Analogs of Propranolol. Synthesis of 3-Alkylamino-1-(3-benzo[*b*]thienyloxy)-2-propanols

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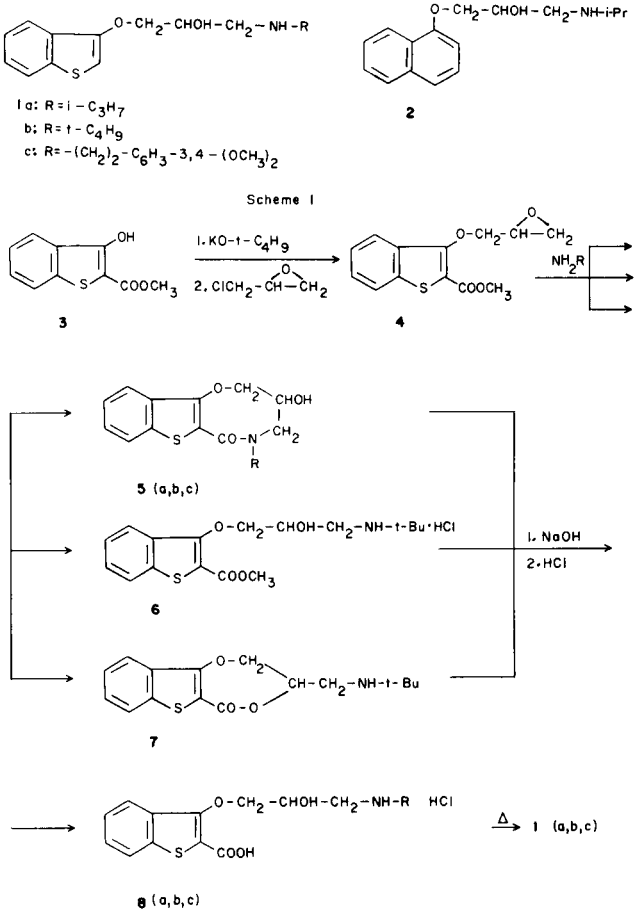
Received January 2, 1980

The synthesis by two alternative routes of 1-(3-benzo[*b*]thienyloxy)-3-isopropylamino-2-propanol hydrochloride (**1a** • HCl), a thiophenic isoster of Propranolol, and related compounds, is reported. The protecting and enolizing properties of the 2-methoxycarbonyl group on benzo[*b*]thiophene-3-one, along with its facile removal, are utilized in the first route. In the second one, conversion of 3-bromobenzo[*b*]thiophene in 1-(3-benzo[*b*]thienyloxy)-2,3-*o*-isopropylidenepropane is the key step. On the other hand, hydrolysis of 1-(3-benzo[*b*]furanyloxy)-2,3-*o*-isopropylidenepropane to the corresponding diol, in order to obtain a furanic isoster of Propranolol (**17a**), was unsuccessful.

J. Heterocyclic Chem., **17**, 937 (1980).

The synthesis of the thiophene isostere **1a** of the β-blocking, antihypertensive and antiarrythmic agent, propranolol **2**, has been claimed by Goldenberg, *et al.* (1). 3-Hydroxybenzo[*b*]thiophene (3-thioindoxyl), an unstable compound, which is extremely prone to air oxidation to thioindigo, was *O*-alkylated with epichlorohydrin. The crude product thus obtained in unreported yield was treated with isopropylamine to yield **1a** which was isolated as an oxalic acid salt in unreported yield.



In this paper, we wish to report two more suitable alternative methods for the synthesis of **1a** and related compounds **1b** and **1c**. Attempts to prepare the corresponding benzo[*b*]furan derivatives **17a,b,c** are also reported.

The first method of preparation (Scheme I) starts from methyl 3-hydroxybenzo[*b*]thiophene-2-carboxylate (**3**). This enol compound is easily available from methyl *o*-nitrobenzoate and ethyl thioglycolate (2) and is stable to air oxidation. It has already been successfully *O*-alkylated with various agents (3). The reaction of the potassium salt of **3**, prepared from potassium *t*-butoxide, with epichlorohydrin in DMSO, led to the epoxide **4** (61% yield). Compound **4** was then made to react with different amines at room temperature for several days. When volatile amines were used (isopropylamine or *t*-butylamine) the reaction was done without any added solvent and with a great excess of the amines. For the case of the high boiling homoveratrylamine, the reaction was carried in isopropyl alcohol and with equimolar amounts.

The reactions with isopropylamine and homoveratrylamine led to the lactamic neutral compounds **5a** (65% yield) and **5c** (62% yield), respectively, along with unidentified oily basic compounds. The reaction with *t*-butylamine afforded a mixture of the neutral lactam compound **5b** (26% yield), the basic lactone compound **7** (21% yield) and the amine compound **6** (48% yield). Structures **5, 6** and **7**, corresponding to one of the two possible regioisomers, have been assigned according to their spectroscopic data and are in agreement with previous reports (4).

Compounds **5a,b,c, 6** and **7** were hydrolyzed by hydroalcoholic sodium hydroxide to the corresponding derivatives **8a,b,c,** which were isolated in their hydrochloride form. The easy thermal decarboxylation found by von Auwers (5) in the case of 3-methoxybenzo[*b*]-thiophene-2-carboxylic acid, also took place in the case of compounds **8a,b,c**. These derivatives when heated *in vacuo* yielded the corresponding compounds **1a,b,c.**

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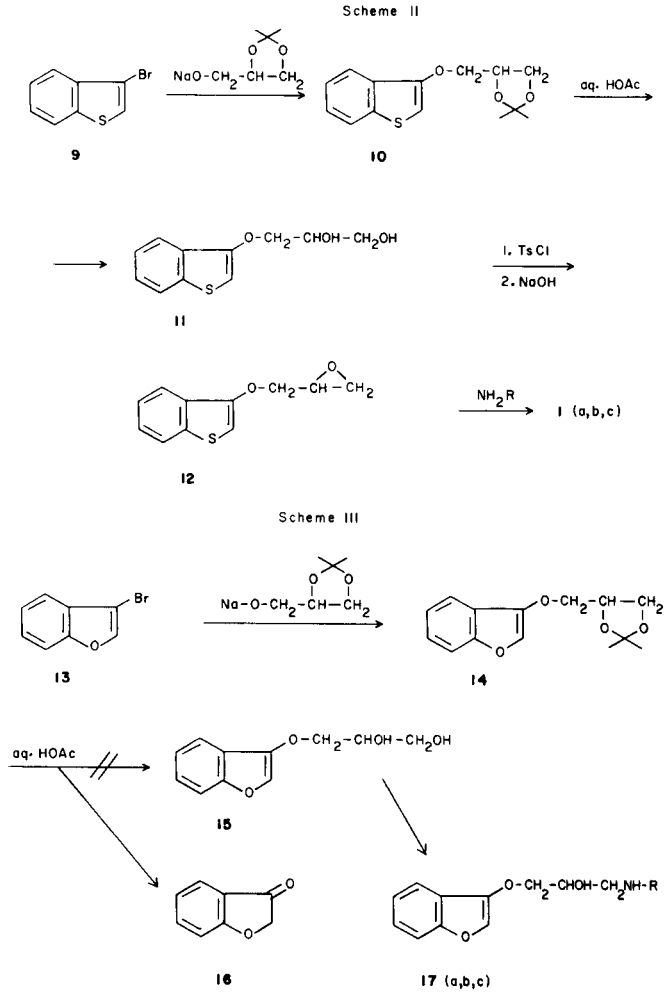

The second method proposed for the synthesis of compounds **1** (Scheme II) starts from commercial benzo[*b*]-thiophene, which is first transformed into its 3-bromo derivative **9**. The conversion of **9** into compound **10** takes into account the Sicé's method for the synthesis of 2- or 3-methoxythiophene from 2- or 3-bromothiophene respectively (6,7). Compound **9** when heated at 90° for 3 days with a solution of an excess of sodium in isopropylideneglycerol, in the presence of cupric oxide and catalytic amounts of potassium iodide afforded **10** (75% yield).

The route from compound **10** to compounds **1a,b,c** is based in the Danilewicz's procedure (8), for the synthesis of (*R*)-(+)-Practolol from *R*(-)-α-(4-acetamidophenyl)-acetone glycerol.

The Sicé's method was also applied to the synthesis of 1-(3-benzo[*b*]furanyloxy)-2,3-*o*-isopropylidenepropane (**14**) from 3-bromobenzo[*b*]furan, in order to obtain compounds **17a,b,c** (Scheme III). Compound **14** was obtained in 70% yield. However, the hydrolysis of **14** led to 3-coumaronone (**16**) and not to the desired diol **15**. Attempts in other weaker acidic conditions (40%, 20%, 5% acetic acid solutions, boric acid) at different temperatures were also unsuccessful, leading always to 3-coumaronone.

EXPERIMENTAL

Melting points were determined on a Gallemkamp capillary apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 257 spectrometer. Proton nuclear magnetic resonance spectra were recorded on a Perkin-Elmer R-12 60MHz spectrometer with TMS as internal reference.

Methyl 3-hydroxybenzo[*b*]thiophene-2-carboxylate (**3**) (2), 3-bromobenzo[*b*]thiophene (**9**) (9) and 3-bromobenzo[*b*]furan (**13**) (10) were obtained according to the literature.

2,3-Epoxy-1-(3-(2-methoxycarbonyl)benzo[*b*]thiophene)propane (**4**).

To a well stirred solution of compound **3** (31.2 g., 0.15 mole) and potassium *t*-butoxide (20.2 g., 0.18 mole) in 250 ml. of DMSO, epichlorohydrin (33.3 g., 28 ml., 0.36 mole) were added dropwise. The mixture was heated at 75° for 24 hours and after cooling to room temperature, the solvent was evaporated at reduced pressure (0.1 mm) and the residual oil was thoroughly extracted with boiling *n*-hexane. The hexane extracts were concentrated to yield 24.1 g. (61%) of compound **4**, as a colorless solid, m.p. 63-64° (*n*-hexane); ir (nujol): ν 1710 (C=O); nmr (deuteriochloroform): δ 2.7-3.0 (d, 2H, CH_2 epoxy), 3.3-3.6 (q, 1H, CH), 3.95 (s, 3H, CH_3), 4.2-4.8 (d, 2H, $-CH_2-O-$), 7.3-8.2 (m, 4H, aromatic protons).

Anal. Calcd. for $C_{13}H_{12}O_4S$: C, 59.08; H, 4.57; S, 12.12. Found: C, 58.92; H, 4.66; S, 12.03.

Reaction of Compound **4** with Secondary Amines.

1. Reaction with Isopropylamine.

A great excess of isopropylamine was added to compound **4** (7.9 g., 0.03 mole). The reaction mixture was left for 4 days at room temperature and then evaporated to dryness. The residue was dissolved in diethyl ether and 4.8 g. of compound **5a** crystallized as a colorless solid, m.p. 183-184°. The ethereal phase was washed with a 1*N* hydrochloric acid solution, dried with sodium sulfate and concentrated to yield an additional crop of 0.9 g. of compound **5a**, overall yield 65%. The analytical sample was obtained by recrystallization from toluene, m.p. 184-185°; ir (nujol): ν 3330 (-OH), 1580 (C=O); nmr (deuteriochloroform): δ 1.1-1.4 (d, 6H, CH_3), 2.9-3.4 (bs, 1H, OH), 3.5-3.8 (d, 2H, $-CH_2-N$), 3.8-4.3 (m, 1H, $-CH-(CH_3)_2$), 4.3-5.0 (m, 3H, $-O-CH_2-CH-OH$), 7.3-8.0 (m, 4H, aromatic protons).

Anal. Calcd. for $C_{15}H_{17}NO_3S$: C, 61.89; H, 5.84; N, 4.81. Found: C, 61.67; H, 5.95; N, 4.71.

2. Reaction with *t*-Butylamine.

A great excess of *t*-butylamine was added to compound **4** (3.0 g., 0.011 mole). The reaction mixture was left for 15 days at room temperature and 0.7 g. (21%) of compound **7** crystallized from the solution as a colorless solid, m.p. 119-121° (methanol); ir (nujol): ν 3320 (-NH), 1670 (C=O); nmr (deuteriochloroform): δ 1.15 (s, 9H, CH_3), 3.0-3.1 (d, 2H, $-CH_2-NH$), 4.4-4.9 (m, 3H, $-O-CH_2-CH-OH$), 5.5-6.5 (1H, NH), 7.4-8.0 (m, 4H, aromatic protons).

Anal. Calcd. for $C_{16}H_{19}NO_3S$: C, 62.93; H, 6.27; N, 4.58. Found: C, 63.22; H, 6.44; N, 4.64.

The filtrate was evaporated under reduced pressure and the residue was dissolved in anhydrous diethyl ether and treated with an hydrogen chloride solution in anhydrous diethyl ether to afford 2.0 g. (48%) of compound **6** as a colorless solid, m.p. 252-254° dec. (methanol); ir (nujol): ν 3360, 3430 (OH, NH), 1660 (C=O); nmr (DMSO-d_6): δ 1.4 (s, 9H, CH_3), 3.95 (s, 3H, $COOCH_3$), 4.6-5.1 (m, 3H, $-O-CH_2-CH-OH$) 5.5-6.5 (1H, NH), 7.4-8.1 (m, 4H, aromatic protons).

Anal. Calcd. for $C_{17}H_{24}ClNO_4S$: C, 54.63; H, 6.42; N, 3.74. Found: C, 54.60; H, 6.18; N, 3.54.

The ethereal extract was concentrated to yield 0.9 g. (26%) of compound **5b** as a colorless solid, m.p. 156-157° (benzene); ir (nujol): ν 3380

(-OH), 1590 (C=O); nmr (deuteriochloroform): δ 1.6 (s, 9H, CH_3), 2.5-2.8 (bs, 1H, OH), 3.7-3.9 (d, 2H, -CH_2-N), 4.1-4.7 (m, 3H, -O-CH_2-CH-OH), 7.4-8.0 (m, 4H, aromatic protons).

Anal. Calcd. for $C_{16}H_{19}NO_3S$: C, 62.93; H, 6.27; N, 4.58. Found: C, 63.07; H, 6.29; N, 4.79.

3. Reaction with 3,4-Dimethoxyphenylethylamine.

3,4-Dimethoxyphenylethylamine (1.8 g., 0.01 mole) was added to a solution of compound **4** (2.64 g., 0.01 mole) in isopropyl alcohol. The reaction mixture was left for 4 days at room temperature and then evaporated to dryness. The residue was dissolved in diethyl ether and 2.3 g. of compound **5c** crystallized out as a colorless solid, m.p. 182-183°. The ethereal phase was washed with a 1*N* hydrochloric acid solution, dried with sodium sulfate and concentrated to yield an additional crop of 0.3 g. of compound **5c**, overall yield 62%. The analytical sample was obtained by recrystallization from ethanol, m.p. 184-185°; ir (nujol): ν 3400 (OH), 1590 (C=O); nmr (deuteriochloroform): δ 2.3-2.7 (bs, 1H, OH), 2.9-3.7 (m, 6H, -CH_2-N-CH_2-CH_2), 3.9 (s, 6H, OCH_3), 4.4-4.7 (m, 3H, -O-CH_2-CH-OH), 6.9 (m, 3H, benzenic protons), 7.4-7.8 (m, 4H, thiophenic protons).

Anal. Calcd. for $C_{22}H_{23}NO_5S$: C, 63.91; H, 5.60; N, 3.38. Found: C, 64.02; H, 5.69; N, 3.61.

3-Alkylamino-1-(3-(2-carboxy)benzo[*b*]thienyloxy)-2-propanol Hydrochlorides (**8**).

1. Hydrolysis of Compounds **5a,b,c** and **7**.

To a stirred solution of the compound **5a, 5b, 5c** or **7** (0.023 mole) in 135 ml. of ethanol, 27 ml. of a 20% aqueous solution of sodium hydroxide were added. The reaction mixture was heated under reflux for 3 hours for compounds **5a, 5b** and **7** and for 24 hours for compound **5c**. The solvent was evaporated *in vacuo*, the residue was dissolved in water and the filtered aqueous solution was treated with a 1*N* hydrochloric acid solution until slightly acid *p*H. The solution was evaporated under reduced pressure without heating to dryness and the residue was treated with absolute ethanol. The remaining insoluble inorganic salts formed in the reaction were filtered. Anhydrous diethyl ether was added to the ethanolic filtrate and the desired compound **8 (a,b,c)** was crystallized.

2. Hydrolysis of Compound **6**.

The hydrolysis procedure was the same as above, except for the use of a double amount of sodium hyroxide. Refluxing time was 3 hours. The following compounds were obtained according to these procedures.

1-(3-(2-Carboxy)benzo[*b*]thienyloxy)-3-isopropylamino-2-propanol Hydrochloride (**8a**).

This compound was obtained as a colorless solid in 50% yield, m.p. 151-152° (ethanol-diethyl ether); ir (nujol): ν 3320 (OH), 1660 (C=O); nmr (deuterium oxide): δ 1.5-1.7 (d, 6H, CH_3), 3.3-4.0 (m, 3H, -CH_2-NH-CH), 4.3-4.7 (m, 3H, -O-CH_2-CH-OH), 7.4-8.0 (m, 4H, aromatic protons); nmr (DMSO-d_6): δ 1.2-1.4 (d, 6H, CH_3), 4.3-4.5 (m, 3H, -O-CH_2-CH-OH), 5.5-6.5 (1H, NH), 7.4-8.3 (m, 4H, aromatic protons), 8.5-9.4 (bs, 1H, COOH), nmr (pyridine): δ 1.5-1.6 (d, 6H, CH_3), 3.5-3.6 (bs, 1H, OH), 3.7-3.9 (m, 3H, CH_2-NH-CH), 4.8-4.9 (m, 3H, -O-CH_2-CH-OH).

Anal. Calcd. for $C_{15}H_{20}ClNO_4S$: C, 52.11; H, 5.79; N, 4.05. Found: C, 51.99; H, 5.88; N, 3.98.

1-[3-(2-Carboxy)benzo[*b*]thienyloxy]-3-*t*-butylamino-2-propanol Hydrochloride (**8b**).

This compound was obtained as a colorless solid in 55% yield from compounds **7** and **5b** and 65% yield from compound **6** m.p. 154-155° (ethanol-diethyl ether); ir (nujol): ν 3310 (OH), 1665 (C=O); nmr (deuterium oxide): δ 1.6 (s, 9H, CH_3), 3.4-3.8 (s, 2H, CH_2-NH), 4.3-4.6 (m, 3H, -O-CH_2-CH-OH), 7.4-8.0 (m, 4H, aromatic protons); nmr (DMSO-d_6): δ 1.4 (s, 9H, CH_3), 4.3-4.6 (m, 3H, -O-CH_2-CH-OH), 5.4-6.4 (1H, NH), 7.4-8.0 (m, 4H, aromatic protons); nmr (pyridine): δ 1.6 (s, 9H, CH_3), 3.1-3.3 (bs, 1H, OH), 3.5-3.8 (s, 2H, CH_2-NH), 4.7-4.8 (m, 3H, -O-CH_2-CH-OH).

Anal. Calcd. for $C_{16}H_{22}ClNO_4S$: C, 53.41; H, 6.12; N, 3.89. Found: C, 53.28; H, 6.17; N, 3.93.

1-[3-(2-Carboxy)benzo[*b*]thienyloxy]-3-(3,4-dimethoxyphenylethylamino)-2-propanol Hydrochloride (**8c**).

This compound was obtained as a colorless solid in 60% yield, m.p. 156-157° (ethanol-diethyl ether); ir (nujol): ν 3320 (OH), 1670 (C=O); nmr (deuterium oxide): δ 3.1-3.5 (m, 6H, CH_2-NH-CH_2-CH_2), 3.9 (s, 6H, OCH_3), 4.3-4.7 (m, 3H, -O-CH_2-CH-OH), 6.9 (m, 3H, benzene protons), 7.4-8.0 (m, 4H, benzothiophene protons); nmr (DMSO-d_6): δ 3.9 (s, 6H, OCH_3), 4.3-4.7 (m, 3H, -O-CH_2-CH-OH), 5.4-6.4 (1H, NH), 6.9 (m, 3H, benzene protons), 7.4-8.0 (m, 4H, benzothiophene protons), 8.5-9.4 (bs, 1H, COOH); nmr (pyridine): δ 2.8-3.0 (bs, 1H, OH), 3.2-3.5 (m, 6H, -CH_2-NH-CH_2-CH_2), 3.9 (s, 6H, OCH_3), 4.7-4.8 (m, 3H, -O-CH_2-CH-OH).

Anal. Calcd. for $C_{21}H_{26}ClNO_6S$: C, 56.47; H, 5.56; N, 2.99. Found: C, 56.39; H, 5.48; N, 3.07.

3-Alkylamino-1-(3-benzo[*b*]thienyloxy)-2-propanol Hydrochlorides (**1a,b,c**·HCl) from Compounds **8a,b,c**.

Compounds **8a,b,c** when heated at 30° above the melting point for 30 minutes at reduced pressure (0.1 mm) afforded oils that were purified by recrystallization from ethanol-diethyl ether. The following compounds were obtained according to this procedure:

1-(3-Benzo[*b*]thienyloxy)-3-isopropylamino-2-propanol Hydrochloride (**1a**·HCl).

This compound was obtained as a colorless solid in 65% yield, m.p. 173-174°; ir (nujol): ν 3300, 3220 (-OH; NH); nmr (DMSO-d_6): δ 1.2-1.4 (d, 6H, CH_3), 4.2-4.4 (m, 3H, -O-CH_2-CH-OH), 5.8-6.2 (1H, NH), 6.8 (s, 1H, thiophene proton), 7.5-8.1 (m, 4H, benzene protons).

Anal. Calcd. for $C_{14}H_{20}ClNO_2S$: C, 55.72; H, 6.63; N, 4.64. Found: C, 55.57; H, 6.58; N, 4.61.

1-(3-Benzo[*b*]thienyloxy)-3-*t*-butylamino-2-propanol Hydrochloride (**1b**·HCl).

This compound was obtained as a colorless solid in 69% yield; m.p. 159-160°; ir (nujol): ν 3300, 3210 (OH, NH); nmr (DMSO-d_6): δ 1.4 (s, 9H, CH_3), 4.2-4.5 (m, 3H, -O-CH_2-CH-OH), 5.7-6.7 (1H, NH), 6.95 (s, 1H, thiophene proton), 7.4-8.1 (m, 4H, benzene protons); nmr (deuterium oxide): δ 1.65 (s, 9H, CH_3), 3.4-3.7 (m, 2H, -CH_2-NH), 4.3-4.6 (m 3H, -O-CH_2-CH-OH), 6.8 (s, 1H, thiophene proton), 7.5-8.1 (m, 4H, benzene protons).

Anal. Calcd. for $C_{15}H_{22}ClNO_2S$: C, 57.07; H, 6.97; N, 4.43. Found: C, 57.01; H, 6.83; N, 4.38.

1-(3-Benzo[*b*]thienyloxy)-3-(3,4-dimethoxyphenylethylamino-2-propanol Hydrochloride (**1c**·HCl).

This compound was obtained as a colorless solid in 63% yield, m.p. 187-189°; ir (nujol): ν 3310, 3220 (OH, NH); nmr (DMSO-d_6): δ 3.75-3.85 (s, 6H, OCH_3), 4.1-4.5 (m, 3H, -O-CH_2-CH-OH), 5.7-6.2 (1H, NH), 6.95 (m, 4H, 3 benzene and 1 thiophene protons), 7.4-8.1 (m, 4H, benzene protons); nmr (deuterium oxide): δ 3.2-3.6 (m, 6H, -CH_2-NH-CH_2-CH_2), 3.85-3.9 (s, 6H, OCH_3), 4.2-4.5 (m, 3H, -O-CH_2-CH-OH), 6.95 (m, 4H, 3 benzene and 1 thiophene protons), 7.4-8.1 (m, 4H, benzene protons).

Anal. Calcd. for $C_{21}H_{26}ClNO_4S$: C, 59.51; H, 6.14; N, 3.30. Found: C, 59.47; H, 6.43; N, 3.28.

1-(3-Benzo[*b*]thienyloxy)-2,3-*o*-isopropylidene propane (**10**).

Sodium (6.2 g., 0.27 mole) was added to 139 ml. (1.13 moles) of isopropylideneglycerol in order to obtain the sodium salt, whereupon 3-bromobenzo[*b*]thiophene (**9**) (9) (21.3 g., 0.1 mole), potassium iodide (0.09 g., 0.00054 mole) and cupric oxide (4.0 g., 0.05 mole) were added. The reaction mixture was heated at 90° for 3 days, cooled at room temperature and the salts so formed were filtered off. The filtrate was distilled to yield, after a forerun of isopropylideneglycerol (80-81° at 11 mm), a main fraction of 24.8 g (75%) of compound **10**; b.p. 172° (0.1 mm), that was crystallized from methanol, m.p. 63-64°; nmr (deuteriochloroform): δ 1.45-1.55 (s, 6H, CH_3), 3.9-4.7 (m, 5H, -O-CH_2-CH-CH_2); 6.4 (s, 1H, thiophene proton), 7.4-8.0 (m, 4H, benzene protons).

Anal. Calcd. for $C_{14}H_{16}O_3S$: C, 63.62; H, 6.10; S, 12.10. Found: C, 63.69; H, 5.96; S, 12.23.

(3-Benzo[*b*]thienyl)glycerol (**11**).

A solution of compound **10** (11 g., 0.04 mole) and 50 ml. of an 80% acetic acid solution was heated at 60-70° for 45 minutes and the solvent was evaporated *in vacuo*. The residue was recrystallized from benzene yielding 7.2 g. (77%) of compound **11** as a colorless solid, m.p. 86-87°; ir (nujol): ν 3500-3000 (broad OH); nmr (deuteriochloroform): δ 1.6-1.8 (bs, 1H, OH, -CH_2OH), 2.6-2.8 (bs, 1H, OH, -CH-OH), 3.8-4.2 (m, 5H, -O-CH_2-CH(OH)-CH_2-OH), 6.45 (s, 1H, thiophene proton), 7.4-8.0 (m, 4H, benzene protons).

Anal. Calcd. for $C_{10}H_{12}O_3S$: C, 56.34; H, 5.71; S, 14.28. Found: C, 56.59; H, 5.70; S, 14.32.

1-(3-Benzo[*b*]thienyloxy)-2,3-epoxypropane (**12**).

p-Toluenesulfonyl chloride (3.8 g., 0.02 mole) was added at −10° to a stirred solution of compound **11** (4.5 g., 0.02 mole) in 45 ml. of anhydrous pyridine. The reaction mixture was left for 24 hours in the refrigerator and then a solution of 17.5 ml. of sulphuric acid in 100 ml. of water was added cooling with an ice-bath. The organic layer was separated and the aqueous layer was extracted with ethyl acetate (2 × 50 ml.). The organic extracts were dried and evaporated *in vacuo* to afford the monotosyl derivative as an oil that was not purified.

The crude product was dissolved in 15.2 ml. of anhydrous DMSO and 7.6 ml. of a 20% aqueous solution of sodium hydroxide were added. The reaction mixture was stirred for 10 minutes, whereupon 33 ml. of water were added. The resulting solution was extracted with ethyl acetate (3 × 50 ml.) and the organic extracts were dried and evaporated to dryness to yield 3.7 g. (90%) of compound **12** as an oil that was not purified.

3-Alkylamino-1-(3-benzo[*b*]thienyloxy)-2-propanol Hydrochlorides (**1a,b,c**·HCl) from Compound **12**.

Synthesis of **1a** and **1b**.

A great excess of amine (isopropylamine or *t*-butylamine) was added to compound **12** (0.01 mole). The reaction mixture was left for 3 days at room temperature and then evaporated to dryness. The residue was dissolved in diethyl ether and the solution was treated with an excess of a solution of hydrogen chloride in dry diethyl ether to furnish **1a** hydrochloride (2.0 g., 67%), m.p. 173-174° (ethanol-diethyl ether) and **1b** hydrochloride (2.0 g., 65%), m.p. 159-160° (ethanol-diethyl ether), respectively, identical in all respects with the compounds previously obtained.

Synthesis of **1c**.

3,4-Dimethoxyphenylethylamine (0.01 mole) was added to a solution of 0.01 mole of compound **12** in isopropyl alcohol. The reaction mixture was left for 3 days at room temperature and then evaporated to dryness. The residue was dissolved in diethyl ether and the solution was treated with an excess of diethyl ether saturated of hydrogen chloride to yield **1c** hydrochloride (2.7 g., 65%), m.p. 187-189° (ethanol-diethyl ether), identical in all respects with **1c** hydrochloride previously obtained.

1-(3-(Benzo[*b*]furanyloxy)-2,3-*o*-isopropylidenepropane (**14**).

The procedure described above for obtaining compound **10** was used for the synthesis of compound **14** from 3-bromobenzo[*b*]furane (10). This compound was obtained in 70% yield and had b.p. 115°C (0.01 mm), m.p. 64-64.5° (ethanol); nmr (deuteriochloroform): δ 1.45-1.5 (s, 6H, CH_3), 3.9-4.8 (m, 5H, -O-CH_2-CH-CH_2); 7.3-7.8 (m, 5H, aromatic protons).

Anal. Calcd. for $C_{14}H_{16}O_4$: C, 67.72; H, 6.49. Found: C, 67.85; H, 6.53.

Hydrolysis of Compound **14**.

A mixture of compound **14** (9.9 g., 0.04 mole) and 48 ml. of an 80% acetic acid solution was heated at 60-70° for 30 minutes and the solvent was evaporated *in vacuo*. The residue was recrystallized from benzene to yield 4.4 g. (83%) of 3-coumaronone **17**, m.p. 100-101°.

Acknowledgment.

We are indebted to M. J. Morcillo for her aid in a part of this work, to Dr. Madroñero for his encouragement and advice, and to our Department of Analyses and Instrumental Techniques for all the analytical and spectral data.

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