

CHEMISTRY

A EUROPEAN JOURNAL

Supporting Information

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A New Strategy for Designing None- C_2 Symmetric Monometallic Bifunctional Catalysts and Their Application in Enantioselective Cyanation of Aldehydes

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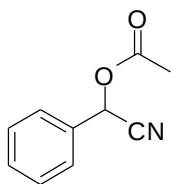
I. General procedure for asymmetric cyanosilylation of aldehydes

A flame-dried reaction vessel was charged with (*R*)-**1** (0.05 mmol, 17.6 mg) under nitrogen, followed by addition of dry methylene chloride (2 mL) and $\text{Ti}(\text{O}i\text{Pr})_4$ (0.05 mmol, 15 μL). After being stirred at room temperature for 1 h, TMSCN (200 μL , 1.5 mmol) was added at $-40\text{ }^\circ\text{C}$, followed by addition of an aldehyde (0.5 mmol) after 10 min. After the reaction mixture was stirred at $-40\text{ }^\circ\text{C}$ for 48 h, aqueous solution of hydrochloric acid (2 M, 3 mL) and ethyl acetate (3 mL) were added at the same temperature. The resulting mixture was stirred vigorously for 3 h at room temperature, and then extracted with ethyl acetate ($3 \times 12\text{ mL}$). The organic layer was separated, dried over MgSO_4 , and evaporated under reduced pressure, affording a residue that was purified by flash chromatography with petroleum ether/ethyl acetate (6:1) to obtain pure cyanohydrins.

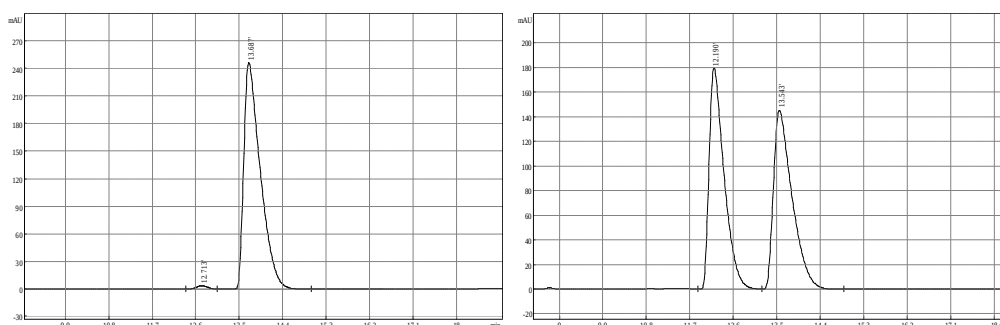
Pure cyanohydrin was treated with acetyl chloride (0.5 mL) and TEA (0.5 mL) in CH_2Cl_2 (4 mL). After being stirred for 1 h, the reaction was quenched by water and the mixture was extracted with ethyl acetate ($3 \times 8\text{ mL}$). The organic extracts were washed with brine, dried over anhydrous sodium sulfate and concentrated by rotoevaporation. The residue was purified by column chromatograph on silica gel with elution with petroleum ether/ethyl acetate (15/1) to give cyano acetate. Enantiomeric excess was determined by chiral HPLC (Chiralcel OD-H) or chiral GC.

The isolated yields of asymmetric cyanosilylation reactions are obtained after acidic hydrolysis, and are the averages of two runs at least. The products are known and their ^1H and ^{13}C NMR spectra agreed with those in the literature.^[1-5] After cyanohydrins were converted to cyano acetates, enantiomeric excesses were determined by HPLC (LabTech 600 series) using Chiralcel OD-H column or by chiral GC analysis on Varian CP-Chirasil DEX CB (0.25 mm $\times$ 25 m) [column temperature: $160\text{ }^\circ\text{C}$ (isothermal); inject temperature: $230\text{ }^\circ\text{C}$; detector temperature: $230\text{ }^\circ\text{C}$; inlet pressure: $5.6 \times 10^4\text{ Pa}$]. The absolute configurations of adducts were assigned by comparison with literature compounds.^[1-5]

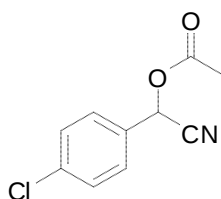
II. Experimental data for the described substances



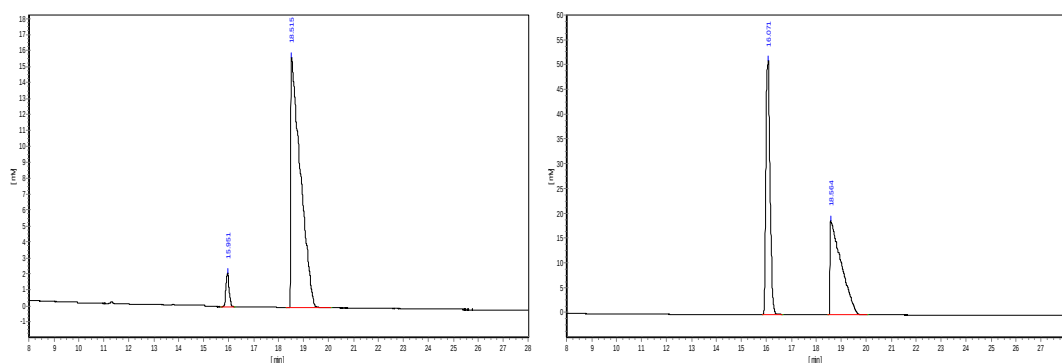
(S)-2-Acetyloxy benzeneacetonitrile:^[1, 2] 97% yield and 98% ee determined by HPLC on a Chiralcel OD column (hexane/2-propanol = 99:1, flow rate = 1.0 mL/min, $t_{\text{minor}} = 12.7$ min, $t_{\text{major}} = 13.7$ min). ^1H NMR (600 MHz, CDCl_3): $\delta = 2.17$ (s, 3H), 6.41 (s, 1H), 7.46-7.55 (m, 5H). ^{13}C NMR (150 MHz, CDCl_3): $\delta = 20.5, 62.8, 116.1, 127.9, 129.3, 130.4, 131.7, 169.0$. GC-MS: m/z : 175 [M^+].



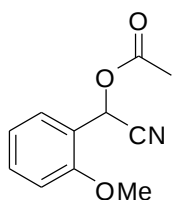
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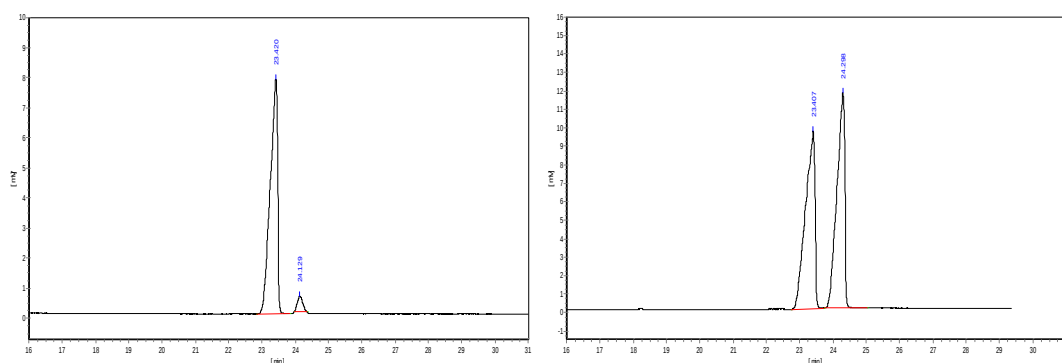
(S)-2-Acetyloxy-2-(4-chlorophenyl) acetonitrile:^[1, 2] 92% yield and 92% ee determined by GC on Varian CP-Chirasil DEX CB (0.25 mm $\times$ 25 m) [column temperature = 160 $^{\circ}\text{C}$ (isothermal), $t_{\text{minor}} = 16.0$ min, $t_{\text{major}} = 18.5$ min]. ^1H NMR (600 MHz, CDCl_3): $\delta = 2.18$ (s, 3H), 6.39 (s, 1H), 7.43-7.48 (m, 4H). ^{13}C NMR (150 MHz, CDCl_3): $\delta = 20.4, 62.1, 115.7, 129.3, 129.5, 130.2, 136.7, 168.8$. GC-MS: m/z : 209 [M^+].



Rank	Time	Quantity	Area	Height
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2	18.515	95.83614	413265	15692
Total		100	431220	17758

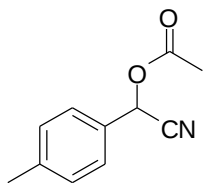


(S)-2-Acetyloxy-2-(2-methoxyphenyl) acetonitrile:^[3] 94% yield and 91% ee determined by GC on Varian CP-Chirasil DEX CB (0.25 mm × 25 m) [column temperature = 155 °C (isothermal), t_{major} = 23.4 min, t_{minor} = 24.1 min]. ^1H NMR (600 MHz, CDCl_3): δ = 2.17 (s, 3H), 3.89 (s, 3H), 6.71 (s, 1H), 6.95 (d, J = 3.5 Hz, 1H), 7.03 (t, J = 7.2 Hz, 1H), 7.42-7.45 (ddd, J = 1.2, 0.6, 1.8 Hz, 1H), 7.56 (2d, J = 1.8, 1.2 Hz, 1H). ^{13}C NMR (150 MHz, CDCl_3): δ = 20.5, 55.7, 58.1, 111.0, 116.2, 119.9, 120.9, 128.8, 131.8, 156.7, 169.0. GC-MS: m/z : 205 [M^+].

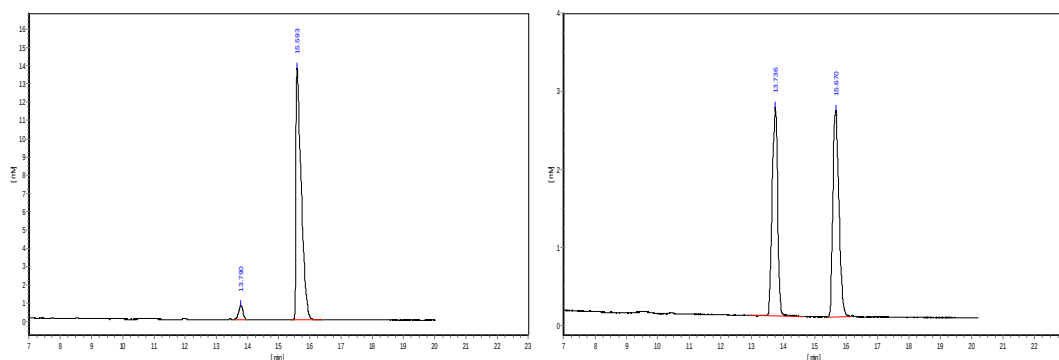


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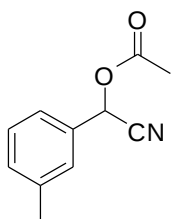
2	24.129	4.68466	5901	522
Total		100	125968	8324



(S)-2-Acetyloxy-2-(4-methylphenyl) acetonitrile:^[2, 3] 87% yield and 92% ee determined by GC on Varian CP-Chirasil DEX CB (0.25 mm × 25 m) [column temperature = 160 °C (isothermal), $t_{\text{minor}} = 13.8$ min, $t_{\text{major}} = 15.6$ min]. ^1H NMR (400 MHz, CDCl_3): $\delta = 2.15$ (s, 3H), 2.38 (s, 3H), 6.37 (s, 1H), 7.24 (d, $J = 8.0$ Hz, 2H), 7.40 (d, $J = 8.4$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3): $\delta = 20.5, 21.3, 62.8, 116.2, 127.9, 128.9, 129.9, 140.7, 169.0$. GC-MS: m/z : 189 [M^+].

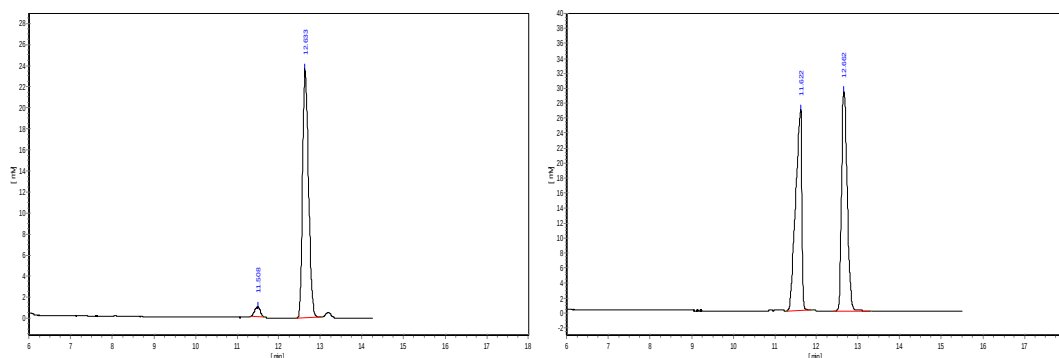


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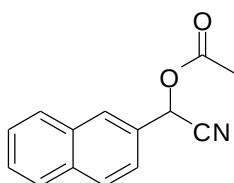


(S)-2-Acetyloxy-2-(3-methylphenyl) acetonitrile:^[1, 2] 93% yield and 93% ee determined by GC on Varian CP-Chirasil DEX CB (0.25 mm × 25 m) [column temperature = 160 °C (isothermal), $t_{\text{minor}} = 11.5$

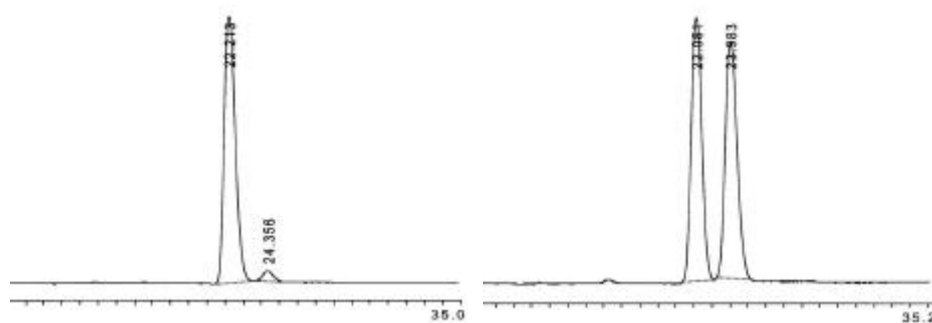
min, $t_{\text{major}} = 12.6$ min]. ^1H NMR (400 MHz, CDCl_3): $\delta = 2.16$ (s, 3H), 2.40 (s, 3H), 6.37 (s, 1H), 7.26-7.34 (m, 4H). ^{13}C NMR (100 MHz, CDCl_3): $\delta = 20.4, 21.3, 62.9, 116.2, 124.9, 128.5, 129.1, 131.1, 131.7, 139.2, 168.9$. GC-MS: m/z : 189 [M^+].



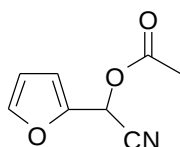
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2	12.633	96.31797	235501	23679
Total		100	244503	24594



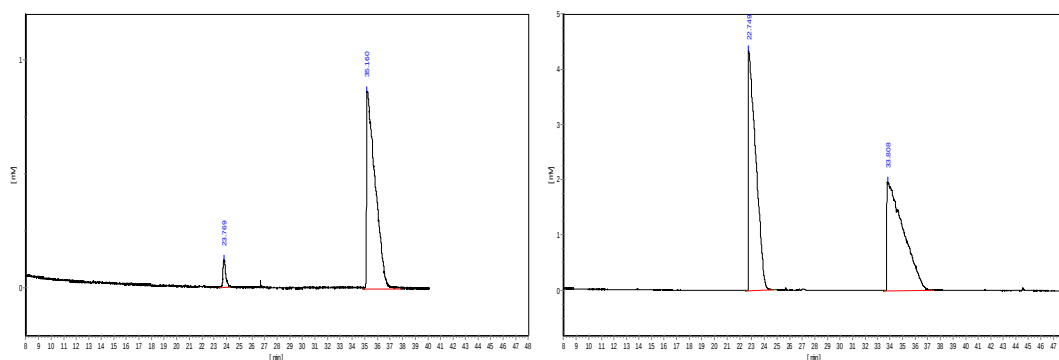
(S)-2-Acetyloxy-2-(2'-naphthyl) acetonitrile: ^[1, 2] 94% yield and 94% ee determined by HPLC on a Chiralcel OD column [hexane/2-propanol = 99:1, flow rate = 1.0 mL/min, $t_{\text{major}} = 22.2$ min, $t_{\text{minor}} = 24.4$ min]. ^1H NMR (600 MHz, CDCl_3): $\delta = 2.20$ (s, 3H), 6.59 (s, 1H), 7.56-7.59 (m, 3H), 7.88-7.94 (m, 3H), 8.03 (s, 1H). ^{13}C NMR (150 MHz, CDCl_3): $\delta = 20.5, 63.0, 116.1, 124.3, 127.1, 127.6, 127.8, 128.0, 128.4, 128.8, 129.4, 132.8, 133.8, 169.0$. GC-MS: m/z : 225 [M^+].



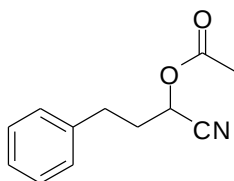
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1	22.213	96.846	9718400	254747
2	24.356	3.154	316419	9009
Total		100	10034819	263756



(S)-2-Acetyloxy-2-(2'-furyl) acetonitrile:^[2, 4] 88% yield and 91% ee determined by GC on Varian CP-Chirasil DEX CB (0.25 mm × 25 m) [column temperature = 105 °C (isothermal), $t_{\text{minor}} = 23.8$ min, $t_{\text{major}} = 35.2$ min]. ^1H NMR (400 MHz, CDCl_3): δ = 2.17 (s, 3H), 6.44 (2d, $J = 3.0, 3.0$ Hz, 1H), 6.47 (s, 1H), 6.68 (2d, $J = 0.6, 0.6$ Hz, 1H), 7.51 (t, $J = 1.2$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ = 20.2, 55.7, 111.1, 112.5, 112.9, 114.0, 145.0, 169.0. GC-MS: m/z : 165 [M^+].

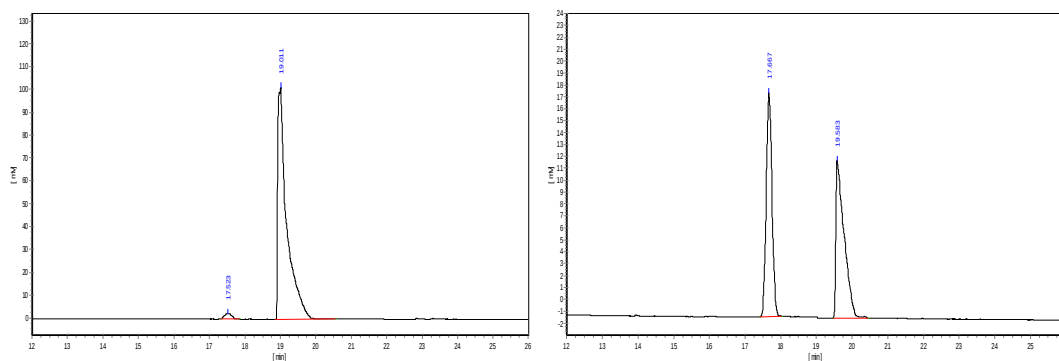


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Total		100	44088	986

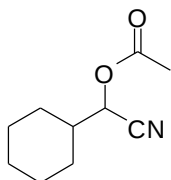


(S)-2-Acetyloxy-4-phenylbutanenitrile:^[5] 98% yield and 97% ee determined by GC on Varian CP-Chirasil DEX CB (0.25 mm × 25 m) [column temperature = 160 °C (isothermal), $t_{\text{minor}} = 17.5$ min, $t_{\text{major}} =$

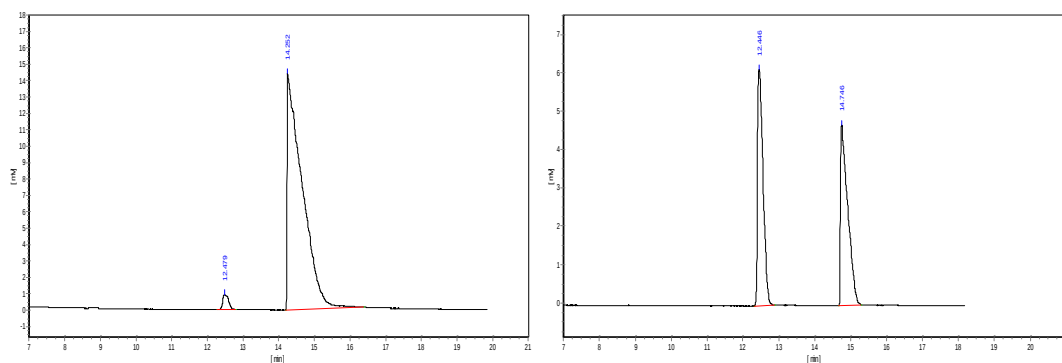
19.0 min]. ^1H NMR (400 MHz, CDCl_3): δ = 2.13 (s, 3H), 2.21-2.27 (m, 2H), 2.82-2.86 (m, 2H), 5.25-5.29 (m, 1H), 7.18-7.34 (m, 5H). ^{13}C NMR (100 MHz, CDCl_3): δ = 20.3, 30.7, 33.8, 60.5, 116.7, 126.7, 128.3, 128.8, 139.0, 169.1. GC-MS: m/z : 203 [M^+].



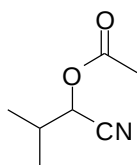
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1	17.523	1.74504	31963	2177
2	19.011	98.25496	1799663	101295
Total		100	1831625	103472



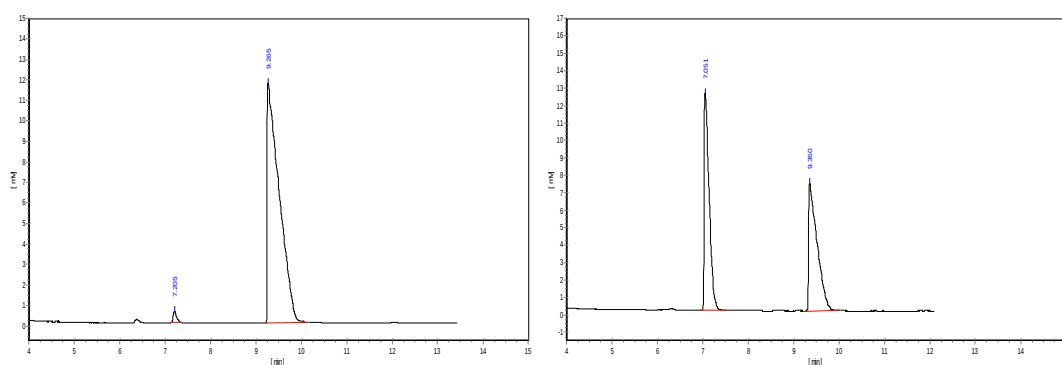
(S)-2-Acetyloxy-2-cyclohexyl-acetonitrile:^[5] 99% yield and 95% ee determined by GC on Varian CP-Chirasil DEX CB (0.25 mm $\times$ 25 m) [column temperature = 140 $^{\circ}\text{C}$ (isothermal), t_{minor} = 12.5 min, t_{major} = 14.3 min]. ^1H NMR (400 MHz, CDCl_3): δ = 1.13-1.30 (m, 5H), 1.70-1.93 (m, 6H), 2.15 (s, 3H), 5.17 (d, J = 6.4 Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ = 20.3, 25.2, 25.3, 25.7, 27.8, 28.1, 40.0, 65.5, 116.1, 169.1. GC-MS: m/z : 181 [M^+].



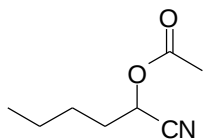
Rank	Time	Quantity	Area	Height
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2	14.252	97.62583	426423	14396
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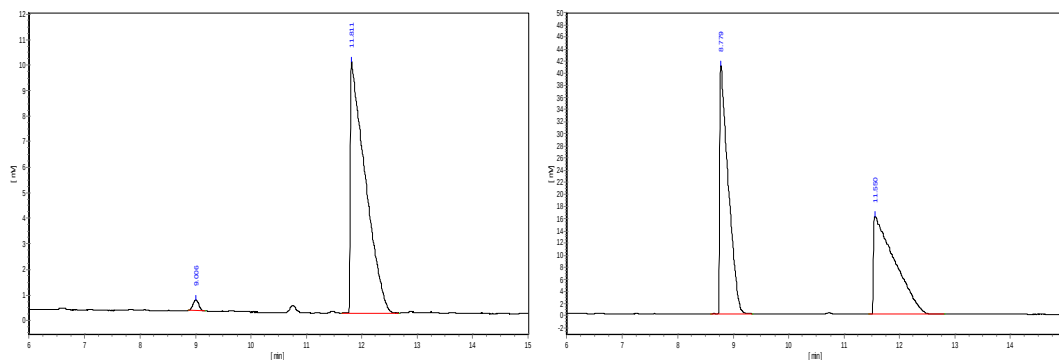
(S)-2-Acetyloxy-3-methyl-butanenitrile.^[5] 93% yield and 98% ee determined by GC on Varian CP-Chirasil DEX CB (0.25 mm × 25 m) [column temperature = 110 °C (isothermal), $t_{\text{minor}} = 7.2$ min, $t_{\text{major}} = 9.3$ min]. ^1H NMR (300 MHz, CDCl_3): $\delta = 1.07$ (q, $J = 6.8$ Hz, 6H), 2.10-2.19 (m, 4H), 5.17 (d, $J = 5.8$ Hz, 1H). ^{13}C NMR (75 MHz, CDCl_3): $\delta = 17.3, 17.7, 20.3, 31.1, 66.3, 116.0, 169.2$. GC-MS: m/z : 141 $[M^+]$.



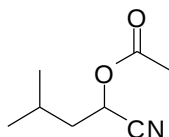
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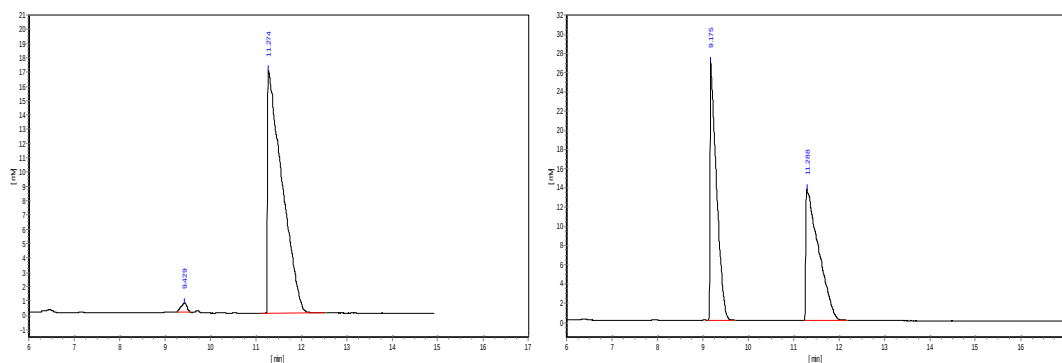
(S)-2-Acetyloxy-hexanenitrile:^[5] 97% yield and 97% ee determined by GC on Varian CP-Chirasil DEX CB (0.25 mm × 25 m) [column temperature = 120 °C (isothermal), $t_{\text{minor}} = 9.0$ min, $t_{\text{major}} = 11.8$ min]. ¹H NMR (400 MHz, CDCl₃): δ = 0.92 (t, $J = 7.2$ Hz, 3H), 1.35-1.53 (m, 4H), 1.88-1.94 (m, 2H), 2.14 (s, 3H), 5.30 (t, $J = 6.4$ Hz, 1H). ¹³C NMR (100 MHz, CDCl₃): δ = 13.6, 20.3, 21.8, 26.5, 31.9, 61.0, 116.8, 169.0. GC-MS: m/z : 156 [$M^+ + H$].



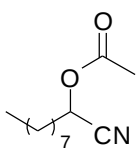
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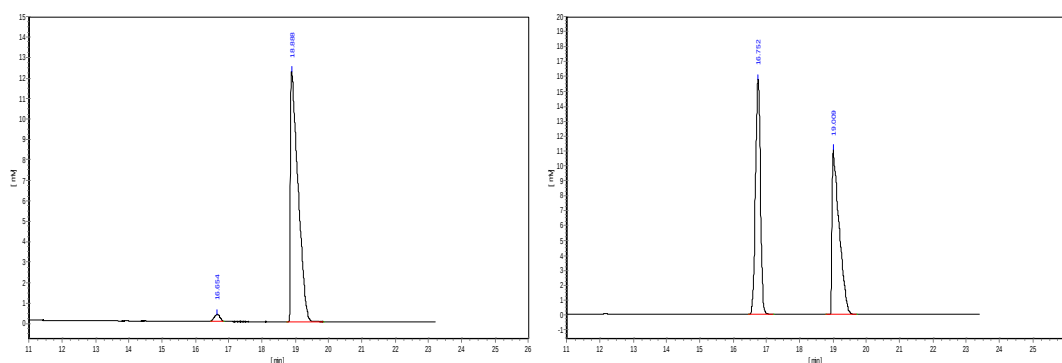
(S)-2-Acetyloxy-4-methyl-pentanenitrile:^[5] 91% yield and 97% ee determined by GC on Varian CP-Chirasil DEX CB (0.25 mm × 25 m) [column temperature = 115 °C (isothermal), $t_{\text{minor}} = 9.4$ min, $t_{\text{major}} = 11.3$ min]. ¹H NMR (300 MHz, CDCl₃): δ = 0.97 (q, $J = 3.3$ Hz, 6H), 1.78-1.88 (m, 3H), 2.14 (s, 3H), 5.33 (t, $J = 7.3$ Hz, 1H). ¹³C NMR (75 MHz, CDCl₃): δ = 20.4, 22.2, 24.5, 40.8, 59.9, 117.1, 169.2. GC-MS: m/z : 156 [$M^+ + H$].



Rank	Time	Quantity	Area	Height
1	9.429	1.34498	5122	605
2	11.274	98.65502	375665	16991
Total		100	380787	17596

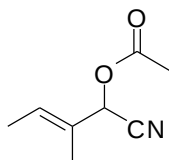


(S)-2-Acetyloxy decanenitrile:^[5] 95% yield and 96% ee determined by GC on Varian CP-Chirasil DEX CB (0.25 mm × 25 m) [column temperature = 155 °C (isothermal), t_{minor} = 16.7 min, t_{major} = 18.9 min]. ¹H NMR (300 MHz, CDCl₃): δ = 0.86 (t, J = 7.0 Hz, 3H), 1.28-1.37 (m, 11H), 1.44-1.52 (m, 2H), 1.86-1.93 (m, 1H), 2.14 (s, 3H), 5.31 (t, J = 6.8 Hz, 1H). ¹³C NMR (75 MHz, CDCl₃): δ = 14.0, 20.4, 22.6, 24.5, 28.8, 29.1, 29.2, 31.7, 32.3, 61.1, 116.9, 169.2. MS (ESI) m/z : 212 [M^+ +H].

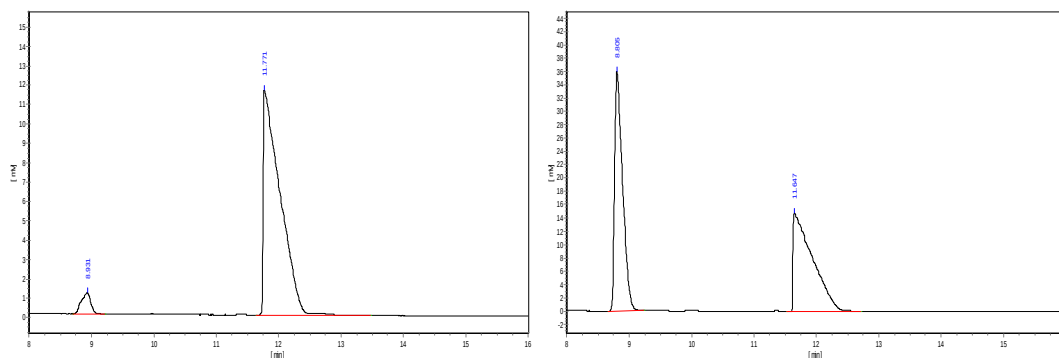


Rank	Time	Quantity	Area	Height
1	16.654	1.94616	3795	318

2	18.888	98.05384	191206	12245
Total		100	195001	12563



(S)-(3E)-2-Acetyloxy-3-methyl-3-pentenitrile:^[5] 85% yield and 90% ee determined by GC on Varian CP-Chirasil DEX CB (0.25 mm × 25 m) [column temperature = 120 °C (isothermal), t_{minor} = 8.9 min, t_{major} = 11.8 min]. ^1H NMR (300 MHz, CDCl_3): δ = 1.70 (d, J = 6.9 Hz, 3H), 1.78 (s, 3H), 2.15 (s, 3H), 5.74 (s, 1H), 5.86-5.92 (m, 1H). ^{13}C NMR (75 MHz, CDCl_3): δ = 12.3, 13.5, 20.4, 66.3, 115.8, 127.3, 129.4, 169.0. GC-MS: m/z : 153 [M^+].



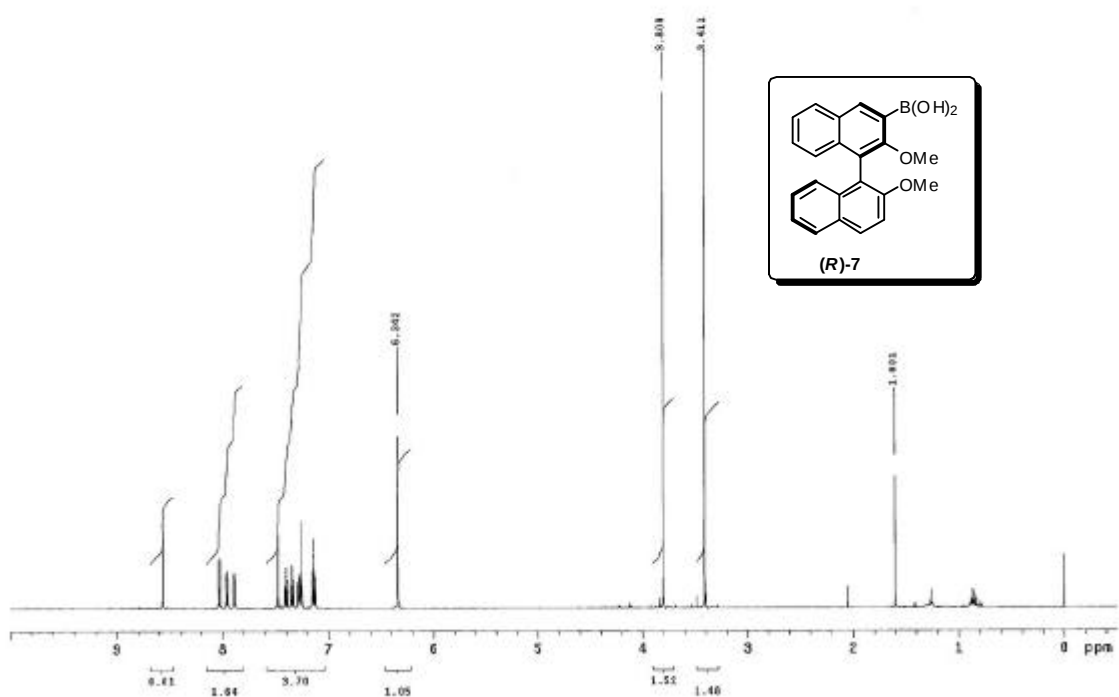
Rank	Time	Quantity	Area	Height
1	8.931	4.99799	11533	1113
2	11.771	95.00201	219218	11615
Total		100	230751	12728

III. References:

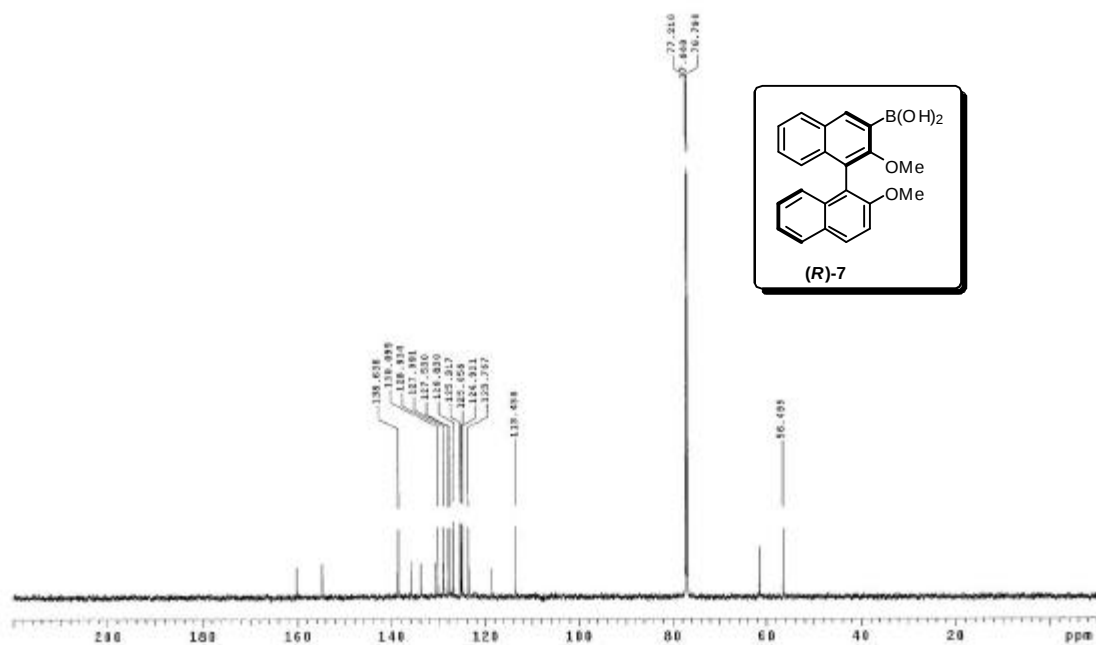
- [1] M. Hatano, T. Ikeno, T. Miyamoto, K. Ishihara, *J. Am. Chem. Soc.* **2005**, *127*, 10776-10777.
- [2] Y. Li, B. He, B. Qin, X. M. Feng, G. L. Zhang, *J. Org. Chem.* **2004**, *69*, 7910-7913.
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- [4] Y. Hamashima, D. Sawada, M. Kanai, M. Shibasaki, *J. Am. Chem. Soc.* **1999**, *121*, 2641-2642
- [5] Y. C. Qin, L. Liu, L. Pu, *Org. Lett.* **2005**, *7*, 2381-2383.

IV. Copies of ^1H and ^{13}C NMR spectra:

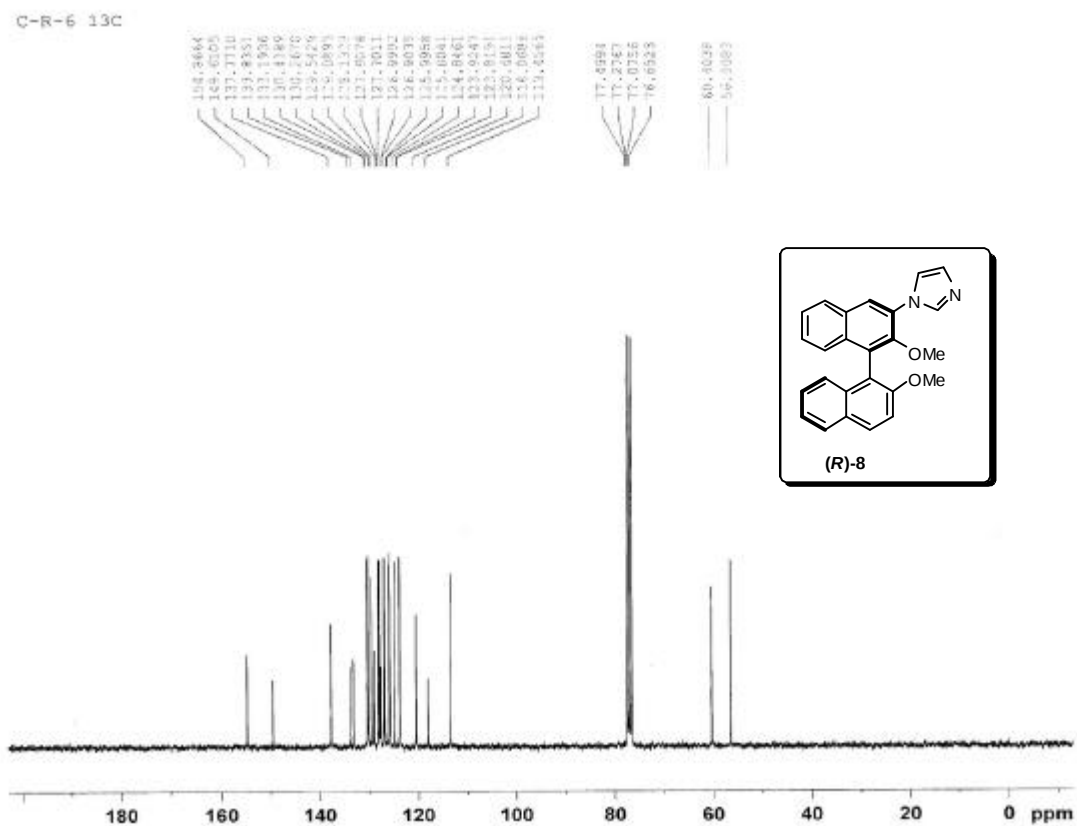
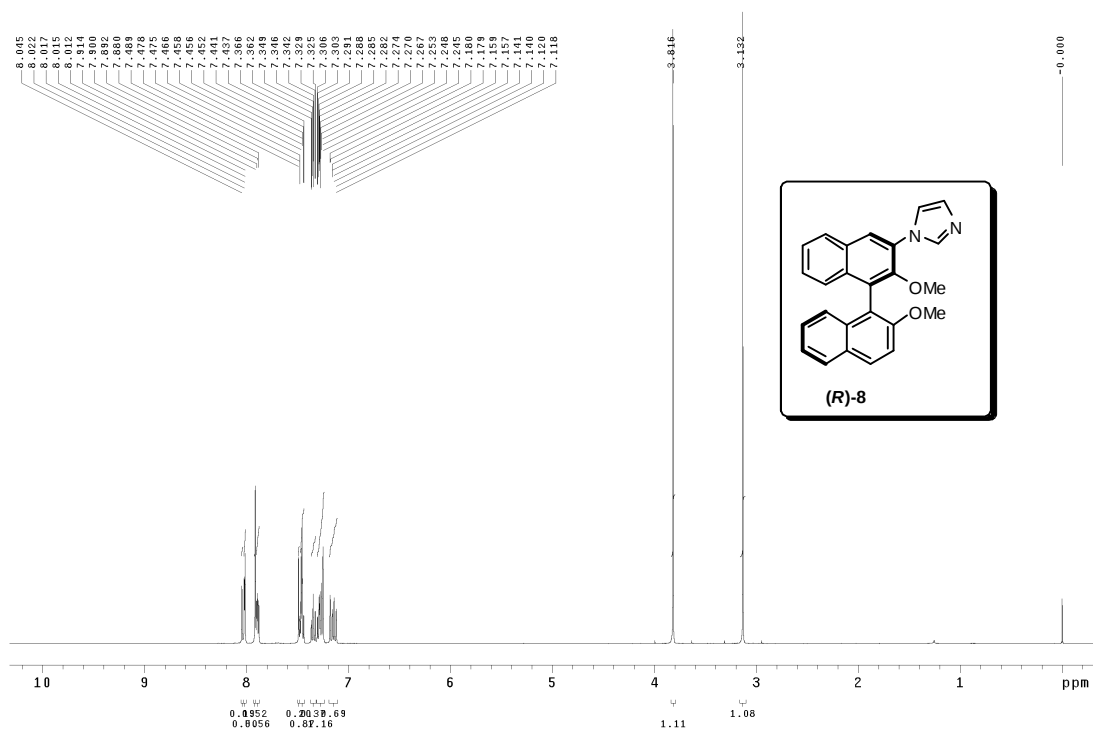
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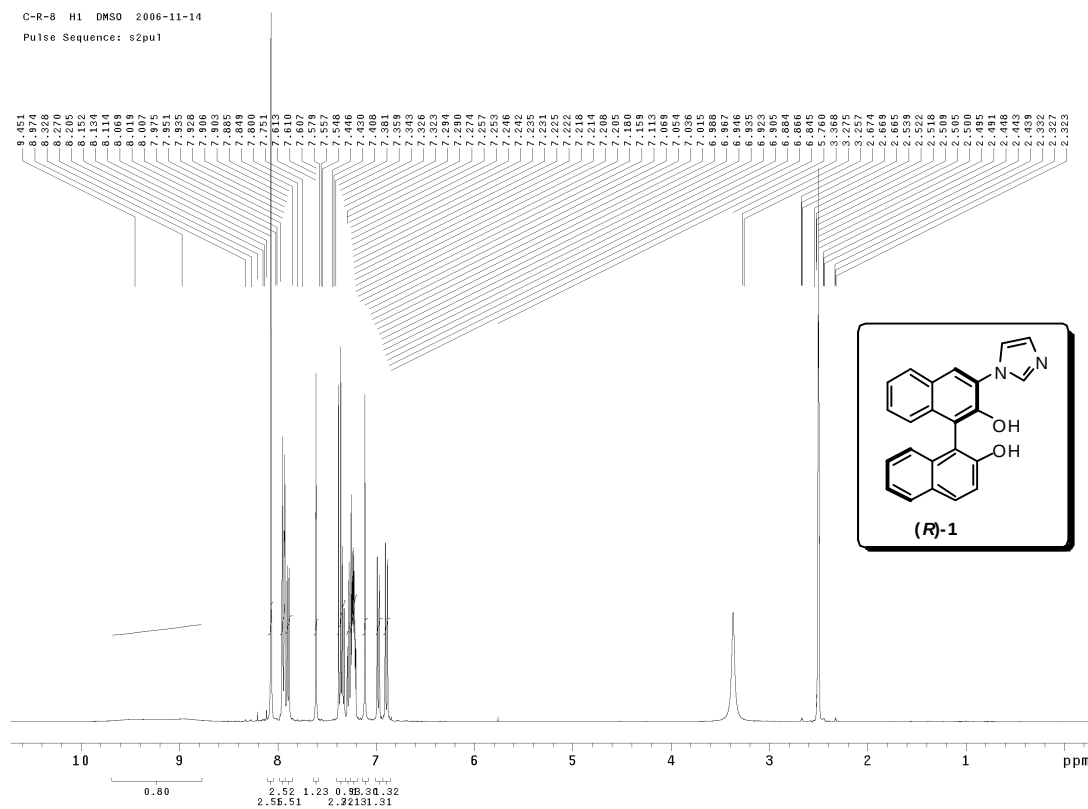
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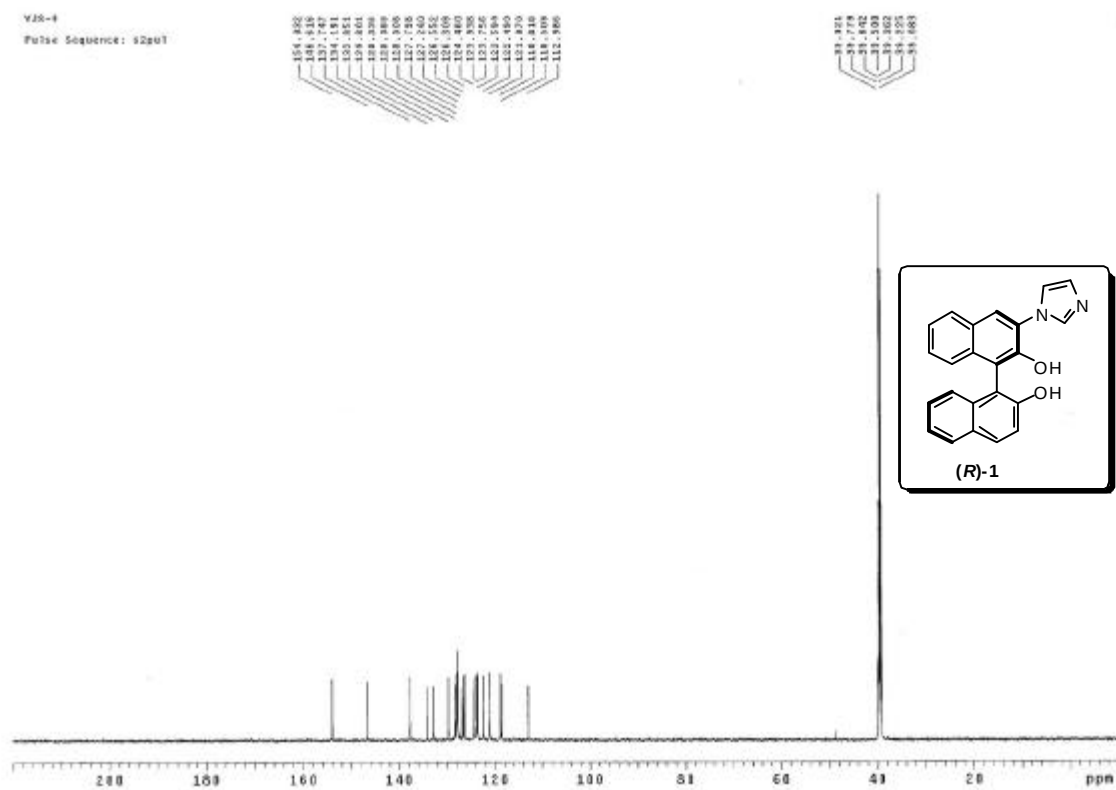
CR-6 H1 CDC13 2006-12-11
Pulse Sequence: s2pu1

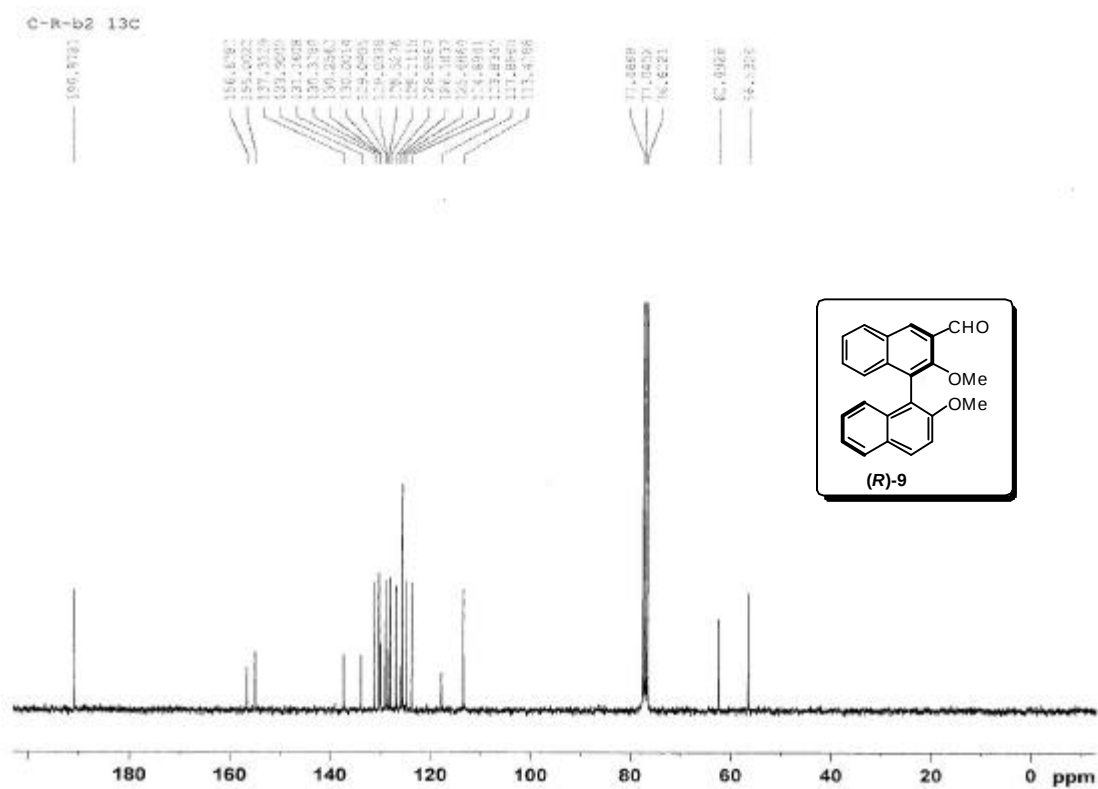
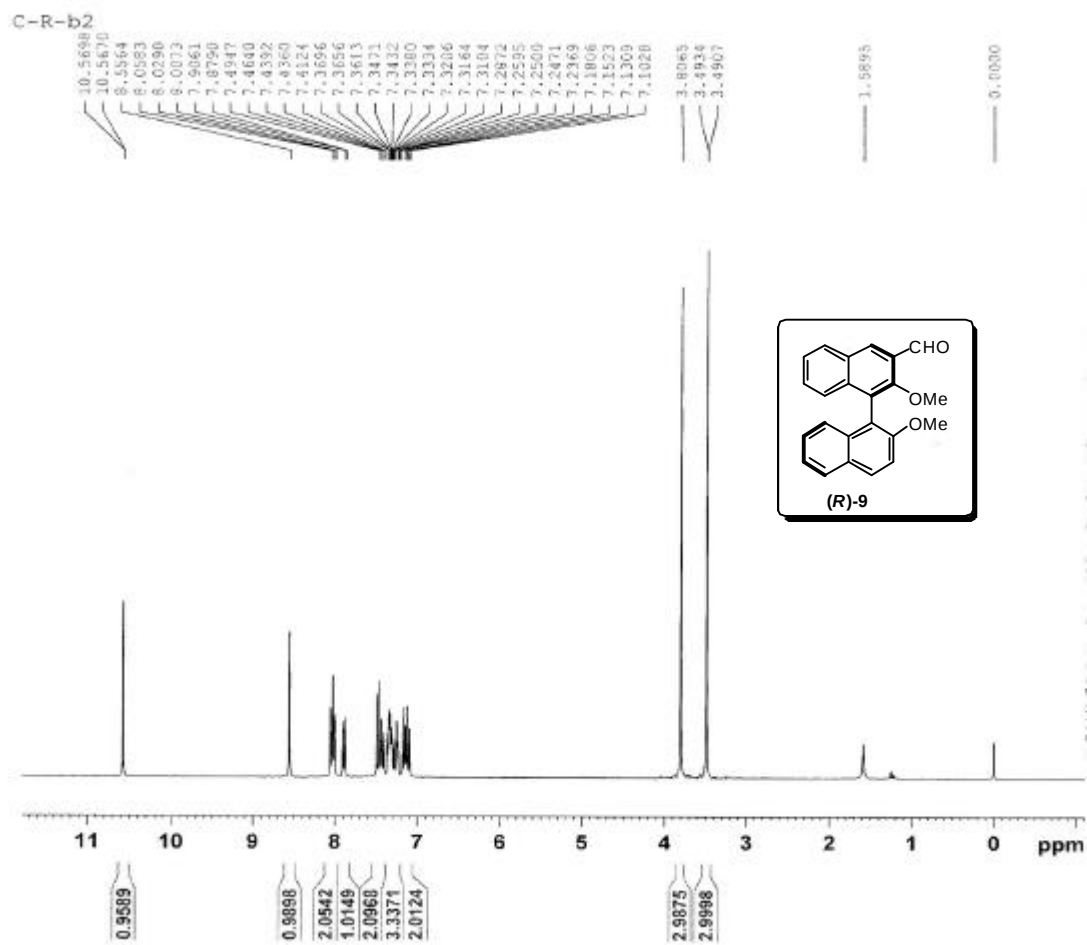


C-R-8 H1 DMSO 2006-11-14
Pulse Sequence: s2pu1

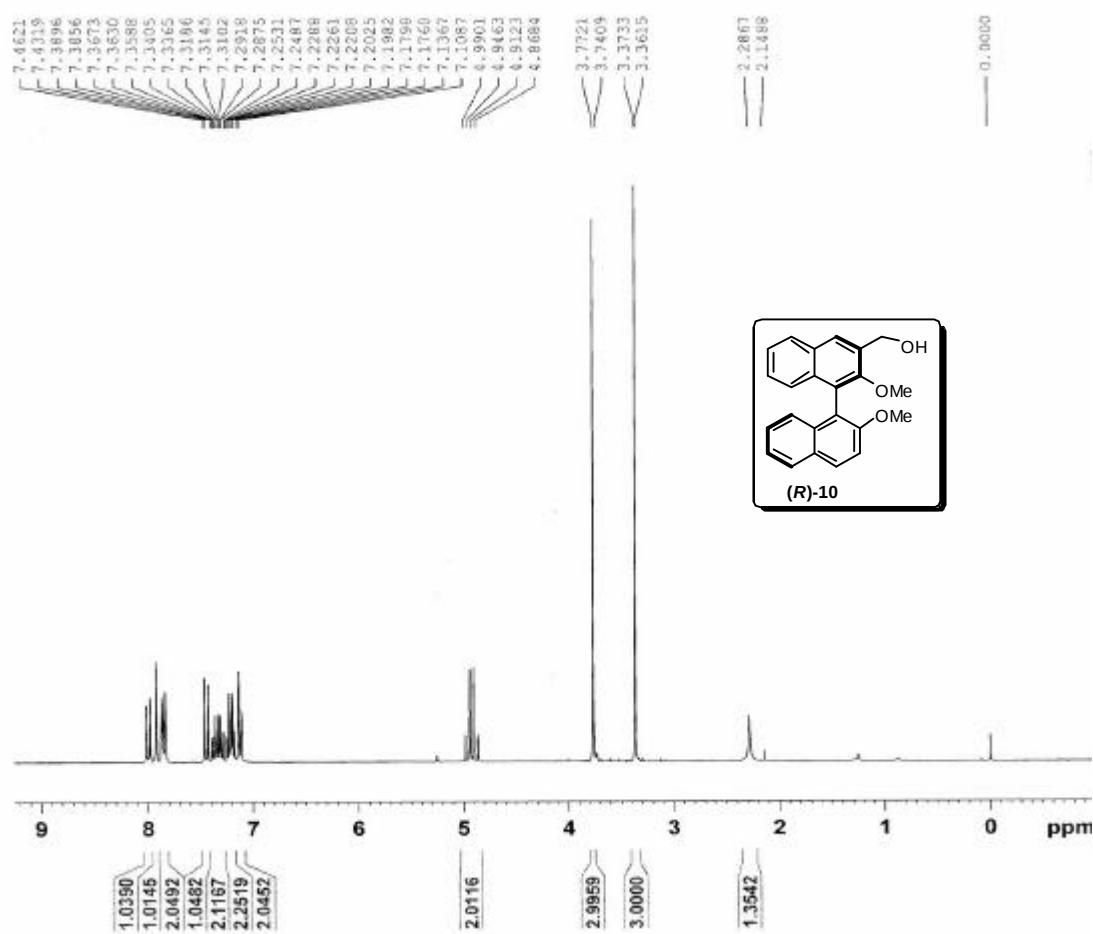


V28-4
Pulse Sequence: s2pu1

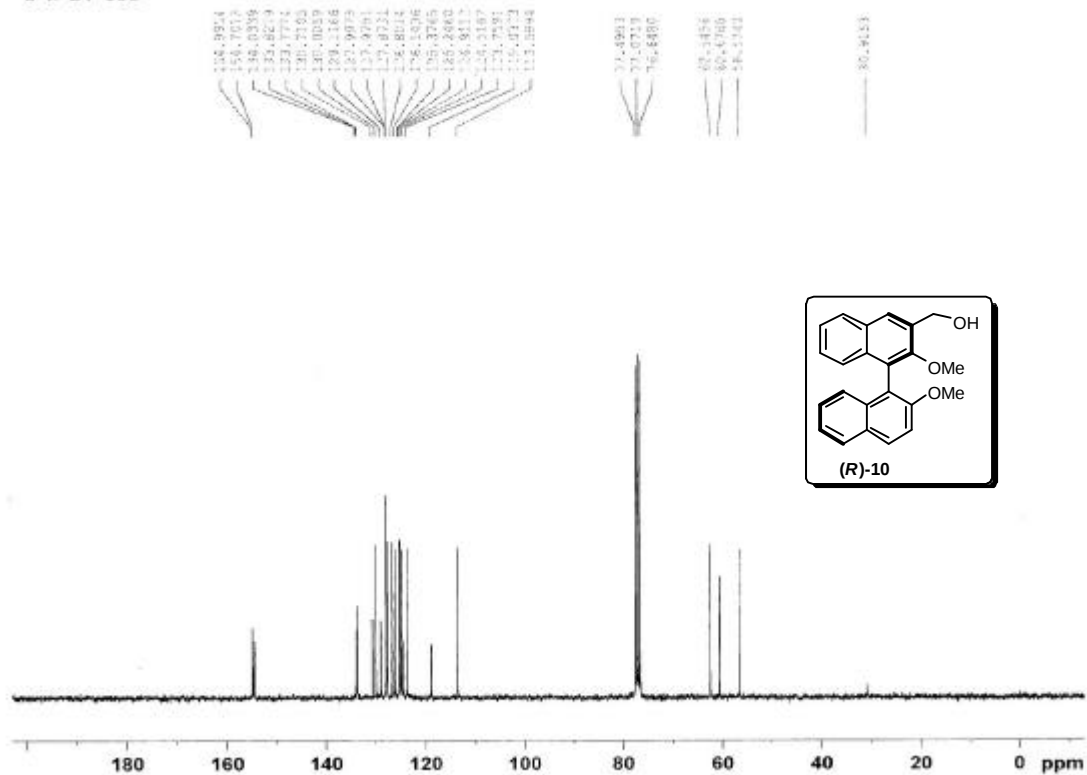


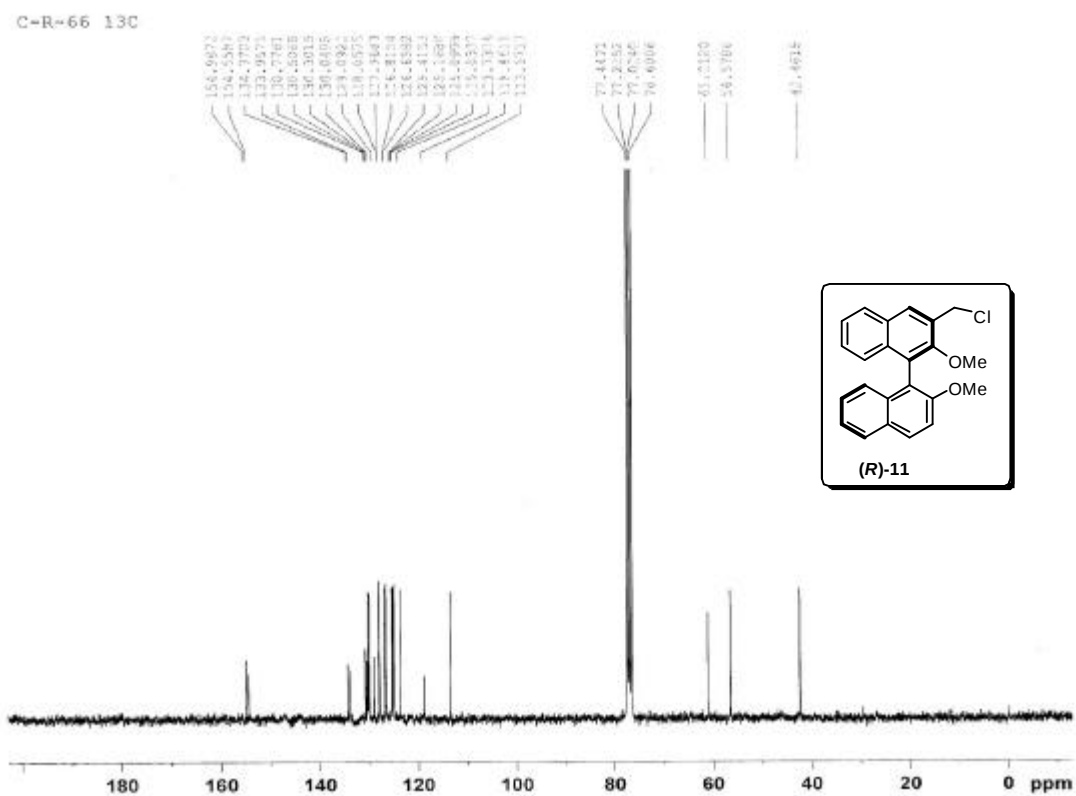
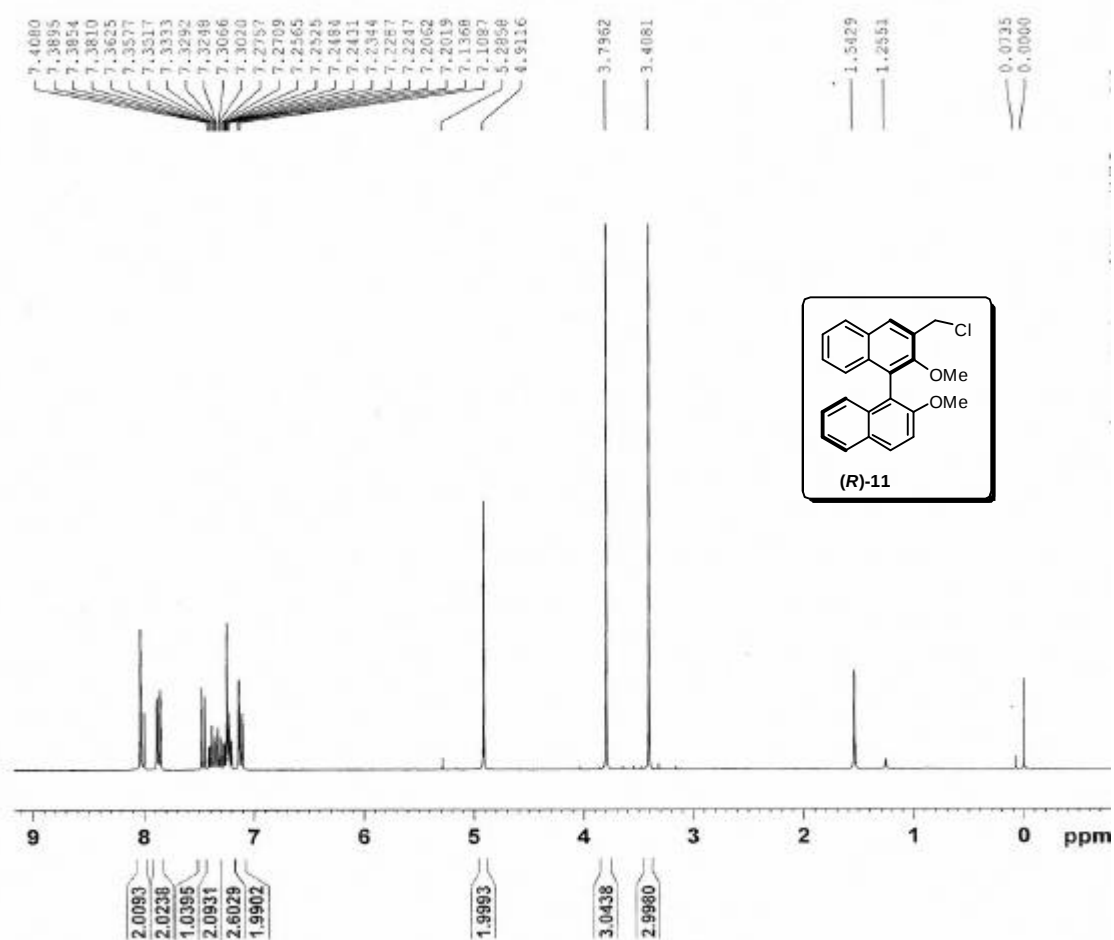


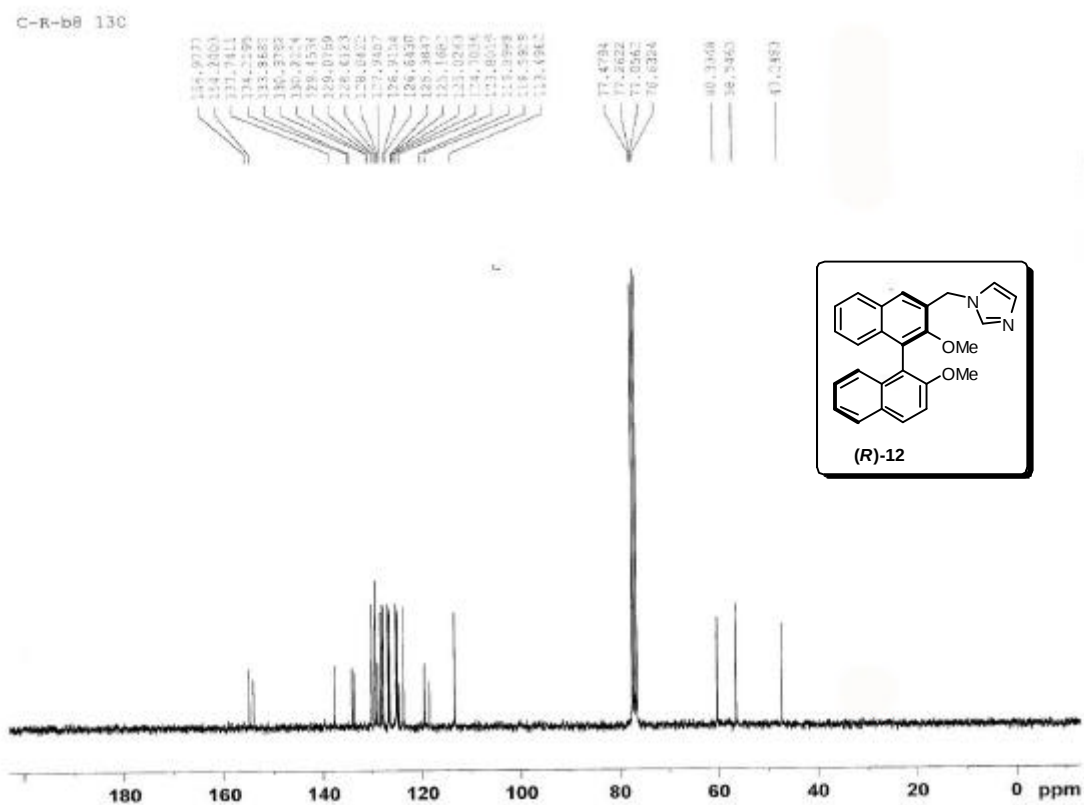
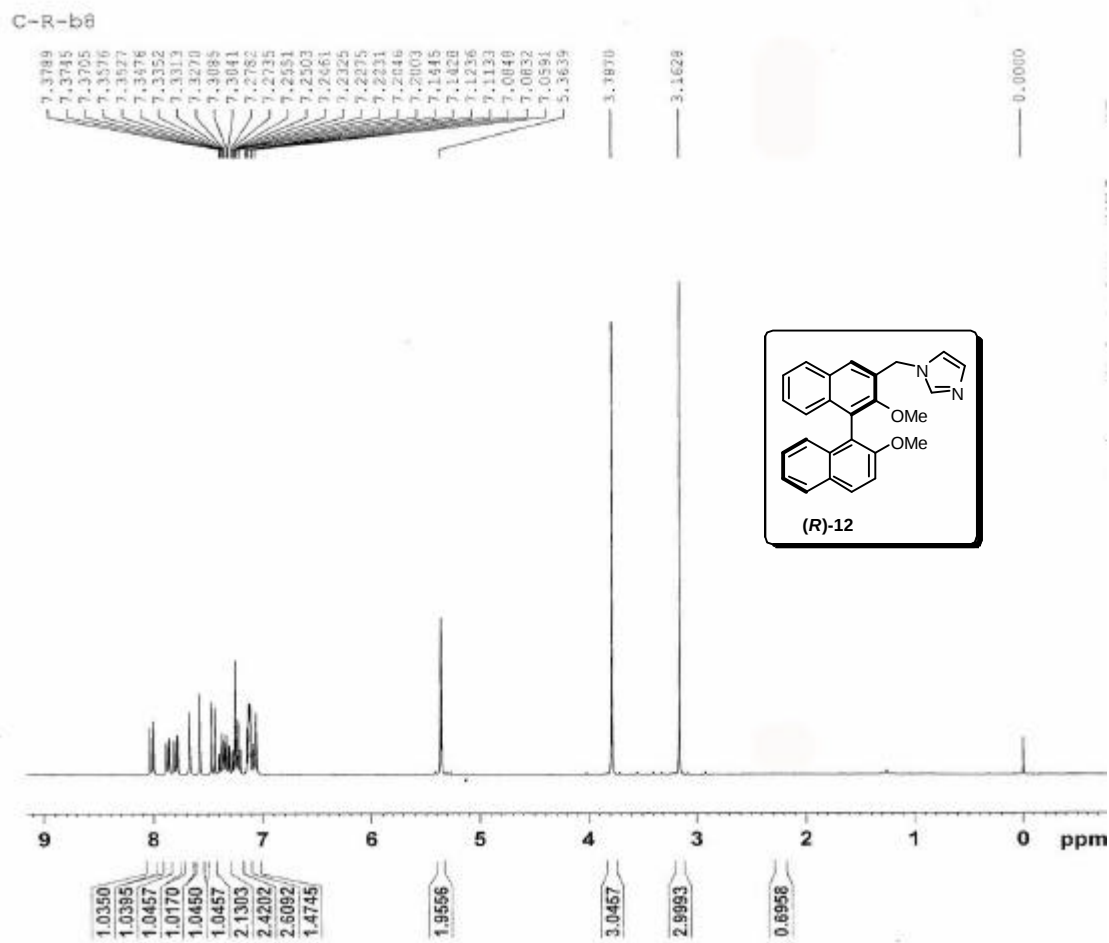
C-R-b4



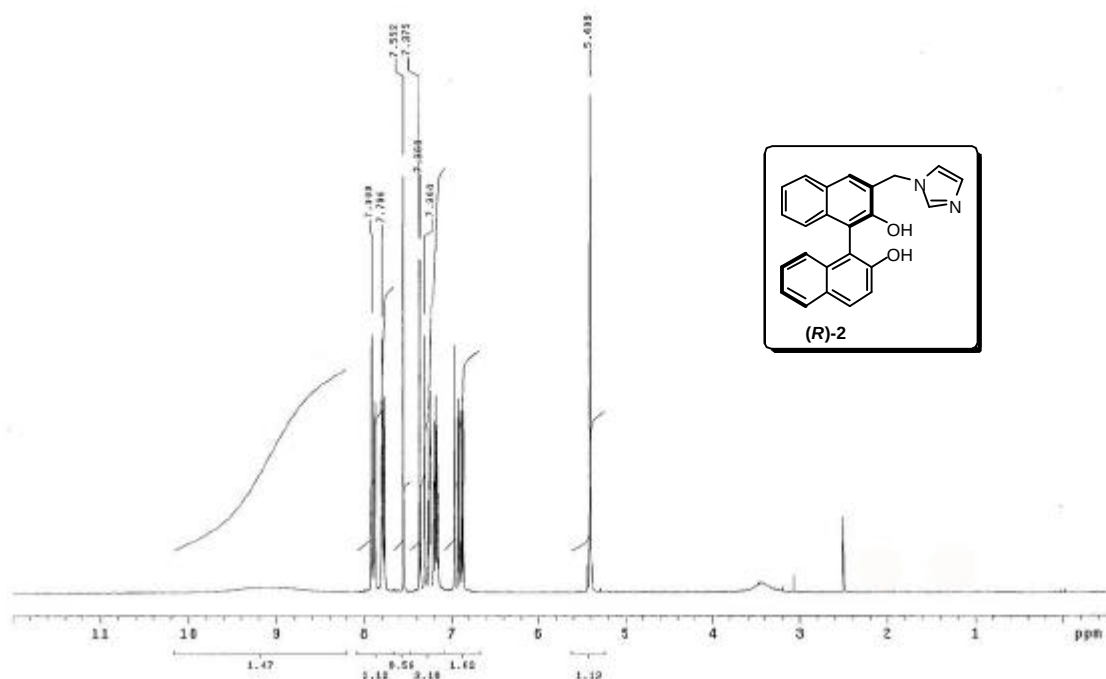
C-R-b4 13C



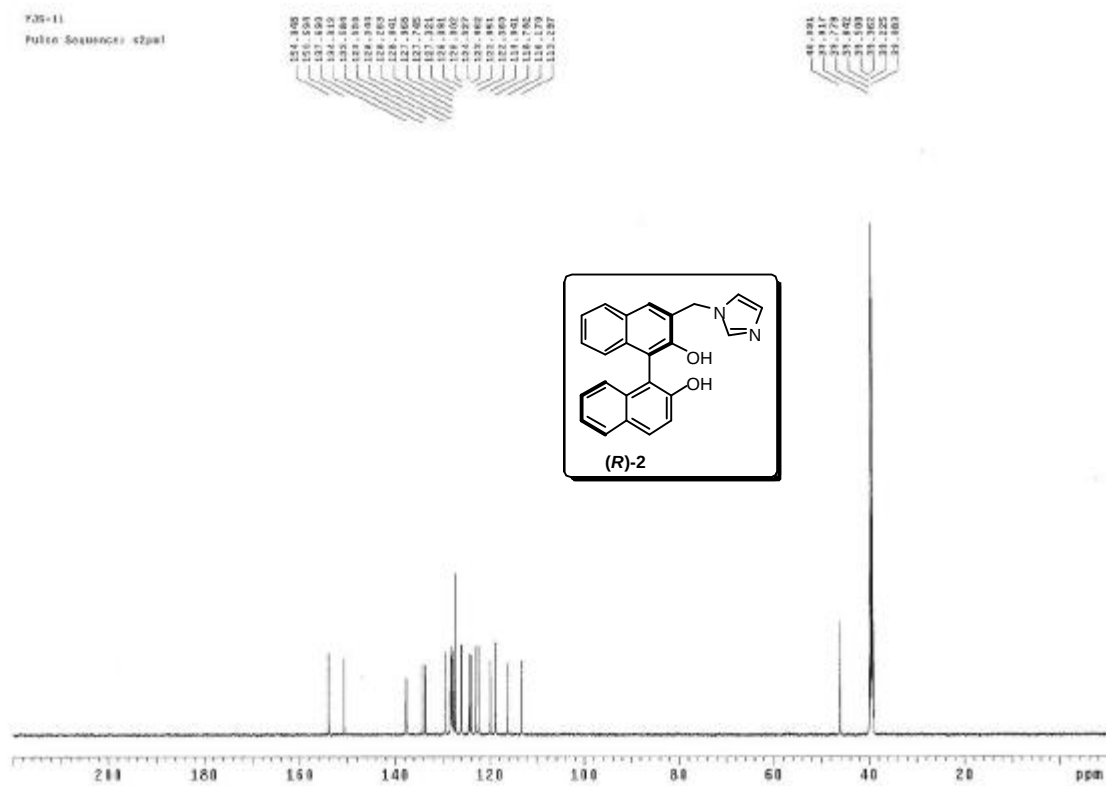




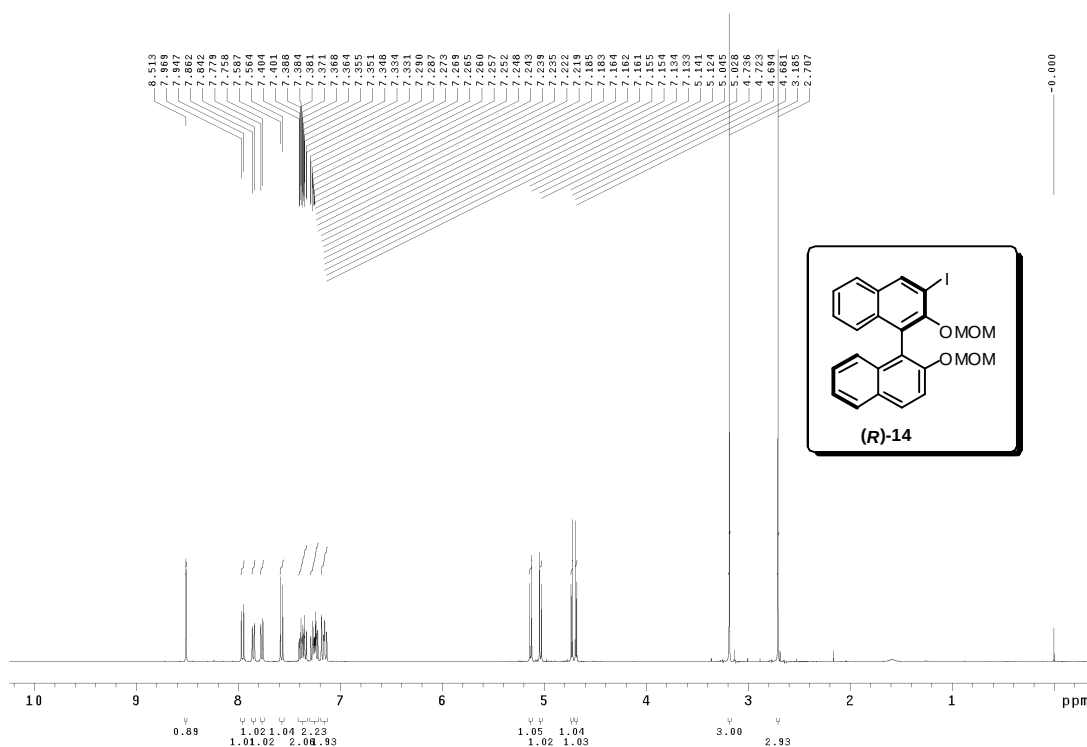
Y35-11
Pulse Sequence: zgpg30



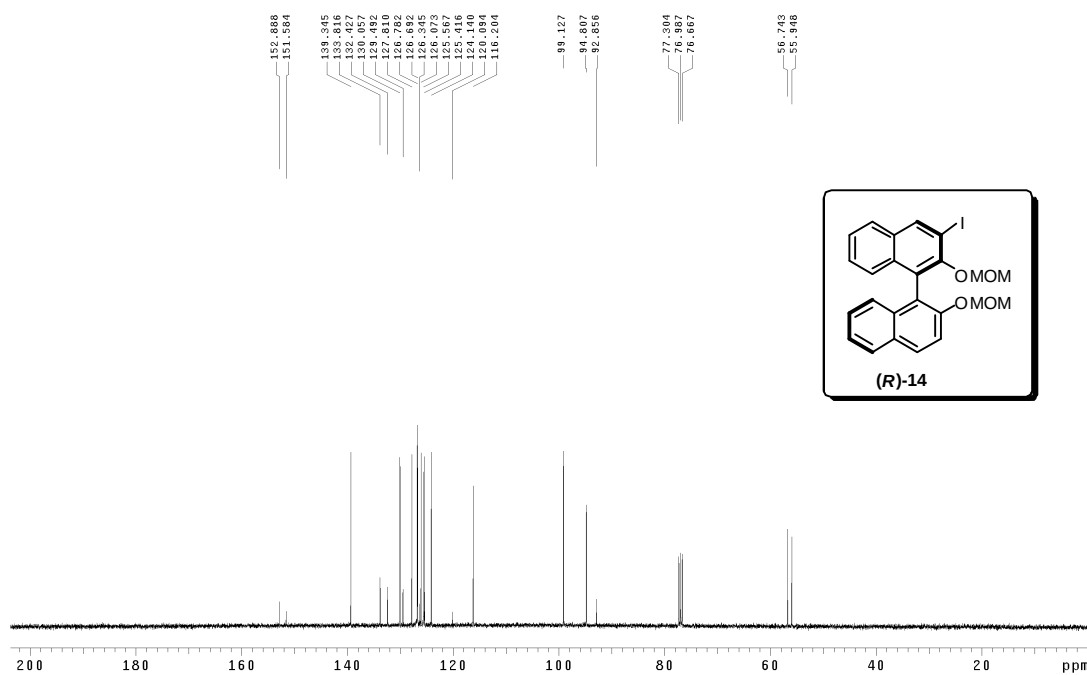
Y35-11
Pulse Sequence: zgpg30



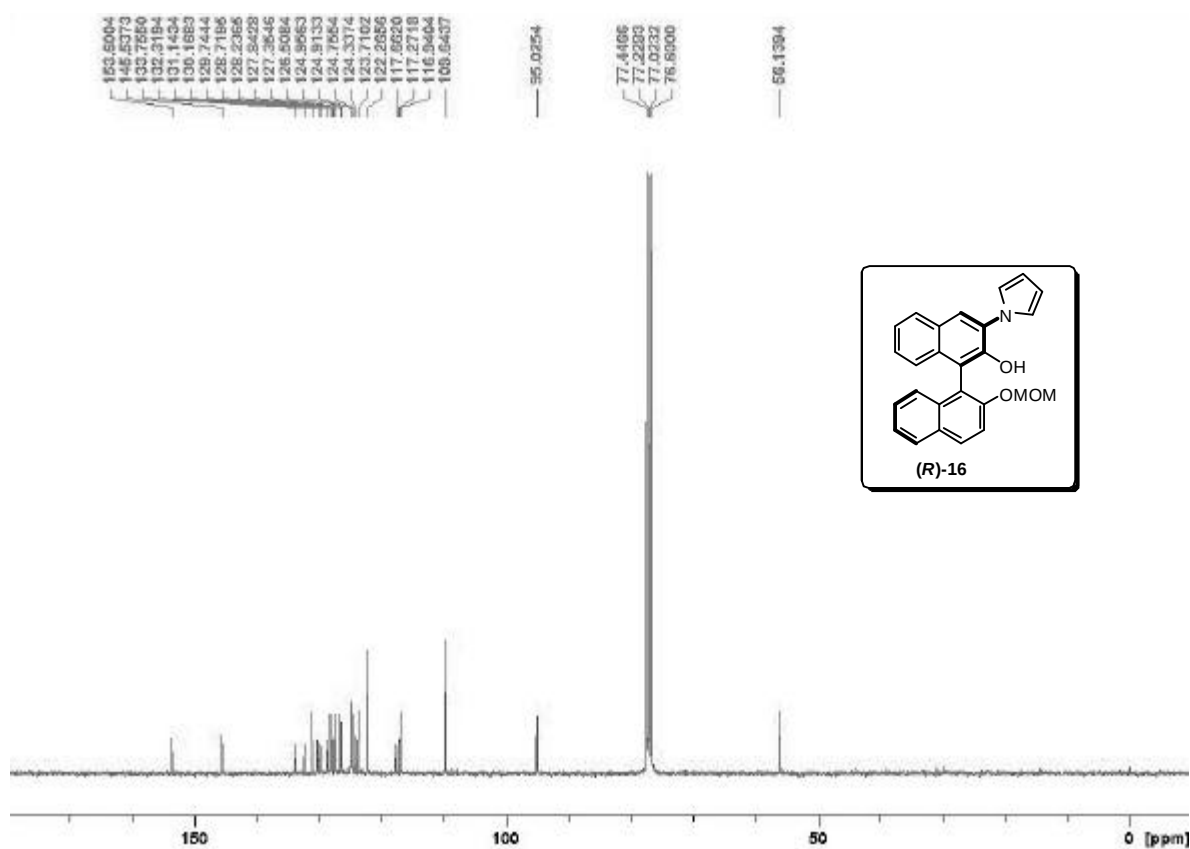
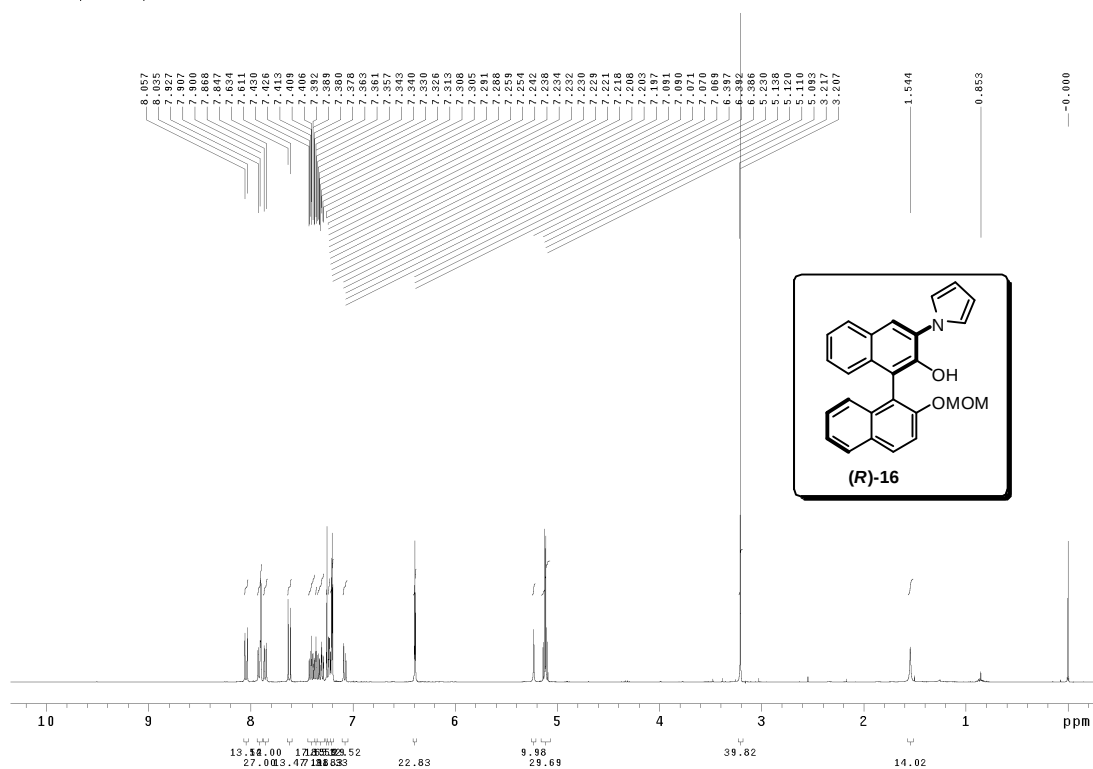
CR-I1 H1 CDC13 2007-4-23
Pulse Sequence: s2pu1



CR-I1-CDCL3-C13-2007-4-24
Pulse Sequence: s2pu1



CR-PR1 H1 CDC13 2007-4-27
Pulse Sequence: s2pu1

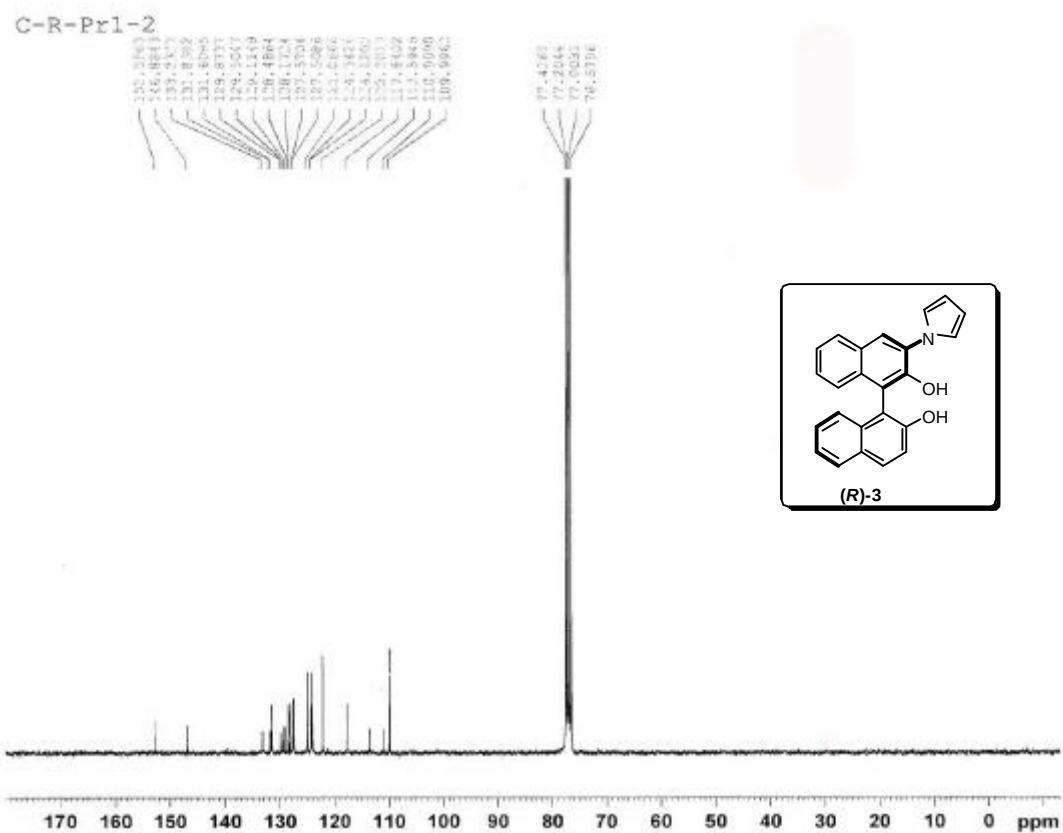


Chemical Structure of (R)-3:

Oc1ccc2cc(O)c3ccccc3c2c1N4C=CC=C4

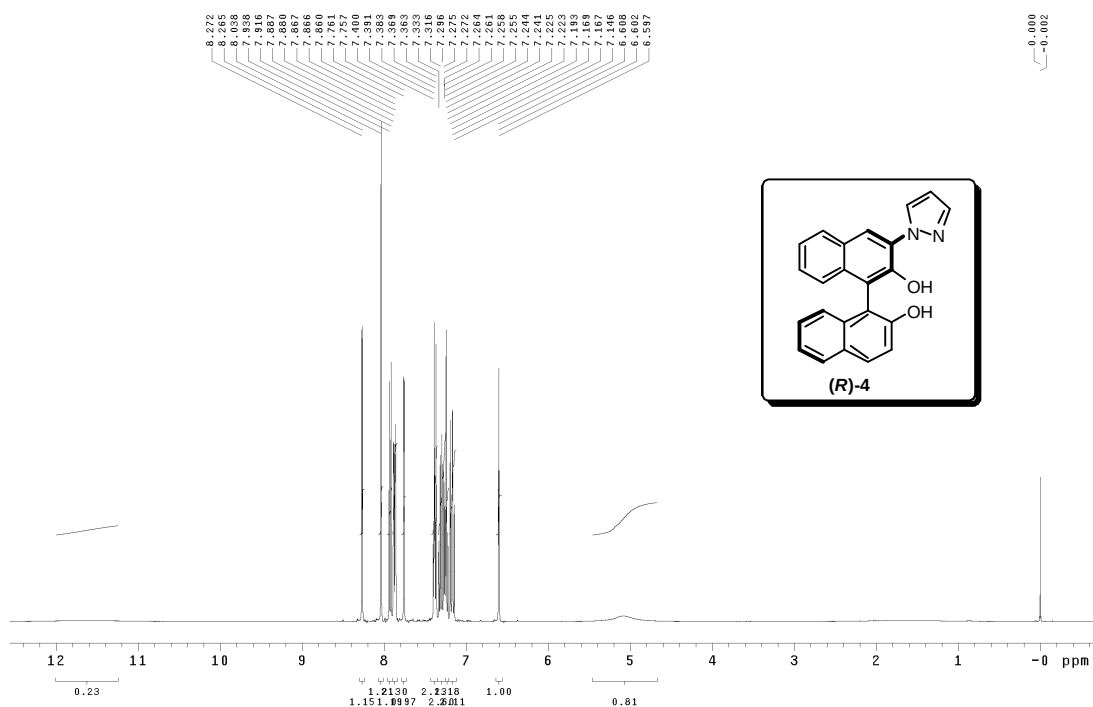
¹H NMR Spectrum Data:

Chemical Shift (ppm)	Integration
7.836, 7.824, 7.820, 7.802, 7.842, 7.836, 7.843, 7.843, 7.874, 7.370, 7.352, 7.352, 7.350, 7.335, 7.327, 7.318, 7.314, 7.312, 7.298, 7.295, 7.286, 7.271, 7.268, 7.257, 7.250, 7.242, 7.236, 7.230, 7.183, 7.131, 7.120, 7.107, 7.106, 7.086, 7.086, 6.339, 6.328, 6.328, 5.280, 4.960 <td>2.76, 2.55, 8.12, 7.42, 8.60, 4.10, 3.10</td>	2.76, 2.55, 8.12, 7.42, 8.60, 4.10, 3.10

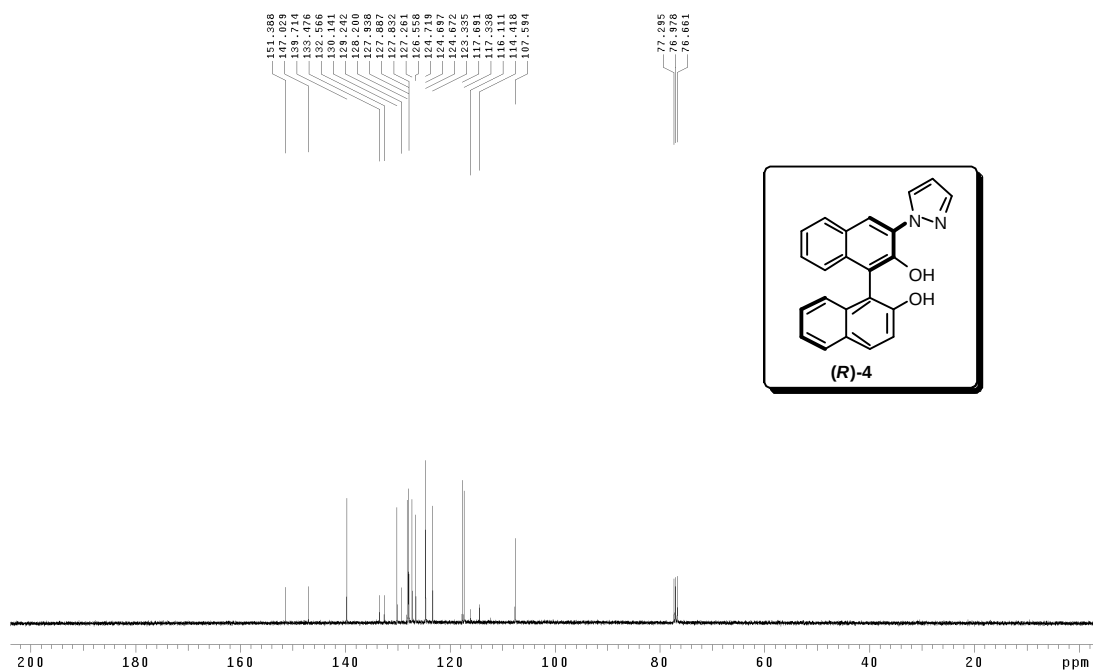


[illegible]

B-OH-PY H1 CDC13 2007-7-13
Pulse Sequence: s2pu1



C-OH-PY1-CDCl3-C13-2007-3-13
Pulse Sequence: s2pu1



¹H NMR spectrum of (R)-18 in CDCl₃.

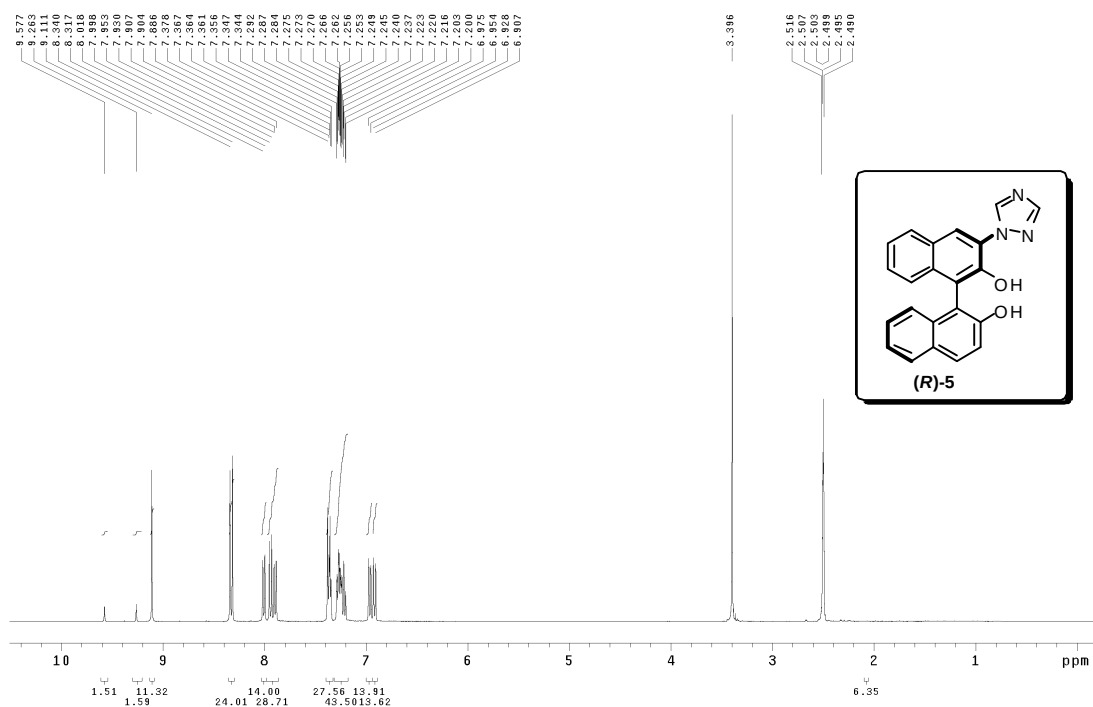
Chemical structure of (R)-18: Oc1c2ccccc2c(c1)C3=CN=CN3C(OC)C4=CC=CC=C4

Peak list (ppm): 8.887, 8.871, 8.219, 8.131, 8.056, 8.042, 7.985, 7.907, 7.890, 7.884, 7.586, 7.412, 7.409, 7.405, 7.400, 7.395, 7.392, 7.387, 7.383, 7.380, 7.375, 7.371, 7.366, 7.363, 7.309, 7.296, 7.296, 7.292, 7.285, 7.284, 7.279, 7.275, 7.271, 7.267, 7.261, 7.256, 7.257, 7.256, 7.146, 7.146, 7.146, 7.125, 5.138, 5.121, 5.088, 5.069, 3.786, -0.000.

Integration values: 0.62, 0.39, 0.63, 0.62, 1.90, 0.61, 0.026, 3.28, 1.30, 0.64, 0.66, 0.66.



C-R-Tr11-DMSO-H1-2007-1-16
Pulse Sequence: s2pu1



C-OH-Tr11-DMSO-C13-2007-3-14
Pulse Sequence: s2pu1

