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2-(4-OXO-3,4-DIHYDRO-2-QUINAZOLINYL-METHYL)BENZOIC ACIDS

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Condensation of 2-cyanomethylbenzoic acid with anthranilic acids gave a series of 2-(4-oxo-3,4-dihydro-2-quinazolinylmethyl)benzoic acids which are structural analogs of the alkaloid glycosminine (2-benzyl-1,2-dihydro-4-quinazolone).

Keywords: anthranilic acids, glycosminine, 2-(4-oxo-3,4-dihydro-2-quinazolinylmethyl)benzoic acids, 2-cyanomethylbenzoic acid.

Condensation of 2-cyanomethylbenzoic acid with amine derivatives is a convenient method for the preparation of various aza-heterocyclic derivatives, in particular of 3-iminoisochroman-1-one [1], 5H-morphanthridine-6,11-dione [2], 3-amino-1-isoquinolinones [3], and condensed isoquinolines with a bridging nitrogen atom [4].

In this work we continue our search [5, 6] for novel synthetic routes to isoquinolines and quinazolines and of condensed systems based on them by studying the reaction of cyano acid **1** with anthranilic acids. It is known [3] that the reaction of the cyano acid **1** with aniline gives 3-anilino-1,2-dihydro-1-isoquinolinone (**3a**). Viewing anthranilic acid as a particular case of a substituted aniline we felt justified in expecting that its condensation with compound **1** would give 2-(1-oxo-1,2-dihydro-3-isoquinolinylamino)benzoic acid (**3b**). Use of ethyl anthranilate in this reaction might be expected to give the ethyl ester of acid **3b**.

Heating a mixture of equimolar amounts of cyano acid **1** with anthranilic acid or ethyl anthranilate in chlorobenzene gave a product which differed from the acid **3b** in its expected spectroscopic properties. Evidently reaction involves the participation of the carboxyl group of the anthranilic acid. The chemical properties of the condensation product and its spectroscopic parameters (Table 1) correspond to the structure 2-(4-oxo-3,4-dihydro-2-quinazolinylmethyl)benzoic acid (**4a**). The material synthesized by us shows amphoteric properties. The action of hydrobromic acid on compound **4a** gives the corresponding hydrobromide and that of sodium hydroxide yields the sodium salt. Using standard methods [7] for the identification of carboxylic acid we have prepared the ethyl (**5a**) and phenacyl (**5b**) esters and the phenylhydrazide (**5c**) derivatives of the acid **4a** (Scheme 1).

In order to clarify the structure of the condensation product we have prepared a series of model compounds. A sample of the previously unknown 2-(1-oxo-1,2-dihydro-3-isoquinolinamino)benzoic acid (**3b**) has been prepared by the nucleophilic substitution of the methoxy group in 3-methoxy-1,2-dihydro-1-isoquinolinone through reaction with anthranilic acid. Condensation of the cyano acid **1** with *m*-aminobenzoic acid and 1,3-benzodioxolan-5-amine in the conditions for the formation of the quinolinone **3a** [3] gave the previously unreported 3-(1-oxo-1,2-dihydro-3-isoquinolinamino)benzoic acid (**3c**) and 3-(1,3-benzodioxolan-5-

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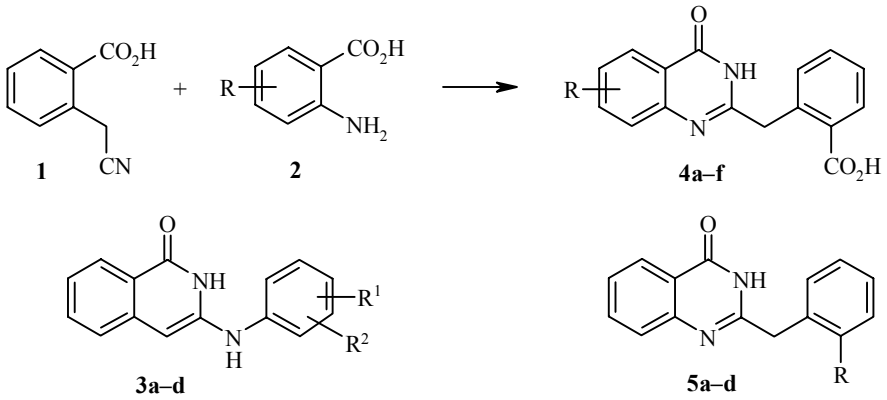
Scheme 1



3 a–c R^1 = H; **a** R^2 = H; **b** R^2 = 2-CO_2H; **c** R^2 = 3-CO_2H; **d** R^1R^2 = 3,4-OCH_2O;
4 a R = H; **b** R = 6'-Br; **c** R = 7'-Cl; **d** R = 7'-CO_2Me; **e** R = 7'-CF_3; **f** R = 6'-Me;
5 a R = CO_2Et; **b** R = CO_2CH_2COPh; **c** R = CONHNHPh; **d** R = H

ylamino)-1,2-dihydro-1-isoquinolinone **(3d)**. The structure of the isoquinolinones **3b-d** has been confirmed by their ^{1}H NMR spectra and the aminoisoquinolinone **3d** has been proved by X-ray crystallographic investigation (see Fig. 1 and Tables 2-4). Conjugation between the π-systems of the isoquinolinone and the benzodioxole bicycles is disturbed as a result of rotation of the latter. The torsional angle $N_{(2)}$–$C_{(3)}$–$C_{(5')}$–$C_{(4')}$ is 73.4(4)° and this is likely a result of the repulsion between the $C_{(4)}$H and $C_{(5')}$ atoms. The distance between them is 0.267 nm whereas the sum of the van der Waal radii is 0.287 nm [8]. An addition, the absence of the conjugation is confirmed by a significant lengthening of the $N_{(3)}$–$C_{(5')}$ bond to 0.1433(3) nm when compared with the mean value of 0.1376 nm [9]. The dioxolane ring exists in an envelope conformation with a deviation of -0.023 nm for atom $C_{(2')}$.

The aminoisoquinolinones **3c,d** have virtually identical electronic spectra (Fig. 2) and this points to the absence in solution of conjugation between the unshared electron pair of atom $N_{(3)}$ and the benzene ring of the benzodioxole. At the same time, the spectrum of the condensation product of anthranilic and *o*-cyanomethylbenzoic acids (quinazolinone **4a**) differs significantly in the long-wavelength region of the absorption spectrum of the aminoisoquinolinones **3c,d**. Moreover, the observed absorption spectrum agrees well with the spectra of other 3,4-dihydro-1-quinazolones [10]. In particular, the correspondence of the UV spectra of

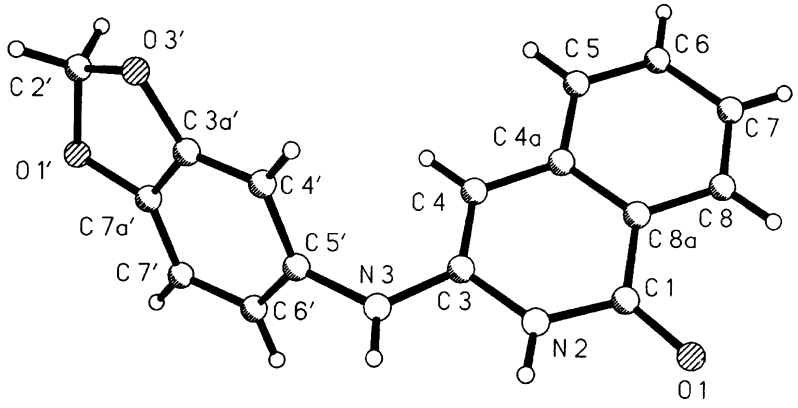


Fig. 1. Molecular structure of the aminoisoquinolinone **3d**.

TABLE 1. Characteristics for 2-(4-Oxo-3,4-dihydro-2-quinazolinylmethyl)benzoic Acids **4**

Compound	Empirical formula	Found, % / Calculated, %			mp, °C*	IR spectrum, ν, cm^{-1} (vibrations of the quinazolone system)		^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz)			Yield, %
		C	H	N				–C<u>H</u>$_2$–, s	arom. H	Other	
4a	$C_{16}H_{12}N_2O_3$	68.73 / 68.57	4.47 / 4.32	0.02 / 9.99	299	1670	1600	4.31	8.06 (1H, d, J_o = 8); 7.87 (1H, d, J_o = 8); 7.71 (1H, t, J_o = 8); 7.55-7.35 (5H, m)	12.6 (1H, s, N<u>H</u>)	85
4b*[2]	$C_{16}H_{11}BrN_2O_3$	53.77 / 53.50	3.21 / 3.09	7.93 / 7.80	319	1670	1600	4.35	8.15 (1H, d, J_m = 2.5); 7.91 (1H, dd, J_o = 8, J_m = 2.5); 7.91 (1H, dd, J_o = 8, J_m = 2.5); 7.54 (1H, td, J_o = 8, J_m = 2.5); 7.45-7.35 (3H, m)	13.0 (1H, N<u>H</u>)	80
4c*[3]	$C_{16}H_{11}ClN_2O_3$	61.25 / 61.06	3.61 / 3.52	8.97 / 8.90	315	1670	1610	4.36	8.06 (1H, d, J_o = 8); 7.91 (1H, d, J_o = 8); 7.56-7.37 (5H, m)	12.44 (1H, s)	80
4d	$C_{18}H_{14}N_2O_5$	64.01 / 63.90	4.23 / 4.17	8.37 / 8.28	279	1670, 1720	1610	4.4	8.2 (1H, d, J_o = 8); 7.80-8.0 (3H, m); 7.2-7.7 (3H, m)	3.90 (3H, s, C<u>H</u>$_3$)	75
4e	$C_{17}H_{11}F_3N_2O_3$	58.97 / 58.93	3.35 / 3.18	8.09 / 8.04	305	1670	1590	4.4	8.3 (1H, d, J_o = 8); 7.9 (1H, d, J_o = 8); 7.3-7.8 (5H, m)		80
4f	$C_{17}H_{14}N_2O_3$	69.54 / 69.38	5.10 / 4.79	9.63 / 9.52	278	1700	1590	4.35	7.8-8.0 (2H, m); 7.3 (5H, m)	2.40 (3H, s, C<u>H</u>$_3$)	82

* Compounds **4a-c** from DMF, **4d-f** from AcOH.

*[2] Found, %: Br 22.41. Calculated, %: Br 22.25.

*[3] Found, %: Cl 11.18. Calculated, %: Cl 11.27.

TABLE 2. Coordinates ($\times 10^4$) and Equivalent Isotropic Thermal Parameters ($Å^2 \times 10^3$) for the Non-hydrogen Atoms in Structure **3d**

Atom	*x*	*y*	*z*	U_{eq}
O(1)	2676(4)	10414(2)	3812(2)	43(1)
O(1')	5398(4)	1547(2)	10270(2)	61(1)
O(3')	2030(4)	3018(2)	10423(2)	58(1)
N(2)	3548(4)	8554(2)	5469(2)	36(1)
N(3)	4868(5)	6766(2)	7193(2)	45(1)
C(8)	-964(5)	9269(3)	3003(2)	40(1)
C(7)	-2655(6)	8646(3)	2678(3)	46(1)
C(6)	-2963(5)	7356(3)	3406(3)	44(1)
C(5)	-1577(5)	6697(3)	4441(3)	38(1)
C(4a)	209(5)	7295(3)	4798(2)	34(1)
C(4)	1703(5)	6637(3)	5868(2)	35(1)
C(3)	3329(5)	7273(2)	6184(2)	34(1)
C(1)	2270(5)	9265(2)	4404(2)	33(1)
C(8a)	493(5)	8611(3)	4055(2)	33(1)
C(5')	5062(5)	5404(3)	7962(2)	36(1)
C(6')	7064(5)	4521(3)	7896(3)	44(1)
C(7')	7361(6)	3188(3)	8631(3)	49(1)
C(7a')	5537(5)	2796(3)	9430(2)	41(1)
C(2')	3015(7)	1636(3)	10718(3)	60(1)
C(3a')	3523(5)	3670(3)	9500(2)	39(1)
C(4a')	3207(5)	4990(3)	8790(2)	40(1)

the product **4a** and the known [11] 2-benzyl-1,2-dihydro-4-quinazolone (**5d**) points to the isoelectronic nature of these chromophores and to the similarity in their structures. The additional fact that the UV spectra of the aminoisoquinolinones **3c,d** do not change in the presence of strong mineral acids whereas the spectra of quinazolinone **5d** and the condensation product of anthranilic and 2-cyanomethylbenzoic acid **4a** undergo identical changes upon protonation (Table 1) are yet a further pointer to the quinazolinone structure for **4a**.

The proposal of a quinazolinone structure for compound **4a** is in agreement with its IR spectrum. The observed differences in the spectra of the quinazolinone **5d** (broad C=O band and the presence of the O–H band) is due to the presence of the carboxyl group and this hinders the identification of the inherent characteristics of the 3,4-dihydro-4-quinazolinone fragment bands [12]. However, such a possibility exists in the case of ester **5a**. Along with the ester C=O group band (1710 cm^{-1}) there are observed bands in the spectrum for the N–H, C=O, and C=N of the quinazolinone at 3170, 1670, and 1610 cm^{-1} respectively.

TABLE 3. Bond Lengths (*l*) in the Aminoisoquinolinone Molecule **3d**

Bond	*l*, nm	Bond	*l*, nm
O(1)–C(1)	0.1253(3)	C(8)–C(8a)	0.1406(4)
C(1)–N(2)	0.1374(3)	N(3)–C(5')	0.1433(3)
C(1)–C(8a)	0.1450(4)	O(1')–C(7a')	0.1386(3)
N(2)–C(3)	0.1376(3)	O(1')–C(2')	0.1424(4)
C(3)–C(4)	0.1352(4)	C(2')–O(3')	0.1438(4)
C(3)–N(3)	0.1384(4)	O(3')–C(3a')	0.1392(3)
C(4)–C(4a)	0.1432(4)	C(3a')–C(4')	0.1376(4)
C(4a)–C(5)	0.1417(4)	C(3a')–C(7a')	0.1380(4)
C(4a)–C(8a)	0.1424(4)	C(4')–C(5')	0.1407(4)
C(5)–C(6)	0.1371(4)	C(5')–C(6')	0.1379(4)
C(6)–C(7)	0.1400(4)	C(6')–C(7')	0.1395(4)
C(7)–C(8)	0.1376(4)	C(7')–C(7a')	0.1369(4)

TABLE 4. Valence Angles (ω) in the Aminoisoquinolinone Molecule **3d**

Valence angle	ω, deg.	Valence angle	ω, deg.
O(1)–C(1)–N(2)	119.3(3)	C(4a)–C(8a)–C(1)	119.4(2)
O(1)–C(1)–C(8a)	124.5(2)	C(3)–N(3)–C(5')	121.5(2)
N(2)–C(1)–C(8a)	116.1(2)	C(7a')–O(1')–C(2')	104.4(2)
C(1)–N(2)–C(3)	125.2(2)	O(1')–C(2')–O(3')	108.5(2)
C(4)–C(3)–N(2)	119.7(2)	C(3a')–O(3')–C(2')	104.2(2)
C(4)–C(3)–N(3)	126.3(2)	C(4')–C(3a')–C(7a')	122.8(3)
N(2)–C(3)–N(3)	114.0(2)	C(4')–C(3a')–O(3')	127.7(3)
C(3)–C(4)–C(4a)	120.2(2)	C(7a')–C(3a')–O(3')	109.4(2)
C(5)–C(4a)–C(8a)	117.8(2)	C(3a')–C(4')–C(5')	115.9(3)
C(5)–C(4a)–C(4)	122.9(2)	C(6')–C(5')–C(4')	120.8(3)
C(8a)–C(4a)–C(4)	119.4(3)	C(6')–C(5')–N(3)	120.0(3)
C(6)–C(5)–C(4a)	121.1(3)	C(4')–C(5')–N(3)	119.2(3)
C(5)–C(6)–C(7)	120.6(3)	C(5')–C(6')–C(7')	122.5(3)
C(8)–C(7)–C(6)	120.1(3)	C(7a')–C(7')–C(6')	116.1(3)
C(7)–C(8)–C(8a)	120.4(3)	C(7')–C(7a')–C(3a')	121.8(3)
C(8)–C(8a)–C(4a)	120.0(3)	C(7')–C(7a')–O(1')	127.8(3)
C(8)–C(8a)–C(1)	120.6(3)	C(3a')–C(7a')–O(1')	110.3(3)

The formation of quinazolinylmethylbenzoic acid **4a** as a result of condensation of acids **1** and **2** can occur through an initial amination of the nitrile group of the cyano acid **1** by the amino group of the anthranilic acid. Such a reaction course cannot be regarded as common since the intermolecular formation of amidines from nitriles which do not contain activating electron-acceptor groups at the α-carbon atom usually needs acid catalysis [13]. We have found that unsubstituted phenylacetonitrile, along with the methyl ester of

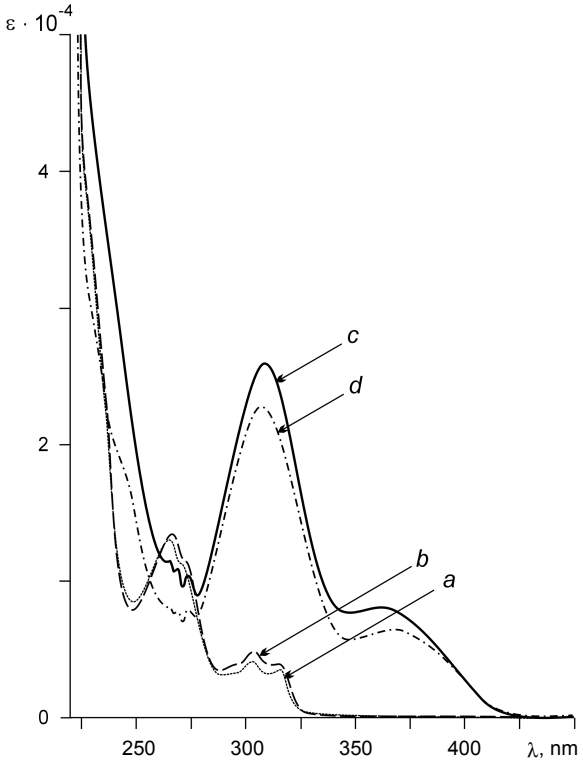


Fig. 2. Electronic spectra of the quinazolinones **4a** (*a*), **5d** (*b*) and isoquinolinones **3c** (*c*) and **3d** (*d*).

2-cyanomethylbenzoic acid, do not react with anthranilic ester or its ester in the conditions for the formation of **4a**. At the same time, in the presence of hydrogen chloride, phenylacetonitrile readily condenses with the anthranilate ester to form the benzylquinazolinone **5d** [14]. In the case of the *o*-cyanomethylbenzoic acid there is evidently a specific activation of the nitrile group by the neighbouring carboxyl. At least, the intermediate formation of the corresponding amidines most clearly explains the formation of the anilinoisoquinolinones **3** recorded above and also 2-(1,3-benzoxazole-2-methyl)- and 2-(1,3-benzothiazole-2-methyl)benzoic acids [1] as a result of condensation of o-cyanomethylbenzoic acid **1** with anilines and *o*-amino(thio)phenols respectively.

The quinazolinylmethybenzoic acid **4a** may be of practical interest as a modified carboxyl group of a structural analog of the alkaloid glycosminine from *Glycosmis arborea* which has been identified [15] as 2-benzylquinazolinone **5d**. On this basis we have introduced a series of substituted anthranilic acids into the condensation with acid **1** to give good yields of 2-(4-oxo-3,4-dihydro-2-quinazolinylmethyl)benzoic acids substituted at the quinazolinone fragment (**4b-f**). Their spectroscopic parameters resemble those discussed for the acid **4a** (Table 1).

EXPERIMENTAL

IR spectra for the compounds were recorded on a Pye-Unicam SP3-300 instrument for KBr tablets. ^{1}H NMR spectra were measured on a Bruker WR-100 (100 MHz) spectrometer using TMS as internal standard. UV Spectra were recorded on a Shimadzu UV-3100 spectrophotometer for 5×10^{-5} M solutions of the compounds in methanol.

X-ray Analysis was carried out on a Siemens P3/PC automatic diffractometer (λMoKα, graphite monochromator, θ/2θ scanning, $2\theta_{max} = 50°$) with the measurement of 2276 independent reflections (R_{int} 0.043). Crystals of **3d** ($C_{16}H_{12}N_2O_3$) are triclinic. At 20°C a = 5.678(2), b = 10.739(4), c = 11.348(4) Å; α = 71.31(3), β = 87.43(3), γ = 81.14(3)°; V = 647.6(4) Å^3; d_{calc} = 1.437 g/cm^3; space group $P\bar{1}$; Z = 2. The structure was solved by a direct method using the program package SHELX-97 [9]. The positions of the hydrogen atoms were revealed in difference synthesis of electron density and refined using the "rider" method with a fixed $U_{iso} = nU_{eq}$ for a non-hydrogen atom bound to the given hydrogen atom (n = 1.5 for methyl groups and 1.2 for remaining hydrogen atoms). Refinement in an F^2 full matrix least squares analysis (190 parameters) in the anisotropic approximation for non-hydrogen atoms with the 2276 reflections gave wR_2 = 0.1583 (R_1 = 0.058 for 1270 reflections with $F > 4\sigma(F)$, S = 0.92). Coordinates for the non-hydrogen atoms are given in Table 2 and bond lengths and valence angles in Tables 3 and 4.

2-Cyanomethylbenzoic acid (1) was prepared in accordance with method [16].

2-Benzyl-3,4-dihydro-4-quinazolinone (5d) was prepared as in method [14].

2-(4-Oxo-3,4-dihydro-2-quinazolinylmethyl)benzoic Acids (4a-f). A mixture of acid **1** (0.32 g, 2 mmol) and the corresponding anthranilic acid **2** (2 mmol) was refluxed for 10 min in chlorobenzene (5 ml). After removal of solvent in vacuo the residue was treated with *i*-PrOH. The precipitate was filtered off and washed with Et_2O.

2-(4-Oxo-3,4-dihydro-2-quinazolinylmethyl)benzoic Acid Hydrobromide (4a·HBr). The quinazolinone **4a** (0.56 g, 2 mmol) was dissolved in refluxing AcOH (10 ml) and concentrated HBr (1 ml) was added. After cooling the reaction mixture, the precipitate formed was filtered off and washed with *i*-PrOH and then Et_2O. Yield 0.6 g (85%); mp 323°C (AcOH). IR spectrum (KBr), ν, cm^{-1}: 1625 (C=N); 1665 (C=O carboxyl group), 1705 (C=O 4-quinazolinone), 2660-2960 (N^+–H), 3280-3560 (O–H). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm, J (Hz): 8.5 (2H, br. s, COOH, N^+H); 8.2 (1H, d, J_o = 8, 5-H); 7.4-8.1 (7H, m, $H_{arom.}$); 4.6 (2H, s, CH_2). Found, %: C 53.47; H 3.77; Br 22.17; N 7.86. $C_{16}H_{12}N_2O_3$·HBr. Calculated %: C 53.21; H 3.63; Br 22.12; N 7.76.

Sodium 2-(4-Oxo-3,4-dihydro-2-quinazolinylmethyl)benzoate. The quinazolinone **4a** (1.4 g, 5 mmol) was dissolved in 2N NaOH (5 ml) at room temperature. The solidified mixture was treated with *i*-PrOH and the precipitate was filtered off and washed with Et_2O. Yield 2 g (80%); mp 280°C (water). IR spectrum (KBr), ν, cm^{-1}: 1620 (C=N), 1665 (C=O), 3420 (N–H). ^1H NMR spectrum (DMSO-d_6), δ, ppm, *J* (Hz): 15.3 (1H, s, NH); 8.05 (1H, d, J_o = 8, 5-H); 7.1-7.8 (7H, m, $H_{arom.}$); 4.1 (2H, s, CH_2). Found, %: C 60.17; H 5.13; N 8.93. $C_{16}H_{11}N_2NaO_3$. Calculated, %: C 63.58; H 3.67; N 9.27.

2-(1-Oxo-1,2-dihydro-3-isoquinolinylamino)benzoic Acid (3b). A mixture of 3-methoxy-1,2-dihydro-1-isoquinoline (0.9 g, 5 mmol) and anthranilic acid (0.7 g, 5 mmol) was refluxed for 4 h in chlorobenzene (10 ml). The precipitate was filtered off and washed with *i*-PrOH and Et_2O. Yield 0.84 g (60%); mp 276°C (DMF). IR spectrum (KBr), ν, cm^{-1}: 1650 (sh.), 1635 (C=O). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 13.2 (1H, s, OH); 11.9 (1H, s, $C_{(3)}NH$); 9.5 (1H, s, $N_{(2)}H$); 6.9-8.0 (8H, m, $H_{arom.}$); 6.3 (1H, s, $C_{(4)}H$). Found %: C 68.62; H 4.38; N 10.05. $C_{16}H_{12}N_2O_3$. Calculated, %: C 68.57; H 4.32; N 9.99.

3-(1-Oxo-1,2-dihydro-3-isoquinolinamino)benzoic Acid (3c). A mixture of 2-cyanomethylbenzoic acid (0.32 g, 2 mmol) and *m*-aminobenzoic acid (0.27 g, 2 mmol) was refluxed for 4 h in chlorobenzene (5 ml). Solvent was removed in vacuo and the residue was treated with *i*-PrOH and the precipitate filtered off. Yield 0.43 g (77%); mp 305°C (DMF). IR spectrum (KBr), ν, cm^{-1}: 1630 (C=N); 1665 (C=O carboxyl group), 1705 (C=O 4-quinazolinone), 2660-2960 (N^+–H), 3280-3560 (O–H). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 10.9 (1H, s, $C_{(3)}NH$); 8.2 (1H, s, $N_{(2)}H$); 7.1-8.1 (8H, m, $H_{arom.}$); 6.1 (1H, s, $C_{(4)}H$). Found, %: 68.59; H 4.40; N 10.09. $C_{16}H_{12}N_2O_3$. Calculated, %: C 68.57; H 4.32; N 9.99.

3-(1,3-Benzodioxolan-5-ylamino)-1,2-dihydro-1-isoquinolinone (3d), A mixture of 2-cyanomethyl-benzoic acid (0.32 g, 2 mmol) and 1,3-benzodioxolan-5-amine (0.54 g, 4 mmol) was refluxed for 2 h in chlorobenzene (5 ml). The solvent was removed in vacuo and the residue treated with Et_2O and filtered off. Yield 0.4 g (73%); mp 235°C (*i*-PrOH). IR spectrum (KBr), ν, cm^{-1}: 1630 (C=N), 1665 (C=O carboxyl group), 1705 (C=O 4-quinazolinone), 2660-2960 (N^+–H), 3280-3560 (O–H). ^1H NMR spectrum (DMSO-d_6), δ, ppm, *J* (Hz): 5.8 (1H, s, $C_{(4)}$–CH); 7.7 (1H, s, $N_{(2)}H$); 6.6-7.5 (6H, m, $H_{arom.}$); 8.0 (1H, d, J_o = 8, 8-H); 10.6 (1H, s, $C_{(3)}$–NH). Found, %: C 68.67; H 4.37; N 10.09. $C_{16}H_{12}N_2O_3$. Calculated, %: C 68.57; H 4.32; N 9.99.

Ethyl Ester of 2-(4-Oxo-3,4-dihydro-2-quinazolinylmethyl)benzoic Acid (5a). Quinazolinone **4a** (0.28 g, 1 mmol) was suspended in absolute EtOH (20 ml). $SOCl_2$ (1 ml, 14 mmol) was added carefully dropwise at 0-5°C. The reaction mixture was then refluxed for 5 h, solvent evaporated off in vacuo, and the residue was treated with a saturated solution of $NaHCO_3$. The residue was filtered off and washed with water, *i*-PrOH, and Et_2O. Yield 0.23 g (70%); mp 176°C (AcOH). IR spectrum (KBr), ν, cm^{-1}: 1250 (C–O), 1610 (C=N), 1670 (C=O quinazolinone), 1710 (C=O ester), 3170 (N–H). ^1H NMR spectrum ($CDCl_3$), δ, ppm, *J* (Hz): 4.5 (2H, q, O–CH_2); 4.3 (2H, s, CH_2); 1.4 (3H, t, *J* = 3, CH_3). Found, %: C 70.63 ;H 5.37; N 9.15. $C_{18}H_{16}N_2O_3$. Calculated, %: C 70.12; H 5.23; N 9.09.

2-Oxo-2-phenylethyl Ester of 2-(4-Oxo-3,4-dihydro-2-quinazolinylmethyl)benzoic Acid (5b). The sodium salt of **4a** (1 g, 3 mmol) was dissolved in water (10 ml) and acidified with two drops of dilute HCl. EtOH (10 ml) was added and then phenacyl bromide (1 g, 5 mmol). The reaction mixture was heated with a reflux condenser on a water bath. After cooling, the precipitate was filtered off and washed with dilute $NaHCO_3$ solution and Et_2O. Yield 0.8 g (68%); mp 215°C (*i*-PrOH). IR spectrum (KBr), ν, cm^{-1}: 1280 (C–O) 1605 (C=N), 1660 (C=O quinazolinone), 1690, 1710 (C=O ester), 3170 (N–H). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 4.6 (2H, s, CH_2); 5.7 (2H, s, O–CH_2); 7.3 (1H, s, NH); 7.4-8.3 (13H, m, $H_{arom.}$). Found, %: C 72.57; H 4.73; N 7.11. $C_{24}H_{18}N_2O_4$. Calculated, %: C 72.35; H 4.55; N 7.03.

2-Phenylhydrazide of 2-(4-Oxo-3,4-dihydro-2-quinazolinylmethyl)benzoic Acid (5c). A mixture of acid **4a** (1 g, 3.6 mmol) and phenylhydrazine (2 ml, 20 mmol) was heated in benzene (20 ml) using a reflux condenser for 30 min. After cooling the reaction mixture the precipitate was filtered off and washed with Et_2O. Yield 0.9 g (70%); mp 273°C (AcOH). IR spectrum (KBr), ν, cm^{-1}: 1605 (C=N), 1650-1670 (broad C=O

quinazolinone, hydrazide), 2750-3200 (broad, N–H). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 4.4 (2H, s, CH_2); 7.1-8.3 (13H, m, $H_{arom.}$); 11.4 (1H, s, NH), 12.6 (2H, br. s, NH). Found, %: C 71.78; H 5.00; N 15.17. $C_{22}H_{18}N_4O_2$. Calculated, %: C 71.34; H 4.90; N 15.13.

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