(*S*)-2-Hydroxycuparene [*p*-(1,2,2-Trimethylcyclopentyl)-*o*-cresol] and 3,4'-Ethylenebisphenol from a Liverwort, *Marchantia polymorpha* Linn.

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(*S*)-2-Hydroxycuparene and 3,4'-ethylenebisphenol have been isolated from *Marchantia polymorpha* Linn., together with a mixture of campesterol, stigmasterol, and β-sitosterol, and other terpenoid constituents. Syntheses of (*R*)-2-hydroxycuparene and of the bisphenol are reported.

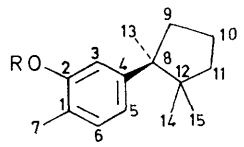
METABOLIC processes in some liverworts (Hepaticae) have already been shown [1] to lead to sesquiterpenoids of unusual stereochemistry. It was therefore interesting to find a novel hydroxycuparene in the liverwort, *Marchantia polymorpha* Linn., with *S*-chirality, whereas the known cuparenes from higher plants [2] are uniformly *R*-chiral; known (*S*)-cuparenes (*e.g.* helicobasidin, deoxyhelicobasidin,[3] and lagopodin A [4]) have been reported as metabolites of the botanically still lower division of the fungi (Phycophyta).

The liquid phenol (I), $C_{15}H_{22}O$, $[\alpha]_D$ −65° (in $CHCl_3$) (benzoate, m.p. 98—99°), obtained from *Marchantia polymorpha* Linn., possessed one methyl group [δ ($CDCl_3$) 2·21] on its aromatic ring and was identified as a cuparene derivative by the unusually shielded resonance (δ 0·55) of one of its alkyl methyl groups: a Dreiding model shows that position 15 † is well within the shielding zone of the aromatic ring. The *ortho*-relationship of the hydroxy-group and the aryl methyl group was deduced from the unchanged position of the aryl methyl resonance on benzoylation; we have found ‡ that the resonance shift (Δδ in deuteriochloroform solution) of an aryl methyl group of a methylphenol on benzoylation is effectively zero for *ortho*-methylphenols, but is *ca.* +0·1 p.p.m. for *meta*- and *para*-methylphenols (see Table) when no marked out-of-plane crowding effects occur.

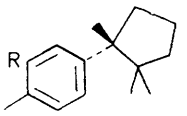
Δδ Values (p.p.m.) for methyl singlets of *x*-methylphenols and their benzoates (solutions in $CDCl_3$; internal standard Me_4Si)

	δ			
x	free phenol	benzoate	δΔ	OH–Me relationship
2	2·20	2·22		
2,4	2·20	2·17		
2,5	2·17	2·17	−0·01 ± 0·02	*o*
2,6	2·21	2·18		
3	2·22	2·35		
2,5	2·22	2·32	+0·11 ± 0·02	*m*
3,5	2·23	2·32		
4	2·23	2·33	+0·09 ± 0·02	*p*
2,4	2·23	2·30		
3,4	2·16 (6H,s)	2·26 (6H,s)	+0·10	*m* + *p*

Structure (I) for the new hydroxy-cuparene was proven by synthesis of the enantiomeric form of the compound from (*R*)-cuparene (III). This was achieved both in a single reaction sequence *via* direct thallation [5] of (*R*)-cuparene (III) to give (IV), and, more satisfactorily, by nitration of (*R*)-cuparene [to give (V)] and replacement of the nitro-group by OH *via* the amino-derivative (VI), which was characterized as its crystalline diacetyl derivative (VII). The latter sequence provided



(I) R = H
(II) R = Bz



(III) R = H (IV) R = OH
(V) R = NO_2 (VI) R = NH_2
(VII) R = NAc_2

further support for the *ortho*-relationship of the aryl methyl and hydroxy-groups in (IV), and hence in (I): the resonance positions of the former were δ ($CDCl_3$) 2·29 for (III), δ (CCl_4) 2·55 for (V), δ (CCl_4) 2·05 for (VI) and (VII), and δ (CCl_4) 2·16 for (IV), thus demonstrating the deshielding and shielding effects expected for adjacent nitro- and amino-groups.

The structural identity and enantiomeric relationship of the *S*- and *R*-forms [(I) and (IV)] were demonstrated by the identity of the i.r., n.m.r., and mass spectra of these compounds and their crystalline acetates and benzoates, by the identical m.p.s of the latter, and by the mirror-image relationship of their o.r.d. curves and $[\alpha]_D$ values.

The plant extract also yielded a mixture of constituents obtained as a chromatographically homogeneous fraction: g.l.c. analysis of this mixture and of its fully hydrogenated products indicated (see Experimental section) that it contained the nortriterpenes campesterol, stigmasterol, and β-sitosterol. Other terpenoid constituents were two alcohols, $C_{15}H_{28}O$ and $C_{20}H_{34}O$ (see Experimental section), which were not fully characterized.

A minor constituent of the plant was found to be 3,4'-ethylenebisphenol (VIII), reported by Asahina and Asano [6] as a degradation product of hydrangenol and

† The numbering of cuparene used here [see (I)] is based on that of *p*-cymene and *p*-menthane.

‡ As first reported (by G. W. P.) at the South African Chemical Institute Convention, Grahamstown, February, 1971.

[1] H. Knoche, G. Ourisson, G. W. Perold, J. Foussereau, and J. Maleville, *Science*, 1969, **166**, 239.

[2] In G. Ourisson, S. Munavalli, and C. Ehret, 'Data Relative to Sesquiterpenoids,' Pergamon, London, 1966, pp. VIII and 8; the structure given for helicobasidin on p. VIII is that of the (*R*)-enantiomer of the natural (*S*)-product.

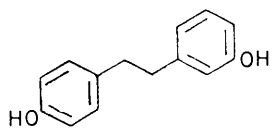
[3] S. Natori, Y. Inouye, and H. Nishikawa, *Chem. and Pharm. Bull. (Japan)*, 1967, **15**, 380.

[4] P. Bollinger, Thesis, Eidgen. Techn. Hochschule, Zürich, 1965; R. H. Thomson, 'Naturally Occurring Quinones,' 2nd edn., Academic Press, London, 1971, p. 131.

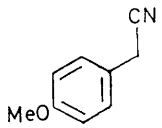
[5] E. C. Taylor, H. W. Altland, R. H. Danforth, G. McGillivray, and A. McKillop, *J. Amer. Chem. Soc.*, 1970, **92**, 3250.

[6] Y. Asahina and J. Asano, *Ber.*, 1930, **63**, 429.

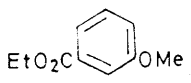
prepared by these authors in low yield.[7] We report a more satisfactory synthesis *via* the condensation of *p*-methoxybenzyl cyanide (IX) with ethyl *m*-methoxybenzoate (X). The product (XI) was converted *via* the imino-ester hydrochloride (XII) into the β-keto-ester (XIII). On alkaline hydrolysis, even in aqueous medium at room temperature only, this β-keto-ester merely suffered a reversal of the condensation reaction, and *p*-methoxyphenylacetic and *m*-methoxybenzoic acids were the only products so isolated. Hydrolysis under drastic acidic conditions,[8] however, afforded the expected decarboxylation product, *p*-methoxybenzyl *m*-methoxyphenyl ketone (XIV), in 60% yield. This ketone, m.p. 59°, had previously been reported (m.p. 61°) [9] as a rearrangement product of the corresponding 1,1-diarylethylene oxide.



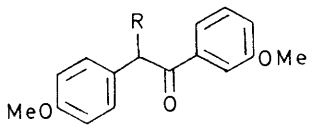
(VIII)



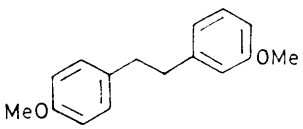
(IX)



(X)



(XI) R = CN
(XII) R = C(OEt)=NH,HCl
(XIII) R = CO_2Et
(XIV) R = H



(XV)

On catalytic hydrogenation over palladium–carbon the ketone (XIV) was hydrogenated but only partly hydrogenolysed; on Clemmensen reduction, however, the product was smoothly converted into the bismethyl ether (XV), which was then demethylated. The resulting bisphenol (VIII) was identical (see Experimental section) with the compound obtained from the plant.

EXPERIMENTAL

M.p.s were taken on a Kofler micro hot-stage apparatus. Spectra were obtained on Unicam SP 1800 (u.v.), Perkin-Elmer 521 (i.r.), A.E.I. MS9 and Varian-MAT CH5 (mass), Hitachi–Perkin-Elmer R20 (n.m.r.), and JASCO ORD/UV-5 (c.d.) spectrometers. I.r. data are for potassium bromide dispersions except where noted otherwise. Optical rotations were determined for chloroform solutions on a Perkin-Elmer 141 polarimeter. N.m.r. data are δ values, relative to tetramethylsilane; separations (*S* in Hz) are quoted as read from the spectra. T.l.c. was carried out on Merck precoated plates of silica gel F254 and results are quoted as hR_F (= 100 × R_F) values; spots were revealed by spraying with chromic acid [10] or, for phenols, with Pauly's reagent.[11] Column chromatography was performed over Merck silica gel (0·05—0·20 mm). Reactions were carried out at room temperature unless specified otherwise. Elemental analyses (Perkin-Elmer C-H-N-analyser) and some n.m.r. spectra were obtained by Mr. T. P. Jwili, and some mass spectra were measured by Mr. A. Zaffirellis.

Air-dried cleaned whole plants (thalli with associated rhizoid mats and some capitula) of *Marchantia polymorpha* Linn., collected in November in Jonkershoek, Stellenbosch, Cape, at about 600 m above sea-level, were milled (269 g) and extracted (Soxhlet; ether) for 44 h; the thimble packing was dried, repacked, and again extracted for 165 h. The dried extracts (3·35 g) on t.l.c. showed four groups of major spots around hR_F 96, 80, 45, and 0 in benzene–ethyl acetate (5 : 1 v/v) and were chromatographed over silica gel (150 g).

(S)-2-*Hydroxycuparene* [(S)-(1,2,2-*Trimethylcyclopentyl*)-*o*-*cresol*].—Combined chromatographic fractions showing major spots around hR_F 80 (system as above) (877 mg) were twice distilled up to 200° (bath) at 0·1 Torr to afford a yellow viscous oil (303 mg), which was chromatographed to give an oil (235 mg) with a strong ' mossy ' odour showing components at hR_F 67 (major) and 50 (minor) in benzene–ethyl acetate (19 : 1 v/v). The major * component, (S)-2-*hydroxycuparene*, was obtained pure (97 mg) in partial recovery by chromatography in benzene–ethyl acetate (39 : 1 v/v); it gave an orange spot with Pauly's reagent; [11] b.p. 100° (bath) at 0·05 Torr (Found: C, 81·9, 82·7; H, 10·2, 10·4. $C_{15}H_{22}O$ requires C, 82·5; H, 10·2%), $[\alpha]_D$ −65° (*c* 1·2), $\lambda_{max.}$ (MeOH) 220 and 276 nm (ε 7000 and 2300), $\lambda_{max.}$ (0·01M-NaOH in MeOH) 240 and 290 nm (ε 5600 and 2700), $\bar{\nu}_{max.}$ ($CHCl_3$) 3600 and 3340br (OH), 2950 and 2870 (CH_3 and CH_2), 1380, 1370, and 1190 cm^{-1} (Me_2C),[12] δ ($CDCl_3$) 7·1—6·8 (3H, m, arom.), 4·65br (1H, OH), and 2·21, 1·23, 1·07, and 0·58 (4 × 3H, s, Me), *m/e* 218 (M^+, 83%), 161 (29), 148 (81), and 136 (100).

Compound (I) (16 mg) was heated in acetic anhydride (130 mg) and sodium acetate (10 mg) for 3 h at 95°, and the neutral product was sublimed at 30—40° and 0·03 Torr to give (S)-2-*acetoxycuparene* (16 mg), m.p. 37·5—38·5° (Found: C, 78·8; H, 9·45. $C_{17}H_{24}O_2$ requires C, 78·4; H, 9·3%), $[\alpha]_D$ −44° (*c* 1·17), $\bar{\nu}_{max.}$ 1760 and 1210 cm^{-1} ($MeCO_2Ar$),[13] δ (CCl_4) 7·1—6·8 (3H, m, arom.), 2·09 (3H, s, $ArO_2C{\cdot}CH_3$), and 2·22, 1·24, 1·04, and 0·56 (4 × 3H, s, Me), *m/e* 260 (M^+).

(S)-2-*Benzoyloxycuparene* was obtained from the compound (I) (17 mg) with benzoyl chloride in 2M-sodium hydroxide; the product was chromatographed and crystallized from hexane (22 mg; m.p. 98—99°) (Found: C, 82·1; H, 8·1. $C_{22}H_{26}O_2$ requires C, 81·9; H, 8·1%), $[\alpha]_D$ −38° (*c* 0·8), $\bar{\nu}_{max.}$ 1732 and 1275, 1260, and 1250 ($PhCO_2Ar$),

* The minor component had the mossy odour; it was a liquid alcohol (Found: C, 82·3; H, 11·8. Calc. for $C_{20}H_{34}O$: C, 82·7; H, 11·8%), $\bar{\nu}_{max.}$ ($CHCl_3$) 3590 and 3450 cm^{-1} (OH), *m/e* 290 (M^+), which was not fully characterized.

[7] Ref. 6, pp. 436—437.

[8] L. Gattermann and H. Wieland, ' Laboratory Methods of Organic Chemistry,' 22nd edn., Macmillan, London, 1934, p. 130.

[9] J. Lévy and R. Pernot, *Bull. Soc. chim. France*, 1931, **49**, 1730, 1734.

[10] H. Ertel and L. Horner, *J. Chromatog.*, 1962, **7**, 268.

[11] ' Chromatography with Particular Consideration of Paper Chromatography,' E. Merck AG, Darmstadt, 2nd edn., p. 144.

[12] K. Nakanishi, ' Infrared Absorption Spectroscopy, Practical,' Holden-Day, San Francisco, 1972, p. 20.

[13] L. J. Bellamy, ' The Infrared Spectra of Complex Molecules,' 2nd edn., Methuen, London, 1962, pp. 179, 182, and 190.

$\bar{\nu}_{max.}$ ($CHCl_3$) 1732 and 1265 cm^{-1} ($PhCO_2Ar$),[14] δ ($CDCl_3$) 8·33—8·18 and 7·65—7·10 (8H, m, arom.) and 2·20, 1·27, 1·05, and 0·60 (4 × 3H, s, Me), δ (CCl_4) 8·2—8·05 and 7·6—6·95 (8H, m, arom.) and 2·16, 1·28, 1·06, and 0·62 (4 × 3H, s, Me), *m/e* 322 (M^+).

3,4′-*Ethylenebisphenol* (VIII).—Combined chromatographic fractions (905 mg) showing major spots around hR_F 45 in benzene–ethyl acetate (5 : 1 v/v) were twice distilled up to 200° (bath) at 0·1 Torr and the distillate (130 mg) was chromatographed. Fractions showing spots at hR_F 37 in benzene–ethyl acetate (6 : 1 v/v) crystallized (17 mg), and from benzene gave needles of the bisphenol, m.p. 108·5—109° (Found: C, 78·7; H, 6·55. Calc. for $C_{14}H_{14}O_2$: C, 78·5; H, 6·6%), $\lambda_{max.}$ (MeOH) 224 and 278 nm (ε 16,000 and 3400), $\lambda_{max.}$ (0·04M-NaOH in MeOH) 223, 243sh, and 282 nm (ε 16,000, 5900, and 3200), $\bar{\nu}_{max.}$ 3350br cm^{-1} (OH), δ ($CDCl_3$) 7·3—6·6 (8H, m, arom.), 4·65 (2H, s, OH), and 2·83 (4H, s, Ar-CH_2), *m/e* 214 (M^+, 31), 107 (100), and 77 (10%); a t.l.c. spot with Pauly's reagent [11] gave a yellow colour with a brown edge. Compound (VIII) (13 mg; crude), was treated with benzoyl chloride (0·1 ml in all) and 1·5M-sodium hydroxide and the product was chromatographed (22 mg) to give the *dibenzoate* (9 mg), m.p. 108—110° (from benzene–hexane) (Found: C, 79·85; H, 5·3. $C_{28}H_{22}O_4$ requires C, 79·6; H, 5·25%), $\bar{\nu}_{max.}$ 1733sh, 1730, 1270, and 1140 cm^{-1} ($PhCO_2Ar$),[14] δ ($CDCl_3$) 8·3—8·1 (4H, m, benzoate *ortho*-H), 7·6—7·0 (14H, m, arom. H), and 2·95 (4H, s, $ArCH_2 \cdot CH_2Ar'$).

Marchantia polymorpha Linn., collected in August at the end of winter at the same site, was milled (1151 g) and extracted with ether as before to yield a dried extract (6·77 g) which on t.l.c. resembled the previous extract in every way. (*S*)-2-Hydroxycuparene (251 mg) was obtained by repeated chromatography only and resembled the sample obtained before in every way. The bisphenol (VIII) could not, however, be isolated from the apposite chromatographic fractions, although a phenolic component was present which on t.l.c. resembled it. These undistilled fractions (584 mg in all) on careful separation did, however, furnish a chromatographically pure sesquiterpenoid alcohol [117 mg; hR_F 64 in benzene–ethyl acetate (4 : 1 v/v), $\bar{\nu}_{max.}$ (CCl_4) 3590 cm^{-1} (OH), *m/e* 224 ($C_{15}H_{28}O$, M^+ only at *ca.* 10 eV), 209 (Found: *m/e* 209·189. Calc. for $C_{14}H_{25}O$: *m/e* 209·191)], and a mixture of triterpenes (302 mg) showing a single t.l.c. spot at hR_F 46 in benzene–ethyl acetate (4 : 1 v/v), and giving needles (from ethanol), m.p. 138—139°, raised to *ca.* 145° on further crystallization (Found: C, 84·9; H, 12·1. Calc. for $C_{29}H_{48}O$: C, 84·4; H, 11·7. Calc. for $C_{29}H_{50}O$: C, 84·0; H, 12·2%), $\bar{\nu}_{max.}$ 3400br cm^{-1} (OH), δ ($CDCl_3$) 5·3 and 5·05 (2 m, olefinic), 3·45br (s, OH), and 1·0 and 0·7 (2 s, Me), *m/e* 414 (M^+ for $C_{29}H_{50}O$, 20%), 412 (M^+ for $C_{29}H_{48}O$, 16%), 400 (20), and 43 (100). This mixture on g.l.c. (1·8 × 0·006 m column; 3% GE SE30 on Chromosorb Q; 258°; N_2 at 5 lb in^{-2}) showed three major components in about equal proportions with retention times of 15·0, 15·8, and 18·3 min, the same values as obtained for authentic campesterol, stigmasterol, and β-sitosterol in that order. The mixture (24 mg) was hydrogenated over platinum (1 Torr; 16 h) to give a saturated product (23 mg), m.p. 135—140° (from methanol), no n.m.r. signals >δ 4 in $CDCl_3$, *m/e* 416 (30%), 402 (20), and 43 (100), which on g.l.c. (as above; N_2 at 7 lb in^{-2}) showed only two major peaks with retention times 13·5 and 16·5 min in the ratio 1 : 2 (retention times for dihydrocampesterol and tetrahydrostigmasterol 13·2 and 16·5 min, respectively).

Synthesis of (R)-2-*Hydroxycuparene*.—(*R*)-Cuparene (170 mg) was obtained from a hydrocarbon mixture (1 g; extracted * from Cupressaceae and containing about 38% of cuparene by g.l.c. analysis) by preparative g.l.c. separation (retention time 7·5 min; 1·8 × 0·006 m glass column; 10% FFAP on Chromosorb Q; 168°; nitrogen at 50 lb in^{-2}; flow rate 200 ml min^{-1}); $[\alpha]_D$ +58° (*c* 1·4) (lit.,[15] +65°), $\bar{\nu}_{max.}$ (neat) 3080, 3050, and 3010 (arom. CH), and 810 cm^{-1} (*p*-disubst. benzene), δ ($CDCl_3$) 7·22 and 7·00 (2, d, *S* 8 Hz, arom.) and 2·29, 1·25, 1·05, and 0·55 (4 s, Me).

(*a*) (*R*)-Cuparene (99 mg) was shaken for 30 min in 0·88M-thallium trifluoroacetate in trifluoroacetic acid (0·625 ml). Lead tetra-acetate (221 mg) in trifluoroacetic acid was added, followed, after 30 min, by triphenylphosphine (131 mg), and the solvent was evaporated off at 45° and 15 Torr. Insoluble chlorides were removed by addition of 5M-hydrochloric acid (4 ml) and a brown oil was recovered (extraction with ether) and boiled for 2 h with 2M-potassium hydroxide. The product was extracted with ether (176 mg), triphenylphosphine oxide (46 mg) was precipitated with light petroleum, and the remainder was chromatographed in benzene–ethyl acetate (500 : 1 v/v) to give slightly impure (*R*)-2-hydroxycuparene (10 mg), b.p. 100—110° (bath) at 0·05 Torr (Found: C, 81·7; H, 9·6. $C_{15}H_{22}O$ requires C, 82·5; H, 10·2%), $[\alpha]_D$ +58°, δ (CCl_4) *ca.* 6·7 (poorly defined m, arom.), 4·3br (OH), and 2·15, 1·20, 1·05, and 0·57 (4 s, Me).

(b) (R)-2-*Nitrocuparene*. To the impure hydrocarbon mixture (5·36 g; see above, containing about 38% cuparene) stirred in concentrated sulphuric acid (2·9 ml) was added a mixture of concentrated nitric (2·7 ml) and sulphuric (4·6 ml) acids during 30 min. The mixture was stirred for a further 18 h, and poured into ice–water to precipitate a solid (1·12 g; insoluble in ether). The ethereal extract of the filtrate was washed with 4M-potassium hydroxide and gave a liquid neutral product (3·70 g), which on chromatography in benzene–light petroleum gave a mixture (hR_F 90 in benzene–light petroleum, 1 : 1 v/v), containing cuparene (by g.l.c.), which was again nitrated in the same way; (R)-2-*nitrocuparene* was eluted as above (hR_F 75; same eluant) and was a liquid (615 mg in all), b.p. 115—120° (bath) at 0·05 Torr (Found: C, 72·6; H, 8·65; N, 5·15. $C_{15}H_{21}NO_2$ requires C, 72·9; H, 8·6; N, 5·7%), $[\alpha]_D$ +3° (*c* 1·14), $\bar{\nu}_{max.}$ (neat) 1530 and 1350 cm^{-1}, δ (CCl_4) 7·93 (1H, d, *S* 2 Hz), 7·45 (1H, dd, *S* 2 and 8 Hz), and 7·18 (1H, d, *S* 8 Hz) (arom.), and 2·55, 1·27, 1·07, and 0·57 (4 × 3H, s, Me), *m/e* 247 (M^+, 74%), 177 (100), and 160 (95).

(R)-2-*Aminocuparene*. (*R*)-2-Nitrocuparene (600 mg) was boiled under reflux with 10M-hydrochloric acid (6 ml), ethanol (6 ml), and granulated tin (600 mg) for 1 h. The mixture was treated with an excess of 12M-sodium hydroxide and extracted with ether (yield 550 mg); the product was chromatographed to give liquid (R)-2-*aminocuparene* (328 mg), b.p. 95—100° (bath) at 0·1 Torr (Found: C, 83·0; H, 10·7; N, 6·05. $C_{15}H_{23}N$ requires C, 82·9; H, 10·7; N, 6·4%), $\bar{\nu}_{max.}$ 3450 and 3370 cm^{-1} (NH_2), δ (CCl_4) 6·85—6·4 (3H, m, arom.), 3·29 (2H, s, NH_2), and 2·05, 1·19, 1·04, and 0·57 (4 × 3H, s, Me), *m/e* 217 (M^+, 84%) and 135 (100). Its *diacetate* was obtained from the amine (29 mg) and acetic anhydride (96 mg) by boiling under reflux for 15 min, then

* Originally obtained by Professor H. Erdtman (*Tetrahedron*, 1958, **4**, 361).

[14] Ref. 13, pp. 179 and 191.

[15] C. Enzell and H. Erdtman, *Tetrahedron*, 1958, **4**, 365.

adding water (20 ml), boiling for 30 min, and extracting with benzene (36 mg); chromatography over alumina and sublimation at 50—70° and 0·05 Torr gave 15 mg of material, m.p. 63—65° (Found: C, 75·9; H, 9·2; N, 4·6. $C_{19}H_{27}NO_2$ requires C, 75·7; H, 9·0; N, 4·65%), $\bar{\nu}_{max.}$ 1715 and 1705, and 1245 and 1225 cm^{-1} (Ac_2N), δ (CCl_4) 7·15—6·85 (3H, m, arom.), 2·15 and 2·13 (2 × 3H, s, NAc_2), and 2·05, 1·27, 1·03, and 0·55 (4 × 3H, s, Me), *m/e* 301 (M^+, 100%) and 259 (30).

(R)-2-*Acetoxycuparene*. (*R*)-Aminocuparene (170 mg) in 10M-hydrochloric acid (5 ml) and ethanol (2 ml) was treated with sodium nitrite (54 mg) in water (2 ml) at 0°. The solution was diluted with water (120 ml) and phosphoric acid (1·37 ml) and boiled for 1 h. The crude phenolic product (165 mg) was extracted with ether, chromatographed [106 mg; hR_F 42 in benzene–ethyl acetate (30 : 1 v/v)], and kept in acetic anhydride (1·5 ml) and sodium acetate (70 mg) at 100° for 3 h to yield (R)-2-*acetoxycuparene* (112 mg), distilled at 100—110° and 15 Torr (93 mg) and crystallized from hexane at −79°; m.p. 38—39° (Found: C, 78·5; H, 9·5. $C_{17}H_{24}O_2$ requires C, 78·4; H, 9·3%), $[\alpha]_D$ +47° (*c* 1·28), $\bar{\nu}_{max.}$ 1760 and 1210 cm^{-1}, δ (CCl_4) 7·0—6·8 (3H, m, arom.), 2·08 (3H, s, $ArO_2C{\cdot}CH_3$), and 2·21, 1·23, 1·03, and 0·57 (4 × 3H, s, Me), *m/e* 260 (M^+, 87%).

(R)-2-*Hydroxycuparene*. (*R*)-2-Acetoxycuparene (24 mg) in M-sodium hydroxide (3 ml) was kept at 100° for 3 h. Ethanol (3 ml) was then added and the mixture was kept for 3 days at 25° and for 1 h under reflux. The product was chromatographed (20 mg) and distilled at *ca.* 100° (bath) and 0·1 Torr to give liquid (R)-2-*hydroxycuparene* (12 mg) (Found: C, 82·45; H, 10·2. $C_{15}H_{22}O$ requires C, 82·5; H, 10·2%), $[\alpha]_D$ +63° (*c* 1·35), $\lambda_{max.}$ (MeOH) 220 and 276 nm (ε 7200 and 2400), $\bar{\nu}_{max.}$ (CCl_4) 3580 and 3450 cm^{-1} (OH), δ (CCl_4) 7·0—6·6 (3H, m, arom.), 4·63 (1H, s, OH), and 2·16, 1·19, 1·03, and 0·55 (4 × 3H, s, Me), *m/e* 218 (M^+, 69%), 161 (36), 148 (92), and 136 (100).

(R)-2-*Benzoyloxycuparene* was obtained from the foregoing compound (14 mg) in 2M-sodium hydroxide by shaking with benzoyl chloride and chromatographing the product; yield 22 mg, m.p. 98—99° (from hexane) (Found: C, 82·4; H, 8·1. $C_{22}H_{26}O_2$ requires C, 81·9; H, 8·1%), $[\alpha]_D$ +38° (*c* 0·7), $\bar{\nu}_{max.}$ 1732, 1275, 1260, and 1250 cm^{-1} ($PhCO_2Ar$) [identical with the spectrum of (*S*)-2-benzoyloxycuparene over the range 4000—400 cm^{-1}], δ (CCl_4) 8·22—8·05 and 7·6—6·95 (8H, m, arom.) and 2·16, 1·27, 1·07, and 0·61 (4 × 3H, s, Me).

Synthesis of 3,4′-*Ethylenebisphenol* (VIII).—*p*-Methoxybenzyl cyanide [16] (2·413 g, 16·5 mmol) and ethyl *m*-methoxybenzoate * (4·348 g, 24·1 mmol) [17] were kept in sodium ethoxide solution [sodium (0·525 g, 22·9 mmol) in absolute ethanol (12 ml)] under reflux at 95° for 15 h; ethanol (6 ml) was evaporated off and the mixture was treated with ice–water (25 ml) and extracted (ether) to give unchanged reactants (3·793 g) in the proportion of *ca.* 1 : 2 [hR_F 78 and 69 in benzene–ethyl acetate (9 : 1 v/v) for the ester and the nitrile in that order]; the aqueous solution was acidified with acetic acid (3 ml) and the condensation product (2·086 g) was recovered (ether) and chromatographed in benzene–ethyl acetate (9 : 1 v/v) to afford viscous 2-*p*-methoxyphenyl-2-*m*-methoxybenzoylacetonitrile (1·885 g, 41% based on starting nitrile), $\bar{\nu}_{max.}$ ($CHCl_3$) 2250w [18] (CN) and 1695s cm^{-1} (C=O), δ ($CDCl_3$) 7·5—6·7 (8H, m, arom.), 5·50 (1H, s, CH), and 3·77 and 3·72 (2 × 3H, s, Me), *m/e* 281 (M^+, 3%), 135 (100), 107 (27), and 77 (19). This product (975 mg) was kept in absolute ethanol (10 ml) containing hydrogen chloride (2·0 g) for 45 h. The solution was then treated with water (20 ml) and kept at 60° for 30 min, and the neutral product was recovered (1·008 g) and chromatographed (benzene–ethyl acetate) to give ethyl 2-*p*-methoxyphenyl-2-*m*-methoxybenzoylacetate (828 mg, 78%), b.p. 140—160° (bath) at 0·04 Torr, $\bar{\nu}_{max.}$ ($CHCl_3$) 1738 (ester C=O) and 1684 cm^{-1} (aryl ketone C=O), δ ($CDCl_3$) 7·5—6·7 (8H, m, arom.), 5·45 (1H, s, CH), 4·16 (2H, q, *S* 7 Hz) and 1·22 (3H, t, *S* 7 Hz) (Et), and 3·75 and 3·70 (2 × 3H, s, Me), *m/e* 328 (M^+, 2%), 135 (97), and 121 (100). This keto-ester (415 mg) in acetic acid–sulphuric acid–water (1 : 1 : 1 v/v; 40 ml) [8] was heated under reflux at 135° for 90 min, after which the evolution of carbon dioxide had ceased. The solution was diluted to 100 ml with water and the neutral product (275 mg) recovered (ether) and chromatographed to give *p*-methoxybenzyl *m*-methoxyphenyl ketone (195 mg, 60%), m.p. 58·5—59° (lit.,[9] 61°) (from benzene–hexane) (Found: C, 74·7; H, 6·2. Calc. for $C_{16}H_{16}O_3$: C, 75·0; H, 6·3%), $\bar{\nu}_{max.}$ 1685 cm^{-1} (aryl ketone), δ ($CDCl_3$) 7·6—6·65 (8H, m, arom.), 4·13 (2H, s, $CH_2{\cdot}CO$), and 3·76 and 3·70 (2 × 3H, s, Me), *m/e* 256 (M^+, 17%), 135 (100), and 121 (47); hR_F 39 in benzene–ethyl acetate (49 : 1 v/v). This ketone (129 mg) was hydrogenated over palladium–carbon (10%; 107 mg) in ethanol (20 ml) and 10M-hydrochloric acid (1·5 ml) for 7 h. The recovered product (107 mg) was chromatographed and fractions showing spots at hR_F 74 (25 mg; for the diarylethane derivative) and 14 (57 mg; for the benzylbenzyl alcohol derivative?) in benzene–ethyl acetate (49 : 1 v/v) were combined (79 mg) and boiled under reflux with amalgamated zinc (3 g), 6M-hydrochloric acid (10 ml), and ethanol (1 ml) for 3 h. The recovered neutral product (71 mg) was chromatographed to give liquid 3,4′-ethylenebisphenol dimethyl ether (67 mg), no i.r. absorption ($CHCl_3$) at 4000—3100 and 2800—1630 cm^{-1}, δ ($CDCl_3$) 7·1—6·5 (8H, m, arom.), 3·67 (6H, s, Me), and 2·79 (4H, s, CH_2), *m/e* 242 (M^+, 9%) and 121 (100). The dimethyl ether (50 mg) was heated in a sealed tube with pyridine hydrochloride (365 mg) at 210° for 5 h; the product was taken up in water and the phenolic product (40 mg) was recovered (ether) and chromatographed to give crystalline 3,4′-ethylenebisphenol (30 mg), hR_F 35 in benzene–ethyl acetate (6 : 1 v/v), m.p. 108—109° (from benzene), identical (mixed m.p. and i.r. spectrum) with the natural product (Found: C, 78·3; H, 6·5. Calc. for $C_{14}H_{14}O_2$: C, 78·5; H, 6·6%), *m/e* 214 (M^+, 11%) and 107 (100). The bisphenol (10 mg) was kept in pyridine (1 ml) and benzoyl chloride (0·1 ml) for 15 h. The product was recovered (20 mg) *via* extraction (ether–benzene) after treatment with water, and chromatographed to give the dibenzoate (14 mg), m.p. 108—110° (from benzene–hexane), identical (mixed m.p. and i.r. spectrum) with the dibenzoate of the natural product (Found: C, 79·6; H, 5·2. Calc. for $C_{28}H_{22}O_4$: C, 79·6; H, 5·25%), *m/e* 422 (M^+, 6%), 211 (10), 105 (100), and 77 (70).

* Obtained by Fischer–Speier esterification of *m*-methoxybenzoic acid (Light & Co.); b.p. 97—100° (bath) at 0·05 Torr.

[16] K. Rorig, J. D. Johnston, R. W. Hamilton, and T. J. Telinski, *Org. Synth.*, Coll. Vol. IV, 1963, p. 576.

[17] Condensation procedure patterned according to P. L. Julian, J. J. Oliver, R. H. Kimball, A. B. Pike, and G. D. Jefferson, *Org. Synth.*, Coll. Vol. II, 1943, p. 487.

[18] Ref. 13, p. 266.

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