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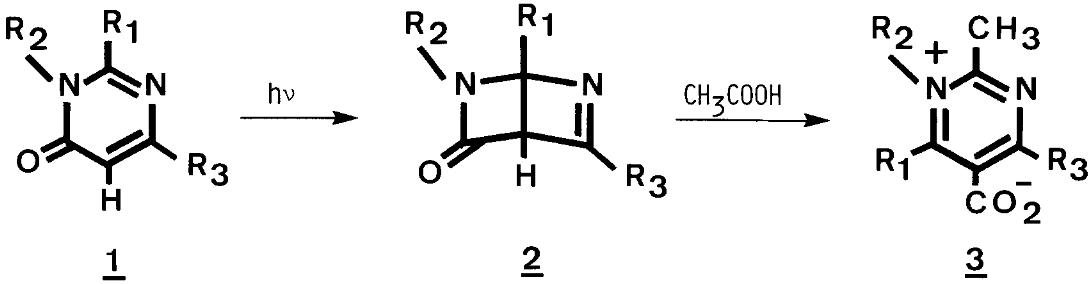
PHOTOCHEMICAL REACTIONS OF 4-PYRIMIDINONES IN ACETIC ACID. FORMATION OF 5-CARBOXYPYRIMIDINIUM BETAINES

Shun-ichi Hirokami,(a) Tamiko Takahashi,(a) Masanori Nagata,(a)
and Takao Yamazaki(b)*
(a) Laboratory of Chemistry, Toyama Medical and Pharmaceutical University, Sugitani 2630, Toyama 930-01, Japan, (b) Faculty of Pharmaceutical Sciences, Toyama Medical and Pharmaceutical University, Sugitani 2630, Toyama 930-01, Japan

Abstract: Irradiation of 4-pyrimidinone 1 in acetic acid solution gave 5-carboxypyrimidinium betaine 3. The photochemical intermediate for the formation of the betaine 3 was the Dewar 4-pyrimidinone 2.

The primary photochemical reaction of 4-pyrimidinone is the formation of the Dewar 4-pyrimidinone by disrotatory electrocyclic reaction.1,2) The Dewar 4-pyrimidinones undergo SN1 and nucleophilic addition reactions in protic solvents as a means of releasing ring strain.1-4) During the course of our studies, we encountered a zwitterionic product which resulted from unusual rearrangement. The structure of the product was confirmed by synthetic method. We wish to report this rearrangement as an interesting example of ring transformation reaction of 4-pyrimidinone.

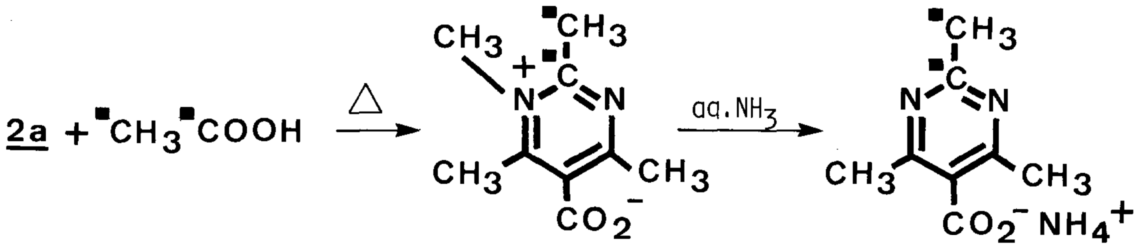
When an acetic acid solution of 1a [λmax(CH_3COOH) 269 nm(ε 3910)] was irradiated at 25°C with a 100 w high pressure mercury lamp through quartz under an argon atmosphere, 5-carboxypyrimidinium betaine 3a5) was obtained in a yield of 69% (based on the consumed 1a). Analogous photolysis of 1b-g gave the betaines 3b-g5) in 55-100% yields. The thermal reaction of acetic acid with the Dewar 4-pyrimidinones (2a, 2e, and 2f)1) in an acetic acid-acetonitrile or in an acetic acid solution at 0-20°C gave the corresponding betaines(3a, 3e, and 3f) in 54, 47, and 61% yields, respectively. The results indicated clearly that the Dewar 4-pyrimidinone 2 is the photochemical intermediate in the formation of the betaine 3.



	R_1	R_2	R_3	Yield of 3 (%)	mp, °C
a	CH_3	CH_3	CH_3	69	223-225 (dec.)
b	C_2H_5	CH_3	CH_3	84	229-231 (dec.)
C	CH_3	CH_3	C_2H_5	55	226-227 (dec.)
d	Ph	CH_3	CH_3	62	204-206 (dec.)
e	CH_3	CH_3	Ph	100	194 (dec.)
f	p-CH_3O-$PhCH_2$	CH_3	t-Bu	83	185-187 (dec.)
g	-$(CH_2)_4$-		CH_3	57	>300

The structure of the product 3a was assigned by its spectral data. To confirm the structure 3a by synthesis, the betaine 3a was converted to 5-ethoxycarbonyl-1,2,4,6-tetramethylpyrimidinium iodide5) in methanol solution containing ethyl iodide at 70°C. The pyrimidinium salt was synthesized from 5-ethoxycarbonyl-2,4,6-trimethylpyrimidine6) with methyl iodide. The synthesized compound was found to be identical (spectra) with that obtained from 3a. When the betaine 3a was treated in an aqueous ammonia solution at 20°C, ammonium 2,3,6-trimethylpyrimidine-5-carboxylate5) was obtained in a quantitative yield. The structure of the ammonium salt was deduced from its spectral data.

In order to determine the positions of two carbon atoms derived from acetic acid, we undertook the reactions of the Dewar 4-pyrimidinone 2a with [1,2-^{13}C] acetic acid in an acetonitrile solution at 0°C and of the formed product 3a* in an aqueous ammonia solution at 20°C. The ^{13}C labeled product 3a* and ammonium salt 4a* were obtained in 57 and 98% yields, respectively. The ^{13}C labeled methyl group is located at position 2, which was readily determined by the symmetry of 4a* based on the ^{1}H and ^{13}C NMR spectra. The ^{1}H and proton-noise-decoupling ^{13}C NMR spectra of 3a* and 4a* in methanol-d_4 exhibited the H-^{13}C, H-^{13}C-^{13}C, and ^{13}C-^{13}C couplings between 2-methyl and C(2). The coupling constants of 3a* are J_{CH} = 132 Hz, J_{HCC} = 7.1 Hz, and J_{CC} = (57.8 ± 0.4) Hz and those of 4a* are J_{CH} = 129 Hz, J_{HCC} = 6.9 Hz, and J_{CC} = (59.4 ± 0.4) Hz. Furthermore, in the mass spectrum of 3a*, two ^{13}C atoms are incorporated in the molecular(M^+) and fragment(M^+-CO_2) ions. No ^{13}C atom is found in the carboxylic group at position 5.



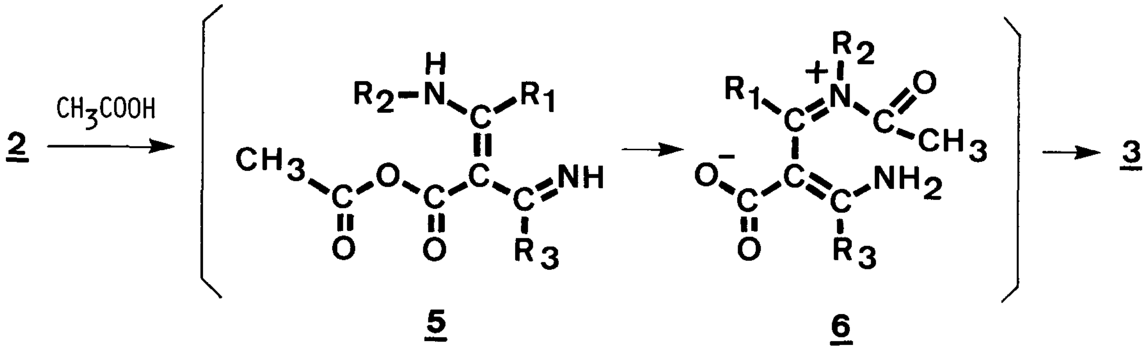
3a*

4a*

The positions of the substituents (R_1, R_2, and R_3) of the betaines 3a-g were determined by the chemical shifts of the ^{1}H and ^{13}C NMR spectra and by the analyses of the fragment peaks of the mass spectra.

A plausible mechanism for the formation of the products is that the carboxylic group of acetic acid adds to the β-lactam carbonyl carbon of 2 with concomitant cleavage of the amide bond to give the mixed anhydride 5. Intramolecular acetylation of the secondary amine gives the zwitterion 6, which undergoes a condensation reaction between the amide carbonyl and the amine to give 3 (Scheme 1).

Scheme 1



Further studies on the scope and mechanism of the ring transformation reaction are now in progress.

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5) Satisfactory spectral and analytical data were obtained for each new compound. Complete spectroscopic details will be provided in a later publication.

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