



Should anionised benzylic sulfones be considered as carbenoids?[†]

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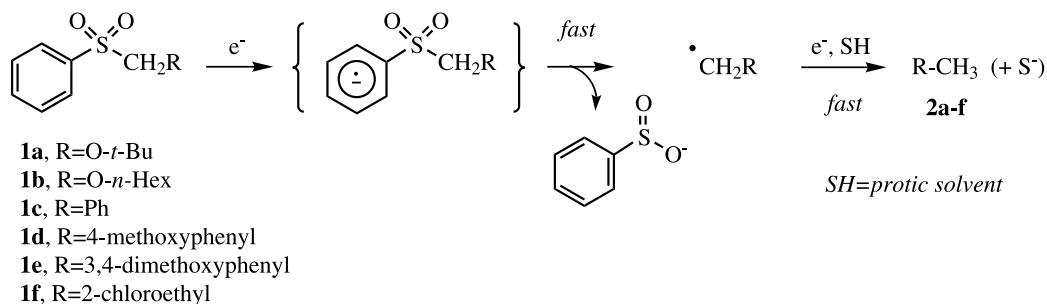
Abstract—Na·Hg reduction of benzyl sulfones **1c–e** in aprotic solvent conditions affords stilbenes **4c–e**, an olefination process best explained by assuming that the corresponding sulfone carbanion, which was formed under these conditions, is decomposed into a carbene species. © 2002 Published by Elsevier Science Ltd.

The reduction of alkyl arylsulfones to form an arylsulfinate and the corresponding hydrocarbon is an essential step of many applications of these compounds in organic synthesis.¹ Most frequently, this is realised by using sodium amalgam (Na·Hg) in a lower alcohol,² but comparable yields and selectivity are achieved by electrolysing these sulfones at a mercury electrode in either methanol^{3a} or moist DMF^{3b} and a mechanism for both processes has been presented (Scheme 1).^{3a}

In the first step, an electron is transferred to the substrate to form a radical anion, which dissociates into a radical and an arylsulfinate. Since this first electron intake occurs at a relatively low potential (ca. –2 V versus SCE), this free radical should immediately be reduced.⁴ Indeed a single two-electron wave is usually observed by sulfone polarography and it is accordingly assumed that these cathodic reductions and, by extension, the Na·Hg-promoted sulfone hydrogenolyses proceed as indicated by the kinetically-limiting formation

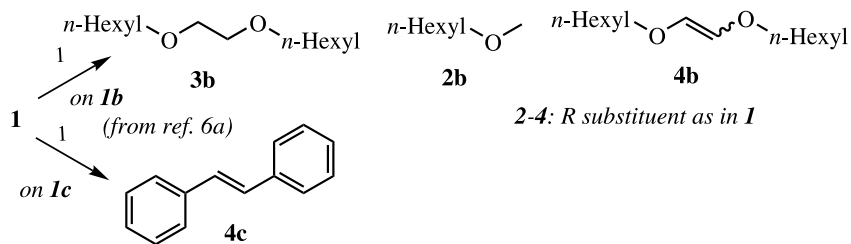
of a radical whose ensuing reduction and protonation affords the observed hydrocarbon.

Recent electrochemistry experiments largely confirm this view.⁵ Of special interest in this study is the observation of two distinct one-electron waves for the cathodic reduction of the sulfone **1a** in steady-state voltammetry: since the *t*-butoxymethyl radical which, according to the above E-C-E mechanism, should form in this case is strongly *nucleophilic*, its reduction into the corresponding carbanion proceeds at a more negative potential as compared with unsubstituted alkyl radicals. Consequently, by operating at a higher (i.e. less negative) potential, the rate at which this radical is converted into the corresponding anion is slowed down and other fates as inter alia dimerisation compete. Likewise, treating the sulfone **1b** with Na·Hg in benzene mainly affords a mixture of the bis-ether of ethyleneglycol **3b** and *n*-hexyl methylether **2b** (Scheme



Scheme 1.

* Corresponding author. E-mail: uguen@chimie.u-strasbg.fr[†] This letter is dedicated to Pr. Marc Julia on the occasion of his 80th birthday as a mark of deep respect and acknowledgement for his guidance.



Scheme 2. Reagents and conditions: 1–6% Na·Hg (2 g/mmol), THF; reflux, 3 days.

2).⁶ Noteworthy, trace amounts (4%) of 1,2-bis-*n*-hexyloxyethylene **4b** were also detected.

While investigating the mechanism of these reductions, one of us made the intriguing discovery that treatment of the benzyl sulfone **1c** with 6% Na·Hg in refluxing THF did not give the expected dimer, i.e. diphenylethane **3c**, but instead stilbene **4c**; toluene (i.e. **2c**), the only identified product by using methanol as a solvent, was detected but not quantified.^{6a}

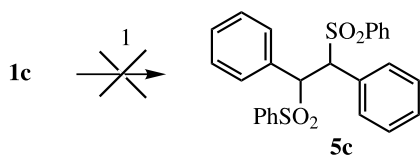
In order to shed some light on this puzzling result and, subsidiarily, to evaluate the potential of this olefination process for preparing more elaborate stilbene derivatives,⁷ these aprotic reduction conditions have been applied to the parent sulfones **1d** and **1e** and the main purpose of this letter is to comment on the results of this study in light of both the above mechanistic considerations and relevant literature.

After having validated the preceding result by treating **1c** with freshly-prepared 6% Na·Hg in refluxing THF for 5 days, great care was exercised to exclude air, the methoxybenzyl sulfones **1d** and **1e** were submitted to these conditions to give similarly **4d** and **4e** and the corresponding toluene derivatives **2d** and **2e**, respectively (Table 1; for the sake of comparison, the result obtained with **1b**, vide supra, is included). In each case, the balance in engaged material was on the whole provided by the unreacted sulfone and no other product could be characterised.⁸

Table 1. Reduction of sulfones **1b–e** by Na·Hg under aprotic solvent conditions^a

Substrate	Solvent	Products (% yield)
1b	Benzene	3b (80), 2b (12), 4b (4)
1c	THF	4c (19), 2c (not determined), 1c (54)
1d	THF	4d (17), 2d (34), 1d (41)
1e	THF	4e (13), 2e (29), 1e (49)

^a All reactions run at 80°C (bath) for 5 days under an argon atmosphere.



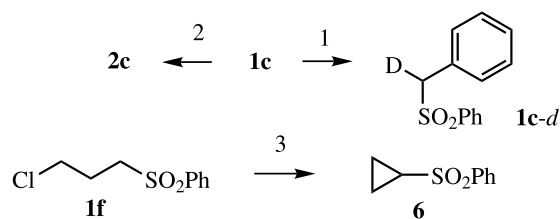
Scheme 3. Reagents and conditions: 1-*t*-Butylperoxide (1 equiv.), benzene; reflux, 16 h.

Since the formation of free radicals in related reduction conditions has been substantiated,^{6b} a possibility was that the initially-produced benzylic radical had time to diffuse out of the reducing area, then to abstract a hydrogen atom from the unreacted sulfone: dimerisation of the resulting α -sulfonyl radical and Na·Hg reduction of the resulting bis-sulfone **5c** would have produced **4c**. Such a free radical pathway seems difficult to conciliate with the result obtained with **1b** however. Removal of a hydrogen atom from this alkoxymethylsulfone should not be disfavoured and it is thus difficult to explain why only a trace of the ethylene derivative **4b** is formed in this case. Such a free-radical pathway was definitively ruled out by treating **1c** by *t*-butylperoxide in refluxing benzene: the bis-sulfone **5c** was not obtained (Scheme 3).

Another conjecture was that due to their lower nucleophilicity as compared with alkoxymethyl radicals, the formed benzylic radicals were instead reduced, the organometal species thus formed being then protonated by the starting sulfone to give the observed toluene derivative. In the event, the contrasting reactivity of sulfones **1c–e** as compared with **1b** (res **1a**) would have originated from some unusual fate of the resulting sulfone anions. Evidence for anionisation of the used sulfone in these ‘aprotic’ reductions was gathered as follows.

Treatment of **1c** by radical-anions derived from aromatic hydrocarbons and either sodium or lithium in THF has previously been shown to afford the corresponding benzylmetal, characterised by trapping experiments with added electrophilic species.^{6a,9}

Demonstration of in situ anionisation of the substrate was acquired by using the related trimesitylborane–lithium reagent (TMBLi), selected for its perfect stability in protic solvent conditions.¹⁰ Hence, whereas addition of a mixture of **1c** and *t*-BuOH to a solution of TMBLi in glyme afforded toluene in high yield (83%, as estimated by GLC) and complete disappearance of the used sulfone, mixing **1c** with this reagent in the same solvent and quenching the reaction mixture with D₂O after 1 h resulted only in partial reduction to furnish toluene, besides labelled **1c** (i.e. **1c–d**) (Scheme 4). Additionally, and independently, treating the chlorosulfone **1f** with Na·Hg in benzene as above gave the cyclopropane sulfone **6** in an interesting 53% yield (based on converted material), alongside 1,6-dichlorohexane **3f** (13%) and chloropropane **2f** (17%). Since in



Scheme 4. Reagents and conditions: (1) TMBLi (2 equiv.), glyme; -78°C , 1 h, then D_2O (52%); (2) addition of **1c** and *t*-BuOH (1 equiv.) to a solution of TMBLi (2 equiv.) in glyme; -78°C , 1 h, then H_2O (83%); (3) 6% Na-Hg (1 g/mmol), benzene; reflux, 6 h (53% isolated yield at ca. 49% conversion).

Table 2. Thermal decomposition of lithiated benzylic sulfones^a

Substrate	Solvent	Stilbene (% yield)
1d	THF	4d (26)
1d	THF	4d (24) ^b
1d	Benzene	4d (29)
1d	THF/HMPT ^c	4d (8)
1e	THF	4e (18)
1e	THF/HMPT ^c	4e (4)

^a All reactions run at 80°C (bath) for 5 days.

^b Trace of air introduced; *p*-anisaldehyde detected as a side product.

^c 3 Equiv.

the latter case any formed free radical would not be more easily reduced than a benzylic radical, it can safely be concluded that, whatever the associated cation (Li or Na), anionisation of benzylic sulfones may occur in the preceding reduction conditions.¹¹

A few decompositions of sulfone anions with formation of a new carbon–carbon double bond have already been reported. Hence, treatment of **1c** by KOH under harsh conditions (200°C) produces stilbene **4c**,^{12a} a similar result being obtained by keeping at room temperature for several days a THF solution of its lithio derivative, i.e. **1c-Li**.^{12b} A related process has also been observed with an alkyl arylsulfone.^{12c} Moreover, the lithio derivative of sulfone **1a** was shown to afford the bis-enolether **4a** in high yield on standing at room temperature.^{12d}

Earlier investigations led to consideration of oxygen as essential for these reactions to occur,^{12c} added tellurium or sulfur proving also beneficial.^{12b} Later, the **1c-Li** species was claimed as being thermally stable in the dark, but to decompose into stilbene **4c** on exposure to UV light or by treatment with nickel salts.^{12e,f}

The stability of anionised benzyl sulfones was re-examined. To this end, the lithio derivatives of **1d** and **1e** were classically prepared in THF using butyllithium then heated at 80°C for 5 days under various solvent conditions and under strictly oxygen-free conditions (Table 2).

In each case, a stilbene slowly formed. Though it is difficult to certify that no trace oxygen (or nickel) was present, this element seems to play no other role than to induce the known^{12f} oxidation of a sulfone anion into the corresponding aldehyde, indeed observed by admitting air with a syringe (entry 2).

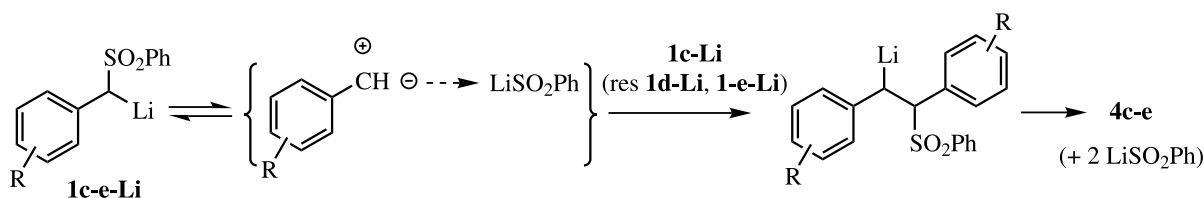
More surprisingly, the rate of this olefination process proved dependent on the basicity of the solvent used, the more dramatic change being observed with added HMPT (entries 4 and 6), another striking result being the slightly, but significantly, higher stability of **1e-Li** as compared to **1d-Li**.

Formation of symmetrical olefins in the decomposition of carbanions stabilised by electronegative heteroelements is well documented and considered as indicative of either a carbenoid or a carbene species.¹³ Anionised sulfones are known to react with various carbenoid species, with elimination of a sulfinate ion, to give an olefinic product.^{12d,14} Since an arylsulfonyl residue can act as a leaving group, the question as to whether the formation of a stilbene by anionisation of the sulfones **1c–e** is due to a carbenoid feature of their sodio (res lithio) derivative is warranted.

A carbenoid *behaviour* has been suggested for the lithio derivative of the alkoxy sulfone **1a** which, indeed, can be condensed with various nucleophilic species, especially lithiosulfones, to afford *t*-butylvinylethers;^{12d} thus explaining the side formation of **4b** in the reduction of **1b** in aprotic conditions (vide supra). However, crystal structures of both benzyl phenylsulfone **1c** and its lithio derivative **1c-Li** have been determined¹⁵ and it is evident that the bond between the benzylic carbon and the sulfur atom is reinforced upon anionisation; a result of the stabilising effect of the sulfonyl group. Accordingly, **1c-Li** should by no means be considered as a carbenoid.¹⁶

As previously suggested by Eisch,^{12e} a more satisfactory picture is that carbenes, and not carbenoids, are involved in these homo-coupling processes. Failure to observe a cyclopropane derivative by treating **1c-Li** with excess cyclohexene has been considered as evidence against the formation of phenylcarbene.^{12b} However, should an α -elimination process be operating, disruption of the carbon–sulfur bond will necessarily be highly endoergic and thus the corresponding transition state will appreciably share a carbene character. Accordingly, this reaction should proceed very slowly, as observed. Moreover, since carbenes are stabilised by added salts,^{13a} solvation by the outcoming lithium sulfinate, as indicated (Scheme 5), would be kinetically beneficial, which possibly explains the detrimental effect of HMPT (Table 2). In the same mood, cyclopropanation of cyclohexene by any solvated carbene species should be preceded by a demanding desolvation, not required for its condensation with **1c-Li** to occur: stilbene **4c** should be the main product, as observed.^{12b,17}

In summary, the electron (base)-induced rearrangement of benzylic sulfones presented in this letter could by no



Scheme 5. Suggested mechanism for the **1c-e**–**4c-e** conversion.

means be considered as a possible alternative to existing methods for preparing stilbenes unless, as demonstrated by Eisch,^{12e} a short UV irradiation or added nickel salts would be used. A few interesting points emerge from this study however. Oxygen appears to play no other role in these reactions than to induce the formation of an aldehyde. Further, unlike alkoxymethylsulfones, the treatment of which by Na·Hg in aprotic medium generates almost exclusively free radicals, the reduction of benzylic sulfones under the same conditions affords successively a benzyl anion, a sulfone anion, then a stilbene: an olefination process best explained by assuming that the formed sulfone carbanion slowly decomposes into, and couples with a carbene. Efforts are now being made to support more firmly this view by trapping experiments.

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- The rate constant for the reduction of a primary alkyl radical by sodium/naphthalene in THF has been estimated to $1.6 \times 10^9 \text{ mol}^{-1} \text{ s}^{-1}$ (Barton, J. F.; Garst, F. E. *J. Am. Chem. Soc.* **1974**, *96*, 523–529).
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- Protocol for the Na·Hg reduction of sulfones in aprotic medium*: Finely ground, freshly prepared 6% Na·Hg (4.2 g) and sulfone **1d** (0.64 g; 2.4 mmol) were placed in a flask equipped with a condenser connected to an argon/vacuum line. The flask was evacuated to 10^{-3} Torr and then filled with argon. THF (15 ml) was added with a syringe and the resulting suspension was perfectly degassed (three ‘freeze and thaw’ cycles), then brought to reflux for 5 days with magnetic stirring. After cooling, ether (50 ml) was added and the resulting mixture was filtered on paper. The clear filtrate thus obtained was washed with brine (3×25 ml), dried (K_2CO_3), then evaporated to give a pasty solid (0.3 g). Chromatography of this residue on silica gel ($\text{CH}_2\text{Cl}_2/\text{hexane}$) afforded successively anisol **3d** (102 mg; 34%), the stilbene **4d** (50 mg; 17%), and finally unreacted **1d** (41%). Selected data: **4d**: Mp 121°C; ^{13}C NMR: 55.41, 114.19, 126.27, 127.5, 130.57, 159.09.
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11. The transient formation of strongly basic species by electrochemical reduction of sulfones has been substantiated (Mabon, G.; Chaoui El Badre, M.; Simonet, J. *Bull. Soc. Chim. Fr.* **1992**, 129, 9–15).
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15. Boche, G.; Marsch, M.; Harms, K.; Sheldrick, G. M. *Angew. Chem., Int. Ed. Engl.* **1985**, 24, 573–575.
16. Though vinylogous with **1a**, probably the same applies to anions of the sulfones **1d** and **1e**. That the lithio derivative of **1a** or related alkoxyethylsulfones are *true* carbenoids is highly questionable anyway: the pK_a of the parent methoxymethyl phenylsulfone is in the same range as those of related alkyl phenylsulfones (**1a** is considerably more acidic than *t*-butyl methylether) and the anion derived from this alkoxyethylsulfone should, accordingly, be structurally related to any sulfone anion, with extensive delocalisation of the negative charge onto the sulfur atom.
17. A similar result is obtained by decomposing the lithio derivative of benzyl chloride in the presence of cyclohexene (Ref. 13b, chapter V). It is interesting to note that the thermal decomposition of the lithio derivative of benzaldehyde tosylhydrazone (Kabalka, G. W.; Wu, Z.; Ju, Y. *Tetrahedron Lett.* **2001**, 42, 4759–4760) has been shown to afford, besides stilbene, trace amounts of benzyl *p*-tolylsulfone; a side condensation (i.e. coupling of phenylcarbene with lithium *p*-toluenesulfinate) which is precisely the reverse of the decomposition being advocated.