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SYNTHESIS OF QUINOLIN-2-ONES BY AN INTRAMOLECULAR KNOEVENAGEL CONDENSATION AND BY TANDEM MICHAEL-KNOEVENAGEL HETEROCYCLIZATION

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The synthesis of 2-(N-R-amino)- and 2-(N-vinylcarbonylamino)acylbenzenes has been carried out and their heterocyclization into quinolin-2-ones under the action of sodium ethylate has been studied.

Keywords: acyl-2-(N-acylamino)benzenes, acyl-2-vinylcarbonylaminobenzenes, quinolin-2-ones, intramolecular Knoevenagel condensation, tandem heterocyclization.

Compounds containing the quinolin-2-one fragment have already been studied systematically as subjects of medicobiological investigations for more than 50 years. Since then it was discovered that quinolin-2-ones as structural units, form part of the composition of a series of natural alkaloids [1]. The investigations led to a remarkable result, but only in practically the last 10-12 years, when new biological targets were discovered and test systems based on them were designed and in practice highly coeffective screening was embodied in the search for new medicinals. It was established that derivatives of quinolin-2-ones may display properties of nonsteroidal selective androgen modulators [2-4] and may show effective action against hepatitis B [5], act as inhibitors of acyl coenzyme A and cholesterol acyltransferase and increase the permeability of calcium activated K^+ channels [6, 7], display high antiproliferative activity [8-11] and the ability to bind to 5-HT_3 receptors [12], to receptors of antibiotics [13], and are inhibitors of various types of kinase [14-17], of farnesyl transferase [18], and affect erectile dysfunction [19]. The established broad spectrum of biological activity of quinolin-2-ones derivatives studied up to the present time, on the one hand, stimulated the search of new medicinals of various profile based on them, and on the other, made urgent the problem of synthesizing new representatives of this class with the prospect of developing for them characteristic forms of biological activity and the potential of using them for practical purposes.

For the synthesis of new derivatives of quinolin-2-ones, we turned to the Knoevenagel intramolecular condensation using as precursor the corresponding derivatives of *ortho*-aminoacylbenzenes. This route to the synthesis of quinolin-2-one, comprising the heterocyclization of 2-(acetylamino)acetophenone under the action of aqueous alcoholic alkaline solution, was used for the first time in [20]. However, many years passed before a series of quinolin-2-ones was synthesized in a similar manner [21, 22]. In all probability, insufficient attention to this method of synthesis was linked with the difficulties of obtaining the starting *ortho*-aminoacylbenzenes.

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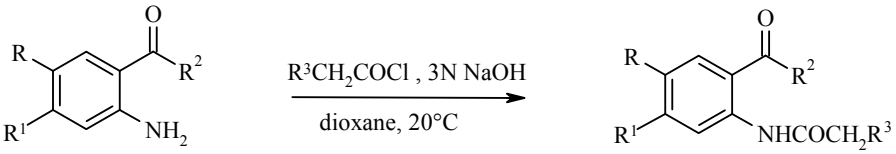
This was confirmed, for example, by the fact that with the development of new approaches to the synthesis of *ortho*-aminoacylbenzenes, the intramolecular Knoevenagel condensation as a method of heterocyclization in quinolin-2-ones became used more intensively [5, 15, 18, 19].

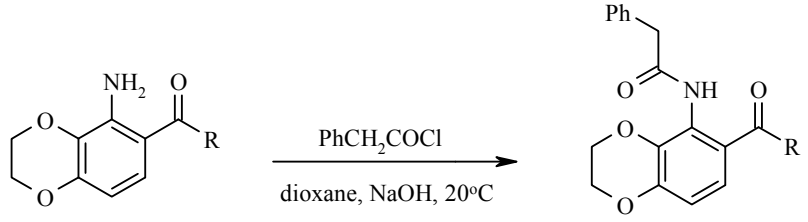
Previously, in a brief communication [23], we showed that by the Knoevenagel reaction it was possible to synthesize the corresponding quinolin-2-ones from *ortho*-amino ketones of the 1,4-benzodioxane series. The condensation occurs in alcohol at 20°C in the presence of an equimolecular quantity of sodium ethylate. In the present work we have studied the behavior of a series of *ortho*-(R-acetylamino)acylbenzenes under the action of the same reagent to obtain functionalized quinolin-2-ones.

The starting *ortho*-(R^3-acetylamino)acylbenzenes **20-49** were obtained by the acylation of *ortho*-acylanilines **1-19** with acid chlorides of substituted acetic acids. Most of the *ortho*-acylanilines **1-5, 7-14, 17-19** used were synthesized as described in [23-28], but 6-amino-7-butyroyl-1,4-benzodioxane (**6**), 6-amino-7-(2-iodobenzoyl)-1,4-benzodioxane (**15**), and 2-amino-4,5-dimethoxyacetophenone (**16**), were obtained by the reduction of the corresponding nitro compounds (see EXPERIMENTAL).



1–17 **20–47**

1–3 R = H, **1** R^1 = *t*-Bu, R^2 = Me; **2** R^1 = H, R^2 = Et; **3** R^1 = Br, R^2 = Et; **4–15** R + R^1 = OCH_2CH_2O,
4 R^2 = Me, **5** R^2 = Et, **6** R^2 = Pr, **7** R^2 = *cyclo*-Pr, **8** R^2 = Ph, **9** R^2 = *p*-MeC_6H_4, **10** R^2 = *m*-FC_6H_4,
11 R^2 = *p*-FC_6H_4, **12** R^2 = *o*-ClC_6H_4, **13** R^2 = *p*-ClC_6H_4, **14** R^2 = *o*-BrC_6H_4, **15** R^2 = *o*-IC_6H_4;
16, 17 R = R^1 = OMe, **16** R^2 = Me; **17** R^2 = *cyclo*-Pr; **20–23** R = H, **20** R^1 = *t*-Bu, R^2 = Me, R^3 = *o*-$MeOC_6H_4$;
21 R^1 = H, R^2 = Et, R^3 = Ph; **22** R^1 = Br, R^2 = Et, R^3 = Ph; **23** R^1 = Br, R^2 = Et, R^3 = *o*-$MeOC_6H_4$;
24–45 R + R^1 = OCH_2CH_2O, **24** R^2 = Me, R^3 = Ph; **25** R^2 = Me, R^3 = *o*-$MeOC_6H_4$; **26** R^2 = Et, R^3 = Ph;
27 R^2 = Pr, R^3 = Me; **28** R^2 = Pr, R^3 = Ph; **29** R^2 = Pr, R^3 = *o*-$MeOC_6H_4$; **30** R^2 = *cyclo*-Pr, R^3 = Ph;
31 R^2 = *cyclo*-Pr, R^3 = *p*-$NO_2C_6H_4$; **32** R^2 = R^3 = Ph; **33** R^2 = *p*-MeC_6H_4, R^3 = *p*-ClC_6H_4O;
34 R^2 = *p*-MeC_6H_4, R^3 = CH_2Br; **35** R^2 = *p*-MeC_6H_4, R^3 = *p*-$NO_2C_6H_4$; **36** R^2 = *m*-FC_6H_4, R^3 = Ph;
37 R^2 = *p*-FC_6H_4, R^3 = CH_2Br; **38** R^2 = *o*-ClC_6H_4, R^3 = *p*-$NO_2C_6H_4$; **39** R^2 = *p*-ClC_6H_4, R^3 = Pr;
40 R^2 = *p*-ClC_6H_4, R^3 = Ph; **41** R^2 = *p*-ClC_6H_4, R^3 = *o*-$MeOC_6H_4$; **42** R^2 = *p*-ClC_6H_4, R^3 = *p*-$NO_2C_6H_4$;
43 R^2 = *o*-BrC_6H_4, R^3 = Ph; **44** R^2 = *o*-IC_6H_4, R^3 = Ph; **45** R_2 = *o*-IC_6H_4, R^3 = *o*-$MeOC_6H_4$;
46, 47 R = R^1 = OMe, **46** R^2 = Me, R^3 = Ph; **47** R^2 = *cyclo*-Pr, R^3 = Ph

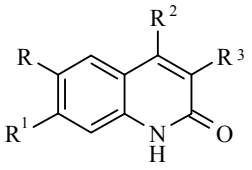


18, 19 **48, 49**

18, 48 R = Me; **19, 49** R = *i*-Pr

All the R-acylaminobenzenes **20-49** had not been obtained previously, their yields and physicochemical characteristics are given in Tables 1-3.

We found further, that if the reaction of *ortho*-arylacetylaminoacylbenzenes **20-26, 28-32, 35, 36, 38, 40-47** was carried out under the conditions described in [23] (equivalent quantity of sodium ethylate, in alcohol, 20°C), the heterocyclization, irrespective of the nature of the substituents in the aromatic ring of the starting anilides, was effected practically regioselectively and the corresponding quinolin-2-ones **50-72** were formed in high yield (see Tables 2, 4-6). The substituents R, R^1, R^2, and R^3 are identical with the substituents of these in the starting anilides respectively.

20–26, 28–32, 35, 36, 38, 40–47 → EtONa (1 equiv.), EtOH, 20°C → 

50–72

TABLE 1. Characteristics of Compounds **20-49**

Compound	Empirical formula	Found, % / Calculated, %			mp, °C*	Yield, %
		C	H	N		
1	2	3	4	5	6	7
20	$C_{21}H_{25}NO_3$	74.01 / 74.31	7.31 / 7.42	3.92 / 4.13	90-91	83
21	$C_{17}H_{17}NO_2$	76.11 / 76.38	6.94 / 6.41	5.03 / 5.24	67-68	88
22	$C_{17}H_{16}BrNO_2$	59.12 / 58.97	4.51 / 4.66	3.88 / 4.05	92-93	85
23	$C_{18}H_{18}BrNO_3$	57.16 / 57.46	4.65 / 4.82	3.51 / 3.72	100-101	76
24	$C_{18}H_{17}NO_4$	69.31 / 69.44	5.32 / 5.50	4.47 / 4.50	132-133	86
25	$C_{19}H_{19}NO_5$	66.72 / 66.85	5.41 / 5.61	4.01 / 4.10	167-168	79
26	$C_{19}H_{19}NO_4$	70.02 / 70.14	5.72 / 5.89	4.26 / 4.31	151-152	87
27	$C_{15}H_{19}NO_4$	64.71 / 64.96	6.81 / 6.91	4.97 / 5.05	128-129	81
28	$C_{20}H_{21}NO_4$	70.43 / 70.78	6.02 / 6.24	3.98 / 4.13	91-92	77
29	$C_{21}H_{23}NO_5$	67.95 / 68.28	6.11 / 6.28	3.64 / 3.79	126-127	68
30	$C_{20}H_{19}NO_4$	71.01 / 71.20	5.47 / 5.68	3.91 / 4.15	137-138	91
31	$C_{20}H_{18}N_2O_6$	62.61 / 62.82	4.56 / 4.74	7.23 / 7.33	122-123	87
32	$C_{23}H_{19}NO_4$	73.65 / 73.98	5.01 / 5.13	3.69 / 3.75	167-168	94
33	$C_{24}H_{20}ClNO_5$	65.61 / 65.83	4.48 / 4.60	3.12 / 3.20	199-201	76
34	$C_{19}H_{18}BrNO_4$	56.21 / 56.45	4.38 / 4.49	3.41 / 3.47	135-136	79
35	$C_{24}H_{20}N_2O_6$	66.31 / 66.66	4.51 / 4.66	6.33 / 6.48	137-138	82
36	$C_{23}H_{18}FNO_4$	70.26 / 70.58	4.51 / 4.63	3.52 / 3.58	157-158	85
37	$C_{18}H_{15}BrFNO_4$	52.71 / 52.96	3.62 / 3.70	3.24 / 3.43	94-95	84
38	$C_{23}H_{17}ClN_2O_6$	60.78 / 61.00	3.61 / 3.78	6.01 / 6.19	191-192	91
39	$C_{20}H_{20}ClNO_4$	64.01 / 64.26	5.16 / 5.39	3.71 / 3.75	114-115	83
40	$C_{23}H_{18}ClNO_4$	67.51 / 67.73	4.31 / 4.45	3.35 / 3.44	138-139	89
41	$C_{24}H_{20}ClNO_5$	65.71 / 65.83	4.44 / 4.60	3.11 / 3.20	156-157	91

TABLE 1 (continued)

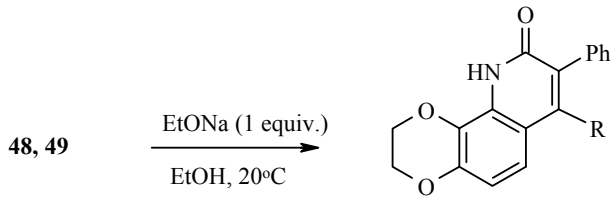
1	2	3	4	5	6	7
42	$C_{23}H_{17}ClN_2O_6$	60.74 / 61.00	3.51 / 3.78	6.04 / 6.19	140-141	77
43	$C_{23}H_{18}BrNO_4$	60.95 / 61.08	3.91 / 4.01	2.93 / 3.10	147-148	76
44	$C_{23}H_{18}INO_4$	54.96 / 55.33	3.41 / 3.63	2.62 / 2.81	158-159	81
45	$C_{24}H_{20}INO_5$	54.21 / 54.46	3.64 / 3.81	2.41 / 2.65	144-145	71
46	$C_{18}H_{19}NO_4$	68.78 / 68.99	5.93 / 6.11	4.21 / 4.47	137-138	90
47	$C_{20}H_{21}NO_4$	70.62 / 70.78	6.09 / 6.24	4.07 / 4.13	121-122	77
48	$C_{18}H_{17}NO_4$	69.22 / 69.44	5.32 / 5.51	4.38 / 4.50	91-92	79
49	$C_{20}H_{21}NO_4$	70.51 / 70.78	6.14 / 6.24	3.98 / 4.13	114-115	81

*Solvents for recrystallization: EtOH (compounds **20-27, 29**, **30, 34, 35, 37, 39, 40, 45, 47-49**) and EtOH–$CHCl_3$, 1:1 mixture (compounds **28, 31-33, 36, 38, 41-44, 46**).

TABLE 2. Mass Spectra of Compounds **20, 26, 32, 36, 40, 59, 64, 67**

Compound	*m/z* (I_{rel}, %)
20	339 $[M]^+$ (4), 218 (46), 191 (26), 176 (8), 148 (23), 132 (10), 121(38), 91 (100), 77 (16), 65 (24), 57 (13), 43 (61)
26	325 $[M]^+$ (69), 296 (35), 234 (78), 207 (65), 188 (20), 178 (83), 91 (100), 77 (8), 65 (41), 57 (44), 51 (13), 39 (27)
32	373 $[M]^+$ (56), 282 (100), 255 (98), 204 (26), 178 (9), 171 (11), 143 (19), 105 (60), 91 (65), 77 (59), 65 (34), 51 (24), 39 (20)
36	391 $[M]^+$ (30), 300 (48), 273 (65), 204 (9), 161 (14), 123 (65), 91 (100), 75 (11), 65 (42), 51 (13), 39 (26)
40	407 $[M]^+$ (41), 318 (35), 316 (100), 290 (55), 289 (98), 204 (9), 141 (16), 139 (21), 98 (14), 91 (43), 59 (26), 43 (36)
59	319 $[M]^+$ (100), 304 (15), 291 (35), 262 (12), 235 (24), 206 (21), 178 (17), 152 (31), 139 (26), 115 (25), 102 (24), 89 (26), 77 (36), 68 (36), 51 (37), 39 (55)
64	434 $[M]^+$ (56), 399 (36), 353 (26), 297 (36), 269 (30), 256 (21), 240 (99), 226 (36), 213 (79), 200 (60), 187 (38), 176 (52), 163 (37), 149 (72), 141 (46), 126 (46), 107 (82), 94 (100), 87 (35), 75 (55), 68 (85), 55 (65), 41 (95)
67	434 $[M]^+$ (100), 386 (6), 240 (29), 214 (12), 200 (10), 187 (25), 176 (16), 163 (10), 140 (10), 120 (21), 106 (58), 99 (28), 87 (26), 75 (41), 68 (84), 50 (42), 44 (61)

5-Phenacetylamino-substituted 6-acyl-1,4-benzodioxanes **48, 49** were cyclized in a similar manner under the same conditions.



73 R = Me; **74** R = *i*-Pr

TABLE 3. ^{1}H NMR Spectra of Compounds **20-49**

Com-pound	Chemical shifts*, δ, ppm (*J*, Hz)
1	2
20	1.35 (9H, s, C(CH$_3$)$_3$); 2.61 (3H, s, CH$_3$CO); 3.79 (2H, s, CH$_2$Ar); 3.87 (3H, s, CH$_3$O); 6.94 (1H, d, *J* = 7.6, H Ar); 6.99 (1H, t, *J* = 7.6, H Ar); 7.12 (1H, dd, *J* = 7.8, *J* = 2.0, H Ar); 7.33 (2H, m, H Ar); 7.78 (1H, d, *J* = 7.8, H Ar); 8.91 (1H, d, *J* = 2.0, H Ar); 11.67 (1H, s, NH)
21	1.21 (3H, t, *J* = 6.6, CH$_2$CH$_3$); 3.02 (2H, q, *J* = 6.6, CH$_2$CH$_3$); 3.77 (2H, s, CH$_2$Ph); 7.11 (1H, dt, *J* = 7.8, *J* = 1.4, H Ar); 7.31 (1H, m, H Ar); 7.41 (4H, m, H Ar); 7.52 (1H, dt, *J* = 7.8, *J* = 1.4, H Ar); 7.89 (1H, dd, *J* = 7.8, *J* = 1.4, H Ar); 8.75 (1H, dd, *J* = 7.8, *J* = 1.4, H Ar); 11.81 (1H, s, NH)
22	1.22 (3H, t, *J* = 7.2, CH$_2$CH$_3$); 2.98 (2H, q, *J* = 7.2, CH$_2$CH$_3$); 3.77 (2H, s, CH$_2$Ph); 7.23 (1H, dd, *J* = 7.8, *J* = 1.9, H Ar); 7.33 (1H, m, H Ar); 7.39 (4H, m, H Ar); 7.73 (1H, d, *J* = 7.8, H Ar); 9.02 (1H, s, H Ar); 11.85 (1H, s, NH)
23	1.19 (3H, t, *J* = 6.4, CH$_2$CH$_3$); 2.97 (2H, q, *J* = 6.4, CH$_2$CH$_3$); 3.79 (2H, s, CH$_2$Ar); 3.88 (3H, s, CH$_3$O); 6.94 (1H, d, *J* = 7.6, H Ar); 6.99 (1H, dt, *J* = 7.8, *J* = 1.2, H Ar); 7.21 (1H, dd, *J* = 8.4, *J* = 2.0, H Ar); 7.32 (2H, m, H Ar); 7.71 (1H, d, *J* = 8.4, H Ar); 9.03 (1H, s, H Ar); 11.68 (1H, s, NH)
24	2.51 (3H, s, CH$_3$CO); 3.75 (2H, s, CH$_2$Ph); 4.24 (2H, m) and 4.31 (2H, m, OCH$_2$CH$_2$O); 7.31 (1H, m, H Ar); 7.33 (1H, s, H Ar); 7.41 (4H, m, H Ar); 8.35 (1H, s, H Ar); 11.65 (1H, s, NH)
25	2.51 (3H, s, CH$_3$CO); 3.71 (2H, s, CH$_2$Ph); 3.85 (3H, s, CH$_3$O); 4.24 (2H, m) and 4.35 (2H, m, OCH$_2$CH$_2$O); 6.87 (1H, d, *J* = 7.8, H Ar); 6.98 (1H, t, *J* = 7.8, H Ar); 7.31 (3H, m, H Ar); 8.36 (1H, s, H Ar); 11.52 (1H, s, NH)
26	1.01 (3H, t, *J* = 7.2, CH$_2$CH$_3$); 2.98 (2H, q, *J* = 7.2, CH$_2$CH$_3$); 3.71 (2H, s, CH$_2$Ph); 4.23 (2H, m) and 4.33 (2H, m, OCH$_2$CH$_2$O); 7.24 (1H, m, H Ar); 7.33 (4H, m, H Ar); 7.62 (1H, s, H Ar); 8.01 (1H, s, H Ar); 11.51 (1H, s, NH)
27	0.91 (3H, t, *J* = 6.8, CH$_2$CH$_2$CH$_3$); 1.11 (3H, t, *J* = 6.4, CH$_2$CH$_3$); 1.61 (2H, m, CH$_2$CH$_2$CH$_3$); 2.38 (2H, q, *J* = 6.4, CH$_2$CH$_3$); 2.96 (2H, t, *J* = 6.7, CH$_2$CH$_2$CH$_3$); 4.25 (2H, m) and 4.35 (2H, m, OCH$_2$CH$_2$O); 7.54 (1H, s, H Ar); 8.07 (1H, s, H Ar); 11.48 (1H, s, NH)
28	0.99 (3H, t, *J* = 7.0, CH$_2$CH$_2$CH$_3$); 1.73 (2H, m, CH$_2$CH$_2$CH$_3$); 2.84 (2H, t, *J* = 6.7, CH$_2$CH$_2$CH$_3$); 3.75 (2H, s, CH$_2$Ph); 4.22 (2H, m) and 4.32 (2H, m, OCH$_2$CH$_2$O); 7.27 (1H, m, H Ar); 7.35 (4H, m, H Ar); 7.38 (1H, s, H Ar); 8.62 (1H, s, H Ar); 11.81 (1H, s, NH)
29	0.98 (3H, t, *J* = 7.2, CH$_2$CH$_2$CH$_3$); 1.74 (2H, m, CH$_2$CH$_2$CH$_3$); 2.85 (2H, t, *J* = 6.9, CH$_2$CH$_2$CH$_3$); 3.75 (2H, s, CH$_2$Ar); 3.86 (3H, s, CH$_3$O); 4.24 (2H, m) and 4.30 (2H, m, OCH$_2$CH$_2$O); 6.92 (1H, d, *J* = 8.2, H Ar); 6.97 (1H, t, *J* = 8.2, H Ar); 7.28 (2H, m, H Ar); 7.36 (1H, s, H Ar); 8.33 (1H, s, H Ar); 11.62 (1H, s, NH)
30	1.01 (2H, m, *cyclo*-Pr); 1.17 (2H, m, *cyclo*-Pr); 2.51 (1H, m, *cyclo*-Pr); 3.70 (2H, s, CH$_2$Ph); 4.26 (2H, m) and 4.32 (2H, m, OCH$_2$CH$_2$O); 7.29 (1H, m, H Ar); 7.37 (4H, m, H Ar); 7.59 (1H, s, H Ar);

TABLE 3 (continued)

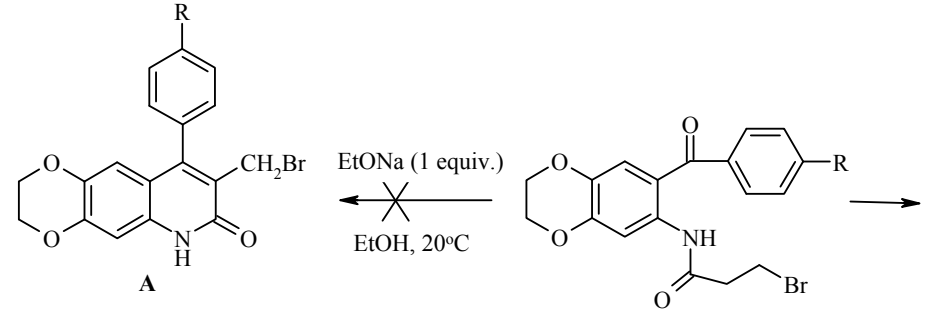
1	2
31	1.03 (2H, m, *c*-Pr); 1.17 (2H, m, *c*-Pr); 2.54 (1H, m, *c*-Pr); 3.81 (2H, s, C<u>H</u>$_2$Ph); 4.26 (2H, m) and 4.32 (2H, m, OCH$_2$CH$_2$O); 7.53 (2H, d, *J* = 8.4, H Ar); 7.62 (1H, s, H Ar); 8.20 (1H, s, H Ar); 8.24 (2H, d, *J* = 8.4, H Ar); 11.84 (1H, s, NH)
32	3.34 (2H, s, C<u>H</u>$_2$Ph); 4.25 (2H, m) and 4.33 (2H, m, OCH$_2$CH$_2$O); 6.88 (1H, s, H Ar); 7.15 (2H, d, *J* = 7.8, H Ar); 7.22 (1H, t, *J* = 7.8, H Ar); 7.28 (2H, m, H Ar); 7.42 (1H, s, H Ar); 7.49 (2H, m, H Ar); 7.62 (3H, m, H Ar); 10.35 (1H, s, NH)
33	2.45 (3H, s, CH$_3$); 4.26 (2H, m) and 4.35 (2H, m, OCH$_2$CH$_2$O); 4.59 (2H, s, C<u>H</u>$_2$OAr); 7.05 (2H, d, *J* = 8.3, H Ar); 7.14 (1H, s, H Ar); 7.28 (4H, m, H Ar); 7.61 (2H, d, *J* = 8.0, H Ar); 8.31 (1H, s, H Ar); 11.92 (1H, s, NH)
33	2.45 (3H, s, CH$_3$); 4.26 (2H, m) and 4.35 (2H, m, OCH$_2$CH$_2$O); 4.59 (2H, s, C<u>H</u>$_2$OAr); 7.05 (2H, d, *J* = 8.3, H Ar); 7.14 (1H, s, H Ar); 7.28 (4H, m, H Ar); 7.61 (2H, d, *J* = 8.0, H Ar); 8.31 (1H, s, H Ar); 11.92 (1H, s, NH)
34	2.45 (3H, s, CH$_3$); 3.02 (2H, t, *J* = 6.8, C<u>H</u>$_2$CH$_2$Br); 3.73 (2H, t, *J* = 6.8, CH$_2$C<u>H</u>$_2$Br); 4.25 (2H, m) and 4.35 (2H, m, OCH$_2$CH$_2$O); 7.12 (1H, s, H Ar); 7.29 (2H, d, *J* = 8.1, H Ar); 7.59 (2H, d, *J* = 8.1, H Ar); 8.28 (1H, s, H Ar); 11.19 (1H, s, NH)
35	2.45 (3H, s, CH$_3$); 3.85 (2H, s, C<u>H</u>$_2$Ar); 4.25 (2H, m) and 4.35 (2H, m, OCH$_2$CH$_2$O); 7.15 (1H, s, H Ar); 7.29 (2H, d, *J* = 7.4, H Ar); 7.54 (2H, d, *J* = 8.1, H Ar); 7.58 (2H, d, *J* = 7.4, H Ar); 8.18 (1H, s, H Ar); 8.22 (2H, d, *J* = 8.1, H Ar); 11.26 (1H, s, NH)
36	3.33 (2H, s, C<u>H</u>$_2$Ph); 4.26 (2H, m) and 4.33 (2H, m, OCH$_2$CH$_2$O); 6.89 (1H, s, H Ar); 7.12 (2H, d, *J* = 7.2, H Ar); 7.22 (1H, t, *J* = 7.2, H Ar); 7.26 (2H, m, H Ar); 7.31 (1H, s, H Ar); 7.34 (1H, m, H Ar); 7.40 (1H, m, H Ar); 7.44 (1H, m, H Ar); 7.51 (1H, m, H Ar); 10.31 (1H, s, NH)
37	3.02 (2H, t, *J* = 7.2, C<u>H</u>$_2$CH$_2$Br); 3.71 (2H, t, *J* = 7.2, CH$_2$C<u>H</u>$_2$Br); 4.25 (2H, m) and 4.35 (2H, m, OCH$_2$CH$_2$O); 7.06 (1H, s, H Ar); 7.17 (2H, m, H Ar); 7.71 (2H, m, H Ar); 8.26 (1H, s, H Ar); 11.11 (1H, s, NH)
38	3.92 (2H, s, C<u>H</u>$_2$Ar); 4.21 (2H, m) and 4.35 (2H, m, OCH$_2$CH$_2$O); 6.85 (1H, s, H Ar); 7.26 (1H, m, H Ar); 7.37 (1H, m, H Ar); 7.45 (2H, m, H Ar); 7.59 (2H, d, *J* = 8.6, H Ar); 8.25 (2H, d, *J* = 8.6, H Ar); 8.36 (1H, s, H Ar); 11.81 (1H, s, NH)
39	0.82 (3H, t, *J* = 6.4, CH$_2$CH$_2$CH$_2$C<u>H</u>$_3$); 1.12 (2H, m, CH$_2$CH$_2$C<u>H</u>$_2$CH$_3$); 1.28 (2H, m, CH$_2$C<u>H</u>$_2$CH$_2$CH$_3$); 2.02 (2H, t, *J* = 6.2, C<u>H</u>$_2$CH$_2$CH$_2$CH$_3$); 4.26 (2H, m) and 4.34 (2H, m, OCH$_2$CH$_2$O); 6.91 (1H, s, H Ar); 7.19 (1H, s, H Ar); 7.54 (2H, d, *J* = 8.0, H Ar); 7.62 (2H, d, *J* = 8.0, H Ar); 9.95 (1H, s, NH)
40	3.41 (2H, s, C<u>H</u>$_2$Ph); 4.23 (2H, m) and 4.33 (2H, m, OCH$_2$CH$_2$O); 6.88 (1H, s, H Ar); 7.10 (2H, d, *J* = 7.5, H Ar); 7.21 (1H, t, *J* = 7.5, H Ar); 7.25 (2H, m, H Ar); 7.28 (1H, s, H Ar); 7.51 (2H, d, *J* = 8.4, H Ar); 7.59 (2H, d, *J* = 8.4, H Ar); 10.22 (1H, s, NH)
41	3.74 (2H, s, C<u>H</u>$_2$Ar); 3.83 (3H, s, CH$_3$O); 4.23 (2H, m) and 4.33 (2H, m, OCH$_2$CH$_2$O); 6.90 (1H, d, *J* = 8.1, H Ar); 6.97 (1H, s, H Ar); 6.98 (1H, t, *J* = 8.1, H Ar); 7.32 (2H, m, H Ar); 7.44 (2H, d, *J* = 8.4, H Ar); 7.60 (2H, d, *J* = 8.4, H Ar); 8.21 (1H, s, H Ar); 10.73 (1H, s, NH)
42	3.85 (2H, s, C<u>H</u>$_2$Ar); 4.22 (2H, m) and 4.31 (2H, m, OCH$_2$CH$_2$O); 7.05 (1H, s, H Ar); 7.46 (2H, d, *J* = 8.4, H Ar); 7.57 (4H, m, H Ar); 8.21 (1H, s, H Ar); 8.22 (2H, d, *J* = 8.6, H Ar); 11.21 (1H, s, NH)
43	3.78 (2H, s, C<u>H</u>$_2$Ph); 4.21 (2H, m) and 4.33 (2H, m, OCH$_2$CH$_2$O); 6.62 (1H, s, H Ar); 7.28 (1H, m, H Ar); 7.36 (4H, m, H Ar); 7.43 (1H, dd, *J* = 7.4, *J* = 1.9, H Ar); 7.47 (1H, dt, *J* = 7.8, *J* = 1.9, H Ar); 7.52 (1H, dt, *J* = 7.4, *J* = 1.3, H Ar); 7.74 (1H, dd, *J* = 7.8, *J* = 1.1, H Ar); 8.11 (1H, s, H Ar); 11.23 (1H, s, NH)
44	3.79 (2H, s, C<u>H</u>$_2$Ph); 4.21 (2H, m) and 4.32 (2H, m, OCH$_2$CH$_2$O); 6.60 (1H, s, H Ar); 7.28 (1H, m, H Ar); 7.36 (6H, m, H Ar); 7.52 (1H, dt, *J* = 7.6, *J* = 1.0, H Ar); 7.95 (1H, d, *J* = 7.8, H Ar); 8.12 (1H, s, H Ar); 11.27 (1H, s, NH)

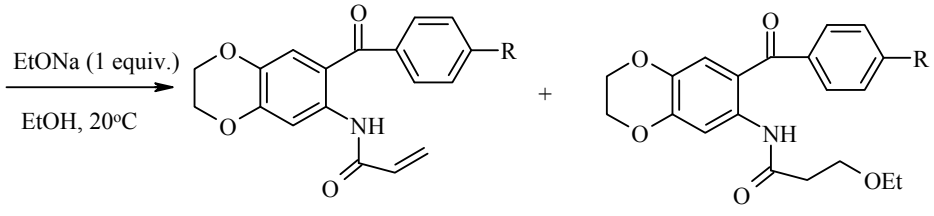
TABLE 3 (continued)

1	2
45	3.69 (2H, s, CH_2Ar); 3.82 (3H, s, OCH_3); 4.17 (2H, m) and 4.32 (2H, m, OCH_2CH_2O); 6.57 (1H, s, H Ar); 6.95 (1H, t, *J* = 8.0, H Ar); 7.03 (1H, d, *J* = 8.0, H Ar); 7.39 (5H, m, H Ar); 7.52 (1H, t, *J* = 8.0, H Ar); 7.94 (1H, d, *J* = 8.0, H Ar); 11.29 (1H, s, NH)
46	2.59 (3H, s, $COCH_3$); 3.75 (2H, s, $C\underline{H}_2Ph$); 3.90 (3H, s, CH_3O); 3.96 (3H, s, CH_3O); 7.25 (1H, s, H Ar); 7.32 (1H, m, H Ar); 7.39 (4H, m, H Ar); 8.54 (1H, s, H Ar); 12.06 (1H, s, NH)
47	1.06 (2H, m, *cyclo*-Pr); 1.22 (2H, m, *cyclo*-Pr); 2.57 (1H, m, *cyclo*-Pr); 3.73 (2H, s, $C\underline{H}_2Ph$); 3.93 (3H, s, CH_3O); 3.96 (3H, s, CH_3O); 7.28 (1H, m, H Ar); 7.37 (4H, m, H Ar); 7.51 (1H, s, H Ar); 8.51 (1H, s, H Ar); 12.01 (1H, s, NH)
48	2.51 (3H, s, $COCH_3$); 3.52 (2H, s, $C\underline{H}_2Ph$); 4.26 (2H, m) and 4.35 (2H, m, OCH_2CH_2O); 6.75 (1H, d, *J* = 8.8, H Ar); 7.30 (1H, d, *J* = 8.8, H Ar); 7.35 (1H, m, H Ar); 7.40 (4H, m, H Ar); 9.02 (1H, s, NH)
49	1.11 (6H, d, *J* = 7.0, $CH(C\underline{H}_3)_2$); 3.35 (1H, sept, *J* = 7.0, $C\underline{H}(CH_3)_2$); 3.75 (2H, s, $C\underline{H}_2Ph$); 4.26 (2H, m) and 4.33 (2H, m, OCH_2CH_2O); 6.74 (1H, d, *J* = 8.9, H Ar); 7.24 (1H, d, *J* = 8.9, H Ar); 7.31 (1H, m, H Ar); 7.38 (4H, m, H Ar); 9.01 (1H, s, NH)

*The ^1H NMR spectra of compounds **20, 21, 24, 25, 28-31**, **33-35, 37, 38, 41, 42, 46-49** were recorded in $CHCl_3$, and of compounds **22, 23, 26, 27, 32, 36, 39, 40, 43-45** in DMSO-d_6.

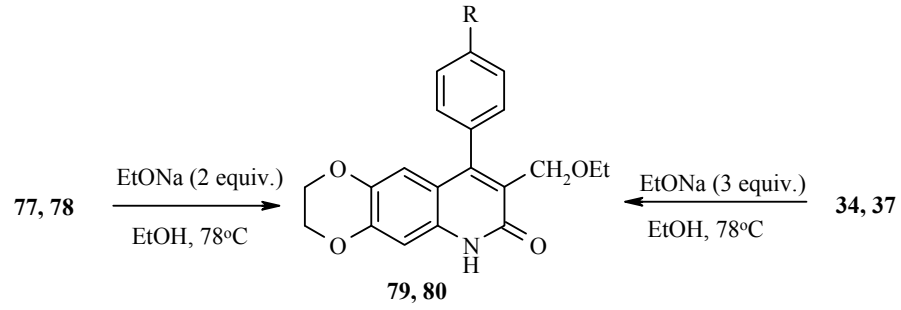
In contrast to this, derivatives of alkyl (compounds **27, 39**) or aryloxy (compound **33**) substituted acetic acids did not react, but derivatives of β-bromopropionic (bromomethylacetic) acid **34, 37** were converted into the products of hydrogen bromide elimination (compounds **75, 76**) and nucleophilic substitution of the halogen atom (compounds **77, 78**), and not into quinolin-2-ones of type A.





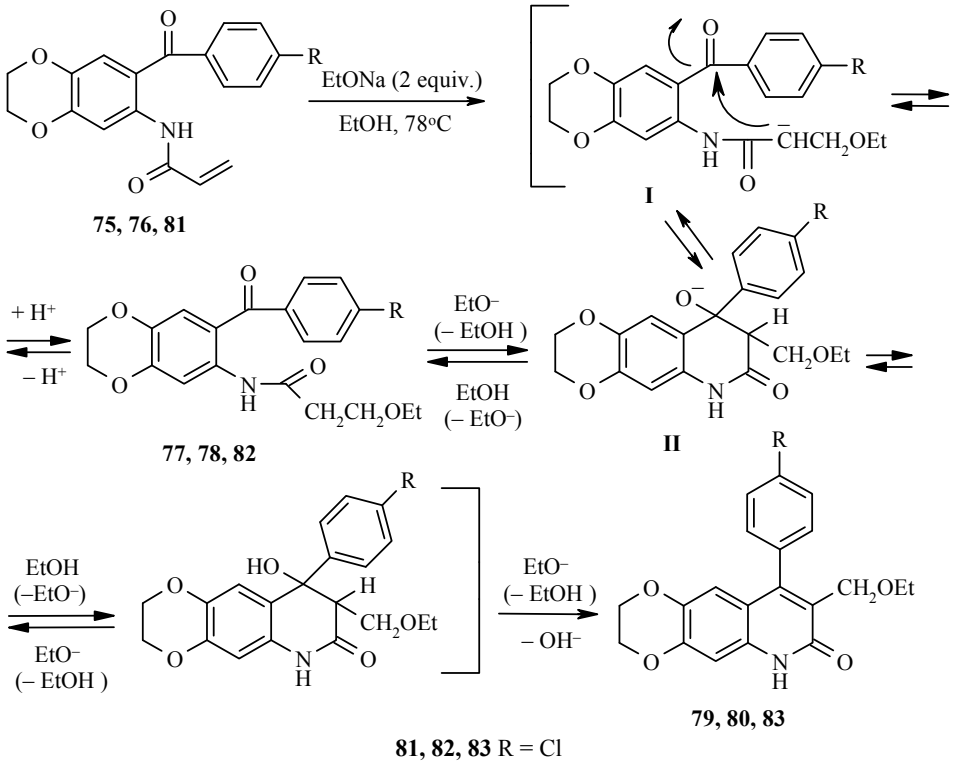
75, 77 R = Me; **76, 78** R = F

It turned out that if the alkoxy derivatives **77, 78** were treated repeatedly with 2 equiv. sodium ethylate, and β-bromomethylacetylamines **34, 37** were reacted with 3 equiv. alcoholate and the reaction was carried out with heating, then in both cases alkoxy-substituted quinolin-2-ones **79, 80** were formed in high yield.



34, 77, 79 R = Me; **37, 78, 80** R = F

When transforming β-haloethylcarbonylamino-substituted acylbenzenes **34, 37** into alkoxy-substituted quinolin-2-ones **79, 80,** two separate and subsequent processes are undergoing. 1) Conversion of the starting anilides **34**, **37** into alkoxyethylcarbonylamino-1,4-benzodioxanes **77**, **78**, in all probability, occurs in an excess of alcoholate by way of both the direct substitution reaction of the halogen atom by an alkoxy group, and addition of ethanol to the α,β-vinyl group of compounds **75, 76**, catalyzed by alcoholate, and 2) subsequent condensation into quinolin-2-ones **79**, **80**.



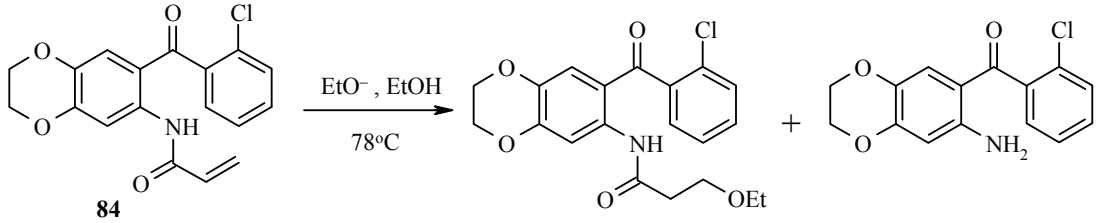
81, 82, 83 R = Cl

Indirect confirmation of the fact that the β-alkoxyethylcarbonyl fragment in compounds **77, 78** may be formed from the vinylcarbonyl substituent in the process of base-catalyzed addition of alcohol according to Michael, is the conversion of 6-acyl-7-vinylcarbonylamino-1,4-benzodioxanes **75, 76, 81** into the corresponding alkoxy-substituted quinolin-2-ones **79, 80, 83** under heterocyclization conditions.

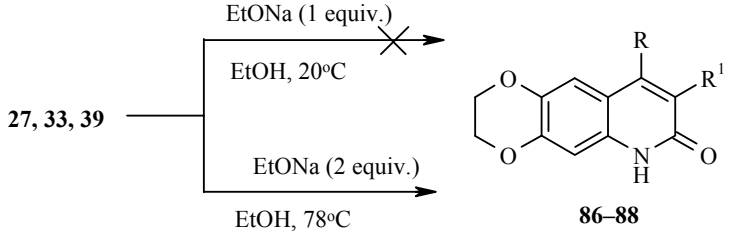
It is seen from the scheme that the formation of quinolinones **79, 80, 83** may occur both through the stage of forming addition products of ethanol to the vinylcarbonyl group according to Michael **77, 78, 82** and through the stage of forming the cyclic ion **II**, obtained in the process of adding alcohol according to a pseudo-Michael reaction involving the carbonyl group in the *ortho*-position to the vinyl-containing substituent. It is interesting that if the reaction of vinylcarbonylamino-substituted acylbenzenes **75, 76, 81** is completed with the formation of the corresponding quinolinones, analogously substituted benzodioxane **84** containing a 2-chloro-benzoyl group in the *ortho*-position is mainly converted into the product of Michael addition **85**. In this way, a partial cleavage of the amide bond is observed with the formation of 7-acyl-6-amino-1,4-benzodioxane **12**.

The obtained result shows that alkoxy-substituted acylaminobenzenes, the immediate precursors of the corresponding quinolinones, may in reality be formed from the vinylcarbonyl fragments by a Michael reaction. Regarding the impossibility of compound **85** to give products of heterocyclization, it is evident that the heterocyclization stage to the corresponding quinolinone is inhibited due to steric factors.

On the whole, irrespective of the fact that whether products of addition according to Michael are formed or heterocyclization into the corresponding quinolin-2-ones is effected through anions of types **I, II** (see scheme on p. 1112), arising at the stage of adding ethylate anion to the double bond of the vinylcarbonyl group, the process of forming alkoxy-substituted quinolin-2-ones (of type **79, 80, 83**) from *ortho*-acylanilides of acrylic acid (of type **75, 76, 81**) under the action of sodium ethylate may be considered as a tandem heterocyclization.



It is interesting to note that if 3 equiv. alcoholate and heating are necessary for complete conversion of β-haloethylcarbonylamino-substituted benzodioxanes **34, 37** into the corresponding quinolin-2-ones **79, 80**, then compounds **27, 33**, and **39** were practically unchanged by the action of 1 equiv. sodium ethylate at 20°C, but underwent complete conversion into the corresponding quinolin-2-ones **86-88** at a substrate–sodium ethylate ratio of 1:2 in boiling alcohol.



27, 86 R = Pr, R^1 = Me; **33, 87** R = *p*-MeC_6H_4, R^1 = *p*-ClC_6H_4O;
39, 88 R = *p*-ClC_6H_4, R^1 = Pr

According to the scheme of the intramolecular variant of the Knoevenagel condensation of *N*-acylamino-substituted acylbenzenes **20-49, 77, 78** studied by us, this conversion may be effected under the action of even catalytic quantities of alcoholate, moreover, this reaction may be initiated by released hydroxide anion [21, 22].

Probably, since the positive charge on the carbon atom of the carbonyl group in the present case is lower than in the classical variant of the Knoevenagel condensation, the process is conducted significantly more slowly. In our case, it is therefore necessary to use a larger quantity of alcoholate to achieve complete conversion of the starting substrates into quinolin-2-ones. In reality, we have established that under the action of catalytic amounts of sodium ethylate chromatographically appreciable quantities of condensation products are formed only after 10-12 h.

TABLE 4. Characteristics of Quinolin-2-ones **50-74, 79, 80, 83, 86-88**

Compound	Empirical formula	Found, % / Calculated, %			mp., °C*	Yield, %
		C	H	N		
1	2	3	4	5	6	7
50	$C_{21}H_{23}NO_2$	78.12 78.47	7.03 7.21	4.11 4.36	238–239	76
51	$C_{17}H_{15}NO$	81.54 81.91	6.23 6.06	5.66 5.62	224–225	69
52	$C_{17}H_{14}BrNO$	62.30 62.21	4.31 4.30	4.28 4.27	232–233	86
53	$C_{18}H_{16}BrNO_2$	60.15 60.35	4.66 4.50	4.15 3.91	237–238	83
54	$C_{18}H_{15}NO_3$	73.61 73.71	4.96 5.15	4.63 4.78	323–324	92
55	$C_{19}H_{17}NO_4$	70.32 70.58	5.17 5.30	4.21 4.33	293–294	93
56	$C_{19}H_{17}NO_3$	74.02 74.25	5.50 5.58	4.38 4.56	311–312	88
57	$C_{20}H_{19}NO_3$	74.38 74.75	5.78 5.96	4.18 4.36	297–298	87
58	$C_{21}H_{21}NO_4$	71.52 71.78	5.88 6.02	4.11 3.99	269–271	81
59	$C_{20}H_{17}NO_3$	74.92 75.22	5.28 5.37	4.24 4.39	301–302	91
60	$C_{20}H_{16}N_2O_5$	65.69 65.93	4.54 4.43	7.78 7.69	402–404	89
61	$C_{23}H_{17}NO_3$	77.69 77.73	4.65 4.82	4.05 3.94	353–354	92
62	$C_{24}H_{18}N_2O_5$	69.23 69.56	4.21 4.38	6.62 6.76	392–394	82
63	$C_{23}H_{16}FNO_3$	73.82 73.99	4.24 4.32	3.73 3.75	354–355	95
64	$C_{23}H_{15}ClN_2O_5$	62.96 63.53	3.57 3.48	6.22 6.44	250–270	86
65	$C_{23}H_{16}ClNO_3$	70.52 70.86	3.96 4.14	3.71 3.59	398–400	93
66	$C_{24}H_{18}ClNO_4$	68.41 68.66	4.19 4.32	3.31 3.34	328–329	92
67	$C_{23}H_{15}ClN_2O_5$	63.32 63.53	3.33 3.48	6.38 6.44	405–407	79
68	$C_{23}H_{16}BrNO_3$	63.36 63.61	3.51 3.71	3.25 3.23	382–383	81
69	$C_{23}H_{16}INO_3$	56.94 57.40	3.17 3.35	2.83 2.91	400–401	88
70	$C_{24}H_{18}INO_4$	56.48 56.38	3.57 3.55	2.59 2.74	322–323	74

TABLE 4 (continued)

1	2	3	4	5	6	7
72	$C_{20}H_{19}NO_3$	74.52 74.74	5.54 5.96	4.31 4.36	281-282	84
73	$C_{18}H_{15}NO_3$	74.00 73.71	5.35 5.15	4.94 4.78	225-226	71
74	$C_{20}H_{19}NO_3$	74.61 74.75	5.93 5.96	4.20 4.36	232-233	65
79	$C_{21}H_{21}NO_4$	71.59 71.78	5.87 6.02	3.91 3.99	268-269	86
80	$C_{20}H_{18}FNO_4$	67.45 67.60	5.16 5.10	3.76 3.94	244-245	95
83	$C_{20}H_{18}ClNO_4$	64.70 64.61	4.95 4.88	3.64 3.77	264-265	93
86	$C_{15}H_{17}NO_3$	69.27 69.48	6.48 6.61	5.26 5.41	269-270	52
87	$C_{24}H_{18}ClNO_4$	68.41 68.66	4.19 4.32	3.21 3.34	321-322	78
88	$C_{20}H_{18}ClNO_3$	67.42 67.51	4.96 5.10	3.88 3.94	325-326	75

*Solvents for recrystallization: EtOH (compounds **50-55, 58**, **70, 73, 74, 79, 80, 83, 86, 88**) and EtOH–$CHCl_3$, 1:1 mixture (compounds **56, 57, 59-69, 71, 72, 87**).

The lower proton mobility of hydrogen atoms in the methylene component of the starting substrates **27, 33, 39, 77, 78** (in comparison with classical substrates) leads to the fact that their heterocyclization into the corresponding quinolin-2-ones succeeds not only because of the increase in alcoholate concentration, but also as a result of an increase in times of the reaction and heating.

It is important to emphasize that under conditions of heterocyclization not only is the Knoevenagel intermolecular condensation not observed but also there is no formation of the isomeric quinolones (quinolin-4-ones) from substrates for which this is possible (compounds **20-29, 46, 48**).

EXPERIMENTAL

The IR spectra were recorded on a UR 20 instrument in nujol (compounds **51, 56, 60, 61, 64, 65, 70, 83**) or hexachlorobutadiene (compounds **59, 80**). The ^1H and ^{13}C NMR spectra were obtained on a Bruker Avance 400 instrument (at 400 MHz and 100 MHz respectively), internal standard was TMS. Mass spectra were recorded on a Finnigan SSQ 7000 (GC-MS type) instrument using a capillary column (30 m × 2 mm, stationary phase DB-1), carrier gas was helium (40 ml/min) with temperature programing from 50 to 300°C (10 deg/min). Ionization energy was 70 eV. Elemental analysis was carried out on a Vario-II CHN analyzer. A check on the purity of compounds obtained and the separation of certain reaction mixtures was effected by TLC on Al_2O_3, activity grade II (according to Brockmann) in the systems ether–petroleum ether (40-70°C), 1:3, or ether–CH_2Cl_2–petroleum ether (40-70°C), 1:1:3 by volume.

1-(7-Nitro-2,3-dihydro-1,4-benzodioxin-6-yl)butan-1-one was obtained by the nitration of 1-(2,3-dihydro-1,4-benzodioxin-6-yl)butan-1-one with acetyl nitrate in Ac_2O as described in [29]. Yield 84%; mp 90-91°C (EtOH). ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.02 (3H, t, *J* = 6.7 $CH_2CH_2C\underline{H}_3$); 1.79 (2H, m, $CH_2C\underline{H}_2CH_3$); 2.78 (2H, t, *J* = 6.8, $C\underline{H}_2CH_2CH_3$); 4.19 (4H, m, OCH_2CH_2O); 6.82 (1H, s, H-5); 7.71 (1H, s, H-8).

TABLE 5. ^{1}H NMR Spectra of Quinolin-2-ones **74, 79, 80, 83, 86-88**

Com-pound	Chemical shifts*, δ, ppm. (*J*, Hz)
1	2
50	1.34 (9H, s, $C(CH_3)_3$); 2.55 (3H, s, CH_3); 3.78 (3H, s, CH_3O); 7.03 (1H, d, *J* = 7.8, H Ar); 7.08 (1H, t, *J* = 7.8, H Ar); 7.25 (1H, dd, *J* = 7.8, *J* = 1.4, H Ar); 7.29 (2H, m, H Ar); 7.41 (1H, dt, *J* = 7.8, *J* = 1.4, H Ar); 7.69 (1H, d, *J* = 9.1, H Ar); 11.85 (1H, s, NH)
51	1.07 (3H, t, *J* = 7.1, $CH_2C\underline{H}_3$); 2.62 (2H, q, *J* = 7.1, $C\underline{H}_2CH_3$); 7.22 (3H, m, H Ar); 7.37 (2H, t, *J* = 8.0, H Ar); 7.44 (2H, t, *J* = 7.6, H Ar); 7.51 (1H, t, *J* = 7.6, H Ar); 7.81 (1H, d, *J* = 8.0, H Ar); 11.82 (1H, s, NH)
52*[2]	1.04 (3H, t, *J* = 6.6, $CH_2C\underline{H}_3$); 2.61 (2H, q, *J* = 6.6, $C\underline{H}_2CH_3$); 7.21 (2H, d, *J* = 7.4, H Ar); 7.37 (2H, m, H Ar); 7.43 (2H, t, *J* = 7.4, H Ar); 7.52 (1H, d, *J* = 1.3, H Ar); 7.74 (1H, d, *J* = 8.4, H Ar); 11.91 (1H, s, NH)
53	0.99 (3H, t, *J* = 6.6, $CH_2C\underline{H}_3$); 2.45 (1H, m) and 2.59 (1H, m, $C\underline{H}_2CH_3$); 3.68 (3H, s, CH_3O); 7.01 (1H, t, *J* = 8.2, H Ar); 7.07 (2H, m, H Ar); 7.37 (2H, m, H Ar); 7.51 (1H, d, *J* = 1.9, H Ar); 7.72 (1H, d, *J* = 8.8, H Ar); 11.80 (1H, s, NH)
54	2.15 (3H, s, CH_3); 4.26 (2H, m) and 4.32 (2H, m, OCH_2CH_2O); 6.80 (1H, s, H Ar); 7.21 (3H, m, H Ar); 7.33 (1H, t, *J* = 7.8, H Ar); 7.40 (2H, t, *J* = 7.8, H Ar); 11.49 (1H, s, NH)
55	2.04 (3H, s, CH_3); 3.68 (3H, s, CH_3O); 4.27 (2H, m) and 4.32 (2H, m, OCH_2CH_2O); 6.79 (1H, s, H Ar); 6.98 (1H, t, *J* = 7.8, H Ar); 7.04 (2H, m, H Ar); 7.17 (1H, s, H Ar); 7.34 (1H, dt, *J* = 7.8, *J* = 1.2, H Ar); 11.40 (1H, s, NH)
56	1.02 (3H, t, *J* = 7.4, $CH_2C\underline{H}_3$); 2.54 (2H, q, *J* = 7.4, $C\underline{H}_2CH_3$); 4.27 (2H, m) and 4.31 (2H, m, OCH_2CH_2O); 6.82 (1H, s, H Ar); 7.17 (2H, d, *J* = 7.4, H Ar); 7.21 (1H, s, H Ar); 7.34 (1H, m, H Ar); 7.41 (2H, m, H Ar); 11.55 (1H, s, NH)
57	0.77 (3H, t, *J* = 7.3, $CH_2CH_2C\underline{H}_3$); 1.46 (2H, m, $CH_2C\underline{H}_2CH_3$); 2.50 (2H, m, $C\underline{H}_2CH_2CH_3$); 4.27 (2H, m) and 4.32 (2H, m, OCH_2CH_2O); 6.82 (1H, s, H Ar); 7.16 (2H, m, H Ar); 7.19 (1H, s, H Ar); 7.34 (1H, m, H Ar); 7.40 (2H, m, H Ar); 11.51 (1H, s, NH)
58	0.71 (3H, t, *J* = 7.2, $CH_2CH_2C\underline{H}_3$); 1.49 (2H, m, $CH_2C\underline{H}_2CH_3$); 2.51 (2H, m, $C\underline{H}_2CH_2CH_3$); 3.76 (3H, s, CH_3O); 4.19 (2H, m) and 4.29 (2H, m, OCH_2CH_2O); 6.30 (1H, s, H Ar); 6.75 (1H, s, H Ar); 7.02 (1H, d, *J* = 8.4, H Ar); 7.03 (1H, t, *J* = 8.4, H Ar); 7.14 (1H, dd, *J* = 8.4, *J* = 1.3, H Ar); 7.37 (1H, m, H Ar); 11.21 (1H, s, NH)
59	0.05 (2H, m, *cyclo*-Pr); 0.73 (2H, m, *cyclo*-Pr); 2.02 (1H, m, *cyclo*-Pr); 4.27 (2H, m) and 4.33 (2H, m, OCH_2CH_2O); 6.79 (1H, s, H Ar); 7.31 (3H, m, H Ar); 7.36 (2H, m, H Ar); 7.58 (1H, s, H Ar); 11.55 (1H, s, NH)
60	0.05 (2H, m, *cyclo*-Pr); 0.71 (2H, m, *cyclo*-Pr); 1.99 (1H, m, *cyclo*-Pr); 4.22 (2H, m) and 4.25 (2H, m, OCH_2CH_2O); 6.61 (1H, s, H Ar); 7.43 (1H, s, H Ar); 7.61 (2H, d, *J* = 8.4, H Ar); 8.14 (2H, d, *J* = 8.4, H Ar); 11.62 (1H, s, NH)
61	4.18 (2H, m) and 4.28 (2H, m, OCH_2CH_2O); 6.36 (1H, s, H Ar); 6.88 (1H, s, H Ar); 7.06 (7H, m, H Ar); 7.28 (3H, m, H Ar); 11.70 (1H, s, NH)
62	2.26 (3H, s, CH_3); 4.19 (2H, m) and 4.30 (2H, m, OCH_2CH_2O); 6.42 (1H, s, H Ar); 6.88 (1H, s, H Ar); 7.02 (2H, d, *J* = 8.0, H Ar); 7.13 (2H, d, *J* = 8.0, H Ar); 7.34 (2H, d, *J* = 8.5, H Ar); 8.01 (2H, d, *J* = 8.5, H Ar); 11.95 (1H, s, NH)
63	4.20 (2H, m) and 4.29 (2H, m, OCH_2CH_2O); 6.35 (1H, s, H Ar); 6.88 (1H, s, H Ar); 6.96 (1H, d, *J* = 8.0, H Ar); 6.98 (1H, d, *J* = 8.5, H Ar); 7.06 (2H, m, H Ar); 7.10 (2H, m, H Ar); 7.15 (2H, m, H Ar); 7.33 (1H, m, H Ar); 11.80 (1H, s, NH)
64	4.21 (2H, m) and 4.32 (2H, m, OCH_2CH_2O); 6.19 (1H, s, H Ar); 6.91 (1H, s, H Ar); 7.31 (2H, m, H Ar); 7.36 (1H, m, H Ar); 7.38 (2H, d, *J* = 8.8, H Ar); 7.47 (1H, d, *J* = 8.0, H Ar); 8.03 (2H, d, *J* = 8.8, H Ar); 12.05 (1H, s, NH)

TABLE 5 (continued)

1	2
65	4.21 (2H, m) and 4.31 (2H, m, OCH_2CH_2O); 6.34 (1H, s, H Ar); 6.88 (1H, s, H Ar); 7.04 (2H, d, *J* = 8.2, H Ar); 7.15 (5H, m, H Ar); 7.36 (2H, d, *J* = 8.2, H Ar); 11.81 (1H, s, NH)
66	3.58 (3H, s, CH_3O); 4.19 (2H, m) and 4.29 (2H, m, OCH_2CH_2O); 6.33 (1H, s, H Ar); 6.75 (1H, t, *J* = 8.0, H Ar); 6.82 (1H, d, *J* = 8.0, H Ar); 6.87 (1H, s, H Ar); 6.89 (1H, dd, *J* = 8.0, *J* = 1.4, H Ar); 7.03 (1H, m, H Ar); 7.14 (2H, m, H Ar); 7.32 (2H, d, *J* = 8.5, H Ar); 11.69 (1H, s, NH)
67	4.21 (2H, m) and 4.33 (2H, m, OCH_2CH_2O); 6.38 (1H, s, H Ar); 6.89 (1H, s, H Ar); 7.20 (2H, d, *J* = 8.1, H Ar); 7.36 (2H, d, *J* = 8.2, H Ar); 7.40 (2H, d, *J* = 8.1, H Ar); 8.13 (2H, d, *J* = 8.2, H Ar); 11.91 (1H, s, NH)
68	4.19 (2H, m) and 4.32 (2H, m, OCH_2CH_2O); 6.15 (1H, s, H Ar); 6.91 (1H, s, H Ar); 7.14 (5H, m, H Ar); 7.22 (2H, m, H Ar); 7.31 (1H, t, *J* = 8.0, H Ar); 7.60 (1H, d, *J* = 8.0, H Ar); 11.51 (1H, s, NH)
69	4.20 (2H, m) and 4.32 (2H, m, OCH_2CH_2O); 6.12 (1H, s, H Ar); 6.89 (1H, s, H Ar); 7.02 (1H, dt, *J* = 7.7, *J* = 1.6, H Ar); 7.11 (1H, m, H Ar); 7.15 (4H, m, H Ar); 7.20 (1H, dd, *J* = 7.7, *J* = 1.6, H Ar); 7.34 (1H, dt, *J* = 7.5, *J* = 1.0, H Ar); 7.82 (1H, d, *J* = 7.5, H Ar); 11.82 (1H, s, NH)
70	3.66 (3H, s, OCH_3); 4.25 (4H, m, OCH_2CH_2O); 6.10 (1H, s, H Ar); 6.82 (1H, m, H Ar); 6.84 (1H, m, H Ar); 6.88 (1H, s, H Ar); 7.04 (4H, m, H Ar); 7.29 (1H, m, H Ar); 7.81 (1H, d, *J* = 8.1, H Ar); 11.71 (1H, br. s, NH)
71	2.23 (3H, s, CH_3); 3.83 (6H, s, $2CH_3O$); 6.89 (1H, s, H Ar); 7.15 (1H, s, H Ar); 7.22 (2H, d, *J* = 7.6, H Ar); 7.33 (1H, m, H Ar); 7.41 (2H, t, *J* = 7.6, H Ar); 11.60 (1H, s, NH)
72	0.05 (2H, m, *cyclo*-Pr); 0.76 (2H, m, *cyclo*-Pr); 2.05 (1H, m, *cyclo*-Pr); 3.86 (6H, s, $2CH_3O$); 6.89 (1H, s, H Ar); 7.35 (5H, m, H Ar); 7.59 (1H, s, H Ar); 11.61 (1H, s, NH)
73*[2]	2.19 (3H, s, CH_3); 4.36 (4H, s, OCH_2CH_2O); 6.78 (1H, d, *J* = 8.6, H Ar); 7.22 (2H, d, *J* = 8.0, H Ar); 7.26 (1H, d, *J* = 8.6, H Ar); 7.35 (1H, t, *J* = 8.0, H Ar); 7.42 (2H, t, *J* = 8.0, H Ar); 10.77 (1H, s, NH)
74*[2]	1.26 (6H, d, *J* = 5.4, $CH(C\underline{H}_3)_2$); 3.09 (1H, sept, $C\underline{H}(CH_3)_2$); 4.35 (4H, m, OCH_2CH_2O); 6.77 (1H, d, *J* = 8.9, H Ar); 7.16 (2H, m, H Ar); 7.39 (1H, m, H Ar); 7.41 (2H, m, H Ar); 7.51 (1H, m, H Ar); 10.68 (1H, br.s, NH)
79	1.16 (3H, t, *J* = 6.8, $OCH_2C\underline{H}_3$); 2.44 (3H, s, CH_3); 3.48 (2H, q, *J* = 6.8, $OC\underline{H}_2CH_3$); 4.20 (2H, s, CH_2OEt); 4.27 (4H, m, OCH_2CH_2O); 6.63 (1H, s, H Ar); 6.94 (1H, s, H Ar); 7.21 (2H, d, *J* = 7.4, H Ar); 7.27 (2H, d, *J* = 7.4, H Ar); 12.12 (1H, s, NH)
80	1.18 (3H, t, *J* = 6.2, $OCH_2C\underline{H}_3$); 3.49 (2H, q, *J* = 6.2, $OC\underline{H}_2CH_3$); 4.23 (2H, m) and 4.31 (2H, m, OCH_2CH_2O); 4.26 (2H, s, CH_2OEt); 6.58 (1H, s, H Ar); 6.97 (1H, s, H Ar); 7.19 (2H, m, H Ar); 7.34 (2H, m, H Ar); 12.25 (1H, br. s, NH)
83	1.19 (3H, t, *J* = 6.2, $OCH_2C\underline{H}_3$); 3.50 (2H, q, *J* = 6.2, $OC\underline{H}_2CH_3$); 4.23 (2H, m) and 4.31 (2H, m, OCH_2CH_2O); 4.26 (2H, s, CH_2OEt); 6.57 (1H, s, H Ar); 6.95 (1H, s, H Ar); 7.31 (2H, d, *J* = 8.0, H Ar); 7.48 (2H, d, *J* = 8.0, H Ar); 12.11 (1H, br. s, NH)
86	0.99 (3H, t, *J* = 7.1, $CH_2CH_2C\underline{H}_3$); 1.49 (2H, m, $CH_2C\underline{H}_2CH_3$); 2.05 (3H, s, CH_3); 2.73 (2H, t, *J* = 6.9, $C\underline{H}_2CH_2CH_3$); 4.25 (2H, m) and 4.29 (2H, m, OCH_2CH_2O); 6.75 (1H, s, H Ar); 7.14 (1H, s, H Ar); 11.36 (1H, s, NH)

TABLE 5 (continued)

1	2
87	2.32 (3H, s, CH_3); 4.21 (2H, m) and 4.29 (2H, m, OCH_2CH_2O); 6.48 (1H, s, H Ar); 6.85 (2H, d, *J* = 8.4, H Ar); 6.89 (1H, s, H Ar); 7.17 (2H, d, *J* = 8.0, H Ar); 7.25 (4H, m, H Ar); 11.94 (1H, s, NH)
88	0.72 (3H, t, *J* = 7.3, $CH_2CH_2C\underline{H}_3$); 1.36 (2H, m, $CH_2C\underline{H}_2CH_3$); 2.18 (2H, m, $C\underline{H}_2CH_2CH_3$); 4.17 (2H, m) and 4.26 (2H, m, OCH_2CH_2O); 6.15 (1H, s, H Ar); 6.83 (1H, s, H Ar); 7.26 (2H, d, *J* = 8.4, H Ar); 7.59 (2H, d, *J* = 8.4, H Ar); 11.65 (1H, s, NH)

* Spectra of quinolinones **50, 74, 79, 80, 83** were recorded in $CDCl_3$, and of **51-73, 86-88** in DMSO-d_6.

*[2] ^{13}C NMR spectra, δ, ppm, compound **52**: 14.1, 23.1, 55.7, 111.6, 118.0, 120.7, 123.2, 125.0, 125.3, 127.5, 129.6, 129.6, 131.2, 140.0, 149.3, 157.3, 161.2; compound **73**: 17.2, 64.7, 64.9, 111.9, 114.9, 117.9, 127.5, 128.3, 130.9, 137.0, 143.9, 161.3; compound **74**: 21.7, 31.8, 64.7, 64.9, 111.3, 112.6, 119.3, 127.5, 128.5, 129.6, 130.2, 137.9, 143.34, 152.62, 161.50.

TABLE 6. IR Spectra of Compounds **51, 56, 59, 60, 61, 64, 65, 70, 80, 83**

Com-pound	ν, cm^{-1}
51	3200–2800 (NH); 1645 (C=O)
56	3000–2400 (NH); 1660 (C=O)
59	3000–2600 (NH); 1640 (C=O)
60	3050–2600 (NH); 1650 (C=O); 1520, 1360 (NO_2)
61	3000–2600 (NH); 1650 (C=O)
64	3000–2400 (NH); 1650 (C=O); 1520, 1370 (NO_2)
65	3000–2400 (NH); 1645 (C=O)
70	3100–2700 (NH), 1650 (C=O)
80	3180–2800 (NH); 1660(C=O)
83	3200–2760 (NH); 1645(C=O)

1-(7-Amino-2,3-dihydro-1,4-benzodioxin-6-yl)butan-1-one (6) was synthesized by the reduction of 1-(7-nitro-2,3-dihydro-1,4-benzodioxin-6-yl)butan-1-one by the procedure of [28]. Yield 77%; mp 65-66°C (EtOH). ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.01 (3H, t, *J* = 6.8, $CH_2CH_2C\underline{H}_3$); 1.71 (2H, m, $CH_2C\underline{H}_2CH_3$); 2.79 (2H, t, *J* = 6.8, $COC\underline{H}_2CH_2CH_3$); 4.18 (2H, m) and 4.28 (2H, m, OCH_2CH_2O); 5.88 (2H, br. s, NH_2); 6.11 (1H, s, H-5); 7.22 (1H, s, H-8). Found, %: C 64.78; H 6.69; N 6.12. $C_{12}H_{15}NO_3$. Calculated, %: C 65.14; H 6.83; N 6.33.

7-Nitro-2,3-dihydro-1,4-benzodioxin-6-yl 2-iodophenyl ketone was obtained by the nitration of (2,3-dihydro-1,4-benzodioxin-6-yl) 2-iodophenyl ketone by the procedure of [27]. Yield 86%; mp 167-168°C (EtOH). ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 4.41 (4H, m, OCH_2CH_2O); 7.03 (1H, s, H Ar); 7.15 (1H, m, H Ar); 7.31 (2H, m, H Ar); 7.67 (1H, s, H-8); 8.04 (1H, d, *J* = 8.0, H Ar). Found, %: C 43.61; H 2.31; N 3.26. $C_{15}H_{10}INO_5$. Calculated, %: C 43.82; H 2.45; N 3.41.

7-Amino-2,3-dihydro-1,4-benzodioxin-6-yl 2-iodophenyl ketone (15) was synthesized analogously to compound **6** by the reduction of 2-iodophenyl 7-nitro-2,3-dihydro-1,4-benzodioxin-6-yl ketone, yield

79%, mp 168-169°C (EtOH). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 4.11 (2H, m) and 4.27 (2H, m, OCH_2CH_2O); 6.32 (1H, s, H-5); 6.65 (1H, s, H-8); 6.96 (2H, br. s, NH_2); 7.43 (1H, d, *J* = 8.1, H Ar); 7.52 (2H, m, H Ar); 7.63 (1H, d, *J* = 8.1, H Ar). Found, %: C 47.12; H 3.01; N 3.51. $C_{15}H_{12}INO_3$. Calculated, %: C 47.27; H 3.17; N 3.68.

4,5-Dimethoxy-2-nitroacetophenone was obtained by the nitration of 3,4-dimethoxyacetophenone, as described in [29]. Yield 64%; mp 121-122°C (EtOH). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 2.51 (3H, s, $COCH_3$); 3.90 (3H, s, OCH_3); 3.95 (3H, s, OCH_3); 7.21 (1H, s, H Ar); 7.62 (1H, s, H Ar).

2-Amino-4,5-dimethoxyacetophenone (16) was syhthesized analogously to compound **6** by the reduction of 4,5-dimethoxy-2-nitroacetophenone. Yield 55%. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.48 (3H, s, $COCH_3$); 3.82 (3H, s, OCH_3); 3.87 (3H, s, OCH_3); 6.09 (1H, s, H Ar); 6.25 (2H, br. s, NH_2); 7.07 (1H, s, H Ar). Found, %: C 61.28; H 6.52; N 6.96. $C_{10}H_{13}NO_3$. Calculated, %: C 61.53; H 6.71; N 7.18.

(*o*-Acylamino)acylbenzenes 20-49 (General Method). The acid chloride of the corresponding acid (10 mmol) and 3 N NaOH solution (10 mmol) were added gradually and at the same time, with stirring to a solution of the corresponding *ortho*-aminoacylbenzene **1-19** in dioxane (25 ml). The reaction mixture was stirred for 30 min and poured into water (250 ml). The precipitated solid was filtered off, washed with water, air-dried, and recrystallized from a suitable solvent. The yields and physicochemical characteristics of the obtained anilides **20-49** are given in Tables 1 and 2.

Interaction of *o*-Acylaminoacylbenzenes 20-49 with Equimolecular Quantities of Sodium Ethylate (General Method). The corresponding acylanilide (2 mmol) was added to a solution of sodium ethylate, prepared from sodium (46 mg, 2 mmol) and ethanol (25 ml). The mixture was stirred at 20°C for 2 h, poured into water (120 ml) and neutralized with 2 N HCl. The precipitated solid was filtered off, washed with alcohol, air-dried, and recrystallized from a suitable solvent. In the case of *o*-acylaminoacylbenzenes **20-26, 28-32, 35, 36, 38**, and **40-49** the corresponding quinolin-2-ones **50-74** were obtained. Yields, physicochemical characteristics, and data of elemental analysis of the obtained heterocycles are given in Tables 3 and 4.

***N*-[7-(4-Methylbenzoyl)-2,3-dihydro-1,4-benzodioxin-6-yl]acrylamide (75) and 3-Ethoxy-*N*-[7-(4-methylbenzoyl)-2,3-dihydro-1,4-benzodioxin-6-yl]propionamide (77).** A mixture (0.74 g) was obtained from 3-bromo-*N*-[7-(4-methylbenzoyl)-2,3-dihydro-1,4-benzodioxin-6-yl]propionamide (**34**) (0.81 g, 2 mmol), chromatography of which on preparative plates of Al_2O_3 gave the starting anilide **34** (0.36 g, 44%), compound **75** (0.21 g, 58%), and compound **77** (0.17 g, 42%). The yields of compounds **75** and **77** were calculated on the anilide consumed in the reaction. Compound **75**: mp 116-117°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 2.44 (3H, s, CH_3); 4.24 (2H, m) and 4.35 (2H, m, OCH_2CH_2O); 5.76 (1H, d, *J* = 10.1, COCH=C$\underline{H}_2$, H-*cis*); 6.30 (1H, dd, *J* = 10.1, *J* = 17.0, COC$\underline{H}$=CH_2); 6.42 (1H, d, *J* = 17.0, COCH=C$\underline{H}_2$, H-*trans*); 7.14 (1H, s) and 8.36 (1H, s, H-5,8); 7.28 (2H, d, *J* = 7.9, H-3',5'); 7.57 (2H, d, *J* = 7.9, H-2',6'); 11.34 (1H, s, NH). Found, %: C 70.65; H 5.13; N 4.22. $C_{19}H_{17}NO_4$. Calculated, %: C 70.58; H 5.30; N 4.33. Compound **77**: viscous oil. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.19 (3H, t, *J* = 6.9, $OCH_2C\underline{H}_3$); 2.43 (3H, s, CH_3); 2.66 (2H, t, *J* = 6.1, $COC\underline{H}_2CH_2O$); 3.55 (2H, q, *J* = 6.9, $CH_3C\underline{H}_2O$); 3.77 (2H, t, *J* = 6.1, $COCH_2C\underline{H}_2O$); 4.23 (2H, m) and 4.32 (2H, m, OCH_2CH_2O); 7.08 (1H, s) and 8.22 (1H, s, H-5,8); 7.26 (2H, d, *J* = 8.2, H-3',5'); 7.56 (2H, d, *J* = 8.2, H-2',6'); 11.01 (1H, s, NH). Found, %: C 68.45; H 5.98; N 3.65. $C_{21}H_{23}NO_5$. Calculated, %: C 68.28; H 6.21; N 3.79.

***N*-[7-(4-Fluorobenzoyl)-2,3-dihydro-1,4-benzodioxin-6-yl]acrylamide (76) and 3-ethoxy-*N*-[7-(4-fluorobenzoyl)-2,3-dihydro-1,4-benzodioxin-6-yl]propionamide (78**) were obtained from 3-bromo-*N*-[7-(4-fluorobenzoyl)-2,3-dihydro-1,4-benzodioxin-6-yl]propionamide (**37**) (0.82 g, 2 mmol) analogously to compound **75**. From the mixture (0.79 g) of reaction products the starting compound **37** (0.43 g, 52%), compound **76** (0.18 g, 52%), and compound **78** (0.19 g, 48%) were separated chromatographically. The yields of compounds **76** and **78** were calculated on the anilide **37** consumed in the reaction. Compound **76**: mp 141-142°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 4.32 (4H, m, OCH_2CH_2O); 5.77 (1H, d, *J* = 10.1, COCH=C$\underline{H}_2$-*cis*); 6.29 (1H, dd, *J* = 10.1, *J* = 16.9, COC$\underline{H}$=CH_2); 6.42 (1H, d, *J* = 16.9, COCH=C$\underline{H}_2$-*trans*); 7.08 (1H, s) and 8.36 (1H, s, H-5,8); 7.16 (2H, m, H Ar); 7.69 (2H, m, H Ar); 11.24 (1H, s, NH). Found, %: C 66.32; H 4.36; N 4.09. $C_{18}H_{14}FNO_4$. Calculated, %: C 66.05; H 4.31; N 4.28. Compound **78**: viscous oil. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.18 (3H, t, *J* = 7.0,

$C\underline{H}_3CH_2O$); 2.66 (2H, t, J = 6.1, $COC\underline{H}_2CH_2O$); 3.55 (2H, q, J = 7.0, $CH_3C\underline{H}_2O$); 3.77 (2H, t, J = 6.1, $COCH_2C\underline{H}_2O$); 4.28 (4H, m, OCH_2CH_2O); 7.02 (1H, s) and 8.21 (1H, s, H-5,8); 7.15 (2H, m, H Ar); 7.71 (2H, m, H Ar); 10.58 (1H, s, NH). Found, %: C 64.18; H 5.29; N 3.71. $C_{20}H_{20}FNO_5$. Calculated, %: C 64.34; H 5.40; N 3.75

Cyclization of (*o*-Acylamino)acylbenzenes 27, 33, 39, 77, 78 was carried out by the general method using sodium ethylate (2 equiv.) in boiling ethanol for 5 h. The corresponding quinolin-2-ones **79, 80, 86-88** were obtained. Yields and physicochemical characteristics are given in Tables 4 and 5.

Cyclization of (*o*-Acylamino)acylbenzenes 34 and 37. Analogously, but at a substrate–sodium ethylate ratio of 1:3, quinolinone **79** (0.31 g, 88%) was obtained from compound **34** (0.4 g, 1 mmol) and also the corresponding quinolin-2-ones **79** and **80** were obtained from compound **37** (0.41 g, 1 mmol).

Interaction of *N*-(7-Aroyl-2,3-dihydro-1,4-benzodioxin-6-yl)acrylamides 75, 76, 81, 84 with Sodium Ethylate. The corresponding anilide (1 mmol) was added to a solution of sodium ethylate prepared from sodium (46 mg, 2 mmol) and ethanol (10 ml). The mixture was refluxed for 2 h, the ethanol was evaporated, the residue was treated with water (30 ml), the resulting solid filtered off, and air-dried. (In the case of compound **84**, after evaporation of the ethanol the reaction products were extracted with $CHCl_3$.) The corresponding quinolin-2-ones **79, 80**, and **83** were obtained from vinylcarbonylaminobenzodioxanes **75, 76**, and **81**. From compound **84,** after chromatography of the reaction mixture on Al_2O_3, *N*-[7-(2-chlorobenzoyl)-2,3-dihydro-1,4-benzodioxin-6-yl]-3-ethoxypropionamide (**85**) (0.24 g, 72%) and 7-amino-2,3-dihydro-1,4-benzodioxin-6-yl 2-chlorophenyl ketone (**12**) (60 mg, 22%) were obtained. Compound **85**: viscous oil. ^{1}H NMR spectrum, δ, ppm (J, Hz): 1.22 (3H, t, J = 7.2, $OCH_2C\underline{H}_3$); 2.74 (2H, t, J = 6.0, $COC\underline{H}_2CH_2O$); 3.58 (2H, q, J = 7.2, $CH_3C\underline{H}_2O$); 3.84 (2H, t, J = 6.0, $COCH_2C\underline{H}_2O$); 4.21 (2H, m) and 4.32 (2H, m, OCH_2CH_2O); 6.85 (1H, s, H Ar); 7.29-7.48 (4H, m, H Ar); 8.42 (1H, s, H Ar); 11.65 (1H, br. s, NH). Found, %: C 61.41; H 5.01; N 3.42. $C_{20}H_{20}ClNO_5$. Calculated, %: C 61.62; H 5.17; N 3.59.

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