318. *Polymerisation of Flavans. Part VI.* Reduction of Flavanoids and Chalcones with Lithium Aluminium Hydride in the Presence of Aluminium Chloride.*

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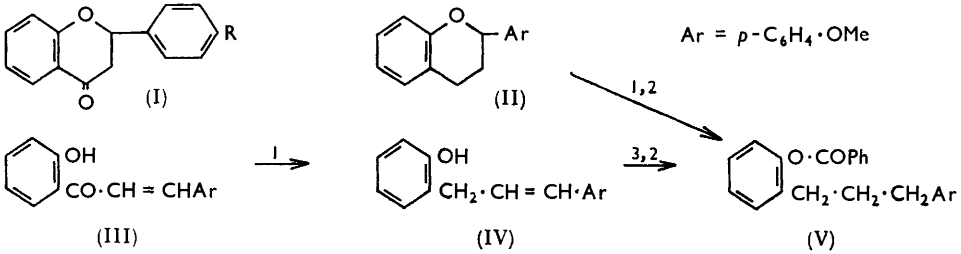
Flavan is obtained in good yield from the action of lithium aluminium hydride and aluminium chloride on flavanone. Di-*p*-methoxybenzyl ether and 4′-methoxyflavan are smoothly hydrogenolysed by the mixed reagent; in the absence of activating groups no hydrogenolysis occurs. (+)-Epicatechin tetramethyl ether, obtained by methylation of the culture fluid from the growth of *Penicillium solitum* on epimerised (+)-catechin, has been reductively cleaved.

Chalcone with the mixed reagent yields diphenylpropene, and 4- and 4′-methoxychalcones yield propenes in which the double bond has migrated. 2′-Hydroxychalcone gives 1-*o*-hydroxyphenyl-3-phenylprop-1-ene whereas 2′-hydroxy-4-methoxychalcone gives 3-*o*-hydroxyphenyl-1-*p*-methoxyphenylprop-1-ene with a little of 1-*o*-hydroxyphenyl 3-*p*-methoxyphenylprop-1-ene. Flavans are conveniently prepared from 2-hydroxychalcones when the mixed reagent is used with a high ratio of aluminium chloride. With a smaller ratio, the corresponding propanones and propanols have been isolated.

EARLIER work[1] has shown that aromatic ketones are smoothly hydrogenolysed by a mixture of lithium aluminium hydride and aluminium chloride to give good yields of the corresponding hydrocarbons. Thus, hydrogenolysis of a flavan-4-one (I) should yield a flavan (II), and this constitutes a convenient preparation of flavan itself (II; Ar = Ph) (yield 88%). However, when reduction of 4′-methoxyflavan-4-one (I; R = OMe) was attempted with the mixed reagent, the products were complex and partly soluble in alkali. It was realised[2] that the heterocyclic oxygen ring had been cleaved and that the *p*-methoxy-group was responsible, since dibenzyl ether is not attacked but di-*p*-methoxybenzyl ether gives 83% of *p*-methoxytoluene. The extension of this reaction to the hydrogenolysis of acetals has been reported[3] and we have found that formaldehyde dibenzyl acetal yields benzyl methyl ether and benzyl alcohol. The cleavage of 4′-methoxyflavan (II) gave 1-*o*-hydroxyphenyl-3-*p*-methoxyphenylpropane, isolated as its benzoyl derivative (V) (55%). This compound was identical with that obtained by hydrogenation and benzoylation of 3-*o*-hydroxyphenyl-1-*p*-methoxyphenylprop-1-ene (IV) obtained from 2′-hydroxy-4-methoxychalcone (III) (see later).



Reagents: 1, $LiAlH_4$–$AlCl_3$; 2, PhCOCl–aq. NaOH; 3, H_2–Pt–EtOH.

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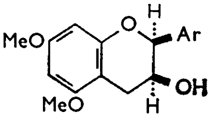
* Part V, *J.*, 1961, 4663.

[1] (*a*) Brown and White, *J.*, 1957, 3755; (*b*) Nystrom and Berger, *J. Amer. Chem. Soc.*, 1958, **80**, 2896; Blackwell and Hickinbottom, *J.*, 1961, 1405.

[2] Brown and Somerfield, *Proc. Chem. Soc.*, 1958, 7.

[3] Eliel and Rerick, *J. Org. Chem.*, 1958, **23**, 1088.

Cleavage of the tetramethyl ethers of (+)-catechin and (—)-epicatechin has been reported in detail,[4] and that of (+)-epicatechin tetramethyl ether (VI) briefly.[5] The latter has been obtained by the growth of *Penicillium solitum* on solutions of epimerised (+)-catechin. After 15 days, paper chromatography showed that (+)-catechin had disappeared but that (+)-epicatechin remained. From the culture fluid, after methylation, three compounds have been isolated. One (*ca.* 3·5%) has been shown to be an ester of (+)-epicatechin tetramethyl ether with an acid of small molecular weight, possibly the half methyl ester of succinic acid as judged from analytical results. A second (*ca.* 9%) was (+)-epicatechin tetramethyl ether, and the third (*ca.* 15%) was probably a polymer since, before methylation, the culture fluid gave a thick precipitate with gelatin solution. Reduction of (+)-epicatechin tetramethyl ether (VI) with the mixed reagent, followed by methylation,[4a,c] gave 49% of unchanged material, 7% of 1-(3,4-dimethoxyphenyl)-3-(2,4,6-trimethoxyphenyl)propan-2-ol (VII) and 4·5% of (+)-2-(3,4-dimethoxyphenyl)-3-(2,4,6-trimethoxyphenyl)propan-1-ol (VIII). The latter with the (—)-propan-1-ol obtained from (+)-catechin tetramethyl ether gave the (±)-propan-1-ol (VIII) whose m. p. was not depressed on admixture with the synthetic compound.[4c] The propan-2-ol (VII) results from hydrogenolysis of the heterocyclic ether link, and the work of Clark-Lewis and Ramsay[6] on the analogous reduction of the tetramethyl ethers of (+)-catechin and (—)-epicatechin indicate that the (+)-propan-1-ol (VIII) probably arises by the migration of a benzyl group.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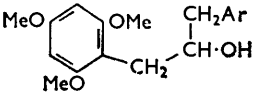
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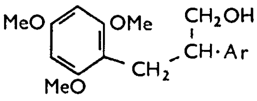
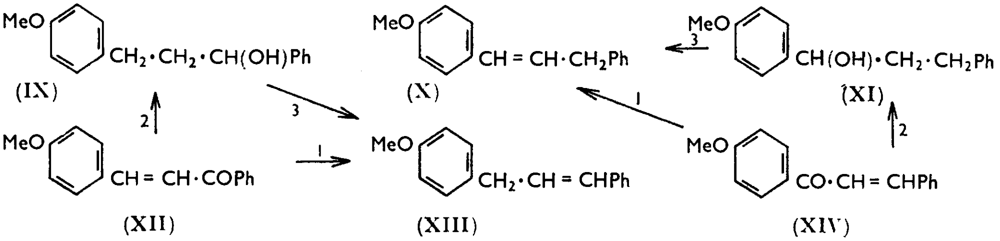

(VIII)

[Ar = 3,4-(MeO)$_2$C$_6$H$_3$]

Consideration of earlier work[7] on the hydrogenolysis of αβ-unsaturated ketones suggested that examination of the reduction of chalcones might lead to convenient preparations of flavans. It was expected that the carbonyl group of a chalcone, being conjugated with a phenyl group, would be reduced to a methylene group,[1] but interest lay in the behaviour of the double bond, since it has been shown[7b] that the reduction of αβ-unsaturated ketones can follow different paths to give several products. Chalcone itself yielded 65% of *trans*-1,3-diphenylpropene and 15% of viscous oil (polymer ?).



Reagents: 1, LiAlH$_4$–AlCl$_3$; 2, LiAlH$_4$; 3, AlCl$_3$.

The reduction of 4-methoxychalcone (XII) in ether for 2 hr. gave 44% of *trans*-3-*p*-methoxyphenyl-1-phenylprop-1-ene (XIII), which was identified by its ultraviolet spectrum

[4] (*a*) Brown and Somerfield, *Proc. Chem. Soc.*, 1958, 236; (*b*) Clark-Lewis, *Proc. Chem. Soc.*, 1959, 388; (*c*) Clark-Lewis, *J.*, 1960, 2433.

[5] Bokadia, Brown, and Somerfield, *Proc. Chem. Soc.*, 1960, 280.

[6] Clark-Lewis and Ramsay, *Proc. Chem. Soc.*, 1960, 359.

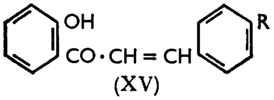
[7] (*a*) Broome and Brown, *Chem. and Ind.*, 1956, 1307; (*b*) Broome, Brown, Roberts, and White, *J.*, 1960, 1406.

($\lambda_{\text{max.}}$ 254 mμ, ε 14,000), together with 43% of polymers (?) whose infrared spectra contained no bands attributable to double bonds. Identification of this prop-1-ene was not possible from its refractive index, since two divergent values are recorded in the literature[8,9] and our value differs from both of these. Moreover, two values are recorded[8,10] for the m. p. of the dibromide. We find that at 0° with a controlled amount of bromine, the true dibromide is produced and that at room temperature this reacts with more bromine to give a compound which contains three bromine atoms per molecule and is presumably a substitution product.

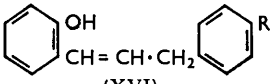
Likewise, 4′-methoxychalcone (XIV) is reduced to the structurally isomeric olefin, *trans*-1-*p*-methoxyphenyl-3-phenylprop-1-ene (X), again with apparent migration of the double bond. As with the isomeric chalcone, reduction during 2 hr. yielded *trans*-olefin (65%) and polymer (?). The olefin was identified by its analysis, refractive index, and ultraviolet spectrum, and by the m. p. of its dibromide. As expected for this olefin, in which the methoxy-group and the double bond are conjugated through a benzene ring, the ultraviolet absorption is of greater intensity ($\lambda_{\text{max.}}$ 257 mμ, ε 28,200) than that of the isomeric olefin. When 4′-methoxychalcone was reduced in ether for only 20 min., some *cis*-olefin (infrared absorption at 678 cm.$^{-1}$) was produced along with the *trans*-olefin. The *cis*-olefin was not obtained pure, since it polymerised (?) on attempted distillation under high vacuum.

It is known[9] that 4- and 4′-methoxychalcones are reduced by lithium aluminium hydride alone to the saturated alcohols (IX) and (XI). These yield the olefins (XIII) and (X) when they are boiled with aluminium chloride in ether. Hence we consider that the course of reaction between these chalcones and the mixed reagent is reduction to the saturated alcohol followed by dehydration to the olefin, which accounts for the migration of the double bond.

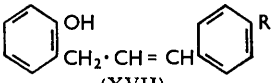
Since it was known[11] that 3-*o*-hydroxyphenyl-1-phenylprop-1-ene (XVII; R = H) gives flavan (no yield stated) on treatment with acid, and, from the experiments described above, that chalcones yield propenes on reduction with the mixed reagent, we investigated the action of the mixed reagent on 2- and 2′-hydroxychalcones (XVIII) and (XV) as a route to flavans. The reduction of 2′-hydroxychalcone (XV; R = H) in tetrahydrofuran gave 46% of a compound, m. p. 67—68°, formulated as 1-*o*-hydroxyphenyl-3-phenylprop-1-ene (XVI; R = H) on the evidence of its ultraviolet spectrum ($\lambda_{\text{max.}}$ 254 mμ, ε 26,730) and the fact that Claisen[11] and Hurd and Schmerling[12] report m. p. 55—56° for the isomer, 3-*o*-hydroxyphenyl-1-phenylprop-1-ene (XVII; R = H). The action of boiling acid on (XVI; R = H) gave only 15% of flavan in 3 hr. and 26% in 12 hr. The action of the mixed reagent on 2′-hydroxy-4-methoxychalcone (XV; R = OMe) gave 76% of 3-*o*-hydroxyphenyl-1-*p*-methoxyphenylprop-1-ene (XVII; R = OMe) and 8% of the corresponding isomer (XVI; R = OMe). Treatment of (XVII; R = OMe) with hot acid gave 83% of 4′-methoxyflavan whereas the (XVI; R = OMe) yielded none. On this basis the above structures have been assigned. Treatment of the crude reduction product from 2′-hydroxy-4-methoxychalcone with hot acid gave directly 50% of 4′-methoxyflavan.



(XV)



(XVI)



(XVII)

The reduction of 2-hydroxychalcones follows a different course. 2-Hydroxychalcone (XVIII; R = R′ = H) and 2-hydroxy-4′-methoxychalcone (XVIII; R = OMe, R′ = H)

[8] Ingold and Shoppee, *J.*, 1929, 447.

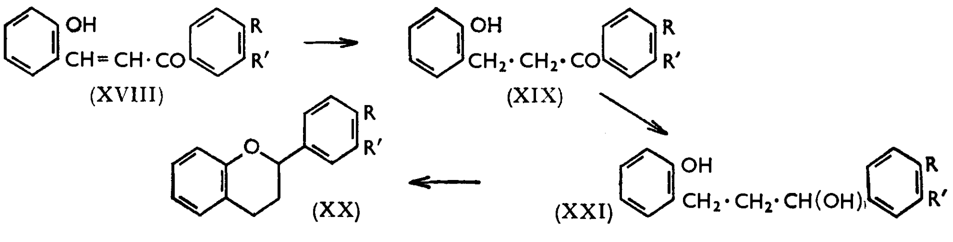
[9] Rondestvedt, *J. Amer. Chem. Soc.*, 1951, **73**, 4509.

[10] Ingold and Piggott, *J.*, 1921, 2381.

[11] Claisen, *Annalen*, 1925, **442**, 210.

[12] Hurd and Schmerling, *J. Amer. Chem. Soc.*, 1937, **59**, 107.

gave, with a ratio of 1 mol. of chalcone : 2·6 mol. of lithium aluminium hydride : 3·75 mol. of aluminium chloride, the corresponding propanones (XIX) with the propanols (XXI) which were separated with difficulty. 2-Hydroxy-4′-methoxychalcone also gave 30% of 4′-methoxyflavan (XX; R = OMe, R′ = H). When the amount of lithium aluminium hydride was increased to 4 mol. and that of aluminium chloride to 20—25 mol.,



a convenient preparation of flavans resulted, since these were easily separated from any phenolic products by filtration through alumina. With a reaction time of 30 min., 2-hydroxychalcone (XVIII; R = R′ = H) gave 17% of flavan (XX; R = R′ = H), 2-hydroxy-4′-methoxychalcone (XVIII; R = OMe, R′ = H) gave 84% of 4′-methoxyflavan (XX; R = OMe, R′ = H), and 2-hydroxy-3′,4′-dimethoxychalcone (XVIII; R = R′ = OMe) gave 51% of 3′,4′-dimethoxyflavan (XX; R = R′ = OMe).

EXPERIMENTAL

Alumina was Spence's grade H or O deactivated, when stated, with acetic acid. Light petroleum refers to the fraction of b. p. 40—60°. Optical rotations were determined in chloroform at room temperature.

Compounds which were readily soluble in ether were reduced and the products isolated by the general procedure previously described.[1a] Tetrahydrofuran was used as solvent when ether was not suitable.

Attempted Reduction of Dibenzyl Ether.—Dibenzyl ether (9·33 g.), n_D^{12} 1·5659, gave an oil which yielded unchanged dibenzyl ether (7·94 g.), b. p. 155—159°/10 mm., n_D^{12} 1·5658.

*Reduction of Flavan-*4*-one* (I; R = H).—Flavanone (2·00 g.) yielded an oil which was chromatographed in light petroleum on alumina (grade O, 5% deactivated) to give flavan (II; Ar = Ph) (1·65 g.) which separated from light petroleum (b. p. 40—45°) as rods, m. p. 43—44° (Found: C, 85·9; H, 6·55. Calc. for $C_{15}H_{14}O$: C, 85·7; H, 6·65%), $\nu_{max.}$ (in Nujol) 752 and 697 cm.$^{-1}$ (aromatic). Borsche and Geyer [13] report m. p. 44°.

*Reduction of Di-*p*-methoxybenzyl Ether.*—Di-*p*-methoxybenzyl ether (5·5 g.) gave a product which was filtered through alumina (grade O, 10% deactivated) in light petroleum to give *p*-methoxytoluene (4·33 g.), b. p. 172·5—173°/757 mm., n_D^{20} 1·5117.

Reduction of Formaldehyde Dibenzyl Acetal.—The acetal (b. p. 174—176°/12 mm., n_D^{16} 1·5489) (9·33 g.) gave a product which was distilled to give the following fractions: (i) b. p. 62—64°/12 mm., n_D^{17} 1·5045 (4·2 g.); (ii) b. p. 64—88°/12 mm., n_D^{17} 1·5158 (1·2 g.); (iii) b. p. 88—89°/12 mm., n_D^{17} 1·5383 (2·9 g.).

A commercial sample of benzyl methyl ether had b. p. 167—168°/745 mm., n_D^{14} 1·5051. Fraction (i) was identical with this specimen in infrared spectrum (natural film) and on a gas-phase chromatogram.

A gas-phase chromatogram of fraction (ii) showed a main peak corresponding to benzyl methyl ether and a small peak identical in elution time with benzyl alcohol. This fraction also showed a hydroxyl band (3401 cm.$^{-1}$, natural film) in its infrared spectrum.

The third fraction was identical in all respects with benzyl alcohol and yielded a naphthylurethane, m. p. and mixed m. p. 134—135°.

Reduction of 4′*-Methoxyflavan* (II).—4′-Methoxyflavan (1·50 g.) gave an oil which was

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[13] Borsche and Geyer, *Ber.*, 1914, **47**, 1154.

treated with 2N-sodium hydroxide (50 ml.) and light petroleum (3 × 20 ml.). The petroleum extracts yielded unchanged 4′-methoxyflavan (0·32 g.). The alkaline extract was benzoylated (Schotten–Baumann) and the product isolated in ether. Chromatography on alumina (grade O, 5% deactivated) in light petroleum (b. p. 60—80°)–benzene (4 : 1 v/v) yielded 1-o-*benzoyloxyphenyl*-3-p-*methoxyphenylpropane* (V) (1·20 g.) which separated from wet methanol as prisms, m. p. 45·5—46·5° (Found: C, 79·7; H, 6·35. $C_{23}H_{22}O_3$ requires C, 79·75; H, 6·35%). The m. p. was unchanged on admixture with a specimen obtained by hydrogenation and benzoylation of 3-*o*-hydroxyphenyl-1-*p*-methoxyphenylprop-1-ene (see below), and the infrared spectra of the two in Nujol were identical.

(+)-*Epicatechin* 5,7,3′4′-*Tetramethyl Ether* (VI).—A solution of (+)-catechin (10·0 g.) in water (2 l.) was sterilised at 110—115° for 25 min. The solution became dark and chromatography on Whatman No. 1 paper in butanol–acetic acid–water (4 : 1 : 5 v/v, top phase; temperature 24°; ferric chloride–potassium ferricyanide spray) showed that appreciable epimerisation of the (+)-catechin had occurred [R_F 0·58, (+)-epicatechin, and 0·67, (+)-catechin]. The solution gave a slight precipitate with gelatin solution. *Penicillium solitum* (from the Central Bureau voor Schimmel Cultures, Baarn, Holland) was grown on this solution to which had been added potassium dihydrogen phosphate (3·0 g.), ammonium nitrate (1·2 g.), calcium chloride hexahydrate (1·0 g.), sodium tetraborate heptahydrate (1·0 g.), zinc sulphate heptahydrate (0·01 g.), ferric chloride hexahydrate (0·01 g.), copper sulphate pentahydrate (0·01 g.), and manganous chloride (0·01 g.). After 15 days there was no spot on the chromatogram corresponding to (+)-catechin but (+)-epicatechin was still present. The fungus was removed from the culture fluid, which was saturated with salt and extracted with ethyl acetate. The aqueous layer, which gave a positive ferric chloride test, was extracted continuously with ethyl acetate for 24 hr. The combined extracts were dried and the solvent was removed to afford a brown powder (3·5 g.) whose aqueous solution gave a thick precipitate with gelatin and on chromatography showed spots at 0·30, 0·41, 0·46, 0·60 [(+)-epicatechin], and 0·84, with a background streak from the origin to the third spot. The powder had $\lambda_{max.}$ (in ethanol) 278 and 385 mμ. Methylation with methyl sulphate–acetone–potassium carbonate, until a test portion gave no colour with ferric chloride–potassium ferricyanide solution, gave a brown syrup which was chromatographed on alumina (200 g. of 10% deactivated grade H). Elution with benzene (400 ml.) afforded a solid which, after several crystallisations from light petroleum–benzene and finally from methanol, gave needles (350 mg.), m. p. 115—125°. Filtration through alumina (10% deactivated grade H) and further recrystallisation raised the m. p. to 135—136°, $[\alpha]_D$ +75° (*c* 3·0) (Found: C, 62·6, 62·85; H, 6·15, 6·25; OMe, 31·4. $C_{24}H_{28}O_9$ requires C, 62·6; H, 6·1; 5 OMe, 33·7%), $\lambda_{max.}$ (in ethanol) 205, 227, and 277 mμ (ε 110,000, 20,200, and 4510), $\nu_{max.}$ (in carbon tetrachloride) 1751 cm.$^{-1}$ (ester). Hydrolysis of the compound (150 mg.) with boiling methanolic potassium hydroxide (5 ml.; 1N) for 30 min. gave (+)-epicatechin tetramethyl ether (110 mg.) as prisms, m. p. and mixed m. p. 144—145°, $[\alpha]_D$ +42° (*c* 3·0). Reduction of the compound with lithium aluminium hydride gave (+)-epicatechin tetramethyl ether.

Further elution of the original column with benzene (600 ml.) followed by benzene–chloroform (9 : 1 v/v; 200 ml.) gave a semicrystalline mass which, after three crystallisations from methanol, afforded (+)-epicatechin tetramethyl ether (VI) (0·90 g.) as prisms, m. p. and mixed m. p. 144—145°, $[\alpha]_D$ +43° (*c* 3·0) (Found: C, 65·75; H, 6·65. Calc. for $C_{19}H_{22}O_6$: C, 65·9; H, 6·35%). Acetic anhydride–pyridine gave the 3-acetate which separated from ethanol as prisms, m. p. 93—95°, $[\alpha]_D$ +73° (*c* 2·4).

Elution with chloroform and methanol gave a brown amorphous solid (1·5 g.).

Reduction of (+)-*Epicatechin* 5,7,3′,4′-*Tetramethyl Ether* (VI).—(+)-Epicatechin tetramethyl ether (2·0 g.) was added to a mixture of lithium aluminium hydride (0·50 g.) and aluminium chloride (3·50 g.) in tetrahydrofuran (150 ml.). The mixture was boiled for 6 hr., treated at 0° with methyl formate (10 ml.) in ether (50 ml.), and then acidified with 2N-sulphuric acid (20 ml.). The organic layer was separated and the aqueous layer was extracted several times with ether. The combined extracts yielded an oil (2·1 g.) which was dissolved in benzene–ether (1 : 1 v/v; 25 ml.) and extracted with Claisen's alkali [potassium hydroxide (175 g.) in methanol (300 ml.) and water (125 ml.)] (5 × 15 ml.). The organic layer gave unchanged (+)-epicatechin tetramethyl ether (0·98 g.), prisms, m. p. and mixed m. p. 145—146°.

The phenolic material (0·80 g.) was recovered from the alkaline extracts and methylated with methyl sulphate–acetone–potassium carbonate for 23 hr. The product was chromatographed on alumina (70 g. of 10% deactivated grade H). Elution with benzene (250 ml.)

afforded an oil which, from ethyl acetate–hexane, gave 1-(3,4-dimethoxyphenyl)-3-(2,4,6-trimethoxyphenyl)propan-2-ol (VII) (140 mg.) as prisms, m. p. 95—96·5° (Found: C, 66·3; H, 7·3; OMe, 43·9. Calc. for $C_{20}H_{26}O_6$: C, 66·3; H, 7·2; 5 OMe, 42·8%).

Elution with benzene (150 ml.) and benzene–ether (9 : 1 v/v; 300 ml.) afforded an oil which, from ethyl acetate–hexane, gave (+)-2-(3,4-*dimethoxyphenyl*)-3-(2,4,6-*trimethoxyphenyl*)*propan*-1-*ol* (VIII) (90 mg.) as needles, m. p. 124·5—125·5°, $[\alpha]_D$ +39·5° (*c* 1·1) (Found: C, 66·4; H, 7·55. $C_{20}H_{26}O_6$ requires C, 66·3; H, 7·2%).

Equal amounts of this (+)-propan-1-ol and the (−)-propan-1-ol from the reduction of (+)-catechin tetramethyl ether were crystallised from ethyl acetate–hexane to give the (±)-propan-1-ol as needles, m. p. and mixed m. p. 107—108°. A mixed m. p. with (±)-1-(3,4-dimethoxyphenyl)-3-(2,4,6-trimethoxyphenyl)propan-2-ol (VII) (m. p. 96—97°) showed depression.

Reduction of Chalcone.—Chalcone (10·0 g.) gave a slightly yellow oil. Chromatography through alumina (grade O) in light petroleum gave a main fraction of mobile oil (6·4 g.) followed by a second fraction of viscous oil (1·5 g.).

The main fraction distilled at 92°/0·15 mm. or 163—164/15 mm. to yield *trans*-1,3-diphenylpropene, n_D^{20} 1·5995 (Found: C, 92·6; H, 7·3. Calc. for $C_{15}H_{14}$: C, 92·8; H, 7·2%), $\lambda_{max.}$ (in ethanol) 204, 252, 284, and 292 mμ (ε 31,600, 20,600, 2500, and 2000), $\nu_{max.}$ (liquid film) 963 cm.$^{-1}$ (*trans*-CH=CH). There was no evidence for the presence of a *cis*-double bond. The compound formed a dibromide (in carbon tetrachloride) which separated from ethanol as needles, m. p. 110°. Böeseken and Elsen [14] record b. p. 164—168°/14 mm., $n_D^{17.5}$ 1·6010, and Dieckmann and Kämmerer [15] give m. p. 110° for the dibromide.

The second fraction gave a glass when distillation under high vacuum was attempted.

Reduction of 4-*Methoxychalcone* (XII).—The chalcone (8·70 g.), added to the mixed reagent in ether by extraction from a thimble during 2 hr., gave an oil which was chromatographed on alumina (grade O; 140 g.) in light petroleum–benzene (3 : 1 v/v). Elution with this solvent mixture gave *trans*-3-*p*-methoxyphenyl-1-phenylprop-1-ene (XIII) (3·60 g.), b. p. 116—118°/0·01 mm., n_D^{17} 1·5912, $\lambda_{max.}$ (in ethanol) 254, 284, and 292 mμ (ε 14,800, 4000, and 1300), $\nu_{max.}$ (liquid film) 966 cm.$^{-1}$ (*trans*-CH=CH). The *dibromide* (prepared in chloroform at 0° with the calculated quantity of bromine) after chromatography on alumina (grade O) in light petroleum, separated from light petroleum as elongated plates, m. p. 82—83° (Found: C, 50·1; H, 4·55; Br, 40·0. $C_{16}H_{16}Br_2O$ requires C, 50·0; H, 4·2; Br, 41·7%). When this preparation was carried out at room temperature without a carefully controlled amount of bromine, products with m. p.s ranging from 74° to 125° were obtained, and pure products could not be isolated from them. Ingold and Piggott [10] record m. p. 74°, and Ingold and Shoppee [8] give m. p. 96° for this dibromide. The dibromide readily took up 1 mol. of bromine at room temperature to yield a *bromodibromide* which separated from light petroleum as needles, m. p. 130—132° (Found: C, 41·8; H, 3·25; Br, 50·4. $C_{16}H_{15}Br_3O$ requires C, 41·5; H, 3·25; Br, 51·8%).

Further elution of the original column with benzene gave a viscous oil (2·0 g.), and with ether a glass (1·55 g.), m. p. 64°, was obtained. Infrared spectra showed that neither of these products contained double bonds.

Action of Aluminium Chloride on 3-p-*Methoxyphenyl*-1-*phenylpropan*-1-*ol* (IX).—A mixture of the propanol (7·0 g.), aluminium chloride (14·0 g.), and ether (300 ml.) was boiled for 1 hr. and worked up in the usual way. The residual oil in light petroleum was put on to alumina grade O; 120 g.). Elution with light petroleum–benzene (3 : 1 v/v) gave *trans*-3-*p*-methoxyphenyl-1-phenylprop-1-ene (XIII) (4·8 g.) as an oil, b. p. 118—120°/0·01 mm., n_D^{19} 1·5910. The ultraviolet and infrared spectra were identical with those of the sample from 4-methoxychalcone (above). The dibromide, obtained as described above, had m. p. 82—83°, unchanged on admixture with the previous sample.

Reduction of 4′-*Methoxychalcone* (XIV).—The chalcone (10·0 g.), added to the mixed reagent as a suspension in ether during 20 min., yielded a yellow oil which was chromatographed on alumina (grade O; 80 g.) in light petroleum. Elution with light petroleum gave the prop-1-ene (X) (4·0 g.), b. p. 120—122°/0·15 mm., n_D^{19} 1·5988 (Found: C, 85·7; H, 7·15. Calc. for $C_{16}H_{16}O$: C, 85·7; H, 7·1%), $\lambda_{max.}$ (in ethanol) 257, 284, and 292 mμ (ε 28,200, 5850, and 3200), $\nu_{max.}$ (liquid film) 966 cm.$^{-1}$ (*trans*-CH=CH). The dibromide, prepared in chloroform at 0°, separated from light petroleum as plates, m. p. 119—120°. Rondestvedt [9] records n_D^{26} 1·6002

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[14] Böeseken and Elsen, *Rec. Trav. chim.*, 1929, **48**, 364.

[15] Dieckmann and Kämmerer, *Ber.*, 1906, **39**, 3049.

for 1-*p*-methoxyphenyl-3-phenylprop-1-ene (X) and Ingold and Shoppee [8] give m. p. 119° for the m. p. of the dibromide.

Elution with light petroleum–benzene (3 : 1 v/v) gave a liquid (1·1 g.) whose infrared spectrum had medium bands at 966 cm.$^{-1}$ (*trans*-CH=CH) and 678 cm.$^{-1}$ (*cis*-CH=CH).

Elution with ether gave a liquid (2·0 g.) whose infrared spectrum had bands at 966 vw and 678s cm.$^{-1}$. When distillation of these two fractions was attempted, some *trans*-olefin volatilised and a glassy involatile solid remained.

A repetition of this reduction, in which the chalcone was added to the reagent by extraction from a thimble during 2 hr., yielded no *cis*-olefin, 65% of pure *trans*-olefin, and polymeric(?) material.

Action of Aluminium Chloride on 1-p-*Methoxyphenyl*-3-*phenylpropan*-1-*ol* (XI).—A solution of the propanol (1·0 g.) and aluminium chloride (2·0 g.) in ether (100 ml.) was boiled for 1 hr. and worked up in the usual way. The residual oil in light petroleum was filtered through alumina (grade O) and converted into the dibromide (1·10 g.), which separated from light petroleum as plates, m. p. 119—120°, unchanged by admixture with the dibromide of *trans*-1-*p*-methoxyphenyl-3-phenylprop-1-ene from the reduction of 4′-methoxychalcone.

Reduction of 2′-*Hydroxychalcone* (XV; R = H).—2′-Hydroxychalcone (8·5 g.), with the mixed reagent in tetrahydrofuran, gave yellow crystals (8·2 g.). A solution of these in ether (250 ml.) was extracted with 2N-sodium hydroxide (6 × 125 ml.). The alkali-soluble portion, recovered by acidification and extraction with ether, was an oil (2·3 g.), and the alkali-insoluble portion was a partly-crystalline yellow oil (5·5 g.). The latter was chromatographed on alumina (10% deactivated grade H; 170 g.). Elution with light petroleum–benzene (3 : 1 v/v) (200 ml.) yielded an oil (0·40 g.) which could not be crystallised even after further chromatography. Further elution with the same solvent mixture (1500 ml.) yielded 1-o-*hydroxyphenyl*-3-*phenylprop*-1-*ene* (XVI; R = H) which separated from light petroleum–benzene as needles (3·5 g.), m. p. 67—68° (Found: C, 85·9; H, 6·6. $C_{15}H_{14}O$ requires C, 85·7; H, 6·7%), $\lambda_{max.}$ (in ethanol) 254 mμ (ε 26,730), $\nu_{max.}$ (in Nujol) 3300 (OH), 970 (*trans*-CH=CH), 765, 740, and 690 cm.$^{-1}$ (aromatic). The only crystalline material isolated from the alkali-soluble product was more (0·13 g.) of the above propene, m. p. and mixed m. p. 66—67°.

The *phenylurethane* separated from aqueous methanol as needles, m. p. 138—139° (Found: C, 80·25; H, 5·85; N, 4·55. $C_{22}H_{19}NO_2$ requires C, 80·15; H, 5·8; N, 4·3%). Claisen,[11] and Hurd and Schmerling [12] give 132° for the m. p. of the urethane of the prop-2-ene.

Flavan.—The above prop-1-ene (XVI; R = H) (0·80 g.) in methanol (20 ml.) was boiled under reflux for 3 hr. The mixture was poured into excess of water and the products extracted with ether. Removal of the solvent and recrystallisation from light petroleum–benzene gave unchanged prop-1-ene (0·56 g., 70%), m. p. and mixed m. p. 66—67°. Evaporation of the mother liquor and chromatography of the residue on alumina (10% deactivated grade H) gave two fractions: (i) light petroleum–benzene (1 : 5 v/v; 60 ml.) yielded flavan (0·12 g., 15%), m. p. and mixed m. p. 43—44°; (ii) benzene (60 ml.) yielded unchanged prop-1-ene (0·08 g., 10%), m. p. and mixed m. p. 66—67°.

A second experiment, in which the mixture was boiled for 12 hr., gave flavan (26%) and unchanged prop-1-ene (72%).

Reduction of 2′-*Hydroxy*-4-*methoxychalcone* (XV; R = OMe).—The chalcone (12·5 g.) with the mixed reagent in tetrahydrofuran gave a partly crystalline oil which, on recrystallisation from light petroleum–benzene (5 : 1 v/v), gave 3-o-*hydroxyphenyl*-1-p-*methoxyphenylprop*-1-*ene* (XVII; R = OMe) (5·0 g.) as needles, m. p, 98·5—99·5° (Found: C, 80·05; H, 6·4. $C_{16}H_{16}O_2$ requires C, 80·0; H, 6·65%), $\lambda_{max.}$ (in ethanol) 205, 262, 290 (infl.), and 310 mμ (infl.) (ε 37,200, 28,800, 4200, and 1900), $\nu_{max.}$ (in dichloromethane) 3580 (OH) and 972 cm.$^{-1}$ (*trans*-CH=CH). The residue from the mother liquors was chromatographed on alumina (10% deactivated grade H; 550 g.). Elution with light petroleum–benzene (3 : 1 v/v) (6 l.) yielded a solid (3·92 g.) which separated from light petroleum–benzene as needles, m. p. and mixed m. p. (with the above propene) 98—99°.

Elution with benzene–ether (2 : 1 v/v) (2 l.) and crystallisation from light petroleum–benzene gave 1-o-*hydroxyphenyl*-3-p-*methoxyphenylprop*-1-*ene* (XVI; R = OMe) (0·95 g.) as needles, m. p. 88—89° (Found: C, 79·9; H, 6·6. $C_{16}H_{16}O_2$ requires C, 80·0; H, 6·65%), $\lambda_{max.}$ (in ethanol) 202, 260, and 300 mμ (infl.) (ε 32,400, 25,100, and 3900), $\nu_{max.}$ (in Nujol) 3413 (OH) and 975 cm.$^{-1}$ (*trans*-CH=CH). The action of boiling ethanolic hydrochloric acid (2 hr.) on this propene yielded no 4′-methoxyflavan.

4′-Methoxyflavan.—(*a*) From 3-*o*-hydroxyphenyl-1-*p*-methoxyphenylprop-1-ene (XVII; R = OMe). A solution of the prop-2-ene (0·30 g.) in ethanol (25 ml.) and concentrated hydrochloric acid (5 ml.) was boiled for 2 hr. under nitrogen. Water (75 ml.) was added and an oil was isolated in ether. Filtration through alumina (5% deactivated grade H) in light petroleum–benzene (1 : 1 v/v) gave 4′-methoxyflavan (0·25 g.) which separated from light petroleum (b. p. 40—45°) as needles, m. p. 83—84°, unchanged on admixture with an authentic specimen (Found: C, 79·75; H, 6·5. Calc. for $C_{16}H_{16}O_2$: C, 80·0; H, 6·65%).

(*b*) From 2′-hydroxy-4-methoxychalcone (XV; R = OMe). The chalcone (2·55 g.) was reduced as described above and the resulting oil was dissolved in ethanol (100 ml.) and concentrated hydrochloric acid (15 ml.), and heated under reflux for 2 hr. Water (600 ml.) was added, the product taken up in ether (120 ml.), and the solution extracted with 2N-sodium hydroxide (10 × 15 ml.), washed with water, dried, and evaporated. The resulting brown oil was chromatographed to yield 4′-methoxyflavan (1·2 g.), m. p. and mixed m. p. 83—84°.

1-o-*Benzoyloxyphenyl*-3-p-*methoxyphenylpropane* (V).—The above propene (XVII; R = OMe) (0·43 g.) was hydrogenated in ethanol (50 ml.) over Adams's catalyst (uptake 1 mol. of hydrogen in 30 min. at 20°/757 mm.). Removal of the catalyst and evaporation gave an oil which was benzoylated (Schotten–Baumann). Isolation with ether and filtration in light petroleum (b. p. 60—80°)–benzene (3 : 1 v/v) through alumina (15 g. of 5% deactivated grade H) gave the benzoyl compound (0·27 g.) which separated from aqueous methanol as needles, m. p. 45—46° (Found: C, 79·3; H, 6·3%).

Reduction of 2-*Hydroxychalcone* (XVIII; R = R′ = H).—(*a*) 2-Hydroxychalcone (11·0 g.) in tetrahydrofuran (150 ml.) was added to a cooled solution of lithium aluminium hydride (5·0 g.) and aluminium chloride (25·0 g.) in tetrahydrofuran (350 ml.), and the mixture was boiled under reflux for 4 hr. Excess of reducing agent was decomposed with wet ether (400 ml.) and dilute sulphuric acid (200 ml.). The layers were separated and the aqueous solution was extracted with more ether (3 × 100 ml.). The combined extracts were extracted with 5N-sodium hydroxide (2 × 500 ml.); a solid appeared. Evaporation of the washed and dried ethereal layer yielded a yellow oil (0·80 g.) which on chromatography gave non-phenolic material (0·11 g.) which could not be crystallised. Acidification and ether extraction of the alkaline solution and of the precipitate yielded a solid (9·0 g.) which was acetylated by using acetic anhydride–pyridine to give a yellow oil which was chromatographed on alumina (10% deactivated grade H; 900 g.). Elution with light petroleum–benzene (4 : 1 v/v; 1200 ml.) yielded an oil (0·30 g.) which could not be crystallised. Further elution with the same solvent mixture (3·5 l.) yielded 3-*o*-acetoxyphenyl-1-phenylpropan-3-one (6·2 g.) which separated from aqueous ethanol as needles, m. p. 66—67°, $\nu_{\text{max.}}$ (in Nujol) 1760 (acetate) and 1690 cm.$^{-1}$ (aryl ketone). Hydrolysis of the acetate with aqueous methanolic potassium hydroxide gave 3-*o*-hydroxyphenyl-1-phenylpropan-3-one (XIX; R = R′ = H) which separated from light petroleum–benzene as plates, m. p. 90—91°, $\nu_{\text{max.}}$ (in Nujol) 3300 (OH) and 1670 cm.$^{-1}$ (aryl ketone). Feuerstein and Kostanecki[16] report m. p. 91—92° for the phenolic ketone, and m. p. 65—66° for its acetate.

Elution with light petroleum–benzene (3 : 1 v/v) yielded a pale yellow oil which could not be crystallised. Hydrolysis with aqueous methanolic potassium hydroxide gave 3-*o*-hydroxyphenyl-1-phenylpropan-3-ol (XXI; R = R′ = H) (2·2 g.) which separated from light petroleum–benzene as needles, m. p. 94·5—95·5° (Found: C, 78·95; H, 7·15. Calc. for $C_{15}H_{16}O_2$: C, 78·95; H, 7·0%), $\lambda_{\text{max.}}$ (in ethanol) 273 and 280 mμ (ε 2570 and 2220). Stoermer *et al.*[17] report m. p. 94°.

(*b*) The chalcone (1·12 g.) in tetrahydrofuran (20 ml.) was added to a mixture of lithium aluminium hydride (0·60 g.) and aluminium chloride (10·7 g.) in tetrahydrofuran (75 ml.), and the solution was boiled under reflux for 30 min. Treatment in the usual way with wet ether, water, and dilute sulphuric acid yielded a yellow oil which was filtered through alumina (grade H) in light petroleum to give flavan (XX; R = R′ = H) (0·18 g.), m. p. and mixed m. p. 43—44°.

Reduction of 2-*Hydroxy*-4′-*methoxychalcone* (XVIII; R = OMe, R′ = H).—(*a*) The chalcone (5·0 g.) with the mixed reagent [lithium aluminium hydride (2·0 g.) and aluminium chloride (10 g.)] in tetrahydrofuran gave a reddish-brown oil (5·1 g.).

(i) Separation with aqueous alkali. The crude product (5·1 g.) in ether (200 ml.) was

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[16] Feuerstein and Kostanecki, *Ber.*, 1898, **31**, 710.

[17] Stoermer, Chydenius, and Schinn, *Ber.*, 1924, **57**, 78.

extracted with 4N-sodium hydroxide (5 × 100 ml.). The ethereal layer yielded an oil (3·25 g.). A white solid had appeared on addition of alkali and this, together with the alkaline solution, was acidified and extracted with ether to yield a red oil (1·4 g.).

The alkali-insoluble oil (3·25 g.) in light petroleum–benzene (3 : 2 v/v) (10 ml.) was chromatographed on alumina (10% deactivated grade H; 100 g.). Elution with light petroleum–benzene (3 : 1 v/v; 100 ml.) yielded a white solid (1·2 g.) which separated from light petroleum as needles, m. p. and mixed m. p. 83—84° with 4′-methoxyflavan (XX; R = OMe, R′ = H). Further elution with light petroleum–benzene yielded oils (1·8 g.) which were acetylated. The resulting oil was chromatographed in light petroleum–benzene (2 : 1 v/v) on alumina (10% deactivated grade H; 150 g.). Elution with the same solvent mixture (750 ml.) yielded an oil (0·70 g.) which, even after further chromatography, was not obtained crystalline; $\nu_{max.}$ (natural film) 1755 cm.$^{-1}$ (acetate). Elution with light petroleum–benzene (3 : 2 v/v; 100 ml.) yielded a solid (0·70 g.) which separated from aqueous ethanol as plates, m. p. 83—84°, unchanged on admixture with authentic 3-*o*-acetoxyphenyl-1-*p*-methoxyphenylpropan-1-one. The infrared spectra of the two samples in Nujol were identical.

The alkali-soluble oil (1·4 g.) was acetylated to give crystals. Recrystallisation from ethanol gave the above acetoxypropanone (0·56 g.) as plates, m. p. and mixed m. p. 83—84°. The oil from the mother liquors was chromatographed on alumina (10% deactivated grade H; 40 g.) and eluted with light petroleum–benzene (2 : 1 v/v) (80 ml.) to give 4′-methoxyflavan (0·20 g.), m. p. and mixed m. p. 83—84°. Further elution with the same solvent mixture yielded the acetoxypropanone (0·31 g.), m. p. and mixed m. p. 82—83°.

(ii) Separation with Claisen's alkali. The crude reduction product (3·9 g.) in ether (200 ml.) was extracted with Claisen's alkali (4 × 50 ml.). Acidification of the alkaline solution and extraction with ether yielded crystals which separated from benzene as prisms, m. p. 116·5—118°, and which were shown to be 1-*p*-methoxyphenyl-3-*o*-hydroxyphenylpropan-1-ol (XXI; R = OMe, R′ = H) by mixed m. p. and infrared comparison.

(*b*) A mixture of the chalcone (1·0 g.), lithium aluminium hydride (0·60 g.), aluminium chloride (10·7 g.), and tetrahydrofuran (100 ml.) was boiled for 30 min. and worked up in the usual way to give a product which on filtration through alumina (grade H) in light petroleum–benzene (19 : 1 v/v) gave 4′-methoxyflavan (XX; R = OMe, R′ = H) (0·79 g., 84%) as plates m. p. and mixed m. p. 82—83°.

When the mixture was boiled for 2·5 hr. the yield of 4′-methoxyflavan was 68%.

Reduction of 2-*Hydroxy*-3′,4′-*dimethoxychalcone* (XVIII; R = R′ = OMe).—A mixture of the chalcone (0·62 g.), lithium aluminium hydride (0·33 g.), aluminium chloride (7·3 g.), and tetrahydrofuran (90 ml.) was boiled for 30 min. and worked up to give a product which on filtration through alumina (grade H) in benzene–ether (9 : 1 v/v) gave 3′,4′-dimethoxyflavan (XX; R = R′ = OMe) (0·30 g.) as prisms (from ethanol), m. p. 99·5—100·5° (Found: C, 75·35; H, 6·55; OMe, 23·45. Calc. for $C_{17}H_{18}O_3$: C, 75·55; H, 6·7; 2OMe, 22·95%). Hathway and Seakins [18] record m. p. 99—100°.

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[18] Hathway and Seakins, *J.*, 1957, 1562.