

CLARIFICATION OF THE MECHANISM OF REARRANGEMENT OF ENOL SILYL ETHER EPOXIDES

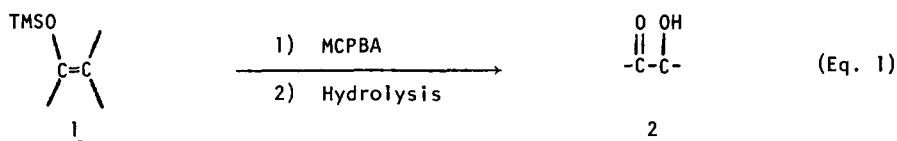
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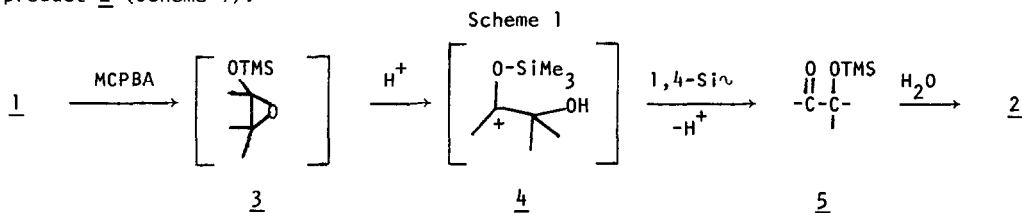
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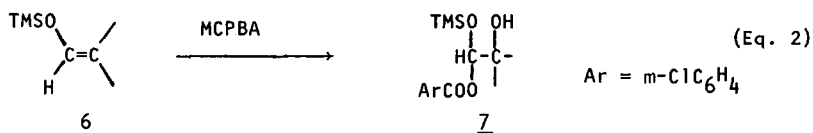
The reaction of enol silyl ethers 1² with m-chloroperbenzoic acid (MCPBA) to afford α -hydroxy ketones 2 has become a generally employed synthetic technique^{3,4} (Eq. 1).



Initial studies^{3b,4a} led to the postulate that the reaction pathway involved the intermediate epoxide 3, which then underwent acid promoted cleavage to afford the carbonium ion 4, and subsequent 1,4-silicon migration gave the α -silyloxy ketone 5. Hydrolysis of 5 afforded the product 2 (Scheme 1).



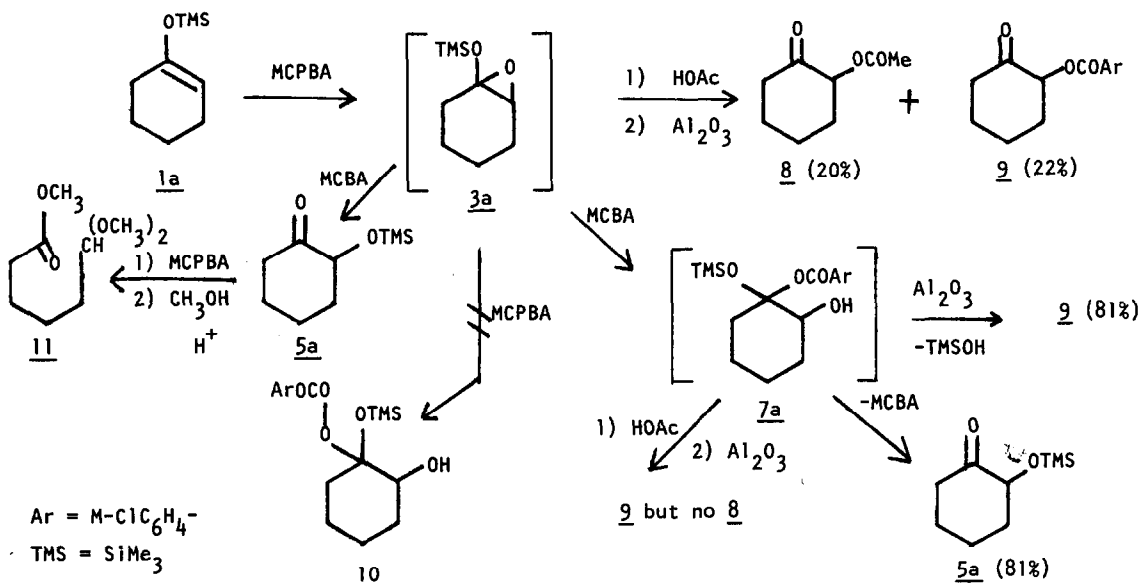
In one instance, a heterocyclic epoxide of type 3 was isolated,^{3b} but numerous other attempts have failed to isolate 3 in the more general carbocyclic case.^{3a,3c,3g,4a,5} Evidence for 4 was obtained when the enol silyl ethers of aldehydes 6 afforded 7^{3c} (Eq. 2). In this case,



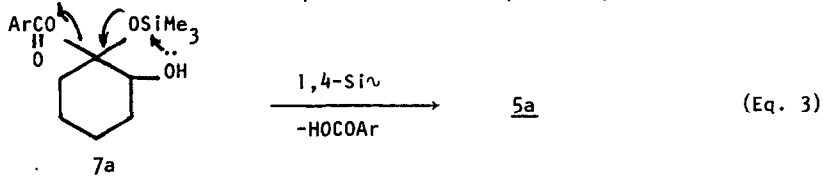
trapping of 4 by *m*-chlorobenzoic acid (MCBA) was competitive with the silicon shift.

We would like to report that intermediates of type 7 are probably generally involved in the mechanistic pathway leading to 5 in the MCPBA oxidation of 1⁶ (Scheme 2).

Scheme 2



Addition of 1a to a solution of MCPBA in either ether or hexane followed by immediate (ca 5 sec) addition of acetic acid and then chromatography over alumina affords a 1:1 mixture (42%) of 8 and 9.^{7,8} Quenching with acetic acid 10 min after the addition of 1a to the MCPBA is complete gives 9 but no 8 after treatment of the reaction mixture with alumina, while normal aqueous workup of the reaction^{3c} after 10 min affords only 5a.⁹ These results indicate that 3a, the initial product of the reaction of 1a with MCPBA, is indeed cleaved by MCBA and that the resulting carbonium ion is trapped to produce 7a. Alumina mediates the transformation of 7a into 9, while in the absence of alumina treatment, 7a is transformed into 5a by the 1,4-silicon shift (Eq. 3). Rapid addition of acetic acid provides a nucleophile capable of competing with



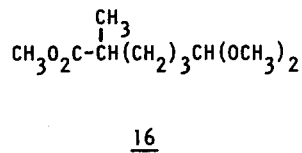
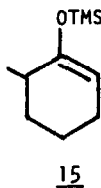
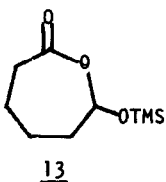
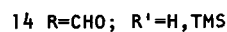
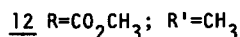
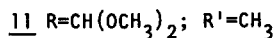
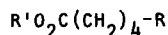
the MCBA for 3a, while addition of acetic acid at a later point has no effect since 3a has already been transformed into 7a.

The established intervention of 7a¹⁰ suggests the intriguing possibility that the use of 2 equivalents of MCPBA in the oxidation of 1 might lead to products which have undergone ring

cleavage, overall the equivalent of ozonolysis of 1a under mild conditions.

Treatment of 1a with MCPBA (2.5 eq) at rt in ether for 18 hr provided a mixture of products (which were isolated after treatment with pTsOH in CH₃OH (rt. 18 h)). Workup and separation by preparative tlc or vpc afforded ester 11 and 12 (1:1.8) in 90% yield. Use of larger excesses of MCPBA resulted in almost exclusive formation of 12. Monitoring the reactions by tlc, confirmed the appearance and disappearance of 5a. This implies that direct capture of 3a by MCPBA did not occur and that 11 and 12 arise by Baeyer-Villiger oxidation of 5a to 13, cleavage, and partial oxidation of the resulting aldehyde 14 by MCPBA.¹¹ Although we were unable to positively confirm the presence of 13 by NMR; evidence in support of this pathway is strong. Oxidation of 5a under comparable conditions with 1.5 eq of MCPBA provides the same mixture of 11 and 12 obtained previously. Further, treatment of 1a with 1.0 eq of MCPBA for 12 hr at rt providing 5a (in situ) followed by further treatment with 1.5 eq of MCPBA again provides, after workup, essentially the same mixture of 11 and 12.

For preparative purposes, use of only 1 eq of MCPBA in the second step allows formation of 11 as the major product (>99:1) in ~70% yield. Finally, the reaction appears to have potential utility since regiospecific oxidation in unsymmetrical cases is possible. Treatment of enol silyl ether 15 as above with successive equivalent portions of MCPBA affords α-methyl ester acetal 16 upon acidic methanol treatment in ~50-60% yield. Only trace amounts of the derived diester appear to be formed. During the Baeyer-Villiger rearrangement, migration of the oxygen substituted carbon occurs exclusively.^{12,13}



ACKNOWLEDGMENT: GMR and JMG acknowledge the financial support of the Research Council of the University of Idaho. RKB, MR and JBM wish to thank the National Cancer Institute of the National Institutes of Health for the award of a research grant (CA-17154) in support of this research.

FOOTNOTES AND REFERENCES:

1. Fellow of the Alfred P. Sloan Foundation (1976-1980); Recipient of a Career Development Award (CA-00273) from the National Cancer Institute of NIH (1976-81).
2. For an excellent review on the synthetic uses of 1, see: J.K. Rasmussen, Synthesis, 91 (1977).
- 3a. G.M. Rubottom, M.A. Vazquez and D.R. Pelegrina, Tetrahedron Lett., 4319 (1974).
- b. A.G. Brook and D.M. Macrae, J. Organomet. Chem., 77, C19 (1974).
- c. A. Hassner, J. Org. Chem., 40, 3427 (1975).
- d. M.E. Jung and C.A. McCombs, Tetrahedron Lett., 2935 (1976).
- e. R.K. Boeckman, Jr. and M. Ramaiah, J. Org. Chem., 42, 1581 (1977).
- f. R.C. Anderson, D.M. Gunn, J. Murray-Rust and J.S. Roberts, J. Chem. Soc. Chem. Commun., 27 (1977).
- g. R.P. Hanzlik and J.M. Hilbert, J. Org. Chem., 43, 610 (1978).
- h. G.M. Rubottom and J.M. Gruber, ibid., 43, 1599 (1978).
4. For oxidation of the closely related ketene acetals, see:
 - a. G.M. Rubottom and R. Marrero, J. Org. Chem., 40, 3783 (1975).
 - b. E. Vedejs, D.A. Engler and J.E. Telschow, ibid., 43, 188 (1978).
5. R.A. Amos and J.A. Katzenellenbogen, J. Org. Chem., 42, 2537 (1977).
6. Presented in part at the 12th Organosilicon Award Symposium, Ames, Iowa, March 11, 1978, section B.
7. It was initially thought that the production of 9 was due to a solvent effect,^{3e} but formation of 9 was subsequently found to be occurring during chromatography of the crude reaction mixture on Woelm activity I alumina.
- 8a. 2-Acetoxycyclohexanone, 8: mp 39.5-40°C (lit. mp 41-42°C; M. Bermann and M Grierth, Justus Liebigs Ann. Chem., 448, 48 (1926)).
- b. 2-(m-Chlorobenzoyloxy)cyclohexanone, 9: mp 62-62°C; NMR (CDCl₃) δ 1.8-2.8(m,8H), 5.5 (m,1H), 7.5 (m,2H), 8.1(m,2H); IR (Nujol) 1730, 1720 cm⁻¹; M⁺ 254, 252. Note that an incorrect mp for 9 was inadvertently reported in ref 3e. Anal. Calcd. for C₁₃H₁₃ClO₃: C, 61.50; H, 5.15. Found: C, 61.67; H, 5.13.
9. 2-Trimethylsilyloxycyclohexanone, 5a: Sample collected with preparative GLPC (5% Se-30; 120°C); NMR (neat) δ 0.06(s,9H), 1.2-2.5(m,8H), 4.09(m,1H); IR (neat) 1725 cm⁻¹; M⁺ 186. Anal. Calcd. for C₉H₁₈SiO₂: C, 58.02; H, 9.74. Found: C, 57.81; H, 9.68.
10. The structure of intermediates 3a and 7a is inferred from their chemical behavior, they have not been isolated or spectroscopically observed.
11. Oxidation of hydroxyl groups has been observed: E.G. Rozantzev and M.B. Neiman, Tetrahedron, 20, 131 (1964).
12. For an example of such an oxidative cleavage, see L. Knof, Ann., 656, 183 (1962).
13. Satisfactory spectral data and high resolution mass spectral or elemental analysis has been obtained for 15 and 16.

(Received in USA 24 July 1978)