Supplementary Material (ESI) for Chemical Communications

Electronic Supplementary Information

A diastereoselective carbocyclisation of allene-hydrazones through the intramolecular allylic transfer reaction

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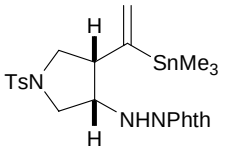
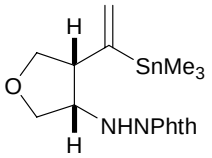
General. All reactions were run in flame-dried glassware under an atmosphere of nitrogen. Dichloromethane was distilled from CaH_2 prior to use. All liquid reagents purchased from the Aldrich were distilled properly prior to use, unless otherwise indicated. Purification was conducted by flash column chromatography on silica gel (230-400 mesh), eluting with a mixture of hexane and ethyl acetate, unless otherwise stated. The reported yields are for chromatographically pure isolated products. FT-IR spectra were recorded on a Nicolet 320. ^{1}H NMR spectra were recorded on a Varian Unity Inova at 500 and/or 300 MHz in $CDCl_3$ as a solvent with TMS or residual chloroform as the internal standard. ^{13}C NMR spectra were measured on a Varian Unity Inova at 125 or 75 MHz in $CDCl_3$ as a solvent. X-ray data was collected with a Siemens P4 diffractometer equipped with a Mo X-ray tube at our departmental X-ray facility.

Typical procedure: 2-[(3*S,4*S**)-1-Tosyl-4-{1-(trimethylstannyl)vinyl}pyrrolidin-3-ylamino]isoindoline-1,3-dione (7a)**: A flame-dried 20 mL Schlenk flask containing $(\pi\text{-allyl})_2Pd_2Cl_2$ (3.42 mg, 0.0096 mmol) was charged with freshly diatilled CH_2Cl_2 (5 mL). After cooling to –40 °C, a solution of **6a** (0.130 g, 0.317 mmol) and hexamethyldistannane (0.115 g, 0.35 mmol) in CH_2Cl_2 (1.5 mL) was added over 20 min while keeping the temperature below –40 °C, and then stirred for 3 h at –40 °C (reaction progress was monitored by TLC). After cooling to –78 °C, a pre-cooled solution of $TiCl_4$ (1.2 mL, 0.36 mmol, freshly prepared 0.3 M in CH_2Cl_2) at –78 °C was added in one portion via a cannular needle. The reaction mixture was allowed to proceed for 2 h at –78 °C, and

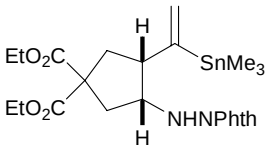


then quenched by the addition of aqueous saturated $NaHCO_3$ solution (pH 7, 7 mL). The aqueous layer was extracted with CH_2Cl_2 (ca 10 mL x 2). The combined organic extracts were washed with saturated brine (1x), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to give the crude product. Final purification was effected by SiO_2 chromatography (Hexanes:EtOAc = 5:1) to afford **7a** (0.151 g, 0.263 mmol, 83%) as a colorless liquid then solidify in the freezer. TLC, R*f* 0.48 (2:1 hexane/EtOAc); IR (film) 3046, 2977, 1722, 1599, 1443, 1368, 1096, 665 cm^{-1}; ^1H NMR (500MHz, $CDCl_3$) δ 0.12 (s, 9H), 2.44 (s, 3H), 2.85-2.87 (m, 1H), 3.12 (dd, *J* = 9.9, 8.4 Hz, 1H), 3.18 (dd, *J* = 9.3, 7.0 Hz, 1H), 3.54 (dd, *J* = 9.9, 8.4 Hz, 1H), 3.55-3.59 (m, 2H), 4.52 (d, *J* = 3.1 Hz, 1H), 5.25 (s, 1H), 5.80 (s, 1H), 7.33 (d, *J* = 8.4 Hz, 2H), 7.71 (d, *J* = 8.4 Hz, 2H), 7.75 (dd, *J* = 5.3, 3.1 Hz, 2H), 7.84 (dd, *J* = 5.3, 3.1 Hz, 2H); ^{13}C NMR (125MHz, $CDCl_3$) δ –8.3, 15.5, 21.8, 52.2, 54.0, 62.3, 123.8, 127.9, 128.9, 130.0, 130.2, 133.5, 134.7, 144.0, 152.7, 166.7; Anal. Calcd for $C_{24}H_{29}N_3O_4SSn$: C, 50.19; H, 5.09; N, 7.32; S, 5.58. Found: C, 49.91; H, 4.88; N, 7.44; S, 5.63.

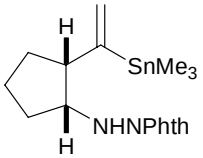
2-[(3*S,4*R**)-4-{1-(Trimethylstannyl)vinyl}-tetrahydrofuran-3-ylamino]-isoindoline-1,3-dione (7b)**: TLC, R*f* 0.49 (2:1 hexane/EtOAc); IR (neat) 3045, 2982, 1719, 1589, 1447, 1375, 1122, 1095, 668 cm^{-1}; ^1H NMR (500MHz, $CDCl_3$) δ 0.28 (s, 9H), 3.28-3.29 (m, 1H), 3.80-3.83 (m, 1H), 3.89-3.91 (m, 1H), 3.95-4.00 (m, 2H), 4.16 (dd, *J* = 8.2, 8.2 Hz, 1H), 4.48 (s, 1H), 5.57 (s, 1H), 6.02 (s, 1H), 7.73 (dd, *J* = 5.6, 3.1 Hz, 2H), 7.84 (dd, *J* = 5.6, 3.1 Hz, 2H). ^{13}C NMR (125MHz, $CDCl_3$) δ –8.3, 52.1, 61.3, 70.4, 72.7, 123.7, 129.7, 130.5, 134.5, 150.4, 167.1; HRMS (EI): calcd. for $C_{17}H_{22}N_2O_3Sn$: 422.0652. Found 426.0644.



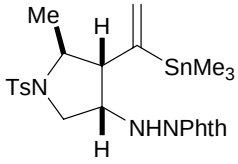
(3*R,4*S**)-Diethyl 3-(1,3-dioxoisoindolin-2-ylamino)-4-{1-(trimethylstannyl)vinyl}-cyclopentane-1,1-dicarboxylate (7c):** TLC, R*f* 0.49 (2:1 hexane/EtOAc); IR (film) 3051, 2970, 1738, 1720, 1595, 1450, 1376, 1225, 1129. 1096, 664 cm^{-1}; ^1H NMR (500MHz, $CDCl_3$) δ 0.26 (s, 9H), 1.31 (t, *J* = 7.0 Hz, 6H), 2.13-2.17 (m, 1H), 2.50 (ddd, *J* = 12.9, 5.1, 1.7 Hz, 1H), 3.03-3.07 (m, 2H), 3.80 (s, 1H), 4.15 (q, *J* = 7.0 Hz, 4H), 5.54 (s, 1H), 6.05 (s, 1H), 7.71 (dd, *J* = 5.3, 3.1 Hz, 2H), 7.82 (dd, *J* = 5.3, 3.1 Hz, 2H); ^{13}C NMR (125MHz, $CDCl_3$) δ –8.5, 14.2, 35.4, 38.2, 51.6, 53.6, 60.7, 61.9, 123.5, 128.3, 130.6, 134.4, 151.9, 167.2, 171.9, 173.4; Calcd for $C_{24}H_{32}N_2O_6Sn$: C, 51.18; H, 5.73; N, 4.97. Found: C, 51.33; H, 5.88; N, 4.69.



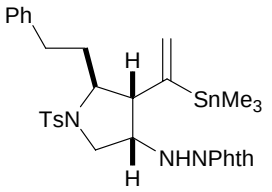
2-[(1*R,2*S**)-2-{1-(Trimethylstannyl)vinyl}cyclopentylamino]isoindoline-1,3-dione (7d)**: TLC, R*f* 0.31 (3:1 hexane/EtOAc); IR (film) 3037, 2989, 1721, 1592, 1444, 1377, 1094, 664 cm^{-1}; ^1H NMR (500MHz, $CDCl_3$) δ 0.13 (s, 9H), 1.40-1.48 (m, 1H), 1.63-1.73 (m, 2H), 1.77-1.89 (m, 2H), 1.90-2.17 (m, 1H), 2.72 (dd, *J* = 11.0, 8.0 Hz, 1H), 3.55-3.59 (m, 1H), 4.64 (s, 1H), 5.10 (s, 1H), 5.78 (s, 1H), 7.72 (dd, *J* = 5.3, 3.1 Hz, 2H), 7.83 (dd, *J* = 5.3, 3.1 Hz, 2H); ^{13}C NMR (125MHz, $CDCl_3$) δ –8.2, 22.5, 31.1, 33.1, 56.8, 64.4, 123.6, 125.5, 130.5, 134.4, 158.0, 167.2; Anal. Calcd for $C_{18}H_{24}N_2O_2Sn$: C, 51.58; H, 5.77; N, 6.68. Found: C, 51.32; H, 5.89; N, 6.53.



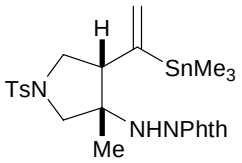
2-[(3*S,4*R**)-5-methyl-1-tosyl-4-{1-(trimethylstannyl)vinyl}pyrrolidin-3-ylamino]-isoindoline-1,3-dione (7e)**: TLC, R*f* 0.29 (2:1 hexane/EtOAc); IR (film) 3048, 2968, 1728, 1595, 1451, 1369, 1091, 665 cm^{-1}; ^1H NMR (500MHz, $CDCl_3$) δ 0.041 (s, 9H), 1.33 (d, *J* = 6.0 Hz, 3H), 2.42 (s, 3H), 2.64 (dd, *J* = 10.0, 10.0 Hz 1H), 3.27-3.37 (m, 2H), 3.41 (dd, *J* = 10.8, 9.0 Hz, 1H), 3.73 (dd, *J* = 10.8, 7.5 Hz, 1H), 4.56 (s, 1H), 5.30 (d, *J* = 2.0 Hz, 1H), 5.82 (d, *J* = 2.0 Hz, 1H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.67 (d, *J* = 8.0 Hz, 2H), 7.75 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.84 (dd, *J* = 5.5, 3.0 Hz, 2H); ^{13}C NMR (125MHz, $CDCl_3$) δ –8.21, 19.9, 21.7, 52.9, 60.4, 60.6, 64.6, 123.8, 127.6, 130.0, 130.2, 131.3, 134.7, 135.7, 143.8, 152.4, 166.6; Anal. Calcd for $C_{25}H_{31}N_3O_4SSn$: C, 51.04; H, 5.31; N, 7.14; S, 5.45. Found: C, 52.75; H, 5.44; N, 7.01; S, 5.29.



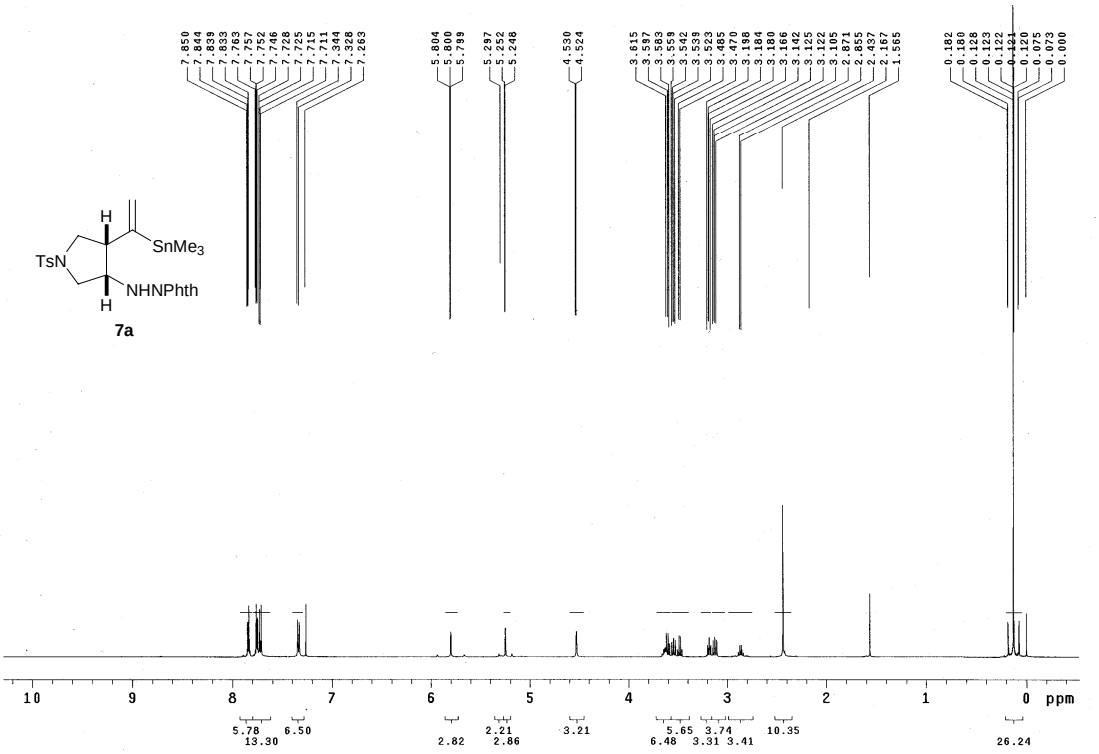
2-[(3*S,4*R**)-5-Phenethyl-1-tosyl-4-{1-(trimethylstannyl)vinyl}pyrrolidin-3-ylamino]isoindoline-1,3-dione (7f)**: TLC, R*f* 0.31 (2:1 hexane/EtOAc); IR (film) 3047, 2763, 1727, 1592, 1452, 1368, 1095, 664 cm^{-1}; ^1H NMR (500MHz, $CDCl_3$) δ 0.06 (s, 9H), 1.87-1.94 (m, *1*H), 2.16-2.23 (m, 1H), 2.61 (dd, *J* = 12.8, 5.5 Hz, 1H), 2.80 (dd, *J* = 12.8, 4.5 Hz, 1H), 2.95 (dd, *J* = 9.5, 9.5 Hz, 1H), 3.26-3.31 (m, 1H), 3.39 (dd, *J* = 11.0, 9.5 Hz, 1H), 3.56 (ddd, *J* = 9.5, 6.5, 2.5 Hz, 1H), 3.81 (dd, *J* = 11.0, 7.0 Hz, 1H), 4.60 (s, 1H), 5.33 (d, *J* = 2.0 Hz, 1H), 5.83 (d, *J* = 2.0 Hz, 1H), 7.14-7.19 (m, 4H), 7.25-7.29 (m, 3H), 7.67 (d, *J* = 8.5 Hz, 2H), 7.76 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.85 (dd, *J* = 5.5, 3.0 Hz, 2H); ^{13}C NMR (125MHz, $CDCl_3$) δ –8.16, 21.7, 30.2, 34.5, 53.4, 60.7, 61.3, 63.5, 123.9, , 126.0, 127.6, 128.6, 128.7, 130.1, 130.2, 131.1, 134.7, 135.9, 142.1, 143.9, 153.3, 166.6; Anal. Calcd for $C_{32}H_{37}N_3O_4SSn$: C, 56.65; H, 5.50; N, 6.19; S, 4.73. Found: C, 56.70; H, 5.52; N, 6.12; S, 4.71.

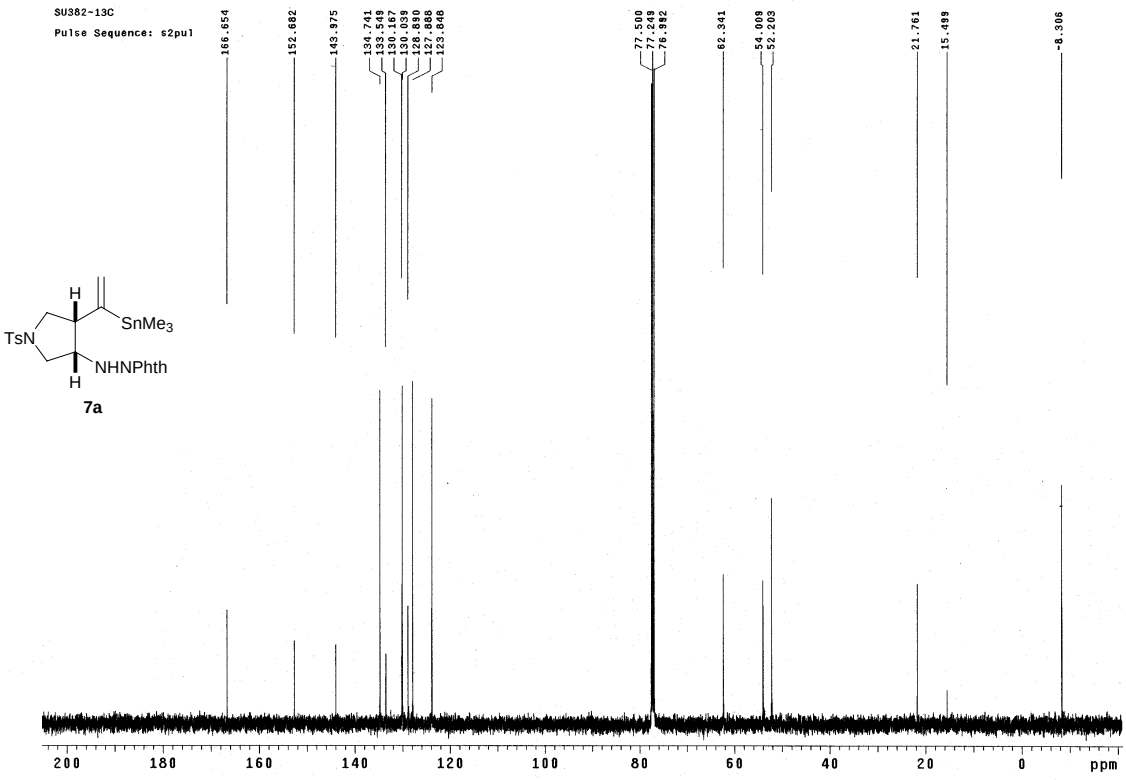


2-[(3*S,4*S**)-3-methyl-1-tosyl-4-{1-(trimethylstannyl)vinyl}pyrrolidin-3-ylamino]-isoindoline-1,3-dione (7g)**: TLC, R*f* 0.38 (2:1 hexane/EtOAc); IR (neat) 3053, 2974, 1725, 1596, 1448, 1376, 1098, 662 cm^{-1}; ^{1}H NMR (300MHz, $CDCl_3$) δ 1.16 (s, 9H), 0.94 (s, 3H), 2.41 (s, 3H), 2.98 (dd, *J* = 8.1, 8.1 Hz, 1H), 3.24 (d, *J* = 10.5 Hz, 1H), 3.35 (dd, *J* = 8.1, 8.1 Hz, 1H), 3.42 (d, *J* = 10.5 Hz 1H), 3.68 (dd, *J* = 8.1, 8.1 Hz, 1H), 4.44 (s, 1H), 5.42 (s, 1H), 5.81 (s, 1H), 7.32 (d, *J* = 8.1 Hz, 2H), 7.73-7.65 (m, 6H); ^{13}C NMR (75MHz, $CDCl_3$) δ –7.36, 19.5, 21.8, 51.6, 55.0, 58.9, 67.6, 123.8, 127.9, 130.0, 130.2, 130.4, 133.8, 134.8, 143.8, 151.6, 167.4; Anal. Calcd for $C_{25}H_{31}N_3O_4SSn$: C, 51.04; H, 5.31; N, 7.14; S, 5.45. Found: C, 51.23; H, 5.57; N, 6.96; S, 5.33.



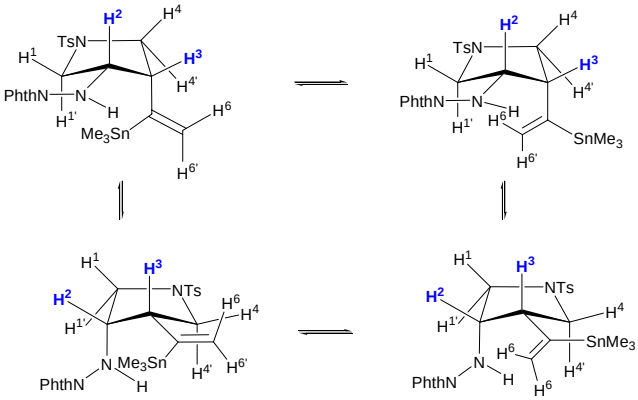
Copies of ^{1}H NMR and ^{13}C NMR spectra for all products and NOE spectra of 7a and 7g

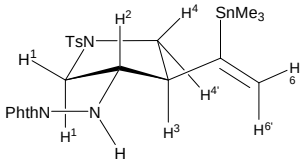




NOE experiments for the compound 7a

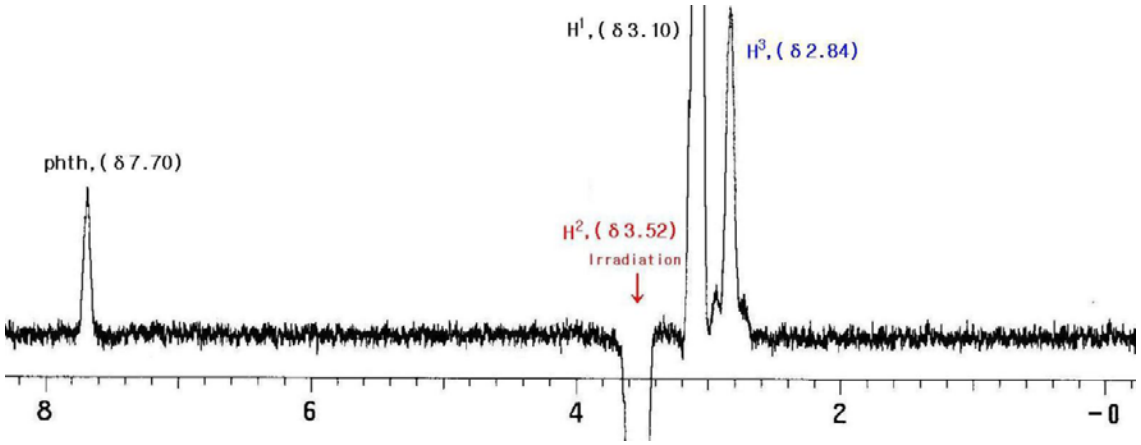
-Conformations

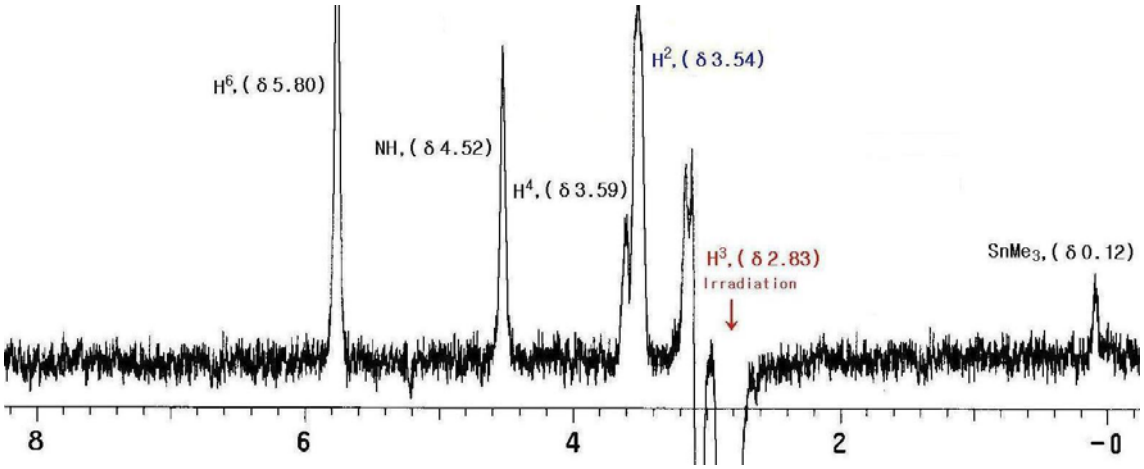


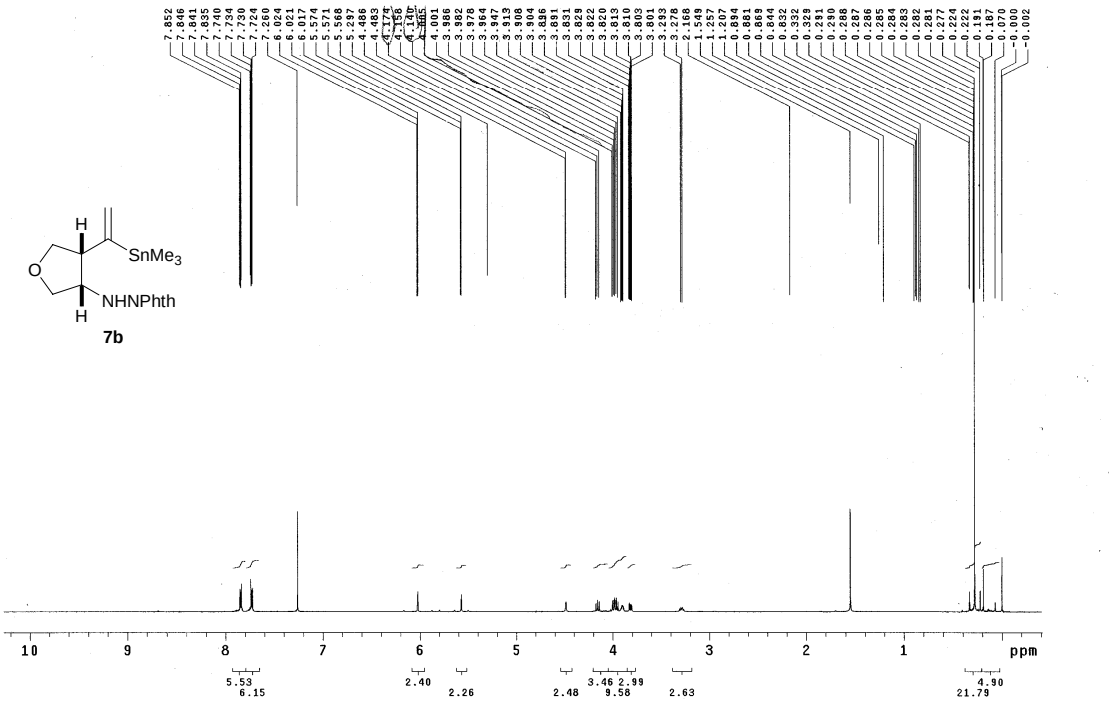


NOE data are not matched with
any conformations of the trans isomer

-NOE spectra



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0.191
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O
NHNPhth
H
7b
10
9
8
7
6
5
4
3
2
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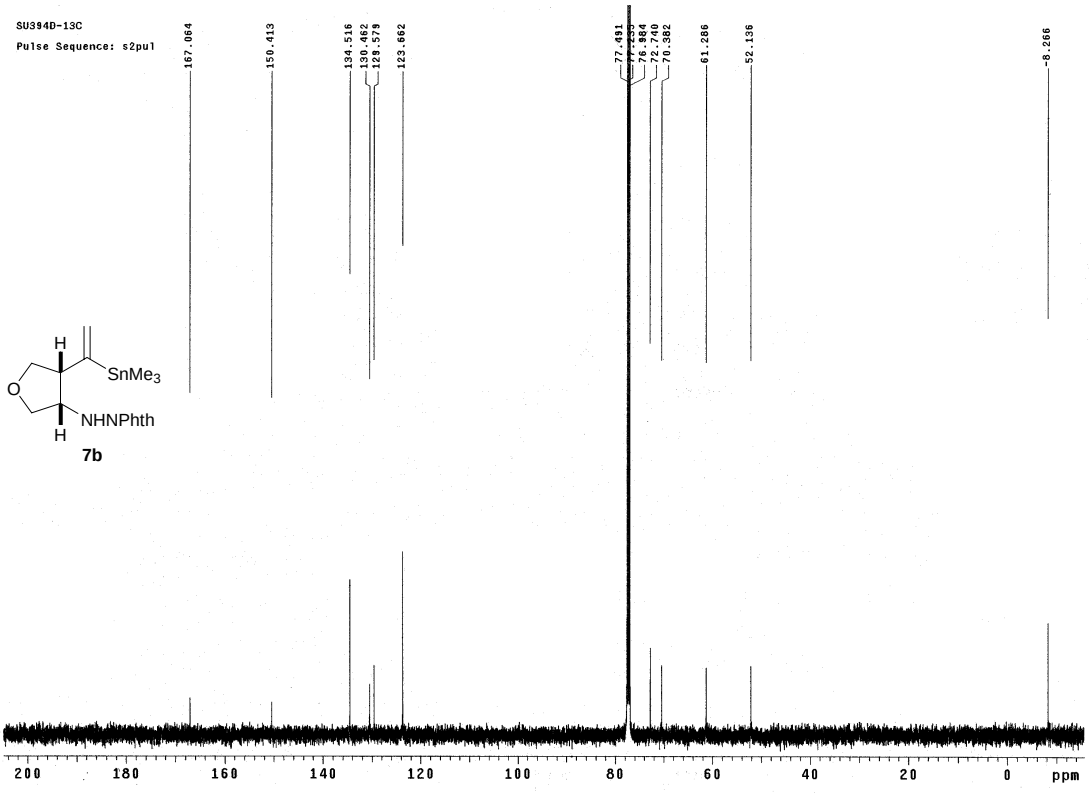
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76.984
72.740
70.382
61.286
52.136
-8.266
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H
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120
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80
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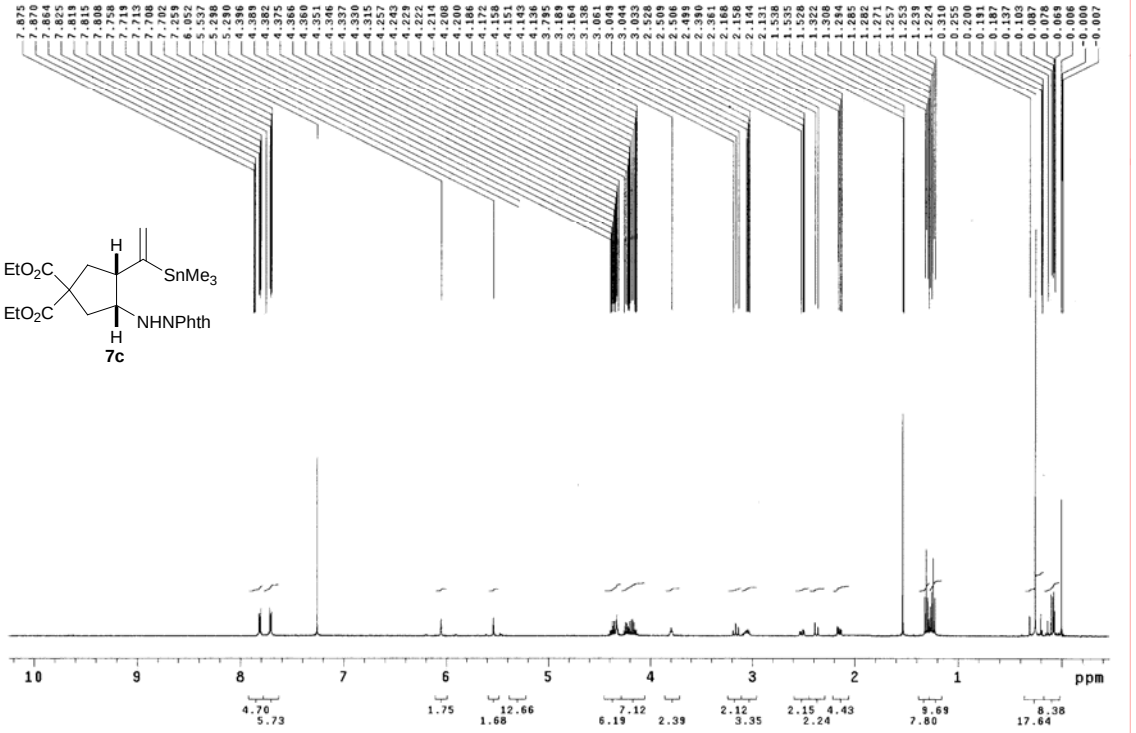
40
20
0
ppm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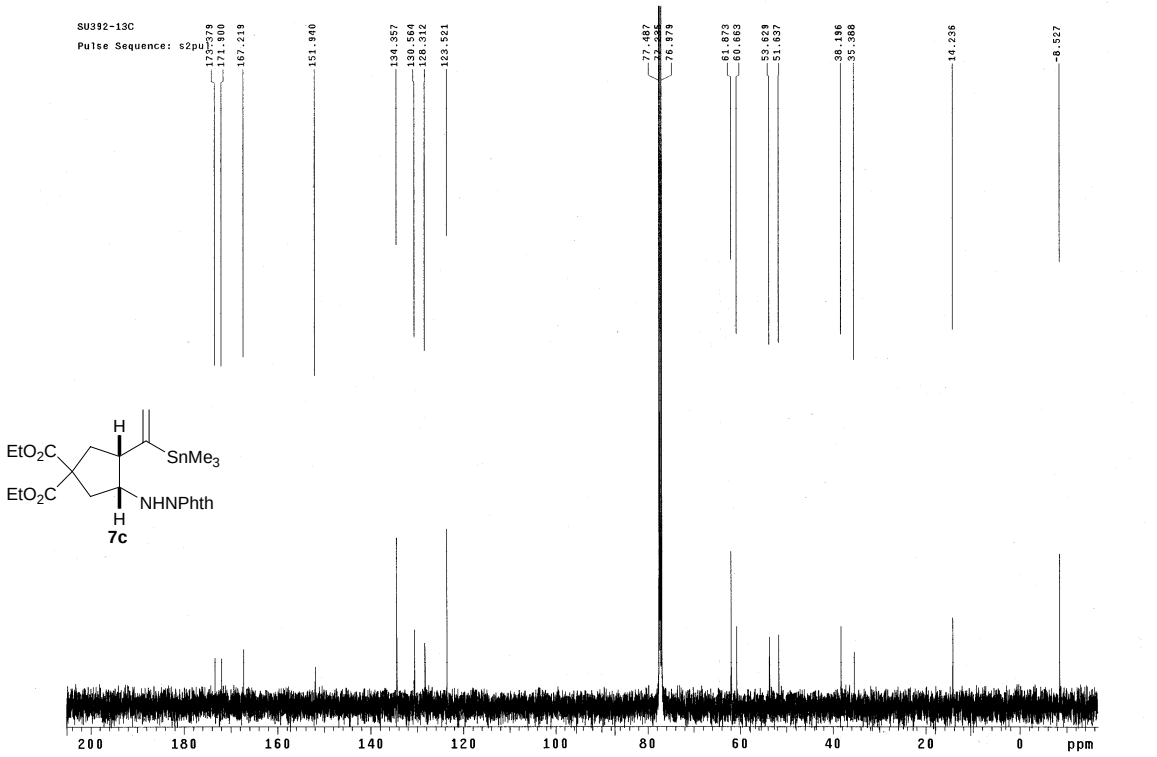
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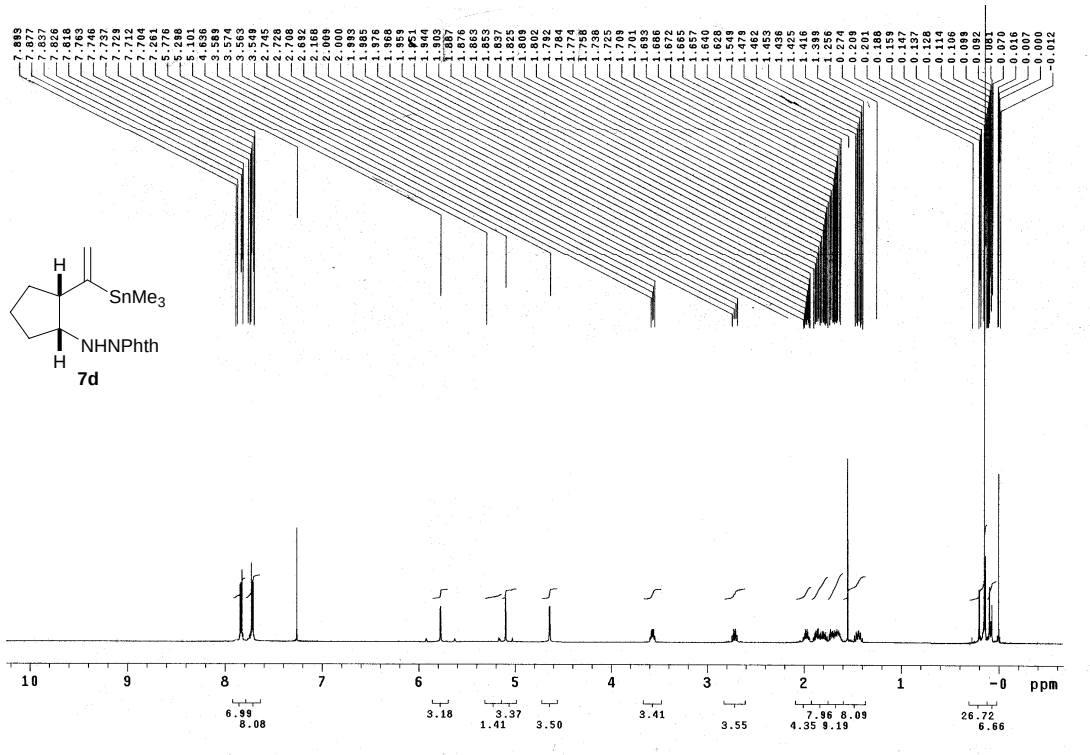
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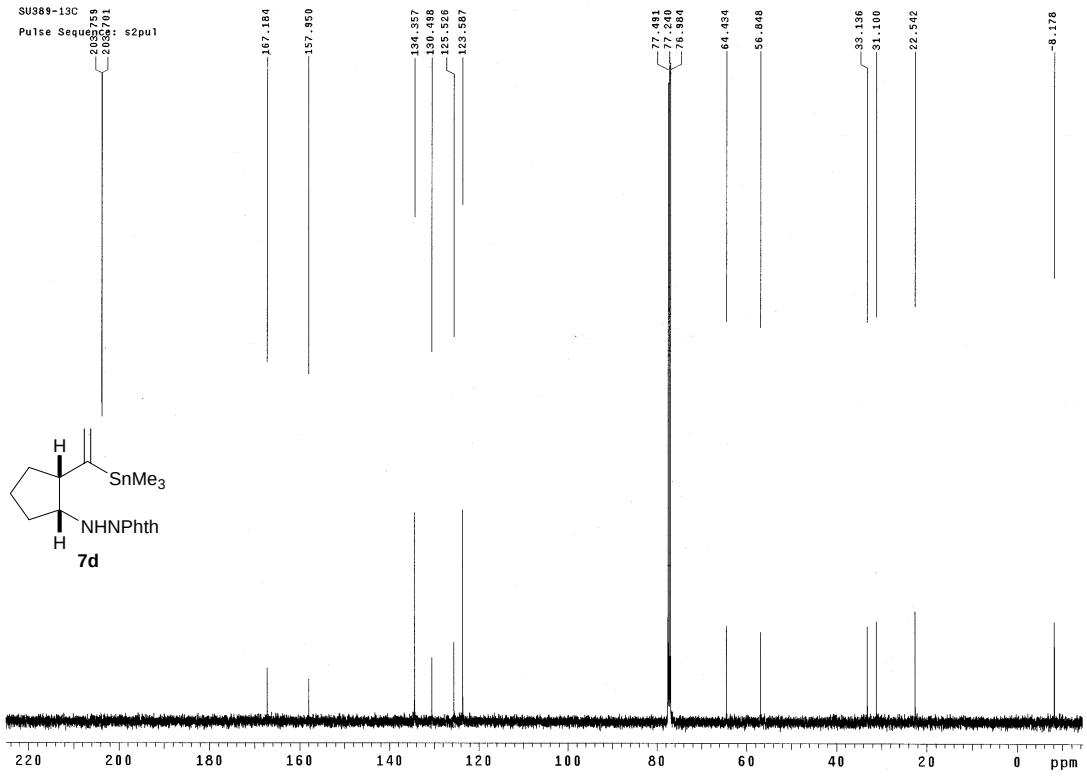
NHNPhth
7d
ppm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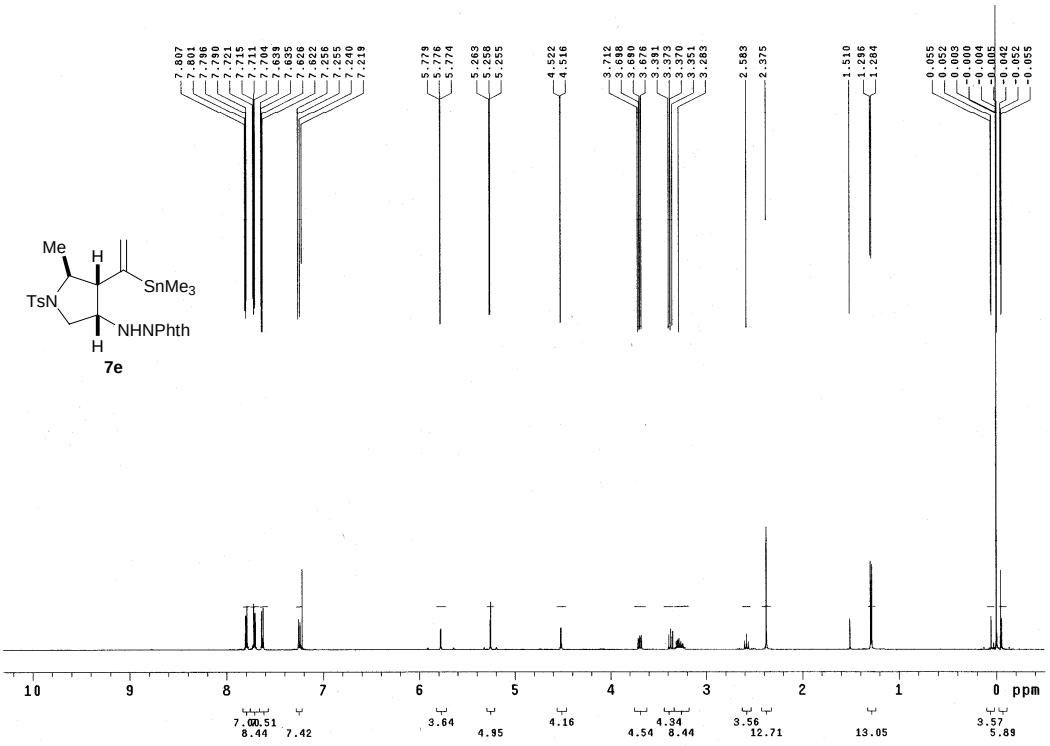
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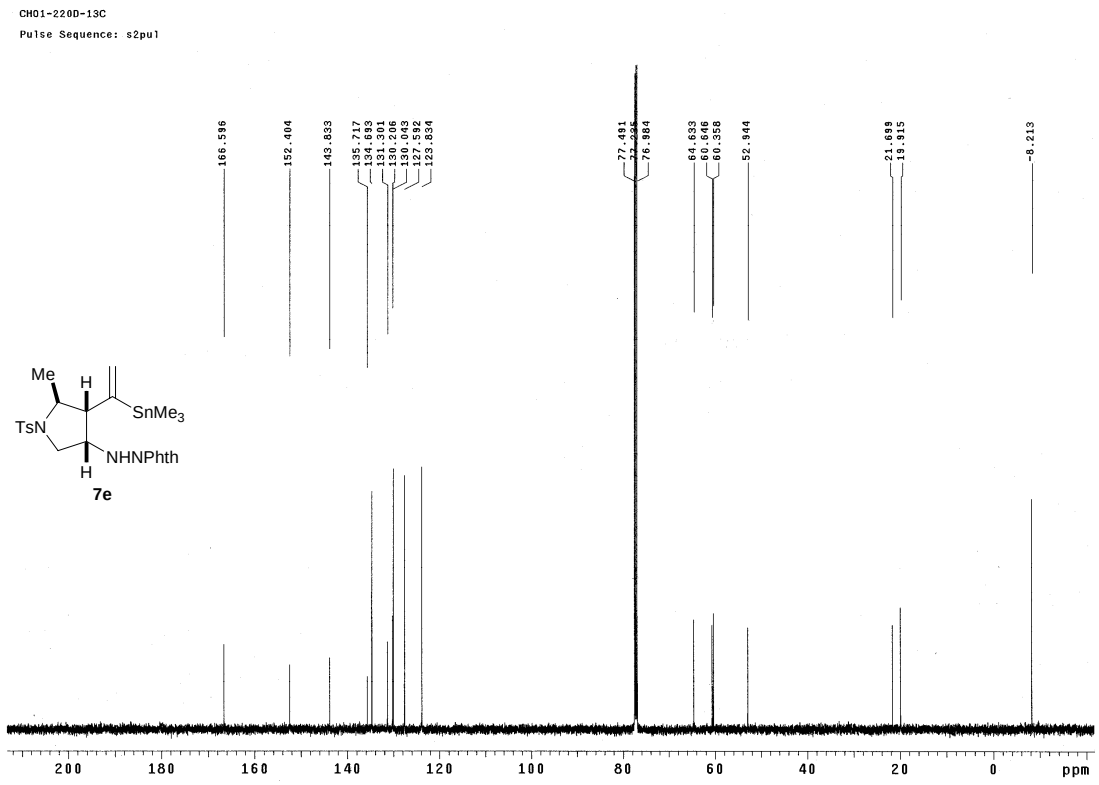
H
7e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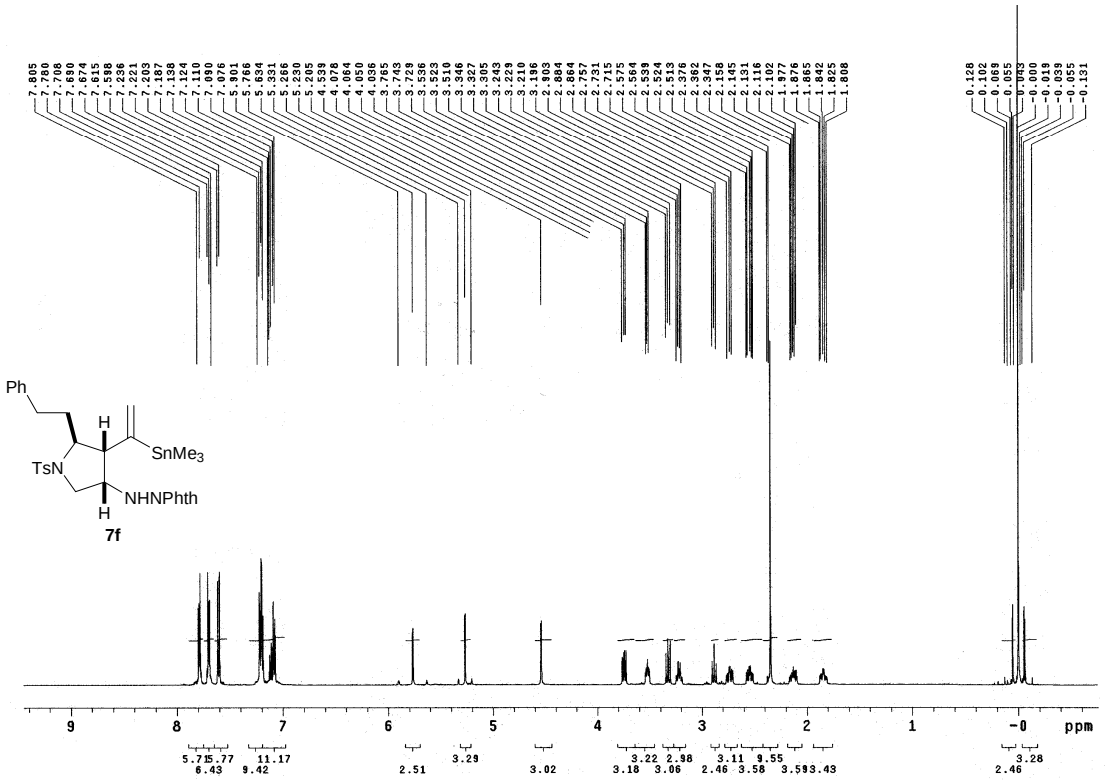
H
7e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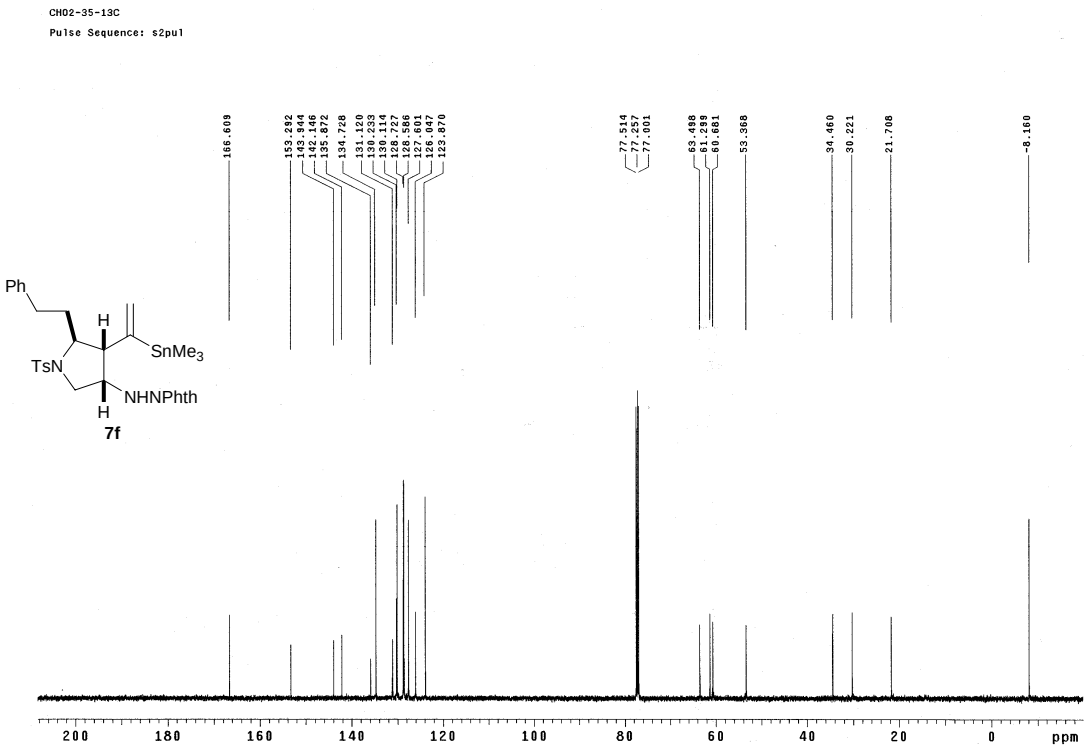
H
7f
ppm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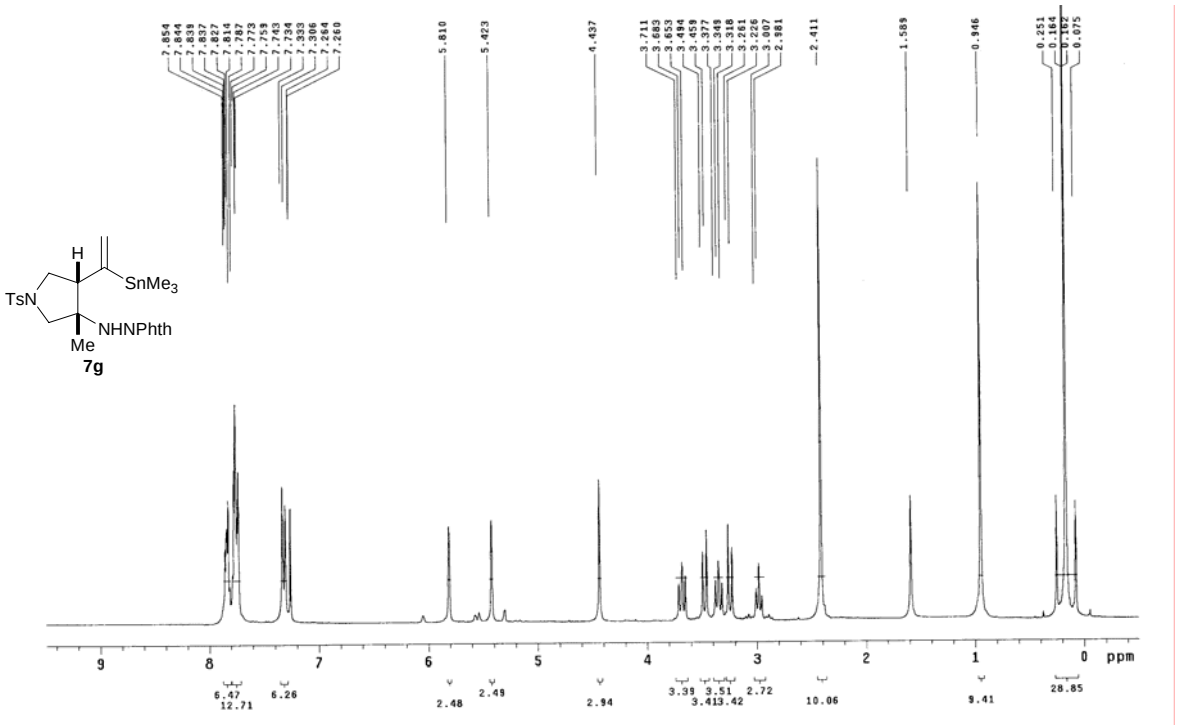
ppm


H
SnMe3
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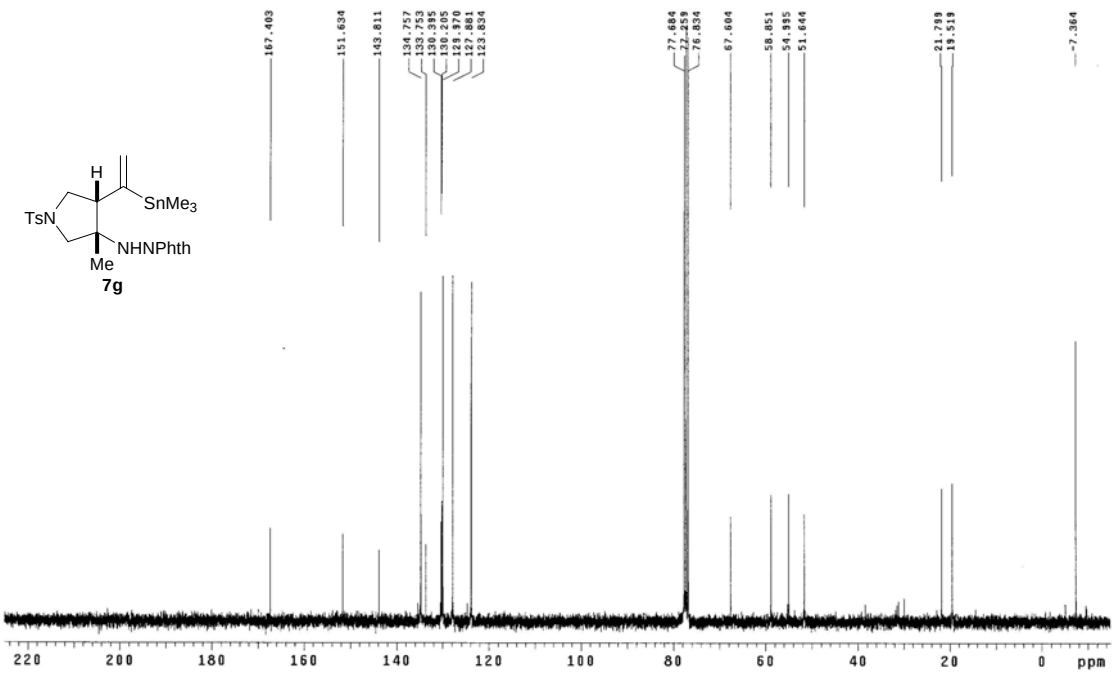
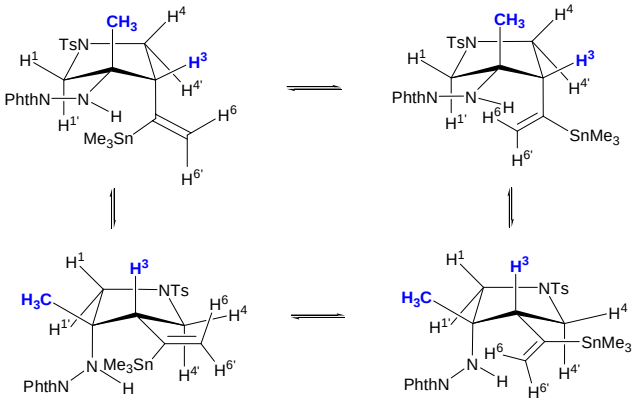
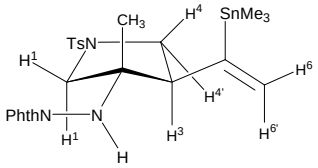
Me
7g


H
SnMe3
TsN
NHNPhth
Me
7g

NOE experiments for the compound 7g

-Conformations





NOE data are not matched with any conformations of the trans isomer

-NOE spectra