Synthesis and Thermolysis of *N*-Heteroarylacetylazides and α-Oximino-α-(*N*-heteroaryl)acetylazides

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Treatment of *N*-heteroarylacethydrazides with an equimolar amount of nitrous acid afforded *N*-heteroaryacetylazides and subsequent thermolysis of these azides gave the analogues of 2,3-dihydroimidazo[1,5-*a*]pyridin-3-one. When some of these cyclized compounds were treated with nitrous acid, the ring opening reaction occurred and recyclized 3-(*N*-heteroaryl)-1,2,4-oxadiazolin-5-ones were obtained. Treatment of *N*-heteroarylacethydrazides with two equivalent moles of nitrous acid afforded α-oximino-α-(*N*-heteroaryl)acetylazides. Thermolysis of these azides gave mixtures of 3-(*N*-heteroaryl)-1,2,4-oxadiazolin-5-one and 3-hydroxy-4-(*N*-heteroaryl)furazan. On the basis of the effects of heterocyclic rings and solvents upon the relative yield of two types of the products, one plausible mechanistic explanation for the decomposition of such azides was proposed. α-Oximino-α-(*H*-heteroaryl)acetylazides were converted into cyano *N*-heterocycles by the action of alkali in good yields.

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Previously, we have investigated the reaction between 2-pyridylacethydrazide and nitrous acid and obtained the following results (1). (a) Treatment of 2-pyridylacethydrazide with an equimolar amount of nitrous acid affords 2-pyridylacetylazide and thermolysis of this azide gives 2,3-dihydroimidazo[1,5-*a*]pyridin-3-one. (b) 2,3-Dihydroimidazo[1,5-*a*]pyridin-3-one rearranges, upon treatment with nitrous acid, to 3-(2-pyridyl)-1,2,4-oxadiazolin-5-one. (c) Treatment of 2-pyridylacethydrazide with excess nitrous acid yields α-oximino-α-(2-pyridyl)acetylazide and subsequent thermolysis of this azide affords 3-(2-pyridyl)-1,2,4-oxadiazolin-5-one. (d) Treatment of α-oximino-α-(2-pyridyl)acetylazide with alkali gives 2-cyanopyridine.

In order to extend the scope of these reactions, the successive study was carried out by using a variety of *N*-heteroarylacethydrazides as starting material. The present paper described mainly the synthesis and thermolysis of *N*-heteroarylacetylazides and α-oximino-α-(*N*-heteroaryl)acetylazides.

Synthesis and Thermolysis of *N*-Heteroarylacetylazides.

6-Methyl-2-pyridylacethydrazide (I) was diazotized with an equimolar amount of sodium nitrite in 10% hydrochloric acid under ice-salt cooling. After neutralization, the resulting azide was extracted with chloroform from the reaction mixture and decomposed *in situ* by heating the dried chloroform solution giving 5-methyl-2,3-dihydroimidazo[1,5-*a*]pyridin-3-one (VIII) in 56% yield. In a similar manner, 1-methyl-2,3-dihydroimidazo[1,5-*a*]pyridine-3-one (IX) and 6-methoxy-2,3-dihydroimidazo[1,5-*b*]-pyridazin-3-one (X) were obtained in 48% and 52% yield, respectively, from the corresponding hydrazides II and III.

The elemental analyses and mass spectra of these compounds agreed with the expected molecular formulae. The ir spectra showed strong carbonyl absorption at about 1680 cm^{-1} and NH absorption between 3200-2000 cm^{-1} as a broad band with several sub-maxima. Such low and broad frequency of the NH band is characteristic of unsaturated cyclic amides, such as α-pyridone and carbostyril, and attributable to the strong hydrogen bonding of the dimer (2). Other spectroscopic data were also consistent with the cyclic structure.

In the synthesis of above compounds, the isolation of intermediate acyl azides in pure form failed due to their thermal instability. Hence, the characterization of the azides was not carried out. However, in the diazotization of 2-quinolylacethydrazide (IV) and 1-isoquinolylacethydrazide (V), analytically pure samples of acetylazide VI and VII were obtained as fairly stable yellow crystals by purification by chromatography on a silica gel column or by recrystallization.

The spectroscopic data of these compounds indicate that they exist as a tautomeric mixture of keto forms VIa, and VIIa and enamine forms VIb, VIIb and the equilibrium lies to the latter form. Namely, the nmr spectra of VI and VII, measured in deuteriochloroform, showed the absorption of the methylene protons of the keto form at 4.06 and 4.38 ppm, respectively, and that of the olefinic proton of the enamine form at 4.84 and 5.55 ppm, respectively. The relative ratio of enamine form and keto form is about 7:1 in the quinoline derivative VI and 10:1 in the isoquinoline derivative VII. The ir spectra, obtained in Nujol mulls, also indicated the predominance of the enamine tautomer. The spectrum of VI showed azide absorption at 2120 and 2150 cm^{-1} as a doublet and carbonyl absorption at 1645 cm^{-1}. Compound VII exhibited azide absorption at 2130 cm^{-1} and carbonyl absorption at 1620 cm^{-1}. However, the characteristic NH absorption was not found in the spectra of both compounds. The unusually

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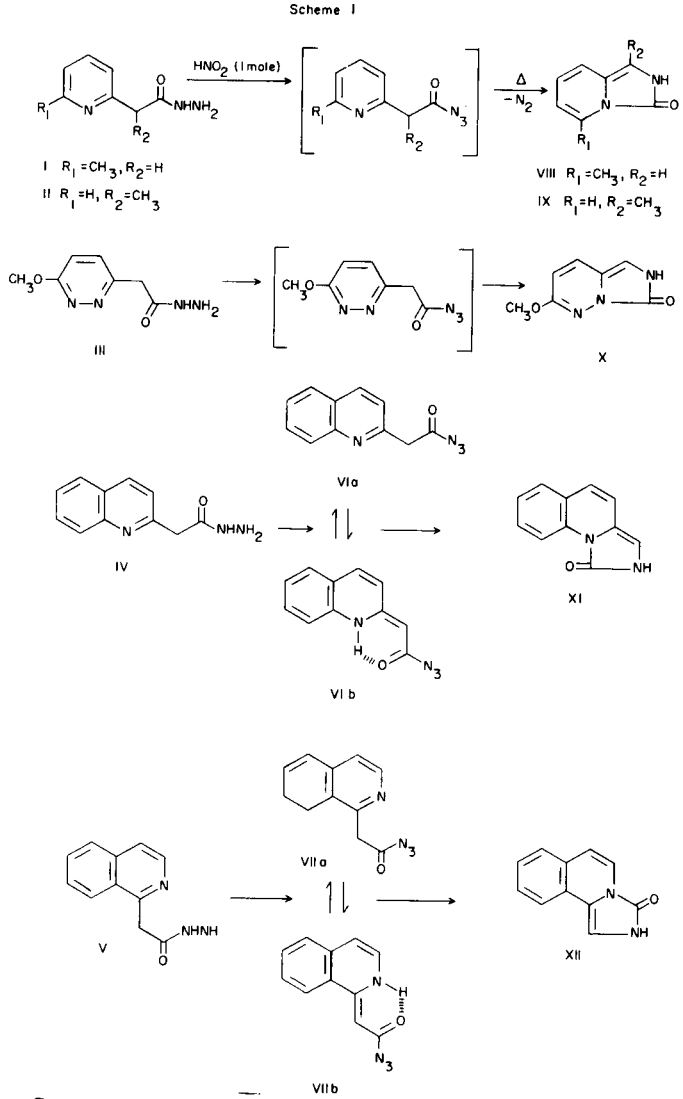
low frequency of the carbonyl absorption and absence of the NH band are well rationalized in terms of the strong conjugated chelation in the enamine tautomers VIb and VIIb. The moderate stability of VI and VII will be explained with this conjugated chelation, because it reduces the character of the acyl azide in these compounds and consequently inhibits the decomposition due to a thermally induced Curtius rearrangement. The uv spectra showed strong absortions in the visible region indicating conjugation in the heterocyclic system which is characteristic for the enamine tautomers.

Similar features of this tautomerism have been observed in many acylmethylquinolines and related compounds (3).

Thermolysis of VI and VII in boiling benzene afforded 1,2-dihydroimidazo[1,5-*a*]quinolin-1-one (XI) and 2,3-dihydroimidazo[5,1-*a*]isoquinolin-3-one (XII) in 83% and 89% yield, respectively.

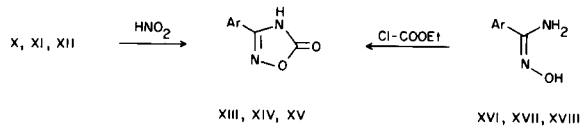
Scheme 1



Conversion of Imidazoazine Derivatives into 3-(*N*-Heteroaryl)-1,2,4-oxadiazolin-5-ones.

Under ice cooling, compounds X, XI and XII were treated with 1.2 molar amounts of sodium nitrite in aqueous acetic acid for one hour. As in the case of the nitrosation of 2,3-dihydroimidazo[1,5-*a*]pyridin-3-one, no nitroso derivative was formed, but the rearranged oxadiazole derivatives XIII, XIV and XV, respectively, were obtained in about 80-90% yield. The structures of these compounds were proved by spectroscopic data and the unequivocal synthesis from the amidoximes XVI, XVII and XVIII.

Scheme 2

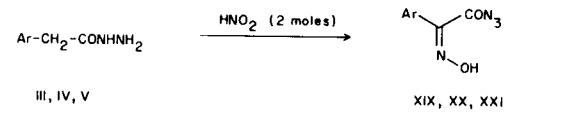


XIII, XVI Ar = 6-Methoxy-3-pyridazinyl
XIV, XVII Ar = 2-Quinolyl
XV, XVIII Ar = 1-Isoquinolyl

Synthesis and Thermolysis of α-Oximino-α-(*N*-heteroaryl)acetylazides.

Under ice-salt cooling, 6-methoxy-3-pyridazinylacethydrazide (III) was treated with a 2.2 molar amount of sodium nitrite in 10% hydrochloric acid. After neutralization, a precipitated white powder was collected by filtration and dried *in vacuo* giving α-oximino-α-(6-methoxy-3-pyridazinyl)acetylazide (XIX) in 81% yield. The ir spectrum showed a broad hydrogen bonded hydroxyl band of the oxime group between 3300-2200 cm^{-1} (ν max = 2750 cm^{-1}), azide absorption at 2180 cm^{-1} and carbonyl absorption at 1680 cm^{-1}. In a similar manner, α-oximino-α-(2-quinolyl)acetylazide (XX) and α-oximino-α-(1-isoquinolyl)acetylazide (XXI) were obtained in 92% and 89% yield, respectively. Their ir spectra showed absorptions similar to those of XIX. These compounds were used for the following reactions without further purification because of their thermal instability.

Scheme 3

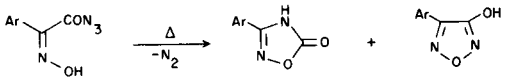


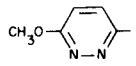
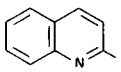
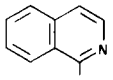
III, XIX Ar = 6-Methoxy-3-pyridazinyl
IV, XX Ar = 2-Quinolyl
V, XXI Ar = 1-Isoquinolyl

When quinolylazide XX was decomposed in boiling chloroform, in contrast to the thermolysis of pyridylazide, two types of product were obtained. The minor product

Table I

Thermolysis of α-Oximino-α-(*N*-heteroaryl)acetylazide



Azide No.	Ar-	Solvent	Product 1,2,4-oxadiazole No.	Yield (%)	Furazan No.	Yield (%)
		Chloroform	XIII	76	XXII	10
XIX						
		Ethanol	XIII	80	XXII	trace
		Chloroform	XIV	17	XXIII	70
XX						
		Ethanol	XIV	77	XXIII	5
		Chloroform	XV	28	XXIV	58
XXI						
		Ethanol	XV	92	XXIV	trace

(17%) was readily identified as 3-(2-quinolyl)-1,2,4-oxadiazolin-5-one (XIV), an anticipated compound, by the comparison of the ir spectrum with that of an authentic sample. The major product (70%) was determined to be 3-hydroxy-4-(2-quinolyl)furazan (XXIII) on the basis of the spectroscopic data and chemical reactions outlined below.

The elemental analysis and mass spectrum showed that this compound was the isomer of XIV. The nmr spectrum showed an absorption for the OH proton at 10.6 ppm as a broad singlet, together with the absorptions of the six protons of the quinoline ring. However, the detection of the characteristic hydroxyl stretching band in the ir spectrum was not observed and can be explained by the proposed structure since in this structure, there is a strong six membered chelation between the hydroxyl group attached to the furazan ring and the nitrogen atom of the quinoline ring, thus it must weaken the intensity of hydroxyl band in the ir spectrum.

Next, we turned our attention to some chemical transformations of compound XXIII. Treatment of XXIII with diazomethane in ether gave the *O*-methylated compound XXV in quantitative yield. The acetate XXVI was prepared by refluxing a solution of XXIII in acetic anhydride. The ir spectrum of XXVI showed the carbonyl absorption at 1790 cm^{-1}. Such carbonyl bands appearing in the high frequency region is characteristic of esters of aromatic or heteroaromatic alcohols. The acetate XXVI was readily hydrolysed to XXIII by heating in 10% hydrochloric acid.

For the further confirmation of the structure of XXIII, the unequivocal synthesis of 3-hydroxy-4-(2-quinolyl)-furazan was attempted. Furazans are most often prepared by heating the corresponding glyoximes in aqueous alkali. Cusmano and Tiberio reported that 3-amino-4-phenylfurazan was obtained from α-oximino-α-phenylacetonitrile by heating with hydroxylamine in aqueous potassium hydroxide *via* the intermediate aminoglyoxime (4). Following this method, 3-amino-4-(2-quinolyl)furazan (XXVIII) was prepared from α-oximino-α-(2-quinolyl)acetonitrile (XXVII) in 16% yield. In this reaction, α-oximino-α-(2-quinolyl)acetic acid (XXIX) was obtained as a by-product in 44% yield. The diazotization and subsequent hydrolysis of the amine function of XXVIII was attempted. However, the ring opening reaction into compound XXVII was

favored over the hydrolysis and the anticipated hydroxyfurazan was not obtained. On the other hand, when methyl α-oximino-α-(2-quinolyl)acetate (XXX) was allowed to react with hydroxylamine in aqueous sodium hydroxide, 3-hydroxy-4-(2-quinolyl)furazan was obtained in 25% yield, along with acid XXIX (12%) and 1,2,4-oxadiazole (XIV) (2%). This compound was found to be identical with compound XXIII by the comparison of ir spectra and mixed melting point determination. From these physical and chemical data, it is doubtless that compound XXIII is 3-hydroxy-4-(2-quinolyl)furazan.

Next, thermolysis of α-oximino-α-(1-isoquinolyl)acetylazide (XXI) and α-oximino-α-(6-methoxy-3-pyridazinyl)-acetylazide (XIX) were carried out. As in the case of pyrolysis of quinolylazide (XX), thermolysis of XXI in chloroform afforded furazan derivative XXIV as a major product (58%) and 1,2,4-oxadiazole derivative XV as a minor product (28%). On the other hand, when pyridazinylazide XIX was thermolysed in chloroform, furazan derivative XXII was obtained only in 10% yield and the 1,2,4-oxadiazole derivative XIII was obtained in 76% yield. This result is similar to that of the thermolysis of α-oximino-α-(2-pyridyl)acetylazide, where the 1,2,4-oxadiazole derivative was obtained as the sole product (1).

These results suggest that in the thermolysis of α-oximino-α-(*N*-heteroaryl)acetylazide, the transition state into 3-hydroxy-4-(*N*-heteroaryl)furazan is stabilized by the heterocyclic nucleus with the following order; 2-quinoline > 1-isoquinoline > 6-methoxy-3-pyridazine > 2-pyridine.

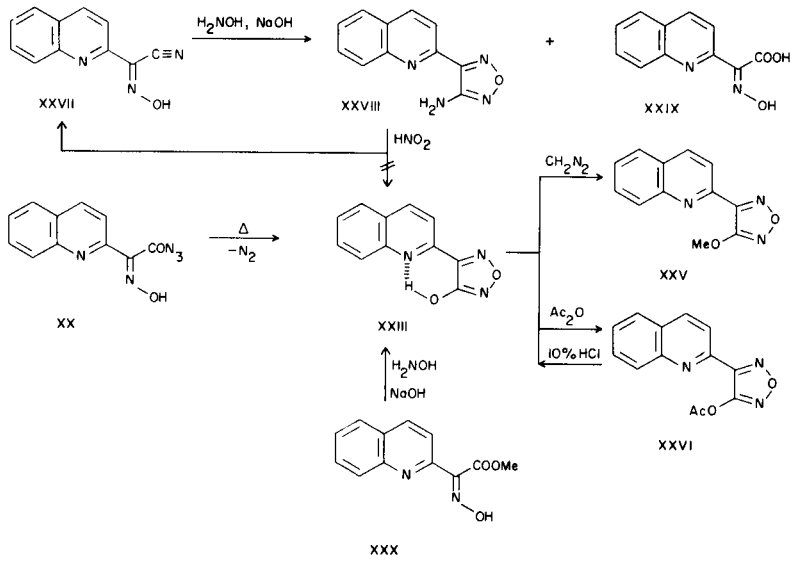
Next, the solvent effect on the yield of furazan and 1,2,4-oxadiazole was examined. When quinolylazide XX was decomposed in boiling ethanol, the relative yield of the two products changed dramatically, that is, 1,2,4-oxadiazole XIV was obtained in 77% yield and furazan XXIII only in 5% yield. Moreover, thermolysis of the isoquinolylazide XXI in ethanol gave the 1,2,4-oxadiazole XV in 92% yield and trace amount of the furazan XXIV. Thermolysis of the pyridazinylazide XIX afforded the 1,2,4-oxadiazole XIII in 80% yield and only a trace amount of furazan XXII.

These remarkable changes in the yields mean that the transition state into the furazan derivative is destabilized in polar protic solvent and that into the 1,2,4-oxadiazole derivative is stabilized. Namely, the transition state into the furazan is less polar than that into the 1,2,4-oxadiazole.

A plausible mechanism which accounts for the observations described above is depicted in Scheme V. α-Oximino-α-(*N*-heteroaryl)acetylazide exists as a tautomeric mixture of oxime form (*A*) and nitrosoenamine form (*B*) in solution. When the azide is subjected to thermolysis, the Curtius rearrangement occurs in tautomer (*A*) giving isocyanate (*D*) which cyclizes into 1,2,4-oxadiazole (*E*). On the other hand, in tautomer (*B*), the assisted decomposition of the azide group with the nitroso group leading to furazan (*G*) *via* transition state (*F*) will be prefered over the Curtius rearrangement, because the contribution of the resonance structure (*B'*) to the ground state of the tautomer reduces the influence of the acyl azide in (*B*) and consequently inhibits the Curtius rearrangement. In addition, the presence of such neighbouring-group participation for the decomposition of the azide group was shown kinetically by Dyall and Kemp in the thermolysis of many phenylazides with unsaturated *ortho* substituents. (5).

Compounds XIX, XX, XXI and pyridine analogues are all colorless crystalline compounds and show a strong hydroxyl band of the oxime group between 3300-2200 cm^{-1}. Therefore, the equilibrium between (*A*) and (*B*) must lie far in the direction of (*A*) in all compounds. However,

Scheme 4



the relative yield of the two types of products, (*E*) and (*G*), must depend not only on the equilibrium constant of the starting tautomers, but also on the difference in the stability of the transition states (*C*) and (*F*). In the thermolysis of bicyclic quinoline or isoquinoline derivatives in a solvent of low polarity (chloroform), it may be assumed that the less polar transition states of type (*F*), where an acidic hydrogen atom associates intramolecularly with a nitrogen and an oxygen atom, are more stable than the polar transition states of type (*C*). Consequently, furazan derivatives become a major product in such cases. However, the loss of the resonance energy due to the destruction of the heteroaromatic ring in the transition states of type (*F*) derived from monocyclic pyridyl or pyridazinylazide must be larger than that in the bicyclic analogues. Therefore, in the thermolysis of such monocyclic azides, the polar transition states of type (*C*) become more stable than type (*F*) even in chloroform and consequently 1,2,4-oxadiazole derivatives are preferentially formed. In ethanol, the polar transition states of type (*C*) must be greatly stabilized, hence pyrolysis of azides in ethanol affords 1,2,4-oxadiazole derivatives as a major product in all cases.

Conversion of α-Oximino-α-(*N*-heteroaryl)acetylazide into Nitrile Derivatives.

Suspension of azide XIX in 10% sodium carbonate was stirred for 3 hours at room temperature giving 3-methoxy-6-cyanopyridazine (XXXI) in 84% yield. In a similar manner, XX and XXI were converted into the corresponding nitriles XXXII and XXXIII in good yields. The structures of these nitriles were confirmed by comparison of their ir spectra with those of authentic samples.

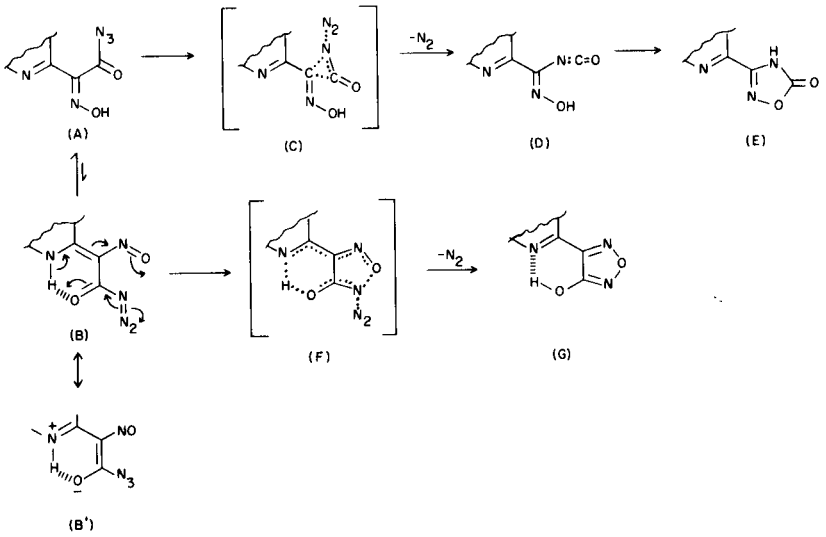
EXPERIMENTAL

All melting points are uncorrected. Mass spectra were recorded on a JEOL JMS-01SG spectrometer. Nmr spectra were recorded on a JEOL JNM-PS-100 or a Hitachi R-20B spectrometer using TMS as an intenal standard. Ir spectra were obtained in Nujol or Fluorolube mulls with a Hitachi EPI-2 spectrometer. Uv spectra were determined for solutions in 95% ethanol with a Hitachi 323 or 124 spectrometer.

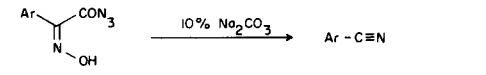
Materials

6-Methyl-2-pyridylacethydrazide (I) and α-(2-pyridyl)propionhydrazide (II) were prepared from 1,6-lutidine and 1-ethylpyridine, respectively, *via* the corresponding carboxylic esters according to the method reported in the literature (6). 6-Methoxy-3-pyridazinylacethydrazide (III), 2-quinolylacethydrazide (IV) and 1-isoquinolylacethydrazide (V) were obtained from the corresponding heterocyclic *N*-oxides in two or three steps using the convenient method recently reported from this laboratory (7).

Scheme 5



Scheme 6



XIX, XX, XXI — XXXI, XXXII, XXXIII

XIX, XXXI — Ar = 6-Methoxy-3-pyridazinyl

XX, XXXII — Ar = 2-Quinolyl

XXI, XXXIII — Ar = 1-Isoquinolyl

5-Methyl-2,3-dihydroimidazo[1,5-*a*]pyridin-3-one (VIII).

A solution of 2.07 g. (30 mmoles) of sodium nitrite in 10 ml. of water was added dropwise to a stirred solution of 4.96 g. (30 mmoles) of 6-methyl-2-pyridylacethydrazide (I) in 50 ml. of 10% hydrochloric acid, keeping the temperature between -5 and 0°. After stirring for an additional 10 minutes, the reaction mixture was made basic with 10% sodium carbonate and extracted with chloroform. The dried extract (magnesium sulfate) was refluxed for 1.5 hours and then evaporated to dryness. The residue was washed with ether and then with a small amount of dichloromethane giving 2.48 g. (56%) of yellow small prisms, m.p. 142.5-144.5°. An analytical sample was obtained by recrystallization from dichloromethane or acetone, m.p. 143-145°; ms: m/e 148 (M^+); nmr (deuteriochloroform): δ 2.68 (s, 3H, CH_3), 5.63 (near d, 1H, H_6), 6.18 (near q, 1H, H_7), 6.37 (s, 1H, H_1), 6.65 (d, 1H, H_8), 11.6 (br s, 1H, NH), $J_{6,7}$ = 6, $J_{7,8}$ = 10; ir: 3130 (NH), 2960 (NH), 2820 (NH) and 1675 cm^{-1} (C=O); uv λ max: 217 (ϵ, 19,800), 269 (ϵ, 6,600), 279 (ϵ, 7,000), 290 (ϵ, 4,800) and 365 nm (ϵ, 2,800).

Anal. Calcd. for $C_8H_8N_2O$: C, 64.85; H, 5.44; N, 18.91. Found: C, 64.69; H, 5.35; N, 19.13.

1-Methyl-2,3-dihydroimidazo[1,5-*a*]pyridin-3-one (IX).

This compound was prepared from α-(2-pyridyl)propionhydrazide (II) in the same manner as described above and purified by recrystallization from benzene, yield 48%, yellow prisms, m.p. 170-173° dec.; ms: m/e 148 (M^+); nmr (deuteriochloroform): δ 2.28 (s, 3H, CH_3), 6.60 (t, 1H, H_6), 6.21 (near q, 1H, H_7), 6.77 (d, 1H, H_8), 7.43 (d, 1H, H_5), 12.3 (br s, 1H, NH), $J_{5,6}$ = 7, $J_{6,7}$ = 7, $J_{7,8}$ = 10 Hz; ir: 3130 (NH), 2920 (NH), 2760 (NH) and 1675 cm^{-1} (C=O); uv λ max: 216 (ϵ, 26,900), 269 (ϵ, 6,600), 276 (ϵ, 6,600) and 388 nm (ϵ, 2,200).

Anal. Calcd. for $C_8H_8N_2O$: C, 64.85; H, 5.44; N, 18.91. Found: C, 65.26; H, 5.55; N, 18.94.

6-Methoxy-2,3-dihydroimidazo[1,5-*b*]pyridazin-3-one (X).

6-Methoxy-3-pyridazinylacethydrazide (III) (1.25 g., 6.9 mmoles) in 30 ml. of 10% hydrochloric acid was treated with 0.48 g. (7 mmoles) of sodium nitrite in 5 ml. of water in a similar manner as described for compound VIII. After neutralization with 10% sodium carbonate, the resulting azide was extracted with chloroform and decomposed by heating under reflux for 1.5 hours as above. Chloroform was evaporated and the residue was recrystallized from ethanol (charcoal) giving 0.60 g. (52%) of X, yellow plates, m.p. 226-229° dec.; ms: m/e 165 (M^+); nmr (DMSO-d_6): δ 3.80 (s, 3H, OCH_3), 6.11 (d, 1H, H_7), 6.79 (s, 1H, H_1), 7.53 (d, 1H, H_8), 11.1 (br s, NH), $J_{7,8}$ = 10 Hz; ir: 3130 (NH), 2960 (NH), 2800 (NH) and 1687 cm^{-1} (C=O); uv λ max: 233 (ϵ, 27,000) and 376 nm (ϵ, 1,900).

Anal. Calcd. for $C_7H_7N_3O_2$: C, 50.91; H, 4.27; N, 25.45. Found: C, 51.15; H, 4.23; N, 25.37.

2-Quinolylacetylazide (VI).

A solution of 1.34 g. (19.4 mmoles) of sodium nitrite in 10 ml. of water was added to a stirred solution of 3.90 g. (19.4 mmoles) of 2-quinolylacethydrazide (IV) in 100 ml. of 10% hydrochloric acid, keeping the temperature between -1 and 1°. After stirring for an additional 10 minutes, the reaction mixture was made basic with 10% sodium carbonate solution. At this time, methanol was added occasionally to the reaction mixture in order to prevent foaming. The precipitated yellow solid was collected by filtration and dried *in vacuo* over phosphorus pentoxide to give 3.70 g. of crude VI. The crude product was digested with cold dichloromethane. The insoluble substance was filtered off by suction and the filtrate was passed rapidly through a short column of silica gel using dichloromethane as eluent. The eluant was evaporated to dryness without heating to give 2.52 g. (61%) of purified VI, m.p. 93-94° dec.; nmr (deuteriochloroform): δ 4.06 (s, CH_2 of ketoform), 4.84 (s, C=C-H of enamine form), 6.58 (dd, H_3 of enamine form), 7.0-8.2 (m, ArH), 12.9 (br s, NH of enamine form), $J_{3,4}$ = 9.5, $J_{3,NH}$ = 1.5 Hz; ir: 2150 (N_3), 2120 (N_3) and 1645 cm^{-1} (C=O); uv λ max: 212 (ϵ, 31,800), 232 (sh) (ϵ, 15,800), 260 (ϵ, 8,900), 269 (ϵ, 9,400), 290 (sh) (ϵ, 14,300), 298 (ϵ, 15,300), 312 (ϵ, 10,900), 390 (ϵ, 8,000), 410 (ϵ, 8,500), and 433 nm (ϵ, 4,800). The decomposition of VI in ethanol is so rapid that the ϵ values are not reliable.

Anal. Calcd. for $C_{11}H_8N_4O$: C, 62.25; H, 3.80; N, 26.40. Found: C, 62.35; H, 3.66; N, 26.45.

1-Isoquinoylacetylazide (VII).

This compound was prepared from 1-isoquinolylacethydrazide (V) in thesame manner as described for compound VI in 54% yield, yellow fine needles, m.p. 123° dec.; nmr (deuteriochloroform): δ 4.38 (s, CH_2 of keto form), 5.55 (s, C=C-H of enamine form), 6.65 (dd, H_4 of enamine form), 7.1-8.1 (m, ArH), 13.3 (br s, NH of enamine form), $J_{3,4}$ = 7, $J_{4,NH}$ = 1.5 Hz; ir: 2130 (N_3) and 1620 cm^{-1} (C=O); uv λ max: 217 (ϵ, 35,800), 259 (ϵ, 13,900), 267 (ϵ, 18,200), 291 (sh) (ϵ, 6,600), 299 (ϵ, 8,500), 324 (ϵ, 4,800), 385 (ϵ, 6,400), 405 (ϵ, 11,200) and 428 nm (ϵ, 11,300). The ϵ values are not accurate due to the instability of VII in ethanol. An analytical sample was purified by recrystallization from dichloromethane/petroleum ether.

Anal. Calcd. for $C_{11}H_8N_4O$: c, 62.25; H, 3.80; N, 26.40. Found: C, 62.13; H, 3.68; N, 26.38.

1,2-Dihydroimidazo[1,5-*a*]quinolin-1-one (XI).

A solution of 1.00 g. (4.7 mmoles) of 2-quinolylacetylazide (VI) in 100 ml. of benzene was refluxed for one hour. After cooling, the precipitated pale orange fine needles were collected by filtration giving 0.72 g. (83%) of compound XI, m.p. 216-218° dec. An analytical sample was prepared by recrystallization from ethanol; ms: m/e 184 (M^+); nmr (DMSO-d_6): 6.62 (d, 1H, H_4), 6.65 (s, 1H, H_3), 6.78 (d, 1H, H_5), 7.0-7.4 (m, 3H, H_6, H_7 and H_8), 8.84 (d, 1H, H_9), 11.15 (br s, 1H, NH), $J_{4,5}$ = 9, $J_{8,9}$ = 8 Hz; ir: 3120 (NH), 3020 (NH), 2810 (NH) and 1684 cm^{-1} (C=O); uv λ max: 209 (ϵ, 39,200), 257 (ϵ, 23,000), 265 (ϵ, 25,200) and 360 nm (ϵ, 5,000).

Anal. Calcd. for $C_{11}H_8N_2O$: C, 71.72; H, 4.38; N, 15.21. Found: C, 71.97; H, 4.32; N, 15.22.

2,3-Dihydroimidazo[5,1-*a*]isoquinolin-3-one (XII).

A mixture of 0.53 g. (2.5 mmoles) of 1-isoquinolylacetylazide (VII) and 30 ml. of benzene was refluxed for one hour. After cooling, the precipitated pale yellow fine needles were collected by filtration giving 0.36 g. of XII, m.p. 196-198°. The filtrate was concentrated and allowed to stand giving 0.05 g. of additional XII, m.p. 196-198°. Total yield was 0.41 g. (89%). An analytical sample was obtained by recrystallization from benzene, m.p. 196-198°; ms: m/e 184 (M^+); nmr (DMSO-d_6): 6.37 (d, 1H, H_6), 7.2-7.5 (m, 5H, ArH), 7.77 (m, 1H, H_{10}), 10.75 (br s, 1H, NH), $J_{5,6}$ = 7.5 Hz; ir: 3100 (NH), 2970 (NH), 2790 (NH) and 1680 cm^{-1} (C=O); uv λ max: 210 (ϵ, 31,700), 259 (ϵ, 31,400), 268 (ϵ, 42,700), and 339 nm (ϵ, 6,100).

Anal. Calcd. for $C_{11}H_8N_2O$: C, 71.72; H, 4.38; N, 15.21. Found: C, 71.99; H, 4.27; N, 15.03.

Conversion of X into 3-(6-Methoxy-3-pyridazinyl)-1,2,4-oxadiazolin-5-one (XIII).

A solution of 0.22 g. (3.2 mmoles) of sodium nitrite in 1 ml. of water was added dropwise to an ice-cooled stirred solution of 0.45 g. (2.7 mmoles) of X in a mixture of 10 ml. of acetic acid and 1 ml. of water. The reaction mixture turned dark blue and then reddish brown. After stirring for one hour, the precipitated pale brown powder was collected by filtration and washed with water to give 0.35 g. of crude XIII, m.p. 215-218° dec. The filtrate and washing solutions were combined and concentrated to a small volume giving 0.08 g. of additional XIII, m.p. 210-214° dec. Total yield was 0.43 g. (82%). The crude products were combined and recrystallized from ethanol (charcoal) giving slightly yellow prisms, m.p. 218.5-219° dec.; ms: m/e 194 (M^+); nmr (DMSO-d_6): δ 4.14 (s, 3H, OCH_3), 7.50 (d, 1H, H_5), 8.17 (d, 1H, H_4), 13.2 (br s, 1H, NH), $J_{4,5}$ = 9 Hz; ir: 3080 (NH), 1803 (C=O) and 1778 cm^{-1} (C=O); uv λ max: 238 nm (ϵ, 11,900).

Anal. Calcd. for $C_7H_6N_4O_3$: C, 43.30; H, 3.12; N, 28.86. Found: C, 43.30; H, 3.01; N, 29.23.

Conversion of XI into 3-(2-Quinolyl)-1,2,4-oxadiazolin-5-one (XIV).

Compound XI (0.20 g., 1.1 mmoles) in a mixture of 10 ml. of acetic acid and 0.5 ml. of water was treated with 0.09 g. (1.3 mmoles) of sodium nitrite in 0.5 ml. of water and worked up in a similar manner as described

above giving 0.18 g. (78%) of compound XIV. Recrystallization from ethanol (charcoal) gave fine colorless needles, m.p. 268.5-270.5° dec.; ms: m/e 213 (M^+); nmr (DMSO-d_6): δ 7.6-8.2 (m, 5H, ArH), 8.58 (d, 1H, H_4), 13.5 (br s, 1H, NH), $J_{3,4}$ = 9 Hz; ir: 3130 (NH) and 1787 cm^{-1} (C=O); uv λ max: 243 (ε, 22,400), 293 (ε, 4,400), 322 (ε, 2,700) and 335 nm (ε, 1,900).

Anal. Calcd. for $C_{11}H_7N_3O_2$: C, 61.97; H, 3.31; N, 19.71. Found: C, 62.12; H, 3.26; N, 19.94.

Conversion of XII into 3-(1-Isoquinolyl)-1,2,4-oxadiazolin-5-one (XV).

Compound XII (0.40 g., 2.2 mmoles) in a mixture of 10 ml. of acetic acid and 5 ml. of methanol was treated with 0.18 g. (2.6 mmoles) of sodium nitrite in 1 ml. of water and worked up in a similar manner as described above giving 0.41 g. (89%) of compound XV. Recrystallization from ethanol (charcoal) gave colorless fine needles, m.p. 242-242.5° dec.; ms: m/e 213 (M^+); nmr (DMSO-d_6): δ 7.83-8.34 (m, 3H, H_5, H_6 and H_7), 8.24 (d, 1H, H_4), 8.83 (d, 1H, H_3), 9.04 (m, 1H, H_8), 12.9 (br s, 1H, NH), $J_{3,4}$ = 6 Hz; ir: 3180 (NH) and 1790 cm^{-1} (C=O); uv λ max: 224 (ε, 41,600), 284 (ε, 4,700) and 327 nm (ε, 6,100).

Anal. Calcd. for $C_{11}H_7N_3O_2$: C, 61.97; H, 3.31; N, 19.71. Found: C, 62.10; H, 3.15; N, 19.67.

The Unequivocal Synthesis of 3-(6-Methoxy-3-pyridazinyl)-1,2,4-oxadiazolin-5-one (XIII).

(1) 6-Methoxy-3-pyridazineamidoxime (XVI).

A mixed solution of 3.26 g. (47 mmoles) of hydroxylamine hydrochloride and 2.49 g. (24 mmoles) of sodium carbonate in 30 ml. of water was added to a solution of 5.26 g. (39 mmoles) of 3-methoxy-6-cyanopyridazine (8) in 100 ml. of ethanol and the reaction mixture was refluxed for 3 hours. After cooling, the precipitated colorless needles were collected by filtration and washed with water giving 3.94 g. of XVI. The filtrate was evaporated and the residue was washed with water and filtered to give 1.78 g. of additional XVI. The crude products were combined and recrystallized from ethanol to give 5.59 g. (85%) of purified XVI, m.p. 200-202°.

Anal. Calcd. for $C_6H_8N_4O_2$: C, 42.85; H, 4.80; N, 33.32. Found: C, 42.77; H, 4.60; N, 33.43.

(2) 3-(6-Methoxy-3-pyridazinyl)-1,2,4-oxadiazolin-5-one (XIII).

Ethyl chloroformate (1.32 g., 12.2 mmoles) was added dropwise to an ice-cooled stirred solution of 1.72 g. (10.2 mmoles) of XVI in 15 ml. of pyridine. After stirring for 3 hours at room temperature, the reaction mixture was poured into ice-water. The precipitate was collected by filtration to give 1.37 g. of the intermediate *O*-ethoxycarbonyl amidoxime, m.p. 149-154°. The filtrate was evaporated and the residue was washed with water. The insoluble substance was collected giving 0.37 g. of the same compound. Both products were combined and heated under nitrogen atmosphere at 180° (bath temperature) for 15 minutes. After cooling, the resultant solid was recrystallized from ethanol (charcoal) giving 0.72 g. (36%) of 3-(6-methoxy-3-pyridazinyl)-1,2,4-oxadiazolin-5-one, m.p. 219-219.5° dec. This compound was shown to be identical with compound XIII prepared from compound X by mixed melting point determination and by comparison of the ir spectra.

The Unequivocal Synthesis of 3-(2-Quinolyl)-1,2,4-oxadiazolin-5-one (XIV).

(1) 2-Quinolineamidoxime (XVII).

This compound was prepared from 2-cyanoquinoline in a similar manner as described for compound XVI and recrystallized from ethanol, yield 93%, m.p. 160-162° (lit. (9) gives m.p. 162-163°).

Anal. Calcd. for $C_{10}H_9N_3$: C, 64.16; H, 4.85; N, 22.45. Found: C, 64.38; H, 4.84; N, 22.61.

(2) 3-(2-Quinolyl)-1,2,4-oxadiazolin-5-one (XIV).

Compound XVII (0.50 g., 2.9 mmoles) in 5 ml. of pyridine was treated with 0.38 g. (3.5 mmoles) of ethyl chloroformate in a similar manner as described above giving 0.71 g. of *O*-ethoxycarbonyl amidoxime, m.p. 137.5-139°. This compound was heated under nitrogen atmosphere at 150-160° (bath temperature) for 40 minutes. The resultant solid (0.55 g.) was recrystallized from ethanol giving 0.31 g. (50%) of 3-(2-quinolyl)-1,2,4-oxadiazolin-5-one, m.p. 266-269° dec. The ir spectrum of this compound was completely identical with that of compound XIV prepared from compound XI.

The Unequivocal Synthesis of 3-(1-Isoquinolyl)-1,2,4-oxadiazolin-5-one (XV).

(1) 1-Isoquinolineamidoxime (XVIII).

This compound was prepared from 1-cyanoisoquinoline in a similar manner as described for compound XVI and recrystallized from ethanol/water, yield 89%, m.p. 127-128.5° (lit. (10) gives m.p. 126-128°).

Anal. Calcd. for $C_{10}H_9N_3O$: C, 64.16; H, 4.85; N, 22.45. Found: C, 64.35; H, 4.71; N, 22.55.

(2) 3-(1-Isoquinolyl)-1,2,4-oxadiazolin-5-one (XV).

Compound XVIII (1.00 g., 5.8 mmoles) in 10 ml. of pyridine was treated with 0.76 g. (7.0 mmoles) of ethyl chloroformate in a similar manner to that described above giving 1.12 g. of *O*-ethoxycarbonyl-amidoxime, m.p. 97-100.5°. This compound was heated under nitrogen atmosphere at 130° (bath temperature) for 40 minutes. The resultant solid was recrystallized from ethanol giving 0.83 g. (67%) of 3-(1-isoquinolyl)-1,2,4-oxadiazolin-5-one, m.p. 241-242.5° dec. The ir spectrum of this compound was completely identical with that of compound XV prepared from compound XII.

α-Oximino-α-(6-methoxy-3-pyridazinyl)acetylazide (XIX).

A solution of 1.82 g. (26.4 mmoles) of sodium nitrite in 5 ml. of water was added dropwise to a stirred solution of 2.00 g. (11.0 mmoles) of 6-methoxy-3-pyridazinylacethydrazide (III) in 30 ml. of 10% hydrochloric acid, keeping the temperature between -4 and -1°. After stirring for an additional 10 minutes, the *p*H of the reaction mixture was adjusted to *ca.*, 4 with 10% sodium bicarbonate solution. The precipitated colorless solid was collected by filtration and washed with water. The residue was dried *in vacuo* over phosphorus pentoxide giving 1.97 g. (81%) of XIX, m.p. *ca.*, 115° (explosively dec.) (rapid heating); ir: 2750 (OH), 2180 (N_3) and 1680 cm^{-1} (C=O). This compound was used for the next reactions without further purification due to its instability.

α-Oximino-α-(2-quinolyl)acetylazide (XX).

2-Quinolylacethydrazide (IV), (12.07 g., 60 mmoles) in 150 ml. of 10% hydrochloric acid was treated with 9.11 g. (132 mmoles) of sodium nitrite in 20 ml. of water and worked up in a similar manner as described for XIX giving 13.36 g. (92%) of XX, m.p. *ca.*, 101° (explosively dec.) (rapid heating); ir: 2720 (OH), 2160 (N_3) and 1678 cm^{-1} (C=O). This compound was used for the next reaction without further purification due to its instability.

α-Oximino-α-(1-isoquinolyl)acetylazide (XXI).

1-Isoquinolylacethydrizide (V) (3.90 g., 19.4 mmoles) in 100 ml. of 10% hydrochloric acid was treated with 3.35 g. (48.5 mmoles) of sodium nitrite in 10 ml. of water and worked up in a similar manner as described for XIX giving 4.18 g. (89%) of XXI, m.p. *ca.*, 123° (explosively dec.) (rapid heating); ir: 2600 (OH), 2180 (N_3), 2150 (N_3) and 1683 cm^{-1} (C=O). This compound was not purified due to its instability.

Thermolysis of XIX.

(a) In chloroform.

A mixture of 1.30 g. (5.8 mmoles) of XIX and 60 ml. of chloroform was refluxed for 2 hours. Chloroform was evaporated and the residue was digested with 30 ml. of dichloromethane. The insoluble solid was collected by filtration giving 0.44 g. of 3-(6-methoxy-3-pyridazinyl)-1,2,4-oxadiazolin-5-one (XIII). The ir spectrum of this compound was identical with that of an authentic sample prepared by the method described above. Recrystallization from ethanol afforded pink needles, m.p. 221-222° dec. The filtered dichloromethane solution was applied to a column of silica gel. Elution with dichloromethane gave 0.11 g. (10%) of 3-hydroxy-4-(6-methoxy-3-pyridazinyl)furazan (XXII). An analytical sample was obtained by recrystallization from ether, colorless prisms, m.p. 146-147°; nmr (deuteriochloroform): δ 4.23 (s, 3H, OCH_3), 7.36 (d, 1H,

H_5), 8.32 (d, 1H, H_4), 9.26 (br s, 1H, OH), $J_{4,5}$ = 9 Hz; uv λ max: 243 (sh) (ε, 7,200), 259 (ε, 8,400) and 314 nm (sh) (ε 2,300).

Anal. Calcd. for $C_7H_6N_4O_3$: C, 43.30; H, 3.12; N, 28.86. Found: C, 43.58; H, 3.01; N, 29.15.

Further elution of the column with ether gave 0.42 g. of XIII. Recrystallization from ethanol afforded colorless needles, m.p. 221-223° dec. The total yield of XIII was 0.86 g. (76%).

(b) In ethanol.

A mixture of 1.00 g. (4.5 mmoles) of XIX and 70 ml. of ethanol was refluxed for one hour. Ethanol was evaporated and the residue was digested with 10 ml. of hot benzene. The insoluble substance was collected by filtration and washed with a small amount of methanol giving 0.49 g. of XIII, m.p. 216-219° dec. Recrystallization from ethanol raised the melting point to 221-223° dec. The filtered benzene solution was applied on a colum of silica gel (2 x 8 cm.). Elution with benzene afforded 0.3 mg. of XXII, which was identified by tlc. Further elution of the column with chloroform afforded 0.21 g. XIII, m.p. 217-219° dec. Recrystallization from methanol raised the melting point to 219-220° dec. The total yield of XIII was 0.70 g. (80%).

Thermolysis of XX.

(a) In chloroform.

A mixture of 3.00 g. (12.4 mmoles) of XX and 300 ml. of chloroform was refluxed for 2 hours. Chloroform was evaporated and the residue was digested with hot chloroform. The insoluble substance was collected by filtration and recrystallized from ethanol giving 0.36 g. of 3-(2-quinolyl)-1,2,4-oxadiazolin-5-one (XIV), m.p. 260-268° dec. Further recrystallization from ethanol/benzene raised the melting point to 269-271.5° dec. The ir spectrum of this compound was identical with that of an authentic sample prepared by the method described above. The filtered chloroform solution was concentrated and applied on a column of silica gel (2.5 x 35 cm.). Elution with chloroform afforded 1.85 g. (70%) of 3-hydroxy-4-(2-quinolyl)furazan (XXIII). An analytical sample was obtained by recrystallization from benzene, yellow needles, m.p. 174-174.5°; ms: m/e 213 (M^+); nmr (deuteriochloroform): δ 7.57-8.45 (m, 6H, ArH), 10.6 (br s, 1H, OH); uv λ max: 243 (ε, 28,700), 254 (sh) (ε, 19,800), 304 (ε, 8,100), 320 (sh) (ε, 6,400) and 333 nm (sh) (ε, 4,200).

Anal. Calcd. for $C_{11}H_7N_3O_2$: C, 61.97; H, 3.31; N, 19.71. Found: C, 62.24; H, 3.21; N, 19.93.

Further elution of the column with ethyl acetate gave crude XIV which was contaminated by a slight amount of oily impurity. Crystallization from ethanol afforded 0.09 g. of XIV, m.p. 250-264° dec. Recrystallization from ethanol (charcoal) raised the melting point to 268-271° dec. The total yeild of XIV was 0.45 g. (17%).

(b) In ethanol.

A mixture of 1.00 g. (4.1 mmoles) of XX and 70 ml. of ethanol was refluxed for one hour. Ethanol was evaporated and the residue was recrystallized from ethanol giving 0.65 g. of XIV, m.p. 265-270.5° dec. Further recrystallization from ethanol raised the melting point to 269-271.5° dec. The mother liquor was evaporated. The residue was dissolved in chloroform and applied on a column of silica gel. Elution with chloroform afforded 0.04 g. (5%) of furazan XXIII, m.p. 172-174°. Further elution with chloroform gave 0.02 g. of XIV, m.p. 263-269° dec. The total yield of XIV was 0.67 g. (77%).

Thermolysis of XXI.

(a) In chloroform.

A mixture of 1.00 g. (4.1 mmoles) of XXI and 100 ml. of chloroform was refluxed for 2 hours. Chloroform was evaporated and the residue was digested with 25 ml. of hot benzene. The insoluble substance was filtered giving 0.19 g. of crude compound of 3-(1-isoquinolyl)-1,2,4-oxadiazolin-5-one (XV). The filtrate was allowed to cool and the precipitated additional XV (0.03 g.) was collected by filtration. Both products were combined and recrystallized fm ethanol giving 0.19 g. of purified XV, m.p. 239-242° dec. The ir spectrum of this compound was identical with that of an authentic sample prepared by the method described above. The filtered benzene solution was applied on a column of silica gel (2.5 x 23 cm.) and eluted with benzene giving 0.51 g. (58%) of 3-hydroxy-4-(1-isoquinolyl)furazan (XXIV), m.p. 166-167.5°. An analytical sample was prepared by recrystallization from ethanol yellow needles, m.p. 166-167.5°; ms: m/e 213 (M^+); nmr (deuteriochloroform): δ 7.91-8.08 (m, 4H, ArH), 8.67 (d, 1H, H_3), 9.31 (m, 1H, H_8), $J_{3,4}$ = 6 Hz; uv λ max: 223 (ε, 32,000), and 331 nm (ε, 6,800).

Anal. Calcd. for $C_{11}H_7N_3O_2$: C, 61.97; H, 3.31; N, 19.71. Found: C, 62.24; H, 3.12; N, 19.78.

Further elution of the colunn with ethyl acetate gave 0.06 g. of XV. The total yield of XV was 0.25 g. (28%).

(b) In ethanol.

A mixture of 1.00 g. (4.1 mmoles) of XXI and 70 ml. of ethanol was refluxed for one hour. After cooling, the precipitated needles were collected by filtration giving 0.49 g. of XV, m.p. 241-242° dec. The filtrate was evaporated and the residue was digested with 10 ml. of hot benzene. After cooling, the insoluble substance was collected by filtration and recrystallized from ethanol (charcoal) giving 0.28 g. of additional XV, m.p. 241.5-243° dec. The filtered benzene solution was applied on a column of silica gel (1.5 x 10 cm.). Elution with benzene afforded 0.01 g. of solid, which was shown to be a mixture of 1-cyanoisoquinoline and furazan XXIV by tlc. This mixture was applied on a preparative scale tlc (silica gel, 20 x 20 cm., thickness 0.2 mm.) and developed with chloroform. 1-Cyanoisoquinoline (6 mg.), m.p. 87-88°, was isolated, but furazan XXIV was not obtained probably due to its decomposition caused by room light (11) *etc.*, during the purification procedure.

Further elution of the column with chloroform afforded 0.04 g. of XV, m.p. 239-242° dec. The total yield of XV was 0.81 g. (92%).

3-Methoxy-4-(2-quinolyl)furazan (XXV).

Under ice-cooling, excess diazomethane in ether was added to a solution of 0.21 g. (1 mmole) of XXIII in 100 ml. of ether. The reaction mixture was allowed to stand overnight in a refrigerator. Ether was evaporated over a steam bath giving 0.23 g. (quantitative) of XXV. An analytical sample was obtained by recrystallization from ether/petroleum ether, slightly pink needles, m.p. 100-103°; ms: m/e 227 (M^+); nmr (deuteriochloroform): δ 4.27 (s, 3H, OCH_3), 7.54-8.37 (m, 6H, ArH); uv λ max: 241 (ε, 10,100), 250 (sh) (ε, 9,100) and 300 nm (ε, 3,300).

Anal. Calcd. for $C_{12}H_9N_3O_2$: C, 63.43; H, 3.99; N, 18.49. Found: C, 63.20; H, 3.89; N, 18.66.

3-Acetoxy-4-(2-quinolyl)furazan (XXVI).

A mixture of 0.21 g. (1 mmole) of XXIII and 2 ml. of acetic anhydride was refluxed for 2 hours. After cooling, the reaction mixture was poured over ice-water and precipitated colorless fine needles were collected by filtration giving 0.21 g. (82%) of XXVI, m.p. 103-104°. An analytical sample was obtained by recrystallization from benzene/ligroin, m.p. 103-105°; nmr: (deuteriochloroform): δ 2.52 (s, 3H, $COCH_3$), 7.49-8.32 (m, 6H, ArH); ir: 1790 cm^{-1} (C=O); uv λ max: 245 (ε, 30,400), 292 (ε, 7,400), 319 (sh) (ε, 4,100) and 332 nm (sh) (ε, 2,600).

Anal. Calcd. for $C_{13}H_9N_3O_3$: C, 61.17; H, 3.55; N, 16.47. Found: C, 61.07; H, 3.42; N, 16.27.

Hydrolysis of XXVI.

A mixture of 0.21 g. (0.8 mmole) of XXVI and 10 ml. of 10% hydrochloric acid was heated over a steam bath for one hour. After cooling, precipitated yellow needles were collected by filtration giving 0.15 g. (88%) of XXIII. The ir spectrum of this compound was identical with that of an authentic sample.

α-Oximino-α-(2-quinolyl)acetonitrile (XXVII).

A solution of 0.97 g. (14 mmoles) of sodium nitrite in 5 ml. of water was added dropwise to a stirred solution of 2.06 g. (12 mmoles) of 2-quinolylacetonitrile (12) in 20 ml. of acetic acid, keeping the temperature between 15 and 25°. After stirring for an additional 10 minutes, 80 ml. of water was added to a reaction mixture. The precipitate was collected and recrystallized from aqueous ethanol (charcoal) giving 2.22 g. (94%) of

XXVII, colorless needles, m.p. 183.5-185° dec.; ms: m/e 197 (M^+); ir: 3490 (OH), 2870 (OH), 2260 (C≡N) and 1645 cm^{-1} (C=N).

Anal. Calcd. for $C_{11}H_7N_3O$: C, 67.00; H, 3.58; N, 21.01. Found: C, 66.98; H, 3.50; N, 21.18.

3-Amino-4-(2-quinolyl)furazan (XXVIII) and α-Oximino-α-(2-quinolyl)acetic acid (XXIX).

A mixture of XXVII (1.00 g., 5 mmoles), hydroxylamine hydrochloride (0.42 g., 6 mmoles), sodium hydroxide (1.04 g., 26 mmoles) and water (20 ml.) was refluxed for one hour. After cooling, precipitated colorless fine needles were collected by filtration giving 0.18 g. (16%) of 3-amino-4-(2-quinolyl)furazan (XXVIII). An analytical sample was prepared by recrystallization from ethanol, m.p. 191.5-192°; ms: m/e 212 (M^+); nmr (deuteriochloroform): δ 5.92 (br s, 2H, NH_2), 7.52-8.38 (m, 6H, ArH); ir: 3370 (NH), 3270 (NH) and 1630 cm^{-1} (NH); uv λ max: 245 (ε, 36,800), 309 (ε, 9,200), 322 (ε, 8,800) and 336 nm (ε, 6,600).

Anal. Calcd. for $C_{11}H_8N_4O$: C, 62.25; H, 3.80; N, 26.40. Found: C, 62.20; H, 3.69; N, 26.73.

The alkaline filtrate was made acidic with hydrochloric acid. The precipitated yellow solid was collected by filtration giving 0.48 g. (44%) of α-oximino-α-(2-quinolyl)acetic acid (XXIX). An analytical sample was obtained by recrystallization from ethanol, yellow needles, m.p. 174.5° dec.; ms: m/e 216 (M^+); nmr (DMSO-d_6): 7.60-8.08 (m, 5H, ArH), 8.42 (d, 1H, H_4), 12.6 (br s, OH), $J_{3,4}$ = 9 Hz.

Anal. Calcd. for $C_{11}H_8N_2O_3$: C, 61.11; H, 3.73; N, 12.96. Found: C, 61.17; H, 3.73; N, 12.98.

An Attempted Conversion of XXVIII into 3-Hydroxy-4-(2-quinolyl)-furazan (XXIII). Formation of α-Oximino-α-(2-quinolyl)acetonitrile (XXVII).

Under ice-cooling, a solution of 80 mg. (1.2 mmole) of sodium nitrite in a minimum amount of water was added dropwise to a solution of 100 mg. (0.5 mmole) of XXVIII in 5 ml. of 50% sulfuric acid. The reaction mixture was allowed to stand for 30 minutes at room temperature, warmed over a steam bath for 10 minutes and cooled by addition of a small piece of ice. The solution was made basic with ammonia water and the insoluble substance was filtered off. Tlc showed that this substance was the mixture of several compounds, not including the desired compound XXIII. The filtrate was made acidic with 10% hydrochloric acid. The precipitate was collected and recrystallized from ether/petroleum ether giving 20 mg. (20%) of XXVII as pale yellow needles. The ir spectrum of this compound was identical with that of an authentic sample prepared by the method described above.

Methyl α-oximino-α-(2-quinolyl)acetate (XXX).

Under ice-salt cooling, a solution of 2.4 g. (35 mmoles) of sodium nitrite in 5 ml. of water was added dropwise to a stirred solution of 7.0 g. (35 mmoles) of methyl 2-quinolylacetate in 30 ml. of 10% hydrochloric acid, keeping the temperature between -3 and 3°. After stirring for 10 minutes, the precipitated white solid was collected by filtration and washed with methanol giving 7.5 g. (80%) of hydrochloride of XXX, m.p. 189-189.5° dec. An analytical sample was prepared by recrystallization from methanol, m.p. 191-192° dec.; ir: 2550 (OH and N^+-H) and 1754 cm^{-1} (C=O).

Anal. Calcd. for $C_{13}H_{11}ClN_2O_3$: C, 54.05; H, 4.16; N, 10.50. Found: C, 54.13; H, 4.19; N, 10.61.

A suspension of recrystallized hydrochloride of XXX (4.5 g.) in 80 ml. of 10% sodium bicarbonate was vigorously stirred at room temperature for several minutes and filtered giving 3.8 g. (98%) of XXX; nmr (DMSO-d_6): δ 3.74 (s, 3H, $COOCH_3$), 7.56-7.88 (m, 3H, ArH), 8.03 (near dd, 2H, ArH), 8.44 (d, 1H, H_4), 13.12 (s, 1H, OH), $J_{3,4}$ = 9 Hz; ir: 2700 (OH) and 1737 cm^{-1} (C=O). This non-recrystallized compound melted once at 121-123°, then solidified and remelted at 152-153°. The double melting point would be attributable to the isomerization of oxime function caused by heating.

The recrystallization from benzene gave colorless needles of the isomerized oxime, m.p. 152-153°; nmr (DMSO-d_6): δ 3.87 (s, 3H, $COOCH_3$), 7.52-8.04 (m, 5H, ArH), 8.43 (d, 1H, H_4), 12.90 (s, 1H, OH), $J_{3,4}$ = 9 Hz; ir: 3230 (OH) and 1709 cm^{-1} (C=O).

Anal. Calcd. for $C_{12}H_{10}N_2O_3$: C, 62.60; H, 4.38; N, 12.17. Found: C, 62.65; H, 4.31; N, 12.24.

The oxime of *syn* configuration to the carbomethoxy group can form intramolecular hydrogen bonding with the ester carbonyl which is anticipated to cause the frequency decrease of the carbonyl absorption in the ir spectrum. Consequently, the configuration of oxime of the recrystallized compound (ν C=O: 1709 cm^{-1}) would be *syn* to the ester group and that of the non-recrystallized compound (ν C=O: 1737 cm^{-1}) *anti*.

The Unequivocal Synthesis of 3-Hydroxy-4-(2-quinolyl)furazan (XXIII).

A mixed solution of recrystallized XXX (1.18 g., 5.1 mmoles), hydroxylamine hydrochloride (0.42 g., 6.1 mmoles) and sodium hydroxide (1.2 g., 30 mmoles) in 7 ml. of water was stirred at room temperature for 4.5 days and warmed on a steam bath for 4 hours. Water (30 ml.) was added to the reaction mixture, warmed and filtered. The filtrate was made acidic with 10% hydrochloric acid and the precipitate was collected by filtration. The residue (0.55 g.) was digested with chloroform and filtered giving 0.13 g. (12%) of α-oximino-α-(2-quinolyl)acetic acid (XXIX), m.p. 174-175° dec. The filtrate was applied on a column of silica gel and eluted with chloroform. From the first fraction, 0.27 g. (25%) of 3-hydroxy-4-(2-quinolyl)furazan was obtained, yellow needles, m.p. 172-174°. This compound was shown to be identical with compound XXIII obtained by the thermolysis of α-oximino-α-(2-quinolyl)acetylazide (XX) by mixed melting point and comparison of ir spectra. Further elution of the column with chloroform afforded 0.02 g. (2%) of 3-(2-quinolyl)-1,2,4-oxadiazolin-5-one (XIV), which was shown to be identical with an authentic sample by comparison of ir spectra.

3-Methoxy-6-cyanopyridazine (XXXI).

A suspension of 0.57 g. (2.6 mmoles) of XIX in 10 ml. of 10% sodium carbonate was stirred at room temperature for 3 hours and filtered giving 0.21 g. of XXXI. The filtrate was extracted with chloroform. The dried extract was evaporated giving 0.08 g. of additional XXXI. The total yield was 0.29 g. (84%). Both products were combined and recrystallized from ether/petroleum ether giving colorless needles, m.p. 92-93.5° (lit. (8) gives m.p. 94-95°). The ir spectrum of this compound was identical with that of an authentic sample prepared by the method reported in literature (8).

2-Cyanoquinoline (XXXII).

A suspension of 0.71 g. (2.9 mmoles) of XX in 20 ml. of 10% sodium carbonate was stirred at room temperature for 3 hours and filtered giving 0.37 g. (83%) of XXXII. Recrystallization from ligroin afforded colorless needles, m.p. 93-94° (lit (13) gives m.p. 94-96°). The ir spectrum of this compound was superimposable upon that of an authentic sample prepared by the method described in literature (13).

1-Cyanoisoquinoline (XXXIII).

A suspension of 0.67 g. (2.8 mmoles) of XXI in 20 ml. of 10% sodium carbonate was stirred at room temperature for 3 hours and filtered giving 0.35 g. (82%) of XXXIII. Recrystallization from ether/petroleum ether afforded colorless needles, m.p. 89-89.5° (lit (14) gives m.p. 87-89°). The ir spectrum of this compound was identical with that of an authentic sample prepared by the method described in literature (14).

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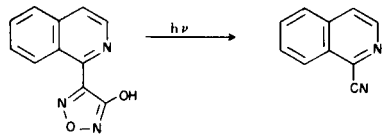
(11) When a mixture of 100 mg. of XXIV and 35 ml. of chloroform in a quartz vessel was irradiated externally with a 100 W. high pressure mercury lamp for 10 hours, 68 mg. (94%) of 1-cyanoisoquinoline, m.p. 88.5-90°, was obtained.



XXIV

Consequently, one of the explanations for the disappearance of XXIV during the purification procedure is the photochemical decomposition, due to room light, of XXIV into 1-cyanoisoquinoline.

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