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ANTHOCYANIDINS AND RELATED COMPOUNDS—VII

REACTIONS OF FLAVYLIUM SALTS WITH 5,5-DIMETHYL-1,3-CYCLOHEXANEDIONE AT pH 5·8

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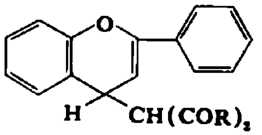
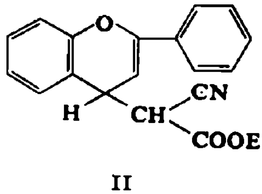
Abstract—Phenolic flavylium salts, substituted and unsubstituted at position 3, condense with 5,5-dimethyl-1,3-cyclohexanedione in aqueous methanolic solutions at pH 5·8 to form novel cyclic flavan derivatives of types Xa and XIa.

PYRYLIUM salts are susceptible to attack by nucleophilic reagents.[1] In 1959, Kröhnke and Dickore reported[2] that the β-diketones, 2,4-pentanedione and dibenzoylmethane, react with flavylium perchlorate in alkaline solutions to yield 4-(diacetylmethyl)- and 4-(dibenzoylmethyl)-flav-2-ene, Ia and Ib, respectively. Under these conditions, ethyl cyanoacetate or malononitrile formed mixtures of compounds of types II and III. These flavenes are easily oxidized[2] in acid solutions, e.g., by air, to substituted flavylium salts. The formation of IV in the reaction of flavylium perchlorate with malonic acid in acetic acid solutions involves an oxidative condensation of this nature.[3] These reactions occur only with flavylium salts which are unsubstituted in the 3-position.[3] We have now determined, however, that the cyclic β-diketone, 5,5-dimethyl-1,3-cyclohexanedione, reacts readily with unsubstituted and 3-methyl phenolic flavylium salts to yield novel flavan derivatives.



Ia, R = Me
Ib, R = C_6H_5



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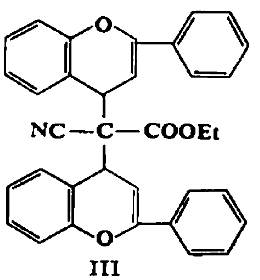

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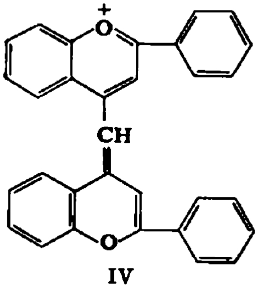

IV

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* A laboratory of the Western Utilization Research and Development Division, Agricultural Research Service, U.S. Department of Agriculture.

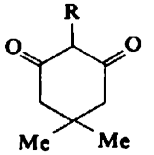
[1] F. M. Dean, *Naturally Occurring Oxygen Ring Compounds*, p. 391. Butterworths, London (1963).

[2] F. Kröhnke and K. Dickore, *Chem. Ber.* **92**, 46 (1959).

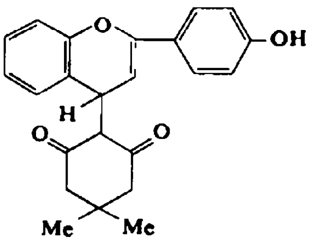
[3] M. Blackburn, G. B. Sankey, A. Robertson and W. B. Whalley, *J. Chem. Soc.* 1573 (1957).

Thus, 4′-hydroxyflavylium chloride condenses with 5,5-dimethyl-1,3-cyclohexanedione (Va) in aqueous methanolic solutions at pH 5·8 to yield (76%) a colorless, crystalline compound, $C_{23}H_{22}O_4$, m.p. 249°. In alcohol it has λ_{max} 268, 225 mμ (Log ϵ 4·03, 4·37). On acetylation (with acetic anhydride and pyridine) and methylation the condensation product forms a monoacetate, $C_{25}H_{24}O_5$, and an alkali-insoluble, monomethyl derivative, $C_{24}H_{24}O_4$, indicating that under these conditions only the 4′-phenolic hydroxyl group is acylated and alkylated.

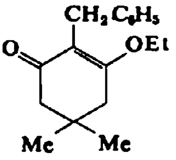
By analogy with the 2,4-pentanedione and dibenzoylmethane products (Ia and Ib) it was anticipated that condensation of 4′-hydroxyflavylium chloride and Va would yield the monoflavenyl-5,5-dimethyl-1,3-cyclohexanedione (VI) the molecular formula of which is identical with that determined for the condensation product. However, comparisons of the chemical and spectral properties of the condensation product with those of 1-benzyl-5,5-dimethyl-1,3-cyclohexanedione (Vb) 2-benzyl-3-ethoxy-2-cyclohexenone (VII) and 4-substituted flav-2-enes clearly exclude structure VI for the product. Thus, (a) 2-alkyl-5,5-dimethyl-1,3-cyclohexanediones enolize with ease and, consequently, dissolve in aqueous alkalies, form colored complexes with ferric salts and form O-alkyl derivatives when heated with alkyl halides in alkaline solutions.[4,5] In agreement with these observations Vb[6] gives an intense red



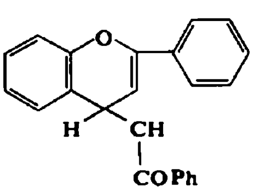
Va, R = H
Vb, R = $C_6H_5CH_2$



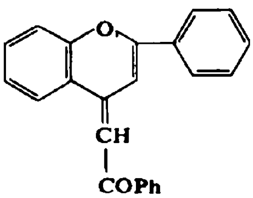
VI



VII



VIII



IX

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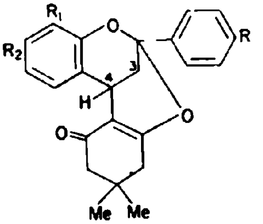
[4] R. B. Woodward and E. R. Blout, *J. Amer. Chem. Soc.* **65**, 562 (1943).

[5] J. Nickl, *Chem. Ber.* **91**, 553 (1958).

[6] R. D. Desai, *J. Chem. Soc.* 1079 (1932).

color with alcoholic ferric chloride, is easily soluble in aqueous alkalies, and forms the alkali-insoluble O-ethyl derivative VII, when treated with ethyl iodide and alcoholic potassium hydroxide. Compound VII and the 4'-hydroxyflavylium condensation product, however, do *not* form colored complexes with ferric chloride and, heated with methyl iodide and alcoholic potash, the phenolic condensation product yields only the alkali-insoluble 4'-monomethyl ether, (b) in absolute ethanol 2,5,5-trimethyl-1,3-cyclohexanedione (λ_{max} 264 mμ, log ϵ 4·13) exists predominantly as the enol.[7] On addition of alkali the enol is ionized, the intensity of absorption increases and the λ_{max} undergoes a pronounced bathochromic shift to 295 mμ.[7] Compound Vb behaves similarly, its λ_{max} in ethanol (264 mμ, Log ϵ 4·06) shifting to 292 mμ in alcoholic sodium ethylate. The spectrum of VII (λ_{max} 268 mμ, log ϵ 4·21) and of the 4'-methyl ether of the condensation product (λ_{max} 267 mμ, log ϵ 3·97), on the other hand, are unaltered on the addition of alkali, (c) in the 5·5–6·5 μ region the IR spectrum of Vb in chloroform has a broad band at 6·26 μ and weaker bands at 5·88 and 5·75 μ. In this region the spectrum of VII and of the 4'-methyl ether of the condensation product are very similar, each having a single sharp band, at 6·19 and 6·15 μ respectively, (d) as previously mentioned, substituted flavenes of types Ia and Ib are oxidized easily by air in acid solutions to flavylium salts. Similarly, 4-phenacylflavenes (VIII) undergo facile dehydrogenation in acetic acid solutions to yield highly colored, crystalline 4-phenacylidene flavenes (IX) which are converted by mineral acids into 4-phenacylflavylium salts.[8,9] In contrast to the pronounced instability of these flavenes, the condensation product is substantially unaffected (90% recovery) when heated in acetic acid solutions, while in acetic acid–hydrochloric acid solutions, it chiefly rearranges, without oxidation, to an isomer,[10] m.p. 207°. These comparisons clearly indicate that neither a flavene nucleus nor a dione (or free enolized dione) grouping are present in the condensation product. The dione grouping is present, however, in a *stabilized* enolic form. On this basis the product is formulated



Xa, R = OH, $R_1 = R_2$ = H
Xb, R = OMe, $R_1 = R_2$ = H
Xc, R = OH, R_1 = OMe, R_2 = H
Xd, R = R_1 = OMe, R_2 = H
Xe, R_2 = OH, R = R_1 = H

as a cyclic flavan derivative (Xa) derived from VI by enolization and subsequent addition of the enolic hydroxyl to the flavene double bond. NMR spectral measurements, particularly on the condensation products derived from 3-methylflavylium salts *vide infra*, are in complete accord with the flavan structure Xa (Table 1). As in

[7] E. G. Meek, J. H. Turnbull and W. Wilson, *J. Chem. Soc.* 2891 (1953).

[8] D. W. Hill, *J. Chem. Soc.* 1255 (1934); 85 (1935).

[9] F. M. Irvine and R. Robinson, *J. Chem. Soc.* 2086 (1927).

[10] To be described in the succeeding paper in this series.

TABLE 1. NMR SPECTRA DATA[a]

	C—CH_3	H_3	H_4	CH_2 (allylic)	CH_2 (ketonic)	$C^{CH}_{CH_3}$
XIb (m.p. 153°)	9·25 (7·0, d)[b]	approx. 7·7[c]	6·05 (2·5, d)	7·58 (s)	7·76 (s)	9·00 (s) 8·89 (s)
XIb (m.p. 120°)	9·31 (7·0, d)	approx. 7·7[c]	6·00 (2·5, d)	7·67 (s)	7·78 (s)	9·10 (s) 8·90 (s)
Xd	—	7·82 (2·8, d)	5·78 (2·8, t)	7·63 (s)	7·78 (s)	9·07 (s) 8·92 (s)
XIIb	9·25 (7·0, d)	7·67 (2·5, d) (7·0, quart)	5·88 (2·5, d)	—	—	—

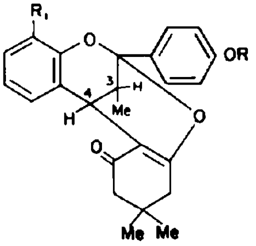
[a] NMR spectra were taken in $CDCl_3$ with tetramethylsilane as internal reference using the Varian A-60 spectrometer.

[b] Recorded shielding value in τ (coupling constant in c/s, multiplicity).

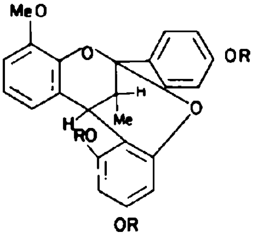
[c] The absorption peaks of the proton, although accounted for by integration, were shadowed by absorption peaks of the methylene groups.

the case of 4'-hydroxyflavylium chloride, 8-methoxy-4'-hydroxyflavylium chloride and 7-hydroxyflavylium chloride react with Va at pH 5·8 to form condensation products $C_{24}H_{24}O_5$ and $C_{23}H_{22}O_4$, respectively. The chemical properties and UV spectra of these products are very similar to those previously described for Xa and, consequently, these products are the corresponding flavan derivatives Xc and Xe.

3-Methylflavylium salts also condense readily with Va at pH 5·8. However, with these flavylium salts the products consist of mixtures of two isomeric compounds, which have similar properties and are apparently stereoisomers. Thus, 3-methyl-8-methoxy-4'-hydroxyflavylium chloride yields a crystalline product (m.p. 211–212°) which, on thin layer chromatography on silicic acid in a variety of solvent systems, migrates as a single species. By fractional crystallization, however, it can be separated with some difficulty into two monohydroxy $C_{25}H_{28}O_5$ compounds, m.p. 256° λ_{max} 266, 225 mμ (log ϵ 4·00, 4·33) and m.p. 226°, λ_{max} 268, 226 mμ (log ϵ 4·04, 4·36). Mixtures of these separated isomers melt at 211–212°, the m.p. of the initial reaction product. Apart from m.p. differences, these isomers and their methyl and acetyl derivatives have virtually identical chemical and spectral properties. They are completely stable in boiling glacial acetic acid. Heated briefly with a mixture of glacial acetic acid and conc. hydrochloric acid, they may be recovered unchanged in approximately 50% yields. Except for this characteristic reluctance to rearrange[10] in strongly acid (and alkaline) solutions, the properties of these isomers closely correspond to those of the flavan derivatives of type Xa. These compounds, therefore, must be stereoisomers of structure XIc, which differ only in the spatial arrangement of the methyl group at position 3. It is noteworthy that XIc is structurally related to the product XIIa, recently obtained[11] from the condensation of 3-methyl-8-methoxy-4'-hydroxyflavylium chloride and phloroglucinol. Compound Va and 3-methyl-4'-hydroxyflavylium chloride react similarly to yield stereoisomers XIa, m.p. 254° (methyl ether, XIb, m.p. 120°) and m.p. 225° (methyl ether, XIb, m.p. 153°). The flavan structures assigned to these stereoisomers has been confirmed by NMR spectral measurements on the methyl ethers XIb. Thus, as in XIIb,[11] the methyl group at position 3



XIa, R — R$_1$ = H
XIb, R = Me, R$_1$ = H
XIc, R$_1$ = Me, R = H



XIIa, R = H
XIIb, R = Me

(>CH—CH$_3$) in XIb, m.p. 120° and 153°, adsorbs as a doublet (J = 7·0 c/s) at 9·31 and 9·25 τ respectively (Table 1, Fig. 1). In the absence of a methyl group at position 3, the methyl ether (Xd) of the condensation product from 8-methoxy-4'-hydroxyflavylium chloride shows a methylene doublet (τ = 2·8 c/s) at 7·82 τ. As expected, the chemical shifts of the protons of the allylic methylene group and of the methylene

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[11] L. Jurd and A. C. Waiss, *Chem. & Ind.* 1708 (1964); *Tetrahedron* **21**, 3707 (1965).

group adjacent to the carbonyl in the cyclohexanone portion of these condensation products are similar to the corresponding shifts in the enol form of Va itself.[12]

The flavan derivatives are not reduced by sodium borohydride. Prolonged treatment of the monomethoxy compound (Xb) with LAH, however, gave a monohydroxy-monomethoxy derivative, $C_{24}H_{26}O_4$. This product is unusual in that the alcoholic hydroxyl group is easily solvolysed. Recrystallized from methanol it forms the corresponding *di*-methoxy compound, $C_{25}H_{28}O_4$. The UV spectrum of the dimethoxy compound, λ_{max} 278, 271, 224 mμ (log ϵ 3·29, 3·37, 4·30), is typical of that of a simple flavan and its IR spectrum in chloroform has a strong bond at 6·02 mμ, indicative of an α,β-unsaturated carbonyl. The reduction product does not

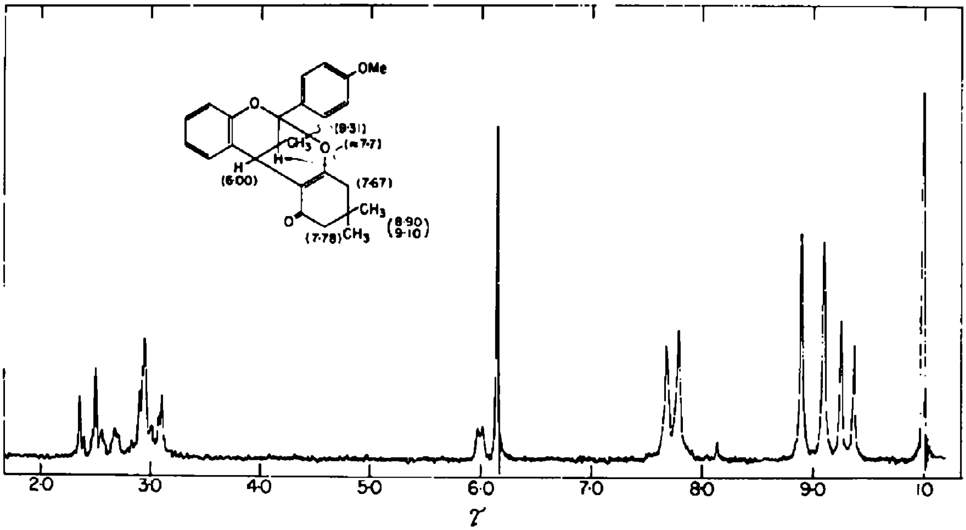
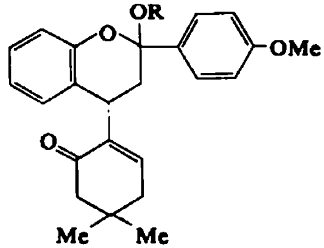
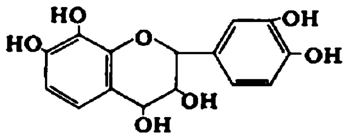


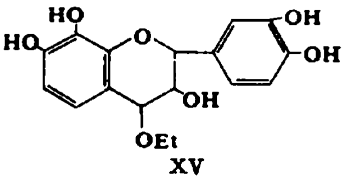
FIG. 1 60 Mc NMR spectrum of XIb (m.p. 120°).



XIIIa, R = H
XIIIb, R = Me



XIV



XV

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[12] *High Resolution* NMR *Spectra Catalog*, Spectrum 512. Varian Associates (1963).

form a colored complex with ferric salts and its spectrum does not undergo a bathochromic shift in alkali. It is, however, highly unstable in acid solutions and forms orange–red, unidentified products. On the basis of these limited data the reduction product and its methyl derivative may be assigned tentative structures XIIIa and b, respectively. Facile solvolysis of a reactive benzylic hydroxyl, *para*- to a hydroxyl or methoxyl group, has been reported for the natural flavan-3,4-diol, isomelaccidin (XIV). Recrystallized from ethanol it forms the monoethyl derivative (XV).[13]

EXPERIMENTAL

UV spectra were determined in EtOH in 1 cm silica cells.

Condensation of 4′-hydroxyflavylium chloride and Va. A solution of 4′-hydroxyflavylium chloride (10·0 g) and Va (20·0 g) in MeOH (100 ml) and aqueous buffer solution, pH 5·8 (100 ml) was heated on a steam-bath for 10 min. Colorless crystals rapidly separated from the highly colored reaction mixture. The mixture was allowed to stand overnight and the crystalline product was collected (10·6 g). Recrystallized from acetone–MeOH, Xa separated as colorless needles, m.p. 249°, which did not give a color with alcoholic $FeCl_3$ λ_{max} 268 (4·03), 226 (4·37) mμ (log ϵ). (Found: C, 76·2; H, 6·16. Calc. for $C_{23}H_{22}O_4$; C, 76·2; H, 6·12%.)

The *acetate* of Xa, prepared by warming the product with acetic anhydride and pyridine, crystallized from MeOH as colorless prisms, m.p. 134°, λ_{max} 264 mμ. (Found: C, 74·4; H, 5·96; CH_3CO—, 10·5. Calc. for $C_{25}H_{24}O_5$: C, 74·2; H, 5·98; 1 CH_3CO—, 10·6%.)

A solution of Xa (2·0 g) and dimethyl sulfate (3·0 ml) in dry acetone (50 ml) was heated under reflux with anhydrous K_2CO_3 (6·0 g) for 2 hr. The colorless reaction mixture was concentrated, diluted with water (150 ml) and allowed to stand for 30 min. The crystalline methyl ether was collected and recrystallized from acetone–MeOH. Compound Xb separated as colorless needles, m.p. 144° (1·6 g) λ_{max} 267 (3·97), 226 (4·36) mμ (log ϵ) and was also obtained by methylation of Xa with MeI and K_2CO_3 in acetone. (Found: C, 76·3; H, 6·40; MeO—, 8·22. Calc. for $C_{24}H_{24}O_4$: C, 76·6; H, 6·43; 1 MeO—, 8·23%.)

A solution of Xa (1·0 g) and KOH (2·0 g) in EtOH (20 ml) and water (5·0 ml) was heated under reflux for 15 min. MeI (15·0 ml) was added and heating was continued for 3 hr. The reaction mixture was concentrated and diluted with water. The solid product crystallized from MeOH as colorless needles, m.p. and m.m.p. with Xb, 144°. Compound Xb, similarly refluxed with MeI and 10% alcoholic KOHaq for 3 hr, was recovered unchanged on addition of water.

Compound Xa (0·2 g) was benzylated by heating it with KI (1·0 g), K_2CO_3 (5·0 g) and benzyl chloride (1·0 ml) in acetone (20 ml) for 3 hr. The filtered acetone solution was evaporated to an oil which was dissolved in boiling Skellysolve F. On cooling, colorless crystals separated. Recrystallized from acetone–MeOH, the *benzyl ether* of Xa separated as colorless, glistening prisms, m.p. 174°, λ_{max} 267, 230 mμ. (Found: C, 79·6; H, 6·24. Calc. for $C_{30}H_{28}O_4$: C, 79·6; H, 6·24%.)

A solution of Xa (1·0 g) in boiling glacial acetic acid (40 ml) and water (10·0 ml) was heated on a steam-bath for 10 min, diluted with water (50 ml) and allowed to cool slowly. Colorless crystals of Xa, m.p. and m.m.p. 249°, separated from the yellow solution (0·90 g). A solution of Xb (0·2 g) in glacial acetic acid (5·0 ml) was heated on a steam-bath for 15 min. Excess of water was added to the yellow solution and Xb separated as colorless needles, m.p. and m.m.p. 144° (0·19 g).

A mixture of Xa (0·2 g), hydroxylamine hydrochloride (1·0 g), sodium acetate (1·0 g), EtOH (20 ml) and water (5·0 ml) was heated on a steam bath for 1 hr and filtered. Water (50 ml) was added to the filtrate, whereupon Xa separated as colorless needles, m.p. and mixed m.p. 249°, λ_{max} 268, 226 mμ.

Condensation of 8-methoxy-4′-hydroxyflavylium chloride and Va. A mixture of 8-methoxy-4′-hydroxyflavylium chloride (2·0 g) and Va (4·0 g) in MeOH (50 ml) and aqueous buffer, pH 5·8 (50 ml) was heated on a steam-bath for 30 min. Colorless crystals separated. After cooling, the product was collected (2·0 g) and recrystallized from acetone–MeOH. Compound Xc separated as colorless needles, m.p. 219°, λ_{max} 266 (4·00), 225 (4·33) mμ (log ϵ). (Found: C, 73·6; H, 6·07; MeO—, 7·84. Calc. for $C_{24}H_{24}O_5$: C, 73·45; H, 6·16; 1 MeO—, 7·91%.)

The *acetate* of the product separated from acetone–MeOH as colorless needles, m.p. 204°, λ_{max}

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[13] J. W. Clark-Lewis and P. I. Mortimer, *J. Chem. Soc.* 4106 (1960).

264 mμ. (Found: C, 71·8; H, 5·97; MeO—, 7·15; CH_3CO—, 9·91. Calc. for $C_{26}H_{26}O_6$: C, 71·9; H, 6·03; 1 MeO—, 7·15; 1 CH_3CO—, 9·92%.)

Compound Xc was methylated as described above. The methyl ether (Xd) crystallized from MeOH as small, colorless needles, m.p. 196°, λ_{max} 266, 226 mμ. (Found: C, 73·4; H, 6·43; MeO—, 14·1. Calc. for $C_{25}H_{26}O_5$: C, 73·8; H, 6·45; 1 MeO—, 15·2%.) Warmed briefly with glacial acetic acid containing a few drops of 10% HClaq, Xd was recovered unchanged.

Condensation of 7-hydroxyflavylium chloride and Va. Reaction of 7-hydroxyflavylium chloride (1·0 g) and Va (2·0 g) at pH 5·8 as previously described gave Xe (0·95 g) which crystallized from MeOH as colorless granular crystals, m.p. 237°, λ_{max} 272 (3·85), inflections at 255 and 224 mμ (log ε), which did not give a color with alcoholic $FeCl_3$. (Found: C, 76·0; H, 6·08. Calc. for $C_{23}H_{22}O_4$: C, 76·2; H, 6·12%.)

The acetate of Xe separated from acetone–MeOH as colorless needles, m.p. 132°, λ_{max} 266 mμ. (Found: C, 74·3; H, 6·02; CH_3CO—, 10·9. Calc. for $C_{25}H_{24}O_5$: C, 74·2; H, 5·98; 1 CH_3CO—, 10·65%.)

Condensation of 3-methyl-4′-hydroxyflavylium chloride and Va. A solution of 3-methyl-4′-hydroxyflavylium chloride[14] (8·0 g) and Va (16·0 g) in MeOH (100 ml) and aqueous buffer solutions, pH 5·8 (100 ml) was warmed for 30 min. Crystals rapidly separated. Recrystallized from MeOH the product separated as colorless prisms, m.p. 211–213° (9·5 g). Dissolved in acetone–MeOH and allowed to crystallize slowly this product deposited minute prisms (m.p. 223–224°), followed by large rhombic prisms (m.p. 253–254°). Specimens of these crystals were separated manually. The crystalline mixture was redissolved in acetone–MeOH and seeded with the crystals, m.p. 223–224°. An isomer of XIa thereby separated as colorless prisms, m.p. 225° (recrystallized) (4·1 g), λ_{max} 267 (3·99), 225 (4·37) mμ (log ε). (Found: C, 76·7: H, 6·40. Calc. for $C_{24}H_{24}O_4$: C, 76·7; H, 6·43%.)

The acetone–MeOH filtrate from the isomer (m.p. 225°) was concentrated and seeded with the crystals, m.p. 253–254°. The second isomer of XIa separated as colorless prisms, m.p. 254–255° (recrystallized) (2·6 g), λ_{max} 270 (4·03), 226 (4·35). (Found: C, 76·7; H, 6·38. Calc. for $C_{24}H_{24}O_4$: C, 76·7; H, 6·43%.) Mixtures of the isomers, m.p. 225° and 254–255°, melted at 211–213°.

The *acetate* of XIa (m.p. 225°) separated from acetone–MeOH as colorless needles, m.p. 156°, λ_{max} 265 mμ. (Found: C, 74·6; H, 6·30; CH_3CO—, 9·81. Calc. for $C_{26}H_{26}O_5$: C, 74·6; H, 6·26; 1 CH_3CO—, 10·6%.) The *acetate* of the isomeric form of XIa (m.p. 254–255°) had m.p. 136°, λ_{max} 265 mμ. (Found: C, 74·8; H, 6·25%.)

Methylation of XIa (m.p. 225°) with MeI, K_2CO_3 and acetone in the usual way, give the *methyl ether* XIb, m.p. 153°, λ_{max} 265, 225 mμ. (Found: C, 77·1; H, 6·67; MeO—, 7·86. Calc. for $C_{25}H_{26}O_4$ C, 76·9; H, 6·71; 1 MeO—, 7·95%.) Methylation of XIa (m.p. 254–255°) in the same way gave an isomeric *methyl ether* XIb, m.p. 120°, λ_{max} 270 (4·02), 227 mμ (log ε). (Found: C, 76·7; H, 6·70; MeO—, 7·83%.)

Condensation of 3-methyl-8-methoxy-4′-hydroxyflavylium chloride and Va. Condensation of this flavylium salt (10 g) and Va in aqueous MeOH at pH 5·8 gave a crystalline product, m.p. 211–212° (11·0 g). Recrystallized from acetone–MeOH, an isomer of XIc, m.p. 256°, λ_{max} 266 (4·00), 225 (4·33) mμ (log ε) separated from the boiling solution (5·5 g). (Found: C, 73·8; H, 6·41. Calc. for $C_{25}H_{26}O_5$: C, 73·9; H, 6·45%.)

Concentration of the acetone–MeOH filtrate gave a second isomer of XIc, m.p. 226–227° (recrystallized), λ_{max} 268 (4·04), 226 (4·36) mμ (log ε). (Found: C, 73·9; H, 6·46%.) Mixtures of the isomers, m.p. 256° and 226° had m.p. 211–212°.

Compound XIc, m.p. 256° (0·5 g) was dissolved in boiling glacial acetic acid (10 ml) and heated for 40 min. The solution remained colorless. On adding excess of water, XIc, m.p. 256°, was recovered (0·5 g).

The *acetate* of XIc (m.p. 256°) crystallized from acetone–MeOH as colorless needles, m.p. 168°, λ_{max} 264 mμ. (Found: C, 72·3; H, 6·36; CH_3CO—, 9·5. Calc. for $C_{27}H_{28}O_6$: C, 72·3; H, 6·29; 1 CH_3CO—, 9·6%.) The *acetate* of XIc (m.p. 226–227°) formed colorless needles, m.p. 144° λ_{max} 265 mμ. (Found: C, 72·5; H, 6·30; CH_3CO—, 9·5%.)

The *methyl ether* of XIc (m.p. 256°) formed colorless needles, m.p. 152°, λ_{max} 264, 226 mμ. (Found: C, 74·4; H, 6·64; MeO—, 14·7. Calc. for $C_{26}H_{28}O_5$: C, 74·3; H, 6·71; 2 MeO—, 14·8%.)

Lithium aluminum hydride reduction of Xb. A solution of Xb (1·0 g) in anhydrous ether (100 ml) was added slowly during 2 hr to a slurry of LAH (1·0 g) in ether (100 ml). The mixture was refluxed

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for an additional 2 hr. Unreacted LAH was decomposed with 50% aqueous MeOH (10 ml) and the etheral solution was added to cold 5% H_2SO_4aq (100 ml). The ethereal layer was washed with water, dried (Na_2SO_4) and evaporated to an oil (A). MeOH (20 ml) was added to the oil. On scratching, long, colorless, silky needles separated (0·95 g). Recrystallized 3 times from MeOH XIIIb was obtained as colorless needles, m.p. 130°. (Found: C, 76·6; H, 7·14; MeO—, 15·8. Calc. for $C_{25}H_{28}O_4$: C, 76·5; H, 7·19; 2 MeO—, 15·8%.)

When an oil (A) was dissolved in ether, concentrated and diluted with Skellysolve F, a granular solid separated. Recrystallized 3 times from a MeOH-free mixture of acetone and ether, colorless prisms were obtained, m.p. 151–152°, λ_{max} 278 (3·21), 271 (3·25), 225 (4·14) mμ (log ϵ). (Found: C, 76·3; H, 6·94; MeO—, 8·24. Calc. for $C_{24}H_{26}O_4$: C, 76·2; H, 6·93; 1 MeO—, 8·21%.)

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