PHOTOCHEMICAL REARRANGEMENT OF FUSED ZWITTERIONIC PYRIDAZINES AND PHOTOCHEMICAL RING CONTRACTION OF FUSED PYRIMIDONE

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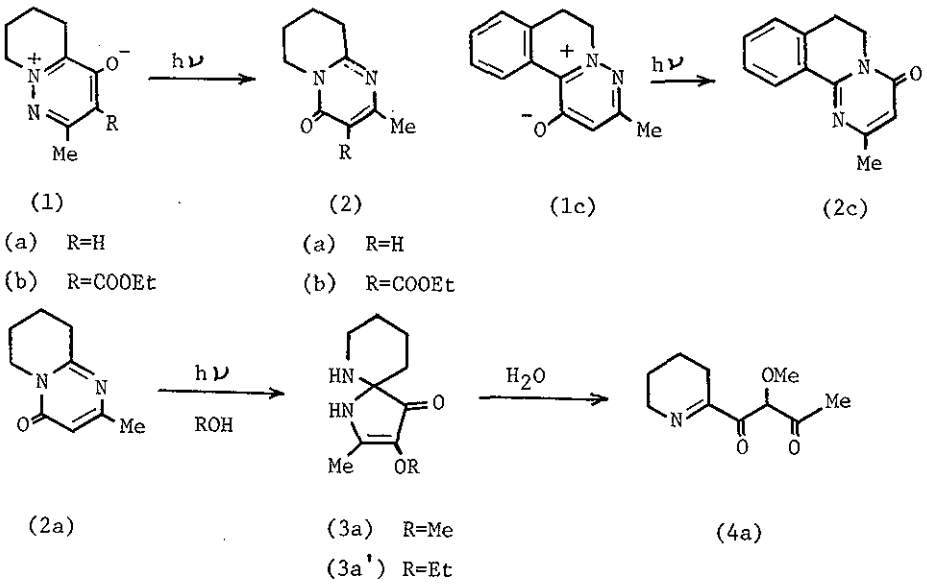
Photolysis of zwitterionic pyridazine (1a-c) in liquid phase afforded pyrimidin-4-ones (2a-c). Photolysis of 6,7,8,9-tetrahydro-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one (2a) in methanol gave 1,6-diaza-3-methoxy-2-methyl-4-oxospiro[4,5]dec-2-ene (3a). Photolysis of (2a) in ethanol gave also 1,6-diaza-3-ethoxy-2-methyl-4-oxospiro[4,5]dec-2-ene (3a'). Hydrolysis of (3a) in methanol or in chloroform containing a small amount of water yielded 2-(α-acetyl-α-methoxyacetyl)-3,4,5,6-tetrahydropyridine (4a).

In the previous report, we described a general method for the preparation of anhydro 1-substituted or 1,6-disubstituted 5-hydroxypyridazinium hydroxides, and showed that the 3-position of the compounds was subjected to both the electrophilic and the nucleophilic substitutions.[1] In the process of the studies on photochemical and thermal 1,3-dipolar cycloaddition of some dipolarophiles such as dimethyl acetylenedicarboxylate and acrylonitrile to fused zwitterionic

pyridazines, photochemical rearrangement of zwitterionic pyridazines to pyrimidones has been found.[2)]

On the other hand, the photochemical reactions of 2-pyridones, carbostyril, 3-pyridazinones and 2-pyrazinone have been described, and the mechanisms of dimerization and isomerization of these compounds have been elucidated.[3-9)]

We wish to report that photochemical rearrangement of fused zwitterionic pyridazines to fused 4-pyrimidones occurs in a liquid phase and that photochemical ring contraction of a fused pyrimidone takes place in methanol and in ethanol, yielding 3-alkoxy-1,6-diaza-2-methyl-4-oxospiro[4,5]dec-2-enes. Particularly, the latter case is the first example of photochemical ring contraction of pyrimidone, which has hitherto been unknown.



(1)
(a) R=H
(b) R=COOEt

(2)
(a) R=H
(b) R=COOEt

(1c)

(2c)

(2a)

(3a) R=Me
(3a') R=Et

(4a)

Chart 1

A solution of anhydro 3-substituted 5,6,7,8-tetrahydro-4-hydroxy-2-methylpyrido[1,2-b]pyridazinium hydroxide (1a-b) (1.5g) in methanol (300ml) was irradiated for 4-10 hr with a 200W high-pressure mercury lamp through a quartz tube under nitrogen at room temperature. The irradiated solutions were concentrated and the residues, eluted from alumina with benzene, were purified to give 6,7,-8,9-tetrahydro-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one (2a) from (1a) in 60-70% yield [mp 82-83° , IR($CHCl_3$)cm^{-1} 1662(C=O) ; UV(MeOH) λmax nm(ε) 228(6100), 274(4700) ; NMR($CDCl_3$, ppm) 1.97 (4H, 7,8-CH_2, quintette, J=3.2 Hz), 2.24 (3H, CH_3, s), 2.92 (2H, 9-CH_2, t, J=6.3 Hz), 3.95 (2H, 6-CH_2, t, J=6.3 Hz), 6.18 (1H, 3-H, s) ; MS m/e 164 (M^+)] and to afford 3-ethoxycarbonyl-6,7,8,9-tetrahydro-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one (2b) from (1b) in 15-20% yield [yellow oil ; IR($CHCl_3$)cm^{-1} 1735(CO-OEt), 1675(C=O) ; UV(MeOH) λmax nm(ε) 225 (4800), 283(5900) ; NMR($CDCl_3$, ppm) 1.38(3H, OCH_2-$\underline{CH_3}$, t, J=7.2 Hz), 1.94 (4H, 7,8-CH_2, quintette, J=3.0 Hz), 2.33 (3H, CH_3, s), 2.90 (2H, 9-CH_2, t, J=6.3 Hz), 3.94 (2H, 6-CH_2, t, J=6.3 Hz), 4.38 (2H, O-$\underline{CH_2}$-CH_3, quartet, J=7.2 Hz) ; MS m/e 236 (M^+)], respectively.

Photolysis of (1a) in ethanol or in benzene instead of methanol gave also (2a) in 60-70% yield. The products (2a) and (2b) were not formed thermally in methanol, even by heating at 64°.

Analogous photo-rearrangement leading to 6,7-dihydro-2-methyl-4H-pyrimido-[2,1-a]isoquinolin-4-one (2c) was observed when anhydro 6,7-dihydro-1-hydroxy-3-methylpyridazino[3,2-a]isoquinolinium hydroxide (1c) was irradiated in methanol under the conditions similar to the case of (2a-b).[2a] After evaporation of methanol, the residue was purified by recrystallization to furnish (2c) in 80-90% yield [mp 114-116° ; IR(KBr)cm^{-1} 1670(C=O) ; UV(MeOH) λmax nm(ε) 248(9990), 302(11900) ; NMR($CDCl_3$, ppm) 2.33 (3H, CH_3, s), 3.03 (2H, 7-CH_2, t, J=6.3 Hz), 4.28 (2H, 6-CH_2, t, J=6.3 Hz), 6.27 (1H, 3-H, s), 7.15-7.60 (3H, 8,9,10-H, m), 8.27-8.47 (1H, 11-H, m) ; MS m/e 212 (M^+)].

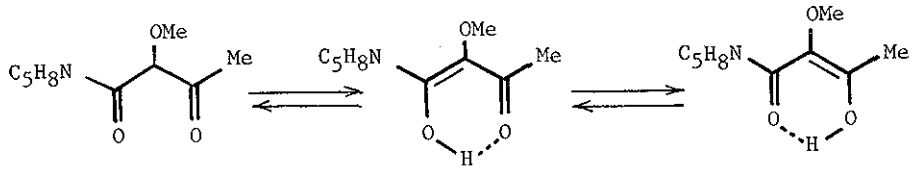
During further investigation of the reaction, several reports on the photochemistry of zwitterionic pyridazine have recently been published.[10-12] In these papers, it is reported that zwitterionic pyridazines rearrange to pyrimidones. These experimental results show that the photochemical rearrangement occurs regardless of the substituents at the pyridazine ring.

Shorter time irradiation of (1a) in methanol gave (2a) mainly, but continued irradiation for about 20 hr until the complete disappearance of the starting material resulted in the formation of (2a) in about 60% yield and 1,6-diaza-3-methoxy-2-methyl-4-oxospiro[4,5]dec-2-ene (3a) in about 20% yield [mp 178-180° ; IR(KBr)cm^{-1} 3430, 3360, 3250(NH and OH), 1710, 1690(C=O) ; UV(MeOH) λmax nm(ε) 271(23300) ; NMR(C_5D_5N, ppm) 2.26 (3H, CH_3, s), 3.32 (3H, OCH_3, s), 5.87 (2H, NH, s) ; MS m/e 196 (M^+)]. Photolysis of the isolated (2a) for 3-5 hr in methanol led to the formation of (3a) in 25-30% yield, thus suggesting that product (3a) was formed by a secondary photolysis of (2a). Retention of piperidine ring moiety and appearance of a quaternary carbon on the photolysis of (2a) were suggested by ^{13}C-NMR spectral data on the reaction produt, thus supporting the structure given to (3a).

Photolysis of (2a) in ethanol for 3-5 hr instead of methanol gave 1,6-diaza-3-ethoxy-2-methyl-4-oxospiro[4,5]dec-2-ene (3a') in 25-30% yield [mp 140-141° ; IR(KBr)cm^{-1} 3450, 3360, 3260(NH and OH), 1720, 1690(C=O) ; UV(MeOH) λmax nm(ε) 271(12100) ; NMR(C_5D_5N, ppm) 1.20 (3H, OCH_2-$\underline{CH_3}$, t, J=7.0 Hz), 2.30 (3H, CH_3, s), 3.62 (2H, O-$\underline{CH_2}$-CH_3, quartet, J=7.0 Hz), 5.93 (2H, NH, s) ; MS m/e 210 (M^+)].

After the concentration of reaction mixture, products (3a) and (3a') were readily crystallized from the resulting residue by adding a small amount of benzene or diethyl ether. The product (3a) was not formed thermally in methanol at 64°. Approximately 50% of starting material (2a) in the experimetal runs was recovered in order to avoid the further photolysis of (3a) or (3a').

Product (3a) decomposed gradually in methanol or in chloroform containing a small amount of water at room temperature, yielding 2-(α-acetyl-α-methoxyacetyl)-3,4,5,6-tetrahydropyridine (4a) [mp 49-50° ; IR(KBr)cm^{-1} 1700(C=O), 1600(C=N) ; UV(MeOH)λmax nm(ε) 248(8320), 304(16600) ; NMR($CDCl_3$, ppm) 1.77 (4H, 4,5-CH_2, quintette, J=3.0 Hz), 2.23 (3H, CH_3, s), 2.73 (2H, 3-CH_2, t, J= 6.0 Hz), 3.43 (2H, 6-CH_2, t, J=6.0 Hz), 3.73 (3H, OCH_3, s), 12.93 (1H, α-CH, s) ; MS m/e 197 (M^+)]. The NMR spectrum ($CDCl_3$) showed an enol-type hydrogen at 12.93 ppm. The signal at 12.93 ppm associated with enol structure disappeared on D_2O treatment, but others were essentially left unchanged. Thus, the structure of (4a) could be depicted by tautomeric form (4a)-A,B,C.



(4a)-A (4a)-B (4a)-C

Chart 2

The mechanistic elucidation for the photochemical ring contraction of pyrimidones is now in progress.

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