

A NEW SYNTHESIS OF 2-AMINO- γ -LACTONES INVOLVING
PHOTOCHEMICAL ADDITION REACTION OF ALCOHOLS TO ENAMIDE

Takeaki Naito and Ichiya Ninomiya*

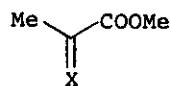
Kobe Women's College of Pharmacy, Motoyamakita, Higashinada,
Kobe 658, Japan

Abstract—Photochemical addition reaction of alcohols to the enamide (2) prepared from pyruvic acid ester has provided a new synthetic method of the 2-amino- γ -lactones (6a-d).

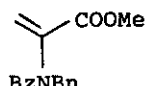
During the course of studies on the cyclization of enamides with various types of structures,^{1,2} we have investigated the photochemical behavior of the enamide (2) which was prepared from pyruvic acid ester and found that a new photochemical addition reaction of alcohols to the enamide provides a new and general synthetic method of the 2-amino- γ -lactones.

Though photocyclization of the N-benzoylenamine type of enamides derived from either cyclic or acyclic ketones has been well known to proceed smoothly to give the isoquinolones,^{1,2} photochemical study of the enamide derived from α -keto-ester hitherto has not been investigated except the intramolecular [2+2] photocycloaddition of the corresponding N-allylenamide.^{3,4}

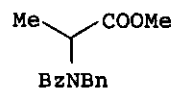
Benzoylation of the imine (1b), which was prepared by condensation⁵ of methyl pyruvate (1a) and benzylamine, gave the enamide (2) in 58% yield [$\nu(\text{CHCl}_3)\text{cm}^{-1}$: 1725 and 1645; $\text{nmr}(\text{CDCl}_3)$ δ :5.90 and 5.23(each s)($\text{CH}_2=\text{C}$)]. Attempted reductive photocyclization of the enamide (2) in the presence of sodium borohydride was unsuccessful due to susceptibility to reduction of the double bond leading to the formation of the corresponding methyl derivative (3). Thus, irradiation of the enamide (2) in methanol under non-oxidative condition with low pressure mercury lamp was carried out. The product was a mixture of two photo-products (4)(10%) and (5a)(20%) which were readily separated by chromatography and characterized by the following spectral analysis and chemical conversion. The first eluted product (4) was found to be the expected photocyclized lactam [m/z : 295 (M^+); $\text{nmr}(\text{CDCl}_3)$ δ :8.20(m, 8-H) and 4.22(dd, $J=6$ and 2.5Hz, 3-H)].



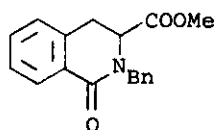
(1a) X=O
(1b) X=NBn



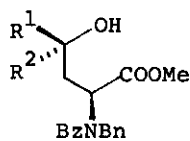
(2)



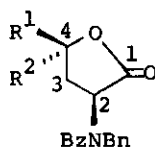
(3)



(4)

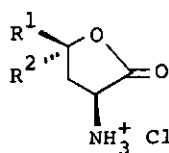


(5a-d)

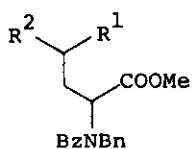


(6a-d)

	R ¹	R ²
a:	H	H
b:	Me	H
c:	H	Me
d:	Me	Me



(7a) R¹=Me, R²=H
(7b) R¹=H, R²=Me



(8a) R¹--O(CH₂)₃--R²
(8b) R¹--(CH₂)₃O--R²
(8c) R¹--(CH₂)₅--R²

(Bn=CH₂Ph)
(Bz=COPh)

The second product (5a) exhibited unassignable broad nmr spectrum. The structure of (5a) was deduced from its chemical conversion by treatment with *p*-toluenesulfonic acid into the 2-amino- γ -lactone (6a) which exhibited the following spectra [m/z : 295 (M^+); $\text{ir}(\text{CHCl}_3)$ cm^{-1} : 1780 and 1640; $\text{nmr}(\text{CDCl}_3)$ at 51°C δ : 4.56 (br td, $J=8.5$ and 3.5 Hz, 4-H), 4.22 (q, $J=8.5$ Hz, 4-H), and 4.14 (m, 2-H)]. Thus, it has been found that the enamide (2) undergoes photoaddition reaction of methanol used as solvent. In order to establish the generality of this photoaddition reaction, we investigated photochemical reaction of the enamide (2) in other alcohols. On irradiation in ethanol, the enamide (2) gave the adducts (5b) and (5c) which were also characterized by their conversion to the corresponding 2-amino- γ -lactones (6b) (24%) [$\text{nmr}(\text{CDCl}_3)$ at 52°C δ : 4.94 (sext, $J=6.5$ Hz, 4-H) and 2.62 (dt, $J=13$ and 8 Hz, 3-H) and 1.94 (ddd, $J=13, 10.5,$ and 4.5 Hz, 3-H) and (6c) (25%) [$\text{nmr}(\text{CDCl}_3)$ at 51°C δ : 4.45 (sext, $J=6.5$ Hz, 4-H) and 2.33 (t-like, $J=8$ Hz, 3-H₂)]. Their stereochemistry was deduced by comparison of their nmr spectra with the authentic 2-amino- γ -lactones⁶ (7a) and (7b) of which the cis-lactone (7a) exhibited two signals at δ : 3.43 (ddd, $J=12, 8.5,$ and 5.5 Hz) and 2.55 (td, $J=12$ and 10 Hz) due to two hydrogens at the 3-position while the trans-lactone (7b) exhibited a single signal at δ : 3.06 (m) due to the same two hydrogens.

Similarly, on irradiation in isopropanol, the adduct (5d) was obtained and characterized as its 2-amino- γ -lactone (6d) in 49% yield. Further, in addition to alcohols, two organic solvents such as tetrahydrofuran and cyclohexane were found to be photochemically incorporated into the enamide (2). Two adducts (8a)(24%) and (8b)(20%) were obtained by irradiation of (2) in tetrahydrofuran and a single adduct (8c)(27%) in cyclohexane, respectively, though the stereochemistry of the former two adducts (8a) and (8b) was not established.

These 2-amino- γ -lactones (6a-d) synthesized in this work are derivatives of biologically important γ -hydroxyamino acids, such as homoserine (constituent of toxic marine cyanophyte),⁷⁻⁹ γ -hydroxynorvaline (constituent of *Boletus satanas* Lenz),^{6,9} and γ -hydroxyleucine (constituent of mushroom toxin phalloin).⁹

Thus, we have established a new synthetic method of the 2-amino- γ -lactones involving photochemical addition reaction of alcohols to the enamide followed by acidic lactonization though mechanistic study of the initial photochemical addition reaction has not been clarified.

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