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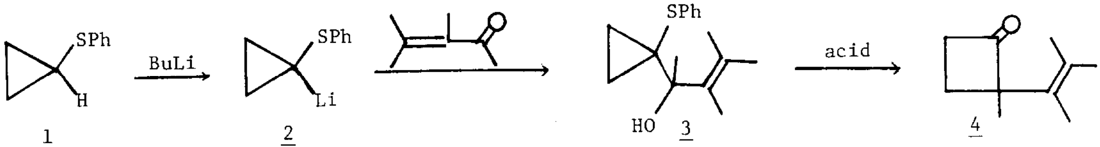
A SYNTHESIS OF 2-VINYLCYLOBUTANONES USING 1-METHOXYCYCLOPROPYLLITHIUM REAGENTS

Theodore Cohen* and James R. Matz
Department of Chemistry, University of Pittsburgh, Pittsburgh, PA 15260, USA

Abstract: A facile synthesis of 2-vinylcyclobutanones consists of reductive lithiation of 1-phenylthio-1-methoxycyclopropanes, addition of enals or enones to the resulting α-lithioethers, and acid catalyzed rearrangement of the allylic alcohols thus produced.

The literature suggests that 2-vinylcyclobutanones are unusually promising intermediates for the versatile elaboration of 5- and 6-member rings[1] and of 8-member rings.[2] However, until recently no general synthetic method for such compounds has been available. The recently explored[3] addition of vinylketene to diolefins lacks sufficient generality and the yields are less than desirable. Only the ingenious procedure of Trost (1 → 4)[4] appeared to have some generality.[5] This methodology was especially attractive to us because of the possibility of substantial further generalization due to our recent discovery that analogues of 2 bearing substituents on the cyclopropyl ring[6] can be readily prepared by reductive lithiation of cyclopropanone thioketals using lithium naphthalenide[7a] or lithium 1-dimethylaminonaphthalenide (LDMAN).[7b] A wide variety of such thioketals is simply available using a new ring closure reaction in a non-connective[8] or connective[9] mode or a complementary procedure of Braun and Seebach[10] which is especially useful for ring-fused cyclopropanone thioketals.



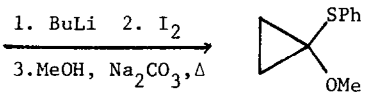
1 2 3 4

However, when we attempted to apply this technology, we found, in agreement with the experience of Trost[4], that substantial experimentation was necessary in each case in order to obtain good yields in the rearrangement step; in the original work,[4] a wide variety of reaction conditions (reagent, temperature and time) were used. In our own work, some cases did not give satisfactory yields even after trying several sets of conditions.[11]

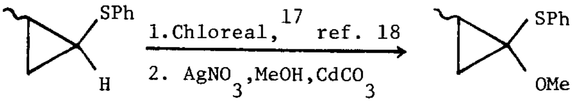
It appeared likely that an analogous procedure in which the phenylthio group is replaced by an alkoxy group would give better results because of (i) the greater ability of oxygen to stabilize a positive charge[4,12] and (ii) the ready acid-catalyzed hydrolysis of the enol ether which is a possible proximate product of the reaction.[13] Indeed, this concept was the inspiration for our development of a general method for producing α-lithioethers by reductive lithiation of α-phenylthioethers.[14] The three methods that we have used so far for the production of 1-methoxy-1-phenylthiocyclopropanes are shown below.[15]

1

ref. 16

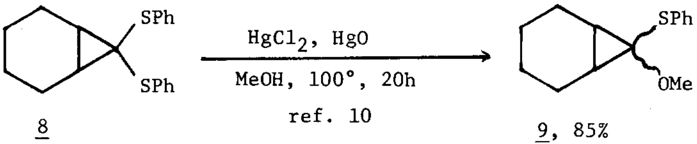


5, 83%



6

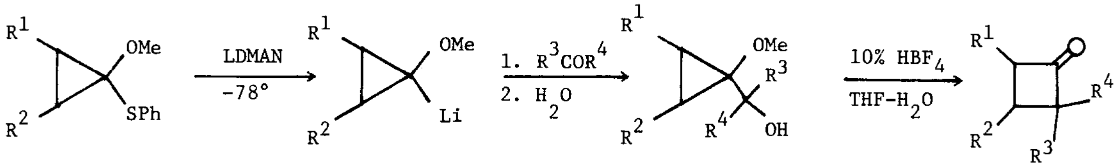
7, 73%



8

9, 85%

The preparation of 2-vinyl or 2-arylcyclobutanones from 5, 7, and 9 is outlined in the Scheme. Reductive lithiation of the latter substances occurs smoothly in THF at -78° by use of 2 equivalents of LDMAN for 45 min.[14] Addition of the conjugated aldehyde or ketone causes instant decolorization of the anions. In most cases the crude 1-cyclopropylallyl alcohols were treated directly with 10% HBF_4 in wet THF (one volume of aqueous 48% HBF_4 mixed with 4 volumes of THF). As hoped, these conditions were generally successful in producing the phenyl- and vinylcyclobutanones in satisfactory yields (Table).[19]



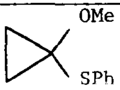
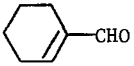
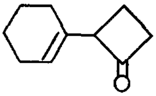
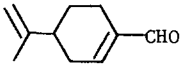
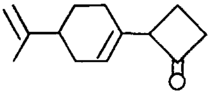
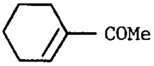
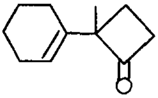
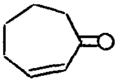
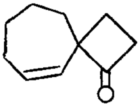
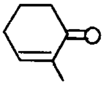
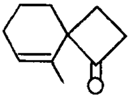
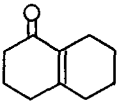
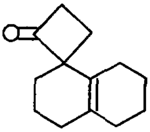
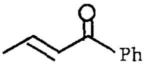
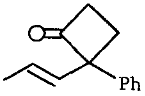
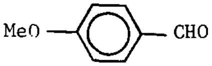
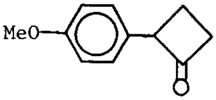
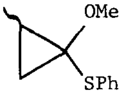
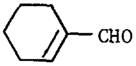
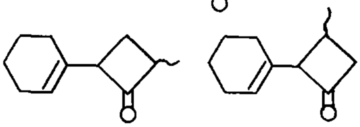
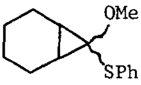
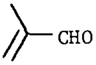
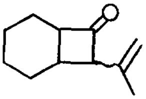
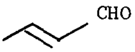
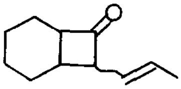
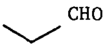
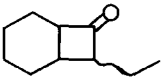
Scheme

Attractive features of this procedure include fair generality with respect to the type of the cyclopropane ring,[20] the clean nature of the products, and the fact that one set of reaction conditions is successful in all cases. The rearrangement of the non-allylic and secondary alcohol intermediate in entry 12 makes it very obvious that considerably milder conditions would probably be successful in most of the other cases in which the alcohol intermediates are far more labile; optimization of rearrangement conditions has not been sought Entry 12 also suggests that this procedure is useful not only for vinylcyclobutanones but for other cyclobutanones as well.

After the completion of this work, Trost and Jungheim[21] reported an alternative and complementary method to produce 2-vinylcyclobutanones. Their procedure utilizes 1-(2',6'-dimethoxyphenylthio) formylcyclopropane and involves a rearrangement analogous to that in Trost's earlier work.[4] This paper also discloses new uses for 2-vinylcyclobutanones involving ring opening reactions. In the accompanying paper,[1] we describe some useful acid-catalyzed ring expansions of these products to 5- and 6-member rings.

Acknowledgment. We thank Dr. Alvin Marcus for recording the mass spectra and the National Institutes of Health for support of this work (GM 22760).

TABLE. Preparation of Cyclobutanones from 1-Phenylthio-1-methoxycyclopropanes

Entry	Mixed Ketal	Carbonyl compound	Cyclobutanone	Combined yield,%
1				63
2	"			50
3	"			82[a]
4	"			55
5	"			68
6	"			79
7	"			15[b]
8	"			64[c]
9				55[d]
10				87
11	"			76[e]
12	"			82

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a. Prepared previously by Trost et al.[4] b. The major product arose by 1,4-addition. c. H. Hanack, E. J. Carnehan, A. Krowizynski, W. Schoberth, L. R. Subramanian, and D. Subramanian, J. Am. Chem. Soc., 101, 100 (1979). d. A 1:1 mixture. e. Prepared previously by Seebach et al.[5]

References and Notes

1. J. R. Matz and T. Cohen, accompanying paper and references cited therein.

2. M. Kahn, Tetrahedron Lett., 4547 (1980).

3. R. W. Holder, H. S. Freiman, and M. F. Stefanchik, J. Org. Chem., 41, 3303 (1976).

4. B. M. Trost, D. E. Keeley, H. C. Arndt, J. H. Rigby, and M. J. Bogdanowicz, J. Am. Chem. Soc., 99, 3080 (1977).

5. A related procedure (SMe in place of SPh) has been applied to substituted cyclopropanes by M. Braun, R. Dammann, and D. Seebach, Chem. Ber., 108, 2368 (1975); however only one case of a vinylcyclobutanone was reported and the yield was low.

6. The deprotonation of substituted analogues of 1 is slow and incomplete.[4]

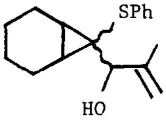
7. (a) T. Cohen, W. M. Daniewski, and R. B. Weisenfeld, Tetrahedron Lett., 4665 (1978); (b) T. Cohen and J. R. Matz, Synth. Commun., 311 (1980).

8. T. Cohen and W. M. Daniewski, Tetrahedron Lett., 2991 (1978).

9. T. Cohen, R. B. Weisenfeld, and R. E. Gapinski, J. Org. Chem., 44, 4744 (1979).

10. M. Braun and D. Seebach, Chem. Ber., 109, 669 (1976).

11. For example, using the conditions most often used by Trost[4] (stannic chloride), the p-anisaldehyde adduct of 2 gave only 39% of 2-p-anisylcyclobutanone and the following compound failed to give any of the desired vinylcylobutanone.



12. Cyclopropanecarboxaldehyde bearing a 1-methoxy group rearranges readily under acid conditions whereas the phenylthio analogue fails to rearrange: B. M. Trost, W. C. Vladuchick, and A. J. Bridges, J. Am. Chem. Soc., 102, 3548 (1980).

13. There are ample precedents for the ready 1,2-rearrangement of cyclopropylcarbinyl cations bearing a 1-oxygen substituent: J. M. Conia and M. J. Robson, Angew. Chem., Int. Ed. Engl., 14, 473 (1975); H. H. Wasserman, M. J. Hearn, and R. E. Cochoy, J. Org. Chem., 45, 2874 (1980), and references cited therein.

14. T. Cohen and J. R. Matz, J. Am. Chem. Soc., 102, 6900 (1980).

15. The conversion of 8 to 9 is not completely general. 1,1-Bis(phenylthio)cyclopropane and its 2-methyl analogue reacted very sluggishly. The analogue of 8 containing a cyclopentane instead of a cyclohexane ring underwent ring opening.

16. K. Tanaka, H. Uneme, and S. Matsui, Chem. Lett., 287 (1980).

17. A. J. Mura, Jr., D. A. Bennett, and T. Cohen, Tetrahedron Lett., 4433 (1975).

18. T. Masuda, N. Furukawa, and S. Oae, Bull. Soc. Chem. Jpn., 51, 2659 (1978).

19. New compounds were characterized by their spectroscopic properties and their exact masses as determined by high resolution mass spectrometry.

20. We are investigating more versatile preparative methods for these substrates.

21. B. M. Trost and L. N. Jungheim, J. Am. Chem. Soc., 102, 7910 (1980).

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