Reaction of *o*-aminobenzohydroxamic acid with aldehydes

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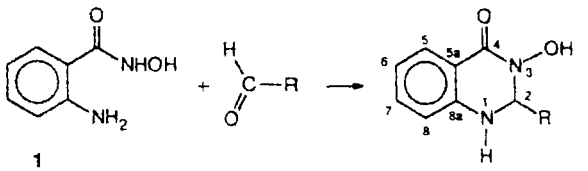
The reaction of *o*-aminobenzohydroxamic acid with aliphatic, aromatic, or heterocyclic aldehydes leads to the formation of derivatives of 3-hydroxy-1,2-dihydroquinazolin-4-one.

Key words: *o*-aminobenzohydroxamic acid, aldehydes, reaction; 3-hydroxy-1,2-dihydroquinazolin-4-ones.

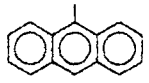
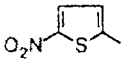
In the last decade, the products of the reaction of *o*-aminobenzohydroxamic acid (**1**) with aromatic and heterocyclic aldehydes have been studied actively as analytical reagents for the determination of various metals.[1–7] But there is no consensus about the structure of such adducts. As a rule, the structure of Schiff's bases is ascribed to them,[1–7] and only in a single paper[8] the product of a similar reaction is considered as a derivative of 3-hydroxy-1,2-dihydroquinazolin-4-one. To clarify a possible area for applying this reaction as well as the structure of the condensation products, we studied the interaction of compound **1** with a series of aliphatic, aromatic, and heterocyclic aldehydes. The main physicochemical characteristics of the products obtained are summarized in Tables 1–3.

It was established that the interaction of acid **1** with aldehydes is of common character and leads to the formation of 3-hydroxy-1,2-dihydroquinazolin-4-ones (HDHQ) **2**–**14**.



1 **2**–**14**

R = Me (**2**), Pr^i (**3**), Ph (**4**), 2-O_2NPh (**5**), 3-O_2NPh (**6**), 4-O_2NPh (**7**), 2-HOPh (**8**), 2-HO-3-CH_2=$CHCH_2$Ph (**9**), 3,4-OCH_2OPh (**10**), 3-O_2N-4-MeOPh (**11**),

 (**12**),  (**13**),  (**14**)

This conclusion also refers to adducts of compound **1** with benzaldehyde[4,7] and salicylaldehyde,[1,3–5] which were described earlier. The main characteristics of these adducts coincide with those obtained in this work (or are very close to them), although these compounds were assumed to have the structure of the corresponding Schiff's bases in the references mentioned above.

Table 1. Melting points, yields, and data from elemental analysis of 2-R-3-hydroxy-1,2-dihydroquinazolin-4-ones

Compound	M.p. /°C	Yield (%)	Found / Calculated (%)			Molecular formula
			C	H	N	
2	102–104	25	61.2 60.7	5.5 5.6		$C_9H_{10}N_2O_2$
3	172–175	23	64.0 64.1	6.7 6.8		$C_{11}H_{14}N_2O_2$
4	170–171	41	70.4 70.0	5.1 5.0	12.1 11.7	$C_{14}H_{12}N_2O_2$
5	224–225	59	59.8 58.9	3.7 3.9	14.1 14.7	$C_{14}H_{11}N_3O_4$
6	187–189	45	59.3 58.9	4.1 3.9	14.2 14.7	$C_{14}H_{11}N_3O_4$
7	124–126	47	60.5 58.9	4.1 3.9	14.1 14.7	$C_{14}H_{11}N_3O_4$
8	178–180	76	65.7 65.6	4.7 4.7		$C_{14}H_{12}N_2O_3$
9	170–172	29	69.3 68.9	5.4 5.4		$C_{17}H_{16}N_2O_3$
10	193–194	43	63.5 63.4	4.2 4.2		$C_{15}H_{12}N_2O_4$
11	168–170	48	57.1 57.1	4.1 4.1		$C_{15}H_{13}N_3O_5$
12	219–220	26	77.3 77.4	5.2 5.0		$C_{22}H_{16}N_2O_2$
13	167–168	47	62.9 62.6	4.3 4.4		$C_{12}H_{10}N_2O_3$
14	162–163	50	50.5 49.7	2.8 2.8	14.3 14.5	$C_{12}H_9N_3O_4S$

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Table 2. ^{1}H NMR spectra of 2-R-3-hydroxy-1,2-dihydroquinazolin-4-ones synthesized

Compound	Solvent	δ							
		H(1) (NH)	H(2)	H(3) (NOH)	H(5)	H(6)	H(7)	H(8)	R
2	$CDCl_3$—DMSO-d_6	4.8 (br)	5.16 (q)		7.84 (d)	6.82 (t)	7.29 (t)	6.65 (d)	1.58 (d, 3 H)
3	$CDCl_3$—DMSO-d_6	4.93 (br)	4.88 (q)		7.68 (d)	6.65 (t)	7.16 (t)	6.57 (d)	0.89 (q); 0.95 (q, 6 H); 2.35 (m, 1 H)
4	$CDCl_3$		5.98 (s)		7.84 (d)	6.82 (t)	7.28 (t)	6.58 (d)	7.4–7.5 (5 H)
5	$CDCl_3$	6.71 (s)	5.36 (s)		7.54–7.70 (m)	6.89 (t)	7.31 (t)	6.59 (d)	7.5–7.7 (m, 2 H); 7.93 (d, 1 H); 8.11 (d, 1 H)
6	DMSO-d_6	7.54 (s)	6.12 (s)	9.9 (br)	7.89 (d)	6.73–6.77	7.28 (t)	6.73–6.77	7.6–7.7 (m, 2 H); 8.21 (d, 1 H); 8.30 (s, 1 H)
7	$CDCl_3$—DMSO-d_6	7.48 (s)	6.05 (s)	9.95 (br)	7.7 (d)	6.72 (t)	7.21 (t)	6.72 (t)	7.70 (d, 2 H); 8.20 (d, 2 H)
8	DMSO-d_6	6.63–6.67 (m)	6.25 (s)	9.89 (br)	7.72 (d)	6.88 (d)	7.05–7.27 (m)	6.63–6.67 (m)	6.63–6.67 (m, 1 H); 7.05–7.27 (m, 3 H)
9	CD_3CN—DMSO-d_6	6.63 (s)	6.22 (s)		7.76 (d)	6.68–6.82 (m)	7.25 (t)	6.68–6.82 (m)	3.40 (d, 2 H); 5.04 (t, 2 H); 5.97 (m, 1 H); 6.68–6.82 (m, 1 H); 7.12 (t, 2 H)
10	CD_3CN—DMSO-d_6		5.87 (s)		7.77 (d)	6.72–6.88 (m)	7.29 (t)	6.72–6.88 (m)	5.97 (s, 2 H); 6.72–6.88 (m, 1 H); 6.90 (d, 1 H); 7.02 (s, 1 H)
11	DMSO-d_6	6.8 (s)	5.89 (s)	9.55 (t)	7.60–7.75 (t)	6.65 (t)	7.28 (t)	6.65 (t)	3.88 (s, 3 H); 7.05 (d, 1 H); 7.60–7.75 (m, 1 H); 7.93 (s, 1 H)
12	DMSO-d_6		6.57 (s)		7.82 (d)	6.89 (t)	7.35 (t)	6.74 (d)	7.53 (q, 5 H); 7.65 (s, 1 H); 8.13 (q, 2 H); 8.69 (s, 1 H)
13	CD_3CN—DMSO-d_6	7.03 (br.s)	5.91 (s)	9.60 (br)	7.72 (d)	6.74 (t)	7.27 (t)	6.74 (t)	6.33 (s, 2 H); 7.44 (s, 1 H)
14	DMSO-d_6	7.3 (br.s)	6.05 (s)	10.05 (br)	7.7 (t)	6.72 (t)	7.33 (t)	6.72 (t)	7.07 (d, 1 H); 7.70 (t, 1 H)

Table 3. ^{13}C NMR spectra of some 3-hydroxy-1,2-dihydroquinazolin-4-ones

Compound	δ (DMSO-d_6)								
	C(2)	C(4)	C(5)	C(5a)	C(6)	C(7)	C(8)	C(8a)	R
2	76.74	161.10	126.80	113.51	113.49	132.91	116.42	146.73	15.825, 17.32, 31.46
4	75.13	163.02	127.17	113.925	114.35	133.64	117.61	146.38	127.43, 128.48, 128.82, 140.11
6	73.83	162.77	127.24	113.70	114.30	133.58	117.81	145.76	121.84, 123.45, 129.90, 142.08, 147.69
7	73.96	162.825	127.39	113.78	114.40	133.70	117.87	145.88	123.62, 128.43, 147.23, 147.68
8	68.80	162.48	126.90 (or 127.19)	113.90	114.53	133.28	117.31	146.20	115.71, 118.83, 125.78, 127.19 (or 126.9), 129.48, 155.08
14	70.76	162.97	127.43	114.19	115.09	134.02	118.65	145.31	128.26, 129.23, 150.17, 151.85

The choice between the structures of HDHQ and Schiff's bases ($RCH{=}NC_6H_4CONHOH$), which are isomeric to them, can be made with adequate reliability in considering the ^1H NMR spectra of the substances under study. The most general and demonstrative is the presence of the signals of protons at position 2 of HDHQ in the range of 4.9—5.2 ppm for adducts based on aliphatic aldehydes and in the range of 5.9—6.5 ppm for products based on aromatic and heterocyclic aldehydes. This is an area characteristic of the protons at position 2 of 1,2-dihydro-4-(3*H*)-quinazolinones.[8,9] In contrast, if the adducts based on aromatic aldehydes had the structure of Schiff's bases, protons of the —CH=N— group would be observed in the range of 8.2—8.5 ppm.[10] However, there are no signals in this range (if no nitro group is present in the aromatic ring). Taking into account the data given as well as the fact that a signal of a proton at 5.95 ppm is observed in the ^1H NMR spectrum of the adduct of acid **1** with pyridine-2-carbaldehyde,[2] we believe that the HDHQ structure should also be ascribed to this compound, and not the structure of a Schiff's base, as proposed previously.[2,6]

Significant evidence of the structure of the products is also the ^{13}C NMR spectra: signals of C(2) are observed in the 70—76 ppm range, which should be expected for HDHQ (δ ^{13}C 68.68[8]), but not for Schiff's bases isomeric to them (ArN=CHR, δ ^{13}C(CH=N) 157—164[11,12]). Additional proof of the HDHQ structure could also be the chemical shift in the ^{15}N NMR spectrum of compound **14**: −304 ppm (with respect to nitromethane), which is characteristic of aromatic amines[13] and differs strongly from the signals characteristic of Schiff's bases (ArN=CHPh, δ ^{15}N −42 to −62 with respect to nitromethane[13]).

Other spectral characteristics of the compounds obtained are also consistent with the HDHQ structure. One can observe the signals of protons of the NH group at 4.8—5.0 ppm for compounds **2** and **3** and at 7.4—7.6 ppm for products **4—14**, as well as the signals of protons of the NOH group in the 9—10 ppm range in the ^1H NMR spectra.

The broad band in the range of 3300—3350 cm^{-1} in IR spectra corresponds to the vibrations of the N—H bond. One of the most intense bands in the IR spectra is the band of the hydroxyamide group, which sometimes appears as a poorly resolved doublet (1610—1615 cm^{-1}).

The HDHQ obtained are crystalline substances with melting points of ~100—230 °C, depending on the nature of the substutuent at position 2.

Experimental

The ^1H, ^{13}C, and ^{15}N NMR spectra were recorded on a Bruker AM-300 spectrometer. The IR spectra were recorded on a UR-20 instrument (KBr). The melting points were measured on a Koffler stage.

3-Hydroxy-2-methyl-1,2-dihydroquinazolin-4-one (2). A triple amount of acetaldehyde was added to acid **1** (0.2 g) in 5—10 mL of 40% ethanol, and the reaction mixture was heated in an ampule at 110 °C for 3 h. The solution was evaporated in air, and the residue was recrystallized twice from 40% ethanol. The yield of compound **2** and the data from elemental analysis are summarized in Table 1.

3-Hydroxy-2-R-1,2-dihydroquinazolin-4-ones (3—14) (general procedure). An equimolar amount of aldehyde (in the case of solids, in the form of hot solutions in 40% ethanol) was added to a solution of acid **1** (0.2 g) in 5 mL of 40% ethanol or methanol obtained while heating. The reaction mixture was refluxed ~5 min and allowed to cool. The product precipitated was filtered off and recrystallized twice from 40% ethanol. The yields are given in Table 1 with respect to the recrystallized compounds.

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