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5. Preparation of Methyl Isopropyl 2,6-dimethyl-4-(3'-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate. 5-Methoxycarbonyl-2,6-dimethyl-4-(3'-nitrophenyl)-1,4-dihydropyridine-3-carboxylic acid (325mg, 1mmol) and triethylamine (0.14ml, 1mmol) was stirred in DMF (5ml) for 10 min 1-Methansulfonyloxy-6-trifluoromethylbenzotri-

azole (FMS) (338mg, 1.2mmol) was added into the solution at 0°C and stirred. After 30 min isopropyl alcohol (0.12ml/1.5mmol) was added and warmed up to 60°C with stirring for 2hr [FOBT intermediate, m.p. = 189-190°C, nmr (CDCl₃): 2.43(s, 3H), 2.45(s, 3H), 3.67(s, 3H), 5.40(s, 1H), 6.75(b, 1H), 7.05-8.25(m, 7H). The reaction mixture was poured into 100ml of water and extracted with methylene chloride. The extract concentrated and the residue was chromatographed on silica gel eluted with toluene: ethyl acetate = 7:3 mixture (87% yield, m.p. = 130-133°C).

Reducing Characteristics of 4-(Borane-dimethylamino)pyridine. Chemoselective Reduction of Aldehydes in the Presence of Ketones

Sunggak Kim* and Sungbong Yang

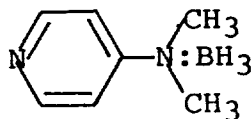
Department of Chemistry, Korea Advanced Institute of Science and Technology, Seoul 130-650

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Tertiary amine-borane and pyridine-borane complexes react with aldehydes and ketones sluggishly at an elevated temperature with transferring only one of the three available hydride equivalents.¹ Therefore, they failed to gain widespread use in synthetic applications in spite of their high stability and good solubility in protic and aprotic solvents, although most amine-borane complexes as hydride reducing agents have been known for a long time.¹

Since 4-dimethylaminopyridine (DMAP),² a highly active acylation catalyst, is expected to coordinate less tightly with borane than pyridine, the ability of hydride transfer in 4-(borane-dimethylamino)pyridine would be greater than that in pyridine-borane complex. Although 4-(borane-dimethylamino)pyridine is commercially available,³ as far as we are aware, there are no reports on the reducing property of the present reagent. Thus, we have briefly investigated its reducing property.

4-(Borane-dimethylamino)pyridine was easily prepared by mixing equimolar amounts of borane-dimethyl sulfide complex and DMAP in ether at room temperature and the desired product was precipitated as white solids. The reagent was soluble in dichloromethane and acetonitrile but insoluble in ether, tetrahydrofuran, ethanol, and water. Furthermore, the reagent was stable under nitrogen at room temperature for several months, whereas it readily decomposed in acidic aqueous solution with evolution of hydrogen gas.



Reduction of acetophenone with equimolar amounts of the reagent in dichloromethane occurred only to an observable extent, yielding 4% of α -methyl benzyl alcohol at room temperature for 24 h, whereas nonyl aldehyde was reduced to nonyl alcohol in 92% yield under the similar condition.

Table 1. Selective Reduction of Aldehydes in the Presence of Ketones with 4-(Borane-dimethylamino)pyridine^a

Starting mixture	% Reduction ^b
Nonyl aldehyde	95
Acetophenone	3
Nonyl aldehyde	98
Diisopropyl ketone	2
Nonyl aldehyde	98
3-Pentanone	10
Nonyl aldehyde	94
2-Undecanone	8
Nonyl aldehyde	96
Isophorone	0
Nonyl aldehyde	94
Carvone	2
Nonyl aldehyde	95
Mesityl oxide	2
Benzaldehyde	94
2-Undecanone	5
Butyraldehyde	87
Cyclohexanone	48

^aThe reaction was carried out with an equal mixture of the aldehyde, the ketone, and the reagent in dichloromethane at room temperature for 24 h. ^bDetermined by GLC using an internal standard.

Therefore, we turned our attention to the possibility of chemoselective reduction of aldehydes in the presence of ketones.⁴ The reaction of an equimolar mixture of nonyl aldehyde and acetophenone with 1 equiv of the reagent at room temperature for 24 h afforded a 95% reduction of nonyl aldehyde along with a 3% reduction of acetophenone. The change of solvent to acetonitrile and the use of 2 equiv of the reagent did not show appreciable enhancement of chemoselectivity

and reactivity. Thus, remaining reductions were carried out with equimolar amounts of an aldehyde, a ketone, and the reagent in dichloromethane at room temperature for 24 h. Table 1 shows some experimental results and illustrates the applicability and the scope of the present method.

A competition between nonyl aldehyde and diisopropyl ketone resulted in a 98% reduction of nonyl aldehyde and only a 2% reduction of the ketone. A competition between aldehydes and α,β -unsaturated ketones such as isophorone and carvone gave similar results, yielding chemoselective reduction of aldehydes along with a few % reduction of α,β -unsaturated ketones. In the case of relatively unhindered simple ketones such as 3-pentanone, 2-undecanone, and cycloheptanone, the chemoselectivity was slightly decreased, as compared with acetophenone and diisopropyl ketone. Furthermore, the reagent reaches a limit with cyclohexanone derivatives. For example, reduction of an equimolar mixture of butyraldehyde and cyclohexanone gave a 87:48 mixture of n-butanol and cyclohexanol under the same condition. Under the present conditions, carboxylic acids and esters were inert to the reagent for 24 h at room temperature and the starting materials were recovered unchanged.

Since boron trifluoride etherate was often utilized as a catalyst for activation of carbonyl compounds in the reduction of amine-borane complexes,⁵ we have briefly studied the reducing property of the reagent in the presence of boron trifluoride etherate. The reduction was carried out with an equimolar mixture of the substrate, the reagent, and boron trifluoride etherate in dichloromethane at room temperature. Under the present conditions, simple aldehydes and ketones such as benzaldehyde, acetophenone, and cycloheptanone were smoothly reduced to the corresponding alcohols in essentially quantitative yields within 2 h. In the case of α,β -unsaturated carbonyl compounds such as t-cinnamyl aldehyde

and mesityl oxide, it was found that the products were a mixture of allylic alcohols and saturated alcohols roughly in an equal ratio, resulting from concomitant 1,2 and 1,4 attack by hydride. Furthermore, reduction of esters occurred to half extent for 24 h at room temperature. Thus, methyl benzoate was reduced to benzyl alcohol in 42% yield along with 54% of the starting material.

In conclusion, 4-(borane-dimethylamino)pyridine is a mild reducing agent which is capable of selective reduction of aldehydes in the presence of ketones and the reducing agent in the presence of boron trifluoride etherate is comparable to sodium borohydride in its reducing property.

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A New Method for β -Lactam Formation from β -Amino Acids Using Benzotriazol-1-yloxytris(dimethylamino)phosphonium Hexafluorophosphate

Sunggak Kim* and Tai Au Lee

Department of Chemistry, Korea Advanced Institute of Science and Technology, Seoul 130-650

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One of the most common synthetic methods for the β -lactam formation is based on the intramolecular condensation of β -amino acids using condensing agents.¹ Among various condensing agents currently available, triphenylphosphine/2,2'-dipyridyl disulfide² and 2-chloro-1-methylpyridinium iodide³ are the most effective and reliable.

In connection with our research program directed toward the development of new methods for β -lactam formation,⁴ we have had an occasion to examine the β -lactam formation from β -amino acids using benzotriazol-1-yloxytris(dimethylamino)phosphonium hexafluorophosphate (BOP reagent).^{5,6} BOP reagent has been successfully utilized in the synthesis of peptides⁵ and esters⁷ as a condensing agent. However, as

far as we know, there are no reports on the application of BOP reagent for the β -lactam formation from β -amino acids. This paper describes a new method for the preparation of β -lactams from β -amino acids by using BOP reagent.

The solvent effect was briefly studied using 3-benzylaminobutyric acid as a model compound with 1.2 equiv of BOP reagent and triethylamine at 80°C for 20 h under a high dilution (0.01M solution). Among solvents employed in this study, acetonitrile gave the best result, yielding 64% of N-benzyl-4-methyl-2-azetidinone. Dichloromethane, N,N'-dimethylformamide, and tetrahydrofuran were much less effective, yielding the corresponding β -lactam in 31%, 30%, and 23% yield, respectively. Furthermore, it was observed