mined using gas chromatography. Fraction 2 was submitted for elemental analysis: n^{20}D 1.5115 (lit.[19] n^{20}D 1.5104)

Anal. Calcd for $C_8H_9NO_2$: C, 63.6; H, 6.0; N, 9.3. Found: C, 63.2; H, 6.0; N, 9.3.

The experiment was repeated using the procedure outlined above except the reactants were refluxed in 100 ml of ethanol to give 1.80 g (35%) of **4** and 5.3 g of crude **9**.

(19) R. C. Weast, Ed., "Handbook of Chemistry and Physics," 49th ed, Chemical Rubber Publishing Co., Cleveland, Ohio, 1968, p C520.

Registry No.—**1**, 492-73-9; **6**, 27784-64-1; **7**, 27784-65-2.

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The Thermal Rearrangement of *O*-(2-Pyridyl) Oximes

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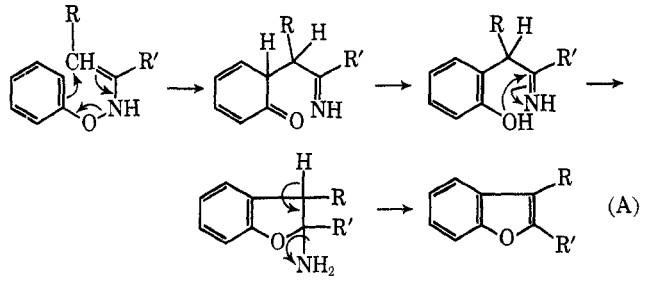
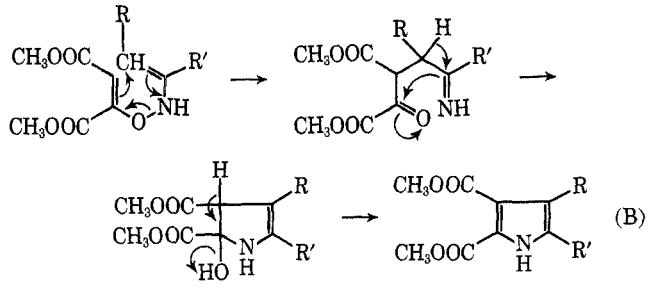
O-(2-Pyridyl) oximes of cyclopentanone, cyclohexanone, acetophenone, 1-indanone, and 1-tetralone (**1a–e**) were prepared by treating the respective oximes with 2-fluoropyridine. On heating, compounds **1** rearranged to yield 3-(2-oxoalkyl)-2-pyridones (**5**), of which two (**5b** and **5e**) were cyclized to the corresponding furo[2,3-*b*]pyridines (**6**). The mechanism of this rearrangement and its relationship to the Fischer indole synthesis are discussed.

Rearrangements of O-substituted oximes containing α-methylene groups have been recently reported by us[1,2] and by others.[3–5]

The rearrangement involves concerted cleavage of the nitrogen–oxygen bond and formation of a new carbon–carbon bond to give initially 4-imino ketones. These highly reactive species, however, cyclize spontaneously forming either furans (path A, observed in the case of *O*-phenyl oximes[6]) or pyrroles (path B, observed in the case of *O*-vinyl oximes[2]).



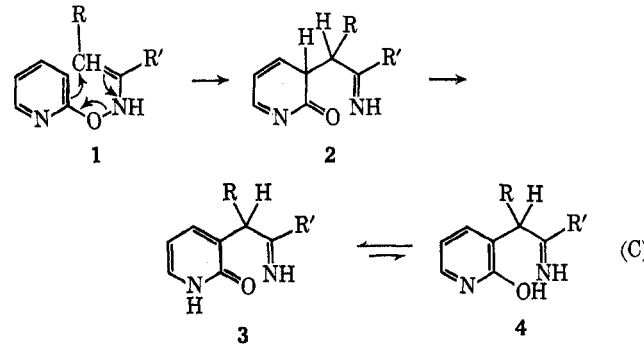
(A)



(B)

Path A is completely analogous to the Fischer indole synthesis[6,7] and involves rearrangement, aromatization to a phenol, and nucleophilic attack by the hydroxyl on the imine. Path B in which the initial intermediate retains the keto form involves a nucleophilic attack by the imine on the carbonyl.

We wish to report now the rearrangement of *O*-(2-pyridyl) oximes (**1**) (path C). We were interested in this peculiar case as it differs from those previously studied. Aromatization of the intermediate **2** should lead to **3**, as 2-hydroxypyridines are known to exist predominantly as 2-pyridones.[8] Cyclization to a furopyridine (path A mechanism) can proceed by nucleophilic action of the hydroxyl group in the minor tautomer **4**, but this course is unlikely in view of the available information on the reactivity of 2-pyridones.[9] On the other hand the amidic carbonyl in the pyridone **3** should be inert toward a nucleophilic attack by the imine (path B mechanism), thus excluding the possibility of cyclization to a pyrrole (7-azaindole in this case).



(C)

Termination of path C at compound **3** and isolation of an uncyclized product would further confirm the mechanisms suggested earlier (paths A and B) and provide new synthetic utility of the rearrangement.

The initial step (**1** → **2**) involves an electrophilic attack on the electron-deficient pyridine ring. It is to be expected that use of an acid catalyst would lead to further deactivation in this step because of protonation of the pyridine nitrogen. A thermal process,[10,11] by

(1) T. Sheradsky, *Tetrahedron Lett.*, 5225 (1966).
(2) T. Sheradsky, *ibid.*, 25 (1970).
(3) A. Mooradian, *ibid.*, 407 (1967).
(4) D. Kaminsky, J. Shavel, and R. I. Meltzer, *ibid.*, 859 (1967).
(5) H. O. House and F. A. Richey, *J. Org. Chem.*, **34**, 1430 (1969).
(6) A. Mooradian and P. E. Dupont, *Tetrahedron Lett.*, 2867 (1967).
(7) T. Sheradsky and A. Elgavi, *Israel J. Chem.*, **6**, 895 (1968).
(8) A. R. Katritzky and J. M. Lagowsky, *Advan. Heterocycl. Chem.*, **1**, 339 (1963).
(9) H. Meislich in "Pyridine and Its Derivatives," Vol. 3, E. Klingsberg, Ed., Interscience, New York, N. Y., 1962, p 509.
(10) J. T. Fitzpatrick and R. D. Hiser, *J. Org. Chem.*, **22**, 1703 (1957).
(11) A. H. Kelly, D. H. McLeod, and J. Parrick, *Can. J. Chem.*, **43**, 296 (1965).

which a number of aza and diazaindoles have been successfully prepared,[12,13] avoids this deactivation.

The starting *O*-(2-pyridyl) oximes (**1a–e**) were prepared by the reaction of the respective oximes with 2-fluoropyridine and potassium *tert*-butoxide at 90°. Use of 2-chloropyridine required higher temperatures and the yields were considerably lower. The compounds prepared are listed in Table I.

TABLE I

O-(2-PYRIDYL) OXIMES[a]

No.	Parent ketone	Mp, °C	Yield, %
1a	Cyclopentanone	Oil	50
1b	Cyclohexanone	68–69	78
1c	Acetophenone	Oil	94
1d	1-Indanone	230	54
1e	1-Tetralone	224	50

[a] Satisfactory analytical data (±0.25 for C, H, and N) were reported for all compounds in the table: Ed.

A previous attempt to carry out thermal rearrangements of *O*-aryl oximes has been reported to yield only intractable tars.[14] Indeed, in our initial experiments with the cyclohexanone derivative **1b**, no defined product could be isolated even on lowering the thermolysis temperature to 130° (boiling 2-ethoxyethanol). However, heating a solution of **1b** in DMSO at 100° for 4 hr afforded 10% yield of a crystalline product which was identified as 3-(2-oxocyclohexyl)-2-pyridone (**5b**). In a similar manner low yields of 3-(2-oxocyclopentyl)-2-pyridone (**5a**) and α-(3-pyridyl-2-one)acetophenone (**5c**) were obtained from **1a** and **1c**, respectively. Better results were obtained with the derivatives of the benzene fused cyclic ketones. The optimal reaction temperature for these compounds was found to be 180° (boiling ethylene glycol). The 1-indanone derivative **1d** gave 3-(1-oxo-2-indanyl)-2-pyridone (**5d**) in 53% yield and the 1-tetralone derivative **1e** yielded 73% of 3-(1-oxo-2-tetralyl)-2-pyridone (**5e**). Compounds **5** were formed presumably by facile hydrolysis of the imino groups in the expected products **3** during work-up. The reaction sequence starting with 1-tetralone oxime is presented in Scheme I.

The structure assignments of compounds **5** as 3-(2-oxoalkyl)-2-pyridones are based mainly on spectral evidence. The infrared spectra exhibit two carbonyl bands at *ca.* 1700 (ketone) and 1650 cm^{-1} (2-pyridone). The ultraviolet spectra indicate the presence of the 2-pyridone moiety, showing absorptions at *ca.* 230 and 300 nm. The loss of hydrogen from and the formation of a new C–C bond between position 3 of the pyridine nucleus and the α position of the ketone is evident from the nuclear magnetic resonance spectra. The absorptions of the pyridine hydrogens have the same shape and positions as those reported for 3-substituted 2-pyridones, including the NH signal at very low field. Spectral data for compounds **5** are presented in Tables II and III. Literature data[15,16] for the model compound 3-methyl-2-pyridone (**7**) are included for comparison.

(12) A. H. Kelly and J. Parrick, *Can. J. Chem.*, **44**, 2455 (1966).
(13) P. A. Crooks and B. Robinson, *ibid.*, **47**, 206 (1969).
(14) A. Mooradian and P. E. Dupont, *J. Heterocycl. Chem.*, **4**, 441 (1967).
(15) W. Brügel, *Z. Electrochem.*, **66**, 159 (1966).
(16) E. Spinner and J. C. B. White, *J. Chem. Soc. B*, 99 (1966).

SCHEME I

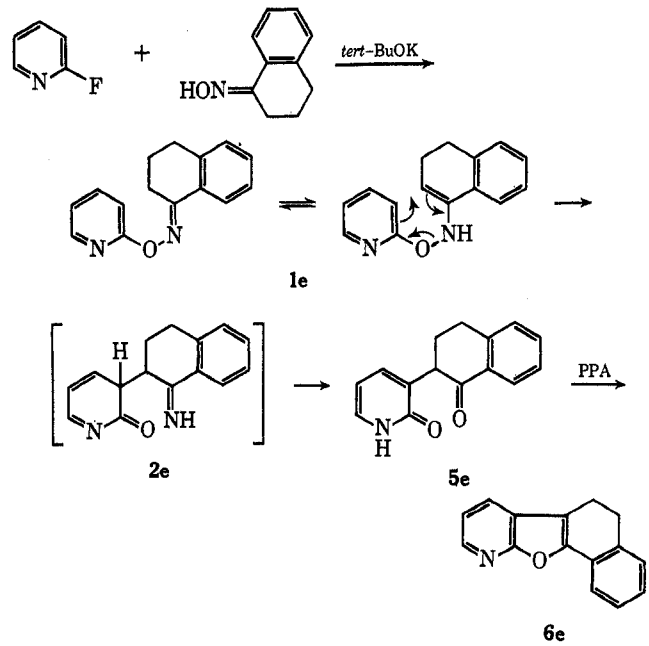


TABLE II

UV AND IR DATA

No.	Ir, cm^{-1}[a] C=O (ketone)	Ir, cm^{-1}[a] C=O (pyridone)	Uv, nm (log ε)[b]
5a	1740	1645	232 (3.70), 300 (3.83)
5b	1715	1650	229 (3.76), 299 (3.80)
5c	1690	1645	237[c] (4.13), 300 (3.82)
5d	1700	1640	240[c] (4.16), 296 (3.97)
5e	1685	1640	239[c] (4.10), 246 (4.09), 298 (3.94)
7[d]		1641	224 (3.85), 294 (3.75)

[a] In Nujol. [b] Solvent ethanol. [c] The low wavelength absorption of the pyridine is obscured by the benzoyl absorption. [d] Data from ref 16.

TABLE III

NMR DATA (δ, PARTS PER MILLION)[a]

No.	Pyridine hydrogens 1 (s)	5 (t)	4 + 6 (d)[b]	α hydrogens
5a	11.86	6.10	7.26	3.23 (t, 1 H)
5b	12.00	6.15	7.24	3.95 (m, 1 H)
5c	11.35	6.17	7.90	4.04 (s, 2 H)
5d	11.50	6.10	7.50	3.65 (dd, 1 H)
5e	11.70	6.08	7.23	3.73 (dd, 1 H)
7[c]	11.95	6.20	7.41	

[a] Solvent DMSO-d_6. [b] Hydrogens 4 and 6 show the same chemical shift; $J_{4+6,5}$ was 6.5–7.0 Hz in all compounds **5** (reported for compound **7**,[15] 6.7 Hz). [c] Reference 15.

The cyclization of the ketones **5** to the corresponding furo[2,3-*b*]pyridines was attempted in both sulfuric and polyphosphoric acids. The cyclohexanone **5b** and 1-tetralone **5e** cyclized smoothly to 5,6,7,8-tetrahydrobenzofuro[2,3-*b*]pyridine (**6b**, 89%) and its benzo derivative (**6e**, 88%), respectively. However, the cyclopentanone **5a** and the 1-indanone **5d** did not cyclize and were recovered unchanged even after heating at 160° in polyphosphoric acid. This substantial difference in reactivity is probably a consequence of the

spatial inaccessibility of the two carbonyl groups in the five-membered ring ketones **5a** and **5d** (also revealed on examination of models). The spectral data for compounds **6b** and **6e** are in accordance with the expected structures and in close agreement with the data published[17] for the unsubstituted furo[2,3-*b*]pyridine.

The results obtained confirm the predictions outlined in the introduction and verify the mechanisms suggested for the Fischer-like reactions of oximes. The reaction can be used in some cases for the synthesis of 3-(2-oxoalkyl)pyridones and subsequent products.

Experimental Section

Melting points are uncorrected. Spectrometers used were: Unicam SP-800 (uv), Perkin-Elmer 257 (ir), and Varian T-60 and HA-100 (nmr).

***O*-(2-Pyridyl) Oximes of Cyclopentanone, Cyclohexanone, and Acetophenone (1a–c).**—A solution containing the oxime (0.02 mol) and *tert*-BuOK (2.2 g, 0.02 mol) in dry DMSO (40 ml) was stirred under nitrogen for 30 min, and 2-fluoropyridine (1.94 g, 0.02 mol) dissolved in 40 ml of DMSO was added. Stirring was continued for 1 hr at room temperature and 1 hr at 90°, and the cooled solution was poured into 300 ml of saturated NaCl solution. Extraction with ethyl acetate (two 200-ml portions), drying ($MgSO_4$), and evaporation yielded the products **1** as yellow oils. Compound **1b** solidified on trituration with petroleum–ether (bp 40–60°) and was crystallized from this solvent. Compounds **1a** and **1c** were chromatographed twice on Florisil.

***O*-(2-Pyridyl) Oximes of 1-Indanone and 1-Tetralone (1d,e).**—These were prepared as described above for **1a–c**. Stirring at 90° was continued for 3 hr The products precipitated on pouring the reaction mixture into water and were collected by filtration and crystallized from methanol

Yields, properties, and analyses of all compounds **1** obtained are given in Table I.

3-(2-Oxocyclohexyl)-2-pyridone (5b) —A solution of **1b** (1 g) in 20 ml of DMSO was heated at 100° for 4 hr under nitrogen and then poured into saturated NaCl solution (100 ml) The mixture was extracted twice with ethyl acetate and the extract dried and evaporated The remaining black tar was chromatographed on Florisil to yield after crystallization from ethyl acetate 0.1 g (10%) of **5b**, mp 192–193°

Anal. Calcd for $C_{11}H_{13}NO_2$: C, 69.09; H, 6.85; N, 7.32. Found: C, 69.45; H, 6.79; N, 7.41.

(17) H. Sliwa, *Bull. Soc. Chim. Fr.*, 646 (1970).

3-(2-Oxocyclopentyl)-2-pyridone (5a) was obtained in the same manner as **5b** above in 12% yield, mp 180–181°.

Anal. Calcd for $C_{10}H_{11}NO_2$: C, 67.78; H, 6.26; N, 7.50. Found: C, 67.50; H, 6.29; N, 7.97.

α-(3-Pyridyl-2-one)acetophenone (5c) was obtained as described for **5b**. The yield was 5% after crystallization from ethanol, mp 202°.

Anal. Calcd for $C_{13}H_{11}NO_2$: C, 73.23; H, 5.20; N, 6.57. Found: C, 73.53; H, 5.07; N, 6.57.

3-(1-Oxo-2-indanyl)-2-pyridone (5d).—A solution of **1d** (1 g) in ethylene glycol (20 ml) was refluxed for 15 hr under nitrogen, cooled, and poured into water. The precipitate was collected and crystallized from ethanol to yield 0.53 g (53%) of **5d**, mp 213–214°.

Anal. Calcd for $C_{14}H_{11}NO_2$: C, 74.65; H, 4.92; N, 6.22. Found: C, 74.62; H, 5.06; N, 6.14.

3-(1-Oxo-2-tetralyl)-2-pyridone (5e).—The procedure described for **5d** was followed. After 20-hr reflux, **5e** was obtained in 73% yield, mp 206–207°.

Anal. Calcd for $C_{15}H_{13}NO_2$: C, 75.30; H, 5.48; N, 5.85. Found: C, 75.04; H, 5.58; N, 5.78.

5,6,7,8-Tetrahydrobenzofuro[2,3-*b*]pyridine (6b).—A solution of **5b** (0.16 g) in 2.2 ml of H_2SO_4 was kept at room temperature for 6 days and then poured into ice water. The solution was made basic by addition of 50% NaOH solution and extracted with ethyl acetate. Drying and evaporation of the ethyl acetate afforded, after crystallization from ethyl acetate, 0.13 g (89%) of **6b**: mp 50–51°; uv λ_{max} (EtOH) 220 nm (log ϵ 5.14), 265 (3.76), 286 (3.92); nmr ($CDCl_3$) δ 1.88 and 2.67 [m, 4 each, $(CH_2)_4$], 7.10 (dd, 1, H-3), 7.65 (d, 1, H-4), 8.17 (d, 1, H-2), $J_{2,3} = 5$, $J_{3,4} = 7.5$ Hz; no carbonyl absorption in the ir.

Anal. Calcd for $C_{11}H_{11}NO$: C, 76.20; H, 6.40; N, 8.09. Found: C, 75.93; H, 6.47; N, 8.12.

5,6-Dihydronaphtho[1′,2′:4,5]furo[2,3-*b*]pyridine (6e).—Compound **5e** (0.15 g) in polyphosphoric acid (3 g) was heated at 160° for 4 hr and poured into ice water. The precipitated product was collected by filtration and crystallized from ethyl acetate–petroleum ether (bp 40–60°) to yield 0.12 g (88%) of **6e**: mp 110°; uv λ_{max} (EtOH) 234 nm (log 4.20), 242 (4.17), 322 (4.44), 336 (4.38); nmr δ 3.03 (m, 4), 7.26 (m, 5), 7.75 (dd, 1, H-4), 8.28 (dd, 1, H-2), $J_{2,3} = 4.9$, $J_{3,4} = 5.2$, $J_{2,4} = 1.7$ Hz; no carbonyl absorption in the ir.

Anal. Calcd for $C_{15}H_{11}NO$: C, 81.43; H, 5.01; N, 6.33. Found: C, 81.40; H, 5.14; N, 6.37.

Registry No.—**1a**, 27921-17-1; **1b**, 27921-18-2; **1c**, 27921-19-3; **1d**, 27921-20-6; **1e**, 27921-21-7; **5a**, 27921-22-8; **5b**, 27921-23-9; **5c**, 24391-89-7; **5d**, 27915-21-5; **5e**, 27915-22-6; **6b**, 27915-23-7; **6e**, 27915-24-8.