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THE REACTION OF 2-AMINOETHYL- AND 3-AMINOPROPYL-SUBSTITUTED HETEROCYCLES WITH 2-FORMYL-1,3-CYCLANEDIONES AND 4-OXO-3,1-BENZOXAZINES

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The reaction of 2-formyl-1,3-cyclohexanedione, its 5,5-dimethyl, 5-phenyl and 5-(2-furyl) derivatives and of 2-formyl-1,3-indanedione and dehydroacetic acid with histamine, 3-(1-imidazolyl)propylamine, 3-(4-morpholyl)propylamine, 3-(2-pyrrolidon-1-yl)propylamine, 2-(1-piperazinyl)ethylamine, tryptamine, and 2-(aminomethyl)pyridine gave fifteen 2-aminomethylene derivatives. The reaction of these amines with 2-methyl-4-oxo-3,1-benzoxazine gave the 3-substituted 2-methyl-4(3H)-quinazolinones and with 4-oxo-2-phenyl-3,1-benzoxazine the monosubstituted N-benzoylanthranilic acid amides.

Keywords: 2-aminoethyl- and 3-aminopropyl-substituted heterocycles, 2-formyl-1,3-cyclanediones, dehydroacetic acid, 4-oxo-3,1-benzoxazines, 2-aminomethylene-1,3-cyclanediones, 3-substituted 4(3H)-quinazolinones, monosubstituted N-benzoylanthranilic acid amides.

In the last decade biologists, medics and chemists have carried out an intensive complex investigation of histamine H_3-receptor agonists and antagonists [1-17] directed towards broadening the treatment of a series of diseases. As reported in [3] the rationale for structure activity relationships amongst histamine H_3-receptors has led us to introduce histamine and certain ethyl- and propylamines with heterocyclic substituents at the β- and, respectively, γ-carbon atoms in the reaction with cyclanediones and benzoxazines. As cyclanediones **1** we used 2-formyl-1,3-cyclohexanedione (**1a**), its 5,5-dimethyl (**1b**), 5-phenyl (**1c**), and 5-(2-furyl) (**1d**) derivatives and 2-formyl-1,3-indanedione (**1e**) and, as amines **2,** histamine (**2a**), 3-(1-imidazolyl)propylamine (**2b**), 3-(4-morpholyl)propylamine (**2c**), 3-(2-pyrrolidon-1-yl)propylamine (**2d**), 2-(1-piperazinyl)ethylamine (**2e**), tryptamine (**2f**), and 2-(aminomethyl)pyridine (**2g**).

Reaction of 2-formyl-1,3-cyclohexanediones **1a-e** with amines **2a-g** give the 2-(aminomethylene)-1,3-cyclanediones (**3-17**) and dehydroacetic acid **1f** reacts with tryptamine **2f** to form the 3-(1-[2-(3-indolyl)ethylamino]ethylidene)-6-methyl-2,4-pyrandione (**18**).

The synthesis of compounds **3-18** was carried out using one of the following four procedures. Reaction of the free amines **2** with the formyl derivatives **1** gave the 2-aminomethylene derivatives **6, 7, 13-15, 17**. To synthesize the compounds **3, 5** and **8**, the amine hydrochlorides **2** were treated with the potassium salts of the corresponding formyl derivatives **1**.

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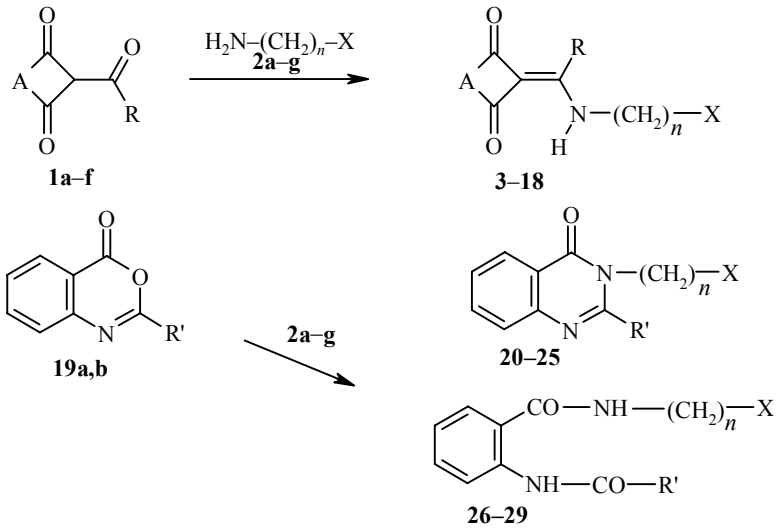
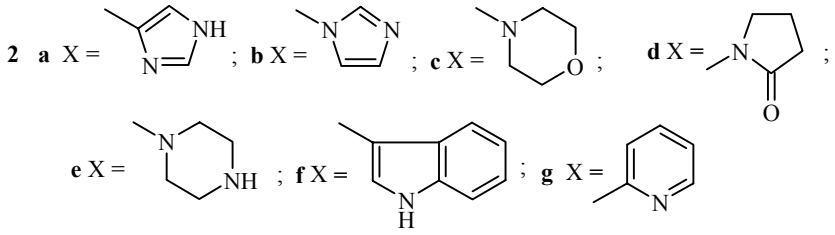


1 **a** A = $(CH_2)_3$; **b** A = $CH_2C(CH_3)_2CH_2$; **c** A = $CH_2CH(Ph)CH_2$; **d** A = $CH_2CH(2\text{-furyl})CH_2$; **e** A = C_6H_4-1,2; **f** A = –O–C(CH_3)=CH–; **a–e** R = H; **f** R = CH_3



a, **e**, **f** *n* = 2; **b–d** *n* = 3, **g** *n* = 1

A**,** *n***,** X = **3a,a**; **4a,b**; **5b,a**; **6b,b**; **7b,d**; **8b,f**; **9c,d**; **10d,b**; **11d,e**; **12e,a**; **13e,b**; **14e,c**; **15e,d**; **16e,f**; **17e,g**; **18f**,**f**; **19**: R' = **a** CH_3; **b** C_6H_5; R'**,** *n***,** X = **20a,a**; **21a,b**; **22a,d**; **23a,f**; **24a,g**; **25b,g**; **26b,a**; **27b,b**; **28b,c**; **29b**,**f**

Compounds **12, 16, 18** were prepared from the 2-acyl-1,3-cyclanediones **1** and the amine hydrochlorides **2** in the presence of $NaHCO_3$. The potassium salts of the 2-formyl-1,3-cyclohexanediones **1** and the free amines **2** in the presence of HCl gave the compounds **4** and **9-11.**

The structure of the 2-aminomethylene-1,3-cyclanediones **3-17** was confirmed by IR and ^{1}H NMR spectroscopic data (Table 1). The ^{1}H NMR spectra of **3-17**, as in the spectra of previously studied compounds of this series [18-22], show characteristic proton signals for the cyclanedione and *trans*-fixed =CH–NH– fragment.

The reaction of the 2-methyl-4-oxo-3,1-benzoxazine (**19a**) with the amines **2a,b,d,f,g**, analogously to its previously studied reactions with amino heterocycles [23, 24], gives the 3-substituted 4(3H)-quinazolinones **20-24**. Treatment of the 4-oxo-2-phenyl-3,1-benzoxazine (**19b**) with 2-(aminomethyl)pyridine (**2g**) also gives the quinazolinone **25**. The reaction of the benzoxazine **19b** with the amines **2a,b,c,f** gave the N-benzoylanthranilic acid amides **26-29**.

The spectra of the quinazolinones **20-25** and the N-benzoylanthranilic acid amides **26-29** are readily distinguishable. The ^{1}H NMR spectra of the latter show two additional signals for the NH group protons (Table 1).

The synthesized compounds were prepared with the aim of investigating their histamine H_3-receptor agonist and antagonist activities since the amines used can be considered as histamine analogs.

TABLE 1. IR and ^{1}H NMR Spectra of Synthesized Compounds

Com-pound	IR spectrum, ν, cm^{-1}	^{1}H NMR spectrum, δ, ppm, *J* (Hz)*
1	2	3
3	1670, 1610 (C=O), 1590, 1575; 3200, 3100 (NH)	$CDCl_3$. 1.85 (2H, m, ^3J = 7,CH_2); 2.25-2.42 (4H, m, $2CH_2$); 2.83 (2H, t, ^3J = 7, CH_2); 3.65 (2H, dt, ^3J = 6, ^3J = 7, CH_2); 6.75 (1H, s, =CH); 7.47 (1H, s, =CH–); 7.96 (1H, d, ^3J = 14, =CH–); 9.31 (1H, br. s, NH); 11.13 (1H, br. m, NH)
4	1665 (C=O), 1610-1570, 1515; 3200, 3140, 3110 (NH)	$CDCl_3$. 1.78-2.43 (8H, m, $4CH_2$); 3.31 (2H, dt, ^3J = 6, ^3J = 7, CH_2); 3.98 (2H, d, ^3J = 7, CH_2); 6.82 (1H, s, =CH–); 7.01 (1H, s, =CH–); 7.42 (1H, s, =CH–); 7.99 (1H, d, ^3J = 14, =CH–); 11.14 (1H, br. m, NH)
5	1675 (C=O), 1600; 3220, 3120 (NH)	DMSO-d_6. 0.94 (6H, s, $2CH_3$); 2.16 (2H, s, CH_2); 2.25 (2H, s, CH_2); 2.78 (2H, t, ^3J = 7,5 Hz, CH_2); 3.72 (2H, dt, ^3J = 6 Hz, ^3J = 7 Hz, CH_2); 6.82 (1H, br. s, =CH–); 7.56 (1H, s, =CH–); 7.96 (1H, d, ^3J = 14 Hz, =CH–); 10.94 (1H, br. m, NH); 11.81 (1H, br. s, NH)
6	1665 (C=O), 1600, 1575, 1545, 1512; 3200, 3140 (NH)	DMSO-d_6. 0.94 (6H, s, $2CH_3$); 2.03 (2H, m, ^3J = 7, CH_2); 2.21 (2H, s, CH_2); 2.26 (2H, s, CH_2); 3.40 (2H, dt, ^3J = 7, ^3J = 5, CH_2); 3.96 (2H, t, ^3J = 7, CH_2); 6.87 (1H, s, =CH); 7.21 (1H, s, =CH–); 7.61 (1H, s, =CH–); 8.01 (1H, d, ^3J = 14, =CH–); 10.85 (1H, br. m, NH)
7	1680, 1670 (C=O), 1605, 1582, 1500; 3200 (NH)	$CDCl_3$. 0.98 (6H, s, $2CH_3$); 1.76-2.43 (6H, m, $3CH_2$); 2.24 (2H, s, CH_2); 2.82 (2H, s, CH_2); 3.33 (6H, m, $3CH_2$); 8.01 (1H, d, ^3J = 14, =CH–); 11.06 (1H, br. m, NH)
8	1668 (C=O), 1585, 1565; 3280, 3190 (NH)	$CDCl_3$. 1.04 (6H, s, $2CH_3$); 2.27 (2H, s, CH_2); 2.36 (2H, s, CH_2); 3.09 (2H, t, ^3J = 7, CH_2); 3.72 (2H, dt, ^3J = 6, ^3J = 7, CH_2); 7.08-7.66 (5H, m, C_6H_4, =CH–); 8.05 (1H, d, ^3J = 13, =CH–); 8.33 (1H, br. s, NH); 12.22 (1H, br. m, NH)
9	1680–1665 (C=O), 1600, 1580, 1560, 1510; 3280, 3220 (NH)	DMSO-d_6. 1.76-2.62 (11H, m, $5CH_2$, CH); 3.22 (6H, m, $3CH_2$); 7.21 (5H, m center, C_6H_5); 8.04 (1H, d, ^3J = 14, =CH–); 10.29 (1H, br. m, NH)
10	1665 (C=O), 1610, 1590, 1575, 1500; 3200, 3160 (NH)	$CDCl_3$. 2.14 (2H, m, ^3J = 7, CH_2); 2.76 (4H, br. s, $2CH_2$); 3.40 (1H, m, CH); 3.42 (2H, dt, ^3J = 6, ^3J = 7, CH_2); 4.05 (2H, t, ^3J = 7, CH_2); 6.05 (1H, m, C_4H_3O); 6.32 (1H, m, C_6H_3O); 6.92 (1H, s, =CH–); 7.12 (1H, s, =CH–); 7.36 (1H, m, C_4H_3O); 7.52 (1H, s, =CH–); 8.12 (1H, d, ^3J = 14, =CH–); 11.24 (1H, br. m, NH)
11	1673 (C=O), 1612, 1688, 1555, 1510; 3350, 3200, 3120 (NH)	DMSO-d_6. 2.06-3.53 (17H, m, $8CH_2$, CH); 5.94 (1H, m, C_4H_3O); 6.23 (1H, m, C_4H_3O); 7.50 (1H, m, C_4H_3O); 7.98 (2H, br. s, =CH–, NH); 10.78 (1H, br.m, NH)
12	1690, 1650 (C=O), 1625, 1590, 1560, 1540; 3280, 3200-3170 (NH)	DMSO-d_6. 2.78 (2H, t, ^3J = 7, CH_2); 3.69 (2H, dt, ^3J = 6, ^3J = 7, CH_2); 6.81 (1H, s, =CH–); 7.53-7.69 (5H, m, C_6H_4, =CH–); 7.69 (1H, d, ^3J = 14, =CH–); 9.54 (1H, br. m, NH); 11.62 (1H, br. s, NH)
13	1690, 1650 (C=O), 1625, 1600, 1570, 1530; 3280, 3150 (NH)	$CDCl_3$. 2.13 (2H, m, CH_2); 3.36 (2H, dt, ^3J = 5, ^3J = 7, CH_2); 4.05 (2H, t, ^3J = 7, CH_2); 6.91 (1H, s, =CH-); 7.12 (1H, s, =CH–); 7.67 (6H, C_6H_4, 2=CH–); 9.25 (1H, br. m, NH)
14	1710, 1675, 1650 (C=O), 1630, 1605-1560; 3280, 3100 (NH)	$CDCl_3$. 1.95 (2H, m, CH_2); 2.48 (6H, m, $3NCH_2$); 3.50 (2H, dt, ^3J = 6, ^3J = 7, NCH_2); 3.82 (4H, m, $2OCH_2$); 7.56-7.84 (5H, m, C_6H_4, =CH–); 9.38 (1H, br. m, NH)
15	1710, 1695, 1645 (C=O), 1635, 1620, 1600, 1500; 3280, 3110, 3090 (NH)	$CDCl_3$. 1.78-2.54 (6H, m, $3CH_2$); 3.47 (6H, m, $3CH_2$); 7.63 (5H, m, C_6H_4,=CH–); 9.44 (1H, br. m, NH)
16	1720-1705 (C=O), 1650-1580, 1565, 1550; 3400, 3200, 3100 (NH)	$CDCl_3$. 3.13 (2H, t, ^3J = 7, CH_2); 3.76 (2H, dt, ^3J = 6, ^3J = 7, CH_2); 7.16-8.08 (10H, m, $2C_6H_4$, 2=CH–); 9.23 (1H, br. m, NH); 12.93 (1H, br. s, NH)
17	1710, 1680, 1670, 1655 (C=O), 1615, 1560; 3250 (NH)	$CDCl_3$. 4.67 (2H, d, ^3J = 6, CH_2); 7.23-7.75 (8H, m, C_6H_4, C_5H_4N); 7.86 (1H, d,^3J = 14, =CH–); 8.67 (1H, m, C_5H_4N); 9.76 (1H, br. m, NH)
18	1715-1700, 1660, 1640 (C=O), 1620, 1580-1550; 3300, 3200 (NH)	DMSO-d_6. 2.02 (3H, s, CH_3); 2.47 (3H, s, CH_3); 3.05 (2H, t, ^3J = 7, CH_2); 3.80 (2H, dt, ^3J = 6, ^3J = 7, CH_2); 5.67 (1H, s, =CH–); 6.97-7.62 (5H, m, C_6H_4, =CH–); 10.98 (1H, br. s, NH); 13.83 (1H, br. m, NH)

TABLE 1 (continued)

1	2	3
20	1665 (C=O), 1600, 1575, 1560; 3130 (NH)	DMSO-d_6. 2.41 (3H, s, CH_3); 2.92 (2H, t, ^3J = 7, CH_2); 4.23 (2H, t, ^3J = 7, CH_2); 6.81 (1H, s, =CH–); 7.50-7.78 (4H, m, C_6H_4, =CH–); 8.09 (1H, dd, ^3J = 8, ^4J = 1.5, $C_{(5)}H$); 11.87 (1H, br. s, NH)
21	1680, 1665 (C=O), 1620, 1600, 1575, 1565, 1520	DMSO-d_6. 2.13 (2H, m, ^3J = 7, CH_2); 2.43 (3H, s, CH_3); 4.07 (2H, t, ^3J = 7, CH_2); 4.15 (2H, t, ^3J = 7, CH_2); 6.89 (1H, s, =CH–); 7.29 (1H, s, =CH–); 7.32-7.63 (4H, m, C_6H_4, =CH–); 8.29 (1H, d, ^3J = 8, $C_{(5)}H$)
22	1660, 1650, 1640 (C=O), 1610, 1600, 1575, 1505	$CDCl_3$. 2.02-2.46 (6H, m, $3CH_2$); 2.65 (3H, s, CH_3); 3.49 (4H, m, $2CH_2$); 4.09 (2H, m, CH_2); 7.36-8.27 (4H, m, C_6H_4)
23	1705, 1660 (C=O), 1600, 1575; 3300 (NH)	DMSO-d_6. 2.73 (3H, s, CH_3); 3.09 (2H, dd, ^3J = 5, ^3J = 9, CH_2); 4.31 (2H, dd, ^3J = 5, ^3J = 9, CH_2); 7.01-7.89 (8H, m, $2C_6H_4$, =CH); 8.21 (1H, d, ^3J = 8, $C_{(5)}H$); 10.91 (1H, br. s, NH)
24	1686 (C=O), 1628, 1590, 1576, 1568, 1504	DMSO-d_6. 2.48 (3H, s, CH_3); 5.45 (2H, s, CH_2); 7.18-8.44 (8H, m, C_6H_4, C_5H_4N)
25	1682 (C=O), 1588, 1568	DMSO-d_6. 5.27 (2H, s, CH_2); 7.11-8.43 (13H, m, C_6H_4, C_5H_4N, C_6H_5)
26	1665, 1655 (C=O), 1605, 1590, 1575, 1535, 1525; 3340, 3100 (NH)	DMSO-d_6. 2.81 (2H, t, ^3J = 6.5, CH_2); 3.57 (2H, dt, ^3J = 6, ^3J = 6.5, CH_2); 6.85 (1H, s, =CH–); 7.21-7.92 (9H, m, C_6H_5, C_6H_4, =CH–); 8.66 (1H, d, ^3J = 8, $C_{(6)}H$); 8.98 (1H, br. t, ^3J = 6, NH); 11.83 (1H, br. s, NH); 12.61 (1H, br. s, NH)
27	1675, 1665 (C=O), 1635, 1600, 1580, 1550, 1515, 1500; 3280, 3230, 3120 (NH)	DMSO-d_6. 1.98 (2H, m, ^3J = 7, CH_2); 3.32 (2H, dt, ^3J = 5.5, ^3J = 7, CH_2); 4.05 (2H, t, ^3J = 7, CH_2); 6.91 (1H, s, =CH–); 7.24 (1H, s, =CH); 7.26-7.98 (9H, m, C_6H_5, C_6H_4, =CH–); 8.72 (1H, d, ^3J = 8, $C_{(6)}H$); 8.94 (1H, br. t, ^3J = 5.5, NH); 12.52 (1H, br. s, NH)
28	1675, 1645 (C=O), 1605, 1585, 1580, 1540-1520, 1500; 3250-3180 (NH)	DMSO-d_6. 1.69 (2H, m, CH_2); 3.28 (2H, m, NCH_2); 3.29 (6H, m, $3NCH_2$); 3.51 (4H, m, $2OCH_2$); 7.04-7.93 (8H, m, C_6H_5, C_6H_4); 8.60 (1H, dd, ^3J = 8, ^4J = 1.5, $C_{(6)}H$); 8.82 (1H, br. t, ^3J = 5, NH); 12.53 (1H, br. s, NH)
29	1675, 1645 (C=O), 1610, 1590, 1580, 1540, 1510; 3270, 3300, 3200 (NH)	DMSO-d_6. 2.98 (2H, m, CH_2); 4.14 (2H, m, CH_2); 6.71-7.90 (15H, m, C_6H_5, C_6H_4,=CH–, 2NH); 8.30 (1H, dd, ^3J = 8, ^4J = 1.7, $C_{(6)}H$); 10.83 (1H, br. s, NH)

TABLE 2. Characteristics for Synthesized Compounds

Com-pound	Empirical formula	Found, % / Calculated, %			Crystallysation solvent	mp, °C	Yield, %
		C	H	N			
1	2	3	4	5	6	7	8
3	$C_{12}H_{15}N_3O_2$	61.57 / 61.79	6.40 / 6.48	17.88 / 18.01	Toluene	164-165	34
4	$C_{13}H_{17}N_3O_2$	62.95 / 63.14	6.81 / 6.93	16.83 / 16.99	Isopropanol	151-153	80
5	$C_{14}H_{19}N_3O_2$	64.11 / 64.35	7.40 / 7.33	16.02 / 16.08	Ethanol	170-171	59
6	$C_{15}H_{21}N_3O_2$	65.20 / 65.43	7.52 / 7.65	15.40 / 15.26	Isopropanol	159-161	76
7	$C_{16}H_{24}N_2O_3$	65.50 / 65.73	8.21 / 8.27	9.40 / 9.58	Ethanol	139-141	95
8	$C_{19}H_{22}N_2O_2$	73.26 / 73.52	7.01 / 7.14	9.20 / 9.02	Ethanol	110-112	60
9	$C_{20}H_{24}N_2O_3$	70.44 / 70.57	7.10 / 7.11	8.08 / 8.08	Isopropanol	113-116	47
10	$C_{17}H_{18}N_3O_3$	65.28 / 65.37	5.74 / 5.81	13.26 / 13.45	Ethanol	88-90	89

TABLE 2 (continued)

1	2	3	4	5	6	7	8
11	$C_{17}H_{23}N_3O_3$	64.11 64.33	7.11 7.31	13.01 13.24	Ethanol	135-136	62
12	$C_{15}H_{13}N_3O_2$	67.19 67.41	4.80 4.90	15.55 15.72	Ethanol–water, 1:1	217-220	45
13	$C_{16}H_{15}N_3O_2$	68.39 68.32	5.21 5.37	15.01 14.94	Ethanol	148-150	57
14	$C_{17}H_{20}N_2O_3$	67.77 67.98	6.60 6.71	9.12 9.33	Ethanol	74-75	46
15	$C_{17}H_{18}N_2O_3$	68.58 68.43	5.96 6.10	9.30 9.39	Ethanol	135-137	85
16	$C_{20}H_{16}N_2O_2$	75.71 75.90	4.98 5.10	8.61 8,85	Ethanol	163-164	50
17	$C_{16}H_{12}N_2O_2$	72.51 72.71	4.50 4.58	10.44 10.60	Ethanol	160-161	71
18	$C_{18}H_{18}N_2O_3$	69.55 69.66	5.80 5.85	8.89 9.03	Ethanol	164-165	90
20	$C_{14}H_{14}N_4O$	66.01 66.12	5.66 5.55	21.81 22.03	Water	241-245	35
21	$C_{15}H_{16}N_4O$	67.01 67.15	5.95 6.01	20.65 20.88	Ethanol	137-140	78
22	$C_{16}H_{19}N_3O_2$	67.12 67.35	6.60 6.72	14.88 14.73	Methanol	73-76	27
23	$C_{19}H_{17}N_3O$	75.02 75.23	5.51 5.65	13.70 13.85	Acetic acid	227-229	56
24	$C_{15}H_{13}N_3O$	71.49 71.69	5.02 5.21	16.60 16.72	Water	80-81	55
25	$C_{20}H_{15}N_3O$	76.50 76.66	4.77 4.82	13.28 13.41	Ethanol	98-100	64
26	$C_{19}H_{18}N_4O_2$	68.18 68.25	5.33 5.43	16.53 16.76	Ethanol–water, 1:3	208-211	30
27	$C_{20}H_{20}N_4O_2$	68.79 68.95	5.82 5.79	16.01 16.08	Isopropanol	135-137	68
28	$C_{21}H_{25}N_3O_3$	68.50 68.64	6.95 6.86	11.40 11.44	Methanol	118-120	49
29	$C_{24}H_{21}N_3O_2$	78.19 78.45	5.15 5.76	11.98 11.44	Acetic acid	258-259	53

EXPERIMENTAL

IR spectra were taken on a Specord IR-75 spectrometer for suspensions of the materials in vaseline oil (1800-1500 cm^{-1}) and in hexachlorobutadiene (3600-2000 cm^{-1}). The frequencies of the stretching bands of the C–H bonds in the region 3050-2800 cm^{-1} are not reported. ^1H NMR spectra were taken on a Bruker WH-90/DS (90 MHz) instrument using $CDCl_3$ or DMSO-d_6 solvents and TMS internal standard.

The β-substituted ethylamines and γ-substituted propylamines were obtained from the Acros and Maybridge companies.

Parameters for the synthesized compounds are given in Tables 1 and 2.

2-[3-(1-Imidazolyl)propylaminomethylene]-5,5-dimethyl-1,3-cyclohexanedione (6), 5,5-Dimethyl-2-[3-(2-oxopyrrolidin-1-yl)propylaminomethylene]-1,3-cyclohexanedione (7), 2-[3-(1-Imidazolyl)propyl-aminomethylene]-1,3-indanedione (13), 2-[3-(4-Morpholyl)propylaminomethylene]-1,3-indanedione (14), 2-[3-(2-Oxopyrrolidin-1-yl)propylaminomethylene]-1,3-indanedione (15), and 2-(2-Pyridyl)methylamino-methylene-1,3-indanedione (17). A solution of an equimolar amount of the free amine **2** in ethanol (15-20 ml), at the same temperature, was added to a solution of the acylcyclanedione **1** (5 mmol) in ethanol (15 ml) which had been heated to reflux. After 2 h, the product was filtered off and recrystallized.

2-[2-(4-Imidazolyl)ethylaminomethylene-1,3-cyclohexanedione (3), 2-[2-(4-Imidazolyl)ethylamino-methylene-5,5-dimethyl-1,3-cyclohexanedione (5), and 2-[2-(3-Indolyl)ethylaminomethylene]-5,5-dimethyl-1,3-cyclohexanedione (8). An aqueous solution of the amine hydrochloride **2** (3 mmol) in water (10 ml), at the

same temperature, was added to a solution of the acylcyclanedione **1** (3 mmol) in water (15 ml) which had been heated to 70-80°C. After 2 h, the product was filtered off and recrystallized.

2-[2-(4-Imidazolyl)ethylaminomethylene]-1,3-indanedione (12), 2-[2-(3-Indolyl)ethylamino-methylene]-1,3-indanedione (16), and 3-(1-[2-(3-Indolyl)ethylamino]ethylidene)-6-methyl-2,4-pyrandione (18). The acylcyclanedione **1** (3 mmol), an equimolar amounts of $NaHCO_3$ and the amine hydrochloride **2** were refluxed for 15 min (in the case of the product **18,** four hours) in ethanol (30 ml). The reaction mixture was cooled, the NaCl filtered off, half of the solvent distilled off, and the product was left in the fridge for one day. The precipitate was filtered off and recrystallized.

2-[3-(1-Imidazolyl)propylaminomethylene]-1,3-cyclohexanedione (4), 2-[3-(2-Oxopyrollidin-1-yl)propylaminomethylene]-5-phenyl-1,3-cyclohexanedione (9), 2-[3-1-(Imidazolyl)propylamino-methylene]-5-(2-furyl)-1,3-cyclohexanedione (10), 2-[2-(1-Piperazinyl)ethylaminomethylene]-5-(2-furyl)-1,3-cyclohexanedione (11). The potassium salt of the corresponding acylcyclanedione **1** (2.5 mmol), an equimolar amount of amine **2**, and 1 drop of concentrated HCl in ethanol (30 ml) were refluxed for 5 min. KCl was filtered off from the hot reaction mixture and the filtrate was left in the fridge for one day. The precipitate was filtered off and recrystallized.

3-[2-(4-Imidazolyl)ethyl]-2-methyl-4(3H)-quinazolinone (20). The benzoxazine **19a** (0.81 g, 5 mmol), hydrochloride **2a** (1.01 g, 5.5 mmol) and K_2CO_3 (1.52 g, 11 mmol) in DMF (30 ml) were refluxed for 1 h. Solvent (20-25 ml) was distilled off on a rotary evaporator and the residue was cooled. The precipitate was filtered off and recrystallized from water.

3-[3-(1-Imidazolyl)propyl]-2-methyl-4(3H)-quinazolinone (21) and 2-Methyl-3-[3-(2-oxopyrrolidin-1-yl)propyl]-4(3H-quinazolinone (22). The benzoxazine **19a** (5 mmol) and an equimolar amount of the amine **2b** or **2d** respectively in glacial acetic acid (15 ml) were refluxed for 8 h. The solvent was evaporated off on a rotary evaporator and the remaining oily product was recrystallized.

3-[2-(3-Indolyl)ethyl]-2-methyl-4(3H)-quinazolinone (23). The benzoxazine **19a** (5 mmol) and hydrochloride **2f** (5 mmol) in glacial acetic acid (15 ml) were refluxed for 4 h. The precipitate formed on cooling was mixed with aqueous $NaHCO_3$ solution, filtered, and recrystallized.

2-Methyl-3-(2-pyridinyl)methyl-4(3H)-quinazolinone (24) and 3-(2-Pyridyl)methyl-2-phenyl-4(3H)-quinazolinone (25). Equimolar amounts of the amine **2g** and benzoxazine **19** were melted in a wide tube for 1.5 h at 150°C (bath temperature). The melt was cooled and recrystallized.

N-Benzoylanthranilic Acid 2-(4-Imidazolyl)ethylamide (26). The benzoxazine **19b** (0.56 g, 2.5 mmol), dihydrochloride **2a** (0.50 g, 2.7 mmol), and K_2CO_3 (0.75 g, 5.4 mmol) in DMF (15 ml) were refluxed for 1 h. The precipitate was filtered off, the filtrate was evaporated to one third volume, and water (30 ml) was added. The precipitated solid was filtered off and recrystallized.

N-Benzoylanthranilic Acid 3-(1-Imidazolyl)propylamide (27) and 3-(4-Morpholyl)propylamide (28). Equimolar amounts of the benzoxazine **19b** and the amine **2b** or **2c** were melted in a wide tube for 1.5 h at 150°C (bath temperature). The melt was cooled and recrystallized.

N-Benzoylanthranilic Acid 2-(3-Indolyl)ethylamide (29). The benzoxazine **19b** and hydrochloride **2f** (each 2.5 mmol) in glacial acetic acid (15 ml) were refluxed for 8 h. The precipitate formed on cooling was filtered off, mixed with aqueous $NaHCO_3$ solution, and again filtered and recrystallized.

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