Reactions of Derivatives of Anthranilic Acid With 3-Chloropropyl Isocyanate

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The urea **1** obtained from anthranilonitrile and 3-chloropropyl isocyanate is converted into 3-(3-chloropropyl)-2,4(1*H*,3*H*)quinazolinedione (**4**) when heated with hydrochloric acid, whereas it undergoes a double cyclization to form 2,3,4,7-tetrahydro-6*H*-pyrimido[1,2-*c*]quinazolin-6-one (**3**) upon heating, or treatment with ammonia. On the other hand, the urea **5** formed from methyl anthranilate and 3-chloropropyl isocyanate cyclizes in three different ways, when treated with ammonia, potassium bicarbonate, or concentrated sulfuric acid, to yield compound **4**, 3,4-dihydro-2*H*,6*H*-[1,3]oxazino[2,3-*b*]quinazolin-6-one (**9**), or 2-[(3-chloropropyl)amino]-4*H*-3,1-benzoxazin-4-one (**6**), respectively. Acid-catalyzed reactions of compound **9** with nucleophilic reagents proceed with opening of the oxazine ring and readily yield various 3-substituted 2,4(1*H*,3*H*)-quinazolinediones.

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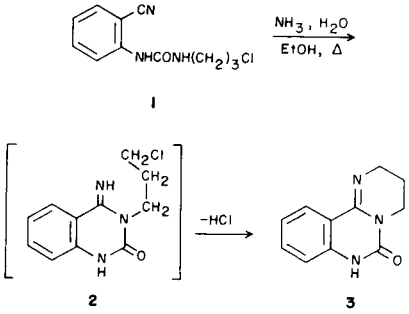
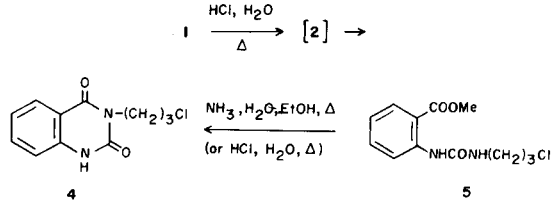
Among many useful cyclizations of anthranilonitrile and methyl anthranilate, their reactions with isocyanates have been shown to lead to quinazolines [1,2] and benzoxazines [2]. In the presence of a leaving group *beta* to the isocyanato group, such reactions can be used to prepare derivatives of imidazo[1,2-*c*]quinazoline and oxazolo[2,3-*b*]quinazoline [3]. This paper is an extenstion of earlier work [3] and describes reactions of anthranilonitrile and methyl anthranilate with 3-chloropropyl isocyanate, which allow convenient synthesis of compounds with the pyrimido[1,2-*c*]-quinazoline and oxazino[2,3-*b*]quinazoline structures.

Anthranilonitrile reacts readily with 3-chloropropyl isocyanate to form the expected urea **1** in quantitative yield. When compound **1** is heated at a temperature 20-30° above its melting point, it undergoes a decomposition resulting in the formation of a hydrochloride salt, treatment of which with aqueous ammonia yields 2,3,4,7-tetrahydro-6*H*-pyrimido[1,2-*c*]quinazolin-6-one (**3**). The same product is obtained in a better state of purity when urea **1** is heated with aqueous-ethanolic ammonia on a steam bath for

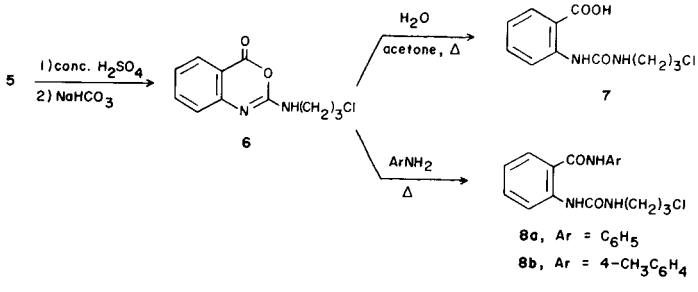


10-15 minutes. It thus appears that the initial cyclization product **2** [1] undergoes a further ring forming reaction to yield the tricyclic product **3**. The structure assigned to this compound is consistent with its infrared and proton nuclear magnetic resonance spectra, as well as with its published melting point [4]. It should perhaps be noted that the literature method of preparation of **3** involves three steps from isatoic anhydride and proceeds with an overall yield of 45% [4], whereas the present method affords this compound in two steps from anthranilonitrile and 93% overall yield.

When cyclization of urea **1** is attempted by heating it briefly with concentrated hydrochloric acid, the product formed is 3-(3-chloropropyl)-2,4(1*H*,3*H*)quinazolinedione (**4**). Under these conditions the imino group of intermediate **2** undergoes hydrolytic cleavage before the tetrahydropyrimidine ring can be formed. The structure of **4** is confirmed by its formation from urea **5** (obtained quantitatively from methyl anthranilate and 3-chloropropyl isocyanate) by the action of either aqueous-ethanolic ammonia,

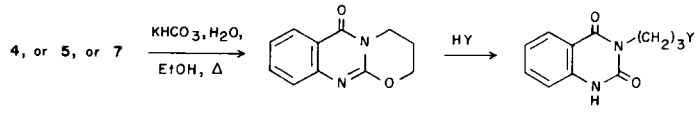


or hydrochloric acid. It is interesting to note that under the same conditions, *i.e.* treatment with hot, concentrated hydrochloric acid, the 2-chloroethyl analog of urea **1** yields a different cyclization product, namely 2-[(2-chloroethyl)-amino]-4*H*-3,1-benzoxazin-4-one [3a]. The homologous



benzoxazinone **6** is prepared readily by the room temperature treatment of urea **5** with concentrated sulfuric acid followed by neutralization with sodium bicarbonate [2]. As for other compounds of this structure [2,3], the carbon, nitrogen double bond in **6** is believed to be endocyclic. This is supported by the observation that, although the NH proton signal in the nmr spectrum of **6** is covered by aromatic proton signals, coupling between the NH and CH_2 protons is indicated by the fact that the signal of the latter is a rough quartet, which is converted into a triplet upon addition of deuterium oxide to the solution. As anticipated, the oxazinone ring of **6** is opened up by treatment with water to form carboxylic acid **7**, and with aniline or *p*-toluidine to form amide **8a**, or **8b**, respectively. The structure of **7** is confirmed by its smooth formation when an aqueous solution of potassium anthranilate is treated with 3-chloropropyl isocyanate and the resulting solution is acidified.

Treatment of quinazolinedione **4** with aqueous-ethanolic potassium bicarbonate yields 3,4-dihydro-2*H*,6*H*-[1,3]-oxazino[2,3-*b*]quinazolin-6-one (**9**). The same compound is obtained by the action of potassium bicarbonate on ester **5**, or, most conveniently, on carboxylic acid **7**. In analogy with the behavior of 2,3-dihydro-5*H*-oxazolo[2,3-*b*]quinazolin-5-one [3a], compound **9** readily undergoes acid catalyzed nucleophilic attack at C-2, which causes the oxazine



ring to open up and conveniently yields a variety of 3-substituted quinazolinediones. Thus, treatment with hydrochloric, hydrobromic, and hydriodic acids gives the corresponding 3-(3-halopropyl)-2,4(1*H*,3*H*)-quinazolinediones **4**, **10a**, and **10b**. Analogous reactions of **9** with aqueous sulfuric acid, acetic acid, or trifluoroacetic acid yield alcohol **10c** and esters **10f, g**, respectively. Ethers **10d, e** and anilino derivative **10h** are obtained by the respective, acid-catalyzed reactions of **9** with methanol, ethanol, and aniline. Finally, the oxazino ring of **9** is also opened up by direct nucleophilic attack at C-2, as by the action of aqueous sodium hydroxide to form the hydroxypropylquinazolinedione **10c**.

EXPERIMENTAL

Melting points were determined in capillaries with a Thomas-Hoover Uni-Melt apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 337 spectrophotometer using mineral oil mulls. Proton nmr spectra were obtained on Varian EM360 and Varian FT80A spectrometers using solutions in hexadeuteriodimethyl sulfoxide and tetramethylsilane as internal standard.

2-[3-(3-Chloropropyl)ureido]benzonitrile (**1**).

A mixture of anthranilonitrile (2.36 g, 0.020 mole) and 3-chloropropyl isocyanate [5] (2.40 g, 0.020 mole) was warmed momentarily to obtain a clear solution, which solidified slowly when allowed to stand at room temperature. After 48 hours, there was obtained **1** (4.70 g, 99%), mp 152-153°, recrystallization of which from ethanol yielded the pure compound as colorless crystals, mp 159-160°; ir: 3340, 3260 (N-H), 2220 (C≡N), 1640 (C=O) cm^{-1}; ^{1}H-nmr: δ 2.0 (quint, 2, $CH_2CH_2CH_2$), 3.3 (q, 2, NCH_2), 3.7 (t, 2, CH_2Cl), 7.0-8.2 (m, 5, ArH, $NHCH_2$), 8.6 (s, 1, NH).

Anal. Calcd. for $C_{11}H_{12}ClN_3O$: C, 55.58; H, 5.09; N, 17.68. Found: C, 55.76; H, 5.31; N, 17.53.

2,3,4,7-Tetrahydro-6*H*-pyrimido[1,2-*c*]quinazolin-6-one (**3**).

Method A.

When **1** (2.0 g, 8.4 mmoles) was heated in an oil bath (170-180°), its partial melting was accompanied by a vigorous reaction, which yielded a solid material. After 5 minutes of heating, the product was cooled and treated with dilute aqueous ammonia to afford yellow-tinged **3** (1.70 g, 100%), mp 237-240°.

Method B.

A mixture of **1** (1.0 g, 4.2 mmoles), ethanol (10 ml), and concentrated aqueous ammonia (5.0 ml) was heated on a steam bath for 15 minutes. The resulting mixture was cooled and diluted with water to yield **3** (0.80 g, 94%), mp 242.5-244°. The pure compound was obtained by recrystallization from ethanol as colorless crystals, mp 244.5-245.5° (lit [4] mp 245-246.5°); ir: 1680 (C=O), 1620 (C=N) cm^{-1}; ^{1}H-nmr: δ 1.85 (quint, 2, $CH_2CH_2CH_2$), 3.50 (t, 2, CH_2), 3.75 (t, 2, CH_2), 6.95-8.00 (m, 4, ArH), 10.6 (s, 1, NH).

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

Method A.

When a mixture of **1** (0.50 g, 2.1 mmoles) and concentrated hydrochloric acid (3.0 ml) was heated on a steam bath for 2 minutes, initial dissolution was followed by formation of a precipitate. The resulting mixture was cooled, mixed with concentrated hydrochloric acid, and filtered to yield **4** (0.35 g, 70%), mp 173-175°.

Method B.

A mixture of **5** (1.0 g, 3.7 mmoles), ethanol (5.0 ml), and concentrated hydrochloric acid (5.0 ml) was heated on a steam bath for 0.5 hour, cooled, and diluted with water to yield **4**, (0.80 g, 91%), mp 168-172°.

Method C.

A mixture of **5** (0.50 g, 1.85 mmoles), ethanol (5.0 ml), and concentrated aqueous ammonia (5.0 ml) was heated on a steam bath for 10 minutes, cooled, and diluted with water to give **4** (0.40 g, 91%), mp 174-176°. Recrystallization of this material from ethanol yielded the pure compound as colorless crystals, mp 174-176° (lit [6] mp 178-179°); ir: 3250, 3200 (N-H), 1720, 1640 (C=O) cm^{-1}; ^{1}H-nmr: δ 2.1 (quint, 2, $CH_2CH_2CH_2$), 3.7 (t, 2, CH_2Cl), 4.1 (t, 2, NCH_2), 6.9-7.9 (m, 4, ArH), 11.4 (s, 1, NH).

Anal. Calcd. for $C_{11}H_{11}ClN_2O_2$: C, 55.36; H, 4.65; N, 11.74. Found: C, 55.40; H, 4.85; N, 11.50.

Method D.

A mixture of **9** (0.60 g, 3.0 mmoles) and concentrated hydrochloric acid (5.0 ml) was heated on a steam bath for 5 minutes and then it was cooled, diluted with water, and filtered to yield **4** (0.55 g, 77%), mp 172-174°.

Methyl 2-[3-(3-Chloropropyl)ureido]benzoate (**5**).

A mixture of methyl anthranilate (4.5 g, 0.030 mole) and 3-chloropropyl isocyanate (3.6 g, 0.030 mole) solidified slowly upon standing at room temperature. After 4 hours, there was obtained **5** (7.9 g, 98%), mp 118-120°, recrystallization of which from ethanol yielded the pure com-

pound as colorless crystals, mp 123-124°; ir: 3320, 3290 (N-H), 1700, 1650 (C=O) cm^{-1}; ^{1}H-nmr: δ 1.95 (quint, 2, $CH_2CH_2CH_2$), 3.25 (q, 2, NCH_2), 3.72 (t, 2, CH_2Cl), 3.90 (s, 3, CH_3), 6.95 (m, 1, ArH), 7.50 (m, 2, ArH, $NHCH_2$), 7.90 (m, 1, ArH), 8.40 (m, 1, ArH), 9.80 (s, 1, ArNH).

Anal. Calcd. for $C_{12}H_{15}ClN_2O_3$: C, 53.24; H, 5.58; N, 10.35. Found: C, 53.41; H, 5.76; N, 10.14.

2-[(3-Chloropropyl)amino]-4*H*-3,1-benzoxazin-4-one (**6**).

A solution of **5** (3.0 g, 11 mmoles) in concentrated sulfuric acid (10 ml) was allowed to stand at room temperature for 3 hours. It was then poured onto crushed ice and the resulting mixture was neutralized with aqueous sodium bicarbonate (10%) and filtered to yield **6** (2.5 g, 94%), mp (partial melting) 129-130°. The pure compound was obtained by recrystallization from benzene/petroleum ether (bp 60-80°) as colorless crystals, mp (partial melting) 135-136°; ir: 3280 (N-H), 1740 (C=O), 1630 (C=N) cm^{-1}; ^{1}H-nmr: δ 2.1 (quint, 2, $CH_2CH_2CH_2$), 3.4 (q, 2, NCH_2), 3.8 (t, 2, CH_2Cl), 7.0-8.2 (m, 5, ArH, NH).

Anal. Calcd. for $C_{11}H_{11}ClN_2O_2$: C, 55.36; N, 4.65; N, 11.74. Found: C, 55.18; H, 4.73; N, 11.54.

Hydrolysis of **6**.

After a mixture of **6** (0.50 g, 2.1 mmoles), acetone (10 ml), and water (5.0 ml) had been refluxed for 1 hour, it was concentrated at the aspirator and the residue was cooled to yield **7** (0.40 g, 74%), mp 150-151° dec.

2-[3-(3-Chloropropyl)ureido]benzoic Acid (**7**).

A solution of anthranilic acid (8.2 g, 0.060 mole) in aqueous potassium bicarbonate (10%, 70 ml) was filtered from traces of insoluble material, chilled, and vigorously shaken with 3-chloropropyl isocyanate (8.0 g, 0.067 mole) for 10 minutes. During this time, the mixture was kept cold by occasional immersion into an ice-water mixture. After it had stood at room temperature for a further 0.5 hour, the mixture was filtered and the chilled filtrate was acidified with concentrated hydrochloric acid to yield **7** (14.3 g, 93%), mp 147-148° dec. The pure compound was obtained by recrystallization from aqueous ethanol as colorless crystals, mp 155-156° dec [7]; ir: 3340, 3300 (NH), 1680, 1650 (C=O) cm^{-1}; ^{1}H-nmr: δ 1.90 (m, 2, $CH_2CH_2CH_2$), 3.25 (m, 2, NCH_2), 3.75 (t, 2, CH_2Cl), 6.80-8.50 (m, 5, ArH, $NHCH_2$), 10.1 (s, 1, ArNH), 13.0 (br, 1, COOH).

Anal. Calcd. for $C_{11}H_{13}ClN_2O_3$: C, 51.47; H, 5.11; N, 10.91. Found: C, 51.72; H, 5.11; N, 10.86.

N-Phenyl-2-[3-(3-chloropropyl)ureido]benzamide (**8a**).

A mixture of **6** (0.20 g, 0.84 mmole) and aniline (0.50 g, 5.4 mmoles) solidified when heated on a steam bath for 3 minutes. Trituration of this material with ethanol yielded **8a** (0.28 g, 100%), mp 192-193°. An analytical sample was obtained as colorless crystals, mp 193-194°, by recrystalization from ethanol; ir: 3350-3200 (N-H), 1670, 1640 (C=O) cm^{-1}; ^{1}H-nmr: δ 1.90 (quint, 2, $CH_2CH_2CH_2$), 3.20 (m, 2, NCH_2), 3.65 (t, 2, CH_2Cl), 6.95-7.75 (m, 9, ArH, $NHCH_2$), 8.25 (m, 1, ArH), 9.40 (s, 1, NH), 10.10 (s, 1, NH).

Anal. Calcd. for $C_{17}H_{18}ClN_3O_2$: C, 61.54; H, 5.47; N, 12.66. Found: C, 61.70; H, 5.68; N, 12.66.

N-(4-Methylphenyl)-2-[3-(3-chloropropyl)ureido]benzamide (**8b**).

As for the previous compound **8a**, from **6** (0.20 g, 0.84 mmole) and *p*-toluidine (0.50 g, 4.7 mmoles), there was obtained **8b** (0.29 g, 100%), mp 183-184°. Recrystallization from ethanol yielded an analytical sample as colorless crystals mp 183-184°; ir: 3330-3180 (N-H), 1660, 1630 (C=O) cm^{-1}; ^{1}H-nmr: δ 1.80 (quint, 2, $CH_2CH_2CH_2$), 3.20 (q, 2, NCH_2), 3.65 (t, 2, CH_2Cl), 6.90-7.80 (m, 8, ArH, $NHCH_2$), 8.25 (m, 1, ArH), 9.45 (s, 1, NH), 10.10 (s, 1, NH).

Anal. Calcd. for $C_{18}H_{20}ClN_3O_2$: C, 62.52; H, 5.83; N, 12.15. Found: C, 62.50; H, 5.84; N, 11.95.

3,4-Dihydro-2*H*,6*H*-[1,3]oxazino[2,3-*b*]quinazolin-6-one (**9**).

Method A.

After a mixture of **5** (1.0 g, 3.7 mmoles), ethanol (10 ml), and aqueous potassium bicarbonate (10%, 10 ml) had been heated on a steam bath for 1 hour, it was diluted with water and chilled to yield a precipitate, which was dried overnight in an evacuated desiccator, over anhydrous calcium chloride. There was obtained **9** (0.50 g, 67%), mp 125-130°.

Method B.

A mixture of **4** (0.30 g, 1.26 mmoles), ethanol (5.0 ml), and aqueous potassium bicarbonate (10%, 5.0 ml) was heated on a steam bath until a clear solution had been obtained and for a further 0.5 hour. It was then diluted with water and chilled to yield **9** (dried as before, 0.16 g, 64%), mp 124-128°.

Method C.

A solution of **7** (4.0 g, 15.6 mmoles) in aqueous potassium bicarbonate (10%, 50 ml) was heated on a steam bath for 1 hour and then was diluted with water and chilled to give **9** (dried as before, 2.7 g, 86%), mp 125-130°. The pure compound was obtained by recrystallization from carbon tetrachloride/petroleum ether (bp 60-80°) as colorless crystals, mp 128-131.5°; ir: 1670 (C=O) cm^{-1}; ^{1}H-nmr: δ 2.20 (quint, 2, $CH_2CH_2CH_2$), 3.95 (t, 2, NCH_2), 4.45 (t, 2, OCH_2), 7.20-8.10 (m, 4, ArH).

Anal. Calcd. for $C_{11}H_{10}N_2O_2$: C, 65.34; H, 4.98; N, 13.85. Found: C, 65.18; H, 5.04; N, 13.61.

3-(3-Bromopropyl)-2,4(1*H*,3*H*)-quinazolinedione (**10a**).

A mixture of **9** (0.20 g, 0.10 mmole) and concentrated hydrobromic acid (5.0 ml) was heated on a steambath for 5 minutes and then it was cooled, diluted with water, and filtered to yield **10a** (0.26 g, 93%), mp 187-189°. The pure compound was obtained by recrystallization from methanol as colorless crystals, mp 189-191°; ir: 3300, 3180 (N-H), 1710, 1640 (C=O) cm^{-1}; ^{1}H-nmr: δ 2.0 (quint, 2, $CH_2CH_2CH_2$), 3.6 (t, 2, CH_2Br), 4.0 (t, 2, NCH_2), 7.1-8.1 (m, 4, ArH), 11.3 (s, 1, NH).

Anal. Calcd. for $C_{11}H_{11}BrN_2O_2$: C, 46.67; H, 3.92; N, 9.89. Found: C, 46.89; H, 4.09; N, 9.74.

3-(3-Iodopropyl)-2,4(1*H*,3*H*)-quinazolinedione (**10b**).

As for previous compound **10a**, from **9** (0.20 g, 0.10 mmole) and concentrated hydriodic acid (5.0 ml), there was obtained **10b** (0.32 g, 97%), mp 200-202°. Recrystallization from methanol gave the pure compound as colorless crystals, mp 201-202°; ir: 3300 (N-H), 1700, 1640 (C=O) cm^{-1}; ^{1}H-nmr: δ 2.1 (quint, 2, $CH_2CH_2CH_2$), 3.3 (t, 2, CH_2I), 4.0 (t, 2, NCH_2), 7.0-8.0 (m, 4, ArH), 11.4 (s, 1, NH).

Anal. Calcd. for $C_{11}H_{11}IN_2O_2$: C, 40.02; H, 3.36; N, 8.49. Found: C, 40.28; H, 3.61; N, 8.45.

3-(3-Hydroxypropyl)-2,4(1*H*,3*H*)-quinazolinedione (**10c**) [8].

Method A.

The solution obtained by heating **9** (0.50 g, 2.5 mmoles) and 10% aqueous sodium hydroxide (10 ml) on a steam bath for 10 minutes was cooled, diluted with water, and acidified with concentrated hydrochloric acid to yield **10c** (0.50 g, 93%), mp 174-176°. An analytical sample was obtained by recrystallization from aqueous ethanol as colorless crystals, mp 175-177°; ir 3500, 3200 (O-H, N-H), 1710, 1630 (C=O) cm^{-1}; ^{1}H-nmr: δ 1.75 (quint, 2, $CH_2CH_2CH_2$), 3.50 (m, 2, CH_2O), 4.00 (t, 2, NCH_2), 4.45 (approx t, 1, OH), 7.10-8.00 (m, 4, ArH), 11.40 (s, 1, NH).

Anal. Calcd. for $C_{11}H_{12}N_2O_3$: C, 60.00; H, 5.49; N, 12.72. Found: C, 59.79; H, 5.65; N, 12.75.

Method B.

After a mixture of **9** (0.50 g, 2.5 mmoles), water (10 ml), and concentrated sulfuric acid (1.0 ml) had been heated on a steam bath for 1 hour, it was cooled and neutralized with 10% aqueous potassium bicarbonate to yield **10c** (0.30 g, 56%), mp 172-175°.

3-(3-Methoxypropyl)-2,4(1*H*,3*H*)-quinazolinedione (**10d**).

After a mixture of **9** (0.50 g, 2.5 mmoles), methanol (10 ml), and concentrated sulfuric acid (1.0 ml) had been refluxed for 1 hour, the solvent was removed at the aspirator and the residue was mixed with water and neutralized with 10% aqueous potassium bicarbonate. There was obtained **10d** (0.45 g, 78%), mp 136-138°, recrystallization of which from

benzene/petroleum ether (bp 60-80°) gave the pure compound as colorless crystals, mp 138-140°; ir: 3200 (N-H), 1710, 1630 (C=O) cm^{-1}; ^{1}H-nmr: δ 1.75 (quint, 2, $CH_2CH_2CH_2$), 3.20 (s, 3, CH_3), 3.35 (t, 2, CH_2O), 3.95 (t, 2, NCH_2), 7.10-8.0 (m, 4, ArH), 11.35 (s, 1, NH).

Anal. Calcd. for $C_{12}H_{14}N_2O_3$: C, 61.53; H. 6.02; N, 11.96. Found: C, 61.42; H, 6.12; N, 12.10.

3-(3-Ethoxypropyl)-2,4(1*H*,3*H*)-quinazolinedione (**10e**).

As for the previous compound **10d**, from **9** (0.50 g, 2.5 mmoles), absolute ethanol (10 ml), and concentrated sulfuric acid (1.0 ml), there was obtained **10e** (0.40 g, 66%), mp 126-130°. Recrystallization from benzene/petroleum ether (bp 60-80°) gave the pure compound as colorless crystals, mp 133-134.5°; ir: 3230-3130 (N-H), 1725, 1630 (C=O) cm^{-1}; ^{1}H-nmr: δ 1.0 (t, 3, CH_3), 1.8 (quint, 2, $CH_2CH_2CH_2$), 3.4 (m, 4, CH_2O), 4.0 (t, 2, NCH_2), 7.0-7.9 (m, 4, ArH), 11.3 (s, 1, NH).

Anal. Calcd. for $C_{13}H_{16}N_2O_3$: C, 62.89; H, 6.50; N, 11.28. Found: C, 62.67; H, 6.61; N, 11.33.

3-(3-Acetoxypropyl)-2,4(1*H*,3*H*)-quinazolinedione (**10f**).

A mixture of **9** (0.60 g, 3.0 mmoles), acetic acid (6.0 ml), and concentrated sulfuric acid (3 drops) was refluxed for 1 hour, then cooled and diluted with water to yield **10f** (0.60 g, 77%), mp 135-140°. An analytical sample was obtained by recrystallization from carbon tetrachloride as colorless crystals, mp 140-141.5°; ir: 3230-3130 (N-H), 1730, 1640 (C=O) cm^{-1}; ^{1}H-nmr: δ 1.95 (s, 3, CH_3), 1.95 (quint, 2, $CH_2CH_2CH_2$), 4.0 (m, 4, $CH_2CH_2CH_2$), 7.1-8.0 (m, 4, ArH), 11.4 (s, 1, NH).

Anal. Calcd. for $C_{13}H_{14}N_2O_4$: C, 59.54; H, 5.38; N, 10.68. Found: C, 59.37; H, 5.48; N, 10.87.

3-(3-Trifluoroacetoxypropyl)-2,4(1*H*,3*H*)-quinazolinedione (**10g**).

A mixture of **9** (0.50 g, 2.5 mmoles) and trifluoroacetic acid (1.0 ml) was refluxed for 5 minutes, then cooled and diluted with water to give **10g** (0.75 g, 96%), mp 151-153°. The pure compound was obtained by recrystallization from benzene/petroleum ether (bp 60-80°) as colorless crystals, mp 154-155°; ir: 3320-3180 (N-H), 1780, 1720, 1650 (C=O) cm^{-1}; ^{1}H-nmr: δ 2.10 (m, 2, $CH_2CH_2CH_2$), 4.05 (m, 2, CH_2), 4.45 (m, 2, CH_2), 7.10-8.0 (m, 4, ArH), 11.5 (s, 1, NH).

Anal. Calcd. for $C_{13}H_{11}F_3N_2O_4$: C, 49.38; H, 3.51; N, 8.86. Found: C, 49.51; H, 3.63; N, 8.66.

3-(3-Phenylaminopropyl)-2,4(1*H*,3*H*)-quinazolinedione (**10h**).

After a mixture of **9** (0.60 g, 3.0 mmoles), benzene (10 ml), aniline (1.0 g, 11 mmoles), and *p*-toluenesulfonic acid (0.10 g) had been refluxed for 1 hour, it was cooled and filtered to yield **10h** (0.78 g, 89%), mp 196-200°. The pure compound was obtained by recrystallization from 1-butanol/ethanol as colorless crystals, mp 200-202°; ir: 3390 (N-H), 1715, 1650 (C=O) cm^{-1}; ^{1}H-nmr: δ 1.90 (quint, 2, $CH_2CH_2CH_2$), 3.10 (q, 2, CH_2NH), 4.05 (t, 2, NCH_2), 5.50 (t, 1, CH_2NH), 6.45-8.05 (m, 9, ArH), 11.4 (s, 1, NH).

Anal. Calcd. for $C_{17}H_{17}N_3O_2$: C, 69.14; H, 5.80; N, 14.23. Found: C, 69.06; H, 5.97; N, 14.26.

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