Table I
Synthesis of Terminal Acetylenes by the Treatment of Lithium Ethynyltrialkylborates–Ethylenediamine with Iodine

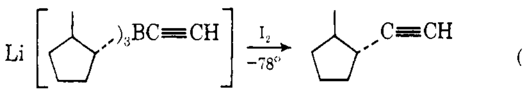
Olefin in R_3B	Product	Yield, %[a]
1-Butene	1-Hexyne	75
2-Butene	3-Methyl-1-pentyne	84
2-Methylpropene	4-Methyl-1-pentyne	94
Cyclopentene	Cyclopentylethyne	85
1-Methylcyclopentene	*trans*-2-Methylcyclopentylethyne	90
Cyclohexene	Cyclohexylethyne	92

[a] Analysis by glpc with yield based on R_3B.

stirred for 2 hr at room temperature and then cooled to −78°. Iodine, 1.27 g (5.0 mmol), in 6 ml of THF was added dropwise to the solution with vigorous stirring. After 90 min at −78°, the solution was brought to room temperature and treated with 5 ml of 40% potassium hydroxide, and the aqueous phase saturated with potassium carbonate. Analysis by glpc revealed the presence of 4.6 mmol (92% yield) of cyclohexylethyne.

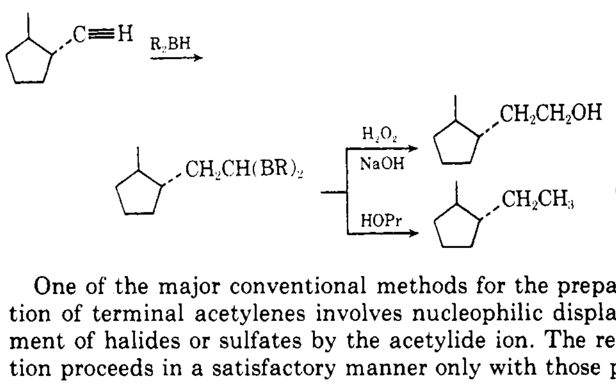
Many reactions of organoboranes proceed to provide products which retain the stereochemistry of the boron-carbon bond.[5] On the other hand, some reactions which proceed through free-radical intermediates involve the loss of such stereochemistry.[6] Accordingly, it appeared desirable to establish the stereochemistry of the present synthesis.

The trialkylborane from 1-methylcyclopentene was selected for this study. Oxidation with alkaline hydrogen peroxide produces 100% *trans*-2-methylcyclopentanol, with only a trace of 1-methylcyclopentanol.[5] The acetylene product obtained from this organoborane was indicated to be a single isomer, presumably the trans derivative (eq 2) by glpc analysis.



(2)

This conclusion was confirmed by dihydroborating the product with dicyclohexylborane (R_2BH). Oxidation with alkaline hydrogen peroxide[7] produced 2-(*trans*-2-methylcyclopentane)ethanol and protonolysis[8] with propionic acid produced *trans*-1-ethyl-2-methylcyclopentane (eq 3). In each case, the isomeric purity of the products was confirmed by glpc comparison with authentic samples of the *cis* and *trans* isomers. In both cases, only the trans isomers could be detected.



(3)

One of the major conventional methods for the preparation of terminal acetylenes involves nucleophilic displacement of halides or sulfates by the acetylide ion. The reaction proceeds in a satisfactory manner only with those primary derivatives which readily participate in S_N2 substitution processes. However, the present procedure accommodates, in addition to primary alkyl groups, highly branched groups, secondary, and alicyclic groups, groups which are often relatively resistant to nucleophilic substitution. Furthermore, the transfer of alkyl groups from boron to the acetylenic carbon with retention further extends the range of applicability of this procedure. Consequently, this development provides a general, stereospecific synthesis of monoalkyl- and monocycloalkylacetylenes under exceptionally mild conditions. The discovery that lithium acetylide–ethylenediamine may be used to prepare lithium ethynyltrialkylborates now makes possible the extension of the many interesting new reactions of the lithium 1-alkynyltriorganoborates[9] to the parent compound.

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(2) The lithium acetylide was prepared by the addition of *n*-butyllithium to acetylene in THF at −78°. Addition of acetone yielded 94% 2-methyl-3-butyn-2-ol, confirming that the lithium acetylide had been formed in high yield. Following an alternative literature procedure [K. Suga, S. Watanabe, and T. Suzuki, *Can. J. Chem.*, **46**, 3041 (1968)] for the preparation of lithium acetylide resulted in a yield of 1-hexyne of only 6%.

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(10) Graduate research assistant on Grant No. GM 10937 from the National Institutes of Health.

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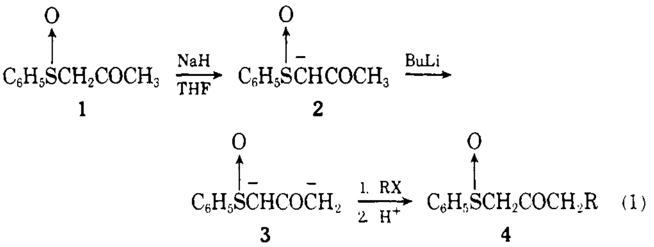
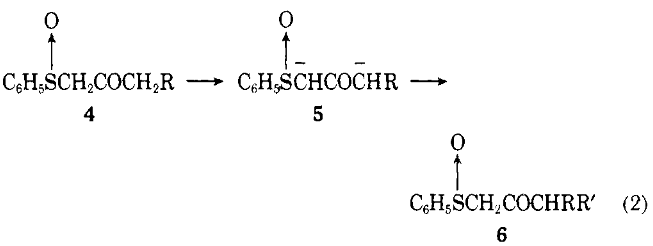
Alkylation of the Dianion of β-Keto Sulfoxides. A Versatile Synthesis of Phenyl (2-Oxoalkyl) Sulfoxides. A General Route to Ketones, 1,4 Diketones, and Aldols

Summary: General synthetic routes to phenyl (2-oxoalkyl) sulfoxides, ketones, 1,4 diketones, and aldols have been realized *via* dianions of β-keto sulfoxides.

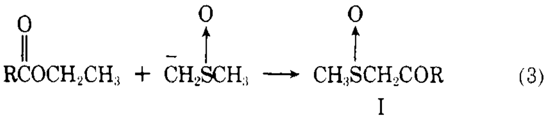
Sir: We wish to report that dianion **3** derived from phenyl (2-oxopropyl) sulfoxide (**1**) can be generated and undergoes specific alkylation at the γ carbon atom (eq 1). In addition, dianions derived from γ-substituted β-keto alkyl sulfoxides undergo exclusive alkylation at the γ carbon (eq 2). The specific alkylation at γ carbon of **1** and **4** *via* dianions **3** and **5**, respectively, makes phenyl (2-oxopropyl) sulfoxide (**1**) a useful reagent in organic synthesis (*vide infra*) and provides a general high yield synthesis of β-keto sulfoxides. Russell[1] and Corey[2] have previously shown that esters react with dimethyl sulfoxide anion to produce β-keto sulfoxides (eq 3). In addition, it had been reported[2] that compounds such as I could be reductively cleaved (aluminum amalgam) to yield methyl ketones. More recently it has been demonstrated that lithiated chloromethyl phenyl sulfoxide reacts with aldehydes affording an adduct which upon treatment with methyllithium produced phenyl (2-oxoalkyl) sulfoxides (eq 4).[3] Procedures for the mono- and dialkylation at the α carbon of β-keto sulfoxides of type I have been reported;[4] however, no report describing the specific γ-alkylation of dianions derived from β-keto sulfoxides (*e.g.*, **3** and **5**) has been reported.[5]



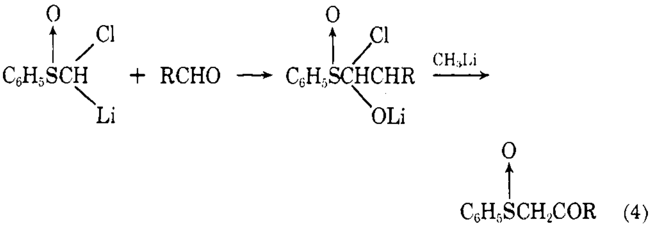
$$\underset{\mathbf{1}}{C_6H_5\overset{\overset{O}{\uparrow}}{S}CH_2COCH_3} \xrightarrow[THF]{NaH} \underset{\mathbf{2}}{C_6H_5\overset{\overset{O}{\uparrow}}{S}\overset{-}{C}HCOCH_3} \xrightarrow{BuLi} \underset{\mathbf{3}}{C_6H_5\overset{\overset{O}{\uparrow}}{S}\overset{-}{C}HCO\overset{-}{C}H_2} \xrightarrow[2.\ H^+]{1.\ RX} \underset{\mathbf{4}}{C_6H_5\overset{\overset{O}{\uparrow}}{S}CH_2COCH_2R} \quad (1)$$



$$\underset{\mathbf{4}}{C_6H_5\overset{\overset{O}{\uparrow}}{S}CH_2COCH_2R} \longrightarrow \underset{\mathbf{5}}{C_6H_5\overset{\overset{O}{\uparrow}}{S}\overset{-}{C}HCO\overset{-}{C}HR} \longrightarrow \underset{\mathbf{6}}{C_6H_5\overset{\overset{O}{\uparrow}}{S}CH_2COCHRR'} \quad (2)$$



$$R\overset{\overset{O}{\|}}{C}OCH_2CH_3 + \overset{-}{C}H_2\overset{\overset{O}{\uparrow}}{S}CH_3 \longrightarrow \underset{\mathbf{I}}{CH_3\overset{\overset{O}{\uparrow}}{S}CH_2COR} \quad (3)$$



$$C_6H_5\overset{\overset{O}{\uparrow}}{S}CH(Cl)Li + RCHO \longrightarrow C_6H_5\overset{\overset{O}{\uparrow}}{S}CH(Cl)CH(OLi)R \xrightarrow{CH_3Li} C_6H_5\overset{\overset{O}{\uparrow}}{S}CH_2COR \quad (4)$$

Treatment of phenyl (2-oxopropyl) sulfoxide[6] (**1**) with sodium hydride in anhydrous THF produced the soluble monoanion **2**, and subsequent metalation of **2** with *n*-butyllithium generated dianion **3**. When a solution of **3** in THF was treated with a variety of alkylating agents, including isopropyl iodide, a facile reaction occurred. The monoalkylated products were isolated in good yield (Table I). Yields have not been optimized.

Table I
Alkylation of Dianion from $C_6H_5S(\rightarrow O)CH_2COCH_3$

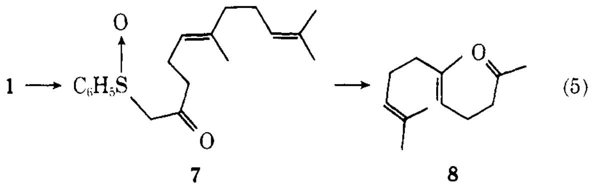
RX	Yield of **4**,[a,b] %
$CH_3CH_2CH_2CH_2I$	78[c]
$(CH_3)_2CHI$	73[c]
$C_6H_5CH_2Cl$	63
$CH_2{=}CHCH_2Br$	65[c]
Geranyl bromide	61
m-Methoxybenzyl bromide	80

[a] All substances exhibited nmr, ir, and analytical data in accord with the assigned structures. [b] Crude yields were on the order of 80–90%. [c] Yield refers to crystalline material obtained by direct crystallization from crude product.

It was evident from the nmr spectra that alkylation occurred exclusively at the γ carbon. Spectral analysis of the crude reaction mixture failed to give any evidence of alkylation at the α carbon atom, dialkylation or O-alkylation. The nmr spectra of **4**[7] have a two-proton singlet at δ 3.75 due to the α-methylene protons. The absence of a three-proton singlet at δ ~2.23 further indicated that alkylation occurred exclusively on the γ carbon.

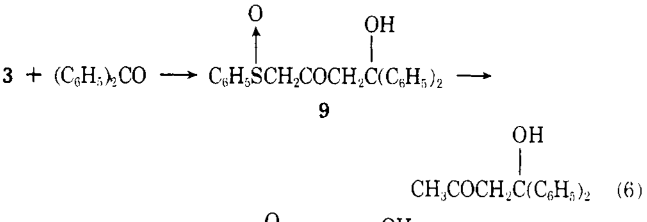
We have also alkylated γ-substituted β-keto sulfoxides. Treatment of phenyl (2-oxoheptyl) sulfoxide (**4**, R = *n*-Bu) with sodium hydride in THF followed by metalation with *n*-BuLi afforded dianion **5** (R = *n*-Bu) which upon addition of benzyl chloride resulted in a 72% isolated pure yield of **6** (R = *n*-Bu; R′ = benzyl). Similarly, allyl bromide, 1,3-dichloro-2-butene, and geranyl bromide underwent γ-alkylation.

Specific alkylation at the γ-carbon atom of **1** provides a general route to phenyl (2-oxoalkyl) sulfoxides which allows for an attractive synthetic route to a wide variety of methyl ketones[8] *via* reductive cleavage of the carbon–sulfur bond.[2] To demonstrate the efficiency of this ketone synthesis, we have carried out the synthesis of geranylacetone (**8**) (eq 5). Sulfoxide **1** (1 equiv, 1 *M* in THF) was converted into monoanion **2** by treatment with a sodium hydride (1.1 equiv) in 1 ml of THF. After stirring at room temperature for 30 min, monoanion **2** was treated with *n*-butyllithium (1.1 equiv). After 20 min, geranyl bromide (1.1 equiv) was added. Stirring was continued for 10 min followed by the usual work-up. There was obtained after chromatography a 61% isolated yield of pure β-keto sulfoxide **7**. Reductive cleavage of **7** with aluminum amalgam in 10% aqueous THF at 80° for ~1 hr afforded a 90% yield of geranylacetone (**8**) which was identical (nmr, ir, mass spectrum, glc) with an authentic sample.[9]

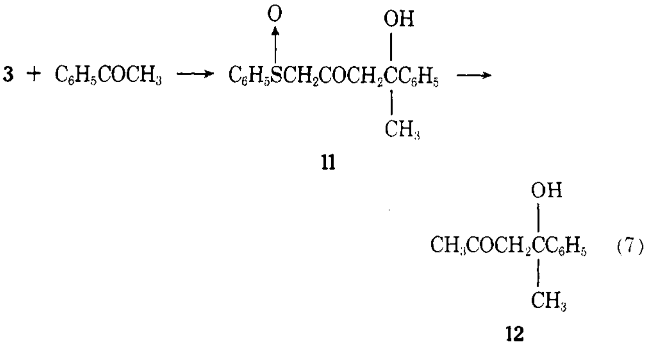


7 **8**

Dianions of β-keto sulfoxides undergo aldol reactions with carbonyl compounds. We have found that reaction of dianion **3** with benzophenone gave the aldol product **9** in 80% yield which upon treatment with Al/Hg afforded the aldol **10** in 90% yield (eq 6). Similarly, acetophenone reacted with dianion **3** affording adduct **11** in 77% yield which upon reductive cleavage afforded aldol **12** in 80% isolated pure yield (eq 7). The synthetic route outlined permits ready access to aldols (*e.g.*, **10** and **12**) which are not readily available by alternate procedures.

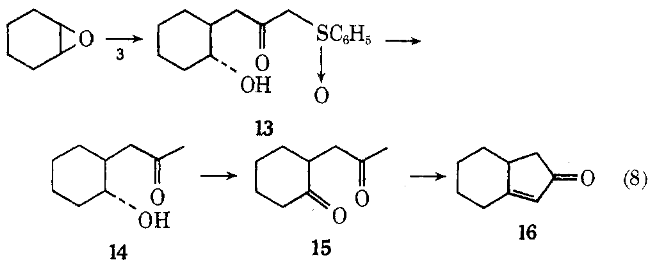


$$\mathbf{3} + (C_6H_5)_2CO \longrightarrow \underset{\mathbf{9}}{C_6H_5\overset{\overset{O}{\uparrow}}{S}CH_2COCH_2\overset{\overset{OH}{|}}{C}(C_6H_5)_2} \longrightarrow CH_3COCH_2\overset{\overset{OH}{|}}{C}(C_6H_5)_2 \quad (6)$$



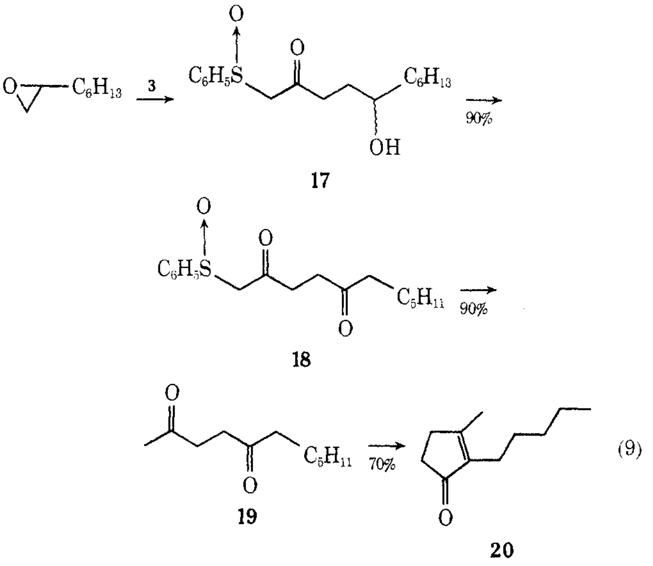
$$\mathbf{3} + C_6H_5COCH_3 \longrightarrow \underset{\mathbf{11}}{C_6H_5\overset{\overset{O}{\uparrow}}{S}CH_2COCH_2\underset{CH_3}{\overset{OH}{C}}C_6H_5} \longrightarrow \underset{\mathbf{12}}{CH_3COCH_2\underset{CH_3}{\overset{OH}{C}}C_6H_5} \quad (7)$$

Finally, we wish to report that dianion **3** reacts with a variety of epoxides,[10] thus providing a convenient route to 1,4 diketones (eq 8). Treatment of cyclohexene oxide with



dianion 3 in THF at room temperature for 24 hr resulted in an 85% crude yield of ketol 13 (a 54% isolated yield of pure 13, mp 104-105°, was obtained by direct crystallization of the crude product). Cleavage of the carbon-sulfur bond was achieved (Al/Hg) in aqueous THF as previously described in 85% yield. Jones oxidation of 14 followed by aldol condensation afforded hydrindenone 16 in 70% overall yield from 14.

To further demonstrate the efficiency of this synthetic scheme, we have carried out the synthesis of dihydrojasmone[11] (20) as illustrated in eq 9. Reaction of the epoxide derived from 1-octene with dianion 3 in THF provided an 80% yield of ketol 17 (17 was in equilibrium with its cyclic hemiacetal). Oxidation followed by reductive cleavage and cyclization afforded dihydrojasmone (20) which exhibited spectral properties in agreement with published data.[11]



This novel and efficient method for the construction of 1,4 diketones makes dianions of β-keto sulfoxides useful intermediates in organic synthesis. In addition, dianion 3 should provide an attractive synthetic route to a wide variety of ketones and aldols.[8]

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References and Notes

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(2) E. J. Corey and M. Chaykovsky, *J. Amer. Chem. Soc.*, **87**, 1345 (1965).
(3) I. Kuwajima and Y. Fukuda, *Tetrahedron Lett.*, 327 (1973).
(4) P. G. Gassman and G. D. Richmond, *J. Org. Chem.*, **31**, 2355 (1966).
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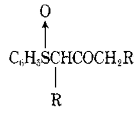
(6) Prepared by treatment of phenyl (2-oxopropyl) sulfide with sodium metaperiodate in aqueous methanol at 0° [C. R. Johnson and H. E. Keiser, *Org. Syn.*, **46**, 78 (1966)].
(7) The nmr spectrum of phenyl (2-oxopropyl) sulfoxide has the following signals: δ (CCl_4) 2.23 (s, 3 H, COMe), 3.80 (s, 2 H, $-CH_2-$), 7.55 (m, 5 H).
(8) One can prepare α- and γ-substituted β-keto sulfoxides (*e.g.*, i) which provides for a general route to ketones (unpublished results, P. A. Grieco and C. S. Pogonowski).



$C_6H_5\overset{\overset{O}{\uparrow}}{S}\underset{\underset{R}{|}}{C}HCOCH_2R'$

i

(9) Kindly provided through the courtesy of Dr. Bernard J. Kane, Glidden-Durkee, Jacksonville, Fla.
(10) In addition to the epoxides cited, propylene oxide undergoes smooth reaction with dianion **3**. A report describing the opening of epoxides with the dianion of ethyl acetoacetate for the preparation of tetrahydrofurylidene acetates has recently appeared [T. A. Bryson, *J. Org. Chem.*, **38**, 3428 (1973)].
(11) H. C. Ho, T. L. Ho, and C. M. Wong, *Can. J. Chem.*, **50**, 2718 (1972), and references cited therein.

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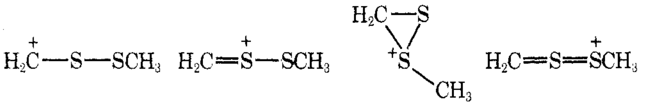
α-Disulfide Carbonium Ions

Summary: Evidence from solvolysis studies on chloromethyl methyl disulfide and spectroscopic studies with various disulfides is taken to indicate that acyclic α-disulfide carbonium ions are far less stable than α-sulfide carbonium ions.

Sir: While carbonium ion stabilization by adjacent thiyl groups is well-known,[1] the stability of α-disulfide carbonium ions has not been reported. In connection with studies involving α-heteroatom-substituted alkyl disulfides[2] we required information on the properties of the methyldithiomethyl cation (shown in various canonical or valence tautomeric representations **1a–1d**) and its alkyl-substituted derivatives. In this communication we present the preliminary results of our investigation.



1a **1b** **1c** **1d**

We have determined the rate of hydrolysis of CH_3SSCH_2Cl[3] under S_N1 conditions, following the general procedure used by Bordwell in his classical study of the hydrolysis of α-chloro sulfides.[1a] The hydrolysis of a ~0.005 *M* solution of the α-chloro disulfide in 50% dioxane–water at 34.85° was followed using either an automatic titrator or a conductivity cell.[4] Least-squares analysis of data obtained from a duplicate run using a photometric titrator[5] automatically maintained at the pH 4.6 Bromphenol Blue end point gave a first-order rate constant of 1.82×10^{-4} sec^{-1} (correlation coefficient 0.995). A comparison of the rate constants for hydrolysis of CH_3SSCH_2Cl and CH_3SCH_2Cl (Table I) indicates a rate retardation for the former of over 6800, providing clear evidence for the decreased stability of $CH_3SSCH_2^+$ compared to $CH_3SCH_2^+$.