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Polysulfones: solid organic catalysts for the chemoselective cleavage of methyl-substituted allyl ethers under neutral conditions†

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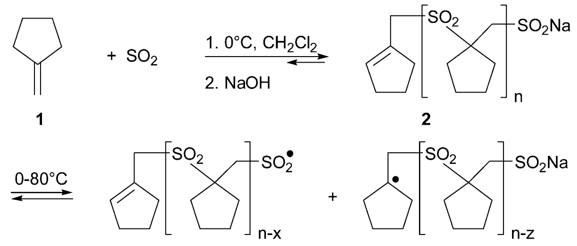
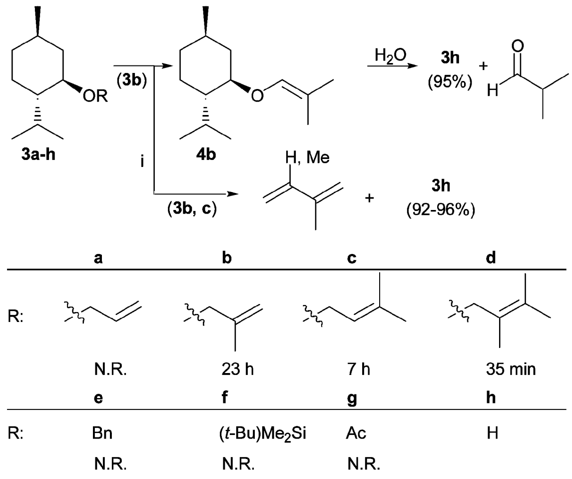
The solid polysulfone made of SO_2 and methylidenecyclopentane catalyzes the cleavage of methyl-substituted allyl ethers and liberates the corresponding alcohols.

Selective protection, deprotection and semi-protection of polyols is a central theme of organic synthesis.[1] We recently reported that methyl-substituted allyl ethers are readily cleaved in the presence of a catalytic amount of diphenyldisulfone. The fastest reactions occur with the most substituted allyl systems, whereas allyl, benzyl and silyl ethers, acetals and esters are not affected.[2] The reactive species involved is the benzenesulfonyl radical ($PhSO_2^{\bullet}$) engendered by thermal (80 °C) homolysis of $(PhSO_2)_2$.[3] We have also shown that solid polysulfones (1 : 1 copolymer of alkenes and SO_2) equilibrate with alkanesulfonyl radicals, which are capable of inducing the isomerization of 2-alkyl substituted alkenes *via* the generation of allyl radical intermediates.[4]



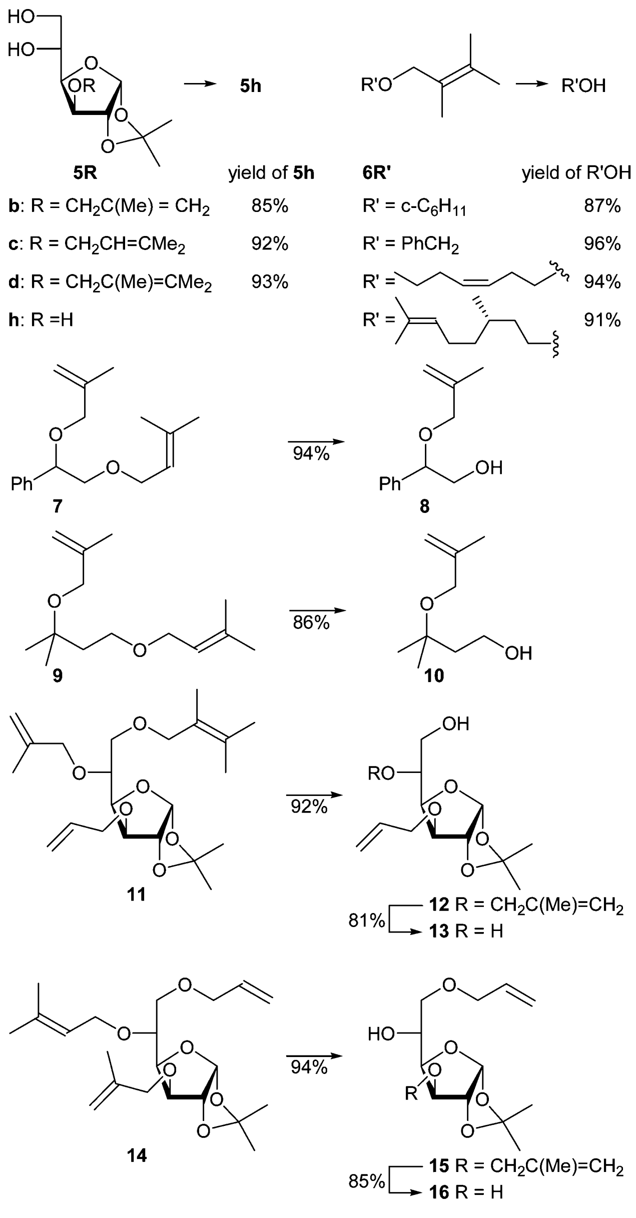
We have now evaluated the possibility of using these polymers instead of $(PhSO_2)_2$ as a source of sulfonyl radicals and have found that the solid polysulfone resulting from the combination of methylidenecyclopentane with SO_2 (**2**) is a better catalyst for the chemoselective cleavage of methyl-substituted allyl ethers than diphenyldisulfone.

Our initial studies used the polysulfone obtained by reaction of methylidenecyclopentane (**1**) in 1 : 5 SO_2/CH_2Cl_2 at 0 °C. The solid



Scheme 1 *Conditions*: 10% (weight) **2**, cyclohexane, 80 °C.

Table 1 Examples of polysulfone induced ether cleavages (in cyclohexane, 10% (weight) **2**, 80 °C)[a]



[a] For the preparations of **5R**, **6R′**, **11–16**, see ref. 2.

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† Electronic supplementary information (ESI) available: detailed procedures for the preparations and complete characterisations. See http://www.rsc.org/suppdata/cc/b4/b410965a/

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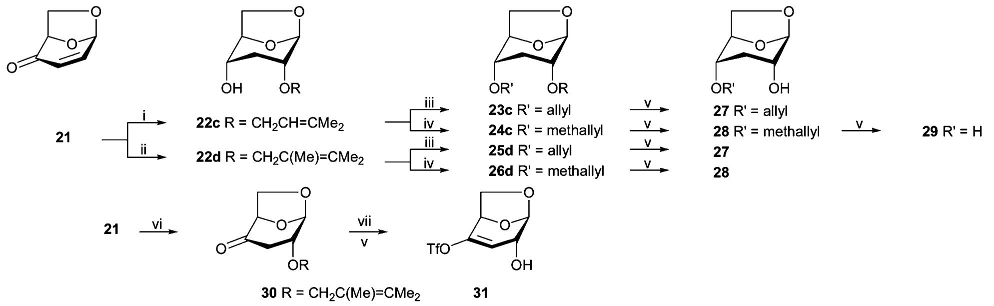
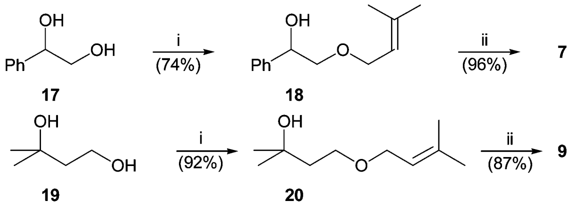


Scheme 3 *Conditions*: (i) prenol, Et_3N, 25 °C, then K-Selectride in THF, −78 °C; (ii) methylprenol, Et_3N, 25 °C, then K-Selectride in THF, −78 °C; (iii) allyl bromide, NaH/THF, 25 °C; (iv) methallyl bromide, NaH, THF, 25 °C; (v) 10% **2**, cyclohexane, 80 °C; (vi) 2,3-dimethylbut-2-en-1-ol, THF, −40 °C; (vii) $(Me_3Si)_2NLi$/HMPA/THF, −80 °C, then quenching with CF_3SO_2Cl, −78 °C, 85%.



Scheme 2 *Conditions*: (i) NaH/DMF, −40 to −10 °C, then prenyl bromide; (ii) NaH/DMF, then methallyl bromide, 20 °C; (iii) KH/THF, then methallyl bromide, 25 °C.

polymer thus obtained was neutralized by 0.1 M $NaOH/H_2O$ (neutralized polysulfone **2**, average molecular weight 200,000) and tested with menthol derivatives **3a–3g**.[2] The latter compounds remained unchanged on heating to 80 °C in CH_2Cl_2 (in a sealed tube) or cyclohexane for 24 h. In the presence of polysulfone **2** (10% weight with respect to **3**), allyl **3a**, benzyl **3e**, silyl ether **3f**, and acetate **3g** were not affected after heating to 80 °C for 24 h. In contrast, methylallyl ether **3b** was isomerized slowly into **4b** (^{1}H NMR) and menthol (**3h**) was recovered after slightly acidic aqueous work-up (Scheme 1). The co-product is isobutyraldehyde. With prenyl (**3c**) and 2-methylprenyl ether (**3d**), faster reactions were observed that liberated menthol (**3h**) together with isoprene and 2,3-dimethylbutadiene, respectively, without aqueous work-up. The reactivity sequence **3d** > **3c** > **3b** ≫ **3a** is the same as that observed for the reactions of these allyl ethers with $(PhSO_2)_2$.[2] The yield of recovered **3h** is better than 90% and no polymeric material is formed concurrently, which was not the case with the $(PhSO_2)_2$ induced cleavages. Thus, soluble $PhSO_2^\bullet$ has a greater tendency to add to alkenes and start polymerization processes than the solid sulfonyl radicals that equilibrate with polysulfone **2**. Polysulfones resulting from the copolymerization (0–30 °C) of SO_2 with methylidenecyclopropane, methylidenecyclobutane, 2-methylidenebicyclo[2.2.1]heptane and 1-methylcyclopentene were also found to catalyze the cleavage of ethers **3b**, **3c** and **3d**, but with lower rates than **2**. Possible mechanisms for the polysulfone-induced allyl ether cleavages are proposed to be the same as those for the $(PhSO_2)_2$ induced cleavages.[2] They also involve the formation of allyl radical intermediates from the methyl-substituted allyl ethers as evidenced by their efficient inhibition by TEMPO and Bu_3SnH. Illustrations of the usefulness of our protection/deprotection method are given in Table 1. In all cases, the liberated alcohols are isolated in high yields. The fact that prenyl (3-methylbut-2-en-1-yl) ethers are cleaved much faster than methallyl (2-methylallyl) ethers allows one to prepare semi-protected polyols in high yield. This is illustrated by the preparations of **8** and **10**, obtained by heating **7** and **9** with **2** at 80 °C in heptane, respectively. Diethers **7** and **9** were obtained readily according to Scheme 2.

A further illustration of the potential of our new protection/deprotection method is the conversion of isolevoglucosenone (**21**) into alcohols **27** and **28**, and into the hydroxyenol triflate **31** (Scheme 3). In the presence of Et_3N,[5] prenol and 2-methylprenol add to the *exo* face of enone **21** giving the corresponding β-allyloxy ketones that are reduced *in situ* with K-Selectride giving alcohols **22c** (75%) and **22d** (80%), respectively. These alcohols were protected as allyl ethers **23c** (85%) and **25d** (78%), respectively, under standard conditions. Similarly, methallyl ethers **24c** (68%) and **26d** (85%) were prepared. In the presence of 10% **2** (weight) heating of **23c** and **24c** in cyclohexane at 80 °C liberated alcohols **27** and **28**, respectively, in quantitative yield. Further heating of allyl ether **27** with **2** to 100 °C left this compound unchanged after 24 h. In contrast, further heating of methallyl ether **28** in the presence of **2** gave diol **29** (75%). Similarly, **25d** and **26d** were converted into **27** (75%) and **28** (78%), respectively.

This work demonstrates for the first time that polysulfones are solid catalysts for the cleavage of methyl substituted allyl ethers. They catalyze the isomerizations of methallyl ethers into the corresponding alkenyl ethers. They also catalyze the elimination of isoprene and 2,3-dimethylbutadiene from 3-methylbut-2-enyl ethers and 2,3-dimethylbut-2-en-1-yl ethers, respectively, whereas allyl ethers are not cleaved. This establishes a new method of selective polyol semi-protection in which the neutral, solid catalyst induces cleavage of ethers with the following reactivity sequence: 2-methylprenyl > prenyl > methallyl ≫ allyl. Acetals, esters, silyl ethers and benzyl ethers stay intact under these conditions as they do not require acidic or basic conditions or heavy metals. In several instances the liberated alcohols are obtained pure after solvent evaporation as the side-products are volatile (isobutyraldehyde, isoprene, 2,3-dimethylbutadiene).

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