PHOTOCHEMISTRY OF 4-PYRIMIDINONES. VII.
REACTION OF DEWAR 4-PYRIMIDINONE WITH METHYLAMINE

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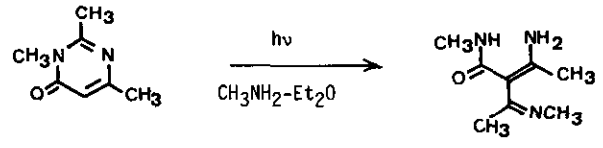
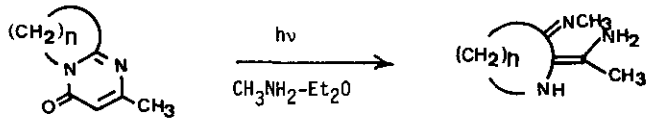
Abstract ---- Irradiation of the 2,3,6-trialkyl-4-pyrimidinones (1) and (5) in methylamine solution at 0°C gave the amidine derivatives (6) and (7). The reaction of Dewar 4-pyrimidinone (9) with methylamine in methylamine-ether gave the di-imine derivative (2) and the amidine derivative (6). The fraction of the amidine (6) increased with increasing methylamine concentration.

Hitherto, we have studied systematically the photochemical reactions of 4-pyrimidinones.[1] In a preliminary communication, we reported the preparation of the di-imine (2) by the photochemical reaction of the monocyclic 4-pyrimidinone (1) in methylamine-ether (1:5) solution and the new synthesis of medium-ring lactams (4) having the reactive di-imine system[2] starting from the fused 4-pyrimidinones (3).[1c] Furthermore, during the course of the investigation, we found that irradiation of the 2,3,6-trimethyl-4-pyrimidinone (1) in liquid methylamine solution gave mainly crystalline amidine (6). The structure of this product (6) was quite different from that of the photochemical product (2) formed in methylamine-ether (1:5) solution. These results prompted us to investigate the influence of methylamine concentration on the photochemical reaction of 4-pyrimidinones.

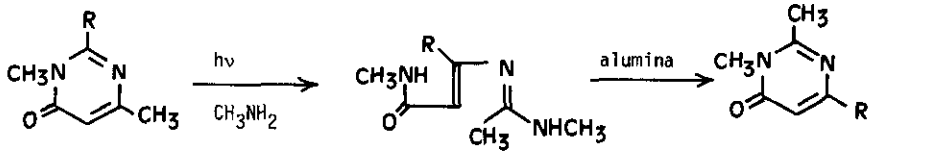


(1) (2)



(3) n = 4 or 5 (4) n = 4 or 5

A solution of 2,3,6-trimethyl-4-pyrimidinone (1) in liquid methylamine was irradiated through quartz under nitrogen atmosphere at 0°C for 24 h. After evaporation of the solvent, the residue was chromatographed on Sephadex LH 20 and was recrystallized from ethyl acetate to isolate N-methyl-3-[(N-methylaminoethylidene)amino]-2-butenamide (6) in 27.2% conversion yield[3] [mp 115-117°C; ν_{max}^{KBr} 3360, 3235, 1650, and 1620 cm^{-1}; δ(DMSO-d_6) 1.80 (6H,br s), 2.65(3H,d,J=4Hz), 2.72(3H, d,J=3Hz), 4.93(1H,s), 6.73-7.37(1H,br), and 7.17-7.83(1H,br); UV(MeOH)nm 274(7.45x10^3) and 221(7.24 x10^3)].[4] Similarly, N-methyl-3-[(N-methylaminoethylidene)amino]-2-pentenamide (7) [mp 109-111°C; ν_{max}^{KBr} 3360, 3230, 1645, and 1620 cm^{-1}; δ(DMSO-d_6) 1.13(3H,t,J=7Hz), 1.90(3H,s), 2.23(2H,q,J=7Hz), 2.57(3H,d,J=4Hz), 2.66(3H,d,J=2Hz), 4.15(1H,s), 6.70-7.30(1H,br), and 7.15-7.80(1H,br)] was obtained in 32.2% conversion yield[5] when 3,6-dimethyl-2-ethyl-4-pyrimidinone (5) was irradiated in liquid methylamine under the same conditions as described above. When these amidine derivatives (6) and (7) were chromatographed on alumina, 4-pyrimidinones (1) and (8) were obtained, respectively. These results indicate that methylamine reacted at position 6 of starting materials, 4-pyrimidinones.

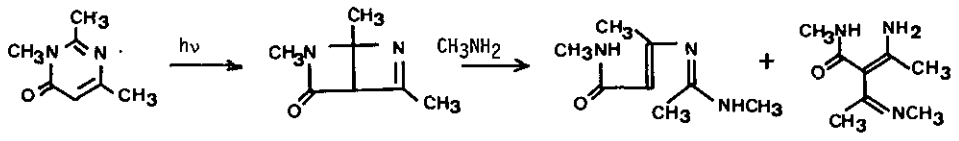


(1) R = CH_3 (6) R = CH_3 (1) R = CH_3

(5) R = CH_2CH_3 (7) R = CH_2CH_3 (8) R = CH_2CH_3

We already reported that irradiation of a liquid ammonia-ether (8:2) solution of 2,3,6-trimethyl 4-pyrimidinone (1) at -40°C gave Dewar 4-pyrimidinone (32%).[1e] To examine exactly the influence of concentration of methylamine, the reactions of Dewar 4-pyrimidinone with methylamine in various concentrations of methylamine-ether solution were carried out.

A solution of (1)(2g) in liquid ammonia-ether (8:2) was irradiated at -40°C for 8 h.[6] After evaporation of the solvent, the residue was dissolved in methylamine-ether (200ml). The solution was left in a strage at -20°C for 7 days. After evaporation of the solvent, the residue was chromatographed on Sephadex LH 20 to give a mixture of the di-imine (2) and the amidine (6). The fraction of (6) to (6) + (2) varied from 0:100 (methylamine:ether = 37:63) to 67:33 (methylamine:ether = 100:0). The results are shown in Figure I and Table I. It is of interest to note that the fraction of amidine (6) increases with increasing methylamine concentration.



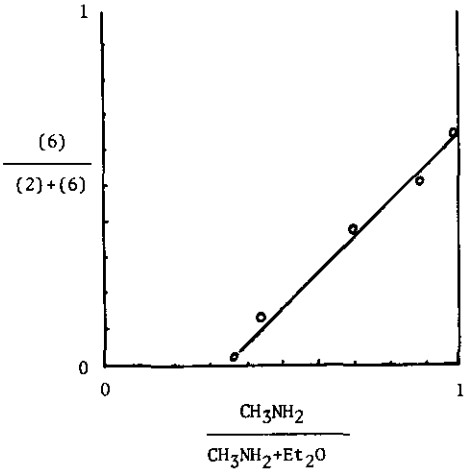
(1) (9) (6) (2)

Table I. Dependence of the amidine (6) on the mole fraction of methylamine-ether solution at -20°C

$\frac{CH_3NH_2}{CH_3NH_2 + Et_2O}$	$\frac{(6)}{(2) + (6)}$
100	67
88	51
70	38
44	12
37	0

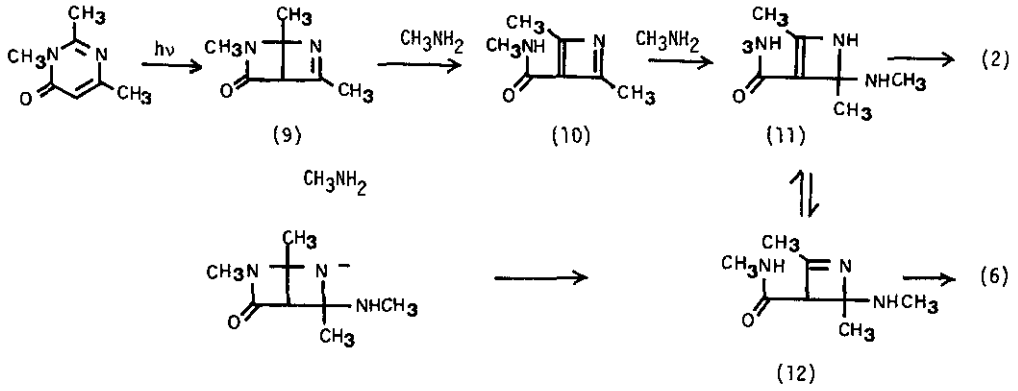
The fraction of (2) and (6) were estimated by integration of the peak areas of the NMR spectra at 35°C.

Figure I. Dependence of the amidine (6) on the mole fraction of methylamine-ether solution at -20°C



The reaction mechanism might be explained as follows. The initial abstraction of the methine proton of (9) by methylamine gives the azacyclobutadiene (10) which then reacts with methylamine to give the azetine (11). The azetine (11) gives the open-chain product (2). Also, (11) isomerizes to (12) which leads to the formation of (6). According to an alternative reaction mechanism it could be assumed that the 1,4 addition of methylamine to Dewar 4-pyrimidinone (9) gives the azetine (12) which leads to the formation of (2) and (6). The fraction of the di-imine (2) and the amidine (6) would be corresponded to the fraction of the formation of (11) and (12). Addition of ether in methylamine solution causes the decrease of the solvent porarity. Therefore, it is considered that the fraction of (12) increases with an increase in the polarity of solvent. However, the influence of the methylamine concentration could not elusidate from the present results.

The photochemistry of 4-pyrimidinones in other amine solution is now in progress.



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1. a) T.Yamazaki, M.Nagata, S.Hirokami, Y.Hirai, and T.Date, Heterocycles, 1978, 9, 505. b) S.Hirokami, Y.Hirai, M.Nagata, T.Yamazaki, and T.Date, J. Org. Chem., 1979, 44, 2083. c) Y.Hirai, T.Yamazaki, S.Hirokami, and M.Nagata, Tetrahedron Lett.,1980, 3067. d) T.Kato, N.Katagiri, U.Izumi, Y.Miura, T.Yamazaki, and Y.Hirai, Heterocycles, 1981, 15, 399. e) S.Hirokami, T.Takahashi, M.Nagata, Y.Hirai, and T.Yamazaki, J. Org. Chem., 1981, 46, 1769.
2. There are some reports on the reactions of di-imine compounds; a) J.Barluenga, S.Fustero, and V.Gotor, Synthesis, 1957, 191. b) J.Barluenga, M.Tomás, v.Bubio, and V.Gotor, Chem. Comm., 1979, 675. c) J.Barluenga, M.Tomás, S.Fustero, and V.Gotor, Synthesis, 1979, 345.
3. The starting material was recovered in 46% yield.
4. Satisfactory elemental analyses were obtained on all new compounds.
5. The starting material was recovered in 52% yield.
6. Dewar 4-pyrimidinone was formed in 32% yield together with 4-pyrimidinone as the starting material. The fractions of Dewar 4-pyrimidinone and 4-pyrimidinone were estimated by integration of the peak areas of the NMR spectra at 35°C.

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