New Epoxidation with *m*-Chloroperbenzoic Acid at Elevated Temperatures

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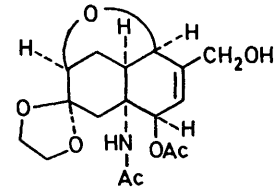
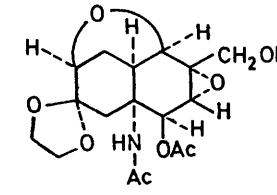
Summary Methyl methacrylate, a cyclic olefin, and two alk-1-enes are efficiently converted into their corresponding epoxides by *m*-chloroperbenzoic acid at elevated temperatures in the presence of a small amount of a radical inhibitor, which prevents thermal decomposition of the peracid.

IN the course of an investigation directed towards a total synthesis of tetrodotoxin,[1] conversion of the olefin (I) into the epoxide (II) was required. This seemingly easy step turned out to be difficult because the double bond in the olefin (I) has exceptionally poor reactivity towards peracids such as *m*-chloroperbenzoic acid, peracetic acid, and performic acid. Epoxidation at an elevated temperature was considered; however, thermal decomposition of the peracid becomes a problem and the possibility that it might be suppressed in the presence of some radical inhibitor was investigated.†



(I)



(II)

† T. M. Luong and D. Lefort observed that the decomposition of perbenzoic acid in cyclohexane at 80 °C is suppressed in the presence of *p*-benzoquinone or hydroquinone (*Bull. Soc. chim. France*, 1962, 827). However, these inhibitors are not effective enough for the present purpose.

Thus, the decomposition of *m*-chloroperbenzoic acid in ethylene dichloride at 90 °C in the presence of several commercially available radical inhibitors was examined.‡ The results in the Table show that decomposition of the peracid is suppressed in the presence of some radical inhibitors, the best of which is 4,4′-thiobis-(6-t-butyl-3-methylphenol) (t.b.p.); 100% recovery was achieved on heating (3 h; 90 °C) *m*-chlorobenzoic acid (20 mg) with t.b.p. (0·2 mg) in ethylene chloride (2 ml), 30% recovery was achieved in the presence of 0·02 mg inhibitor.

TABLE

Decomposition of m-*chloroperbenzoic acid in the presence of radical inhibitors*[a]

Radical Inhibitor	Peracid remaining[b] (%) After 1 h heating	After 3 h heating
4,4′-Thiobis-(6-t-butyl-3-methylphenol)	100	100
2,6-Di-t-butyl-4-methylphenol	90	77
4,4′-Butylidenebis-(6-t-butyl-3-methylphenol	91	20
Dilauryl 3,3′-thiodipropionate	93	<10
Distearyl 3,3′-thiodipropionate	55	<10
Hydroquinone	~30[c]	—
None	27	—

[a] *m*-Chloroperbenzoic acid (20 mg) was heated at 90 °C in ethylene dichloride (2·0 ml) containing 0·2 mg inhibitor; [b] Determined iodimetrically; [c] The end point of the iodimetric titration is not very clear because of the yellow colour developed on heating.

Accordingly the olefin (I) was treated with 1·2 equiv. of *m*-chloroperbenzoic acid in ethylene dichloride containing a small amount of t.b.p., at 90° for 2 h, to afford the desired epoxide (II) (> 95%).§

To extend the procedure to general use, the epoxidation of oct-1-ene, dodec-1-ene, and methyl methacrylate was examined. These olefins are known to have a poor reactivity towards peracids and hence trifluoroperacetic acid has been used for epoxidation of these.[2,3] Oct-1-ene, dodec-1-ene, or methyl methacrylate (100 mg) was heated (90°, 1 h) in ethylene dichloride (5 ml) containing *m*-chloroperbenzoic acid (1·2 equiv.) and t.b.p. (1—2 mg), the yield of epoxide is almost quantitative (g.l.c.).

The new procedure has advantages over the use of trifluoroperacetic acid which has to be used in basic or buffered solution to prevent opening of the epoxide ring by CF_3CO_2H generated from the peracid.[3]

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§ Epoxidation of (I) with *m*-chloroperbenzoic acid (excess) at 90 °C in the absence of the radical inhibitor gave a complex mixture.

[1] Y. Kishi, M. Aratani, H. Tanino, T. Fukuyama, F. Nakatsubo, T. Goto, S. Inoue, H. Kakoi, and S. Sugiura, Abstracts of the Third International Congress on Heterocyclic Chemistry, Sendai, 1971, p. 49.

[2] D. Swern, G. N. Billen, and J. T. Scanlan, *J. Amer. Chem. Soc.*, 1946, **68**, 1504; W. D. Emmons, A. S. Pagano, and J. P. Freeman, *ibid.*, 1954, **76**, 3472.

[3] W. D. Simmons and A. S. Pagano, *J. Amer. Chem. Soc.*, 1955, **77**, 89.