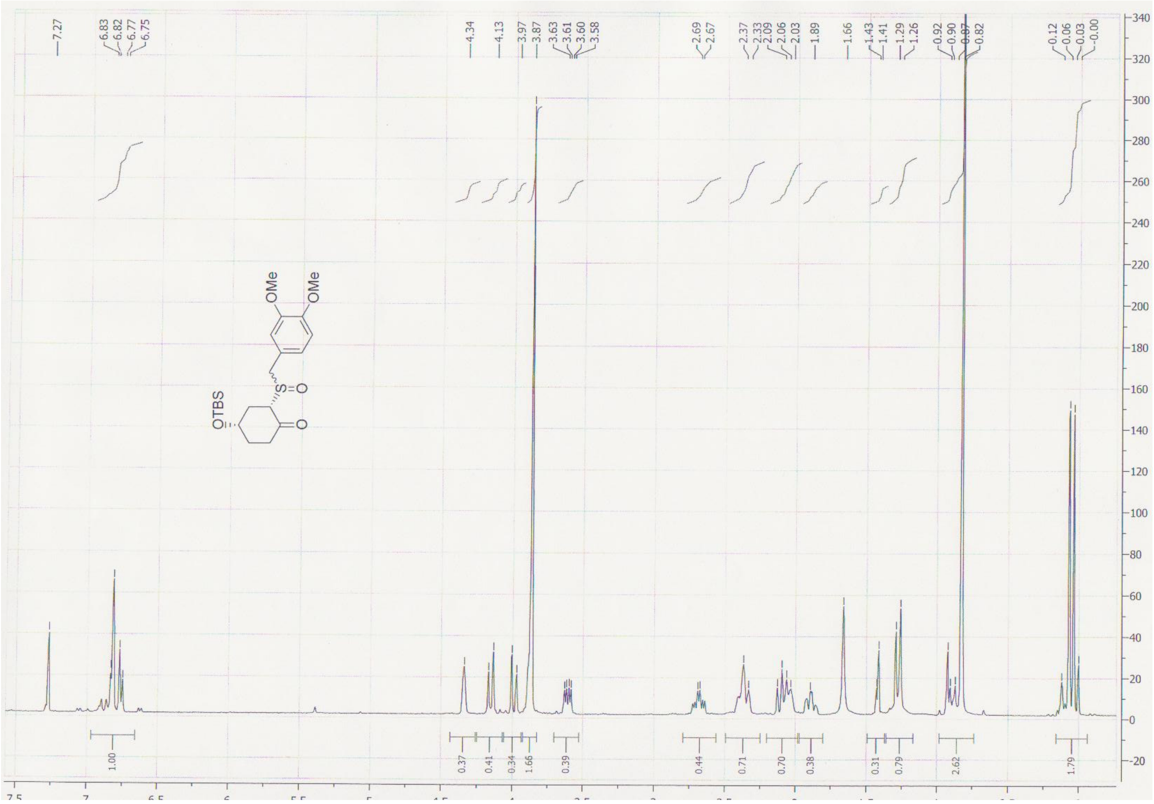
149.26
122.33
122.08
112.74
111.44
77.32
77.00
76.68
70.09
64.01
56.62
55.97
55.88
55.41
31.55
30.70
29.08
25.75
18.01
-4.52
-4.61
OTBS
OH
S=O
OMe
OMe
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
650
600
550
500
450
400
350
300
250
200
150
100
500
0
-500

Compound **24**


7.27
6.83
6.82
6.77
6.75
4.34
4.13
3.97
3.87
3.63
3.61
3.60
3.58
2.69
2.67
2.37
2.33
2.09
2.06
2.03
1.89
1.66
1.43
1.41
1.29
1.26
0.92
0.90
0.87
0.82
0.12
0.06
0.03
-0.00
OTBS
S
O
O
OMe
OMe
1.00
0.37
0.41
0.34
1.66
0.39
0.44
0.71
0.70
0.38
0.31
0.79
2.62
1.79
340
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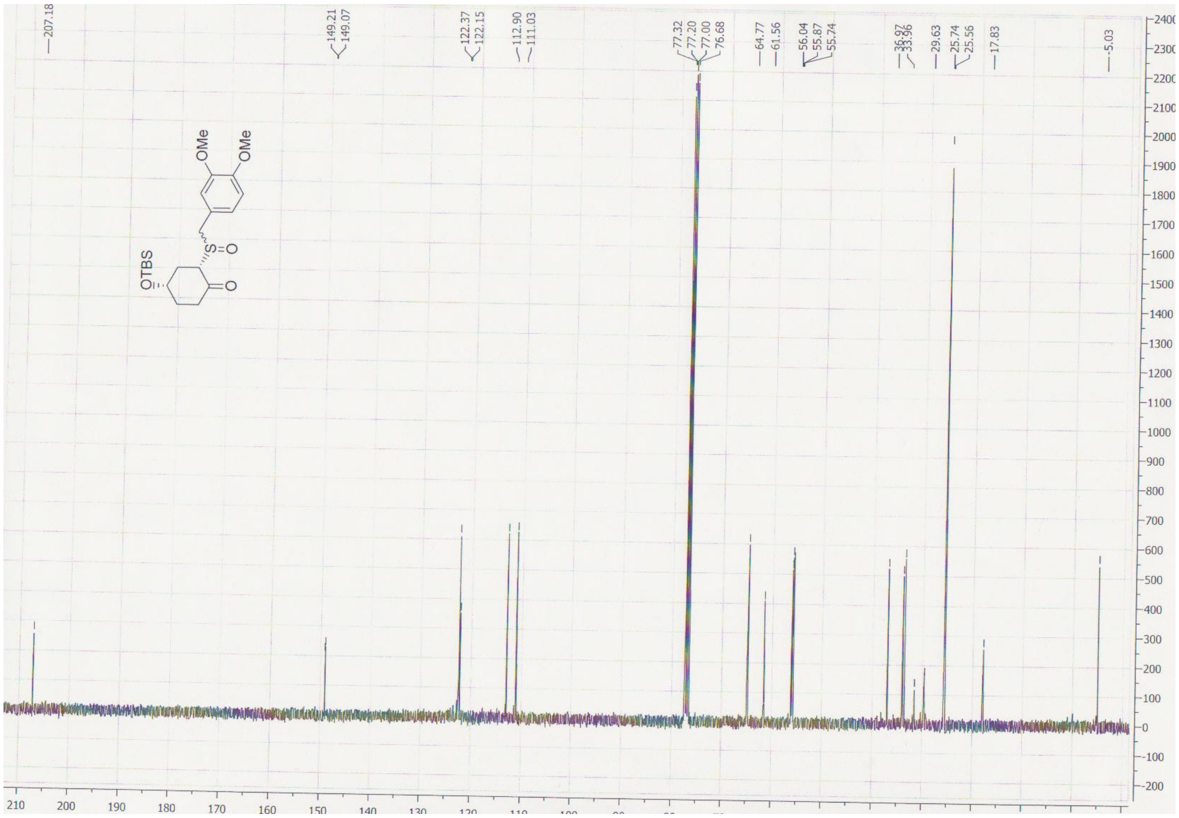
300
280
260
240
220
200
180
160
140
120
100
80
60
40
20
0
-20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77.32
77.20
77.00
76.68
64.77
61.56
56.04
55.87
55.74
36.97
33.96
29.63
25.74
25.56
17.83
-5.03
OTBS
S
O
O
OMe
OMe
2400
2300
2200
2100
2000
1900
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
-200
210
200
190
180
170
160
150
140
130