Tetrahedron, 1965, Vol. 21, pp. 3707 to 3714. Pergamon Press Ltd. Printed in Northern Ireland

ANTHOCYANIDINS AND RELATED COMPOUNDS—VIII

CONDENSATION REACTIONS OF FLAVYLIUM SALTS WITH 5,5-DIMETHYL-1,3-CYCLOHEXANEDIONE IN ACID SOLUTIONS

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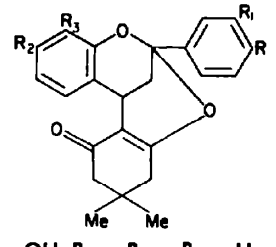
(*Received* 29 *April* 1965; *in revised form* 14 *June* 1965)

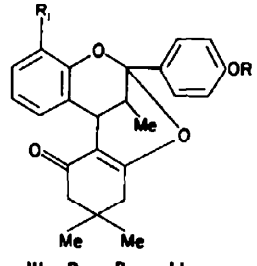
Abstract—4'-Hydroxyflavylium salts, unsubstituted at position 3, react with 5,5-dimethyl-1,3-cyclohexanedione in acid solutions to yield *para*-hydroxyphenacyl-5-keto-tetrahydroxanthene derivatives, e.g., Va, isomeric with the flavan derivatives, e.g., IIa, formed at pH 5·8. These flavans isomerize to the tetrahydroxanthenes in both acid and alkaline media.

7-Hydroxy- and 3-methyl-4'-hydroxyflavylium salts yield flavan derivatives, eq. IIIa, IId, when condensed either in acid solutions or at pH 5·8. Isomerization of these flavans to corresponding tetrahydroxanthenes has not been detected.

IN THE preceding paper[1] it has been reported that 5,5-dimethyl-1,3-cyclohexanedione (I) reacts with flavylium salts at pH 5·8 to form structurally similar flavan derivatives of types II and III. In acid solutions, however, 4'-hydroxyflavylium salts, unsubstituted at position 3, undergo a unique condensation with I to yield novel *para*-hydroxyphenacyl-5-ketotetrahydroxanthene derivatives, which are isomeric with the



IIa, R = OH, $R_1 = R_2 = R_3 = H$
IIb, R = $OCOC_6H_5$, $R_1 = R_3 = R_3 = H$
IIc, R = OH, R_2 = OMe, $R_1 = R_3 = H$
IId, R_3 = OH, $R = R_1 = R_3 = H$
IIe, R = OH, R_1 = OMe, $R_2 = R_3 = H$



IIIa, $R = R_1 = H$
IIIb, R = H, R_1 = OMe

corresponding flavans obtained at pH 5·8. 7-Hydroxy- and 3-methyl-4'-hydroxyflavylium salts, on the other hand form flavan derivatives under both conditions.

Thus, 4'-hydroxyflavylium chloride reacts with I in aqueous acetic acid–hydrochloric acid solutions to yield (73%) a colorless compound, $C_{23}H_{22}O_4$, m.p. 207°, which is isomeric with the phenolic flavan IIa (m.p. 249°) previously obtained at pH 5·8.

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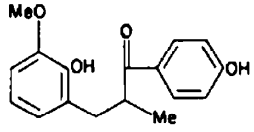
[1] L. Jurd and B. J. Bergot, *Tetrahedron* **21**, 3697 (1965).

Condensation in aqueous acetic acid solutions, without hydrochloric acid, yields both the flavan IIa (57%) and the isomer (28%).

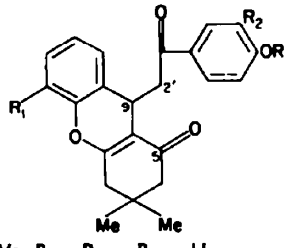
Like IIa, the isomer, m.p. 207°, does not form colored complexes with ferric salts, and it yields an alkali-insoluble monomethyl and monoacetyl derivative when methylated and acetylated respectively. In ethanol it has λ_{max} 281 mμ (log ϵ 4·36). On addition of sodium ethylate the spectrum undergoes an immediate, pronounced bathochromic shift of 51 mμ to give λ_{max} 332 mμ (Fig. 1). These spectral properties differ markedly from those of the flavan IIa (Fig. 2) and, in addition, indicate the presence of a *para*-hydroxyphenacyl grouping in this new compound. In support of this interpretation, the spectra of *para*-hydroxyacetophenone (λ_{max} 278 mμ) and of the dihydrochalcone IV (λ_{max} 279 mμ)[2] undergo similar 50 mμ bathochromic shifts in alkali to give λ_{max} 328 and 329 mμ respectively. Furthermore, whereas the IR



IV

spectrum of IIa in chloroform has a single "carbonyl" band at 6·15 mμ, arising from

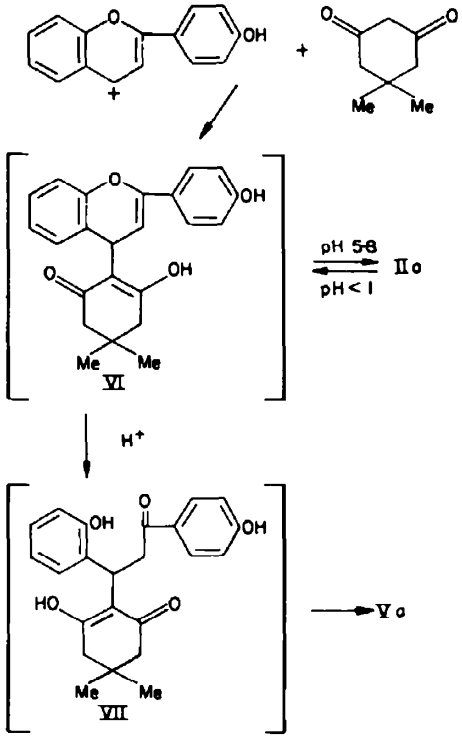
the —O—C=C—C— grouping of the cyclohexenone portion of the molecule, the isomer has two "carbonyl" bands, at 6·01 and 6·15 mμ. The α,β-unsaturated carbonyl group is relatively unreactive and IIa does not form an oxime when warmed with hydroxylamine hydrochloride and sodium acetate. Under the same conditions, however, the isomer forms a mono-oxime, whose λ_{max} in alcohol (263 mμ) shifts to 288 mμ in alkali. The λ_{max} of the oxime of *para*-hydroxyacetophenone shifts similarly from 259 mμ in alcohol to 288 mμ in alkali. On the basis of these observations the product, m.p. 207°, is formulated as 5-keto-7,7-dimethyl-9-(4-hydroxyphenacyl)-5,6,7,8-tetrahydroxanthene (Va). As indicated in Fig. 4, the NMR spectrum of the methyl derivative (Vb) of this compound is in full accord with the proposed structure. The two proton absorption centered at 6·75τ, appearing as the AB part of ABX system, is apparently due to the C_2' methylene group. The proton at C_9 showed a multiplet at 5·5τ.



Va, $R = R_1 = R_2 = H$
Vb, $R = Me$, $R_1 = R_2 = H$
Vc, $R = COC_6H_5$, $R_1 = R_2 = H$
Vd, $R_1 = OMe$, $R = R_2 = H$
Ve, $R_2 = OMe$, $R = R_1 = H$

[2] Unpublished observations.

Warmed briefly in glacial acetic acid–hydrochloric acid solutions, the flavan (IIa) rearranges readily to the isomer Va. Since flav-2-enes easily hydrolyse to dihydrochalcones[3] in acid solutions, this rearrangement, as well as the direct condensation in acid solutions, must involve initial formation of the substituted flav-2-ene (VI) hydrolysis to the intermediate dihydrochalcone (VII) and subsequent ring closure to Va:



As in the case of 4′-hydroxyflavylium chloride, 8-methoxy-4′-hydroxyflavylium chloride condenses with I in acid solutions to form the xanthene (Vd) corresponding to the flavan (IIc) formed at pH 5·8. 3′-Methoxy-4′-hydroxyflavylium chloride also reacts smoothly with I in acid solutions to form the xanthene derivative (Ve), λ_{max} 280 mμ (log ϵ 4·27) in ethanol and λ_{max} 352 mμ (log ϵ 4·39) in alcoholic sodium ethylate.[4] This flavylium salt, however differs from the 4′-hydroxy- and 8-methoxy-4′-hydroxyflavylium salts in that condensation with I at pH 5·8 yields both the xanthene (Va) and the isomeric flavan (IIe) λ_{max} 271 mμ (log ϵ 3·98) in ethanol, λ_{max} 289 mμ (log ϵ 4·51) in alcoholic sodium ethylate.

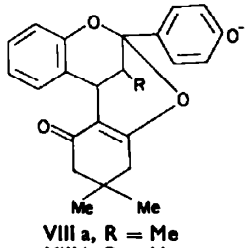
Unlike the above flavylium salts, 3-methyl-4′-hydroxy-, 3-methyl-8-methoxy-4′-hydroxy-, and 7-hydroxyflavylium salts react with I in acid solutions to form flavan derivatives, identical with those obtained by condensation at pH 5·8, viz., IIIa, IIIb, and IId respectively. Thus, although the formation of undetected xanthene derivatives in small quantities cannot be categorically excluded in these latter reactions,

[3] J. W. Gramshaw, A. W. Johnson and T. J. King, *J. Chem. Soc.* 4040 (1958).

[4] 3-Methoxy-4-hydroxyacetophenone, λ_{max} 275 mμ (ethanol), undergoes a virtually identical bathochromic shift of 70 mμ to give λ_{max} 345 mμ in sodium ethylate.

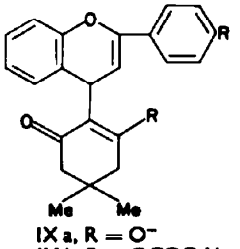
it is evident that the presence of a 3-methyl group or the absence of a 4'-hydroxyl largely, if not completely, inhibits acid isomerization of these flavans.

Effects of alkali on phenolic flavan derivatives. The UV spectra of phenolic flavans of both types II and III *in neutral solutions*, e.g., alcohol, are virtually identical, having a λ_{max} at 265–270 mμ and 225 mμ. The methyl and acetyl derivatives of these flavans also have similar spectra (λ_{max} at 264–266 mμ) and the spectra of the methyl ethers are unaffected by alkali. In the presence of alkali, however, the UV spectra of the phenolic flavans IIa, IIc and IIe undergo characteristic changes, which distinctly differ from those of the flavans, e.g., IIIa, derived from 3-methyl-4'-hydroxyflavylium salts. Thus, in alcohol IIIa (isomer m.p. 254°) has λ_{max} 270, 226 mμ (log ϵ 4·03, 4·35). On addition of sodium ethylate the spectrum undergoes a bathochromic shift to give a shoulder at 278 mμ and a strong peak at 250 mμ (log ϵ 4·42). The stereoisomer (IIIa, m.p. 224°) undergoes similar changes and, on long standing, these alkali spectra are unchanged (Fig. 3). The bathochromic shift observed with IIIa indicates that in this case alkali merely ionizes the 4' phenolic hydroxyl group with the formation of the stable phenoxide ion VIIIa. The phenolic flavan (IIa) has λ_{max} 268, 226 mμ (log ϵ 4·03, 4·37) in alcohol. Addition of sodium



VIII a, R = Me
VIII b, R = H

ethylate results in an *initial* bathochromic shift similar to the above to give a shoulder at 278 mμ and a peak at 251 mμ. In 5 min, however, the alkali spectrum undergoes a pronounced change to give λ_{max} 286 mμ (log ϵ 4·43) (Fig. 2). No further change occurs on standing for 24 hr. These spectral changes suggest that, whereas the 3-methyl phenoxide ion (VIIIa) is stable in alkaline solutions, the ion VIIIb is highly unstable and ring opens to the ionized enol (IXa). In support of this interpretation,



IX a, R = O⁻
IX b, R = OCOC$_6$H$_5$

IIa, dissolved in cold aqueous ethanolic sodium hydroxide and treated immediately with benzoyl chloride, forms a monobenzoate (IIb; m.p. 157°), identical with that prepared by benzoylation of IIa under mild conditions in pyridine. When a solution of IIa in cold aqueous ethanolic sodium hydroxide is allowed to stand for 15 min before addition of benzoyl chloride, however, a crystalline dibenzoate, m.p. 167–168°,

presumably IXb, is obtained. Finally, if a solution of IIa in aqueous sodium hydroxide is heated to boiling, isomerization to the tetrahydroxanthene derivative occurs and benzoylation then yields a benzoate (Ve; m.p. 182°), identical with that prepared by benzoylation of Va in pyridine.

Thus, phenolic flavans derived from 4'-hydroxyflavylium salts are unstable in both acid and alkaline media, with facile opening of one or both or the heterocyclic rings. Subsequent reclosure under the appropriate conditions then leads to the isomeric 5-ketotetrahydroxanthene derivatives. The 3-methyl flavan derivatives, on the other hand, are relatively stable to both acids and alkalis. A satisfactory explanation of this entirely unexpected stabilizing effect of the 3-methyl group has not, at this time, been found.

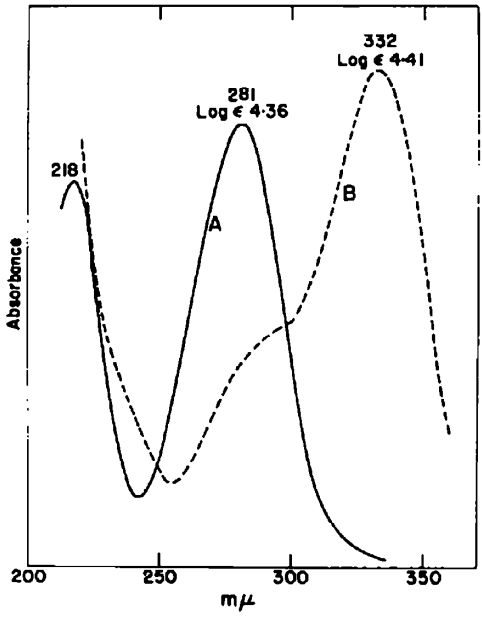


FIG. 1 Ultraviolet spectra of Va in (A) ethanol, (B) 0·02M ethanolic sodium ethylate.

EXPERIMENTAL

Condensation of 4'-hydroxyflavylium chloride and 5,5-dimethyl-1,3-cyclohexanedione(I) *at pH* < 1. A mixture of 4'-hydroxyflavylium chloride (5·0 g) and I (10·0 g) was heated to boiling with glacial acetic acid (50 ml) and 5% HClaq (50 ml). The clear solution first obtained rapidly began to deposit slightly yellow crystals. The mixture was warmed on a steam-bath for 5 min, cooled and filtered. The crystalline product was washed thoroughly with 50% aqueous acetic acid and recrystallized from MeOH; Va separated as colorless needles, m.p. 207°, λ_{max}^{EtOH} 281 (4·36), λ_{max}^{NaOEt} 332 (4·41) mμ (log ε) (5·1 g). It did not give a color with alcoholic $FeCl_3$ nor a positive test with Gibbs reagent. (Found: C, 76·3; H, 6·17. Calc. for $C_{23}H_{22}O_4$: C, 76·2; H, 6·12%.)

The product (0·2 g) was acetylated in warm acetic anhydride (2·0 ml) and pyridine (0·5 ml). The acetate of Va crystallized from MeOH as colorless needles, m.p. 125°, λ_{max}^{EtOH} 252 mμ. (Found: C, 74·1; H, 5·97; CH_3CO—, 10·6. Calc. for $C_{25}H_{24}O_5$: C, 74·2, H, 5·98; CH_3CO—, 10·6%.)

Compound Va (0·4 g) was warmed on a steam-bath for 30 min with sodium acetate (2·0 g), hydroxylamine hydrochloride (2·0 g), EtOH (20 ml) and water (10 ml). Water (40 ml) was added and the solution cooled. The crystalline product was recrystallized from aqueous MeOH. The oxime of Va thereby separated as colorless needles (0·35 g), m.p. 210–211°, λ_{max}^{EtOH} 264 mμ, λ_{max}^{NaOEt} 289 mμ. (Found: C, 72·8; H, 6·16; N, 4·15. Calc. for $C_{23}H_{23}O_4N$: C, 73·2; H, 6·14; N, 3·71%.)

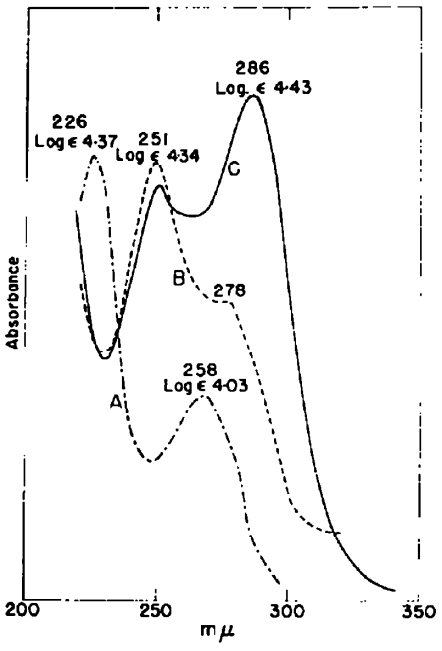


FIG. 2 Ultraviolet spectra of IIa in (A) ethanol, (B) 0·02M ethanolic sodium ethylate, measured immediately, (C) 0·02M ethanolic sodium ethylate, measured after 5 min.

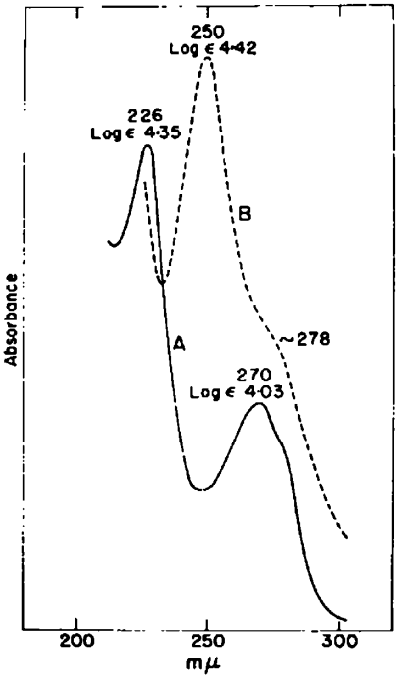


FIG. 3 Ultraviolet spectra of IIIa (m.p. 254°) in (A) ethanol, (B) 0·02M sodium ethylate. The spectrum (B) does not change on standing.

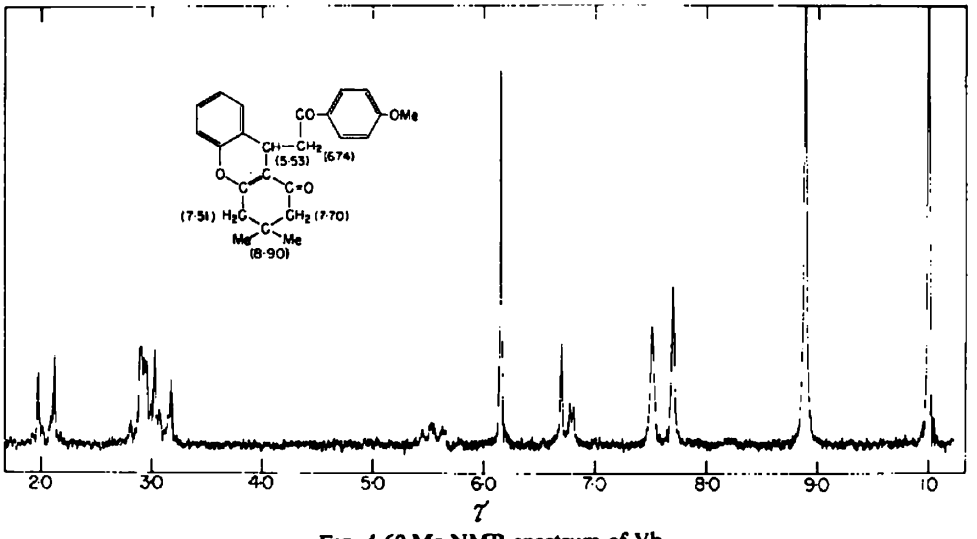


FIG. 4 60 Mc NMR spectrum of Vb.

Compound Va (1·0 g) was heated under reflux with a mixture of dimethyl sulfate (5 ml), K_2CO_3 (10 g) and acetone (75 ml) for 1·5 hr. Water (250 ml) was added and the mixture was cooled to 0° for 3 hr. Colorless crystals formed. Recrystallized from MeOH, the *methyl ether*(Vb) separated as colorless needles, m.p. 107–108°, λ_{max}^{EtOH} 279 mμ (0·85 g). (Found: C, 76·7, H, 6·43; MeO—, 8·30. Calc. for $C_{24}H_{24}O_4$: C, 76·6; H, 6·43; 1 MeO—, 8·23%.)

Condensation of 4′-*hydroxyflavylium chloride and* I *in dilute acetic acid.* A solution of 4′-hydroxyflavylium chloride (1·0 g) and I (2·0 g) in 50% aqueous acetic acid (20 ml) was heated for 10 min, cooled and filtered. The crystalline product was recrystallized from tetrahydrofuran–MeOH yielding the flavan derivative (IIa) m.p. and m.m.p. 249° (0·80 g). The tetrahydrofuran–MeOH filtrate from IIa was concentrated and allowed to stand. Colorless needles, m.p. 196°, λ_{max}^{EtOH} 281 mμ, λ_{max}^{NaOEt} 332 mμ, separated (0·40 g). Recrystallized from MeOH, Va was obtained, m.p. and m.m.p. 207°.

Isomerization of IIa *to* Va. The flavan derivative (IIa; 2·0 g) was heated to boiling with a mixture of glacial acetic acid (30 ml) and 10% HClaq (5·0 ml). The clear, yellow solution was diluted with water (20 ml) and allowed to cool. Slightly yellow needles rapidly separated. After 24 hr the product was collected and recrystallized successively from aqueous MeOH and MeOH yielding Va as colorless glistening needles, m.p. and m.m.p. 207°, λ_{max}^{EtOH} 281 mμ, λ_{max}^{NaOEt} 332 mμ (1·1 g).

Condensation of 8-*methoxy*-4′-*hydroxyflavylium chloride and* I *at pH* < 1. 8-Methoxy-4′-hydroxyflavylium chloride (5·0 g), condensed with I (10·0 g) in glacial acetic acid (50 ml) and 5% HClaq (50 ml) as described above, deposited crystalline Vd which recrystallized from acetone–MeOH as colorless, fluffy needles, m.p. 212°, λ_{max}^{EtOH} 282 mμ, λ_{max}^{NaOEt} 332 mμ. Vd does not give a color with alcoholic $FeCl_3$. Mixed with the isomeric flavan derivative IIc (m.p. 219°, obtained by condensation at pH 5·8) it melts at 192°. (Found: C, 73·7; H, 6·18; MeO—, 7·94. Calc. for $C_{24}H_{24}O_5$: C, 73·45; H, 6·16; 1 MeO—, 7·91%.)

The *oxime* of Vd, prepared by heating it with hydroxylamine hydrochloride and sodium acetate as described above, crystallized from MeOH as colorless needles, m.p. 204°, λ_{max}^{EtOH} 263 mμ, λ_{max}^{NaOEt} 291 mμ. (Found: C, 71·0; H, 6·16; N, 3·05. Calc. for $C_{24}H_{25}O_5N$: C, 70·7; H, 6·18; N, 3·44%.)

The *methyl ether* of Vd, prepared by reaction with dimethyl sulfate and K_2CO_3 in acetone, crystallized from MeOH as colorless prisms, m.p. 126–127°. (Found: C, 73·9; H, 6·56. Calc. for $C_{26}H_{26}O_5$: C, 73·9; H, 6·45%.)

Condensation of 3′-*methoxy*-4′-*hydroxyflavylium chloride and* I *at pH* < 1. 3′-Methoxy-4′-hydroxyflavylium chloride (2·0 g) and I (4·0 g), warmed briefly with glacial acetic acid (20 ml) and 5% HClaq (20 ml), formed Ve (2·2 g) which recrystallized from acetone–MeOH as slightly pink prisms, m.p. 173–174°, λ_{max}^{EtOH} 280 (4·27), 225 (4·38) mμ (log ε), λ_{max}^{NaOEt} 352 (4·39), 287 (4·00), 252 (4·07) mμ (log ε). (Found: C, 73·3; H, 6·10; MeO—, 8·23. Calc. for $C_{24}H_{24}O_6$: C, 73·45; H, 6·16; 1 MeO, 7·91%.)

Acetyl and methyl derivatives of Ve were not crystallized. The crystalline benzyl derivative was prepared by heating with benzyl chloride (1 ml), KI (1 g), K_2CO_3 (5 g) and acetone (20 ml) for 2 hr. The filtered acetone solution was evaporated to an oil. This crystallized from benzene–Skellysolve F. Recrystallized from MeOH the *benzyl ether* of Ve separated as colorless prisms, m.p. 104–106°. (Found: C, 77·1; H, 6·30. Calc. for $C_{31}H_{28}O_6$: C, 77·15; H, 6·27%.)

Condensation of 3′-*methoxy*-4′-*hydroxyflavylium chloride and* I *at ph* 5·8. The flavylium salt (5·0 g) was warmed with I (10·0 g) in MeOH (50 ml) and aqueous buffer solution, pH 5·8 (50 ml) for 20 min and allowed to stand at 0° for 3 days. An oil percipitated and was separated by decantation. The decantate was poured into cold 5% HClaq (1 l.). The precipitated brown solid was collected at once, combined with the oil, and dissolved in MeOH. Ve separated as colorless prisms, m.p. and m.m.p. 173–174°, λ_{max}^{NaOEt} 352, 287, 252 mμ (3·0 g). Addition of water to the MeOH filtrate precipitated the crude isomeric flavan derivative. Recrystallized 4 times from aqueous MeOH, the flavan derivative (IIe) was obtained as colorless prisms, m.p. 92–95°, λ_{max}^{EtOH} 271 (3·98), 225 mμ (log ε) (1·7 g). Elemental analyses indicate that IIe crystallizes with MeOH of crystallization. (Found: C, 71·2; H, 6·54; MeO–, 13·1. Calc. for $C_{24}H_{24}O_5$: C, 73·45; H, 6·16; 1 MeO—, 7·91. Calc. for $C_{24}H_{24}O_5 \cdot CH_3OH$: C, 70·7; H, 6·65; 2 MeO—, 14·6%.)

The *acetate* of the flavan (IIe) crystallizes from MeOH as colorless plates, m.p. 136–138°. (Found: C, 71·9; H, 5·98; CH_3CO—, 9·59. Calc. for $C_{26}H_{26}O_6$: C, 71·9; H, 6·03; 1 CH_3CO—, 9·92%.)

The flavan (IIe; 0·2 g) was dissolved in glacial acetic acid (2·0 ml) containing 2 drops of 10% HClaq and warmed for 2 min. Colorless crystals (0·14 g) separated from the orange-red solution on

addition of water. Recrystallized from MeOH Ve was obtained, m.p. and m.m.p. 173–174°, λ_{max}^{EtOH} 280 mμ.

Condensation of 3-*methyl*-8-*methoxy*-4'-*hydroxyflavylium chloride and* I *at pH* < 1. A solution of the 3-methylflavylium salt (4·0 g) and I in glacial acetic acid (40 ml), conc. HCl (10 ml) and water (30 ml) was heated on a steam-bath for 5 min and allowed to stand overnight. An oily precipitate separated. The mixture was diluted with water (200 ml) and the sticky product was collected and dissolved in warm acetone–MeOH. On concentration and cooling, the stereoisomers IIIb separated as a mixture of colorless prisms, m.p. 212–213°,[1] λ_{max}^{EtOH} 267, 225 mμ, λ_{max}^{NaOEt} 250 mμ (2·4 g). Fractionally crystallized from acetone–MeOH as previously described,[1] this mixture was resolved into the isomer, m.p. and m.m.p. 256°, λ_{max}^{EtOH} 266, 225 mμ, λ_{max}^{NaOEt} 249 mμ, and the isomer, m.p. and m.m.p. 226°; λ_{max}^{EtOH} 268, 225 mμ, λ_{max}^{NaOEt} 250 mμ.

The isomer (IIIb, mμ 256; 0·2 g) was redissolved in glacial acetic acid (5 ml) and 5% HClaq (5·0 ml), heated to boiling for 1 min, and allowed to cool. Water was added and the solid product was recrystallized from acetone–MeOH. Unreacted IIIb, m.p. and m.m.p. 256°, separated (0·09 g).

3-Methyl-4'-hydroxyflavylium chloride (1·0 g), condensed similarly with I (2·0 g) in glacial acetic acid–HCl, gave colorless prisms (0·85 g), m.p. 211–213°, λ_{max}^{EtOH} 269, 226 mμ; λ_{max}^{NaOEt} 249, inflection at ~278 mμ, identical with the stereoisomeric mixture obtained at pH 5·8. Recrystallized once from acetone–MeOH the isomer IIIa, m.p. and m.m.p. 253–254°, was separated (0·24 g).

Condensation of 7-*hydroxyflavylium chloride and* I *at pH* < 1. A solution of 7-hydroxyflavylium chloride (1·0 g) and I (2·0 g) in glacial acetic acid (10·0 ml) and 5% HClaq (10·0 ml) was heated on a steam-bath for 5 min and allowed to cool. Crystals rapidly separated from the orange-red solution. Recrystallized from acetone–MeOH the flavan derivative IIc separated as glistening, cream-colored prisms, m.p. 237°, λ_{max}^{EtOH} 272, inflections at ~250 and 224 mμ; λ_{max}^{NaOEt} 264, inflection at ~285 mμ, (0·63 g). The *acetate* of the product crystallized from MeOH as colorless prisms, m.p. and m.m.p. with the acetate[1] of IIc, 132°.

Benzoylation of Va. (a) The tetrahydroxanthene derivative Va (0·3 g) was warmed with pyridine (2·0 ml) and benzoyl chloride (1·5 ml). After 5 min excess of water was added. The solid benzoate was collected after 1 hr and crystallized from acetone–MeOH. The monobenzoate Ve separated as colorless needles, m.p. 182–183°, λ_{max}^{EtOH} 251 (4·45), 231 (4·42) mμ (log ε). (Found: C, 77·2; H, 5·59. Calc. for $C_{30}H_{26}O_6$: C, 77·2; H, 5·62%.)

(b) Compound Va (0·2 g) was dissolved in 10% NaOHaq (10·0 ml), cooled and shaken with benzoyl chloride (2·0 ml) for 10 min. A crystalline solid separated. Excess of $NaHCO_3$aq was added and the product was recrystallized from acetone–MeOH. The benzoate, described above, was obtained, m.p. and m.m.p. 182–183°. Alkaline hydrolysis of this benzoate yielded Va, m.p. 207°.

Benzoylation of IIa. (a) The flavan derivative IIa (0·5 g) was warmed with pyridine (5·0 ml) and benzoyl chloride (1·5 ml) for 5 min, diluted with water (50 ml) and allowed to stand for 1 hr. The oily benzoate was collected and crystallized from acetone–MeOH. The benzoate IIb separated as colorless, felted needles, m.p. 157°, λ_{max}^{EtOH} 230 (4·44), inflection at 263 (4·08) mμ (log ε). (Found: C, 77·3; H, 5·62. Calc. for $C_{30}H_{26}O_6$: C, 77·2; H, 5·62%.)

(b) Compound IIa (0·5 g) was heated to boiling with EtOH (10·0 ml), the mixture was cooled, treated with 10% NaOHaq (20 ml) and allowed to stand at room temp for 15 min. Benzoylchloride (10·0 ml) was then added and the mixture was agitated for 5 min and 10% NaOHaq (20 ml) added and the agitation was continued for 5 min. Sat. $NaHCO_3$aq was added and the mixture refrigerated for 2 hr. The oily product was extracted with ether. The ether solution was washed well in water, dried (Na_2SO_4) and evaporated. The oily residue was dissolved in Skellysolve F (50 ml). On cooling, colorless crystals separated. Recrystallized from acetone–MeOH the *dibenzoate* IXb separated as colorless prisms, m.p. 167–168° (0·30 g), λ_{max}^{EtOH} 238 (4·74), inflection at 271 mμ (log ε). (Found: C, 77·9; H, 5·36. Calc. for $C_{37}H_{30}O_8$: C, 77·9; H, 5·30%.)

(c) Compound IIa (2·0 g) was dissolved in boiling 10% NaOHaq (50 ml). The yellow solution was cooled and treated with benzoyl chloride (6·0 ml). After shaking for 5 min, sat. $NaHCO_3$aq (50 ml) was added and the mixture was refrigerated for 2 hr. The solid benzoate was collected and recrystallized from acetone–MeOH. The benzoate Ve of the xanthene derivative was obtained as colored needles, m.p. and m.m.p. 181–182°, λ_{max}^{EtOH} 251, 230 mμ (1·1 g).

Acknowledgments—The author is indebted to Dr. R. Lundin for the NMR spectrum of Va, to J. Bergot for assistance in determining ultraviolet spectra and to L. M. White and Miss G. Secor for elemental analyses.