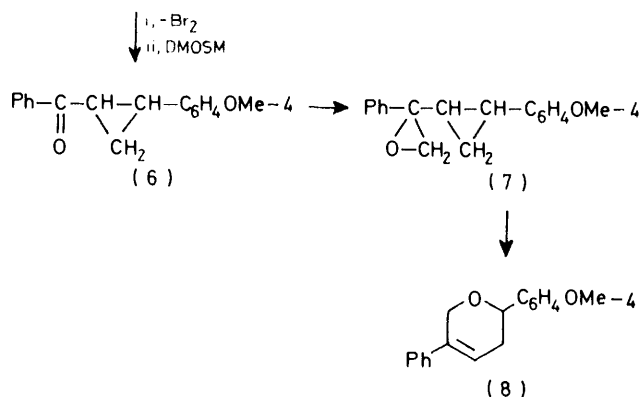
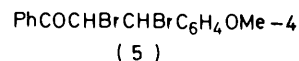
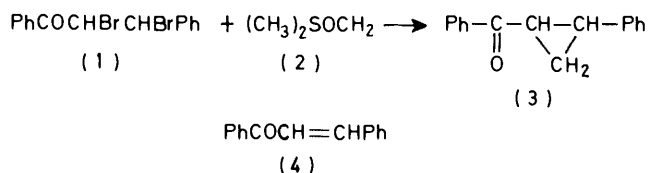


Cyclopropyl Epoxides. Reactions of Some $\alpha\beta$ -Dibromoketones with Dimethylloxosulphonium Methylide

By John A. Donnelly,* M. John Fox, and James G. Hoey, Chemistry Department, University College, Dublin 4, Ireland

2,3-Dibromo-3-phenylpropionophenones eliminated both bromine and hydrogen bromide on reaction with dimethylloxosulphonium methylide (DMOSM); the resulting $\alpha\beta$ -unsaturated ketones formed cyclopropyl ketones which, when suitably substituted, continued to react with DMOSM, forming a variety of heterocyclic products. A contiguous cyclopropyl epoxide underwent ring-opening oxymercuration with mercuric acetate *via* 5-oxypent-2-en-1-ols. A cyclopropylcyclopropane analogue of the epoxide was stable at 300 °C.

CHALCONES (4) react¹ readily with dimethylloxosulphonium methylide (DMOSM) (2) to form, often quantitatively, cyclopropyl ketones (3). These ketones can be converted² into cyclopropyl epoxides (7) by reaction

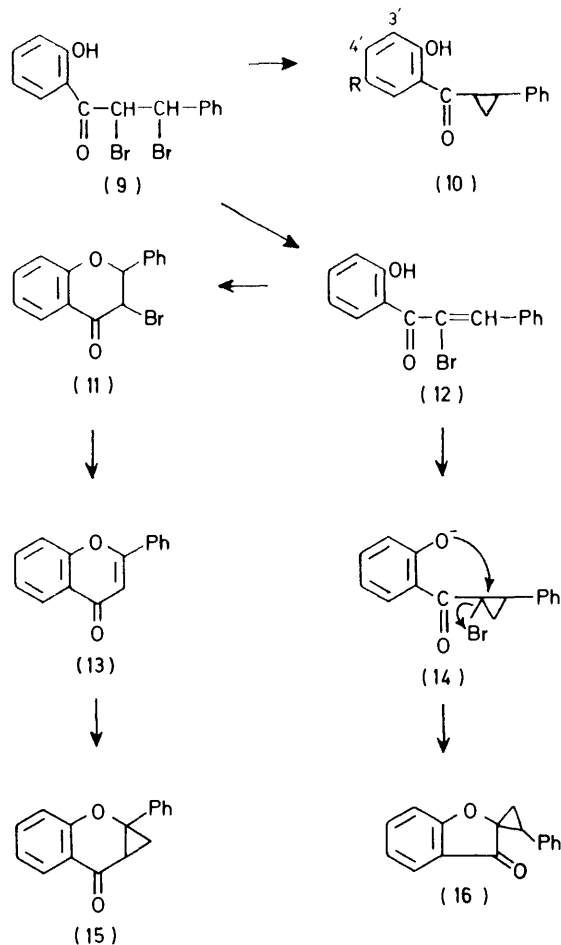


with DMOSM or dimethylsulphonium methylide (DMSM). The cyclopropyl ketones and epoxides are useful³ for the synthesis of a wide variety of compounds. Bravo *et al.*,⁴ have shown that α -halogeno-ketones readily form cyclopropyl ketones by reaction with DMOSM. Described here are some reactions of $\alpha\beta$ -dihalogeno-ketones and related compounds with DMOSM.

Simple chalcone dibromide (1) reacted with DMOSM (2) to form *cis*- and *trans*-1-benzoyl-2-phenylcyclopropane (3). Thus the ylide or the solvent, dimethylsulphoxide,⁵ acts as a debrominating agent, converting the dihalide (1) into chalcone (4) before the ylide adds to give the cyclopropyl ketone (3) isomers. The more reactive system, 4-methoxychalcone dibromide (5), reacted more extensively and formed 2-(4-methoxyphenyl)-5-phenyl-3,6-dihydro-2*H*-pyran (8). The dihydropyran presumably results from dehalogenation of

the chalcone dibromide (5) to a chalcone, followed by reaction⁶ of the latter with DMOSM to form the dihydropyran (8) *via* a cyclopropyl ketone (6) and a cyclopropyl epoxide (7).

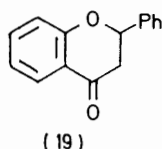
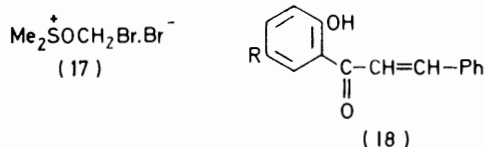
An *o*-hydroxy-substituent was incorporated into the chalcone dibromide system to trap intermediates in the methylide reaction and to divert its course. 2'-Hydroxychalcone dibromide (9), on reaction with DMOSM, gave, among several products, 1-(5-bromo-2-hydroxybenzoyl)-2-phenylcyclopropane (10; R = Br). This is the product of side-chain dehalogenation followed by nuclear halogenation and side-chain methylation. Also iso-



lated were 1-(2-hydroxybenzoyl)-2-phenylcyclopropane (10; R = H), a possible precursor of the previous cyclopropyl ketone (10; R = Br); 2'-phenylspiro[coumaran-2,1'-cyclopropan]-3-one (16), presumed to result from dehydrobromination⁷ of the substrate (9) to an α -bromochalcone (12), followed by conversion of the latter into a bromocyclopropyl ketone (14) and cyclization in the presence of the basic methyide to the spirocyclopropyl-coumaranone (16); and 2,3-methanoflavanone (15), resulting from cyclization of the α -bromochalcone (12) to 3-bromoflavanone (11), dehydrobromination to flavone (13) (which was also isolated), and methylenation⁸ to the cyclopropyl ketone (15).

The isolation of a nuclear halogenated product (10; R = Br) might indicate that debromination in the presence of DMOSM yields an effective brominating agent (17) but it is more likely, however, that nuclear halogenation is due to the conversion⁹ of the hydrogen bromide, eliminated in the formation of the other products, into bromine by the solvent dimethyl sulphoxide (DMSO).

The nuclear halogenated product (10; R = Br) was synthesized directly from 2'-hydroxy-5'-bromochalcone (18; R = Br) by reaction with DMOSM. 1-(2-Hydroxybenzoyl)-2-phenylcyclopropane (10; R = H) was similarly prepared from either 2'-hydroxychalcone (18;

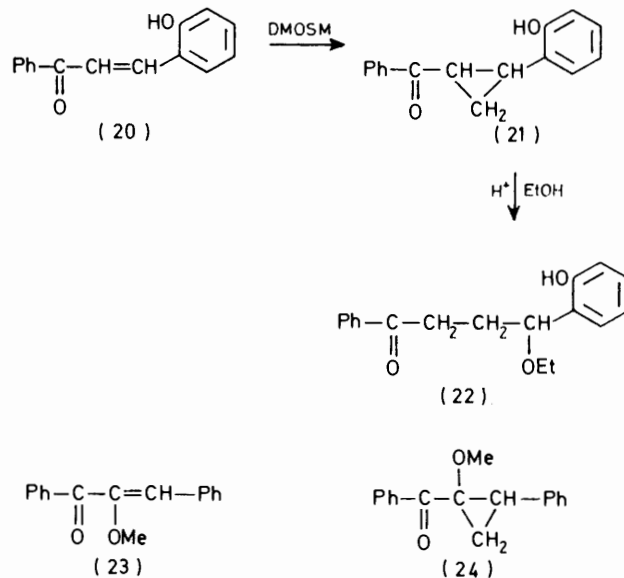


R = H) or flavanone (19); the latter undoubtedly isomerizes to the chalcone (18; R = H) before methylenation. In other reactions of chalcones with DMOSM, it was found that 2-hydroxychalcone (20) formed an unstable cyclopropyl ketone (21) which reacted with ethanol to give 4-ethoxy-4-(2-hydroxyphenyl)-1-phenylbutan-1-one (22). α -Methoxychalcone (23) gave a cyclopropyl ketone (24), but in poor yield.

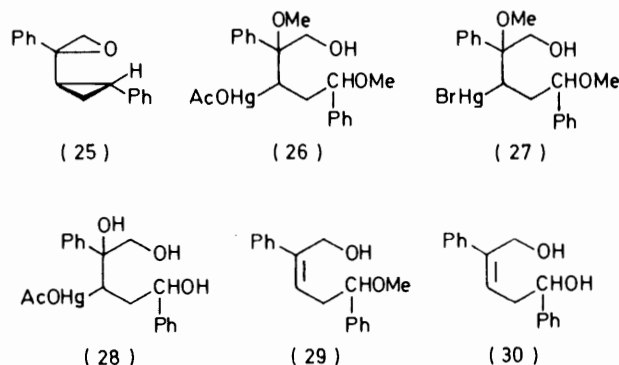
Cyclopropyl ketones react readily with DMOSM or DMSM to form,² as earlier mentioned, cyclopropyl epoxides. These epoxides rearrange^{2b,3b} spontaneously or under mildly acidic conditions to produce, mainly, a variety of cyclic products. These rearrangements are believed to be initiated by ring-opening of the heterocyclic ring. Described now is an attempt to initiate reaction by electrophilic mercuriation of the cyclopropane ring.¹⁰

trans-1-Phenyl-2-(2-phenyloxiran-2-yl)cyclopropane (25) was unreactive towards mercuric acetate in either diethyl ether or DMSO, with or without sodium acetate

or sodium perchlorate as catalyst.¹¹ In methanol, however, two diastereoisomers of the organomercurial (26) were obtained; these were quantitatively converted into diastereoisomers of the bromomercurial (27) by



potassium bromide. Mercuriation of the cyclopropyl epoxide (25) in aqueous tetrahydrofuran gave two diastereoisomers of the 3-acetoxymercuriopentan-1,2,5-triol (28), which were also converted into the corresponding bromomercurials. The structure of these mercuriation products suggested that the cyclopropyl epoxide (25) had ring-opened to the corresponding (*E*)-1-hydroxy-5-methoxypent-2-ene (29) and (*E*)-1,5-dihydroxypent-2-ene (30) prior to oxymercuriation. In agreement, these two pent-2-enes (29) and (30), prepared by solvolysis of the cyclopropyl epoxide (25), on oxymercuriation gave the same products (26) and (28) as were obtained by direct oxymercuriation of the cyclopropyl epoxide (25). The formation of only two of the

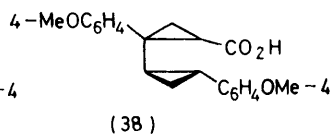
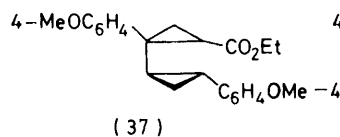
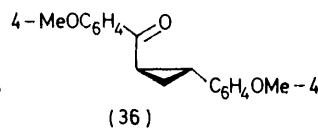
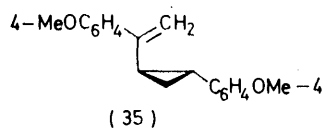
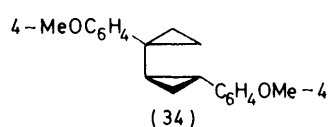
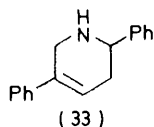
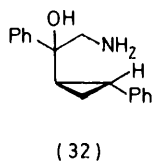
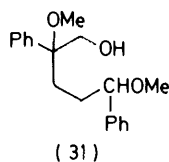


four possible diastereoisomers by each (*E*)-pent-2-ene is in keeping with a cyclic mercurinium ion intermediate¹² leading to exclusive *trans* addition.

Demercuriation of 3-acetoxymercurio-2,5-dimethoxy-2,5-diphenylpentan-1-ol (26) with sodium borohydride in

ethanol gave approximately equal amounts of the normal demercuration product, 2,5-dimethoxy-2,5-diphenylpentan-1-ol (31), and the deoxymercuration product (*E*)-1-hydroxy-5-methoxy-2,5-diphenylpent-2-ene (29). When the reaction was carried out in methanol, only the deoxymercuration product (29) was obtained. Deoxymercuration is usually carried out¹³ in acidic conditions; in basic media epoxides and ketones are formed.¹⁴

trans-1-Phenyl-2-(2-phenyloxiran-1-yl)cyclopropane (25) reacted cleanly with methanol-ammonia to form



trans-1-(2-amino-1-hydroxy-1-phenylethyl)-2-phenylcyclopropane (32) but an attempted synthesis of the tetrahydropyridine (33) by pyrolysis of the hydrochloride of this hydroxy-amine (32) failed, as the conditions for a reasonably clean reaction were not found.

It was observed that the contiguous dicyclopropane system in *trans*-1-(4-methoxyphenyl)-2-[1-(4-methoxyphenyl)cyclopropyl]cyclopropane (34), the alicyclic analogue of the thermally (room-temperature) unstable cyclopropyl epoxides,⁶ was stable at 300 °C. The dicyclopropane (34) was prepared in poor yield by a Simmons-Smith reaction on the vinyl cyclopropane (35) using a zinc-silver couple. No reaction occurred when the usual zinc-copper couple was used. *trans*-1-(4-Methoxyphenyl)-1-[2-(4-methoxyphenyl)cyclopropyl]-ethylene (35) was synthesized by the Wittig reaction of the cyclopropyl ketone (36) with triphenylphosphonium methylide. The dicyclopropane (34) was not obtainable by the reaction of the vinylcyclopropane (35) with diazomethane, even in the presence of copper salts.

In an effort to improve the synthesis of the dicyclo-

propane (34), the vinyl cyclopropane (35) was treated with ethyl diazoacetate. The four diastereoisomers of the cyclopropyl ester (37) were isolated, in two pairs. Both pairs gave the corresponding pairs of cyclopropyl carboxylic acids (38) on hydrolysis but these acids were not decarboxylated by copper sulphate in quinoline, black copper oxide in benzene, or by heating to 330 °C.

EXPERIMENTAL

¹H N.m.r. spectra were obtained for all products at 60 MHz in deuteriated chloroform with tetramethylsilane as internal reference. Chemical shifts are given in p.p.m. (δ). M.p.s were taken with a Kofler hot-stage apparatus. The usual work-up consisted of diluting with water, extracting with ether, washing the ether extract with water and aqueous saturated sodium chloride, drying the extract over anhydrous sodium sulphate, removing the solvent, and fractionating the residue by thick layer chromatography over silica gel; products are mentioned in order of decreasing *R_F* values.

Chalcone Dibromide.—A solution of the dibromide (1) (3.0 g) in DMSO (60 ml) was added to a solution of DMOSM¹ (*ca.* 1.9 g) in DMSO (40 ml). After 3 min and the usual work-up, a mixture¹ of *cis*- and *trans*-1-benzoyl-2-phenylcyclopropane (3) (1.25 g) was obtained, m.p. 35–60° [from light petroleum (b.p. 60–80°)] (lit.,¹ 45–50°) (Found: C, 86.1; H, 6.5. Calc. for C₁₆H₁₄O: C, 86.5; H, 6.3%).

4-Methoxychalcone Dibromide.—A solution of the dibromide (5) (4.0 g) in DMSO (80 ml) was added to a solution of DMOSM (*ca.* 3.8 g) in DMSO (100 ml). After 3 min the usual work-up gave 2-(4-methoxyphenyl)-5-phenyl-3,6-dihydro-2H-pyran (8) (2.3 g), m.p. 149–150° (from ethanol) (lit.,¹⁵ 149–150°) (Found: C, 81.3; H, 6.6. Calc. for C₁₆H₁₆O₂: C, 81.2; H, 6.8%).

2'-Hydroxychalcone Dibromide.—A solution of the dibromide (9) (2.3 g) in DMSO (60 ml) was added to a solution of DMOSM (*ca.* 1.9 g) in DMSO (60 ml). After 3 min and the usual work-up, the following were obtained: 1-(2-Hydroxybenzoyl)-2-phenylcyclopropane (10; R = H) (21 mg), m.p. 62.5–63° [from light petroleum (b.p. 60–80°)] (Found: C, 80.4; H, 6.2. C₁₆H₁₄O₂ requires C, 80.6; H, 5.9%), δ 1.39–2.06 (m, CH₂), 2.54–3.00 (m, 1- and 2-H), 6.66–7.53 (m, Ar), 7.79 (q, 6'-H), and 11.09 (s, OH); 1-(5-bromo-2-hydroxybenzoyl)-2-phenylcyclopropane (10; R = Br) (20 mg), m.p. 85–86° [from light petroleum (b.p. 60–80°)] (Found: C, 60.9; H, 4.3. C₁₆H₁₃BrO₂ requires C, 60.6; H, 4.1%), δ 1.47–2.08 (m, CH₂), 2.69–2.92 (m, 1- and 2-H), 6.86 (d, 3'-H, *J* 9 Hz), 7.09–7.41 (m, Ph), 7.51 (q, 4'-H *J* 3 and 9 Hz), 7.96 (d, 6'-H, *J* 3 Hz), and 12.38 (s, OH); 2'-phenylspiro[*coumaran*-2,1'-*cyclopropan*]-3-one (16) (40 mg), m.p. 102–103° [from light petroleum (b.p. 60–80°)] (lit.,¹⁶ 104°) (Found: C, 81.7; H, 5.2. Calc. for C₁₆H₁₂O₂: C, 81.3; H, 5.1%); 2,3-methanoflavanone (15) (40 mg), m.p. 64–65° [from light petroleum (b.p. 60–80°)] (lit.,¹⁷ 64°); and flavone (13) (6 mg), m.p. 95–97° (lit.,¹⁸ 96–97°).

A solution of 5'-bromo-2'-hydroxychalcone (18; R = Br) (2.0 g) in DMSO (40 ml) was added to a solution of DMOSM (*ca.* 1.5 g) in DMSO (50 ml). After 3 min and the usual work-up (except that chromatography was omitted), 1-(5-bromo-2-hydroxybenzoyl)-2-phenylcyclopropane (10; R = Br) (1.67 g), m.p. 85–86°, was obtained.

A solution of 2'-hydroxychalcone (18; R = H) (5.0 g) or

flavanone (19) (5.0 g) in DMSO (100 ml) was added to a solution of DMOSM (*ca.* 3.8 g) in DMSO (100 ml). After 3 min and the usual work-up, 1-(2-hydroxybenzoyl)-2-phenylcyclopropane (10; R = H) (4.5 g from chalcone; 4.8 g from flavanone), m.p. 62–63°, was obtained.

2-Hydroxychalcone (20).—A solution of the chalcone (20) (5.0 g) in DMSO (100 ml) was added to a solution of DMOSM (*ca.* 3.7 g) in DMSO (100 ml). After 3 min and the usual work-up, the oily product was refluxed in ethanol. Removal of the solvent gave 4-ethoxy-4-(2-hydroxyphenyl)-1-phenylbutan-1-one (22) (5.1 g), m.p. 79° [from light petroleum (b.p. 60–80°)] (Found: C, 76.1; H, 7.0. $C_{18}H_{20}O_3$ requires C, 76.0; H, 7.1%), δ 1.19 (t, Me, *J* 7 Hz), 2.37 (m, 3-CH₂), 3.19 (t, 2-CH₂, *J* 7 Hz), 3.65 (m, OCH₂), 4.60 (t, 4-CH, *J* 7 Hz), and 8.36 (s, OH).

α -Methoxychalcone (23).—A solution of DMOSM (*ca.* 0.42 g) in DMSO (13 ml) was added to a solution of α -methoxychalcone (23) (0.9) in DMSO (7 ml). After 1.5 h, the usual work-up gave 1-benzoyl-1-methoxy-2-phenylcyclopropane (24) as an oil (0.13 g) (Found: C, 80.7; H, 6.3. $C_{17}H_{16}O_2$ requires C, 80.7; H, 6.4%), δ 1.64 (q, 3-H, *J* 8 and 6 Hz), 2.07 (q, 3-H, *J* 10 and 6 Hz), 2.89 (q, 2-H, *J* 8 and 10 Hz), 3.07 (s, OMe), and 7.18–8.36 (m, Ar).

trans-1-Phenyl-2-(2-phenyloxiran-1-yl)cyclopropane (25).—Mercuric acetate (2 g) was added to a solution of this cyclopropyl epoxide (25) (1 g), a mixture¹⁵ of diastereoisomers, in methanol (50 ml). After 48 h the solvent was removed, the residue extracted with chloroform, and the extract washed and dried. Removal of the solvent gave a mixture of two inseparable diastereoisomers of 3-acetoxymercurio-2,5-dimethoxy-2,5-diphenylpentan-1-ol (26) (1.8 g), m.p. 131–138° (from aqueous ethanol) (Found: C, 45.1; H, 4.8. $C_{21}H_{26}HgO_5$ requires C, 45.1; H, 4.7%), δ 1.70–2.00 (m, 4-CH₂), 2.03 (s, Ac), 2.58–2.85 (m, 3-CH), 3.05 (br s, OH), 3.16 (s, OMe), 3.18 (s, OMe), 3.22 (s, OMe), 4.08 (br s, 1-CH₂), 3.80–4.30 (m, 5-CH), 7.32 (s, Ph), and 7.40 (s, Ph). A solution of the 3-acetoxymercurio-pentan-1-ol (26) (0.5 g) in chloroform (25 ml) was washed with saturated aqueous potassium bromide (8 ml) and dried. Removal of the solvent gave a mixture of two inseparable diastereoisomers of 3-bromomercurio-2,5-dimethoxy-2,5-diphenylpentan-1-ol (27) (0.5 g), m.p. 123–124° (from aqueous ethanol) (Found: C, 39.3; H, 3.9. $C_{15}H_{22}BrHgO_3$ requires C, 39.4; H, 4.0%), δ 1.80–2.15 (m, 4-CH₂), 2.30 (br s, OH), 2.95–3.05 (m, 3-CH), 3.18 (s, 2- and 5-OMe), 3.90–4.30 (m, 1-CH₂, 5-CH), 7.32 (s, Ph), and 7.40 (s, Ph).

Mercuric acetate (1.41 g) was added to a solution of the cyclopropyl epoxide (25) (1 g) in aqueous tetrahydrofuran (50%; 20 ml). After 24 h, the mixture was extracted with chloroform and the extract washed with water and dried. Removal of the solvent gave a mixture of two inseparable diastereoisomers of 3-acetoxymercurio-2,5-diphenylpentane-1,2,5-triol (28) (1.5 g), m.p. 127–132° (from aqueous ethanol) (Found: C, 43.2; H, 3.9. $C_{19}H_{22}HgO_5$ requires C, 43.0; H, 4.2%), δ 2.00 (s, Ac), 2.00–2.60 (m, 4-CH₂), 2.65–2.90 (m, 3-CH), 3.00 (br s, OH), 3.74 (br s, 1-CH₂), 4.90–5.20 (m, 5-CH), and 7.48 (br s, Ar). A solution of the 3-acetoxymercurio-1,2,5-triol (28) (0.1 g) in chloroform (5 ml) was washed with saturated aqueous potassium bromide (10 ml) and dried. Removal of the solvent gave a mixture of two inseparable diastereoisomers of 3-bromomercurio-2,5-diphenylpentane-1,2,5-triol (85 mg), m.p. 150–156° (from aqueous ethanol) (Found: C, 37.3; H, 3.7. $C_{17}H_{18}BrHgO_3$ requires C, 37.0; H, 3.5%), δ 2.10–2.90 (m, OH), 2.10–2.70 (m, 4-CH₂), 2.70–2.90 (m, 3-

CH), 3.77 (br s, 1-CH₂), 4.94–5.24 (m, 5-CH), 7.34 (s, Ph), 7.49 (s, Ph), and 7.52 (s, Ph).

Mercuric acetate (2 g) was added to a solution of (*E*)-1-hydroxy-5-methoxy-2,5-diphenylpent-2-ene⁶ (29) (1 g) in methanol (40 ml). After 48 h, the solvent was removed and the residue extracted with chloroform. The extract was washed and dried. Removal of the solvent gave a mixture of diastereoisomers of 3-acetoxymercurio-2,5-dimethoxy-2,5-diphenylpentan-1-ol (26) (1.5 g), m.p. 136–138° (from aqueous ethanol).

Mercuric acetate (1.41 g) was added to a solution of (*E*)-1,5-dihydroxy-2,5-diphenylpent-2-ene⁶ (30) (1 g) in aqueous tetrahydrofuran (50%; 20 ml). After 24 h, the mixture was extracted with chloroform and the extract washed with water and dried. Removal of the solvent gave a mixture of two diastereoisomers of 3-acetoxymercurio-2,5-diphenylpentane-1,2,5-triol (28) (1.5 g), m.p. 127–132° (from aqueous ethanol).

Deoxymercuriation.—Sodium borohydride (0.1 g) was added to an ice-cold solution of 3-acetoxymercurio-2,5-dimethoxy-2,5-diphenylpentan-1-ol (26) (0.4 g) in methanol (10 ml). After 15 min, water (10 ml) was added and the mixture was boiled. The usual work-up gave (*E*)-1-hydroxy-5-methoxy-2,5-diphenylpent-2-ene (29) (0.1 g). The above reaction of the 3-acetoxymercurio-pentan-1-ol (26) (0.58 g) in ethanol (20 ml) gave (*E*)-1-hydroxy-5-methoxy-2,5-diphenylpent-2-ene (29) (0.1 g) and two inseparable diastereoisomers of 2,5-dimethoxy-2,5-diphenylpentan-1-ol (31) as an oil (0.12 g) (Found: C, 75.7; H, 8.1. $C_{19}H_{24}O_3$ requires C, 76.0; H, 8.1%), δ 1.44–2.20 (m, CH₂CH₂), 3.00 (s, OMe), 3.08 (s, OMe), 3.12 (s, OMe), 3.25 (s, OMe), 3.50–4.55 (m, 5-CH, 1-CH₂), 4.03 (br s, OH), 7.30 (s, Ph), and 7.35 (s, Ph).

trans-1-(2-Amino-1-hydroxy-1-phenylethyl)-2-phenylcyclopropane (32).—A solution of trans-1-phenyl-2-(2-phenyloxiran-2-yl)cyclopropane (25) (1 g) in methanolic ammonia (20%; 15 ml) was heated in a sealed tube at 180 °C for 5 h. It was then cooled, filtered, and evaporated to dryness, giving the cyclopropylethylamine (32) (0.6 g), m.p. 115–116° (from benzene) (Found: C, 80.6; H, 7.9; N, 5.5. $C_{17}H_{19}NO$ requires C, 80.6; H, 7.6; N, 5.5%), δ 0.50–2.10 (m, cyclopropyl), 2.55 (br s, NH₂), 2.58 (br s, OH), 3.03 (s, CH₂), and 6.80–7.60 (m, Ar). Aqueous hydrochloric acid (10%; 3 ml) was added to a solution of the cyclopropylethylamine (32) (1 g) in propan-2-ol (50 ml). The water was then removed by azeotropic distillation with propan-2-ol and the solution was concentrated, filtered, and diluted with ethyl acetate (50 ml). trans-1-(2-Amino-1-hydroxy-1-phenylethyl)-2-phenylcyclopropane hydrochloride separated, m.p. 210–212° (from propan-2-ol) (Found: C, 70.5; H, 6.9; Cl, 12.2; N, 4.8. $C_{17}H_{20}ClNO$ requires C, 70.5; H, 7.0; Cl, 12.2; N, 4.8%), δ 0.50–2.00 (m, cyclopropyl), 3.09 (s, OH), 3.37 (s, CH₂), 6.60–7.60 (m, Ar), and 7.70–8.30 (very br s, NH₃).

trans-1-(4-Methoxyphenyl)-2-[1-(4-methoxyphenyl)cyclopropyl]cyclopropane (34).—A solution of *n*-butyllithium (*ca.* 2.4 g) in hexane (23 ml) was added dropwise under nitrogen to methyltriphenylphosphonium bromide (12.72 g) in diethyl ether (200 ml). After 4 h, trans-1-(4-methoxybenzoyl)-2-(4-methoxyphenyl)cyclopropane¹⁵ (36) (7 g) in diethyl ether (100 ml) was added. After a further 4 h, the mixture was filtered and the solvent removed, giving trans-1-(4-methoxyphenyl)-1-[2-(4-methoxyphenyl)cyclopropyl]ethylene (35) (5.63 g), m.p. 84–85° [from light petroleum (b.p. 40–60°)] (Found: C, 81.6; H, 6.9. C_{19} -

H₂₀O₂ requires C, 81.4; H, 7.2%), δ 1.15—2.05 (m, cyclopropyl), 3.80 (s, OMe \times 2), 4.75 (s, H_a), 5.30 (s, H_b), and 6.80—7.61 (m, Ar).

Zinc dust (1.16 g) was added to a stirred hot solution of silver acetate (0.1 g) in acetic acid (25 ml). After 30 s, the supernatant liquid was decanted and the residual zinc-silver couple was washed with acetic acid and anhydrous diethyl ether. Di-iodomethane (4.8 g) in diethyl ether (50 ml) was added dropwise. After 1 h, the cyclopropylethylene (35) (2 g) in ether (20 ml) was added and the mixture was refluxed for 48 h, cooled, treated with pyridine (3.5 ml), and, after 1 h, filtered. The ether layer was washed with water and saturated aqueous sodium chloride and dried. Removal of the solvent, followed by chromatography of the residue on silica gel gave the *cyclopropylcyclopropane* (34) as an oil (0.140 g) (Found: C, 81.4; H, 7.7. C₂₀H₂₂O₂ requires C, 81.6; H, 7.5%), δ 0.55—1.75 (m, cyclopropyl), 3.75 (s, OMe \times 2), and 6.75—7.41 (m, Ar).

Ethyl diazoacetate (4 g) was added to a mixture of copper sulphate (0.3 g) and the cyclopropylethylene (35) (4 g) in dry benzene (50 ml) at 40 °C. The mixture was refluxed for 2 h and cooled to 30 °C. Ethyl diazoacetate (6 g) was added in lots, one lot (1 g) every 30 min. The mixture was cooled, filtered, and evaporated to dryness. Chromatography of the residual oil on silica gel gave two fractions, each containing two of the four possible isomers of trans-1-[2-ethoxycarbonyl-1-(4-methoxyphenyl)cyclopropyl]-2-(4-methoxyphenyl)cyclopropane (37). The mixture of isomers with the larger R_F value was obtained as an oil (1.82 g) (Found: C, 75.5; H, 7.2. C₂₃H₂₆O₄ requires C, 75.4; H, 7.2%), δ 0.71—2.23 (m, cyclopropyl and Me), 3.79 (s, OMe), 3.82 (s, OMe), 4.11 (q, OCH₂), 4.18 (q, OCH₂), and 6.72—7.48 (m, Ar). The mixture of isomers with the smaller R_F value was obtained as an oil (2.280 g) (Found: C, 75.5; H, 7.4. C₂₃H₂₆O₄ requires C, 75.4; H, 7.2%), δ 0.65—2.11 (m, cyclopropyl), 1.14 (t, Me, *J* 7 Hz), 3.91 (s, OMe \times 2), 4.03 (q, OCH₂), 4.36 (q, OCH₂), and 6.87—7.52 (m, Ar).

Aqueous sodium hydroxide (10%; 4 ml) was added to a solution of the first-mentioned ester mixture above (0.815 g) in ethanol (15 ml). The mixture was refluxed for 1.5 h, cooled, and poured into hydrochloric acid (10%; 5 ml). The usual work-up, but without chromatography, gave a mixture of two isomers of trans-1-[2-carboxy-1-(4-methoxy-

phenyl)cyclopropyl]-2-(4-methoxyphenyl)cyclopropane (38) (0.480 g), m.p. 117—118° (from ethanol) (Found: C, 74.2; H, 6.4. C₂₁H₂₂O₄ requires C, 74.5; H, 6.6%), δ 0.51—2.19 (m, cyclopropyl), 3.82 (s, OMe \times 2), 6.71—7.43 (m, Ar), and 10.16 (br s, CO₂H). Aqueous sodium hydroxide (10%; 5 ml) was added to a solution of the second-mentioned ester mixture above (0.666 g) in ethanol (10 ml). The mixture was refluxed for 2 h, cooled, and poured into hydrochloric acid (10%; 5 ml). The usual work-up, but without chromatography, gave a mixture of the other two possible isomers of the cyclopropyl carboxylic acid (38) (0.435 g) as an oil (Found: C, 74.3; H, 6.4. C₂₁H₂₂O₄ requires C, 74.5; H, 6.6%), δ 0.61—1.99 (m, cyclopropyl), 3.76 (s, OMe), 3.79 (s, OMe), 6.76—7.19 (m, Ar), and 9.10 (br s, CO₂H).

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