

论文

消旋17-苯-18,19,20-失三碳前列腺素F<sub>2α</sub>甲酯及其15-差向异构体的合成

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摘要:

从中间体(4)出发,经醛(5),与磷叶立德(3)或2-酮-4-苯丁烷磷酸酯(11)钠缩合成(6),再钠硼氢还原得3' $\alpha$ -醇(7A)及其差向异构体(7B),经硅胶柱色谱分开,分别经二异丁基铝氢还原,与溴化5-三苯磷戊酸之Wittig试剂缩合,得17-苯-18,19,20-失三碳前列腺素F<sub>2α</sub>(9A)及其15-差向异构体(9B),再用重氮甲烷甲酯化,分别得相应的17-苯-18,19,20-失三碳前列腺素F<sub>2α</sub>甲酯(10A)及其15-差向异构体(10B)。

关键词: 前列腺素合成 17-苯-18,19,20-失三碳前列腺素F<sub>2α</sub> 堕胎剂 黄体消散剂

SYNTHESIS OF dl-17-PHENYL-18,19,20-TRINORPROSTAGLANDIN F<sub>2α</sub> METHYL ESTER AND ITS 15-EPIMER

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Abstract:

d,l-17,Phenyl-18,19,20-trinorprostaglandin (PG) F<sub>2α</sub> methyl ester (10A) and its 15-epimer (10B) were synthesized in an attempt to develop new PG congeners with better bioselectivities and higher potency in terminating pregnancy. Wittig-Horner reaction of aldehyde (6) with the ylide (3) of 4-phenyl-2-oxo-n-butyl-triphenylphosphonium bromide gave 42% yield of 1' 2'-unsaturated 3'-ketone (6). Reduction of (6) with sodium borohydride in absolute methanol at -3°C yielded a mixture of epimers, 3' $\alpha$ -alcohol (7A) and 3'  $\beta$ -alcohol (7B), which were separated by column chromatography on silica gel with diethyl ether as eluent to yield 42% (7A) and 36% (7B) respectively. Treatment of (7A) with an excess of di-isobutylaluminium hydride in ethylene glycol dimethylether and diethyl ether under nitrogen at -78°C afforded the intermediate lactol (SA) as colorless semisolid in 80% yield. Subjected to Wittig condensation with a 5-fold excess of Wittig reagent generated in situ from 4-carboxybutyl triphenylphosphonium bromide and dimethyl sodium in dimethylsulfoxide, (8A) was transformed to d, l-17-phenyl-18, 19, 20-trinor PGF<sub>2α</sub> (9A) in yields of about 77%. Methylation of (9A) with ethereal diazomethane yielded the corresponding methyl ester (10A). By similar transformations, d,l-15-epi-17-phenyl-18, 19, 20-trinor PGF<sub>2α</sub> methyl ester (10B) was obtained through intermediates (SB) and (9B). Preliminary bioassays showed that (9A) exhibited activities more potent than that of d,l-15-methyl PGF<sub>2α</sub> methyl ester in terminating early pregnancy in mice.

Keywords: Luteolytic agent Prostaglandin synthesis 17-Phenyl-18, 19, 20-trinor PGF<sub>2α</sub> Abortifacient

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