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CONVERSION OF α,β-UNSATURATED ALDEHYDES AND ESTERS INTO CYCLOPROPANES

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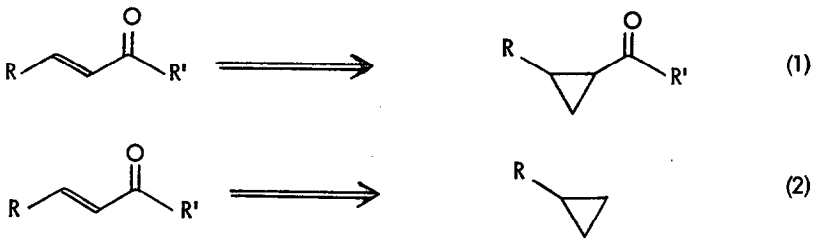
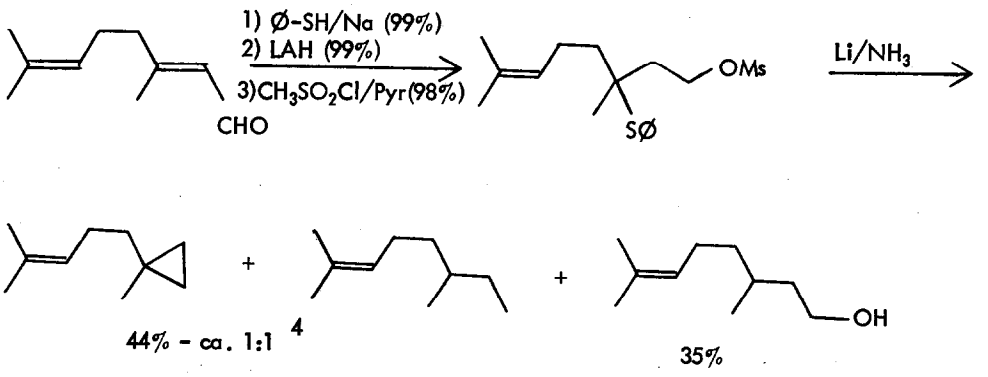
There are a variety of methods for converting the double bond of Michael acceptors into cyclopropanes (eq. 1).[2] In contrast, there is no direct way to prepare the cyclopropane as in equation 2.[3]



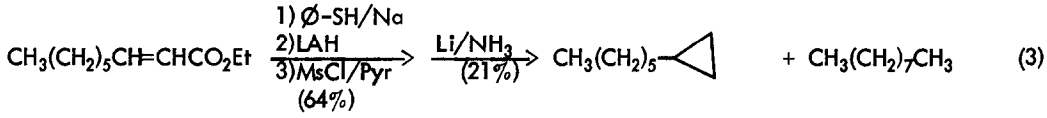
We wish to report a 4-step procedure for this latter transformation (eq. 2, R'=H, OR'). The reaction sequence is illustrated for citral in Scheme 1. The carbonyl oxygen is converted into a leaving group while the beta carbon is made nucleophilic by the Birch reduction of the thiophenyl moiety.

Scheme 1

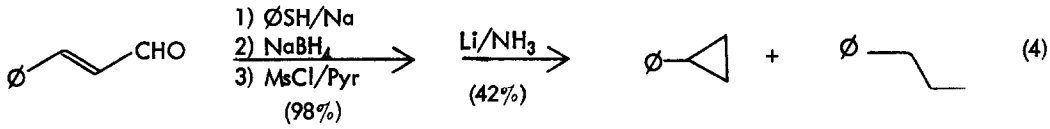


The cyclopropane and open chain analogue are formed in a 44% yield[4] along with a 35% yield of citronellol. The hydrocarbon side product apparently arises by reductive cleavage of both the thiophenyl and mesylate groups.[5] The citronellol is the result of loss of the thiophenyl group and known acyl cleavage of the mesylate.[6] Leaving groups other than mesylate were tried in an attempt to reduce the side reactions; however, tosylate, benzoate, pivalate, diethylphosphate, methoxide and chloride failed to yield any cyclopropane (as judged by ^{1}H nmr) and iodide gave only a small amount. Similarly, adding hexamethylphosphoramide, running the reaction at -78° or substituting calcium for lithium gave no improvement. An attempt to prepare the p-nitrophenyl analogue also failed.

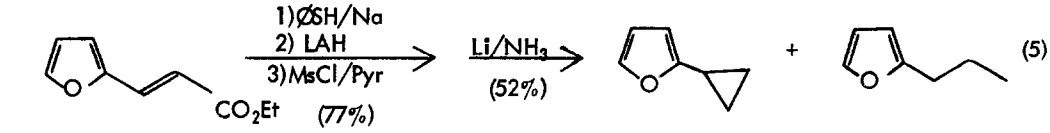
Several other systems were examined. Ethyl-2-nonenoate gave a 21% yield (.7 g: bp 130-138°) of a 1:1 mixture (by vpc and ^{1}H nmr) of 1-cyclopropylhexane and nonane (eq. 3).[7] Cinnamaldehyde similarly yielded a 4:1 mixture (by both vpc and ^{1}H nmr) of cyclopropylbenzene and n-propylbenzene



in 42% yield (.7 g: bp 95° (25 mm)) (eq. 4).[8] Ethyl furylacrylate gave the corresponding cyclopropane



and 2-n-propylfuran in a 13:1 ratio (by ^{1}H nmr) in 52% yield (1.1 g: bp 120-123°) (eq. 5).[9] Carvone



and 1-dodecen-3-one were converted into the necessary thiophenyl mesylate precursors but yielded no cyclopropanes upon treatment with lithium and ammonia. Thus, the procedure appears to be limited to unsaturated aldehydes and esters where the corresponding mesylate is primary.

This novel transformation provides a general method for converting α,β-unsaturated aldehydes and esters into cyclopropanes--an otherwise difficult task.

Typical experimental procedure for citral is as follows: Sodium (.3 g) was reacted with 50 ml of 95% EtOH and 15.4 g (140 mmol) of thiophenol was added. Citral (16.97 g, 100 mmol) was added and after 40 hours the ethanol was removed at reduced pressure. The residue was dissolved in 250 ml ether and washed with 5% NaOH and aqueous NaCl, dried ($MgSO_4$) and concentrated to give 27.5 g (99%) of the Michael type adduct. Reduction with $LiAlH_4$ (1.9 g, 50 mmol) in 60 ml dry ether gave, after work up with dilute HCl, 27.4 g (99%) of the alcohol. A portion of this alcohol (14.0 g, 50 mmol) was dissolved in 15.8 g (200 mmol) of pyridine and 7.44 g (65 mmol) of mesyl chloride was added. After

10 hr at room temperature the reaction mixture was poured into ice water and extracted with ether. This was washed with 5% HCl and aqueous NaCl, dried ($MgSO_4$) and concentrated to give 17.6 g (98%) of the mesylate. This ester (14.3 g, 40 mmol) was dissolved in 250 ml ether and 600 ml liquid ammonia. Lithium was added until the characteristic blue color persisted. After 2 1/2 hr at reflux, solid ammonium chloride was added and the ammonia was allowed to evaporate. The remaining ether was washed with 5% NaOH and aqueous NaCl, dried ($MgSO_4$) and concentrated to yield 7.98 g. This was vacuum distilled: (1) bp 83-85° (70 mm), 2.4 g; (2) bp 70-75° (.1 mm), 2.2 g. Fraction 1 is the mixture of cyclopropane and acyclic compound (44%) (see footnote 4) while fraction 2 had ir, nmr, tlc and vpc identical with citronellol (35%).

Acknowledgment:

We wish to thank Dr. Richard H. Cox for assistance with the ^{13}C nmr spectra and the UGA Office of General Research for partial support of this work.

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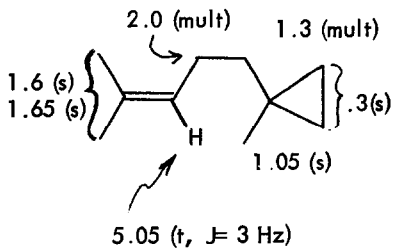
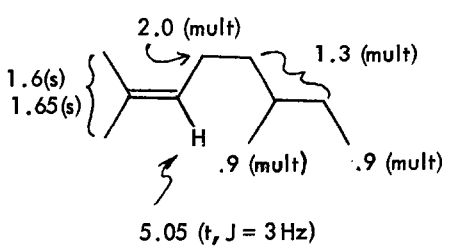
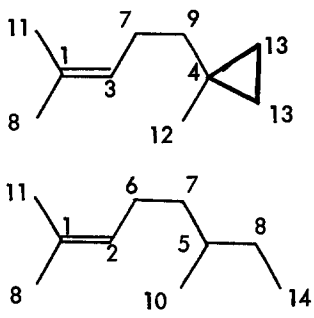
1. Undergraduate research participant.
2. For example: (a) Sulfur ylides, E. J. Corey and M. Chaykovsky, J. Am. Chem. Soc., 87, 1353 (1965) and C. R. Johnson, G. F. Katekar, R. F. Huxol and E. R. Janiga, ibid., 93, 3771 (1971); (b) Pyrazolines, W. J. Greenlee and R. B. Woodward, ibid., 98, 6075 (1976); (c) Carbenes, U. Mende, B. Raduchel, W. Skuballa and H. Vorbruggen, Tetrahedron Lett., 629 (1975); (d) Simmons-Smith Reaction, H. E. Simmons, T. L. Cairns, S. A. Vladuchick and C. M. Hoiness, Org. Reactions, 20, 1 (1973).
3. There are several methods for preparing the corresponding cyclopropanols: (a) Pyrazolines, J. P. Freeman, J. Org. Chem., 29, 1379 (1964); (b) Clemmenson Reduction, C. W. Jefford and A. F. Boschung, Helv. Chim. Acta., 59, 962 (1976); (c) Protected Cyanohydrin Anions, G. Stork, J. C. Depezay and J. d'Angelo, Tetrahedron Lett., 389 (1975).
4. These two products are inseparable--having the same polarity on silica gel tlc and showing only one peak at various temperatures upon vpc analysis (SF-96 column). The one to one ratio derives from ^{13}C nmr data-- carbons 2 and 3 showing about the same intensity. The authentic acyclic product was prepared by $LiAlH_4$ reduction of the tosylate of citronellol and showed the same polarity (tlc) and bp (vpc) as the mixture. Pertinent ^1H nmr data (100 MHz, CCl_4, δ) are as follows:





Analogous ^{13}C nmr data ($CDCl_3$, δ) are as follows (assignments confirmed by off-resonance decoupling):



1	130.80	8	25.75
2	125.24	9	22.78
3	125.13	10	19.17
4	39.80	11	17.60
5	36.92	12	15.41
6	34.24	13	13.12
7	29.55	14	11.41

5. Mesylates are known to cleave under Birch conditions: R. E. Ireland, "Organic Synthesis", Prentice-Hall, Englewood Cliffs, N.J., 1969, p. 90.

6. (a) W. Nagata, T. Sugasawa, M. Narisada, T. Wakabayashi and Y. Hayase, J.Am.Chem.Soc., 85, 2342 (1963); (b) J.F.W.McOmie, "Protective Groups in Organic Chemistry," Plenum Press, 1973.

7. This mixture could be separated by preparative vpc (SF-96 column): 60 MHz 'H nmr (CCl_4)δ 1-cyclopropylhexane- .1 (2H, mult, cyclopropyl), .5 (3H, mult, cyclopropyl), .9 (3H, mult, methyl), 1.4 (10H, br.s, aliphatic chain); nonane- .9 (6H, mult, methyl), 1.3 (14H, br.s., aliphatic chain). A 12% yield (.5 g) of 1-nonanol was also isolated: 60 MHz 'H nmr (CCl_4) δ .9 (3H, mult, methyl), 1.3 (14 H, br.s., aliphatic chain), 2.5 (1H, br.s., OH) 3.5 (2H, t, J=5, methylene).

8. Separation by preparative vpc (SF-96 column) gave pure products: 60 MHz 'H nmr (CCl_4) δ cyclopropylbenzene- .8 (4H, mult, cyclopropyl), 1.8 (1H, mult, benzylic), 7.1 (5H, mult, aromatic), n-propylbenzene- .9 (3H, t, J = 7, methyl), 1.6 (2H, mult, methylene), 2.6 (2H, t, J = 7, methylene), 7.2 (5H, mult, aromatic).

9. These two products are inseparable by tlc and vpc: 60 MHz 'H nmr (CCl_4)δ .8 (mult, cyclopropyl), 1.8 (mult, cyclopropyl and methylene), 2.6 (t, methylene), 5.85 (d, furan), 6.2 (dd, furan), 7.2 (d, furan).