

Highly efficient, catalytic bis addition reactions of allyl phenyl sulfone to vinyl sulfones[☆]

Greg A. N. Felton and Nathan L. Bauld*

Department of Chemistry and Biochemistry, The University of Texas, Austin, TX 78712, USA

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Abstract—Highly efficient, electrocatalytic additions of allyl phenyl sulfone to a variety of vinyl sulfones have been accomplished. The additions are catalyzed by electrogenerated bases derived from the reactant itself, and furnish 90–94% yields of highly polar molecules in which 1 mol of allyl phenyl sulfone has added consecutively, selectively, and in a linear addition mode to 2 mol of the vinyl sulfone. Essentially no products are observed which incorporate other than 2 mol of the vinyl sulfone. An addition to a difunctional alkene, divinylsulfone, yields a novel cyclization product, albeit in more moderate yield (41%). The use of tetraalkylammonium salts, as opposed to lithium salts, as electrolytes has been found to provide electrogenerated bases of especially high reactivity.

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1. Introduction

The buildup of basicity around the cathode during an electrolytic reduction has long been known.¹ A prominent example of this phenomenon is the production of sodium hydroxide by electrolysis of water.² However, the application of this concept for the purpose of organic synthesis did not begin until the late 1960's. Since that time, a modest variety of applications of electrogenerated bases (EGB's) to organic synthesis have been reported.¹ The typical approach has been to provide (usually in stoichiometric amount) an additive (called a pro-base), which serves as a precursor to the active base. In the context of another investigation, the present authors have noted that bases generated at vitreous carbon cathodes in the electrolysis of certain substrates in acetonitrile solution containing quaternary ammonium salts (as opposed to lithium salts) as electrolytes possess an especially high level of reactivity. The present work reports the exploitation of this electrochemical system and the corresponding reactive EGB's to effect exceptionally efficient and highly electrocata-

lytic additions of allyl phenyl sulfone (via its conjugate base) to a variety of vinyl sulfones.

A novel aspect of these reactions is that, in contrast to most of the earlier applications of EGB's to organic synthesis, one of the reactants (allyl phenyl sulfone) also serves as the pro-base in the presently reported chemistry, so that no foreign pro-base need be added. Another especially novel aspect of these reactions is that they furnish high (90–94%) yields of highly polar molecules in which 1 mol of allyl phenyl sulfone has added consecutively, selectively, and in a linear addition mode to 2 mol of the vinyl sulfone. Essentially no products are observed, which incorporate other than 2 mol of the vinyl sulfone. Finally, an addition to a difunctional alkene, divinylsulfone, yields a novel cyclization product, albeit in more moderate yield (41%).

2. Dimerization of allyl phenyl sulfone

In the initial phase of this research, the reactivity of the EGB formed under our electrochemical conditions and the efficiency of base-catalyzed Michael-type additions under such conditions, was demonstrated in a study of the self-addition of allyl phenyl sulfone (**1a**). This reaction was found to afford the dimer **2a** in 81% yield, with a catalytic factor of at least 11.3³ (equivalent to a

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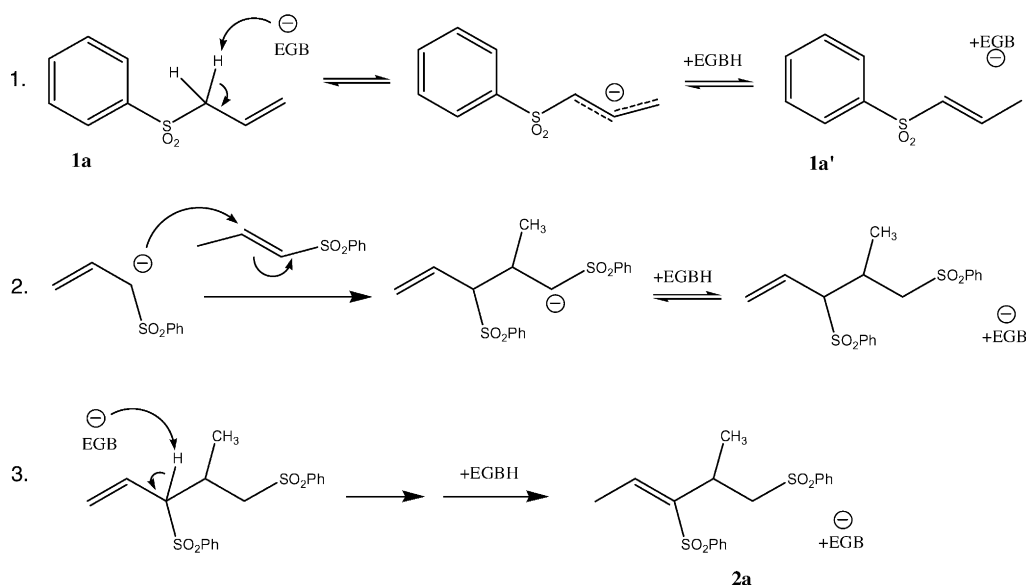
* Corresponding author. Tel.: +1-512-471-3017; fax: +1-512-471-8696; e-mail addresses: greg_felton@hotmail.com; bauld@mail.utexas.edu

0.087 F mol⁻¹ process). This same dimer has been reported in the literature in one other instance, as a product of a cathodic reduction of the isomeric molecule phenyl *trans*-propenyl sulfone, a substrate which would furnish the same conjugate base as allyl phenyl sulfone.⁴ In that study, the yield of **2a** obtained was only 56% (catalytic factor of at least 10). Further, an anion radical mechanism was proposed for the formation of **2a**, which we consider inconsistent with typical anion radical behavior. Rather, the base-catalyzed Michael-type addition illustrated in Scheme 1 is presently proposed.

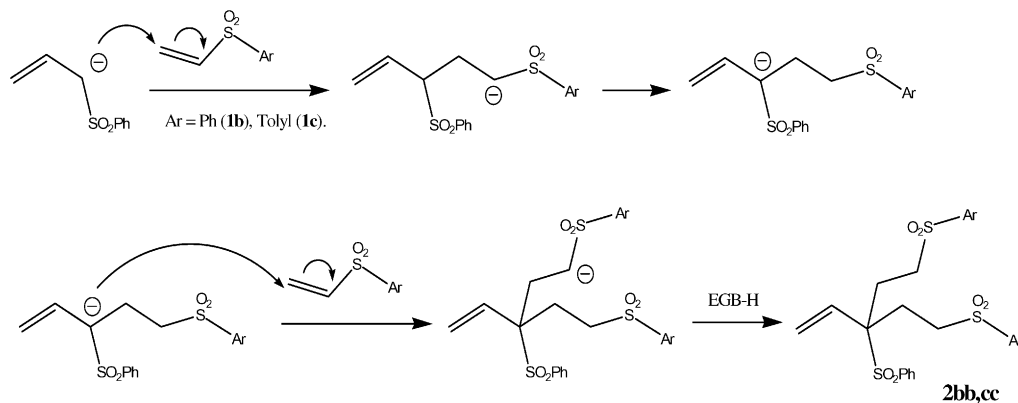
The mechanism of generation of the EGB is by no means certain, but appears to involve the initial reduction of **1a** to the corresponding anion radical. It is possible that this anion radical is itself the EGB, which initiates the deprotonation of **1a**. Alternatively, the anion radical may deprotonate adventitious water,⁵ yielding hydroxide ion as the EGB. Interestingly, the structure of the dimeric product reveals that the conjugate base adds not to the unactivated double bond of **1a**, but to the activated, electron deficient double bond of its position isomer, phenyl propenyl sulfone (**1a'**), which would be produced by a rapid, base-catalyzed equilibration of **1a** and **1a'** (step 1 of Scheme 1). The latter isomer has in fact been detected (NMR) in these reacting solutions. The addition of the conjugate base of **1a/1a'** to the β position of **1a'** yields a dimer carbanion, which is subsequently protonated either by **1a**, to yield more conjugate base, or by the conjugate acid of the EGB, to regenerate the EGB. It is noted that the protonation of the dimer carbanion by **1a** should be exergonic, since the latter carbanion has a greater degree of delocalization. Finally, the double bond of the initially produced dimer undergoes base-catalyzed position isomerization (step 3 of Scheme 1). It is of interest that subsection of **1a** to typical base catalysis conditions yields no detectable amount of dimer **2b**, but rather produces various oligomers and condensation products.⁶

3. Additions of allyl phenyl sulfone to electron deficient substrates

In view of the observation that the conjugate base of **1a** undergoes efficient conjugate addition to phenyl propenyl sulfone, it appeared likely that cross additions to vinyl sulfones, might be even more efficient. Such vinyl sulfones would not be susceptible to deprotonation, so that they could not fulfill the carbanion role but could serve as ideal Michael acceptors. However, a plausible possibility was that additions of the conjugate base of **1a** to these receptors might generate a mixture of dimers, trimers, oligomers, and even higher polymers. The addition reactions of **1a** with phenyl and tolyl vinyl sulfone (substrates **1b** and **1c**) under our conditions somewhat surprisingly lead to quite high yields of single compounds, which are not dimers, but trimers, in which the conjugate base of **1a** has added to two and only two molecules of the receptor. Further, even when a 2.06:1 ratio of receptor to **1a** is used, the 'trimers' are generated cleanly and in high yield, unaccompanied by any of the dimer of **1a**. The proposed general mechanism for the formation of these linear trimers is given in Scheme 2. Preferential addition of the conjugate base of **1a** to the vinyl sulfone component as opposed to the propenyl sulfone is expected based not only upon steric effects, which are minimal in the case of the vinyl sulfone, but also because of the concentration of **1a'** never rises to a very high level in these solutions (presumably <2% of the mixture of **1a** and **1a'**). The addition of the dimer carbanion to another mole of the vinyl sulfone then follows rapidly and equally selectively, leading to a trimer carbanion. Interestingly, these reactions do not form significant amounts of tetramers, oligomers or polymers, so that there is no apparent tendency of this latter carbanion to add to any further molecules of the vinyl sulfone. It appears reasonable to propose that the pronounced difference in nucleophilic reactivity between the trimer carbanion and the dimer carbanion is the



Scheme 1. Mechanism of electrogenerated base-catalyzed dimerization of allyl phenyl sulfone.



Scheme 2. Proposed mechanism of the linear cross addition of allyl phenyl sulfone with 2 mol of a vinyl sulfone.

Table 1. Yields and catalytic factors for the dimerization of allyl phenyl sulfone, and the cross addition of this sulfone, to several electron deficient alkenes

| Substrate | Product | Yield (%) | Catalytic factor ^a |
|-----------------------------------|--|-------------------|-------------------------------|
| No additional substrate | 2b : Dimer 1a' : Propenyl vinyl sulfone | 81.3 2.1 | 11.3 |
| 1b : Phenyl vinyl sulfone | 2bb : Trimer | 90.8 | 12.7 |
| 1c : Tolylyl vinyl sulfone | 2cc : Trimer | 94.5 | 7.4 |
| 1d : Divinyl sulfone | 2d : Cyclic dimer | 41.0 ^b | 6.3 ^b |

^a Catalytic factor based upon total charge used and moles of limiting reagent **1a**.

^b Corrected for 21.1% of **1a** that was recovered.

result of increased steric hindrance at the carbanion site of the trimer (Table 1).

4. Carbanion-mediated versus anion radical mediated reaction mechanisms

The isomerization of allyl phenyl sulfone to phenyl propenyl sulfone is required by the structure of the dimeric product obtained from the former sulfone. It appears logical, and even essential, to propose a base-catalyzed mechanism for this isomerization, which would require the intermediacy of the common conjugate base of both sulfones. Since this conjugate base is obviously present in the reaction medium, and since the Michael addition of this base/nucleophile to electron deficient double bonds is highly precedented, it appears likely that **2a** is formed via an exclusively carbanion-mediated process. Incidentally, the final double bond isomerization also would appear to require a base-catalyzed process. The formation of the specific trimers observed in the cross additions⁷ also appears to be rather uniquely consistent with a carbanion mechanism. Further, the highly catalytic nature of these reactions is consistent with electrogenerated base-catalyzed chemistry. Such high catalytic factors have not been observed in the case of anion radical chemistry.^{7,8} Still another relevant observation is that the anion radical of phenyl vinyl sulfone undergoes a rapid cyclobutadimerization

reaction.⁹ No such product is observed in the case of the cross addition of **1a** to phenyl vinyl sulfone.¹⁰ Finally, the absence of anion radical pathways is further indicated by the observation that when the electrolyte is changed to lithium perchlorate, the dimerization of **1a** does not proceed. No reaction is observed, even after the passage of several F mol⁻¹, yet this electrolyte is known to favor anion radical promoted cyclizations,⁷ whilst allowing at best limited base reactivity.¹¹

5. A novel cyclization

The reaction of **1a** with **1d** gives a rather unexpected and novel product, the eight-membered ring product **2d** (Fig. 1). The yield of this product (41%) is more modest than those observed in the previously described linear dimerizations and trimerizations, but the coupling of the conjugate base of allyl phenyl sulfone once at the position α to the phenylsulfonyl group and then again γ to it, to yield an eight-membered ring is rather novel. As in the previously described reactions, coupling undoubtedly occurs first at the α position, followed rapidly by intramolecular addition from the γ position (Scheme 3). Presumably, the preference for reaction at the γ position to give a cyclooctene derivative over addition from the α position, to give an eight-membered ring product derives from the circumstance that the α carbon is now tertiary, and much more highly hindered than the γ carbon, which is primary.

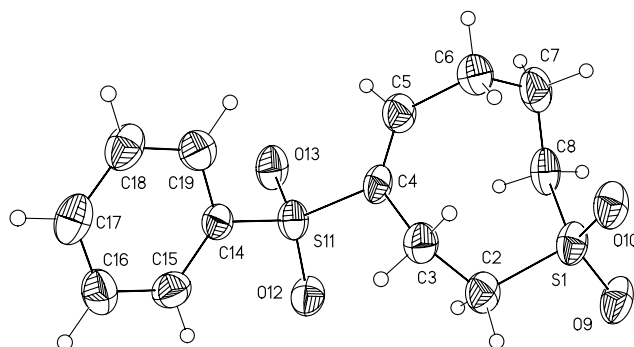
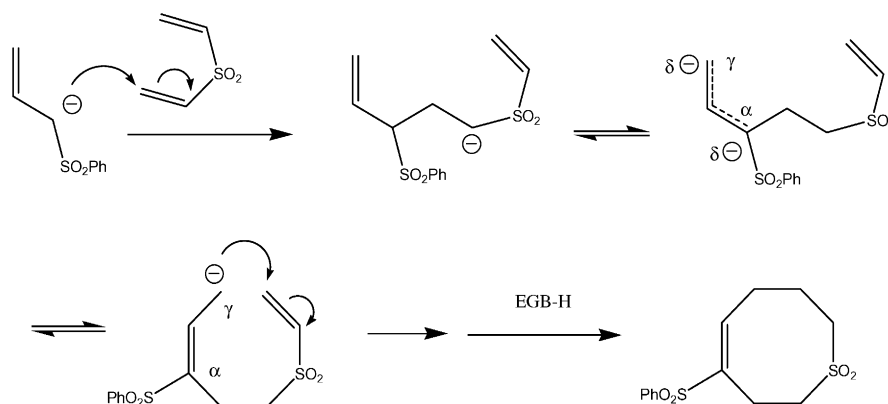


Figure 1. View of **2d** showing the atom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level.



Scheme 3. Proposed mechanism for the addition/cyclization of allyl phenyl sulfone to divinylsulfone.

There is no higher order oligomer (such as trimer) formation, such as would be expected if the ring closure step were slower than addition to another molecule of **1d**. Presumably the intramolecularity of the cyclization process provides the basis for the kinetic preference for cyclization over oligomerization. The maximized yield given above is obtained when the ratio of **1d** to **1a** is greater than 3:1. In contrast to the other reactions, unreacted **1a** is generally recovered from this cyclization. When the ratio of **1d** to **1a** is less than 3:1, the formation of some **2b** is also observed.

6. Summary

Highly efficient, electrocatalytic additions of allyl phenyl sulfone to a variety of vinyl sulfones have been accomplished.¹² The additions are catalyzed by electrogenerated bases derived from the reactant itself, and furnish 90–94% yields of highly polar molecules in which 1 mol of allyl phenyl sulfone has added consecutively, selectively, and in a linear addition mode to 2 mol of the vinyl sulfone. Essentially no products are observed which incorporate other than 2 mol of the vinyl sulfone. An addition to a difunctional alkene, divinylsulfone, yields a novel cyclization product, albeit in more moderate yield (41%). The use of tetraalkylammonium salts, as opposed to lithium salts, as electrolytes has been found to provide electrogenerated bases of especially high reactivity.

Acknowledgements

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10. These results have been repeated in our group, with yields in excess of 80%, with the exact same cell, solution, electrolyte, and reduction potentials as the reactions reported here.
11. Unpublished research in this group has established a complete suppression of competing EGB pathways in intramolecular anion radical mediated cycloadditions, when the electrolyte is changed from alkylammonium salts to lithium perchlorate, to be published.
12. Sample experimental and novel compound characterizations: Electrolysis of 72 mg (0.018 M) of **1a** and 137 mg (0.037 M) of **1b** (2.06:1 relative to **1a**) was carried out for 3.0 C, at –2.5 V, in a 0.1 M Et₄NBF₄ acetonitrile solution, in a divided cell, with glassy carbon electrodes. Voltage versus silver wire in porous glass. Upon benzene extraction and PTLC separation, 186 mg (90.8%) of **2bb** was recovered. Formation of the trimer occurred with a charge based catalytic factor of 12.7. *E*-3,5,7-Tris(phenylsulfonyl)-2-pentene (**2bb**): ¹H NMR (300 MHz, CDCl₃): 2.24 (4H, m), 3.05 (2H, m), 3.37 (2H, m), 4.98 (1H, d, 17.4 Hz), 5.37 (1H, d, 11.1 Hz), 5.61 (1H, dd, 11.1, 17.1 Hz), 7.49 (2H, m), 7.65 (9H, m), 7.91 (4H, m); LRMS (CI+): 519, 351. *E*-3,5,7-Tris(4-methylphenylsulfonyl)-2-pentene (**2cc**): ¹H NMR (300 MHz, CDCl₃): 2.22 (4H, m), 2.46 (6H, s), 3.01 (2H, m), 3.31 (2H, m), 4.98 (1H, d, 17.4 Hz), 5.37 (1H, d, 11.1 Hz), 5.61 (1H, dd, 11.1, 17.4 Hz), 7.37 (4H, m), 7.45 (2H, t, 7.2 Hz), 7.64 (3H, m), 7.78 (4H, br d, 8.7 Hz); LRMS (CI+): 547, 405; HRMS (CI+): Calcd: 547.128279. Found: 547.128911. 1-Phenylsulfonyl-5-thia-5,5-dioxacyclohept-1-ene (**2d**): ¹H NMR (300 MHz, CDCl₃): 2.02 (2H, p, 6.6 Hz), 2.60 (2H, m), 2.70 (2H, t, 6.3 Hz), 3.12 (2H, t, 6.3 Hz), 3.22 (2H, t, 5.4 Hz), 7.18 (1H, t, 9.3 Hz), 7.58 (2H, br t, 7.8 Hz), 7.70 (2H, br t, 7.8 Hz), 7.81 (1H, br d, 7.8 Hz); LRMS (CI+): 301. Crystallographic data (excluding structure

factors) for **2bb** and **2d**, have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 231694 and CCDC 231693, respectively. Copies of the data can be obtained,

free of charge, via www.ccdc.cam.ac.uk/data_request/cif or on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).