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Studies of Heteroaromaticity. XLVI.[1] Syntheses of 2,5-Disubstituted 1,3,4-Oxadiazoles Containing Nitrofuran Nucleus

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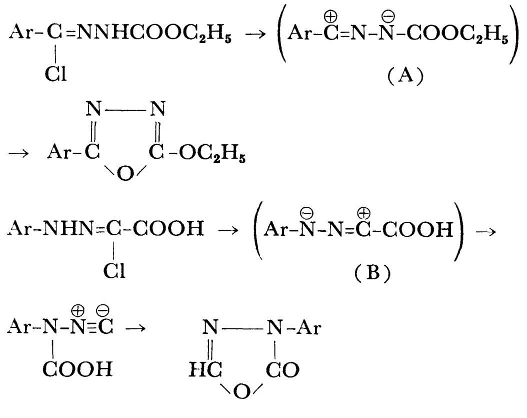
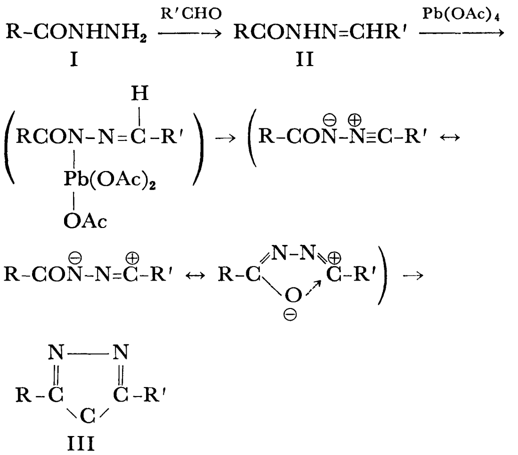
In a previous paper, we reported that aroyl and ary nitrile oxides have a similar reactivity in the 1,3-dipolar cycloaddition.[2] In continuation of our studies on similar reactivity of the nitrile imines,[3] this paper describes our attempts to prepare *N*-aroyl nitrile imines. 1-α-chlorobenzylidene-2-ethoxycarbonylhydrazine is reported to cyclize by triethylamine to 2-phenyl-5-ethoxy-1,3,4-oxadiazole[4] and in a similar manner, aryhydrazonochloroacetic acids cyclize to 4-aryl-5-oxo-1,3,4-oxadizol-2-ines.[5] Both cyclization reactions might be explained by postulating intermediate *N*-ethoxycarbonyl benzonitrile imine (A) and *C*-carboxynitrile imine (B), respectively.



As in the preparation of the nitrile imines,[3] lead tetraacetate-oxidation of the readily available aroylhydrazones (II) from aroylhydrazines (I) was carried out at room temperature. The products were characterized as 2,5-disubstituted 1,3,4-oxadiazoles (III), simple oxidation products of aroylhydrazones which provide general procedure for the preparation of 2,5-disubstituted 1,3,4-oxadiazoles.[6] The recent appearance of an article on a similar subject[7] prompted us to write this note. A sequence of the reaction and the mechanism postulated for the preparation of III are given below.



The results are summarized in Tables 1 and 2.

Experimental[8]

Starting Materials. Aroylhydrazines (Ia:[9] 5-nitro-2-furoyl, Ib:[10] 5-nitro-2-furylacroyl, and Ic:[11] benzoylhydrazine) and 5-nitro-2-furylacrolein[12] were prepared by the known procedures. All the other aldehydes were commercial products.

General Procedure. *Conversion of I to II.* A mixture of 0.6 g (3.5 mmol) of 5-nitro-2-furoylhydrazine

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[1] Part XLV: T. Sasaki, K. Kanematsu and A. Kakehi, *Chem. Commun*, **1970**, 1030.

[2] T. Sasaki, T. Yoshioka and Y. Suzuki, This Bulletin, **43**, 2991 (1970).

[3] T. Sasaki and T. Yoshioka, *ibid.*, **43**, 1254 (1970).

[4] T. Bacchetti, *Gazz. Chem. Ital.*, **91**, 866 (1961).

[5] M. O. Losinskii and P. S. Pelkis, *Zh. Obshch. Khim.*, **32**, 526 (1962); **33**, 2231 (1963).

[6] A. Hetzheim and K. Mockel, "Advances in 1,3,4-Oxadiazole Chemistry," in "Advances in Heterocyclic Chemistry," Vol. 7, A. R. Katritzky and A. J. Boulton Ed., Academic Press, New York (1966), p. 190.

[7] W. A. F. Glaston, J. B. Aylward and R. O. C. Norman, *J. Chem. Soc., C*, **1969**, 2587.

[8] The melting points were measured on a micro hot stage and are not corrected. The microanalyses were carried out with a Perkin-Elmer Model 240 Elemental Analyzer. The ultraviolet spectra were obtained on a JASCO ORD/UV-5 and the infrared spectra on a JASCO IR-S spectrometer.

[9] M. Amorosa and L. Lipparini, *Ann. Chim.* (Rome), **45**, 724 (1955).

[10] T. Sasaki, *Chem. Pharm. Bull.* (Tokyo), **2**, 95 (1954).

[11] T. Curtius and H. Franzen, *Ber.*, **35**, 3421 (1902).

[12] H. Saikachi and H. Ogawa, *J. Amer. Chem. Soc.*, **80**, 3462 (1958).

Table 1. acylhydrazones

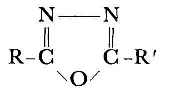
$RCONHN{=}CHR'$

II

R	R'	Product	Mp. °C	Yield %	Found (Calcd) C%	H%	N%	UV λ_{max}^{EtOH} mμ ($\varepsilon\times10^{-4}$)	IR ν_{CO}^{KBr} cm^{-1}
NF-*	C_6H_5-	IIa	212—214	85	55.58 (55.60	3.58 3.50	16.35 16.21)	322 (1.7), 298 (1.58), 280 (1.7)	1665
NF-	p-Cl-C_6H_4-	IIb	226—229	80	48.95 (49.08	2.75 2.72	14.25 14.31)		1665
NF-	p-CH_3-C_6H_4-	IIc	210—214	70	57.20 (57.14	4.15 4.06	15.45 15.38)		1670
NFCH=CH-	C_6H_5-	IId	218—220	90	58.85 (58.94	3.95 3.89	14.80 14.73)		1660
C_6H_5-	NF-	IIe	215—219	90	55.55 (55.60	3.65 3.50	16.15 16.21)		1660
C_6H_5-	NFCH=CH-	IIf	233—235	90	59.05 (58.94	3.78 3.89	14.75 14.73)		1640

* NF: 5-nitro-2-furyl

Table 2. Oxadiazoles



III

R	R'	Product	Mp °C	Yield %	Found (Calcd) C%	H%	N%	UV λ_{max}^{EtOH} mμ ($\varepsilon\times10^{-4}$)	IR $\nu_{C=N}^{KBr}$ cm^{-1}
NF-	C_6H_5-	IIIa	231—232	80	56.15 (56.03	2.85 2.74	16.45 16.34)	332 (1.55) 266 (1.14)	1610
NF-	p-Cl-C_6H_4-	IIIb	216—217	75	49.35 (49.42	2.15 2.06	14.55 14.41)	330 (1.8) 268 (1.4)	1615
NF-	p-CH_3-C_6H_4-	IIIc	180—182	85	57.65 (57.56	3.45 3.34	15.55 15.49)	336 (1.68) 268 (1.29)	1610
NFCH=CH-	C_6H_5-	IIId*	216—218	40	59.45 (59.36	3.35 3.20	14.95 14.84)	368 (2.34) 292 (1.06) 233 (1.16)	1605
C_6H_5-	NF-	IIIa	227—231	70					1610
C_6H_5-	NFCH=CH-	IIId	215—217	30					1605

* A. Sugihara and M. Ito, *Yakugaku Zasshi*, **85**, 744 (1965); mp 205—206°C.

(Ia) and 0.4 g (3.5 mmol) of benzaldehyde was refluxed in 40 m*l* of ethanol for 7 hr. After cooling, the precipitates were collected and recrystallized from ethanol to give 0.85 g (85%) of 1-benzylidene-2-(5-nitro-2-furoyl)-hydrazine (IIa). The results of similar reactions using several aroyhydrazines and aromatic aldehydes are summarized in Table 1.

Conversion of II to III. To a stirred suspension of 0.5 g (2 mmol) of IIa in 100 m*l* of dichloromethane was added 1.3 g (3 mmol) of lead tetraacetate at room temperature. The mixture was stirred at room temperature for 2 days. After filtering off the undissolved materials, the solvent was removed under reduced pressure. The residue was recrystallized from ethanol-benzene-tetrahydrofuran to afford 0.38 g (80%) of 2-(5-nitro-2-furyl)-5-phenyl-1,3,4-oxadiazole (IIIa), 231—232°C (decomp.). Analytical and spectral data are summarized in Table 2.