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Studies on Heteroaromaticity. XXIX.[1] Synthesis and Reactions of 1-(5-Nitro-2-furoyl)aziridine Oxime

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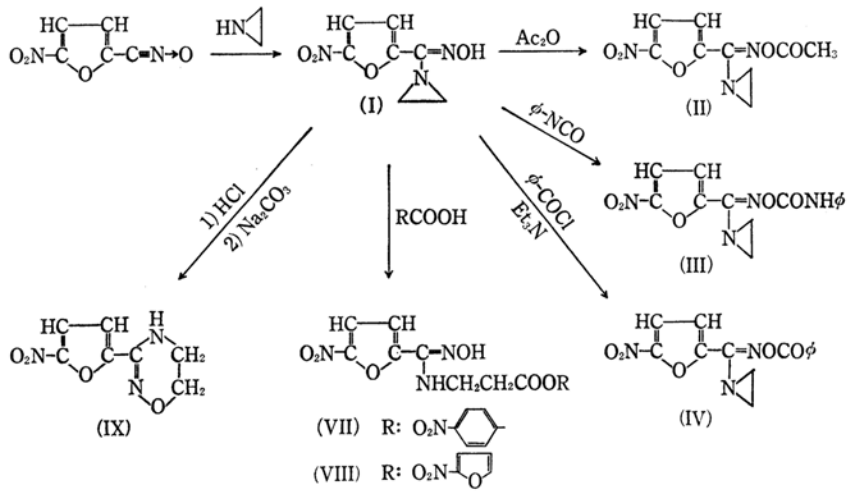
In the previous papers,[2,3] we have reported the ring-opening reactions of β-(5-nitro-2-furyl)-acryloylaziridine and *N*-[β-(5-nitro-2-furyl)vinyl]-*N'*-ethyleneurea with acid, base or nucleophilic reagents affording oxazoline derivatives similar to general activated aziridine derivatives,[4] but in low yields.

This paper deals with the synthesis and reactions of 1-(5-nitro-2-furoyl)aziridine oxime (I), which was readily prepared from 5-nitro-2-furonitrile oxide[5] and aziridine in ether at 0°C in 80% yield. This structure was confirmed by the elemental analysis and the spectral data; an absorption at 3200 cm^{-1} in the infrared spectrum and a signal at 7.75 τ (singlet, 4H, $-CH_2-CH_2-$) in the NMR spectrum indicate the presence of an OH group and aziridine ring respectively. The aziridine ring in I was comparably stable and it did not react at all with aniline or *p*-toluidine even when it was refluxed in toluene for 8 hr. By addition of a catalytic amount of boron trifluoride etherate to a dry ethereal solution of I and aniline, however, I polymerized even at room temperature. Treatmet of I with acetic anhydride at room temperature, with phenyl isocyanate in refluxing benzene, or with benzoyl chloride in the presence of triethylamine at room temperature, gave the corresponding *O*-substituted oximates, II, III, and IV, in high yields respectively.

(V) (VI)

Aziridines V possessing unsaturated substituents on the nitrogen are known to undergo ring expansion to yield 1-azacyclopentene derivatives VI.[6] It was of interest to determine whether or not the similar processes would occur in our aziridine oxime.

All attempts for ring-expansion of I by treating it in refluxing ethanol with organic acids like *p*-nitrobenzoic acid or 5-nitro-2-furoic acid were unsuccessful and only resulted in the cleavage of the aziridine ring to form products, VII and VIII, in low yields. The infrared spectra of VII and VIII showed common absorptions at 3500,



1) Part XXVIII of this series: T. Sasaki and M. Ando, *Yuki Gosei Kagaku Kyokai-shi* (*J. Soc. Org. Synth. Chem., Japan*), **27** 169 (1969).
2) T. Sasaki and T. Yoshioka, *ibid.*, **25**, 658 (1967).
3) T. Sasaki and T. Yoshioka, This Bulletin, **41**, 1258 (1968).
4) G. E. Ham, *J. Org. Chem.*, **29**, 3052 (1964).
5) T. Sasaki and T. Yoshioka, This Bulletin, **40**, 2604 (1967).
6) P. Scheider, *J. Org. Chem.*, **32**, 2628 (1967).

3400 (ν_{NH}), 1720, and 1715 (ν_{CO}) cm^{-1} and their ultraviolet absorption spectra manifested patterns similar to that of *N*-methyl-(5-nitro-2-furan)carbonamidoxime which is known to be a tautomeric mixture between its amino oxime and amino alcohol.[7] However, when I was treated with a mineral acid such as hydrochloric acid in acetone at room temperature for 1 day, an oily product was obtained, which was further treated with an aqueous sodium carbonate solution to afford 3-(5-nitro-2-furyl)-4,5-dihydro-6*H*-1,2,4-oxadiazine (IX), mp 195—197°C, in 51% yield; this structure was confirmed by the elemental analysis and the spectral data. The infrared spectrum showed absorptions at 3200 (sharp, ν_{NH}) and 1620 ($\nu_{C=N}$) cm^{-1} and the NMR signals appeared at around 2.6 τ (broad, 1H, NH), 6.10 (triplet, 2H, $-CH_2O-$) and 6.61 (multiplet, 2H, $-CH_2N-$), all supporting the presence of 4,5-dihydro-6*H*-1,2,4-oxadiazine ring in IX.

About the mechanism of the formation of IX from I, this reaction seems to proceed through two discrete steps; the first step is the cleavage of the ring by acid treatment and the second one is the ring closure by alkaline treatment, as have been reported by Rajagopalan and Talaty.[8]

All the results are summarized in the above scheme.

Experimental[9]

1-(5-Nitro-2-furoyl)aziridine Oxime (I). 5-Nitro-2-furohydroxamoyl chloride[7] (0.95 g) was dissolved in 20 m*l* of dry ether. To this solution was added a solution of 1.0 m*l* of aziridine in 5 m*l* of dry ether with stirring at 0—5°C. After 3 minutes' stirring at the same temperature, aziridine hydrochloride was filtered off and the filtrate was kept standing overnight in an ice box. The precipitates were collected, washed with ethanol and recrystallized from ethanol to afford 0.7 g (80%) of I as light yellow crystals, mp 172°C (decomp). IR (KBr) cm^{-1}: 3200 (broad, ν_{OH}), 1630 ($\nu_{C=N}$). UV λ_{max}^{EtOH} mμ (ε): 348 (11600), 250 (8000). NMR (DMSO-d_6) τ: −1.25 (singlet, 1 H, OH, disappeared on deuteration), 2.28 and 2.92 (each doublet, 1 H, J=3.8 cps, nitrofuran ring protons), 7.65 (singlet, 4 H, $-CH_2-CH_2-$).

Found: C, 42.82; H, 3.73; N, 20.82%. Calcd for $C_7H_7O_4N_3$: C, 42.64; H, 3.58; N, 21.32%.

1-(5-Nitro-2-furoyl)aziridine Oxime *O*-Acetylate (II). A solution of 0.4 g of I in 6 m*l* of acetic anhydride was allowed to stand at room temperature overnight. Removal of the unreacted acetic anhydride *in vacuo* afforded an oil. It was treated with 10 m*l* of water to give yellow precipitates, which were recrystallized from ethanol - petroleum ether to give 0.27 g (55%) of II, mp 129°C. IR (KBr) cm^{-1}: 1760 (ν_{CO}). UV λ_{max}^{EtOH} mμ (ε): 326 (16500), 250 (10200).

Found: C, 44.94; H, 3.69; N, 17.42%. Calcd for $C_9H_9O_5N_3$: C, 45.19; H, 3.79; N, 17.57%.

1-(5-Nitro-2-furoyl)aziridine Oxime *O*-Phenylcarbamate (III). A mixture of 0.23 g of I and 0.3 m*l* of phenyl isocyanate in 20 m*l* of dry benzene was refluxed for 4 hr. After removal of the solvent under reduced pressure, the residue was recrystallized from ethanol to give 0.27 g (71%) of III, mp 145°C. IR (KBr) cm^{-1}: 3360 (ν_{NH}), 1750 (ν_{CO}). UV λ_{max}^{EtOH} mμ (ε): 330 (15500), 237 (22000).

Found: C, 53.00; H, 3.84; N, 18.49%. Calcd for $C_{14}H_{12}O_5N_4$: C, 53.16; H, 3.82; N, 17.72%.

1-(5-Nitro-2-furoyl)aziridine Oxime *O*-Benzoate (IV). A mixture of 0.3 g of I and 4 m*l* of benzoyl chloride was dissolved in a mixture of 10 m*l* of tetrahydrofuran and 10 m*l* of dry ether. To this solution was added 0.4 m*l* of triethylamine in 5 m*l* of dry ether at room temperature with stirring. After stirring was continued for 3 hr, the solids which separated were filtered, washed with water and recrystallized from ethanol to give 0.76 g (80%) of IV as light yellow crystals, mp 166°C. IR (KBr) cm^{-1}: 1735 (ν_{CO}). UV λ_{max}^{EtOH} mμ (ε): 325 (15300), 254 (12100), 232 (14800).

Found: C, 56.05; H, 3.72; N, 13.94%. Calcd for $C_{14}H_{11}O_5N_3$: C, 55.81; H, 3.68; N, 13.95%

Reaction of I with Organic Acids. A solution of 0.4 g of I and 0.35 g of *p*-nitrobenzoic acid in 30 m*l* of ethanol was refluxed for 7 hr. The solvent was removed under reduced pressure and the oily residue was treated with 20 m*l* of ethanol - water (1 : 2). The solids which separated were filtered and recrystallized from ethanol - petroleum ether to give 0.36 g (50%) of VII as yellow crystals, mp 122°C. IR (KBr) cm^{-1}: 3500 (ν_{NH}), 3200 (ν_{OH}), 1720 (ν_{CO}). UV λ_{max}^{EtOH} mμ (ε): 360 (5900), 295 (9600), 254 (19200).

Found: C, 45.88; H, 3.29; N, 15.70%. Calcd for $C_{14}H_{12}O_8N_4$: C, 46.16; H, 3.32; N, 15.38%.

Similarly, 0.25 g (30%) of VIII, mp 134—136°C, was obtained from 0.4 g of I and 0.37 g of 5-nitro-2-furoic acid after 4 hr's refluxing in 15 m*l* of ethanol and worked up as above. IR (KBr) cm^{-1}: 3490 (ν_{NH}), 3400 (ν_{OH}), 1715 (ν_{CO}). UV λ_{max}^{EtOH} mμ (ε): 360 (6200), 294 (16500), 234 (10300).

Found: C, 40.91; H, 2.84; N, 15.92%. Calcd for $C_{12}H_{10}O_9N_4$: C, 40.68; H, 2.85; N, 15.82%.

3-(5-Nitro-2-furyl)-4,5-dihydro-6*H*-1,2,4-oxadiazine (IX). To a solution of 0.4 g of I in 8 m*l* of acetone was added a mixture of 2 m*l* of concentrated hydrochloric acid and 5 m*l* of acetone at 0—5°C for 0.5 hr with stirring. Stirring was continued at room temperature for 1 day. After a distillable fraction was removed under reduced pressure, an oily residue was dissolved in 10 m*l* of water and the solution was made alkaline with an aqueous sodium carbonate solution and then, stored overnight in an ice box. The precipitates were collected, washed with water and recrystallized from

7) T. Sasaki and T. Yoshioka, *Yuki Gosei Kagaku Kyokai-shi* (*J. Soc. Org. Synth. Chem., Japan*), **25**, 665 (1967).

8) P. Rajagopalan and C. N. Talaty, *J. Am. Chem. Soc.*, **88**, 5048 (1966).

9) All melting points were determined on a Yanagimoto electric micromelting point apparatus and uncorrected. All the infrared and ultraviolet spectra were recorded on a JASCO Model IR-S infrared spectrometer and on a Hitachi Model ESP-2 recording spectrometer respectively. The NMR spectra were taken on a Varian A-60 apparatus with tetramethylsilane as an internal standard and the chemical shifts are presented in terms of τ-values.

ethanol to give 0.24 g (51%) of IX as brown crystals, mp 197°C. IR (KBr) cm^{-1}: 3200 (sharp, ν_{NH}), 1620 ($\nu_{C=N}$). UV λ_{max}^{EtOH} mμ (ε): 348 (7300), 304 (7600), 240 (6800). NMR (DMSO-d_6) τ: 2.88 and 2.90 (each doublet, 1 H, J=3.8 cps, nitrofuran ring protons), 2.6 (broad, 1 H, NH, disappeared on deuteration), 6.10 (triplet, 2 H, J=4.0 cps, CH_2), 6.61 (multiplet, 2 H, CH_2).

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