One-step synthesis of 5-acetyl-2-amino-4-aryl-3-cyano-4*H*-pyrano[3,2-*b*]indoles. Molecular and crystal structure of 5-acetyl-2-amino-4-(4´-chloro-3´-nitrophenyl)-3-cyano-4*H*-pyrano[3,2-*b*]indole

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A one-step procedure was developed for the synthesis of 5-acetyl-2-amino-4-aryl-3-cyano-4*H*-pyrano[3,2-*b*]indoles involving the three-component reaction of 1-acetylindol-3(2*H*)-one with aromatic aldehydes and malononitrile in ethanol in the presence of triethylamine as the catalyst. The structure of 5-acetyl-2-amino-4-(4´-chloro-3´-nitrophenyl)-3-cyano-4*H*-pyrano[3,2-*b*]indole was established by X-ray diffraction analysis.

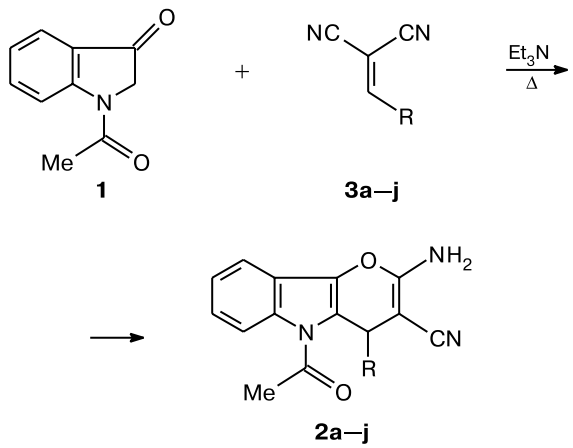
Key words: 1-acetylindol-3(2*H*)-one, 5-acetyl-2-amino-4-aryl-3-cyano-4*H*-pyrano[3,2-*b*]indoles, three-component reaction, X-ray diffraction analysis.

Substituted 2-amino-4-aryl-3-cyano-4*H*-pyrans exhibit biological activities, which gave impetus to the extensive development of regio- and stereoselective procedures for the synthesis of these compounds.[1—9] From this viewpoint, 2-amino-4-aryl-3-cyano-4*H*-pyrans annelated with fragments of coumarin,[10] substituted benzenes,[11] quinolines,[12] naphthalene,[13] and pyrazolone,[14,15] which exhibit anticoagulant, antisclerotic, antitumor activities, and other practically important properties, are of most interest. Of particular interest are pyrans annelated with another biologically active molecule, *viz.*, indole.[9,16] The latter compounds were prepared by condensation of 1-acetylindol-3(2*H*)-one (**1**) with aromatic aldehydes followed by the reactions of the resulting 1-acetyl-2-arylidene-1*H*-indol-3-ones with malononitrile.

With the aim of developing simpler procedures for the synthesis of substituted pyrano[3,2-*b*]indoles **2**, we studied the reactions of 1-acetylindol-3(2*H*)-one (**1**) with unsaturated nitriles **3** and investigated the three-component reaction of compound **1**, aromatic aldehydes **4**, and malononitrile **5**. Earlier, products of the reaction of indolone **1** with malononitrile **5** have been erroneously assigned the structures of acyclic Michael adducts.[17] Later on, their structures were corrected.[16] To reliably establish the structures of these products, we studied these compounds by various physicochemical methods, including X-ray diffraction analysis.

The reactions of 1-acetylindol-3(2*H*)-one (**1**) with unsaturated nitriles **3a—j** were carried out on heating in EtOH in the presence of Et_3N over a short period of time.[18] Under these conditions, the reactions proceeded with high regioselectivity to give 5-acetyl-2-amino-4-aryl-3-cyano-4*H*-pyrano[3,2-*b*]indoles **2a—j** in good yields (Scheme 1, Tables 1 and 2, method *A*).

Scheme 1



2,3: R = Ph (**a**), 2-FC_6H_4 (**b**), 3-FC_6H_4 (**c**), 4-FC_6H_4 (**d**), 2-ClC_6H_4 (**e**), 4-ClC_6H_4 (**f**), 3-BrC_6H_4 (**g**), 2-$NO_2C_6H_4$ (**h**), 3-pyridyl (**i**), 2-C_4H_2SBr-5 (**j**)

Initially, treatment of 1-acetylindol-3(2*H*)-one (**1**) with triethylamine affords enolate anion **6** (Scheme 2),

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Table 1. Physicochemical characteristics and mass-spectrometric data for compounds **2a—w**

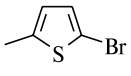
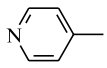
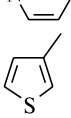
Compound	R	M.p./°C	Yield (%) (method)	Found / Calculated (%)			Molecular formula	MS, m/z ($[M]^+$)
				C	H	N		
2a	Ph	313—315	59 (*A*) 80 (*B*)	73.06 72.95	4.87 4.56	11.43 12.77	$C_{20}H_{15}N_3O_2$	329
2b	2-FC_6H_4	285—287	51 (*A*)	68.91 69.16	4.31 4.03	12.45 12.10	$C_{20}H_{14}FN_3O_2$	347
2c	3-FC_6H_4	280—282	56 (*A*)	69.34 69.16	3.75 4.03	11.75 12.10	$C_{20}H_{14}FN_3O_2$	347
2d	4-FC_6H_4	276—278	76 (*A*) 69 (*B*)	68.81 69.16	3.89 4.03	12.50 12.10	$C_{20}H_{14}FN_3O_2$	347
2e	2-ClC_6H_4	294—296	63 (*A*)	66.37 66.02	3.57 3.85	11.20 11.55	$C_{20}H_{14}ClN_3O_2$	364
2f	4-ClC_6H_4	260—262	90 (*A*) 73 (*B*)	65.85 66.02	3.57 3.85	11.90 11.55	$C_{20}H_{14}ClN_3O_2$	364
2g	3-BrC_6H_4	273—275	71 (*A*)	58.65 58.82	3.45 3.43	10.34 10.29	$C_{20}H_{14}BrN_3O_2$	408
2h	2-$NO_2C_6H_4$	263—265	59 (*A*)	64.52 64.17	4.02 3.74	14.62 14.97	$C_{20}H_{14}N_4O_4$	374
2i		268—269	91 (*A*)	68.84 69.09	3.96 4.24	17.32 16.97	$C_{19}H_{14}N_4O_2$	330
2j		257—259	18 (*A*) 26 (*B*)	52.52 52.17	3.18 2.90	10.49 10.14	$C_{18}H_{12}BrN_3O_2S$	414
2k	2-$CF_3C_6H_4$	271—273	44 (*B*)	63.83 63.48	3.81 3.53	10.23 10.58	$C_{21}H_{14}F_3N_3O_2$	397
2l	3-ClC_6H_4	279—281	57 (*B*)	65.67 66.02	4.13 3.85	11.15 11.55	$C_{20}H_{14}ClN_3O_2$	364
2m	2,3-$Cl_2C_6H_3$	271—273	67 (*B*)	60.28 60.45	2.99 3.27	10.18 10.58	$C_{20}H_{13}Cl_2N_3O_2$	397
2n	2,4-$Cl_2C_6H_3$	257—259	81 (*B*)	60.10 60.45	3.56 3.27	10.23 10.58	$C_{20}H_{13}Cl_2N_3O_2$	397
2o	2-BrC_6H_4	291—293	54 (*B*)	58.47 58.82	3.71 3.43	9.89 10.29	$C_{20}H_{14}BrN_3O_2$	408
2p	4-BrC_6H_4	255—257	82 (*B*)	58.77 58.82	3.48 3.43	10.31 10.29	$C_{20}H_{14}BrN_3O_2$	408
2q	5-Br-2-F-C_6H_3	268—270	46 (*B*)	56.52 56.34	3.33 3.05	10.86 9.86	$C_{20}H_{13}BrFN_3O_2$	426
2r	3-$NO_2C_6H_4$	274—276	61 (*B*)	63.82 64.17	3.46 3.74	14.62 14.97	$C_{20}H_{14}N_4O_4$	374
2s	4-Cl-3-NO_2-C_6H_3	266—268	95 (*B*)	58.93 58.75	3.04 3.18	13.36 13.71	$C_{20}H_{13}ClN_4O_4$	409
2t		251—253	55 (*B*)	68.87 69.09	4.19 4.24	16.86 16.97	$C_{19}H_{14}N_4O_2$	330
2u		269—271	67 (*B*)	64.83 64.48	4.16 3.88	12.19 12.54	$C_{18}H_{13}N_3O_2S$	335
2v		295—297	72 (*B*)	64.31 64.48	3.60 3.88	12.89 12.54	$C_{18}H_{13}N_3O_2S$	335
2w	4-$MeOOCC_6H_4$	273—275	72 (*B*)	67.87 68.22	4.69 4.39	10.50 10.85	$C_{22}H_{17}N_3O_4$	387

Table 2. Spectroscopic characteristics of compounds **2a—w***

Compound	^{1}H NMR, δ (*J*/Hz)				IR, ν/cm^{-1}			
	COMe (s, 3 H)	H(4) (s, 1 H)	NH_2 (br.s, 2 H)	H arom.	δ(NH_2)	CO	CN	NH_2
2a	2.48	5.24	6.78	7.02—7.10 (m, 2 H); 7.21—7.45 (m, 5 H); 7.61 (d, 1 H, H(9), *J* = 8.6); 8.08 (d, 1 H, H(6), *J* = 7.8)	1665	1687	2220	3216, 3250, 3324, 3378
2b	2.58	5.62	6.75	6.90—6.95 (m, 1 H); 7.05—7.12 (m, 2 H); 7.20—7.25 (m, 1 H); 7.38 (t, 2 H, *J* = 5.5); 7.61 (d, 1 H, H(9), *J* = 8.6); 7.98 (d, 1 H, H(6), *J* = 7.8)	1668	1695	2218	3210, 3248, 3321, 3375
2c	2.58	5.35	6.78	6.90—6.69 (m, 3 H); 7.29—7.40 (m, 3 H); 7.61 (d, 1 H, H(9), *J* = 8.6); 8.00 (d, 1 H, H(6), *J* = 7.8)	1665	1697	2217	3218, 3250, 3332, 3380
2d	2.52	5.31	6.89	7.00—7.18 (m, 4 H); 7.33—7.49 (m, 2 H); 7.59 (d, 1 H, H(9), *J* = 8.6); 8.01 (d, 1 H, H(6), *J* = 7.8)	1667	1700	2221	3218, 3258, 3323, 3390
2e	2.50	5.75	6.72	6.90 (s, 1 H); 7.11—7.20 (m, 2 H); 7.35—7.40 (m, 3 H); 7.60 (d, 1 H, H(9), *J* = 8.6); 7.98 (d, 1 H, H(6), *J* = 7.8)	1664	1702	2220	3208, 3246, 3320, 3380
2f	2.4	5.28	6.83	7.03—7.10 (m, 2 H); 7.25—7.41 (m, 4 H); 7.60 (d, 1 H, H(9), *J* = 8.6); 7.98 (d, 1 H, H(6), *J* = 7.8)	1667	1695	2219	3220, 3250, 3322, 3387
2g	2.52	5.28	6.79	7.03 (d, 1 H, *J* = 8.3); 7.20—7.42 (m, 5 H); 7.61 (d, 1 H, H(9), *J* = 8.6); 7.98 (d, 1 H, H(6), *J* = 7.8)	1662	1691	2208	3219, 3251, 3330, 3393
2h	2.58	6.15	6.80	7.12 (d, 1 H, *J* = 7.76); 7.33—7.42 (m, 3 H); 7.50—7.63 (m, 2 H); 7.80 (d, 1 H, H(9), *J* =8.6); 7.95 (d, 1 H, H(6), *J* = 7.8)	1669	1700	2218	3210, 3240, 3320, 3420
2i	2.58	5.31	6.80	7.23—7.45 (m, 4 H); 7.60 (d, 1 H, H(9), *J* = 8.6); 7.92 (d, 1 H, H(6), *J* = 7.8); 8.30—8.45 (m, 2 H, H(6), H(2))	1666	1696	2215	3215, 3252, 3338, 3370
2j	2.67	5.60	6.72	6.90—7.10, 7.25—7.48 (both m, 2 H each); 7.58 (d, 1 H, H(9), *J* = 8.6); 7.98 (d, 1 H, H(6), *J* = 7.8)	1660	1700	2210	3210, 3240, 3322, 3400
2k	2.58	5.78	6.78	7.03 (d, 1 H, *J* = 7.1); 7.40—7.49 (m, 4 H); 7.60—7.70 (m, 2 H); 7.83 (d, 1 H, H(6), *J* = 7.8)	1666	1694	2208	3216, 3250, 3325, 3380
2l	2.52	5.28	6.80	7.00—7.08 (m, 2 H); 7.19—7.42 (m, 4 H); 7.60 (d, 1 H, H(9), *J* = 8.6); 7.98 (d, 1 H, H(6), *J* = 7.8)	1663	1694	2215	3210, 3250, 3335, 3388
2m	2.58	5.85	6.88	7.15—7.21 (m, 1 H); 7.32—7.42 (m, 4 H); 7.61 (d, 1 H, H(9), *J* = 8.6); 7.90 (d, 1 H, H(6), *J* = 7.8)	1663	1699	2218	3210, 3248, 3323, 3378
2n	2.40	5.72	6.80	6.90—6.97, 7.19—7.25 (both m, 1 H each); 7.31—7.45 (m, 3 H); 7.60 (d, 1 H, H(9), *J* = 8.6); 7.85 (d, 1 H, H(6), *J* = 7.8)	1664	1704	2224	3208, 3232, 3328, 3360
2o	2.55	5.76	6.78	6.86 (d, 1 H, *J* = 7.7); 7.13—7.62 (m, 6 H); 7.98 (d, 1 H, H(6), *J* = 7.7)	1664	1698	2217,	3212, 3248, 3325, 3380
2p	2.50	5.25	6.78	7.00—7.08 (m, 2 H); 7.35—7.44 (m, 4 H); 7.60 (d, 1 H, H(9), *J* = 8.6); 7.98 (d, 1 H, H(6), *J* = 7.8)	1670	1690	2210	3250, 3310, 3320, 3370
2q	2.62	5.58	6.90	7.02—7.12 (m, 2 H); 7.35—7.44 (m, 3 H); 7.62 (d, 1 H, H(9), *J* = 8.6); 7.90 (d, 1 H, H(6), *J* = 7.8)	1665	1695	2217	3205, 3223, 3242, 3390
2r	2.51	5.50	6.98	7.38—7.64 (m, 5 H); 7.89 (s, 1 H); 7.95 (d, 1 H, H(9), *J* = 8.6); 8.10 (d, 1 H, H(6), *J* = 7.8)	1665	1690	2215	3210, 3250, 3338, 3360
2s	2.60	5.38	7.00	7.35—7.43, 7.63—7.72 (both m, 3 H each); 7.90 (d, 1 H, H(6), *J* = 7.8)	1663	1696	2220	3215, 3248, 3325, 3395
2t	2.53	5.27	6.87	7.06 (br.s, 2 H, H(2), H(5)); 7.48 (t, 2 H, H(7), H(8), *J* = 7.1); 7.61 (d, 1 H, H(9), *J* = 8.6); 7.93 (d, 1 H, H(6), *J* = 7.8); 8.45 (br.s, 2 H, H(3), H(5))	1660 1665	1702 1700	2202 2214	3190, 3240, 3320, 3340 3215, 3250,
2u	2.52	5.43	6.75	6.84 (d, 1 H, H(4), *J* = 5.0); 7.08 (s, 1 H, H(2)); 7.30—7.40 (m, 3 H, H(5), H(8), H(7)); 7.59 (d, 1 H, H(9), *J* = 8.6); 8.08 (d, 1 H, H(6), *J* = 7.8)				3330, 3378

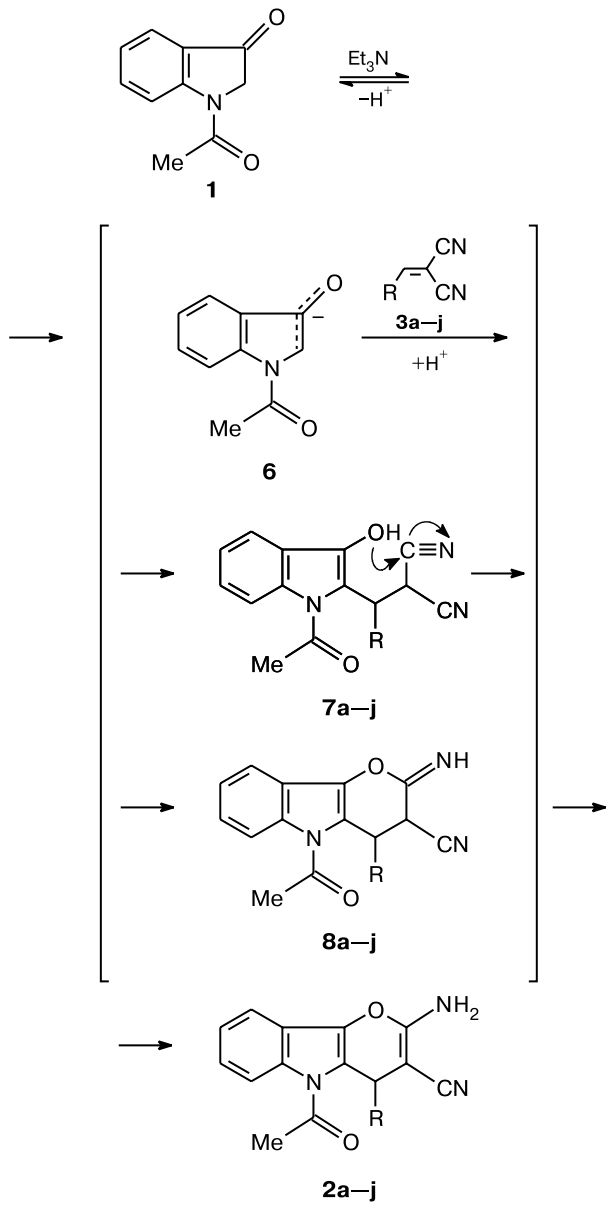
(*to be continued*)

Table 2 (*continued*)

Compound	^{1}H NMR, δ (*J*/Hz)				IR, ν/cm^{-1}			
	COMe (s, 3 H)	H(4) (s, 1 H)	NH_2 (br.s, 2 H)	H arom.	δ(NH_2)	CO	CN	NH_2
2v	2.62	5.64	6.68	6.90 (c, 2 H); 7.22 (c, 1 H); 7.29—7.42 (m, 2 H); 7.60 (d, 1 H, H(9), *J* = 8.6); 8.03 (d, 1 H, H(6), *J* = 7.8)	1663	1697	2218	3215, 3245, 3332, 3378
2w	2.53	5.38	7.11	3.83 (s, 3 H, 4'-COOMe); 7.14—7.23 (m, 2 H); 7.38—7.49 (m, 2 H, H(8), H(7)); 7.62 (d, 1 H, H(9), *J* = 8.6); 7.92 (m, 2 H); 8.00 (d, 1 H, H(6), *J* = 7.8)	1680	1700, 1670	2215	3200, 3240, 3320, 3440

* The assignments of the signals for H(9) and H(6) were made based on the experimental data published earlier.[19]

Scheme 2



which is involved in the Michael reaction with arylidenemalononitriles **3**. In a basic medium, Michael adducts **7** undergo intramolecular cyclization to give iminopyrans **8**. The tautomeric transformation of the latter compounds gives rise to 5-acetyl-2-amino-4-aryl-3-cyano-4*H*-pyrano[3,2-*b*]indoles **2**.

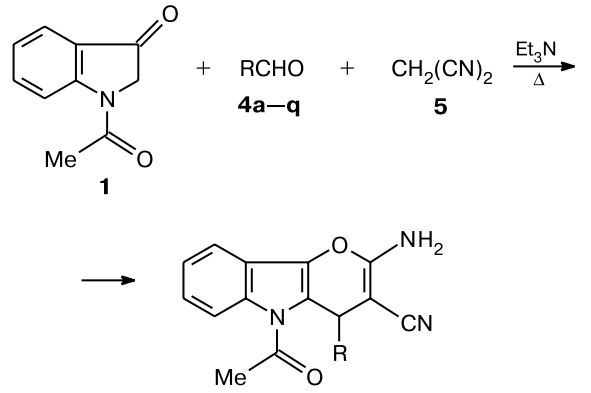
The direction of the reaction depends on the nature of the aryl substituent in arylidenemalononitrile **3**. For example, unsubstituted benzylidenemalononitrile **3a**, its substituted analogs containing the nitro group (**3h**) or halogen atom (**3b—g**), and derivatives of pyridine (**3i**) and thiophene (**3j**) aldehydes are readily involved in these reactions. The reactions with arylidenemalononitriles containing one or two alkoxy groups do not proceed at all. Most likely, this fact is associated with a decrease in the electrophilicity of the C_β atom of unsaturated nitrile due to the presence of electron-releasing substituents.

Pyrans **2** can be prepared according to a simpler one-step procedure (without the preliminary synthesis of arylidenemalononitriles **3**), *viz.*, by the three-component reaction of acetylindol-3(2*H*)-one **1**, malononitrile **5**, and the corresponding aldehyde **4** (Scheme 3, see Table 1, method *B*). This reaction has been used earlier for the synthesis of substituted 2-amino-4*H*-pyrans. For example, condensation of aldehydes, malononitrile, and ethyl acetoacetate afforded 2-amino-4-aryl-3-cyano-5-ethoxycarbonyl-6-methyl-4*H*-pyrans.[7]

The reaction was carried out on heating in EtOH in the presence of Et_3N over a short period of time. Under these conditions, the reaction proceeded regioselectively to form pyrans **2**. The latter method gives the target products in lower yields than those obtained according to the method *A*. However, taking into account the preliminary synthesis of unsaturated nitriles **2**, these yields are ~10—15% higher.

Some compounds, in particular, annelated pyran **2t** (R = 4-pyridyl), can be prepared only according to the method *B*. Thus, in attempting to prepare unsaturated nitrile **3** (R = 4-pyridyl) from pyridine-4-carbaldehyde (**4n**) and malononitrile (**5**), we obtained substituted cyclohexene **9** [7] (Scheme 4).

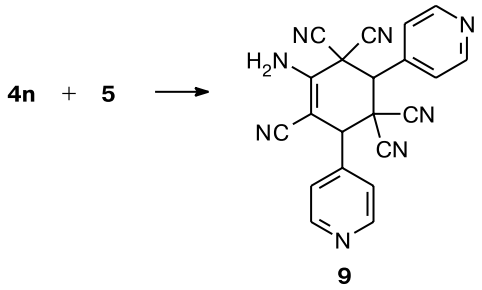
Scheme 3



2a,d,f,j—w

R = Ph (**4a, 2a**); 4-FC_6H_4 (**4b, 2d**); 4-ClC_6H_4 (**4c, 2f**); 2-C_4H_2SBr-5 (**4d, 2j**); 2-$CF_3C_6H_4$ (**4e, 2k**); 3-ClC_6H_4 (**4f, 2l**); 2,3-$Cl_2C_6H_3$ (**4g, 2m**); 2,4-$Cl_2C_6H_3$ (**4h, 2n**); 2-BrC_6H_4 (**4i, 2o**); 4-BrC_6H_4 (**4j, 2p**); 5-Br-2-FC_6H_3 (**4k, 2q**); 3-$NO_2C_6H_4$ (**4l, 2r**); 4-Cl-3-$NO_2C_6H_3$ (**4m, 2s**); 4-pyridyl (**4n, 2t**); 3-C_4H_3S (**4o, 2u**); 2-C_4H_3S (**4p, 2v**); 4-$MeOOCC_6H_4$ (**4q, 2w**)

Scheme 4



The structures of compounds **2a—w** were confirmed by physicochemical and spectroscopic methods (see Tables 1 and 2).

According to the Cambridge Structural Database, data on the structures of systems containing the annelated 2-amino-4-aryl-3-cyano-4*H*-pyran or 1-acetylindole fragments analogous to compounds **2** are lacking in the literature.

X-ray diffraction analysis of compound **2s** (Fig. 1, Tables 3 and 4) showed that the substituted 4*H*-pyran heterocycle adopts a strongly flattened chair confor-

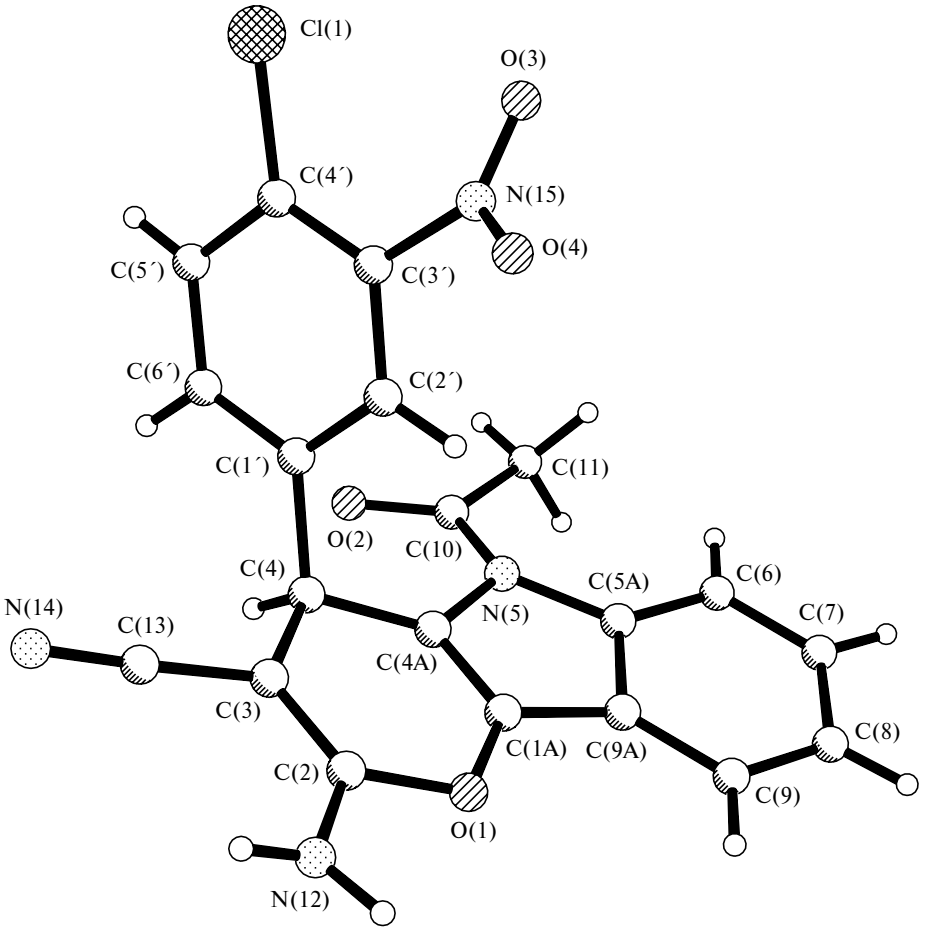


Fig. 1. Molecular structure of 5-acetyl-2-amino-4-(4′-chloro-3′-nitrophenyl)-3-cyano-4*H*-pyrano[3,2-*b*]indole (**2s**).

Table 3. Bond lengths (*d*) in the structure of **2s**

Bond	*d*/Å	Bond	*d*/Å
Cl(1)—C(4′)	1.727(3)	C(4)—C(1′)	1.527(4)
O(1)—C(1A)	1.374(3)	C(5A)—C(6)	1.386(5)
O(1)—C(2)	1.376(4)	C(5A)—C(9A)	1.406(4)
O(2)—C(10)	1.215(4)	C(6)—C(7)	1.370(5)
O(3)—N(15)	1.218(4)	C(7)—C(8)	1.389(5)
O(4)—N(15)	1.208(4)	C(8)—C(9)	1.376(5)
N(5)—C(10)	1.389(4)	C(9)—C(9A)	1.388(4)
N(5)—C(4A)	1.418(4)	C(10)—C(11)	1.490(5)
N(5)—C(5A)	1.424(4)	C(1′)—C(6′)	1.382(4)
N(12)—C(2)	1.330(4)	C(1′)—C(2′)	1.389(4)
N(14)—C(13)	1.149(4)	C(2′)—C(3′)	1.391(4)
N(15)—C(3′)	1.467(4)	C(3′)—C(4′)	1.371(5)
C(1A)—C(4A)	1.333(4)	C(4′)—C(5′)	1.383(5)
C(1A)—C(9A)	1.429(4)	C(5′)—C(6′)	1.381(4)
C(2)—C(3)	1.361(4)	O(1W)—C(1W)	1.173(6)
C(3)—C(13)	1.417(4)	C(1W)—C(2W)	1.468(7)
C(3)—C(4)	1.516(4)	C(1W)—C(3W)	1.478(7)
C(4)—C(4A)	1.488(4)		

mation. The O(1) and C(4) atoms deviate from the C(2)—C(3)—C(1A)—C(4A) plane (within 0.011 Å) in opposite directions by −0.042 and 0.028 Å, respectively. The folding angles along the C(1A)...C(2) and C(3)...C(4A) lines are rather small (3.4 and 1.9°, respectively). The conformation of this ring can be represented as a flattened sofa with the O(1) atom deviating from the plane through the five atoms of the ring (planar to within 0.011 Å) by −0.032 Å. It should be noted that the heterocycles in substituted 4*H*-pyrans studied earlier[3,20,21] are less flattened and adopt boat conformations with a more pronounced folding. Both the dihedral angle between the planar pyrrole heterocycle and the planar fragment of the pyran ring and the dihedral angle between the pyrrole ring and the Ph substituent (C(5A)...C(9A)) are small (6.4 and 4.2°, respectively), which is indicative of a flattening of the tricyclic fragment as a whole. The twist of the pseudoaxial aryl substituent with respect to the planar fragment of the pyran ring is 82.5°. The rotation of the nitro group with respect to the Ph ring by 44.2° is caused by the presence of the Cl atom at the adjacent atom (nonbonded Cl(1)...O(3) distance (2.926(4) Å) is smaller than the sum of the van der Waals radii of the atoms[22]). It should be noted that the aryl substituent is twisted due to the presence of the nitro group toward the plane of the heterocycle, *i.e.*, it is in the *anti* orientation relative to the H atom at the C(4) atom. The observed spatial arrangement of the acetyl group gives rise to the O(2)...H(4A) nonbonded interaction, which can be considered[23,24] as an intramolecular contact (C(4)...O(2), 2.771(4) Å; C(4)—H(4A), 1.0 Å; O(2)...H(4A), 2.42 Å; C(4)—H(4A)...O(2) angle, 101°). As can be seen from Table 3, there is a noticeable redistribution of the bond lengths in the planar N(12)—C(2)=C(3)—C(13)≡N(14) fragment, which is attributable to conjugation. The remaining geometric parameters of the compounds under study have the expected values.[25] In the crystal, molecules **2s** are linked in infinite chains through the intermolecular hydrogen bonds N(12)—H(12A)...N(14) ($1.5 - x$, $3.5 - y$, $-z$) (N(12)...N(14), 3.101(4) Å; N(12)—H(12A), 0.88 Å; H(12A)...N(14), 2.27 Å; N(12)—H(12A)...N(14) angle, 158°) and N(12)—H(12B)...O(2) (x, $1 + y$, z) (N(12)...O(2), 2.966(4) Å; N(12)—H(12B), 0.88 Å; H(12B)...O(2), 2.10 Å; N(12)—H(12B)...O(2) angle, 166°). It should be noted that the O atom of the acetone molecule of solvation forms a rather weak intermolecular hydrogen bond with the pyran molecule, *viz.*, C(11)—H(11C)...O(1W) ($1 - x$, y, $0.5 - z$) (C(11)...O(1W), 3.271(4) Å;

Table 4. Bond angles (ω) in the structure of **2s**

Angle	ω/deg	Angle	ω/deg	Angle	ω/deg
C(1A)—O(1)—C(2)	115.3(2)	C(4A)—C(4)—C(1′)	112.2(2)	N(5)—C(10)—C(11)	119.0(3)
C(10)—N(5)—C(4A)	122.0(3)	C(3)—C(4)—C(1′)	111.0(2)	N(14)—C(13)—C(3)	177.1(3)
C(10)—N(5)—C(5A)	129.1(3)	C(1A)—C(4A)—N(5)	108.2(3)	C(6′)—C(1′)—C(2′)	118.6(3)
C(4A)—N(5)—C(5A)	107.3(2)	C(1A)—C(4A)—C(4)	124.2(3)	C(6′)—C(1′)—C(4)	121.0(3)
O(4)—N(15)—O(3)	124.3(3)	N(5)—C(4A)—C(4)	127.1(3)	C(2′)—C(1′)—C(4)	120.4(3)
O(4)—N(15)—C(3′)	117.8(3)	C(6)—C(5A)—C(9A)	120.1(3)	C(1′)—C(2′)—C(3′)	119.6(3)
O(3)—N(15)—C(3′)	117.9(3)	C(6)—C(5A)—N(5)	132.1(3)	C(4′)—C(3′)—C(2′)	121.4(3)
C(4A)—C(1A)—O(1)	126.0(3)	C(9A)—C(5A)—N(5)	107.8(3)	C(4′)—C(3′)—N(15)	122.1(3)
C(4A)—C(1A)—C(9A)	110.9(3)	C(7)—C(6)—C(5A)	118.4(3)	C(2′)—C(3′)—N(15)	116.5(3)
O(1)—C(1A)—C(9A)	123.0(3)	C(6)—C(7)—C(8)	121.9(3)	C(3′)—C(4′)—C(5′)	119.1(3)
N(12)—C(2)—C(3)	127.2(3)	C(9)—C(8)—C(7)	120.4(3)	C(3′)—C(4′)—Cl(1)	122.4(3)
N(12)—C(2)—O(1)	110.8(3)	C(8)—C(9)—C(9A)	118.7(3)	C(5′)—C(4′)—Cl(1)	118.4(3)
C(3)—C(2)—O(1)	122.0(3)	C(9)—C(9A)—C(5A)	120.6(3)	C(6′)—C(5′)—C(4′)	119.9(3)
C(2)—C(3)—C(13)	117.6(3)	C(9)—C(9A)—C(1A)	133.5(3)	C(5′)—C(6′)—C(1′)	121.4(3)
C(2)—C(3)—C(4)	126.0(3)	C(5A)—C(9A)—C(1A)	105.7(3)	O(1W)—C(1W)—C(2W)	120.9(6)
C(13)—C(3)—C(4)	116.3(2)	O(2)—C(10)—N(5)	119.3(3)	O(1W)—C(1W)—C(3W)	122.2(6)
C(4A)—C(4)—C(3)	106.2(2)	O(2)—C(10)—C(11)	121.7(3)	C(2W)—C(1W)—C(3W)	116.9(5)

C(11)—H(11C), 0.98 Å; H(11C)...O(1W), 2.31 Å; C(11)—H(11C)...O(1W) angle, 166°).

Apparently, intramolecular contacts are formed in Michael adducts **7** (see Scheme 2), whose subsequent cyclization affords one of two possible isomers containing the Ph substituent in the axial position.

The IR spectra of annelated pyrans are characterized by the presence of bending and stretching absorption bands of the amino group at 1660—1680 and 3190—3440 cm^{-1}, respectively. The conjugated cyano group of the enaminonitrile fragment of the pyran ring is manifested in the region of 2202—2221 cm^{-1}. The absorption band of the carbonyl group of the *N*-acetyl fragment has a somewhat higher frequency (1687—1702 cm^{-1}) than the expected value. This shift is, apparently, associated with the deviation of the acetyl group from the plane of the indole system and disruption of conjugation with the N atom (as was demonstrated by X-ray diffraction analysis of compound **2s**).

The ^1H NMR spectroscopic data for the compounds under consideration are also not contradictory with the structures of annelated pyrans **2**. Thus, the ^1H NMR spectra have signals for the protons of the acetyl substituent (δ 2.48—2.67), aryl substituents, and indole fragment (δ 6.90—8.45) along with the characteristic signal for the H(4) proton (δ 5.24—6.15), which is shifted downfield by 1.0—1.2 ppm compared to that observed in the spectra of nonannelated 2-amino-4-aryl-3-cyanopyrans.[7] The slightly broadened signal for the protons of the amino group (δ 6.68—7.11) is also characteristic.

Experimental

The melting points were measured on a Kofler hot-stage apparatus. The IR spectra were recorded on a Specord IR-75 instrument in KBr pellets. The ^1H NMR spectra were measured on a Bruker AM-300 instrument at natural isotopic abundance. The mass spectra (EI, 70 eV) were obtained on a Funnigan MAT INCOS-50 instrument. The course of the reactions and purities of the products were monitored by TLC on Silufol UV-254 plates.

Synthesis of 5-acetyl-2-amino-4-aryl-3-cyano-4*H*-pyrano[3,2-*b*]indoles 2 (general procedure). ***A.*** K Triethylamine (0.3 mL) was added to a solution of equimolar amounts of compound **1**[26] (1.75 g, 0.01 mol) and arylidenemalononitrile **3a—j** in EtOH (30 mL) at 40—60 °C. The reaction mixture was kept at 20 °C for 24 h. The precipitate that formed was filtered off, washed with EtOH and hexane, and recrystallized from MeCN. The characteristics of compounds **2a—j** are given in Tables 1 and 2.

B. Triethylamine (0.3 mL) was added to a solution of equimolar amounts of compound **1** (1.75 g, 0.01 mol), aldehyde **4a—q**, and malononitrile **5** (0.66 g, 0.01 mol) in EtOH (30 mL) at 40—60 °C. The reaction mixture was kept and treated as described above. The characteristics of compounds **2a,d,f,j—w** are given in Tables 1 and 2.

X-ray diffraction study of compound 2s. Colorless crystals of compound **2s** were prepared by slow crystallization from acetone during two days. Crystals of **2s** ($C_{20}H_{13}ClN_4O_4 \cdot C_3H_6O$) are monoclinic, at –80 °C: a = 23.77(3) Å, b = 8.877(6) Å, c = 23.09(2) Å, β = 117.23(6)°, V = 4332(7) $Å^3$, Z = 8, d_{calc} = 1.432 g cm^{-3}, space group $C2/c$. The unit cell parameters and intensities of 3509 reflections were measured on an automated four-circle Siemens P3/PC diffractometer (λ(Mo-Kα) radiation, graphite monochromator, θ/2θ scan technique, θ_{max} = 27°). The structure was solved by direct methods and refined by the full-matrix least-square method with anisotropic thermal parameters for all nonhydrogen atoms. The positions of the H atoms were calculated geometrically and refined using the riding model. The final values of the reliability factors were as follows: R_1 = 0.057 based on 2381 independent reflections with $I > 2\sigma(I)$ and wR_2 = 0.146 based on 3382 independent reflections. All calculations were carried out with the use of the SHELXL-97 program package. The bond lengths and bond angles are given in Tables 3 and 4, respectively. The coordinates and isotropic equivalent thermal parameters of the nonhydrogen atoms were deposited with the Cambridge Structural Database.

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