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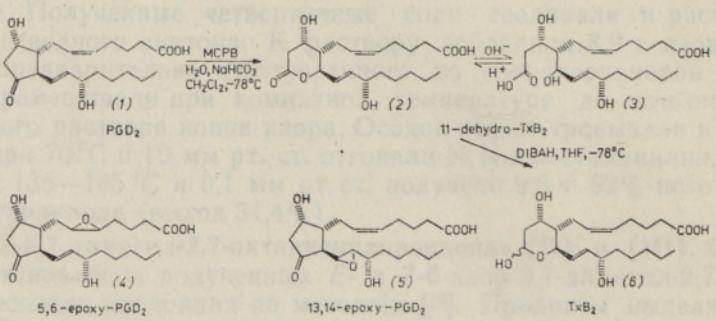
A SHORT WAY TO 11-DEHYDRO-TxB_2 AND TxB_2 FROM PGD_2

I. JÄRVING, Külliki VARVAS, Aino VAHEMETS, N. SAMEL, Ü. LILLE. 11-DEHÜDRO-TxB_2 JA TxB_2 SAAMINE PGD_2-st

И. ЯРВИНГ, Кюллики ВАРВАС, Айно ВАХЕМЕТС, Н. САМЕЛЬ, Ю. ЛИЛЛЕ. КРАТКИЙ ПУТЬ СИНТЕЗА 11-ДЕГИДРО-TxB_2 И TxB_2 ИЗ PGD_2

The most common approach in the studies aimed at measuring the thromboxane A_2 production *in vivo* is to monitor the stable hydrolysis product TxB_2 in plasma. However, the measured levels of TxB_2 in plasma vary greatly, even in the studies based on identical assay methods. To circumvent this problem, a prominent TxB_2 metabolite in the circulation as well as urine 11-dehydro-TxB_2 is recommended to use [1].

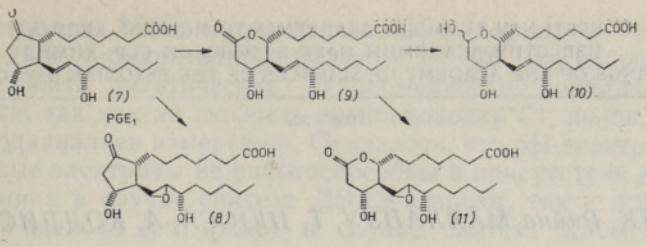
In order to synthesize 11-dehydro-TxB_2 we propose the Baeyer-Williger oxidation which converts PGD_2 (1) directly to the corresponding δ-lactone (2). The possible by-products are monoepoxides (4) and (5), diepoxide and lactone epoxides.



The yield of 11-dehydro-TxB_2 using *m*-chloroperbenzoic acid (MCPB) as an oxidant was up to 30%, whereas the content of the open dicarboxylic acid form (3) did not exceed 2%. The total amount of PGD_2 epoxides was 8%. About 60% of the initial PGD_2 remained nonconsumed and was recovered in the course of separation of the reaction mixture by preparative normal-phase HPLC.

Attempts to oxidize PGD_2 with other reagents such as hexafluoroacetone/H_2O_2 or CH_3COOH/H_2O_2/alkali were unsuccessful.

The Baeyer-Williger oxidation of PGE_1 and PGE_2 as model compounds led to similar products with the exception of a complete lack of acyclic diacid form of lactones.



The oxidation of PGE_1 (7) with MCPB in dry acetonitrile afforded epoxide (8) in 80% yield. When the reaction was carried out in the acetonitrile-water mixture in the presence of $NaHCO_3$, the main product was lactone (9), 40%.

The δ-lactones obtained were easily reduced with diisobutylaluminium-hydride (DIBAH) into TxB_2 (6) or its analogs (10) derived from E-type prostaglandins.

The synthesized compounds were identified by ^{13}C NMR spectra at the Institute of Chemical Physics and Biophysics by T. Pehk.

REFERENCES

1. *Kumlin, M., Granström, M.* Radioimmunoassay for 11-dehydro-TxB_2. A method for monitoring thromboxane production in vivo. — Prostaglandins, 1986, **32**, N 5, 741—767.

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