THE REMARKABLE FLUORESCENCE OF CERTAIN COUMARIN DERIVATIVES

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In a previous paper[1] the important structural features that affect the fluorescence of hydroxycoumarins and chromones were discussed. Amongst coumarin derivatives certain 3-carbethoxy and 3-carboxyumbelliferones exhibited remarkable fluorescence; besides the intensity being great the fluorescence was very prominent and bright even in neutral alcoholic solutions. Hence it became a matter of interest to test if besides the above two groups others containing a carbonyl would give rise to the same effect and further if the remarkable capacity of these 3-substituted compounds to fluoresce in neutral solution would persist even after the 7-hydroxy group is modified by etherification. The present paper records the synthesis of a number of derivatives of 7-hydroxycoumarin not prepared till now. They are prepared from β-resorcylic aldehyde, orcylic aldehyde and 4-O-methylresorcylic aldehyde the last of which occurs in several plant materials by condensation with ethyl acetoacetate, ethyl benzoylacetate and diethyl malonate using piperidine as the condensing agent. The preparation and properties are briefly embodied in Table I. A detailed study of their properties has been made with particular reference to the fluorescence exhibited by them in neutral, alkaline and acid solutions. Also for purposes of comparison a number of previously known compounds have been re-examined for their fluorescence under the same conditions as adopted for the new compounds. The results are discussed towards the end of this paper.

Experimental

The condensations of the hydroxy-aldehydes with the esters were effected in the presence of piperidine. The practical details were nearly the same in all the cases but for some slight modifications in the method of purification. The following is a typical experiment:—

A solution of orcylic aldehyde (0·1 g.) and ethyl acetoacetate (5 drops) in alcohol (1 c.c.) was treated with piperidine (3 drops) and the resulting solution left overnight in a stoppered test-tube. It was then rendered acid

with dilute hydrochloric acid when a solid separated out contaminated with some oily matter. After pouring out the aqueous solution the mixture was stirred with ether (10 c.c.) when the oily impurity alone dissolved leaving behind a better-looking solid. The clear supernatant liquid was decanted off and the residual solid washed again with ether (10 c.c.) by decantation. Two crystallisations from hot alcohol gave 3-acetyl-5-methyl-7-hydroxy-coumarin in the form of rhombic and rectangular plates melting at 224–25°.

The reactants for the preparation of the other coumarin derivatives, their physical properties and chemical composition are summarised in Table I. The sample of 4-O-methyl-resorcylic aldehyde used in the preparation of the 7-methoxy-coumarins was obtained from the root of *Decalepis Hamiltonii*[2]. 3-Carboxy-7-methoxy-coumarin was obtained from the 3-carbethoxy compound by treatment with cold 10% alcoholic potash during 24 hours. In all cases alcohol was used as the solvent for the crystallisations.

The visible fluorescence of the compounds was studied in very dilute solutions under illumination by daylight. First the colours in concentrated sulphuric acid and in alcoholic solutions were observed; subsequently part of the alcoholic solution was rendered faintly acid with one drop of dilute sulphuric acid and another part alkaline with one drop of dilute sodium hydroxide. It was noticed in all cases that dilution of the alcoholic solution with tap water (pH 7·2) produced an effect which was comparable to that of the addition of alkali; this effect was not observed when distilled water was the diluent.

To test if the organic solvent employed had any marked influence on the fluorescence exhibited by these 3-substituted coumarins the behaviour of 3-carbethoxy-7-hydroxy-coumarin was studied in typical hydroxylic and non-hydroxylic solvents. The colour of the fluorescence was as follows: in rectified spirit, absolute alcohol and anhydrous methyl alcohol-brilliant blue with violet tinge; in chloroform, acetone and ether—weak blue becoming deeper on the addition of a little water; in benzene—very feeble blue; in petroleum ether—almost absent.

Discussion

From the results given in Table II it is clear that the presence of a carbethoxyl, carboxyl or acetyl group in position 3 of 7-hydroxy and 7-methoxycoumarins enhances the fluorescent property of these compounds so much that they exhibit bright fluorescence even in neutral alcoholic solutions. The hydroxy compounds differ from the methoxy series in the following characteristics: (1) The former produce bright fluorescence in neutral and alkaline media and the intensity is considerably diminished in acid

TABLE I

Phenolic aldehyde	Ester condensed	Product	Gross appearance	Microscopic appearance	M.P.	Formula	Required		Found	
							% C	% H	% C	% H
Resorcylic aldehyde	Ethyl benzoyl acetate	3-benzoyl-7-hydroxy coumarin	Light pale yellow clusters	Stout needles and narrow rectangular prisms	236–37°	$C_{16}H_{10}O_4$	72·2	3·8	72·6	4·2
Orcylic aldehyde	Ethyl acetoacetate	3-acetyl-5-methyl-7-hydroxycoumarin	Citron yellow glistening powder	Rhombic and rectangular prisms	224–25°	$C_{12}H_{10}O_4$, $\frac{1}{2}H_2O$	63·5	4·8	63·8	5·1
,,	Ethyl benzoyl acetate	3-benzoyl-5-methyl-7-hydroxycoumarin	Pale yellow woolly clusters	Long rectangular prisms	231–32°	$C_{17}H_{12}O_4$	72·9	4·3	72·5	4·6
4-O-methyl resorcylic aldehyde	Ethyl acetoacetate	3-acetyl-7-methoxycoumarin	Glistening lemon yellow needles	Thin rectangular plates	168–69°	$C_{12}H_{10}O_4$	66·1	4·6	65·8	4.6
,,	Ethyl benzoyl acetate	3-benzoyl-7-methoxy-coumarin	Light white clusters	Long stout fibrous needles	153°	$C_{17}H_{12}O_4$	72·9	4·3	73·2	4·2
,,	Diethyl malonate	3-carbethoxy-7-methoxy coumarin	White glistening powder	Rectangular plates	134°	$C_{13}H_{12}O_5$	62·9	4·8	62·5	4·8
		3-carboxy-7-methoxy-coumarin	White glistening flakes	Plates and prisms	195°	$C_{11}H_8O_5$	60·0	3·6	60·0	3·4

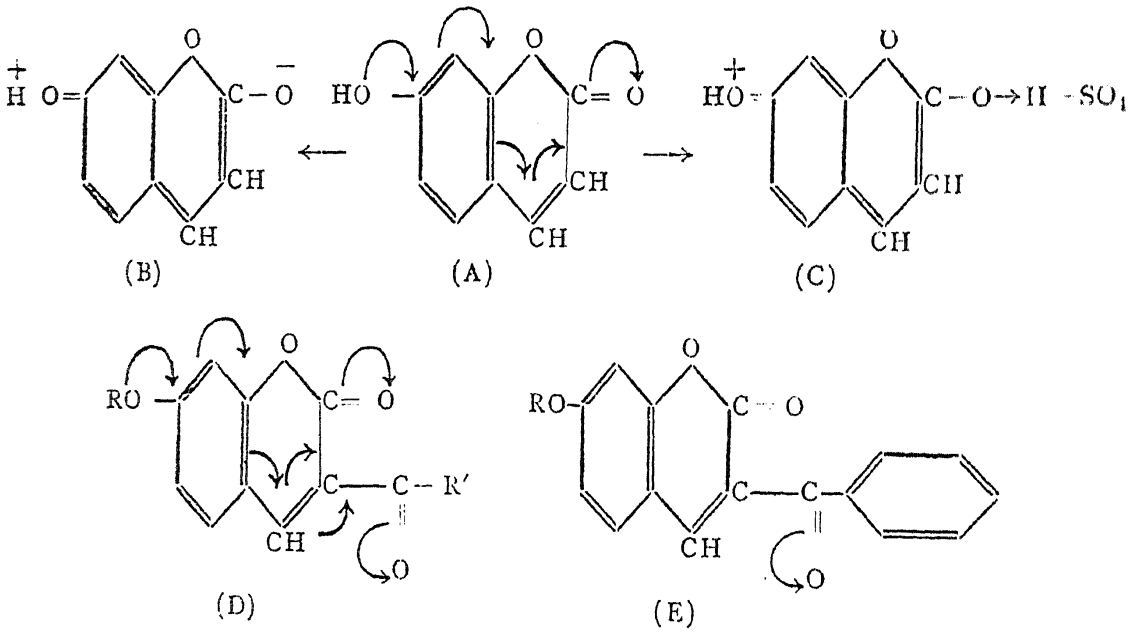
TABLE II

Colour of the Fluorescence

Compound	In concentrated sulphuric acid	In alcohol	In alcoholic solution after addition of one drop of dilute acid	In alcoholic solution after addition of one drop of dilute alkali
3-Carbethoxy-7-hydroxycoumarin[3]	Bright blue violet	Bright blue with violet tinge	Not qualitatively affected, just a bit less intense	Bright pure blue (solution is pale yellow in colour)
3-Carboxy-7-hydroxycoumarin[3] ..	,,	,,	,,	Bright pure blue (solution not coloured yellow)
3-Acetyl-7-hydroxy coumarin ..	Pale blue	Violet blue	Very pale violet	Bright pure blue (solution yellow)
3-Benzoyl-7-hydroxy-coumarin ..	Nil (solution deep yellow)	Nil (solution colour less)	Nil	Nil (even a solution in tap water has yellow colour)
3-Carbethoxy-5-methyl-7-hydroxy-coumarin[4]	Pale blue	Bright blue with violet tinge	Considerably reduced	Bright blue (solution pale yellow)
3-Carboxy-5-methyl-7-hydroxy-coumarin[4]	,,	,,	,,	,,
3-Acetyl-5-methyl-7-hydroxy-coumarin	Pale bluish green (solution pale yellow)	Blue with green tinge	Very pale violet	Bright blue with green tinge (solution yellow)
3-Benzoyl-5-methyl-7-hydroxy-coumarin	Nil (solution deep yellow)	Nil (pale yellow solution)	Nil (solution colourless)	Nil (solution deep yellow ; even tap water gives pale yellow solution)
3-Carbethoxy-7-methoxycoumarin	Bright violet blue	Pale violet	Not affected	Fluorescence lost ; (solution yellow) either addition of acid or large dilution restores violet fluorescence
3-Carboxy-7-methoxycoumarin ..	,,	Violet blue	,,	Flourescence lost (solution colourless); either addition of acid or large dilution restores violet fluorescence (sodium salt sparingly soluble)
3-Acetyl-7-methoxycoumarin ..	Blue (solution pale yellow)	Very pale violet	Very pale violet	Deep yellow solution ; bright blue fluorescence on dilution with water or alcohol.
3-Benzoyl-7-methoxy-coumarin	Nil (solution deep yellow)	Nil	Nil	Nil (solution very pale yellow)

media. The reverse is the case with the latter. (2) The fluorescence of the hydroxy compounds is blue whereas that of the methoxy series is more on the violet side. The 3-benzoyl compounds differ markedly from the others. The solids as well as their solutions are markedly coloured yellow and they exhibit no visible fluorescence under any condition.

In explaining fluorescence and in looking for a correlation between it and chemical constitution it has to be borne in mind that the phenomenon has two important aspects, (1) absorption of light by the molecule and (2) emission of fluorescence. For exhibiting visible fluorescence the molecule should possess suitable light absorption and the fluorescent band should fall in the visible region. It may therefore be said that the constitutional factors which affect absorption are of primary importance. Possibility of resonance as the result of electron mobility is now recognised as the essential cause of absorption colour and this may also be considered as one of the deciding factors for fluorescence emission.



[R = H or CH_3; R′ = OH, OEt or CH_3]

Though resonance exists in umbelliferone (A) it is not sufficient to produce fluorescence. Only charged molecules present in solution in aqueous alkali or concentrated sulphuric acid exhibit this property. The structures of these molecules may be represented by (B) and (C) respectively. In 7-methoxy-coumarin, structures (A) and (C) alone are possible since dilute alkali does not react with it. The introduction of a carbonyl group in position 3 in the shape of a carbethoxyl, carboxyl or acetyl enhances resonance as shown in (D) since two carbonyl groups take part and hence these compounds fluoresce even in neutral alcoholic solution. This may be further

accentuated in the case of the 7-hydroxy compounds (R = H) by the capacity of the phenolic hydroxyl to undergo ionisation. The effect of acid in diminishing fluorescence in this case may be due to the hindrance offered by it to this ionisation. Such a possibility does not exist in regard to the 7-methoxy compounds. On the other hand the weakening of fluorescence of the methoxy compounds on adding alkali may be attributed to the influence of the negative hydroxyl ions of the alkali in preventing the polarisation of the carbonyl group and thus diminishing resonance. Further the alkaline solutions are coloured yellow and the fluorescence is not easily visible. Dilution with water not only weakens this absorption colour but it also diminishes the concentration of the hydroxyl ions and thus fluorescence is rendered again prominent.

In the case of the 3-benzoyl compounds (E) the introduction of a new benzene ring has brought about far-reaching changes. Since this ring can act as an electron sink as well as an electron source resonance is obviously increased and it is evident from the deep colour of the compounds. But the fluorescence band has either shifted to the infra-red or all emission is inhibited as the result of degradation of the absorbed light into heat.

Summary

A number of umbelliferone derivatives with acetyl, benzoyl, carbethoxyl or carboxyl groups in the 3-position have been prepared of which 6 are new. The fluorescence exhibited by these has been studied and the results are discussed.

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