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REACTION OF 3-ARYLAMINOBENZOFURO-, 3-ARYLAMINOBENZOTHIENO-, AND 3-ARYLAMINO-INDOLO[2,3-*c*]PYRYLIUM SALTS WITH NUCLEOPHILIC REAGENTS

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We have studied the reactions of 3-arylaminobenzofuro-, 3-arylaminobenzothieno-, and 3-arylaminoindolo[2,3-c]pyrylium salts with ammonium acetate, primary amines, and hydrazine hydrate. In an alcoholic medium, primary amines and hydrazine hydrate open up the pyrylium ring to form arylamides of 2-(N-benzylmethylketimine)hetaryl-3-acetic acids or the corresponding hydrazones, where further heterocyclization does not occur. Upon treatment with ammonium acetate in acetic acid, 2-aryl-1-methylhetero[2,3-c]pyridin-3-(2H)-ones are formed along with their 2-unsubstituted analogs.

Keywords: 3-arylaminobenzothieno[2,3-*c*]pyrylium, 3-arylaminobenzofuro[2,3-*c*]pyrylium, 3-aryl-aminoindolo[2,3-*c*]pyrylium, 2-N-aryl-1-methylhetero[2,3-*c*]pyridin-3(2H)-ones, recyclization.

Pyrylium salts are interesting systems for studying reaction with nucleophilic reagents [1, 2]. The functional groups in the cation affect the electronic structure and consequently the chemical properties of these salts, and participate in ring formation processes [3, 4]. In continuing research on synthesis and conversions of condensed pyrylium salts [5, 6], we have studied the reactions of 3-arylaminobenzofuro- (**1**), 3-arylaminobenzothieno- (**2**), and 3-arylaminoindolo[2,3-*c*]pyrylium (**3**) perchlorates with nucleophilic reagents. With the aim of determining the effect of the arylamino group on the reactivity of the pyrylium ring condensed with different benzannelated heterocycles, we have calculated the electronic structure parameters of salts **1a-3a** within the coupled multiparameter perturbation theory of the PPP method [7, 8]. The parameters of the π-electron Hamiltonian and the resonance integrals are analogous to those assumed for the carbon and nitrogen atoms [9, 10] and the oxygen atom of the furan ring [11], and the thiophene sulfur atom in [12]. The effect of substituents on the electronic structure parameters of the compounds was taken into account within perturbation theory describing chemical substitution [13].

Based on analysis of the electronic structure parameters of the cations for salts **1a-3a**, we showed that charge localization is observed mainly in the pyrylium ring and on the hetero atoms O, N, and it decreases somewhat as we go to the corresponding anhydro forms of these compounds **4a-6a.**

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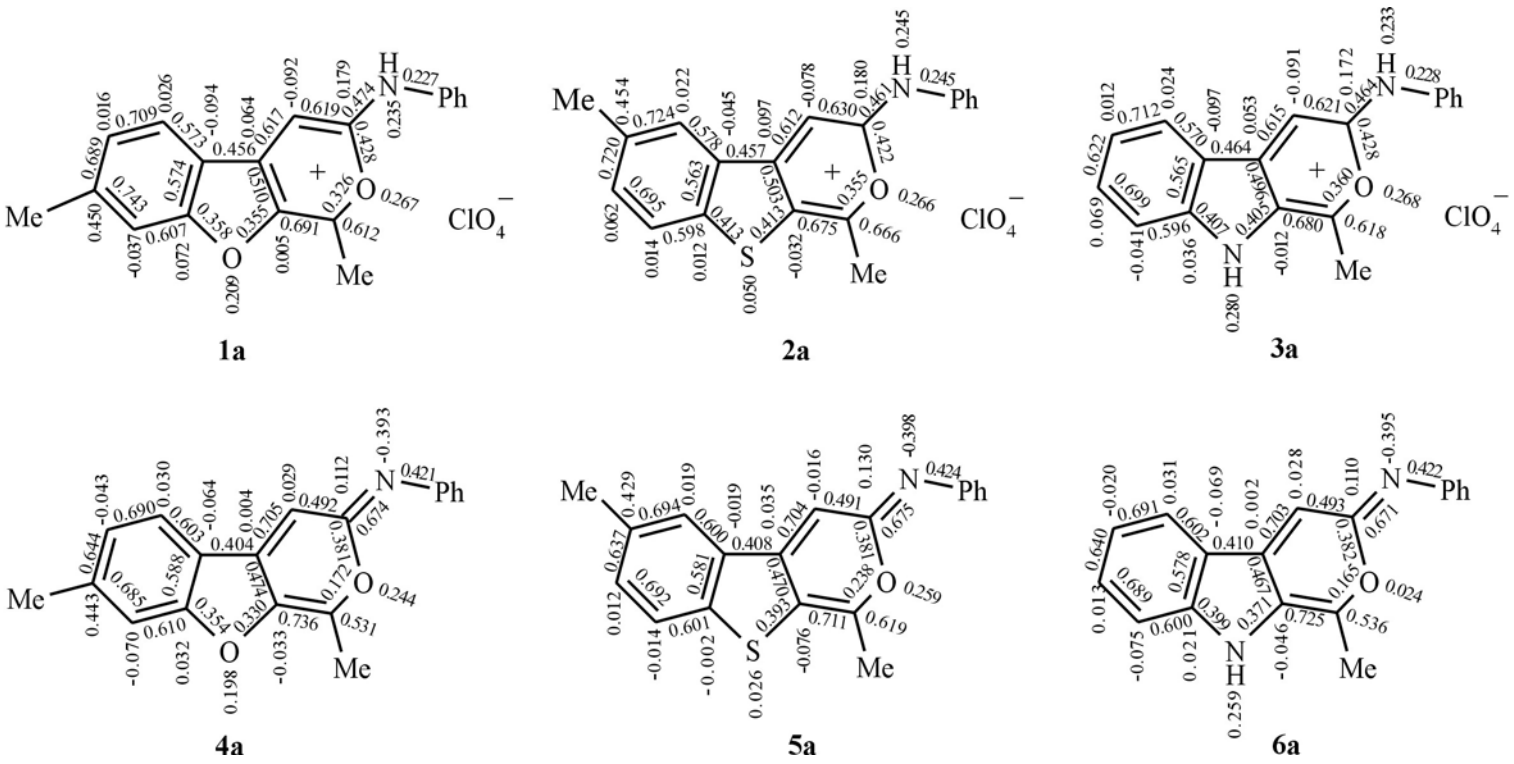


Fig. 1. Molecular diagrams for the salts **1a-3a** and the corresponding anhydro forms **4a-6a**.

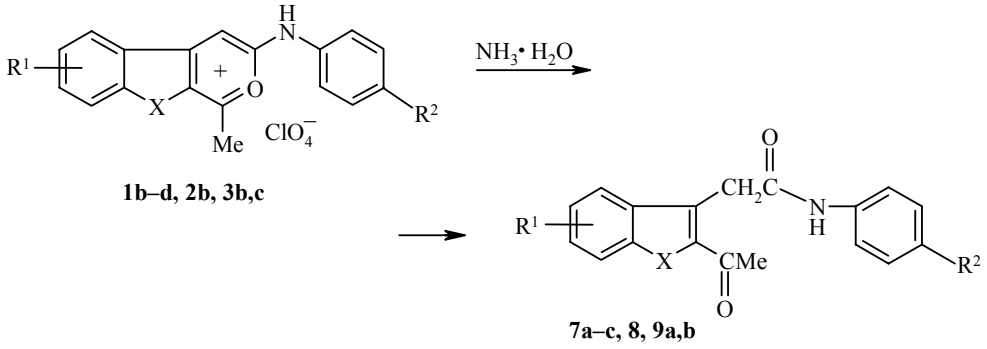
We note that the values of the residual π-electron charges on the nitrogen and oxygen atoms remain virtually unchanged. Analysis of short-range bond orders P_{ik} for compounds **1a-3a** and the corresponding anhydrido forms **4a-6a** showed that in the pyrylium ring, the $C_{(1)}$–O and $C_{(3)}$–O bonds are the weakest.

For quantum-chemical treatment of intramolecular cyclizations based on the Fukui index approach [14] within a statistical model of reactivity, as the reactivity indices we selected the long-range bond orders $P_{ik}(0)$. In this case, the magnitude defines the possibility and rate of cyclization, while the sign defines the stereospecificity of the process.

Among the possible molecular rearrangements of the structures under consideration, cyclization at the $C_{(1)}$–N bond is of practical interest in compounds **1a-3a** ($P^{1a}_{C(1)–N}$ = 0.103; $P^{1b}_{C(1)–N}$ = 0.106; $P^{1c}_{C(1)–N}$ = 0.100), the probability of which increases in the case of the anhydro forms ($P^{2a}_{C(1)–N}$ = 0.145; $P^{2b}_{C(1)–N}$ = 0.149; $P^{2c}_{C(1)–N}$ = 0.145).

According to the above discussion, the 1 position in the pyrylium cation is most susceptible to attack by a nucleophilic reagent.

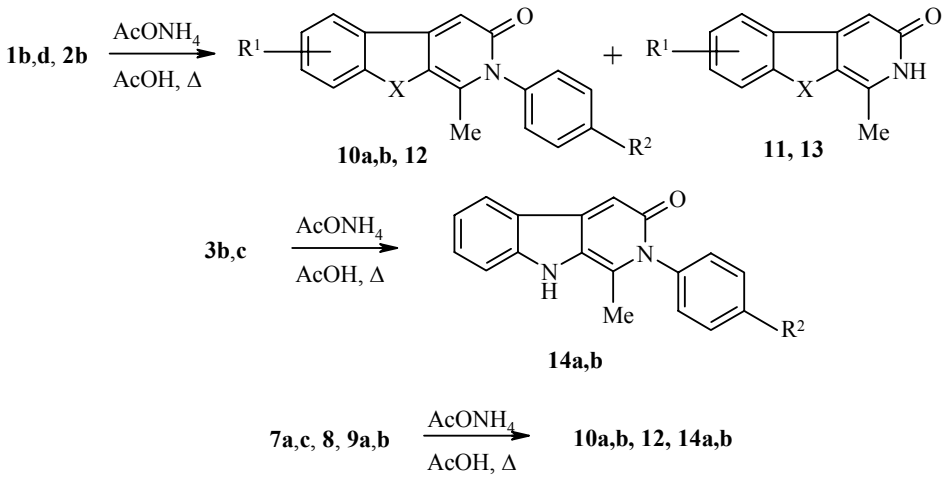
We studied the reactions of 3-arylaminoheteropyrylium perchlorates **1b-d, 2b, 3b,c** with nucleophilic reagents such as ammonia, primary and secondary amines, and hydrazine hydrate. We found significant differences between the properties of compounds **1-3** and the properties of analogously constructed 1,3-dialkyl- and 1-alkyl-3-aryl-substituted pyrylium salts [1, 2, 15]. Thus reaction of perchlorates **1b-d, 2b, 3b,c** with an aqueous alcoholic solution of ammonia does not occur according to the traditional route for pyrylium salts (leading to pyridine bases) but rather occurs with opening of the pyrylium ring and formation of 2-acetylhetaryl-3-acetic acid arylamides **7a-c, 8, 9a,b**, identical to compounds we obtained earlier from the corresponding pyrones and arylamines [16].



1, **7** X = O, R^1 = Me-7; **1b**, **7a** R^2 = Me; **1c**, 7**b** R^2 = Cl; **1d**, **7c** R^2 = Br; **2b**, **8** X = S, R^1 = Me-6, R^2 = Me; **3**, **9** X = NH, R^1 = H; **3b**, **9a** R^2 = Me; **3c**, **9b** R^2 = OMe

When perchlorates **1b,d** and **2b** were boiled with ammonium acetate in acetic acid, in each case two products were isolated: from salt **1b** we obtained 1,7-dimethyl-2-(4-methylphenylamino)benzofuro[2,3-*c*]-pyridin-3(2H)-one (**10a**) (64%) and 1,7-dimethylbenzofuro[2,3-*c*]pyridin-3(2H)-one (**11**) (36%); from salt **1d** we obtained 2-(4-bromophenyl)-1,7-dimethylbenzofuro[2,3-*c*]pyridin-3(2H)-one (**10b**) (60%) and pyridinone **11** (40%); from salt **2b** we obtained 1,6-dimethyl-2-(4-methylphenyl)(benzothieno[2,3-*c*]pyridin-3(2H)-one (**12**) (55%) and 1,6-dimethylbenzothieno[2,3-*c*]pyridin-3(2H)-one (**13**) (45%). Compound **11** is identical to the sample obtained from 1-methyl-3-hydroxybenzofuro[2,3-*c*]pyrylium borofluoride (according to TLC and ^{1}H NMR [4]). Under the indicated conditions, from perchlorates **3b,c** we obtained only 2-aryl-1-methylindolo-[2,3-*c*]pyridin-3(2H)-ones (**14a,b**) in 72% and 74% yields respectively.

Formation of products **11, 13** is connected with addition of the nucleophile at the 3 position of the pyrylium ring. Indirect evidence for nucleophilic attack at this position comes from the fact that the pyridones **10a,b, 12, 14a,b** are formed exclusively upon reaction of the keto amides **7a,c, 8, 9a,b** with ammonium acetate in acetic acid.



10, **11** X = O, R^1 = Me-7; **10 a** R^2 = Me, **b** R^2 = Br; **12**, **13** X = S, R^1 = Me-6, R^2 = Me;
14 a R^2 = Me, **b** R^2 = OMe

The structure of 2-(4-bromophenyl)-1,7-dimethylbenzofuro[2,3-*c*]pyridin-3(2H)-one **10b** was established using X-ray diffraction (Fig. 2, Tables 1-3).

The six-membered heterocycle of compound **10b** is planar within 0.02 Å. In the $O_{(2)}$–$C_{(1)}$–$C_{(2)}$–$C_{(3)}$–$C_{(10)}$ moiety, we observe strong delocalization of the electron density, as indicated by the lengthening of the $O_{(2)}$–$C_{(1)}$ bond to 1.228(5) Å compared with the average value of 1.210 Å [17] and the $C_{(2)}$–$C_{(3)}$ bond to 1.361(6) Å (average value 1.330 Å), and shortening of the $C_{(1)}$–$C_{(2)}$ bond to 1.426(6) Å (average value 1.464 Å), $C_{(3)}$–$C_{(10)}$ to 1.412(6) Å (average value 1.464 Å). The bromophenyl substituent at the $N_{(1)}$ atom is rotated practically perpendicular to the plane of the heterocycle [torsional angle $C_{(11)}$–$N_{(1)}$–$C_{(12)}$–$C_{(17)}$ 106.3(5)°]. Breakdown of the conjugation leads to lengthening of the $N_{(1)}$–$C_{(12)}$ bond to 1.453(5) Å (average value 1.390 Å). In the tricyclic moiety, the benzene and pyridine rings are rotated relative to each other by a 6.3° angle. The bond lengths in the five-membered ring are appreciably different from those in the furan ring. They all are considerably lengthened (Table 2), which indicates appreciable weakening of the conjugation in that moiety. In the crystal, we observe shortened intermolecular contacts $H_{(13)}\cdots O_{(2')}$ (x, 0.5 – y, z – 0.5) 2.33 Å (the sum of the van der Waals radii is 2.45 Å [18]), Br(1)···H(6') (1 + x, 0.5 – y, 0.5 + z) 3.08 Å (3.23 Å).

When pyrylium perchlorates **1b-d, 2b, 3b,c** react with benzylamine or furfurylamine in alcohol, addition of the primary amine occurs at the 1 position of the pyrylium ring. Subsequent breaking of the $C_{(1)}$–O bond leads to formation of 2-(1-benzyliminoethyl)hetaryl-3-acetic acid arylamides **15a-c, 16, 17a,b**, which are stable under the reaction conditions and do not undergo further heterocyclization. This is the first example of isolation of intermediates in reactions of pyrylium salts with primary amines, which were postulated earlier by Dimroth and other researchers [19-21].

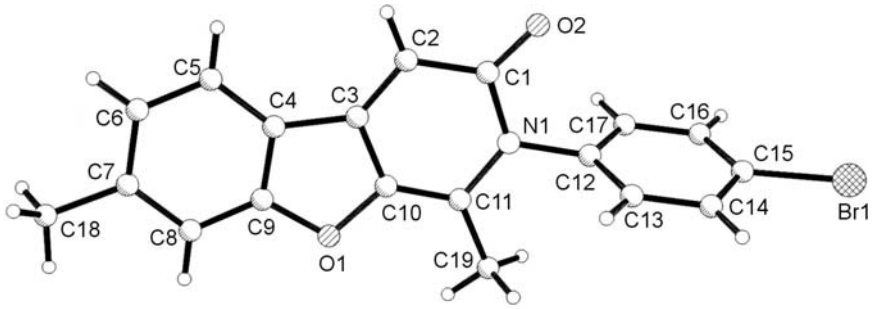
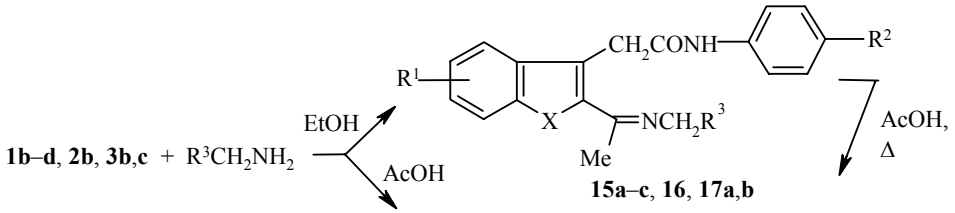
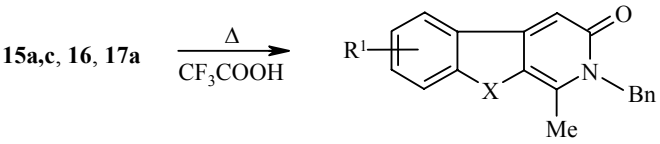


Fig. 2. Structure of 2-(4-bromophenyl)-1,7-dimethylbenzofuro[2,3-*c*]pyridin-3(2H)-one **10b**.

TABLE 1. Coordinates of Non-hydrogen Atoms (*x, y, z*) and Equivalent Isotropic Thermal Parameters U_{eq}, Å^2, in the Structure of **10b**

Atom	$x \cdot 10^4$	$y \cdot 10^4$	$z \cdot 10^4$	U_{eq}
$Br_{(1)}$	5880(1)	3675(1)	595(1)	74(1)
$N_{(1)}$	1914(2)	3434(3)	-699(5)	36(1)
$O_{(1)}$	-19(2)	4706(2)	-2410(4)	45(1)
$O_{(2)}$	2078(2)	1850(2)	13(4)	43(1)
$C_{(1)}$	1579(3)	2505(4)	-440(6)	35(1)
$C_{(2)}$	655(3)	2394(3)	-761(6)	38(1)
$C_{(3)}$	166(3)	3147(3)	-1384(6)	33(1)
$C_{(4)}$	-753(3)	3294(3)	-1928(6)	34(1)
$C_{(5)}$	-1500(3)	2711(4)	-1935(6)	43(1)
$C_{(6)}$	-2270(3)	3086(4)	-2651(6)	47(1)
$C_{(7)}$	-2310(3)	4004(4)	-3361(6)	44(1)
$C_{(8)}$	-1576(3)	4595(3)	-3323(6)	38(1)
$C_{(9)}$	-810(3)	4214(4)	-2577(6)	38(1)
$C_{(10)}$	572(3)	4045(3)	-1686(6)	36(1)
$C_{(11)}$	1430(3)	4216(3)	-1331(6)	34(1)
$C_{(12)}$	2857(3)	3550(3)	-395(6)	32(1)
$C_{(13)}$	3415(3)	3535(3)	-1767(7)	44(1)
$C_{(14)}$	4314(3)	3599(4)	-1513(7)	51(1)
$C_{(15)}$	4638(3)	3644(4)	185(8)	47(1)
$C_{(16)}$	4094(3)	3680(4)	1579(7)	47(1)
$C_{(17)}$	3187(3)	3617(3)	1307(6)	44(1)
$C_{(18)}$	-3170(3)	4355(4)	-4199(7)	59(2)
$C_{(19)}$	1853(3)	5166(3)	-1575(6)	46(1)





15 X = O, **15 a–c** R^1 = Me-6, **a** R^2 = Me, R^3 = Ph, **b** R^2 = Cl, R^3 = 2-furyl, **c** R^2 = Br, R^3 = Ph; **18** X = O, R^1 = Me-7; **16**, **19** X = S, **16** R^1 = Me-5, R^2 = Me, R^3 = Ph, **19** R^1 = Me-6, **17**, **20** X = NH; **17** R^1 = H, **a** R^2 = Me, R^3 = Ph; **b** R^2 = MeO, R^3 = 2-furyl, **20** R^1 =H

Reaction of pyrylium salts **1b-d, 2b, 3b,c** with benzylamine and furfurylamine in acetic acid, in contrast to the reaction in alcohol, leads to the corresponding 2-aryl-1-methylheteropyridin-3(2H)-ones **10a-c, 12, 14a,b** and probably also occurs through intermediate formation of ketimines **15a-c, 16, 17a,b**, which in acid medium undergo ring closure to form pyridones **10a-c, 12, 14a,b** respectively. To test this hypothesis, we studied heterocyclization of ketimines **15-17** under acid catalysis conditions. We showed that when they are boiled in acetic acid, the pyridones **10, 12, 14** are formed in good yields.

TABLE 2. Bond Lengths (*l*) in the Structure of **10b**

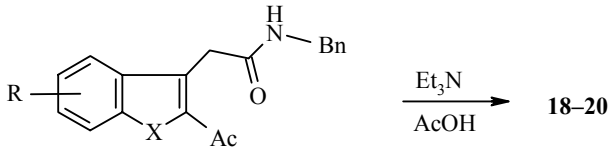
Bond	*l*, Å	Bond	*l*, Å	Bond	*l*, Å
$Br_{(1)}–C_{(15)}$	1.903(5)	$C_{(10)}–C_{(11)}$	1.343(6)	$C_{(4)}–C_{(9)}$	1.373(7)
$N_{(1)}–C_{(1)}$	1.401(6)	$C_{(12)}–C_{(13)}$	1.360(6)	$C_{(5)}–C_{(6)}$	1.379(6)
$O_{(1)}–C_{(9)}$	1.384(5)	$C_{(13)}–C_{(14)}$	1.376(6)	$C_{(7)}–C_{(8)}$	1.383(6)
$O_{(2)}–C_{(1)}$	1.228(5)	$C_{(15)}–C_{(16)}$	1.359(7)	$C_{(8)}–C_{(9)}$	1.387(6)
$C_{(2)}–C_{(3)}$	1.361(6)	$N_{(1)}–C_{(11)}$	1.392(6)	$C_{(11)}–C_{(19)}$	1.480(6)
$C_{(3)}–C_{(4)}$	1.460(6)	$N_{(1)}–C_{(12)}$	1.453(5)	$C_{(12)}–C_{(17)}$	1.383(6)
$C_{(4)}–C_{(5)}$	1.391(6)	$O_{(1)}–C_{(10)}$	1.390(5)	$C_{(14)}–C_{(15)}$	1.376(7)
$C_{(6)}–C_{(7)}$	1.386(7)	$C_{(1)}–C_{(2)}$	1.426(6)	$C_{(16)}–C_{(17)}$	1.390(6)
$C_{(7)}–C_{(18)}$	1.520(6)	$C_{(3)}–C_{(10)}$	1.412(6)		

TABLE 3. Bond Angles (ω) in the Structure of **10b**

Angle	ω, deg.	Angle	ω, deg.	Angle	ω, deg.
$C_{(11)}–N_{(1)}–C_{(1)}$	125.3(4)	$C_{(10)}–C_{(11)}–N_{(1)}$	115.6(4)	$C_{(5)}–C_{(4)}–C_{(3)}$	133.8(4)
$C_{(1)}–N_{(1)}–C_{(12)}$	116.0(4)	$N_{(1)}–C_{(11)}–C_{(19)}$	120.8(4)	$C_{(5)}–C_{(6)}–C_{(7)}$	122.1(5)
$O_{(2)}–C_{(1)}–N_{(1)}$	119.9(4)	$C_{(13)}–C_{(12)}–N_{(1)}$	120.1(4)	$C_{(8)}–C_{(7)}–C_{(18)}$	120.1(5)
$N_{(1)}–C_{(1)}–C_{(2)}$	115.6(4)	$C_{(12)}–C_{(13)}–C_{(14)}$	121.4(4)	$C_{(7)}–C_{(8)}–C_{(9)}$	116.7(4)
$C_{(2)}–C_{(3)}–C_{(10)}$	119.9(4)	$C_{(16)}–C_{(15)}–C_{(14)}$	121.8(4)	$C_{(4)}–C_{(9)}–C_{(8)}$	123.3(4)
$C_{(10)}–C_{(3)}–C_{(4)}$	104.3(4)	$C_{(14)}–C_{(15)}–Br_{(1)}$	119.2(4)	$C_{(11)}–C_{(10)}–O_{(1)}$	125.2(4)
$C_{(9)}–C_{(4)}–C_{(3)}$	106.5(4)	$C_{(12)}–C_{(17)}–C_{(16)}$	118.8(5)	$O_{(1)}–C_{(10)}–C_{(3)}$	111.6(4)
$C_{(6)}–C_{(5)}–C_{(4)}$	117.6(5)	$C_{(11)}–N_{(1)}–C_{(12)}$	118.6(4)	$C_{(10)}–C_{(11)}–C_{(19)}$	123.5(4)
$C_{(8)}–C_{(7)}–C_{(6)}$	120.6(4)	$C_{(9)}–O_{(1)}–C_{(10)}$	105.1(3)	$C_{(13)}–C_{(12)}–C_{(17)}$	120.2(4)
$C_{(6)}–C_{(7)}–C_{(18)}$	119.3(4)	$O_{(2)}–C_{(1)}–C_{(2)}$	124.4(4)	$C_{(17)}–C_{(12)}–N_{(1)}$	119.5(4)
$C_{(4)}–C_{(9)}–O_{(1)}$	112.3(4)	$C_{(3)}–C_{(2)}–C_{(1)}$	120.2(4)	$C_{(13)}–C_{(14)}–C_{(15)}$	117.9(5)
$O_{(1)}–C_{(9)}–C_{(8)}$	124.5(4)	$C_{(2)}–C_{(3)}–C_{(4)}$	135.7(4)	$C_{(16}–C_{(15)}–Br_{(1)}$	119.0(4)
$C_{(11)}–C_{(10)}–C_{(3)}$	123.2(4)	$C_{(9)}–C_{(4)}–C_{(5)}$	119.7(4)	$C_{(15)}–C_{(16)}–C_{(17)}$	119.7(4)

In trifluoroacetic acid, heterocyclization of ketimines **15a,c, 16, 17a** occurs with formation of the corresponding 2-benzyl-1-methylhetero[2,3-*c*]pyridin-3(2H)-ones **18-20**.

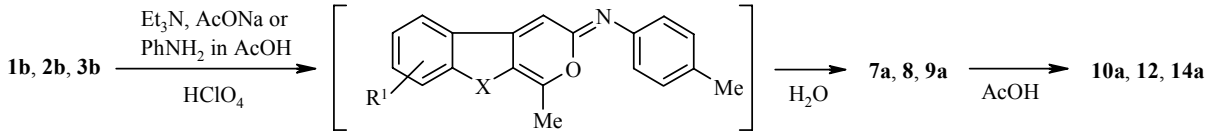
The structure of 2-benzyl-1,7-dimethylbenzofuro[2,3-*c*]pyridin-3(2H)-one (**18**), 2-benzyl-1,6-dimethylbenzothieno[2,3-*c*]pyridin-3(2H)-one (**19**) and 2-benzyl-1-methylindolo[2,3-*c*]pyridin-3(2H)-one (**20**) was confirmed by an alternate synthesis from 2-acetylhetaryl-3-acetic acid benzylamides **21-23**. Samples of compounds **18-20** obtained by the different methods have identical characteristics (mp and ^{1}H NMR data).



21–23

21 X = O, R = Me-6; **22** X = S, R = Me-5; **23** X = NH, R = H

2-Arylheteropyridin-3(2H)-ones **10a, 12, 14a** were also synthesized by reaction of pyrylium salts **1b-3b** with triethylamine, sodium acetate, or aniline in acetic acid. Under these conditions, aniline acts as a base rather than as a reagent. Formation of the products **10a, 12, 14a** obviously occurs through the corresponding anhydro bases **4b-6b**, their further conversion to the corresponding keto amides **7a, 8, 9a** and cyclization of the latter.

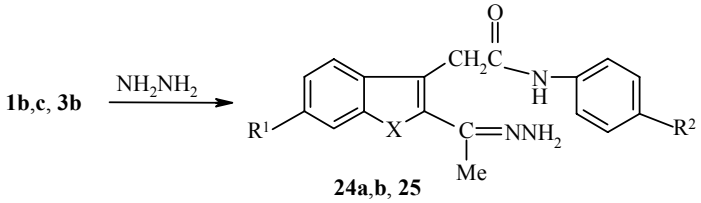


4b–6b

4b R^1 = Me-7, **5b** R^1 = Me-6, **6b** R^1 = H

Our attempts to obtain the anhydro bases **4b-6b** by treatment of the pyrylium salts **1b, 2b,** and **3b** with triethylamine in THF were unsuccessful due to the tendency of these bases toward hydrolysis, which during their purification led to keto amides **7a, 8**, and **9a**.

Hydrazine hydrate reacts with the pyrylium salts **1b,c, 3b** like primary amines. The reaction stops in the step of formation of hydrazones of 2-acetylhetaryl-3-acetic acid arylamides **24a,b, 25**. The same hydrazones **24a,b, 25** may also be obtained from 2-acetylhetaryl-3-acetic acid arylamides **7a,b, 9a** and hydrazine hydrate.



24a,b, 25

24 X = O, R^1 = Me, **a** R^2 = Me, **b** R^2 = Cl, **25** X = NH, R^1 = H, R^2 =Me

TABLE 4. Characteristics of Synthesized Compounds

Compound	Empirical formula	Found, % / Calculated, %					mp, °C	Yield, %
		C	H	Hal	N	S		
12a	$C_{27}H_{26}N_2O_2$	79.18 / 79.00	6.24 / 6.38	—	6.92 / 6.82	—	175-176	98
12b	$C_{24}H_{21}ClN_2O_3$	68.31 / 68.49	4.88 / 5.03	8.55 / 8.42	6.79 / 6.66	—	172-173	90
12c	$C_{26}H_{23}BrN_2O_2$	65.75 / 65.69	5.04 / 4.88	16.69 / 16.81	5.72 / 5.89	—	205	96
13	$C_{27}H_{26}N_2OS$	75.87 / 76.02	6.25 / 6.14	—	6.44 / 6.57	7.60 / 7.52	150-152	91
14a	$C_{26}H_{25}N_3O$	79.04 / 78.96	6.22 / 6.37	—	10.46 / 10.62	—	172-173	79
14b	$C_{24}H_{23}N_3O_3$	71.67 / 71.80	5.70 / 5.77	—	10.63 / 10.47	—	169-170	63
15	$C_{20}H_{17}NO_2$	79.32 / 79.19	5.77 / 5.65	—	4.51 / 4.62	—	205	92
16	$C_{20}H_{17}NOS$	75.06 / 75.20	5.49 / 5.36	—	4.52 / 4.38	9.95 / 10.04	223-224	91
17	$C_{19}H_{16}N_2O$	79.26 / 79.14	5.68 / 5.59	—	9.56 / 9.71	—	288	89
18	$C_{20}H_{19}NO_3$	74.86 / 74.75	5.83 / 5.96	—	4.21 / 4.36	—	134-135	96
19	$C_{20}H_{19}NO_2S$	71.31 / 71.19	5.45 / 5.68	—	4.04 / 4.15	9.36 / 9.50	196-197	80
20	$C_{19}H_{18}N_2O_2$	74.40 / 74.49	6.02 / 5.92	—	9.03 / 9.14	—	173	97
21a	$C_{20}H_{21}N_3O_2$	71.75 / 71.62	6.22 / 6.31	—	12.61 / 12.53	—	191	97
21b	$C_{19}H_{18}ClN_3O_2$	64.26 / 64.14	5.03 / 5.10	9.87 / 9.96	11.73 / 11.81	—	201	96
22	$C_{19}H_{20}N_4O$	71.16 / 71.23	6.23 / 6.29	—	17.54 / 17.49	—	107	95

TABLE 5. ^{1}H NMR Spectra of Synthesized Compounds

Com-pound	δ, ppm, SSCC (*J*, Hz)
15a	2.20 (3H, s, CH_3-4'); 2.46 (6H, s, CH_3C=N and CH_3-6); 4.10 (2H, s, CH_2CO); 4.80 (2H, s, CH_2N=); 6.95 (2H, d, *J* = 8.5, H-3',5'); 7.11 (2H, d, *J* = 8.5, H-2',6'); 7.17-7.32 (5H, m, H_{arom}); 7.45 (1H, s, H-7); 7.47 (1H, d, *J* = 8.0, H-5); 7.59 (1H, d, *J* = 8.0, H-4); 10.25 (1H, s, NH)
15b	2.42 (6H, s, CH_3C=N and CH_3-6); 3.95 (2H, s, CH_2CO); 4.77 (2H, s, CH_2N=); 6.36 (2H, m, H*$_{fur}$-3,4); 7.11 (1H, d, *J* = 8.0, H-5); 7.20 (2H, d, *J* = 8.7, H-2',6'); 7.29 (2H, d, *J* = 8.7, H-3',5'); 7.40 (1H, s, H-7); 7.52 (1H, d, H_{fur}-5); 7.53 (1H, d, *J* = 8.0, H-4); 10.51 (1H, s, NH)
15c	2.42 (6H, s, CH_3C=N and CH_3-6); 4.07 (2H, s, CH_2CO); 4.76 (2H, s, CH_2N=); 7.11 (1H, d, *J* = 8.0, H-5); 7.17-7.43 (10H, m, H_{arom}); 7.56 (1H, d, *J* = 8.0, H-4); 10.40 (1H, s, NH)
16	2.15 (3H, s, CH_3-4'); 2.42 (3H, s, CH_3-5); 2.49 (3H, s, CH_3C=N); 4.13 (2H, s, CH_2CO); 4.79 (2H, s, CH_2N=); 6.91 (2H, d, *J* = 8.3, H-3',5'); 7.03 (2H, d, *J* = 8.3, H-2',6'); 7.24-7.31 (5H, m, H_{arom}); 7.46 (1H, d, *J* = 8.2, H-6); 7.78 (1H, s, H-4); 7.84 (1H, d, *J* = 8.2, H-7); 10.48 (1H, s, NH)
17a	2.14 (3H, s, CH_3-4'); 2.50 (3H, s, CH_3C=N); 3.93 (2H, s, CH_2CO); 4.84 (2H, s, CH_2N=); 6.87 (2H, d, *J* = 8.5, H-3',5'); 6.96 (2H, d, *J* = 8.5, H-2',6'); 7.04 (1H, t, *J* = 8.0, H-6); 7.18 (1H, t, *J*= 8.0, H-5); 7.24 (5H, m, H_{arom}); 7.42 (1H, d, *J* = 8.1, H-7); 7.64 (1H, d, *J* = 7.7, H-4); 10.50 (1H, s, NHCO); 11.38 (1H, s, $N_{(1)}H$)
17b	2.47 (3H, s, CH_3C=N); 3.63 (3H, s, CH_3O-4'); 3.85 (2H, s, CH_2CO); 4.81 (2H, s, CH_2N=); 6.40 (2H, m, H_{fur}-3,4); 6.70 (2H, d, *J* = 9.0, H-3',5'); 7.02 (1H, t, *J* = 8.0, H-6); 7.14 (2H, d, *J* = 9.0, H-2',6'); 7.16 (1H, t, *J* = 8.0, H-5); 7.39 (1H, d, *J* = 8.0, H-7); 7.55 (1H, m, H_{fur}-5); 7.62 (1H, d, *J* = 7.8, H-4); 10.50 (1H, s, NHCO); 11.38 (1H, s, $N_{(1)}H$)
18	2.44 (6H, s, CH_3-1,7); 5.40 (2H, s, CH_2); 6.86 (1H, s, H-4); 7.13-7.34 (7H, m, H_{arom}); 7.92 (1H, d, *J* = 8.0, H-5)
19	2.43 (3H, s, CH_3-6); 2.48 (3H, s, CH_3-1); 5.50 (2H, s, CH_2); 7.17-7.40 (6H, m, H-4 and H_{phenyl}); 7.46 (1H, d, *J* = 8.2, H-7); 7.77 (1H, d, *J* = 8.2, H-8); 8.09 (1H, s, H-5)
20	2.51 (3H, s, CH_3-1); 5.49 (2H, s, CH_2); 6.89 (1H, s, H-4); 7.05 (1H, t, *J* = 7.8, H-7); 7.11 (2H, d, *J* = 8.0, H-2',6'); 7.19-7.33 (4H, m, H-3',4',5',8); 7.43 (1H, t, *J* = 8.0, H-6); 7.97 (1H, d, *J* = 7.6, H-5); 10.48 (1H, s, $N_{(9)}H$)
21	2.46 (3H, s, CH_3-6); 2.56 (3H, s, $COCH_3$); 4.05 (2H, s, CH_2CO); 4.28 (2H, d, *J* = 5.8, CH_2); 7.15-7.30 (6H, m, H_{arom}); 7.49 (1H, s, H-7); 7.64 (2H, d, *J* = 8.2, H-4); 8.53 (1H, t, *J* = 5.8, NH)
22	2.46 (3H, s, CH_3-5); 2.60 (3H, s, $COCH_3$); 4.25 (2H, s, CH_2); 4.42 (2H, d, *J* = 5.8, CH_2); 7.21-7.43 (6H, m, H_{arom}); 7.85 (1H, d, *J* = 8.0, H-7); 7.92 (1H, s, H-4); 8.67 (1H, t, *J* = 5.8, NH)
23	2.60 (3H, s, $COCH_3$); 4.03 (2H, s, CH_2); 4.26 (2H, d, *J* = 5.8, CH_2); 7.05 (1H, t, *J* = 8.0, H-6); 7.16-7.31 (6H, m, H_{arom}); 7.43 (1H, d, *J* = 8.2, H-7); 7.71 (1H, d, *J* = 8.2, H-4); 8.38 (1H, t, *J* = 5.8, NH); 11.59 (1H, s, $N_{(1)}H$)
24a	2.14 (3H, s, CH_3-7); 2.22 (3H, s, CH_3-4'); 2.40 (3H, s, CH_3C=N); 3.87 (2H, s, CH_2); 6.99 (2H, s, NH_2); 7.07 (2H, d, *J* = 7.8, H-3',5',5); 7.34 (1H, s, H-7); 7.43 (2H, d, *J* = 7.8, H-2',6',4); 10.20 (1H, s, NH)
24b	2.17 (3H, s, CH_3-6); 2.43 (3H, s, CH_3C=N); 3.89 (2H, s, CH_2); 6.97 (2H, s, NH_2); 7.07 (1H, d, *J* = 8.0, H-5); 7.30 (2H, d, *J* = 8.6, H-2',6'); 7.32 (1H, s, H-7); 7.46 (1H, d, *J* = 8.0, H-4); 7.60 (2H, d, *J* = 8.6, H-3',5'); 10.44 (1H, s, NH)
25	2.21 (6H, s, CH_3C=N and CH_3-4'); 3.80 (2H, s, CH_2); 6.77 (2H, s, NH_2); 6.95-7.12 (4H, m, H-3',5',5,6); 7.33 (1H, d, *J* = 7.7, H-7); 7.41 (2H, d, *J* = 8.2, H-2',6'); 7.54 (1H, d, *J* = 7.7, H-4); 10.50 (1H, s, CONH); 11.09 (1H, s, $N_{(1)}H$)

* H_{fur}: here and elsewhere, the proton of the 2-furyl substituent.

Thus when the 3-arylamino-1-methylhetero[2,3-*c*]pyrylium salts **1-3** enter into reactions with nucleophilic reagents in alcohol, addition of the nucleophile at the position 1 of the pyrylium moiety and opening of the pyrylium ring occur, while in the analogous reaction in acetic acid, subsequent heterocyclization of the addition products occurs to form derivatives of 2-aryl-1-methylbenzofuro-, 2-aryl-1-methylbenzothieno-, and 2-aryl-1-methylindolo[2,3-*c*]pyridin-3(2H)-ones.

EXPERIMENTAL

The ^{1}H NMR spectra were taken on a Gemini-200 (200 MHz) in DMSO-d_6, internal standard TMS. The purity of the products obtained was monitored using TLC on Silufol UV-254 plates in the system toluene–ethanol, 4:1. The reaction products were analyzed by HPLC on a Laboratory Pristroje (Prague) chromatograph. Detector, RIDK-102 differential refractometer; column 3 × 150 mm; stationary phase, Separon C18; mobile phase, methanol–water, 7:3.

Reaction of Perchlorates 1b-d, 2b, 3b,c with an Aqueous Alcoholic Solution of Ammonia. 2-Acetylhetaryl-3-acetic Acid Arylamides (7a-c, 8, 9a,b). 25% ammonia solution (5 ml) was added to a suspension of the pyrylium salt **1b-d, 2b, 3b,c** (50 mmol) in alcohol (25 ml). The precipitate formed was filtered out and recrystallized from 2-propanol (products **7a-c**) or aqueous DMF (products **8, 9a,b**). We obtained **2-acetyl-6-methylbenzo[*b*]furan-3-ylacetic acid 4-methylphenylamide (7a)** (92%, mp 172-173°C), **2-acetyl-6-methylbenzo[*b*]furan-3-ylacetic acid 4-chlorophenylamide (7b)** (89%, mp 175-176°C), **2-acetyl-6-methylbenzo-[*b*]furan-3-ylacetic acid 4-bromophenylamide (7c)** (91%, mp 192-193°C), **2-acetyl-5-methylbenzo[*b*]thiophene-3-ylacetic acid 4-methylphenylamide (8)** (90%, mp 205-206°C), **2-acetylindol-3-ylacetic acid 4-methylphenylamide (9a)** (93%, mp 229-230°C), **2-acetylindol-3-ylacetic acid 4-methoxyphenylamide (9b)** (92%, mp 224-225°C).

The listed products are identical (mp) to the amides described previously in [16].

Reaction of Perchlorates (1c,d, 2b, 3b,c) with Ammonium Acetate in Acetic Acid. 1-Methylhetero[2,3-*c*]pyridin-3(2H)-ones (11, 13). 2-Aryl-1-methylhetero[2,3-*c*]pyridin-3(2H-ones (10a-c, 12, 14a,b). A mixture of perchlorate **1b,d, 2b, 3b,c** (26 mmol) and ammonium acetate (1 g) in 98% acetic acid (15 ml) was boiled for 3 h. The mixture was cooled down; the pyridones **11, 13** precipitating during the reaction was filtered out, washed with alcohol, and crystallized from DMF. The filtrate was poured into water (100 ml) and neutralized with a 10% aqueous solution of ammonia. The precipitating products **10a,b, 12, 14a,b** were filtered out and crystallized from 2-propanol. Compounds **10a,b, 11a, 12, 14a,b** are identical to those described in the literature (mp) [15].

Reaction of Perchlorates (1b-d, 2b, 3b,c) with Triethylamine (Procedure A), Sodium Acetate (B) or Aniline (C) in Acetic Acid. 2-Aryl-1-methylhetero[2,3-*c*]pyridin-3(2H)-ones (10a-c, 12, 14a,b). A. Triethylamine (3 ml) was added to a suspension of pyrylium salt **1b-d, 2b, 3b,c** (0.01 mol) in acetic acid (30 ml). The solution was boiled for 2 h and then cooled down. Water (100 ml) was added, and the mixture was neutralized with a 10% aqueous solution of ammonia. The precipitate formed was filtered out and recrystallized from 2-propanol. We obtained pyridones **10a-c, 12, 14a,b** in close to quantitative yields.

B. The above-indicated products were synthesized similarly, using sodium acetate (3 g) instead of triethylamine. Yields, %: **10a**, 93%; **10b**, 89%, **10c**, 92%; **12**, 90%; **14a**, 78%, **14b**, 83%.

C. The same products were obtained using aniline (3 ml). Yields, %: **10a**, 75%; **10b**, 72%; **10c**, 78%; **12**, 76%; **14a**, 68%; **14b**; 70%. Samples of 2-arylpyridones **10a-c**, **12**, **14a,b** obtained by procedures A, B, C did not result in depression of the melting point when mixed with samples obtained by reaction of salts **1b-d**, **2b**, **3b,c** with $AcONH_4$ in AcOH (see above).

2-[(1-Benzyl(furfuryl)iminoethyl)]hetaryl-3-acetic Acid Arylamides (15a-c, 16, 17a,b) (General Procedure). Benzylamine or furfurylamine (5 ml) was added to a suspension of the pyrylium salt **1b-d, 2b, 3b,c** (0.01 mol) in 2-propanol (50 ml). The mixture obtained was boiled for 1 h and then cooled down, and water (20 ml) was added. The precipitate was filtered out and washed with water. We obtained the products **15a-c, 16, 17a,b**, which were crystallized from 2-propanol (**15a,c, 17a,b**), methanol (**15b**), or a 1:3 benzene–hexane mixture (**16**).

Cyclization of 2-[(1-Benzyl(furfuryl)iminoethyl)]hetaryl-3-acetic Acid Arylamides (15a-c, 16, 17a,b) in Acetic Acid. Pyridinones (10a-c, 12, 14a,b). A solution of compound **15a-c, 16, 17a,b** (1 g) in acetic acid (10 ml) was boiled for 3 h and then cooled down, diluted with water (30 ml), and treated with a 10% aqueous solution of ammonia until pH > 7 was reached. The precipitate was filtered out and washed with water.

We obtained 2-arylpyridones (%): **10a** (92%), **10b** (89%), **10c** (91%), **12** (85%), **14a** (95%), **14b** (87). Samples of compounds **10a-c, 12, 14a,b** did not result in a depression of the melting point when mixed with samples obtained by reaction of salts **1b-d, 2b, 3b,c** with triethylamine.

Cyclization of Arylamides 15a-c, 16, 17a in Trifluoroacetic Acid. 2-Benzyl-1-methylhetero[2,3-*c*]-pyridin-3(2H)-ones (18-20). Cyclization of compounds **15a-c, 16a, 17a,b** in trifluoroacetic acid was carried out by the method of cyclization in acetic acid. The products obtained, **18-20**, were crystallized from 2-propanol. Yields, %: **18**, 92%; **19**, 91%; **20**, 89%.

2-Acetyl-1,6-dimethylbenzofuran-3-ylacetic Acid Benzylamide (21), 2-Acetyl-1,5-dimethylbenzothiophen-3-ylacetic Acid Benzylamide (22), and **2-Acetyl-1-methylindol-3-ylacetic Acid Benzylamide (23).** We obtained benzylamides **21-23** by boiling 1,7-dimethylbenzofuro[2,3-*c*]-3-pyrone with benzylamine in 2-propanol or by boiling 1,6-dimethylbenzothieno[2,3-*c*]-3-pyrone and 1-methylindolo[2,3-*c*]-3-pyrone with benzylamine in DMF, using the procedure for synthesis of the corresponding arylamides in [16]. The reaction products were purified by recrystallization from 2-propanol.

Cyclization of Benzylamides 21-23. 2-Benzyl-1-methylhetero[2,3-*c*]pyridin-3(2H)-ones (18-20) (General Procedure). Triethylamine (0.05 mol) was added to a solution of benzylamides **21-23** (0.01 mol) in acetic acid (30 ml). The mixture was boiled for 1.5 h, cooled down, and poured into water. An ammonia solution was added until pH ≥ 7 was reached. The precipitate of pyridinone **18-20** was filtered out, washed with water, dried, and crystallized from alcohol. The synthesized samples of compounds **18-20** did not result in depression of the melting point when mixed with samples obtained by cyclization of arylamides **15-17** in trifluoroacetic acid (see above).

Hydrazones of 2-Acetylhetaryl-3-ylacetic Acid Arylamides (24a,b, 25). A. Hydrazine hydrate (5 ml) was added to a suspension of the salt **1b,c,3b** (0.01 mol) in methyl alcohol (50 ml) and the mixture was boiled for 0.5 h. After cooling, water (50 ml) was added to the reaction mixture. The precipitate was filtered out and washed with water. Hydrazones **24a,b** obtained were crystallized from methanol; **25** was obtained from 2-propanol.

B. Hydrazones **24a,b, 25** were also obtained from arylamide **7a,b, 9a** (0.01 mol) respectively according to the procedure described above, using 2-propanol instead of methanol.

X-ray Diffraction Study of 2-(4-Bromophenyl)-1,7-dimethylbenzofuro[2,3-*c*]pyridin-3(2H)-one (10b). The crystals of compound **10b** are monoclinic, $C_{19}H_{14}NO_2Br$, at 20°C a = 15.159(5), b = 13.888(4), c = 7.623(3) Å; β = 91.19(3)°; V = 1604.5(9) Å^3; M_r = 368.22; Z = 4; space group $P2_1/c$; d_{calc} = 1.524 g/cm^3; μ(MoKα) = 2.571 mm^{-1}; F(000) = 744. The unit cell parameters and intensities of 3245 reflections (2782 independent reflections, R_{int} = 0.083) were measured on a Siemens P3/PC automatic 4-circle diffractometer (MoKα, graphite monochromator, 2θ/θ scanning, $2\theta_{max}$ = 50°).

The structure was deciphered by the direct method using the SHELX-97 software package [21]. Correction for absorption was done by the semiempirical method from the results of ψ-scanning (T_{max} = 0.982, T_{min} = 0.555). The positions of the hydrogen atoms were determined from an electron density difference synthesis and refined using the "horse and rider" model with $U_{iso} = nU_{eq}$ (n = 1.5 for the methyl groups and n = 1.2 for the remaining hydrogen atoms). The structure was refined by full-matrix least-squares on F^2 in the anisotropic approximation for nonhydrogen atoms to wR_2 = 0.12 using 2782 reflections (R_1 = 0.045 using 1201 reflections with $F > 4\sigma(F)$, S = 0.918). The final atomic coordinates are given in Table 1; the bond lengths and bond angles are given in Tables 2 and 3.

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