The products of reaction were in general separated by fractional distillation through Widmer or modified Widmer columns carrying spirals 15 cm. in length.[39] Solid products were recrystallized. The products were characterized by analysis and by comparison of their physical constants with those reported in the literature or found for substances prepared by other methods. A considerable number of ethers were prepared by the Williamson synthesis in order that their properties might be compared with those of products of hydrogenation (Table IV).

The structure of a number of compounds was ascertained by oxidizing them to a benzoic or a substituted benzoic acid. For this purpose 1 to 2 g. of the compound was oxidized with potassium permanganate in the usual manner. Benzoic acid, m. p. 120–121°, was obtained from 1-phenyl-2-methoxycyclohexane, 1-phenyl-2-ethoxycyclohexane, 1-phenyl-3-ethoxycyclohexane, cetyl ether of 1-phenyl-2-hydroxycyclohexane and 1-phenyl-2-hydroxy-5-ethylcyclohexane. Phthalic anhydride, m. p. 129–131°, was obtained from 2-ethyl-1,2,3,4-tetrahydro-1-naphthol and 1-ethyl-1,2,3,4-tetrahydro-2-naphthol. *m*-Ethoxybenzoic acid,[40] m. p. 136–137°, was obtained from 1-cyclohexyl-3-methoxybenzene, *p*-ethoxybenzoic acid,[41] m. p. 195–196°, from *p*-cyclohexylphenetole, *o*-ethoxybenzoic acid,[41] m. p. 19–20°, from 1-cyclohexyl-2-ethoxybenzene and *o*-methoxybenzoic acid,[42] m. p. 98–100°, from 1-cyclohexyl-2-methoxybenzene.

Summary

The monohydroxynaphthalenes and diphenyls and their ethers have been submitted to partial hydrogenation over Raney nickel and copper–chromium oxide. Over Raney nickel hydrogenation takes place exclusively in the oxygenated ring of naphthol-2 and of 2- and 3-hydroxydiphenyl, while naphthol-1 and 4-hydroxydiphenyl accept hydrogen in both rings, but predominantly in the non-oxygenated ring. The ethers of naphthol-1, and of 3- and 4-hydroxydiphenyl over Raney nickel show a greater tendency to react in the non-oxygenated ring than do the phenols.

The phenols showed a much greater tendency to hydrogenate in the oxygenated ring over copper–chromium oxide. This fact coupled with the inactivity of the ethers toward hydrogen over copper–chromium oxide leads to the conclusion that with this catalyst the hydrogenation of the phenol in the oxygenated ring involves the tautomeric ketone.

While no effort has been made to prepare in high yields the completely hydrogenated alcohols and ethers corresponding to the five phenols referred to above, there is no doubt that they may be made in excellent yields by catalytic hydrogenation over Raney nickel, with the possible exception of those from naphthol-1 for which a yield of 34% is reported.

Tetralin has been made for the first time over copper–chromium oxide. This catalyst has the advantage in this case over Raney nickel that further hydrogenation does not occur at 200°. Tetralin may be made with Raney nickel at 100° or lower.

It has been shown that there is no great difference between the ease of hydrogenation of methyl, ethyl, dodecyl and cetyl aryl ethers.

MADISON, WISCONSIN RECEIVED NOVEMBER 29, 1937

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(29) Martha E. Smith and Adkins, THIS JOURNAL, **60**, 657 (1938).

(40) Fritsch, *Ann.*, **329**, 71 (1903).

(41) Cohen and Dudley, *J. Chem. Soc.*, **97**, 1737 (1910).

(42) Graebe, *Ann.*, **340**, 210 (1905).

[A COMMUNICATION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

Hydrogenation of Pyrones[1]

BY RALPH MOZINGO AND HOMER ADKINS

The chromones, flavonols and anthocyanidins offer an attractive field for studies in selective hydrogenation which may be of some value to synthetic organic chemistry. To that end the reaction of hydrogen with various pyrones has been investigated.

It has been observed many times in this Laboratory that rapid hydrogenations give better yields of the chief product and fewer products due to side or subsequent reactions. This matter becomes of decisive importance in the hydrogenation of compounds containing several functional groups. Impurities, inadequate amounts of catalyst, inactive catalysts, too low temperatures or pressures, or a poor choice of solvent may serve to prolong the period of reaction to such an extent that a hopeless mixture of products is obtained. On the other hand, too high a temperature may induce reactions which could otherwise be avoided. Most of the hydrogenations described in this paper were carried out at the lowest temperature at which a rapid hydrogena-

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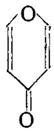
[1] This investigation was supported in part by a grant from the Wisconsin Alumni Research Foundation.

tion could be secured. Most of those which involved the possibility of two or more reactions were completed in less than half an hour, and several in less than ten minutes. The temperature range in which reaction was carried out is given in Table I. The lower figure represents beginning of a fairly rapid absorption of hydrogen while the higher figure represents the maximum value indicated by the potentiometer indicator and controller. In general the reactions were carried out near that temperature at which the drop in pressure of hydrogen, due to reaction, was just greater than the rise in pressure due to the heating of the steel vessel. The hydrogenations with one exception were carried out in a steel vessel having a volume of 270 ml. which contained the hydrogen acceptor dissolved in 50 to 120 ml. of dry ethanol. The apparatus and catalyst preparation have been recently described in detail.[2]

γ-Pyrone, I, reacts rapidly (fifteen minutes) with hydrogen over copper-chromium oxide at 120–125°. Both the alkene and the carbonyl linkages are hydrogenated so that a 50% yield of γ-hydroxytetrahydropyran, III, was isolated. There also was obtained a 23% yield of tetrahydropyrone, II. The yield of this ketone could undoubtedly be increased by stopping the hydrogenation after the absorption of two moles of hydrogen. For this purpose Raney nickel and a lower temperature would be preferable.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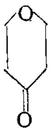
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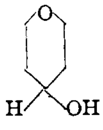
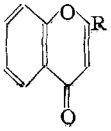

III

Such a benzopyrone as 2-ethylchromone (R is C_2H_5 in IV) may react with hydrogen in several different ways. The alkene linkage or the carbonyl linkage may be hydrogenated or both reactions may occur, hydrogenolysis may occur at the carbinyl, or at the ether linkage, and lastly the benzenoid nucleus may be hydrogenated, as indicated in formulas V to X, inclusive.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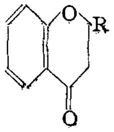
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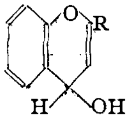
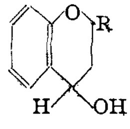
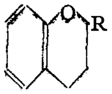

VI


VII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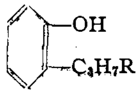
IX


X

All of these products have been obtained under various conditions, four of them in yields of 30 to 84%. Fortunately the two (VI and IX) which were not obtainable in good yields are the two which are probably most readily available by other means. The catalyst, the temperature and duration of reaction are the chief variables in a hydrogenation which, in addition to structure, determines the proportion of reaction products. The effects of such variations are shown by the data in Table I.

Ethylchromone reacted with hydrogen at 110–113° over copper-chromium oxide to give a mixture of 2-ethylchromanone, V, 2-ethylchromen-4-ol, VI, and 2-ethyl-4-hydroxychroman, VII. At a higher temperature only the latter was produced, the optimum temperature being 150–155°, where the yield was 84%, Winans similarly obtaining the 2-methyl-4-hydroxychroman, m. p. 87–88°, in 84% yield.[3]

The saturated ketone V is not produced in any considerable amount over copper-chromium oxide, since it is so readily converted to the alcohol. However, over Raney nickel at 120–130° it was isolated in a yield of 30%. A pure sample of the unsaturated alcohol VI could not be obtained since it distilled over with unreacted ethylchromone. These two compounds could not be separated by the most careful fractionation, even from 50 g. of the mixture. However, the alcohol was separated as a pyrylium chloride and as a chloroplatinate. The amount of the 2-ethylchromen-4-ol was estimated by a polarographic analysis[4] and by the use of the Grignard machine. These methods indicated that the fraction of b. p. 134–136° (2.5 mm.) contained about 30% of the alcohol, which corresponds to a yield of 4 to 7% from 2-ethylchromone.

When hydrogen reacted with 2-ethylchromone (or V, VI, or VII) at 165–175° over copper-chromium oxide for several hours, hydrogenolysis occurred with the formation of 2-ethylchroman, VIII, in excellent yields. This was the expected reaction, since VII is a substituted benzyl alcohol. Cleavage at the ether linkage also took place with

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(2) Adkins, "Reactions of Hydrogen," University of Wisconsin Press, Madison, 1937, pp. 11, 29; for references to THIS JOURNAL see **58**, 715 (1936).

(3) C. F. Winans, Ph.D. Thesis, University of Wisconsin, Madison, 1933.

(4) Borcherdt, Meloche and Adkins, THIS JOURNAL, **59**, 2171 (1937).

TABLE I

DATA ON HYDROGENATIONS

In dry ethanol under 100–200 atm. of hydrogen

Moles	Compound	Temp., °C.	Time, min.	G.	Catalyst	% yield of products
0.15	γ-Pyrone (3.3)[a]	120–125	15	2	CuCrO	50 γ-OH-Tetrahydropyran
						23 γ-Tetrahydropyrone
.10	2-Et-chromone (2.0)	150–155	40	2	CuCrO	84 2-Et-4-OH-chroman
.05	2-Et-chromone (1.6)	120–130	16	3	Ni(R)	30 2-Et-chromanone
						46 2-Et-4-OH-chroman
.15	2-Et-chromone (1.0)	140–150	92	2	CuCrO	29 2-Et-chromanone
						47 2-Et-chromone
						8 2-Et-4-OH-chroman
.30	2-Et-chromone (1.3)	110–113	5	5	CuCrO	15 2-Et-chromone
						16 2-Et-chromanone
						5 2-Et-chromen-4-ol
						29 2-Et-4-OH-chroman
.30	2-Et-chromone (1.1)	110–117	99	3	CuCrO	22 2-Et-chromone
						6 2-Et-chromen-4-ol
						37 2-Et-4-OH-chroman
.10	2-Et-chromone (2.0)	100–108	21	3	Ni(R)	77 2-Et-4-OH-chroman
.10	2-Et-chromone (3.4)	166–175	348	2	CuCrO	73 2-Et-chroman
						5 *o*-Amylphenol
.12	2-Et-chroman (3.1)	200	180	3	Ni(R)	92 2-Et-hexahydrochroman
.05	2-Me-3-Ph-7-OH-chromone (1.4)	120–125	22	2	CuCrO	30 Original substance
						60 Product (alcohol?)
.05	2-Me-3-Ph-7-OH-chromone (3.0)	131–138	24	2	CuCrO	67 2-Me-3-Ph-7-OH-chroman
.10	Flavone (1.6)	140–149	19	2	CuCrO	24 Flavone
						13 Flavonone
						.. Flaven-4-ol
						27 β-4-OH-Flavan
.10	Flavone	85	12	5	Ni(R)	52 Flavone
						20 β-4-OH-Flavan
.10	Flavone (1.7)	140–150	8	2	CuCrO	18 Flavone
						.. Flaven-4-ol
						21 β-4-OH-Flavan
.10	Flavanone (1.2)	135–145	3	2	CuCrO	85 β-4-OH-Flavan
.11	Flavanone (2.2)	145–155	380	2	CuCrO	53 *o*-OH-1,3-di-Ph-propane
						10 β-4-OH-Flavan
						24 Flavan
.40	Flavanone[b]	120–135	42	10	CuCrO	93 β-4-OH-Flavan
.10	Flavanone (2.2)	155–165	436	2	CuCrO	47 *o*-OH-1,3-di-Ph-propane
						34 Flavan
.09	β-4-OH-Flavan (1.0)	160–170	79	2	CuCrO	36 *o*-OH-1,3-di-Ph-propane
						26 Flavan
.06	Flavonol (0.7)	140–147	7	2	CuO	39 Flavonol
						17 3,4-di-OH-Flavan

[a] The figures in parentheses represent the moles of hydrogen absorbed per mole of compound. [b] The hydrogenation was carried out in a large bomb in 700 ml. of ethanol.

the formation of small quantities of *o*-amylphenol. The benzenoid nucleus in 2-ethylchroman was hydrogenated at 200° over Raney nickel to give in over 90% yield a product of b. p. 96–97° (18 mm.), of the hexahydrochroman or octahydrobenzopyran, X.

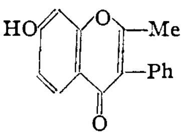
The proportion of products obtained in the hydrogenation of flavone (2-phenylchromone) differs considerably from that obtained from 2-ethylchromone. On account of the physical characteristics of the products, there was a greater mechanical loss in fractionation and the yields reported are considerably lower than would correspond to the amounts of the various compounds produced. The saturated ketone flavanone corresponding to formula V, where R is phenyl, was obtained in a maximum yield of only 13%, while the unsaturated alcohol flaven-4-ol was separated and estimated as in the case of the 2-ethyl-chromen-4-ol. The saturated alcohol β-4-hydroxyflavan VII was obtained in a maximum yield of 65% at 140–150° in a very rapid hydrogenation (eight minutes) over copper–chromium oxide.

The hydrogenation of flavanone V proceeded very smoothly. At 120–135° over copper–chromium oxide absorption almost stopped after forty-two minutes and a 93% yield of β-4-hydroxyflavan was obtained. However, when an attempt was made to push the reaction further at 145–165°, hydrogenolysis at the hydroxyl group was not the chief reaction. In no case was flavan VIII found in a greater yield than 34%. The chief product corresponding to IX was *o*-hydroxy-1,3-diphenylpropane, which was isolated in yields of about 50%. This latter yield could without question be increased by continued hydrogenation for the reaction was not allowed to go to completion. When β-4-hydroxyflavan VII was submitted to hydrogenolysis the phenol IX was also obtained in a higher yield than flavan VIII. Thus it is apparent that phenyl in the 2-position of a chromone labilizes the ether linkage toward hydrogenolysis to a greater extent than does ethyl.

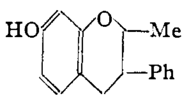
The oxygen in the ring of flavone and β-4-hydroxyflavan may be considered to be of the benzyl aryl ether type, *i. e.*, —C=C—O. . . . C—C=C—, and so should be hydrogenolyzed much more readily than the alkyl aryl ether type, *i. e.*, —C=C—O—C—C—C—, found in the corresponding ethylchromone.[5]

It is of interest that Karrer, Yen and Reichstein[6] obtained two geometrical isomers when they reduced flavone to β-4-hydroxyflavan with titanium trichloride. Catalytic hydrogenation over copper–chromium oxide as described above gave only the higher melting isomer in sufficient amount for identification.

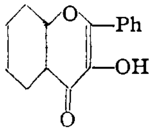
The 2-methyl-3-phenyl-7-hydroxychromone, XI, over copper–chromium oxide at 120–125° rapidly took up two moles of hydrogen per mole of compound reacting. The product was an oil which could not be purified and which did not give a solid 3,5-dinitrobenzoate. Whether the product was the saturated alcohol or a benzopyran could not therefore be ascertained. The alcohol which is the more likely compound might consist of four racemic mixtures so that it is not surprising that the product was an oil. Upon further action of hydrogen, however, the 2-methyl-3-phenyl-7-hydroxychroman, XII, was obtained.



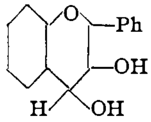
XI



XII



XIII



XIV

Flavonol or 3-hydroxyflavone, XIII, is so acidic that upon attempted hydrogenation over copper–chromium oxide the catalyst was deactivated rapidly and only 17% of the 3,4-dihydroxyflavan, XIV, was obtained. Presumably for a similar reason attempts to hydrogenate quercitin in dioxane over copper–chromium oxide or Raney nickel showed no reaction, even at 200°.

Preparation of Materials.—The methods used in the synthesis of substances to be hydrogenated were, with one exception, modifications in scale or detail of procedures previously described. All liquids were distilled over Raney nickel before being submitted to hydrogenation. The solids, except flavonol, were dissolved in the solvent for recrystallization, and heated with Raney nickel before they were allowed to recrystallize. These operations were of course for the removal of halogen-containing impurities.

Neither the method of Lowenbein[7] nor that of Feuerstein[8] and Kostanecki were found satisfactory for the preparation of pure flavone in good yields. Using Lowenbein's method in 5 to 8 times the quantities reported by him, yields from 70 to 80% were obtained based upon the flavanone, but the melting point of the product even after six to twelve recrystallizations was lower than we have found for pure flavone. The preferred method involved, as a first step, the condensation of ethyl benzoate with *o*-hydroxyacetophenone, under the influence of sodium ethoxide. This reaction has never hitherto been achieved. However, the discovery of Magnani[9] and McElvain that ethyl benzoate and acetophenone could be condensed if sodium ethoxide was added to the mixture of the ester and ketone at about 150°, made it possible to develop a new and excellent method for the preparation of flavone.

***o*-Hydroxydibenzoylmethane.**—In a one-liter 3-necked flask were placed 600 g. (4 mols) of ethyl benzoate and 68 g. (0.5 mol) of freshly distilled *o*-hydroxyacetophenone. The flask was fitted with a downward condenser and with an efficient sealed stirrer capable of agitating a viscous mixture. The flask was heated to 150–160° in an oil-bath; then 85 g. (1.25 mols) of fresh sodium ethoxide was added during twenty to thirty minutes. After a few additions of ethoxide, alcohol began to distil out of the reaction mixture and thereafter the evolution of alcohol

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(5) Van Duzee and Adkins, THIS JOURNAL, **57**, 147 (1935).

(6) Karrer, Yen and Reichstein, *Helv. Chim. Acta*, **13**, 1308 (1930).

(7) Lowenbein, *Ber.*, **57**, 1516 (1924).

(8) Feuerstein and Kostanecki, *ibid.*, **31**, 1758 (1898).

(9) Magnani, Ph.D. Thesis, University of Wisconsin, Madison, Wisconsin, 1937.

was quite vigorous after each addition of the ethoxide. The additions were made as soon as the alcohol evolution subsided. During the ethoxide addition, a gentle stream of air was kept passing through the flask by means of a water pump attached to the distillate receiver, so that the alcohol vapor was prevented from rising in the third arm of the flask and interfering with the ethoxide addition. The reaction mixture was stirred after the addition of the ethoxide until no more distillate (65–75 g.) came over.

The reaction mixture while stirring was continued was cooled to room temperature by running water. Then 300 ml. of water was added to the reaction mass, and the resulting aqueous and nonaqueous layers were transferred to a separatory funnel. One hundred twenty ml. of glacial acetic acid and 300 ml. of ether were then added and, after vigorous shaking, the organic layer was separated and washed with 200 ml. of water. The combined water layers were then shaken with 200-ml. portions of ether until the ether no longer became colored. The ether extracts were combined and most of the ether removed by distillation.

The remaining ether and excess ester were removed under reduced pressure. The recovered ester, b. p. 80–83° (8 mm.), amounted to 475–500 g. After the ester was removed, the temperature of the oil-bath was raised slowly to 130°. When no more distilled at this temperature, the remaining oil, while still warm, was poured into a flask and allowed to crystallize. This crude *o*-hydroxydibenzoylmethane was recrystallized twice by dissolving in ethyl alcohol and cooling to 0°. The yield of *o*-hydroxydibenzoylmethane was 68–85 g. (61–73%), melting point 119–120°. The acetyl derivative, prepared by the method of Müller,[10] melted at 118–118.5°.

Flavone.—Fifty grams of *o*-hydroxydibenzoylmethane in a solution of 10 ml. of sulfuric acid in 250 ml. of glacial acetic acid was heated on a steam-bath for one hour. The resulting solution was poured into 2 liters of water when the flavone separated as an oil which solidified on standing, The solid was filtered off, washed with water, and, after breaking up into small pieces, was air-dried. The dry product was transferred to a 2-liter flask and crystallized from petroleum ether (b. p. 100 to 140°). The resulting mother liquor was then concentrated to about 300 ml. and a second crop of crystals was obtained on cooling. The yield was 41–45 g. (89–97%) of a very slightly yellow product which melted at 97–98°. After recrystallizing twice more from petroleum ether (b. p. 100–140°) the product was pure white and melted at 99–100°.

***o*-Hydroxyacetophenone** was prepared by the method given for *o*- and *p*-propiophenol by Miller and Hartung.[11] The preparation was made on three times the scale used by them and the procedure for isolating the product modified as follows. The cold, partly solidified oil separating after acidification was diluted with benzene, and the water layer extracted with benzene. The benzene was removed by distillation. The residue was distilled at 17 mm. until the solid *p*-isomer began to collect in the condenser. The distillate was then fractionated through a Widmer column and the fraction boiling at 90–110° (17 mm.) saved. Upon refractionation there was obtained 370–440 g. (28 to 30% of theoretical) of pure product boiling at 105.5–106 (17 mm.) with $n^{25}\text{D}$ 1.5559.

Flavonol, m. p. 169–169.5°, (from *n*-butanol) was obtained in 37–46% yield by the method of Kostanecki and Szabranski.[12] The method was modified in that butyl nitrite instead of amyl nitrite was used and the quantity of alcohol was reduced to a liter for 45 g. of flavanone.

2-Ethylchromone was prepared by a development of the method described by Heilbron, Hey and Lowe.[13] Forty-eight grams of sodium was powdered under xylene in a 2-liter round-bottomed flask. The xylene was decanted, the flask surrounded by an ice-bath, fitted with a reflux condenser with a drying tube, and dropping funnel. To the well-cooled sodium was added *very* slowly a mixture of 120 g. of *o*-hydroxyacetophenone in 300 ml. of ethyl propionate. Great care must be taken that the reaction has started before any considerable quantity of the reactants are in the flask, otherwise the reaction goes with explosive violence. It may be necessary to allow the flask to warm up a little in order to permit the reaction to start. As the reaction *proceeds* the rate of addition of the reactants is increased so that all of the reactants may be added in one or two hours. As soon as the vigorous reaction had subsided the ice-bath was removed and the mixture heated on a steam-bath for an hour or so until the sodium had disappeared. The reaction mixture was then poured with stirring on 600 g. of ice, to which was later added 190 ml. of acetic acid and 700 ml. of water. The oily layer was separated and the water extracted three times with ether. After the distillation of the ether 20 ml. of concd. hydrochloric acid and 20 ml. of acetic acid were added to the residue, and the mixture heated for one-half to one hour. The mixture was fractionated through a Widmer column; all material boiling below 80° (7 mm.) was discarded. Most of the unreacted *o*-hydroxyacetophenone came off between 80 and 88° (7 mm.). The crude ethylchromone was then distilled at 2 mm. Upon refractionation through a Widmer column there was obtained 26–30 g. of *o*-hydroxyacetophenone, 86–88° (7 mm.) and 68–77 g. of ethylchromone, 124–126° (2 mm.), m. p. 20–20.5°, $n^{25}\text{D}$ 1.5832.

Flavanone, m. p. 76–77° (from methanol and then from petroleum ether), was prepared in 63% yield from 136 g. of *o*-hydroxyacetophenone and 107 g. of benzaldehyde[14] without isolating the intermediate *o*-hydroxybenzalacetophenone, as in the original method.[7]

γ-Pyrone, m. p. 31–32°, b. p. 101–102 (17 mm.), was obtained in 61–73% yields from crude chelidonic acid,[15] according to the method of Willstätter and Pummerer.[16]

2,4-Dihydroxyphenyl benzyl ketone was prepared by the method of Chapman and Stephen[17] using 10 to 20 times the amounts given in their procedure. Instead of extracting the imino hydrochloride with dilute hydrochloric acid, the ether was distilled and the crude hydrochloride hydrolyzed and recrystallized from dilute alcohol.

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(10) Müller, *J. Chem. Soc.*, **107**, 875 (1915).

(11) Miller and Hartung, "Organic Syntheses," Vol. XIII, John Wiley and Sons, Inc., New York, 1933, p. 90.

(12) Kostanecki and Szabranski, *Ber.*, **37**, 2819 (1904).

(13) Heilbron, Hey and Lowe, *J. Chem. Soc.*, 1312 (1934).

(14) "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, 1932, p. 71.

(15) "Organic Syntheses," Vol. XVII, John Wiley and Sons, Inc., New York, 1937, p. 40.

(16) Willstätter and Pummerer, *Ber.*, **37**, 3745 (1904).

(17) Chapman and Stephen, *J. Chem. Soc.*, **123**, 406 (1923).

TABLE II

ANALYTICAL DATA

Compound	Formula	Carbon, %			Hydrogen, %		
		Calcd.	Found		Calcd.	Found	
2-Ethyl-4-hydroxychroman	$C_{11}H_{14}O_2$	74.16	74.20	74.24	7.86	7.86	7,77
2-Methyl-4-hydroxychroman	$C_{10}H_{12}O_2$	73.17	73.30		7.32	7.33	
2-Ethyl-4-(3,5-dinitrobenzoxy)-chroman	$C_{16}H_{16}N_2O_7$	58.08	58.27	58.26	4.28	4.42	4.40
2-Ethylchromanone	$C_{11}H_{12}O_2$	75.00	74.82	74.89	6.82	6.96	6.90
2-Ethylchroman	$C_{11}H_{14}O$	81,41	81.16	81.28	8.64	8.65	8.74
2-Methyl-3-phenyl-7-hydroxychroman	$C_{16}H_{16}O_2$	80.00	80.03	80.12	6.67	6.70	6.75
2-Methyl-3-phenyl-7-(3,5-dinitrobenzoxy)-chroman	$C_{23}H_{18}N_2O_7$	63.59	63.37		4.15	3.98	
γ-Hydroxytetrahydropyran	$C_5H_{10}O_2$	58.82	58.76	58.89	9.80	9.75	9.91
3,4-Dihydroxyflavan	$C_{15}H_{14}O_3$	74.38	74.36	74.23	5.79	5.97	5.90
2-Ethylhexahydrochroman	$C_{11}H_{20}O$	78.57	78.51		11.90	12.33	
o-(3,5-Dinitrobenzoxy)-1,3-diphenylpropane	$C_{22}H_{16}N_2O_6$	N (calcd.)	6.90		(found)	6.93	6.91
2-Ethyl benzopyrylium chloroplatinate	$C_{22}H_{24}PtCl_8 \cdot 2H_2O$	Pt (calcd.)	24.4		(found)	24.3	24.4
Flavylium chloroplatinate	$C_{30}H_{24}PtCl_8 \cdot 2H_2O$	Pt (calcd.)	21.8		(found)	21.6	21.5

2-Methyl-3-phenyl-7-hydroxychromone, m. p. 242–243°, was obtained in 90% yield by the method of Baker and Robinson.[18]

Quercitin, m. p. 313–314° (uncorr.), was obtained (104 g.) from the dried scales of red onions (8.5 kg.) by a modification of the method of Perkin and Hummel.[19] The preparation of quercitin was carried out under the direction of Karl Paul Link in his Laboratory.

Separation and Characterization of Products.—The products of hydrogenation were in general separated by fractional distillation with the type of equipment and method recently described.[20] The modified Widmer column used had a helix 25 cm. in length with 0.5 turn per cm. The Widmer had a spiral 15 cm. in length with one turn of the helix per cm. Solids from fractional distillation or those which could not be distilled were recrystallized. Analytical data for compounds not hitherto prepared are given in Table II.

From 2-Ethylchromone.—The fractions from the hydrogenation of 2-ethylchromone were characterized in the following manner. The fraction which boiled at 137–139° at 3 mm. (94–96° at 0.3 mm.) solidified on cooling. On recrystallizing from petroleum ether (b. p. 60–68°), long white feathery needles, m. p. 78–79°, resulted. The 2-ethyl-4-hydroxychroman thus obtained gave one mole of methane per mole of compound when treated with methylmagnesium iodide in the Grignard machine.[21] The 3,5-dinitrobenzoate, m. p. 141–142° (from ethanol), was obtained on heating for fifteen minutes with 3,5-dinitrobenzoyl chloride in pyridine. The fractions boiling at 128–133° (26 mm.) were refractionated and gave a product boiling at 130–131° (26 mm.); $n^{25}\mathrm{D}$ 1.5236. This fraction gave only a small amount of methane with methylmagnesium iodide, indicating that there was no free hydroxyl. It failed to give a 3,5-dinitrobenzoate; analysis showed only one oxygen, it did not react with the 2,4-dinitrophenylhydrazine reagent and it is 2-ethylchroman.

o-Amylphenol has been prepared previously as having a boiling point of 122–124° (10 mm.).[22] The compound was obtained from the higher boiling intermediate fraction (131–135° at 26 mm.) from 2-ethylchromone. The total quantity was estimated, by use of the Grignard machine, after the first distillation of the product. Because of the small quantity it was identified as the aryloxy acetic acid, m. p. 76–77°.

2-Ethylchromanone, b. p. 115–116° (2 mm.), $n^{25}\mathrm{D}$ 1.5440, gave a 3,5-dinitrobenzoate melting at 221–222°.

The fraction from 2-ethylchromone which distilled over at 134–136° (2.5 mm.) contained in addition to unreacted 2-ethylchromone a certain amount of 2-ethyl-chromen-4-ol. The mixture reacted with methylmagnesium iodide in the Grignard machine to give an amount of methane corresponding to 29% of the alcohol. Polarographic analysis indicated that the mixture from this same sample contained 68% of 2-ethylchromone,[23] or 32% of the unsaturated alcohol. On treatment of the mixture of the ketone and alcohol with dry hydrogen chloride, a hygroscopic hydrochloride separated. The hydrochloride was not stable in air and gave no definite melting point. However, in water–alcohol solution it gave a chloroplatinate, m. p. 165–166° which was analyzed after being washed with acetone and dry ether.

From Flavone.—The products from the hydrogenation of flavone were separated and characterized as follows. The reaction product was crystallized fractionally from dioxane and water to obtain β-hydroxyflavan. The resulting mixture was then distilled to remove the flavanone, and the residue, which consisted largely of unchanged flavone, was recrystallized from petroleum ether (b. p. 100–140°). From the petroleum ether in this crystallization, a small amount of material came out as an oil on evaporation. This gave a dark red hydrochloride with dry hydrogen chloride in ether. Flavone was identified by melting point and mixed melting point of 99–100°. The 2,4-dinitrophenylhydrazone was prepared and melted at 282–283°. Flavanone was identified as the 2,4-dinitrophenylhydrazone, m. p. 254–255°. β-4-Hydroxyflavan has been prepared previously by Karrer, Yen and Reichstein. It was identified by comparison of its melting point, 147–148°, and that of its acetyl derivative, β-4-acetoxyflavan, 98–99°, with those of Karrer, Yen and Reichstein,[6] 148–149° and 97–98°, respectively. Flavan separated by

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(18) Baker and Robinson, *J. Chem. Soc.*, 2349 (1925).

(19) Perkin and Hummel, *ibid.*, **69**, 1296 (1896); Kostanecki, Lampe and Tambor, *Ber.*, **37**, 1405 (1904).

(20) Martha E. Smith and Adkins, THIS JOURNAL, **60**, 657 (1938).

(21) Kohler and Richtmyer, *ibid.*, **52**, 3736 (1930).

(22) Sandulesco and Girard, *Bull. soc. chim.*, [4] **47**, 1312 (1930).

(23) R. H. Baker, unpublished results.

TABLE III

2,4-DINITROPHENYLHYDRAZONES

2,4-Dinitrophenyl-hydrazone of	M. p., °C.	Color	Recryst. from	Carbon, %				Hydrogen, %			
				Calcd.	Found			Calcd.	Found		
Flavone[a]	282–283	Dark red	Dioxane	62.68	62.66	62.66		3.48	3.61	3.40	
Flavanone	254–255	Scarlet	Butanol-1	62.38	62.59	62.30		3.96	4.06	3.97	
2-Ethylchromone	249–250	Dark red	Dioxane	57.63	57.45	57.63	57.54	3.96	3.94	3.91	4.00
2-Ethyl-chromanone	221–222	Scarlet	(Dioxane alcohol)	57.30	57.36	57.27		4.50	4.67	4.59	

[a] % Nitrogen: calcd. 13.93; found 14.02.

fractional distillation, and was identified by the melting point, 44–44.5°, compared to 44–45° from the literature.[24]

Flaven-4-ol was characterized by conversion of the rather unstable red chloride (flavylium chloride) into the chloroplatinate which melted at 199–200° after being washed with acetone and dry ether. A 3,5-dinitrobenzoate could not be obtained.

o-Hydroxy-1,3-diphenylpropane,[25] b. p. 133–135 (0.3 mm.), $n^{25}\text{D}$ 1.5786, was treated with 3,5-dinitrobenzoyl chloride in pyridine to give an ester, m. p. 143–143.5°.

From Other Hydrogenations.—2-Methyl-3-phenyl-7-hydroxychroman, b. p. 172–174° (0.3 mm.), was soluble in alkali, gave one mole of methane in the Grignard machine and gave a 3,5-dinitrobenzoate, m. p. 169–170°, from *n*-butanol.

3,4-Dihydroxyflavan, m. p. 123–124° from dioxane and water, gave two moles of methane in the Grignard machine.

γ-Hydroxytetrahydropyran, b. p. 119–120° (23 mm.), gave one mole of methane in the Grignard machine and a 3,5-dinitrobenzoate, m. p. 98–99°.

Tetrahydro-γ-pyrone, b. p. 94–98° (23 mm.), gave with benzaldehyde a β,β′-dibenzal-tetrahydro-γ-pyrone,[26] m. p. 184–185°.

2,4-Dinitrophenylhydrazones of the Chromones.—Oximes and phenylhydrazones of the chromones and flavones have never been reported.[27] However, since the carbonyl group reacts with a Grignard reagent,[28] and as shown above is hydrogenated as readily as in other ketones, an attempt was made to prepare such hydrazones by the method of Brady.[29]

The 2,4-dinitrophenylhydrazones of flavone, flavanone, 2-ethylchromone and 2-ethylchromanone were prepared and have the properties and analyses shown in Table III. In all cases 20 ml. of a fresh solution of 1 g. of 2,4-dinitrophenylhydrazine in 2 ml. of concentrated sulfuric acid and 15 ml. of 95% alcohol and about 0.005 mole of the sample were mixed and heated to boiling and allowed to stand in a stoppered flask for twenty-four to seventy-two hours, after which time no more precipitate formed. The solution was diluted, if necessary, with a one molar solution of sulfuric acid in water and the precipitate washed with the dilute acid.

It was possible, but not probable, that the oxygen containing ring had opened during the preparation of the hydrazone. To test this possibility the 2,4-dinitrophenylhydrazine derivative of *o*-hydroxydibenzoylmethane was prepared and compared with the derivative of flavone. The latter melted at 282–283°, while the former had a m. p. of 119–120°.

Summary

γ-Pyrone, 2-ethylchromone, 2-ethylchroman, 2-methyl-3-phenyl-7-hydroxychromone, flavone, flavanone, β-4-hydroxyflavan, flavonol, and quercitin have been submitted to the action of hydrogen over copper–chromium oxide and (or) Raney nickel catalysts. With the exception of quercitin all of these compounds were hydrogenated to various products depending upon the catalyst, temperature and duration of reaction. The relationship of these variables to the yield and character of the products has been summarized in Table I and in the discussion.

A new synthesis for flavone, involving *o*-hydroxydibenzoylmethane, has been described, which gives better yields of a higher melting product than has hitherto been reported. Phenylhydrazones of chromones have been prepared for the first time.

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