Synthesis of 4(3*H*)-Quinazolinones from Derivatives of Methyl 2-Isothiocyanatobenzoate

William D. Dean and Eleftherios P. Papadopoulos

Department of Chemistry, University of New Mexico,
Albuquerque, New Mexico 87131

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Ethyl *N*-(2-methoxycarbonylphenyl)thiocarbamate (**2**), *N*-(2-ethoxycarbonylphenyl)-4-methoxythiobenzamide (**3b**), and 2-(4-methoxyphenyl)-4*H*-3,1-benzothiazin-4-one (**4a**), react with nucleophilic reagents containing at least one primary amino group to yield a variety of 2-substituted and 2,4-disubstituted 4(3*H*)-quinazolinones, as well as some tricyclic and tetracyclic products.

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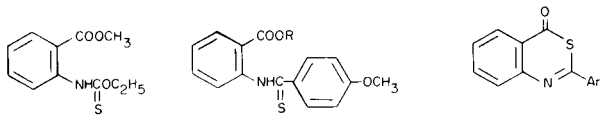
Although the chemistry of methyl 2-isothiocyanatobenzoate (**1**) has been investigated extensively (1), reactions of derivatives of this reagent suitable for preparation of heterocyclic compounds have not attracted much attention. In this paper, we report on the results of reactions of three derivatives of isothiocyanate **1**, ethyl *N*-(2-methoxycarbonylphenyl)thiocarbamate (**2**), *N*-(2-ethoxycarbonylphenyl)-4-methoxythiobenzamide (**3b**), and 2-(4-methoxyphenyl)-4*H*-3,1-benzothiazin-4-one (**4a**) (Scheme 1) with nucleophilic reagents. All three compounds can be

Scheme 1



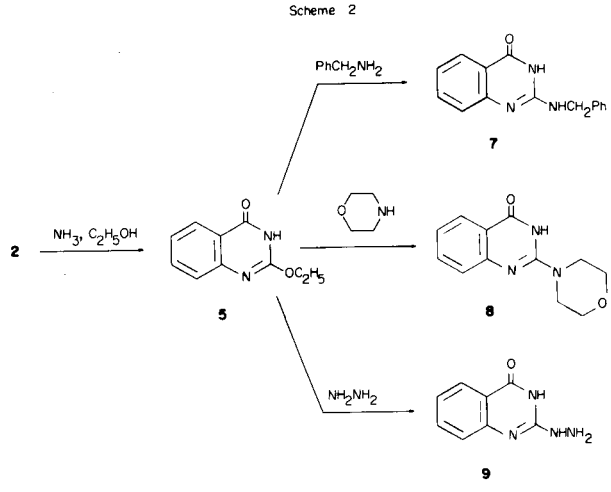
2 **3a**, R = CH_3; **3b**, R = C_2H_5 **4a**, Ar = 4-$CH_3OC_6H_4$ **4b**, Ar = 4-$CH_3C_6H_4$

expected to react with reagents containing a primary amino group at both carbonyl and thiocarbonyl (potential thiocarbonyl for **4a** to from a 4(3*H*)-quinazolinone with elimination of methanol, or ethanol and/or hydrogen sulfide.

Reactions of Compound **2**.

When thiocarbamate **2**, which is readily obtainable from isothiocyanate **1** and ethanol is treated with ethanolic ammonia at room temperature (closed flask) for four days, 2-ethoxy-4(3*H*)-quinazolinone (**5**) is formed as product, whereas an analogous treatment on a steam bath leads to a mixture of **5** and 2-amino-4(3*H*)-quinazolinone (**6**) (2). Although a logical intermediate in the conversion of **2** into **6**, compound **5** actually reacts very slowly with ammonia. Thus, heating of **5** with ethanolic ammonia (closed flask) at 100° for four days causes only partial (20%) conversion into **6** and about 65% of **5** is recovered. However, **5** reacts readily with benzylamine, morpholine, and to undergo nucleophilic substitution at C-2 yielding 2-benzylamino- (**7**), 2-(4-morpholino)- (**8**), and 2-hydrazino-4(3*H*)-quinazolinone (**9**), respectively (Scheme 2). These

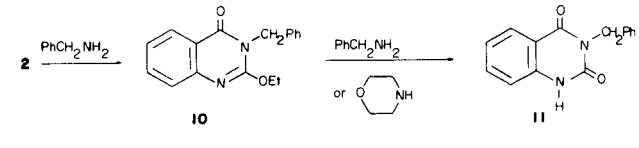
Scheme 2



results, together with the observation that **5** does not react with aniline, either when the neat reagent is used at 100°, or its solution in refluxing toluene, indicate that the reactivity of amines with respect to nucleophilic substitution at C-2 of **5** roughly parallels their basicity. It is interesting to note that treatment of **5** with aniline and anilinium chloride at 100° results in the formation of 2,4(1*H*,3*H*)-quinazolinedione. Presumably, protonation of **5** provides a good leaving group and, instead of the C-2 of the heterocyclic ring, the nucleophile in this case attacks either the α-C or the β-C of the ethyl group to cause respectively an S_N2 or an E_2 reaction to occur.

Thiocarbamate **2** reacts with benzylamine in refluxing ethanol to give an almost quantitative yield of 3-benzyl-2-ethoxy-4(3*H*)-quinazolinone (**10**). In view of the behavior

Scheme 3

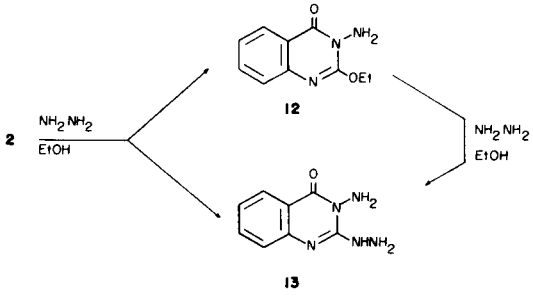


hydrazine of **5** toward nucleophiles, the analogous reactivity of **10** was briefly examined. It was found that this compound does not react with benzylamine at 100°,

whereas at 150° a reaction takes place which yields 3-benzyl-2,4(1*H*,3*H*)-quinazolinedione (**11**). The same result is observed when **10** is heated with morpholine at 100° (Scheme 3). Steric hindrance at C-2 of the heterocycle is the probable reason why these reagents prefer to attack the α-C (S_N2) or β-C (E_2) of the ethyl group of **10**. Inspection of a molecular model of this compound shows that the benzyl and ethoxy groups can shield the C-2 on both faces of the heterocyclic ring.

When thiocarbamate **2** is treated with the less basic aniline in a variety of refluxing solvents, little or no hydrogen sulfide is evolved and the starting material is largely recovered. An attempt to use forcing conditions by boiling **2** with aniline resulted in an undesired reaction yielding 3-phenyl-1*H*,3*H*-quinazolin-4-one-2-thione. On the other hand, the reaction of **2** with hydrazine proceeds as anticipated. When an equivalent amount of hydrazine is used in room-temperature ethanol, the product is

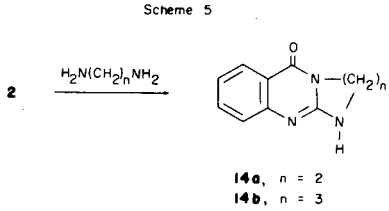
Scheme 4



3-amino-2-ethoxy-4(3*H*)-quinazolinone (**12**), whereas use of an excess of hydrazine in refluxing ethanol yields 3-amino-2-hydrazino-4(3*H*)-quinazolinone (**13**) (Scheme 4). The former compound may well be an intermediate in the formation of the latter, since treatment with hydrazine in refluxing ethanol converts **12** into **13**.

The fact that **12** undergoes nucleophilic substitution at C-2 when treated with hydrazine suggested reactions of thiocarbamate **2** with 1,2- and 1,3-dinucleophilic reagents aiming at the formation of a third ring fused at positions 2 and 3 of the quinazolinone structure. As anticipated, **2** was found to react with 1,2-ethanediamine in refluxing benzene and with 1,3- propanediamine in refluxing toluene to yield the tricyclic 2,3-dihydro-1*H*-imidazo-[2,1-*b*]quinazolin-5-one (**14a**) and 1,2,3,4-tetrahydro-6*H*-pyrimido[2,1-*b*]quinazolin-6-one (**14b**) (Scheme 5). Although the analogous reaction of **2** with 2-aminoethanethiol yields the expected 2,3-dihydro-5*H*-thiazolo[2,3-*b*]-

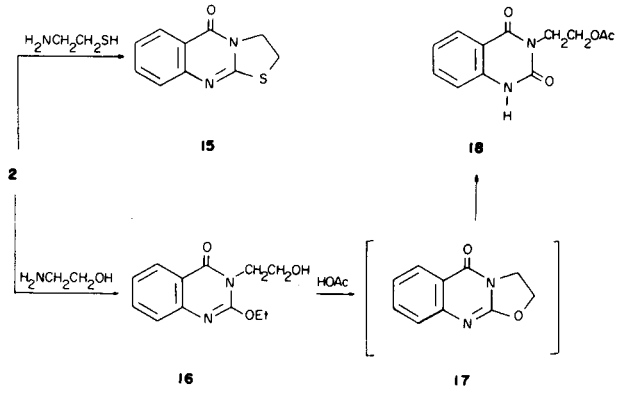
Scheme 5



14a, n = 2
14b, n = 3

quinazolin-5-one (**15**), when 2-aminoethanol is used as reagent 2-ethoxy-3-(2-hydroxyethyl)-4(3*H*)-quinazolinone (**16**) is isolated as the product (Scheme 6). An attempt to cyclize this compound into the oxazolo derivative **17** by re-

Scheme 6



fluxing it in acetic acid led instead to 3-(2-acetoxyethyl)-2,4(1*H*,3*H*)-quinazolinedione (**18**). This result indicates that the expected product (**17**) is formed, but reacts further with acetic acid to form **18** (3).

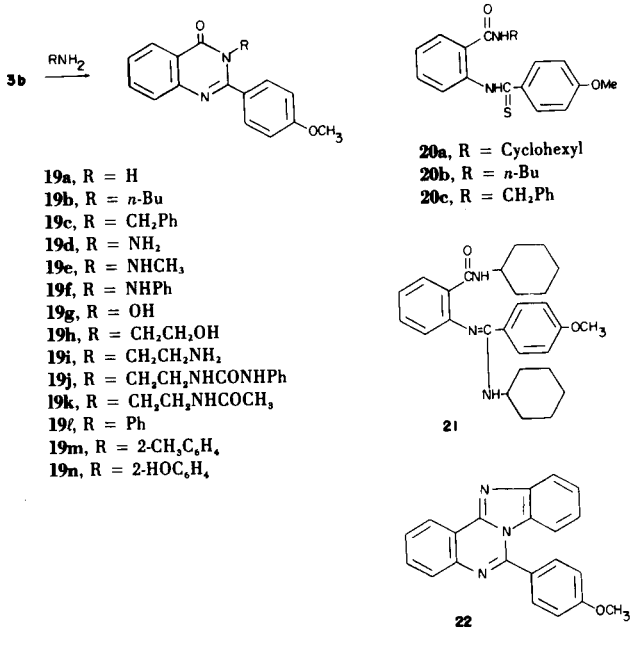
Reaction of Compound **3b**.

In analogy with the formation of *N*-ethoxycarbonylthioamides (4), preparation of thioamide **3a** was attempted by the aluminum chloride catalyzed reaction of anisole with isothiocyanate **1**. The product isolated from this reaction, however, is not **3a**, as evidenced by its proton nmr spectrum, which shows the absence of an ester methyl group, and by its ir spectrum, which contains only a low wavenumber (1650 cm^{-1}) carbonyl band. These data, together with the melting point of the pure compound, indicate that the product actually is 2-(4-methoxyphenyl)-4*H*-3,1-benzothiazin-4-one (**4a**) (5). It is likely that the initial adduct of anisole and **1** cyclizes to form **4a** under the strongly acidic reaction conditions. Indeed, thioamide **3b** is converted into **4a** upon refluxing in acetic acid. Since the analogous reaction of **1** with toluene and aluminum chloride gives the corresponding benzothiazinone (**4b**) in poor yield (26%), whereas with benzene only tars are obtained, it may be concluded that a fairly strongly activated aromatic ring is required for the reaction to be successful. The heterocyclic ring of **4a** is opened up easily by the ac-

tion of sodium ethoxide in ethanol and thus thioamide **3b** becomes readily available.

When **3b** is heated with ethanolic ammonia at 100° (closed flask), 2-(4-methoxyphenyl)-4(3*H*)-quinazolinone (**19a**) is formed. Analogous reactions of **3b** with *n*-butylamine and benzylamine yield 3-butyl- (**19b**) and 3-benzyl-2-(4-methoxyphenyl)-4(3*H*)-quinazolinone (**19c**), respectively (Scheme 7). A similar treatment with cyclohexylamine, however, does not yield a cyclized product but a mixture of *N*-(2-cyclohexylcarbamoylphenyl)-4-methoxythiobenzamide (**20a**) and *N*-cyclohexyl-*N'*-(2-cyclohexylcarbamoylphenyl)-4-methoxybenzamidine (**21**). The structure assignments of these compounds are based on spectroscopic and analytical data. Thus the proton nmr spectrum of **20a** shows the presence of amide, aromatic, cyclohexyl, and methoxy protons in a ratio of 2:8:11:3, whereas the spectrum of **21** exhibits twice as many cyclohexyl protons. The fact that a limited duration reaction of **3b** with cyclohexylamine yields **20a** and only a trace of **21** may be taken to signify that the latter compound is formed by the further reaction of **20a** with cyclohexylamine. The failure of the reaction with cyclohexylamine to yield a cyclized product should probably be attributed to the somewhat sterically hindered nature of the nitrogen atom of this reagent. Although thioamide **20a** is recovered unchanged after it has been heated with triethylamine in ethanol, an analogous treatment with ammonia converts **20a** into **19a** possibly through an amidine-type intermediate analogous to **21**.

Scheme 7



The reaction of thioamide **3b** with hydrazine yields 3-amino-2-(4-methoxyphenyl)-4(3*H*)-quinazolinone (**19d**), as evidenced by a two-proton singlet (NH_2) in the nmr spectrum of the product, which disappears upon addition of deuterium oxide to the solution. Furthermore, treatment of this product with nitrous acid causes deamination (6) and yields quinazolinone **19a**. Methylhydrazine and phenylhydrazine react with **3b** in an analogous manner and yield 2-(4-methoxyphenyl)-3-methylamino- (**19e**) and 2-(4-methoxyphenyl)-3-phenylamino-4(3*H*)-quinazolinone (**19f**) respectively. An attempt to force formation of a 7-membered heterocyclic ring through use of *N,N'*-dimethylhydrazine as reagent was unsuccessful. Very little hydrogen sulfide was evolved and only a tar was obtained as product. On the other hand, **3b** reacts as expected with hydroxylamine to form 3-hydroxy-2-(4-methoxyphenyl)-4(3*H*)-quinazolinone (**19g**).

Thioamide **3b** reacts with 2-aminoethanol to yield a product identified as 3-(2-hydroxyethyl)-2-(4-methoxyphenyl)-4(3*H*)-quinazolinone (**19h**) on the basis of its nmr spectrum, which exhibits a pair of two-proton triplets for the methylene protons, as well as a one-proton singlet for the hydroxy proton. An analogous reaction with 2-aminoethanethiol was unsuccessful, but treatment of **3b** with 1,2-ethanediamine gave the anticipated 3-(2-aminoethyl)-2-(4-methoxyphenyl)-4(3*H*)-quinazolinone (**19i**). This compound was isolated as an oil which could not be distilled without decomposition and was characterized by the presence in its nmr spectrum of the signals expected from the aminoethyl group protons. Treatment of **19i** with phenyl isocyanate yields the expected urea **19j**, the spectral and microanalytical data of which confirm its structure. It is interesting to note that when the reaction of **3b** with 1,3-ethanediamine is run in refluxing acetic acid, the isolated product is the *N*-acetyl derivative (**19k**) of the aminoethyl compound **19i**. In contrast to *N*-ethoxycarbonylthioamides which react readily with aromatic amines to form *N*-aryl-*N'*-ethoxycarbonylamidines (7), no reaction occurs when **3b** is treated with aniline in refluxing ethanol, or toluene, whereas under drastic conditions extensive decomposition takes place.

Reactions of Benzothiazinone **4a**.

This compound, prepared by a different method (5), has been reported to react in refluxing ethanol with ammonia at C-2, but with benzylamine at C-4 to yield respectively an internal amidinium salt and *N*-(2-benzylcarbamoylphenyl)-4-methoxythiobenzamide (**20c**) (8). We have found that quinazolinones **19a** and **19c** are the respective products where **4a** is heated with ethanolic ammonia (closed flask) at 100°, or refluxed with benzylamine. Similarly, heating of **4a** with *n*-butylamine on a steam bath yields quinazolinone **19b**. Use of cyclohexylamine, however, results in the formation of a mixture of thioamide **20a** and amidine **21**, exactly as for the analogous reaction of thioamide **3b**. The formation of quinazolinones **19b** and **19c** by the above reaction very likely involves the in-

termediate formation of thioamides **20b** and **20c** (8b). Indeed, **20c** is readily converted into **19c** upon brief boiling in benzylamine.

As observed with other 2-substituted-4*H*-3,1-benzothiazin-4-ones (8), compound **4a** reacts with aromatic amines to yield 2,3-disubstituted 4(3*H*)-quinazolinones. We have found, however, that this reaction is greatly facilitated by an acidic catalyst. Thus, whereas the reaction of **4a** with aniline to yield 2-(4-methoxyphenyl)-3-phenyl-4(3*H*)-quinazolinone (**19ℓ**) requires over 5 hours of refluxing for completion, the same reaction run in the presence of hydrochloric acid is complete within 20 minutes. An analogous treatment of **4a** with *o*-toluidine yields 2-(4-methoxyphenyl)-3-(2-methylphenyl)-4(3*H*)-quinazolinone (**19m**).

When benzothiazinone **4a** is allowed to react with *o*-aminophenol in refluxing acetic acid, 3-(2-hydroxyphenyl)-2-(4-methoxyphenyl)-4(3*H*)-quinazolinone (**19n**) is formed as product. The structure assigned to this compound is consistent with its ir and nmr spectra and is further supported by its solubility in 10% aqueous sodium hydroxide and a positive ferric chloride test. The analogous reaction of **4a** with *o*-phenylenediamine leads to 6-(4-methoxyphenyl)benzimidazo[1,2-*c*]quinazoline (**22**). In this case, the initial cyclization is followed by condensation of the second amino group of the reagent with the carbonyl at position 4 of the intermediate quinazolinone to form an imidazole ring. The structure of this product is supported by its ir spectrum, which indicates the absence of carbonyl and amino groups, and by its proton nmr spectrum, which exhibits only aromatic and methoxy protons in a ratio of 4:1. An attempt to obtain a tricyclic product by allowing benzothiazinone **4a** to react in a similar manner with 1,2-ethanediamine resulted instead in the formation of 3-(2-acetamidoethyl)-2-(4-methoxyphenyl)-4(3*H*)-quinazolinone (**19k**), just like the analogous reaction of thioamide **3b**.

EXPERIMENTAL (9)

Ethyl-*N*-(2-methoxycarbonylphenyl)thiocarbamate (**2**) (1a).

A mixture of 10.0 g (0.052 mole) of methyl 2-isothiocyanatobenzoate (**1**) (1b) and 25 ml of absolute ethanol was allowed to reflux for 16 hours. The solid which precipitated upon cooling of the solution was washed with cold ethanol to provide 9.8 g (79% of **2**, mp 60-65°). Recrystallization from ethanol gave the pure compound in the form of colorless crystals, mp 69-70° [lit (1a) mp 70°]; ir: 3200 (N-H), 1690 (C=O) cm^{-1}; nmr (deuteriochloroform): δ 1.4 (t, 3, CH_2CH_3), 3.9 (s, 3, OCH_3), 4.6 (q, 2, CH_2), 7.0-7.7 (m, 2, ArH), 7.9-8.1 (m, 1, ArH), 8.5-8.6 (m, 1, ArH).

2-Ethoxy-4(3*H*)-quinazolinone (**5**).

A mixture of 1.0 g (4.2 mmoles) of thiocarbamate **2** and 20 ml of ethanolic ammonia (10) was allowed to stand in a closed flask, at room temperature, for 4 days. After evaporation of the solvent, the residue was washed with water to yield 0.75 g (94%) of **5**, mp 168-172°. Recrystallization from ethanol gave pure **5** as colorless crystals, mp 175.5-176.5° [lit (11) mp 179°]; ir: 1670 (C=O) cm^{-1}; nmr (deuteriochloroform): δ 1.4 (t, 3, CH_3), 4.6 (q, 2, CH_2), 7.2-7.8 (m, 3, ArH), 8.2-8.3 (m, 1, ArH), 11.0 (s, 1, NH).

2-Benzylamino-4(3*H*)-quinazolinone (**7**).

A mixture of 0.20 g (1.0 mmole) of **5**, 0.21 g (2.0 mmoles) of benzylamine, and 3 ml of toluene was refluxed for a period of 24 hours. The solid that precipitated upon cooling was washed with ethanol to give 0.22 g (88%) of **7** as colorless crystals, mp 215-217° [lit (12) mp 213.5-214.5°]; ir: 3580, 3340 (N-H), 1670 (C=O) cm^{-1}; nmr: δ 4.6 (m, 2, CH_2), 6.7 (m, 1, $NHCH_2$), 7.0-7.7 (m, 8, ArH), 7.8-8.0 (m, 1, ArH), 11.0 (s, 1, NHCO).

2-(4-Morpholino)-4(3*H*)-quinazolinone (**8**).

A mixture of **5** (0.28 g, 1.5 mmoles), morpholine (0.22 g, 2.5 mmoles), and 3 ml of toluene was allowed to reflux for 22 hours. Upon cooling, there precipitated 0.21 g (62%) of **8** as colorless crystals, mp 237-239° [lit (13) mp 237°]; ir: 1670 (C=O) cm^{-1}; nmr: δ 3.6 [s, 8, $(CH_2)_4$], 7.0-7.7 (m, 3, ArH), 7.8-8.0 (m, 1, ArH), 11.3 (s, 1, NH).

2-Hydrazino-4(3*H*)-quinazolinone (**9**).

A mixture of 0.28 g (1.5 mmoles) of **5**, 0.10 g (3.1 mmoles) of hydrazine and 4 ml of ethanol was refluxed for 16 hours. Upon cooling, there precipitated 0.25 g of crude **9**, mp 253° dec. Recrystallization from ethanol yielded 0.19 g (73%) of pure **9** as colorless crystals, mp 360° dec [lit (13) mp 360° dec]; ir: 1670 (C=O) cm^{-1}; nmr: δ 7.1-7.9 (m, 3, ArH), 8.1-8.2 (m, 1, ArH).

Reaction of **5** with Aniline in the Presence of Anilinium Chloride.

A mixture of 0.30 g (1.6 mmoles) of **5**, 3 ml of aniline and 0.30 g of anilinium chloride was heated on a steam bath for 2.5 hours. The resulting mixture was neutralized with aqueous sodium bicarbonate and steam distilled to yield a residue, which was washed with aqueous ethanol to give 0.19 g (73%) of 2,4(1*H*,3*H*)-quinazolinedione, mp 345-348° [lit (15) mp 356°]; ir: 1700, 1660 (C=O) cm^{-1}; nmr: δ 7.0-7.3 (m, 2, ArH), 7.5-8.0 (m, 2, ArH), 11.4, 11.5 (overlaping s, 2, NH). These spectra were superimposable on those of an authentic sample.

3-Benzyl-2-ethoxy-4(3*H*)-quinazolinone (**10**).

A mixture of 0.50 g (2.1 mmoles) of thiocarbamate **2**, 0.50 g (4.7 mmoles) of benzylamine, and 5 ml of ethanol was refluxed for 22 hours. The resulting solution was cooled and mixed with water to yield 0.55 g (93%) of **10**, mp 95-96°. Recrystallization from ethanol gave the pure compound as colorless crystals, mp 96-97°; ir: 1670 (C=O) cm^{-1}; nmr (deuteriochloroform): δ 1.4 (t, 3, CH_3), 4.5 (q, 2, CH_2CH_3), 5.3 (s, 2, CH_2Ph), 6.9-7.9 (m, 8, ArH), 8.2-8.3 (m, 1, ArH).

Anal. Calcd. for $C_{17}H_{16}N_2O_2$: C, 72.84; H, 5.75; N, 9.99. Found: C, 72.96; H, 5.81; N, 10.15.

Reaction of **10** with Benzylamine and Morpholine.

Quinazoline **10** (0.30 g, 1.1 mmoles) was heated with 1 ml of benzylamine, at 150° (oil bath), for 12 hours. The glass that was formed upon cooling of the reaction mixture was triturated with ethyl ether to yield 0.10 g (37%) of 3-benzyl-2,4(1*H*,3*H*)-quinazolinedione (**11**), mp 220-223° [lit (14) mp 227°]; ir: 1710, 1650 (C=O) cm^{-1}; nmr δ 5.2 (s, 2, CH_2), 7.3 (s, 5, ArH), 7.0-8.1 (m, 4, ArH), 11.1 (s, 1, NH). Evaporation of the filtrate led to the recovery of 0.12 g of starting material.

In a similar manner, 0.30 g (1.1 mmoles) of **10** was heated with 1 ml of morpholine on a steam bath for 16 hours to give 0.13 g (48%) of crude **11**, mp 213-217°, spectroscopically identical with the product of the previous reaction. Evaporation of the filtrate yielded 0.10 g of unreacted **10**.

3-Amino-2-ethoxy-4(3*H*)-quinazolinone (**12**).

A mixture of thiocarbamate **2** (0.50 g, 2.1 mmoles), hydrazine (0.66 g, 2.1 mmoles), and ethanol (3 ml) was allowed to stand at room temperature until evolution of hydrogen sulfide had stopped (4 days). Filtration yielded 0.30 g of **12**, mp 94-96° and concentration of the filtrate afforded an additional 0.10 g of **12**, mp 90-92° (total yield, 93%). The pure compound was obtained by recrystallization from ethanol as colorless crystals, mp 99.5-100°; ir: 3325, 3300, 3200 (N-H), 1660 (C=O) cm^{-1}; nmr: δ 1.4 (t, 3,

CH_3), 4.5 (q, 2, CH_2), 5.7 (s, 2, NH_2), 7.1-7.9 (m, 3, ArH), 8.0-8.1 (m, 1, ArH).

Anal. Calcd. for $C_{10}H_{11}N_3O_2$: C, 58.53; H, 5.40; N, 20.48. Found: C, 58.37; H, 5.61; N, 20.34.

3-Amino-2-hydrazino-4(3*H*)-quinazolinone (**13**).

Method A.

A mixture of 0.50 g (2.1 mmoles) of **2**, 0.70 g (0.022 mole) of hydrazine, and 5 ml of ethanol was refluxed until evolution of hydrogen sulfide had stopped (3 hours). Upon cooling, there precipitated 0.40 g (100%) of **13**, mp 219-221° [lit (16) mp 219-220°]; ir: 3325, 3300, 3200 (N-H), 1650 (C=O) cm^{-1}; nmr: δ 4.5 (br s, 2, NHNH_2), 5.5 (s, 2, NNH_2), 7.1-7.9 (m, 4, ArH, NH), 8.0-8.2 (m, 1, ArH).

Method B.

A mixture of 0.10 g (0.49 mmole) of **12**, 2 ml of ethanol, and 2 drops of hydrazine was refluxed for 2.5 hours. Filtration of the cooled reaction mixture yielded 0.050 g (53%) of **13**, mp 212-214°.

2,3-Dihydro-1*H*-imidazo[2,1-*b*]quinazolin-5-one (**14a**).

Method A.

A mixture of thiocarbamate **2** (0.50 g, 2.1 mmoles), ethylenediamine (0.20 g, 3.3 mmoles), and benzene (5 ml) was refluxed for a period of 16 hours. Upon cooling, there was collected 0.29 g (74%) of crude **14a**, mp 250-255°. Recrystallization from ethanol gave the pure compound, mp 264-265° [lit (17) mp 266-268°]; ir: 1660 (C=O) cm^{-1}; nmr: δ 3.5-3.8 (m, 2, CH_2NH), 4.0-4.3 (m, 2, CH_2NCO), 7.0-7.4 (m, 2, ArH), 7.5-8.1 (m, 3, ArH, NH).

Method B.

A mixture of 0.50 g of **2** and 2 ml of ethylenediamine was heated on a steam bath for 21 hours. Following addition of 3 ml of ethanol, heating was continued for a further 3 hours. The mixture was then cooled and filtered to yield 0.25 g (64%) of **14a**, mp 263-265°.

1,2,3,4-Tetrahydro-6*H*-pyrimido[2,1-*b*]quinazolin-6-one (**14b**).

A mixture of 1.0 g (4.2 mmoles) of **2**, 0.45 g (6.1 mmoles) of 1,3-propanediamine, and 7 ml of toluene was refluxed for 8 hours. Filtration of the cooled reaction mixture yielded 0.69 g (82%) of **14b**, mp 235-237°. The pure compound was obtained by recrystallization from ethanol as colorless crystals, mp 237-238° [lit (18) mp 227-229°]; ir: 1660 (C=O) cm^{-1}; nmr: δ 2.0 (m, 2, $CH_2CH_2CH_2$), 3.3 (m, 2, CH_2NH), 4.0 (m, 2, CH_2NCO), 7.0-7.3 (m, 2, ArH), 7.5-8.1 (m, 3, ArH, NH).

Anal. Calcd. for $C_{11}H_{11}N_3O$: C, 65.66; H, 5.51; N, 20.88. Found: C, 65.58; H, 5.49; N, 21.04.

2,3-Dihydro-5*H*-thiazolo[2,3-*b*]quinazolin-5-one (**15**).

A mixture of 0.50 g (2.1 mmoles) of **2**, 0.34 g (3.0 mmoles) of 2-aminoethanethiol hydrochloride, and 7 ml of pyridine was allowed to reflux for 20 hours. Evaporation of the solvent under reduced pressure yielded a yellow oil, which solidified upon trituration with 10% aqueous sodium hydroxide to give 0.25 g (58%) of crude **15**, mp 146-152°. Recrystallization from ethanol afforded the pure compound as colorless crystals, mp 157-159° [lit (1c) mp 155-156°]; ir: 1770 (C=O) cm^{-1}; nmr (deuteriochloroform): δ 3.5 (t, 2, SCH_2), 4.6 (t, 2, NCH_2), 7.2-7.9 (m, 3, ArH), 8.2-8.3 (m, 1, ArH).

2-Ethoxy-3-(2-hydroxyethyl)-4(3*H*)-quinazolinone (**16**).

Thiocarbamate **2**, (1.0 g, 4.2 mmoles) was refluxed in 10 ml of tetrahydrofuran with 0.60 g (9.8 mmoles) of 2-aminoethanol for a period of 22 hours. Upon cooling of the reaction mixture there precipitated 0.80 g (82%) of **16**, mp 76-79°. The pure compound was obtained by recrystallization from ethanol as colorless crystals, mp 84-85°; ir: 3350 (O-H), 1680 (C=O) cm^{-1}; nmr: δ 1.4 (t, 3, CH_3), 2.8 (br t, 1, OH), 3.9 (m, 2, CH_2CH_2OH), 4.3 (t, 2, CH_2CH_2OH), 4.6 (q, 2, CH_2CH_3), 7.2-7.8 (m, 3, ArH), 8.1-8.2 (m, 1, ArH).

Anal. Calcd. for $C_{12}H_{14}N_2O_3$: C, 61.53; H, 6.02; N, 11.96. Found: C, 61.69; H, 6.06; N, 12.02.

3-(2-Acetoxyethyl)-2,4(1*H*,3*H*)-quinazolinedione (**18**).

Quinazolinone **16** (0.050 g, 0.21 mmole) was refluxed in 1 ml of acetic acid for 4 hours. Upon cooling there precipitated 0.050 g (96%) of **18**, mp 165-167 [lit (3) mp 167-168.5°].

2-(4-Methoxyphenyl)-4*H*-3,1-benzothiazin-4-one (**4a**).

Anhydrous aluminum chloride (32.0 g, 0.24 mole) was added in 6-8 portions to a stirred and occasionally cooled mixture of anisole (26.0 g, 0.24 mole) and methyl 2-isothiocyanatobenzoate (23.3 g, 0.12 mole). After the reaction mixture had stood at room temperature for 1 hour, the resulting brown, tarry product was hydrolyzed by careful addition of a mixture of concentrated hydrochloric acid, water and ice to yield 16.0 g (50%) of crude **4a**, mp 165-170°. Recrystallization from ethanol gave the pure substance, mp 174-175° [lit (5) mp 173°]; ir: 1650 (C=O) cm^{-1}; nmr (deuteriochloroform): δ 3.9 (s, 3, CH_3), 6.9-7.1 (m, 2, ArH), 7.2-7.7 (m, 1, ArH), 7.8-8.3 (m, 5, ArH).

2-(4-Methylphenyl)-4*H*-3,1-benzothiazin-4-one (**4b**).

This compound was prepared by the same method as **4a**. Following recrystallization of the crude product from ethanol, there was obtained a 26% yield of **4b**, mp 128-129° [lit (5) mp 130°]; ir: 1650 (C=O) cm^{-1}; nmr (deuteriochloroform): 2.4 (s, 3, CH_3), 7.2-7.4 (m, 2, ArH), 7.5-7.7 (m, 1, ArH), 7.8-8.1 (m, 4, ArH), 8.3-8.4 (m, 1, ArH).

N-(2-Ethoxycarbonylphenyl)-4-methoxythiobenzamide (**3b**).

Benzothiazinone **4a** (1.5 g, 5.6 mmoles) was added in small portions to a solution of sodium ethoxide obtained from 0.13 g (5.6 mmoles) of sodium and 50 ml of absolute ethanol. After the resulting mixture had been stirred at room temperature for 0.5 hour, it was filtered to remove traces of insoluble material. Acidification of the filtrate with concentrated hydrochloric acid and washing of the resulting precipitate successively with water and ethanol yielded 1.6 g (91%) of **3b**, mp 114-116°. The pure compound was obstained as yellow crystals by recrystallization from ethanol, mp 115-116° [lit (19) mp 110°]; ir: 3200 (br, N-H), 1680 (C=O) cm^{-1}; nmr: 1.2 (t, 3, CH_3), 3.8 (s, 3, OCH_3), 4.2 (q, 2, CH_2CH_3), 7.0-7.2 (m, 2, ArH), 7.3-7.8 (m, 2, ArH), 7.9-8.1 (m, 4, ArH), 12.0 (s, 1, NH).

Anal. Calcd. for $C_{17}H_{17}NO_3S$: C, 64.74; H, 5.43; N, 4.44. Found: C, 64.76; H, 5.41; N, 4.43.

Cyclization of Thioamide **3b** into Benzothiazinone **4a**.

After a mixture of 0.50 g (1.6 mmole) of **3b** and 5 ml of acetic acid had been refluxed for 16 hours, it was cooled to yield 0.30 g (70%) of **4a** mp 173.5-175°. Partial evaporation of the filtrate led to the recovery of 0.10 g of unreacted **3b**.

2-(4-Methoxyphenyl)-4(3*H*)-quinazolinone (**19a**).

Method A.

A mixture of 0.50 g (1.6 mmoles) of thioamide **3b** and 10 ml of ethanolic ammonia was heated in a pressure bottle, on a steam bath, for 18 hours. Upon cooling there precipitated 0.30 g (75%) of **19a**, mp 245-246°. The pure compound was obtained by recrystallization from *N,N*-dimethylformamide as colorless crystals, mp 246-247° [lit (20) mp 245-246°].

Method B.

In a similar manner, from 0.50 g (1.9 mmoles) of benzothiazinone **4a** and 10 ml of ethanolic ammonia heated at 100° for 16 hours, there was obtained 0.30 g (64%) of **19a**, mp 240-243°.

Method C.

Thioamide **20a** (0.17 g, 0.46 mmole) was heated with 15 ml of ethanolic ammonia (closed flask) on a steam bath for a period of 3 days. The solid which precipitated upon cooling was washed with ethanol to afford 0.11 g (95%) of **19a**, mp 245-246°.

3-Butyl-2-(4-methoxyphenyl)-4(3*H*)-quinazolinone (**19b**).

Method A.

Thioamide **3b** (0.50 g, 1.6 mmoles) was heated with 2 ml of *n*-butylamine on a steam bath for 2 hours. The cooled reaction product was dissolved in ethyl ether and this solution was washed with three portions of 1% hydrochloric acid. Evaporation of the ether solution yielded an oil which, after dissolution in 5% hydrochloric acid and reprecipitation with 10% aqueous sodium hydroxide, gave 0.30 g (61%) of **19b**, mp 60-61°. The pure substance was obtained by recrystallization from petroleum ether (bp 30-60°), mp 63.5-64.5°; ir: 1670 (C=O) cm^{-1}; nmr (deuteriochloroform): δ 0.8-1.8 (m, 7, $CH_3CH_2CH_2$), 3.9 (s, 3, OCH_3), 4.1 (m, 2, $CH_2C_3H_7$), 7.0-7.1 (m, 2, ArH), 7.4-7.8 (m, 5, ArH), 8.3-8.4 (m, 1, ArH).

Anal. Calcd. for $C_{19}H_{20}N_2O_2$: C, 74.00; H, 6.54; N, 9.08. Found: C, 74.17; H, 6.37; N, 9.04.

Method B.

In a similar manner, from 0.50 g (1.9 mmoles) of benzothiazinone **4a** and 3 ml of *n*-butylamine heated at 100° for 3 hours, there was obtained 0.12 g (21%) of **19b**, mp 63-64°.

3-Benzyl-2-(4-methoxyphenyl)-4(3*H*)-quinazolinone (**19c**).

Method A.

A mixture of 0.35 g (1.1 mmoles) of thioamide **3b** and 2 ml of benzylamine was boiled until evolution of hydrogen sulfide had stoped (20 minutes). After it had been cooled, the reaction mixture was dissolved in ethyl ether and the resulting solution was washed with three 10-ml portions of 1% hydrochloric acid. Partial evaporation of the ether solution yielded two crops of crystals: 0.29 g, mp 139.5-140.5° and 0.02 g, mp 137-139° (total yield, 82%). Pure **19c** was obtained by recrystallization from ethanol as colorless crystals, mp 139.5-140.5°; ir: 1670 (C=O) cm^{-1}; nmr (deuteriochloroform): δ 3.8 (s, 3, CH_3), 5.3 (s, 2, CH_2), 6.8-7.8 (m, 7, ArH), 8.3-8.4 (m, 1, ArH).

Anal. Calcd. for $C_{22}H_{18}N_2O_2$: C, 77.16; H, 5.30; N, 8.19. Found: C, 77.29; H, 5.18; N, 8.30.

Method B.

In a similar manner, from 0.50 g (1.9 mmoles) of benzothiazinone **4a** and 2 ml of benzylamine boiled for 25 minutes, there was obtained 0.54 g (84%) of **19c**, mp 133-137°.

Method C.

A mixture of 0.30 g (0.80 mmole) of thioamine **20c** (8b) and 2 ml of benzylamine was refluxed for 0.5 hour. Upon cooling and dilution with ethanol there was obtained 0.20 g (74%) of **19c**, mp 139-140°.

N-(2-Cyclohexylcarbamoylphenyl)-4-methoxythiobenzamide (**20a**) and *N*-Cyclohexyl-*N'*-(2-cyclohexylcarbamoylphenyl)-4-methoxybenzamidine (**21**).

Method A.

Thioamide **3b** (0.50 g, 1.6 mmoles) was heated with 4 ml of cyclohexylamine, on a steam bath, for 24 hours. The reaction mixture was dissolved in ethyl ether and this solution was extracted with three 10-ml portions of 2% hydrochloric acid. Evaporation of the ether solution yielded 0.15 g (25%) of **20a**, mp 174.5-176°, and recrystallization from aqueous ethanol afforded the pure compound as yellow crystals, mp 177-178°; ir: 3275 (N-H), 1675 (C=O) cm^{-1}; nmr: δ 1.0-2.0 [m, 10, $(CH_2)_5$], 3.6-4.2 (m, 1, NCH), 3.9 (s, 3, CH_3), 6.4 (br d, 1, CONH), 6.9-7.1 (m, 2, ArH), 7.2-7.7 (m, 3, ArH), 8.0-8.2 (m, 2, ArH), 9.1-9.3 (m, 1, ArH), 12.6 (s, 1, NHCS).

Anal. Calcd. for $C_{21}H_{24}N_2O_2S$: C, 68.45; H, 6.56; N, 7.60. Found: C, 68.61; H, 6.67; N, 7.67.

Upon standing for 24 hours, the combined aqueous acid extracts deposited 0.25 g (36%) of crude **21**, mp 188-192°. Recrystallization of this material from ethanol afforded pure **21**, mp 195-196°; ir: 3260 (N-H), 1625 (C=O) cm^{-1}; nmr: δ 1.1-2.2 [m, 20, $(CH_2)_{10}$], 3.8 (s, 3, CH_3), 4.0 (m, 2, CHN), 4.8 (br d, 1, NH), 6.2-6.4 (m, 1, CONH), 6.7-7.3 (m, 6, ArH), 8.1-8.3 (m, 1, ArH), 9.2-9.4 (m, 1, ArH).

Anal. Calcd. for $C_{27}H_{35}N_3O_2$: C, 74.79; H, 8.14; N, 9.69. Found: C, 74.82; H, 8.10; N, 9.64.

Method B.

After thioamide **3b** (0.20 g, 0.63 mmole) had been heated with 1 ml of cyclohexylamine on a steam bath for 1.5 hours, addition of a small amount of ethyl ether precipitated 0.15 g (65%) of **20a**, mp 174-175°. The filtrate was diluted with ethyl ether and extracted with three 10-ml portions of 2% hydrochloric acid. Basification of the combined extracts with 10% aqueous sodium hydroxide caused precipitation of a trace amount of **21**.

Method C.

Benzothiazinone **4a** (0.30 g, 1.1 mmoles) was heated with 2 ml of cyclohexylamine on a steam bath for 16 hours. Addition of ethanol to the reaction mixture precipitated 0.30 g of a crude product, mp 181-190°. Recrystallization of this material from aqueous ethanol yielded 0.15 g (38%) of **20a**, mp 174-175°. The filtrate, upon standing, deposited 0.10 g (21%) of **21**, mp 197-198°.

3-Amino-2-(4-methoxyphenyl)-4(3*H*)-quinazolinone (**19d**).

A mixture of 0.50 g (1.6 mmoles) of thioamide **3b**, 0.10 g (3.1 mmoles) of hydrazine, and 7 ml of ethanol was refluxed for 3 hours. The precipitate formed upon cooling was washed with cold ethanol to yield 0.43 g (100%) of **19d**, mp 182-183°. Recrystallization from ethanol did not cause any change in the mp [lit (21) mp 185°]; ir: 3300, 3200 (N-H), 1670 (C=O) cm^{-1}; nmr (deuteriochloroform): δ 3.9 (s, 3, CH_3), 5.1 (s, 2, NH_2), 6.9-7.1 (m, 2, ArH), 7.3-7.9 (m, 5, ArH), 8.2-8.4 (m, 1, ArH).

Deamination of Quinazolinone **19d** into **19a** (6).

To a solution of 0.15 g of **19d** in 1 ml of concentrated hydrochloric acid was added 0.10 g of sodium nitrite dissolved in 3 ml of water and the resulting mixture was diluted with 5 ml of water and was allowed to stand at room temperature overnight. The precipitate was then collected by filtration and washed with ethanol to yield a colorless solid, mp 246-247°, identified as **19a** by its ir and nmr spectra, as well as a mixture melting point with an authentic sample.

2-(4-Methoxyphenyl)-3-methylamino-4(3*H*)-quinazolinone (**19e**).

A mixture of 0.25 g (0.79 mmole) of **3b** and 2 ml of methylhydrazine was heated on a steam bath for 1.5 hours. Upon addition of water to the resulting solution and filtration, there was obtained 0.14 g (64%) of essentially pure **19e**, mp 123.5-124.5°. Recrystallization from aqueous ethanol did not change this mp; ir: 3300 (N-H), 1660 (C=O) cm^{-1}; nmr (deuteriochloroform): δ 2.5 (d, 3, CH_3N), 3.9 (s, 3, CH_3O), 6.1 (q, 1, NH), 6.9-7.1 (m, 2, ArH), 7.3-8.1 (m, 5, ArH), 8.3-8.4 (m, 1, ArH).

Anal. Calcd. For $C_{16}H_{15}N_3O_2$: C, 68.31; H, 5.37; N, 14.94. Found: C, 68.46; H, 5.31; N, 14.95.

2-(4-Methoxyphenyl)-3-phenylamino-4(3*H*)-quinazolinone (**19f**).

A mixture of 0.50 g (1.6 mmoles) of **3b**, 0.25 g (2.3 mmoles) of phenylhydrazine, and 5 ml of ethanol was refluxed for 6 days. Filtration of the cooled reaction mixture and washing of the precipitate with cold ethanol yielded 0.40 g (73%) of crude **19f**, mp 163-165°. The pure compound was obtained by recrystallization from ethanol as colorless crystals, mp 172-173° [lit (21) mp 174°]; ir: 3220 (N-H), 1675 (C=O) cm^{-1}; nmr (deuteriochloroform): δ 3.8 (s, 3, CH_3), 6.6-7.9 (m, 13, ArH), 8.2-8.3 (m, 1, ArH).

3-Hydroxy-2-(4-methoxyphenyl)-4(3*H*)-quinazolinone (**19g**).

A mixture of 0.50 g (1.6 mmoles) of thioamide **3b**, 0.22 g (3.2 mmoles) of hydroxylamine hydrochloride and 5 ml of pyridine was refluxed for 16 hours. Evaporation of the solvent under reduced pressure yielded 0.58 g of crude product, mp 195-200° and recrystallization from ethanol afforded pure **19g** (0.20 g, 47%), mp 207-208° [lit (8) mp 211°]; ir: 1650 (C=O) cm^{-1}; nmr: δ 3.9 (s, 3, CH_3), 6.9-7.1 (m, 2, ArH), 7.3-8.0 (m, 5, ArH), 8.1-8.2 (m, 2, ArH).

3-(2-Hydroxyethyl)-2-(4-methoxyphenyl)-4(3*H*)-quinazolinone (**19h**).

Method A.

A mixture of 0.25 g (0.79 mmole) of **3b**, 0.10 g (1.6 mmoles) of 2-aminoethanol and 3 ml of ethanol was refluxed for 4.5 hours. Upon cooling there precipitated 0.15 g (65%) of crude **19h**, mp 148-150°, and recrystallization from ethanol gave the pure compound as colorless crystals, mp 152-153°; ir: 3350 (O-H), 1660 (C=O) cm^{-1}; nmr: δ 3.7 (m, 2, CH_2OH), 3.9 (s, 3, OCH_3), 4.2 (m, 2, CH_2CH_2OH), 5.7 (s, 1, OH), 6.9-7.1 (m, 2, ArH), 7.5-7.9 (m, 5, ArH), 8.2-8.3 (m, 1, ArH).

Anal. Calcd. for $C_{17}H_{16}N_2O_3$: C, 68.91; H, 5.44; N, 9.45. Found: C, 69.06; H, 5.58; N, 9.42.

Method B.

A mixture of 0.50 g (1.9 mmoles) of benzothiazinone **4a**, 0.33 g (5.4 mmoles) of 2-aminoethanol, and 7 ml of pyridine was allowed to reflux for 19 hours. The solvent was removed under reduced pressure and the residue was triturated with ethyl ether to yield 0.50 g (91%) of crude **19h**, mp 146-153°.

3-(2-Aminoethyl)-2-(4-methoxyphenyl)-4(3*H*)-quinazolinone (**19i**) and 2-(4-Methoxyphenyl)-3-[2-(3-phenylureido)ethyl]-4(3*H*)-quinazolinone (**19j**).

A mixture of 0.25 g (0.79 mmole) of **3b**, 0.10 g (1.7 mmole) of ethylenediamine, and 3 ml of tetrahydrofuran was allowed to reflux for 24 hours. The resulting solution was evaporated under reduced pressure to yield 0.20 g of an oil identified as 3-(2-aminoethyl)-2-(4-methoxyphenyl)-4(3*H*)-quinazolinone (**19i**) on the basis of its spectral data; ir: 3350 (N-H), 1650 (C=O) cm^{-1}; nmr (deuteriochloroform): δ 1.1 (s, 2, NH_2), 2.9 (t, 2, CH_2NH_2), 3.9 (s, 3, CH_3), 4.1 (t, 2, NCH_2), 6.9-7.1 (m, 2, ArH), 7.3-7.7 (m, 5, ArH), 8.2-8.3 (m, 1, ArH).

To a solution of this oil in dry ethyl ether was added phenyl isocyanate (10 drops) and the resulting mixture was allowed to stand for 24 hours. Evaporation of the solvent and crystallization of the residue from ethanol yielded 0.13 g (39%) of crude **19j**, mp 211-213°. The pure compound was obtained as colorless crystals by recrystallization from ethanol, mp 220-220.5°; ir: 3330 (N-H), 1680, 1630 (C=O) cm^{-1}; nmr: δ 3.3 (m, 2, CH_2NH), 3.7 (s, 3, CH_3), 4.1 (m, 2, NCH_2), 6.1 (br t, 1, CH_2NH), 6.9-7.9 (m, 12, ArH), 8.1-8.2 (m, 1, ArH), 8.6 (s, 1, NHPh).

Anal. Calcd. for $C_{24}H_{22}N_4O_3$: C, 69.55; H, 5.35; N, 13.52. Found: C, 69.47; H, 5.33; N, 13.54.

3-(2-Acetamidoethyl)-2-(4-methoxyphenyl)-4(3*H*)-quinazolinone (**19k**).

Method A.

A mixture of thioamide **3b** (0.50 g, 1.6 mmoles), ethylenediamine (0.50 g, 8.3 mmoles), and 3 ml of acetic acid was refluxed for a period of 18 hours. The resulting solution was condensed under reduced pressure to an oil which, upon neutralization with 10% aqueous sodium bicarbonate and washing with water, yielded 0.15 g of **19k**, mp 183-185°. Upon standing, the washings deposited a further 0.35 g of **19k**, mp 180-183° (total yield, 92%). Recrystallization from benzene gave the pure compound as colorless crystals, mp 185-185.5°; ir: 3270 (N-H), 1675, 1630 (C=O) cm^{-1}; nmr: δ 1.8 (s, 3, CH_3CO), 3.4 (m, 2, CH_2NH), 3.9 (s, 3, CH_3O), 4.2 (m, 2, NCH_2), 6.5 (m, 1, NH), 6.9-7.1 (m, 2, ArH), 7.3-7.8 (m, 5, ArH), 8.2-8.3 (m, 1, ArH).

Anal. Calcd. for $C_{19}H_{19}N_3O_3$: C, 67.64; H, 5.68; N, 14.05. Found: C, 67.80; H, 5.72; N, 14.27.

Method B.

Following the procedure described above, from 0.30 g (1.1 mmoles) of benzothiazinone **4a**, 0.30 g (5.0 mmoles) of ethylene diamine, and 4 ml of acetic acid, there was obtained 0.19 g (51%) of crude **19k**, mp 175-180°.

2-(4-Methoxyphenyl)-3-phenyl-4(3*H*)-quinazolinone (**19ℓ**).

A mixture of 0.20 g (0.74 mmole) of benzothiazinone **4a**, 3 ml of aniline, and 3 drops of concentrated hydrochloric acid was boiled until evolution of hydrogen sulfide had stopped (20 minutes). The resulting mixture was neutralized with 10% aqueous sodium bicarbonate and then subjected to steam distillation to remove the excess of aniline. The residue crystallized upon cooling to 0.23 g (96%) of **19ℓ**, mp 152-154°. Recrystallization from ethanol yielded the pure compound, mp 154-155° [lit (22) mp 148°]; ir: 1660 (C=O) cm^{-1}; nmr (deuteriochloroform): δ 3.7 (s, 3, CH_3), 6.6-6.8 (m, 2, ArH), 7.0-7.8 (m, 10, ArH), 8.3-8.4 (m, 1, ArH).

Anal. Calcd. for $C_{21}H_{16}N_2O_2$: C, 76.80; H, 4.91; N, 8.54. Found: C, 76.88; H, 4.82; N, 8.54.

2-(4-Methoxyphenyl)-3-(2-methylphenyl)-4(3*H*)-quinazolinone (**19m**).

A mixture of 0.34 g (1.3 mmoles) of **4a**, 5 ml of *o*-toluidine, and 5 drops of concentrated hydrochloric acid was refluxed for 0.5 hour. The cooled reaction mixture was dissolved in ethyl ether and the resulting solution was washed with four 5-ml portions of 5% hydrochloric acid and finally with water. Evaporation of the solvent yielded 0.35 g (80%) of **19m**, mp 148-149°. Recrystallization from ethanol gave the pure compound as colorless crystals, mp 148.5-149°; ir: 1670 (C=O) cm^{-1}; nmr (deuteriochloroform): δ 2.1 (s, 3, CH_3), 3.8 (s, 3, OCH_3), 6.6-6.8 (m, 2, ArH), 7.1-7.8 (m, 9, ArH), 8.3-8.4 (m, 1, ArH).

Anal. Calcd. for $C_{22}H_{18}N_2O_2$: C, 77.16; H, 5.30; N, 8.19. Found: C, 77.11; H, 5.31; N, 8.31.

3-(2-Hydroxyphenyl)-2-(4-methoxyphenyl)-4(3*H*)-quinazolinone (**19n**).

A mixture of 0.50 g (1.9 mmoles) of **4a**, 0.30 g (2.8 mmoles) of *o*-aminophenol, and 5 ml of acetic acid was refluxed for 21 hours. Removal of the solvent under reduced pressure left an oil, which crystallized upon trituration with ethyl ether to a broad melting solid. This was recrystallized from aqueous ethanol to yield 0.25 g (39%) of pure **19n**, mp 230-231°; ir: 1675 (C=O) cm^{-1}; nmr: δ 3.7 (s, 3, CH_3), 6.8-7.9 (m, 11, ArH), 8.1-8.2 (m, 1, ArH), 9.9 (s, 1, OH).

Anal. Calcd. for $C_{21}H_{16}N_2O_3$: C, 73.24; H, 4.68; N, 8.13. Found: C, 73.19; H, 4.79; N, 8.32.

6-(4-Methoxyphenyl)benzimidazo[1,2-*c*]quinazoline (**22**).

A mixture of 0.50 g (1.9 mmoles) of **4a**, 0.30 g (2.8 mmoles) of *o*-phenylenediamine, and 5 ml of acetic acid was refluxed for 16 hours. After removal of the solvent under reduced pressure, the oily residue was crystallized by trituration with ethyl ether to yield 0.20 g (33%) of **22**, mp 247-248°. Recrystallization from ethanol yielded the pure compound as colorless crystals, mp 252-252.5°; nmr (deuteriochloroform): δ 3.9 (s, 3, CH_3), 6.7-8.1 (m, 11, ArH), 8.7 (m, 1, ArH).

Anal. Calcd. for $C_{21}H_{15}N_3O$: C, 77.52; H, 4.65; N, 12.91. Found; C, 77.74; H, 4.85; N, 13.04.

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