Tetrahedron, 1966, Vol. 22, pp. 1789 to 1795. Pergamon Press Ltd. Printed in Northern Ireland

FLAVONOIDS—II[1]

STEREOCHEMISTRY OF ISOAURONES

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(*Received* 30 *November* 1965)

Abstract—Isoaurones (anhydrolactones of 2-hydroxy-α-benzylmandelic acids), trimethylanhydrohazeyl lactone[2a] and its 5-methyl-4′-methoxy analogue (VI) are shown to be *trans*- stilbene derivatives and are isomerized to *cis*-compounds by pyridine. The stereochemistry has been established by a stereoselective synthesis of the derived *cis*-stilbene-α-carboxylic acid VII ($R = CH_3$, $R' = H$) and confirmed by UV and NMR studies. A mechanism for isomerization has been suggested.

RING opening of dihydroflavonols to 2-hydroxy-α-benzylmandelic acids has been observed by several workers. Further acid treatment yields isoaurones(anhydrolactones) probably through the intermediate saturated benzofuranones(lactones)[2]. 4′-Methoxy-6-methyldihydroflavonol[3] with aqueous sodium carbonate gave a stable lactone (II). The intermediate in the preparation of the dihydroflavonol (I) by the "Rasoda" reaction viz. 2′-acetoxy-5′-methylphenyl α-bromo-β-hydroxy-β-(4-methoxyphenyl)-ethyl ketone[4] or the starting 2′-acetoxy-4-methoxy-5′-methylchalcone dibromide[5] under similar conditions gave the lactone (II) in one step. Methylation and ethylation of (II) furnished an *o*-methoxy acid (III; $R = CH_3$, $R' = H$), its methyl and ethyl esters, an *o*-ethoxy acid and its ethyl ester. An independent synthesis of the *o*-methoxy acid (III; $R = CH_3$, $R' = H$) was achieved from 2′,4-dimethoxy-5′-methylchalcone epoxide (cf. Ref. 6). Acetate of the lactone (II) with ethanolic sodium hydroxide gave 2-hydroxy-4′-methoxy-5-methyl-*trans*-stilbene-α-carboxylic acid (V; $R = R' = H$) which on heating above its m.p. gave 4′-methoxy-5-methyl-*trans*-isoaurone (VI) identical with that synthesized by condensation of 2-hydroxy-5-methylphenylacetic acid[7] and anisaldehyde together with the *cis*-isoaurone (IX) the constitution of which will be discussed later. *trans* Geometry of the acid (V; $R = R' = H$) and the isoaurone (VI) comes from the consideration of the preferred conformation of the acetate (IV) during β-elimination and has been confirmed as follows. Methylation of the isoaurone (VI) or the stilbene-α-carboxylic acid (V; $R = R' = H$) gave 2,4′-dimethoxy-5-methyl-stilbene-α-carboxylic acid (V; $R = CH_3$, $R' = H$) different from VII ($R = CH_3$, $R' = H$) obtained by Perkin

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[1] Part I, K. G. Marathe, *J. Univ. Poona* **14**, 63 (1959).

[2a] T. Oyamada, *J. Chem. Soc. Japan* **55**, 755, 785 (1934); [b] M. Kotake and T. Kubota, *Liebigs Ann.* **544**, 253 (1940); [c] J. Gripenberg, *Acta Chim. Scand.* **7**, 1323 (1953); [d] D. Molho and M. Chadenson, *Bull. Soc. Chim. Fr.* 453 (1959).

[3] K. G. Marathe, K. R. Chandorkar and S. D. Limaye, *Rasayanam* **II**, 48 (1952).

[4] G. V. Bhide and S. D. Limaye, *Rasayanam* **II**, 55 (1955).

[5] Aüwers and Anschütz, *Chem. Ber.* **54**, 1543 (1921).

[6] E. Rohrman, R. G. Jones and H. A. Shonle, *J. Amer. Chem. Soc.* **66**, 1856 (1944).

[7] O. Dann, J. Lang and H. Vohl, *Liebigs Ann.* **635**, 116 (1960).

condensation of 2-methoxy-5-methylphenylacetic acid[7] and anisaldehyde. Zimmerman[8] has shown that Perkin condensation is stereoselective and yields *cis*-stilbene-α-carboxylic (α-phenyl-*trans*-cinnamic) acids. It follows that the acids (V; R = R′ = H and R = CH_3, R′ = H) and isoaurone (VI) are *trans*-stilbene derivatives. Similar conformational preference in dehydration was also observed when 2-methoxy-5-methyl-α-anisylmandelic acid (III; R = CH_3, R′ = H) was refluxed with acetic anhydride containing sodium acetate and the product was the *trans*-acid (V; R = CH_3, R′ = H).

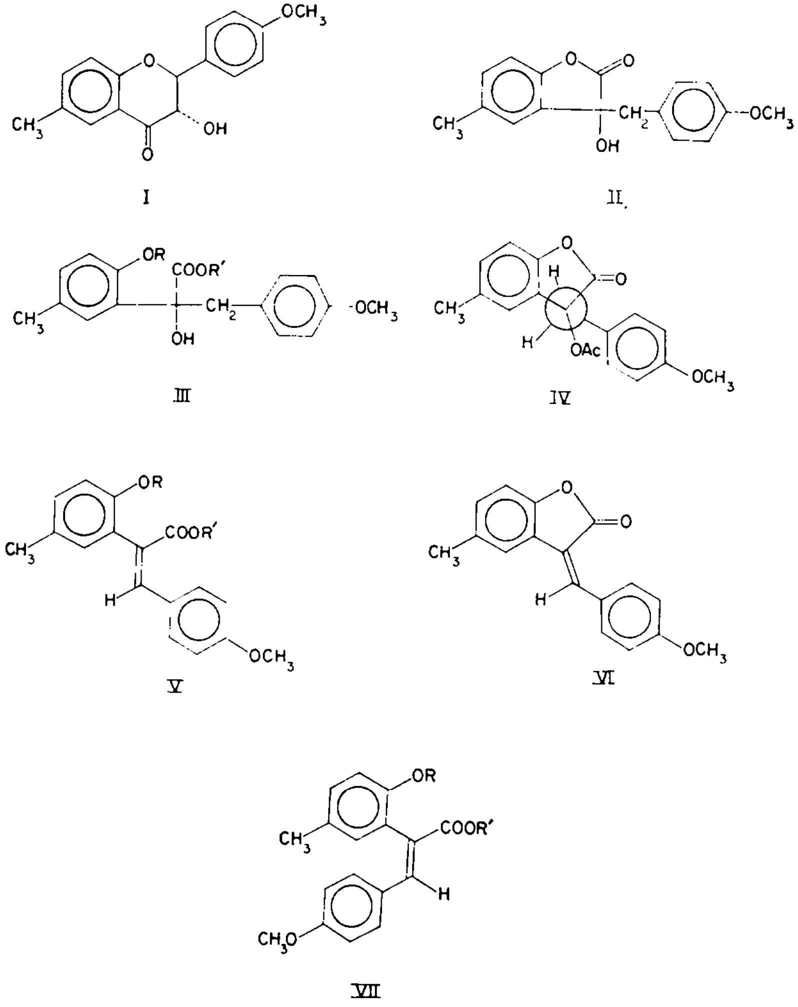

FIG. 1

Attempts to prepare an O-acetate of the acid (V; R = R′ = H) with acetic anhydride regenerated the *trans*-isoaurone (VI) while pyridine–acetic anhydride gave a compound m.p. 85° identical with the earlier mentioned product obtained in Perkin condensation together with the *trans*-isoaurone (VI). On hydrolysis with

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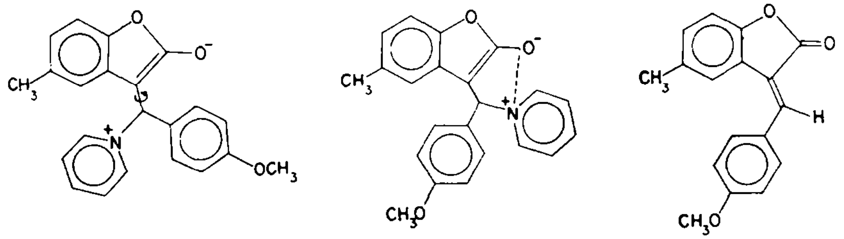
[8] H. E. Zimmerman and L. Ahramjian, *J. Amer. Chem. Soc.* **81**, 2086 (1959).

ethanolic sodium hydroxide it gave an acid m.p. 178° which on methylation yielded the earlier mentioned 2,4'-dimethoxy-5-methyl-*cis*-stilbene-α-carboxylic acid (VII; $R = CH_3$, $R' = H$). On heating above its m.p. the acid, m.p. 178°, regenerated the starting compound m.p. 85°. Moreover, on refluxing with ethanol the compound m.p. 85° was isomerized to *trans*-isoaurone (VI). All these facts could be accommodated by considering the lactone m.p. 85° as 4'-methoxy-5-methyl-*cis*-isoaurone (IX) and the acid m.p. 178° as the corresponding *cis*-stilbene acid (VII; $R = R' = H$). It was also noticed that with pyridine alone the *trans*-acid (V; $R = R' = H$) remained unchanged yielding *trans*-isoaurone (VII) after acidification of the reaction mixture while isoaurone (VI) was isomerized to the *cis*-compound (IX).

Of all the mechanisms for the base induced isomerizations of α,β-unsaturated carbonyl compounds,[9] attack by the nucleophile on the positively polarized β-carbon leading to the formation of the enolate anion (VIII) provides an explanation for the above *trans-cis* isomerization. In elimination reactions the stereochemistry of the product is controlled by the conformation of the transition intermediate.[8] In our case the intermediate σ-complex (VIII) is stabilized in the conformation (VIII') by electrostatic interaction leading to the formation of *cis*-isoaurone (IX).



VIII VIII' IX

FIG. 2

Methyl ethers of naturally occurring dihydroflavonols, fustin, alpinone, pinobanksin, ampelopsin and dihydrorobinetin are known to yield isoaurones (anhydrolactones) and in addition, some of these have been synthesized.[10] We believe that all these are *trans*-isoaurone derivatives. In all these cases the intermediate saturated lactones of the type (II) undergo facile dehydration due to the presence of a resonance electron donating methoxy group *para* to the reaction center leading to the formation of a benzyl carbonium ion in contrast to the stable saturated lactone reported above.[11]

In order to generalize the above isomerization we have synthesized trimethyl hazeic acid from racemic trimethylfustin[12] and converted it into anhydrotrimethylhazeyl lactone[2a] to which we now assign *trans*-configuration. This with pyridine gave 3',4',6-trimethoxy-*cis*-isoaurone, m.p. 152°. Both the lactones yielded *cis*- and *trans*-2-hydroxy- and 2-methoxy-3',4,4'-trimethoxystilbene-α-carboxylic acids. The

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[9] Patai and Rappoport, *J. Chem. Soc.* 396 (1962) and Refs cited therein.

[10] J. Gripenberg and B. Juselius, *Acta Chim. Scand.* **8**, 734 (1954); D. Molho and J. Coillard, *Bull. Soc. Chim. Fr.* 78 (1956). These authors did not study the stereochemistry.

[11] A stable saturated lactone m.p. 107–108° has also been isolated in the case of unsubstituted dihydroflavonol. (cf. Ref. 3) and K. G. Marathe, Ph.D. Thesis p. 82. Poona Univ. (1954).

[12] R. C. Shah, C. G. Joshi and A. B. Kulkarni, *Chem. & Ind.* 1062 (1955).

former compounds could be converted into the starting isomeric isoaurones by heating above their m.p.

In contrast with the isoaurones, 4′-methoxy-5-methylaurone (which we consider as *trans* compound) remained unchanged with pyridine and this is in accord with the proposed mechanism for isomerization.

p*K* Values of 2-methoxy-5-methylstilbene-α-carboxylic acids are in agreement with the proposed stereochemistry so also are the UV spectra of these and other stilbene-α-carboxylic acid derivatives. However, the UV spectra of isoaurones are very similar. Probably, the rigid five membered lactone ring has altered the bond angles removing steric strain to coplanarity; as open chain *cis*- and *trans*-2′-hydroxy-2-methoxy-5′-methyl-3′-nitrochalcones show a considerable difference in spectra.

TABLE 1. UV ABSORPTION MAXIMA OF *cis* AND *trans* STILBENE-α-CARBOXYLIC ACID DERIVS., ISOAURONES AND CHALCONES

Stilbene-α-carboxylic acid		λ_{max}	$\varepsilon_{max} \times 10^{-4}$
2,4′-Dimethoxy-5-methyl-	*cis*	285	2·5
	trans	289	2·9
2,3′,4,4′-tetramethoxy	*cis*	309	1·7
	trans	315	2·3
2-Hydroxy-3′,4,4′-trimethoxy	*cis*	315	1·8
	trans	309	2·4
2-Hydroxy-4′-methoxy-5-methyl	*cis*	292	2·5
	trans	278–282	2·6
2,4′-Dimethoxy-5-methyl-	*cis*	307–308	2·6
(methyl ester)	*trans*	316	3·5
Isoaurones			
4′-Methoxy-5-methyl	*cis*	380	2·6
	trans	380	2·5
3′,4′,6-Trimethoxy	*cis*	390	2·2
	trans	392–395	2·1
Chalcones			
2′-Hydroxy-2-methoxy-5′-methyl-3′-nitro	*cis*	343, 276, 241	0·61, 0·66 2·1
	trans	375, 310, 264	1·9, 1·1, 1·2

Regarding the stereochemistry of isoaurones (VI and IX) though there is indication in their IR spectra[13] the resolution of the instrument was not enough to arrive at a decision, however, NMR spectra showed that the assigned structures are correct. The spectrum of the *trans*-isoaurone (VI) showed a singlet (3H) at 2·3 δ (Ar—CH_3), a singlet (3H) at 3·8 δ (OCH_3), two sets of doublets (4H) at 8·1 δ and 6·85 δ indicative of a *p*-disubstituted benzene. A sharp singlet (1H) at 7·35 δ has been ascribed to a vinyl proton under the strong deshielding influence of the aromatic ring. The NMR spectrum of the *cis*-isoaurone (IX) showed the presence of the *trans*-compound (VI) as well though it could not be detected on TLC. The signal due to vinyl proton appeared at 6·95–6·9 δ. This value is in conformity with the one reported for a vinyl

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[13] A. Hassner and T. C. Mead, *Tetrahedron* **20**, 2201 (1965).

proton under the influence of a carbonyl group.[14] The doublets due to *p*-disubstituted benzene appeared at 7·55 δ and 6·9 δ and a singlet (3H) due to Ar—CH_3 at 2·25 δ.[15]

EXPERIMENTAL

UV spectra were measured in EtOH solution and IR spectra for Nujol suspensions.

3-*Anisyl*-3-*hydroxy*-5-*methyl*-2(3H)-*benzofuranone* (II)

A suspension of 4′-methoxy-6-methyldihydroflavonol (1 g) in 1N NaOH or sat. Na_2CO_3aq (50 ml) was refluxed for 2·5 hr. The precipitated Na salt of 4′-methoxy-6-methylflavonol was collected. The filtrate was acidified and kept for 48 hr. The precipitated brown mass on trituration with EtOH and crystallization from benzene gave II (0·3 g) m.p. 152°. λ_{max} 281 (0·56), 276 infl. (0·51) mμ ($\varepsilon_{max} \times 10^{-4}$), ν_{max} 2·9 (OH), 5·5 (CO)μ. (Found: C, 71·5; H, 5·4. $C_{17}H_{16}O_4$ requires: C, 71·8; H, 5·6%.)

2′-Acetoxy-5′-methyl-α-bromo-β-hydroxy-β-(4-methoxy-phenyl)-ethyl ketone and 2′-acetoxy-4-methoxy-5′-methylchalcone dibromide on similar treatment gave II (0·24 g and 0·05 g resp.).

Acetate IV. Prepared by the Ac_2O–pyridine method, m.p. 101° (EtOH) λ_{max} 280 (0·39), 275 (0·38) mμ ($\varepsilon_{max} \times 10^{-4}$), ν_{max} 5·5 (lactone CO), 5·67 (ester CO) μ. (Found: C, 69·6; H, 5·2. $C_{19}H_{18}O_5$ requires: C, 69·9; H, 5·5%.)

α-*Anisyl*-2-*methoxy*-5-*methylmandelic acid* (III; $R = CH_3$, $R' = H$)

(a) To a suspension of II (0·57 g) in 1N NaOH (10 ml), dimethylsulphate (0·7 ml) was added dropwise. After 1 hr water (10 ml) was added. Extraction with ether and acidification of the alkaline layer yielded a product which on extraction with $NaHCO_3$aq afforded III ($R = CH_3$, $R' = H$; 0·2 g) m.p. 166° (EtOH) λ_{max} 277–282 (0·64) mμ ($\varepsilon_{max} \times 10^{-4}$). (Found: C, 68·0; H, 6·1. $C_{18}H_{20}O_5$ requires: C, 68·3; H, 6·3%.)

The ether layer afforded *methyl 2-methoxy-5-methyl-α-anisylmandelate* (III; $R = R' = CH_3$) m.p. 134° λ_{max} 276 (0·44) and 281 (0·43) mμ ($\varepsilon_{max} \times 10^{-4}$). (Found: C, 68·7; H, 6·3. $C_{19}H_{22}O_5$ requires: C, 69·0; H, 6·7%.) Hydrolysis yielded III ($R = CH_3$, $R' = H$).

(b) A suspension of 2′,4-dimethoxy-5′-methylchalcone epoxide[16] (2 g) in EtOH (20 ml) was refluxed with 5N NaOH (80 ml) for 2 hr. Dilution with water and working up as above gave III ($R = CH_3$, $R' = H$; 1 g) m.p. 166° alone or admixed with the above sample.

The ethyl ester (III; $R = CH_3$, $R' = C_2H_5$; EtOH–*p*-toluenesulphonic acid method) m.p. 90° (from EtOH) λ_{max} 276 (0·46) and 281 (0·45) mμ ($\varepsilon_{max} \times 10^{-4}$). (Found: C, 69·4; H, 6·7. $C_{20}H_{24}O_5$ requires: C, 69·7; H, 6·9%.)

The benzofuranone (II) with diethyl sulphate afforded III ($R = C_2H_5$, $R' = H$) m.p. 175° λ_{max} 278–281 (0·63) mμ ($\varepsilon_{max} \times 10^{-4}$). (Found: C, 68·8; H, 6·3. $C_{19}H_{22}O_5$ requires: C, 69·08; H, 6·7%) and *ethyl 2-ethoxy-5-methyl-α-anislymandelate* (III; $R = R' = C_2H_5$) m.p. 65°. (Found: C, 70·1; H, 6·9. $C_{21}H_{26}O_5$ requires: C, 70·39; H, 7·3%.)

2-*Hydroxy*-4′-*methoxy*-5-*methyl-trans-stilbene*-α-*carboxylic acid* (V; $R = R' = H$)

A suspension of IV (1 g) in 2N NaOH or sat. Na_2CO_3aq (50 ml) was refluxed for 2 hr. The crude product on working up gave 2-*hydroxy*-4′-*methoxy*-5-*methyl*-trans-*stilbene*-α-*carboxylic acid* (0·55 g) m.p. 152° (from EtOH) ν_{max} 2·95, 5·85 (α,β-unsat·COOH); 6·2 (conj. C=C) μ. (Found: C, 71·5; H, 5·3. $C_{17}H_{16}O_4$ requires: C, 71·8; H, 5·6%.)

4′-*Methoxy*-5-*methyl*-trans-*isoaurone* (VI)

(a) The above acid (V; $R = R' = H$; 0·5 g) was heated at 155–160° in an oil bath for 0·5 hr. The melt on crystallization from EtOH gave 4′-*methoxy*-5-*methyl*-trans-*isoaurone* (0·3 g) m.p. 136–137° ν_{max} 5·65 (lactone CO), 6·25 (conj. C=C) μ. (Found: C, 76·4; H, 5·1. $C_{17}H_{14}O_3$ requires: C, 76·7; H, 5·3%.) The isoaurone on refluxing with 2N NaOH regenerated the trans stilbene acid (V; $R = R' = H$).

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[14] D. N. Kevill, E. D. Weiler and N. H. Cromwell, *J. Org. Chem.* **29**, 1276 (1964).

[15] We are indebted to Drs. G. R. Bedford of Imperial Chemical Industries Ltd., Pharmaceuticals Division, Macclesfield, Cheshire, England and P. M. Nair for NMR and A. J. Mukhedkar for UV spectra.

[16] H. K. Pendse and S. D. Limaye, *Rasayanam* II, 74 (1955).

(b) A mixture of 2-hydroxy-5-methyl-phenylacetic acid (1·65 g), anisaldehyde (2·52 g), triethylamine (1 ml) and Ac_2O (2 ml) was refluxed for 6 hr. Acidification with HCl gave a gum which was triturated with EtOH and filtered. The insoluble residue was crystallized from EtOH yielding IX, m.p. 85°, described below. The filtrate on standing for 8 hr gave a solid which was crystallized from EtOH yielding *4′-methoxy-5-methyl-trans-isoaurone* VI (0·5 g) m.p. alone or when mixed with the above sample 136–137°.

2,4′-Dimethoxy-5-methyl-trans-*stilbene-α-carboxylic acid* V ($R = CH_3$, $R' = H$).

(a) Methylation of the above VI or V ($R = R' = H$) as described for the lactone II gave *2,4′-dimethoxy-5-methyl*-trans-*stilbene-α-carboxylic acid* m.p. 192°, pK_a (50% EtOH) 6·1. (Found: C, 72·5; H, 6·0. $C_{18}H_{18}O_4$ requires: C, 72·5; H, 6·0%), and *methyl 2,4′-dimethoxy-5-methyl*-trans *stilbene-α-carboxylate* m.p. 97°. (Found: C, 72·8; H, 6·2. $C_{19}H_{20}O_4$ requires: C, 73·0; H, 6·4%.) The ester on hydrolysis yielded the above acid m.p. 192°.

(b) α-Anisyl-2-methoxy-5-methylmandelic acid (0·5 g) was refluxed with AcONa and Ac_2O for 2 hr. The resulting gummy mass on extraction with $NaHCO_3$aq yielded 2,4′dimethoxy-5-methyl-*trans*-stilbene-α-carboxylic acid m.p. 192°.

2,4′-Dimethoxy-5-methyl-cis-*stilbene-α-carboxylic acid* VII ($R = CH_3$, $R' = H$)

A mixture of 2-methoxy-5-methylphenylacetic acid (1·8 g), anisaldehyde (2·52 g), triethylamine (1 ml) and Ac_2O (2 ml) was heated on water bath for 2 hr. Acidification and extraction with $NaHCO_3$aq afforded 2,4′-dimethoxy-5-methyl-*cis*-stilbene-α-carboxylic acid (0·9 g) m.p. 192°, pK_a (50% EtOH) 6·6. (Found: C, 72·29; H, 5·7%.) Its mixed m.p. with the *trans* acid m.p. 192° V ($R = CH_3$, $R' = H$) showed a depression of 26°.

Attempted O-*acetylation of the* trans-*acid* V ($R = R' = H$)

(a) The *trans* V ($R = R' = H$) on treatment with Ac_2O for 24 hr regenerated the *trans*- VI.

(b) *4′-Methoxy-5-methyl*-cis-*isoaurone* IX. A solution of the above acid (0·6 g) in Ac_2O (6 ml) and pyridine (9 ml) was set aside for 24 hr. Addition of water and HCl precipitated a product which after 2 hr period was crystallized from EtOH giving *4′-methoxy-5-methyl*-cis-*isoaurone* IX (0·4 g) m.p. 85° ν_{max} 5·6 (lactone CO, doublet[13]), 6·2 (conj. C═C) μ. (Found: C, 76·4; H, 5·6%.) It gave a single spot on TLC on silica gel.

(c) The *trans* V ($R = R' = H$; 0·3 g) in pyridine (5 ml) was set aside for 24 hr. Acidification and working up after 2 hr afforded the *trans*- VI (0·05 g) m.p. 136–137°.

(d) A solution of the *trans*- VI (0·3 g) in pyridine (5 ml) on usual work up after 24 hr afforded the *cis*- IX (0·17 g) m.p. 85° alone or mixed with the above sample.

3′,4′,6-*Trimethoxy*-cis-*isoaurone*

(a) *Trimethylhazeic acid.* A suspension of (±) trimethylfustin[12] (1 g) in 1N NaOH (50 ml) was refluxed for 2 hr. Acidification and extraction with $NaHCO_3$aq afforded trimethylhazeic acid (0·55 g) m.p. 138° (lit.,[2a] m.p. 138°). (Found: C, 61·9; H, 5·5. Calc. for $C_{18}H_{20}O_7$: C, 62·07; H, 5·75%.)

(b) *Anhydrotrimethylhazeyl lactone.* A suspension of the above trimethylhazeic acid (1 g) in conc. HCl (20 ml) was refluxed for 45 min. Addition of water precipitated a product which was crystallized from EtOH giving anhydrotrimethylhazeyl lactone (0·9 g) m.p. 185–187° (lit.,[2a] m.p. 185°) ν_{max} 5·67 (lactone CO), 6·15 (C═C) μ. (Found: C, 68·9; H, 5·0. Calc. for $C_{18}H_{16}O_5$: C, 69·2; H, 5·1%.)

(c) A solution of anhydrotrimethylhazeyl lactone (0·2 g) in pyridine (16 ml) on usual work up after 24 hr afforded *3′,4′,6-trimethoxy*-cis-*isoaurone* (0·1 g) from EtOH, m.p. 152° ν_{max} 5·6 (lactone CO), 6·15 (conj. C═C) μ. (Found: C, 69·1; H, 4·8%.)

The above *cis*-isoaurone (0·2 g) on refluxing with EtOH (5 ml) for 2 hr afforded the starting *trans*-isoaurone (0·1 g) from EtOH, m.p. 185° alone or mixed with the sample above.

2-Hydroxy-3′,4,4′-trimethoxy-trans- *and* -cis-*stilbene-α-carboxylic acids*

Anhydrotrimethylhazeyl lactone (0·5 g) was refluxed with 2N NaOH for 1 hr. Acidification and extraction with $NaHCO_3$aq afforded *2-hydroxy-3′,4,4′-trimethoxy*-trans-*stilbene-α-carboxylic acid* (0·2 g) m.p. 152° from EtOH, ν_{max} 2·87, 5·9 (COOH), 6·2 μ. (Found: C, 65·2; H, 5·1. $C_{18}H_{18}O_6$ requires: C, 65·5; H, 5·4%.)

On similar treatment 3′,4′,6-trimethoxy-*cis*-isoaurone (0·5 g) afforded 2-*hydroxy*-3′,4,4′-*trimethoxy*-cis-*stilbene-α-carboxylic acid* (0·2 g) m.p. 185° (EtOH) ν_{max} 2·85, 5·92 (COOH), 6·2 μ. (Found: C, 64·9; H, 5·0%.)

Both the acids on heating above their m.ps regenerated the starting *trans*- and *cis*-3′,4′,6-trimethoxy-isoaurones m.p. 185° and 152° respectively.

2,3′,4,4′-*Tetramethoxy*-trans- *and* -cis-*stilbene-α-carboxylic acids*

The above *trans*- and *cis*-trimethoxyisoaurones or the corresponding stilbene acids on methylation afforded 2,3′,4,4′-*tetramethoxy-trans*- and -*cis-stilbene-α-carboxylic acids* m.p. 172° from EtOH. (Found: C, 66·1; H, 5·5. $C_{19}H_{20}O_6$ requires: C, 66·3, H, 5·8%) and m.p. 193–194° from EtOH. (Found: C, 65·9; H, 5·6%) resp.

trans *and* cis 2′-*Hydroxy*-2-*methoxy*-5′-*methyl*-3′-*nitrochalcones*

A mixture of 2-hydroxy-5-methyl-3-nitroacetophenone[17] (2 g), 2-methoxybenzaldehyde (3 ml), EtOH (25 ml) and 10N NaOH (6 ml) was allowed to stand for 24 hr. Acidification and crystallization from AcOH afforded *trans*-2′-hydroxy-2-methoxy-5′-methyl-3′-nitrochalcone (2 g) m.p. 163°. (Found: N, 4·23. $C_{17}H_{15}O_5N$ requires: N, 4·5%.)

Addition of water to the mother liquor from the crystallization of the above chalcone gave a product which on rapid crystallization from EtOH afforded *cis*-2′-hydroxy-2-methoxy-5′-methyl-3-nitrochalcone m.p. 92°. (Found: N, 4·25%).

Both *trans*- and *cis*-chalcones gave the same *acetate* (Ac_2O–AcONa) m.p. 104°. (Found: N, 4·15; $C_{19}H_{17}O_6N$ requires: N, 3·9%.)

The *cis*-chalcone m.p. 92° on refluxing with AcOH for 2 hr afforded the *trans*-compound m.p. 163° and both with alkaline H_2O_2 yielded 2′-methoxy-6-methyl-8-nitroflavonol m.p. 278° from AcOH. (Found: N, 4·2; $C_{17}H_{13}O_6N$ requires: N, 4·3%.)

Acknowledgements—The authors express their sincere thanks to Professor Sir C. K. Ingold, F.R.S. for helpful discussions in formulating the mechanism, and Professors Eva M. Philbin and S. K. K. Jatkar for their interest.

[17] H. Bredereck, G. Lehmann, C. Schönfeld and E. Fritzsche, *Chem. Ber.* **72B,** 1414 (1939).