A COLOUR REACTION OF CERTAIN PHENOLIC ETHERS AND THEIR DERIVATIVES WITH NITRIC ACID

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In the course of work on the synthesis and study of anthoxanthins and their degradation products in this laboratory a number of derivatives of phenolic ketones became available. It was noticed that some of them gave a blue colour reaction with concentrated nitric acid. It appears to be characteristic of certain structural combinations and comes in handy for distinguishing between closely related compounds and isomers belonging not only to the abovementioned group of phenolic ketones, but also to simpler (phenolic ethers) and more complex types (chalkones and flavanones) of compounds.

In order to describe the colour reaction, phloroacetophenone dimethyl ether could be taken as a typical example. When a small quantity of this substance is treated with concentrated nitric acid the solid goes into solution producing a brilliant blue colour. On standing, this colour gradually changes through an intermediate violet to a bright scarlet red which is stable. This colour change becomes more rapid when the solution is heated. The blue is not obtained with other mineral acids even when used in conjunction with nitric acid. Dilute nitric acid also fails to produce it; its solvent capacity is also very small as compared with the concentrated acid. It should be emphasised here that the appearance of a definite blue or green colour immediately or within a few minutes after the substance is treated with nitric acid can alone be taken as a positive test or reaction and not any other colour such as yellow, orange red or brown commonly given by most organic compounds. The following is a list of compounds (not exhaustive) yielding positive tests:—

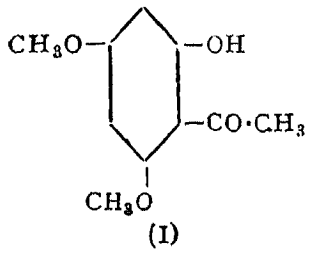
(1) *Phenolic ethers.*—Resorcinol-dimethyl and diethyl ethers and orcinol dimethyl ether give an intense emerald green colour immediately. The trimethyl ether of phloroglucinol produces a deep blue colour in about two minutes.

(2) *Aldehydes.*—Resorcylic-aldehyde-4-methyl ether gives a green colour within a minute while phloroglucin-aldehyde-4: 6-dimethyl ether gives an immediate blue colour.

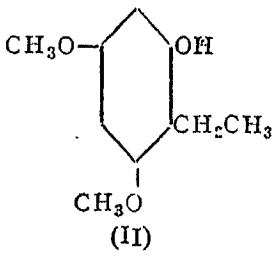
(3) *Ketones.*—4-Methyl and 4-ethyl ethers of β-resacetophenone and its dimethyl ether and γ-resacetophenone-monomethyl ether give a greenish blue colour within two minutes. Immediate pure blue colour is formed by the following:—Phloroacetophenone-4: 6-dimethyl-, diethyl-, dibenzyl-, 4-benzyl-6-methyl, and 2: 4: 6-trimethyl ethers; ω-methoxy-phloroacetophenone-4: 6-dimethyl and diethyl ethers; ω-ethoxy-phloroacetophenone-4: 6-diethyl ether, phlorobenzophenone-4: 6-dimethyl and 4: 6: 2′- trimethyl ethers and ω-phenyl-phloroacetophenone-4: 6-dimethyl ether.

(4) *Acids and their derivatives.*—β-Resorcylic acid-4-methyl ether gives a green colour in a minute; it is rather sparingly soluble. The dimethyl ether, its acid chloride and its anhydride give immediate blue colour. β-Resorcylic-ester-4-methyl and 2: 4-dimethyl ethers, everninic acid and its methyl ester and the dimethyl ether of methyl orsellinate give a similar colour.

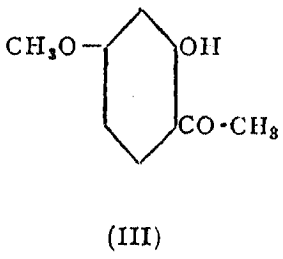
Catechol, quinol, pyrogallol and hydroxy quinol and their methyl ethers do not give this test. Even resorcinol, orcinol and phloroglucinol and their partial methyl ethers do not give it; only their fully methylated ethers do and they represent the simplest types. It would therefore appear to be a characteristic of the fully alkylated ethers of the three meta-hydroxy-phenols. One hydroxyl could be free if it is protected by a carbonyl group in the neighbouring position. Examples of these are given above in (2), (3) and (4). This should be connected with the effect of chelation known to exist in the case of orthohydroxy-carbonyl compounds. Support for this explanation is provided by the following comparisons. Compounds (I) and (III) give positive tests whereas the related compounds (II), (IV) and (V) do not. It should be emphasised that a carbonyl group is capable of protecting only one hydroxyl group by chelation and hence phloroacetophenone-4-methyl and 4-benzyl ethers and γ-resacetophenone give negative reaction. As could be expected free phloroacetophenone and resacetophenone do not respond to the test.



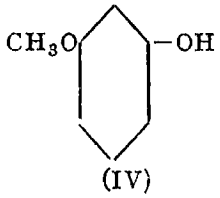
(I)



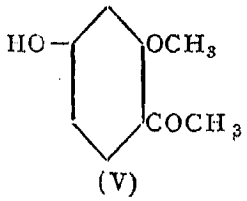
(II)



(III)



(IV)

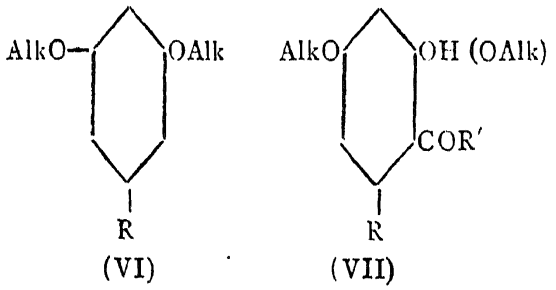


(V)

A large variation in the nature of the carbonyl group is permissible since aldehydes, ketones, including ω-alkoxy and ω-aryl ketones, acids and esters behave alike. Though protection of the hydroxyls by benzyl groups leads to positive reaction, protection by acyl groups like benzoyl gives only negative test (*e.g.*) 2: 4-dibenzoyl-phloroglucinaldehyde.

Further substitution with methyl or methoxyl groups in the nuclear positions of phloroacetophenone-2: 4-dimethyl ether or in the 3 and 5 positions of β-resorcylic acid- and β-resacetophenone-4-methyl ethers produces negative reaction. Typical examples are 2-hydroxy-3: 4- and 2-hydroxy-4: 5-dimethoxy acetophenones, 2-hydroxy-3: 4: 6, 2-hydroxy-3: 4: 5- and 2-hydroxy-4: 5: 6-trimethoxy acetophenones, 2-hydroxy- ω: 3: 5: 6-tetramethoxy acetophenone, 2-hydroxy-3-methyl-4-methoxy- and 2-hydroxy-3-methyl-4: 6-dimethoxy acetophenones, and 2-hydroxy-3-methyl-4-methoxybenzoic ester. These do not give the test.

A consideration of all the above particulars would indicate that the structural requirements for this colour reaction with nitric acid can be represented as given below:



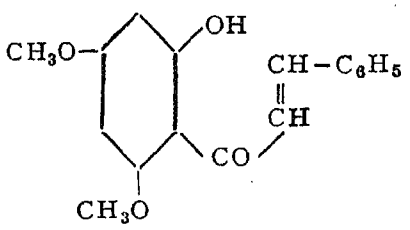
(VI) (VII)

R = H, CH_3 or OAlk.

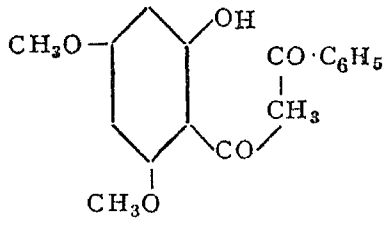
R′ = H, CH_3, CH_2 aryl, C_6H_5, CH_2 OAlk., OH, OAlk.

Consequently it offers a ready means of distinction between these types and others that may be obtained by the degradation of flavones, flavonols and related compounds. Further in the methylation of derivatives of resorcinol and phloroglucinol, besides the normal methyl ethers, C-methyl compounds are frequently met with. The latter do not give the test and can thus be differentiated from the former. For example the methyl ether of 2-hydroxy-3-methyl-4-methoxy benzoic acid gives no blue colour, whereas the ester of 4-O-methyl-β-resorcylic acid does. Similarly the C-methyl and O-methyl derivatives obtained from phloroglucinol by methylation behave differently.

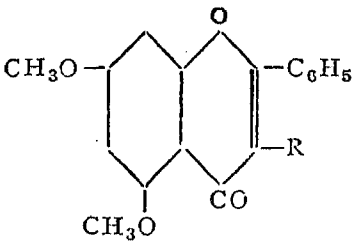
Another direction in which the reaction is useful is for the characterisation of flavanones. Ethers of chalkone (VIII), diketone (IX), flavone (X), and coumaranone (XI) derived from phloroglucinol do not give the test, whereas flavanone ethers (XII) resemble phloroacetophenone-dimethyl ether and give the test strongly.



(VIII)

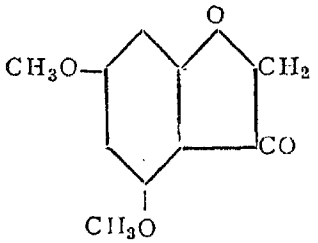


(IX)

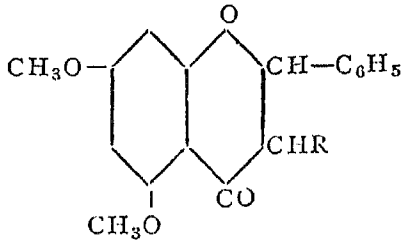


R=H or OCH_3

(X)

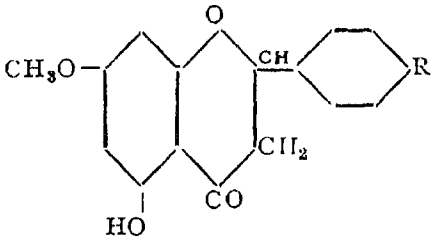


(XI)



R=H or OCH_3

(XII)



R=H, OH or OCH_3

(XIII)

The observation that a free hydroxyl in the 5-position of flavanones (XIII) is no hindrance to this test makes the characterisation of flavanones more easy, because partial methylation of hydroxy flavanones leaving this 5-hydroxyl free is readily carried out and this keeps the flavanone ring in tact.[1] On the other hand, complete methylation results in the opening of the ring and formation of chalkone derivatives. The presence of methyl ether groups and even free hydroxyl groups in the side phenyl nucleus does not seem to affect the reaction. The scope is indicated by the following list of flavanones:—5:7-dihydroxy flavanone, naringenin (5: 7: 4′-trihydroxy flavanone) and isosakuranetin (5: 7-dihydroxy-4′-methoxy flavanone) do not give the test whereas 7-methoxy-5-hydroxy flavanone, sakuranetin (7-methoxy-5: 4′-dihydroxy flavanone), sakuranetin-monomethyl ether (7: 4′-dimethoxy-5-hydroxy flavanone), naringenin-trimethyl ether (5: 7: 4′-trimethoxy flavanone) and hesperetin-trimethyl-ether (5: 7: 3′: 4′-tetramethoxy-flavanone) give positive test. In this connection should be mentioned the earlier observation of Asahina and co-workers[2] that sakuranetin gives an indigo blue colour with nitric acid and isosakuranetin does not.

Summary

A characteristic blue or green colour reaction with concentrated nitric acid is given by the fully alkylated ethers of resorcinol and phloroglucinol and by a number of carbonyl derivatives of them. n the case of these carbonyl compounds one orthohydroxyl could be free. Certain flavanone derivatives of phloroglucinol also give this test whereas chalkones, flavones, diketons and coumaranones do not. It is useful for the differentiation and characterisation of closely related and isomeric compounds belonging to the above categories.

References

1. Narasimhachari and Seshadri .. *Proc. Ind. Acad. Sci.*, A, 1948, **27**, 223.
2. Asahina, *et al.* .. *J. Pharm. Soc. Japan*, 1927, **550**, 1007.