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FORMATION OF α,β-EPOXY SYSTEMS FROM β-PEROXY CARBON FREE RADICALS

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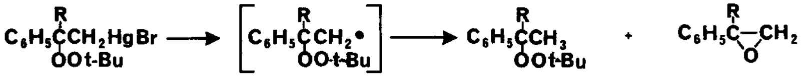
Abstract: The conversion of β-peroxy carbon free radicals to α,β-epoxides is a facile process of broad scope and may be a key step in the biosynthesis of clavulones.

In 1971 Bloodworth and Bylina reported that the reduction of the peroxy mercurial 1 by sodium borohydride in aqueous tetrahydrofuran (THF) afforded in addition to the expected demercurated peroxide (2), styrene oxide (3) in a ratio of 4:1.[1] The analogous reaction of the tertiary peroxide 4 also gave a mixture of peroxide (5) and epoxide (6) with the latter predominating by as much as 6:1. It was proposed[1] that epoxide formation occurs by intramolecular attack of the carbon radical produced by the borohydride demercuration[2] on the nearest peroxy oxygen with displacement of the t-butylperoxy radical. The generality of this process is relevant to a proposed biosynthesis[3a] of the clavulones (see Chart I).[3b] We report herein four additional and diverse examples of the transformation of β-peroxy carbon radicals to α,β-epoxy systems which indicate that this process is both general and feasible biosynthetically.

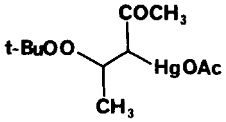


1 R=H
4 R=CH$_3$

2 R=H
5 R=CH$_3$

3 R=H
6 R=CH$_3$

The reaction of the β-peroxy mercurial 7[4] in THF at 0° with a slight excess of sodium borohydride in basic aqueous solution afforded an E/Z mixture of epoxy ketones 8 as the sole products.



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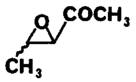
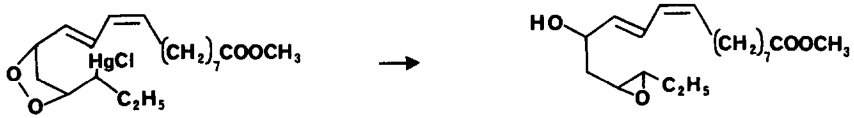


8

Peroxymercuration of 2-cyclohexen-1-ol with t-butyldimethylsilyl hydroperoxide[5] - mercuric trifluoroacetate at -90° in methylene chloride, removal of solvent in vacuo and reduction of a THF solution of the resulting peroxy mercurial with aqueous borohydride afforded 66% of trans-2,3-epoxycyclohexanol, identical in all respects with an authentic sample.[6] In a similar way 2-cyclopenten-1-ol was converted to trans-2,3-epoxycyclopentanol.

Finally, of closest relevance to clavulone biosynthesis is the reduction of the peroxy mercurial 9[7] which proceeded at -78° in THF using sodium trimethoxy borohydride under argon to form as major product the epoxy alcohol 10[8] which was isolated in 40% yield after chromatography on silica gel.

The transformation of β-peroxy carbon radicals to α,β-epoxy systems is clearly a facile process.[9]



9 **10**

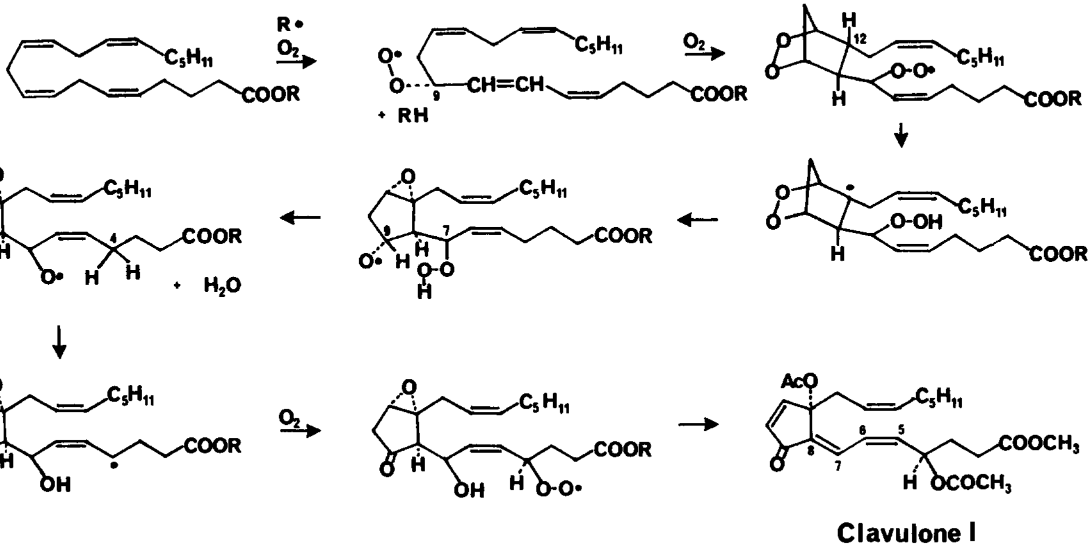


CHART I

References and Notes

1. A. J. Bloodworth and G. S. Bylina, J. Chem. Soc. Perkin I, 2433 (1972).
2. Much evidence has been accumulated in recent years that the reduction of organomercurials by sodium borohydride generates radicals. See inter alia (a) F. G. Bordwell and M. L. Douglass, J. Am. Chem. Soc., 88, 993 (1966); (b) D. J. Pasto and J. A. Gontarz, ibid., 91, 719 (1969); (c) G. M. Whitesides and J. San Filippo, ibid., 92, 6611 (1970); (d) B. Giese, Chem. Ber., 112, 3766 (1979).
3. (a) E. J. Corey, Experientia, in press; (b) H. Kikuchi, Y. Tsukitani, K. Iguchi, and Y. Yamada, Tetrahedron Letters, 23, 5171 (1982); 24, 1549 (1983).
4. A. J. Bloodworth and R. J. Bunce, J. Chem. Soc. (C), 1453 (1971).
5. Prepared from t-butyldimethylsilyl chloride, imidazole and dry ethereal hydrogen peroxide followed by extractive isolation and chromatography on Florisil.
6. P. Chamberlin, M. L. Roberts and G. H. Whitham, J. Chem. Soc. (B), 1374 (1970).
7. The preparation of 9 was accomplished by the sequence: (1) conversion of linolenic acid to the 13-hydroperoxide by oxidation with soybean lipoxygenase, (2) esterification with diazomethane, (3) internal peroxymercuration in THF with mercuric chloroacetate, and (4) extractive isolation from aqueous sodium chloride.
8. The structures of 9 and 10 were confirmed by UV absorption and 270 MHz pmr data.
9. This research was assisted financially by a grant from the National Science Foundation.

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