Synthesis of Derivatives of Thiophene Using Methyl 2-Isothiocyanatobenzoate

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Received April 26, 2000

A variety of 2-substituted thiophenes is readily obtained from 2-(2-thienyl)-4*H*-3,1-benzothiazin-4-one (**2**), which is formed when thiophene reacts with methyl 2-isothiocyanatobenzoate (**1**) in the presence of anhydrous stannic chloride.

J. Heterocyclic Chem., **38**, 343 (2001).

Methyl 2-isothiocyanatobenzoate (**1**) has been used extensively for the synthesis of a wide variety of heterocyclic compounds [1-16]. In this paper we report the results of a brief investigation of the use of this reagent for the synthesis of a number of derivatives of thiophene, which parallel the results of an earlier reported synthesis of derivatives of pyrrole [11].

In the presence of anhydrous stannic chloride, thiophene reacts with **1** to form 2-(2-thienyl)-4*H*-3,1-benzothiazin-4-one (**2**), presumably by cyclization of the initially formed *N*-(2-methoxycarbonylphenyl)thiophene-2-thiocarboxamide (**3**). The thiazinone ring of **2** opens up readily upon treatment with nucleophilic reagents. Thus, sodium methoxide in methanol converts **2** to thioamide **3**, which is oxidized by hydrogen peroxide to the corresponding amide, *N*-(2-methoxycarbonylphenyl)thiophene-2-carboxamide (**4**). Brief heating of **2** with ethanolic ammonia yields *N*-(2-aminocarbonylphenyl)thiophene-2-thiocarboxamide (**5**), whereas a more prolonged treatment results in cyclization and formation of 2-(2-thienyl)-4(3*H*)-quinazolinone (**6**). Analogous reactions of **2** with hydrazine and methylhydrazine lead to 3-amino-2-(2-thienyl)-4(3*H*)-quinazolinone (**7a**) and 3-methylamino-2-(2-thienyl)-4(3*H*)-quinazolinone (**7b**), respectively. Deamination of **7a** with nitrous acid [17] yields the anticipated quinazolinone **6**. Also, the thiazinone ring of **2** undergoes ring opening in aqueous

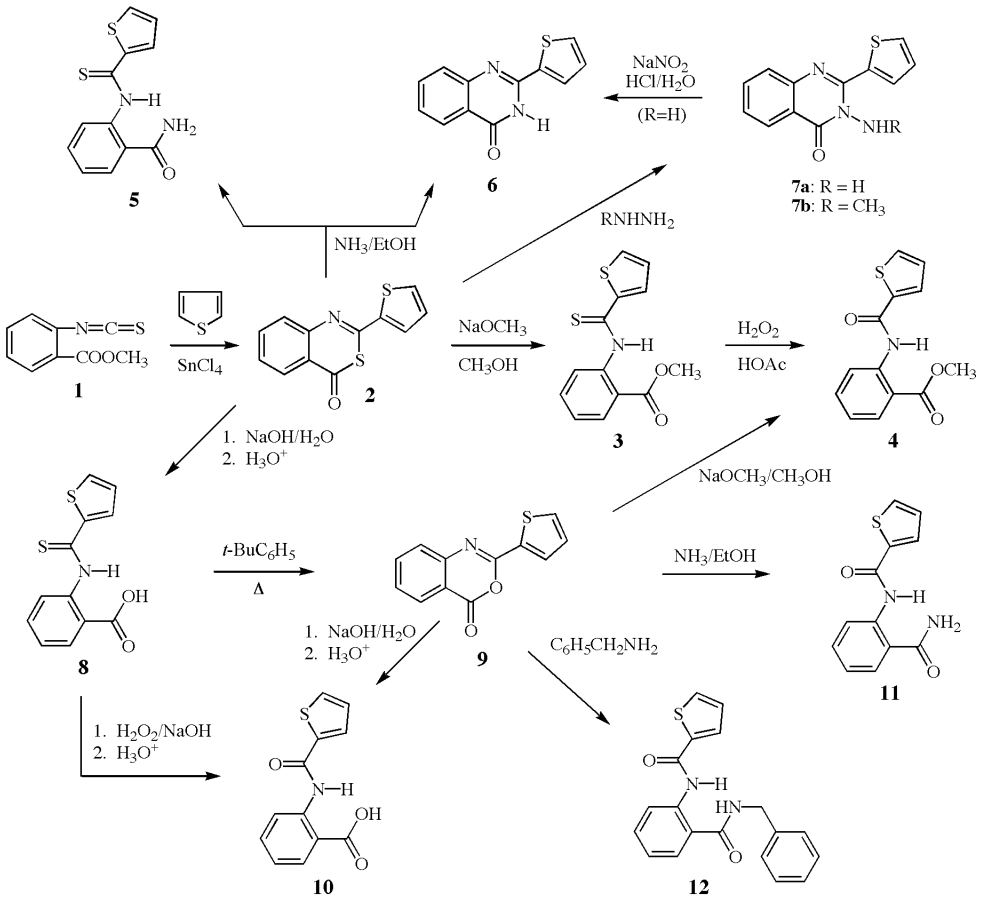
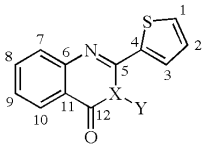
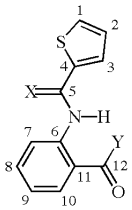


Table 1

^{13}C-nmr Shifts in Dimethyl-d_6 Sulfoxide





Compound	X	Y	Compound	X	Y
2	S	–	**3**	S	OCH_3
6	N	H	**4**	O	OCH_3
7a	N	NH_2	**5**	S	NH_2
7b	N	$NHCH_3$	**8**	S	OH
9	O	–	**10**	O	OH
			11	O	NH_2
			12	O	$NHCH_2Ph$

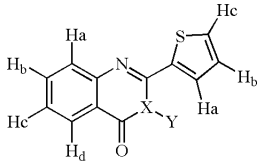
	1	2	3	4	5	6	7	8	9	10	11	12	Y		
2	133.1	128.8	130.1	140.9	154.7	147.8	130.8	136.5	129.0	124.4	119.2	182.2			
3	134.9	128.5	125.2	148.0	187.2	139.5	127.0	133.0	127.4	130.6	125.3	166.2	52.6(CH_3)		
4	132.5	128.4	128.9	139.4	159.4	139.9	120.7	134.3	123.3	130.7	116.9	168.0	52.6(CH_3)		
5	135.0	128.8	125.4	149.2	185.3	139.4	122.7	131.5	124.3	128.5	123.9	170.4			
6	132.1	128.5	129.4	137.3	148.6	147.8	125.9	134.7	126.3	126.9	120.8	161.8			
7a	133.6	127.1	133.9	135.2	149.4	146.9	127.0	134.4	126.2	126.0	119.3	161.1			
7b	134.5	126.8	133.6	134.6	149.2	146.9	127.1	134.6	126.8	126.0	119.9	160.5	36.6(CH_3)		
8	135.2	128.7	125.0	148.7	186.6	140.3	125.4	133.1	126.6	131.3	123.9	168.4			
9	133.4	128.7	131.6	133.6	153.0	146.0	126.3	136.8	128.6	128.1	116.6	158.3			
10	132.5	128.4	128.7	139.6	159.4	140.8	119.8	134.3	122.9	131.3	116.4	170.0			
11	132.6	128.4	128.8	139.9	159.3	140.0	119.9	132.2	122.6	128.4	118.8	171.2			
12	132.4	128.4	128.5	139.2	159.3	139.8	120.3	132.3	122.9	128.3	119.9	168.6	138.9(*i*) 128.2(*m*)	127.2(*o*) 126.9(*p*)	42.6(CH_2)

sodium hydroxide to give, after acidification, carboxylic acid **8**. Upon refluxing in *t*-butylbenzene, **8** undergoes cyclization with loss of hydrogen sulfide to form 2-(2-thienyl)-4*H*-3,1-benzoxazin-4-one (**9**). The structure of this compound is established by its rapid hydrolysis to carboxylic acid **10**, which is also obtained by oxidation of compound **8** with hydrogen peroxide. Similarly, the oxazinone ring of **9** undergoes ring opening upon treatment with sodium methoxide, ammonia, and benzylamine to afford ester **4**, amide **11**, and *N*-benzylamide **12**, respectively.

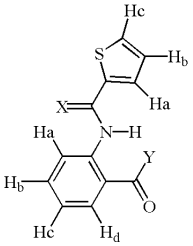
The structures assigned to compounds **2**-**12** are consistent with their infrared, proton nmr, and C-13 nmr spectra. Table 1 contains the C-13 nmr spectroscopic data for all of the compounds mentioned above. Use of HMQC and HMBC along with literature data of model compounds [18-22] allowed the assignments of signals to specific carbon atoms of these compounds.

EXPERIMENTAL

Reagent grade solvents were used without further purification. Melting points were determined in capillaries with a Thomas-Hoover Uni-Melt apparatus and are uncorrected. Infrared spectra were recorded on a Beckman IR-33 spectrophotometer using mineral oil mulls. Proton and carbon-13 nmr spectra were obtained in DMSO-d_6 on a Bruker AC250 spectrometer. Chemical shifts are in ppm (δ) relative to TMS as internal standard. The symbols used to describe proton nmr spectra in the following experimental procedures are shown on the structures below.



2, **6**, **7a**, **7b**, **9**



3–**5**, **8**, **10**–**12**

X and Y as in Table 1.

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

A mixture of thiophene (2.0 g, 23.8 mmol), methyl 2-isothiocyanatobenzoate (3.41 g, 17.6 mmol) and stannic chloride (5 ml, 42.7 mmol) was stirred at room temperature for 16 hours. To the resulting dark green semi solid was added ice, water and

concentrated hydrochloric acid. The aqueous solution was decanted and the sticky solid was triturated first with hexane and then with ethanol to give 2.45 g (57%) of **2**, mp 125-127°. Recrystallization from ethanol gave the pure compound as buff crystals, mp 127-128°; ir: 1650 (C=O) cm^{-1}; ^1H nmr: δ 7.25 (dd, 1H, thiophene H_b, J = 4.8, 3.9 Hz), 7.62 (dt, 1H, ArH_c, J = 7.5, 1.1 Hz), 7.81 (dd, 1H, ArH_a, J = 7.8, 0.7 Hz), 7.83 (dd, 1H, thiophene H_a, J = 3.8, 1.0 Hz), 7.94 (dt, 1H, ArH_b, J = 7.8, 1.5 Hz), 7.98 (dd, 1H, thiophene H_c, J = 5.0, 0.9 Hz), 8.11 (dd, 1H, ArH_d, J = 7.9, 1.3 Hz).

Anal. Calcd. for $C_{12}H_7NOS_2$: C, 58.75; H, 2.88; N, 5.71. Found: C, 58.58; H, 2.74; N, 5.63.

N-(2-Methoxycarbonylphenyl)thiophene-2-thiocarboxamide (**3**).

A mixture of compound **2** (0.50 g, 2.04 mmol), sodium methoxide (0.30 g, 5.55 mmol) and methanol (10 ml) was heated in a water bath for 5 minutes. The resulting mixture was diluted with water (20 ml), acidified with concentrated hydrochloric acid and filtered to give 0.55 g (97%) of compound **3**, mp 128-129°. Recrystallization from methanol gave the pure compound as buff crystals, mp 129.5-131°; ir: 1690 (C=O) cm^{-1}; ^1H nmr: δ 3.76 (s, 3H, CH_3), 7.23 (dd, 1H, thiophene H_b, J = 4.8, 3.9 Hz), 7.43 (dt, 1H, ArH_c, J = 7.7, 1.1 Hz), 7.68 (dt, 1H, ArH_b, J = 7.8, 1.5 Hz), 7.83 (dd, 1H, thiophene H_a, J = 3.8, 1.1 Hz), 7.86 (dd, 1H, thiophene H_c, J = 5.0, 1.0 Hz), 7.93 (dd, 1H, ArH_d, J = 7.9, 1.1 Hz), 7.95 (dd, 1H, ArH_a, J = 7.8, 1.5 Hz), 11.8 (s, 1H, NH).

Anal. Calcd. for $C_{13}H_{11}NO_2S_2$: C, 56.29; H, 4.00; N, 5.05. Found: C, 56.00; H, 3.84; N, 5.01.

N-(2-Methoxycarbonylphenyl)thiophene-2-carboxamide (**4**).

Method A.

A mixture of compound **3** (0.23 g, 0.83 mmol), acetic acid (2 ml) and 30% hydrogen peroxide (2 ml) was allowed to stand for 2 hours. The resulting mixture was diluted with water and filtered to give 0.14 g (65%) of compound **4** as a buff solid, mp 170-171°. Recrystallization from petroleum ether (bp 35-60°)/ethyl acetate gave the pure compound, mp 170-171°; ir: 3255 (N-H), 1690, 1630 (C=O) cm^{-1}; ^1H nmr: δ 3.85 (s, 3H, CH_3), 7.19 (dt, 1H, ArH_c, J = 7.5, 1.1 Hz), 7.24 (dd, 1H, thiophene H_b, J = 5.0, 3.8 Hz), 7.63 (dt, 1H, ArH_b, J = 7.8, 1.6 Hz), 7.77 (dd, 1H, thiophene H_a, J = 3.8, 1.1 Hz), 7.87 (dd, 1H, thiophene H_c, J = 5.0, 1.0 Hz), 7.96 (dd, 1H, ArH_d, J = 7.9, 1.5 Hz), 8.34 (dd, 1H, ArH_a, J = 8.4, 0.9 Hz), 11.5 (s, 1H, NH).

Anal. Calcd. for $C_{13}H_{11}NO_3S$: C, 59.76; H, 4.24; N, 5.36. Found: C, 59.51; H, 4.10; N, 5.43.

Method B.

A mixture of compound **9** (0.30 g, 1.31 mmol), sodium methoxide (0.15 g, 2.80 mmol) and methanol (10 ml) was heated briefly and then was allowed to stand at room temperature for 1 hour. Dilution with water (30 ml) and filtration gave 0.30 g (88%) of **4**, mp 169-171°.

N-(2-Aminocarbonylphenyl)thiophene-2-thiocarboxamide (**5**).

A mixture of compound **2** (0.50 g, 2.04 mmol) and ethanolic ammonia (ethanol saturated with ammonia at 0°, 10 ml) was heated briefly in a stoppered flask on a water bath and the resulting solution was allowed to stand at room temperature for 1 hour. Dilution with water (30 ml) and acidification with concentrated hydrochloric acid gave 0.50 g (93%) of compound **5**, mp 200-202°. Recrystallization from ethanol afforded the pure compound as buff crystals, mp 204-205°; ir: 3430, 3150 (N-H), 1640 (C=O) cm^{-1}; ^1H nmr: δ 7.23 (dd, 1H, thiophene H_b, J = 5.1, 3.9 Hz), 7.33 (dt, 1H, ArH_c, J = 7.6, 1.1 Hz), 7.58 (dt, 1H, ArH_b, J = 7.8, 1.5 Hz), 7.73 (dd, 1H, thiophene H_a, J = 3.8, 1.1 Hz), 7.86 (dd, 1H, thiophene H_c, J = 5.1, 1.0), 7.88 (dd, 1H, ArH_d, J = 7.9, 1.4 Hz), 8.39 (s, 2H, NH_2), 8.87 (dd, 1H, ArH_a, J = 8.9, 0.9 Hz), 13.2 (s, 1H, NH).

Anal. Calcd. for $C_{12}H_{10}N_2OS_2$: C, 54.94; H, 3.84; N, 10.68. Found: C, 55.02; H, 3.72; N, 10.68.

2-(2-Thienyl)-4(3*H*)-quinazolinone (**6**).

Method A.

A mixture of compound **2** (0.60 g, 2.45 mmol) and ethanolic ammonia (ethanol saturated with ammonia at 0°, 12 ml) was heated in a closed flask on a water bath for 16 hours. The resulting solution was cooled and filtered to give 0.45 g (80%) of **6**, mp 282.5-284°. Recrystallization from ethanol gave the pure compound as buff crystals, mp 284-286° (lit [23] mp 288-289°; lit [24] mp 285-286°); ir: 3195(N-H), 1675 (C=O) cm^{-1}; ^1H nmr: δ 7.22 (dd, 1H, thiophene H_b, J = 4.9, 3.8 Hz), 7.49 (dt, 1H, ArH_c, J = 7.8, 1.0 Hz), 7.64 (d, 1H, ArH_a, J = 8.2 Hz), 7.79 (dt, 1H, ArH_b, J = 7.7, 1.5 Hz), 7.85 (dd, 1H, thiophene H_c, J = 5.0, 1.0 Hz), 8.11 (d, 1H, ArH_d, J = 7.9 Hz), 8.21 (dd, 1H, thiophene H_a, J = 3.8, 1.1 Hz), 12.6 (s, 1H, NH).

Anal. Calcd. for $C_{12}H_8N_2OS$: C, 63.14; H, 3.53; N, 12.27. Found: C, 63.01; H, 3.67; N, 12.26.

Method B.

To an ice cold mixture of compound **7a** (0.30 g, 1.23 mmol) and concentrated hydrochloric acid (2 ml) was added sodium nitrite (0.20 g) dissolved in cold water (6 ml). After the evolution of nitrogen had ceased, the mixture was diluted with water (10 ml) and was allowed to stand for 2 hours. Following filtration, the product was washed thoroughly with 10% aqueous sodium hydrogen carbonate to give 0.25 g (89%) of **6,** mp 281-284°.

3-Amino-2-(2-thienyl)-4(3*H*)-quinazolinone (**7a**).

Hydrazine (95%, 2 ml) was added to compound **2** (0.50 g, 2.04 mmol) and the mixture was heated in a water bath for 30 minutes. After cooling, water was added and the mixture was filtered to give 0.50 g (100%) of **7a**, mp 198-199.5°. Recrystallization from ethanol gave the pure compound as buff crystals, mp 198-200°; ir: 3350 (N-H), 1675 (C=O), 1615 (C=N) cm^{-1}; ^1H nmr: δ 5.95 (s, 2H, NH_2), 7.21 (dd, 1H, thiophene H_b, J = 5.1, 3.9 Hz), 7.49 (dt, 1H, ArH_c, J = 7.6, 1.2 Hz), 7.66 (dd, 1H, ArH_a, J = 8.2, 1.0 Hz), 7.81 (dt, 1H, ArH_b, J = 7.7, 1.5 Hz), 7.85 (dd, 1H, thiophene H_c, J = 5.1, 1.2 Hz), 8.12 (dd, 1H, ArH_d, J = 8.0, 1.1 Hz), 8.41 (dd, 1H, thiophene H_a, J = 3.9, 1.2 Hz).

Anal. Calcd. for $C_{12}H_9N_3OS$: C, 59.24; H, 3.73; N, 17.27. Found: C, 59.28; H, 3.66; N, 17.23.

3-Methylamino-2-(2-thienyl)-4(3*H*)-quinazolinone (**7b**).

A mixture of compound **2** (0.50 g, 2.04 mmol) and methylhydrazine (2 ml) was heated in a water bath for 30 minutes. The product was mixed with water (20 ml) and the resulting semisolid was triturated with ethanol to give 0.20 g (39%) of compound **7b**, mp 122-124°. Recrystallization from ethanol gave the pure compound, mp 127-128°; ir: 3320 (N-H), 1665 (C=O), 1605 (C=N) cm^{-1}; ^1H nmr: δ 2.68 (d, 3H, CH_3, J = 5.6 Hz), 6.72 (q, 1H, NH, J = 5.6 Hz), 7.22 (dd, 1H, thiophene H_b, J = 4.8, 3.9 Hz), 7.49 (dt, 1H, ArH_c, J = 7.9, 0.9 Hz), 7.66 (d, 1H, ArH_a, J = 8.0 Hz), 7.81

(dt, 1H, ArH_b, J = 7.6, 1.3 Hz), 7.86 (dd, 1H, thiophene H_c, J = 5.0, 1.1 Hz), 8.12 (dd, 1H, ArH_d, J = 8.0, 1.5 Hz), 8.36 (dd, 1H, thiophene H_a, J = 3.9, 1.1Hz).

Anal. Calcd. for $C_{13}H_{11}N_3OS$: C, 60.68; H, 4.31; N, 16.33. Found: C, 60.80; H, 4.25; N, 16.38.

N-(2-Carboxyphenyl)thiophene-2-thiocarboxamide (**8**).

Benzothiazinone **2** (0.50 g, 2.04 mmol) was heated with 10% aqueous sodium hydroxide (10 ml) in a water bath for 30 minutes to obtain a clear solution. Ice water was added to the cooled solution which was acidified with concentrated hydrochloric acid to give 0.50 g (93%) of compound **8**, mp 164-165°. This product was recrystallized from methanol to give pure **8**, mp 165-166°; ir: 1655 (C=O) cm^{-1}; ^1H nmr: δ 7.22 (dd, 1H, thiophene H_b, J = 5.0, 3.8 Hz), 7.39 (dt, 1H, ArH_c, J = 7.6, 1.1 Hz), 7.65 (dt, 1H, ArH_b, J = 7.8, 1.6 Hz), 7.78 (dd, 1H, thiophene H_a, J = 3.8, 1.1 Hz), 7.84 (dd, 1H, thiophene H_c, J = 5.0, 1.0 Hz), 8.00 (dd, 1H, ArH_d, J = 7.9, 1.5 Hz), 8.34 (dd, 1H, ArH_a, J = 8.6, 0.8 Hz), 12.1 (s, 1H, NH).

Anal. Calcd. for $C_{12}H_9NO_2S_2$: C, 54.73; H, 3.45; N, 5.32. Found: C, 54.88; H, 3.61; N, 5.32.

2-(2-Thienyl)-4*H*-3,1-benzoxazin-4-one (**9**).

A mixture of compound **8** (1.63 g, 6.19 mmol) and *t*-butylbenzene (20 ml) was refluxed for 18 hours, and allowed to cool. The resulting mixture was diluted with petroleum ether (bp 63-75°; 50 ml) and filtered to give 1.08 g (76%) of **9**, mp 132-134°. Recrystallization from petroleum ether (bp 35-60°)/ethyl acetate gave the pure compound as buff crystals, mp 134-135° (lit[25] mp 133-134°; lit [26] mp 125-127°); ir: 1770 (C=O), 1615 (C=N) cm^{-1}; ^1H nmr: δ 7.28 (dd, 1H, thiophene H_b, J = 5.0, 3.8 Hz), 7.58 (dt, 1H, ArH_c, J = 7.6, 1.1 Hz), 7.63 (dd, 1H, ArH_a, J = 7.9, 0.7 Hz), 7.92 (dt, 1H, ArH_b, J = 7.8, 1.6 Hz), 7.93 (dd, 1H, thiophene H_c, J = 5.0, 1.2 Hz), 7.98 (dd, 1H, thiophene H_a, J = 3.8, 1.2 Hz), 8.11 (dd, 1H, ArH_d, J = 7.8, 1.1 Hz).

Anal. Calcd. for $C_{12}H_7NO_2S$: C, 62.88; H, 3.08; N, 6.11. Found: C, 62.86; H, 3.02; N, 5.90.

N-(2-Carboxyphenyl)thiophene-2-carboxamide (**10**).

Method A.

A mixture of compound **9** (0.20 g, 0.87 mmol) and 10% aqueous sodium hydroxide (5 ml) was heated in a water bath for 5 minutes to form a solution which was diluted with water (30 ml), cooled and acidified with concentrated hydrochloric acid to give 0.18 g (84%) of **10,** mp 208-210°. Recrystallization from petroleum ether (bp 35-60°)/ethyl acetate gave the pure compound mp 210-211° (lit[26] mp 210-212°); ir: 3310 (N-H), 1670, 1690 (C=O) cm^{-1}; ^1H nmr: δ 7.18 (dt, 1H, ArH_c, J = 7.5, 0.9 Hz), 7.25 (dd, 1H, thiophene H_b, J = 4.8, 3.9 Hz), 7.63 (dt, 1H, ArH_b, J = 7.8, 1.5 Hz), 7.73 (dd, 1H, thiophene H_a, J = 3.8, 1.0 Hz), 7.90 (dd, 1H, thiophene H_c, J = 5.0, 1.0 Hz), 8.03 (dd, 1H, ArH_d, J = 7.9, 1.5 Hz), 8.55 (d, 1H, ArH_a, J = 8.3 Hz), 12.1 (s, 1H, NH).

Anal. Calcd. for $C_{12}H_9NO_3S$: C, 58.29; H, 3.67; N, 5.66. Found: C, 58.56; H, 3.76; N, 5.42.

Method B.

To a chilled solution of compound **8** (0.20 g, 0.76 mmol) in 10% aqueous sodium hydroxide (2 ml) was added 30% hydrogen peroxide (2 ml) and the resulting mixture was kept in an ice bath for 2 minutes. After a 15 minute period of standing at room temperature, a second portion (2 ml) of 30% hydrogen peroxide was added. The mixture was allowed to stand for 30 minutes and then it was diluted with water (20 ml) and acidified with concentrated hydrochloric acid to give 0.16 g (85%) of **10**, mp 210-211°.

N-(2-Aminocarbonylphenyl)thiophene-2-carboxamide (**11**).

A mixture of compound **9** (0.60 g, 2.63 mmol) and ethanolic ammonia (10 ml) was kept in a stoppered flask at room temperature for 2 hours and was then filtered to give 0.56 g (86%) of **11**, mp 182-183°. Recrystallization from petroleum ether (bp 35-60°)/ethyl acetate gave the pure compound mp 182-183° (lit [26] mp 280-283°); ir: 3450, 3360, 3200 (N-H), 1655, 1620 (C=O) cm^{-1}; ^1H nmr: δ 7.16 (dt, 1H, ArH_c, J = 7.6, 1.2 Hz), 7.25 (dd, 1H, thiophene H_b, J = 5.0, 3.8 Hz), 7.55 (dt, 1H, ArH_b, J = 7.9, 1.5 Hz), 7.69 (dd, 1H, thiophene H_a, J = 3.8, 1.1 Hz), 7.88 (dd, 1H, ArH_d, J = 8.0, 1.3 Hz), 7.89 (dd, 1H, thiophene H_c, J = 5.0, 1.0 Hz), 8.41 (s, 2H, NH_2), 8.55 (dd, 1H, ArH_a, J = 8.0, 1.0 Hz), 13.0 (s, 1H, NH).

Anal. Calcd. for $C_{12}H_{10}N_2O_2S$: C, 58.52; H, 4.09; N, 11.37. Found: C, 58.79; H, 4.23; N, 11.19.

N-[2-(Benzylaminocarbonyl)phenyl]thiophene-2-carboxamide (**12**).

A mixture of compound **9** (0.68 g, 2.98 mmol), benzene (10 ml) and benzylamine (0.40 g, 3.74 mmol) was refluxed for 30 minutes. Filtration of the cooled reaction mixture gave 0.93 g (93%) of **12**, mp 153-155°. The pure compound was obtained by recrystallization from petroleum ether (bp 35- 60°)/ethyl acetate as buff crystals, mp 155-156° (lit [26] mp 156-158°) ; ir: 3290 (N-H), 1652, 1615 (C=O) cm^{-1}; ^1H nmr: δ 4.53 (d, 2H, CH_2, J = 5.9 Hz), 7.20 (dt, 1H, ArH_c, J = 7.7, 1.2 Hz), 7.24 (dd, 1H, thiophene H_b, J = 5.0, 3.7 Hz), 7.27-7.38 (m, 5H, PhH), 7.56 (dt, 1H, ArH_b, J = 7.8, 1.4 Hz), 7.69 (dd, 1H, thiophene H_a, J = 3.9, 1.1 Hz), 7.88 (dd, 1H, thiophene H_c, J = 5.0, 1.1 Hz), 7.90 (dd, 1H, ArH_d, J = 7.8, 1.3 Hz), 8.52 (dd, 1H, ArH_a, J = 8.4, 1.0 Hz), 9.46 (t, 1H, CH_2NH, J = 5.8 Hz), 12.5 (s, 1H, NH).

Anal. Calcd. for $C_{19}H_{16}N_2O_2S$: C, 67.84; H, 4.79; N, 8.33. Found: C, 68.11; H, 4.91; N, 8.24.

REFERENCES AND NOTES

[1] J. C. Howard and G. Klein, *J. Org. Chem*., **27**, 3701 (1962).

[2] E. Cherbuliez, B. Willhalm, O. Espejo, S. Jaccard and J. Rabinowitz, *Helv. Chim. Acta*, **50**, 1440 (1967).

[3] E. Cherbuliez, B. Willhalm, S. Jaccard and J. Rabinowitz, *Helv. Chim. Acta*, **50**, 2563 (1967).

[4] E. Cherbuliez, O. Espejo, B. Willhalm and J. Rabinowitz, *Helv. Chim. Acta*, **51**, 241 (1968).

[5] P. Thieme and H. Koenig, *Synthesis*, 426 (1973).

[6] J. Becher and E. G. Frandsen, *Acta Chem. Scand. Ser. B*, **30**, 863 (1976).

[7] V. P. Arya, R. S. Grewal, C. L. Kaul, J. David and V. Honkan, *Indian J. Chem. Sect. B*, **15**, 133 (1977).

[8] H. J. Kabbe, *Liebigs Ann. Chem*., 398 (1978).

[9] C. Nguyen, Y. Saegusa and Y. Iwakura, *J. Heterocyclic Chem*., **19**, 541 (1982).

[10] W. D. Dean and E. P. Papadopoulos, *J. Heterocyclic Chem*., **19**, 1117 (1982).

[11] V. Looney-Dean, B. S. Lindamood and E. P. Papadopoulos, *Synthesis*, 68 (1984).

[12] K. Kottke, H. Kuehmstedt, I. Graefe and D. Knoke,

Pharmazie, **45**, 528 (1990).

[13] I. Graefe, K. Kottke, H. Kuehmstedt and D. Knoke, *Pharmazie*, **45**, 530 (1990).

[14] J. Garin, E. Melendez, F. L. Merchan, P. Merino, J. Orduna and T. Tejero, *J. Heterocyclic Chem*., **28**, 359 (1991).

[15] P. Wippich, C. Hendreich, M. Guetschow and S. Leistner, *Synthesis*, 741 (1996).

[16] O. Morgenstern, R. Schuster, M. Finke and P. H. Richter, *Pharmazie*, **51**, 458 (1996).

[17] M. N. Sheng and A. R. Day, *J. Org. Chem*., **28**, 736 (1963).

[18] E. Kolehmainen, K. Laihia, R. Kauppinen, D. Rasala and A. Puchala, *J. Phys. Org. Chem*., **8**, 577 (1995).

[19] B. S. Joshi, Y. Bai, M. S. Puar, K. K. Dubose and S. W. Pelletier, *J. Nat. Prod*., **57**, 953 (1994).

[20] M. Chakrabarty, A. Batabyal, M. S. Morales-Rios and P. Joseph-Nathan, *Monatsh. Chemie*, **126**, 789 (1995).

[21] S. L. Spassov, I. A. Atanassova and M. A. Haimova, *Magn. Reson. Chem*., **23**, 795 (1985).

[22] V. J. Robinson and R. W. Spencer, *Can. J. Chem*., **66**, 416 (1988).

[23] A. Couture, H. Cornet, and P. Grandclaudon, *Synthesis*, 1009 (1991).

[24] E. P. Papadopoulos, *J. Org. Chem*., **39**, 2540 (1974).

[25] A. I. Eid, N. N. Aboul-Enein, S. El-Difrawy, M. Bibers, S. El-Hawary, *Eur. J. Med. Chem.-Chim. Ther.*, **14**, 463 (1979).

[26] A. A. El-Khamry, S. El-Nagdy, M. E. Shaban, *Egypt. J. Chem*., **31**, 241 (1988).