BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN VOL. 42 3008—3010 (1969)

Studies of Heteroaromaticity. XXXI.[1] New Reactions of Aromatic Amidoximes with Diketene

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(Received March 22, 1969)

While diketene is known to react with thiourea, amidines and guanidines affording uraciles,[2-4] no report has been given on the reactions with amidoximes. As a continuation of the previous papers[1,5] concerning the reactivity of aromatic amidoximes, this note deals with their new reactions with diketene.

Treatment of *p*-nitrobenzamidoxime (Ia) with a small excess amount of diketene in refluxing toluene afforded a quantitative yield of colorless product (IIIa); the infrared spectrum in a potassium bromide pellet showed a strong carbonyl absorption at 1720 cm^{-1} and the NMR spectrum in deuteriochloroform exhibited chemical shifts at 1.70 τ (singlet, 4 H, *p*-substituted phenyl protons), 5.81 (singlet, 2 H, methylene) and 7.60 (singlet, 3 H, methyl). From these data and microanalysis, compound IIIa was concluded as 3-(*p*-nitrophenyl)-5-acetonyl-1,2,4-oxadiazole. This result is of interest, when compared with our previous report[6] that 3-(5-nitro-2-furyl)-5-methylisoxazole was prepared by the reaction of diketene with 5-nitro-2-furhydroxamoyl chloride. Similarly, the products, IIIb and IIIc, were obtained from *m*-nitrobenzamidoxime (Ib) and 5-nitro-2-furamidoxime (Ic) respectively. These results are summarized in Table 1.

When treated with diketene in acetic acid or in pyridine at room temperature, Ic afforded a quantitative yield of 5-nitro-2-furamidoxime *O*-acetoacetate (IIc), a ring-opened product of IIIc, as thin yellow crystals of mp 136—138°C, which was readily cyclized to IIIc by refluxing in toluene. This provides good evidence that the formation of IIIc from Ic might proceeds *via* an intermediate IIc and that this reaction is initiated by the nucleophilic attack of diketene to the hydrogen of hydroxime, not to that of amine.[7] When diketene was replaced by ethylene carbonate, phenyl glycidyl ether or β-propiolactone in the above reactions, no reactions could be observed.

When the *N*-phenyl- (IVc) or the *N*-methylamidoxime (IVc′) was treated with diketene instead of Ic under the reaction conditions similar

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[1] Part XXX of this series: T. Sasaki and T. Yoshioka, This Bulletin, **42**, 556 (1969).

[2] R. Lacy, *J. Chem. Soc.*, **1954**, 839.

[3] Y. Iwakura and K. Nakakubo, *Nippon Kagaku Zasshi (J. Chem. Soc. Japan, Pure Chem. Sect.)*, **57**, 947 (1951).

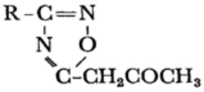
[4] N. Khromov-Borisov and R. Karlinskaya, *Zhur. Obschchei Khim.*, **26**, 1728 (1956).

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

[6] T. Sasaki and T. Yoshioka, This Bulletin, **42**, 258 (1969).

[7] T. Kato, *Yuki Gosei Kagaku Kyokai-shi (J. Soc. Org. Synth. Chem. Japan)*, **26**, 311 (1968).

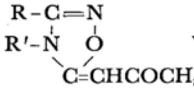
TABLE 1. OXADIAZOLES



III

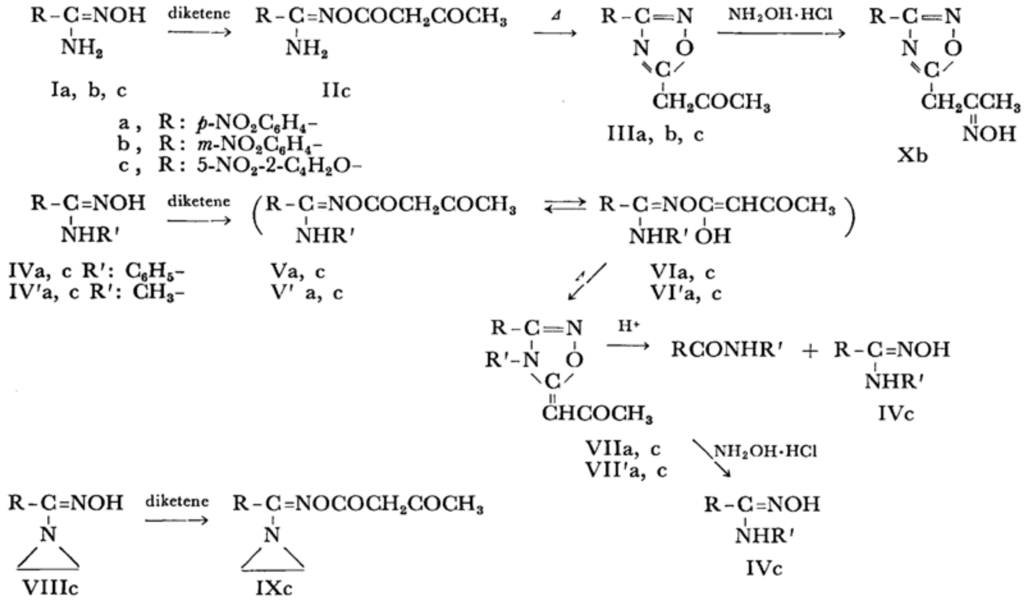
R	Product	Mp °C	Yield %	Found (Calcd) C%	H%	N%	UV λ_{max}^{EtOH} mμ ($\varepsilon\times10^{-4}$)
p-NO_2-C_6H_4-	IIIa	143—144	95	53.15 (53.44	3.61 3.67	16.67 17.00)	274 (1.4)
m-NO_2-C_6H_4-	IIIb	150—151	95	53.68 (53.44	3.80 3.67	16.75 17.00)	262 (1.0)
5-NO_2-2-C_4H_2O-	IIIc	108—110	85	45.58 (45.57	2.95 2.98	17.94 17.72)	310 (1.3)

TABLE 2. OXADIAZOLINES



VII

R	R′	Product	Mp °C	Yield %	Found (Calcd) C%	H%	N%	UV λ_{max}^{EtOH} mμ ($\varepsilon\times10^{-4}$)
p-NO_2-C_6H_4-	C_6H_5-	VIIa	220—222	95	63.47 (63.15	4.55 4.65	12.74 13.00)	292 (3.7) 250 (1.2)
p-NO_2-C_6H_4-	CH_3-	VIIa′	221—223	95	54.98 (55.17	3.97 4.24	15.75 16.09)	294 (3.6) 246 (1.2)
5-NO_2-2-C_4H_2O-	C_6H_5-	VIIc	235—237	90	57.63 (57.51	3.58 3.54	13.57 13.42)	304 (3.5)
5-NO_2-2-C_4H_2O-	CH_3-	VIIc′	195—196	90	47.97 (47.81	3.64 3.61	16.21 16.21)	



to those of N-non-substituted amidoximes, the product, VIIc or VIIc′, showed a different UV-spectral pattern, as seen by comparing Tables 1 and 2. The NMR spectrum of the product VIIa′ from N-methyl p-nitrobenzamidoxime (IVa′) and diketene showed a methine signal at 4.92τ, in addition to those at 7.88 (singlet, 3 H, methyl), 6.78 (singlet, 3 H, methyl), and 2.04 (quartet, 4H, $J=9$ cps, p-nitrophenyl protons). Similarly, the NMR spectrum of the product VIIa from the N-phenyl amidoxime (IVa) and diketene showed a methine signal at 5.45τ, in addition to those at 7.91 (singlet, 3 H, methyl), 2.40 (singlet, 5 H, N-phenyl protons) and 2.0 (quartet, 4 H, $J=9$ cps, p-nitrophenyl protons). Acidic hydrolysis of VIIc afforded a 50% yield of 5-nitro-2-furanilide, mp

171—173°C[8] together with a 30% yield of IVc, which was also produced directly from VIIc and hydroxylamine hydrochloride in boiling ethanol, though IIIb afforded the corresponding ketoxime (Xb) under similar reaction conditions. The mechanism for the formation of VII from IV might be explained similarly by the intermediate formation of a simple adduct (V) which is in tautomeric equilibrium with its enol form (VI), and VI is cyclized to VII after removal of water. In fact, an oily product obtained from IVc and diketene in acetic acid at room temperature was thermally converted to VIIc.

Similar treatment of 1-(5-nitro-2-furoyl)aziridine oxime (VIIIc) with diketene afforded a simple addition product (IXc); this structure was confirmed on the basis of analytical and spectral data.

As previously reported about VIIIc,[1] IXc remained also unchanged upon treatment with sodium iodide in boiling acetone.

Experimental

NMR spectra were measured by a Varian A-60 spectrometer at 60 Mc using tetramethylsilane as an internal standard and DMSO-d_6 as a solvent, unless otherwise stated. The chemical shifts were expressed in τ-values.

3-(*p*-Nitrophenyl) - 5 - acetonyl - 1,2,4 - oxadiazole (IIIa). A mixture of Ia (0.5 g) and diketene (1 m*l*) was refluxed in toluene (20 m*l*) for 10 hr. After removing toluene under reduced pressure from the reaction mixture, water was added to the residue and extraction was carried out with ether. The ether layer was washed with dilute hydrochloric acid. The residue obtained after removing ether was recrystallized from a mixture of ethanol and petroleum ether to afford IIIa. Similar treatment of Ib and Ic afforded the corresponding oxadiazoles, IIIb and IIIc, respectively. All the results are summarized in Table 1.

5-Nitro-2-furamidoxime *O*-Acetoacetate (IIc). A mixture of Ic (0.5 g) and diketene (0.5 m*l*) was dissolved in acetic acid (10 m*l*) and the solution was stirred for 2 hr at room temperature. The precipitated crystals were collected and recrystallized from a mixture of ethanol and benzene to afford 0.35 g of IIc. Further 0.3 g of IIc were obtained from the filtrate. The total yield was over 90%. Mp 136—138°C. ν_{max}^{KBr} 3570, 3400 (NH), 1770 (OCO), 1720 (CO) cm^{-1}.

Found: C, 42.47; H, 3.46; N, 16.25%. Calcd for $C_9H_9O_6N_3$: C, 42.36; H, 3.56; N, 16.47%.

When the same procedure was applied to Ic in pyridine instead of acetic acid, a quantitative yield of IIc was also obtained.

The Thermal Conversion of IIc to IIIc. IIc (0.4 g) was dissolved in toluene (25 m*l*) and the solution was refluxed for ten days. The precipitates were filtered after cooling and recrystallized from a mixture of ethanol and benzene to afford 0.1 g (30%) of Ic, which was identified by IR-spectral comparison with a specimen prepared by the above method. The filtrate was condensed under reduced pressure and the residue was recrystallized from a mixture of benzene and petroleum ether to afford 0.2 g (50%) of IIIc. When this thermal conversion was carried out in the presence of diketene, IIIc was obtained almost quantitatively.

3-(5-Nitro-2-furyl)- methyl- 5 -acetonylidene - 1,2, 4-oxadiazoline (VIIc). A mixture of IVc (0.5 g) and diketene (1 m*l*) was dissolved in toluene (20 m*l*) and the solution was refluxed for 11 hr. The reaction mixture was condensed and ethanol was added to the residue. The resulting crystals were filtered and recrystallized from ethanol several times to give 0.6 g (90%) of thin yellow needles, VIIc, having a mp 195—196°C (decomp.). ν_{max}^{KBr} 1660 (CO) cm^{-1}. The results are given in Table 2.

Acidic Hydrolysis of VIIc. VIIc (0.4 g) was added to a mixture of concd. hydrochloric acid (0.6 m*l*) and water (20 m*l*) and the mixture was stirred at 85—90°C for 7 hr. The crystals precipitated after cooling were collected and recrystallized from a mixture of benzene and petroleum ether to give 0.24 g (50%) of 5-nitro-2-furanilide.[8] The filtrate was made alkaline with sodium carbonate and the resulting crystals were collected and characterized as *N*-phenyl 5-nitro-2-furamidoxime IVc by IR-spectral comparison with a specimen prepared by another method.[5] The yield was 30% (0.2 g).

1-(5-Nitro-2-furyl)aziridine Oxime *O*-Acetoacetate (IXc). VIIIc (0.46 g) and diketene (1 m*l*) were dissolved in toluene (20 m*l*) and the solution was refluxed for 10 hr. After removing toluene under reduced pressure, the residual oil was recrystallized from ethanol to give 0.6 g (90%) of IXc, mp 195—196°C (decomp.). ν_{max}^{EtOH} ($\varepsilon \times 10^{-4}$) 320 (1.4), 245 (1.1) m$\mu$. ν_{max}^{KBr} 1775 (OCO), 1710 (CO) cm^{-1}.

Found: C, 46.71; H, 3.89; N, 14.96%. Calcd for $C_{11}H_{11}O_6N_3$: C, 46.98; H, 3.94; N, 14.94%.

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[8] R. Marquis, *Ann. Chim.*, (8), **4**, 196 (1905).