BENZIMIDAZOLE DERIVATIVES.

XXXIII.* 1,4-BENZOQUINONYL DERIVATIVES OF AZOLES

V. N. Komissarov and A. M. Simonov

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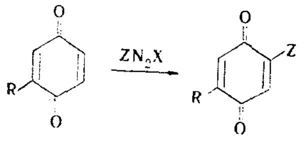
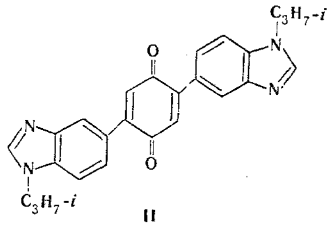
Benzoquinonyl derivatives of azoles were obtained by the Meerwein reaction of 1,4-benzoquinone with heterocyclic diazo compounds. Reactions involving the addition of hydrogen chloride, reduction of the quinoid ring, and quaternization of the heteroring were carried out for these compounds. A method for the preparation of 1-quinonylbenzimidazoles was developed.

In previously investigated quinones of the benzimidazole, indole, and other heterocycle series the quinone ring was included in a heterocyclic system [2-4]. Papers devoted to the study of quinonyl derivatives of some nitrogen heterocycles (pyrrole, triazole, etc.) [5, 6] have appeared only recently. Quinones connected by a single bond to benzimidazole, benzothiazole, and benzoxazole rings have been unknown up until now. It seemed of interest to study methods for their synthesis and their properties and bactericidal activity, which is expressed extremely strongly in a number of quinones [7].

The Meerwein reaction, which has not been described in the quinone series for heterocyclic diazo compounds, proved to be a rather convenient method for the preparation of quinonyl-substituted azoles. 1,4-Benzoquinone and its phenyl derivative were subjected to this transformation. The yields of monoheteryl-substituted 1,4-benzoquinones (Ia-f) are 27-47%, and a bisheteryl-substituted quinone (II) is simultaneously obtained in yields up to 12%. Bis-substituted quinone II can also be obtained by subjecting Ib to the Meerwein reaction in aqueous acetone. A considerable amount of a mixture of side products is also formed in the reaction.



I a-f



II

I a,b,d-f R=H; I c R=C_6H_5; a-c Z= 1-R'-benzimidazol-5-yl(a R'=CH_3; b,e R'= =i-C_3H_7); d Z= 6-benzothiazolyl Z=4-(2-benzimidazolyl)phenyl; f Z=4-(2-benzoxazolyl)phenyl

The quinonylazoles obtained were subjected to quaternization, 1,4-addition with hydrohalic acids, and reduction to hydroquinones.

In order to obtain 1-quinonyl derivatives of benzimidazole, 1-(2,5-dimethoxyphenyl)-5-nitrobenzimidazole [8] was subjected to demethylation, and the resulting

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*See [1] for communication XXXII.

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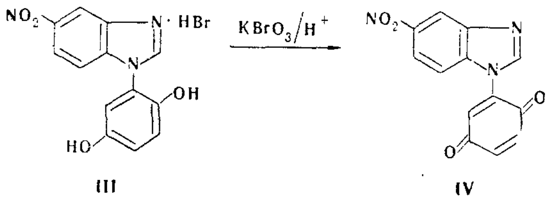
hydroquinone derivative (III), which is stable only in the form of the hydrobromide, was oxidized with potassium bromate to quinone IV.



EXPERIMENTAL

The IR spectra of mineral-oil suspensions of the compounds were recorded with a UR-20 spectrometer.

2-(4-Aminophenyl)benzimidazole. This compound, with mp 237° [10], was obtained by the method in [9] by heating o-phenylenediamine and p-aminobenzoic acid in polyphosphoric acid.

2-(4-Aminophenyl)benzoxazole. This compound was obtained in 60% yield by the method in [9] by heating o-aminophenol and p-aminobenzoic acid in a mixture with an equal amount (by weight) of polyphosphoric acid at 165-170° for 4 h. The product was purified by filtration of a chloroform solution of it through a layer of aluminum oxide to give pinkish needles with mp 176-177° (from benzene). Found: C 74.5; H 4.6%. $C_{13}H_{10}N_2O_2$. Calculated: C 74.3; H 4.8%.

1-Methyl-5-(p-benzoquinonyl)benzimidazole (Ia). A solution of 1.4 g (0.02 mole) of sodium nitrite in 10 ml of water was added at 0° to a solution of 2.94 g (0.02 mole) of 1-methyl-5-aminobenzimidazole [11] in 20 ml of water and 8 ml of concentrated hydrochloric acid. After 30 min, the excess nitrous acid was removed with urea, sodium acetate was added to pH 5, and the solution of diazonium salt was added to a solution of 2.16 g (0.02 mole) of p-benzoquinone in 200 ml of water, during which nitrogen was evolved quite vigorously. After 2.5 h, the bright-red precipitate was removed by filtration and dried at 80°, and Ia was extracted with three 100-ml portions of boiling chloroform. The chloroform solution was chromatographed with a column filled with aluminum oxide, and the first orange-colored fraction was collected. The solvent was removed from this fraction by distillation to give 1.8 g (40%) of dark-orange needles with mp 206-207° (from benzene). The product was soluble in alcohol and acetone but insoluble in petroleum ether. It was readily soluble in dilute acids. IR spectrum: $\nu_{C=O}$ 1660 and 1642 cm^{-1}. Found: C 70.4; H 4.4; N 11.5%. $C_{14}H_{10}N_2O_2$. Calculated: C 70.8; H 4.3; N 11.8%.

Quinones Ib-f (Table 1) were obtained by similar methods from the appropriate amines.

2,5-Bis(1-isopropyl-5-benzimidazolyl)-1,4-benzoquinone (II). This compound was obtained in 34% yield by arylation of Ib in aqueous acetone (1:3) by means of the 1-isopropyl-5-benzimidazolediazonium salt. The product crystallized with a molecule of water to give a substance with mp 139-140° (from alcohol containing benzene).

1-Methyl-5-(2,5-dihydroxyphenyl)benzimidazole. A stream of sulfur dioxide was bubbled into a suspension of 1.2 g of quinone Ia in 20 ml of alcohol and 10 ml of water until the mixture was completely decolorized. Water (40 ml) and 20 ml of 10% sodium hydrocarbonate were added to the solution, and the resulting precipitate was removed by filtration and washed with water to give 0.96 g (80%) of a product that was quite soluble in acids and alkalis. The picrate was obtained as orange needles with mp 200-201° (from aqueous alcohol). Found: C 51.2; H 3.1%. $C_{14}H_{12}N_2O_2 \cdot C_6H_3N_3O_7$. Calculated: C 51.2; H 3.2%.

1-Methyl-5-(p-benzoquinonyl)benzimidazole Methiodide. A 0.48-g (2 mmole) sample of Ia was dissolved by heating in 20 ml of alcohol, 1 ml (0.016 mole) of methyl iodide was added, and the mixture was refluxed for 2.5 h. The solvent was removed by distil-

TABLE 1. 1,4-Benzoquinonyl Derivatives of Azoles

Compound	mp, °C	Empirical formula	Found, %			Calc., %.			$\nu_{C=O}$, cm⁻¹	Yield, %
			C	H	N	C	H	N		
Ib	166—167	$C_{16}H_{14}N_2O_2$	72,5	5,4	10,7	72,2	5,3	10,5	1663, 1635	30
Ic	210—211	$C_{22}H_{18}N_2O_2$	59,2	4,1	12,2	58,8	3,7	12,3	—	30
Id	209—210	$C_{13}H_7NO_2S$	64,6	3,0	5,9	64,7	2,9	5,8	1650, 1639	27
Ie	187—188	$C_{19}H_{12}N_2O_2$	72,3	4,2	—	72,6	4,0	—	1667, 1620	28
If	218—219	$C_{19}H_{11}NO_3$	75,6	3,9	4,8	75,7	3,7	4,7	1668, 1620	46
II	139—140	$C_{26}H_{24}N_4O_2\cdot H_2O$	70,9	5,6	12,9	70,5	5,9	12,7	1640	12

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*Compound Ic was obtained by arylation of phenyl-p-benzoquinone in aqueous acetone (1:1:5) by the method used to obtain Ia.

lation to a volume of 7 ml, and the residual solution was cooled to precipitate 0.41 g (53%) of yellow needles with mp 213-214° (dec., from alcohol). IR spectrum $\nu_{C=O}$ 1670, 1640 cm^{-1}. Found: C 47.8; H 3.6; N 7.4%. $C_{15}H_{13}IN_2O_2$. Calculated: C 47.4; H 3.4; N 7.4%.

1-Methyl-5-(2,5-dihydroxy-4-chlorophenyl)benzimidazole Hydrochloride. A 0.24 g (1 mmole) sample of Ia was dissolved in 40 ml of acetone and 1 ml of concentrated hydrochloric acid, and the solution was allowed to stand overnight. The acetone was removed by distillation, and the hydrochloride was recrystallized from 10% hydrochloric acid to give 0.2 g (77%) of a product with mp 291° (from alcohol containing ether). Found: C 54.1; H 4.3; N 9.2%. $C_{14}H_{11}ClN_2O_2\cdot HCl$. Calculated: C 54.0; H 3.9; N 9.0%.

1-(2,5-Dihydroxyphenyl)-5-nitrobenzimidazole Hydrobromide (III). A solution of 2 g of 1-(2,5-dimethoxyphenyl)-5-nitrobenzimidazole [8] in 40 ml of 48% hydrobromic acid was refluxed for 4 h, after which it was evaporated to a volume of 10 ml at 20-30 mm. Water (40 ml) was added to the residue, and the mixture was refluxed with activated charcoal and filtered. On standing, the filtrate yielded 2.3 g (98%) of needles of III with mp 217-218° (from water). The product was soluble in alcohol but insoluble in ether. Found: C 44.6; H 2.3; Br 22.4%. $C_{13}H_9N_3O_4\cdot HBr$. Calculated: C 44.3; H 2.1; Br 22.7%.

1-(p-Benzoquinonyl)-5-nitrobenzimidazole (IV). A solution of 0.56 g (0.03 mole) of potassium bromate in 5 ml of water was added to a heated (to 50°) solution of 3.52 g (0.01 mole) of III in 100 ml of water acidified with 10 ml of 5% sulfuric acid. The precipitated flakes of the quinone were removed by filtration and washed with water. The yield of product with mp 198-200° (dec.) was quantitative. Because of the low stability of IV in solutions, it could not be purified by recrystallization or by chromatography.

LITERATURE CITED

1. B. I. Khristich, G. M. Suvorova, and A. M. Simonov, Khim. Geterotsikl. Soedin., 1398 (1974).
2. É. R. Zakhs and L. S. Éfros, Zh. Obshch. Khim., 34, 956, 962, 1633 (1964).
3. A. V. Luk'yanov, V. A. Aleshina, V. G. Voronin, and Yu. S. Tsizin, Zh. Vsesoyuzn. Khim. Obshchestva, 15, 467 (1970).
4. Yu. S. Tsizin and M. V. Rubtsov, Khim. Geterotsikl. Soedin., 682 (1969).
5. I. I. Grandberg and A. N. Kost, Zh. Obshch. Khim., 29, 1099 (1959).
6. W. Gauss, H. Heitzer, and S. Petersen, Ann., 764, 131 (1972).
7. M. M. Shemyakin, A. S. Khokhlov, M. N. Kolosov, L. Ya. Bergel'son, and V. A. Antonov, Chemistry of Antibiotics [in Russian], Vol. 1, Izd. Akad. Nauk SSSR, Moscow (1961).
8. A. F. Pozharskii, V. V. Kuz'menko, and A. M. Simonov, Khim. Geterotsikl. Soedin., 1109 (1971).
9. D. W. Hein, R. J. Alheim, and J. J. Leavitt, J. Amer. Chem. Soc., 79, 427 (1957).
10. O. Kym, Ber., 33, 2848 (1900).
11. K. Bernhauer and G. Reber, Biochem. Z., 335, 463 (1962).