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FLAVONOIDS—VI*

THE PREPARATION AND REACTIONS OF THE EPOXIDES OF 2′-HYDROXY-CHALCONE DERIVATIVES

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Abstract—The epoxides of 2′-methoxy-, 2′-benzyloxy- and 2′-*p*-nitro-benzyloxy-chalcone have been prepared. They are resistant to alkalis, and undergo with acids, particularly hydrogen chloride, two kinds of transformation depending on the O-substituent: (a) formation of flavanon-3-ol, (b) formation of chlorohydrins. With $SnCl_4$ in benzene the epoxides give the corresponding chlorohydrins. The mechanisms and structural problems of the reactions are discussed.

Several workers have investigated the preparation and properties of chalcone epoxides.[1–4] While the epoxides of simple chalcones can readily be prepared, epoxidation with alkaline peroxide of chalcones containing an unsubstituted free 2′-hydroxyl group has not been accomplished. Under these conditions, either the so-called Algar-Flynn-Oyamada reaction occurs, resulting in flavon-3-ol,[5,6] or a flavonon-3-ol is obtained from 2′-hydroxy-chalcones.[7,8] According to Oyamada[6] and Murakami and Irie,[7] the flavanone formed from the chalcone is oxidized in the course of the reaction to flavanon-3-ol. Reichel *et al.*, however, presume that the hydrogen peroxide reacts exclusively with the 2′-hydroxy-chalcone and that a HOO^- ion attaches itself to the double bond of the chalcone, followed by the isomerization of this intermediate to flavanon-3-ol. Even Algar and Flynn,[5] as well as other authors[9] suppose that oxidation of 2′-hydroxychalcones with alkaline peroxide involves the intermediary formation of the corresponding epoxides. These reactive epoxides are transformed in alkaline media into flavanon-3-ol as a result of the nucleophilic attack by the hydroxyl or phenolate ion.[10]

Marathey[11] was the first to report the preparation of a 2′-hydroxychalcone epoxide derivative by treating the bromohydrine derived from 2′-acetoxy-3′, 4′-benzo-4-methoxy-chalkone dibromide, with sodium acetate. The resulting 2′-acetoxy-3′, 4′-benzo-4-methoxychalcone epoxide gives 4′-methoxy-7, 8-benzoflavanon-3-ol on treatment with sodium carbonate in acetone.

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* Part V: R. Bognár, I. Farkas and M. Rákosi, *Magyar Kémiai Folyóirat* **67**, 253 (1961).

[1] E. Weitz and A. Scheffer, *Ber. Dtsch. Chem. Ges.* **54**, 2327 (1921).

[2] W. B. Black and R. E. Lutz, *J. Amer. Chem. Soc.* **75**, 5990 (1953).

[3] H. H. Wasserman and N. E. Aubry, *J. Amer. Chem. Soc.* **77**, 590 (1955).

[4] H. E. Zimmerman, L. Singer and B. S. Thyagarajan, *J. Amer. Chem. Soc.* **81**, 108 (1959).

[5] J. Algar and J. P. Flynn, *Proc. Roy. Irish Acad.* B. **42**, 1 (1934); *Chem. Abstr.* **29**, 161 (1935).

[6] T. Oyamada, *Bull. Chem. Soc. Japan* **10**, 182 (1935); *Chem. Abstr.* **29**, 4358 (1935).

[7] M. Murakami and T. Irie, *Proc. Imp. Acad. Tokyo* **11**, 229 (1935); *Chem. Abstr.* **29**, 6598 (1935).

[8] L. Reichel and J. Steudel, *Liebigs Ann.* **553**, 83 (1942).

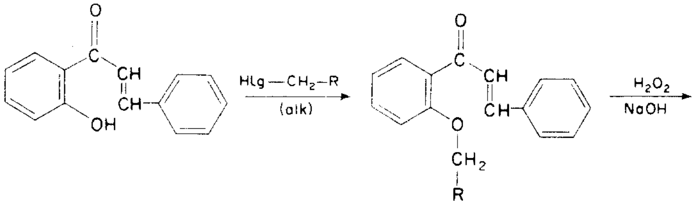
[9] T. S. Wheeler, *Rec. Chem. Prog.* **18**, 133 (1958); R. Bognár and M. Rákosi, *Acta Chim. Hung.* **14**, 369 (1958).

[10] R. Bognár, *Acta Univ. Debreceniensis* VI/2. 99 (1959–60).

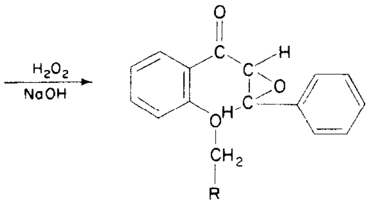
[11] M. G. Marathey, *Sci. and Cult. India* **20**, 135 (1954); *Chem. Abstr.* **49**, 14753 (1955).

The epoxidation and some reactions of substituted 2′-hydroxychalcone derivatives has been investigated and it has been established that epoxide formation takes place when the hydroxyl group is substituted, and that the epoxides are intermediates in the formation of flavanon-3-ols.

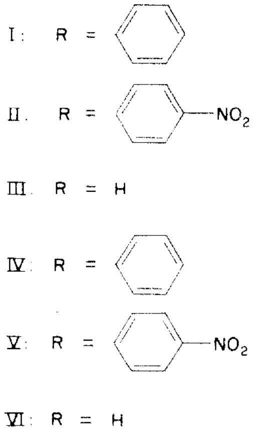
The following O-substituted chalcones, 2′-benzyloxy-(I), 2′-p-nitrobenzyloxy-(II) and 2′-methoxy-chalcone (III) have been prepared by reacting the 2′-hydroxychalcones with benzyl chloride, *p*-nitrobenzyl bromide and methyl iodide respectively.



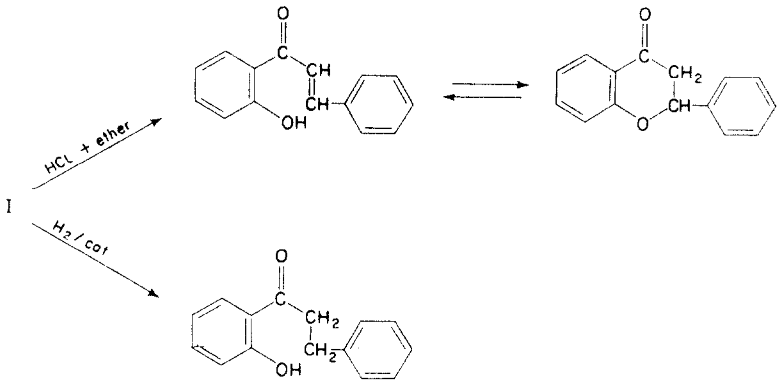
I, II, III



IV, V, VI



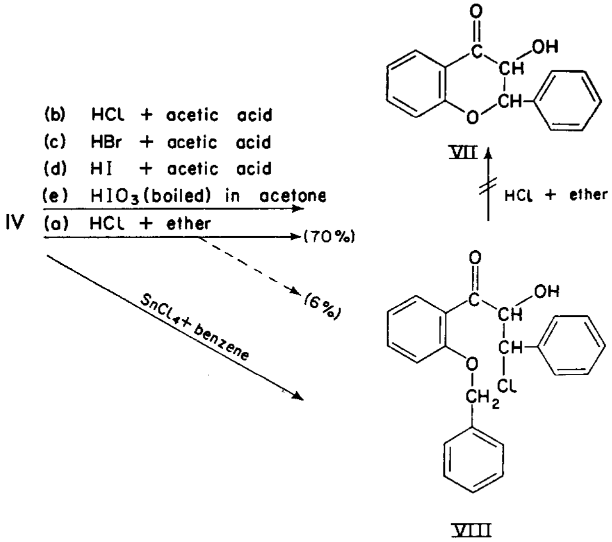
2′-Benzyloxy-chalcone (I) gives 2′-hydroxy-chalcone, and flavanone on treatment with ethereal hydrogen chloride; catalytic hydrogenation leads to 2′-hydroxy-phenyl-propiophenone.



2′-*p*-Nitrobenzyloxy-chalcone (II), like 2′-methoxy-chalcone (III), cannot be hydrolysed with ethereal hydrogen chloride. According to Weitz and Scheffer,[1] the above 2′-hydroxy-chalcone derivatives, give over 90% yield of the corresponding crystalline chalcone epoxides IV, V and VI (the α, β-epoxyketone derivatives) when treated with hydrogen peroxide in the presence of sodium hydroxide. Sodium hydroxide (3 per cent) in water or alcohol does not open the epoxide ring of the 2′-*p*-benzyloxy-chalcone epoxide (IV) even on prolonged heating at 140° in a bomb. According to Stenmark,[12] the epoxide (IV) can be titrated in dioxane solution with hydrochloric acid, but the action of acid does not consist of simple epoxide ring fission with the formation of the halohydrin as would be expected.

At room temperature in ethereal solution saturated with hydrogen chloride the epoxide (IV) decomposes rapidly to give a good yield (70 per cent) of a halogen-free product which separates as crystalline *flavanon-3-ol* (VII). The latter is also formed in high yields when 2′-benzyloxy-chalcone-epoxide in glacial acetic acid is treated at room temperature with HCl, HBr, or HI, or if boiled with iodic acid in acetone solution. The benzyl-halogenide formed as a by-product can be identified in the reaction mixture.

The reaction with hydrogen chloride in ether gives in addition to flavanon-3-ol a small amount (10 per cent or less) of the corresponding halohydrin, as a result of a simultaneous side reaction. The latter product may be prepared in high yields, in fact it is the chief product if, according to House[13], 2′-benzyloxy-chalcone epoxide in benzene is reacted with $SnCl_4$. In this way 1-(*2′-benzyloxy-benzoyl*)-*2-phenyl-ethylene-chlorohydrin* (VIII) is obtained in very good yield and is identical with the halohydrin obtained as a by-product in the formation of flavanon-3-ol in the HCl–ether reaction. The structure of the halohydrins has not been investigated but they are probably anlogous to the chlorohydrins prepared by House who showed that an α-hydroxy-β-chloro-ketone was obtained from benzalacetophenone-epoxide.



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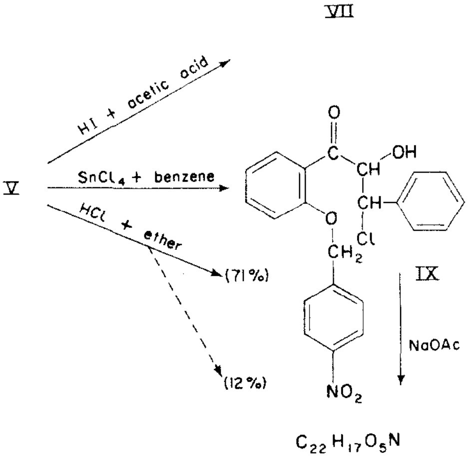
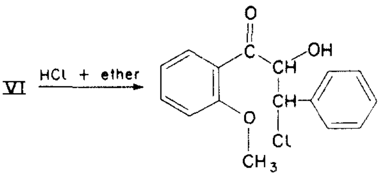
[12] G. A. Stenmark, *Analyt. Chem.* **29**, 1367 (1957).
[13] H. O. House, *J. Org. Chem.* **21**, 1306 (1956).

2′-*p*-Nitrobenzyloxy-chalcone-epoxide (V) gives 1-(2′-*p*-nitrobenzyloxy-benzoyl)-2-phenyl-ethylene chlorohydrin (IX) on treatment either with ethereal HCl or with $SnCl_4$ in benzene solution, and no flavanon-3-ol was isolated from the reaction products. Only by warming in acetic acid with hydrogen iodide could a small yield (under 10 per cent) of flavanon-3-ol (VII) be obtained from *p*-nitrobenzyloxy-chalcone epoxide.

A thorough investigation of the reaction mixture has revealed another side reaction during the HCl + ether reaction of 2′-*p*-nitrobenzyloxy-chalcone-epoxide. After the separation of the chlorohydrin it is possible to isolate a crystalline nitrogenous substance. This same compound may be obtained as the main product from the chlorohydrin, if its alcoholic solution is warmed for a short time in the presence of sodium acetate. Its empirical formula corresponds to 2′-*p*-nitrobenzyloxy-chalcone epoxide and it is believed that it is possibly the corresponding *cis*-epoxide.



The above methods are not suitable for preparing flavanon-3-ol from 2′-methoxy-chalcone-epoxide (VI). The corresponding chlorohydrin (X) is obtained in very good yield (80 per cent) in ethereal hydrogen chloride solution.



X

On the basis of these reactions the following conclusions may be drawn:

(1) 2′-Hydroxy-chalcone epoxides can be prepared if the OH-group in the 2′-position is substituted.

(2) The epoxides are stable to alkalis, i.e., fission of the epoxide ring does not occur.

(3) With $SnCl_4$ in benzene the epoxides give the corresponding chlorohydrins in good yield.

(4) The action of acids, particularly hydrogen halides, depends on the substituents and may result in

(*a*) formation of flavanon-3-ol by splitting off the O-substituent, or

(*b*) formation of the corresponding halohydrin with retention of the original O-substituent.

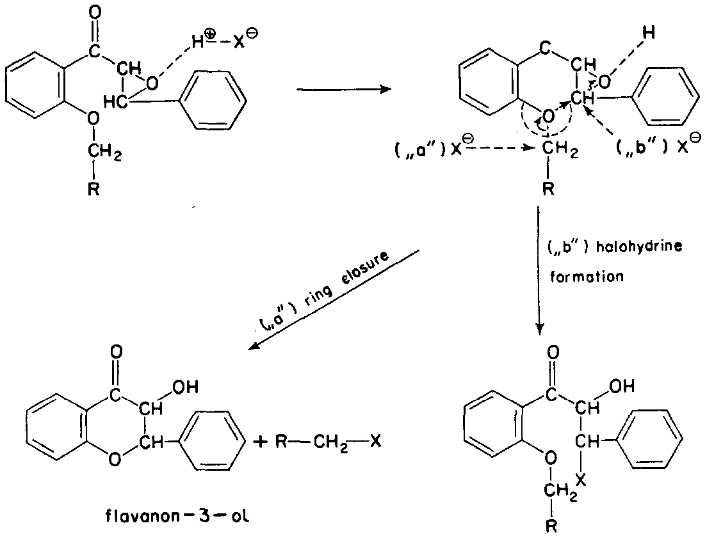
In connection with the course and mechanism of these two reactions, the following may be concluded:

(*a*) The formation of flavanone does not take place via the halohydrin as an intermediate, but proceeds directly from the epoxide, since according to our observations 2′-benzyloxy chlorohydrin is not affected by hydrogen chloride in ether. This is further confirmed by the formation of flavanon-3-ol by the action of iodic acid on the epoxide.

(*b*) It is reasonable to suppose that the O-benzyl group is split off simultaneously with the formation of the flavanon-3-ol, since 2′-benzyloxy-chalcone itself decomposes only very slowly in ethereal HCl. While the formation of flavonol from the epoxide starts after a few minutes, in the case of 2′-benzyloxy-chalcone it is only after 15 hours under similar conditions that the splitting of the benzyl group occurs. Therefore, it is not probable that the splitting off of the benzyl group precedes the formation of the pyranone ring.

(*c*) In those cases, where due to the O-substituents the ethereal C—O bond is split with difficulty or not at all, the flavanon-3-ol formation is poor (e.g. in V) or it fails entirely (e.g. in VI). In these instances the main products are the halohydrins.

On the basis of these arguments, the formation of flavanon-3-ol and of the chlorohydrin, result from one of two alternative nucleophilic reactions, may be formulated as follows:



Concerning the stereochemistry of the compounds and the steric course of the reactions, the following conclusions may be drawn:

Based on the work of Zimmermann[4] and Lutz *et al.*[2,14] it may be assumed that the

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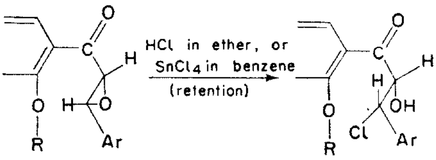
[14] R. E. Lutz and J. O. Weiss, *J. Amer. Chem. Soc.* 77, 1814 (1955).

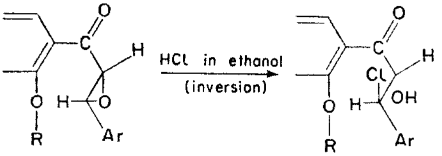
epoxides obtained with alkaline peroxides are *trans*. These authors have established that irrespective of the *cis* or *trans* structure of the starting chalcone, *trans*-epoxides are formed. According to Lutz, *cis*-chalcone is stable towards alkalis, so that it is not a case of the formation of *trans*-chalcone by the isomerization of the *cis*-compound; according to Zimmermann the chalcone epoxide formation is a characteristic "stereoselective" reaction.

Depending on whether the opening of the *trans*-epoxides has taken place with retention or with inversion, the resulting chlorohydrin will have *threo* or *erythro* configuration.

According to House,[13] the action of ethereal HCl or of $SnCl_4$ in benzene usually



Chlorohydrin with threo config.

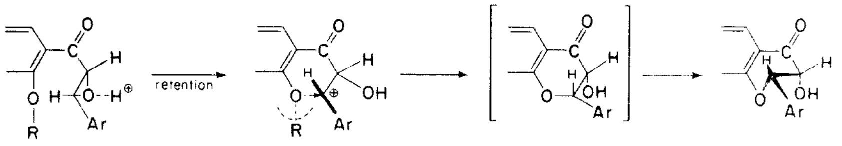


Chlorohydrin with erythro config.

results in products with the *threo* configuration. It is probable that in the present work the $SnCl_4$ as well as the hydrogen chloride have led to chlorohydrins with *threo* configuration, since the experimental conditions were the same as those used by House.[13]

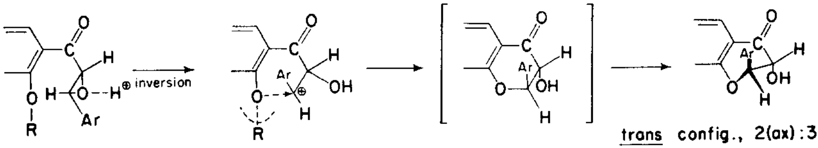
During the formation of flavanon-3-ol there are also two possibilities for the opening of the epoxide ring. If the configuration is retained during fission, then the flavanon-3-ol obtained will have *cis* configuration, and probably (2eq):(3ax) conformation. If, however, the pyranone ring formation, i.e., the opening of the epoxide followed by the nucleophylic attack of the O is accompanied by inversion, then *trans* flavanon-3-ol with (2eq):(3eq) conformation will result.

(a) *If the configuration is retained during ring closure:*

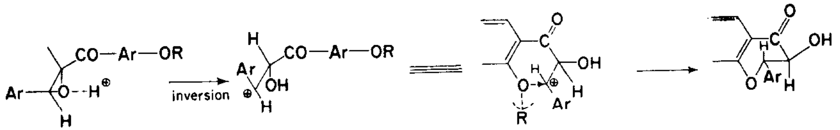


cis config., 2(eq):3(ax) flavanon-3-ol

(b) *If inversion takes place during ring closure:*



trans config., 2(ax):3(ax)-flavanon-3-ol (d-, or l-form)



trans config., 2(eq): 3(eq)-flavanon-3-ol (d-, or l-form)

The formation of flavanon-3-ol is accompanied by ring closure, and as the reaction probably follows an internal S_N2 mechanism, inversion may be expected. The flavanon-3-ols formed in this way are the same as those obtained by the direct oxidation of the chalcone with alkaline peroxide. Mahesh and Seshadri,[15] and Bognár and Rákosi[16] have independently suggested that in these compounds the phenyl and hydroxyl groups are in the *trans* configuration and have (2eq):(3eq) conformation.

EXPERIMENTAL

2′-*Benzyloxy-chalcone* (I)

(a) *from 2′-hydroxy-chalcone.* 2′-Hydroxychalcone (22·4 g, 0·1 mole) was dissolved in warm ethanol (180 ml) followed by the addition of 50% aqueous NaOH (40 g) and benzyl chloride (26·0 g, 0.2 mole). The mixture was stirred and heated under reflux on the water bath for 2 hr. The initially precipitated sodium salt of 2′-hydroxychalcone gradually dissolved, and sodium chloride separated. The reaction mixture diluted with a large volume of water was extracted with ether and the dried extract (Na_2SO_4) distilled after removal of the solvent. The benzyl alcohol, ethyl benzyl ether and unreacted benzyl chloride were distilled under red press at 80–100° leaving a yellowish-red, thick, syrupy liquid which solidified on standing and rubbing with a glass rod. The 2’-benzyloxy-chalcone (21 g, 67%) recrystallized from ethyl alcohol in pale yellow, long needles m.p. 84·5–85·5°; soluble in acetone, benzene, and ether, sparingly soluble in cold methanol and ethanol. (Found: C, 84·38; 84·18; H, 5·70; 5·76; $C_{22}H_{18}O_2$ requires: C, 84·05; H, 5·77%.)

The U.V. spectrum of a 0·001 molar solution in ethanol has λ_{max} at 306 mμ (Fig. on p. 151).

(b) *from the sodium salt of 2′-hydroxychalcone* 2′-Hydroxy-chalcone (22·4 g was dissolved in a small quantity of acetone and 50% aqueous NaOH added (20–30 ml). The mixture was shaken at room temp until complete separation of the orange coloured crystalline sodium salt, yield 90% after washing with acetone and drying. The sodium salt (24·6 g, 0·1 mole) was suspended in a solution of benzyl chloride (19·0 g, 0·15 mole in acetone 100 ml), the mixture boiled for 2 hr with stirring and then treated as under (a) yielding 24·0 g; 76%. The benzylation may also be carried out in ethanol, to give a yield of 60–70%.

Catalytic hydrogenation of 2′-benzyloxy-chalcone

2′-Benzyloxy-chalcone (0·5 g) in ethanol (60 ml) was hydrogenated at atm press and room temp in the presence of palladized charcoal (10–12% Pd). In 1 hr 74·6 ml H_2 at N.T.P. was absorbed (calculated for 2 moles of H_2: 71·3 ml). The solution, free from catalyst, was evaporated to 10–15 ml

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[15] V. B. Mahesh and T. R. Seshadri, *Proc. Ind. Acad. Sci.* **41**, 210 (1955).

[16] R. Bognár and M. Rákosi, *Chem. & Ind.* 188 (1956); *Acta Chim. Hung.* **14**, 369 (1958).

in vacuo, decolorized and left to crystallize. The product, m.p. 33–34°, was identical with authentic[17] 2′-hydroxy-phenyl-propiophenone by mixed m.p. determination.

The action of hydrogen chloride on 2′-benzyloxychalcone

2’Benzyloxychalcone (0·65 g) was dissolved in anhydrous ether (10 ml) saturated with HCl and allowed to stand 6 hr at room temp.

Evaporation of one half of the solution yielded the starting compound with only traces of phenolic material with free hydroxyl groups. The other half after standing an additional 15–16 hr yielded 2′-hydroxychalcone (0·24 g). It was identified by m.p., mixed m.p., and conversion into flavanone.

2′-Benzyloxychalcone epoxide

2′-Benzyloxy-chalcone (3·14 g) was dissolved in acetone (30 ml) and a mixture of 15% H_2O_2 (5 ml), 2 N NaOH (5 ml) and methanol (10 ml) was added. The mixture was shaken for 1 hr and occasionally brought to boiling point. Then an equal volume of water was added causing crystallization. Recrystallization from alcohol or acetone yielded pure 2′-benzyloxy-chalcone epoxide in colourless prisms. (3·1 g, 94%); m.p. 111·5–113°. (Found: C, 80·06; 79·78; H, 5·39, 5·52, $C_{22}H_{18}O_3$ requires: C, 79·98; H, 5·49%).

Epoxide determination: 0·0715 g required 0·0076 g HCl; calc. weight of HCl required for the fission of the epoxide ring: 0·0079 g.

The U.V. spectrum of the 0·001 molar solution in ethanol has two maxima: $\lambda_{max_1} = 259$ mμ and $\lambda_{max_2} = 315$ mμ (Fig. on p. 151).

Flavanon-3-ol (VII) *from 2′-benzyloxy-chalcone-epoxide* (IV)

(a) *The action of ethereal hydrogen chloride.* 2′-Benzyloxy-chalcone-epoxide (3·30 g) was dissolved in ether (30 ml) saturated with dry hydrogen chloride at 0° and shaken for 20 min at room temp. The prismatic crystals of the epoxide dissolved and shiny crystals separated yielding altogether 1·97 g (70%) of the product. Recrystallization from alcohol resulted in colourless needles, m.p. 178–180°, with no m.p. depression with authentic flavanon-3-ol. The U.V. spectrum was also identical with that of flavanon-3-ol obtained from 2′-oxy-chalcone by the action of alkaline peroxide. ($\lambda_{max_1} =$ 252 mμ; $\lambda_{max_2} = 321$ mμ) (Found: C, 74·48; H, 4·98, 4·92. $C_{15}H_{12}O_2$ requires: C, 74·98; H, 5·04%.)

After the separation of flavanon-3-ol, the ethereal solution on evaporation yielded an oily residue (1·6 g) smelling of benzyl chloride. This was dissolved in alcohol, purified with active charcoal, and crystallized. A small quantity (0·12 g, 6%) of a product, m.p. 106–107·5°, containing chlorine was obtained, identical with the halohydrin prepared according to House. (See below.)

(b) *The action of hydrogen chloride in acetic acid.* 2′-Benzyloxy-chalcone-epoxide (3·30 g) was dissolved in 20 ml hot acetic acid, 20 drops conc HCl added and the solution left at room temp. On addition of water (50 ml), precipitation began. The product was recrystallized from alcohol (1·78 g; 69%, m.p. 178–180°). Attempts to obtain crystalline products from the mother-liquor were unsuccessful.

(c) *The action of hydrogen bromide in glacial acetic acid.* 2′-Benzyloxy-chalcone-epoxide (0·66 g) when treated as under (b), but substituting a corresponding amount of HBr for the HCl, yielded 0·38 g (67%) flavanone-3-ol.

(d) *The action of hydrogen iodide in glacial acetic acid,* 2′-Benzyloxy-chalcone-epoxide (0·66 g) when treated with HI as under (b) and (c), gave 0·30 g (50%) flavanon-3-ol. In this case again it was not possible to isolate the halohydrin.

(e) *The action of iodic acid in acetone.* 2′-Benzyloxy-chalcon-epoxide (0·66 g) was dissolved in acetone (15 ml) and iodic acid (0·4 g) in water (5 ml) was added and the mixture heated under reflux for 15 min. The clear filtrate free from oily by-product, was diluted with water, when flavanon-3-ol separated as shiny crystals (0·35 g, 62%).

1-(*2′-Benzyloxy-benzoyl*)-*2-phenyl-ethylene-chlorohydrin* (VIII)

2′-Benzyloxy-chalcone-epoxide (1·0 g) was dissolved in anhydrous benzene (50 ml). On the addition of $SnCl_4$ (1 ml) the solution turned dark. After ½ hr at room temp, cold water (100 ml) was

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[17] R. Bognár and M. Rákosi, *Acta Chim. Hung.* **13,** 217 (1957); K. Freudenberg and L. Orthner, *Ber. Dtsch. Chem. Ges.* **65,** 1748 (1922).

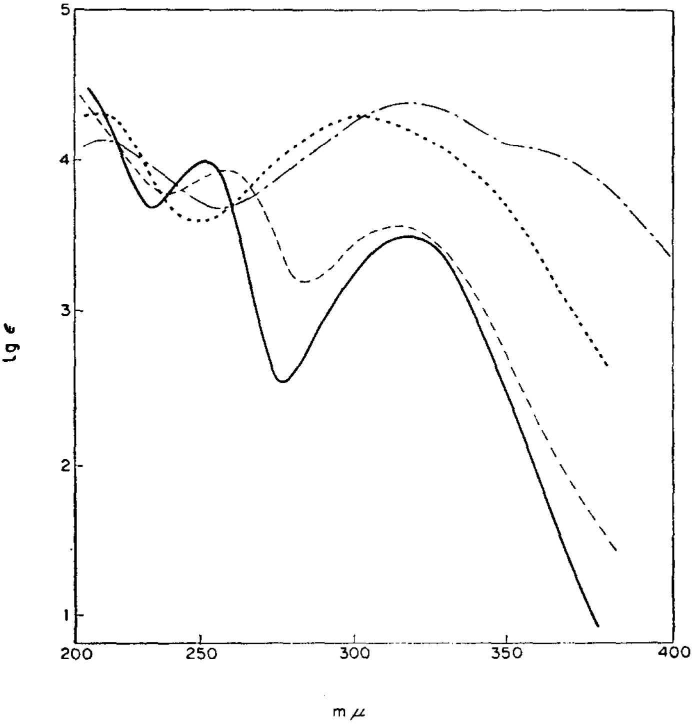

FIG. 1. U.V. spectra.

- · - · - 2′-Hydroxy-chalcone
· · · · · · · 2′-Benzyloxy-chalcone
– – – – – 2′-Benzyloxy-chalcone epoxide
——— Flavanon-3-ol.

added and the benzene layer washed with water, dried (Na_2SO_4) and evaporated. The impure chlorohydrin (1·02 g, 92%) recrystallized from alcohol as colourless needles; (0·98 g; 88%) m.p. 106–107°. (Found: Cl, 9·65; 9·62. $C_{22}H_{19}O_3Cl$ required: Cl, 9·70%). This was identical with the by-product obtained by treating 2′-benzyloxy-chalkone-epoxide with ethereal hydrogen chloride (see above). A mixed m.p. of the two products was not depressed.

The action of ethereal hydrogen chloride on 2′-benzyloxy-chalcone halohydrin

Halohydrin (0·73 g) in ether (15 ml) saturated with HCl was allowed to stand 48 hr, and then evaporated *in vacuo* and the yellowish residue recrystallized from alcohol yielding a compound (0·64 g, 86%; m.p. 106–107°) identical with the starting material. When the mother liquor used for the recrystallization was evaporated, a small quantity of oil remained; its alcoholic solution gave a brown colour with 1% ferric chloride.

2′-p-*Nitrobenzyloxy-chalcone* (II)

The sodium salt of 2′-hydroxy-chalcone (24·6 g, 1 mol) was suspended in a solution of *p*-nitrobenzylbromide (22 g, 0·1 mole) in acetone (150 ml) and the mixture boiled under reflux for ½ hr. The sodium salt dissolved, sodium bromide separated and the dark red mixture became orange. Water was added to the warm solution until it turned cloudy. The needle shaped crystals were separated from the cold solution, washed and dried (30 g; 83%). The crude product was recrystallized from excess acetone to give pure material (28 g; 78%), m.p. 131–131·5°. (Found : C, 73·61, 73·60; H, 4·75, 4·80; N, 3·78, 3·76. $C_{22}H_{17}O_4N$ requires: C, 73·43; H, 4·77; N, 3·9%.)

2′-p-*Nitrobenzyloxy-chalcone epoxide* (V)

(a) 2′-*p*-Nitrobenzyloxy-chalcone (0·72 g) was dissolved in hot methanol (50 ml) and 30% hydrogen peroxide (2 ml) and 2N NaOH (1·5–2 ml) added. After shaking at room temp for ½ hr, a colourless crystalline precipitate separated. About an equal volume of water was added with stirring to complete the separation of the crystalline material (0·75 g; 98%; m.p. 170–175°) which recrystallized from acetone or alcohol. The epoxide forms colourless prisms (0·68 g; 91%; m.p. 176·5–178°). Additional recrystallization from glacial acetic acid left the m.p. unchanged. (Found: C, 70·42, 70·45; H, 4·45. 4·56; N, 3·62, 3·68. $C_{22}H_{17}O_5N$ requires: C, 70·39; H, 4·57; N, 3·73%.)

(b) The epoxide formation can also be carried out in acetone. 2′-*p*-Nitrobenzyloxy-chalcone (3·59 g) in hot acetone (80–100 ml) yielded 86% (3·25 g) of pure recrystallized epoxide when treated with 30% hydrogen peroxide (5 ml) and 2 N NaOH (5 ml) in the presence of methanol (10 ml).

1-(2′-p-*Nitrobenzyloxy-benzoyl*)-2-*phenyl-ethylene chlorohydrin* (IX)

(a) *By the action of hydrogen chloride in ether.* 2′-*p*-Nitrobenzyloxy-chalcone epoxide (3·75 g) was suspended in ether (20 ml) saturated with HCl and the mixture allowed to stand for 20 hr. The chlorohydrin was recrystallized from alcohol or carbon tetrachloride as colourless needles (3·10 g; 71%) m.p. 144–146° dec. (Found: Cl, 8·51, 8·58; N, 3·42, 3·46; $C_{22}H_{18}O_5NCl$ requires: Cl, 8·61; N, 3·42%.)

After the separation of the impure halohydrin, pet ether (b.p. 60–90°) was added and the yellow oil which separated solidified after a few days standing at 5°. This product recrystallized from alcohol and then from a mixture of benzene and pet ether as pale yellow platelets (0·45 g; 12%, m.p. 123–124°) and was identical with the unknown halogen-free derivative, which was prepared in good yield by the action of sodium acetate on the halohydrin (q.v.).

(b) *With* $SnCl_4$ *in benzene.* The epoxide (1·0 g) was suspended in dry benzene (80 ml) and $SnCl_4$ (2 ml) added giving a yellow solution. After 15 min, cold water (100 ml) was added causing the thick, dark brown oil which had separated to dissolve in the benzene layer and the mixture carefully heated on the water bath. This benzene layer was separated, washed with water and dried (Na_2SO_4), and evaporated *in vacuo*. The chlorohydrin was recrystallized from alcohol as colourless needles (0·7 g; m.p. 140–144°). On evaporating the mother liquor a further 0·15 g of product separated. From the combined products, a further recrystallization gave altogether 0·78 g (71%) m.p. 144–146° dec, and identical with the product of process (a) by mixed m.p. determination.

Product of unknown structure resulting from the action of sodium-acetate on p-*nitrobenzyloxy-chalkone chlorohydrin*

Halohydrin (0·82 g, 0·002 mole) and sodium acetate (0·32 g, 0·004 mole) were dissolved in ethanol (10 ml), refluxed for 15–20 min and the homogeneous solution allowed to cool. The crystals which separated (0·54 g; 72%), washed free from sodium acetate with water, recrystallized from benzene–pet ether as pale yellow platelets (0·50 g; 67%); m.p. 124–125°.

This compound did not depress the m.p. of the halogen-free by-product obtained when the epoxide was treated with ethereal HCl (see above). It gave no colour with ferric chloride and did not react with *o*-phenylene-diamine. On the basis of its analysis (C: 69·89, 69·82; H: 4·78, 4·75%), its nitrogen content and the absence of halogen, it is probable that its empirical formula is the same as that of the original 2′-*p*-nitrobenzyloxy-chalcone epoxide, ($C_{22}H_{17}O_5N$), and it may be an isomer of this compound. This supposition requires additional analytical and experimental proof.

Flavanon-3-*ol* (VII) *from* 2′-p-*nitrobenzyloxy-chalcone epoxide* (V)

2′-*p*-Nitrobenzyloxy-chalcone (0·75 g) epoxide was dissolved in acetic acid (10 ml) and HI (1 ml; sp. gr. 1·4) added. The mixture was allowed to stand for 5–6 hr at room temp and then diluted with water. The resinous material which separated was extracted several times with alcohol and the solution purified with activated carbon and evaporated to a small volume. A small quantity (0·04–0·05 g) of flavanon-3-ol was obtained.

2′-*Methoxy-chalcone-epoxide* (III)

2′-Methoxychalcone (1·2 g) was dissolved in methanol (20 ml) and 30% hydrogen peroxide (2 ml) and 2N NaOH (2 ml) added. The mixture was boiled under reflux for 15 min. Colourless needles of the epoxide (1·15 g; 90%; m.p. 124–127°; lit,[18] m.p. 125°) separated on cooling and was suitable for the preparation of the chlorohydrin without further purification.

1-(2′-*Methoxy-benzoyl-2-phenyl*)-*ethylene-chlorohydrin* (X)

The 2′-methoxy-chalcone-epoxide (1·1 g) was dissolved in dry ether (15 ml), saturated with HCl and the solution left for 6–7 hr at room temp. The mixture was then evaporated *in vacuo*, and the yellowish-brown residue recrystallized from alcohol. A good yield (0·92 g; 80%) of the chlorohydrin was obtained, m.p. 103–104°. (Found: Cl, 12·47, 12·42; $C_{16}H_{14}O_2Cl$ requires: Cl: 12·25%.)

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[18] C. Enebäck and J. Gripenberg, *Acta Chem. Scand.* **11**, 866 (1957).