Bis(sulfonyl) Ketones: A New Oxyallyl Cation Source

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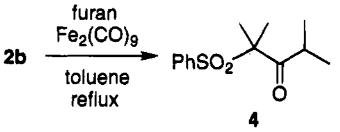
Oxyallyl cation cycloaddition reactions possess vast potential for complex molecule synthesis. We envisaged α,α′-bis(sulfonyl) ketones (BSKs, e.g., **2b**) as new oxyallyl cation precursors which could be used in intermolecular as well as intramolecular cycloadditions. The sulfone moiety would not interfere with tether installation and would later serve as the leaving group during oxyallyl cation generation. Sulfone group ionization via reductive cleavage of β-keto sulfones[1] or with Lewis acid assistance[2] has been reported. Harmata has used allyl sulfones as precursors to allyl cations[3] and oxyallyl cations.[4] In addition, β-keto sulfones are chemically robust, eliminating the need for purification immediately prior to use, a problem with some other common oxyallyl cation progenitors. Herein we report our initial studies of α,α′-bis(sulfonyl) ketones as oxyallyl cation precursors.

Keto sulfone **2b** is efficiently prepared from isopropyl phenyl sulfone **1**[5] (Scheme 1). Attempted generation[6] and trapping[7] of oxyallyl cation **3** from BSK **2b** afforded unilateral desulfonylation product **4** only (eq 1).[8]

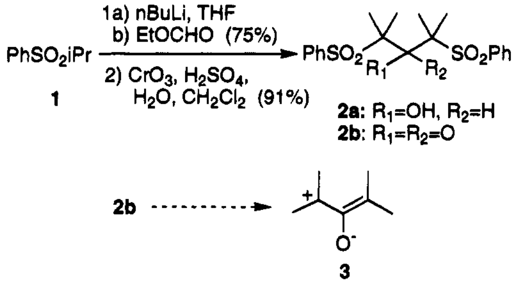


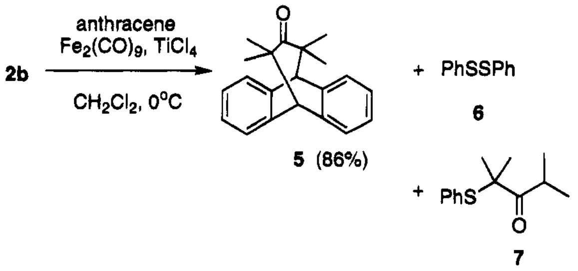
(1)

Reasoning that ionization of the second sulfone moiety required Lewis acid assistance,[2] we BSK **2b** with $Fe_2(CO)_9$ and $TiCl_4$ in the presence of anthracene[7] providing [4 + 3] cycloadduct **5** in good yield (eq 2).

A survey of Lewis acids revealed that $TiCl_4$ was most effective, but it also resulted in polymerization of several of the dipolarophiles examined (e.g., isoprene, cyclopentadiene). Addition of Lewis bases (THF, Ph_3P) in an attempt to attenuate the Lewis acidity of $TiCl_4$[9] resulted in drastic reductions in cycloadduct yields and high levels of unreacted **2b** in the crude reaction product. Varying amounts (0–20%) of disulfide **6** and keto sulfide **7** were also present in the crude product mixtures. Disulfide **6** results from dimerization of thiophenoxy radical, formed by reduction of benzenesulfinate ion under the reaction conditions.[10] Keto sulfide **7** presumably arises from thiophenoxide capture by oxyallyl cation **3**.

Scheme 1





(2)

Exploration of various metal carbonyl compounds in the reaction revealed that $Fe(CO)_5$, $Fe_2(CO)_9$, and $Co_2(CO)_8$ were of approximately equal effectiveness. Of these, $Fe(CO)_5$ was chosen for routine use due to low cost, high solubility in CH_2Cl_2, and ease of removal.[11]

Cycloadditions with various substrates using these optimized condition are summarized in Table 1. In each case reported, the chief products were the expected oxyallyl cation derived cycloadduct, with small amounts of diphenyl disulfide **6** and keto sulfide **7**. Activated mono- (entries 1 and 2) or *trans*-1,2-disubstituted olefins (entry 3) gave good yields of cyclopentanones, while *cis*-1,2-disubstituted olefins (entries 4–6) failed to provide detectable levels of cycloadducts.[12] Arylalkynes undergo cycloaddition to afford β,γ-cyclopentenones in good yield (entries 7 and 8), while an unactivated alkyne did not (entry 9). This appears to be the first report of successful alkyne-oxyallyl cation cycloaddition.[13] Reaction of BSK-derived oxyallyl cation **3** with furan gives bicyclic adduct **12a** in good yield (entry 10).[7] Substituted furans (entries 11–12) and cyclopentadiene (entry 13) gave lower yields, presumably due to competing $TiCl_4$-induced dipolarophile polymerization.

One problem typically associated with other methods of oxyallyl cation generation is the necessity to use large excesses of dipolarophile to obtain good yields of cycloadducts.[6] Tetramethyl oxyallyl cation **3** was trapped in

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[1] Simpkins, N. S. *Tetrahedron* **1990**, *46*, 6951. Roberts, D. W.; Williams, D. C. *Tetrahedron* **1987**, *43*, 1027. Magnus, P. D. *Tetrahedron* **1977**, *33*, 2019.

[2] Trost, B. M.; Neilson, J. B.; Hoogsteen, K. *J. Am. Chem. Soc.* **1992**, *114*, 5432 and references cited therein.

[3] Harmata, M.; Herron, B. F. *J. Org. Chem.* **1993**, *58*, 7393.

[4] Harmata, M.; Gamlath, C. B. *J. Org. Chem.* **1988**, *53*, 6154. Harmata, M.; Gamlath, C. B.; Barnes, C. L. *Tetrahedron Lett.* **1990**, *31*, 5981. Harmata, M.; Fletcher, V. R.; Claasen, R. J. *J. Am. Chem. Soc.* **1991**, *113*, 9861. Harmata, M.; Gamlath, C. B.; Barnes, C. L. *Tetrahedron Lett.* **1993**, *34*, 265.

[5] Lamothe, M.; Anderson, M. B.; Fuchs, P. L. *Synth. Commun.* **1991**, *21*, 1675.

[6] Noyori, R.; Hayakawa, Y. *Org. React.* **1983**, *29*, 163. Hoffmann, H. M. R. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 1. Mann, J. *Tetrahedron* **1986**, *42*, 4611.

[7] Anthracene, furan, and cyclopentadiene are excellent oxyallyl cation acceptors. See ref 6.

[8] Spectral data for **4**: Meanwell, N. A.; Johnson, C. R. *Synthesis* **1982**, 283.

[9] Suzuki, I.; Yamamoto, Y. *J. Org. Chem.* **1993**, *58*, 4783.

[10] In a control experiment, $PhSO_2Na$ afforded a 50% yield of **6** when reacted with $Fe(CO)_5$ and $TiCl_4$.

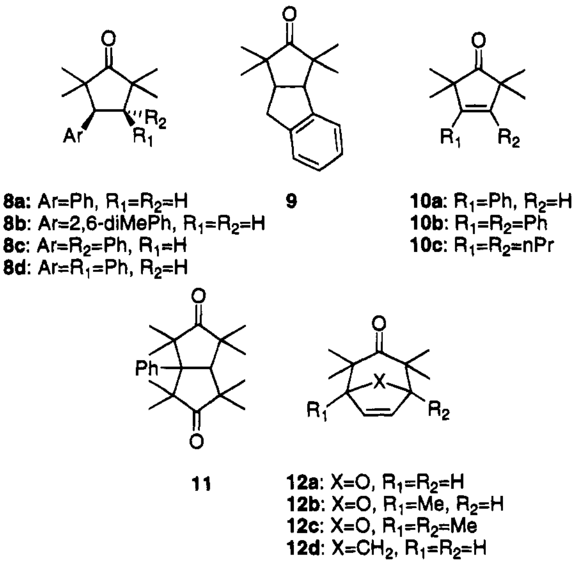
[11] Facile removal of unreacted $Fe(CO)_5$ (bp 103 °C) is readily achieved on a rotary evaporator.

[12] In a similar example, *trans*-β-methylstyrene underwent oxyallyl cation cycloaddition more slowly than styrene. Noyori, R.; Yokayama, K.; Hayakawa, Y. *J. Am. Chem. Soc.* **1973**, *95*, 2722.

[13] In previously reported attempts, oxyallyl cations underwent electrophilic addition (but not cycloaddition) to alkynes: Cowling, A. P.; Mann, J. *J. Chem. Soc., Chem. Commun.* **1978**, 1006. Padwa, A.; Bullock, W. H.; Dyszlewski, A. D.; McCombie, S. W.; Shankar, B. B.; Ganguly, A. K. *J. Org. Chem.* **1991**, *56*, 3556. Allyl cations have, however, undergone cycloaddition reactions with alkynes as exemplified by Johnson's synthesis of longifolene: Volkmann, R. A.; Andrews, G. C.; Johnson, W. S. *J. Am. Chem. Soc.* **1975**, *97*, 4777.

0022-3263/95/1960-1104$09.00/0

Table 1. BSK 2b-Derived Oxyallyl Cation Cycloaddition Reactions



8a: Ar=Ph, R_1=R_2=H
8b: Ar=2,6-diMePh, R_1=R_2=H
8c: Ar=R_2=Ph, R_1=H
8d: Ar=R_1=Ph, R_2=H

9

10a: R_1=Ph, R_2=H
10b: R_1=R_2=Ph
10c: R_1=R_2=nPr

11

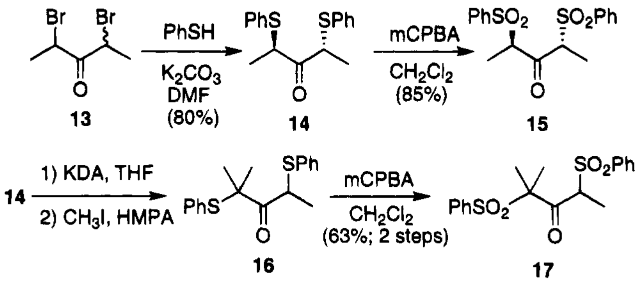
12a: X=O, R_1=R_2=H
12b: X=O, R_1=Me, R_2=H
12c: X=O, R_1=R_2=Me
12d: X=CH_2, R_1=R_2=H

entry	substrate	product	yield (%)
1	styrene	**8a**	70
2	2,6-dimethylstyrene	**8b**	68
3	*trans*-stilbene	**8c**	65
4	*cis*-stilbene	**8d**	0
5	indene	**9**	0
6	**10a**	**11**	0
7	phenylacetylene	**10a**	92
8	diphenylacetylene	**10b**	70
9	4-octyne	**10c**	0
10	furan	**12a**	77
11	2-methylfuran	**12b**	trace
12	2,5-dimethylfuran	**12c**	38
13	cyclopentadiene	**12d**	32
14	anthracene	**5**	86

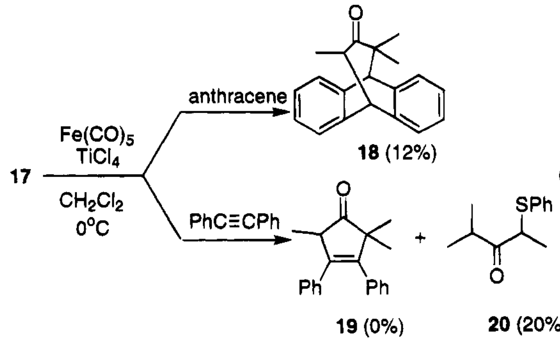
synthetically useful yields using only 1.2 equiv of **2b** per equiv of dipolarophile. In this way the BSK methodology for oxyallyl cation generation may be superior to other methods.

In order to explore the possibility of generating less highly-substituted oxyallyl cations, BSKs **15** and **17** were prepared in a straightforward manner (Scheme 2). Reaction of dibromide **13** (produced as a mixture of diastereomers from 3-pentanone and Br_2/PBr_3[14]) with thiophenoxide affords ketosulfide **14** as a single diastereomer. Keto sulfone **15** could not be alkylated in acceptable yield under any conditions examined. However, keto sulfide **14** was readily methylated to afford trisubstituted keto sulfide **16** in good yield.

Scheme 2



Treatment of **15** with anthracene, $Fe(CO)_5$, and $TiCl_4$ under the same conditions employed for **2b** afforded only unreacted **15**. We speculate that this failure to react is stereoelectronic in nature. If it was due to oxyallyl cation instability (relative to tetramethyl oxyallyl cation **3**), unilateral desulfonylation would probably have been observed. BSK **17** proved somewhat more reactive, providing a low yield of anthracene cycloadduct **18** (eq 3). Similar reaction with diphenylacetylene afforded only oxyallyl cation capture product **20**, while furan gave a complex mixture.



(3)

Mechanistic explorations, studies directed toward leaving groups which will require weaker Lewis acids, as well as work toward use of BSKs in intramolecular oxyallyl cation cycloaddition chemistry are currently underway and will be reported in due course.

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Supplementary Material Available: General experimental procedures and characterization data for all new compounds (6 pages).

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