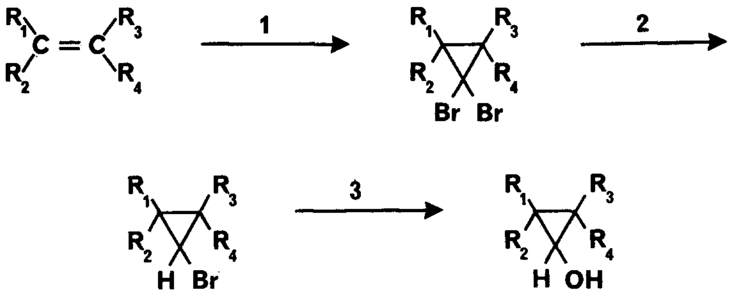
Tetrahedron Letters No.33, pp. 2859-2862, 1969. Pergamon Press. Printed in Great Britain.

OXYGENATION OF CYCLOPROPYLLITHIUMS: A CONVENIENT SYNTHESIS OF CYCLOPROPANOLS

Daniel T. Longone and William D. Wright (1)
Department of Chemistry, University of Michigan, Ann Arbor, Michigan 48104

(Received in USA 26 May 1969; received in UK for publication 16 June 1969)

We report a particularly convenient and efficient synthesis of cyclopropanols (2). The method involves the oxygenation of cyclopropyllithiums, prepared from cyclopropyl bromides by reaction with the metal. An overall synthetic scheme is shown below.



Reagents: 1 t-BuOK/CHBr$_3$; 2 (n-Bu)$_3$SnH; 3 Li/Et$_2$O, O$_2$, NH$_4^+$.

The synthesis of a cyclopropyl bromide from an alkene by dibromocarbene insertion (3) and tri-n-butyltin hydride reduction (4) is well known and easily effected with a variety of alkenes. The two-step conversion of alkene to cyclopropyl bromide gives, both in our hands and as reported in the literature, average yields of about 60%. Conversion of bromide to cyclopropyllithium is

Table I

Conversion of Cyclopropyl Bromides
to Cyclopropanols

Bromide (RBr)[a]	RLi Yield,[b] %	ROH Yield,[c] %
Cyclopropyl	55	28
2-Ethylcyclopropyl[d]	90	70
2,2-Dimethylcyclopropyl	90	55
cis-2,3-Dimethylcyclopropyl	95	70
trans-2,3-Dimethylcyclopropyl	100	69
2,2,3-Trimethylcyclopropyl	96	61
2,2,3,3-Tetramethylcyclopropyl	87	63[e]
Bicyclo[4.1.0]heptyl[f]	98	48[e]

[a] 1-Bromide unless otherwise indicated. [b] Determined by the method of Watson and Eastham (ref 7). [c] Based on RLi and determined by glpc analysis unless otherwise indicated. [d] New compound: satisfactory combustion analysis and spectra. [e] Isolated yield by distillation. [f] 7-Bromide.

nearly quantitative in most cases, and oxygenation of the latter affords the corresponding cyclopropanol in good yield (Table I). Based on availability of precursors and reagents, efficiency of conversions, and simplicity of technique, the synthesis reported here is an attractive method for the preparation of secondary cyclopropanols.

As an example of the experimental procedure used, we describe the preparation of *trans*-2,3-dimethylcyclopropanol. The lithium intermediate was prepared from 9.44 g (0.0634 mol) of 1-bromo-*trans*-2,3-dimethylcyclopropane and 1.18 g (0.170 g-atom) of Li (5) in diethyl ether, according to the procedure of Seyferth and Cohen (6), and was formed in quantitative yield as determined by Watson-Eastham titration (7) using 1,10-phenanthroline as the indicator. Oxygenation was performed by passing dry, CO_2-free oxygen through the cold (-71°) solution of trans-2,3-dimethylcyclopropyllithium for 1.0 hr. After hydrolysis with 15 ml satd NH_4Cl, the ether layer was separated, dried, and concentrated at reduced pressure to give 3.74 g of liquid. Analysis on a 20-ft Carbowax 20M column (20% on 60/80 prep grade Chrom W) at 126° showed the presence of essentially one component (R_t 30 min), which was collected and identified as trans-2,3-dimethylcyclopropanol by comparison of nmr and ir spectra with those of an authentic sample (8).

An interesting feature of the metalation-oxygenation sequence (Table II) is that oxygenation of a cyclopropyllithium derived from a syn/anti mixture of bromides in which the less stable bromide is the major isomer (4), leads preferentially to the more stable cyclopropanol. By analogy to the work of Walborsky and Aronoff (9), reaction of bromide with lithium probably involves considerable loss of stereochemical integrity; however, it is not known if the cyclopropyllithium intermediate is predominantly syn or anti, and hence the stereochemical course of the oxygenation step is unclear. Work in progress will resolve these questions.

Table II

Comparison of Syn/Anti Ratios[a] for Cyclopropyl Bromides (RBr) and Derived Cyclopropanols (ROH)

	Syn/Anti Ratio[a]	
R Group	RBr	ROH
2-Ethylcyclopropyl	3:2	1:2
cis-2,3-Dimethylcyclopropyl	4:1	1:2
2,2,3-Trimethylcyclopropyl	3:1	2:3
Bicyclo[4.1.0]heptyl	7:2	3:4

[a] Syn refers to that isomer in which the larger number of alkyl groups is cis to Br or OH.

Acknowledgment. We are grateful to the National Institutes of Health, U. S. Public Health Service (Grant HD01807), and to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research. We would also like to thank Professor U. Schöllkopf for furnishing us with nmr and ir spectra of several cyclopropanols for use in identification.

References and Notes

1. American Chemical Society-Petroleum Research Fund Fellow, 1968-69.
2. For reviews of previous work on the synthesis of cyclopropanols, see: (a) U. Schöllkopf, Angew. Chem. Intern. Ed. Engl., 7, 588 (1968); (b) C. H. DePuy, Accounts Chem. Res., 1, 33 (1968).
3. W. von E. Doering and A. K. Hoffman, J. Amer. Chem. Soc., 76, 6162 (1954).
4. D. Seyferth, H. Yamazaki, and D. L. Alleston, J. Org. Chem., 28, 703 (1963).
5. Lithium Corporation of America 1/8" diam wire (0.02% Na) was used for all metalations. The use of a high-speed stirrer is recommended for these reactions.
6. D. Seyferth and H. M. Cohen, J. Organometal. Chem., 1, 15 (1963).
7. S. C. Watson and J. F. Eastham, ibid., 9, 165 (1967).
8. U. Schöllkopf, J. Paust, A. Al-Azrak, and H. Schumacher, Chem. Ber., 99, 3391 (1966).
9. H. M. Walborsky and M. S. Aronoff, J. Organometal. Chem., 4, 418 (1965).