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Studies on Pyrazolo[3,4-*d*]pyrimidine Derivatives. XIII.[1] Aryl Migration of 4-Aroyl-1*H*-pyrazolo[3,4-*d*]pyrimidines to 4-Aryl-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidine-4-carboxylic Acids

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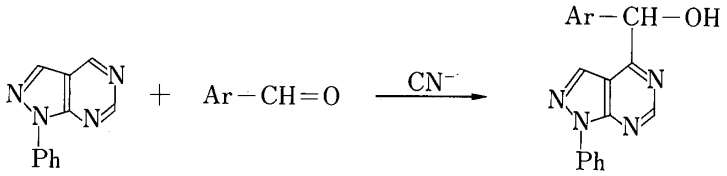
When a mixture of 4-aroyl-1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidines (**3**) and sodium hydroxide in dimethyl sulfoxide (DMSO) was stirred for 1 h at room temperature, migration of the aryl group to the 4-position occurred, *i.e.*, the benzilic acid rearrangement, resulting in the formation of 4-aryl-4,5-dihydro-1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidine-4-carboxylic acids (**4**).

Potassium ferricyanide oxidized the carboxylic acids (**4**) to the corresponding 4-aryl-1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidines (**5**) with elimination of carbon dioxide.

Reaction of **5** with sodium hydroxide in DMSO caused ring fission of the pyrazole portion, to give the corresponding 6-anilino-4-aryl-5-pyrimidinecarbonitriles (**11**).

Keywords——4-aroyl-1*H*-pyrazolo[3,4-*d*]pyrimidine; 4-aryl-4,5-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidine-4-carboxylic acid; 4-aryl-1*H*-pyrazolo[3,4-*d*]pyrimidine; 4-substituted 6-anilino-5-pyrimidinecarbonitrile; aryl migration; benzilic acid rearrangement; ring fission

It has been reported that the chemical properties of the C^4-atom of the 1*H*-pyrazolo[3,4-*d*]pyrimidine ring system are similar to these of the carbonyl carbon.[2] For example, the benzoin type condensation between 1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidine (**1**) and aromatic aldehydes in the presence of cyanide ion results in the formation of α-aryl-1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidine-4-methanols (**2**), as shown in Chart 1.[2] In connection with the



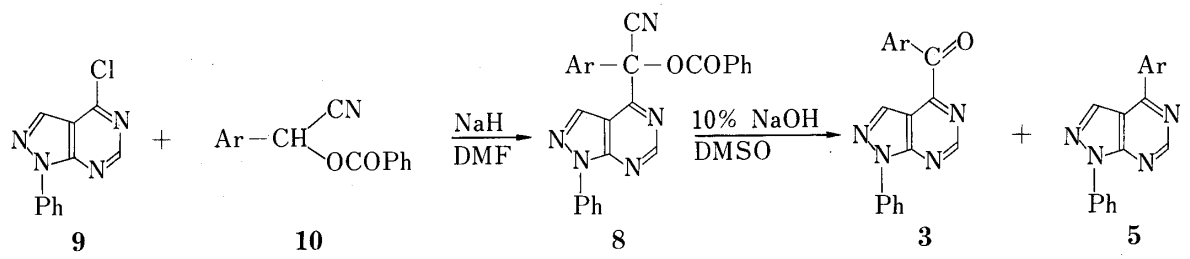
1 **2**

Chart 1

benzoin condensation, it was expected that a benzilic acid rearrangement of 4-aroyl-1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidines (**3**) to 4-aryl-4,5-dihydro-1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidine-4-carboxylic acids (**4**) might proceed. Thus, we carried out the reaction of **3** with sodium hydroxide in dimethyl sulfoxide (DMSO), and found that the aryl group migrates to the C^4 ring carbon, providing **4**. In the course of this study, we also found that ring fission of the pyrazole portion takes place on the reaction of 4-aryl-1-phenyl-1*H*-pyrazolo[3,4-*d*]-pyrimidines (**5**) with sodium hydroxide in DMSO. In the present paper we describe our detailed investigation of the aryl migration and the ring fission.

Hamana *et al.*[3] reported that α-aryl-α-benzoyloxy-2-quinolineacetonitriles (**6**) are easily convertible to the corresponding 2-aroylquinolines (**7**) by alkaline hydrolysis. Application of

this method to α-aryl-α-benzoyloxy-1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidine-4-acetonitriles (**8**), which were easily prepared by the reaction of 4-chloro-1-phenyl-1*H*-pyrazolo[3,4-*d*]-pyrimidine (**9**) with *O*-benzoylmandelonitriles (**10**)[4,5] in the presence of sodium hydroxide in *N,N*-dimethylformamide (DMF), yielded the starting ketones (**3**) except **3b** and **3c**. Thus, **8** was hydrolyzed with sodium hydroxide in DMSO to give the ketones (**3**)[2] together with 4-arylpyrazolopyrimidines (**5**) in poor yields (Tables I and II). Compounds **3b** and **3c** were prepared by benzoin condensation between **1** and the corresponding anisaldehydes, followed by oxidation, as already reported.[2]



a: Ar=C_6H_5, **d**: Ar=*o*-C_6H_4–Cl, **e**: Ar=*p*-C_6H_4–Cl, **f**: Ar=*p*-C_6H_4–Br, **g**: Ar=*p*-C_6H_4–F, **h**: Ar=*p*-C_6H_4–CN, **i**: Ar=*p*-C_6H_4–NO_2

Chart 2

TABLE I. Reaction of **9** with **10** in the Presence of NaH in DMF

9	10	Reaction time (min)	Reaction temp. (°C)[a]	Product	
				8	Yield (%)
9	**10a**	30	r.t.	**8a**	44
9	**10b**	30	r.t.	**8b**	—[b]
9	**10c**	30	r.t.	**8c**	—[b]
9	**10d**	30	40—50	**8d**	33
9	**10e**	30	r.t.	**8e**	58
9	**10f**	30	r.t.	**8f**	60
9	**10g**	30	r.t.	**8g**	58
9	**10h**	30	r.t.	**8h**	57
9	**10i**	10	0	**8i**	60

a) r.t. = room temperature.
b) **8b** and **8c** were not isolated.

TABLE II. Alkaline Hydrolysis of **8** in DMSO

8	Product			
	3	Yield (%)	5	Yield (%)
8a	**3a**	62	**5a**	Trace
8d	**3d**	58	**5d**	3
8e	**3e**	58	**5e**	4
8f	**3f**	56	**5f**	3
8g	**3g**	57	**5g**	2
8h	**3h**	28	**5h**	—[a]
8i	**3i**	20	**5i**	17

a) Compound **5h** was not isolated.

TABLE III. Melting Points and Elemental Analyses of **3**, **4**, **5**, and **8**

Compd.	mp (°C)	Formula	Analysis (%) Calcd (Found)			MS *m/e* M^+
			C	H	N	
3f	180[a]	$C_{18}H_{11}BrN_4O$	57.01	2.92	14.77	
			(56.56	2.96	14.70)	
3g	152—153[a]	$C_{18}H_{11}FN_4O$	67.92	3.48	17.60	
			(68.26	3.64	17.68)	
3h	208[a]	$C_{19}H_{11}N_5O$	70.15	3.41	21.53	
			(70.24	3.65	21.15)	
4a	249—250[b]	$C_{18}H_{14}N_4O_2$	67.91	4.43	17.60	
			(67.73	4.50	17.35)	
4b	230—232[b]	$C_{19}H_{16}N_4O_3$	65.51	4.63	16.08	
			(65.43	4.63	16.16)	
4c	244—245[b]	$C_{19}H_{16}N_4O_3$	65.51	4.63	16.08	
			(65.11	4.68	15.98)	
4d	219—220[b]	$C_{18}H_{13}ClN_4O_2$	61.28	3.71	15.88	
			(60.88	3.80	15.65)	
4e	231[b]	$C_{18}H_{13}ClN_4O_2$	61.28	3.71	15.88	
			(60.71	3.89	15.77)	
4f	223—225[b]	$C_{18}H_{13}BrN_4O_2$	54.42	3.30	14.10	
			(53.95	3.41	14.07)	
4g	229—230[b]	$C_{18}H_{13}FN_4O_2$	64.28	3.90	16.66	
			(63.99	3.95	16.61)	
4h	178—179[b]	$C_{19}H_{13}N_5O_2$	66.46	3.82	20.40	
			(65.59	3.98	20.21)	
5b	143—145[d]	$C_{18}H_{14}N_4O$	71.51	4.67	18.53	
			(71.64	4.68	18.68)	
5c	150—151[d]	$C_{18}H_{14}N_4O$	71.51	4.67	18.53	
			(71.49	4.70	18.51)	
5d	98—100[d]	$C_{17}H_{11}ClN_4$	66.56	3.61	18.26	
			(66.55	3.75	18.17)	
5e	188—190[d]	$C_{17}H_{11}ClN_4$	66.56	3.61	18.26	
			(66.56	3.72	18.40)	
5f	209—210[d]	$C_{17}H_{11}BrN_4$	58.14	3.16	15.95	
			(58.11	3.18	15.93)	
5g	148—149[d]	$C_{17}H_{11}FN_4$	70.34	3.82	19.30	
			(69.93	3.99	19.04)	
5h	235—237[c]	$C_{18}H_{11}N_5$	72.71	3.73	23.56	
			(72.40	3.68	23.50)	
5i	235—236[a]	$C_{17}H_{11}N_5O_2$	64.35	3.49	22.07	
			(64.44	3.60	22.04)	
8a[f]	106—110[b]	$C_{26}H_{17}N_5O_2$ $1/2C_6H_6$	74.03	4.28	14.88	431
			(73.83	4.28	14.83)	
8d	161—163[b]	$C_{26}H_{16}ClN_5O_2$	67.03	3.46	15.03	
			(67.05	3.45	15.29)	
8e	190—191[b]	$C_{26}H_{16}ClN_5O_2$	67.03	3.46	15.03	
			(66.98	3.51	14.91)	
8f	178—179[e]	$C_{26}H_{16}BrN_5O_2$	61.19	3.16	13.72	
			(60.83	3.21	13.96)	
8g	170—171[b]	$C_{26}H_{16}FN_5O_2$	69.48	3.59	15.58	
			(69.17	3.65	15.53)	
8h	167—168[e]	$C_{27}H_{16}N_6O_2$	71.04	3.53	18.41	
			(71.32	3.71	18.28)	
8i	182—185[b]	$C_{26}H_{16}N_6O_4$	65.54	3.39	17.64	476
			(64.84	3.44	17.66)	

a) Yellow needles. *b*) Colorless prisms. *c*) Slightly yellow prisms.
d) Colorless needles. *e*) Colorless scales. *f*) Recrystallization from petr. ether–benzene.

TABLE IV. IR and NMR Spectral Data for **3**, **4**, **5**, and **8**

Compd.	IR ν_{max}^{KBr} cm^{-1}	NMR (in $CDCl_3$) ppm[a]					
		C^3–H (s)	C^6–H (s)	Aromatic H (m)	NH (br s)	OH (br s)	OCH_3 (s)
3f	1670 (C=O)	8.58	9.12	7.16—8.29 (9H)			
3g	1660 (C=O)	8.61	9.18	6.98—8.58 (9H)			
3h[b]	1670 (C=O), 2250 (C≡N)	8.50	9.33	7.42—8.22 (9H)			
4a[c]	1720 (C=O), 3300 (NH or OH)	7.50	—[d]	6.90—8.07 (12H)	—[d]	8.82	
4b[c]	1720 (C=O), 3335 (NH or OH)	7.32	—[d]	6.55—8.06 (11H)	—[d]	8.15	3.77
4c[c]	1720 (C=O), 3200 (NH or OH)	7.52	—[d]	6.78—8.10 (11H)	—[d]	8.84	3.71
4d[c]	1720 (C=O), 3330 (NH or OH)	7.38	—[d]	7.00—8.15 (10H)	6.12	8.41	
4e[c]	1720 (C=O), 3200 (NH or OH)	7.48	—[d]	6.85—8.00 (12H)	—[d]	—[d]	
4f[c]	1720 (C=O), 3200 (NH or OH)	—[d]	—[d]	6.91—7.91 (12H)	—[d]	8.80	
4g[c]	1638 (C=O), 3200 (NH or OH)	7.46	—[d]	6.86—8.11 (11H)	6.13	—[d]	
4h[c]	1640 (C=O), 2250 (C≡N), 3200 (NH or OH)	—[d]	—[d]	6.81—8.13 (13H)	—[d]	—[d]	
5b		8.11	9.04	6.89—8.30 (9H)			3.82
5c		8.39	8.98	6.92—8.37 (9H)			3.85
5d		8.09	9.07	7.07—8.30 (9H)			
5e		8.37	9.00	7.15—8.30 (9H)			
5f		8.38	9.02	7.14—8.28 (9H)			
5g		8.30	8.98	6.92—8.27 (9H)			
5h[b]	2225 (C≡N)	8.97	9.21	7.10—8.46 (9H)			
5i[c]	1350, 1520 (NO_2)	8.47	8.72	7.07—8.32 (9H)			
8a	1740 (C=O)	8.27	8.99	7.11—8.23 (15H)			
8d	1745 (C=O)	8.35	8.94	7.08—8.29 (14H)			
8e	1745 (C=O)	8.30	8.98	7.12—8.23 (14H)			
8f	1750 (C=O)	8.28	8.97	7.06—8.23 (14H)			
8g	1725 (C=O)	8.40	8.99	6.86—8.25 (14H)			
8h	1735 (C=O), 2250 (C≡N)	8.31	8.95	7.14—8.25 (14H)			
8i	1740 (C=O), 1350, 1520 (NO_2)	8.42	9.04	7.00—8.30 (14H)			

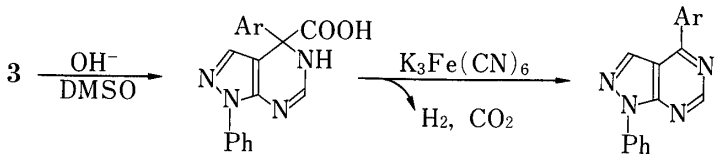
a) br s, broad singlet; m, multiplet; s, singlet.
b) NMR in CF_3COOD.
c) NMR in DMSO-d_6.
d) Overlapping with aromatic H.

The compounds **3a**—**3e**, **3i**, and **5a** thus obtained were identified by comparison with authentic specimens prepared by other routes.[1,2,6] The structures of **3f**—**3h**, **8a**, and **8d**—**8i** were suggested by their elemental analyses (Table III) and confirmed by analyses of their infrared (IR) absorption and nuclear magnetic resonance (NMR) spectra (Table IV). The IR spectra of **8** did not show any absorption band of the cyano group. This is compatible with the reported absence of the absorption band of a cyano group located at an electron-deficient carbon, such as in *O*-benzoyl-*p*-nitromandelonitrile (**10i**).[5]

Even if the yield were poor, the formation of 4-arylpyrazolopyrimidines (**5**) seems to

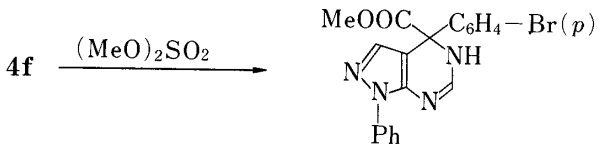
originate from the aryl migration of the ketones (**3**). This strongly supported our expectation, described in the introduction, that the benzilic acid rearrangement of the ketones (**3**) may proceed, and therefore we carried out the following experiments.

When a mixture of the ketones (**3**) and sodium hydroxide in DMSO was stirred, migration of the aryl group occurred, resulting in the formation of the corresponding acids (**4**) in good yields (Table V). The acids (**4**) formed their sodium salts with aqueous sodium carbonate, and were easily convertible to the corresponding 4-arylpyrazolopyrimidines (**5**) in high yields by potassium ferricyanide oxidation with elimination of carbon dioxide (Table VI). Dimethyl sulfate reacted with **4f** to give the corresponding methyl ester (**12f**). Based on the results obtained in the above experiments, as well as the elemental analyses (Table III) and the spectral data (Table IV), the structures of **4** and **5** were confirmed.



4 **5**

a: Ar=C_6H_5, **b**: Ar=*o*-C_6H_4–OMe, **c**: Ar=*p*-C_6H_4–OMe, **d**: Ar=*o*-C_6H_4–Cl, **e**: Ar=*p*-C_6H_4–Cl, **f**: Ar=*p*-C_6H_4–Br, **g**: Ar=*p*-C_6H_4–F, **h**: Ar=*p*-C_6H_4–CN



12f

Chart 3

TABLE V. Aryl Migration of **3** to **4** with OH^- in DMSO

3	Product	
	4	Yield (%)
3a	**4a**	86
3b	**4b**	83
3c	**4c**	59
3d	**4d**	84
3e	**4e**	90
3f	**4f**	82
3g	**4g**	86
3h	**4h**	82
3i	**5i**	22
	4i	54

TABLE VI. Oxidation of **4** with $K_3Fe(CN)_6$ to **5**

4	Product	
	5	Yield (%)
4a	**5a**	85
4b	**5b**	82
4c	**5c**	81
4d	**5d**	75
4e	**5e**	81
4f	**5f**	83
4g	**5g**	81
4h	**5h**	72

This migration can be considered to be a type of benzilic acid rearrangement.[7,8] The aryl group of the anion (A), which is generated by the equilibrium between the ketones (**3**) and a strong base such as hydroxide ion in DMSO,[9] undergoes a 1, 2 shift, in which the migration terminus is the slightly electron-deficient C^4 ring atom,[2,6] leading to the salt of the carboxylic acids (**4**), as shown in Chart 4.

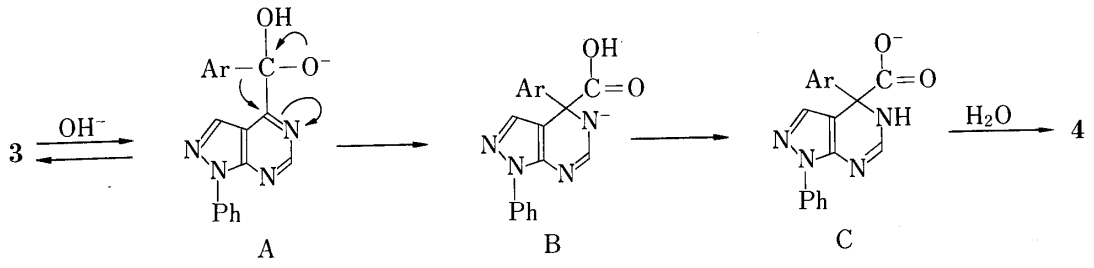


Chart 4

However, in the case of the *p*-nitrobenzoyl derivative (**3i**) the corresponding carboxylic acid (**4i**) was not isolated, and 4-(*p*-nitrophenyl)pyrazolopyrimidine (**5i**, 22%) was obtained together with 6-anilino-4-(*p*-nitrophenyl)-5-pyrimidinecarbonitrile (**11i**, 54%). It is assumed that the first step in the reaction is formation of the carboxylic acid (**4i**), which could not be isolated due to its high susceptibility to oxidation. Subsequent oxidation of **4i** with elimination of carbon dioxide presumably yields **5i**. Compound **11i** seems to be formed by ring fission between N^1 and N^2 of the resulting **5i** (Chart 5).

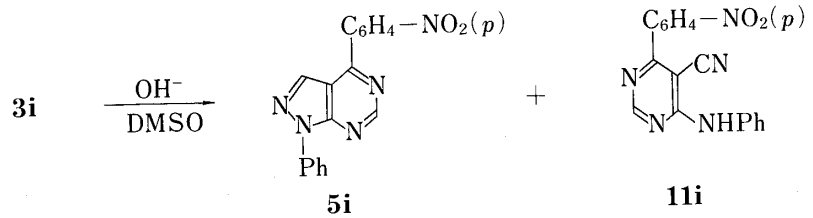
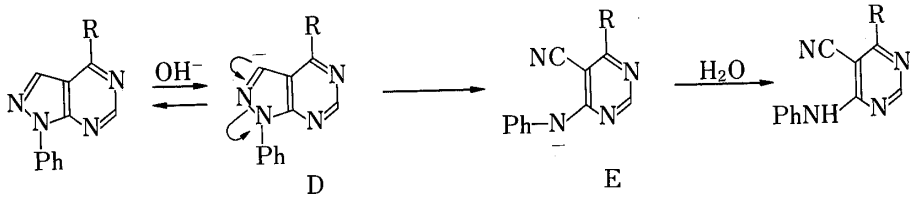


Chart 5

We were interested in this ring fission, and carried out the following experiments. Thus, when a mixture of 4-substituted pyrazolopyrimidines (**1**, **5a**, **5c**, **5i**, and **5j**) and sodium hydroxide in DMSO was stirred, ring fission occurred and the corresponding 4-substituted pyrimidinecarbonitriles (**11k**, **11a**, **11c**, **11i**, and **11j**) were obtained in good yields.



	R	
1	H	**11k**
5a	C_6H_5	**11a**
5c	*p*-C_6H_4–OMe	**11c**
5i	*p*-C_6H_4–NO_2	**11i**
5j	Me	**11j**

Chart 6

Compounds **11a** and **11k** were identified by comparison with corresponding authentic specimens prepared by other routes.[10,11] The structures **11c**, **11i**, and **11j** were suggested by their elemental analyses, and confirmed by analyses of their IR and NMR spectra, as described later.

No reaction was observed when the 3-methyl derivative of **1** (**13**)[12] was subjected to the same ring fission, supporting the proposed mechanism (Chart 6), which involves the ring fission between N^1 and N^2 of the initially formed anion (D).

Experimental

All melting points are uncorrected. IR spectra were recorded on a Jasco IRA-1 grating IR spectrometer. NMR spectra were measured at 60 Mc and 23 °C on a Hitachi R-24 high resolution NMR spectrometer using tetramethylsilane as an internal standard. Mass spectra (MS) were recorded on a Hitachi RMS-4 mass spectrometer. Samples were vaporized in a direct inlet system.

***O*-Benzoylmandelonitriles (10)**——These compounds (**10**) were prepared according to the method reported by Francis *et al.*[4] A mixture of 10 mmol of aromatic aldehydes, 10 mmol of BzCl and 10 mmol of KCN in 5 ml of H_2O was vigorously shaken for 30 min at room temperature. The separated crystals were collected, washed with H_2O, dried, and recrystallized from petr. ether to give **10**.

O-Benzoyl-*o*-chloromandelonitrile (**10d**): mp 51—53 °C, yield 83%. *Anal.* Calcd for $C_{15}H_{10}ClNO_2$: C, 66.31; H, 3.71; N, 5.16. Found: C, 66.22; H, 3.61; N, 5.11. IR ν_{max}^{KBr} cm^{-1}: 1740 (C=O). NMR (in $CDCl_3$) ppm: 6.84 (1H, s, Ar–CH<(CN, O–)), 7.12—8.21 (9H, m, aromatic H).

O-Benzoyl-*p*-bromomandelonitrile (**10f**): mp 55—56 °C, yield 63%. *Anal.* Calcd for $C_{15}H_{10}BrNO_2$: C, 56.98; H, 3.19; N, 4.43. Found: C, 57.36; H, 3.26; N, 4.49. IR ν_{max}^{KBr} cm^{-1}: 1735 (C=O), NMR (in $CDCl_3$) ppm: 6.53 (1H, s, Ar–CH<(CN, O–)), 7.09—8.19 (9H, m, aromatic H).

O-Benzoyl-*p*-fluoromandelonitrile (**10g**): mp 70—71 °C, yield 71%. *Anal.* Calcd for $C_{15}H_{10}FNO_2$: C, 70.58; H, 3.95; N, 5.49. Found: C, 70.59; H, 4.04; N, 5.48. IR ν_{max}^{KBr} cm^{-1}: 1735 (C=O). NMR (in $CDCl_3$) ppm: 6.58 (1H, s, Ar–CH<(CN, O–)), 6.90—8.14 (9H, m, aromatic H).

O-Benzoyl-*p*-cyanomandelonitrile (**10h**): mp 99—100 °C, yield 59%. *Anal.* Calcd for $C_{16}H_{10}N_2O_2$: C, 73.27; H, 3.84; N, 10.68. Found: C, 73.25; H, 3.85; N, 10.69. IR ν_{max}^{KBr} cm^{-1}: 1740 (C=O), 2250 (C≡N). NMR (in $CDCl_3$) ppm: 6.64 (1H, s, Ar–CH<(CN, O–)), 7.03—8.15 (9H, m, aromatic H).

α-Aryl-α-benzoyloxy-1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidine-4-acetonitriles (8)——A mixture of 1.15 g (5 mmol) of 4-chloro-1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidine (**9**), 5 mmol of **10**, and 0.24 g (5 mmol) of NaH (50% in oil) in 25 ml of DMF was stirred under the reaction conditions described in Table I. The reaction mixture was poured into an excess of ice–H_2O mixture, and the separated crystals were collected and extracted with $CHCl_3$. The extract was washed with H_2O, dried over Na_2SO_4, and chromatographed on a column of SiO_2. Elution with benzene gave **8**, which was purified by recrystallization from $CHCl_3$–MeOH. The yields are shown in Table I, the melting points and elemental analysis data in Table III, and spectral data in Table IV.

Hydrolysis of 8——A mixture of 1 mmol of **8** and 1 ml of 10% NaOH in 12 ml of DMSO was stirred for 1 h at room temperature. The reaction mixture was poured into an excess of ice–H_2O mixture. The separated crystals were collected, and extracted with $CHCl_3$. The extract was washed with H_2O, dried over Na_2SO_4, and chromatographed on a column of SiO_2. The first elution with benzene gave the ketones (**3**) which were recrystallized from petr. ether–benzene. The second elution gave **5**, which was recrystallized from petr. ether or benzene.

The yields of **3** and **5** are shown in Table II, melting points and elemental analysis data in Table III, and spectral data in Table IV.

4-Aryl-4,5-dihydro-1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidine-4-carboxylic Acids (4)——A mixture of 1 mmol of **3** and 1 ml of 50% NaOH in 12 ml of DMSO was stirred for 1 h at room temperature. The reaction mixture was poured into an excess of ice–H_2O, neutralized with AcOH, and allowed to stand for 1 d at room temperature. The separated crystals were collected, washed with H_2O, dried, and recrystallized from MeOH to give **4**. The yields are shown in Table V, melting points and elemental analysis data in Table III, and spectral data in Table IV.

Oxidation of 4 with $K_3Fe(CN)_6$——A solution of 500 mg of $K_3Fe(CN)_6$ in 5 ml of H_2O was added to a mixture of 100 mg of **4**, 12 ml of benzene, and 1 ml of 50% NaOH, and the mixture was vigorously shaken for 1 h at room temperature. The benzene solution was dried over Na_2SO_4, and evaporation of the benzene gave 4-aryl-1*H*-pyrazolo[3,4-*d*]pyrimidines (**5**). The yields are listed in Table VI.

Methyl 4-(*p*-Bromophenyl)-4,5-dihydro-1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidine-4-carboxylate (12f)——A solution of 100 mg (0.25 mmol) of **4f** and 288 mg (3 mmol) of dimethyl sulfate dissolved in sodium methoxide solution (45 mg (2 mmol) of Na in 14 ml of MeOH) was refluxed for 1.5 h. After removal of MeOH under reduced pressure, the residue was neutralized with 2 N Na_2CO_3 and extracted with $CHCl_3$. The $CHCl_3$ extract was washed with H_2O, dried over Na_2SO_4, and chromatographed on a column of Al_2O_3. The first elution with $CHCl_3$ gave **12f**, as a yellow oil, in 37% yield (40 mg). MS *m/e*: 410 (M^+), 412 ($M^+ + 2$). IR ν_{max}^{neat} cm^{-1}: 1740 (C=O). NMR (in $CDCl_3$) ppm: 7.49 (1H, s, C^3–H), 7.00—7.90 (11H, m, aromatic H and NH), 3.81 (3H, s, OCH_3).

Reaction of 4-(*p*-Nitrobenzoyl)-1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidine (3i) with NaOH in DMSO——A mixture of 345 mg (1 mmol) of **3i** and 1 ml of 50% NaOH in 12 ml of DMSO was stirred for 1 h at room temperature. The reaction mixture was poured into an excess of ice–H_2O mixture. The separated crystals were collected, washed with H_2O, dried, and recrystallized from benzene to give 4-(*p*-nitrophenyl)-1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidine (**5i**),

mp 235—236 °C, as yellow needles in 22% yield (70 mg). Elemental analysis data are shown in Table III, and spectral data in Table IV.

The separated crystals, obtained by neutralization of the filtrate with AcOH, were collected, washed with H_2O, dried, and recrystallized from $CHCl_3$–MeOH to give 6-anilino-4-(*p*-nitrophenyl)-5-pyrimidinecarbonitrile (**11i**), mp 226—227 °C, as yellow needles in 54% yield (170 mg). *Anal.* Calcd for $C_{17}H_{11}N_5O_2$: C, 64.35; H, 3.49; N, 22.07; Found: C, 63.98; H, 3.61; N, 21.94. IR ν_{max}^{KBr} cm^{-1}: 1350, 1520 (NO_2), 2220 (C≡N), 3325 (NH). NMR (in DMSO-d_6) ppm: 9.38 (1H, br s, exchangeable with D_2O, NH), 8.68 (1H, s, C^2–H), 7.80—8.46 (9H, m, aromatic H).

4-Substituted 6-Anilino-5-pyrimidinecarbonitriles (11)——A mixture of 1 mmol of 4-substituted 1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidines and 1 ml of 50% NaOH in 12 ml of DMSO was stirred for 3 h at room temperature. The reaction mixture was poured into an excess of ice–H_2O mixture, and neutralized with AcOH. The separated crystals were collected, washed with H_2O, and recrystallized from benzene to give the corresponding 4-substituted 6-anilino-5-pyrimidinecarbonitriles (**11**).

From 1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidine (**1**), 4-anilino-5-pyrimidinecarbonitrile (**11k**),[11] mp 171—173 °C, was obtained as yellow needles in 61% yield.

From **5a**, 6-anilino-4-phenyl-5-pyrimidinecarbonitrile (**11a**),[10] mp 236—238 °C, was obtained as colorless scales in 79% yield.

From **5c**, 6-anilino-4-(*p*-methoxyphenyl)-5-pyrimidinecarbonitrile (**11c**), mp 209—211 °C, was obtained as colorless needles in 81% yield. *Anal.* Calcd for $C_{18}H_{14}N_4O$: C, 71.51; H, 4.67; N, 18.53. Found: C, 71.66; H, 4.64; N, 18.55. IR ν_{max}^{KBr} cm^{-1}: 2220 (C≡N), 3330 (NH). NMR (in DMSO-d_6) ppm: 9.41 (1H, br s, exchangeable with D_2O, NH), 8.45 (1H, s, C^2–H), 6.83—8.70 (9H, m, aromatic H), 3.77 (3H, s, OCH_3).

From **5i**, **11i** was obtained in 83% yield.

From 4-methyl-1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidine (**5j**), 6-anilino-4-methyl-5-pyrimidinecarbonitrile (**11j**), mp 154—155 °C, was obtained as yellow needles from petr. ether–benzene in 59% yield. *Anal.* Calcd for $C_{12}H_{10}N_4$: C, 68.55; H, 4.79; N, 26.65. Found: C, 68.87; H, 4.75; N, 26.59. IR ν_{max}^{KBr} cm^{-1}: 2230 (C≡N), 3310 (NH). NMR (in $CDCl_3$) ppm: 8.52 (1H, s, C^2–H), 7.04—7.62 (6H, m, aromatic H and NH), 2.54 (3H, s, CH_3).

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References and Notes

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