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THE ACID CATALYZED REARRANGEMENT OF ADDUCTS FORMED FROM LITHIO CYCLOPROPYLPHENYL SULFIDE AND ENONES

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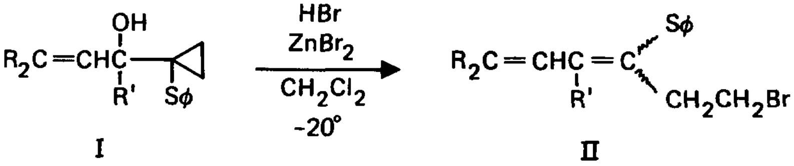
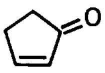
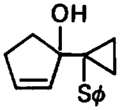
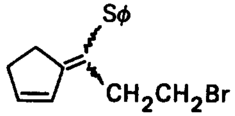
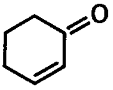
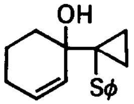
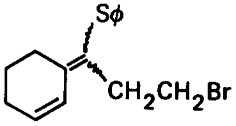
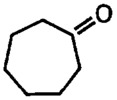
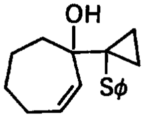
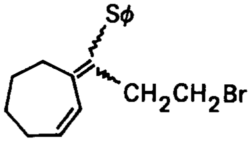
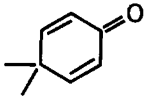
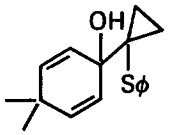
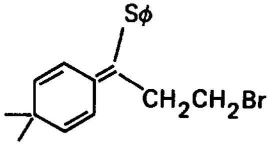
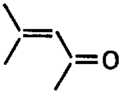
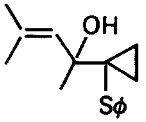
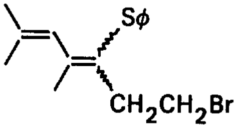
It is known that many cyclopropyl carbinyl alcohols undergo ring opening in acidic media under conditions of reversible product formation to yield the corresponding homoallylic derivatives, and this technique has been employed by various workers in the synthesis of homoallylic alcohols and other derivatives.[1] The conformational requirements of the ring opening are such that in many cases considerable stereoselectivity has been observed in the olefin formation. In a previous paper[3] we described the unexpected deep-seated rearrangement and attending hydrolysis which occurred when the adducts of saturated aldehydes and ketones with lithio cyclopropylphenyl sulfide[4] were treated with strong nonaqueous acids. In these cases, it seemed that rapid ring expansion and hydrolysis preempted the expected cyclopropylcarbinyl-homoallylic rearrangement. In this report we describe the results of treating the corresponding adducts of enones I with strong acid (see below).



In contrast with the saturated derivatives, the adducts did not undergo hydrolytic rearrangement even when treated with aqueous acid. Instead, ionization was accompanied by ring opening to generate the corresponding β-haloethylvinyl sulfides in excellent yields (see Table I). The most effective reagent for promoting this transformation was found to be a mixture of zinc bromide and aqueous hydrobromic acid.[2c] Under these conditions, the ring opening was fast even at -20°. The rearrangement was quite general, and a number of selected examples are shown in Table I. In every case, the yields were high and the homoallylic bromides produced were pure enough for subsequent transformations without further purification.[5]

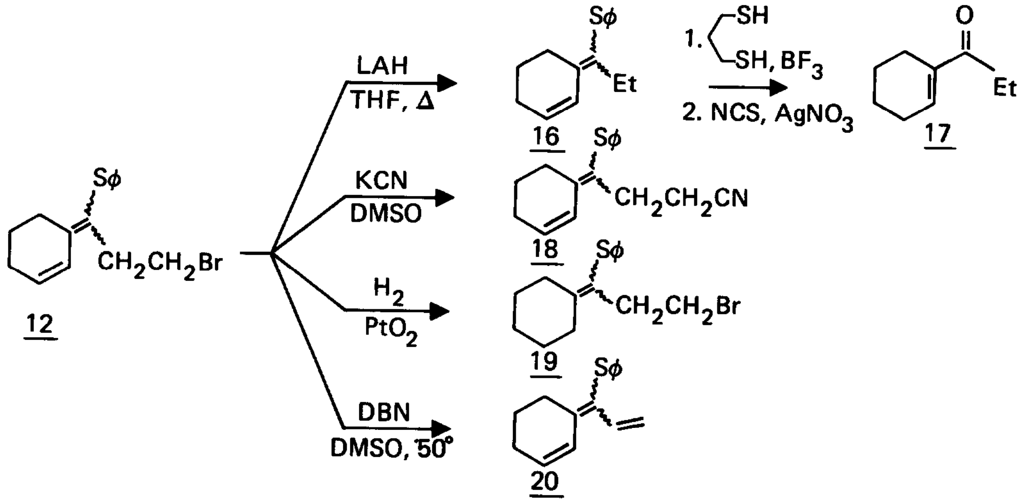
Table I.

 1	 6	 11 (85%)[a]
 2	 7	 12 (90%)
 3	 8	 13 (83%)
 4	 9	 14 (85%)
 5	 10	 15 (90%)

[a] Isolated yields

Examination of the crude reaction mixtures by nmr indicated that the ring opening was not stereospecific and resulted in mixtures of the possible geometric isomers. The respective isomer ratios were easily measured by integration of the separated resonances in the vinyl region. The low stereospecificity of the ring opening was anticipated based on the conformational model proposed by Johnson and coworkers for the rearrangement.[2c] It is interesting that the product 14 was produced in good yield from the corresponding adduct 9 in spite of the strongly acidic conditions. The dienyl alcohol 9 is normally prone to methyl migration and subsequent aromatization under cationic conditions. In this case, however, nmr analysis of the crude reaction mixtures indicated <5% of this rearrangement product was present

The corresponding β-bromoethylvinyl sulfides 11-15 are potentially useful synthetic intermediates capable of further transformations as illustrated below for the derivative 12.



The halogen of the β-bromoethylvinyl sulfides was readily displaced by a variety of nucleophiles. For example, heating 12 with KCN in DMSO for 6 hours produced the nitrile 18 in 90% yield. Dehalogenation of 12 was effected in good yield by refluxing with lithium aluminum hydride in THF for 6 hours. Attempted hydrolysis of the resulting dienyl sulfide 16 using standard techniques[6] proved unsuccessful. However, 16 could be first thioketalized with 1 mole of 1,3-dimercaptopropane and the resulting dithane derivative hydrolyzed in the usual fashion to yield the ketone 17 in 60% overall from 16. The dienyl sulfides (e.g., 12) could be selectively hydrogenated over platinum oxide to yield the corresponding vinyl sulfides.[7] This provided a route to the homoallylic halides which were unavailable from the rearrangement of the saturated cyclopropyl carbinyl adducts (see preceding communication). Finally, dehydrohalogenation of the β-haloethyldienyl sulfides was effected by the use of 1,5-diazabicyclo[4.3.0]non-5-ene (DBN) in DMSO (50°) to yield conjugated trienes such as 20 in good yield.

General Procedure for the Rearrangement of Unsaturated Cyclopropyl Carbinyl Alcohols

The HBr-ZnBr solution was prepared by mixing 5 ml of 48% aqueous hydrobromic acid with 6.75g of anhydrous zinc bromide. To 0.78g of this solution which had been cooled to -20° was added 1 mmole of the corresponding alcohol in 2 ml of dry methylene chloride. The reaction mixture was stirred for 10 minutes at -20°, 30 minutes at 0°, and poured into 50 ml of saturated $NaHCO_3$ solution. The aqueous phase was extracted with ether and the combined organic extracts were washed with water and dried over $MgSO_4$. The crude homoallylic bromides were isolated in a form pure enough for subsequent transformations simply by evaporation of the solvent at reduced pressures.

Further investigation of the acid catalyzed rearrangement and the chemistry of the resulting β-haloethyldienyl sulfides is proceeding.

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7. The heterogeneous hydrogenation, while ultimately producing the desired vinyl sulfide in good yield, required the continuous addition of catalyst in order to proceed to completion presumably due to poisoning of the catalyst.

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