5-HYDROXY AND METHOXY FLAVYLIUM SALTS

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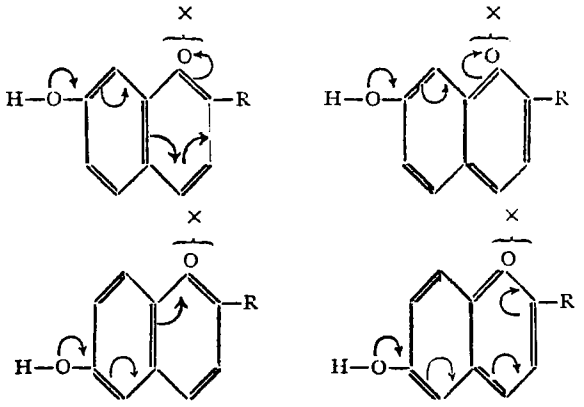
Received January 25, 1944

Starting from γ-resorcylic aldehyde[1] typical 5-hydroxy and-methoxy flavylium salts have now been prepared mainly with a view to study their fluorescence in solutions. Improved procedures for the preparation of the aldehyde and its methyl ether are described in the experimental part of this paper. By adopting them better yields are obtained and the operations are made easier. Attempts to condense the aldehyde with acetophenone itself have not been successful, but condensation has been effected with hydroxy substituted acetophenones and their acetates. In their colour reactions these new flavylium salts are less intense as compared with the 7-substituted isomers and their fluorescence in solutions is almost negligible.

Fluorescence emission of flavylium salts is maximum in concentrated sulphuric acid solutions, less intense in alcohol and minimum in aqueous medium. Only those that are very intense in sulphuric acid give detectable fluorescence in aqueous acid solutions. Ridgway and Robinson[2] reported that most simply constituted flavylium salts exhibit fluorescence in concentrated sulphuric acid though only a few having methoxyl or hydroxyl in the 7 or 6 positions retain it on dilution with water. The 7th position is the most favourable and the 6th comes next. They found that the 8th position is definitely inhibitive since 8-methoxy compounds had an almost negligible fluorescence even in sulphuric acid solution. From the results presented in this paper the 5th position seems to be similarly unfavourable. Further, Pelargonidin does not give fluorescence in alcoholic solutions though it contains a hydroxyl group in position 7 ; the 5-hydroxyl present in this molecule seems to have a definite inhibitory effect. If the 5-hydroxyl is modified by glucoside formation, is methylated or benzoylated or replaced altogether by a methyl group fluorescence reappears.[3] Flavylium salts with 7 : 8 combination of hydroxyl groups have been recently prepared by Robinson and Vasey.[4] They have not recorded any fluorescence; it is possible it was not noticeable in alcoholic or aqueous solutions. Detailed data do not seem to be available relating to the influence of the hydroxyl groups in the 3-position and in the side phenyl nucleus. In general as the number of these groups increases absorption colour is intensified. Visible

fluorescence also seems to increase up to a particular stage, but later on is lost either due to the shifting of the fluorescence band to the infra-red or due to degeneration of the energy into heat.

In some previous publications[5] the structural characters governing fluorescence in coumarins were discussed. With regard to the above-mentioned influence of the position of the hydroxy and methoxy groups on fluorescence emission, the similarity between flavylium salts and coumarins[5] is striking. It may be fortuitous or may be due to similar mechanisms functioning in both groups of compounds. The following suggestion may, however, be made. If we take into consideration only solutions in concentrated sulphuric acid in which the resemblance is closest, coumarins can form hydroxy pyrylium salts. For either of the structural formulæ that could be given for the pyrylium salts resonance originating from 7 and 6 positions may be represented as below. It is possible that the conditions represented by them are the optimum for producing visible fluorescence. The effect should be comparatively inferior from the 6th position since electromeric changes cannot be so facile as when the 7th position is involved.



R=Substituted Phenyl or OH

Experimental

γ-Resorcylic aldehyde was prepared by the decarboxylation of 2:4-dihydroxy-3-formyl benzoic acid (Shah and Laiwalla[1]). Using a modified procedure for the decarboxylation and for the subsequent purification, the preparation was rendered more easy and the yield enhanced.

The aldehydo acid (6·5 g) and water (100 c.c.) were taken in an open pyrex conical flask (250 c.c. capacity) which was placed in an autoclave containing about 200 c.c. of water. The autoclave was closed tight and heated at 108–10° for eight hours. The contents were allowed to cool,

pressure released, and the autoclave opened. The reddish-brown solid product found in the flask was extracted with ether repeatedly and the ethereal solution evaporated. A reddish oily residue (about 5 g.) was left behind which solidified in the course of a few hours. It was purified by dissolving in acetone and treating the solution with petroleum ether when an amorphous brown impurity was deposited. The liquid was filtered and the filtrate carefully concentrated when pale yellow needles of γ-resorcylic aldehyde (3·5 gm.) were obtained.

The monomethyl ether of the above aldehyde was originally prepared in an indirect way by Limaye.[6] Direct methylation using aqueous alkali and dimethyl sulphate or methyl iodide gave mainly the dimethyl ether. The mono-methyl ether could, however, be obtained directly from γ-resorcylic aldehyde by adopting the following procedure for the methylation.

γ-Resorcylic aldehyde (0·1 g.) was dissolved in anhydrous benzene (20 c.c.) and treated with one molecular proportion of dimethyl sulphate in benzene solution and anhydrous potassium carbonate in excess (2·3 g.). After refluxing for 15 hours the mixture was treated with 10 c.c. of cold water in order to dissolve the potassium carbonate. The benzene layer was then separated and washed with a little water. It was then repeatedly extracted with aqueous sodium hydroxide (3%). The alkaline layer was acidified with hydrochloric acid, when the monomethyl ether of γ-resorcylic aldehyde separated out as a fine crystalline mass. It then crystallised from boiling water as clusters of long needles melting at 76–77° C.; yield 65%. (Limaye m.p. 75° C.)

3 : 5 : 4′-*Trihydroxy-flavylium chloride*.—γ-Resorcylic aldehyde (0·2 g.) and ω : *p*-dihydroxy acetophenone (0·2 g.) were dissolved in dry ethyl acetate, the solution saturated at 0° with dry hydrogen chloride and the gas passed slowly for a further period of 4 hours. The solution turned gradually red and after about an hour began to deposit bright red crystals of the flavylium chloride. It was kept overnight in a refrigerator and the crystals were filtered and washed with anhydrous ether. On recrystallisation from 2% aqueous methyl alcoholic hydrochloric acid, bright red needles with metallic lustre were obtained. Yield 63%. The product did not melt below 300° C. (Found: C, 61·4; H, 3·4; $C_{15}H_{11}O_4$ Cl requires C, 62·0 and H, 3·8%.)

5-*Methoxy*-3 : 4′-*dihydroxy-flavylium chloride* was prepared from the monomethyl ether of γ-resorcylic aldehyde adopting exactly the procedure given above. It was a dark red solid with a characteristic metallic sheen and appearing under the microscope as rhombic plates. It melted at 258-60°. (Found: C, 63·5; H, 4·0; $C_{16}H_{12}O_4$ Cl requires C, 63·1 and H, 4·3%.)

3:5:3':4'-*Tetrahydroxy-flavylium chloride*.—For preparing this substance γ-resorcylic aldehyde had to be condensed with ω: 3:4-triacetoxy acetophenone. On previous occasions when this ketone had to be used for flavylium salt synthesis a mixture of anhydrous ethyl acetate and anhydrous alcohol was used as solvent. Flavylium condensation and deacetylation took place simultaneously. In the present case, however, probably due to complex changes taking place with γ-resorcylic aldehyde (*cf.* phloroglucinaldehyde) in the presence of alcohol and hydrogen chloride, only brown amorphous substances insoluble in methyl alcoholic hydrogen chloride were obtained. Consequently the flavylium condensation and deacetylation had to be effected separately.

Through a solution of γ-resorcylic aldehyde (0·1 g.) and ω: 3:4-triacetoxy acetophenone (0·2 g.) in anhydrous ethyl acetate was passed a current of dry hydrogen chloride at ice temperature for about 3 to 4 hours. After keeping the contents in a refrigerator at 0° overnight they were filtered and the reddish brown solid washed with anhydrous ether. The product was dissolved in hot 2% aqueous alcoholic hydrochloric acid and treated with an equal volume of 20% sodium hydroxide. The resulting brown solution was raised to boiling and after a minute acidified with concentrated hydrochloric acid. The bright red solution of the flavylium chloride thus obtained was cooled and then treated with further quantities of hydrochloric acid so that the concentration of the acid in the mixture was finally about 10%. On leaving it in a refrigerator, a fine reddish brown solid was deposited. It was freely soluble in 1% alcoholic hydrogen chloride and 2% aqueous hydrochloric acid. It was crystallised by dissolving in the former solvent and adding concentrated hydrochloric acid. The pure substance appeared as bright red needles which did not melt below 300°C.; (Yield 50%.) (Found: C, 58·1; H, 3·8; $C_{15}H_{11}O_5Cl$ requires C, 58·7 and H, 3·6%.)

3:5:3':4':5'-*Pentahydroxy-flavylium chloride* was prepared from γ-resorcylic aldehyde and ω: 3:4:5: tetra-acetoxy acetophenone adopting the above procedure. It was obtained as a reddish brown micro-crystalline solid which did not melt below 300°C. (Found: C, 55·3; H, 3·7; $C_{15}H_{11}O_6Cl$ requires C, 55·8 and H, 3·4%.)

The following table gives a summary of the colour reactions exhibited by the 5-hydroxy and 5-methoxy flavylium chlorides prepared above. A solution of each substance in 1% alcoholic hydrochloric acid was employed for all tests except 4 and 9 and the colour produced by the addition of various reagents recorded. For 4 the solid was used and for 9 an alcoholic solution without acid.

Reagent	3 : 5 : 4'-Trihydroxy	5-Methoxy-3 : 4'-dihydroxy	3 : 5 : 3' : 4'-Tetrahydroxy	3 : 5 : 3' : 4' 5'-Pentahydroxy
1. Colour of the solution	Red—no fluorescence	Orange red—no fluorescence	Deep red	Deep reddish purple
2. 1% HCl ..	Do.	Do.	Red	Red—precipitation
3. 20% HCl ..	Orange—precipitation—no fluorescence	Do.	Light red	Precipitation
4. Conc. H_2SO_4 ..	Orange—very feeble green fluorescence ; lost on dilution with water	Orange—very feeble green fluorescence ; lost on dilution with water	Red—no fluorescence	Red—no fluorescence
5. Na Acetate ..	Pink—fades rapidly	Pink —fades rapidly	Bluish pink—fades rapidly	First violet changing to blue and fades rapidly
6. Na HCO_3 ..	Purple—fades slowly	Pink—fades slowly	Blue—fades rapidly	Blue—fades rapidly
7. Na_2CO_3 ..	Purple-dichroic blue—fades slowly	Violet-red—fades slowly	Deep blue—rapidly fades	Deep blue—rapidly fades
8. NaOH ..	Reddish-purple —rapidly fades to yellow	Violet-red—rapidly fades to very pale yellow	Blue-green—rapidly fades to yellowish brown	Blue-green and then quickly turns brown
9. $FeCl_3$ ..	Nil	Nil	Blue	Blue

Summary

Starting from γ-resorcylic aldehyde some typical 5-hydroxy and methoxy flavylium salts have been prepared and studied. They exhibit negligible fluorescence even in concentrated sulphuric acid. The structural factors that affect fluorescence in flavylium salts are discussed and comparison effected with coumarins.

REFERENCES

1. Shah and Laiwalla .. *J. C. S.*, 1938, 1828.
2. Ridgway and Robinson .. *Ibid.*, 1924, 215.
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6. Limaye *Rasayanam*, 1936, **1**, 12.