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Supporting Information

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Umpolung of Hemiaminals: Titanocene-Catalyzed Dehydroxylative Radical Coupling Reactions with Activated Alkenes**

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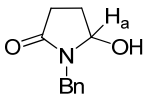
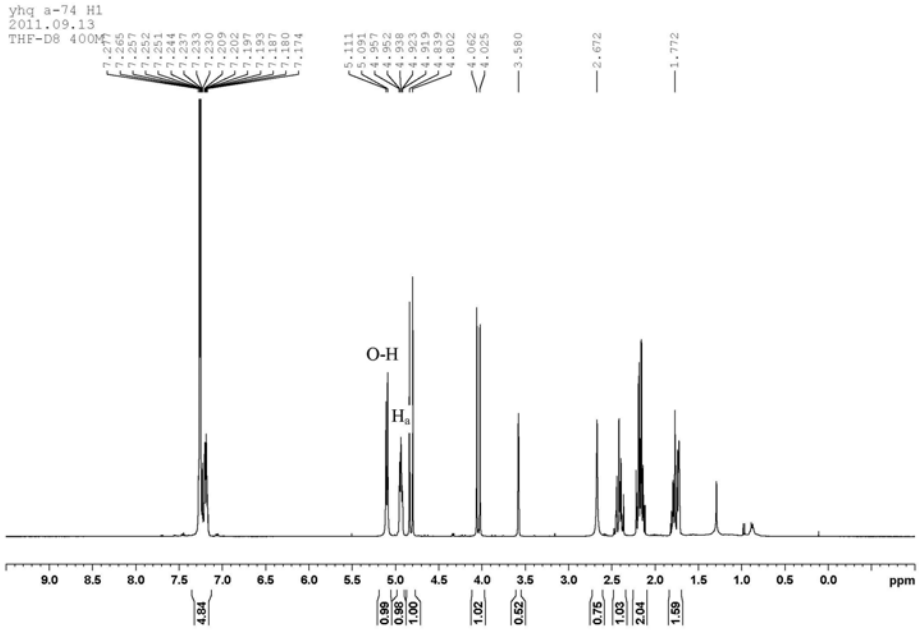
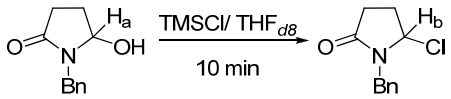
General. Infrared spectra were measured with a Nicolet Avatar 360 FT-IR spectrometer using film KBr pellet techniques. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ on a Bruker Av400 or 500 spectrometer with tertramethylsilane (TMS) as an internal standard. Chemical shifts are expressed in δ (ppm) units downfield from TMS. Mass spectra were recorded by Bruke Dalton Esquire 3000 plus LC-MS apparatus (ESI direct injection). HRMS spectra were recorded on a QSTAR Pulsar/LC/MS/MS System, ESI-QTOF instrument (Applied Biosystem, Canada). Melting points were determined on a Yanaco MP-500 melting point apparatus and are corrected.

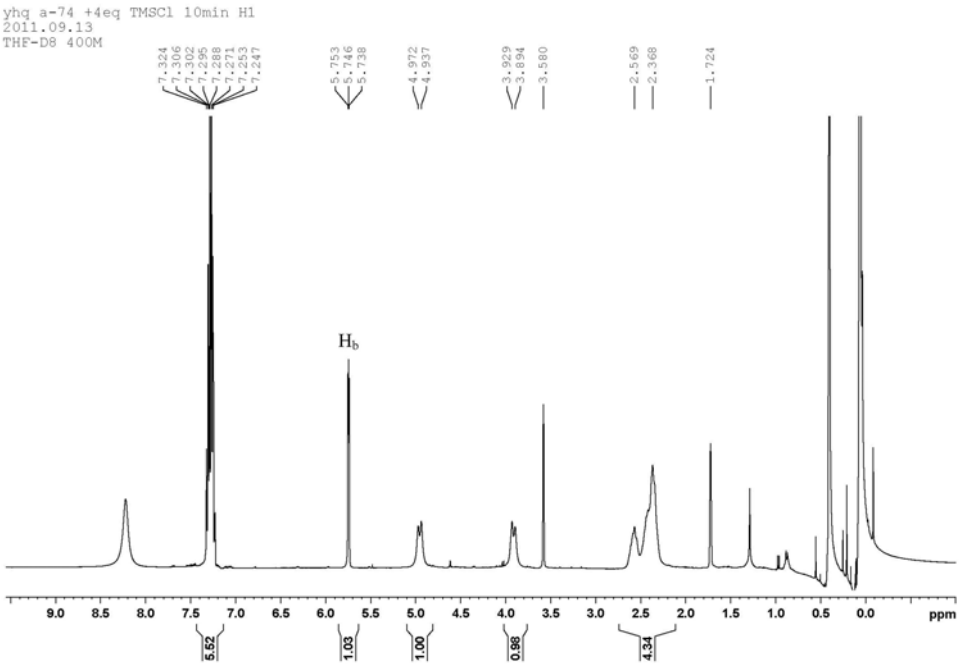
Materials. THF used in the reactions were dried by distillation over metallic sodium and benzophenone; dichloromethane were distilled over CaH. Silica gel (Zhifu, 300~400 mesh) was used for column chromatography, eluting (unless otherwise stated) with ethyl acetate/ hexane mixture. The Cp_2TiCl_2 and Mg used in this study are commercially available.

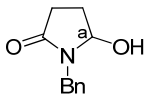
TMSCl-promoted chlorination of hemiaminal 1 in THF-d_8[1]







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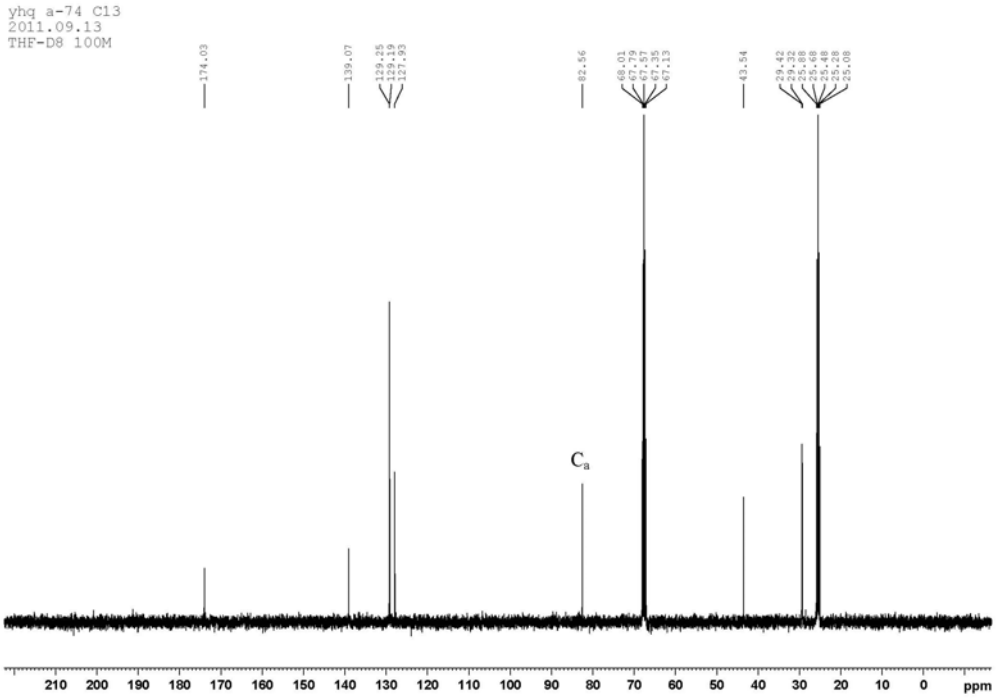
OH
Bn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67.57
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67.13
43.54
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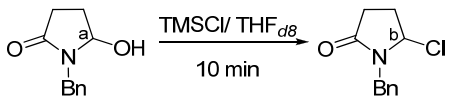
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TMSCl/ THFd8
10 min
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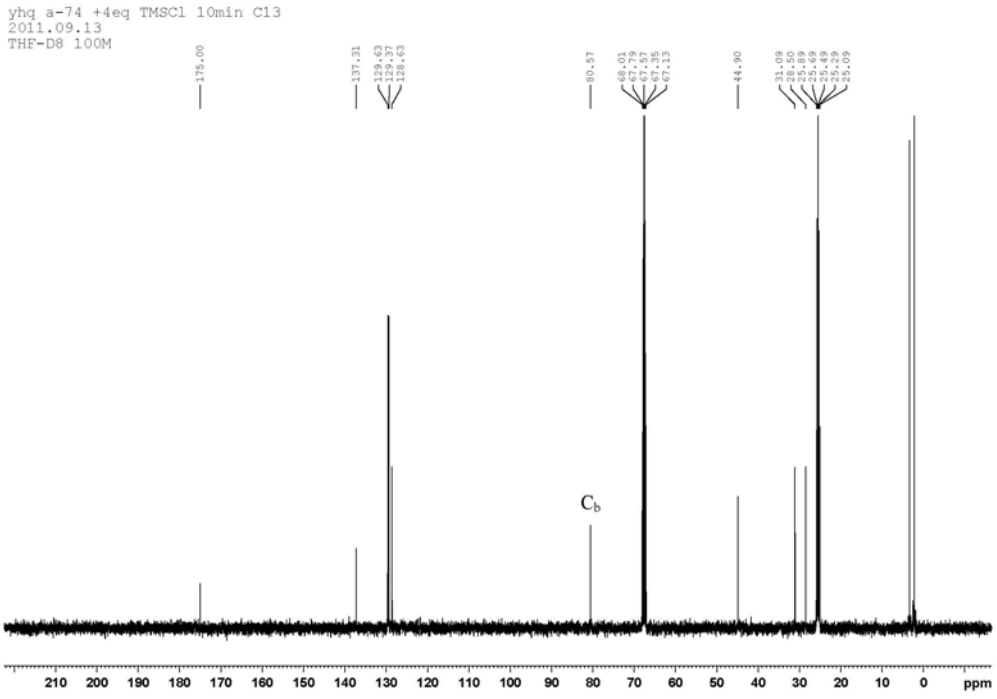
O
N
Cl
Bn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67.13
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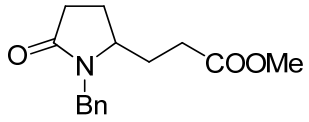
25.58
25.49
25.29
25.09
Cb
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

Titanocene-catalyzed Cross Coupling of Hemiaminals with Activated Alkenes

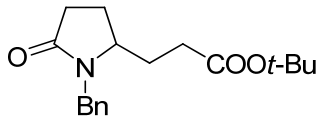
General procedure for the cross-coupling of hemiaminals with α,β-unsaturated compounds: To a suspension mixture of titanocene dichloride (3.1 mg, 0.0125 mmol) and Mg (chips: 60.0 mg, 2.5 mmol or powder: 24.0 mg, 1.0 mmol) in anhydrous THF (1.5 mL) was added dropwise TMSCl (0.25 mL, 2.0 mmol) at room temperature under N_2. The mixture was stirred until it turned green (about 10 min). A solution of a hemiaminal (0.5 mmol) and an α,β-unsaturated compound (1.0 mmol) in anhydrous THF (1.0 mL), then *t*-BuOH (0.2 mL, 2.0 mmol) were added subsequently. The color of the mixture turned to orange. The reaction mixture was stirred for 2~3 h until the color turned back to light green, filtered, washed with EtOAc (15.0 mL). The filtrate was washed with brine (5.0 mL) and dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel to afford the desired cross-coupling products **2a~2k** and **6a~6e**. In some cases, the byproducts **3, 4** and **7** were isolated as side products.

1-Benzyl-5-[2-(methyloxycarbonyl)ethyl]pyrrolidin-2-one (2a)



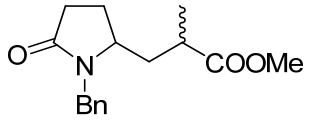
Following **the general procedure**, the cross-coupling of hemiaminal **1** with methyl acrylate afforded **2a**[2] in 93% yield as a colorless oil. IR (film) ν_{max} 3050, 2944, 2869, 1738, 1679, 1489, 1434, 1413 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.62-1.76 (m, 2H), 2.02-2.16 (m, 2H), 2.17-2.34 (m, 2H), 2.35-2.54 (m, 2H), 3.46 (dddd, apparent tdd, *J* = 8.2, 5.2, 3.0 Hz, 1H, H-5), 3.65 (s, 3H, OMe), 3.97 (d, *J* = 15.0 Hz, 1H, PhCH), 4.99 (d, *J* = 15.0 Hz, 1H, PhCH), 7.22-7.36 (m, 5H, Ph-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.4, 27.7, 29.0, 30.0, 44.0, 51.7, 55.9, 127.4, 128.0 (2C), 128.6 (2C), 136.5, 173.0, 174.9; MS (ESI, *m/z*): 284 (M + Na^+, 100%). HRMS calcd for $[C_{15}H_{19}NNaO_3]^+$ (M + Na^+): 284.1257; found: 284.1259.

1-Benzyl-5-[2-(*tert*-butyloxycarbonyl)ethyl]pyrrolidin-2-one (2b)



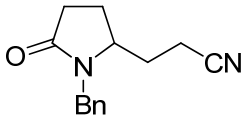
Following **the general procedure**, the cross-coupling of hemiaminal **1** with *tert*-butyl acrylate afforded **2b**[3] in 93% yield as a colorless oil.

1-Benzyl-5-[2-(methyloxycarbonyl)propyl]-pyrrolidin-2-one (2c)



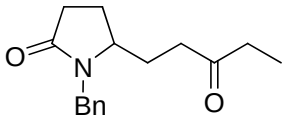
Following **the general procedure**, the cross-coupling of hemiaminal **1** with methyl methacrylate afforded **2c**[3] as an inseparable diastereomeric mixture (diastereomeric ratio: = 55 : 45) in a combined yield of 91%.

1-Benzyl-5-(2-cyanoethyl)pyrrolidin-2-one (2d)



Following **the general procedure**, the cross-coupling of hemiaminal **1** with acrylonitrile afforded **2d**[3] in 94% yield as a colorless oil.

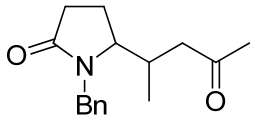
1-Benzyl-5-(3-oxopentyl)pyrrolidin-2-one (2e)



Following **the general procedure**, the cross-coupling of hemiaminal **1** with ethyl vinyl ketone afforded **2e** in 64% yield as a colorless oil. IR (film) ν_{max}: 3030, 2973, 2937, 1712, 1684, 1496, 1445, 1418, 1374, 1255, 1114 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.95 (t, J = 7.3 Hz, 3H), 1.50-1.62 (m, 2H), 1.88-2.06 (m, 2H), 2.16-2.46 (m, 6H), 3.39 (dddd, apparent tdd, J = 8.3, 5.3, 3.0 Hz, 1H), 3.93 (d, J = 15.0 Hz, 1H), 4.87 (d, J = 15.0 Hz, 1H), 7.15-7.27 (m, 5H, Ph-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 7.7, 23.5, 26.3, 30.1, 35.9, 36.7, 44.1, 56.2, 127.4, 128.0 (2C), 128.6 (2C), 136.6,

175.0, 210.0; MS (ESI, *m/z*): 282 (M + Na^+); HRMS calcd for $[C_{16}H_{21}NNaO_2]^+$ (M + Na^+): 282.1465; found: 282.1473.

1-Benzyl-5-(4-oxopentyl-2-yl)pyrrolidin-2-one (2f)

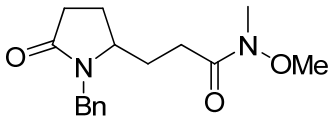


Following **the general procedure**, the cross-coupling of hemiaminal **1** with (*E*)-pen-3-en-2-one afforded **2f** as an inseparable diastereomeric mixture (diastereomeric ratio: = 56 : 44) in a combined yield of 45%. IR (film) ν_{max}: 3029, 2963, 1682, 1421, 1359, 1260, 1168 cm^{-1}; MS (ESI, *m/z*): 282 (M + Na^+). HRMS calcd for $[C_{16}H_{21}NNaO_2]$ (M + Na^+): 282.1465; found: 282.1465.

Major diastereoisomer (data read from spectrum of the diastereomeric mixture): ^1H NMR (400 MHz, $CDCl_3$) δ 0.78 (d, *J* = 6.9 Hz, 3H), 1.53-1.69 (m, 1H), 1.73-2.08 (m, 2H), 1.96 (s, 3H), 2.11-2.41 (m, 3H), 2.44-2.56 (m, 1H), 3.34-3.42 (m, 1H), 3.89 (d, *J* = 14.9 Hz, 1H), 4.81 (d, *J* = 14.9 Hz, 1H), 7.16-7.28 (m, 5H, Ph-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.3, 18.6, 28.8, 30.2, 30.4, 42.7, 44.4, 61.0, 127.5, 128.3 (2C), 128.64 (2C), 136.4, 175.5, 207.1.

Minor diastereoisomer (data read from spectrum of the diastereomeric mixture): ^1H NMR (400 MHz, $CDCl_3$) δ 0.70 (d, *J* = 6.8 Hz, 3H), 1.53-1.69 (m, 1H), 1.73-2.08 (m, 2H), 2.00 (s, 3H), 2.11-2.41 (m, 3H), 2.44-2.56 (m, 1H), 3.34-3.42 (m, 1H), 3.82 (d, *J* = 14.8 Hz, 1H), 5.00 (d, *J* = 14.8 Hz, 1H), 7.16-7.28 (m, 5H, Ph-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.0, 17.8, 28.5, 30.2, 30.5, 44.0, 46.8, 59.3, 127.5, 128.2 (2C), 128.57 (2C), 136.3, 175.2, 206.7.

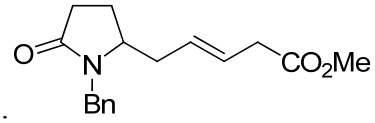
1-Benzyl-5-[2-(*N*-methoxy-*N*-methylaminecarbonyl)ethyl]pyrrolidin-2-one (2g)



Following **the general procedure**, the cross-coupling of hemiaminal **1** with *N*-methoxy-*N*-methylacrylamide afforded **2g** in 55% yield as a colorless oil. IR (film) ν_{max}: 3029, 2937, 1681, 1420, 1256, 1174 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ

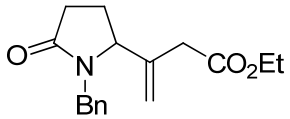
1.57-1.69 (m, 2H), 1.94-2.09 (m, 2H), 2.18-2.48 (m, 4H), 3.09 (s, 3H), 3.43 (dddd, apparent tdd, J = 8.3, 5.4, 3.0 Hz, 1H), 3.58 (s, 3H), 3.93 (d, J = 15.0 Hz, 1H), 4.93 (d, J = 15.0 Hz, 1H), 7.15-7.27 (m, 5H, Ph-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.4, 26.8, 27.2, 30.1 (2C), 44.0, 56.2, 61.2, 127.4, 128.0 (2C), 128.5 (2C), 136.6, 175.0; MS (ESI, *m/z*): 313 (M + Na^+); HRMS calcd for $[C_{16}H_{22}N_2NaO_3]^+$ (M + Na^+): 313.1523; found: 313.1523.

(*E*)-1-Benzyl-5-[4-(methyloxycarbonyl)but-2-enyl]pyrrolidin-2-one (2h)



Following **the general procedure**, the cross-coupling of hemiaminal **1** with (*E*)-methyl penta-2,4-dienoate afforded **2h** in 62% yield as a colorless oil. IR (film) ν_{max}: 3029, 2951, 1736, 1682, 1436, 1420, 1250, 1168 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.62-1.73 (dddd, J = 4.8, 6.0, 8.4, 13.0 Hz, 1H), 1.90-2.02 (dddd, J = 7.1, 8.0, 9.8, 13.0 Hz, 1H), 2.05-2.16 (m, 1H), 2.22-2.44 (m, 3H), 2.95 (d, J = 7.0 Hz, 2H), 3.42 (ddd, J = 4.4, 7.7, 11.7 Hz, 1H), 3.59 (s, 3H), 3.91 (d, J = 15.1 Hz, 1H), 4.90 (d, J = 15.1 Hz, 1H), 5.31 (ddd, J = 15.3, 7.7, 6.6 Hz, 1H), 5.53 (ddd, J = 15.3, 7.5, 6.4 Hz, 1H), 7.11-7.27 (m, 5H, Ph-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.1, 29.9, 35.7, 37.6, 44.0, 51.7, 56.1, 125.9, 127.3, 127.8 (2C), 128.3, 128.5 (2C), 136.5, 171.8, 175.1; MS (ESI, *m/z*): 310 (M + Na^+); HRMS calcd for $[C_{17}H_{21}NNaO_3]^+$ (M + Na^+): 310.1414; found: 310.1410.

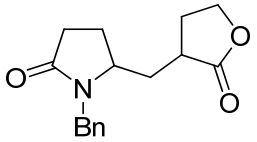
1-Benzyl-5-[4-(ethyloxycarbonyl)prop-2-enyl]pyrrolidin-2-one (2i)



Following **the general procedure**, the cross-coupling of hemiaminal **1** with ethyl buta-2,3-dienoate afforded **2i** in 72% yield as a colorless oil. IR (film) ν_{max}: 3457, 3064, 3031, 2981, 1733, 1689, 1496, 1444, 1417, 1239, 1158, 1032 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.17 (t, J = 7.2 Hz, 3H), 1.69-1.79 (m, 1H), 2.01-2.14 (m, 1H), 2.33 (ddd, J = 4.8, 10.0, 17.2 Hz, 1H), 2.45 (ddd, apparent dt, J = 17.2, 8.7 Hz, 1H),

2.87 (s, 2H), 3.63 (d, J = 13.5 Hz, 1H), 3.90 (dd, J = 3.8, 8.8 Hz, 1H), 4.06 (q, J = 7.2 Hz, 2H), 4.99 (d, J = 13.5 Hz, 1H), 5.00 (s, 1H), 5.12 (s, 1H), 7.13-7.27 (m, 5H, Ph-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 23.6, 29.6, 37.4, 44.2, 61.0, 61.6, 116.6, 127.5, 128.4 (2C), 128.5 (2C), 136.5, 140.2, 170.8, 175.2; MS (ESI, *m/z*): 310 (M + Na^+); HRMS calcd for $[C_{17}H_{21}NNaO_3]^+$ (M + Na^+): 310.1414; found: 310.1416.

1-Benzyl-5-[(2-oxotetrahydrofuran-3-yl)methyl]pyrrolidin-2-one (2j)

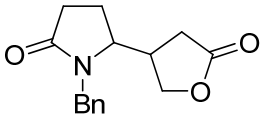


Following **the general procedure**, the cross-coupling of hemiaminal **1** with 3-methylenedihydrofuran-2(3*H*)-one afforded **2j** as an inseparable diastereomeric mixture (diastereomeric ratio: = 56 : 44) in a combined yield of 92%. IR (film) ν_{max}: 3500, 3029, 2927, 1767, 1682, 1495, 1446, 1420, 1375, 1254, 1214, 1174, 1023, cm^{-1}; MS (ESI, m/z): 296 (M + Na^+). HRMS calcd for $[C_{16}H_{19}NNaO_3]^+$ (M + Na^+): 296.1257; found: 296.1263.

Major diastereoisomer (data read from spectrum of the diastereomeric mixture): ^{1}H NMR (400 MHz, CDCl3) δ 1.41 (ddd, J = 6.7, 9.0, 14.0 Hz, 1H), 1.56-1.74 (m, 2H), 1.77-1.98 (m, 1H), 2.00-2.52 (m, 5H), 3.73 (m, 1H), 3.99 (d, J = 15.0 Hz, 1H), 4.02-4.11 (m, 1H), 4.20-4.28 (m, 1H), 4.84 (d, J = 15.0 Hz, 1H), 7.13-7.28 (m, 5H, Ph-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.0, 29.8, 29.9, 33.7, 35.7, 44.3, 55.6, 66.3, 127.5, 127.9 (2C), 128.6 (2C), 136.4, 174.9, 178.4.

Minor diastereoisomer (data read from spectrum of the diastereomeric mixture): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.56-1.74 (m, 2H), 1.77-1.98 (m, 1H), 2.00-2.52 (m, 6H), 3.33 (m, 1H), 3.88 (d, J = 15.1 Hz, 1H), 4.02-4.11 (m, 1H), 4.20-4.28 (m, 1H), 4.99 (d, J = 15.1 Hz, 1H), 7.13-7.28 (m, 9H, Ph-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.6, 28.9, 29.9, 33.6, 35.6, 44.0, 54.9, 66.3, 127.6, 127.9 (2C), 128.6 (2C), 136.1, 174.7, 178.5.

1-Benzyl-5-(5-oxotetrahydrofuran-3-yl)pyrrolidin-2-one (2k)

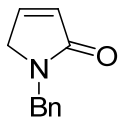


Following **the general procedure**, the cross-coupling of hemiaminal **1** with furan-2(5*H*)-one afforded **2k** as an inseparable diastereomeric mixture (diastereomeric ratio: = 58 : 42) in a combined yield of 62%. IR (film) ν_{max}: 3458, 3030, 2921, 1776, 1682, 1495, 1417, 1262, 1177, 1025 cm^{-1}; MS (ESI, *m/z*): 282 ($M + Na^+$). HRMS calcd for $[C_{15}H_{17}NNaO_3]^+$ ($M + Na^+$): 282.1101; found: 282.1108.

Major diastereoisomer (data read from spectrum of the diastereomeric mixture): ^1H NMR (400 MHz, $CDCl_3$) δ 1.58-1.69 (m, 1H), 1.98-2.18 (m, 2H), 2.24 (dd, *J* = 9.2, 18.2 Hz 1H), 2.35-2.53 (m, 2H), 2.78-2.91 (m, 1H), 3.53-3.62 (m, 1H), 3.85-3.96 (m, 1H), 4.02 (d, *J* = 15.3 Hz, 1H), 4.30 (dd, *J* = 8.2, 9.4 Hz, 1H), 4.78 (d, *J* = 15.3 Hz, 1H), 7.11-7.16 (m, 2H, Ph-H), 7.19-7.30 (m, 3H, Ph-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.0, 28.7, 29.7, 36.8, 45.0, 58.4, 69.6, 127.6, 128.8 (2C), 128.9 (2C), 136.0, 175.3, 175.7.

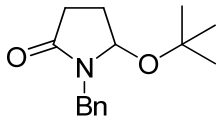
Minor diastereoisomer (data read from spectrum of the diastereomeric mixture): ^1H NMR (400 MHz, $CDCl_3$) δ 1.58-1.69 (m, 1H), 1.98-2.18 (m, 2H), 2.35-2.53 (m, 2H), 2.57 (dd, *J* = 9.8, 18.0 Hz, 1H), 2.78-2.91 (m, 1H), 3.53-3.62 (m, 1H), 3.85-3.96 (m, 2H), 4.13 (d, *J* = 15.3 Hz, 1H), 4.68 (d, *J* = 15.3 Hz, 1H), 7.11-7.16 (m, 2H, Ph-H), 7.19-7.30 (m, 3H, Ph-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.6, 29.7, 31.0, 36.0, 45.1, 59.0, 67.7, 127.8, 128.8 (2C), 128.9 (2C), 136.1, 175.5, 175.9.

1-Benzyl-1,5-dihydropyrrol-2-one (3)



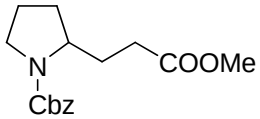
Byproduct **3**[4]: a colorless oil. IR (film) ν_{max} 3030, 2930, 1735, 1673, 1496, 1452, 1358, 1247, 1168, 1077 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.87 (s, 2H), 4.64 (s, 2H), 6.23 (dt, *J* =1.8, 6.0 Hz, 1H), 7.05 (dt, *J* =1.7, 6.0 Hz, 1H), 7.23-7.35 (m, 5H, Ph-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 45.9, 52.2, 127.5, 127.9, 128.0 (2C), 128.7 (2C), 137.2, 142.8, 171.4; MS (ESI, *m/z*): 174, ($M + H^+$).

1-Benzyl-5-*tert*-butyloxypyrrolidin-2-one (4)



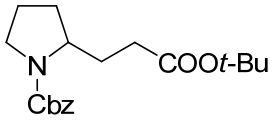
Byproduct **4**: a white solid. Mp 88-90 °C (EtOAc/ Hex = 1: 8). IR (film) ν_{max} 3026, 2928, 2876, 1644, 1492, 1455, 1336, 1260, 1078 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.2 (s, 9H, *t*-Bu), 1.91 (dddd, *J* = 1.6, 3.5, 9.7, 13.3 Hz, 1H), 2.19 (dddd, *J* = 6.2, 8.0, 9.9, 13.3 Hz, 1H), 2.36 (ddd, *J* = 3.5, 9.9, 17.0 Hz, 1H), 2.64 (ddd, *J* = 8.0, 9.7, 17.0 Hz, 1H), 3.96 (d, *J* = 15.4 Hz, 1H, PhCH), 4.94 (dd, *J* = 1.6, 6.2 Hz, 1H), 5.49 (d, *J* = 15.4 Hz, 1H, PhCH), 7.18-7.38 (m, 5H, Ph-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.4 (3C), 28.6, 28.7, 42.7, 73.7, 82.2, 127.2, 127.5 (2C), 128.4 (2C), 137.2, 174.8; MS (ESI, *m/z*): 270 (M + Na^+, 100%). HRMS calcd for $[C_{15}H_{21}NNaO_2]^+$ (M + Na^+): 270.1470; found: 270.1472.

1-(Benzyloxycarbonyl)-2-[2-(methyloxycarbonyl)ethyl]pyrrolidine (6a)



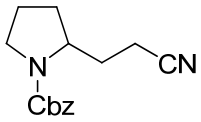
Following **the general procedure**, the cross-coupling of hemiaminal **5** with methyl acrylate afforded **6a** in 81% yield as a colorless oil. IR (film) ν_{max} 3025, 2945, 2868, 1733, 1699, 1438, 1412 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.56-1.62 (m, 1H), 1.64-1.70 (m, 1H), 1.74-1.92 (m, 4H), 2.18-2.38 (m, 2H), 3.28-3.35 (m, 1H), 3.36-3.47 (m, 1H), 3.55 (s br, 3H, OCH_3), 3.78-3.82 (m, 1H), 5.05 (s br, 2H, $PhCH_2$), 7.19-7.32 (m, 5H, Ph-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.5, 29.5, 30.3, 30.9, 46.4, 51.5, 57.0, 66.6, 127.8 (2C), 128.4 (3C), 136.9, 155.1, 173.6; MS (ESI, *m/z*): 314 (M + Na^+, 100%). HRMS calcd for $[C_{16}H_{21}NNaO_4]^+$ (M + Na^+): 314.1363; found: 314.1363.

1-(Benzyloxycarbonyl)-2-[2-(*tert*-butyloxycarbonyl)ethyl]pyrrolidine (6b)



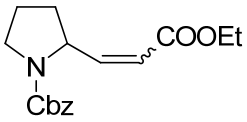
Following **the general procedure**, the cross-coupling of hemiaminal **5** with *tert*-butyl acrylate afforded **6b**[5] in 86% yield as a colorless oil.

1-(Benzyloxycarbonyl)-2-(2-cyanoethyl)pyrrolidine (6c)



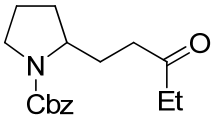
Following **the general procedure A**, the cross-coupling of hemiaminal **5** with acrylonitrile afforded **6c**[5] in 71% yield as a colorless oil.

(*Z*/*E*)-1-(Benzyloxycarbonyl)-2-[2-(ethyloxycarbonyl)ethenyl]pyrrolidine (6d)



Following **the general procedure**, the cross-coupling of hemiaminal **5** with ethyl propiolate afforded **6d**[5] in 74% yield (*E*-isomer: 41%, *Z*-isomer: 33%).

1-(Benzyloxycarbonyl)-2-[2-(ethylcarbonyl)ethyl]pyrrolidine (6e)



Following **the general procedure**, the cross-coupling of hemiaminal **5** with ethyl vinyl ketone afforded **6e**[6] in 80% yield as a colorless oil. IR (film) ν_{max}: 3028, 2949, 1733, 1695, 1408, 1412 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.01 (t, J = 4.0 Hz, 3H, CH_3), 1.55-1.73 (m, 2H), 1.75-1.95 (m, 4H), 2.20-2.50 (m, 4H), 3.30-3.40 (m, 1H), 3.40-3.50 (m, 1H), 3.80-3.92 (m, 1H), 5.09 (d, J = 12.4 Hz, 1H, PhCH), 5.15 (d, J = 12.4 Hz, 1H, PhCH), 7.25-7.42 (m, 5H, Ph-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 7.7, 23.3, 28.5, 30.4, 35.6, 39.1, 46.3, 56.9, 66.6, 127.8 (2C), 128.2, 128.3 (2C), 136.8,

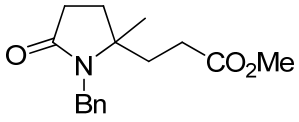
155.1, 211.0; MS (ESI, *m/z*): 312 (M + Na^+, 100%).

General procedure for the cross-coupling of hemiaminals 8, 10 and 12 with α,β-unsaturated compounds:

To a cooled (–20 °C) solution of 1-benzylsuccimide (385 mg, 2.0 mmol) in CH_2Cl_2 (15 mL) was added dropwise a solution of alkyl/ aryl magnesium bromide in Et_2O (1.5 M, 3.3 mL, 5.0 mmol). The mixture was stirred for 4 h at –20 °C. The reaction was quenched with saturated aqueous NH_4Cl (5 mL). After extraction with ethyl acetate (3× 10 mL), the combined organic layers were washed with brine (4 mL), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was filtered through Silica gel (zhifu, 100-200 mesh) to afford the crude hemiaminals **8, 10 and 12** which were used in the next step without further purification.

To a suspension mixture of titanocene dichloride (3.1 mg, 0.0125 mmol) and Mg (chips: 60 mg, 2.5 mmol or powder: 24 mg, 1.0 mmol) in anhydrous THF (1.5 mL) was added dropwise TMSCl (0.25 mL, 2.0 mmol) at room temperature under N_2. The mixture was stirred until it turned green (about 10 min). A solution of a hemiaminal (0.5 mmol) and an α,β-unsaturated compound (1.0 mmol) in anhydrous THF (1.0 mL), then *t*-BuOH (0.2 mL, 2.0 mmol) were added subsequently. The color of the mixture turned to orange. The reaction mixture was stirred for 2~3 h until the color turned back to light green, filtered, washed with EtOAc (15.0 mL). The filtrate was washed with brine (5.0 mL) and dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel to afford the desired cross-coupling products **9a**~**9c**, **11a**~**11c**, **13a**~**13c**.

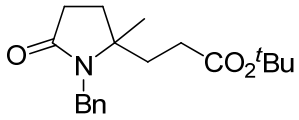
1-Benzyl-5-methyl-5-[2-(methyloxycarbonyl)ethyl]pyrrolidin-2-one (9a)



Following **the general procedure**, with methyl magnesium iodide as Grignard

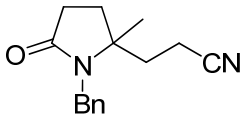
reagent, the cross-coupling of hemiaminal **8** with methyl acrylate afforded **9a** in 82% yield as a colorless oil. IR (film) ν_{max}: 3029, 2967, 1736, 1682, 1404, 1299, 1198 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.04 (s, 3H), 1.67-1.90 (m, 4H), 1.99 (ddd, *J* = 5.6, 10.3, 16.2 Hz, 1H), 2.12 (ddd, *J* = 6.3, 10.0, 16.2 Hz, 1H), 2.36-2.44 (m, 2H), 3.55 (s, 3H), 4.23 (d, *J* = 15.3 Hz, 1H), 4.43 (d, *J* = 15.3 Hz, 1H), 7.13-7.26 (m, 5H, Ph-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.4, 28.8, 29.6, 30.7, 34.0, 42.9, 51.7, 63.1, 127.1, 127.9 (2C), 128.4 (2C), 138.5, 173.2, 174.9; MS (ESI, *m/z*): 298 ($M + Na^+$, 100%); HRMS calcd for $[C_{16}H_{21}KNO_3]^+$ ($M + K^+$): 314.1153; found: 314.1160.

1-Benzyl-5-methyl-5-[2-(*tert*-butyloxycarbonyl)ethyl]pyrrolidin-2-one (9b)



Following **the general procedure**, with methyl magnesium iodide as Grignard reagent, the cross-coupling of hemiaminal **8** with *tert*-butyl acrylate afforded **9b** in 77% yield as a colorless oil. IR (film) ν_{max}: 3036, 2975, 2932, 1727, 1686, 1496, 1403, 1367, 1155 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.03 (s, 3H), 1.33 (s, 9H), 1.64-1.75 (m, 3H), 1.80-1.95 (m, 2H), 1.97-2.08 (m, 1H), 2.34-2.42 (m, 2H), 4.24 (d, *J* = 15.3 Hz, 1H), 4.42 (d, *J* = 15.3 Hz, 1H), 7.11-7.27 (m, 5H, Ph-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.3, 27.9 (3C), 29.6, 30.2, 30.7, 34.0, 42.8, 63.1, 80.4, 127.0, 127.8 (2C), 128.3 (2C), 138.5, 172.0, 174.8; MS (ESI, *m/z*): 340 ($M + Na^+$, 100%); HRMS calcd for $[C_{19}H_{27}NNaO_3]^+$ ($M + Na^+$): 340.1883; found: 340.1884.

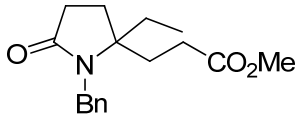
1-Benzyl-5-methyl-5-(2-cyanoethyl)pyrrolidin-2-one (9c)



Following **the general procedure**, with methyl magnesium iodide as Grignard reagent, the cross-coupling of hemiaminal **8** with acrylonitrile afforded **9c** in 84% yield as a colorless oil. IR (film) ν_{max}: 3030, 2969, 2934, 2246, 1682, 1405, 1358, 1168 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.13 (s, 3H), 1.70-1.80 (m, 3H), 1.84-1.93 (m, 2H), 2.00-2.06 (m, 1H), 2.40 (ddd, apparent dt, *J* = 9.3, 6.6 Hz, 2H), 4.20 (d, *J* =

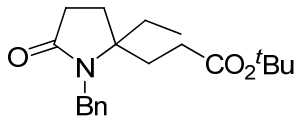
15.3 Hz, 1H), 4.46 (d, J = 15.3 Hz, 1H), 7.19-7.24 (m, 5H, Ph-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.0, 25.7, 29.2, 30.2, 34.8, 42.8, 62.7, 118.9, 127.5, 127.8 (2C), 128.6 (2C), 138.0, 174.6; MS (ESI, *m/z*): 265 (M + Na^+, 100%); HRMS calcd for $[C_{15}H_{18}N_2NaO]^+$ (M + Na^+): 265.1311; found: 265.1318.

1-Benzyl-5-ethyl-5-[2-(methyloxycarbonyl)ethyl]pyrrolidin-2-one (11a)



Following **the general procedure**, with ethyl magnesium bromide as Grignard reagent, the cross-coupling of hemiaminal **10** with methyl acrylate afforded **11a** in 81% yield as a colorless oil. IR (film) ν_{max}: 3029, 2966, 1736, 1681, 1408, 1303, 1197 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.65 (t, J = 7.3 Hz, 3H), 1.41 (dq, apparent q, J = 7.3 Hz, 1H), 1.50 (dq, apparent q, J = 7.3 Hz, 1H), 1.66-1.80 (m, 3H), 1.80-1.90 (m, 2H), 2.00-2.11 (m, 1H), 2.37 (ddd, J = 2.0, 7.5, 9.6 Hz, 2H), 3.51 (s, 3H), 4.19 (d, J = 15.1 Hz, 1H), 4.38 (d, J = 15.1 Hz, 1H), 7.12-7.23 (m, 3H, Ph-H), 7.26 -7.32 (m, 2H, Ph-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 7.7, 26.5, 28.3, 30.0, 32.1, 33.5, 43.1, 51.6, 66.4, 127.2, 128.38 (2C), 128.40 (2C), 138.3, 173.3, 175.5; MS (ESI, *m/z*): 312 (M + Na^+, 100%); HRMS calcd for $[C_{17}H_{23}NNaO_3]^+$ (M + Na^+): 312.1570; found: 312.1573.

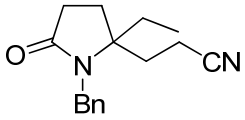
1-Benzyl-5-ethyl-5-[2-(*tert*-butyloxycarbonyl)ethyl]pyrrolidin-2-one (11b)



Following **the general procedure**, with ethyl magnesium bromide as Grignard reagent, the cross-coupling of hemiaminal **10** with *tert*-butyl acrylate afforded **11b** in 72% yield as a white solid. Mp 79-80 ^{o}C (EtOAc/ Hex = 1: 3); IR (film) ν_{max}: 3028, 2972, 2929, 1727, 1682, 1587, 1407, 1366, 1152 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.65 (t, J = 7.4 Hz, 3H), 1.31 (s, 9H), 1.40 (dq, apparent q, J = 7.4 Hz, 1H), 1.49 (dq, apparent q, J = 7.4 Hz, 1H), 1.65-1.81 (m, 5H), 1.93-1.99 (m, 1H), 2.35-2.40 (m, 2H), 4.19 (d, J = 15.1 Hz, 1H), 4.38 (d, J = 15.1Hz, 1H), 7.15-7.23 (m, 3H, Ph-H),

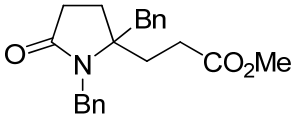
7.29-7.31 (m, 2H, Ph-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 7.7, 26.6, 28.0 (3C), 29.7, 30.0, 32.1, 33.6, 43.1, 66.4, 80.4, 127.2, 128.38 (2C), 128.44 (2C), 138.4, 172.2, 175.6; MS (ESI, *m/z*): 354 (M + Na^+, 100%); HRMS calcd for $[C_{20}H_{29}NNaO_3]^+$ (M + Na^+): 354.2040; found: 354.2041.

1-Benzyl-5-ethyl-5-(2-cyanoethyl)pyrrolidin-2-one (11c)



Following **the general procedure**, with ethyl magnesium bromide as Grignard reagent, the cross-coupling of hemiaminal **10** with acrylonitrile afforded **11c** in 83% yield as a colorless oil. IR (film) ν_{max}: 3030, 2968, 2934, 2246, 1678, 1496, 1409, 1358, 711 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.72 (t, *J* = 7.3 Hz, 3H), 1.48 (dq, apparent q, *J* = 7.3 Hz, 1H), 1.60 (dq, apparent q, *J* = 7.3 Hz, 1H), 1.67-1.81 (m, 4H), 1.83-1.98 (m, 2H), 2.39 (ddd, *J* = 2.1, 7.5, 9.7 Hz, 2H), 3.92 (d, *J* = 15.0 Hz, 1H), 4.66 (d, *J* = 15.0 Hz, 1H), 7.18-7.32 (m, 5H, Ph-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 7.5, 11.6, 26.2, 29.7, 31.5, 34.8, 43.1, 66.1, 119.0, 127.8, 128.4 (2C), 128.8 (2C), 137.9, 175.4; MS (ESI, *m/z*): 279 (M + Na^+, 100%); HRMS calcd for $[C_{16}H_{20}N_2NaO]^+$ (M + Na^+): 279.1468; found: 279.1463.

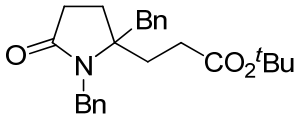
1-Benzyl-5-benzyl-5-[2-(methyloxycarbonyl)ethyl]pyrrolidin-2-one (13a)



Following **the general procedure**, with benzyl magnesium chloride as Grignard reagent, the cross-coupling of hemiaminal **12** with methyl acrylate afforded **13a** in 75% yield as a white solid. Mp 98-99 ^{o}C (EtOAc/ Hex = 1: 3); IR (film) ν_{max}: 3062, 3028, 2950, 1737, 1682, 1495, 1435, 1404, 1304, 1198, 1170 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.47-1.66 (m, 2H), 1.73-2.10 (m, 6H), 2.58 (d, *J* = 13.7 Hz, 1H), 2.83 (d, *J* = 13.7 Hz, 1H), 3.48 (s, 3H), 4.16 (d, *J* = 15.1 Hz, 1H), 4.75 (d, *J* = 15.1 Hz, 1H), 6.95-7.02 (m, 2H, Ph-H), 7.12-7.25 (m, 6H, Ph-H), 7.29-7.36 (m, 2H, Ph-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.9, 28.2, 29.4, 33.4, 43.6, 44.0, 51.6, 66.7, 127.0, 127.2,

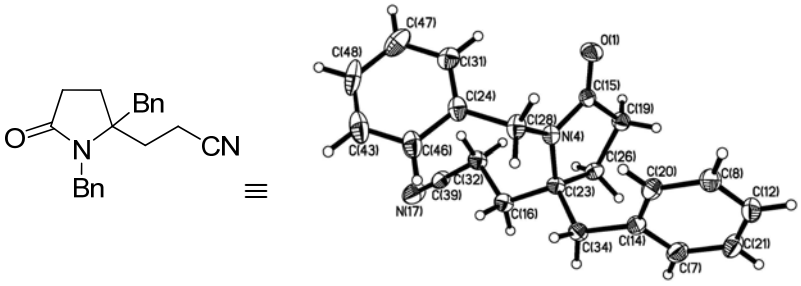
128.3 (2C), 128.4 (2C), 128.5 (2C), 130.0 (2C), 135.7, 138.4, 173.1, 175.8; MS (ESI, *m/z*): 374 (M + Na^+, 100%); HRMS calcd for $[C_{22}H_{25}NNaO_3]^+$ (M + Na^+): 374.1727; found: 374.1730.

1-Benzyl-5-benzyl-5-[2-(*tert*-butyloxycarbonyl)ethyl]pyrrolidin-2-one (13b)



Following **the general procedure**, with benzyl magnesium chloride as Grignard reagent, the cross-coupling of hemiaminal **12** with *tert*-butyl acrylate afforded **13b** in 68% yield as a colorless oil. IR (film) ν_{max}: 3435, 3029, 2976, 2929, 1727, 1683, 1495, 1455, 1404, 1367, 1314, 1151 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.29 (s, 9H), 1.48-1.68 (m, 2H), 1.68-1.83 (m, 3H), 1.89-2.01 (m, 2H), 2.01-2.11 (m, 1H), 2.59 (d, *J* = 13.7 Hz, 1H), 2.82 (d, *J* = 13.7 Hz, 1H), 4.18 (d, *J* = 15.1 Hz, 1H), 4.74 (d, *J* = 15.1 Hz, 1H), 6.96-7.03 (m, 2H, Ph-H), 7.13-7.26 (m, 6H, Ph-H), 7.31-7.36 (m, 2H, Ph-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.1, 28.0 (3C), 29.5, 29.8, 33.8, 43.6, 44.0, 66.8, 80.5, 127.0, 127.3, 128.4 (2C), 128.48 (2C), 128.53 (2C), 130.1 (2C), 135.9, 138.6, 172.0, 175.9; MS (ESI, *m/z*): 416 (M + Na^+, 100%); HRMS calcd for $[C_{25}H_{31}NNaO_3]^+$ (M + Na^+): 416.2196; found: 416.2208.

1-Benzyl-5-benzyl-5-(2-cyanoethyl)pyrrolidin-2-one (13c)

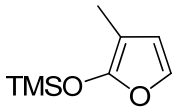


Following **the general procedure**, with benzyl magnesium chloride as Grignard reagent, the cross-coupling of hemiaminal **12** with acrylonitrile afforded **13c**[7] in 81% yield as a white solid. M.p. 164-165 ^oC (EtOAc/ Hex = 1: 2); IR (film) ν_{max}: 3029, 2928, 2245, 1681, 1495, 1454, 1403, 1356, 1151, 1083 cm^{-1}; ^1H NMR (400 MHz,

$CDCl_3$) δ 1.46-1.57 (m, 1H), 1.58-1.71 (m, 2H), 1.78-1.95 (m, 3H), 1.99 (ddd, *J* = 3.3, 10.0, 13.4 Hz, 1H), 2.08 (ddd, *J* = 3.3, 10.1, 13.4, Hz, 1H), 2.63 (d, *J* = 13.8 Hz, 1H), 2.91 (d, *J* = 13.8 Hz, 1H), 4.00 (d, *J* = 15.1 Hz, 1H), 4.95 (d, *J* = 15.1 Hz, 1H), 6.98-7.05 (m, 2H, Ph-H), 7.18-7.37 (m, 8H, Ph-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.6, 26.4, 29.1, 34.5, 43.6, 43.7, 66.4, 119.0, 127.4, 127.9, 128.3 (2C), 128.7 (2C), 129.0 (2C), 130.0 (2C), 135.0, 138.1, 175.7; MS (ESI, *m/z*): 341 (M + Na^+, 100%); HRMS calcd for $[C_{21}H_{22}N_2NaO]^+$ (M+Na^+): 341.1624; found: 341.1630.

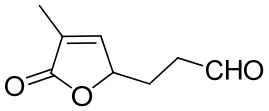
Total Synthesis of (±)-9,10-*epi*-stemoamide

3-Methyl-2-(trimethylsilyloxy)furan (15)



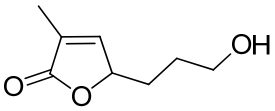
To a cooled solution (ice-bath) of 3-methyl-5*H*-furan-2-one **14** (2.50 g, 25.0 mmol) and Et_3N (4.2 mL, 30.0 mmol) in CH_2Cl_2 (50 mL) was added TMSOTf (4.5 mL, 25.0 mmol) dropwise over 15 min under N_2. The reaction mixture was stirred at the same temperature for 60 min, then allowed to warm to room temperature. After 30 min, the reaction mixture was diluted with petroleum ether (30-60 °C, 100 mL) and transferred to a separatory funnel. The top layer was decanted, and concentrated under reduced pressure (200 mbar). The residue was purified by distillation under reduced pressure (pressure: 93 mbr, temp. 85 °C) to give silyloxyfuran **15**[8] (3.30 g, yield: 78%) as a pale yellow oil. IR (film) ν_{max}: 3086, 2955, 1764, 1644, 1246, 1096, 844 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.28 (s, 9H, Me_3Si), 1.82 (s, 3H, CH_3), 6.10 (d, *J* = 6.8 Hz, 1H, CH=), 6.76 (d, *J* = 6.8 Hz, 1H, OCH=); ^{13}C NMR (100 MHz, $CDCl_3$) δ 0.1 (3C), 8.4, 92.3, 113.5, 131.3, 152.7.

(±)-3-(4'-Methyl-5'-oxo-2',5'-dihydrofuran-2'-yl)propanal (16)



To a solution of pyrrolidine (0.28 mL, 3.4 mmol) in CH_2Cl_2 (65 mL), water (1.22 mL, 67.8 mmol), acetic acid (0.13 mL, 2.3 mmol) and acrolein (0.75 mL, 11.3 mmol) were added under N_2 at –40 ºC. After being stirred for 10 min, 3-methyl-2-(trimethylsilyloxy)furan **15** (2.30 g, 13.5 mmol) was added slowly. The resulting solution was stirred at –40 ºC for 18 h. The reaction was quenched with H_2O (10 mL) then extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (Et_2O/ PE 30-60 °C = 1: 1) to give compound **16** (1.11 g, yield: 64%) as a colorless oil. IR (film) ν_{max}: 3081, 2960, 2914, 1753, 1655, 1442, 1344, 1208, 1069 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.72-1.84 (m, 1H), 1.90 (t, J = 1.8 Hz, 3H, CH_3), 2.18 (dddd, 1H, J = 4.4, 4.4, 7.3, 14.5 Hz), 2.55-2.72 (m, 2H, H-2), 4.91-4.98 (m, 1H), 6.98-7.02 (m, 1H, =CH), 9.78 (s, 1H, CHO); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.6, 25.4, 38.9, 79.6, 130.5, 148.1, 173.8, 200.5; MS (ESI, *m*/*z*): 177 ($M + Na^+$, 100%). HRESIMS calcd for $[C_8H_{10}NaO_3]^+$ ($M + Na^+$): 177.0522; found: 177.0525.

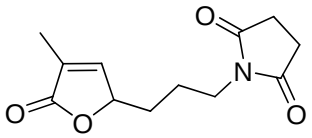
(±)-5-(3'-Hydroxypropanyl)-3-methyl-2(5*H*)-furanone (17)



To a solution of 3-(4-methyl-5-oxo-2,5-dihydrofuran-2-yl)propanal **16** (450 mg, 2.9 mmol) in THF (29.0 mL) was added a 1.0 M solution of BH_3 in THF (3.0 mL, 3.0 mmol) dropwise at –30 °C. The resulting solution was stirred for 1 h at the same temperature, and then quenched with H_2O (10 mL). The mixture was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (eluent: EtOAc/ Hex = 1: 1) to give compound **17** (420 mg, yield: 93%) as a colorless oil.[9] IR (film)

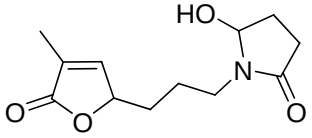
ν_{max}: 3413, 3079, 2927, 2873, 1753, 1658, 1444, 1344, 1208, 1045, 1023 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.62-1.72 (m, 3H), 1.76 (s br, 1H, OH), 1.82-1.89 (m, 1H), 1.90 (t, J = 1.9 Hz, 3H, CH_3), 3.65-3.72 (m, 2H), 4.92-4.98 (m, 1H, H-5), 7.02-7.05 (m, 1H, =CH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.6, 28.0, 30.0, 62.1, 80.9, 130.0, 148.7, 174.3; MS (ESI, m/z): 179 ($M + Na^+$, 100%).

(±)-1-(3-(4-Methyl-5-oxo-2,5-dihydrofuran-2-yl)propyl)pyrrolidine-2,5-dione (18)



To a suspension of alcohol **17** (374 mg, 2.4 mmol), Ph_3P (681 mg, 2.6 mmol), and succinimide (238 mg, 2.4 mmol) in THF (8.0 mL) was added DIAD (0.55 mL, 2.6 mmol) under N_2 at room temperature. The resulting mixture was stirred overnight and then concentrated under reduced pressure. The residue was purified by flash column chromatography (eluent: EtOAc/Hex = 1: 2) to give the cyclic imide **18** (517 mg, yield: 91%) as a colorless oil.[9] IR (film) ν_{max}: 3079, 2941, 1752, 1697, 1438, 1404, 1344, 1252, 1210, 1162, 1112, 1027 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.53-1.62 (m, 1H), 1.63-1.82 (m, 3H), 1.90 (t, J = 1.7 Hz, 3H, CH_3), 2.70 (s br, 4H), 3.48-3.58 (m, 2H), 4.86-4.94 (m, 1H), 6.94-7.07 (m, 1H, =CH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.6, 23.5, 28.2 (2C), 30.7, 38.2, 80.2, 130.4, 148.1, 173.9, 177.2; MS (ESI, m/z): 260 ($M + Na^+$, 100%).

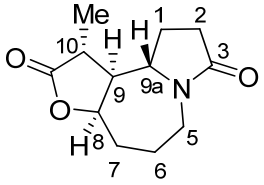
(±)-5-Hydroxy-1-(3-(4-methyl-5-oxo-2,5-dihydrofuran-2-yl)propyl)pyrrolidin-2-one (19)



To a solution of cyclic imide **18** (408 mg, 1.7 mmol) in MeOH (5.0 mL) was added $NaBH_4$ (650 mg, 17.0 mmol) portionwise at −10 °C. The resulting solution was stirred for 15 min at the same temperature, quenched with water (10 mL), extracted with cold

CH_2Cl_2 (5 × 10 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (eluent: EtOAc) to give the carbinol lactam **19** (378 mg, yield: 92%) as a colorless oil.[9] IR (film) ν_{max}: 3339, 3072, 2928, 1751, 1666, 1462, 1338, 1282, 1162, 1102, 1059 cm^{-1}; ^1H NMR (diastereomeric mixture, 400 MHz, $CDCl_3$) δ 1.45-1.85 (m, 5H), 1.90 (s, 3H, CH_3), 2.20-2.40 (m, 2H), 2.45-2.65 (m, 1H), 3.24-3.35 (m, 1H), 3.36-3.50 (m, 1H), 4.47 and 4.49 (2s br, 1H, OH, D_2O exchangeable), 4.90-4.99 (m, 1H), 5.16-5.27 (m, 1H), 6.98-7.08 (m, 1H, =CH); ^{13}C NMR (diastereomeric mixture, 100 MHz, $CDCl_3$) δ 10.5, 23.4, 23.5, 28.26, 28.30, 28.9, 30.69, 30.74, 39.4, 39.8, 80.7, 80.9, 83.2, 83.5, 129.9, 130.0, 148.9, 149.0, 174.5, 175.0; MS (ESI, *m*/*z*): 262 (M + Na^+, 100%).

(±)-9,10-Di-*epi*-stemoamide (20)



A suspension of titanocene dichloride (12.5 mg, 0.05 mmol) was stirred with Mg (22 mg, 0.90 mmol) in anhydrous THF (1.0 mL) for 10 min at room temperature under N_2. The mixture was cooled with an ice-bath, and then TMSCl (50 μL, 0.40 mmol) was added dropwise to it. After being stirred for 30 min, a solution of carbinol lactam **19** (24 mg, 0.10 mmol) in anhydrous THF (1.0 mL) was added via a syringe pump over 4 h. The mixture was allowed to warm up to room temperature, and stirred for 10 h. The reaction mixture was filtered, and washed with EtOAc (3.0 mL). The filtrate was washed with brine (1.0 mL) and dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (eluent: EtOAc) to give compound **20** (7.1 mg, yield: 32%) as a white amorphous solid.[9,10] IR (film) ν_{max}: 2936, 1768, 1680, 1459, 1430, 1381, 1299, 1254, 1193, 1139, 1008 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.38 (d, J = 7.1 Hz, 3H, Me), 1.54-1.69 (m,

1H), 1.80-1.96 (m, 3H), 2.05-2.14 (m, 1H), 2.22-2.62 (m, 5H), 2.76 (ddd, J = 3.6, 10.6, 13.8 Hz, 1H), 3.62 (ddd, J = 1.2, 7.8, 9.9 Hz, 1H), 4.15 (dt, J = 13.8, 4.6 Hz, 1H), 4.62 (ddd, J = 3.0, 7.8, 10.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.9, 23.9, 25.4, 28.9, 30.0, 39.1, 44.0, 50.8, 60.5, 80.6, 174.7, 177.8; MS (ESI, *m*/*z*): 246 (M + Na^+, 100%). HRESIMS calcd for $[C_{12}H_{17}NNaO_3]^+$ (M + Na^+): 246.1101; found: 246.1104.

(±)-20 synthesized in this work	**(±)-20** in ref. 10a
^{1}H NMR ($CDCl_3$, 400 MHz)	
1.38 (d, J = 7.1 Hz, 3H, Me)	1.39 (d, J = 7.2 Hz, 3H)
1.54-1.69 (m, 1H)	1.55-1.70 (m, 1H)
1.80-1.96 (m, 3H)	1.80-2.00 (m, 3H)
2.05-2.14 (m, 1H)	2.07-2.15 (m, 1H)
2.22-2.62 (m, 5H)	2.23-2.62 (m, 5H)
2.76 (ddd, J = 13.8, 10.6, 3.6 Hz, 1H)	2.78 (ddd, J = 14.0, 10.6, 3.4 Hz, 1H)
3.62 (ddd, J = 9.9, 7.8, 1.2 Hz, 1H)	3.63 (m, 1H)
4.15 (dt, J = 13.8, 4.6 Hz, 1H)	4.19 (dt, J = 14.0, 4.5 Hz)
4.62 (ddd, J = 10.6, 7.8, 3.0 Hz, 1H)	4.62 (ddd, J = 10.6, 7.5, 3.0 Hz, 1H)
^{13}C NMR ($CDCl_3$, 100 MHz)	
15.9	15.9
23.9	24.0
25.4	25.5
28.9	28.9
30.0	30.1
39.1	39.1
44.0	44.1
50.8	50.8
60.5	60.6
80.6	80.7
174.7	174.6
177.8	177.9

Reference

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7. CCDC-911087 contains the supplementary crystallographic data for compound **15c**. This data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
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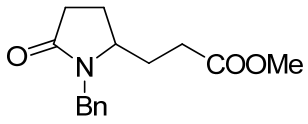
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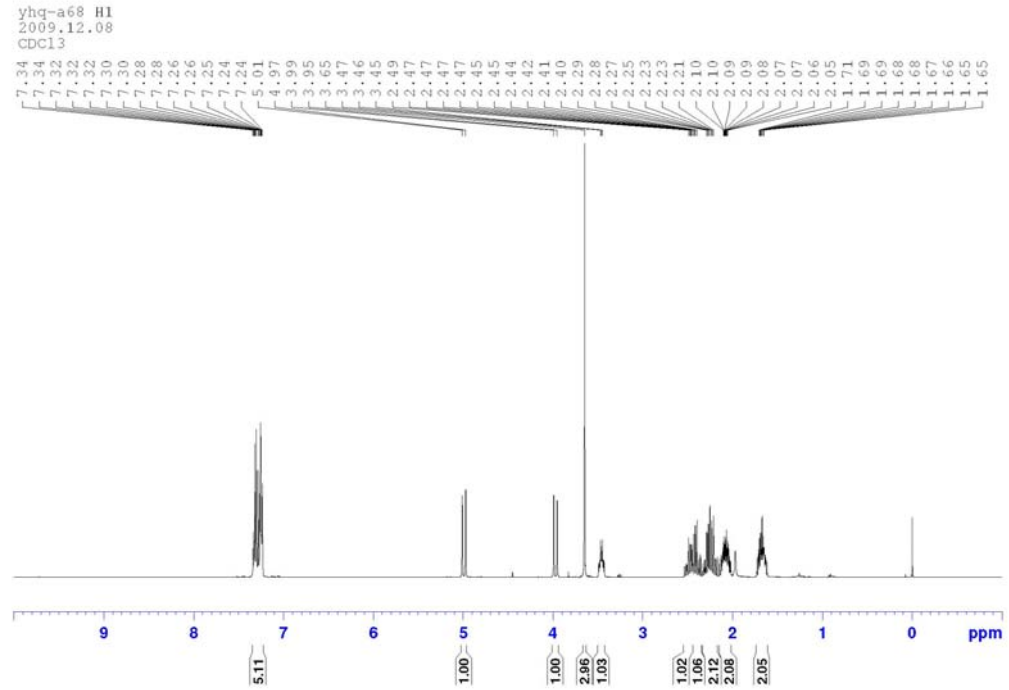
2a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2009.12.08
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5.01 4.97 3.99 3.95 3.65 3.47 3.46 3.45 2.49 2.47 2.47 2.47 2.47 2.45 2.45 2.44 2.42 2.41 2.40 2.29 2.28 2.27 2.25 2.23 2.21 2.10 2.10 2.09 2.09 2.08 2.07 2.07 2.06 2.05 1.71 1.69 1.69 1.68 1.68 1.67 1.66 1.65 1.65
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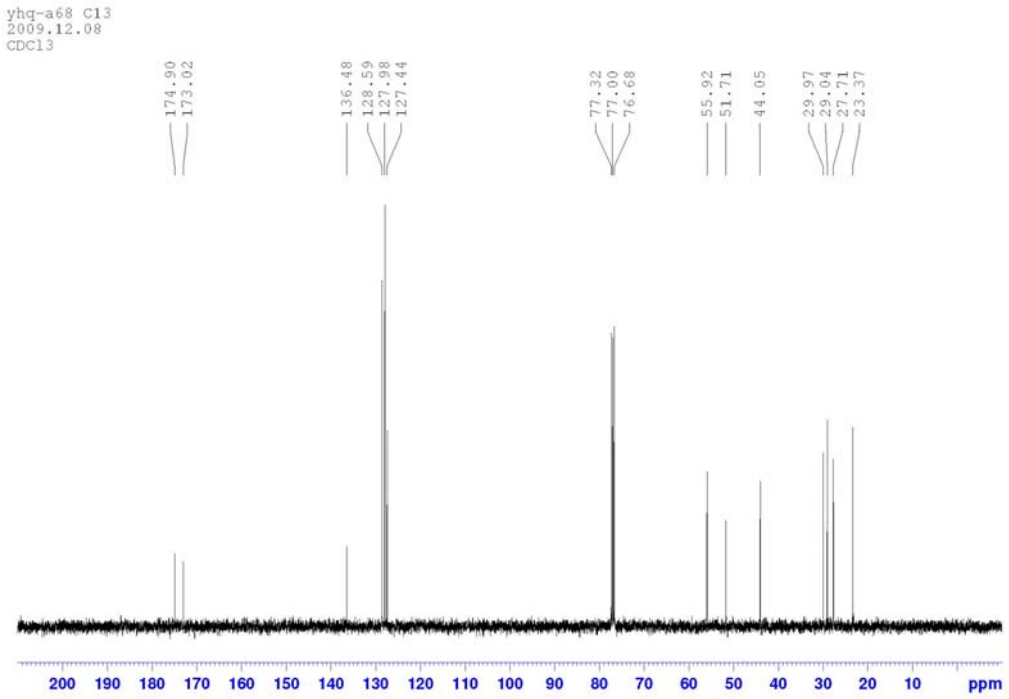
5.11 1.00 1.00 2.96 1.03 1.02 1.06 2.12 2.08 2.05


yhq-a68 C13
2009.12.08
CDCl3
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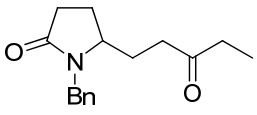
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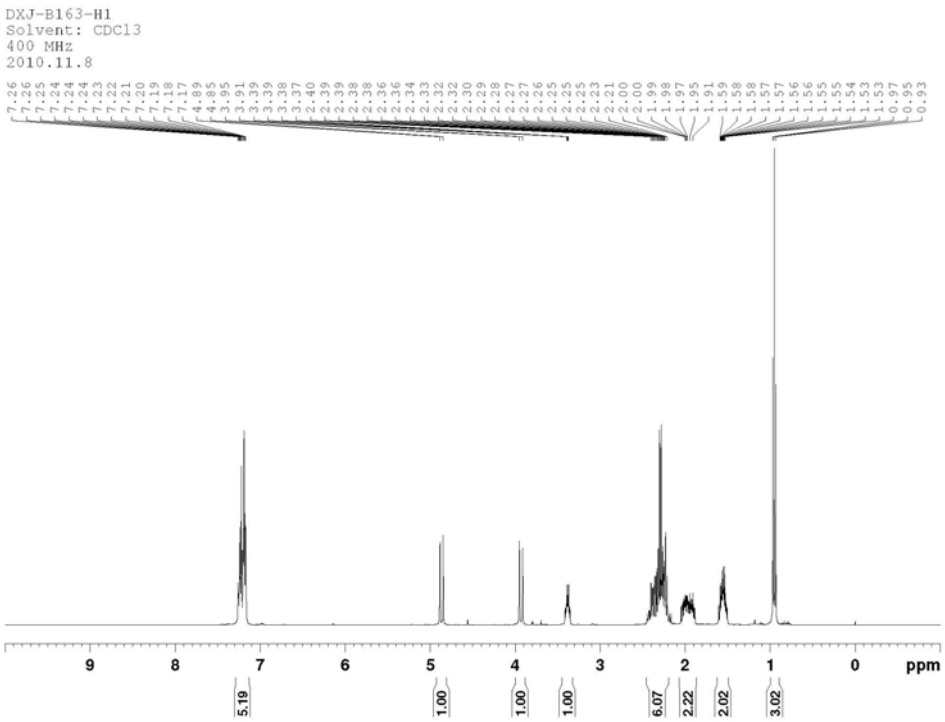
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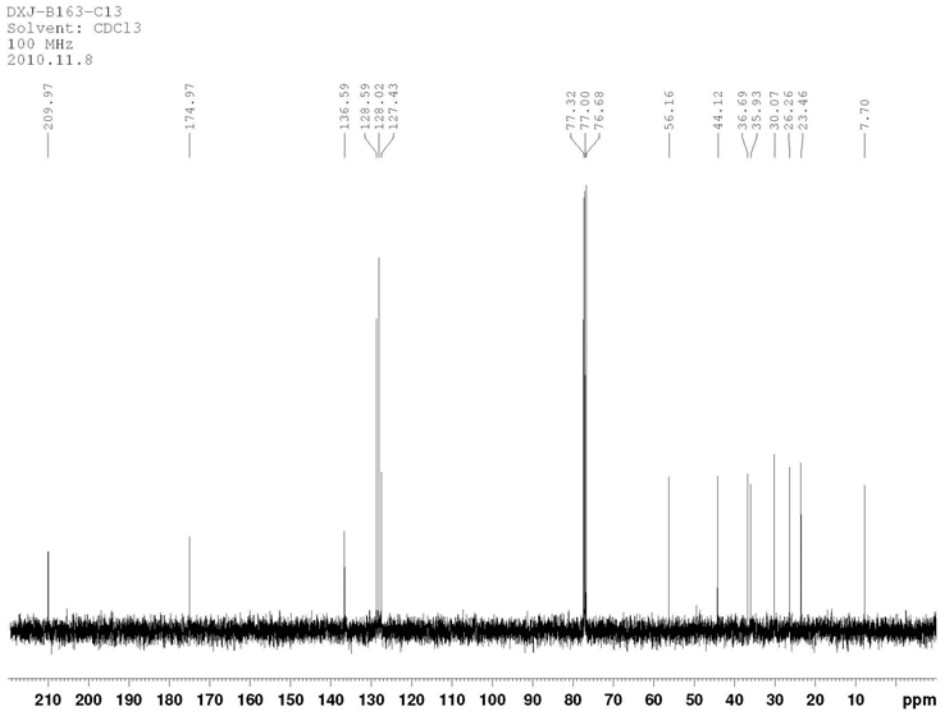
3.02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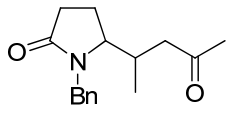
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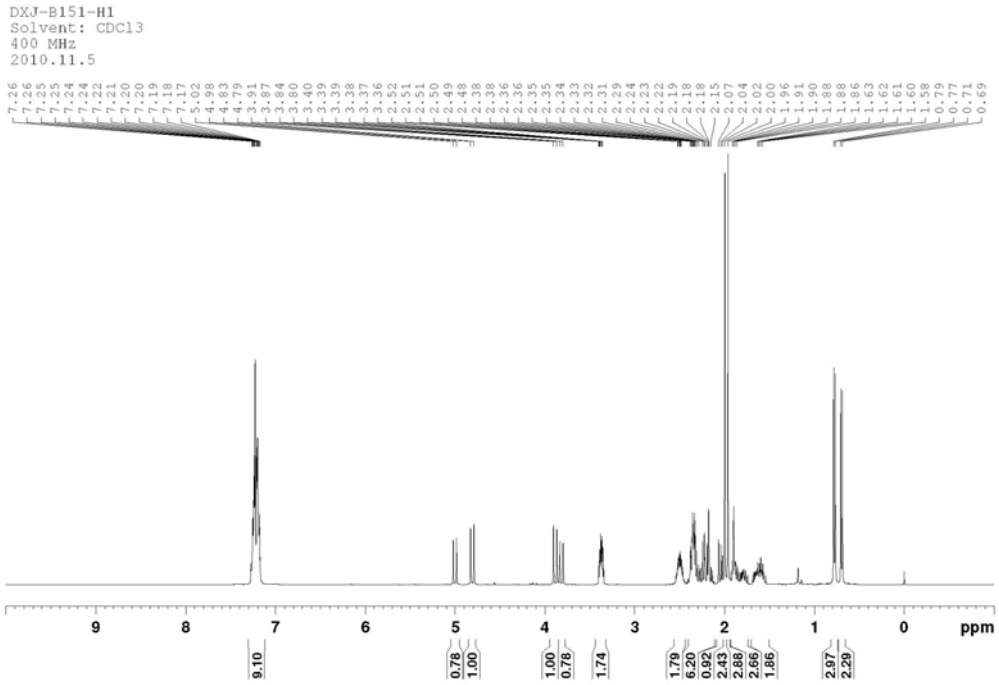
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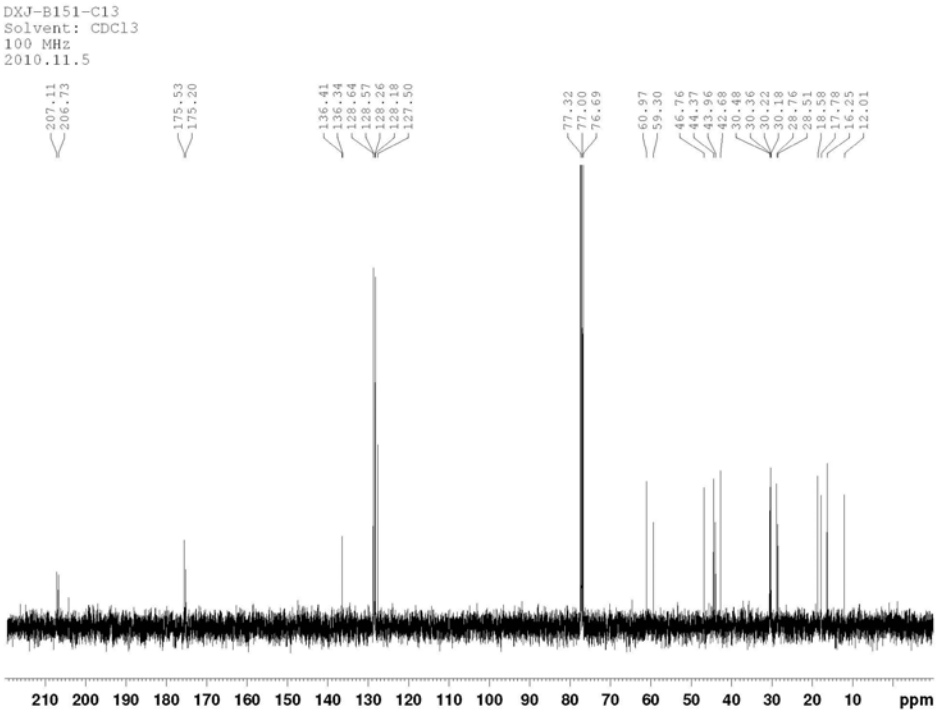
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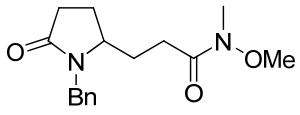
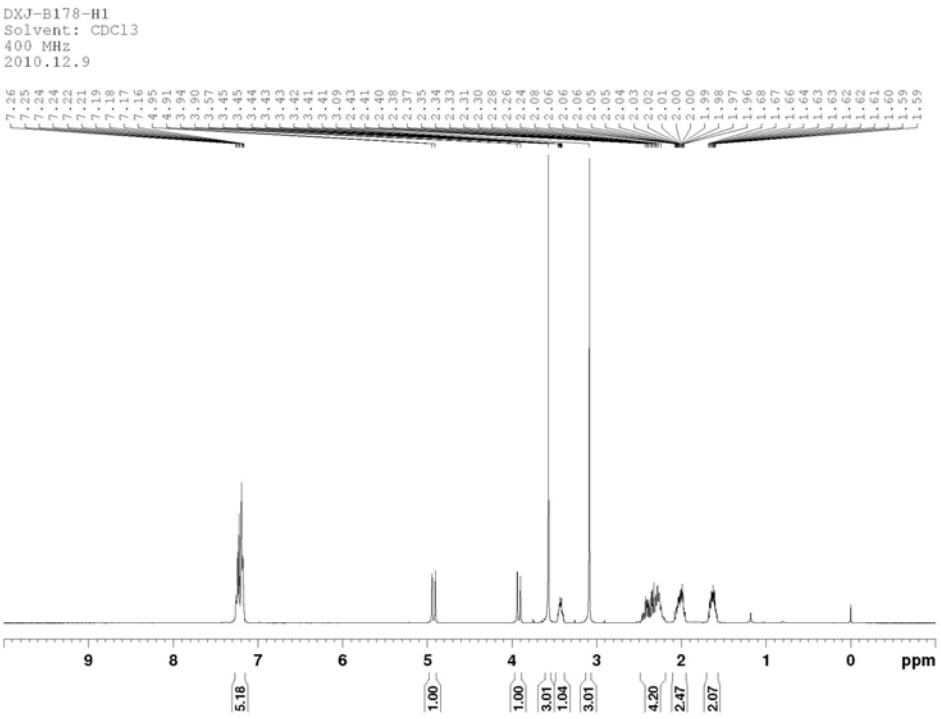
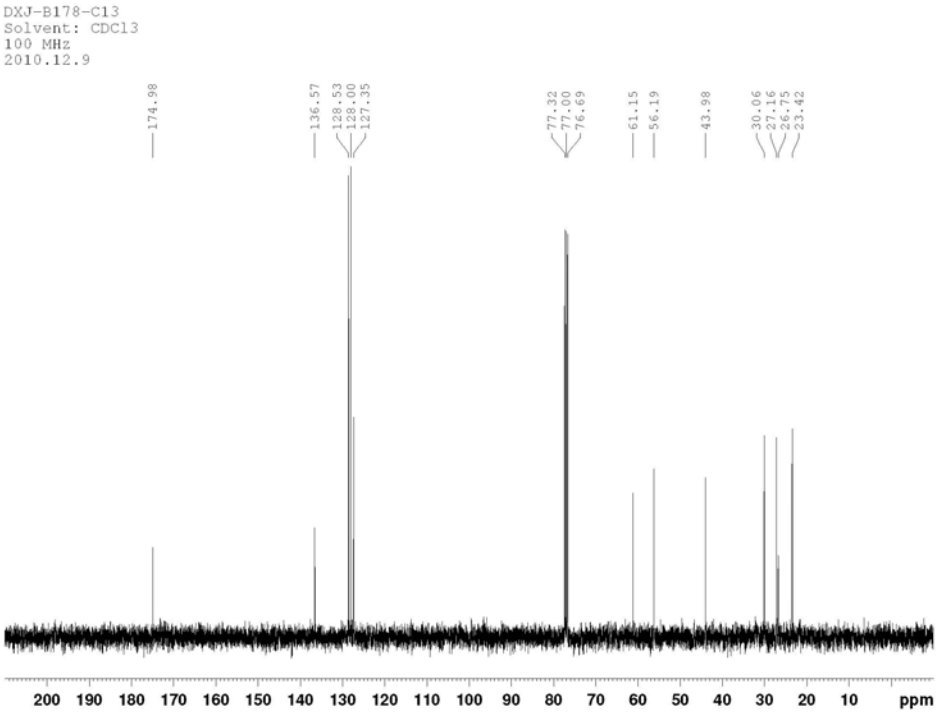
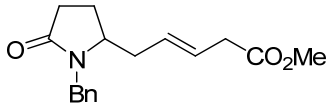
2010.11.5
ppm


O
N
Bn
O
N
OMe

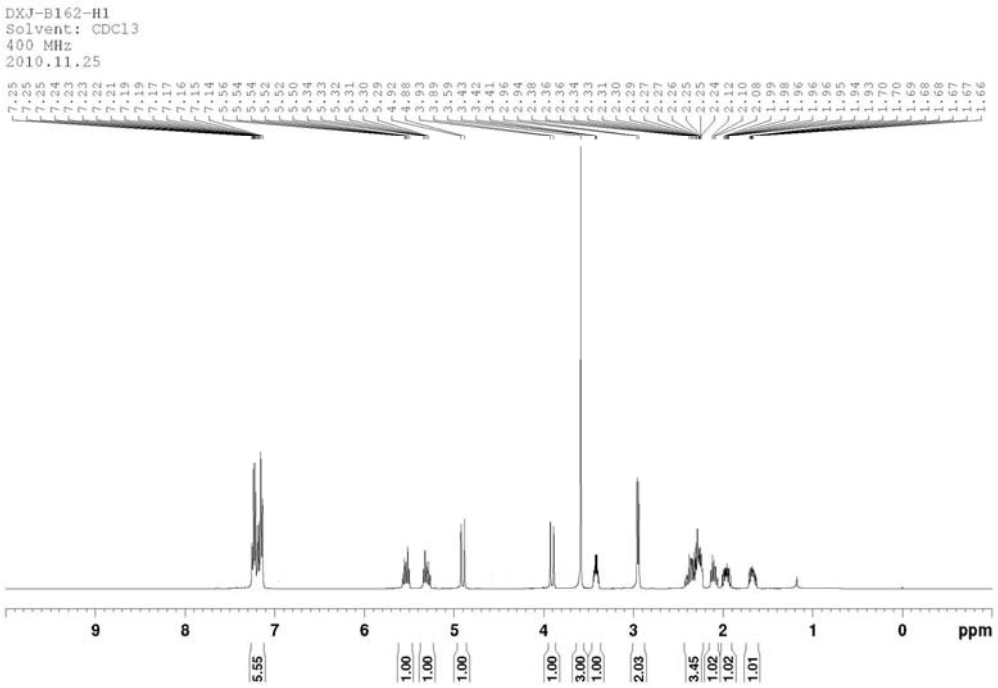
2g

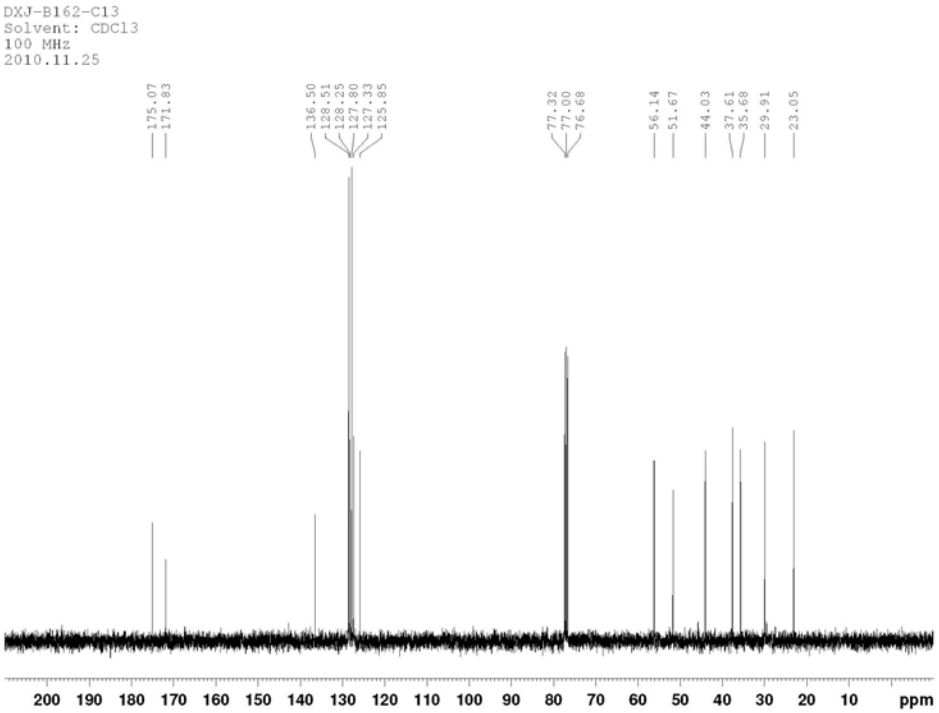

DXJ-B178-H1
Solvent: CDCl3
400 MHz
2010.12.9
7.26 7.25 7.24 7.24 7.22 7.21 7.19 7.18 7.17 7.16 4.95 4.91 3.94 3.90 3.57 3.45 3.45 3.44 3.43 3.43 3.42 3.41 3.41 3.09 2.43 2.41 2.40 2.38 2.37 2.35 2.34 2.33 2.31 2.30 2.28 2.26 2.24 2.08 2.06 2.06 2.06 2.05 2.05 2.04 2.03 2.02 2.01 2.00 2.00 1.99 1.98 1.97 1.96 1.68 1.67 1.66 1.64 1.63 1.63 1.62 1.62 1.61 1.60 1.59 1.59
9 8 7 6 5 4 3 2 1 0 ppm
5.18 1.00 1.00 3.01 1.04 3.01 4.20 2.47 2.07

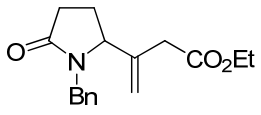

DXJ-B178-C13
Solvent: CDCl3
100 MHz
2010.12.9
174.98 136.57 128.53 128.00 127.35 77.32 77.00 76.69 61.15 56.19 43.98 30.06 27.16 26.75 23.42
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


O
N
Bn
CO2Me

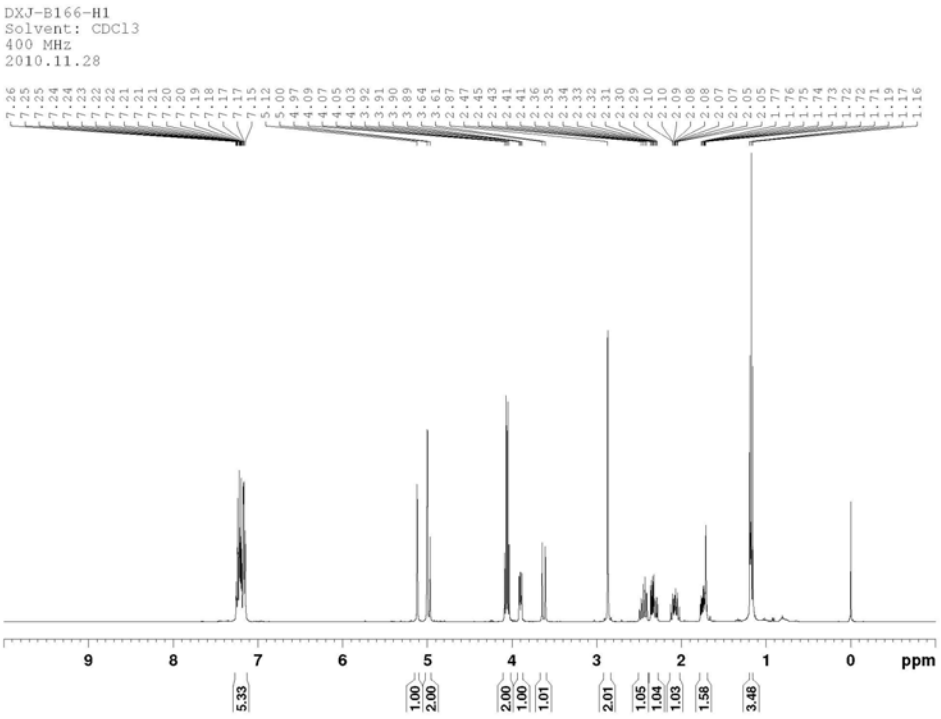
2h

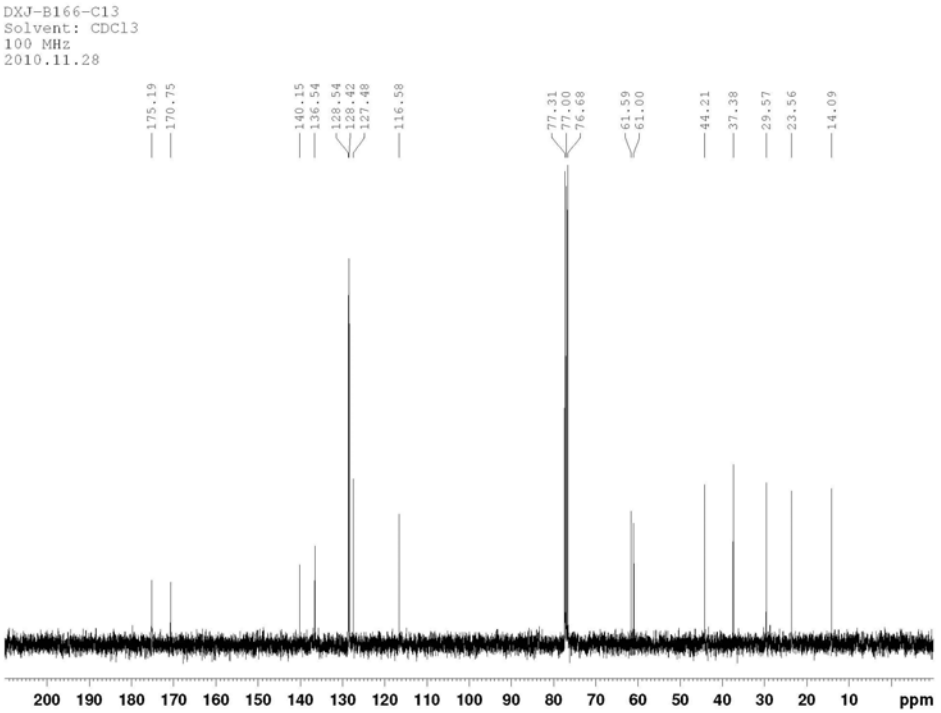

DXJ-B162-H1
Solvent: CDCl3
400 MHz
2010.11.25
ppm

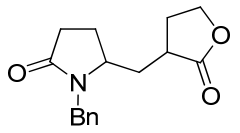

DXJ-B162-C13
Solvent: CDCl3
100 MHz
2010.11.25
ppm


O
N
Bn
CO2Et

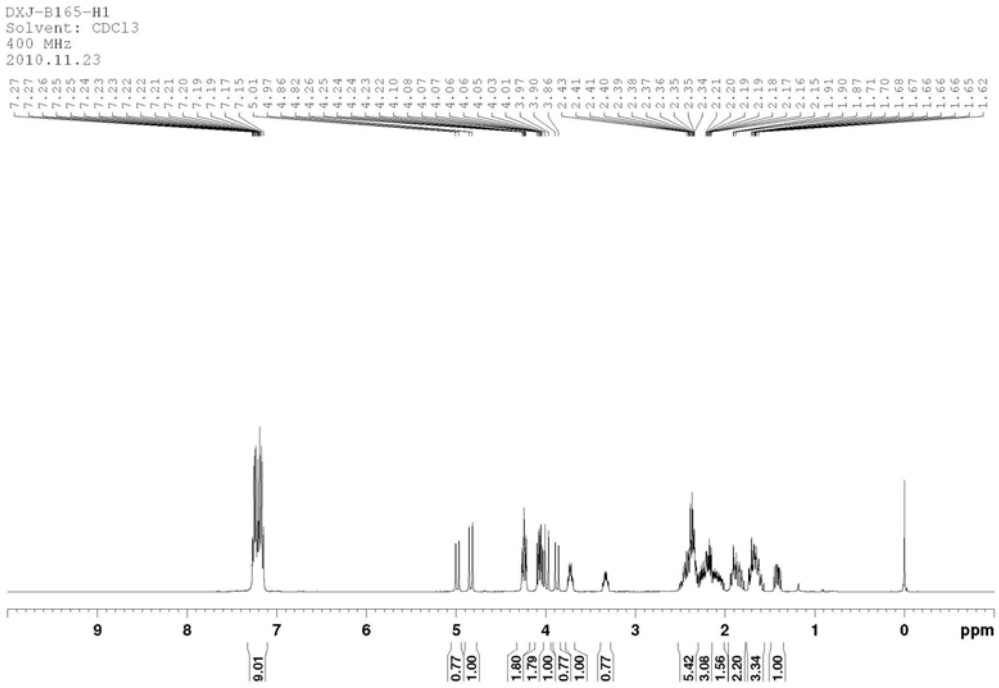
2i

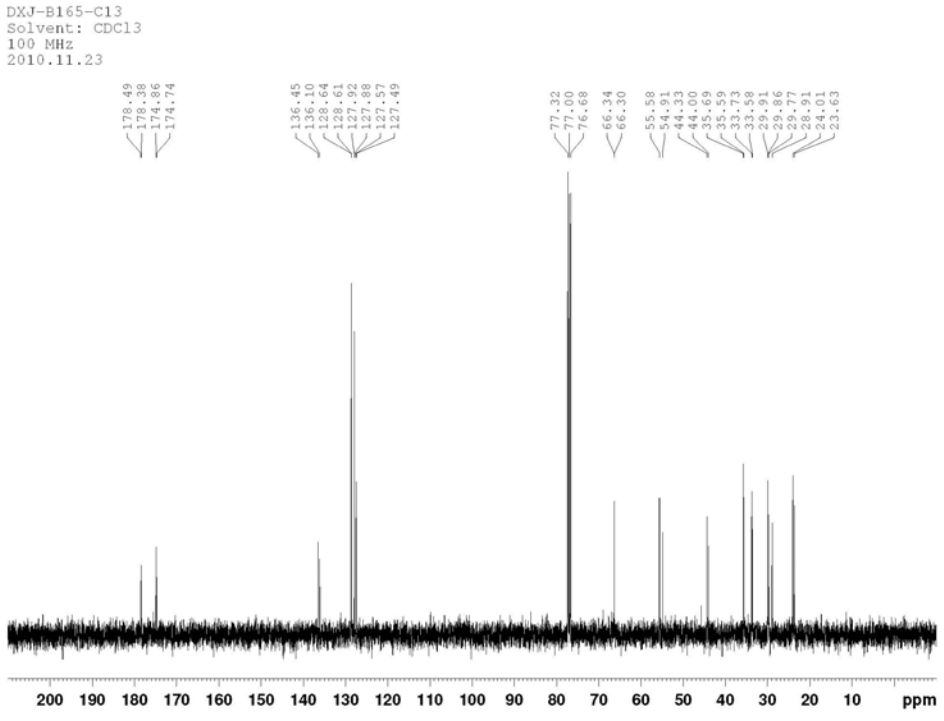

DXJ-B166-H1
Solvent: CDCl3
400 MHz
2010.11.28
ppm

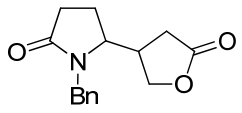

DXJ-B166-C13
Solvent: CDCl3
100 MHz
2010.11.28
ppm


O
O
N
Bn
O
O

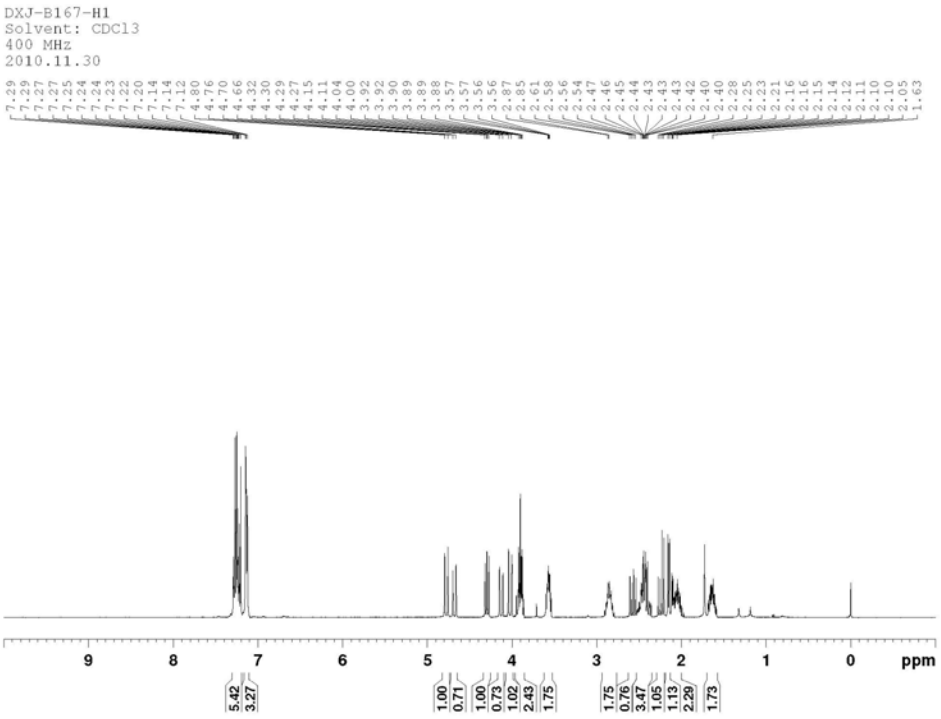
2j

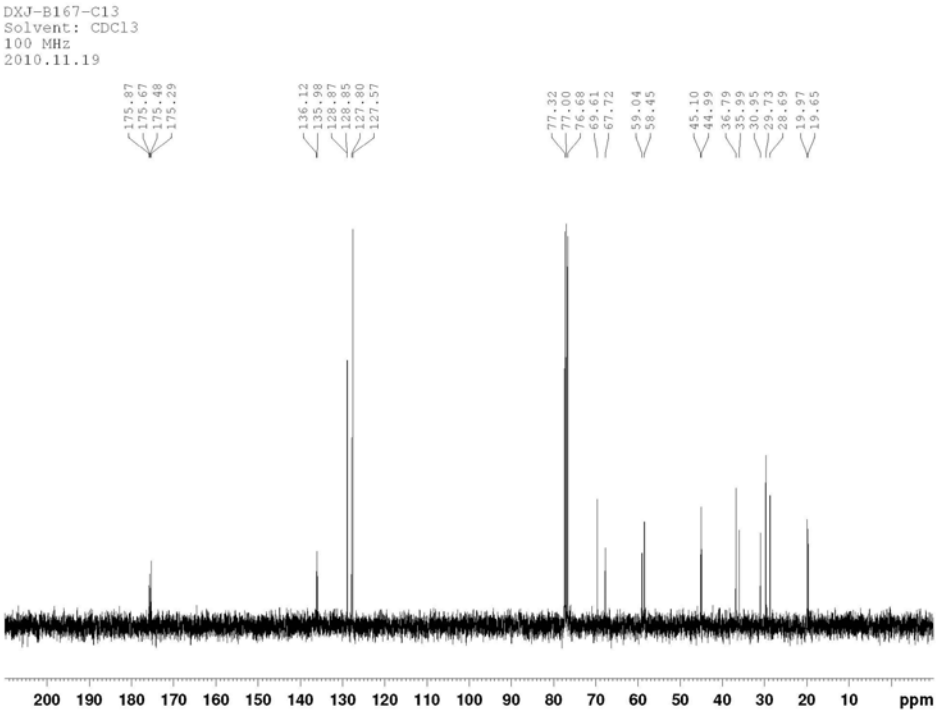

DXJ-B165-H1
Solvent: CDCl3
400 MHz
2010.11.23
ppm

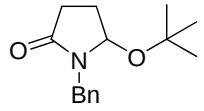

DXJ-B165-C13
Solvent: CDCl3
100 MHz
2010.11.23
ppm


O
N
Bn
O
O

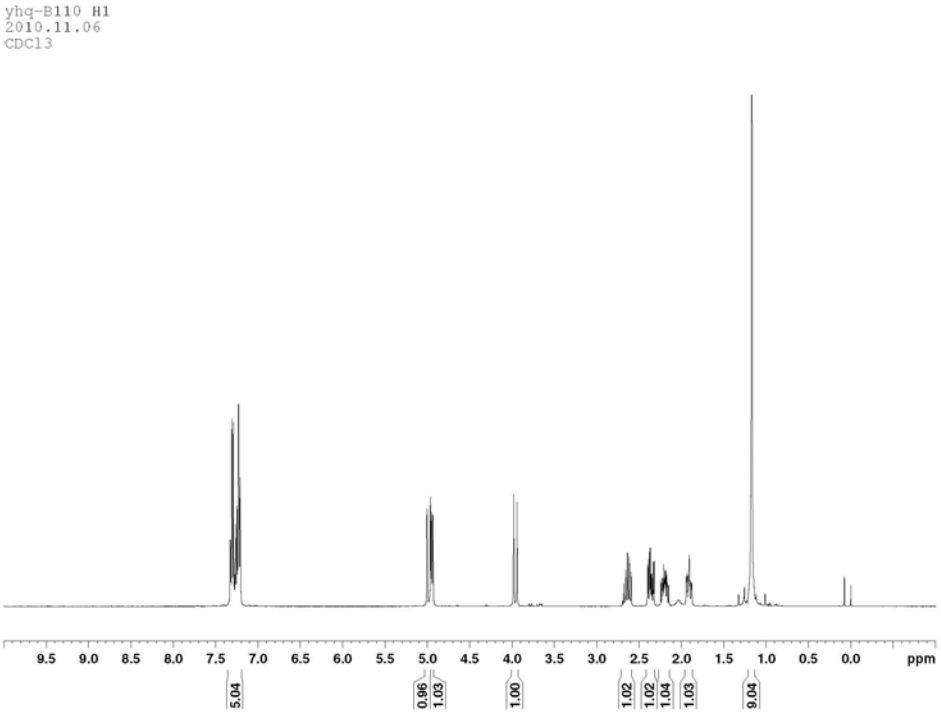
2k

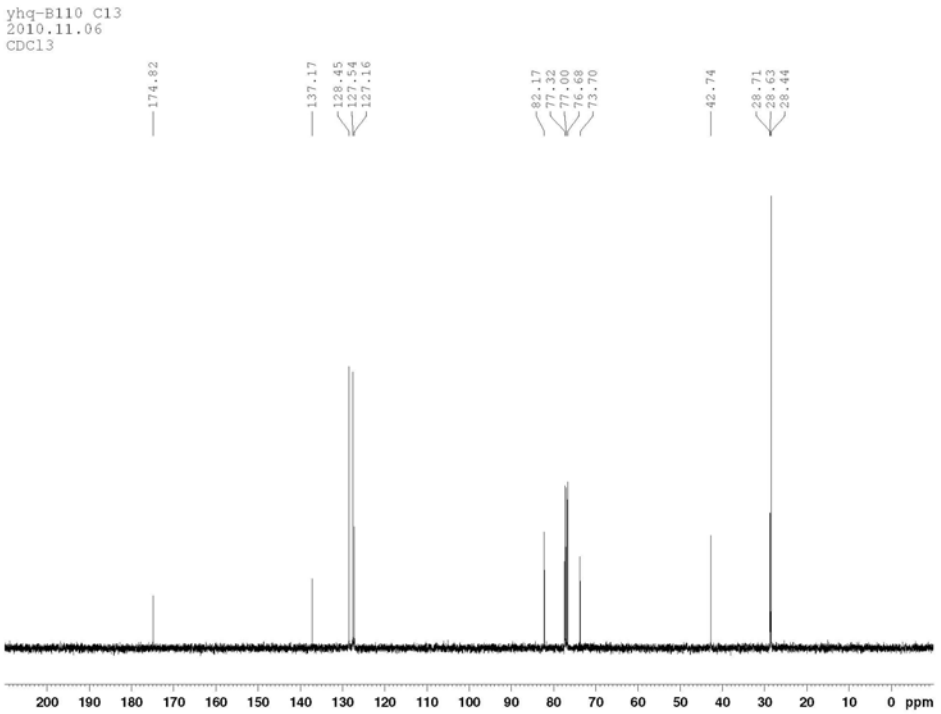

DXJ-B167-H1
Solvent: CDCl3
400 MHz
2010.11.30
ppm
5.42
3.27
1.00
0.71
1.00
0.73
1.02
2.43
1.75
1.75
0.76
3.47
1.05
1.13
2.29
1.73

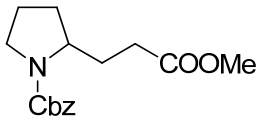

DXJ-B167-C13
Solvent: CDCl3
100 MHz
2010.11.19
ppm


O
N
Bn
O

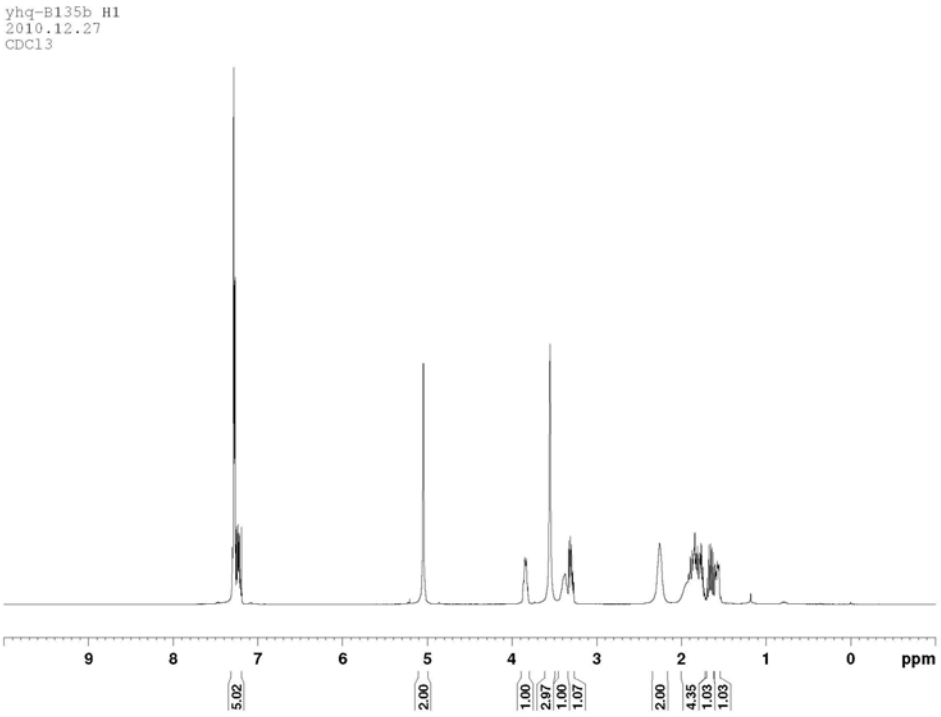
4

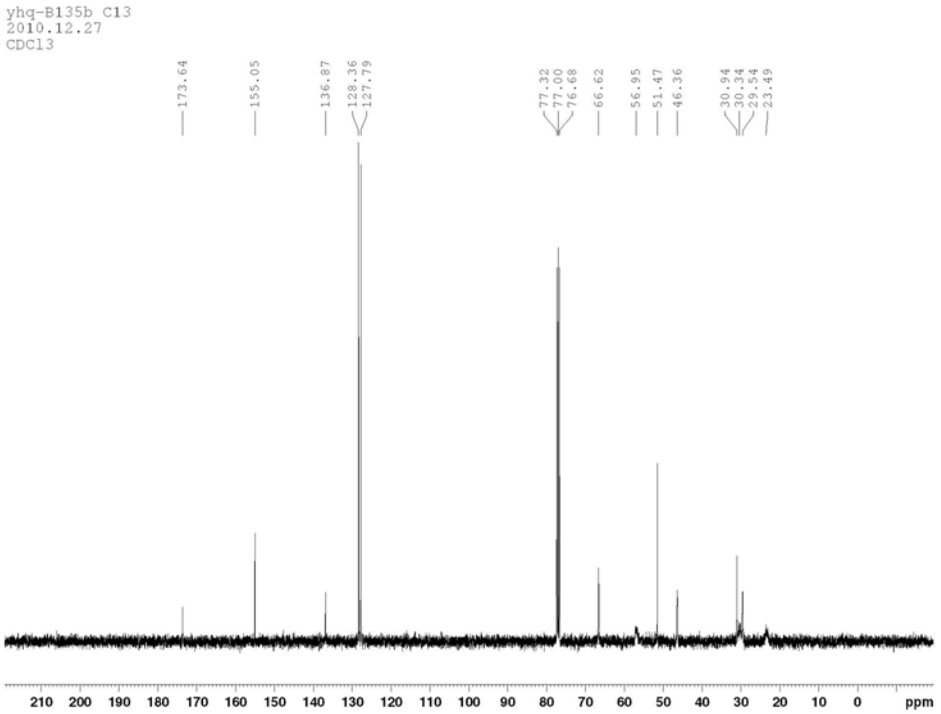

yhq-B110 H1
2010.11.06
CDCl3
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
5.04
0.96
1.03
1.00
1.02
1.02
1.04
1.03
9.04

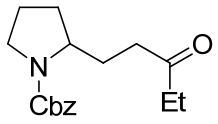

yhq-B110 C13
2010.11.06
CDCl3
174.82
137.17
128.45
127.54
127.16
82.17
77.32
77.00
76.68
73.70
42.74
28.71
28.63
28.44
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


COOMe
N
Cbz

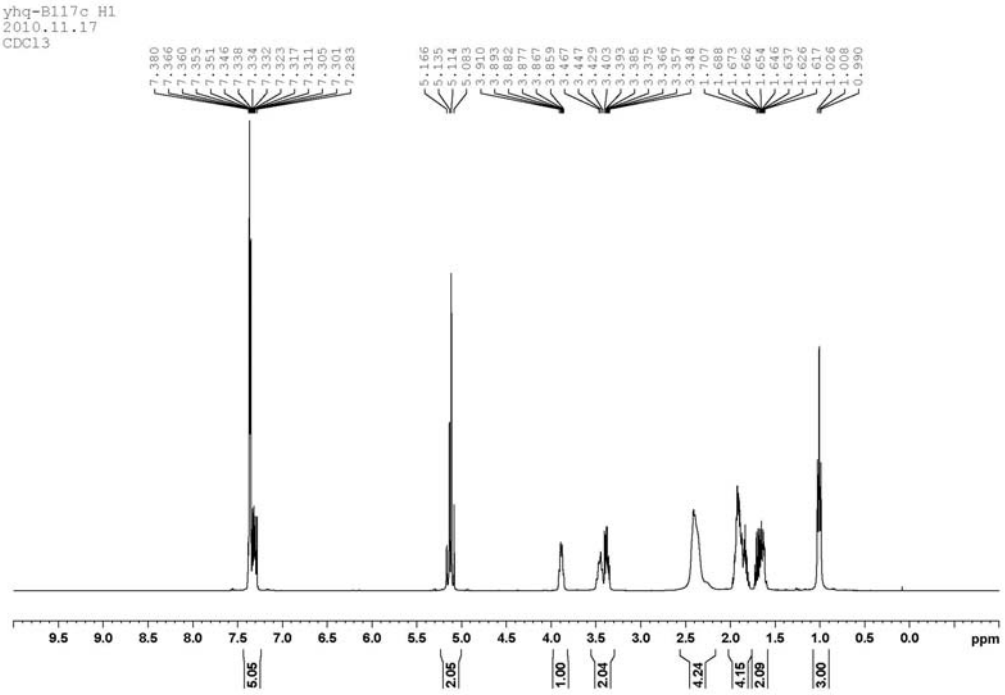
6a

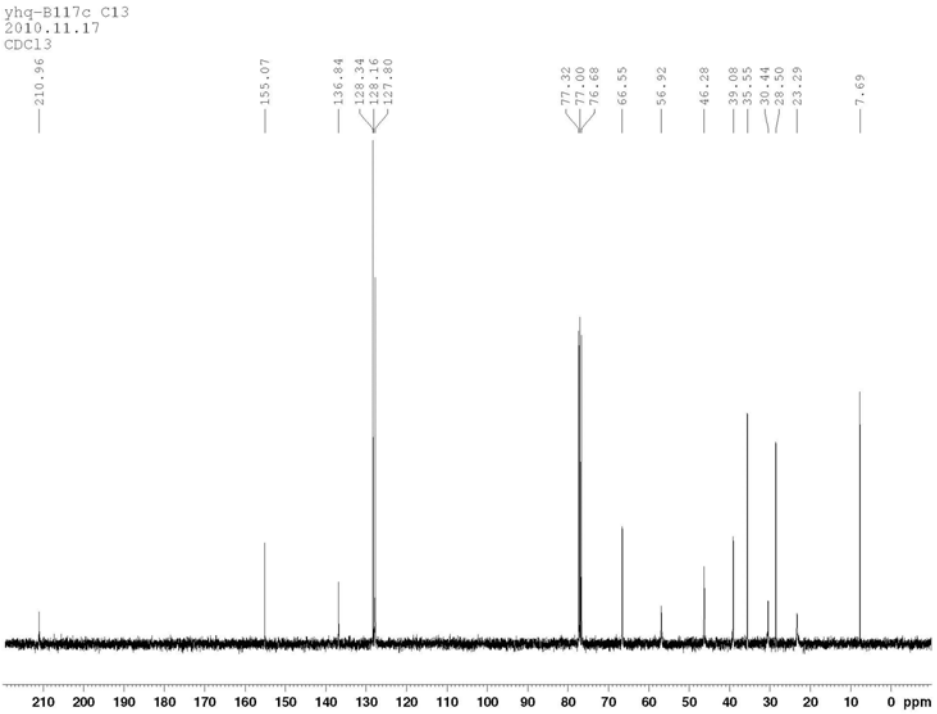

yhq-B135b H1
2010.12.27
CDCl3
9
8
7
6
5
4
3
2
1
0
ppm
5.02
2.00
1.00
2.97
1.00
1.07
2.00
4.35
1.03
1.03

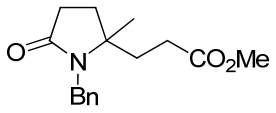

yhq-B135b C13
2010.12.27
CDCl3
173.64
155.05
136.87
128.36
127.79
77.32
77.00
76.68
66.62
56.95
51.47
46.36
30.94
30.34
29.54
23.49
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


N
Cbz
O
Et

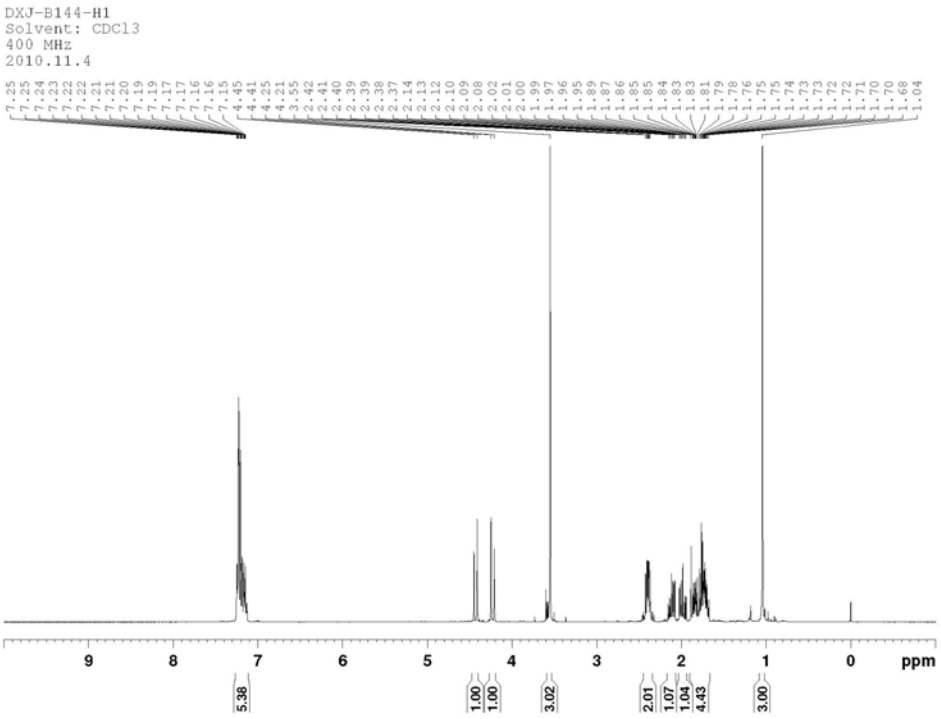
6e

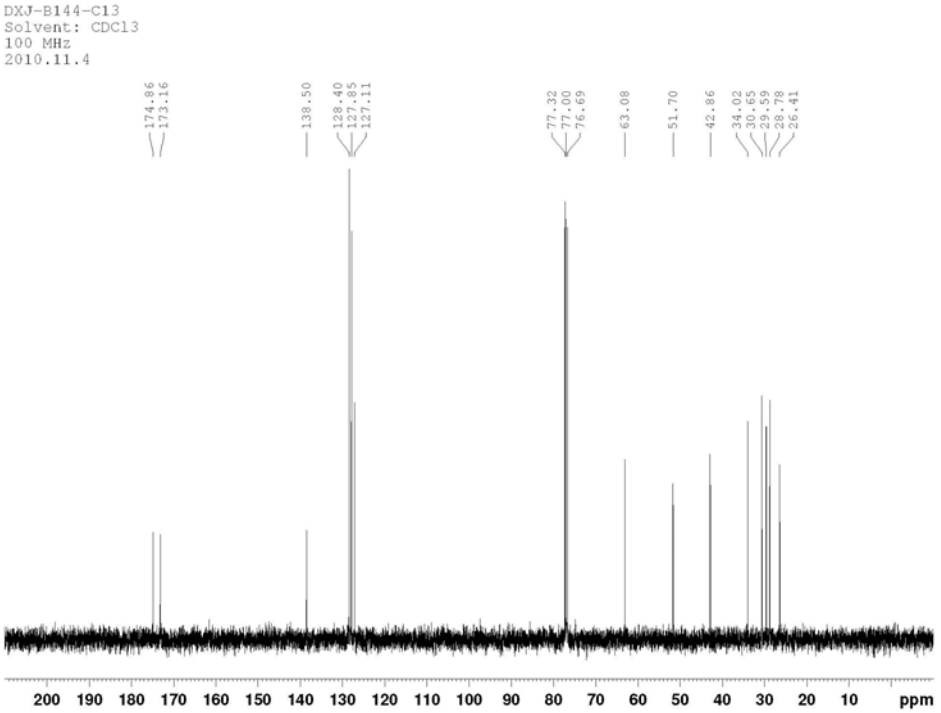

yhq-B117c H1
2010.11.17
CDCl3
7.380
7.366
7.360
7.353
7.351
7.346
7.338
7.334
7.332
7.323
7.317
7.311
7.305
7.301
7.283
5.166
5.135
5.114
5.083
3.910
3.893
3.882
3.877
3.867
3.859
3.467
3.447
3.429
3.403
3.393
3.385
3.375
3.366
3.357
3.348
1.707
1.688
1.673
1.662
1.654
1.646
1.637
1.626
1.617
1.026
1.008
0.990
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
5.05
2.05
1.00
2.04
4.24
4.15
2.09
3.00

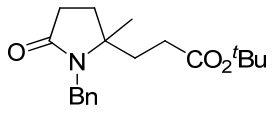

yhq-B117c C13
2010.11.17
CDCl3
210.96
155.07
136.84
128.34
128.16
127.80
77.32
77.00
76.68
66.55
56.92
46.28
39.08
35.55
30.44
28.50
23.29
7.69
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


O
N
Bn
CO2Me

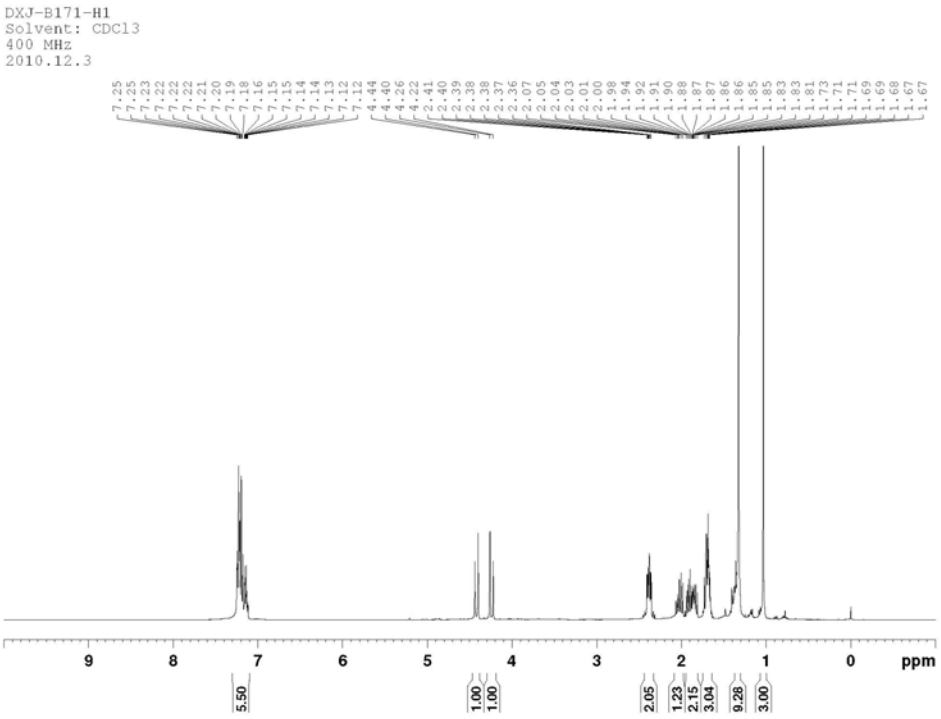
9a

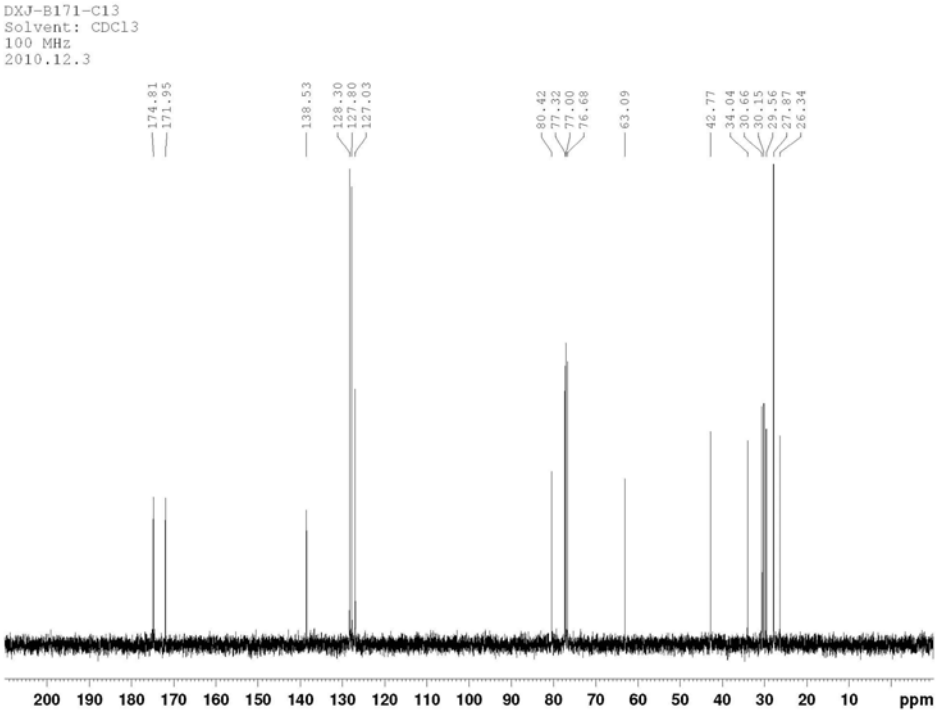

DXJ-B144-H1
Solvent: CDCl3
400 MHz
2010.11.4
ppm

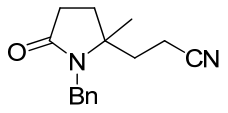

DXJ-B144-C13
Solvent: CDCl3
100 MHz
2010.11.4
ppm


O
N
Bn
CO2tBu

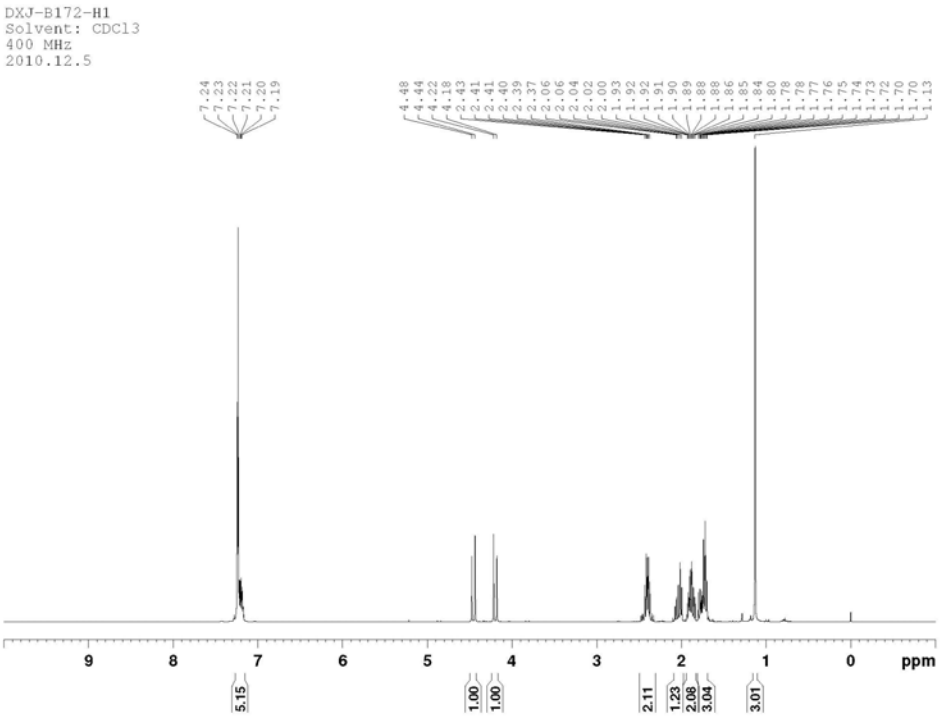
9b

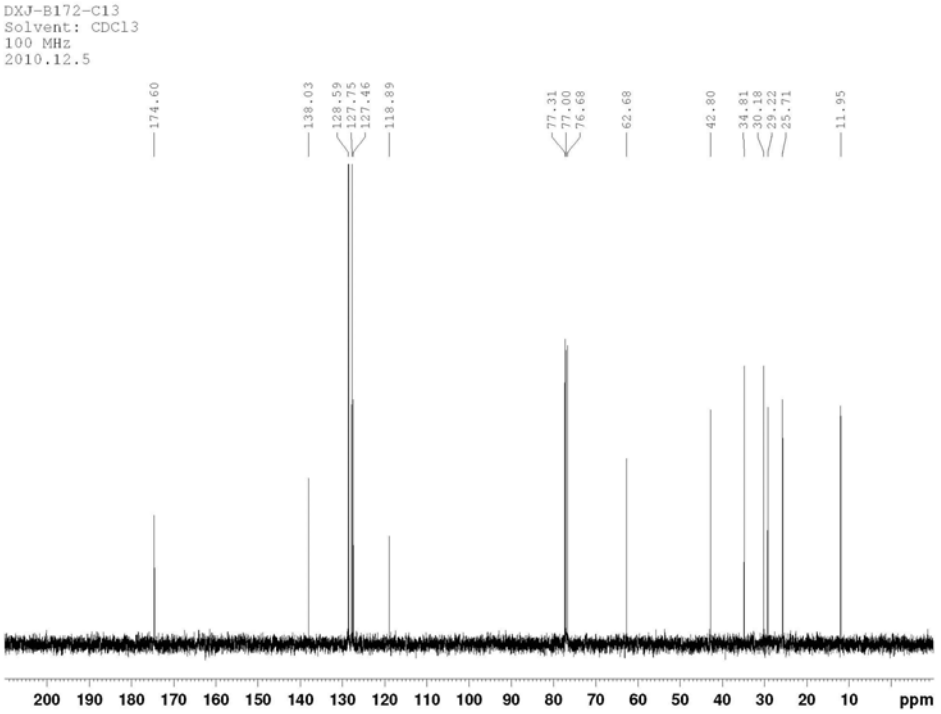

DXJ-B171-H1
Solvent: CDCl3
400 MHz
2010.12.3
ppm

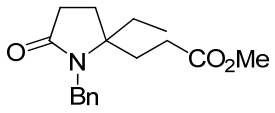

DXJ-B171-C13
Solvent: CDCl3
100 MHz
2010.12.3
ppm


O
N
Bn
CN

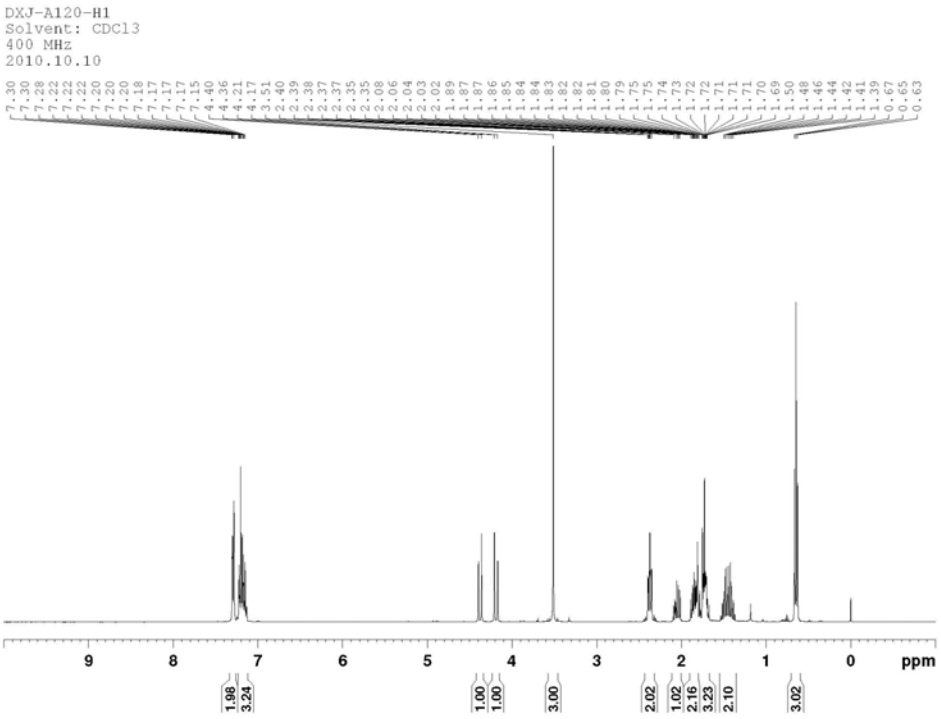
9c

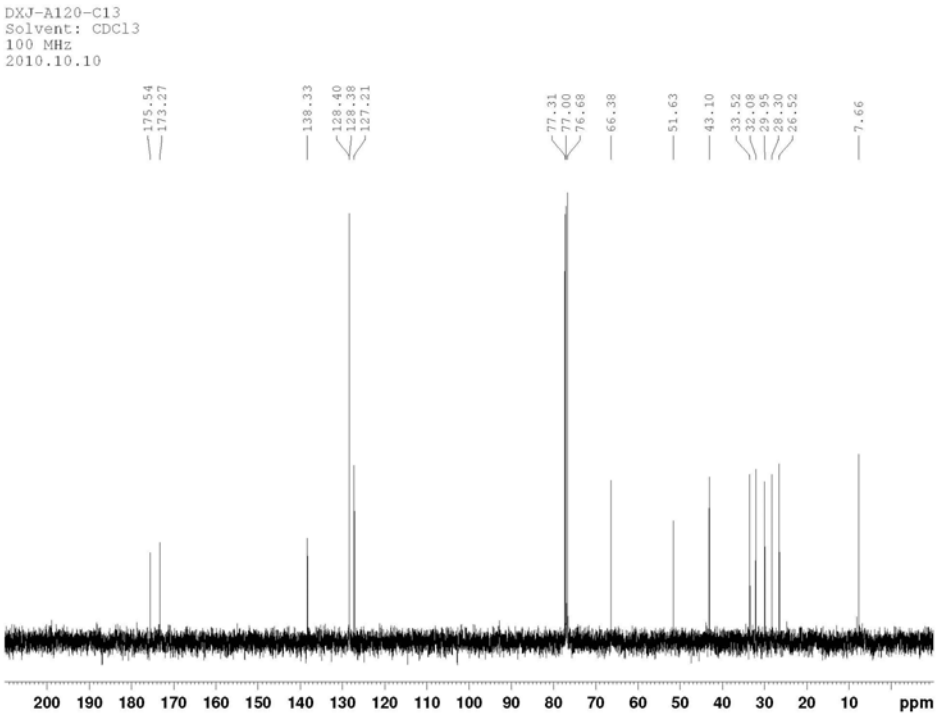

DXJ-B172-H1
Solvent: CDCl3
400 MHz
2010.12.5
7.24
7.23
7.22
7.21
7.20
7.19
4.48
4.44
4.22
4.18
2.43
2.41
2.41
2.40
2.39
2.37
2.06
2.06
2.04
2.02
2.00
1.93
1.92
1.92
1.91
1.90
1.89
1.88
1.88
1.86
1.85
1.84
1.80
1.78
1.78
1.77
1.76
1.75
1.74
1.73
1.72
1.70
1.70
1.13
9
8
7
6
5
4
3
2
1
0
ppm
5.15
1.00
1.00
2.11
1.23
2.08
3.04
3.01

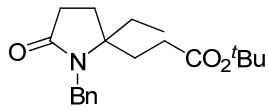

DXJ-B172-C13
Solvent: CDCl3
100 MHz
2010.12.5
174.60
138.03
128.59
127.75
127.46
118.89
77.31
77.00
76.68
62.68
42.80
34.81
30.18
29.22
25.71
11.95
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


O
N
Bn
CO2Me

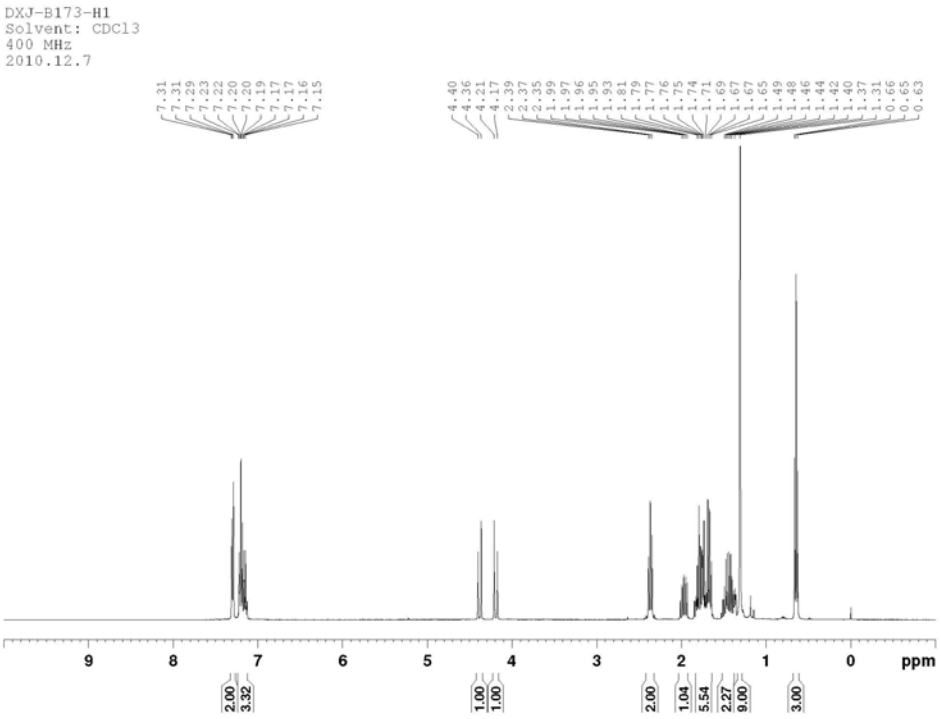
11a

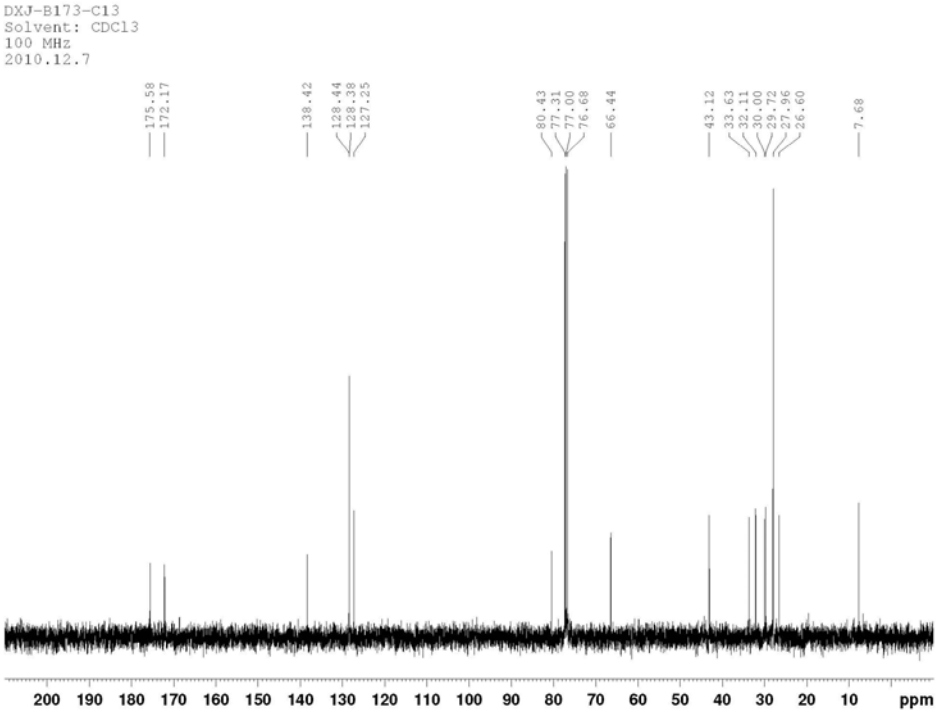

DXJ-A120-H1
Solvent: CDCl3
400 MHz
2010.10.10
ppm
1.98
3.24
1.00
1.00
3.00
2.02
1.02
2.16
3.23
2.10
3.02

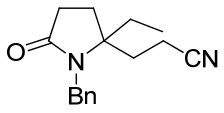

DXJ-A120-C13
Solvent: CDCl3
100 MHz
2010.10.10
175.54
173.27
138.33
128.40
128.38
127.21
77.31
77.00
76.68
66.38
51.63
43.10
33.52
32.08
29.95
28.30
26.52
7.66
ppm


O
N
Bn
CO2tBu

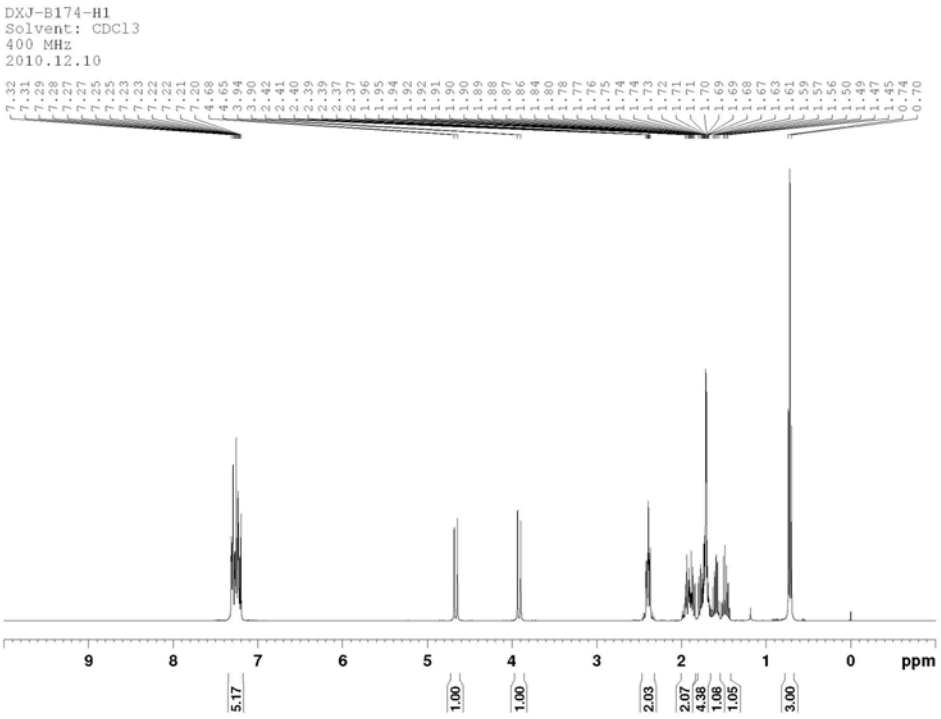
11b

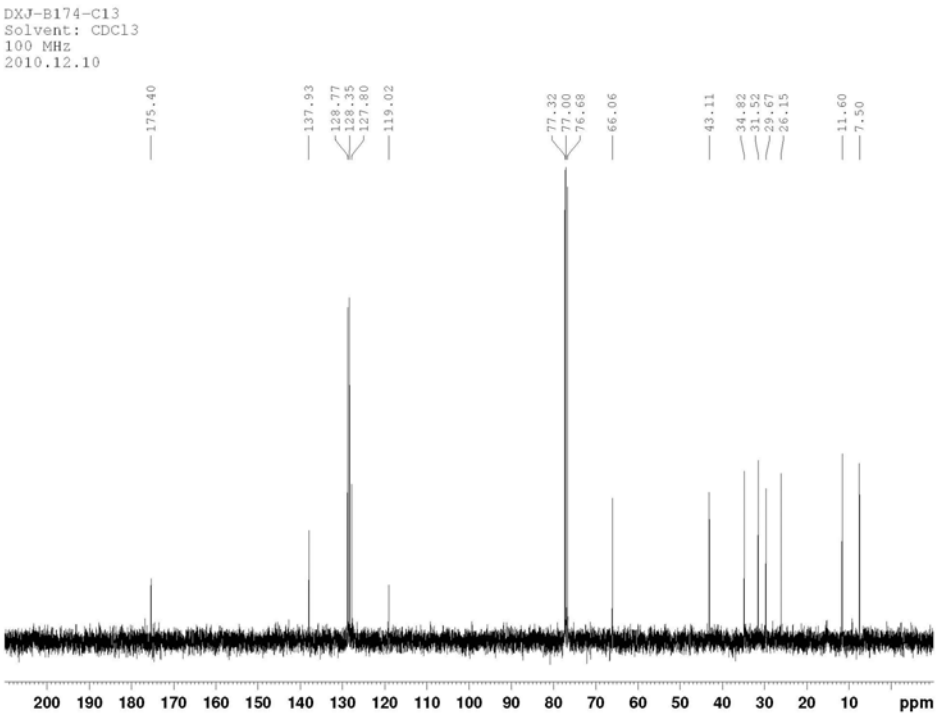

DXJ-B173-H1
Solvent: CDCl3
400 MHz
2010.12.7
7.31
7.31
7.29
7.23
7.22
7.20
7.20
7.19
7.17
7.17
7.16
7.15
4.40
4.36
4.21
4.17
2.39
2.37
2.35
1.99
1.97
1.96
1.95
1.93
1.81
1.79
1.77
1.76
1.75
1.74
1.71
1.69
1.67
1.67
1.65
1.49
1.48
1.46
1.44
1.42
1.40
1.37
1.31
0.66
0.65
0.63
9
8
7
6
5
4
3
2
1
0
ppm
2.00
3.32
1.00
1.00
2.00
1.04
5.54
2.27
9.00
3.00

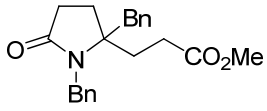

DXJ-B173-C13
Solvent: CDCl3
100 MHz
2010.12.7
175.58
172.17
138.42
128.44
128.38
127.25
80.43
77.31
77.00
76.68
66.44
43.12
33.63
32.11
30.00
29.72
27.96
26.60
7.68
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


O
N
Bn
CN

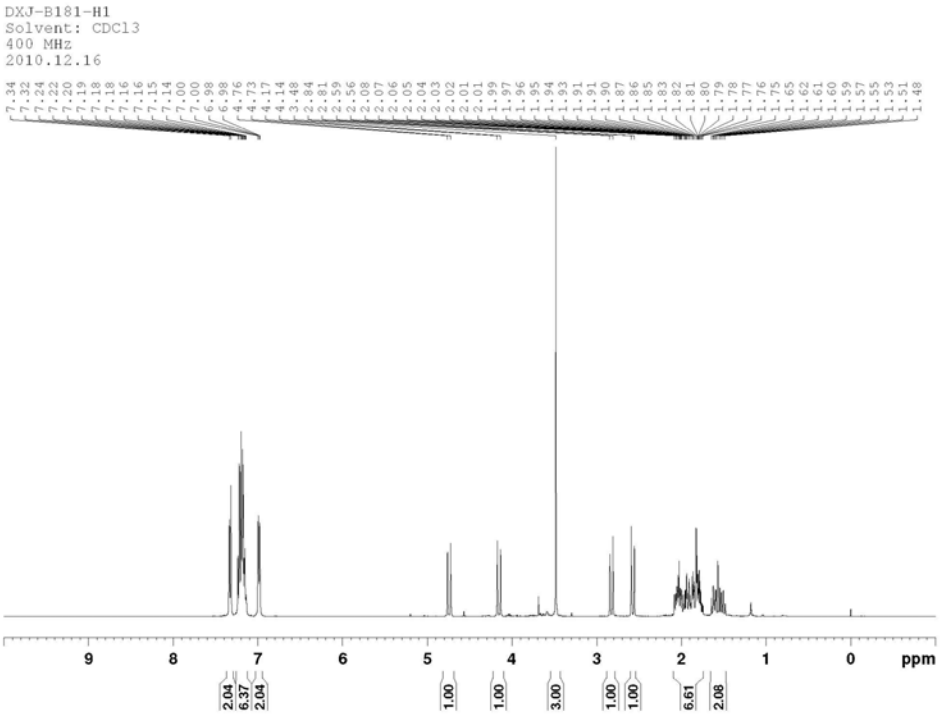
11c

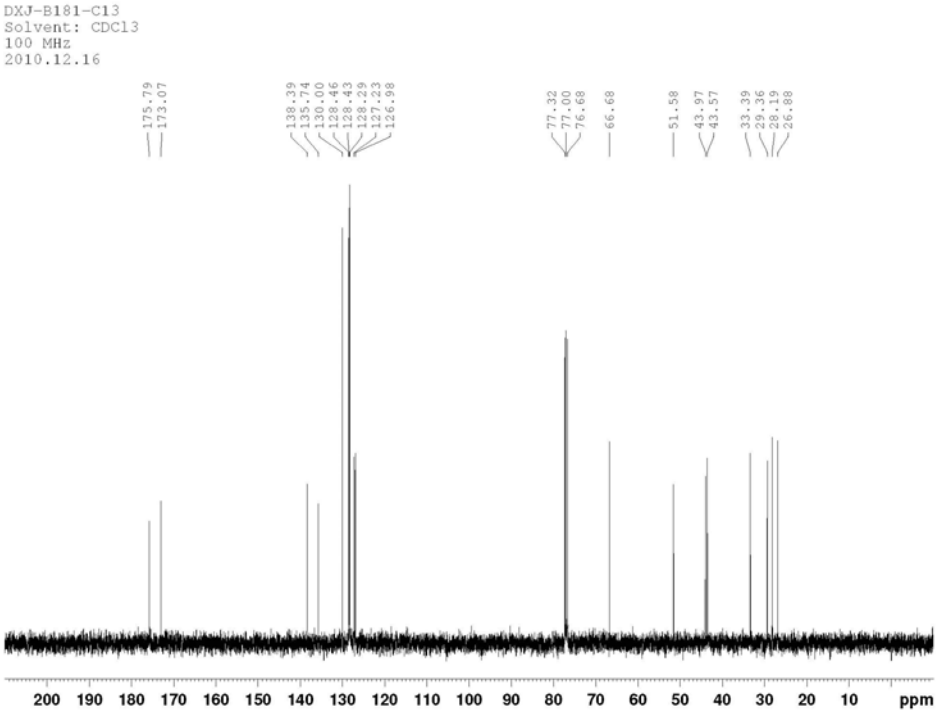

DXJ-B174-H1
Solvent: CDCl3
400 MHz
2010.12.10
ppm
5.17
1.00
1.00
2.03
2.07
4.38
1.08
1.05
3.00

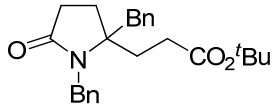

DXJ-B174-C13
Solvent: CDCl3
100 MHz
2010.12.10
175.40
137.93
128.77
128.35
127.80
119.02
77.32
77.00
76.68
66.06
43.11
34.82
31.52
29.67
26.15
11.60
7.50
ppm


Bn
O
N
CO2Me
Bn

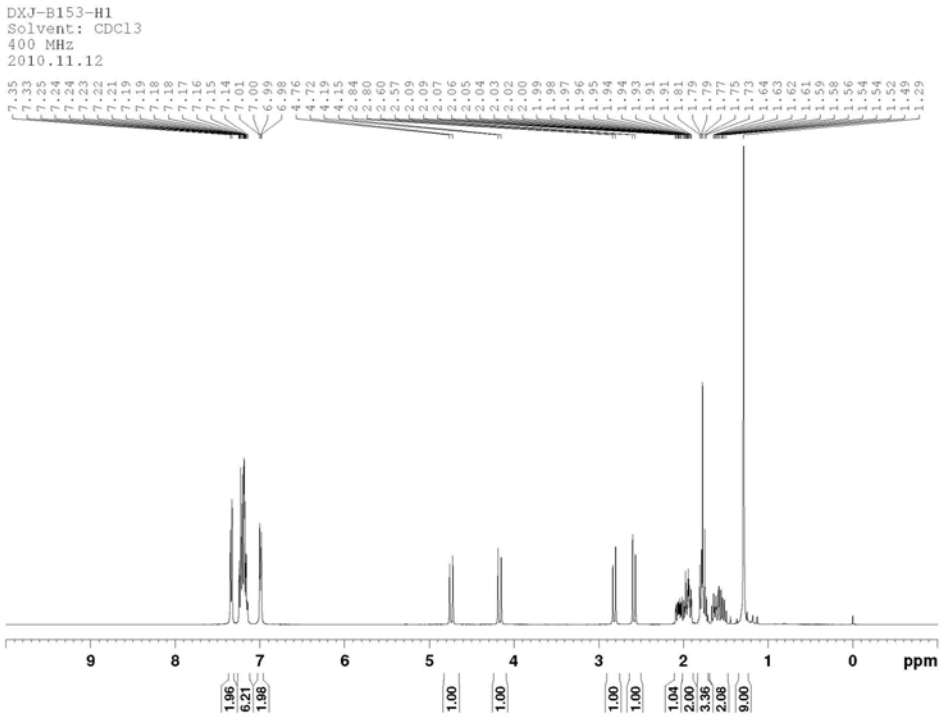
13a

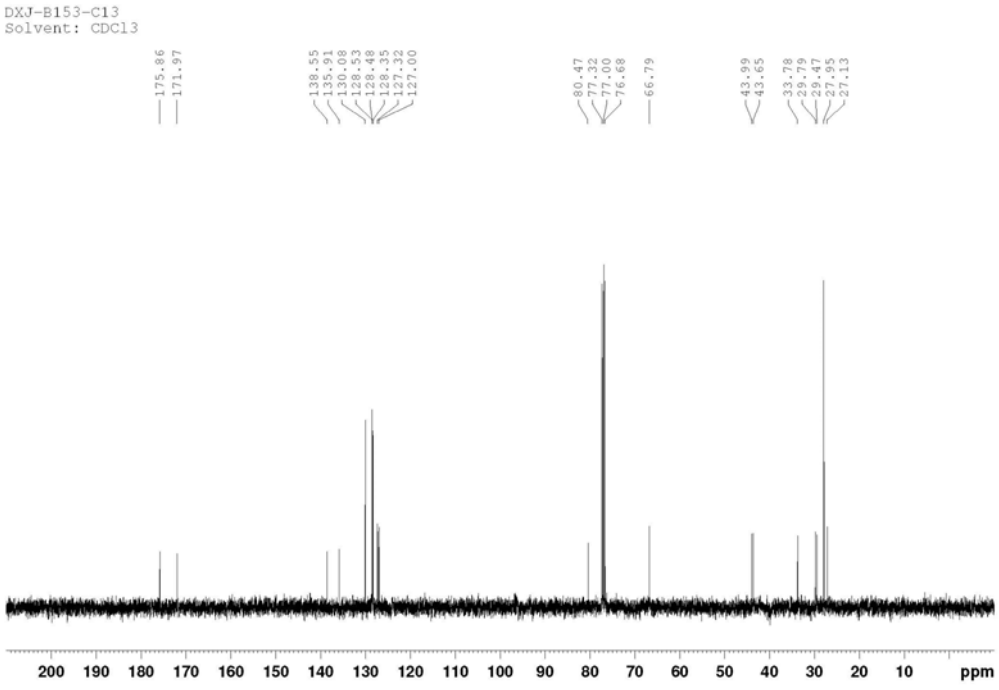

DXJ-B181-H1
Solvent: CDCl3
400 MHz
2010.12.16
7.34 7.32 7.24 7.22 7.20 7.19 7.18 7.18 7.16 7.15 7.14 7.00 7.00 6.98 6.98 4.76 4.73 4.17 4.14 3.48 2.84 2.81 2.59 2.56 2.08 2.07 2.06 2.05 2.04 2.03 2.02 2.01 2.01 1.99 1.97 1.96 1.95 1.94 1.93 1.91 1.91 1.90 1.87 1.86 1.85 1.83 1.82 1.81 1.80 1.79 1.78 1.77 1.76 1.75 1.65 1.62 1.61 1.60 1.59 1.57 1.55 1.53 1.51 1.48
9 8 7 6 5 4 3 2 1 0 ppm
2.04 6.37 2.04 1.00 1.00 3.00 1.00 1.00 6.61 2.08

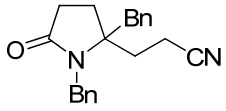

DXJ-B181-C13
Solvent: CDCl3
100 MHz
2010.12.16
175.79 173.07 138.39 135.74 130.00 128.46 128.43 128.29 127.23 126.98 77.32 77.00 76.68 66.68 51.58 43.97 43.57 33.39 29.36 28.19 26.88
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


Bn
O
N
Bn
CO2tBu

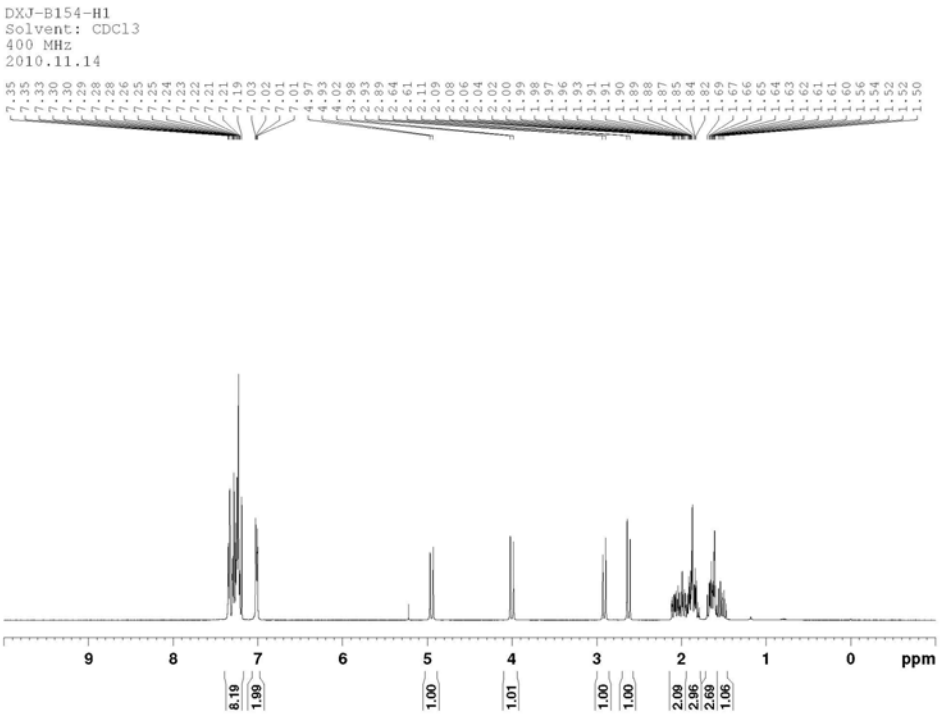
13b

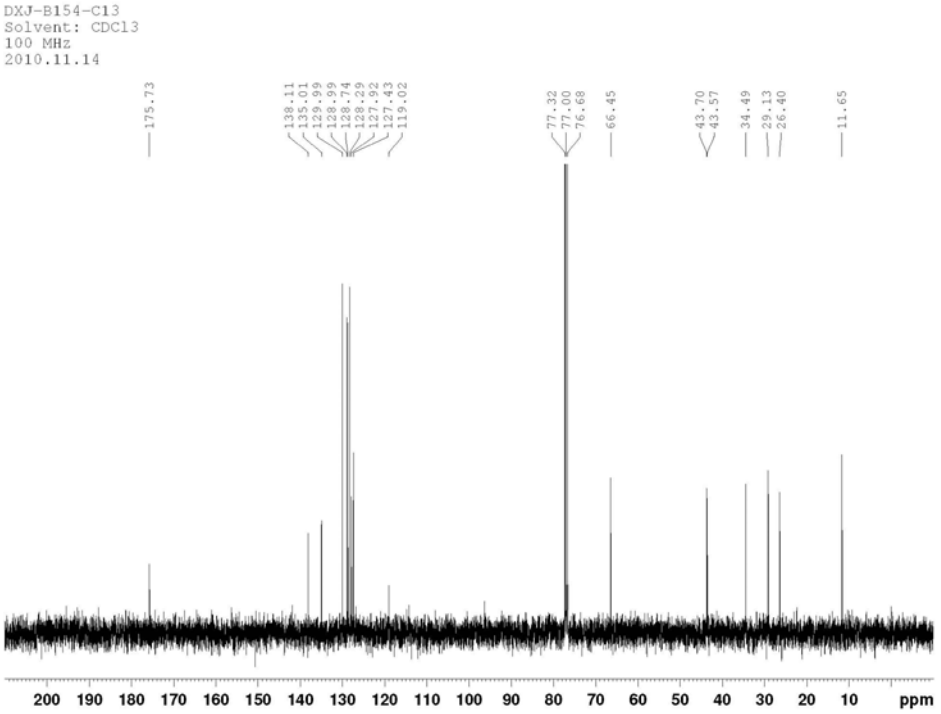

DXJ-B153-H1
Solvent: CDCl3
400 MHz
2010.11.12
ppm

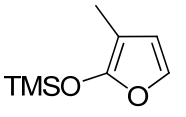

DXJ-B153-C13
Solvent: CDCl3
ppm


Bn
O
N
CN
Bn

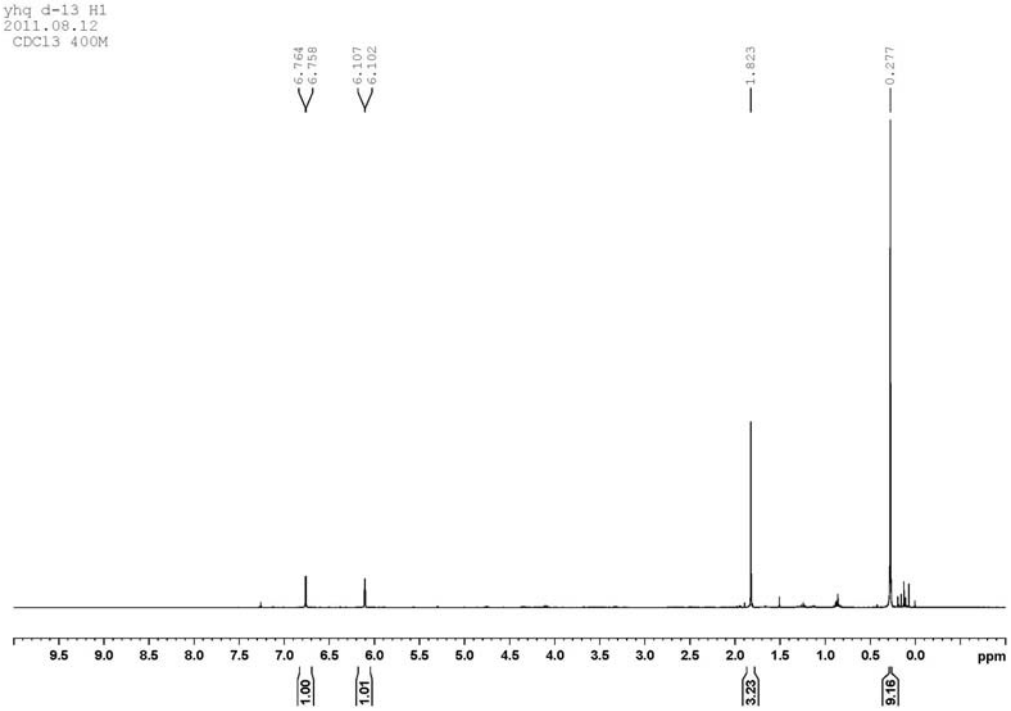
13c

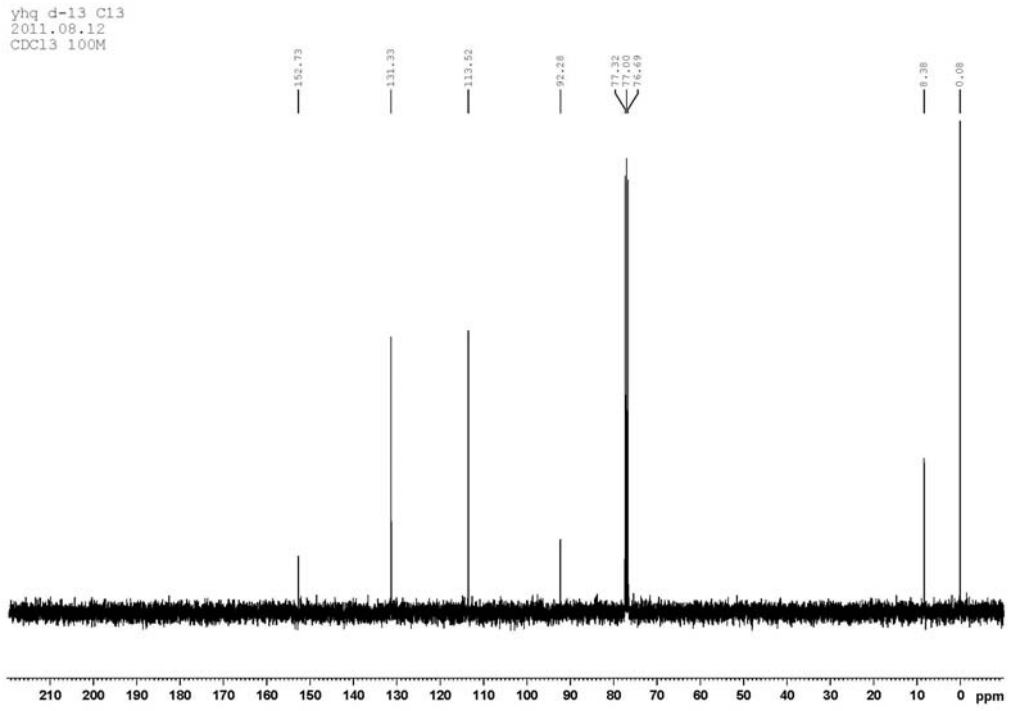

DXJ-B154-H1
Solvent: CDCl3
400 MHz
2010.11.14
ppm
8.19
1.99
1.00
1.01
1.00
1.00
2.09
2.96
2.69
1.06

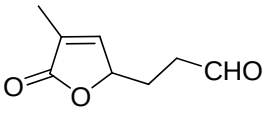

DXJ-B154-C13
Solvent: CDCl3
100 MHz
2010.11.14
175.73
138.11
135.01
129.99
128.99
128.74
128.29
127.92
127.43
119.02
77.32
77.00
76.68
66.45
43.70
43.57
34.49
29.13
26.40
11.65
ppm


TMSO
O

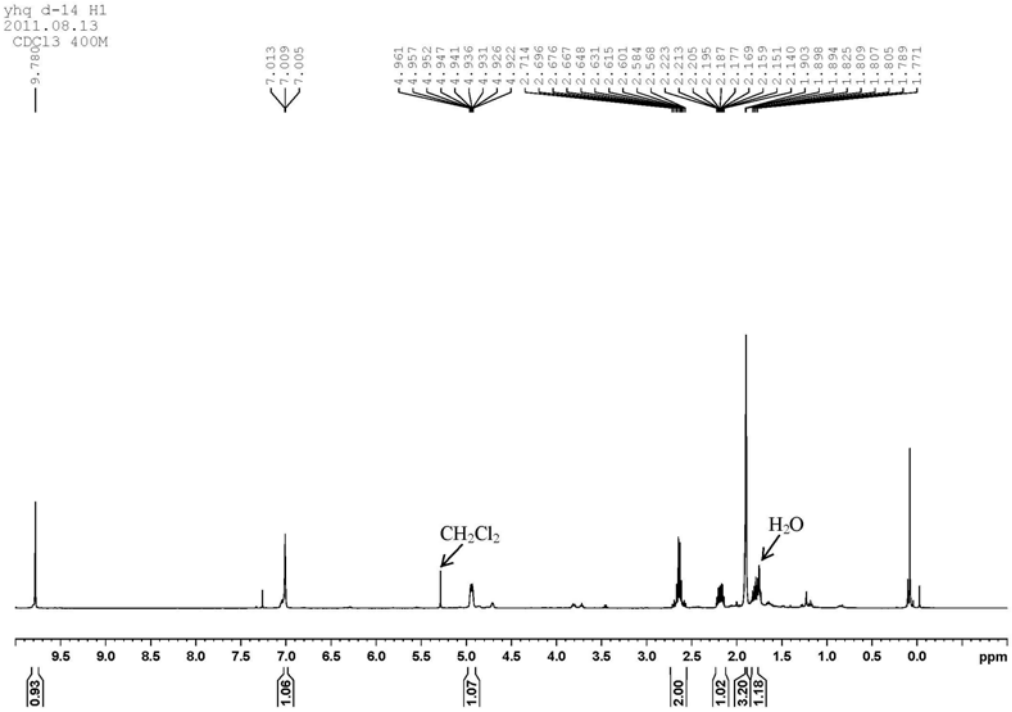
15

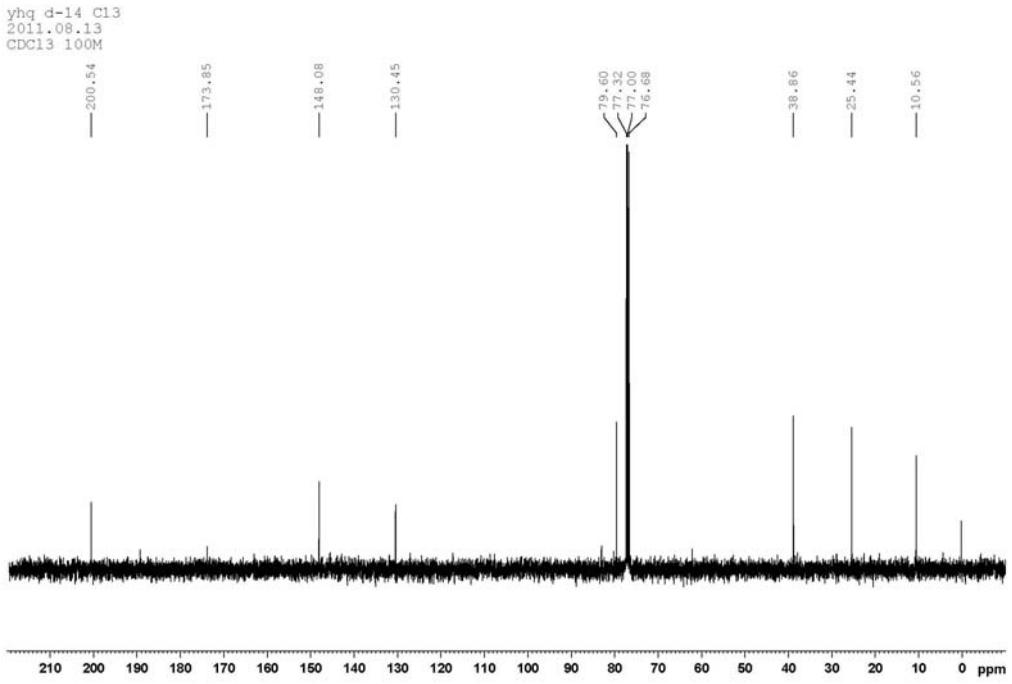

yhq d-13 H1
2011.08.12
CDCl3 400M
6.764
6.758
6.107
6.102
1.823
0.277
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
1.00
1.01
3.23
9.16

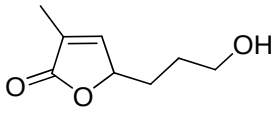

yhq d-13 C13
2011.08.12
CDCl3 100M
152.73
131.33
113.52
92.28
77.32
77.00
76.69
8.38
0.00
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


O
O
CHO

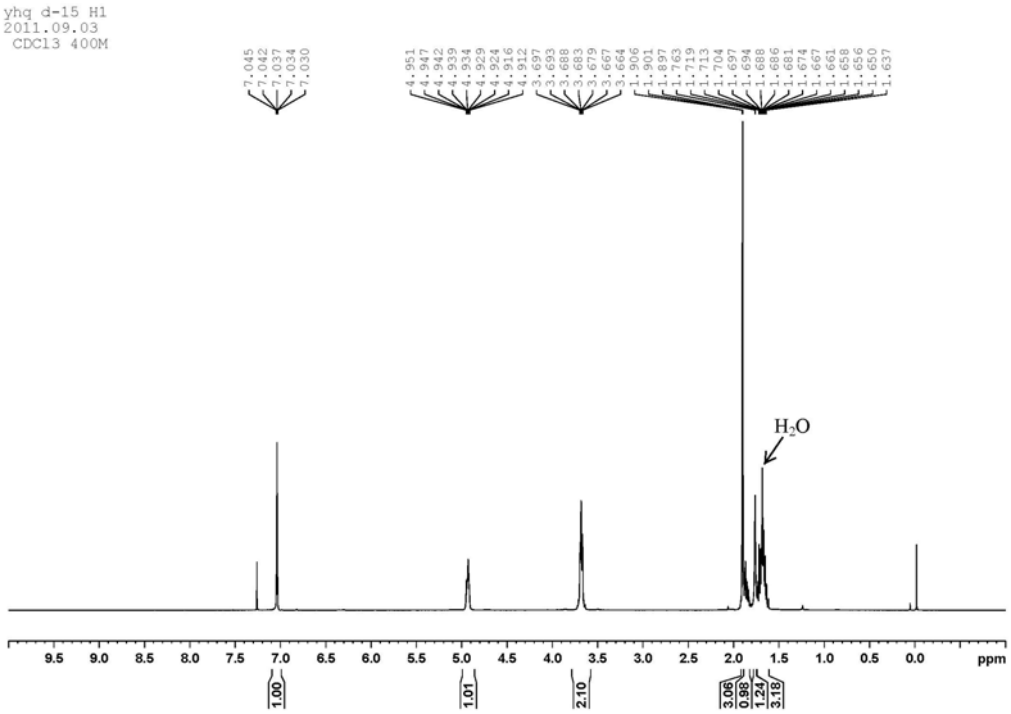
16

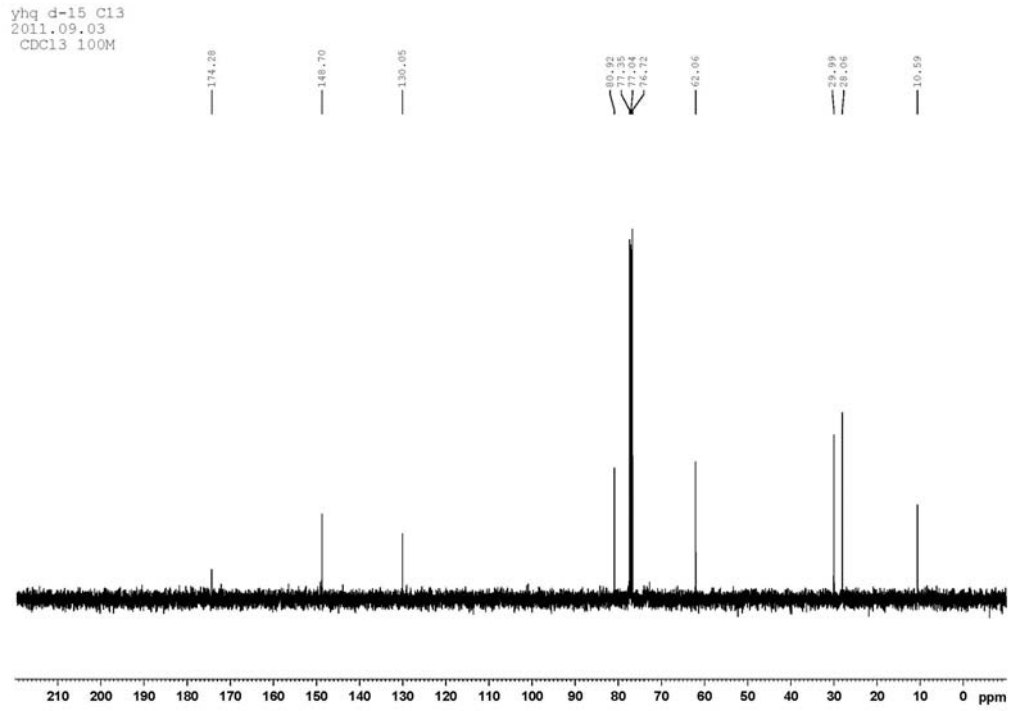

yhq d-14 H1
2011.08.13
CDCl3 400M
9.780
7.013
7.009
7.005
4.961
4.957
4.952
4.947
4.941
4.936
4.931
4.926
4.922
2.714
2.696
2.676
2.667
2.648
2.631
2.615
2.601
2.584
2.568
2.223
2.213
2.205
2.195
2.187
2.177
2.169
2.159
2.151
2.140
1.903
1.898
1.894
1.825
1.809
1.807
1.805
1.789
1.771
CH2Cl2
H2O
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
0.93
1.06
1.07
2.00
1.02
3.20
1.18

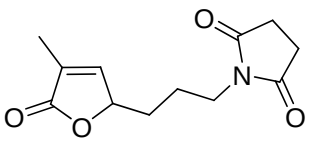

yhq d-14 C13
2011.08.13
CDCl3 100M
200.54
173.85
148.08
130.45
79.60
77.32
77.00
76.68
38.86
25.44
10.56
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


OH
O
O

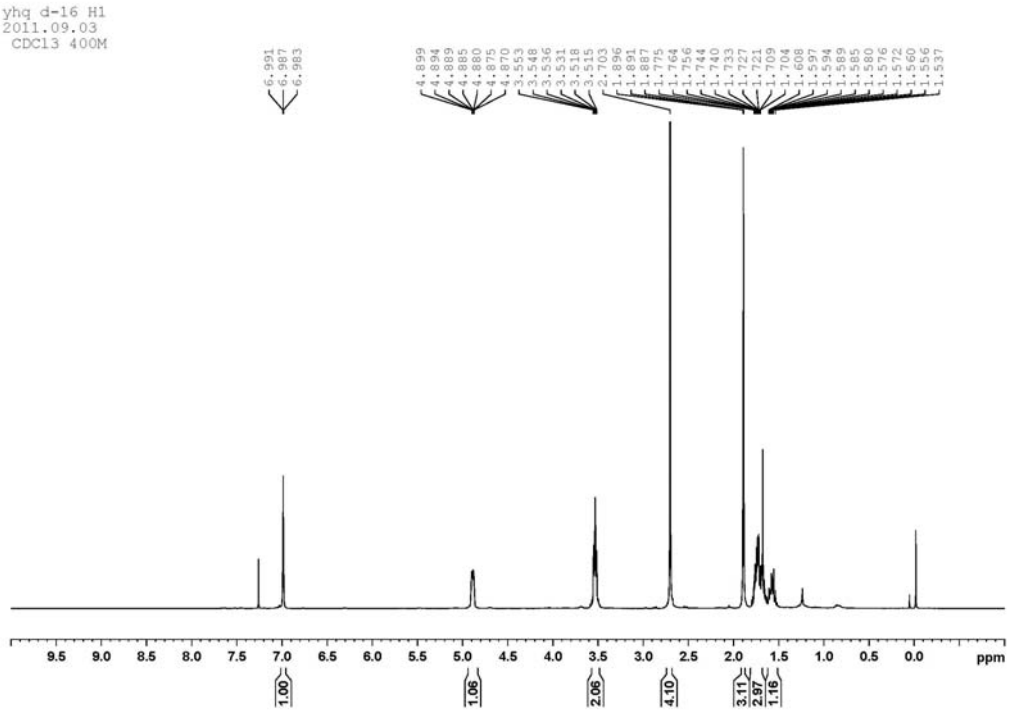
17

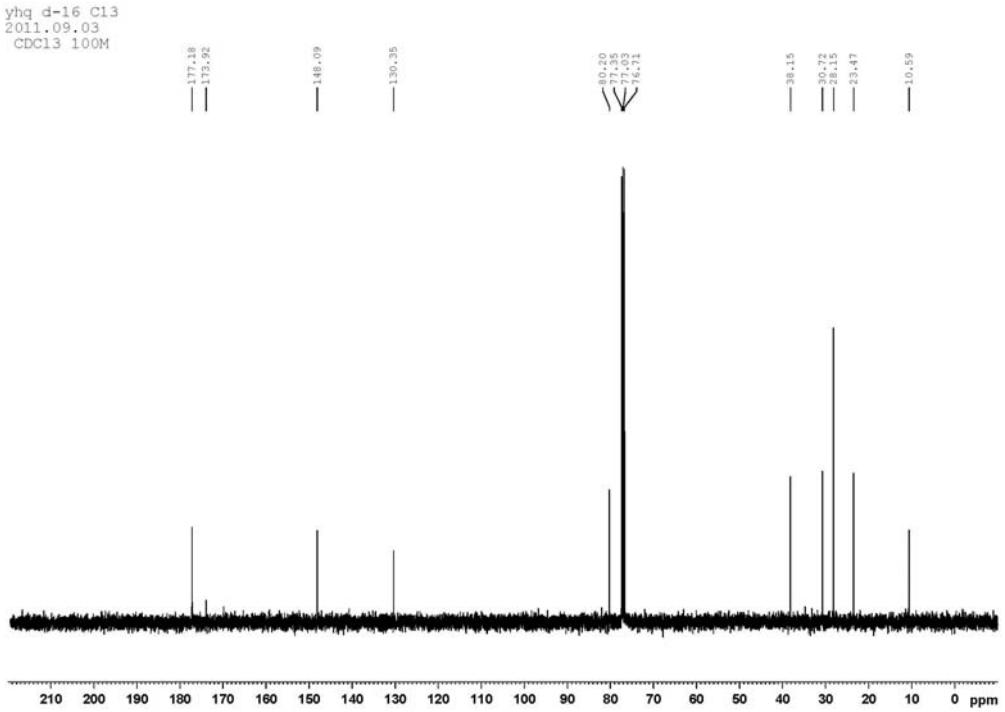

yhq d-15 H1
2011.09.03
CDCl3 400M
H2O
ppm

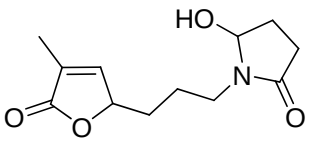

yhq d-15 C13
2011.09.03
CDCl3 100M
ppm



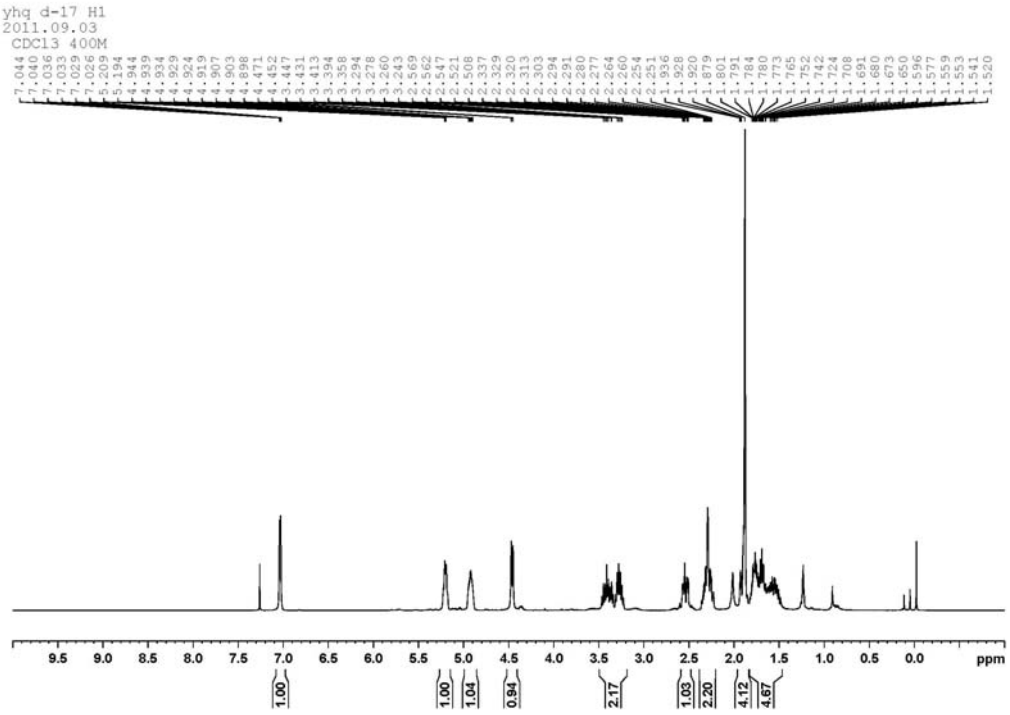
18

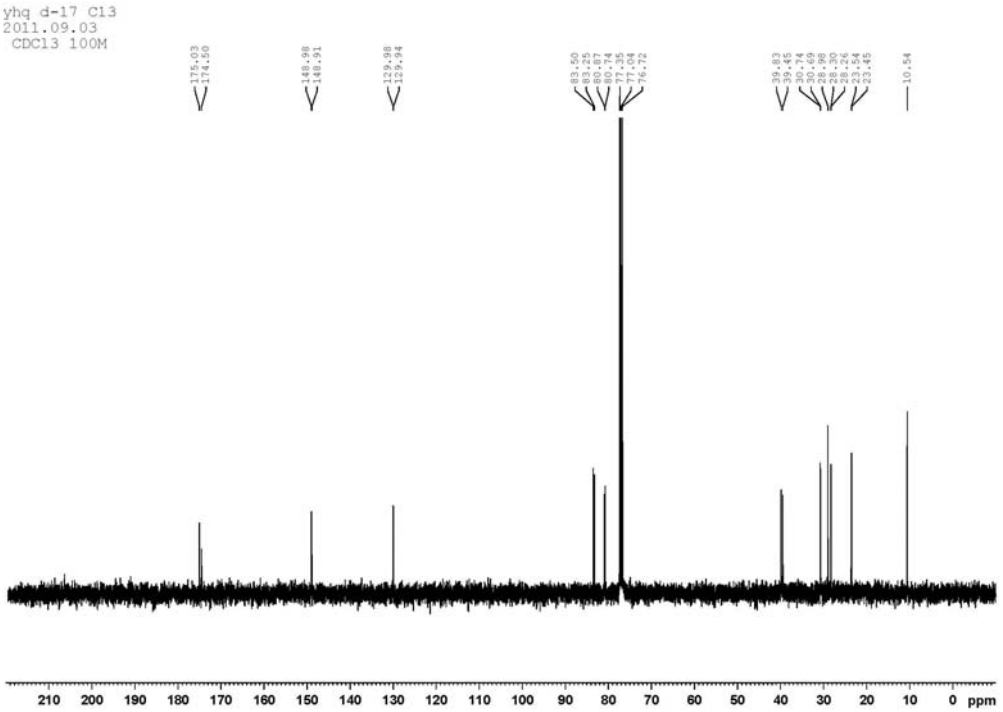

yhq d-16 H1
2011.09.03
CDCl3 400M
6.991
6.987
6.983
4.899
4.894
4.889
4.885
4.880
4.875
4.870
3.553
3.548
3.536
3.531
3.518
3.515
2.703
1.896
1.891
1.887
1.775
1.764
1.756
1.744
1.740
1.733
1.727
1.721
1.709
1.704
1.608
1.597
1.594
1.589
1.585
1.580
1.576
1.572
1.560
1.556
1.537
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
1.00
1.06
2.06
4.10
3.11
2.97
1.16

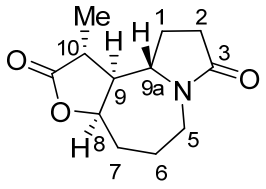

yhq d-16 C13
2011.09.03
CDCl3 100M
177.18
173.92
148.09
130.35
80.20
77.35
77.03
76.71
38.15
30.72
28.15
23.47
10.59
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


HO
N
O
O
O

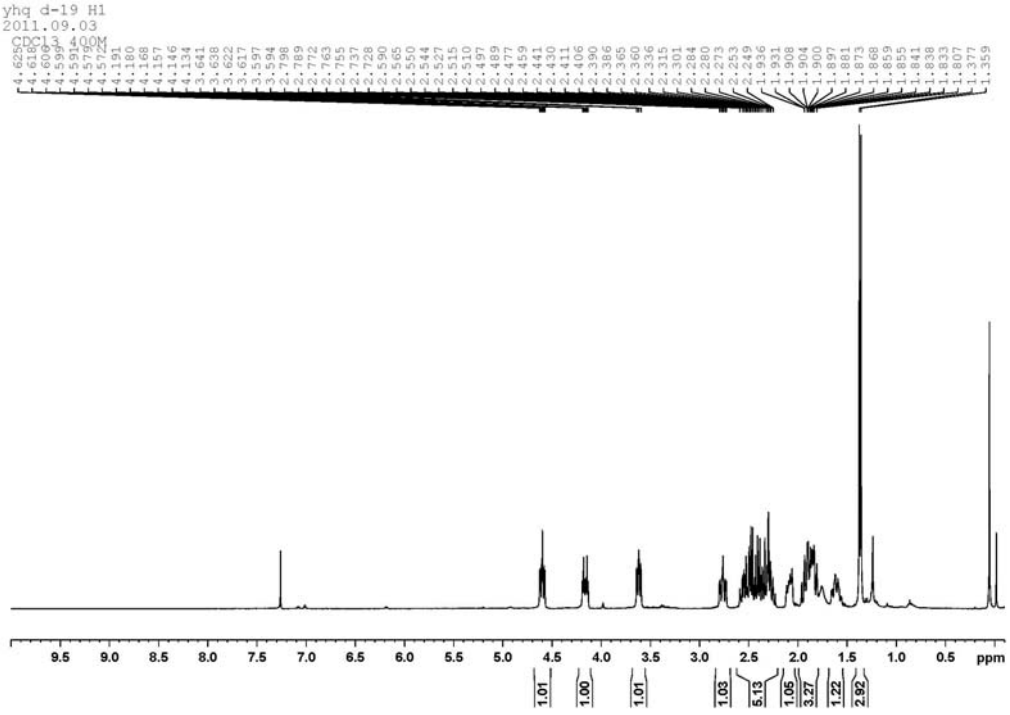
19

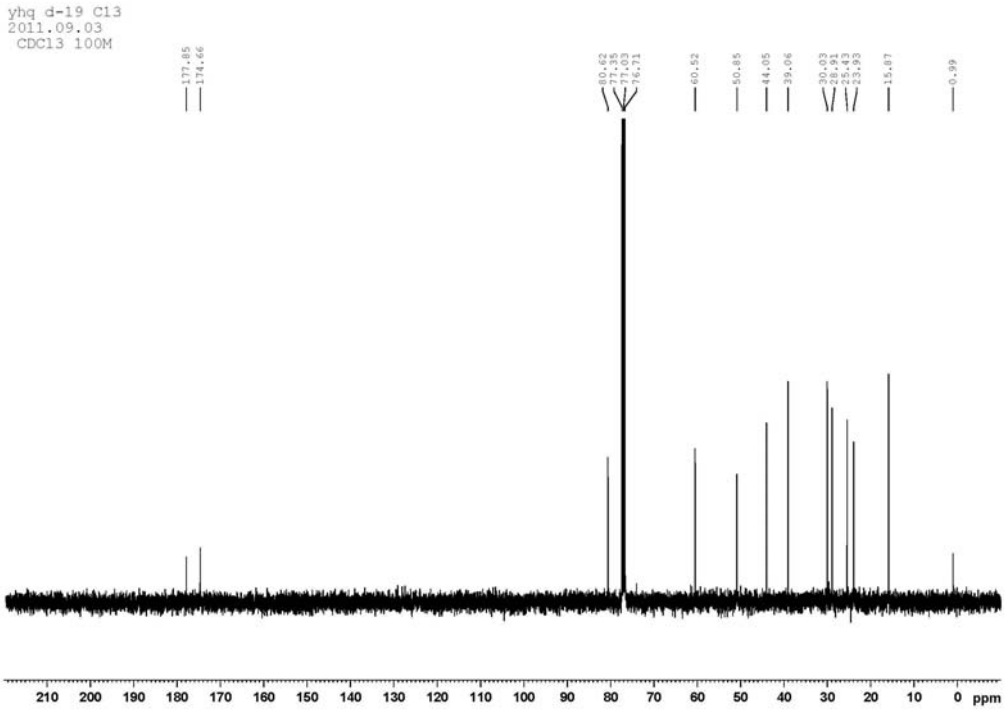

yhq d-17 H1
2011.09.03
CDCl3 400M
ppm


yhq d-17 C13
2011.09.03
CDCl3 100M
ppm


Me
H
H
1
2
10
3
O
O
9
9a
N
O
H
8
5
7
6

20


yhq d-19 H1
2011.09.03
CDCl3 400M
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.01 1.00 1.01 1.03 5.13 1.05 3.27 1.22 2.92


yhq d-19 C13
2011.09.03
CDCl3 100M
177.85
174.66
80.62
77.35
77.03
76.71
60.52
50.85
44.05
39.06
30.03
28.91
25.43
23.93
15.87
0.99
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm