CHEMISTRY LETTERS, pp. 1341-1342, 1976. Published by the Chemical Society of Japan

AN ALTERNATIVE SYNTHESIS OF PROSTAGLANDIN INTERMEDIATES[1]

Makiko KOBAYASHI, Seizi KUROZUMI*, Takeshi TORU, and Sachio ISHIMOTO

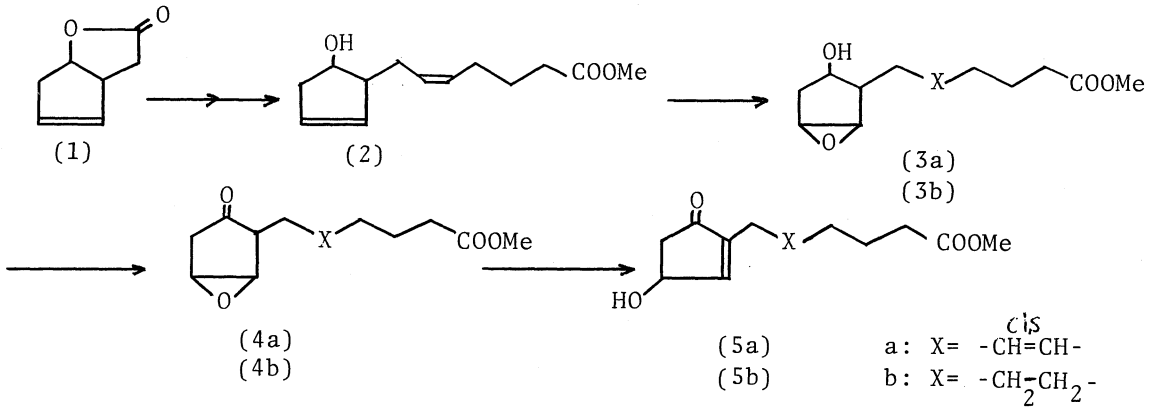
Institute for Biomedical Research, Teijin Ltd.,

4-3-2 Asahigaoka, Hino, Tokyo 191

An alternative synthesis of prostaglandin intermediates, 2-substituted 4-hydroxycyclopent-2-en-1-one (5a) and (5b), from readily available lactone (1) is described.

Since utilization of conjugate addition to enone systems opened a simple and efficient method for the synthesis of prostaglandins (PG's)[2], the preparation of key intermediates, 2-substituted 4-hydroxycyclopent-2-en-1-ones, has been intensively studied.[3] In this paper we wish to report a modified procedure for the preparation of the synthons (5a) and (5b) as depicted in the scheme. Our procedure involves selective epoxidation[4] of the olefin in the ring of cyclopentenol (2) giving epoxyalcohol (3a) with a double bond in the side chain of the molecule. This reaction avoids the previously reported sequence[3b] of the Wittig reaction of the labile epoxylactol.

Selective epoxidation (room temp., 2hr) of cyclopentenol derivative (2), prepared by the procedure of Grieco and Reep,[5] with 72.5% t-butyl hydroperoxide and vanadyl acetylacetonate[4] gave epoxyalcohol (3a)[91% yield, ir(neat) 3500, 1730, 840 cm^{-1}; nmr ($CDCl_3$) δ 5.70-5.26 (m, 2H), 4.12-3.70 (m, 1H), 3.78-3.40 (m, 2H), 3.63 (s, 3H); mass (m/e), 240 (M^+)].



Epoxyalcohol (3a) was oxidized with the Jones reagent in acetone (0°C, 20 min) to afford the corresponding ketone (4a) [93% yield; ir (neat) 1745, 840 cm^{-1}; nmr (CCl_4) δ 5.70-5.30 (m, 2H), 3.80-3.50 (m, 2H), 3.60 (s, 3H)]. Rearrangement of (4a) was carried out by the method developed by Stork et al.,[3c] to afford PGE_2-type synthon (5a)[3,6] in 65% yield [totally 48% yield from lactone (1)]. The PGE_1-type synthon (5b) could also be prepared in a similar manner via catalytic reduction. Hydrogenation of (3a) on Pd-charcoal in methanol gave epoxyalcohol (3b) [97% yield; ir (neat) 3500, 1730, 840 cm^{-1}; nmr ($CDCl_3$) δ 3.90-3.65 (m, 1H), 3.54-3.31 (m, 2H), 3.63 (s, 3H); mass (m/e) 242 (M^+)]. Compound (3b) was oxidized to the corresponding ketone (4b) [92% yield; ir (neat) 1745, 840 cm^{-1}; nmr (CCl_4) δ 3.85-3.40 (m, 2H), 3.60 (s, 3H)], which was transformed to PGE_1-type synthon (5b)[3e,3f,6] (72% yield) in the overall yield of 47% from lactone (1).

Acknowledgment: The authors are grateful to Drs. Y. Noguchi and S. Tsunoda of Teijin Ltd. for their encouragement.

References and Notes

1) Prostaglandin Chemistry-Part IX. Part VIII; T. Tanaka, S. Kurozumi, T. Toru, S. Miura, M. Kobayashi, and S. Ishimoto, Tetrahedron in press.

2) For reviews; (a) N. S. Crossley, Chem. and Ind. (London), 334 (1976) and (b) Von W. Bartmann, Angew. Chem., 37, 143 (1975).

3) (a) L. Gruber, T. Tömösközi, E. Major, and G. Kovács, Tetrahedron Lett., 3792 (1974);
(b) M. B. Floyd, Syn. Comm., 4, 317 (1974);
(c) G. Stork, C. Kowalski, and G. Garcia, J. Amer. Chem. Soc., 97, 3258 (1975);
(d) J. B. Heather, R. Sood, P. Price, G. P. Peruzzotti, S. S. Lee, and C. J. Sih, Tetrahedron Lett., 2313 (1973);
(e) C. J. Sih, J. B. Heather, G. P. Peruzzotti, P. Price, R. Sood, and L. F. H. Lee, J. Amer. Chem. Soc., 95, 1676 (1973);
(f) C. J. Sih, J. B. Heather, R. Sood, P. Price, G. P. Peruzzotti, L. F. H. Lee, and S. S. Lee, ibid., 97, 865 (1975).

4) (a) K. B. Sharpless and R. C. Michaelson, ibid., 95, 6136 (1973);
(b) S. Tanaka, H. Yamamoto, H. Nozaki, K. B. Sharpless, R. C. Michaelson, and J. D. Cutting, ibid., 96, 5254 (1974).

5) P. A. Grieco and J. J. Reap, J. Org. Chem., 38, 3413 (1973).

6) The product gave satisfactory spectral data.

(Received September 24, 1976)