Synthesis of Allenyl Prostaglandins

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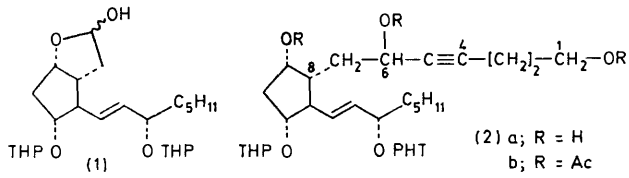
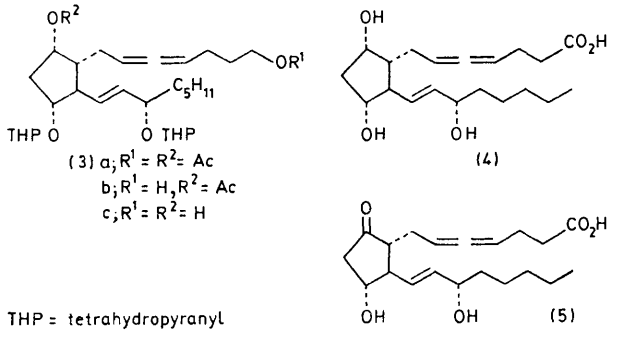
Summary A substituted acetylenic carbinol acetate is converted efficiently into a dialkylated allene by treatment with several equivalents of lithium dialkylcopper in diethyl ether solution; this organocopper reaction involves a reductive process followed by rearrangement and acetate elimination.

WE report the synthesis of two novel prostaglandins belonging to the E and F series, which incorporate a propadiene group at C-4,5.

Reaction of the hemi-acetal (**1**)[1] with the di-lithium salt of pent-4-yn-1-ol under nitrogen provides a mixture of the stereoisomeric acetylenic C-6 carbinols (**2a**) [ν_{max} 3350 and

2225 cm^{-1}; δ 0·90 (Me) and 5·50 p.p.m. (m, 2 vinylic H)].† Esterification with acetyl chloride in pyridine furnishes the tri-acetate (**2b**) [80% overall from (**1**)]. Treatment of





(**2b**) with $LiMe_2Cu$ (4 equiv.) in ether solution, at −78° under argon, affords as the only isolated compound (75%) the disubstituted allene (**3a**).‡

The noteworthy features of this reaction are its simplicity and the exclusive formation of the disubstituted allene (**3a**), with no alkylation of the allene.[2] This reaction thus consists of a reductive process followed by rearrangement and displacement.[3]

Low-temperature alkaline hydrolysis of (**3a**) with K_2CO_3 (1·1 equiv.) in aqueous MeOH gives the monohydroxy-derivative (**3b**). Jones oxidation[4] followed by base treatment of the C-9 acetate and hydrolysis (aqueous AcOH) of the tetrahydropyranyl ether groups yield the (±)-PGF allenyl analogue (**4**),‡ an oil, purified by preparative t.l.c.

Hydrolysis (methanolic K_2CO_3; 3 equiv.) of (**3a**) at room temperature gives the diol (**3c**).‡ Oxidation of (**3c**) with chromic acid[4] (3·3 equiv.) at −15° furnishes the keto-acid, which is then hydrolysed with aqueous AcOH thus affording after t.l.c. the liquid (±)-PGE allenyl analogue (**5**)‡.

Compounds (**3**)—(**5**) are isomeric mixtures of allenes, since alkylation of (**1**) is not stereospecific and thus provides (**2a**) as a mixture of isomers at C-6.

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† Satisfactory elementary analyses or mass spectra were obtained for all new compounds.

‡ N.m.r. and i.r. spectra consistent with their formulation.

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