Supporting Information

Unprecedented Effects of Achiral Oxazolidinones on Enantioselective Radical-Mediated Conjugate Additions Using a Chiral Zinc Triflate

Masatoshi Murakata,* Hideyuki Tsutsui, and Osamu Hoshino*

Faculty of Pharmaceutical Sciences, Science University of Tokyo, Shinjuku-ku, Tokyo 162-0826, Japan

General.

All melting points were measured on a Yanagimoto (hot plate) melting point apparatus and are uncorrected. IR spectra were performed with a Horiba FT–210 spectrophotometer or a Jasco FT/IR-410 spectrophotometer. ^{1}H NMR (400 MHz or 500 MHz) and ^{13}C NMR (100 MHz or 125 MHz) spectra were recorded with a JEOL JNM-LA400 spectrometer or a JEOL JNM-LA500 spectrometer in $CDCl_3$ solution using tetramethylsilane as an internal standard, unless otherwise noted. Mass spectra were measured on a JEOL JMS-SX102A spectrometer. Specific rotation was measured on a JASCO P-1030 digital polarimeter. The enantiomeric excess (ee) of **4**–**8** was determined by HPLC analysis using chiral columns (DAICEL). Column chromatography was performed on silica gel. Thin-layer chromatography was carried out on precoated (0.2 mm) Merck silica gel F-254 plates.

^{1}H spectral data for the chiral zinc complexes: chemical shifts are referenced to methylene chloride. $Zn(OTf)_2$ was obtained from Aldrich Chemical Co. and used without further purification. CD_2Cl_2 was distilled under argon from CaH_2 prior to use. Solutions for the measurements were prepared under argon atmosphere. [**2a**] = [**12**] = [$Zn(OTf)_2$] = [**3**] = 50 mM, which is identical to the concentration of a solution used in the present asymmetric reactions.

The preparations of 1–3, 1a, 2a, and 9–12

3-Cinnamoyl-2-oxazolidinone (**1**) was prepared according to the method described in the literature.[1]

Compounds **1a**, **9**, **10** and **11** were obtained from commercial sources and were used without further purification.

4,4-Diphenyl-2-oxazolidinone (2a).

To a suspension of 92% $LiAlH_4$ (3.63 g, 88 mmol) in THF (80 mL) was added diphenylglycine (10 g, 44.1 mmol) at 0 ˚C, and the mixture was refluxed for 4 h. After successive addition of water (3.6 mL), 15% NaOH (3.6 mL), and water (10.8 mL), the mixture was dried over K_2CO_3 and filtered. The solvent was removed under reduced pressure, and the crude product was rinsed with Et_2O to give diphenylglycinol (8.5 g, 91%): mp 126–129 ˚C; ^{1}H NMR δ 2.25 (3H, br), 4.10 (2H, s), 7.20–7.38 (10H, m); ^{13}C NMR δ 62.4, 70.0, 126.7, 126.9, 128.3, 145.9; IR (KBr) 3350, 3300, 3150, 2850, 1610, 1500, 1450 cm^{-1}; MS (FAB+) *m/z* 214 (M^++H); HRMS (FAB+) calcd for $C_{14}H_{16}NO$ (M^++H) 214.1232 (M^+), found 214.1234 (M^+). To a solution of this product (diphenylglycinol: 6.0 g, 28.1 mmol) in CH_2Cl_2 (150 mL) was added triphosgene (2.8 g, 9.4 mmol) and Et_3N (5.7 g, 56.4 mmol) at 0 ˚C, and the resulting mixture was stirred for 12 h at rt. The mixture was washed successively with 0.5N HCl, water, saturated aqueous $NaHCO_3$ and brine, and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the crude product was rinsed with Et_2O to give **2a** (6.0 g, 90%) as colorless crystals.[2]

4,4-Diphenyl-2-oxazolidinone (2a). Colorless needles; mp 178–179 ˚C (benzene–hexane). ^{1}H NMR (CD_2Cl_2; at rt) δ 4.88 (2H, s), 7.24–7.40 (10H, m), 7.54 (1H, brs). ^{1}H NMR (CD_2Cl_2; at –30 ˚C) δ 4.89 (2H, s), 7.26–7.38 (10H, m), 8.14 (1H, brs). ^{13}C NMR (CD_2Cl_2; at rt) δ 67.0, 77.3, 126.3, 128.3, 129.2, 143.5, 159.5. ^{13}C NMR (CD_2Cl_2; –30 ˚C) δ 66.7, 77.0, 125.9, 128.0, 128.9, 142.9, 159.6. IR (nujol) 3209, 1759, 1470, 1396, 1286, 1245 cm^{-1}. MS *m/z* 239 (M^+); HRMS calcd for $C_{15}H_{13}NO_2$ 239.0945 (M^+), found 239.0951 (M^+). Anal. Calcd for $C_{15}H_{13}NO_2$: C, 75.30; H, 5.48. Found: C, 75.26; H, 5.46.

3-Cinnamoyl-4,4-diphenyl-2-oxazolidinone (2).

Under argon atmosphere, to a solution of 4,4-diphenyl-2-oxazolidinone **2a** (3.0 g, 12.6 mmol) in THF (60 mL) was added a solution of BuLi in hexane (1.5 N, 12.6 mmol) at –78 ˚C, and the mixture was stirred for 1 h at the same temperature. A solution of cinnamoyl chloride (2.1 g, 12.6 mmol) in THF (10 mL) was added at the same temperature, and the reaction mixture was stirred for 2 h. The whole was warmed to rt, and was stirred for 12 h. After addition of aqueous NH_4Cl, the mixture was extracted with AcOEt (100 mL x 2). The combined organic extracts were washed with brine, and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the crude product was purified by column chromatography (hexane–AcOEt) to afford **2** (4.0 g, 86%) as colorless crystals.

3-Cinnamoyl-4,4-diphenyl-2-oxazolidinone (2). Colorless needles; mp 144–145 ˚C (benzene–hexane). ^{1}H NMR (CD_2Cl_2) δ 4.82 (2H, s), 7.35–7.44 (13H, m), 7.59–7.62 (2H, m), 7.69 (1H, d, *J*=15.8 Hz), 7.83 (1H, d, *J*=15.8 Hz). ^{13}C NMR (CD_2Cl_2) δ 71.8, 79.1, 118.9, 128.3, 128.5, 128.7, 128.8, 129.3, 131.0, 135.0, 139.7, 146.1, 154.4, 165.3. IR (nujol) 3026, 1767, 1682,

1614, 1495, 1342, 1209 cm^{-1}. MS *m/z* 369 (M^+); HRMS calcd for $C_{24}H_{19}NO_3$ 369.1356 (M^+), found 369.1355 (M^+). Anal. Calcd for $C_{24}H_{19}NO_3$: C, 78.03; H, 5.18. Found: C, 78.20; H, 5.18.

(*S*,*S*)-2,2'-(1-Ethylpropylidene)bis(4-phenyl-4,5-dihydrooxazole) (3).

(*S*,*S*)-2,2'-(1-Ethylpropylidene)bis(4-phenyl-4,5-dihydrooxazole) (**3**) was prepared by a method similar to that described in the literature.[3]

(*S*,*S*)-2,2'-(1-Ethylpropylidene)bis(4-phenyl-4,5-dihydrooxazole) (3). Colorless needles; mp 63–64 ˚C (Et_2O–petroleum ether). $[\alpha]^{25}_D$ –180.4 (*c* 1.1, EtOH). ^{1}H NMR δ 0.96 (6H, t, *J*=14.1), 2.08–2.23 (4H, m), 4.12 (2H, t, *J*=8.3), 4.66 (2H, dd, *J*=8.3, 10.0 Hz), 5.26 (2H, dd, J=8.3, 10.0 Hz). ^{13}C NMR δ 8.5, 25.6, 47.0, 69.6, 75.0, 126.7, 127.5, 128.7, 142.4, 168.9. IR (nujol) 2972, 1651, 1454, 1352, 1223 cm^{-1}. MS *m/z* 362 (M^+); HRMS calcd for $C_{23}H_{26}N_2O_2$ 326.1993 (M^+), found 326.2016 (M^+). Anal. Calcd for $C_{23}H_{26}N_2O_2$: C, 76.21; H, 7.23. Found: C, 76.30; H, 7.20.

***N*-Methyl-4,4-diphenyl-2-oxazolidinone (12).**

To a suspension of 60% NaH (380 mg, 9.5 mmol) in DMF (20 mL) was added a solution of 4,4-diphenyl-2-oxazolidinone **2a** (1.5 g, 6.3 mmol) in DMF (10 mL) at 0 ˚C, and the mixture was stirred for 30 min. The resulting mixture was warmed to rt, and was stirred for 30 min. MeI (1.8 g, 12.7 mmol) was added at 0 ˚C, and the whole was warmed to rt, and was stirred for 3 h. After addition of water (50 mL), the mixture was extracted with AcOEt–benzene (2:1, 150 mL). The organic extract was washed successively with water (50 mL x 2) and brine, and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the crude product was purified by column chromatography (hexane–AcOEt) to afford **12** (1.5 g, 94%) as colorless crystals.

***N*-Methyl-4,4-diphenyl-2-oxazolidinone (12).** Colorless needles; mp 125–126 ˚C (Et_2O–hexane). ^{1}H NMR (CD_2Cl_2; at rt) δ 2.61 (3H, s), 4.65 (2H, s), 7.22–7.28 (4H, m), 7.36–7.46 (6H, m). ^{1}H NMR (CD_2Cl_2; at –30 ˚C) δ 2.58 (3H, s), 4.63 (2H, s), 7.22–7.26 (4H, m), 7.35–7.44 (6H, m). ^{13}C NMR δ 28.2, 70.5, 76.2, 127.4, 128.3, 128.8, 140.0, 158.4 . IR (nujol) 1743, 1485, 1448, 1359, 1344, 1247 cm^{-1}. MS *m/z* 253 (M^+); HRMS calcd for $C_{16}H_{15}NO_2$ 253.1101 (M^+), found 253.1101 (M^+).

The enantioselective radical-mediated conjugate additions

$Zn(OTf)_2$ was obtained from commercial sources (Aldrich Chemical Co.) and was used without further purification.

The ees of **4** and **6**–**8** were determined directly by HPLC using a chiral column.

The ee of **5** was determined by a chiral HPLC analysis of benzyl 4,4-dimethyl-3-phenylpentanoate **14**, which was obtained by hydrolysis of **5** followed by esterification.

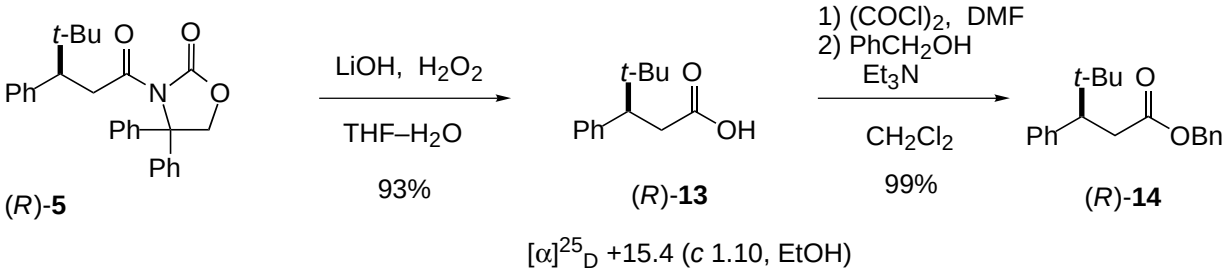
The stoichiometric enantioselective conjugate additions: Typical procedure

A mixture of 98% $Zn(OTf)_2$ (74.2 mg, 0.2 mmol), **3** (72.4 mg, 0.2 mmol) and **2a** (47.8 mg, 0.2 mmol) in CH_2Cl_2 (2 mL) was stirred for 1 h at rt to become a clear solution. The resulting clear solution was cooled to –78 ˚C. A solution of **2** (73.8 mg, 0.2 mmol) in CH_2Cl_2 (2 mL) was added, and the mixture was stirred for 30 min at –78 ˚C. *tert*-BuI (48 μL, 0.4 mmol), Bu_3SnH (111μL, 0.4 mmol), and a solution of triethylborane in hexane (1 N: 0.4 mL, 0.4 mmol) were added successively, and the mixture was allowed to stand for 12 h at the same temperature. After addition of AcOH (0.4 mL) at –78 ˚C, the mixture was stirred for 1 h. H_2O was added, and the mixture was extracted with CH_2Cl_2 (20 mL x 2). The organic layer was washed with saturated aqueous $NaHCO_3$ and brine successively, and dried over $MgSO_4$. After filtration, the solvent was removed under reduced pressure. The residue was taken up in MeCN. The mixture was washed with hexane. Concentration followed by purification through column chromatography (hexane–AcOEt) gave (*R*)-**5** (82.0 mg, 96%).

The ee was determined by HPLC analysis of **14** obtained from the hydrolysis of **5** followed by esterification (Scheme 1). The absolute configuration was determined by chemical correlation with (*S*)-4,4-dimethyl-3-phenylpentanoic acid **13**. To a solution of (*R*)-**5** (76.8 mg, 0.18 mmol) and LiOH (9.6 mg, 0.4 mmol) in THF–H_2O (3:1, 4 mL) was added 31% H_2O_2 (219.4 mg, 2 mmol) at 0 ˚C. The mixture was stirred for 12 h at rt. After addition of aqueous Na_2SO_3, the resulting mixture was stirred for 30 min at rt. After addition of benzene (20 mL), the layers were then separated. The aqueous phase was washed with benzene (20 mL), and then acidified with aqueous 0.5 N HCl. The resulting mixture was extracted with CH_2Cl_2 (20 mL x 2). The organic layer was washed with brine, and dried over $MgSO_4$. After filtration, the solvent was removed under reduced pressure to give (*R*)-**13** (34.5 mg, 93%). To a solution of **13** (33.0 mg, 0.16 mmol) in CH_2Cl_2 (3 mL) were added $(COCl)_2$ (25.4 mg, 0.2 mmol) and a catalytic amount of DMF at 0 ˚C. The whole was stirred for 30 min at 0 ˚C. The solvent was removed under reduced pressure, and the crude product was dissolved in CH_2Cl_2 (2 mL). This solution was added to a solution of BnOH (19.5 mg, 0.18 mmol) and Et_3N (20.2 mg, 0.2 mmol) in CH_2Cl_2 (1 mL) at 0 ˚C. The whole was stirred for 1 h at rt. After addition of saturated aqueous $NaHCO_3$, the mixture was extracted with CH_2Cl_2 (20 mL x 2). The organic layer was washed with brine, and

dried over $MgSO_4$. Concentration followed by purification through preparative thin-layer chromatography (hexane–AcOEt = 3:1) gave (*R*)-**14** (46.9 mg, 99%).

Scheme 1



(*R*)-**5** (*R*)-**13** (*R*)-**14**

$[\alpha]^{25}_D$ +15.4 (*c* 1.10, EtOH)

(*S*)-**13**: Imajo, S.; Kuritani, H.; Shingu, K.; Nakagawa, M. *J. Org. Chem.* **1979**, *44*, 3587–3589.

(*R*)-3-(4,4-Dimethyl-3-phenylpentanoyl)-4,4-diphenyl-2-oxazolidinone (5). Colorless crystals; mp 110–115 ˚C. $[\alpha]^{26}_D$ +12.8 (*c* 1.20, $CHCl_3$). ^{1}H NMR δ 0.89 (9H, s), 2.99 (1H, dd, *J*=3.7, 16.0 Hz), 3.08 (1H, dd, *J*=3.7, 12.0 Hz), 3.98 (1H, dd, *J*=12.0, 16.0 Hz), 4.39 (1H, d, *J*=9.0 Hz), 4.71 (1H, d, *J*=9.0 Hz), 6.58–6.60 (2H, m), 7.03–7.08 (2H, m), 7.15–7.35 (11H, m). ^{13}C NMR δ 28.0, 33.7, 36.8, 51.9, 71.2, 77.7, 126.4, 126.9, 127.6, 127.8, 128.0, 128.17, 128.21, 128.3, 138.6, 139.6, 141.6, 154.0, 172.3, due to overlap (CH x 2), not all carbons resonances were visible. IR (nujol) 2951, 2924, 2854, 1768, 1713, 1601, 1462, 1377 cm^{-1}. MS *m/z* 427 (M^+); HRMS calcd for $C_{28}H_{29}NO_3$ 427.2148 (M^+), found 427.2132 (M^+).

(*R*)-4,4-Dimethyl-3-phenylpentanoic acid (13) Colorless solid. $[\alpha]^{25}_D$ +15.4 (*c* 1.10, EtOH). ^{1}H NMR δ 0.87 (9H, s), 2.71 (1H, dd, *J*=11.0, 15.6 Hz), 2.79 (1H, dd, *J*=4.3, 15.6 Hz), 2.92 (1H, dd, *J*=4.3, 11.0 Hz), 7.12–7.26 (5H, m). ^{13}C NMR δ 28.0, 33.8, 35.5, 51.9, 126.5, 127.7, 129.4, 141.4, 178.7. IR (nujol) 3587–2364, 2954, 2925, 2854, 1697, 1601 cm^{-1}. MS *m/z* 206 (M^+); HRMS calcd for $C_{13}H_{18}O_2$ (M^+) 206.1306, found 206.1309 (M^+).

(*S*)-**13**: Imajo, S.; Kuritani, H.; Shingu, K.; Nakagawa, M. *J. Org. Chem.* **1979**, *44*, 3587–3589.

(*R*)-Benzyl 4,4-Dimethyl-3-phenylpentanoate (14) Colorless semisolid. $[\alpha]^{26}_D$ +5.0 (*c* 0.86, $CHCl_3$); 88% ee [HPLC: Chiralcel OJ, hexane:2-propanol = 50:1, flow rate 1 mL/min, *Rt* 21 min for (*S*)-isomer and 27 min for (*R*)-isomer]. ^{1}H NMR δ 0.88 (9H, s), 2.79–2.87 (2H, m), 3.00 (1H, dd, *J*=5.7, 10.1 Hz), 4.89 (2H, s), 7.06–7.33 (10H, m). ^{13}C NMR δ 27.9, 33.7, 35.7, 52.3, 66.1, 126.4, 127.6, 127.96, 128.00, 128.4, 129.4, 135.9, 141.3, 173.0. IR (neat) 2960, 1736 cm^{-1}. MS *m/z* 296 (M^+). HRMS calcd for $C_{20}H_{24}O_2$ (M^+) 296.1775, found 296.1770 (M^+).

The catalytic enantioselective conjugate additions: General procedure

A mixture of 98% $Zn(OTf)_2$ (0.2 mmol), **3** (0.2 mmol) and **2a** (0.2 mmol) in CH_2Cl_2 (2 mL) was stirred for 1 h at rt to become a clear solution. The resulting clear solution was cooled to –78 ˚C. A solution of **2** (0.4 or 0.8 mmol) in CH_2Cl_2 (2 mL) was added, and the mixture was stirred for 30 min at –78 ˚C. *tert*-BuI (0.8 or 1.6 mmol), Bu_3SnH (0.8 or 1.6 mmol), and a solution

of triethylborane in hexane (1 N, 0.4 mmol) were added successively, and the mixture was allowed to stand for 12 h at the same temperature. The reactions were monitored by analytical thin-layer chromatographic (TLC) methods (silica gel). When TLC analysis showed the starting material, an additional portion of a solution of triethylborane (0.4 mmol) was added, and the mixture was stirred for an additional 12 h at –78 ˚C. After the reaction was complete (TLC, benzene), AcOH (0.4–0.8 mL) was added at –78 ˚C, and the mixture was stirred for 1 h. H_2O was added, and the mixture was extracted with CH_2Cl_2 (20 mL x 2). The organic layer was washed with saturated aqueous $NaHCO_3$ and brine successively, and dried over $MgSO_4$. After filtration, the solvent was removed under reduced pressure. The residue was taken up in MeCN. The mixture was washed with hexane. Concentration followed by purification through column chromatography (hexane–AcOEt) gave **5**–**8** in 72–84% ees and 72–94% yields as shown in Table 3.

Spectroscopic data of 4 and 6–8

(*S*)-3-(4,4-Dimethyl-3-phenylpentanoyl)-2-oxazolidinone (4). Colorless semisolid. $[\alpha]^{27}_D$ +15.4 (*c* 1.07, $CHCl_3$); 52% ee [HPLC: Chiralcel OD, hexane:2-propanol = 9:1, flow rate 1 mL/min, *Rt* 35 min for (*S*)-isomer and 40 min for (*R*)-isomer]. ^{1}H NMR δ 0.92 (9H, s), 3.11 (1H, dd, *J*=3.7, 11.3 Hz), 3.16 (1H, dd, *J*=3.7, 16.8 Hz), 3.72 (1H, dd, *J*=11.3, 16.8 Hz), 3.74 (1H, m), 3.82 (1H, m), 4.23 (1H, m), 4.29 (1H, m), 7.15–7.27 (5H, m). ^{13}C NMR δ 28.0, 33.8, 35.7, 42.5, 51.6, 61.9, 126.2, 127.6, 129.3, 141.8, 153.6, 172.8. IR (neat) 2958, 2867, 1771, 1698, 1492, 1478, 1451, 1392, 1368, 1314, 1259, 1225 cm^{-1}. MS *m/z* 275 (M^+). HRMS calcd for $C_{16}H_{21}NO_3$ (M^+) 275.1521, found 275.1543 (M^+).

(*R*)-3-(4-Methyl-3-phenylpentanoyl)-4,4-diphenyl-2-oxazolidinone (6). Colorless semisolid; mp 84–85 ˚C. $[\alpha]^{26}_D$ +13.7 (*c* 1.08, $CHCl_3$); 84% ee [HPLC: Chiralcel OD, hexane:2-propanol = 75:1, flow rate 0.25 mL/min, *Rt* 68 min for (*S*)-isomer and 72 min for (*R*)-isomer]. ^{1}H NMR δ 0.73 (3H, d, *J*=6.7 Hz), 0.93 (3H, d, *J*=6.7 Hz), 1.82 (1H, m), 2.95 (1H, m), 3.09 (1H, dd, *J*=4.4, 16.3 Hz), 3.76 (1H, dd, *J*=11.2, 16.3 Hz), 4.42 (1H, d, *J*=9.0 Hz), 4.71 (1H, d, *J*=9.0 Hz), 6.64–6.69 (2H, m), 7.08–7.12 (2H, m), 7.17–7.33 (11H, m). ^{13}C NMR δ 20.5, 20.7, 33.5, 39.9, 48.5, 71.1, 77.8, 126.3, 127.0, 127.6, 128.0, 128.20, 128.23, 128.3, 128.8, 138.7, 139.5, 143.0, 154.0, 172.0, due to overlap (CH x 2), not all carbons resonances were visible. IR (nujol) 2953, 2923, 2854, 1770, 1709, 1603, 1456, 1377, 1273 cm^{-1}. MS *m/z* 413 (M^+). HRMS calcd for $C_{27}H_{27}NO_3$ (M^+) 413.1991, found 413.1985 (M^+).

(*R*)-3-(3-Cyclohexyl-3-phenylpropanoyl)-4,4-diphenyl-2-oxazolidinone (7). Amorphous. $[\alpha]^{27}_D$ +9.2 (*c* 0.68, $CHCl_3$); 84% ee [HPLC: Chiralcel OD, hexane:2-propanol = 75:1, flow rate 0.25 mL/min, *Rt* 63 min for (*S*)-isomer and 67 min for (*R*)-isomer]. ^{1}H NMR δ 0.73–1.82 (11H, m), 2.98 (1H, m), 3.13 (1H, dd, *J*=4.6, 16.4 Hz), 3.70 (1H, dd, *J*=11.0, 16.4 Hz), 4.42 (1H, d, *J*=9.0 Hz), 4.71 (1H, d, *J*=9.0 Hz), 6.68–6.70 (2H, m), 7.08–7.10 (2H, m), 7.12–7.33 (11H, m).

^{13}C NMR δ 26.3, 30.8, 31.0, 39.7, 43.1, 47.6, 71.1, 77.8, 126.3, 127.0, 127.6, 128.0, 128.18, 128.20, 128.24, 128.3, 128.8, 138.7, 139.6, 143.2, 154.0, 172.1. IR (neat) 3027, 2924, 2852, 1780, 1713, 1492, 1448, 1373, 1265 cm^{-1}. MS *m/z* 453 (M^+). HRMS calcd for $C_{30}H_{31}NO_3$ (M^+) 453.2304, found 453.2311 (M^+).

(*S*)-3-(3-phenylpentanoyl)-4,4-diphenyl-2-oxazolidinone (8). Colorless oil. $[\alpha]^{25}_D$ +12.5 (*c* 0.50, $CHCl_3$); 72% ee [HPLC: Chiralcel OD, hexane:2-propanol = 75:1, flow rate 0.25 mL/min, *Rt* 83 min for (*R*)-isomer and 88 min for (*S*)-isomer]. ^{1}H NMR δ 0.75 (3H, t, *J*=7.3 Hz), 1.54–1.67 (2H, m), 3.05 (1H, m), 3.07 (1H, dd, *J*=5.5, 17.7 Hz), 3.58 (1H, dd, *J*=10.7, 17.7 Hz), 4.49 (1H, d, *J*=9.2 Hz), 4.71 (1H, d, *J*=9.2 Hz), 6.83–6.85 (2H, m), 7.14–7.35 (13H, m). ^{13}C NMR δ 12.0, 29.6, 42.8, 43.3, 71.1, 77.9, 126.4, 127.1, 127.8, 127.9, 128.0, 128.2, 128.30, 128.32, 128.4, 138.8, 139.5, 143.9, 154.0, 171.6. IR (neat) 3027, 2962, 2927, 1776, 1714, 1602, 1493, 1450, 1375, 1258 cm^{-1}. MS *m/z* 399 (M^+). HRMS calcd for $C_{26}H_{25}NO_3$ (M^+) 399.1833, found 399.1841 (M^+).

The determination of the absolute configurations of 4–8

The absolute configurations of **4** and **5** were determined by chemical correlation with (*S*)-4,4-dimethyl-3-phenylpentanoic acid **13**. For **5**, see: experiment (the enantioselective radical-mediated conjugate additions: typical procedure, Scheme 1).[4]

The absolute configuration of **6** was determined by chemical correlation with (*S*)-4-methyl-3-phenylpentanoic acid **15**.[5]

The absolute configuration of **7** was determined by converting to (*R*)-3-cyclohexyl-3-phenyl-1-propanal **18**.[6]

The absolute configuration of **8** was determined by chemical correlation with (*R*)-3-phenylpentanoic acid **19**.[7]

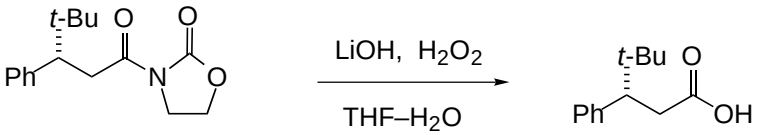
Compound **13** shown in Scheme 2 was synthesized from **4** having 52% ee (entry 3 in Table 1).

Compound **15** shown in Scheme 3 was synthesized from **6** having 50% ee [HPLC: Chiralcel OD, hexane:2-propanol = 75:1, flow rate 0.25 mL/min, *Rt* 66 min for (*S*)-isomer and 71 min for (*R*)-isomer].

Compounds **16–18** shown in Scheme 4 were synthesized from **7** having 84% ee (entry 7 in Table 3).

Compound **19** shown in Scheme 5 was synthesized from **8** having 71% ee (entry 9 in Table 3).

Scheme 2.

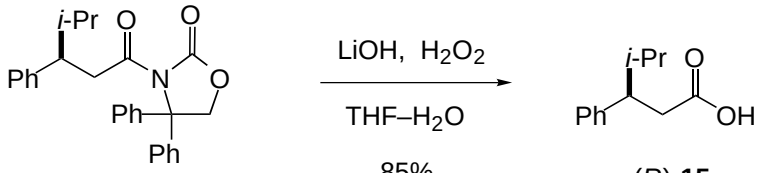


(*S*)-**4** 83% (***S***)-**13**

$[\alpha]^{26}_{D}$ –8.9 (*c* 1.12, EtOH)

(*S*)-**13**: Imajo, S.; Kuritani, H.; Shingu, K.; Nakagawa, M. *J. Org. Chem.* **1979**, *44*, 3587–3589

Scheme 3.

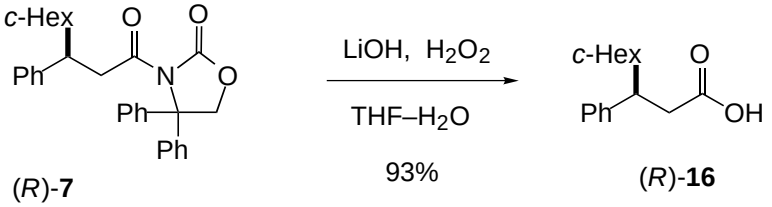


(*R*)-**6** 85% (*R*)-**15**

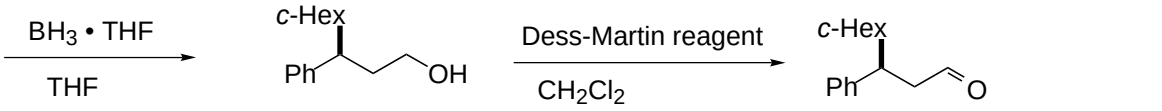
$[\alpha]^{25}_{D}$ +16.1 (*c* 1.17, $CHCl_3$)

(*S*)-**15**: Lardicci, L.; Salvadori, P.; Caporusso, A. M.; Menicagli, R.; Belgodere, E. *Gazz. Chim. Ital.* **1972**, *102,* 64–84; Sibi, M. P.; Ji, J.; Wu, J. H.; Gürtler, S.; Porter, N. A. *J. Am. Chem. Soc*. **1996**, *118*, 9200–9201.

Scheme 4.



(*R*)-**7** 93% (*R*)-**16**

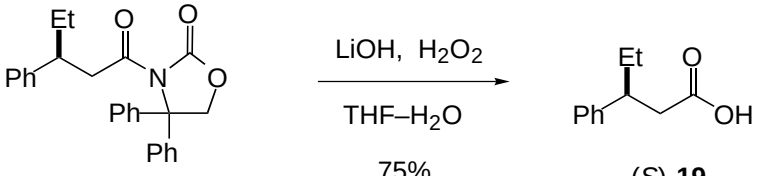


94% (*R*)-**17** (*R*)-**18**

$[\alpha]^{22}_{D}$ +12.4 (*c* 1.17, pentane) $[\alpha]^{23}_{D}$ +1.5 (*c* 1.08, benzene)

(*S*)-**17**, (*S*)-**18**: Ahlbrecht, H.; Enders, D.; Santowski, L.; Zimmermann, G. *Chem. Ber*. **1989**, *122*, 1995–2004

Scheme 5.



(***S***)-**8** 75% (*S*)-**19**

$[\alpha]^{26}_{D}$ +34.7 (*c* 0.73, benzene)

(*R*)-**19**: Lardicci, L.; Menicagli, R.; Salvadori, P. *Gazz. Chim. Ital*. **1968**, *98*, 738–759; Sibi, M. P.; Shay, J J.; Ji, J. *Tetrahedron Lett*. **1997**, *38*, 5955–5958. (*S*)-**19**: Soai, K.; Machida, H.; Yokota, N. *J. Chem. Soc*. *Perkin Trans.1* **1987**, 1909–1914.

Spectroscopic data

For **13**, see experiment (the enantioselective radical-mediated conjugate additions: typical procedure, Scheme 1).

(*R*)-4-Methyl-3-phenylpentanoic acid (15) Colorless solid. $[\alpha]^{25}_{D}$ +16.1 (*c* 1.17, $CHCl_3$). ^{1}H NMR δ 0.74 (3H, d, *J*=6.7 Hz), 0.92 (3H, d, *J*=6.7 Hz), 1.85 (1H, dq, *J*=13.7, 6.7 Hz), 2.60 (1H, dd, *J*=9.7, 15.6 Hz), 2.78 (1H, dd, *J*=5.5, 15.6 Hz), 2.86 (1H, m), 7.12–7.27 (5H, m). ^{13}C NMR δ 20.1, 20.5, 33.1, 38.1, 48.4, 126.4, 128.1, 128.2, 142.5, 179.0. IR (neat) 3500–2500, 2960, 1696, 1417, 1296 cm^{-1}. MS *m/z* 192 (M^+); HRMS calcd for $C_{12}H_{16}O_3$ (M^+) 192.1149 found 192.1144 (M^+).

(*R*)-3-Cyclohexyl-3-phenylpropanoic acid (16). Colorless crystals; mp 58–60 ˚C. $[\alpha]^{26}_{D}$ +23.0 (*c* 1.22, $CHCl_3$). ^{1}H NMR δ 0.75–1.80 (11H, m), 2.57 (1H, dd, *J*=9.5, 15.6 Hz), 2.80 (1H, dd, *J*=5.5, 15.6 Hz), 2.88 (1H, m), 7.10–7.12 (2H, m), 7.18 (1H, m), 7.24–7.28 (2H, m). ^{13}C NMR δ 26.4, 30.6, 30.9, 38.0, 42.8, 47.6, 126.3, 128.1, 128.2, 142.7, 179.1. IR (neat) 3400–2326, 3025, 2922, 2849, 1697, 1601 cm^{-1}. MS *m/z* 232 (M^+); HRMS calcd for $C_{15}H_{20}O_2$ (M^+) 232.1462, found 232.1470 (M^+).

(*R*)-3-Cyclohexyl-3-phenylpropanol (17). Colorless oil; $[\alpha]^{22}_{D}$ +12.4 (*c* 1.17, pentane). ^{1}H NMR δ 0.75–2.12 (13H, m), 2.44 (1H, m), 3.38 (1H, m), 3.45 (1H, m), 7.11–7.12 (2H, m), 7.18 (1H, m), 7.26–7.29 (2H, m). ^{13}C NMR δ 26.5, 31.0, 31.3, 35.5, 43.2, 48.6, 61.6, 126.0, 128.1, 128.4, 143.9. IR (neat) 3726–2500, 3347, 2926, 2852, 1600 cm^{-1}. MS *m/z* 218 (M^+); HRMS calcd for $C_{15}H_{22}O$ (M^+) 218.1669, found 218.1673 (M^+).

(*R*)-3-Cyclohexyl-3-phenylpropanal (18). Colorless oil; bp 70–100 ˚C / 1 mmHg (bulb-to-bulb distillation). $[\alpha]^{23}_{D}$ +1.5 (*c* 1.08, benzene). ^{1}H NMR δ 0.78–1.26 (5H, m), 1.43–1.82 (6H, m), 2.72 (1H, ddd, *J*=2.5, 9.5, 16.5 Hz), 2.83 (1H, ddd, *J*=1.9, 5.5, 16.5 Hz), 2.97 (1H, m), 7.13–7.14 (2H, m), 7.19 (1H, m), 7.26–7.30 (2H, m), 9.60 (1H, dd, *J*=1.9, 2.5 Hz). ^{13}C NMR δ 26.4, 30.7, 31.1, 43.1, 46.2, 47.1, 126.5, 128.3, 128.4, 142.8, 202.6. IR (neat) 3028, 2925, 2851, 2716, 1725, 1600 cm^{-1}. MS *m/z* 216 (M^+); HRMS calcd for $C_{15}H_{20}O$ (M^+) 216.1513, found 216.1515 (M^+).

(*S*)-3-phenylpentanoic acid (19). Colorless oil; bp 170–200 ˚C / 3 mmHg (bulb-to-bulb distillation). $[\alpha]^{26}_{D}$ +34.7 (*c* 0.73, benzene). ^{1}H NMR δ 0.79 (3H, t, *J*=7.3 Hz), 1.61 (1H, m), 1.73 (1H, m), 2.60 (1H, dd, *J*=7.9, 15.6 Hz), 2.66 (1H, dd, *J*=7.3, 15.6 Hz), 2.98 (1H, m), 7.16–7.22 (3H, m), 7.25–7.30 (2H, m). ^{13}C NMR δ 11.8, 29.1, 41.1, 43.5, 126.5, 127.5, 128.4, 143.6, 178.7. IR (neat) 3600–2500, 3029, 2964, 2926, 1709, 1602 cm^{-1}. MS *m/z* 178 (M^+); HRMS calcd for $C_{11}H_{14}O_2$ (M^+) 178.0993, found 178.0994 (M^+).

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(1) (a) Narasaka, K.; Iwasawa, N.; Inoue, M.; Yamada, T.; Nakashima, M.; Sugimori, J. *J. Am. Chem. Soc.* **1989**, *111*, 5340–5345. (b) Evans, D. A.; Chapman, K. T.; Bisaha, J. *J. Am. Chem. Soc.* **1988**, *110*, 1238–1256.

(2) Hassner, A; Lorber, M. E.; Heathcock, C. *J. Org. Chem*. **1967**, *32*, 540–549.

(3) (a) Evans, D. A.; Peterson, G. S.; Johnson, J. S.; Barnes, D. M.; Campos, K. R.; Woerpel, K. A. *J. Org. Chem*. **1998**, *63*, 4541–4544. (b) Corey, E. J.; Imai, N.; Zhang, H.-Y. *J. Am. Chem. Soc*. **1991**, *113*, 728–729.

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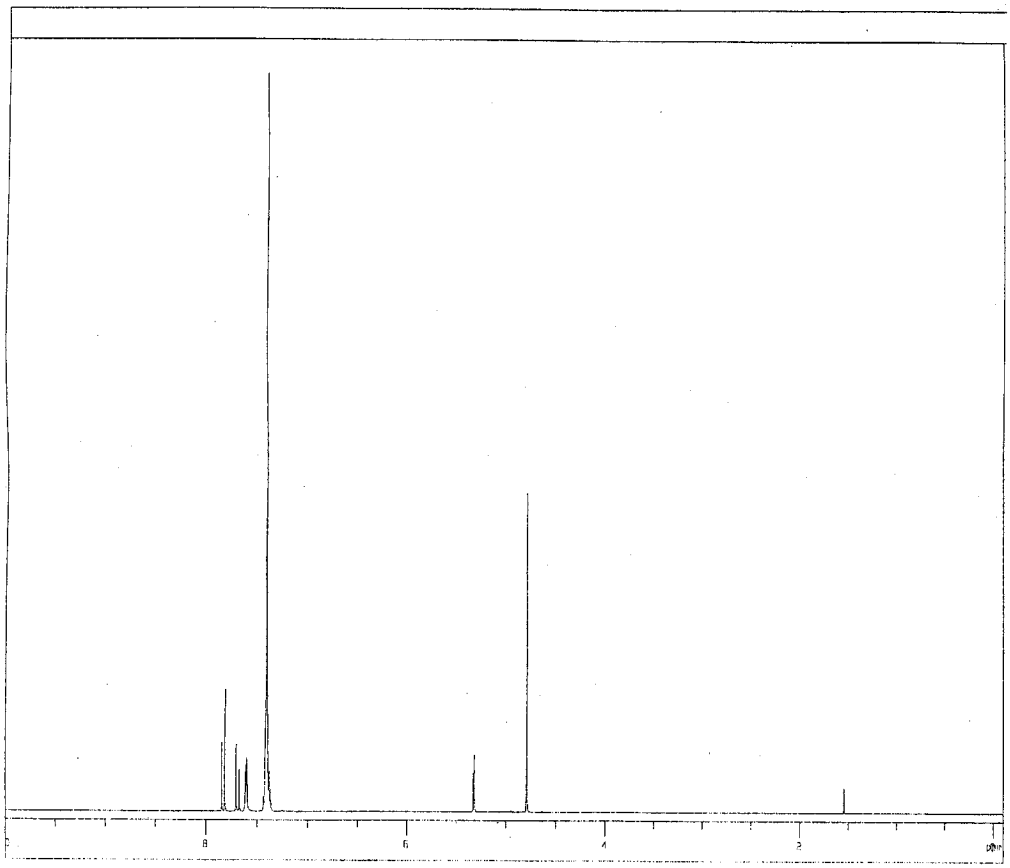
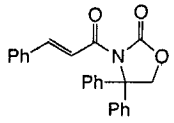
(6) For the antipode, see: Ahlbrecht, H.; Enders, D.; Santowski, L.; Zimmermann, G. *Chem. Ber*. **1989**, *122*, 1995–2004.

(7) Lardicci, L.; Menicagli, R.; Salvadori, P. *Gazz. Chim. Ital.* **1968**, *98*, 738–759. Sibi, M. P.; Shay, J. J.; Ji, J. *Tetrahedron Lett*. **1997**, *38*, 5955–5958. For the antipode, see: Soai, K.; Machida, H.; Yokota, N. *J. Chem. Soc. Perkin Trans.1* **1987**, 1909–1914.





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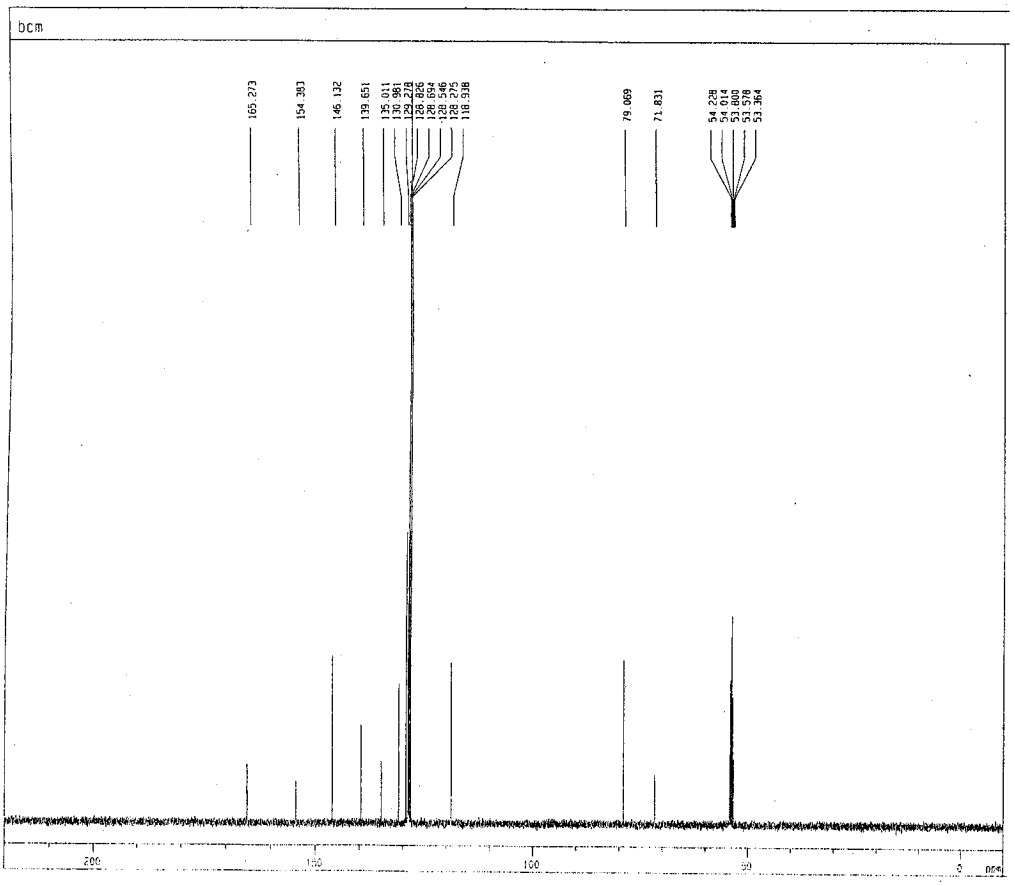

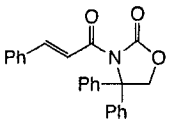

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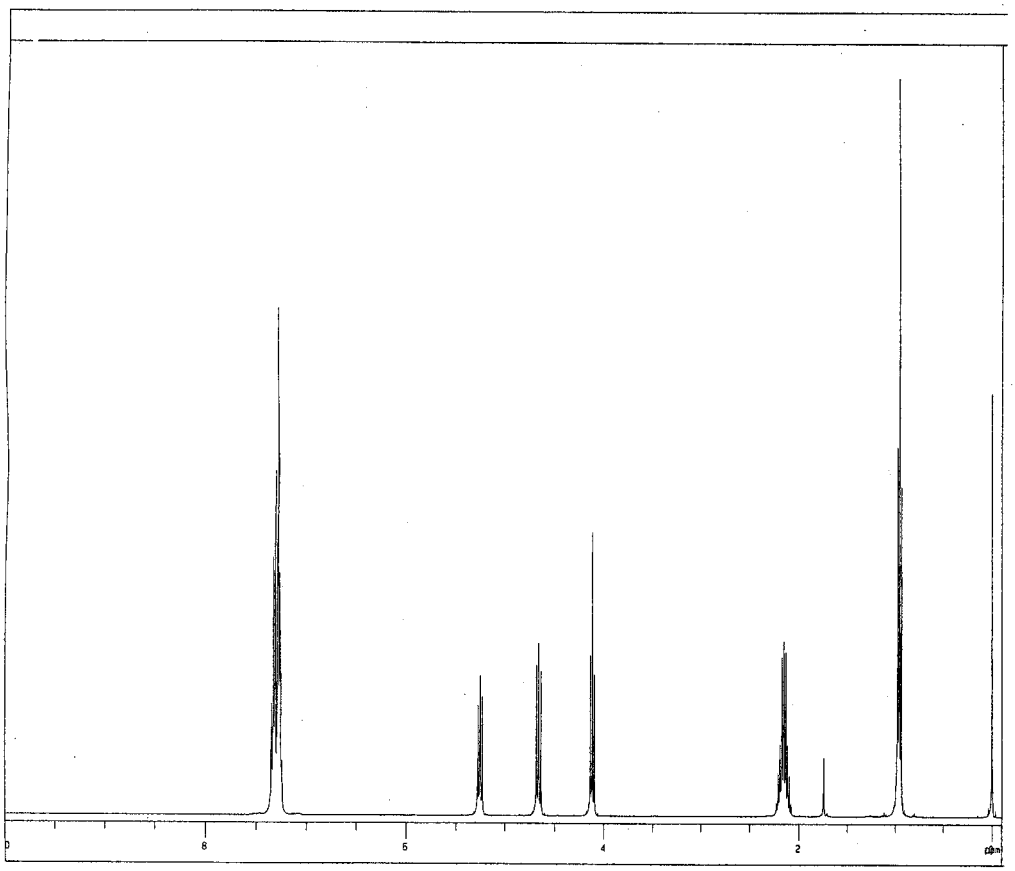

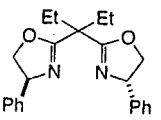

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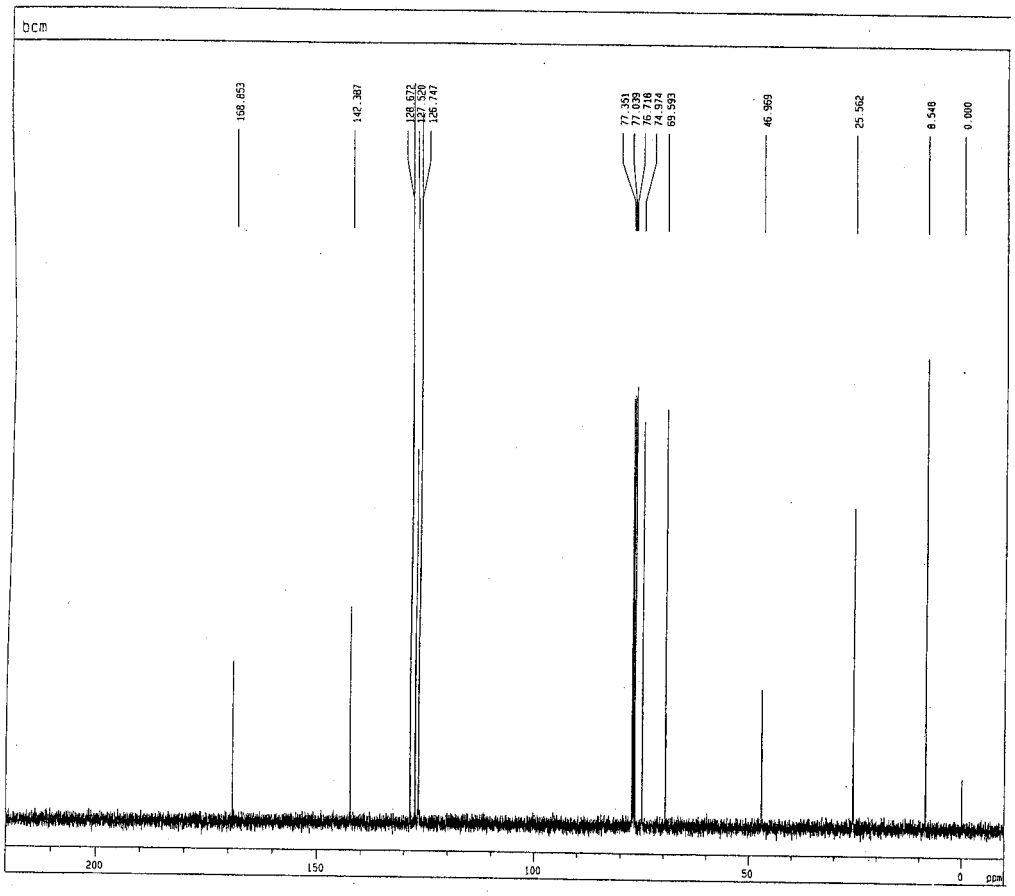

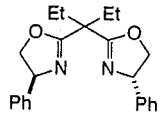

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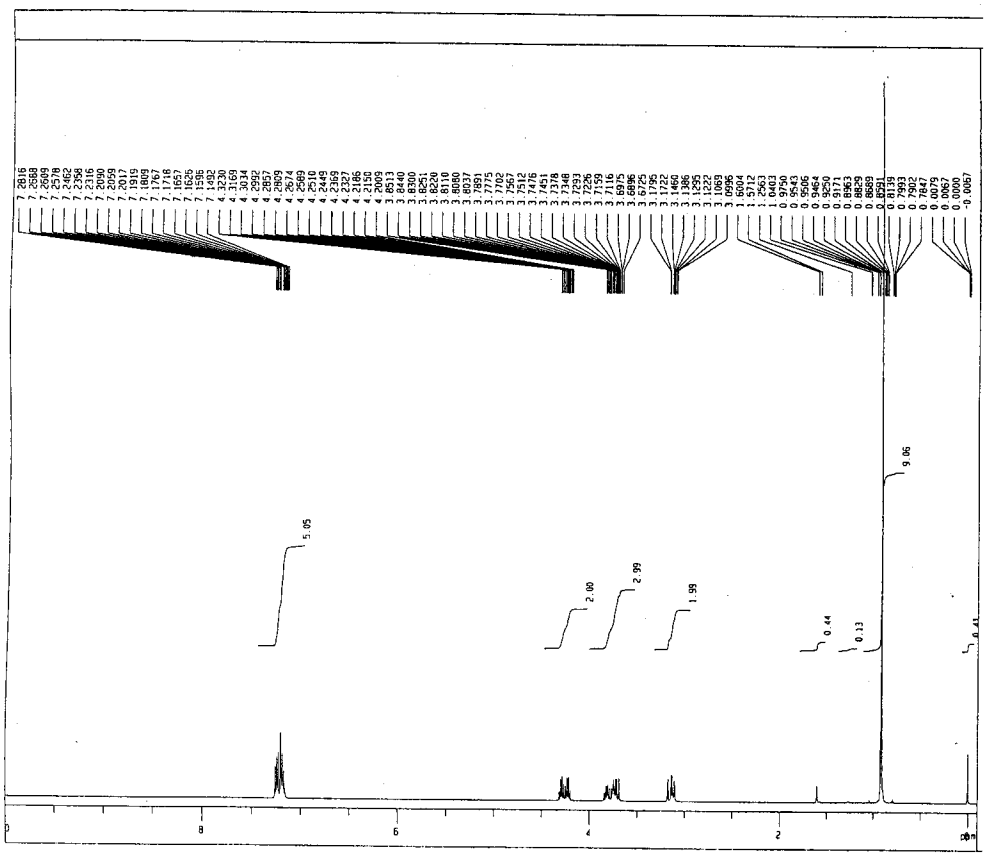

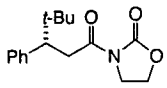

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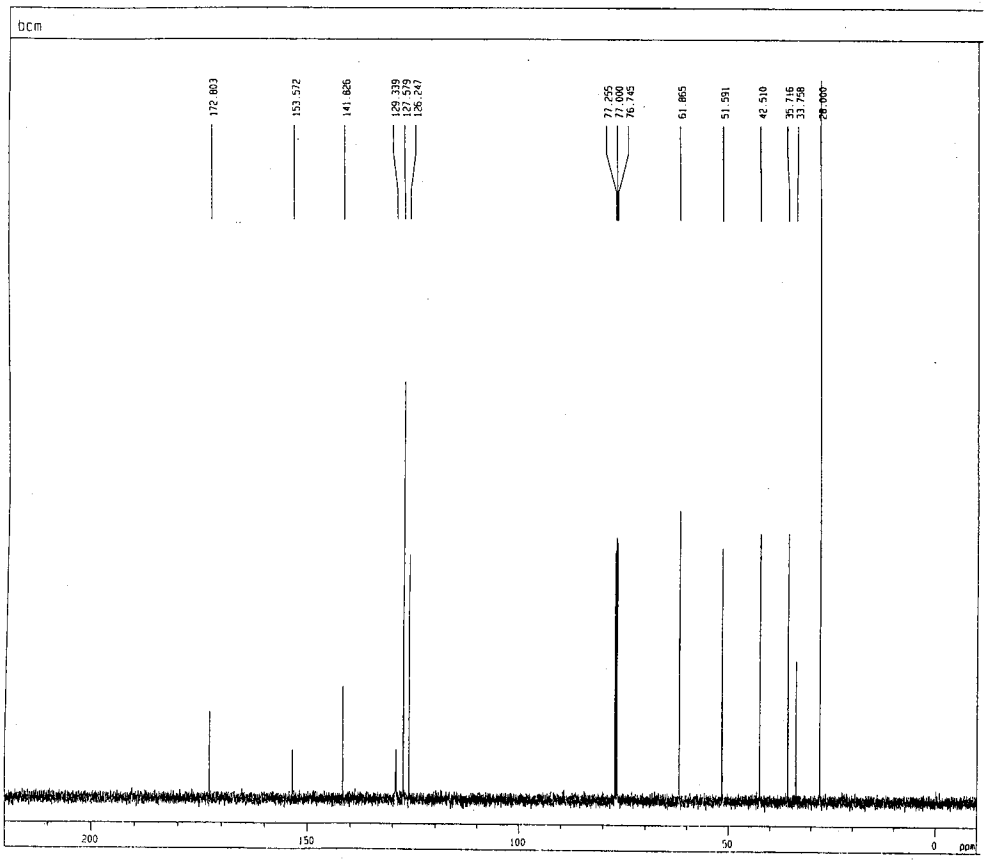

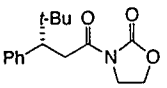

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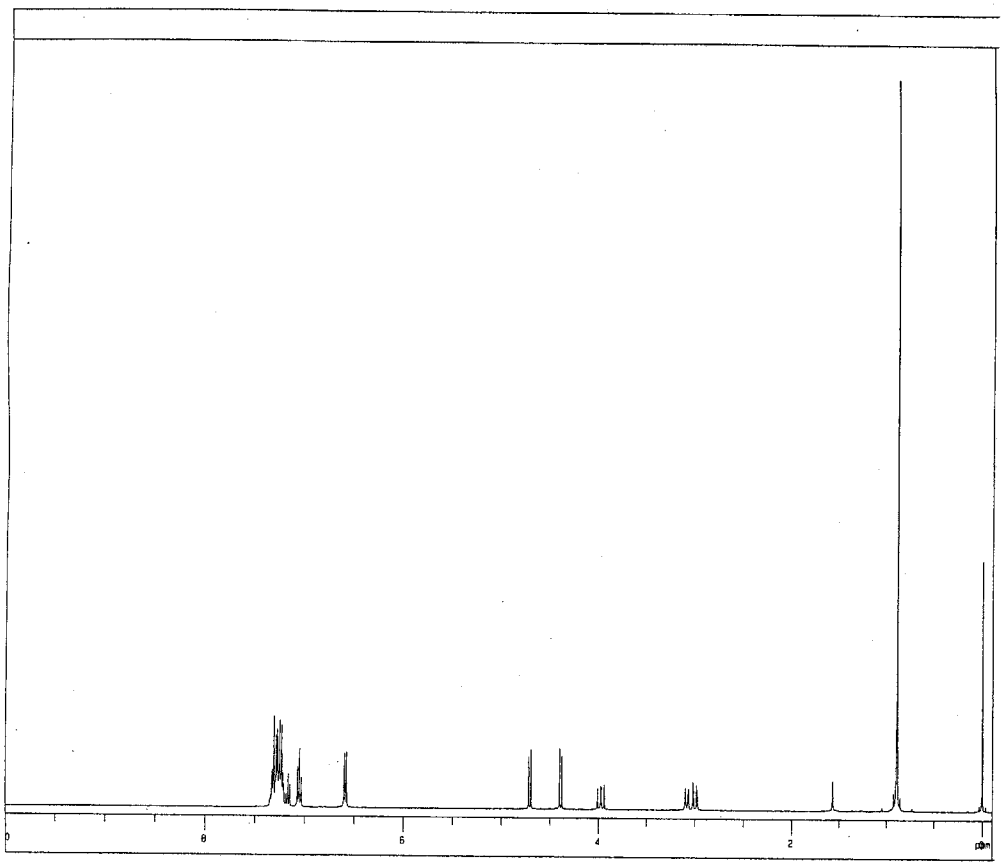

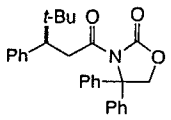

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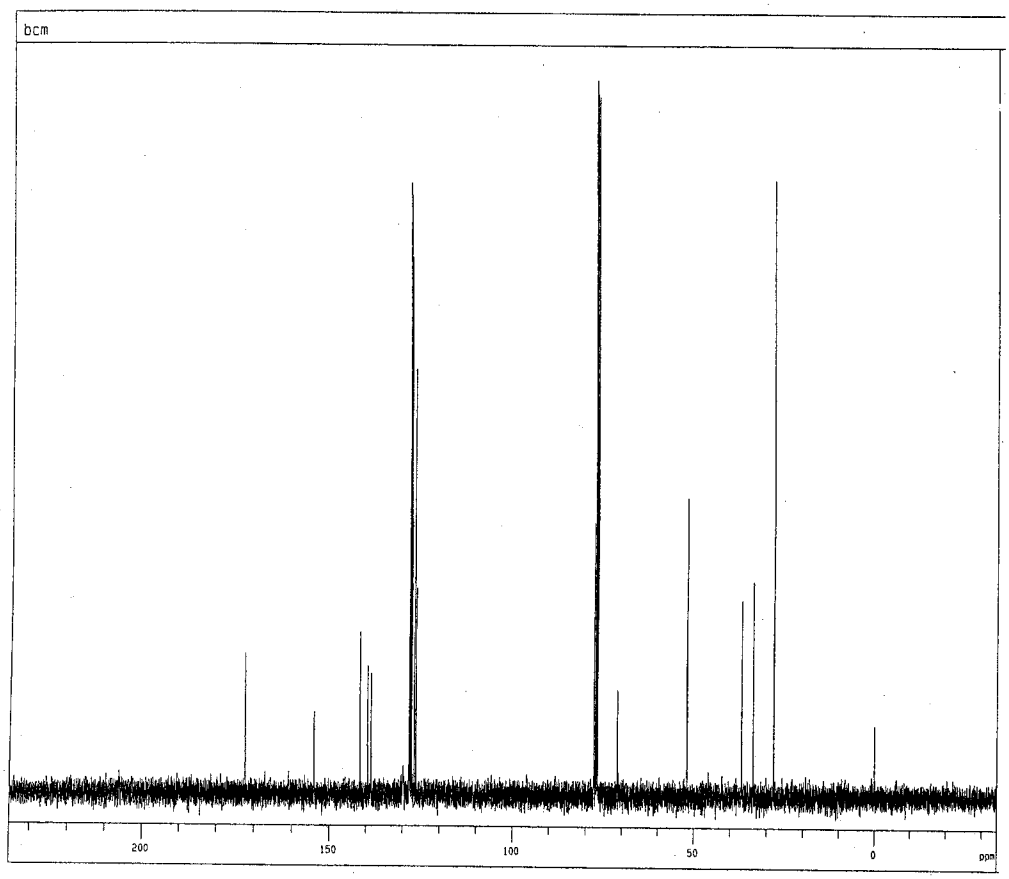

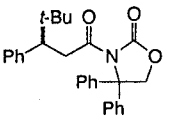

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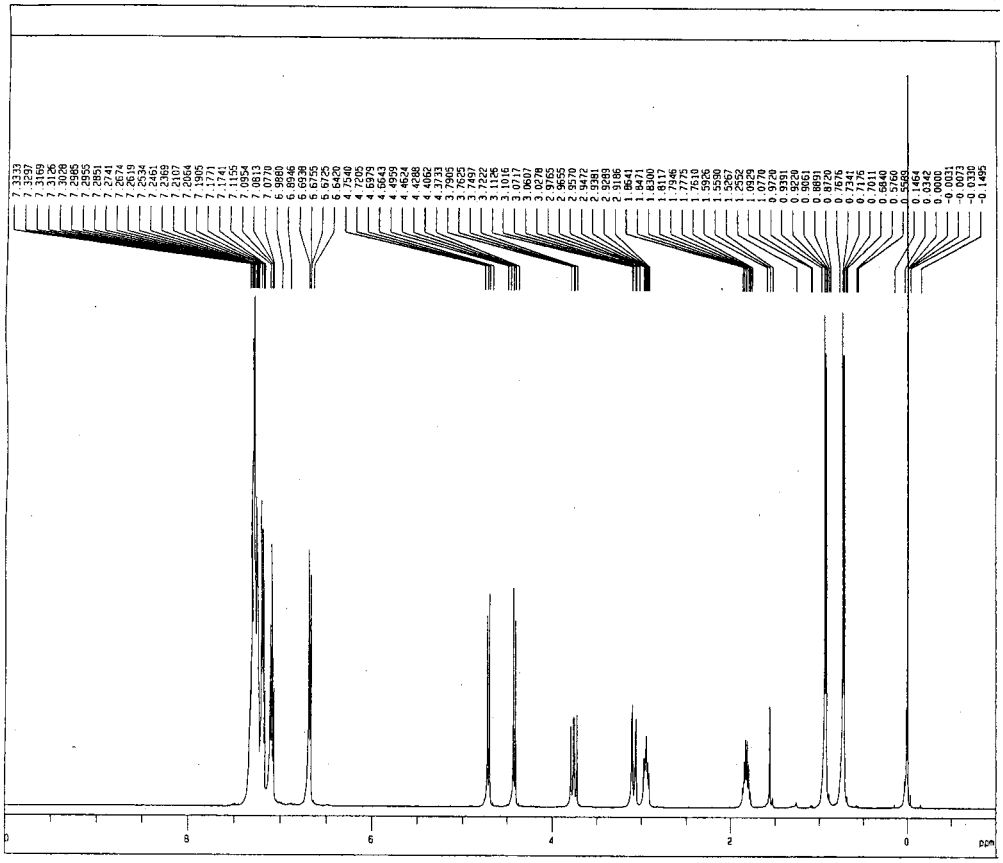

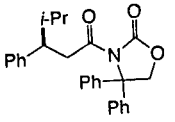

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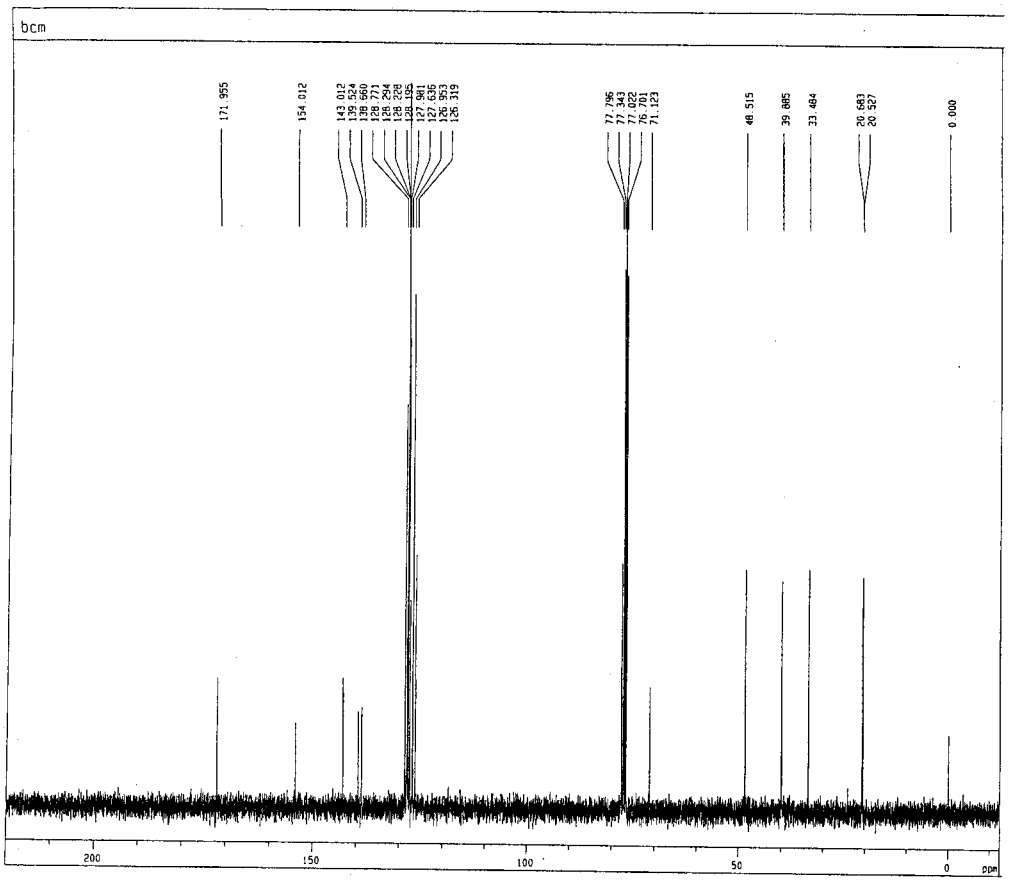

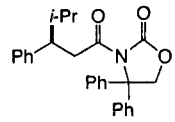

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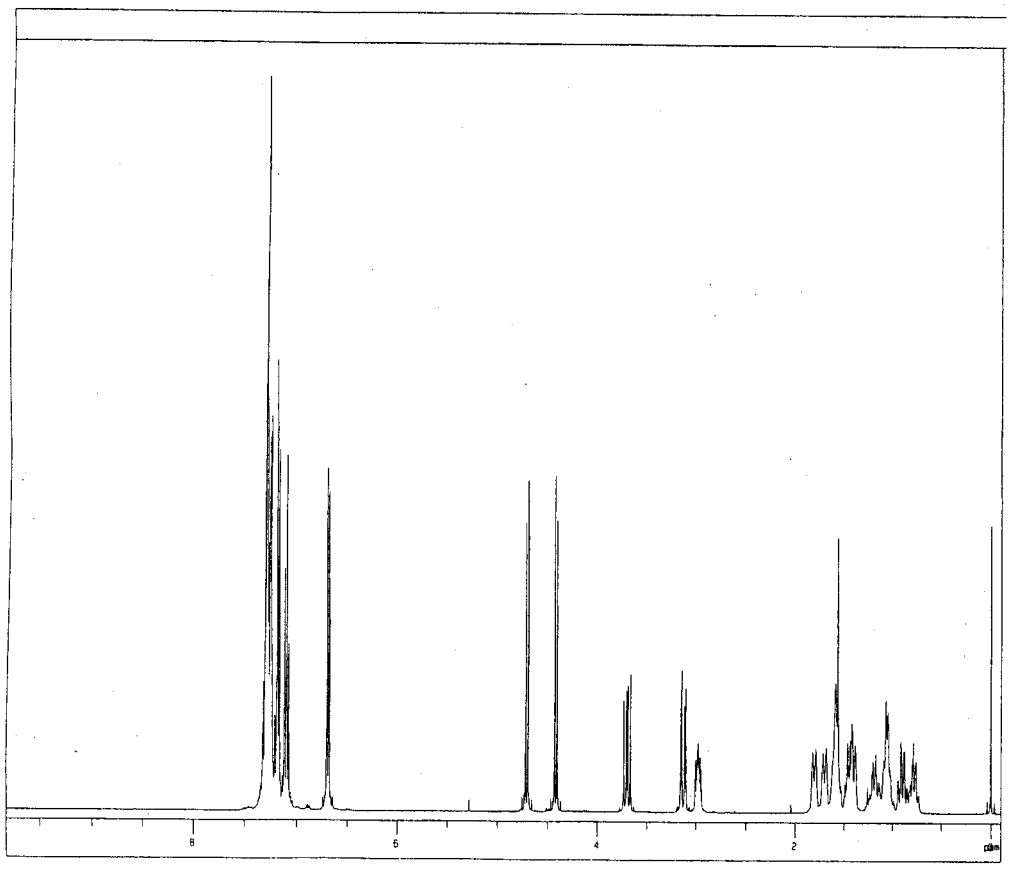

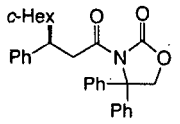

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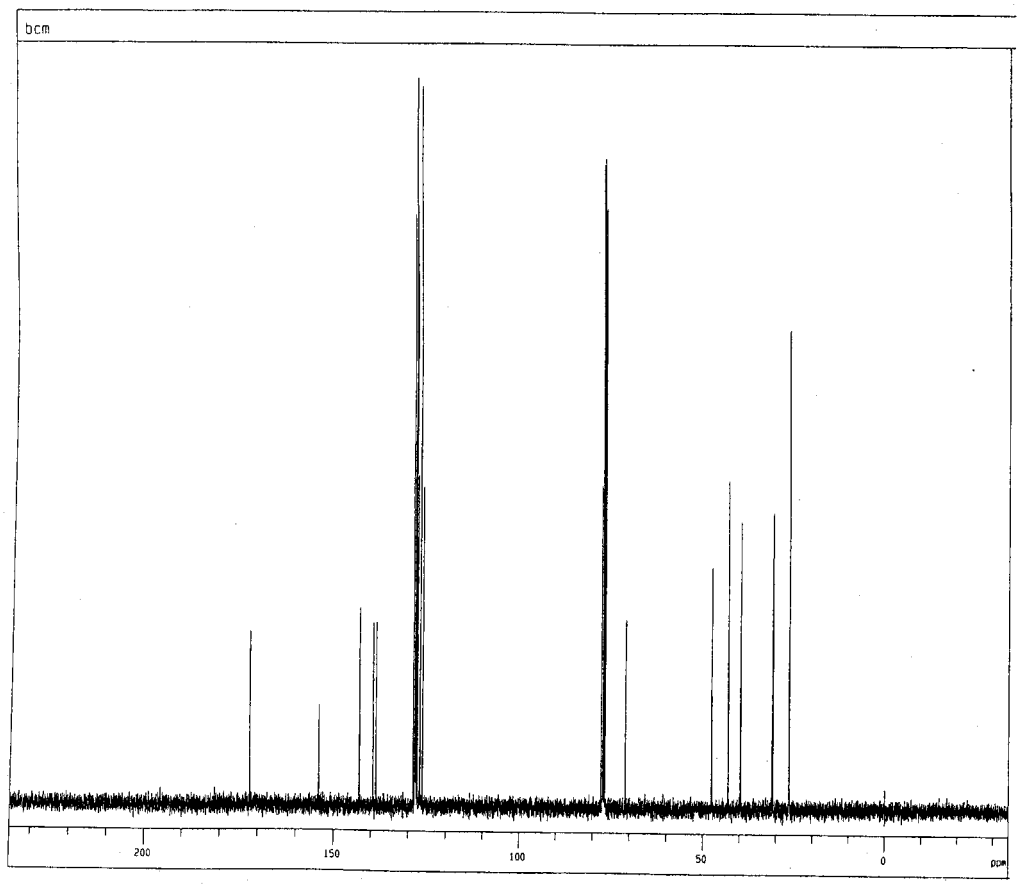

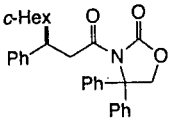

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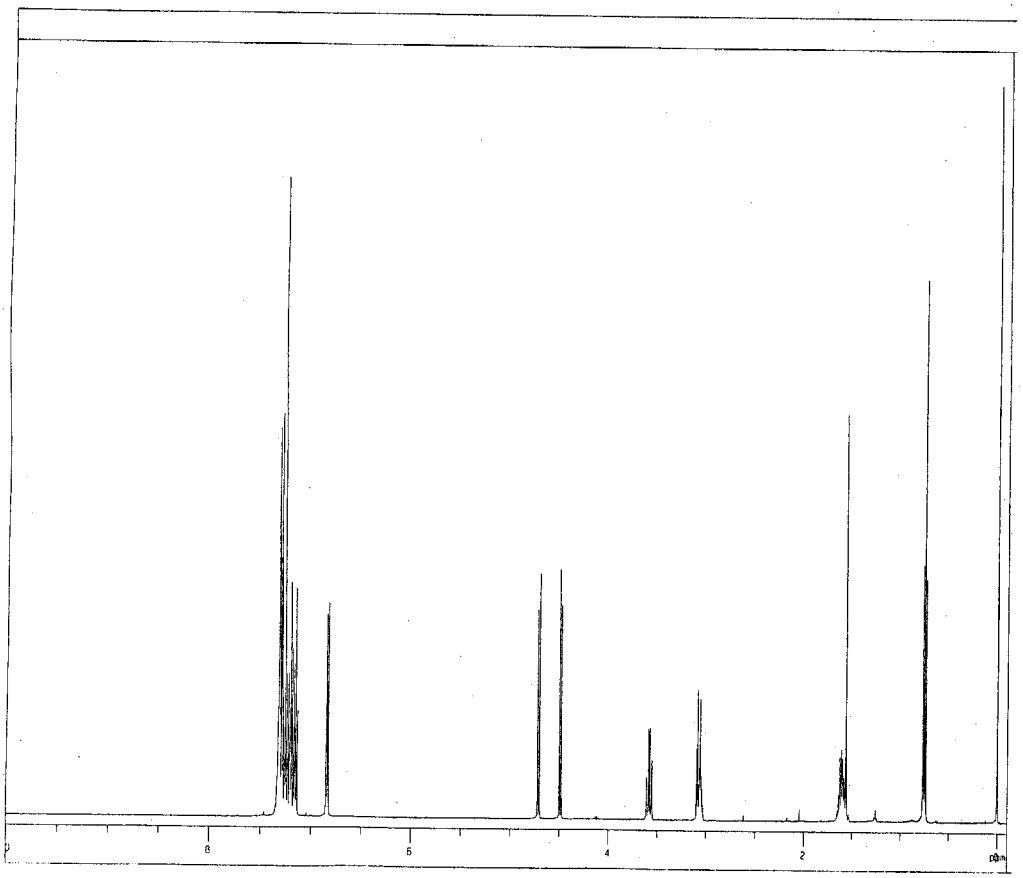

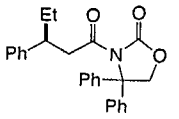

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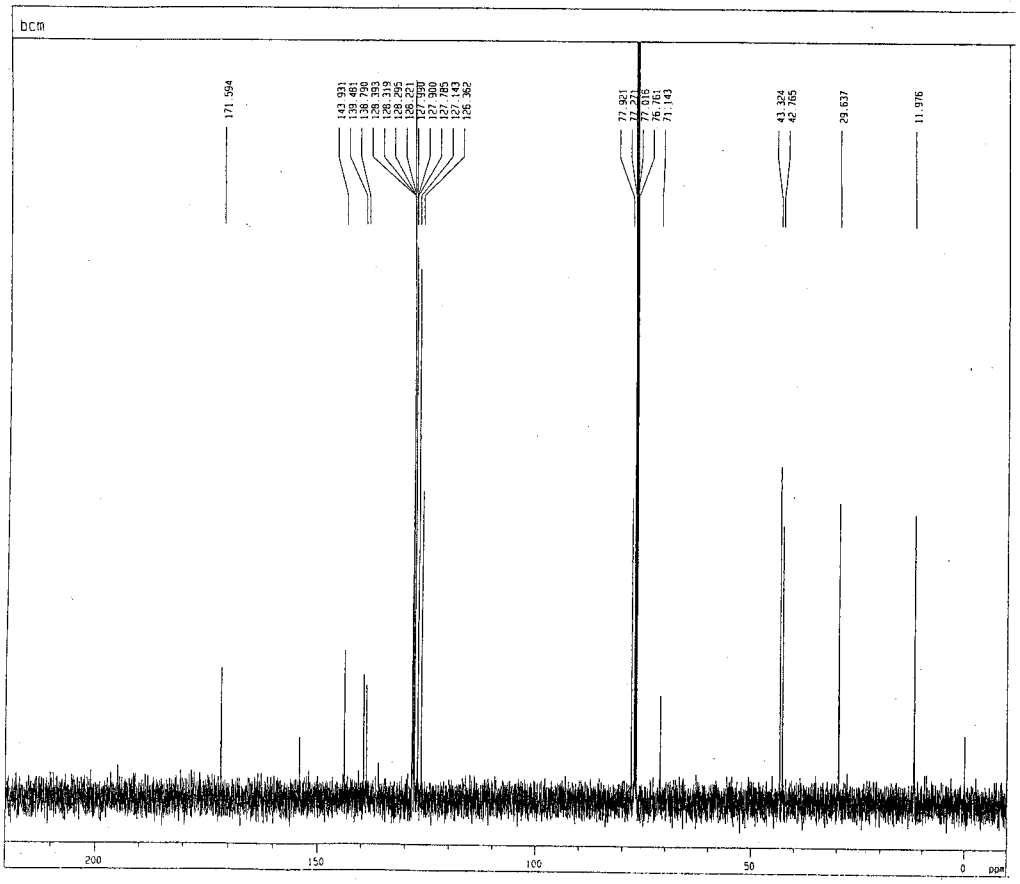

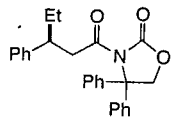

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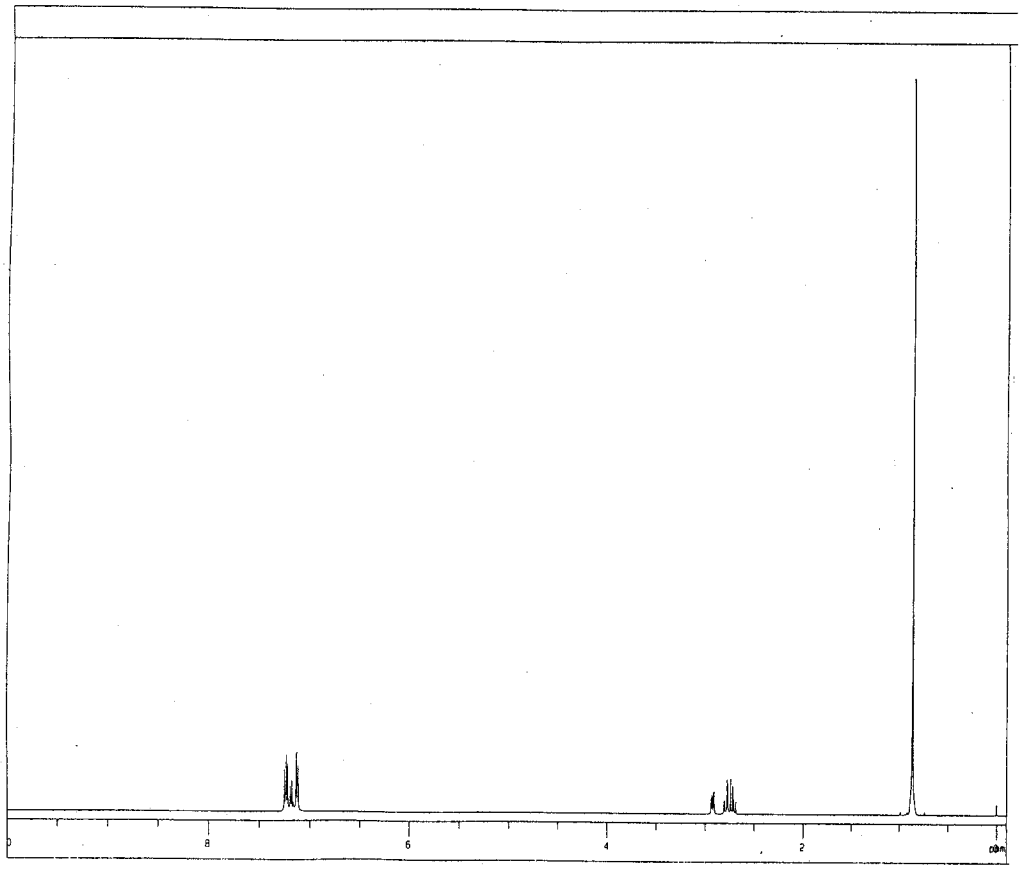

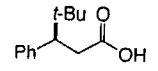

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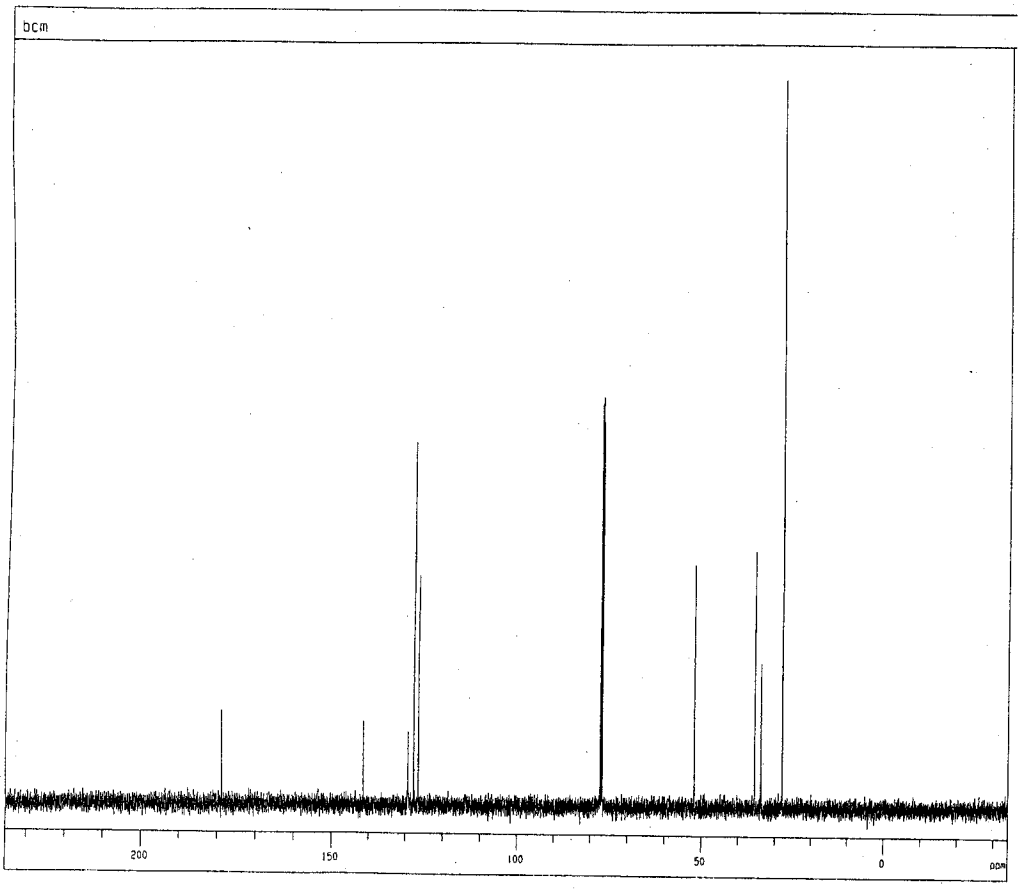

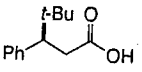

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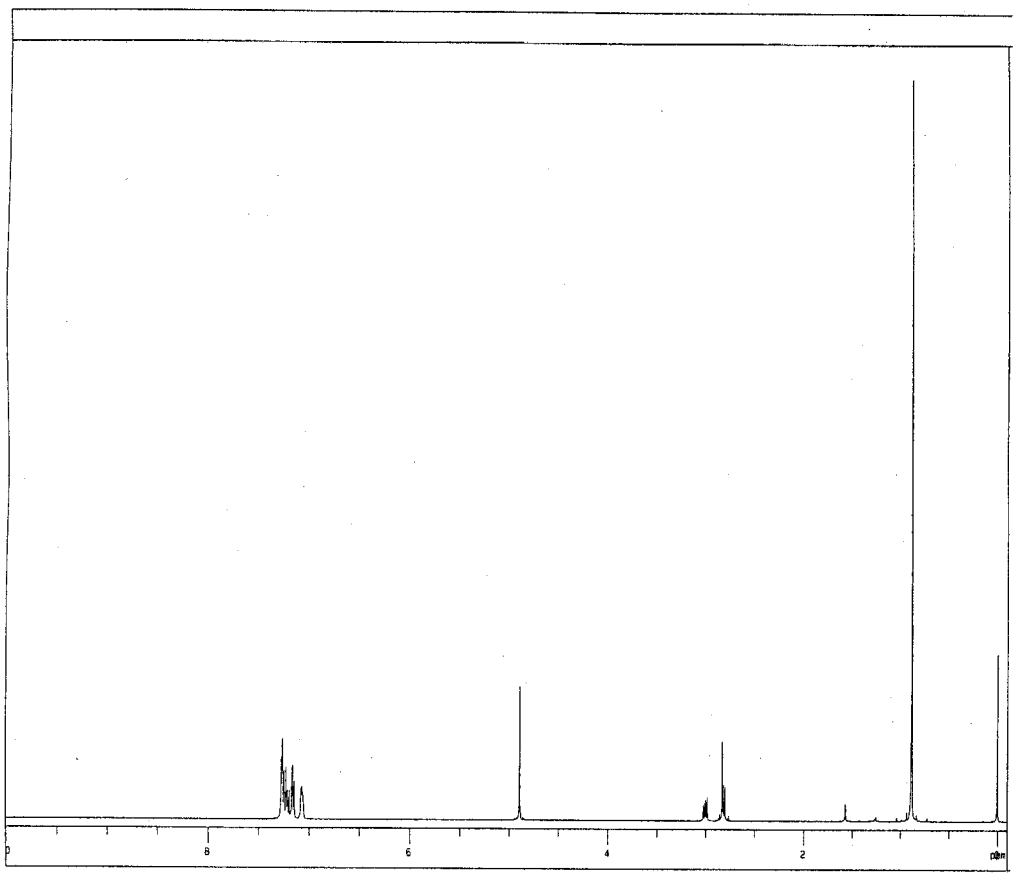

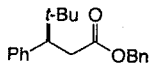

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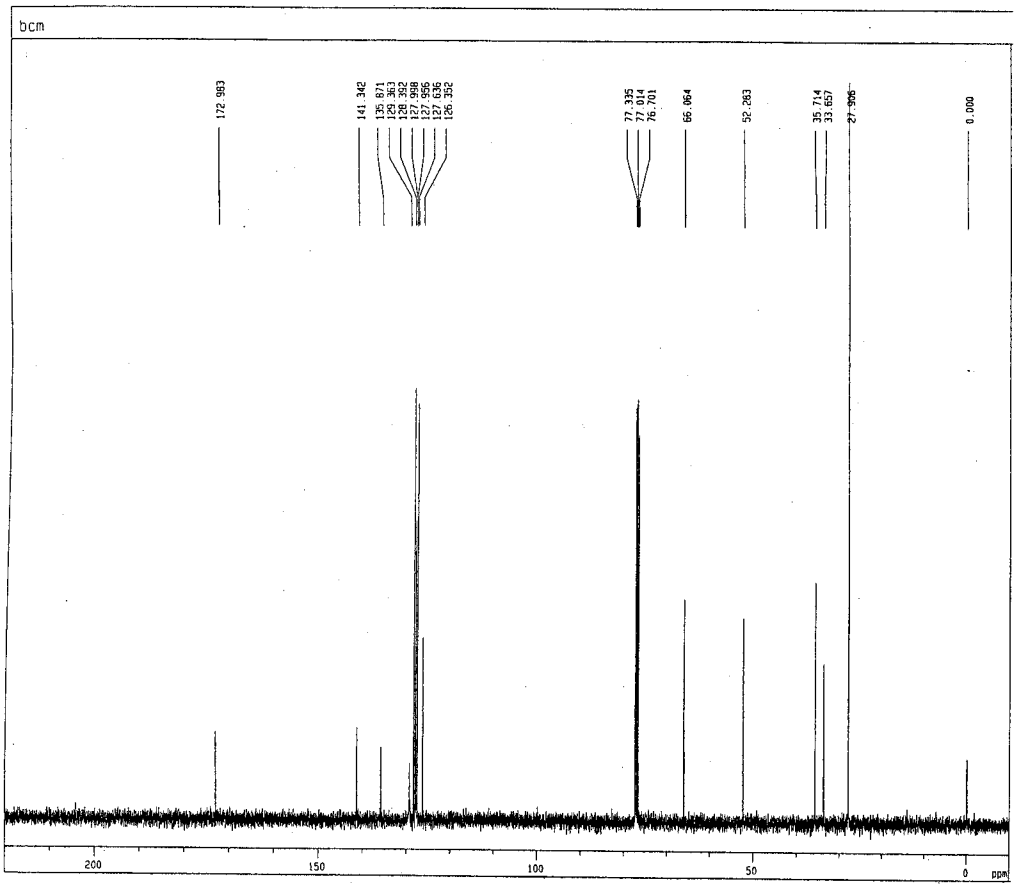
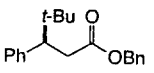
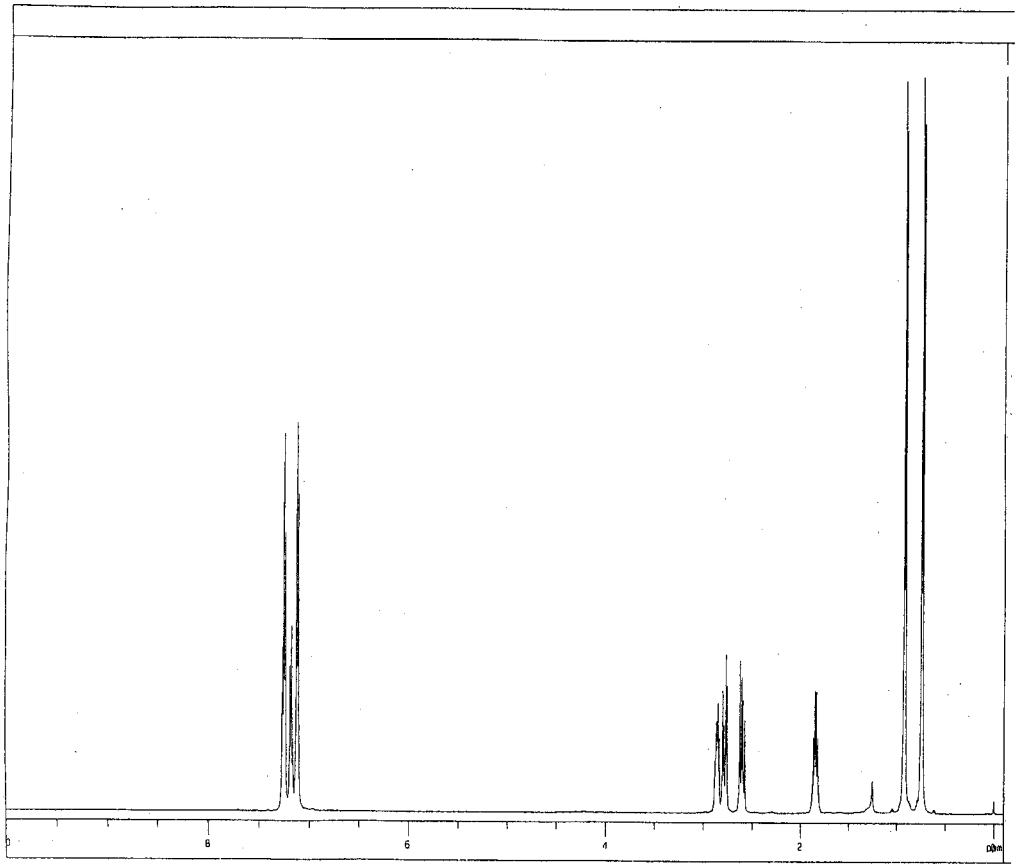
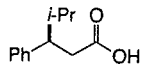


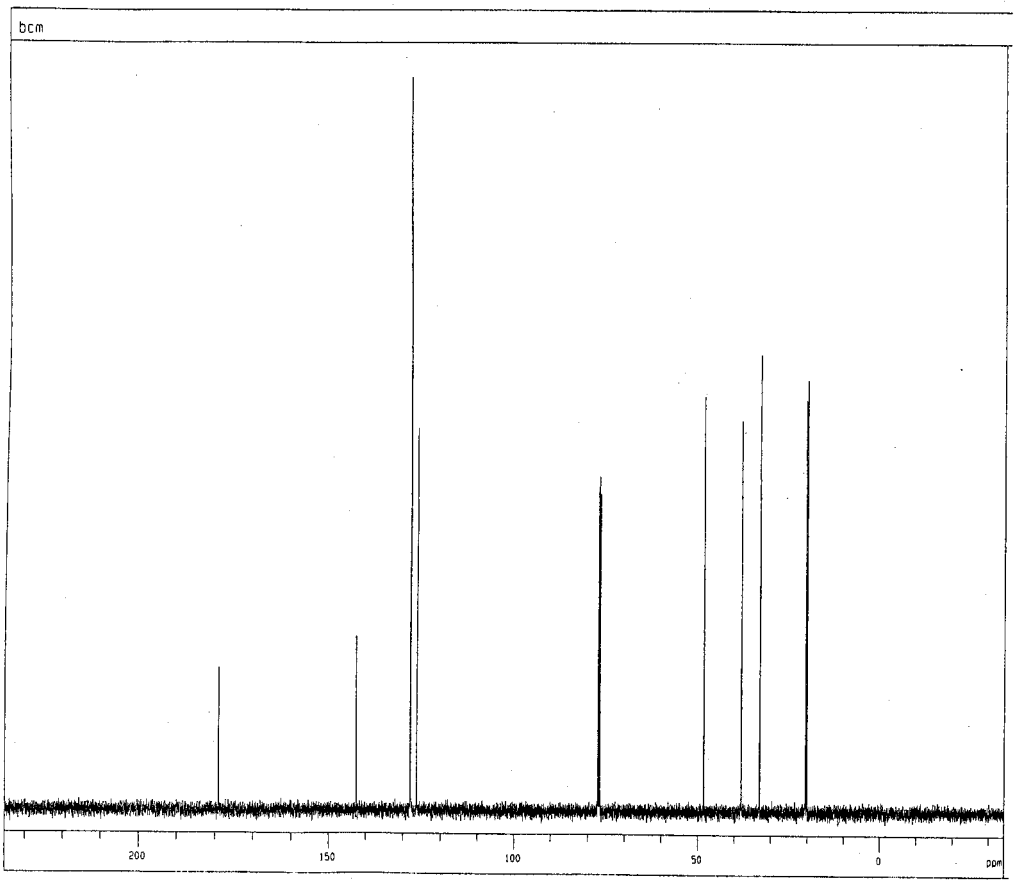


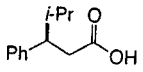
(*R*)-**14** / $CDCL_3$



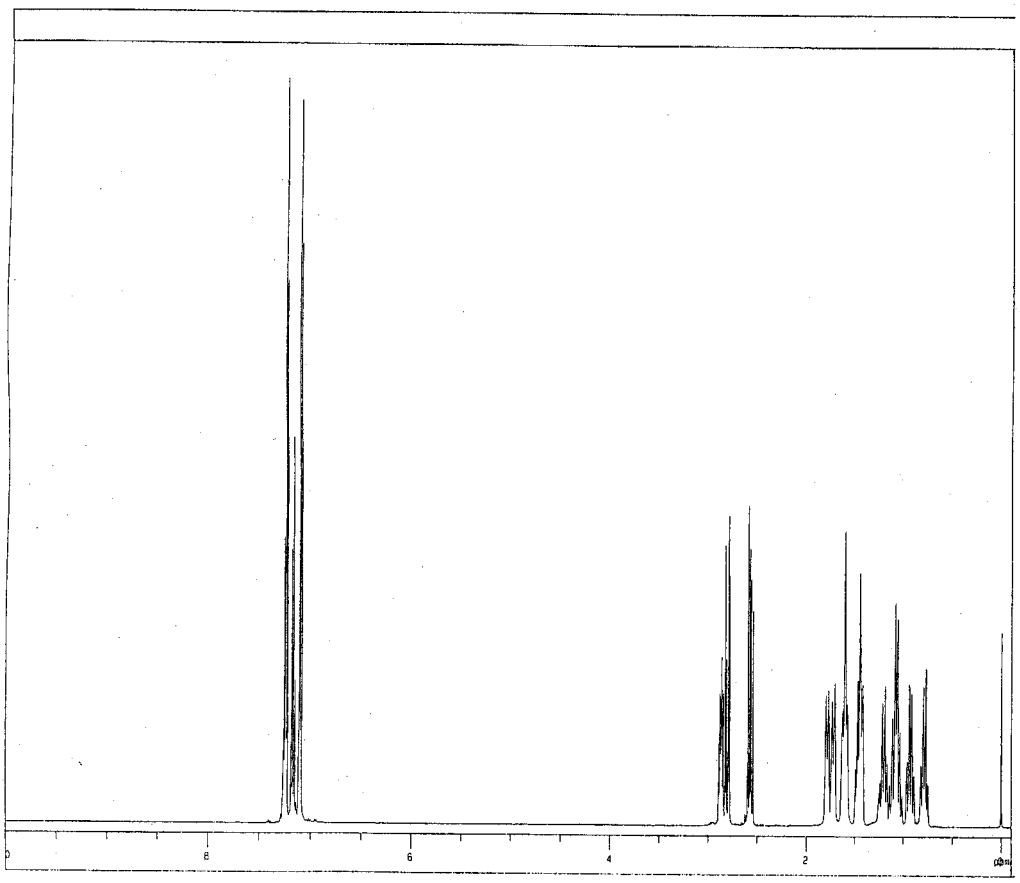


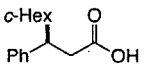
(*R*)-**15** / $CDCL_3$



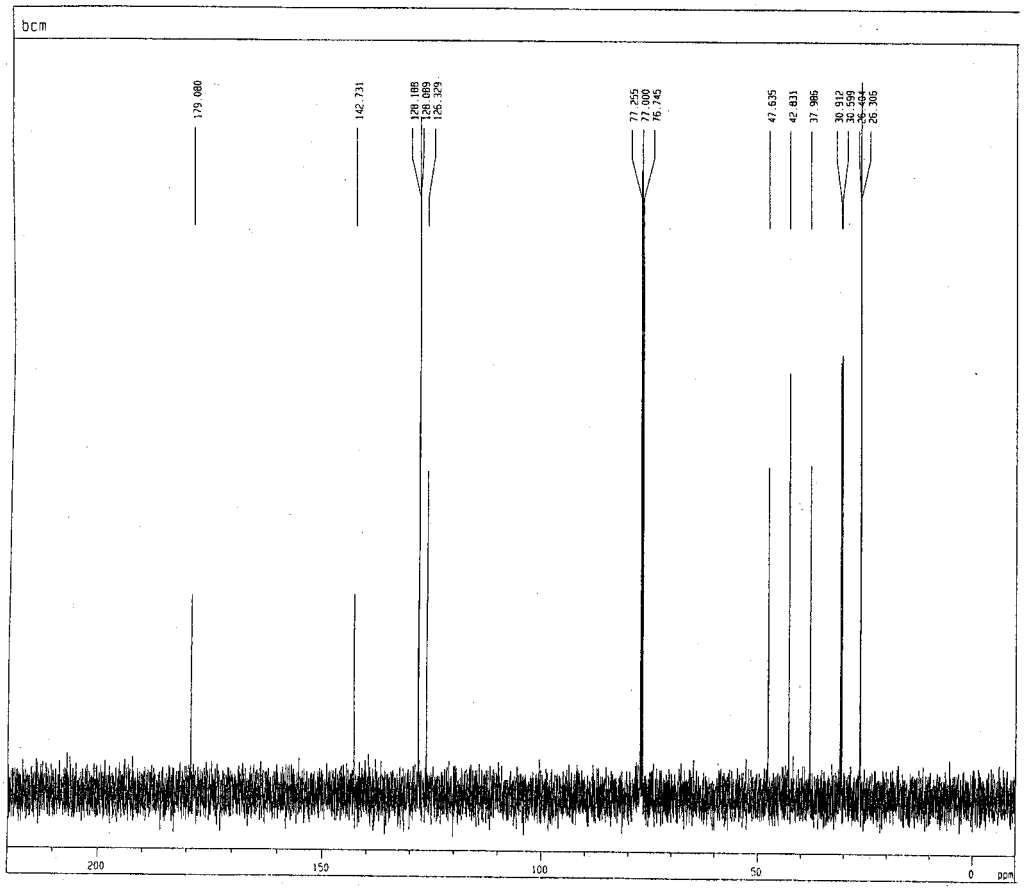


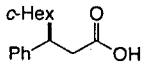
(*R*)-**15** / $CDCL_3$



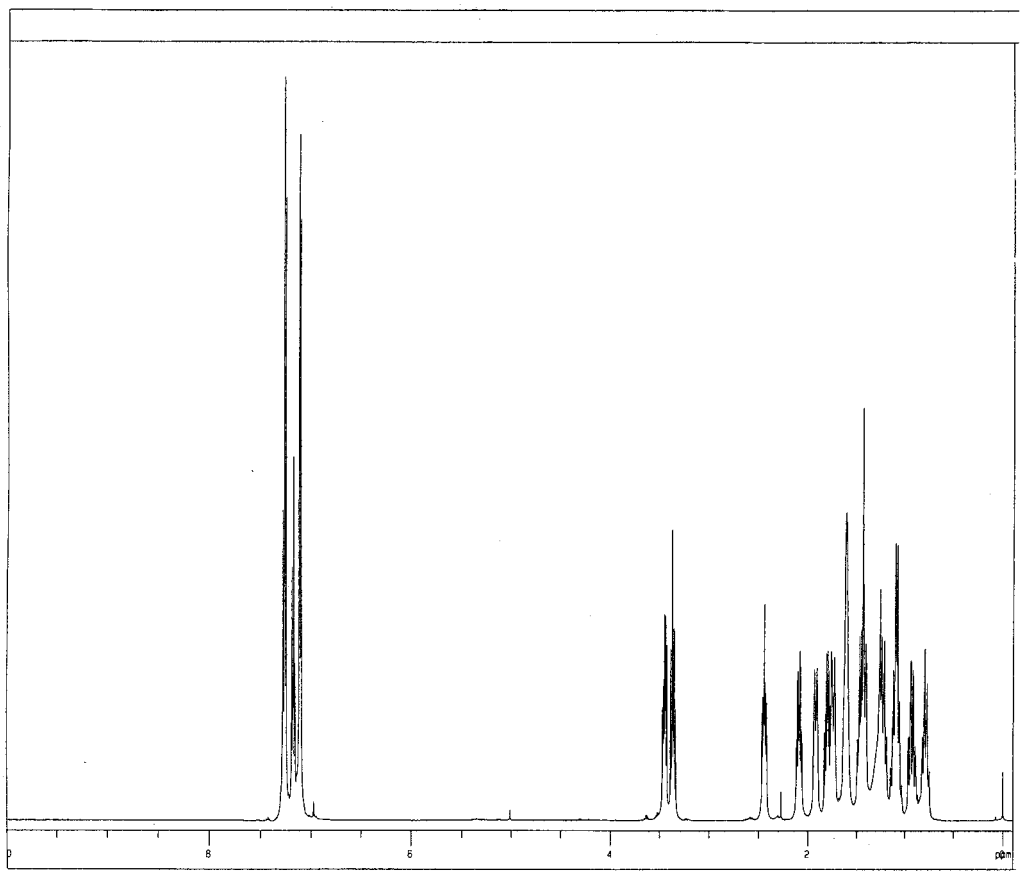


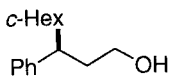
(*R*)-**16** / $CDCL_3$



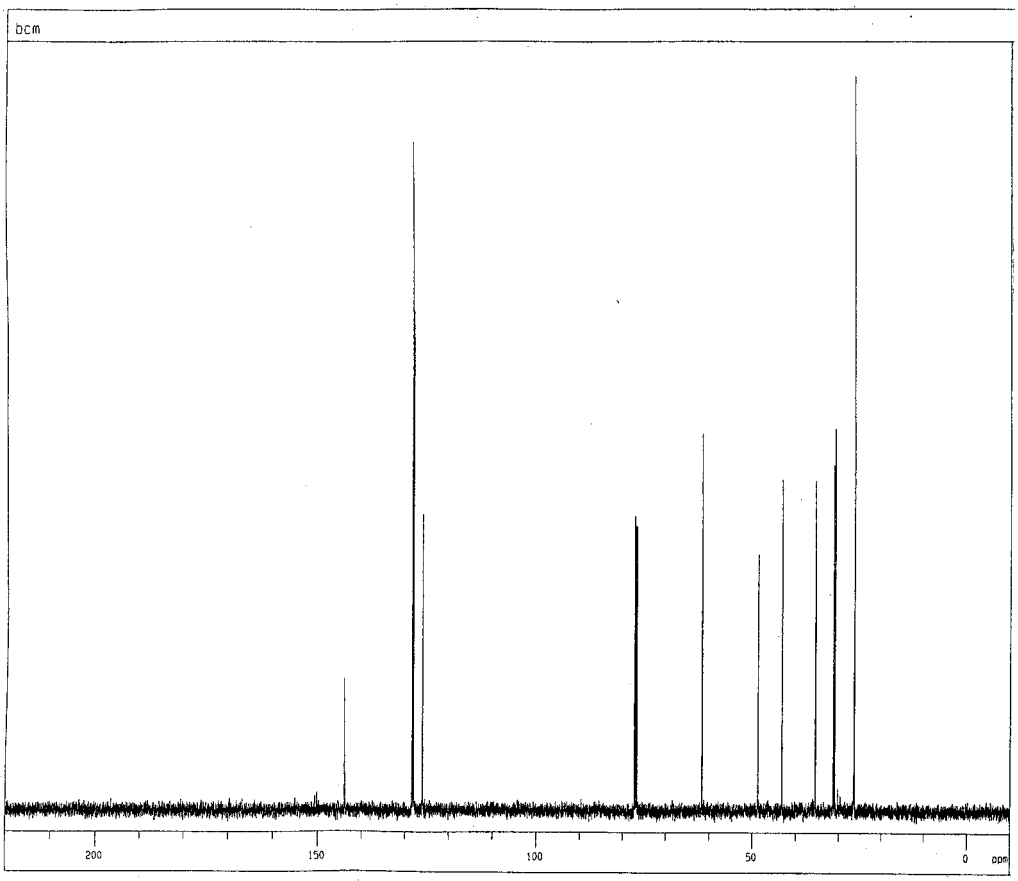


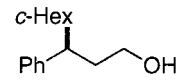
(*R*)-**16** / $CDCL_3$



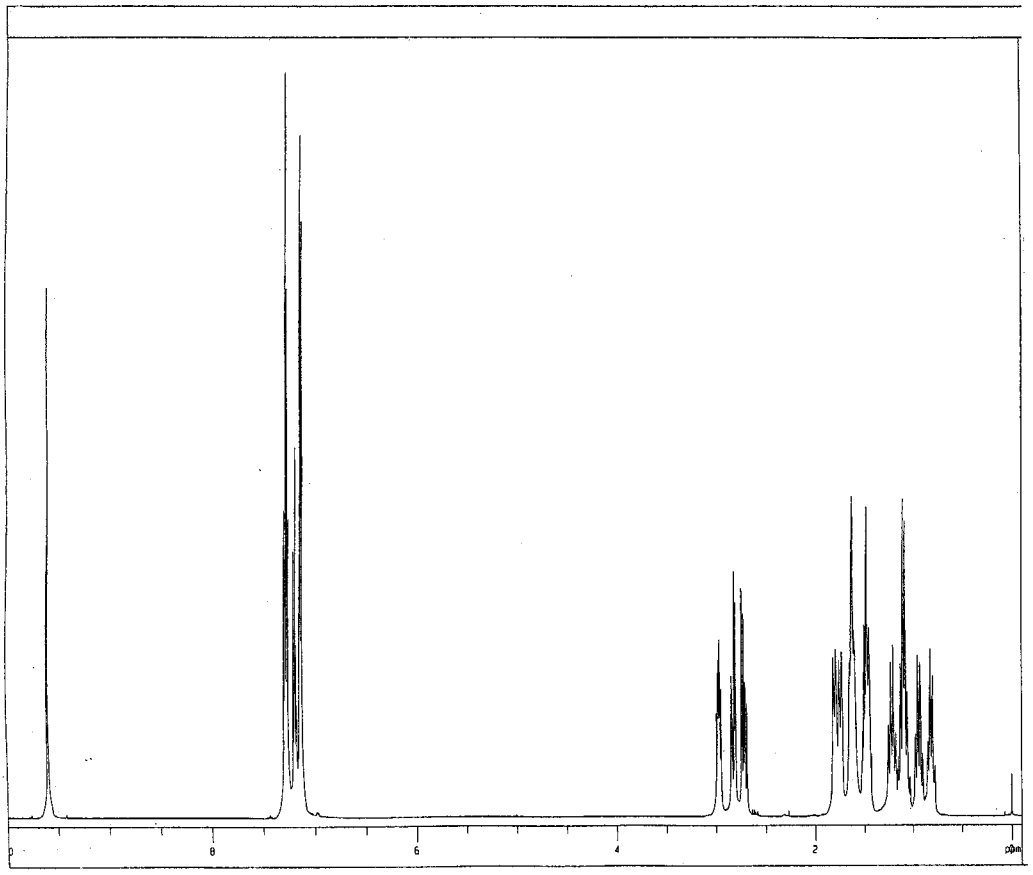


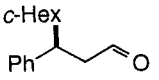
(*R*)-**17** / $CDCL_3$



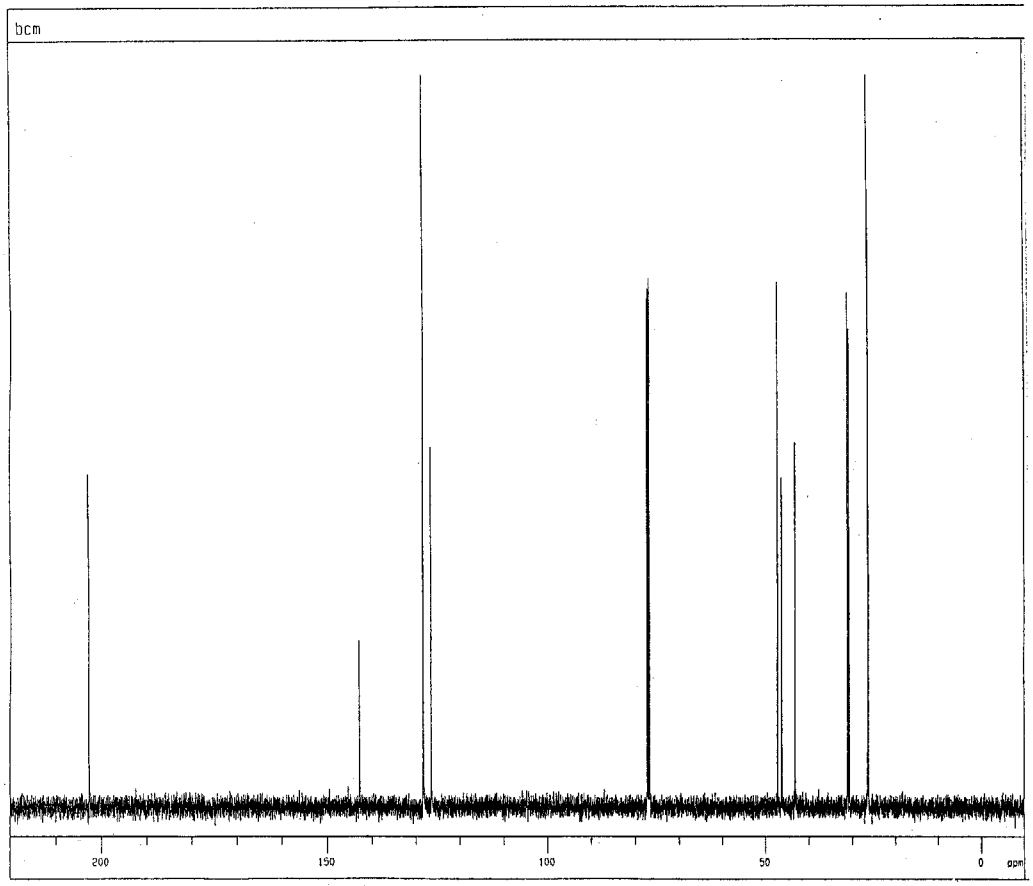


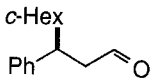
(*R*)-**17** / $CDCL_3$



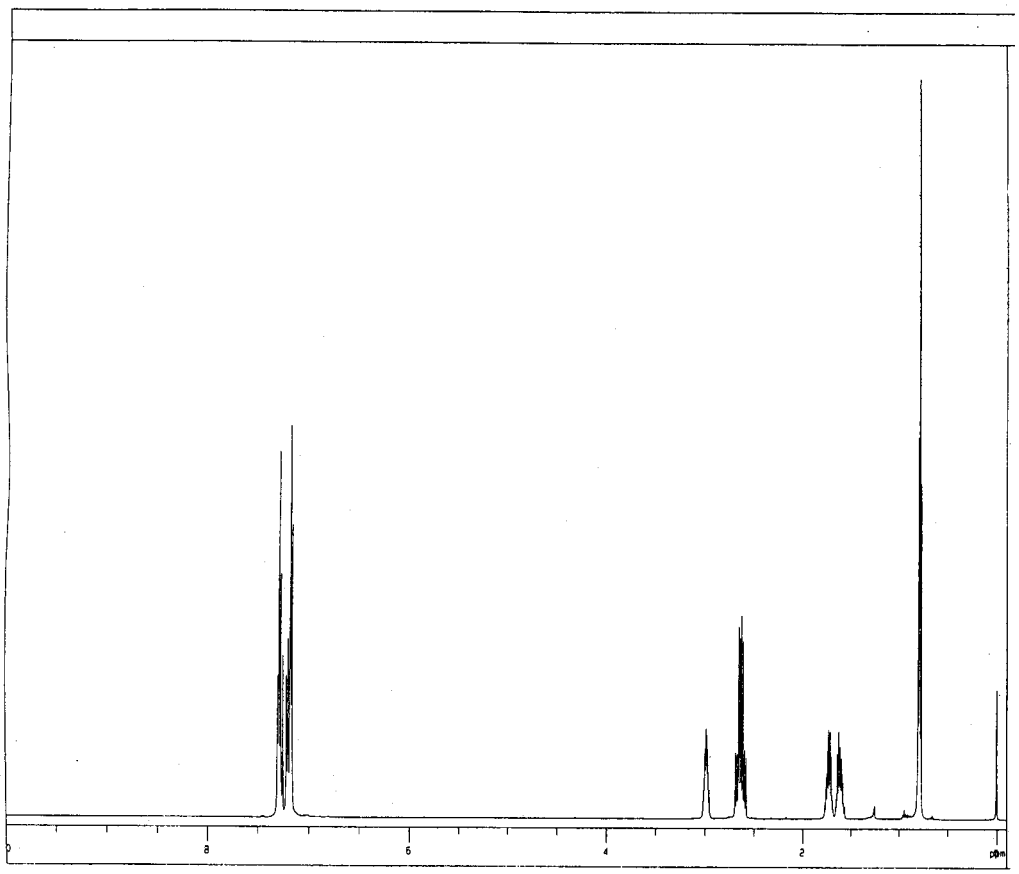


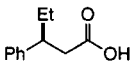
(*R*)-**18** / $CDCL_3$



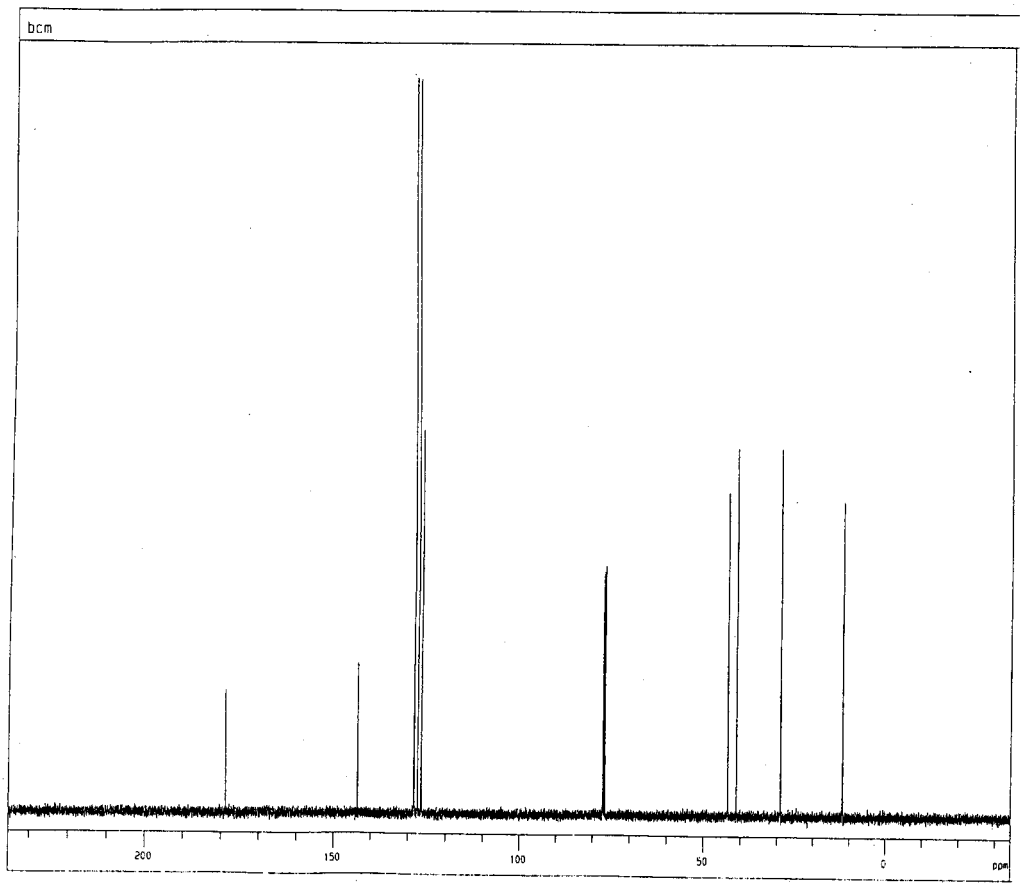


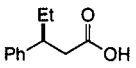
(*R*)-**18** / $CDCL_3$



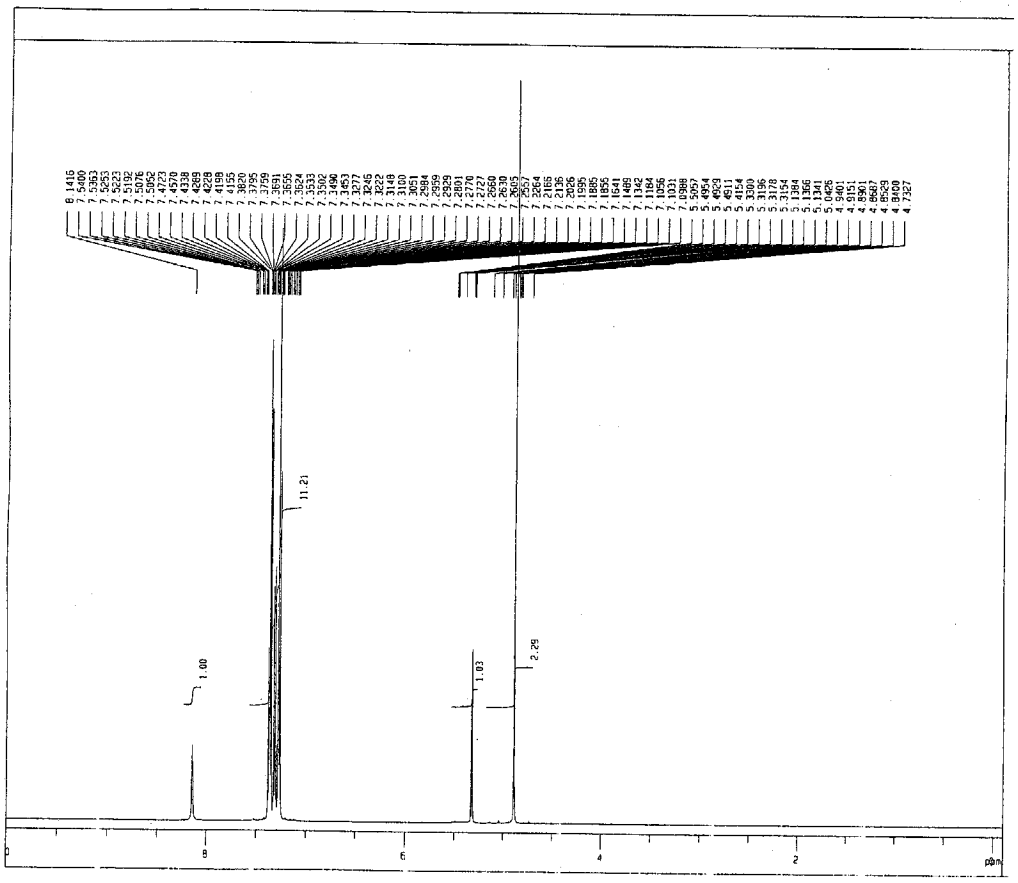


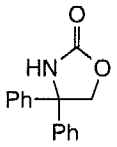
(*S*)-**19** / $CDCL_3$



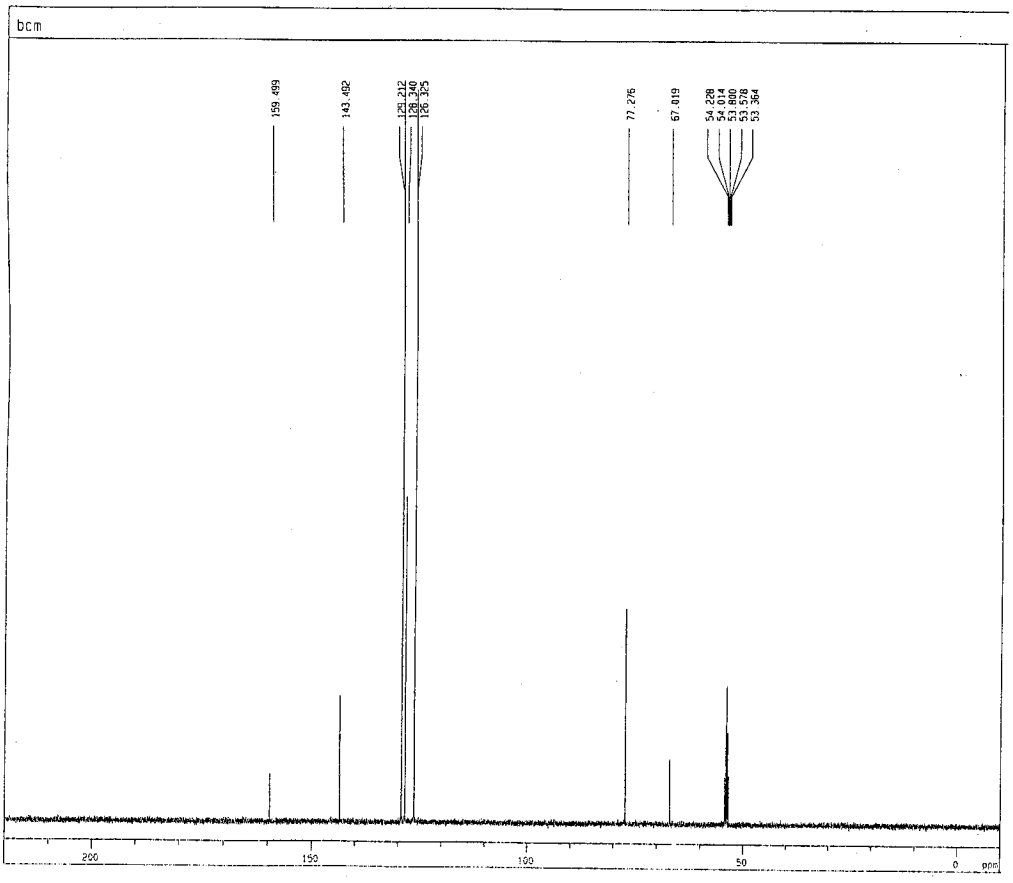


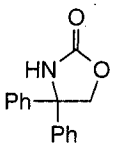
(*S*)-**19** / $CDCL_3$



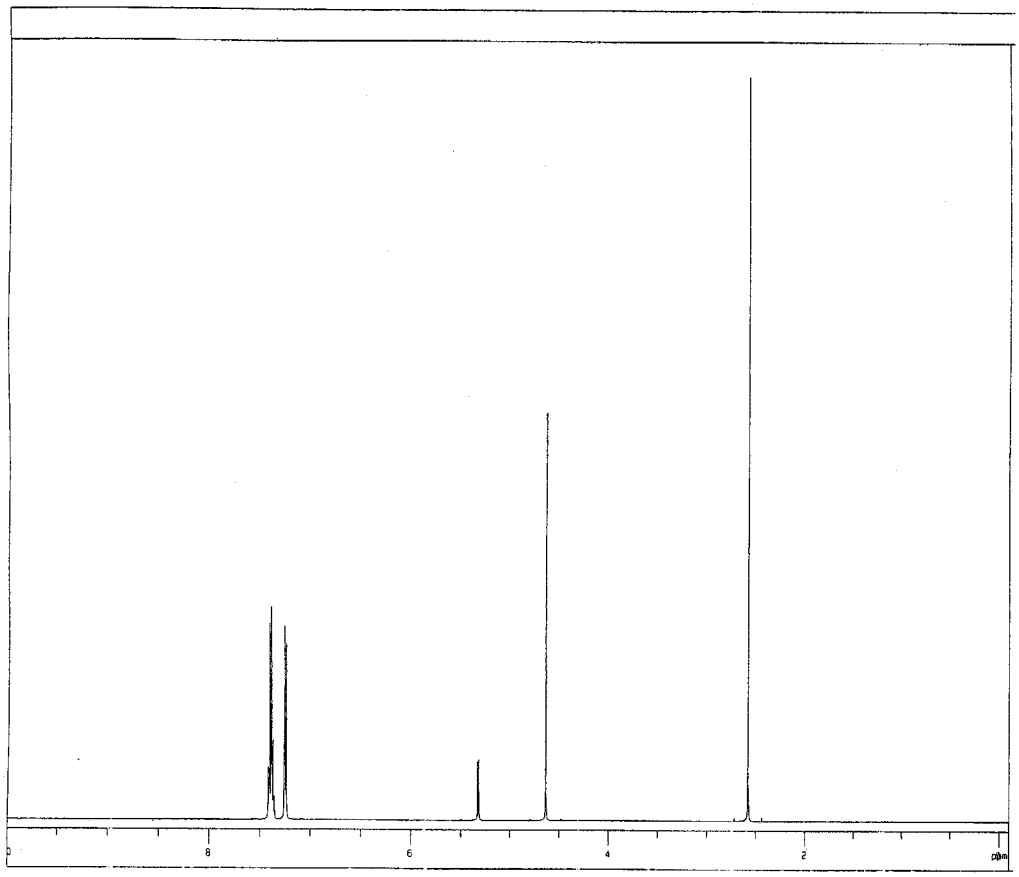


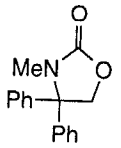
2a / CD_2Cl_2
at –30°C



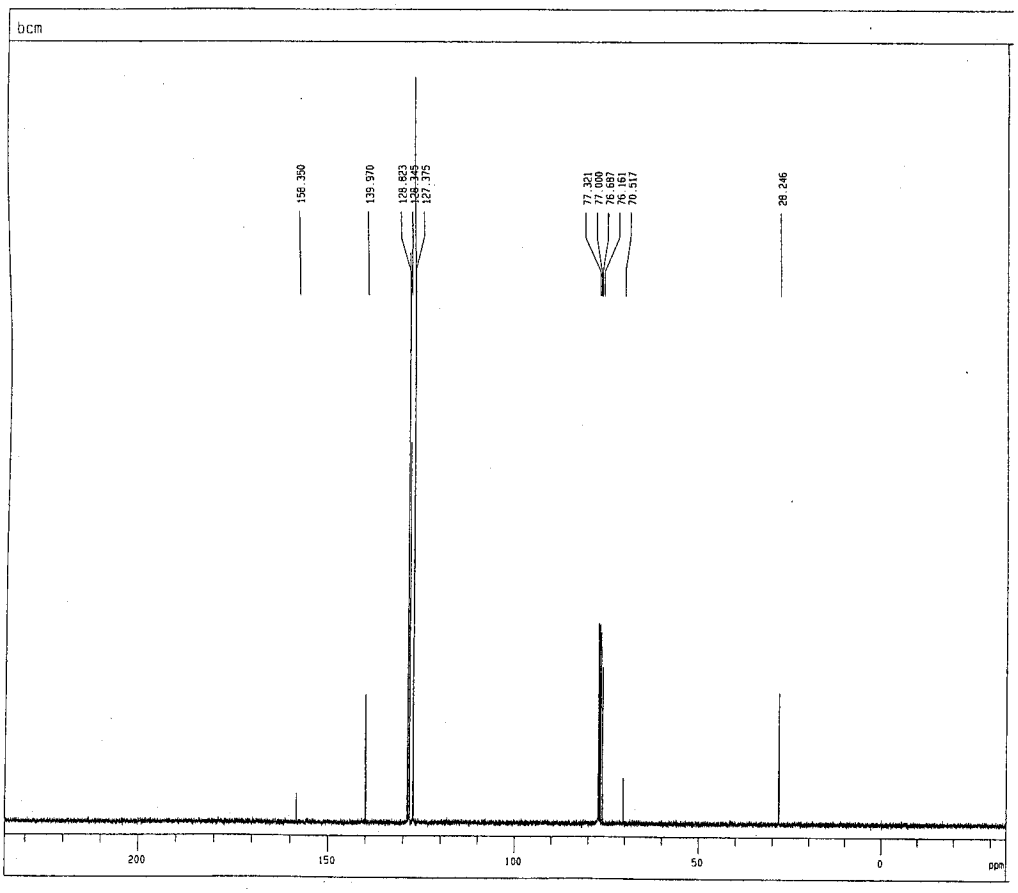


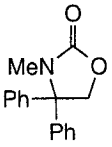
2a / CD_2Cl_2
at rt



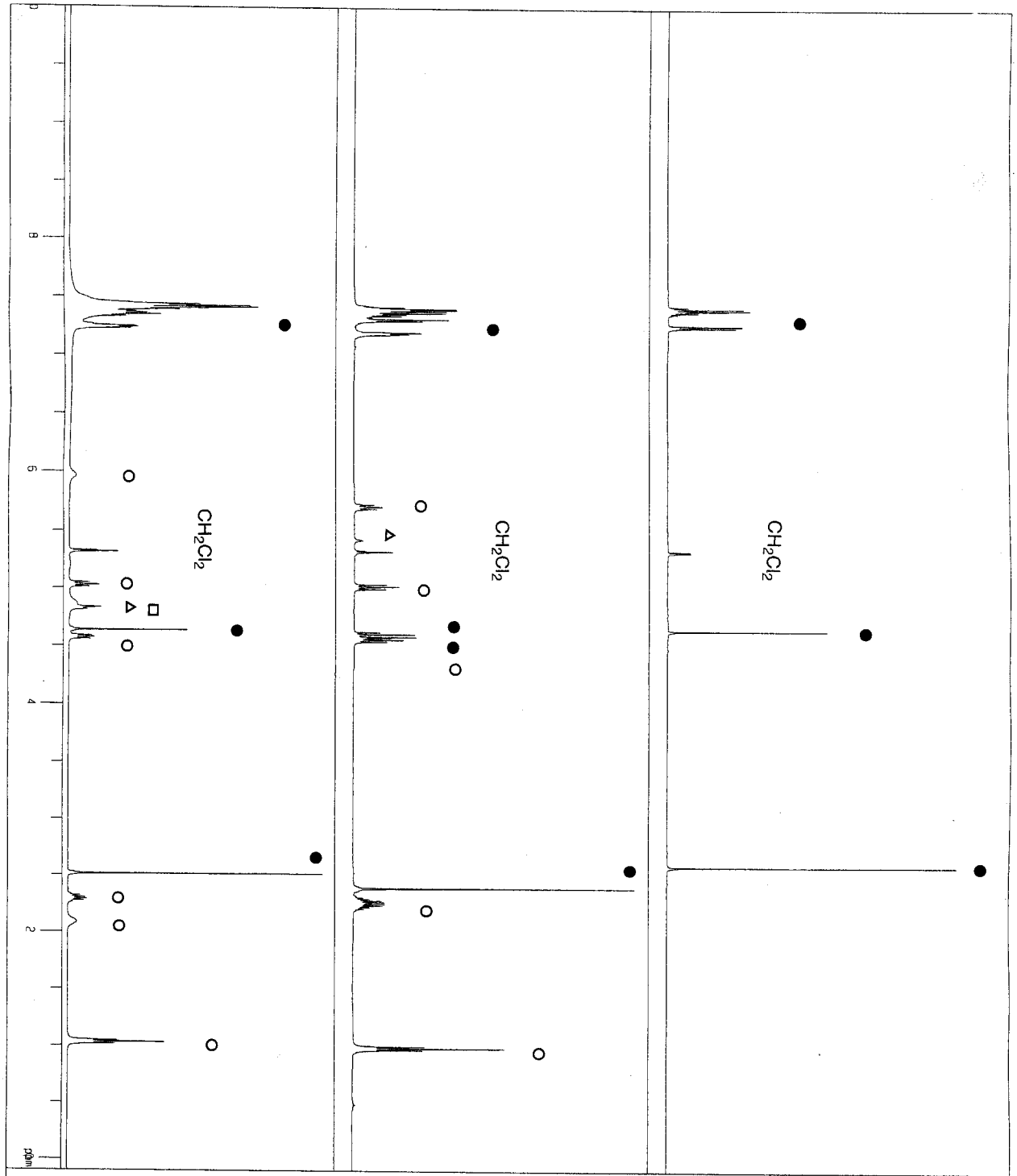


12 / CD_2Cl_2
at –30°C





12 / $CDCl_3$
at rt

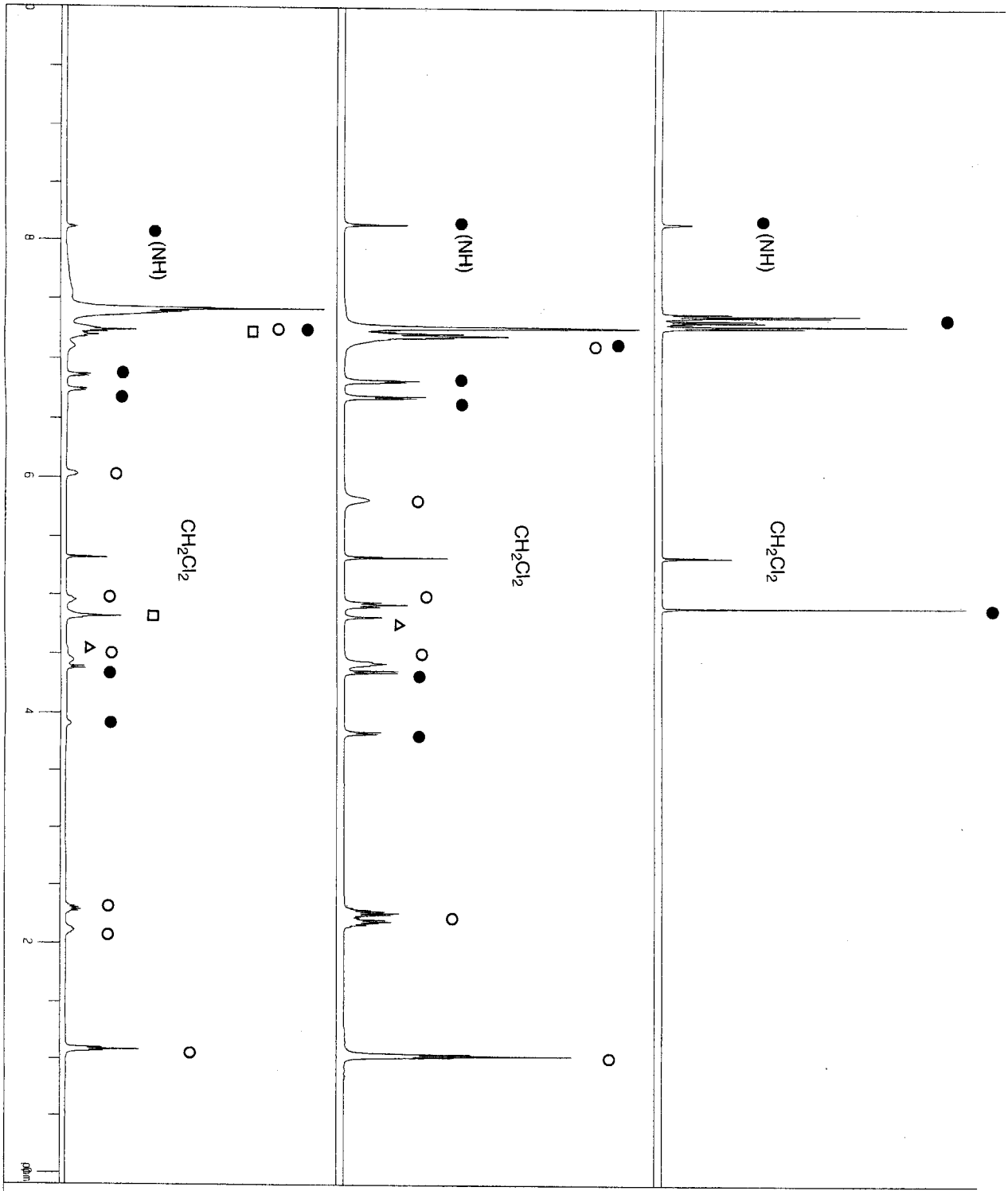


12 / CD_2Cl_2 at –30˚C

3, $Zn(OTf)_2$ and **12** / CD_2Cl_2 at –30˚C

3, $Zn(OTf)_2$, **12** and **2** / CD_2Cl_2 at –30˚C

● : **12**
○ : **3**
□ : **2**
△ : H_2O (contamination)



2a / CD_2Cl_2 at –30°C

3, $Zn(OTf)_2$ and **2a** / CD_2Cl_2 at –30°C

3, $Zn(OTf)_2$, **2a** and **2** / CD_2Cl_2 at –30°C

● : **2a** (CH_2)
○ : **3**
□ : **2**
△ : H_2O (contamination)