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Studies on Aromatic Nitro Compounds. III.[1] Reaction of 2-Nitronaphthalene and 6-Nitroquinoline with Malononitrile in the Presence of Amine

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The reactions of 2-nitronaphthalene (I) and 6-nitroquinoline (IV) with malononitrile in the presence of an amine were examined. I reacted with malononitrile and morpholine to form 4-(1-cyano-2-naphthylcarbamoyl)morpholine (IIIa) in 43% yield. When piperidine or pyrrolidine was used in place of morpholine, I yielded the urea derivative (IIIb or IIIc) corresponding to IIIa. From the reaction of I with cyclohexylamine, the urea derivative (IIId) and 2-cyclohexyl-1-imino-3-oxo-1,2,3,4-tetrahydrobenzo[*f*]quinazoline (VIIId) were obtained in yields of 25 and 24%, respectively. On the other hand, the reaction of I with benzylamine gave only the quinazoline derivative (VIIIe) corresponding to VIIId. Similarly, IV reacted with malononitrile and an amine to give the corresponding urea and/or quinazoline derivatives (Va—d and/or Xd, e). The structures of III, V, VIII and X were confirmed by comparison with authentic samples prepared by an alternative route.

Keywords——2-nitronaphthalene; 6-nitroquinoline; amines; malononitrile; urea derivatives; quinazoline derivatives; 2-ethoxycarbonylaminonaphthalene-1-carbonitrile; 6-ethoxycarbonylaminoquinoline-5-carbonitrile

Dieckmann *et al.*[2] have reported that phenylcarbamoyl cyanide reacts with aniline to form diphenylurea. In the preceding paper[1] we showed that the reaction of 2-nitronaphthalene (I) with malononitrile in the presence of potassium hydroxide gives the potassium salt of 1,1-dicyano-2-hydroxy-2-(1-cyano-2-naphthylamino)ethylene *via* the intermediate (II), 1-cyano-2-naphthylcarbamoyl cyanide, as shown in Chart 1.

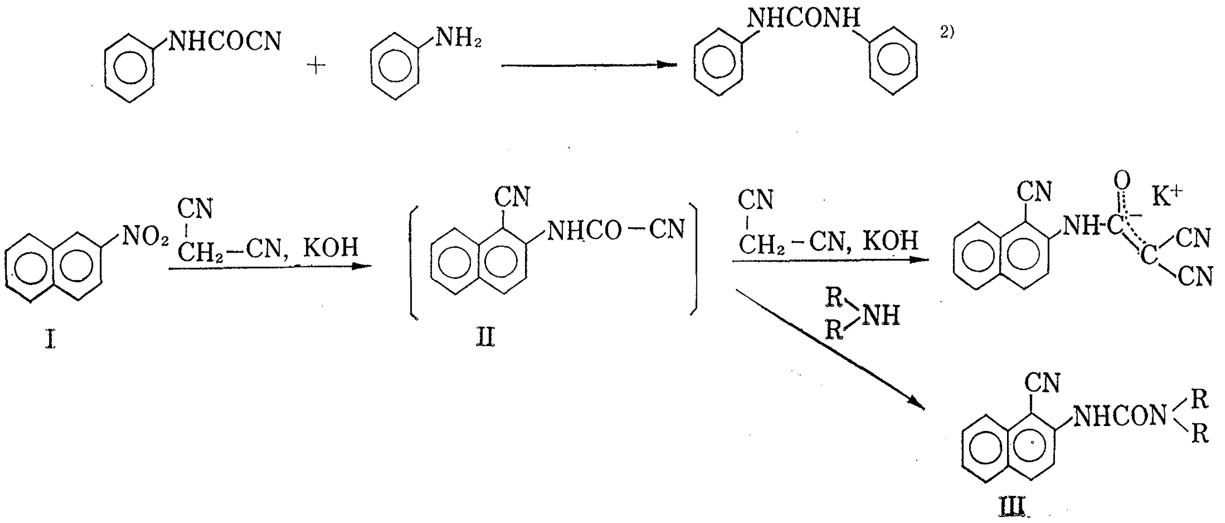


Chart 1

The proposed intermediacy of II suggests the possibility that when this reaction is carried out in the presence of an amine, II initially formed may react with an amine to produce a urea derivative (III). The present paper deals with the reactions of 2-nitronaphthalene and 6-nitroquinoline with malononitrile and an amine.

When I was treated with malononitrile, morpholine and potassium hydroxide in dimethylformamide (DMF) at room temperature for 24 hr, 4-(1-cyano-2-naphthylcarbamoyl)morpholine (IIIa), colorless needles, mp 210°, was obtained. The use of I, malononitrile, morpholine and potassium hydroxide in a 1: 1.2: 3: 2 molar ratio gave IIIa in the best yield (43%) (Table I). Therefore, these conditions were also used in the case of the other amines.

Table I. Reaction[a] of 2-Nitronaphthalene with Malononitrile, Morpholine and Potassium Hydroxide

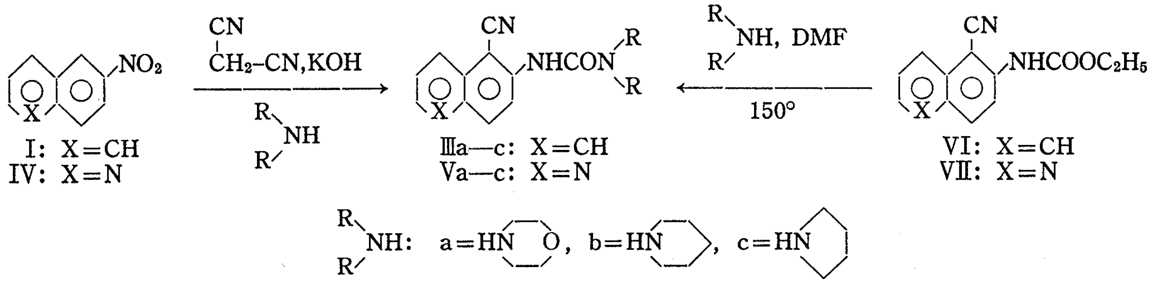
Ia	Molar ratio			Yield of IIIa (%)
	$CH_2(CN)_2$	KOH	 HN O	
1	1.2	1	3	14
1	1.2	2	2	22
1	1.2	2	3	43
1	1.2	3	3	5

a) All reactions were carried out in DMF with stirring for 24 hr at room temperature.

The infrared (IR) spectrum of IIIa displayed a nitrile band at 2200 cm^{-1} and a carbonyl band at 1640 cm^{-1}, and its proton magnetic resonance (PMR) spectrum revealed a pair of one-proton doublets at δ 7.62 (J=9 Hz) and δ 8.18 (J=9 Hz) due to the C_3- and C_4-protons of the naphthalene ring, a multiplet at δ 7.52—8.16 assignable to four protons of C_5—C_8, and a broad singlet at δ 9.05 due to an amine proton, besides the morpholine proton signals. These data are consistent with the proposed structure. Furthermore, the structure of IIIa was confirmed by comparison with an authentic sample prepared from 2-ethoxycarbonylaminonaphthalene-1-carbonitrile by the method described later in this paper.

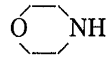
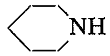
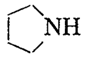
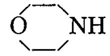
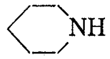
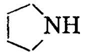
Piperidine and pyrrolidine reacted with I under the same conditions to form 1-(1-cyano-2-naphthylcarbamoyl)-piperidine (IIIb) and -pyrrolidine (IIIc) in 56 and 58% yields, respectively.

Similarly, the reactions of 6-nitroquinoline (IV) with morpholine, piperidine and pyrrolidine proceeded to give 4-(5-cyano-6-quinolylcarbamoyl)morpholine (Va), 1-(5-cyano-6-quinolylcarbamoyl)-piperidine (Vb) and -pyrrolidine (Vc) in 48, 54 and 39% yields, respectively. Some properties of III and V are shown in Table II, and their spectral data are listed in Tables III and IV.



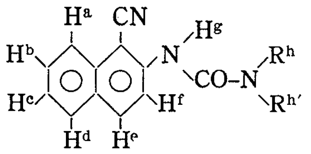
In order to confirm the structures of III and V, we synthesized III and V by an alternative route. A solution of 2-ethoxycarbonylaminonaphthalene-1-carbonitrile[1)] (VI) and morpholine (2 equiv.) in DMF was heated at 150° for 3 hr, yielding the desired IIIa in 83% yield. VI similarly reacted with piperidine and pyrrolidine to produce IIIb and IIIc in yields of 79 and 78%, respectively. In a similar manner, 6-ethoxycarbonylaminoquinoline-5-carbonitrile (VII) prepared from 6-aminoquinoline-5-carbonitrile[3)] provided Va, Vb and Vc in 54, 76 and 89% yields, respectively.

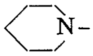
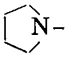
TABLE II. Some Properties of III and V

Compd. No.	R\NH/R'	Yield (%)	mp (°C)[a] ( ): Recrystn. solvent	Formula	Analysis (%) Calcd (Found) C	H	N
IIIa		43	210 (acetone)	$C_{16}H_{15}N_3O_2$	68.31 (68.14	5.38 5.39	14.94 14.65)
IIIb		56	177 (acetone)	$C_{17}H_{17}N_3O$	73.09 (72.72	6.13 6.12	15.04 14.86)
IIIc		58	161 (acetone–petr. benzine)	$C_{16}H_{15}N_3O$	72.43 (72.43	5.70 5.61	15.84 15.90)
Va		48	160 (ether)	$C_{15}H_{14}N_4O_2$	63.82 (63.87	5.00 4.94	19.85 19.94)
Vb		54	185—186 (acetone)	$C_{16}H_{16}N_4O$	68.55 (68.77	5.75 5.69	19.99 20.15)
Vc		39	163—164 (benzene–*n*-hexane)	$C_{15}H_{14}N_4O$	67.65 (67.77	5.30 5.24	21.04 21.14)

a) All compounds are colorless needles.

TABLE III. Some Spectral Data for III

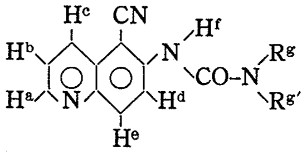


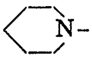
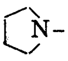
Compd. No.	R\N/R'	IR ν_{max}^{KBr} cm^{-1} NH	CN	CO	Proton NMR spectra (ppm) in DMSO-d_6 solution (J in Hz) Hᵉ	Hᶠ	Hª	Hᵈ	Hᵇ	Hᶜ	Hᵍ	Hʰʰ'	MS m/e (M⁺)
IIIa		3240	2200	1640	8.18 7.62 (d, $J_{e,f}=9$)		7.90—8.10 (m)		7.52—7.90 (m)		9.05 (br. s)	3.44—3.81 (8H, m)	281
IIIb		3260	2200	1640	8.15 7.62 (d, $J_{e,f}=9$)		7.88—8.18 (m)		7.46—7.88 (m)		9.05 (br. s)	1.60(6H, m) 3.52(4H, m)	279
IIIc		3370	2200	1680	8.17 7.86 (d, $J_{e,f}=9$)		7.89—8.11 (m)		7.46—7.78 (m)		8.61 (br. s)	1.80—2.18 (4H, m) 3.25—3.68 (4H, m)	265

Abbreviations: d, doublet; br.s, broad singlet; m, multiplet.

Subsequently, the reactions of I and IV with a primary amine were examined (Chart 2). The treatment of I with cyclohexylamine, malononitrile and potassium hydroxide afforded N-cyclohexyl-N'-(1-cyano-2-naphthyl)urea (IIId) and 2-cyclohexyl-1-imino-3-oxo-1,2,3,4-tetrahydrobenzo[*f*]quinazoline (VIIId) in yields of 25 and 24%, respectively. Although VIIId had the molecular composition $C_{18}H_{19}N_3O$, which is the same as that of IIId, VIIId was obviously not identical with the latter compound. The IR spectrum of VIIId exhibited an absorption band at 1690 cm^{-1} indicative of a carbonyl group, but lacked a characteristic nitrile band. Taylor *et al.*[4] have reported that treatment of N-phenyl-N'-methyl-N'-(*o*-cyanophenyl)urea with sodium methoxide affords 1-methyl-2-oxo-3-phenyl-4-imino-1,2,3,4-tetrahydroquinazoline, which is converted to 1-methyl-2,4-dioxo-3-phenyl-1,2,3,4-tetrahydroquinazoline on hydrolysis. Therefore, these findings suggest that IIId underwent intramolecular cyclization to VIIId. In fact, IIId was readily cyclized to VIIId in 77% yield by treatment with sodium ethoxide in refluxing ethanol. VIIId was further hydrolyzed to 2-cyclohexyl-1,3-dioxo-1,2,3,4-tetrahydrobenzo[*f*]quinazoline (IXd) when heated with hydrochloric acid. The structure of IXd was confirmed by comparison with an authentic sample.[1] Simil-

Table IV. Some Spectral Data for V



Compd. No.	R\N/R	IR ν_{max}^{KBr} cm^{-1} NH	CN	CO	Proton NMR spectra (ppm) in $CDCl_3$ solution (J in Hz) H^a	H^b	H^c	H^d	H^e	H^f	H$^{g'}$	MS m/e (M$^+$)
Va		3180	2200	1628	8.89 (d, $J_{d,e}$=9.5) (d.d, $J_{a,b}$=4.5, $J_{a,c}$=1.5, Jb, c=9.5)	7.50	8.28	8.21	8.61	7.37 (br. s)	3.55—3.66(4H, m) 3.76—3.87(4H, m)	282
Vb		3240	2200	1640	8.81 (d, $J_{d,e}$=9.5) (d.d, $J_{a,b}$=4.5, $J_{a,c}$=1.5, $J_{b,c}$=9.5)	7.47	8.19	8.08	8.51	7.50 (br. s)	1.67(6H, m) 3.57(4H, m)	280
Vc		3360	2200	1680	8.85 (d, $J_{d,e}$=9) (d.d, $J_{a,b}$=4.2, $J_{a,c}$=1.6, $J_{b,c}$=8.8)	7.48	8.24	8.15	8.77	7.24 (br. s)	1.96—2.17(4H, m) 3.53—3.66(4H, m)	266

Abbreviations: d, doublet; d.d, doublet of doublets; br.s, broad singlet; m, multiplet.

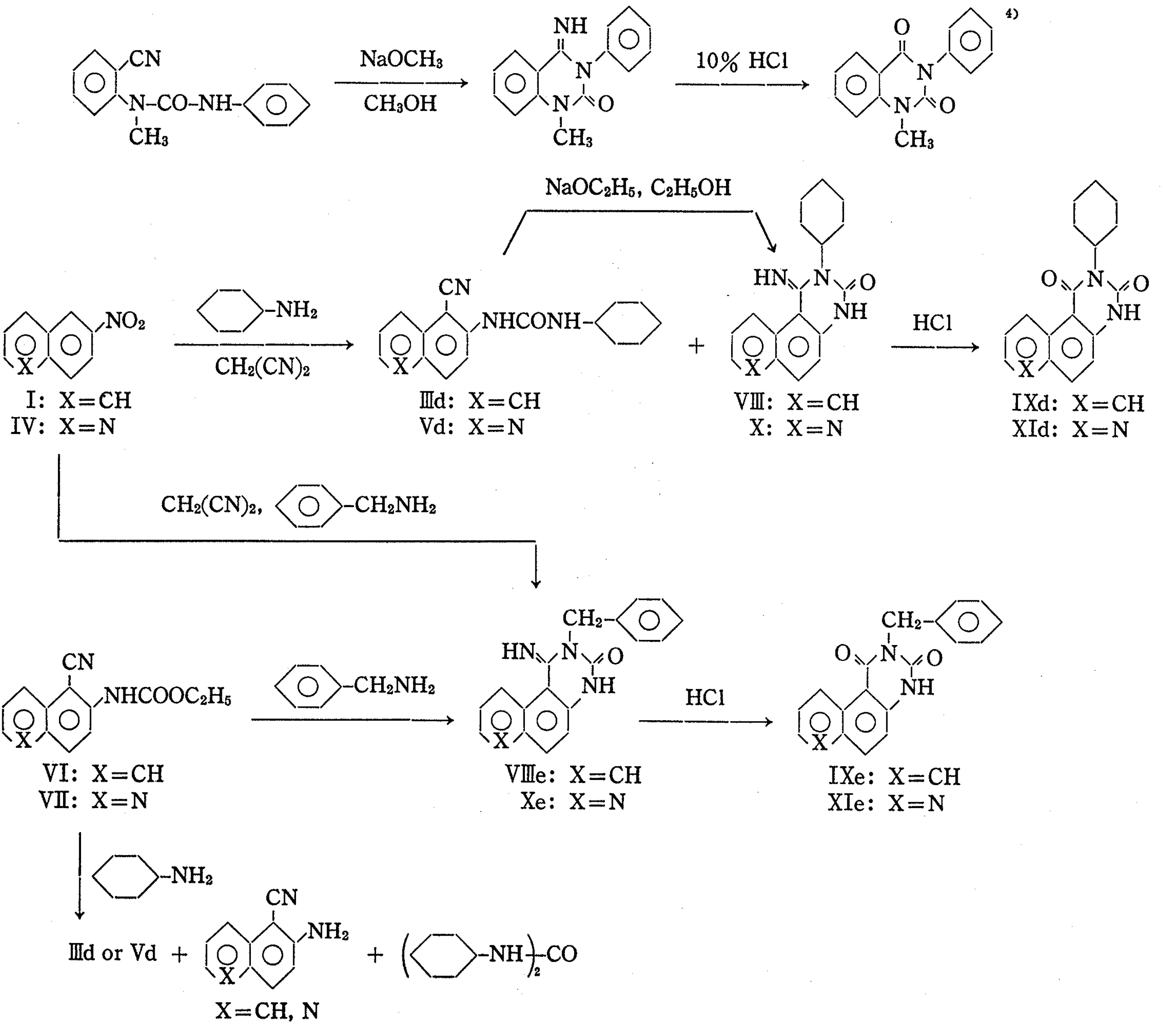


Chart 2

arly, IV reacted with cyclohexylamine to form N-cyclohexyl-N′-(5-cyano-6-quinolyl)urea (Vd) and 2-cyclohexyl-1-imino-3-oxo-1,2,3,4-tetrahydropyrido[3,2-*f*]quinazoline (Xd) in 0.5 and 44% yields, respectively. On treatment with sodium ethoxide, Vd underwent cyclization to Xd which, on acidic hydrolysis, was converted to 2-cyclohexyl-1,3-dioxo-1,2,3,4-tetrahydropyrido[3,2-*f*]quinazoline (XId) in 80% yield. The structural assignments of Xd and XId were made on the basis of elemental analysis and their spectral data (see "Experimental").

On the other hand, the reactions of I and IV with benzylamine gave only the quinazoline derivatives [VIIIe (49%), Xe (48%)], and no formation of the urea derivatives was noted. Both VIIIe and Xe were hydrolyzed to the corresponding 1,3-dioxoquinazolines (IXe, XIe) when heated with hydrochloric acid. The IR spectrum of IXe was identical with that of an authentic sample.[1]

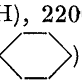
Finally, the reaction of VI with cyclohexylamine (2 equiv.) at 150° for 3 hr resulted in the formation of IIId (48%) and 2-aminonaphthalene-1-carbonitrile (26%) together with a small amount of dicyclohexylurea, whereas IIId was produced in 72% yield when 1.2 equivalents of cyclohexylamine was used. 2-Aminonaphthalene-1-carbonitrile and dicyclohexylurea seem to be formed by the reaction of IIId with cyclohexylamine. VII was also allowed to react with cyclohexylamine (2 equiv.) to give Vd (31%), 6-aminoquinoline-5-carbonitrile (29%) and dicyclohexylurea. Interestingly, the reactions of VI and VII with benzylamine, as well as the reactions of I and IV with benzylamine, gave only the quinazoline derivatives [VIIIe (78%), Xe (91%)], no urea derivatives being isolated.

Of particular interest is the formation of III(V) on the reaction of I(IV) with an amine. This reaction seems to provide a convenient method for synthesizing *o*-cyanoarylureas from aromatic nitro compounds. Further studies are in progress to explore the scope of the reaction.

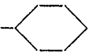
Experimental

DMF was prepared by distillation from calcium hydride and was stored over molecular sieve 4A. All melting points are uncorrected. IR spectra were recorded on an IRA-2 spectrophotometer. PMR spectra were taken on a Hitachi R-22 spectrometer at 90 MHz or a JNM-MH-100 spectrometer at 100 MHz using tetramethylsilane as an internal standard. Mass spectra were measured with a JEOL model JMS-01SG spectrometer.

Reactions of 2-Nitronaphthalene (I) and 6-Nitroquinoline (IV) with Malononitrile and a Secondary Amine. General Procedure——I or IV (0.01 mol) was added in small portions at room temperature to a stirred solution of malononitrile (0.792 g, 0.012 mol), KOH (1.12 g, 0.02 mol) and the amine (0.03 mol) in DMF (10 ml). The mixture was stirred for 24 hr, poured into ice-water, and extracted with $CHCl_3$. The $CHCl_3$ layer was washed with water, dried over Na_2SO_4, and then concentrated *in vacuo*. The residue was purified by column chromatography on alumina with $CHCl_3$ as the eluent to give the urea derivatives (IIIa, b, c and Va, b, c) in the yields shown in Table II.

Reaction of I with Cyclohexylamine——The nitro compound (I) (1.73 g, 0.01 mol) was treated with a solution of malononitrile (0.012 mol), cyclohexylamine (0.03 mol) and KOH (0.02 mol) in DMF (10 ml) by the procedure described above. Purification was carried out by column chromatography on alumina with $CHCl_3$ as the eluent. The first fraction gave I (60 mg). The material in the second fraction was recrystallized from acetone to yield N-cyclohexyl-N′-(1-cyano-2-naphthyl)urea (IIId: 740 mg, 25%) as colorless needles, mp 225°. *Anal.* Calcd for $C_{18}H_{19}N_3O$: C, 73.69; H, 6.53; N, 14.33. Found: C, 73.40; H, 6.50; N, 14.00. MS *m/e*: 293 (M^+). IR ν_{max}^{KBr} cm^{-1}: 3320 (NH), 2200 (CN), 1635 (CO). PMR (in DMSO-d_6) δ: 1.25—2.00 (10H, m), 3.61 (1H, m), 7.25 (1H, m, –N$\underline{H}$–), 7.43—8.09 (4H, m, C_{5-8}–H), 8.18 (1H, d, $J_{3,4}=9$ Hz, C_3–H), 8.47 (1H, d, $J_{3,4}=9$ Hz, C_4–H), 8.80 (1H, br.s, $>$N$\underline{H}$). The third fraction gave 2-cyclohexyl-1-imino-3-oxo-1,2,3,4-tetrahydrobenzo[*f*]quinazoline (VIIId: 710 mg, 24%), which was recrystallized from $CHCl_3$–MeOH to give colorless needles, mp 325° (dec.). *Anal.* Calcd for $C_{18}H_{19}N_3O$: C, 73.69; H, 6.53; N, 14.33. Found: C, 73.32; H, 6.45; N, 14.13. MS *m/e*: 293 (M^+). IR ν_{max}^{KBr} cm^{-1}: 3360 (NH), 1690 (CO). PMR (in DMSO-d_6) δ: 1.00—2.20 (10H, m), 4.55 (1H, m), 7.23 (1H, d, $J_{5,6}=9$ Hz, C_5–H), 7.31—7.96 (3H, m, C_{7-9}–H), 7.97 (1H, d, $J_{5,6}=9$ Hz, C_6–H), 8.80 (1H, m, C_{10}–H), 9.06 (1H, br.s, $\rangle$C=N$\underline{H}$), 10.72 (1H, br.s, $\diagdown$CON$\underline{H}\diagup$).

Reaction of IV with Cyclohexylamine——The nitro compound (IV) (1.74 g, 0.01 mol) was treated with a solution of malononitrile (0.012 mol), cyclohexylamine (0.03 mol) and KOH (0.02 mol) in DMF (10 ml) by the procedure described above. The reaction mixture was poured into ice-water and the precipitate was collected by filtration, washed with water, and dried. The combined filtrate and washings were extracted with $CHCl_3$.

The $CHCl_3$ extract was washed with water, dried over Na_2SO_4, and concentrated *in vacuo*. The residue and the above precipitate were combined and chromatographed on alumina with $CHCl_3$–acetone (9: 1) as the eluent. The first product to appear was N-cyclohexyl-N′-(5-cyano-6-quinolyl)urea (Vd: 16 mg, 0.5%), mp 233° (from benzene), colorless needles. *Anal.* Calcd for $C_{17}H_{18}N_4O$: C, 69.37; H, 6.16; N, 19.04. Found: C, 69.67; H, 6.15; N, 18.99. MS *m/e*: 294 (M^+). IR ν_{max}^{KBr} cm^{-1}: 3320 (NH), 2200 (CN), 1635 (CO). PMR (in DMSO-d_6) δ: 1.00—2.20 (10H, m), 3.54 (1H, m), 7.22 (1H, m, –N$\underline{H}$–), 7.65 (1H, d.d, $J_{2,3}=4$ and $J_{3,4}=8.2$ Hz, C_3–H), 8.16 (1H, d, $J_{7,8}=9.7$ Hz, C_7–H), 8.27 (1H, d.d, $J_{2,4}=2$ and $J_{3,4}=8.2$ Hz, C_4–H), 8.63 (1H, d, $J_{7,8}=9.7$ Hz, C_8–H), 8.83 (1H, d.d, $J_{2,3}=4$ and $J_{2,4}=2$ Hz, C_2–H), 8.82 (1H, br. s, ∖N$\underline{H}$CO∕). The second product to appear was 2-cyclohexyl-1-imino-3-oxo-1,2,3,4-tetrahydropyrido[3,2-*f*]quinazoline (Xd: 1.28 g, 44%), mp 314° (dec.) (from MeOH), colorless needles. *Anal.* Calcd for $C_{17}H_{18}N_4O$: C, 69.37; H, 6.16; N, 19.04. Found: C, 69.45; H, 6.18; N, 18.98. MS *m/e*: 294 (M^+). IR ν_{max}^{KBr} cm^{-1}: 3350 (NH), 1690 (CO). PMR (in DMSO-d_6) δ: 1.00—2.10 (10H, m), 4.35 (1H, m), 7.45 (1H, d, $J_{5,6}=9$ Hz, C_5–H), 7.56 (1H, d.d, $J_{8,9}=4.2$ and $J_{9,10}=8.5$ Hz, C_9–H), 8.07 (1H, d, $J_{5,6}=9$ Hz, C_6–H), 8.72 (1H, br. s, ⟩C=N$\underline{H}$), 8.79 (1H, d.d, $J_{8,9}=4.2$ and $J_{8,10}=1.5$ Hz, C_8–H), 10.22 (1H, m, C_{10}–H), 10.86 (1H, br.s, ∖N$\underline{H}$CO∕).

Reaction of I with Benzylamine——I (1.73 g, 0.01 mol) was added to a stirred solution of malononitrile (0.792 g, 0.012 mol), KOH (1.12 g, 0.02 mol) and benzylamine (3.21 g, 0.03 mol) in DMF at room temperature. The mixture was stirred for 24 hr, then poured into ice-water and the precipitate was collected, washed with water, dried, and then washed with ether to remove the unchanged I (120 mg, 7%). Recrystallization from MeOH–$CHCl_3$ gave 2-benzyl-1-imino-3-oxo-1,2,3,4-tetrahydrobenzo[*f*]quinazoline (VIIIe: 1.48 g, 49%) as colorless needles, mp 238° (dec.). *Anal.* Calcd for $C_{19}H_{15}N_3O$: C, 75.73; H, 5.02; N, 13.95. Found: C, 75.76; H, 4.83; N, 14.00. MS *m/e*: 301 (M^+), IR ν_{max}^{KBr} cm^{-1}: 3340 (NH), 1690 (CO). PMR (in HMPA-d_{18}) δ: 5.32 (2H, s, –C$\underline{H}_2$–), 7.36 (5H, s, phenyl H), 7.24—7.76 (3H, m, $C_{5,8,9}$–H), 7.90 (1H, m, C_7–H), 8.05 (1H, d, $J_{5,6}=8.7$ Hz, C_6–H), 8.18 (1H, br. s, ⟩C=N$\underline{H}$), 10.16 (1H, m, C_{10}–H), 11.24 (1H, br.s, ∖N$\underline{H}$CO∕).

Reaction of IV with Benzylamine——The nitro compound (IV) (0.01 mol) was treated with a solution of malononitrile (0.012 mol), KOH (0.02 mol) and benzylamine (0.03 mol) in DMF (10 ml) by the procedure described for VIIIe. The reaction mixture was poured into ice-water and the precipitate was collected by filtration, washed with water, and dried to give 2-benzyl-1-imino-2-oxo-1,2,3,4-tetrahydropyrido[3,2-*f*]-quinazoline (Xe: 1.79 g). The filtrate was extracted with $CHCl_3$, the $CHCl_3$ layer was concentrated *in vacuo*, the residue was chromatographed on alumina with $CHCl_3$ as the eluent, and the same compound (Xe: 0.229 g) was obtained. Xe was recrystallized from acetone to give colorless needles, 1.433 g (48%), mp 264° (dec.). *Anal.* Calcd for $C_{18}H_{14}N_4O$: C, 71.51; H, 4.67; N, 18.53. Found: C, 71.69; H, 4.40; N, 18.76. MS *m/e*: 302 (M^+). IR ν_{max}^{KBr} cm^{-1}: 3340 (NH), 1690 (CO). PMR (in HMPA-d_{18}) δ: 5.60 (2H, s, –C$\underline{H}_2$–Ph), 7.40—7.90 (6H, m, C_9–H and phenyl H), 8.08 (1H, d, $J_{5,6}=9.5$ Hz, C_5–H), 8.26 (1H, d, $J_{5,6}=9.5$ Hz, C_6–H), 8.75 (1H, br.s, ⟩C=N$\underline{H}$), 9.02 (1H, d.d, $J_{8,9}=4$ and $J_{8,10}=1.5$ Hz, C_8–H), 10.82 (1H, m, C_{10}–H), 12.50 (1H, br. s, ∖N$\underline{H}$CO∕).

Cyclization of N-Cyclohexyl-N′-(1-cyano-2-naphthyl)urea (IIId) to 2-Cyclohexyl-1-imino-3-oxo-1,2,3,4-tetrahydrobenzo[*f*]quinazoline (VIIId)——Sodium metal (50 mg) was dissolved in abs. EtOH (20 ml) and IIId (586 mg) was added. After the mixture had been refluxed for 8 hr, the EtOH was removed *in vacuo*, the residue was neutralized with aq.AcOH, and the precipitate was collected by filtration, washed with water and dried. The combined filtrate and washings were made alkaline with K_2CO_3 and extracted with $CHCl_3$. The $CHCl_3$ extract and the above precipitate were combined and chromatographed over silica gel with $CHCl_3$ as the eluent. The first fraction gave IIId (30 mg, 5%). The second fraction gave VIIId (450 mg, 77%) which was recrystallized from MeOH–$CHCl_3$ to give colorless needles, mp 335° (dec.).

Cyclization of N-Cyclohexyl-N′-(5-cyano-6-quinolyl)urea (Vd) to 2-Cyclohexyl-1-imino-3-oxo-1,2,3,4-tetrahydropyrido[3,2-*f*]quinazoline (Xd)——Xd (200 mg) was added to an NaOEt–EtOH solution prepared from Na (17 mg) and abs.EtOH (10 ml), and the mixture was refluxed for 4 hr. After removal of the EtOH *in vacuo*, the crystalline residue was washed with water, dried, and then recrystallized from MeOH to yield Xd (180 mg, 90%) as colorless needles, mp 314° (dec.).

Hydrolysis of 2-Cyclohexyl- and 2-Benzyl-1-imino-3-oxo-1,2,3,4-tetrahydrobenzo[*f*]quinazolines (VIIId and VIIIe)——A solution of VIIId or VIIIe (2 mmol) and AcOH (5 ml) in 20% HCl (5 ml) was heated at 120° for 8 hr with stirring. The reaction mixture was cooled, then the precipitate was collected, washed with water, and dried. Recrystallization from MeOH–$CHCl_3$ to give 2-cyclohexyl- or 2-benzyl-1,3-dioxo-1,2,3,4-tetrahydrobenzo[*f*]quinazoline (IXd or IXe). These compounds were identical with authentic samples.[1)] IXd (410 mg, 70%), colorless needles, mp 293—294° (dec.). IXe (340 mg, 55%), colorless needles, mp 284° (dec.).

Hydrolysis of 2-Cyclohexyl- and 2-Benzyl-1-imino-3-oxo-1,2,3,4-tetrahydropyrido[3,2-*f*]quinazolines (Xd and Xe)——A solution of Xd or Xe (2 mmol) in 10% HCl (10 ml) was heated at 120° for 3 hr with stirring. The resulting mixture was cooled and the precipitate was collected, washed with water, dried, and then recrystallized from MeOH to give 2-cyclohexyl- or 2-benzyl-1,3-dioxo-1,2,3,4-tetrahydropyrido[3,2-*f*]quinazoline (XId or XIe). XId (470 mg, 80%), colorless needles, mp 312.5—313° (dec.). *Anal.* Calcd for $C_{17}H_{17}N_3O_2 \cdot 1/2H_2O$: C, 67.09; H, 5.96; N, 13.81. Found: C, 66.98; H, 6.10; N, 13.49. MS *m/e*: 295 (M^+). IR ν_{max}^{KBr} cm^{-1}: 3240 (NH), 1710, 1655 (CO). PMR (in HMPA-d_{18}) δ: 1.12—2.16 (10H, m, –C$\underline{H}_2$–), 4.96 (1H, m,

>C$\underline{H}$–), 7.86 (1H, d.d, $J_{8,9}$=4 and $J_{9,10}$=9.6 Hz, C_9–H), 8.00 (1H, d, $J_{5,6}$=9 Hz, C_5–H), 8.29 (1H, d, $J_{5,6}$=9 Hz, C_6–H), 8.98 (1H, d.d, $J_{8,9}$=4 and $J_{8,10}$=2 Hz, C_8–H), 10.05 (1H, d.d, $J_{8,10}$=2 and $J_{9,10}$=9.6 Hz, C_{10}–H). XIe (530 mg, 88%), colorless needles, mp 291.5° (dec.). *Anal.* Calcd for $C_{18}H_{13}N_3O_2$: C, 71.27; H, 4.32; N, 13.86. Found: C, 71.04; H, 4.16; N, 13.64. MS *m/e*: 303 (M^+). IR ν_{max}^{KBr} cm^{-1}: 3200 (NH), 1705, 1650 (CO). PMR (in DMSO-d_6) δ: 5.18 (2H, s, –C$\underline{H}_2$–), 7.35 (5H, s, phenyl H), 7.58 (1H, d, $J_{5,6}$=9 Hz, C_5–H), 7.63 (1H, d.d, $J_{8,9}$=4.5 and $J_{9,10}$=9 Hz, C_9–H), 8.22 (1H, d, $J_{5,6}$=9 Hz, C_6–H), 8.85 (1H, d.d, $J_{8,9}$=4.5 and $J_{8,10}$=1.2 Hz, C_8–H), 9.85 (1H, m, C_{10}–H), 11.97 (1H, br.s, >NH).

Reaction of 2-Ethoxycarbonylaminonaphthalene-1-carbonitrile (VI) and 6-Ethoxycarbonylaminoquinoline-5-carbonitrile (VII) with a Secondary Amine. General Procedure——A stirred mixture of VI or VII (2 mmol) and the amine (4 mmol) in DMF (5 ml) was heated at 150° for 3 hr. After removal of the solvent *in vacuo*, the residue was washed with ether, and then recrystallized from the solvent listed in Table II to give the urea derivatives (IIIa, b, c and Va, b, c).

Reaction of VI with Cyclohexylamine——a) A solution of VI (500 mg, 2.08 mmol) and cyclohexylamine (413 mg, 4.17 mmol) in DMF (5 ml) was heated at 150° for 3 hr with stirring. The reaction mixture was cooled, and deposited dicyclohexylurea (64 mg, mp 225—226°, lit.[5] mp 229—230°) was collected by filtration. The filtrate was concentrated *in vacuo*, and the crystalline residue was extracted with ether. The ether extract gave 2-aminonaphthalene-1-carbonitrile (90 mg, 26%), mp 131.5° (from $CHCl_3$), which was identical with an authentic sample.[6] The ether-insoluble substance was recrystallized from acetone to afford N-cyclohexyl-N'-(1-cyano-2-naphthyl)urea (IIId: 280 mg, 48%) as colorless needles, mp 225°.

b) A solution of VI (500 mg) and cyclohexylamine (248 mg, 2.51 mmol) in DMF (5 ml) was heated at 150° for 3 hr. After removal of the solvent by evaporation *in vacuo*, the residue was recrystallized from acetone to give IIId (440 mg, 72%), mp 225°.

Reaction of VII with Cyclohexylamine——A stirred solution of VII (482 mg, 2 mmol) and cyclohexylamine (396 mg, 4 mmol) in DMF (5 ml) was heated at 150° for 3 hr. The mixture was cooled, and deposited dicyclohexylurea (97 mg) was removed by filtration. The filtrate was concentrated *in vacuo*, and the residue was extracted with ether. The ether extract was purified by column chromatography on alumina with $CHCl_3$ as the eluent to give 6-aminoquinoline-5-carbonitrile (97 mg, 29%), which was identical with an authentic sample.[3] The ether-insoluble residue was chromatographed on alumina. Elution with $CHCl_3$ gave N-cyclohexyl-N'-(5-cyano-6-quinolyl)urea (Vd: 182 mg, 31%), which was recrystallized from benzene to produce colorless needles, mp233°.

Reaction of VI and VII with Benzylamine——A mixture of VI or VII (2 mmol) and benzylamine (4 mmol) in DMF (5 ml) was heated at 150° for 3 hr with stirring. After removal of the DMF *in vacuo*, the crystalline residue (VIIIe or Xe) was washed with ether. 2-Benzyl-1-imino-3-oxo-1,2,3,4-tetrahydrobenzo[*f*]quinazoline (VIIIe: 459 mg, 78%) was recrystallized from $CHCl_3$–MeOH to give colorless needles, mp 238° (dec.). 2-Benzyl-1-imino-3-oxo-1,2,3,4-tetrahydropyrido[3,2-*f*]quinazoline (Xe: 552 mg, 91%) was recrystallized from acetone to produce colorless needles, mp 264° (dec.).

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