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SULFONYL CARBANIONS IN SYNTHESIS. I.
A NOVEL ROUTE TO α,β-UNSATURATED CARBONYL COMPOUNDS.

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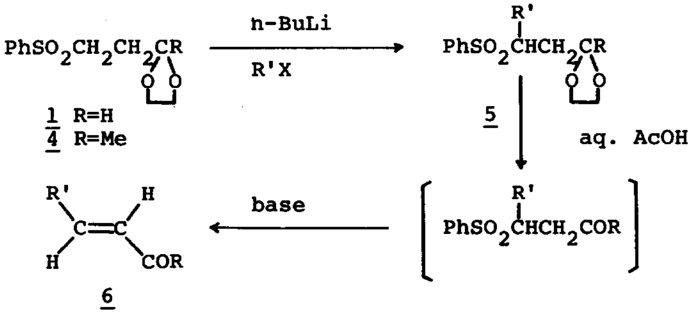
Michael-type addition of nucleophiles to α,β-unsaturated carbonyl compounds is a well-known reaction. This means that the β-carbon of the system can only act as an electrophile and never as a nucleophile. We have found, however, that the situation can be changed by (1) the introduction of benzenesulfonyl group to the β-carbon by normal Michael addition, and (2) protection of the acyl group by acetalization or ketalization. The resulting sulfone acetal or ketal now acts as a strong nucleophile and thus various electrophiles can be introduced on the β-carbon of the original α,β-unsaturated system. This communication deals with the utilization of sulfone acetals 1, 2, and 3,[1] and sulfone ketal 4[2] as synthons of β-acylvinyl anions.[3]

Investigation has shown that the carbanions of 1 and 4 could readily be formed at low temperature (-75°) by treatment with n-butyllithium in anhydrous THF. Alkylation of the resulting anions with a variety of alkyl halides occurred in exellent yields[4] to provide monoalkylated products 5.



The protecting group of the crbonyl was removed by heating 5 for 1 hr in acetic acid and water (1:1). The crude γ-aldehyde or γ-keto sulfones obtained were then treated with base to afford α,β-unsaturated compounds 6 in high yields. The elimination of benzenesulfinic acid was generally attained in about 30 min at room temperature. The trans geometry of 6 was confirmed by ir (960-975 cm^{-1}) and nmr (J_{trans}=15-16 Hz) analyses. Specific examples of 6 prepared by these methods are summarized in Table I.

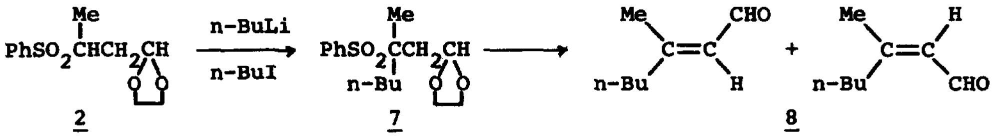
Table I Yields of Alkylated Products 5 and α,β-Unsaturated Carbonyl Compounds 6.

R	R'X	5(%)	6(%) [a]
H	$Me(CH_2)_3I$	77	- [b]
H	$PhCH_2Br$	87	- [b]
H	$Me(CH_2)_7Br$	92	70(A), 85(B)
H	$PhCH_2CH_2Br$	83	80(B)
Me	$Me(CH_2)_7Br$	91	71(C)
Me	$PhCH_2CH_2Br$	87	72(C)

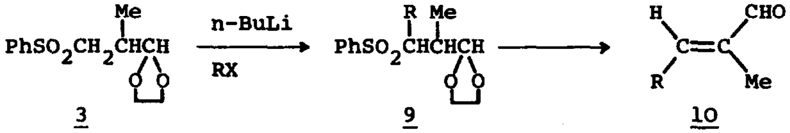
[a] A, B, and C in parentheses indicate the following basic conditons employed for the elimination of benzenesulfonyl group; A: 1% aq. NaOH, B: Et_3N-THF-H_2O, C: 10% aq. Triton B.

[b] Hydrolysis and β-elimination of the benzenesulfonyl group were not attempted.

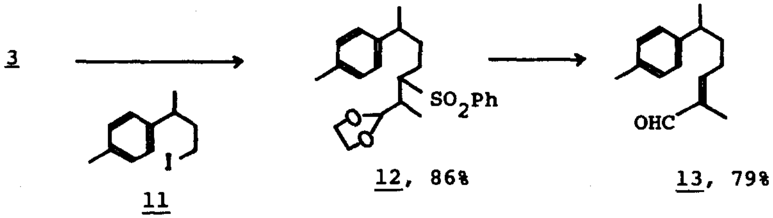
The next application of the method would be the synthesis of trisubstituted olefins. For this purpose, sulfone acetal 2 was prepared either from the sulfone acetal 1 and methyl iodide or from crotonaldehyde and thiophenol according to the general procedure.[1] Geminal alkylation of the sulfone acetal 2 with n-butyl iodide proceeded smoothly under the similar conditions described above to afford the adduct 7. The crude product 7 was successively treated with aq. acid and base to give the desired α,β-unsaturated aldehyde 8 in 83% over all yield. The nmr spectrum of 8, however, revealed that the product was a mixture of E- and Z-isomers in the ratio of 67:33.[5]



Now we have turned our attention to the sulfone acetal 3. Alkylation of the anion derived from 3 with alkyl halides (n-C_4H_9I and $PhCH_2CH_2Br$) gave 9 in excellent yields. Hydrolysis followed by base treatment afforded α,β-unsaturated aldehydes 10 (R=n-C_4H_9 and R=CH_2CH_2Ph) in 73-76% over all yields. In these cases, the nmr spectra[6] indicated that the products solely consisted of the E-isomer and thus were not contaminated with the Z-isomer.



The simplicity and high stereoselectivity of the method provided us the information leading to a facile stereoselective synthesis of some terpenes bearing functionality at the head position. One of the examples of such terpenes is nuciferal, which was found in the volatile oil of the leaves of Torreya nucifera Sieb. et Zuss.[7] Starting from readily available iodide 11[8] and 3, and using the same procedure as described above, we have synthesized (±)-nuciferal 13[9] in the yield shown below. The nmr and ir spectra of the final product were completely identical with those of the natural product.



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1. The sulfone acetals 1 (mp 67-68°), 2, and 3 were prepared by the oxidation of corresponding sulfide acetals with m-chloroperbenzoic acid.
2. The sulfone ketal 4 (mp 33-34°) was obtained by the Michael addition of benzenesulfinic acid to methyl vinyl ketone, followed by ketalization with ethylene glycol.
3. (a) E. J. Corey, B. W. Erickson, and R. Noyori, J. Amer. Chem. Soc., 93, 1724 (1971); (b) T. Nakai, H. Shiono, and M. Okawara, Tetrahedron Lett., 3625 (1974).
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5. The isomer ratio of the products in the directed aldol condensations was also ca. 7:3, (a) G. Wittig and H. Reiff, Angew. Chem. intern. Edit., 7, 7 (1968); (b) F. Nakatsubo, Y. Kishi, and T. Goto, Tetrahedron Lett., 381 (1970).
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9. For the recent compilations for the synthesis of this compound, see (a) V. K. Honward and A. S. Rao, Current Sci. (India), 34, 534 (1965); (b) O. P. Vig, B. Vig, and I. Raj, J. Indian Chem. Soc., 42, 673 (1965); (c) G. Büchi and H. Wüest, J. Org. Chem., 34, 1122 (1969); (d) D. A. Evans, G. C. Andrews, T. T. Fujimoto, and D. Wells, Tetrahedron Lett., 1389 (1973); (e) D. A. Evans and G. C. Andrews, Accounts Chem. Res., 7, 147 (1974).