A New Convenient Synthesis of Ethenyl Ethers

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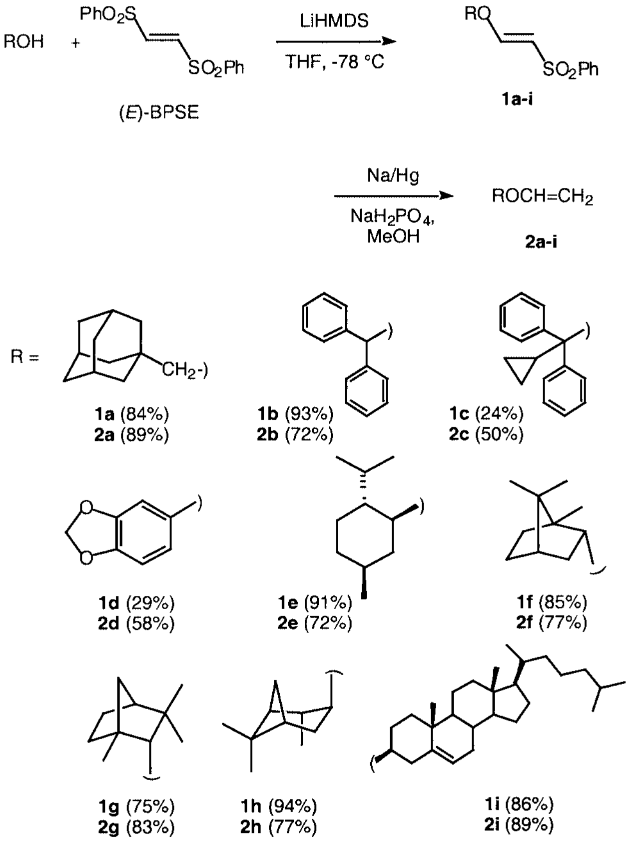
Abstract: Addition-elimination of an alcohol to 1,2-bis(phenylsulfonyl)ethylene afforded β-alkoxyvinyl sulfones which were submitted to reductive elimination with 6% sodium amalgam to produce the corresponding ethenyl ethers in high yields and purity.

Key words: β-alkoxyvinylsulfones, ethenyl ethers, bis(phenylsulfonyl)ethylene, reductive desulfonylation

Ethenyl ethers ($ROCH=CH_2$) are widespread compounds in organic synthesis as they display a high and diversified reactivity. Indeed, beside being used as dienophiles in every type of cycloaddition (hetero [4+2],[1] inverse-electron-demand [4+2],[2] photochemical or dipolar [2+2],[3] dipolar [3+2][4] and cation radical[5] cycloadditions), they can participate as substrates in many reactions such as metathesis,[6] Claisen rearrangements,[7] addition of organometallics,[8] metallation at the α-carbon,[9] etc.[10]

Ethenyl ethers are usually obtained either through Reppe vinylation[11] directly from the alcohol and acetylene at high pressures and temperatures[12] or through mercury(II) acetate mediated trans-etherification of ethyl vinylether[13] or high temperature base-induced elimination reactions.[14] Even though the synthesis of simple ethenyl ethers is no more a challenge and direct vinylation is performed industrially in multi-thousand tons scale, at the laboratory scale all actual methods present drawbacks and disadvantages especially because of the hazard of handling acetylene at the drastic reaction conditions which are needed when dealing with reluctant, hindered alcohols. We now report a new alternative synthetic protocol for the preparation of ethenyl ethers which can be applied to highly hindered substrates and which is based on the use of the safe and crystalline bis(phenylsulfonyl)ethylene (BPSE)[15] via a rather mild substitution-reductive desulfonylation reaction sequence. In other words, BPSE is utilized as a substitute for acetylene as it was in other instances to replace acetylene in cycloaddition reactions.[15] This methodology has been applied to several alcohols with a special attention to chiral enantiopure alcohols because of prospectable work in asymmetric synthesis.[16]

The reaction sequence, which has been used for the preparation of ethenyl ethers **2a-i** and the yields obtained are shown in the Scheme.



Scheme

Primary, secondary as well as tertiary and phenolic (with poorer yields, though) hydroxyl groups are represented. It should be emphasized that even strongly hindered alcohols such as fenchol and norborneol efficiently afford the respective β-alkoxyvinyl sulfones **1f** and **1g**.[17] As an improvement over the formerly reported reaction procedure,[18] it was noticed that when the reaction of an alcohol with BPSE was carried out in THF with LiHMDS[19] instead of NaH, the addition-elimination product **1** was produced exclusively and no formation of the β-phenylsulfonyl acetal **3** resulting from a second alkoxide addition to **1** was observed (Figure).

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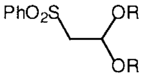

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Figure

The configuration of the β-alkoxyvinyl sulfones **1a-i** is *trans* in any case, i.e. they possess the same configuration as the starting BPSE, thus confirming the stereospecificity of the reaction.

The reductive desulfonylation occurred under mild reaction conditions using the standard sodium amalgam reduction of arylsulfonyl derivatives in buffered (NaH_2PO_4) methanolic solution.[20] After completion, the crude reaction mixture was filtered over Celite and washed with dichloromethane, then extracted with the same solvent and washed with 5% aqueous $NaHCO_3$. Careful evaporation of the organic phase afforded the crude enol ether, which was highly pure in all cases, with the exception of **2c** where a comparable amount of cyclopropyldiphenylmethane was also formed. In this latter case, the high stability of the cyclopropyldiphenylmethyl radical may be responsible for such an observation. It should be noted that the intrinsic reactivity of enol ethers towards water even under slightly acidic conditions would inevitably result in hydrolytic cleavage of the =HC–O– bond. Actually, purification by silica gel chromatography proved detrimental as it resulted in very poor recovery of the desired vinyl ether.

Other reducing agents previously reported to promote reductive desulfonylation - lithium naphthalenide,[21] magnesium in methanol[22] - were also tested but led to inferior results.

In conclusion, the above procedure represents a novel preparative method for the production of parent vinyl ethers. The methodology - which avoids the use of acidic reaction conditions - is of general utility and constitutes a valuable alternative to the existing intrinsically hazardous and/or noxious methodologies. The case of enol ether **2i**, which has been recently reported from vinylation of cholesterol with gaseous acetylene at high pressure and temperature,[12] is illustrative of the mildness of the method and of its potentiality. Extension of our methodology to more complex molecules such as carbohydrates is currently investigated in our laboratory.

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(16) It should be noted that the enantiopure ethenyl ethers chosen by us carry the chiral auxiliary at the minimum distance from the reactive site. References 1–10 have been selected from the vast recent literature about uses of ethenyl ethers in asymmetric synthesis.

(17) *General Procedure for the Synthesis of b-Alkoxy Vinyl Sulfones* (**1a-i**): To a stirred reaction mixture containing 0.1 g (0.32 mmol) of (*E*)-BPSE and the alcohol (0.32 mmol) in anhydrous THF (5 mL) was added 0.32 mL (0.32 mmol) of LiHMDS (1 M solution in hexane) at –78 °C. The mixture was allowed to stir overnight, then quenched with water, extracted with EtOAc and dried over $MgSO_4$. Evaporation of the solvents left a white solid which was purified by flash chromatography (petroleum ether or toluene–EtOAc). The physical properties of the products matched the reported data (Ref. 18)or agreed with the proposed structure. For example: (*E*)-*1*-(*2-Bornyloxy*)-*2-phenylsulfonyl ethylene*(**1f**): Colourless solid; mp 108 °C; $[\alpha]_D^{20} = -60$ (c = 1.1, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$): δ = 7.89–7.87 (m, 2 H, H_{ortho}), 7.60–7.48 (m, 4 H, H_{meta}, H_{para}, H-1), 5.64 (d, 1 H, H-2, J_{vic} = 12.1 Hz), 4.14 (m, 1 H, CHO), 2.25 (m, 1 H), 1.91 (m, 1 H), 1.72 (m, 2 H), 1.24 (m, 2 H), 1.06 (dd, 1 H, H-3e, *J* = 3.2, 13.6 Hz), 0.87 (s, 6 H, CH_3), 0.85 (s, 3 H, CH_3); ^{13}C NMR (62.89 MHz, $CDCl_3$): δ = 161.3 (C-1), 143.0 (C_{IVar}), 132.9 (C_{para}), 129.4 (C_{meta}), 127.1 (C_{ortho}), 106.9 (C-2), 89.0 (CHO), 49.8, 48.2 (C_{IV}), 45.1 (CH), 36.3, 28.0, 26.8 (CH_2), 19.8, 19.0, 13.7 (CH_3); IR (KBr): 1609 cm^{-1} (C=C); MS *m/z* (IS): 321 $[M+H]^+$, 338 $[M+NH_4]^+$, 343 $[M+Na]^+$. (*E*)-*1*-(*2-Fenchyloxy*)-*2-phenylsulfonyl ethylene* (**1g**): Colourless solid; mp 67 °C; $[\alpha]_D^{20} = +9$ (c = 1.26, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$): δ = 7.88–7.85 (m, 2 H, H_{ortho}), 7.58–7.48 (m, 4 H, H_{meta}, H_{para}, H-1), 5.76 (d, 1 H, H-2, J_{vic} = 11.9 Hz), 3.55 (s, 1 H, CHO), 1.70–1.66 (m, 3 H), 1.54–1.45 (m, 2 H), 1.21–1.17 (m, 1 H), 1.08–1.02 (m, 7 H), 0.82 (s, 3 H, CH_3); ^{13}C NMR (62.89 MHz, $CDCl_3$): δ = 162.5 (C-1), 143.0 (C_{IVar}), 132.9 (C_{para}), 129.4 (C_{meta}), 127.0 (C_{ortho}), 107.0 (C-2), 97.8 (CHO), 49.5 (C_{IV}), 48.5 (CH), 41.4 (CH_2), 40.3 (C_{IV}), 31.0 (CH_3), 26.3, 26.0 (CH_2), 20.8, 19.6 (CH_3); IR (KBr): 1624, 1602 cm^{-1} (C=C); MS *m/z* (IS): 321 $[M + H]^+$, 338 $[M + NH_4]^+$, 343 $[M + Na]^+$.

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