M − 200), 135 (73), 118 (93); the ir spectrum was superimposable on that of the product of the direct amination of adenine.

***N*-Amino-7-pivaloyloxymethyladeninium Mesitylenesulfonate (6).** In a procedure similar to that used for the preparation of **4**, 0.5 g of MSH and 150 mg of 7-Pom-adenine[15] gave 185 mg (67%) of compound **6**: mp 230–231°; λ_{max} (H_2O) ($\epsilon \times 10^{-3}$) at pH 1 266 (8.76), at pH 7 261 (10.3), at pH 12 269 (12.5); nmr δ 1.10 (s, 9, Pom CH_3's), 2.17 (s, 3, *p*-CH_3), 2.50 (s, *o*-CH_3's superimposed on solvent), 6.38 (s, 3, 1 H exchanges with D_2O, Pom CH_2, and NH), 6.72 (s, 2, *m*-H's), 8.38 and 8.55 (ss, 2, purine H's); mass spectrum (70 eV), *m/e* (rel intensity), 264 (21, M − 200), 200 (26, M − 264), 179 (24), 150 (30), 135 (20), 57 (100).

Anal. Calcd for $C_{20}H_{28}N_6O_5S \cdot \frac{1}{2}H_2O$: C, 50.73; H, 6.17; N, 17.75. Found: C, 50.60; H, 5.99; N, 17.65.

Cleavage of the 7-Pom Group of 6. A solution of 120 mg of the *N*-amino-7-Pom-adeninium mesitylenesulfonate in methanol saturated with ammonia was allowed to stand at 25° for 6 hr. The solution was evaporated to dryness *in vacuo*, the residue was washed with ether, and the solid was collected by centrifugation. Recrystallization from methanol gave **2a** in chromatographic purity (tlc): yield, 66%; mp 243–244°, λ_{max} (H_2O) at pH 1 257, at pH 7 265, at pH 12 270; nmr δ 2.18 (s, 3, *p*-CH_3), 2.50 (s, *o*-CH_3's superimposed on solvent), 6.51 (s, 1, exchanged with D_2O, NH), 6.72 (s, 2, *m*-H's), 8.43 and 8.52 (ss, 2, purine H's); mass spectrum (70 eV), *m/e* (rel intensity), 200 (43, M − 150), 150 (65, M − 200), 135 (17), 118 (100); the ir spectrum was superimposable on that of the product of direct amination of adenine and on the spectrum of the 9-Pom (4) cleavage product.

***s*-Triazolo[5,1-*i*]purine (7).** Triethyl orthoformate (5 ml) was added to a suspension of **2a** (680 mg, 1.95 mmol) in 25 ml of dry dimethylformamide. The mixture was heated at reflux for 5 min, allowed to cool, and the volatile material was removed *in vacuo*. The resulting solid was suspended in methanol and filtered to afford **7**: 226 mg (95% yield); mp >300°; the uv spectra were identical with reported spectra;[16] λ_{max} (H_2O) at pH 1 261, 273, at pH 7 262 and 277, at pH 12 290; nmr δ 8.48 (s, 1), 8.60 (s, 1), 9.58 (s, 1); mass spectrum (70 eV) *m/e* (rel intensity), 160 (100, M). This compound is weakly fluorescent, showing an emission maximum of 349 nm upon excitation at 291 nm.

Registry No.—**2a**, 52500-49-9; **2b**, 52500-50-2; **4**, 52500-52-4; **6**, 52500-54-6; **7**, 4022-94-0; *O*-mesitylenesulfonylhydroxylamine, 36016-40-7; adenine, 73-24-5; 9-pivaloyloxymethyladenine, 18997-21-2; 7-pivaloyloxymethyladenine, 18997-22-3; triethyl orthoformate, 122-51-0.

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Synthesis of 2-Cyano, 2-Acyl, and 2-Carboxamido Derivatives of 3-Aminobenzo[*b*]thiophene Involving Nitro Displacement

James R. Beck* and Joseph A. Yahner

Lilly Research Laboratories, Greenfield, Indiana

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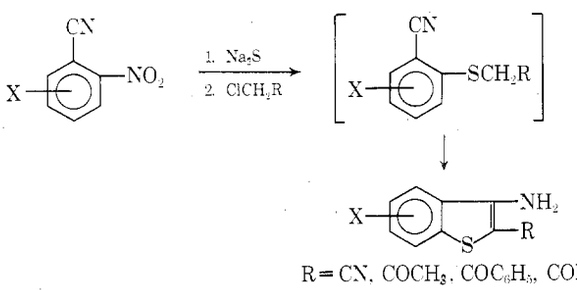
Until recently, 3-aminobenzo[*b*]thiophenes, substituted at the 2 position with cyano or acyl functions, were inaccessible. Clarke and coworkers[1] reported the synthesis of 3-aminobenzo[*b*]thiophene-2-carbonitrile by the reaction of *o*-mercaptobenzonitrile[2] with chloroacetonitrile in aqueous alkali. Similarly prepared were 3-aminobenzo[*b*]thien-2-yl methyl and phenyl ketones using chloroacetone and phenacyl chloride, respectively. The same authors[3] also described the preparation of the methyl ketone from 3-chloro-1,2-benzisothiazole[4] and pentane-2,4-dione in the presence of sodium ethoxide. A facile synthesis of N-substituted 3-aminobenzo[*b*]thien-2-yl ketones from 3-chloro-1,2-benzisothiazolium chlorides[5] and methyl ketones has been reported by Böshagen and Geiger.[6] In an earlier paper,[7] we described the preparation of methyl 3-aminobenzo[*b*]thiophene-2-carboxylate esters from *o*-nitrobenzonitriles and methyl thioglycolate in the presence of base. The reaction involved displacement of the activated nitro group by thioglycolate anion and subsequent base-catalyzed ring closure. Attempts to extend the scope of this procedure for the synthesis of the analogous 2-cyano and 2-acyl derivatives were frustrated by the instability or inaccessibility of the required mercaptan reagents.

We now wish to report two related processes, both involving nitro displacement, for the preparation of these compounds. In the first, an *o*-nitrobenzonitrile was allowed to react with sodium sulfide in aqueous DMF. The nitro group was readily displaced at ice bath temperature, and the anion of the corresponding *o*-mercaptobenzonitrile was formed (Scheme I). *In situ* alkylation with chloroacetonitrile, chloroacetone, or phenacyl chloride, with subsequent sulfide-catalyzed cyclization, yielded the corresponding 3-aminobenzo[*b*]thiophene-2-carbonitriles, 3-aminobenzo[*b*]thien-2-yl methyl ketones, or phenyl ketones, respectively. The procedure was also used as an alternate method of synthesis for 3-aminobenzo[*b*]thiophene-2-carboxamides[8] when chloroacetamide was utilized as the alkylating agent. The derivatives prepared and the yields obtained are summarized in Table I. When the starting nitrile was 2-chloro-5-nitrobenzonitrile, the 2-cyano (**10**) and 2-benzoyl (**11**) derivatives of 3-amino-5-nitrobenzo[*b*]thiophene were readily formed by a process involving active chlorine displacement.

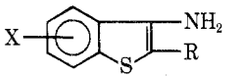
Scheme I



R = CN, $COCH_3$, COC_6H_5, $CONH_2$

When *o*-nitrobenzonitrile or 6-nitro-*o*-anisonitrile was subjected to the initial reaction conditions, sulfide displacement did not occur even at 100° during an extended

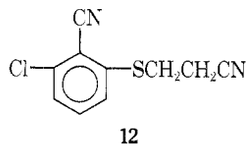
Table I
3-Aminobenzo[*b*]thiophenes[a]



Compd	X	R	Mp, °C	Yield, %	Crystn solvent[b]
1	4-Cl	CN	181–182	66	A
2	6-Cl	CN	215–216	75	A
3	4-NO_2	CN	177–179	84	A
4	4-Cl	$COCH_3$	101–103	68	B
5	4-NO_2	$COCH_3$	136–137	83	A
6	4-Cl	COC_6H_5	126–127	60	B
7	4-NO_2	COC_6H_5	139–141	60	A
8	4-Cl	$CONH_2$	225–227	69	A
9	4-NO_2	$CONH_2$	238–239	65	C
10	5-NO_2	CN	272–273	87	D
11	5-NO_2	COC_6H_5	205–207	90	C
13	H	CN	155–156[c]	70	A
14	H	$COCH_3$	147–149[d]	67	E
15	4-OCH_3	CN	173–176	50	D

[a] Satisfactory analytical data (±0.3% for C, H, N) were reported for all new compounds listed in the table. [b] A = alcohol; B = alcohol–water; C = acetonitrile; D = DMF–water; E = benzene–hexane. [c] Lit.[1] mp 155–156°. [d] Lit.[1] mp 145.5–147°.

period of time. In the second process, this problem was overcome with the use of 3-mercaptopropionitrile[9] anion. In this reaction sequence, the *o*-nitrobenzonitrile was allowed to react with the mercaptan anion in aqueous DMF containing excess potassium hydroxide. Displacement occurred rapidly at ice bath temperature, and an equilibrium mixture was formed involving the cyanoethyl thioether and the corresponding *o*-mercaptobenzonitrile anion. When the reaction was quenched soon after addition of the mercaptan, the cyanoethyl thioether could be isolated and characterized, as in the case of **12**. Addition of the alkylating



12

agent and subsequent ring closure yielded the desired product. Compounds prepared by this method were 3-aminobenzo[*b*]thiophene-2-carbonitrile (**13**), 3-aminobenzo[*b*]thien-2-yl methyl ketone (**14**), and 3-amino-4-methoxybenzo[*b*]thiophene-2-carbonitrile (**15**).

These two procedures provide a convenient, rapid route to 3-aminobenzo[*b*]thiophenes, substituted at the 2 position with cyano, acyl, or carboxamido functions, from readily available *o*-nitrobenzonitriles.

Experimental Section[10]

Materials. 2-Chloro-6-nitrobenzonitrile, 4-chloro-2-nitrobenzonitrile, 2-chloro-5-nitrobenzonitrile, and *o*-nitrobenzonitrile were commercially available. 2,6-Dinitrobenzonitrile[7] and 6-nitro-*o*-anisonitrile[11] were prepared by procedures described in the literature.

General Procedure for Aminobenzo[*b*]thiophenes (1–11). To a mechanically stirred, cold solution (ice bath) containing 30 mmol of the substituted *o*-nitrobenzonitrile in 100 ml of DMF was added dropwise a solution containing 36 mmol of sodium sulfide (nonahydrate) in 20 ml of water. The mixture was stirred in the cold for 15 min and the alkylating agent (3 ml of chloroacetonitrile for **1–3** and **10**; 3 ml of chloroacetone for **4** and **5**; 36 mmol of phenacyl chloride for **6, 7,** and **11**; 36 mmol of chloroacetamide for **8** and **9**) was added dropwise or portionwise. The ice bath was removed and the mixture was stirred for an additional time (30 min for **1–5** and **10**; 1 hr for **6–9** and **11**). It was poured into ice water and the crude product was collected and crystallized from the appropriate solvent (Table I).

2-Chloro-6-[(2-cyanoethyl)thio]benzonitrile (12). A solution of 3 g of potassium hydroxide in 15 ml of water was added dropwise to a stirred, cold solution (ice bath) containing 5.5 g (30 mmol) of 2-chloro-6-nitrobenzonitrile and 3.1 g (36 mmol) of 3-mercaptopropionitrile[9] in 60 ml of DMF. The mixture was stirred in the cold for 10 min and then poured into ice water. The solid was collected and crystallized from alcohol to yield 2.7 g (40%) of product, mp 96–97°.

General Procedure for Aminobenzo[*b*]thiophenes 13–15. To a stirred, cold solution (ice bath) containing 30 mmol of the substituted *o*-nitrobenzonitrile and 3.1 g (36 mmol) of 3-mercaptopropionitrile[9] in 60 ml of DMF was added dropwise a solution of 5 g of potassium hydroxide in 15 ml of water. The mixture was stirred in the cold for 15 min (30 min for preparation of **14**), and the alkylating agent (3 ml of chloroacetonitrile for **13** and **15**; 3.5 ml of chloroacetone for **14**) was added dropwise. After it had been stirred in the cold for an additional 2 hr, the mixture was poured into ice water. The crude product was collected and crystallized from the appropriate solvent (Table I).

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Registry No.—**1,** 52673-85-5; **2,** 52673-86-6; **3,** 52673-87-7; **4,** 52673-88-8; **5,** 52673-89-9; **6,** 52673-90-2; **7,** 52673-91-3; **8,** 52673-92-4; **9,** 52673-93-5; **10,** 52673-94-6; **11,** 52673-95-7; **12,** 52673-96-8; **13,** 34761-14-3; **14,** 22720-75-8; **15,** 52673-97-9; 2-chloro-6-nitrobenzonitrile, 6575-07-1; 4-chloro-2-nitrobenzonitrile, 34662-32-3; 2-chloro-5-nitrobenzonitrile, 16588-02-6; *o*-nitrobenzonitrile, 612-24-8; 2,6-dinitrobenzonitrile, 35213-00-4; 6-nitro-*o*-anisonitrile, 38469-85-1; sodium sulfide, 1313-82-2; chloroacetonitrile, 107-14-2; chloroacetone, 78-95-5; phenacyl chloride, 532-27-4; chloroacetamide, 79-07-2; 3-mercaptopropionitrile, 1001-58-7.

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A New Synthesis of $N^{\alpha},N^{G,G}$-Tribenzyloxycarbonyl-L-arginine and Related Derivatives

Edward L. Smithwick, Jr.,* and Robert T. Shuman

Eli Lilly & Company, Indianapolis, Indiana 46225

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Among the guanidino protected arginine derivatives[1] used in peptide synthesis, $N^{\alpha},N^{G,G}$-tribenzyloxycarbonylarginine (II)[2,3] has proven to be a useful intermediate for the addition of an arginine residue to the amino terminus of a synthetic peptide. The considerable difficulty with which II is prepared, however, has discouraged its use in peptide synthesis except in special cases, *e.g.,* the synthesis of L-arginyl-L-arginyl sequences.

We report herein a procedure for the preparation of II and closely related derivatives which is experimentally simple and which consistently provides product yields substantially greater than the procedure[2,3] heretofore used. The salient features of the procedure involve the use of an