# Synthesis of heterocyclic compounds from 4-formylpyrazoles*

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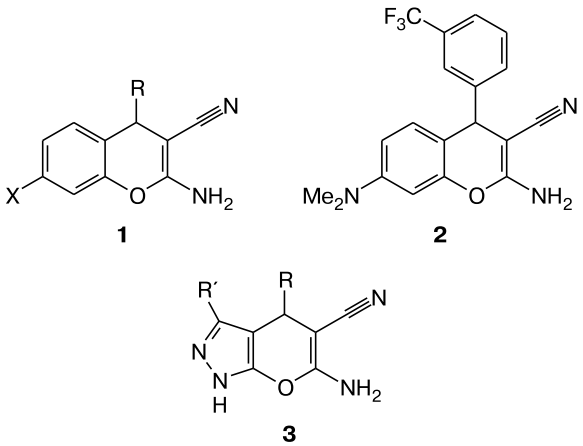
Formylation of pyrazole and 2,5-dimethylpyrazole gave a number of pyrazole-containing aldehydes, which can be used to obtain chromenes, tetrahydrochromenes, 1,4-dihydropyrano[2,3-*c*]pyrazoles, pyrano[3,2-*c*]chromenes, thiochromeno[4,3-*b*]pyrans, pyrano[3,2-*c*]-quinolines, and thiazolo[3,2-*a*]pyridines.

**Key words:** pyrazole, 2,5-dimethylpyrazole, 1-alkyl-1*H*-pyrazole-4-carbaldehyde, "domino" reactions, Knoevenagel condensation, dicyanomethylidene derivatives, chromenes, tetrahydrochromenes, 1,4-dihydropyrano[2,3-*c*]pyrazoles, pyrano[3,2-*c*]chromenes, thiochromeno[4,3-*b*]pyrans, pyrano[3,2-*c*]quinolines, thiazolo[3,2-*a*]pyridines.

A great number of publications concerned with 2-amino-3-cyano-4*H*-chromenes **1** (X = H) is due to the high biological activity of heterocyclic compounds of this class.[1—24] Chromenes exhibit antibacterial,[1—4,16] antituberculosis,[4] fungicidal,[4—6] and anthelmintic[7] activity; some of them can act as antioxidants.[8] Many 2-amino-3-cyano-4*H*-chromenes show antitumor activity.[9—24] Specifically, 4-(3-trifluoromethylphenyl)-4*H*-chromene (**2**) (chromeceptin) can trigger the apoptosis of cancer cells.[11—14] Some tests have revealed high anticancer activity of compounds **1** for X = OR and $NR_2$ in low concentrations.[15—24] Some 6-amino-4-aryl(hetaryl)-5-cyano-1,4-dihydropyrano[2,3-*c*]pyrazoles **3** can act as bactericides[25,26] and inhibitors of kinases,[27,28] P-glycoprotein,[29] Scr-homologs of tyrosine phosphatase (SHP-2),[30] and autotaxin (ATX).[31]




**1**

**2**

**3**

**1:** R = Ar, Het; X = H, OH, OMe, OEt, Hal, $NH_2$, NHEt, $NMe_2$, $NEt_2$
**3:** R = Ar, Het; R′ = Alk, Ar

The most convenient routes to such compounds involve base-catalyzed reactions of condensation products of malononitrile and aldehydes with appropriate carbonyl compounds and *meta*-substituted phenols. These reactions follow a "domino" pattern involving the Knoevenagel condensation, the Michael addition, and the hetero-Thorpe—Ziegler reaction for two, three, and four reaction components.[32] Using this approach, one can obtain libraries of compounds with widely varied substituents. This has become of special interest since the discovery of a correlation between the activity of 2-amino-4-aryl(hetaryl)-3-cyano-7-hydroxy(dimethylamino, diethylamino)-4*H*-chromenes **1** and the structures of substituents in positions 7, 6, and 4.[15—24]

The literature data on 4-pyrazolylpyrans of the type **1** (X = H) or **3** are scarce;[33—42] some of them produce molluscicidal,[33] antibacterial, and fungicidal effects.[36,38,40—42] Pyrans containing an N-alkylpyrazole fragment virtually have not been documented. However, the starting aldehydes for the synthesis of libraries of such compounds are fairly accessible. *N*-Alkylpyrazoles **7** prepared by alkylation of pyrazole **4** or 3,5-dimethylpyrazole (**5**) can be transformed into *N*-alkyl-4-formylpyrazoles **8** in high yields under the conditions of the Vilsmeier reaction[43—45] (Scheme 1).

We obtained and characterized a number of new aldehydes **8a—g**. Aldehydes **8a**,**c**,**d**,**f** are colorless or faintly yellowish liquids that are well soluble in water and common organic solvents but hexane. Compounds **8b**,**e** are virtually odorless, colorless or slightly colored solids, while aldehyde **8g** is a viscous oil; the solubilities of the last three

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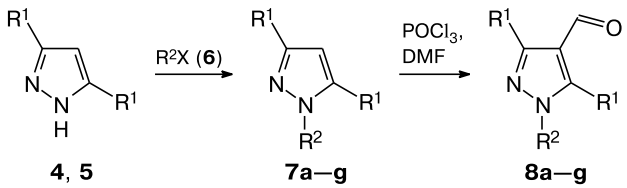
**Scheme 1**




**4**, **5** **7a—g** **8a—g**

**4:** $R^1$ = H; **5**: $R^1$ = Me; **6**: $R^2$ = Me, Et, $Pr^i$, All; X = Br, I
**7**, **8:** $R^1$ = H, $R^2$ = Me (**a**); $R^1$ = $R^2$ = Me (**b**); $R^1$ = H, $R^2$ = Et (**c**); $R^1$ = H, $R^2$ = $Pr^i$ (**d**); $R^1$ = Me, $R^2$ = $Pr^i$ (**e**); $R^1$ = H, $R^2$ = All (**f**); $R^1$ = Me, $R^2$ = All (**g**)

compounds in water are appreciably lower. The $^1$H NMR spectra of compounds **8a**,**c**,**d**,**f** show characteristic signals for the protons of the 1-alkyl(allyl) substituent, signals for the H(3) and H(5) protons at δ 7.96 and 8.41, and a signal for the formyl proton at δ 9.78 (Table 1). In the $^1$H NMR spectra of compounds **8b**,**e**,**g**, the signals for the protons of the methyl groups in positions 3 and 5 appear at δ 2.29—2.31 and 2.45—2.48. The IR spectra of compounds **8** feature a band at 1660—1680 $cm^{-1}$ (C=O); an increase in the number of alkyl groups slightly increases (by 10—15 $cm^{-1}$) the wavenumber. The UV-Vis spectra of these aldehydes show two bands at 202—206 (low intensity) and 246—252 nm (high intensity). The 1-alkyl substituents produce no effect on the positions or intensities of the absorption bands in the UV-Vis spectra. However, introduction of two methyl groups into positions 3 and 5 of the pyrazole ring results in slight (4—7 nm) bathochromic shifts of both bands.

We employed aldehydes **8** for the synthesis of heterocyclic compounds. Attempted three-component synthesis of pyrans from an aldehyde, malononitrile, and a carbonyl compound gave only resinous products. Using a two-component synthesis, we obtained *N*-alkylpyrazolylmethylidenemalononitriles **9a**—**g** and determined their physicochemical characteristics. Compounds **9a**—**g** are colorless or faintly colored solids that are well soluble in most organic solvents, moderately soluble in ethanol (the solubility becomes much better when more alkyl groups are present), and poorly soluble in water and hexane.

Like the $^1$H NMR spectra of compounds **8a**,**c**,**d**,**f**, the spectra of compounds **9a**,**c**,**d**,**f** (Table 2) show characteristic signals for the 1-alkyl(allyl) substituent and signals for the H(3) and H(5) protons of the pyrazole ring. The signal for the proton at the double bond of the dicyanoethenyl substituent appears at δ 8.27—8.37. The IR spectra of compounds **9** feature a band at 2222—2234 $cm^{-1}$ (C≡N). For 3- and 5-unsubstituted pyrazoles **9**, this band appears as

**Table 1.** Elemental analysis data and $^1$H NMR, IR, and UV-Vis spectra of 4-formylpyrazoles **8a**—**g**

| Compound | Found / Calculated (%) | | | Molecular formula | $^1$H NMR (DMSO-$d_6$), δ (*J*/Hz) | IR, ν/$cm^{-1}$ | UV-Vis, $\lambda_{max}$/nm (ε) |
|---|---|---|---|---|---|---|---|
| | C | H | N | | | | |
| **8a** | 54.49<br>54.54 | 5.56<br>5.49 | 25.42<br>25.44 | $C_5H_6N_2O$ | 3.90 (s, 3 H, $NCH_3$); 7.96, 8.41 (both s, each 1 H, CH of pyrazole); 9.78 (s, 1 H, CHO) | 1679 (CO), 1541, 1459, 1385 | 246 (10900), 202 (3600) |
| **8b** | 60.67<br>60.85 | 7.38<br>7.30 | 20.15<br>20.28 | $C_7H_{10}N_2O$ | 2.29, 2.45 (both s, each 3 H, $CH_3$); 3.68 (s, 3 H, $NCH_3$); 9.81 (s, 1 H, CHO) | 2956, 2848, 1660 (CO), 1556, 1544, 1508 | 252 (13800), 206 (7700) |
| **8c** | 57.98<br>58.05 | 6.61<br>6.50 | 22.43<br>22.57 | $C_6H_8N_2O$ | 1.39 (t, 3 H, $CH_3$, *J* = 7.0); 4.19 (q, 2 H, $NCH_2CH_3$, *J* = 7.0); 7.97, 8.46 (both s, each 1 H, CH of pyrazole); 9.78 (s, 1 H, CHO) | 1680 (CO), 1540, 1460, 1390 | 246 (9900), 202 (3500) |
| **8d** | 60.80<br>60.85 | 7.34<br>7.30 | 20.19<br>20.28 | $C_7H_{10}N_2O$ | 1.43 (d, 6 H, $(CH_3)_2CH$, *J* = 6.6); 4.57 (m, 1 H, $(CH_3)_2CHN$); 7.98, 8.50 (both s, each 1 H, CH of pyrazole); 9.78 (s, 1 H CHO) | 1682 (CO), 1543, 1456, 1418, 1394, 1371 | 247 (13200), 202 (4400) |
| **8e** | 64.98<br>65.03 | 8.60<br>8.49 | 16.73<br>16.85 | $C_9H_{14}N_2O$ | 1.34 (d, 6 H, $(CH_3)_2CH$, *J* = 6.2); 2.31, 2.48 (both s, each 3 H, $CH_3$); 4.52 (m, 1 H, $(CH_3)_2CHN$); 9.83 (s, 1 H CHO) | 2989, 2749, 1666 (CO), 1541, 1485, 1428, 1397 | 252 (14600), 206 (6600) |
| **8f** | 61.73<br>61.75 | 5.96<br>5.92 | 20.62<br>20.58 | $C_7H_8N_2O$ | 4.83 (d, 2 H, $NCH_2CHCH_2$, *J* = 5.7); 5.15 (d, 1 H, $NCH_2CHCHH$, *J* = 17.2); 5.24 (d, 1 H, $NCH_2CHCHH$, *J* = 10.3); 6.03 (m, 1 H, $NCH_2CHCH_2$); 8.00, 8.45 (both s, each 1 H, CH of pyrazole); 9.84 (s, 1 H, CHO) | 2846, 2814, 2799, 2777, 1671 (CO), 1545, 1465, 1419, 1393 | 245 (13600), 202 (4300) |
| **8g** | 65.78<br>65.83 | 7.41<br>7.37 | 16.99<br>17.06 | $C_9H_{12}N_2O$ | 2.31, 2.41 (both s, each 3 H, $CH_3$); 4.68 (d, 2 H, $NCH_2CHCH_2$, *J* = 4.4); 4.97 (d, 1 H, $NCH_2CHCHH$, *J* = 16.8); 5.17 (d, 1 H, $NCH_2CHCHH$, *J* = 9.9); 5.92 (m, 1 H, $NCH_2CHCH_2$); 9.84 (s, 1 H, CHO) | 1681 (CO), 1545, 1495, 1435, 1404, 1397 | 252 (21000), 206 (11200) |

**Table 2.** Elemental analysis data and $^1$H NMR, IR, and UV-Vis spectra of *N*-alkylpyrazolylmethylidenemalononitriles **9a—g**

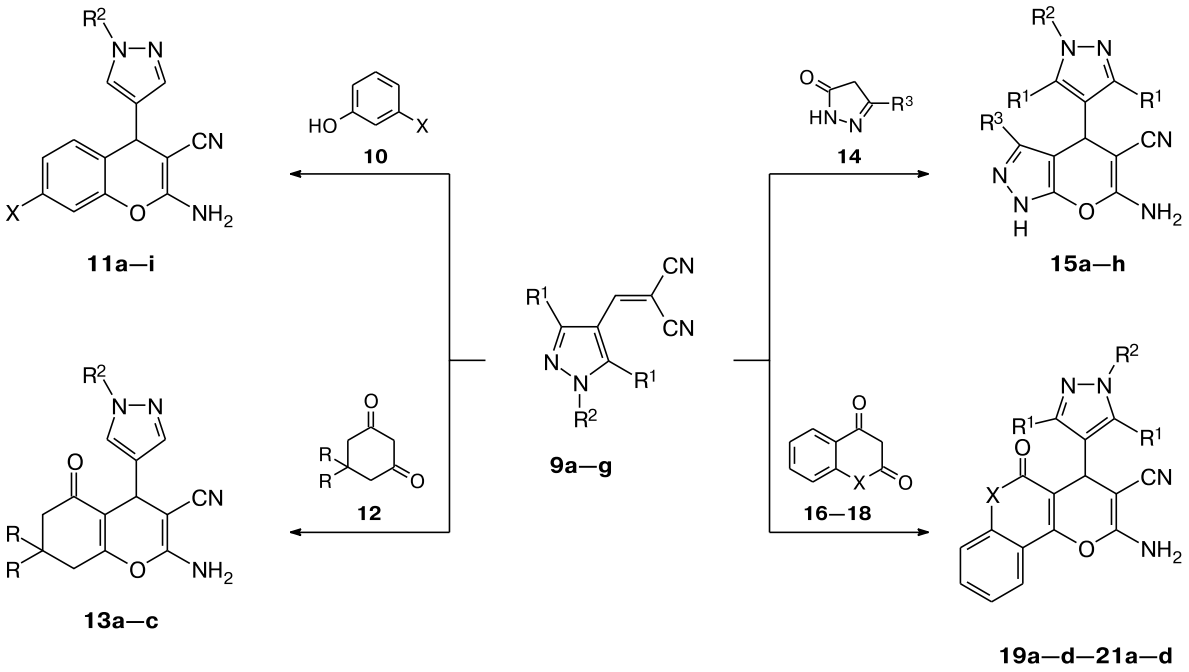
| Compound | Found / Calculated (%) | | | Molecular formula | $^1$H NMR (DMSO-$d_6$), δ (*J*/Hz) | IR, ν/cm$^{-1}$ | UV-Vis, $\lambda_{max}$/nm (ε) |
|---|---|---|---|---|---|---|---|
| | C | H | N | | | | |
| **9a** | 60.59<br>60.75 | 3.96<br>3.82 | 35.36<br>35.42 | $C_8H_6N_4$ | 3.96 (s, 3 H $NCH_3$); 8.08 (s, 1 H, CH of pyrazole); 8.37 (s, 1 H, $CHC(CN)_2$); 8.47 (s, 1 H, CH of pyrazole) | 3124, 3100, 3040, 2224 (CN), 2232 (CN), 1600, 1492, 1212, 1172, 1152, 1068, 1020 | 317 (30450), 217 (6950) |
| **9b** | 60.67<br>64.50 | 7.38<br>7.30 | 20.15<br>20.28 | $C_{10}H_{10}N_4$ | 2.27, 2.37 (both s, each 3 H, $CH_3$); 3.73 (s, 3 H, $NCH_3$); 8.27 (s, 1 H, $CHC(CN)_2$) | 3020, 2932, 2228 (CN), 1592, 1512, 1452, 1396, 1376, 1356, 1236, 1176, 1036 | 329 (3300), 218 (1100) |
| **9c** | 62.74<br>62.78 | 4.70<br>4.68 | 32.48<br>32.54 | $C_9H_8N_4$ | 1.39 (t, 3 H, $CH_3$, $J$ = 6.9); 4.26 (q, 2 H, $CH_3C\underline{H}_2N$, $J$ = 6.9); 8.11 (s, 1 H, CH of pyrazole); 8.35 (s, 1 H, $CHC(CN)_2$); 8.49 (s, 1 H, CH of pyrazole) | 3124, 3035, 2986, 2230 (CN), 2221 (CN), 1592, 1532, 1522, 1476, 1448, 1385, 1233, 1217, 1173, 1147, 1103, 1082, 1015 | 317 (28900), 217 (6200) |
| **9d** | 64.45<br>64.50 | 5.44<br>5.41 | 30.06<br>30.09 | $C_{10}H_{10}N_4$ | 1.41 (d, 6 H, $(C\underline{H}_3)_2CH$, $J$ = 6.5); 4.65 (m, 1 H, $(CH_3)_2C\underline{H}N$); 8.11 (s, 1 H, CH of pyrazole); 8.32 (s, 1 H, $CHC(CN)_2$); 8.46 (s, 1 H, CH of pyrazole) | 3119, 3052, 2988, 2921, 2855, 2294, 2232, 2224 (CN), 1716, 1599, 1530, 1520, 1453, 1383, 1338, 1240, 1186, 1147, 1081, 1019 | 320 (21200), 217 (5200) |
| **9e** | 67.18<br>67.27 | 6.67<br>6.59 | 26.13<br>26.15 | $C_{12}H_{14}N_4$ | 1.36 (d, 6 H, $(C\underline{H}_3)_2CH$, $J$ = 6.5); 2.30, 2.40 (both s, each 3 H, $CH_3$); 4.58 (m, 1 H, $(CH_3)_2C\underline{H}N$); 8.27 (s, 1 H, $CHC(CN)_2$) | 2984, 2941, 2878, 2319, 2223 (CN), 1596, 1498, 1454, 1422, 1381, 1367, 1357, 1263, 1134, 1186, 1161, 1059 | 328 (22300), 217 (6000) |
| **9f** | 65.22<br>65.21 | 4.40<br>4.38 | 30.38<br>30.42 | $C_{10}H_8N_4$ | 4.90 (d, 2 H, $NC\underline{H}_2CHCH_2$, $J$ = 5.1); 5.15 (d, 1 H, $NCH_2CHC\underline{H}H$, $J$ = 17.2); 5.24 (d, 1 H, $NCH_2CHCH\underline{H}$, $J$ = 10.3); 6.02 (m, 1 H, $NCH_2C\underline{H}CH_2$); 8.13 (s, 1 H, CH of pyrazole); 8.37 (s, 1 H, $CHC(CN)_2$); 8.49 (s, 1 H, CH of pyrazole) | 3123, 3036, 2986, 2903, 2230, 2222 (CN), 1876, 1714, 1594, 1528, 1469, 1435, 1420, 1384, 1337, 1290, 1224, 1195, 1167, 1146, 1118, 1015, 1003 | 320 (28300), 217 (5900) |
| **9g** | 67.88<br>67.90 | 5.73<br>5.70 | 26.39<br>26.40 | $C_{12}H_{12}N_4$ | 2.28, 2.36 (both s, each 3 H, $CH_3$); 4.99 (d, 2 H, $NC\underline{H}_2CHCH_2$, $J$ = 5.1); 5.19 (d, 1 H, $NCH_2CHC\underline{H}H$, $J$ = 17.9); 5.24 (d, 1 H, $NCH_2CHCH\underline{H}$, $J$ = 10.0); 6.02 (m, 1 H, $NCH_2C\underline{H}CH_2$); 8.30 (s, 1 H, $CHC(CN)_2$) | 2948, 2336, 2224 (CN), 1644, 1564, 1508, 1456, 1420, 1384, 1336, 1292, 1260, 1160, 1072, 1044, 1028, 988 | 327 (27500), 218 (11500) |

two peaks (rather than one peak observed for the 3- and 5-substituted derivatives). The intense band at 1600 cm$^{-1}$ is due to the stretching vibrations of the double bond of the dicyanoethenyl group. The UV-Vis spectra contain two bands at 217 (low intensity) and 317—330 nm (high intensity). As with aldehydes **8**, the 1-alkyl(allyl) substituents do not affect the spectral pattern; however, introduction of two methyl groups into positions 3 and 5 of the pyrazole ring results in a bathochromic shift (13—14 nm) of the lower-frequency band.

*N*-Alkylpyrazolylmethylidenemalononitriles **9** were used in reactions with carbonyl compounds and *meta*-substituted phenols (Scheme 2).

Reactions of compounds **9** with phenols **10** gave the corresponding 4*H*-chromenes **11**. The highest yields were achieved for resorcinol (X = OH), while the use of 3-(*N*,*N*-diethylamino)phenol (X = $NEt_2$) provided the lowest yields. Chromenes **11a—i** are high-melting colorless (X = O), yellow (X = $NH_2$), or dark brown solids (X = $NAlk_2$); their structures were confirmed by physicochemical data. The $^1$H NMR spectra of these compounds (Table 3) show signals for the protons of the aliphatic groups and the aromatic and pyrazole rings (δ 7.18—7.20, 7.40—7.48) as well as broadened signals for the protons of the 2-amino substituent (δ 6.69—6.75). The spectra of chromenes **11b**,**e**,**h** additionally contain signals for the protons of the 7-amino substituent (δ 6.65—6.67) and signals for the C(4)H protons of the pyran ring (δ 4.48—4.58).[32] The higher-field signals correspond to the chromenes containing the $NH_2$ group in the benzene ring. For 7-dialkyl-

**Scheme 2**




X = O (**16**), S (**17**), NH (**18**)

| **9** | $R^1$ | $R^2$ |
|---|---|---|
| **a** | H | Me |
| **b** | Me | Me |
| **c** | H | Et |
| **d** | H | $Pr^i$ |
| **e** | Me | $Pr^i$ |
| **f** | H | All |
| **g** | Me | All |

| **11**, **13** | X (R) | $R^2$ |
|---|---|---|
| **11a** | OH | $Pr^i$ |
| **11b** | $NH_2$ | $Pr^i$ |
| **11c** | $NMe_2$ | $Pr^i$ |
| **11d** | OH | Et |
| **11e** | $NH_2$ | Et |
| **11f** | $NEt_2$ | Et |
| **11g** | $NMe_2$ | Me |
| **11h** | $NH_2$ | Me |
| **11i** | OH | Me |
| **13a** | Me | All |
| **13b** | Me | Et |
| **13c** | H | Et |

| **15** | $R^1$ | $R^2$ | $R^3$ |
|---|---|---|---|
| **a** | Me | $Pr^i$ | $Pr^i$ |
| **b** | Me | $Pr^i$ | Ph |
| **c** | Me | $Pr^i$ | Me |
| **d** | Me | All | Me |
| **e** | H | All | $Bu^t$ |
| **f** | Me | Me | $Pr^i$ |
| **g** | Me | Me | Et |
| **h** | H | $Pr^i$ | $Bu^t$ |

| **19—21** | X | $R^1$ | $R^2$ |
|---|---|---|---|
| **19a** | O | H | Me |
| **19b** | O | Me | Me |
| **19c** | O | H | Et |
| **19d** | O | Me | $Pr^i$ |
| **20a** | S | Me | $Pr^i$ |
| **20b** | S | H | Me |
| **20c** | S | Me | Me |
| **20d** | S | H | Et |
| **21a** | NH | H | Me |
| **21b** | NH | Me | $Pr^i$ |
| **21c** | NH | H | Et |
| **21d** | NH | Me | Me |

aminochromenes **11c**,**f**,**g**, the signal for the C(4)H proton is slightly (by ~0.06 ppm) shifted downfield. The downfield shift of this signal is also observed in the spectra of 7-hydroxychromenes **11a**,**d**,**i**.

The IR spectra of compounds **11** show a strong band at 2185—2196 $cm^{-1}$ due to the nitrile group, which is characteristic of 2-amino-3-cyanopyrans.[32] Such a frequency decrease results from conjugation of the nitrile group with the pyran ring.

The UV-Vis spectra of 7-hydroxychromenes **11a**,**d**,**i** consist of three wide absorption bands with $\lambda_{max}$ = 202—204 (ε = 55 200—35 400), 233—231 (ε = 21 000—15 400), and 267—272 nm (low intensity). The absorption maximum of the last band experiences a slight hypsochromic shift when moving from the methyl through ethyl to isopropyl substituent at the N atom of the pyrazole ring. The UV-Vis spectra of 7-aminochromenes **11b**,**e**,**h** additionally show a low-intensity band with $\lambda_{max}$ = 425—434 nm (ε = 2400—300), which experiences a slight bathochromic shift (6—9 nm) and becomes considerably more intense for 7-dialkylamino derivatives. Another absorption band of 7-aminochromenes **11b**,**e**,**h** has $\lambda_{max}$ = 270—272 nm and is virtually insensitive to the alkyl group at the N atom of the pyrazole ring. For 7-dialkylaminochromenes, this band experiences a strong bathochromic shift (36—40 nm). A similar but smaller bathochromic shift (12—15 nm) is observed for the absorption band with $\lambda_{max}$ = 245—248 nm in the spectra of 7-aminochromenes **11b**,**e**,**h**. The shortest-wavelength band of 7-aminochromenes **11b**,**e**,**h** and **11c**,**f**,**g** has $\lambda_{max}$ = 211—214 nm, and its position is virtually affected by neither the alkyl group of the pyrazole ring nor the alkyl groups of the 7-amino substituent.

Reactions of compounds **9** with dimedone (**12**, R = Me) and cyclohexane-1,3-dione (**12**, R = H) gave hydrogenated 4*H*-chromenes **13a**—**c** in good yields. The $^1$H NMR spectra of compounds **13** (see Table 3) show signals for

**Table 3.** Elemental analysis data and $^1$H NMR, IR, and UV-Vis spectra of 2-amino-3-cyano-4-pyrazolyl-4*H*-chromenes **11a—i** and 2-amino-3-cyano-4-pyrazolyl-5,6,7,8-tetrahydro-4*H*-chromenes **13a—c**

| Compound | Found / Calculated (%) | | | Molecular formula | $^1$H NMR (DMSO-$d_6$), δ (*J*/Hz) | IR, ν/cm$^{-1}$ | UV-Vis, $\lambda_{max}$/nm (ε) |
|---|---|---|---|---|---|---|---|
| | C | H | N | | | | |
| **11a** | 64.79<br>64.85 | 5.51<br>5.44 | 19.01<br>18.91 | $C_{16}H_{16}N_4O_2$ | 1.35 (d, 6 H, $(CH_3)_2CH$, *J* = 6.2); 4.40 (m, 1 H, $(CH_3)_2CHN$); 4.58 (s, 1 H, CH of pyran); 6.35 (s, 1 H, $CH_{Ar}$); 6.51 (d, 1 H, $CH_{Ar}$, *J* = 8.1); 6.74 (s, 2 H, $NH_2$); 6.93 (d, 1 H, $CH_{Ar}$, *J* = 8.1); 7.19, 7.48 (both s, each 1 H, CH of pyrazole); 9.62 (br.s, 1 H, OH) | 3421, 3338, 2980, 2806, 2691, 2600, 2189 (CN), 1646, 1621, 1587, 1508, 1463, 1406, 1347, 1309, 1157 | 267 (8300), 232 (15400), 204 (39000) |
| **11b** | 65.02<br>65.07 | 5.87<br>5.80 | 23.75<br>23.71 | $C_{16}H_{17}N_5O$ | 1.35 (d, 6 H, $(CH_3)_2CH$, *J* = 5.5); 4.41 (m, 1 H, $(CH_3)_2CHN$); 4.48 (s, 1 H, CH of pyran); 5.19 (s, 2 H, $NH_2$); 6.16 (s, 1 H, $CH_{Ar}$); 6.30 (d, 1 H, $CH_{Ar}$, *J* = 7.3); 6.65 (s, 2 H, $NH_2$); 6.76 (d, 1 H, $CH_{Ar}$, *J* = 7.3); 7.18, 7.46 (both s, each 1 H, CH of pyrazole) | 3440, 3368, 3315, 3234, 3191, 2979, 2933, 2874, 2195 (CN), 1652, 1604, 1572, 1512, 1463, 1407, 1332, 1247, 1207, 1177 | 427 (560), 272 (8300), 245 (22500), 211 (50800) |
| **11c** | 66.79<br>66.85 | 6.61<br>6.55 | 21.58<br>21.66 | $C_{18}H_{21}N_5O$ | 1.35 (d, 6 H, $(CH_3)_2CH$, *J* = 4.0); 2.85 (s, 6 H, $NMe_2$); 4.40 (m, 1 H, $(CH_3)_2CHN$); 4.56 (s, 1 H, CH of pyran); 6.19 (s, 1 H, $CH_{Ar}$); 6.48 (d, 1 H, $CH_{Ar}$, *J* = 7.0); 6.69 (s, 2 H, $NH_2$); 6.92 (d, 1 H, $CH_{Ar}$, *J* = 7.1); 7.19, 7.47 (both s, each 1 H, CH of pyrazole) | 3429, 3318, 3235, 3220, 3185, 2978, 2931, 2898, 2815, 2632, 2196 (CN), 1638, 1600, 1556, 1521, 1443, 1397, 1367, 1316, 1291 | 430 (1300), 308 (3200), 260 (31000), 214 (42000) |
| **11d** | 63.75<br>63.82 | 5.06<br>5.00 | 19.76<br>19.85 | $C_{15}H_{14}N_4O_2$ | 1.31 (t, 3 H, $CH_3$, *J* = 6.9); 4.00 (q, 2 H, $CH_3CH_2N$, *J* = 6.9); 4.57 (s, 1 H, CH of pyran); 6.36 (s, 1 H, $CH_{Ar}$); 6.51 (d, 1 H, $CH_{Ar}$, *J* = 7.9); 6.75 (s, 2 H, $NH_2$); 6.92 (d, 1 H, $CH_{Ar}$, *J* = 8.1); 7.20, 7.47 (both s, each 1 H, CH of pyrazole); 9.64 (br.s, 1 H, OH) | 3487, 3398, 3346, 3216, 3196, 3108, 3038, 2991, 2936, 2816, 2717, 2686, 2636, 2185 (CN), 1651, 1618, 1593, 1505, 1493, 1462, 1399, 1357, 1307 | 270 (11500), 231 (21000), 202 (55200) |
| **11e** | 64.11<br>64.04 | 5.37<br>5.37 | 24.83<br>24.90 | $C_{15}H_{15}N_5O$ | 1.31 (t, 3 H, $CH_3$, *J* = 6.8); 4.05 (q, 2 H, $CH_3CH_2N$, *J* = 6.8); 4.50 (s, 1 H, CH of pyran); 5.20 (s, 2 H, $NH_2$); 6.18 (s, 1 H, $CH_{Ar}$); 6.31 (d, 1 H, $CH_{Ar}$, *J* = 7.7); 6.67 (s, 2 H, $NH_2$); 6.76 (d, 1 H, $CH_{Ar}$, *J* = 7.9); 7.20, 7.45 (both s, each 1 H, CH of pyrazole) | 3451, 3363, 3323, 3159, 2988, 2957, 2875, 2185 (CN), 1662, 1632, 1611, 1575, 1511, 1448, 1400, 1359, 1325, 1275 | 425 (300), 270 (4300), 248 (16000), 214 (29900) |
| **11f** | 67.62<br>67.63 | 6.90<br>6.87 | 20.81<br>20.76 | $C_{19}H_{23}N_5O$ | 1.05 (t, 6 H, $CH_3CH_2N$, *J* = 6.0); 1.31 (t, 3 H, $CH_3CH_2N$, *J* = 6.6); 3.31 (m, 2 H, $CH_3CH_2N$*); 4.04 (q, 2 H, $CH_3CH_2N$, *J* = 6.5); 4.55 (s, 1 H, CH of pyran); 6.12 (s, 1 H, $CH_{Ar}$); 6.42 (d, 1 H, $CH_{Ar}$, *J* = 6.7); 6.68 (s, 2 H, $NH_2$); 6.88 (d, 1 H, $CH_{Ar}$, *J* = 7.8); 7.21, 7.47 (both s, each 1 H, CH of pyrazole) | 3363, 3321, 3264, 3190, 3109, 2997, 2936, 2894, 2873, 2684, 2602, 2187 (CN), 1655, 1627, 1608, 1557, 1515, 1441, 1409, 1378, 1282, 1271, 1251 | 434 (1100), 310 (3000), 262 (23000), 213 (28300) |
| **11g** | 65.04<br>65.07 | 5.86<br>5.80 | 23.69<br>23.71 | $C_{16}H_{17}N_5O$ | 2.85 (s, 6 H, $NMe_2$); 3.74 (s, 3 H, $NCH_3$); 4.55 (s, 1 H, CH of pyran); 6.19 (s, 1 H, $CH_{Ar}$); 6.48 (d, 1 H, $CH_{Ar}$, *J* = 7.3); 6.68 (s, 2 H, $NH_2$); 6.89 (d, 1 H, $CH_{Ar}$, *J* = 8.0); 7.18, 7.41 (both s, each 1 H, CH of pyrazole) | 3353, 3309, 3139, 3114, 2941, 2872, 2807, 2632, 2188 (CN), 1661, 1626, 1561, 1518, 1444, 1408, 1364, 1317, 1274 | 430 (2400), 308 (3700), 260 (26000), 214 (79000) |
| **11h** | 62.88<br>62.91 | 4.96<br>4.90 | 26.16<br>26.20 | $C_{14}H_{13}N_5O$ | 3.76 (s, 3 H, $NCH_3$); 4.48 (s, 1 H, CH of pyran); 5.18 (s, 2 H, $NH_2$); 6.16 (s, 1 H, $CH_{Ar}$); 6.30 (d, 1 H, $CH_{Ar}$, *J* = 8.1); 6.65 (s, 2 H, $NH_2$); 6.73 (d, 1 H, $CH_{Ar}$, *J* = 8.1); 7.17, 7.40 (both s, each 1 H, CH of pyrazole) | 3465, 3415, 3374, 3332, 3242, 3206, 3182, 3060, 2973, 2945, 2872, 2664, 2192 (CN), 1875, 1663, 1640, 1620, 1577, 1557, 1514, 1449, 1400, 1331, 1309, 1274, 1247, 1212 | 425 (2100), 270 (6400), 248 (16000), 212 (35300) |

(*to be continued*)

**Table 3** (*continued*)

| Compound | Found / Calculated (%) | | | Molecular formula | $^1$H NMR (DMSO-d$_6$), δ (*J*/Hz) | IR, ν/cm$^{-1}$ | UV-Vis, $\lambda_{max}$/nm (ε) |
|---|---|---|---|---|---|---|---|
| | C | H | N | | | | |
| **11i** | 62.63<br>62.68 | 4.55<br>4.51 | 20.91<br>20.88 | $C_{14}H_{12}N_4O_2$ | 3.75 (s, 3 H $NCH_3$); 4.57 (s, 1 H, CH of pyran); 6.36 (s, 1 H, $CH_{Ar}$); 6.51 (d, 1 H, $CH_{Ar}$, *J* = 6.6); 6.75 (s, 2 H, $NH_2$); 6.91 (d, 1 H, $CH_{Ar}$, *J* = 7.7); 7.19, 7.43 (both s, each 1 H, CH of pyrazole); 9.63 (br.s, 1 H, OH) | 3419, 3121, 3086, 3053, 3027, 2928, 2712, 2673, 2626, 2196 (CN), 1656, 1621, 1588, 1561, 1503, 1481, 1467, 1405, 1352, 1308 | 272 (8900), 233 (13400), 202 (35400) |
| **13a** | 66.59<br>66.65 | 6.24<br>6.21 | 17.32<br>17.27 | $C_{16}H_{18}N_4O_2$ | 0.93, 1.02 (both s, each 3 H, $CH_3$); 2.23 (m, 2 H, $CH_2$); 2.43 (s, 2 H, $CH_2$); 4.17 (s, 1 H, CH of pyran); 4.66 (d, 2 H, CHH=CHC$\underline{H}_2$, *J* = 4.0); 5.03 (d, 1 H, C$\underline{H}$H=CHCH$_2$, *J* = 16.9); 5.14 (d, 1 H, CH$\underline{H}$=CHCH$_2$, *J* = 9.9); 5.95 (m, 1 H, CHH=C$\underline{H}$CH$_2$); 6.93 (s, 2 H, $NH_2$); 7.17, 7.40 (both s, each 1 H, CH of pyrazole) | 3518, 3384, 3158, 2962, 2926, 2892, 2877, 2194 (CN), 1679, 1662 (CO), 1607, 1555, 1452, 1410, 1370, 1335, 1248 | 290 (3500), 236 (25300) |
| **13b** | 65.42<br>65.37 | 6.39<br>6.45 | 17.88<br>17.94 | $C_{16}H_{17}N_5O$ | 0.95, 1.03 (both s, each 3 H, $CH_3$); 1.30 (t, 3 H, C$\underline{H}_3$CH$_2$, *J* = 6.8); 2.22 (m, 2 H, $CH_2$); 2.44 (s, 2 H, $CH_2$); 4.03 (q, 2 H, $CH_3$C$\underline{H}_2$, *J* = 6.8); 4.16 (s, 1 H, CH of pyran); 6.92 (s, 2 H, $NH_2$); 7.14, 7.42 (both s, each 1 H, CH of pyrazole) | 3385, 2957, 2933, 2895, 2872, 2195 (CN), 2185, 1682, 1652 (CO), 1609, 1556, 1463, 1408, 1368, 1248, 1215 | 291 (2500), 236 (25400) |
| **13c** | 63.43<br>63.37 | 6.71<br>5.67 | 19.68<br>19.71 | $C_{15}H_{16}N_4O_2$ | 1.31 (t, 3 H, C$\underline{H}_3$CH$_2$, *J* = 6.8); 1.92, 2.30 (both m, each 2 H, $CH_2$); 2.50 (s, 2 H, $CH_2$)**; 4.03 (q, 2 H, $CH_3$C$\underline{H}_2$, *J* = 6.8); 4.16 (s, 1 H, CH of pyran); 6.91 (s, 2 H, $NH_2$); 7.16, 7.42 (both s, each 1 H, CH of pyrazole) | 3374, 2956, 2936, 2894, 2662, 2188 (CN), 1680, 1650 (CO), 1609, 1557, 1453, 1422, 1409, 1366, 1246, 1252 | 290 (2800), 236 (21000) |

* Masked by the signal of water.
** Overlap with the signal of the solvent.

the aliphatic protons, signals for the protons of the pyrazole ring (δ 7.17 and 7.42), and signals for the protons of the amino group (δ 6.91—6.92). The spectra of 7,7-dimethyl-5,6,7,8-tetrahydrochromenes **13a**,**b** reveal magnetic nonequivalence of the protons of the methyl groups in position 7 (δ 0.93 and 1.02, respectively), which results from a special conformation of their molecules. The protons of the methylene group of the cyclohexane ring are magnetically nonequivalent as well, which results in an increased number of spectral lines. The IR spectra feature absorption bands due to the nitrile group at 2194 (for **13a**,**b**) and 2188 cm$^{-1}$ (for **13c**) and absorption bands due to the carbonyl group at 1650, 1652, and 1665 cm$^{-1}$, respectively. The UV-Vis spectra consist of two wide absorption bands at 236 (high intensity) and 290 nm (low intensity).

Using 5-substituted pyrazol-3-ones **14** in reactions with compounds **9**, we obtained a number of 6-amino-5-cyano-4-pyrazolyl-1,4-dihydropyrano[2,3-*c*]pyrazoles **15** (see Scheme 2). The structure of compounds **15a**—**d**,**f**,**g** allows intramolecular interactions between the methyl groups in positions 3 and 5 of the 4-pyrazolyl substituent and the group at the C(3) atom of the annulated pyrazole ring. This is most pronounced in the $^1$H NMR spectra of compounds **15a**—**c**,**f** (Table 4). Such interactions between the methyl groups and a bulky substituent in position 3 of the pyranopyrazole molecule make the rotation of the pyrazolyl substituent so hindered that the signals for the methyl protons of the isopropyl group become magnetically nonequivalent and appear as two doublets. The structures of compounds **15** are confirmed by the characteristic signals at δ 4.59—4.91 for the C(4)H protons of the pyran ring and by the signals at δ 6.67—6.77 for the protons of the amino group.[41]

The IR spectra of compounds **15** feature absorption bands at 2206—2180 cm$^{-1}$ (C≡N), which agrees well with data for pyranopyrazoles.[32] The UV-Vis spectra show three absorption bands of medium intensity. When the 4-pyrazolyl substituent contains two methyl groups, the middle band experiences a slight bathochromic shift. For 3-phenyl derivative **15b**, the lowest-frequency band experiences a hypsochromic shift by 10 nm and all the bands become much more intense (the hyperchromic effect).

Reactions of compounds **9** with coumarin **16** and its heteroanalogs (thiocoumarin **17** and 2,4-dihydroxyquinoline **18**) afforded 2-amino-3-cyano-5-oxo-4-pyrazolyl-4*H*,5*H*-pyrano[3,2-*c*]chromenes **19**, 2-amino-3-cyano-5-oxo-4-pyrazolyl-4*H*,5*H*-thiochromeno[4,3-*b*]pyrans **20**, and 2-amino-3-cyano-5-oxo-4-pyrazolyl-5,6-dihydro-4*H*-pyrano[3,2-*c*]quinolines **21**, respectively. The $^1$H NMR

**Table 4.** Elemental analysis data and $^1$H NMR, IR, and UV-Vis spectra of 6-amino-5-cyano-4-pyrazolyl-1,4-dihydropyrano[2,3-*c*]-pyrazoles **15a—h**

| Compound | Found / Calculated (%) | | | Molecular formula | $^1$H NMR (DMSO-$d_6$), δ (*J*/Hz) | IR, ν/cm$^{-1}$ | UV-Vis, $\lambda_{max}$/nm (ε) |
|---|---|---|---|---|---|---|---|
| | C | H | N | | | | |
| **15a** | 63.49<br>63.51 | 7.13<br>7.11 | 24.81<br>24.69 | $C_{18}H_{24}N_6O_2$ | 0.80, 0.94 (both d, each 3 H, $(CH_3)_2CH$, *J* = 6.2); 1.28 (m, 6 H, $(CH_3)_2CHN$); 1.82, 2.05 (both s, each 3 H, $CH_3$); 2.50 (m, 1 H, $(CH_3)_2CH$)*; 4.37 (m, 1 H, $(CH_3)_2CHN$); 4.59 (s, 1 H, CH of pyran); 6.67 (s, 2 H, $NH_2$); 12.02 (br.s, 1 H, NH) | 3505, 3395, 3362, 3119, 2979, 2962, 2924, 2873, 2196 (CN), 1638, 1603, 1567, 1526, 1486, 1432, 1402, 1365, 1353, 1333, 1318, 1298, 1255, 1218 | 260 (6800), 231 (6100), 201 (10200) |
| **15b** | 65.02<br>67.36 | 5.87<br>5.92 | 23.75<br>24.44 | $C_{21}H_{22}N_6O$ | 1.09, 1.18 (both d, each 3 H, $(CH_3)_2CH$, *J* = 4.4); 1.71, 2.07 (both s, each 3 H, $CH_3$); 4.26 (m, 1 H, $(CH_3)_2CHN$); 4.91 (s, 1 H, CH of pyran); 6.77 (s, 2 H, $NH_2$); 7.31 (m, 5 H, $CH_{Ar}$); 12.76 (br.s, 1 H, NH) | 3600, 3395, 3303, 3145, 2977, 2948, 2921, 2873, 2180 (CN), 1649, 1610, 1563, 1503, 1488, 1449, 1435, 1401, 1384, 1371, 1346, 1325, 1259, 1221 | 250 (25500), 230 (18700), 201 (34500) |
| **15c** | 67.69<br>67.63 | 6.91<br>6.87 | 20.88<br>20.76 | $C_{16}H_{20}N_6O$ | 1.29 (m, 6 H, $(CH_3)_2CH$); 1.75, 1.83, 2.08 (all s, each 3 H, $CH_3$); 4.38 (m, 1 H, $(CH_3)_2CHN$); 4.56 (s, 1 H, CH of pyran); 6.69 (s, 2 H, $NH_2$); 12.01 (br.s, 1 H, NH) | 3682, 3317, 3185, 3051, 2978, 2933, 2875, 2346, 2206 (CN), 1645, 1618, 1597, 1558, 1487, 1434, 1398, 1350, 1316, 1280, 1258, 1215 | 260 (9800), 230 (9100), 201 (14300) |
| **15d** | 61.85<br>61.92 | 5.92<br>5.85 | 27.16<br>27.08 | $C_{15}H_{14}N_4O_2$ | 1.77, 1.81, 2.03 (all s, each 3H, $CH_3$); 4.57 (m, 3 H, CH of pyran and $NCH_2CHCH_2$); 4.70 (d,1 H, $NCH_2CHCHH$, *J* = 16.9); 5.07 (d, 1 H, $NCH_2CHCHH$, *J* = 9.2); 5.89 (m, 1 H, $NCH_2CHCH_2$); 6.69 (s, 2 H, $NH_2$); 12.03 (br.s, 1 H, NH) | 3550, 3300, 3116, 3042, 2961, 2921, 2196 (CN), 2182, 1650, 1616, 1601, 1564, 1534, 1490, 1432, 1393, 1356, 1331, 1314, 1303, 1214 | 259 (8000), 229 (8100), 200 (13800) |
| **15e** | 62.86<br>62.95 | 6.27<br>6.21 | 25.83<br>25.91 | $C_{17}H_{20}N_6O$ | 1.09 (s, 9 H, $Bu^t$); 4.64 (s, 1 H, CH of pyran); 4.68 (d, 2 H, $NCH_2CHCH_2$, *J* = 4.4); 5.00 (d, 1 H, $NCH_2CHCHH$, *J* = 15.8); 5.13 (d, 1 H, $NCH_2CHCHH$, *J* = 10.3); 5.94 (m, 1 H, $NCH_2CHCH_2$); 6.68 (s, 2 H, $NH_2$); 7.18, 7.41 (both s, each 1 H, CH of pyrazole); 12.09 (br.s, 1 H, NH) | 3327, 3252, 3227, 3193, 3095, 3077, 2971, 2940, 2913, 2879, 2198 (CN), 1660, 1603, 1589, 1556, 1517, 1482, 1443, 1422, 1396, 1372, 1360, 1307, 1293, 1277, 1261, 1230 | 260 (9000), 225 (9800), 200 (15600) |
| **15f** | 67.62<br>67.63 | 6.90<br>6.87 | 20.81<br>20.76 | $C_{16}H_{20}N_6O$ | 1.76 (m, 3 H, $CH_3CH_2$, $CH_3$); 2.04 (s, 3 H, $CH_3$); 2.48 (m, 2 H, $CH_3CH_2$)*; 3.58 (s, 3 H, $CH_3$); 4.58 (s, 1 H, CH of pyran); 6.67 (s, 2 H, $NH_2$); 12.04 (br.s, 1 H, NH) | 3440, 3318, 3152, 2973, 2956, 2921, 2894, 2870, 2191 (CN), 2141, 1657, 1610, 1591, 1567, 1520, 1492, 1477, 1433, 1408, 1386, 1324, 1290, 1224 | 260 (11900), 231 (11200), 201 (18700) |
| **15g** | 60.34<br>60.39 | 6.16<br>6.08 | 28.09<br>28.17 | $C_{15}H_{18}N_6O$ | 1.29 (m, 6 H, $(CH_3)_2CH$); 1.75, 1.83, 2.08 (all s, each 3 H, $CH_3$); 4.38 (m, 1 H, $(CH_3)_2CHN$); 4.56 (s, 1 H, CH of pyran); 6.69 (s, 2 H, $NH_2$); 12.01 (br.s, 1 H, NH) | 3336, 3312, 3253, 2967, 2932, 2882, 2696, 2519, 2353, 2345, 2192 (CN), 2142, 1655, 1619, 1607, 1558, 1524, 1488, 1469, 1436, 1398, 1375, 1365, 1274, 1220 | 260 (9500), 231 (12400), 201 (13100) |
| **15h** | 62.48<br>62.56 | 6.86<br>6.79 | 25.66<br>25.75 | $C_{17}H_{22}N_6O$ | 1.05 (s, 9 H, $Bu^t$); 1.33 (m, 6 H, $(CH_3)_2CH$); 4.42 (m, 1 H, $(CH_3)_2CHN$); 4.62 (s, 1 H, CH of pyran); 6.67 (s, 2 H, $NH_2$); 7.14, 7.39 (both s, each 1 H, CH of pyrazole); 12.03 (br.s, 1 H, NH) | 3650, 3476, 3264, 3137, 3104, 3080, 2975, 2937, 2871, 2819, 2666, 2196 (CN), 1644, 1606, 1573, 1508, 1484, 1447, 1401, 1367, 1291, 1263, 1228, 1213 | 260 (12400), 225 (12400), 200 (24100) |

* Masked by the signal of the solvent.

spectra of these compounds (Table 5) show signals for the protons of the benzene ring, a signal for the amino group, a signal for the C(4)H proton of the pyran ring, and signals of the aliphatic substituents in the pyrazole ring. For compounds **21**, the spectra additionally contain a wide signal for the N(6)H proton. Note that although the spectral regions relating to the protons of the benzene ring are generally similar, the lowest-field signals for these protons in chromeno[3,2-*c*]pyrans **19** and pyrano[3,2-*c*]quinolines **21** appear at δ 7.85—7.89, while analogous signals in the spectra of thiochromeno[4,3-*b*]pyrans **20** appear at δ 8.34—8.37.

The UV-Vis spectra of products **19**—**21** are rather complicated because of superposition of many absorption bands. The positions of the absorption bands are virtually insensitive to the number of alkyl substituents in the pyrazole ring; however, an increase in their number produces a hyperchromic effect on the band intensities. Chromenes **19** are characterized by $\lambda_{max}$ = 203 nm, while replacement of the O atom by the S atom results in a strong bathochromic shift of this band to $\lambda_{max}$ = 236 nm in the spectra of thiochromenes **20**. For pyranoquinolines **21**, the maximum of this band appears at 228 nm. In addition, the UV-Vis spectra of compounds **21** show three closely spaced lines arranged in a nearly regular triplet with a center at 322 nm, which is absent from the spectra of compounds **19** and **20**.

The IR spectra of products **19**—**21** are also complicated. The stretching vibrations of the carbonyl group are manifested by a band at 1669—1679 $cm^{-1}$ in the spectra of compounds **19** and **20** and by two bands in the spectra of compounds **21**: one at 1670—1672 $cm^{-1}$ (amide band I due to the C=O stretching vibrations) and the other at 1648—1651 $cm^{-1}$ (amide band II due to the NH bending vibrations). A strong band at 2180—2198 $cm^{-1}$ (conjugated C≡N) is also characteristic. In addition, each of these heteroanalogs specifically absorbs at 1373—1375, 1553—1554, and 1378—1382 $cm^{-1}$ (for **19**—**21**, respectively).

**Table 5.** Elemental analysis data and $^1$H NMR, IR, and UV-Vis spectra of 2-amino-3-cyano-5-oxo-4-(1*H*-pyrazolyl)-4*H*,5*H*-pyranochromenes **19a**—**d**, 2-amino-3-cyano-5-oxo-4-(1*H*-pyrazolyl)-4*H*,5*H*-thiochromeno[4,3-*b*]pyrans **20a**—**d**, and 2-amino-3-cyano-5-oxo-4-pyrazolyl-5,6-dihydro-4*H*-pyrano[3,2-*c*]quinolines **21a**—**d**

| Compound | Found / Calculated (%) | | | Molecular formula | $^1$H NMR (DMSO-$d_6$), δ (*J*/Hz) | IR, ν/$cm^{-1}$ | UV-Vis, $\lambda_{max}$/nm (ε) |
|---|---|---|---|---|---|---|---|
| | C | H | N | | | | |
| **19a** | 63.81<br>63.75 | 3.80<br>3.78 | 17.51<br>17.49 | $C_{17}H_{12}N_4O_3$ | 3.75 (s, 3 H, $CH_3N$); 4.43 (s, 1 H, CH of pyran); 7.30 (s, 1 H, CH of pyrazole); 7.32 (s, 2 H, $NH_2$); 7.47 (m, 2 H, $CH_{Ar}$); 7.58 (s, 1 H, CH of pyrazole); 7.70, 7.86 (both m, each 1 H, $CH_{Ar}$) | 3419, 3307, 3281, 3249, 3121, 3111, 2875, 2195 (CN), 1711, 1678, 1644, 1602, 1533, 1497, 1456, 1405, 1373, 1302 | 308 (6700), 285 (8000), 245 (12500), 213 (25600), 203 (32000) |
| **19b** | 65.43<br>65.51 | 4.66<br>4.63 | 15.99<br>16.08 | $C_{19}H_{16}N_4O_3$ | 1.93, 2.13 (both s, each 3 H, $CH_3$); 3.59 (s, 3 H, $CH_3N$); 4.39 (s, 1 H, CH of pyran); 7.25 (s, 2 H, $NH_2$); 7.45 (m, 2 H, $CH_{Ar}$); 7.68, 7.87 (both m, each 1 H, $CH_{Ar}$) | 3412, 3298, 3155, 2962, 3121, 3111, 2875, 2188 (CN), 1699, 1677, 1647, 1610, 1563, 1495, 1458, 1438, 1374, 1326, 1305 | 307 (11800), 278 (11700), 246 (22600), 211 (42500), 205 (47400) |
| **19c** | 66.97<br>67.01 | 5.35<br>5.36 | 14.81<br>14.88 | $C_{18}H_{14}N_4O_3$ | 1.30 (t, 3 H, $CH_3$, *J* = 7.2); 4.03 (q, 2 H, $CH_3C\underline{H}_2N$, *J* = 7.2); 4.42 (s, 1 H, CH of pyran); 7.31 (br.s, 3 H, CH of pyrazole, $NH_2$); 7.48 (m, 2 H, $CH_{Ar}$); 7.61 (s, 1 H, CH of pyrazole); 7.69, 7.85 (both m, each 1 H, $CH_{Ar}$) | 3354, 3311, 3265, 3143, 3109, 2978, 2942, 2198 (CN), 1724, 1672, 1648, 1609, 1555, 1494, 1456, 1395, 1375, 1352, 1328, 1306 | 307 (10700), 283 (12000), 245 (18700), 213 (38100), 205 (46100) |
| **19d** | 65.47<br>65.51 | 4.75<br>4.63 | 16.22<br>16.08 | $C_{19}H_{16}N_4O_3$ | 1.29 (d, 6 H, $(C\underline{H}_3)_2CH$, *J* = 5.9); 1.92, 2.15 (both s, each 3 H, $CH_3$); 3.44 (m, 1 H, $(CH_3)_2C\underline{H}N$); 4.41 (s, 1 H, CH of pyran); 7.26 (br.s, 2 H, $NH_2$); 7.47 (m, 1 H, $CH_{Ar}$); 7.70 (m, 2 H, $CH_{Ar}$); 7.89 (d, 1 H, $CH_{Ar}$, *J* = 7.0) | 3565, 3360, 3144, 3114, 2962, 2979, 2949, 2934, 2656, 2192 (CN), 1728, 1712, 1671, 1642, 1610, 1557, 1494, 1455, 1437, 1374, 1326, 1310 | 308 (10100), 277 (10600), 245 (17600), 213 (39300), 203 (45000) |
| **20a** | 63.19<br>64.27 | 5.24<br>5.14 | 14.17<br>14.28 | $C_{21}H_{24}N_4O_2S$ | 1.33 (d, 6 H, $(C\underline{H}_3)_2CH$, *J* = 5.9); 1.92, 2.15 (both s, each 3 H, $CH_3$); 4.38 (m, 1 H, $(CH_3)_2C\underline{H}N$, 4.56 (s, 1 H, CH of pyran); 7.26 (br.s, 2 H, $NH_2$); 7.62 (m, 1 H, $CH_{Ar}$); 7.70 (m, 2 H, $CH_{Ar}$); 8.37 (d, 1 H, $CH_{Ar}$, *J* = 7.3) | 3463, 3250, 3070, 2985, 2938, 2832, 2194 (CN), 1677, 1631, 1590, 1554, 1489, 1475, 1435, 1397, 1349, 1310 | 330 (6300), 300 (10200), 260 (12600), 255 (15700), 236 (50600) |

(*to be continued*)

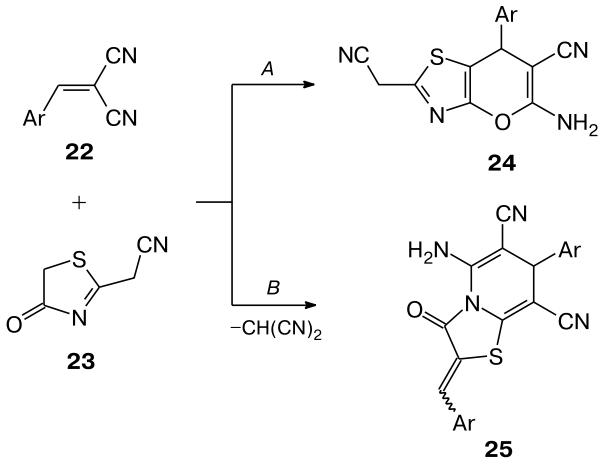
**Table 5** (*continued*)

| Compound | Found / Calculated (%) | | | Molecular formula | $^1$H NMR (DMSO-$d_6$), δ (*J*/Hz) | IR, ν/cm$^{-1}$ | UV-Vis, $\lambda_{max}$/nm (ε) |
|---|---|---|---|---|---|---|---|
| | C | H | N | | | | |
| **20b** | 60.59<br>60.70 | 3.71<br>3.60 | 16.49<br>16.66 | $C_{17}H_{12}N_4O_2S$ | 3.73 (s, 3 H, $CH_3N$); 4.59 (s, 1 H, CH of pyran); 7.22 (s, 1 H, CH of pyrazole); 7.38 (s, 2 H, $NH_2$); 7.50 (s, 1 H, CH of pyrazole); 7.60 (m, 1 H, $CH_{Ar}$); 7.69 (m, 2 H, $CH_{Ar}$); 8.34 (d, 1 H, $CH_{Ar}$, *J* = 7.3) | 3396, 3315, 3273, 3198, 3110, 2940, 2197 (CN), 1670, 1625, 1608, 1587, 1483, 1436, 1405, 1360, 1309 | 330 (5300), 300 (6700), 260 (9400), 255 (10700), 236 (51100) |
| **20c** | 62.55<br>62.62 | 4.48<br>4.43 | 15.51<br>15.37 | $C_{19}H_{16}N_4O_2S$ | 1.90, 2.11 (both s, each 3 H, $CH_3$); 3.58 (s, 3 H, $CH_3N$); 4.53 (s, 1 H, CH of pyran); 7.27 (br.s, 2 H, $NH_2$); 7.61 (m, 1 H, $CH_{Ar}$); 7.69 (m, 2 H, $CH_{Ar}$); 8.36 (d, 1 H, $CH_{Ar}$, *J* = 7.3) | 3301, 3124, 3070, 2980, 2946, 2919, 2196 (CN), 1672, 1623, 1603, 1558, 1554, 1510, 1479, 1432, 1421, 1396, 1353, 1300 | 330 (6600), 300 (12300), 260 (14600), 255 (19300), 236 (62600) |
| **20d** | 61.62<br>61.70 | 4.08<br>4.03 | 15.89<br>15.99 | $C_{18}H_{14}N_4O_2S$ | 1.29 (t, 3 H, $CH_3$, *J* = 7.2); 4.02 (q, 2 H, $CH_3C\underline{H}_2N$, *J* = 7.2); 4.59 (s, 1 H, CH of pyran); 7.23 (s, 1 H, CH of pyrazole); 7.39 (br.s, 2 H, $NH_2$); 7.53 (s, 1 H, CH of pyrazole); 7.60 (m, 1 H, $CH_{Ar}$); 7.69 (m, 2 H, $CH_{Ar}$); 8.34 (d, 1 H, $CH_{Ar}$, *J* = 7.3) | 3395, 3316, 3273, 3223, 3201, 3069, 2977, 2198 (CN), 1670, 1624, 1610, 1589, 1553, 1483, 1433, 1408, 1358, 1309 | 330 (6300), 300 (11900), 260 (14000), 255 (19600), 236 (33700) |
| **21a** | 63.93<br>63.94 | 4.15<br>4.10 | 21.87<br>21.93 | $C_{17}H_{13}N_5O_2$ | 3.74 (s, 3 H, $CH_3N$); 4.48 (s, 1 H, CH of pyran); 7.19 (s, 1 H, CH of pyrazole); 7.25 (s, 2 H, $NH_2$); 7.34 (m, 2 H, $CH_{Ar}$); 7.49 (s, 1 H, CH of pyrazole); 7.56 (m, 1 H, $CH_{Ar}$); 7.86 (d, 1 H, $CH_{Ar}$, *J* = 6.6); 11.78 (s, 1 H, NH) | 3353, 3284, 3131, 3075, 3028, 2967, 2912, 2867, 2748, 2183 (CN), 1679 (CO, amide band I), 1652 (NH, amide band II), 1630, 1608, 1584, 1562, 1500, 1489, 1437, 1414, 1401, 1380, 1323, 1294 | 336 (6400), 322 (8300), 310 (6400), 272 (6400), 243 (19200), 228 (53640), 215 (44700), 202 (26800) |
| **21b** | 67.09<br>67.18 | 5.73<br>5.64 | 18.58<br>18.65 | $C_{21}H_{21}N_5O_2$ | 1.28 (d, 6 H, $(C\underline{H}_3)_2CH$, *J* = 5.8); 1.93, 2.16 (both s, each 3 H, $CH_3$); 3.44 (m, 1 H, $(CH_3)_2C\underline{H}N$); 4.44 (s, 1 H, CH of pyran); 7.07 (s, 2 H, $NH_2$); 7.29 (m, 2 H, $CH_{Ar}$); 7.56, 7.89 (both m, each 1 H, $CH_{Ar}$); 11.62 (s, 1 H, NH) | 3507, 3355, 3176, 3075, 3020, 2973, 2930, 2899, 2867, 2197 (CN), 1677 (CO, amide band I), 1651 (NH, amide band II), 1630, 1606, 1581, 1558, 1503, 1488, 1434, 1382, 1352, 1327, 1309 | 336 (5300), 322 (7100), 310 (5600), 272 (7500), 243 (16900), 228 (47300), 215 (37500), 202 (27300) |
| **21c** | 64.67<br>64.86 | 4.63<br>4.54 | 20.89<br>21.01 | $C_{18}H_{15}N_5O_2$ | 1.29 (t, 3 H, $CH_3$, *J* = 7.2); 4.02 (q, 2 H, $CH_3C\underline{H}_2N$, *J* = 7.2); 4.48 (s, 1 H, CH of pyran); 7.19 (s, 1 H, CH of pyrazole); 7.26 (s, 2 H, $NH_2$); 7.31 (m, 2 H, $CH_{Ar}$); 7.51 (s, 1 H, CH of pyrazole); 7.55, 7.85 (both m, each 1 H, $CH_{Ar}$); 11.78 (s, 1 H, NH) | 3322, 3290, 3204, 3146, 2990, 2981, 2952, 2906, 2893, 2735, 2190 (CN), 1689, 1669 (CO, amide band I), 1658 (NH, amide band II), 1632, 1601, 1557, 1501, 1469, 1431, 1413, 1382, 1319 | 336 (4700), 322 (6000), 310 (4800), 272 (2900), 243 (14700), 228 (40700), 215 (36000), 202 (24000) |
| **21d** | 65.48<br>65.69 | 5.07<br>4.93 | 20.09<br>20.16 | $C_{19}H_{17}N_5O_2$ | 1.28 (d, 6 H, $(C\underline{H}_3)_2CH$, *J* = 5.8); 1.93, 2.16 (both s, each 3 H, $CH_3$); 3.44 (m, 1 H, $(CH_3)_2C\underline{H}N$); 4.44 (s, 1 H, CH of pyran); 7.07 (br.s, 2 H, $NH_2$); 7.30 (m, 2 H, $CH_{Ar}$); 7.56, 7.88 (both m, each 1 H, $CH_{Ar}$); 11.62 (s, 1 H, NH) | 3333, 3289, 3185, 3123, 3072, 2979, 2953, 2919, 2735, 2194 (CN), 1682, 1672 (CO, amide band I), 1648 (NH, amide band II), 1635, 1601, 1582, 1554, 1498, 1430, 1408, 1378, 1348, 1325 | 336 (6950), 322 (10400), 310 (8300), 272 (10500), 243 (24300), 228 (63900), 215 (55600), 202 (27800) |

The yields of pyrans **11**, **13**, **15**, and **19**—**21** range from moderate (25—45%) for phenols and pyrazolones to high (60—80%) for coumarin and its heteroanalogs. This scatter is probably associated with the reversibility of the Thorpe—Ziegler and Michael reactions.

Earlier, ambiguous results have been obtained in reactions of aryl(hetaryl)idenemalononitriles **22** with 2-(4-oxo-4,5-dihydro-1,3-thiazol-2-yl)acetonitrile (**23**) containing two active methylene groups. These reactions reportedly yield either 5-amino-7-aryl-6-cyano-2-cyanomethyl-7*H*-pyrano[2,3-*d*]thiazoles **24** (see Ref. 33) or the corresponding 2,3-dihydro-3-oxo-7*H*-[1,3]thiazolo[3,2-*a*]pyridines **25** (Scheme 3).[46—49]

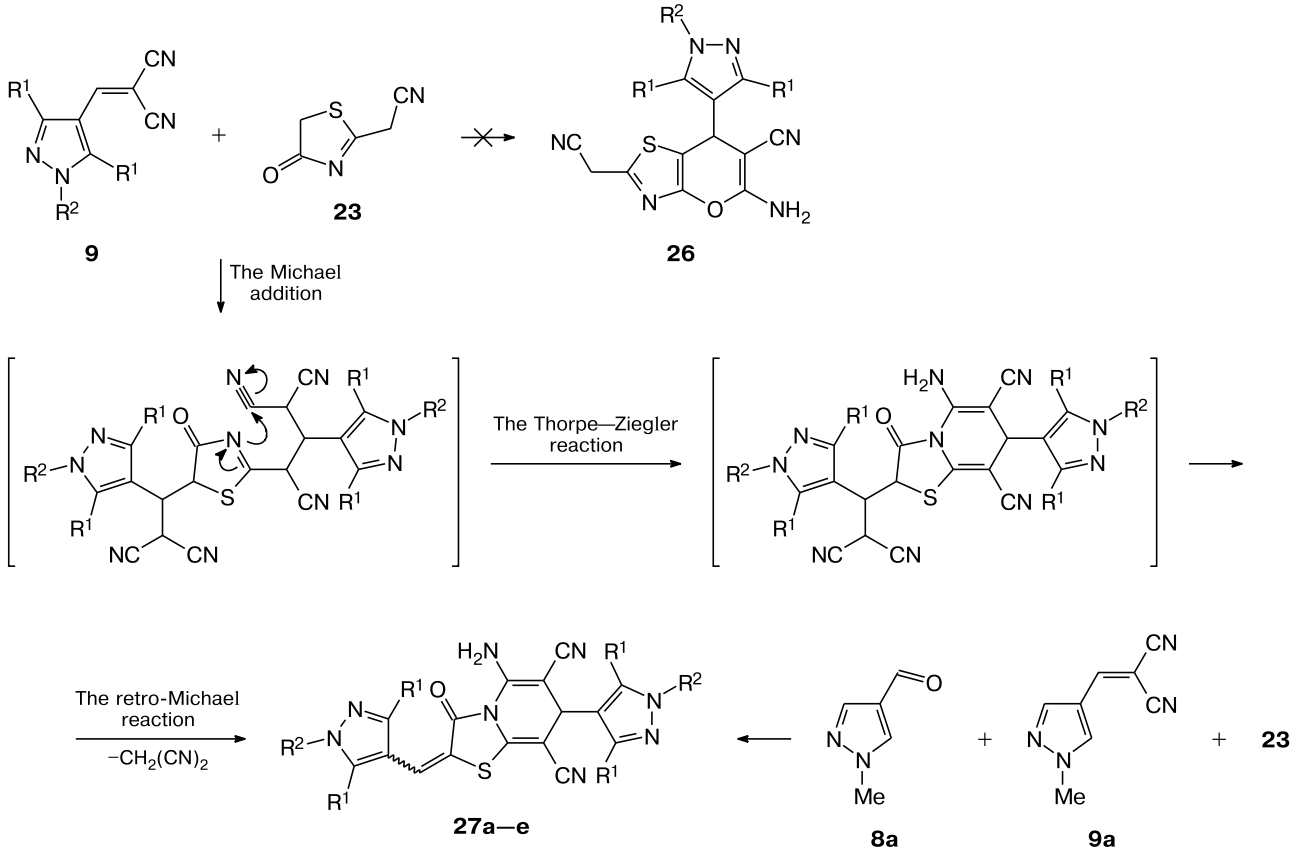
**Scheme 3**




For this reason, we found it interesting to study reactions of pyrazolylmethylidenemalononitriles **9** with thiazolone **23**. Compounds **9** react with cyanomethylthiazolone **23** in EtOH in the presence of $Et_3N$ to give colored (from lemon yellow to orange) products in low yields. The highest yields were achieved when two equivalents of compound **9** were used. This suggests that the reaction follows pathway *B* (see Scheme 3) leading to thiazolopyridines **27** rather than pyranothiazoles **26** (Scheme 4). One can assume that the formation of compounds **27** involves the following pattern of a "domino" reaction: Michael addition → Thorpe—Ziegler reaction → retro-Michael reaction. The possible sequence of the last two reactions remains a subject of debate.

To optimize the synthetic procedure, we carried out a three-component reaction between equimolar amounts of aldehyde **8a**, *N*-methylpyrazolylmethylidenemalononitrile **9a**, and thiazolone **23**. Thiazolopyridine **27c** was obtained in good yield. This reaction also follows the "domi-

**Scheme 4**




**27**: $R^1$ = H, $R^2$ = Et (**a**); $R^1$ = $R^2$ = Me (**b**); $R^1$ = H, $R^2$ = Me (**c**); $R^1$ = H, $R^2$ = $Pr^i$ (**d**); $R^1$ = H, $R^2$ = All (**e**)

no" pattern: Michael addition → Thorpe—Ziegler reaction → Knoevenagel condensation (see Scheme 4).

Structures **27** were confirmed by spectroscopic data. The $^1$H NMR spectra show signals for the protons of two pyrazole fragments, a signal at δ 7.6—7.9 for the proton at the exocyclic double bond, and no signal for the methylene group (Table 6). The presence of absorption bands at 2212 and 2188—2200 cm$^{-1}$ in the IR spectra indicates the conjugation of the nitrile groups.[32,50] This is evidence in favor of structure **27** and so is the presence of strong absorption bands at 1648—1662 cm$^{-1}$ (C=O). Elemental analysis data correspond to the molecular formulas of compounds **27**. The high degree of conjugation in structures **27** accounts for their intense color. They strongly absorb at ~370 nm, which is near the visible region of the UV-Vis spectrum.

## Experimental

$^1$H NMR spectra were recorded on a Bruker AM-300 instrument in DMSO-$d_6$. IR spectra were recorded on a Bruker instrument (KBr pellets). UV-Vis spectra were recorded on a Specord M80-2 instrument in MeOH. Melting points were measured on a Kofler hot stage and are given uncorrected.

1-Alkylpyrazoles **7** used in the synthesis of 1-alkyl-1*H*-pyrazole-4-carbaldehydes **8a**—**c** were prepared according to known procedures.[44,51,52] 1-Methylpyrazole (**7a**),[51] b.p. 126 °C; 1,3,5-trimethylpyrazole (**7b**),[52] b.p. 171 °C; 1-ethylpyrazole (**7c**), b.p. 137—138 °C (*cf.* Ref. 44: b.p. 126 °C). Pyrazole, 3,5-dimethylpyrazole, malononitrile, phenols **10**, dimedone, cyclohexane-1,3-dione, pyrazolones **14**, 4-hydroxycoumarin (**16**), and 4-hydroxyquinolin-2-one (**18**) were commercial chemicals (Acros). 4-Hydroxythiocoumarin (**17**) (m.p. 154 °C) and 2-(4-oxo-4,5-dihydro-1,3-thiazol-2-yl)acetonitrile (**23**) were synthesized as described earlier.[53,54] Commercial DMF for the Vilsmeier reaction was kept over $CaH_2$ (2 g per 100 mL) for at least 24 h and distilled *in vacuo* immediately before use. Other solvents were purified simply by distillation.

**Synthesis of 1-alkyl-1*H*-pyrazole-4-carbaldehydes 8a—f (general procedure). Method *A*.** A 500-mL four-neck flask equipped with a mercury-sealed mechanical stirrer, a thermometer, a dropping funnel, a gas inlet, and a reflux condenser capped with a calcium chloride tube was purged two times with dry argon and charged with a mixture of an appropriate *N*-alkylpyrazole (1 mol) and freshly distilled dry DMF (1.15 mol). The flask was cooled on a bath filled with a mixture of ice and NaCl. Freshly distilled $POCl_3$ (1.15 mol) was added dropwise under argon at 0 °C to the stirred mixture. The addition rate was such as to prevent the temperature from rising above 20 °C. After the addition of $POCl_3$ was completed, the cooling bath was removed. The reaction mixture was stirred at room temperature for 1 h, turning dark red. Then the reaction mixture was stirred for 18 h on a boiling water bath, turning brown. On cooling, the resulting thick mixture was poured with stirring into a 2-L beaker filled

**Table 6.** Elemental analysis data and $^1$H NMR, IR, and UV-Vis spectra of 7*H*-thiazolo[3,2-*a*]pyridines **27a**—**e**

| Compound | Found / Calculated (%) C | H | N | Molecular formula | $^1$H NMR (DMSO-$d_6$), δ (*J*/Hz) | IR, ν/cm$^{-1}$ | UV-Vis, $\lambda_{max}$/nm (ε) |
|---|---|---|---|---|---|---|---|
| **27a** | 57.29<br>57.40 | 4.45<br>4.34 | 26.53<br>26.78 | $C_{20}H_{18}N_8OS$ | 1.38 (m, 6 H, $C\underline{H}_3CH_2$); 4.12, 4.24 (both q, each 2 H, $CH_3C\underline{H}_2$, *J* = 6.4); 4.54 (s, 1 H, CH of pyridine); 7.38 (s, 2 H, $NH_2$); 7.44 (s, 1 H, CH of pyrazole); 7.76 (s, 2 H, CH of pyrazole); 7.86 (s, 1 H, CH of pyrazole); 8.28 (s, 1 H, CH) | 3400 ($NH_2$), 2212 (CN), 2196 (CN), 1700, 1652 (CO), 1612, 1568 | 368 (20900), 297 (14600), 274 (17600), 221 (33400) |
| **27b** | 59.12<br>59.18 | 5.03<br>4.97 | 24.87<br>25.09 | $C_{22}H_{22}N_8OS$ | 2.02, 2.16, 2.19, 2.28 (all s, each 3 H, $CH_3$); 3.64, 3.70 (both s, each 3 H, $NCH_3$); 4.58 (s, 1 H, CH of pyridine); 7.46 (s, 2 H, $NH_2$); 7.63 (s, 1 H, CH) | 3440 ($NH_2$), 2212 (CN), 2188 (CN), 1692, 1648 (CO), 1604, 1548 | 371 (27300), 284 (19600), 221 (25000) |
| **27c** | 55.29<br>55.37 | 3.68<br>3.61 | 28.59<br>28.70 | $C_{18}H_{48}N_8OS$ | 3.83, 3.94 (both s, each 3 H, $NCH_3$); 4.53 (s, 1 H, CH of pyridine); 7.39 (s, 2 H, $NH_2$); 7.44, 7.71, 7.76, 7.85 (all s, each 1 H, CH of pyrazole); 8.25 (s, 1 H, CH) | 3384 ($NH_2$), 2212 (CN), 2200 (CN), 1700, 1662 (CO), 1608, 1540 | 367 (20500), 299 (10800), 277 (122000), 221 (16600) |
| **27d** | 59.05<br>59.18 | 5.08<br>4.97 | 24.93<br>25.09 | $C_{22}H_{22}N_8OS$ | 1.40 (m, 12 H, $CH(C\underline{H}_3)_2$); 4.23 (q, 1 H, $NC\underline{H}(CH_3)_2$, *J* = 6.4); 4.53 (s, 1 H, CH of pyridine); 4.65 (q, 1 H, $NC\underline{H}(CH_3)_2$, *J* = 6.4); 7.44 (m, 3 H, $NH_2$, CH of pyrazole); 7.78, 7.87, 7.85 (all s, each 1 H, CH of pyrazole); 8.29 (s, 1 H, CH) | 3452 ($NH_2$), 2208 (CN), 2192 (CN), 1708, 1652 (CO), 1608, 1540 | 369 (316000), 300 (14700), 278 (16400), 230 (22200) |
| **27e** | 59.64<br>59.71 | 4.15<br>4.10 | 25.22<br>25.32 | $C_{22}H_{18}N_8OS$ | 4.57 (s, 1 H, CH of pyridine); 4.75 (d, 2 H, $NC\underline{H}_2CH{=}CH_2$, *J* = 3.0); 4.88 (d, 2 H, $NC\underline{H}_2CH{=}CH_2$, *J* = 3.0); 5.00—5.30 (m, 5 H, CH of pyridine, $CH_2CH{=}C\underline{H}_2$); 6.00 (m, 2 H, $CH_2C\underline{H}{=}CH_2$); 7.45 (s, 2 H, $NH_2$); 7.49, 7.75, 7.78, 7.91 (all s, each 1 H, CH of pyrazole); 8.29 (s, 1 H, CH) | 3420 ($NH_2$), 2212 (CN), 2196 (CN), 1700, 1648 (CO), 1612, 1564 | 367 (22100), 303 (8400), 278 (9700), 231 (14200) |

with crushed ice (1 kg) (in some experiments, the mixture became too thick to be poured out, and its liquefaction by heating was required). After the ice melted roughly by half, solid-state KOH was added in small portions with stirring to pH ~9 (to avoid a temperature rise above 60 °C, some ice was added to the mixture). On cooling to 35—40 °C, the product was extracted with $CHCl_3$ (6×100 mL). The extract was dried with anhydrous $Na_2SO_4$ and concentrated on a rotary evaporator. The residue was either distilled *in vacuo* or recrystallized from ethanol.

**1-Methyl-1*H*-pyrazole-4-carbaldehyde (8a).** Yield 40%, a yellowish liquid solidifying in storage, b.p. 90—92 °C (10 Torr) (*cf.* Ref. 43: b.p. 106—108 °C (20 Torr)), m.p. 28 °C (*cf.* Ref. 55: m.p. 30 °C).

**1,3,5-Trimethyl-1*H*-pyrazole-4-carbaldehyde (8b).** Yield 86%, colorless crystals, m.p. 81 °C (EtOH) (*cf.* Ref. 45: m.p. 79 °C), b.p. 136—138 °C (8 Torr) (*cf.* Ref. 45: b.p. 132 °C (12 Torr)).

**1-Ethyl-1*H*-pyrazole-4-carbaldehyde (8c).** Yield 58%, yellowish liquid, b.p. 96—98 °C (7 Torr) (*cf.* Ref. 44: b.p. 46—48 °C (5 Torr)), $n_D^{20}$ 1.5179 (*cf.* Ref. 44: $n_D^{20}$ 1.5183).

The spectra and elemental analysis data for compounds **8a—c** are given in Table 1.

**Method *B*.** In contrast to method ***A***, intermediate *N*-alkylpyrazoles were not isolated in the individual state. A 500-mL round-bottomed three-neck flask equipped with a mercury-sealed mechanical stirrer, a reflux condenser, and a thermometer was charged with pyrazole or 2,5-dimethylpyrazole (1 mol), calcined $K_2CO_3$ (1 mol), DMF (150 mL), and an appropriate alkyl halide ($Pr^iI$ or AllBr, 1.2 mol). The reaction mixture was heated to 80 °C with stirring and kept quiet at this temperature for 24 h. On cooling, the reaction mixture was diluted with $CH_2Cl_2$ (250 mL) and filtered. The filter cake was washed with $CH_2Cl_2$ (150 mL). The combined filtrates were fractionated on a heated Vigreux column ($h$ = 70 cm), while collecting a fraction with b.p. <100 °C at atmospheric pressure. Then the still bottoms were evaporated almost to dryness under reduced pressure (100—150 Torr) to collect a fraction with b.p. >100 °C (with reference to 760 Torr). This fraction consisting of *N*-alkylpyrazole and DMF was further treated with $POCl_3$ (1.15 mol) as described in method ***A***.

**1-Isopropyl-1*H*-pyrazole-4-carbaldehyde (8d).** Yield 65%, a colorless liquid with a keen pyridine odor, b.p. 100—102 °C (7 Torr), $n_D^{20}$ 1.5165.

**1-Isopropyl-3,5-dimethyl-1*H*-pyrazole-4-carbaldehyde (8e).** Yield 87%, colorless crystals, m.p. 115 °C (EtOH).

**1-Allyl-1*H*-pyrazole-4-carbaldehyde (8f).** Yield 61%, a colorless liquid with a keen pyridine odor, b.p. 106—107 °C (5 Torr), $n_D^{20}$ 1.5298.

**1-Allyl-3,5-dimethyl-1*H*-pyrazole-4-carbaldehyde (8g).** Yield 55%, yellowish viscous liquid, b.p. 138—139 °C (6 Torr), $n_D^{20}$ 1.5293.

The spectra and elemental analysis data for compounds **8d—g** are given in Table 1.

**Synthesis of *N*-alkylpyrazolylmethylidenemalononitriles 9a—g (general procedure).** Triethylamine (1 mL) was added to a solution of an appropriate 1-alkylpyrazole-4-carbaldehyde (0.1 mol) and malononitrile (0.1 mol) in EtOH (100 mL). The reaction mixture was refluxed for 30 min, cooled, diluted with water (100 mL), and left at 0 °C for 8 h. The precipitate that formed was filtered off, washed on the filter with water, cold (0 °C) 50% aqueous EtOH (20 mL), and hexane, and dried in a desiccator over $P_2O_5$. In most cases, the compounds obtained were analytically pure. When needed, they were recrystallized from a small amount of EtOH.

**2-[(1-Methyl-1*H*-pyrazol-4-yl)methylidene]malononitrile (9a).** Yield 87%, colorless crystals, m.p. 136 °C (EtOH).

**2-[(1,3,5-Trimethyl-1*H*-pyrazol-4-yl)methylidene]malononitrile (9b).** Yield 83%, colorless crystals, m.p. 112 °C (EtOH).

**2-[(1-Ethyl-1*H*-pyrazol-4-yl)methylidene]malononitrile (9c).** Yield 58%, colorless crystals, m.p. 92 °C (EtOH).

**2-[(1-Isopropyl-1*H*-pyrazol-4-yl)methylidene]malononitrile (9d).** Yield 75%, colorless crystals, m.p. 73 °C (EtOH).

**2-[(1-Isopropyl-3,5-dimethyl-1*H*-pyrazol-4-yl)methylidene]-malononitrile (9e).** Yield 77%, colorless crystals, m.p. 115 °C (EtOH).

**2-[(1-Allyl-1*H*-pyrazol-4-yl)methylidene]malononitrile (9f).** Yield 81%, colorless crystals, m.p. 90 °C (EtOH).

**2-[(1-Allyl-3,5-dimethyl-1*H*-pyrazol-4-yl)methylidene]malononitrile (9g).** Yield 85%, colorless crystals, m.p. 52 °C (EtOH).

The spectra and elemental analysis data for compounds **9a—g** are given in Table 2.

**Synthesis of 2-amino-3-cyano-4-pyrazolyl-4*H*-chromenes 11a—i, 2-amino-3-cyano-4-pyrazolyl-5,6,7,8-tetrahydro-4*H*-chromenes 13a—c, 6-amino-5-cyano-4-pyrazolyl-1,4-dihydropyranopyrazoles 15a—h, 2-amino-3-cyano-5-oxo-4-(1*H*-pyrazolyl)-4*H*,5*H*-pyranochromenes 19a—d, and 2-amino-3-cyano-5-oxo-4-(1*H*-pyrazolyl)-4*H*,5*H*-thiochromeno[4,3-*b*]pyrans 20a—d (general procedure).** A mixture of *N*-alkylpyrazolylmethylidenemalononitrile **9** (1 mmol), a carbonyl compound (or *meta*-substituted phenol) (1.1 mmol), and $Et_3N$ (2—3 drops) was refluxed in EtOH (10 mL) for 1 h. On cooling, the reaction mixture was diluted with water (10 mL) and left at 0 °C for 8 h. The precipitate that formed was filtered off, washed with cold (0 °C) ethanol and hexane, and dried in air. In most cases, the compounds obtained were analytically pure. When needed, they were recrystallized from a small amount of ethanol.

**2-Amino-7-hydroxy-4-(1-isopropyl-1*H*-pyrazol-4-yl)-4*H*-chromene-3-carbonitrile (11a).** Yield 57%, colorless powder, m.p. 169 °C.

**2,7-Diamino-4-(1-isopropyl-1*H*-pyrazol-4-yl)-4*H*-chromene-3-carbonitrile (11b).** Yield 53%, yellow powder, m.p. 198 °C.

**2-Amino-7-dimethylamino-4-(1-isopropyl-1*H*-pyrazol-4-yl)-4*H*-chromene-3-carbonitrile (11c).** Yield 38%, brown powder, m.p. 202 °C (EtOH).

**2-Amino-4-(1-ethyl-1*H*-pyrazol-4-yl)-7-hydroxy-4*H*-chromene-3-carbonitrile (11d).** Yield 55%, colorless powder, m.p. 232 °C.

**2,7-Diamino-4-(1-ethyl-1*H*-pyrazol-4-yl)-4*H*-chromene-3-carbonitrile (11e).** Yield 47%, yellow powder, m.p. 179 °C.

**2-Amino-7-diethylamino-4-(1-ethyl-1*H*-pyrazol-4-yl)-4*H*-chromene-3-carbonitrile (11f).** Yield 41%, brown powder, m.p. 148 °C (EtOH).

**2-Amino-7-dimethylamino-4-(1-methyl-1*H*-pyrazol-4-yl)-4*H*-chromene-3-carbonitrile (11g).** Yield 35%, brown powder, m.p. 208 °C (EtOH).

**2,7-Diamino-4-(1-methyl-1*H*-pyrazol-4-yl)-4*H*-chromene-3-carbonitrile (11h).** Yield 49%, yellow powder, m.p. 142 °C.

**2-Amino-7-hydroxy-4-(1-methyl-1*H*-pyrazol-4-yl)-4*H*-chromene-3-carbonitrile (11i).** Yield 45%, colorless powder, m.p. 253 °C (EtOH).

The spectra and elemental analysis data for compounds **11a—i** are given in Table 3.

**4-(1-Allyl-1*H*-pyrazol-4-yl)-2-amino-7,7-dimethyl-5,6,7,8-tetrahydro-4*H*-chromene-3-carbonitrile (13a).** Yield 51%, colorless powder, m.p. 94 °C.

**2-Amino-4-(1-ethyl-1*H*-pyrazol-4-yl)-7,7-dimethyl-5,6,7,8-tetrahydro-4*H*-chromene-3-carbonitrile (13b).** Yield 65%, colorless powder, m.p. 158 °C.

**2-Amino-4-(1-ethyl-1*H*-pyrazol-4-yl)-5,6,7,8-tetrahydro-4*H*-chromene-3-carbonitrile (13c).** Yield 58%, colorless powder, m.p. 157 °C (EtOH).

The spectra and elemental analysis data for compounds **13a—c** are given in Table 3.

**6-Amino-3-isopropyl-4-(1-isopropyl-3,5-dimethyl-1*H*-pyrazol-4-yl)-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (15a).** Yield 57%, colorless powder, m.p. 242 °C.

**6-Amino-4-(1-isopropyl-3,5-dimethyl-1*H*-pyrazol-4-yl)-3-phenyl-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (15b).** Yield 63%, colorless powder, m.p. 156 °C.

**6-Amino-4-(1-isopropyl-3,5-dimethyl-1*H*-pyrazol-4-yl)-3-methyl-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (15c).** Yield 58%, colorless powder, m.p. 154 °C.

**4-(1-Allyl-3,5-dimethyl-1*H*-pyrazol-4-yl)-6-amino-3-methyl-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (15d).** Yield 45%, colorless powder, m.p. 158 °C.

**4-(1-Allyl-1*H*-pyrazol-4-yl)-6-amino-3-*tert*-butyl-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (15e).** Yield 47%, colorless powder, m.p. 206 °C.

**6-Amino-3-isopropyl-4-(1,3,5-trimethyl-1*H*-pyrazol-4-yl)-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (15f).** Yield 51%, colorless powder, m.p. 145 °C (EtOH).

**6-Amino-3-ethyl-4-(1,3,5-trimethyl-1*H*-pyrazol-4-yl)-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (15g).** Yield 60%, colorless powder, m.p. 256 °C.

**6-Amino-3-*tert*-butyl-4-(1-isopropyl-1*H*-pyrazol-4-yl)-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (15h).** Yield 55%, colorless powder, m.p. 226 °C.

The spectra and elemental analysis data for compounds **15a—h** are given in Table 4.

**2-Amino-4-(1-methyl-1*H*-pyrazol-4-yl)-5-oxo-4*H*,5*H*-pyrano[3,2-*c*]chromene-3-carbonitrile (19a).** Yield 87%, colorless powder, m.p. 235 °C.

**2-Amino-5-oxo-4-(1,3,5-trimethyl-1*H*-pyrazol-4-yl)-4*H*,5*H*-pyrano[3,2-*c*]chromene-3-carbonitrile (19b).** Yield 83%, colorless powder, m.p. 256 °C (EtOH).

**2-Amino-4-(1-ethyl-1*H*-pyrazol-4-yl)-5-oxo-4*H*,5*H*-pyrano[3,2-*c*]chromene-3-carbonitrile (19c).** Yield 68%, colorless powder, m.p. 225 °C.

**2-Amino-4-(1-isopropyl-3,5-dimethyl-1*H*-pyrazol-4-yl)-5-oxo-4*H*,5*H*-pyrano[3,2-*c*]chromene-3-carbonitrile (19d).** Yield 75%, colorless powder, m.p. 246 °C (EtOH).

**2-Amino-4-(1-isopropyl-3,5-dimethyl-1*H*-pyrazol-4-yl)-5-oxo-4*H*,5*H*-thiochromeno[4,3-*b*]pyran-3-carbonitrile (20a).** Yield 77%, colorless powder, m.p. 252 °C (EtOH).

**2-Amino-4-(1-methyl-1*H*-pyrazol-4-yl)-5-oxo-4*H*,5*H*-thiochromeno[4,3-*b*]pyran-3-carbonitrile (20b).** Yield 81%, faintly colored bright leaflets, m.p. 260 °C (EtOH).

**2-Amino-5-oxo-4-(1,3,5-trimethyl-1*H*-pyrazol-4-yl)-4*H*,5*H*-thiochromeno[4,3-*b*]pyran-3-carbonitrile (20c).** Yield 85%, colorless powder, m.p. 237 °C.

**2-Amino-4-(1-ethyl-1*H*-pyrazol-4-yl)-5-oxo-4*H*,5*H*-thiochromeno[4,3-*b*]pyran-3-carbonitrile (20d).** Yield 80%, cream-colored powder, m.p. 216 °C.

**Synthesis of 2-amino-5-oxo-4-pyrazolyl-5,6-dihydro-4*H*-pyrano[3,2-*c*]quinoline-3-carbonitriles 21 (general procedure).** A mixture of *N*-alkylpyrazolylmethylidenemalononitrile **9** (1 mmol), 4-hydroxyquinolin-2-one (**18**) (1.1 mmol), and $Et_3N$ (2—3 drops) was refluxed in EtOH (10 mL) for 1 h. On cooling, the reaction mixture was stirred with 10% $NaHCO_3$ (1 mL) for 10 min, diluted with water (10 mL), and left at 0 °C for 8 h. The precipitate that formed was filtered off, washed with 10% $NaHCO_3$ (5 mL), ice water, cold (0 °C) EtOH, and hexane, and dried in air. In most cases, the compounds obtained were analytically pure. When needed, they were recrystallized from a small amount of ethanol.

**2-Amino-4-(1-methyl-1*H*-pyrazol-4-yl)-5-oxo-5,6-dihydro-4*H*-pyrano[3,2-*c*]quinoline-3-carbonitrile (21a).** Yield 85%, cream-colored powder, m.p. 247 °C (EtOH).

**2-Amino-4-(1-isopropyl-3,5-dimethyl-1*H*-pyrazol-4-yl)-5-oxo-5,6-dihydro-4*H*-pyrano[3,2-*c*]quinoline-3-carbonitrile (21b).** Yield 82%, colorless powder, m.p. 262 °C.

**2-Amino-4-(1-ethyl-1*H*-pyrazol-4-yl)-5-oxo-5,6-dihydro-4*H*-pyrano[3,2-*c*]quinoline-3-carbonitrile (21c).** Yield 79%, cream-colored powder, m.p. 265 °C.

**2-Amino-5-oxo-4-(1,3,5-trimethyl-1*H*-pyrazol-4-yl)-5,6-dihydro-4*H*-pyrano[3,2-*c*]quinoline-3-carbonitrile (21d).** Yield 86%, cream-colored powder, m.p. 330 °C.

The spectra and elemental analysis data for compounds **19—21** are given in Table 5.

**Synthesis of 2,3-dihydro-7*H*-thiazolo[3,2-*a*]pyridines 27a—c (general procedure).** ***A.*** 2-(4-Oxothiazol-2-yl)acetonitrile **23** (1 mmol) was added to a hot (60 °C) solution of appropriate *N*-alkylpyrazolylmethylidenemalononitrile **9** (2 mmol) in EtOH (10 mL). The reaction mixture was refluxed to complete homogenization. Then $Et_3N$ (2—3 drops) was added, and the reflux was continued for an additional 30 min. On cooling, the precipitate that formed was filtered off, washed with EtOH and hexane, and dried. In most cases, the compounds obtained were analytically pure. When needed, they were recrystallized from a small amount of EtOH. The spectra and elemental analysis data for compounds **27a—e** are given in Table 6.

**5-Amino-7-(1-ethyl-1*H*-pyrazol-4-yl)-2-[(1-ethyl-1*H*-pyrazol-4-yl)methylidene]-3-oxo-2,3-dihydro-7*H*-[1,3]thiazolo-[3,2-*a*]pyridine-6,8-dicarbonitrile (27a).** Yield 81%, yellow powder, m.p. 253 °C (decomp.).

**5-Amino-3-oxo-7-(1,3,5-trimethyl-1*H*-pyrazol-4-yl)-2-[(1,3,5-trimethyl-1*H*-pyrazol-4-yl)methylidene]-2,3-dihydro-7*H*-[1,3]thiazolo[3,2-*a*]pyridine-6,8-dicarbonitrile (27b).** Yield 81%, orange powder, m.p. 250 °C (decomp.).

**5-Amino-7-(1-methyl-1*H*-pyrazol-4-yl)-2-[(1-methyl-1*H*-pyrazol-4-yl)methylidene]-3-oxo-2,3-dihydro-7*H*-[1,3]thiazolo[3,2-*a*]pyridine-6,8-dicarbonitrile (27c).** Yield 76%, yellow powder, m.p. 260 °C (decomp.).

**5-Amino-7-(1-isopropyl-1*H*-pyrazol-4-yl)-2-[(1-isopropyl-1*H*-pyrazol-4-yl)methylidene]-3-oxo-2,3-dihydro-7*H*-[1,3]thiazolo[3,2-*a*]pyridine-6,8-dicarbonitrile (27d).** Yield 58%, yellow powder, m.p. 262—264 °C.

**7-(1-Allyl-1*H*-pyrazol-4-yl)-2-[(1-allyl-1*H*-pyrazol-4-yl)-methylidene]-5-amino-3-oxo-2,3-dihydro-7*H*-[1,3]thiazolo-[3,2-*a*]pyridine-6,8-dicarbonitrile (27e).** Yield 79%, orange powder, m.p. 266 °C.

***B.*** Triethylamine (2—3 drops) was added to a hot solution of compound **9a** (158 mg, 1 mmol), 4-formyl-1-methylpyrazole (**8a**) (110 mg, 1 mmol), and thiazolone **23** (140 mg, 1 mmol) in EtOH (10 mL). The reaction mixture was refluxed for 30 min. On cooling, the precipitate that formed was filtered off, washed with EtOH and hexane, and dried. The yield of compound **27c** was 320 mg (81%). The melting point and spectral characteristics of this sample are identical with those of compound **27c** obtained according to method ***A***.

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