pyridyl)phenylphosphine *P*-oxide[13] was suggested to proceed via a benzilic acid rearrangement; a similar mechanistic course can be tentatively considered plausible for this decarbonylation reaction.

In conclusion, it appears that ketones which possess two electron-withdrawing aryl groups will undergo decarbonylation under mild reaction conditions. Work is continuing in order to ascertain the breadth of this reaction and to gain further insight into the mechanistic rationale.

Acknowledgment. Supported in part by the National Institutes of Health (GM 20985).

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Received October 17, 1978

Diisobutylaluminum 2,6-Di-*tert*-butyl-4-methylphenoxide. Novel Stereoselective Reducing Agent for Prostaglandin Synthesis

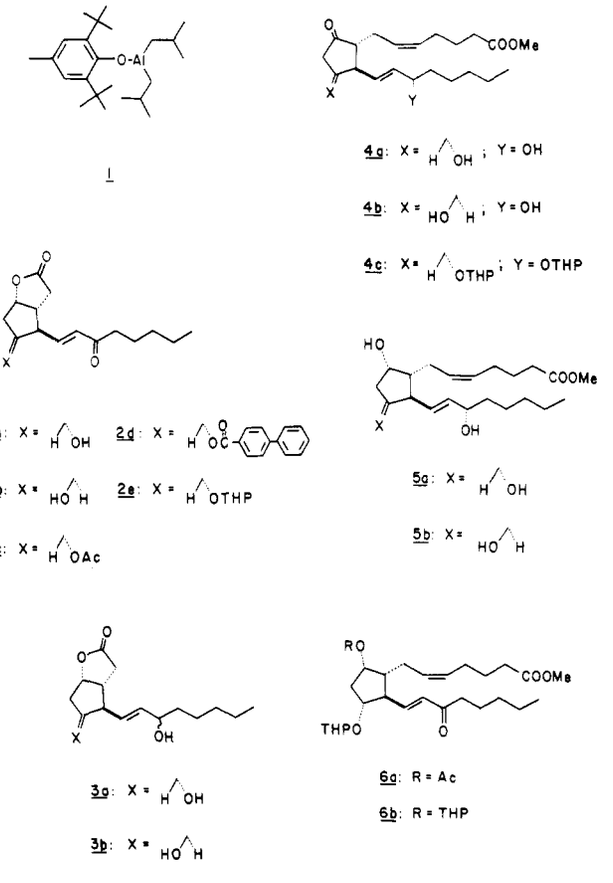
Summary: In an effort to explore the selective reducing agents suitable for prostaglandin synthesis, diisobutylaluminum 2,6-di-*tert*-butyl-4-methylphenoxide (**1**) is found to be among the best. Reduction of the C-15 ketone **2a** with **1** in toluene at −78 °C produced the desired α-alcohol **3a** in 95% yield with 92% stereoselectivity. The procedure is suitable for the synthesis of prostaglandin derivatives and related polyfunctional natural products.

Sir: At the heart of almost any prostaglandin synthesis[1] whose ultimate goal is the stereoselective approach must lie a methodology which controls stereochemistry at C-15.[2] In consonance with this fact we have been interested for many years in devising an efficient approach to the stereocontrolled reduction of the C-15 ketone. The present method utilizes the title compound as the key reagent for a *simple* and *practical* solution to this problem.

A solution of diisobutylaluminum 2,6-di-*tert*-butyl-4-methylphenoxide (**1**)[3,4] can be prepared from diisobutylaluminum hydride (1.76 M solution in toluene) and 2,6-di-*tert*-butyl-4-methylphenol (molar ratio 1:1 to 1:2)[5] in toluene at 0 °C for 1 h. Reaction of **1** (10 equiv) with the enone **2a** in toluene (~0.2 M reagent) first at −78 °C for 2 h was complete after warming to −20 to −40 °C for 1 h. The reaction was terminated by addition of hydrochloric acid (~1 M) and the product was extracted with ethyl acetate. Short-path chromatographic separation to remove the recovered phenol gave the allylic alcohol **3a** in 95% yield. The ratio of 15*S* to 15*R* (prostanoic acid numbering) isomers in several runs was 92:8 by high-pressure liquid chromatographic analysis.[6]

Starting from the C-11 isomeric **2b** and using the same procedure as applied for the synthesis of **3a,** there was produced in 94% isolated yield the alcohol **3b** (15*S*/15*R* = 85:15).[6] Similarly starting from PGE_2 methyl ester (**4a**) there was obtained $PGF_{2\alpha}$ methyl ester (**5a**) in 95% yield and 100% selectivity.[7] Furthermore, reaction of **1** with the C-11 epimeric PGE_2 methyl ester **4b** again furnished the C-11 epimeric $PGF_{2\alpha}$ methyl ester (**5b**) exclusively and efficiently (92% yield).[8]

In contrast to the highly selective reduction of hydroxy ketones, the acetate **2c** afforded the corresponding allylic alcohols without any stereoselectivity (15*S*/15*R* = ~1:1).[6] Analogously, no stereoselectivity could be observed using



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p-phenylbenzoyl ester **2d** as the substrate.[9]

It was previously reported[2a] that the reduction of **2** at −120 to −130 °C favored the formation of 15*S* alcohol when a bulky hydride was used together with a special protecting group at C-11 which is capable of shielding the s-cis enone side chain. Thus, the present high selectivity can be attributed not only to the significant frontal steric bulk of **1**[10] but also to the substantial screening effect of s-cis enone chain to inhibit the α approach of the reagent. Thus, the excess aluminum reagent which is strongly coordinated at the C-11 hydroxyl function appears to play an important role as an exogenous directing group to block α approach of the reagent as well as to maintain s-cis enone conformation.

On the basis of this hypothesis, we examined the reduction of THP ethers **2e, 4c, 6a,** and **6b** using the reagent **1** under the standard conditions. It was thought that moderate selectivity for formation of 15*S* alcohol should be observed in these cases, since the aluminum reagent may be coordinated with ethers rather weakly.[11] The substrates and the observed 15*S*/15*R* (or 9α/9β) ratios are as follows: **2e,** 66:34; **4c,** 85:15; **6a,** 74:26; **6b,** 74:26.[6]

The reduction process which is described herein should be extremely useful for complex or polyfunctional molecules. As is clear from the examples cited above the yields are high, selectivities are unique, and there is little variation in optimal conditions. The advantages of the reagent are also considerable for the operational simplicity and wide availability of starting materials.

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(4) The reagent **1** is stable enough to be stored under argon at 0 °C for several weeks.

(5) Only 1 equiv of phenol is involved in the reaction and ~1 equiv of hydrogen gas evolution is observed during this operation.

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(10) The desired stereoselective reductions were observed only with 2,6-di-*tert*-butyl-4-methylphenol or 2,6-di-*tert*-butylphenol. No or lower selectivities were observed using other phenols: 2,4,6-tri-*tert*-butylphenol, 2-*tert*-butyl-4-methylphenol, 2,4-di-*tert*-butylphenol, 2,6-diisopropylphenol, *p*-cresol, and 2,6-dimethylphenol. The details of these results will be published in a full paper.

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Received December 17, 1978