stirred for one-half hour at 40–45°, an additional 50 g. of sodium amalgam was added and the mixture allowed to stand for six hours at room temperature (without stirring). The yellow solution was filtered, heated to boiling and diluted with water until a permanent turbidity appeared. Upon cooling an amorphous, light yellow precipitate formed. This was crystallized from dilute alcohol, and formed colorless crystals (612 mg.), m. p. 158–159°. It did not depress the m. p. of β-4-hydroxy-4',5,7-trimethoxyflavane obtained by catalytic hydrogenation. The monoacetate melted at 127–128°; mixed m. p. 127–128°.

The alkaline mother liquor from which the flavane separated was acidified, and yielded, after purification, 204 mg. of 2'-hydroxy-4',6',4-trimethoxychalcone, m. p. and mixed m. p. with an authentic specimen, 114–115° (lit.,[20,21] 113–114°). The carbon bisulfide mother liquor from which the chalcone was crystallized yielded upon evaporation 1.04 g. of a yellow oil which afforded no crystalline material but which gave a deep carmine color with concentrated hydrochloric acid.

A repetition of the above procedure, except that the reduction was carried out under purified nitrogen, yielded 494 mg. of the β-4-hydroxyflavane and 115 mg. of the chalcone from 1.0 g. of the flavanone.

C. The Reduction of 2'-Hydroxy-4',6'-trimethoxychalcone.—The reduction of 2.00 g. of 2'-hydroxy-4',6',4-trimethoxychalcone with sodium amalgam was carried out substantially as in the preceding example. There was isolated 473 mg. of β-4-hydroxy-4',5,7-trimethoxyflavane, 650 mg. of unchanged chalcone and 600 mg. of a light yellow oil which gave a deep carmine color with concentrated hydrochloric acid.

D. The Reduction of 2',4',6',3,4-Pentamethoxychalcone with Sodium Amalgam.—To a solution of 0.50 g. of 2',4',6',3,4-pentamethoxychalcone in 80 ml. of 70% alcohol was added 10 g. of 3% sodium amalgam and the mixture allowed to stand at 50° for four hours. After the addition of a further 10 g. of sodium amalgam the reduction was allowed to proceed for another four hours at room temperature. The yellow solution was filtered and diluted with water. The oil which separated was rubbed with ether, with the formation of a colorless solid (37 mg.). This was crystallized from benzene, forming tiny, pale yellow needles, m. p. 234–236° dec. The compound gave an intense carmine color when treated with concentrated hydrochloric acid and instantly decolorized bromine in carbon tetrachloride solution. For these reasons the compound is formulated as the bis-pinacol of the chalcone rather than of the dihydrochalcone.

Anal. Calcd. for $C_{40}H_{46}O_{12}$: C, 66.84; H, 6.45; OCH_3, 43.17. Found: C, 66.59; H, 6.66; OCH_3, 42.95.

III. Attempted Isolation of Reduction Products from Polyhydroxyflavanones.—The reduction of hesperetin, naringenin, homoeriodictyol, liquiritigenin or 7-hydroxy-4'-ethoxyflavanone by any of the above methods did not lead to isolable products which could be identified.

Summary

The colored sodium amalgam reduction products of polyhydroxy- and polymethoxyflavanones are not flavylium salts, but are derived from a mixture of reduction products. Predominant among these are the 4-hydroxyflavanes resulting from reduction of the flavanone carbonyl group, and which it has been shown are converted into deeply colored substances upon treatment with strong acids.

LOS ANGELES, CALIFORNIA

RECEIVED SEPTEMBER 12, 1945

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[20] Bargellini, *Gazz. chim. ital.*, **44**, II, 421 (1914); *Chem. Abstr.*, **9**, 1042 (1915).

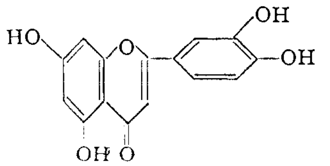
[21] Shinoda and Sato, *J. Pharm. Soc. Japan*, **50**, 265 (1930); *Chem. Abstr.*, **24**, 4046 (1930).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF CALIFORNIA, LOS ANGELES]

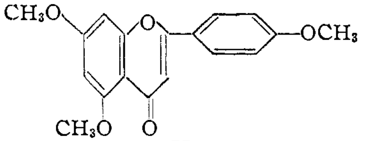
Flavanones and Related Compounds. III. The Reduction of Luteolin and Apigenin Trimethyl Ether with Sodium Amalgam

BY T. A. GEISSMAN AND R. O. CLINTON

When flavones such as luteolin (I) and apigenin trimethyl ether (II) are reduced with sodium amalgam and the reaction mixture acidified, deeply colored substances are formed



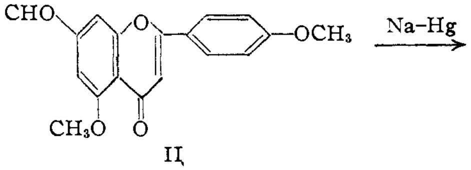
I



II

An analogous result is obtained when a flavonol such as rutin (quercetin-3-rutinoside) or quercetin pentamethyl ether (but not quercetin itself) is reduced[1] in the same way.

The simplest explanation of this reaction, and one that has been offered by Asahina,[1] is that the colored substances are flavylium salts, and that they arise by the reduction of the flavone carbonyl group to yield the pseudo-base III, which upon treatment with acid forms the flavylium ion IV. Taking the reduction of II as an example



II

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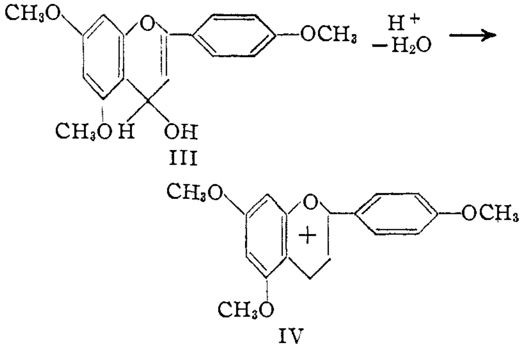
[1] Asahina and Inubuse, *Ber.*, **61**, 1646 (1928); **64**, 1256 (1931); Asahina, Nakagome and Inubuse, *ibid.*, **62**, 3016 (1929).



That such a reaction may occur is possible, but the results presented here show that in the cases of a typical polyhydroxy- and polymethoxyflavone the colors produced in this reduction procedure are due chiefly not to flavylium salts, but to the same substances which are formed in the analogous reduction of the correspondingly substituted flavanones.[2] It has been demonstrated[2] that in the case of the sodium amalgam reduction of flavanones flavylium salts are not formed, and it was suggested that the colored substances arise from substituted 4-hydroxyflavanes.

In Figs. 1 and 2 are shown absorption spectra of solutions prepared by reducing I and II and the corresponding flavanones, eriodictyol and naringenin trimethyl ether, in the standard way described in the preceding paper of this series.[2] The correspondence between these spectra is fair when consideration is taken of the fact that the reduction procedure probably leads to mixtures, and that several of the probable reduction products can give rise to colored ions under the influence of strong acids. That the predominant color-producing substance is the same in each pair of examples is indicated by these data. The inflections in the absorption spectra of the flavone reduction products in the region of 475 mμ. may be an indication that some of the flavylium salt is also present in each case. It is to be noted that corresponding inflections are not present in the curves for the flavanone reduction products.

The formation of the same final reduction products from a flavone and the corresponding flavanone by sodium amalgam can be explained by assuming the reduction of the flavone to proceed in two stages: reduction of the double-bond conjugated with the carbonyl group, yielding a flavanone; and reduction of the flavanone in the manner previously described.[2] The reduction by sodium amalgam of an α,β-unsaturated ketone to the dihydro compound is a well-known reaction. The lack of better correspondence between the spectra of the reduction products of a flavone and the similarly substituted flavanone may be due to reduction to some extent of the flavone according to the scheme II → III.

More direct proof that the sodium amalgam reduction of a flavone proceeds through the flavanone is found in the isolation of the products of the reaction between sodium amalgam and 4′,5,7-trimethoxyflavone (II). There were isolated β-4-hydroxy-4′,5,7-trimethoxyflavane, 2′-hydroxy-4′,6′4-trimethoxychalcone, and an uncrystallizable yellow oil which yielded a deep carmine color with concentrated hydrochloric acid.

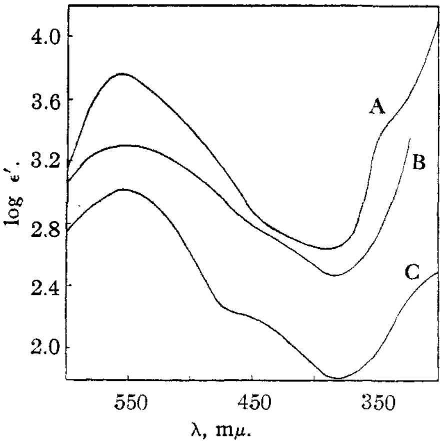


Fig. 1.—Reduction of: A, eriodictyol, Pt-H_2; B, eriodictyol, sodium amalgam; C, luteolin, sodium amalgam. (See ref. 2, footnote 15, for definition of ε′ values.)

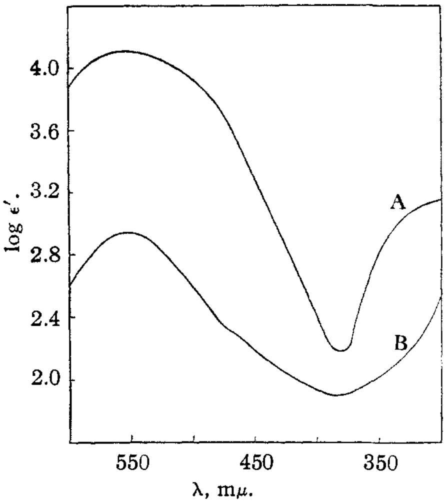


Fig. 2.—Reduction with sodium amalgam of: A, 4′,5,7-trimethoxyflavanone; B, 4′,5,7-trimethoxyflavone.

Similar attempts to isolate pure reduction products from the reaction between sodium amalgam and luteolin (I) were unsuccessful. The products of this reaction were evidently unstable and were converted into colored substances in the course of attempts at purification.

Experimental[3]

The procedure for carrying out the sodium amalgam reductions for spectrophotometric purposes has been de-

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(2) Geissman and Clinton, THIS JOURNAL, 68, 700 (1946).

(3) Melting points are corrected.

scribed.[2] The absorption spectra were measured with a Beckman Quartz Spectrophotometer.

The Reduction of 4′,5,7-Trimethoxyflavone.—A solution of 1.5 g. of 4′,5,7-trimethoxyflavone in 100 ml. of 50% alcohol was stirred with 50 g. of 3% sodium amalgam for one-half hour at 40–45°, and allowed to stand for six hours at room temperature with an additional 50 g. of sodium amalgam. The solution was filtered, heated to boiling, diluted with water until turbid, and allowed to cool. The precipitate which formed was crystallized from dilute alcohol, affording 148 mg. of colorless crystals of β-4-hydroxy-4′,5,7-trimethoxyflavane[2]; monoacetate, m. p. 127–128°.

The alkaline mother liquor from which the flavane separated was acidified with dilute acetic acid, and the yellow precipitate crystallized from carbon bisulfide. There was obtained 62 mg. of 2′-hydroxy-4,4′,6′-trimethoxychalcone, m. p. and mixed m. p. with an authentic specimen, 114–115° (lit.[4] 113–114°).

Summary

The sodium amalgam reduction of polyhydroxy- and polymethoxyflavones leads to the same colored reduction products as the reduction of the corresponding flavanones. There is some evidence that some of the flavylium salt is formed in the former case, but this is not the predominant product.

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(4) Bargellini, *Gazz. chim. ital.*, **44**, II, 421 (1914) (*Chem. Abstr.*, **9**, 1042 (1915)); Shinoda and Sato, *J. Pharm. Soc. Japan*, **50**, 265 (1930) (*Chem. Abstr.*, **24**, 4046 (1930)).

Los Angeles, California

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[Communication No. 1060 from the Kodak Research Laboratories]

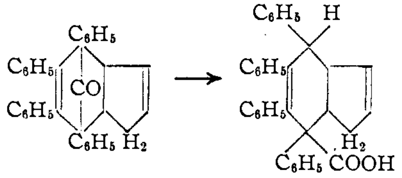
The Action of Alkaline Reagents upon Carbonyl Bridge Compounds. I

By C. F. H. Allen, J. E. Jones and J. A. VanAllan

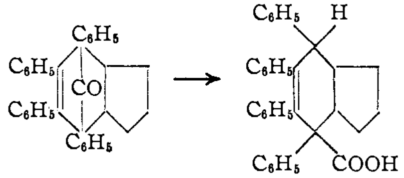
It has been found that in tricyclic carbonyl bridge compounds of the indenone group, the carbonyl bridge is cleaved at one end by the action of strongly alkaline reagents.[1,2] The reaction consists in the addition of one molecule of water, the carbonyl group being converted to a carboxyl group. Since the generality of this reaction had not been determined, all the available carbonyl bridge compounds were submitted to alkaline treatment. These compounds may be placed in two series; one is highly phenylated, whereas in the other, the two phenyl groups at the ends of the bridge are replaced by methyl groups. In this paper the results of treating the first, phenylated series with alkaline reagents are described.

The reaction appears to be fairly general. The action of alkaline reagents upon highly phenylated carbonyl bridge compounds results in the cleavage of the bridge at one end, with consequent formation of a carboxylic acid. Most of the substances treated had simpler structures than the indenones, and fewer functional groups. In spite of this, many secondary reactions often reduce the yield of the primary product. However, quantitative measurements showed that exactly one equivalent of alkali was used for the carbonyl bridge.

The interpretation of the reaction involved in the action of alkaline reagents on indenones containing carbonyl bridges was complicated by the possibility that the indenone keto group might be the one cleaved.[1] The behavior of the compounds, II and III, with alkali indicates, however, the correctness of the earlier interpretation that the keto group in the side chain was not involved. The tetraphenylindene derivative, I,[3] gives a practically quantitative yield of the acid, II, with either alcoholic potassium hydroxide or sodium ethoxide, and the corresponding indane derivative, III, gives the analogous carboxyindane, IV.

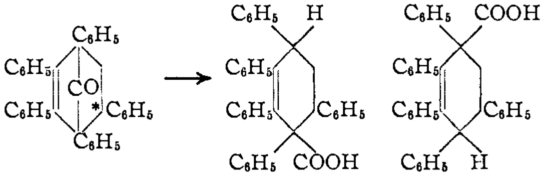


I II



III IV

The pentaphenylated bicyclic ketone, V, gave a mixture of two acids, VI or VII, with potassium hydroxide in ethanol or dioxane, but in methanol a mixture of the two corresponding methyl esters was obtained.



V VI VII

The esters were also formed from the mixed acids by treatment with thionyl chloride, followed by methanol. When piperidine was used, piperidine salts of the acid were formed, but about 10% of an isomeric ketone, Va, was also found. This suggests that the ketone, V, is really a mixture of

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(1) Allen and Gates, This Journal, **64**, 2120 (1942).

(2) Allen and VanAllan, *J. Org. Chem.*, **10**, 333 (1945).

(3) Grummitt, Klopper and Blenkhorn, This Journal, **64**, 604 (1942).