Supplementary Materials

Substitution of Secondary Propargylic Phosphates with Aryl-Lithium-based Copper Reagents

Yuichi Kobayashi [1,2,*], Takayuki Hirotsu [1], Yosuke Haimoto [3], Narihito Ogawa [3]

[1] Department of Bioengineering, Tokyo Institute of Technology, 4259 Nagatsuta-cho, Midori-ku, Yokohama 226-8501, Japan
[2] Present address: Organization for the Strategic Coordination of Research and Intellectual Properties, Meiji University, 1-1-1 Higashimita, Tama-ku, Kawasaki 214-8571, Kanagawa, Japan
[3] Department of Applied Chemistry, Meiji University, 1-1-1 Higashimita, Tama-ku, Kawasaki 214-8571, Kanagawa, Japan
[†] Correspondence: ykobayas@bio.titech.ac.jp

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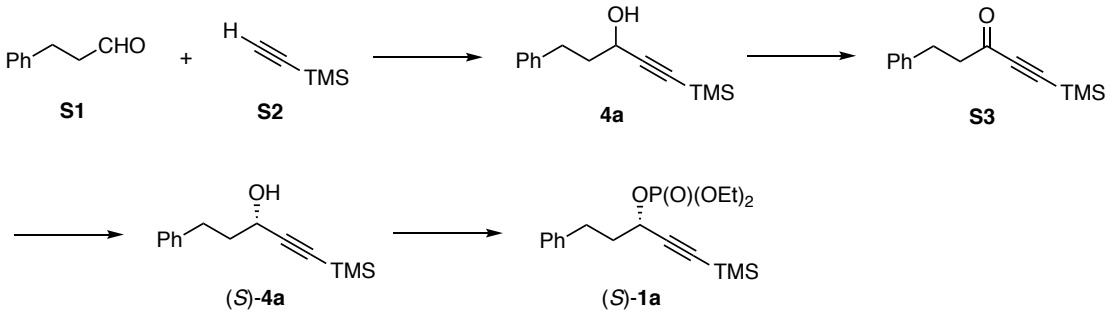
1. Synthesis of phosphates

1.1. General information

According to the previous method [S1], racemic phosphates **1a**–**c** and **7** and enantiomerically enriched phosphates (*S*)-**1a** (97–98% ee), (*S*)-**7** (96% ee), and (*S*)-**8** (95% ee) were synthesized. Among them, synthesis of (*S*)-**1a**, (*S*)-**7**, and (*S*)-**8** are described herein.

*1.2. (S)-Diethyl (5-phenyl-1-(trimethylsilyl)pent-1-yn-3-yl) phosphate [(S)-**1a**]*



To a solution of TMS acetylene **S2** (11.0 mL, 77.8 mmol) in THF (90 mL) was added *n*-BuLi (1.67 M, 34.0 mL, 56.8 mmol) dropwise at –70 °C. After the addition, the solution was stirred at –70 °C for 30 min and added aldehyde **S1** (5.0 mL, 38.0 mmol). The solution was gradually warmed to –30 °C over 2 h and poured into saturated NH_4Cl with vigorous stirring. The mixture was extracted with EtOAc three times. The combined extracts were dried over $MgSO_4$ and concentrated to give an oil, which was purified by chromatography on silica gel with hexane/EtOAc to afford **4a** (8.06 g, 91% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.19 (s, 9 H), 1.78 (d, J = 5.4 Hz, 1 H), 1.94–2.02 (m, 2 H), 2.80 (t, J = 8.0 Hz, 2 H), 4.36 (dt, J = 5.4, 6.6 Hz, 1 H), 7.15–7.33 (m, 5 H).

To a mixture of alcohol **4a** (1.45 g, 6.24 mmol) and Celite (5.53 g) in CH_2Cl_2 (30 mL) was added PCC (1.66 g, 7.70 mmol) portionwise. The mixture was stirred at rt for 15 h, diluted with hexane, and filtered through a pad of Celite. The filtrate was concentrated and the crude product was purified by chromatography on silica gel with hexane/EtOAc to afford ketone **S3** (1.28 g, 88% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.26 (s, 9 H), 2.84–3.02 (m, 4 H), 7.18–7.37 (m, 5 H).

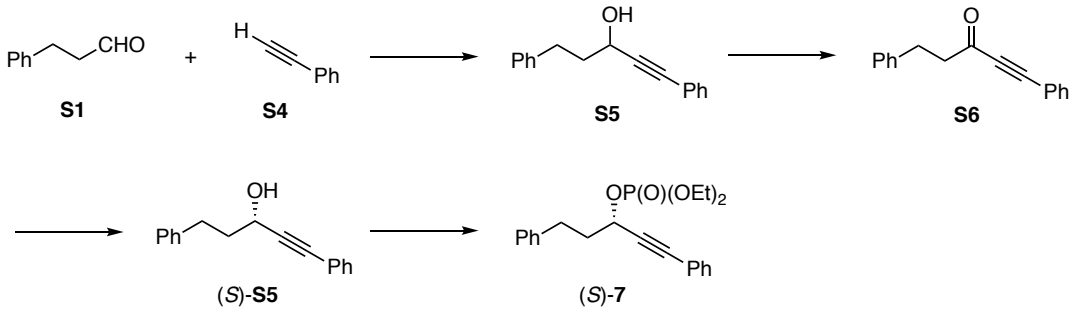
A mixture of RuCl[(1*S*,2*S*)-TsDPEN](*p*-cymene) (56 mg, 0.088 mmol) and KOH (15 mg, 0.266 mmol) in CH_2Cl_2 (1 mL) was stirred at rt for 5 min. The mixture was washed with H_2O three times and the CH_2Cl_2 solution was transferred to another flask. The solution was dried

over CaH_2, decanted through a plug of cotton, and concentrated to afford a purple solid, which was dissolved in *i*-PrOH (1.2 mL) and added to a solution of ketone **S3** (669 mg, 2.90 mmol) in *i*-PrOH (6 mL). The solution was stirred at rt for 14 h and concentrated. The resulting residue was purified by chromatography on silica gel with hexane/EtOAc to produce alcohol (*S*)-**4a** (651 mg, 96% yield). The ^{1}H NMR spectrum was identical with that for racemic **4a** delineated above.

To an ice-cold solution of alcohol (*S*)-**4a** (941 mg, 4.05 mmol) and *N*-methylimidazole (0.49 mL, 6.15 mmol) in CH_2Cl_2 (20 mL) was added diethyl chlorophosphate (1.17 mL, 8.07 mmol) dropwise. The solution was stirred at rt for 20 h and poured into saturated $NaHCO_3$. The mixture was extracted with CH_2Cl_2 twice. The combined extracts were dried over $MgSO_4$ and concentrated. The remaining oil was purified by chromatography on silica gel with hexane/EtOAc to afford phosphate (*S*)-**1a** (1.40 g, 94% yield): 97% ee by chiral HPLC analysis (Chiralcel OD-H, hexane/*i*-PrOH (98:2), 0.3 mL/min, 40 °C, t_R/min = 25.6 (minor) and 27.1 (major)); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.19 (s, 9 H), 1.35 (t, J = 7.0 Hz, 6 H), 2.06–2.23 (m, 2 H), 2.80 (t, J = 7.6 Hz, 2 H), 4.07–4.22 (m, 4 H), 4.99 (dt, J = 7.6, 6.4 Hz, 1 H), 7.17–7.35 (m, 5 H).

The ^{1}H NMR spectra of **4a** and **S3** and (*S*)-**1a** were consistent with the reported data.[S1]

1.3. (S)-1,5-Diphenylpent-1-yn-3-yl diethyl phosphate [(S)-7]

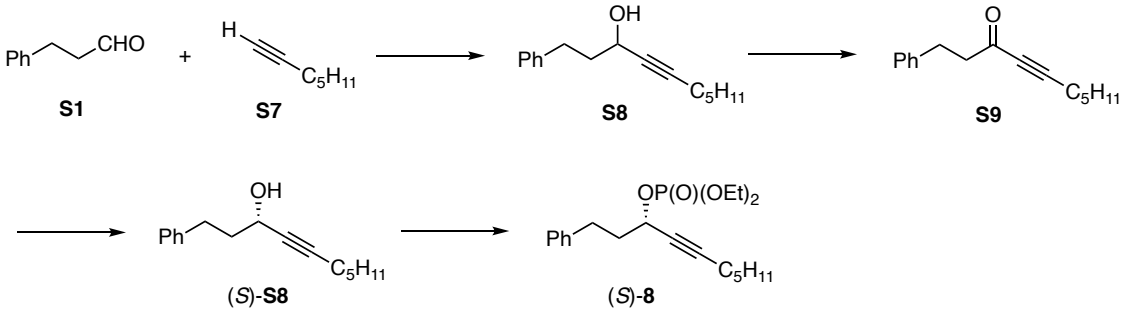


According to the above method for the synthesis of (*S*)-**1a**, a hexane solution of *n*-BuLi (1.65 M, 6.90 mL, 11.4 mmol) was added to a solution of Ph acetylene **S4** (1.70 mL, 15.5 mmol) in THF (10 mL) at –70 °C. After 30 min at –70 °C, aldehyde **S1** (1.0 mL, 7.60 mmol) was added. The solution was stirred at –70 °C for 1 h and poured into saturated NH_4Cl to afford alcohol **S5**, which was passed through a short column of silica gel with hexane/EtOAc. A mixture of **S5**, PCC (2.07 g, 9.60 mmol), and Celite (3.95 g) in CH_2Cl_2 (12 mL) was stirred at rt for 3 h and fitered through a pad of Celite. The product was purified by chromatography

on silica gel to afford ketone **S6** (801 mg, 45% yield from **S1**): ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.94–3.11 (m, 4 H), 7.18–7.50 (m, 8 H), 7.54–7.60 (m, 2 H). A mixture of RuCl[(1*S*,2*S*)-TsDPEN](*p*-cymene) (64.2 mg, 0.101 mmol) and KOH (18.5 mg, 0.33 mmol) in CH_2Cl_2 (1 mL) was stirred at rt for 5 min to afford the purple catalyst, which was mixed with ketone **S6** (743.2 mg, 3.17 mmol) in *i*-PrOH (16 mL). The solution was stirred at rt for 16 h to produce alcohol (*S*)-**S5** (741 mg, 97% yield) after chromatography on silica gel: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.92 (d, J = 5.7 Hz, 1 H), 2.08–2.18 (m, 2 H), 2.87 (t, J = 7.8 Hz, 2 H), 4.60 (dt, J = 5.7, 6.5 Hz, 1 H), 7.16–7.43 (m, 10 H).

Diethyl chlorophosphate (0.92 mL, 6.34 mmol) was added to an ice-cold solution of alcohol (*S*)-**S5** (748 mg, 3.17 mmol) and *N*-methylimidazole (0.76 mL, 9.53 mmol) in CH_2Cl_2 (6 mL). The solution was stirred at rt for 24 h and poured into saturated $NaHCO_3$. The crude product was purified by chromatography on silica gel with hexane/EtOAc to afford phosphate (*S*)-**7** (902 mg, 77% yield): 96% ee by chiral HPLC analysis (Chiralcel OD-H, hexane/*i*-PrOH (98:2), 0.3 mL/min, 25 °C, t_R/min = 65.4 (minor) and 77.5 (major)); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.34 (dt, J = 1.2, 7.2 Hz, 3 H), 1.35 (dt, J = 1.5, 7.2 Hz, 3H), 2.18–2.37 (m, 2 H), 2.88 (t, J = 8.0 Hz, 2 H), 4.07–4.24 (m, 4 H), 5.21 (q, J = 6.8 Hz, 1 H), 7.17–7.37 (m, 8 H), 7.42–7.48 (m, 2 H). The ^{1}H NMR spectrum of (*S*)-**7** was consistent with the reported data.[S1]

*1.4. (S)-Diethyl (1-phenyldec-4-yn-3-yl) phosphate [(S)-**8**]*



According to the above method for the synthesis of (*S*)-**1a**, a hexane solution of *n*-BuLi (1.65 M, 6.90 mL, 11.4 mmol) was added to a solution of 1-heptyne (**S7**) (2.0 mL, 15.4 mmol) in THF (10 mL) at –70 °C. After 30 min at –70 °C, aldehyde **S1** (1.0 mL, 7.60 mmol) was added. The solution was stirred at –70 °C for 1 h and poured into saturated NH_4Cl to afford alcohol **S8**, which was passed through a short column of silica gel with hexane/EtOAc. A mixture of **S8**, PCC (2.22 g, 10.3 mmol), and Celite (5.22 g) in CH_2Cl_2 (20 mL) was stirred

at rt for 2 h and fitered through a pad of Celite. The product was purified by chromatography on silica gel to afford ketone **S9** (983 mg, 57% yield from **S1**): ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.91 (t, J = 7.0 Hz, 3 H), 1.24–1.44 (m, 4 H), 1.55–1.63 (m, 2 H), 2.36 (t, J = 7.0 Hz, 2 H), 2.87 (ddd, J = 8.4, 6.8, 2.0 Hz, 2 H), 2.93–3.02 (m, 2 H), 7.17–7.37 (m, 5 H). A mixture of RuCl[(1*S*,2*S*)-TsDPEN](*p*-cymene) (80.3 mg, 0.126 mmol) and KOH (25.4 mg, 0.453 mmol) in CH_2Cl_2 (1 mL) was stirred at rt for 5 min to afford the purple catalyst, which was mixed with ketone **S9** (914.5 mg, 4.01 mmol) in *i*-PrOH (20 mL). The solution was stirred at rt for 20 h to produce alcohol (*S*)-**S8** (803.3 mg, 87% yield) after chromatography on silica gel: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.91 (t, J = 7.2 Hz, 3 H), 1.22–1.44 (m, 4 H), 1.48–1.60 (m, 2 H), 1.73 (d, J = 5.4 Hz, 1 H), 1.96–2.09 (m, 2 H), 2.23 (dt, J = 2.1, 7.2 Hz, 2 H), 2.79 (t, J = 7.8 Hz, 2 H), 4.34–4.43 (m, 1 H), 7.17–7.37 (m, 5 H).

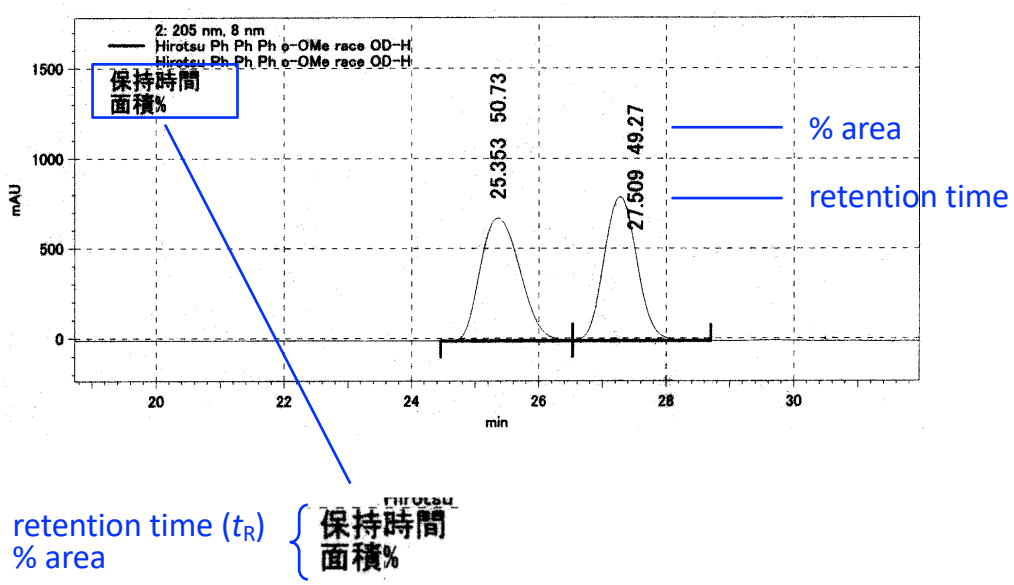
Diethyl chlorophosphate (1.00 mL, 6.90 mmol) was added to an ice-cold solution of alcohol (*S*)-**S8** (803.3 mg, 3.49 mmol) and *N*-methylimidazole (0.84 mL, 10.5 mmol) in CH_2Cl_2 (7 mL). The solution was stirred at rt for 14 h and poured into saturated $NaHCO_3$. The crude product was purified by chromatography on silica gel with hexane/EtOAc to afford phosphate (*S*)-**8** (1.05 g, 82% yield): 95% ee by chiral HPLC analysis (Chiralcel OD-H, hexane/*i*-PrOH (98:2), 0.3 mL/min, 25 °C, t_R/min = 61.9 (minor) and 64.9 (major)); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.90 (t, J = 7.2 Hz, 3 H), 1.23–1.42 (m, 10 H), 1.44–1.59 (m, 2 H), 2.02–2.20 (m, 2 H), 2.24 (dt, J = 2.1, 7.2 Hz, 2 H), 4.04–4.22 (m, 4 H), 4.97–5.04 (m, 1 H), 7.18–7.37 (m, 5 H). The ^{1}H NMR spectrum of (*S*)-**8** was consistent with the reported data.[S1]

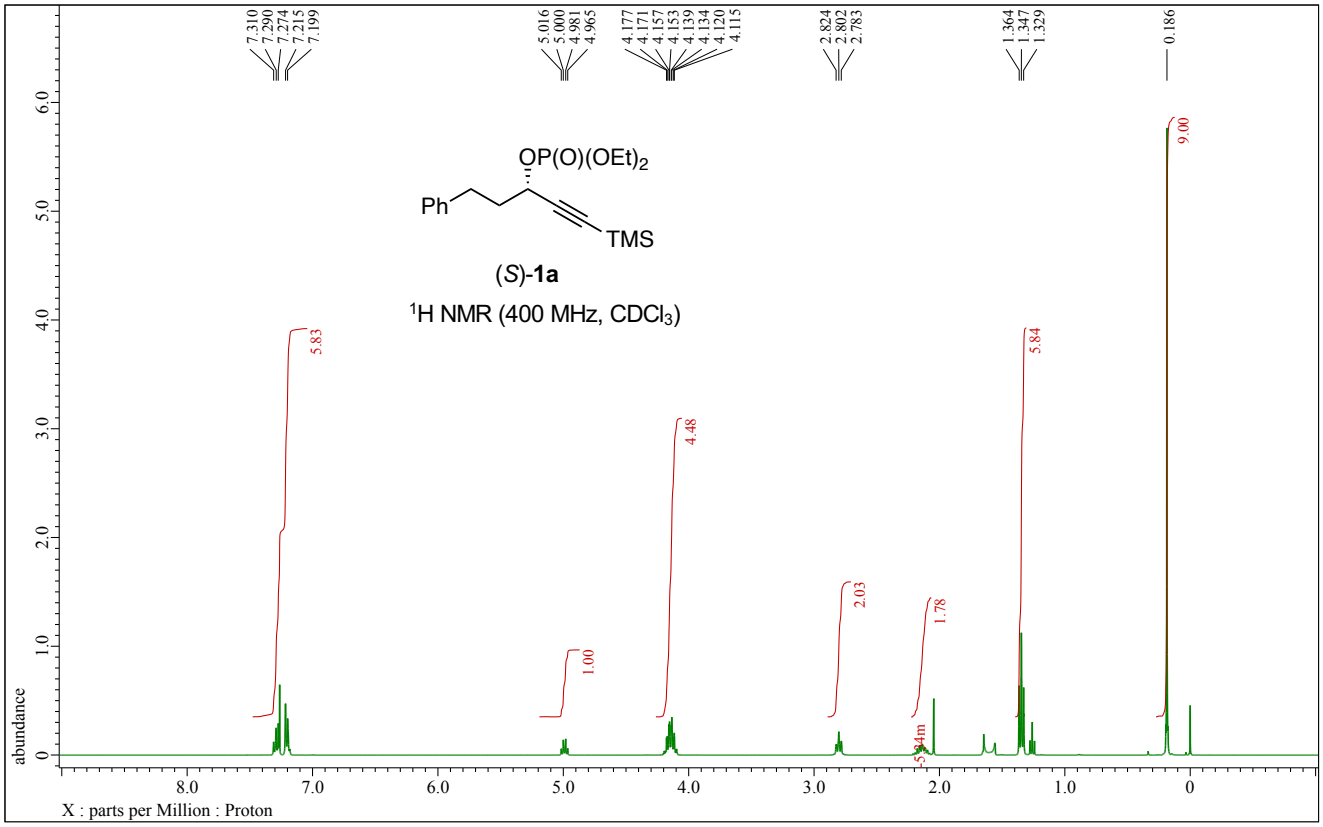
2. Reference

S1. Kobayashi, Y.; Takashima, Y.; Motoyama, Y.; Isogawa, Y.; Katagiri, K.; Tsuboi, A.; Ogawa, N. *Chem. Eur. J.* **2021**, *27*, 3779–3785.

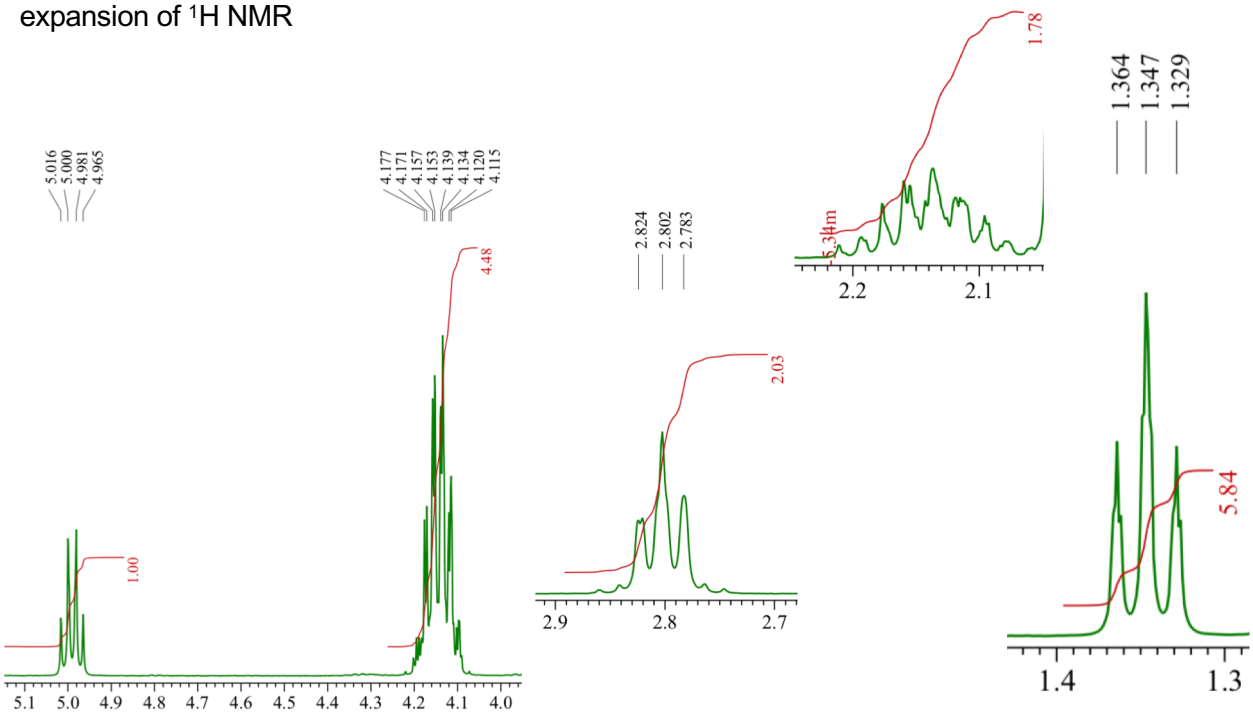
3. NMR spectra and chiral HPLC

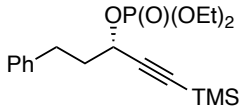
Explanatory notes of HPLC chromatograms and translation of Jpn indication to Engl.





expansion of ^{1}H NMR

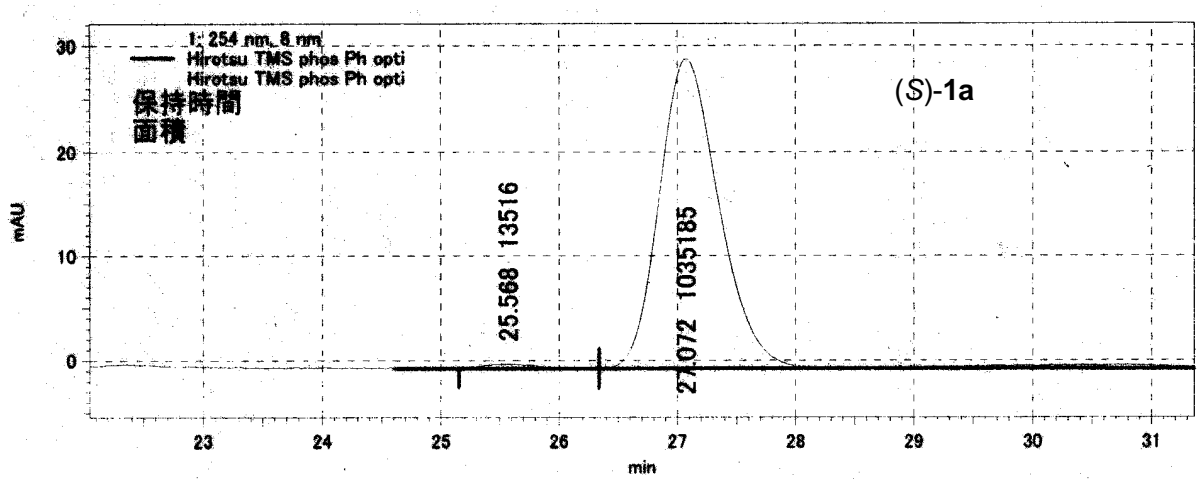


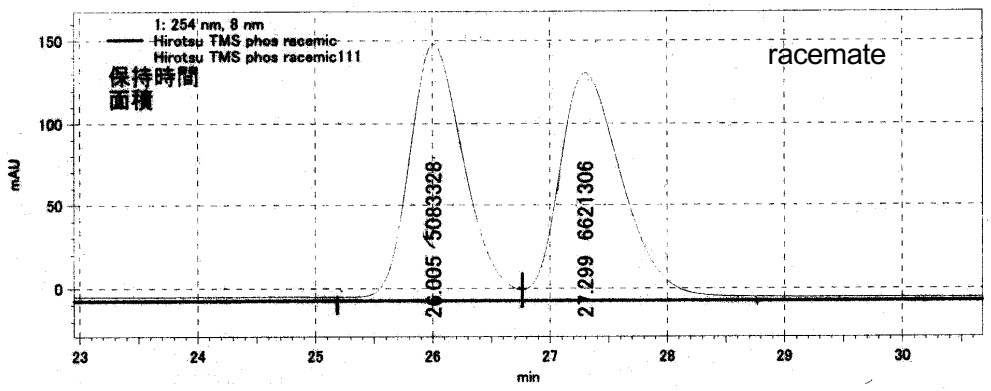


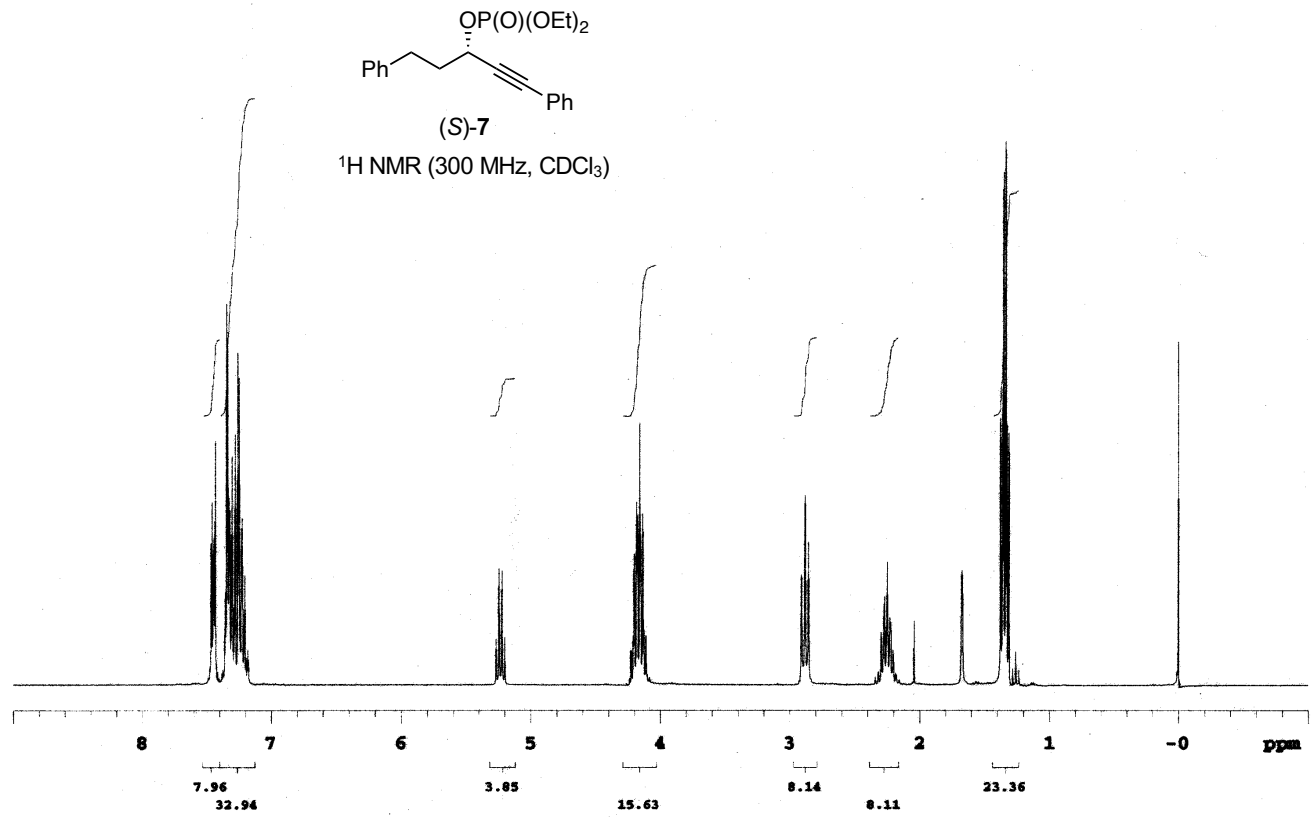
(*S*)-**1a**

ee
= (1035185 – 13516) x 100 / (1035185 + 13516)
= 97.4
≈ 97%

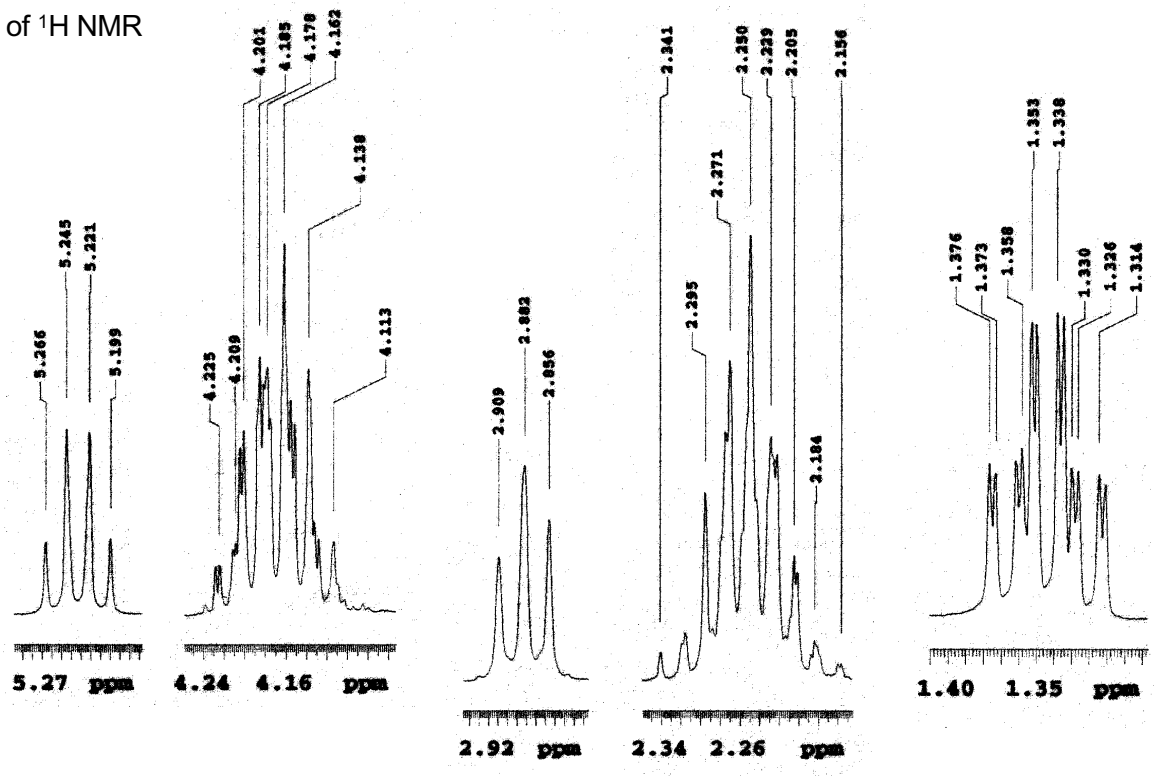
Chiralcel OD-H, hexane/*i*-PrOH = 98:2, 0.3 mL/min,40 °C

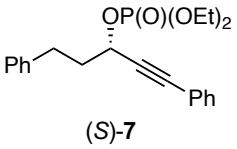






expansion of ^{1}H NMR

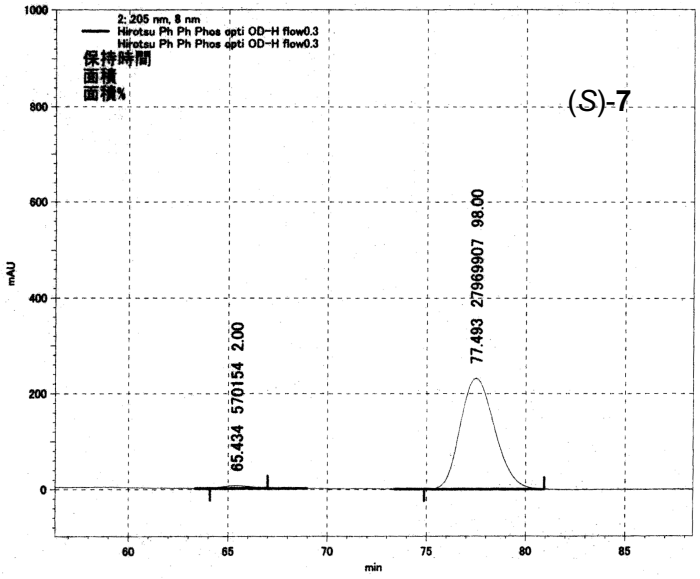


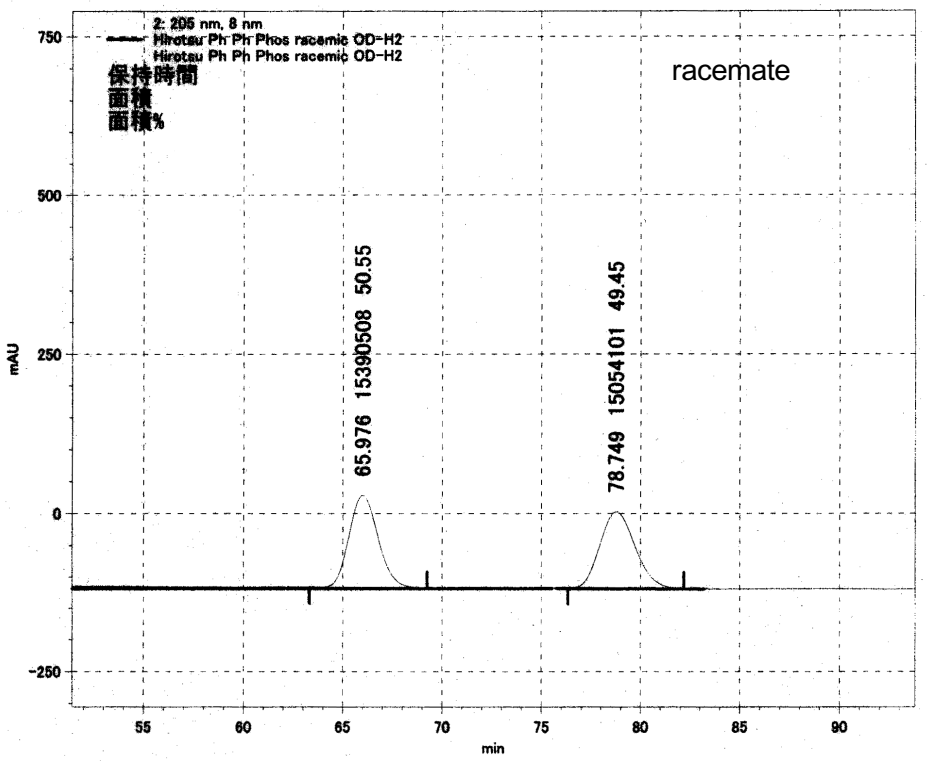


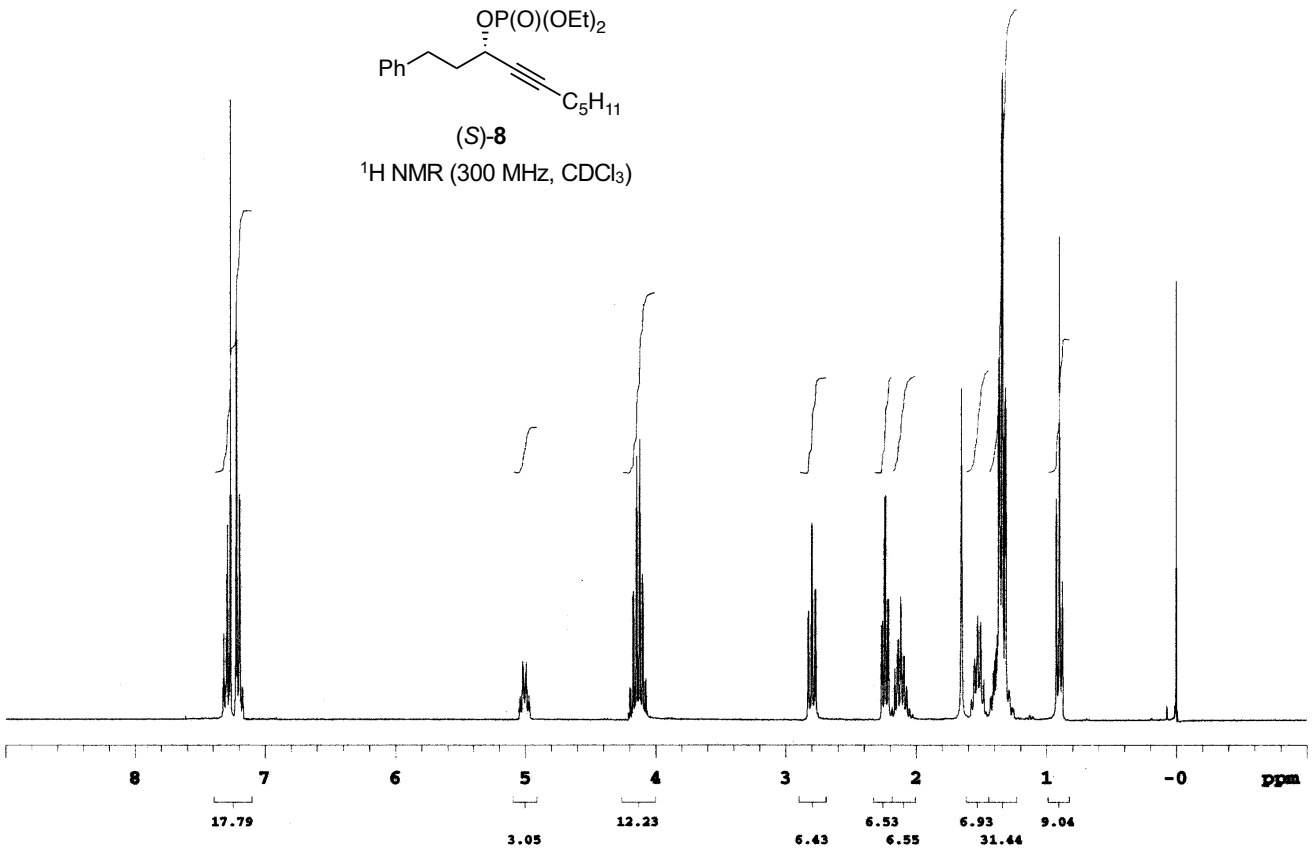
(*S*)-**7**

ee
= (98.00 – 2.00) x 100 / (98.00 + 2.00)
= 96.0

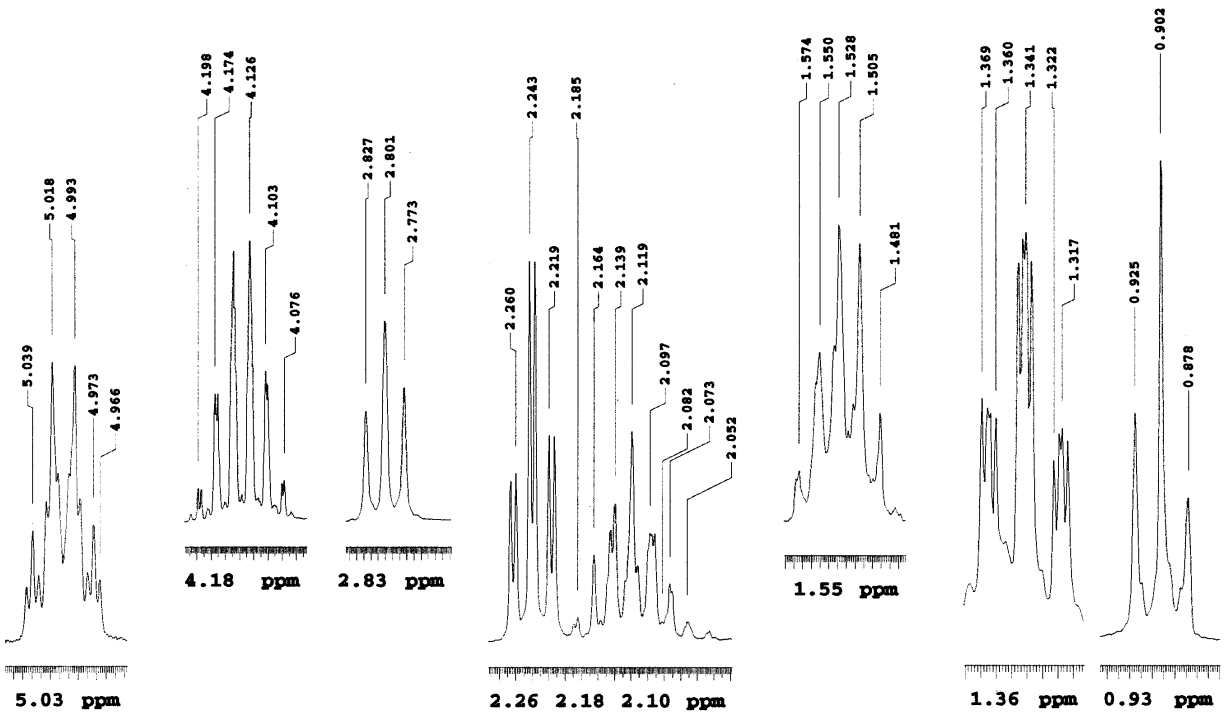
Chiralcel OD-H, hexane/*i*-PrOH = 98:2, 0.3 mL/min, 25 °C

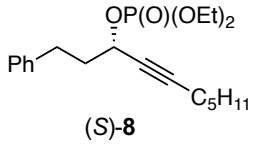






expansion of ^{1}H NMR

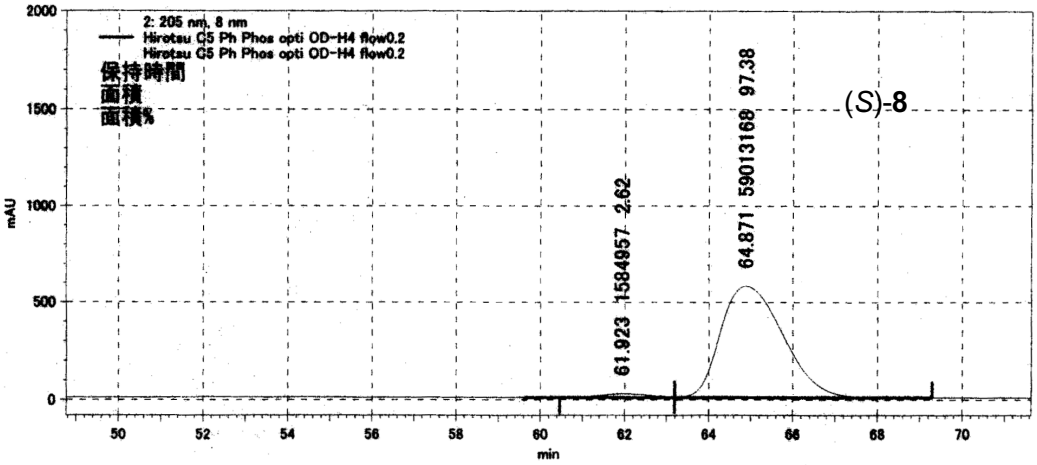


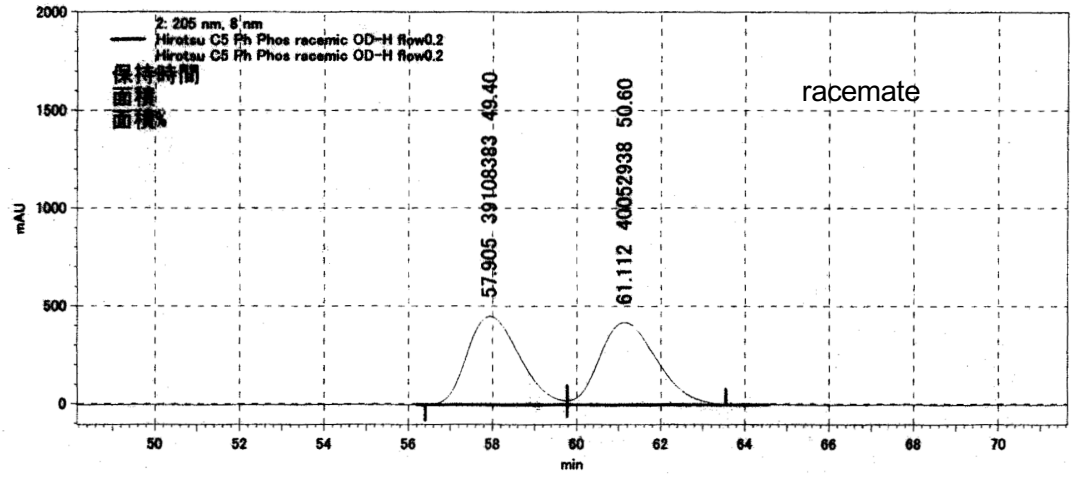


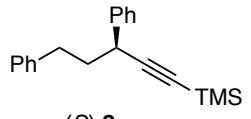
(*S*)-**8**

ee
= (97.38 – 2.62) x 100 / (97.38 + 2.62)
= 94.76
≈ 95%

Chiralcel OD-H, hexane/*i*-PrOH = 98:2, 0.3 mL/min, 25 °C



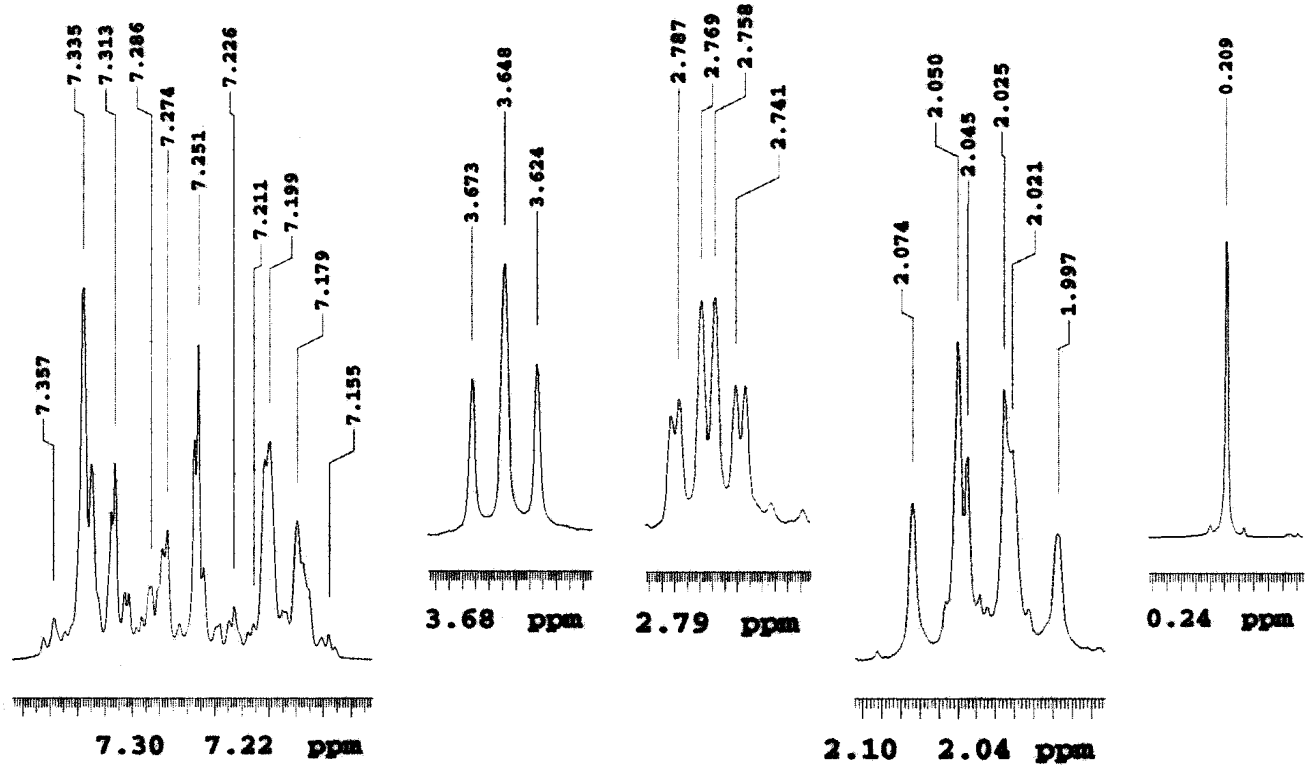


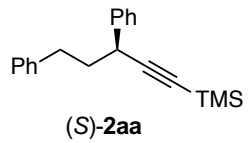


(*S*)-**2aa**

^{1}H NMR (300 MHz, $CDCl_3$)

expansion of ^{1}H NMR

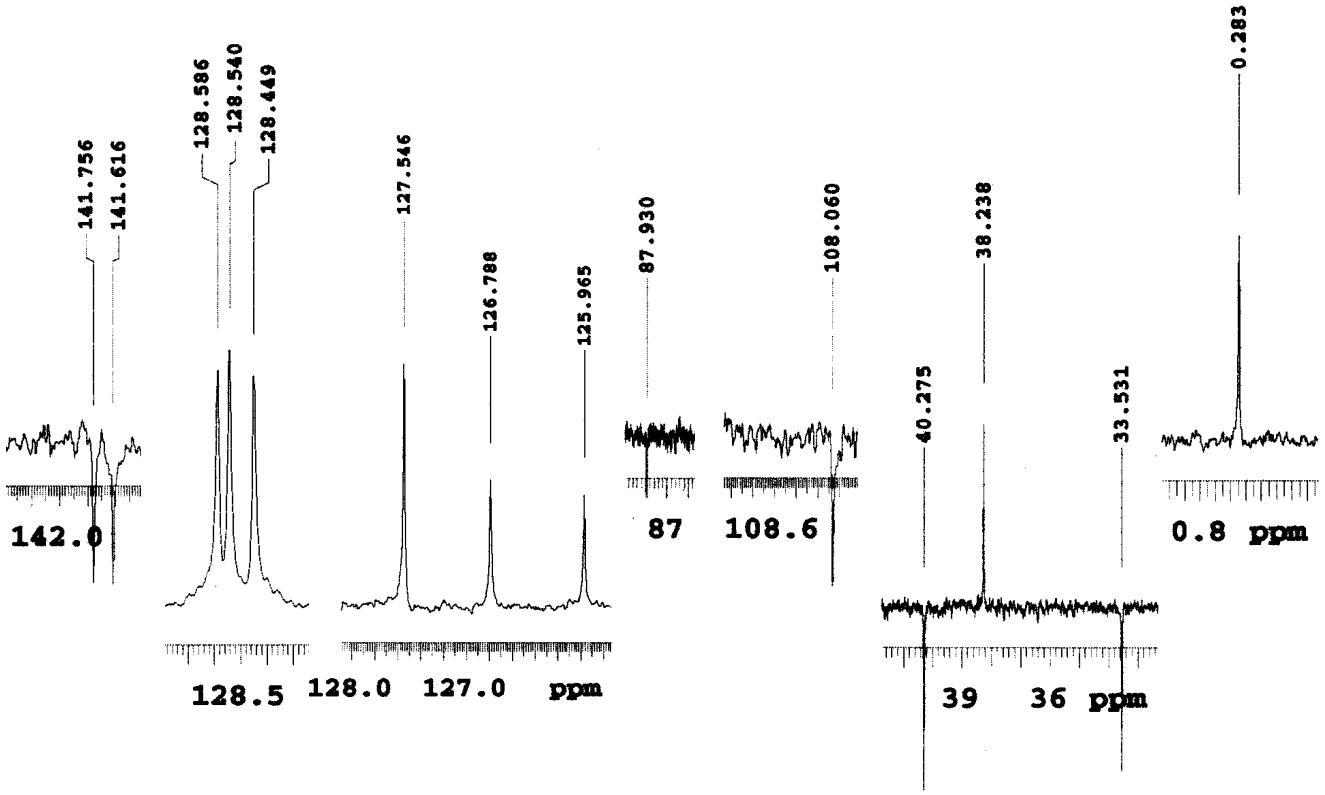


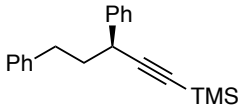


(*S*)-**2aa**

^{13}C NMR (75 MHz, $CDCl_3$)

Expansion of ^{13}C–APT NMR



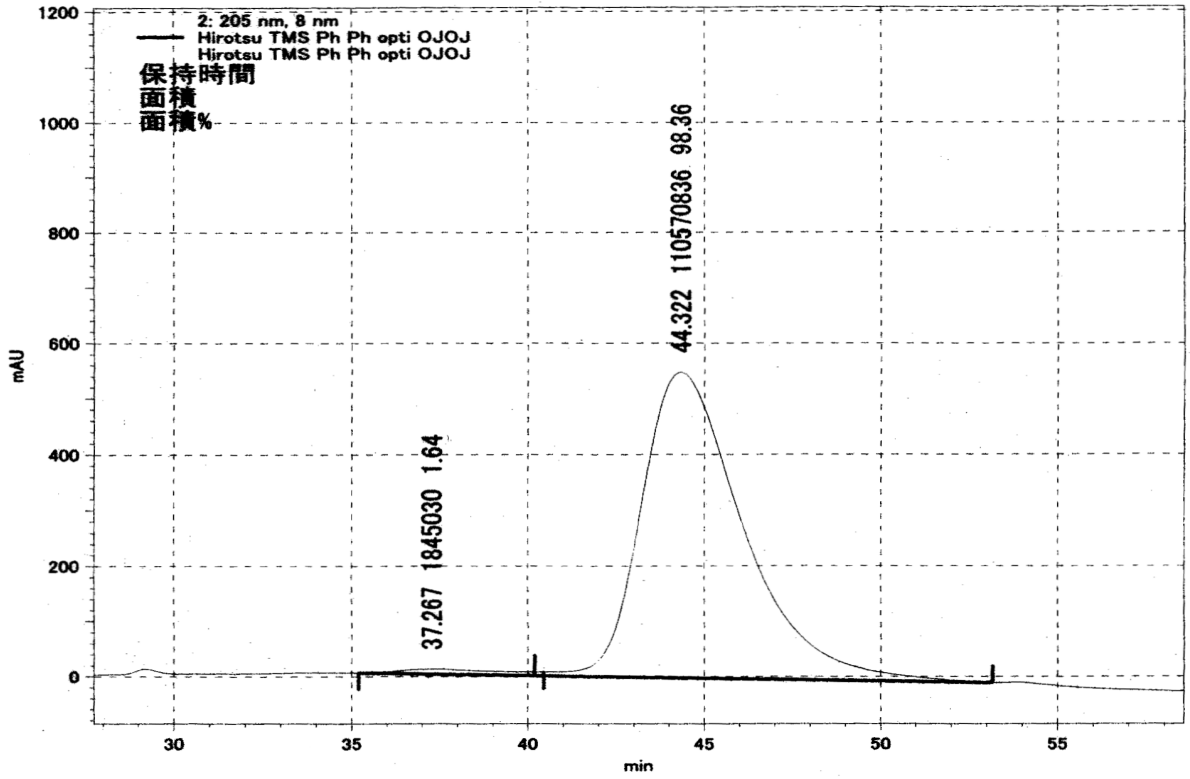


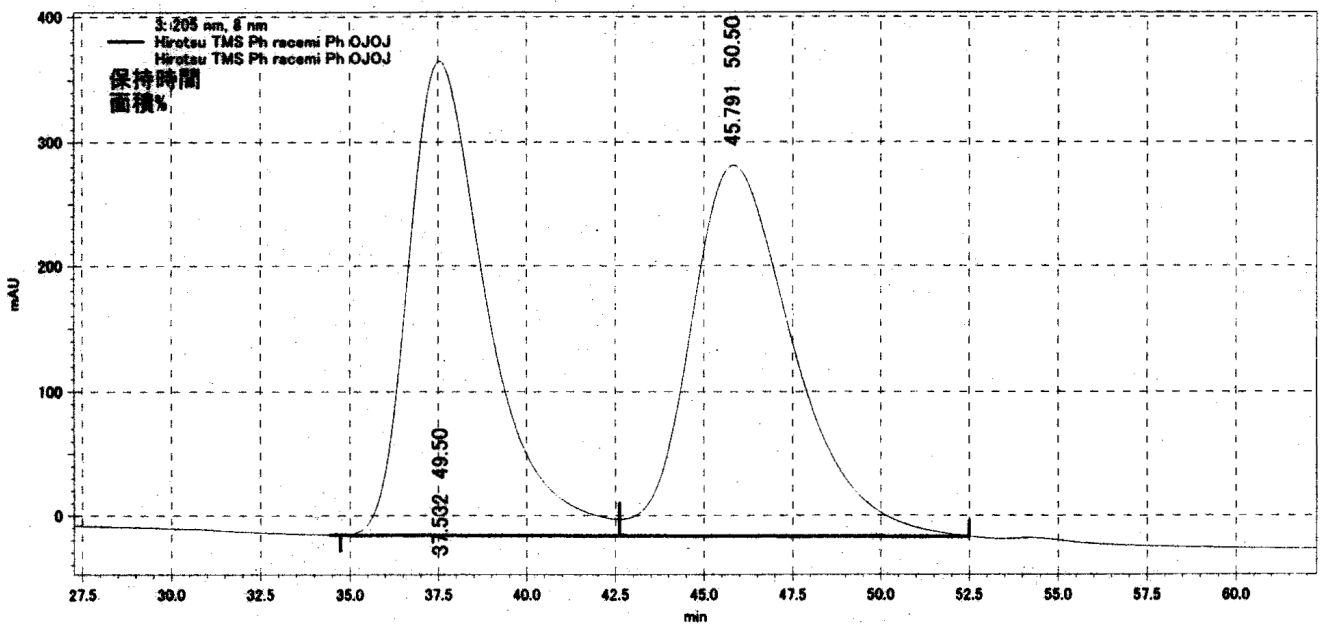
(*S*)-**2aa**

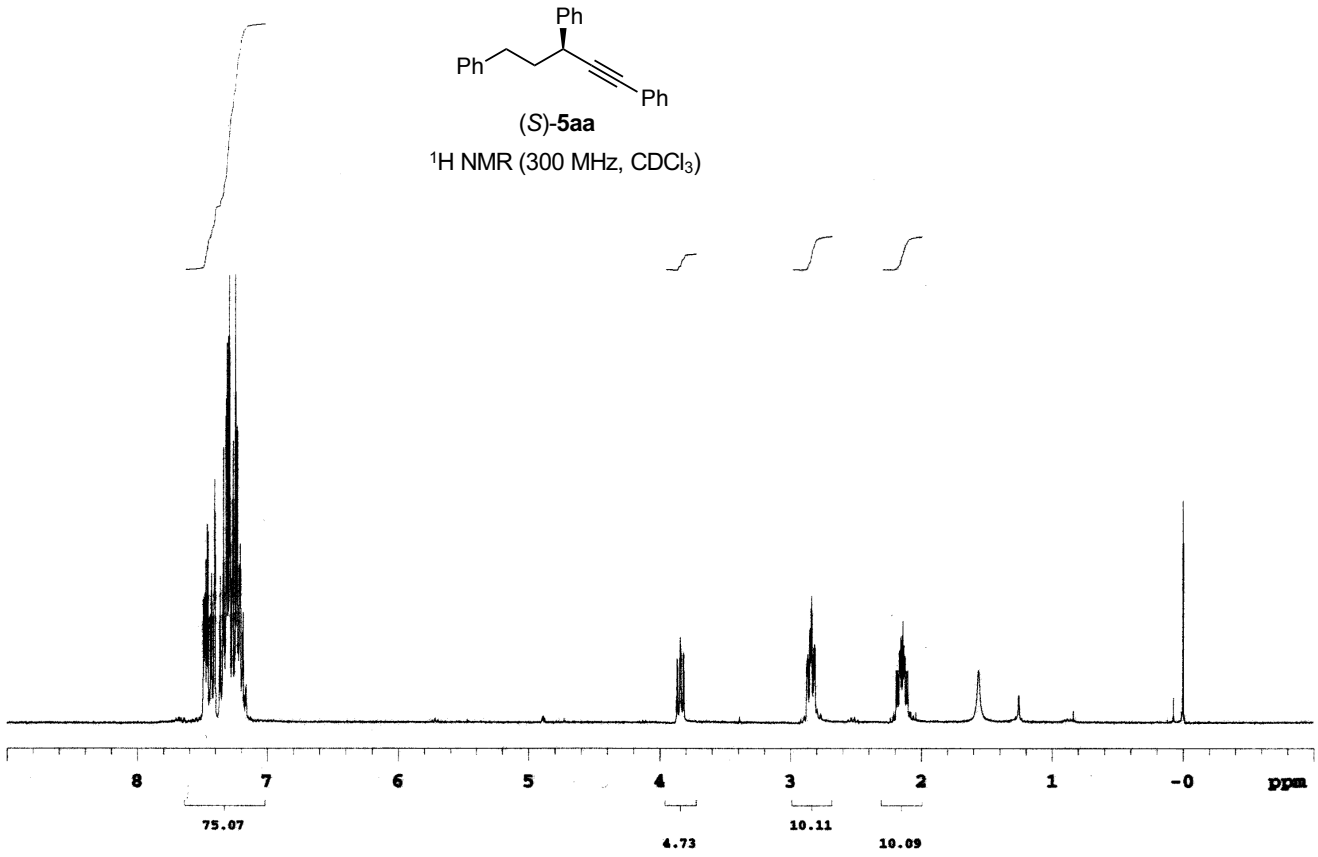
ee
= (98.36 – 1.64) x 100 / (98.36 + 1.64)
= 96.72
≈ 97%

es
= 97 x 100 / 98 = 99%

Chiralcel OJ-H, hexane/*i*-PrOH = 99.9:0.1, 0.2 mL/min, 25 °C



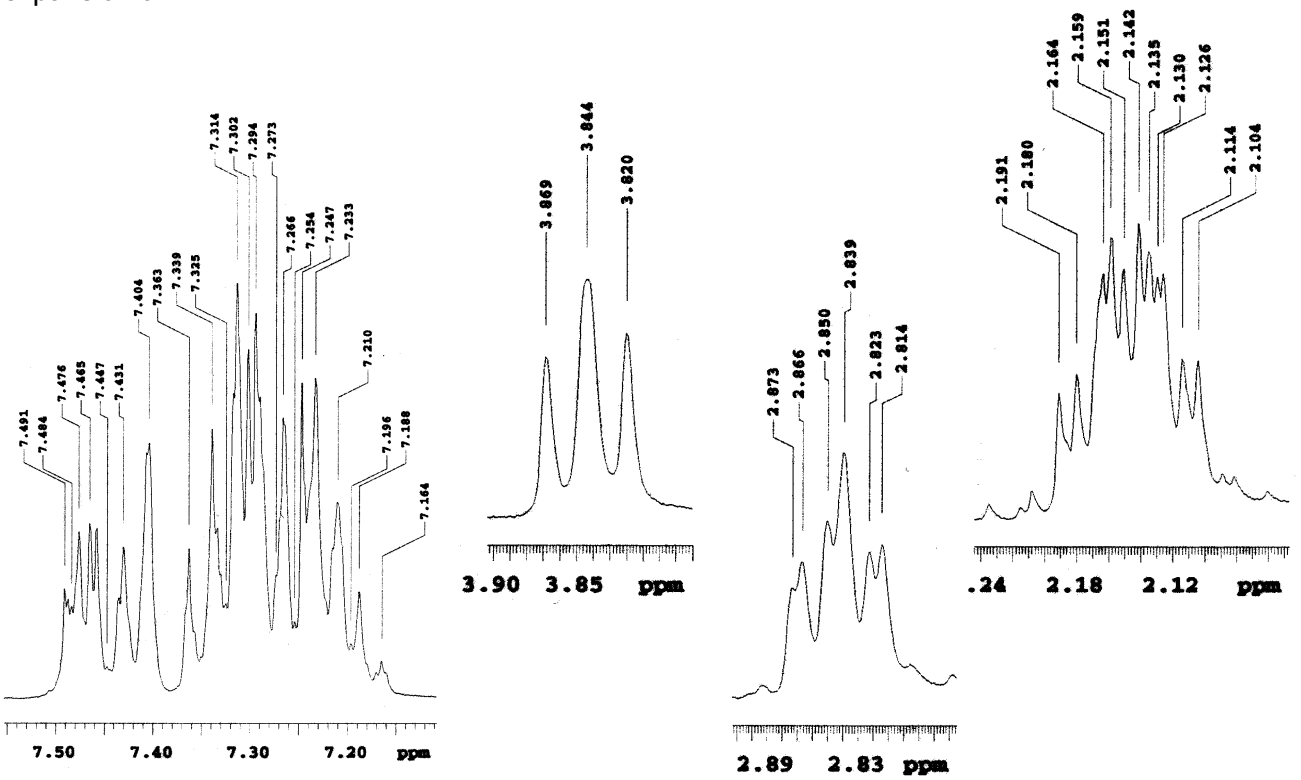


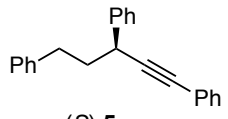


(*S*)-**5aa**

^{1}H NMR (300 MHz, $CDCl_3$)

expansion of ^{1}H NMR

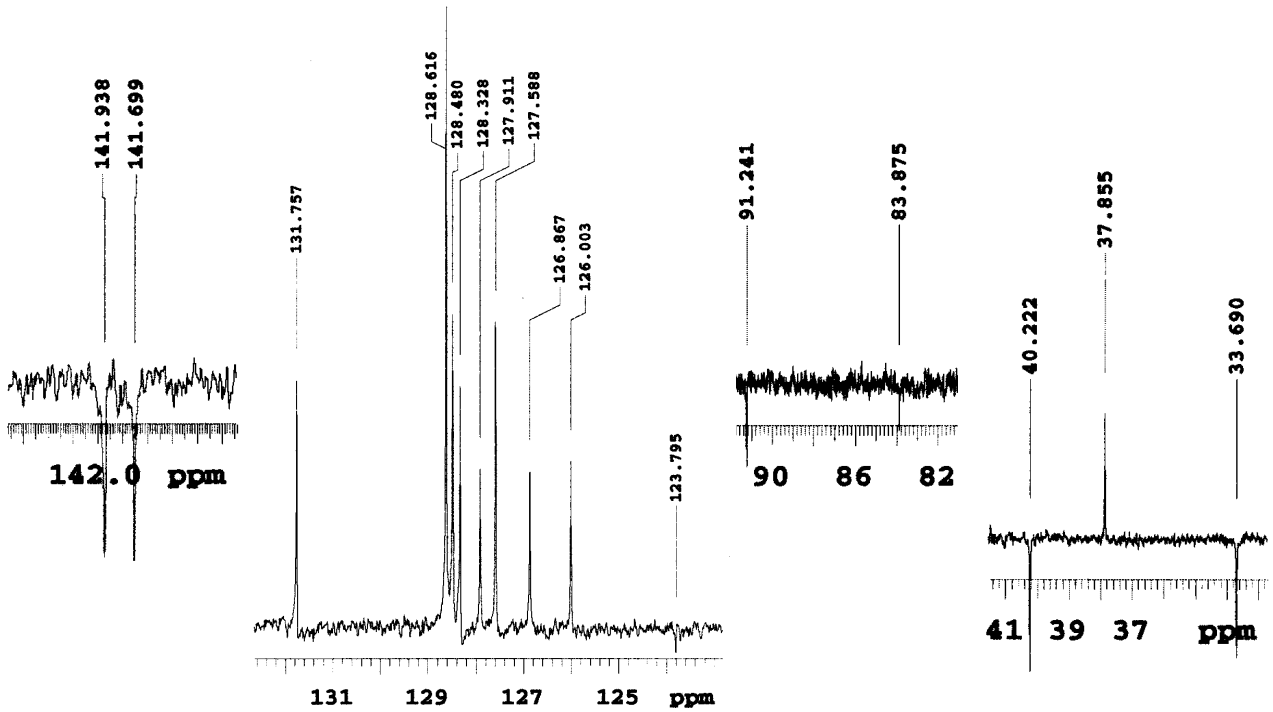




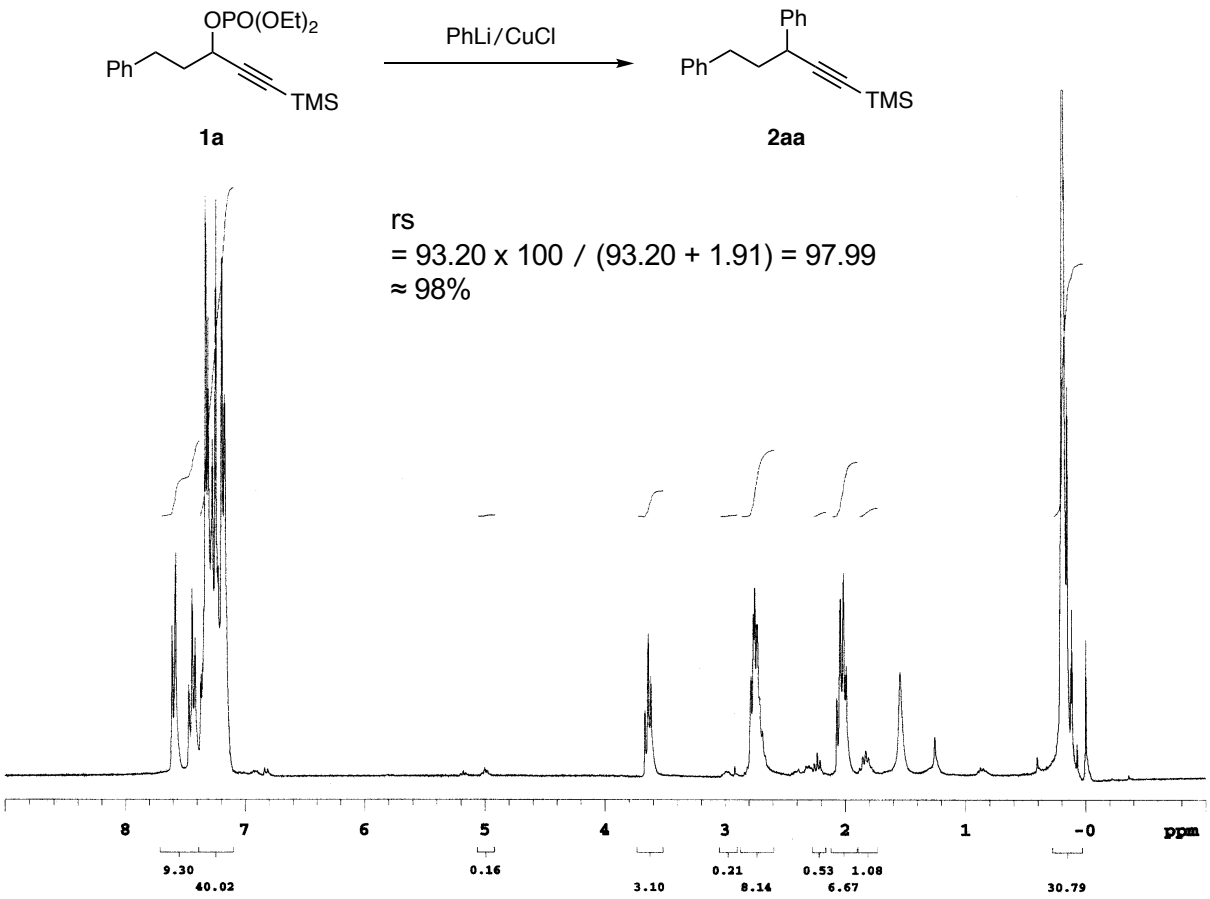
(*S*)-**5aa**

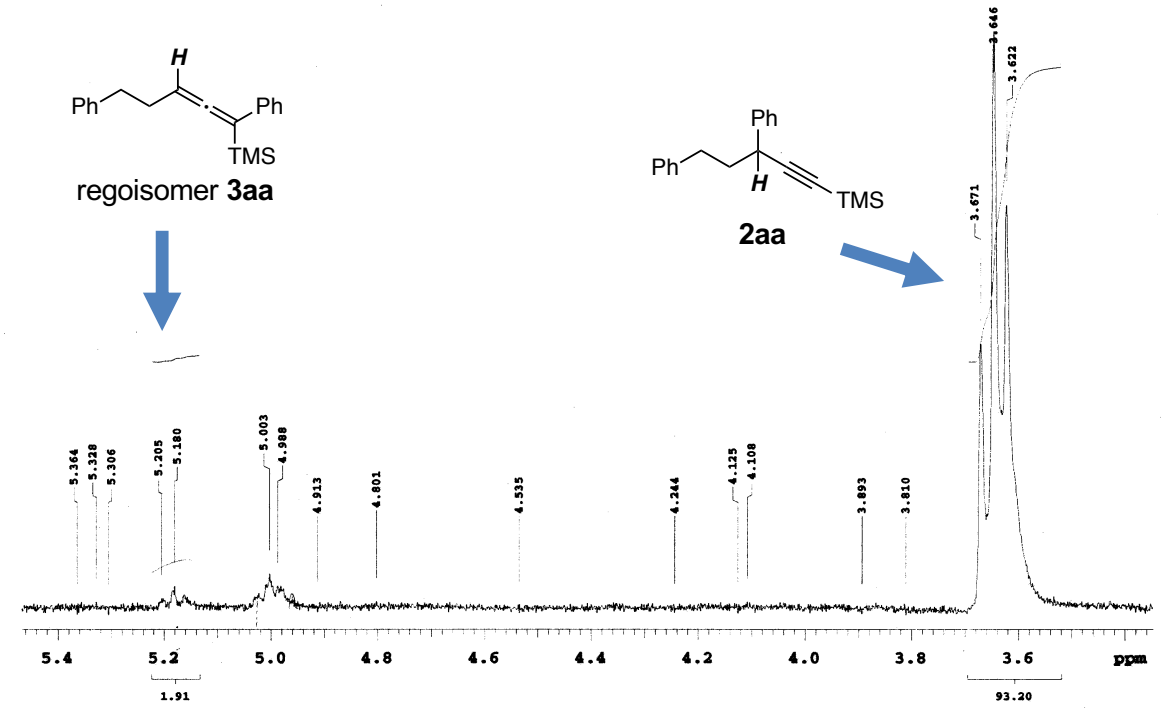
^{13}C NMR (75 MHz, $CDCl_3$)

Expansion of ^{13}C–APT NMR

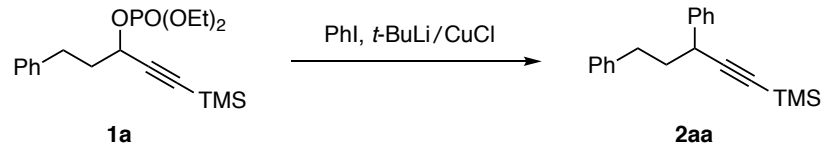


^{1}H NMR (300 MHz, $CDCl_3$) of crude **2aa**
Table 1, Entry 7 (Method A)

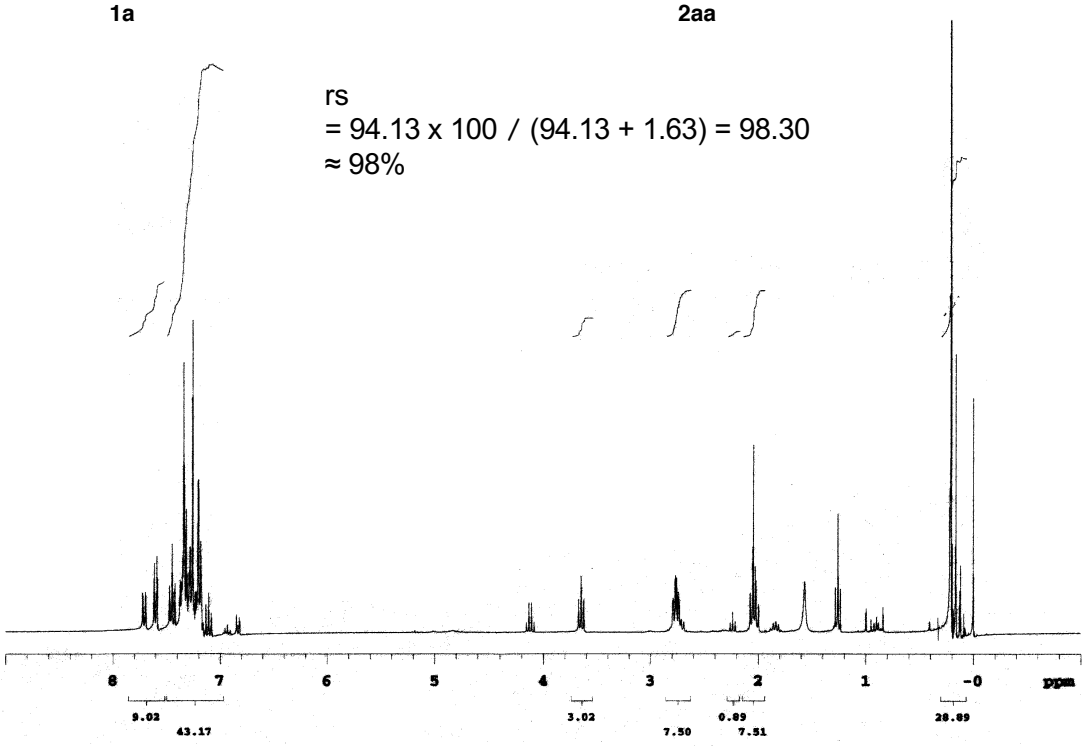


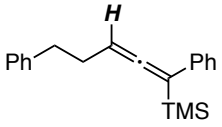


^{1}H NMR (300 MHz, $CDCl_3$) of crude **2aa**
Table 1, Entry 8 (Method B)

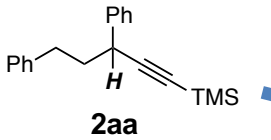


1a **2aa**



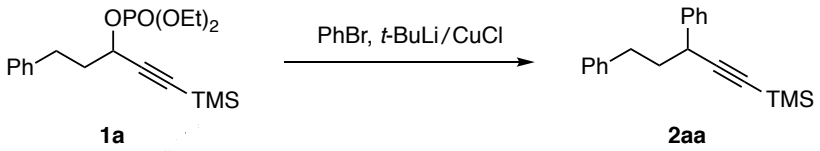


regoisomer **3aa**

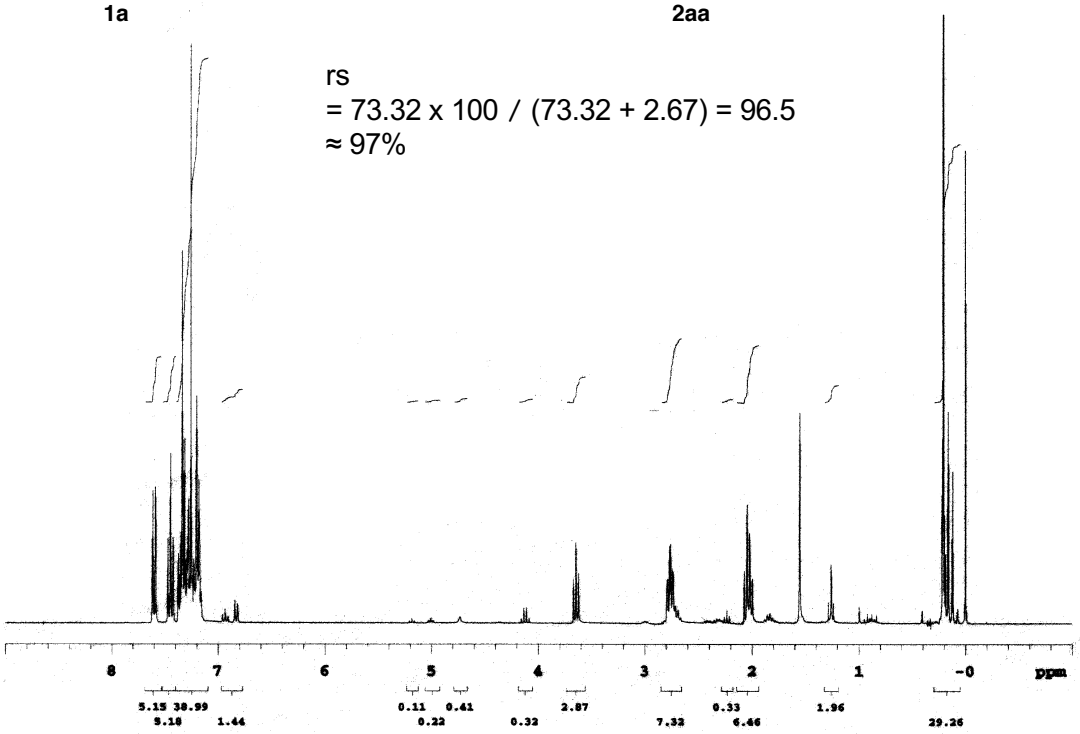


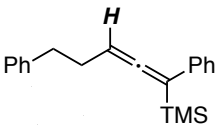
2aa

^{1}H NMR (300 MHz, $CDCl_3$) of crude **2aa**
Table 1, Entry 9 (Method C)

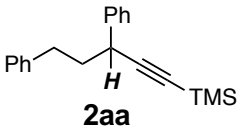


1a **2aa**

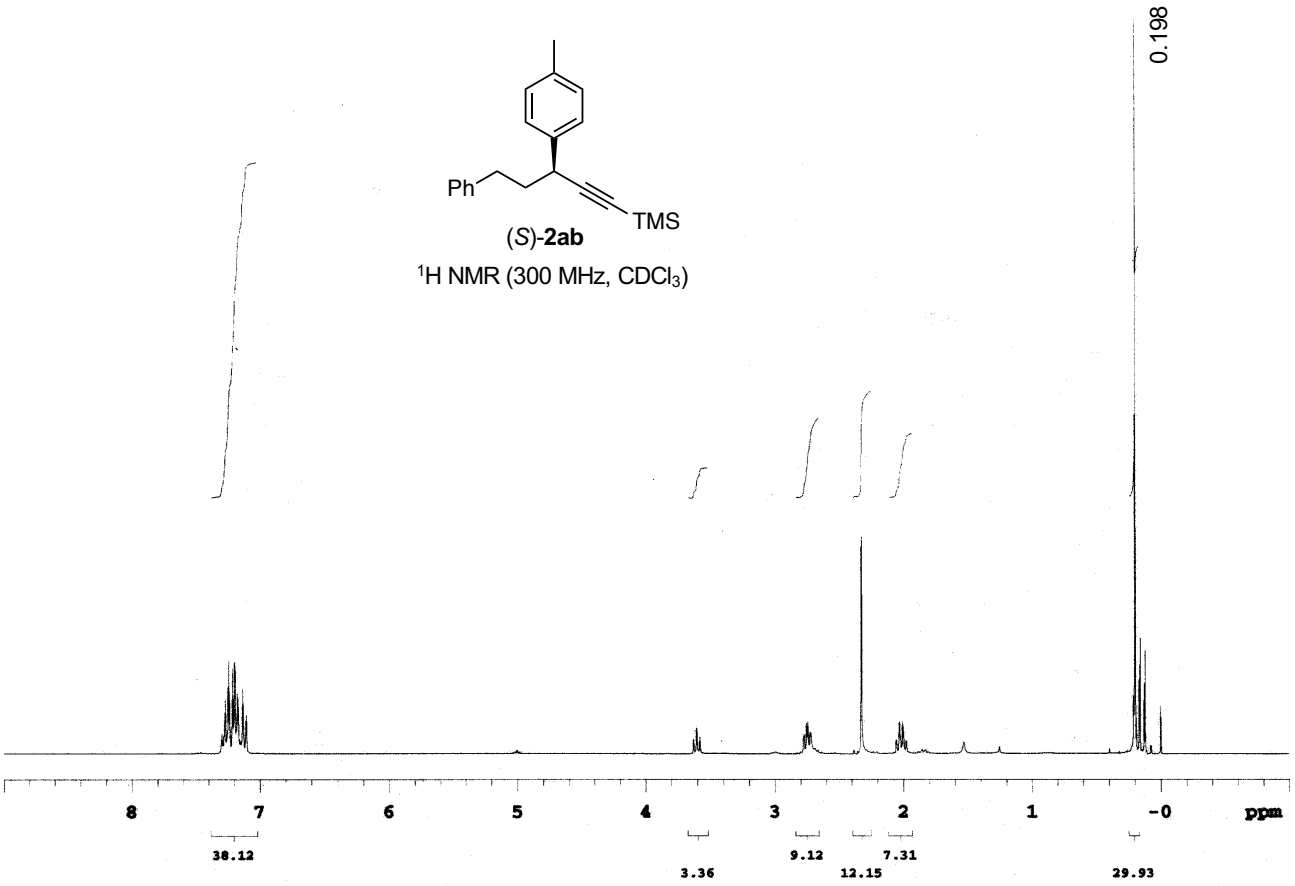




regoisomer **3aa**



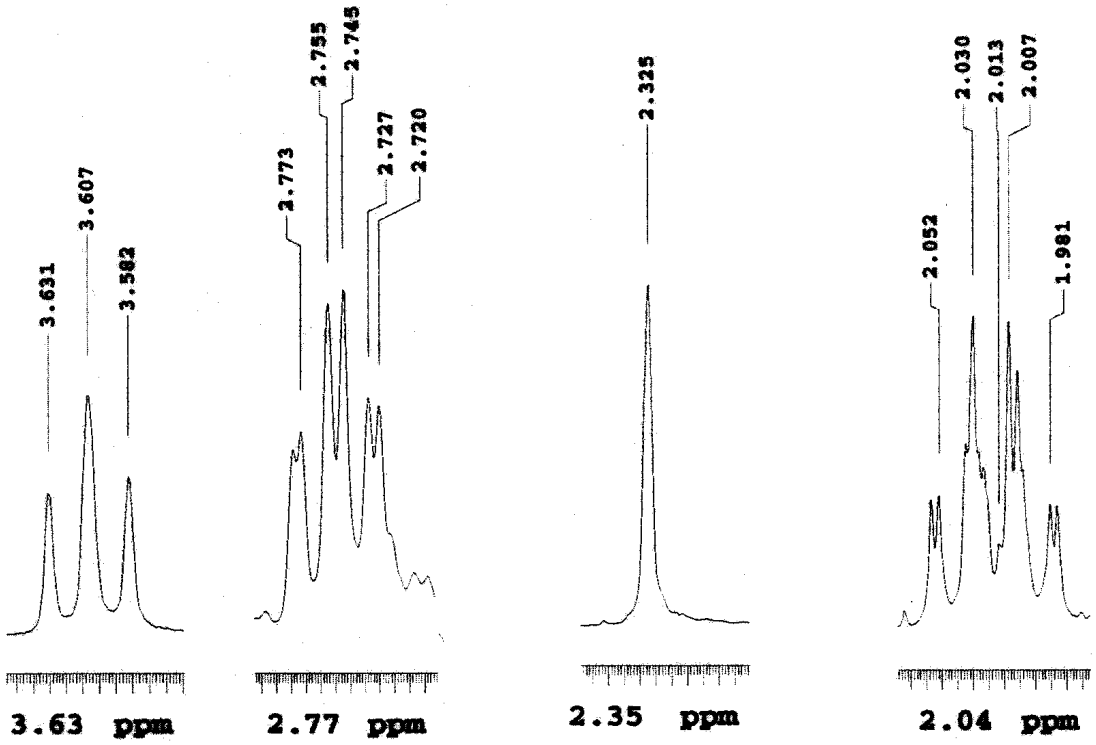
2aa

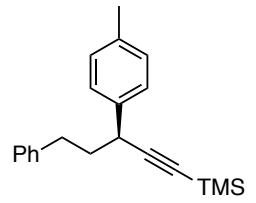


(*S*)-**2ab**

^{1}H NMR (300 MHz, $CDCl_3$)

expansion of ^{1}H NMR

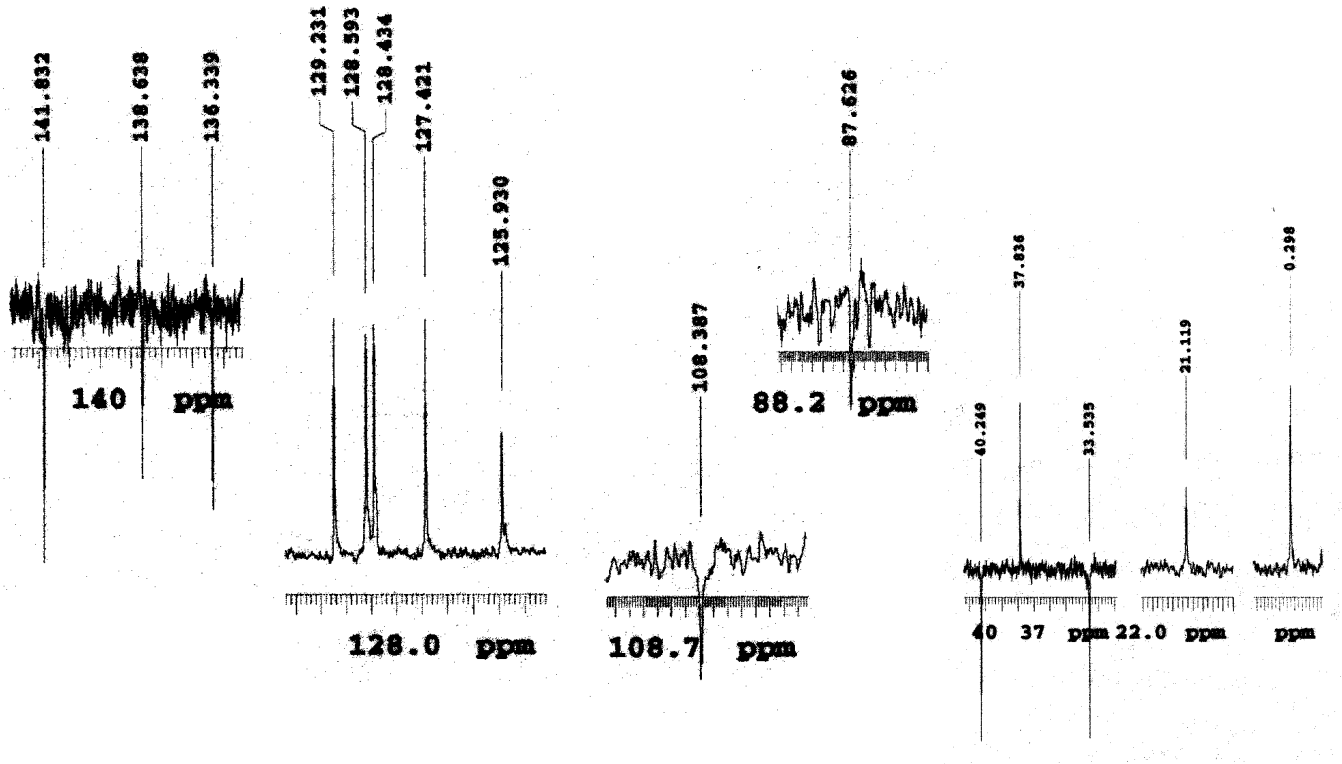


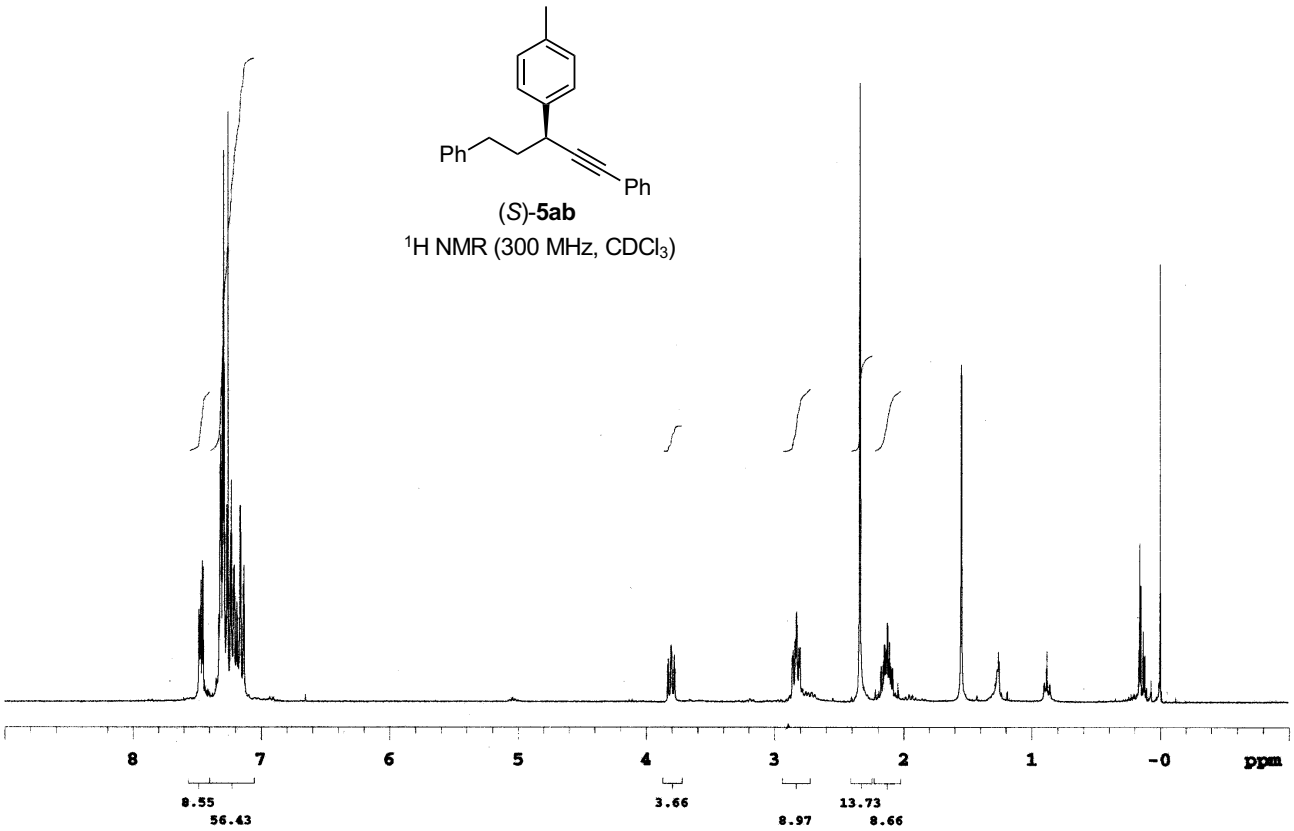


(*S*)-**2ab**

^{13}C NMR (75 MHz, $CDCl_3$)

Expansion of ^{13}C–APT NMR

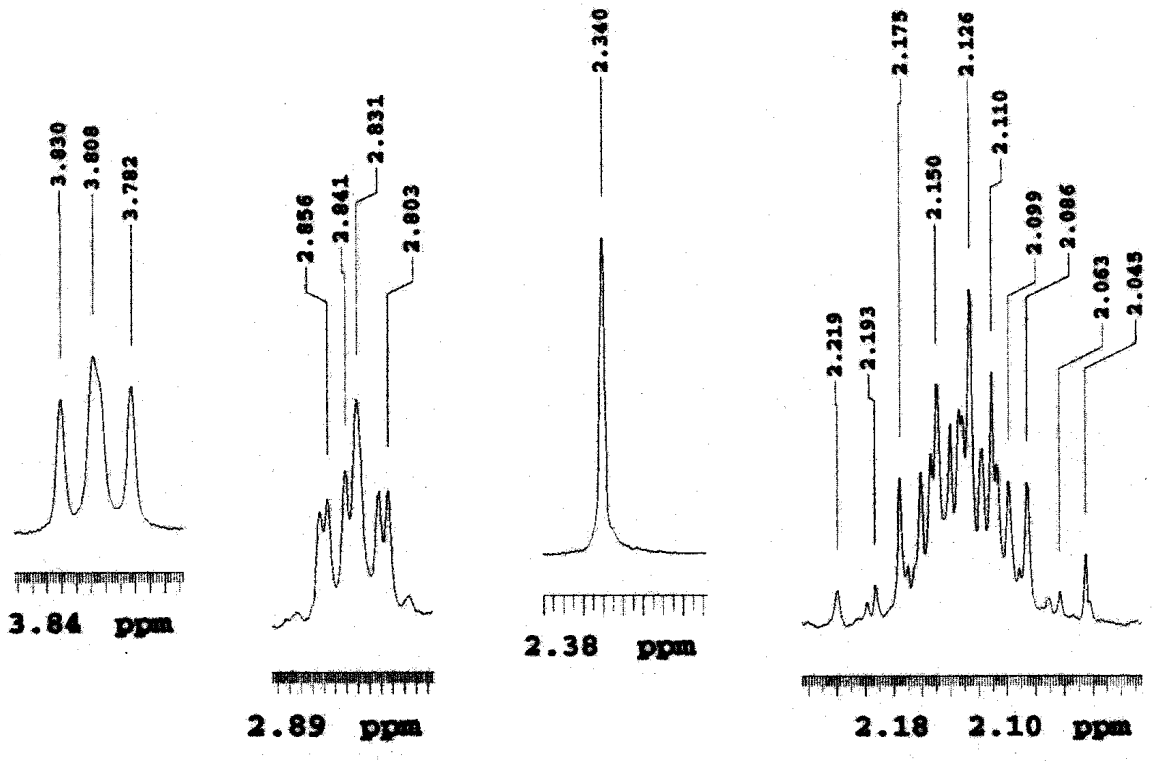


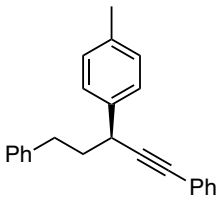


(*S*)-**5ab**

^{1}H NMR (300 MHz, $CDCl_3$)

expansion of ^{1}H NMR



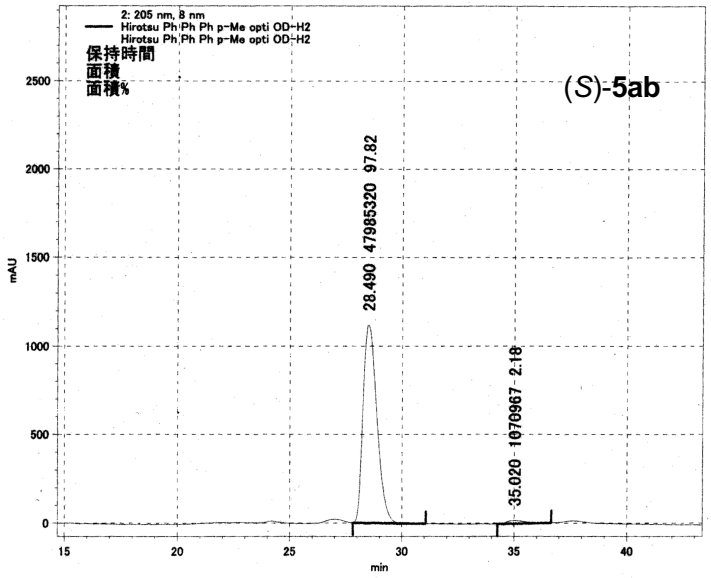


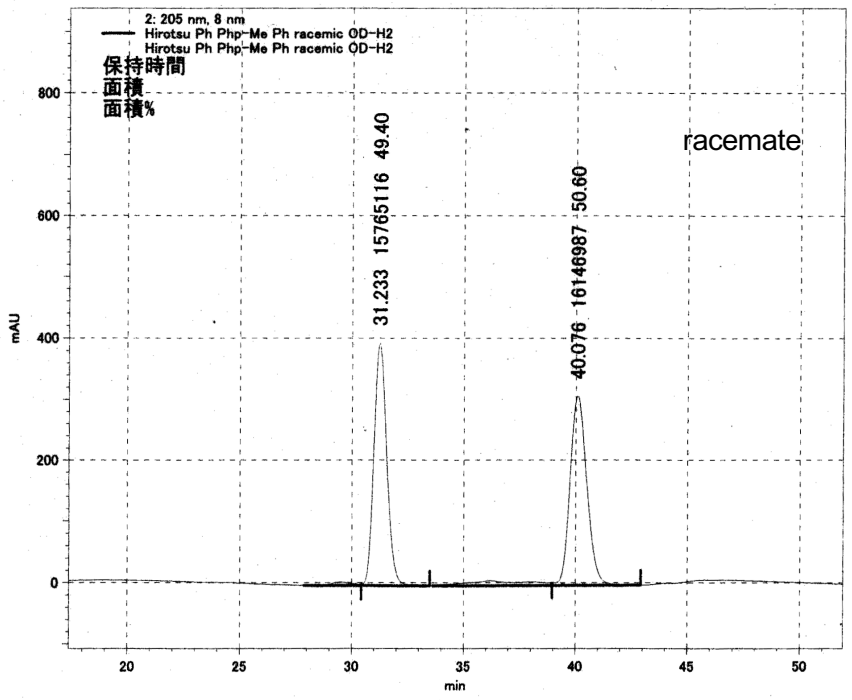
(*S*)-**5ab**

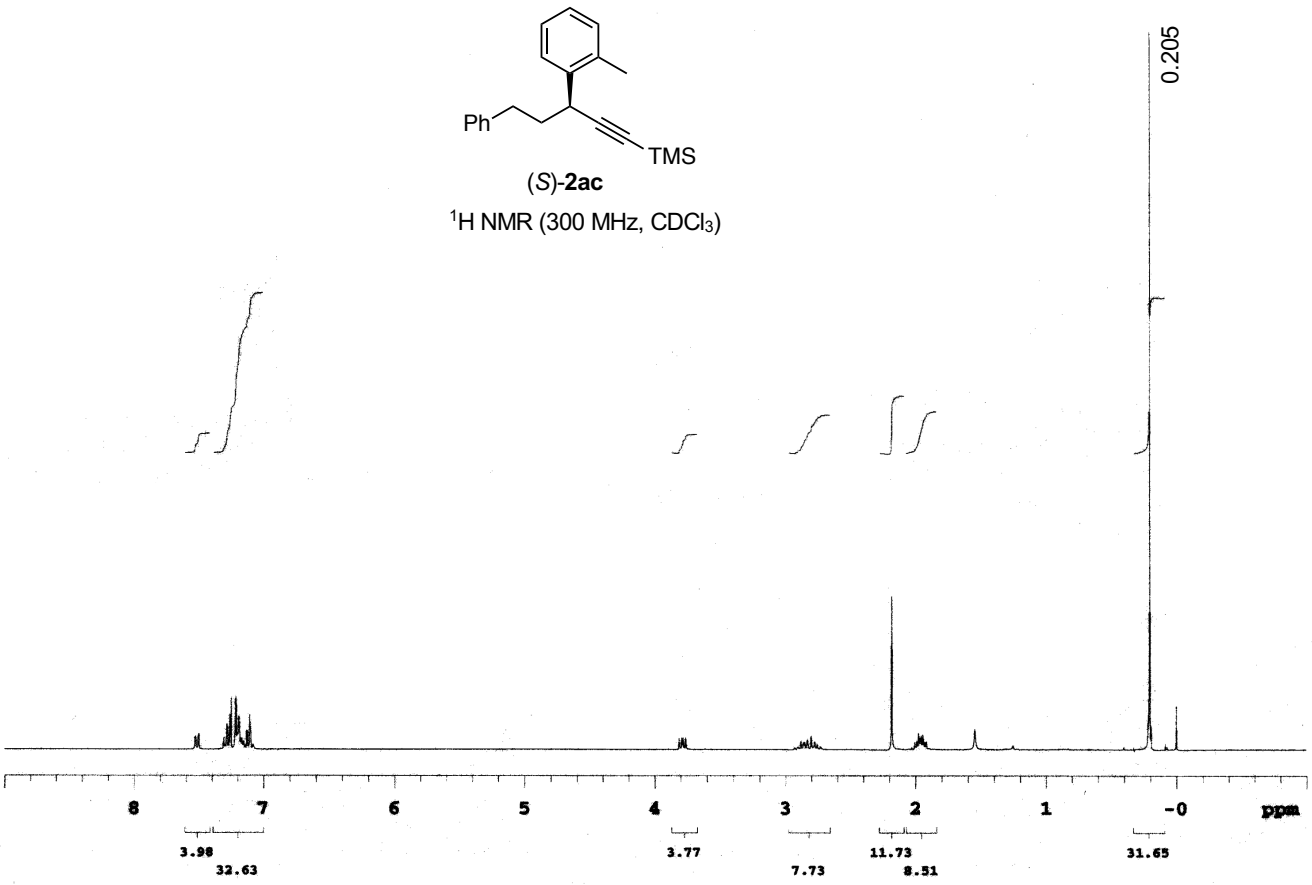
ee
= (97.82 – 2.18) x 100 / (97.82 + 2.18) = 96.0%

es
= 96 x 100 / 98 = 98%

Chiralcel OD-H, hexane/*i*-PrOH = 99.8:0.2, 0.3 mL/min, 25 °C



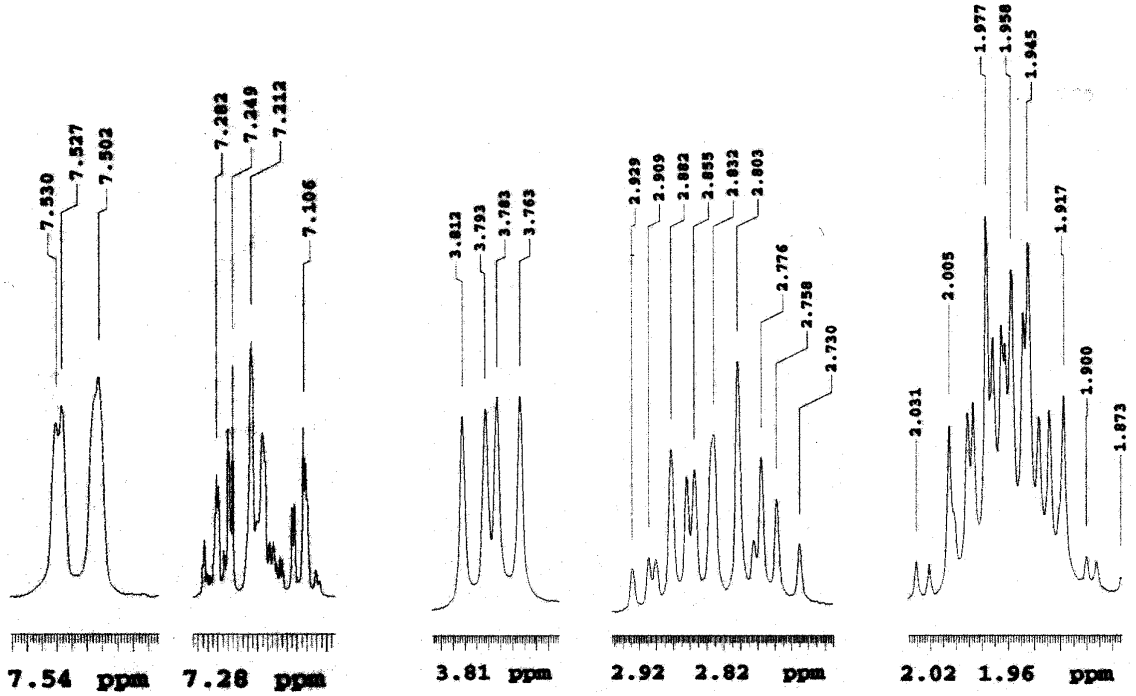


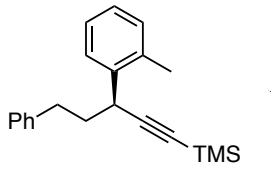


(*S*)-**2ac**

^{1}H NMR (300 MHz, $CDCl_3$)

expansion of ^{1}H NMR

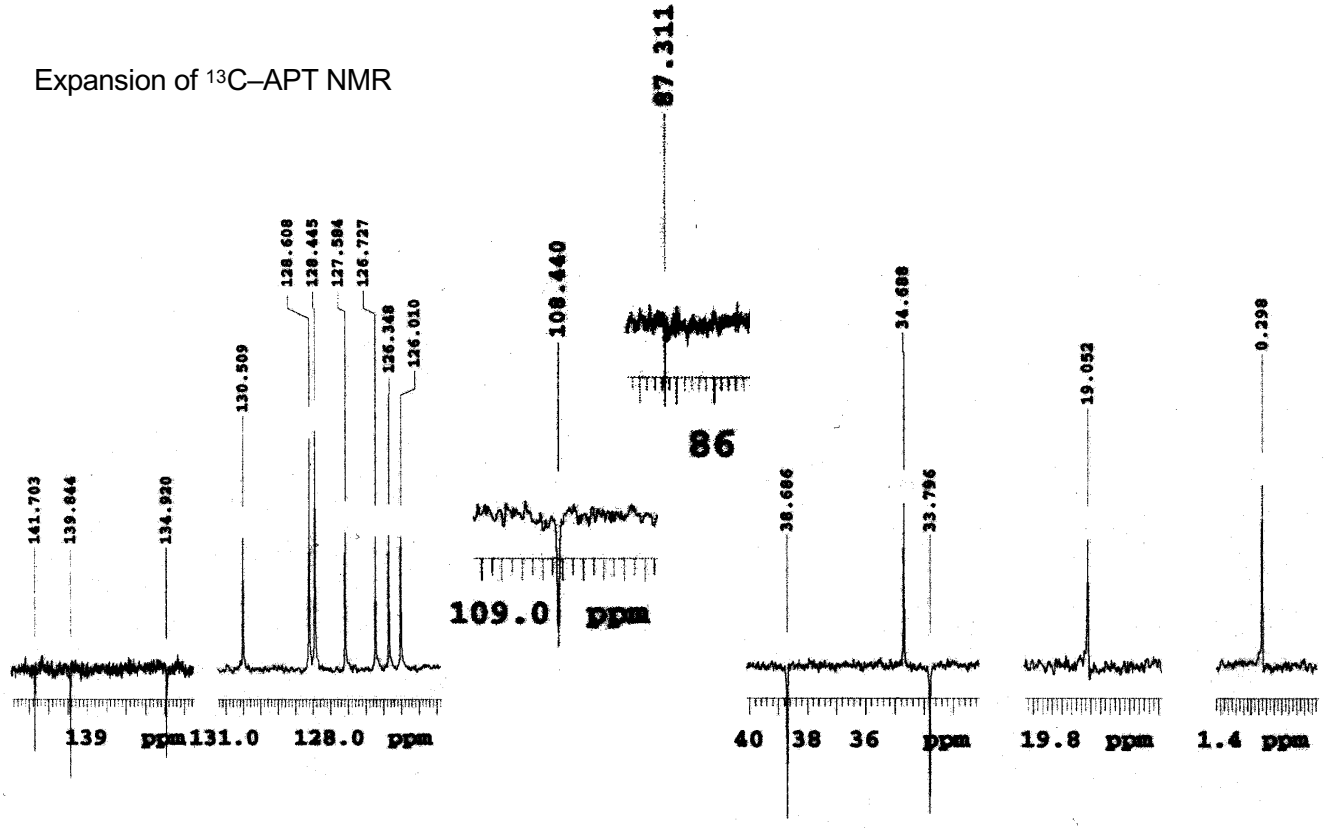


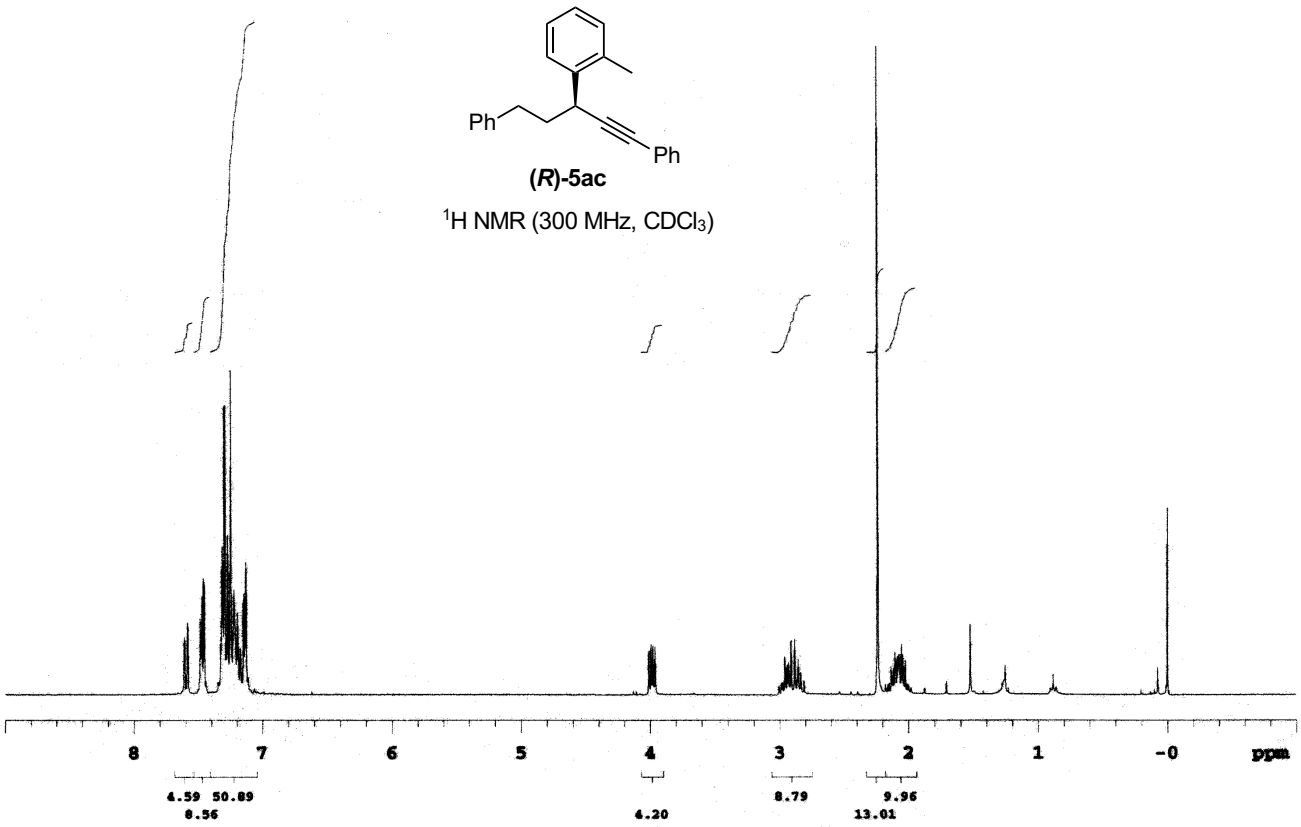


(*S*)-**2ac**

^{13}C NMR (75 MHz, $CDCl_3$)

Expansion of ^{13}C–APT NMR

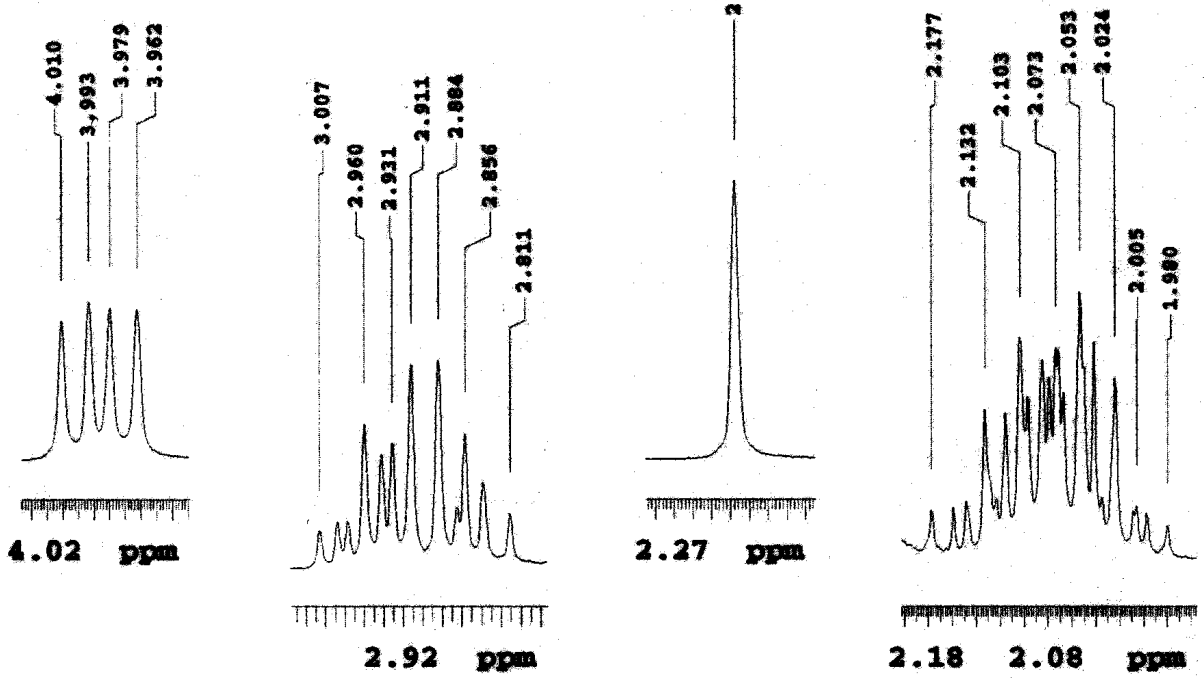


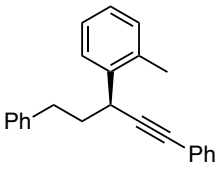


(*R*)-5ac

^{1}H NMR (300 MHz, $CDCl_3$)

expansion of ^{1}H NMR



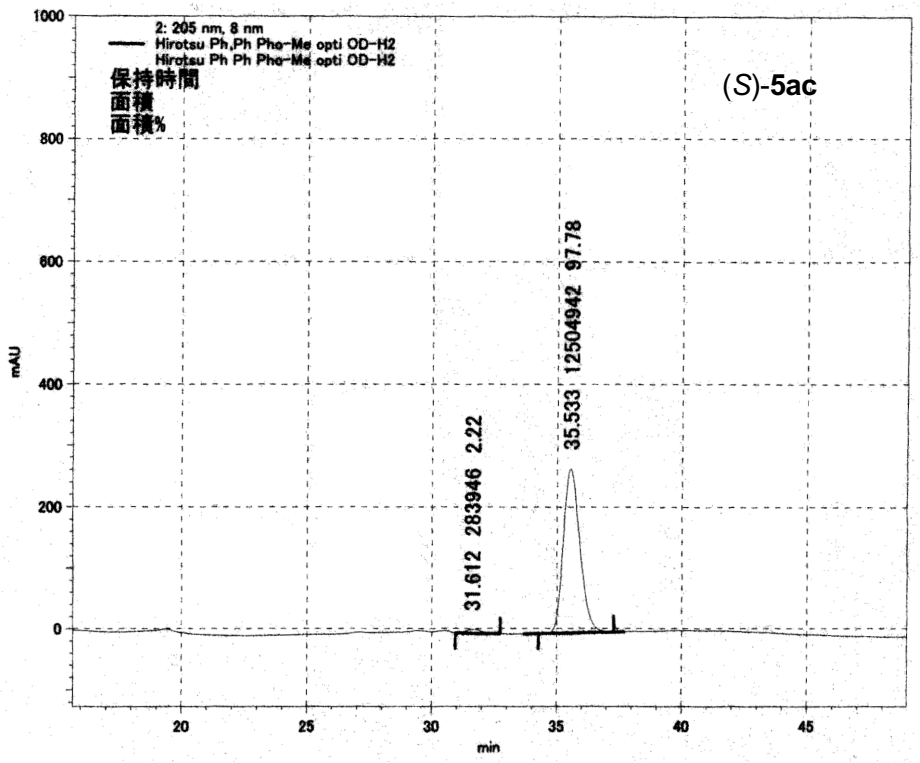


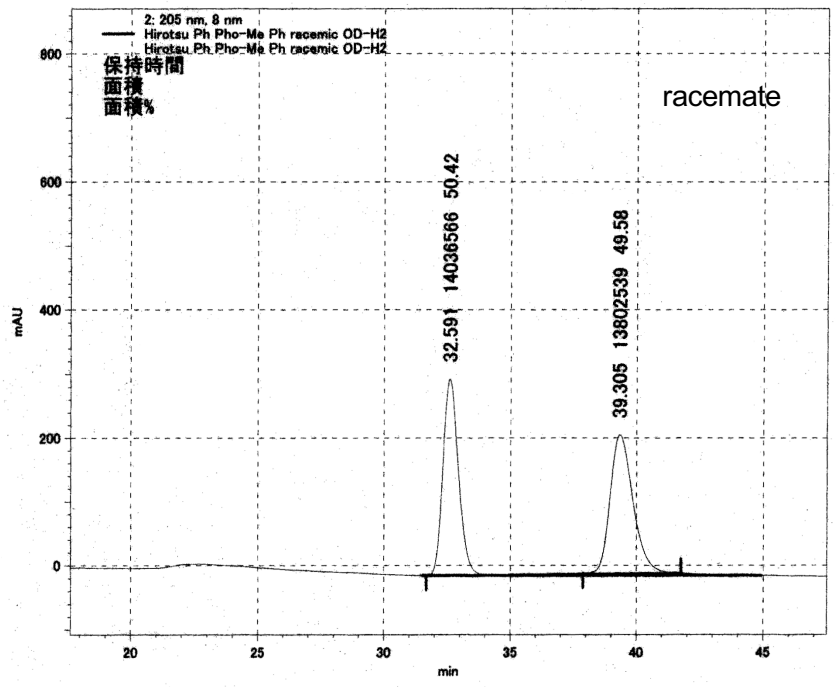
(*R*)-**5ac**

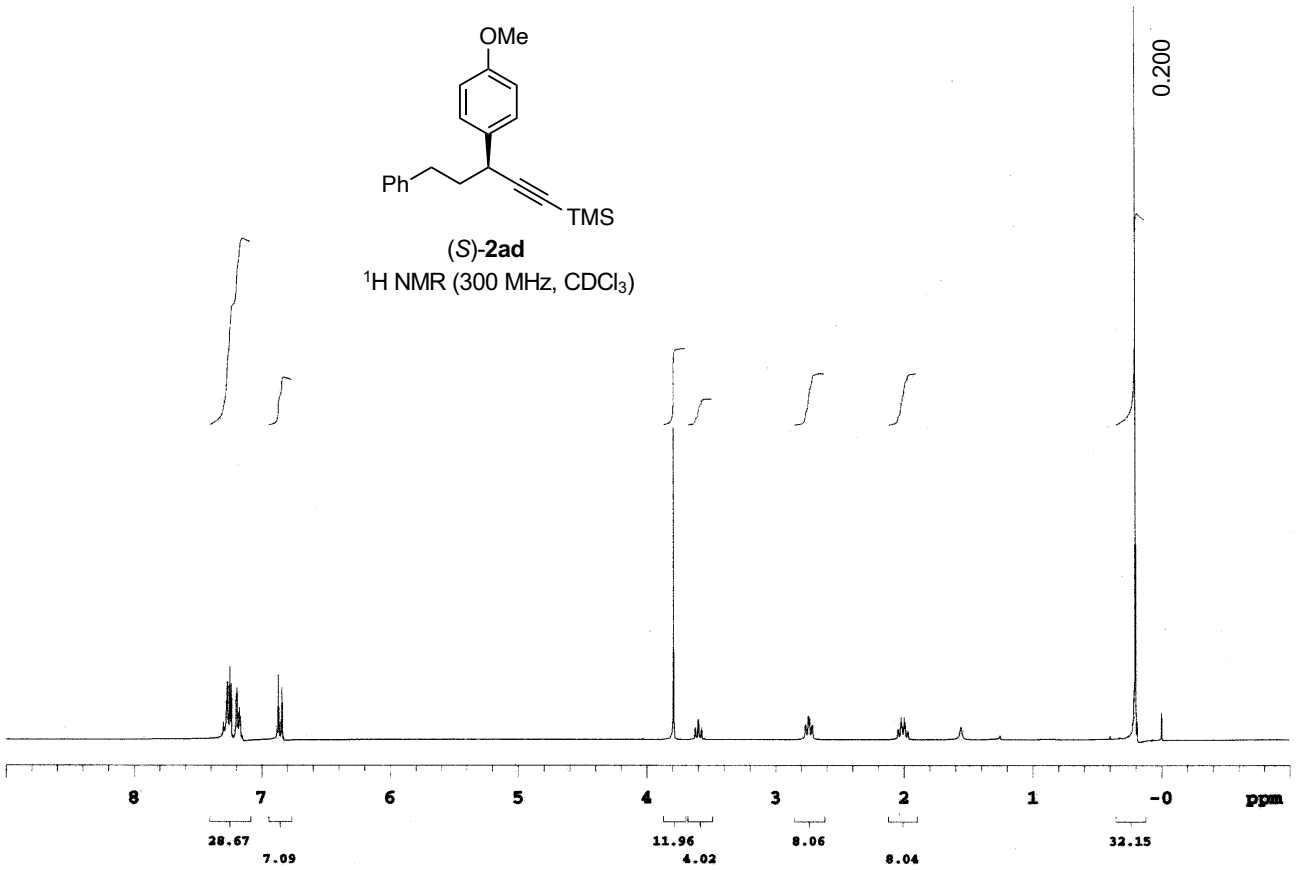
ee
= (97.78 – 2.22) x 100 / (97.78 + 2.22) = 96.0%

es
= 96 x 100 / 98 = 98%

Chiralcel OD-H, hexane/*i*-PrOH = 99.8:0.2, 0.3 mL/min, 25 °C



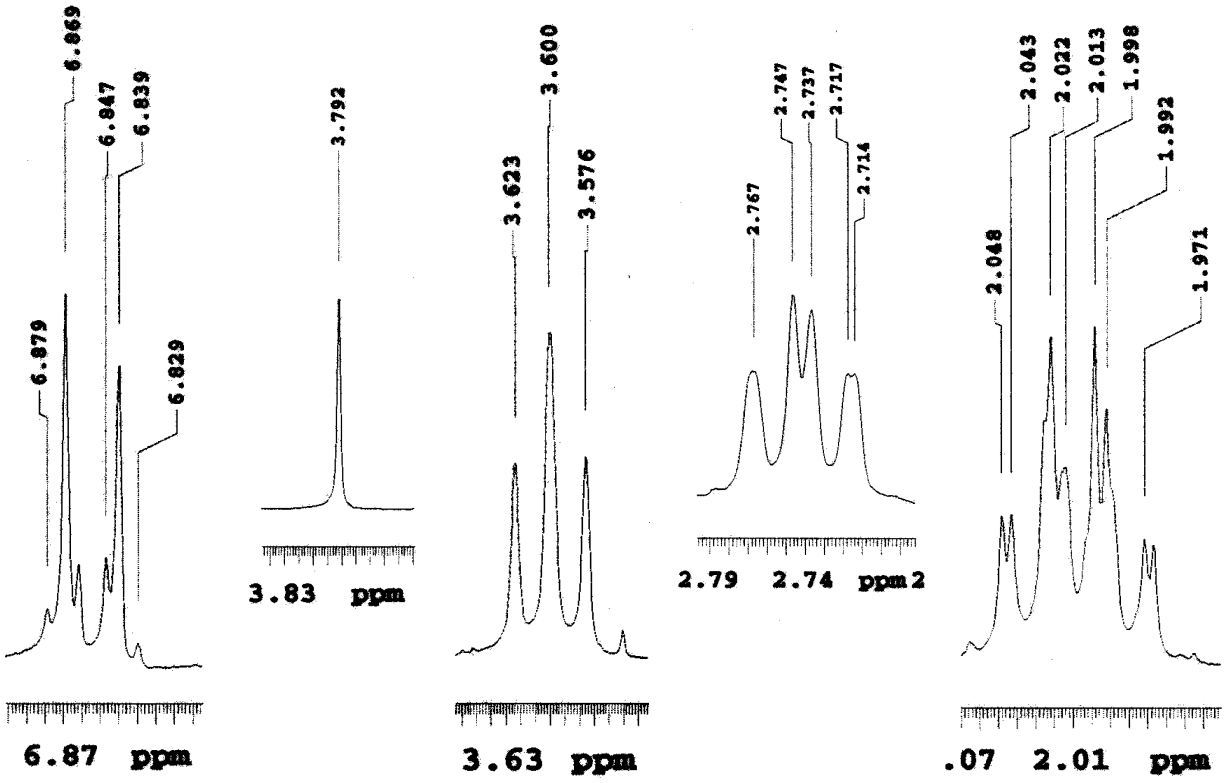


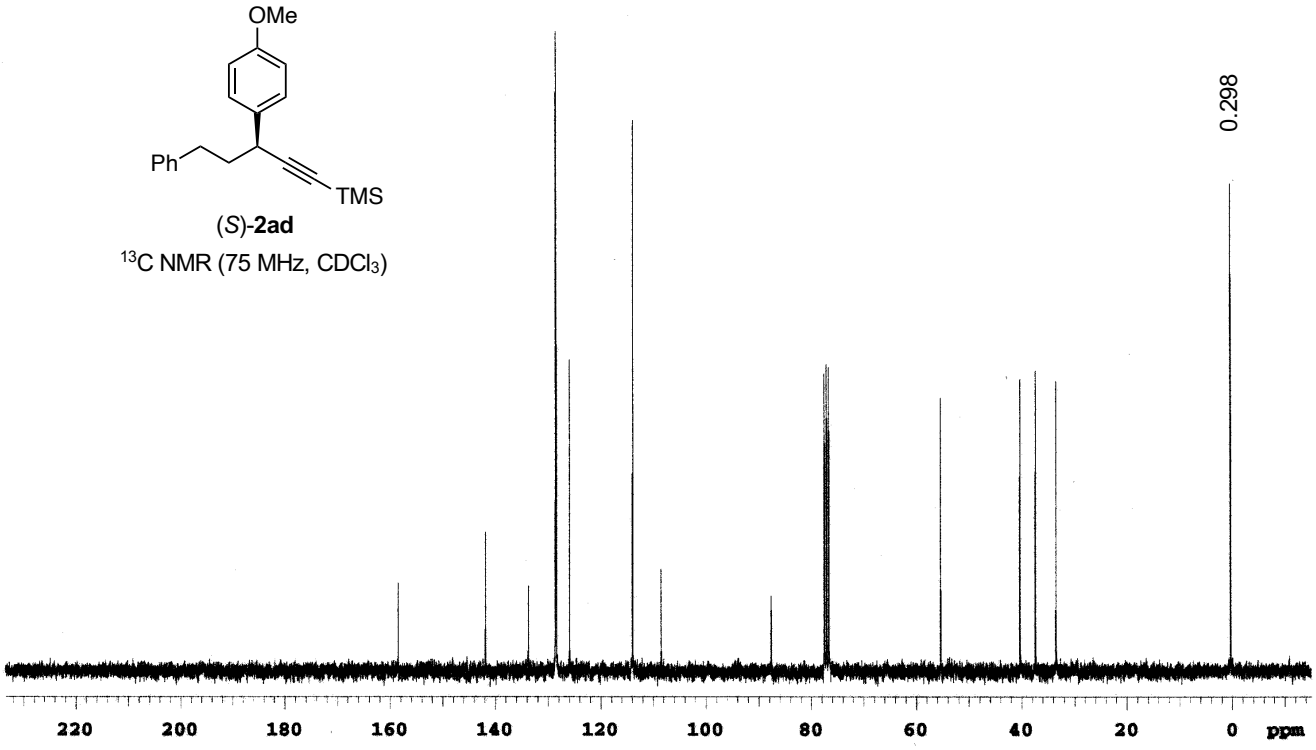


(*S*)-**2ad**

^{1}H NMR (300 MHz, $CDCl_3$)

expansion of ^{1}H NMR

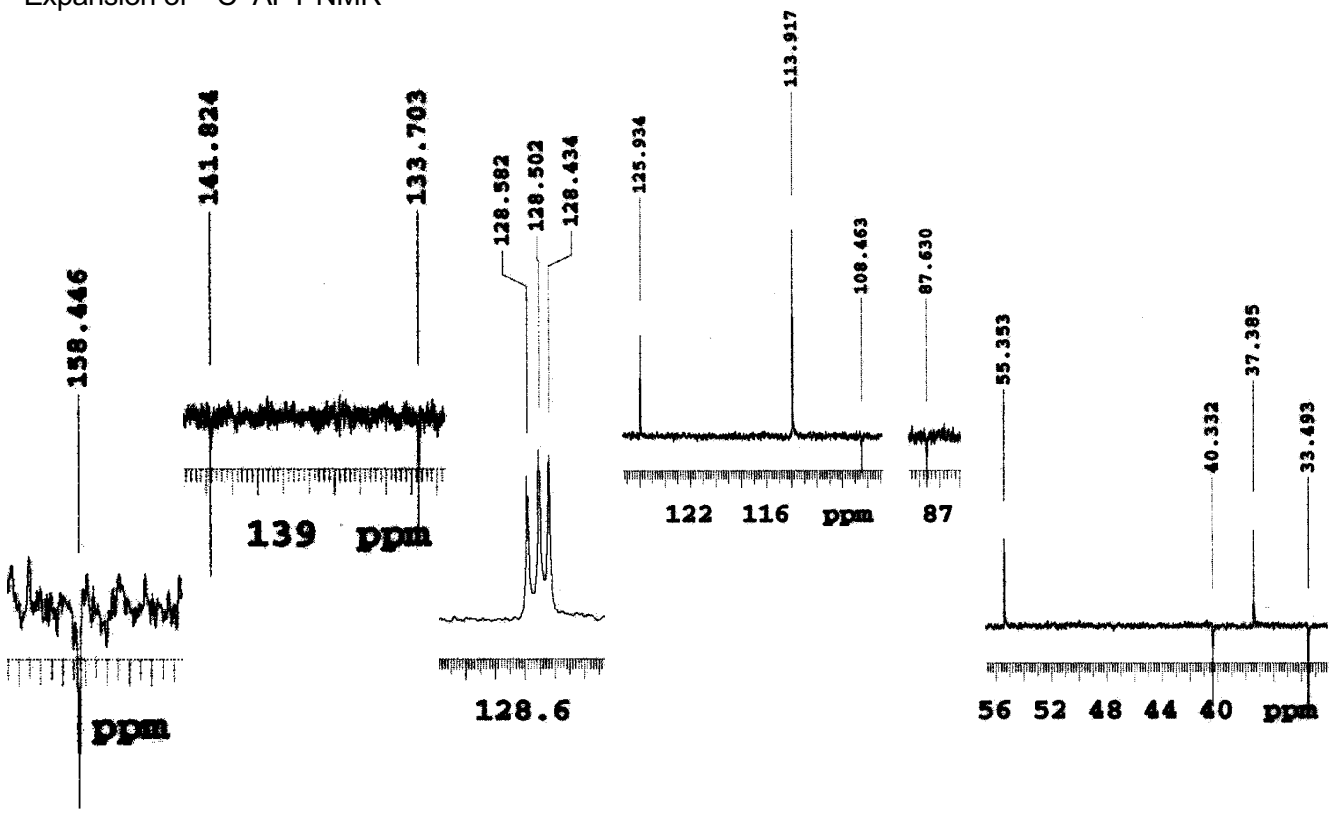


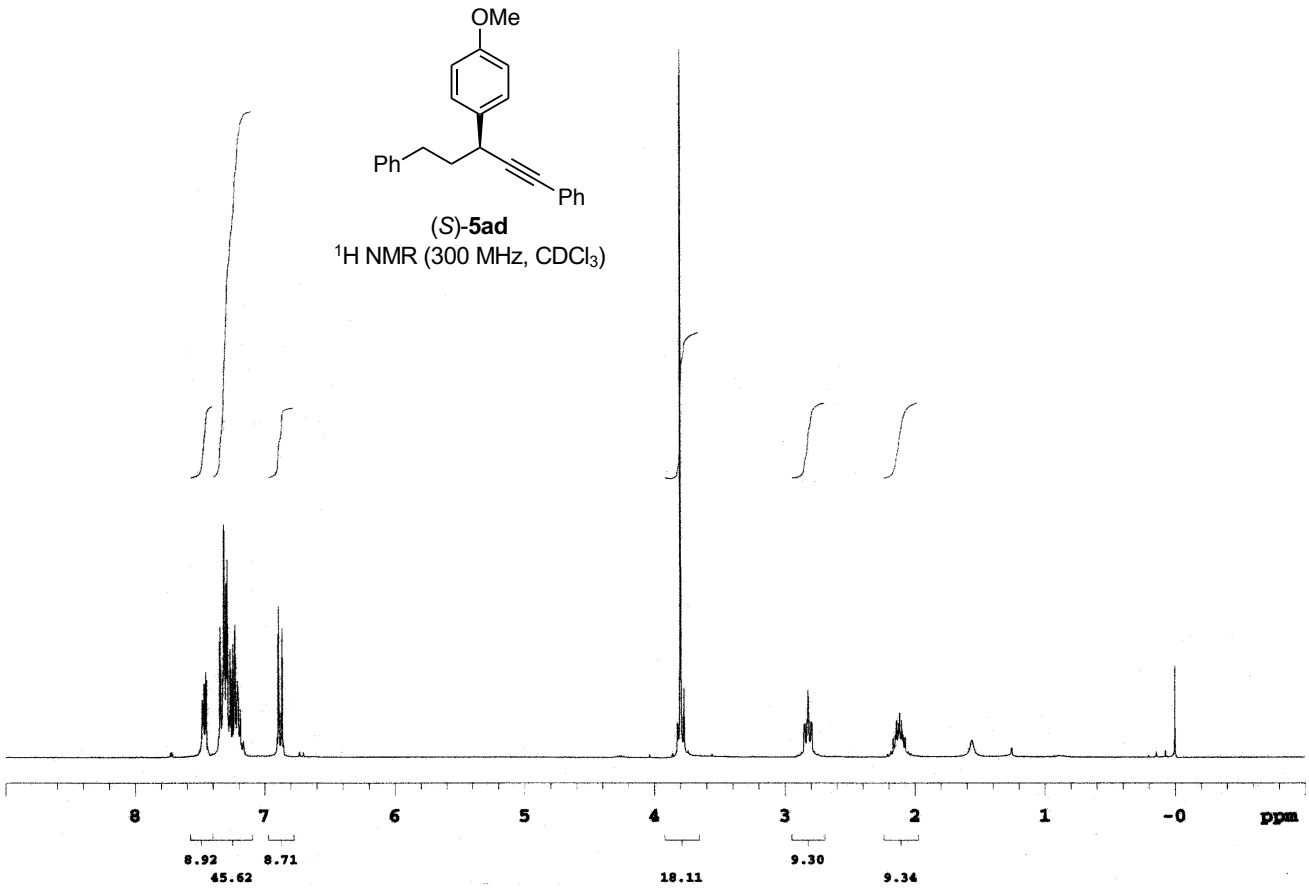


(*S*)-**2ad**

^{13}C NMR (75 MHz, $CDCl_3$)

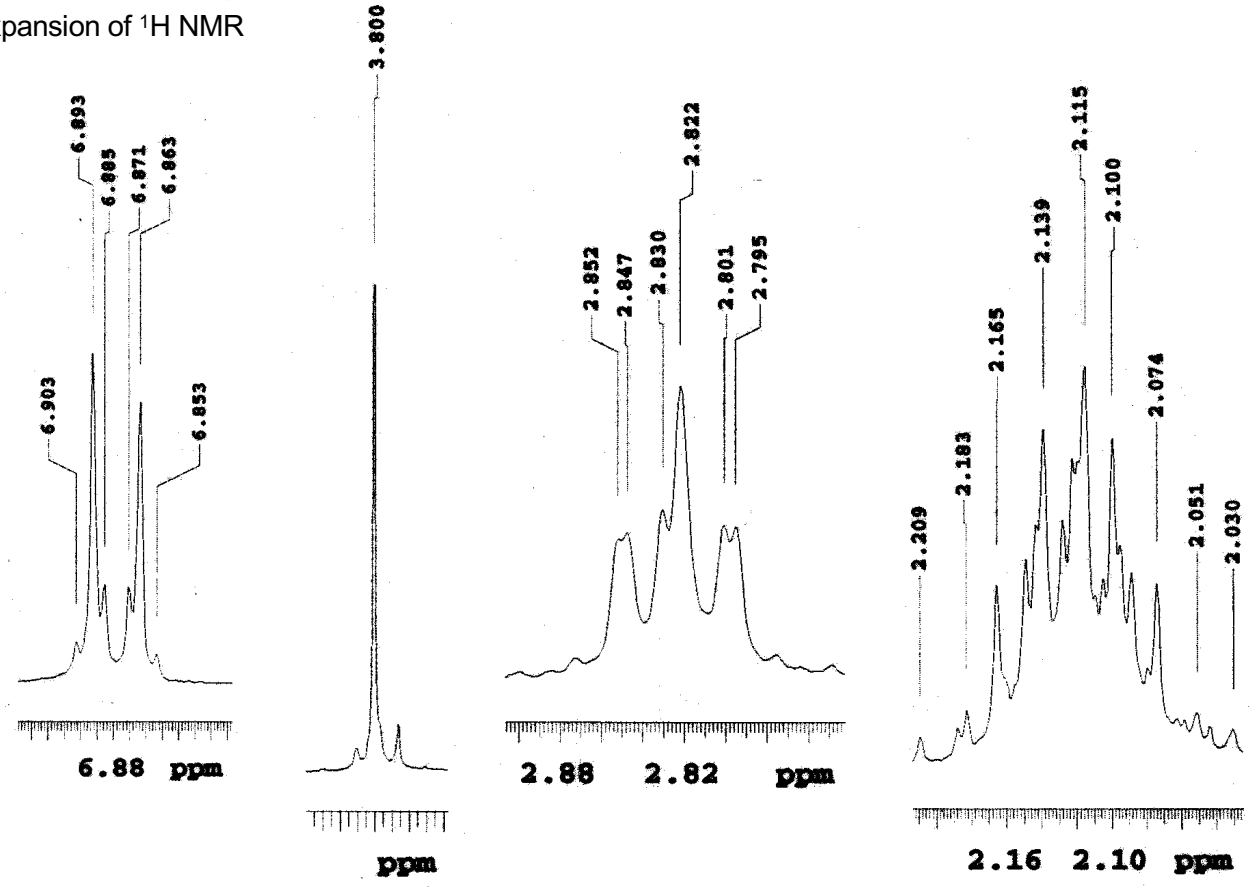
Expansion of ^{13}C–APT NMR

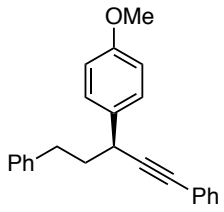




(*S*)-**5ad**
^{1}H NMR (300 MHz, $CDCl_3$)

expansion of ^{1}H NMR



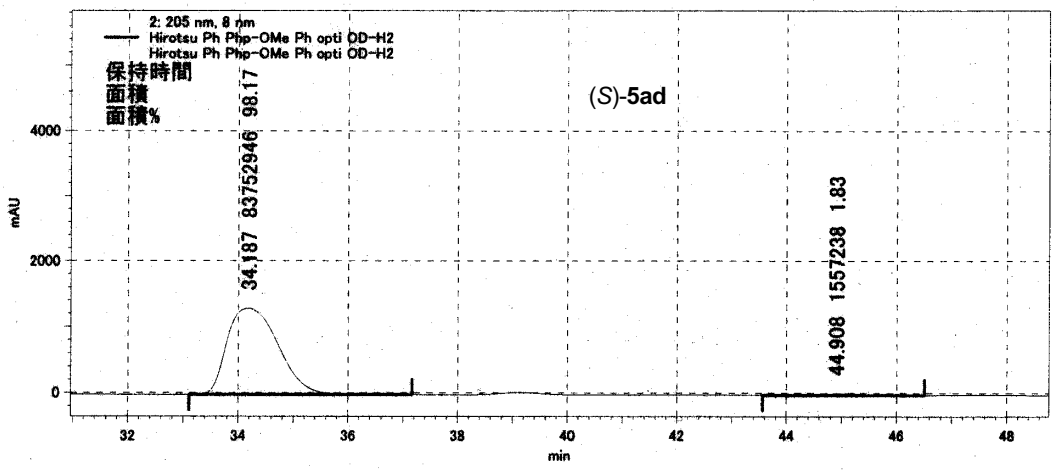


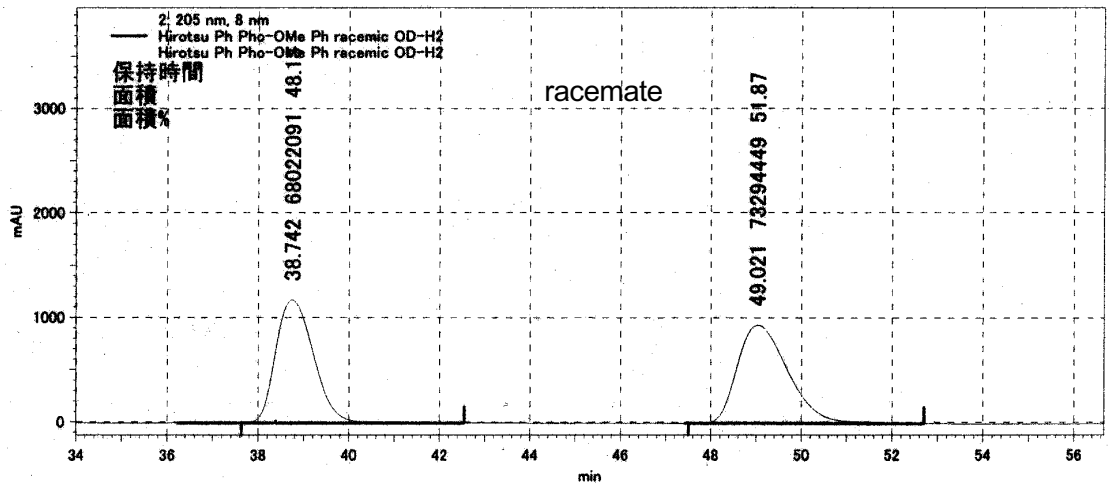
(*S*)-**5ad**

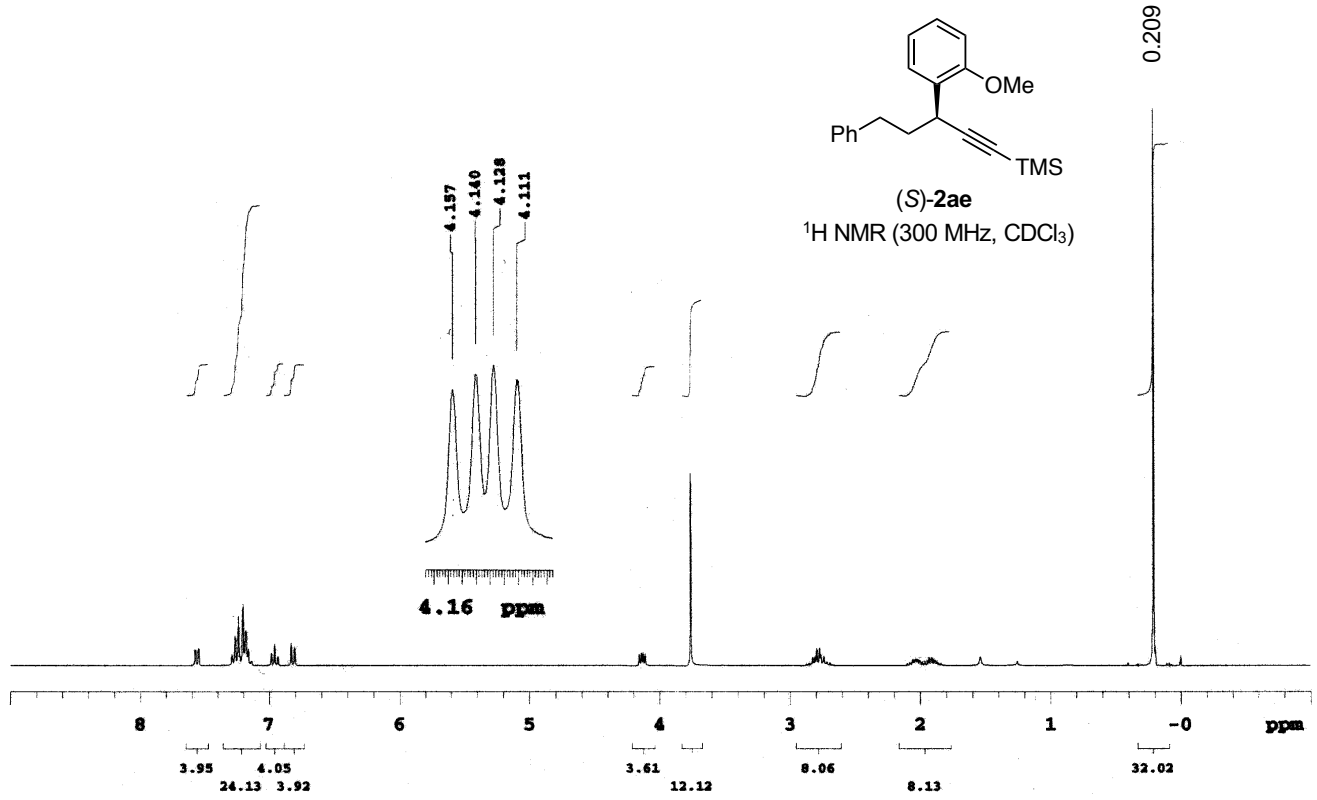
ee
= (98.17 – 1.83) x 100 / (98.17 + 1.83) = 96.3
≈ 96%

es
= 96 x 100 / 98 = 98%

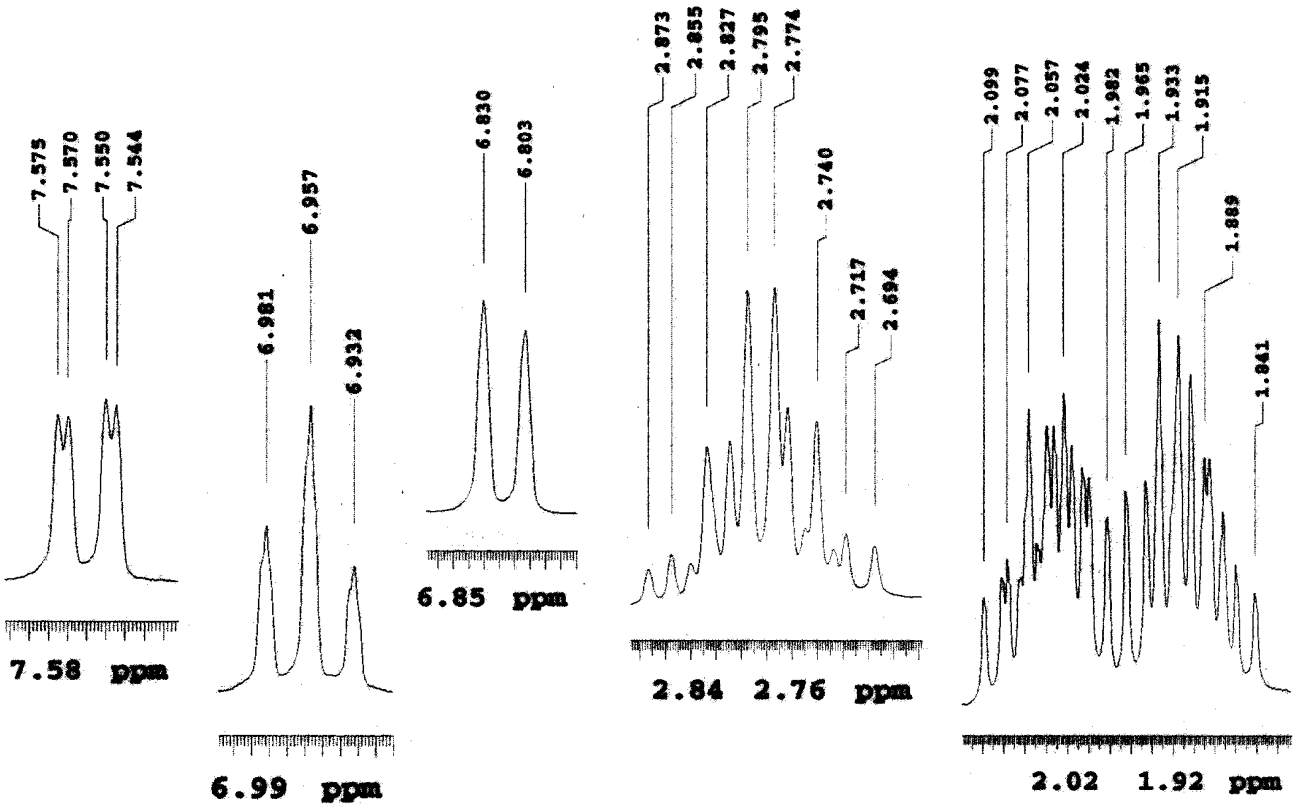
Chiralcel OD-H, hexane/*i*-PrOH = 99.5:0.5, 0.3 mL/min, 25 °C

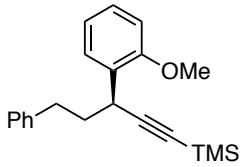






expansion of ^{1}H NMR

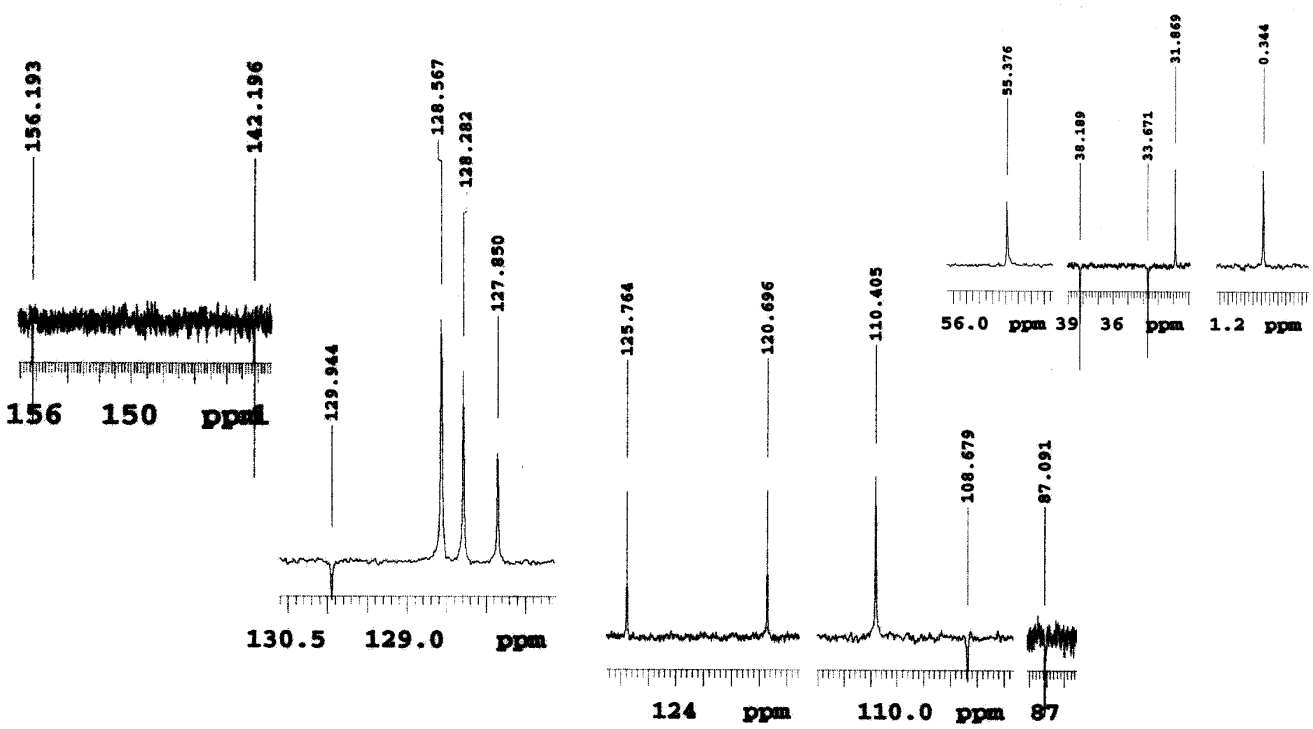


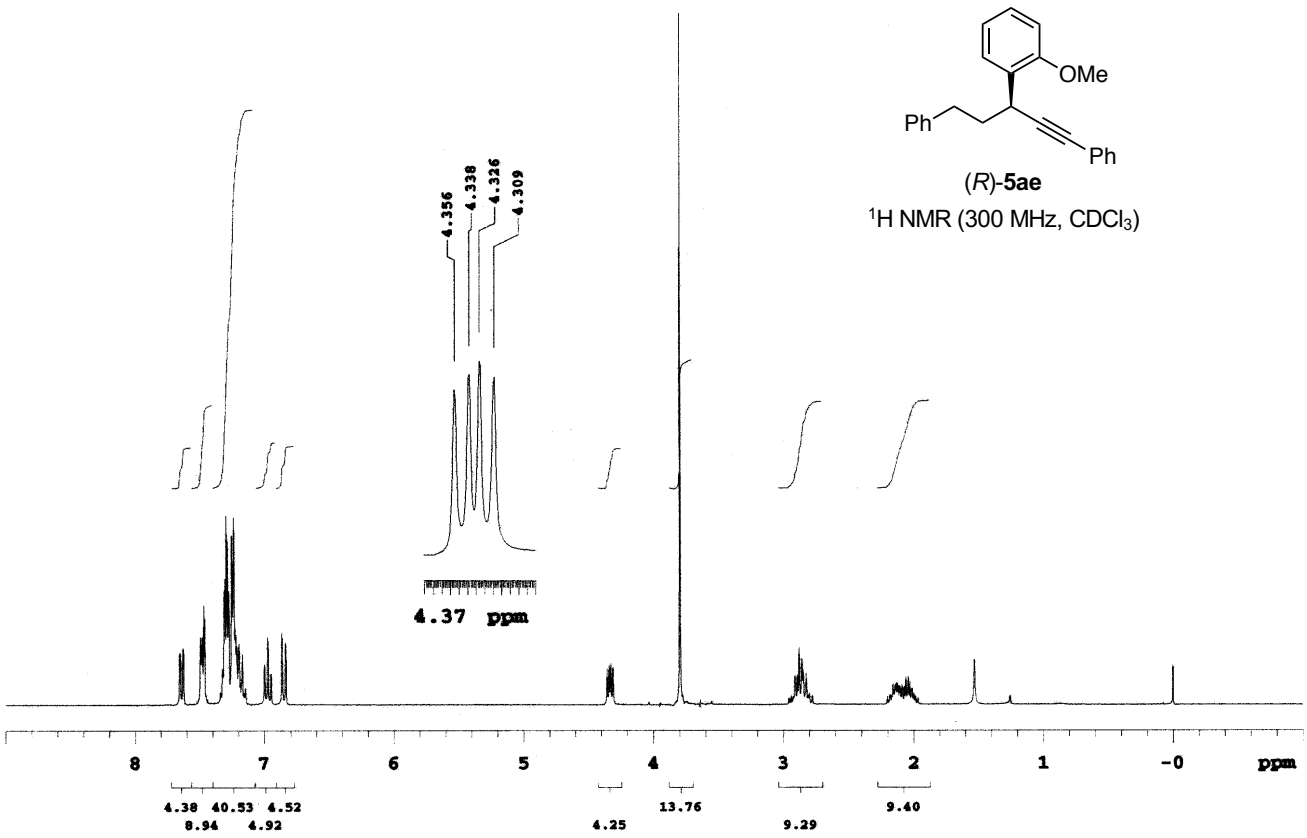


(*S*)-**2ae**

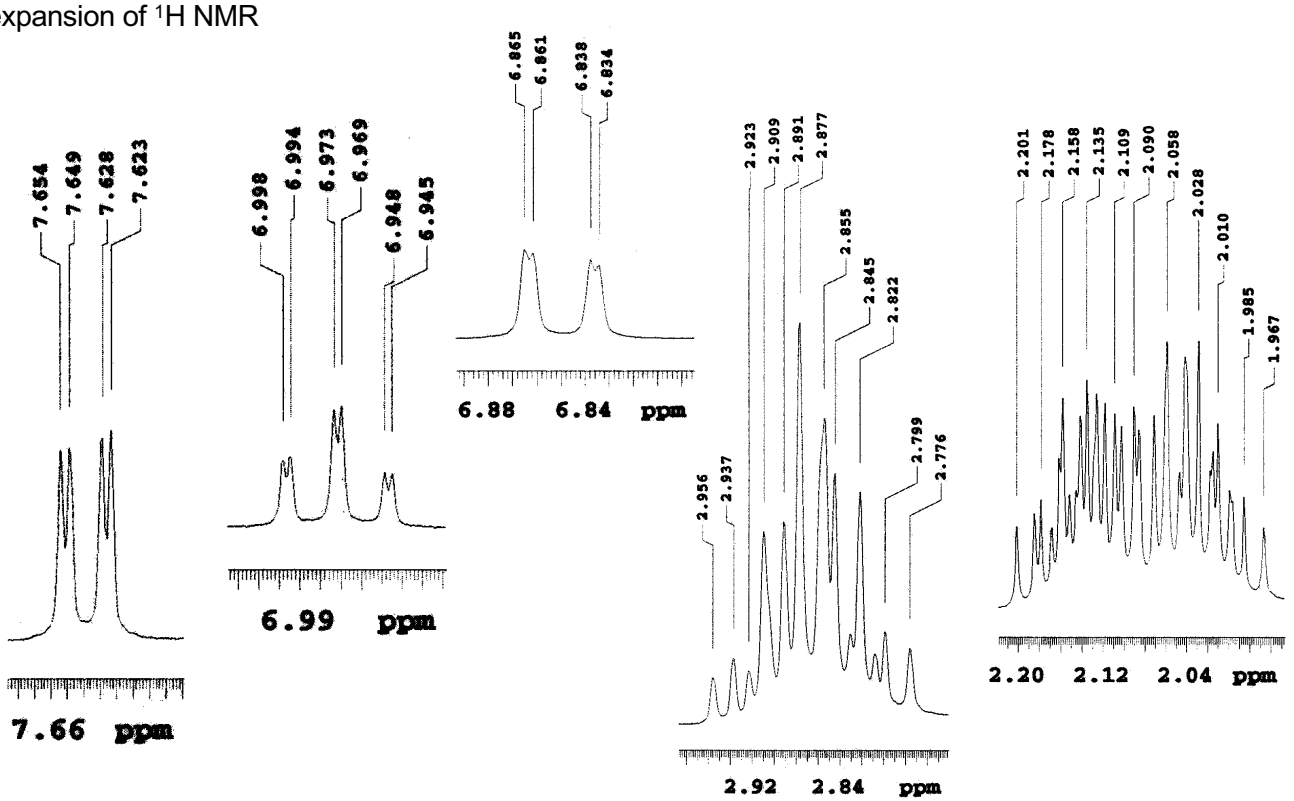
^{13}C NMR (75 MHz, $CDCl_3$)

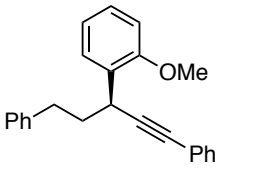
Expansion of ^{13}C–APT NMR





expansion of ^{1}H NMR

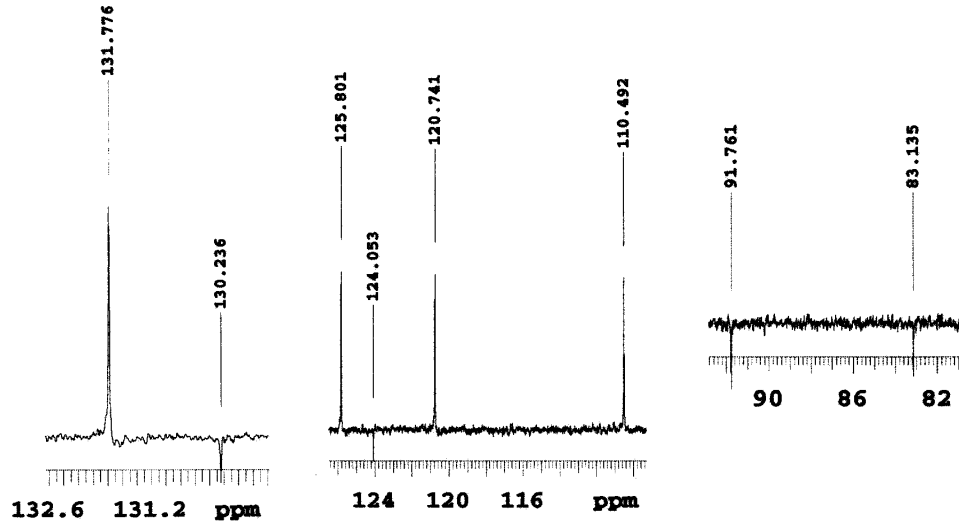


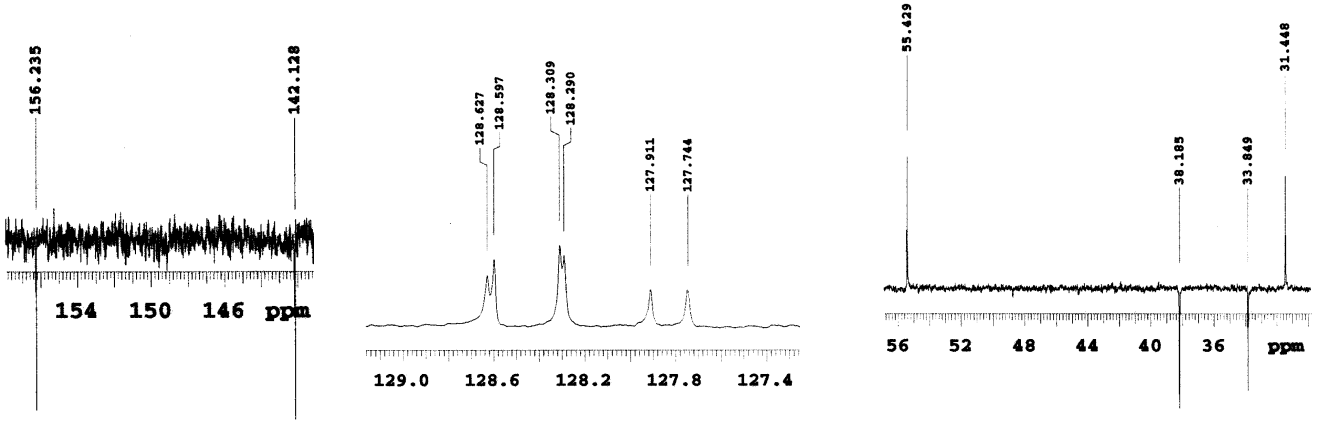


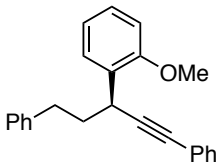
(*R*)-**5ae**

^{13}C NMR (75 MHz, $CDCl_3$)

Expansion of
^{13}C–APT NMR





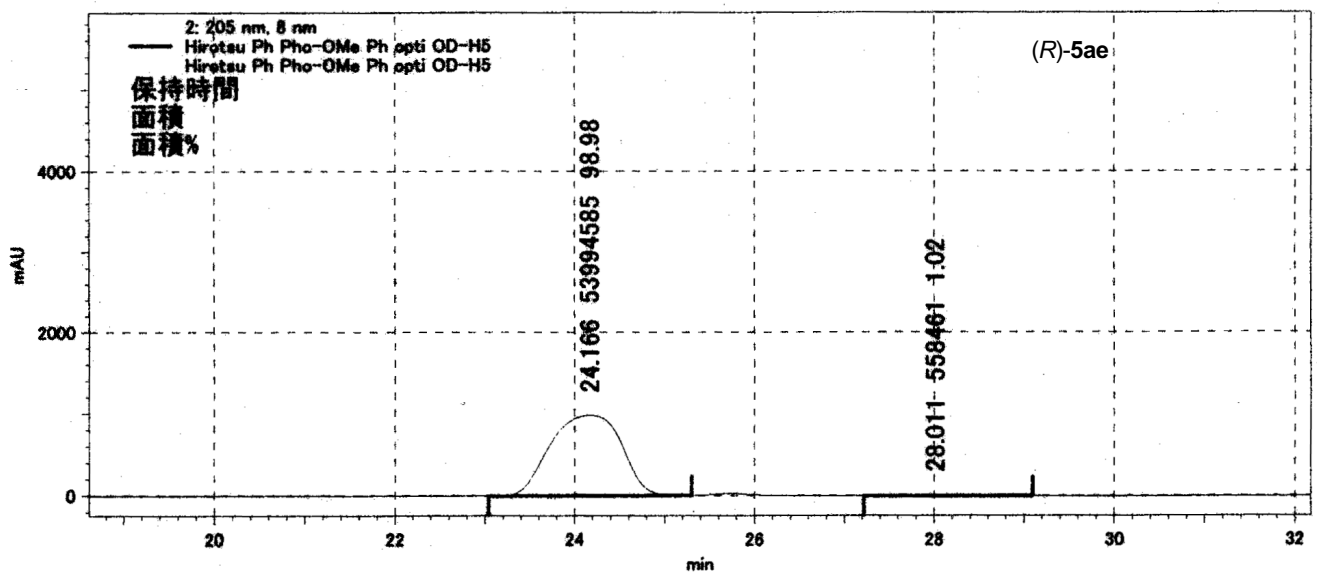


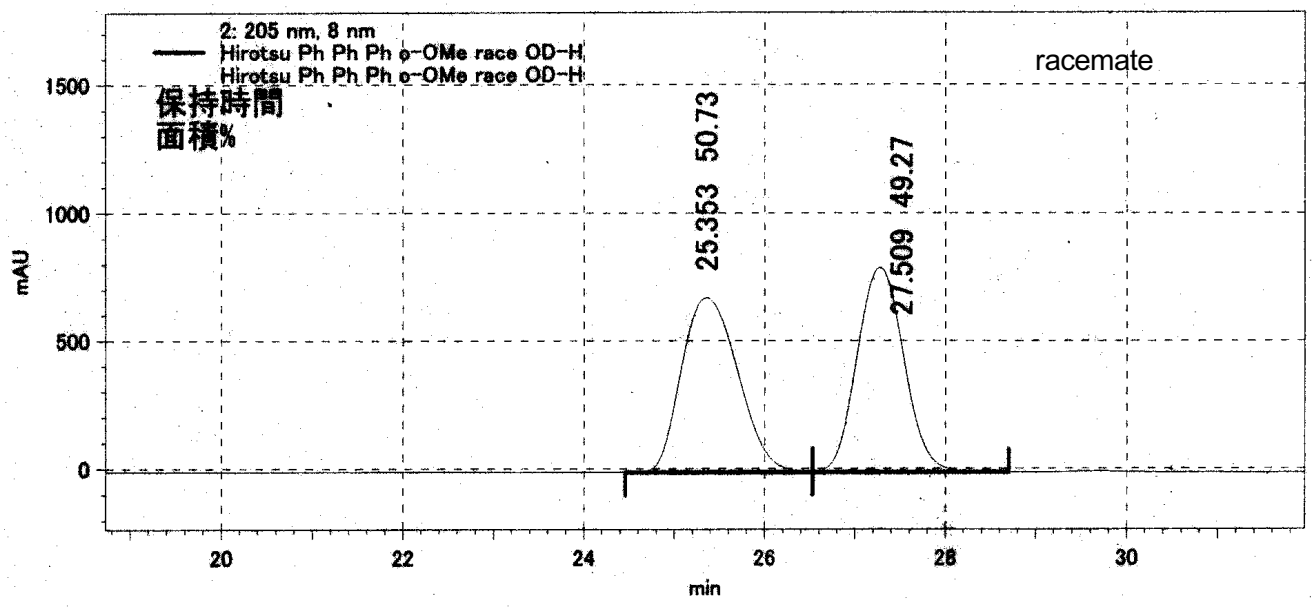
(*R*)-**5ae**

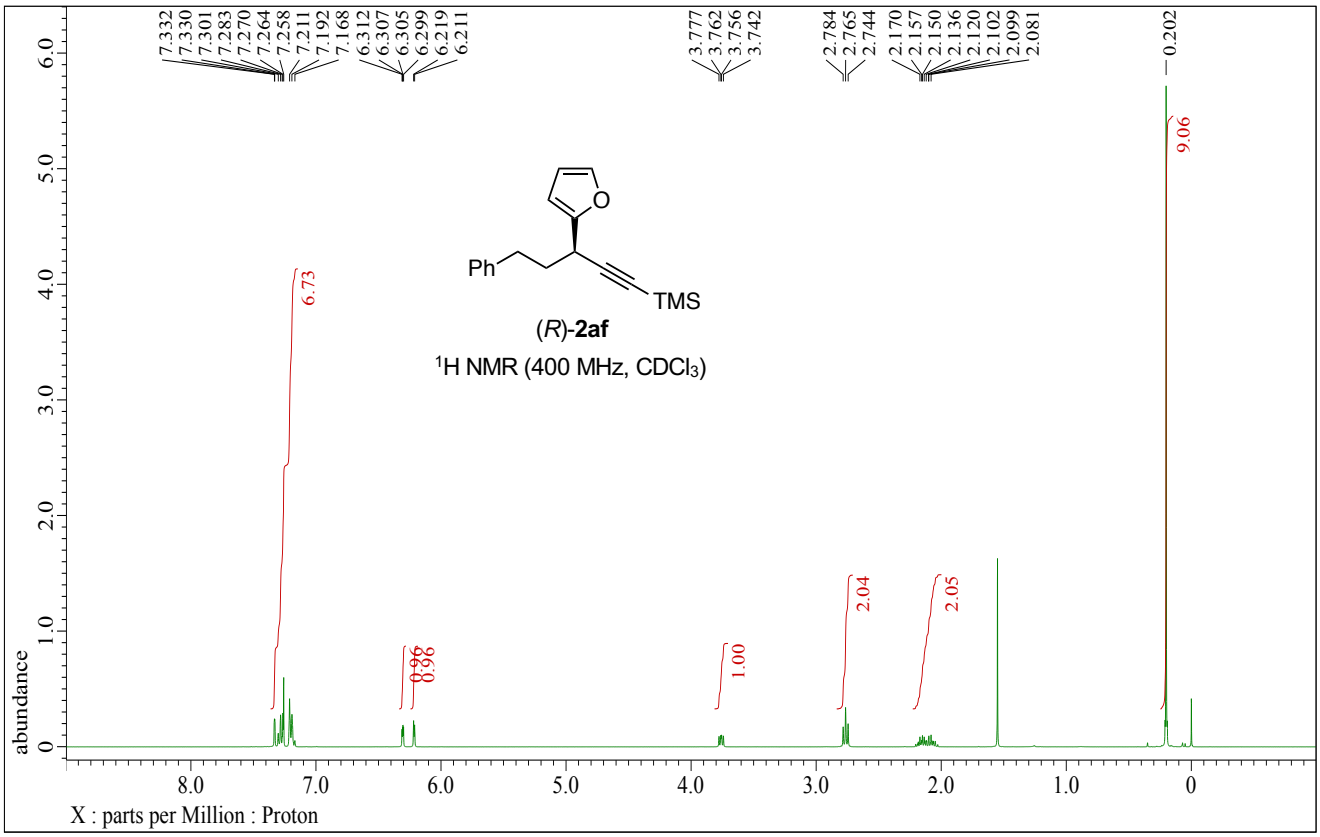
ee
= (98.98 – 1.02) x 100 / (98.98 + 1.02) = 97.96%

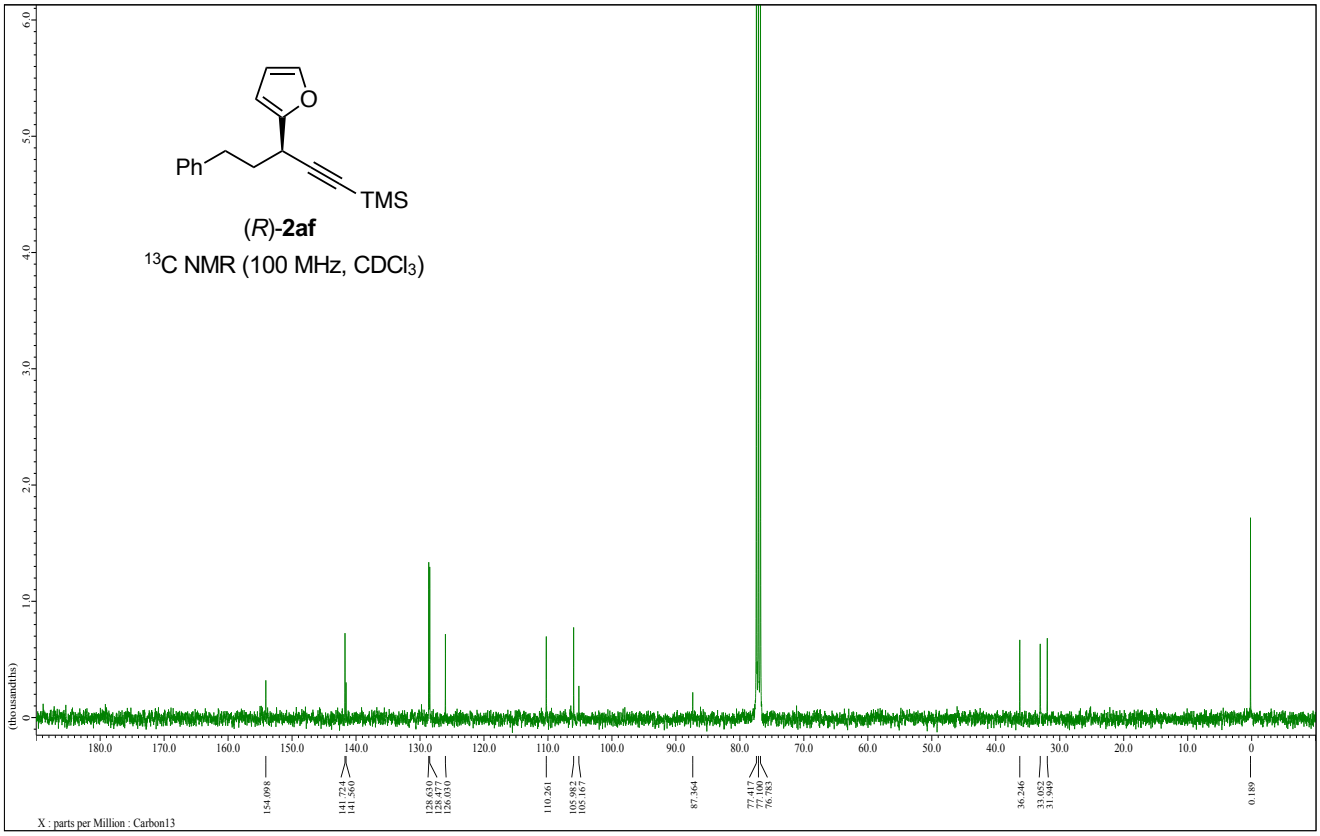
es
= 97.96 x 100 / 98 = 99.96
≈ >99%

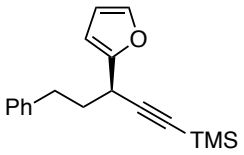
Chiralcel OD-H, hexane/*i*-PrOH = 99.5:0.5, 0.3 mL/min, 25 °C





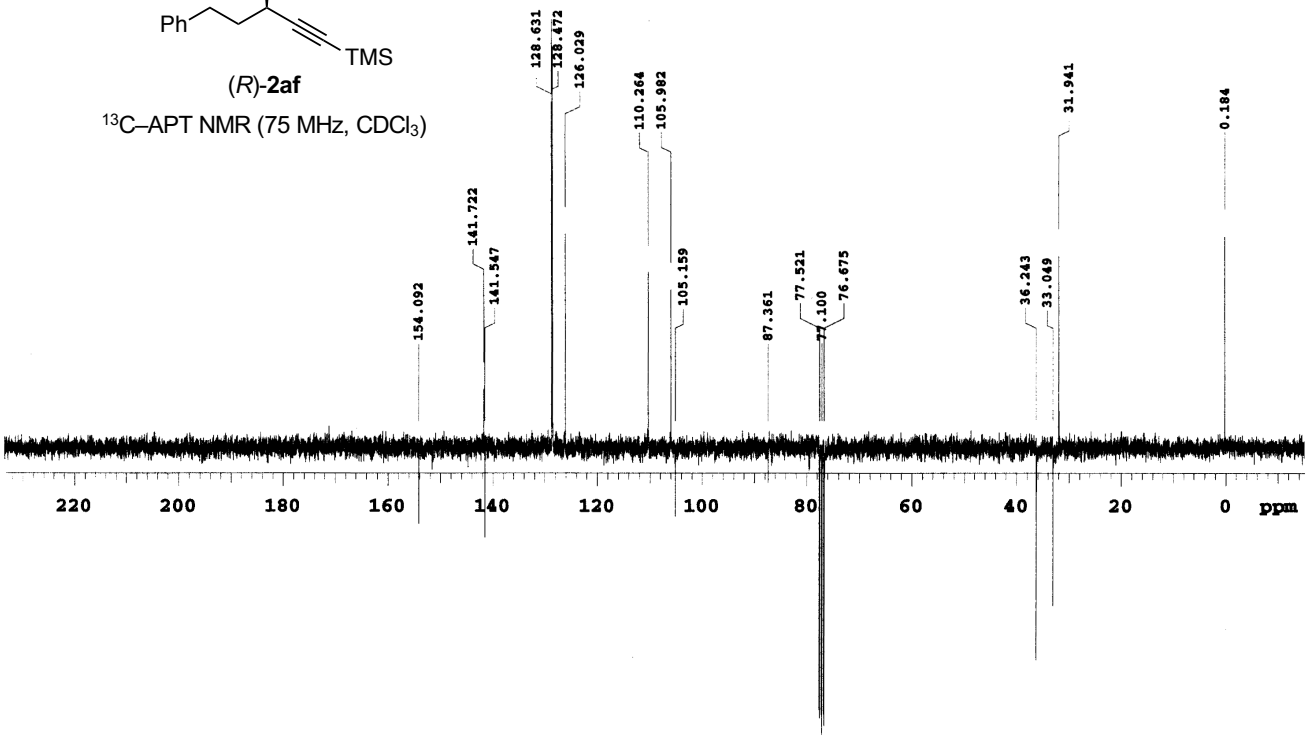

7.332
7.330
7.301
7.283
7.270
7.264
7.258
7.211
7.192
7.168
6.312
6.307
6.305
6.299
6.219
6.211
3.777
3.762
3.756
3.742
2.784
2.765
2.744
2.170
2.157
2.150
2.136
2.120
2.102
2.099
2.081
0.202
9.06
6.73
0.96
0.96
1.00
2.04
2.05
abundance
X : parts per Million : Proton
Ph
TMS
O
(R)-2af
1H NMR (400 MHz, CDCl3)


Ph
TMS
O
(R)-2af
13C NMR (100 MHz, CDCl3)
X : parts per Million : Carbon13

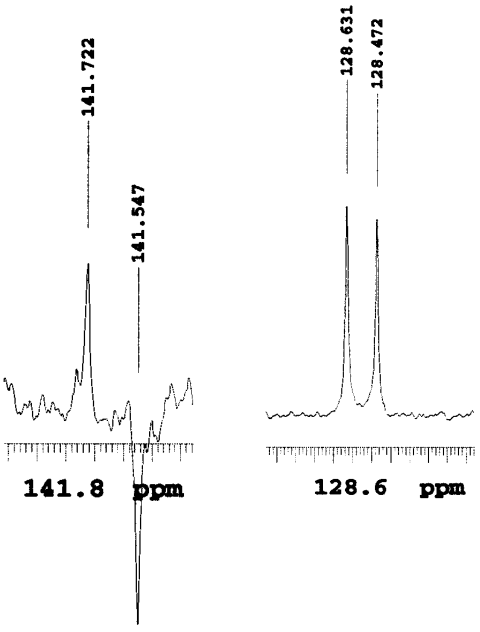


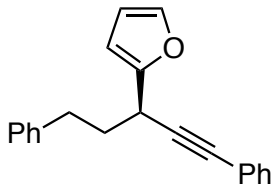
(*R*)-**2af**

^{13}C–APT NMR (75 MHz, $CDCl_3$)



Expansion of ^{13}C–APT NMR

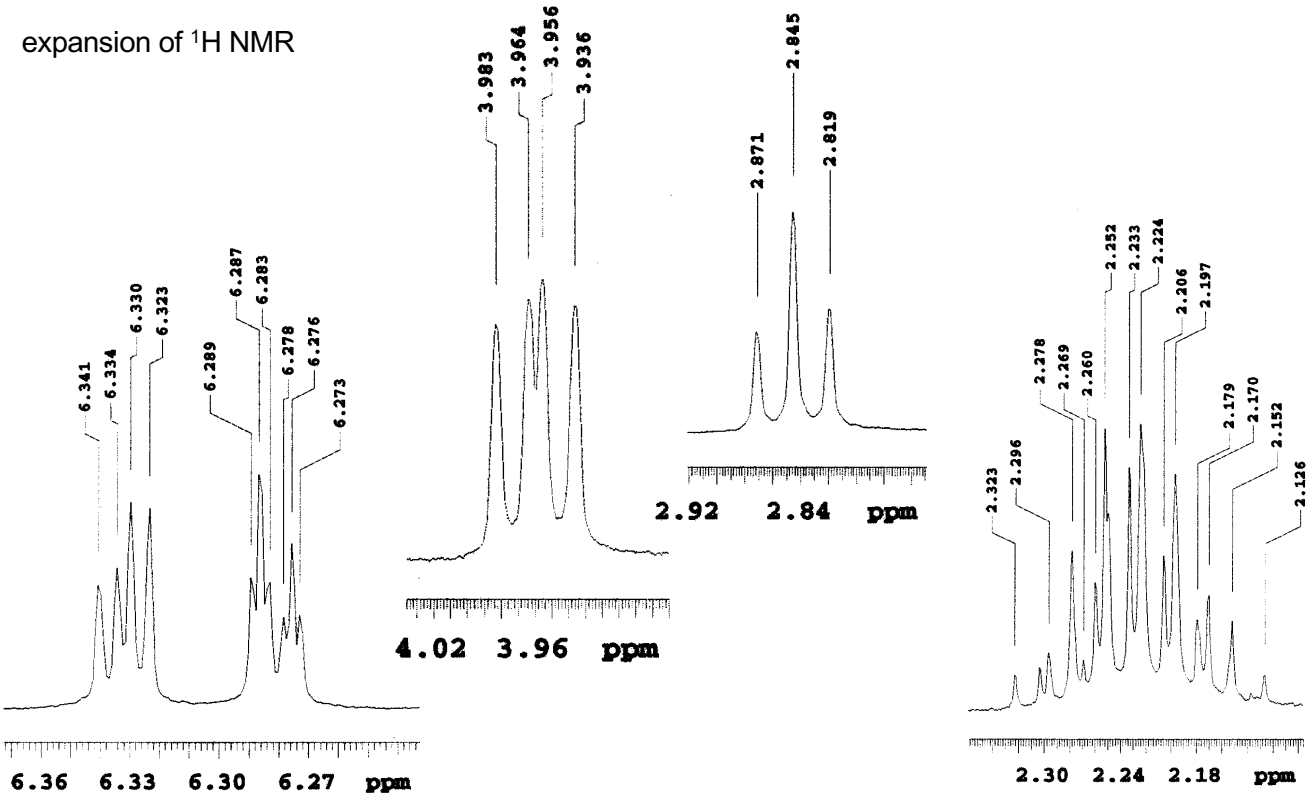


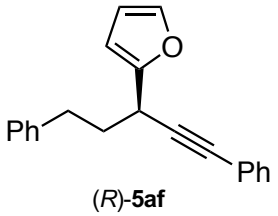


(*R*)-**5af**

^{1}H NMR (300 MHz, $CDCl_3$)

expansion of ^{1}H NMR



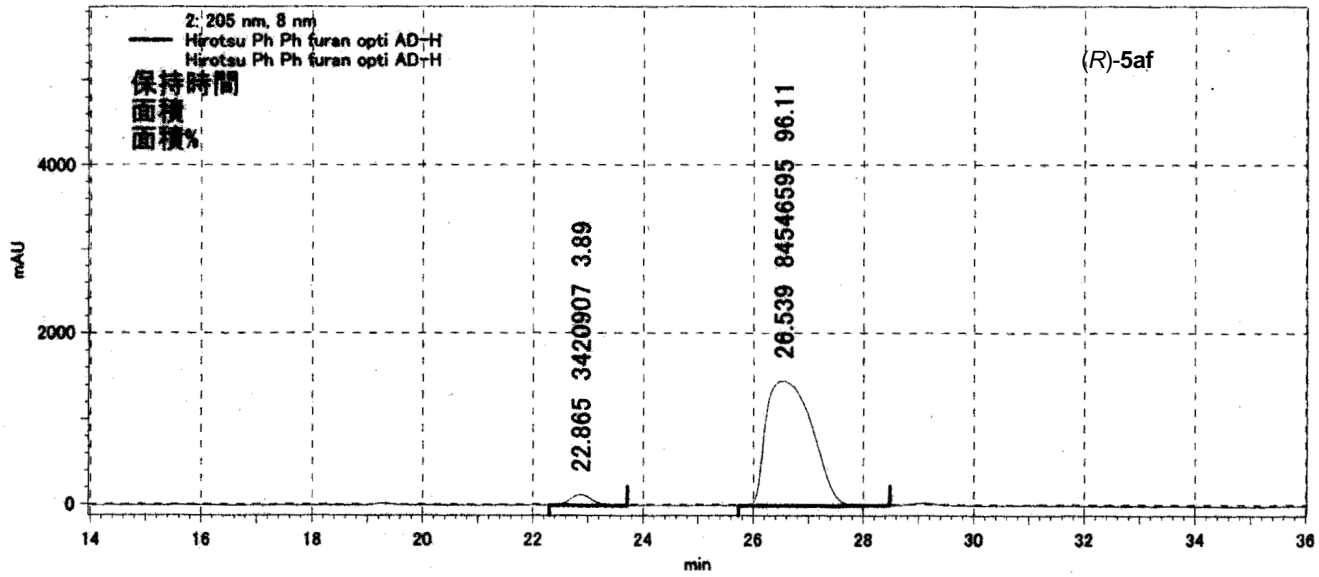


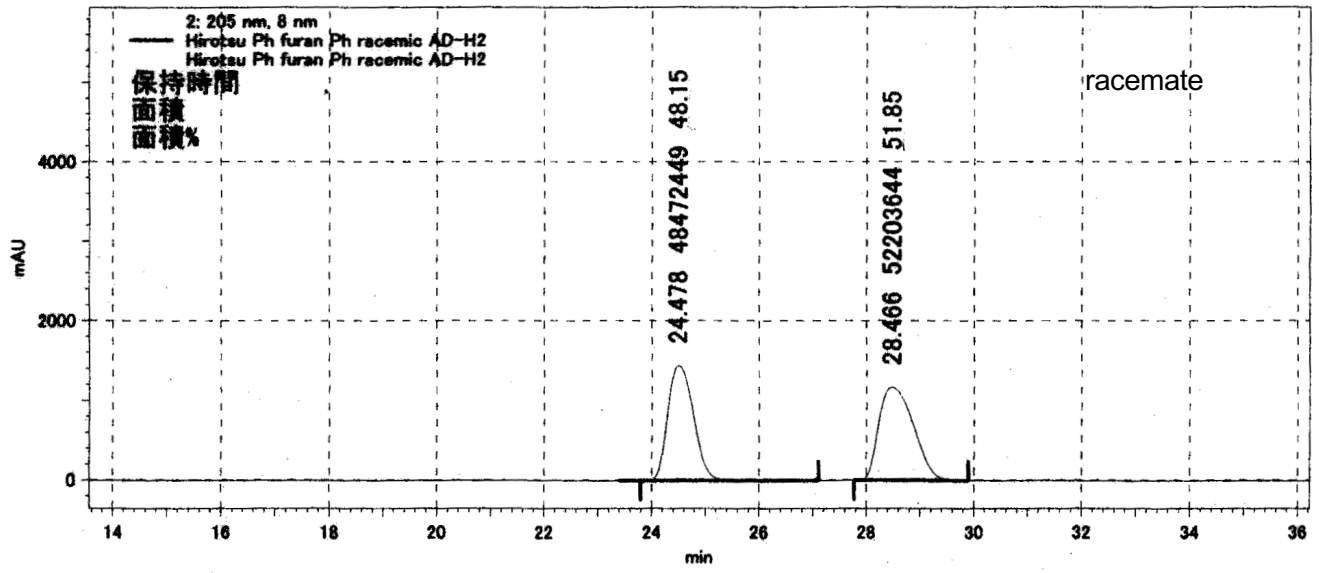
(*R*)-**5af**

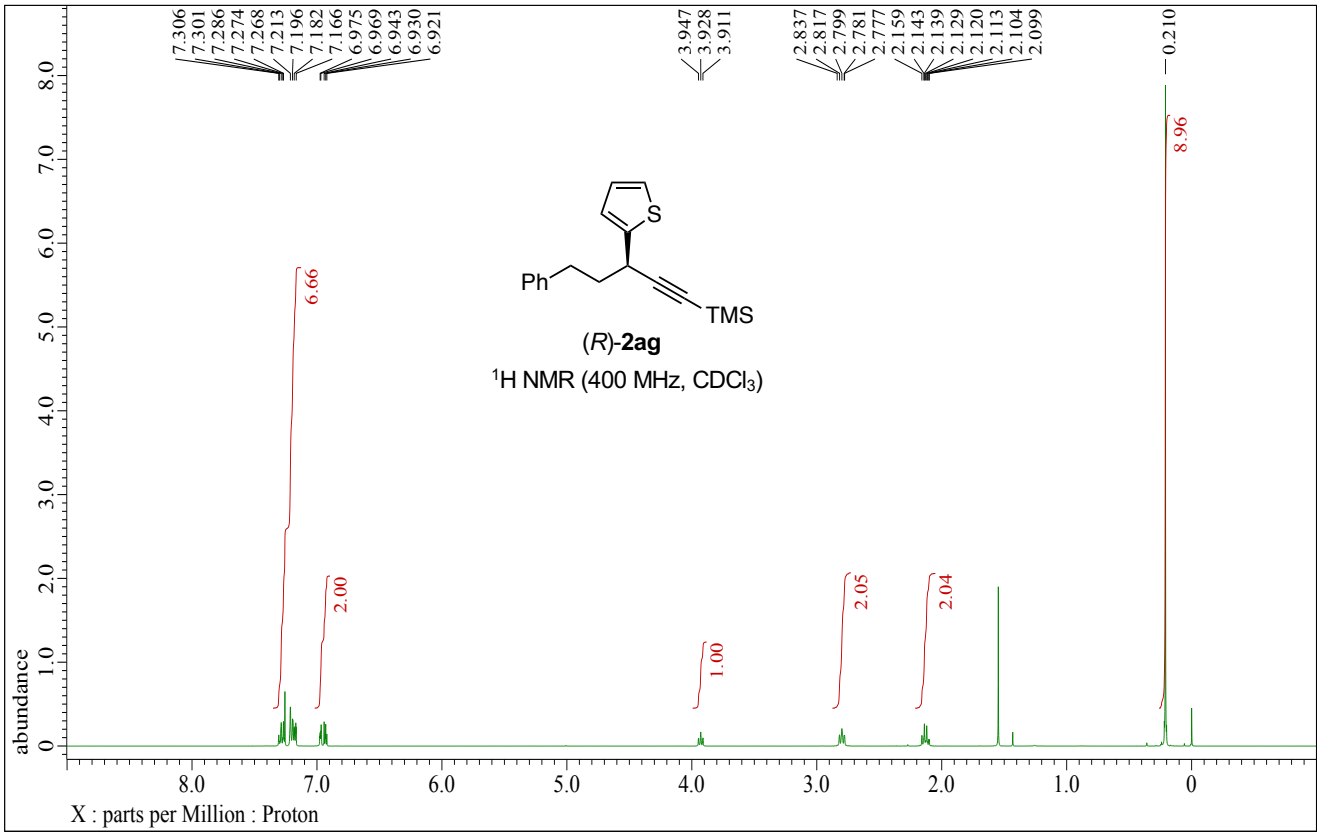
ee
= (96.11 – 3.89) x 100 / (96.11 + 3.89) = 92.22
≈ 92%

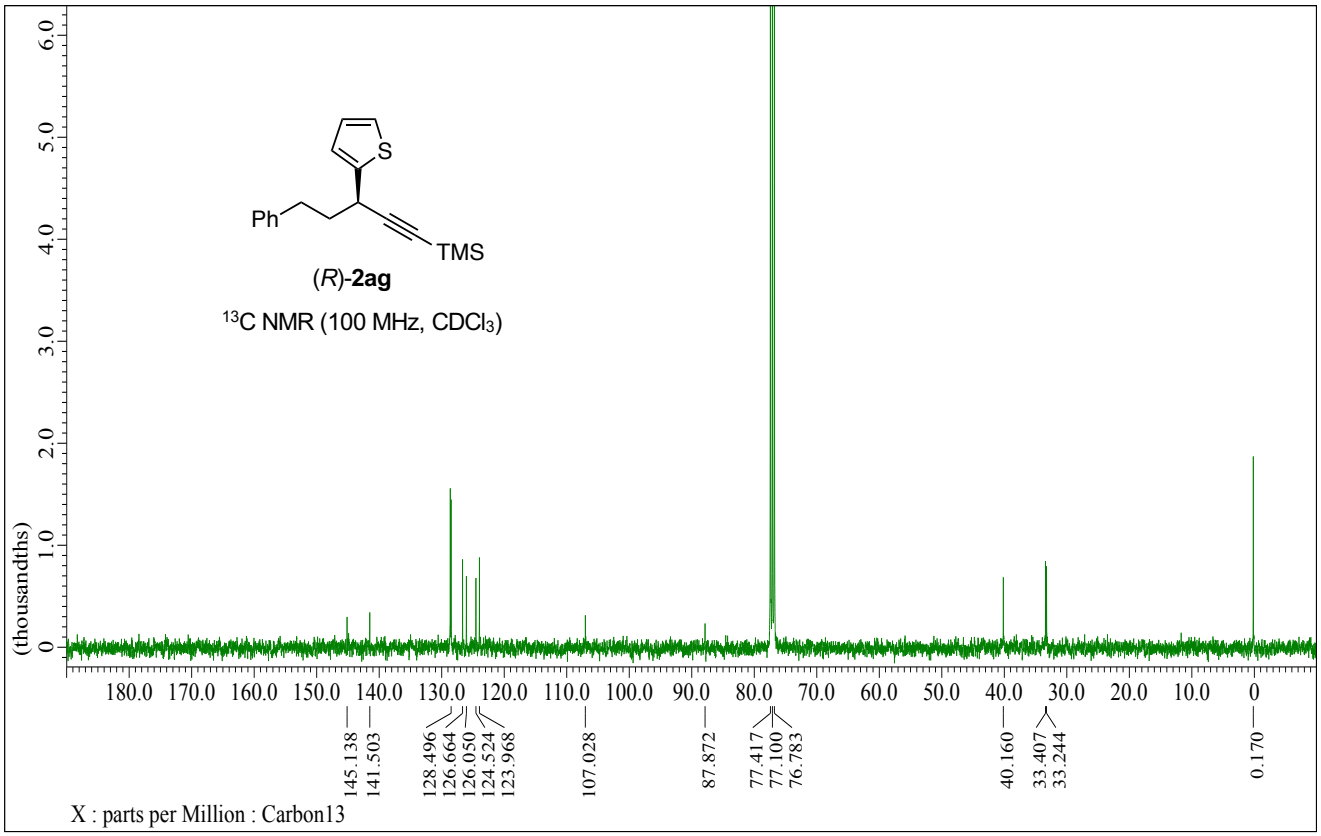
es
= 92 x 100 / 97 = 94.8
≈ 95%

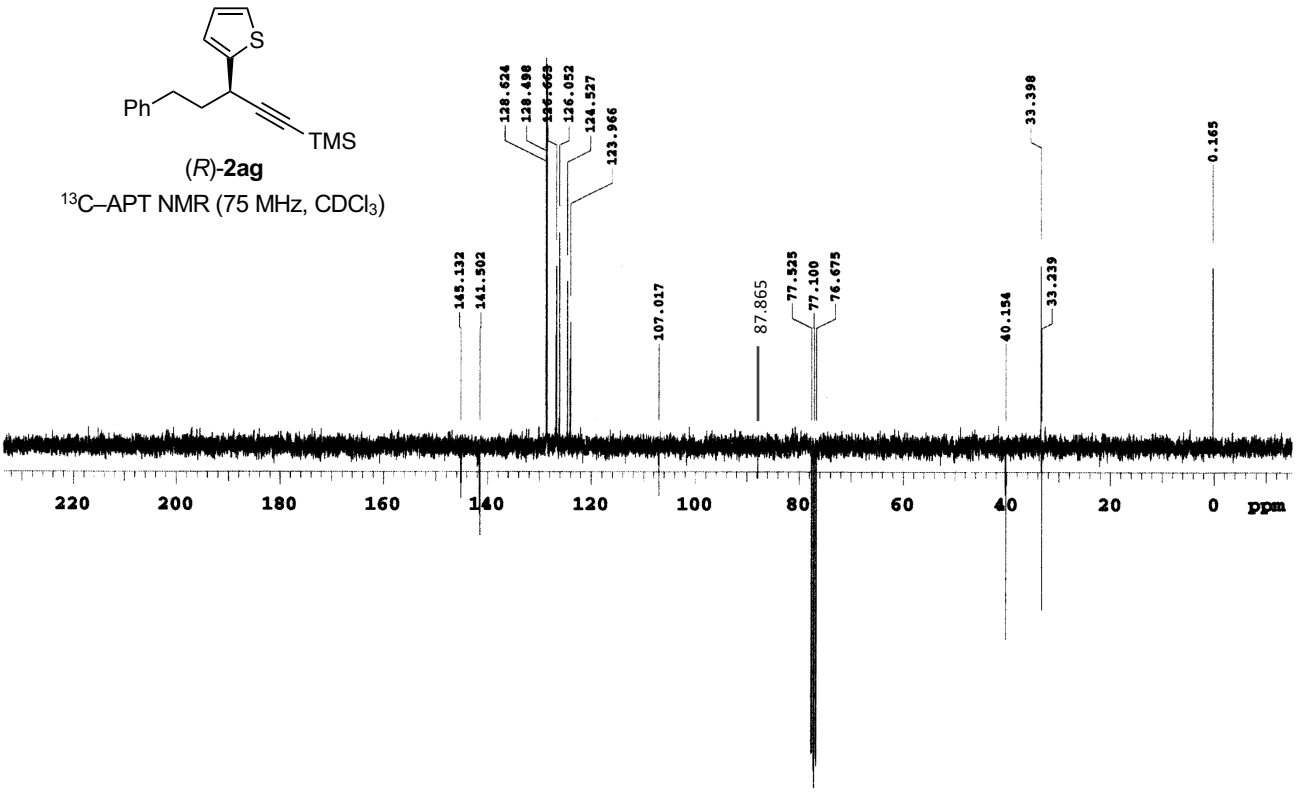
Chiralpak AD-H, hexane/*i*-PrOH = 99.5:0.5, 0.3 mL/min, 25 °C






7.306
7.301
7.286
7.274
7.268
7.213
7.196
7.182
7.166
6.975
6.969
6.943
6.930
6.921
3.947
3.928
3.911
2.837
2.817
2.799
2.781
2.777
2.159
2.143
2.139
2.129
2.120
2.113
2.104
2.099
0.210
8.96
6.66
2.00
1.00
2.05
2.04
S
Ph
TMS
(R)-2ag
1H NMR (400 MHz, CDCl3)
abundance
X : parts per Million : Proton

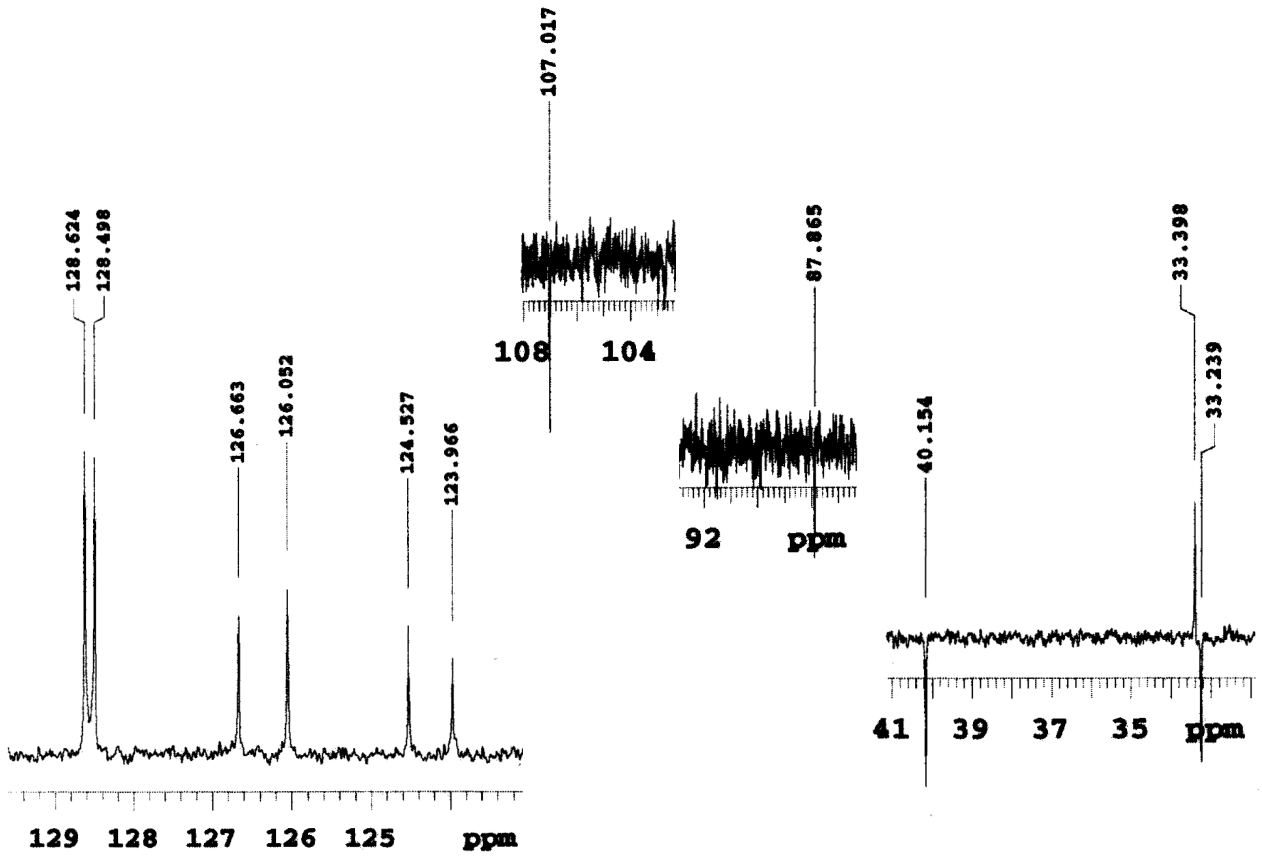

S
Ph
TMS
(R)-2ag
13C NMR (100 MHz, CDCl3)
(thousandths)
145.138
141.503
128.496
126.664
126.050
124.524
123.968
107.028
87.872
77.417
77.100
76.783
40.160
33.407
33.244
0.170
X : parts per Million : Carbon13

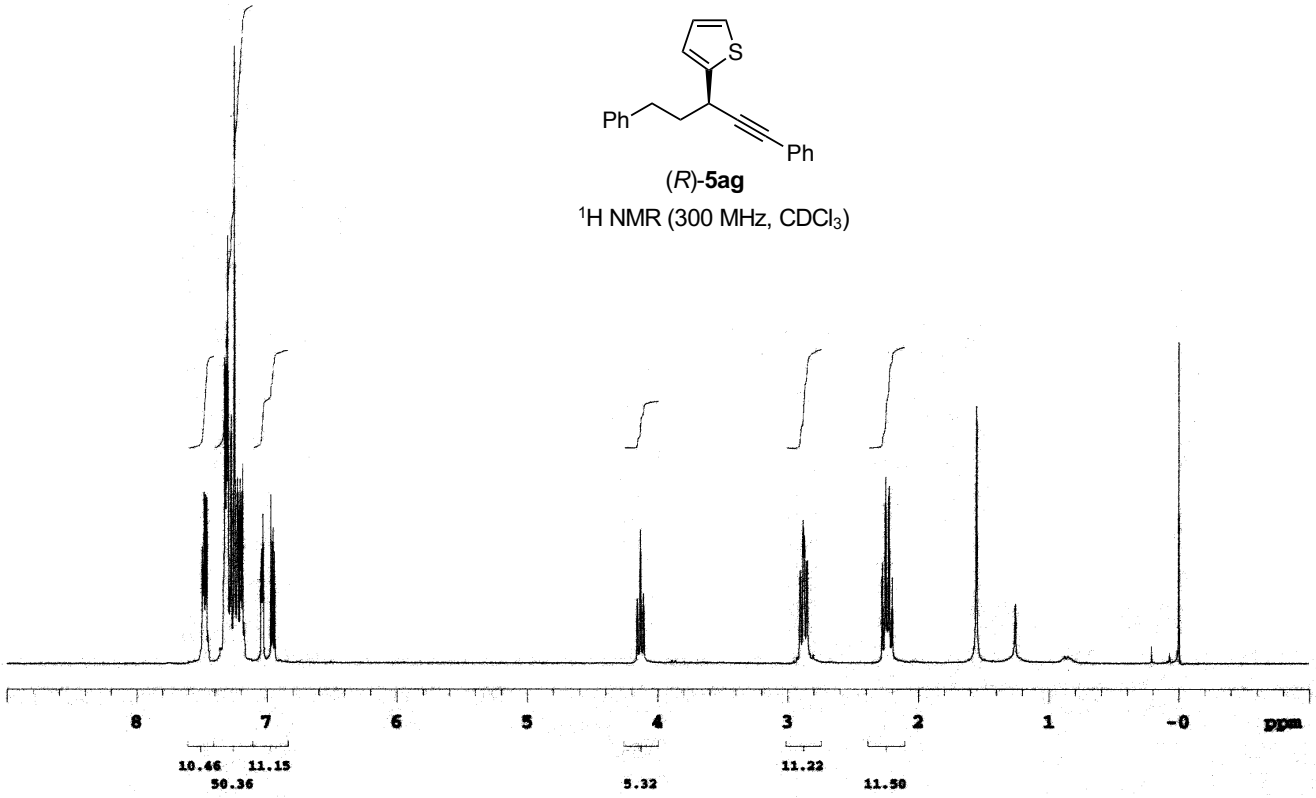


(*R*)-**2ag**

^{13}C–APT NMR (75 MHz, $CDCl_3$)

Expansion of ^{13}C–APT NMR

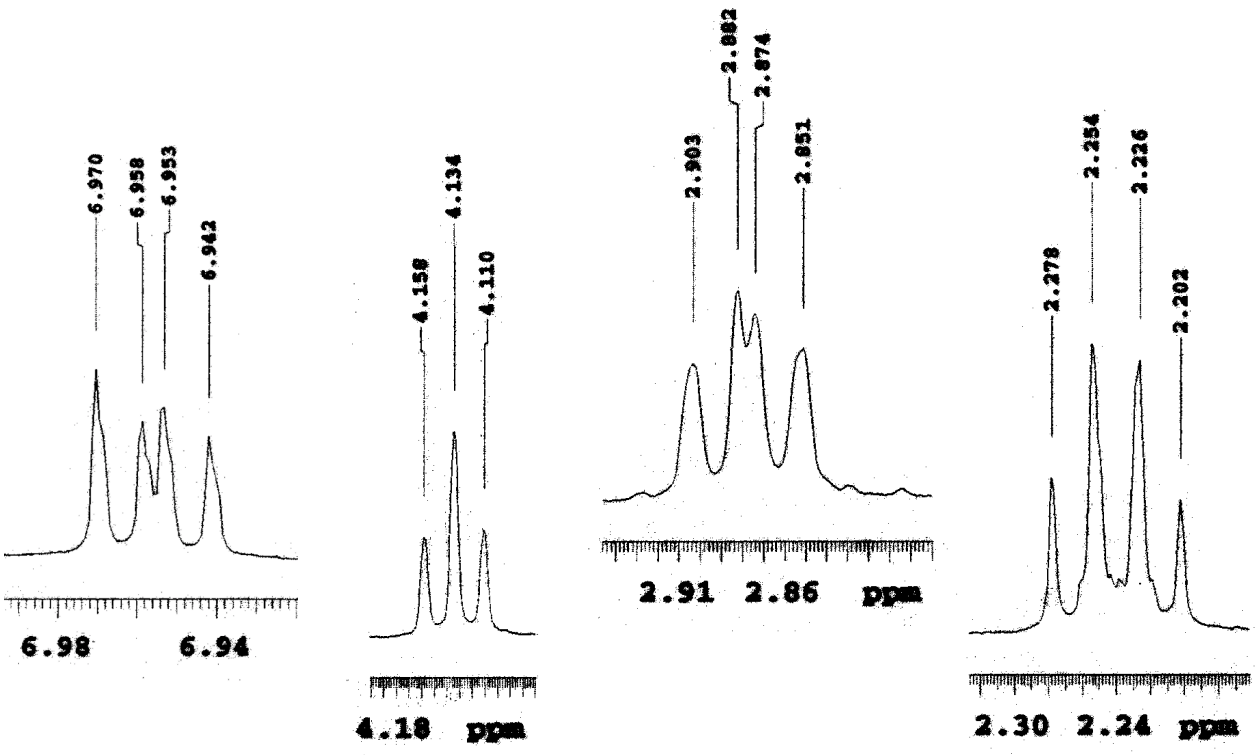


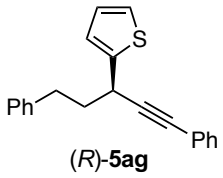


(*R*)-**5ag**

^{1}H NMR (300 MHz, $CDCl_3$)

expansion of ^{1}H NMR



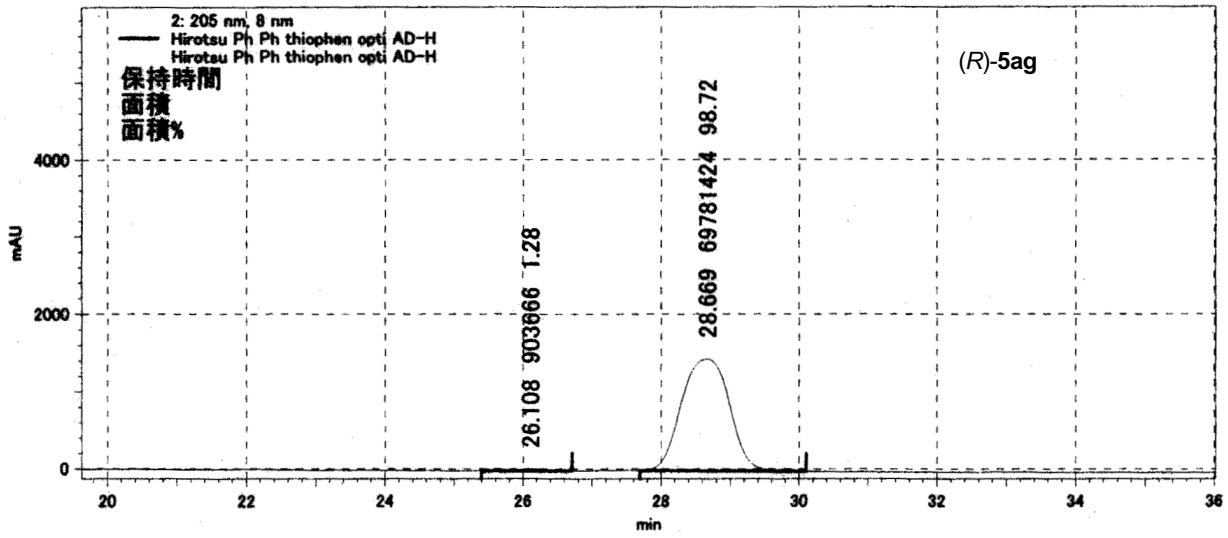


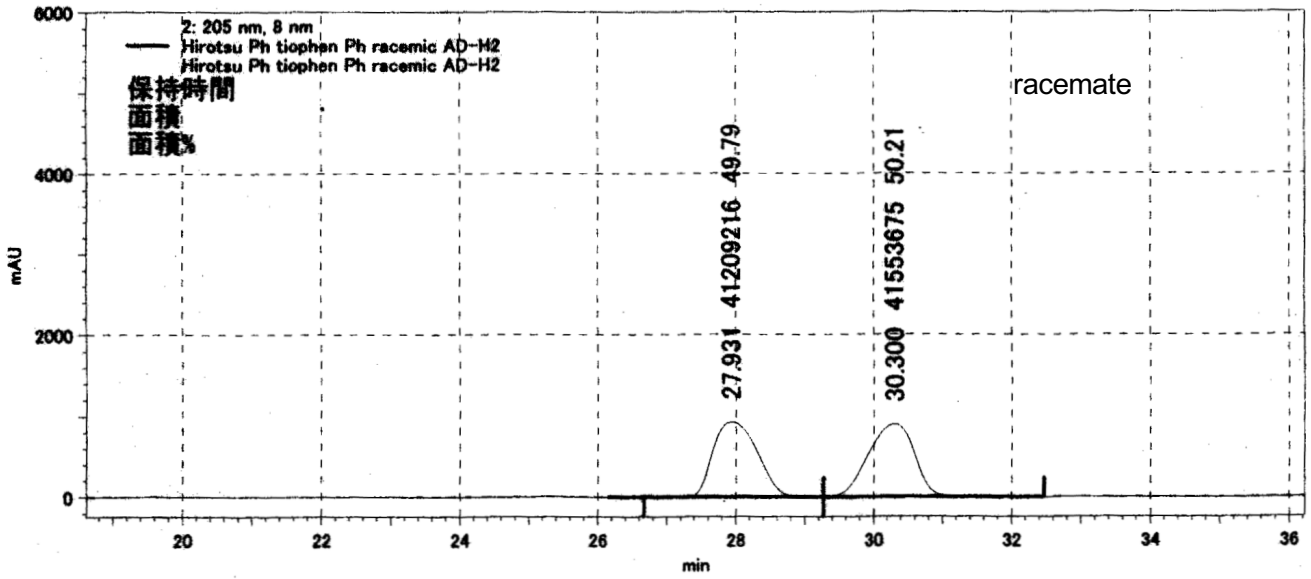
(*R*)-**5ag**

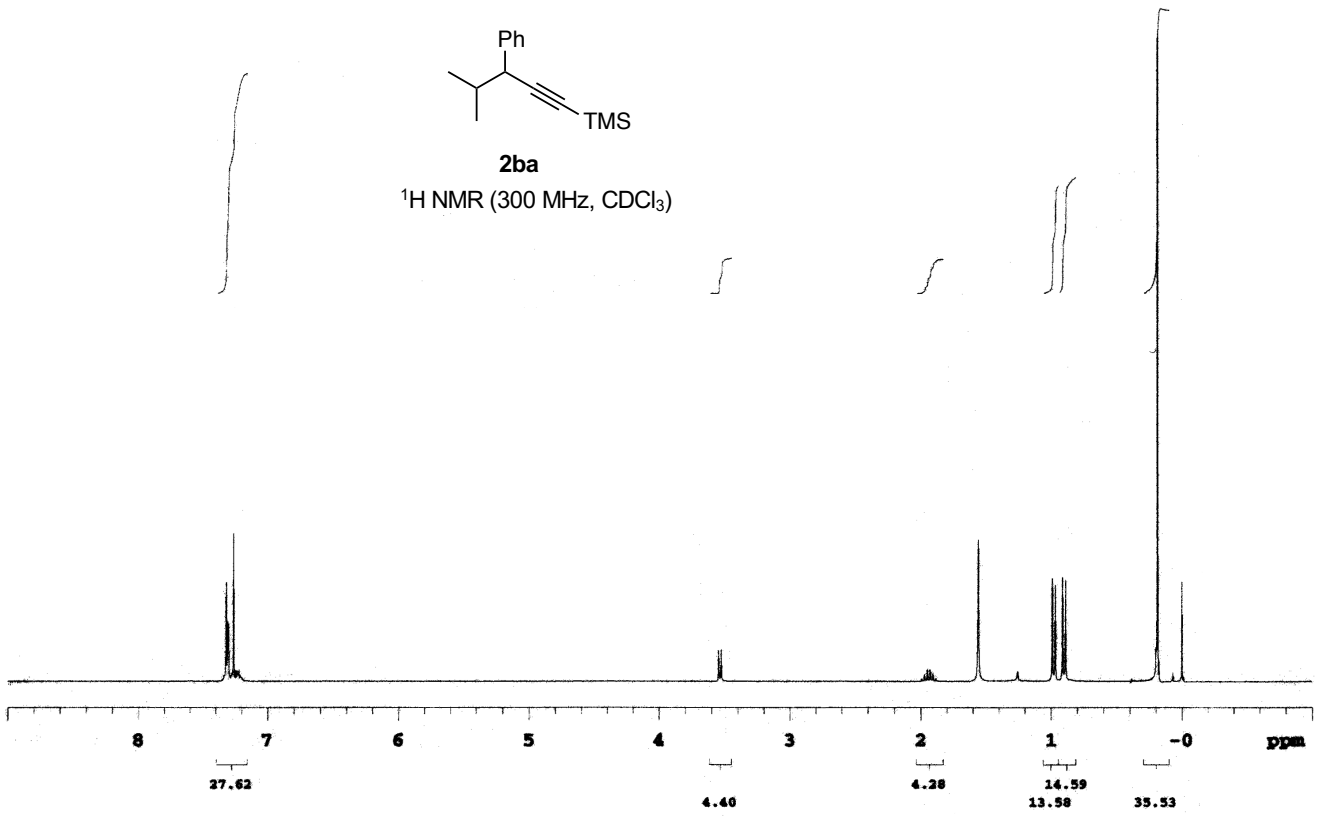
ee
= (98.72 – 1.28) x 100 / (98.72 + 1.28) = 97.44
≈ 97%

es
= 97 x 100 / 98 = 99%

Chiralpak AD-H, hexane/*i*-PrOH = 99.5:0.5, 0.3 mL/min, 25 °C



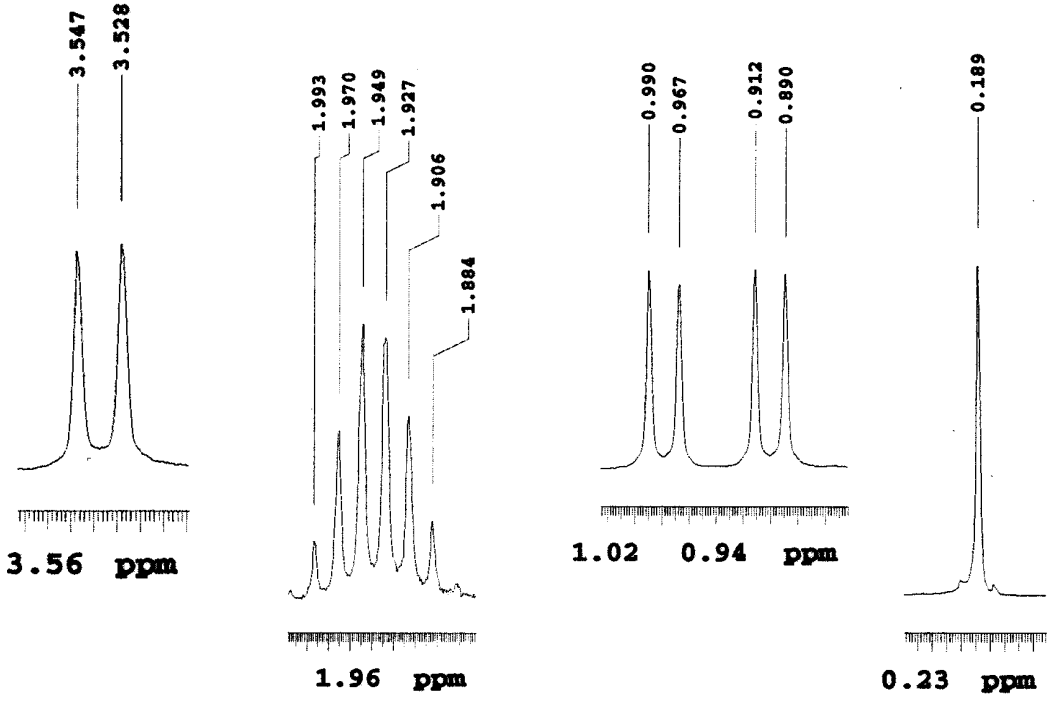


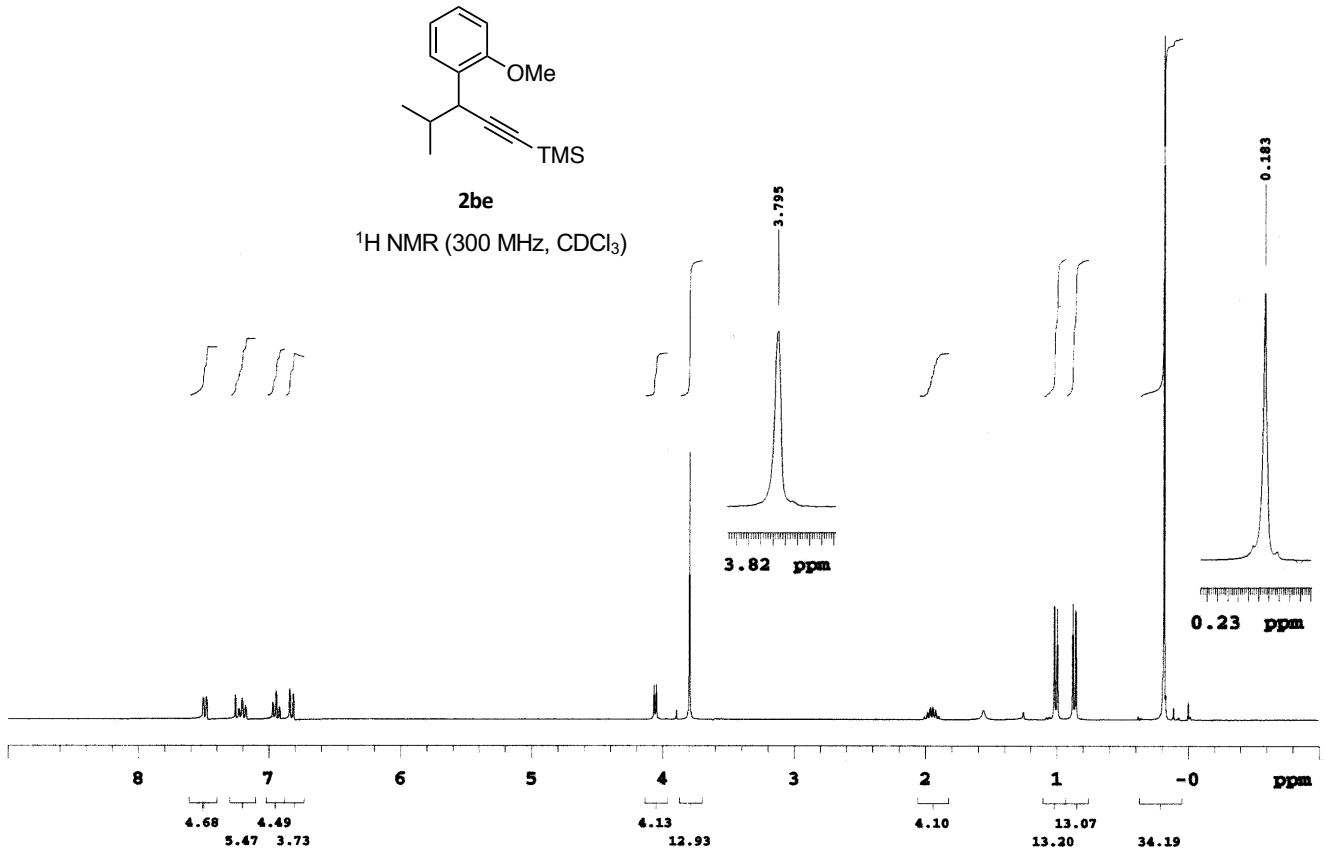


2ba

^{1}H NMR (300 MHz, $CDCl_3$)

expansion of ^{1}H NMR

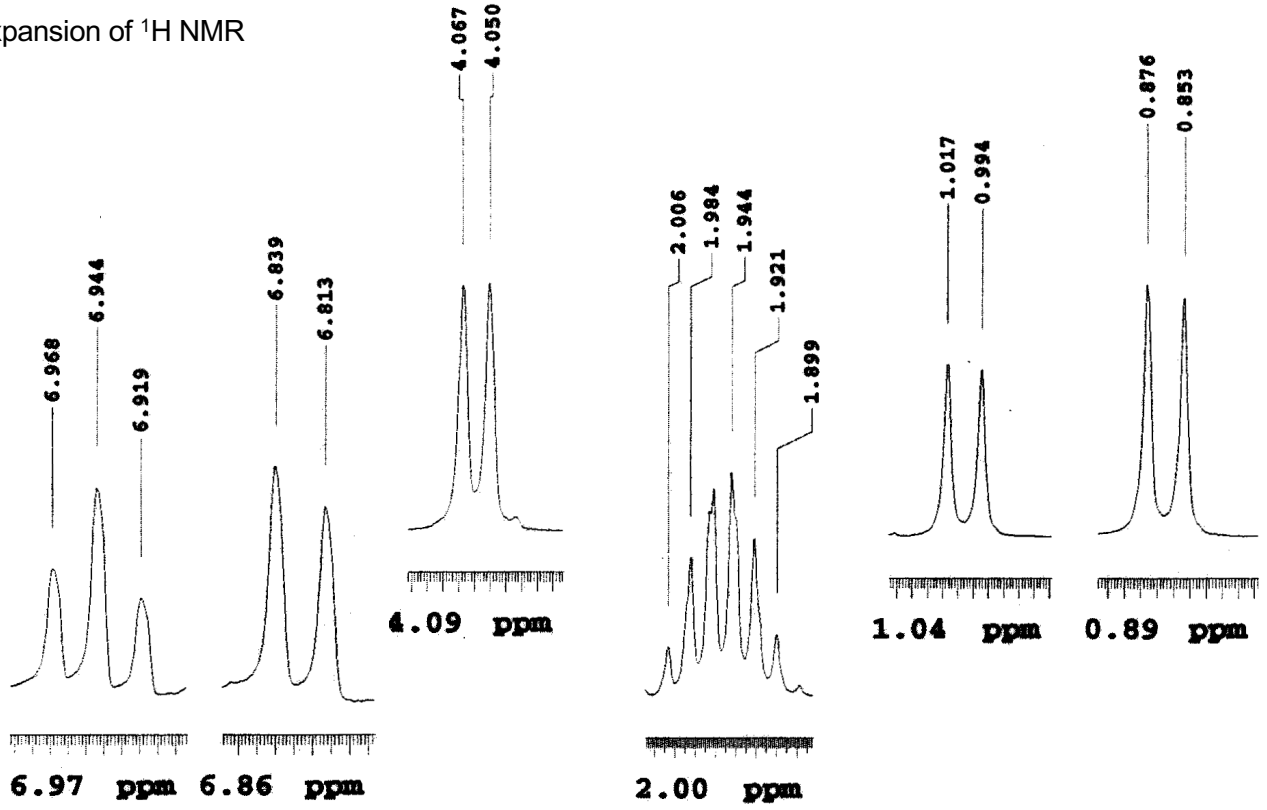


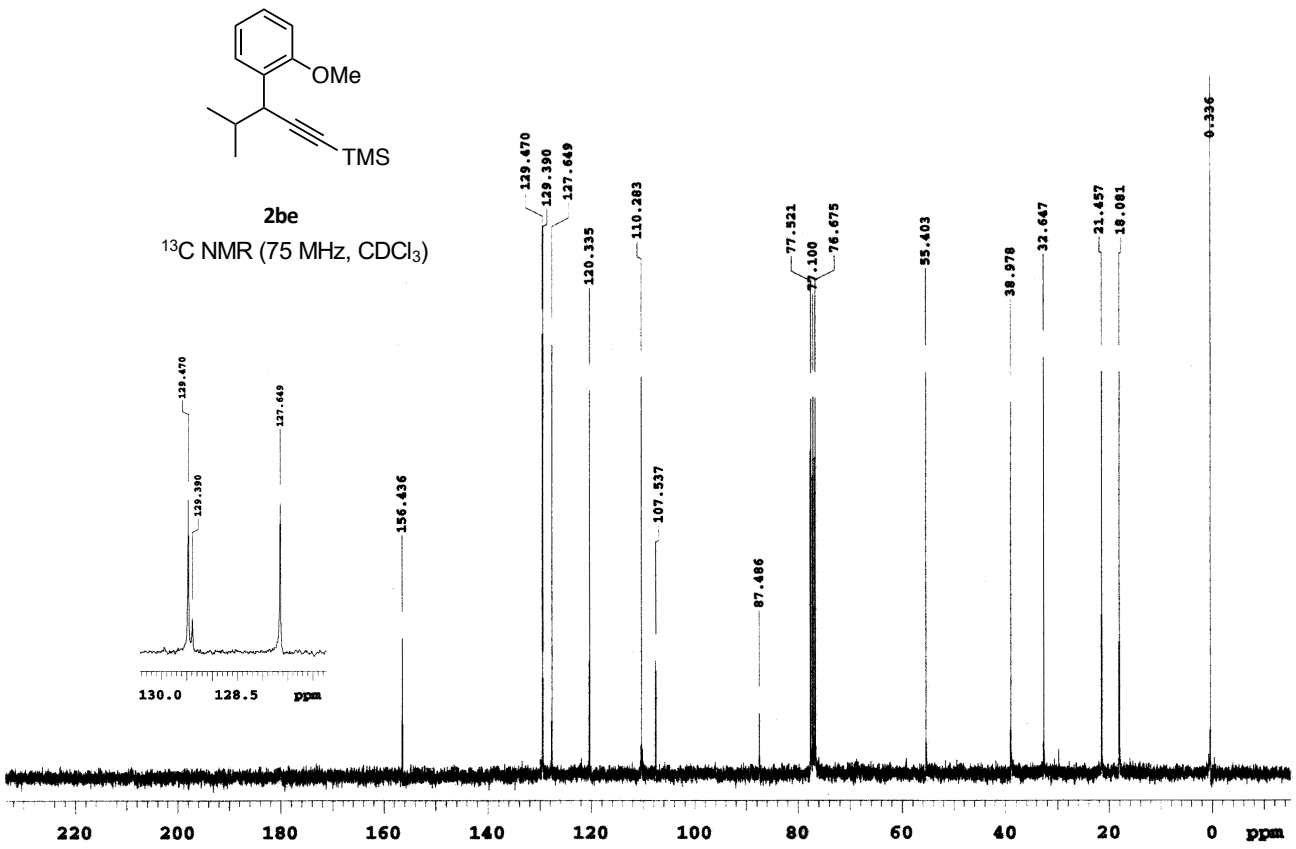


2be

^{1}H NMR (300 MHz, $CDCl_3$)

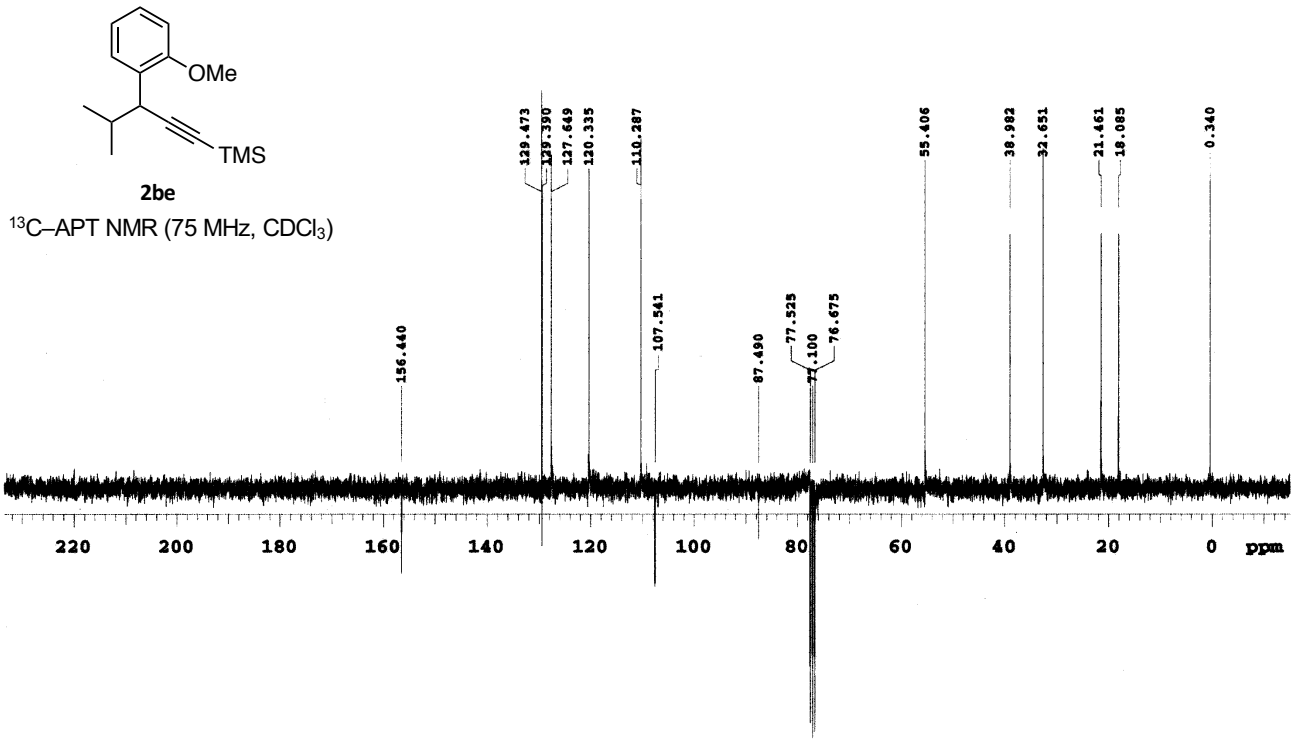
expansion of ^{1}H NMR





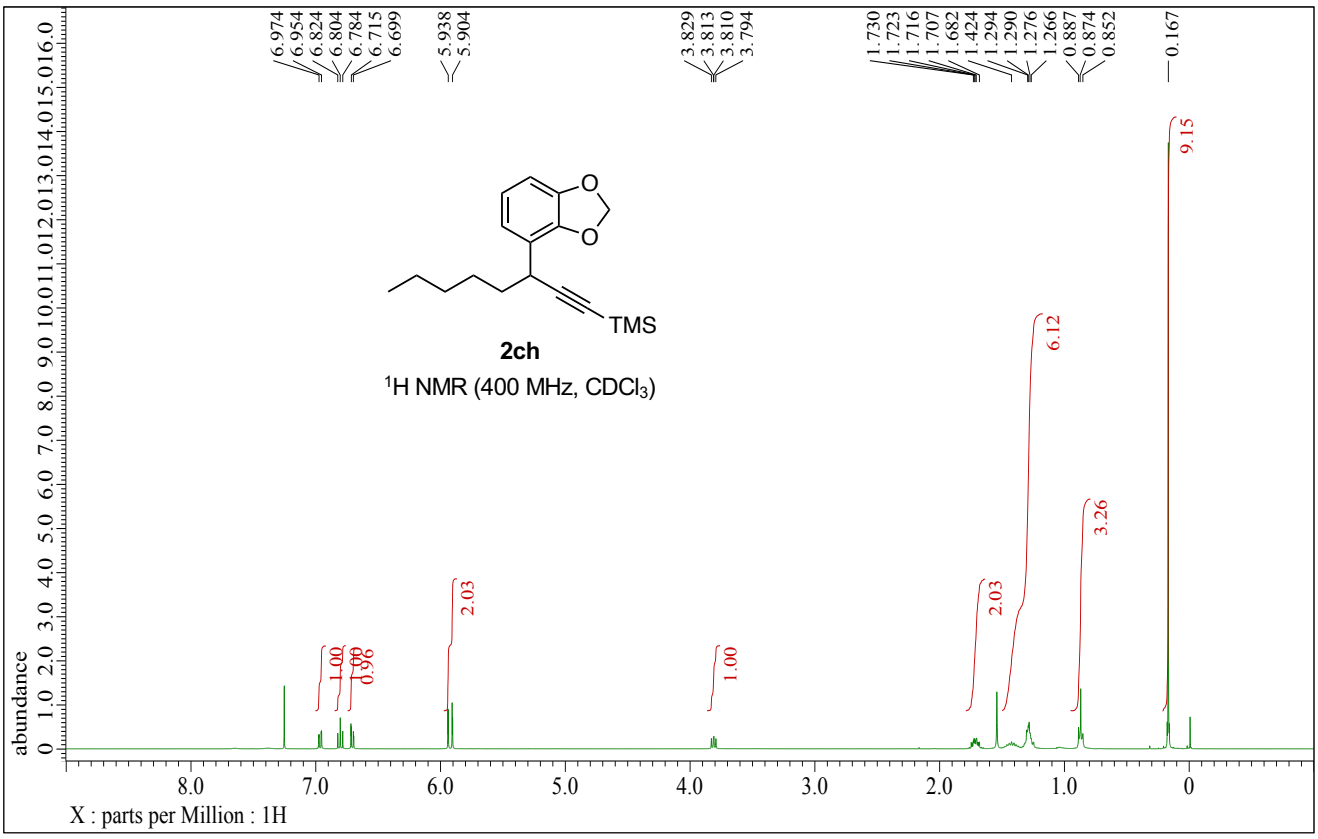
2be

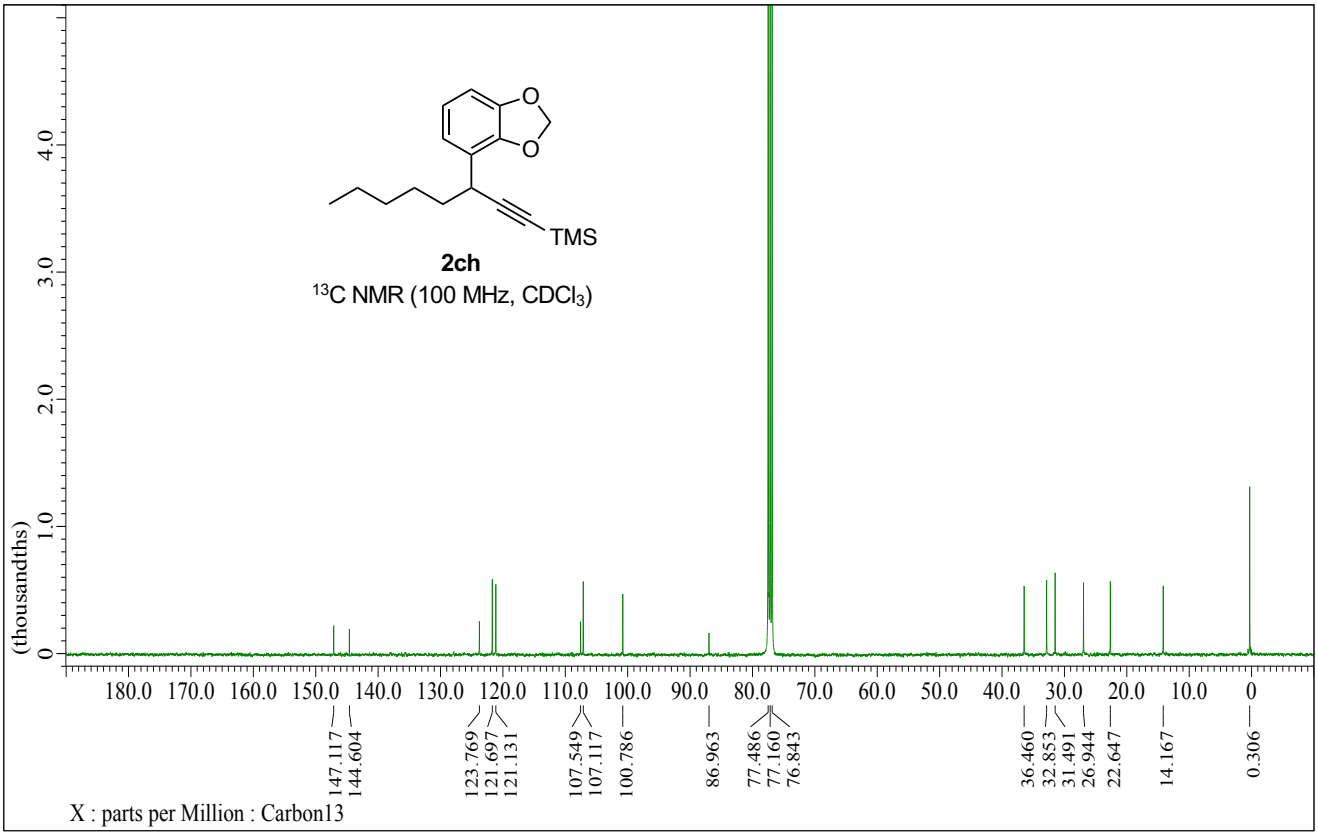
^{13}C NMR (75 MHz, $CDCl_3$)

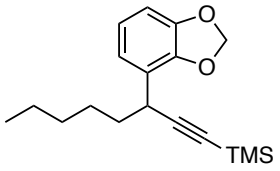


2be

^{13}C–APT NMR (75 MHz, $CDCl_3$)

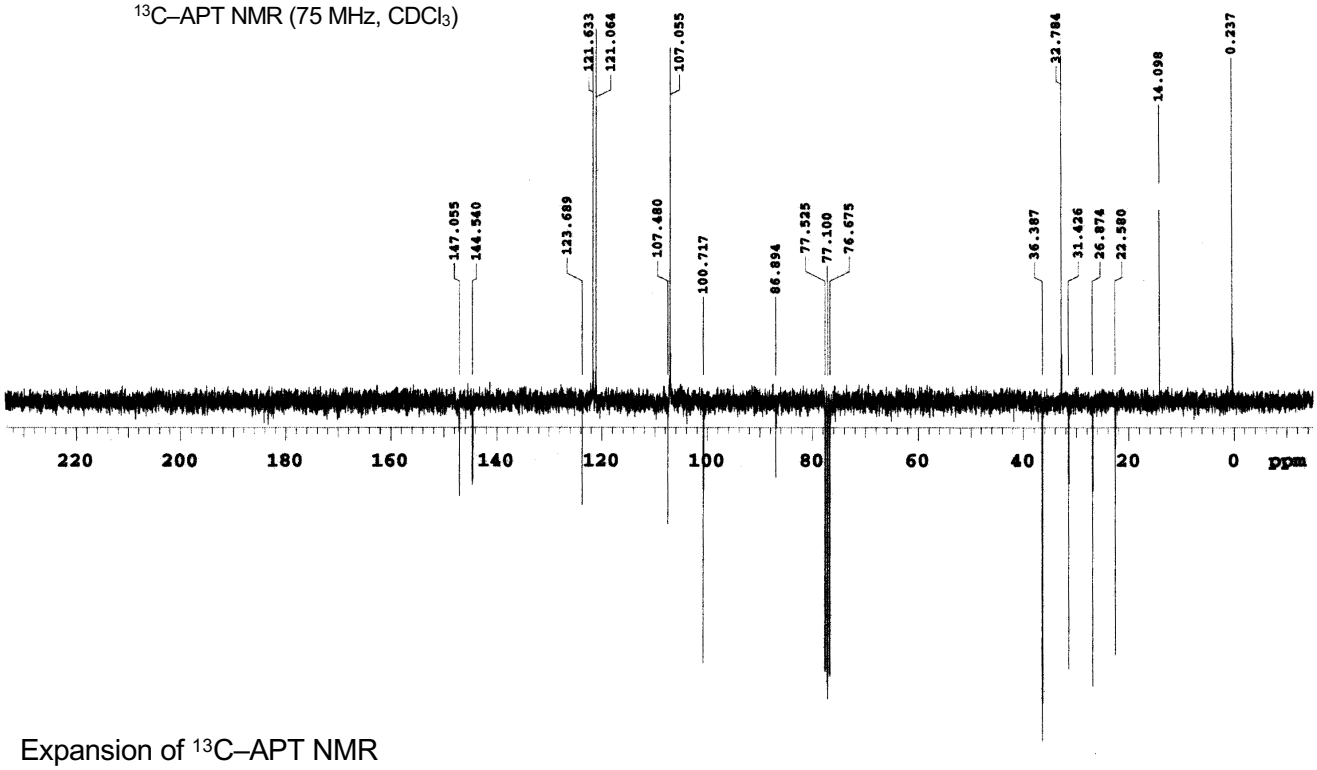

6.974
6.954
6.824
6.804
6.784
6.715
6.699
5.938
5.904
3.829
3.813
3.810
3.794
1.730
1.723
1.716
1.707
1.682
1.424
1.294
1.290
1.276
1.266
0.887
0.874
0.852
0.167
9.15
6.12
3.26
2.03
2.03
1.00
1.00
1.00
0.96
TMS
2ch
1H NMR (400 MHz, CDCl3)
abundance
X : parts per Million : 1H


TMS
2ch
13C NMR (100 MHz, CDCl3)
(thousandths)
147.117
144.604
123.769
121.697
121.131
107.549
107.117
100.786
86.963
77.486
77.160
76.843
36.460
32.853
31.491
26.944
22.647
14.167
0.306
X : parts per Million : Carbon13

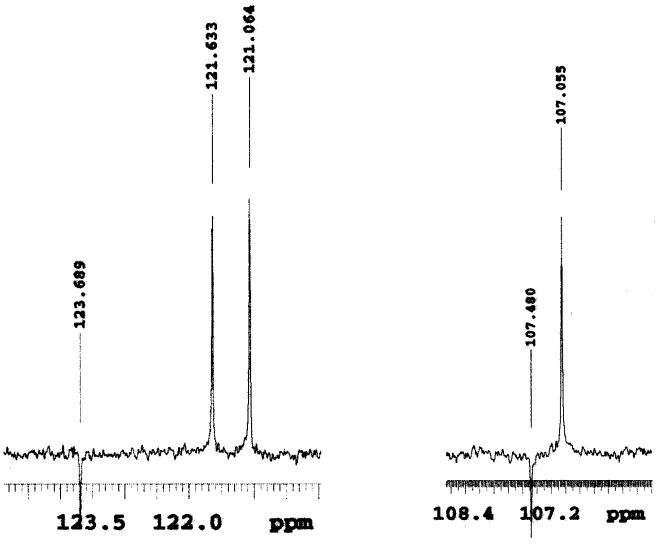


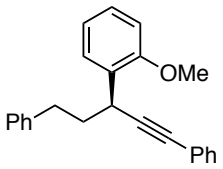
2ch

^{13}C–APT NMR (75 MHz, $CDCl_3$)



Expansion of ^{13}C–APT NMR



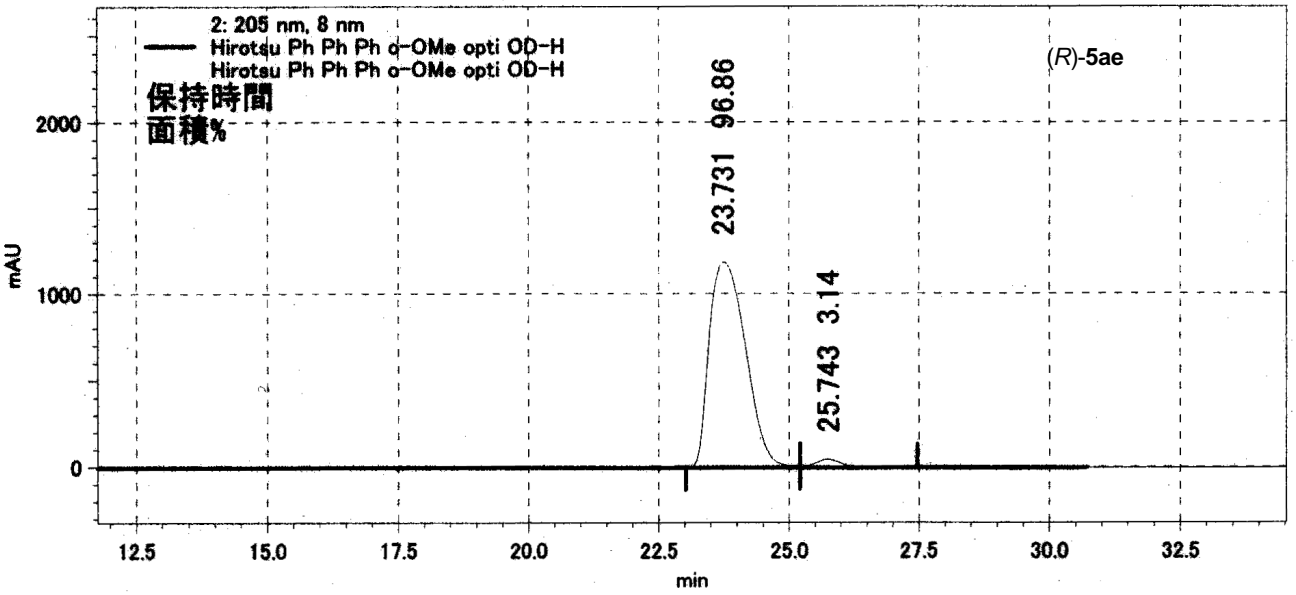


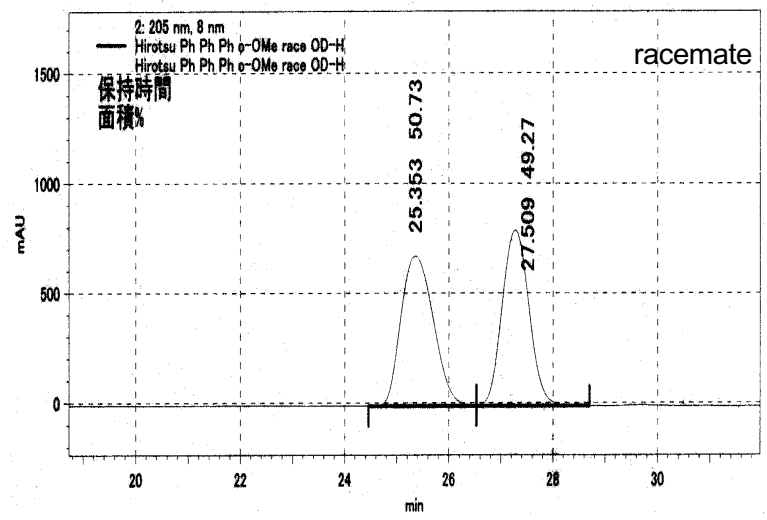
(*R*)-**5ae**

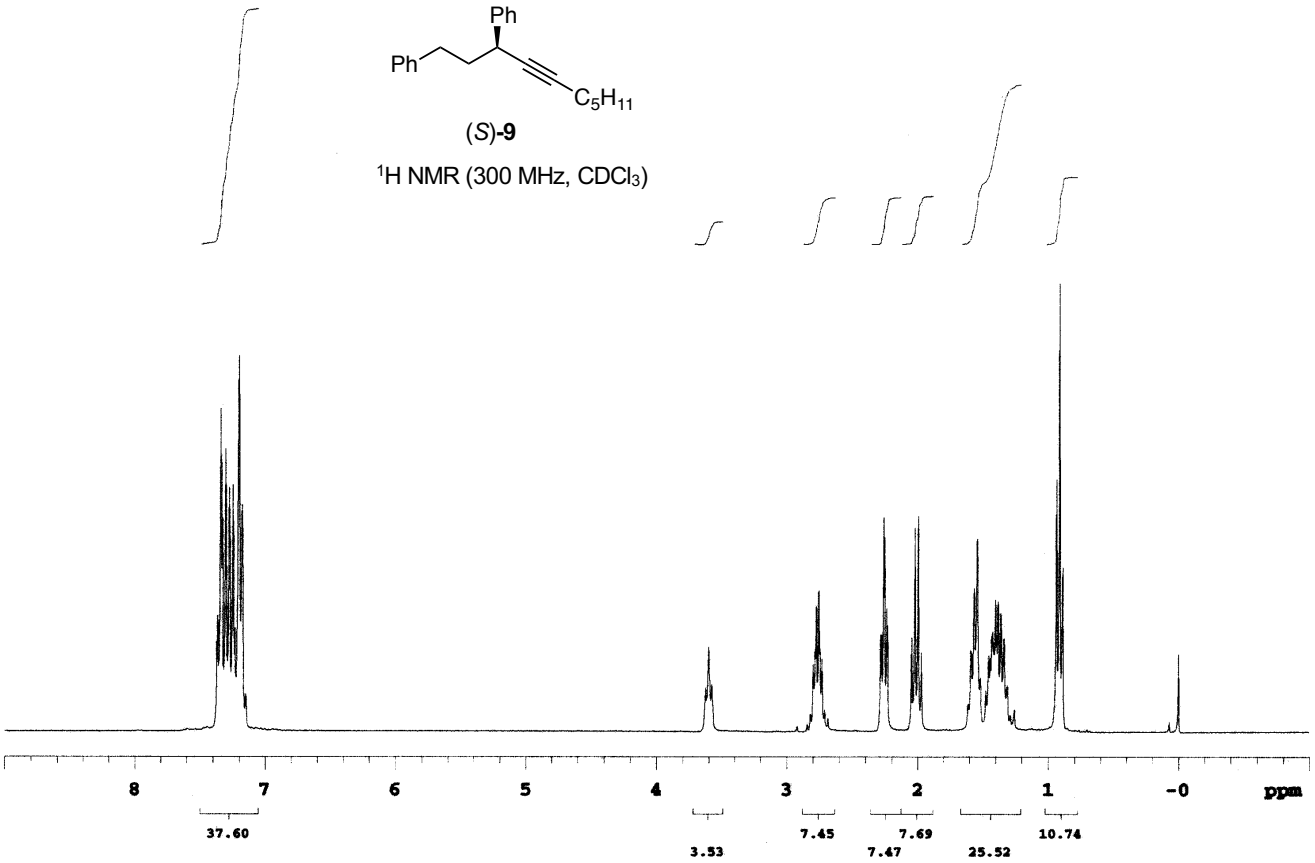
ee
= (96.86 – 3.14) x 100 / (96.86 + 3.14) = 93.72
≈ 94%

es
= 94 x 100 / 96 = 97.92
≈ 98%

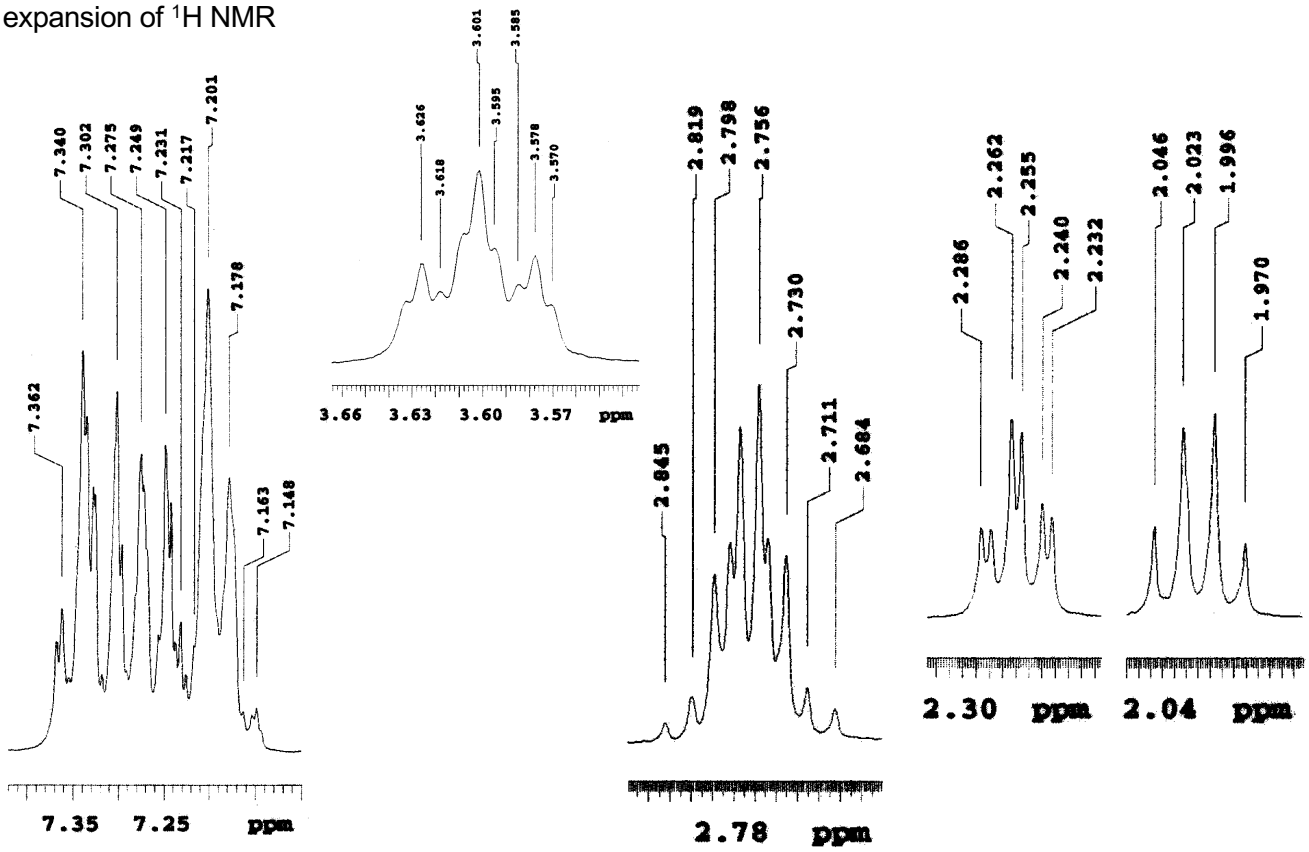
Chiralcel OD-H, hexane/*i*-PrOH = 99.5:0.5, 0.3 mL/min, 25 °C

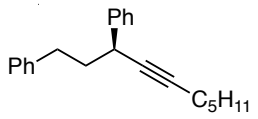






expansion of ^{1}H NMR

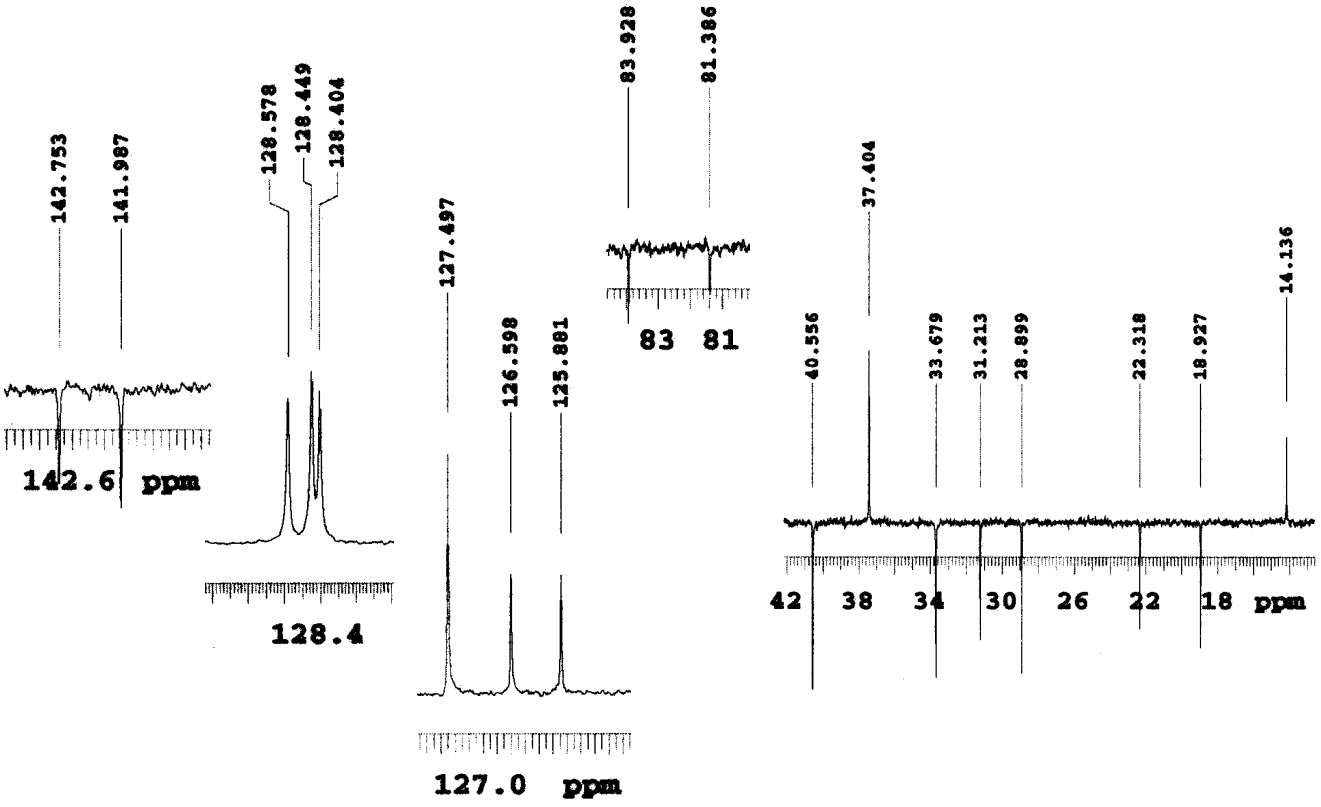


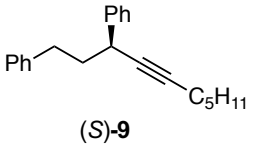


(*S*)-**9**

^{13}C NMR (75 MHz, $CDCl_3$)

Expansion of ^{13}C–APT NMR



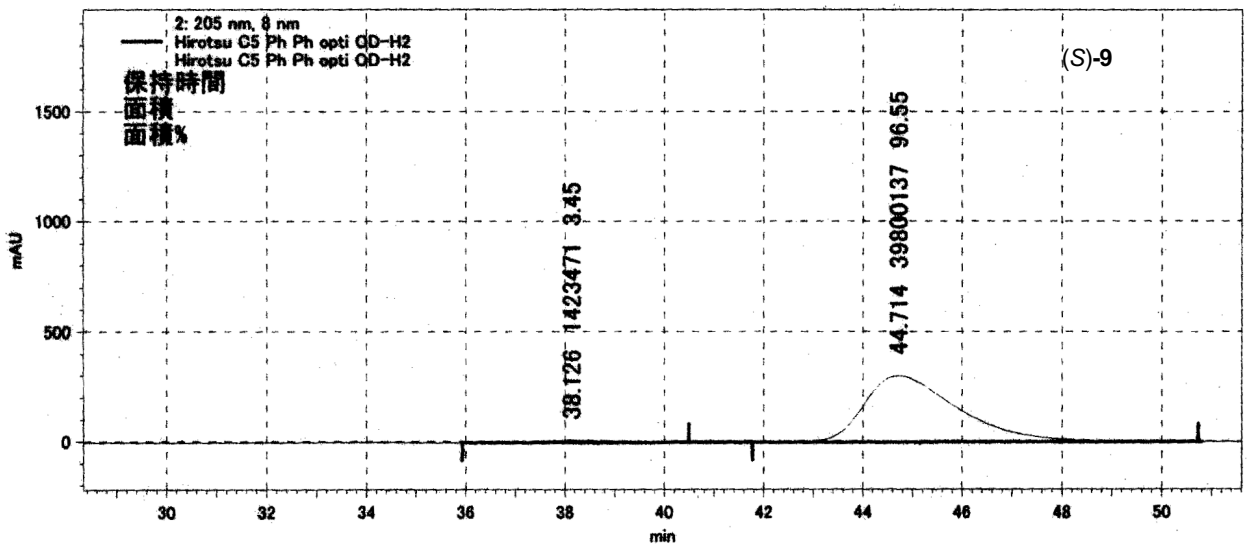


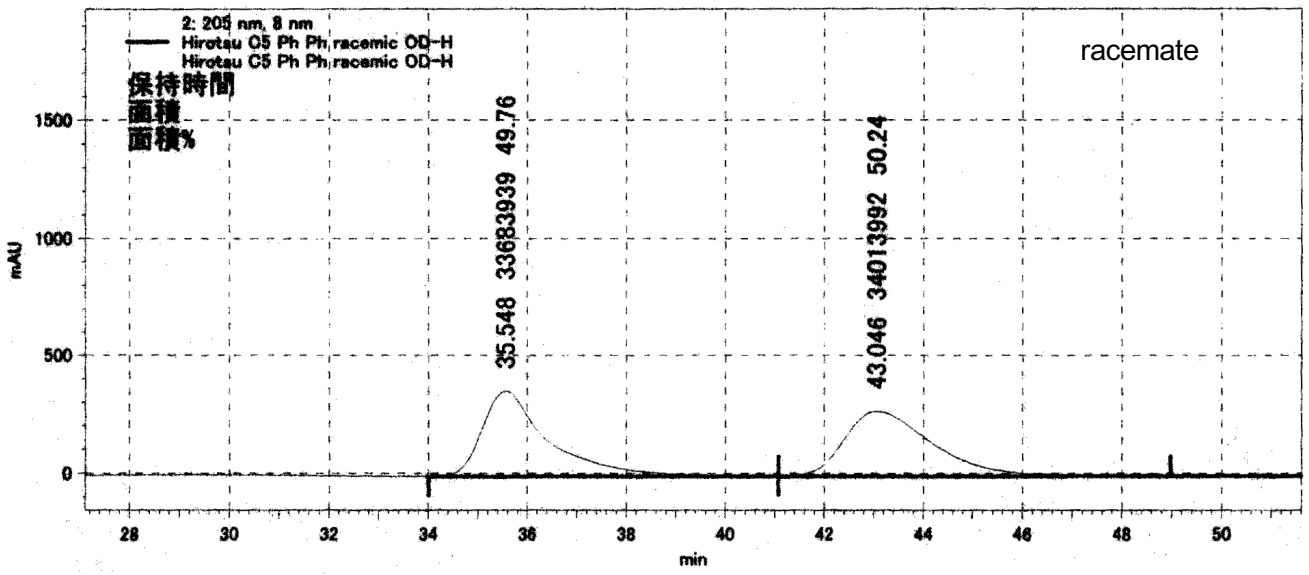
(*S*)-**9**

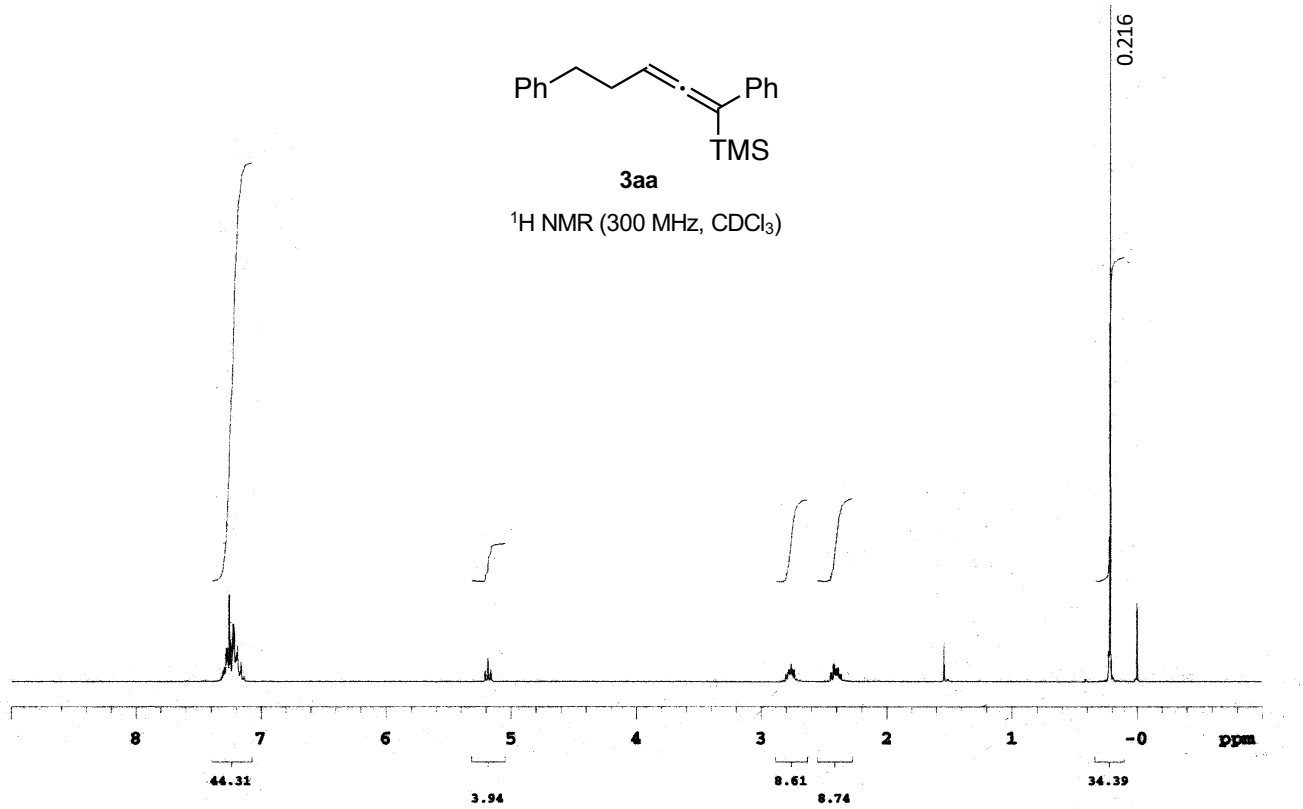
ee
= (96.55 – 3.45) x 100 / (96.55 + 3.45) = 93.1
≈ 93%

es
= 93 x 100 / 95 = 97.89
≈ 98%

Chiralcel OJ-H, hexane/*i*-PrOH = 99.9:0.1, 0.3 mL/min, 25 °C



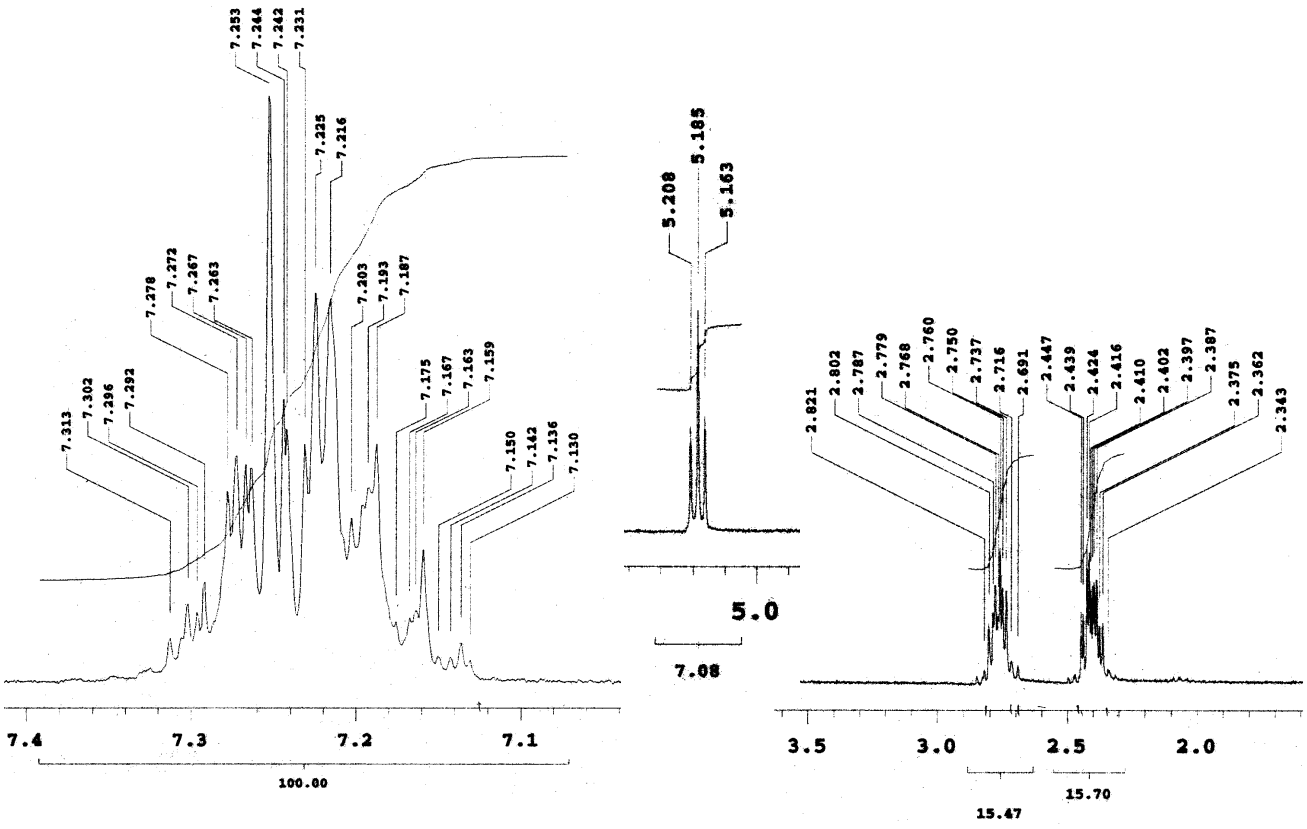


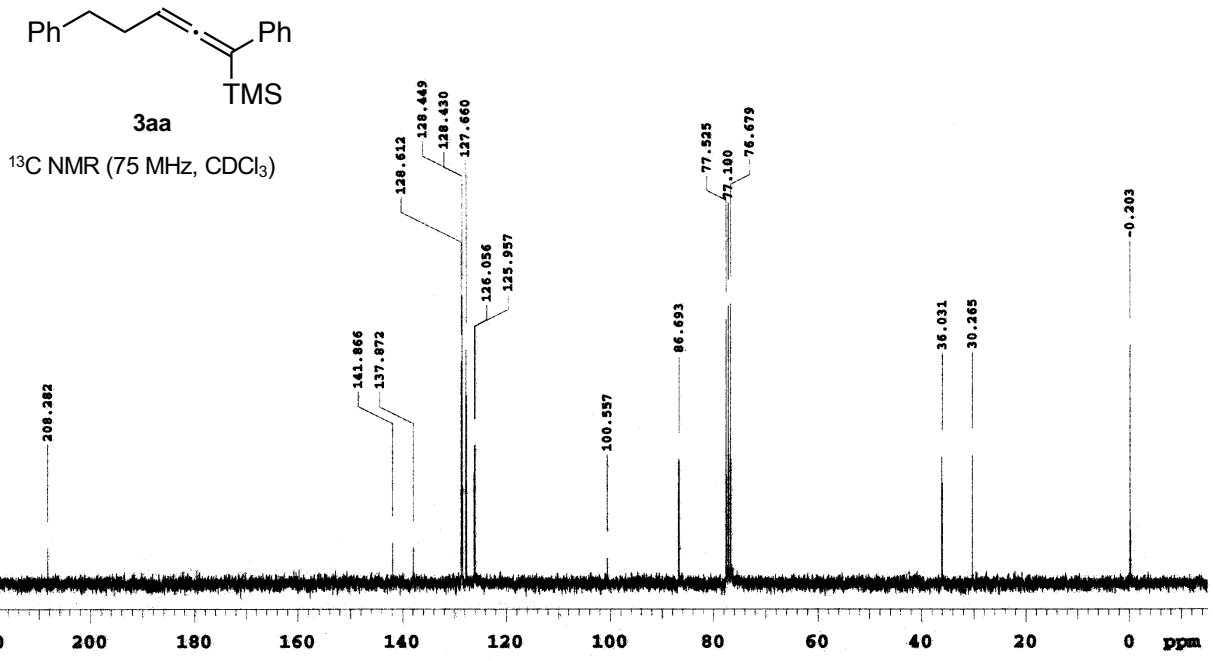


3aa

^{1}H NMR (300 MHz, $CDCl_3$)

expansion of ^{1}H NMR





3aa

^{13}C NMR (75 MHz, $CDCl_3$)

Expansion of ^{13}C–APT NMR
(up, minus; down, plus)