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A NEW ROUTE TO SULFONIUM YLIDES. DIPHENYLSULFONIUM ISOPROPYLIDE

E. J. Corey, Manfred Jautelat, and Wolfgang Oppolzer
Department of Chemistry, Harvard University, Cambridge, Massachusetts 02138

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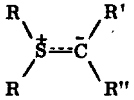
The stabilities of sulfonium ylides (**1**) vary with structure in a manner which is consistent with their description as α-sulfonio-substituted carbanions. If R' and/or R" in **1** are π-electron withdrawing groups (e.g., carbonyl), the ylides are easily generated by the action of mild bases on the corresponding sulfonium cations and usually are sufficiently stable to permit isolation by ordinary procedures (1-3). In contrast,



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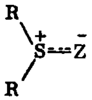

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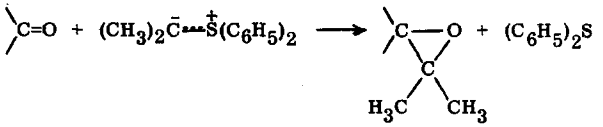
if R' and R" in **1** are hydrogen, as in the case of dimethylsulfonium methylide, **2**, R = CH_3, Z = CH_2, the conversion of sulfonium salt to ylide requires a strong base (e.g., *t*-butoxide ion or methylsulfinyl carbanion) (4-6) and the ylide is both aerobically and thermally unstable (rapid decomposition at temperatures above 10° under nitrogen). Sulfonium *n*-alkylides **1**, R' = H, R" = *n*-alkyl, are even less stable than sulfonium methylides and can be generated efficiently from sulfonium salts only by careful selection of base, solvent, reaction temperature, and other operating conditions. For example, diphenylsulfonium ethylide, **2**, R = C_6H_5, Z = $CHCH_3$, decomposes with a half life of *ca.* 5 hr at -20° and rapidly at 0° in tetrahydrofuran under nitrogen (7). It can be produced in high yield at -76° using as base *t*-butyllithium (7) or lithium dialkylamides (7); however, bases such as methyl-, *n*-butyl-, or phenyllithium are unsatisfactory (7,8). Despite their tendency to undergo spontaneous decomposition, sulfonium methylides and *n*-alkylides can be applied successfully to a variety of synthetically useful processes, e.g., nucleophilic methylene transfer to carbonyl groups to form oxiranes in high yield (4,6,7,9,10).

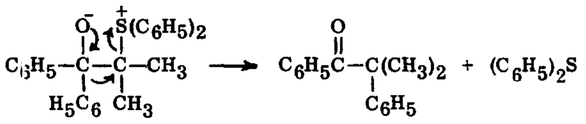
Ylides of type **1** in which *both* R' and R" groups are alkyl are expected to be the least stable of all sulfonium alkylides and the most difficult to prepare. This note reports an especially convenient and practical procedure for the generation of such an ylide, diphenylsulfonium isopropylide, and the application of this intermediate to oxirane synthesis.

Diphenylethylsulfonium fluoborate, prepared (11) from diphenylsulfide and triethyloxonium fluoborate (12), was converted to the corresponding ylide **2**, R = C_6H_5, Z = $CHCH_3$, in dimethoxyethane solution at -70°

in the presence of 1 equivalent of methylene chloride by treatment with 1.1 equivalents of lithium diisopropylamide in dimethoxyethane. Addition of methyl iodide (1.1 equivalents) led to the formation of a precipitate of diphenylisopropylsulfonium iodide in 2.5-3 hr at -70 to -50°, and subsequent treatment with an additional 1.1 equivalents of lithium diisopropylamide at -70° (-78° bath) produced after 0.5-1 hr at -70° a turbid orange solution of diphenylsulfonium isopropylide 2, $R = C_6H_5$, $Z = C(CH_3)_2$. Addition to this reagent of 1 equivalent of benzaldehyde, heptanal, dodecanal, or cyclohexanone resulted in the formation of oxirane in 74-82% (isolated) yield according to the equation:



For the aldehydes, reaction for 2 hr at -60 to -70° was sufficient for complete conversion; for the ketone 1 hr at -70° and 2 hr between -50 and -30° was sufficient. Complete consumption of the sulfonium isopropylide is evident from the fading of the orange color of the solution. Benzophenone, which is much less reactive, was transformed completely only after 14 hr at -20°; in this case in addition to oxirane (37% yield) a rearrangement product (3) (13) was formed (49% yield) probably by the pathway:



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The ketone 3 does not originate from oxirane in this case, since the latter is stable under the conditions of reaction and isolation.

Comment is required on the choice of conditions for the above described generation of diphenylsulfonium isopropylide.

1. Methyl iodide is the most satisfactory reagent for methylation of diphenylsulfonium ethylide; the bromide and chloride are not sufficiently reactive, whereas trimethyloxonium fluoborate, although reactive, affords lower yields.

2. The intermediate diphenylisopropylsulfonium iodide readily decomposes to diphenyl sulfide and isopropyl iodide, and it is best used *in situ* and immediately.

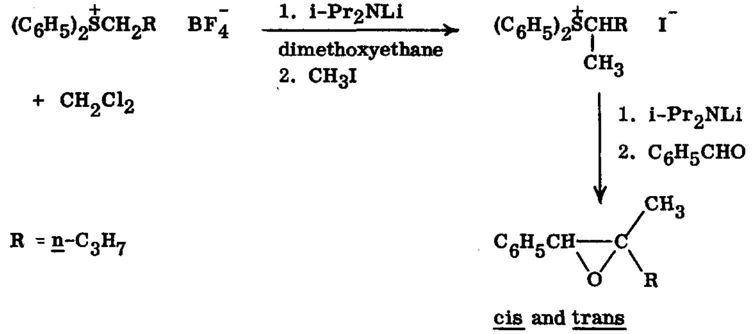
3. Dimethoxyethane is a much better solvent for the various sulfonium salts than is tetrahydrofuran, and its use is especially important in the conversion of diphenylisopropylsulfonium iodide to the corresponding isopropylide.

4. In general, sterically crowded lithium reagents, e.g., *t*-butyllithium, are the most satisfactory bases for the generation of sulfonium alkylides, and *n*-alkyllithium reagents are poor (7,8). However, *t*-butyllithium is sufficiently reactive with dimethoxyethane to be of no use in that medium at -70°, and lithium diisopropylamide in dimethoxyethane leads to only *ca.* 30% yield of ylide from diphenylisopropylsulfonium

iodide. In contrast, the combination of lithium diisopropylamide and methylene chloride in dimethoxyethane, which is equivalent to dichloromethyllithium (14-16), is an excellent reagent for the generation of diphenylsulfonium isopropylide from the sulfonium iodide.

An alternative but less satisfactory procedure for the generation of the isopropylide 2, R = C_6H_5, Z = $C(CH_3)_2$, involves the separate preparation of diphenylisopropylsulfonium fluoborate from diphenyl sulfide, silver fluoborate, and neat isopropyl iodide in large excess (yield ca. 55%) and subsequent ylide generation from the fluoborate in tetrahydrofuran at -70° using t-butyllithium as base (17). In this way oxiranes were obtained from benzaldehyde and cyclohexanone in 55-60% yield.

The alkylation route to dialkyl-substituted ylides is obviously capable of extension to other systems. The following transformation, carried out in good yield in a single reactor without isolation of intermediates, is indicative:



Further aspects of the newly-discovered route to alkyl-substituted ylides and their effective application to synthesis will be reported in due course. The following is a typical experimental procedure (18).

2,2-Dimethyl-3,3-pentamethyleneoxirane. A solution of 3.0 g (0.01 mole) of diphenylethylsulfonium fluoborate and 0.85 g (0.01 mole) of methylene chloride in 100 ml of dry dimethoxyethane (distilled from lithium aluminum hydride) under nitrogen was cooled to -70° and treated with 0.011 mole of a cold solution of lithium diisopropylamide (reagent prepared freshly by the addition of 7.0 ml of 1.6 M n-butyllithium in hexane to 1.12 g of diisopropylamine in 10 ml of dimethoxyethane at -70°). The yellow-green solution which resulted became cloudy after 10 min. After 30 min at -70° the solution was treated with 1.50 g (0.0105 mole) of methyl iodide and the reaction mixture was maintained at -70 to -50° for 2 hr, at the end of which time 0.011 mole of lithium diisopropylamide solution was again added at -70°; an orange color was produced rapidly. After 1 hr at -70°, 0.98 g (0.01 mole) of cyclohexanone was added, and the mixture was maintained for 1 hr at -70° and 2 hr between -70 and -50°. The colorless reaction mixture was treated with water (200 ml) and extracted with four portions of pentane. The pentane extract was washed with water, dried over sodium sulfate, concentrated, and subjected to distillation at 10 mm to afford 1.15 g (82%) of 2,2-dimethyl-3,3-pentamethyleneoxirane, bp 54° (10 mm) (residue, mainly diphenylsulfide 1.9 g); nmr singlet due to methyls at 1.31 ppm downfield from tetramethylsilane and an unsharp peak due to methylene protons at

1.58 ppm (ratio CH_3 : CH_2 protons 0.59).

Anal. Calcd. for $C_9H_{16}O$: C, 77.09; H, 11.50. Found: C, 77.21; H, 11.47.

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15. Solutions of dichloromethyllithium in dimethoxyethane are much less stable than those in tetrahydrofuran (at -70° the former undergo extensive decomposition in 15 min); therefore, with dimethoxyethane as solvent, dichloromethyllithium should be generated in situ.
16. We have shown in separate experiments that lithium diisopropylamide converts methylene chloride to dichloromethyllithium in high yield at -70° in tetrahydrofuran [>85% yield of bisdichloromethylmercury obtained with mercuric chloride (14)], and also that externally generated dichloromethyllithium in tetrahydrofuran converts diphenylisopropylsulfonium iodide and diphenylethylsulfonium iodide to the corresponding ylides.
17. The greater solubility of diphenylisopropylsulfonium fluoborate as compared to the iodide in tetrahydrofuran allows the use of that solvent with the fluoborate.
18. This work was supported by the National Institutes of Health and the National Science Foundation.