Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry


# Supporting information

## Very High Stereoselectivity in Organocatalyzed Desymmetrizing Aldol Reactions of 3-Substituted Cyclobutanones

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## 1. General information:

$^{1}$H NMR spectra were recorded on VARIAN 250, 300 or 500 MHz spectrometers at ambient temperature with $CDCl_3$ as solvent and TMS as internal standard. Data are reported as follows: chemical shifts (δ), multiplicity, integration and coupling constants. $^{13}$C NMR spectra were recorded on the same instruments, operating respectively, at 62, 75 or 124 MHz at ambient temperature with $CDCl_3$ as solvent. Infrared spectra were recorded on a Nicolet Nexus 670 FT-IR spectrophotometer. Low resolution mass spectral analyses were recorded on an Agilent 5973N (Cpsil 32m) in E.I. (70 eV) or C.I. ($NH_3$) mode. Relative intensities are given in parentheses. High resolution mass spectra (HRMS) was recorded on a Finnigan MAT-95 spectrometer using Positive Electro Ionization (ESI) mode. Enantiomeric excesses of aldol products were determined by hplc on a HITACHI L7100 instrument fitted with a HITACHI L-7400 UV detector, using a Daicel Chiralpac AD-H, Chiralcel OD-H or Chiralcel OJ analytical column with *i*-PrOH/hexane as eluent, using authentic racemic samples for reference comparison. Optical rotation values were obtained on a Perkin-Elmer 241 or a PolAAr 32 polarimeter. Microanalyses were carried out on a PerkinElmer 2400 Series II. Analytical thin layer chromatography was performed using 0.25 mm silica gel 60-F plates. Flash chromatography was performed using columns of 70-200 mesh Merk silica gel. Yields refer to chromatographically pure materials. Where a compound has been obtained as a mixture of diastereomers, the NMR data and the chiral hplc data (*ee* values) are reported for the major component.

(±)-Proline and aldehydes **2** were obtained commercially. (2*S*)-*N*-(2-Pyrrolidine-2-carbonyl)-benzenesulfonamide (**II**) was prepared by the literature procedure.[1] 3-Substituted cyclobutanones **1** were prepared by the literature procedures.[2]

[1] A. J. A. Cobb, D. M. Shaw, D. A. Longbottom, J. B. Gold, S. V. Ley, *Org. Biomol. Chem.* 2005, **3**, 84.
[2] a) L. R. Krepski, A. Hasser, *J. Org. Chem.* 1978, **43**, 2879; b) A. Malkov, F. Friscourt, M. Bell, M. E. Swarbrick, P. Kocovsky, *J. Org. Chem*. 2008, **73**, 3996.

**2. Experimental procedures for the synthesis of optically active 2,3-disubstituted cyclobutanones 3 and characterization data.**

**General procedure for the synthesis of authentic racemic samples:** To a solution of aldehyde **2** (0.5 mmol) and 3-substituted cyclobutanone **1** (10 mmol) in DMSO (2 mL) was added (±)-proline (0.05 mmol). The resulting mixture was stirred at room temperature for 96 h. The reaction was quenched with saturated aqueous ammonium chloride (10 mL). The reaction mixture was extracted several times with EtOAc (2 × 10 mL) and the combined organic layers were dried over anhydrous $Na_2SO_4$. After removal of solvent, the residue was purified by flash column chromatography to give the corresponding aldol product **3** .

**General procedure for the enantioselective organocatalyzed aldol reactions:** To a solution of aldehyde **2** (0.5 mmol) and 3-substituted cyclobutanone **1** (10 mmol) in anhydrous $CH_2Cl_2$ (2 mL) was added (2*S*)-*N*-(2-Pyrrolidine-2-carbonyl)-benzenesulfonamide **II** (0.05 mmol). The resulting mixture was stirred at room temperature for 96 h. The reaction was quenched with saturated aqueous ammonium chloride (10 mL). The reaction mixture was extracted with EtOAc (2 × 10 mL) and the combined organic layers were dried over anhydrous $Na_2SO_4$. After removal of solvent, the residue was purified by flash column chromatography to give the corresponding aldol product **3**.

**2-(hydroxy(4-nitrophenyl)methyl)-3-phenyl-cyclobutanone 3aa:** Purified using flash column chromatography (hexane/ether, 1:1) to give the title compound (71% yield) as a mixture of diastereoisomers (dr = 98:2). Orange oil. IR (neat): 3460, 1700 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$) δ: 3.25 (ddd, 1H, $J$ = 2.4 Hz, $J$ = 8.4 Hz, $J$ = 18.0 Hz), 3.41 (ddd, 1H, $J$ = 1.8 Hz, $J$ = 9.0 Hz, $J$ = 17.4 Hz), 3.56 (q, 1H, $J$ = 8.4 Hz), 3.76 (tt, 1H, $J$ = 2.1 Hz, $J$ = 6.7 Hz), 5.13 (d, 1H, $J$ = 6.6 Hz), 7.07-7.29 (m, 5H), 7.54 (d, 2H, $J$ = 8.7 Hz), 8.14 (d, 2H, $J$ = 9.0 Hz). $^{13}C$ NMR (75 MHz, $CDCl_3$) δ: 32.7, 52.5, 72.3, 72.8, 123.7, 126.3, 126.9, 127.2, 128.7, 141.5, 147.5, 147.9, 206.7. MS *m/z*: 297 ($M^+$-18 (80)), 251 (14), 234 (63), 204 (100), 189 (44), 165 (18), 115 (100), 89 (34). Anal. Calcd. for

$C_{17}H_{15}NO_4$; C, 68.88; H, 5.09; N, 4.71. Found: C, 68.80; H, 5.12; N, 4.62. The *ee* was determined to be 99% *ee* by HPLC (Chiralcel AD-H column, hexane/*i*-PrOH = 90:10, flow rate 1.0 mL/min, λ = 254 nm) $t_R$(major) = 18.71 min, $t_R$(minor) = 16.68 min.

**2-(hydroxy(4-cyanophenyl)methyl)-3-phenyl-cyclobutanone 3ab:** Purified using flash column chromatography (hexane/ether, 5:1→1:1) to give the title compound (76 % yield) as a mixture of diastereoisomers (dr = 97:3). Orange oil. IR (neat): 3450, 1720 $cm^{-1}$. $^1$H NMR (300 MHz, $CDCl_3$) δ: 3.08 (br s, 1H), 3.22 (ddd, 1H, *J* = 2.1 Hz, *J* = 8.1 Hz, *J* = 17.4 Hz), 3.37 (ddd, 1H, *J* = 2.1 Hz, *J* = 8.7 Hz, *J* = 17.7 Hz), 3.52 (q, 1H, J = 8.7 Hz), 3.67-3.73 (m, 1H), 5.05 (d, 1H, *J* = 6.3 Hz), 7.06 (d, 2H, *J* = 6.6 Hz), 7.18-7.30 (m, 3H), 7.47 (d, 2H, *J* = 8.1 Hz), 7.57 (d, 2H, *J* = 6.6 Hz). $^{13}$C NMR (75 MHz, $CDCl_3$) δ: 32.6, 52.4, 72.5, 72.9, 111.7, 118.5, 126.3, 126.9, 127.1, 128.7, 132.3, 141.6, 146.0, 206.7. MS *m/z*: 259 ($M^+$-18 (40)), 230 (20), 216 (15), 190 (9), 104 (100), 78 (10). Anal. Calcd. for $C_{18}H_{15}NO_2$: C, 77.96; H, 5.45; N, 5.05. Found: C, 77.91; H, 5.49; N, 5.09. The *ee* was determined to be 98% *ee* by HPLC (Chiralcel OD-H column, hexane/*i*-PrOH = 85:15, flow rate 1.0 mL/min, λ = 254 nm) $t_R$(major) = 20.61 min, $t_R$(minor) = 19.18 min.

**2-(hydroxy(4-chlorophenyl)methyl)-3-phenyl-cyclobutanone 3ac:** Purified using flash column chromatography (hexane/ether, 5:1→1:1) to give the title compound (64 % yield) as a mixture of diastereoisomers (dr = 98:2). Yellow oil. IR (neat): 3440, 1710 $cm^{-1}$. $^1$H NMR (500 MHz, $CDCl_3$) δ: 3.25 (ddd, 1H, *J* = 2.7 Hz, *J* = 8.7 Hz, *J* = 15 Hz), 3.39 (ddd, 1H, *J* = 1.8 Hz, *J* = 8.7 Hz, *J* = 17.4 Hz), 3.51 (q, 1H, *J* = 8.4 Hz), 3.76 (tt, 1H, *J* = 2.1 Hz, *J* = 7.5 Hz), 5.00 (d, 1H, *J* = 6.3 Hz), 7.06 (d, 2H, *J* = 6.9 Hz), 7;20-7.40 (m, 7H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ: 32.7, 52.1, 72.9, 73.4, 126.5, 126.8, 128.0, 128.8, 128.9, 131.6, 139.2, 141.9, 207.4. MS *m/z*: 268 ($M^+$-18 (38)), 233 (87), 205 (75), 189 (40), 164 (43), 136 (34), 104 (100), 78 (15). Anal. Calcd. for $C_{17}H_{15}ClO_2$: C, 71.21; H, 5.27. Found: C, 71.28; H, 5.21. The *ee* was determined to be 84% *ee* by HPLC (Chiralcel AD-H column, hexane/*i*-PrOH = 95:5, flow rate 1.0 mL/min, λ = 254 nm) $t_R$(major) = 36.30 min, $t_R$(minor) = 38.40 min.

**2-(hydroxy(4-fluorophenyl)methyl)-3-phenyl-cyclobutanone 3ad:**

Purified using flash column chromatography (hexane/ether, 5:1→1:1) to give the title compound (66 % yield) as a mixture of diastereoisomers (dr = 96:4). Yellow oil. IR (neat): 3454, 1780 $cm^{-1}$. $^{1}H$ NMR (500 MHz, $CDCl_3$) δ: 3.17 (ddd, 1H, *J* = 2.5 Hz, *J* = 8.5 Hz, *J* = 17.5 Hz), 3.30 (ddd, 1H, *J* = 2.0 Hz, *J* = 9.0 Hz, *J* = 17.5 Hz), 3.42 (q, 1H, *J* = 8.5 Hz), 3.65 (t, 1H, *J* = 6.9 Hz) , 4.92 (d, 1H, *J* = 6.7 Hz), 6.91-7.32 (m, 9H). $^{13}C$ NMR (124 MHz, $CDCl_3$) δ: 32.7, 51.9, 72.9, 73.5, 126.5, 126.7, 128.4 (d, *J* = 8.2 Hz), 128.6, 136.5, 142.0, 162.5 (d, *J* = 12.0 Hz), 207.6. MS *m/z*: 270 ($M^+$-18 (3)), 207 (4), 161 (22), 125 (100), 105 (33), 91(20), 77 (19). Anal. Calcd. for $C_{17}H_{15}FO_2$: C, 75.54; H, 5.59. Found: C, 75.50; H, 5.61. The *ee* was determined to be 81% *ee* by HPLC (Chiralcel AD-H column, hexane/*i*-PrOH = 95:5, flow rate 1.0 mL/min, λ = 254 nm) $t_R$(major) = 29.30 min, $t_R$(minor) = 22.45 min.

**2-((4-(trifluoromethyl)phenyl)(hydroxy)methyl)-3-phenyl-cyclobutanone 3ae:** Purified using flash column chromatography (hexane/ether, 5:1→1:1) to give the title compound (51 % yield) as a mixture of diastereoisomers (dr = 98:2). Yellow oil. IR (neat): 3441, 1775 $cm^{-1}$. $^{1}H$ NMR (500 MHz, $CDCl_3$) δ: 3.26 (ddd, 1H, *J* = 2.5 Hz, *J* = 8.4 Hz, *J* =17.5 Hz), 3.39 (ddd, 1H, *J* = 2.0 Hz, *J* = 9.0 Hz, *J* = 17.5 Hz), 3.53 (q, 1H, *J* = 8.5 Hz), 3.75 (br t, 1H, *J* = 7.5 Hz), 5.09 (d, 1H, *J* = 6.5 Hz), 7.04 (d, 2H, *J* = 7.0 Hz), 7.19-7.29 (m, 3H), 7.51 (d, 2H, *J* = 8.5 Hz), 7.58 (d, 2H, *J* = 8.0 Hz). $^{13}C$ NMR (124 MHz, $CDCl_3$) δ: 32.7, 52.2, 72.9, 73.3, 125.5, 125.6, 126.4, 126.8, 126.9, 128.7, 141.7, 144.6 (d, *J* = 1.3 Hz), 207.0. MS *m/z*: 320 ($M^+$-18 (15)), 301 (4), 161 (40), 145 (9), 127 (11), 104 (100), 77 (12). Anal. Calcd. for $C_{18}H_{15}F_3O_2$: C, 67.5; H, 4.72. Found: C, 67.3; H, 4.70. The *ee* was determined to be 91% *ee* by HPLC (Chiralcel AD-H column, hexane/*i*-PrOH = 90:10, flow rate 1.0 mL/min, λ = 254 nm) $t_R$(major) = 11.57 min, $t_R$(minor) = 13.74 min.

**2-(hydroxy(3-nitrophenyl)methyl)-3-phenyl-cyclobutanone 3af:** Purified using flash column chromatography (hexane/ether, 5:1→1:1) to give the title compound (51 % yield) as a mixture of diastereoisomers (dr = 99:1). Yellow oil. IR (neat): 3478, 1779 $cm^{-1}$. $^{1}H$ NMR (500 MHz,

$CDCl_3$) δ: 2.95 (br s, 1H), 3.27 (dd, 1H, *J* = 8.9 Hz, *J*= 17.6 Hz), 3.43 (dd, 1H, *J*= 8.9 Hz, *J*= 17.6 Hz), 3.56 (q, 1H, *J*= 8.4 Hz), 3.77 (m, 1H), 5.14 (d, 1H, *J*= 6.8 Hz), 7.09 (d, 2H, *J*= 7.7 Hz), 7.20 (d, 1H, *J*= 7.1 Hz), 7.25 (m, 2H), 7.50 (t, 1H, *J* = 8.0 Hz), 7.74 (d, 1H, *J*= 7.5 Hz), 8.12 (d, 1H, *J* = 8.3 Hz), 8.23 (s, 1H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ: 32.9, 52.6, 72.6, 73.1, 121.5, 123.0, 126.4, 127.0, 128.8, 129.6, 132.5, 141.4, 142.5, 142.8, 148.3, 206.8. MS *m/z*: 297 ($M^+$ (3)), 279 (6), 255 (30), 239 (74), 220 (40), 193 (12), 150 (34), 104 (100), 77 (39). Anal. Calcd. for $C_{17}H_{15}NO_4$: C, 68.68; H, 5.09, N, 4.71. Found: C, 68.70; H, 5.11, N, 4.72. The *ee* was determined to be 95% *ee* by HPLC (Chiralcel AD-H column, hexane/*i*-PrOH = 90:10, flow rate 1.0 mL/min, λ = 254 nm) $t_R$(major) = 23.62 min, $t_R$(minor) = 21.42 min.

**3-(4-chlorophenyl)-2-(hydroxy(4-nitrophenyl)methyl)cyclobutanone 3ba:** *Syn* and *anti* diastereomers were separated by flash column chromatography (hexane/ether, 5:1→1:1) to yield two samples. *Anti*-**3ba** (69 % yield). Yellow oil. IR (neat): 3460, 1700 cm$^{-1}$. $^1$H NMR (300 MHz, $CDCl_3$) δ: 3.22 (ddd, 1H, *J* = 2.5 Hz, *J* = 8.4 Hz, *J* =17.5 Hz), 3.41 (ddd, 1H, *J* = 2.0 Hz, *J* = 9.0 Hz, *J* = 17.5 Hz), 3.54 (q, 1H, *J* = 8.5 Hz), 3.71 (br t, 1H, *J* = 7.0 Hz), 5.14 (d, 1H, *J* = 6.5 Hz), 7.04 (d, 2H, *J* = 7.0 Hz), 7.25 (m, 2H), 7.57 (d, 2H, *J* = 8.6 Hz), 8.19 (d, 2H, *J* = 8.6 Hz). $^{13}$C NMR (75 MHz, $CDCl_3$) δ: 32.3, 52.6, 72.4, 72.9, 123.9, 126.5, 127.3, 127.8, 128.8, 128.9, 140.1, 147.7, 205.9. MS *m/z*: 313 ($M^+$-18 (13)), 296 (11), 278 (9), 203 (19), 189 (20), 138 (100), 101 (18), 75 (8). Anal. Calcd. for $C_{17}H_{14}ClNO_4$: C, 61.55; H, 4.25; N, 4.22. Found: C, 61.51; H, 4.30; N, 4.18. The *ee* was determined to be 97% *ee* by HPLC (Chiralcel OJ column, hexane/*i*-PrOH = 80:20, flow rate 1.0 mL/min, λ = 254 nm) $t_R$(major) = 38.85 min, $t_R$(minor) = 48.35 min. *Syn*-**3ba'** (8 % yield). White solid, mp: 144 °C. IR (KBr): 3487, 1780 cm$^{-1}$. $^1$H NMR (250 MHz, $CDCl_3$) δ: 3.18 (ddd, 1H, *J* = 2.5 Hz, *J* = 8.4 Hz, *J* =17.5 Hz), 3.45 (ddd, 1H, *J* = 2.0 Hz, *J* = 9.0 Hz, *J* = 17.5 Hz), 3.69-3.72 (m, 1H), 3.83 (q, 1H, *J* = 8.5 Hz), 5.39 (d, 1H, *J* = 6.5 Hz), 6.90 (d, 2H, *J* = 8.4 Hz), 7.17 (d, 2H, *J* = 8.4 Hz), 7.52 (d, 2H, *J* = 8.6 Hz), 8.17 (m, 2H). $^{13}$C NMR (62 MHz, $CDCl_3$) δ: 30.1, 52.9, 69.8, 73.5, 123.8, 126.5, 127.8, 128.8, 140.8, 147.4, 148.3, 206.2. MS *m/z* (CI, $NH_3$): 349 ($M^+$+18 (100)),

331 (4), 284 (9), 242 (8), 139 (17), 137 (38), 122 (22). HRMS (ESI) calcd for M-H ($C_{17}H_{14}ClNO_4$): 330.0539; found 330.0543.

**3-(4-bromophenyl)-2-(hydroxy(4-nitrophenyl)methyl)cyclobutanone 3ca:** Purified using flash column chromatography (hexane/ether, 1:1) to give the title compound (63 % yield) as a mixture of diastereoisomers (dr = 96:4). Yellow solid. IR (neat): 3505, 1784 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$) 2.86 (m, 1H), 3.21 (ddd, 1H, *J* = 2.5 Hz, *J* = 8.0 Hz, *J* = 17.5 Hz), 3.41 (ddd, 1H, *J* = 2.0 Hz, *J* = 9.5 Hz, *J* = 18.0 Hz), 3.53 (q, 1H, *J* = 8.5 Hz), 3.65-3.75 (m, 1H), 5.14 (d, 1H, *J* = 6.5 Hz), 6.98 (d, 2H, *J* = 8.5 Hz), 7.40 (d, 2H, *J* = 8.5 Hz), 7.56 (d, 2H, *J* = 8.5 Hz), 8.19 (d, 2H, *J* = 8.5 Hz). $^{13}C$ NMR (124 MHz, $CDCl_3$) δ: 32.3, 52.5, 72.3, 72.9, 120.9, 123.9, 127.3, 128.2, 131.9, 140.6, 147.7, 205.8. MS *m/z*: 377 ($M^+$(2)), 360 (5), 358 (5), 240 (10), 242 (11), 184 (94), 182 (100), 150 (22), 115 (24), 103 (63), 77 (81), 51 (60), 43 (26). Anal. Calcd. For $C_{17}H_{14}BrNO_4$: C, 54.27; H, 3.75; N, 3.72. Found: C, 54.47.; H, 3.65; N, 4.80. The *ee* was determined to be 89% *ee* by HPLC (Chiralcel AD-H column, hexane/*i*-PrOH = 90:10, flow rate 1.0 mL/min, λ = 254 nm) $t_R$(major) = 48.13 min, $t_R$(minor) = 45.54 min.

**2-(hydroxy(4-nitrophenyl)methyl)-3-(*p*-tolyl)cyclobutanone 3da:** Purified using flash column chromatography (hexane/ether, 1:1) to give the title compound (74 % yield) as a mixture of diastereoisomers (dr = 93:7). Yellow solid. IR (neat): 3521, 1781 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$) δ: 2.31 (s, 3H), 2.93-3.11 (m, 1H), 3.23 (ddd, 1H, *J* = 2.4 Hz, *J* = 8.4 Hz, *J* = 17.4 Hz), 3.36 (ddd, 1H, *J* = 2.1 Hz, *J* = 8.7 Hz, *J* = 17.4 Hz), 3.53 (q, 1H, *J* = 8.4 Hz), 3.71 (tt, 1H, *J* = 2.2 Hz, *J* = 6.6 Hz)), 5.13 (d, 1H, *J* = 6.6 Hz), 6.97 (d, 2H, *J* = 8.1 Hz), 7.08 (d, 2H, *J* = 7.2 Hz), 7.55 (d, 2H, *J* = 8.7 Hz), 8.16 (d, 2H, *J* = 8.7 Hz). $^{13}C$ NMR (75 MHz, $CDCl_3$) δ: 20.9, 32.4, 52.6, 72.5, 72.8, 123.7, 125.4, 126.2, 127.3, 129.4, 136.7, 138.5, 147.9, 207.1. MS *m/z*: 293 ($M^+$-18 (35)), 278 (14), 218 (8), 202 (20), 118 (100). Anal. Calcd. For $C_{18}H_{17}NO_4$: C, 69.44; H, 5.50; N, 4.50. Found: C, 69.21; H, 5.38; N, 4.80. The *ee* was determined to be 83% *ee* by HPLC (Chiralcel OD-H column, hexane/*i*-PrOH = 85:15, flow rate 1.0 mL/min, λ = 254 nm) $t_R$(major) = 16.79 min, $t_R$(minor) = 11.99 min.

**3-*n*-hexyl-2-(hydroxy(4-nitrophenyl)methyl)cyclobutanone 3ea:** Purified using flash column chromatography (hexane/ether, 1:1) to give the title compound (70 % yield) as a mixture of diastereoisomers (dr = 98:2). Orange oil. IR (neat): 3440, 1730 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$) δ: 0.84 (t, 3H, *J* = 7.5 Hz), 1.00-1.50 (m, 10H), 2.22 (q, 1H, *J* = 7.5 Hz), 2.69 (ddd, 1H, *J* = 2.4 Hz, *J* = 7.5 Hz, *J* = 17.4 Hz), 2.70-2.90 (m, 1H), 3.04-3.17 (m, 2H), 4.97 (d, 1H, *J* = 7.5 Hz), 7.56 (d, 2H, *J* = 9.0 Hz), 8.23 (d, 2H, *J* = 9.0 Hz). $^{13}C$ NMR (75 MHz, $CDCl_3$) δ: 13.9, 22.4, 27.6, 28.2, 28.8, 31.5, 35.8, 50.6, 71.1, 72.9, 123.8, 127.1, 147.6, 148.3, 208.5. MS *m/z*: 287 ($M^+$-18 (25)), 270 (100), 241 (28), 217 (15), 175 (16), 128 (68), 101 (14). Anal. Calcd. for $C_{17}H_{23}NO_4$: C, 66.86; H, 7.59; N, 4.59. Found: C, 66.89; H, 7.50; N, 4.68. The *ee* was determined to be >99% *ee* by HPLC (Chiralcel OD-H column, hexane/*i*-PrOH = 85:15, flow rate 1.5 mL/min, λ = 254 nm) $t_R$(major) = 6.76 min, $t_R$(minor) = 5.87 min.

**2-(hydroxy(4-nitrophenyl)methyl)-3-phenethyl-cyclobutanone 3fa:** Purified using flash column chromatography (hexane/ether, 1:1) to give the title compound (60 % yield) as a mixture of diastereoisomers (dr = 99:1). Orange oil. IR (neat): 3486, 1773 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$) δ: 1.56-1.79 (m, 2H), 2.14-2.27 (m, 1H), 2.35-2.45 (m, 1H), 2.50-2.59 (m, 1H), 2.67 (ddd, 1H, *J* = 4.8 Hz, *J* = 7.5 Hz, *J* = 17.4 Hz), 3.05 (ddd, 1H, *J* = 2.4 Hz, *J* = 8.7 Hz, *J* = 17.4 Hz), 3.11-3.18 (m, 1H), 4.90 (d, 1H, *J* = 7.5 Hz), 7.02 (d, 2H, *J* = 6.9 Hz), 7.19-7.29 (m, 2H), 7.44 (d, 2H, *J* = 8.4 Hz), 8.17 (d, 2H, *J* = 8.7 Hz). $^{13}C$ NMR (75 MHz, $CDCl_3$) δ: 27.5, 33.9, 37.2, 50.5, 71.0, 72.4, 123.7, 125.35, 125.36, 126.1, 127.0, 128.1, 128.4, 140.7, 148.2, 207.8. MS *m/z*: 307 ($M^+$-18 (23)), 290 (58), 203 (42), 142 (25), 128 (49), 105 (22), 91 (100), 65 (12). Anal. Calcd. for $C_{19}H_{19}NO_4$: C, 70.14; H, 5.89; N, 4.31. Found: C, 69.85; H, 5.63; N, 4.70. The *ee* was determined to be 98% *ee* by HPLC (Chiralcel AD-H column, hexane/*i*-PrOH = 80:20, flow rate 1.0 mL/min, λ = 254 nm) $t_R$(major) = 10.48 min, $t_R$(minor) = 9.73 min.

**3-(4-chlorophenyl)-2-((4-(trifluoromethyl) phenyl)(hydroxy) methyl) cyclobutanone 3be:** Purified using flash column chromatography (hexane/ether, 5:1→1:1) to give the title compound (70 % yield) as a

mixture of diastereoisomers (dr = 90:10). Yellow oil. IR (neat): 3450, 1740 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$) δ: 3.21(ddd, 1H, J = 2.7 Hz, *J* = 8.4 Hz, *J* = 17.4 Hz), 3.38 (ddd, 1H, *J* = 2.4 Hz, *J* = 8.7 Hz, *J* = 17.7 Hz), 3.49 (q, 1H, *J* = 8.7 Hz), 3.66-3.72 (m, 1H), 5.08 (d, 1H, *J* = 6.6 Hz), 6.97 (d, 2H, *J* = 8.4 Hz), 7.22 (d, 2H, *J* = 8.4 Hz), 7.50 (d, 2H, *J* = 8.4 Hz), 7.60 (d, 2H, *J* = 8.4 Hz). $^{13}C$ NMR (75 MHz, $CDCl_3$) δ:32.1, 52.1, 72.7, 73.4, 125.7 (d, *J* = 14.7 Hz), 126.9, 127.8, 128.6, 128.8, 132.7, 140.2, 144.5, 206.3. MS *m/z*: 336 ($M^+$-18 (36)), 301 (11), 267 (26), 204 (17), 189 (14), 138 (100), 103 (17). Anal. Calcd. for $C_{18}H_{14}ClF_3O_2$; C, 60.94; H, 3.98. Found: C, 60.99; H, 3.90. The *ee* was determined to be 92% *ee* by HPLC (Chiralcel AD-H column, hexane/*i*-PrOH = 95:5, flow rate 1.0 mL/min, λ = 254 nm) $t_R$(major) = 30.54 min, $t_R$(minor) = 25.03 min.

**4-[(2-Hexyl-4-oxo-cyclobutyl)-hydroxy-methyl]-benzonitrile 3eb:** Purified using flash column chromatography (hexane/ether, 5:1→1:1) to give the title compound (60 % yield) as a mixture of diastereoisomers (dr = 98:2). Orange oil. IR (neat): 3450, 1760 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$) δ: 0.86 (t, 3H, *J* = 7.2 Hz), 0.96-1.45 (m, 10H), 2.19 (q, 1H, *J* = 7.8 Hz, *J* = 15.0 Hz), 2.67 (ddd, 1H, *J* = 2.4 Hz, *J* = 7.5 Hz, *J* = 17.4 Hz), 3.02-3.15 (m, 2H), 4.90 (d, 1H, *J* = 7.8 Hz), 7.49 (d, 2H, *J* = 8.7 Hz), 7.66 (d, 2H, *J* = 8.4 Hz). $^{13}C$ NMR (75 MHz, $CDCl_3$) δ: 13.9, 22.4, 27.6, 28.1, 28.8, 31.5, 35.7, 50.5, 71.1, 73.0, 111.8, 118.5, 127.0, 132.3, 146.4, 205.6. MS *m/z*: 267 ($M^+$-18 (58)), 197 (29), 183 (47), 168 (32), 154 (100), 140 (35), 127 (82), 101 (8), 55 (15). Anal. Calcd. for $C_{18}H_{23}NO_2$: C, 75.76; H, 28.12; N, 4.91. Found: C, 75.69; H, 28.20; N, 4.97. The *ee* was determined to be 83% *ee* by HPLC (Chiralcel AD-H column, hexane/*i*-PrOH = 99:1, flow rate 1 mL/min, λ = 254 nm) $t_R$(major) = 20.36 min, $t_R$(minor) = 25.30 min.

**4-{[2-(4-bromo-phenyl)-4-oxo-cyclobutyl]-hydroxy-methyl}-benzonitrile 3cb:** Purified using flash column chromatography (hexane/ether, 5:1→1:1) to give the title compound (64 % yield) as a mixture of diastereoisomers (dr = 96:4). Yellow oil. IR (neat): 3441, 1771 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$) δ: 3.10 (ddd, 1H, *J* = 2.5 Hz, *J* =

8.0 Hz, *J* = 17.5 Hz), 3.29 (ddd, 1H, *J* = 2.0 Hz, *J* = 9.0 Hz, *J* = 17.5 Hz), 3.41 (q, 1H, *J* = 8.5 Hz), 3.58-3.64 (m, 1H), 4.98 (d, 1H, *J* = 6.0 Hz), 6.88 (d, 2H, *J* = 8.0 Hz), 7.31 (d, 2H, *J* = 8.5 Hz), 7.41 (d, 2H, *J* = 8.0 Hz), 7.52 (d, 2H, *J* = 8.5 Hz). $^{13}$C NMR (124 MHz, $CDCl_3$) δ: 32.0, 52.2, 72.3, 72.9, 111.9, 118.4, 120.0, 127.2, 128.0, 132.4, 132.5, 140.7, 145.9, 206.0. MS *m/z*: 355 ($M^+$-18 (3)), 339 (22), 258 (16), 230 (56), 182 (100), 127 (18), 103 (23). Anal. Calcd. for $C_{18}H_{14}BrNO_2$; C, 60.69; H, 3.96; N 3.93 Found: C, 60.67; H, 3.97; N 3.91. The *ee* was determined to be 89% *ee* by HPLC (Chiralcel OJ column, hexane/*i*-PrOH = 75:25, flow rate 1.0 mL/min, λ = 254 nm) $t_R$(major) = 31.18 min, $t_R$(minor) = 46.53 min.

**The synthesis of 4-(4-chlorophenyl)-dihydro-5-(hydroxy(4-nitrophenyl)methyl)furan-2(*3H*)-one 4:** To solution of **3ba** (131 mg, 0.5 mmol) in anhydrous $CH_2Cl_2$ (5 mL) were added $NaHCO_3$ (87 mg) and m-CPBA (270 mg, 1.5 mmol). The mixture was stirred at 25 °C until the reaction was complete (monitored by TLC). The reaction was quenched with saturated aqueous $Na_2S_2O_3$ (10 mL). The mixture was extracted with EtOAc (2 × 10 mL) and the combined organic layers were dried over anhydrous $Na_2SO_4$. After removal of solvent, the residue was purified by flash chromatography (petroleum ether/EtOAc, 2:1) to give **4** (140 mg) as a white solid in 81% yield; mp: 148-150 °C. $[\alpha]_D^{20}$= +18 (*c* 0.33, $CHCl_3$). $^1$H NMR (300 MHz, $CDCl_3$) δ: 2.65 (dd, 1H, *J* = 8.4 Hz, *J* = 18.5 Hz), 2.99 (dd, 1H, *J* = 9.0 Hz, *J* = 18.0 Hz), 3.77 (dd, 1H, *J* = 6.9 Hz, *J* = 8.7 Hz), 4.62 (dd, 1H, *J* = 3.3 Hz, *J* = 6.9 Hz), 4.88 (br s, 1H), 7.11 (d, 2H, *J* = 7.2 Hz), 7.31 (d, 2H, *J* = 7.5 Hz), 7.5 (d, 2H, *J* = 7.8 Hz), 8.14 (d, 2H, *J* = 7.5 Hz) . $^{13}$C NMR (75 MHz, $CDCl_3$) δ: 37.4, 42.6, 73.4, 88.7, 124.15, 128.08, 128.2, 128.7, 134.2, 138.3, 146.6, 148.2, 174.3. MS *m/z*: 195 ($M^+$-120 (27)), 153 (100), 103 (26), 77 (22), 51 (16). Anal. Calcd. for $C_{17}H_{14}ClNO_5$: C, 58.72; H, 4.06; N, 4.03. Found: C, 58.60; H, 4.31; N, 4.42.

**3. Single-crystal X-ray structure analyses for 4 and 3ba'.**

Details of the crystal data, data collection and refinement are given in Table 1. The diffraction intensities were collected with graphite-monochromated MoKα radiation (λ = 0.71073 Å). Data collection and cell refinement were carried out using a Bruker Kappa X8 APEX II diffractometer. The temperature of the crystal was maintained at the selected value (100 ± 1 K) by means of a 700 Series Cryostream cooling device. Intensity data were corrected for Lorenz-polarization and absorption factors. The structures were solved by direct methods using SHELXS-97,[3] and refined against $F^2$ by full-matrix least-squares methods using SHELXL-97[4] with anisotropic displacement parameters for all non-hydrogen atoms. All calculations were performed by using the crystal structure crystallographic software package WINGX.[5] The structures were drawn (Figures 1 and 2) using ORTEP3.[6] Hydrogen atoms were located on a difference Fourier map and introduced into the calculations as a riding model with isotropic thermal parameters.

The cif files CCDC 752280 (compound **4**) and CCDC 796934 (compound **3ba'**) contain the crystallographic data for this compounds. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_ request/cif.

[3] G. M. Sheldrick, SHELXS-97, *Program for crystal structure solution*, University of Göttingen, Göttingen, Germany, 1997.
[4] G. M. Sheldrick, SHELXL-97, *Program for the refinement of crystal structures from diffraction data*, University of Göttingen, Göttingen, Germany, 1997.
[5] L. J. Farrugia, *J. Appl. Cryst*., 1999**, 32**, 837.
[6] L. J. Farrugia, *J. Appl. Cryst*., 1997, **30**, 565.

**Table 1.** Crystal data and structure refinement for compounds **4** and **3ba'**.

| Compound | **4** | **3ba'** |
|---|---|---|
| Empirical formula | $C_{17}H_{14}ClNO_5$ | $C_{17}H_{14}ClNO_4$ |
| Crystal size ($mm^3$) | 0.12 × 0.05 × 0.02 | 0.31 × 0.12 × 0.02 |
| Formula weight ($g\ mol^{-1}$) | 347.74 | 331.74 |
| Temperature (K) | 100(1) | 100(1) |
| Crystal system | monoclinic | monoclinic |
| Space group | $P\,2_1$ | $P\,-1$ |
| **Unit cell dimensions** | | |
| *a (Å)* | 9.2365(4) | 8.7119(13) |
| *b (Å)* | 9.7935(4) | 12.7240(18) |
| *c (Å)* | 17.7681(8) | 15.850(2) |
| *α (°)* | 90 | 66.646(3) |
| *β (°)* | 101.569(3) | 80.311(3) |
| *γ (°)* | 90 | 70.794(3) |
| *V* ($Å^3$) | 1574.61(12) | 1521.8(4) |
| *Z* | 4 | 4 |
| $D_{calc.}$ ($Mg.m^{-3}$) | 1.467 | 1.448 |
| Absorption coefficient ($mm^{-1}$) | 0.270 | 0.271 |
| F (0 0 0) | 720 | 688 |
| Index ranges | –13 < h < 13, –14 < k < 13, –25 < l < 25 | –12 < h < 13, –17 < k < 20, –25 < l < 21 |
| Reflections collected | 37 446 | 25 995 |
| Independent reflections (Rint) | 9 323 (0.0938) | 11 075 (0.0288) |
| Observed reflections [ $I > 2\sigma(I)$] | 5 216 | 7 614 |
| Refinement method | Full matrix least squares on $F^2$ | Full matrix least squares on $F^2$ |
| Final *R* indices [$I > 2\sigma I$] | $R1 = 0.0671$, $wR2 = 0.1311$ | $R1 = 0.0484$, $wR2 = 0.1216$ |
| *S* | 1.023 | 1.044 |
| Flack Parameter[7] | 0.01(9) | / |
| $(\Delta/\sigma)_{max}$ | 0.000 | 0.002 |
| $(\Delta\rho)_{max,\,min}$ [e $Å^{-3}$] | 0.682 ; –0.731 | 0.581 ; –0.394 |

[7] H. D. Flack, *Acta Cryst.* 1983, **A39**, 876.

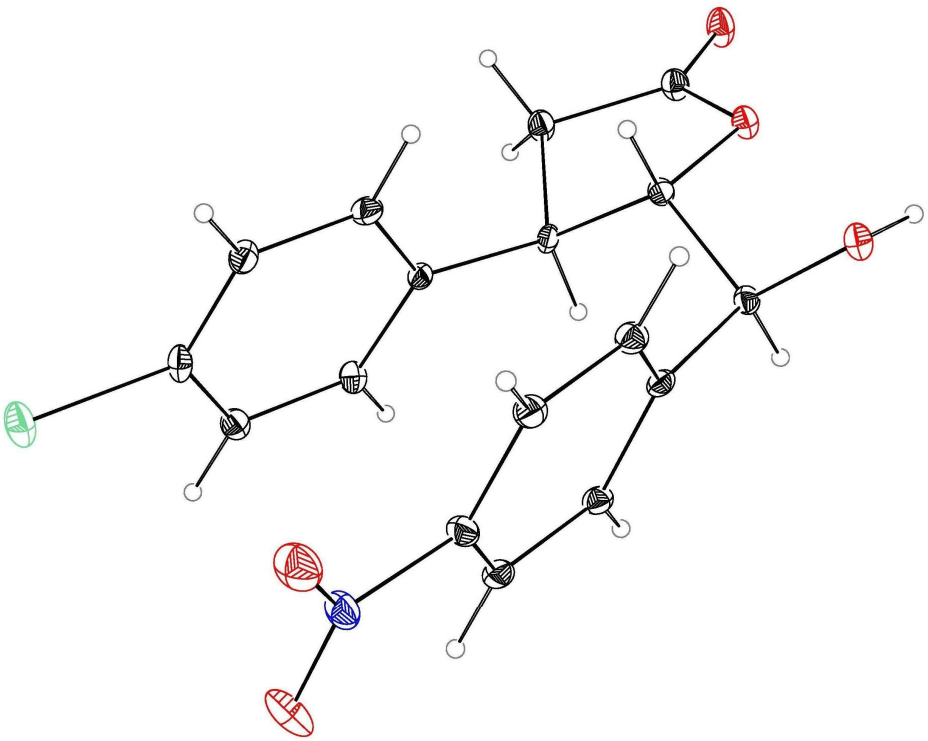


**Fig. 1** Crystal structure of compound **4**. Displacement ellipsoids are drawn at the 50% probability level. Only one molecule is shown for the sake of clarity.

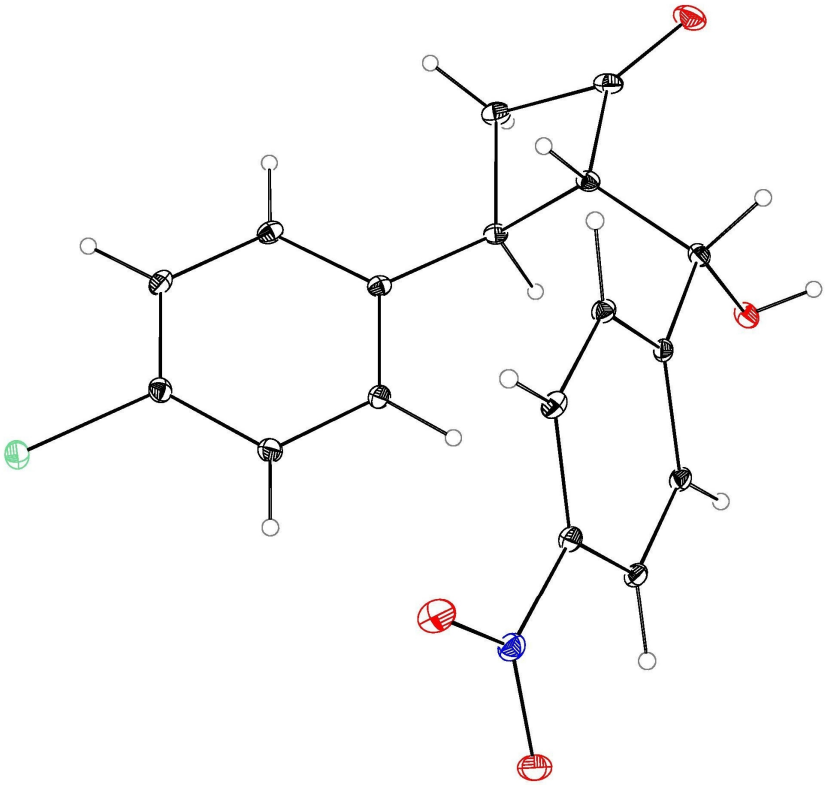
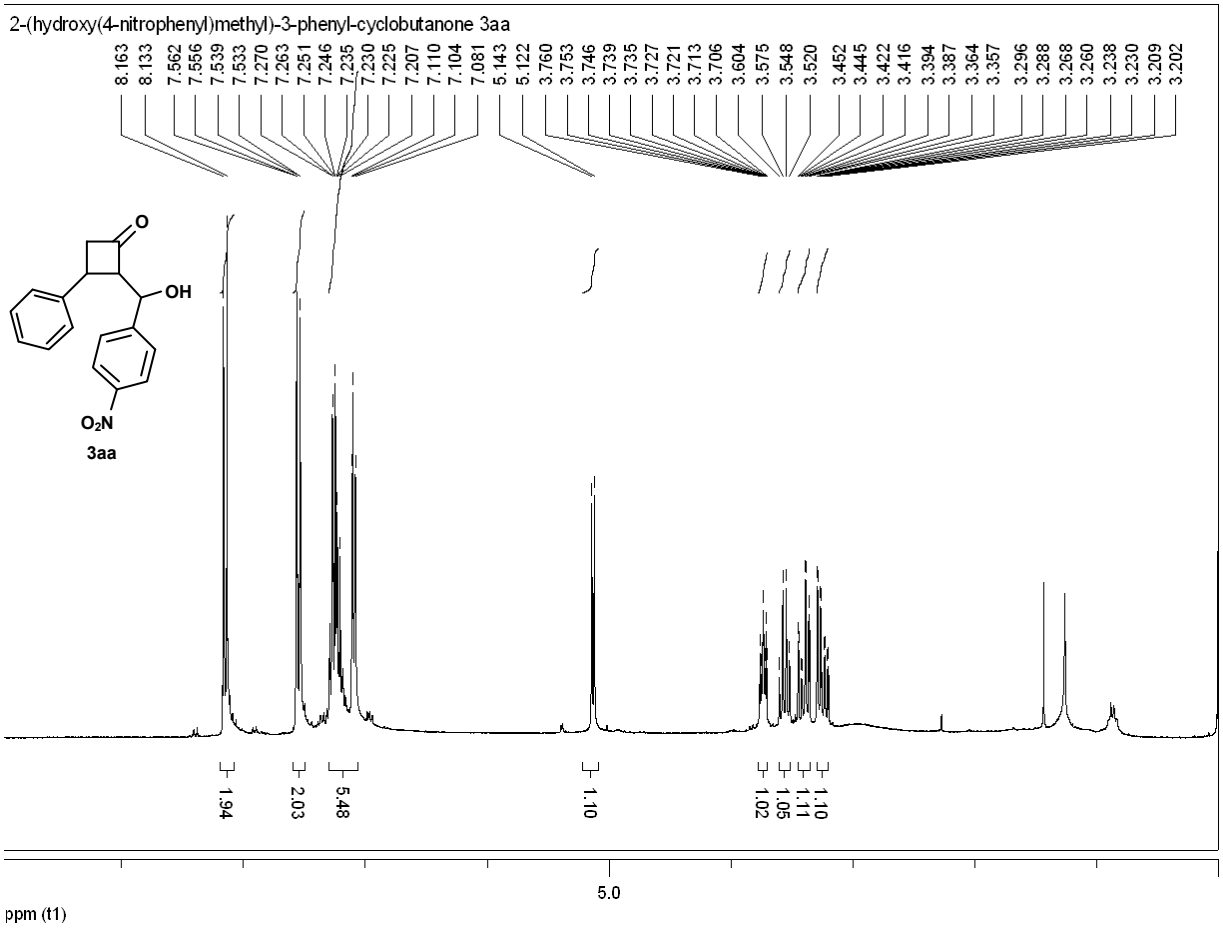
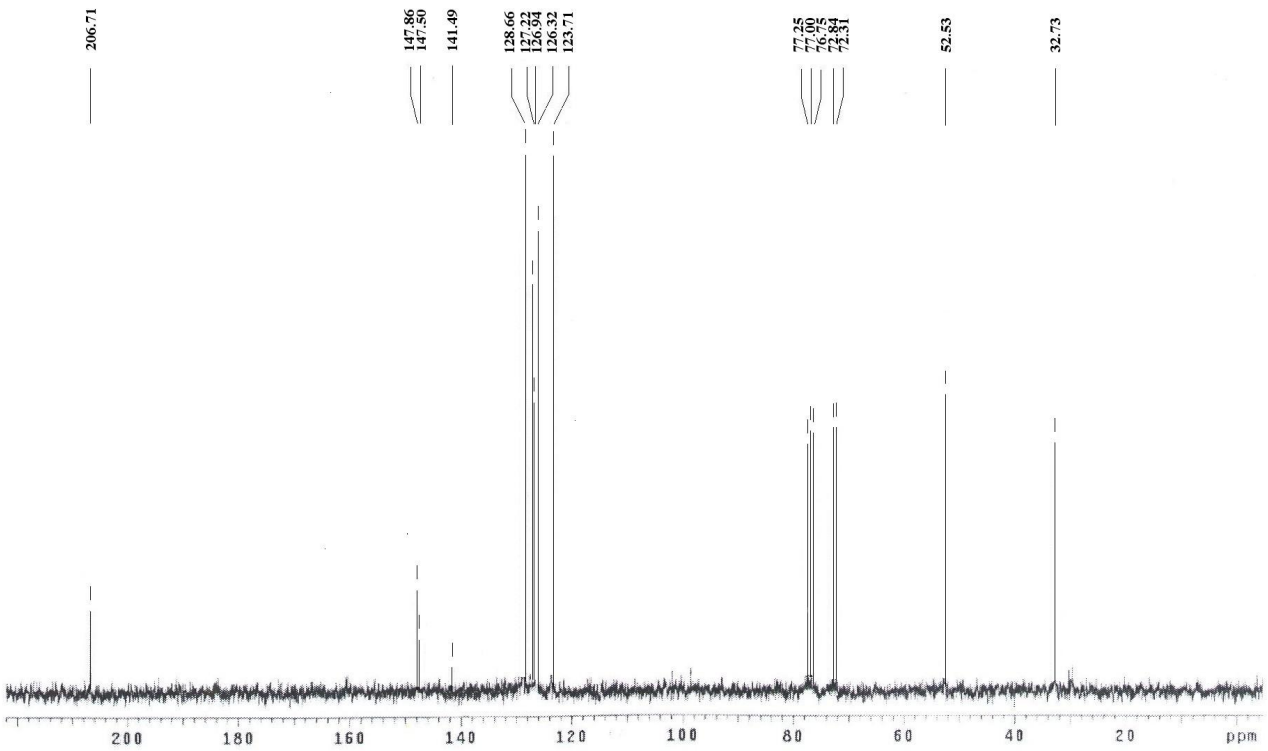
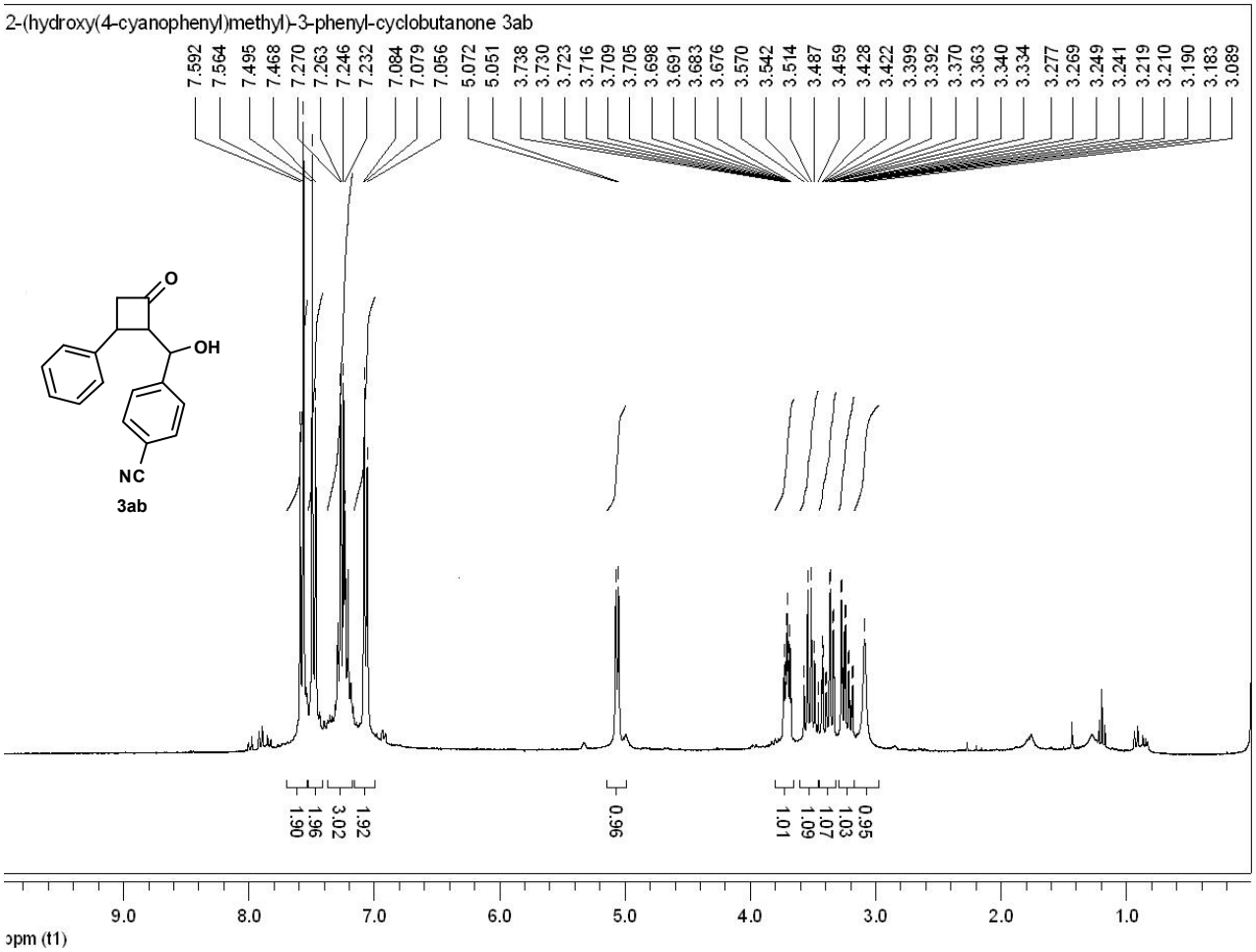


**Fig. 2** Crystal structure of compound **3ba'**. Displacement ellipsoids are drawn at the 50% probability level. Only one molecule is shown for the sake of clarity.

# 4 Copies of NMR spectra of 2,3-disubstituted cyclobutanones 3:

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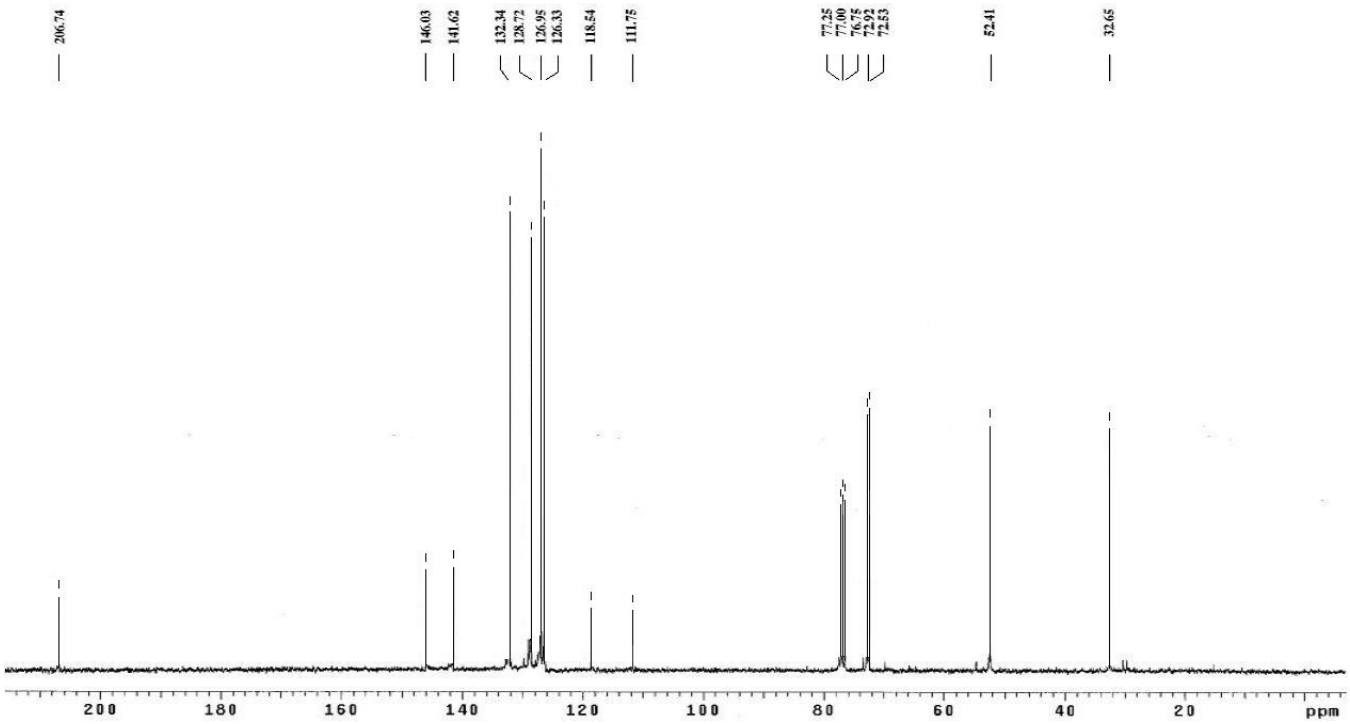
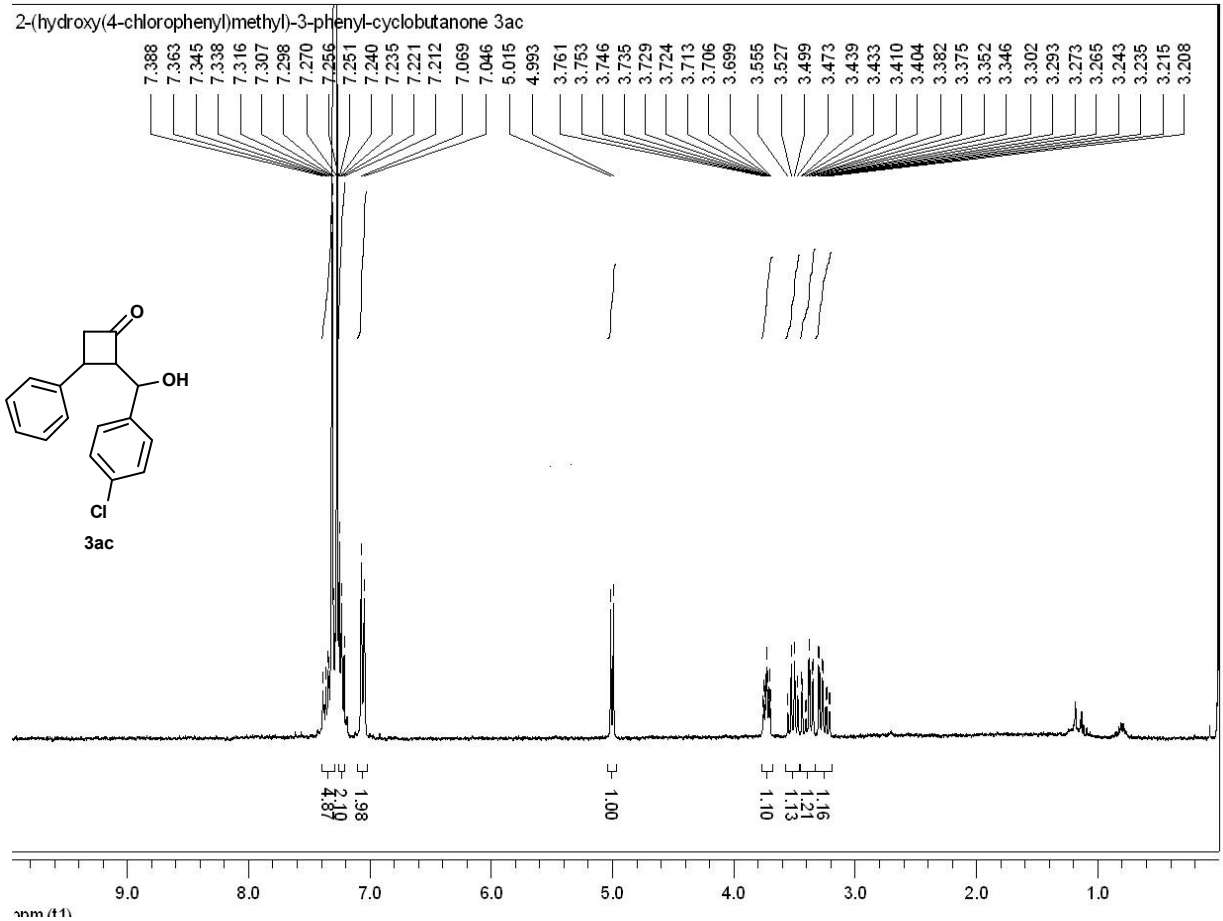
O
OH
NC
3ab
1.90 1.96 3.02 1.92 0.96 1.01 1.09 1.07 1.03 0.95
9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0
ppm (f1)


206.74
146.03 141.62 132.34 128.72 126.95 126.33 118.54 111.75
77.25 77.00 76.75 72.92 72.53
52.41
32.65
200 180 160 140 120 100 80 60 40 20 ppm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O
OH
Cl
3ac
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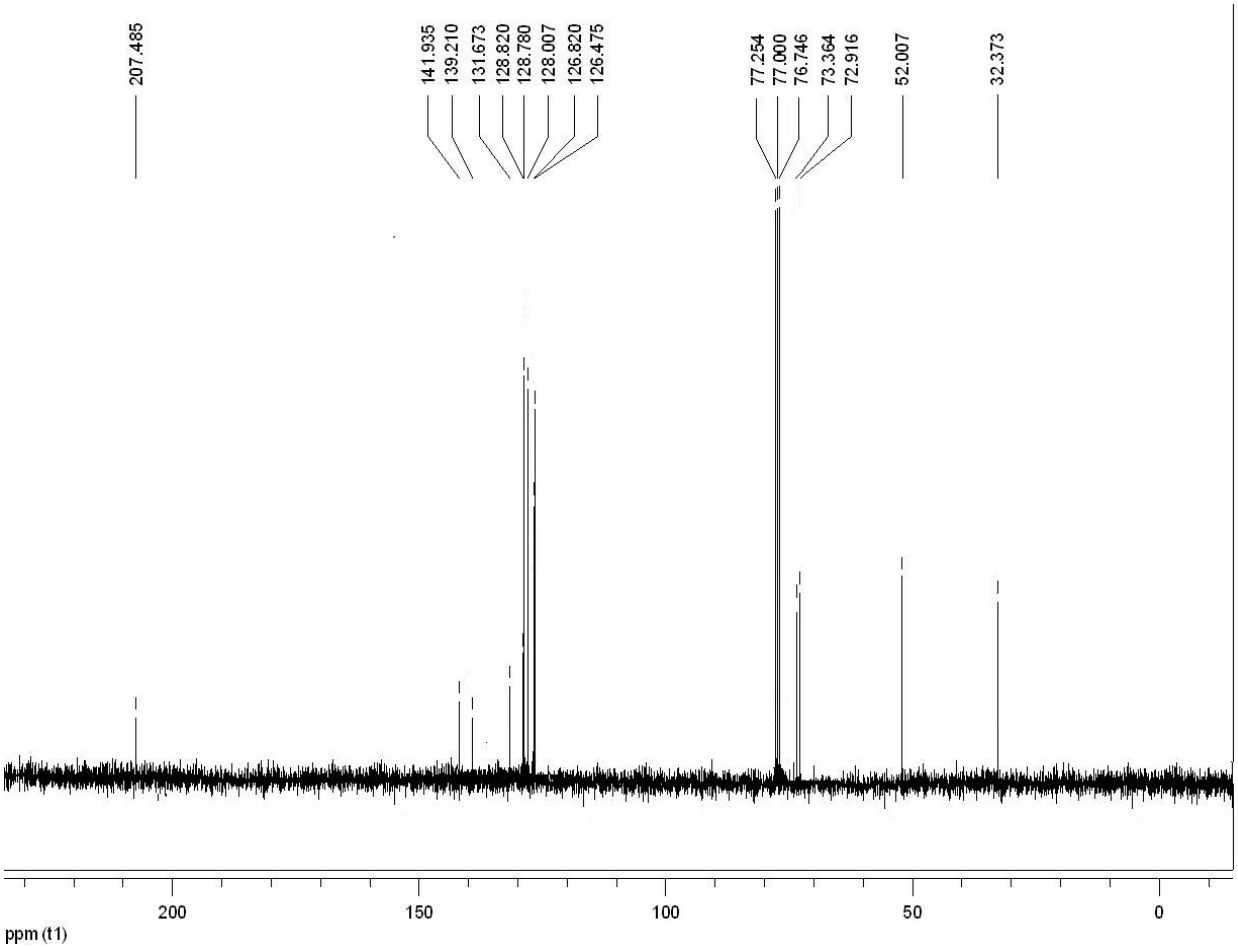
ppm (t1)


207.485
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77.254 77.000 76.746 73.364 72.916
52.007
32.373
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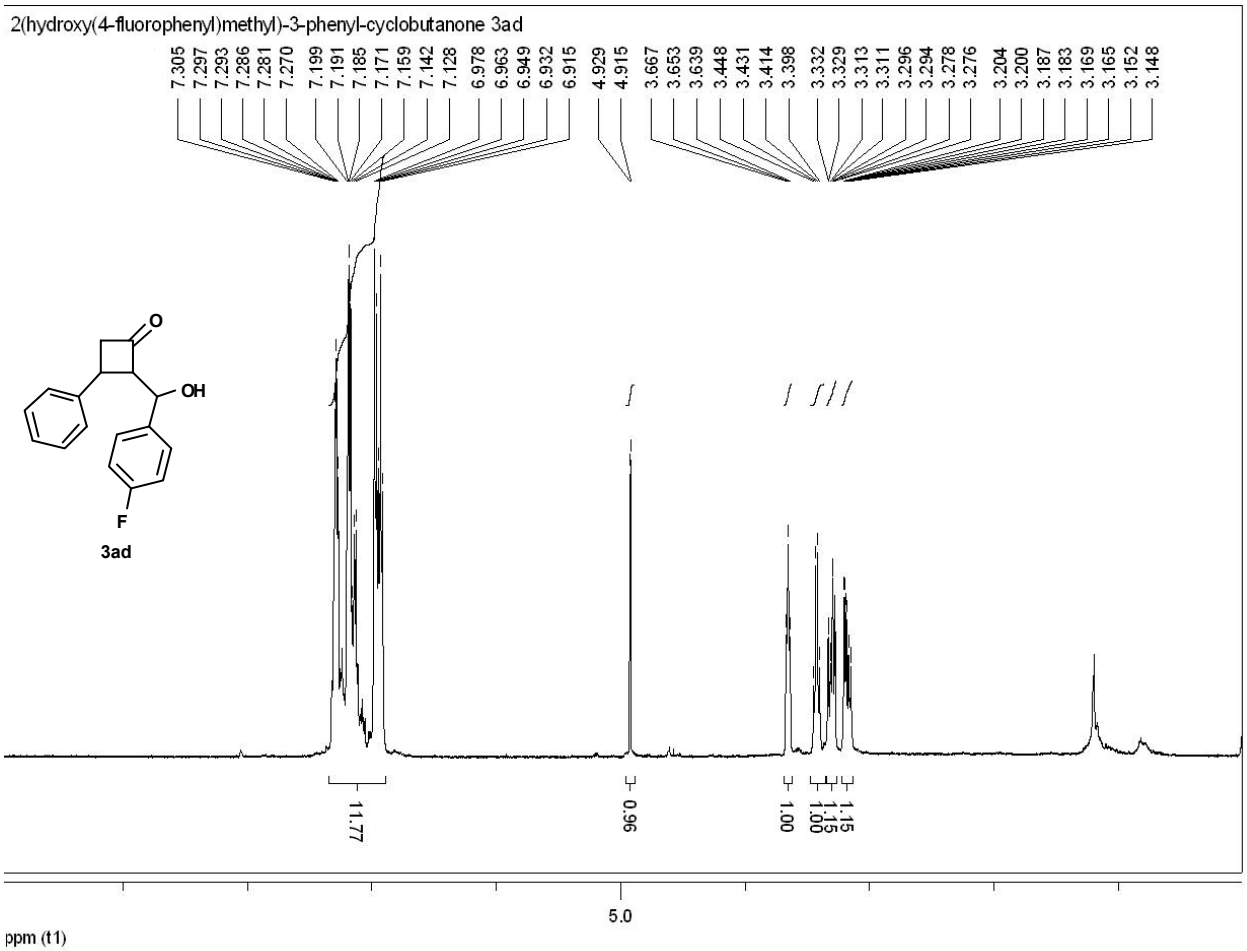
ppm (t1)


2(hydroxy(4-fluorophenyl)methyl)-3-phenyl-cyclobutanone 3ad
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O
OH
F
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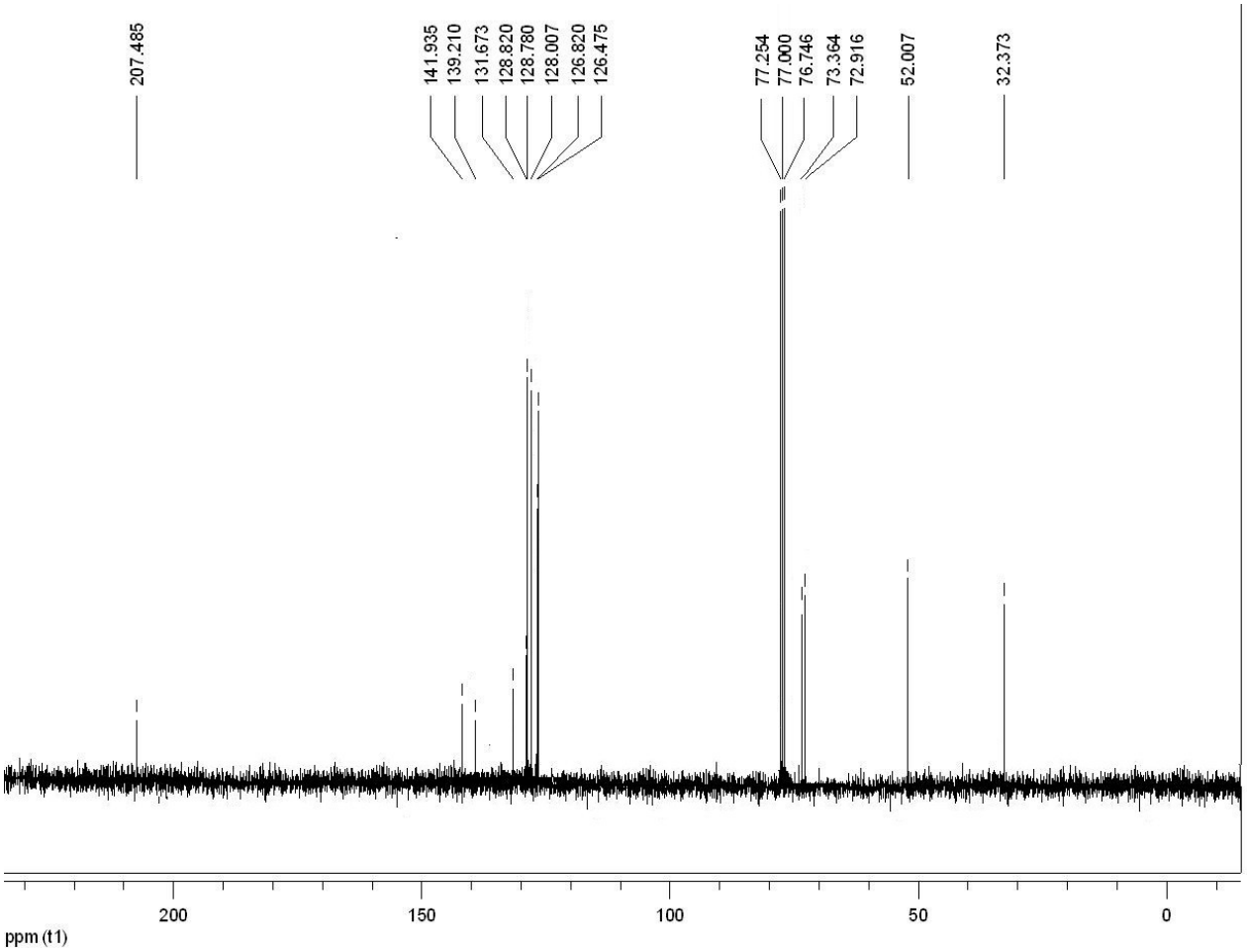
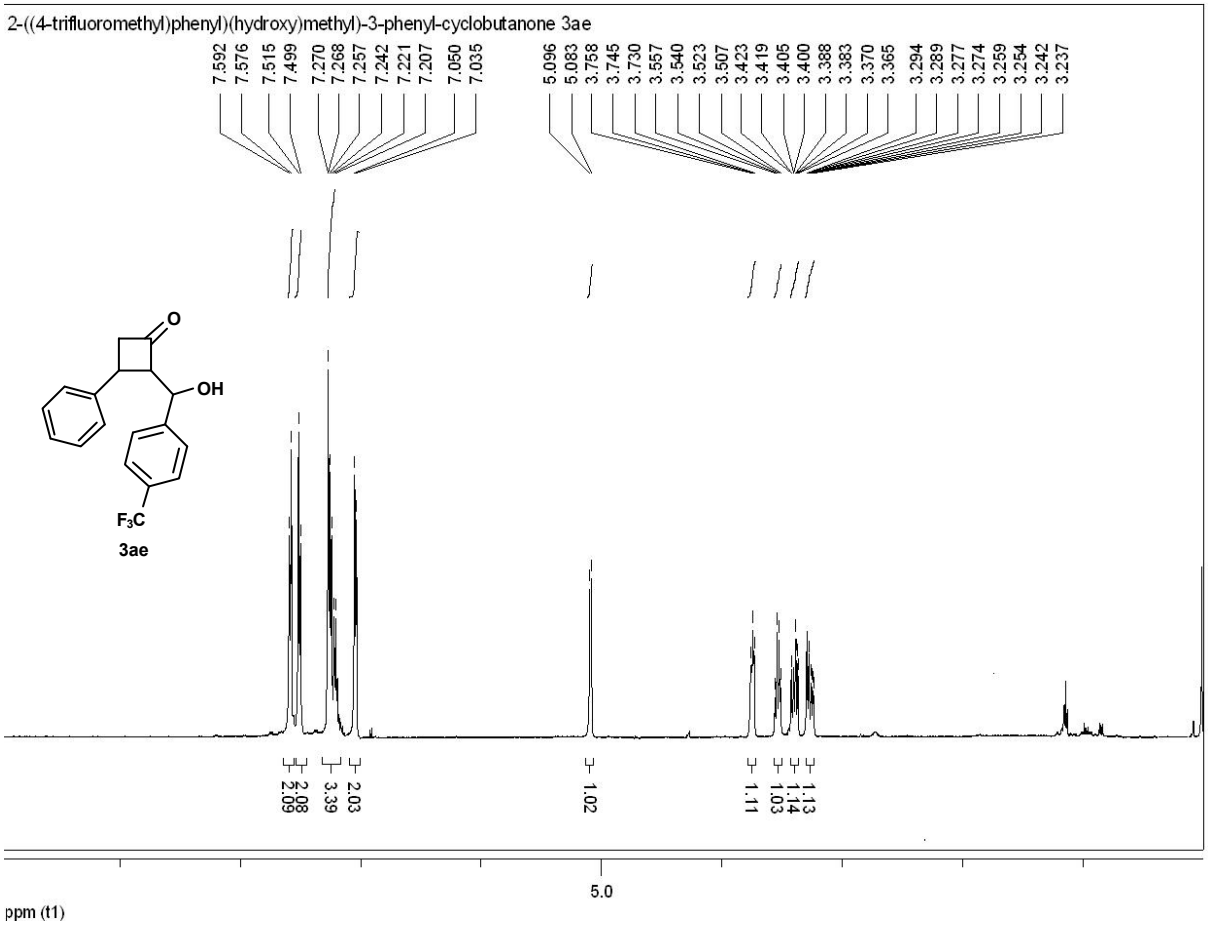
1.00
1.00
1.15
5.0
ppm (t1)


207.485
141.935 139.210 131.673 128.820 128.780 128.007 126.820 126.475
77.254 77.000 76.746 73.364 72.916
52.007
32.373
200
150
100
50
0
ppm (t1)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5.096 5.083 3.758 3.745 3.730 3.557 3.540 3.523 3.507 3.423 3.419 3.405 3.400 3.388 3.383 3.370 3.365 3.294 3.289 3.277 3.274 3.259 3.254 3.242 3.237
O
OH
F3C
3ae
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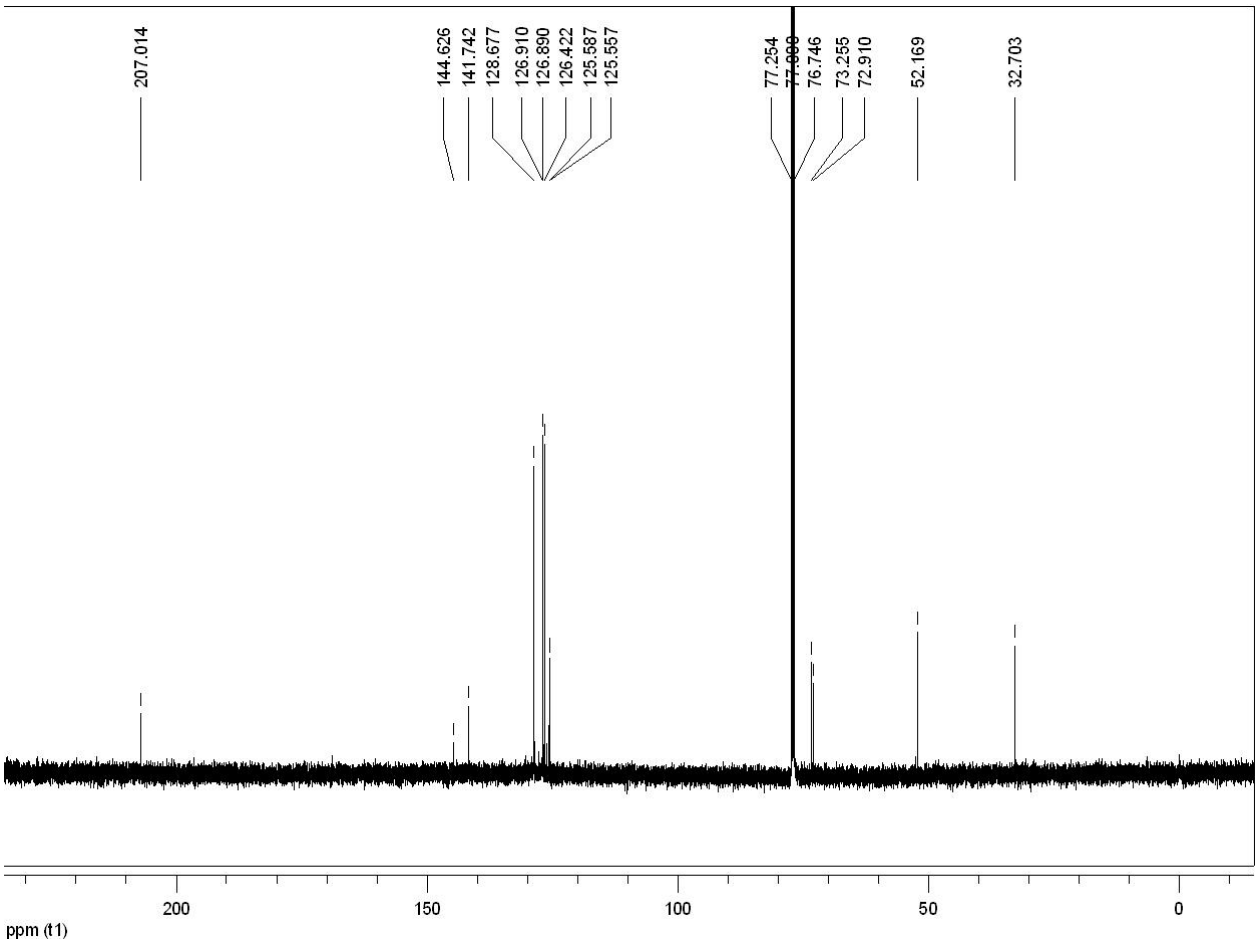
5.0
ppm (t1)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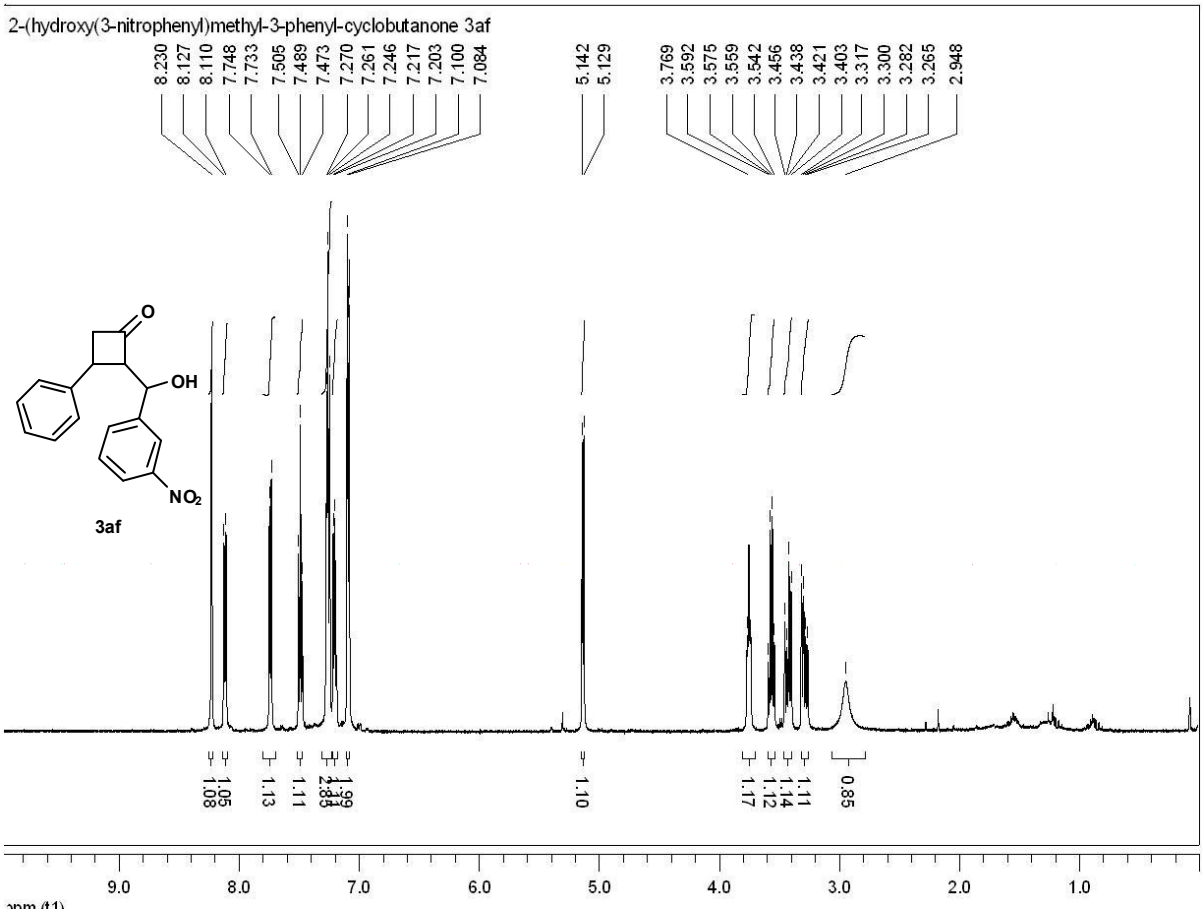
150
100
50
0
ppm (t1)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7.733
7.505
7.489
7.473
7.270
7.261
7.246
7.217
7.203
7.100
7.084
5.142
5.129
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3.592
3.575
3.559
3.542
3.456
3.438
3.421
3.403
3.317
3.300
3.282
3.265
2.948
O
OH
NO2
3af
1.08
1.05
1.13
1.11
1.99
1.10
1.17
1.12
1.14
1.11
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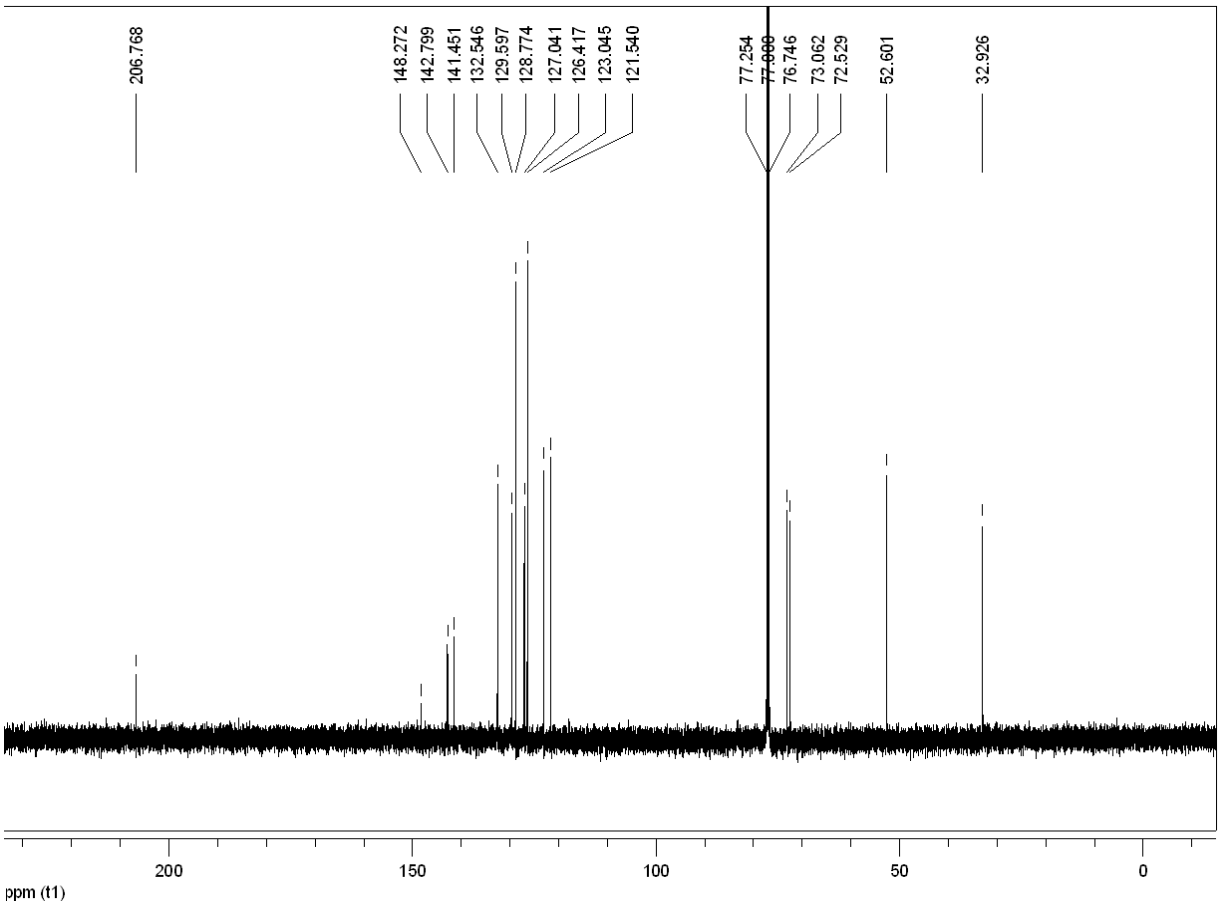
3.0
2.0
1.0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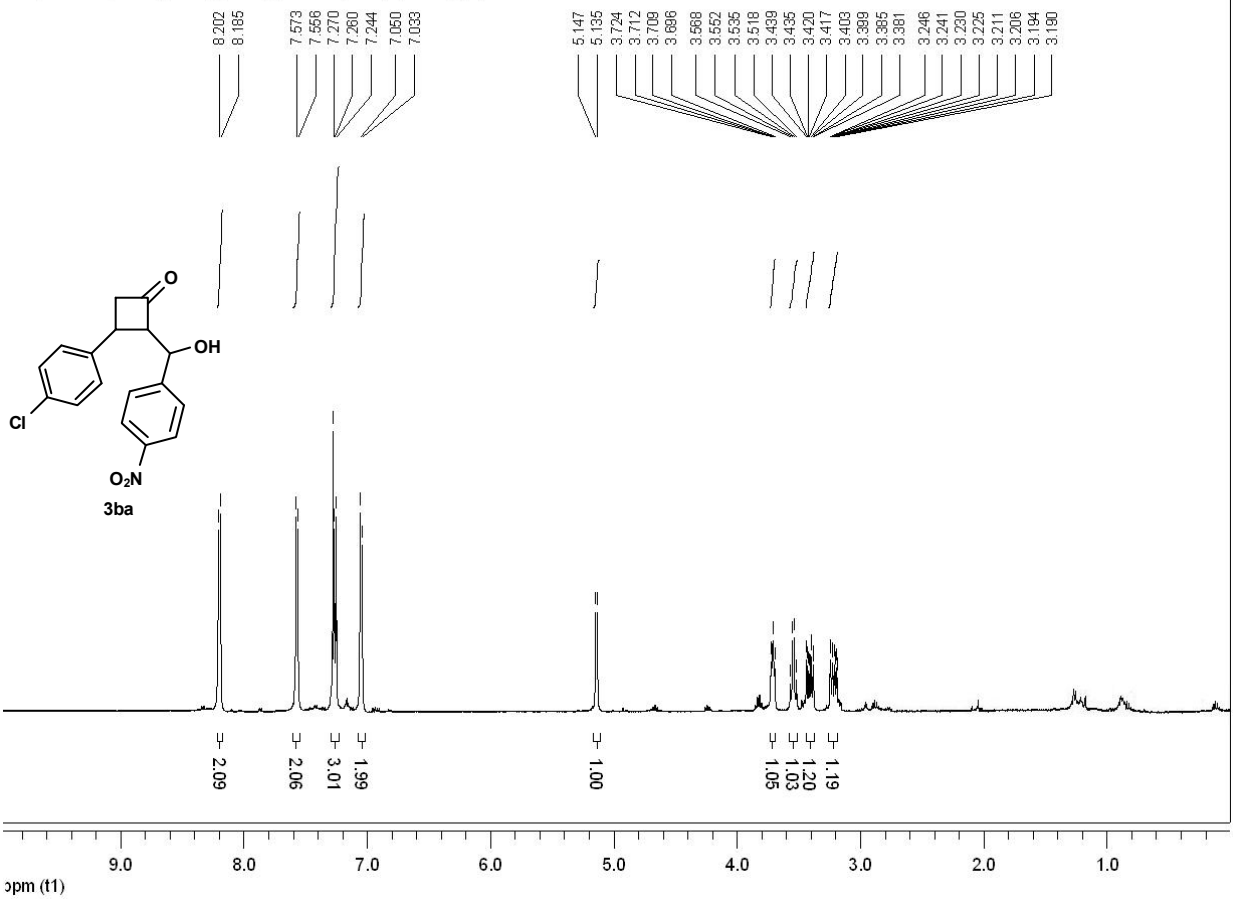
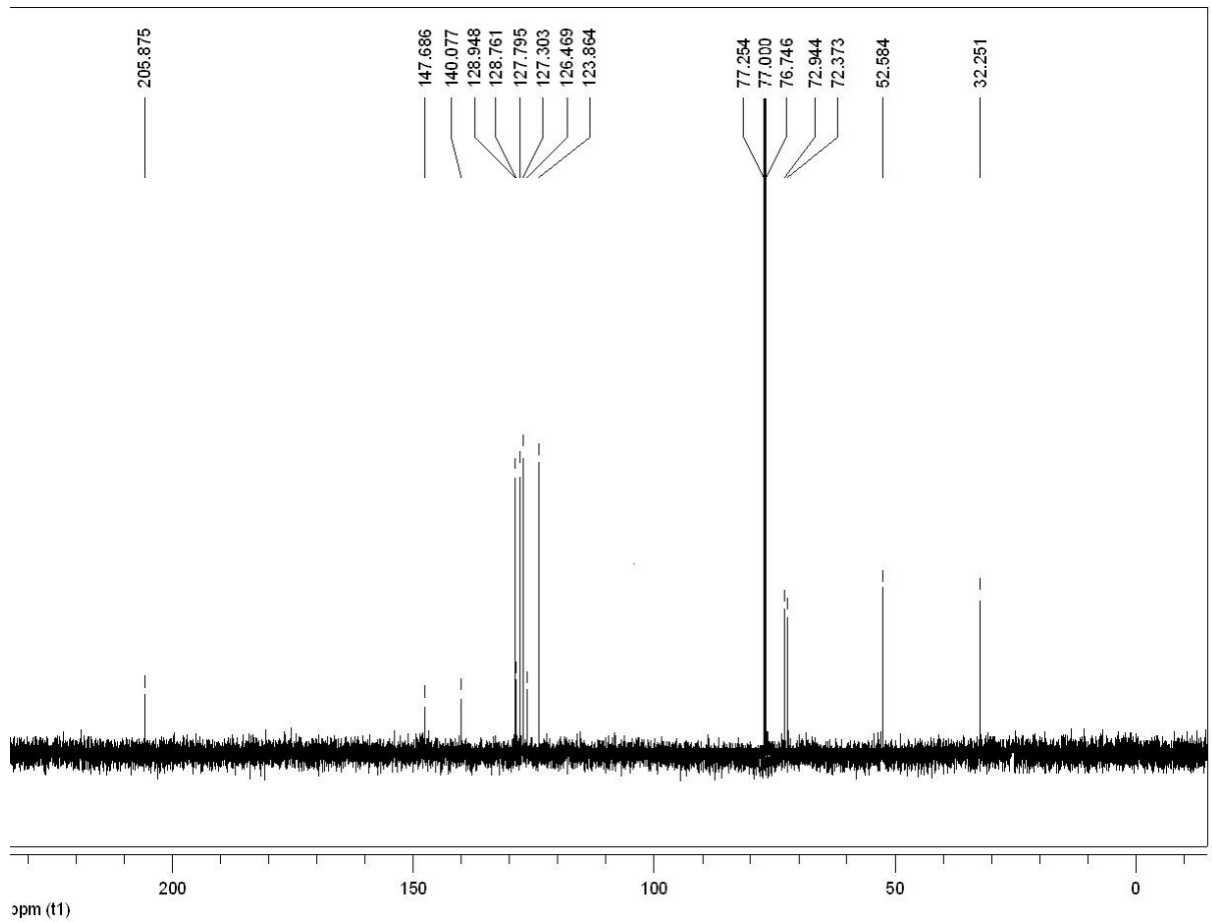
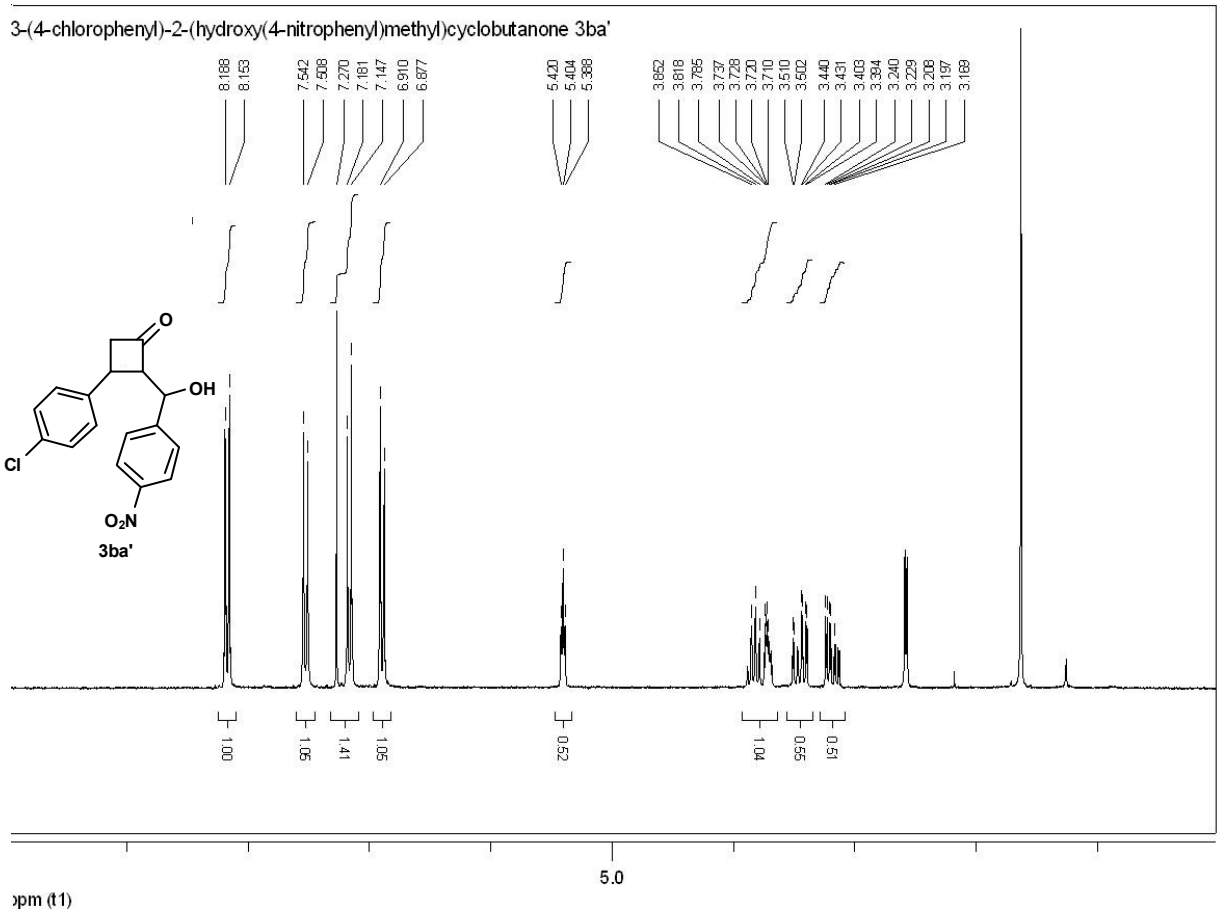
132.546
129.597
128.774
127.041
126.417
123.045
121.540
77.254
77.000
76.746
73.062
72.529
52.601
32.926
200
150
100
50
0
ppm (t1)

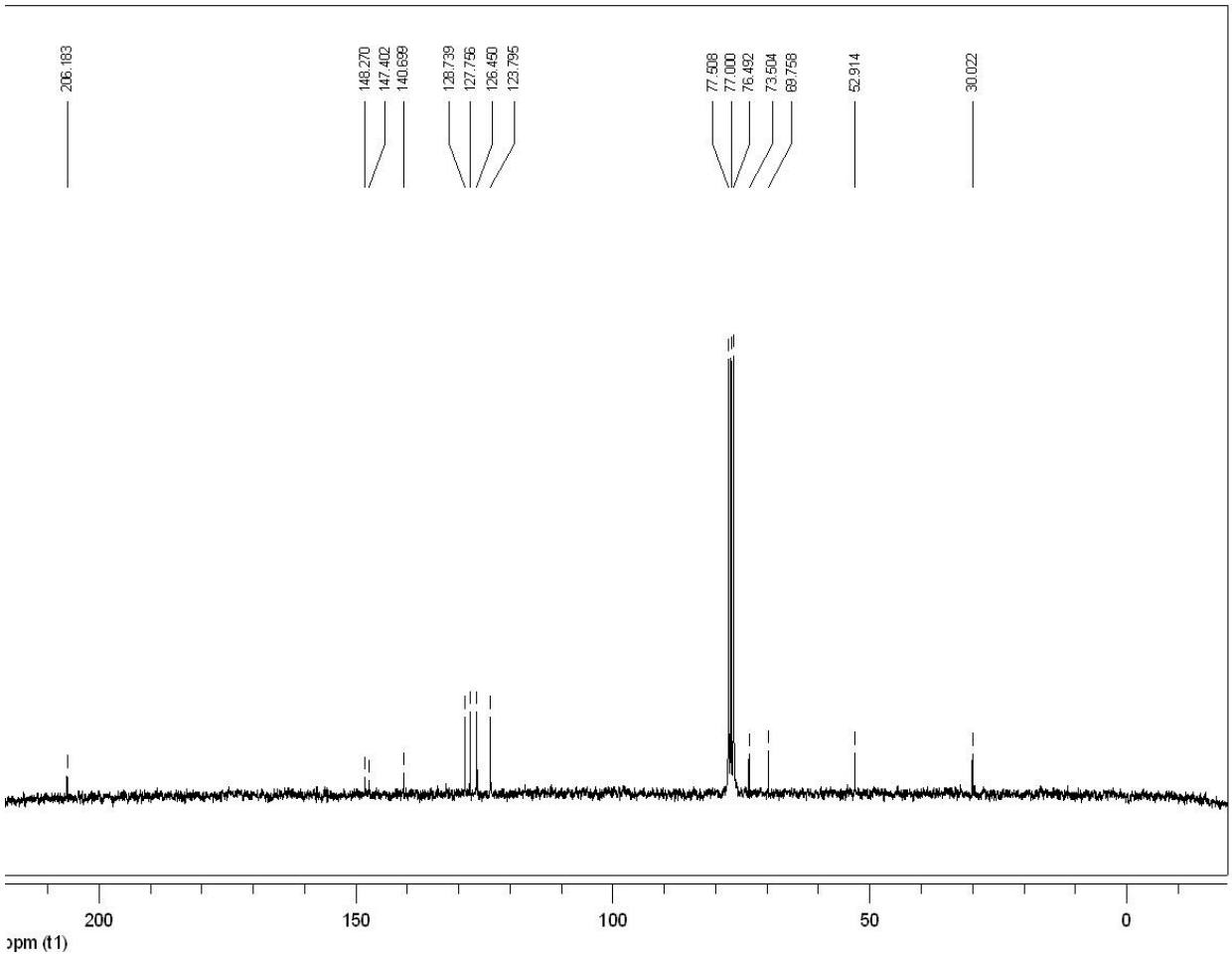
3-(4-chlorophenyl)-2-(hydroxy(4-nitrophenyl)methyl)cyclobutanone 3ba

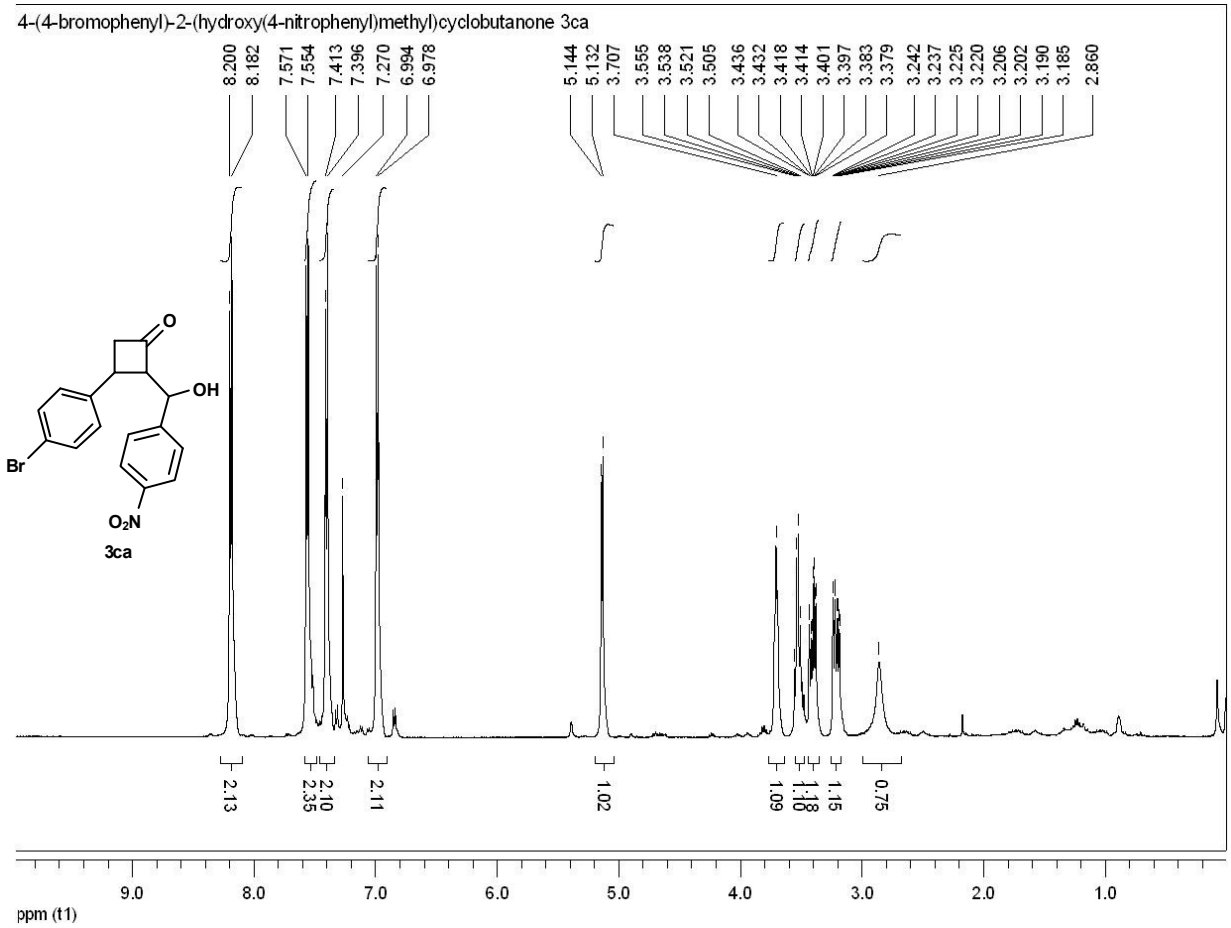


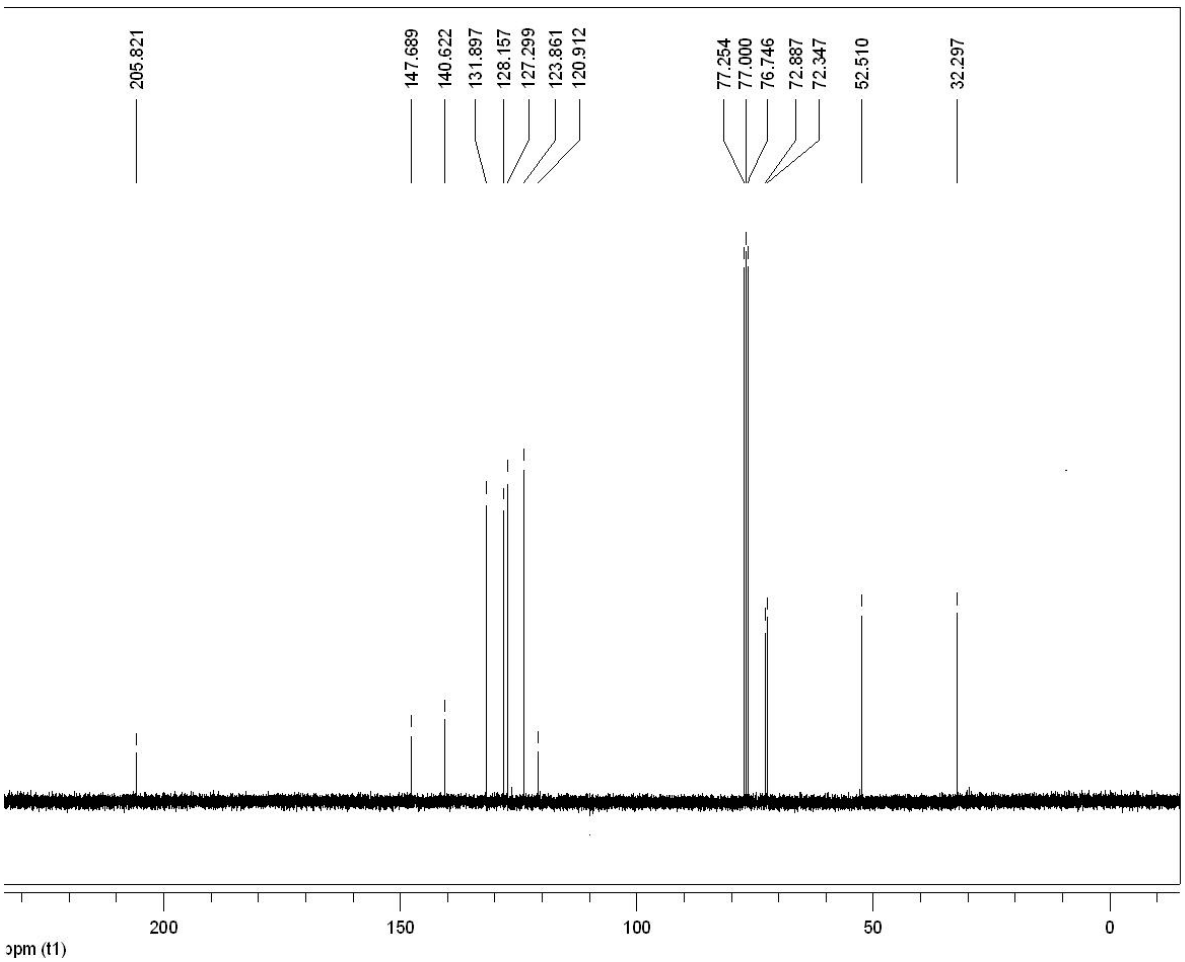



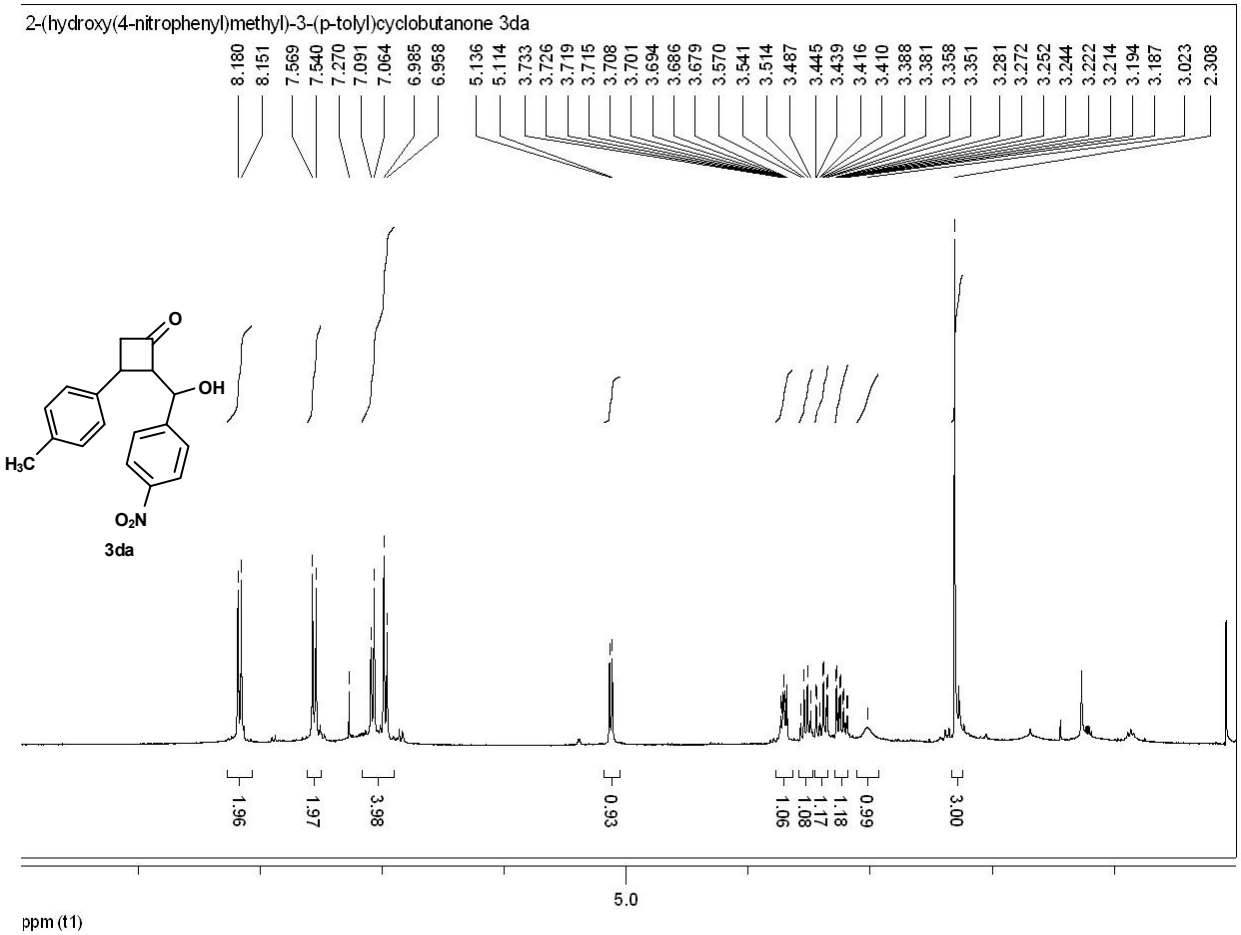
3-(4-chlorophenyl)-2-(hydroxy(4-nitrophenyl)methyl)cyclobutanone 3ba'

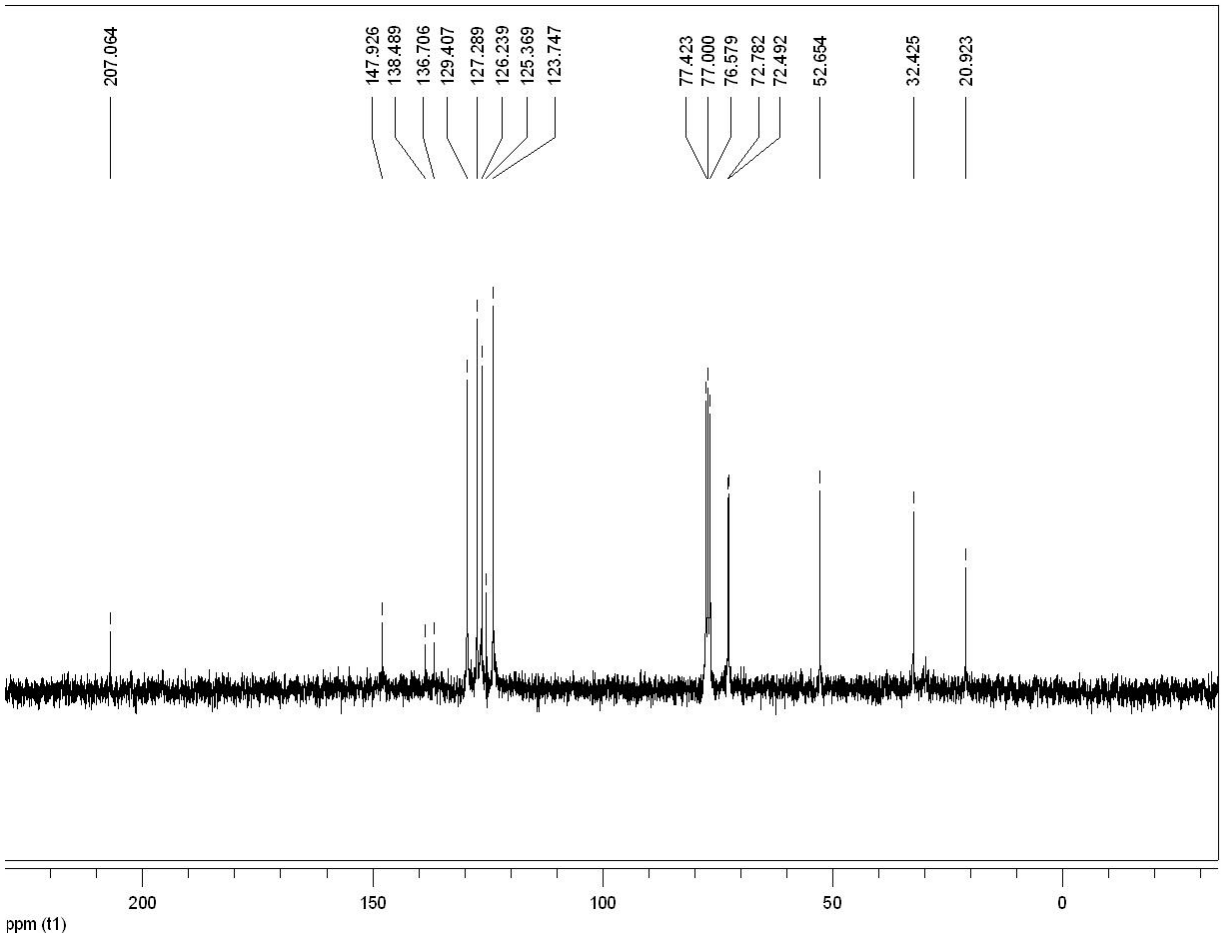


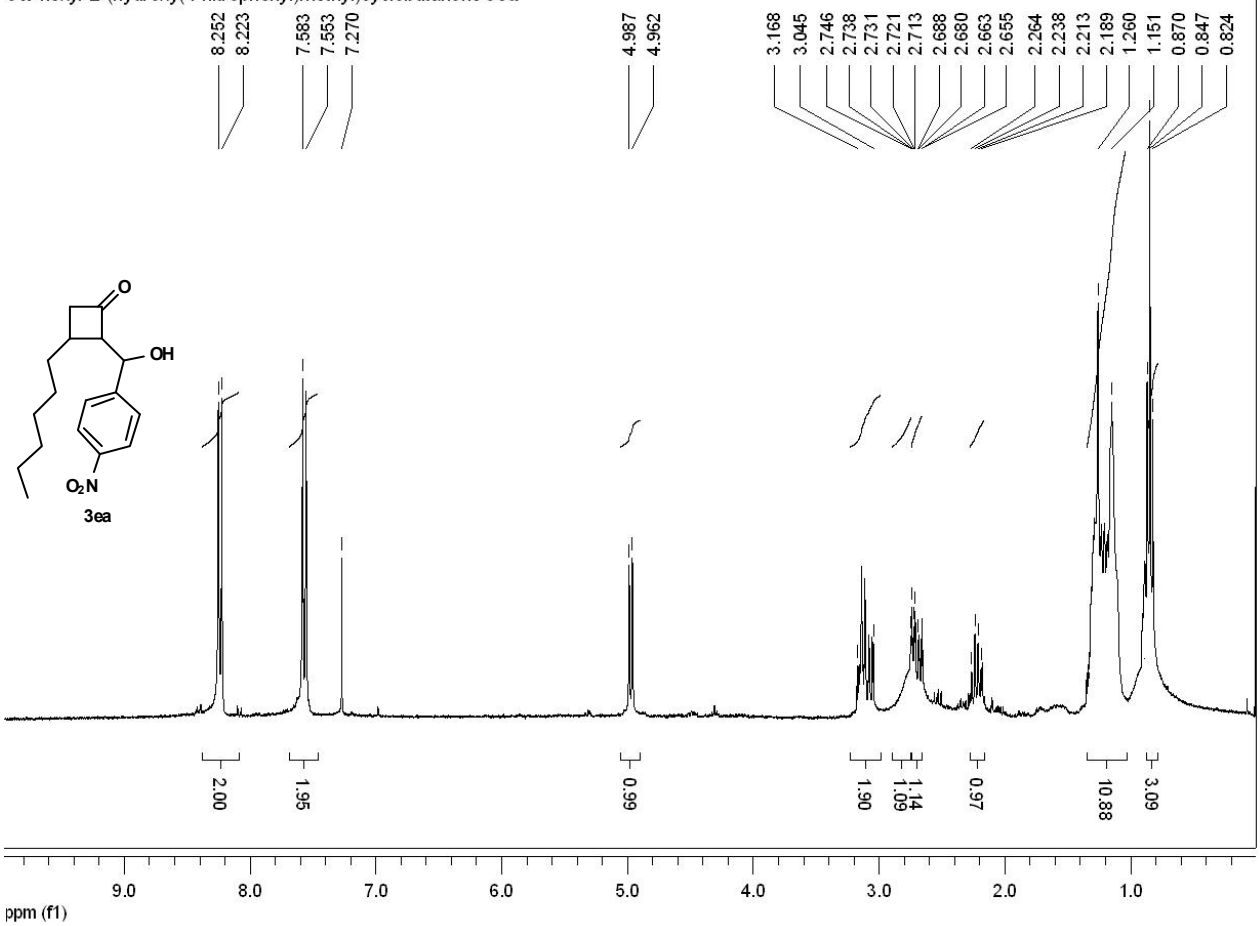

4-(4-bromophenyl)-2-(hydroxy(4-nitrophenyl)methyl)cyclobutanone 3ca
8.200
8.182
7.571
7.554
7.413
7.396
7.270
6.994
6.978
5.144
5.132
3.707
3.555
3.538
3.521
3.505
3.436
3.432
3.418
3.414
3.401
3.397
3.383
3.379
3.242
3.237
3.225
3.220
3.206
3.202
3.190
3.185
2.860
O
OH
Br
O2N
3ca
2.13
2.35
2.10
2.11
1.02
1.09
1.18
1.10
1.15
0.75
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)

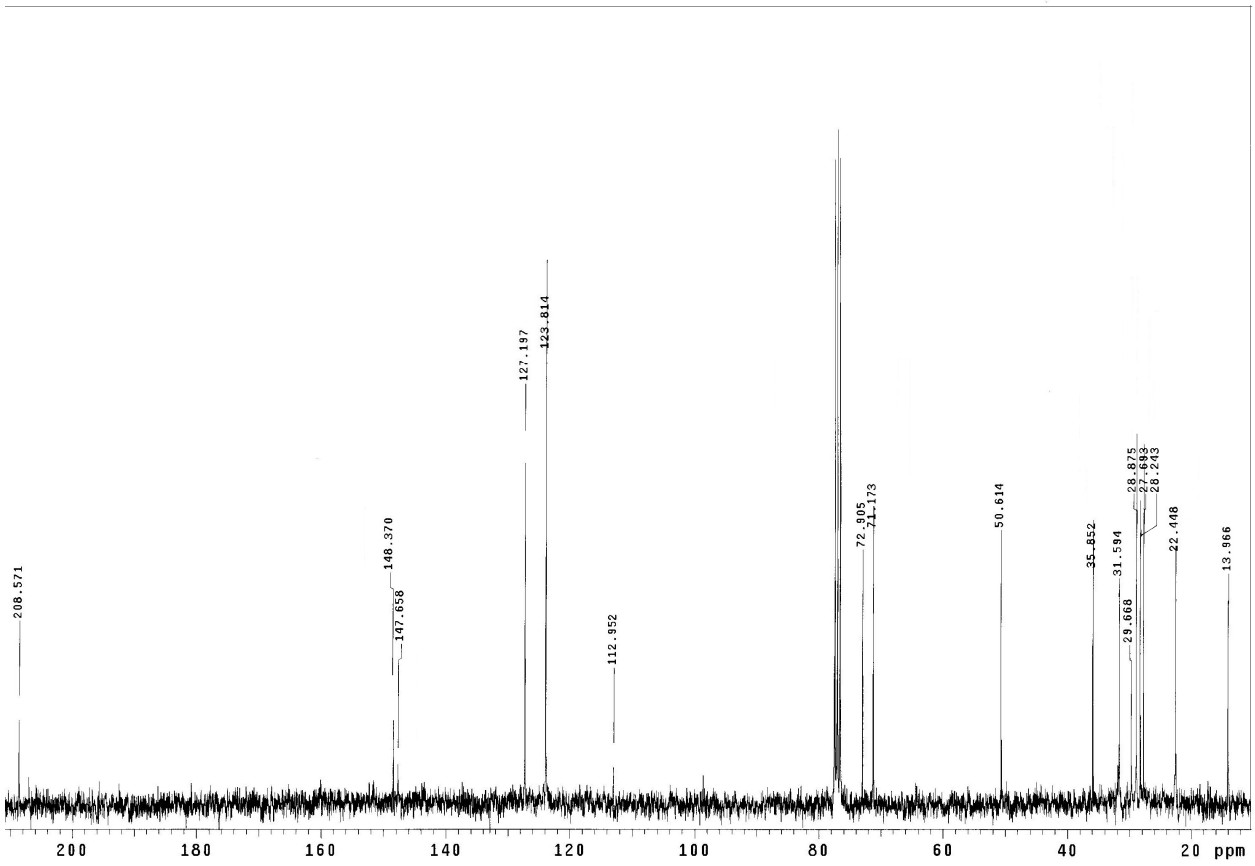

205.821
147.689
140.622
131.897
128.157
127.299
123.861
120.912
77.254
77.000
76.746
72.887
72.347
52.510
32.297
200
150
100
50
0
ppm (t1)

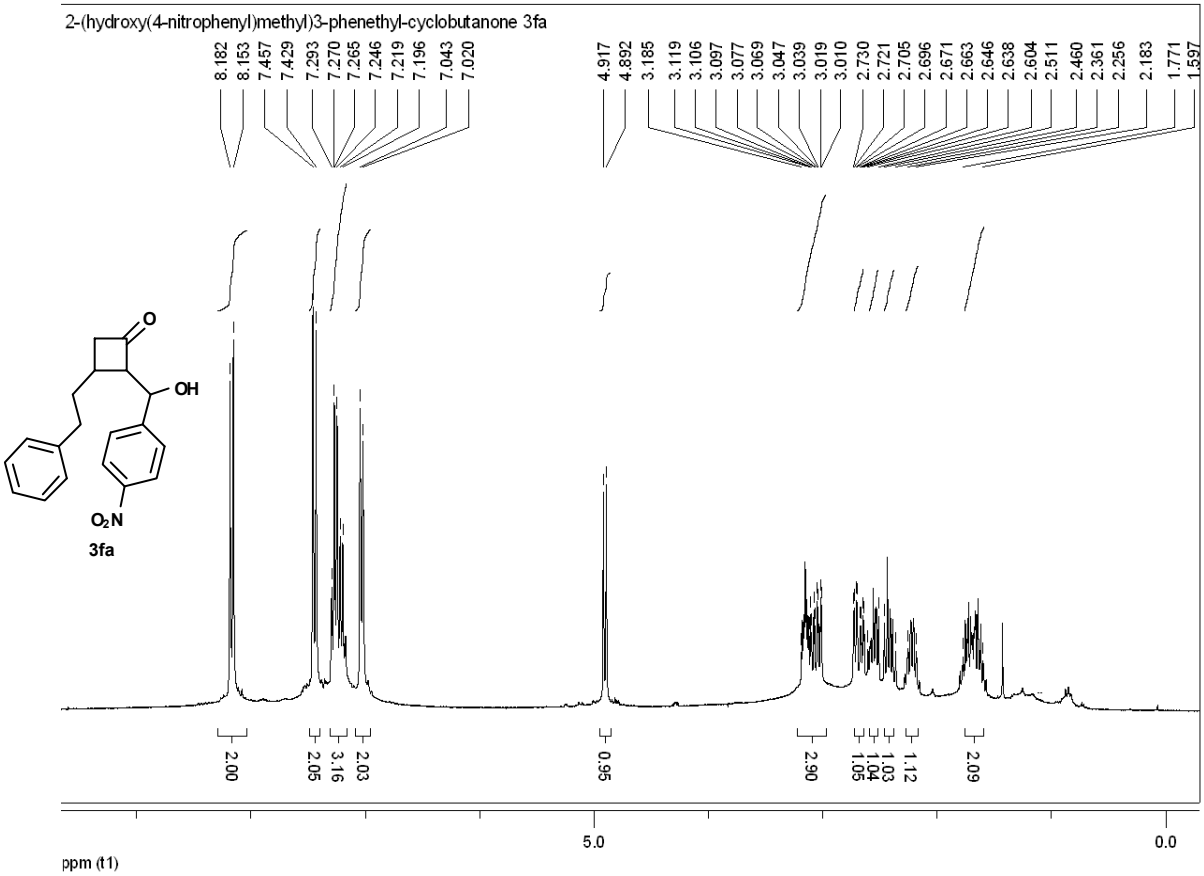

2-(hydroxy(4-nitrophenyl)methyl)-3-(p-tolyl)cyclobutanone 3da
8.180
8.151
7.569
7.540
7.270
7.091
7.064
6.985
6.958
5.136
5.114
3.733
3.726
3.719
3.715
3.708
3.701
3.694
3.686
3.679
3.570
3.541
3.514
3.487
3.445
3.439
3.416
3.410
3.388
3.381
3.358
3.351
3.281
3.272
3.252
3.244
3.222
3.214
3.194
3.187
3.023
2.308
O
OH
H3C
O2N
3da
1.96
1.97
3.98
0.93
1.06
1.08
1.17
1.18
0.99
3.00
5.0
ppm (t1)

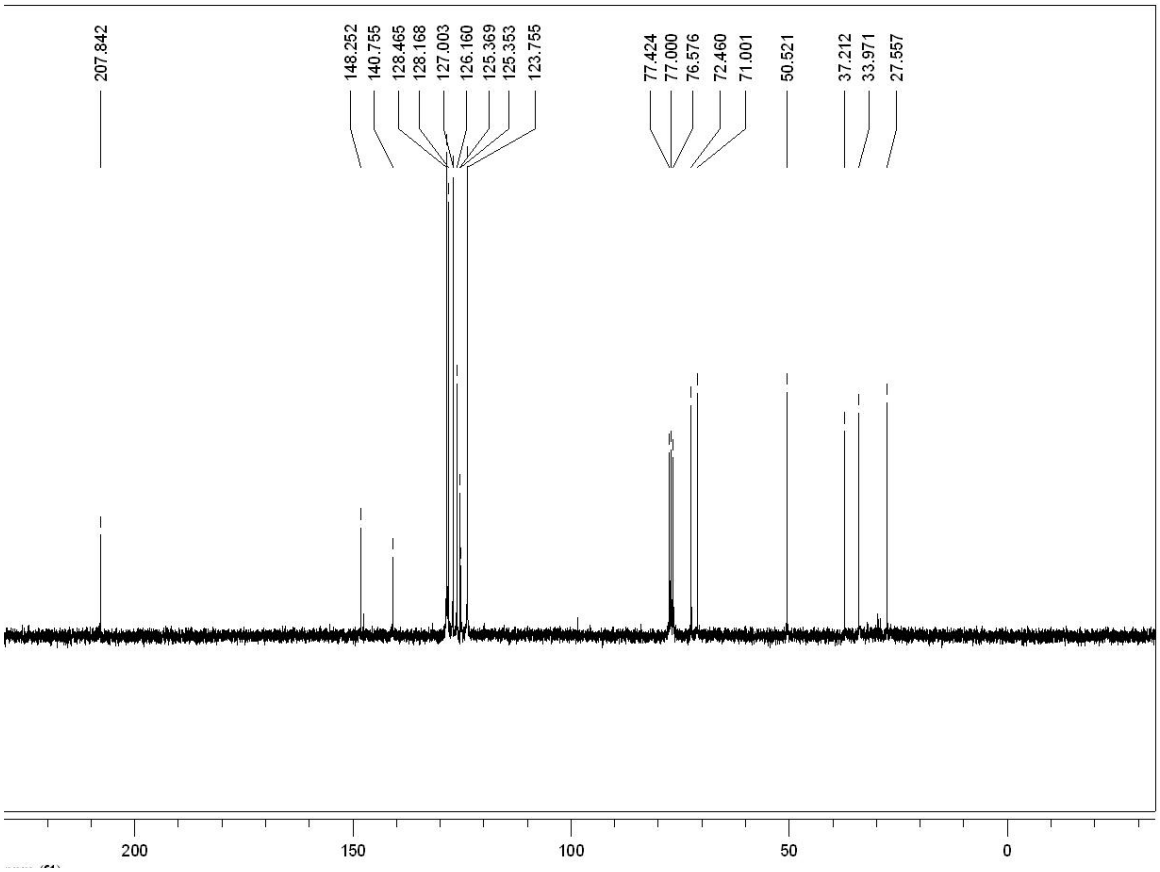

207.064
147.926
138.489
136.706
129.407
127.289
126.239
125.369
123.747
77.423
77.000
76.579
72.782
72.492
52.654
32.425
20.923
200
150
100
50
0
ppm (t1)

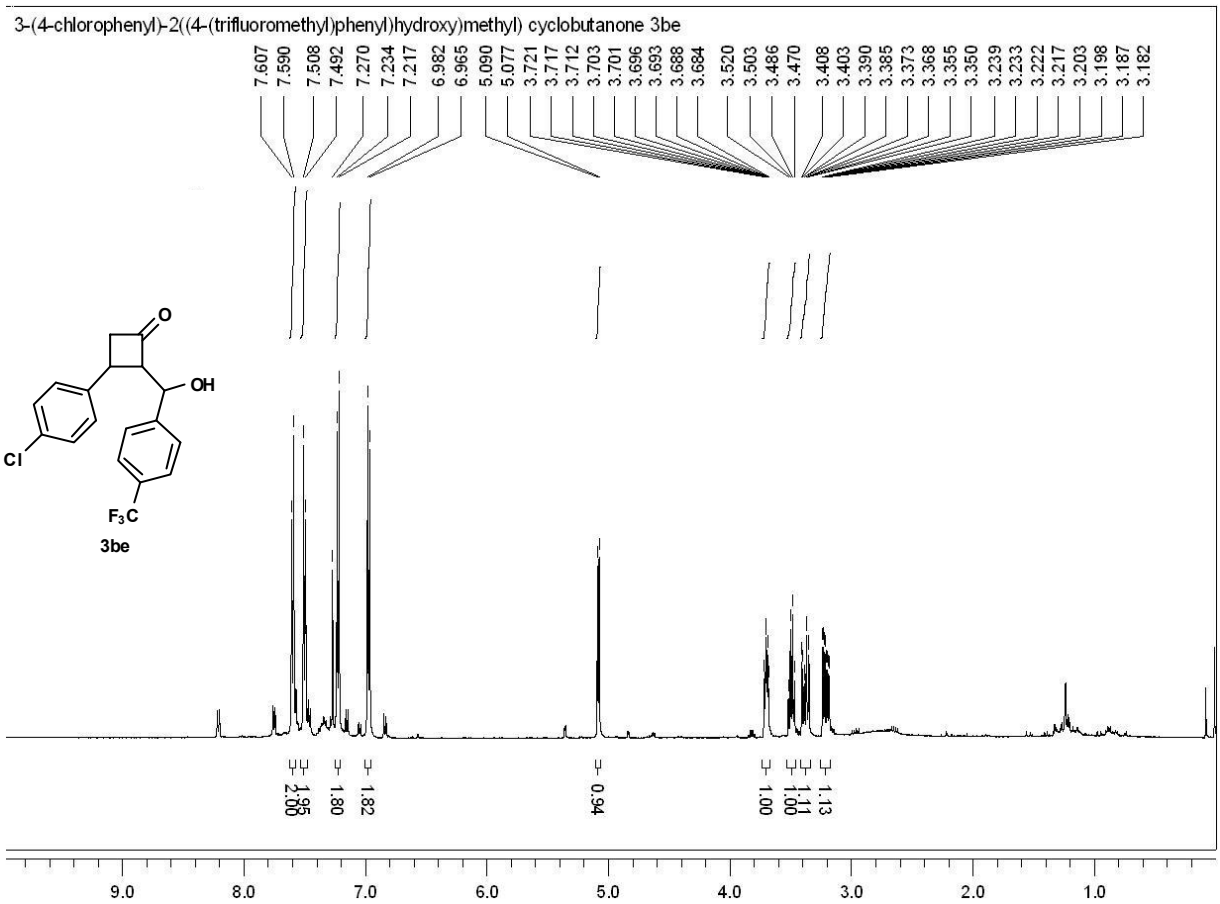
3-*n*-hexyl-2-(hydroxy(4-nitrophenyl)methyl)cyclobutanone **3ea**

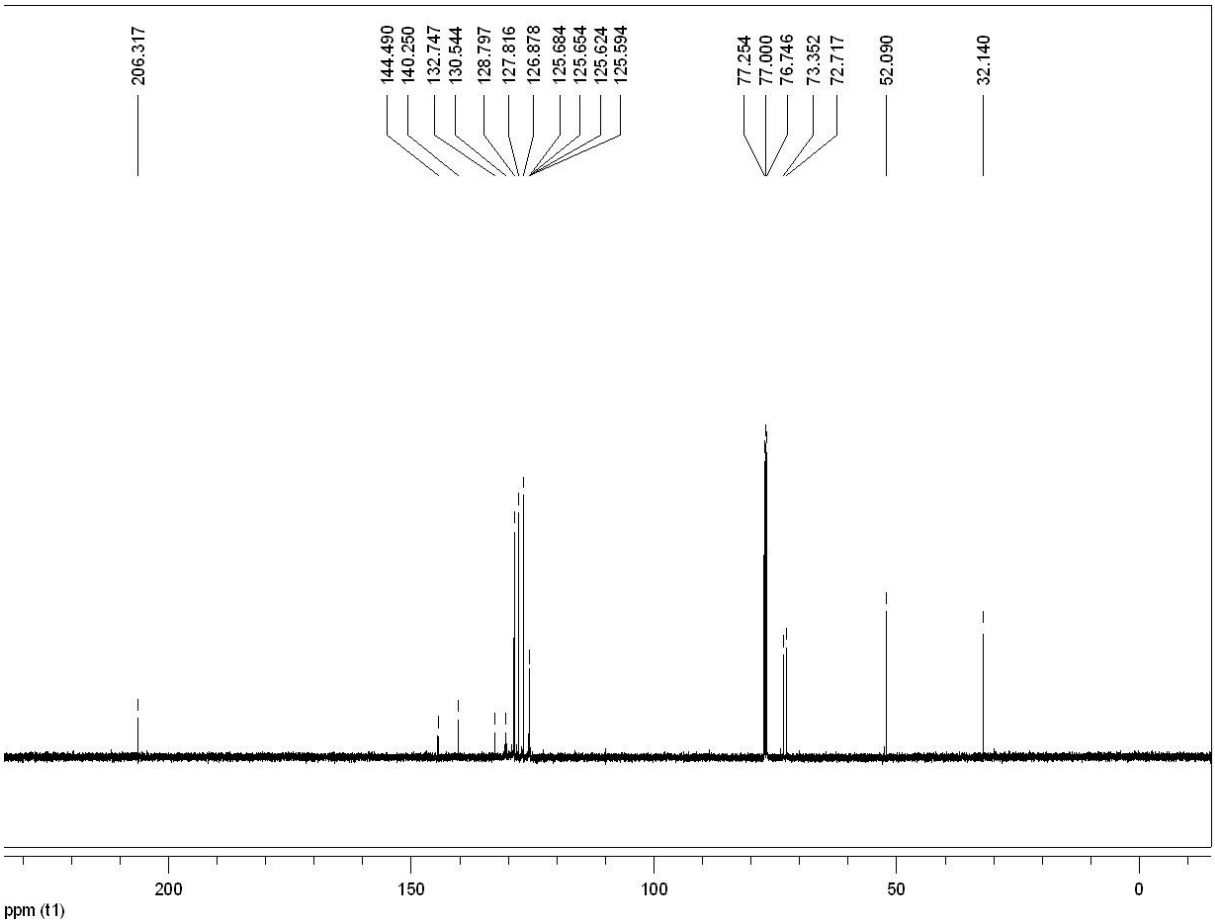


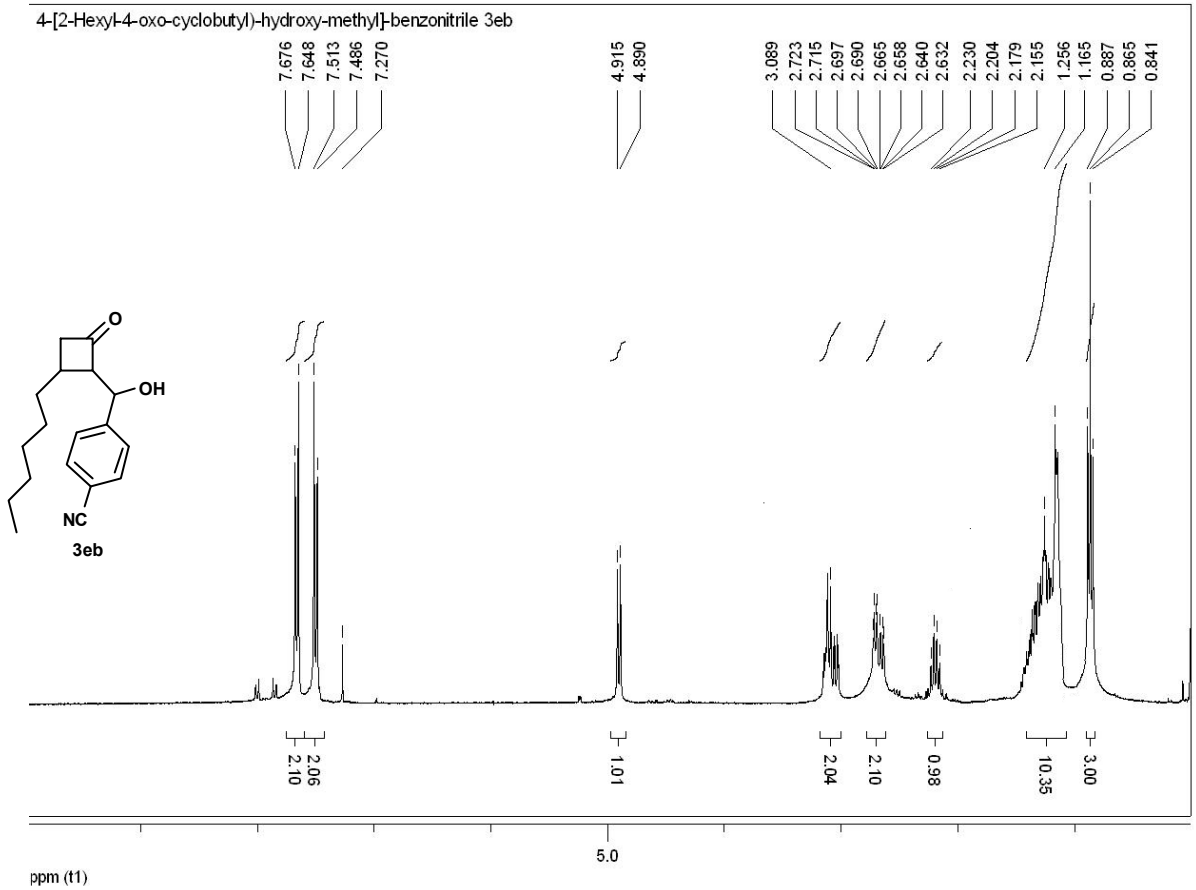



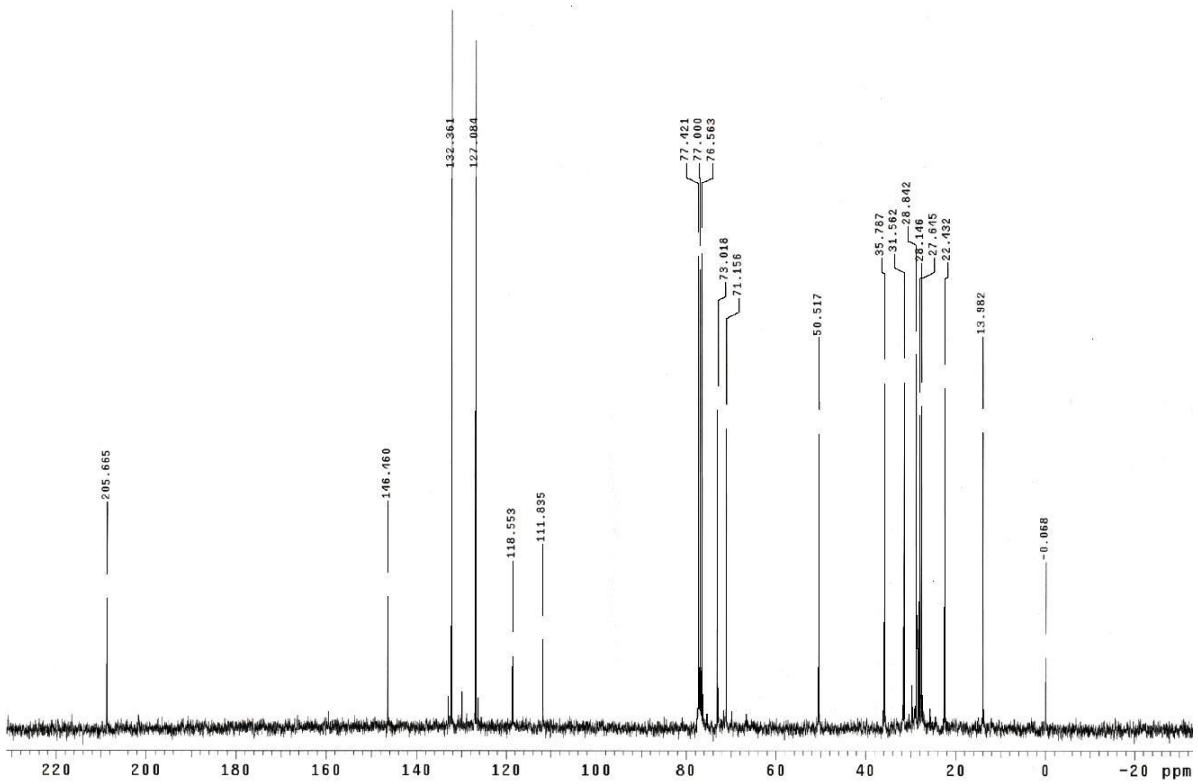

2-(hydroxy(4-nitrophenyl)methyl)3-phenethyl-cyclobutanone 3fa
8.182
8.153
7.457
7.429
7.293
7.270
7.265
7.246
7.219
7.196
7.043
7.020
4.917
4.892
3.185
3.119
3.106
3.097
3.077
3.069
3.047
3.039
3.019
3.010
2.730
2.721
2.705
2.696
2.671
2.663
2.646
2.638
2.604
2.511
2.460
2.361
2.256
2.183
1.771
1.597
O
OH
$O_2N$
3fa
2.00
2.05
3.16
2.03
0.95
2.90
1.05
1.04
1.03
1.12
2.09
5.0
0.0
ppm (t1)


207.842
148.252
140.755
128.465
128.168
127.003
126.160
125.369
125.353
123.755
77.424
77.000
76.576
72.460
71.001
50.521
37.212
33.971
27.557
200
150
100
50
0

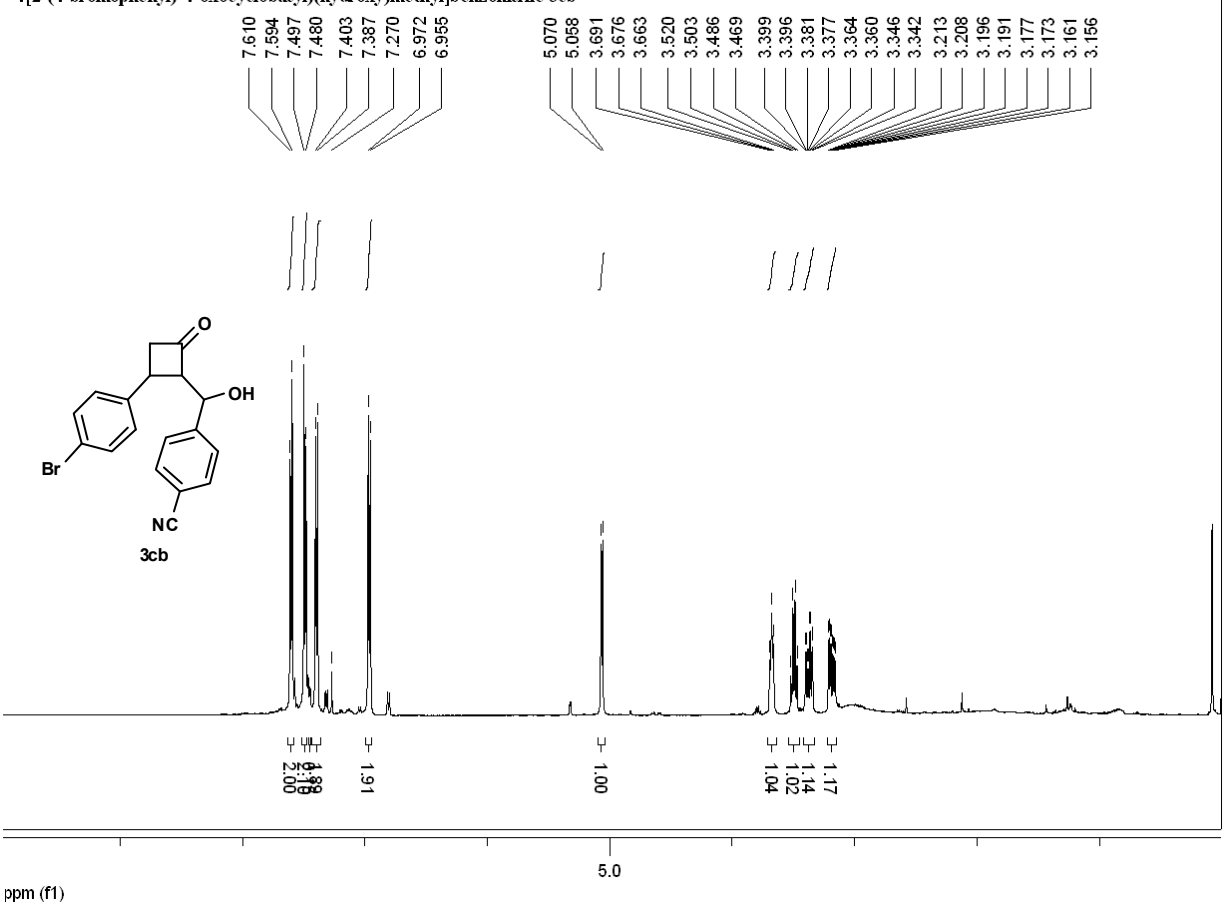

3-(4-chlorophenyl)-2((4-(trifluoromethyl)phenyl)hydroxy)methyl) cyclobutanone 3be
7.607 7.590 7.508 7.492 7.270 7.234 7.217 6.982 6.965 5.090 5.077 3.721 3.717 3.712 3.703 3.701 3.696 3.693 3.688 3.684 3.520 3.503 3.486 3.470 3.408 3.403 3.390 3.385 3.373 3.368 3.355 3.350 3.239 3.233 3.222 3.217 3.203 3.198 3.187 3.182
O
OH
Cl
F3C
3be
2.00 1.95 1.80 2.82 0.94 1.00 1.00 1.11 1.13
9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0

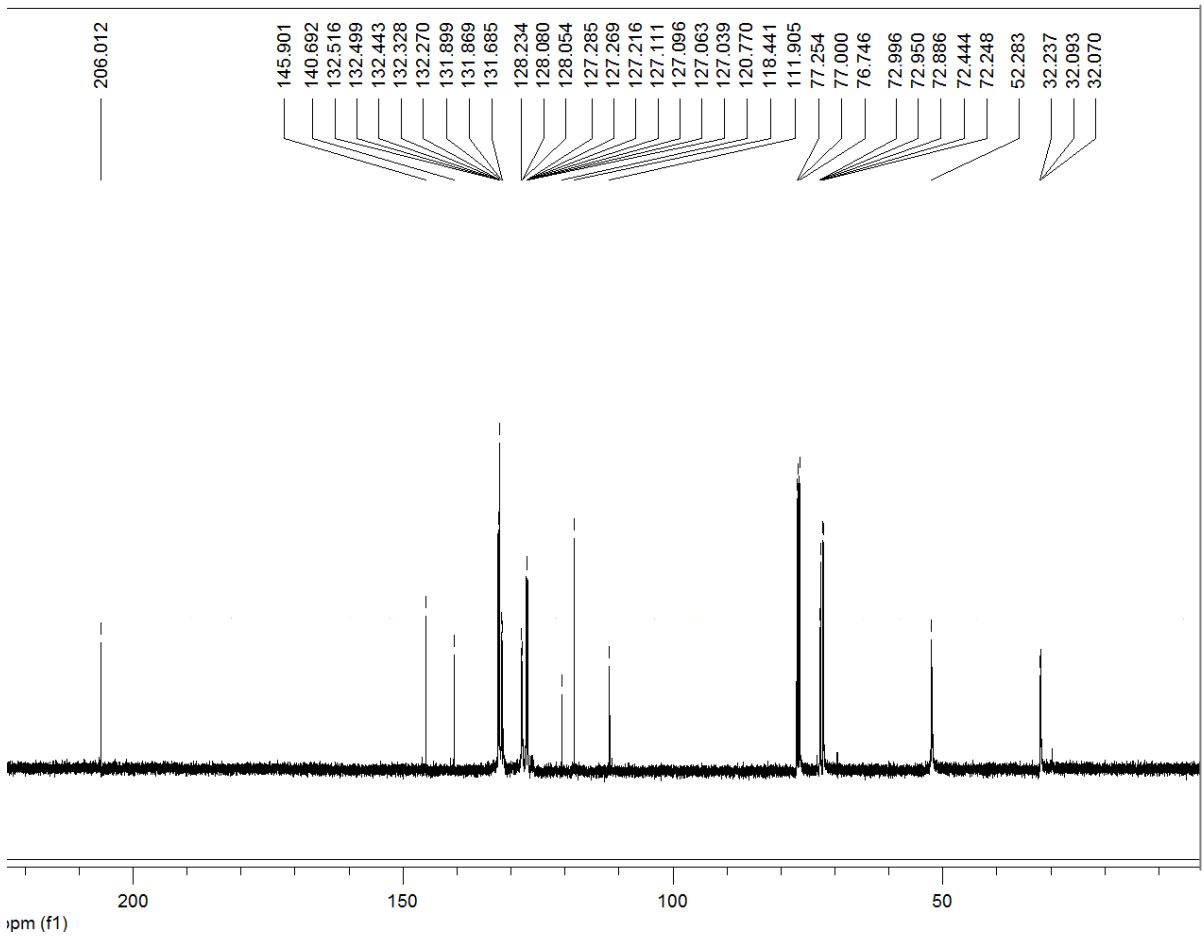

206.317
144.490 140.250 132.747 130.544 128.797 127.816 126.878 125.684 125.654 125.624 125.594
77.254 77.000 76.746 73.352 72.717
52.090
32.140
200 150 100 50 0
ppm (t1)

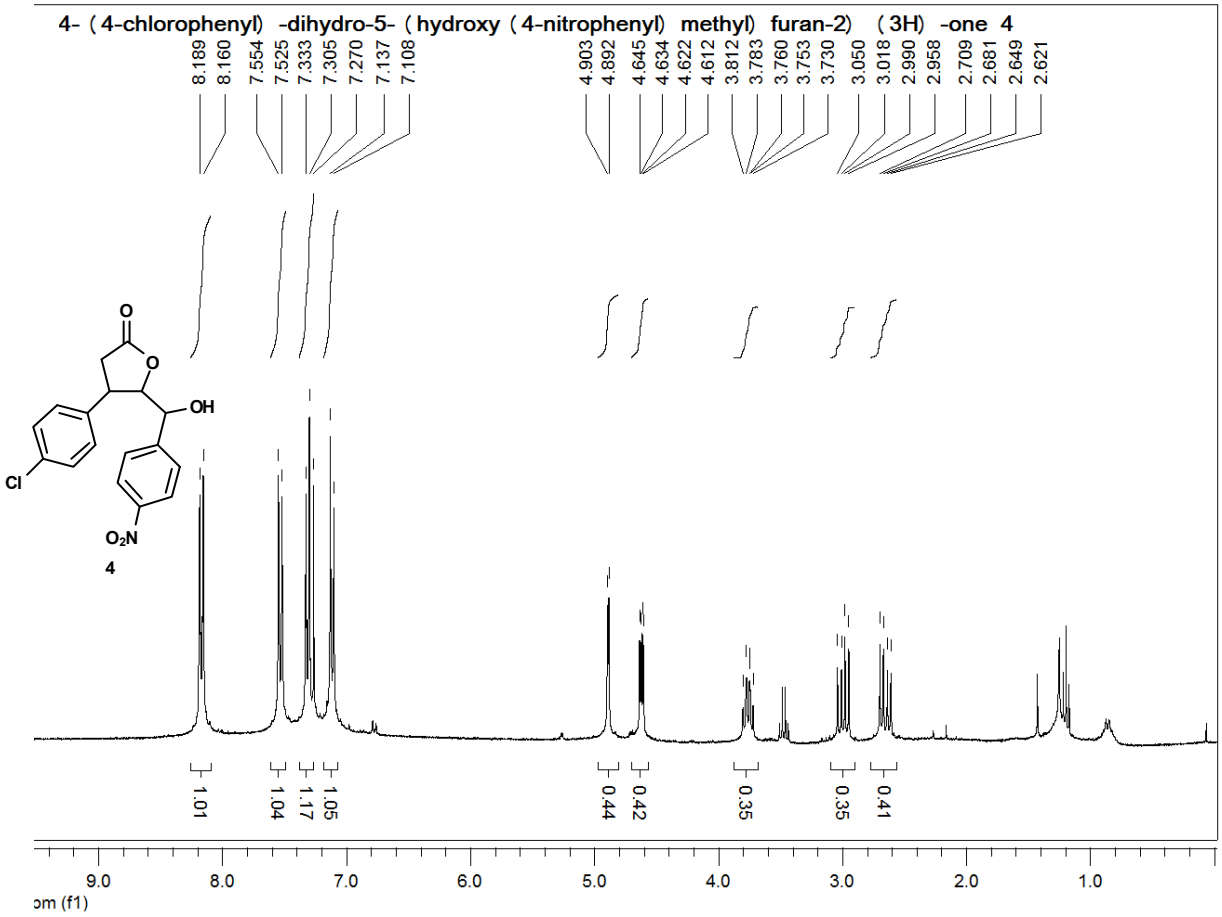

4-[2-Hexyl-4-oxo-cyclobutyl)-hydroxy-methyl]-benzonitrile 3eb
7.676
7.648
7.513
7.486
7.270
4.915
4.890
3.089
2.723
2.715
2.697
2.690
2.665
2.658
2.640
2.632
2.230
2.204
2.179
2.155
1.256
1.165
0.887
0.865
0.841
O
OH
NC
3eb
2.10
2.06
1.01
2.04
2.10
0.98
10.35
3.00
5.0
ppm (t1)

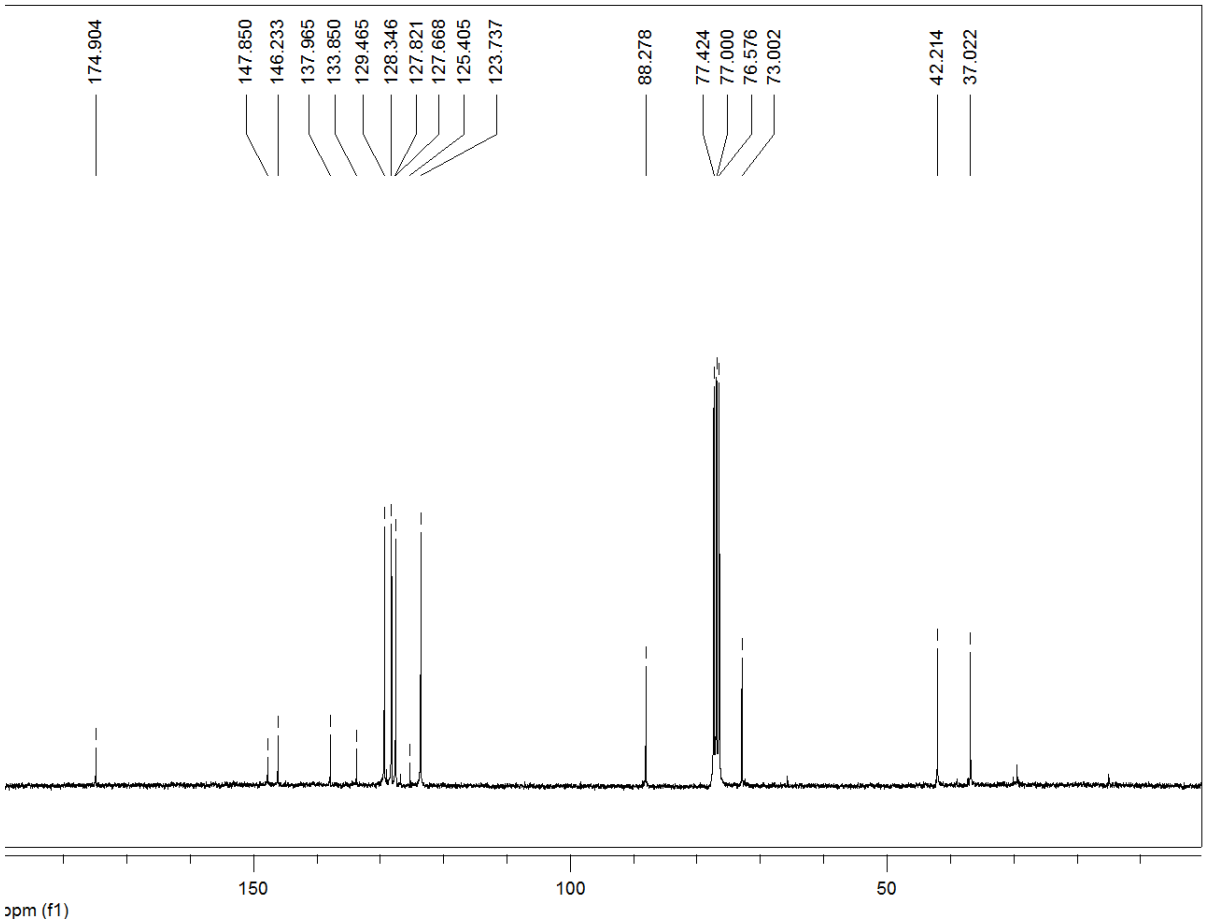

205.665
146.160
132.361
122.084
118.553
111.835
77.421
77.000
76.563
73.018
71.156
50.517
35.787
31.562
28.842
28.146
27.645
22.432
13.982
-0.068
220
200
180
160
140
120
100
80
60
40
20
0
-20 ppm

4[2-(4-bromophenyl)-4-oxocyclobutyl)(hydroxy)methyl]benzonitrile 3cb



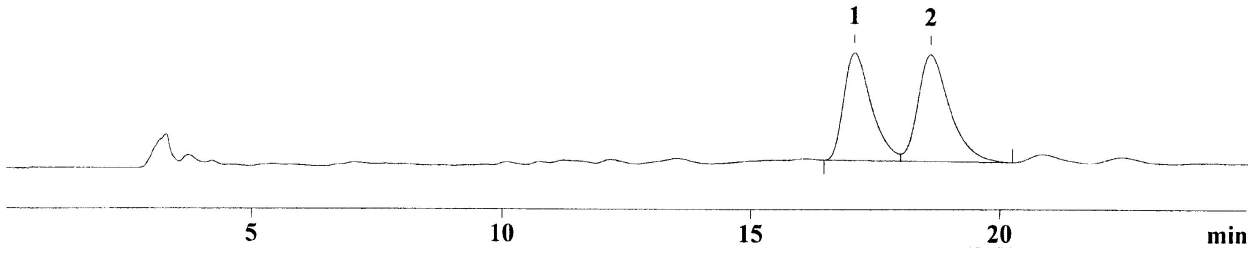



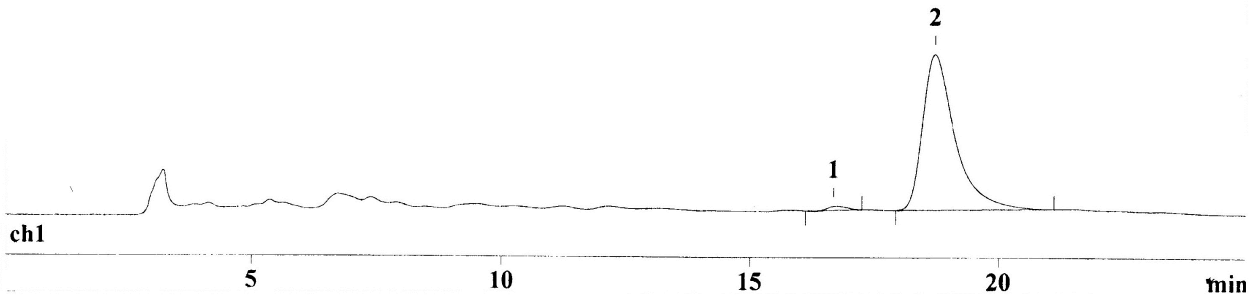

4- (4-chlorophenyl) -dihydro-5- (hydroxy (4-nitrophenyl) methyl) furan-2) (3H) -one 4
8.189
8.160
7.554
7.525
7.333
7.305
7.270
7.137
7.108
4.903
4.892
4.645
4.634
4.622
4.612
3.812
3.783
3.760
3.753
3.730
3.050
3.018
2.990
2.958
2.709
2.681
2.649
2.621
O
O
OH
Cl
O2N
4
1.01
1.04
1.17
1.05
0.44
0.42
0.35
0.35
0.41
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ɔm (f1)


174.904
147.850
146.233
137.965
133.850
129.465
128.346
127.821
127.668
125.405
123.737
88.278
77.424
77.000
76.576
73.002
42.214
37.022
150
100
50
ɔpm (f1)

## 5. Copies of HPLC traces of new aldol adducts:

**3aa**: Chiracel AD-H column (hexane/i-PrOH = 90:10, flow rate 1.0 mL/min, λ = 254 nm)

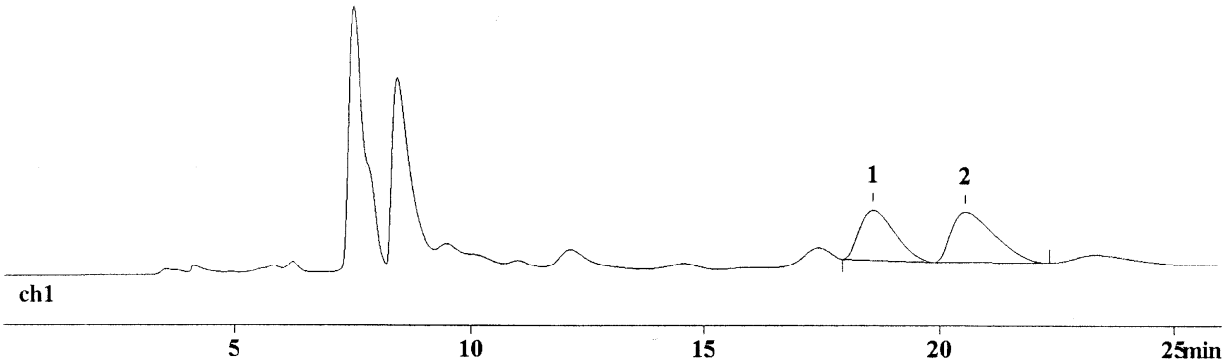


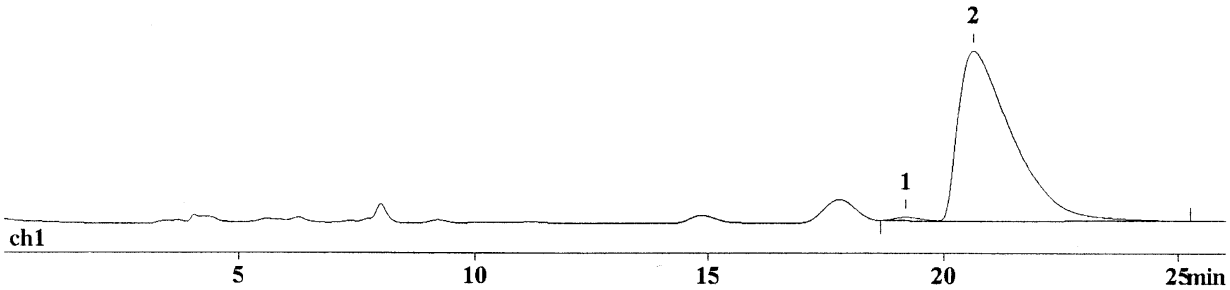




Quantitation method: Absolute concentration
Standard component: No
Normalization: 100.00

| No | Retention min | Area mV*sec | Area % | Name |
|---|---|---|---|---|
| 1 | 16.68 | 8.017 | 0.52 | |
| 2 | 18.71 | 1533.532 | 99.48 | |
| 2 | 33.41 | 1541.549 | 100.00 | |

**3ab** :Chiracel OD-H column (hexane/i-PrOH = 85 :15, flow rate 1.0 mL/min, λ = 254 nm)

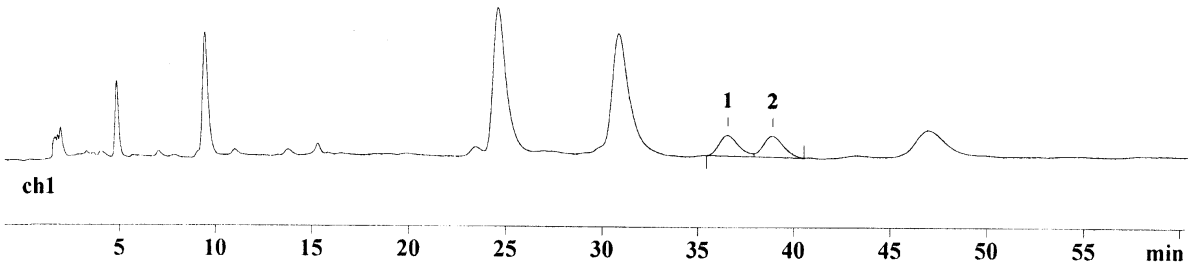


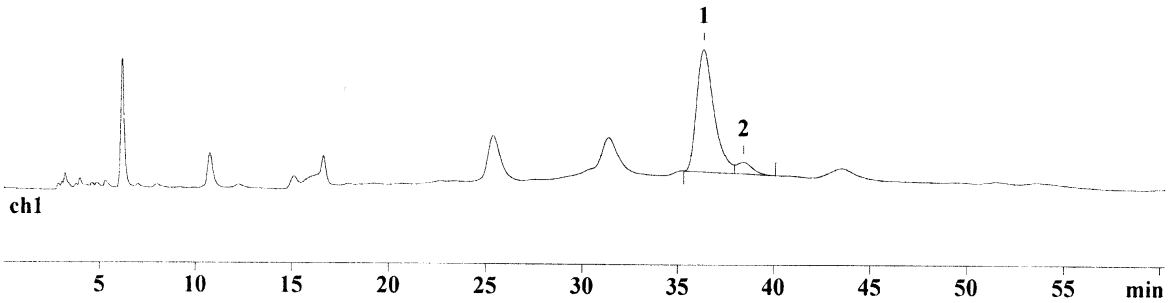




Quantitation method: Absolute concentration

| No | Retention min | Area mV*sec | Area % | Name |
|---|---|---|---|---|
| 1 | 19.18 | 309.545 | 0.94 | |
| 2 | 20.61 | 32547.334 | 99.06 | |
| 2 | 26.03 | 32856.879 | 100.00 | |

**3ac**: Chiracel AD-H column (hexane/i-PrOH = 95 :5, flow rate 1.0 mL/min, λ = 254 nm)

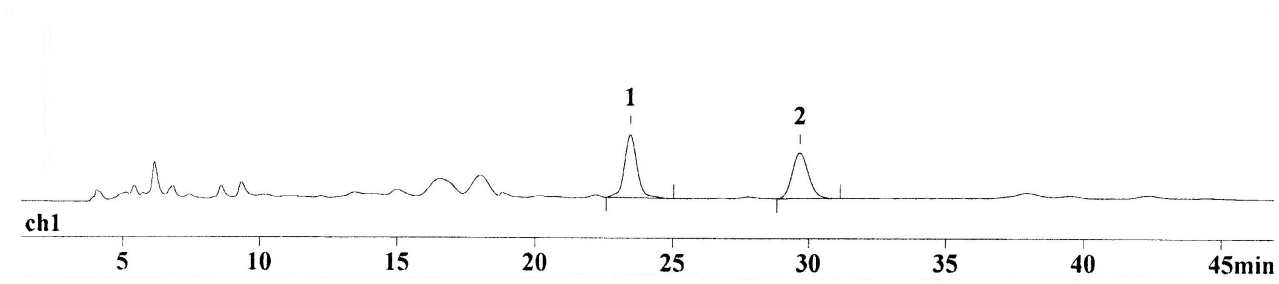


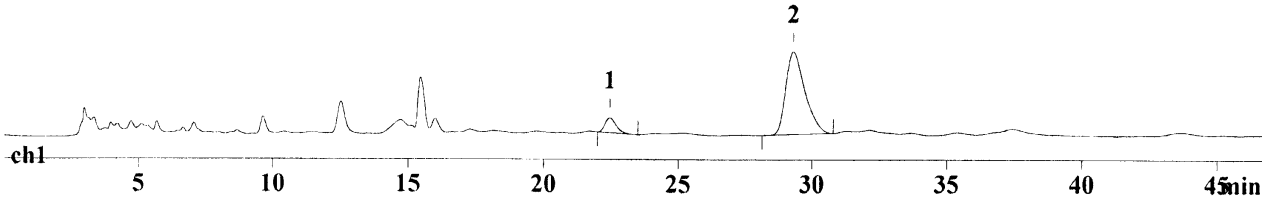




Quantitation method: Absolute concentration
Standard component: No
Normalization: 100.00

| No | Retention min | Area mV*sec | Area % | Name |
|---|---|---|---|---|
| 1 | 36.30 | 2029.270 | 92.06 | |
| 2 | 38.40 | 174.999 | 7.94 | |
| 2 | 80.39 | 2204.270 | 100.00 | |

**3ad** :Chiracel AD-H column (hexane/i-PrOH = 95 :05, flow rate 1.0 mL/min, λ = 254 nm)

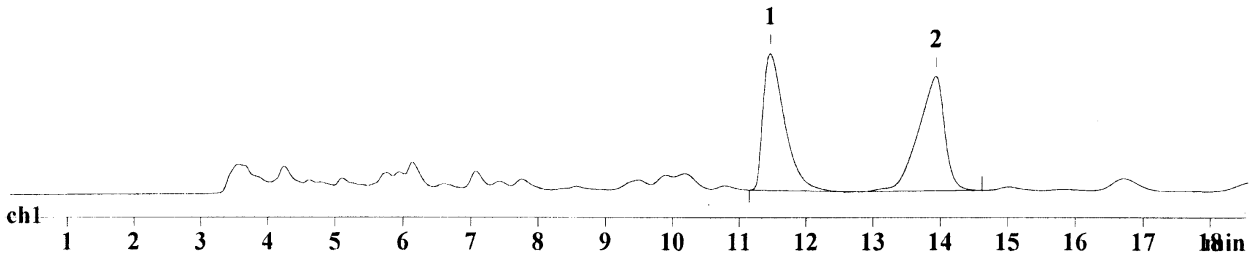


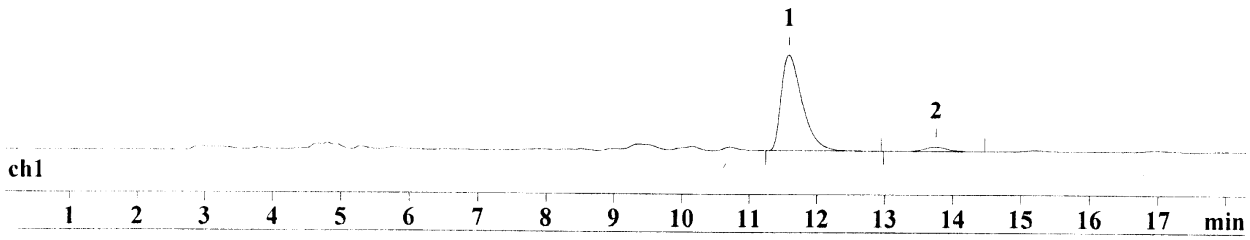




Quantitation method: Absolute concentration
Standard component: No
Normalization: 100.00

| No | Retention min | Area mV*sec | Area % | Name |
|---|---|---|---|---|
| 1 | 22.45 | 856.030 | 9.33 | |
| 2 | 29.30 | 8320.673 | 90.67 | |
| 2 | 46.66 | 9176.703 | 100.00 | |

**3ae** :Chiracel AD-H column (hexane/i-PrOH = 90 :10, flow rate 1.0 mL/min, λ = 254 nm)

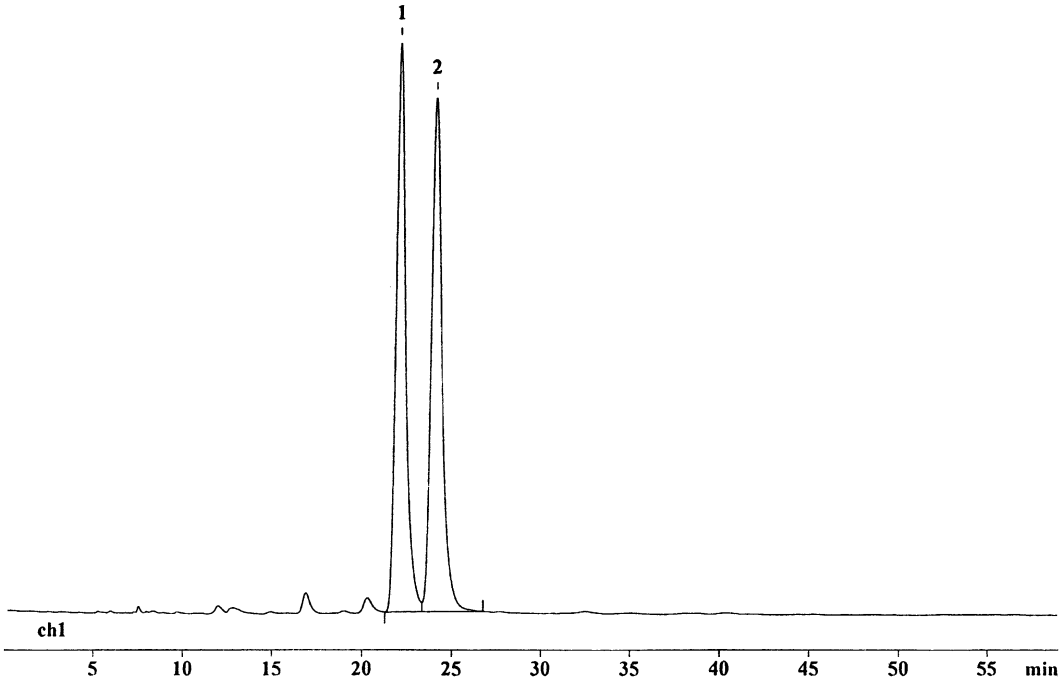


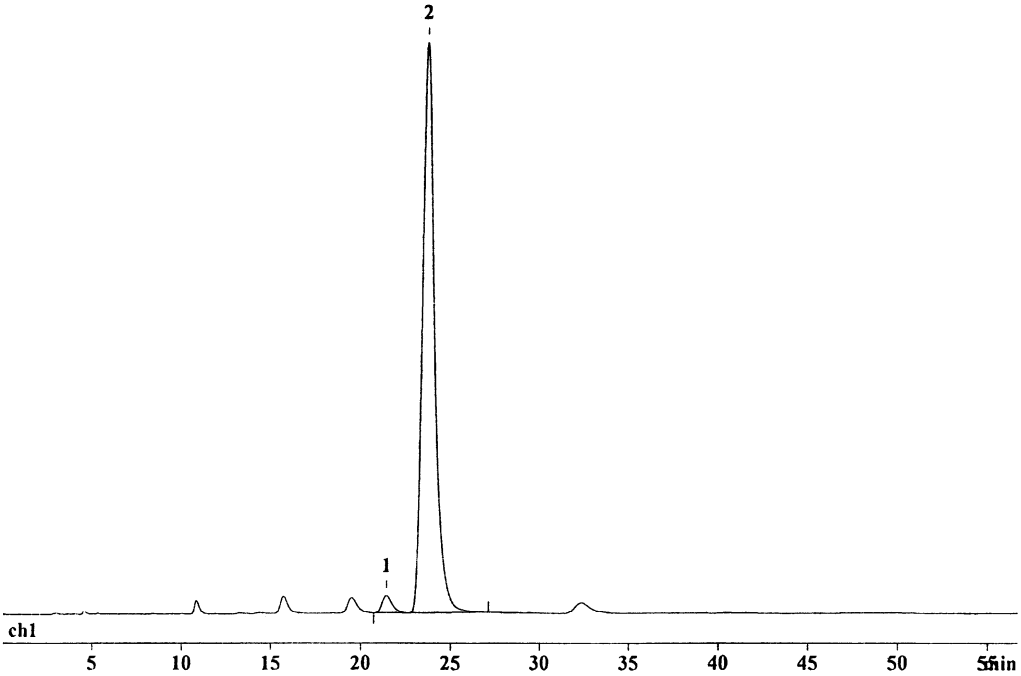




Quantitation method: Absolute concentration
Standard component: No
Normalization: 100.00

| No | Retention min | Area mV*sec | Area % | Name |
|---|---|---|---|---|
| 1 | 11.57 | 9352.377 | 95.40 | |
| 2 | 13.74 | 451.295 | 4.60 | |
| 2 | 29.50 | 9803.673 | 100.00 | |

**3af**: Chiracel AD-H column (hexane/i-PrOH = 90 :10, flow rate 1.0 mL/min, λ = 254 nm)

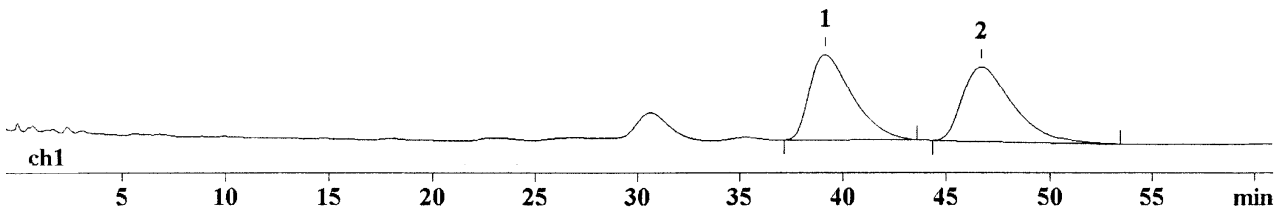


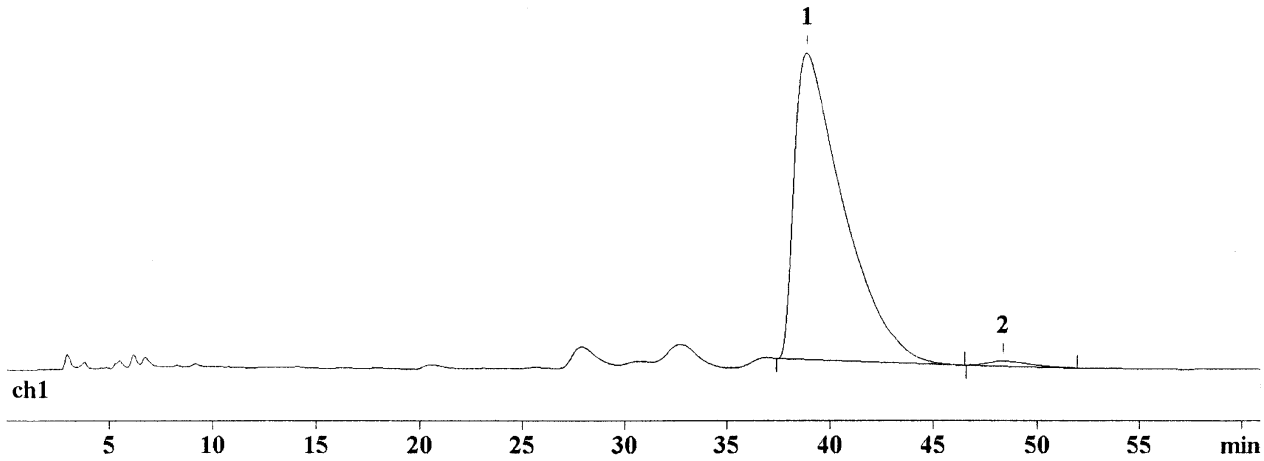




Quantitation method: Absolute concentration
Standard component: No
Normalization: 100.00

| No | Retention min | Area mV*sec | Area % | Name |
|---|---|---|---|---|
| 1 | 21.42 | 657.400 | 2.63 | |
| 2 | 23.62 | 24360.435 | 97.37 | |
| 2 | 56.65 | 25017.835 | 100.00 | |

**3ba** :Chiracel OJ column (hexane/i-PrOH = 80 :20, flow rate 1.0 mL/min, λ = 254 nm)

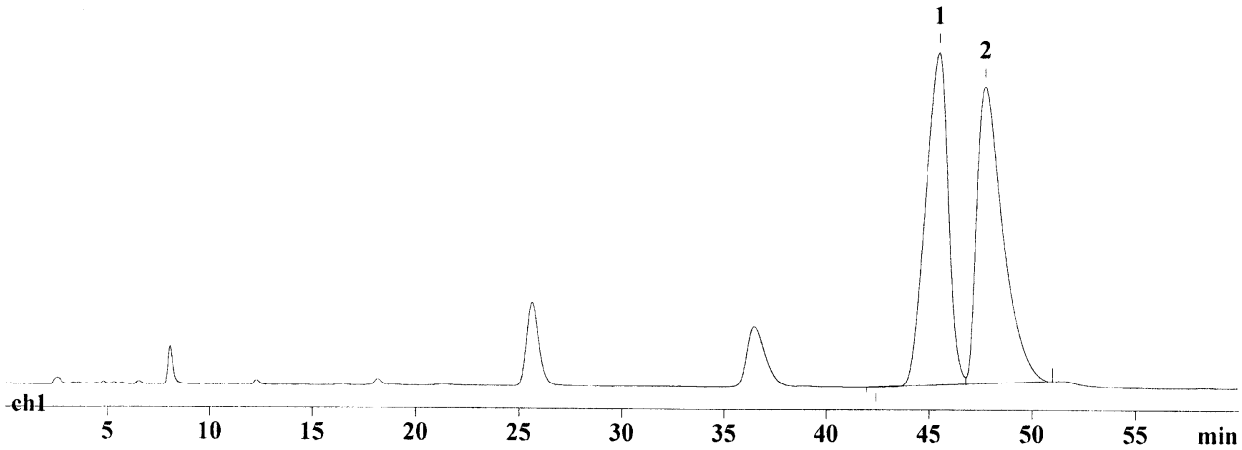


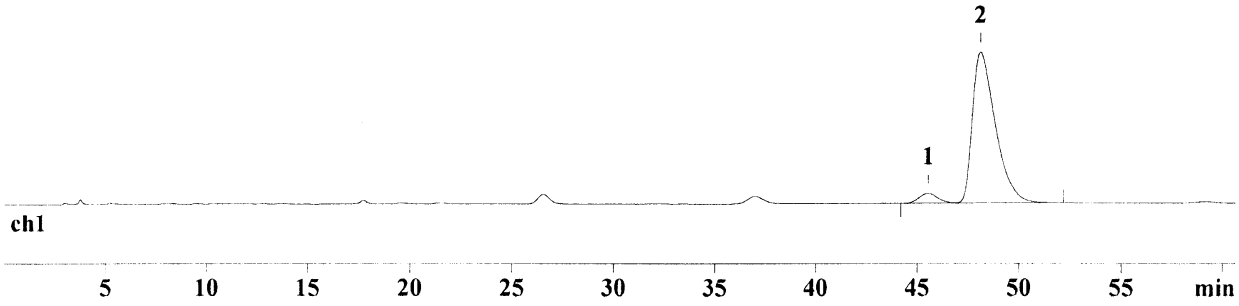




Quantitation method: Absolute concentration

| No | Retention min | Area mV*sec | Area % | Name |
|---|---|---|---|---|
| 1 | 38.85 | 84505.036 | 98.73 | |
| 2 | 48.35 | 1089.283 | 1.27 | |
| 2 | 70.00 | 85594.320 | 100.00 | |

**3ca** :Chiracel AD-H column (hexane/i-PrOH = 90 :10, flow rate 1.0 mL/min, λ = 254 nm)

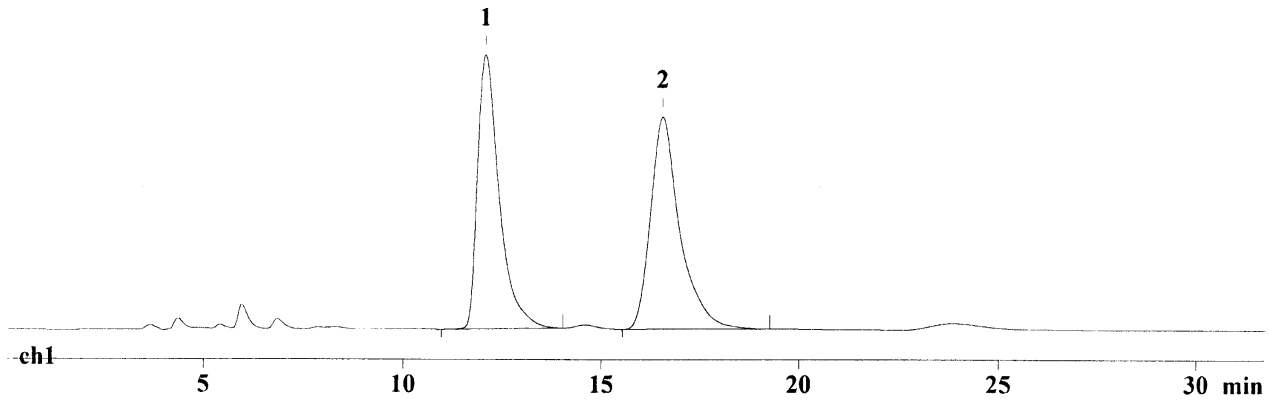


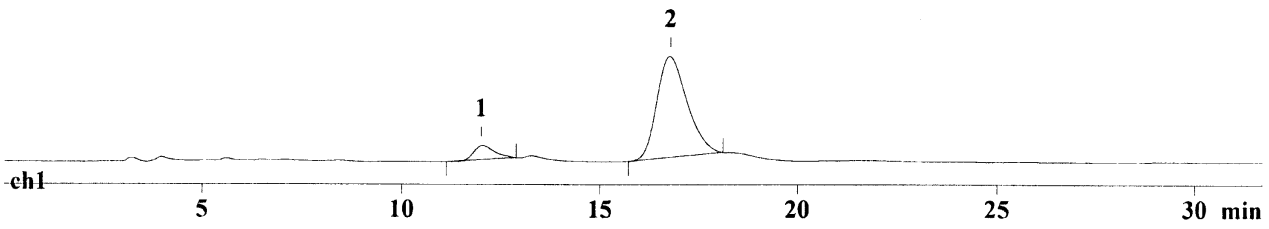




Quantitation method: Absolute concentration
Standard component: No
Normalization: 100.00

| No | Retention min | Area mV*sec | Area % | Name |
|---|---|---|---|---|
| 1 | 45.54 | 1290.192 | 5.27 | |
| 2 | 48.13 | 23176.501 | 94.73 | |
| 2 | 76.59 | 24466.693 | 100.00 | |

**3da** :Chiracel OD-H column (hexane/i-PrOH = 85 :15, flow rate 1.0 mL/min, λ = 254 nm)

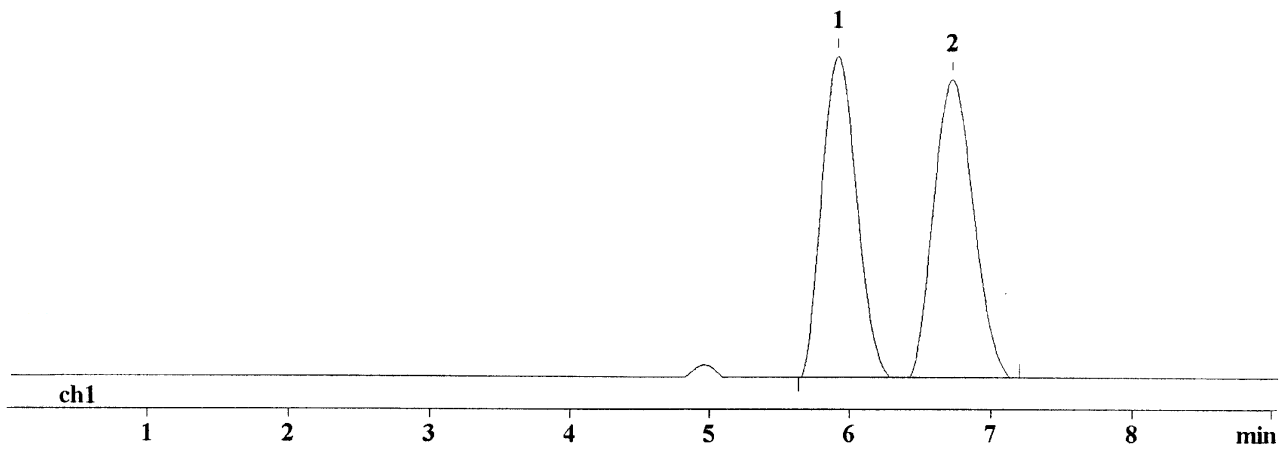


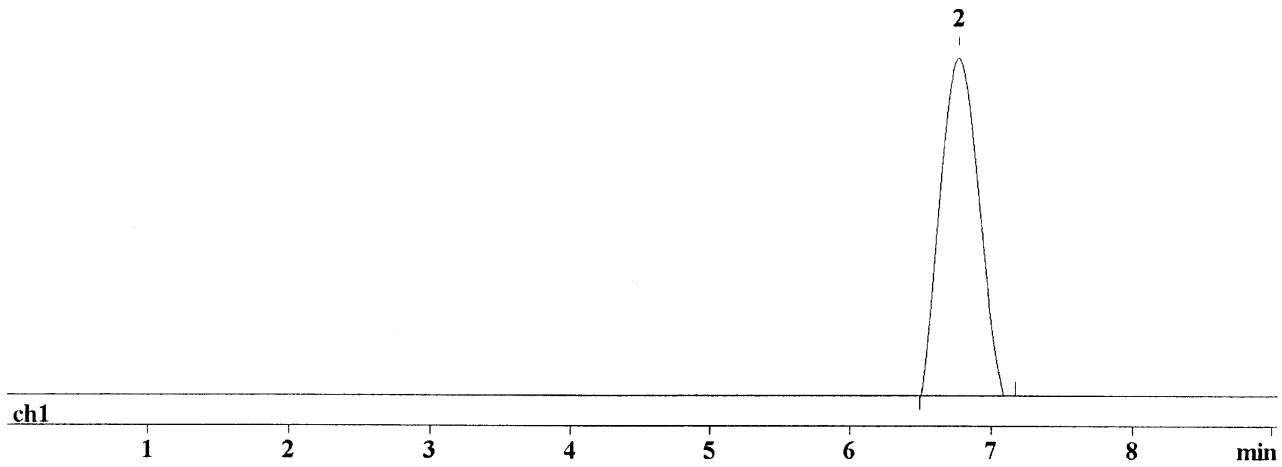




Quantitation method: Absolute concentration

| No | Retention min | Area mV*sec | Area % | Name |
|---|---|---|---|---|
| 1 | 11.99 | 2062.660 | 8.70 | |
| 2 | 16.79 | 21648.538 | 91.30 | |
| 2 | 31.72 | 23711.198 | 100.00 | |

**3ea** :Chiracel OD-H column (hexane/i-PrOH = 85 :15, flow rate 1.0 mL/min, λ = 254 nm)



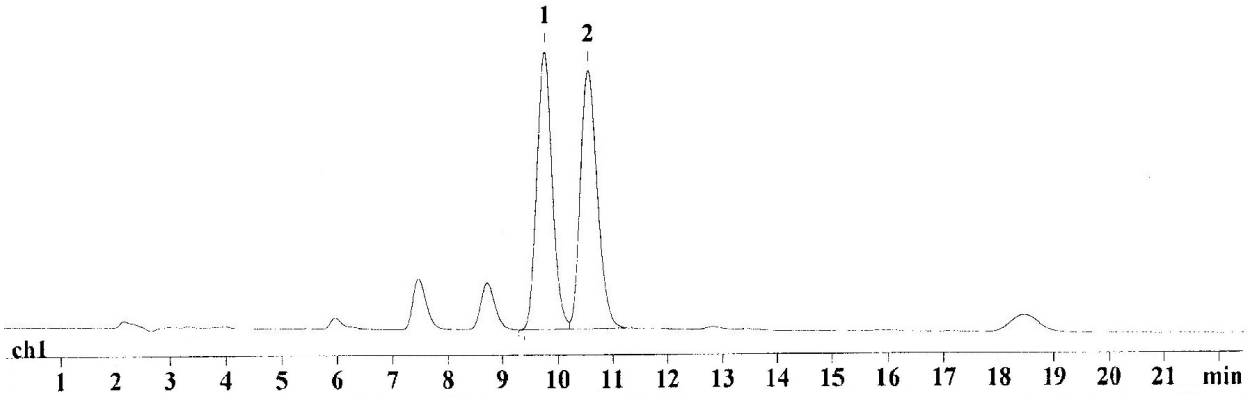



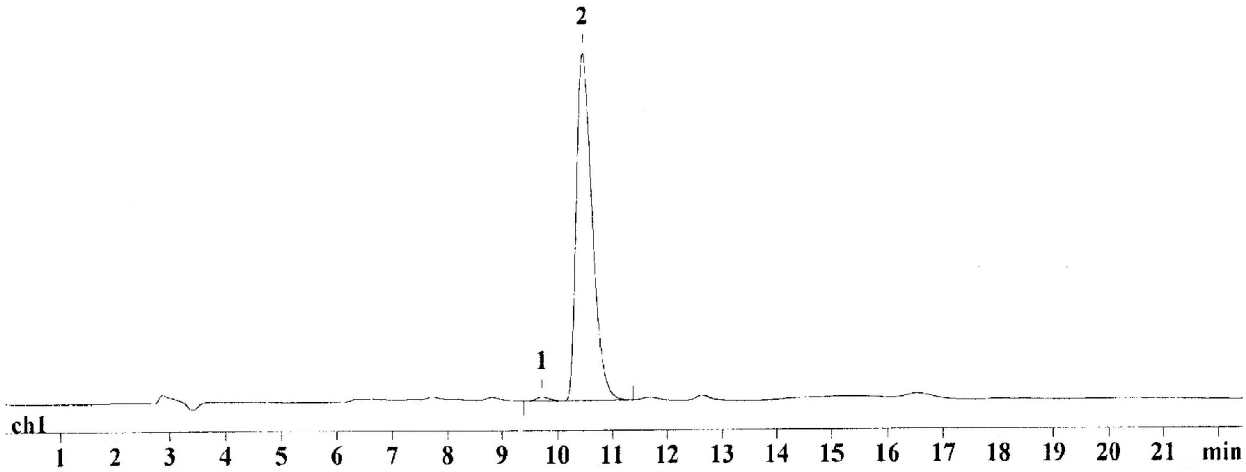

Quantitation method: Absolute concentration

| No | Retention min | Area mV*sec | Area % | Name |
|---|---|---|---|---|
| 1 | 6.76 | 6395.389 | 100.00 | |

This report has been created by IC Metrodata for Windows
METROHM LTD

**3fa** :Chiracel AD-H column (hexane/i-PrOH = 80 :20, flow rate 1.0 mL/min, λ = 254 nm)

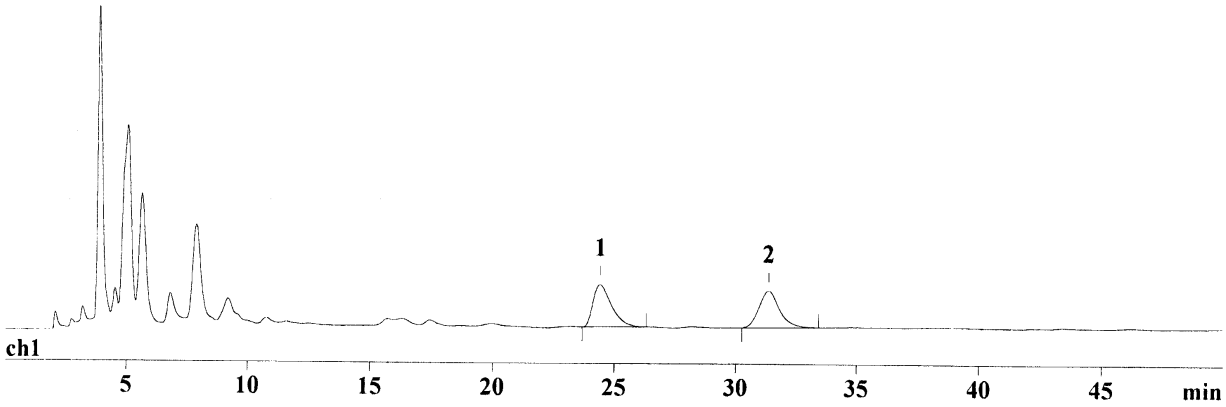


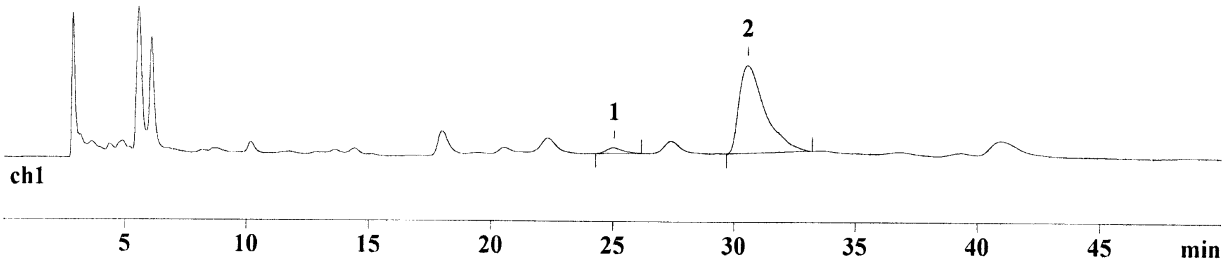




Quantitation method: Absolute concentration

| No | Retention min | Area mV*sec | Area % | Name |
|---|---|---|---|---|
| 1 | 9.73 | 140.633 | 0.95 | |
| 2 | 10.48 | 14705.299 | 99.05 | |
| 2 | 22.45 | 14845.932 | 100.00 | |

**3be**: Chiracel AD-H column (hexane/i-PrOH = 95 :5, flow rate 1.0 mL/min, λ = 254 nm)

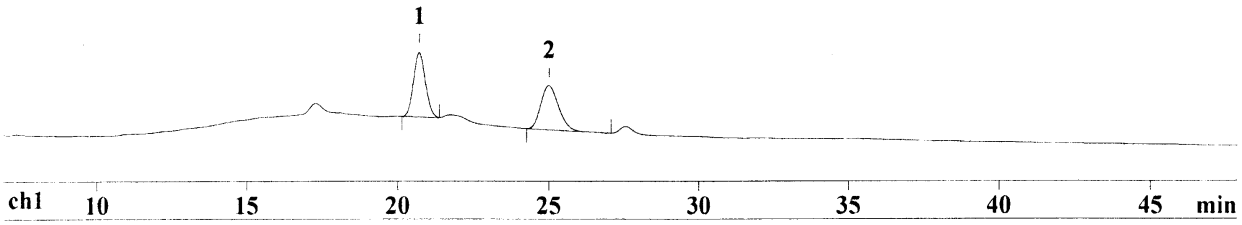


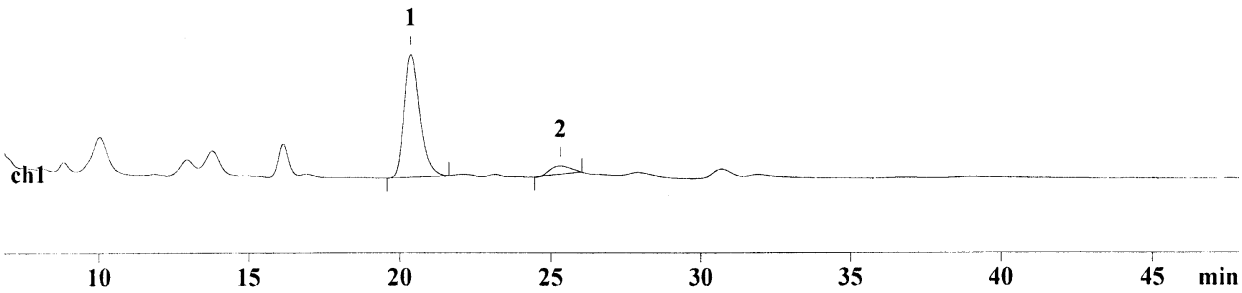




Quantitation method: Absolute concentration
Standard component: No
Normalization: 100.00

| No | Retention min | Area mV*sec | Area % | Name |
|---|---|---|---|---|
| 1 | 25.03 | 74.409 | 4.06 | |
| 2 | 30.54 | 1756.510 | 95.94 | |
| 2 | 62.41 | 1830.919 | 100.00 | |

**3eb** :Chiracel AD-H column (hexane/i-PrOH = 99 :1, flow rate 1.0 mL/min, λ = 254 nm)

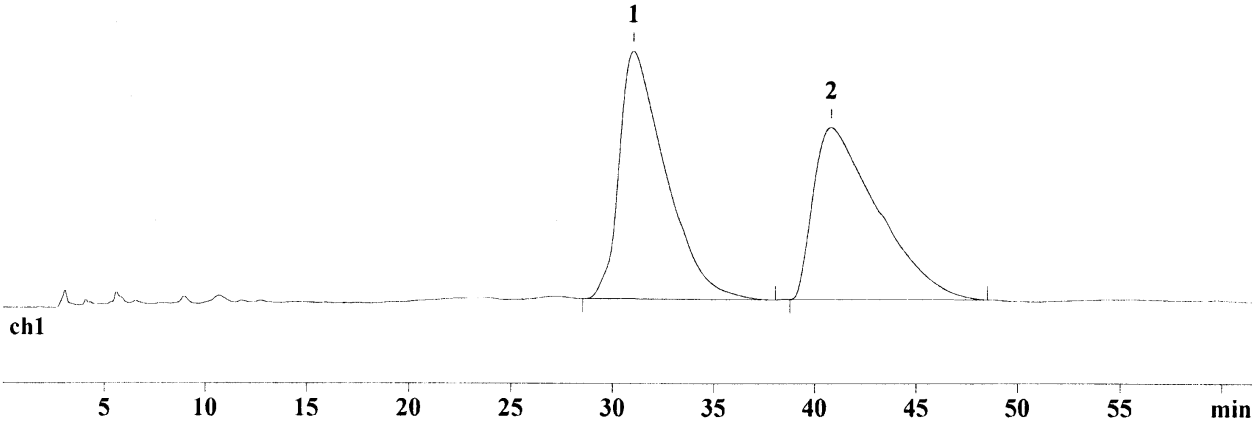


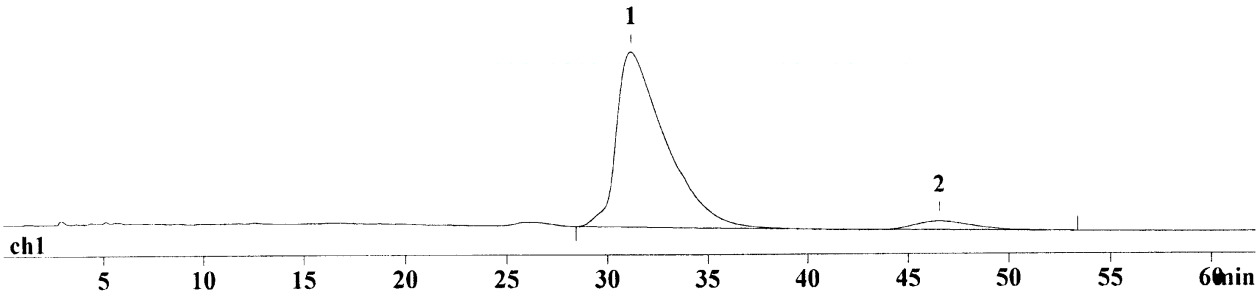




Quantitation method: Absolute concentration
Standard component: No
Normalization: 100.00

| No | Retention min | Area mV*sec | Area % | Name |
|---|---|---|---|---|
| 1 | 20.36 | 3129.401 | 91.51 | |
| 2 | 25.30 | 290.162 | 8.49 | |
| 2 | 49.79 | 3419.563 | 100.00 | |

**3cb** :Chiracel OJ column (hexane/i-PrOH = 75:25, flow rate 1.0 mL/min, λ = 254 nm)




Quantitation method: Absolute concentration
Standard component: No
Normalization: 100.00

| No | Retention min | Area mV*sec | Area % | Name |
|---|---|---|---|---|
| 1 | 31.18 | 13973.634 | 94.45 | |
| 2 | 46.53 | 821.743 | 5.55 | |
| 2 | 62.17 | 14795.377 | 100.00 | |