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THE ACID CATALYZED REARRANGEMENT OF THE ADDUCTS OF LITHIO CYCLOPROPYLPHENYL SULFIDE WITH ALDEHYDES AND KETONES

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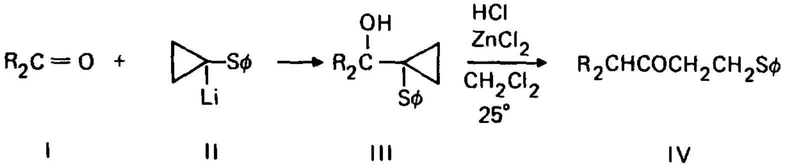
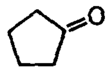
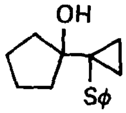
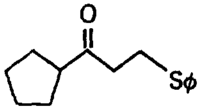
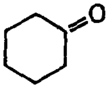
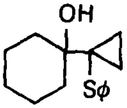
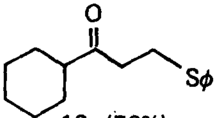
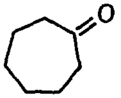
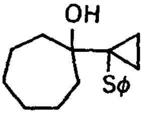
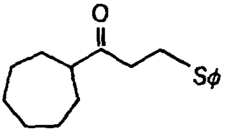
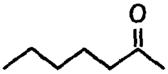
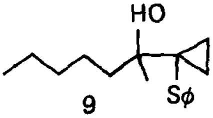
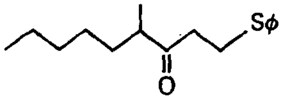
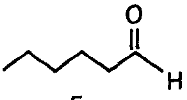
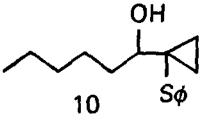
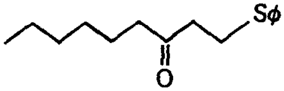
The acid catalyzed ring opening of cyclopropyl carbinyl alcohols to the corresponding homoallylic derivatives is well known[1] and has been utilized by a number of workers for stereospecific olefin syntheses.[2] It seemed reasonable, therefore, that the incorporation of a heteroatom (e.g., S, Se) into appropriate positions of the three-membered ring could lead upon ring opening to synthetically useful masked carbonyl derivatives.

Trost and coworkers have demonstrated that the anion II generated by deprotonation of cyclopropylphenyl sulfide by butyl lithium readily adds to aldehydes, ketones and enones to yield the corresponding cyclopropyl carbinyl alcohols.[3] These workers have also reported the rearrangement of the adducts under various acidic conditions to a wide variety of synthetically useful cyclobutanone derivatives. We report here that the use of strongly acidic, nonaqueous conditions, in particular ($ZnCl_2$, HCl, CH_2Cl_2), converts the same cyclopropylcarbinyl alcohols into ring opened γ-ketosulfides as shown below. The ultimate result of this transformation is the utilization of the anion II as a linear three carbon aldehyde equivalent. During this process, a 1,2-carbonyl transposition of the original carbonyl compound is also effected.



The desired cyclopropylcarbinyl alcohols were produced in good yield by the addition of II to the corresponding carbonyl compound as previously described.[3] All of the adducts 6-10 were purified by Kugelrohr distillation and treated directly with freshly fused zinc chloride and anhydrous hydrogen chloride in methylene chloride. Under these conditions, the alcohols were readily transformed into the γ-ketosulfides 11-15 (see Table I).[4]

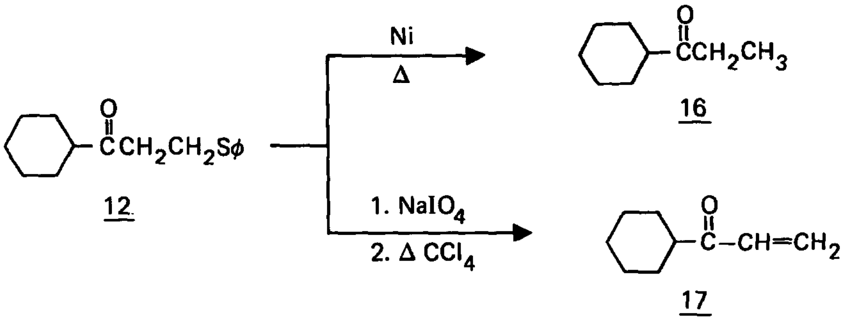
Table I

 1	 6	 11 (60%)[a]
 2	 7	 12 (70%)
 3	 8	 13 (62%)
 4	 9	 14 (61%)
 5	 10	 15 (45%)

[a] Isolated yields of purified product

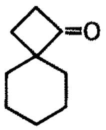
The reaction is reasonably general although the isolated yields of the rearranged γ-ketosulfides from the aldehyde adducts tend, in general, to be lower than those of the corresponding ketones. In some runs, the γ-ketosulfides were contaminated with small amounts of the corresponding β-chloroethylketones. This result is not surprising, as the only source of thiophenoxide in the reaction mixture was the initial adduct itself. In order to eliminate this problem, the crude reaction mixtures were stirred with a solution of lithium thiophenoxide in ether for a few hours which transformed the β-chloroethyl compound into the desired γ-ketosulfide.

The γ-ketosulfides 11-15, while stable and easily purified, are subject to a number of useful chemical transformations. Two of these are shown below, using cyclohexyl-β-thiophenoxyethyl ketone 12 as a typical example.

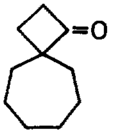


The desulfurization was accomplished in good yield by refluxing the γ-ketosulfide with Raney nickel in acetone. The oxidative elimination to the corresponding enones was most conveniently performed in two steps; first by oxidation with sodium metaperiodate, followed by the subsequent elimination of phenysulfenic acid by refluxing in carbon tetrachloride in the presence of calcium carbonate. These two transformations demonstrate the ultimate use of the anion II as an acyl anion equivalent of either propionaldehyde or acrolein.

The mechanism of formation of γ-ketosulfides from the corresponding cyclopropylcarbinyl derivatives is of some interest in light of the reports of Trost and coworkers which describe the formation of cyclobutanones from many of these materials under a variety of acidic conditions.[3] In this respect, when the progress of the transformation of 7 was monitored by IR at short reaction times, a strong carbonyl absorption characteristic of cyclobutanones[5] appeared at 1775 cm^{-1}. This high frequency absorption decreased with reaction time and was gradually replaced by the strong absorption at 1710 cm^{-1} of the γ-ketosulfide 12. This suggested that a rapid ring expansion and hydrolysis to the corresponding cyclobutanone was occurring which was subsequently transformed more slowly into the isolated γ-ketosulfide via an unusual electrophilically initiated ring opening.[6] In support of this hypothesis, it was observed that the cyclobutanones 18 and 19, which were synthesized by the treatment of 7 and 8 with aqueous fluoroboric acid, were readily converted to the γ-ketosulfides 12 and 13 by treatment with the $HCl-ZnCl_2$ reagent in the presence of two equivalents of thiophenol.[7] On this basis, it seems likely that a primary source of the γ-ketosulfides are the corresponding cyclobutanones produced by the acid catalyzed ring expansion of the cyclopropyl carbinyl derivatives.[8]



18



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GENERAL PROCEDURE FOR THE REARRANGEMENT OF SATURATED CYCLOPROPYL CARBINYL ALCOHOLS

The cyclopropyl carbinyl alcohols were all prepared using the procedure of Trost and coworkers.[3] Anhydrous hydrogen chloride was slowly bubbled through a stirred suspension of 114 mg (1 mmole) of freshly fused zinc chloride in 20 ml of methylene chloride for 1 hour. The acidic mixture was then cooled to 0° and 1 mmole of the alcohol in 2 ml of methylene chloride was added in one portion. The flask was then sealed and allowed to stir at 25° for 48-72 hrs. The contents of the flask were poured into saturated sodium bicarbonate solution and extracted with ether. The ether was dried over $MgSO_4$, decanted and stirred (under nitrogen) with 2 mmole of lithium thiophenoxide at 25° for 16 hrs. The ethereal solution was washed with 5% sodium hydroxide, water and dried over $MgSO_4$. The γ-ketosulfides were easily separated from small amounts of diphenyldisulfide by either column or thick layer chromatography on silica gel.

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3. a) B. M. Trost, D. E. Keeley and M. J. Bogdanowicz, J. Am. Chem. Soc. 95, 3068 (1973); b) B. M. Trost, D. E. Keeley, J. Am. Chem. Soc. 96, 1252 (1974); c) B. M. Trost, D. E. Keeley, H. C. Arndt and M. J. Bogdanowicz, J. Am. Chem. Soc. 99, 3088 (1977).

4. Analytical and spectral data in accord with the proposed structures were obtained and are available upon request.

5. L. J. Bellamy, "The Infrared Spectra of Complex Molecules," Vol. I, John Wiley and Sons, New York, N.Y., 1975.

6. a) P. Doyle, R. H. B. Galt and R. J. Pierce, Tet. Lett., 2903 (1973). b) F. Bourelle-Wargnier, Tet. Lett., 1589 (1974); c) F. Bourelle-Wargnier and R. Jeanie-Carlier, Tet. 32, 2725 (1976).

7. In the absence of a good nucleophile, in this case thiophenol, the starting materials disappeared very slowly to form a complex mixture of products.

8. A number of regiospecific ring opening reactions of cyclobutanone derivatives have been induced by treatment with strong electrophiles. The results of these experiments will be described in a future publication.

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