[Contribution from the Chemical Department, University of Bristol]

THE REDUCTION OF QUERCETIN

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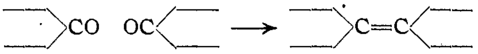
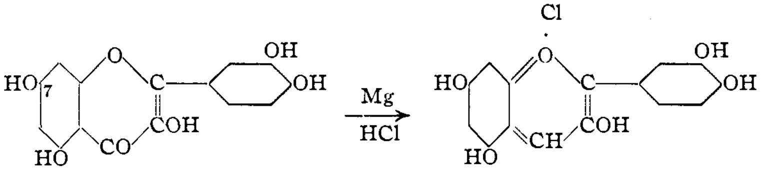
Whereas fluorone, xanthone, thioxanthone, acridone, anthraquinone and their derivatives yield dimolecular products on reduction in acid solution,[1]

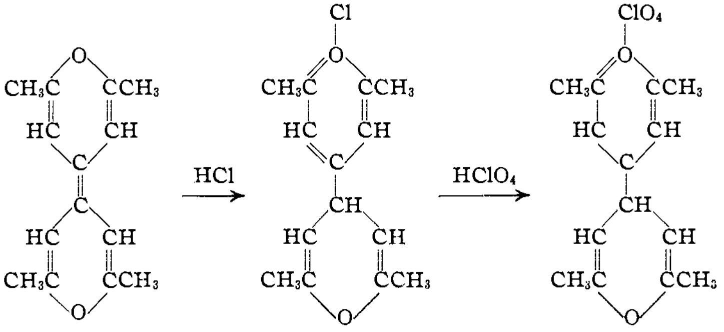


quercetin (I), under identical conditions, gives cyanidin chloride (II).[2]



I II

This is remarkable, considering that other pyrone derivatives behave normally, as shown by Baeyer and Piccard,[3] who found, for example, that dimethylpyrone, if reduced with zinc dust and hydrochloric acid, yields substance III, from which the crystalline perchlorate (IV) may be obtained.



III IV

This abnormal behavior of quercetin, as recorded by Willstätter and Mallison, and the importance of the production of cyanidin chloride from quercetin to the chemistry of the anthocyanidins, has led us to re-investigate this reaction.

The results obtained by us lead to the conclusion that quercetin behaves normally, giving the dimolecular product (V).

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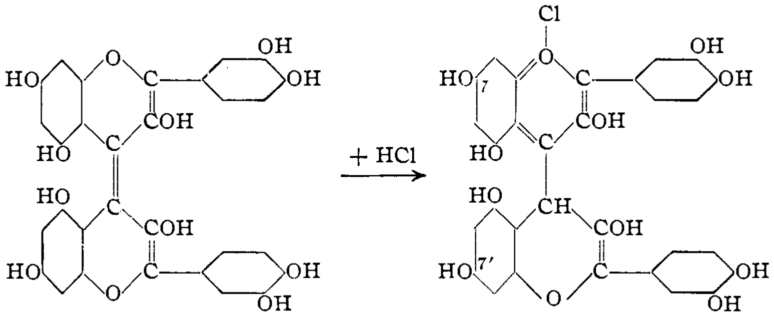
[1] See Houben, "Die Methoden der organischen Chemie," 3rd ed., Vol. II, **1925**, pp. 270 ff.

[2] Willstätter and Mallison, *Sitzb. Preuss. Akad. Wiss.*, 769 (1914).

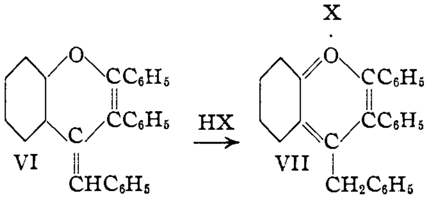
[3] Baeyer and Piccard, *Ann.*, **384**, 208 (1911); **407**, 346 (1914).



V

Following the nomenclature xanthylene (VIII), suggested by Kostanecki and Gurgenjanz[4] for the dimolecular reduction product from xanthone, the name *quercetylene chloride* is suggested for substance (V). The remarkable similarity between quercetylene chloride, $C_{30}H_{21}O_{12}Cl + 2H_2O$, and cyanidin chloride, $C_{15}H_{11}O_6Cl$, which not only resemble each other in almost all respects, but require exactly the same carbon content (C, 55.8), easily accounts for the fact that Willstätter and Mallison should have assumed that they had synthesized cyanidin chloride, since owing to the scarcity of material (0.165 g.) at their disposal, no chlorine analysis, which would have clearly emphasized the difference between these two substances, was possible.

The conversion of the intermediary reduction product, quercetylene, into quercetylene chloride (V), is in agreement with the observations of Baeyer and Piccard, already referred to, and also with the observations made by Löwenbein and Rosenbaum,[5] showing for example that a substance having structure (VI) is easily converted by acids into the pyryllium derivative (VII).

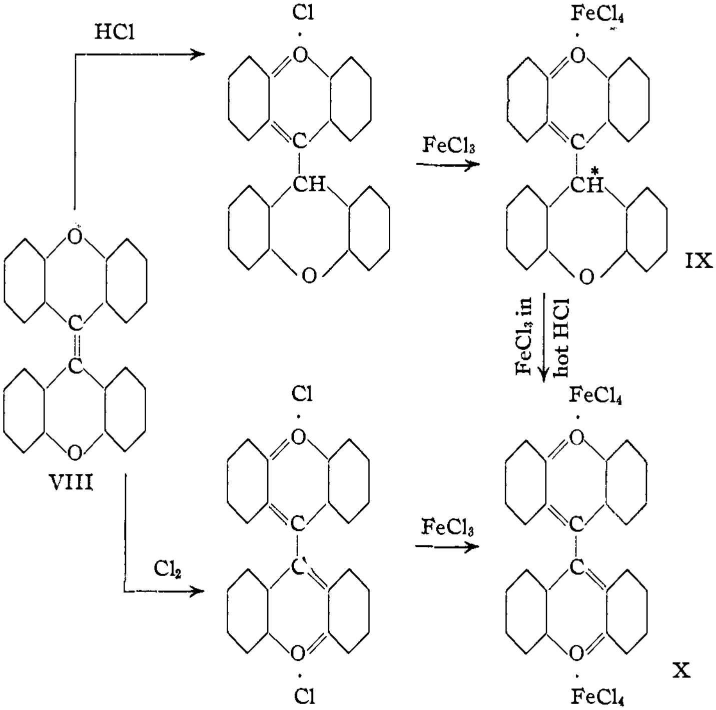


To test further our mechanism for the production of quercetylene chloride, we have also investigated xanthylene (VIII), from which we have obtained the ferrichloride (IX), and the diferrichloride (X), which were prepared according to the following scheme. The preparation of chlorides from xanthylene, however, presented some difficulties, which is to be expected in the light of Gomberg and Cone's[6] observation on the influence of hydroxyl groups on chloride formation.

[4] Kostanecki and Gurgenjanz, *Ber.*, **28**, 2310 (1895).

[5] Löwenbein and Rosenbaum, *Ann.*, **448**, 233, 246 (1926).

[6] Gomberg and Cone, *ibid.*, **370**, 142–208 (1909).



The reduction of rhamnetin, 7, methylquercetin (compare I), which according to Robertson and Robinson[7] is reduced to rhamnetinidin chloride, 7-methylcyanidin chloride (compare II), also proceeds normally, leading to 7,7′-dimethylquercetylene chloride (compare VII). This product, freshly prepared, contains loosely bound hydrochloric acid, which it easily loses on standing, and then gives correct analytical values for 7,7′-dimethylquercetylene chloride. This loss of hydrochloric acid accounts for the unsatisfactory analytical data commented on by Robertson and Robinson,[8] who did not analyze for chlorine, and therefore assumed the increase in carbon content to be due to loss of water of crystallization.

Experimental

Quercetylene Chloride (V).—(1) The reduction product (0.2252 g.), prepared according to Willstätter and Mallison,[9] was purified by dissolving in 25 cc. of methyl alcohol, to which 25 cc. of 12% hydrochloric acid was added, the solution being concentrated on a water-bath. In this manner three fractions, resembling cyanidin chloride in their general properties, were obtained.

Anal. Subs. (dried in desiccator), 5.145, 4.555, 4.638 mg.: CO_2, 10.503, 9.284, 9.435 mg.: H_2O, 1.957, 1.577, 1.732 mg. Subs. (dried in desiccator), 3.70, 7.40, 5.507

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[7] Robertson and Robinson, *J. Chem. Soc.*, 2205 (1927).

[8] Ref. 7, p. 2206.

[9] Willstätter and Mallison, *Sitzb. Preuss. Akad. Wiss.*, 775 (1914).

mg.: AgCl, 0.879, 1.610, 1.196 mg. Subs. (dried by standing in high vacuum over NaOH for six days), 4.783 mg.: AgCl, 1.037 mg. Calcd. for $C_{30}H_{21}O_{12}Cl + 2H_2O$: C, 55.80; H, 3.91; Cl, 5.51. Found: C, 55.67, 55.58, 55.47; H, 4.23, 3.87, 4.15; Cl, 5.88, 5.38, 5.37, 5.36.

(2) To a boiling solution of 10 g. of quercetin in 300 cc. of acetic anhydride, 40 g. of zinc dust was added in three portions, causing the solution to turn deep red. After heating for forty-five minutes over a Bunsen flame, the cooled solution was poured into 500 cc. of 5% hydrochloric acid, the zinc dust being carefully extracted with hot glacial acetic acid. The light yellow colored reduction product was dissolved in 175 cc. of absolute alcohol and heated for two and one-half hours with 75 cc. of concentrated hydrochloric acid, during which time the solution turned deep red; 50 cc. of water was added, and the solution concentrated, a further 50 cc. of water being added after some time. The solid (8.5 g.) which separated was collected, dried and then dissolved in 75 cc. of alcohol, to which was added 75 cc. of 12% hydrochloric acid. On concentration of the solution, 5.3 g. of prismatic crystals, containing only 3% of chlorine, was obtained. This product was rejected. On further concentration, 2.4 g. of a substance containing 5.5% of chlorine was obtained and dissolved in 50 cc. of methyl alcohol, the solution being concentrated in the presence of 50 cc. of 12% hydrochloric acid. Well-defined prisms which resembled the reduction product of Willstätter and Mallison in every respect were obtained.

Anal. Subs. (dried in desiccator), 9.108, 4.032 mg.: CO_2, 18.649, 8.237 mg.: H_2O, 3.361, 1.520 mg. Subs. (dried in desiccator), 5.132 mg.: AgCl, 1.098 mg. Calcd, for $C_{30}H_{21}O_{12}Cl + 2H_2O$: C, 55.80; H, 3.91; Cl, 5.51. Found: C, 55.85, 55.71; H. 4.11, 4.19; Cl, 5.29.

7,7′-Dimethylquercetylene Chloride (Compare V).—The reduction with zinc dust (40 g.) in acetic anhydride (100 cc.) was carried out according to Robertson and Robinson,[7] with the exception that not rhamnetin, but tetra-acetylrhamnetin (4.5 g.) was employed for the reaction. The use of acetylrhamnetin offered the advantage that instead of an ill-defined, sticky product, as observed by Robertson and Robinson, a definite yellow solid was obtained. The hydrolysis of this acetylated reduction product, as well as its purification, was carried out according to these workers, and the product obtained corresponded to theirs.

Anal. (Air-dried product) Subs., 3.191, 4.568 mg.: CO_2, 6.047, 8.657 mg.: H_2O, 1.304, 1.882 mg. Subs., 3.806 mg.: AgCl, 1.445 mg. Subs., 4.136 mg.: AgI, 2.608 mg. (Pregl–Zeisel). Calcd. for $C_{16}H_{13}O_6Cl + 2H_2O$ (rhamnetinidin chloride): C, 51.54; H, 4.56; Cl, 9.53; OCH_3, 8.32. Found: C, 51.68; 51.65; H, 4.57, 4.61; Cl, 9.39; OCH_3, 8.32. (Dried in desiccator.) Subs. (after standing for twenty-four hours), 5.219 mg.: AgCl, 1.558 mg. Found: Cl, 5.39. Subs. (after standing for four days), 5.613, 5.388 mg.: AgCl, 1.176, 1.101 mg. Found: Cl, 5.18, 5.06. Subs. (after standing for five days), 3.843 mg.: AgCl, 0.796 mg. Subs. (after standing for twelve days), 6.932 mg.: CO_2, 14.419 mg.: H_2O, 2.937 mg. Subs. (after standing for fifteen days), 8.332 mg.: CO_2, 17.362 mg.: H_2O, 3.520 mg. Calcd. for $C_{32}H_{25}O_{12}Cl + 2H_2O$: Cl, 5.25; C, 57.1; H, 4.34. Found: Cl, 5.12; C, 56.73, 56.84; H, 4.74, 4.73.

In connection with these analyses it is noteworthy that true pyryllium compounds have constant chlorine content; thus, for example, 3,5,7,3′,4′-pentahydroxyflavylium chloride, prepared according to Pratt and Robinson,[10] remains constant after standing in a desiccator for many months.

Anal. Subs., 5.494 mg.: AgCl, 2.301 mg. Calcd. for $C_{15}H_{11}O_6Cl + H_2O$: Cl, 10.42. Found: Cl, 10.36.

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[10] Pratt and Robinson, *J. Chem. Soc.*, **127**, 172 (1925).

Xanthylene Ferrichlorides

Monoferrichloride (IX).—Into a suspension of 0.22 g. of xanthylene in 50 cc. of alcohol, gaseous hydrogen chloride was passed for fifteen hours at 0°. After standing overnight in the ice chest, the solution was filtered from the unchanged xanthylene (0.12 g.), and to the yellow solution a concentrated solution of ferric chloride in concentrated hydrochloric acid was added, until a cloudiness was produced, the solution being kept cool. The solution was diluted with concentrated hydrochloric acid, when, on standing, the ferrichloride separated in glittering, yellowish-brown scales which could not be recrystallized without decomposition, either from glacial acetic acid, benzene or alcohol. The product did not melt below 320°.

Anal. Subs., 4.549 mg.: CO_2, 9.199 mg.: H_2O, 1.317 mg. Subs., 6.650 mg.: AgCl, 6.879 mg. Calcd. for $C_{26}H_{17}O_2FeCl_4$: C, 55.81; H, 3.04; Cl, 25.40. Found: C, 55.15; H, 3.24; Cl, 25.66.

Diferrichloride (X).—To a suspension of 0.5 g. of xanthylene in 5 cc. of glacial acetic acid was added 5 cc. of glacial acetic acid saturated with chlorine. The reddish-brown solid formed was dissolved in 25 cc. of concentrated hydrochloric acid and to the red filtered solution was added a concentrated solution of ferric chloride in concentrated hydrochloric acid. The brick-red solid (0.4 g.) was crystallized from a large quantity of glacial acetic acid, brick-red, glittering prismatic needles which did not melt below 320°, being obtained.

Anal. Subs., 5.101, 4.388 mg.: CO_2, 7.802, 6.679 mg.: H_2O, 1.100, 0.895 mg. Subs., 8.085 mg.: AgCl, 12.236 mg. Calcd. for $C_{26}H_{16}O_2Fe_2Cl_8$: C, 41.27; H, 2.12; Cl, 37.57. Found: C, 41.71; 41.51; H, 2.41, 2.28; Cl, 37.44.

If, to a hot solution of 0.5 g. xanthylene in 250 cc. of glacial acetic acid, a concentrated solution of ferric chloride in concentrated hydrochloric acid was added, a deep red solution was produced instantaneously, deep red needles being deposited on standing. The product (0.7 g.) crystallized from a large quantity of glacial acetic acid in carmine-colored needles which did not melt at 320°. They proved to be a mixture of the mono- and diferrichlorides. This is in agreement with the results of Löwenbein,[11] who has shown that the hydrogen atom marked* in Formula (IX) is easily oxidized by ferric chloride in the pyryllium series. The production of a mixture consisting of (IX) and (X) is therefore evident.

Anal. Subs., 8.163, 5.244 mg.: CO_2, 13.098, 8.471 mg.: H_2O, 2.218, 1.403 mg. Subs., 3.528 mg.: AgCl, 4.867 mg. Calcd. for $C_{26}H_{17}O_2FeCl_4$; C, 55.81; H, 3.04; Cl, 25.40. Calcd. for $C_{26}H_{16}O_2Fe_2Cl_8$: C, 41.27; H, 2.12; Cl, 37.57. Found: C, 43.76, 44.06; H, 3.04, 2.99; Cl, 34.13.

In conclusion we wish to thank Miss C. M. Fear for all the analytical data recorded in this communication.

Summary

It is shown that the reduction of quercetin leads to a dimolecular reduction product, quercetylene chloride, instead of to cyanidin chloride, as stated in the literature; and that a similar reduction product, 7,7′-dimethylquercetylene chloride, is obtained from rhamnetin.

BRISTOL, ENGLAND

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[11] Löwenbein, *Ber.*, **57**, 1517 (1924).