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PREPARATIVE METHODS FOR (Z)-2-METHOXY-1-PHENYLTHIO-1,3-BUTADIENES. REARRANGEMENT DURING COPPER(I)-INDUCED ELIMINATION OF THIOPHENOL FROM SOME γ,δ-UNSATURATED THIOACETALS

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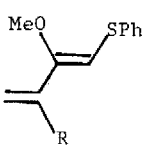
Abstract: (Z)-2-Methoxy-1-phenylthio-1,3-butadienes which are substituted with an alkyl group at the 4-position are not preparable by copper(I)-induced elimination of thiophenol from 4-alkyl-2-methoxy-1,1-bis(phenylthio)-3-alkenes; a 2-step stereospecific synthesis of one such diene (18) is described.

Recent work from this laboratory has demonstrated that treatment of certain unsaturated or vinylogous bis(phenylthio)acetals with the benzene complex of copper(I) trifluoromethanesulfonate (cuprous triflate) in the presence of a hindered amine results in the elimination of benzenethiol and the production of quite satisfactory yields of 1,3-butadienes substituted with a phenylthio group.[1,2] One such diene, which is particularly simple to prepare (eq. 1) in a totally stereospecific manner (despite the fact that the diene produced is the thermodynamically unstable isomer[1]) and which exhibits high reactivity, regioselectivity,[3] and stereoselectivity in Diels-Alder reactions,[1,4,6] is (Z)-2-methoxy-1-phenylthio-1,3-butadiene (3).

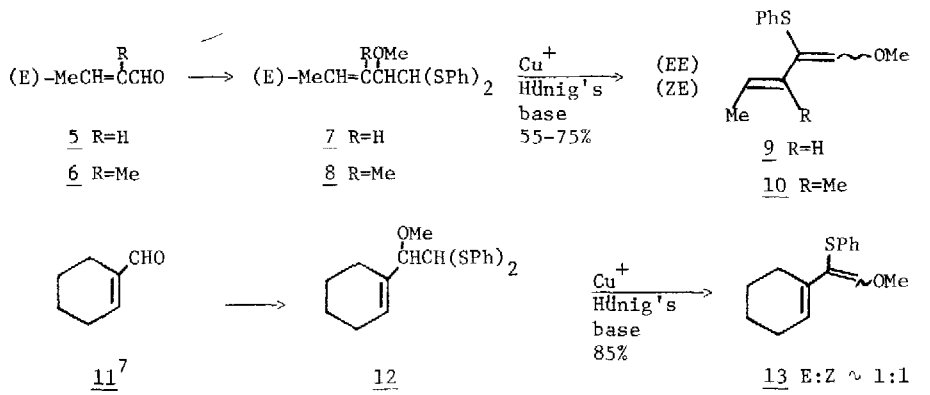
(1) $CH_2=\overset{R}{\overset{|}{C}}CHO \xrightarrow[2.\ Me_2SO_4]{1.\ LiCH(SPh)_2} CH_2=\overset{ROMe}{\overset{|}{C}}CHCH(SPh)_2 \xrightarrow[\text{Hünig's base}]{Cu^+}$ 

1 R=H
2 R=Me

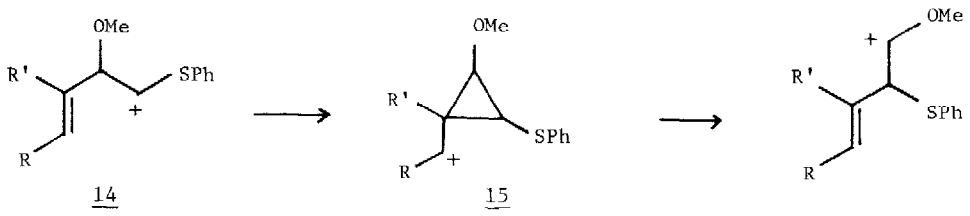
3 R=H
4 R=Me

We have now found that 4 can also be prepared in this way with complete stereospecificity starting from methacrolein (2); the yield in the elimination step ranges from 60 to 85%, with 70-75% being typical. However, it was found that the thioacetals 7, 8, and

12, prepared from the unsaturated aldehydes 5, 6, and 11,[7] respectively, undergo copper(I)-induced loss of thiophenol to produce stereoisomeric pairs of products rather than single stereoisomers. Furthermore, the ^{1}H NMR spectra of these products, although similar to those expected from dienes analogous to 3 and 4, also contained features not in accord with our expectations based on the spectra of 3 and 4. For example, the protons on C-1 and C-4 of the products of these eliminations absorb close to δ 6.6 and 6.0 ppm, respectively, whereas the corresponding protons of 3 and 4 absorb near 5.7 and 4.9-5.5, respectively. The lack of stereospecificity in the elimination and the NMR data made it appear very likely that the positions of the methoxy and phenylthio groups were interchanged as compared to their positions in 3 and 4. Verification of this hypothesis was obtained by cleavage of these three products with chlorotrimethylsilane/sodium iodide which provided α-phenylthio-α,β-unsaturated aldehydes rather than α'-phenylthio-α,β-unsaturated ketones.[8] The structures of the dienes from 7, 8, and 12 are thus 9, 10 and 13, respectively.



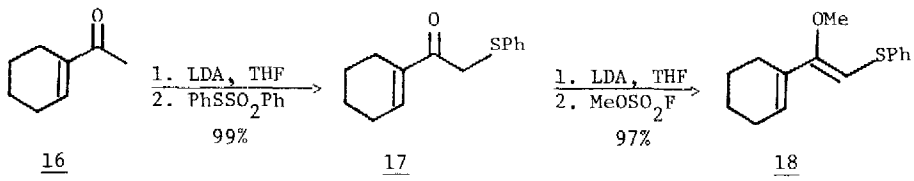
Thus, alkyl groups at the 4-position of the diene system cause a rearrangement during copper(I)-induced elimination, presumably at the carbonium ion stage. This finding can be readily rationalized if the homoallylic cation (14), formed upon removal of thiophenoxide ion by copper(I), undergoes a 1,2-vinyl migration by way of the cyclopropylcarbinyl cation intermediate 15; it is clear that the stability of 15 is greater when R = alkyl than when R = H. This pinacolic 1,2-vinyl migration resembles the pinacolic 1,2-alkyl migration which we used earlier for the ring expansion and chain extension of aldehydes and ketones.[9,10]



14 15

This limitation on our ability to prepare certain 2-methoxy-1-phenylthio-1,3-butadienes was disappointing especially in view of our belief that such dienes in which the C3-C4 vinyl group was incorporated into a ring would be particularly valuable in the construction of molecules of natural origin. A method was therefore sought and found to prepare such a diene in another way. The successful procedure is outlined in the scheme. Commercially available 1-acetylcyclohexene (16) is sulfenylated in 99% yield by adding it to a solution of lithium diisopropylamide (LDA) in tetrahydrofuran (THF) at -78° followed by treatment of the pale yellow solution with phenyl benzenethiosulfonate in the same solvent.[11] The sulfenylated ketone (17) in THF is then added over a one hour period to LDA in THF at -78° and, after the solution has been stirred for a further 30 min, hexamethylphosphoric triamide (2 eq.) is added followed by methyl fluorosulfonate (Magic Methyl, Aldrich, 1.5 eq).[12] The reaction is quenched with NH_4Cl and worked up in the usual way to produce 97% of the stereochemically homogeneous diene (18); the stereochemical outcome is not surprising in view of the steric congestion expected in the E-isomer even if only a moderate degree of planarity of the diene system is maintained. This procedure is not applicable to the preparation of 3; the methylation fails completely and the sulfenylation of methyl vinyl ketone proceeds in very poor yield.[13] Thus, the presently disclosed procedure nicely complements that proceeding by cuprous triflate elmination.[4b]

SCHEME



16 17 18

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References and Notes

1. T. Cohen, A. J. Mura, Jr., D. W. Shull, E. R. Fogel, R. J. Ruffner, and J. R. Falck, J. Org. Chem., 41, 3218 (1976); T. Cohen, R. J. Ruffner, D. W. Shull, E. R. Fogel, and J. R. Falck, Org. Synth., 59, 202 (1980).

2. T. Cohen, R. E. Gapinski and R. R. Hutchins, J. Org. Chem., 44, 3599 (1979).

3. In many cases the regiochemistry appears to be completely dominated by the phenylthio group.[1,4] Trost has reported similar but less pronounced regiocontrol in the 2,3- and 1,4-isomers.[5]

4. (a) Unpublished observations of Zenyk Kosarych. (b) Our work on the uses of the diene discussed in the current paper will be submitted for publication in due course.

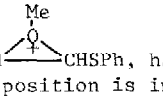
5. B. M. Trost, W. C. Vladuchick, and A. J. Bridges, J. Am. Chem. Soc., 102, 3554 (1980); B. M. Trost and A. J. Bridges, ibid, 98, 5017 (1976); B. M. Trost, J. Ippen, and W. C. Vladuchick, ibid., 99, 8116 (1977).

6. T. Cohen, R. J. Ruffner, D. W. Shull, W. M. Daniewski, R. M. Ottenbrite, and P. B. Alston, J. Org. Chem., 43, 4052 (1978).

7. H. Taguchi, S. Tanaka, H. Yamamoto, and H. Nozaki, Tetrahedron Lett., 2465 (1973).

8. Z. Kosarych and T. Cohen, Tetrahedron Lett., accompanying paper in this issue.

9. T. Cohen, D. Kuhn, and J. F. Falck, J. Am. Chem. Soc., 97, 4749 (1975).

10. An alternative mechanism in which the methoxy group of 14 undergoes a 1,2-migration to produce RCH=C(R')$\overset{+}{C}$HCH(OMe)SPh which then undergoes 1,2-phenylthio group migration is less satisfactory. It appears likely that the first rearrangement would be a 1,2-hydride transfer to form a particularly stable cation were it not for the participation of the electrons of the migrating group. In the case of oxygen the species, RCH=C(R')CH  CHSPh, has negligible charge at C-4 and the necessity of an alkyl group at that position is inexplicable.

11. B. M. Trost and G. S. Massiot, J. Am. Chem. Soc., 99, 4405 (1977).

12. For an example of O-methylation of an enolate under similar conditions, see: J. B. Press and H. Shechter, Tetrahedron Lett., 2677 (1972). See also: ref. 5 and C. J. Heiswolf and H. Kloosterziel, Recl. Trav. Chim. Pays-Bas 89, 1153 (1970); J. P. Boisset, J. Boyer, and J. Rouzaud, C. R. Hebd. Seances Acad. Sci., Ser. C, 263, 1253 (1966).

13. A two step procedure for preparing the same sulfenylation product of methyl vinyl ketone has recently appeared: A. G. Schultz, W. W. Fu, R. D. Lucci, E. G. Kurr, K. M. Lo, and M. Boxer, J. Am. Chem. Soc., 100, 2140 (1978).

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