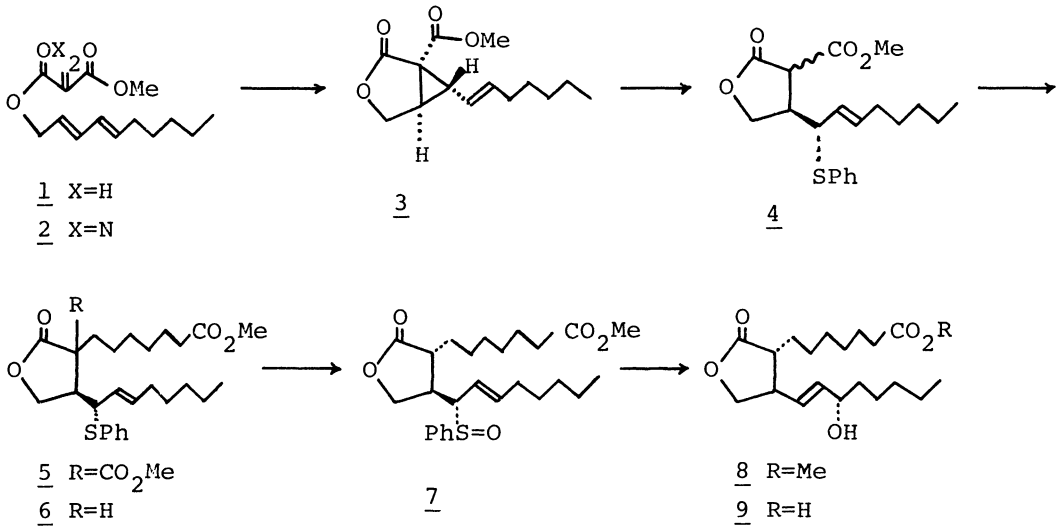
CHEMISTRY LETTERS, pp. 189-190, 1978. Published by the Chemical Society of Japan

STEREOSELECTIVE SYNTHESIS OF 10-OXA-11-DEOXY-PROSTAGLANDIN E_1 [1]

Daiei TUNEMOTO, Yuriko TAKAHATAKE, and Kiyosi KONDO*
Sagami Chemical Research Center, Nishi-Ohnuma 4-4-1, Sagamihara
Kanagawa 229

Intramolecular carbenoid reaction of methyl trans,trans-2,4-decadienyl diazomalonate afforded a bicyclic lactone, from which 10-oxa-11-deoxy-prostaglandin E_1 was synthesized stereoselectively in moderate overall yield, via regio- and stereoselective ring-opening reaction of cyclopropane moiety and [2,3]sigmatropic rearrangement of allylic sulfoxide.

A stereoselective synthesis of 11-deoxy-prostaglandin(PG)E_1 and of a precursor to PGA series[2], based on the combination of a regioselective addition of thiophenoxide to bicyclo[3.1.0]hexan-2-one derivative and a [2,3]sigmatropic rearrangement of allylic sulfoxide, has recently been reported from this laboratory[3]. The method opened a new route for stereoselective generation of α-hydroxy group on 15-position of prostaglandins. As a token of the generality of this concept, we have now applied the reaction sequence to the synthesis of 10-oxa-11-deoxy-PGE_1. The latter compound was formerly prepared by the reduction of a 15-keto intermediate and thus the product was a mixture of 15α- and 15β-prostanoids[4]. The following scheme summarizes our approach to the target compound.



1 X=H
2 X=N
3
4
5 R=CO_2Me
6 R=H
7
8 R=Me
9 R=H

Reaction of trans,trans-2,4-decadienol[2] with methyl chloroformylacetate in ether in the presence of $PhNMe_2$ gave methyl trans,trans-2,4-decadienyl malonate

1[5] in 89% yield; ν_{max}1760, 1738, 1659, and 990 cm^{-1}. The malonate 1 was transformed into the diazo ester 2 by treatment with p-TsN_3/Et_3N in acetonitrile[6] (98%, ν_{max}2125, 1765, 1740, and 990 cm^{-1}). When 2 was refluxed in toluene in the presence of Cu powder, the key intermediate, i.e., bicyclic lactone 3, was obtained in 70% yield: bp 152∿158°C/0.4 mmHg; ν_{max}1780, 1725, 1240, 1050, and 960 cm^{-1}; NMR (CCl_4) δ0.87 (t, J=6Hz, 3H), 1.10∿1.60 (m, 6H), 1.84∿2.14 (m, 2H), 2.18 (dd, J=5, J=8Hz, 1H), 2.63 (t, J=5Hz, 1H), 3.69 (s, 3H), 4.07 (d, J=9Hz, 1H), 4.26 (dd, J=5, J=9Hz, 1H), 5.22 (dd, J=8, J=15Hz, 1H), and 5.73 (dt, J=7, J=15Hz, 1H). Treatment of 3 with PhSK in t-BuOH at room temperature afforded the desired ring-opening product 4 in 60% yield; ν_{max}1788 and 1743 cm^{-1}. Condensation of 4 with methyl 7-iodoheptanoate with the aid of t-BuOK in DMSO at room temperature afforded the diester 5 in 98% yield; ν_{max}1780, 1741, and 1725 cm^{-1}. Decarboxylation was achieved by heating 5 in HMPA in the presence of NaCN at 80° to produce the lactone ester 6 in 83% yield; ν_{max}1780 and 1740 cm^{-1}. Oxidation of 6 with m-CPBA in MeOH[2] followed by [2,3]sigmatropic rearrangement of the resulting allylic sulfoxide 7 by treatment with $(MeO)_3P$[7] produced 10-oxa-11-deoxy-PGE_1 methyl ester 8 in 61% overall yield from 6. Hydrolysis of the ester 8 with aqueous methanolic KOH gave the desired 10-oxa-11-deoxy-PGE_1 9 (mp 57∿59°C) in almost quantitative yield. All of the spectroscopic data of 8 and 9 as well as the mp of 9 were consistent with the reported values[4,8].

REFERENCES AND NOTES

1) Presented at the 36th Annual Meeting of the Chemical Society of Japan, Osaka, Japan, April, 1977.
2) K. Kondo, T. Umemoto, Y. Takahatake, and D. Tunemoto, Tetrahedron Lett., 113 (1977).
3) A similar approach has also been published by D. F. Taber, J. Am. Chem. Soc., 99, 3513 (1977).
4) For nonstereoselective synthesis of this oxa-PG, see (a) J. Himizu, S. Harigaya, A. Ishida, K. Yoshikawa, and M. Sato, Japan Kokai 48-8773; (b) F. C. Hauser and R. C. Huffman, Tetrahedron Lett., 905 (1974).
5) Satisfactory elemental analyses and spectra were obtained for all new compounds.
6) M. Regitz, Angew. Chem. Int. Ed. Engl., 6, 733 (1967).
7) J. G. Miller, W. Kurz, K. G. Unch, and G. Stork, J. Am. Chem. Soc., 96, 6774 (1974), and references cited therein. For a comprehensive review of the rearrangement of allylic sulfoxide, see D. A. Evans and G. C. Andrews, Acc. Chem. Res., 7, 147 (1974).
8) The reported melting points (ref. 4a) of 15-α and 15-β isomers of 10-oxa-11-deoxy-PGE_1 were as follows: 60∿61°C (α) and 93∿94°C (β).

(Received December 9, 1977)