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PHOTOCHEMISTRY OF 4(3H)-PYRIMIDIN-4-ONES. FORMATION OF MEDIUM-RING LACTAMS.

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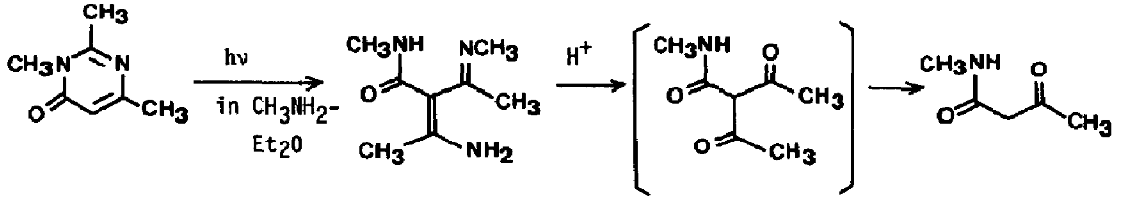
Abstract: Upon irradiation, 4(3H)-pyrimidin-4-one(1) afforded a di-imine derivative(2), which, when hydrolyzed in an acidic methanol solution, gave N-methyl acetoacetamide(3). On the other hand, the fused 4(3H)-pyrimidin-4-ones, (4) and (5), gave medium-ring lactams(6) and (7), which were hydrolyzed in an acidic methanol solution to give (8) and (9), respectively.

We previously reported the photochemical rearrangement of 2,3,6-trialkyl-4(3H)-pyrimidin-4-ones to β-lactams in alcoholic solutions.1),2) These β-lactams have an alkoxy group arising from solvolysis at the β position to carbonyl group. Accordingly, if this photochemical reaction of 4(3H)-pyrimidin-4-ones is carried out in other protic solvents, it would offer a utility as an efficient tool for the synthesis of β-lactams having various substituents. Furthermore, during the course of the investigation, we found an interesting acid-catalyzed rearrangement of fused β-lactams obtained by the photochemical reaction of 4(3H)-pyrimidin-4-ones.3) These results promoted us to investigate the photochemical reaction of 4(3H)-pyrimidin-4-ones in various solvents.

In this paper we report on the photochemistry of 4(3H)-pyrimidin-4-ones in a mixed methylamine-ether solution(1:5). Irradiation of 2,3,6-trimethyl-4(3H)-pyrimidin-4-one(1) in a mixed methylamine-ether solution(1:5) in a quartz vessel with a 200W high pressure mercury lamp for

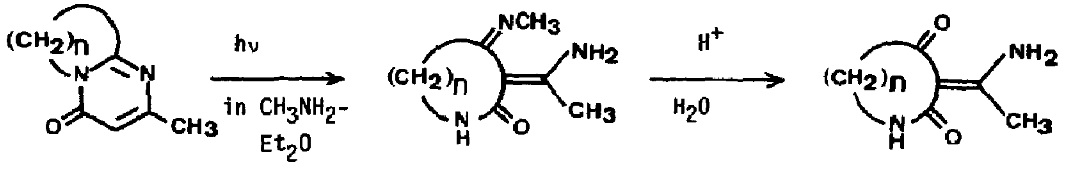
24h at 0° afforded N-methyl-2-aminoethylidene-3-methylimino-butanoamide(2). The isolated yield of (2) was 13.5%. The starting material was recovered in 67% yield. [mp 128 ∿ 131°; ν_{max}^{KBr} 3360, 3200, and 1620 cm^{-1}; UV(MeOH)nm 335(4.12×10^3), 278(1.06×10^4)]4),5) This photoproduct(2) was hydrolyzed in methanol solution containing water(11%) and a catalytic amount of acetic acid(1%) for 24h at room temperature to give N-methyl acetoacetamide(3)6) in 60% yield.



(1) (2) (3)

When six membered fused 4(3H)-pyrimidin-4-one(4) in a mixed methylamine-ether solution(1:5) was irradiated under the same conditions, 2-(aminoethylidene)-3-methylimino-7-heptanelactam (6), a medium-ring lactam [mp 185 ∿ 187°; ν_{max}^{KBr} 3340, 3275, 3160, 3030, 1640, and 1610 cm^{-1}; δ(DMSO-d_6) 1.00-2.00(m, 4H), 1.80(s, 3H), 1.87-2.37(m, 2H), 2.67-3.50(m, 2H), 3.07(s, 3H), 7.35 (br.t, J=6Hz, 1H), 7.33-10.16(br., 2H); UV(MeOH)nm 305(7.85×10^3), 268(5.69×10^3)] was obtained. The isolated yield of (6) was 30.0%. The starting material was recovered in 51% yield.

Similarly, 2-(aminoethylidene)-3-methylimino-8-octanelactam(7), a medium-ring lactam [mp 166 ∿ 168°; ν_{max}^{KBr} 3415, 3270, 3060, 1660, and 1630 cm^{-1}; δ(DMSO-d_6) 0.87-1.90(m, 6H), 1.78(s, 3H), 1.93-2.47(m, 2H), 2.60-3.50(m, 2H), 3.12(s, 3H), 7.45(br.t, J=6Hz, 1H), 7.50-9.30(br., 2H); UV(MeOH)nm 311(8.32×10^3), 272(4.06×10^3)] was obtained in 22.4% isolated yield when seven membered fused 4(3H)-pyrimidin-4-one(5) was irradiated in a mixed methylamine-ether solution (1:5) under the same conditions as described above. The starting material was recovered in 61.2% yield. When these medium-ring lactams(6) and (7) were treated with an acidic methanol solution(11% water and 1% acetic acid) for 24h at room temperature enamino ketone derivatives (8) and (9)3) were obtained in 91% and 84% yields, respectively.

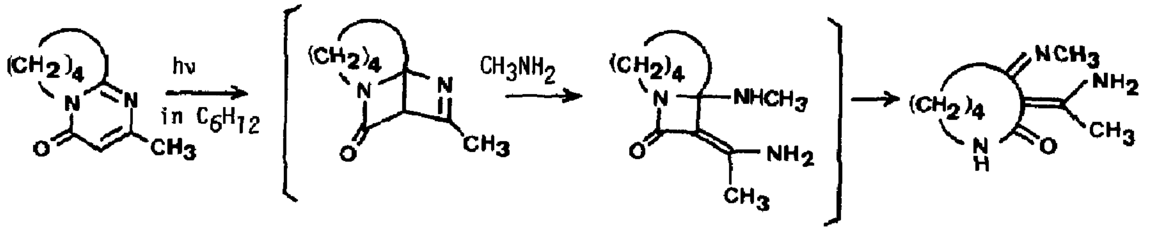


(4) n = 4
(5) n = 5

(6) n = 4
(7) n = 5

(8) n = 4
(9) n = 5

The photolysis of (4) in cyclohexane at 10° was carried out in order to obtain further information about the reaction mechanism. The photolyzed mixture, when treated with a mixed methylamine-ether solution(1:5) after irradiation, afforded medium-ring lactam(6) in 10.2% isolated yield. This result shows that the Dewar type intermediate(X) formed initially by an electrocyclic reaction[7] of 4(3H)-pyrimidin-4-one would react with methylamine to give β-lactam(Y), followed by cleavage of the brigehead N-C bond to afford the final product, (6).



(4) (X) (Y) (6)

Thus, we have found a new synthesis of 8 and 9 membered lactams having the reactive di-imine system[8] by carring out the photochemical reaction of fused 4(3H)-pyrimidin-4-ones in the mixed methylamine-ether solution. The application of the present method to the synthesis of 10 and 11 membered lactams is now in progress.

References and Notes

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4) This compound(2) existed in an equilibrium mixture of (2a) and (2b) in solvents. Therefore, the PMR spectrum of (2) was complicated and the relative intensities of the signals were varied with both solvent and temperature.

(2a) (2b)

5) Satisfactory elemental analyses were obtained on all new compounds.

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