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-diemthylamino)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

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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 disulfide[2] and 2-chloro-1-methylpyridinium iodide[3] are the most effective and reliable.

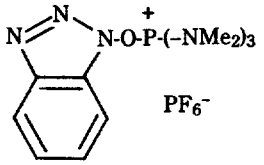
In connection with our research program directed toward the development of new methods for β-lactam formation,[4] we have had an occasion to examine the β-lactam formation from β-amino acids using benzotriazol-1-yloxytris(dimethylamino)phosphonium hexafluorophosphate (BOP reagent).[5,6] BOP reagent has been successfully utilized in the synthesis of peptides[5] and esters[7] 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

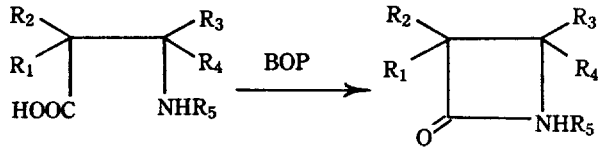
Table 1. Synthesis of β-Lactams from β-Amino Acids Using BOP Reagent[a]

β-lactams	isolated yield, %
$R_1 = CH_3$; $R_2 = OPh$; $R_3 = Ph$; $R_4 = H$; $R_5 = CH_2Ph$	99
$R_1 = R_4 = H$; $R_2 = OPh$; $R_3 = Ph$; $R_5 = CH_2Ph$	73
$R_1 = R_2 = R_4 = H$; $R_3 = CH_3$; $R_5 = CH_2Ph$	64
$R_1 = R_2 = H$; $R_3 = R_4 = CH_3$; $R_5 = CH_2Ph$	93
$R_1 = R_2 = R_3 = H$; $R_4 = n\text{-}C_3H_7$; $R_5 = CH_2Ph$	75
$R_1 = R_2 = R_3 = H$; $R_4 = CH_3$; $R_5 = n\text{-}C_8H_{17}$	59
$R_1 = R_2 = R_3 = R_4 = H$; $R_5 = c\text{-}C_6H_{11}$	76
$R_1 = R_3 = R_4 = H$; $R_2 = CH_3$; $R_5 = CH_2Ph$	46(38)[b]
$R_1 = R_3 = R_4 = H$; $R_2 = CH_3$; $R_5 = c\text{-}C_6H_{11}$	68(22)[b]
$R_1 = R_2 = R_3 = H$; $R_4 = CH_3$; $R_5 = H$	10

[a]The reaction was carried out in acetonitrile (0.01M solution) at 80 °C for 20 h. [b]The yield of isolated cyclic dimer.



BOP



that the reaction in acetonitrile under a low dilution (0.1M) afforded the desired β-lactam in 25% yield together with 34% of a cyclic dimer under the similar conditions. Thus, remaining reactions were normally carried out with 1.2 equiv of BOP reagent and triethylamine in acetonitrile (0.01M) at 80 °C for 20 h.

As shown in Table 1, the present method was successfully applied to a variety of structurally different N-substituted β-amino acids. Most N-substituted β-amino acids were cyclized to afford the corresponding β-lactams in excellent yields. In the case of 3-benzyl(or 3-cyclohexyl)amino-2-methylpropionic acid, 8-membered dimer was obtained as a byproduct along with the desired β-lactam. However, the present method appeared to have a limit in the formation of β-lactams from N-unsubstituted β-amino acids.

A typical procedure for β-lactams from β-amino acids is examplified as follows. To a suspended solution of 3-benzylamino-3-methylbutyric acid (207 mg, 1.0 mmol) and BOP reagent (530 mg, 1.2 mmol) in acetonitrile (100 m*l*) was added triethylamine (120 mg, 1.2 mmol) at room temperature. After being stirred at 80 °C for 20 h, the reaction mixture was concentrated under reduced pressure and the residue was passed through a short silica gel column using ethyl acetate and hexane (2:3) as an eluant to yield 1-benzyl-4,4-dimethyl-2-azetidinone (176 mg, 93%) as an oil.

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