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7. The B(9) resonance for 6-SB_9H_{11} is at +17.3 with J_{BH} = 170 Hz. The B(9) resonance for the alkenyl thiaborane investigated here is found at +35 ppm. The remainder of the spectrum differs little from that of 6-SB_9H_{11}.
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Synthesis of Prostaglandins IV. Facile Synthesis of Luteolytic Prostaglandin Fenprostalene

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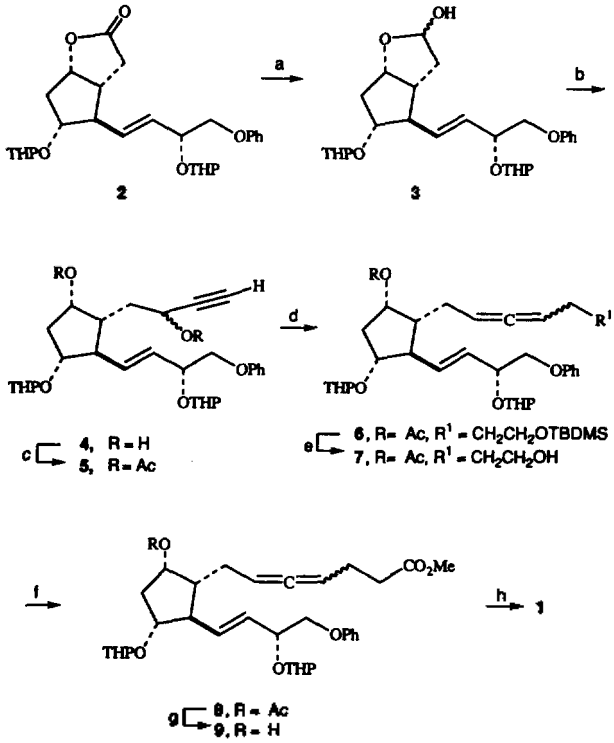
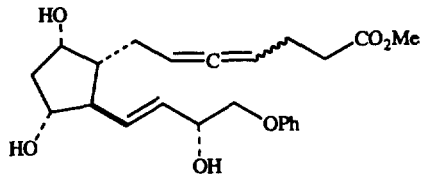
Prostaglandins (PGs) are a family of extremely potent natural hormones with a remarkable range of biological and pharmaceutical properties. The unavailability of a suitable natural source coupled with their potential drug utility has led to the clinical development of a number of synthetic PG analogs. Among them, fenprostalene (**1**), a 4,5,6-allenic



Scheme 1. *Reagents and conditions*: a, DIBAH, toluene, −78 ℃, 2 h; b, see Table 1, 82-93%; c, Ac_2O, cat. DMAP, NEt_3, CH_2Cl_2, rt., 3 h, 91%; d, $TBDMSOCH_2CH_2CH_2MgBr$, $CuI{\cdot}P(OEt)_3$, THF, −40 ℃, 10 min, 76%; e, TBAF, THF, rt, 3 h, 99%; f, i. PDC/CH_2Cl_2, rt, 20 h, ii. PDC/DMF, MeOH, rt, 20 h, 84%; g, K_2CO_3, MeOH, rt, 14 h; then 1 N HCl, 0 ℃ (89%); h, AcOH-H_2O-THF, 40 ℃, 20 h, 65%.

16-phenoxy PGF analog, has been found to possess a luteolytic activity in various animal species.[1] Luteolytic PGs have an important place in veterinary medicine. Thus, the PGs can be used to control the bovine estrus cycle; stemming from this are the benifits of artificial insemination.

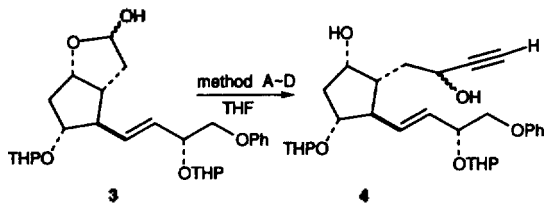


1, fenprostalene

The introduction of allenic side chain attracted substantial synthetic efforts of many organic chemists. Since its development[2], a number of synthetic methods for the preparation of allenic prostaglandins have been reported[3].

The introduction of allenyl group in prostaglandins was done by the reaction of propargylic ester with lithium dimethylcuprate[2] or by using an orthoester Claisen rearrangement of propargylic alcohol intermediate.[3c] The specificity for the formation of protonated allene from propargylic ester depends on the various factors like the kind of propargylic derivatives, cuprate reagents, reaction temperature, work-up conditions, etc.[4] Therefore, the possibilities for the formation of alkylated allene and alkylated acetylene was a main drawback for the synthesis of allenic prostaglandin derivatives.[3a,5]

Table 1. Preparation of Propargyl alcohl **4**



Method	Conditions	Yield (%)
A	i. H−≡−$SnBu_3$/n-BuLi, −78℃ ~*rt*. ii. n-BuLi, −78℃ ~*rt*.	82
B	i. H−≡−$SiMe_3$/n-BuLi, −78℃ ~*rt*. ii. TBAF, *rt*.	93
C	H−≡−H/n-BuLi, −78℃ ~*rt*.	82
D	H−≡−MgBr, 0℃ ~*rt*.	91

We describe herein a convenient synthesis of **1** *via* facile introduction of protonated allenyl group starting with the known lactone **2**.[6]

The basic strategy of this synthesis involves efficient ring opening of lactol **3** with metal acetylides, subsequent acetylation and facile introduction of three-carbon unit with formation of allenyl group (Scheme 1).

We intended to develop a simple synthetic route to fenprostalene (**1**) by the direct reaction of lactol with metal acetylide and acetylation of the resulting diol since our synthetic strategy need not differentiate two hydroxy groups in C-6 and C-9 (PG numbering) positions. The lactone **2** was reduced with DIBALH in toluene at −78 ℃ to the lactol **3**, which was sufficiently pure to be used without purification.

Firstly, the reaction of the lactol **3** was examined with several metal acetylides (Table 1). When the lactol **3** was treated with lithium acetylide-ethylendiamine complex in THF or DMF as the solvent, the reaction did not completed due to the low reactivity of lithium acetylide-ethylenediamine complex. But, the reactions of the lactol **3** with lithium anion of 5 equivalents of ethynyltri-*n*-butyltin or trimethylsilylacetylene in tetrahydrofuran (−78 ℃ ~*r.t.*) proceeded smoothly to afford the propargylic alcohol **4** in 82% and 93% yield, respectively (method A and B). The propargylic alcohol **4** was also obtained by the reaction of the lactol with **5** equivalents of lithium acetylide or ethynylmagnesium bromide (method C and D). The reaction of lactol with ethynylmagnesium bromide (method D) seems to be appropriate and efficient since the reaction with lithium tri-*n*-butylstannanylacetylide or lithium trimethylsilylacetylide necessitate additional deprotecting step. The resulting propargylic alcohol **4** was transformed to the propargylic acetate **5** with an excess amount of acetic anhydride and triethylamine in the presence of a catalytic amount of 4-dimethylaminopyridine (DMAP) in 91% yield.

The propargylic acetate was further converted to the protonated allene with concomitant three-carbon homologation through cuprate-based Grignard reaction. The reaction of propargylic acetate **5** with 3-*t*-butyldimethylsilyloxypropylmagnesium bromide and catalytic amount of $CuI{\cdot}P(OEt)_3$ at −40 ℃ in THF afforded cleanly the allenic acetate **6** in 76% yield. The fenprostalene (**1**)[2] was formed from the allenic acetate **6** by the following sequential reactions; deprotection of silyl group with *tetra-n*-butylammonium fluoride (TBAF) (98%), consecutive oxidation with pyridinium dichromate (PDC)/CH_2Cl_2 and PDC/MeOH/DMF (84%), deprotection of acetyl group in **8** with methanolic potassium carbonate (89%), and deprotection of tetrahydrofuranyl group with acetic acid/H_2O/THF (19 : 11 : 3) (65%). The spectroscopic properties of **1** were in accord with those described in the literature.[2]

In conclusion, the synthesis of luteolytic prostaglandin fenprostalene (**1**) has been achieved in 8 steps and ~30% overall yield starting from lactone **2**. The efficacy of our synthesis relies on the facile introduction of allenic moiety with concomitant three-carbon homologation. The synthetic steps were also shortened by direct reaction of the lactol **3** with ethynylmagnesium bromide followed by acetylation.

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Nucleophilic Additions to 5-Hydroxymethyl-2-pyrrolidinone: Synthesis of Chiral 2,5-Disubstituted Pyrrolidines

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2,5-Disubstituted pyrrolidines occur as many bioactive natural products,[1] and C_2 symmetric 2,5-disubstituted pyrrolidi-