shown by the synthesis of 6, 7, and the novel 8 as pure substances. No other products were detected by NMR analysis before fractionation. Iodobutene 6 had previously been obtained by Knunjants and Pervova[8] in moderate yield, from the same starting compound by means of triethyl phosphite. They found that the best results (25% yield) were obtained at elevated temperatures.

Aminophosphine 9 did not show high diastereoselectivity in the formation of alkenes, as both *E* and *Z* isomers were found where possible (2, 7, and 8). As is apparent from the results summarized in Table I, the order of reactivity of different halogens is I > Br > Cl > F, also in a highly selective manner. The abstraction of fluorine and bromine was found only in the case of the partially fluorinated alkene 3, and the possible competing reaction of dehydrofluorination was not observed. Finally, 9 differs markedly not only from other reducing agents known to effect dehalogenation, such as phosphites, but even from the very similar tris(dimethylamino)phosphine. The latter did not yield perfluoroallyl chloride under the same conditions or under longer reaction times and higher temperature, although it did give a 1,2 debromination reaction (cf. Table I).

In conclusion, aminophosphines are promising reagents for the synthesis of haloalkenes by selective dehalogenation. The limited examples demonstrated in this work using tris(diethylamino)phosphine suggests many other potential applications for this readily available reagent.

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Supplementary Material Available: ^1H and ^{19}F NMR spectra of 3 and ^{19}F NMR spectra of 6–8 (5 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

An Improved Procedure for Retro-Cycloaddition of Adducts from Steroidal 5,7-Dienes and 4-Phenyl-1,2,4-triazoline-3,5-dione

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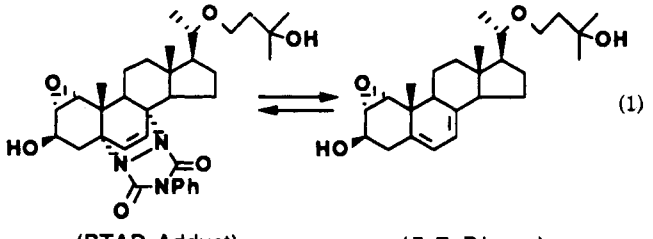
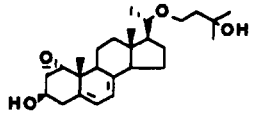
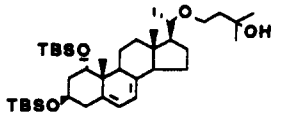
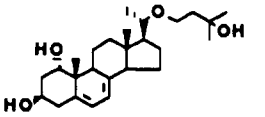
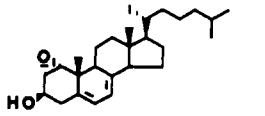
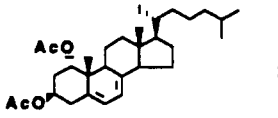
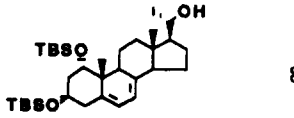
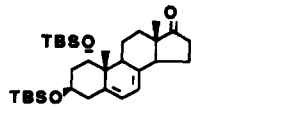
Retro-cycloaddition of adducts from steroidal 5,7-dienes and 4-phenyl-1,2,4-triazoline-3,5-dione (PTAD) to regenerate the 5,7-diene systems is one of the most important reactions in the steroid–vitamin D chemistry (eq 1).[1] The



(1)

Table I. Steroidal 5,7-Dienes Prepared from PTAD Adducts by Retro-Cycloaddition (140 °C, DMI)

entry/ compd	reaction time (h)	5,7-dienes	yield[a] (%)	lit.
1	2		84	
2	2		76	5
3	1.5		68	5
4	2.5		87	6
5	1		84	7
6	2.5		87	8
7	5		83	8

[a] Yields refer to pure 5,7-dienes isolated.

formation of the adducts generally proceeds smoothly and quantitatively;[1] however, the yields of the retro-cycloaddition of the adducts are not always satisfactory under the known conditions (e.g., $LiAlH_4$,[1] Na/EtOH,[1] hydrazine hydrate,[1] furan,[1] pyrolysis,[1] K_2CO_3/DMSO or DMF,[2] tetramethylguanidine[3] or γ-collidine,[3] or KOH/EtOH[4]). We now wish to report an improved procedure which involves heating adducts alone in 1,3-dimethyl-2-imidazolidinone (DMI).

In a typical procedure, the PTAD adduct in DMI is stirred at 140 °C for 1–5 h. After the usual workup, the 5,7-diene is obtained in 68–87% yields. The results are summarized in Table I.

When DMF or DMSO was used as a solvent instead of DMI, the retro-cycloaddition of the adducts proceeded very slowly and in poor yields, while in the case of xylene the reaction did not occur. The present procedure for retro-cycloaddition is very useful due to its simplicity and high yield with acid-, base-, or $LiAlH_4$-sensitive substituents remaining intact.

Experimental Section

General Procedure for Retro-Cycloaddition. A solution of the PTAD adduct (entry 1) (327 mg, 0.55 mmol) in DMI (32.7 mL) was stirred at 140 °C (bath temperature) for 2 h. The reaction

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mixture was poured into H_2O (30 mL) and extracted with AcOEt (15 mL × 3). The extract was washed with saturated NaCl and dried over $MgSO_4$. Removal of the solvent in vacuo left a solid which was chromatographed on a silica gel flash column with CH_2Cl/EtOH = 20/1 to give the 5,7-diene (entry 1) (193 mg, 84%) as a pale yellow powder: mp 164–165 °C; IR (KBr) 3350, 2995, 2905, 1395, 1380, 1170, 1110, 1080, 1065, 855 cm^{-1}; ^1H-NMR ($CDCl_3$), δ 0.61 (3 H, s), 1.02 (3 H, s), 1.22 (3 H, d, J = 7.2 Hz), 1.24 (6 H, s), 3.00 (1 H, d, J = 3.6 Hz), 3.20–3.38 (1 H, br), 3.32 (1 H, d, J = 3.6 Hz), 3.44–3.56 (1 H, m), 3.78–3.92 (2 H, m), 5.32–5.40 (1 H, m), 5.68 (1 H, brd, J = 5.7 Hz); MS m/z 416 (M^+), 68 (100); UV (EtOH) λ_{max} 289, 278, 267 nm. The other 5,7-dienes shown in Table I are known compounds and have the following melting points: entry 2, 148–149.5 °C;[5] entry 3, 186.5–187.5 °C;[5] entry 4, 112–113 °C; entry 5, 118–119 °C;[7] entry 6, 169 °C;[8] entry 7, 120.5–121.5 °C. The physical and spectral properties agree with the literature data.[5-8]

Acknowledgment. We thank to Dr. Masatomo Hamana, Professor Emeritus of Kyushu University for his encouragement.

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N,O-Bis(phenoxycarbonyl)hydroxylamine: A New Reagent for the Direct Synthesis of Substituted *N*-Hydroxyureas

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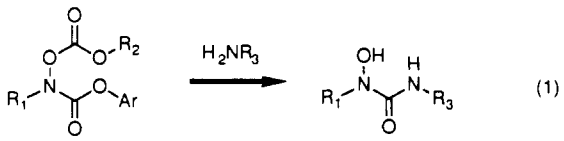
A series of potent, selective, orally active inhibitors of the enzyme 5-lipoxygenase has been investigated which contain the *N*-hydroxyurea as a necessary component for biological activity.[1] Inhibitors of 5-lipoxygenase represent a promising new therapy for a variety of disorders involving leukotriene mediators.[2] One objective in this pharmaceutical discovery research was to devise efficient synthetic methods for the preparation of substituted *N*-hydroxyureas.[3]

A common method for the preparation of *N*-hydroxyureas has been the treatment of hydroxylamines with an isocyanate or potassium cyanate. The hydroxylamines themselves can be obtained from acid-catalyzed reduction of the corresponding oxime using borane pyridine.[4]

Alternatively, Miller has demonstrated that O-substituted hydroxamates can be alkylated with alcohols using the Mitsunobu reaction (Scheme I).[5,6] *N*-(Benzyloxycarbonyl)hydroxylamine derivatives or the commercially available *N,O*-bis(*tert*-butyloxycarbonyl)hydroxylamine gave high yields of the adducts **5** under these conditions (Scheme I). These alkylated products require *deprotection* to give the hydroxylamine **6** which can then be treated with an isocyante to provide the requisite *N*-hydroxyureas. Both of the above methods typically require acidic conditions or hydrogenolysis and the intermediacy of a hydroxylamine. We required a method utilizing a suitably protected hydroxylamine that could be alkylated by the Mitsunobu reaction and could also be deprotected under nonacidic conditions without hydrogenolysis.

After examining derivatives of hydroxylamine and several commercially available chloroformates we reasoned that *N*-(phenoxycarbonyl)hydroxylamines of the general formula **1** should, on treatment with an amine, directly give the corresponding *N*-hydroxyurea **2** (eq 1). This was



(1)

1 **2**

based on the well-known conversion of phenylcarbonates to *O*-carbamoyl derivatives,[7] the preparation of *N,N'*-disubstituted ureas by both the aminolysis of phenylcarbamates[8,9] and the consecutive addition of amines to bis(4-nitrophenyl)carbonate,[10] as well as the reported conversion of diphenyl cyanocarboimidates to *N*-cyano-*N,N'*-disubstituted guanidines by stepwise addition of amines.[11] Adaptation of a literature procedure for preparation of *N,O*-bis(benzyloxycarbonyl)hydroxylamine,[12] but substituting phenyl chloroformate, gave crystalline *N,O*-bis(phenoxycarbonyl)hydroxylamine (**1a**) (Scheme II). This stable crystalline material reacted smoothly with a variety of alcohols in the Mitsunobu reaction (triphenylphoshine/diisopropyl azodicarboxylate[13]/THF) (Scheme III). After chromatography (silica gel) these adducts **8** were treated with ammonia in various solvents. Under these conditions, the carbonate is rapidly cleaved to give the *N*-hydroxyphenylurethane **10** which can be isolated.[14] Prolonged exposure to ammonia converts the intermediate *N*-hydroxyphenylurethanes **10** to the desired *N*-hydroxyureas **11**.

Good yields were obtained in the alkylation of the hydroxylamine derivative **1a** with several alcohols (Table I).

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