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SPONTANEOUS DIHYDROXYLATION OF α-OXO ENOL ETHERS BY AIR

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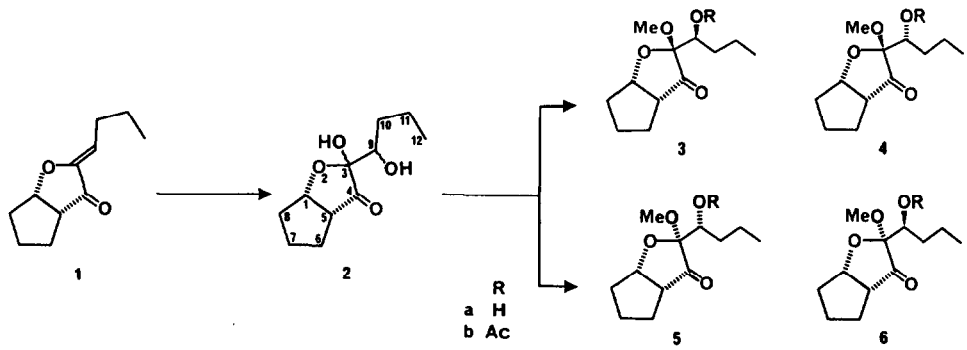
Summary *Unexpected dihydroxylation of 7-oxo-prostacyclin and a related α-oxo enol ether by air is reported.*

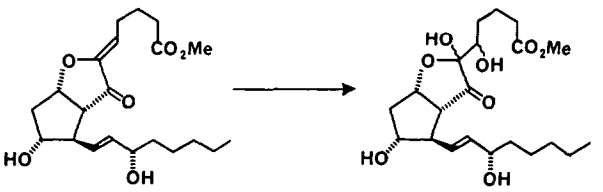
During the synthesis[1] of 7-oxo-PGI_2, a hydrolytically stable prostacyclin mimic[2], capricious deterioration of 7-oxo-PGI_2 methyl ester could occasionally be observed on attempted recovery from pure chromatographic elutes by rotatory evaporation of the solvent. Model experiments with 1 revealed the role of air in this transformation, namely in argon only 1 could be recovered unchanged.

On exposure to air a slow consumption of the oily 1 took place affording 2 as an unseparable mixture of diastereomers in 67% yield [i.r. 3350 (broad, OH), 1720 (C=O) cm^{-1}]. Complete consumption of 1 required 8-10 days. The rate of the reaction was considerably increased, however, by the presence of catalytic amount of α,α'-azo-isobutyronitrile (AIBN). A reaction of preparative value occured when the etheral solution of 1 was exposed to air at λ = 254 nm in presence of AIBN (89% isolated yield of 2). The separation of diastereomers could be achieved by successive blocking of the hydroxyl



groups. Treatment of the methanolic solution of 2 with catalytic amount of $BF_3.EtO_2$ gave chromatographically separable methyl ketals (3a+4a) and (5a+6a), respectively in a ratio 2:1 in yield 86% [4]. Subsequent acetylation (Ac_2O, 4-dimethylaminopyridine, CH_2Cl_2, r.t, 4 h) allowed further separation of both epimeric mixtures affording

3b:4b:5b:6b in ratio 2:1:2:1, respectively. The chemical structure of these compounds was unequivocally established by ^{1}H-NMR spectroscopy[5] although the configuration at C-9 could only be assigned tentatively.



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Dihydroxylated products 7 obtained from 7-oxo-PGI_2 methyl ester were separated and characterized as above. This transformation resulted in complete loss of antiaggregatory activity[2].

REFERENCES AND NOTES

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5. The elemental analyses and spectral data for the new compounds were in accordance with the structures assigned, and only selected data are listed.

   1: ^{1}H-NMR (C_6D_6, 80MHz): 5.70 (t, J = 8Hz 1H), 4.55 (m, 1H), 2.40 (m, 1H) 2.28 (m, 2H), 1.90 (m, 2H) 1.15-1.70 (m, 6H), 0.95 (t, J = 5Hz, 3H).

   2: ^{1}H-NMR (C_6D_6, 80MHz): 4.8 (m, 1H), 3.95 (m, 1H), 2.70 (m, 1H), 1.20-2.20 (m, 11H), 1.00 (t, J = 5Hz, 3H).

   3b: ^{1}H-NMR (C_6D_6, 80MHz): 5.10 (t, J = 6Hz, 1H), 4.90 (m, 1H), 3.20 (s, 3H), 2.75 (m, 1H), 2.05 (s, 3H), 1.15-2.30 (m, 10H), 0.95 (t, J = 5 Hz, 3H).

   4b: ^{1}H-NMR (C_6D_6, 80MHz): 5.25 (t, J = 8Hz, 1H), 4.95 (m, 1H), 3.30 (s, 3H), 2.85 (m, 1H), 2.00 (s, 3H), 1.10-2.25 (m, 10H), 0.90 (t, J = 5Hz, 3H).

   5b: ^{1}H-NMR (C_6D_6, 80MHz): 5.15 (dd J = 9Hz, 2Hz, 1H), 4.80 (m, 1H), 3.20 (s, 3H), 2.85 (m, 1H), 2.05 (s, 3H), 1.10-2.25 (m, 10H), 0.90 (t, J = 5Hz, 3H).

   6b: ^{1}H-NMR (C_6D_6, 80MHz): 5.35 (dd, J = 10Hz, 3Hz, 1H), 4.80 (m, 1H), 3.35 (s, 3H), 2.75 (m, 1H), 2.05 (s, 3H), 1.15-2.30 (m, 10H) 0.95 (t, J = 5Hz, 3H).

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