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The first synthesis of 7-prenylisatin

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CONTENTS

Experimental

General

Melting points were determined on an X–5 digital microscope melting point apparatus (Yuhua, China) and are uncorrected. Several commercially available solvents were dried by standard procedures before use: DMF (CaH_2), THF (Na). Other commercial reagents were analytical grade and used without further purification. IR spectra were run for KBr discs (and neat for liquid samples) on a Perkin–Elmer L 120-000A apparatus (ν_{max} in cm^{-1}). ^1H NMR and ^{13}C NMR spectra were recorded with a Bruker ARX-400 (400 MHz for ^1H NMR and 100 MHz for ^{13}C NMR) spectrometer using TMS as an internal standard (chemical shifts in δ values, *J* in Hz). High–resolution MS data were obtained on Agilent-6520 QTOF LC/MSD spectrometer, using ESI ionization. Column chromatography was performed on silica gel (200–300 mesh, Qingdao Haiyang Chemical Co., Ltd, Qingdao, China). Analytical TLC was performed on plates pre-coated with silica gel (GF254, 0.25 mm, Qingdao Haiyang Chemical Co., Ltd, Qingdao, China) and iodine vapor was used to develop color on the plates.

tert-Butyl (2-methylbut-3-en-2-yl) carbonate

To a solution of 2-methylbut-3-en-2-ol (4.3 g, 50 mmol) in dry THF (90 ml) *n*-BuLi in hexane (2.5 M, 20 ml, 50 mmol) was added under N_2 at 0 °C over 20 min. The clear solution was stirred at 0 °C for 30 min and then di-*tert*-butyl dicarbonate (10.9 g, 50.0 mmol) was added in one portion. The clear solution was allowed to warm to room temperature and further stirred for 5 h when the resulting mixture became white thick suspension. After the reaction was quenched with saturated $NaHCO_3$ solution (200 ml) and the organic phase was washed

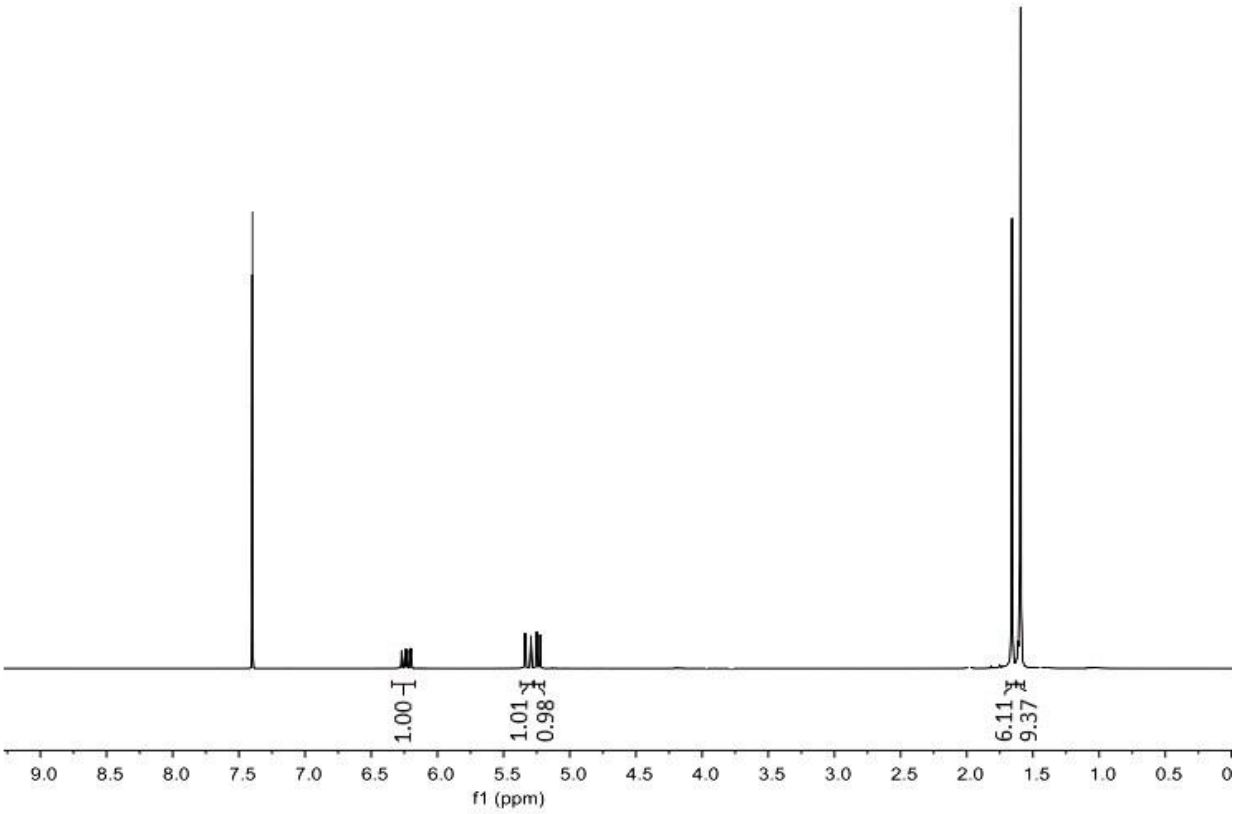
successively by water, saturated brine, dried over anhydrous $MgSO_4$ and evaporated under reduced pressure to give 8.7 g (94%) of *tert*-butyl (2-methylbut-3-en-2-yl) carbonate as light yellow liquid, which was used without further purification. IR (KBr): 1100, 1160, 1230, 1278, 1360, 1390, 1455, 1735, 2946, 2990 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.61 (s, 9H, 3Me), 1.70 (s, 6H, 2Me), 5.23 (d, 1H, CH_2, *J* 10.6 Hz), 5.30 (d, 1H, CH_2, *J* 17.2 Hz), 6.25 (dd, 1H, CH, *J* 17.2 and 10.6 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 24.3 (Me), 26.0 (Me), 79.5 ($Me_2\underline{C}$), 79.7 ($Me_3\underline{C}$), 111.2 (CH_2), 140.3 (CH), 150.1 (C=O); HRMS (ESI) Calcd for $C_{10}H_{19}O_3$ $(M+H)^+$: 187.1329, found: 187.1322.

N-(2-Methylbut-3-en-2-yl)aniline

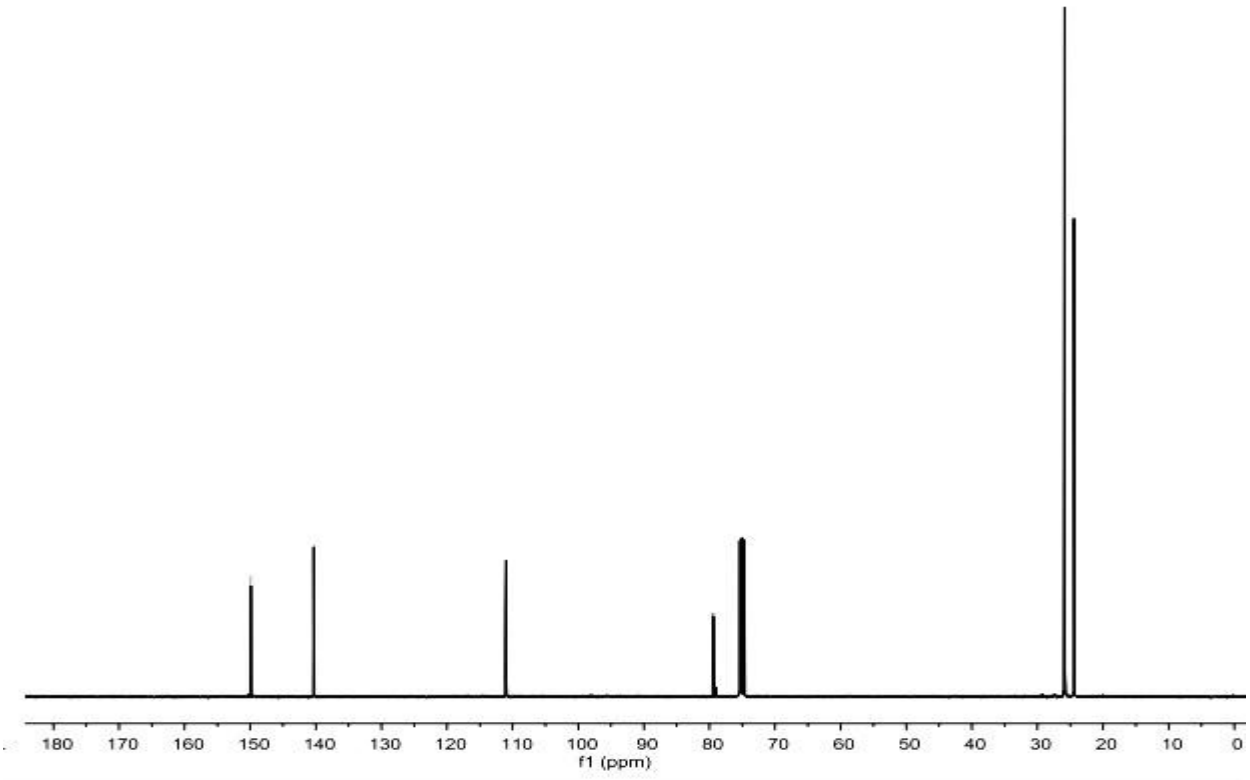
A mixture of *tert*-butyl (2-methylbut-3-en-2-yl) carbonate (7.4 g, 40 mmol), aniline (3.0 g, 32 mmol) and $Pd(PPh_3)_4$ (0.74 g, 0.64 mmol) in THF-DMF (60 ml : 3 ml) was stirred at room temperature for 24 h (monitored by TLC, EtOAc–Petroleum ether 1:10, R_f 0.45). Most of solvent was evaporated *in vacuo*, the residue was diluted with water (50 ml) and was extracted with EtOAc (3 × 20 ml). The organic solution was combined and washed by brine, dried (anhydrous $MgSO_4$) and concentrated *in vacuo* to give crude product, which was chromatographed over silica gel (EtOAc–petroleum ether, 1:20) to afford 3.9 g (76%) of *N*-(2-methylbut-3-en-2-yl)aniline as yellow liquid. IR (KBr): 1257, 1316, 1497, 1605, 2979, 3401 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.40 (s, 6H, 2Me), 3.62 (brs, 1H, NH), 5.16-4.97 (m, 2H, CH_2), 6.03-5.87 (m, 1H, CH), 6.63-6.48 (m, 3H, Ar), 7.04 (t, 2H, Ar, *J* 8.0 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 29.7 (Me), 55.9 ($Me_2\underline{C}$), 114.8 (CH_2), 117.0 (Ar), 118.8 (Ar), 129.9 (Ar), 145.1 (CH), 147.5 (Ar); HRMS (ESI) Calcd for $C_{11}H_{16}N$ $(M+H)^+$: 162.1277, found: 162.1272.

2-(3-Methylbut-2-en-1-yl)aniline **2**

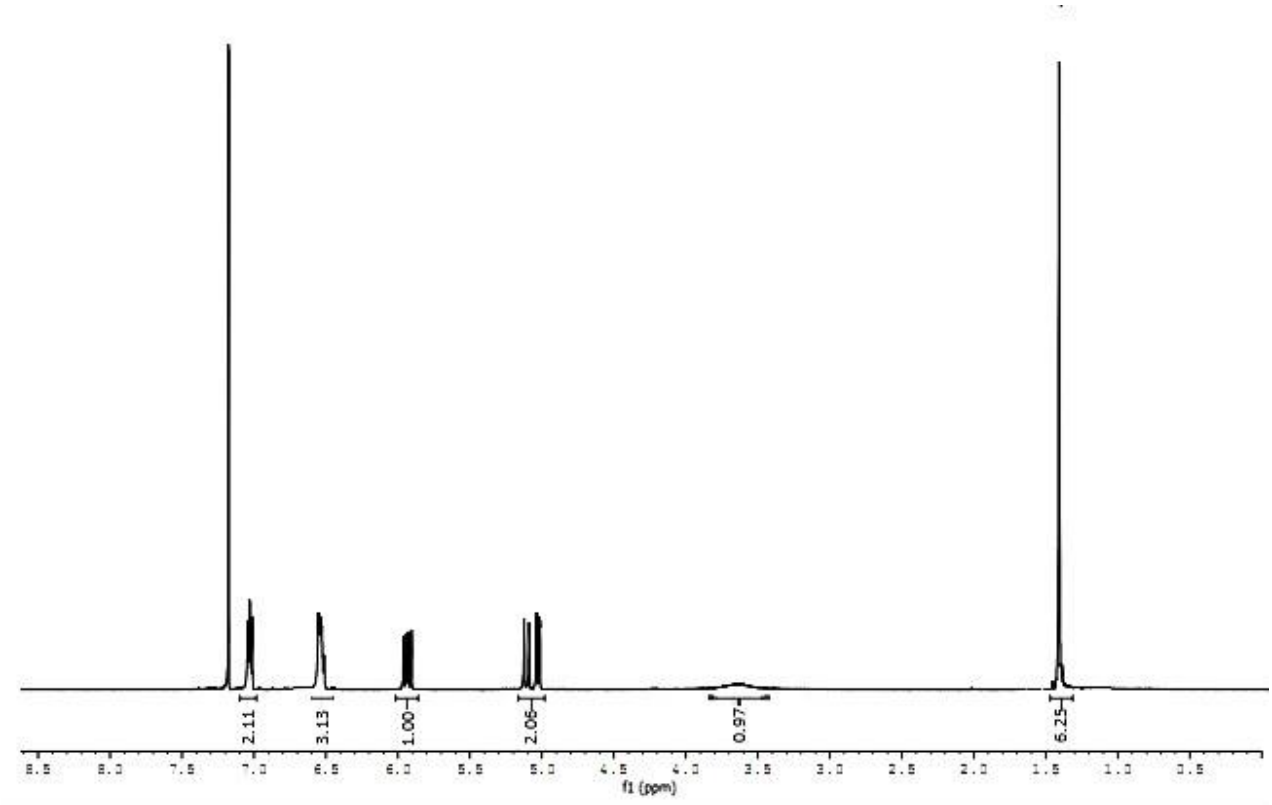
A suspension of *N*-(2-methylbut-3-en-2-yl)aniline (3.7 g, 23 mmol) and *p*-TsOH monohydrate (0.44 g, 2.3 mmol) in CH_3CN–H_2O (60 ml : 6 ml) was heated for 12 h at 70 °C. CH_3CN was removed *in vacuo*, and the residue was extracted with EtOAc (3 × 20 ml). The organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. The crude residue was purified by the column chromatography on silica gel (EtOAc–petroleum ether, 1:20) to afford 2.1 g (57%) of **2** as yellow liquid. IR (KBr): 1260, 1300, 1470, 1620, 2950, 3385 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.63 (s, 6H, 2Me), 2.63 (t, 2H, CH_2, *J* 5.8 Hz), 3.63 (brs, 2H, NH_2), 4.90-4.82 (m, 1H, CH), 6.64-6.53 (m, 1H, Ar), 6.90-6.72 (m, 2H, Ar), 7.06 (t, 1H, Ar, *J* 7.6 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 17.6 (Me), 25.7 (Me), 33.8 (CH_2), 113.7 (Ar), 116.2 (CH), 119.5 (Ar), 123.7 (Ar), 128.7 (Ar), 129.3 (CH), 131.9 (Ar), 143.5 (Ar); HRMS (ESI) Calcd for $C_{11}H_{16}N$ $(M+H)^+$: 162.1277, found: 162.1273.



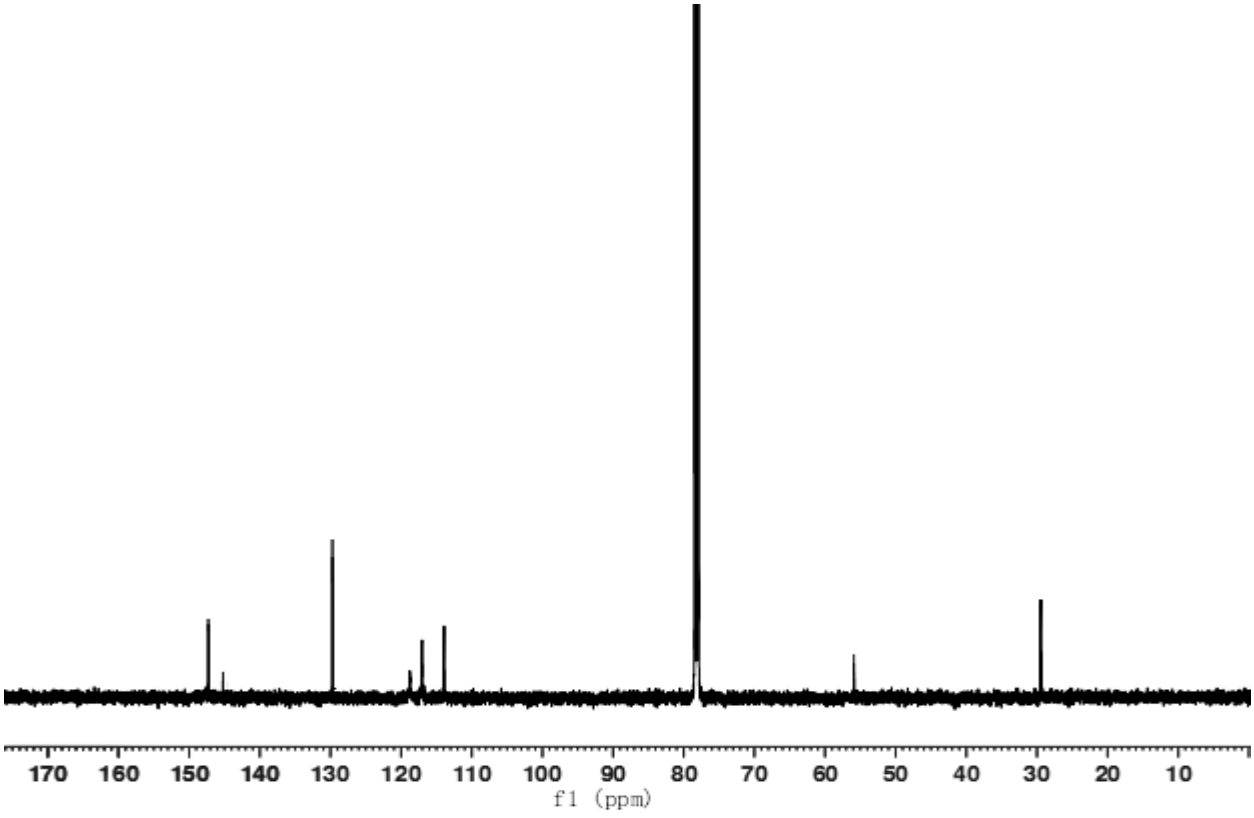
^{1}H NMR spectrum of *tert*-butyl (2-methylbut-3-en-2-yl) carbonate



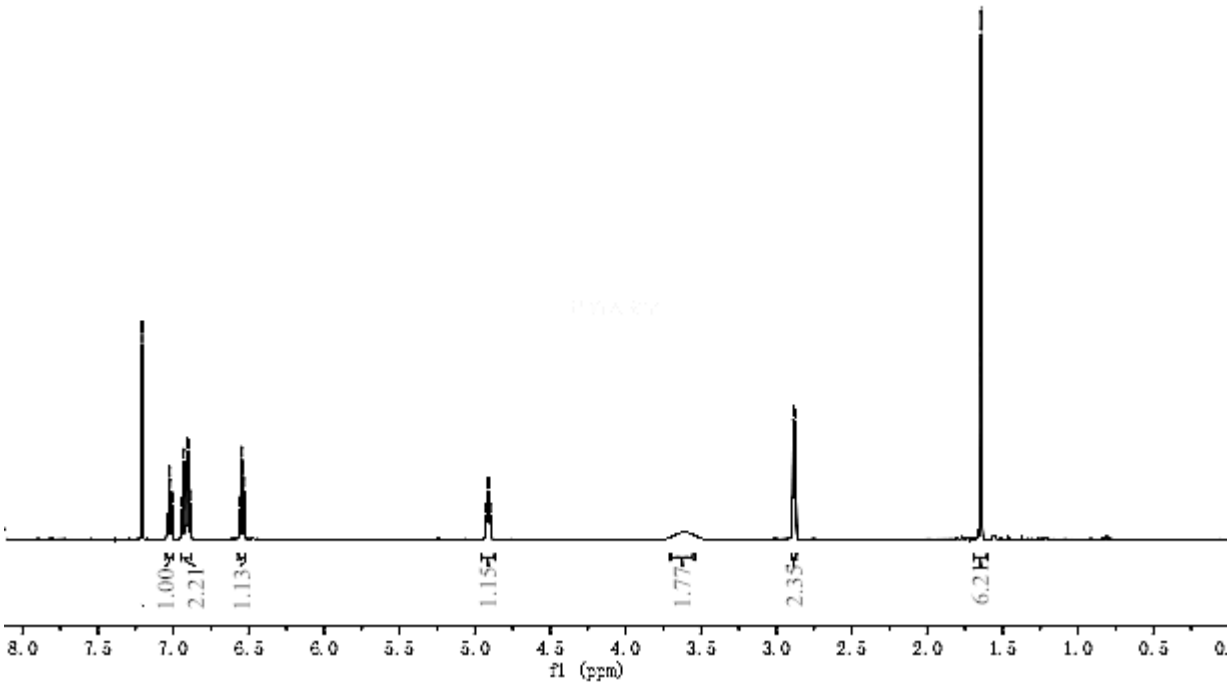
^{13}C NMR spectrum of *tert*-butyl (2-methylbut-3-en-2-yl) carbonate



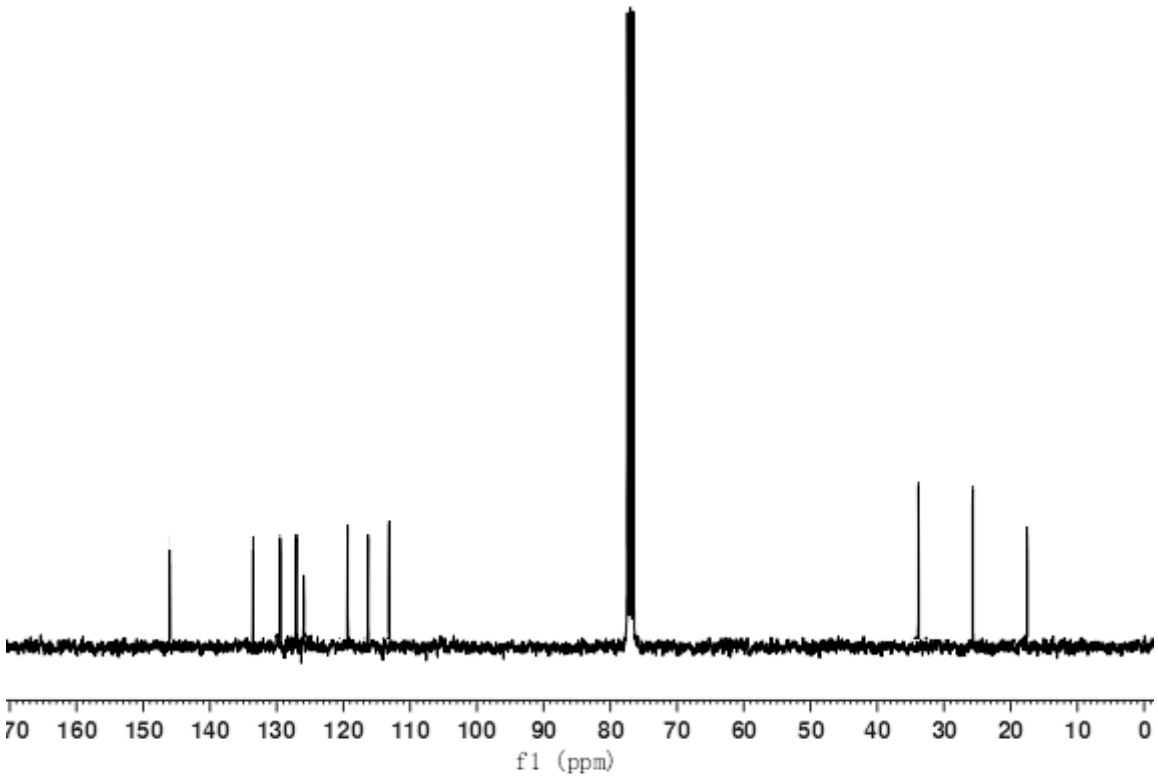
^{1}H NMR spectrum of *N*-(2-methylbut-3-en-2-yl)aniline



^{13}C NMR spectrum of *N*-(2-methylbut-3-en-2-yl)aniline



^{1}H NMR spectrum of 2-(3-methylbut-2-en-1-yl)aniline **2**



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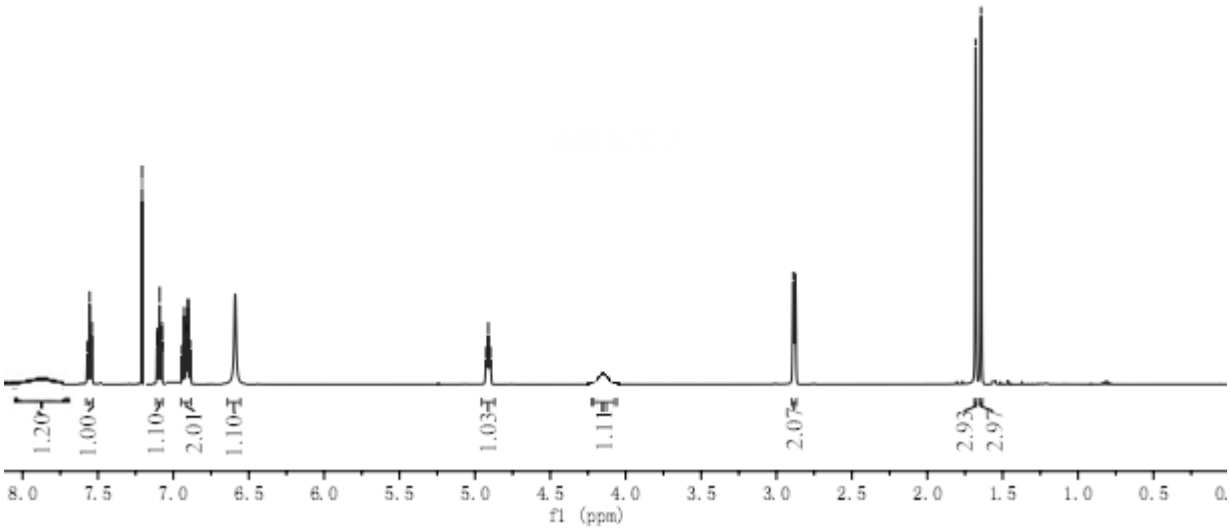
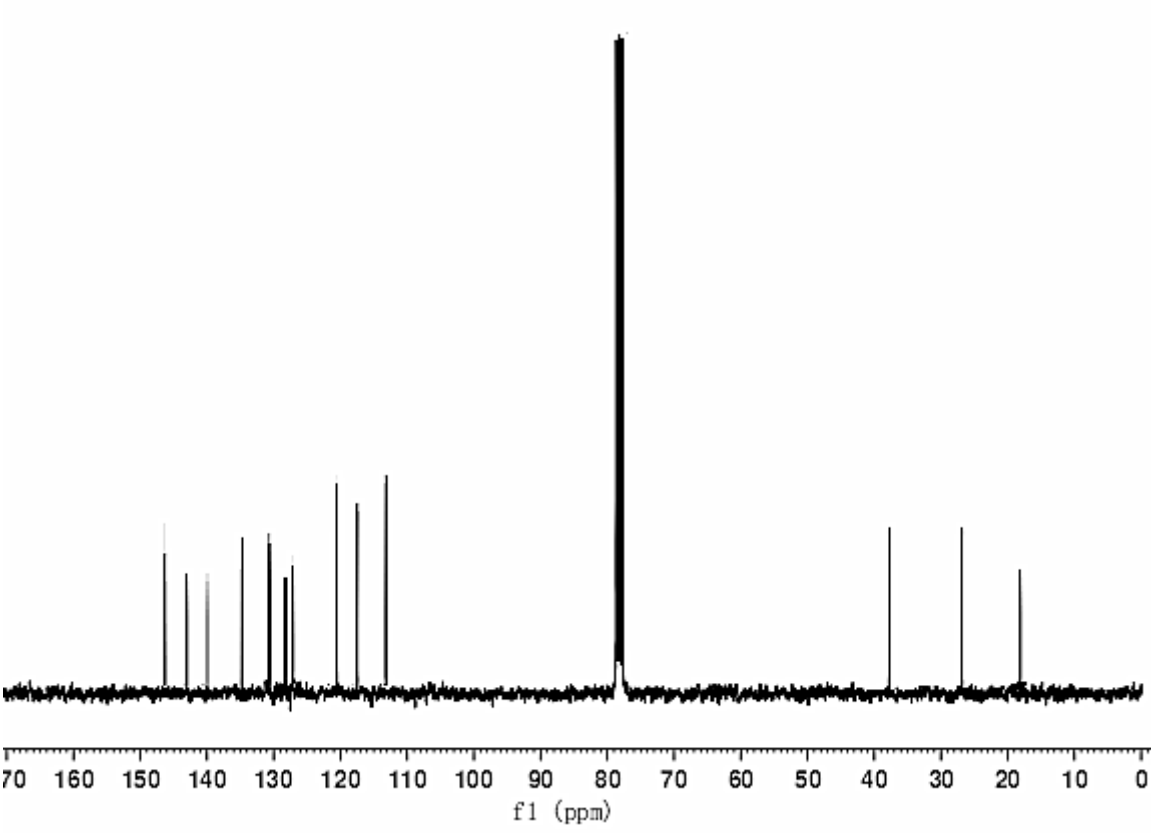
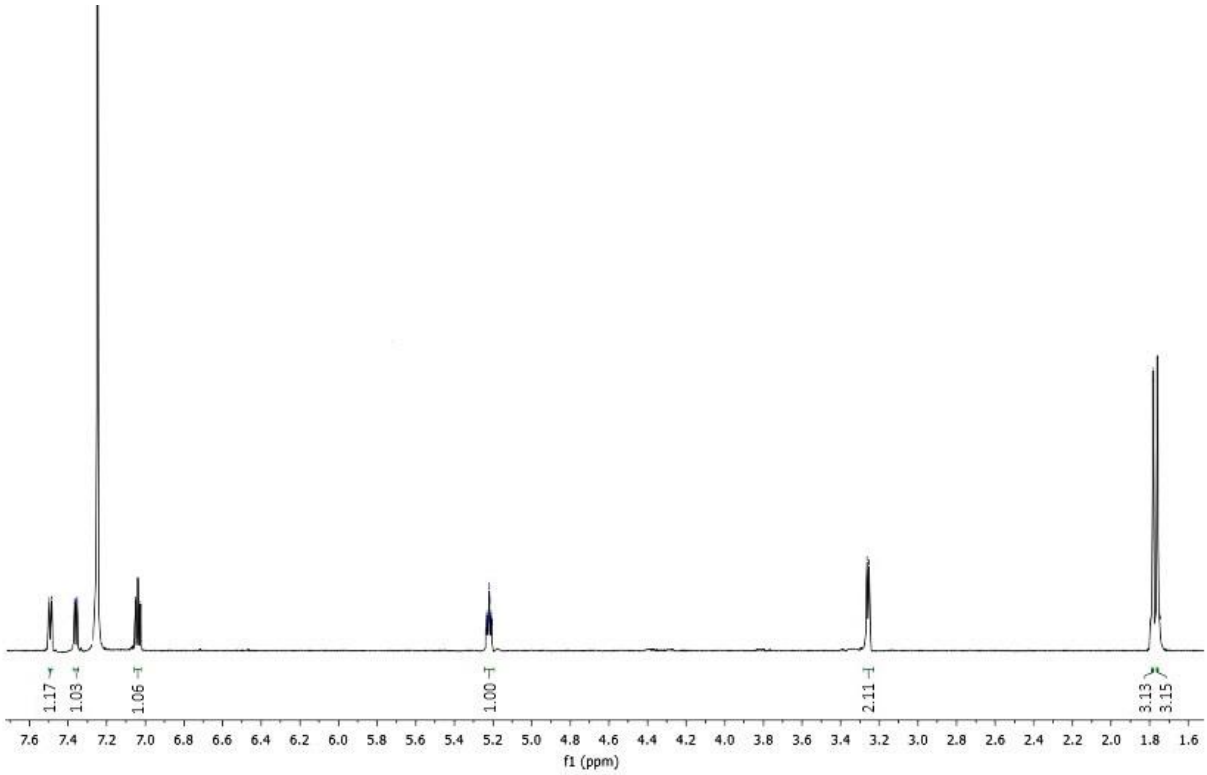


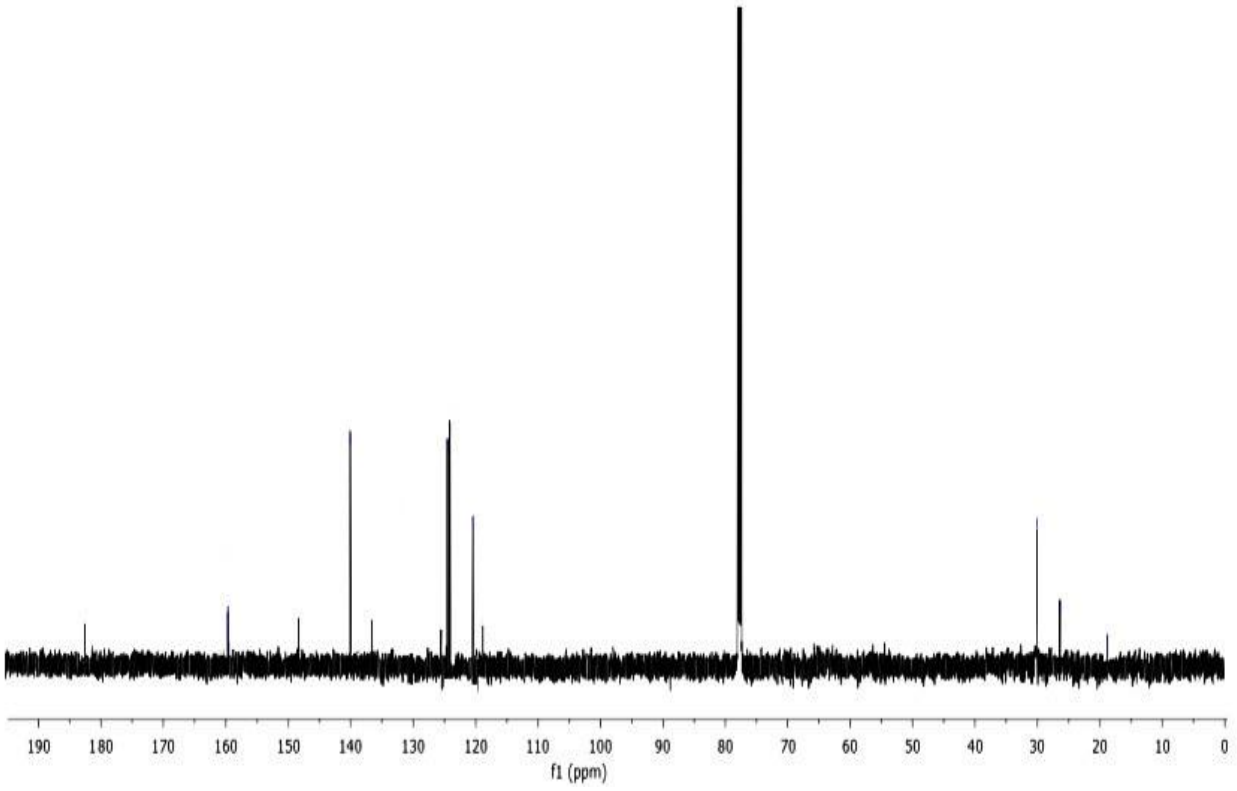
^{1}H NMR spectra of (*E*)-2-(hydroxyimino)-*N*-(2-(3-methylbut-2-en-1-yl)phenyl)acetamide **3**



^{13}C NMR spectrum of (*E*)-2-(hydroxyimino)-*N*-(2-(3-methylbut-2-en-1-yl)phenyl)acetamide **3**



^{1}H NMR spectrum of 7-prenylisatin **1**



^{13}C NMR spectrum of 7-prenylisatin **1**