equilibrated with alkali and then chromatographed on alumina and had a specific activity of 410 mC/mmole.

7-Ketocholesterol from cholesterol acetate-7α-H³. Cholesterol acetate-7α-H³ was oxidized with *tert*-butyl chromate[10] and the crude 7-ketocholesterol acetate obtained was directly hydrolyzed by heating under reflux for 1 hr. in 1% methanolic potassium hydroxide solution. After the usual workup of the hydrolyzate, the product was chromatographed on silica gel and the pure material, obtained from the ethyl acetate-benzene eluates and recrystallized from methanol, had a specific activity of 70 mC/mmole.

Cholesterol-7α-D from 7α-bromocholesterol acetate. This reduction was carried out as described above, except that the palladium-on-calcium carbonate was prereduced with carrier free deuterium and that carrier free deuterium was used for the reduction proper. The deutero compound had two absorption bands in the C-D stretching region at 2155 and 2130 cm.$^{-1}$

3β-Hydroxypregn-5-en-20-one-7α-H³ from 3β-acetoxy-7α-bromopregn-5-en-20-one. The 3β-acetoxy-7α-bromopregn-5-en-20-one was prepared as indicated by Antonucci *et al.*[14] and the bromo compound was then reduced with a tritium-hydrogen mixture containing 0.5 C/mmole as described for the 7α-bromocholesterol acetate. The crude reaction product was hydrolyzed, worked up in the usual manner and finally chromatographed on silica gel. The pure pregnenolone had a specific activity of 325 mC/mmole.

3β,17β-Dihydroxypregn-5-en-20-one-7α-H³ from 3β, 17α-dihydroxypregn-5-en-20-one 3β-acetate. The bromination with *N*-bromosuccinimide followed by the reduction with tritium was carried out as described above. In this case the specific radioactivity amounted to 135% of the calculated amount.

3β-Hydroxyandrost-5-en-17-one-7α-H³ from 3β-acetoxy-7α-bromoandrost-5-en-17-one. This preparation had already been described.[6]

SHREWSBURY, MASS.

(14) R. Antonucci, S. Bernstein, D. Giancola, and K. J. Sax, *J. Org. Chem.*, 16, 1126 (1951).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, FACULTY OF SCIENCE, CAIRO UNIVERSITY, AND THE LABORATORIES OF THE MEMPHIS CHEMICAL COMPANY, CAIRO]

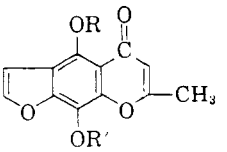
Experiments with Furochromones. A Color Test for Hydroxyfurochromones and Related Substances with Uranyl Acetate

AHMED MUSTAFA, NICOLAS A. STARKOVSKY, AND (MISS) EKRAM ZAKI

Received August 18, 1959

Syntheses for 8-(ω)-carboxymethoxy)-5-methoxy- (Ik) and 5-(ω-carboxymethoxy)-2-methylfuro-4′,5′,6,7-chromone (IId) are described. Whereas oxidation of IId with chromic acid effects the destruction of the furan ring with the formation of 5-(ω-carboxymethoxy)-6-formyl-7-hydroxy-2-methylchromone (IIIb), controlled oxidation with hydrogen peroxide in alkaline medium gives the corresponding furanosalicylic acid (Vc). The furanosalicylic acids Va–b and Vd are similarly obtained. Alkaline hydrolysis of Ik and IId results in the formation of the corresponding benzofuran derivatives (IVa–b) respectively. Hydroxyfurochromones and related substances (*cf.* Table I) give a color reaction with uranyl acetate solution. The importance of the free hydroxyl group in the *peri*- position to the carbonyl group is stressed (*cf.* Table II).

The recent publication of the preparation of a number of active water soluble derivatives of 2-methyl-5-hydroxy-8-methoxy-6,7-furochromone by the introduction of solubilizing groups, e.g., amino-,[1] or carboxyl group[2] prompts us to report some related work which we carried out some time ago.



Ia. R = R′ = CH_3
b. R = CH_2COOH; R′ = CH_3
c. R = H; R′ = CH_3
d. R = $CH_2COOC_2H_5$; R′ = CH_3
e. R = R′ = H
f. R = R′ = $CH_2COOC_2H_5$
g. R = R′ = CH_2COOH
h. R = H; R′ = CH_2COOH
i. R = H; R′ = $CH_2COOC_2H_5$
j. R = CH_3; R′ = $CH_2COOC_2H_5$
k. R = CH_3; R′ = CH_2COOH
l. R(R′) = $CH_2COOC_2H_5$; R′(R) = CH_2COOH.

(1) J. P. Fourneau, *Ann. Pharm. Franç.*, 11, 685 (1953).
(2) C. Musante and S. Fattuta, *Ann. Chim.* (Rome), 45, 918 (1955); L. Ritter and H. Kunsch, German Patent, 952,899, Nov. 22, 1956; *Chem. Abstr.*, 53, 2258 (1959).

The synthesis of 5-(ω-carboxymethoxy)-8-methoxy-2-methylfuro-4′,5′,6,7-chromone (Ib) by Mukerjee and Seshadri[3] now has been confirmed in our laboratories. The isomeric khellin derivative, namely, 8-(ω-carboxymethoxy)-5-methoxy-2-methylfuro-4′,5′,6,7-chromone (Ik) is now, similarly, prepared by allowing khellin-hydroquinone (Ie) to react with ethyl chloroacetate to yield Ii which, upon hydrolysis, produces Ik in an overall yield *ca.* 50% based on Ia used.

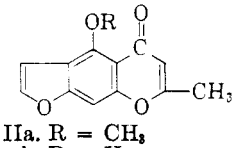
Refluxing 5,8-di(ω-carboxymethoxy)-2-methylfuro-4′,5′,6,7-chromone (Ig)[4] with 20% hydrochloric acid and/or 60% hydrobromic acid[5] does not accomplish the preparation of 8-(ω-carboxy-

(3) S. K. Mukerjee and T. R. Seshadri, *Proc. Indian Acad. Sci.*, 35A, 323 (1952).
(4) A. Schönberg and A. Sina, *J. Am. Chem. Soc.*, 72, 3396 (1950).
(5) These are common reagents to effect selective demethylation of chromones in position 5, without causing an undesired rearrangement (*cf.* H. Abu-Shady and T. O. Soine, *J. Am. Pharm. Assoc.*, 41, 325 (1952); S. K. Mukerjee and T. R. Seshadri (ref. 3).

methoxy) - 5 - hydroxy - 2 - methyl - furo - 4′,5′,6,7-chromone (Ih). This may be attributed to the lower solubility of (Ig).

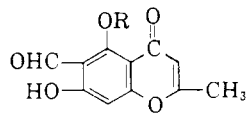
The stability of Ig toward these reagents is in contrast to the facile selective demethylation of Ia in position 5 by the same reagents, as well as by a number of other reagents.[6]

Similarly, 5-(ω-carboxymethoxy)-2-methylfuro-4′,5′,6,7-chromone (IId) has been prepared by allowing 5-norvisnagin (IIb), readily obtained by demethylation of the natural analog of Ia, namely, visnagin (IIa), to react with ethylchloroacetate, followed by hydrolysis of the intermediate ester (IIc).



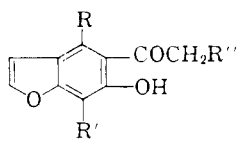
IIa. R = CH_3
b. R = H
c. R = $CH_2COOC_2H_5$
d. R = CH_2COOH

We now have found that when IId is treated with chromic acid, under the same experimental conditions described for the oxidation of IIa,[7] destruction of the furan ring and formation of 5-(ω-carboxymethoxy) - 6 - formyl - 7 - hydroxy - 2 - methylchromone (IIIb) takes place.

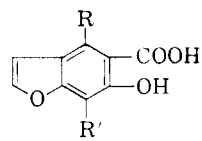


IIIa. R = CH_3
b. R = CH_2COOH

Recently, it has been shown that by controlled oxidation of Ia and IIa with hydrogen peroxide in alkaline medium[7] that 6-hydroxy-4,7-dimethoxybenzofuran-5-carboxylic acid (Ve) and 6-hydroxy-4-methoxybenzofuran-5-carboxylic acid (Vf) are obtained respectively. The furanosalicylic acid derivatives (Va–d) are now obtained, in a similar manner, by the controlled oxidation of Ig, Ik, IId, and Ib respectively.



IV

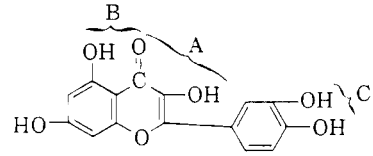


V

IVa. R = OCH_3; R′ = OCH_2COOH; R″ = H
b. R = OCH_2COOH; R′ = H; R″ = H
c. R = R′ = OCH_3; R″ = H
d. R = OCH_3; R′ = R″ = H
e. R = R′ = OCH_3; R″ = $COCH_3$
f. R = OCH_3; R′ = H; R″ = $COCH_3$
g. R = OCH_3; R′ = Br; R″ = H
Va. R = R′ = OCH_2COOH
b. R = OCH_3; R′ = OCH_2COOH
c. R = OCH_2COOH; R′ = H
d. R = OCH_2COOH; R′ = OCH_3
e. R = R′ = OCH_3
f. R = OCH_3; R′ = H

While the alkaline hydrolysis of Ia and IIa to khellinone (IVc) and visnaginone (IVd) respectively are already known,[8] the hydrolysis of the furochromones described in this paper has not been investigated. Thus, when Ik and IId are subjected to alkaline hydrolysis, the corresponding benzofuran derivatives (IVa–b) are obtained respectively.

Color Test. Color tests have been occasionally described for hydroxyflavones having a hydroxyl group in the *α-* or *peri*-position to the carbonyl group.[9,10] Their chelating ability has recently been studied by Hörhammer and Hänsel (*cf.* VI).[11,12]



VI

With a view to finding a color reaction for the naturally occurring hydroxyfurochromones[13] and hydroxychromones,[14] having a free hydroxyl group in the position *peri* to the carbonyl group,[15] we now have undertaken the study of the behavior of a number of these compounds toward uranyl acetate solution. Thus, when 2 ml. of a 0.05% ethyl alcohol solution (ethyl alcohol for spectroscopic measurement) of the chromone derivative was treated with 1 ml. of 0.1% aqueous uranyl acetate solution, a

(6) A. Schönberg and G. Aziz, *J. Am. Chem. Soc.*, **75**, 3265 (1953); W. Asker, A. F. A. M. Shalaby, and S. M. A. D. Zayed, *J. Org. Chem.*, **23**, 1781 (1958); N. A. Starkovsky, *Egyptian J. Chem.* **2**, 111 (1959).

(7) A. Schönberg, N. Badran, and N. A. Starkowsky, *J. Am. Chem. Soc.*, **75**, 4992 (1953).

(8) P. Fantl and S. I. Salem, *Biochem. Zeit*, **226**, 166 (1930); E. Späth and W. Gruber, *Ber.*, **74**, 1492 (1941).

(9) K. Tauböck, *Naturwissenschaften*, **30**, 439 (1942).

(10) C. W. Wilson, *J. Am. Chem. Soc.*, **61**, 2303 (1939).

(11) L. Hörhammer and R. Hänsel, *Arch. Pharm.*, **285**, 438 (1952); **286**, 425 (1953).

(12) L. Hörhammer, R. Hänsel, and W. Hieber, *Naturwissenschaften*, **41**, 529 (1954).

(13) Khellin (Ia) gives a intense red-violet color with potassium or sodium hydroxide pellets in the presence of little water (*cf.* Abd El-Rahman, masters' thesis, Fouad I University, Cairo (1943); I. Fahmy, N. Badran, and M. Messeid, *J. Pharm. Pharmacol.*, I, 529, 535 (1949). The application of this test for a colorimetric estimation of khellin (G. Anrep, M. Kenawy, G. Barsoum, and I. Fahmy, *Gazz. Fac. Med.*, Cairo, **14**, 1 (1947)) has been questioned (*cf.* A. Schönberg and A. Sina, *J. Chem. Soc.*, 3344 (1950)).

(14) The color test for 2-methylchromones with *m*-dinitrobenzene in the presence of dilute alkali has been reported to be inconclusive in the case of 2-methylchromones containing a free phenolic group [A. Schönberg and M. M. Sidky, *J. Org. Chem.*, **21**, 476 (1956)]. This may result because many of these chromones dissolve in alkali with a reddish-brown color [*Cf.* A. Schönberg and A. Sina, *J. Chem. Soc.*, 3344 (1950)].

(15) The possibility of chelation in furochromones, having a free hydroxyl group in position *peri* to the carbonyl group, *e.g.*, 5-norkhellin (VIIa), has recently been discussed (*cf.* A. Schönberg and G. Aziz, *J. Am. Chem. Soc.*, **75**, 3265 (1953)).

color developed, followed by the separation of an insoluble metal salt complex, upon dilution with water in some cases (cf. Table I). The limit for the detection of norvisviagin (IIb), taken as an example, with urnayl acetate solution is 5γ/ml., and the limit for the detection of uranium in uranyl acetate solution with IIb reagent is 5.6γ/ml. The color formed is readily destroyed on addition of mineral acids and even with an excess of dilute acetic acid solution, as well as with alkaline buffers (*p*H 9 and above) and with aqueous sodium hydroxide solution (4%), with the formation of the yellow sodium salt. Hydroxyfurochromones and hydroxychromones, listed in Table I, give no color with boric-citric or boric-oxalic acids reagents.[9,10]

TABLE I

COMPOUNDS GIVING A POSITIVE TEST[a]

Compound	Color
5-Norkhellin (VIIa)[d]	Red, green, violet-brown[b]
5-Norvisnagin (VIIb)[e]	Red, green, scarlet-red[b]
8-(Carbethoxymethoxy)-5-hydroxy-2-methylfuro-4′,5′,6,7-chromone (VIIc)	Red, green, orange-red[b]
5-Norkhellol (VIId)[f]	Red, green, deep-red
8-(*N*,*N*-Diethylaminoethoxy)-5-hydroxy-2-methylfuro-4′,5′,6,7-chromone (VIIe)[g]	Red, green
5,8-Dinorkhellin (VIIf)[h]	Violet-red, green changing immediately to red-brown, brown
5,6-Di-nor-isokhellin (VIII)[i]	Deep wine-red, green, violet-brown
6-Formyl-5-hydroxy-7-methoxy-2-methylchromone (IXc)	Bulky yellow precipitate, wine-red, yellow
6-Formyl-5,7-dihydroxy-2-methylchromone (IXe)[j]	Yellow precipitate, wine-red, yellow
Eugenitin (IXg)[j]	Red, deep violet-black, deep orange
7-Nor-eugenitin (IXh)[j]	Red, deep violet-black, buff-brown
5,6,7-Trihydroxy-2-methylchromone (IXa)[k]	Wine-red, brown, pale-brown
5,6,7-Trihydroxyflavone (IXb)[l]	Red-brown, brownish black, brown
6,7-Dihydroxy-5-methoxy-2-methylchromone (IXo)[m]	Brick-red, deep green, orange-brown
6,7-Dihydroxy-5-methoxyflavone (IXp)[n]	Red-brown, deep green, red
o-Hydroxyacetophenone	Yellow, violet
2-Hydroxy-4-methoxyacetophenone	Yellow, red-violet
ω-Acetokhellinone (IVe)	Yellow, red
ω-Acetovisnaginone (IVf)	Yellow, red
Khellinone (IVc)[o]	Orange, green
Visnaginone (IVd)[o]	Yellow, green
7-Bromovisnaginone (IVg)	Brownish-yellow, green

The importance of the free hydroxyl group in the position *peri* to the carbonyl group is stressed, as hydroxychromones with protected hydroxyl groups in the *peri* position give no color (*cf.* Table II). Morover, although the two isomeric chromones, 6-formyl-5-hydroxy-7-methoxy- (IXc) and 6-formyl-5-methoxy-7-hydroxy-2-methylchromone (IXd), give a wine-red color with ferric chloride, only IXc gives a bulky yellow precipitate with uranyl acetate solution.

TABLE II

COMPOUNDS GIVING A NEGATIVE TEST[c]

Compound	Color
6-Formyl-5-methoxy-7-hydroxy-2-methylchromone (IXd)[j]	Wine-red
6-Formyl-7-hydroxy-5-methoxy-8-nitro-2-methylchromone (IXi)[j]	Orange
6-Formyl-7-hydroxy-5-methoxy-2-hydroxymethylchromone (IXj)[m]	Wine-red
6-Formyl-7-hydroxy-5-(ω-carboxy-methoxy)-2-methylchromone (IXk)	Wine-red
6-Formyl-7-hydroxy-5-methoxyflavone (IXl)[n]	Red
6-Formyl-7-hydroxy-5-methoxy-8-bromo-2-methylchromone (IXm)[m]	Wine-red
6-Hydroxy-5,7-dimethoxy-2-methylchromone (IXn)[p]	Pale-brown developed gradually

[a] The colors given refer to the color developed with uranyl acetate, ferric chloride solution, and the color of the precipitate formed after dilution of the reaction mixture of uranyl acetate and the chromone derivative with water, respectively. [b] The precipitate is readily extractable with chloroform to give deep-red solution. [c] The given color refers to the color developed with aqueous ferric chloride solution. [d] See ref. 3, 5, 6. [e] A. Schönberg and N. Badran, *J. Am. Chem. Soc.*, **73**, 2960 (1951). [f] See ref. 6. [g] See ref. 1. [h] V. V. S. Murti and T. R. Seshadri, *Proc. Indian Acad. Sci.*, **30A**, 107 (1949). [i] J. R. Clarke and A. Robertson, *J. Chem. Soc.*, 302 (1949). [j] See ref. 7. [k] S. K. Mukerjee and T. R. Seshadri, *J. Sci. Ind. Research (India)*, **13B**, 400 (1954); D. K. Charkravorty, S. K. Mukerjee, V. V. S. Murti, and T. R. Seshadri, *Proc. Indian Acad. Sci.*, **35A**, 34 (1952). [l] See ref. 18. [m] A. Schönberg, N. Badran, and N. A. Starkowsky, *J. Am. Chem. Soc.*, **77**, 1019 (1955). [n] A. Schönberg, N. Badran, and N. A. Starkowsky, *J. Am. Chem. Soc.*, **77**, 5390 (1955). [o] See ref. 8. [p] See ref. 17.

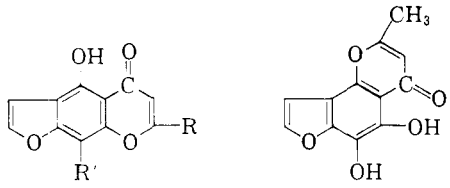
5,6,7-Trihydroxy-2-methylchromone (IXa) and 5,6,7-trihydroxyflavone (IXb), similar to IXe and IXf, have two chelate forming groups in the molecule and can form complexes with uranyl acetate. In contrast to the behavior of IXd and IXl, which give no color, red precipitates are formed in the case of IXo–p (without free hydroxyl groups in the *peri* position) with the same reagent, showing that the hydroxyl groups in positions 6 and 7 are capable of forming chelates,[16] as IXn gives no color.

o-Hydroxyacetophenone and IVc–g are ring-opened analogs of the 5-hydroxychromones and have the same chelating structure. Thus, a yellow

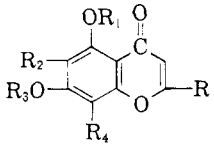
(16) *Cf.* The unability of polyhydroxyflavanols, *e.g.* Vl, to form chelates by group C (ref. 12).

color developed when their cold solutions were treated with uranyl acetate solution (*cf.* Table I). Acetophenone gives no color with the same reagent.

The application of the color development for a colorometric estimation of hydroxyfurochromones (VIIa–c) and the spectrophotometrical study of the chloroform-soluble complex formation of these chromones with uranyl acetate is under investigation. This color test is of value for structural study.



VIIa. R = CH_3; R′ = OCH_3
b. R = CH_3; R′ = H
c. R = CH_3; R′ = $OCH_2COOC_2H_5$
d. R = CH_2OH; R′ = H
e. R = CH_3; R′ = $OCH_2CH_2N(C_6H_5)_2$
f. R = CH_3; R′ = OH



IXa. R = CH_3; R_1 = R_3 = R_4 = H; R_2 = OH
b. R = C_6H_5; R_1 = R_3 = R_4 = H; R_2 = OH
c. R = R_3 = CH_3; R = R_4 = H; R_2 = CHO
d. R = R_1 = CH_3; R_2 = CHO; R_3 = R_4 = H
e. R = CH_3; R_2 = CHO; R_1 = R_3 = R_4 = H
f. R = CH_3; R_2 = CHO; R_1 = R_3 = H; R_4 = NO_2
g. R = R_2 = R_3 = CH_3; R_1 = R_4 = H
h. R = R_2 = CH_3; R_1 = R_3 = R_4 = H
i. R = R_1 = CH_3; R_2 = CHO; R_3 = H; R_4 = NO_2
j. R = CH_2OH; R_1 = CH_3; R_2 = CHO; R_3 = R_4 = H
k. R = CH_3; R_1 = CH_2COOH; R_2 = CHO; R_3 = R_4 = H
l. R = C_6H_5; R_1 = CH_3; R_2 = CHO; R_3 = R_4 = H
m. R = R_1 = CH_3; R_2 = CHO; R_3 = H; R_4 = Br
n. R = R_1 = R_3 = CH_3; R_2 = OH; R_4 = H
o. R = R_1 = CH_3; R_2 = R_3 = OH; R_4 = H
p. R = C_6H_5; R_1 = CH_3; R_2 = R_3 = OH; R_4 = OH

EXPERIMENTAL[17]

5,8-Di-(ω-carbethoxymethoxy)-2-methylfuro-4′,5′,6,7-chromone (If). To a solution of 8 g. of 5,8-di-norkhellin (Ie)[h] in 100 ml. of dry acetone was added 8 g. of anhydrous potassium carbonate, 6.5 ml. of ethylchloroacetate, and 0.5 g. of sodium iodide. The reaction mixture was refluxed for 12 hr., then 4 g. of anhydrous potassium carbonate, 2.5 ml. of ethylchloroacetate and 40 ml. of acetone were added, and refluxing was extended for a further period of 28 hr. Acetone was then driven off and the residue was digested with cold water and the reaction mixture made acidic to methyl red by addition of dilute acetic acid. The colorless solid that separated on cooling was filtered off, washed with water, and extracted with cold sodium carbonate solution (5%). The insoluble part was crystallized from 50% ethanol m.p. 125–127°, and was identified as If (m.p. and mixed m.p.[4]); yield was *ca.* 6 g.

The sodium carbonate solution was treated with cold dilute hydrochloric acid, and the solid obtained gave upon crystallization from ethyl alcohol colorless crystals, m.p. 198–200°.

Anal. Calcd. for $C_{18}H_{16}O_9$: C, 57.44; H, 4.25. Found: C, 57.40; H, 4.23.

5(8)-(ω-Carbethoxymethoxy)-8(5)-(w-carboxymethoxy)-2-methylfuro-4′,5′,6,7-chromone (Il) is soluble in sodium carbonate solution (5%) and is almost insoluble in sodium bicarbonate solution (5%). It gives a crimson-red color when treated with sodium hydroxide pellets.[18]

The free dibasic acid (Ig) was readily obtained from either If or Il upon treatment with dilute sulfuric acid according to the procedure described by Schönberg and Sina.[4] Ig was unaffected when refluxed with 20% hydrochloric acid and/or with hydrobromic acid (60%) for 15 min.

8-(ω-Carbethoxymethoxy)-5-hydroxy-2-methylfuro-4′,5′,6,7-chromone (Ii) was obtained according to the procedure described above for the preparation of If. The reaction mixture was refluxed for 12 hr. only; acetone was driven off and the solution of the reaction residue in water was acidified with dilute acetic acid. The solid obtained was filtered off, washed with water, and crystallized from dilute ethyl alcohol as yellow plates, m.p. 129–130°. Yield is *ca.* 7 g.

Anal. Calcd. for $C_{16}H_{14}O_7$: C, 60.37; H, 4.40. Found: C, 60.30; H, 4.53.

8-(ω-Carboxymethoxy)-5-hydroxy-2-methylfuro-4′,5′,6,7-chromone (Ih). A solution of 1 g. of Ii in 25 ml. of glacial acetic acid was treated with a mixture of 20 ml. of water and 1 ml. of concentrated sulfuric acid. The reaction mixture was refluxed for 20 min. and cooled. The solid obtained was collected by filtration and was crystallized from ethyl alcohol as colorless crystals (0.7 g.), m.p. 220–222°.

Anal. Calcd. for $C_{14}H_{10}O_7$: C, 57.93; H, 3.44. Found: C, 57.88; H, 3.57.

8-(ω-Carbethoxymethoxy)-5-methoxy-2-methylfuro-4′,5′,6 7-chromone (Ij). A mixture of 1 g. of Ii, in 40 ml. of dry acetone, 3 g. of anhydrous potassium carbonate, and 2 ml. of methyl iodide, was refluxed for 20 hr. It was filtered and evaporated to dryness. The solid was crystallized from 20% ethyl alcohol as colorless crystals (*ca.* 1.0 g.), m.p. 110–112°. Ij gives a red color when treated with sodium hydroxide pellets.

Anal. Calcd. for $C_{17}H_{16}O_7$: C, 61.44; H, 4.81. Found: C, 61.52; H, 4.98.

8-(ω-Carboxymethoxy)-5-methoxy-2-methylfuro-4′,5′,6,7-chromone (Ik). Hydrolysis of 1 g. of Ij was carried out as described for Ih. The crude Ik, thus obtained, was crystallized from ethyl alcohol as colorless needles (*ca.* 0.75 g.), m.p. 278°.

Anal. Calcd. for $C_{15}H_{12}O_7$: C, 59.21; H, 3.94. Found: C, 59.44; H, 3.94. It is soluble in sodium carbonate solution with effervescence and gives a red color with sodium hydroxide pellets.

5-(ω-Carbethoxymethoxy)-2-methylfuro-4′,5′,6,7-chromone (IIc). 5-Norvisnagin (IIb)[17] (1 g.) was treated with ethylchloroacetate as described for If to give after crystallization from ethyl alcohol, 1 g. of colorless needles of IIc, m.p. 134–135°.

Anal. Calcd. for $C_{16}H_{14}O_6$: C, 63.57; H, 4.63. Found: C, 63.59; H, 4.72. It gives a red color with sodium hydroxide pellets.

5-(ω-Carboxymethoxy)-2-methylfuro-4′,5′,6,7-chromone (IId). One gram of IIc was treated with sulfuric acid as described above to give an almost quantitative yield of IId. It was crystallized from glacial acetic acid as colorless plates, m.p. 246–248°, and gives a violet color with sodium hydroxide pellets.

Anal. Calcd. for $C_{14}H_{10}O_6$: C, 61.31; H, 3.65. Found: C, 61.78; H, 3.86.

Oxidation of IId. (a) *Chromic acid.* Oxidation of 1 g. of IId with chromic acid according to the procedure described for IIa[7] gave colorless needles of 5-(ω-carboxymethoxy)-6-

(17) All melting points are uncorrected. Microanalysis was carried out by Dr. A. Bernhardt, Mülheim, and Drs. G. Weiler and F. Strauss, Oxford.

(18) A. Schönberg and A. Sina, *J. Chem. Soc.*, 3344 (1950).

formyl-7-hydroxy-2-methylchromone (IIIb) from ethyl alcohol, m.p. 202–204° (dec.). Yield was *ca.* 65%.

Anal. Calcd. for $C_{13}H_{10}O_7$: C, 56.11; H, 3.59. Found: C, 55.83; H, 3.76.

(b) *Hydrogen peroxide.* Oxidation of IId with hydrogen peroxide in alkaline medium according to the procedure described for the oxidation of IIa[7] led to the formation of yellowish needles of 4-(ω-carboxymethoxy)-6-hydroxybenzofuran-5-carboxylic acid (Vc), m.p. 229–230° (dec.). It gives a blue color when its alcoholic solution is treated with aqueous ferric chloride solution.

Anal. Calcd. for $C_{11}H_8O_7$: C, 52.38; H, 3.17. Found: C, 52.35; H, 3.58.

Oxidation with hydrogen peroxide in alkaline medium. (a) Ig. One gram of Ig gave upon oxidation with hydrogen peroxide in alkaline medium[7] 4,7-di-(ω-carboxymethoxy)-6-hydroxybenzofuran-5-carboxylic acid (Va) as colorless needles from water (*ca.* 0.5 g.), m.p. 222–223° (dec.). It gives a blue color with ferric chloride.

Anal. Calcd. for $C_{13}H_{10}O_{10}$, H_2O: C, 45.34; H, 3.48. Found: C, 45.42; H, 3.70.

(b) Ik. Similarly, oxidation of 1 g. of Ik with the same reagents under the same experimental conditions, led to the formation of colorless needles from ethyl alcohol (*ca.* 0.6 g.) of 7-(ω-carboxymethoxy)-6-hydroxy-4-methoxybenzofuran-5-carboxylic acid (Vb), m.p. 192–194° (dec.). It gives a blue color with ferric chloride.

Anal. Calcd. for $C_{12}H_{10}O_8$: C, 51.06; H, 3.54. Found: C, 51.28; H, 4.18.

(c) Ib. Oxidation of 1 g. of Ib[2] with hydrogen peroxide, as described for Ig, led to the formation of colorless needles from ethyl alcohol of 4-(ω-carboxymethoxy)-6-hydroxy-7-methoxybenzofuran-5-carboxylic acid (Vd) (*ca.* 0.5 g.), m.p. 202–203° (dec.). It gives a blue color with ferric chloride.

Anal. Calcd. for $C_{12}H_{10}O_8$: C, 51.06; H, 3.54. Found: C, 51.03; H, 4.18.

Alkaline hydrolysis. (a) Ik. Refluxing 1 g. of Ik with aqueous sodium hydroxide solution (40 ml.; 15%) for 2 hr., followed by cooling the reaction mixture and acidification with cold dilute hydrochloric acid, gave pale-yellow needles from dilute ethyl alcohol of 5-acetyl-7-(ω-carboxymethoxy)-6-hydroxy-4-methoxybenzofuran (IVa) (ca. 0.6 g.), m.p. 171–172°. It gives a green color with ferric chloride.

Anal. Calcd. for $C_{13}H_{12}O_7$: C, 55.71; H, 4.28. Found: C, 55.73; H, 4.61.

(b) IId. Similarly, treatment of 1 g. of IId with sodium hydroxide under the above mentioned conditions led to the formation of canary-yellow needles from ethyl alcohol (*ca.* 0.4 g.) of 5-acetyl-4-(ω-carboxymethoxy)-6-hydroxybenzofuran (IVb), m.p. 217–218° (dec.). It gives a blue color with ferric chloride.

Anal. Calcd. for $C_{12}H_{10}O_6$: C, 57.60; H, 4.00. Found: C, 57.51; H, 4.10.

Preparation of 6-Formyl-5-hydroxy-7-methoxy-2-methylchromone (IXc). One half gram of 6-formyl-5,7-dimethoxy-2-methylchromone[7] was refluxed for 1 hr. with a mixture of 10 ml. of concentrated hydrochloric acid and 10 ml. of water. The solid obtained upon cooling the reaction mixture was collected and crystallized from ethyl alcohol as colorless crystals (250 mg.), m.p. 250° (dec.).

Anal. Calcd. for $C_{12}H_{10}O_5$: C, 61.53; H, 4.27. Found: C, 61.63; H, 4.14.

IXc is insoluble in aqueous sodium hydroxide solution (5%) and acquires a yellow color when treated with 50% sulfuric acid. It gives a violet-red color with ferric chloride.

CAIRO, U.A.R.

[FROM THE DEPARTMENT OF CHEMISTRY AND PHARMACEUTICAL CHEMISTRY, MEDICAL COLLEGE OF VIRGINIA]

Palladium Catalysts. X.[1,2] Substrate-Specific and Stereospecific Centers

ROBERT L. BEAMER,[3] J. DOYLE SMITH, JOHN ANDRAKO, AND WALTER H. HARTUNG

Received June 22, 1959

It is postulated that a hydrogenation catalyst prepared by depositing palladium on a suitable carrier consists of centers differing from each other not only in their reactivity toward specific substrates but toward specific stereoisomers of those substrates. Thus, centers effective for the hydrogenation of a given compound differ appreciably from those effective for another compound or even for a stereoisomer. Conditions are outlined for determining the validity of these postulates, and experimental results thus far obtained are in harmony therewith. For example, with identical catalysts the Schiff base formed with benzylamine and a racemic acyloin takes up hydrogen considerably faster than does the Schiff base formed with the D(−)acyloin. Other examples are also given.

Reactions depending on heterogenous catalysis are surface phenomena.[4] Studies of adsorption, reaction kinetics, poisoning, and promoter action lead to the conclusion that the catalytically active surface is nonuniform and that not all areas are equally active.[5]

In previous papers of this series it has been found that for palladium-on-carbon the catalytic properties are influenced by factors such as the presence of other metals,[6] by the ratio of metal to carrier,[7] and by the nature of the anion present when the pal-

(1) For number IX see R. W. Meschke and W. H. Hartung, *J. Org. Chem.* **25**, 137 (1960).

(2) This investigation was supported by Public Health Service Grant RG-5895, National Institutes of Health. For this assistance the authors express grateful appreciation.

(3) Present address: School of Pharmacy, University of South Carolina, Columbia, S. C.

(4) H. S. Taylor and R. M. Burns, *J. Am. Chem. Soc.* **43**, 1284 (1921).

(5) A. B. Kistiakowsky, E. W. Flosdorf, and H. S. Taylor, *J. Am. Chem. Soc.* **49**, 2200 (1927); H. S. Taylor and S. C. Liang, *J. Am. Chem. Soc.*, **69**, 1306, 2989 (1947); R. N. Pease and L. Stewart, *J. Am. Chem. Soc.*, **47**, 1235 (1925); E. B. Maxted *et al.*, *J. Chem. Soc.* **1933**, 502; **1935**, 393; 1938, 1228, 2071; W. W. Russell, *J. Chem. Ed.* **22**, 163 (1945).

(6) W. H. Hartung and Y. T. Chang, *J. Am. Chem. Soc.* **74**, 5927 (1952).

(7) J. G. Young and W. H. Hartung, *J. Org. Chem.* **18**, 1659 (1953).