Thienyl Analogues of the Alkaloids. Part II.[1] 3-Thienyl Analogues of Ephedrine and ψ-Ephedrine

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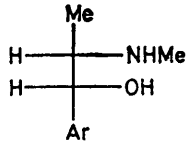
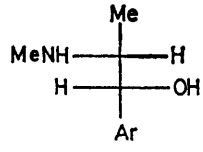
The synthesis, from 3-propionylthiophen, of the 3-thienyl analogues of ephedrine and ψ-ephedrine, and the resolution of the latter are described. An account is also given of alternative approaches to these isosteres from 2,5-dichloro- and 2,5-dibromo-3-propionylthiophen.

In an extension of our previous work [1] on the 2-thienyl analogues of the ephedrines we now report the synthesis of the corresponding 3-thienyl compounds. 3-Propionylthiophen was prepared from 3-bromothiophen by an adaptation of the method of MacDowell and Greenwood;[2] a crystalline by-product of the reaction of 3-bromothiophen with copper(I) cyanide in quinoline was identified as 2,4,6-tri-(3-thienyl)-1,3,5-triazine. Side-chain bromination of 3-propionylthiophen and reaction of the resulting α-bromoketone with methylamine in ether afforded the unstable α-methylaminoketone, which was reduced immediately with sodium borohydride. The mixture of diastereoisomers (Ia) and (IIa) so obtained was separated by treatment with picric acid in ether, the *erythro*-isomer (Ia) forming an ether-insoluble picrate.



(I)



(II)

Ar = 2,5-di-X-3-thienyl

a; X=H
b; X=Cl
c; X=Br

Configurational assignments were made on the basis of the n.m.r. spectra, the smaller vicinal coupling constant

[1] J. M. Barker, D. J. Byron, and P. R. Huddleston, *J. Chem. Soc.* (*C*), 1969, 2183.

[2] D. W. H. MacDowell and T. D. Greenwood, *J. Heterocyclic Chem.*, 1965, **2**, 44.

and lower chemical shift of ArC*H* being associated with the *erythro*-isomer in both ephedrine [3] and the 2-thienyl analogue [1] (see Table).

Chemical shift and coupling constant of ArC*H*

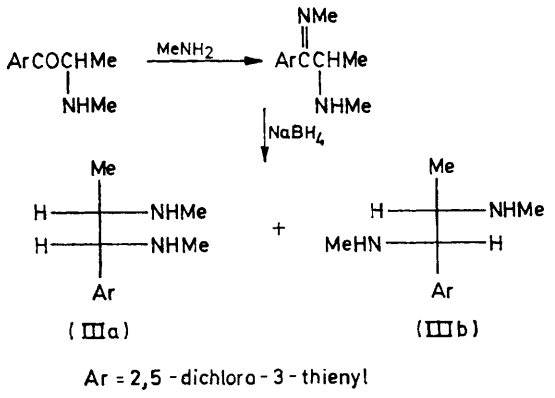
	threo		*erythro*	
	τ	*J*/Hz	τ	*J*/Hz
Ephedrine [3]			5·24	4·0
ψ-Ephedrine [3]	5·81	8·3		
2-Thienyl analogues [1]	5·49	7·7	5·07	4·3
3-Thienyl analogues	5·64	7·5	5·35	4·3
2,5-Dichloro-3-thienyl analogues	5·57	9·0	5·16	3·8
2,5-Dibromo-3-thienyl analogues	5·40	8·4	5·00	3·8

threo-2-Methylamino-1-(3-thienyl)propan-1-ol (IIa) was resolved through its salts with (+)- and with (−)-tartaric acid, but attempts to resolve the *erythro*-isomer (Ia) with tartaric, di-*p*-toluoyltartaric, mandelic, or camphorsulphonic acid failed.

In view of the relative inaccessibility of 3-propionylthiophen we explored the possibility of synthesising the alkaloid analogue from 2,5-dichloro-3-propionylthiophen, by the reaction sequence described above, with removal of the blocking halogen atoms at the last stage. The mixture of diastereoisomers (Ib) and (IIb) could not be separated satisfactorily by the picrate method, but pure (±)-*erythro*-1-(2,5-dichloro-3-thienyl)-2-methylaminopropan-1-ol (Ib) was isolated through its copper complex (prepared after the method of ref. 4). However, the *threo*-isomer (IIb) could not be obtained although its presence in the crude reduction product was demonstrated by n.m.r. spectroscopy. Also isolated from the reaction mixture was (±)-*erythro*-1-(2,5-dichloro-3-thienyl)-1,2-bismethylaminopropane (IIIa), identified through its n.m.r. spectrum (by analogy with the ephedrines) and analysis of the picrate; although n.m.r. spectroscopy showed the *threo*-diamine (IIIb) to be present also we were unable to isolate it. Presumably these diamines arise through reduction of the Schiff's base formed between methylamine and the α-methylaminoketone.

No dehalogenation of (Ib) took place with zinc–acetic acid; [5] sodium bis-2-methoxyethoxyaluminium hydride [6] and sodium amalgam–ethanol [7] both achieved some reduction but led to intractable mixtures.

Because of the unsatisfactory results in the 2,5-dichloro-series we investigated the corresponding 2,5-dibromo-3-thienyl compounds. Reaction of 2,5-dibromothiophen with propionyl chloride gave the desired starting material, 2,5-dibromo-3-propionylthiophen, together with 5-bromo-2-propionylthiophen and tetrabromothiophen. Electrophilic displacement is common in polybromothiophens [8] and we were unable to find reaction conditions that gave consistently high yields of 2,5-dibromo-3-propionylthiophen. As in the dichloro-series, we were only able to obtain the (±)-*erythro*-base (Ic) pure from the mixture of diastereoisomers (Ic) and (IIc) and again zinc–acetic acid [9] failed to give satisfactory dehalogenation.



The relative proportions of the diastereoisomers in the crude borohydride reduction product in each of the three reaction sequences described was determined approximately by n.m.r. spectroscopy. The results [(Ia) : (IIa) 3 : 1; (Ib) : (IIb) 2 : 1; (Ic) : (IIc) 3 : 2] indicate that the reduction proceeds according to the hydrogen bonded model of Cram's rule.[10] It is of interest to note that the diastereoisomer ratio of the diamines [(IIIa) : (IIIb) 2 : 1] implies that reduction of the Schiff's base is also governed by the same stereochemical considerations.

EXPERIMENTAL

M.p.s are uncorrected. I.r. spectra were determined on a Perkin-Elmer 337 spectrometer, and n.m.r. spectra on a JEOL JNM–C–60HL 60 MHz instrument (internal standard tetramethylsilane). Light petroleum refers to the fraction b.p. 40—60° unless otherwise stated.

3-Cyanothiophen [2] had b.p. 79—80° at 15 mmHg, $\nu_{max.}$ (film) 2235 cm^{-1}; the solid residue from distillation was crystallised from ethanol to give fine needles of 2,4,6-*tri*-(3-*thienyl*)-1,3,5-*triazine*, m.p. 163—164° (Found: C, 54·7; H, 2·9; N, 12·7. $C_{15}H_9N_3S_3$ requires C, 55·0; H, 2·7; N, 12·8%), τ ($CDCl_3$) 1·48 (m), 2·00 (m), and 2·69 (m), $\nu_{max.}$ (KBr) 1520, 1435, 1320 (*s*-triazine bands [11]), and 840 cm^{-1} (C–C inter-ring stretching [12]). Pure triazine (1·5 g) was obtained in a preparation yielding 3-cyanothiophen (61 g).

Reaction of 3-cyanothiophen with ethylmagnesium bromide (*cf.* ref. 2) afforded 3-propionylthiophen,[13] b.p. 98—100° at 15 mmHg.

3-(α-*Bromopropionyl*)*thiophen*.[14]—To a stirred solution

[3] J. B. Hyne, *Canad. J. Chem.*, 1961, **39**, 2536; G. G. Lyle and L. K. Keefer, *J. Org. Chem.*, 1966, **31**, 3921.
[4] Z. Földi, T. Földi, and A. Földi, *Chem. and Ind.*, 1955, 1297; *Acta Chim. Acad. Sci. Hung.*, 1957, **11**, 339.
[5] *E.g.* D. W. H. MacDowell, T. B. Patrick, B. K. Frame, and D. L. Gleison, *J. Org. Chem.*, 1967, **32**, 1226.
[6] M. Capka and V. Chvalovsky, *Coll. Czech. Chem. Comm.*, 1969, **34**, 2782.
[7] *E.g.* E. Profft and H. Mitternacht, *J. prakt. Chem.*, 1962, **16**, 13.
[8] *E.g.* L. Gattermann and M. Romer, *Ber.*, 1886, **19**, 688.
[9] *E.g.* S. Gronowitz, *Acta Chem. Scand.*, 1959, **13**, 1045.
[10] S. Yamada and K. Koga, 'Selective Organic Transformations,' ed. B. S. Thyagarajan, Wiley-Interscience, New York and London, vol. 1, 1970.
[11] H. Schroeder, *J. Amer. Chem. Soc.*, 1959, **81**, 5658.
[12] R. D. Spencer, *Spectrochim. Acta*, 1965, **21**, 1543.
[13] E. Campaigne and H. L. Thomas, *J. Amer. Chem. Soc.*, 1955, **77**, 5365.
[14] Since this work was carried out this compound has been described in a patent, A. L. A. Pons, *et al.*, G.P. 2,042,504/1971 (*Chem. Abs.*, 1971, **74**, 125,485w).

of 3-propionylthiophen (21·1 g) in dichloromethane (250 ml), bromine (25·6 g) in dichloromethane (20 ml) was added dropwise at room temperature. After a further 30 min the solution was washed with water, sodium hydrogen sulphite solution, water, then dried ($MgSO_4$), and evaporated. Distillation gave 3-(*α-bromopropionyl*)*thiophen* (29·8 g, 90%) as an oil, b.p. 139—141° at 15 mmHg (Found: C, 39·0; H, 3·0. C_7H_7BrOS requires C, 38·4; H, 3·2%), τ (CCl_4) 8·18 (d, *J* 6·5 Hz, $CHCH_3$), 4·95 (q, *J* 6·5 Hz, $CHCH_3$), and 1·73—2·80 (m, Ar), $\nu_{max.}$ (film) 1685 cm^{-1}.

(±)-erythro- *and* threo-2-*Methylamino*-1-(3-*thienyl*)*propan*-1-*ol* (Ia) *and* (IIa).—A solution of 3-(α-bromopropionyl)-thiophen (29 g) in ether (100 ml) was mixed with methylamine (10 g) in ether (500 ml) and the whole was set aside for 2 days. The suspension was washed with aqueous ammonia (*d* 0·88), dried ($MgSO_4$), and evaporated to give a dark oil (22 g) which was dissolved in methanol (150 ml) and reduced immediately with sodium borohydride (6 g) and 4M-sodium hydroxide (6 ml). After 3 h the solvent was removed under reduced pressure and the residue was suspended in water and extracted several times with ether. The combined organic solutions were exhaustively extracted with 2M-hydrochloric acid, the acid solution was basified with sodium hydroxide solution, saturated with sodium chloride, and the basic material was isolated with ether. Distillation gave a pale-yellow oil (11 g), b.p. 139—142° at 15 mmHg, which partially crystallised on standing. The distillate (4·4 g) was added to a saturated solution of picric acid (4·4 g) in ether; after several days the *picrate* of (±)-erythro-2-*methylamino*-1-(3-*thienyl*)*propan*-1-*ol* (5·8 g) was collected. An analytical sample formed yellow granules (from water), m.p. 168—170° (Found: C, 41·9; H, 4·0; N, 13·7. $C_{14}H_{16}N_4O_8S$ requires C, 42·0; H, 4·0; N, 14·0%). The picrate (5·5 g) was shaken with saturated aqueous lithium hydroxide and the solution was extracted with ether (2 × 100 ml). Evaporation of the washed and dried ($MgSO_4$) ethereal solution left an oily solid (2·7 g) which was crystallised repeatedly from light petroleum to afford (±)-erythro-2-*methylamino*-1-(3-*thienyl*)*propan*-1-*ol* (Ia) (1·1 g), m.p. 66—68° (Found: C, 56·1; H, 7·5; N, 7·9. $C_8H_{13}NOS$ requires C, 56·2; H, 7·6; N, 8·2%), τ [$(CD_3)_2SO$] 9·17 (d, *J* 6·5 Hz, $CHCH_3$), 7·70 (s, $NHCH_3$), 7·12—7·68 (m, $CHCH_3$), 5·33 (d, *J* 4·3 Hz, ArC*H*), and 2·46—3·0 (m, Ar), $\nu_{max.}$ (KBr) 3300sh cm^{-1} (NH) superimposed on a broad OH band.

The ethereal filtrate from the picrate preparation was washed free of picric acid, dried ($MgSO_4$), and evaporated and the oil obtained was extracted with light petroleum (charcoal). When concentrated the solution deposited (±)-threo-2-*methylamino*-1-(3-*thienyl*)*propan*-1-*ol* (IIa) (0·5 g), m.p. 108—110°. The analytical sample had m.p. 113—114° (Found: C, 55·7; H, 7·5; N, 7·8%), τ [$(CD_3)_2SO$] 9·23 (d, *J* 6·5 Hz, $CHCH_3$), 7·72 (s, $NHCH_3$), 7·14—7·60 (m, $CHCH_3$), 5·63 (d, *J* 6·5 Hz, ArC*H*), and 2·44—2·98 (m, Ar), $\nu_{max.}$ (KBr) 3300sh cm^{-1} (NH) superimposed on a broad OH band.

Resolution of (±)-threo-2-*Methylamino*-1-(3-*thienyl*)*propan*-1-*ol* (IIa).—A solution of the racemate (600 mg) and (+)-tartaric acid (540 mg) in ethanol (9 ml) was boiled for a few min and then set aside in the refrigerator for 72 h. The solid was filtered off and crystallised thrice from ethanol to give (−)-threo-2-*methylammonio*-1-(3-*thienyl*)*propan*-1-*ol* (+)-*tartrate* (230 mg), m.p. 168—169° (decomp.) (Found: C, 45·8; H, 6·1; N, 3·8. $C_{12}H_{19}NO_7S,0{\cdot}5C_2H_5OH$ requires C, 45·4; H, 6·4; N, 4·1%), $[\alpha]_D^{25}$ (water) −17·2° (*c* 0·46). The (−)-threo-*free base* recovered from this salt had m.p. 108—110°, $[\alpha]_D^{25}$ (ethanol) −39·0° (*c* 0·4).

The combined mother liquors from the preparation and crystallisation of the (+)-tartrate were evaporated, the solid was dissolved in water, the solution was basified with 4M-sodium hydroxide, saturated with sodium chloride, and extracted with dichloromethane. The mixture of bases so obtained was treated with (−)-tartaric acid (380 mg) as described above, affording (+)-threo-2-*methylammonio*-1-(3-*thienyl*)*propan*-1-*ol* (−)-*tartrate* (270 mg), m.p. 167—169° (decomp.) (Found: C, 45·4; H, 5·8; N, 3·9%), $[\alpha]_D^{25}$ (water) +15·6° (*c* 0·4). The (+)-threo-*free base* had m.p. 108—110°, $[\alpha]_D^{25}$ (ethanol) +37·1° (*c* 0·4).

3-(*α-Bromopropionyl*)-2,5-*dichlorothiophen*.—2,5-Dichloro-3-propionylthiophen, prepared by a Friedel–Crafts reaction in dichloromethane (instead of carbon disulphide [15]) had b.p. 128—132° at 15 mmHg, m.p. 63—64·5° (from ethanol) (lit.,[15] 60°), τ (CCl_4) 8·80 (t, *J* 6·5 Hz, CH_2CH_3), 7·10 (q, *J* 6·5 Hz, CH_2CH_3), and 2·84 (s, Ar), $\nu_{max.}$ (CCl_4) 1685 cm^{-1}. The 2,4-*dinitrophenylhydrazone* (orange needles from ethyl acetate) had m.p. 206—207° (Found: C, 40·2; H, 2·7; N, 14·4. $C_{13}H_{10}Cl_2N_4O_4S$ requires C, 40·1; H, 2·6; N, 14·4%). The ketone (53 g) was treated with bromine (41·6 g) as described above for 3-propionylthiophen to give 3-(*α-bromopropionyl*)-2,5-*dichlorothiophen* (65·2 g, 89%), b.p. 117—118° at 0·6 mmHg (Found: C, 29·5; H, 1·6. $C_7H_5BrCl_2OS$ requires C, 29·2; H, 1·8%), τ (CCl_4) 8·08 (d, *J* 6·5 Hz, $CHCH_3$), 4·85 (q, *J* 6·5 Hz, $CHCH_3$), and 2·75 (s, Ar), $\nu_{max.}$ (film) 1700 cm^{-1}.

(±)-erythro-1-(2,5-*Dichloro*-3-*thienyl*)-2-*methylaminopropan*-1-*ol* (Ib).—The foregoing bromoketone (39·4 g) in ether (50 ml) was added to methylamine (*ca.* 10 g) in ether (500 ml). After 2 days at room temperature the mixture was shaken with aqueous ammonia (*d* 0·88) and the ether layer was washed with brine, dried ($MgSO_4$), and evaporated to yield a thick syrup (32·7 g). Acidification of the ammonia solution provided 2,5-dichloro-3-thenoic acid (750 mg), m.p. 148—150° (from water) (lit.,[16] 147—148°), alone and mixed with authentic material.

The crude α-methylaminoketone was dissolved in a mixture of methanol (250 ml) and 4M-sodium hydroxide (9 ml) and was reduced by the addition of sodium borohydride (5·4 g), in portions, with ice-cooling. Next day the solvent was removed, the syrupy residue was taken up in dichloromethane, and extracted with 5M-hydrochloric acid (6 × 50 ml). The extract was basified (30% sodium hydroxide solution), the mixture was saturated with sodium chloride, and the basic material (21·7 g) was isolated with dichloromethane. Trituration with ice-cold ether gave a solid (A) and an ether solution (B); (A) (10·3 g) was dissolved in ethanol (100 ml) and M-sodium hydroxide (80 ml) and saturated aqueous copper(II) sulphate solution was run in until copper(II) hydroxide commenced to separate. The lilac copper complex [10·25 g, m.p. 149° (decomp.)] was filtered off (filtrate C) and dissolved in 2M-hydrochloric acid (100 ml), Kieselguhr was added, and hydrogen sulphide was passed through the solution until precipitation of copper was complete. The solids were filtered off, the filtrate was made basic (4M-sodium hydroxide solution), and the organic material was extracted with dichloromethane. Thus was obtained (±)-erythro-1-(2,5-*dichloro*-3-*thienyl*)-2-*methylaminopropan*-1-*ol* (Ib) (6·2 g), m.p. 108—110°

[15] N. P. Buu-Hoï and D. Lavit, *J. Chem. Soc.*, 1958, 1721.
[16] H. D. Hartough and L. Conley, *J. Amer. Chem. Soc.*, 1947, **69**, 3096.

(needles from light petroleum) (Found: C, 40·1; H, 4·5; N, 5·4. $C_8H_{11}Cl_2NOS$ requires C, 40·0; H, 4·6; N, 5·8%), τ ($CDCl_3$) 9·12 (d, *J* 6·5 Hz, $CHCH_3$), 7·60 (s, $NHCH_3$), 7·43 (s, NH and OH), 7·35 (m, $CHCH_3$), 5·16 (d, *J* 3·8 Hz, ArC*H*), and 3·15 (s, Ar), $\nu_{max.}$ (KBr) 3300sh cm^{-1} (NH) superimposed on a broad OH band.

Ether solution (B) was evaporated and the residue was distilled to give an oil (9·1 g), b.p. 97—112° at 0·2 mmHg. Treatment with copper(II) sulphate as described above gave a sticky precipitate (discarded); the alkaline ethanol filtrate was combined with filtrate (C), and ethanol was removed *in vacuo*. The remaining aqueous phase was extracted with ether, and the ether solution was washed with 2M-ammonium hydroxide until colourless, dried, and evaporated, yielding an oil (4·9 g). The oil was shaken vigorously with a solution of copper(II) sulphate pentahydrate (5·0 g) in water (50 ml), M-sodium hydroxide (40 ml) was added, and shaking was continued for 10 min. Next day the royal-blue complex was filtered off, washed with dichloromethane until the washings were colourless, and decomposed with hydrogen sulphide as described previously. A portion (200 mg) of the resulting oil, b.p. 150° (bath) at 2 mmHg, was chromatographed on silica gel (20 g). After initial elution with chloroform (7 × 10 ml), 9 : 1 chloroform–methanol eluted (±)-erythro-1-(2,5-*dichloro*-3-*thienyl*)-1,2-*bismethylaminopropane* (IIIa), τ (CCl_4) 9·16 (d, *J* 6·5 Hz, $CHCH_3$), 8·45 (s, N*H*), 7·75 (s, $CH_3CHNHCH_3$), 7·60 (s, $ArCHNHCH_3$), 7·25 (m, $CHCH_3$), 6·28 (d, *J* 4·0 Hz, ArC*H*), and 3·14 (s, Ar), *picrate* m.p. 199—201° (from aqueous ethanol) (Found: C, 36·5; H, 3·5; N, 14·9. $C_{15}H_{17}Cl_2N_5O_7S$ requires C, 37·1; H, 3·5; N, 14·5%). N.m.r. showed subsequent fractions to contain increasing amounts of the threo-*diamine* (IIIb), τ (CCl_4) 6·67 (d, *J* 8·5 Hz, ArC*H*), but this was not obtained pure.

2,5-*Dibromo*-3-*propionylthiophen*.—Aluminium chloride (67 g) in dichloromethane (200 ml) was stirred with ice-cooling whilst propionyl chloride (40 g) in dichloromethane (60 ml) was added slowly. After 30 min a solution of 2,5-dibromothiophen (96 g) in dichloromethane (75 ml) was added dropwise during 45 min. The mixture was stirred for periods of 1 h at 0°, at room temperature and at 30°, then cooled, and poured onto a mixture of crushed ice and concentrated hydrochloric acid. Work-up and distillation of the organic phase gave two principal fractions. (i) The first had b.p. 86—108° at 0·6 mmHg; crystallisation from light petroleum (b.p. 60—80°) gave 5-bromo-2-propionylthiophen (18·8 g), m.p. 53—55° (lit.,[17] 57°), τ (CCl_4) 8·81 (t, *J* 6·5 Hz, CH_3), 7·20 (q, *J* 6·5 Hz, CH_2), and 2·80 (q, *J* 4·0 Hz, Ar), 2,4-*dinitrophenylhydrazone*, m.p. 241—242° (deep-red needles from ethyl acetate) (Found: C, 38·8; H, 3·0; N, 13·5. $C_{13}H_{11}BrN_4O_4S$ requires C, 39·1; H, 3·0; N, 14·0%). (ii) The second had b.p. 120—124° at 0·6 mmHg; this, when crystallised from benzene–light petroleum gave 2,5-*dibromo*-3-*propionylthiophen* (29·7 g), m.p. 108—110° (Found: C, 27·8; H, 2·5. $C_7H_6Br_2OS$ requires C, 28·2; H, 2·0%), τ (CCl_4) 8·84 (t, *J* 6·5 Hz, CH_3), 7·08 (q, *J* 6·5 Hz, CH_2), and 2·88 (s, Ar), $\nu_{max.}$ (KBr) 1655 cm^{-1}, 2,4-*dinitrophenylhydrazone*, m.p. 195—196° (orange needles from ethyl acetate) (Found: C, 31·9; H, 2·0; N, 11·3. $C_{13}H_{10}Br_2N_4O_4S$ requires C, 32·6; H, 2·1; N, 11·7%).

Refractionation of the combined mother liquors provided a further 7·9 g of 5-bromo-2-propionylthiophen and a higher boiling fraction (7·5 g) which was shown (g.l.c.; 5 ft × ⅛ in 5% Carbowax 20M on Celite at 155°) to consist of 2,5-dibromo-3-propionylthiophen and a substance of greater retention time. The latter, separated by chromatography of a sample (1·5 g) of the mixture on alumina (25 g) with light petroleum (2 × 10 ml), was identified as tetrabromothiophen, m.p. and mixed m.p. with authentic material 116—117°.

2,5-*Dibromo*-3-(α-*bromopropionyl*)*thiophen*.—Reaction of the ketone (11·3 g) with bromine (6·4 g) as described above gave the α-*bromoketone* (12·2 g, 85%) as a yellow oil, b.p. 128—134° at 0·4 mmHg. which crystallised on storage in the refrigerator and had m.p. 64° (from ethanol) (Found: C, 22·4; H, 1·2. $C_7H_5Br_3OS$ requires C, 22·3; H, 1·3%). τ ($CDCl_3$) 8·15 (d, *J* 6·5 Hz, CH_3), 4·66 (q, *J* 6·5 Hz, $CHCH_3$), and 2·89 (s, Ar), $\nu_{max.}$ (film) 1680 cm^{-1}.

(±)-erythro-1-(2,5-*Dibromo*-3-*thienyl*)-2-*methylaminopropan*-1-*ol* (Ic).—Reaction of the preceding α-bromoketone (20 g) in ether (100 ml) with methylamine (*ca.* 4 g) in ether (250 ml) as before and reduction with an excess of sodium borohydride gave a mixture of bases (9·8 g). This was shaken with copper(II) sulphate pentahydrate (3·8 g) in water (34 ml), M-sodium hydroxide (28·7 ml) and dichloromethane (40 ml) were added, and the whole was shaken again. The lilac solid (5·3 g), m.p. 164° (decomp.), was collected, washed with dichloromethane, and decomposed as previously described, giving (±)-erythro-1-(2,5-*dibromo*-3-*thienyl*)-2-*methylaminopropan*-1-*ol* (Ic). An analytical sample had m.p. 144—146° (from aqueous ethanol) (Found: C, 29·1; H, 3·4; N, 4·4. $C_8H_{11}Br_2NOS$ requires C, 29·1; H, 3·3; N, 4·3%), τ ($CDCl_3$) 9·15 (d, *J* 6·5 Hz, $CHCH_3$), 7·65 (s, NH and OH), 7·50 (s, $NHCH_3$), 6·75—7·17 (m, $CHCH_3$), 4·97 (d, *J* 3·8 Hz, ArC*H*), and 3·19 (s, Ar), $\nu_{max.}$ (KBr) 3300sh cm^{-1} (NH) superimposed on a broad OH band.

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[17] N. P. Buu-Hoï and Nguyen-Hoán, *Rec. Trav. chim.*, 1949, **68**, 5.