[CONTRIBUTION FROM THE NOVES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

# THE CONVERSION OF p-QUINONEMONOXIME TO p-AZOXYPHENOL

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The rearrangement of p-quinonemonoxime (I) to 1-azacyclohepta-3,6-diene-2,5-dione (II), described by Beckmann and Liesche (1), has additional current interest because the stated product, at least in its tautomeric forms (IIa, IIb), can be construed as an aza- $\gamma$ -tropolone (2, 3). It was considered desirable to repeat the work of Beckmann and Liesche (1) for the purpose of establishing the structure of the conversion product unequivocally and to investigate its chemistry.



At the outset, it was realized that the conditions used for the conversion were atypical for the "Beckmann rearrangement," which normally requires an acid medium. The rearrangement of *p*-quinonemonoxime was described as occurring upon treatment of I with benzenesulfonyl chloride in pyridine and subsequent heating (1). The conditions employed actually have closer resemblance to those which effect the Neber conversion of the sulfonate ester of a ketoxime to an  $\alpha$ -aminoketone (4), although such a rearrangement is precluded in this case by the fact that the  $\alpha$ -carbons in the benzenesulfonic ester of *p*-quinonemonoxime (III) are unsaturated. An examination of the evidence upon which Beckmann and Liesche (1) based the assignment of structure II revealed the absence of degradative and unequivocal synthetic proof. However, the analysis reported was satisfactory for the composition C<sub>6</sub>H<sub>5</sub>NO<sub>2</sub> required by 1-azacyclohepta-3,6-diene-2,5-dione (II). Also reported for the compound, m.p. 224°, were: a

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molecular weight determination; the properties of alkali solubility, non-reactivity with hydroxylamine and phenylhydrazine, and formation of metal salt precipitates; and a benzoyl derivative, m.p. 189–190°, (nitrogen 0.48% off in analysis) which returned the original compound on alkaline hydrolysis. It was obviously necessary to accumulate further evidence in order to confirm or reject the seven-membered-ring structure (II).

When we followed the directions of Beckmann and Liesche (1) for the conversion of p-quinonemonoxime, we obtained a product, m.p. 234-235°, which crystallized as yellow needles from 50% aqueous ethanol. The properties of this compound corresponded to those described earlier (1), but the analysis indicated a composition,  $C_{12}H_{10}N_2O_3$ , wherein the ratio of nitrogen to oxygen precluded the possibility of structure II as correct and suggested some dimeric relation to I. Moreover, the infrared absorption spectrum of the conversion product revealed maxima indicative of hydroxyl (3345 cm.<sup>-1</sup>), benzene ring, (1598 cm.<sup>-1</sup>), general phenol-like absorption (1286-1209 cm.<sup>-1</sup>), and para-benzenoid substitution (835 cm.<sup>-1</sup>). Diacetyl (m.p. 166–166.5°) and dibenzoyl (m.p. 194–194.5°) derivatives were prepared which had elementary analyses also consistent with formulation of the original product as  $C_{12}H_{10}N_2O_3$ . From the infrared evidence and the microanalytical data, especially the empirical nitrogen-tooxygen ratio, we concluded that the product in hand was p-azoxyphenol (IV). The physical and chemical properties reported for p-azoxyphenol, m.p.  $224^{\circ}(5)$ , and its derivatives: diacetyl, m.p. 163° (5) or 169° (6), and dibenzoyl, m.p. 187-190° (7), were in accord with this hypothesis. Accordingly, for direct proof, we synthesized by unequivocal means p-azoxyphenol, p, p'-diacetoxyazoxybenzene, and p, p'-dibenzoxyazoxybenzene, and we compared these with samples of the p-quinonemonoxime conversion product and its diacetyl and dibenzoyl derivatives. Mixture melting point behavior and infrared absorption spectra served to establish conclusively the identity of the corresponding samples in each group.



Thus, the product obtained by treating p-quinonemonoxime (I) with benzenesulfonyl chloride in pyridine at room temperature for 12 hours, followed by heating the mixture for 20 minutes, cooling, acidification, and subsequent extraction (1), has been shown to be p-azoxyphenol (IV). The only data of Beckmann and Liesche not in accord with this fact are the analytical and molecular weight figures, and we regard these as either fortuitous or in error. Attempts to determine the molecular weight in this laboratory by the Rast camphor method gave erratic and inconclusive results. The melting point and the nitrogen analysis of Beckmann's benzoyl derivative are in satisfactory agreement with those required for p, p'-dibenzoxyazoxybenzene, so that there is little doubt but that the earlier workers (1) obtained compound IV, rather than the "Beckmann rearrangement" product (II), from I.

It is interesting to speculate on the course of this conversion of p-quinonemonoxime to p-azoxyphenol and to consider extension of the reaction with a view to mechanistic studies and synthetic possibilities. Even as it is described in the earlier reference (1) and in this preliminary study, the conversion of I to IV constitutes one of the best methods for the synthesis of p-azoxyphenol. The use of p-quinonemonoxime and benzenesulfonyl chloride in the molar proportion of 9 to 7 was found to give the best yield (45%) of p-azoxyphenol, when the range of mixture proportions from 1:1 to 3:1 was explored. No improvement in yield was realized when the reagents (benzenesulfonyl chloride and pyridine) were carefully dried before use. The yield of IV was lower when  $\alpha$ -picoline, 2,6-lutidine, or triethylamine was employed in place of pyridine, and no azoxy compound was produced when the basic medium was aqueous sodium carbonate or sodium hydroxide. We feel that the optimum time and temperature conditions may not be indicated in the directions of Beckmann and Liesche (1) and those provided here, but that at least the extremes of the conditions indicated are less satisfactory. That is, merely heating the reactants for 20 minutes on the steam-bath, without the preliminary 12-hour period at room temperature, gave a lower yield of p-azoxyphenol (ca. 23%), whereas omission of the heating period following the 12 hours at room temperature permitted the isolation of the benzenesulfonic ester  $(III)^2$  of p-quinonemonoxime in 60% yield.

An important clue to the mechanism of the conversion of I to IV was obtained from the following facts. When p-quinonemonoxime (I) was heated alone in pyridine containing pyridine hydrochloride, no p-azoxyphenol could be isolated from the reaction mixture and at least 90% of the starting material was recovered. When the benzenesulfonic ester (III) of p-quinonemonoxime was treated similarly (in the absence of I), a negligible amount of p-azoxyphenol (IV) was produced. By contrast, when an equimolar mixture of p-quinonemonoxime and its benzenesulfonic ester was heated under the same conditions, a good yield of *p*-azoxyphenol resulted. It is therefore apparent that the over-all transformation,  $I \rightarrow IV$ , probably proceeds through partial conversion of I to III, followed by interaction of these two compounds. p-Quinonemonoxime (I) would be expected to dissociate to sufficient extent in hot pyridine (9) to produce a resonance-stabilized anion (V). The anion V could displace the benzenesulfonate anion from the nitrogen (10) of the benzenesulfonic ester (III), with the formation of the N-oxide (VI) of p-quinoneazine (11). An extended quinoid system of the type present in VI is known to take on hydrogen extremely readily (11), and in this case, p-azoxyphenol would result. The over-all yield of p-azoxyphenol from p-quinonemonoxime, which has not exceeded 50% in our experience, suggests that disproportionation probably takes place in order to provide for

<sup>2</sup> Beckmann and Liesche (1) formulated this product as *p*-nitrosophenyl benzenesulfonate, but previous evidence (8) and our infrared data indicate that the compound is the ester of the quinoid form (III).



the reduction of compound VI. Substantiation of our hypothesis requires further study of possible nucleophilic displacements at nitrogen in compounds of type III and an examination of hydrogen donors which would account for the overall reduction occurring in the transformation of I to IV.

## EXPERIMENTAL<sup>3, 4</sup>

p-Quinonemonoxime (p-Nitrosophenol). The procedure of Bridge (8) as modified by Tseng and Hu (12) was used. A solution of 60 g. (0.64 mole) of phenol, 27 g. (0.68 mole) of sodium hydroxide, and 66.8 g. (0.78 mole) of potassium nitrite in 1.5 l. of water was cooled to  $-3^{\circ}$ . To this solution was added with stirring 150 g. (1.42 moles) of sulfuric acid in 400 cc. of water at a rate sufficiently slow to maintain the temperature of the reaction mixture at  $-3^{\circ}$  to 0°. The addition required 1–1.5 hours, after which the reaction mixture was stirred for an additional 2 hours with continued cooling. The brownish crystalline precipitate was filtered. The product was washed on the funnel with 100 cc. of ice-water and then air-dried. The yield of p-quinonemonoxime was 56.3 g. (72%), m.p. 137° (dec.), and the compound was of sufficient purity for use directly [reported m.p. 126° (8), 144° (13)].

### CONVERSIONS OF *p*-QUINONEMONOXIME

A. To the benzenesulfonic ester (III). A mixture of 6.0 g. (0.048 mole) of p-quinonemonoxime with 8.64 g. (0.048 mole) of benzenesulfonyl chloride in 70 cc. of pyridine was allowed to stand at 25° for 12 hours. The reaction mixture was acidified with 25% sulfuric acid and the resulting precipitate was collected. The product was purified by recrystallization, with decolorization, from ether. The yield was 7.7 g. (60%) as yellow needles, m.p. 132.5–133° [reported, 131° (1)].

Anal. Calc'd for C12H9NO4S: C, 54.73; H, 3.44; N, 5.32.

Found: C, 54.85; H, 3.48; N, 5.17.

The infrared spectrum of this compound had an absorption band at 1649 cm.<sup>-1</sup>, attributable to C=N and/or C=O, and therefore indicative that the compound was an ester of the *p*-quinonemonoxime rather than the *p*-nitrosophenol form.

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<sup>&</sup>lt;sup>3</sup> All melting points are corrected.

<sup>&</sup>lt;sup>4</sup> The authors are indebted to Mrs. Katherine Pih, Miss Emily Davis, and Mrs. Esther Fett for microanalyses and to Miss Helen P. Miklas for determination of the infrared absorption spectra.

B. To p-azoxyphenol (IV). A mixture of 9.0 g. (0.073 mole) of p-quinonemonoxime with 10.0 g. (0.057 mole) of benzenesulfonyl chloride in 70 cc. of pyridine was allowed to stand at 25° for 12 hours. The reaction mixture was then heated on the steam-bath for 20 minutes, cooled, and acidified with 25% sulfuric acid. The resulting black mixture was extracted with ether. The ether extract was treated with Norit, filtered, and evaporated to crystallization or evaporated to a small volume and benzene added. The insoluble material was collected, washed with benzene, and dried. Recrystallization from 50% aqueous ethanol gave yellow needles, m.p. 234-235°, with decomposition; yield 3.8 g. (45%).

Anal. Calc'd for C6H5NO2: C, 58.54; H, 4.09; N, 11.38.

Calc'd for C<sub>12</sub>H<sub>10</sub>N<sub>2</sub>O<sub>8</sub>: C, 62.60; H, 4.38; N, 12.17.

Found: C, 62.81; H, 4.41; N, 12.23.

The compound was found to have infrared absorption maxima at 3345, 1598, and 835 cm.<sup>-1</sup>, together with several maxima in the region 1286-1209 cm.<sup>-1</sup>.

The *diacetyl* derivative was prepared by treatment with acetic anhydride in pyridine (14), and recrystallized from ethanol as pale yellow, hairlike needles, m.p. 166-166.5°.

Anal. Calc'd for C<sub>16</sub>H<sub>14</sub>N<sub>2</sub>O<sub>5</sub>: C, 61.15; H, 4.49; N, 8.92.

Found: C, 61.29; H, 4.46; N, 8.89.

The dibenzoyl derivative was prepared by treatment with benzoyl chloride in pyridine (14) and recrystallized as pale yellow leaflets from ethyl acetate, m.p. 194-194.5°.

Anal. Cale'd for C28H18N2O5: C, 71.24; H, 4.14; N, 6.39.

Found: C, 71.45; H, 4.30; N, 6.43.

### UNEQUIVOCAL SYNTHESES

A. p, p'-Diacetoxyazoxybenzene. The procedure of Wohl (6) was used to convert p-nitrophenyl acetate to p, p'-diacetoxyazoxybenzene. A mixture of 15.2 g. (0.084 mole) of pnitrophenyl acetate, 15.2 g. (0.23 gram-atom) of zinc dust, 2.3 g. (0.043 mole) of ammonium chloride, 127 cc. of benzene, and 228 cc. of water was stirred at 25° for 4 hours and then filtered. The precipitate was extracted with boiling ether, the dried ether solution was evaporated to dryness, and the residue (1.1 g.) was recrystallized from ethanol. The two liquid layers composing the filtrate (see above) were separated, and the aqueous layer was extracted once with benzene. The combined benzene solutions were evaporated to dryness, and the residue, after washing with ethanol and drying, amounted to 1.6 g. (combined yield, 20%). The product was recrystallized, with decolorization, from ethanol as yellow needles, m.p. 165-166°. This compound did not depress the melting point of the diacetyl derivative of the p-quinonemonoxime conversion product, and their infrared absorption spectra, as determined in a Nujol mull, were identical.

B. p, p'-Dibenzoxyazoxybenzene. The procedure used was similar to that described above, which is the method of Wohl (6), modified slightly. The product was obtained in 10% yield after recrystallization from ethyl acetate as yellow leaflets, m.p. 193.5-194.5°. This compound was identical, as established by melting point and infrared spectrum, with the dibenzovl derivative of the p-quinonemonoxime conversion product.

C. p-Azoxyphenol. A mixture of 2.1 g. of authentic p, p'-diacetoxyazoxybenzene and 35 cc. of 10% aqueous potassium hydroxide solution was heated under reflux until all the material went into solution (35 minutes). The solution was cooled, and carbon dioxide was bubbled through until no further precipitate formed. A quantitative yield (1.5 g.) of p-azoxyphenol was obtained. Recrystallization from 50% aqueous ethanol gave yellow needles, m.p. 233-233.5°, with decomposition, which did not depress the melting-decomposition point of the p-quinonemonoxime conversion product, and which had an identical infrared absorption spectrum (determined in a Nujol mull).

### SUMMARY

The product resulting from the treatment of p-quinonemonoxime with benzenesulfonyl chloride in pyridine at 25°, followed by a short heating period, was described by Beckmann and Liesche as a seven-membered-ring compound, 1-azacyclohepta-3,6-diene-2,5-dione. We have now established that the product is in reality p-azoxyphenol, and we have advanced a hypothesis to account for this unusual conversion, p-quinonemonoxime to p-azoxyphenol.

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