Registry No.—4-Hydroxy-4-methylcyclohexadienone, 23438-23-5.

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A Simple Procedure for the Epoxidation of Acid-Sensitive Olefinic Compounds with *m*-Chloroperbenzoic Acid in an Alkaline Biphasic Solvent System[1]

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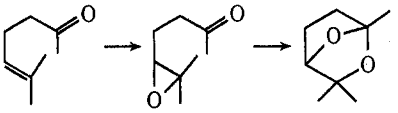
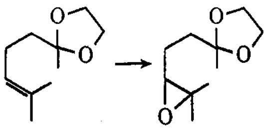
The epoxidation of acid-sensitive olefins or the epoxidation of olefins yielding acid-sensitive epoxides are typically conducted in the presence of a buffer such as solid sodium carbonate, sodium bicarbonate, or disodium hydrogen phosphate.[2] During the course of our research we found the solid buffer–single solvent procedure to be unsuited for certain acid-sensitive compounds. We wish to report a mild and simple epoxidation procedure using a two-phase system which proved superior to the single solvent method for the epoxidation of acid-sensitive compounds.

The epoxide 2, derived from 6-methylhept-5-en-2-one (1), is known to undergo very facile rearrangement to 1,3,3-trimethyl-2,7-dioxabicyclo[2.2.1]heptane (3).[3] This rearrangement occurs thermally and is acid catalyzed. The preparation of the unstable epoxide, 2, has previously been accomplished by careful epoxidation of 1 in methylene chloride using peracetic acid–sodium acetate.[3a] When we attempted to prepare 2 using *m*-chloroperbenzoic acid–sodium bicarbonate we obtained a mixture of 2 and 3 in approximately equal proportion (as estimated by nmr[4]). Epoxidation of 1 with *m*-chloroperbenzoic acid in a dichloromethane–aqueous sodium bicarbonate biphasic system led to the formation of 2 in high yield (83–85%) with no detectable amounts of the rearranged product, 3.[4]

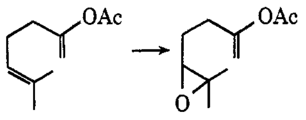


1 **2** **3**

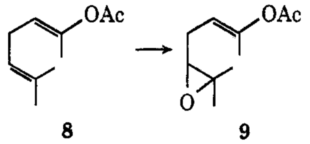
Similar biphase epoxidation of the ketal 4 and enol acetates 6 and 8 proceeded smoothly to give 5, 7, and 9, respectively, in 80–85% yields.[5,6]



4 **5**



6 **7**



8 **9**

In a study of the scope of this reaction we examined the biphasic epoxidation of simple mono-, di-, and trisubstituted olefins.[7] Table I[8] gives the results of this study and it is evident that the two-phase epoxidation procedure can be extended to mono- and disubstituted olefins. Furthermore, the yields of epoxides were comparable to those obtained by a single solvent procedure.[8]

TABLE I

TWO-PHASE EPOXIDATION OF OLEFINS WITH *m*-CHLOROPERBENZOIC ACID

Compd	Olefin–peracid ratio, *M*	Reaction time, hr	Product[a]	Yield, %[b]
Cyclohexene	1:1	4	Cyclohexene oxide[c,e]	71
1-Hexene	1:1	9	1,2-Epoxyhexane[d]	56
Limonene	1:1	2	1,2-Epoxy-*p*-menth-8-ene[e]	85
Limonene	1:2	4	1,2,8,9-Diepoxy-*p*-menthane[e]	66
Limonene	1:3	4	1,2,8,9-Diepoxy-*p*-menthane[e]	68

[a] Products were characterized by nmr, ir, glc, and mass spectrometry. [b] Yields were calculated by glc. [c] Reference 8a. [d] Reference 8b. [e] Reference 8c.

In the case of limonene (*p*-mentha-1,8-diene) the two-phase epoxidation procedure was compared with the epoxidation using *m*-chloroperbenzoic acid in dichloromethane. With 1 equiv of peracid both procedures gave selective epoxidation of the trisubstituted double bond in identical yields (a slightly longer reaction time was required in the two-phase system).

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[1] This research was supported by Grant 1 R01 CA11880 from the National Cancer Institute, National Institutes of Health.

[2] D. Swern in "Organic Peroxides," Vol. II, D. Swern, Ed., Wiley-Interscience, New York, N. Y., 1971, pp 355–533.

[3] (a) E. Klein and W. Rojahn, *Dragoco Rep. Engl. Ed.*, **14**, 155 (1967); (b) Y. Gaoni, *J. Chem. Soc. C*, 2925 (1968).

[4] 5,6-Epoxy-6-methylhepten-2-one (**2**) quantitatively rearranged to **3** during attempted glc analysis; so the crude reaction mixture, following workup, was analyzed by nmr. In the nmr spectrum of **2** (CCl$_4$) the C-1 methyl appeared at τ 7.87 and in the spectrum of **3** the C-1 methyl appeared at τ 8.52.

[5] **4** was prepared from **1** by *p*-toluenesulfonic acid catalyzed ketalization; **6** and **8** were prepared from **1** by BF$_3$-catalyzed enol acetylation (the two isomers could be separated by spinning band distillation and preparative glc). All compounds were characterized by mass spectrometry, ir, and nmr (including spin-decoupling studies).

[6] For an example of epoxidation of an isolated double bond in the presence of an enol acetate, see R. B. Moffet and G. Slomp, Jr., *J. Amer. Chem. Soc.*, **76**, 3678 (1954).

[7] Water is known to decrease the rate of peracid epoxidation of olefins and the presence of aqueous sodium bicarbonate would be expected to increase the rate of peracid decomposition.[2]

[8] (a) G. B. Payne, P. H. Deming, and P. H. Williams, *J. Org. Chem.*, **26**, 659 (1961); (b) D. J. Pasto and C. C. Cumbo, *ibid.*, **30**, 1271 (1965); (c) B. A. Arbuzov and B. M. Mikhailow, *J. Prakt. Chem.*, **127**, 92 (1932) [*cf. Chem. Abstr.*, **24**, 4285 (1932)].

With 2 equiv of peracid both procedures afforded diepoxide in identical yields.

The two-phase epoxidation method is illustrated in the following procedure for the synthesis of **9**. Solid *m*-chloroperbenzoic acid (2.029 g, 0.01 mol[9]) was slowly added in small portions to a magnetically stirred mixture of **8** (1.68 g, 0.01 mol) in dichloromethane (100 ml) and 0.5 *M* aqueous sodium bicarbonate (30 ml, pH 8.3). The mixture was stirred at room temperature for a period of 2 hr following the addition of the peracid (the consumption of peracid was tested with starch–iodide paper) and the two phases were separated. The organic phase was washed successively with 1 *N* sodium hydroxide (30 ml) and water (30 ml) and dried (Na_2SO_4). The methylene chloride was removed under reduced pressure to yield 1.7 g of crude product which was shown by glc to contain 86% of the desired product, **9**: ir (CCl_4)[10] 1760 (C═O), 1698 (C═C), 1391, 1383, 1374, 1239, 1215, and 1153 cm^{-1}; nmr (CCl_4) τ 8.73 (s, 6 H, C-7 and C-8), 8.13 (br s, 3 H, C-1), 7.93 (s, 3 H, $-COCH_3$), 7.53 (m, 2 H, C-4), 7.35 (m, 2 H, C-5), and 4.88 (t of q, $J_{3,4}$ = 6.5, $J_{3,1}$ = 0.8 Hz, 1 H, C-3).

The epoxidation procedure described herein should be very useful for the preparation of acid-sensitive epoxides. The reactivity of the peracid is slightly diminished in the aqueous biphasic media; however, the system is still sufficiently reactive to epoxidize simple monosubstituted double bonds.

Registry No.—**1,** 110-93-0; **2,** 16262-93-4; **3,** 16194-31-3; **4,** 3695-38-3; **5,** 39810-29-2; **6,** 39810-30-5; **7,** 39810-31-6; **8,** 39810-32-7; **9,** 39810-33-8; *m*-chloroperbenzoic acid, 937-14-4.

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[9] The calculated molarity of the *m*-chloroperbenzoic acid was based on the 85% purity of the commercial peracid.

[10] The ir of isomeric enol acetate **7** showed absorptions at 1764 (C═O), 1675 (C═C), 1385, 1374, 1225, 1200, and 1170 cm^{-1}. The nmr spectra of **7** and **9** were also quite different.