

On the Reaction of 3-Cyanochromones with Phenyl- and Methylhydrazines: Structural Revision and a Simple Synthesis of Chromeno[4,3-*c*]pyrazol-4-Ones

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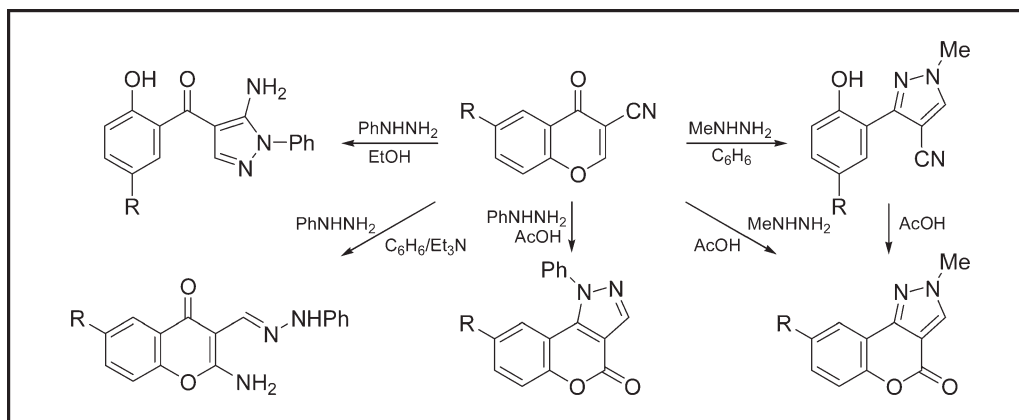
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Received October 1, 2009

DOI 10.1002/jhet.370

Published online 3 May 2010 in Wiley InterScience (www.interscience.wiley.com).



Reactions of 3-cyanochromones with phenylhydrazine gave the corresponding 5-amino-4-salicyloyl-1-phenylpyrazoles, 2-aminochromone-3-carbaldehyde *N*-phenylhydrazones, and 1-phenylchromeno[4,3-*c*]pyrazol-4(1*H*)-one, depending on the reaction conditions. With methylhydrazine, 3-(2-hydroxyaryl)-1-methylpyrazole-4-carbonitriles and 2-methylchromeno[4,3-*c*]pyrazol-4(2*H*)-ones were obtained in moderate to high yields.

J. Heterocyclic Chem., **47**, 629 (2010).

INTRODUCTION

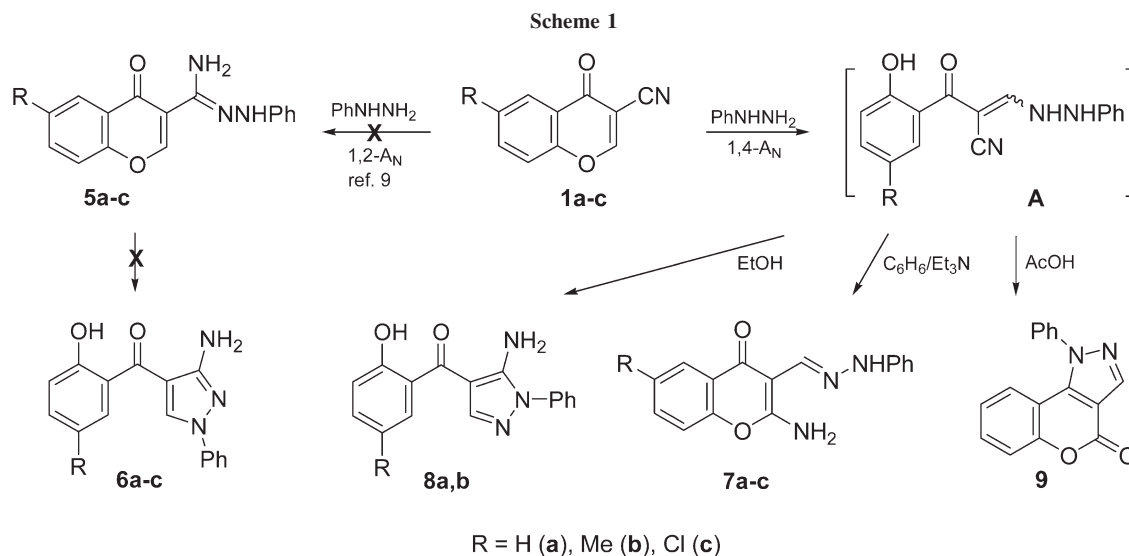
The chemistry of 3-cyanochromones has been developed since the mid-1970s after the simple and convenient Vilsmeier-Haack method was proposed for the synthesis of 3-formylchromones from 2-hydroxyacetophenones, DMF, and POC_l₃ [1]. Treatment of 3-formylchromones with hydroxylamine via 3-formylchromone-3-oximes leads to 3-cyanochromones **1** [2,3]. In addition, **1** can be synthesized directly from 2-hydroxyacetophenones and hydroxylamine under the Vilsmeier-Haack conditions [4] and from O-methylated chromone-3-oximes [5].

The introduction of the electron-withdrawing CN group at the 3-position of the chromone system changes crucially the reactivity of the pyrone ring with respect to nucleophiles, and provides a broad synthetic potential of 3-cyanochromones **1** [6]. The diversity of properties of these compounds is due to the fact that, being highly reactive geminally activated push-pull alkenes (α,β -unsaturated ketones and nitriles simultaneously) with a good leaving group at the β -carbon atom, whose role is played by the phenolate anion (a fragment of the enol

ether), they acquire the ability to undergo a nucleophilic 1,4-attack followed by additional transformations related to γ -pyrone ring opening and heterocyclizations at the C-4 atom and/or at the cyano group. However, although nucleophilic 1,4-addition occurs easily, which is clearly demonstrated by the transformation of 3-cyanochromones **1** into 2-amino-3-formylchromones under basic conditions [3,7], the reactions of **1** with dinucleophiles were further interpreted from both the viewpoint of 1,4-addition at the C-2 atom (this direction is equivalent to the 1,2-attack at the CHO group of 2-amino-3-formylchromone) and 1,2-addition to the cyano group, which inevitably led to contradictory results [6,8,9].

RESULTS AND DISCUSSION

Recently [10], we reported on the ring transformations of the chromones **1** to 2-aminochromone-3-carboxamide, 3-amino-4*H*-chromeno[3,4-*d*]isoxazol-4-one, and 3-(diaminomethylene)chroman-2,4-dione under the action of hydroxylamine in alkaline medium, some of which were previously incorrectly formulated [6]. Now we were



interested in the course of the reactions of 3-cyanochromones **1** with phenyl- and methylhydrazines. The reaction with phenylhydrazine has already been the subject of investigations and to the intermediate was assigned the structure **5** without NMR spectral data [9]. The authors believed that the reaction occurred via 1,2-addition of phenylhydrazine to the cyano group of **1a-c** to give amidohydrazone **5a-c**, which on prolonged refluxing in ethanol afforded 3-aminopyrazoles **6a-c** [6,9]. On the other hand, it was claimed that refluxing benzene induces the initial 1,4-addition of phenylhydrazine producing ultimately the phenylhydrazone derivatives **7** [8]. It should be noted that the pyrazole structure **6** was not established with certainty and in the light of our previous results [10] it seemed more logical to us that the more nucleophilic nitrogen atom of the phenylhydrazine would attack at the 2-position of the chromone rather than at the CN group.

We studied repeatedly the reactions of chromones **1** with phenylhydrazine under the conditions described in refs. 8 and 9 and confirmed the structure of compounds **7a-c**, which can easily be prepared in refluxing benzene in the presence of Et_3N for 0.5 h (for **1c** this reaction occurs both in benzene and ethanol without Et_3N , whereas for **1b** the reaction in benzene without Et_3N gives a complex mixture of isomeric open-chain intermediates and **7b**). However, we were unable to reproduce the claimed synthesis of **6a-c**; instead, 5-amino-1-phenyl-4-salicyloylpyrazoles **8a,b** as mixtures with **7a,b** were obtained in refluxing ethanol (**8a:7a** = 82:18 and **8b:7b** = 76:26). When these mixtures were treated with 20% sulfuric acid in ethanol [9], 5-aminopyrazoles **8a,b** were isolated as pure compounds in 44–49% yields. Refluxing an ethanolic solution of **1c** with phenylhydrazine afforded only the hydrazone **7c** with no traces of **8c**.

On the basis of ^1H and ^{13}C NMR spectroscopy and using 2D HSQC, HMBC, and NOESY experiments we found that the reaction products of **1a,b** and phenylhydrazine were, in fact, 5-amino-1-phenyl-4-salicyloylpyrazoles **8a,b** (Scheme 1). The structural assignment for these compounds as the 5-aminopyrazoles was based on the presence of a NOESY cross-peak from the ortho protons of the phenyl (δ 7.55–7.60 ppm, H-2'', H-6'') onto the NH_2 group and the absence of cross-peak between pyrazole H-3 proton and *ipso*-C of N-Ph in the HMBC spectrum (for **8a**). In addition, all the signals in the ^1H and ^{13}C NMR spectra of compound **8a** were assigned on the basis of 2D ^1H – ^{13}C HSQC and HMBC experiments. Besides the signals expected for the aromatic protons, the ^1H NMR spectra of **8a,b** in $\text{DMSO}-d_6$ showed three singlets due to the NH_2 group (δ 7.1 ppm), pyrazole H-3 proton (δ 7.7 ppm) and phenolic hydroxyl (δ 10.5–10.8 ppm). It is concluded that the series of the reported products such as **5**, was not in fact obtained. Moreover, based on the similarities between the ^1H NMR spectral data of **8** with those reported for **6** in CDCl_3 [9], it is clearly evident that the structure **6** should be revised to **8**.

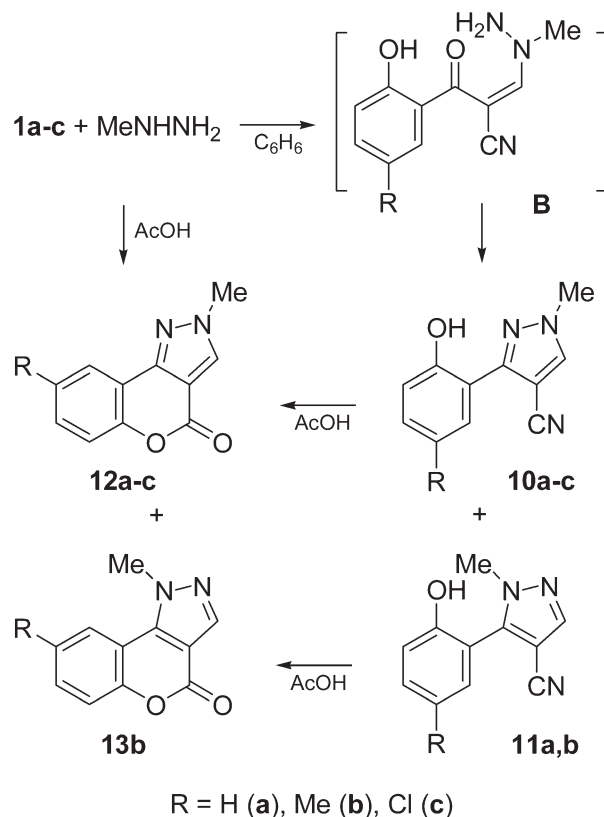
We also found that chromone **1a**, when treated with phenylhydrazine in refluxing AcOH, underwent transformation into 1-phenylchromeno[4,3-*c*]pyrazol-4(1*H*)-one **9** (55% yield). This observation is in line with other report on the condensation of 3-cyano-2-methylchromone with arylhydrazines, which leads to 1-aryl-3-methylchromeno[4,3-*c*]pyrazol-4(1*H*)-ones [11], and not to the claimed earlier 4-methyl-2-phenylchromeno[4,3-*c*]pyrazol-3(2*H*)-one [12]. Previously, compound **9** was obtained by the reactions of phenylhydrazine with chromone-3-carboxylic acid [13], 4-chloro-3-coumarincarbaldehyde [14], and 4-azido-3-coumarincarbaldehydes [15].

Products **7–9** can result from the initial nucleophilic 1,4-addition of phenylhydrazine to the C-2 atom of **1** to give, as a mixture of isomers, the open chain intermediate **A**, further transformation of which is controlled by the nucleophilicity of the OH and NH groups and depends on the reaction conditions. Two different reaction paths for **A** may be envisaged. In refluxing ethanol, intramolecular addition of the NHPPh function to the CN group with subsequent hydrogen shift leads to 5-amino-pyrazole **8** as a major product. The alternative cyclization of **A** involving the phenolic hydroxyl and the cyano group to form hydrazone **7** occurs in refluxing benzene in the presence of Et₃N. When **1** was allowed to react with phenylhydrazine in refluxing acetic acid, the initially formed hydrazone **7** could not be isolated and underwent intramolecular cyclization at the keto group to give chromeno[4,3-*c*]pyrazol-4(1*H*)-one **9**. Thus, the initial Michael addition of phenylhydrazine to **1** leads to three different types of products and the 1,2-addition at the CN group was not observed at all (Scheme 1). This clearly indicates that the C-2 atom of 3-cyanochromone is more susceptible to nucleophilic attack than the CN group. Note that in its reaction with sodium azide, it behaves as a simple aryl nitrile to form 3-(1*H*-tetrazol-5-yl)chromone [2a,16].

It is of interest that chromones **1** react in different manner with methylhydrazine to provide a completely different regiochemistry pattern. When an equimolar mixture of **1a–c** and methylhydrazine was refluxed in benzene for 0.5 h, 3-arylpyrazoles **10a–c** were obtained in 40–46% yields (Scheme 2). This reaction exhibits high regioselectivity and pyrazole **10c** was isolated as the single product. However, in the case of **10a,b**, some amount of 5-arylpyrazoles **11a,b** was observed (7 and 25%, respectively). The determination of the isomers ratio can easily be performed by ¹H NMR spectroscopic analysis. The ¹H NMR spectra of compounds **10a–c** in DMSO-*d*₆ consisted of a characteristic singlet due to the phenolic hydroxyl in the region of δ 9.8–10.4 ppm and two singlets due to the resonances of the pyrazole proton and the MeN group at δ 8.56–8.58 and 3.94 ppm. The IR spectra are also of diagnostic value in this 4-cyanopyrazole series (ν_{CN} = 2230 cm⁻¹).

The formation of these pyrazoles may be rationalized by initial 1,4-addition of the more nucleophilic secondary nitrogen atom of methylhydrazine on the C-2 atom of **1** with concomitant opening of the pyrone ring to give intermediate **B**. Further, the intramolecular heterocyclization occurs between the NH₂ group and the carbonyl, which seems more reactive than the cyano group. Compounds **10a–c**, so obtained, were then allowed to react under more vigorous conditions (boiling acetic acid for 5 h). This afforded coumarins **12a–c** in high yields (70–92%), which were also obtained directly

Scheme 2



from **1a–c** and methylhydrazine under the same reaction conditions, however, better yields were achieved if the transformation was performed in a two-step approach. The regioisomeric compounds **13** were not detected, except for the reactions of **1b**, in which case the ¹H NMR spectra of the products showed the presence of **13b** (25–28%) along with compound **12b** as the major product (Scheme 2).

Spectral data and melting point of **12a** were consistent with previous reported [17], this confirms the regiochemistry of the reaction with methylhydrazine. Interestingly, although the chemistry of the tricyclic chromeno[4,3-*c*]pyrazol-4-one system has been well documented [11–15], we have found that compound **12a** has been obtained only very recently from chromeno[4,3-*b*][1,5]benzodiazepin-7(8*H*)-one and methylhydrazine [17], while derivatives **12b,c** are hitherto unreported. In conjunction with the pharmaceutical importance known for the fused heterocycles incorporating a coumarin moiety [18], this simple synthesis of chromeno[4,3-*c*]pyrazol-4-ones from readily available 3-cyanochromones is noteworthy and will complement the published synthetic methods.

In conclusion, 3-cyanochromone represents a very reactive system and its reactions with phenyl- and

methylhydrazines give a variety of products. As the identity of some of these products was in doubt, we have reinvestigated the reaction with phenylhydrazine and found that by varying the conditions, 5-amino-4-salicyloyl-1-phenylpyrazoles, 2-aminochromone-3-carbaldehyde *N*-phenylhydrazones, and 1-phenylchromeno[4,3-*c*]pyrazol-4(1*H*)-one could be prepared in moderate to good yields. With methylhydrazine, 3-(2-hydroxyaryl)-1-methylpyrazole-4-carbonitriles and 2-methylchromeno[4,3-*c*]pyrazol-4(2*H*)-ones were obtained. A simple and convenient synthesis of chromeno[4,3-*c*]pyrazol-4-ones was developed and the generality of this method is being investigated further.

EXPERIMENTAL

¹H (400 MHz) and ¹³C (100 MHz) NMR spectra were recorded on a Bruker DRX-400 spectrometer in DMSO-*d*₆ with TMS as the internal standard. IR spectra were recorded on Perkin–Elmer Spectrum BX-II instrument (KBr) and Bruker Alpha instrument (ATR, ZnSe). Elemental analyses were performed at the Microanalysis Services of the Institute of Organic Synthesis, Ural Branch, Russian Academy of Sciences. Melting points are uncorrected. All solvents used were dried and distilled per standard procedures. The starting 3-cyanochromones **1a–c** were prepared according to described procedures [16].

General procedure for the preparation of 2-aminochromone-3-carbaldehyde *N*-phenylhydrazones (7a–c). A solution of chromone **1** (1.2 mmol), phenylhydrazine (130 mg, 1.2 mmol) and two drops of Et₃N in benzene (5 mL) was refluxed for 0.5 h and the reaction mixture cooled. The deposited phenylhydrazone **7** was filtered and washed with benzene. For **1c** this reaction occurs both in benzene and ethanol without Et₃N.

2-Aminochromone-3-carbaldehyde *N*-phenylhydrazone (7a). Yield 46%, mp 274–275°C (lit. [8a] mp 270°C); IR (KBr): 3317, 3256, 3109, 1646, 1600, 1532 cm^{−1}; ¹H NMR (DMSO-*d*₆): δ 6.71 (tt, 1H, H-4', *J* = 7.3, 1.0 Hz), 6.85–6.89 (m, 2H, H-2', H-6'), 7.19–7.24 (m, 2H, H-3', H-5'), 7.41 (ddd, 1H, H-6, *J* = 7.8, 7.2, 1.0 Hz), 7.45 (dd, 1H, H-8, *J* = 8.4, 1.0 Hz), 7.68 (ddd, 1H, H-7, *J* = 8.4, 7.2, 1.7 Hz), 8.02 (dd, 1H, H-5, *J* = 7.8, 1.7 Hz), 8.45 (s, 1H, HC=N), 8.98 (br s, 2H, NH₂), 10.10 (s, 1H, NH). Anal. Calcd for C₁₆H₁₃N₃O₂: C, 68.81; H, 4.69; N, 15.05. Found: C, 68.83; H, 4.72; N, 15.06.

2-Amino-6-methylchromone-3-carbaldehyde *N*-phenylhydrazone (7b). Yield 79%, mp 298–300°C (lit. [8a] mp 275°C); IR (ATR, ZnSe): 3243, 1640, 1604, 1594, 1549, 1520 cm^{−1}; ¹H NMR (DMSO-*d*₆): δ 2.40 (s, 3H, Me), 6.71 (tt, 1H, H-4', *J* = 7.4, 1.0 Hz), 6.85–6.89 (m, 2H, H-2', H-6'), 7.19–7.23 (m, 2H, H-3', H-5'), 7.34 (d, 1H, H-8, *J* = 8.4 Hz), 7.48 (ddq, 1H, H-7, *J* = 8.4, 2.3, 0.6 Hz), 7.82 (br d, 1H, H-5, *J* = 2.0 Hz), 8.45 (s, 1H, HC=N), 8.93 (br s, 2H, NH₂), 10.07 (s, 1H, NH). Anal. Calcd for C₁₇H₁₅N₃O₂: C, 69.61; H, 5.15; N, 14.33. Found: C, 69.53; H, 5.06; N, 14.41.

2-Amino-6-chlorochromone-3-carbaldehyde *N*-phenylhydrazone (7c). Yield 71%, mp 308–310°C (lit. [8a] mp 290°C); IR (ATR, ZnSe): 3375, 3245, 1610, 1600, 1579, 1529 cm^{−1}; ¹H NMR (DMSO-*d*₆): δ 6.72 (tt, 1H, H-4', *J* = 7.4, 1.2 Hz), 6.86–6.89 (m, 2H, H-2', H-6'), 7.19–7.24 (m, 2H, H-3', H-5'),

7.51 (d, 1H, H-8, *J* = 8.8 Hz), 7.71 (dd, 1H, H-7, *J* = 8.8, 2.7 Hz), 7.94 (d, 1H, H-5, *J* = 2.7 Hz), 8.42 (s, 1H, HC=N), 9.07 (br s, 2H, NH₂), 10.14 (s, 1H, NH). Anal. Calcd for C₁₆H₁₂ClN₃O₂: C, 61.25; H, 3.86; N, 13.39. Found: C, 60.91; H, 3.88; N, 13.01.

5-Amino-4-salicyloyl-1-phenylpyrazole (8a). This compound was prepared from chromone **1a** and phenylhydrazine according to the procedure described previously for **6a** [9]. Yield 44%, mp 143–144°C (lit. [9] mp 144°C); ¹H NMR (DMSO-*d*₆): δ 6.94 (ddd, 1H, H-5', *J* = 7.7, 7.3, 0.9 Hz), 6.97 (dd, 1H, H-3', *J* = 8.4, 0.9 Hz), 7.15 (s, 2H, NH₂), 7.40 (ddd, 1H, H-4', *J* = 8.4, 7.3, 1.6 Hz), 7.45 (m, 1H, H-4''), 7.55–7.61 (m, 5H, H-6', H-2'', H-3'', H-5'', H-6''), 7.74 (s, 1H, H-3), 10.79 (s, 1H, OH); ¹H NMR (CDCl₃): δ 6.08 (s, 2H, NH₂), 6.97 (td, 1H, H-5', *J* = 7.5, 1.0 Hz), 7.04 (dd, 1H, H-3', *J* = 8.4, 0.9 Hz), 7.43–7.49 (m, 2H, H-4', H-4''), 7.55–7.58 (m, 4H, H-2'', H-3'', H-5'', H-6''), 7.90 (dd, 1H, H-6', *J* = 7.9, 1.6 Hz), 7.97 (s, 1H, H-3), 11.84 (s, 1H, OH); ¹³C NMR (DMSO-*d*₆): δ 104.35 (C4), 116.94 (C3'), 119.02 (C5'), 123.75 (C2'', C6''), 124.81 (C1'), 127.72 (C4''), 129.44 (C6'), 129.53 (C3'', C5''), 132.61 (C4'), 137.39 (C1''), 141.89 (C3), 150.65 (C5), 157.04 (C2'), 189.03 (C=O); MS (EI): *m/z* (%) 279 [M]⁺ (45), 159 [M+1–HOC₆H₄CO]⁺ (100), 158 [M–HOC₆H₄CO]⁺ (29), 121 [HOC₆H₄CO]⁺ (27), 93 [HOC₆H₄]⁺ (15), 77 [Ph]⁺ (34), 69 (30). Anal. Calcd for C₁₆H₁₃N₃O₂: C, 68.81; H, 4.69; N, 15.05. Found: C, 68.51; H, 4.86; N, 15.01.

5-Amino-4-(2-hydroxy-5-methylbenzoyl)-1-phenylpyrazole (8b). This compound was prepared from chromone **1b** and phenylhydrazine according to the procedure described previously for **6b** [9]. Yield 49%, mp 148–149°C (lit. [9] mp 151°C); IR (ATR, ZnSe): 1597, 1573, 1531 cm^{−1}; ¹H NMR (DMSO-*d*₆): δ 2.28 (s, 3H, Me), 6.86 (d, 1H, H-3', *J* = 8.2 Hz), 7.11 (s, 2H, NH₂), 7.20 (dd, 1H, H-4', *J* = 8.2, 2.0 Hz), 7.36 (d, 1H, H-6', *J* = 2.0 Hz), 7.43–7.47 (m, 1H, H-4''), 7.55–7.60 (m, 4H, H-2'', H-3'', H-5'', H-6''), 7.75 (s, 1H, H-3), 10.53 (s, 1H, OH). Anal. Calcd for C₁₇H₁₅N₃O₂: C, 69.61; H, 5.15; N, 14.33. Found: C, 69.74; H, 5.36; N, 14.26.

1-Phenylchromeno[4,3-*c*]pyrazol-4(1*H*)-one (9). A solution of chromone **1a** (250 mg, 1.46 mmol) and phenylhydrazine (160 mg, 1.48 mmol) in 5 mL of glacial acetic acid was heated at reflux for 4 h. The resulting reaction mixture was then diluted with water (15 mL) and the solid that formed was filtered, washed with water, dried, and recrystallized from acetonitrile to give **9** as colorless needles in 55% yield (210 mg), mp 192–193°C (lit. [13] mp 191°C, lit. [14] mp 183–185°C, lit. [15] mp 209–210°C). ¹H NMR (DMSO-*d*₆): δ 7.07 (dd, 1H, H-9, *J* = 8.0, 1.8 Hz), 7.11 (ddd, 1H, H-8, *J* = 8.0, 6.8, 1.0 Hz), 7.47 (dd, 1H, H-6, *J* = 8.4, 1.0 Hz), 7.54 (ddd, 1H, H-7, *J* = 8.4, 6.8, 1.8 Hz), 7.59–7.62 (m, 2H, Ph), 7.68–7.71 (m, 3H, Ph), 8.35 (s, 1H, H-3).

General procedure for the preparation of 3-(2-hydroxyaryl)-1-methylpyrazole-4-carbonitriles (10a–c). A solution of chromone **1** (1.0 mmol) and methylhydrazine (55 mg, 1.2 mmol) in 4 mL of benzene was refluxed for 0.5 h. The resulting reaction mixture was then diluted with hexane (5 mL) and the solid that formed was filtered and washed with benzene/hexane mixture (1:1) to give **10** as yellow crystals.

3-(2-Hydroxyphenyl)-1-methylpyrazole-4-carbonitrile (10a). Yield 40%, mp 155–156°C; IR (KBr): 3130, 2229, 1621, 1586, 1542, 1506, 1462 cm^{−1}; ¹H NMR (DMSO-*d*₆): (10a, 93%) δ

3.94 (s, 3H, MeN), 6.91 (td, 1H, H-5', $J = 7.5$, 1.1 Hz), 6.97 (dd, 1H, H-3', $J = 8.2$, 1.1 Hz), 7.29 (ddd, 1H, H-4', $J = 8.2$, 7.3, 1.7 Hz), 7.50 (dd, 1H, H-6', $J = 7.7$, 1.7 Hz), 8.57 (s, 1H, H-5), 10.05 (s, 1H, OH); 5-(2-hydroxyphenyl)-1-methylpyrazole-4-carbonitrile (**11a**, 7%) δ 3.72 (s, 3H, Me), 6.98 (td, 1H, H-5', $J = 7.5$, 1.0 Hz), 7.06 (dd, 1H, H-3', $J = 8.2$, 1.0 Hz), 7.30 (dd, 1H, H-6', $J = 7.7$, 1.7 Hz), 7.41 (ddd, 1H, H-4', $J = 8.2$, 7.3, 1.7 Hz), 8.09 (s, 1H, H-3), 10.05 (br s, 1H, OH); MS (EI): m/z (%) 199 [M]⁺ (100), 171 (20), 156 (22), 42 (27). Anal. Calcd for C₁₁H₉N₃O: C, 66.32; H, 4.55; N, 21.09. Found: C, 65.96; H, 4.58; N, 20.74.

3-(2-Hydroxy-5-methylphenyl)-1-methylpyrazole-4-carbonitrile (10b). Yield 42%, mp 150–151°C; IR (KBr): 3176, 3120, 2230, 1621, 1591, 1543, 1503, 1467 cm⁻¹; ¹H NMR (DMSO-*d*₆): (**10b**, 75%) δ 2.24 (s, 3H, Me), 3.94 (s, 3H, MeN), 6.86 (d, 1H, H-3', $J = 8.3$ Hz), 7.08 (dd, 1H, H-4', $J = 8.3$, 2.0 Hz), 7.30 (d, 1H, H-6', $J = 2.0$ Hz), 8.56 (s, 1H, H-5), 9.79 (br s, 1H, OH); 5-(2-hydroxy-5-methylphenyl)-1-methylpyrazole-4-carbonitrile (**11b**, 25%) δ 2.26 (s, 3H, Me), 3.70 (s, 3H, MeN), 6.95 (d, 1H, H-3', $J = 8.3$ Hz), 7.10 (d, 1H, H-6', $J = 2.0$ Hz), 7.21 (dd, 1H, H-4', $J = 8.3$, 2.0 Hz), 8.08 (s, 1H, H-3), 10.07 (br s, 1H, OH). Anal. Calcd for C₁₂H₁₁N₃O: C, 67.59; H, 5.20; N, 19.71. Found: C, 67.18; H, 5.15; N, 19.42.

3-(5-Chloro-2-hydroxyphenyl)-1-methylpyrazole-4-carbonitrile (10c). Yield 46%, mp 213–214°C; IR (KBr): 3122, 2231, 1621, 1580, 1541, 1498, 1461 cm⁻¹; ¹H NMR (DMSO-*d*₆): δ 3.94 (s, 3H, MeN), 6.98 (d, 1H, H-3', $J = 8.7$ Hz), 7.33 (dd, 1H, H-4', $J = 8.7$, 2.7 Hz), 7.43 (d, 1H, H-6', $J = 2.7$ Hz), 8.58 (s, 1H, H-5), 10.37 (br s, 1H, OH). Anal. Calcd for C₁₁H₈ClN₃O: C, 56.54; H, 3.45; N, 17.98. Found: C, 56.54; H, 3.64; N, 17.85.

General procedure for the preparation of 2-methylchromeno[4,3-*c*]pyrazol-4(2H)-ones (12a–c). A solution of pyrazole **10** (1.0 mmol) in 3 mL of glacial acetic acid was refluxed for 5 h. The resulting reaction mixture was then diluted with water (10 mL) and the solid that formed was filtered, washed with water, and dried to give **12** as colorless crystals.

2-Methylchromeno[4,3-*c*]pyrazol-4(2H)-one (12a). Yield 92%, mp 209–210°C (lit. [17] mp 210°C); ¹H NMR (DMSO-*d*₆): δ 4.09 (d, 3H, Me, $J = 0.5$ Hz), 7.38 (ddd, 1H, H-8, $J = 7.7$, 7.3, 1.2 Hz), 7.44 (ddd, 1H, H-6, $J = 8.4$, 1.2, 0.4 Hz), 7.55 (ddd, 1H, H-7, $J = 8.4$, 7.3, 1.7 Hz), 7.99 (ddd, 1H, H-9, $J = 7.7$, 1.7, 0.4 Hz), 8.79 (q, 1H, H-3, $J = 0.5$ Hz). Anal. Calcd for C₁₁H₈N₂O₂: C, 66.00; H, 4.03; N, 13.99. Found: C, 65.64; H, 4.08; N, 13.84.

2,8-Dimethylchromeno[4,3-*c*]pyrazol-4(2H)-one (12b). Yield 70%, mp 158–160°C; IR (ATR, ZnSe): 1743, 1591, 1557, 1524 cm⁻¹; ¹H NMR (DMSO-*d*₆): (**12b**, 72%) δ 2.43 (s, 3H, Me), 4.09 (s, 3H, NMe), 7.22 (d, 1H, H-6, $J = 8.5$ Hz), 7.28 (dd, 1H, H-7, $J = 8.5$, 2.0 Hz), 7.76 (br s, 1H, H-9), 8.67 (s, 1H, H-3); 1,8-dimethylchromeno[4,3-*c*]pyrazol-4(1H)-one (**13b**, 28%) δ 2.49 (s, 3H, Me), 4.36 (s, 3H, NMe), 7.35 (d, 1H, H-6, $J = 8.5$ Hz), 7.40 (dd, 1H, H-7, $J = 8.5$, 2.0 Hz), 7.94 (br s, 1H, H-9), 8.07 (s, 1H, H-3). Anal. Calcd for

C₁₂H₁₀N₂O₂: C, 67.28; H, 4.71; N, 13.08. Found: C, 66.96; H, 4.81; N, 13.06.

8-Chloro-2-methylchromeno[4,3-*c*]pyrazol-4(2H)-one (12c). Yield 92%, mp 228–230°C; IR (ATR, ZnSe): 1747, 1736, 1589, 1554, 1511 cm⁻¹; ¹H NMR (DMSO-*d*₆): δ 4.10 (s, 3H, Me), 7.38 (d, 1H, H-6, $J = 8.8$ Hz), 7.47 (dd, 1H, H-7, $J = 8.8$, 2.5 Hz), 7.91 (d, 1H, H-9, $J = 2.5$ Hz), 8.74 (s, 1H, H-3). Anal. Calcd for C₁₁H₇ClN₂O₂: C, 56.31; H, 3.01; N, 11.04. Found: C, 55.96; H, 2.88; N, 11.42.

Acknowledgment. This work was financially supported by the RFBR (Grant 06-03-32388).

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