A New Synthesis of Indoles Particularly Suitable for the Synthesis of Tryptamines and Tryptamine Itself †

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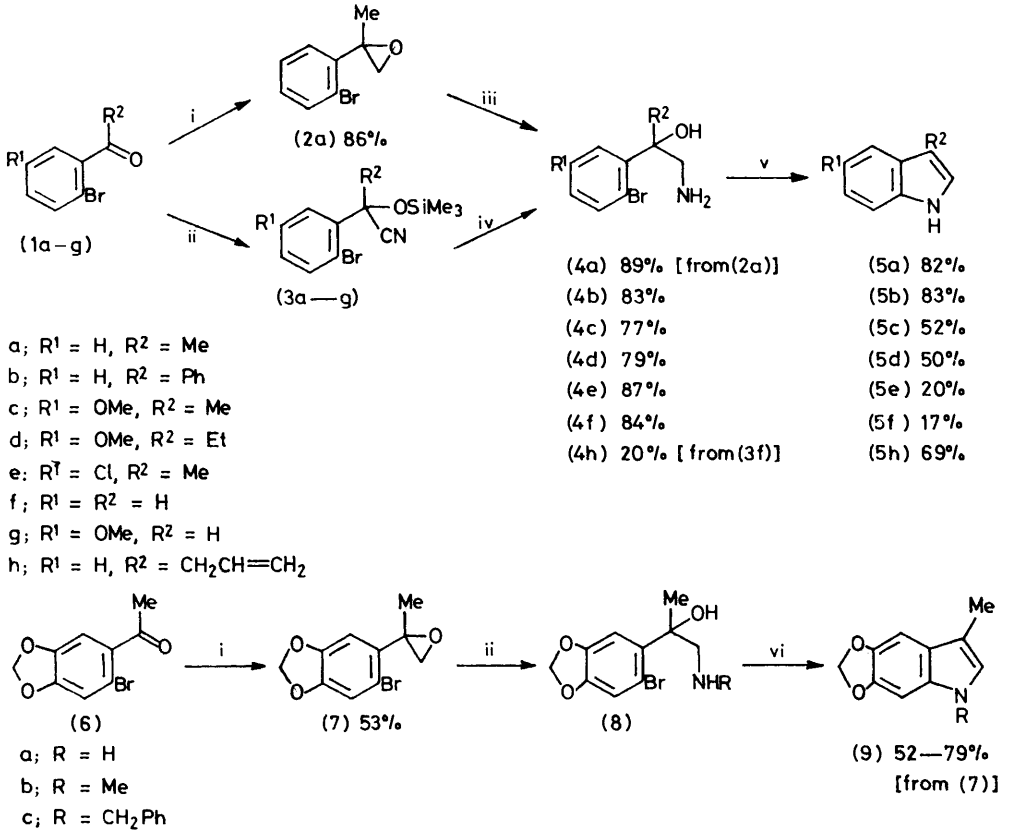
2-Amino-1-*o*-bromophenylethanols (4) give indoles (5) when heated to 140—170 °C in a solution of ammonia in methanol. The reaction is suitable for the synthesis of a wide variety of 1-, 3-, 5-, and 6-substituted indoles and, because the starting materials are easy to make, it is particularly suitable for the synthesis of *N*(b)-di-substituted tryptamines (15). Tryptamine itself can be made in 31% yield (based on *o*-bromobenzoic acid) by using benzyl groups as the *N*(b)-substituents, and removing them by hydrogenolysis.

In studying a benzyne route to indoles,[1] we observed that the amino-alcohol (4a), prepared by treating the epoxide (2a) with ammonia in methanol for 50 h at 105 °C, was concurrently giving skatole (5a) directly. These conditions are unlikely to give rise to a benzyne intermediate, and the result was, therefore, somewhat surprising. the other being the reaction described above, based on the opening of epoxides (2). The latter has the advantage that *N*-substituents can be accommodated: thus the epoxide (7), on treatment with ammonia, methylamine, or benzylamine, gave the corresponding indoles (9a—c) directly. The epoxides (2), however, cannot



Scheme 1 *Reagents*: i, $Me_2SO{:}CH_2$; ii, Me_3SiCN; iii, NH_3–MeOH; iv, $LiAlH_4$; v, NH_3–MeOH, 160 °C, 72h; vi, RNH_2–MeOH

After 72 h at 160 °C the intermediate (4a) was no longer present and the yield of skatole was quite good (82%). Tambute [2] has independently observed a similar reaction. We now report that the reaction (4) ⟶ (5) is suitable for preparing a wide range of indoles (Scheme 1), including indole itself, and that *it is particularly well adapted to the synthesis of tryptamines* (15) (Scheme 2).

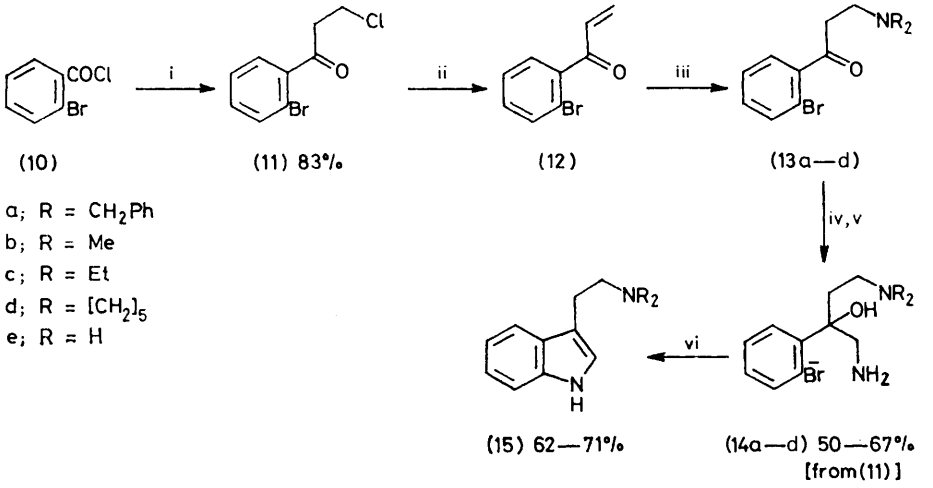
The key intermediates (4) can, no doubt, be made by a variety of methods; we have principally used two, one being reduction of cyanohydrin silyl ethers (3) and always be made from the corresponding ketones (1), whereas the cyanohydrin silyl ethers (3) in our experience usually can. Another route was used to prepare the amino-alcohol (4c): the trimethylsilyl ether of *o*-bromobenzaldehyde cyanohydrin was treated first with lithium di-isopropylamide and then with allyl bromide. The crude product was then reduced with lithium aluminium hydride.

The indole-forming reaction (4) ⟶ (5) is compatible not only with a range of *N*-substituents but also with a range of benzene-ring and 3-substituents (R^1 and R^2)

† There are no reprints of this paper.

(indole numbering), as shown by the success of the reaction with compounds (4a—h). Other solvents, like dimethylformamide (DMF) and hexamethylphosphoric triamide (HMPT) gave lower yields, and the ammonia (or other amine) was an essential ingredient.

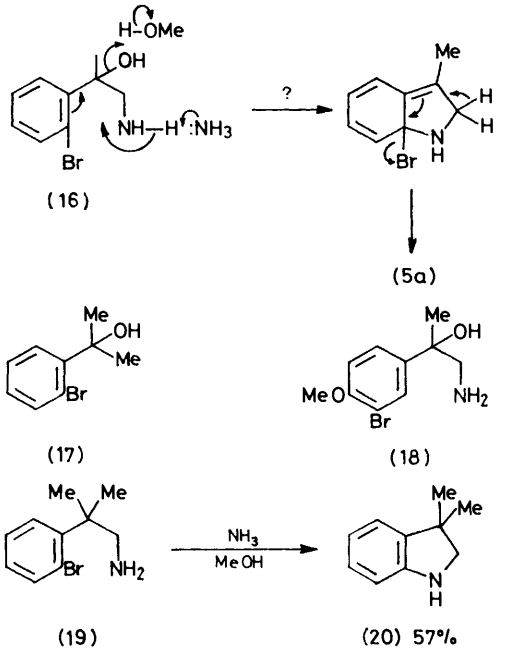
The 3-position of indoles is nucleophilic, and the synthesis of tryptamines (15) from 3-unsubstituted indoles involves, therefore, some form of umpolong.[3] Our route to indoles (Scheme 2), however, starts with



SCHEME 2 *Reagents*: i, $CH_2=CH_2$–$AlCl_3$; ii, $AlCl_3$; iii, HNR_2; iv, Me_3SiCN; v, $LiAlH_4$; vi, NH_3–MeOH

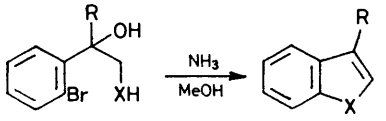
the carbon atom destined to become C-3 electrophilic, and no umpolong is needed to make the intermediates (11)—(14) of a tryptamine synthesis. Thus *o*-bromobenzoyl chloride (10) reacts with ethylene in the presence of aluminium chloride to give the β-chloro-ketone (11), and this ketone readily gave the unsaturated ketone (12) on treatment with triethylamine. The unsaturated ketone reacted with secondary amines like dibenzylamine to give the β-amino-ketones (13), which gave cyanohydrin silyl ethers in good yield. These could be reduced to the amino-alcohols (14) and, on heating in methanolic ammonia, the amino-alcohols gave tryptamines (15). In the case of the dibenzyl derivative (15a), hydrogenolysis gave tryptamine itself (15e) in an overall yield of 31%, based on *o*-bromobenzoic acid. The yield compares very favourably with other tryptamine syntheses [4,5] not based on indole itself. Thus, Szantay's route,[5] one of the better ones, gives an overall yield of 23% based on aniline and 1-bromo-3-chloropropane.

Our first thought on the mechanism of the key reaction (4) ⟶ (5) was that a benzyne mechanism was less likely than a reaction in which the amino-group displaces the hydroxy-group in a process, represented in its most general form by (16), with a variety of possible alternatives differing in the timing of the various events. Three special observations helped to clarify this picture. (i) The alcohol (17), which differed from (4a) only in having no amino-group, was recovered unchanged after being heated in methanolic ammonia for 170 h at 160 °C. (ii) The alcohol (18), which we had already shown [1] did give the corresponding indole under ' benzyne conditions ', was also recovered unchanged after being heated in methanolic ammonia for 170 h at 160 °C. These two observations showed that the benzyne mechanism was indeed very unlikely. (iii) The amine (19), on the other hand, gave the indoline (20) in 57% yield after being heated in methanolic ammonia for 170 h at 160 °C. This implies that the amino-group can attack an unactivated benzene ring more easily than we, at least, expected. We also found that the amino-alcohol (4e; Cl for Br) was slower to react than (4e) itself, and that other leaving groups (OMe and OTs) in place of the bromide were ineffective. The reaction forming indole itself was also



slower, as a result, no doubt, of the absence of a geminally disubstituted atom at the future C-3. These observations are consistent with what we now believe the mechanism to be: rate-determining nucleophilic

attack by the amino-group in the benzene ring to give a tetrahedral intermediate (more stabilised by the



(21) (22)

a; X = O, R = Me
b; X = O, R = Ph
c; X = S, R = Me
d; X = S, R = Ph

bromo-group than by chloro or methoxy), followed by expulsion of the bromide ion, followed by aromatisation of the indole ring.

The reaction is applicable to the synthesis of other benzoheterocycles, but the yields are generally rather lower. Thus we have prepared the benzofurans (22a) (86%) and (22b) (57%) and the benzothiophens (22c) (51%) and (22d) (53%), but when we heated *o*-bromoacetophenone oxime or hydrazone in methanolic ammonia, only 10% yields of 3-methylbenzisoxazole and 3-methylbenzindazole were obtained.

EXPERIMENTAL

Preparation of the Ketones and Aldehydes (1) *and* (6).—*o-Bromobenzaldehyde* (1f). Finely powdered *N*-bromo-succinimide (71.2 g, 0.4 mol) was added to a solution of *o*-bromotoluene (34.2 g, 0.2 mol) in carbon tetrachloride (500 ml) containing benzoyl peroxide (0.5 g) and the mixture heated under reflux for 20 h, while irradiating with a Hanovia 250 W mercury-vapour lamp.[6] After cooling to 0 °C and removing the succinimide by filtration, the solvent was evaporated *in vacuo* and the residue distilled to give *o-bromobenzylidene dibromide* (62.5 g, 95%), b.p. 93—95 °C/0.5 mmHg (Found: C, 25.4, H, 1.65, Br, 72.9; $C_7H_5Br_3$ requires C, 25,6; H, 1.53; Br, 72.9%), $\nu_{max.}$ (film) 3 090 and 3 010 cm^{-1} (ArC–H); $\tau(CDCl_3)$ 2.20—2.95 (4 H, m) and 3.15 (1 H, s), *m/e* 332, 330; 328, and 326 (33, 100, 100, and 33%, M^+). The *o*-bromobenzylidene dibromide (62.5 g, 0.19 mol) in acetone (400 ml) was hydrolysed by adding with stirring a solution of silver nitrate (65 g; 3.39M) in water (400 ml) over 10 min. After an additional 30 min, the precipitated silver bromide was removed by filtration, washed with acetone (100 ml), and the filtrate extracted with ether (3 × 200 ml). The ether was dried ($MgSO_4$), evaporated *in vacuo*, and the residue was distilled to give *o*-bromobenzaldehyde (1f) [31.5 g, 84% (based on *o*-bromotoluene)], b.p. 64 °C/0.5 mmHg (lit.,[7] b.p. 118 °C/12 mmHg), $\nu_{max.}$ (film) 3 050 and 3 000 w (ArC–H) and 1 700 s cm^{-1} (C=O); $\tau(CDCl_3)$ −0.35 (1 H, s) and 1.95—2.70 (4 H, m). Alternative hydrolysis procedures [8] gave substantially lower yields of the aldehyde (1f).

2'-Bromoacetophenone (1a). A solution of *o*-bromobenzaldehyde (1f) (18.5 f, 0.1 mol) in ether (20 ml) was slowly added to a stirred solution of methylmagnesium iodide (0.13 mol) in ether (100 ml), under nitrogen, at a rate which maintained gentle reflux. The mixture was then heated under reflux for a further 20 h, allowed to cool and poured into ice-cold hydrochloric acid (2M; 100 ml). The ether layer was separated, and the aqueous layer was saturated with sodium chloride and extracted with ether (3 × 50 ml). The combined ether extracts were washed successively with water (50 ml), saturated sodium hydrogen carbonate solution (2 × 50 ml), and water (50 ml), and then dried ($MgSO_4$) and evaporated *in vacuo*. Distillation of the pale yellow residue gave 1-(2-bromophenyl)ethanol (18.0 g, 90%), b.p. 90—92 °C/2 mmHg (lit.,[9] 104—105 °C/5 mmHg). This alcohol (18.0 g, 90 mmol) in anhydrous dichloromethane (20 ml) was added to a stirred suspension of pyridinium chlorochromate [10] (29.1 g, 135 mmol) in dichloromethane (200 ml) and stirred for 3 h. Ether (200 ml) was added, and the supernatant liquid decanted from the precipitated black gum. The insoluble residue was washed with ether (3 × 50 ml) and the combined extracts were evaporated to a small volume (*ca.* 50 ml) and passed through a short pad of Florosil (50 g). Removal of the solvent *in vacuo* and distillation gave the ketone (1a) (16.1 g, 89%), b.p. 117 °C/14 mmHg (lit.,[7] b.p. 112 °C/10 mmHg).

o-Bromobenzophenone (1b). *o*-Bromobenzoyl chloride and benzene were combined in a Friedel–Crafts reaction as outlined by Koopal [11] (97%), b.p. 136—138 °C/1 × 10^{-3} mmHg (lit.,[12] 151—153 °C/0.05 mmHg).

2-Bromo-5-methoxybenzaldehyde (1g). Bromine (16.0 g, 0.1 mol) in chloroform (150 ml) was added dropwise to a stirred solution of *m*-methoxybenzaldehyde (13.6 g, 0.1 mol) in chloroform (100 ml) at room temperature and the mixture was then heated under reflux for 48 h, when the evolution of hydrogen bromide had ceased. After cooling, the reaction mixture was washed successively with sodium hydrogen carbonate solution (5%; 200 ml) and water (100 ml), dried ($MgSO_4$), and evaporated *in vacuo* to give the bromide (11.9 g, 55%) as plates, m.p. 76—78 °C (from hexane) (lit.,[13] m.p. 76 °C).

5-Bromo-2-methoxybenzaldehyde [(12d) *in ref.* 1]. This compound was prepared similarly from *o*-methoxybenzaldehyde (59%) as plates, m.p. 114—116 °C (from EtOH) (lit.,[14] m.p. 113.5—115 °C).

3-Bromo-4-methoxybenzaldehyde [(12b) *in ref.* 1]. Bromine (48.0 g, 0.30 mol) was added over 1 h to a stirred solution of *p*-anisaldehyde (40.8 g, 0.30 mol) in acetic acid (90%, 200 ml) containing a trace of iodine. The temperature of the mixture rose to 45 °C during the addition. After cooling, the mixture was poured into water (200 ml), solid sodium metabisulphite was added, and the mixture was extracted with ether (2 × 100 ml). The organic extract was washed with a saturated solution of sodium hydrogen carbonate (2 × 250 ml) and water (50 ml), and then dried ($MgSO_4$) and evaporated. Distillation of the residue gave the aldehyde (24.0 g, 37%), b.p. 108—110 °C/1 mmHg (lit.[15] 158—162 °C/15 mmHg).

2-Bromo-5-methoxyacetophenone (1c). Treatment of 2-bromo-5-methoxybenzaldehyde (1g) with methylmagnesium iodide, as described in the preparation of (1a), gave *1-(2-bromo-5-methoxyphenyl)ethanol* (14.7 g, 85%) as plates, m.p. 66 °C (from EtOH) (Found: C, 46.5; H, 4.95. $C_9H_{11}BrO_2$ requires C, 46.7; H, 4.80%), $\nu_{max.}$ (film) 3 460 s cm^{-1} (OH); $\tau(CDCl_3)$ 2.61 (1 H, d, *J* 9.5 Hz), 2.83 (1 H, d, *J* 3 Hz), 3.32 (1 H, dd, *J* 9.5 and 3 Hz), 4.82 (1 H, q, *J* 6.5 Hz), 6.17 (3 H, s), 7.30—7.60 (1 H, disappears on shaking with D_2O), and 8.48 (3 H, d, *J* 6.5 Hz). Oxidation of the alcohol (14.7 g, 0.063 mol), as described in the preparation of (1a), gave the ketone (1c) (12.5 g, 85%), b.p. 102 °C/0.4 mmHg (lit.,[16] 105 °C/0.65 mmHg).

2-Bromo-5-methoxypropiophenone (1d). Treatment of 2-bromo-5-methoxybenzaldehyde (1g) with ethylmagnesium iodide as in the preparation of (1a), gave 1-(2-*bromo*-5-

methoxyphenyl)propanol (16.7 g, 92%) as needles, m.p. 63 °C (from EtOH) (Found: C, 49.0; H, 5.30. $C_{10}H_{13}BrO_2$ requires C, 49.0; H, 5.35%), $\nu_{max.}$ ($CHCl_3$) 3 560 s cm^{-1} (OH); τ($CDCl_3$) 2.60 (1 H, d, *J* 9.5 Hz), 2.88 (1 H, d, *J* 3.0 Hz), 3.33 (1 H, dd, *J* 9.5 and 3.0 Hz), 5.05 (1 H, dd, *J* 6.0 and 1.0 Hz), 6.21 (3 H, s), 7.27 br (1 H, disappears with D_2O), 8.12—8.57 (2 H, m), and 9.02 (3 H, t, *J* 6.0 Hz); *m/e* 244, 246 (25, 7, M^+) and 215 and 217 (100, 38, $M - C_2H_5$).

Oxidation of the alcohol gave the *ketone* (1d) (13.5 g, 82%), b.p. 99—101 °C/0.05 mmHg (Found: C, 49.1; H, 4.55. $C_{10}H_{11}BrO_2$ requires C, 49.3; H, 4.50%), $\nu_{max.}$ (film) 3 080 and 3 020 w (ArC–H), and 1 695 s cm^{-1} (C=C); τ($CDCl_3$) 2.47—3.30 (3 H, m), 6.20 (3 H, s), 7.07 (2 H, q, *J* 7.5 Hz), and 8.77 (3 H, t, *J* 7.5 Hz); *m/e* 242, 244 (28, 28%, M^+) and 213, 215 (100, 100, $M - C_2H_3$).

3-*Bromo*-4-*methoxyacetophenone* [(12a) *in ref.* 1]. Modifying the Friedel–Crafts procedure described by Kimoto and his co-workers [17] by substituting dichloromethane for carbon-disulphide and conducting the reaction at −20 °C for 5 h gave the ketone (14.2 g, 62%), as needles, m.p. 88 °C (from EtOH) (lit.,[17] m.p. 85—87 °C) (Found: C, 47.1; H, 3.9; Br, 34.8. Calc. for $C_8H_9BrO_2$: C, 47.2, H, 3.9; Br, 34.9%).

5-*Bromo*-2-*methoxyacetophenone* [(12c) *in ref.* 1]. The ketone was obtained by the same Friedel–Crafts procedure described above (15.9 g, 69%), b.p. 120 °C/2 mmHg (lit.,[17] b.p. 130—135 °C/4 mmHg).

2-*Bromo*-5-*chloroacetophenone* (1e) and 2,5-*dichloroacetophenone* (1e; Cl for Br) were prepared (49% and 73%) by Friedel–Crafts acetylation of the dihalogenobenzenes using known procedures.[18]

2-*Bromopiperonal*.—Bromine (107 g, 0.67 m) was added dropwise to a stirred solution of piperonal (100 g, 0.66 mol) in chloroform (500 ml) at 0 °C over 2 h. The mixture was then heated under reflux until the evolution of hydrogen bromide had ceased (36 h), allowed to cool, and extracted successively with 5% aqueous solutions of sodium hydrogen carbonate and sodium hydrogen sulphite. The organic extracts were washed with water, dried ($MgSO_4$), and evaporated *in vacuo* to give a solid residue. Washing the residue with ether–light petroleum (b.p. 60—80 °C) (1 : 1, 200 ml) removed the unchanged piperonal, leaving 2-bromopiperonal (117 g, 73%) as plates, m.p. 129 °C (from EtOH) (lit.,[19] m.p. 129 °C), $\nu_{max.}$ (Nujol) 1 700 s cm^{-1} (C=O); τ(CCl_4) −0.15 (1 H, s), 2.67 (1 H, s), 2.87 (1 H, s), and 3.36 (2 H, s); *m/e* 228, 230 (100, 100% M^+), and 199, 201, (24, 24, M − CHO). This procedure gave better yields than that (54%) described by Parijs.[20]

5-*Acetyl*-6-*bromo*-2H-[1,3]*benzodioxole* (6).—2-Bromopiperonal (30.0 g, 0.124 mol) was converted into 5-bromo-6-(1-hydroxyethyl)-2*H*-[1,3]benzodioxole by treatment with methylmagnesium iodide as described in the preparation of (1b). Oxidation of the crude alcohol with pyridinium chlorochromate gave the *ketone* (6) (26.3 g, 82%), as plates, m.p. 55 °C (from EtOH) (Found: C, 44.2; H, 2.85; Br, 32.9. $C_9H_9BrO_3$ requires C, 44.2; H, 2.90; Br, 32.8%), $\nu_{max.}$ ($CHCl_3$) 3 080 and 3 010w (ArC–H) and 1 695s cm^{-1} (C=O); τ ($CDCl_3$) 2.97 (2 H, s), 3.96 (2 H, s), 7.40 (3 H, s); *m/e* 242 (50, 50%, M^+), 227, 229 (100, 100 $M - CH_3$); $\lambda_{max.}$ (EtOH) 231, 277, and 305 nm (ε 14 930, 3 690, and 3 650).

Preparation of the Epoxides (2) *and* (7).—2-(2-*Bromophenyl*)-2-*methyloxiran* (2a). (a) Sodium hydride [2.85 g, 50% dispersion in oil, 60 mmol, washed with dry light petroleum (b.p. 30—40 °C)] and trimethylsulphoxonium iodide [21] (12.98 g, 59 mmol) were added to dry dimethyl sulphoxide (DMSO) (20 ml) and the mixture stirred until the rapid evolution of hydrogen had ceased (*ca.* 45 min.). 2-Bromoacetophenone (1a) (5.97 g, 30 mmol) in a mixture of dry tetrahydrofuran (THF) and DMSO (2 : 1; 15 ml) was added with stirring, which was continued for 1 h at room temperature and then 1 h at 50 °C. The cooled mixture was poured into water and extracted with ether (3 × 50 ml). The organic extracts were washed with water (3 × 25 ml), dried ($MgSO_4$), and evaporated *in vacuo* to give a brown oil. Distillation gave the *oxiran* (2a) (5.5 g, 86%), b.p. 108—110 °C/14 mmHg (Found: C, 50.8; H, 4.4. C_9H_9BrO requires C, 50.8; H, 4.25%), $\nu_{max.}$ (film) 1 240, 940, and 865 m cm^{-1} (C·O·C); τ($CDCl_3$) 2.5—3.2 (4 H, m), 7.14 (1 H, d, *J* 5.5 Hz), 7.35 (1 H, d, *J* 5.5 Hz), and 8.45 (3 H, s); *m/e* 212, 214 (13, M^+), 182, 184 (23, $M - CH_2O$), 133 (53, M − Br), and 103 (100%, $M - CH_2OBr$).

(b) *m*-Chloroperbenzoic acid (18.1 g, 0.1 mol [based on 95% pure material]) was added in small portions to a stirred solution of 2-bromo-α-methylstyrene (see below) (20.0 g, 0.1 mol) in a mixture of dichloromethane (500 ml) and aqueous sodium hydrogen carbonate (250 ml of a 0.5 M-solution). The resulting solution was vigorously stirred until a positive starch–iodide test (for peroxy-acid) was no longer obtained (*ca.* 30 h), and the two phases were separated. The organic extract was then washed successively with aqueous sodium hydroxide (1M; 300 ml) and water (50 ml), and then dried (Na_2SO_4) and evaporated *in vacuo*. The resulting oil was chromatographed on Florosil (750 g) with chloroform as eluant to give the *oxiran* (2a) (17.2 g, 70%), identical with that obtained by method (a).

2-*Bromo*-α-*methylstyrene*.—Methyl 2-bromobenzoate (53.75 g, 0.25 mol) and methylmagnesium iodide (from 96 g MeI) were combined following the published procedure.[22] The product (48.4 g, 91%) had b.p. 80—82 °C/1 mmHg, the b.p. quoted [22] as being that of the styrene. It was, however, the tertiary *alcohol* (17), $\nu_{max.}$ (film) 3 460s cm^{-1}; τ($CDCl_3$) 2.20—3.1 (4 H, m), 6.9—7.4br (1 H, s, disappears with D_2O), and 8.25 (6 H, s), *m/e* 196, 198 (100%, $M - H_2O$), 181, 183 (13%, $M^+ - H_2O$-CH_3), and 102 (56%, $M^+ - H_2O$–CH_3Br). The tertiary alcohol (39.4 g, 0.2 mol) was distilled from fused potassium hydrogen sulphate (24 g) at 125 mmHg to give the styrene (28.5 g, 72%), b.p. 40—42 °C/0.6 mmHg (Found, C, 54.9; H, 4.70; Br, 40.4 Calc. for C_9H_9Br: C, 54.8; H, 4.60; Br, 40.5%); $\nu_{max.}$ (film) 1 645 cm^{-1}; τ($CDCl_3$) 2.18—2.90 (4 H, m), 4.70 (1 H, m), 5.0 (1 H, m), and 7.83 (3 H, s).

5-*Bromo*-6-(2-*methyloxiran*-2-*yl*)-2H-[1,3]*benzodioxole* (7).—Sodium hydride [40 mmol; a 50% oil dispersion washed with dry light petroleum (b.p. 30—40 °C)] was suspended in anhydrous DMSO (100 ml) under dry nitrogen and stirred at 70—80 °C until a clear solution was obtained (0.5 h). After cooling, *S*-methyl-*S*-phenyl-*N*-*p*-tolylsulphonylsulphinylimine (11.7 g, 40 mmol) was added and the mixture stirred at room temperature until the solution became clear (1—2 h). 5-Acetyl-6-bromo-2*H*-[1,3]benzodioxole (6) (9.2 g, 38 mmol) in DMSO (30 ml) was added and the solution stirred at room temperature for 18 h, poured into water (250 ml), and extracted with n-pentane (3 × 100 ml). The pentane extracts were washed with water (2 × 50 ml), dried ($MgSO_4$), and evaporated *in vacuo*. Distillation gave the *oxiran* (7) (8.10 g, 53%), b.p. 145—148 °C/1 × 10^{-4} mmHg (Found: C, 46.9; H, 3.60; Br, 31.3; $C_{10}H_9BrO_3$ requires C, 46.7; H, 3.50; Br, 31.1%), $\nu_{max.}$ 3 095 and

3 030 w (ArC–H), 1 260, 950, and 820s cm^{-1} (C·O·C); τ($CDCl_3$) 3.04 (2 H, s), 4.04 (2 H, s), 7.05, (1 H, d, *J* 5.5 Hz), 7.18 (1 H, d, *J* 5.5 Hz), and 8.38 (3 H, s); *m/e* 256, 258 (73%, M^+), and 227, 229 (100%, M^+ – CHO).

Preparation of the Amino-alcohols (4) *and* (14).—1-*Amino*-2-(2-*bromophenyl*)*propan*-2-*ol* (4a). (a) The oxiran (2) (1.0 g, 4.7 mmol) in methanol (20 ml) previously saturated at 0 °C with ammonia was heated in a sealed tube for 4 h at 110 °C. The brown residue obtained by evaporation was partitioned between ether (20 ml) and hydrochloric acid (2M; 20 ml). The aqueous layer was basified to pH 13 with sodium hydroxide solution (2M), saturated with sodium chloride, and extracted with ether (3 × 50 ml). The combined organic extracts were washed with water (30 ml), dried ($MgSO_4$), and evaporated *in vacuo* to give the *amino-alcohol* (4a) (0.95 g, 89%), characterised as its N-*benzoyl derivative*, prisms, m.p. 118—119 °C (from benzene) (Found: C, 57.5; H, 4.8; N, 4.2. $C_{16}H_{16}BrNO_2$ requires C, 57.5; H, 4.8; N, 4.2%); τ(CCl_4) 2.95—3.2 (9 H, m), 4.7br (1 H, m, NH), 5.92br (2 H, d), and 8.33 (3 H, s).

(b) Trimethylsilyl cyanide (2.7 g, 27 mmol) and anhydrous zinc iodide (10 mg) were added to *o*-bromoacetophenone (1a) (5.0 g, 25 mmol) and the mixture heated at 50 °C for 20 h (or, in the general case, until i.r. studies indicated the disappearance of the carbonyl group from the starting ketone). The intermediate cyanohydrin ether was diluted with THF (10 ml), and added to a suspension of lithium aluminium hydride (1.50 g, 39 mmol) in THF (30 ml) at a rate which maintained a gentle reflux. The mixture was heated under reflux for a further 1.5 h, and the excess of hydride destroyed with a saturated solution of sodium sulphate. The granular precipitate was filtered off, washed with ether (3 × 50 ml), and the filtrate extracted with hydrochloric acid (1M; 2 × 30 ml). The aqueous layer was washed with ether (20 ml) basified to pH 13 with sodium hydroxide solution (2M), saturated with sodium chloride, and extracted with ether (4 × 50 ml). The organic extracts were dried ($MgSO_4$) and evaporated *in vacuo* to give the *amino-alcohol* (4a) (4.5 g, 78%) as a red oil, identical to that obtained by method (a) above. The following amino-alcohols were obtained by method (b).

(a) 2-*Amino*-1-(2-*bromophenyl*)-1-*phenylethanol* (4b) (83%), plates, m.p. 136—138 °C (sublimed at 150 °C and 0.2 mmHg) (Found: C, 57.4; H, 4.9; N, 4.8. $C_{14}H_{14}BrNO$ requires C, 57.5; H, 4.85; N, 4.8%), $\nu_{max.}$ (Nujol) 3 200—2 600 m cm^{-1} (OH); τ($CDCl_3$) 2.21—3.10 (9 H, m), 6.32 (1 H, d, *J* 6 Hz), 6.76 (1 H, d, *J* 6 Hz), and 7.58br (3 H, disappears slowly on shaking with D_2O); *m/e* (no M^+), 261, 263 (80% 70%, $M^+ - CH_2NH_2$) and 183, 185 (100%, $BrC_6H_4CO^+$); $\lambda_{max.}$ (EtOH) 217 and 268 nm (ε 12 000 and 1 100).

(b) 1-*Amino*-2-(2-*bromo*-5-*methoxyphenyl*)*propan*-2-*ol* (4c) (77%) as a red gum, $\nu_{max.}$ (film) 3 300 m,br (OH) and 1 565 m cm^{-1} (NH_2); τ($CDCl_3$) 2.53 (1 H, d, *J* 2.5 Hz), 2.58 (1 H, d, *J* 9.0 Hz), 3.37 (1 H, dd, *J* 2.5 and 9.0 Hz), 6.20 (3 H, s), 6.36 (1 H, d, *J* 13.0 Hz), 7.17 (1 H, d, *J* 13.0 Hz), 7.70br (3 H, disappears with D_2O) and 8.34 (3 H, s); *m/e* (no M^+), 242, 244 (100%, *M* – OH) and 229, 231 (11%, 10%, $M - CH_2NH_2$).

(c) 1-*Amino*-2-(2-*bromo*-5-*methoxyphenyl*)*butan*-2-*ol* (4d) (79%) as a red gum, $\nu_{max.}$ (film) 3 300 m,br, (OH) and 1 575m cm^{-1} (NH_2); τ($CDCl_3$) 2.53 (1 H, d, *J* 2.5 Hz), 2.58 (1 H, d, *J* 9.0 Hz), 3.37 (1 H, dd, *J* 2.5 and 9.0 Hz), 6.20 (3 H, s), 6.90 (1 H, d, *J* 13.0 Hz), 7.21 (1 H, d, *J* 13.0 Hz), 7.50 (3 H, br disappears with D_2O), 8.27 (2 H, q, *J* 7.0 Hz), and 9.27 (3 H, t, *J* 7.0 Hz) (Found: M^+, 273.036 1, 275.033 9. $C_{11}H_{16}BrNO_2$ requires 273.0363, 275.0344), *m/e* 273, 275 (1%, 1%, M^+), 243, 245 (100%, $M - CH_2NH_2$) and 213, 215 (39%, 44%, CH_3O – Br – $C_6H_3CO^+$).

(d) 1-*Amino*-2-(2-*bromo*-5-*chlorophenyl*)*propan*-2-*ol* (4e) (87%), plates, m.p. 68 °C [from ether–light petroleum (b.p. 60—80 °C)] (Found: C, 41.2; H, 4.25; N, 5.5. $C_9H_{11}BrClNO$ requires C, 40.9; H, 4.20; H, 5.30%), $\nu_{max.}$ (film) 3 420br (OH), cm^{-1}; τ($CDCl_3$) 2.15—2.78 (3 H, m), 6.24 (1 H, of AB, d, *J* 4 Hz), 7.20 (1 H of AB, d, *J* 4 Hz), 8.03br (3 H, disappears with D_2O), and 8.40 (3 H, s); *m/e* (no M^+), 233, 235, 237 (24%, 100%, 76% $M^+ - CH_2NH_2$) and 217, 219, 221 [5%, 19%, 14% (Br) (Cl) $C_6H_4CO^+$].

(e) 1-*Amino*-2-(2,5-*dichlorophenyl*)*propan*-2-*ol* (4e; Cl for Br) (84%), needles, m.p. 122—124 °C (from ether) (Found: C, 49.2; H, 5.10, N, 6.3. $C_9H_{11}Cl_2NO$ requires C, 49.2; H, 5.20; N, 6.3%), $\nu_{max.}$ ($CHCl_3$) 3 420 m (OH) and 1 550 w cm^{-1} (NH_2); τ($CDCl_3$) 1.9—2.15br (1 H), 2.50—2.95 (2 H, m), 6.33 (1 H, d, *J* 12 Hz), 7.15 (1 H, d, *J* 12 Hz), 7.75br (3 H, exchanged slowly with D_2O), and 8.35 (3 H, s); *m/e* (no M^+), 190, 192, 194 (68%, 44%, 7%, $M^+ - CH_2NH_2$) and 185, 187 (100%, 33%, M^+ – Cl).

(f) 2-*Amino*-1-(2-*bromophenyl*)*ethanol* (4f) (84%), plates, m.p. 83—85 °C (sublimed at 90 °C and 10^{-3} mmHg) (Found: C, 44.4; H, 4.65; N, 6.6. $C_8H_{10}BrNO$ requires C, 44.4; H, 4.65; N, 6.5%), $\nu_{max.}$ (Nujol) 3 340, 3 275, 3 180, 1 560 (NH_2), and 2 700br cm^{-1} (OH); τ($CDCl_3$) 2.37—3.00 (4 H, m), 5.02 (1 H, dd, *J* 3.5 and 8.0 Hz, methine H), 7.97 (1 H, dd, *J* 13.0 and 3.5 Hz, 1 H of methylene), 7.34 (1 H, dd, *J* 8.0 and 13.0 Hz, 1 H of methylene), and 7.50br (3 H, disappears with D_2O); *m/e* (no M^+), 198, 200 (36%, 65%, *M* – OH) and 185, 187 (100%, $M - CH_2NH_2$).

(g) 1-*Amino*-2-(3-*bromo*-4-*methoxyphenyl*)*propan*-2-*ol* [(13a) in ref. 1] (83%), a viscous oil, b.p. 134—136 °C/0.25 mmHg, $\nu_{max.}$ (film) 3 400 s cm^{-1} (OH); τ($CDCl_3$) 2.33 (1 H, d, *J* 2.5 Hz), 2.62 (1 H, dd, *J* 2.5 and 8.0 Hz), 3.10 (1 H, d, *J* 8.0 Hz), 6.19 (3 H, s), 7.06 (1 H, d, *J* 12.5 Hz), 7.28 (1 H, d, *J* 12.5 Hz), 7.90br (3 H, disappears with D_2O) and 8.55 (3 H, s); *m/e* 259, 261 (2%, M^+), 242, 244 (3%, *M* – OH) and 229, 231 (100%, $M - CH_2NH_2$); *hydrochloride*, plates, m.p. 173 °C (from ether) (Found: C, 40.7; H, 5.10; N, 4.7. $C_{10}H_{14}BrCNO_2$ requires C, 40.6; H, 4.8; N, 4.7%).

(h) 2-*Amino*-1-(3-*bromo*-4-*methoxyphenyl*)*ethanol* [13b) in ref. 1] (79%), plates, m.p. 89—91 °C (sublimed at 110 °C and 10^{-3} mmHg), $\nu_{max.}$ (Nujol) 3 300br (OH) and 1 565m cm^{-1} (NH_2); τ(DMSO) 2.54 (1 H, d, *J* 2.0 Hz), 2.78 (1 H, dd, *J* 2.0 and 8.0 Hz), 3.08 (1 H, d, *J* 8.0 Hz), 5.58 (1 H, m), 6.17 (3 H, s), 6.90br (3 H, disappears with D_2O), and 7.28—7.54 (2 H, m) (Found: $M^+ - CH_2NH_2$, 214.968, 216.970 2, $C_8H_8BrO_2$ requires 214.970 6, 216.968 8), *m/e* 245, 247 (2%, M^+), 215, 217 (10%, 11%, $M^+ - CH_2NH_2$), and 186, 188 (100%, $M^+ - CH_2NH_2 - H_2O$).

(i) 1-*Amino*-2-(5-*bromo*-2-*methoxyphenyl*)*propan*-2-*ol* [(13c) in ref. 1] (aluminium chloride was used in place of zinc iodide), (77%) as a pale yellow gum, $\nu_{max.}$ (film) 3 360 m,br (OH) and 1 570 w cm^{-1} (NH_2); τ($CDCl_3$) 2.31 (1 H, d, *J* 2.0 Hz), 2.69 (1 H, dd, *J* 2.0 and 9.0 Hz), 3.27 (1 H, d, *J* 9.0 Hz), 6.18 (3 H, s), 6.71 (1 H, d, *J* 13.0 Hz), 7.25 (1 H, d, *J* 13.0 Hz), 7.66br (3 H, disappears with D_2O), and 8.49 (3 H, s); *m/e* 259, 261 (1%, M^+), 241, 243 (16%, 24%, $M^+ - H_2O$) and 229, 231 (100%, 99%, $M^+ - CH_2NH_2$); *hydrochloride*, plates, m.p. 216 °C (from EtOH) (Found: C, 40.3; H, 5.0; N, 4.7. $C_{10}H_{15}BrClNO_2$ requires C, 40.5; H, 5.10; N, 4.7%).

(j) 2-*Amino*-1-(2-*chlorophenyl*)*ethanol* [(8) in ref. 1, R^1 = R^2 = H, Cl for Br] (84%), plates, m.p. 63 °C (sublimed at 80 °C and 0.2 mmHg) (lit.[23] b.p. 108—112 °C/0.25 mmHg) (Found: C, 56.0; H, 5.8; N, 8.1; Cl, 20.8. Calc. for $C_8H_{10}ClNO$; C, 56.0; H, 5.80; N, 8.2; Cl, 20.7%), $\nu_{max.}$ (Nujol) 3 450, 3 300, 1 625 (NH_2), and 2 700br cm^{-1} (OH); τ(DMSO) 2.36—3.04 (4 H, m), 5.19 (1 H, dd, *J* 3.0 and 7.5 Hz, methine H), 7.18 (1 H, dd, *J* 3.0 and 13.0 Hz, 1 H of methylene), 7.33 (3 H, s, disappears with D_2O), and 7.52 (1 H, dd, *J* 7.5 and 13.0 Hz, 1 H of methylene); *m/e* (no M^+), 141, 143 (28%, 100%, $M - CH_2NH_2$).

(k) 2-*Amino*-1-(2-*bromo*-5-*methoxyphenyl*)*ethanol* [(8) in ref. 1, R^1 = OMe, R^2 = H] [aluminium chloride (10 mg) was used in place of zinc iodide], (82%) as a pale yellow gum, $\nu_{max.}$ (film) 3 460, 3 290, 1 570 m (NH_2), and 3 150br cm^{-1} (OH); τ($CDCl_3$) 2.62 (1 H, d, *J* 9.0 Hz), 2.85 (1 H, d, *J* 2.5 Hz), 3.32 (1 H, dd, *J* 2.5 and 9.0 Hz), 2.85 (1 H, d, *J* 2.5 Hz), 3.32 (1 H, dd, *J* 2.5 and 9.0 Hz), 5.08 (1 H, dd, *J* 3.0 and 8.0 Hz, methine H), 6.20 (3 H, s), 6.98 (1 H, dd, *J* 3.0 and 12.0 Hz, 1 H of methylene), 7.32 (1 H, dd, *J* 8.0 and 12.0 Hz, 1 H of methylene), 7.44br (3 H, disappears with D_2O); *m/e* 245, 247 (7%, M^+) and 215, 217 (80%, 100%, $M - CH_2NH_2$); *hydrochloride*, plates, m.p. 190 °C (sublimed at 10^{-3} mmHg and 150 °C) (Found: C, 38.2; H, 4.60; N, 5.1. $C_9H_{13}BrClNO_2$ requires C, 38.2; H, 4.65; N, 5.0%).

(l) 1-*Amino*-2-(2-*bromophenyl*)-4-(NN-*dibenzylamino*)-*butan*-2-*ol* (14a), 20 h at 60 °C were necessary, and aluminium chloride was used in place of zinc iodide, (67%) red oil, $\nu_{max.}$ (film) 3 200br (OH) and 1 560m cm^{-1} (NH_2); τ($CDCl_3$) 2.44—3.18 (14 h, m), 6.24 (4 H, s), 6.25 (1 H, d, *J* 13 Hz), 6.86 (1 H, d, *J* 13 Hz), and 7.32—7.84 (4 H, m) (Found: $M^+ - CH_2NH_2$, 408.092 6, 410.095 3. $C_{23}H_{23}BrNO$ requires $M^+ - CH_2NH_2$, 408.096 1. 410.094 2), *m/e* (no M^+), 420, 422 (14%, $M - H_2O$) and 407, 409 (100%, $M^+ - CH_3NH_2$).

(m) 1-*Amino*-2-(2-*bromophenyl*)-4-*dimethylaminobutan*-2-*ol* (14b) [as for (14a)], (50%) $\nu_{max.}$ (film) 3 340, 3 290, 1 560 (NH_2), and 3 200br cm^{-1} (OH); τ($CDCl_3$) 2.00—3.06 (4 H, m), 6.58 (1 H, d, *J* 13.0 Hz), 6.72br (3 H, disappears with D_2O), 7.06 (1 H, d, *J* 13.0 Hz), 7.60—8.00 (4 H, m), and 7.92 (6 H, s) (Found: $M^+ - CH_3NH_2$, 255.024 9, 257.026 1. $C_{11}H_{14}BrNO$ requires $M - CH_3NH_2$, 255.025 7, 257.023 8), *m/e* 286, 288 (0.4%, M^+), 256, 258 (2%, $M^+ - CH_2NH_2$) and 183, 185 (100%, *o*-$BrC_6H_4CO^+$).

(n) 1-*Amino*-2-(2-*bromophenyl*)-4-*diethylaminobutan*-2-*ol* (14c) [as for (14a)], (65%) $\nu_{max.}$ (film) 3 190br (OH), 3 080, 3 020w (ArC–H), and 1 560m cm^{-1} (NH_2); τ($CDCl_3$) 1.91—3.03 (4 H, m), 6.24—7.00br (3 H, disappears with D_2O), 6.62 (1 H, d, *J* 13.0 Hz), 7.18—8.00 (8 H, m), and 9.07 (6 H, t, *J* 7.0 Hz) (Found: $M^+ - CH_2NH_2$, 284.063 9, 286.063 3. $C_{13}H_{19}BrNO$ requires $M - CH_2NH_2$, 284.064 3, 286.063 0); *m/e* 314, 316 (2%, M^+), 296, 298 (15%, $M^+ - H_2O$), and 284, 286 (100%, $M - CH_2NH_2$).

(o) 1-*Amino*-2-(2-*bromophenyl*)-4-*piperidinobutan*-2-*ol* (14d) [as for (14a)], (64%), $\nu_{max.}$ (film) 3 160br (OH), 3 080, 3 060, 3 020w (ArC–H), and 1 560w cm^{-1} (NH_2); τ($CDCl_3$) 1.94—3.08 (4 H, m), 6.38 (1 H, d, *J* 13.0 Hz), 6.61br (3 H, disappears with D_2O), 7.03 (1 H, d, *J* 13.0 Hz), 7.20—8.06 (8 H, m), and 8.18—8.66 (6 H, m) (Found: $M^+ - CH_2NH_2$, 296.063 3, 298.063 6. $C_{14}H_{19}BrNO$ requires $M - CH_2NH_2$, 296.064 8, 298.062 9); *m/e* (no M^+), 296, 298 (12%, $M - CH_2NH_2$) 183, 185 (25%, *o*-$BrC_6H_4CO^+$), and 106 (100%, $C_6H_5COH^+$).

1-*Amino*-2-(2-*bromophenyl*)*pent*-4-*en*-2-*ol* (4h).—A solution of lithium di-isopropylamide (25 mmol) in THF (25 ml) was prepared by adding a solution of n-butyl-lithium (40 mol of a 1.6M solution in hexane; 25 mmol) to di-isopropylamine (3.55 ml, 25 mmol) in THF at −78 °C. The mixture was stirred under nitrogen for 10 min at −78 °C and a solution of (3f) in THF (10 ml) was added by syringe through a septum cap. A deep purple colour developed immediately and the mixture was stirred for a further 10 min at −78 °C to complete the formation of the anion. Freshly distilled allyl bromide (2.17 ml, 25 mmol) in THF (5 ml) was added and the mixture stirred at −78 °C for 3 h, and then allowed to warm to 15 °C over a further 3 h. The resulting solution was added to a cooled suspension of lithium aluminium hydride (30 mmol) in THF (25 ml) and heated under reflux for 2 h. After cooling, the excess hydride was destroyed with a saturated solution of sodium sulphate. The white granular precipitate so obtained was filtered off, washed well with ether (100 ml), and the total filtrate, including washings, extracted with hydrochloric acid (2M; 50 ml). The aqueous phase was separated, washed with ether (25 ml), basified to pH 13 with sodium hydroxide solution (2M), saturated with sodium chloride, and extracted with ether (3 × 50 ml). The organic extracts were washed with water (25 ml), dried ($MgSO_4$), and evaporated *in vacuo* to give the *amino-alcohol* (4h) (1.28 g, 20%) as a red gum, $\nu_{max.}$ (film) 3 300s,br (OH), 1 650m (C=C), 1 560m (NH_2), 995 and 915 cm^{-1} (CH=CH_2); τ($CDCl_3$) 2.20—3.15 (4 H, m), 4.05—4.64 (1 H, m), 4.92—5.18 (2 H, m), 6.36 (1 H, d, *J* 13.0 Hz), 7.18 (1 H, d, *J* 13.0 Hz), 7.25br (3 H, disappears with D_2O), and 7.38—7.62 (2 H, m) (Found: 224.991 5, 226.989 6. $C_{10}H_{10}BrO$ requires 224.991 4, 226.989 5); *m/e* 255, 257 (3%, M^+), 225, 227 (16%, $M - CH_2NH_2$), and 183, 185 (100%, *o*-$BrC_6H_4CO^+$).

Preparation of the Indoles (5), (9), *and* (15).—3-*Methylindole* (5a). 1-Amino-2-(2-bromophenyl)propan-2-ol (4a) (900 mg, 3.9 mmol) in anhydrous methanol (25 ml) previously saturated at 0 °C with ammonia was heated in a sealed tube for 72 h at 160 °C. The solvent was evaporated *in vacuo* and the residue partitioned between ether (50 ml) and hydrochloric acid (2M; 50 ml). The aqueous phase was further extracted with ether (3 × 25 ml) and the combined organic extract was washed with water (25 ml) and dried ($MgSO_4$). Removal of the solvent *in vacuo* gave 3-methylindole (5a) (425 mg, 82%), identical (mixed m.p., i.r., and n.m.r.) with authentic material. A closely similar reaction with (4a; Cl for Br) also gave (5b) in 70% yield.

The following indoles were prepared by a similar procedure except that, for the indoles (9a—c), the oxiran (7) was heated in methanol with the corresponding amine, and no attempt was made to isolate the corresponding amino-alcohols; for the tryptamines (15), the acid-work-up was omitted.

(a) 3-*Phenylindole* (5b). 72 h at 150 °C, (83%), plates m.p. 89 °C (lit.,[24] m.p. 88—89 °C) (Found: C, 87.1; H, 5.75; N, 7.4. Calc. for $C_{14}H_{11}N$. C, 87.0; H, 5.70; N, 7.3%), $\nu_{max.}$ (Nujol) 3 480m cm^{-1} (NH); *m/e* 193 (100%, M^+), 192 (11%, $M - H$), and 164 (22%, $-CH_2N$). The following variations were tried in the case of 3-phenylindole (i) As above, but using benzylamine in place of ammonia; only 3-phenylindole (5b) was produced (83%). (ii) Ethanol was used in place of methanol without affecting the yield significantly (81%). (iii) t-Butyl alcohol was used in place of methanol with a small drop in yield (74%). (iv) Ethylene glycol was used in place of methanol with a

small drop in yield (69%). (v) When ethanolamine was used in place of the ammoniacal methanol, no reaction occurred after 72 h at 150 °C; starting material was recovered (95%). (vi) The following ammoniacal solvents gave lower yields: hexamethylphosphoric triamide (55%); dimethylformamide (35%); acetonitrile (22%); and dimethyl sulphoxide (20%). (vii) Aqueous ammonium hydroxide or water or methanol without the ammonia each gave complex mixtures of products.

(b) 3-*Allylindole* (5h). 120 h, at 160 °C, (69%), b.p. 128—129 °C/0.1 mmHg (lit.,[25] 120 °C/0.05 mmHg). The spectroscopic data (i.r., n.m.r., and mass spectrum) were identical with those reported.

(c) 5-*Methoxy*-3-*methylindole* (5c). 100 h at 160 °C, (52%), identical (i.r., n.m.r. and mass spectrum) with that obtained by the benzyne route.

(d) 3-*Ethyl*-5-*methoxyindole* (5d). 100 h at 160 °C, (50%), identical (mixed m.p., i.r., n.m.r., and mass spectrum with that obtained by the benzyne route.

(e) 5-*Chloro*-3-*methylindole* (5e). From (4e), 200 h, at 160 °C, (20%), plates, m.p. 114—116 °C (from EtOH–ether) (Found: C, 64.6; H, 4.7; N, 7.9. C_9H_8ClN requires C, 64.8; H, 4.8; N, 8.3%), $\nu_{max.}$ ($CHCl_3$) 3 500 m cm^{-1} (NH); τ($CDCl_3$) 2.05—2.40br (1 H, disappears with D_2O), 2.54 (1 H, d, *J* 9.0 Hz), 2.75 (1 H, d, *J* 2.5 Hz), 2.93 (1 H, dd, *J* 2.5 and 9.0 Hz), 3.11 (1 H, m), and 7.70 (3 H, s) (Found: M^+, 165.034 0, 167.031 3. C_9H_8ClN requires M^+, 165.034 5, 167.031 5), $\lambda_{max.}$ (EtOH) 231, 281, 287, and 296 nm (ε 23 000, 4 900, 5 200, and 4 700). Heating (4e; Cl for Br) for 400 h at 160 °C gave the same indole (22%). The addition of catalytic or equivalent amounts of cuprous chloride, cuprous iodide, or nickel bromide to the ammoniacal methanol solutions described above made no difference to the yield of (5e).

(f) *Indole* (5f). (a) From (4f), 240 h at 160 °C (17%), plates, m.p. 52 °C (from EtOH) (lit.,[7] m.p. 52 °C); (b) from (4f; Cl for Br), 240 h at 160 °C (13%), identical (t.l.c., mixed m.p., i.r., n.m.r., and mass spectrum) with an authentic sample.

(g) 7-*Methyl*-5H-[1,3]*dioxolo*[4,5-f]*indole* (9a). 120 h at 160 °C, (79%), plates, m.p. 87—89 °C [from ether–light petroleum (b.p. 60—80 °C)] (Found: C, 68.7; H, 5.35; N, 7.9. $C_{10}H_9NO_2$ requires C, 68.5; H, 5.20; N, 7.9%), $\nu_{max.}$ ($CHCl_3$) 3 475 m cm^{-1} (NH); τ($CDCl_3$) 2.08—2.60br (1 H), 3.04 (1 H, s), 3.18 (1 H, m), 3.22 (1 H, s), 4.08 (2 H, s), and 7.72 (3 H, s); *m/e* 175 (100%, M^+); $\lambda_{max.}$ (EtOH) 228, 286, and 312 nm (ε 12 865, 4 400, and 7 900).

(h) 5,7-*Dimethyl*-5H-[1,3]*dioxolo*[4,5-f]*indole* (9b). Using methylamine (0.62 g, 20 mmol) in place of ammonia and heating for 300 h at 160 °C, (52%), needles, m.p. 73—75 °C (sublimed at 100 °C and 1.0 mmHg), $\nu_{max.}$ ($CHCl_3$) 3 080 and 3 020m (ArC–H), 2 960 and 2 885w (aliphatic C–H), 1 235, and 1 040 s cm^{-1} (=C–O–C); τ($CDCl_3$) 3.12 (1 H, s), 3.32 (1 H, s), 3.35 (1 H, s), 4.12 (2 H, s), 6.40 (3 H, s), and 7.78 (3 H, s) (Found: 189.078 5. $C_{11}H_{11}NO_2$ requires 189.078 9); *m/e* 189 (100%, M^+) and 131 (14%, $M^+ - CO - CH_2O$).

(i) 5-*Benzyl*-7-*methyl*-5H-[1,3]*dioxolo*[4,5-f]*indole* (9c). Using benzylamine (0.87 g, 8.2 mmol) in place of ammonia and heating for 300 h at 160°, (60%), plates, m.p. 80—82 °C (sublimed at 110 °C and 10^{-3} mmHg) (Found: C, 76.6; H, 5.65; N, 5.1. $C_{17}H_{15}NO_2$ requires C, 76.9; H, 5.70; N, 5.3%), $\nu_{max.}$ ($CHCl_3$) 2 920, 2 850, and 2 780w (saturated CH stretch), 1 240s, and 1 037s cm^{-1} (=C–O–C); τ($CDCl_3$) 2.64—3.00 (5 H, m), 3.07 (1 H, s), 3.24 (1 H, s), 3.34 (1 H, s), 4.12 (2 H, s), 4.86 (2 H, s), and 7.75 (3 H, s); *m/e* 265 (100%, M^+) and 174 (52%, $M^+ - CH_2Ph$).

(j) 3-(2-*Dimethylaminoethyl*)*indole* (15b). 170 h at 160 °C (62%), plates, m.p. 46 °C [from EtOH – light petroleum (b.p. 60—80 °C)] (lit.,[26] m.p. 45—47 °C) identical (t.l.c., mixed m.p., i.r., n.m.r. and mass spectrum) with an authentic sample.

(k) 3-(2-*Diethylaminoethyl*)*indole* (15c). 170 h at 160 °C, followed by chromatography on Florosil (50 g) with chloroform–methanol (4 : 1) as eluant gave (15c) (71%), needles, m.p. 87—89 °C (from EtOH) (lit.,[27] m.p. 85—88 °C) identical (t.l.c., mixed m.p., i.r., n.m.r. and mass spectrum) with an authentic sample.

(l) N-(2-*Indol*-3-*ylethyl*)*piperidine* (15d). 170 h at 160 °C (63%), colourless needles, m.p. 152 °C (lit.[28] m.p. 151—152 °C) identical (t.l.c., mixed m.p., i.r., and mass spectrum) with an authentic sample.

(m) 3-(2-*Aminoethyl*)*indole* (15e). Starting with (14a), 170 h at 160 °C followed by evaporation *in vacuo* gave a solid residue of (15a) which was taken up in ethanol (15 ml) containing perchloric acid (3 drops), and hydrogenated in the presence of 10% palladium–charcoal for 12 h.[29] The catalyst was removed by filtration, washed with ethanol (2 × 20 ml), and the filtrate concentrated *in vacuo* to give (15e) (203 mg, 56%) as needles, m.p. 115 °C [from EtOH–light petroleum (b.p. 60—80 °C)] (lit.,[7] 116—117 °C), identical (t.l.c., mixed m.p., i.r., n.m.r., and mass spectrum) with an authentic sample.

The authentic samples of the tryptamines (15b), (15c), and (15d) were made from indole-3-acetic acid and the appropriate amine by the method of Shaw.[30]

2′-*Bromo*-3-*chloropropiophenone* (11).—Ethylene was passed through a stirred solution of the complex formed between *o*-bromobenzoyl chloride (10) (18.8 g, 0.085 mol) and aluminium chloride (11.5 g, 0.085 mol) in tetrachloroethane (150 ml) for 48 h at room temperature.[31] The reddish brown solution was poured into a mixture of ice and dilute hydrochloric acid and then extracted with ether (3 × 25 ml), and water (3 × 25 ml), dried ($MgSO_4$), and evaporated *in vacuo* to give a mixture of the ketones (11) and (12). Dry hydrogen chloride was passed through a solution of this mixture in dry ether (100 ml) at 0 °C. Evaporation of the solvent under reduced pressure and distillation gave the *ketone* (11) (17.2 g, 83%), b.p. 84 °C/0.3 mmHg (with decomposition), $\nu_{max.}$ (film) 3 080 and 3 020w ArC–H), and 1 700s (C=O) cm^{-1}; τ($CDCl_3$) 2.27—2.85 (4 H, m), 6.14 (2 H, t, *J* 6 Hz), and 6.60 (2 H, t, *J* 6 Hz) (Found: M^+, 245.944 2, 247.941 7, 249.939 8. C_9H_8BrClO requires 245.944 6, 247.942 7, 249.939 0), *m/e* 210, 212 (32%, $M^+ - HCl$) and 183, 185 [100%, $M^+ - (CH_2)_2Cl$].

2′-*Bromo*-3-NN-*dibenzylaminopropiophene* (13a).—Triethylamine (10.1 g, 0.1 mol) was added to a stirred solution of the ketone (11) (6.2 g, 0.025 mol) in ether (25 ml) and stirring continued for 30 min. The precipitate was filtered off and washed with ether, and the filtrates concentrated *in vacuo*. Triethylamine was added to the resulting solution, and the whole procedure repeated, until precipitation was complete. (The disappearance of the CH_2CH_2Cl signals and the growth of the $CH{=}CH_2$ signals in the n.m.r. spectrum is a useful guide). Dibenzylamine (7.43 g, 0.025 mol) in ether (10 ml) was then added to the ketone (12) in ether (25 ml) and kept at 30 °C until the n.m.r. spectrum shows the disappearance of the $CH{=}CH_2$ signals (usually 1—2 h). The ether was evaporated to give the β-*amino-ketone* (13a) as a yellow oil, $\nu_{max.}$ (film) 3 095 and 3 080w (ArC–H) and

1 700 s cm^{-1} (C=O); τ($CDCl_3$) 2.6—3.05 (14 H, m), 6.27 (4 H, s), 6.45 (2 H, s), and 7.05 (2 H, s) (Found: M^+, 409.085 2, 407.082 9. $C_{23}H_{22}BrNO$ requires M^+, 409.086 4, 407.083 3), *m/e* 316, 318 (67%, $M^+ - CH_2Ph$), and 210, 212 (100% *o*-$BrC_6H_4COCH{=}CH_2^+$).

The following β-amino-ketones were made similarly except that for the low-boiling amines an excess of amine (0.035 mol) was used.

(a) *2′-Bromo-3-NN-dimethylaminopropiophenone* (13b). $\nu_{max.}$ (film) 3 095 and 3 080w (Ar–H), 1 700 cm^{-1} s (C=O); τ($CDCl_3$) 2.40—3.15 (4 H, m), 7.15 (2 H, t, *J* 6.0 Hz), 7.55 (2 H, t, *J* 6.0 Hz), and 8.03 (6 H, s) (Found: M^+, 255.027 1, 257.022 3. $C_{11}H_{14}BrNO$ requires 255.025 7, 257.023 8), *m/e* 210, 212 (22%, 24%, $M^+ - Me_2NH$), and 183, 185 (100%, *o*-$BrC_6H_4CO^+$).

(b) *2′-Bromo-3-NN-diethylaminopropiophenone* (13c). $\nu_{max.}$ (film) 3 110 and 3 050w (ArC–H) and 1 708 cm^{-1} s (C=O); τ($CDCl_3$) 2.30—2.94 (4 H, m), 6.80—7.16 (4 H, 2t overlapping), 7.51 (4 H, q, *J* 7.5 Hz, 2 × CH_2CH_3), 9.03 (6 H, t, *J* 7.5 Hz, 2 × CH_2CH_3) (Found: 283.056 7, 285.055 9, $C_{13}H_{18}BrNO$ requires 283.057 0 and 285.055 2), *m/e* 254, 256, (30%, 28%, $M^+ - Et$), and 183, 185 (100%, *o*-$BrC_6H_4CO^+$).

(c) *2′-Bromo-3-N-piperidinopropiophenone* (13d). $\nu_{max.}$ (film) 3 080w (ArC–H) and 1 675 s cm^{-1} (C=O); τ($CDCl_3$) 1.90—2.50 (4 H, m), 6.60 (2 H, t, *J* 6.0 Hz), 7.00 (2 H, t, *J* 6.0 Hz), 7.1—7.45 (4 H, m), and 7.85—8.45 (6 H, m) (Found: 295.055 6, 297.056 5, $C_{14}H_{18}BrNO$ requires 295.057 0, 297.055 1), *m/e* 295, 297 (1%, M^+), 183, 185 [11%, 10% $M - C_5H_{10}N(CH_2)_2$], and 98 (100% $C_5H_{10}NCH_2^+$). None of the ketones (13) gave an epoxide on treatment either with Corey's reagent [21] or with Johnson's.[32]

2-(2-Bromophenyl)-2-methylpropionitrile.—A solution of 2-bromobenzyl cyanide [33] (5.0 g 25.5 mmol) was added *via* a syringe to a stirred solution of lithium di-isopropylamide in dry THF (200 ml) [prepared from di-isopropylamine (7.2 ml, 51 mmol) and n-butyl-lithium (39.3 ml of a 1.3M solution in hexane, 51 mmol)] at −78 °C under nitrogen. A black colour developed immediately and the mixture was stirred for a further 10 min to complete the formation of the anion. A solution of methyl iodide (14.5 g, 51 mmol) in THF (50 ml) was added and the mixture stirred at −78 °C for 1 h, allowed to warm to room temperature over a further 1 h, and then poured into water (250 ml) and extracted with ether (3 × 50 ml). The organic extracts were washed with hydrochloric acid (2M; 50 ml) and water (50 ml), dried ($MgSO_4$), and evaporated *in vacuo*. Distillation of the residue gave the *nitrile* (4.5 g, 79%), b.p. 82 °C/0.5 mmHg, $\nu_{max.}$ (film) 2 230m cm^{-1} (CN); τ($CDCl_3$) 2.30—3.05 (4 H, m) and 8.15 (6 H, s) (Found: M^+, 222.999 3, 224.996 7. $C_{10}H_{10}BrN$ requires 222.999 6, 224.997 7), *m/e* 208, 210 (100%, $M^+ - CH_3$), and 180, 182 (86%, $M^+ - CH_3CN$).

2-(2-Bromophenyl)-2-methylpropylamine (19).—A solution of 2-(2-bromophenyl)-2-methylpropiononitrile (4.0 g, 17.8 mmol) in dry THF (10 ml) was added to a suspension of lithium aluminium hydride (1.00 g, 25 mmol) in THF (50 ml) at a rate which maintained a gentle reflux. The mixture was heated under reflux for a further 2 h, allowed to cool, and the excess hydride was destroyed with a saturated solution of sodium sulphate. The granular precipitate was filtered off, washed with ether (3 × 50 ml), and extracted with hydrochloric acid (2M, 50 ml). The aqueous layer was washed with ether (20 ml), basified to pH 13 by the addition of sodium hydroxide solution (2M), saturated with sodium chloride, and extracted with ether (4 × 50 ml). The organic extracts were washed with water, dried ($MgSO_4$), and evaporated *in vacuo* to give the *amine* (19) (3.41 g, 84%), $\nu_{max.}$ (film) 3 340, 3 260, and 1 560 cm^{-1} (NH_2); τ(DMSO) 2.37—3.08 (4 H, m), 6.78 (2 H, s), and 8.53 (6 H, s) (Found: $M^+ - NH_2$, 211.012 3, 213.010 7. $C_{10}H_{12}Br$ requires 211.012 1, 213.010 2), *m/e* (No M^+), 211, 213 (21%, $M^+ - NH_2$), 196, 198 (22, $M^+ - CH_2NH_2$), and 148 (100%, $M^+ - Br$).

3,3-Dimethylindoline (20).—2-(2-Bromophenyl)-2-methylpropylamine (19) (900 mg, 4.0 mmol) in dry methanol (25 ml), previously saturated at 0 °C with ammonia, was heated in a sealed tube for 170 h at 160 °C. The solvent was evaporated *in vacuo* and the residue was chromatographed on silica (50 g) with chloroform as eluant to give the indoline (20) (330 mg, 57%), needles, m.p. 34 °C [from light petroleum (b.p. 60—80 °C)] (lit.,[34] m.p. 34 °C), the spectroscopic data (i.r., n.m.r. and mass spectrum) were identical with those reported.[35]

2-(2-Bromophenyl)propane-1,2-diol (21a).— *o*-Bromo-α-methylstyrene (7.0 g, 34 mmol) was added dropwise to a stirred solution of *N*-methylmorpholine *N*-oxide hydrate (7.3 g, 42 mmol) and osmium tetraoxide [40 mg dissolved in t-butyl alcohol (8 ml)] in aqueous acetone (75 ml) under nitrogen [36] and the mixture stirred overnight. A slurry of sodium hydrosulphite (1.0 g) and Florisil (12.0 g) in water (80 ml) was added, and the mixture stirred for a further 30 min. The Florisil was filtered off, washed with acetone (25 ml), and the filtrate neutralised to pH 7 by the careful addition of dilute sulphuric acid (2M). The acetone was then evaporated *in vacuo*, the pH adjusted to pH 2, the solution saturated with sodium chloride, and extracted with ethyl acetate (3 × 50 ml). The ethyl acetate was dried ($MgSO_4$) and evaporated *in vacuo*, and the residue distilled to give the *diol* (21a) (6.0 g, 77%), b.p. 117 °C/0.4 mmHg (Found: C, 47.1; H, 4.60; Br, 34.3. $C_9H_{11}BrO_2$ requires C, 46.8; H, 4.80; Br, 34.6%), $\nu_{max.}$ (Nujol) 3 250s, br cm^{-1} (OH); τ($CDCl_3$) 1.95—3.00 (4 H, m), 5.73 (1 H, d, *J* 12 Hz), 6.10 (1 H, d, *J* 12 Hz), 6.25br (2 H, disappears with D_2O), and 8.37 (3 H, s); *m/e* 183, 185 (6% 6%, $BrC_6H_4CO^+$).

3-Methylbenzofuran (22a).—2-(2-Bromophenyl)propane-1,2-diol (21a) (1.0 g, 4.3 mmol) was suspended in anhydrous methanol (20 ml) saturated at 0 °C with ammonia, and heated in a sealed tube at 160 °C for 580 h. After cooling, the solvent was evaporated *in vacuo* and the residue chromatographed on silica (75 g). Elution with chloroform gave 3-methylbenzofuran (22a) (0.31 g, 54%), identical (i.r., n.m.r., and mass spectrum) with an authentic sample, and 2-(2-bromophenyl)propane-1,2-diol (21a) (0.38 g). The effective yield of (22a) (based on unrecovered starting material) was 86%.

1-(2-Bromophenyl)-1-phenylethane-1,2-diol (21b).—The *diol* was obtained in 61% yield by the method given for the preparation of (21a), b.p. 158—160 °C/0.5 mmHg, $\nu_{max.}$ (neat) 3 500s cm^{-1} (OH); τ(CCl_4) 2.05—3.25 (9 H, m), 6.02 (2 H, s), and 6.63br (2 H, disappears with D_2O) (Found: $M^+ - CH_2OH$, 261.993 0, 263.993 3. $C_{13}H_{13}BrO_2$ requires 261.994 7, 263.992 8), *m/e* (no M^+), 261, 263 (100%, $M^+ - CH_2OH$) and 183, 185 (67%, *o*-$BrC_6H_4CO^+$).

3-Phenylbenzofuran (22b).—1-(2-Bromophenyl)-1-phenylethane-1,2-diol (21b) (584 mg, 2.0 mmol) was suspended in anhydrous methanol (25 ml), saturated at 0 °C with ammonia, and heated in a sealed tube for 168 h at 160 °C. After cooling, the solvent was evaporated *in vacuo* and the residue was chromatographed on silica (30 g). Elution

with chloroform gave (22b) (220 mg, 57%) as plates, m.p. 42 °C (ether) (lit.,[37] m.p. 42 °C), $\nu_{max.}$ (neat) 3 080 and 3 020w cm^{-1} (ArC–H), $\tau(CDCl_3)$ 2.22—3.18 (10 H, m); *m/e* 194 (100%, M^+).

2-(2-*Bromophenyl*)-1-*mercaptopropan*-3-*ol* (1c). 2-(2-Bromophenyl)-2-methyloxiran (2b) (5.0 g, 23.5 mmol) and sodium hydrogen sulphide (0.14 g, 2.5 mmol) were suspended in anhydrous methanol (35 ml), saturated at 0 °C with hydrogen sulphide, and heated in a sealed tube for 6 h at 110 °C. After cooling, the solvent was evaporated under reduced pressure and the residue was chromatographed on Florosil (250 g). Elution with chloroform gave 2-(2-*bromophenyl*)-1-*mercaptopropan*-3-*ol* (21c) (4.01 g, 71%) further purified by distillation, b.p. 96 °C/0.6 mmHg, $\nu_{max.}$ (neat) 2 590w (SH) and 3 510s cm^{-1} (OH); $\tau(CDCl_3)$ 2.07—3.00 (4 H, m), 6.20 (1 H, dd, *J* 7.0 and 14.0 Hz, 1 H of methylene), 6.92br (1 H, disappears with D_2O), 7.14 (1 H, dd, *J* 11.5 and 14.0 Hz, 1 H of methylene), 8.28 (3 H, s), and 9.18 (1 H, dd, *J* 7.0 and 11.5 Hz, SH) (Found: $M^+ - CH_2SH$, 198.975 8, 200.973 8. C_8H_8BrO requires 198.976 0, 200.975 2), *m/e* (no M^+), 199, 201 (100%, 100% $M - CH_2SH$), 183, 185 (15%, 15%, $BrC_6H_4CO^+$), and 166 (18%, M — HBr), Further elution gave 2,7-*bis*-(2-*bromophenyl*)-4,5-*dithiaoctane*-2,7-*diol* as a mixture of diastereoisomers, $\nu_{max.}$ (film) 3 500s cm^{-1} (OH); $\tau(CDCl_3)$ 2.16—3.02 (8 H, m), 6.07 (1 H, d, *J* 5.5 Hz), 6.21 (1 H, d, *J* 5.5 Hz), 6.62 (1 H, d, *J* 3.0 Hz), 6.77 (1 H, d, *J* 3.0 Hz), 6.70—6.92 (2 H, br disappears with D_2O), and 8.24 (6 H, s).

3-*Methylbenzothiophen* (22c).—2-(2-Bromophenyl)-1-mercaptopropan-3-ol (21c) (494 mg, 2 mmol) was suspended in methanol (25 ml) saturated at 0 °C with ammonia, and heated in a sealed tube for 168 h at 160 °C. After cooling, the solvent was evaporated *in vacuo* and the residue was chromatographed on silica (25 g). Elution with chloroform gave 3-methylbenzothiophen (22c) (151 mg, 51%) as a pale yellow oil, b.p. 104 °C/9 mmHg (lit.,[38] b.p. 125—127 °C/25 mmHg). $\nu_{max.}$ (film) 3 110 and 3 000 m cm^{-1} (ArC–H); $\tau(CDCl_3)$ 2.16—2.52 (2 H, m), 2.64—2.96 (2 H, m), 3.07 (1 H, s) and 7.63 (3 H, s) (Found: M^+, 148.032 3. C_9H_8S requires M, 148.034 7).

1-(2-*Bromophenyl*)-2-*mercapto*-1-*phenylethanol* (21d).—The major product from (2c) using the conditions described for the preparation of (21c) was 1,6-*bis*-(2-*bromophenyl*)-1,6-*diphenyl*-3,4-*dithiahexane*-1,6-*diol* (92%), as a mixture of diastereoisomers, $\nu_{max.}$ (film) 3 500s cm^{-1} (OH); $\tau(CDCl_3)$ 2.10—2.32 (2 H, m), 2.48—3.12 (16 H, m), 5.66—6.40 (4 H, complex), and 6.00—6.40br (2 H, disappears with D_2O); *m/e* 614, 616, 618 (0.1%, M^+), 535, 537 (3%, M^+ — Br), and 261, 263 (100%, *o*-$BrC_6H_4CO^+C_6H_5$). Reduction of this disulphide with lithium aluminium hydride gave the *mercaptoethanol* (21d), $\nu_{max.}$ (film) 3 500 s (OH) and 2 590 w cm^{-1} (SH); $\tau(CDCl_3)$ 2.12—3.08 (9 H, m), 5.68—6.38 (2 H complex), and 7.93 (1 H, d, *J* 10 Hz) (Found: $M^+ - H_2O$, 289.971 9, 291.970 0. $C_{13}H_{10}BrS$ requires 289.972 4, 291.970 6), *m/e* (no M^+), 290, 292 (30%, $M^+ - H_2O$) and 261, 263 (100%, *o*-$BrC_6H_4CO^+C_6H_5$).

3-*Phenylbenzothiophen* (22d).—From (21d), (53%), b.p. 134 °C/1 mmHg (lit.,[39] b.p. 132—135 °C/1 mmHg) $\nu_{max.}$ (film) 3 090 and 3 010w cm^{-1} (ArC–H), $\tau(CDCl_3)$ 2.02—2.17 (1 H, m) and 2.34—2.94 (9 H, m); *m/e* 210 (100%, M^+) and 178 (38%, M^+ — S).

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REFERENCES

[1] I. Fleming and M. Woolias, preceding paper.
[2] A. Tambute, *Compt. rend.*, 1974, **278C**, 1239.
[3] D. Seebach and M. Kolb, *Chem. and Ind.*, 1974, 687.
[4] T. Kametani, S. Takano, S. Hibino, and M. Takeshita, *Synthesis*, 1972, 475 and references therein; M. Julia, J. Bagot and O. Siffert, *Bull. Soc. chim. France*, 1973, 1424.
[5] C. Szantay, L. Szabo, and G. Kalaus, *Synthesis*, 1974, 354.
[6] H. Gilman, C. G. Brannen, and R. K. Ingham, *J. Amer. Chem. Soc.*, 1956, **78**, 1689.
[7] ' Dictionary of Organic Compounds ', ed. I. Heilbron, Eyre and Spottiswoode, London, 1969.
[8] M. J. S. Dewar and A. P. Marchand, *J. Amer. Chem. Soc.*, 1966, **98**, 3318; E. L. Eliel and K. W. Nelson, *J. Chem. Soc.*, 1955, 1628.
[9] K. Kaji, H. Nagashima, K. Mashimo, Y. Naka, and K. Shigezane, *Gifu Yakka Daigaku Kivo*, 1966, **16**, 45.
[10] E. J. Corey and J. W. Suggs, *Tetrahedron Letters*, 1975, 2647.
[11] M. S. Koopal, *Rec. Trav. chim.*, 1915, **34**, 115.
[12] E. Bergmann, *J. Org. Chem.*, 1939, **4**, 1.
[13] R. Pschorr, *Annalen*, 1912, **391**, 23.
[14] W. H. Perkin, *Annalen*, 1868, **145**, 301.
[15] M. S. Gibson, G. W. Prenton, and J. M. Walthew, *J. Chem. Soc.* (*C*), 1970, 2234.
[16] W. J. Horton and D. E. Robertson, *J. Org. Chem.*, 1960, **25**, 1016.
[17] S. Kimoto, K. Asaki, M. Kozuka, and A. Ayada, *J. Pharm. Soc. Japan*, 1953, **73**, 506.
[18] T. de Crauw, *Rec. Trav. chim.*, 1931, **50**, 753.
[19] E. Oertly and A. Pictet, *Ber.*, 1910, **43**, 1336.
[20] A. H. Parijs, *Rec. Trav. chim.*, 1930, **49**, 17.
[21] E. J. Corey and M. J. Chaykovsky, *J. Amer. Chem. Soc.*, 1962, **84**, 867 and 1965, **87**, 1353.
[22] E. A. Khrustaleva, M. A. Bulatov and S. S. Spasskii, *Tr. Inst. Khim. Akad. Nauk S.S.R., Ural Filial.*, 1966, **13**, 13; *Chem. Abs.*, 1968, **68**, 87339.
[23] A. A. Santilli and T. S. Osdene, *J. Org. Chem.*, 1964, **29**, 1998.
[24] E. Fischer and T. Schmidt, *Ber.*, 1888, **21**, 1811.
[25] B. Cardillo, G. Casnati, A. Pochini, and A. Ricca, *Tetrahedron*, 1967, **23**, 3771.
[26] F. A. Hochstein and A. M. Paradies, *J. Amer. Chem. Soc.*, 1957, **79**, 5735.
[27] T. Nogradi, *Monatsh.*, 1957, **88**, 768.
[28] R. C. Elderfield, B. Fischer, and J. M. Lagowski, *J. Org. Chem.*, 1957, **22**, 1376.
[29] A. F. Ames, D. E. Ames, C. R. Coyne, T. F. Grey, I. M. Lockhart, and R. S. Ralph, *J. Chem. Soc.*, 1959, 3388.
[30] E. Shaw, *J. Amer. Chem. Soc.*, 1955, **77**, 4319.
[31] M. G. Perrier, *Bull. Soc. chim. France*, 1904, **31**, 859.
[32] C. G. Overberger and J. H. Saunders, *Org. Synth.*, Coll. Vol. 3, 1955, 204.
[33] M. Julia and H. Gaston-Breton, *Bull. Soc. chim. France*, 1966, 1335.
[34] M. Kates and L. Marion, *Canad. J. Chem.*, 1951, **29**, 37.
[35] A. H. Jackson and A. E. Smith, *Tetrahedron*, 1965, **21**, 989.
[36] V. VanRheenan, R. C. Kelly, and D. Y. Cha, *Tetrahedron Letters*, 1976, 1973.
[37] R. Stoermer and O. Kippe, *Ber.*, 1903, **36**, 3992.
[38] E. G. G. Werner, *Rec. Trav. chim.*, 1949, **68**, 509.
[39] S. Dayagi, I. Goldberg, and U. Shmueli, *Tetrahedron*, 1970, **26**, 411