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CONDENSED DIAZEPINES. SYNTHESIS OF 1-ARYL-3,5-DIHYDRO-4H-1-BENZOFURO-[2,3-*d*][1,2]DIAZEPIN-4-ONES

A. B. Eresko[1], V. S. Tolkunov[1], and S. V. Tolkunov[1]*

The cyclocondensation of (2-aroyl-1-benzofuran-3-yl)acetic acids and their methyl esters with hydrazine hydrate under various experimental conditions has been studied. Optimal conditions have been found for obtaining 1-aryl-3,5-dihydro-4H-1-benzofuro[2,3-d][1,2]diazepin-4-ones.

Keywords: (2-aroyl-1-benzofuran-3-yl)-acetic acids, 1-aryl-3,5-dihydro-4H-1-benzofuro[2,3-*d*][1,2]diazepin-4-ones, hydrazine hydrate, condensed diazepines, polyphosphoric acid, benzoylation, cyclization.

1-Aryl-3,5-dihydro-4H-2,3-benzodiazepin-4-ones are actively studied in connection with the anticonvulsive activity detected in them [1-4]. Known routes to obtain them are based on the interaction of 2-aroyl-4,5-dimethoxyphenylacetic acids or their esters with hydrazine [1-6]. Of the heterocyclic analogs of 2,3-benzodiazepin-4-ones only 3H-[1,2]diazepino[5,6-*b*]indoles, obtained by the cyclocondensation of the ethyl ester of [2-formyl(acetyl)indol-2-yl]acetic acid with hydrazine hydrate are known [7-9]. Similar conversions have not been described in the 1-benzofuran series. As was shown in our preliminary publication [10], heterocyclization of hydrazones of (2-acyl-1-benzofuran-3-yl)acetic acid leads to the corresponding azine, but heterocyclization of hydrazones of arylamides of (2-acetyl-1-benzofuran-3-yl)acetic acid, depending on the conditions, takes place with the formation of 2-amino-1-methyl-1-benzofuro[2,3-*c*]pyridin-3-one or azines of arylamides of (2-acetyl-1-benzofuran-3-yl)acetic acid.

In the present work the reaction of methyl esters of (2-aroyl-1-benzofuran-3-yl)acetic acids **2a-g** and (2-aroyl-1-benzofuran-3-yl)acetic acids **4a-c** with hydrazine hydrate has been investigated. The initial esters **2a-g** were obtained by acylation of the methyl ester of (6-methyl-1-benzofuran-3-yl)acetic acid (**1**) with aroyl(heteroyl) chlorides in the presence of aluminum chloride.

Acylation of methyl ester **1** with benzoic, veratric, and thiophene-2-carboxylic acids in polyphosphoric acid (PPA) leads to 7-methyl-1-phenyl-3H-pyrano[3,4-*b*][1]benzofuran-3-one (**3a**), 7-methyl-1-(thien-2-yl)-3H-pyrano[3,4-*b*][1]benzofuran-3-one (**3b**), and 1-(3,4-dimethoxyphenyl)-7-methyl-3H-pyrano[3,4-*b*][1]benzofuran-3-one (**3c**), from which (2-aroyl-1-benzofuran-3-yl)acetic acids **4a-c** were obtained by alkaline hydrolysis.

* To whom correspondence should be addressed, e-mail: s_tolkunov@yahoo.com

[1]L. M. Litvinenko Institute of Physical-Organic Chemistry and Coal Chemistry, National Academy of Sciences of Ukraine, Donetsk 83114, Ukraine.

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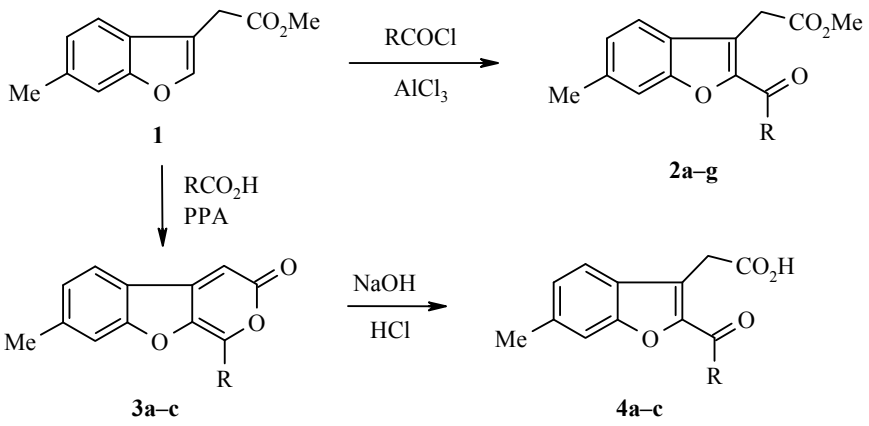
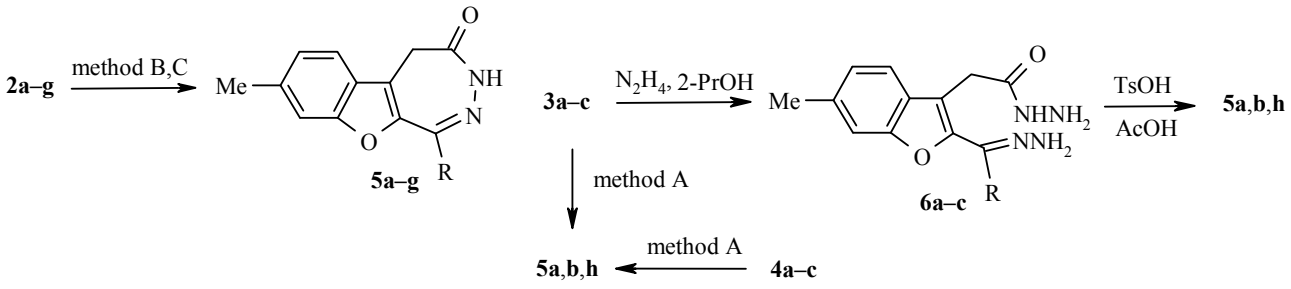
Only on using veratric acid was a high yield of pyrone **3** (85%) obtained. In the remaining cases this method gives poor yields and substances were purified with difficulty, consequently we did not use it in the synthesis of other derivatives.



2 a R = Ph, **b** R = 2-thienyl, **c** R = 3-MeOC$_6$H$_4$, **d** R = 2-MeOC$_6$H$_4$, **e** R = 4-ClC$_6$H$_4$, **f** R =4-MeC$_6$H$_4$, **g** R = 2-ClC$_6$H$_4$; **3**, **4 a** R = Ph, **b** R = 2-thienyl, **c** R = 3,4-(MeO)$_2$C$_6$H$_3$

The heterocyclization of (2-aroyl-6-methyl-1-benzofuran-3-yl)acetic acids **4a-c** proceeded readily on extended boiling (20 h) with a fivefold quantity of hydrazine hydrate in ethyl cellosolve in the presence of catalytic amounts of acetic acid (method A). 1-Aryl-8-methyl-3,5-dihydro-4H-1-benzofuro[2,3-*d*][1,2]diazepin-4-ones **5a,b,h** were obtained in yields up to 50%. Under analogous conditions the heterocyclization of the methyl esters of (2-aroyl-1-benzofuran-3-yl)acetic acids **2a-g** leads to a mixture of the hydrazide-hydrazones and the corresponding diazepines **5a-g** with a predominance of the latter (according to data of ^{1}H NMR spectroscopy and chromato-mass spectra).



5 a R = Ph, **b** R = 2-thienyl, **c** R = 3-MeOC$_6$H$_4$, **d** R = 2-MeOC$_6$H$_4$, **e** R = 4-ClC$_6$H$_4$, **f** R = 4-MeC$_6$H$_4$, **g** R = 2-ClC$_6$H$_4$, **h** R = 3,4-(MeO)$_2$C$_6$H$_3$; **6 a** R = Ph, **b** R =2-thienyl, **c** R = 3,4-(MeO)$_2$C$_6$H$_3$

Treatment of the obtained mixture of reaction products with the acetic acid in the presence of catalytic amounts of *p*-toluenesulfonic acid enabled the preparation of diazepines **5a-g** in 40-60% yield (method B).

Attempts to optimize method B, using keto esters **2a-g**, hydrazine hydrate, the acetic acid, and *p*-toluenesulfonic acid as catalyst gave better yields of the final diazepines than in the two-stage procedure and more dirty reaction products. The best results were obtained on heterocyclization of esters **2a-g** with a fivefold quantity of hydrazine acetate in ethyl cellosolve (method C). Boiling keto acids **4a-c** in ethyl cellosolve with hydrazine dihydrochloride did not lead to diazepines.

Pyrones **3a-c** in method A were converted into diazepines in up to 40% yield, but on boiling in 2-propanol gave only hydrazide-hydrazones **6a-c**, which may be converted into the corresponding diazepines by boiling in acetic acid with *p*-toluenesulfonic acid as catalyst.

In the ^{1}H NMR spectra of diazepines **5a-h** the signals of the CH_2 group protons were displayed in 3.60 region, and of the NH group in 11.0 region ppm. The following were characteristic of the chromato-mass spectra of compounds **5a** and **5f**. For **5a** retention time was 0.714 min (99.26%), *m/z* 291.2 ($[M + 1]^+$ calculated 290.11), for **5f** retention time was 0.718 min (98.52%), *m/z* 305.0 ($[M + 1]^+$ calculated 304.12).

Table 1. Characteristics of the Synthesized Compounds **1-6**

Compound	Empirical formula	Found, % / Calculated, %					mp, °C	Yield, % (method)
		C	H	Cl	N	S		
1	$C_{12}H_{12}O_3$	70.41 / 70.58	5.84 / 5.92				—*	92
2a	$C_{19}H_{16}O_4$	74.12 / 74.01	5.17 / 5.23				117-118	76
2b	$C_{17}H_{14}O_4S$	65.06 / 64.95	4.40 / 4.49			10.11 / 10.20	101-103	64
2c	$C_{20}H_{18}O_5$	70.85 / 70.99	5.44 / 5.36				79-80	74
2d	$C_{20}H_{18}O_5$	70.87 / 70.99	5.42 / 5.36				81-82	80
2e	$C_{19}H_{15}ClO_4$	66.69 / 66.58	4.49 / 4.41	10.29 / 10.34			134-136	62
2f	$C_{20}H_{18}O_4$	74.39 / 74.52	5.70 / 5.63				83-85	62
2g	$C_{19}H_{15}ClO_4$	66.46 / 66.58	4.32 / 4.41	10.27 / 10.34			79-80	66
3a	$C_{18}H_{12}O_3$	78.15 / 78.25	4.31 / 4.38				186-187	10
3b	$C_{16}H_{10}O_3S$	68.18 / 68.07	3.50 / 3.57			11.28 / 11.36	164-166	25
3c	$C_{20}H_{16}O_5$	71.31 / 71.42	4.86 / 4.79				194-195	85
4a	$C_{18}H_{14}O_4$	73.59 / 73.46	4.70 / 4.79				171-172	92
4b	$C_{16}H_{12}O_4S$	64.09 / 63.99	3.95 / 4.03			10.61 / 10.68	146-148	42
4c	$C_{20}H_{18}O_6$	67.64 / 67.79	5.24 / 5.12				189-190	90
5a	$C_{18}H_{14}N_2O_2$	74.34 / 74.47	4.94 / 4.86		9.57 / 9.65		214-216	57 (A), 20 (B)
5b	$C_{16}H_{12}N_2O_2S$	64.70 / 64.85	4.00 / 4.08		9.40 / 9.45	10.75 / 10.82	197-198	33 (A), 35 (B)
5c	$C_{19}H_{16}N_2O_3$	71.35 / 71.24	5.10 / 5.03		8.67 / 8.74		203-205	42 (B), 53 (C)
5d	$C_{19}H_{16}N_2O_3$	71.36 / 71.24	4.94 / 5.03		8.81 / 8.74		184-186	18 (B), 21 (C)
5e	$C_{18}H_{13}ClN_2O$	66.69 / 66.57	4.11 / 4.03	10.81 / 10.92	8.70 / 8.63		229-231	63 (B), 61 (C)
5f	$C_{19}H_{16}N_2O_2$	75.09 / 74.98	5.20 / 5.30		9.12 / 9.20		210-211	43 (B)
5g	$C_{18}H_{13}ClN_2O_2$	66.45 / 66.57	4.10 / 4.03	10.82 / 10.92	8.59 / 8.63		211-212	20 (C)
5h	$C_{20}H_{18}N_2O_4$	78.42 / 78.56	5.25 / 5.18		7.95 / 8.00		208-210	40 (A)
6a	$C_{18}H_{18}N_4O_2$	67.21 / 67.07	5.70 / 5.63		17.30 / 17.38		191-192	46
6b	$C_{16}H_{16}N_4O_3S$	58.71 / 58.52	4.80 / 4.91			9.93 / 9.76	170-171	39
6c	$C_{20}H_{22}N_4O_4$	62.71 / 62.82	5.87 / 5.80		14.54 / 14.62		168-170	41

*Bp 150°C (9 mm Hg).

TABLE 2. ^{1}H NMR Spectra of Compounds **1-6**

Com-pound	Chemical shifts, δ, ppm (*J*, Hz)
1	2
1	2.47 (3H, s, 6-CH_3); 3.68 (3H, s, CO_2CH_3); 3.70 (2H, s, CH_2); 7.04 (1H, d, *J* = 8.0, H-5); 7.27 (1H, s, H-7); 7.41 (1H, d, *J* = 8.0, H-4); 7.66 (1H, s, H-2)
2a	2.53 (3H, s, 6-CH_3); 3.68 (3H, s, CO_2CH_3); 4.14 (2H, s, CH_2); 7.18 (1H, d, *J* = 8.0, H-5); 7.42 (1H, s, H-7); 7.54 (2H, t, *J* = 8.0, H-3',5'); 7.62 (2H, m, H-4,4'); 8.08 (2H, d, *J* = 8.0, H-2',6')
2b	2.55 (3H, s, 6-CH_3); 3.68 (3H, s, CO_2CH_3); 4.19 (2H, s, CH_2); 7.18 (1H, d, *J* = 8.0, H-5); 7.27 (1H, t, *J* = 4.0, H-4'); 7.46 (1H, s, H-7); 7.61 (1H, d, *J* = 8.0, H-4); 7.91 (1H, d, *J* = 4.0, H-5'); 8.39 (1H, d, *J* = 4.0, H-3')
2c	2.54 (3H, s, 6-CH_3); 3.70 (3H, s, CO_2CH_3); 3.90 (3H, s, 3'-OCH_3); 4.17 (2H, s, CH_2); 7.18 (2H, m, H-5,5'); 7.43 (1H, d, *J* = 1.6, H-7); 7.45 (1H, dd, *J* = 8.0, *J* = 1.6, H-4); 7.56 (1H, d, *J* = 2.1, H-2'); 7.63 (1H, dd, *J* = 8.0, *J* = 2.1, H-4'); 7.70 (1H, d, *J* = 8.0, H-6')
2d	2.49 (3H, s, 6-CH_3); 3.68 (3H, s, CO_2CH_3); 3.76 (3H, s, 2'-OCH_3); 4.07 (2H, s, CH_2); 7.04 (1H, t, *J* = 8.0, H-5'); 7.08 (1H, d, *J* = 8.0, H-3'); 7.12 (1H, d, *J* = 8.0, H-5); 7.27 (1H, s, H-7); 7.35 (1H, d, *J* = 8.0, H-4); 7.51 (1H, t, *J* = 8.0, H-4'); 7.57 (1H, d, *J* = 8.0, H-6')
2e	2.54 (3H, s, 6-CH_3); 3.69 (3H, s, CO_2CH_3); 4.18 (2H, s, CH_2); 7.20 (1H, d, *J* = 8.0, H-5); 7.42 (1H, s, H-7); 7.56 (2H, d, *J* = 8.0, H-3',5'); 7.65 (1H, d, *J* = 8.0, H-4); 8.11 (2H, d, *J* = 8.0, H-2',6')
2f	2.46 (3H, s, 4'-CH_3); 2.53 (3H, s, 6-CH_3); 3.68 (3H, s, CO_2CH_3); 4.16 (2H, s, CH_2); 7.18 (1H, d, *J* = 8.0, H-5); 7.33 (2H, d, *J* = 8.0, H-3',5'); 7.39 (1H, s, H-7); 7.60 (1H, d, *J* = 8.0, H-4); 7.99 (2H, d, *J* = 8.0, H-2',6')
2g	2.48 (3H, s, 6-CH_3); 3.67 (3H, s, CO_2CH_3); 4.14 (2H, s, CH_2); 7.15 (1H, d, *J* = 8.0, H-5); 7.29 (1H, s, H-7); 7.42–7.54 (4H, m, H-3'–6'); 7.62 (1H, d, *J* = 8.0, H-4)
3a	2.51 (3H, s, 7-CH_3); 6.69 (1H, s, H-4); 7.19 (1H, d, *J* = 8.0, H-6); 7.38 (1H, s, H-8); 7.50–7.62 (3H, m, H-3'–5'); 7.95 (1H, d, *J* = 8.0, H-5); 8.11 (2H, d, *J* = 8.0, H-2',6')
3b	2.54 (3H, s, 7-CH_3); 6.50 (1H, s, H-4); 7.16 (1H, d, *J* = 8.0, H-6); 7.25 (1H, t, *J* = 4.0, H-4'); 7.31 (1H, s, H-8); 7.73 (1H, d, *J* = 4.0, H-5'); 7.85 (2H, m, H-5,3')
3c	2.51 (3H, s, 7-CH_3); 3.89 (3H, s, 3'-OCH_3); 3.91 (3H, s, 4'-OCH_3); 6.43 (1H, s, H-4); 7.01 (1H, d, *J* = 8.0, H-5'); 7.12 (1H, d, *J* = 8.0, H-6); 7.27 (1H, s, H-8); 7.53 (1H, s, H-2'); 7.70 (1H, d, *J* = 8.0, H-6'); 7.82 (1H, d, *J* = 8.0, H-5)
4a	2.52 (3H, s, 6-CH_3); 4.08 (2H, s, CH_2); 7.18 (1H, d, *J* = 8.2, H-5); 7.41 (1H, s, H-7); 7.50–7.64 (3H, m, H-3'–5'); 7.66 (1H, d, *J* = 8.2, H-4); 8.06 (2H, d, *J* = 8.2, H-2',6'); 12.28 (1H, s, COOH)
4b	2.53 (3H, s, 6-CH_3); 4.10 (2H, s, CH_2); 7.17 (1H, d, *J* = 8.0, H-5); 7.26 (1H, t, *J* = 4.0, H-4'); 7.44 (1H, s, H-7); 7.63 (1H, d, *J* = 8.0, H-4); 7.91 (1H, d, *J* = 4.0, H-5'); 8.37 (1H, d, *J* = 4.0, H-3'); 12.10 (1H, br. s, COOH)
4c	2.52 (3H, s, 6-CH_3); 3.87 (3H, s, 3'-OCH_3); 3.90 (3H, s, 4'-OCH_3); 4.11 (2H, s, CH_2); 7.01 (1H, d, *J* = 8.2, H-5'); 7.12 (1H, d, *J* = 8.2, H-6'); 7.29 (1H, s, H-2'); 7.41 (1H, s, H-7); 7.68 (1H, d, *J* = 8.0, H-5); 7.98 (1H, d, *J* = 8.0, H-4); 12.10 (1H, s, COOH)
5a	2.49 (3H, s, 8-CH_3); 3.66 (2H, s, CH_2); 7.16–7.74 (8H, m, H arom); 11.18 (1H, s, NH)
5b	2.52 (3H, s, 8-CH_3); 3.64 (2H, s, CH_2); 7.10 (1H, t, *J* = 4.0, H-4'); 7.17 (1H, d, *J* = 8.0, H-7); 7.38 (1H, s, H-9); 7.46 (1H, d, *J* = 4.0, H-5'); 7.65 (1H, d, *J* = 4.0, H-3'); 7.67 (1H, d, *J* = 8.0, H-6); 11.08 (1H, s, NH)
5c	2.50 (3H, s, 8-CH_3); 3.65 (2H, s, CH_2); 3.83 (3H, s, 3'-OCH_3); 6.97 (1H, d, *J* = 8.0, H-4'); 7.16 (1H, d, *J* = 8.0, H-7); 7.28–7.32 (4H, m, H-2',5',6',9); 7.66 (1H, d, *J* = 8.0, H-6); 11.09 (1H, s, NH)
5d	2.47 (3H, s, 8-CH_3); 3.60 (3H, s, 2'-OCH_3); 3.67 (2H, s, CH_2); 7.00–7.06 (2H, m, H-3',5'); 7.12 (1H, d, *J* = 8.0, H-7); 7.20 (1H, s, H-9); 7.44 (1H, t, *J* = 8.0, H-4'); 7.51 (1H, d, *J* = 8.0, H-6'); 7.62 (1H, d, *J* = 8.0, H-6); 11.06 (1H, s, NH)
5e	2.51 (3H, s, 8-CH_3); 3.67 (2H, s, CH_2); 7.18 (1H, d, *J* = 8.0, H-7); 7.31 (1H, s, H-9); 7.44 (2H, d, *J* = 8.0, H-3',5'); 7.69 (1H, d, *J* = 8.0, H-6); 7.75 (2H, d, *J* = 8.0, H-2',6'); 11.23 (1H, s, NH)
5f	2.41 (3H, s, 4'-CH_3); 2.48 (3H, s, 8-CH_3); 3.63 (2H, s, CH_2); 7.22 (4H, m, H arom); 7.63 (3H, m, H arom); 11.09 (1H, s, NH)
5g	2.47 (3H, s, 8-CH_3); 3.73 (2H, s, CH_2); 7.15 (1H, d, *J* = 8.0, H-7); 7.23 (1H, s, H-9); 7.46 (3H, br. s, H-4'–6'); 7.62 (1H, d, *J* = 8.0, H-6); 7.67 (1H, d, *J* = 8.0, H-3'); 11.31 (1H, s, NH)

TABLE 2 (continued)

1	2
5h	2.51 (3H, s, 8-CH_3); 3.62 (2H, s, CH_2); 3.83 (3H, s, 3'-OCH_3); 3.87 (3H, s, 4'-OCH_3); 6.91 (1H, d, *J* = 8.0, H-5'); 7.17 (1H, d, *J* = 8.0, H-7); 7.26 (1H, d, *J* = 8.0, H-6'); 7.32 (1H, s, H-9); 7.35 (1H, s, H-2'); 7.67 (1H, d, *J* = 8.0, H-6); 10.95 (1H, s, NH)
6a	2.42 (3H, s, 6-CH_3); 3.60 (2H, s, CH_2); 4.10 (2H, br. s, =NNH_2); 6.67 (2H, s, CONHN$\underline{H_2}$); 7.16–7.70 (8H, m, H arom); 8.90 (1H, s, NH)
6b	2.55 (3H, s, 6-CH_3); 4.08 (2H, br. s, =NNH_2); 4.19 (2H, s, CH_2); 6.66 (2H, s, CONHN$\underline{H_2}$); 7.18 (1H, d, *J* = 8.0, H-5); 7.27 (1H, t, *J* = 4.0, H-4'); 7.46 (1H, s, H-7); 7.61 (1H, d, *J* = 8.0, H-4); 7.91 (1H, d, *J* = 4.0, H-5'); 8.39 (1H, d, *J* = 4.0, H-3'); 8.85 (1H, s, NH)
6c	2.54 (3H, s, 6-CH_3); 3.92 (3H, s, 3'-OCH_3); 3.95 (3H, s, 4'-OCH_3); 4.00 (2H, br. s, =NNH_2); 6.64 (2H, s, CONHN$\underline{H_2}$); 7.01 (1H, d, *J* = 8.0, H-5'); 7.17 (1H, d, *J* = 8.0, H-5); 7.37 (1H, s, H-7); 7.63 (1H, s, H-2'); 7.68 (1H, d, *J* = 8.0, H-4); 7.85 (1H, d, *J* = 8.0, H-6'); 8.97 (1H, s, NH)

EXPERIMENTAL

The ^{1}H NMR spectra were recorded on a Bruker Avance II 400 instrument in DMSO-d_6, internal standard was TMS. Chromato-mass spectra were obtained on an Agilent 1100 LC/MSD VL spectrometer, method of ionization was APCI (chemical positive ionization at atmospheric pressure). Parameters of the chromatographic column were length 50 mm, diameter 4.6 mm, stationary phase ZORBAX SB-C18, solvent acetonitrile–water, 95:5, 0.1% trifluoroacetic acid, gradient elution, solvent supply rate 3.0 ml/min. The characteristics of the synthesized compounds are given in Tables 1 and 2.

Methyl Ester of (6-Methyl-1-benzofuran-3-yl)acetic Acid (1). Acetyl chloride (4 g, 50 mmol) was added with cooling to a solution of (6-methyl-1-benzofuran-3-yl)acetic acid (9.5 g, 50 mmol) in dry methanol (50 ml). The mixture was allowed to stand for 2 days, poured into 5% $NaHCO_3$ solution (200 ml), and extracted with chloroform. The solvent was evaporated in vacuum, and the residue distilled in vacuum.

Methyl Ester of (2-Aroyl-1-benzofuran-3-yl)acetic Acids 2a-g (General Method). A solution of ester **1** (1.02 g, 5.0 mmol) in methylene chloride (5 ml) was added to a mixture of aluminum chloride (0.86 g, 6.5 mmol) and the appropriate aroyl chloride (6.0 mmol) in dry methylene chloride (10 ml), and the mixture was stirred for 3 h at 25-30^{o}C. The reaction mixture was poured onto ice (40 g) with hydrochloric acid (7 ml), and extracted with methylene chloride. The extract was washed with a dilute solution of salt and with water, dried over Na_2SO_4, and evaporated. The residue was recrystallized from 2-propanol.

7-Methyl-1-phenyl-3H-pyrano[3,4-*b*][1]benzofuran-3-one (3a), 7-Methyl-1-(thien-2-yl)-3H-pyrano-[3,4-*b*][1]benzofuran-3-one (3b), 1-(3,4-Dimethoxyphenyl)-7-methyl-3H-pyrano[3,4-*b*][1]benzofuran-3-one (3c) (General Method). Ester **1** (6.1 g, 30 mmol) and the appropriate benzoic acid (50 mmol) were added to PPA, prepared from H_3PO_4 (22 g) and P_2O_5 (44 g), and the mixture stirred for 1.5 h at 100^{o}C. The reaction mixture was poured into water (400 ml), neutralized with K_2CO_3 to weakly alkaline in the medium (pH 9). The solid was filtered off and recrystallized from methanol.

(2-Benzoyl-6-methyl-1-benzofuran-3-yl)acetic Acid (4a), [6-Methyl-2-(thiophen-2-ylcarbonyl)-1-benzo-furan-3-yl]acetic Acid (4b), [2-(3,4-Dimethoxybenzoyl)-6-methyl-1-benzofuran-3-yl]acetic Acid (4c) (General Method). Compound **3a-c** (10 mmol) was added to an aqueous solution (30 ml) containing NaOH (1.0 g, 25 mmol), and the mixture heated to complete solution. The solution was cooled and acidified with formic acid . The precipitated solid was filtered off, washed with water, dried, and recrystallized from 2-propanol.

1-Aryl(hetaryl)-3,5-dihydro-4H-1-benzofuro[2,3-*d*][1,2]diazepin-4-ones 5 (General Method). A. A mixture of the appropriate (2-aroyl-1-benzofuran-3-yl)acetic acid **4a-c** or pyrone **3a-c** was boiled for 20 h with hydrazine hydrate (5 mmol) in ethyl cellosolve (10 ml) in the presence of catalytic quantities (3-4 drops) of acetic acid. The reaction mixture was diluted with water. The precipitated solid was filtered off and washed with water. The product was recrystallized from 2-propanol.

B. A mixture of the appropriate ester of (2-aroyl-6-methyl-1-benzofuran-3-yl)acetic acid **2** (1 mmol) with hydrazine hydrate (5 mmol) in ethyl cellosolve (10 ml) was boiled for 20 h in the presence of catalytic amounts (3-4 drops) of acetic acid. The reaction mixture was diluted with water. The precipitated solid was filtered off and washed with water. The dried solid was boiled in acetic acid for 5 h in the presence of catalytic amounts of *p*-toluenesulfonic acid. The solvent was removed in vacuum. The residue was triturated with water, the solid filtered off, and washed with water. The product was recrystallized from 2-propanol.

C. A mixture of the appropriate ester of (2-aroyl-1-benzofuran-3-yl)acetic acid **2** (1 mmol) and hydrazine acetate (5 mmol) in ethyl cellosolve (10 ml) was boiled for 20 h. The reaction mixture was diluted with water. The precipitated solid was filtered off, and washed with water. The product was recrystallized from 2-propanol.

Hydrazide-hydrazones of (2-aroyl-1-benzofuran-3-yl)acetic acids 6a -c. A mixture of the appropriate pyrone **3a-c** (1 mmol) was boiled for 20 h with hydrazine hydrate (5 mmol) in 2-propanol (15 ml). The reaction mixture was diluted with water. The precipitated solid was filtered off and recrystallized from 2-propanol.

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