Communication

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Reactions of α,β-unsaturated *N*-benzenesulfonyl Imine - *N*-[(2*E*)-3-phenyl-2-propen-1-ylidene]benzenesulfonamide with Methyllithium

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α,β-Unsaturated *N*-benzenesulfonyl imine **1** was treated with 1.1 eq methyllithium to afford 1,2-addition adduct as a sole product. However, when compound **1** was treated with 2 eq MeLi, 1,2-addition product, benzenesulfonamide derivative **3** and 2*H*-1,2-benzothiazine 1,1-dioxide derivatives **4** and **5** were isolated.

Keywords: Nucleophilic addition; α,β-Unsaturated sulfonyl imine; 1,2-Addition; Cyclization.

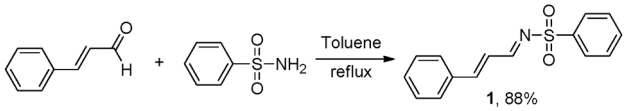
INTRODUCTION

Nucleophilic addition reaction to electron-deficient olefins is one of the most important methods for C-C or C-heteroatom formation in organic synthesis.[1] The reactions of α,β-unsaturated imine with different nucleophile provide a convenient route for the preparation of functionalized organic compounds[2] and are increasingly being used for the asymmetric synthesis to chiral compounds[3] and natural products.[4] However, the addition of organolithium compounds to α,β-unsaturated imine tends to favour 1,2-addition for most substrates, and when successful, 1,4-addition will not afford.[3b,3g] In this paper, we reported that the reaction of α,β-unsaturated *N*-benzenesulfonyl imine with methyllithium. When two equivalents of MeLi was added, not only afforded 1,2-addition product, but also generated benzenesulfonamide derivatives and 2*H*-1,2-benzothiazine 1,1-dioxide derivatives.

RESULTS AND DISCUSSION

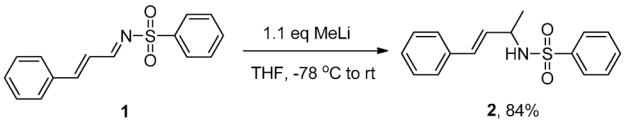
α,β-Unsaturated *N*-benzenesulfonyl imine **1** have been successfully synthesized by the condensation reaction of *trans*-cinnamaldehyde and benzenesulfonamide in toluene at refluxing temperature to give the important precursor in 88% yield (Scheme 1).[5]

Scheme 1 Synthesis of Compound **1**



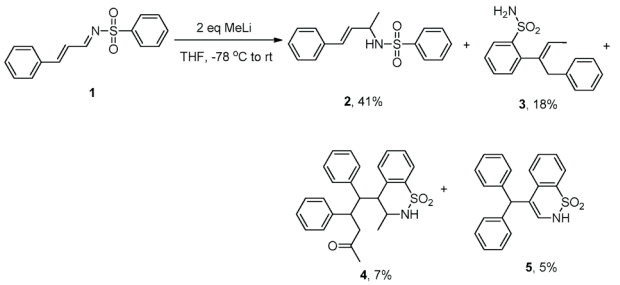
When α,β-unsaturated *N*-benzenesulfonyl imine **1** was treated with 1.1 eq MeLi at -78 °C and stirred at rt for 24 h, only 1,2-addtion addition adduct **2** was obtained in 84% yield (Scheme 2).

Scheme 2 Reaction of Compound **1** with 1.1 eq MeLi



However, when α,β-unsaturated *N*-benzenesulfonyl imine **1** was treated with 2 eq MeLi at -78 °C and stirred at rt for 24 h, four compounds, **2**, **3**, **4**, and **5**, were isolated in yields of 41%, 18%, 7%, and 5%, respectively. The structures of compounds **3**, **4**, and **5** were confirmed by X-ray crystallography (Scheme 3).

Scheme 3 Reaction of Compound **1** with 2 eq MeLi



The result shows that compound **3** was produced from phenyl anion addition at conjugated C=C bond for ring-closing reaction and followed by ring-opening reaction to give compound **3**.

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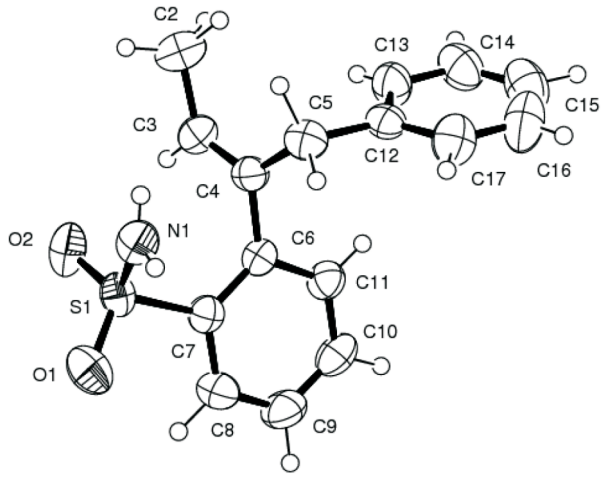


Fig. 1. The X-ray crystal structure of **3**.

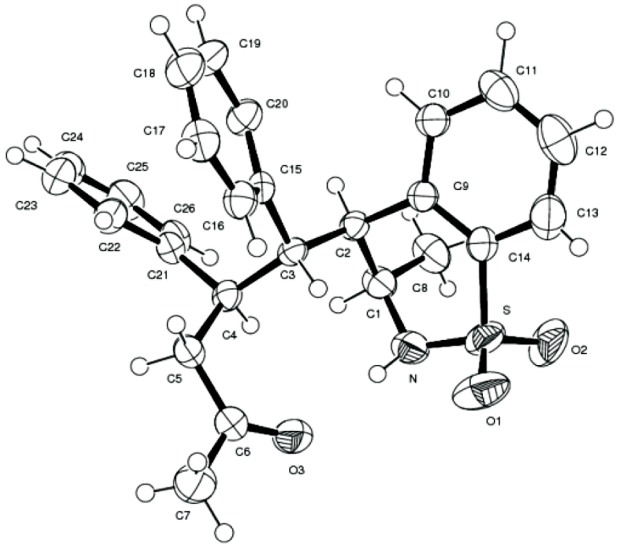
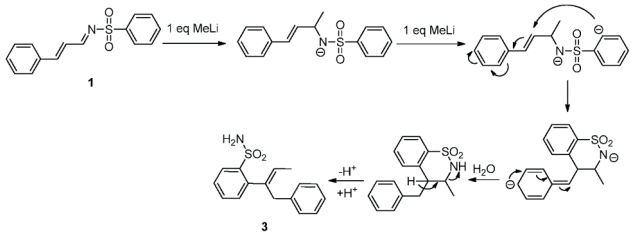


Fig. 2. The X-ray crystal structure of **4**.

Scheme 4 Plausible mechanism for the formation of Compound **3**



Compound **4** was obtained from the formation of benzylic anion which was attacked to another molecule and followed by cyclization to give six-membered ring finally hydration and oxidation to form compound **4**.

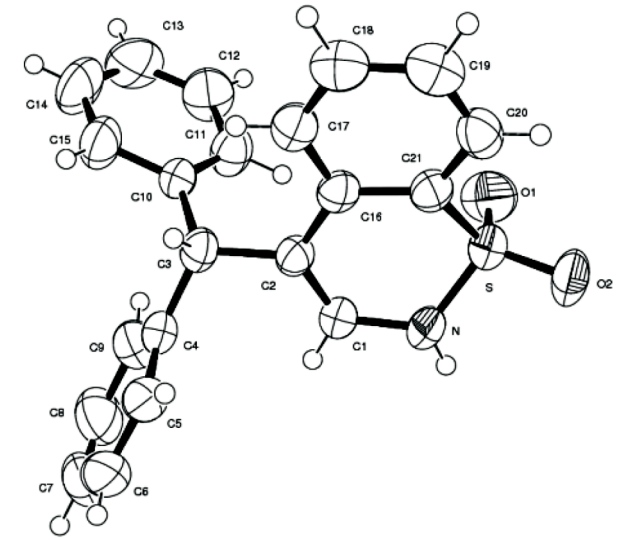
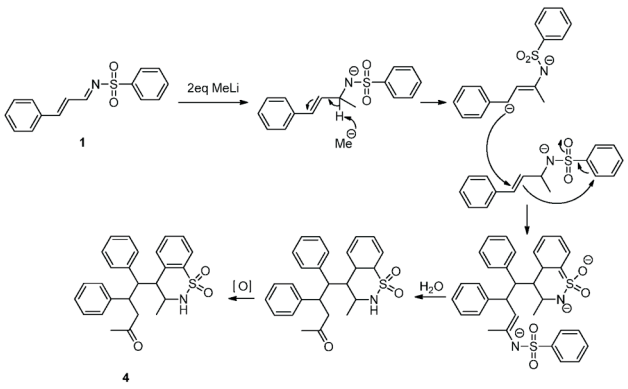


Fig. 3. The X-ray crystal structure of **5**.

Scheme 5 Plausible mechanism for the formation of Compound **4**



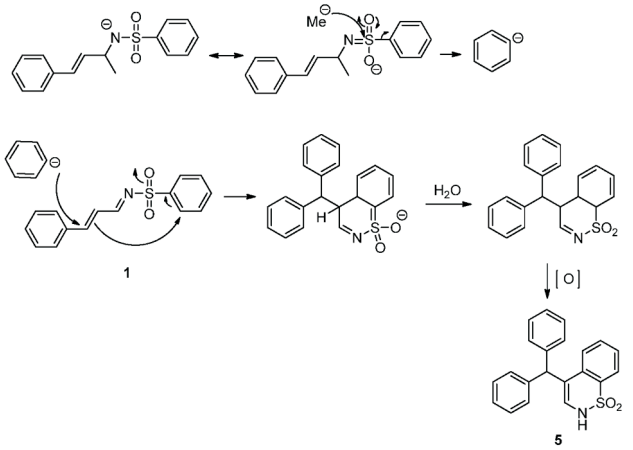
Compound **5** was formed from MeLi addition to sulfonyl group to leave a phenyl anion[6] due to the pKa of Me-H is 48[7] and the pKa of Ph-H is 43.[8] Phenyl anion underwent 1,4-addition of **1** followed by ring-closing reaction and oxidation to produce compound **5** (Scheme 6).

In conclusion, α,β-unsaturated *N*-benzenesulfonyl imine reacted with 1.1 eq methyllithium will afford 1,2-addition adduct only. When 2 eq of MeLi was added, not only afforded 1,2-addition product, but also formed benzenesulfonamide derivative **3** and 2*H*-1,2-benzothiazine 1,1-dioxide derivatives **4** and **5**.

EXPERIMENTAL

General information: Melting points were measured with a Barloworld SMP3 melting point apparatus and were uncor-

Scheme 6 Plausible mechanism for the formation of Compound **5**



rected. NMR spectra were measured in $CDCl_3$ solution with a Bruker AC-300 MHz NMR spectrometer, with $CHCl_3$ (7.26 ppm) as the internal standard. Carbon-13 NMR were measured in $CDCl_3$ solution on a 75 MHz NMR spectrometer and referenced to $CDCl_3$ (77.1 ppm). Chemical shifts (δ) are expressed in ppm downfield from tetramethylsilane. Coupling constants (J) are expressed in hertz (Hz). Mass spectra were measured with a Finnigan/Thermo Quest MAT 95XL mass spectrometer. The elemental analyses were recored on a Elementar vario EL III elemental analyzer. Infrared spectra were recorded on KBr pellets. Flash chromatography was performed on silica gel (230 mesh). Column chromatography was performed on silica gel (70-230 mesh). Solvents are of reagent grade.

Preparation of *N*-[(2*E*)-3-phenyl-2-propen-1-ylidene]-benzenesulfonamide (1):[5] To a solution of *trans*-cinnamaldehyde (26.4 g, 0.2 mol) and benzenesulfonamide (31.4 g, 0.2 mol) in 1 L toluene was stirred for 120 h at reflux under a Dean-Stark trap. Toluene was removed on a rotary evaporator to yield a pale yellow solid (47.7 g, 88%). The NMR data are consistent with those reported in the literature.[9]

Reaction of *N*-[(2*E*)-3-phenyl-2-propen-1-ylidene]-benzenesulfonamide (1) with 1.1 eq Methyllithium: Methyllithium (1.5 M in ether, 11 mL, 16.5 mmol) was added dropwise from a dropping funnel to a stirred solution of compound **1** (4.08 g, 15 mmol) in 100 mL of dry THF at -78 °C. The mixture was allowed to warm to rt and stirred for 24 h. The mixture was poured into a 400 mL beaker with 100 g of crushed ice and added 50 mL CH_2Cl_2. The organic layer was separated and washed with water and brine, and then dried over anhydrous $MgSO_4$. After filtration, the solvent was removed on a rotary evaporator and the residue was purified by flash column chromatography to give compound **2** (3.62 g, 84%). The NMR data are consistent with those reported in the literature.[10] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.91-7.87 (m, 2H), 7.50-7.14 (m, 8H), 6.32 (d, 1H, J = 15.8 Hz), 5.86 (dd, 1H, J = 15.8, 6.7 Hz), 4.77 (s, 1H), 4.14-4.08 (m, 1H), 1.27 (d, 3H, J = 6.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.2 (C), 136.3 (C), 132.5 (CH), 130.7 (CH), 130.1 (CH), 129.0 (CH), 128.5 (CH), 127.8 (CH), 127.2 (CH), 126.4 (CH), 51.8 (CH), 22.0(CH_3). MS *m/z* (%) 287 (M^+, 13), 77 (100), 130 (45), 144 (45), 146 (62). HRMS (EI) calcd for $C_{16}H_{17}NO_2S$ *m/z* 287.0980 (M^+), found 287.0984.

Reaction of *N*-[(2*E*)-3-phenyl-2-propen-1-ylidene]-benzenesulfonamide (1) with 2 eq Methyllithium: Methyllithium (1.5 M in ether, 20 mL, 30 mmol) was added dropwise from a dropping funnel to a stirred solution of compound **1** (4.08 g, 15 mmol) in 100 mL of dry THF at -78 °C. The mixture was allowed to warm to rt and stirred for 24 h. The mixture was poured into a 400 mL beaker with 100 g of crushed ice and added 50 mL CH_2Cl_2. The organic layer was separated and washed with water and brine, and then dried over anhydrous $MgSO_4$. After filtration, the solvent was removed on a rotary evaporator and the residue was purified by column chromatography and HPLC to give compounds **2** (1.77 g, 41%), **3** (0.78 g, 18%), **4** (0.46 g, 7%), **5** (0.26 g, 5%). Compound **3**: mp 111-112 °C; IR (neat, cm^{-1}) 3034, 3275, 3061, 1950, 1715, 1557, 1492, 1467, 1453, 1329, 1157, 894, 759, 734, 703; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.01-7.96 (m, 1H), 7.34-6.80 (m, 8H), 5.72 (q, 1H, J = 6.8 Hz), 4.64 (s, 2H), 3.90 (s, 2H), 2.02 (d, 3H, J = 6.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.0 (C), 140.2 (C), 139.5 (C), 139.1 (C), 131.9 (CH), 129.1 (CH), 128.6 (CH), 127.2 (CH), 127.0 (CH), 126.4 (CH), 38.4 (CH_2), 14.5 (CH_3). MS *m/z* (%) 287 (M^+, 7), 206 (32), 191 (100), 91 (33). HRMS (EI) calcd for $C_{16}H_{17}NO_2S$ *m/z* 287.0980 (M^+), found 287.0977. X-ray: CCDC 1051436. Compound **4**: mp 193-195 °C; IR (neat, cm^{-1}) 3200, 3056, 2918, 2863, 1697, 1494, 1347, 1166, 769, 709, 597, 566; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.78-7.75 (m, 1H), 7.74-6.23 (m, 14H), 4.85-4.70 (m, 1H), 4.10-4.00 (m, 1H), 3.17-3.10 (m, 1H), 3.08-2.91 (m, 2H), 2.70 (dd, 1H, J = 18.8, 3.1 Hz), 2.2 (s, 3H), 1.56 (d, 3H, J = 7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.1 (C), 140.0 (C), 137.1 (C), 136.5 (C), 131.4 (CH), 131.2 (CH), 130.5 (CH), 129.3 (CH), 128.2 (CH), 127.9 (CH), 127.4 (CH), 127.3 (CH), 127.2 (CH), 125.1 (CH), 55.1 (CH) 52.0 (CH), 47.0 (CH_2), 46.1 (CH), 38.8 (CH), 30.6 (CH_3), 19.0 (CH_3). MS *m/z* (%) 433 (M^+, 1), 286 (61), 237 (43), 180 (30), 179 (100), 91 (28). HRMS (EI) calcd for $C_{26}H_{27}NO_3S$ *m/z* 433.1712 (M^+), found 433.1716. X-ray: CCDC 1051438. Compound **5**: mp 160-162 °C; IR (neat, cm^{-1}) 3240, 3032, 1697, 1493, 1309, 1168, 810, 774, 747, 696; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.95-7.91 (m, 1H), 7.49-7.15 (m, 14H), 5.92 (s, 1H), 5.63 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.6 (C), 133.5 (C), 132.5 (C), 132.1 (CH),

129.6 (CH), 128.8 (CH), 127.7 (CH), 127.6 (CH), 127.0 (CH), 125.0 (CH), 121.8 (CH), 51.2 (CH). MS *m/z* (%) 347 (M^+, 100), 266 (75), 206 (31), 167 (30), 165 (37). HRMS (EI) calcd for $C_{21}H_{17}NO_2S$ *m/z* 347.0980 (M^+), found 347.0989. X-ray: CCDC 1051439.

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