INVESTIGATION OF AZOCOUPLING OF 3-HYDROXYQUINOLINE AND 4-HYDROXYISOQUINOLINE

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Previous investigations have shown that the introduction of a condensed benzene ring and the substituent into the molecule of 3-hydroxypyridine has an effect on the reactivity of the β -pyridol ring and the orientation of electrophilic substitution. Thus, in 3-hydroxyquinoline, containing an annelated benzene ring in the 5,6-positions of the β -pyridol ring, aromatic substitution has a different orientation from that in 3hydroxypyridine [1]. At the same time, electrophilic reactions in 4-hydroxyisoquinoline in which the benzene ring is added in the 4,5-positions of the β -pyridol ring proceed in the same direction as in 3-hydroxypyridine [2].

We were interested in investigating the chemical behavior of 3-hydroxyquinoline (I) and 4-hydroxyisoquinoline (II) in the reaction of azocoupling. Phenyldiazonium, p-bromophenyldiazonium, p-nitrophenyldiazonium, p-sulfophenyldiazonium, p-tolyldiazonium, and p-methoxyphenyldiazonium chlorides were selected as the diazo-components. Azocoupling was conducted in weakly alkali medium. The yield of azo-products was 80-90%. The azo-compounds obtained are crystalline substances, practically insoluble in water, with the exception of p-sulfobenzene-azo-3-hydroxyquinoline and 4-hydroxyisoquinoline. The color of the azocompounds varied from bright red to dark cherry, depending on the substituent in the benzene ring



The azo-derivatives (I) obtained were reduced to amino compounds. An analysis of the PMR spectrum of amino-3-hydroxyquinoline (Fig. 1) indicated that the amino group is in the 4-position of the quinoline ring. Thus, the single signal from the protons of the pyridine ring at 4.37 ppm was ascribed to the proton of C_2H , and the intensity of this signal was four times as great as the intensity of the remaining signals from the protons of the benzene ring. Thus, azocoupling of (I), analogously to β -naphthol, is directed into the 4-position of the quinoline ring. Attempts at bis-substitution, like β -naphthol, proved unsuccessful.

The structure of the azo-products (II) was confirmed by counter synthesis of 3-amino-4-hydroxyisoquinoline, obtained by reduction both of azo-derivatives of 4-hydroxyisoquinoline and of 3-nitro-4-hydroxyisoquinoline. In the PMR spectrum of 3-amino-4-hydroxyisoquinoline in the region of a weak magnetic field at 4.49 ppm there is a signal characteristic of the proton of C_1H . The intensity of this signal is one fourth the intensity of the signals from the protons of the benzene ring, situated in a stronger magnetic field (3.76 ppm).

Thus, azocoupling of (II), in contrast to α -naphthol and β -pyridol, is directed in the o- and not in the p-position to the hydroxy group. However, further azocoupling of 3-benzeneazo-4-hydroxy isoquinoline is directed in the p-position to the hydroxy group, with the formation of 1,3-bis (benzeneazo)-4-hydroxy iso-quinoline.

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EXPERIMENTAL METHOD

The PMR spectrum of 4-amino-3-hydroxyquinoline was taken on an NA-100 spectrometer. The in-vestigated compounds were ~10 mole % solutions in D₂O with NaOD. Dioxane was used as an internal standard. The PMR spectrum of 3-amino-4-hydroxyisoquinoline was taken in 10 mole % D₂O with an addition of D₂SO₄.

Method of Azocoupling

A solution of phenyldiazonium chloride (0.003 M) was added to 20 ml of a solution of 0.45 g (I) or (II) and 0.018 g NaOH, cooled to 5-10°, maintaining the pH of the medium in the range 7-8.5. The reaction mass was exposed for 1 h, the precipitate formed removed, washed with water, dried, and crystallized from methanol. The azo-derivatives (I) and (II) were obtained; the yields and physicochemical constants are cited in Table 1.

4-Amino-3-hydroxyquinoline

To a solution of 0.5 g 4-benzeneazo-3-hydroxyquinoline in 8 ml concentrated HCl, heated to $50-60^{\circ}$, we added 0.95 g stannous chloride. The temperature was raised to $90-95^{\circ}$ and the reaction mixture mixed at this temperature for 30 min; the solution was cooled, the precipitate of 4-amino-3-hydroxyquinoline hydrochloride that formed as needles was removed, washed with acetone, and crystallized from methanol. Yield 0.34 g (85%); mp 280-282°. Found: C 54.68; H 4.68; N 14.6; Cl 17.85%. C₉H₉N₂OCI. Calculated: C 54.8; H 4.59; N 14.2; Cl 18.2%.

3-Amino-4-hydroxyisoquinoline

<u>From 3-Azo-derivatives of 4-Hydroxyisoquinoline</u>. The reduction of azo-derivatives of 4-hydroxyisoquinoline was conducted according to the method described above for 4-benzeneazo-3-hydroxyquinoline. Yield of 3-amino-4-hydroxyisoquinoline 80%, mp 196-198°. According to the data of [3]: mp 195-197°.

-R	mp, °C		Yield,		Found, %			Empirical	Calculated, %		
	(1)	(11)	(1)	(11)	C	н	N	formula	C	H	N
H NO2 Br SO3H OCH3 CH3	$\begin{array}{ c c c c c c c c c c c c c c c c c c c$	106—108 197—199 216—219 	90 92 88 85 82 81	90 92 86 82 78 70	71,961,4654,91 $68,8973,04$	4,533,363,12 $$	16,97 18,94 12,77 12,6 14,85 15,85	C ₁₅ H ₁₁ N ₃ O C ₁₅ H ₁₀ N ₄ O ₃ C ₁₅ H ₁₀ N ₃ BrO C ₁₅ H ₁₁ N ₃ O ₄ S C ₁₆ H ₁₃ N ₃ O ₂ C ₁₆ H ₁₃ N ₃ O	$72,20\\61,20\\54,80\\54,7\\68,8\\73,0$	4,40 3,40 3,04 3,34 4,65 4,94	16,86 19,0 12,8 12,7 15,0 16,0

TABLE 1. Azo-Derivatives of 3-Hydroxyquinoline (I) and 4-Hydroxyisoquinoline (II)

From 3-Nitro-4-hydroxyisoquinoline. A 0.38 g portion of 3-nitro-4-hydroxyisoquinoline was reduced by the method described above. 3-Amino-4-hydroxyisoquinoline was obtained in the form of yellow needles; yield 0.30 g (75%); mp 195-197° (MeOH). Mixed samples of 3-amino-4-hydroxyisoquinoline, produced according to the two methods, give no depression of the melting points.

1,3-Bis (benzeneazo) -4-hydroxyisoquinoline

Produced from (II) with 2 equivalents of phenyldiazonium chloride; yield 75%; mp 116-118°. Found: C 71.44; H 4.42; N 19.32%. $C_{21}H_{15}N_5O$. Calculated: C 71.36; H 4.25; N 19.8%.

CONCLUSIONS

1. The azocoupling of 3-hydroxyquinoline and 4-hydroxyisoquinoline was investigated.

2. The azo-group in 3-hydroxyquinoline is a substituent in the 4-position of the quinoline ring.

3. Azocoupling of 4-hydroxyisoquinoline is initially directed in the 3-position and then in the 1-position of the isoquinoline ring.

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