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Studies on Organosulfur Compounds. XII.[1] Syntheses and Pharmacological Activities of 2-Heterocyclic Substituted 4(3H)-Quinazolinones

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Four useful procedures for preparing a series of new 2-pyridyl-4(3*H*)-quinazolinones were investigated and twelve quinazolinones were evaluated for hypnotic activity. Some of them showed a definite hypnotic effect in intraperitoneal doses above 100 mg/kg, whose structure–activity relationship demonstrated that 3-pyridyl and 4-pyridyl substitution at 2-position of 4 (3*H*)-quinazolinone ring and *o*-fluorophenyl and *o*-chlorophenyl at 3-position are appropriate for the manifestation of hypnotic activity. A maximum hypnotic effect was observed in 2-(4-pyridyl)-3-(*o*-fluorophenyl)-4(3*H*)-quinazolinone (1), the potency of which was equal to methaqualone in mice.

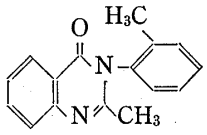
Diverse synthetic methods to obtain compounds having a 4(3*H*)-quinazolinone ring system have been investigated.[3] Numerous 4(3*H*)-quinazolinones, particularly those with 2,3-disubstituents, have been prepared and evaluated for pharmacological activities[4] since Gujral and his co-workers[5] first reported that some 4(3*H*)-quinazolinones exhibited a potent hypnotic action in experimental animals. It is well known that quinazolinone derivatives show an activity on the central nervous system, and 2-methyl-3-*o*-tolyl-4(3*H*)-quinazolinone (methaqualone) and 2-methyl-3-(*o*-chlorophenyl)-4(3*H*)-quinazolinone (mecloqualone) are known as a potent hypnotic.[6] Although there are several reports on the problem of structure–activity relationship of quinazolinones on their activities, none of them give a general view. Approaches to this problem can be expected only if one restricts his attention to groups of compounds having a quinazolinone ring system of similar structure. 4(3*H*)-Quinazolinones with substituents in 2- and 3-positions are one such group and, in particular, those substituted with alkyl, aryl, or amino have been evaluated for their pharmacological activity but derivatives with a heterocyclic group in 2-position have received relatively limited attention.[7]

Our previous paper, with a view to obtaining a more fully refined structure specificity on the methaqualone-like action, reported a convenient synthetic method to obtain 4(3*H*)-quinazolinones substituted with 2-pyridyl or 4-pyridyl at 2-position by the modified Willgerodt-Kindler reaction, in which a mixture of picoline, aromatic amine, and anthranilic acid was heated in the presence of sulfur, and by the modified Niementowski reaction by cyclization

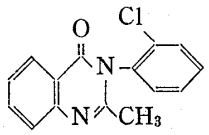
1) Part XI: T. Hisano and M. Ichikawa, *Chem. Pharm. Bull.* (Tokyo), **22**, 2051 (1974).
2) Location: *a) Oe-honmachi, Kumamoto, 862, Japan; b) Tashiro-daikanmachi, Tosu, Saga, 841, Japan.*
3) T. Hisano, *Org. Prep. Proced. Int.*, **5**, 145 (1973).
4) W.L.F. Armarego, *Adv. Heterocycl. Chem.*, **1**, 253 (1963).
5) M.L. Gujral, P.N. Saxena, and R.S. Tiwari, *Indian J. Med. Res.*, **43**, 637 (1955); M.L. Gujral, P.N. Saxena, and B.K. Khanna, *J. Indian Med. Profess.*, **3**, 1098 (1956); M.L. Gujral, K.N. Sacreen, and R. P. Kohli, *Indian J. Med. Res.*, **45**, 207 (1957).
6) G.B. Jackman, V. Petrow, and O. Stephensor, *J. Pharm. Pharmacol.*, **12**, 529 (1960); J. Klosa, *Prackt. Chem.*, **14**, 84 (1961).
7) A. Buzas and C. Hoffman, *Bull. Soc. Chim. France*, **26**, 1889 (1959); S. Peterson, H. Herlinger, E. Tietze, and W. Stiefken, *Angew. Chem.*, **74**, 855 (1962); S. Somasekhra, W.S. Dighe, P.R. Mankad, and F.A. Mukerjee, *Indian J. Chem.*, **2**, 369 (1964).

of anthranilic acid with thiopicolino-anilides in the presence of nitrogen bases.[8] In our preliminary experiments, it was found that 2-(4-pyridyl)-3-*o*-tolyl-4(3*H*)-quinazolinone (A) and its derivatives possess potent hypnotic and anticonvulsive activity in mice, which are equal to or more potent than methaqualone.[9]

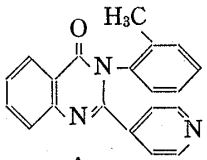
The present paper deals with the synthesis and hypnotic activity of 4(3*H*)-quinazolinones, substituted with 4-pyridyl (**1**—**4**), 3-pyridyl (**5**—**11**), and 2-thienyl (**12**) at 2-position, which were synthesized in analogy with structural features of the mecloqualone-like compounds and to examine the activity of 4(3*H*)-quinazolinones having a heterocyclic group at 2-position (Table I).



methaqualone



mecloqualone



A

Syntheses

In the synthesis of 2-pyridyl-3-chlorophenyl-4(3*H*)-quinazolinones, the modified Willgerodt-Kindler reaction as mentioned above cannot be used, since a new dechlorination occurred during quinazolinone cyclization process by the use of chloroanilines as the aromatic amine series.[10] In the synthesis of 2-(3-pyridyl) derivatives, 3-picoline is unreactive under this reaction condition. Therefore, four synthetic methods for the mecloqualone-like compounds were investigated further, as described in Chart 1.

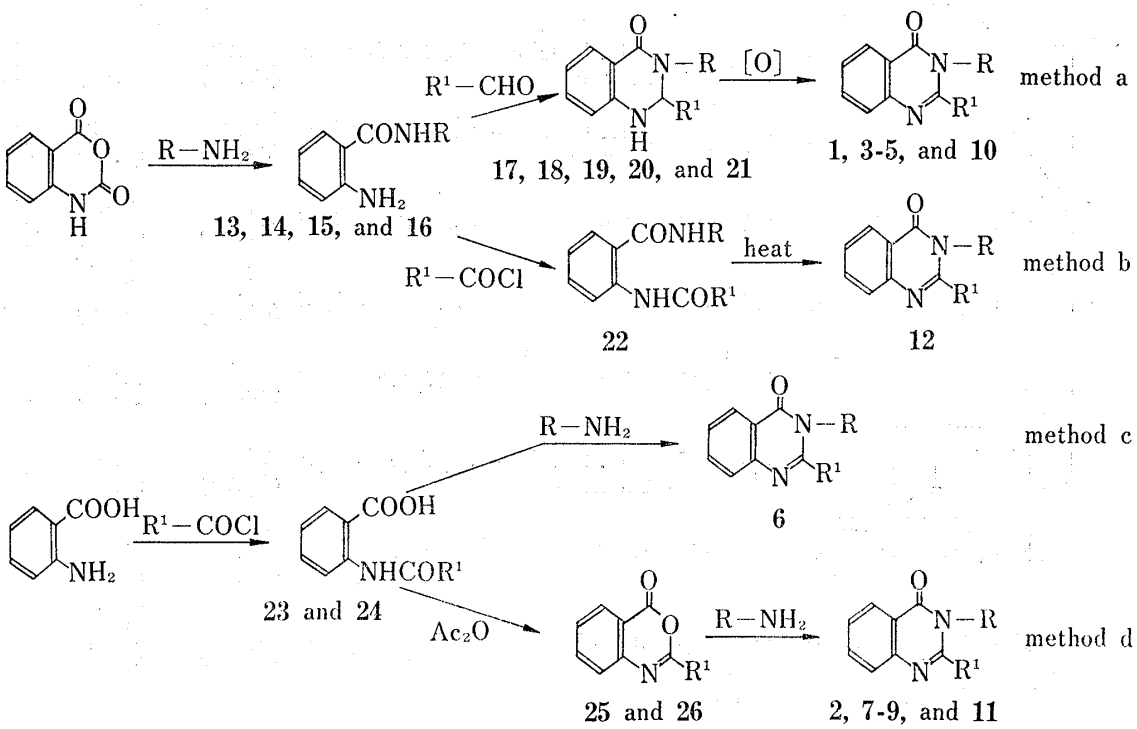
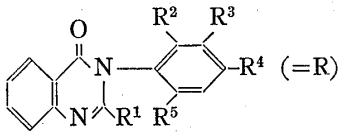


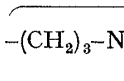
Chart 1

8) T. Hisano, T. Nishi, and M. Ichikawa, *Yakugaku Zasshi*, **92**, 582 (1972).
9) T. Hisano, M. Ichikawa, G. Kito, and T. Nishi, *Chem. Pharm. Bull.* (Tokyo), **20**, 2575 (1972).
10) T. Hisano and Y. Yabuta, *Chem. Pharm. Bull.* (Tokyo), **22**, 316 (1974).

In method a, N-substituted 2-aminobenzamides[11] (**13**—**16**), obtained from isatoic anhydride and amines, were condensed with aldehydes to give the corresponding 4-oxo-1,2,3,4-tetrahydroquinazolines (**17**—**21**) as an intermediate, which were oxidized with potassium permanganate in acetone to obtain the desired 4(3*H*)-quinazolinones (**1**, **3**—**5**, and **10**) in a good yield (Tables II and III). Compound **12**, shown in method b, was prepared by the

Table I. 3-Substituted 2-Heterocycle-4(3*H*)-quinazolinones



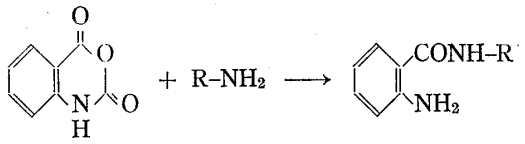
Compd. No.	R^1	R				mp[a] (°C)	Recrystn. solvent[b]	Formula	Method	Analysis (%) Calcd. (Found)		
		R^2	R^3	R^4	R^5					C	H	N
1		F	H	H	H	198—199	MeOH	$C_{19}H_{12}ON_3F$	a	71.92 (72.18)	3.81 (3.53)	13.24 (13.25)
2		Cl	H	H	H	173—174	petr. benzine–benzene	$C_{19}H_{12}ON_3Cl$	d	68.37 (68.15)	3.63 (3.47)	12.59 (12.38)
3		$-C_2H_5$				101—103	petr. benzine–benzene	$C_{15}H_{13}ON_3$	a	71.69 (72.36)	5.21 (5.17)	16.72 (16.69)
4						192—194	petr. benzine–benzene	$C_{18}H_{12}ON_4$	a	71.99 (71.68)	4.03 (4.15)	18.65 (18.45)
5		F	H	H	H	156—157	petr. benzine–benzene	$C_{19}H_{12}ON_3F$	a	71.92 (72.24)	3.81 (3.82)	13.24 (13.18)
6		Cl	H	H	H	117—118	petr. benzine–benzene	$C_{19}H_{12}ON_3Cl$	c	68.37 (68.67)	3.63 (3.57)	12.59 (12.73)
7		Cl	Cl	H	H	161—162	ether	$C_{19}H_{11}ON_3Cl_2$	d	61.98 (61.82)	3.01 (3.21)	11.41 (11.23)
8		Cl	H	Cl	H	174—176	MeOH	$C_{19}H_{11}ON_3Cl_2$	d	61.98 (61.73)	3.01 (3.15)	11.41 (11.21)
9		Cl	H	H	CH_3	147—149	ether	$C_{20}H_{14}ON_3Cl$	d	69.07 (69.15)	4.06 (4.23)	12.03 (12.15)
10						185—186	petr. benzine–benzene	$C_{18}H_{12}ON_4$	a	71.99 (71.75)	4.03 (3.94)	18.65 (18.38)
11						155—156	EtOH	$C_{20}H_{22}O_2N_4$	d	68.55 (68.69)	6.33 (6.23)	15.99 (15.80)
12		CH_3	H	H	H	137—138	MeOH	$C_{19}H_{14}ON_2S$	b	71.68 (71.92)	4.43 (4.41)	8.80 (9.08)
MTQ	CH_3	CH_3	H	H	H	115						

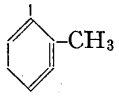
a) All melting points are uncorrected.
b) All compounds were colorless prisms except **8** crystallized as colorless needles and **12** as light brown prisms.
MTQ=methaqualone

11) *a*) G. Satzinger and Herrmann, Br. Patent 1292773 [*C. A.*, **78**, 496 (1973)]; *b*) R.H. Clark and F.C. Wagner, *J. Org. Chem.*, **9**, 55 (1944); *c*) T.H. Haskell, F.E. Peterson, D. Watson, N.R. Plesoas, and T. Culbertson, *J. Med. Chem.*, **13**, 697 (1970); *d*) C. Mehner, *Prakt. Chem.* (2), **63**, 283 (1901).

ring closure of N-(*o*-tolyl)-2-(2-thenoylamino)benzamide (**22**), formed from N-(*o*-tolyl)-2-aminobenzamide (**16**) with 2-thiophenecarbonyl chloride,[11b,12] since a precursor of **12** such as the above intermediate was unstable under this reaction condition.

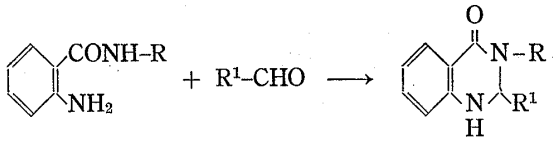
TABLE II. N-Substituted 2-Aminobenzamides

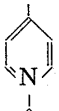
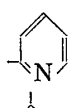
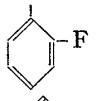


Compd. No.	R	mp[a] (°C)	Recrystn. solvent[b]	Yield[c] (%)	Formula	Analysis (%) Calcd. (Found) C	H	N
13		123—125[d]	benzene	63	$C_{13}H_{11}ON_2F$	67.82 (67.65)	4.82 (4.91)	12.17 (12.30)
14	$-C_2H_5$	102—104[e]	MeOH	98	$C_9H_{12}ON_2$	65.83 (65.59)	7.37 (7.31)	17.06 (17.20)
15		132—134[f]	MeOH	58	$C_{12}H_{11}ON_3$	67.59 (67.35)	5.20 (5.12)	19.71 (19.83)
16		104[g]	benzene	70	$C_{14}H_{14}ON_2$	74.31 (74.52)	6.24 (6.41)	12.38 (12.15)

a) All melting points are uncorrected. *b*) All compounds were colorless prisms. *c*) calcd. on the basis of isatoic anhydride
d) reported[11a] mp 123—124° *e*) reported[11b] mp 102—104° *f*) reported[11c] mp 132—133° *g*) reported[11d] mp 104°

TABLE III. 4-Oxo-1,2,3,4-tetrahydroquinazolines



Compd. No.	R^1	R	mp[a] (°C)	Recrystn. solvent[b]	Yield[c] (%)	Formula	Analysis (%) Calcd. (Found) C	H	N
17			230—231	MeOH	78	$C_{19}H_{14}ON_3F$	71.46 (71.52)	4.42 (4.38)	13.16 (13.01)
18		$-C_2H_5$	147—148	benzene	60	$C_{15}H_{15}ON_3$	71.13 (70.95)	5.97 (5.83)	16.59 (6.44)
19			188—190	benzene	83	$C_{18}H_{14}ON_4$	71.51 (70.99)	4.67 (4.35)	18.53 (18.28)
20			211—213	MeOH	84	$C_{19}H_{14}ON_3F$	71.46 (71.35)	4.42 (4.51)	13.16 (13.25)
21			156—157	benzene	94	$C_{18}H_{14}ON_4$	71.51 (71.30)	4.67 (4.70)	18.53 (18.63)

a) All melting points are uncorrected.
b) All compounds were colorless prisms.
c) calcd. on the basis of N-substituted 2-aminobenzamides

12) *a*) S. Hayano, H.J. Havera, W.G. Strycker, and E. Hong, *J. Med. Chem.*, **12**, 936 (1969); *b*) J.R. Feldman and E.C. Wagner, *J. Org. Chem.*, **7**, 31 (1942).

2-Picolinoylaminobenzoic acids (**23** and **24**) were used as the starting material in methods c and d, for the possibility of using the modified Niementowski 4(3*H*)-quinazolinone synthesis. Compound 6 was readily prepared in one step by heating **23** with *o*-chloroaniline in the presence of phosphorus trichloride (method c).[13,14] In method d, the N-acylanthranilic acids were heated with acetic anhydride to give the corresponding benzoxazin-4-ones[12a,15] which were reacted with amines. The procedure given here can be used conveniently to prepare the desired 4(3*H*)-quinazolinones (**2**, **7**—**9**, and **11**).

Hypnotic Effect

Materials——Twelve derivatives of 4(3*H*)-quinazolinones were prepared as described above. The compounds shown in Table I are sparingly soluble in water, suspended in normal saline solution with the aid of 0.5% tragacanth, and methaqualone, supplied by Eisai Co. Ltd., Tokyo, was used as a reference drug. Male mice of ddN strain weighing 18—22 g were used as experimental animals.

Method——Hypnotic effect was selected for the first screening. A group of 5 to 6 mice was used for each test compound. Each of four graded doses such as 30, 100, 300, and 1000 mg/kg of test compounds was given intraperitoneally to each group of mice. The behavior and toxic signs were observed for 120 min and the period needed for recovery from complete loss of righting reflex was determined as the sleeping time. A complete loss of the reflex for more than 2 min was regarded as a positive hypnotic effect.

The sleeping time of 10 compounds and of methaqualone is shown in Table IV. A significant effect was demonstrated in a dose of 100 mg/kg of compound **1**, 300 mg/kg of **2**, and 300 mg/kg of **6**. Methaqualone showed a definite hypnotic effect in doses above 100 mg/kg.

Table IV. Effect of Compounds on Righting Reflex in Mice

Compd. No.	Dose (mg/kg) (intraperitoneal)	Period until sleep (min)	Sleeping time (min)	No. of sleeping mice (30 min<)
1	30	12.0	3.5	1/6
	100	4.2	111.2	6/6
	300	4.0	657.2	5/5
2	30	5.8	8.0	4/6
	100	4.8	13.3	5/6
	300	2.5	447.2<	6/6
3	300	4.8	78.5	6/6
4	300	6.0	210.7	6/6
5	100	3.5	27.2	6/6
	300	2.8	395.5	6/6
6	30	2.8	11.6	5/6
	100	2.2	38.4	6/6
	300	2.1	1554.1<	6/6
8	300	34.5	23.0	4/6
9	300	21.0	2.8	1/6
10	300	6.0	112.2	6/6
11	300	5.5	7.1	5/6
Methaqualone	30	11.5	5.5	2/6
	100	1.7	119.7	5/5
	300	2.3	699.7	6/6

13) K.-H. Boltze, H.-D. Dell, H. Lehwald, D. Lorenz, and M. Rüberg-Schweer, *Arzneimittel-forsch.*, **13**, 688 (1963).
14) E. Marchetti, G. Bergesi, and G. Mattalia, *Ann. Chim.* (Rome), **52**, 836 (1962) [*C. A.*, **59**, 1638 (1963)].
15) D.T. Zentmyer and E.C. Wagner, *J. Org. Chem.*, **14**, 967 (1949).

Discussion

As previously stated,[8,9] among the 2-heterocyclic derivatives are 2-(4-pyridyl)-3-*o*-tolyl-4(3*H*)-quinazolinone (A) which may act as a more potent hypnotic than methaqualone in mice and others substituted with 2-pyridyl group at 2-position which have a tendency to augment pharmacological activities when an *o*-methyl group is introduced into the phenyl substituent at 3-position. On the basis of these data, we have developed the structure specificity on the mode of the methaqualone-like action, although there have been very few studies on 2-heterocycle substituted quinazolinones. Obviously the *o*-tolyl group at 3-position in the 4(3*H*)-quinazolinone ring is a decisive factor for the hypnotic action. Other structural factors are still uncertain.

In the present study, attempts were made to determine whether, and if any, what kind of halogen group in the phenyl substituent at 3-position in combination with the pyridyl group at 2-position in the 4(3*H*)-quinazolinone ring might affect the pharmacological activity, because mecloqualone, as well as methaqualone, is utilized in therapy as a hypnotic.

The structure-activity relationship for the hypnotic effect of 12 analogs is summarized below.

1) The compound **12**, having a thienyl substituent at 2-position, is inactive. Substitution of 3-position with a pyridyl, ethyl, and so forth (*e.g.*, compounds **3**, **4**, **10**, and **11**), other than a phenyl group, markedly decreases the activity.

2) Introduction of an *o*-fluoro or *o*-chloro into the phenyl substituent at 3-position seems to be effective (*e.g.*, compounds **1**, **2**, **5**, and **6**). In contrast, the progressive introduction of *m*- or *p*-chloro, or *p*-methyl group into the same position (*e.g.*, compounds **7**, **8**, and **9**) markedly diminished the activity compared to the original compound **6**. A-like compounds with a fluoro group showed a definite hypnotic effect at 100 mg/kg doses (**1** and **2**).

3) Potentiation of the activity due to the position of halogen group in the phenyl ring at 3-position and of pyridyl group at 2-position was found in the combination of *o*-fluoro and 4-pyridyl. It is concluded that a maximum hypnotic activity will be found in structures like 2-(4-pyridyl)-3-(*o*-fluorophenyl)-4(3*H*)-quinazolinone (**1**), which is equal to 2-methyl-3-*o*-tolyl-4(3*H*)-quinazolinone (methaqualone) in mice.

Experimental

Method a. General Method——A mixture of 6.5 g (0.040 mol) of isatoic anhydride and 0.044 mol of an amine was heated at 120° for 4 hr. The reaction mixture was treated with a small amount of MeOH in an ice bath. The resulting solid was collected by suction and recrystallized to colorless crystals (**13**—**16**) as shown in Table II.

2-(3-Pyridyl)-3-(2-pyridyl)-4-oxo-1,2,3,4-tetrahydroquinazoline (**21**): A mixture of 2.1 g (0.010 mol) of N-(2-pyridyl)-2-aminobenzamide (**15**) and 1.6 g (0.015 mol) of pyridine-3-carbaldehyde in 50 ml of EtOH was refluxed for 5 hr. The solvent was removed and the residue was recrystallized from benzene to 2.8 g (94%) of colorless prisms, mp 156—157°. IR ν_{max}^{KBr}: 1645 cm^{-1} ($\nu_{c=o}$). *Anal.* Calcd. for $C_{18}H_{14}ON_4$: C, 71.51; H, 4.67; N, 18.53. Found: C, 71.63; H, 4.53; N, 18.71.

Other tetrahydroquinazolines (**17**, **18**, **19**, and **20**) were prepared by this procedure (Table III).

2-(3-Pyridyl)-3-(2-pyridyl)-4 (3*H*)-quinazolinone (**10**): To a solution of 1.5 g (0.005 mol) of **21** in 60 ml of acetone was gradually added 1.2 g (0.0075 mol) of $KMnO_4$ with stirring and the mixture was refluxed for additional 1 hr. The hot reaction mixture was filtered by suction and then the precipitate was washed with hot MeOH. The filtrate and washings were combined and concentrated to give a crystalline mass which was recrystallized from a mixture of petr. benzine and benzene to 0.9 g (60%) of colorless prisms, mp 185—186°. IR ν_{max}^{KBr}: 1675 cm^{-1} ($\nu_{c=o}$). *Anal.* Calcd. for $C_{18}H_{12}ON_4$: C, 71.99; H, 4.03; N, 18.65. Found: C, 71.75; H, 3.94; N, 18.38.

Other 4(3*H*)-quinazolinones (**1**, **3**, **4**, and **5**) were prepared by this procedure (Table I).

Method b——2-(2-Thenoylamino)-N-(*o*-tolyl)benzamide (**22**): To a solution of 5.0 g (0.022 mol) of N-(*o*-tolyl)-2-aminobenzamide (**16**) dissolved in a mixture of 30 ml of benzene and 5 ml of pyridine, a solution of 3.5 g (0.024 mol) of 2-thiophenecarbonyl chloride in 10 ml of benzene was added dropwise and the mixture was refluxed for 1 hr. After evaporation of the solvent *in vacuo*, H_2O was added to the residue and the mixture was allowed to stand overnight. The separated colorless crystals were collected by suction and recrystal-

lized from dimethylformamide-EtOH to 4.8 g (65%) of colorless prisms, mp 203—205°. *Anal.* Calcd. for $C_{19}H_{16}O_2N_2S$: C, 67.84; H, 4.79; N, 8.33. Found: C, 67.75; H, 4.68; N, 8.28.

2-(2-Thienyl)-3-(*o*-tolyl)-4(3*H*)-quinazolinone (**12**): Without a solvent, 4.1 g (0.012 mol) of N-(*o*-tolyl)-2-(2-thenoylamino)benzamide (**22**) was heated in an oil bath at 230—240° for 20 hr. The reaction mixture was cooled, dissolved in a small portion of $CHCl_3$, and then applied to the top of a column packed with 50 g of Al_2O_3 (300 mesh). The product (**12**) was eluted with $CHCl_3$. From the first effluent fraction, a crude crystalline mass was obtained and recrystallized from MeOH to 2.1 g (54%) of light brown prisms, mp 137—138°. IR ν_{max}^{KBr}: 1683 cm^{-1} ($\nu_{C=O}$). *Anal.* Calcd. for $C_{19}H_{14}ON_2S$: C, 71.68; H, 4.43; N, 8.80. Found: C, 71.92; H, 4.41; N, 9.08.

Method c——2-Isonicotinoylaminobenzoic Acid (**24**): To a mixture of 13.7 g (0.1 mol) of anthranilic acid and 13.5 g (0.11 mol) of isonicotinic acid in 25 ml of toluene, 15 ml of $POCl_3$ was added dropwise at room temperature with stirring and then heated in an oil bath under reflux for 30 min. After cooling in an ice bath, a crystalline mass was collected by suction and dissolved in 10% aq. Na_2CO_3 soln. The alkaline solution was neutralized with 10% HCl and separated crystals were collected by suction, washed with H_2O, dried, and recrystallized from MeOH, giving 2-isonicotinoylaminobenzoic acid (**24**) as colorless prisms, mp 275—278°, in 60% yield. *Anal.* Calcd. for $C_{13}H_{10}O_3N_2$: C, 64.46; H, 4.16; N, 11.57. Found: C, 64.50; H, 4.25; N, 11.52.

2-Nicotinoylaminobenzoic acid (**23**) (mp 260°; reported[15] mp 263—264°) was prepared from anthranilic acid and nicotinic acid in the same manner as above.

2-(3-Pyridyl)-3-(*o*-chlorophenyl)-4(3*H*)-quinazolinone (**6**): To a solution of 8.0 g (0.033 mol) of 2-nicotinoylaminobenzoic acid (**23**) and 4.6 g (0.036 mol) of *o*-chloroaniline dissolved in 30 ml of dry xylene, 2.7 g (0.020 mol) of PCl_3 was added dropwise at 0—5°. The mixture was stirred for 1 hr at room temperature and then refluxed with stirring for 3 hr. After the reaction was completed, the solvent was evaporated *in vacuo* and the residue dissolved in a small portion of $CHCl_3$ was chromatographed over 70 g of Al_2O_3 (300 mesh), chloroform being used as eluant. From the first effluent fraction, a crude crystalline mass was obtained and recrystallized from petr. benzine–benzene to 6.8 g (62%) of colorless prisms, mp 117—118°. IR ν_{max}^{KBr}: 1685 cm^{-1} ($\nu_{C=O}$). *Anal.* Calcd. for $C_{19}H_{12}ON_3Cl$: C, 68.37; H, 3.63; N, 12.59. Found: C, 68.67; H, 3.67; N, 12.73.

Method d——2-(4-Pyridyl)-4*H*-3,1-benzoxazin-4-one (**26**): A mixture of 0.05 mol of 2-isonicotinoylaminobenzoic acid and 40.8 g (0.4 mol) of Ac_2O was heated under reflux for 3 hr. After the reaction was completed, an excess of Ac_2O was evaporated under reduced pressure, and the residue solidified on chilling flask. The crude benzoxazone was recrystallized from a mixture of benzene and petr. benzine with activated charcoal to 2-(4-pyridyl)-4*H*-3,1-benzoxazin-4-one (**26**) as light yellow prisms, mp 183—185°, in 80% yield. *Anal.* Calcd. for $C_{13}H_8O_2N_2$: C, 69.64; H, 3.60; N, 12.50. Found: C, 69.80; H, 3.43; N, 12.44.

2-(3-Pyridyl)-4*H*-3,1-benzoxazin-4-one (**25**) (mp 150—152°; reported[15] mp 153°) was prepared from from 2-nicotinoylaminobenzoic acid (**23**) in the same manner as that for **26**.

2-(3-Pyridyl)-3-(2-chloro-6-methylphenyl)-4(3*H*)-quinazolinone (**9**): A mixture of 2.2 g (0.014 mol) of 2-(3-pyridyl)-4*H*-3,1-benzoxazin-4-one (**25**) and 2.0 g (0.014 mol) of 2-chloro-6-methylaniline was heated in an oil bath at 210—220° for 20 hr. The reaction mixture was cooled, dissolved in ether, and the solution was purified by chromatography (Al_2O_3), using ether as eluant, in the same manner as above. From the first effluent fraction, 2.9 g (58%) of colorless prisms (**9**), mp 147—149°, was obtained. IR ν_{max}^{KBr}: 1690 cm^{-1} ($\nu_{C=O}$). *Anal.* Calcd. for $C_{20}H_{14}ON_3Cl$: C, 69.07; H, 4.06; N, 12.08. Found: C, 69.15; H, 4.23; N, 12.15.

Other compounds (**2**, **7**, **8**, and **10**) were prepared similarly (Table I).

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