

Cyclization of β -Amino Acids to β -Lactams by Using Diphenyl 2-(3-oxo-2,3-dihydro-1,2-benzisulfonazolyl) phosphonate

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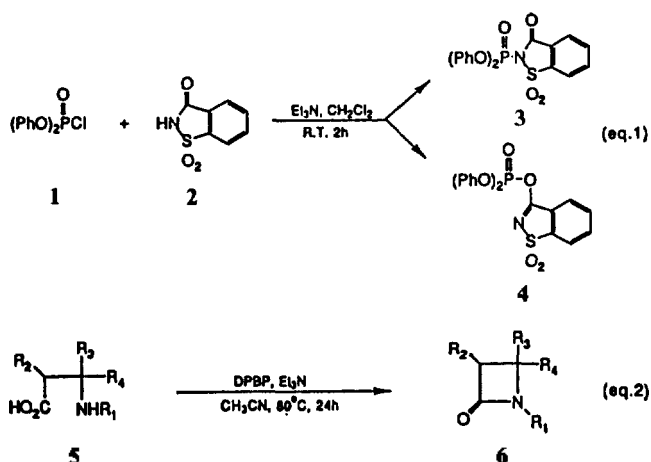
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A great deal of synthetic work has been already carried out in the formation of β -lactams from β -amino acids. One of the popular synthetic methods for the β -lactams formation is based on the intramolecular cyclization of β -amino acids using condensing agents¹. Among various organophosphorus condensing agents currently available, triphenylphosphine-tetrahalomethane², triphenylphosphine /2,2'-dipyridyl disulfide³, bis[5'-nitro-2'-pyridyl]-2,2'-trichloroethylphosphate⁴, N,N'-bis[2-oxo-3-oxazolidinyl]phosphorodiamidic chloride⁵, tris[2-oxo-3-oxazoliny]phosphine oxide⁶, diphenyl 2-oxo-3-oxazolinyphosphonate⁷, and benzotriazol-1-yloxytris(dimethylamino) phosphonium hexafluorophosphate⁸ are the most effective and reliable.

Recently, our group has studied the synthesis of condensing agents⁹. In the previous paper¹⁰, we have described the application of diethyl 2-(3-oxo-2,3-dihydro-1,2-benzisulfonazolyl)phosphonate. This paper describes further utility of saccharin (3-oxo-2,3-dihydro-1,2-benzisulfonazole, 2) moiety which plays an important role in a facile preparation of β -lactam derivatives (6) from β -amino acids (5) by using diphenyl 2-(3-oxo-2,3-dihydro-1,2-benzisulfonazolyl)phosphonate (DPBP reagent, 3).



DPBP reagent was conveniently obtained by the reaction of diphenyl chlorophosphate (1) with saccharin (2), and triethylamine in dichloromethane at room temperature for 2 h (Eq. 1). Phosphorylation of 2 might be expected to give either the O- or N-phosphoryl product, because of its well-known tautomerism. The reaction of 1 with 2 in dichloromethane at 25°C gave preferentially N-phosphoryl product 3.

Table 1. Synthesis of β -Lactams from β -Amino Acids

Description	Isolated yield (%)
R ¹ =CH ₂ Ph, R ² =H, R ³ =R ⁴ =CH ₃	97
R ¹ =CH ₂ Ph, R ² =R ³ =H, R ⁴ =CH ₃	80
R ¹ =CH ₂ Ph, R ² =CH ₃ , R ³ =R ⁴ =H	59
R ¹ =CH ₂ Ph, R ² =R ³ =H, R ⁴ =CH ₂ CH ₃	85
R ¹ =CH ₂ Ph, R ² =R ³ =H, R ⁴ =CH ₂ CH ₂ CH ₃	90
R ¹ =CH ₂ Ph, R ² =R ³ =H, R ⁴ =CO ₂ CH ₂ Ph	53
R ¹ =CH ₂ Ph, R ² =R ³ =H, R ⁴ =CO ₂ CH ₃	59
R ¹ =CH ₂ Ph, R ² =R ³ =R ⁴ =H	15
R ¹ =CH ₂ CH ₂ Ph, R ² =R ³ =H, R ⁴ =CH ₃	58
R ¹ =CH ₂ CH ₂ Ph, R ² =H, R ³ =R ⁴ =CH ₃	89

The structure of DPBP (3) was assigned on the basis of infrared spectroscopy. The IR spectrum showed the carbonyl absorption band at 1750 cm⁻¹. The reagent 3 is white crystalline solid and can be stored in a refrigerator for several weeks without any decomposition, and generally used without further purification.

We have briefly studied solvent effects using 3-benzylaminobutanoic acid, 1.2 equivalent of DPBP reagent and triethylamine at 80°C for 24 h. Among various solvents employed in this study, acetonitrile gave the best results, yielding 68% of 1-benzyl-4-methyl-2-azetidinone. Tetrahydrofuran and dichloromethane were much less effective, yielding the corresponding β -lactam in 66% and 63% yield, respectively.

Some experimental results are summarized in Table 1. N-substituted β -amino acids were cyclized to the corresponding β -lactams in good yields but N-unsubstituted β -amino acids gave very poor results.

Experimental

A typical procedure for the preparation of diphenyl 2-(3-oxo-2,3-dihydro-1,2-benzisulfonazolyl)phosphonate (Eq. 1): To a stirred solution of saccharin (400 mg, 2.2 mmol) and diphenyl chlorophosphate (709 mg, 2.6 mmol) in dichloromethane (10 ml) was added triethylamine (260 mg, 2.6 mmol) at room temperature. After being stirred for 2 h, the reaction mixture was evaporated in vacuo. The chromatographic purification on silica gel (CH₂Cl₂-EtOAc) gave the reagent 3 in essentially quantitative yield (823 mg, 90%) as a white crystalline solid melting at 109-110°C.

The representative experimental procedure for the reaction of β -amino acid with diphenyl 2-(3-oxo-2,3-dihydro-1,2-benzisulfonazolyl)phosphonate (Eq. 2): To a mixture of 3-benzyl amino-3-methylbutanoic acid (310 mg, 1.5 mmol) and DPBP reagent (748 mg, 1.8 mmol) in acetonitrile (150 ml) was added triethylamine (360 mg, 3.6 mmol) at room temperature. After being stirred for 24 h at 80°C, the reaction mixture was concentrated under reduced pressure and the residue was passed through silica gel column using ether-chloroform (2 : 1) as an eluent to yield 1-benzyl-4,4-dimethyl-2-azetidinone (257 mg, 97% yield) as an oil.

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Emission Spectra of the Uranyl Ion in Aqueous Solutions at 77 K

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The deactivation mechanism of the photo-excited dioxo-uranium(VI) (uranyl) ion, $^*UO_2^{2+}$ in aqueous solutions has been studied extensively since the late 1970s.¹⁻⁷ However, the mechanism remains a matter of controversy. The luminescence of $^*UO_2^{2+}$ in aqueous solutions has been reported to decay exponentially or not with the lapse of time depending on experimental conditions. It is of greatest interest that the luminescence decay is biexponential in the aqueous solutions where the uranyl ion is predominant. Marcantonatos *et al.* measured lifetimes with a single photon counting nanosecond spectrometer, and interpreted the biexponential decay in terms of exciplex formation between $^*UO_2H^{2+}$ and UO_2^{2+} .²⁻⁴ In their interpretation the formation of UO_2^+ and U(IV) ions are involved, but no evidence has been observed yet for the formation of the U(IV) ion even by the long-time exposure of UO_2^{2+} ion in aqueous solutions to light. On the other hand, Formosinho *et al.* studied excited uranyl decays using nanosecond flash-photolysis apparatus with a pulsed nitrogen laser.^{5,6} They proposed the deactivation mechanism

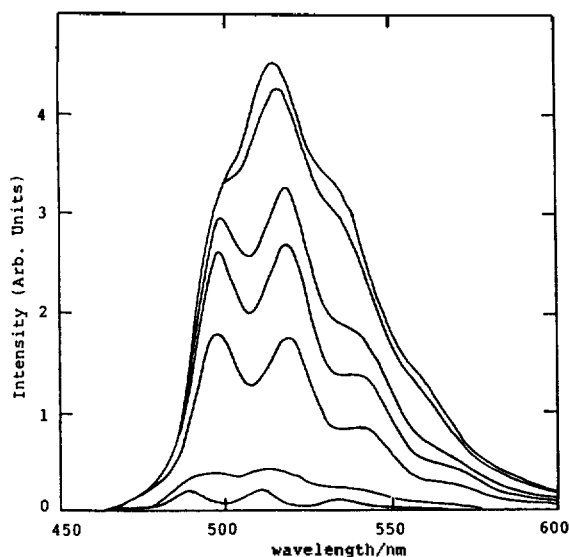


Figure 1. Emission spectra of uranyl ion in aqueous perchlorate solutions as a function of pH at ambient temperature: $[UO_2^{2+}]_T = 0.01$ M; pH (from the bottom) = 2.24, 3.01, 3.36, 3.49, 3.64, 3.76, and 3.82.

involving a reversible crossing process between two almost degenerate states of $^*UO_2^{2+}$. It has been reported that the luminescence decay of $^*UO_2^{2+}$ is four times or more faster than that of the other emitting species or state (*X).

In order to establish the identity of *X , we investigated emission spectra of UO_2^{2+} ion in aqueous solutions at ambient temperature and 77 K. The emission spectra were measured by using a Hitachi model 850 fluorescence spectrophotometer. Uranyl perchlorate solutions were prepared from $[UO_2(H_2O_9)](ClO_4)_2$, which was synthesized by the same method as described in a previous paper.⁸ The total uranyl ion concentration, $[UO_2^{2+}]_T$ of all sample solutions was 0.01 M (1 M = 1 mol dm⁻³). The pH readings of the solutions were carried out on a Toa IM-20E pH meter. The pH was adjusted with NaOH and HClO₄ solutions.

Figure 1 shows the emission spectra (excitation at 337 nm) of UO_2^{2+} ion in aqueous solutions as a function of pH at ambient temperature. The spectra changed markedly with increasing pH and thereby increasing hydrolysis products of UO_2^{2+} ion. The major hydrolysis products are known to be $(UO_2)_2(OH)_2^{2+}$ and $(UO_2)_3(OH)_5^+$ ions.⁹ The red shift of the bands corresponding to the $0' \rightarrow 0''$ transition is considered to be due to the formation of the hydrolysis products. This fact is in good agreement with the low-field shift of ¹⁷O NMR resonances of uranyl oxygen atoms by the hydrolysis because ¹⁷O chemical shifts of uranyl oxygen atoms in uranyl complexes increase with the decrease in their lowest electronic transition energies.^{10,11} The other characteristic aspect of the emission spectra is that band intensities increased significantly as hydrolysis proceeded. The intensities varied with pH to a greater degree than did those expected only from a consideration of change in the distribution of uranyl species in the ground state. For example, the emission spectrum at pH 3.36 is considerably different from that of $^*UO_2^{2+}$ at pH 2.24, in spite of the fact that the ratio of $[(UO_2)_2(OH)_2^{2+}]$ to $[UO_2^{2+}]$ is only ca. 0.05 at pH 3.36.