

THE REARRANGEMENT OF O-ARYL OXIMES

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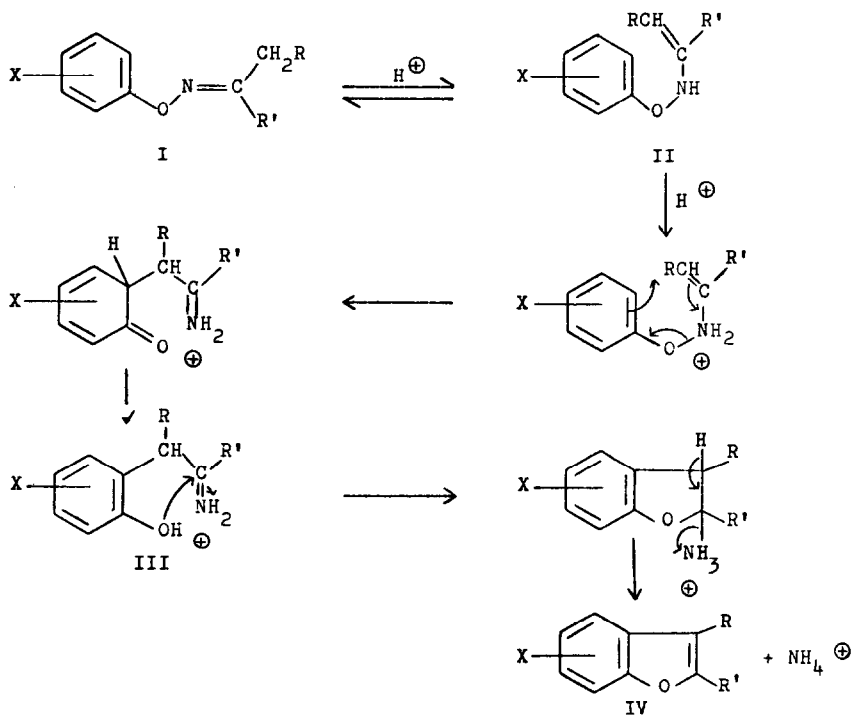
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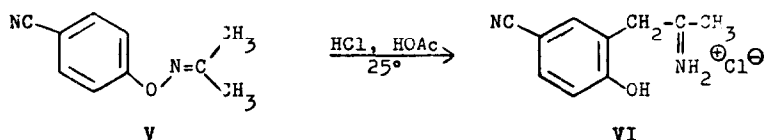
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In an earlier communication (2) it was suggested that the rearrangement of O-aryloximes to benzofurans occurs in a manner analogous to the mechanism proposed for the Fischer indole synthesis. (3)

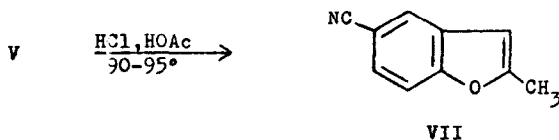


We wish now to report the rearrangement of O-aryl oximes to ortho-hydroxyaryl ketimine salts (III), possible intermediates in the formation of benzofurans (IV).

Thus, when p-(isopropylideneaminoxy)-benzonitrile (V) was allowed to stand in the presence of two equivalents of hydrogen chloride in glacial acetic acid, an exothermic reaction took place which resulted in the precipitation of 3-(2-imino-propyl)-4-hydroxybenzonitrile hydrochloride (VI) in high yield.



Heating the O-aryl oxime (V) with hydrogen chloride-acetic acid on the steam bath for fourteen hours afforded the benzofuran (VII) as the major product.



Similarly, heating the imine hydrochloride (VI) with hydrogen chloride-acetic acid on the steam bath for fourteen hours also yielded the benzofuran (VII) as the major product. In an effort to ascertain that the imine hydrochloride (VI) and the benzofuran (VII) are formed consecutively and not by parallel reactions, the O-aryl oxime was again subjected to heating with hydrogen chloride-acetic acid and the reaction stopped when all the starting material had been consumed (as shown by TLC). This yielded the imine hydrochloride (VI) as the major product. Thus the major portion of benzofuran (VII) which is obtained upon heating the O-aryl oxime (V) with hydrogen chloride-acetic acid must be formed at the expense of the initially generated ortho-hydroxyaryl ketimine salt (VI).

The method of preparation of O-aryl oximes has already been touched upon in our first communication. The condensation of the sodium salt of an oxime with an activated aryl halide, preferably fluoride, gives stable, easily handled, usually solid oximes. New oximes used for this communication are O-(p-nitrophenyl)cyclopentanone oxime (mp 128-130°), yield 66%, analyses for  $C_{11}H_{12}N_2O_3$ : C, 60.27; H, 5.37; N, 12.66; p-(isopropylideneaminoxy)-benzonitrile (mp 100-103°), yield 73%, analyses for  $C_{10}H_{10}N_2O$ : C, 69.27; H, 5.95; N, 16.15; O-[p-(phenylsulfonyl)phenyl]acetone oxime (mp 130-134°), yield 82%, analyses for  $C_{15}H_{15}NO_3S$ : C, 62.58; H, 5.27; N, 4.83. O-phenylacetophenone oxime was made by the method of Sheradsky (4). 2-Methyl-5-benzofurancarbonitrile has mp 76-78°; analyses for  $C_{10}H_7NO$ : C, 76.31; H, 4.36; and N, 8.92.

The rearrangement of O-aryloximes is done with approximately 1.5 N hydrogen chloride in acetic acid at room temperature. About a 30-100% excess of hydrogen chloride is used. After twenty-four hours if the imine salt has not precipitated, precipitation is induced by scratching or by the addition of ether.

As might be expected, treatment of the imine hydrochlorides with water rapidly resulted in the corresponding ketones. Hydrolytic yields are excellent. The preparation of known compounds, two (5) and six (6), as well as the infra-red and nmr spectra, leaves no doubt as to the structure of our products. The conversion of such phenolic ketones to benzofurans is well known (7).

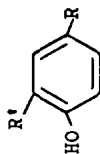
Further studies related to the reaction mechanism and scope are continuing.

#### References

1. This paper is taken in part from a thesis to be submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Department of Chemistry at Rensselaer Polytechnic Institute.
2. Aram Mooradian, Tetrahedron Letters, 407 (1967); See also ref. 4.
3. C. M. Robinson and R. Robinson, J. Chem. Soc., 125, 827 (1924).
4. T. Sheradsky, Tetrahedron Letters, 5225 (1966).
5. W. J. Hale and C. A. Robertson, Am. Chem. J., 39, 683 (1908).
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7. W. J. Hale, Ber., 45, 1600 (1912).

TABLE I

## Substituted Phenols



R	R'	Yield, %	Mp, °C	Formula	Found, %		
					C	H	N
1. NO <sub>2</sub>	-CH <sub>2</sub> C(=NH <sub>2</sub> Cl)CH <sub>3</sub>	93	171	C <sub>9</sub> H <sub>10</sub> N <sub>2</sub> O <sub>3</sub> ·HCl	46.98	4.74	12.05
2. NO <sub>2</sub>	-CH <sub>2</sub> COCH <sub>3</sub>	71	188-190	C <sub>9</sub> H <sub>9</sub> NO <sub>4</sub>	55.21	4.55	7.30
3. NO <sub>2</sub>		70, 88	207(dec)	C <sub>11</sub> H <sub>12</sub> N <sub>2</sub> O <sub>3</sub> ·HCl	13.85 <sup>c</sup>		10.82
4. NO <sub>2</sub>		66	177-179	C <sub>11</sub> H <sub>11</sub> NO <sub>4</sub>	59.46	4.99	6.13
5. H	-CH <sub>2</sub> C(=NH <sub>2</sub> Cl)C <sub>6</sub> H <sub>5</sub>	49 <sup>a</sup>	210	C <sub>14</sub> H <sub>13</sub> NO·HCl	14.59 <sup>c</sup>		5.55
6. H	-CH <sub>2</sub> COC <sub>6</sub> H <sub>5</sub>	93	123-131	2,4-Dinitrophenylhydrazones, mp 196-198 <sup>5,d</sup>			
7. CN	-CH <sub>2</sub> C(=NH <sub>2</sub> Cl)CH <sub>3</sub>	72, 97	205	C <sub>10</sub> H <sub>10</sub> N <sub>2</sub> O·HCl	56.80	5.18	13.13
8. CN	-CH <sub>2</sub> COCH <sub>3</sub>	89	145-149	C <sub>10</sub> H <sub>9</sub> NO <sub>2</sub>	68.70	5.06	7.98
9. C <sub>6</sub> H <sub>5</sub> SO <sub>2</sub> -	-CH <sub>2</sub> C(=NH <sub>2</sub> Cl)CH <sub>3</sub>	96	198	C <sub>15</sub> H <sub>15</sub> NO <sub>3</sub> ·HCl	54.90	4.93	10.82 <sup>b</sup>
10. C <sub>6</sub> H <sub>5</sub> SO <sub>2</sub> -	-CH <sub>2</sub> COCH <sub>3</sub>	96	170-172	C <sub>15</sub> H <sub>14</sub> O <sub>4</sub> S	62.37	4.97	11.12 <sup>c</sup>

<sup>a</sup>Overall from O-phenylhydroxylamine.<sup>b</sup>Chlorine analysis.<sup>c</sup>Sulfur analysis.<sup>d</sup>Mixed melting point.