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BY-PRODUCTS FORMED IN TRANSFORMATIONS OF PROSTAGLANDIN E_1

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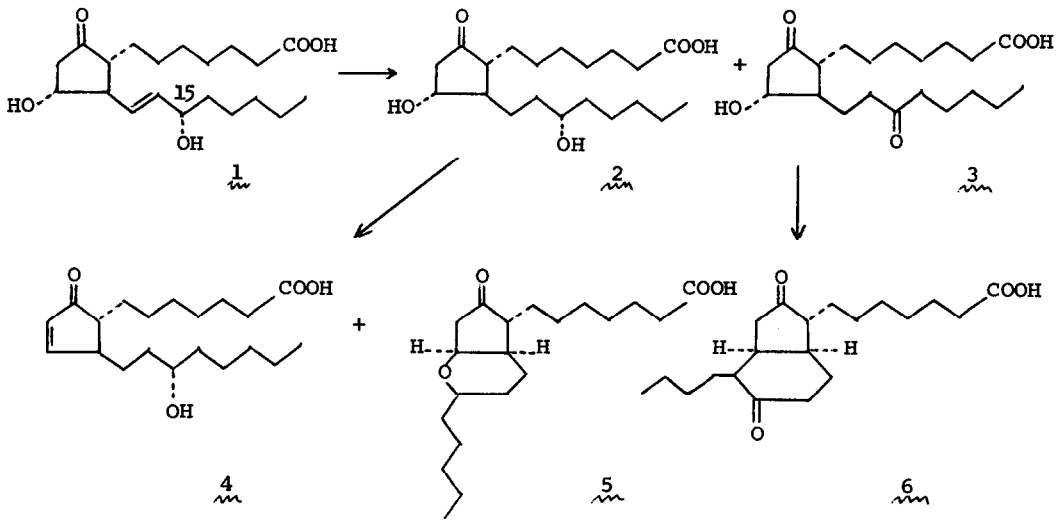
Hydrogenation of prostaglandin E_1 over platinum group catalysts yields 13,14-dihydroprostaglandin E_1 in only moderate ($\sim$45 - 60%) yield[1]. With 10% palladium on carbon in ethyl acetate we obtained 2 in 55 - 60% yield as well as a more mobile by-product (15 - 20%) shown to be 9,15-dioxo-11α-hydroxyprostanoic acid 3. Identification of the latter was based on physical measurements, especially the mass spectrum of its methyl ester, which was essentially identical with the published spectrum of 3[2]. Formation of 3 presumably involves double bond migration (Δ-13 $\rightleftharpoons$ Δ-14) on the catalyst surface at a rate competitive with hydrogenation. This side reaction was avoided by carrying out the hydrogenation over Raney nickel in dioxane, under which conditions 2 was the sole product.

Dehydration of 2 to 13,14-dihydroprostaglandin A_1, 4 in 90% aqueous acetic acid at 60°[3] gave, in addition to 4 (45 - 50%) and its 15-acetate ($\sim$5%), a more mobile substance (30 - 35%) identified as 11,15-epoxy-9-oxoprostanoic acid 5. Its uv spectrum showed the absence of cyclopentenone functionality. Carboxyl and cyclopentanone functionalities were shown to be present by its ir spectrum, and its nmr spectrum ($CDCl_3$) indicated the presence of 2H alpha to ether oxygen (1H multiplets at 3.73 and 4.34 δ). The mass spectrum of the methyl ester had major peaks at 352 (M^+), 334 (M^+-H_2O), 321 (M^+-OCH_3), 309 ($M^+-C_3H_7$), 303 ($M^+-H_2O-OCH_3$) and 281 ($M^+-C_5H_{11}$). Cyclic ether 5 evidently arises from 4 by intramolecular addition of the C-15 hydroxyl group to the Δ-10 double bond.

The 11α-hydroxy-9,15-dione 3 showed no uv absorption after warming in methanolic sodium hydroxide, suggesting formation of the Michael product 6 via the expected intermediate cyclopentenone[4].



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4. Cf. P. F. Beal, III, J. C. Babcock and F. H. Lincoln, Proceedings of the Second Nobel Symposium - Prostaglandins, Interscience, N. Y. (1967), p. 227. Assignment of cis stereochemistry at the ring junctions of 5 and 6 is based on inspection of models.