Dehydrosulfonylation of Conjugated Enyne Sulfones: Convenient Synthesis of Diyne Compounds

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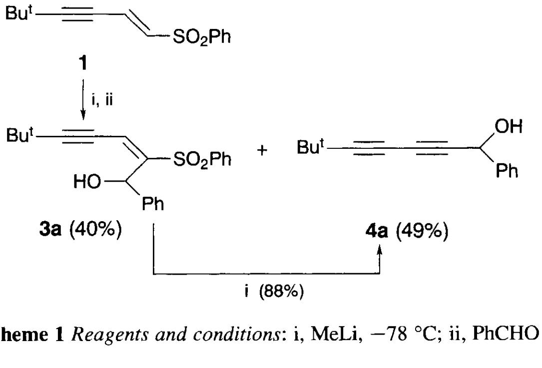
α-Lithio conjugated enyne sulfones, easily generated from enyne sulfones **1** and **2** and MeLi, upon reaction with carbonyl compounds followed by treatment with MeLi afford the 2,4-diynols **4a–g** and **5a–c** in high yields.

Some conjugated diacetylenes showing antibacterial or antifungal activity have been isolated from fungi and plants,[1] and artificial phospholipids containing conjugated acetylenes are good tools for the preparation of phospholipid polymers by photochemical cross-linking.[2] The most widely used method for the synthesis of conjugated diacetylenes is the oxidative coupling reaction of acetylenes (Cadiot–Chodkiewicz reaction); however, this acetylenic coupling reaction has several disadvantages, such as the formation of 1-haloalkynes and contamination by symmetrical diynes in the synthesis of unsymmetrical diynes.[3] The only alternative methods available for the synthesis of 1,3-diynes are the fluoride-mediated dehydrochlorination of (*Z*)-1-chloro-alk-1-en-3-ynes[3] and the metallation–elimination of (*Z*)-1-methoxybut-1-en-3-yne with Bu^{n}Li.[4]

α-Lithiation of conjugated enyne sulfones and successive treatment with electrophiles, was found to result in the dehydrosulfonylation of enyne sulfones, affording diyne compounds. The dehydrosulfonylation of vinyl sulfones, a potentially convenient method for the production of conjugated acetylene derivatives, has to be reported. We here report the unprecedented dehydrosulfonylation of enyne sulfones and a novel one-pot synthesis of diyne alcohols.

Reaction of 2,2-dimethyl-6-benzenesulfonylhex-3-yn-5-ene **1** with benzaldehyde, resulted in the formation of diyne alcohol **4a** (49% yield), together with the normal adduct **3a** (Scheme 1). Although variously-substituted vinyl sulfones undergo deprotonation at the α-position of the sulfonyl group upon treatment with MeLi at −90 °C,[5] dehydrosulfonylation has not been observed.[5] The enyne sulfone **3** was treated with 2 equiv. of MeLi at −78 °C to give the diyne alcohol **4** in 88% yield. This result suggested that the α-substituted conjugated enyne sulfone easily underwent deprotonation of a β-hydrogen of the sulfonyl group and successive desulfonylation. If these processes can be achieved in a one-pot reaction, this could become a useful synthetic method for the preparation of various diyne alcohols from enyne sulfones.

We examined the one-pot synthesis of diyne alcohols from enyne sulfones **1** and **2**, as shown in Table 1. After the reaction of α-lithio enyne sulfone **1** with benzaldehyde, 1 mol. equiv. of MeLi was added to the reaction mixture to give the diyne alcohol **4a** in good yield (entry 1).† The phenethyl-substituted butadiynol **4b** was obtained in high yield from 3-phenylpropanal (entry 2). Cycloalkanones also gave satisfactory results (entries 3 and 4). The α-lithio enyne sulfone **1** underwent 1,2-addition to cyclohexenone and the intermediate was transformed to the enediynol **4e** in 73% yield. Reaction with hept-2-ynal gave 1,4,6-triyn-3-ol **4g** in good yield. *n*-Butyl-substituted enyne sulfone **2** was treated similarly and gave the diynols **5a–c** in good yields.



Scheme 1 *Reagents and conditions*: i, MeLi, −78 °C; ii, PhCHO

The reaction mechanism is shown in Scheme 2. α-Lithio enyne sulfone **7** is easily generated by treatment of the (*E*)-enyne sulfone **6** with MeLi at −78 °C, and reacts with carbonyl compounds without isomerisation to give (*E*)-enynol **8**. Treatment of **8** with MeLi causes deprotonation of a β-vinyl hydrogen and the synchronous *syn*-elimination of the sulfonyl group to give the diynol **11**.

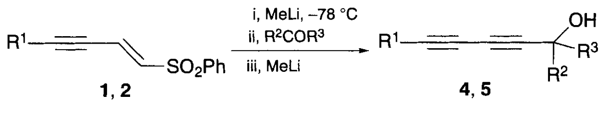
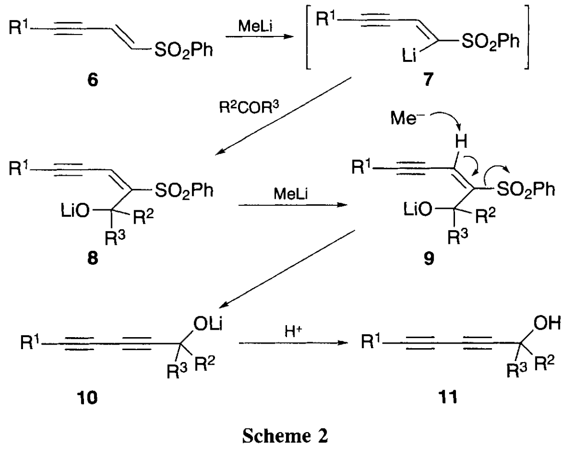


Table 1 Synthesis of diyne alcohols

Entry	Enyne sulfone	R^1	Electrophile R^2	R^3	Product (% yield)
1	**1**	Bu^t	H	Ph	**4a** (85)
2	**1**	Bu^t	H	Ph(CH$_2$)$_2$	**4b** (94)
3	**1**	Bu^t	–(CH$_2$)$_4$–		**4c** (82)
4	**1**	Bu^t	–(CH$_2$)$_5$–		**4d** (94)
5	**1**	Bu^t	–CH=CH(CH$_2$)$_3$–		**4e** (73)
6	**1**	Bu^t	H	furyl	**4f** (79)
7	**1**	Bu^t	H	Bu^{n}C≡C	**4g** (70)
8	**2**	Bu^n	H	Ph	**5a** (59)
9	**2**	Bu^n	H	Ph(CH$_2$)$_2$	**5b** (66)
10	**2**	Bu^n	–(CH$_2$)$_5$–		**5c** (60)



Scheme 2

This method can be extended to the syntheses of alkadiynes and alkadiynamines. These will be reported in a full paper.

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Footnote

† Preparation of **4a**: a benzene (60 ml) solution of methyl phenyl sulfone (3.12 g, 20 mmol) was added dropwise to a diethyl ether (40 ml) solution of EtMgBr [30 mmol, prepared from EtBr (3.27 g, 30 mmol) and Mg (0.72 g, 30 mmol)] at 0 °C, and the resulting mixture stirred for 1 h at room temp., followed by the dropwise addition of a diethyl ether (20 ml) solution of 4,4-dimethylpent-2-ynal (2.20 g, 20 mmol) at 0 °C. This was stirred overnight and then worked up as usual. The raw product was purified by column chromatography on silica gel eluting with EtOAc–*n*-hexane (1 : 10) to give 2,2-dimethyl-6-benzenesulfonylhex-3-yn-5-ol (3.70 g, 70%) as a pale yellow oil. Methanesulfonyl chloride (1.29 g, 11.3 mmol) was added dropwise to a mixture of this yellow oil (3.00 g, 11.3 mmol) and Et_3N (2.28 g, 22.6 mmol) at room temp., the mixture was stirred for 2 h and then worked up. Purification of the raw product by column chromatography on silica gel eluting with EtOAc–*n*-hexane (1 : 20) gave **1** (2.80 g, 59%) as colourless prisms, mp 92–94 °C. A diethyl ether solution of MeLi (2.0 ml, 1.0 mol dm^{-3} solution) was added dropwise to a diethyl ether (2 ml) solution of **1** (0.25 g, 1.0 mmol) at −78 °C under an Ar atmosphere, and stirred for 5 min, then a diethyl ether (1 ml) solution of benzaldehyde (0.21 g, 2.0 mmol) was also added. A diethyl ether solution of MeLi (2.0 ml, 1.0 mol dm^{-3} solution) was added to the resultant mixture of **3a**, which was then stirred for 10 min at −78 °C and then worked up. The raw product was separated by preparative TLC on silica gel to give the 2,2-dimethyl-7-phenyl-3,5-diyn-7-ol **4a** (0.18 g, 85%) as colourless needles, mp 47–49 °C (decomp.).

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