Synthesis and Antimalarial Effects of [1]Benzothieno[3,2-*f*]quinazoline-1,3-diamine (1)

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Bromination of 2-dibenzothiophenamine has been shown to afford 1-bromo-2-dibenzothiophenamine rather than the previously reported 3-isomer. This material was converted to the 1-cyano derivative and cyclized with chloroformamidine hydrochloride to [1]benzothieno-[3,2-*f*]quinazoline-1,3-diamine. Both this and the corresponding 7,7-dioxide were devoid of antimalarial activity.

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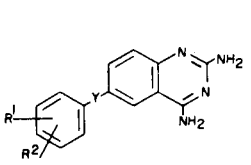
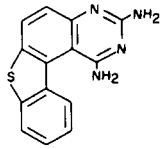
A variety of 6-[(aryl)thio, sulfinyl and sulfonyl]-2,4-quinazolinediamines (**1**) have been shown to possess exceptional antimalarial properties (2). The suppressive antimalarial potency of the 6-[(aryl)thio]-2,4-quinazolinediamines against *Plasmodium berghei* is generally enhanced by 5-methyl substitution.



1 Y = S, SO, SO$_2$



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Based on the hypothesis that the activity of these compounds against cycloguanil- and pyrimethamine-resistant plasmodia may be related to the inhibition of tetrahydrofolate coenzymes within the interconversion cycle, further structural modifications were sought which would mimic the structure of these coenzymes and forestall the formation and interconversion of one-carbon derivatives allied with the tetrahydrofolate coenzymes. Thus the synthesis of the fused prototype [1]benzothieno[3,2-*f*]quinazoline-1,3-diamine (**2**) was deemed of interest.

The synthetic approach to this material (Scheme I) required 1-bromo-2-dibenzothiophenamine (**4**) as the key intermediate. A survey of the literature indicated that bromination of *N*-2-dibenzothiophenylacetamide and of *N*-2-dibenzothiophenylbenzamide gave the 3-bromo derivatives (3,4). A recent report (5) claimed that the position of bromination of certain aromatic amines could be changed by using hydrobromic acid in dimethyl sulfoxide as the brominating agent. Our application of this technique to 2-dibenzothiophenamine (**3**) afforded a homogeneous monobromo derivative in 74% yield. The nmr spectrum (Table I) of this material indicated quite clearly that it was the desired 1-bromo-2-dibenzothiophenamine (**4**). Thus, H-3 which appears as a pair of doublets centered at δ 6.82, representing coupling with H-1 (J = 2) and H-4 (J = 9) in the spectrum of 2-dibenzothiophenamine (**3**) appears in that of 1-bromo-2-dibenzothiophenamine (**4**) as a doublet centered at δ 6.92 with *ortho* coupling (J = 9) to H-4. In addition, the H-9 multiplet has been deshielded by the bromine from δ 8.0(7) to 9.2. Campaigne *et al.*, (8) noted a similar deshielding affect by the aldehyde substituent at the 1 position on H-9 when comparing the spectrum of 4-methoxydibenzothiophene with that of

Scheme I

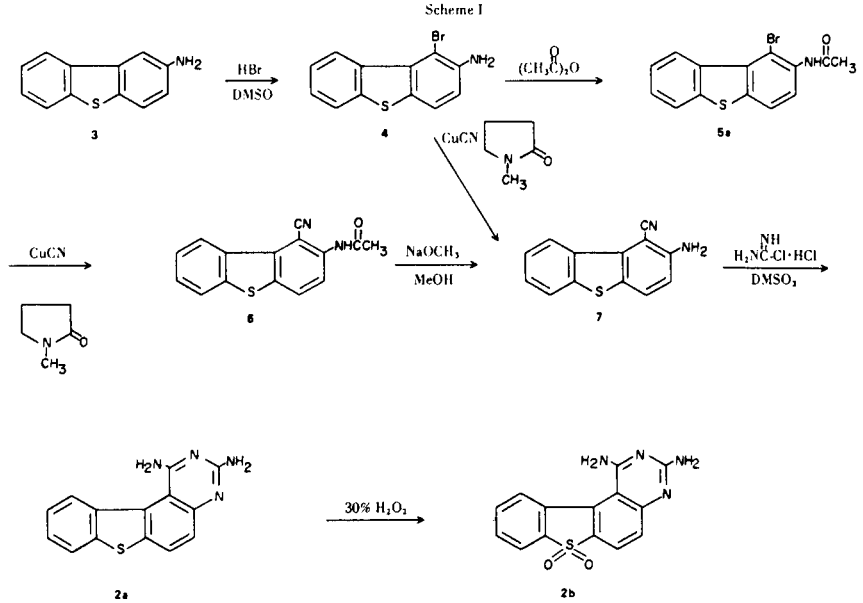
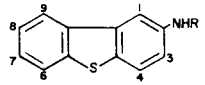


Table I

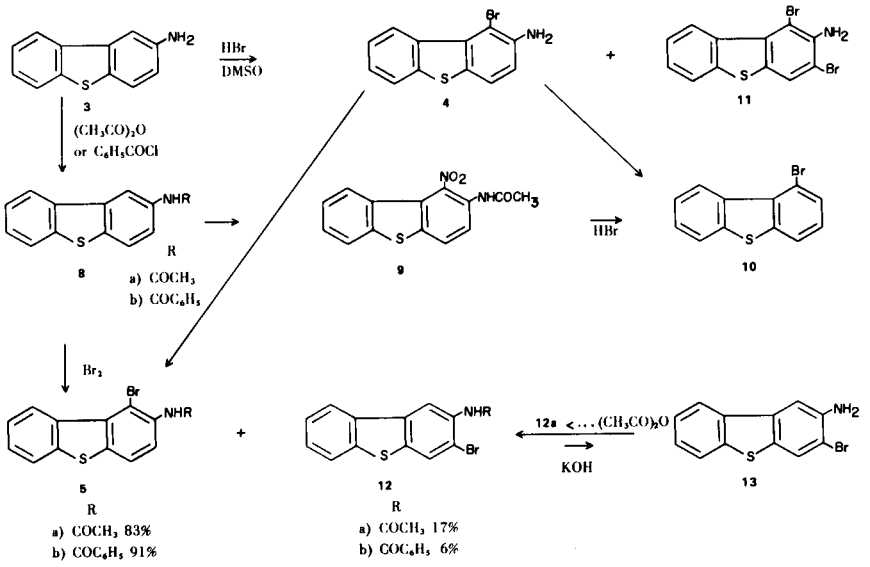
Nmr Spectra (a) of Substituted Dibenzothiophenes



Compound	M.p. °C	δ (ppm from TMS) H-1	H-3	H-4	H-6	H-7,8	H-9	NH(H_2)	R	Solvent (a)
2-Dibenzothiophenamine (**3**)	133-135°	7.38, d (b)	6.82, dd (b,c)	7.55, d (c)	7.75, m	7.3, 2m	8.0, m	3.7, s	—	C
1-Bromo-2-dibenzothiophenamine (**4**)	133-135°	—	6.92, d (c)	7.53, d (c)	7.80, m	7.4, 2m	9.2, m	4.26, s	—	C
1,3-Dibromo-2-dibenzothiophenamine (**11**)	176-178°	—	—	8.22, s	8.0, m	7.4, 2m	9.12, m	5.5, s	—	D
3-Bromo-2-dibenzothiophenamine (**13**)	153-154° (d)	7.49, s	—	7.87, s	7.8, m	7.4, 2m	8.0, m	4.2, s	—	C
2-Amino-1-dibenzothiophenecarbonitrile (**7**)	194-195°	—	6.83, d (c)	7.71, d (c)	7.8, m	7.45, 2m	8.8, m	4.58, s	—	C
N-2-Dibenzothiophenylacetamide (**8a**)	177-179°	8.57, d (b)	7.61, dd (b,c)	7.8, d (c)	8.0, m	7.45, 2m	8.1, m	10.15, s	2.1, s	D
N-(1-Nitro-2-dibenzothiophenyl)acetamide (**9**)	209-210°	—	7.67, d (c)	8.29, d (c)	8.16, m	7.6, 2m	7.6, m	10.0, s	2.1, s	D
1-Bromodibenzothiophene (**10**)	79-80° (e)	—	7.42, dd (c)	7.55, dd (b,c)	8.1, m	7.6, 2m	9.05, m	—	—	D
N-(1-Bromo-2-dibenzothiophenyl)acetamide (**5a**)	197-199°	—	7.56, d (c)	8.04, d (c)	8.1, m	7.5, 2m	9.2, m	9.7, s	2.1, s	D
N-(3-Bromo-2-dibenzothiophenyl)acetamide (**12a**)	239-240° (f)	8.41 or 8.37, s	—	8.37 or 8.41, s	8.0, m	7.5, 2m	8.3, m	9.64, s	2.1, s	D
N-2-Dibenzothiophenylbenzamide (**8b**)	197-199° (g)	8.78, d (b)	7.85, dd (b,c)	*ca.* 8.0, d (h)	*ca.* 8.0, m (h)	7.5, 2m	8.2, m	10.5, s	7.5 (3H) 8.0 (2H)	D
N-(1-Bromo-2-dibenzothiophenyl)benzamide (**5b**)	201-202°	—	*ca.* 7.6 (h)	8.12, d (c)	8.1, m	7.6, 2m	9.2, m	9.78, s	7.6 (3H), 8.05 (2H)	D
N-(3-Bromo-2-dibenzothiophenyl)benzamide (**12b**)	188-189° (i)	8.42 or 8.45, s	—	8.45 or 8.42, s	*ca.* 8.05, m (h)	*ca.* 7.5, 2m (h)	8.35 m	10.25, s	7.55 (3H), 8.0 (2H)	D
[1]Benzothieno[3,2-*f*]quinazoline-1,3-diamine (**2a**)	296-298° dec.	—	7.3, d (c)	8.05, d (c)	8.04, m	7.4, 2m	8.76, m	(j)	—	D

(a) A Bruker WH-90 instrument was used to determine the spectra. C = deuterated chloroform; D = deuterated dimethyl sulfoxide; s = singlet; d = doublet; dd = double doublets; m = multiplet. δ Values for multiplets refer to center of the resonances. (b) J = 2 Hz. (c) J = 9 Hz. (d) Literature (3) had previously reported 135°. (e) Literature reports m.p. 84°; δ H-2 = 8.07, dd (b,c). (f) Previously reported (3) at 199-200°. (g) Literature (10) reports 199-200°. (h) Overlapping absorption prevents accurate assignment. (i) Previously reported (4) as 201-202°. (j) $2NH_2$: δ 6.15, s, and 6.95, s.

Scheme II



4-methoxydibenzothiophene-1-carboxaldehyde.

Further evidence that this material was indeed 1-bromo-2-dibenzothiophenamine was provided by the following studies (See Scheme II). Nitration of *N*-2-dibenzothiophenylacetamide (**8a**) gave *N*-(1-nitro-2-dibenzothiophenyl)acetamide (**9**), which was treated with hydrobromic acid (9) to afford 1-bromodibenzothiophene (**10**). Characterization of the 1-bromodibenzothiophene had been accomplished by its comparison with a sample prepared by deamination of 1-bromo-4-dibenzothiophenamine (6). The I-bromodibenzothiophene thus obtained was identical in all respects with the material obtained by deaminating 1-bromo-2-dibenzothiophenamine (**4**).

When we used excess hydrobromic acid in the bromination of **3**, a second product, which analyzed for a dibromo derivative, was isolated. Assignment of structure of the compound as 1,3-dibromo-2-dibenzothiophenamine (**11**) is based on the nmr spectrum which reveals a singlet at δ 8.22. This singlet represents H-4, deshielded to that region by the bromine substituents. The H-3 of 1,4-dibromo-2-dibenzothiophenamine, the other possible product whose nmr spectrum would display a singlet, would be expected to appear further upfield (*ca.* δ 7.0-7.5) due to the counteracting shielding effect of the neighboring amine substituent. (Note that the apparent small deshielding effect on H-6 is in fact a result of the change of solvent. This proton absorbs at *ca.* δ 7.8 in deuterated chloroform and at δ 8.0-8.1 in deuterated dimethyl sulfoxide.)

The melting points of the 1-bromo-2-dibenzothiophenamine (133-135°) and its acetamide (197-199°) were curiously close to those reported in the literature (3) for the 3-bromo isomers (135-135.5°; 199-200°). Therefore, the bromination of *N*-2-dibenzothiophenylacetamide (**8a**) with bromine in acetic acid was duplicated (additional solvent and slight heating were needed to bring about complete reaction). Analytical results indicated the crude product to be a monobrominated dibenzothiophene. Vpc data demonstrated the presence of a mixture of a major product (83%) and a minor one (17%). The purified major product proved identical (tlc, nmr, ir) to *N*-(1-bromo-2-dibenzothiophenyl)acetamide (**5a**) obtained by acetylation of the hydrobromic acid/dimethylsulfoxide product. Efforts to isolate the minor isomer were unsuccessful.

N-2-Dibenzothiophenylbenzamide (**8b**) (10) was then brominated using conditions described in the literature (4). Once again two products were present in the reaction mixture (91% and 6% by vpc). The major product, isolated in 76% yield, had a melting point (201-202°) identical to that reported by the literature (4) for the 3-bromo derivative. However, the nmr spectrum of the compound (See Table I, **5b**) demonstrated the multiplet at δ 9.2 characteristic of H-9 deshielded by the 1-bromo function. We concluded, therefore, that this was *N*-(1-bromo-2-dibenzothiophenyl)benzamide (**5b**). Hydrolysis provided once again 1-bromo-2-dibenzothiophenamine (**4**). A small amount of the minor isomer was isolated and its nmr spectrum (See Table I, **12b**) suggests that it is the elusive 3-bromo derivative. Thus H-1 and H-4 appear as sharp singlets at δ 8.42 and 8.44, adjacent to the H-9 multiplet at δ 8.35. Campaigne and Ashby (11) observed that the spectrum of 3-bromo-2-methyldibenzothiophene displayed a similar pattern. This material (**12b**) was hydrolyzed to 3-bromo-2-dibenzothiophenamine (**13**) which in turn was treated with acetic anhydride to give *N*-(3-bromo-2-dibenzothiophenyl)acetamide (**12a**) (See Table I for melting points and nmr spectra of these products). According to thin layer chromatography, **12a** was identical to the minor

product resulting from the bromination of **8a**.

We, therefore, conclude that 1-bromo-2-dibenzothiophenamine and derivatives have been previously incorrectly assigned as the 3-bromodibenzothiophenes (3,4). The structure proof previously presented (3) based upon the hydrolysis, deamination, and oxidation of the bromination product to give 3-bromodibenzothiophene 5,5-dioxide which had been prepared by applying the Sandmeyer reaction to 3-dibenzothiophenamine 5,5-dioxide (12) appeared sound and we are unable to explain the conflicting results obtained. It is of interest that chlorination of *N*-2-dibenzothiophenylacetamide with sulfuryl chloride was observed to give the 1-chloro derivative (4).

The 1-bromo-2-dibenzothiophenamine thus prepared was then utilized in the sequence outlined in Scheme I to obtain the desired [1]benzothieno[3,2-*f*]quinazoline-1,3-diamine (**2**). The intermediate 2-amino-1-dibenzothiophenecarbonitrile (**7**) could be obtained directly from 1-bromo-2-dibenzothiophenamine (**4**) in low (6%) yield. However, treatment of *N*-(1-bromo-2-dibenzothiophenyl)-acetamide with cuprous cyanide followed by hydrolysis produced **7** in better overall yield (26%). Cyclization with chloroformamidine hydrochloride (13) provided the desired **2**. Treatment with 30% hydrogen peroxide afforded [1]benzothieno[3,2-*f*]quinazoline-1,3-diamine 7,7-dioxide.

Both [1]benzothieno[3,2-*f*]quinazoline-1,3-diamine (**2**) and its dioxide were administered in a single dose to mice infected with a normal drug-sensitive strain of *P. berghei* (14) and were devoid of antimalarial activity at 640 mg./kg. They were also tested *in vitro* against *Streptococcus faecalis* (MGM-2), normal (UC-76) and drug-resistant (S18713) *Staphylococcus aureus*, *Pseudomonas aeruginosa* (28), *Escherichia coli* (Vogel), and *Shigella sonnei* (C-10) using a modification of the gradient procedure of Szybalski (15) and Webb and Washington (16). Inhibition of *S. faecalis* at a concentration as low as 2.0 μg./ml. by [1]-benzothieno[3,2-*f*]quinazoline-1,3-diamine was demonstrated.

EXPERIMENTAL (17)

2-Dibenzothiophenamine (**3**).

A solution of 51 g. (0.22 mole) of 2-nitrodibenzothiophene (18) in 100 ml. of methanol and 400 ml. of tetrahydrofuran was hydrogenated over 7 g. of Raney-Nickel at room temperature and at an initial pressure of 50 p.s.i.g. for 20 hours. The reaction mixture was then filtered, concentrated to dryness *in vacuo*, and the residue was recrystallized form methanol to afford 26 g. (59%) of product, m.p. 133-135°. The literature (6) reports m.p. 129°. The filtrate afforded an additional 8.5 g., m.p. 133-135° (total yield 78%).

Anal. (first crop) Calcd. for $C_{12}H_9NS$: C, 72.33; H, 4.55; N, 7.03. Found: C, 71.99; H, 4.75; N, 7.23.

1-Bromo-2-dibenzothiophenamine (**4**).

A procedure of Pan and Fletcher (5) was followed. To a stirred solution of 10 g. (0.05 mole) of 2-dibenzothiophenamine in 75 ml. of dimethyl sulfoxide was added at a very slow drop rate 5.9 ml. (0.05 mole) of 48% hydrobromic acid. The solution was stirred overnight. An additional 0.6 ml. of hydrobromic acid was added, and the solution was heated under gentle reflux for 1.5 hours, allowed to cool and poured into 1 liter of cold water. The mixture was made basic with concentrated ammonium hydroxide and filtered. The filter cake was washed with water, air dried, dissolved in benzene, and chromatographed over 240 g. of silica gel, eluting with benzene. That portion of the eluant containing the product, as determined by tlc (silica/benzene, $R_f \cong 0.29$), was evaporated to dryness *in vacuo* to give 11.4 g. (82%) of the product which could be used in the next reaction as is. Recrystallization from ethanol afforded 8.85 g. of purified material, m.p. 133-135°. The filtrate was concentrated to give an additional 1.37 g., m.p. 133-135°; total yield, 10.22 g. (73.5%).

Anal. Calcd. for $C_{12}H_8BrNS$: C, 51.82; H, 2.90; N, 5.04. Found: C, 51.63; H, 3.07; N, 5.06.

1,3-Dibromo-2-dibenzothiophenamine (**11**).

The quantities and procedure used were identical to that described above for the preparation of **4** except that an additional 2.5 ml. rather than 0.6 ml. of 48% hydrobromic acid was added after the mixture had stirred overnight. The solution was then heated under reflux 1 hour and stirred overnight to afford 1.5 g. of **11**, $R_f \cong 0.36$ (silica-benzene). The filtrate was diluted with water, made basic, and filtered. The filter cake was taken up in 150 ml. of benzene and filtered to collect 3.8 g. of **4**. The benzene filtrate was chromatographed over 200 g. of silica gel to afford 0.8 g. of **11** and 5.6 g. of **4**. The two crops of **11** were combined and recrystallized from a 50:50 mixture of toluene:methanol to give 1.62 g. (9%) of **11**, m.p. 176-178°.

Anal. Calcd. for $C_{12}H_7Br_2NOS$: C, 40.36; H, 1.98; N, 3.92; Br, 44.76. Found: C, 40.48; H, 2.17; N, 3.83; Br, 44.68.

N-2-Dibenzothiophenylacetamide (**8a**).

To a warm solution of 10 g. (0.05 mole) of 2-dibenzothiophenamine in 230 ml. of benzene was added 6.6 ml. of acetic anhydride. The acetamide which separated upon standing, was collected to afford 11 g. (91%), m.p. 177-179°, lit. (6) reports 178°.

N-(1-Nitro-2-dibenzothiophenyl)acetamide (**9**).

The procedure of Gilman and Wilder (9) was followed. To a stirred mixture of 7.5 g. (0.031 mole) of *N*-2-dibenzothiophenylacetamide in 325 ml. of glacial acetic acid was added over 0.5 hour, 6.5 ml. of fuming nitric acid (90%). The temperature was not allowed to rise above 28° during the addition. The mixture was stirred one hour, cooled to 16° and filtered to afford 6.4 g. (72%) of product, m.p. 205-210°. Recrystallization from methanol gave 5.1 g. (57%), m.p. 209-210° [lit. (9) m.p. 209-210°].

Anal. Calcd. for $C_{14}H_{10}N_2O_3S$: C, 58.73; H, 3.52; N, 9.79. Found: C, 58.59; H, 3.73; N, 9.79.

1-Bromodibenzothiophene (**10**).

Method A. Treatment of *N*-(1-nitro-2-dibenzothiophenyl)acetamide (**9**) with 30% Hydrobromic Acid (9).

A mixture of 2 g. (0.007 mole) of *N*-(1-nitro-2-dibenzothiophenyl)acetamide in 40 ml. of 30% hydrobromic acid and 40 ml. of ethanol was heated under reflux for 1 hour, diluted with 100 ml. of water and allowed to cool. The precipitate which was collected appeared to be a mixture, (tlc - silica gel/benzene), of the starting material, hydrolyzed starting material and the desired product. It was chromatographed over 50 g. of silica gel, with benzene, to afford 0.95 g. of crude product. The red semi-solid was extracted twice with boiling methanol and the extract was

again evaporated to give 0.61 g. Two recrystallizations from methanol-water gave 0.2 g. of 1-bromodibenzothiophene, m.p. 79-80°, lit. (9) m.p. 84°.

Anal. Calcd. for $C_{12}H_7BrS$: C, 54.77; H, 2.68; Br, 30.37. Found: C, 54.64; H, 2.87; Br, 30.58.

Method B. Deamination of 1-Bromo-2-dibenzothiophenamine.

A procedure of Gilman and Avakian (3) was followed. To a suspension of 1.5 g. (0.0054 mole) of 1-bromo-2-dibenzothiophenamine in 45 ml. of ethanol was added cautiously a mixture of 12 ml. of concentrated sulfuric acid and 6 ml. of water. The mixture was heated to 80° and to it was added slowly 3.6 g. (0.052 mole) of sodium nitrite. The yellow suspension was heated under reflux for 25 minutes, allowed to cool and filtered. The filtrate was diluted with water, made basic with ammonium hydroxide, and filtered to collect 0.74 g. (52%) of crude product, m.p. 74-78°. Recrystallization from methanol-water gave analytically pure material, m.p. 79-80° which showed no depression in a mixed melting point determination with a sample of 1-bromodibenzothiophene obtained by Method A.

Anal. Calcd. for $C_{12}H_7BrS$: C, 54.77; H, 2.68; N, 0.0; Br, 30.37. Found: C, 54.78; H, 2.63; N, 0.0; Br, 30.16.

N-(1-Bromo-2-dibenzothiophenyl)acetamide (**5a**).

Method A.

To a solution of 10.5 g. (0.0378 mole) of 1-bromo-2-dibenzothiophenamine in 500 ml. of benzene was added 5 ml. of acetic anhydride. The mixture was allowed to stand several hours and then filtered to collect 10.15 g. (83.9%) of white crystalline product, m.p. 197-199°.

Anal. Calcd. for $C_{14}H_{10}BrNOS$: C, 52.51; H, 3.15; N, 4.38. Found: C, 52.59; H, 3.26; N, 4.41.

Method B.

The following is a modified procedure of Gilman and Avakian (3). Bromine (2.9 g., 0.018 mole) in acetic acid (18 ml.) was added dropwise to a solution of *N*-2-dibenzothiophenylacetamide (**8a**) (4 g., 0.017 mole) in acetic acid (140 ml.), and the solution was stirred overnight at room temperature. Tlc (alumina-30 parts ethyl acetate:70 parts benzene) demonstrated the presence of starting material as well as products. An additional 1 g. of bromine was added and the solution was stirred at 60° for 2 hours, allowed to cool, and poured into 600 ml. of water containing sodium bisulfite (*ca.* 0.1 g.). The resulting precipitate was collected, washed with water, and dried to afford 5.18 g., (m.p. 176-186°) which according to tlc (30 parts ethyl acetate:70 parts benzene) and vpc was a mixture of *N*-(1-bromo-2-dibenzothiophenyl)acetamide (**5a**) ($R_f \cong 0.3$, 83%) and another product ($R_f \cong 0.4$, 17%) which was later shown to be **12a**. Recrystallization from ethanol afforded 2.1 g. of *N*-(1-bromo-2-dibenzothiophenyl)acetamide (**5a**), m.p. 197-199°, which was identical (ir, nmr) with the material obtained by Method A.

N-2-Dibenzothiophenylbenzamide (**8b**).

This compound was prepared as described by Gilman and Wilder (10), m.p. 197-199°, lit. (10) reports 199-200°.

Bromination of *N*-2-Dibenzothiophenylbenzamide.

This procedure was reported by Gilman and Wilder (4). To a solution of 5 g. (0.017 mole) of *N*-2-dibenzothiophenylbenzamide in 200 ml. of chloroform was added a solution of 2.7 g. (0.017 mole) of bromine and a crystal of iodine in chloroform (30 ml.). The reaction mixture was heated under reflux for 2.5 hours, cooled, washed with water, and evaporated to give 6.3 g. (100%) of crude product. Tlc (silica-benzene) and vpc indicated the presence of a major product (R_f = *ca.* 0.24, 91%) and a minor one (R_f = *ca.* 0.31, 6%). Recrystallization from methyl cellosolve afforded 4.8 g. (76%) of the major product (vpc 100%), m.p. 201-202° which was determined by means of nmr to be *N*-(1-bromo-2-dibenzothiophenyl)benzamide (**5b**).

Anal. Calcd. for $C_{19}H_{12}BrNOS$: C, 59.69; H, 3.17; N, 3.57; S, 8.39; Br, 20.91. Found: C, 59.68; H, 3.33; N, 3.57; S, 8.19; Br, 20.86.

Hydrolysis in refluxing ethanolic potassium hydroxide afforded 1-bromo-2-dibenzothiophenamine (**4**).

Crude *N*-(3-bromo-2-dibenzothiophenyl)benzamide (**12b**), the minor product, was isolated from the recrystallization filtrate and purified by two recrystallizations from methyl cellosolve to give 0.1 g., m.p. 188-189°.

Anal. Calcd. for $C_{19}H_{12}BrNOS$: C, 59.69; H, 3.17; N, 3.57; S, 8.39. Found: C, 59.67; H, 3.31; N, 3.72; S, 8.35.

3-Bromo-2-dibenzothiophenamine (**13**).

A mixture of 0.1 g. (0.00026 mole) of *N*-(3-bromo-2-dibenzothiophenyl)benzamide in 1.3 ml. of 13% aqueous potassium hydroxide and 6 ml. of ethanol was heated under reflux for 11 hours, diluted with *ca.* 1 ml. of water, and cooled to afford 0.07 g. (100%) of product, m.p. 152-153°. Recrystallization from ethanol gave 0.04 g., m.p. 153-154°.

Anal. Calcd. for $C_{12}H_8BrNS$: C, 51.81; H, 2.90; N, 5.04; Br, 28.73. Found: C, 51.97; H, 3.07; N, 5.05; Br, 29.14.

N-(3-Bromo-2-dibenzothiophenyl)acetamide (**12a**).

A warm solution of 0.03 g. (0.0001 mole) of **13** in 9 ml. of benzene was treated with 0.02 ml. (0.0002 mole) of acetic anhydride to afford 24 mg. (80%) of product, m.p. 239-240°. Tlc (alumina - 30 parts ethylacetate:70 parts benzene) indicated that this product was identical with the minor product resulting from the bromination of *N*-2-dibenzothiophenylacetamide (**8a**).

Anal. Calcd. for $C_{14}H_{10}BrNOS$: C, 52.51; H, 3.15; N, 4.38; Br, 24.96. Found: C, 52.51; H, 3.15; N, 4.60; Br, 24.97.

N-(1-Cyano-2-dibenzothiophenyl)acetamide (**6**).

A mixture of 0.64 g. (0.002 mole) of *N*-(1-bromo-2-dibenzothiophenyl)acetamide, 0.24 g. (0.0027 mole) of cuprous cyanide and 3 ml. of 1-methyl-2-pyrrolidinone was stirred at 145° for 5 hours, cooled and poured into water. The precipitate that formed was collected, washed with water and extracted with 30 ml. of boiling ethanol. Upon cooling, the extract afforded 0.2 g. (37.5%) of the desired product, m.p. 217-218°.

Anal. Calcd. for $C_{15}H_{10}N_2OS$: C, 67.65; H, 3.79; N, 10.52. Found: C, 67.40; H, 4.24; N, 10.60.

The infrared spectrum (potassium bromide disc) contained a sharp CN peak at 2220 cm^{-1}.

2-Amino-1-dibenzothiophenecarbonitrile (**7**).

This compound was first prepared in the following manner: A mixture of 2.98 g. (0.0107 mole) of 1-bromo-2-dibenzothiophenamine, 1.26 g. (0.0141 mole) of cuprous cyanide and 10.7 ml. of 1-methyl-2-pyrrolidinone was stirred at 140° for 0.5 hours. The mixture was allowed to cool and then triturated with water. The dark solid was extracted with boiling ethanol and the extract was treated with charcoal, filtered through Celite and evaporated to dryness *in vacuo*. The residue was extracted with boiling benzene and again evaporated to dryness. The residue was then chromatographed over 40 g. of silica gel, eluting with benzene. That portion of the eluant containing the product as determined by thin layer chromatography (silica/benzene, $R_f \cong 0.25$) was concentrated *in vacuo* to an off-white solid. Recrystallization from 95% aqueous ethanol gave 0.16 g. (6.6%) of the product, m.p. 194-195°.

Anal. Calcd. for $C_{13}H_8N_2S \cdot 0.05H_2O$: C, 69.34; H, 3.62; N, 12.44; H_2O, 0.36. Found: C, 69.06; H, 3.70; N, 12.49; H_2O, 0.14.

The yield was considerably improved by heating a mixture of 0.27 g. (0.001 mole) of **6**, 0.06 g. (0.011 mole) of sodium methoxide and 20 ml. of methanol under reflux for 4 hours. The cooled mixture afforded 0.18 g. (82%) of the product **7**.

[1]Benzothieno[3,2-*f*]quinazoline-1,3-diamine (**2a**).

A mixture of 1.5 g. (0.0067 mole) of 2-amino-1-dibenzothiophenecarbonitrile, 0.96 g. (0.0083 mole) of chloroformamidine hydrochloride (13) and 5.9 g. of sulfonylbis[methane] was heated to 155° and kept at that temperature for 40 minutes. The slightly cooled reaction mixture was taken up in 250 ml. of hot water, filtered to remove dark insolubles and made basic with ammonium hydroxide. The precipitate that formed was collected, washed with water and recrystallized from *N,N*-dimethylformamide to give 1.4 g. (78.6%) of the title compound, m.p. 296-298° dec.

Anal. Calcd. for $C_{14}H_{10}N_4S$: C, 63.13; H, 3.78; N, 21.05. Found: C, 63.08; H, 4.07; N, 21.11.

[1]Benzothieno[3,2-*f*]quinazoline-1,3-diamine 7,7-Dioxide (**2b**).

A mixture of 2.87 g. (0.0108 mole) of [1]benzothieno[3,2-*f*]-quinazoline-1,3-diamine, 11.5 ml. of 30% hydrogen peroxide, and 48 ml. of glacial acetic acid was stirred at room temperature for 2 days. An additional 1 ml. of hydrogen peroxide was added and the mixture was stirred at 45° for 8 hours and at room temperature for 3 days and then poured into iced sodium hydroxide. The precipitate was collected, washed with water and recrystallized from *N,N*-dimethylformamide containing a small amount of water to give 0.87 g. (27%) of product, m.p. >300°.

Anal. Calcd. for $C_{14}H_{10}N_4O_2S$: C, 56.36; H, 3.38; N, 18.78. Found: C, 56.06; H, 3.57; N, 18.76.

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