Reactions of 3-cyanochromones with primary amines: structures of the products

V. Ya. Sosnovskikh,[a] V. S. Moshkin,[a] and M. I. Kodess[b]*

[a]A. M. Gorky Ural State University,
51 prosp. Lenina, 620083 Ekaterinburg, Russian Federation.
Fax: +7 (343) 261 5978. E-mail: Vyacheslav.Sosnovskikh@usu.ru
[b]I. Ya. Postovsky Institute of Organic Synthesis, Ural Branch of the Russian Academy of Sciences,
22 ul. S. Kovalevskoi, 620041 Ekaterinburg, Russian Federation.

Reactions of 3-cyanochromones with primary aromatic amines in boiling benzene gave mixtures of *Z*- and *E*-3-arylamino-2-(2-hydroxyaroyl)acrylonitriles and 2-amino-3-(aryliminomethyl)chromones. The latter can easily be obtained in the individual state when the reaction is carried out in the presence of triethylamine. In the case of primary aliphatic amines, the open-chain reaction product immediately undergoes cyclization into 3-alkyliminomethyl-2-aminochromones. The structures of the products were examined by 1D and 2D ^{1}H, ^{13}C, and ^{15}N NMR spectroscopy in DMSO-d_6 and $CDCl_3$.

Key words: 3-cyanochromones, primary amines, recyclization, 2-amino-3-(aryliminomethyl)chromones, 3-alkyliminomethyl-2-aminochromones, 3-arylamino-2-(2-hydroxyaroyl)acrylonitriles, ^{1}H, ^{13}C, and ^{15}N NMR spectroscopy.

The intensive development of the chemistry of 3-cyanochromones was triggered by the discovery of a simple and convenient route to 3-formylchromones involving the Vilsmeier—Haack reaction of 2-hydroxyacetophenones with DMF and $POCl_3$ in 1973 (see Refs 1—3). Treatment of 3-formylchromones with hydroxylamine affords, through the formation of chromone 3-oximes, 3-cyanochromones **1** in good yields.[4—6] Recently, chromones **1** have been obtained by the Vilsmeier—Haack reaction[7] directly from 2-hydroxyacetophenones and hydroxylamine and from *O*-methylated chromone 3-oximes.[8]

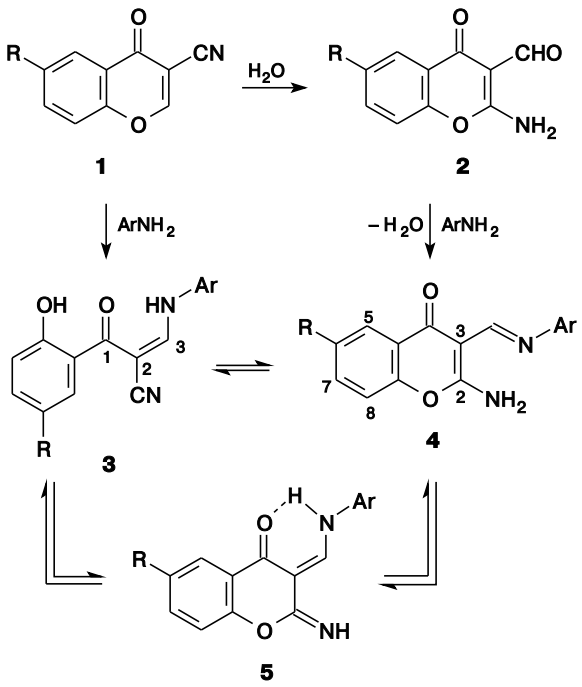
Introduction of a cyano group into position 3 of chromones radically changes the reactivity of the pyrone ring toward nucleophilic reagents and opens up a broad synthetic scope of this important oxygen-containing heterocyclic system. Being essentially *gem*-activated alkenes (simultaneously α,β-unsaturated ketones and nitriles), 3-cyanochromones **1** exhibit a variety of properties and can undergo additional transformations through opening of the γ-pyrone ring and heterocyclizations at the carbonyl or cyano group because of the presence of a good leaving group (phenolate anion).[9] For instance, when treated with morpholine in aqueous DMF,[10] with *n*-propylamine in ethanol,[11] or with aqueous NaOH,[6] chromone **1** easily undergoes recyclization into 2-amino-3-formylchromone **2** and acts as its chemical equivalent in reactions with active methylene compounds.[9] However, data on reactions of 3-cyanochromones **1** with primary amines are very scarce. It has been only reported[12] that reactions of 3-cyanochromone and 3-cyano-6-methylchromone with *p*-toluidine yield equilibrium mixtures of an open-chain tautomer (amino enone **3**) and two cyclic tautomers **4** and **5** (Scheme 1). It is also known[13] that 2-amino-3-formylchromones **2** react with aniline to give 2-amino-3-(phenyliminomethyl)chromones **4**. In the present work, we endeavored for the first time to determine the structures of the products obtained by reactions of 3-cyanochromones **1** with aromatic and aliphatic amines using 1D and 2D NMR spectroscopy in DMSO-d_6 and $CDCl_3$.

Results and Discussion

The closely related structural analogs of chromones **4** are 3-aminomethylidenechromane-2,4-diones **6**, which exist as mixtures of *E*- and *Z*-isomers stabilized by intramolecular hydrogen bonds (IntraHB) between the ketone or lactone carbonyl group and the amino group. The ^{1}H NMR spectra of these compounds show two sets of signals (doublets at δ 12—14 and ~9 with J = 13—14 Hz for the amino and vinylic protons, respectively[14,15]). However, in contrast to 2-hydroxychromones mainly existing as 4-hydroxycoumarins **7**,[16] less acid 2-aminochromones **8** does not tend toward tautomerization into the coumarin system[17] and, because of the push-pull character of the double bond of the pyrone ring, are thermodynamically

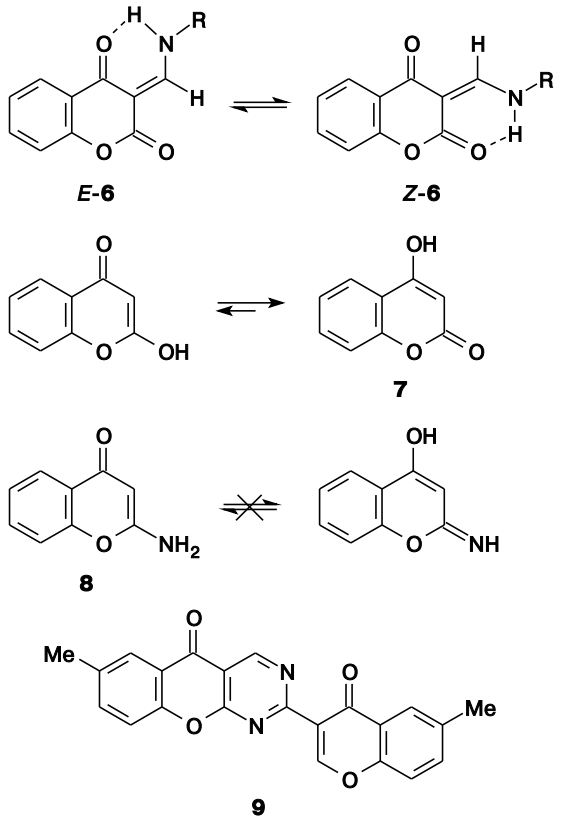
Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 3, pp. 602—611, March, 2010.

Scheme 1



R = H, Me

Scheme 2



stable (Scheme 2). This casts doubt on the presumed dynamic equilibrium between the chromone system **4** and compounds **3** and **5** (Scheme 1).

In connection with this, we studied again reactions of chromones **1** with aromatic amines in boiling benzene for 4 h (procedure ***A***)[12]. The results obtained are summarized in Table 1 and Scheme 3. It turned out that 3-cyanochromones **1** (R = H (**a**), Me (**b**), or Cl (**c**)) react with aniline, *p*-toluidine, and 2,4-xylidine to give mainly mixtures of *Z*- and *E*-acrylonitriles **3** and chromones **4**; only the reaction of compound **1b** with aniline afforded the *Z*- and *E*-isomers of acrylonitrile **3b** without an impurity of product **4b**. With 4-methoxy- and 4-bromoanilines and 2-aminopyridine, chromones **4f,h—j** were obtained as the sole reaction products, while 4-nitroaniline remained inert to compound **1a** under these and more drastic conditions. Reactions of aliphatic amines (such as benzylamine, phenethylamine, and isopropylamine) with chromones **1a,b** in boiling benzene proceed through the formation of acrylonitriles to give chromones **4m—p** in good yields (48—65%). A reduction in the reflux time from 4 h to 5—30 min (procedure ***B***) did not afford intermediate acrylonitriles **3** in the individual state: apart from the

Table 1. Compositions of products **3** and **4** in DMSO-d_6 and $CDCl_3$ (from ^{1}H NMR spectra)

Product	R	Ar	Method *A* *Z*-**3** : *E*-**3** : **4** (%)	Method *B* **1** : *Z*-**3** : *E*-**3** : **4** (%)
3a + **4a**	H	Ph	30 : 52 : 18[a]	25 : 27 : 44 : 4[a] (5)[b]
3b	Me	Ph	35 : 65 : 0[a]	
3b	Me	Ph	77 : 23 : 0[c]	
3c + **4c**	Cl	Ph	24 : 40 : 36[a]	4 : 26 : 45 : 25[a] (15)[b]
3d + **4d**	H	4-MeC_6H_4	8 : 15 : 77[a]	
3d + **4d**	H	4-MeC_6H_4	25 : 0 : 75[c,d]	
3e + **4e**	Me	4-MeC_6H_4	35 : 60 : 5[a]	
3e + **4e**	Me	4-MeC_6H_4	84 : 10 : 6[c,d]	
4f	H	4-$MeOC_6H_4$	0 : 0 : 100[a]	0 : 30 : 44 : 26[a] (5)[b]
4f	H	4-$MeOC_6H_4$	0 : 0 : 100[c]	
3g + **4g**	Me	4-$MeOC_6H_4$	30 : 50 : 20[a]	0 : 34 : 53 : 13[a] (5)[b]
3g + **4g**	Me	4-$MeOC_6H_4$	76 : 7 : 17[c]	
4h	Cl	4-$MeOC_6H_4$	0 : 0 : 100[a]	
4i	H	4-BrC_6H_4	0 : 0 : 100[a]	
4j	H	2-C_5H_4N	0 : 0 : 100[a]	
3k + **4k**	H	2,4-$Me_2C_6H_3$	56 : 17 : 27[a]	16 : 82 : 2 : 0[c] (30)[b]
3l + **4l**	Me	2,4-$Me_2C_6H_3$	60 : 22 : 18[a]	
3l + **4l**	Me	2,4-$Me_2C_6H_3$	87 : 4 : 9[c]	
4m	H	CH_2Ph	0 : 0 : 100[a,c]	
4n	H	$(CH_2)_2Ph$	0 : 0 : 100[a]	
4o	H	*i*-Pr	0 : 0 : 100[a]	
4p	Me	CH_2Ph	0 : 0 : 100[a]	

[a] In DMSO-d_6.
[b] The reflux time (min).
[c] In $CDCl_3$.
[d] Earlier,[12] this product has been reported to be an equilibrium mixture of compounds **3**, **4**, and **5**.

Z- and *E*-isomers of products **3**, the reaction mixtures always contained impurities of chromones **1** and/or **4** (^{1}H NMR data). At the same time, compounds **4a—e,g,k,l** can easily be obtained in 64—98% yields when the starting reagents are refluxed in benzene for 4 h in the presence of triethylamine (procedure ***C***). Compounds **4** are analytically pure even without recrystallization. The exception is chromone **4p**, which contains a 6% impurity (^{1}H NMR data) of the earlier described[11] dimer 7-methyl-2-(6-methyl-4-oxo-4*H*-chromen-3-yl)-5*H*-chromeno[2,3-*d*]pyrimidin-5-one (**9**) (Scheme 2).

The reaction studied involves nucleophilic 1,4-addition of an amine to the C(2) atom of chromone **1** followed by opening of the pyrone ring and formation of intermediate **3**. The latter undergoes irreversible cyclization into final product **4** through addition of the phenolic hydroxyl to the cyano group (Scheme 3). The rate of this intramolecular cyclization depends on the substituents in the chromone and aniline molecules. The first step of the reaction is rapid, which is evident from the experimental data obtained according to procedure ***B***. The cyclization rate is probably determined by the acidity of the phenolic hydroxyl and the basicity of the amine used. Although a detailed examination of this problem was beyond the scope of this study, the above assumption is supported by the following experimental facts.

(1) Addition of a catalytic amount of Et_3N (procedure ***C***) promoting the deprotonation of the phenolic hydroxyl substantially accelerates the cyclization and affords chromones **4** without an impurity of the open-chain form **3**.

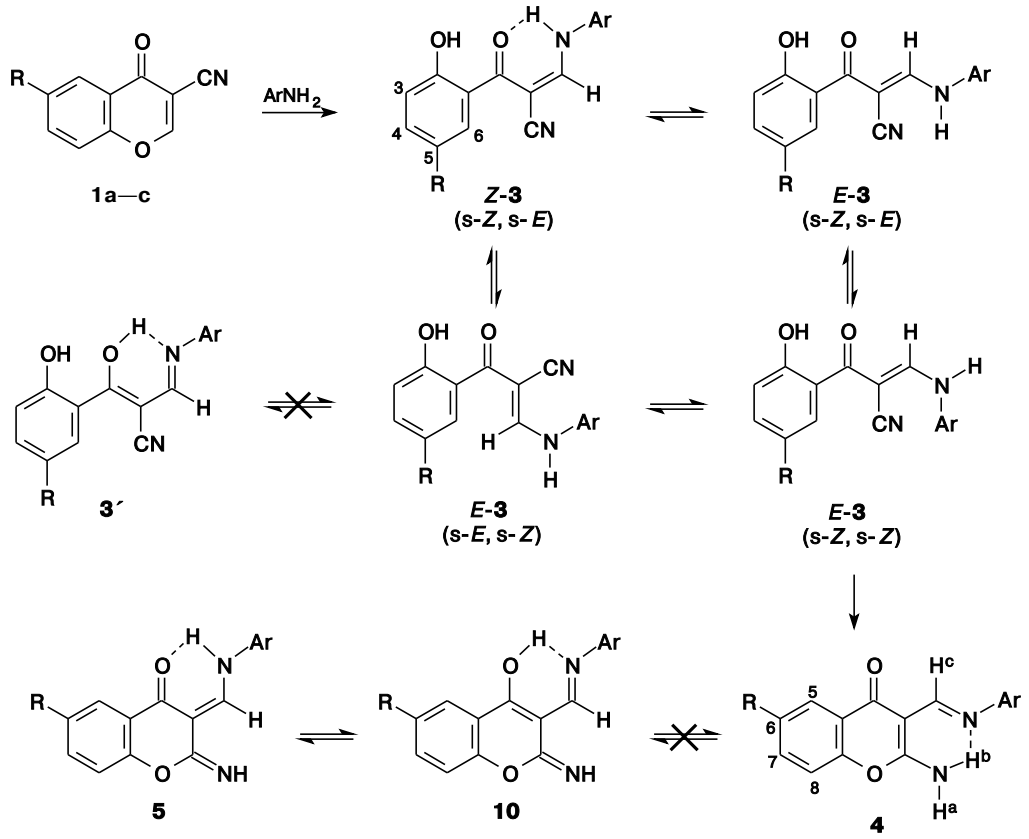
(2) Being stronger bases, aliphatic amines always yield final products **4** only, while intermediate acrylonitriles **3** are not detected even in trace amounts.

(3) In the presence of the electron-donating Me group in position 6 of chromone, the phenolic fragment is less acid and thus the cyclization is inhibited. As a result, the reaction products either contain no chromone **4** at all (as with **3b**) or its content is low (**3e,g,l**). As expected, the electron-withdrawing Cl atom produces an opposite effect (**4c,h**).

(4) Product **3b** is stable for a day in $CDCl_3$; in more basic DMSO-d_6, it undergoes spontaneous cyclization into compound **4b** with simultaneous decomposition to the starting reagents 3-cyano-6-methylchromone and aniline over the same period of time.

Compounds **3** and **4** and their mixtures are yellow or colorless high-melting solids; they are soluble in DMSO and moderately soluble in chloroform. The ^{1}H NMR spectra (400 MHz) of chromones **4** are given in Table 2; the

Scheme 3



R = H (**1a**), Me (**1b**), Cl (**1c**)

Table 2. ^{1}H NMR spectra of chromones **4a—p**

Imine	R	Ar	^{1}H NMR, δ, *J*/Hz			
			H^a (br.s)	H^b (br.s)	H^c	R, H(5)—H(8), Ar
4a[a]	H	Ph	9.43	10.64	8.98 (s)	7.19—7.26 (m, 3 H, H(4′), H(2′), H(6′)); 7.38—7.47 (m, 4 H, H(6), H(8), H(3′), H(5′)); 7.72 (ddd, 1 H, H(7), *J* = 8.4, 7.2, 1.7); 8.05 (ddd, 1 H, H(5), *J* = 8.1, 1.7, 0.4)
4a[b]	H	Ph	6.03	11.40	9.15 (s)	7.20—7.40 (m, 7 H, H(6), H(8), Ph); 7.60 (ddd, 1 H, H(7), *J* = 8.2, 7.4, 1.7); 8.24 (dd, 1 H, H(5), *J* = 7.9, 1.7)
4b[a]	Me	Ph	9.36	10.60	8.97 (s)	2.41 (s, 3 H, Me); 7.18—7.25 (m, 3 H, H(4′), H(2′), H(6′); 7.35 (d, 1 H, H(8), *J* = 8.4); 7.37—7.43 (m, 2 H, H(3′), H(5′)); 7.52 (ddq, 1 H, H(7), *J* = 8.4, 2.3, 0.5); 7.84 (br.d, 1 H, H(5), *J* = 2.0)
4c[a]	Cl	Ph	9.55	10.68	8.95 (s)	7.19—7.26 (m, 3 H, H(4′), H(2′), H(6′)); 7.38—7.43 (m, 2 H, H(3′), H(5′)); 7.52 (d, 1 H, H(8), *J* = 8.8); 7.76 (dd, 1 H, H(7), *J* = 8.8, 2.7); 7.96 (d, 1 H, H(5), *J* = 2.7)
4d[a]	H	4-MeC_6H_4	9.38	10.68	8.97 (s)	2.31 (s, 3 H, Me); 7.13—7.22 (m, 4 H, Ar); 7.41—7.47 (m, 2 H, H(6), H(8)); 7.72 (ddd, 1 H, H(7), *J* = 8.4, 7.2, 1.7); 8.05 (dd, 1 H, H(5), *J* = 7.9, 1.7)
4d[b]	H	4-MeC_6H_4	6.10	11.70	9.13 (s)	2.36 (s, 3 H, Me); 7.10—7.20 (m, 4 H, Ar); 7.25 (d, 1 H, H(8), *J* = 8.2); 7.35 (td, 1 H, H(6), *J* = 7.6, 0.8); 7.58 (ddd, *J* = 8.2, 7.4, 1.7); 8.23 (dd, 1 H, H(5), *J* = 7.8, 1.7)
4e[a]	Me	4-MeC_6H_4	9.32	10.65	8.97 (s)	2.31 and 2.41 (both s, 3 H, Me); 7.13—7.22 (m, 4 H, Ar); 7.34 (d, 1 H, H(8), *J* = 8.4); 7.52 (dd, 1 H, H(7), *J* = 8.4, 2.3); 7.83 (br.d, 1 H, H(5), *J* = 2.0)
4e[b]	Me	4-MeC_6H_4	5.98	11.20	9.13 (s)	2.36 and 2.43 (both s, 3 H, Me); 7.10—7.30 (m, 5 H, Ar, H(8)); 7.38 (dd, 1 H, H(7), *J* = 8.4, 2.0); 8.01 (d, 1 H, H(5), *J* = 2.0)
4f[a,c]	H	4-MeOC_6H_4	9.34	10.70	8.97 (s)	3.77 (s, 3 H, MeO); 6.94—6.99 (m, 2 H, Ar); 7.21—7.26 (m, 2 H, Ar); 7.41—7.46 (m, 2 H, H(6), H(8)); 7.71 (ddd, 1 H, H(7), *J* = 8.5, 7.3, 1.7); 8.05 (dd, 1 H, H(5), *J* = 7.8, 1.6)
4f[b]	H	4-MeOC_6H_4	6.02	11.65	9.12 (s)	3.83 (s, 3 H, MeO); 6.90—6.94 (m, 2 H, Ar); 7.20—7.24 (m, 2 H, Ar); 7.26 (dd, 1 H, H(8), *J* = 8.3, 1.0); 7.36 (ddd, 1 H, H(6), *J* = 7.8, 7.3, 1.0); 8.23 (dd, 1 H, H(5), *J* = 7.8, 1.7)
4g[a]	Me	4-MeOC_6H_4	9.28	10.66	8.96 (s)	2.41 (s, 3 H, Me); 3.77 (s, 3 H, MeO); 6.94—6.98 (m, 2 H, H(3′), H(5′)); 7.21—7.25 (m, 2 H, H(2′), H(6′)); 7.34 (d, 1 H, H(8), *J* = 8.4); 7.51 (ddq, 1 H, H(7), *J* = 8.4, 2.3); 7.83 (br.d, 1 H, H(5), *J* = 2.0)
4g[b]	Me	4-MeOC_6H_4	5.93	11.25	9.12 (s)	2.44 (s, 3 H, Me); 3.83 (s, 3 H, MeO); 6.90—6.93 (m, 2 H, H(3′), H(5′)); 7.20—7.24 (m, 3 H, H(8), H(2′), H(6′)); 7.38 (dd, 1 H, H(7), *J* = 8.5, 2.3); 8.01 (br.d, 1 H, H(5), *J* = 2.0)
4h[a]	Cl	4-MeOC_6H_4	9.46	10.74	8.95 (s)	3.77 (s, 3 H, MeO); 6.95—6.99 (m, 2 H, H(3′), H(5′)); 7.22—7.27 (m, 2 H, H(2′), H(6′)); 7.51 (d, 1 H, H(8), *J* = 8.8); 7.75 (dd, 1 H, H(7), *J* = 8.8, 2.7); 7.96 (d, 1 H, H(5), *J* = 2.7)
4i[a,d]	H	4-BrC_6H_4	9.47	10.52	8.97 (s)	7.22 (d, 2 H, H(2′), H(6′), *J* = 8.7); 7.42—7.46 (m, 2 H, H(6), H(8)); 7.56 (d, 2 H, H(3′), H(5′), *J* = 8.7); 7.72 (ddd, 1 H, H(7), *J* = 8.5, 7.2, 1.7); 8.05 (dd, 1 H, H(5), *J* = 7.8, 1.7)
4j[a]	H	2-C_5H_4N	9.58	10.89	9.75 (s)	7.22 (ddd, 1 H, H(5′), *J* = 7.3, 4.8, 1.0); 7.36 (dt, 1 H, H(3′), *J* = 8.1, 1.0); 7.42—7.47 (m, 2 H, H(6), H(8)); 7.73 (ddd, 1 H, H(7), *J* = 8.4, 7.2, 1.7); 8.06 (dd, 1 H, H(5), *J* = 7.8, 1.7); 8.47 (ddd, 1 H, H(6′), *J* = 4.8, 2.0, 0.7)
4k[a]	H	2,4-$Me_2C_6H_3$	9.39	10.79	8.90 (s)	2.26 and 2.28 (both s, 3 H, Me); 6.96 (d, 1 H, H(6′), *J* = 7.8); 7.03—7.07 (m, 2 H, H(3′), H(5′)); 7.44 (td, 1 H, H(6), *J* = 7.8, 1.0); 7.72 (ddd, 1 H, H(7), *J* = 8.4, 7.2, 1.7); 7.60 (dd, 1 H, H(5), *J* = 7.8, 1.7)

(*to be continued*)

Table 2 (*continued*)

Imine	R	Ar	^{1}H NMR, δ, *J*/Hz			
			H^a (br.s)	H^b (br.s)	H^c	R, H(5)—H(8), Ar
4l[a]	Me	2,4-$Me_2C_6H_3$	9.33	10.76	8.90 (s)	2.26, 2.28 and 2.41 (all s, 3 H, Me); 6.96 (d, 1 H, H(6′), 7.03—7.07 (m, 4 H, H(3′), H(5′)); 7.35 (d, 1 H, 7.52 (dd, 1 H, H(7), *J* = 8.4, 2.2); 7.84 (br.d, 1 H, H(5), *J* = 2.0)
4l[b]	Me	2,4-$Me_2C_6H_3$	6.06	11.25	9.07 (s)	2.32, 2.36 and 2.43 (all s, 3 H, Me); 7.03—7.10 (m, 4 H, H(8) Ar); 7.38 (dd, 1 H, H(7), *J* = 8.4, 2.0); 6.78 (br.s, 1 H, H(5))
4m[b]	H	CH_2Ph	6.31	11.60	8.83 (s)	4.74 (s, 2 H, CH_2); 7.16 (dd, 1 H, H(8), *J* = 8.4, 1.0); 7.27—7.39 (m, 6 H, Ph); 7.54 (ddd, 1 H, H(7), *J* = 8.4, 7.3, 1.5); 8.17 (dd, 1 H, H(5), *J* = 7.8, 1.5)
4m[a]	H	CH_2Ph	8.98	10.80	8.85 (s)	4.75 (s, 2 H, CH_2); 7.25—7.37 (m, 5 H, Ph); 7.39 (ddd, 1 H, H(6), *J* = 8.0, 7.3, 1.0); 7.40 (dd, 1 H, H(8), *J* = 8.4, 1.0); 7.68 (ddd, 1 H, H(7), *J* = 8.4, 7.3, 1.7); 8.02 (dd, 1 H, H(5), *J* = 8.0, 1.7)
4m[e]	H	CH_2Ph	—	—	9.50 (br.s)	4.90 (br.s, 2 H, CH_2); 7.28—7.42 (m, 7 H, H(6), H(8), Ph); 7.64 (t, 1 H, H(7), *J* = 7.5); 8.07 (d, 1 H, H(5), *J* = 7.5)
4n[a]	H	$(CH_2)_2Ph$	8.86	10.82	8.63 (s)	2.91 (t, 2 H, CH_2, *J* = 7.2); 3.78 (t, 2 H, NCH_2, *J* = 7.2); 7.17—7.32 (m, 5 H, Ph); 7.36 (dd, 1 H, H(8), *J* = 8.4, 1.0); 7.37 (ddd, 1 H, H(6), *J* = 8.0, 7.3, 1.0); 7.66 (ddd, 1 H, H(7), *J* = 8.4, 7.3, 1.7); 7.98 (dd, 1 H, H(5), *J* = 8.0, 1.7)
4o[a]	H	Pr^i	8.84	10.94	8.70 (s)	1.20 (d, 6 H, 2 Me, *J* = 6.3); 3.56 (sept, 1 H, CH, *J* = 6.3); 7.35—7.40 (m, 2 H, H(6), H(8)); 7.67 (ddd, 1 H, H(7), *J* = 8.3, 7.2, 1.7); 7.99 (dd, 1 H, H(5), *J* = 7.9, 1.7)
4o[f]	H	Pr^i	—	—	8.70 (s)	1.21 (d, 6 H, 2 Me, *J* = 6.3); 3.59 (sept, 1 H, CH, *J* = 6.3); 7.35—7.40 (m, 2 H, H(6), H(8)); 7.67 (ddd, 1 H, H(7), *J* = 8.3, 7.2, 1.7); 8.00 (dd, 1 H, H(5), *J* = 7.9, 1.7)
4p[a,g]	H	CH_2Ph	8.92	10.74	8.84 (s)	2.39 (s, 3 H, Me); 4.74 (s, 2 H, CH_2); 7.24—7.38 (m, 5 H, Ph); 7.29 (d, 1 H, H(8), *J* = 8.5); 7.48 (dd, 1 H, H(7), *J* = 8.5, 2.2); 7.80 (d, 1 H, H(5), *J* = 2.2)

[a] In DMSO-d_6.
[b] In $CDCl_3$.
[c] The signals for the NH protons disappear upon the addition of CD_3CO_2D.
[d] ^{13}C NMR (DMSO-d_6), δ: 95.05 (C(3)), 116.73 (C(8)), 117.64 (C(4′)), 121.83 (C(4a)), 123.15 (C(2′), C(6′)), 125.09 (C(6)), 125.22 (C(5)), 132.03 (C(3′), C(5′)), 133.50 (C(7)), 150.27 (C(1′)), 152.86 (C(8a)), 156.46 (C=N), 164.25 (C(2)), 173.89 (C(4)).
[e] $CDCl_3$ + CD_3CO_2D.
[f] DMSO-d_6 + CD_3CO_2D.
[g] The product contains dimer **9** as an impurity (6%). ^{1}H NMR (DMSO-d_6), δ: 2.48 (s, 6 H, 2 Me); 7.68 (d, 1 H, H(8), *J* = 8.6 Hz); 7.71 (d, 1 H, H(8′), *J* = 8.6 Hz); 7.71 (dd, 1 H, H(7), *J* = 8.6 Hz, *J* = 2.3 Hz); 7.79 (dd, 1 H, H(7′), *J* = 8.6 Hz, *J* = 2.3 Hz); 7.98 (br.s, 1 H, H(5)); 8.01 (br.s, 1 H, H(5′)); 9.09 (s, 1 H, H(2)); 9.56 (s, 1 H, CH=N).

^{1}H NMR spectra of *Z*- and *E*-acrylonitriles **3** in $CDCl_3$ and DMSO-d_6 at 25 °C are summarized in Tables 3 and 4, respectively. In the case of reactions of chromones **1** with primary amines according to procedure ***A***, the ^{1}H NMR spectra of the products show one to three sets of signals of different intensities. This allowed assignment of all low-field signals for the OH, NH, and =CH protons in *Z*- and *E*-**3**; however, signals for the aromatic protons were assigned incompletely because of their overlap.

Our primary task was to identify the tautomeric form of the final products in the reactions of chromones **1** with primary amines (procedures ***A*** and ***C***). Because the ^{1}H NMR spectra of these products show three low-field singlets for the H^a, H^b, and H^c protons, we excluded from consideration amino enone structure **5**, which is a nitrogen analog of 3-aminomethylidenechromane-2,4-diones **6** (earlier,[12] structure **5** was assigned to open-chain form **3** with similar spectroscopic characteristics). We gave preference to imino enamine **4** rather than imino enol **10** upon analysis of the chemical shifts of the signals for the N atoms in compound **4i** at δ 98.9 (NH_2) and 287.4 (N=C) (2D ^{1}H—^{15}N HMQC and HMBC). The spectrum of tau-

Table 3. ^{1}H NMR spectra of acrylonitriles *Z*- and *E*-**3a,b,d,e,g,k,l** in $CDCl_3$

Enamine	R	Ar	^{1}H NMR, δ, *J*/Hz			
			OH	NH (br.d)	=CH (d)	R, H(3)—H(6), Ar
Z-**3a**	H	Ph	11.41 (s)	12.44 (*J* = 13.4)	8.06 (*J* = 13.4)	6.95 (ddd, 1 H, H(5), *J* = 8.1, 7.4, 1.0); 7.01 (dd, 1 H, H(3), *J* = 8.2, 1.0); 7.20—7.30 (m, 3 H, Ar); 7.40—7.50 (m, 3 H, H(4), Ar); 8.40 (dd, 1 H, H(6), *J* = 8.1, 1.6)
E-**3a**	H	Ph	11.90 (s)	18.12 (*J* = 15.2)	8.82 (*J* = 15.2)	6.95 (ddd, 1 H, H(5), *J* = 8.1, 7.4, 1.0); 7.02 (dd, 1 H, H(3), *J* = 8.2, 1.0); 7.20—7.30 (m, 3 H, Ar); 7.40—7.50 (m, 3 H, H(4), Ar); 8.31 (dd, 1 H, H(6), *J* = 8.1, 1.6)
Z-**3b**[a]	Me	Ph	11.17 (s)	12.45 (*J* = 13.4)	8.05 (*J* = 13.4)	2.34 (s, 3 H, Me); 6.91 (d, 1 H, H(3), *J* = 8.4); 7.22—7.32 (m, 4 H, H(2′), H(6′), H(4′), H(4)); 7.46 (t, 2 H, H(3′), H(5′), *J* = 7.9); 8.19 (br.d, 1 H, H(6), *J* = 1.5)
E-**3b**[b]	Me	Ph	11.68 (s)	8.18 (*J* = 15.2)	8.80 (*J* = 15.2)	2.35 (s, 3 H, Me); 6.92 (d, 1 H, H(3), *J* = 8.4); 7.21—7.50 (m, 6 H, H(4), Ar); 8.10 (br.d, 1 H, H(6), *J* = 1.7)
Z-**3d**	H	4-MeC_6H_4	11.70 (br.s)	12.45 (*J* = 13.5)	8.01 (*J* = 13.5)	2.38 (s, 3 H, Me); 6.94 (ddd, 1 H, H(5), *J* = 8.1, 7.4, 1.0); 7.00 (dd, 1 H, H(3), *J* = 8.2, 1.0); 7.10—7.20 (m, 4 H, Ar); 7.46 (ddd, 1 H, H(4), *J* = 8.2, 7.4, 1.6); 8.39 (dd, 1 H, H(6), *J* = 8.1, 1.6)
Z-**3e**	Me	4-MeC_6H_4	11.21 (br.s)	12.45 (*J* = 13.5)	8.01 (*J* = 13.5)	2.33 and 2.38 (both s, 3 H, Me); 6.90 (d, 1 H, H(3), *J* = 8.4); 7.10—7.30 (m, 5 H, H(4), Ar); 8.18 (br.d, 1 H, H(6), *J* = 1.5)
E-**3e**	Me	4-MeC_6H_4	11.71 (br.s)	8.07 (*J* = 15.2)	8.77 (*J* = 15.2)	2.34 and 2.37 (both s, 3 H, Me); 6.92 (d, 1 H, H(3), *J* = 8.4); 7.10—7.30 (m, 5 H, H(4), Ar); 8.10 (br.d, 1 H, H(6), *J* = 1.5)
Z-**3g**	Me	4-$MeOC_6H_4$	11.25 (br.s)	12.49 (*J* = 13.4)	7.94 (*J* = 13.4)	2.33 (s, 3 H, Me); 3.84 (s, 3 H, MeO); 6.90 (d, 1 H, H(3), *J* = 8.4); 6.94—7.20 (m, 4 H, Ar); 7.26 (dd, 1 H, H(4), *J* = 8.4, 2.3); 8.18 (br.d, 1 H, H(6), *J* = 1.5)
E-**3g**	Me	4-$MeOC_6H_4$	11.72 (br.s)	8.15 (*J* = 15.2)	8.70 (*J* = 15.2)	2.34 (s, 3 H, Me); 3.84 (s, 3 H, MeO); 7.02—7.20 (m, 5 H, H(3), Ar); 7.28 (dd, 1 H, H(4), *J* = 8.4, 2.3); 8.10 (br.d, 1 H, H(6), *J* = 1.5)
Z-**3k**	H	2,4-$Me_2C_6H_3$	11.46 (br.s)	12.60 (*J* = 13.3)	8.03 (*J* = 13.3)	2.35 and 2.40 (both s, 3 H, Me); 6.95 (ddd, 1 H, H(5), *J* = 8.1, 7.2, 1.1), 7.01 (dd, 1 H, H(3), *J* = 8.3, 1.1); 7.10—7.16 (m, 3 H, Ar); 7.46 (ddd, 1 H, H(4), *J* = 8.3, 7.2, 1.6); 8.40 (dd, 1 H, H(6), *J* = 8.1, 1.6)
Z-**3l**	Me	2,4-$Me_2C_6H_3$	11.22 (br.s)	12.61 (*J* = 13.2)	8.02 (*J* = 13.2)	2.34, 2.35 and 2.40 (all s, 3 H, Me); 6.91 (d, 1 H, H(3), *J* = 8.3); 7.07—7.16 (m, 3 H, Ar); 7.26 (dd, 1 H, H(4), *J* = 8.3, 2.0); 8.19 (br.d, 1 H, H(6), *J* = 1.5)
E-**3l**	Me	2,4-$Me_2C_6H_3$	11.73 (br.s)	8.09 (*J* = 15.2)	8.71 (*J* = 15.2)	2.30—2.40 (masked, 9 H, 3 Me); 6.90—7.16 (m, 5 H, H(3), H(4), Ar); 8.10 (br.s, 1 H, H(6))

[a] ^{13}C NMR ($CDCl_3$), δ: 20.60 (Me), 82.38 (C(2)), 118.05 (C(2″), C(6″)), 118.15 (C(3′)), 119.35 (C(1′)), 120.34 (CN), 126.92 (C(4″)), 128.17 (C(5′)), 129.08 (C(6′)), 130.22 (C(3″), C(5″)), 136.78 (C(4′)), 137.84 (C(1″)), 155.03 (C(3)), 159.26 (C(2′)), 193.14 (C(1)).
[b] ^{13}C NMR ($CDCl_3$), δ: 84.02 (C(2)), 129.44 (C(6′)), 137.98 (C(1″)), 154.45 (C(3)), 160.06 (C(2′)), 188.90 (C(1)) (the signals were identified only in part).

tomer **10** would contain two low-field signals for the imine N atoms (Scheme 3).

As another piece of evidence for structure **4**, note that the lowest-field signal in the ^{13}C NMR spectrum of compound **4i** at δ 173.9 correlates well with the signal for the group C=O in chromones[18] and that the chemical shifts of the signals for the H(5)—H(8) protons at δ 7.42—8.05 are very close to those for the corresponding aromatic protons in 2-amino-3-formyl- and 2-amino-3-carbamoylchromones.[19] The nonequivalence of the NH_2 protons in chromones **4a—p**, which appear in DMSO-d_6 as slightly broadened singlets at δ 8.8—9.6 (H^a) and 10.4—10.9 (H^b) and disappear upon addition of CD_3CO_2D, is probably due to IntraHB between the H^b proton and the imine N atom. The results are hindered rotation about the C(2)—N bond, the *E*-configuration of the imino group, and the stabilization of the s-*cis*-conformer (see Scheme 3). The azomethine H^c proton in these compounds resonates in a narrow range (δ 8.6—9.0). The exception is α-pyridyl-containing compound **4j**: the signal for the H^c proton ap-

Table 4. ^{1}H NMR spectra of acrylonitriles *Z*- and *E*-**3a—g,k,l** in DMSO-d_6

Enamine	R	Ar	^{1}H NMR, δ, *J*/Hz			
			OH	NH	=CH	R, H(3)—H(6), Ar
Z-**3a**	H	Ph	10.18 (s)	12.32 (br.d, *J* = 13.5)	8.55 (d, *J* = 13.5)	6.86—6.95 (m, 2 H, H(3), H(5)); 7.29—7.38 (m, 5 H, H(4), H(6), H(3′), H(4′), H(5′)); 7.56—7.59 (m, 2 H, H(2′), H(6′))
E-**3a**	H	Ph	10.21 (br.s)	11.03 (br.s)	8.14 (br.s)	6.86—6.95 (m, 2 H, H(3), H(5)); 7.29—7.38 (m, 7 H, H(4), H(6), Ph)
Z-**3b**[a]	Me	Ph	9.93 (s)	12.31 (br.d, *J* = 13.5)	8.54 (d, *J* = 13.5)	2.23 (s, 3 H, Me); 6.81 (d, 1 H, H(3), *J* = 8.2); 7.10—7.16 (m, 2 H, H(4), H(6)); 7.24 (tt, 1 H, H(4′), *J* = 7.4, 1.0); 7.41—7.46 (m, 2 H, H(3′), H(5′)); 7.55—7.59 (m, 2 H, H(2′), H(6′))
E-**3b**[b]	Me	Ph	9.95 (br.s)	10.99 (br.s)	8.13 (br.s)	2.23 (s, 3 H, Me); 6.82 (d, 1 H, H(3), *J* = 8.2); 7.10—7.16 (m, 2 H, H(4), H(6)); 7.18 (tt, 1 H, H(4′), *J* = 7.4, 1.0); 7.28—7.32 (m, 2 H, H(2′), H(6′)); 7.36—7.41 (m, 2 H, H(3′), H(5′))
Z-**3c**	Cl	Ph	10.43 (s)	12.26 (br.d, *J* = 13.6)	8.57 (d, *J* = 13.6)	6.94 (d, 1 H, H(3), *J* = 8.8); 7.17—7.40 (m, 3 H, H(4), H(6), H(4′)); 7.44 (br.t, 2 H, H(3′), H(5′), *J* = 7.8); 7.58 (br.d, 2 H, H(2′), H(6′), *J* = 7.8)
E-**3c**	Cl	Ph	10.39 (br.s)	11.09 (br.s)	8.14 (br.s)	6.94 (d, 1 H, H(3), *J* = 8.8); 7.17—7.42 (m, 7 H, H(4), H(6), Ph)
Z-**3d**	H	4-MeC_6H_4	10.17 (s)	12.33 (br.d, *J* = 13.6)	8.51 (d, *J* = 13.6)	2.31 (s, 3 H, Me); 6.85—6.95 (m, 2 H, H(3), H(5)); 7.20—7.48 (m, 6 H, H(4), H(6), Ar)
E-**3d**	H	4-MeC_6H_4	10.25 (br.s)	10.99 (br.s)	8.11 (br.s)	2.27 (s, 3 H, Me); 6.85—6.95 (m, 2 H, H(3), H(5)); 7.20—7.48 (m, 6 H, H(4), H(6), Ar)
Z-**3e**	Me	4-MeC_6H_4	9.92 (s)	12.32 (br.d, *J* = 13.5)	8.49 (d, *J* = 13.5)	2.23 and 2.31 (both s, 3 H, Me); 6.81 (d, 1 H, H(3), *J* = 8.2); 7.10—7.16 (m, 2 H, H(4), H(6)); 7.22—7.25 (m, 2 H, Ar); 7.44—7.47 (m, 2 H, Ar)
E-**3e**	Me	4-MeC_6H_4	9.95 (br.s)	10.95 (br.s)	8.08 (br.s)	2.22 and 2.27 (both s, 3 H, Me); 6.82 (d, 1 H, H(3), *J* = 8.2); 7.10—7.16 (m, 2 H, H(4), H(6)); 7.19 (s, 4 H, Ar)
Z-**3f**	H	4-$MeOC_6H_4$	10.16 (s)	12.37 (br.d, *J* = 13.6)	8.44 (d, *J* = 13.6)	3.78 (s, 3 H, MeO); 6.85—7.02 (m, 4 H, H(3), H(5), Ar); 7.29—7.36 (m, 2 H, H(4), H(6)); 7.50—7.54 (m, 2 H, Ar)
E-**3f**	H	4-$MeOC_6H_4$	10.26 (br.s)	10.96 (br.s)	8.05 (br.s)	3.74 (s, 3 H, MeO); 6.85—7.02 (m, 4 H, H(3), H(5), Ar); 7.22—7.26 (m, 2 H, Ar), 7.29—7.36 (m, 2 H, H(4), H(6))
Z-**3g**	Me	4-$MeOC_6H_4$	9.91 (s)	12.35 (br.d, *J* = 13.5)	8.42 (d, *J* = 13.5)	2.23 (s, 3 H, Me); 3.78 (s, 3 H, MeO); 6.81 (d, 1 H, H(3), *J* = 8.3); 6.94—7.01 (m, 2 H, Ar); 7.10—7.15 (m, 2 H, H(4), H(6)); 7.50—7.53 (m, 2 H, Ar)
E-**3g**	Me	4-$MeOC_6H_4$	9.96 (br.s)	10.93 (br.s)	8.03 (br.s)	2.22 (s, 3 H, Me); 3.74 (s, 3 H, MeO); 6.81 (d, 1 H, H(3), *J* = 8.3); 6.94—7.01 (m, 2 H, Ar); 7.10—7.15 (m, 2 H, H(4), H(6)); 7.22—7.26 (m, 2 H, Ar)
Z-**3k**	H	2,4-$Me_2C_6H_3$	10.14 (s)	12.65 (br.d, *J* = 13.0)	8.61 (d, *J* = 13.0)	2.28 and 2.34 (both s, 3 H, Me); 6.88 (td, 1 H, H(5), *J* = 7.5, 1.0), 6.92 (dd, 1 H, H(3), *J* = 8.6, 1.0); 7.05—7.15 (m, 2 H, H(3′), H(5′)); 7.29—7.34 (m, 2 H, H(4), H(6)); 7.60 (d, 1 H, H(6′), *J* = 8.2)
E-**3k**	H	2,4-$Me_2C_6H_3$	10.16 (br.s)	10.47 (br.s)	7.73 (br.s)	2.24 and 2.25 (both s, 3 H, Me); 6.84—6.94 (m, 2 H, H(5), H(3)); 7.05—7.15 (m, 3 H, Ar); 7.26—7.34 (m, 2 H, H(4), H(6))

(*to be continued*)

Table 4 (*continued*)

Enamine	R	Ar	^{1}H NMR, δ, *J*/Hz			
			OH	NH	=CH	R, H(3)—H(6), Ar
Z-**3l**	Me	2,4-$Me_2C_6H_3$	9.90 (s)	12.66 (br.d, *J* = 13.0)	8.60 (d, *J* = 13.0)	2.23, 2.28 and 2.33 (all s, 3 H, Me); 6.82 (d, 1 H, H(3), *J* = 8.5); 7.01—7.15 (m, 4 H, H(4), H(6), H(3′), H(5′)); 7.59 (d, 1 H, H(6′), *J* = 8.2)
E-**3l**	Me	2,4-$Me_2C_6H_3$	9.92 (br.s)	10.44 (br.s)	7.72 (br.s)	2.20, 2.24 and 2.25 (all s, 3 H, Me); 6.78 (d, 1 H, H(3), *J* = 8.5); 7.01—7.15 (m, 5 H, H(4), H(6), Ar)

[a] ^{13}C NMR (DMSO-d_6), δ: 19.91 (Me), 85.48 (C(2)), 116.27 (C(3′)), 118.19 (C(2″), C(6″)), 119.92 (CN), 125.77 (C(4″)), 126.59 (C(1′)), 127.24 (C(5′)), 128.24 (C(6′)), 129.62 (C(3″), C(5″)), 132.45 (C(4′)), 138.46 (C(1″)), 152.67 (C(2′)), 153.59 (C(3)), 193.05 (C(1)).
[b] ^{13}C NMR (DMSO-d_6), δ: 19.91 (Me), 86.75 (C(2)), 116.17 (C(3′)), 116.73 (CN), 118.33 (C(2″), C(6″)), 125.20 (C(4″)), 125.63 (C(1′)), 127.70 (C(5′)), 129.19 (C(6′)), 129.62 (C(3″), C(5″)), 132.56 (C(4′)), 139.78 (C(1″)), 152.83 (C(2′)), 154.23 (C(3)), 189.69 (C(1)).

pears at δ 9.75 because of the deshielding of the pyridine N atom (see Table 2).

Out of two NH_2 protons in chromone **4i**, a cross peak with the high-field N atom is produced only by the H^b proton (δ 10.52) involved in IntraHB (^{1}H—^{15}N HMQC data). The H^a proton (δ 9.47) linked by an intermolecular hydrogen bond (InterHB) to basic DMSO-d_6 molecules produces no cross peak, which has been noted earlier for 2-amino-3-carbamoylchromone.[19] At the same time, in $CDCl_3$ incapable of forming InterHB to acid hydrogen atoms, the signal for H^a appears as a broadened singlet at δ 5.9—6.3, while the signal for H^b is shifted downfield (δ 11.3—11.7) because of IntraHB (compounds **4d,e,f,g,l,m**). This agrees well with the presumed formation of InterHB and IntraHB in solutions of chromones **4** in DMSO-d_6 (see Table 2). Upon addition of CD_3CO_2D to a solution of compound **4m** in $CDCl_3$, the singlet for the azomethine H^c proton is shifted downfield by 0.67 ppm and the singlet for the CH_2 group, by 0.16 ppm, which indicates deuteration of the imine N atom in this solvent.

The ^{1}H—^{15}N HMBC spectrum of compound **4i** contains three cross peaks with a low-field signal for the N atom. These are produced by the azomethine H^c proton (δ 8.97), the *ortho*-protons of the 4-bromophenyl substituent, and the H^b proton (a very weak cross peak). The last correlation is most likely due to the coupling through the hydrogen bond ($^{1h}J_{N,H}$) rather than the long-range spin-spin coupling with $^5J_{N,H}$ (see Ref. 20). All the signals in the ^{1}H and ^{13}C NMR spectra of compound **4i** were assigned from 2D experiments (^{1}H—^{13}C HSQC and HMBC) and the NOESY spectrum. The latter revealed positive cross peaks between both NH_2 protons and water because of chemical exchange. Apparently, IntraHB in compound **4i** is weakened and does not prevent the H^b proton from participating in the exchange process.

3-Arylamino-2-(2-hydroxyaroyl)acrylonitriles **3** obtained from chromone **1** under the action of aromatic amines *via* the opening of the pyrone ring are typical representatives of push-pull alkenes with the highly polarized bond C(2)=C(3) and, accordingly, the lowered energy barrier to rotation about this bond, which allows them to exist in solution as an equilibrium mixture of geometric *Z*- and *E*-isomers. In addition, compounds **3** can be regarded as amide vinylogs with hindered rotation about the formally single bonds C(1)—C(2) and C(3)—N because of the delocalized π-electron density, which may give rise to conformers (rotamers) in the equilibrium mixture. However, the ^{1}H NMR spectra of compounds **3** in both $CDCl_3$ and DMSO-d_6 show only two sets of signals for the *Z*- and *E*-isomers. The major isomer in $CDCl_3$ is the *Z*-isomer with IntraHB between the C=O and NH groups, while the major isomer in DMSO-d_6 is the *E*-isomer with the NH proton involved in intermolecular hydrogen bonding to solvent molecules.

All essential signals in the ^{1}H and ^{13}C NMR spectra for this series of compounds were assigned from 2D experiments (^{1}H—^{13}C HSQC and HMBC) for compound **3b** obtained from 3-cyano-6-methylchromone and aniline (the product contained no impurity of chromone **4b**). The most informative cross peaks in the HMBC spectrum (DMSO-d_6) are as follows: C(2)/H(3), CN/H(3), C(1″)/H(3), C(1)/H(3), C(3′)/OH, C(1′)/OH, and C(2′)/OH. The 2D ^{1}H—^{15}N HMQC spectrum of a mixture of *Z*-**3b** and *E*-**3b** in DMSO-d_6 exhibits only one cross peak between the doublet for the NH proton (δ_H 12.3) in *Z*-**3b** and the signal for the N atom at δ_N 137.6 (in $CDCl_3$, δ_N 140.2). Therefore, the N atom also belongs to the *Z*-isomer (direct correlations with the *E*-isomer were not revealed in this experiment). The chemical shift of the amine N atom in the *E*-isomer (δ_N 132.1) was determined from the 2D ^{1}H—^{15}N HMBC data: its signal shows a cross peak with the *ortho*-protons of the phenyl substituent (a similar cross peak is observed for the *Z*-isomer).

In the ^{1}H NMR spectra of compounds **3** in $CDCl_3$, the major set of signals for the *Z*-isomer includes a broadened doublet for the NH proton (δ 12.4—12.6) because of its participation in the formation of a strong IntraHB to the carbonyl O atom, a distinct doublet for the vinylic proton (δ 7.9—8.1, ^3J = 13.2—13.5 Hz), and a singlet for the hydrogen-bonded phenolic hydroxyl (δ 11.2—11.7). The minor set of signals (*E*-isomer) consists of a broadened doublet for the free NH proton (δ 8.1—8.2), a distinct doublet for the =CH group (δ 8.7—8.8, ^3J = 15.2 Hz), and a singlet for the phenolic OH group bound by IntraHB (δ 11.7—11.9). These data correlate well with the assumption that compounds **3** exist in $CDCl_3$ as equilibrium mixtures of the *Z*-isomer (because of IntraHB, it is the s-*Z*,s-*E*-rotamer about the bonds C(1)—C(2) and C(3)—N, respectively) and the *E*-isomer in the same conformation. The considerable chemical shift difference (Δδ ~4.4 ppm) for the NH proton in *Z*-**3** and *E*-**3** is due to the cleavage of IntraHB, which is inevitable for this isomerization. The downfield shift of the signal for the =CH proton (Δδ ~0.8 ppm) is associated with the deshielding effect of the carbonyl group in the *E*-isomer with the s-*Z*-conformation with respect to the C(1)—C(2) bond (see Scheme 3, Table 3).

In DMSO-d_6, the minor set of signals, except for **3k,l**, includes a broadened doublet for the NH proton (δ 12.3—12.7; the width of each component of the doublet does not exceed 2.5 Hz), a distinct doublet for the =CH group (δ 8.4—8.6, ^3J = 13.5—13.6 Hz), and a singlet for the phenolic hydroxyl bound by InterHB (δ 9.9—10.4). Thus, these signals relate to the IntraHB-stabilized *Z*-isomer with the s-*Z*,s-*E*-conformation. The major set of signals in this solvent includes three broadened singlets in sufficiently narrow ranges (δ 7.7—8.1, 10.4—11.1, and 9.9—10.4). We assigned these signals to the vinylic proton, the NH protons bound by InterHB to DMSO-d_6 molecules (the line width exceeds 20 Hz), and the phenolic hydroxyl of the *E*-isomer with the s-*Z*-conformation about the C(3)—N bond, respectively. The correct assignment of the last signal to the OH proton is indirectly confirmed by a noticeable influence of the substituent in position 5 of the phenol residue on the chemical shift of this signal. A rigorous proof is provided by the cross peaks between the phenolic proton and the C(1′), C(2′), and C(3′) atoms in the 2D HMBC spectrum of compound **3b**. In so far as the preferable form of β-oxo imines is amino enone rather than imino enol (mainly because the hydrogen bond NH···O=C is stronger than the bond OH···N=C),[21—24] the existence of acrylonitriles **3** in DMSO-d_6 as imino enol **3′** is very unlikely. For rotamers about the C(3)—N bond, the reported[25—27] coupling constants are ^3J = 13—14 Hz (s-*E*-conformation) and ^3J = 7—8 Hz (s-*Z*-conformation). The latter constant is not always detectable because of intermolecular NH exchange, the exchange rate being dependent on the amount of water in the solvent and the concentration of the rotamer. When moving from *Z*-**3** to *E*-**3**, the chemical shift of the signal for the =CH proton in DMSO-d_6 is shifted upfield by ~0.4 ppm (by 0.88 ppm for compounds **3k,l** containing the *ortho*-Me group in the aniline residue)—in contrast to the solution in $CDCl_3$, in which the signal for this atom is shifted downfield—and seems to be an average for the corresponding rotamers s-*Z*,s-*Z* and s-*E*,s-*Z* in rapid equilibrium with each other (see Scheme 3, Table 4).

As noted above, the aromatic protons were identified incompletely because of the overlap of their signals; yet some conclusions can be drawn. First, the ^{1}H NMR spectra of *Z*-**3** and *E*-**3** in $CDCl_3$ show the signals for the H(3) and H(5) protons in the range expected for the phenol fragment (δ 6.90—7.02). Along with other factors, this is an important argument for open-chain amino enone **3**. In the case of the earlier proposed cyclic structure **5**, the corresponding signals would be shifted downfield (δ 7.1—7.2). Second, the low-field signal for the H(6) proton at δ 8.3—8.4 (R = H) and 8.1—8.2 (R = Me) in $CDCl_3$ confirms that the OH and C=O groups are bound by IntraHB in both *Z*-**3** and *E*-**3**; as a result, the phenol ring is coplanar with the enone fragment and the H(6) proton is deshielded by the CN group. Third, in DMSO-d_6, the H(3) and H(5) protons resonate at δ 6.78—6.95 and the H(4) and H(6) protons resonate at δ 7.2—7.4 (R = H) and 7.1—7.2 (R = Me), as expected for the open-chain forms *Z*-**3** and *E*-**3**. This is due to cleavage of the intramolecular hydrogen bond O—H···O=C in this solvent and the non-coplanarity of the phenol ring with the amino enone residue. Fourth, in DMSO-d_6, the H(2′) and H(6′) protons of the aniline ring in *Z*-**3** are more strongly deshielded than the corresponding protons in *E*-**3**. This agrees with the assumption that *E*-**3** exists as the s-*Z*-rotamer about the C(3)—N bond, in which the aryl substituent is not coplanar, for steric reasons, with the amino enone fragment and becomes less conjugated with the delocalized system. In this respect, the most demonstrative is the isomer *E*-**3e**, in which the signal for the *p*-tolyl substituent appears as a singlet at δ 7.19 (4 H).

The IR spectra of chromones **4a**—**p** in pellets with KBr show absorption bands at 3200—3240 (NH_2 stretches), 1650—1660 (C=O stretches), and 1600—1610 cm^{-1} (C=C stretches). The presence of the open-chain form **3** is manifested by a characteristic band of the cyano group at 2200—2206 cm^{-1}.

To sum up, the set of products in noncatalytic reactions of 3-cyanochromones with aromatic amines in benzene depends substantially on the substituent in position 6 of chromone and, to a less degree, on the substituents in the aniline component. Base-catalyzed reactions of this type yield 2-amino-3-(aryl/alkylimino)methylchromones as the sole products. 3-Cyano-6-methylchromone is the most suitable reagent for the synthesis of intermediate acrylonitriles as mixtures of their *Z*- and *E*-isomers.

Experimental

IR spectra were recorded on a Perkin-Elmer Spectrum BX-II instrument (KBr pellets). ^{1}H, ^{13}C, and ^{15}N NMR spectra were recorded on a Bruker DRX-400 spectrometer in DMSO-d_6 or $CDCl_3$ (400.1, 100.6, and 40.5 MHz, respectively) with Me_4Si as the internal standard and with liquid ammonia as the external standard.

The ^{1}H NMR spectra of 2-amino-3-(aryl/alkyliminomethyl)-chromones **4a**—**p** are given in Table 2. The ^{1}H NMR spectra of the *Z*- and *E*-isomers of 3-anilino-2-salicyloylacrylonitriles **3** in $CDCl_3$ and DMSO-d_6 are given in Tables 3 and 4. The yields, melting points, elemental analysis data, and IR spectra of chromones **4** are summarized in Table 5.

3-Cyanochromones **1** were prepared as described earlier.[28] To identify the signals in the ^{1}H and ^{13}C NMR spectra of compound **3b**, all signals for 3-cyano-6-methylchromone were assigned from 2D experiments (^{1}H—^{13}C HSQC and HMBC). ^{1}H NMR (DMSO-d_6), δ: 2.45 (s, 3 H, Me); 7.65 (d, 1 H, H(8), J = 8.6 Hz); 7.72 (ddq, 1 H, H(7), J = 8.6 Hz, J = 2.2 Hz, J = 0.6 Hz); 7.85 (dq, 1 H, H(5), J = 2.2 Hz, J = 0.6 Hz); 9.20 (s, 1 H, H(2)). ^{13}C NMR (DMSO-d_6), δ: 20.36 (Me), 100.75 (C(3)), 113.27 (CN), 118.63 (C(8)), 122.31 (C(4a)), 124.27 (C(5)), 136.55 (C(7)), 136.97 (C(6)), 153.63 (C(8a)), 165.16 (C(2)), 172.44 (C(4)).

Reactions of 3-cyanochromones with amines. Procedure *A*. A solution of chromone **1** (1.0 mmol) and an amine (1.0 mmol) was refluxed in benzene (4 mL) for 4 h. The reaction mixture was cooled and the precipitate that formed was filtered off, washed with benzene, and dried.

Procedure *B* is similar but the reflux time was varied (see Table 1).

Procedure *C* is similar with procedure ***A*** but two drops of triethylamine were added.

Procedures ***A*** and ***C*** were used to obtain 2-amino-3-(phenyliminomethyl)chromone (**4a**), 2-amino-6-methyl-3-(phenyliminomethyl)chromone (**4b**), 2-amino-6-chloro-3-(phenyliminomethyl)chromone (**4c**), 2-amino-3-(4-tolyliminomethyl)-

Table 5. Physicochemical properties, elemental analysis data, and IR spectra of chromones **4a**—**p**

Chromone	Yield (%)	M.p. /°C	Molecular formula	Found / Calculated (%)			IR, ν/cm^{-1}
				C	H	N	
4a[a]	81	216—218	$C_{16}H_{12}N_2O_2$	72.85 72.72	4.40 4.58	10.48 10.60	3216, 3048, 1654, 1600, 1563, 1517
4b	98	230—232	$C_{17}H_{14}N_2O_2$	73.56 73.37	5.33 5.07	10.28 10.07	3203, 3070, 1650, 1608, 1565, 1512
4c	76	338—340	$C_{16}H_{11}ClN_2O_2$	64.10 64.33	3.71 3.71	9.47 9.38	3204, 3052, 1652, 1600, 1564, 1516
4d[b]	68	200—202	$C_{17}H_{14}N_2O_2$	73.22 73.37	5.18 5.07	10.14 10.07	3210, 3047, 1656, 1605, 1562, 1518
4e[c]	77	228—230	$C_{18}H_{16}N_2O_2$	74.12 73.95	5.35 5.52	9.74 9.58	3195, 3017, 1657, 1609, 1564, 1502
4f	64	233—235	$C_{17}H_{14}N_2O_3$	69.26 69.38	4.56 4.79	9.45 9.52	3197, 3037, 1656, 1607, 1564, 1501
4g	87	236—238	$C_{18}H_{16}N_2O_3$	70.25 70.12	4.98 5.23	8.99 9.09	3205, 3077, 1652, 1607, 1573, 1507
4h	87	290—292	$C_{17}H_{13}ClN_2O_3$	62.06 62.11	3.64 3.99	8.60 8.52	3190, 3015, 1649, 1598, 1564
4i	80	253—255	$C_{16}H_{11}BrN_2O_2$	55.86 56.00	3.35 3.23	7.98 8.16	3211, 3075, 1655, 1605, 1564, 1519
4j	81	243—244	$C_{15}H_{11}N_3O_2$	67.70 67.92	4.13 4.18	15.90 15.84	3185, 3042, 1614, 1575, 1554, 1510
4k	80	236—238	$C_{18}H_{16}N_2O_2$	73.86 73.95	5.47 5.52	9.48 9.58	3200, 1662, 1616, 1573, 1544
4l	76	243—245	$C_{19}H_{18}N_2O_2$	74.40 74.49	6.06 5.92	9.21 9.14	3197, 3007, 1656, 1608, 1563, 1508
4m	57	155—156	$C_{17}H_{14}N_2O_2$	73.10 73.37	4.85 5.07	10.09 10.07	3198, 1664, 1611, 1562
4n	48	139—141	$C_{18}H_{16}N_2O_2$	74.23 73.95	5.54 5.52	9.72 9.58	3227, 1663, 1607, 1554
4o	65	194—195	$C_{13}H_{14}N_2O_2$	67.50 67.81	5.83 6.13	12.12 12.17	3237, 1665, 1612, 1566
4p[d]	64	174—175	—	—	—	—	3200, 1660, 1610, 1568

[a] *Cf.* Ref. 13: m.p. 210—214 °C.
[b] *Cf.* Ref. 12: m.p. 211 °C.
[c] *Cf.* Ref. 12: m.p. 210 °C.
[d] The product was isolated as a mixture with dimer **9** (6%).

chromone (**4d**), 2-amino-6-methyl-3-(4-tolyliminomethyl)-chromone (**4e**), 2-amino-3-(4-methoxyphenyliminomethyl)-chromone (**4f**), 2-amino-3-(4-methoxyphenyliminomethyl)-6-methylchromone (**4g**), 2-amino-6-chloro-3-(4-methoxyphenyliminomethyl)chromone (**4h**), 2-amino-3-(4-bromophenyliminomethyl)chromone (**4i**), 2-amino-3-(2-pyridyliminomethyl)-chromone (**4j**), 2-amino-3-(2,4-dimethylphenyliminomethyl)-chromone (**4k**), 2-amino-3-(2,4-dimethylphenyliminomethyl)-6-methylchromone (**4l**), 2-amino-3-(benzyliminomethyl)chromone (**4m**), 2-amino-3-(phenethyliminomethyl)chromone (**4n**), 2-amino-3-(isopropyliminomethyl)chromone (**4o**), and 2-amino-3-benzyliminomethyl-6-methylchromone (**4p**).

This work was financially supported by the Russian Foundation for Basic Research (Project No. 06-03-32388).

References

1. H. Harnisch, *Liebigs Ann. Chem.*, 1972, **765**, 8.
2. A. Nohara, T. Umetani, Y. Sanno, *Tetrahedron Lett.*, 1973, 1995.
3. A. Nohara, T. Umetani, Y. Sanno, *Tetrahedron*, 1974, **30**, 3553.
4. A. Nohara, *Tetrahedron Lett.*, 1974, 1187.
5. S. Klutchko, M. P. Cohen, J. Shavel, M. von Strandtmann, *J. Heterocycl. Chem.*, 1974, **11**, 183.
6. U. Petersen, H. Heitzer, *Liebigs Ann. Chem.*, 1976, 1659.
7. G. J. Reddy, D. Latha, C. Thirupathaiah, K. S. Rao, *Tetrahedron Lett.*, 2004, **45**, 847.
8. R. P. Hsung, C. A. Zificsak, L.-L. Wei, L. R. Zehnder, F. Park, M. Kim, T.-T. T. Tran, *J. Org. Chem.*, 1999, **64**, 8736.
9. C. K. Ghosh, S. K. Karak, *J. Heterocycl. Chem.*, 2005, **42**, 1035.
10. A. Nohara, T. Ishiguro, K. Ukawa, H. Sugihara, Y. Maki, Y. Sanno, *J. Med. Chem.*, 1985, **28**, 559.
11. C. K. Ghosh, N. Tewari, *J. Org. Chem.*, 1980, **45**, 1964.
12. C. K. Ghosh, C. Ghosh, A. Patra, *Indian J. Chem.*, 1998, **37B**, 387.
13. H. Hagen, G. Nilz, H. Walter, A. Landes, W. Freund, DE Patent 4 039 281, 1992; *Chem. Abstr.*, 1992, **117**, 111473.
14. C. Bandyopadhyay, K. R. Sur, R. Patra, A. Sen, *Tetrahedron*, 2000, **56**, 3583.
15. M. A. Ibrahim, *ARKIVOC*, 2008, **xvii**, 192.
16. W. R. Porter, W. F. Trager, *J. Heterocycl. Chem.*, 1982, **19**, 475.
17. W. Basinski, *Pol. J. Chem.*, 1995, **69**, 376.
18. V. Ya. Sosnovskikh, B. I. Usachev, M. I. Kodess, *Izv. Akad. Nauk, Ser. Khim.*, 2002, 1671 [*Russ. Chem. Bull.*, *Int. Ed.*, 2002, 51, 1817].
19. V. Ya. Sosnovskikh, M. I. Kodess, V. S. Moshkin, *Izv. Akad. Nauk, Ser. Khim.*, 2009, 1218 [*Russ. Chem. Bull.*, *Int. Ed.*, 2009, 6].
20. I. Alkorta, J. Elguero, G. S. Denisov, *Magn. Reson. Chem.*, 2008, **46**, 599.
21. K. Saito, T. Yamaguchi, *J. Chem. Soc., Perkin Trans. 2*, 1979, 1605.
22. S.-F. Tan, K.-P. Ang, H. L. Jayachandran, A. J. Jones, W. R. Begg, *J. Chem. Soc.*, *Perkin Trans. 2*, 1982, 513.
23. A. L. Nivorozhkin, H. Toftlund, P. C. Stein, F. Jensen, *J. Chem. Soc.*, *Perkin Trans. 2*, 1993, 2423.
24. K. Neuvonen, C. Zewi, H. Lönnberg, *Acta Chem. Scand.*, 1996, **50**, 1137.
25. A. Gómez-Sanchez, R. Paredes-León, J. Campora, *Magn. Res. Chem.*, 1998, **36**, 154.
26. J. Wójcik, W. Domalewski, K. Kamienska-Trela, L. Stefaniak, S. I. Vdovienko, I. I. Gerus, M. G. Gorbunova, *Magn. Res. Chem.*, 1993, **31**, 808.
27. L. Kozerski, P. Krajewski, E. Bednarek, *Magn. Res. Chem.*, 1995, **33**, 745.
28. A. Nohara, H. Kuriki, T. Saijo, H. Sugihara, M. Kanno, Y. Sanno, *J. Med. Chem.*, 1977, **20**, 141.

Received May 5, 2009;
in revised form August 31, 2009