The oxime, prepared according to the directions of Shriner and Fuson,[18b] melted at 76–77° when recrystallized as plates from ethanol–water.

*Anal.* Calcd. for $C_{10}H_{17}NO$: C, 71.80; H, 10.25. Found: C, 72.03; H, 10.42.

Ultraviolet irradiation of the oxime in benzene solution for thirty-six hours resulted in complete recovery of the material melting at 76–77°.

The semicarbazone,[18a] shiny flakes when recrystallized from methanol, melted at 199.5–200.5°.

*Anal.* Calcd. for $C_{11}H_{19}N_3O$: C, 63.16; H, 9.09. Found: C, 63.17; H, 9.12.

The 2,4-dinitrophenylhydrazone, prepared by the method of Shriner and Fuson,[18c] formed red microcrystals from absolute ethanol, m. p. 194.5–196°.

*Anal.* Calcd. for $C_{16}H_{20}N_4O_4$: N, 16.87. Found: N, 16.80.

***d*-Phellandric Acid.**—To a mixture of 2920 ml. of petroleum ether (80–110°) and 488 ml. of *n*-butyl alcohol were added 45 g. (0.27 mole) of *dl*-phellandric acid and 101 g. (0.27 mole) of quinine trihydrate. The solution was heated to 60°, filtered hot, allowed to cool slowly to room temperature and finally chilled overnight in an icebox. The precipitated salt was filtered and recrystallized from the same solvent mixture. A second 45-g. portion of acid was treated in the same manner, and the two batches of salt combined and recrystallized seven times. The rotation did not change during the last two crystallizations. There was obtained 24 g. of quinine salt, m. p. 141–143°, $[\alpha]^{25}D$ −100° (0.0288 g./ml. of methanol).

*Anal.* Calcd. for $C_{30}H_{40}N_2O_4$: C, 73.14; H, 8.18. Found: C, 73.34; H, 8.43.

The quinine salt was dissolved in chloroform and decomposed by shaking with 12 ml. of 5% aqueous potassium hydroxide. The chloroform layer was discarded. The aqueous layer was washed twice with chloroform and then acidified. The precipitated acid was collected on a filter, washed with water and air-dried. It weighed 6.4 g., $[\alpha]^{25}D$ +63° (0.0223 g./ml. of methanol).

The partially resolved acid was dissolved in 300 ml. of a mixture of 1 volume of *n*-butyl alcohol to 20 volumes of petroleum ether (80–110°), and an excess of *l*-α-phenylethylamine was added. The mixture was heated on a steam-cone, then allowed to cool slowly as before. After eighteen recrystallizations from the same solvent mixture the rotation of the salt remained constant. There was obtained 1.27 g. of salt, m. p. 151–152°; $[\alpha]^{25}D$ +70.0° (0.0266 g./ml. of methanol solution).

*Anal.* Calcd. for $C_{18}H_{27}NO_2 \cdot H_2O$: C, 70.32; H, 9.51. Found: C, 70.66; H, 9.58.

This salt was decomposed in the same manner as the quinine salt to yield optically pure *d*-phellandric acid, m. p. 143–144°, $[\alpha]^{26}D$ +112.2° (0.02054 g./ml. of methanol solution) (lit.,[5b] m. p. 144–145°, $[\alpha]^{20}D$ +112.8° (0.02083 g./ml. of methanol solution)).

*Anal.* Calcd. for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.25; H, 9.62.

## Summary

The structure of the terpene phellandral has been confirmed by the total synthesis of *dl*-phellandral and the resolution of *dl*-phellandric acid.

URBANA, ILLINOIS RECEIVED MAY 31, 1949

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

# Flavanones and Related Compounds. VI. The Polarographic Reduction of Some Substituted Chalcones, Flavones and Flavanones

BY T. A. GEISSMAN AND S. L. FRIESS[1]

The study of the behavior at the dropping-mercury electrode of substances belonging to the $C_6$–$C_3$–$C_6$ (flavonoid) group of naturally occurring plant substances[2] has been continued. A more detailed examination has been made of some of the questions raised in the earlier part of this work, and a study has now been made of a group of flavones having hydroxyl and acetoxyl groups in the 5-, 7- and 4′-positions.[3] In addition, fourteen flavanones and sixteen chalcones, containing hydroxyl, methoxyl and acetoxyl groups in various positions in both aromatic rings, were examined. In each group the parent compound was included.

The objectives of this study included (1) a correlation between the kind and degree of substitution and the resulting variation in the ease of reduction at the electrode; (2) an evaluation of the most probable electrode mechanism; and (3) an attempt to account for the observed $E_{1/2}$ values on the basis of the proposed electrode reaction and the relative degrees of resonance stabilization of the reactants and products of the electrode reaction.

## Experimental

The polarographic runs were made in 50% buffer–50% isopropyl alcohol mixtures at a temperature of 25 ± 0.1°, the $E_{1/2}$ values being measured against the saturated calomel electrode (S.C.E.). The *p*H values recorded for the various buffer mixtures used in the polarographic runs are the nominal ones given by the Beckman *p*H meter. They are in general about 1 *p*H unit higher than those of the aqueous buffer solutions alone.

In the case of the chalcones, the polarograph, buffers and dropping-mercury electrode were those used in the earlier study. Later, a Fisher Electropode was used, the runs with the flavones and flavanones being made with this instrument.

The capillary used for the runs on the flavones

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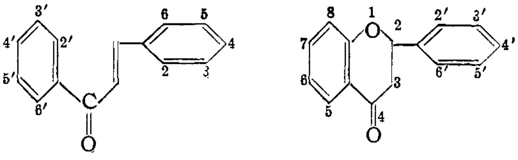
[2] Engelkemeir, Geissman, Crowell and Friess, THIS JOURNAL, **69**, 155 (1947).

[3] Chalcones, flavones and flavanones are numbered as follows:



and flavanones had the following characteristics: drop time at zero applied voltage = 3.78 sec.; $m$ = 1.63 mg./sec.; $m^{2/3}t^{1/6}$ = 1.73. In the case of these series the buffers were all acetic acid–tetramethylammonium hydroxide mixtures. This buffer was adopted as a standard despite its poor buffering power at the higher $p$H values, since it was felt best to avoid possible complexities which the use of different (acetate, phosphate and borate) buffers might involve.[4]

Each run was carried out in duplicate, using in most cases different amounts of compound for each polarogram. The curves obtained for such duplicate runs gave reproducible half-wave potentials and wave heights proportional (by measurement, or estimation by inspection) to the sample weights.

In order to compare the Elecdropode with the instrument formerly used, a run was made on flavonol (3-hydroxyflavone), a compound not otherwise included in the present discussion. The value of the half-wave potential for this compound was found in the previous work to be −1.33 volts at $p$H 7.7; the value on the Elecdropode was −1.30 volts at $p$H 7.5. No systematic correction was applied, however, to the values found on either instrument since attention was chiefly directed to the differences observed within each group of related substances.

Since it was considered possible that certain chalcones having 2′-hydroxyl groups might be converted in solution into equilibrium mixtures containing some of the isomeric flavanone, particularly since a thirty-minute deoxygenation period preceded each run, a run was made using a mixture of 2′-hydroxychalcone and flavanone, at $p$H 7.5. The $E_{1/2}$ value for flavanone (−1.37 v.) was unaffected by the presence of the chalcone, and no wave was observed to occur at this point when 2′-hydroxychalcone was run alone under identical conditions. At no time was there any evidence that a flavanone gave rise to the corresponding chalcone, or *vice versa*, under the conditions of the polarographic runs carried out in this work.

Most of the compounds used were on hand or were prepared by known methods.[5]

Each compound was purified before use by recrystallization from an appropriate solvent. **5-Acetoxyflavone** was prepared by the acetylation of the hydroxy compound with acetic anhydride–pyridine. It formed white needles from alcohol, m. p. 121–122°. This changed on recrystallization to the value of 145° reported by Sugasawa.[6] In view of this behavior the compound was analyzed: Calcd. for $C_{17}H_{12}O_4$: C, 72.85; H, 4.32. Found: C, 72.96; H, 4.52.

**Naringenin triacetate** was prepared from purified naringenin by Asahina's method.[7] The colorless needles, recrystallized from ethyl acetate–petroleum ether, melted at 82–84°.

*Anal.* Calcd. for $C_{21}H_{18}O_8$: C, 63.32; H, 5.55; OAc, 32.4. Found: C, 63.28; H, 5.10; OAc, 31.3.

**Flavanone** was prepared by refluxing 2′-hydroxychalcone in alcoholic hydrochloric acid solution.[8]

## Results

In Table I are given summaries of the half-wave potentials and $i_d/c$ values ($i_d$ in microamperes, $c$ in millimoles/liter) for the compounds studied. In general, $i_d/c$ values were measured only for those curves which were clearly separated from adjoining waves. In a number of cases the amount of compound selected for a run proved to be incompletely soluble in the standard volume of buffer–isopropyl alcohol used in the polarograph cell; in such cases the concentration was not known with certainty and no $i_d/c$ value is reported. Enough examples of $i_d/c$ are given, however, to establish the range within which these values fall for each class of compounds studied. It is seen that most of the flavanones give single-wave, the flavones double-wave and the chalcones triple-wave polarograms. Some exceptions to this are observed, and this is regarded in most cases to be the result of the fusion of two waves into a single one. The results can most conveniently be discussed by directing attention to each class of compound separately.

**Flavones.**—In Fig. 1 are shown polarograms (plotted from Elecdropode readings) for 4′-hydroxyflavone, its acetate and its methyl ether. The two-step nature of the waves is evident, and is in contrast to the single wave of more highly substituted flavones[2] (*e. g.*, quercetin). This point was re-examined by repeating one of the earlier runs on kampferol (3,5,7,4′-tetrahydroxyflavone). This compound showed a single well-defined wave at −1.49 v. in a buffer of $p$H 6.1.[8a] Although some of the compounds show but one wave, it seems likely that this may be the result of the fusion of two steps which occur closely enough together to obscure the plateau between them. This is indicated by the

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[4] Furman and Stone, This Journal, **70**, 3055 (1948), in a polarographic study of some anthraquinones, found differences in the nature and position of the wave exhibited by a given compound when buffers of the same $p$H but different composition were used.

[5] Geissman and Clinton, *ibid.*, **68**, 597 (1946).

[6] Sugasawa, *J. Chem. Soc.*, 1483 (1934).

[7] Asahina and Inubuse, *Ber.*, **61B**, 1514 (1928).

[8] Kostanecki and Szabranksi, *ibid.*, **37**, 2635 (1904).

[8a] The single-wave polarograms of quercetin, kampferol and some related substances were interpreted in the earlier work[2] as indicating a single-electron reduction of these substances, a conclusion which was supported by wave analyses which gave "$n$" values of about 1. It appears from the present results that this conclusion was incorrect, and that in the case of these compounds the polarograms were actually those of two-electron processes in which two, one electron waves appeared as a single fused wave. An inspection of the diffusion current constants supports this view. In at least one case reported in that paper[2] a double wave was noted (quercetin tetramethyl ether), and it is noteworthy that when the "break" in this curve was ignored, and it was treated as a single wave, the diffusion current constant calculated from the total wave height was in line with those calculated for waves which did not show a distinct "break."

observation that in some series of runs at increasing *p*H the separation between the waves progressively decreases before the fusion into a simple wave occurs.

TABLE I[a]

| | | *p*H 6.1 | | *p*H 7.5 | | *p*H 8.6 | | *p*H 9.6 | |
|---|---|---|---|---|---|---|---|---|---|
| | Flavones | $E_{1/2}$ | $i_d/c$ | $E_{1/2}$ | $i_d/c$ | $E_{1/2}$ | $i_d/c$ | $E_{1/2}$ | $i_d/c$ |
| 1 | Unsubstituted | −1.26 | 1.53 | −1.26 | 1.99 | −1.41 | .. | −1.42 | .. |
| | | −1.38 | .. | −1.44 | .. | −1.75 | .. | −1.75$^b$ | .. |
| 2 | 4’-Hydroxy | −1.25 | 1.62 | −1.35 | 1.37 | −1.53 | .. | −1.54 | .. |
| | | −1.49 | 2.34 | −1.50 | 1.29 | .... | .. | .... | .. |
| 3 | 5-Hydroxy | −1.28 | 1.58 | −1.33 | .. | −1.37$^c$ | .. | −1.37$^c$ | .. |
| | | −1.41 | .. | −1.45 | .. | −1.51 | .. | −1.51 | .. |
| | | | | | | −1.65 | .. | −1.65 | .. |
| | | | | −1.36$^c$ | | | | | |
| 4 | 7-Hydroxy | −1.26 | 1.23 | −1.50 | 1.26 | −1.59 | .. | −1.60 | .. |
| | | −1.51 | 2.95 | −1.64 | .. | .... | .. | .... | .. |
| 5 | 4’-Acetoxy | −1.14 | 1.48 | −1.23 | 1.47 | −1.37 | .. | −1.37 | .. |
| | | −1.37 | 2.16 | −1.39 | 1.65 | −1.73$^b$ | .. | −1.73$^b$ | .. |
| 6 | 5-Acetoxy | −1.15 | 1.56 | .... | .. | −1.35 | .. | .... | .. |
| | | −1.31 | 1.60 | .... | .. | .... | .. | .... | .. |
| 7 | 7-Acetoxy | −1.14 | 1.24 | .... | .. | −1.38 | .. | .... | .. |
| | | −1.41 | 1.88 | .... | .. | −1.72 | .. | .. | .. |
| 8 | 4′-Methoxy | −1.20 | 1.09 | .... | .. | −1.47 | .. | .... | .. |
| | | −1.37 | .. | | | | | | |
| | Flavanones | | | | | | | | |
| 9 | Unsubstituted | −1.29 | 2.78 | −1.37 | 2.62 | .... | .. | −1.51 | 2.43 |
| 10 | 4’-Hydroxy | −1.29 | .. | −1.37 | .. | −1.51 | 0.62 | −1.52 | 0.73 |
| 11 | 4′,5-Dihydroxy | −1.39 | 2.47 | −1.45 | 2.25 | −1.53 | 1.72 | −1.54 | 1.91 |
| 12 | 4′,7-Dihydroxy | −1.45 | 2.20 | −1.57 | 2.25 | −1.58 | 0.83 | −1.59 | 0.67 |
| | | | | | | −1.84 | .. | −1.84 | |
| 13 | 4′,5,7-Trihydroxy | −1.57 | 2.18 | −1.62 | 2.24 | −1.65 | .82 | −1.66 | .57 |
| 14 | 3′,4’,5,7-Tetrahydroxy | −1.54 | 2.44 | −1.61 | 1.98 | −1.65 | .73 | −1.66 | .70 |
| 15 | 3’-Methoxy-4’,5,7-trihydroxy | −1.55 | 2.49 | −1.59 | 1.99 | −1.65 | .91 | −1.65 | .60 |
| 16 | 4′-Methoxy | −1.28 | 2.81 | −1.34 | 2.41 | −1.51 | 2.19 | −1.52 | .. |
| 17 | 4’,7-Dimethoxy | −1.40 | 2.28 | −1.46 | .. | −1.64 | 2.25 | −1.64 | 2.24 |
| | | | | −1.60 | .. | | | | |
| 18 | 4′,5,7-Trimethoxy | −1.36 | .. | −1.43 | .. | −1.68 | .. | −1.69 | .. |
| 19 | 4′,7-Dimethoxy-5-hydroxy | −1.50 | .. | −1.53 | .. | −1.65 | .. | −1.67 | .. |
| 20 | 4’-Acetoxy | −1.26 | .. | −1.52 | .. | .... | .. | −1.49 | .. |
| 21 | 4’,5-Diacetoxy | −1.22 | .. | −1.27 | .. | .... | .. | −1.46 | 1.91 |
| | | −1.37 | | −1.43 | | | | | |
| 22 | 4′,5,7-Triacetoxy | −1.19 | .. | −1.25 | .. | .... | .. | −1.38 | .. |
| | Chalcones | | | | | | | | |
| 23 | Unsubstituted | −0.89 | 1.71 | −0.93 | 1.38 | −1.08$^d$ | 3.58 | −1.10$^d$ | 3.55 |
| | | −1.12 | 1.82 | −1.12 | 1.60 | 1.62 | 2.71 | −1.63 | 2.62 |
| | | −1.44 | 0.68 | −1.60$^e$ | 0.53 | | | | |
| 24 | 2’-Hydroxy | −0.93 | 2.10 | −0.98 | 1.87 | −1.01 | 1.70 | −1.02 | 1.40 |
| | | −1.12 | 1.77 | −1.20 | 1.72 | −1.25 | 1.49 | −1.25 | 1.34 |
| | | −1.47 | 2.62 | −1.58 | 1.98 | −1.64 | 0.73 | −1.63 | 0.80 |
| 25 | 2’,4-Dihydroxy | −1.04 | 1.43 | −1.11 | 1.40 | −1.16 | 1.27 | −1.16 | 1.22 |
| | | −1.19 | 1.31 | −1.24 | 1.43 | −1.35 | 1.34 | −1.35 | 1.35 |
| | | −1.44 | 2.07 | −1.55 | 2.25 | −1.64 | 0.76 | −1.64 | 0.85 |
| 26 | 2’,3,4-Trihydroxy | .... | .. | −1.18$^f$ | 2.56 | .... | .. | .... | .. |
| | | | | 1.55 | 1.75 | | | | |
| 27 | 2’,4,4-Trihydroxy | −1.10 | 0.75 | −1.13 | 1.40 | −1.24 | 1.02 | −1.27 | 0.83 |
| | | −1.25 | 1.59 | −1.28 | 1.42 | −1.43 | 1.15 | −1.44 | 1.32 |
| | | −1.55 | 1.67 | −1.66 | 1.80 | −1.90 | 0.96 | −1.92 | 0.92 |
| 28 | 2′,4′,3-Trihydroxy | .... | .. | −1.16$^d$ | 2.15 | .... | .. | .... | .. |
| | | | | 1.69 | 1.89 | | | | |
| 29 | 2’,4’,3,4-Tetrahydroxy | −1.15$^d$ | 2.54 | −1.25$^d$ | 2.37 | −1.25 | .. | −1.25 | .. |
| | | 1.57 | 1.94 | 1.69 | 1.82 | −1.40 | .. | −1.40 | .. |
| | | | | | | −1.85 | .. | −1.87 | .. |

TABLE I (*Continued*)

| | | *p*H 6.1 | | *p*H 7.5 | | *p*H 8.6 | | *p*H 9.6 | |
|---|---|---|---|---|---|---|---|---|---|
| | Chalcones | $E_{1/2}$ | $i_d/c$ | $E_{1/2}$ | $i_d/c$ | $E_{1/2}$ | $i_d/c$ | $E_{1/2}$ | $i_d/c$ |
| 30 | 4'-Hydroxy | .... | .. | $-1.13^{d,f}$ | 2.70 | .... | .. | .... | .. |
| | | | | 1.79 | | | | | |
| 31 | 4',4-Dihydroxy | .... | .. | −1.10 | 1.35 | .... | .. | .... | .. |
| | | | | −1.24 | 1.32 | | | | |
| | | | | −1.72 | 0.65 | | | | |
| 32 | 4'-Methoxy | .... | .. | −1.01 | 1.35 | .... | .. | .... | .. |
| | | | | −1.21 | 1.32 | | | | |
| | | | | −1.68 | 0.65 | | | | |
| 33 | 4',4-Dimethoxy | −0.94 | .. | −1.04 | .. | −1.13 | .. | −1.10 | .. |
| | | −1.18 | .. | −1.22 | .. | −1.26 | .. | −1.23 | .. |
| | | −1.45 | .. | −1.62 | .. | −1.73 | .. | −1.73 | .. |
| 34 | 2'-Hydroxy-4,4',6'-trimethoxy | $-1.13^{d}$ | .. | $-1.19^{d}$ | .. | −1.19 | .. | −1.20 | .. |
| | | | | | | −1.34 | .. | −1.34 | .. |
| | | 1.58 | .. | −1.72 | .. | −1.85 | .. | −1.85 | .. |
| 35 | 2',4',6',4-Tetramethoxy | $-1.03^{d}$ | 0.85 | $-1.09^{d}$ | 0.88 | $-1.28^{d}$ | 1.71 | −1.28 | 1.32 |
| | | −1.24 | 0.88 | −1.24 | 1.17 | | | | |
| 36 | 2',3',4'-Trihydroxy | .... | .. | $-1.15^{d,f}$ | 3.55 | .... | .. | .... | .. |
| | | | | −1.77 | 1.15 | | | | |
| 37 | 2'-Hydroxy-6'-methoxy-3,4-methylenedioxy | −0.93 | .. | .... | .. | .... | .. | .... | .. |
| | | −1.05 | .. | | | | | | |
| | | −1.47 | .. | | | | | | |
| 38 | 2'-Hydroxy-4',6',3,4-tetramethoxy | $-1.03^{d}$ | .. | .... | .. | .... | .. | .... | .. |
| | | −1.13 | .. | | | | | | |

[a] Half-wave potentials are measured *vs.* the saturated calomel electrode; $i_d/c$ values are in microamperes/millimole/liter. [b] Very small wave. [c] Triple wave with small breaks. [d] Single (fused) wave. [e] Small symmetrical wave. [f] Slight maximum in wave.

Figure 2 shows the variation in half-wave potential with *p*H for a number of the compounds examined. The abrupt shift in $E_{1/2}$ at *p*H values in the region 8–9 has been observed not only in this series but also in the case of similarly substituted chalcones and flavanones. A similar behavior has been used in the case of a series of substituted benzaldehydes by Baker, Davies and Hemming.[9] The same effect was noted in the first part of this study.[2]

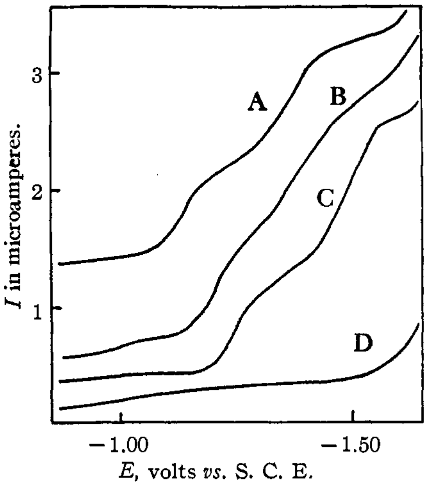

Fig. 1.—Polarograms of flavones at *p*H 6.1: A, 4'-acetoxyflavone; B, 4'-methoxyflavone; C, 4'-hydroxyflavone; D, buffer blank.

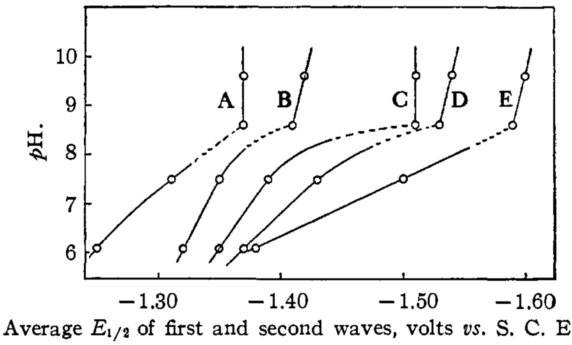

Fig. 2.—Variation of half-wave potential with *p*H: A, 4'-acetoxyflavone; B, flavone; C, 5-hydroxyflavone; D, 4'-hydroxyflavone; E, 7-hydroxyflavone.

Compared with flavone itself, the 5-, 7- and 4'-hydroxy compounds are more difficultly reducible and the corresponding acetyl derivatives more readily reducible. Since the presence of two waves makes it possible to base comparisons on

TABLE II

AVERAGE $E_{1/2}$ VALUES OF FIRST AND SECOND WAVES

| Flavone | *p*H 6.1 | *p*H 7.5 | *p*H 8.6 |
|---|---|---|---|
| 4'-OH | −1.37 | −1.43 | −1.53 |
| 5-OH | −1.35 | −1.39 | −1.51 |
| 7-OH | −1.38 | −1.43 | −1.59 |
| 4'-OAc | −1.25 | −1.31 | −1.37 |
| 5-OAc | −1.23 | .... | −1.37 |
| 7-OAc | −1.27 | .... | −1.38 |
| 4'-OMe | −1.29 | .... | −1.47 |
| Unsubst. | −1.32 | −1.35 | −1.41 |

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(9) Baker, Davies and Hemming, *J. Chem. Soc.*, 692 (1940).

either wave or on their average value, the effects of the substituents are best seen when the latter basis is adopted (Table II), although at *p*H 7.5 and 8.6 the effects are clearly apparent on either basis (Table I). 4′- and 7-hydroxyflavone show substantially the same values of $E_{1/2}$ in the range below *p*H 8.6, while 5-hydroxyflavone shows lower $E_{1/2}$ values at all *p*H's. A series of studies by Scaramelli[10,11] on hydroxybenzaldehydes and their ethers has shown a similar relationship between the effects of an ortho-(corresponding to 5- in the flavones) and a para-(corresponding to 7-) hydroxyl group, *p*- and *o*-hydroxybenzaldehydes being more difficultly reducible than benzaldehyde, but the ortho- compound being more easily reduced than the para-. Similar results are reported for the corresponding hydroxyacetophenones.[12,13]

Although the differences in $E_{1/2}$ values for the three hydroxyflavones and their derivatives are small, their reproducibility and the essential simplicity of the structures of these compounds is such that these effects are properly subject to interpretation. The decreased acidity of the 5-hydroxyl group in chromone derivatives (and in general, of hydroxyl groups *peri* to carbonyl groups in other systems) is a well-known property manifested by its greater difficulty of methylation with diazomethane and in the diminished solubility of 5-hydroxyflavone derivatives in aqueous alkali. It is to be expected, then, that throughout the *p*H range used in this work the anionic character of the 5-hydroxyl group would be less than that of the 7- or the 4′-hydroxyl group. Since, as will be shown in the sequel, there is good reason to ascribe the effects of these hydroxyl groups upon the ease of reduction of the carbonyl group to their ability to release electrons into the ring, the greater anionic character of the 7-hydroxyl group would allow it to have a greater effect upon the reducibility of the carbonyl group than the 5-hydroxyl group. The greater (negative) $E_{1/2}$ value of 7-hydroxyflavone than of 4′-hydroxyflavone at *p*H 9.6 may be ascribed to the greater acidity of the 7-hydroxyl group and its assumption of a greater degree of anionic character at this *p*H. Although at lower *p*H values, where the effects of un-ionized hydroxyl groups are probably predominant, very small differences in *pK* values would not be apparent, at higher *p*H values the increasing role of the anionic oxygen atoms should cause an increasingly wider separation of their effects. On the basis of these considerations the $E_{1/2}$ values of the hydroxylated flavones are in accord with expectations.

At a low *p*H (6.1) the hydroxyflavones and flavone itself show almost identical $E_{1/2}$ values for the first wave, the second wave only showing the greater ease of reduction of the parent compound. Since flavone contains the same heterocyclic oxygen atom as the hydroxyl-substituted derivatives, it is probable that this oxygen atom is of the greatest influence in affecting the ease of carbonyl reduction in all of these compounds, the effects of the nuclear hydroxyl groups superimposing themselves markedly upon this effect only at *p*H values which permit them to assume an appreciable amount of anionic character.

An examination of the diffusion current constants ($i_d/c$) for the flavones (Table I) shows that these are of about the same order of magnitude. The approximately twofold variation over all the values measured follows no consistent pattern. The values appear to be those of one-electron steps, since they correspond closely in order of magnitude with those observed by Pasternak[14] for a group of related substances. For example, Pasternak finds $i_d/c$ values of approximately 2, with variations of about ±0.3, in most cases, for steps involving one-electron electrode reactions of a number of carbonyl compounds. An inspection of Table I shows that for the flavones examined, $i_d/c$ values of comparable magnitude were found. Closer agreement than is actually found need not be expected in view of the considerable structural differences in the compounds examined by Pasternak and in this work. Smith and his co-workers[15] likewise found diffusion current constants of approximately the same magnitude (*ca.* 4, for two-electron steps) for a series of hydroxychromanes and -coumaranes.[15a]

Wave analyses, by means of the equation

$$E = \text{constant} - \frac{0.059}{n} \log \frac{i}{i_d - i}$$

for a number of the compounds studied give *n* values of about 1 for each wave. This result, while not a demonstration that these are actually one-electron steps, since it is not known whether these are reversible processes, is at least consistent with the view that each wave represents a one-electron process. Müller[16] takes the view that while such wave analyses may not be strictly valid for irreversible processes, the *n* values so obtained may be regarded as approximations to the nearest integer of the number of electrons involved in the wave. In Figs. 3 and 4 are shown

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(10) Scaramelli, *Atti accad. Italia, Rend.* [7] 1, 764 (1940); *C. A.*, **37**, 1408 (1943).

(11) Scaramelli, *Boll. sci. facoltà chim. ind. Bologna*, 235–238 (1940); *C. A.*, **37**, 1408 (1943).

(12) Scaramelli, *ibid.*, 768–770 (1940); *C. A.*, **37**, 1408 (1943).

(13) Scaramelli, *ibid.*, 122–123 (1941); *Chem. Zent.*, **115**, I, 417 (1944).

(14) Pasternak, *Helv. Chim. Acta*, **31**, 753 (1948). This article, which became available to us after this paper was submitted for publication, deals with compounds related to those we studied, and offers an interpretation of their behavior substantially in agreement with our original proposals.

(15) Smith, Kolthoff, Wawzonek and Ruoff, THIS JOURNAL, **63**, 1018 (1941).

(15a) Comparisons of this kind are valid only if the characteristics of the electrodes used are the same or nearly so. In the cases selected for comparison this is the case; for example, the dropping-mercury electrode used by Smith, *et al.*, had $m^{2/3}t^{1/6} = 1.63$; ours had $m^{2/3}t^{1/6} = 1.73$.

(16) Müller, *Annals N. Y. Acad. Sci.*, **40**, 91 (1940).

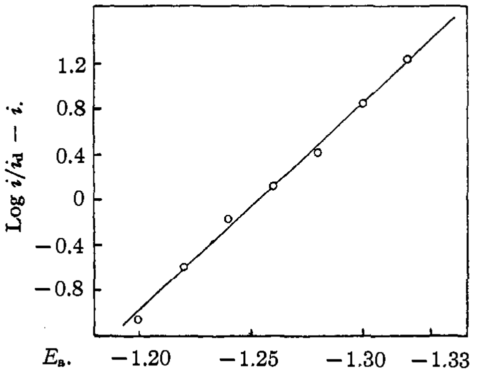


Fig. 3.—Wave analysis of first wave of 7-hydroxyflavone at *p*H 6.1.

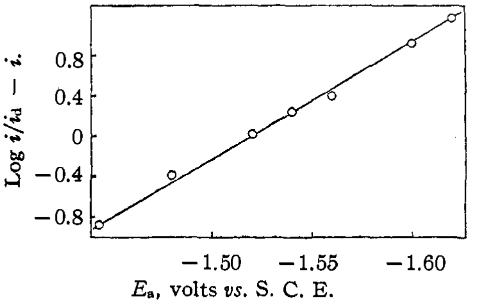


Fig. 4.—Wave analysis of second wave of 7-hydroxyflavone at *p*H 6.1.

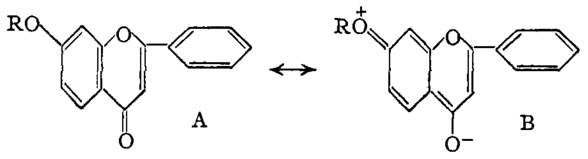
wave analyses for both waves of 7-hydroxyflavone. The values of *n* found from these and several other such wave analyses are given in Table III.

TABLE III

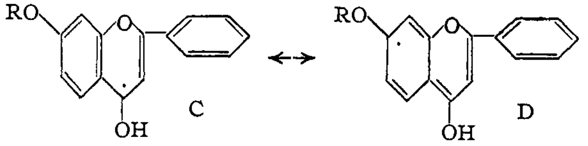
| Flavone | *p*H | 1/slope of *E vs.* log $i(i_d - i)$ | *n* |
|---|---|---|---|
| 7-OH (1) | 6.1 | −0.055 | 1.1 |
| 7-OH (2) | 6.1 | − .081 | 0.7 |
| 7-OH | 9.6 | − .112 | .5 |
| 3-OH | 7.5 | − .064 | .9 |
| 4'-OAc | 8.6 | − .070 | .8 |

The polarographic reduction of organic compounds in distinct one-electron steps has been interpreted in a number of cases[14,16,17,18,19] as indicating the intermediate existence of a "semiquinone," or free radical, at the electrode. The behavior of the flavonoid compounds (of all three classes) studied in the course of the present work, can be accounted for in the light of the effects of structure upon the stabilization of the free radical produced in an initial, one-electron, electrode reaction. It is possible to arrive at a consistent treatment of the observed results if it is assumed that a greater degree of stabilization of the free radical as compared with the unreduced form (the oxidant) should result in a greater ease of reduction, as compared with another substance in which the substituents reduce the relative stabilization of the radical with respect to the oxidant.

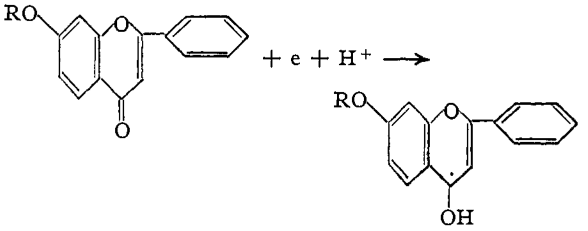
For illustration, consider the 7-substituted flavones. The forms A↔B are among those contributing to the structure of the resonance hybrid of the unreduced form



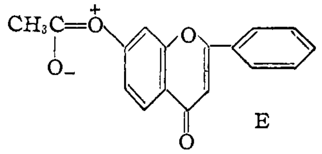
and forms C↔D may be considered among those contributing to the structure of the one-electron-reduced product (the free radical), where forms



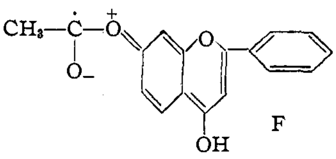
C, etc., may be considered to be the immediate product of the initial electrode reaction, according to the equation



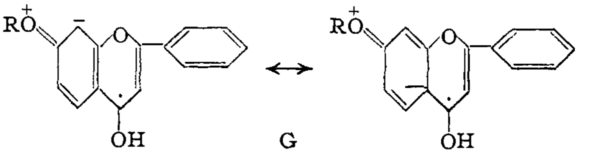
In the acetoxy compound (R = $CH_3CO$-), the stabilization of the oxidant will be diminished as a result of contributions from the opposing effect E



while that of the radical will be enhanced by a form F



It is apparent that when R = $CH_3$, form B will be relatively more effective than form D, since the latter will be opposed by forms G



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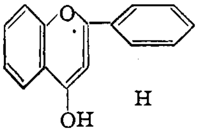
(17) Brdička, *Z. Elektrochem.*, **47**, 314 (1941).

(18) Tokuoka, *Coll. Czech. Chem. Comm.*, **1**, 392 (1935).

(19) Baker, Davies and Hemming, *J. Chem. Soc.*, 692 (1940).

and consequently it is to be expected that the acetoxy compound should be more easily reduced than the methyl ether.

It is seen from Table I and Fig. 5 that flavanones show single-wave polarograms, and undergo an initial electrode reaction involving one electron. A reason for two-step waves in the case of flavones can therefore be suggested. The greater stabilization of a form such as $C \leftrightarrow D$, through participation of the chromone ring as in H



H

allows it to persist at the electrode and to be reduced further in a second electrode reaction. A flavanone, on the other hand, lacks the added possibilities for stabilization of the radical through the participation of such forms as H, and consequently undergoes disproportionation or dimerization in the free radical stage before a second electrode step can ensue, giving rise to a product which is not reducible at the electrode in the range of voltage used.

**Flavanones.**—An examination of the diffusion current constants for the flavanones studied shows that these are in most cases somewhat greater than those characteristic of a one-electron potential-determining electrode reaction. An unusual and unexplained feature of the $i_d/c$ values for some of the flavanones is the sharp drop (from about 2 microamperes/mmole./liter to less than 1) noticed at high *p*H values. Wave analyses for a representative number of the compounds give *n* values of about 1, but the *E vs.* log $(i/i_d - i)$ plots showed a tendency to deviate from straight lines, vitiating even the approximate nature of this check on the number of electrons involved in the wave being analyzed.

The relative ease of reducibility of each flavanone can be related to the unsubstituted compound (9) as a standard. With increasingly more negative $E_{1/2}$ values, indicating increasing difficulty of reduction, the $E_{1/2}$ values of Table I may be used directly as a measure of the ease of reduction, and a correlation can be found between these values and particular kinds of nuclear substitution present.

It is seen by a comparison of the $E_{1/2}$ values at a *p*H of 6.1 for the flavanones 9, 10, 16 and 17 that the introduction at the 4′-position of the electron-supplying groups hydroxyl or methoxyl, or of the electron-withdrawing acetoxyl group, leads to no significant effect upon the ease of reduction relative to the unsubstituted flavanone. In view of the manner in which such substituents act to affect the ease of reduction of the flavones discussed above, this comparison demonstrates that substitution in a position not conjugated with the carbonyl group, and therefore incapable of affecting it by resonance, leads to no influence on the ease of reduction of such substituted compounds. The non-effectiveness of substitution in the 2-phenyl group is further illustrated by a comparison of the $E_{1/2}$ values for compounds 14 and 15.

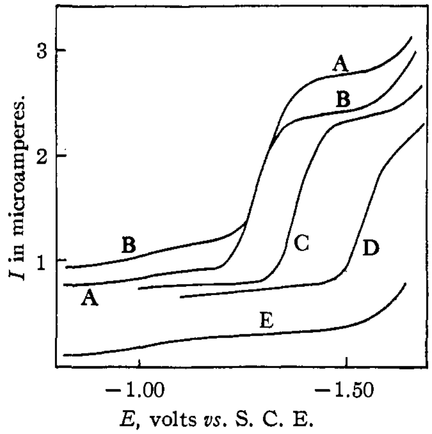


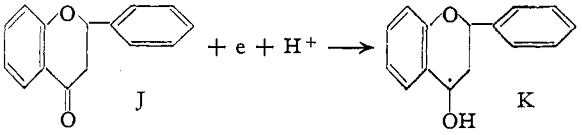
Fig. 5.—Flavanone polarograms at *p*H 6.1: A, flavanone; B, 4′-hydroxyflavanone; C, 4′,5-dihydroxyflavanone; D, 4′,5,7-trihydroxyflavanone; E, buffer blank.

In the resonance-effective (*i. e.*, with respect to the carbonyl group) 5- and 7-positions, however, the effect of varying substitution is marked. The effect of substitution in the 5-position is shown by comparing the $E_{1/2}$ values for 9 (−1.29), 10 (−1.39), and the first wave of 21 (−1.22). Since a substituent in the 4′-position is ineffective, it is seen from this comparison that for the carbonyl-conjugated 5-position, substitution of an electron-supplying hydroxyl group increased the difficulty of reduction while an electron-withdrawing acetoxyl group decreases the difficulty of reduction as compared with flavanone (9).

The relative effectiveness of electron supply by the hydroxyl and methoxyl groups, so far as these reductions are concerned, is shown (with reference to position 7) by a comparison of the $E_{1/2}$ values for compounds 9 (−1.29), 12 (−1.45) and 17 (−1.40). Here, the order of electron supply, interpreted from the relative ease of reducibility, is OH > OMe > H, as would be expected.

The effect of the acetoxyl group with respect to electron supply is shown, for example, by a comparison of flavanone 9 with 13, 18 and 22. The acetoxyl group is evidently electron-attractive relative to hydrogen, an effect clearly shown by the behavior of flavanone 22 in this series.

It is further evident from an inspection of the $E_{1/2}$ values for the flavanones examined that a multiplicity of substituents in resonance-important positions leads to additivity of their effects upon the ease of reduction. Among the comparisons that can be cited to show this are: (1) increasing difficulty of reduction in the series 10, 11, 12, 13 (see Fig. 5), and (2) increasing ease of reduction in the series 20, 21, 22. The magnitude of the $i_d/c$ values indicates that the electrode reaction involves a two-electron change, although the $n$ values from wave analyses indicate one-electron steps. An examination of the change in $E_{1/2}$ with $p$H shows that (Fig. 6) hydrogen ion also participates in this reaction. It is therefore likely that the electrode process involves the potential-determining reaction



The occurrence of only a single step of reduction can be ascribed to the instability of the primary electrode product K, which lacks the stabilization from the (unconjugated) 2-phenyl group found with the fully conjugated flavones and chalcones, and which immediately adds a second electron in a rapid second stage to yield a single-wave polarogram with a wave height corresponding to a two-electron reduction.

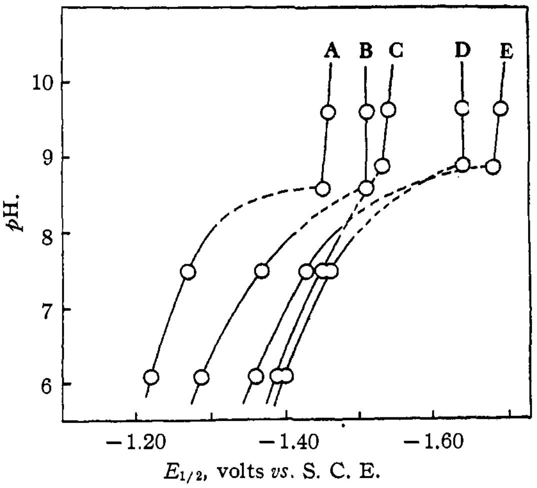


Fig. 6.—Variation of half-wave potential with $p$H: A, 4',5-diacetoxyflavanone; B, flavanone; C, 4',5-dihydroxyflavanone; D, 4',7-dimethoxyflavanone; E, 4',5,7-trimethoxyflavanone.

The arguments, based upon substitution effects, that favor this mechanism are virtually the same as those previously advanced in the discussion of the flavones. The substitution of electron-releasing groups such as hydroxyl or methoxyl in positions conjugated with the carbonyl group causes increased resonance stabilization in form J, relative to the unsubstituted state, but no increased (or decreased) stabilization of the reaction product K. Hence, this kind of substitution leads to increasing difficulty of the production of K by electrode reduction, as compared to the unsubstituted molecule, and is reflected in a shift of the half-wave potentials to the more negative values observed.

**Chalcones.**—The complex nature of the waves given by the chalcones studied is apparent from the data given in Table I. Figure 7 shows clearly the kind of curves from which these values were obtained. These polarograms are those of chalcone and of three chalcones carrying one, two and three hydroxyl groups in positions joined by conjugation with the carbonyl group.

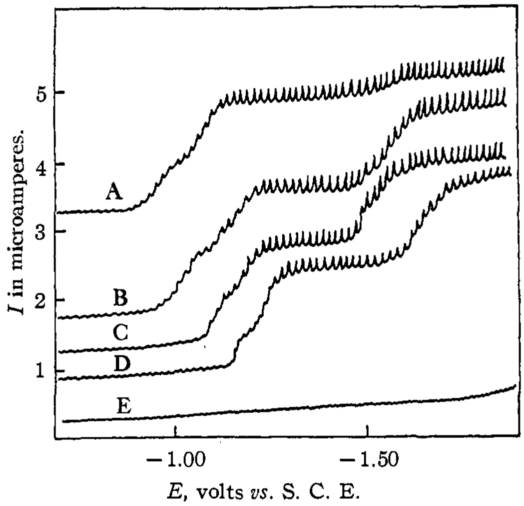


Fig. 7.—Chalcone polarograms (at $p$H 7.7): A, chalcone; B, 2'-hydroxychalcone; C, 2',4-dihydroxychalcone; D, 2',4',4-trihydroxychalcone; E, buffer blank.

The diffusion current constants ($i_d/c$), while somewhat more variable than those found for the flavones and flavanones, appear to fall in the range typical of one-electron electrode reactions; the values for chalcones are in the majority of cases in the range of 1–2. Wave analyses have been carried out for a number of the polarograms, the values found for $n$ being summarized in Table IV. In Fig. 8 are shown plots of $E$ vs. log $(i/i_d - 1)$ for the three waves of chalcone (23). The agreement between the evaluation of $n$ by this method and by estimation from diffusion current constants is shown by the data of Table IV, in which the $n$ values range from 0.7–1.4 for the

TABLE IV

| Chalcone | $p$H | 1/slope at $E = E_{1/2}$ | | $n$ |
|---|---|---|---|---|
| Unsubstituted | 8.9 | First | −0.068 | 1.1 |
| | 8.9 | Second | − .066 | 1.1 |
| | 6.1 | First | − .062 | 1.0 |
| | 6.1 | Second | − .054 | 0.9 |
| | 6.1 | Third | − .049 | .8 |
| 2'-Hydroxy | 6.1 | First | − .051 | .9 |
| | 6.1 | Second | − .039 | .7 |
| | 6.1 | Third | − .080 | 1.3 |
| | 9.6 | First | − .063 | 1.0 |
| | 9.6 | Second | − .057 | 1.0 |
| | 9.6 | Third | − .069 | 1.2 |
| 2',4',3,4-Tetrahydroxy | 6.1 | First (fused) | − .082 | 1.4 |
| | 6.1 | Third | − .050 | 0.8 |
| 2',4',6',4-Tetramethoxy | 8.9 | First (fused) | − .059 | 1.0 |

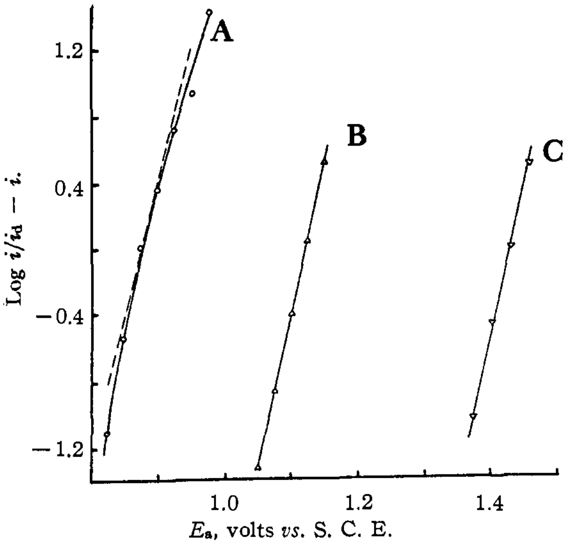
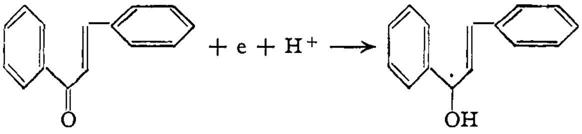


Fig. 8.—Wave analyses for the three waves of chalcone at *p*H 6.1: A, first wave; B, second wave; C, third wave.

fourteen cases listed. It appears that the conclusion is a sound one that the waves of the chalcone polarograms represent one-electron potential-determining reactions.

Of the three waves, the first two appear to depend upon the degree of hydroxylation of the chalcones. The third shows no such regular dependence upon structure. These relationships are shown more clearly in Figs. 9 and 10, in which are plotted $E_{1/2}$ values as functions of the *p*H at which they were measured (Fig. 9, averaged first and second waves; Fig. 10, third waves). The $E_{1/2}$ values become essentially *p*H-independent above *p*H values of about 8–9; and between *p*H 6–8 the slopes of the curves are reasonable approximations to 0.06 v./*p*H unit. This indicates the participation of hydrogen ions in the electrode reactions.

The dependence of the half-wave potentials upon the degree of hydroxylation resembles that observed in the cases of flavone and flavanone derivatives. The following initial electrode reaction is suggested



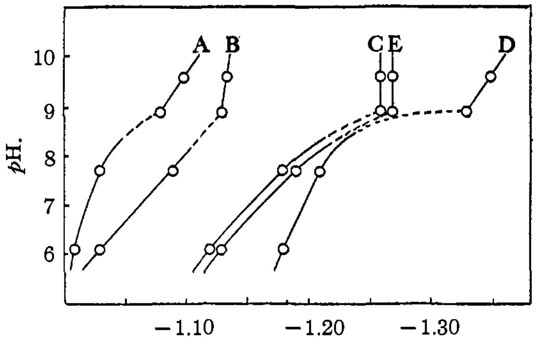


Fig. 9.—Variation of half-wave potential with *p*H: A, chalcone; B, 2'-hydroxychalcone; C, 2',4-dihydroxychalcone; D, 2',4',4-trihydroxychalcone; E, 2'-hydroxy-4',6',4-trimethoxychalcone.

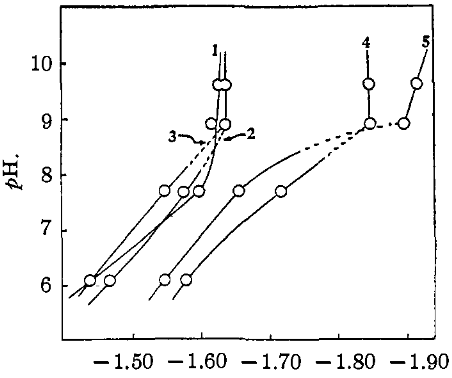


Fig. 10.—1, chalcone; 2, 2'-hydroxychalcone; 3, 2',4-dihydroxychalcone; 4, 2'-hydroxy-4',6',4-trimethoxychalcone; 5, 2',4',4-trihydroxychalcone.

The free radical produced can be stabilized by resonance involving a number of contributing forms, the important ones being represented by structures having the free electron on the *β*-carbon atom or at three positions in each of the aromatic rings. As in the case of the flavones, the considerable stabilization afforded by the participation of a number of structures makes it possible for a second electrode reaction to occur at higher potentials, leading to further reduction rather than to dimerization or disproportionation. The second wave can be the result of more than one kind of reduction of the free radical, but appears to be subject to the same kind of structural influences as affect the first wave. This is shown by the nature of the dependence of its half-wave potential upon structure and the fact that the effects of *p*H changes upon the first wave are also shown by the second wave.

The third waves show what appear at first sight to be erratic variation with those changes in substitution which cause regular variations in the first two waves. The data suggest the possibility

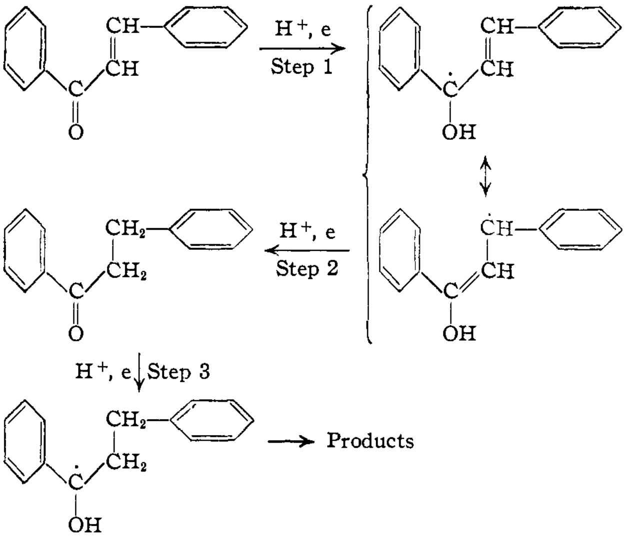
TABLE V

| Compound | $E_{1/2}(NH_4Cl)^a$ | $E_{1/2}$ at *p*H 6.1$^b$ |
|---|---|---|
| 2-OH Acetophenone | −1.46 | .... |
| 2'-OH Chalcone | .... | −1.47 |
| 2',4-diOH Chalcone | .... | −1.44 |
| 2,4-diOH Acetophenone | −1.60 | .... |
| 2',4',4-triOH Chalcone | .... | −1.55 |
| 2',4',3,4-tetraOH Chalcone | .... | −1.57 |

[a] Scaramelli[12] used 0.1 *N* ammonium chloride in 50% ethanol–water. [b] From Table I.

that the third wave represents the reduction of a substance which no longer possesses an $\alpha,\beta$-unsaturated carbonyl system, but which contains a structural element such as a carbonyl group attached to an aromatic ring. This supposition is supported by the observation that the third wave occurs at $E_{1/2}$ values in the range of those reported by Scaramelli[12] for hydroxylated acetophenone derivatives. The values in Table V show this correspondence.

From the considerations of the foregoing discussion, the following sequence of steps at the electrode can be suggested (using chalcone as a typical example).



This sequence of electrode reactions makes it possible to account for the occurrence of three waves, and also for the considerably greater ease of reduction of chalcones than of similarly substituted flavones and flavanones. If one compares the considerably greater possibility for resonance stabilization of the initial free radical, as compared with the original chalcone, with the corresponding differences between the unreduced and free-radical forms of flavones and flavanones, it is seen that the chalcone free radical is *preferentially* stabilized to the greatest degree, that of a flavone next, and that of a flavanone least. This is completely in accord with the relative ease of reduction at the electrode of chalcone > flavone > flavanone.

## Summary

A study has been made of the effect of substitution of hydroxyl, alkoxyl and acetoxyl groups upon the ease of reduction of a group of flavones, flavanones and chalcones at the dropping-mercury electrode. When these groups are present in positions conjugated with the carbonyl groups in these compounds, hydroxyl and methoxyl groups decrease, and acetoxyl groups increase, the ease of reduction.

The results have been interpreted in terms of one-electron electrode reactions and the relative stabilities of the unreduced compounds and the initial free radicals produced in the first stage of the electrode process.

Flavanones give single-wave, flavones double-wave and chalcones triple-wave polarograms. It is suggested that these behaviors are due to the successive reduction at the electrode of the unreduced compound and one-electron-reduced intermediates.

LOS ANGELES, CALIFORNIA RECEIVED JULY 5, 1949

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[CONTRIBUTION NO. 17 FROM THE THERMODYNAMICS LABORATORY OF THE PETROLEUM EXPERIMENT STATION, BUREAU OF MINES]

# Experimental Vapor Heat Capacities and Heats of Vaporization of 2-Methylpentane, 3-Methylpentane and 2,3-Dimethylbutane[1]

BY GUY WADDINGTON, J. C. SMITH,[2] D. W. SCOTT AND H. M. HUFFMAN

This paper is a further contribution from the thermodynamic research program of the Petroleum and Natural-Gas Branch of the Bureau of Mines. The vapor heat capacities and heats of vaporization of 2,2-dimethylbutane and *n*-hexane have already been measured in this Laboratory.[3] Similar data for the three remaining hexanes are presented here. In the case of the heat-capacity measurements, the temperature range was from approximately the normal boiling point of the compound to 200°. Heats of vaporization were determined at temperatures corresponding to saturated pressures of about one-quarter, one-half and one atmosphere.

## Experimental

**Apparatus and Method.**—Since the apparatus and experimental procedures used were essentially as described in detail in an earlier paper,[4] only a brief account of them will be given here.

A measured, constant flow of hydrocarbon vapor was produced by electrical heating in a cycling vaporizer. This was passed through a flow calorim-

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[1] Not subject to copyright.

[2] Present address: Army Chemical Center, Edgewood, Maryland.

[3] Waddington and Douslin, THIS JOURNAL, **69**, 2275 (1947).

[4] Waddington, Todd and Huffman, *ibid.*, **69**, 22 (1947).