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Studies on Aromatic Nitro Compounds. V.[1] A Simple One-Pot Preparation of *o*-Aminoaroylnitriles from Some Aromatic Nitro Compounds

YUKIHIKO TOMIOKA, KIMIKO OHKUBO, and MOTOYOSHI YAMAZAKI*

Faculty of Pharmaceutical Sciences, Fukuoka University, 8–19–1 Nanakuma, Jonan-ku, Fukuoka 814–01, Japan

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The reactions of 3-, 5-, 6-, 7- and 8-nitroquinolines, 1- or 2-nitronaphthalene and *m*-substituted (CF_3, $COCH_3$ and COC_6H_5) nitrobenzenes with ethyl cyanoacetate and potassium hydroxide in dimethylformamide, followed by hydrolysis of the reaction mixture with hydrochloric acid or sodium hydroxide, gave the corresponding *o*-aminoaroylnitriles.

Keywords——nitroquinoline; nitronaphthalene; nitrobenzene; ethyl cyanoacetate; hydrolysis; *o*-aminoaroylnitrile; pyrimidin-4(3*H*)-one

The versatility of *o*-aminoaroylnitriles as synthetic intermediates lies principally in the ease with which *o*-aminoaroylnitriles may be transformed to a variety of heterocycles, in particular, condensed pyrimidines.[2] However, the established procedures for the preparation of *o*-aminoaroylnitriles are elaborate and tedious in some cases. For example, 2-amino-1-naphthalenecarbonitrile[3a] is prepared by the following procedure. As the first step, 2-acetamido-1-bromonaphthalene[4] is obtained by bromination of 2-acetamidonaphthalene with bromine. Secondly, 2-acetamido-1-bromonaphthalene is treated with copper(I) cyanide in pyridine to give 2-acetamido-1-naphthalenecarbonitrile. Finally, hydrolysis of 2-acetamido-1-naphthalenecarbonitrile with sodium hydroxide affords 2-amino-1-naphthalenecarbonitrile. Recently, we showed that 6-nitroquinoline reacts with ethyl cyano-

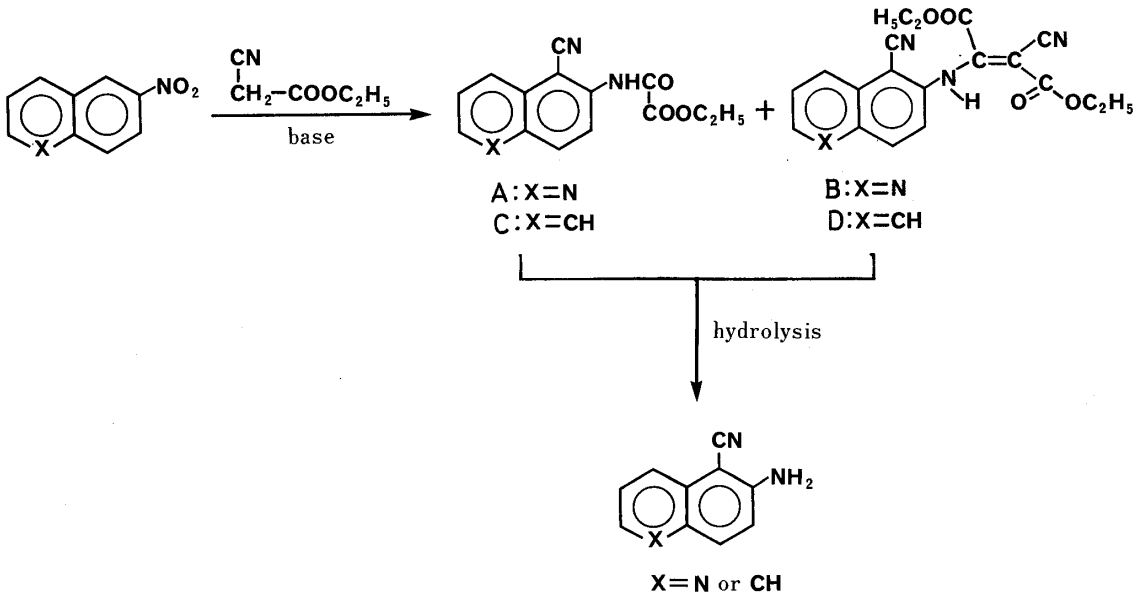
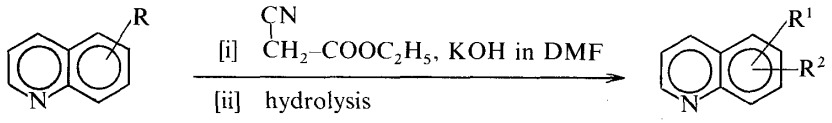


Chart 1

acetate in the presence of a base to give ethyl *N*-(5-cyano-6-quinolyl)oxamate (A) and diethyl 2-cyano-3-(5-cyano-6-quinolylamino)fumarate (B),[5] and in a similar fashion 2-nitronaphthalene provides ethyl *N*-(1-cyano-2-naphthyl)oxamate (C) and diethyl 2-cyano-3-(1-cyano-2-naphthylamino)fumarate (D).[1]

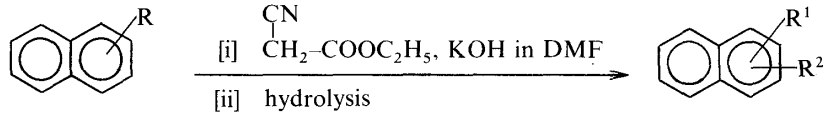
Although the mechanism of the above reaction has not been established, both the oxamate (A or C) and the fumarate (B or D) are converted to 6-amino-5-quinolinecarbonitrile

TABLE I. Synthesis of *o*-Aminoaroylnitriles (II) from Some Aromatic Nitro Compounds (I)



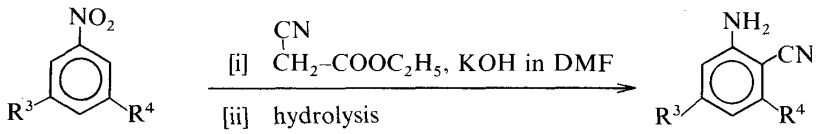
Ia: R = 3-NO_2
Ib: R = 5-NO_2
Ic: R = 6-NO_2
Id: R = 7-NO_2
Ie: R = 8-NO_2

IIa: R^1 = 3-NH_2, R^2 = 4-CN
IIb: R^1 = 5-NH_2, R^2 = 6-CN
IIc: R^1 = 6-NH_2, R^2 = 5-CN
IId: R^1 = 7-NH_2, R^2 = 8-CN
IIe: R^1 = 8-NH_2, R^2 = 7-CN



If: R = 1-NO_2
Ig: R = 2-NO_2

IIf: R^1 = 1-NH_2, R^2 = 2-CN
IIg: R^1 = 2-NH_2, R^2 = 1-CN



Ih: R^3 = CF_3, R^4 = H
Ii: R^3 = $COCH_3$, R^4 = H
Ij: R^3 = COC_6H_5, R^4 = H
Ik: R^3 = R^4 = CF_3

IIh: R^3 = CF_3, R^4 = H
IIi: R^3 = $COCH_3$, R^4 = H
IIj: R^3 = COC_6H_5, R^4 = H
IIk: R^3 = R^4 = CF_3

Substrate	Product	Yield of II (%)		Reaction conditions: [i] Temp. (°C)		Time (h)		[ii] Solvent	Temp. (°C)	Time (h)
		A	B	A	B	A	B			
Ia	IIa	83		R.T.		24		20% HCl	Reflux	5
Ib	IIb	15	39	50	R.T.	48	24	10% HCl	Reflux	3
Ic	IIc	84		R.T.		24		10% HCl	Reflux	3
Id	IId	43	44	R.T.	R.T.	24	2	10% HCl	Reflux	3
Ie	IIe	32	42	50	R.T.	48	24	10% HCl	Reflux	0.5
If	IIf	47	54	50	50	72	24	5% NaOH	Reflux	0.5
Ig	IIg	64	75	R.T.	R.T.	24	24	5% NaOH	Reflux	1
Ih	IIh	54	53	R.T.	R.T.	24	24	5% NaOH	Reflux	1
Ii	IIi	29	45	R.T.	R.T.	24	24	5% NaOH	R.T.	24
Ij	IIj	40	47	R.T.	R.T.	24	24	5% NaOH	R.T.	24
Ik	IIk	51	75	R.T.	0	24	1	5% NaOH	Reflux	1

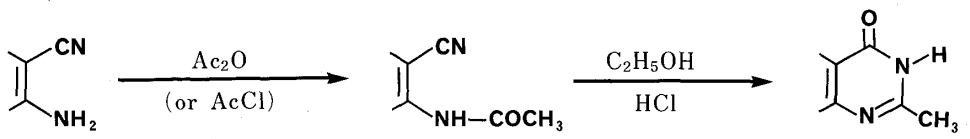
A: All reactions were carried out with the use of I, ethyl cyanoacetate and potassium hydroxide in a 1 : 3 : 3 molar ratio, except in the cases of Ib, Ie and If, for which a 1 : 5 : 5 molar ratio of I to ethyl cyanoacetate and potassium hydroxide was used. B: All reactions were carried out with the use of I, ethyl cyanoacetate, potassium hydroxide and potassium cyanide in a 1 : 3 : 2 : 1 molar ratio. R.T. = room temperature.

or 2-amino-1-naphthalenecarbonitrile on hydrolysis. This reaction suggests a promising new method for synthesizing *o*-aminoaroylnitriles from aromatic nitro compounds. In order to explore the scope and limitations of the above reaction, studies were carried out with various aromatic nitro compounds. Table I summarizes the results.

A mixture of 3-nitroquinoline (Ia: 0.03 mol), ethyl cyanoacetate (0.09 mol) and potassium hydroxide (0.09 mol) in dimethylformamide (DMF) was stirred for 24 h at room temperature, then the DMF was removed *in vacuo*, and the residue was hydrolyzed with hydrochloric acid to give 3-amino-4-quinolinecarbonitrile (IIa) in 83% yield. In a similar manner, 5-nitro- (Ib), 6-nitro- (Ic), 7-nitro- (Id), and 8-nitroquinolines (Ie), and 1- or 2-nitronaphthalene (If or Ig) gave *o*-aminoaroylnitriles (IIb—g) corresponding to IIa. In the case of Ib, although the reaction was carried out for 48 h at 50 °C with Ib, ethyl cyanoacetate and potassium hydroxide in a 1:5:5 molar ratio, the yield of 5-amino-6-quinolinecarbonitrile (IIb) was only 15%. When the reaction was carried out for 24 h at room temperature with Ib, ethyl cyanoacetate, potassium hydroxide and potassium cyanide in a molar ratio 1:3:2:1, the yield of IIb increased to 39%. Similarly, I (e—g, i—k) gave II (e—g, i—k) in somewhat higher yields.

m-Nitro-α,α,α-trifluorotoluene (Ih), *m*-nitroacetophenone (Ii), *m*-nitrobenzophenone (Ij) and 3,5-bis(trifluoromethyl)nitrobenzene (Ik), in which electron-withdrawing groups occupy the positions *meta* to the nitro group provided the expected 2-amino-4-trifluoromethylbenzonitrile (IIh), 2-amino-4-acetylbenzonitrile (IIi), 2-amino-4-benzoylbenzonitrile (IIj), 6-amino-2,4-bis(trifluoromethyl)benzonitrile (IIk), respectively, whereas in the case of nitrobenzene, no reaction occurred and nitrobenzene was recovered unchanged. Although the detailed features of the *o*-aminoaroylnitrile formation remain to be further explored, electron-withdrawing groups seem to facilitate the introduction of a cyano group into the aromatic ring.

The structures of IIa,[6] 6-amino-5-quinolinecarbonitrile (IIc),[5] 1-amino-2-naphthalenecarbonitrile (IIf)[7] and 2-amino-1-naphthalenecarbonitrile (IIg)[3] were confirmed by direct comparison with authentic samples. The structural assignments of II (b, d, e, h—k) were made on the basis of elemental analysis, the spectral data and the following chemical reactions.



II III IV

Chart 2

It is well known that *o*-acylaminoaroylnitriles are converted to condensed pyrimidines by acid or base.[2] On acetylation with acetic anhydride, II (b, d, e, h—j) gave the corresponding *o*-acetamidoaroylnitriles III (b, d, e, h—j), whereas IIk was recovered unchanged under the same conditions. Compound IIk was allowed to react with acetyl chloride in pyridine to give 6-acetamido-2,4-bis(trifluoromethyl)benzonitrile (IIIk). On treatment with hydrogen chloride in ethanol, III (b, d, e, h—k) were cyclized to the corresponding condensed pyrimidines IV (b, d, e, h—k). The structures of IV (b, d, e, h—k) were deduced on the basis of the analytical (Table II) and spectral (Table III) data. The results suggest that the cyano group of II (b, d, e, h—k) occupies the position *ortho* to the amino group. In the proton nuclear magnetic resonance (^{1}H-NMR) spectra of IIi and IIj, the proton signals at C_3 in IIi and IIj appeared as doublets (δ 7.38, J = 1.4 Hz and δ 7.09, J = 1.5 Hz for IIi and IIj, respectively), while the proton signals at C_5 appeared as doublets of doublets (δ 7.12, J = 8.2 Hz and 1.4 Hz and δ 6.89, J = 8.2 Hz and 1.5 Hz for IIi and IIj, respectively), indicating that the cyano groups are attached

to C_1 in IIi and IIj.

On the basis of the present results, this reaction seems to provide a convenient method for synthesizing *o*-aminoaroylnitriles, IIa—k, from the corresponding aromatic nitro compounds, Ia—k.

Experimental

DMF was prepared by distillation from calcium hydride and was stored over molecular sieve 4A. All melting points are uncorrected. Infrared (IR) spectra were recorded on an IRA-2 spectrophotometer. ^{1}H-NMR spectra were taken on a Hitachi R-22 spectrometer at 90 MHz with tetramethylsilane as an internal standard. Mass spectra (MS) were measured with a JEOL model JMS-01SG spectrometer and a JEOL model JMS-D 300 mass spectrometer.

General Procedure for the Preparation of *o*-Aminoaroylnitriles (IIa—k)——A nitro compound (Ia—k: 0.03 mol) was added to a stirred solution of ethyl cyanoacetate and KOH (or KOH and KCN) in the molar ratio shown in Table I in DMF (90 ml), and the mixture was stirred for the specified time at the specified temperature (Table I). After the solvent had been removed *in vacuo*, the residue was hydrolyzed with 10 or 20% HCl or 5% NaOH (60 ml). The reaction mixture was extracted with $CHCl_3$. In the case of acidic hydrolysis, the reaction mixture was basified with 10% NaOH, and extracted with $CHCl_3$. The $CHCl_3$ extract was dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on alumina with $CHCl_3$ as the eluent.

3-Amino-4-quinolinecarbonitrile (IIa): Recrystallization from MeOH gave IIa as slightly yellow needles, mp 221 °C (lit.[6] mp 213—214 °C).

5-Amino-6-quinolinecarbonitrile (IIb): Recrystallization from $CHCl_3$ gave IIb as yellow prisms, mp 209—211 °C. *Anal.* Calcd for $C_{10}H_7N_3$: C, 70.99; H, 4.17; N, 24.84. Found: C, 70.78; H, 3.90; N, 24.45. MS *m/z*: 169 (M^+). IR ν_{max}^{KBr} cm^{-1}: 3400, 3345, 3215 ($-NH_2$), 2190 (CN). ^{1}H-NMR (in DMSO-d_6) δ: 7.09 (2H, br s, $-N\underline{H}_2$), 7.28 (1H, d, $J_{7,8}=9$ Hz, C_7-H), 7.59 (1H, dd, $J_{3,4}=9$, $J_{2,3}=4.5$ Hz, C_3-H), 7.65 (1H, d, $J_{7,8}=9$ Hz, C_8-H), 8.84 (1H, dd, $J_{3,4}=9$, $J_{2,4}=1.5$ Hz, C_4-H), 9.00 (1H, dd, $J_{2,3}=4.5$, $J_{2,4}=1.5$ Hz, C_2-H).

6-Amino-5-quinolinecarbonitrile (IIc): Recrystallization from $CHCl_3$ gave IIc as pale yellow prisms, mp 181 °C (lit.[5] mp 181 °C).

7-Amino-8-quinolinecarbonitrile (IId): Recrystallization from $CHCl_3$ gave IId as yellow prisms, mp 240—242 °C. *Anal.* Calcd for $C_{10}H_7N_3$: C, 70.99; H, 4.17; N, 24.84. Found: C, 71.11; H, 3.96; N, 25.18. MS *m/z*: 169 (M^+). IR ν_{max}^{KBr} cm^{-1}: 3375, 3340, 3200 ($-NH_2$), 2198 (CN). ^{1}H-NMR (in DMSO-d_6) δ: 7.01 (2H, s, $-N\underline{H}_2$), 7.22 (1H, d, $J_{5,6}=9$ Hz, C_6-H), 7.33 (1H, dd, $J_{2,3}=4.5$, $J_{3,4}=9$ Hz, C_3-H), 7.91 (1H, d, $J_{5,6}=9$ Hz, C_5-H), 8.20 (1H, dd, $J_{2,4}=1.5$, $J_{3,4}=9$ Hz, C_4-H), 8.85 (1H, dd, $J_{2,3}=4.5$, $J_{2,4}=1.5$ Hz, C_2-H).

8-Amino-7-quinolinecarbonitrile (IIe): Recrystallization from MeOH gave IIe as yellow prisms, mp 157—159 °C. *Anal.* Calcd for $C_{10}H_7N_3$: C, 70.99; H, 4.17; N, 24.84. Found: C, 71.12; H, 3.99; N, 25.19. MS *m/z*: 169 (M^+). IR ν_{max}^{KBr} cm^{-1}: 3440, 3340, 3200 ($-NH_2$), 2200 (CN). ^{1}H-NMR (in DMSO-d_6) δ: 6.98 (2H, br s, $-N\underline{H}_2$), 7.10 (1H, d, $J_{5,6}=8.5$ Hz, C_6-H), 7.44 (1H, d, $J_{5,6}=8.5$ Hz, C_5-H), 7.64 (1H, dd, $J_{2,3}=4.5$, $J_{3,4}=9$ Hz, C_3-H), 8.57 (1H, dd, $J_{2,4}=1.5$, $J_{3,4}=9$ Hz, C_4-H), 8.86 (1H, dd, $J_{2,3}=4.5$, $J_{2,4}=1.5$ Hz, C_2-H).

1-Amino-2-naphthalenecarbonitrile (IIf): Recrystallization from MeOH gave IIf as colorless columns, mp 108 °C (lit.[7] mp 107—108 °C).

2-Amino-1-naphthalenecarbonitrile (IIg): Recrystallization from $CHCl_3$ gave IIg as colorless scales, mp 131.5 °C (lit.[3] 132—133 °C).

2-Amino-4-trifluoromethylbenzonitrile (IIh): Recrystallization from CH_2Cl_2 gave IIh as pale yellow needles, mp 89—89.5 °C (lit.[8] 86—89 °C). High-resolution MS *m/z*: Calcd for $C_8H_5F_3N_2$, 186.0404. Obsd. 186.0406. IR ν_{max}^{KBr} cm^{-1}: 3440, 3355, 3240 ($-NH_2$), 2200 (CN), 1339, 1174, 1128 (CF_3). ^{1}H-NMR (in DMSO-d_6) δ: 6.55 (2H, br s, $-N\underline{H}_2$), 6.87 (1H, dd, $J=8.5$, 2 Hz, C_5-H), 7.18 (1H, d, $J=2$ Hz, C_3-H), 7.65 (1H, d, $J=8.5$ Hz, C_6-H).

2-Amino-4-acetylbenzonitrile (IIi): Recrystallization from ether gave IIi as yellow prisms, mp 139—140 °C. *Anal.* Calcd for $C_9H_8N_2O$: C, 67.48; H, 5.03; N, 17.49. Found: C, 67.13; H, 4.89; N, 17.27. MS *m/z*: 160 (M^+). IR ν_{max}^{KBr} cm^{-1}: 3420, 3360, 3240 ($-NH_2$), 2200 (CN), 1675 (>CO). ^{1}H-NMR (in DMSO-d_6) δ: 2.54 (3H, s, $-COC\underline{H}_3$), 6.29 (2H, s, $-N\underline{H}_2$), 7.12 (1H, dd, $J=8.2$, 1.4 Hz, C_5-H), 7.38 (1H, d, $J=1.4$ Hz, C_3-H), 7.54 (1H, d, $J=8.2$ Hz, C_6-H).

2-Amino-4-benzoylbenzonitrile (IIj): Recrystallization from CH_2Cl_2 gave IIj as yellow prisms, mp 141—142 °C. *Anal.* Calcd for $C_{14}H_{10}N_2O$: C, 75.65; H, 4.54; N, 12.61. Found: C, 75.61; H, 4.17; N, 12.50. MS *m/z*: 222 (M^+). IR ν_{max}^{KBr} cm^{-1}: 3460, 3380, 3260 ($-NH_2$), 2240 (CN), 1650 (>CO). ^{1}H-NMR (in DMSO-d_6) δ: 6.37 (2H, s, $-N\underline{H}_2$), 6.89 (1H, dd, $J=8.2$, 1.5 Hz, C_5-H), 7.09 (1H, d, $J=1.5$ Hz, C_3-H), 7.44—7.84 (6H, m, aromatic H).

6-Amino-2,4-bis(trifluoromethyl)benzonitrile (IIk): Recrystallization from petr. ether gave IIk as pale yellow plates, mp 84—86 °C. High-resolution MS *m/z*: Calcd for $C_9H_4F_6N_2$, 254.0278. Obsd. 254.0272. IR ν_{max}^{KBr} cm^{-1}: 3520, 3380, 3260 ($-NH_2$), 2240 (CN), 1284, 1182, 1140 (CF_3). ^{1}H-NMR (in DMSO-d_6) δ: 7.10 (1H, s), 7.16 (2H, br s, $-N\underline{H}_2$), 7.47 (1H, s).

Acetylation of II (b, d, e, h—j)——A solution of II (b, d, e, h—j) (5 mmol) in Ac_2O (5 ml) was refluxed for 2 h. After the Ac_2O had been evaporated off under reduced pressure, the residue was poured into ice water. The

TABLE II. Some Properties of III and IV

Compd. No.	Yield (%)	mp (°C) (Recrystn. solvent)	Appearance	Formula	Analysis (%) Calcd (Found)		
					C	H	N
IIIb	50	198—200 (Acetone)	Colorless needles	$C_{12}H_9N_3O$	68.23 (68.30	4.30 4.04	19.90 19.78)
IIId	76	181 (Acetone)	Colorless cotton	$C_{12}H_9N_3O$	68.23 (68.27	4.30 4.03	19.90 19.57)
IIIe	30	212 (Acetone)	Colorless prisms	$C_{12}H_9N_3O$	68.23 (68.44	4.30 4.08	19.90 19.66)
IIIh	84	131—132 (Petr. ether–ether)	Colorless columns	$C_{10}H_7F_3N_2O$	b)		
IIIi	68	130 (Acetone)	Colorless needles	$C_{11}H_{10}N_2O_2$	65.33 (65.44	4.98 4.81	13.86 13.68)
IIIj	91	148—149 (Acetone)	Colorless prisms	$C_{16}H_{12}N_2O_2$	72.71 (72.67	4.58 4.35	10.60 10.40)
IIIk	39	124—125 (Petr. ether–ether)	Colorless prisms	$C_{11}H_6F_6N_2O$	c)		
IVb	70	334—335 (MeOH)	Colorless needles	$C_{12}H_9N_3O$	68.23 (68.49	4.30 4.02	19.90 19.73)
IVd	77	251—252 (MeOH)	Colorless cotton	$C_{12}H_9N_3O$	68.23 (68.22	4.30 4.01	19.90 20.06)
IVe	80	278—280 (MeOH)	Colorless needles	$C_{12}H_9N_3O$	68.23 (67.77	4.30 4.01	19.90 19.43)
IVh	83	234—236 (MeOH)	Colorless needles	$C_{10}H_7F_3N_2O$	d)		
IVi	75	242—243 (MeOH)	Yellow prisms	$C_{11}H_{10}N_2O_2$	65.33 (64.86	4.98 4.95	13.86 13.52)
IVj	64	227—228 (MeOH)	Yellow needles	$C_{16}H_{12}N_2O_2$	72.71 (72.57	4.58 4.32	10.60 10.42)
IVk	19[a)]	221 (Ether)	Colorless needles	$C_{11}H_6F_6N_2O$	e)		

a) 6-Amino-2,4-bis(trifluoromethyl)benzonitrile (IIk: 42%) was isolated as the major product. *b*) High-resolution MS *m/z*: Calcd for $C_{10}H_7F_3N_2O$, 228.05101. Obsd. 228.05165. *c*) High-resolution MS *m/z*: Calcd for $C_{11}H_6F_6N_2O$, 296.03841. Obsd. 296.03801. *d*) High-resolution MS *m/z*: Calcd for $C_{10}H_7F_3N_2O$, 228.05101. Obsd. 228.05217. *e*) High-resolution MS *m/z*: Calcd for $C_{11}H_6F_6N_2O$, 296.03841. Obsd. 296.03838.

precipitate was collected, washed with water, dried, and recrystallized from the solvent indicated in Table II to give III (b, d, e, h—j).

6-Acetamido-2,4-bis(trifluoromethyl)benzonitrile (IIIk)——A solution of IIk (5 mmol) and acetyl chloride (10 mmol) in pyridine (3 ml) was heated at 70 °C for 8 h. The solvent was removed *in vacuo*, and the residue was purified by column chromatography on silica gel with CH_2Cl_2 as the eluent to give IIIk. The yields and the spectral data of III (b, d, e, h—k) are given in Tables II and III.

Conversion of III (b, d, e, h—j) into Condensed Pyrimidines IV (b, d, e, h—j)——A solution of III (b, d, e, h—j) (1 mmol) in abs. EtOH (10 ml) was saturated with dry HCl under ice cooling, and the reaction mixture was refluxed for 1 h. After removal of the EtOH, the residue was basified with aq. NH_4OH. The precipitate was collected, washed with ice water, dried and recrystallized from MeOH to furnish 2-methylpyrido[2,3-*h*]quinazolin-4(3*H*)-one (IVb), 3-methylpyrido[2,3-*f*]quinazolin-1(2*H*)-one (IVd), 2-methylpyrido[3,2-*h*]quinazolin-4(3*H*)-one (IVe), 2-methyl-7-trifluoromethyl-4(3*H*)-quinazolinone (IVh), 7-acetyl-2-methyl-4(3*H*)-quinazolinone (IVi), or 7-benzoyl-2-methyl-4(3*H*)-quinazolinone (IVj).

Preparation of 5,7-Bis(trifluoromethyl)-2-methyl-4(3*H*)-quinazolinone (IVk)——A solution of IIIk (1 mmol) in abs. EtOH (10 ml) was saturated with dry HCl under ice cooling, and then the reaction mixture was refluxed for 1 h.

TABLE III. Some Spectral Data for III and IV

Compd. No.	IR ν_{max}^{KBr} cm^{-1}			^{1}H-NMR spectra (ppm) in DMSO-d_6 solution (J in Hz)
	NH	CN	CO	
IIIb	3235	2210	1660	2.26 (3H, s, >N–COCH$_3$), 7.70 (1H, dd, J=8.5, 4.2, C$_3$-H), 8.00 (1H, d, J=9, C$_7$-H), 8.10 (1H, d, J=9, C$_8$-H), 8.50 (1H, dd, J=8.5, 1.5, C$_4$-H), 9.09 (1H, dd, J=4.2, 1.5, C$_2$-H), 10.57 (1H, br s, >NH)
IIId	3305	2225	1720	2.25 (3H, s, >N–COCH$_3$), 7.62 (1H, dd, J=8.2, 4.2, C$_3$-H), 7.94 (1H, d, J=9, C$_6$-H), 8.25 (1H, d, J=9, C$_5$-H), 8.47 (1H, dd, J=8.2, 2, C$_4$-H), 9.03 (1H, dd, J=4.2, 2, C$_2$-H), 10.50 (1H, br s, >NH)
IIIe	3220	2220	1670 1657	2.28 (3H, s, >N–COCH$_3$), 7.73 (1H, dd, J=8.5, 4.2, C$_3$-H), 7.83 (1H, d, J=8.5, C$_6$-H), 7.98 (1H, d, J=8.5, C$_5$-H), 8.50 (1H, dd, J=8.5, 1.8, C$_4$-H), 9.09 (1H, dd, J=4.2, 1.8, C$_2$-H), 10.49 (1H, br s, >NH)
IIIh	3330 3240	2240	1707	2.18 (3H, s, >N–COCH$_3$), 7.67 (1H, dd, J=8, 2, C$_5$-H), 8.06 (1H, d, J=2, C$_3$-H), 8.07 (1H, d, J=8, C$_6$-H), 10.38 (1H, br s, >NH)
IIIi	3320	2200	1722 1708 1672	2.15 (3H, s, >N–COCH$_3$), 2.62 (3H, s, aromatic COCH$_3$), 7.81 (1H, dd, J=8, 1.5, C$_5$-H), 7.96 (1H, d, J=8, C$_6$-H), 8.08 (1H, d, J=1.5, C$_3$-H), 10.27 (1H, br s, >NH)
IIIj	3340	2225	1705 1648	2.13 (3H, s, >N–COCH$_3$), 7.45—8.08 (8H, m), 10.31 (1H, br s, >NH)
IIIk	3250 3200	2235	1678	2.20 (3H, s, >N–COCH$_3$), 8.04 (1H, s, C$_5$-H), 8.37 (1H, s, C$_3$-H), 10.64 (1H, br s, >NH)
IVb	3155		1670[a]	2.53 (3H, s, C$_2$-CH$_3$), 7.64 (1H, dd, J=8.5, 4.5, C$_9$-H), 7.96 (1H, dd, J=9, 1, C$_6$-H), 8.25 (1H, d, J=9, C$_5$-H), 9.03 (1H, dd, J=4.5, 2, C$_8$-H), 9.18 (1H, ddd, J=8.5, 2, 1, C$_{10}$-H)
IVd	3170		1672[a]	2.46 (3H, s, C$_3$-CH$_3$), 7.62 (1H, dd, J=8.2, 4.5, C$_8$-H), 7.69 (1H, d, J=9, C$_5$-H), 8.25 (1H, d, J=9, C$_6$-H), 8.45 (1H, dd, J=8.2, 2, C$_7$-H), 9.07 (1H, dd, J=4.5, 2, C$_9$-H)
IVe	3170		1678[a]	2.57 (3H, s, C$_2$-CH$_3$), 7.75 (1H, dd, J=8, 4.5, C$_8$-H), 7.88 (1H, d, J=8.5, C$_5$-H), 8.13 (1H, d, J=8.5, C$_6$-H), 8.47 (1H, dd, J=8, 2, C$_7$-H), 9.09 (1H, dd, J=4.5, 2, C$_9$-H)
IVh	3180		1683	2.42 (3H, s, C$_2$-CH$_3$), 7.69 (1H, dd, J=9, 2, C$_6$-H), 7.82 (1H, d, J=2, C$_8$-H), 8.26 (1H, d, J=9, C$_5$-H), 12.43 (1H, br s, >NH)
IVi	3200 3160		1682 1600	2.39 (3H, s, C$_2$-CH$_3$), 2.68 (3H, s, C$_7$-COCH$_3$), 7.86 (1H, dd, J=8, 2, C$_6$-H), 8.06 (1H, d, J=2, C$_8$-H), 8.14 (1H, d, J=8, C$_5$-H), 12.28 (1H, br s, >NH)
IVj	3160		1678 1653	2.40 (3H, s, C$_2$-CH$_3$), 7.45—7.87 (7H, m, C$_{6,8}$-H and -COPh), 8.21 (1H, d, J=8.5, C$_5$-H), 12.34 (1H, br s, >NH)
IVk	3190		1690	2.43 (3H, s, C$_2$-CH$_3$), 7.96 (1H, s, C$_6$-H), 8.13 (1H, s, C$_8$-H), 12.50 (1H, br s, >NH)

Abbreviations: br s, broad singlet; d, doublet; dd, doublet of doublets; m, multiplet; s, singlet. *a*) The amido proton signal could not be detected.

After removal of the EtOH, the residue was basified with aq. NH_4OH. The precipitate was collected, washed with ice water, dried and recrystallized from ether to afford IVk (57 mg, 19%) as colorless needles. The mother liquor of crystallization was evaporated to dryness. The residue was purified by column chromatography on alumina with $CHCl_3$ as the eluent to give IIk (124 mg, 42%). The yields of IV (b, d, e, h—k) are given in Table II and the spectral data are listed in Table III.

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References and Notes

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