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A general, selective synthesis of ω-hydroxyethenyl ethers

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Abstract—A general selective synthesis of β-, γ- and δ-hydroxyethenyl ethers, a class of compounds containing two mutually reactive functionalities positioned at an interacting distance, is based on the reaction of diols with 1,2-bis-(phenylsulfonyl)ethylene (BPSE) followed by reductive elimination of the resulting β-phenylsulfonyl acetals with sodium amalgam. © 2002 Elsevier Science Ltd. All rights reserved.

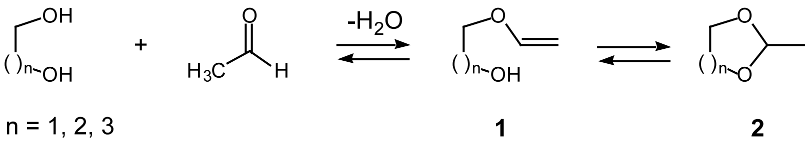
ω-Hydroxyethenyl (or -vinyl) ethers **1** represent a rare class of organic compounds which contain at an interacting distance two functional groups which—except under basic conditions—are highly reactive to one another. Indeed β-, γ- and δ-hydroxyvinyl ethers are possible intermediates in the generation of cyclic acetals **2** via the standard condensation of diols with aldehydes as shown in Scheme 1 for the parent vinyl ether.

Of course, while the saturated acetals **2** are widely used as protective groups and thus devoid of per se practical reactivity, β-, γ- and δ-hydroxyvinyl ethers **1** are most promising from a synthetic viewpoint either for the reactivity of the vinyl ether itself[1] or for the extra potentiality offered by the close proximity of the hydroxyl function. Compounds **1** can be particularly valuable when derived from chiral enantiopure diols in which the presence of the hydroxyl function can play an important role in the transmission of the chiral information.[2]

Some preparations of hydroxyethenyl ethers are reported in the literature. The proposed methods can be summarised as: (i) vinylation of diols with acetylene itself or haloethylenes;[3] (ii) preparation of vinyl ethers containing a carbonyl group followed by reduction or addition of organometallics;[4] (iii) addition of vinylmetals to endoperoxides.[5] None of the reported procedures represent a selective synthesis and they all contain inherent drawbacks and disadvantages such as length, availability of the starting material, hazard in handling acetylene, scope and selectivity, etc.

Herewith we report the first general synthetic methodology for a selective synthesis of this class of compounds, which is based on the two-step pathway shown in Scheme 2.

The reaction of diols with either (*Z*)- or (*E*)-isomers of 1,2-bis-(phenylsulfonyl)ethylene (BPSE) leads in high yields to the respective β-phenylsulfonyl acetals **3a**–**f**.[6,7] These compounds are stable crystalline substances which are highly resistant to hydrolysis[7] and can thus be stored indefinitely as precursors of the hydroxyenol ethers. Phenylsulfonylacetals other than **3a**–**f** are also available.[7,8] Significantly, acetals **3g** and **3h** display 1,3-dioxocane and 1,3-dioxacyclotridecane rings, respectively. Though they are produced in quite poor yield (11 and 2%, respectively) and have not been further processed to the respective hydroxyethenyl ethers, they are indicative of the scope of the reaction.



Scheme 1.

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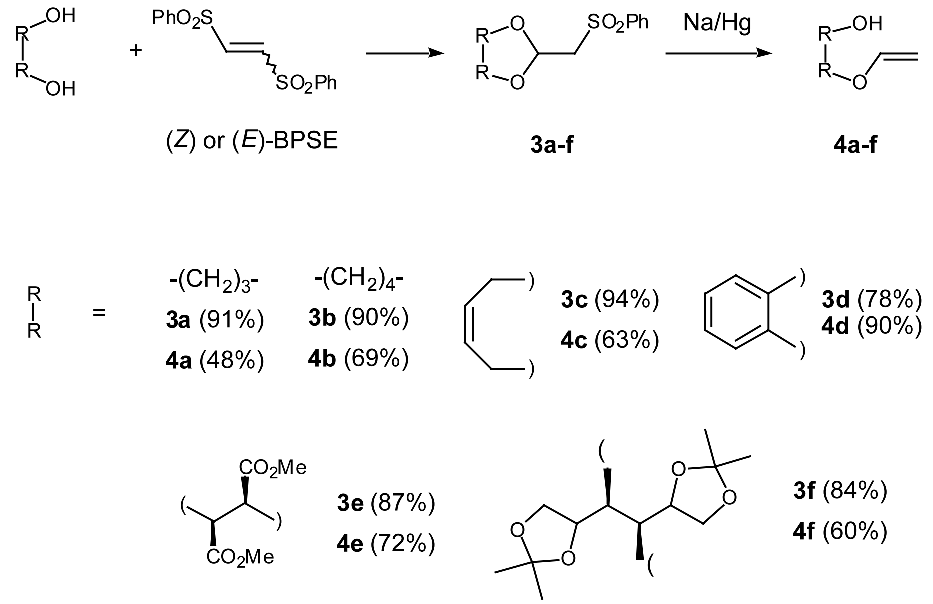
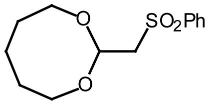
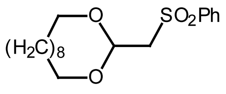


Scheme 2.

At the outset, the reduction of **3a**–**f** using 6% sodium amalgam was thought to proceed with formation of the ethylidene acetals **5** via a standard desulfonylation pathway (Scheme 3).

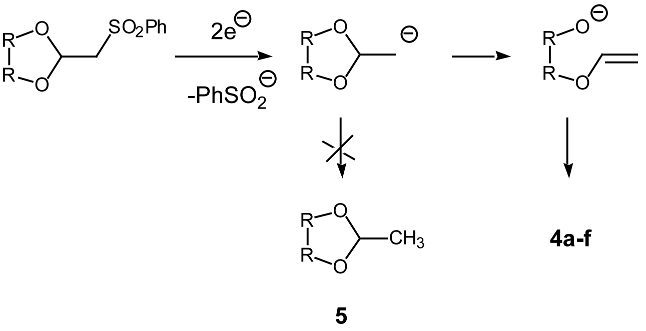


3g



3h

Contrary to such an expectation the sodium amalgam reduction selectively led in all cases to the corresponding hydroxyethenyl ethers **4a**–**f** in fair to good yields. No products of type **5** could be detected, thus confirming the selectivity of the reaction. The preferred formation of a hydroxyethenyl ether over that of the ethylidene acetal can be easily rationalised with the β-elimination of the carbanion with formation of the thermodynamically more stable alkoxide anion as can be observed in related instances (Scheme 3).[9] The basic reaction conditions maintained throughout the reaction sequence ensure survival of the otherwise delicate products while the clean sodium amalgam reduction and the work-up procedure allows for the isolation of the hydroxyethenyl ether with such purity grade that they do not require further purification.



Scheme 3.

In conclusion, the present methodology represents a broad general synthetic protocol for the preparation of hydroxyethenyl ethers. The method highlights the potentiality of BPSE as acetylene substitute in organic synthesis.[10] The high reactivity of BPSE associated with its crystallinity makes the reactions easy to be performed and the products highly versatile for the preparation of several classes of compounds which are otherwise not easily available by other means.

Typical procedure for the synthesis of β-phenylsulfonylacetals 3a–f from diols. A solution of the diol (0.32 mmol) in anhydrous THF (2 mL) was treated with NaH (2 equiv.) and a few crystals of Bu_4NBr as phase transfer agent, while stirring under argon at 0°C. After 30 min, BPSE (0.32 mmol) was added and the mixture was allowed to stir overnight, then quenched with water, extracted with EtOAc and dried over $MgSO_4$. After evaporation of the solvent, the residue was purified by silica gel column chromatography (petroleum ether/EtOAc). Yields reported in Scheme 2.

Typical procedure for the synthesis of hydroxyethenyl ethers 4a–f. To a solution of the acetal **3** in anhydrous MeOH (100 mg/5 mL), 6% sodium amalgam (8 g/0.44 mmol of compound) and solid phosphate buffer NaH_2PO_4 (4 g/0.44 mmol of compound) was added. The reaction mixture was monitored (TLC) at room temperature until complete consumption of the acetal, then filtered over Celite, washed with dichloromethane and extracted. The organic phase was washed with water (pH maintained neutral/basic), dried over K_2CO_3 and concentrated under vacuum to afford the hydroxyethenyl ether **4**. Yields reported in Scheme 2.

Acknowledgements

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