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1,3-Rearrangement of Allylic Sulphones: Rearrangement-Cyclisation of Allylic 4-Pentenyl Sulphones

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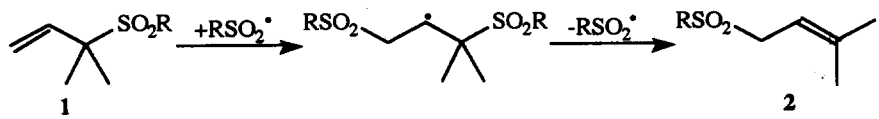
Abstract: Allylic alkyl sulphones CH_2:CHC(Me)$_2SO_2R$ (R=Me, Et, *i*Pr, *t*Bu, CH_2SiMe_3, $CH_2CH_2SiMe_3$, and $CH_2CH(OH)Me$ underwent 1,3–rearrangement on treatment with benzoyl peroxide in tBuOH. 1,3-Rearrangement did not occur in cases (R=CH_2Ph, CH_2COMe) where the intermediate sulphonyl radical $RSO_2^{\cdot}$ could undergo loss of sulphur dioxide to form a resonance-stabilised alkyl radical. Allylic 4-pentenyl sulphones undergo rearrangement with accompanying cyclisation of the intermediate radical, this process is more efficient if the allylic sulphone bears an electron withdrawing group at the β-position.

In earlier investigations[1] we reported that acyclic allylic *p*-tolyl sulphones such as **1** (R=*p*Tol) underwent 1,3-rearrangement upon treatment with benzoyl peroxide (BPO) in CCl_4, or with *p*TolSO_2Na in aqueous AcOH. The mechanism proposed for the rearrangement under both sets of conditions was a free radical chain involving, as propagating steps, sulphonyl radical addition to the double bond of the allylic sulphone followed by β-scission of the resulting β-sulphonyl alkyl radical (Scheme 1). Other workers[2] have also contributed to the understanding of such 1,3–rearrangements.



1 **2**

Scheme 1

We have recently extended our study of the scope of this 1,3-rearrangement reaction to include allylic alkyl sulphones **1** (R=alkyl). CCl_4 was unsatisfactory as a solvent for the BPO-induced rearrangement of sulphone **1** (R=Me) due to competing abstraction from the solvent and S_H2' substitution of the sulphone by the resulting $Cl_3C^{\cdot}$ radicals. However, the rearrangement proceeded satisfactorily upon treatment with BPO in *t*BuOH, or with $MeSO_2Na$ in aqueous AcOH. Sulphones **1** (R=Et, *i*Pr, *t*Bu, CH_2SiMe_3, $CH_2CH_2SiMe_3$, $CH_2CH(OH)Me$) also underwent rearrangement upon treatment with BPO in *t*BuOH (Table 1). The BPO-induced rearrangements were typically accomplished by heating a solution of the sulphone (concentration 0.1-1.0M) containing 0.2 equivalents BPO under reflux in *t*BuOH for 24-60h, with the prenyl sulphones **2** being isolated in 48-71% yield. Sulphone **1** (R=*t*Bu), however, rearranged only slowly under the standard conditions and an increased concentration of the substrate was required for the rearrangement to proceed effectively. This resistance to rearrangement of **1** (R=*t*Bu) was ascribed to competing loss of sulphur dioxide from the intermediate *t*Bu$SO_2^{\cdot}$ radical, evidence for which was the detection (by ^{1}H n.m.r. and GCMS) of **2** (R=Ph) as a minor by-product from the rearrangement of **1** (R=*t*Bu) in the presence of BPO.

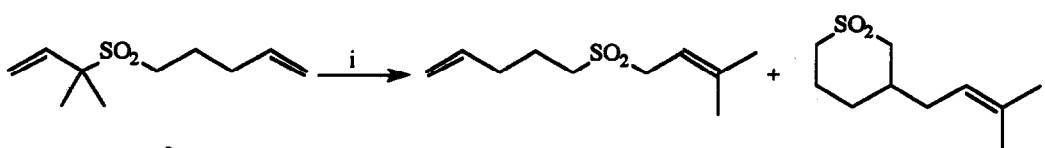
Rearrangement was unsuccessful in cases where the intermediate sulphonyl radical could undergo loss of sulphur dioxide to give a resonance-stabilised alkyl radical. Thus sulphones **1** (R=CH_2Ph, CH_2COMe) were recovered largely unchanged after treatment with BPO in *t*BuOH. The minor products from the attempted rearrangement reactions provided evidence for competing loss of sulphur dioxide from the intermediate $RSO_2^{\bullet}$ radical in these cases[3]. From the attempted rearrangement of sulphone **1** (R=CH_2Ph), the phenyl sulphone **2** (R=Ph), 1,2-diphenylethane, and 2-methyl-5-phenyl-2-pentene were detected as minor products, while from the attempted rearrangement of sulphone **1** (R=CH_2COMe), **2** (R=Ph) and 6-methyl-5-hepten-2-one were detected.

Table 1. BPO-Induced Rearrangement of Allylic Sulphones 1

Entry	R	Concentration of **1** / M	Reaction Time / h	Yield of **2** / %
1	Me	0.1	24	55
2	Et	0.1	60	62
3	*i*Pr	0.1	48	48
4	*t*Bu	5	48	63
5	CH_2SiMe_3	0.1	48	58
6	$CH_2CH_2SiMe_3$	1	48	71
7	$CH_2CH(OH)Me$	1	48	56

We considered that allylic 4-pentenyl sulphones were potentially interesting substrates in the 1,3-rearrangement reaction, since cyclisation of the intermediate 4-pentenesulphonyl radical might occur, leading to cyclic products. Few reports of cyclisation reactions involving 4-pentenesulphonyl radicals have appeared in the literature, but in the cases reported,[4] 6-membered ring cyclic sulphones, formed *via* 6-*endo* cyclisation, predominate. In contrast, cyclisation of the corresponding carbon-centred (5-hexenyl) radicals, occurs with high selectivity in favour of the 5-*exo* mode,[5] and the reaction has been widely applied in synthesis.

When sulphone **3** was subjected to the BPO / *t*BuOH conditions, the compound was found to be surprisingly resistant to rearrangement, with the reaction proceeding much less readily than the 1,3-rearrangement of substrates, such as **1** (R=Me, Et), in which the alkyl group of the allylic sulphone is saturated. Thus, a 1M solution of sulphone **3** heated for 24h with 0.2 equivalents of BPO gave, after chromatography, recovered **3** (23% yield), the acyclic 1,3-rearranged sulphone **4** (8% yield) and the cyclic sulphone **5** (14% yield).

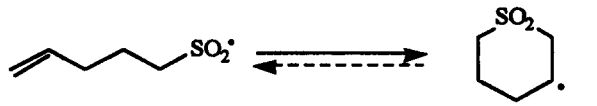


3 **4** **5**

Reagents and conditions: i. 0.2eq. BPO, *t*BuOH, Δ, 24h.

Scheme 2

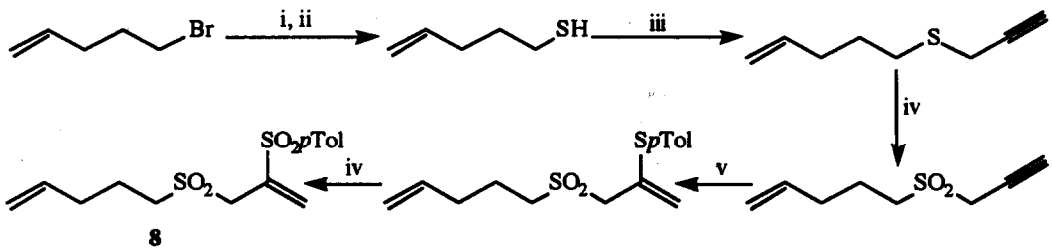
The behaviour of sulphone **3** under the rearrangement conditions can be rationalised by considering the nature of the cyclised and uncyclised radicals. The uncyclised radical **6** is an electrophilic sulphonyl radical which can be expected to add rapidly to the relatively electron rich βγ double bond of the allylic sulphone **3**. The cyclised radical **7**, however, is a nucleophilic alkyl radical, expected to add only slowly to the βγ double bond of sulphone **3**. The cyclisation process shown in Scheme 3 therefore results in the transformation of sulphonyl radical **6**, which can carry the radical chain efficiently, to nucleophilic radical **7**, which carries the chain inefficiently. The slow rate of the rearrangement and observed product ratio are consistent with the cyclisation of radical being rapid compared to the rate of addition to the allylic sulphone **3**, with the equilibrium in favour of the cyclic form **7**.



6 electrophilic radical — **7** nucleophilic radical

Scheme 3

On the basis of the above rationalisation, we predicted that the formation of the cyclic sulphone should be favoured by incorporating an electron withdrawing group at the β-position of the allylic sulphone, in order to increase the efficiency of capture of the nucleophilic radical **7**[6]. We therefore prepared the bis-sulphone **8** using the route shown in Scheme 4[7].



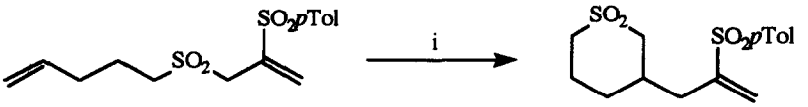
8

Reagents and conditions: i. Thiourea, EtOH, Δ; ii. NaOH, aq. EtOH, room temp.; iii. NaOMe, MeOH, then $HC{\equiv}CCH_2Cl$, room temp.; iv. OXONE, aq. MeOH, room temp.; v. *p*TolSH, Et_3N (cat.), PhH, room temp.

Scheme 4

As predicted, the rearrangement of sulphone **8** to give the cyclic sulphone **9** proceeded much more readily than the corresponding rearrangement of sulphone **3**. Thus, a 0.1M solution of sulphone **8** heated for 24h with 0.1 equivalents of BPO gave, after chromatography, 25% yield of recovered **8**, together with 45% yield of the cyclic sulphone **9** (60% based on consumed starting material). Repeating the experiment with 0.2 equivalents of BPO resulted in complete consumption of the starting material, but only 37% yield of sulphone **9** was obtained. A possible problem is the sulphone **9** contains an electron deficient double bond and may compete with **8** for the cyclic radical **7**, so that consumption of the product may compete with its formation when conversion of the starting material is near completion. However, the reasonable efficiency of the rearrangement of sulphone **8**

suggests that it may be possible to apply sulphonyl radical cyclisation successfully in synthesis, provided the electronic nature of the radicals involved is taken into account.



8 **9**

Reagents and conditions: i. 0.1eq. BPO, *t*BuOH, Δ, 8h.

Scheme 5

The results described above confirm that the free radical 1,3-rearrangement reaction can be extended to allylic alkyl sulphones, and are consistent with the S_H2' mechanism proposed for this reaction.

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