

CONVERSION OF CYCLOPROPYL BROMIDES TO CYCLOPROPYLOXY DERIVATIVES

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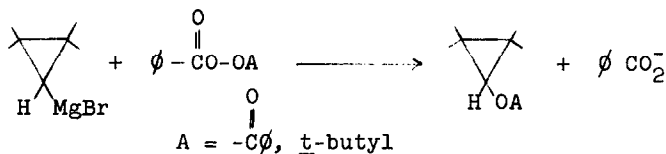
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(Received in USA 8 August 1967)

We report the first synthetically useful conversion of cyclopropyl halides to the corresponding cyclopropyloxy derivatives. The method developed utilizes cyclopropyl carbanions, derived from the bromides, as agents for nucleophilic attack on the oxygen atom of an appropriate substrate. Such reversal of the normal nucleophilic and electrophilic roles of the atoms involved obviates the difficulties inherent in the orthodox S_N1 and S_N2 reactions of the halide and allows for a net nucleophilic substitution.

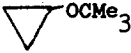
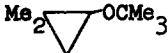
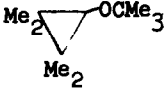
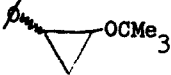
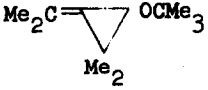
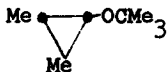
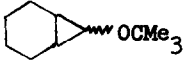
Treatment of cyclopropyl Grignard reagents with benzoyl peroxide or *t*-butyl perbenzoate affords the corresponding cyclopropyl benzoates and *t*-butyl ethers (1), respectively:



The *t*-butyl ethers are particularly useful because they are converted in high yields to the corresponding acetates by reaction with acetyl bromide, acetyl fluoroborate or acetic anhydride/ BF_3 -etherate. The last reagent is convenient to use and provides optimum yields of acetates under mild reaction conditions.

The yields (2) of *t*-butyl ethers range from 20 to 60% (see TABLE).

TABLE
 Yields of t-Butyl Ethers^a

	42%		
	28		30% ^b
	60		52
	20		20% ^b

^aYields are based on Grignard reagent and, unless otherwise indicated, product isolation by distillation procedures.

^bVPC analysis and isolation.

An example of the experimental procedure utilized is the preparation of cis- and trans- 2-phenylcyclopropyl t-butyl ether (from the corresponding mixed bromides) and subsequent conversion to acetates. To a solution of 0.13 mole of the Grignard reagent in 200 ml of tetrahydrofuran was added, over a 10-min period, 19.4g (0.100 mole) of t-butyl perbenzoate in 20ml of tetrahydrofuran. The reaction medium was held at -10 to -5° during the addition and then at 0° with stirring for an additional 2 hr. Saturated ammonium chloride solution was added to dissolve all salts, the aqueous layer extracted with ether and the combined ether phases washed with dilute base, dried, and concentrated. Fractional distillation gave 4.0g of phenylcyclopropane and 11.2g (59%) of cis- and trans- 2-phenylcyclopropyl t-butyl ether. The ether (1.2g) was treated with 3 ml of acetic anhydride and 100 μ l of BF₃-etherate at room temperature. After 2 hr the system was

quenched with dilute NaOH. The ether extract afforded 1.0g (90%) of cis- and trans-2-phenylcyclopropyl acetate. In a similar manner and in comparable yields, the requisite t-butyl ethers gave cyclopropyl, 2,2,3,3-tetramethylcyclopropyl and 2,2-dimethylcyclopropyl acetates.

The reaction of cyclopropyl Grignard reagents with benzoyl peroxide affords the cyclopropyl benzoates in low yields (< 20%). For this reason the preparation of the acetates via the t-butyl ethers is the preferred route to the esterified cyclopropanols. Cyclopropanols are readily obtained from the acetates by reductive cleavage with methyl lithium or lithium aluminum hydride (3). The reactions reported here and the availability of structurally diverse halocyclopropanes provide an attractive general route to cyclopropanols.

The reactions of cyclopropyl Grignard reagents with benzoyl peroxide and t-butyl perbenzoate probably occur by other than a free radical pathway. A reasonable cyclic mechanism has been proposed for the related reactions of other Grignard species with these substrates (4):



Mechanistic and stereochemical considerations are currently being examined.

ACKNOWLEDGEMENT: We are grateful to the National Institutes of Health, U. S. Public Health Service for support of this work through grant HD01807.

REFERENCES

1. All compounds in this paper have been fully characterized by elemental analyses and infrared and nmr spectroscopy.

2. We have not yet made a careful study of the effect of reaction conditions on product yields. Several tertiary cyclopropyl halides, exo- and endo- 7-chloro-7-phenylbicyclo [4.1.0.] heptane and 1-chloro-1-phenyl-2,2,3,3-tetramethylcyclopropane, failed to give cyclopropyloxy derivatives.
3. Cf. C. H. DePuy, G. M. Dappen, K. L. Eilers, and R. A. Klein, J. Org. Chem., 29, 2813(1964).
4. S.-O. Lawesson and N. C. Yang, J. Am. Chem. Soc., 81, 4230(1959). See also, S.-O. Lawesson, C. Frisell, D. Z. Denney, and D. B. Denney, Tetrahedron, 19, 1229(1963).