# SUPPORTING INFORMATION

## Rhodium/Phosphoramidite-Catalyzed Asymmetric Arylation of Aldehydes with Arylboronic Acids

Richard B. C. Jagt,[a] Patrick Y. Toullec,[a] Johannes G. de Vries,*[b]

Ben L. Feringa,*[a] Adriaan J. Minnaard*[a]

[a] *Department of Organic and Molecular Inorganic Chemistry, Stratingh Institute, University of Groningen, Nijenborgh 4, 9747 AG, Groningen, The Netherlands*

[b] *DSM Research, Life Sciences - Advanced Synthesis & Catalysis, P.O. box 18, 6160 MD Geleen, The Netherlands*

**General remarks:** All air and moisture sensitive manipulations were carried out under a dry nitrogen atmosphere using standard Schlenk techniques. $^{1}$H-NMR, $^{31}$P-NMR, and $^{13}$C-NMR spectra were recorded on a Varian 400 (400, 162, and 101 MHz) in $CDCl_3$. Mass spectra (HRMS) were recorded on an AEI MS-902. Optical rotations were measured on a Schmidt and Haensch Polartronic MH8. $Rh(acac)(C_2H_4)_2$ was purchased from Strem and used without further purification. Dioxane was distilled from sodium. All other chemicals were purchased from Acros and used as received unless stated otherwise. Flash chromatography was performed using silica gel 60 Å (Merck, 230-400 mesh). Phosphoramidite ligands **L1**[1] and **L2**[2] were prepared according to literature procedures.

## Catalytic arylboronic acid addition reactions

**General procedure for Table 1, entries 1-7.** In a flame dried Schlenk tube flushed with nitrogen, 1.55 mg (6.0 µmol, 3 mol%) of $Rh(acac)(C_2H_4)_2$ and 14.0 µmol (7.5 mol%) of one of the enantiomers of phosphoramidite **L1** were dissolved in 2 mL of solvent. After stirring for 15 min at room temperature, 0.2 mmol of substrate **1a** and 0.6 mmol of phenylboronic acid (**2a,** 3 equiv) were added and the resulting mixture was stirred at reflux. After 4 h the reaction mixture was cooled to RT and quenched with 2 mL of a 12.5% aqueous ammonia solution. After 20 minutes the water-layer was extracted with 3 x 5 mL of ethylacetate, the combined organic layers dried on $Na_2SO_4$, and evaporated under reduced pressure.

**General procedure for Table 2, entries 1-11.** In a flame dried Schlenk tube flushed with nitrogen, 1.55 mg (6.0 µmol, 3 mol%) of $Rh(acac)(C_2H_4)_2$ and 6.5 µmol (3.5 mol%) phosphoramidite (*S*,*S*)-**L2** were dissolved in 2 mL of 2-propanol. After stirring for 15 min at room temperature, 0.2 mmol of substrate **1** and 0.6 mmol of arylboronic acid **2** (3 equiv) were added and the resulting mixture was stirred at reflux. After 4 h the reaction mixture was cooled to RT and evaporated under reduced pressure. Products were purified by flash chromatography ($SiO_2$, pentane:EtOAc = 20:1).

**(*R*)-(4-chlorophenyl)phenylmethanol (3a).** Obtained as a solid in 91% isolated yield (Table 2, entry 1); mp 47.4-48.4 °C; $^{1}$H NMR ($CDCl_3$) δ = 7.21-7.30 (m, 9H), 5.75 (s, 1H), 2.11 (bs, 1H); $^{13}$C NMR

($CDCl_3$) δ = 143.40, 142.17, 133.25, 128.62 (2), 128.57 (2), 127.84 (3), 126.49 (2), 75.59; HRMS calcd for $C_{13}H_{11}O^{37}Cl$: ***m/z*** 220.0469, found: 220.0461; The ee was determined on a Chiralcel AD column with heptane : isopropanol = 95 : 5, flow = 1.0 mL/ min. Retention times: 11.3 [(***R***)-enantiomer] and 12.1 [(***S***)-enantiomer] min; $[\alpha]^{20}_D$ = -10.4 (***c*** 1.08, $CHCl_3$, Table 2, entry 1, 60%), lit.[3] $[\alpha]^{26}_D$ = -18.6 (***c*** 0.86, $CHCl_3$, 94%, (***R***)).

**(*R*)-(4-trifluoromethylphenyl)phenylmethanol (3b).** Obtained as a solid in 94% isolated yield (Table 2, entry 2); mp 71.9-73.0 °C; $^1$H NMR ($CDCl_3$) δ = 7.45-7.56 (m, 4H), 7.21-7.31 (m, 5H), 5.83 (s, 1H), 2.19 (bs, 1H); $^{13}$C NMR ($CDCl_3$) δ = 147.48, 143.13, 129.21 (q, $J_{CF}$ = 32.1 Hz), 128.75 (2), 128.08, 126.64 (2), 126.61 (2), 125.39 (2q, $J_{CF}$ = 3.7 Hz), 124.19 (q, $J_{CF}$ = 286.4 Hz), 75.75; HRMS calcd for $C_{14}H_{11}OF_3$: ***m/z*** 252.0762, found: 252.0774; The ee was determined on a Chiralcel AD column with heptane : isopropanol = 98 : 2, flow = 1.0 mL/ min. Retention times: 17.0 [(***R***)-enantiomer] and 20.2 ((***S***)-enantiomer) min; $[\alpha]^{20}_D$ = -19.4 (***c*** 1.05, $CHCl_3$, Table 2, entry 2, 51% ee), lit.[4] $[\alpha]^{22}_D$ = -34.6 (***c*** 0.19, $C_6H_6$, 94%, (***R***)).

**(*R*)-(4-phenylphenyl)phenylmethanol (3c).** Obtained as a solid in 93% isolated yield (Table 2, entry 3); mp 74.0-74.6 °C; $^1$H NMR ($CDCl_3$) δ = 7.21-7.57 (m, 14H), 5.84 (s, 1H), 2.38 (bs, 1H); $^{13}$C NMR ($CDCl_3$) δ = 143.69, 142.77, 140.71, 140.41, 128.71 (2), 128.50 (2), 127.57, 127.23, 127.18 (2), 127.02 (2), 126.93 (2), 126.51 (2), 75.96; HRMS calcd for $C_{19}H_{16}O$: ***m/z*** 260.1201, found: 260.1203; The ee was determined on a Chiralcel AD column with heptane : isopropanol = 98 : 2, flow = 1.0 mL/ min. Retention times: 36.8 [(***S***)-enantiomer] and 41.9 min [(***R***)-enantiomer]; $[\alpha]^{20}_D$ = -3.2 (***c*** 1.01, $CHCl_3$, Table 2, entry 3, 59% ee).

**(*R*)- and (*S*)-(4-tolyl)phenylmethanol (3d).** The (*R*)-enantiomer was obtained as a solid in 80% isolated yield (Table 2, entry 4) and the (*S*)-enantiomer was obtained as a solid in 93% isolated yield (Table 2, entry 6); mp 51.4-52.9 °C; $^1$H NMR ($CDCl_3$) δ = 7.09-7.33 (m, 9H), 5.76 (s, 1H), 2.29 (s, 3H), 2.19 (bs, 1H); $^{13}$C NMR ($CDCl_3$) δ = 143.89, 140.90, 137.22, 129.13 (2), 128.39 (2), 127.40, 126.47 (2), 126.40 (2), 76.03, 21.07; HRMS calcd for $C_{14}H_{14}O$: ***m/z*** 198.1045, found: 198.1053; The ee was determined on a Chiralcel AD column with heptane : isopropanol = 98 : 2, flow = 1.0 mL/ min. Retention

times: 20.6 [(*R*)-enantiomer] and 21.7 [(*S*)-enantiomer] min; $[\alpha]^{20}_D$ = +5.2 (*c* 0.92, $CHCl_3$, Table 2, entry 4, 60% ee), $[\alpha]^{20}_D$ = -4.0 (*c* 0.76, $CHCl_3$, Table 2, entry 6, 47% ee), lit.[5] $[\alpha]^{20}_D$ = +8.4 (*c* 0.50, $CHCl_3$, 97% ee, (*R*)).

**(*R*)-(4-methoxyphenyl)phenylmethanol (3e).** Obtained as a viscous oil in 61% isolated yield (Table 2, entry 5); $^1$H NMR ($CDCl_3$) δ = 7.20-7.34 (m, 7H), 6.82 (m, 2H), 5.76 (s, 1H), 3.74 (s, 3H), 2.20 (bs, 1H); $^{13}$C NMR ($CDCl_3$) δ = 158.99, 143.96, 136.12, 128.40 (2), 127.86 (2), 127.38, 126.35 (2), 113.82 (2), 75.76, 55.24; HRMS calcd for $C_{14}H_{14}O_2$: *m/z* 214.0994, found: 214.0992; The ee was determined on a Chiralcel AD column with heptane : isopropanol = 95 : 5, flow = 1.0 mL/ min. Retention times: 16.7 [(*R*)-enantiomer] and 17.8 [(*S*)-enantiomer] min; $[\alpha]^{20}_D$ = +16.9 (*c* 0.44, $C_6H_6$, Table 2, entry 5, 60% ee), lit.[6] $[\alpha]^{20}_D$ = +18.7 (*c* 1.86, $C_6H_6$,(*R*)).

**(*R*)-(3-methoxyphenyl)phenylmethanol (3f).** Obtained as an oil in 96% isolated yield (Table 2, entry 8); $^1$H NMR ($CDCl_3$) δ = 7.19-7.35 (m, 6H), 6.90 (m, 2H), 6.77 (m, 1H), 5.74 (s, 1H), 3.74 (s, 3H), 2.38 (bs, 1H); $^{13}$C NMR ($CDCl_3$) δ = 159.64, 145.41, 143.61, 129.44, 128.42, 128.19, 127.52, 126.46 (2), 118.84, 112.89, 112.02, 76.06, 55.14; HRMS calcd for $C_{14}H_{14}O_2$: *m/z* 214.0994, found: 214.1002; The ee was determined on a Chiralcel AD column with heptane : isopropanol = 98 : 2, flow = 1.0 mL/ min. Retention times: 34.3 [(*S*)-enantiomer] and 36.0 [(*R*)-enantiomer] min; $[\alpha]^{20}_D$ = -8.7 (*c* 0.99, $CHCl_3$, Table 2, entry 8, 61% ee).

**(*R*)-(2-methoxyphenyl)phenylmethanol (3g).** Obtained as an oil in 89% isolated yield (Table 2, entry 9); $^1$H NMR ($CDCl_3$) δ = 7.18-7.36 (m, 7H), 6.83-6.93 (m, 2H), 6.02 (s, 1H), 3.76 (s, 3H), 2.99 (bs, 1H); $^{13}$C NMR ($CDCl_3$) δ = 156.70, 143.24, 131.94, 128.67, 128.11 (2), 127.82, 127.10, 126.51 (2), 120.76, 110.73, 72.21, 55.36; HRMS calcd for $C_{14}H_{14}O_2$: *m/z* 214.0994, found: 214.1003; The ee was determined on a Chiralcel AD column with heptane : isopropanol = 95 : 5, flow = 1.0 mL/ min. Retention times: 13.1 (minor) and 14.2 (major) min; $[\alpha]^{20}_D$ = +18.2 (*c* 0.77, $CHCl_3$, Table 2, entry 9, 50% ee).

**(*R*)-(1-naphthyl)phenylmethanol (3h).** Obtained as a viscous oil in 67% isolated yield (Table 2, entry 10); $^1$H NMR ($CDCl_3$) δ = 7.99 (m,

1H), 7.74-7.85 (m, 2H), 7.59 (m, 1H), 7.21-7.47 (m, 8H), 6.49 (s, 1H), 2.16 (bs, 1H); $^{13}$C NMR ($CDCl_3$) δ = 143.05, 138.73, 133.88, 130.63, 128.73, 128.50, 128.45, 128.29, 127.64, 127.00, 126.11, 125.94, 125.56, 125.29, 124.57, 123.94, 73.63; HRMS calcd for $C_{17}H_{14}O$: *m/z* 234.1045, found: 234.1053; The ee was determined on a Chiralcel AD column with heptane : isopropanol = 98 : 2, flow = 1.0 mL/ min. Retention times: 35.1 [(*S*)-enantiomer] and 38.8 [(*R*)-enantiomer] min; $[\alpha]^{20}_D$ = +29.6 (*c* 0.54, $C_6H_6$, Table 2, entry 10, 52% ee), lit.[6] $[\alpha]^{20}_D$ = +59.5 (*c* 0.88, $C_6H_6$, >98% ee, (*R*)).

**(*S*)- and (*R*)-(2-naphthyl)phenylmethanol (3i).** The (S)-enantiomer was obtained as a solid in 92% isolated yield (Table 2, entry 7) and the (*R*)-enantiomer was obtained as a solid in 92% isolated yield (Table 2, entry 11); mp 70.9-71.2 °C; $^1$H NMR ($CDCl_3$) δ = 7.75-7.85 (m, 4H), 7.20-7.47 (m, 8H), 5.95 (s, 1H), 2.36 (bs, 1H); $^{13}$C NMR ($CDCl_3$) δ = 143.59, 141.09, 133.22, 132.85, 128.51 (2), 128.29, 128.04, 127.64 (2), 126.68 (2), 126.15, 125.94, 125.00, 124.74, 76.32; HRMS calcd for $C_{17}H_{14}O$: *m/z* 234.1045, found: 234.1051; The ee was determined on a Chiralcel OD-H column with heptane : isopropanol = 90 : 10, flow = 0.5 mL/ min. Retention times: 24.3 [*S*-enantiomer] and 28.0 [*R*-enantiomer] min; $[\alpha]^{20}_D$ = -4.8 (*c* 1.37, $C_6H_6$, Table 2, entry 7, 53% ee), $[\alpha]^{20}_D$ = +6.7 (*c* 1.62, $C_6H_6$, Table 2, entry 11, 75% ee), lit.[6] $[\alpha]^{20}_D$ = +7.4 (*c* 0.76, $C_6H_6$, 94% ee, (*R*)).

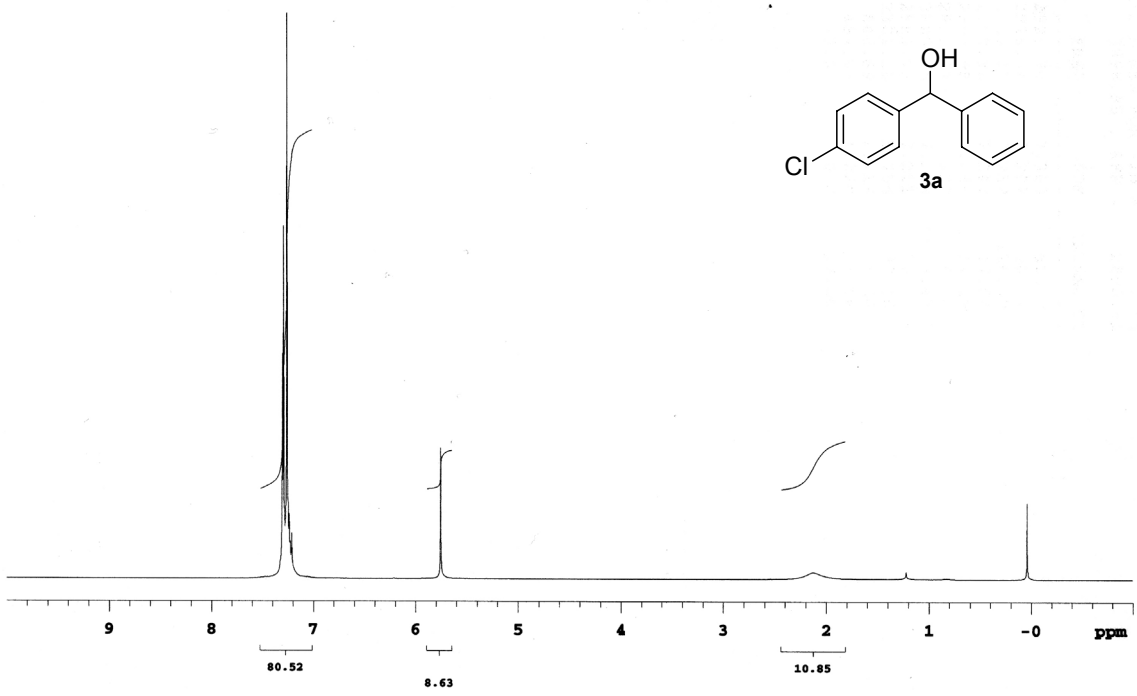
## Identification of borate ester 4

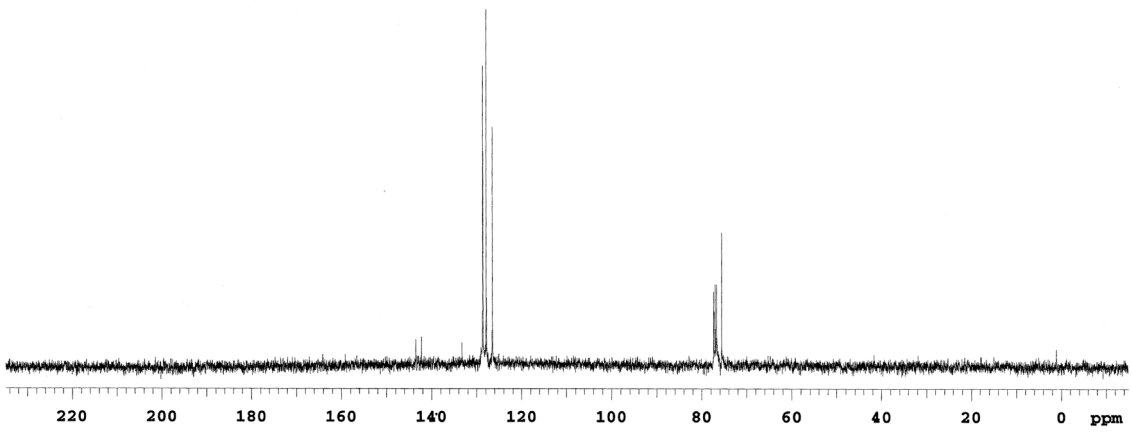
In a flame dried Schlenk tube flushed with nitrogen, 1.55 mg (6.0 µmol, 3 mol%) of $Rh(acac)(C_2H_4)_2$ and 14.0 µmol (7 mol%) of one of the enantiomers of phosphoramidite **L1** were dissolved in 2 mL of dry dioxane. After stirring for 15 min at room temperature, 0.2 mmol of substrate **1a** and 0.4 mmol of phenylboronic acid **2a** (2 equiv) were added and the resulting mixture was stirred at reflux. After 4 h the reaction mixture was cooled to RT. The reaction mixture was passed through a silica-plug and the solvent evaporated under reduced pressure. According to $^1$H-NMR, a mixture was obtained of 9% starting material **1a**, 36% product **3a**, and 55% borate ester **4** with a characteristic benzhydrilic proton at 6.21 ppm. Negative ion ESI-MS using diluted $NH_3$ (aq.) as a base, gave a specific isotope pattern for $C_{13}H_{11}BO_3^-.NH_3$ ($M-NH_4^+$): m/z 277.1 (15%,

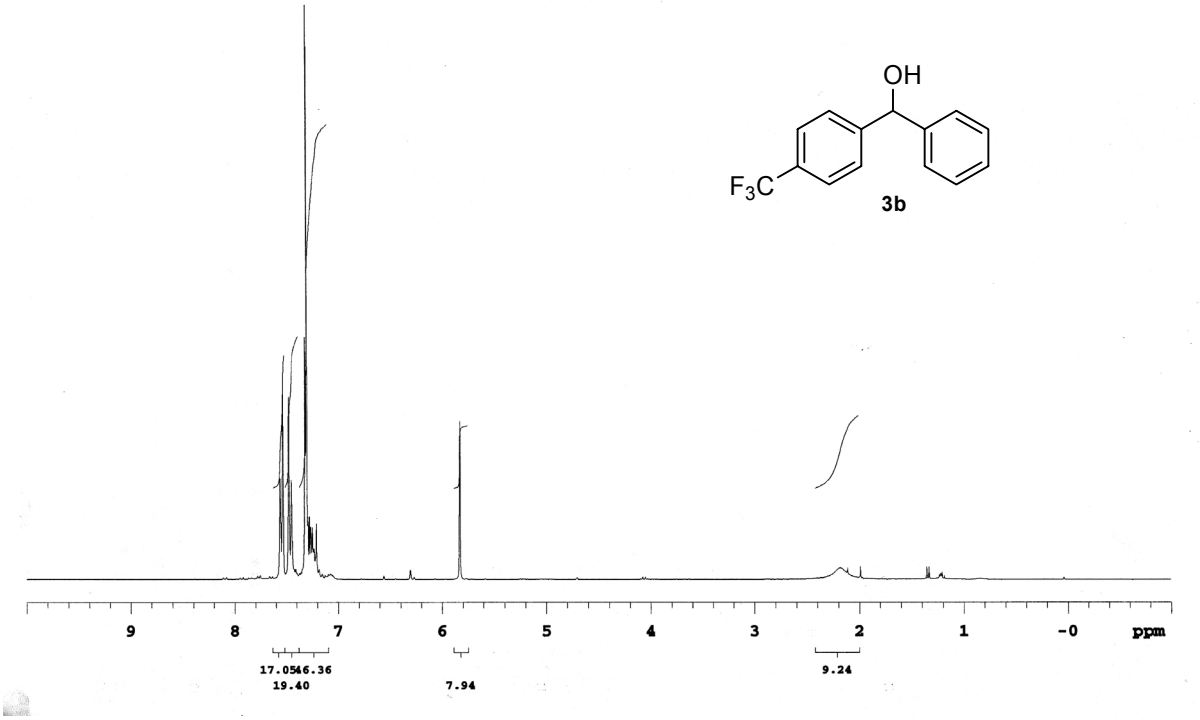
$^{10}B$, $^{35}Cl$), 278.1 (100%, $^{11}B$, $^{35}Cl$), 279.0 (25%, $^{10}B$, $^{37}Cl$), 280.0 (25%, $^{11}B$, $^{37}Cl$). Usual work-up of the mixture with aqueous ammonia 12.5% (***vide supra***), followed by flash chromatography ($SiO_2$, pentane:EtOAc = 20:1) gave the product **3** in 89% isolated yield.

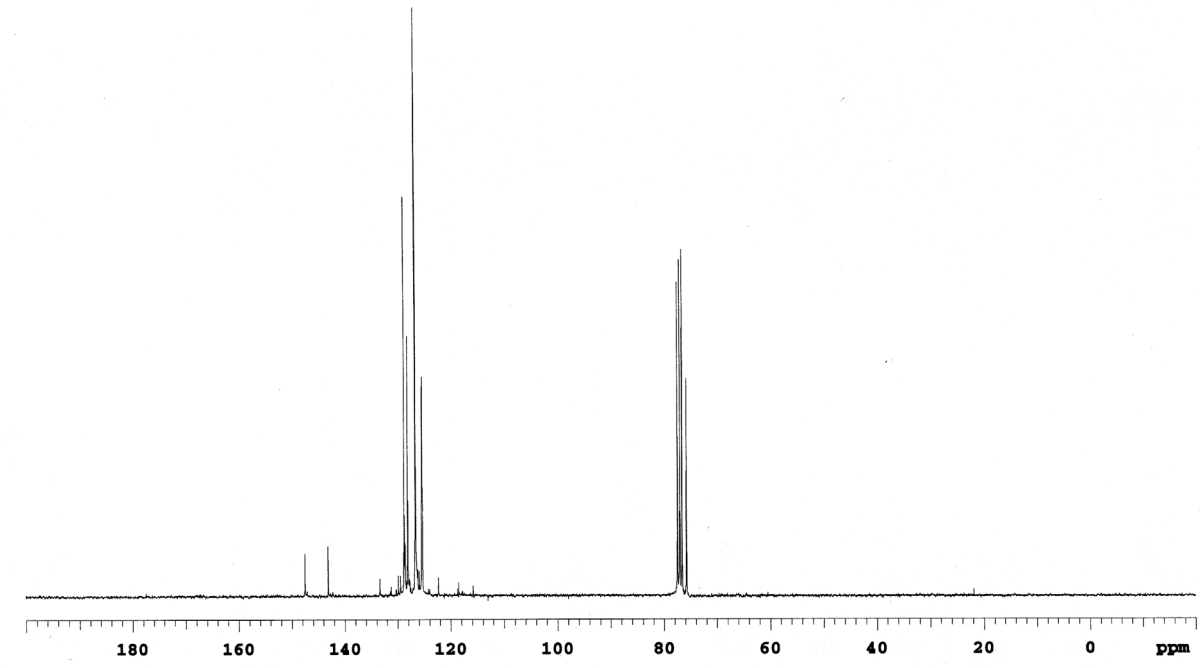
## References

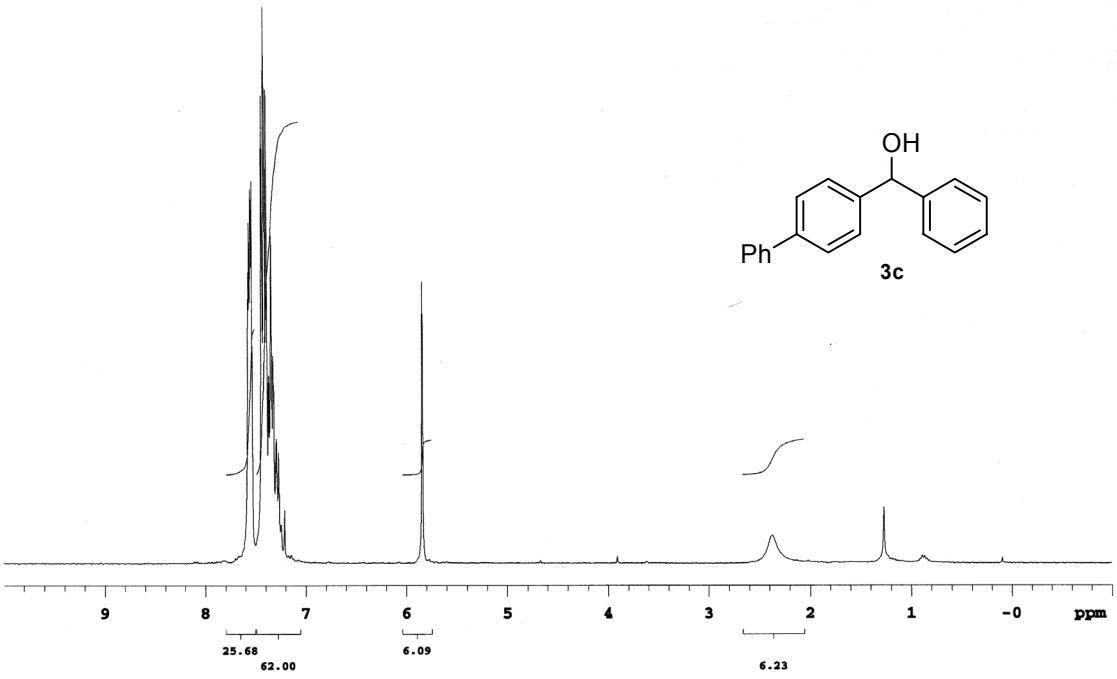

1 J.-G. Boiteau, R. Imbos, A. J. Minnaard, B. L. Feringa, ***Org. Lett.***, 2003, **5**, 681.
2 L. A. Arnold, R. Imbos, A. Mandoli, A. H. M. de Vries, R. Naasz, B. L. Feringa, ***Tetrahedron***, 2000, **56**, 2865.
3 K. Soai, Y. Kawase, A. Oshio, ***J. Chem. Soc. Perkin Trans.***, 1991, **6**, 183.
4 S. Stanchev, R. Rakovska, N. Berova, G. Snatzke, ***Tetrahedron: Asymmetry***, 1995, **6**, 183.
5 S. Nakamura, M. Oda, H. Yasuda, T. Toru, ***Tetrahedron***, 2001, **57**, 8469.
6 D. Seebach, A. K. Beck, S. Roggo, A. Wonnacott, ***Chem. Ber.***, 1985, **118**, 3673.


OH
Cl
3a
9
8
7
6
5
4
3
2
1
-0
ppm
80.52
8.63
10.85

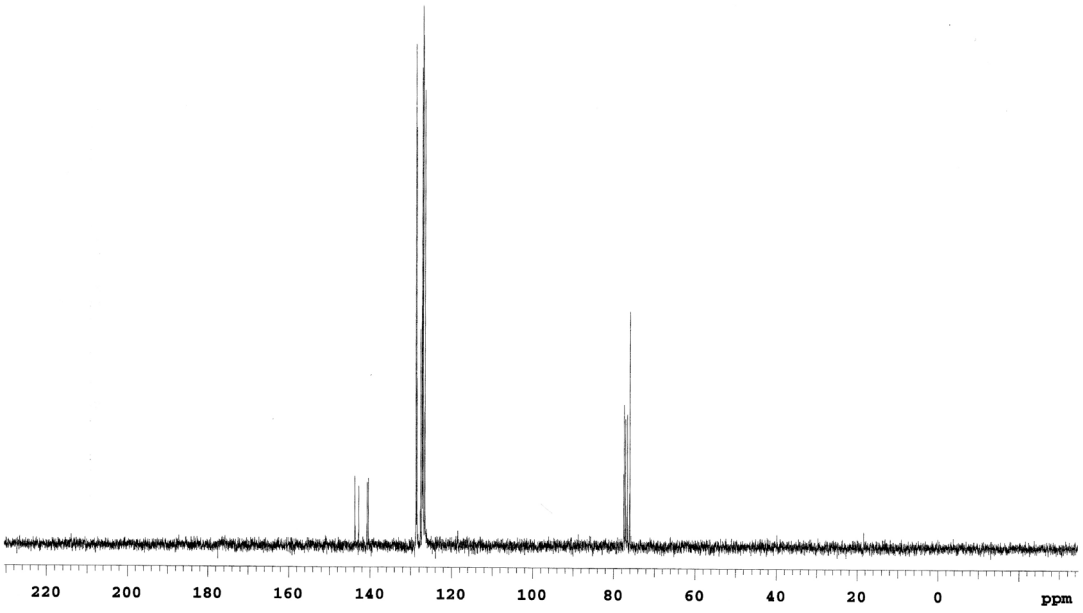

220
200
180
160
140
120
100
80
60
40
20
0
ppm

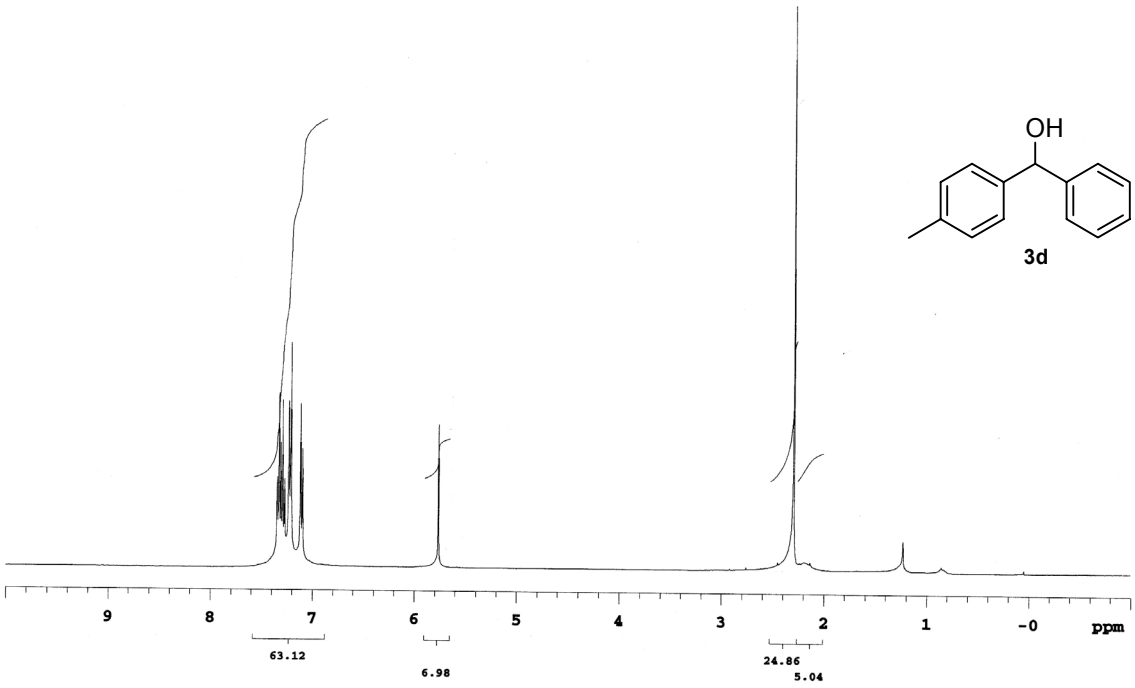

OH
F3C
3b
9
8
7
6
5
4
3
2
1
-0
ppm
17.05
46.36
19.40
7.94
9.24

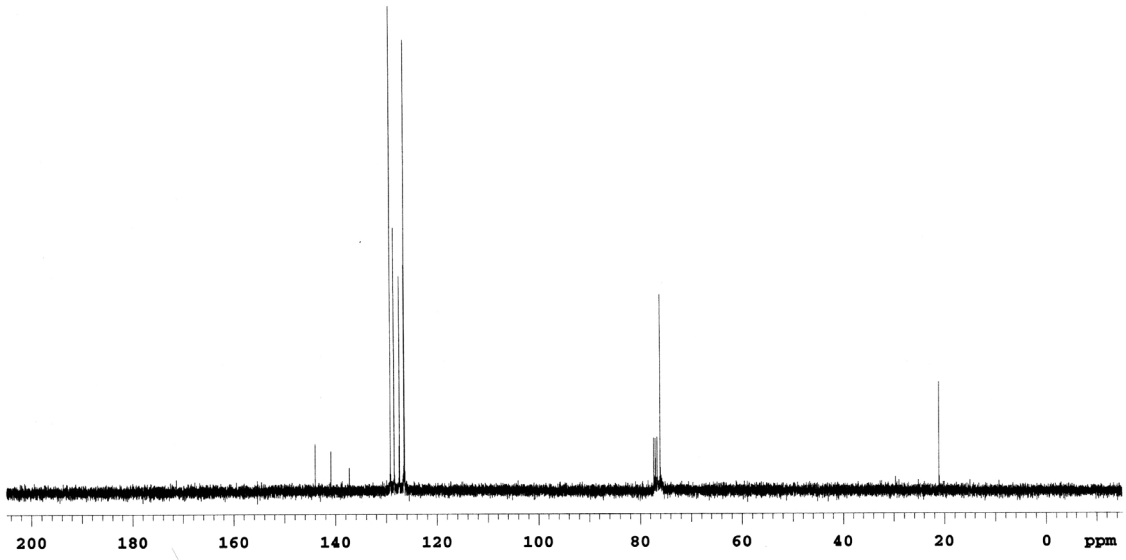

180
160
140
120
100
80
60
40
20
0
ppm

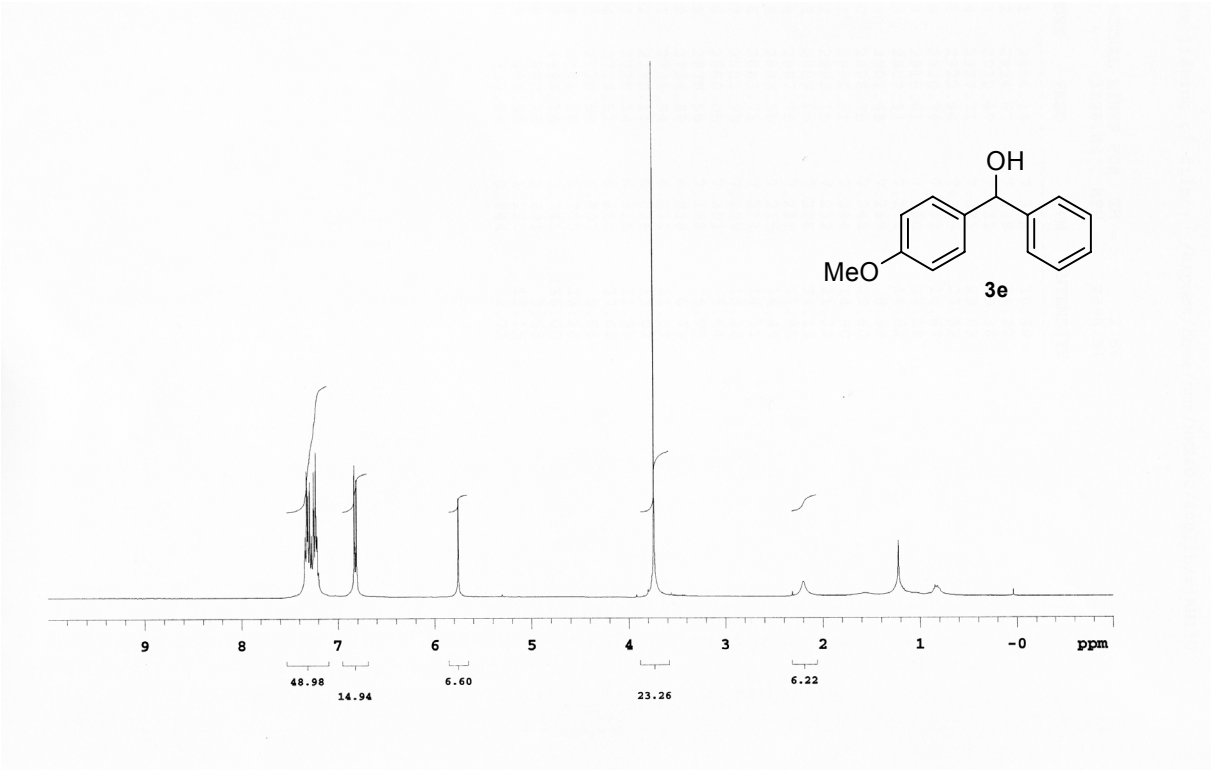

OH
Ph
9
8
7
6
5
4
3
2
1
-0
ppm
25.68
62.00
6.09
6.23

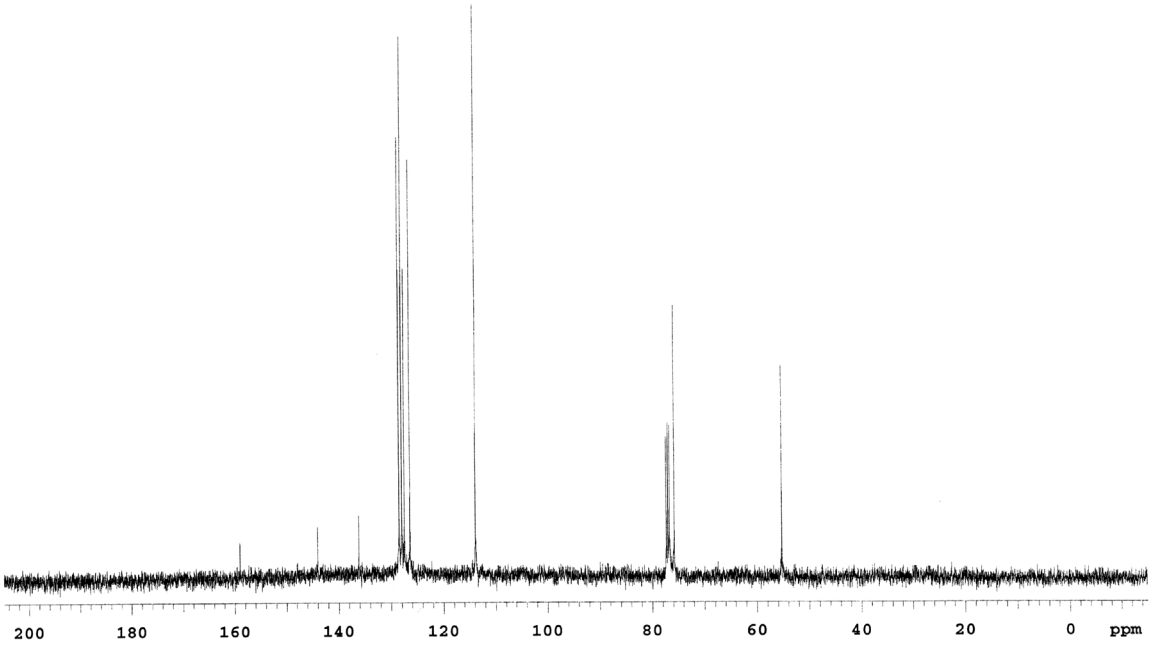
**3c**

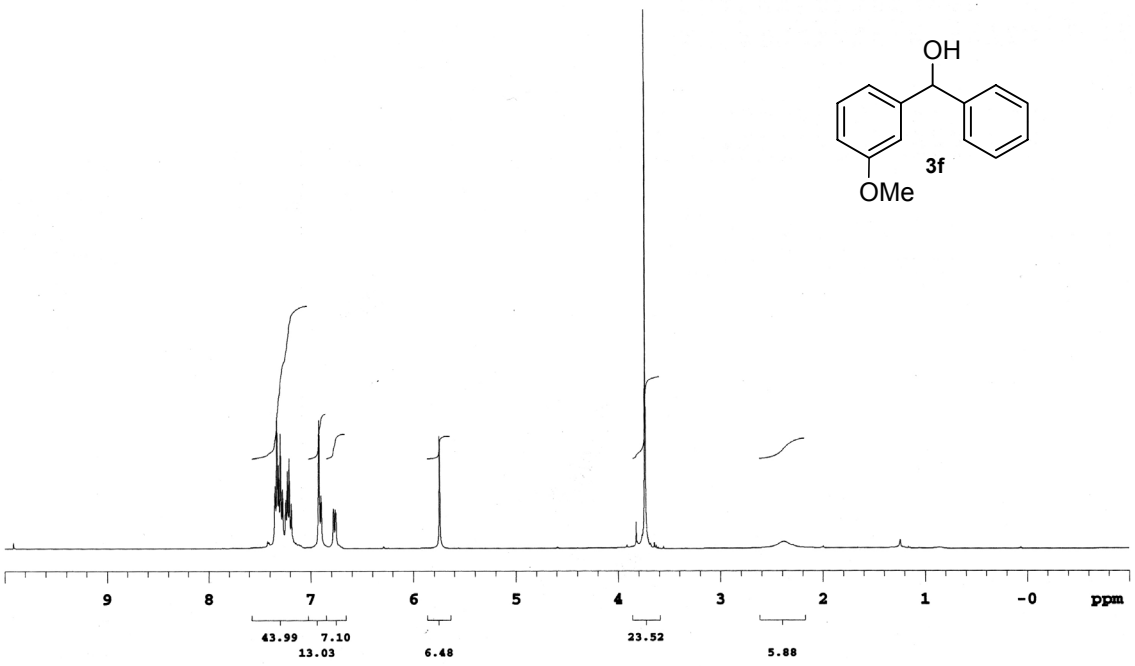

220
200
180
160
140
120
100
80
60
40
20
0
ppm

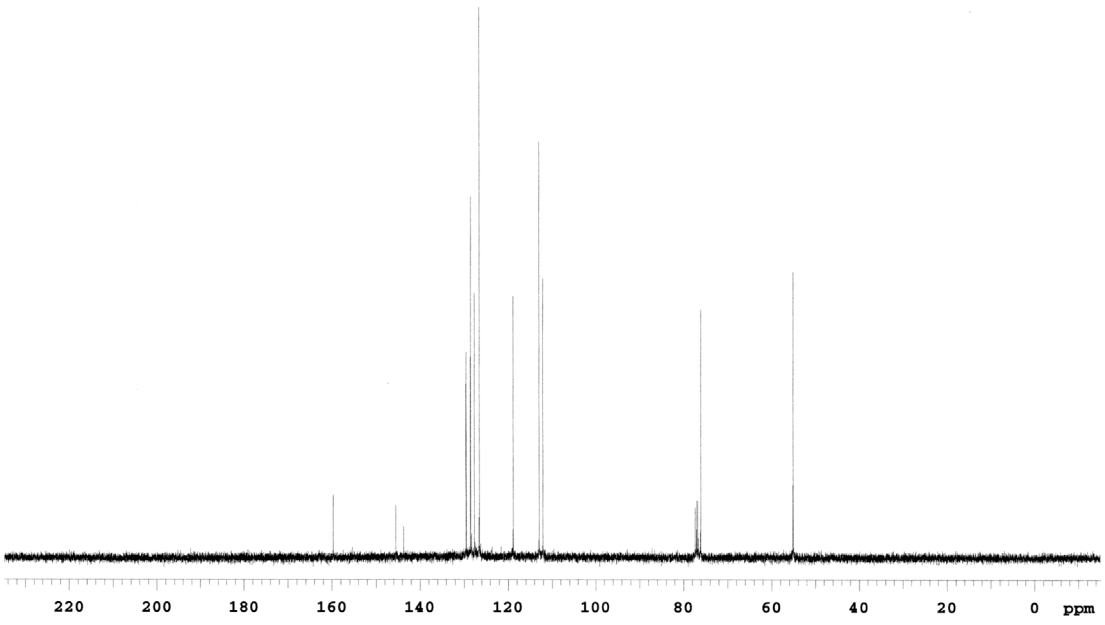

OH
3d
9
8
7
6
5
4
3
2
1
-0
ppm
63.12
6.98
24.86
5.04

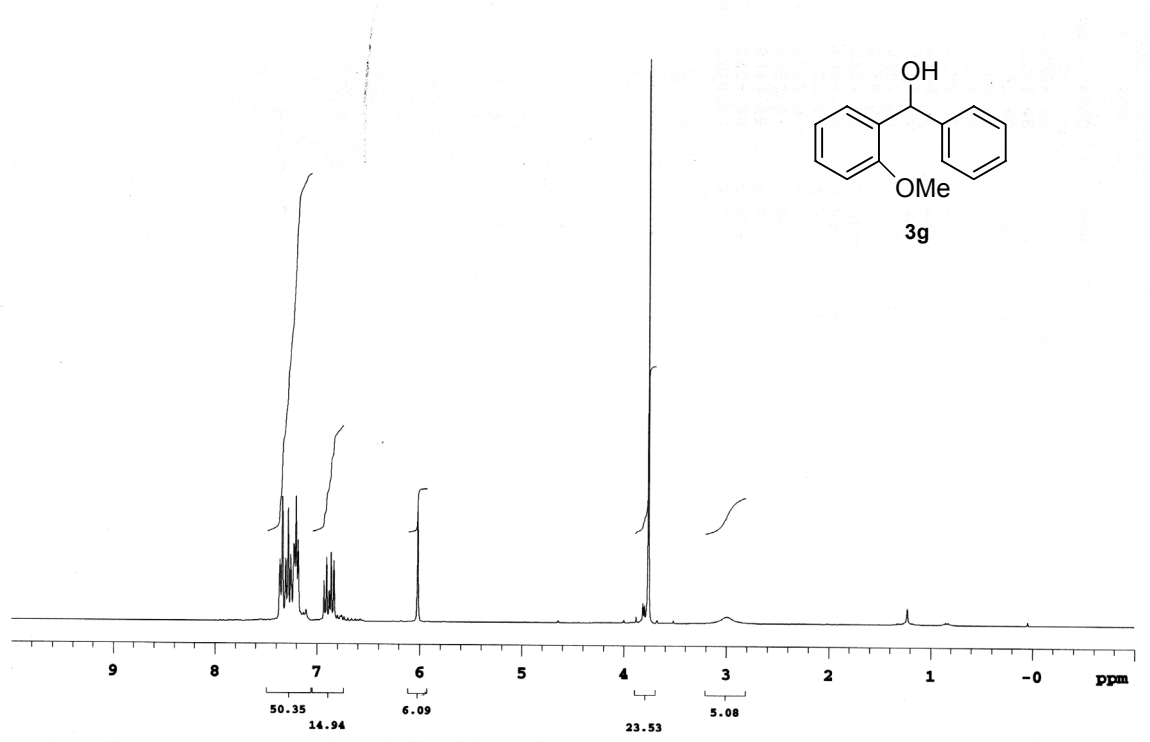

200
180
160
140
120
100
80
60
40
20
0
ppm


OH
MeO
3e
9
8
7
6
5
4
3
2
1
-0
ppm
48.98
14.94
6.60
23.26
6.22

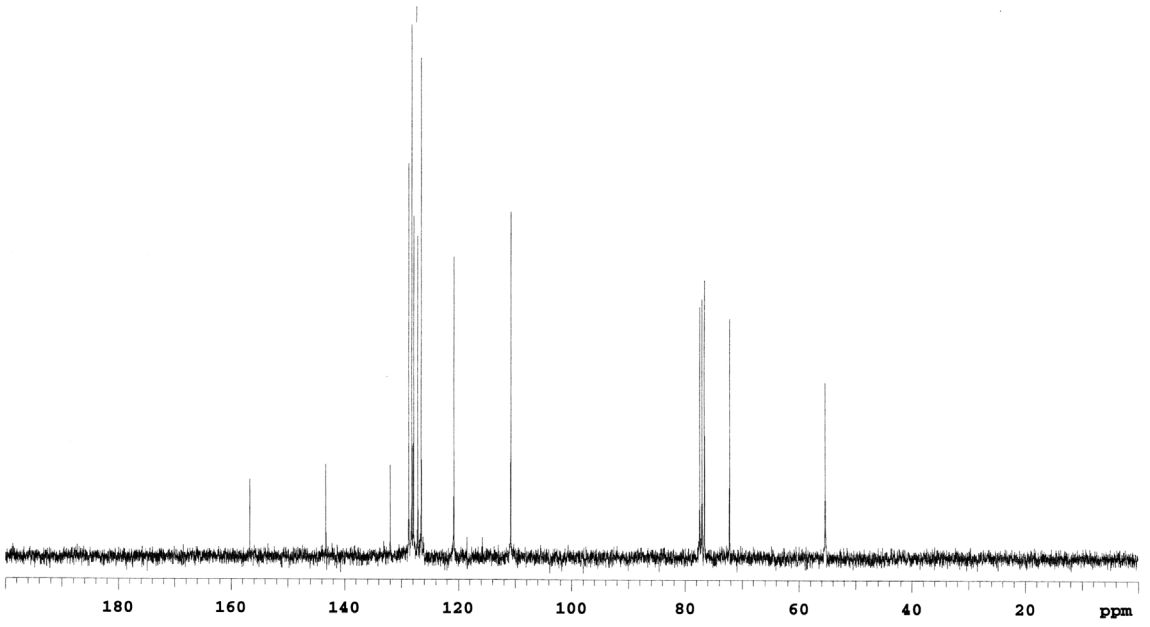

200
180
160
140
120
100
80
60
40
20
0
ppm

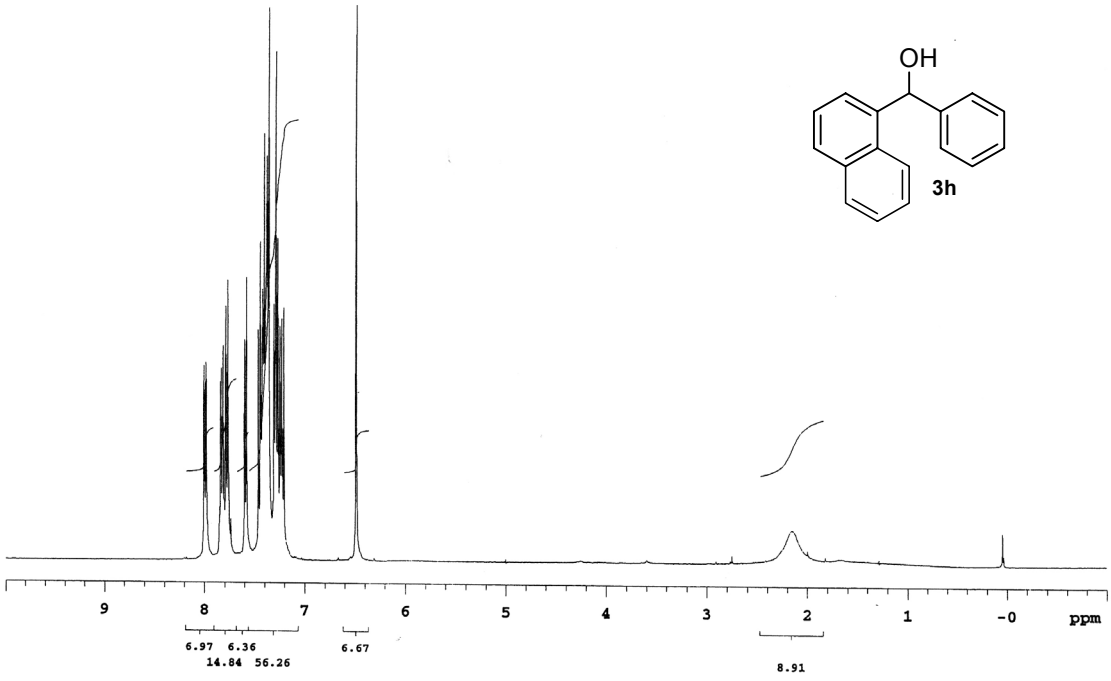

OH
OMe
3f
9
8
7
6
5
4
3
2
1
-0
ppm
43.99
7.10
13.03
6.48
23.52
5.88

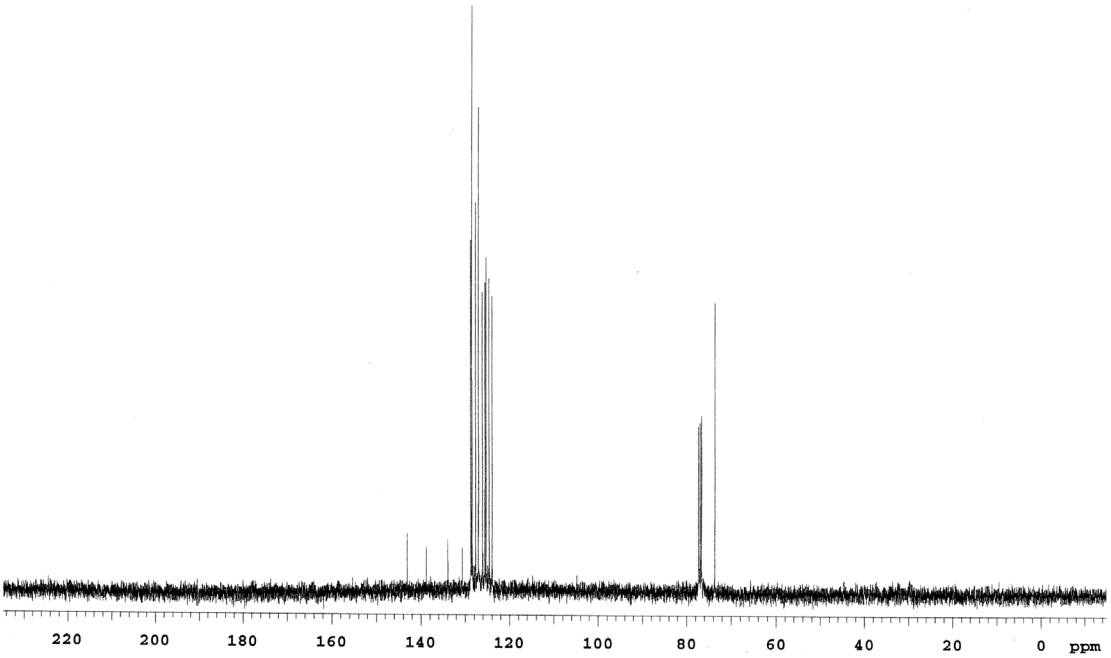

220
200
180
160
140
120
100
80
60
40
20
0
ppm

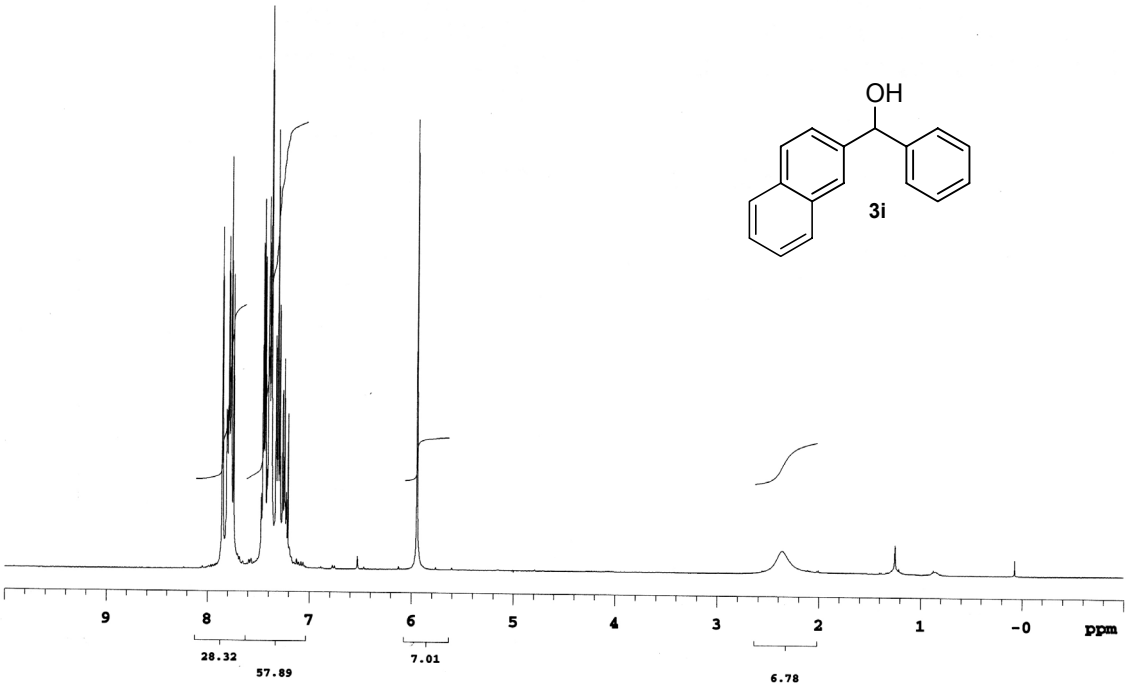

OH
OMe
9
8
7
6
5
4
3
2
1
-0
ppm
50.35
14.94
6.09
23.53
5.08

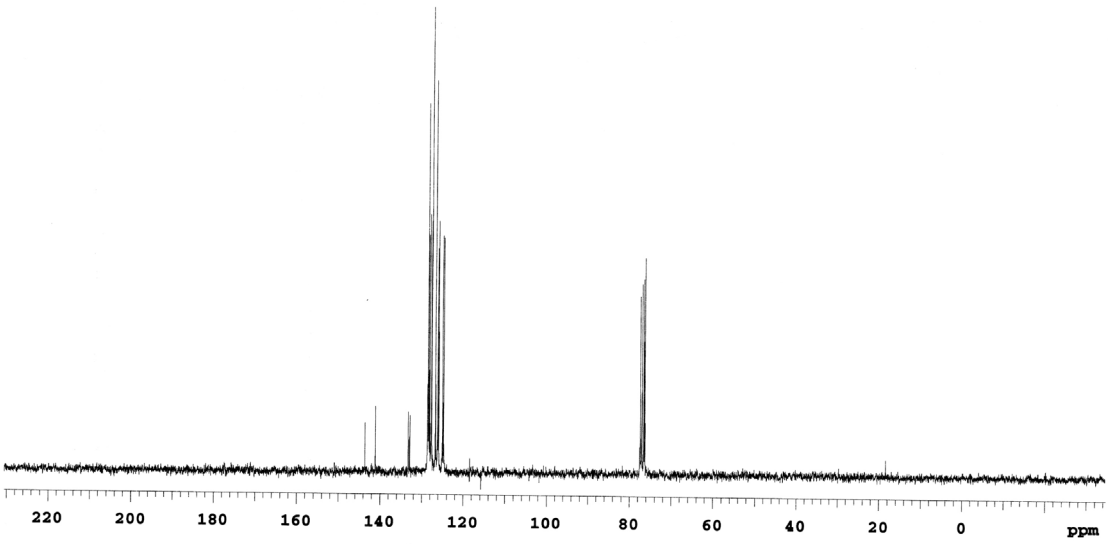
**3g**


180
160
140
120
100
80
60
40
20
ppm


OH
3h
9
8
7
6
5
4
3
2
1
-0
ppm
6.97
6.36
14.84
56.26
6.67
8.91


220
200
180
160
140
120
100
80
60
40
20
0
ppm


OH
3i
9
8
7
6
5
4
3
2
1
-0
ppm
28.32
57.89
7.01
6.78


220
200
180
160
140
120
100
80
60
40
20
0
ppm