Enantioselective Construction of Quaternary α-Carbon Centers on α-Amino Phosphonates via Catalytic Asymmetric Allylation

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Supporting Information

General and Materials. Specific rotations were measured with a JASCO P-1020 polarimeter. NMR spectra were obtained with a Varian GEMINI-2000 spectrometer (7.0 T). Toluene and THF were distilled from Na–benzophenone ketyl under nitrogen. [Pd(π-allyl)(cod)]BF_4,[1] **1**,[2] and **4**[3] was prepared according to the literature procedures. Other materials were purchased and used without further purification.

Dimethyl (*S*)-[1-(*N*-Acetylamino)-2-oxo-1-{(*E*)-3-phenyl-2-propenyl}propyl]phosphonate (3a). The enantiomeric excess was determined by HPLC analysis with a chiral stationary phase column, SUMICHIRAL OA-4100 (hexane/1,2-dichloroethane/ethanol = 15/5/1): White solid; $[\alpha]^{20}_D$ = +9.6 (*c* 2.25, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 2.04 (s, 3H), 2.41 (s, 3H), 3.18 (dt, *J* = 8.3, 14.7 Hz), 3.63–3.76 (m, 1H), 3.79 (d, *J* = 11.1 Hz, 3H), 3.89 (d, *J* = 10.8 Hz, 3H), 5.95 (dt, *J* = 15.6, 7.5 Hz, 1H), 6.47 (d, *J* = 15.6 Hz, 1H), 6.70 (d, *J* = 6.6 Hz, 1H), 7.17–7.35 (m, 5H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 23.6, 26.0, 33.5, 53.7 (d, *J* = 7.0 Hz), 54.6 (d, *J* = 6.9 Hz), 69.5 (d, *J* = 142.7 Hz), 122.5 (d, *J* = 10.4 Hz), 126.2, 127.5, 128.5, 134.6, 136.7, 169.7 (d, *J* = 5.8 Hz), 201.7; ^{31}P{^{1}H} NMR (121.5 MHz, $CDCl_3$, 85% H_3PO_4 aq) δ 21.7; HRMS (FAB) Calcd for $C_{16}H_{23}NO_5P$: 340.1314. Found: 340.1319 (M + H^+).

Dimethyl [1-(*N*-Acetylamino)-2-oxo-1-{(*E*)-3-phenyl-2-propenyl}butyl]phosphonate (3b). The enantiomeric excess was determined by HPLC analysis with a chiral stationary phase column, SUMICHIRAL OA-4100 (hexane/1,2-dichloroethane/ethanol = 23/7/1): Colorless oil; $[\alpha]^{20}_D$ = +18.6 (*c* 1.33, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 1.11 (t, *J* = 7.2 Hz, 3H), 2.03 (s, 3H), 2.69 (dq, *J* = 18.0, 7.2 Hz, 1H), 2.90 (dq, *J* = 18.0, 7.2 Hz, 1H), 3.19 (dt, *J* = 8.2, 14.5 Hz, 1H), 3.66–3.80 (m, 1H), 3.77 (d, *J* = 11.1 Hz, 3H), 3.88 (d, *J* = 10.8 Hz, 3H), 5.92 (dt, *J* = 15.6, 7.7 Hz, 1H), 6.47 (d, *J* = 15.6 Hz, 1H), 6.74 (d, *J* = 6.6 Hz, 1H), 7.18–7.34 (m, 5H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 8.1, 23.6, 31.4, 33.5, 53.5 (d, *J* = 8.1 Hz), 54.6 (d, *J* = 5.8 Hz), 69.4 (d, *J* = 141.6 Hz), 122.6 (d, *J* = 10.5 Hz), 126.1, 127.5, 128.4, 134.5, 136.7, 169.6 (d, *J* = 5.7 Hz), 204.7; ^{31}P{^{1}H} NMR

(121.5 MHz, $CDCl_3$, 85% H_3PO_4 aq) δ 21.9; HRMS (FAB) Calcd for $C_{17}H_{25}NO_5P$: 354.1470. Found: 354.1480 ($M + H^+$).

Dimethyl [1-(*N*-Acetylamino)-2-oxo-2-phenyl-1-{(*E*)-3-phenyl-2-propenyl}ethyl]phosphonate (3c). The enantiomeric excess was determined by HPLC analysis with a chiral stationary phase column, CHIRALPAK AD (hexane/2-propanol = 85/15): Colorless oil; $[\alpha]^{20}_D$ = +86.0 (*c* 1.13, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$, TMS) δ 1.92, 3.40 (dddd, *J* = 1.1, 8.1, 14.6, 20.1 Hz, 1H), 3.61 (dddd, *J* = 1.3, 6.6, 9.6, 14.6 Hz, 1H), 3.81 (d, *J* = 10.8, 3H), 3.83 (d, *J* = 11.1 Hz, 3H), 6.03 (ddd, *J* = 6.6, 8.1, 15.6 Hz, 1H), 6.29 (d, *J* = 15.6 Hz, 1H), 6.84 (d, *J* = 7.8 Hz, 1H), 7.17–7.30 (m, 5H), 7.40–7.48 (m, 2H), 7.50–7.57 (m, 1H), 8.09–8.15 (m, 2H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 23.3, 36.2, 54.2 (d, *J* = 8.1 Hz), 54.5 (d, *J* = 7.0 Hz), 68.6 (d, *J* = 141.6 Hz), 123.2 (d, *J* = 6.9 Hz), 126.2, 127.5, 128.1, 128.5, 128.9, 132.5, 134.8, 136.1, 137.0, 169.4 (d, *J* = 8.1 Hz), 195.7; $^{31}P\{^1H\}$ NMR (121.5 MHz, $CDCl_3$, 85% H_3PO_4 aq) δ 22.7; HRMS (FAB) Calcd for $C_{21}H_{25}NO_5P$: 402.1470. Found: 402.1460 ($M + H^+$).

Dimethyl [1-(*N*-Acetylamino)-1-{(*E*)-2-hexenyl}-2-oxopropyl]phosphonate (3d). The enantiomeric excess was determined by HPLC analysis with a chiral stationary phase column, SUMICHIRAL OA-4100 (hexane/1,2-dichloroethane/ethanol = 50/15/1): Colorless oil; $[\alpha]^{20}_D$ = +14.7 (*c* 1.40, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$, TMS) δ 0.85 (t, *J* = 7.4 Hz, 3H), 1.33 (sextet, *J* = 7.4 Hz, 2H), 1.93 (q, *J* = 7.2 Hz, 2H), 2.05 (s, 3H), 2.37 (s, 3H), 2.92 (ddd, *J* = 8.3, 12.0, 14.6 Hz, 1H), 3.53–3.66 (m, 1H), 3.76 (d, *J* = 11.1 Hz, 3H), 3.88 (d, *J* = 11.1 Hz, 3H), 5.12 (dt, *J* = 15.2, 7.2 Hz, 1H), 5.55 (dt, *J* = 15.2, 6.9 Hz, 1H), 6.65 (d, *J* = 5.4 Hz, 1H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 13.4, 22.3, 23.8, 26.0, 32.8, 34.6, 53.6 (d, *J* = 8.2 Hz), 54.7 (d, *J* = 5.8 Hz), 69.8 (d, *J* = 143.9 Hz), 122.1 (d, *J* = 11.6 Hz), 136.3, 169.3 (d, *J* = 4.7 Hz), 201.9; $^{31}P\{^1H\}$ NMR (121.5 MHz, $CDCl_3$, 85% H_3PO_4 aq) δ 21.8; HRMS (FAB) Calcd for $C_{13}H_{25}NO_5P$: 306.1470. Found: 306.1461 ($M + H^+$).

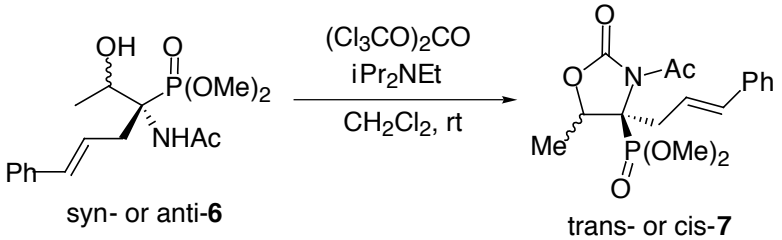
Dimethyl [1-(*N*-Acetylamino)-2-oxo-1-(2-propenyl)propyl]phosphonate (3e). The enantiomeric excess was determined by HPLC analysis with a chiral stationary phase column, SUMICHIRAL OA-4100 (hexane/1,2-dichloroethane/ethanol = 15/5/1): Colorless oil; $[\alpha]^{20}_D$ = +30.5 (*c* 1.82, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$, TMS) δ 2.06 (s, 3H), 2.36 (s, 3H), 2.99 (dt, *J* = 8.1, 14.7 Hz, 1H), 3.50–3.66 (m, 1H), 3.78 (d, *J* = 10.8 Hz, 3H), 3.88 (d, *J* = 10.8 Hz, 3H), 5.09–5.21 (m, 2H), 5.51–5.67 (m, 1H), 6.74 (d, *J* = 5.7 Hz); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 23.5, 25.9, 34.0, 53.6 (d, *J* = 6.9 Hz), 54.5 (d, *J* = 5.8 Hz), 69.2 (d, *J* = 143.8 Hz), 119.7, 131.1 (d, *J* = 10.5 Hz), 169.5 (d, *J* = 5.8 Hz), 201.7; $^{31}P\{^1H\}$ NMR (121.5 MHz, $CDCl_3$, 85% H_3PO_4 aq) δ 21.7; HRMS (FAB) Calcd for $C_{10}H_{19}NO_5P$: 264.1001. Found: 264.0998 ($M + H^+$).

Methyl 1-(*N*-Acetylamino)-1-(dimethylphosphono)-5-phenyl-4-pentenoate (5). The enantiomeric excess was determined by HPLC analysis with a chiral stationary phase column, SUMICHIRAL OA-4100 (hexane/1,2-dichloroethane/ethanol = 23/7/1): Colorless oil; $[\alpha]^{20}_{D}$ = +14.7 (*c* 1.40, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 2.03 (s, 3H), 3.22 (dt, *J* = 8.1, 15.1 Hz, 1H), 3.46–3.58 (m, 1H), 3.84 (d, *J* = 11.1 Hz, 3H), 3.86 (s, 3H), 3.87 (d, *J* = 10.8 Hz, 3H), 6.05 (dt, *J* = 15.9, 7.2 Hz, 1H), 6.37 (d, *J* = 6.3 Hz, 1H), 6.48 (d, *J* = 15.9 Hz, 1H), 7.19–7.36 (m, 5H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 23.6, 34.8, 53.5, 54.1 (d, *J* = 6.9 Hz), 54.6 (d, *J* = 6.9 Hz), 64.1 (d, *J* = 145.0 Hz), 123.0 (d, *J* = 9.3 Hz), 126.3, 127.6, 128.5, 134.7, 137.0, 169.1, 169.4 (d, *J* = 6.9 Hz); ^{31}P{^{1}H} NMR (121.5 MHz, $CDCl_3$, 85% H_3PO_4 aq) δ 21.4; HRMS (FAB) Calcd for $C_{16}H_{23}NO_6P$: 355.1263. Found: 356.1270 (M + H$^+$).

Dimethyl (2*S*,3*S*)-[1-(*N*-Acetylamino)-2-hydroxy-1-{(*E*)-3-phenyl-2-propenyl}propyl]phosphonate (*syn*-6). Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 1.27 (d, *J* = 6.3 Hz, 3H), 2.07 (s, 3H), 2.62–2.80 (m, 1H), 2.94 (ddd, *J* = 7.1, 14.7, 18.6 Hz, 1H), 3.81 (d, *J* = 10.5 Hz, 3H), 3.83 (d, *J* = 10.5 Hz, 3H), 4.23 (dq, *J* = 3.9, 6.3 Hz, 1H), 5.86 (s, 1H), 6.35 (dt, *J* = 15.9, 7.1 Hz, 1H), 6.49 (d, *J* = 15.9 Hz, 1H), 7.22–7.41 (m, 5H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 17.1 (d, *J* = 8.2 Hz), 24.2, 37.3, 53.0 (d, *J* = 8.1 Hz), 53.7 (d, *J* = 6.9 Hz), 64.9 (d, *J* = 154.3 Hz), 68.4, 123.6, 126.4, 128.7, 134.9, 136.8, 171.1; ^{31}P{^{1}H} NMR (121.5 MHz, $CDCl_3$, 85% H_3PO_4 aq) δ 28.3.

Dimethyl (2*S*,3*R*)-[1-(*N*-Acetylamino)-2-hydroxy-1-{(*E*)-3-phenyl-2-propenyl}propyl]phosphonate (*anti*-6). Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 1.40 (d, *J* = 6.3 Hz, 3H), 2.06 (s, 3H), 2.68 (ddd, *J* = 9.1, 11.7, 14.7 Hz, 1H), 3.47–3.59 (m, 1H), 3.82 (d, *J* = 10.8 Hz, 3H), 3.84 (d, *J* = 10.2 Hz, 3H), 4.04 (dq, *J* = 24.5, 6.3 Hz, 1H), 6.15 (ddd, *J* = 6.0, 9.1, 15.9 Hz, 1H), 6.37 (d, *J* = 3.3 Hz, 1H), 6.49 (d, *J* = 15.9 Hz, 1H), 7.19–7.39 (m, 5H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 18.4, 24.3, 33.6, 52.7 (d, *J* = 7.0 Hz), 54.1 (d, *J* = 8.1 Hz), 64.1 (d, *J* = 149.6 Hz), 69.6, 123.5 (d, *J* = 9.3 Hz), 126.2, 127.5, 128.5, 134.4, 137.0, 170.6 (d, *J* = 5.7 Hz); ^{31}P{^{1}H} NMR (121.5 MHz, $CDCl_3$, 85% H_3PO_4 aq) δ 27.5; HRMS (FAB) Calcd for $C_{16}H_{25}NO_5P$: 342.1470. Found: 342.1455 (M + H$^+$).

Assignments of Relative Configurations between 2- and 3-Position of *syn*- and *anti*-6. For determination of relative configuration of **6**, both of the diastereomers were converted into cyclic carbamate **7** as follows (Scheme S-1): To a solution of *syn*- or *anti*-**6** (46.7



syn- or anti-**6** trans- or cis-**7**

mg, 137 μmol) and diisopropylethylamine (60 μl, 344 μmol) in CH_2Cl_2 (0.5 ml) was added bis(trichloromethyl) carbonate (26.7 mg, 90.0 μmol) at 0 ˚C. The mixture was stirred at room temperature for 22 h. After 28% NH_3 aq (0.1 ml) was added, the mixture was passed through a short column of Na2SO4 (EtOAc) and evaporated under reduced pressure. The residue was purified by preparative TLC (EtOAc/MeOH) to give *trans*- or *cis*-**7**, respectively. *trans*-**7** (from *syn*-**6**): Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 1.63 (d, *J* = 6.6 Hz, 3H), 2.49 (s, 3H), 2.60–2.70 (m, 1H), 3.26 (dt, *J* = 15.0, 9.9 Hz, 1H), 3.77 (d, *J* = 11.1 Hz, 3H), 3.99 (d, *J* = 11.1 Hz, 3H), 4.96 (dq, *J* = 13.0, 6.6 Hz, 1H), 5.99 (ddd, *J* = 5.7, 9.5, 15.5 Hz, 1H), 6.46 (d, *J* = 15.5 Hz, 1H), 7.20–7.38 (m, 5H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 14.4 (d, *J* = 2.3 Hz), 24.3, 31.6 (d, *J* = 4.6 Hz), 52.4 (d, *J* = 8.2 Hz), 55.7 (d, *J* = 7.0 Hz), 66.1 (d, *J* = 164.8 Hz), 75.6 (d, *J* = 2.3 Hz), 121.4 (d, *J* = 11.6 Hz), 126.4, 128.0, 128.7, 136.48, 136.53, 152.7, 171.4; ^{31}P{^{1}H} NMR (121.5 MHz, $CDCl_3$, 85% H_3PO_4 aq) δ 24.2; HRMS (FAB) Calcd for $C_{17}H_{23}NO_6P$: 368.1263. Found: 368.1262 (M + H^+). *cis*-**7** (from *anti*-**6**): Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 1.65 (d, *J* = 6.6 Hz, 3H), 2.55 (s, 3H), 2.70–2.81 (m, 1H), 3.28–3.41 (m, 1H), 3.85 (d, *J* = 10.5 Hz, 3H), 3.90 (d, *J* = 10.8 Hz, 3H), 4.58 (dq, *J* = 20.4, 6.6 Hz, 1H), 6.00 (dt, *J* = 15.6, 7.7 Hz, 1H), 6.48 (*J* = 15.6 Hz, 1H), 7.23–7.35 (m, 5H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 16.1 (d, *J* = 3.5 Hz), 25.1, 35.1 (d, *J* = 5.8 Hz), 53.3 (d, *J* = 6.9 Hz), 54.0 (d, *J* = 6.9 Hz), 66.8 (d, *J* = 161.3 Hz), 76.6, 121.2 (d, *J* = 10.4 Hz), 126.4, 128.0, 128.7, 136.4, 136.5, 153.3, 170.9; ^{31}P{^{1}H} NMR (121.5 MHz, $CDCl_3$, 85% H_3PO_4 aq) δ 21.7; HRMS (FAB) Calcd for $C_{17}H_{23}NO_6P$: 368.1263. Found: 368.1256 (M + H^+).

Representative results of ^{1}H{^{1}H} nOe experiments of the cyclic carbamates, *trans*- and *cis*-**7**, were summarized in Figure S-1. These nOe enhancements suggested that alcohol **6** obtained preferentially by the reduction of **3a** in MeOH possesses *syn*-(2*S**,3*S**)-configuration and that in ^{t}BuOH was *anti*-(2*S**,3*R**).

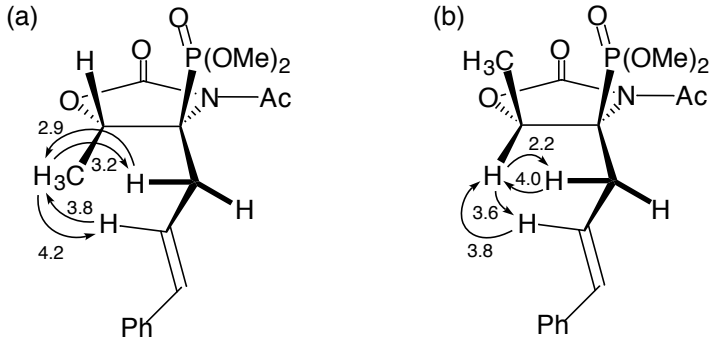


Figure S-1. Representative results of ^{1}H{^{1}H} nOe (% enhancement) of cyclic carbamates of **6** obtained through the reduction of **3a** (a) in MeOH, and (b) in ^{t}BuOH.

Determinations of Absolute Configurations of *syn*-6. The absolute configuration of *syn*-**6**, obtained by the reduction of **3a** with Bu_4NBH_4 in MeOH, were determined by Trost's method as follows: A solution of *syn*-**6** (8.1 mg, 24 μmol), (*R*)-*O*-methylmanderic acid (7.9 mg, 48 μmol), DCC (15.5 mg, 75 μmol) and DMAP (0.3 mg, 2.5 μmol) in CH_2Cl_2 (0.3 ml) was stirred for 28 h at room temperature. The mixture was filtered and evaporated under reduced pressure. The residue was purified by preparative TLC, giving *O*-methylmandelate of *syn*-**6** (7.3 mg, 63% yield) as a mixture of the diastereomers. The diastereo ratio corresponded with the enantiomeric excess of starting **3a** approximately.

Representative results of ^{1}H NMR measurement of the mixtures are summarized in Figure S-2. The results indicate the absolute configurations of *syn*-**6** to be (2*S*,3*S*), respectively.

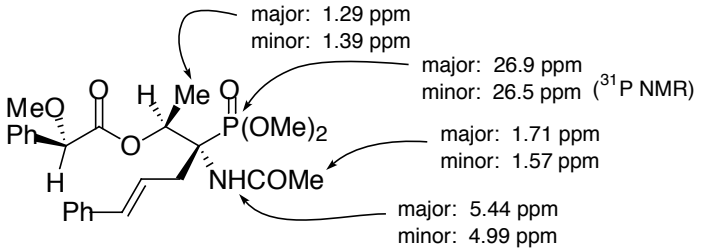


Figure S-2. Representative ^{1}H NMR chemical shifts for (*R*)-*O*-methylmandelate derivative of *syn*-**6**.

References

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(2) Kitamura, M.; Tokunaga, M.; Pham, T.; Lubell, W. D.; Noyori, R. *Tetrahedron Lett.* **1995**, *36*, 5769.

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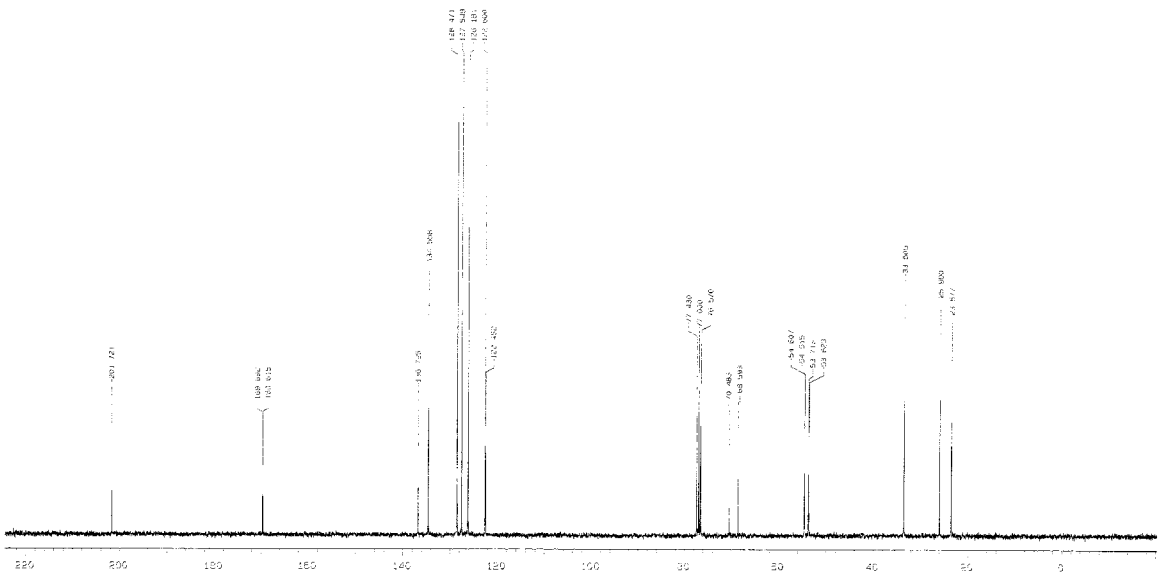

Figure S-1. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of **3a**.

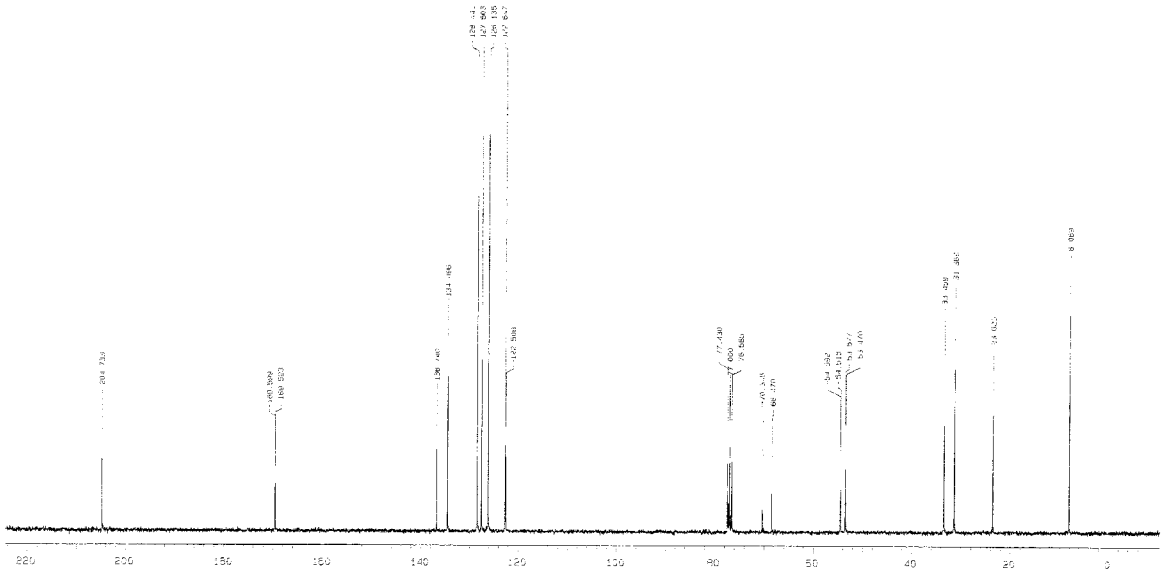

Figure S-2. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of **3b**.

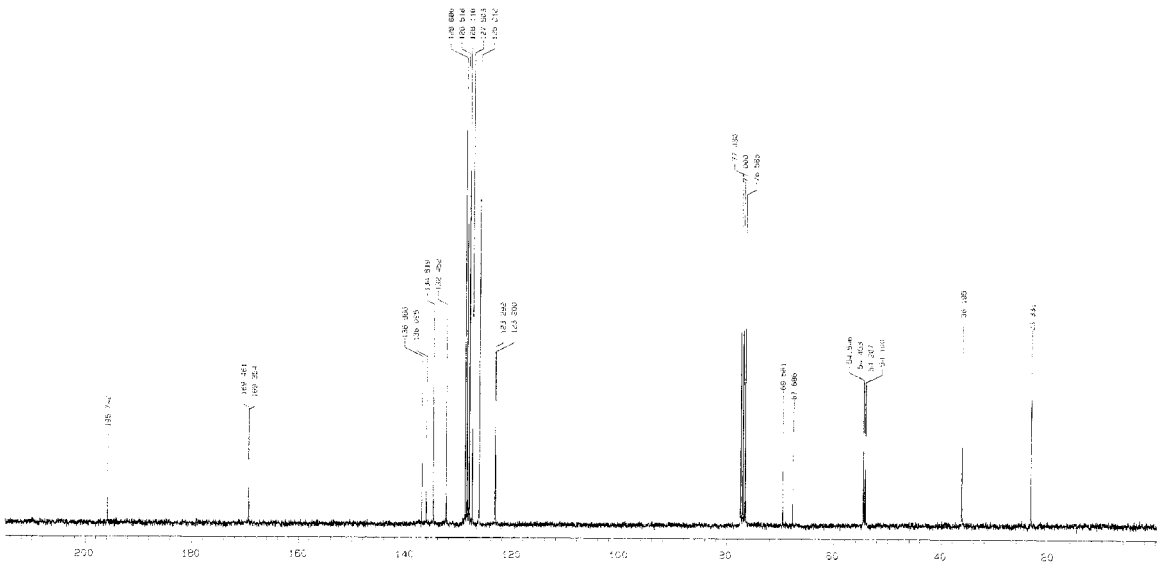

Figure S-3. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of **3c**.

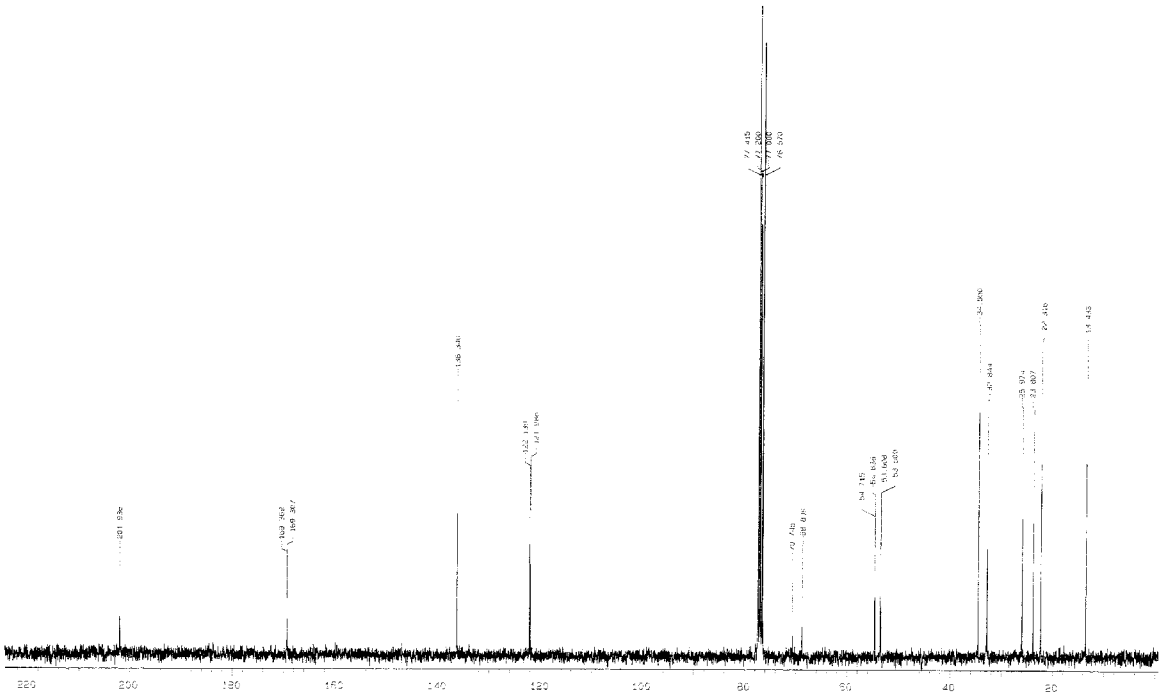

Figure S-4. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of **3d**.

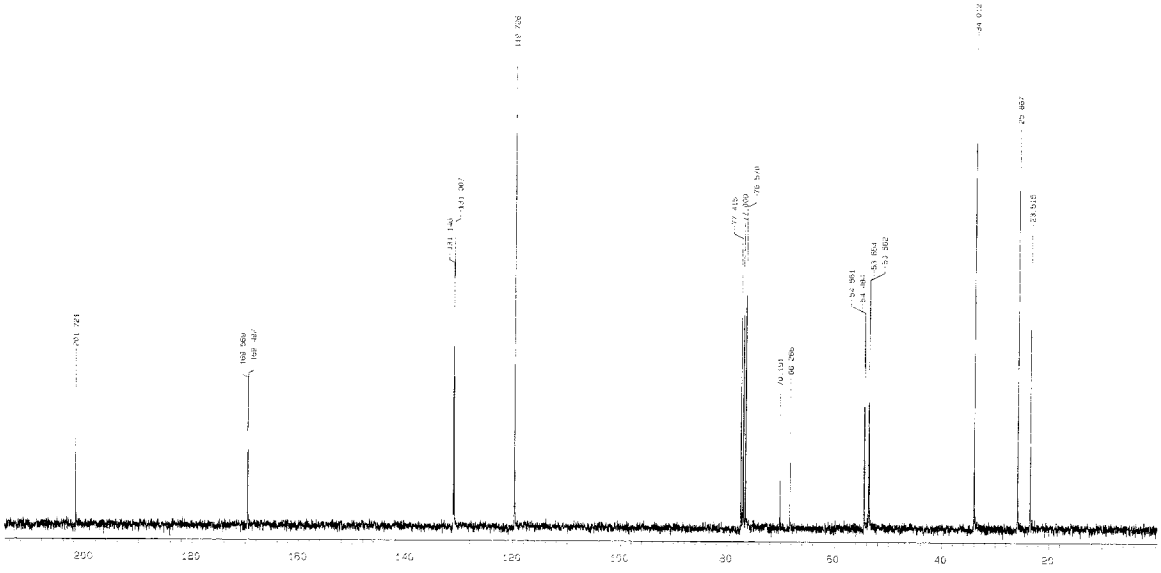

Figure S-5. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of **3e**.

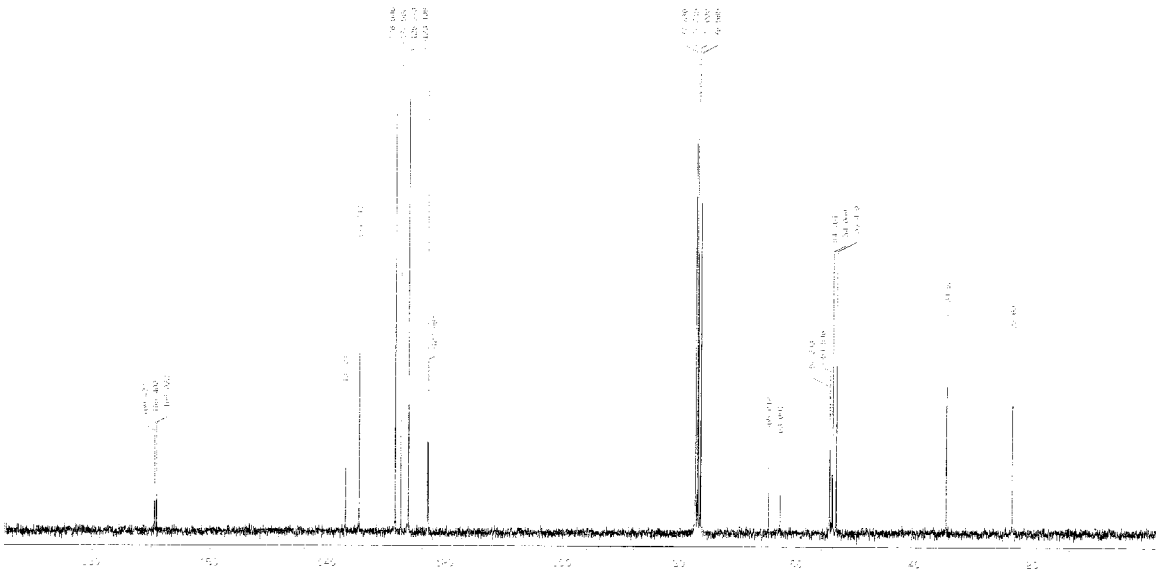

Figure S-6. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of **5**.

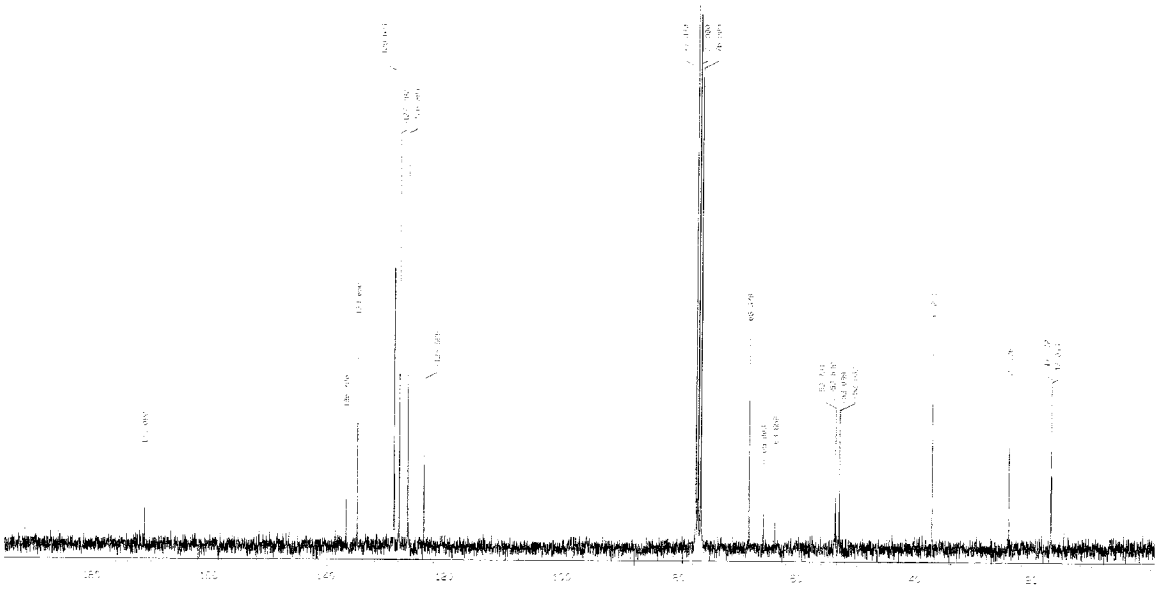

Figure S-7. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of *anti*-**6**.

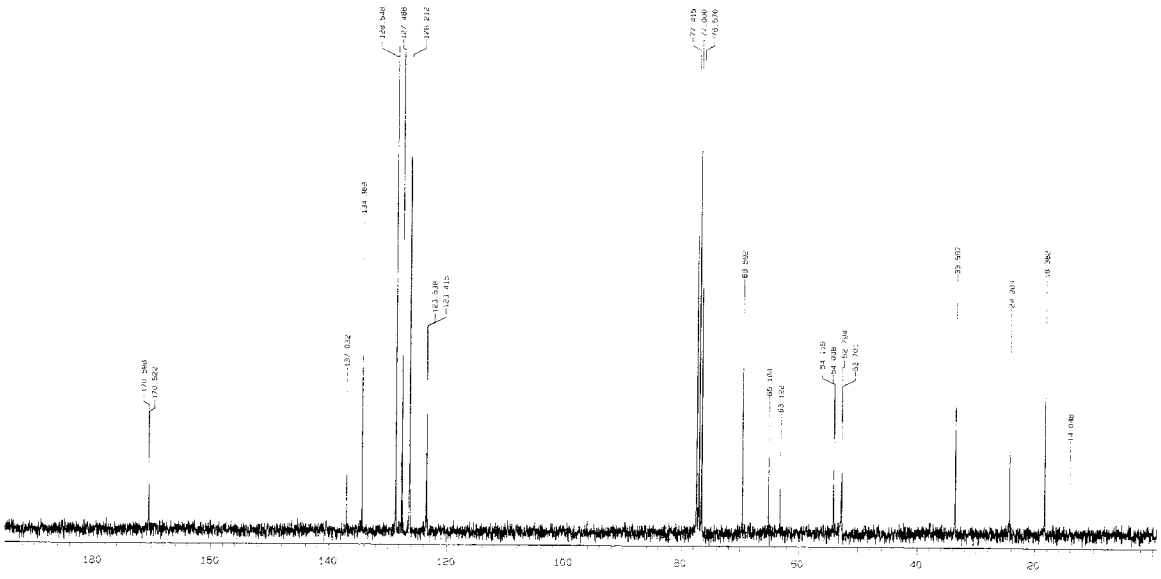

Figure S-8. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of *syn*-**6**.