Angewandte Chemie
Eine Zeitschrift der Gesellschaft Deutscher Chemiker

Supporting Information

69451 Weinheim, Germany

A Green Chemistry Method for the Synthesis of Compounds with Adjacent Quaternary Stereogenic Centers: Parallel Syntheses of (+)- and (-)-α-Cuparenone by Radical Combination in Crystalline Solids [**]

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[**] This work was supported by the National Science Foundation through grant CHE0551938

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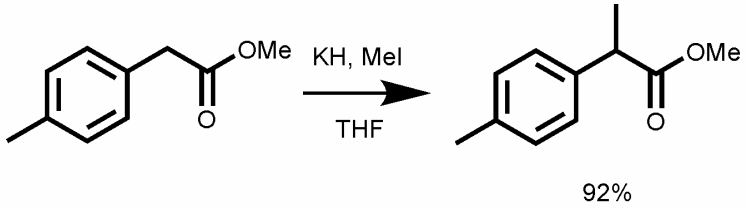
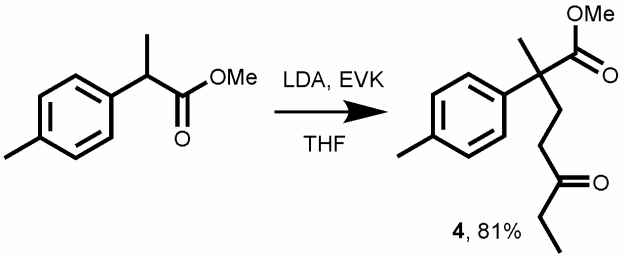
I. General: Tetrahydrofuran (THF) was distilled over sodium-benzophenone ketyl. Diisopropylamine and methylene chloride were distilled over CaH_2. Commercial reagents of the highest purity available were used without further purification. ^1H and ^{13}C NMR spectra were obtained with a Bruker ARX400, ARX 500 or DRX500 spectrometer in $CDCl_3$ (internal reference). IR spectra were obtained with a Perkin-Elmer FT-IR spectrum-100 spectrometer (equipped with ATR accessory) either as neat solids, thin films or as neat oils. High resolution mass spectra were obtained by electron ionization. GC was conducted on a HP5890 gas chromatograph with a 0.2 mm x 25 m x 0.11μm HP-1 and HP-5 (cross linked methyl silicone gum) capillary column. Chiral GC analysis was carried out with the Supelco β-dex 120 column. Melting points were uncorrected. Moisture sensitive reactions were carried out in oven-dried glassware under argon atmosphere.

II. Synthesis of Methyl 2-methyl-2-(*p*-tolyl)-5-oxoheptanoate (4).



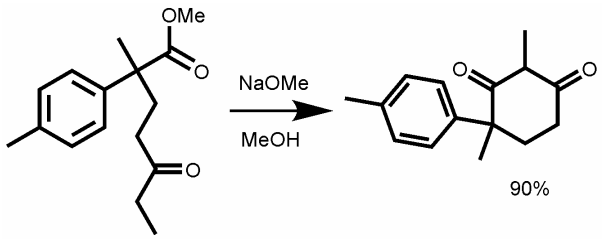
Methyl 2-(*p*-tolyl)-propionate: A 250 mL round bottom flask equipped with a magnetic stirring bar was charged with potassium hydride (0.812 g, 20.2 mmol). THF (50 mL) was added and the mixture was cooled to 0 °C in an ice-bath. *p*-tolylacetic acid methylester **3** (commercially available) (3.02 g, 18.4 mmol) in 50 mL of THF was added dropwise with stirring over 20 min, and the resulting light yellow solution was warmed to room temperature and continued to stir for an additional 30 min. Methyl iodide (1.15 mL, 18.5 mmol) was added and the reaction mixture was allowed to stir for 14h at room temperature. The reaction mixture was quenched with water (100 mL) and the product was extracted with ether (2 × 50 mL). The organic layers were combined, washed with brine, and dried over anhydrous $MgSO_4$. Removal of solvent *in vacuo* afforded 3.01 g as a light yellow oil, which was used in the next step without further purification. Yield: 92%. ^1H NMR: δ 1.48 (d, J = 7.2 Hz, 3H), 2.32 (s, 3H), 3.64 (s, 3H), 3.66(q, J = 7.4 Hz, 1H), 7.13 (d, J = 8.0 Hz, 2H), 7.18 (d, J = 8.1 Hz, 2H). ^{13}C NMR: δ 18.58, 20.98, 44.96, 51.93, 127.28,

129.29, 136.73, 137.56, 175.13. IR (neat): 2980, 2952, 2876, 1738, 1515, 1454, 1434, 1335, 1253, 1206, 1165, 1064, 819, 784, 728 cm^{-1}. EI HRMS: calculated for $C_{11}H_{14}O_2$ 178.0994, found 178.0994.

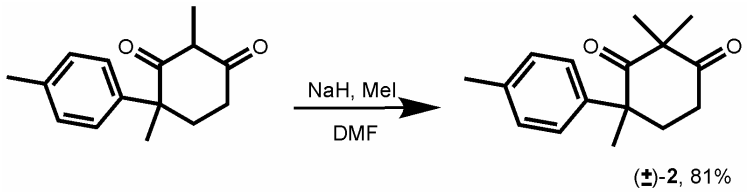


Methyl 2-methyl-5-oxo-2-*p*-tolylheptanoate: To a 250 mL round bottom flask equipped with a magetic stirring bar were added THF (50 mL) and diisopropylamine (3.47 mL, 24.8 mmol). After cooling the mixture to 0 °C, *n*-butyllithium (1.6M in hexanes, 24.1 mmol) was added dropwise. Stirring was continued at 0 °C for 20 min and the flask was then transferred to a Dry ice/acetone bath. Ester (3.90 g, 21.9 mmol) in 15 mL of THF was added dropwise over 10 min, and the resulting mixture was stirred at –78 °C for 1 h. Ethyl vinyl ketone (2.20 mL, 22.1 mmol) was added dropwise and mixture was stirred for 2 h at –78 °C and then 2 h at 0 °C. After the mixture was warmed to room temperature, water (80 mL) was added to quench the reaction and the product was extracted with ether (3 × 50 mL). The combined organic layer was washed with brine, dried over $MgSO_4$, and concentrated to give a yellow viscous oil. Purification by column chromatography (30% ethyl acetate/hexanes) yielded 4.65 g (81%) of **4** as a colorless oil. ^{1}H NMR: δ 1.01 (t, *J* = 7.3 Hz, 3H), 1.53 (s, 3H), 2.24-2.31 (m, 4H), 2.31 (s, 3H), 2.34 (q, *J* = 7.3 Hz, 2H), 3.66 (s, 3H), 7.13 (d, *J* = 8.3 Hz, 2H), 7.16 (d, *J* = 8.6 Hz, 2H). ^{13}C NMR: δ 7.78, 20.90, 23.08, 32.90, 35.88, 38.01, 49.28, 52.15, 125.86, 129.19, 136.53, 139.91, 176.47, 210.84. IR (neat): 2978, 2942, 1732, 1715, 514, 1461, 1378, 1242, 1114, 818 cm^{-1}. EI HRMS: calculated for $C_{16}H_{22}O_3$ 262.1569, found 262.1569.

III. Synthesis of 2,2,4-Trimethyl-4-(*p*-tolyl)-1,3-cyclohexanedione [(±)-2)].



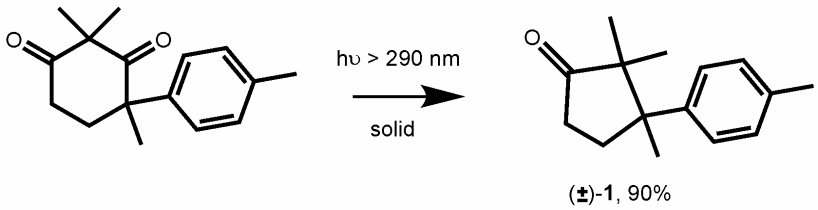
2,4-Dimethyl-4-(*p*-tolyl)-1,3-cyclohexanedione. A 50 mL round bottom flask equipped with a magnetic stirring bar was charged with anhydrous methanol (25 mL). Elemental sodium (1.21 g, 52.6 mmol) was added and the mixture was stirred at room temperature until all the sodium had reacted. Ketoester **4** (3.1 g, 11.8 mmol) in 2 mL of MeOH was added dropwise and the resulting mixture was refluxed for 18 h. After the mixture was cooled to room temperature, 1N HCl (25 mL) was added to quench the reaction and the product was extracted with ethyl acetate (3 × 20 mL). The combined organic layer was washed with brine, dried over $MgSO_4$, and concentrated to a pale yellow solid. Tituration with ether gave 2.7 g (100%) of monomethyated cyclohexanedione as a white solid, further purification of which was unnecessary. Spectroscopic data indicated that diketone existed entirely in its enol form. m.p. 165.4-167.6 °C. ^{1}H NMR (DMSO-d_6): δ 1.24 (s, 3H), 1.62 (s, 3H), 1.87-1.95 (m, 1H), 2.03-2.06 (m, 1H), 2.24 (s, 3H), 2.24-2.40 (m, 2H), 7.04 (d, *J* = 8.5 Hz, 2H), 7.08 (d, *J* = 8.3 Hz, 2H), 10.22 (br, 1H). ^{13}C NMR (DMSO-d_6): δ 8.90, 21.43, 27.45, 27.97, 34.35, 48.15, 110.48, 126.89, 129.76, 136.16, 141.65, 170.75, 201.13. IR (KBr): 3253, 2924, 1595, 1512, 1447, 1383, 1357, 1335, 1257, 1094, 1072, 810 cm^{-1}. EI HRMS: calculated for $C_{15}H_{18}O_2$ 230.1307, found 230.1306.



2,2,4-Trimethyl-4-(*p*-tolyl)-1,3-cyclohexanedione. To a 50 mL three-necked round bottom flask equipped with a water condenser and a magnetic stirring bar were added NaH (0.129 g, 5.42 mmol), diketone (1.10 g, 4.78 mmol) and anhydrous DMF (18 mL). The reaction mixture was heated at 75 °C with stirring for 30 min. Methyl iodide (0.753 g, 5.31 mmol) was then added and the mixture was allowed to stir at 75°C for another 2.5 h. Water (20 mL) was added to quenched the reaction and product was extracted with ether (3

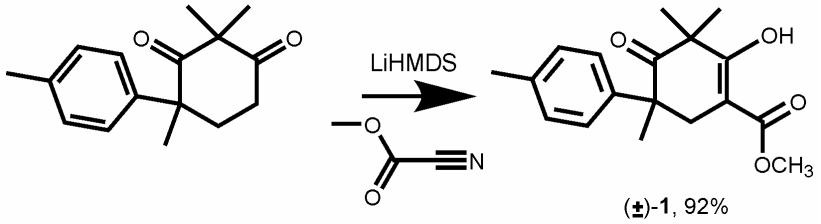
× 20 mL). The combined organic layer was washed successively with 1N HCl, water, and brine, dried over $MgSO_4$ and concentrated *in vacuo* to give 1.1 g from yellow oil. GC analysis indicated that the desired cyclohexanedione ±-**2** and the corresponding O-alkylated product were formed in a 5:1 ratio in 81% overall yield. Column chromatography ($CHCl_3$) followed by recrystallization from 80:20 hexane/ether in the freezer (-15°C) afforded **2** as clear, colorless crystals. m.p. 63.1-65.6 °C; ^{1}H NMR: δ 1.14 (s, 3H), 1.32 (s, 3H), 1.39 (s, 3H), 2.14-2.19 (m, 1H), 2.30 (s, 3H), 2.60-2.75 (m, 3H), 7.02 (d, *J* = 8.3 Hz, 2H), 7.12 (d, *J* = 8.5 Hz, 2H). ^{13}C NMR: δ 20.89, 23.55, 23.95, 27.96, 28.16, 34.36, 52.29, 58.93, 126.12, 129.77, 136.38, 137.20, 210.61, 212.75. IR (KBr): 3027, 2980, 2970, 2871, 1726, 1697, 1510, 1466, 1418, 1379, 1277, 1006, 820 cm^{-1}. EI HRMS: calculated for $C_{16}H_{20}O_2$ 244.1463, found 244.1463.

IV. Solid state synthesis of (±)-(α)-**Cuparenone**.



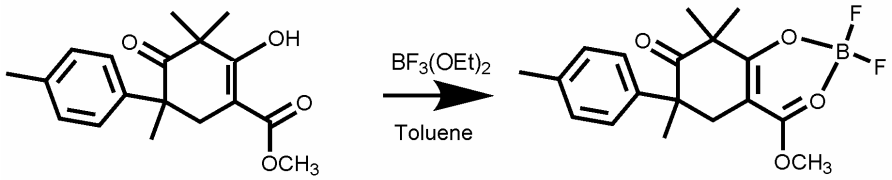
(±)-(α)-Cuparenone (±-1). Finely ground powders of ±-**2** (20 mg) were placed in between two Pyrex microscope slides, secured with masking tape. The entire setup was placed inside a sealed plastic bag and immersed in an isopropanol bath with the internal temperature maintained between –20 °C and –25 °C. Sample was irradiated with an Hanovia medium pressure Hg lamp for 12 h, at which point melting was observed initially at the border of the powder sample. GC analysis indicated a conversion of 70% to the natural product had been achieved. Spectroscopic data of ±-**1** were in agreement with published data. ^{1}H NMR (500 MHz): δ 0.61 (s, 3H), 1.17 (s, 3H), 1.26 (s, 3H), 1.89-1.94 (m, 1H), 2.34 (s, 3H), 2.44-2.46 (m, 1H), 2.50-2.56 (m, 1H), 2.66-2.71 (m, 1H), 7.16 (d, *J* = 8.2 Hz, 2H), 7.27 (d, *J* = 8.2 Hz, 2H). ^{13}C NMR (125 MHz): δ 18.41, 20.83, 22.12, 25.34, 29.66, 33.78, 48.32, 53.21, 126.39, 128.91, 135.81, 141.91, 222.63. IR (neat): 2969, 2924, 1738, 1515, 1460, 1375, 1275, 1095, 1055, 817 cm^{-1}. EI HRMS: calculated for $C_{15}H_{20}O$ 216.1514, found 216.1510.

V. Synthesis of chiral Precursors 7A and 7B:



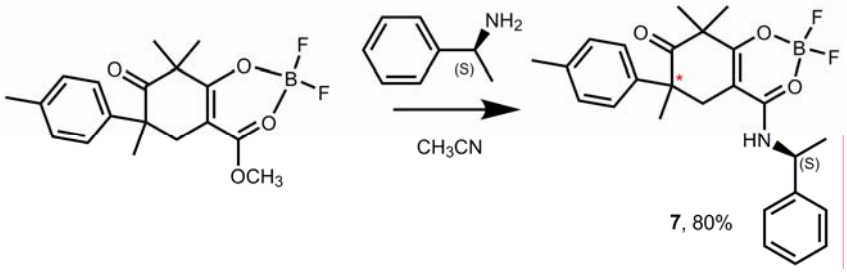
(±)-**1**, 92%

β-ketoester (±)**-5**: A solution of diketone (630mg, 2.6mmol) in 5 mL dry THF was cooled to -78° C, and 1.1 eq of LiHMDS (lithium bistrimethyl silylamide, 2.84 mL) was added. After stirring the reaction mixture for 1 h, methylcyanoformate (1.1 *eq*, 0.23 mL) was added and the reaction was stirred for additional 30 mins. The reaction was warmed to room temperature and quenched with saturated ammonium chloride solution. The product was extracted using ether and dried over $MgSO_4$. The β-ketoester **5** was purified by column chromatography with ether: hexane = 2:8. The product (700 mg, 90%) was crystallized in ether to obtain colorless plate like crystals. m.pt : 97.5-101° C. ^{1}H NMR (500 MHz, $CDCl_3$): 0.97 (s, 3H), 1.35 (s, 3H), 1.41 (s, 3H), 2.3 (s, 3H), 2.43 (d, 1H, J = 16.5 Hz), 3.35 (d, 3H, J = 16.5 Hz), 3.92 (s, 1H), 7.03 (d, *J* = 8.0 Hz, 2H), 7.11 (d, *J* = 8.0 Hz, 2H), 12.28 (s, 1H). IR (neat): 3250, 2969, 2856, 1711, 1660, 1621, 1355, 1514, 1442, 1226, 1189, 1039, 820 cm^{-1}.



(±)-**6**, 100%

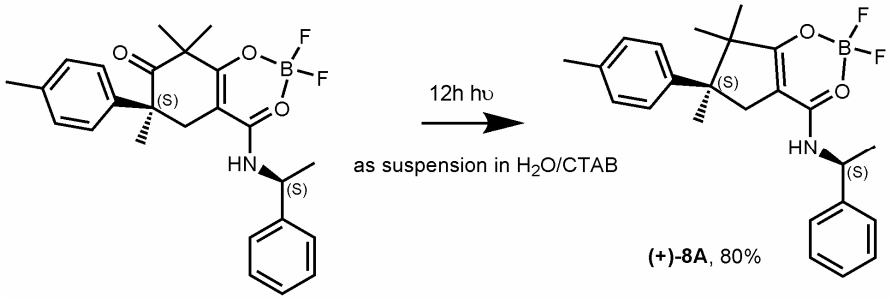
2,2-Difluoro-4-methoxy-1,3,2-dioxaborinane (±)**-6**: To a solution of 1,3 ketoester **5** (610mg, 0.002 mmol) in toluene (5 mL), 3 equivalents of $BF_3.OEt_2$ (0.76 mL) was added and the reaction was stirred at room temperature overnight. The solvent was removed in rotovap and the precipitated material was washed several times with petroleum ether/ EtOAC = 5/1, yielding pure product (692 mg, 98%). The product **6** was dried in vacuum to yield a dirty white powder, which was then recrystallized in ether. ^{1}H NMR (500 MHz, $CDCl_3$): 1.05 (s, 3H), 1.4 (s, 3H), 1.43 (s, 3H), 2.31 (s, 3H), 2.49 (d, 1H, J = 16.0 Hz), 3.32 (d, 1H, J = 16.0 Hz), 4.24 (s, 3H), 6.94 (d, *J* = 8.0 Hz, 2H), 7.12 (d, *J* = 8.0 Hz, 2H). IR (neat): 2987, 2856, 1713, 1605, 1525, 1505, 1398, 1378, 1346, 1176, 1044, 823 cm^{-1}.



2-Difluoroboryloxy-3,3,5-trimethyl-4-oxo-N-[(S)-1-phenylethyl]-5-p-tolylcyclohex-1-enecarboxamide (**7**): The dioxaborinane ester complex (±)**-6** (786 mg) was dissolved in 5 mL of acetonitrile and to the solution 1.3 *eq*. of α-methyl benzylamine was added and the solution was stirred at room temperature for 6-8 h. The reaction solvent was evaporated in vacuo and the residue was redissolved in EtOAC and the organic layer was washed with water and organic layer was dried over $MgSO_4$ and the solvent was removed in vacuo. The two diastereomers were separated in analytical TLC plates with R_f values of 0.3 (diastereomer 2) and 0.4 (diastereomer 1) using EtOAc/Hexane = 2:8. The same solvent system was used to separate the crude (ca. 780 mg) by column chromatography using silica gel 60 Geduran® with particle size of 40-63 μm. The column used had a 4.7 cm diameter and it was packed to a height of 30 cm. About 216 (10 ml) fractions were collected. The unreacted starting material was recovered as the corresponding ester **5** (the BF_2 group of **6** cleaves off in silica). The product **7** diastereomers (800 mg, 80% yield) formed in 1:1 ratio were separated. Diastereomer **7A** was recrystallized from ether to obtain needle shaped colorless crystals and diastereomer **7B** was crystallized in EtOAC : Hexane = 2:8 to obtain clear plate like crystals. **Diastereomer 7A**: m.p. 224-227 °C. $[\alpha]_D^{23.3}$ = +60 $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): 0.94 (s, 3H), 1.34 (s, 3H), 1.43 (s, 3H), 1.76 (d, 3H, J = 7.5 Hz), 2.32 (s, 3H), 2.43 (d, 1H, J = 15.0 Hz), 2.84 (d, 1H, J = 15.0 Hz), 5.4 (m, 1H), 6.18 (bd, 1H), 6.95 (d, *J* = 8.0 Hz, 2H), 7.13 (d, *J* = 8.0 Hz, 2H), 7.38-7.48 (m, 4H). ^{13}C NMR (125 MHz): δ 20.8, 20.81, 24.0, 25.1, 26.55, 29.2, 29.6, 49.3, 50.4, 51.2, 90.8, 126.1, 126.22, 128.54, 129.08, 129.5, 136.0, 137.3, 140.21, 166.65, 179.0, 211.2. IR (neat): 2969, 2924, 1738, 1515, 1460, 1375, 1275, 1095, 1055, 817 cm^{-1}. IR (neat): 3368, 2925, 2854, 1713, 1593, 1582, 1524, 1497, 1455, 1414, 1379, 1353, 1045, 911 cm^{-1}. **Diastereomer 7B**, m.p. 192-198° C; $[\alpha]_D^{23.0}$ = -237 ($CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): 0.95 (s, 3H), 1.35 (s, 3H), 1.45 (s, 3H), 1.72 (d, 3H, J = 7.5 Hz), 2.28 (s, 3H), 2.5 (d, 1H, J = 15.0 Hz), 2.81 (d, 1H, J = 15.0 Hz), 5.41 (m, 1H), 6.15 (bd, 1H), 6.84 (d, *J* = 8.0 Hz, 2H), 7.04 (d, *J* = 8.0 Hz, 2H), 7.4-7.5 (m, 4H). ^{13}C NMR (125 MHz): δ 20.7, 21.11, 24.1, 24.9, 26.53, 29.22,

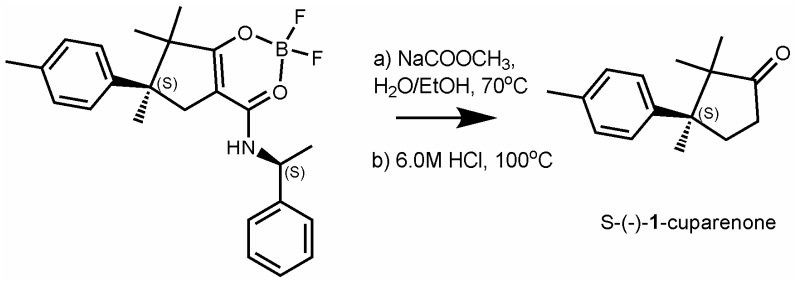
29.6, 49.4, 50.5, 51.1, 90.7, 126.2, 126.5, 128.6, 129.1, 129.4, 136.15, 137.4, 139.82, 166.65, 178.9, 211.25. IR (neat): 3368, 2925, 2854, 1713, 1593, 1582, 1524, 1497, 1455, 1414, 1379, 1353, 1045, 911 cm^{-1}.

VI. Solid state synthesis of homochiral cuparenone amides.



(S)-2-(difluoroboryloxy)-3,3,4-trimethyl-N-[(S))-1-phenylethyl]-4-p-tolylcyclopent-1-enecarboxamide (S,S)-(+)-**8** and (R)-2-(difluoroboryloxy)-3,3,4-trimethyl-N-[(S))-1-phenylethyl]-4-p-tolylcyclopent-1-enecarboxamide (R,S)-(-)-**8**): 100 mg diketone precursor (**7a** or **7b**) was dissolved in 2 mL of acetone and was added into 25 mL of H_2O/CTAB (0.16mM) solution while vortexing the solution. Thus the nanocrystals suspension obtained was irradiated while stirring the solution in a 450W medium pressure mercury lamp for 10-12 hours. The reaction conversion was monitored using TLC which showed the formation of the product eluting just above the starting material in ethylacetate: hexane = 2:8. The product [(+)-**8** or (-)-**8**] was isolated using column chromatography (yield: 80%). **S,S-cuparenoneamide** [(S,S)-(+)-**8**] ^{1}H NMR (500 MHz, $CDCl_3$): 0.7 (s, 3H), 1.31 (s, 3H), 1.38 (s, 3H), 1.68 (d, 3H, J = 7.5 Hz), 2.24 (d, 1H, J = 12.6 Hz), 2.33 (s, 3H), 3.16 (d, 1H, J = 12.6 Hz), 5.36 (m, 1H), 5.76 (bd, 1H), 7.13 (d, *J* = 8.2 Hz, 2H), 7.21 (d, *J* = 8.2 Hz, 2H), 7.3-7.46 (m, 4H). **R,S-cuparenoneamide** [(R,S)-(-)-**8**] ^{1}H NMR (500 MHz, $CDCl_3$): 0.71 (s, 3H), 1.32 (s, 3H), 1.39 (s, 3H), 1.7 (d, 3H, J = 7.5 Hz), 2.23 (d, 1H, J = 12.6 Hz), 2.34 (s, 3H), 3.2 (d, 1H, J = 12.6 Hz), 5.37 (m, 1H), 5.63 (bd, 1H), 7.13 (d, *J* = 8.2 Hz, 2H), 7.21 (d, *J* = 8.2 Hz, 2H), 7.3-7.46 (m, 4H).

VII. Solid state synthesis of homochiral cuparenones.



S-(+)-Cuparenone ((+)-**1)** and R-(-)-Cuparenone ((-)-**1)**: To 50 mg of the cuparenoneamide [**(+)-8** or **(-)-8**] in H_2O/EtOH mixture = 4:1, 5 eq of sodium actetate was added and the reaction mixture was refluxed for 3-4 h. Later, to the same solution 6.0 M HCl was added and the reaction was continued to reflux at 120° C for 48 h. The reaction mixture was warmed to room temperature and extracted with ether and dried over $MgSO_4$. The R or S cuparenone (S-(+)-**1** or R-(-)-**1**) was obtained as pure white solid after column chromatography with Hexane:ether = 9:1 (90% yield) Optical rotation $[\alpha]_D^{25}$ = +171.0 ($CHCl_3$) for S-(+)-**1** and $[\alpha]_D^{25}$ = -168.0 ($CHCl_3$) for R-(-)-**1**.

VIII. Literature precedence for (±)-α-cuparenone and chiral cuparenone synthesis.

1. Synthesis of ±-α-cuparenone.

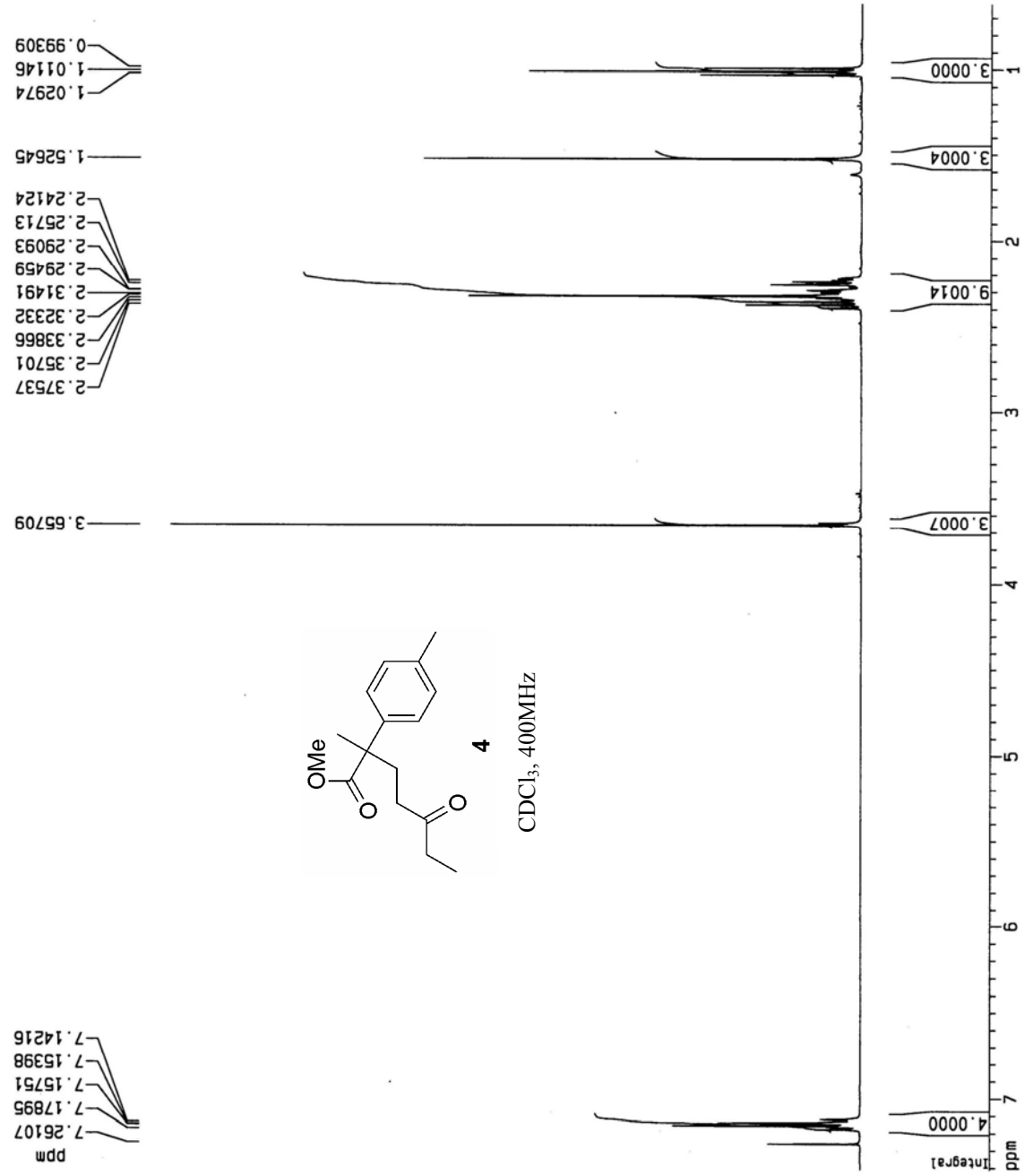
Literature	Starting Material	Number of steps	Overall Yield (%)
Parker *et al.,*[1] 1962	*p*-Toluamide	15	Yields not reported
Noyori *et al.,*[2] 1978	2-*p*-Tolyl propene	1	18
Wenkert *et al.,*[3] 1978	*p*-Cymene	8	5
Halazy *et al.,*[4] 1982	*p*-Methyl acetophenone	4	37
Greene *et al.,*[5] 1983	*p*-Tolyl propene	4	35
Gadwood *et al.,*[6] 1983	*p*-Methyl acetophenone	3	26
Eilbracht *et al.,*[7] 1984	3-Methyl-3-*p*-tolylpentanedioic acid	6	17
Srikrishna *et al.,*[8] 1990	*p*-Methyl acetophenone	8	10
Ho, T-L *et al.,*[9] 1997	α,p-Dimethylstyrene	6	8
Kulkarni *et al.,*[10] 1997	*p*-Methyl acetophenone	5	38
Cossy *et al.,*[11] 1997	2-Methylcyclopentane 1,3-dione	4	55
Ashutosh Pal *et al.,*[12] 1999	Unsaturated cyano ester	8	18
Chavan *et al.,*[13] 1999	*p*-Methyl acetophenone	5	56
Avila-Zarraga *et al.,*[14] 2000	4-methylphenyl acetonirile	5	~9
Paul, T *et al.,*[15] 2003	Unsaturated cyano ester	4	30
Bernard *et al.,*[16] 2005	Cyclopropylphenyl selenide	4	37
Our work	*p*-Tolylacetic acid methyl ester	4	59

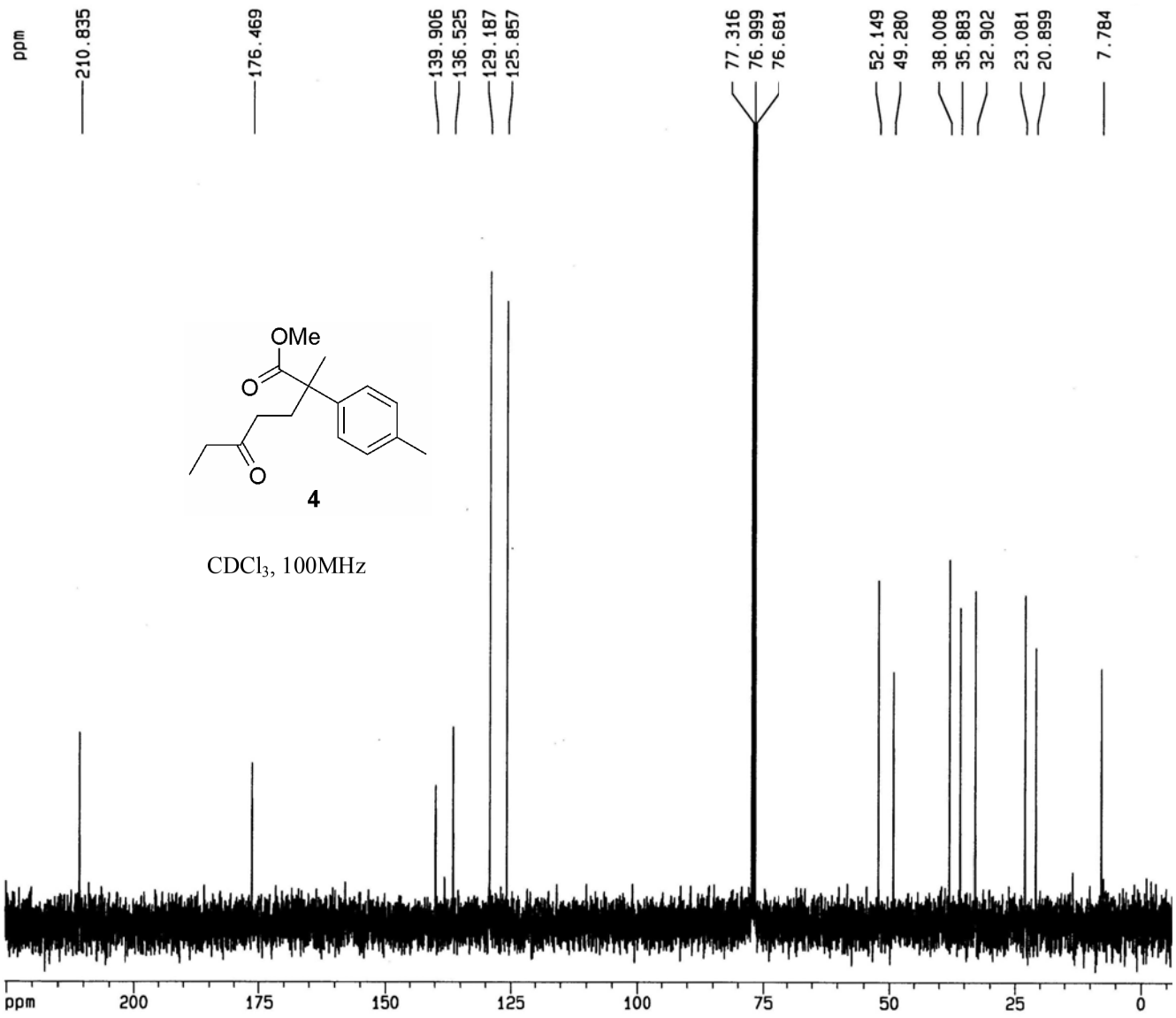
Synthesis of (+) and (-)-α-cuparenones.

Literature	Starting Material	No. of steps	Overall Yield (%) [%ee][§]
Posner *et al.*,[17] 1984	2-Cyclopentenone to (+)-α-cuparenone	8	5 [71]
Taber *et al.*,[18]1985	*p*-Tolyl acetic acid to (+)-α-cuparenone	7	0.5 [96]
Kametani *et al.*,[19] 1985	*trans*-3-*p*-Tolyl but-2-enoic acid	14	5 [9]
Meyers *et al.*,[20] 1986	*p*-Tolyl acetic acid to (-)-α-cuparenone	8	29 [97.6]
Greene *et al.*,[21] 1987	1-Methyl-4-vinyl benzene to (-)-α-cuparenone	7	18 [99]
Asaoka *et al.*,[22] 1988	Silyl cyclohexanone deri- vative to (+)α-cuparenone	12	1.5
Takano, *et al.*,[23] 1989	Dicyclopentadiene to (+)-α-cuparenone	13	0.5
Gharpure *et al.*,[24] 1989	2-Methyl-2-*p*-tolyl succinnic acid	6.5	6.5 [96]
Fadel *et al.*,[25] 1991	Chiral α,α-succinate derivative to (+)-α-cuparenone	11	22
Nemoto *et al.*,[26] 1992	Methyl *p*-tolyl acetate to (+) or (-)-α-cuparenone	9	3
Canet *et al.*,[27] 1992	*p*-Methyl acetophenone to (+) or (-)α-cuparenone	12	12
Honda *et al.*,[28] 1993	*p*-Methyl acetophenone to (+)-α-cuparenone	9	6
Maruoka *et al.*,[29] 1996	*p*-Me 4-*p*-tolylcyclo hexa- none to (+)-α-cuparenone	7	10 [70]
Kosaka *et al.*,[30] 1997	*cis*-butene 1,4-diol to (-)-α-cuparenone	14	3.6
Nakashima *et al.*, [31] 2000	**(±)**-Cyclopenten-1-ol to (+)/(-)α-cuparenone	17	5.6
Satoh *et al.*,[32] 2003	*p*-Methyl acetophenone to (+)-α-cuparenone	9	32
Spino *et al.*,[33] 2004	*p*-Menthone-3-carboxylate to (+)-α-cuparenone	9	12
Our work	Methyl-2-tolyl-acetate	9	36 [99]

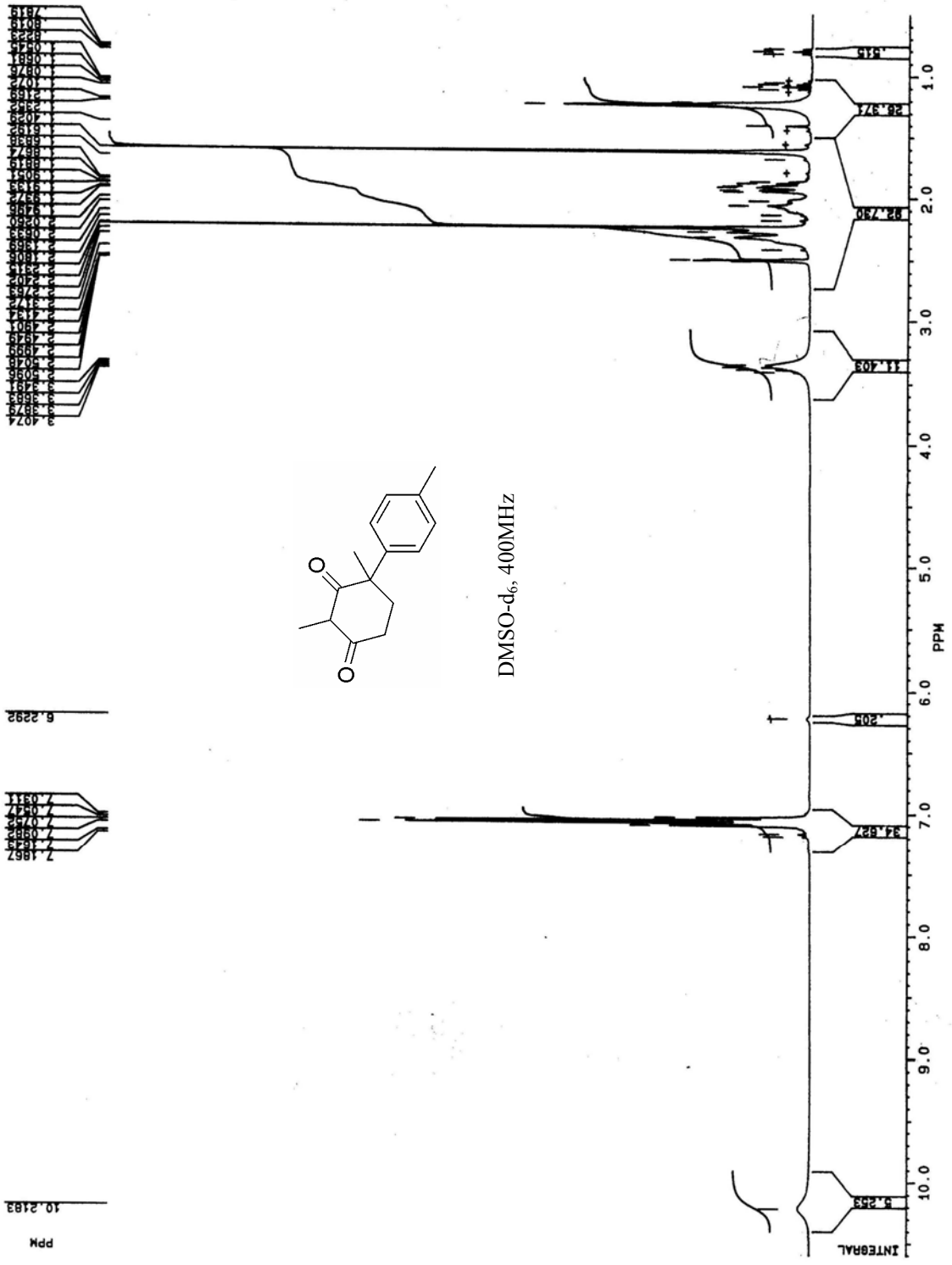
[§] Only %ee values explicitly reported are included.

IX. Spectral Characterization

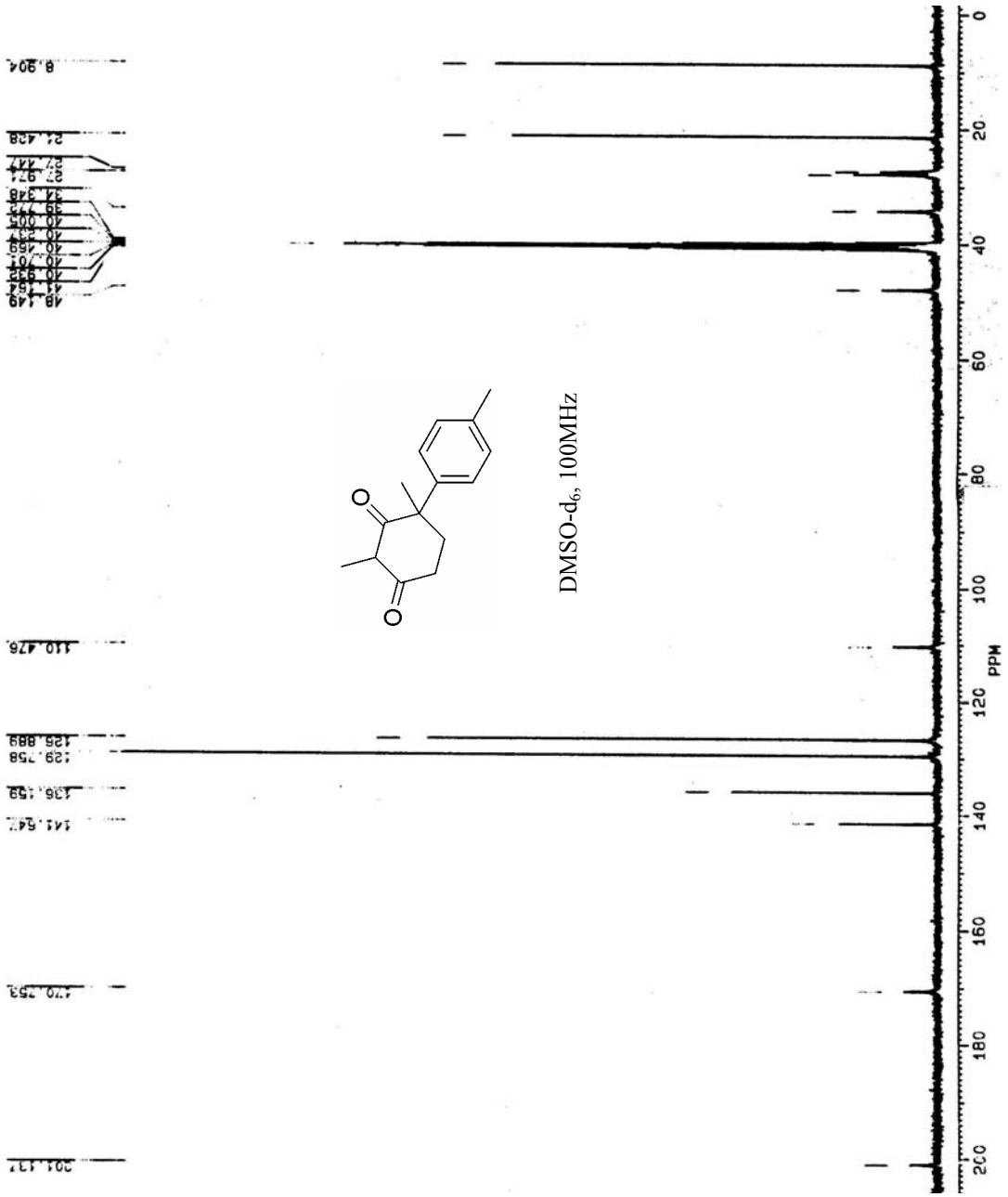


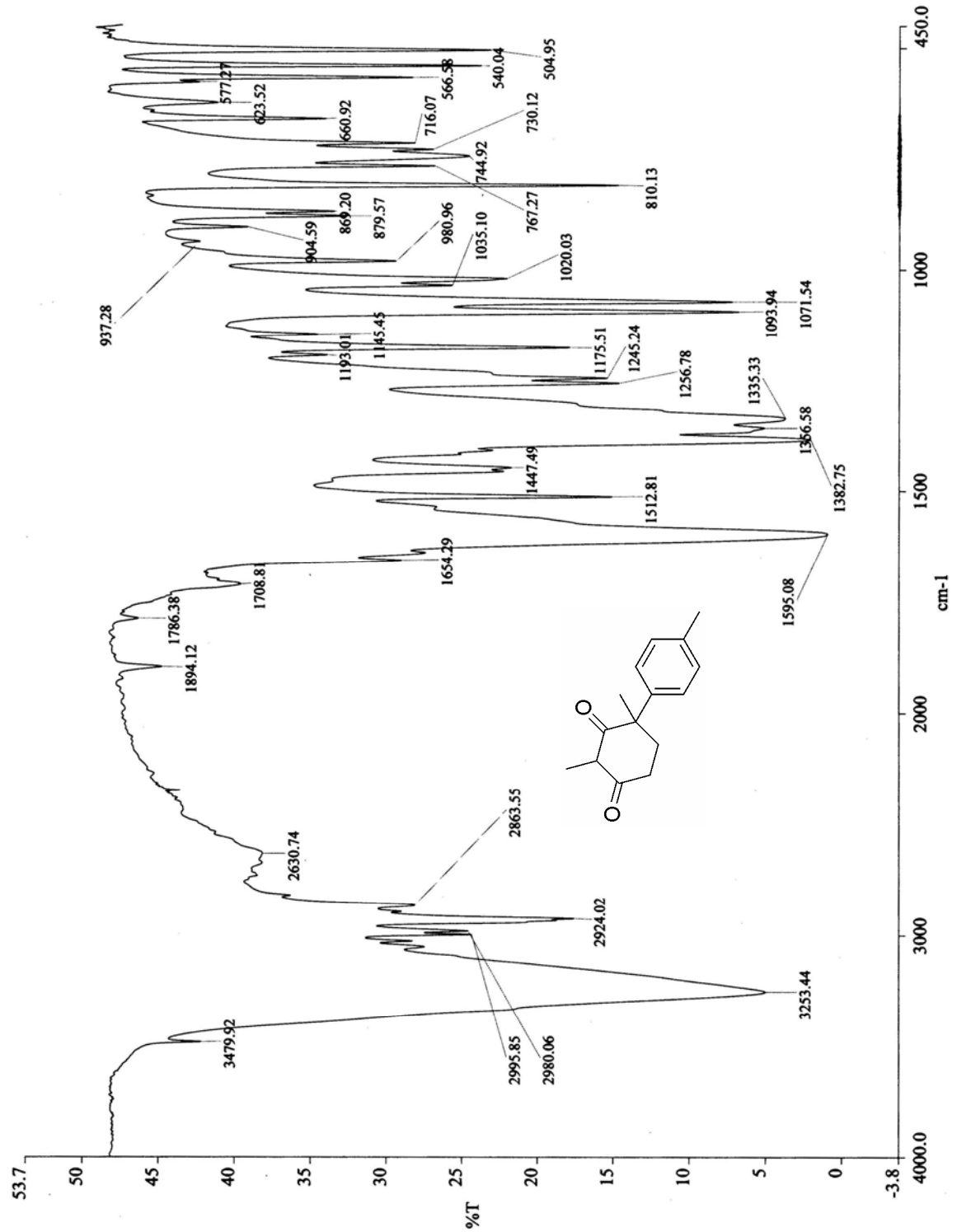

ppm
210.835
176.469
139.906
136.525
129.187
125.857
77.316
76.999
76.681
52.149
49.280
38.008
35.883
32.902
23.081
20.899
7.784
OMe
O
O
4
CDCl3, 100MHz
ppm
200
175
150
125
100
75
50
25
0

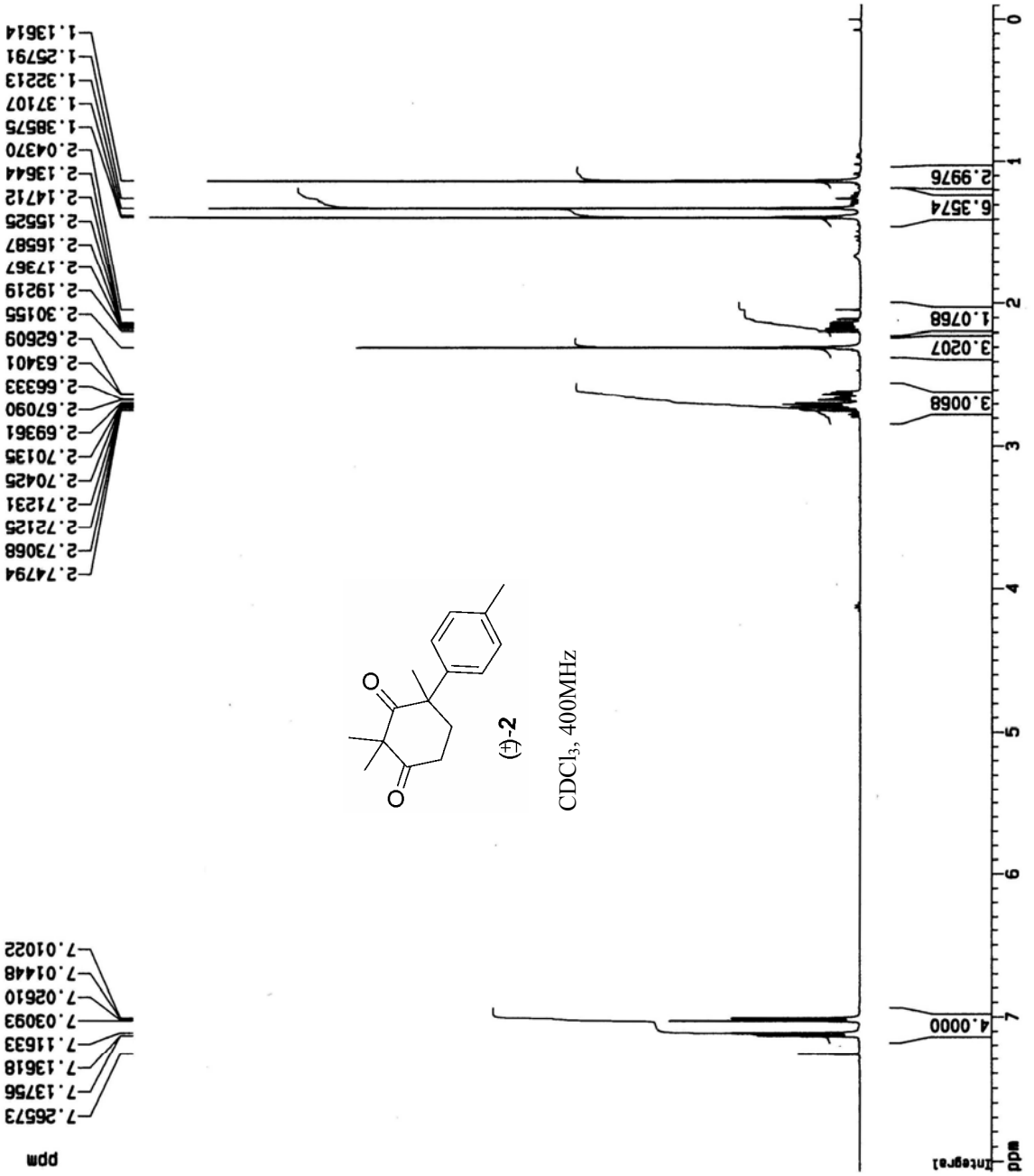
82.04
%T
23.29
4000
3500
3000
2500
2000
1500
1000
cm-1
OMe
O
O
4
2973.8; 44.94%T
2942.3; 47.25%T
1731.6; 26.03%T
1514.6; 51.21%T
1460.8; 49.57%T
1434.1; 53.47%T
1411.3; 59.71%T
1377.7; 52.63%T
1241.8; 39.19%T
1192.0; 53.56%T
1155.5; 54.63%T
1114.3; 47.39%T
1065.2; 63.48%T
1020.1; 64.45%T
986.3; 67.09%T
945.3; 77.18%T
922.5; 76.10%T
863.6; 72.42%T
817.8; 57.03%T
772.4; 73.62%T
735.2; 75.90%T

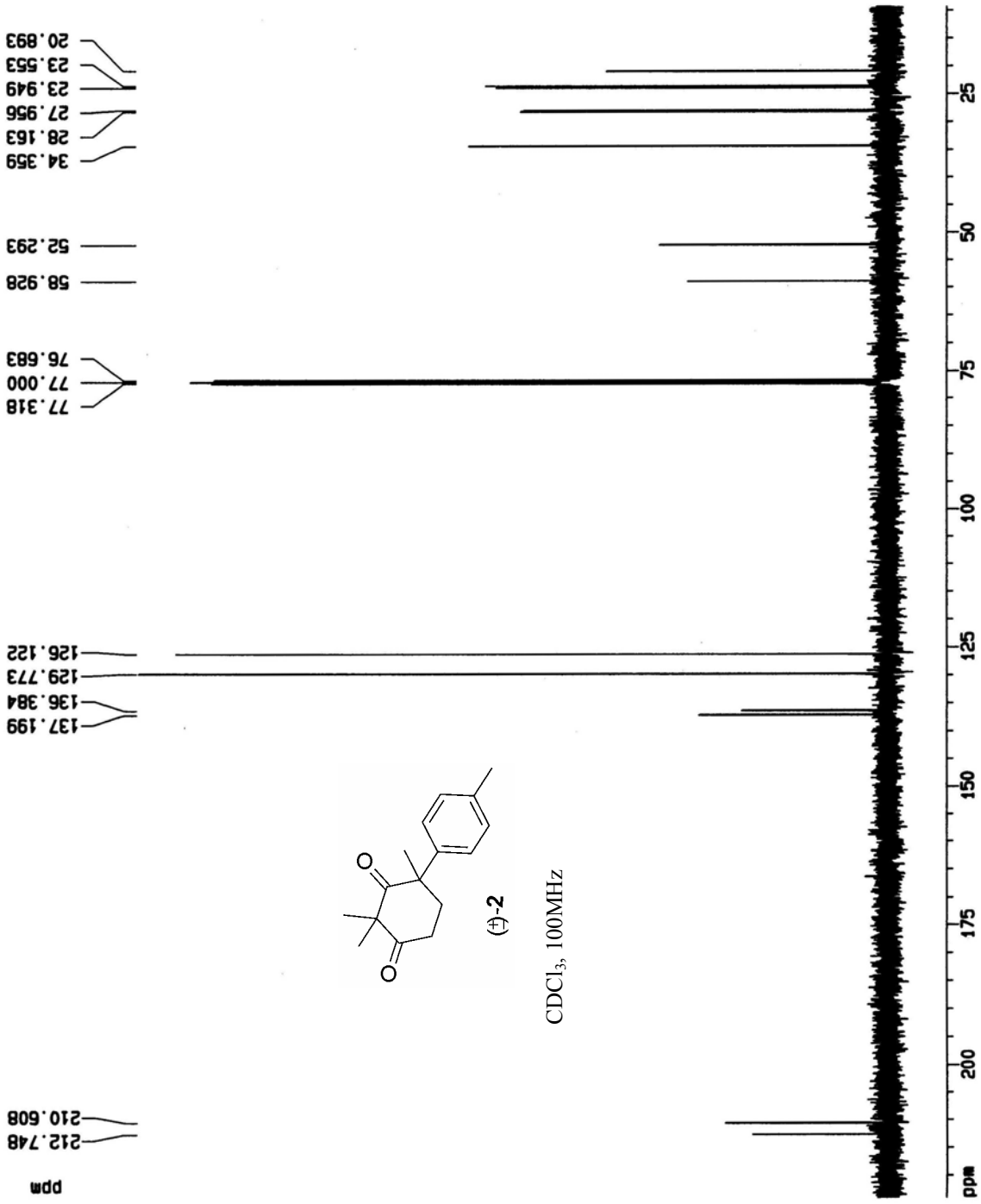


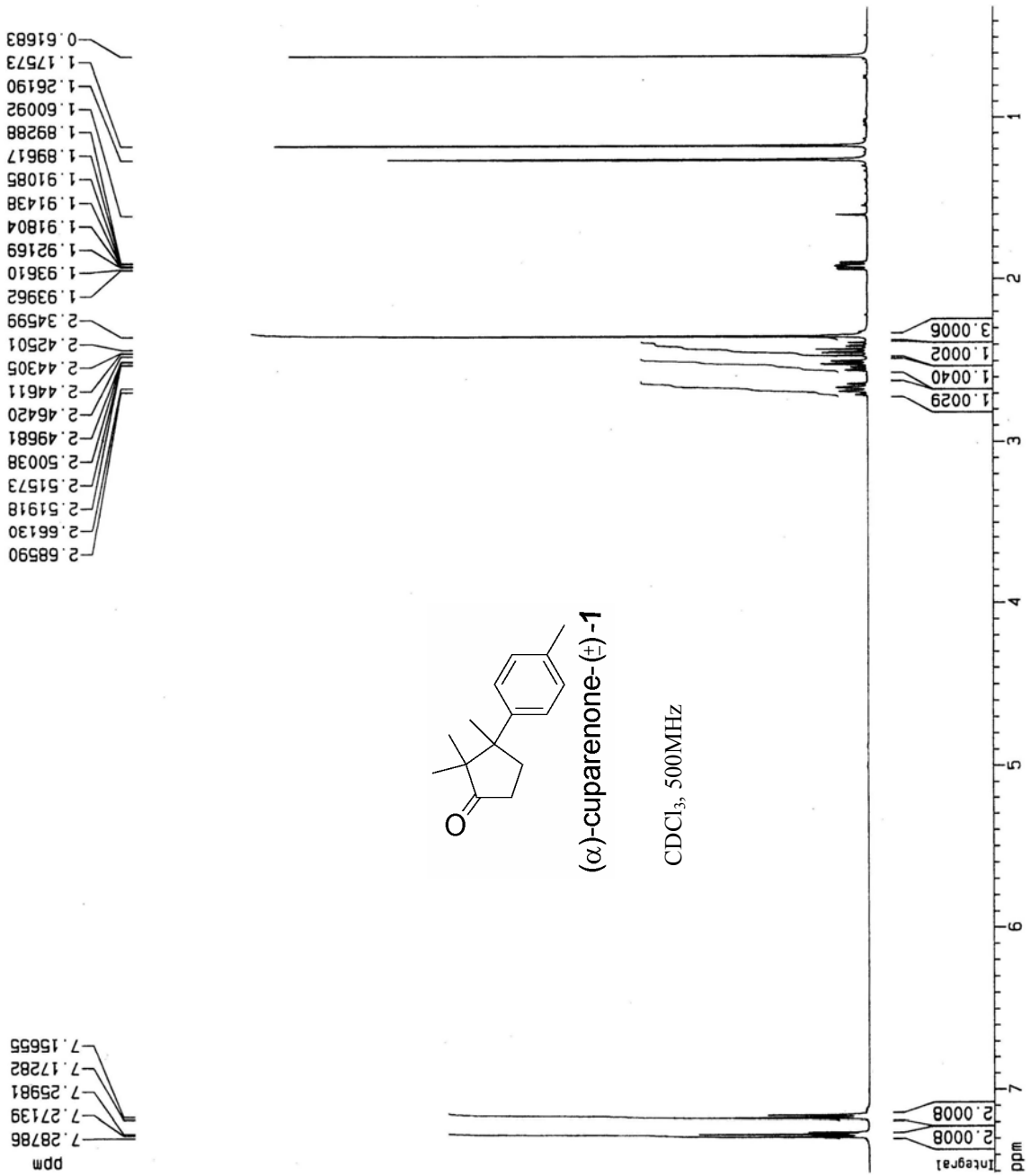
$CDCl_3$, 400MHz

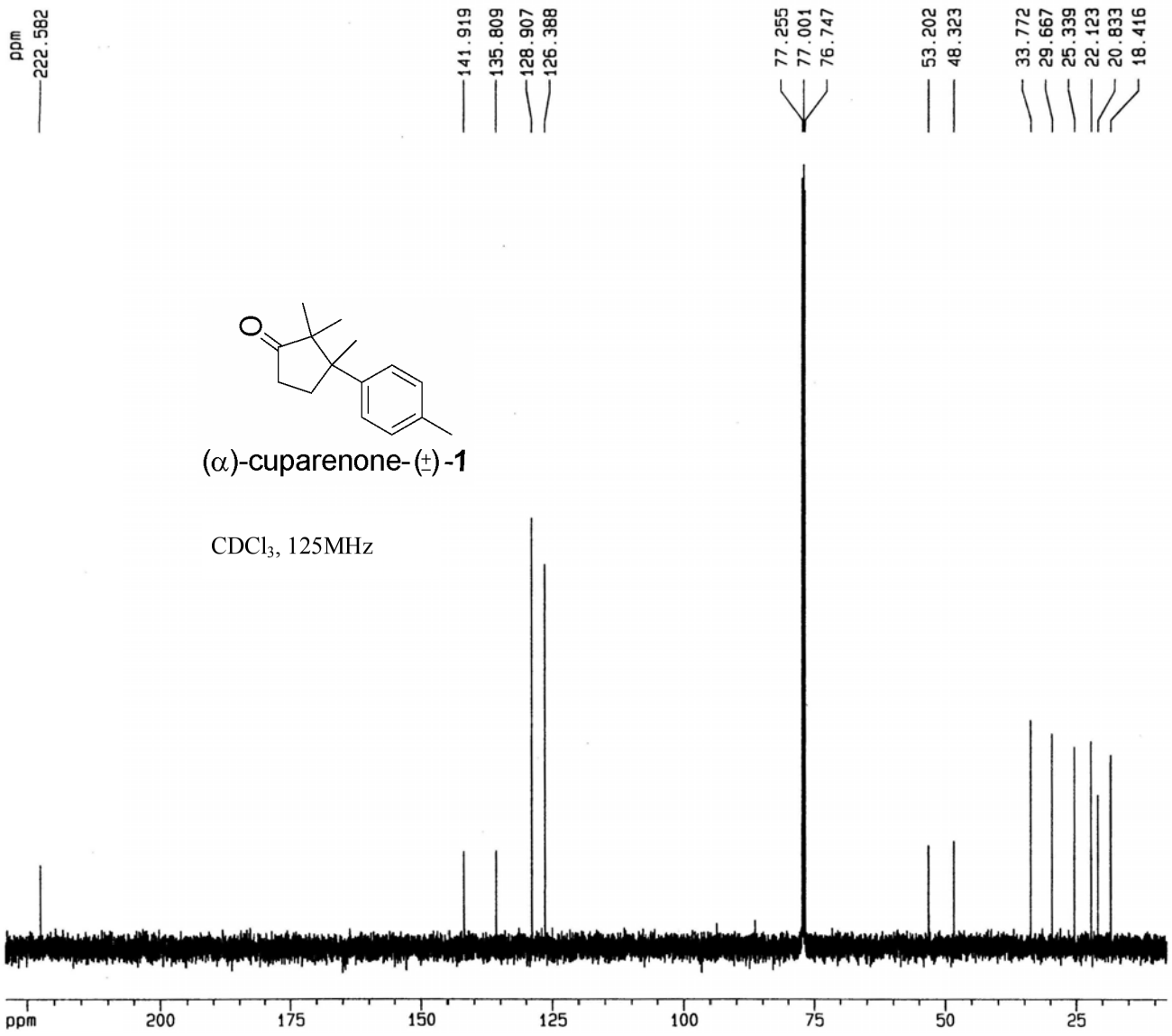

DMSO-d6, 100MHz
PPM
0
20
40
60
80
100
120
140
160
180
200

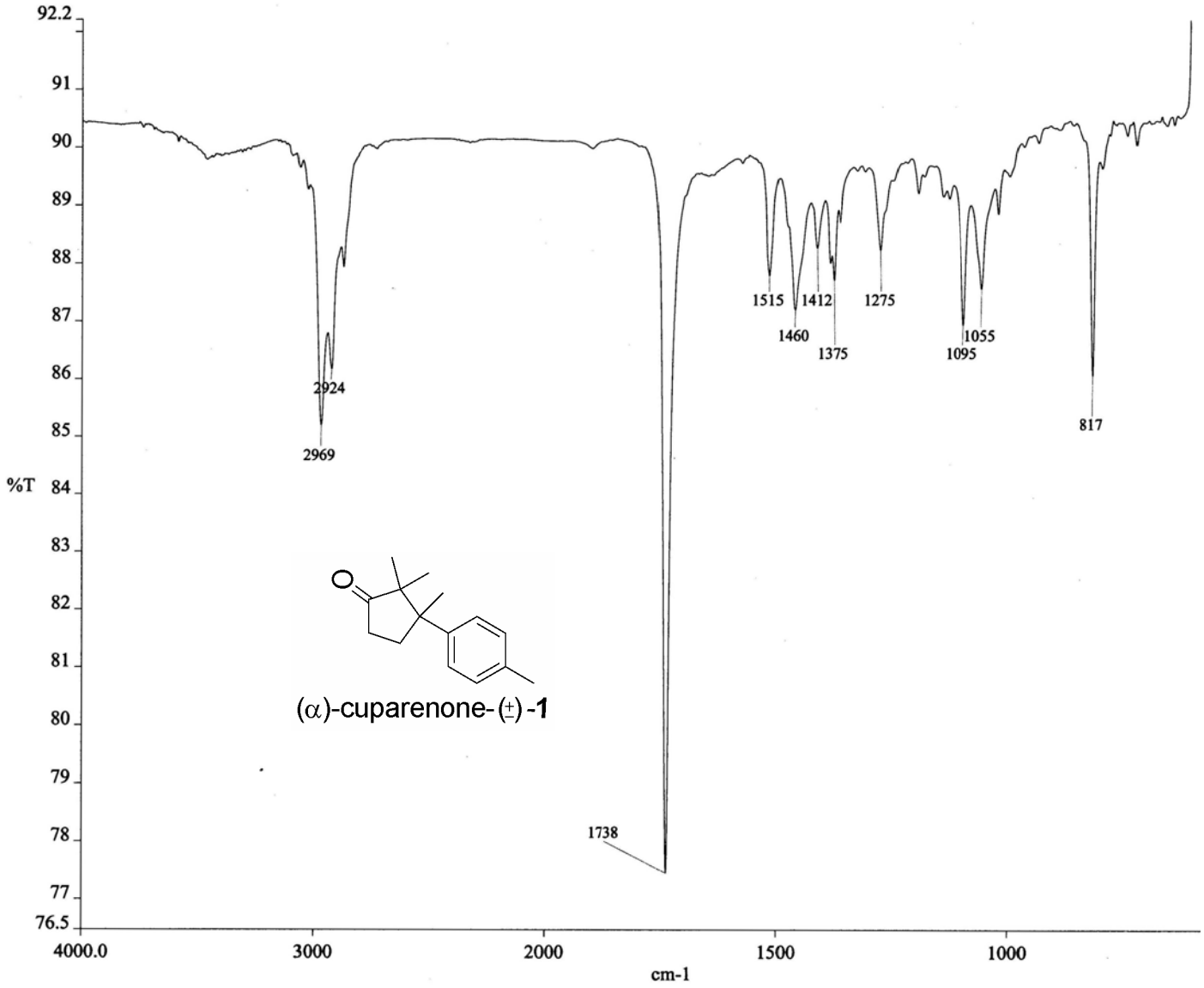

53.7
50
45
40
35
30
25
20
15
10
5
0
-3.8
%T
4000.0
3000
2000
1500
1000
450.0
cm-1
3479.92
3253.44
2995.85
2980.06
2924.02
2863.55
2630.74
1894.12
1786.38
1708.81
1654.29
1595.08
1512.81
1447.49
1382.75
1366.58
1335.33
1256.78
1245.24
1175.51
1145.45
1193.01
1093.94
1071.54
1035.10
1020.03
980.96
937.28
904.59
879.57
869.20
810.13
767.27
744.92
730.12
716.07
660.92
623.52
577.27
566.58
540.04
504.95
O
O

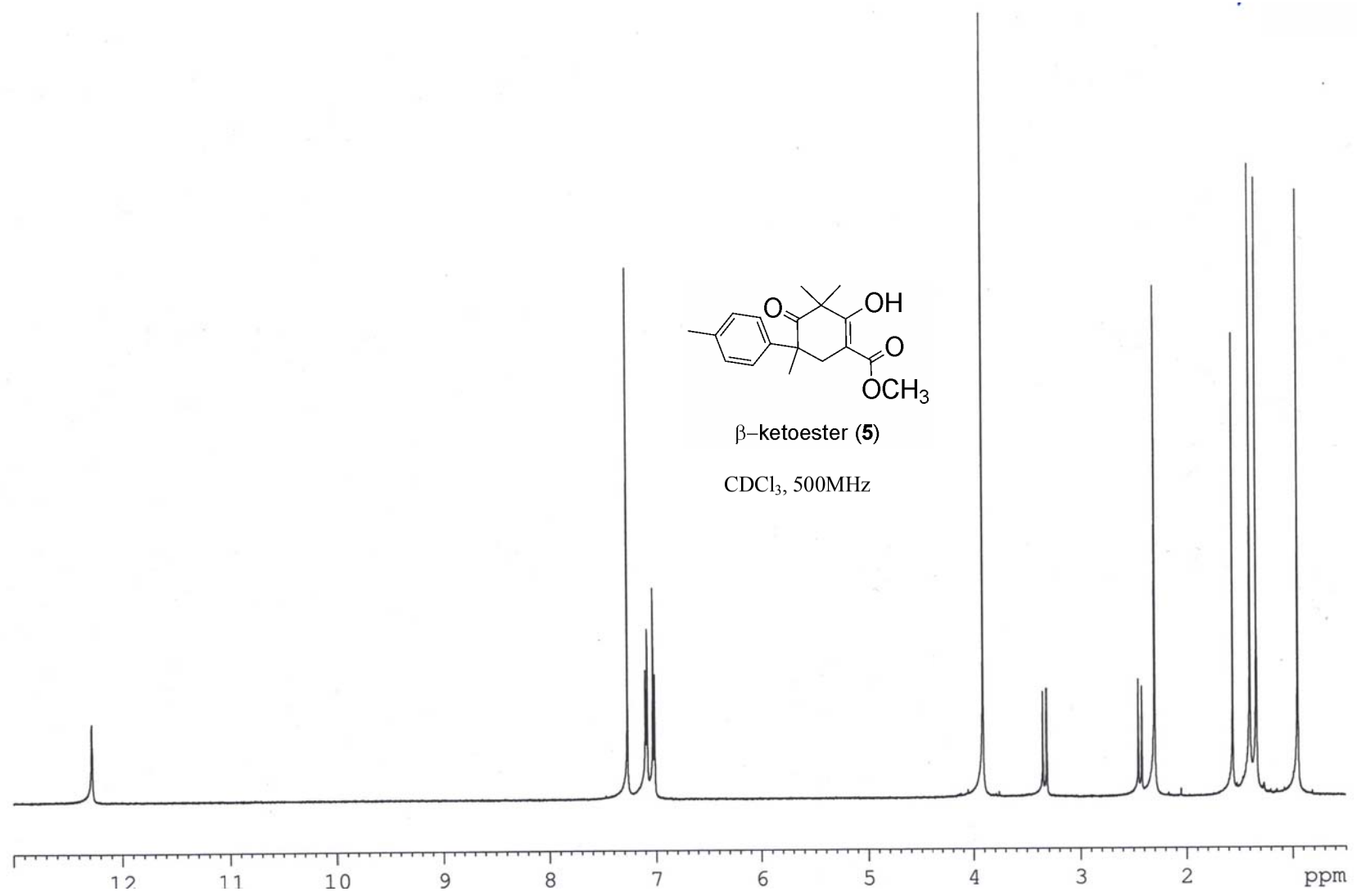

(±)-2
$CDCl_3$, 400MHz
ppm
Integral

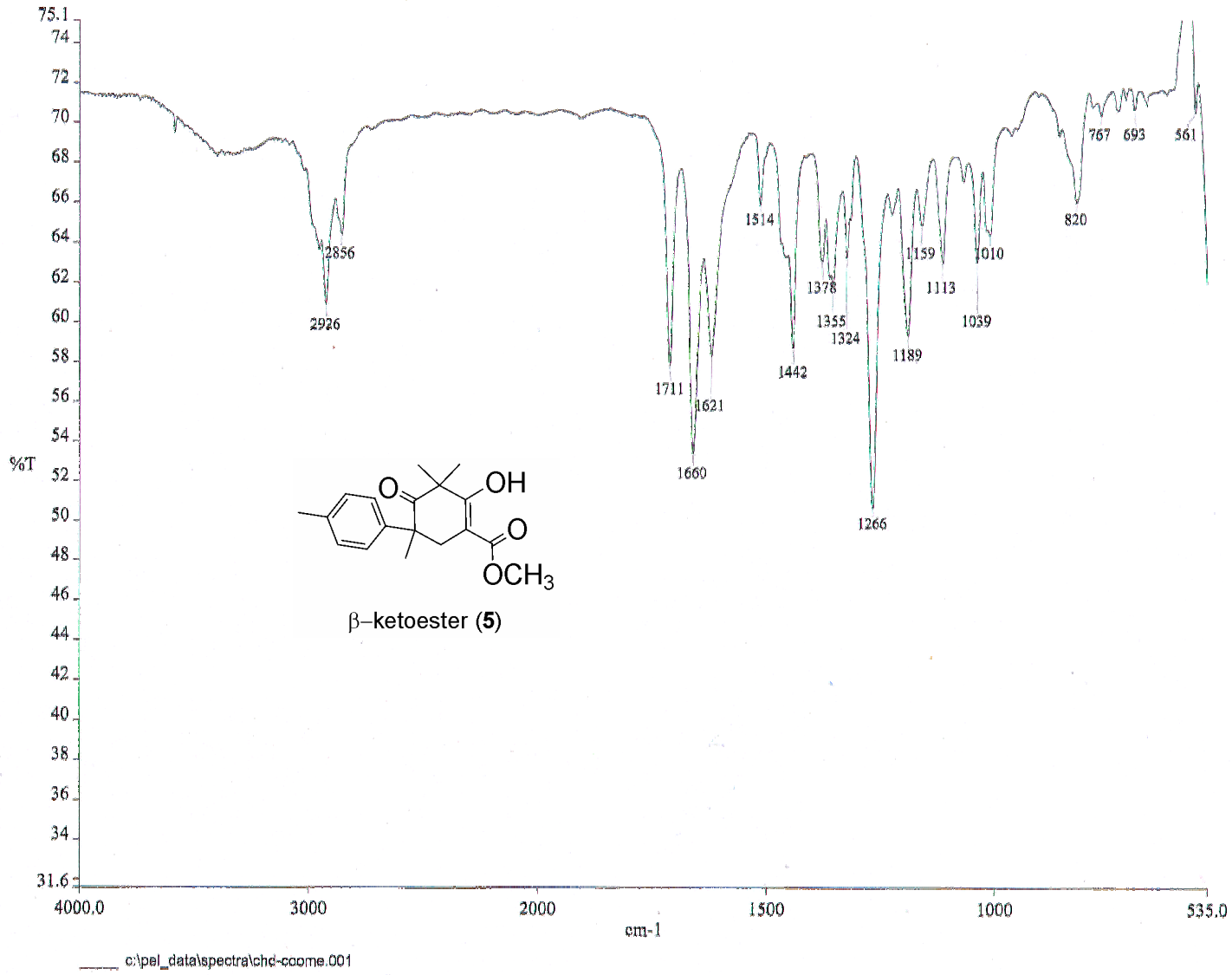

ppm
212.748
210.608
137.199
136.384
129.773
126.122
77.318
77.000
76.683
58.928
52.293
34.359
28.163
27.956
23.949
23.553
20.893
25
50
75
100
125
150
175
200
ppm
O
O
(±)-2
CDCl3, 100MHz


(α)-cuparenone-(±)-1
CDCl3, 500MHz
O
ppm
Integral
7.28786
7.27139
7.25981
7.17282
7.15655
2.68590
2.66130
2.51918
2.51573
2.50038
2.49681
2.46420
2.44611
2.44305
2.42501
2.34599
1.93962
1.93610
1.92169
1.91804
1.91438
1.91085
1.89617
1.89288
1.86092
1.84190
1.81573
0.81683
2.0008
2.0008
1.0029
1.0040
1.0002
3.0006

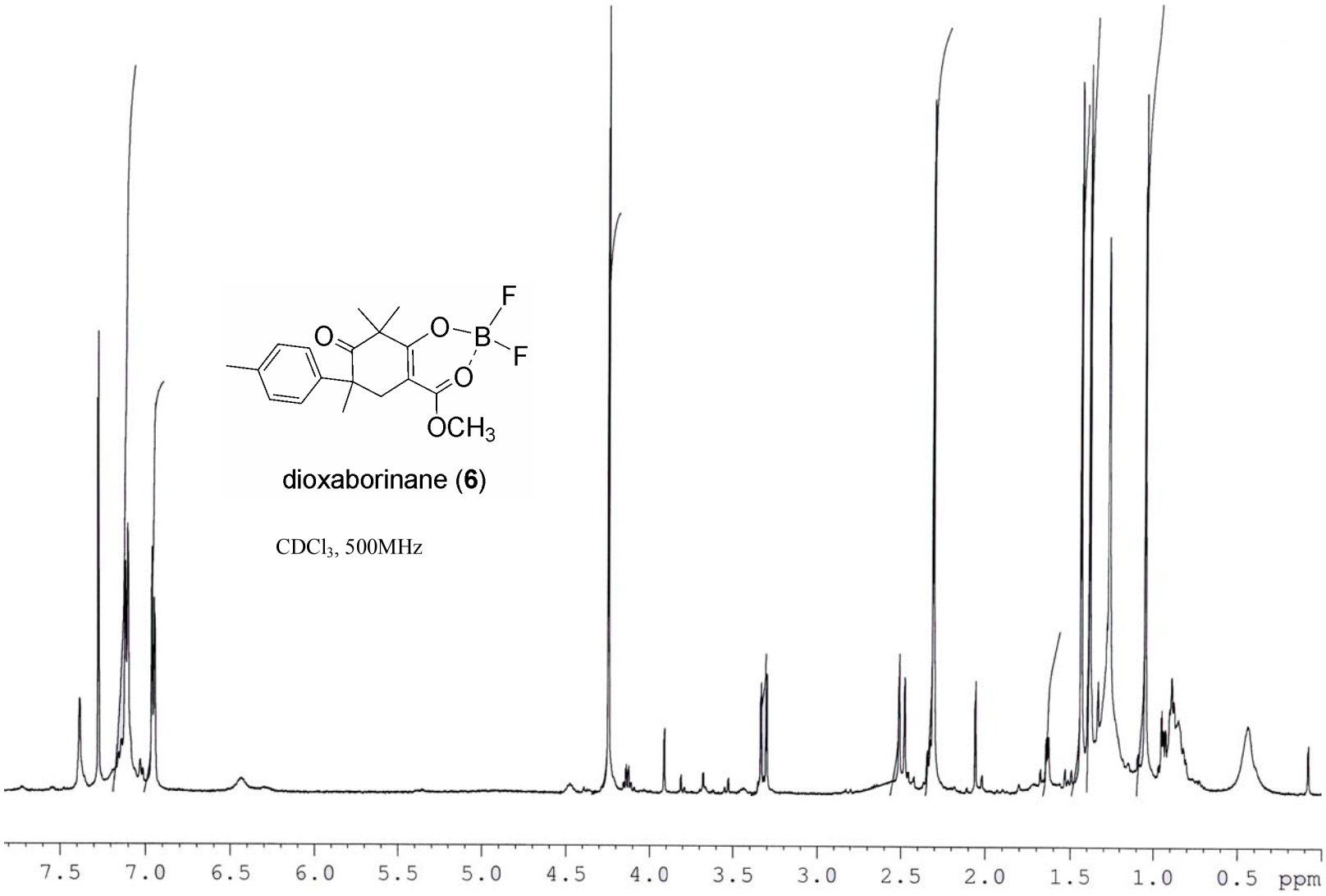

ppm
222.582
141.919
135.809
128.907
126.388
77.255
77.001
76.747
53.202
48.323
33.772
29.667
25.339
22.123
20.833
18.416
(α)-cuparenone-(±)-1
CDCl3, 125MHz
ppm
200
175
150
125
100
75
50
25


92.2
91
90
89
88
87
86
85
84
83
82
81
80
79
78
77
76.5
%T
4000.0
3000
2000
1500
1000
cm-1
2969
2924
1738
1515
1460
1412
1375
1275
1095
1055
817
(α)-cuparenone-(±)-1


O
OH
O
OCH3
β–ketoester (5)
CDCl3, 500MHz
12
11
10
9
8
7
6
5
4
3
2
ppm

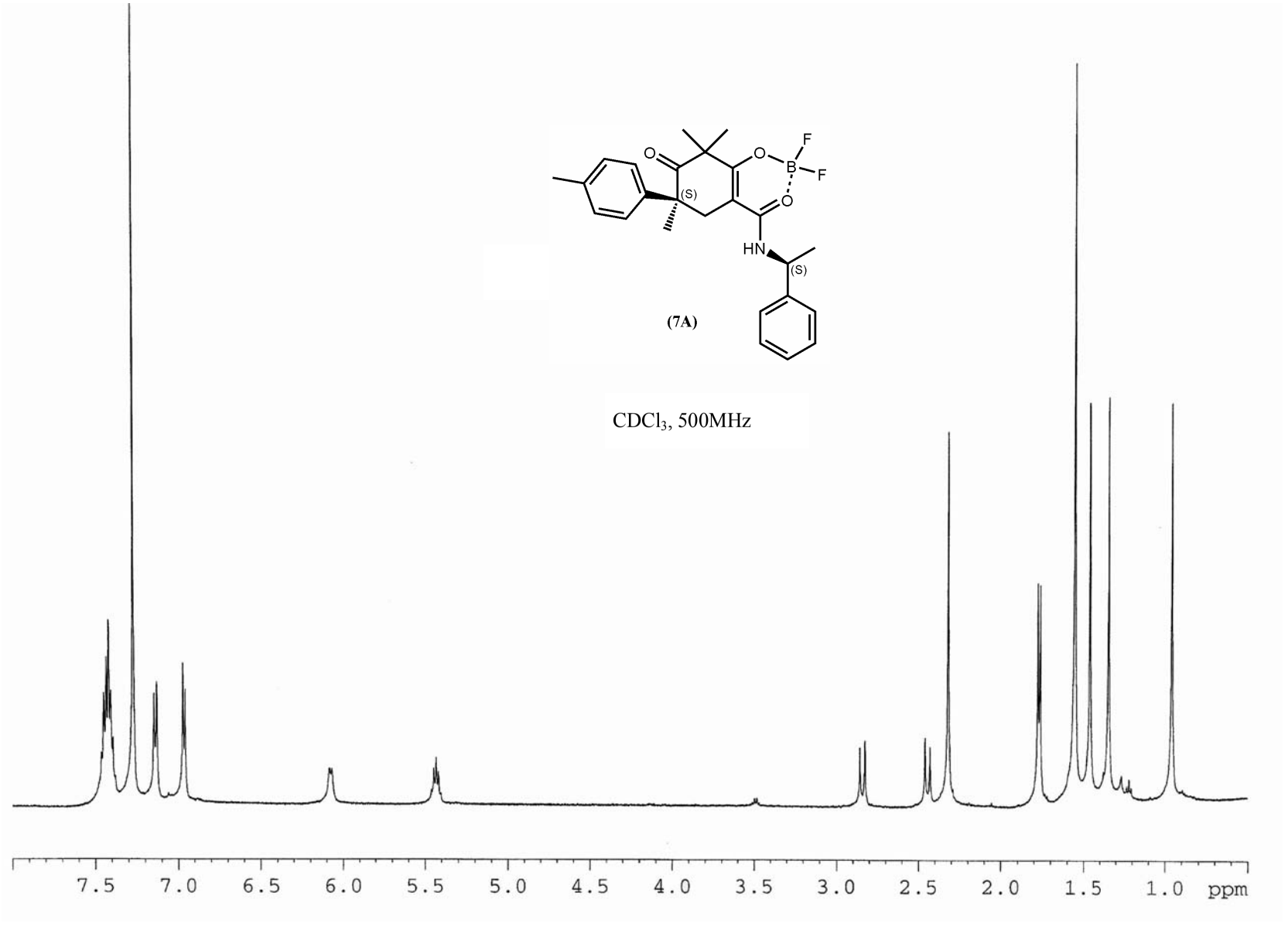


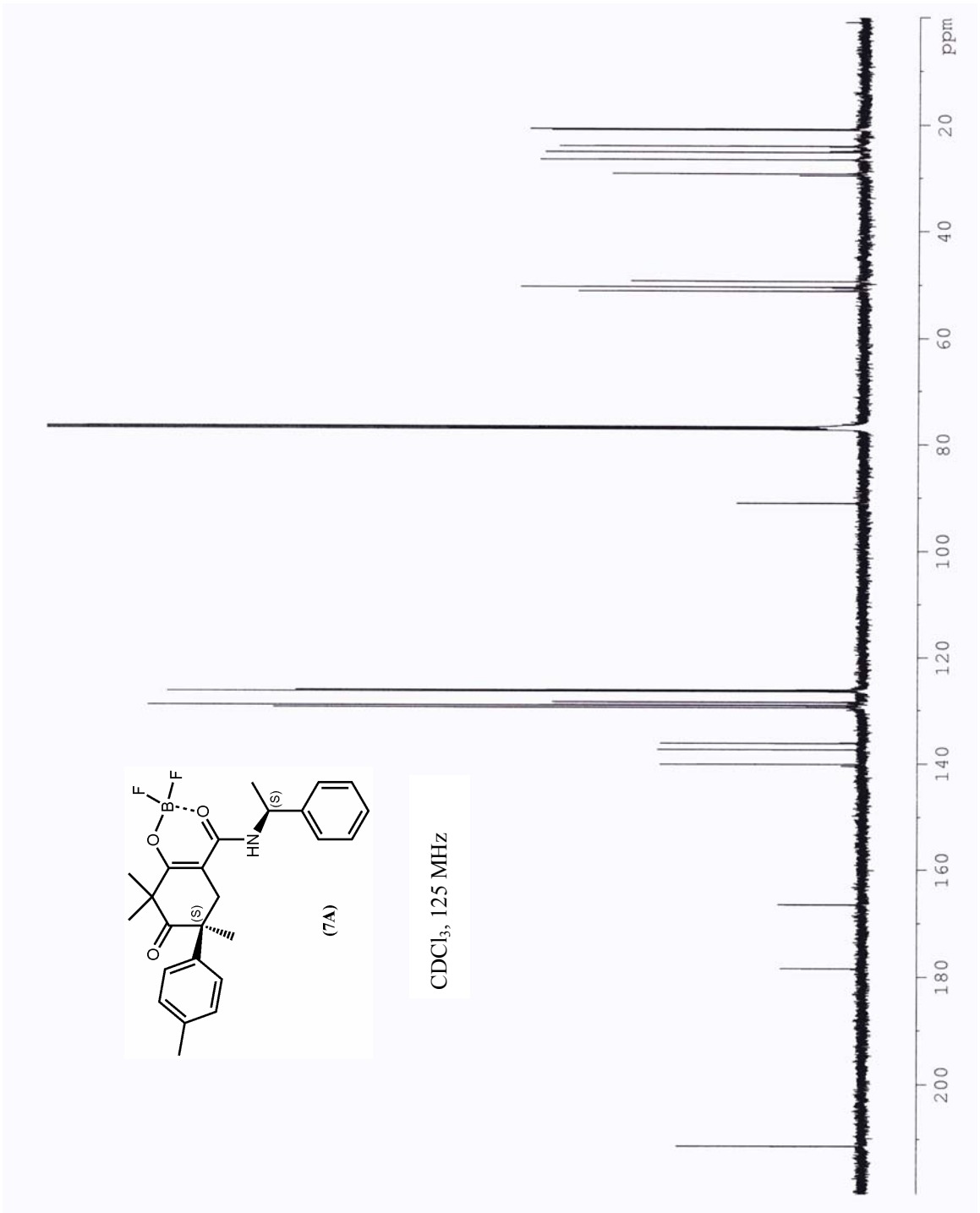
β–ketoester (**5**)

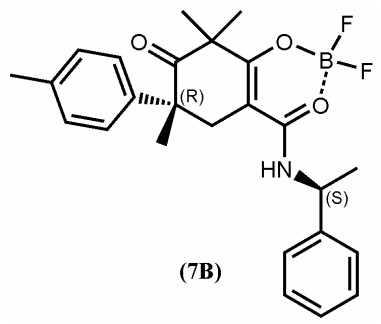


dioxaborinane (**6**)

$CDCl_3$, 500MHz

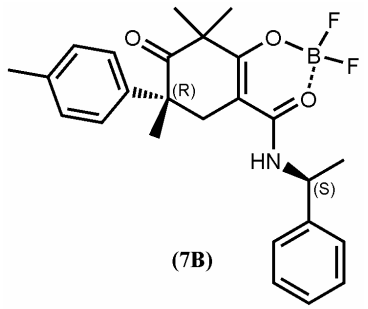

O
O
B
F
F
O
(S)
HN
(S)
(7A)
CDCl3, 500MHz
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm


F
B
F
O
O
O
HN
(S)
(S)
(7A)
CDCl3, 125 MHz
ppm
200
180
160
140
120
100
80
60
40
20



(7B)

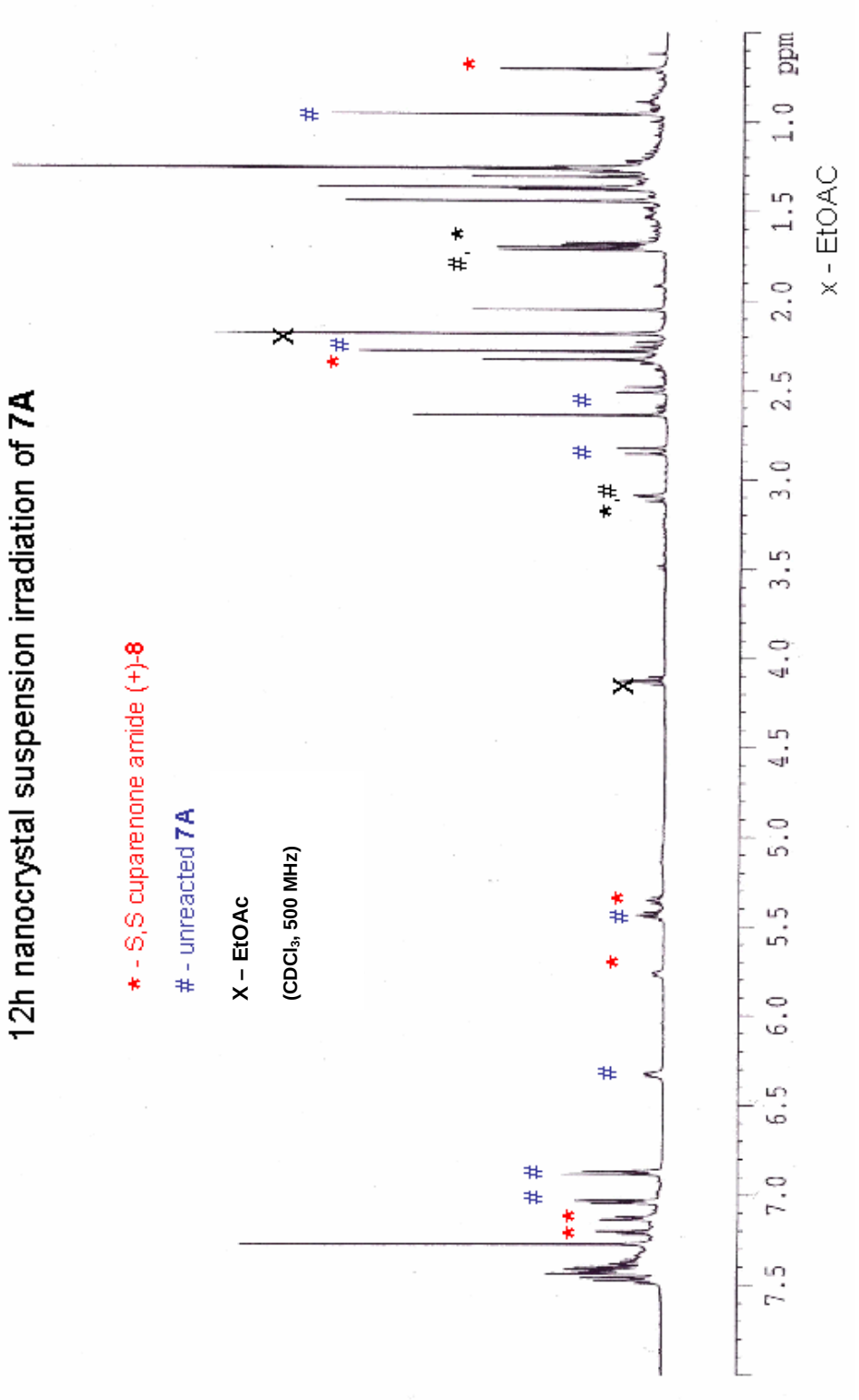
$CDCl_3$, 500MHz

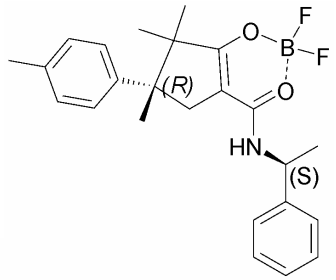


(7B)

$CDCl_3$, 125 MHz

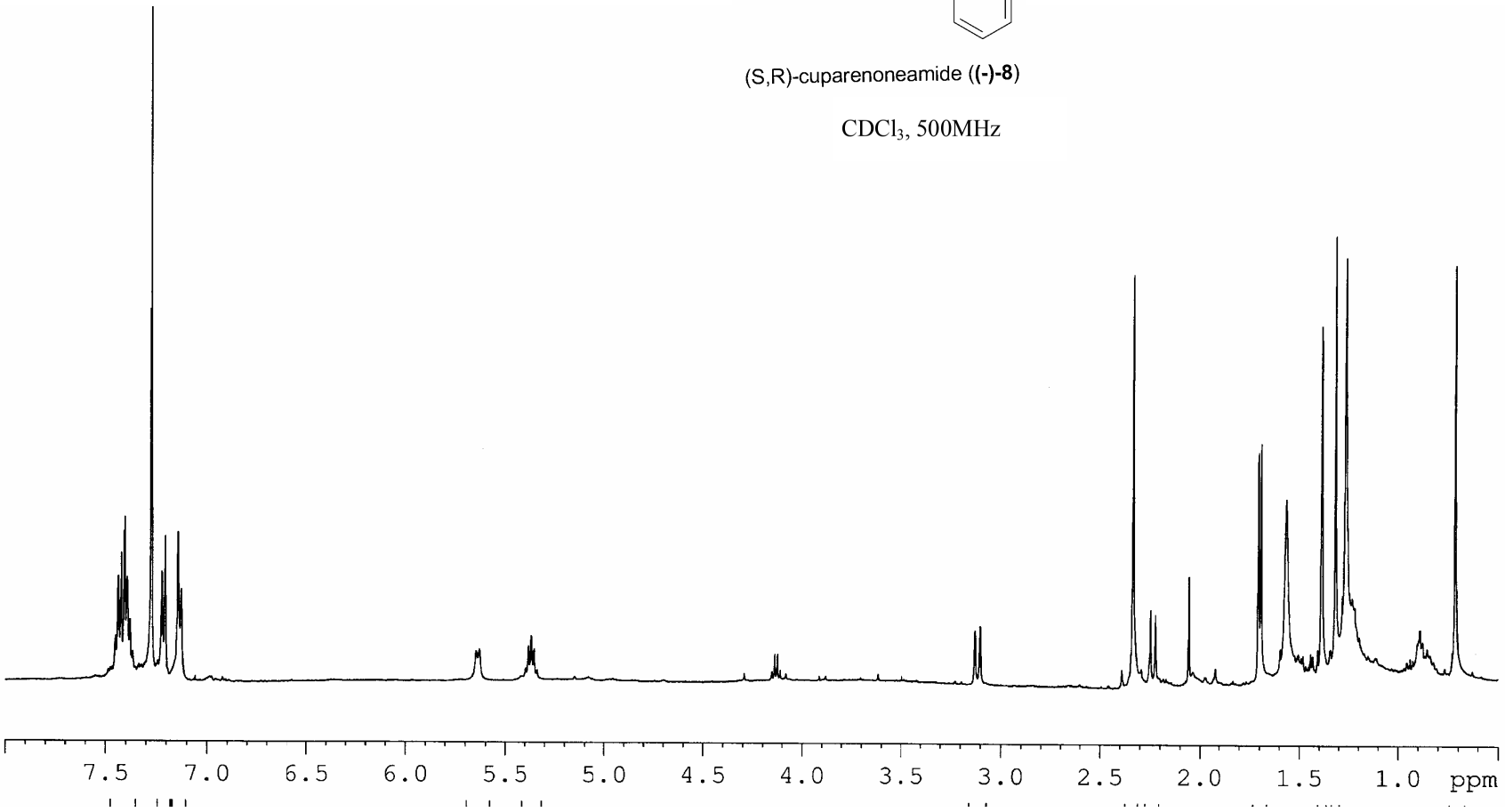
NMR Spectrum from suspension photolysis of (S,S)-(+)-7 showing the formation of (S,S)-(+)-8.

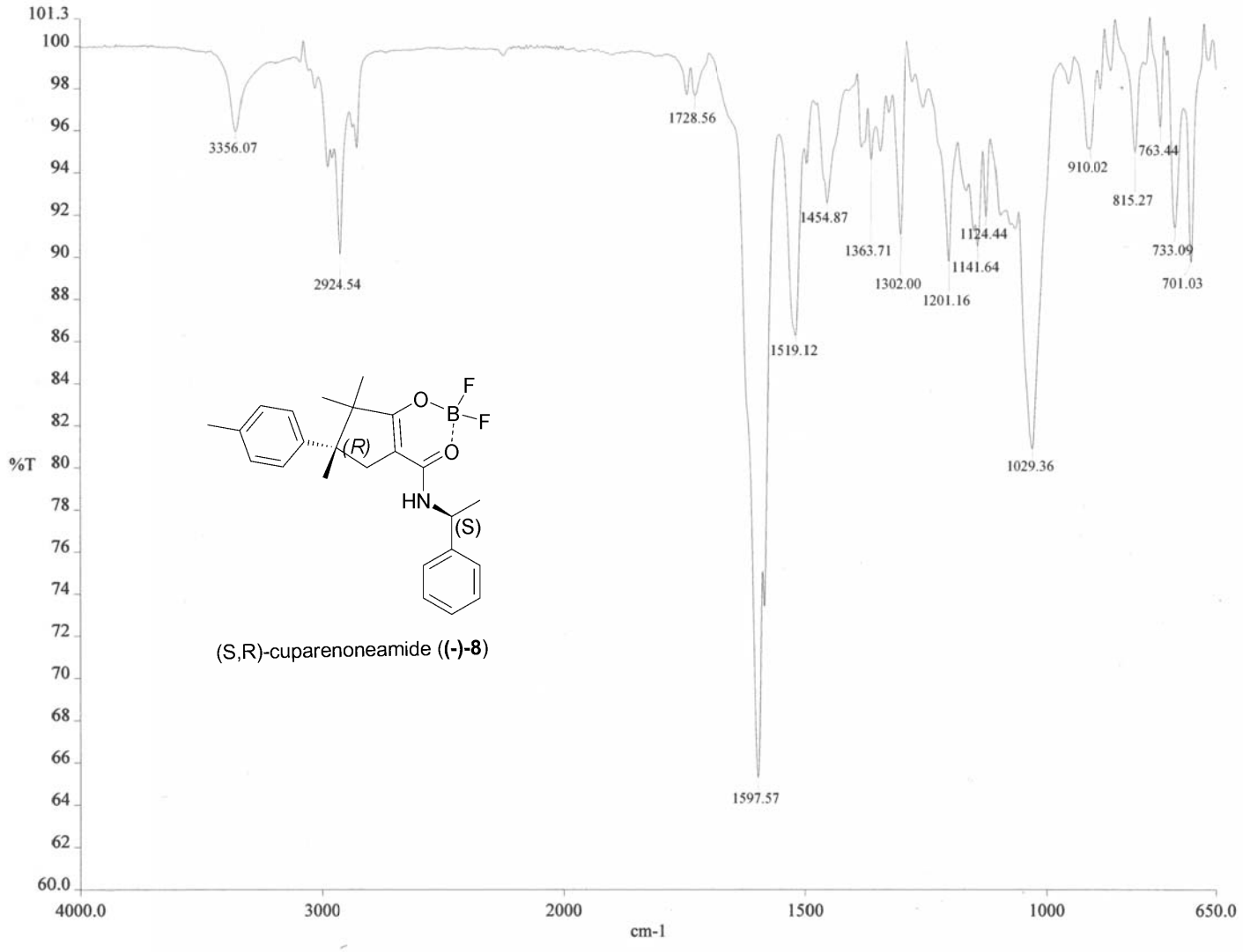




(S,R)-cuparenoneamide (**(-)-8**)

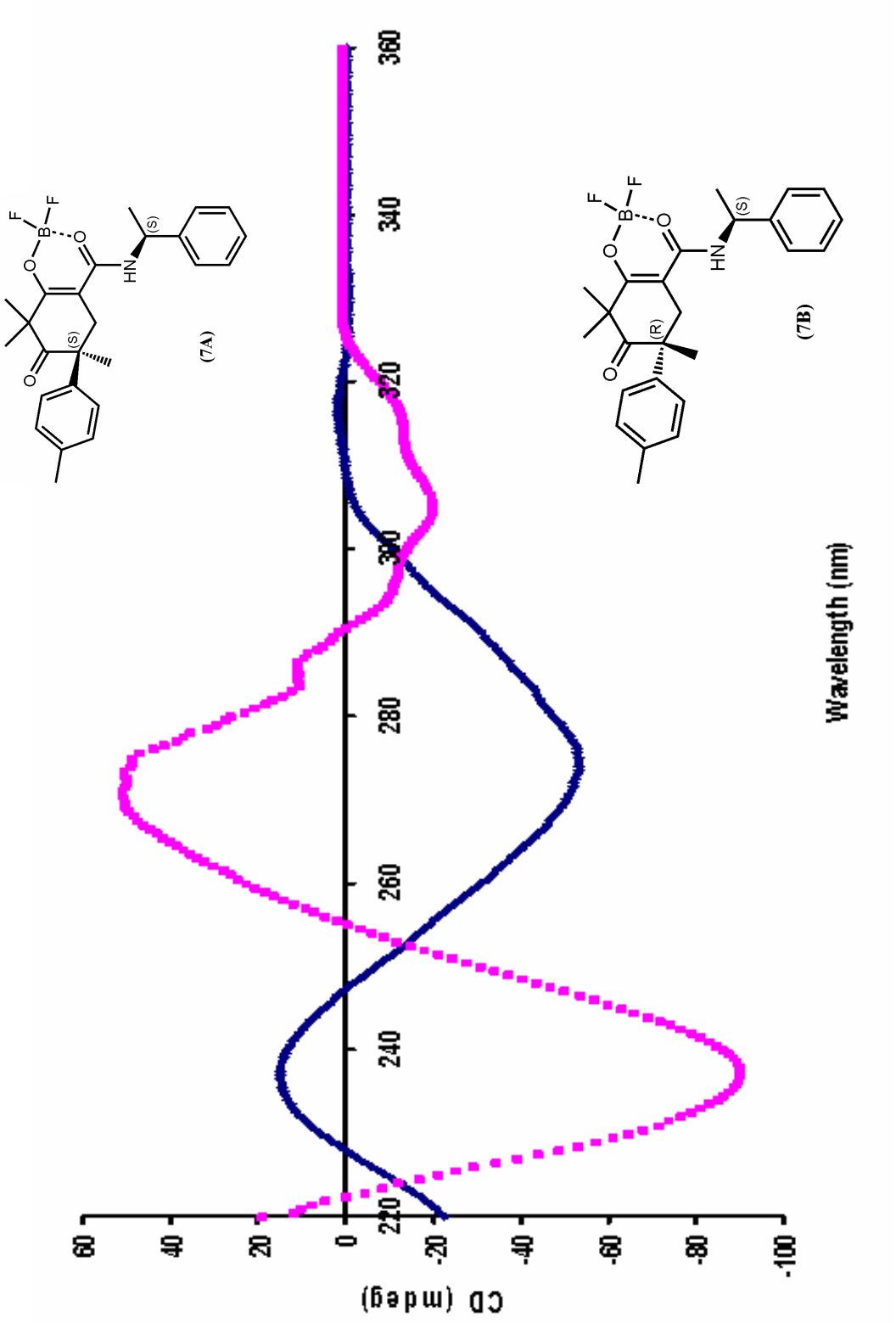
$CDCl_3$, 500MHz



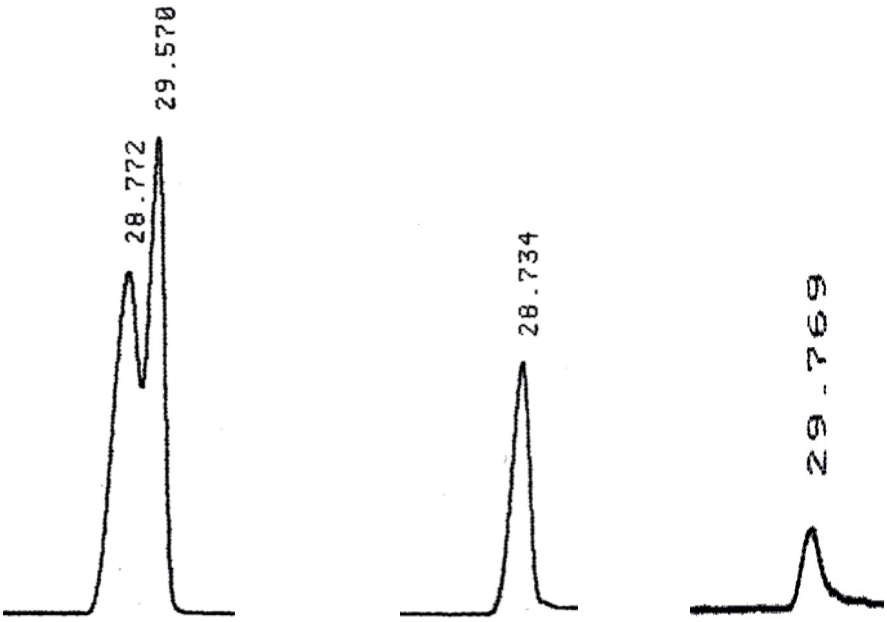


(S,R)-cuparenoneamide (**(-)-8**)

Circular dichroism spectra of (S,S)-(+)-7 and (S,R)-(-)-7 in CH_2Cl_2.



Analysis of the racemic and chiral cyclohexadienone precursors via chiral GC



(a) (b) (c)

(a): (±)-**2**

(b) (-)-**2** obtained *via* hydrolysis of (+)-7A*

(c) (+)-**2** obtained *via* hydrolysis of (-)-7B *

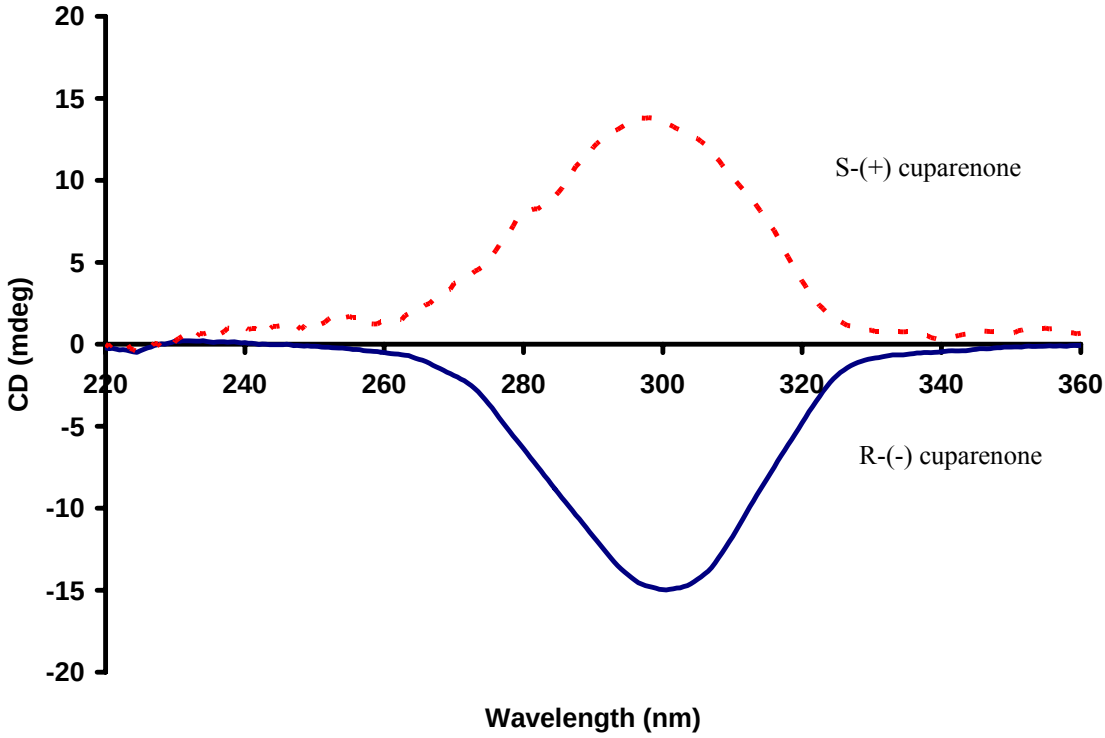
There is a change in the sign of optical rotation upon removal of the chiral auxiliary to obtain the optically pure diketone. However, the optical rotation of the two natural products is the same as that of their corresponding ketoamide precursors.

SUPELCO-Chiral GC column: β-DEX-120, 30 m x 0.2 mm; film thickness 0.25μm.

GC Conditions: Injector temperature, 250 °C; Detector temperature, 280°C

Program: Initial Temperature, 145 °C; Initial time, 33 min; Ramp, 10 °C/min; Final temperature: 200 °C; Final time: 10 min

Circular dichroism spectra of (S)-(+)-α-cuparenone and (R)-(-)-α-cuparenone in CH_2Cl_2.



X. References:

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