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SYNTHESIS OF SUBSTITUTED 6-AMINO-4-ARYL-5-CYANO-2H,4H-PYRANO[2,3-*c*]PYRAZOLES. CRYSTAL AND MOLECULAR STRUCTURE OF 6-AMINO-5-CYANO-3-METHYL-4-(2',4',6'-TRIETHYLPHENYL)-2H,4H-PYRANO[2,3-*c*]PYRAZOLE

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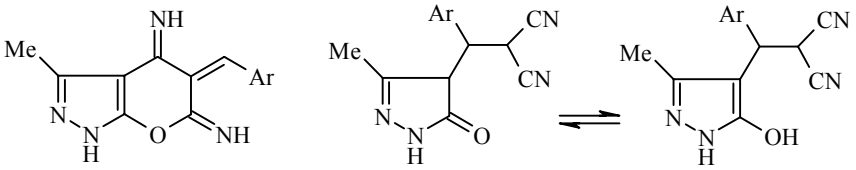
Substituted 6-aminopyrano[2,3-c]pyrazoles were synthesized by the two-component condensation of arylidenemalononitriles and substituted 5-pyrazolones or three-component condensation of aromatic aldehydes, malononitrile, and substituted 5-pyrazolones. It was established by X-ray crystallographic analysis that pyranopyrazoles exist in the 2H and not the 1H tautomeric form.

Keywords: Michael adduct, pyrazole, pyran, pyranopyrazole, X-ray crystallographic analysis.

Substituted 6-aminopyrano[2,3-*c*]pyrazoles were first obtained by the reaction of 3-methyl-5-pyrazolone with tetracyanoethylene [1]. Later different methods were developed for the synthesis of these compounds from arylidenemalononitriles and 3-methyl-5-pyrazolone or 4-arylidene-3-methyl-5-pyrazolones and malononitrile and also by the three-component condensation of aromatic aldehydes, malononitrile, and 3-methyl-5-pyrazolone [2-5].

There is still no common opinion about the structure of the products of these reactions. Thus, the authors in [6] assigned the structure of diiminopyranopyrazole (**1**) to the products of the reactions of arylidenemalononitriles and 3-methyl-5-pyrazolone. More recently it was established that the reaction takes place through the tautomeric Michael adducts **2** ⇄ **3**, the structure of which was not finally resolved. However, it was shown that these adducts undergo cyclization in the presence of bases to 6-amino-4-aryl-5-cyano-3-methyl-1H,4H-pyrano[2,3-*c*]pyrazoles (**4**) [3, 4], which can exist in the tautomeric form **5**.



1 **2** **3**

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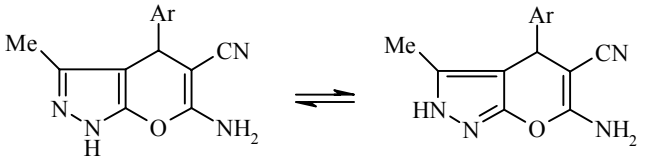
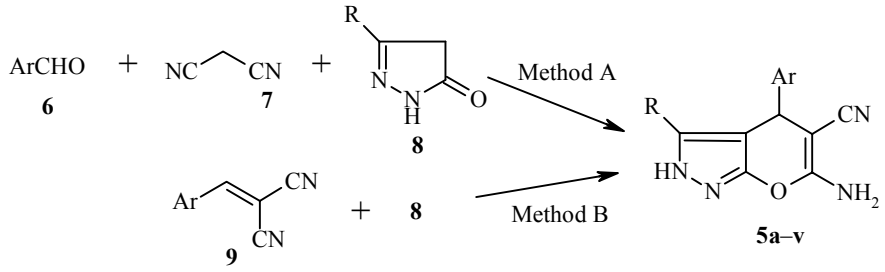


4 **5**

Recently we synthesized new 6-amino-5-cyano-3-methylpyrano[2,3-*c*]pyrazoles **4** ⇄ **5**, containing alkyl, spirocyclohexyl, and spiropiperidine substituents at position 4. The structure of these compounds was also studied by X-ray crystallographic analysis, about which we reported previously [7-9]. However, to judge from the data in [10] the question of the structure of the preferred tautomers of the pyranopyrazoles remains open.

In order to extend the range of methods available for the synthesis of pyranopyrazoles, to determine the structure of the products of these reactions, and to study the effect of the substituent at position 3 of the pyranopyrazoles **5** on the proton attached to one of the nitrogen atoms of the pyrazole ring we synthesized new pyranopyrazoles, using sterically hindered polyalkylbenzaldehydes, heterocyclic aldehydes, and 5-pyrazolones containing not only a methyl substituent but also phenyl, methoxymethylene, trifluoromethyl, *tert*-butyl, and other substituents at position 3. We proved the structure of one of the pyranopyrazoles conclusively by X-ray crystallographic analysis.

By varying the methods for the synthesis of pyranopyrazoles described above and using new substituted aldehydes and 5-pyrazolones we came to the conclusion that the simplest method for the production of pyranopyrazoles with sufficiently high yields is three-component condensation (method A, Scheme). Thus, when equimolar amounts of compounds **6**, **7**, and **8** were heated briefly in ethanol in the presence of triethylamine as catalyst the required compounds **4** ⇄ **5** were obtained with yields of 52-95%. In the case of sterically hindered aldehydes **6**, however, these compounds can also be obtained by two-component condensation (method B) of the previously synthesized arylidenemalonitriles **9** and 5-pyrazolones **8**.



6 **7** **8** **9** **5a–v**

5a-e R = Me; **f**, **g** R = Et; **h**, **i** **R =** *n*-Pr, **j**, **k** R = *t*-Bu; **l**, **m** R = Ph; **n-p** R = CF_3; **q**, **r** R = $MeOCH_2$; **s** R = $MeOCOCH_2$; **t-v** R = 4-$MeC_6H_4SCH_2$; **5 a** Ar = 2,4,6-$Me_3C_6H_2$; **b** Ar = 2,4,6-Me_3-3-O_2NC_6H; **c** Ar = 2,4,6-Me_3-3,5-$(O_2N)_2C_6$; **d** Ar = 2,4,6-Me_3-3-$EtOCH_2C_6H$; **e** Ar = 2,4,6-$Et_3C_6H_2$; **f**, **h**, **t** Ar = 2-C_4H_3S; **g**, **u** Ar = 2,5-$(MeO)_2C_6H_3$; **i**, **k**, **m**, **s**, **v** Ar = 2,3,4-$(MeO)_3C_6H_2$; **j** Ar = 2-$MeOC_6H_4$; **l** Ar = 2,4,5-$(MeO)_3C_6H_2$; **n** Ar = 2-$CF_3C_6H_4$; **o** Ar = 3-C_5H_4N; **p** Ar = 2-$(OCH_2$-(2'-$ClC_6H_4))C_6H_4$; **q** Ar = 2-MeC_6H_4; **r** 2-C_4H_3O

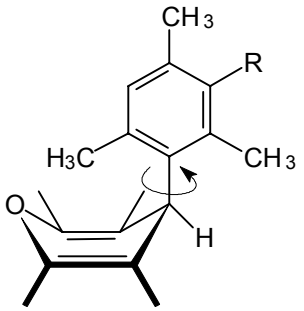
The compounds **5** that we obtained were stable analytically pure colorless powders, which could be recrystallized from ethanol or acetonitrile. The structure of all the obtained products was confirmed by various methods (Tables 1 and 2). The IR spectra of the compounds contain absorption bands for the stretching and deformation vibrations of the amino and cyano groups. In the ^1H NMR spectra there are signals for the protons of the aryl, alkyl, amino, and other groups.

TABLE 1. The Characteristics of 6-Amino-4-aryl-5-cyano-2H,4H-pyrano[2,3-*c*]pyrazoles **5a-v**

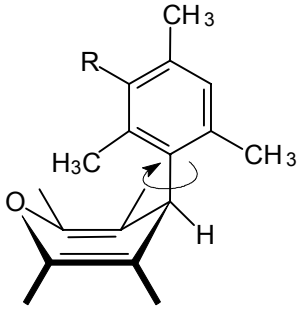
Compound	Empirical formula	Found, % / Calculated, %			mp, °C	Yield, %
		C	H	N		
5a	$C_{17}H_{18}N_4O$	69.30 / 69.36	6.27 / 6.16	18.98 / 19.04	225-228	52
5b	$C_{17}H_{17}N_5O_3$	60.20 / 60.17	5.06 / 5.05	20.75 / 20.64	255-260	76
5c	$C_{17}H_{16}N_6O_5$	53.06 / 53.13	4.17 / 4.20	21.94 / 21.87	263-269	83
5d	$C_{20}H_{24}N_4O_2$	65.52 / 65.56	5.93 / 6.05	15.42 / 15.29	235-238	74
5e	$C_{20}H_{24}N_4O$	71.35 / 71.40	7.20 / 7.19	16.53 / 16.65	257-260	76
5f	$C_{13}H_{12}N_4OS$	57.24 / 57.33	4.41 / 4.44	20.63 / 20.58	237-238	93
5g	$C_{17}H_{18}N_4O_3$	62.47 / 62.57	5.45 / 5.56	17.25 / 17.17	188-194	84
5h	$C_{14}H_{14}N_4OS$	58.82 / 58.72	4.92 / 4.93	19.47 / 19.57	193-198	85
5i	$C_{19}H_{22}N_4O_4$	61.57 / 61.61	5.94 / 5.99	15.11 / 15.13	193-194	95
5j	$C_{18}H_{20}N_4O_2$	66.70 / 66.65	6.27 / 6.21	17.30 / 17.27	227-229	97
5k	$C_{20}H_{24}N_4O_4$	62.41 / 62.48	6.31 / 6.29	14.66 / 14.57	209-214	90
5l	$C_{22}H_{20}N_4O_4$	65.31 / 65.34	4.99 / 4.98	13.86 / 13.85	188-196	82
5m	$C_{22}H_{20}N_4O_4$	65.39 / 65.34	5.11 / 4.98	13.76 / 13.85	225-228	83
5n	$C_{15}H_8F_6N_4O$	48.21 / 48.14	2.08 / 2.15	14.99 / 14.97	260-264	71
5o	$C_{13}H_8F_3N_5O$	50.92 / 50.82	2.57 / 2.62	22.87 / 22.79	219-221	98
5p	$C_{21}H_{14}ClF_3N_4O_2$	56.51 / 56.45	3.22 / 3.16	12.50 / 12.54	206-212	57
5q	$C_{16}H_{16}N_4O_2$	64.90 / 64.85	5.32 / 5.44	18.78 / 18.91	204-205	59
5r	$C_{13}H_{12}N_4O_3$	57.27 / 57.35	4.38 / 4.44	20.54 / 20.58	194-197	54
5s	$C_{19}H_{20}N_4O_6$	57.12 / 57.00	4.94 / 5.04	14.10 / 13.99	194-196	88
5t	$C_{19}H_{16}N_4OS_2$	60.02 / 59.98	4.12 / 4.24	14.63 / 14.73	213-215	86
5u	$C_{23}H_{22}N_4O_3S$	63.57 / 63.58	5.20 / 5.10	12.95 / 12.89	191-193	96
5v	$C_{24}H_{24}N_4O_4S$	62.14 / 62.06	5.15 / 5.21	12.07 / 12.06	188-191	76

It follows from the NMR spectra that both electron-withdrawing and electron-donating substituents at position 3 of the pyranopyrazoles have an extremely insignificant effect on the hydrogen atom attached to one of the nitrogen atoms. The change in the chemical shift of this proton in the NMR spectra is very small, and it is therefore impossible to give preference to either of structures **4** or **5**.

A special feature of the ^{1}H NMR spectra of compounds **5b** and **5d** (R = NO_2, CH_2OEt) is the splitting of the signals for the protons of the phenyl ring and its substituents (Tables 1 and 2). In the case of compound **5d** there is splitting of equal intensity in the signals for the C(4)H proton of the pyran ring and the protons of the OCH_2 substituent in the phenyl ring. This is due to the increase in the volume of the substituent at position 3 of the phenyl, the mutual screening of these atoms, and restricted rotation about the C_{Ar}–C_{pyran} bond.



sp-isomer (A)



ap-isomer (B)

R = NO_2, CH_2OEt

The ^{1}H NMR spectra, recorded at various temperatures (20, 60, 120°C), indicate the formation of stable *syn*-periplanar (A) and *anti*-periplanar (B) atropoisomers. Thus, at 60°C the ^{1}H NMR spectra of compounds **5b** and **5d** remain unchanged, while at 120°C rotation occurs about the axis of the C(4)–C(1') bond, and the previously split signals of the protons merge and look like broad singlets.

TABLE 2. The Characteristics of 6-Amino-4-aryl-5-cyano-2H,4H-pyrano[2,3-*c*]pyrazoles **5a-v**

Compound	IR spectrum, ν, cm^{-1}		^{1}H NMR spectrum, δ, ppm, coupling constants, *J* (Hz)
	CN	NH_2	
1	2	3	4
5a	2190	3196, 3312, 3396	1.63 (3H, s, C(3)–CH_3); 1.83 (3H, s, CH_3); 2.20 (3H, s, CH_3); 2.42 (3H, s, CH_3); 5.12 (1H, s, C(4)H); 6.71 (1H, s, C_6H_2); 6.85 (1H, s, C_6H_2); 6.79 (2H, s, NH_2); 12.02 (1H, s, NH)
5b	2192	3176, 3308, 3392	*1.69 (3H, s, C(3)–CH_3); 1.75+1.90 (*^{2}3H, ss, C(2')–CH_3); 2.19 (3H, s, C(4')–CH_3); 2.33+*^{3}2.50 (*^{2}3H, ss, C(6')–CH_3); 5.28 (1H, s, C(4)H); 6.99 (2H, s, NH_2); 7.07+7.20 (*^{2}1H, ss, C(5')H); 12.17 (1H, br. s, NH); *^{4}1.69 (3H, s, C(3)–CH_3); 1.76-*^{3}2.55 (6H, weak resolution m, C(2')–CH_3, C(6')–CH_3); 2.19 (3H, s, C(4')–CH_3); 5.28 (1H, s, C(4)H); 6.33 (2H, br. s, NH_2); 7.07 (1H, br. s, C(5')H); 11.78 (1H, br. s, NH)
5c	2196	3084, 3256	1.75 (3H, s, C(3)–CH_3); 1.84 (3H, s, CH_3); 2.14 (3H, s, CH_3); 2.43 (3H, s, C(4')–CH_3); 5.48 (1H, s, C(4)H); 7.17 (2H, s, NH_2); 12.26 (1H, s, NH)
5d	2190	3184, 3308, 3376	*1.12 (3H, m, $OCH_2C\underline{H}_3$); 1.60 (3H, s, C(3)–CH_3); 1.82+1.89 (*^{2}3H, ss, C(2')–CH_3); 2.29 (3H, s, C(4')–CH_3); 2.40+2.45 (*^{2}3H, ss, C(6')–CH_3); 3.44 (2H, m, $OC\underline{H}_2CH_3$); 4.37+4.49 (*^{2}2H, ss, C(3')–CH_2O); 5.15+5.27 (*^{2}1H, ss, C(4)H); 6.75+6.89 (*^{2}1H, ss, C(5')H); 6.82 (2H, s, NH_2); 12.00 (1H, s, NH); *^{3}1.15 (3H, t, ^3J = 7.9, $OCH_2C\underline{H}_3$); 1.63 (3H, s, C(3)–CH_3); 1.81-2.66 (6H, weak resolution m, C(2')–CH_3, C(6')–CH_3); 2.29 (3H, s, C(4')–CH_3); 3.48 (2H, q , ^3J = 7.9, $OC\underline{H}_2CH_3$); 4.47 (2H, br. s, C(3')–CH_2O); 5.26 (1H, br. s, C(4)H); 6.12 (2H, br. s, NH_2); 6.82 (1H, br. s, C(5')H); 11.58 (1H, br. s, NH)
5e	2192	2968, 3136, 3252	0.80 (3H, t, ^3J = 7.2, C(4')–($CH_2C\underline{H}_3$)); 1.24 (6H, m, C_6H_2–($CH_2C\underline{H}_3$)$_2$–2',6'); 1.60 (3H, s, C(3)–CH_3); 2.25-*^{3}2.83 (6H, m, ($C\underline{H}_2CH_3$)$_3$); 5.12 (1H, s, C(4)H); 6.79 (2H, s, NH_2); 6.83 (1H, s, C_6H_2); 6.88 (1H, s, C_6H_2); 12.00 (1H, s, NH)

TABLE 2 (continued)

1	2	3	4
5f	2196	2972, 3111, 3236	0.98 (3H, t, ^3J = 7.2, 3H, $CH_2C\underline{H}_3$); 2.31 (2H, q , ^3J = 7.2, $C\underline{H}_2CH_3$); 4.95 (1H, s, C(4)H); 6.69 (2H, s, NH_2); 6.91 (1H, dd, ^3J = 2.6, ^3J = 5.2, C(4')H); 6.98 (1H, d, ^3J = 2.6, C(3')H); 7.27 (1H, d, ^3J = 5.2, C(5')H); 12.02 (1H, s, NH)
5g	2196	3180, 3328	0.82 (3H, t, ^3J = 7.2, $CH_2C\underline{H}_3$); 2.21 (2H, q , ^3J = 7.2, $C\underline{H}_2CH_3$); 3.65 (3H, s, C(2')–OCH_3); 3.75 (3H, s, C(5')–OCH_3); 4.95 (1H, s, C(4)H); 6.52 (1H, d, ^4J = 3.3, C(6')H); 6.67 (2H, br. s, NH_2); 6.77 (1H, dd, ^4J = 3.3, ^3J = 8.5, C(4')H); 6.94 (1H, d, ^3J = 8.5, C(3')H); 11.95 (1H, br. s, NH)
5h	2196	3184, 3248	0.80 (3H, t, ^3J = 7.1, CH_3); 1.38 (2H, q , ^3J = 7.1, $CH_3C\underline{H}_2$); 2.28 (2H, m, C(3)–$C\underline{H}_2$); 4.90 (1H, s, C(4)H); 6.62 (2H, s, NH_2); 6.90 (1H, dd, ^3J = 2.6, ^3J = 5.2, C(4')H); 6.96 (1H, d, ^3J = 2.6, C(3')H); 7.28 (1H, d, ^3J = 5.2, C(5')H); 12.00 (1H, s, NH)
5i	2200	2960, 3212, 3328	0.62 (3H, t, ^3J = 7.5, $C\underline{H}_3CH_2$); 1.18 (2H, m, $CH_3C\underline{H}_2$); 2.14 (2H, m, C(3)–CH_2); 3.70, 3.74, 3.79 (9H, sss, 2',3',4'–C_6H_2–($OC\underline{H}_3$)$_3$); 4.73 (1H, s, C(4)H); 6.69 (2H, s, NH_2); 6.73 (2H, s, $C_6\underline{H}_2$–$(OMe)_3$); 11.92 (1H, s, NH)
5j	2190	2972, 3164, 3288	1.02 (9H, s, $C(CH_3)_3$); 3.81 (3H, s, OCH_3); 5.11 (1H, s, C(4)H); 6.37 (2H, s, NH_2); 6.83 (2H, d, J = 4.4, C_6H_4); 6.95 (1H, d, J = 8.2, C_6H_4); 7.14 (1H, weak resolution m, C_6H_4); 11.86 (1H, s, NH)
5k	2194	3112, 3260	1.01 (9H, s, $C(CH_3)_3$); 3.71, 3.74, 3.78 (9H, sss, 2',3',4'-C_6H_2–($OC\underline{H}_3$)$_3$); 4.82 (1H, s, C(4)H); 6.57 (2H, br. s, NH_2); 6.63 (1H, d, ^3J = 8.5, C_6H_2); 6.71 (1H, d, ^3J = 8.5, C_6H_2); 11.82 (1H, s, NH)
5l	2196	3120, 3272	3.58 (3H, s, C(2')–OCH_3); 3.77 (3H, s, C(5')–OCH_3); 3.78 (3H, s, C(4')–OCH_3); 5.14 (1H, s, C(4)H); 6.45 (3H, br. s, NH_2+C(6')H); 6.58 (1H, s, C(3')H); 7.25 (3H, m, C_6H_5); 7.40 (2H, d, ^3J = 6.6, C_6H_5); 12.59 (1H, s, NH)
5m	2202	3120, 3220	3.70, 3.71, 3.80 (9H, sss, 2',3',4'–C_6H_2–($OC\underline{H}_3$)$_3$); 5.09 (1H, s, C(4)H); 6.56 (2H, s, NH_2); 6.59 (1H, d, ^3J = 8.5, C_6H_2); 6.65 (1H, d, ^3J = 8.5, C(5')H); 7.24 (3H, m, C_6H_5); 7.39 (2H, d, ^3J = 7.2, C_6H_5); 12.60 (1H, s, NH)
5n	2208	3124, 3280	5.11 (1H, s, C(4)H); 7.09 (2H, br. s, NH_2); 7.26 (1H, d, ^3J = 7.2, C_6H_4); 7.46 (1H, m, C_6H_4); 7.61 (1H, m, C_6H_4); 7.79 (1H, d, ^3J = 7.9, C_6H_4); 14.19 (1H, br. s, NH)
5o	2184	3168, 3312	4.78 (1H, s, C(4)H); 6.99 (2H, s, NH_2); 7.29 (1H, m, C_5H_4N); 7.48 (1H, dt, J = 2.0, J = 7.8 C_5H_4N); 8.37 (1H, d, J = 2.0, C_5H_4N); 8.43 (1H, dd, J = 2.0, J = 4.6, C_5H_4N); 13.94 (1H, br. s, NH)
5p	2182	3164, 3292	5.10 (3H, m, C(4)H+CH_2O); 6.84 (2H, br. s, NH_2); 6.90-7.47 (8H, m, $(C_6H_4)_2$); 13.79 (1H, br. s, NH)
5q	2196	3130, 3256, 3340	2.29 (3H, s, C(2')–CH_3); 2.92 (3H, s, OCH_3); 3.77 (1H, d, ^2J = 12.5, $C\underline{H}_2$–O); 3.89 (1H, d, ^2J = 12.5, $C\underline{H}_2$–O); 4.89 (1H, s, C(4)H); 6.72 (2H, s, NH_2); 7.00 (1H, weak resolution m, C_6H_4); 7.13 (3H, weak resolution m, C_6H_4); 12.39 (1H, s, NH)
5r	2202	3204, 3310	3.11 (3H, s, OCH_3); 4.18 (2H, s, C(3)–CH_2–O); 4.81 (1H, s, C(4)H); 6.20 (1H, d, ^3J = 3.1, C(3')H); 6.36 (1H, dd, ^3J = 3.1, ^3J = 5.2, C(4')H); 6.88 (2H, br. s, NH_2); 7.51 (1H, d, ^3J = 5.2, C(5')H); 12.49 (1H, br. s, NH)
5s	2192	2948, 3204, 3332	3.19 (1H, d, ^2J = 16.9, C(3)CH_2); 3.39 (1H, d, ^2J = 16.9, C(3)CH_2); 3.41 (3H, s, $COOCH_3$); 3.64 (3H, s, C(2')–OCH_3); 3.74 (3H, s, C(3')–OCH_3); 3.77 (3H, s, C(4')–$OC\underline{H}_3$); 4.70 (1H, s, C(4)H); 6.72 (2H, s, C_6H_2); 6.74 (2H, br. s, NH_2); 12.14 (1H, br. s, NH)
5t	2198	3156, 3264	2.29 (3H, s, CH_3); 3.59 (1H, d, ^2J = 14.4, SCH_2); 3.90 (1H, d, ^2J = 14.4, SCH_2); 4.60 (1H, s, C(4)H); 6.89-7.42 (9H, m, NH_2+C_6H_4+C_4H_3S); 12.42 (1H, br. s, NH)

TABLE 2 (continued)

1	2	3	4
5u	2200	3150, 3248	2.27 (3H, s, CH_3); 3.59 (1H, d, ^2J = 13.8, SCH_2); 3.81 (1H, d, ^2J = 13.8, SCH_2); 3.64 (6H, s, 2',5'–C_6H_3–$(OCH_3)_2$); 4.72 (1H, s, C(4)H); 6.49 (1H, d, ^4J = 3.3, C(6')H); 6.77 (3H, dd, ^4J = 3.3, ^3J = 8.5, NH_2+C(4')H); 6.91 (1H, d, ^3J = 8.5, C(3')H); 7.07 (4H, m, C_6H_4); 12.24 (1H, s, NH)
5v	2192	3324, 3364	2.29 (3H, s, C<u>H</u>$_3$–C_6H_4–S); 3.58 (1H, d, ^2J = 13.8, SCH_2); 3.63+3.71+3.78 (9H, sss, 2',3',4'–$(CH_3O)_3$–C_6H_2); 3.79 (1H, d, ^2J = 13.8, SCH_2); 4.58 (1H, s, C(4)H); 6.61 (2H, br. s, NH_2); 6.69 (2H, m, C_6H_2); 7.09 (4H, m, S–C_6H_4); 12.14 (1H, br. s, NH)

* ^{1}H NMR spectra measured at 20 and 60°C.
*^{2} Total number of protons corresponding the *sp*- and *ap*-isomers.
*^{3} The signals of the protons partly overlap with the signals of the protons of DMSO.
*^{4} The ^{1}H NMR spectra measured at 120°C.

As also in the previously studied *syn*-periplanar isomers of 1,4-dihydropyridines [11-13], 4,5-dihydrothiophenes [14], and other hydrogenated heterocycles [11, 15, 16] containing a 2-nitrophenyl or α,β-picolinium substituent at the sp^3-hybridized carbon atom, the phenyl substituent in compounds **5b** and **5d** is in the pseudoaxial position and is turned in the *anti*-periplanar direction in relation to the planar part of the "bottom of the boat" in the flattened pyran ring (Fig. 1). In such a position the screening of the hydrogen atoms of the phenyl substituent and C(4)H of the pyran ring is different.

The structure of the 4H-pyran **5e**, condensed with a pyrazole ring, was established conclusively for the first time by X-ray crystallographic analysis (Fig. 1, Tables 3 and 4).

In the molecule of **5e** the conformation of the pyran ring is a very strongly flattened boat; the C(2) and C(4a) atoms project from the plane of "the bottom of the boat" (the deviation of its atoms from the average plane is ±0.001 Å) by 0.074 and 0.022 Å respectively, which corresponds to bending of the ring along the O(1)–C(3) line through 6.6°, C(4)–C(7a) through 1.8°, and C(2)–C(4a) through 4.4°. It should be noted that the pyran ring in our previously investigated molecules of 2-amino-3-ethoxycarbonyl-4-(3-fluorophenyl)-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-benzo[*b*]pyran (**10**) [17] and 2-amino-3-ethoxycarbonyl-4-(2-fluorophenyl)-4H-naphtho[2,1-*b*]pyran (**11**) [18] and also in the molecule of 2-amino-3-cyano-5-ethoxycarbonyl-6-methyl-4-phenyl-4H-pyran (**12**) [19] has a boat conformation but with more substantial projection from the plane of

TABLE 3. The Bond Lengths (*d*) in the Molecule of **5e**

Bond	*d*, Å	Bond	*d*, Å	Bond	*d*, Å
O(1)–C(2)	1.367(2)	C(4a)–C(7a)	1.387(3)	C(12)–C(21)	1.510(3)
O(1)–C(7a)	1.367(3)	C(5)–C(6)	1.351(2)	C(13)–C(14)	1.369(3)
C(2)–C(3)	1.365(3)	C(5)–C(23)	1.487(4)	C(14)–C(15)	1.383(4)
C(2)–N(8)	1.339(3)	N(6)–N(7)	1.361(3)	C(14)–C(19)	1.518(4)
C(3)–C(4)	1.531(3)	N(7)–C(7a)	1.323(2)	C(15)–C(16)	1.396(3)
C(3)–C(9)	1.419(2)	C(9)–N(10)	1.146(2)	C(16)–C(17)	1.518(3)
C(4)–C(4a)	1.501(2)	C(11)–C(12)	1.413(3)	C(17)–C(18)	1.532(4)
C(4)–C(11)	1.542(2)	C(11)–C(16)	1.409(2)	C(19)–C(20)	1.447(8)
C(4)–C(5)	1.382(3)	C(12)–C(13)	1.396(3)	C(21)–C(22)	1.480(6)

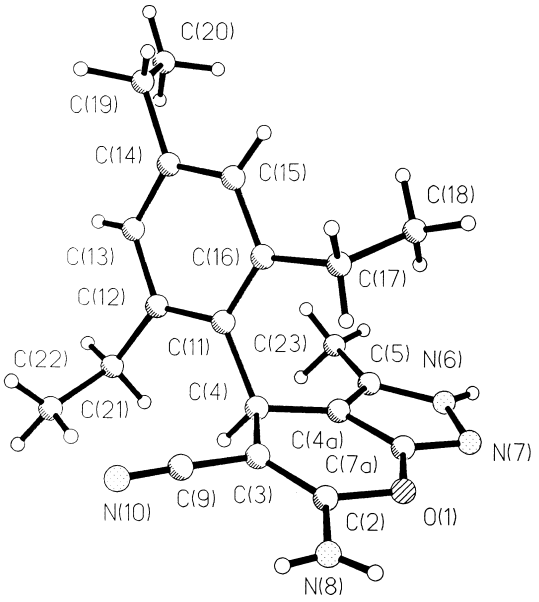


Fig. 1. A general view of the molecule of 6-amino-5-cyano-3-methyl-4-(2',4',6'-triethylphenyl)-2H,4H-pyrano[2,3-*c*]pyrazole (**5e**) according to data from X-ray crystallographic analysis. (The numbering of the atoms does not correspond to the numbering used in the text.)

heterocycle of the other atoms – O(1) and C(4). The dihedral angle (measured with an accuracy of ±0.003°) between the planar pyrazole ring and "the bottom of the boat" of the pyran ring is 1.6°, i.e., the bicyclic system is in fact planar. The intramolecular nonbonding contacts (Table 6) give rise to rotation of the pseudoaxial aryl substituent in relation to the "bottom of the boat" in the six-membered heterocycle by 98.6° and have some effect on the length of the bonds at the C(4) atom. Thus, the lengths of the C(3)–C(4) bond 1.531(3) and C(4)–C(11) bond 1.542(2) Å are increased in comparison with the length of the C(4)–C(4a) bond 1.501(2) Å and the standard length [20] of the C(sp^2)–C(sp^3) bond 1.507 Å.

In the molecule of **5e**, as also in the molecules **10-12**, conjugation is observed in the planar fragment N(8)–C(2)=C(3)–C(9)≡N(10), containing NH_2 and CN groups at the C(2)=C(3) bond. This leads to appreciable redistribution of the bond lengths (shortening of N(8)–C(2) and C(3)–C(9) and lengthening of C(2)=C(3)) compared with the usual values [20].

TABLE 4. The Bond Angles (ω) in the Molecule of **5e**

Angle	ω, deg.	Angle	ω, deg.	Angle	ω, deg.
C(2)–O(1)–C(7a)	115.2(1)	C(4)–C(4a)–C(7a)	123.3(2)	C(11)–C(12)–C(21)	124.5(2)
N(7)–N(6)–C(5)	113.5(2)	C(5)–C(4a)–C(7a)	103.4(1)	C(13)–C(12)–C(21)	116.5(2)
N(6)–N(7)–C(7a)	102.0(2)	N(6)–C(5)–C(4a)	106.4(2)	C(12)–C(13)–C(14)	123.0(2)
O(1)–C(2)–N(8)	110.3(2)	N(6)–C(5)–C(23)	122.6(2)	C(13)–C(14)–C(15)	117.3(2)
O(1)–C(2)–C(3)	123.5(2)	C(4a)–C(5)–C(23)	131.0(2)	C(13)–C(14)–C(19)	120.6(3)
N(8)–C(2)–C(3)	126.2(2)	O(1)–C(7a)–N(7)	119.4(2)	C(15)–C(14)–C(19)	122.0(2)
C(2)–C(3)–C(4)	125.5(2)	O(1)–C(7a)–C(4a)	125.8(2)	C(14)–C(15)–C(16)	122.9(2)
C(2)–C(3)–C(9)	119.7(2)	N(7)–C(7a)–C(4a)	114.7(2)	C(11)–C(16)–C(15)	119.0(2)
C(4)–C(3)–C(9)	119.7(2)	N(10)–C(9)–C(3)	177.9(2)	C(11)–C(16)–C(17)	124.6(2)
C(3)–C(4)–C(4a)	106.2 (1)	C(4)–C(11)–C(12)	119.2 (1)	C(15)–C(16)–C(17)	116.5 (2)
C(3)–C(4)–C(11)	115.8 (1)	C(4)–C(11)–C(16)	121.8 (2)	C(16)–C(17)–C(18)	113.3 (2)
C(4a)–C(4)–C(11)	112.6 (1)	C(12)–C(11)–C(16)	118.8 (2)	C(14)–C(19)–C(20)	114.3 (3)
C(4)–C(4a)–C(5)	133.2 (2)	C(11)–C(12)–C(13)	119.0 (2)	C(12)–C(21)–C(22)	114.3 (3)

TABLE 5. The Atomic Coordinates ($\times 10^4$; for H $\times 10^3$) in the Molecule of **5e**

Atom	*x*	*y*	*z*	Atom	*x*	*y*	*z*
O(1)	3275(2)	5837 (1)	4518(1)	H(6)	101(3)	272 (3)	381(2)
N(6)	1128(3)	3539 (2)	3822(1)	H(8a)	345(4)	863 (3)	488(2)
N(7)	2550(3)	3790 (2)	4265(1)	H(8b)	468(4)	731 (3)	512(2)
N(8)	3746(3)	7808 (2)	4883(2)	H(4)	-144(3)	769 (2)	375(2)
N(10)	771(3)	10667 (2)	3716(2)	H(13)	-322(3)	924 (2)	80(2)
C(2)	2693(3)	7267 (2)	4399(1)	H(15)	226(3)	733 (2)	12(2)
C(3)	1253(3)	8006 (2)	3849(1)	H(17a)	355(3)	668 (2)	245(2)
C(4)	-89(3)	7380 (2)	3391(1)	H(17b)	442(3)	709 (2)	136(2)
C(4a)	577(3)	5822 (2)	3629(1)	H(18a)	300(4)	456 (2)	198(2)
C(5)	-79(3)	4715 (2)	3438(1)	H(18b)	553(4)	461 (2)	157(2)
C(7a)	2158(3)	5174 (2)	4139(1)	H(18c)	361(3)	495 (2)	89(2)
C(9)	964(3)	9481 (2)	3764(1)	H(19a)	2(4)	876 (3)	-112(2)
C(11)	-211(3)	7812 (2)	2286(1)	H(19b)	-153(3)	972 (2)	-108(2)
C(12)	-2031(3)	8565 (2)	1975(2)	H(20a)	-309(4)	756 (3)	-67(2)
C(13)	-2184(4)	8824 (3)	971(2)	H(20b)	-204(3)	790 (2)	-179(2)
C(14)	-641(4)	8392 (3)	263(2)	H(20c)	-139(4)	674 (3)	-91(2)
C(15)	1146(4)	7693 (3)	578(2)	H(21a)	-501(3)	926 (2)	234(2)
C(16)	1408(3)	7393 (2)	1569(1)	H(21b)	-406(3)	845 (2)	321(2)
C(17)	3456(3)	6610 (3)	1793(2)	H(22a)	-518(4)	1090 (2)	341(2)
C(18)	4040(4)	5082 (3)	1564(3)	H(22b)	-371(4)	1125 (3)	258(2)
C(19)	-926(6)	8627 (4)	-815(2)	H(22c)	-300(4)	1039 (2)	335(2)
C(20)	-1989(8)	7731 (5)	-1099(3)	H(23a)	-189(3)	384 (3)	283(2)
C(21)	-3864(4)	9126 (3)	2659(2)	H(23b)	-311(4)	506 (2)	332(2)
C(22)	-3953(5)	10478 (5)	3013(4)	H(23c)	-188(3)	521 (3)	238(2)
C(23)	-1755(4)	4689 (3)	2935(2)				

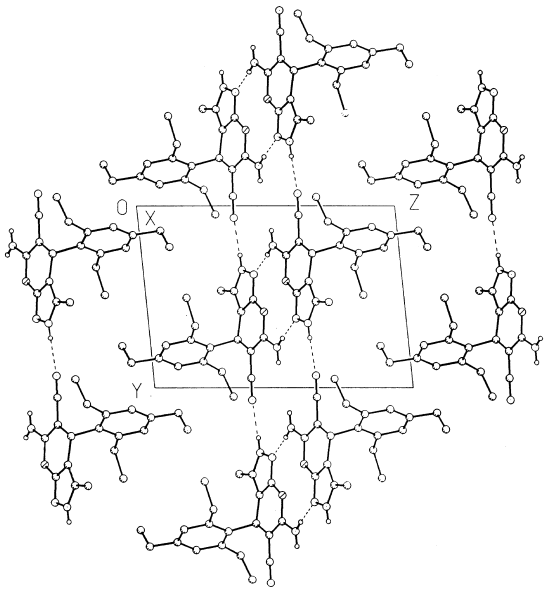


Fig. 2. A *bc* projection of the crystal structure of **5e**.
The dashed lines indicate intermolecular N–H···N hydrogen bonds.

TABLE 6. The Short Nonbonding Intramolecular Contacts in the Molecule of **5e***

Length	*d*, Å	Length	*d*, Å	Length	*d*, Å
C(3) . . C(16)	3.281(3)	C(4) . . C(23)	3.387(3)	C(9) . . C(11)	3.154(3)
C(3) . . C(17)	3.319(3)	C(4a) . . C(16)	3.109(3)	C(12) . . H(4)	2.56(3)
C(4) . . C(17)	3.087(3)	C(4a) . . C(17)	3.156(3)	C(21) . . H(4)	2.50(3)
C(4) . . C(21)	3.027(3)	C(5) . . C(11)	3.256(3)	H(4) . . H(21b)	2.05(3)

* The sums of the van der Waals radii [22] of C and H are 2.90 Å, and twice the van der Waals radii of C and H amounts to 3.40 and 2.40 Å respectively.

In the crystal intermolecular hydrogen bonds N(6)–H(6)···N(10) (*x*, *y* - 1, *z*) [N(6)–N(10) 2.970(3), N(6)–H(6) 0.84(3), H(6)–N(100) 2.13(3) Å, angle N(6)–H(6)–N(10) 178(2)°] and N(8)–H(8b)···N(7) (1 - *x*, 1 - *y*, 1 - *z*) [N(8)–N(7) 3.019(3), N(8)–H(8b) 0.80(2), H(8b)–N(7) 2.22(3) Å, angle N(8)–H(8b)–N(7) 171(2)°] link the molecules of **5e** into ribbons along the *b* axis (Fig. 2). The second hydrogen atom of the $N(8)H_2$ group does not form hydrogen bonds and shortened contacts.

It can be concluded on the basis of the data presented above that the pyranopyrazoles **5a-v** exist in the 2H and not the 1H tautomeric form, as was previously considered [1-6].

EXPERIMENTAL

The melting points were determined on a Kofler bench. The IR spectra were recorded on Specord M-80 and Perkin-Elmer 577 instruments for tablets in potassium bromide (1/200). The ^{1}H NMR spectra were measured on a Bruker AC-300 spectrometer (300 MHz) in DMSO-d_6 with reference to TMS.

The crystals of compound **5e** ($C_{20}H_{24}N_4O$, M = 336.43 g/mol) are triclinic, at 20°C: a = 7.114(2), b = 9.974(3), c = 13.858(4) Å; α = 81.92(2), β = 80.77(2), γ = 74.22(2)°; V = 933.0(6) Å^3; d_{calc} = 1.198 g/cm^3; Z = 2; space group P1. The unit cell parameters and the intensities of 4870 unique reflections were measured on a Siemens P3/PS four-circle automatic diffractometer (λMoKα, graphite monochromator, θ/2θ scan to θ_{max} = 28°). The structure was interpreted by the direct method, revealing all the non-hydrogen atoms, and refined by full-matrix least-squares treatment in anisotropic approximation for the non-hydrogen atoms in 3862 reflections with $I > 3\sigma(I)$. All the hydrogen atoms were revealed objectively by Fourier difference syntheses but on account of the large thermal vibrations were included in the refinement with fixed temperature parameters U = 0.05 Å^2. The final divergence factor was R = 0.064 (R_w = 0.064). All the calculations were performed using the SHELXTL PLUS software [21] (PC version). The atomic coordinates are given in Table 5. (The thermal parameters can be obtained from the authors.)

6-Amino-4-aryl-5-cyano-2H,4H-pyrano[2,3-*c*]pyrazoles (5). A. A mixture of the aromatic aldehyde **6** (10 mmol) and malononitrile **7** (11 mmol) in ethanol (20 ml) was stirred and heated until the reagents had dissolved, and triethylamine (0.5 ml) was added. After 15 min 5-pyrazolone **8** (11 mmol) was added. The reaction mass was heated to boiling, filtered, and left to crystallize. The precipitate was filtered off and washed with ethanol and hexane.

B. Compounds **5** were obtained similarly to method A from arylidenemalononitrile **9** (10 mmol) and 5-pyrazolone **8** (11 mmol).

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