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STEREOSELECTIVE OLEFINIC CYCLIZATION ASSISTED BY THE SELENYL GROUP ——— BIOGENETIC-TYPE SYNTHESIS OF CAPARRAPI OXIDE

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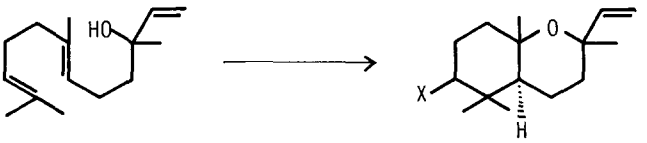
Summary: The acid catalysed cyclization of β-hydroxy selenide (4), which was prepared from nerolidol (1) *via* the epoxide (3), was carried out to give bicyclic ether (5) directly which was further transformed into caparrapi oxide (6).

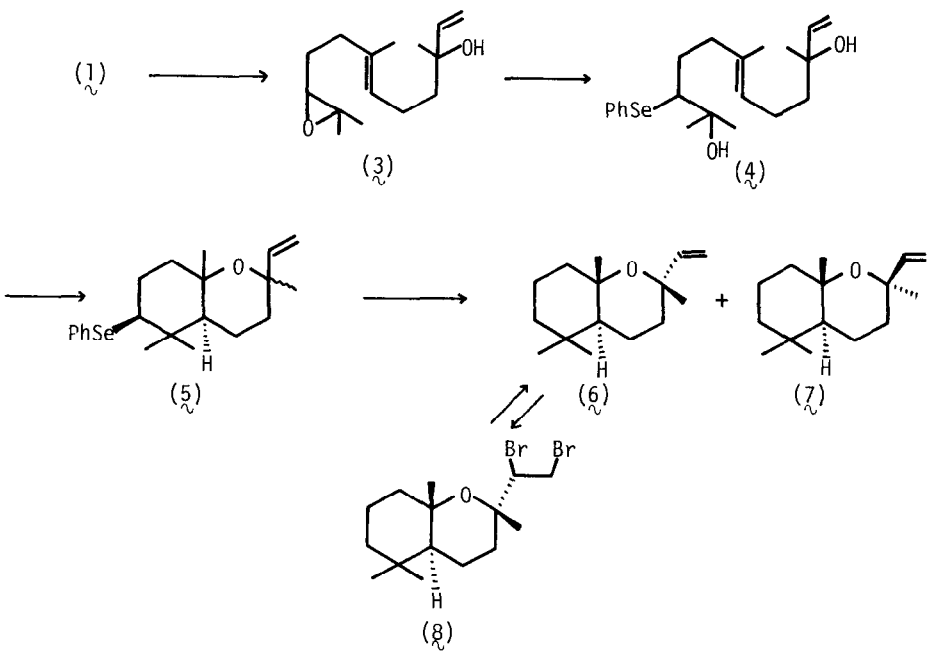
Studies concerning the polyolefinic cyclization have been accumulated in the literatures and such reactions have been proven to be one of the most effective way to construct polycyclic carbon frameworks.[1] Recently attention has been focused on the incorporation of bromine atoms into cyclic systems *via* bromonium ion initiated polyolefinic cyclization[2] because of increasing occurrence of bromine-containing natural products from marine organisms.[3] It could be easily speculated by the coupling of our first findings[4] that the acidic treatment of olefinic β-hydroxy selenides afforded cyclic selenides resulting from the participation of olefins with seleniranium ions formed *in situ* and the known procedure[6] for the conversion of carbon-selenium bonds into carbon-halogen linkages would lead to a net brominative cyclization. In case of the cyclization reactions[7,8] of nerolidol (1) by using various types of reagents, bicyclic systems, shown in scheme 1 could not be formed[7] or could be formed only in low yield.[8] Therefore we investigated the cyclization of β-hydroxy selenide (4) to examine whether such bicyclic selenide (5) could be formed directly or not. Here we wish to report the direct formation of 5 by acidic treatment of 4.



(1) (2)

Scheme 1

The epoxide (3), prepared by treatment of nerolidol (1) with m-chloroperbenzoic acid in dichloromethane and saturated sodium hydrogencarbonate aqueous solution, was treated with phenylselenium anion[9] generated in situ by reduction of diphenyldiselenide with sodium borohydride gave the β-hydroxy selenide (4) in 62 % yield [$\nu_{max}^{CHCl_3}$ 3600 cm^{-1}; δ (CCl_4) 1.20 (6H, s, 2 × Me), 1.30 (3H, s, Me), 1.57 (3H, s, Me), 3.0 (1H, dd, J = 3 and 11 Hz, PhSeCH-), 4.83 - 6.70 (4H, m, olefinic protons), and 7.07 - 7.67 (5H, m, aromatic protons); m/e 394, 396 (M^+)]. The β-hydroxy selenide (4) thus obtained was then subjected to acid catalysed cyclization as follow. A solution of 4 in dichloromethane containing trifluoroacetic acid was stirred for 5 min at 0°C to afford the bicyclic selenide (5) in 21 % yield [m/e 376, 378 (M^+)] as a diastereoisomeric mixture at C-8 position. The stereochemistry at the selenium-bearing carbon was easily deduced by the appearance of axial proton as a broad doublet of doublets (J = 4 and 12 Hz) at 3.0 ppm in its nmr spectrum. To confirm the structure including the stereochemistry at all the chiral centers, 5 was treated under nitrogen with tri-n-butyltin hydride to remove the phenylseleno group by reduction[10] to yield a ca. 1 : 1 mixture of bicyclic ethers (6 and 7) in 77.3 % yield. Although the separation of 6 and 7 was somewhat difficult, this was overcome by taking advantage of faster bromination of caparrapi oxide (6) with equatrial vinyl group than its C-8 epimer (7) with axial vinyl group by monitoring its nmr spectrum followed by separating the dibromide (8) thus obtained from 7 by passing through silica gel column with n-hexane-benzene as eluent. The dibromide (8) was then subjected to reductive elimination of bromine by zinc powder in ether and acetic acid to regenerate caparrapi oxide (6). The compounds 6 and 7 thus obtained were identical with authentic samples in their nmr specrta.[11]



Scheme 2

Thus we could confirm the stereochemical course in the cyclization of β-hydroxy selenide (4) giving the bicyclic ether (5). Conversion of phenylseleno group into other functional groups is now under investigation.

References and Notes

1 For reviews: See a) M. Julia, Acc. Chem. Res., 8, 152 (1975); b) W. S. Johnson, Bioorg. Chem., 5, 51 (1976); c) W. S. Johnson, Angew. Chem. Int. Edn. Engl., 15, 9 (1976); d) J. K. Sutherland in "Stereoselective Synthesis of Natural Products", Proceedings of the Seventh Workshop Conference, Hoechst, Schloss Reisensburg, 24 - 27, September, 1978, Eds. W. Bartmann and E. Winterfeldt, Excerpta Medica, Amsterdam-Oxford, 1979, pp. 142 - 150; e) M. Matsuki, M. Kodama, and S. Ito, Tetrahedron Lett., 2901 (1979); f) M. B. Gravestock, D. R. Morton, S. G. Boots, and W. S. Johnson, J. Am. Chem. Soc., 102, 800 (1980); g) E. E. Van Tamelen and D. G. Loughhead, ibid., 102, 869 (1980); h) Y. Yamada, S. Nakamura, K. Iguchi, and K. Hosaka, Tetrahedron Lett., 22, 1355 (1981).

2 a) A. G. González, J. D. Martin, C. Pérez, and M. A. Ramirez, Tetrahedron Lett., 137 (1976); b) L. E. Wolinsky and D. J. Faulkner, J. Org. Chem., 41, 597 (1976); c) T. Kato, I. Ichinose, A. Kamoshida, and Y. Kitahara, J. Chem.

Soc. Chem. Commun., 518 (1976); d) T. R. Hoye and M. J. Kurth, J. Org. Chem., 43, 3693 (1978); e) T. R. Hoye and M. J. Kurth, J. Am. Chem. Soc., 101, 5065 (1979); f) T. Kato and I. Ichinose, J. Chem. Soc. Perkin Trans. I, 1051 (1980).

3 a) P. J. Sheuer, "Chemistry of Marine Natural Products", Academic Press, New York, N.Y., 1973; b) J. T. Baker and V. Murphy, "Compounds from Marine Organisms", CRC Press, Cleveland, Ohio, 1976, Vol. 1; c) D. J. Faulkner and W. Fenical, "Marine Natural Products Chemistry", Plenum Press, New York, 1977.

4 a) T. Kametani, K. Suzuki, H. Kurobe, and H. Nemoto, J. Chem. Soc. Chem. Comm., 1128 (1979); b) Idem, Chem. Pharm. Bull., 29, 105 (1981); c) T. Kametani, H. Kurobe, and H. Nemoto, J. Chem. Soc. Chem. Commun., 762 (1980); d) Idem, J. Chem. Soc. Perkin Trans. I, 756 (1981). After first proposal for the general procedure of carbon-carbon bond formation via selenium-mediated olefinic cyclization, the same type of cyclization of alkenyl-substituted β-dicarboxy compounds has been reported.[5]

5 a) W. P. Jackson, S. V. Ley, and A. J. Whittle, J. Chem. Soc. Chem. Commun., 1173 (1980); b) W. P. Jackson, S. V. Ley, and J. A. Morton, ibid., 1028 (1980).

6 a) M. Sevrin, W. Dumont, L. Hevesi, and A. Krief, Tetrahedron Lett., 2647 (1976); b) M. Sevrin and A. Krief, J. Chem. Soc. Chem. Commun., 656 (1980).

7 T. R. Hoye and M. J. Kurth, J. Org. Chem., 44, 3461 (1979).

8 T. Kato, K. Ishii, I. Ichinose, Y. Nakai, and T. Kumagai, J. Chem. Soc. Chem. Commun., 1106 (1980).

9 K. B. Sharpless and R. F. Laner, J. Am. Chem. Soc., 95, 2697 (1973).

10 D. L. J. Clive, G. Chittattu, and C. K. Wong, J. Chem. Soc. Chem. Commun., 41 (1978).

11 P. Lombardi, R. C. Cookson, H. P. Weber, W. Renold, A. Hauser, K. H. Schulte-Elte, B. Willhalm, W. Johmmen, and G. Ohloff, Helv, Chim. Acta, 59, 1158 (1976).

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