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REGIOSELECTIVE REACTION OF PHENYLSULFENYL ALLYLIC CARBANION WITH EPOXIDE AND SYNTHESIS OF PROSTAGLANDIN INTERMEDIATE

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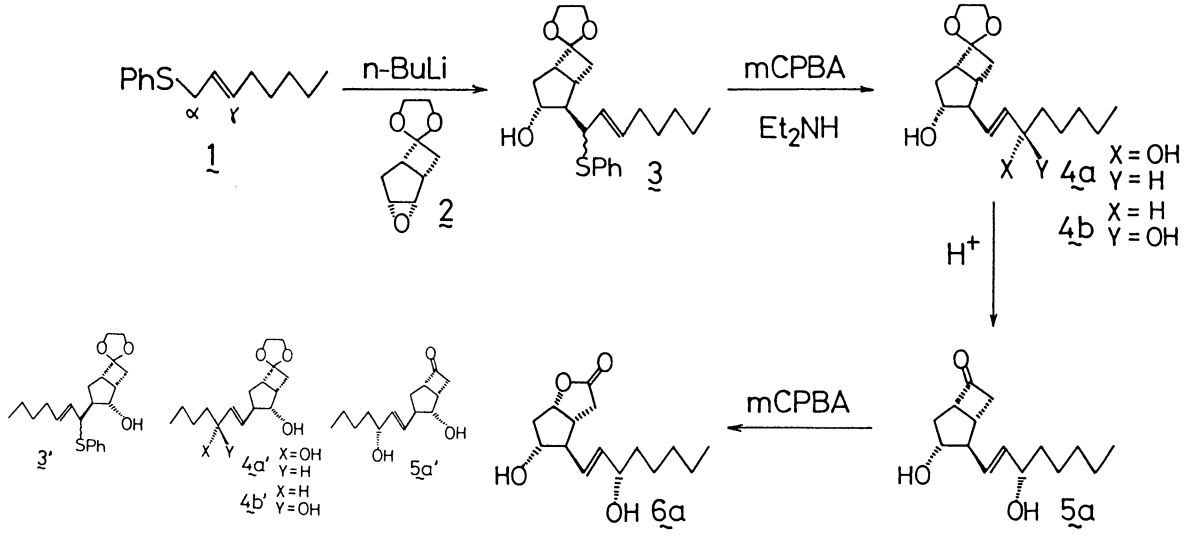
An ambident nucleophile derived from 1-phenylsulfenyloct-2-ene reacts at the α-carbon with epoxide. The reaction has been employed for the preparation of a key intermediate for synthesis of prostaglandins.

1-Phenylsulfenyloct-2-ene (1) is a useful and inexpensive synthetic equivalent to form the ω-chain of prostaglandins. Actually, PGE was synthesized effectively via 1,4-addition reaction of the allylic carbanion derived from 1 with cyclopentenone derivatives.[1] We report here a further application of the carbanion to the synthesis of prostaglandin intermediate 6a via reaction with epoxide 2.[2] The synthesis was carried out as shown below.



The carbanion, prepared from 1 by treatment with butyllithium in tetrahydrofuran at -45 °C, was treated with the epoxide 2 at -78 °C to give 3. The product (87% yield) was a diastereomeric mixture of 3 and 3' which could not be separated by chromatographic procedure. We could not detect a product resulted from the reaction at the γ-position of phenylsulfenyl allylic carbanion with the epoxide.[3] Therefore, the mixture was converted to allylic alcohol 4 by treating with m-chloroperbenzoic acid (mCPBA) and then with diethylamine in methanol.[4] The products were separated to two parts by silica gel column chromatography (AcOEt/hexane=1/3 as eluent). The polar part (Rf=0.44; AcOEt) and the less polar part (Rf=0.56; AcOEt) were assigned to 4a and 4b which contained one of the regioisomers (4a' or 4b') respectively. The acid hydrolysis of 4a to 5a and of 4b

to 5b were carried out separately. The desired product 5a (Rf=0.62; AcOEt, 84%)[5] and a regioisomer 5a' or 5b' (Rf=0.44; AcOEt, 13%)[6] were separated from the reaction mixture by column chromatography on silica gel (AcOEt/hexane=1/2). Similarly, 5b (Rf=0.65; AcOEt, 75%)[7] and 5a' or 5b' (Rf=0.60; AcOEt, 17%)[8] were obtained. The total yield of 5a was 30% and that of 5b was 26% based on the epoxide 2. The Baeyer-Villiger oxidation of 5a afforded the prostaglandin intermediate 6a in 86% yield.[9]

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References

1) J. Nokami, T. Ono, A. Iwao, and S. Wakabayashi, Bull. Chem. Soc. Jpn., 55, 3043(1982).

2) A similar reaction (sulfur-stabilized allylic carbanion with epoxide) has been reported; a) 1,3-bis(methylthio)allyllithium; E. J. Corey, B. W. Erickson, and R. Noyori, J. Am. Chem. Soc., 93, 1724(1971); b) carbanion derived from dihydrothiopyran; K. Kondo, A. Negishi, and D. Tunemoto, J.C.S. Chem. Commun., 1311(1972); S. Torii, H. Tanaka, and Y. Tomotaki, Chem. Lett., 1541(1974); c) intramolecular reaction of the carbanion derived from epoxygeranyl phenylsulfide; M. Kodama, Y. Matsuki, and S. Ito, Tetranedron Lett., 1121(1976).

3) The reaction of the carbanion with cyclohexene oxide gave the α-product (ca. 90% yield) and a trace of γ-product, though that with propylene oxide gave a mixture of α- and γ-products in the ratio of ca. 4/1 (quantitative yield).

4) The sulfide (5.56 g, 14.3 mmol) in 10 ml of methanol was treated with mCPBA (2.45 g, 14.2 mmol) at 0 °C for 10 min and followed with diethylamine (4.4 ml, 42.5 mmol) at r.t. for 10 h. It was impossible to convert the isolated pure sulfoxide to the corresponding allylic alcohol 4.

5) 5a: ^{13}C-NMR ($CDCl_3$) 213.75(s), 133.65(d), 131.37(d), 79.74(d), 72.54(d), 62.46(d), 55.31(d), 52.38(t), 37.68(t), 37.15(t), 33.75(d), 31.64(t), 25.08(t), 22.50(t), 14.00(q) ppm.

6) 5a' or 5b': ^{13}C-NMR ($CDCl_3$) 212.58(s), 135.17(d), 132.24(d), 77.81(d), 72.76(d), 61.29(d), 46.70(d), 46.05(t), 37.03(t), 31.93(d), 31.64(t), 31.11(t), 25.02(t), 22.56(t), 14.00(q) ppm.

7) 5b: ^{13}C-NMR ($CDCl_3$) 214.15(s), 133.36(d), 131.02(d), 79.86(d), 72.25(d), 62.75(d), 54.90(d), 52.44(t), 38.14(t), 37.21(t), 33.87(d), 31.70(t), 25.14(t), 22.62(t), 14.06(q) ppm.

8) 5a' or 5b': ^{13}C-NMR ($CDCl_3$) 212.40(s), 134.77(d), 130.13(d), 77.70(d), 71.95(d), 61.23(d), 46.05(d), 45.94(t), 37.09(t), 31.99(d), 31.64(t), 31.05(t), 25.08(t), 22.50(t), 14.00(q) ppm.

9) 5a (2 mmol) was treated with mCPBA (2 mmol) in the presence of sodium bicarbonate in CH_2Cl_2 (10 ml) at -78 °C for 4 h, then saturated aqueous sodium bicarbonate was added to the reaction mixture. From the CH_2Cl_2 extracts, 6a was obtained in 86% yield after column chromatography on silica gel (AcOEt).

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