Tetrahedron. Vol 26, pp. 2545 to 2554. Pergamon Press 1970. Printed in Great Britain

FLAVANOID EPOXIDES—VII[1]

FLAVINDOGENIDE CHLOROHYDRINS[2]

J. R. DOHERTY, D. D. KEANE, K. G. MARATHE, W. I. O'SULLIVAN and E. M. PHILBIN
Department of Chemistry, University College, Belfield, Dublin 4, Ireland

and

R. M. SIMONS and P. C. TEAGUE
Department of Chemistry, University of South Carolina, Columbia, S.C., U.S.A.

(*Received in the UK* 27 *January* 1970; *Accepted for publication* 4 *February* 1970)

Abstract—Three of the four possible isomeric 3-hydroxy-β-chloroflavindogenide chlorohydrins have been prepared by the action of hydrogen chloride in benzene–ether on flavindogenide epoxides.[1] The configurations of the chlorohydrins have been determined and the structures of the epoxides from which they are derived have been correlated. Attempts to prepare the fourth isomeric flavindogenide halohydrin are described. The mechanism of the epoxide ring opening reaction is discussed.

RESULTS

trans,trans-FLAVINDOGENIDE epoxides (IIIb, c)[3] on treatment with dry hydrogen chloride in benzene–ether caused the epoxide ring to open with inversion of configuration at the point of attack (*trans*-opening) to yield *erythro,trans*-chlorohydrins (VIIb, c). Cyclization of the latter compounds with base regenerated the original epoxides. On the other hand, treatment of *trans,cis*- (IVb, c) and of *cis,trans*- (Vb, c) and *cis,cis*- (VIb, c) flavindogenide epoxides with hydrogen chloride in benzene–ether caused the epoxide ring to open with retention of configuration (*cis*-opening) to give *threo,cis*- (VIIIb, c), *erythro,trans*- (VIIb, c) and *erythro,cis*-chlorohydrins (IXb, c) respectively. Cyclization of chlorohydrins (VIIIb, c) gave *cis,cis*-epoxides (VIb, c) and cyclization of chlorohydrins (IXb, c) yielded *trans,cis*-epoxides (IVb, c). Although the crude reaction mixtures were not analysed for other products, the consistently high yields (in the order of 90%) for the reactions indicated almost exclusive formation of the of the products shown in Scheme 1.

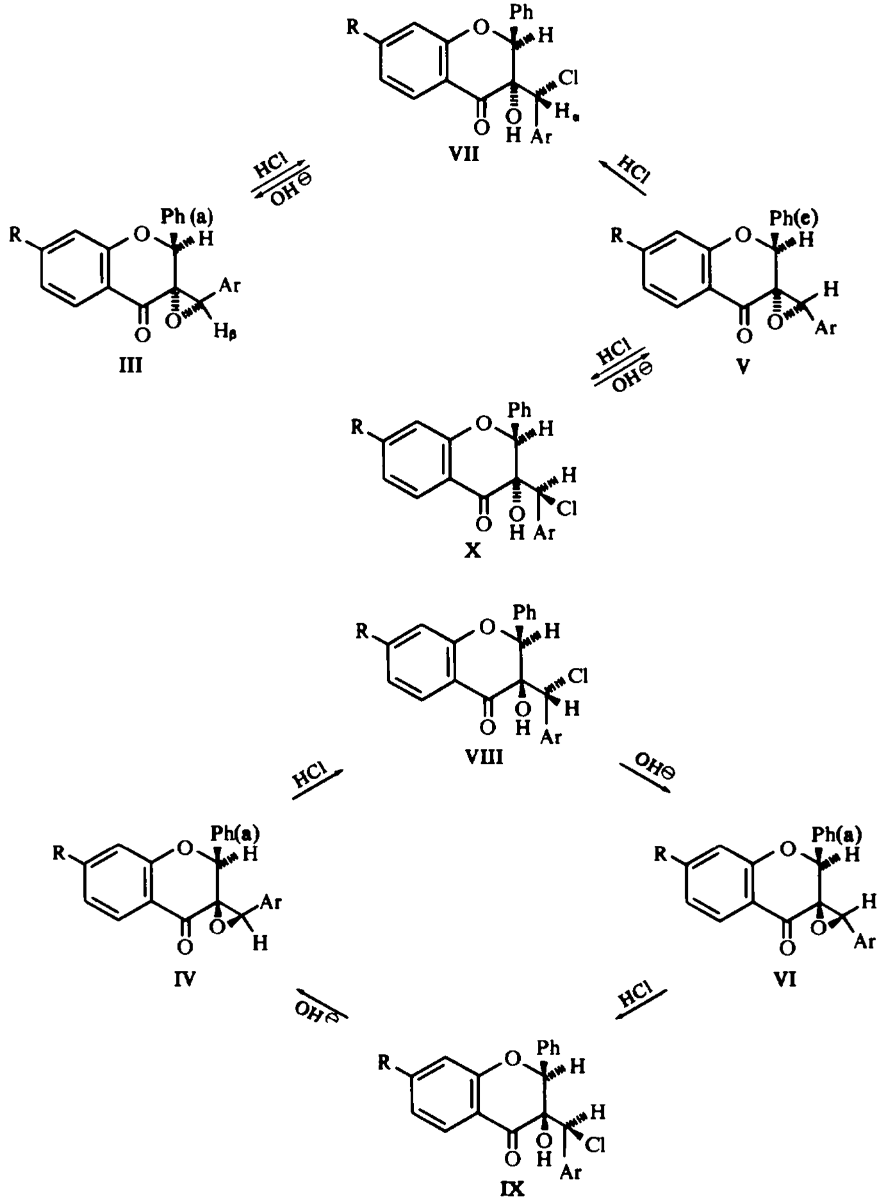
The unsubstituted flavindogenide epoxides (IIIa, IVa) did not yield chlorohydrins. This may be due to the absence of the activating *p*-OMe group in the side chain aryl group.

Attempts were made to prepare the fourth isomeric halohydrin by S_N2 replacement of chlorine by iodine in the *erythro,trans*-chlorohydrin (VIIb). Cyclization of the new *threo,trans*-halohydrin (XI) should in turn yield the required *cis,trans*-epoxide (Vb; Scheme 2).

---

* The terms *erythro*- and *threo*- prefixed to chlorohydrins refer to the configurations about the 3-α bond and the terms *cis*- and *trans*- refer to the relative positions of the phenyl group at the 2-position and the OH group at the 3-position. It should be remembered that the β-position in flavindogenide epoxides corresponds to the α-position in the chlorohydrins.

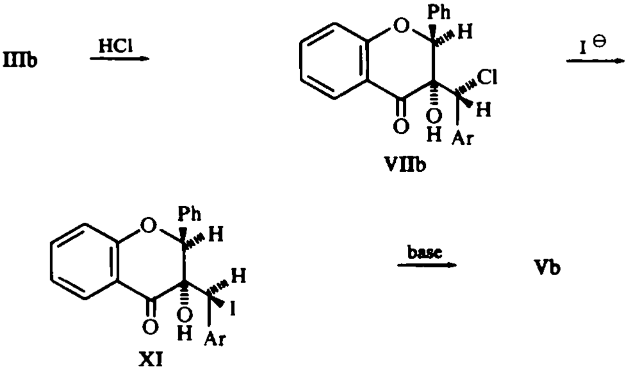
SCHEME 1



a; $R=H$; $Ar=C_6H_5$
b: $R=H$; $Ar=C_6H_4$-p-OMe
c: $R=OMe$; $Ar=C_6H_4$-p-OMe

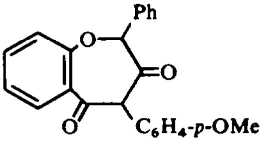
However, treatment of the chlorohydrin (VIIb) with sodium iodide gave, not iodohydrin (XI), but 2-phenyl-4-(4-methoxyphenyl)-2,3,4,5-tetrahydrobenzo-1-oxepin-3,5-dione (XII), which was identical with an authentic sample obtained by the action of boron trifluoride on *trans,trans*-3-anisylideneflavanone epoxide.[4]

SCHEME 2

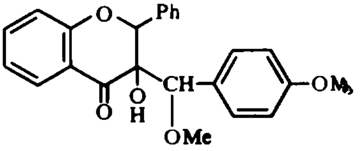


$Ar = C_6H_4\text{-}p\text{-}OMe$

Another possible route to the unknown *threo,trans*-chlorohydrin (Xb) was by *trans*-opening of the epoxide ring in epoxide (Vb). Treatment of Vb with hydrogen chloride using methanol as solvent gave the methoxy-derivative (XIII) and not the expected chlorohydrin. When the reaction was carried out in isopropyl alcohol a compound thought to be the fourth chlorohydrin (Xb) was obtained. This compound is very unstable, and decomposes with the evolution of hydrogen chloride both in solution and in the solid state to produce a higher melting compound. The compound regenerates epoxide (Vb) when it is treated with sodium hydroxide solution. The NMR spectrum of the crude product is not inconsistent with structure Xb, but further work is required for its characterization.



XII

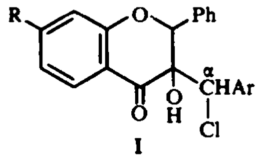


XIII

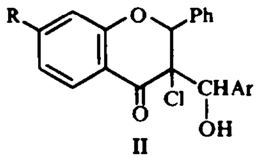
Two α-deuterated chlorohydrins (VIII'c and IX'c) were prepared by the action of anhydrous hydrogen chloride on β-deuterated epoxides (IV'c and VI'c) in benzene–ether. The chemical shifts of the α- and of the 2-protons of the third chlorohydrin (VIIc) were so similar to those of (VIIIc) that the α-deuterated (VIIc) was not prepared.

DISCUSSION

The structures of the chlorohydrins (VIIb, VIIIb and IXb) and (VIIc, VIIIc and IXc) are supported by elemental analyses, IR and NMR spectral data (Table 1) and by their reactions.



I



II

That the chlorohydrins have the 3-hydroxy-α-chloro (I) rather than the alternative 3-chloro-α-hydroxy (II) structure was shown by the following. (a) The chlorohydrins were resistant to oxidation by Jones's Reagent, where it is expected a benzylic OH group would be readily oxidized. A control sample, benzhydrol, was readily oxidized by the reagent. (b) The position of the OH was confirmed by taking the NMR spectra of the chlorohydrins (VIIc, VIIIc and IXc) in deuterated DMSO. In this solvent the rate of proton exchange is so reduced that the effect of vicinal coupling in primary or secondary alcohols becomes observable. That no coupling of the α- and hydroxyl-protons occurs in this solvent confirms the 3-position of the OH group. (c) The IR spectra of the chlorohydrins show strong H-bonding of the OH peaks in carbon tetrachloride. Dilution studies showed that the OH and CO bands had nearly the same relative intensities at high and low dilutions, indicating that the H-bonding is intermolecular.[5] (d) The chlorohydrins do not liberate iodine from an acidified potassium iodide solution as would be expected from α-haloketones.[6]

These results are consistent with structure I which is the chlorohydrin resulting from the expected[7] direction of ring opening of a 1-keto-2-aryl epoxide, the β-carbon being more stable with a developing positive charge in the transition state than the α-carbon.

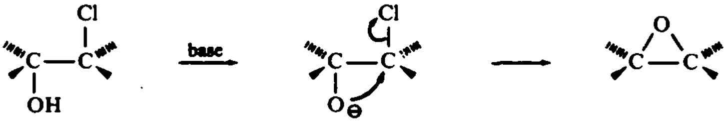
The four isomeric flavindogenide epoxides can be inter-related by examining the chlorohydrins (VIIb, VIIIb, IXb) which they yield and the epoxides produced on subsequent ring closure.[*] Although the opening of an epoxide ring may occur in a *cis* or *trans* manner (depending in certain cases on reaction conditions) to produce structurally different chlorohydrins,[7] chlorohydrins, under basic conditions form epoxides by a *trans* nucleophilic S_N2 displacement (Scheme 3).

The formation of chlorohydrin VIIb from epoxide IIIb with subsequent ring closure under basic conditions to regenerate epoxide IIIb indicates that the epoxide ring in IIIb opened with inversion of configuration at the point of attack (*trans*-opening). On the other hand treatment of epoxides (IVb, Vb and VIb) with hydrogen chloride in benzene–ether give chlorohydrins (VIIIb, VIIb and IXb) which on cyclodehydrohalogenation gave epoxides (VIb, IIIb and IVb), different from the starting epoxides,

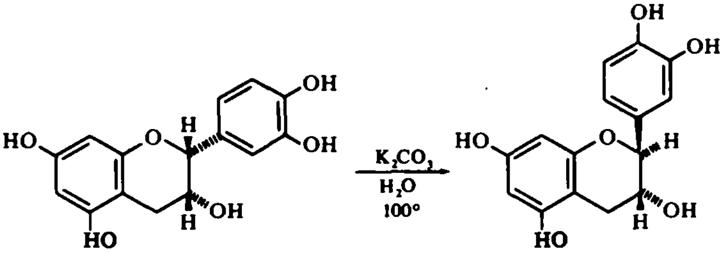
---

[*] The reactions of *cis*- and *trans*-3-anisylideneflavanones and of *cis*- and *trans*-3-anisylidene-7-methoxyflavanones and their derivatives are in most respects completely analogous. The discussion is based on the results obtained with the former compounds except in those cases where differences exist or where data are available only for the 3-anisylidene-7-methoxyflavanone derivatives. The tables and figures include data for both systems when it is available.

SCHEME 3



indicating that the epoxide ring opened with retention of configuration. This conclusion presumes that the configuration of the C atom at the 2-position remained unchanged. However, there was the possibility that an epimerization occurred at the 2-position under the basic conditions of the cyclodehydrohalogenation reactions. This type of epimerization has been observed[9] by Freudenberg *et al.* when (−)-epicatechin (XIV) was converted into (−)-catechin (XV) by aqueous base.



XIV XV

However, 3-anisylideneflavonone epoxides (IVb and VIb) were stable under the basic conditions used for the cyclization reactions.

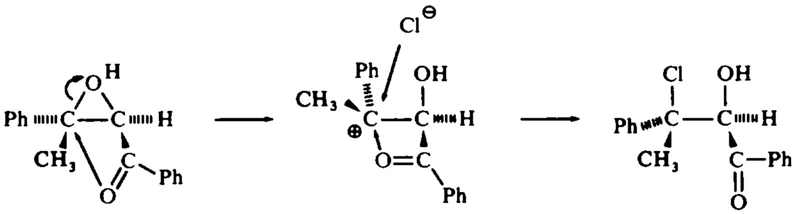
Since treatment of the epoxides with hydrochloric acid followed by recyclization of the chlorohydrins formed does not involve a change in stereochemistry at the C-2 and C-3, the relative configurations at these positions must be the same in epoxides (IIIb and Vb) and in epoxides (IVb and VIb) it follows that the relative geometry of the CO and the β-aryl groups differs in each of these pairs of isomers.

The above evidence on its own is insufficient to enable actual configurations to be assigned to the epoxides but taken in conjunction with the results obtained from the peracid epoxidation reactions and with the spectroscopic evidence the assignments can be made.

The configurations of the three chlorohydrins (VIIb, VIIIb and IXb) (Scheme 1) were derived from the known stereochemistry of the epoxides (Vb, VIb and IVb) which they produced on *trans* cyclodehydrohalogenation. The question remains as to why three of the epoxides (IVb, Vb and VIb) react with retention (*cis*-opening) and one (IIIb) with inversion of configuration (*trans*-opening) when treated with hydrogen chloride.

The mechanism for *cis*-opening of the oxirane ring in epoxide compounds is uncertain; however, a number of pathways have been proposed.[7] Wasserman and Aubrey[10] suggested that in epoxy aroyl systems a double inversion occurs which involves participation of the CO group as shown in Scheme 4.

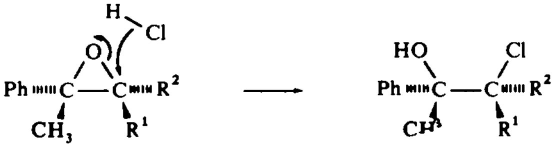
SCHEME 4



In the case of flavindogenide epoxide this mechanism is not applicable as the CO group is remote from the β-carbon during cleavage.

It has been proposed[7, 10] that a four-centre mechanism operates in the *cis*-opening of dypnone oxides by hydrochloric acid and in the *cis*-opening of *trans*-chalcone oxides by boron trifluoride.[11]

SCHEME 5



A modification of this mechanism (Fig 2 or 3) in which the reacting C atom has a high degree of carbonium ion character was put forward by Brewster.[12] An ion pair (as in Fig 3) is considered as being held in a solvent cage so that *cis* attack by the chloride ion is favoured.

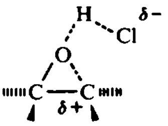


FIG 2

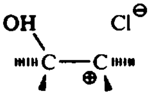
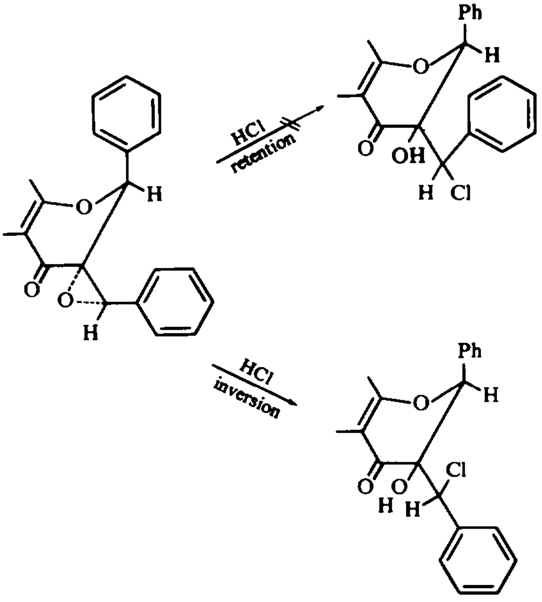


FIG 3

In the *cis*-opening of flavindogenide epoxides the four centre mechanism, or a modification of it, is likely to be involved.

An inspection of models (Dreiding) shows that there is no steric inhibition to *cis*-ring opening by a four centre mechanism in the case of the *cis,cis*- (VIb), *cis,trans*- (Vb) and *trans,cis*- (IVb) epoxides. However, in the case of the *trans,trans*-isomer (IIIb) there is some steric compression between the phenyl group at the 2-position and the side-chain aryl group. A transition state leading to opening of the epoxide ring with retention would initially release strain as the C-β-position would attain more sp^2 character allowing the phenyl and aryl groups to separate further from each other, but on *cis*-attack by the chlorine atom (or ion) it would attain sp^3 character with the consequent return of the non-bonded interaction between the 2- and β-(α) aryl groups. Instead, *trans*-attack by the Cl atom of a second molecule of hydrogen chloride (or chloride ion) would be more energetically favoured leading to inversion of configuration at the β-carbon with consequent release of strain.

SCHEME 6



EXPERIMENTAL

Formation of chlorohydrins

erythro,trans-3-(α-*Chloroanisyl*)-3-*hydroxyflavanone* (VIIb)

A. *trans,trans*-3-Anisylideneflavanone epoxide (IIIb; 2 g) was dissolved in dry benzene–ether (3 :2; 50 ml) presaturated with dry HCl gas. The resulting soln was stirred for 30 min. On removal of the solvent a yellow oil was obtained which crystallized from benzene to give *chlorohydrin* VIIb (1·7 g), m.p. 164–165° (dec). (Found: C, 70·0; H, 4·7; Cl, 8·4; MeO, 8·3. $C_{23}h_{19}O_4Cl$ requires: C, 70·0; H, 4·9; Cl, 9·0; MeO, 7·9%). ν_{max} (KBr) 3482 (OH), 1690 cm^{-1} (C = O). The compound gave a negative potassium iodide test.

B. *cis,trans*-3-Anisylideneflavanone epoxide (Vb) in a similar expt gave chlorohydrins VIIb, m.p. 163° (dec). A mixed m.p. determination with the product from the previous expt showed no depression.

threo, cis-3(α-*Chloroanisyl*)-3-*hydroxyflavanone* (VIIIb)

trans,cis-3-Anisylideneflavanone epoxide (IVb; 4g) on treatment with HCl in benzene–ether as described in the preceding expt gave 3·5 g product, m.p. 106–115°, which on purification on silica gel using ether as eluent, followed by recrystallization from cyclohexane gave *chlorohydrin* VIIIb, m.p. 125–127° (dec). (Found: C, 70·4; H, 5·1; Cl, 9·0. $C_{23}H_{19}O_4Cl$ requires: C, 70·0; H, 4·9; Cl, 9·0%). ν_{max} (CCl_4) 3485 (OH), 1708 cm^{-1} (C = O) (no change in ν_{max} observed on dilution.

erythro,cis-3-(α-*Chloroanisyl*)-3-*hydroxyflavanone* (IXb)

cis,cis-3-Anisylideneflavanone epoxide (VIb; 1 g) on treatment with HCl in benzene–ether gave a gum (0·8 g) which on purification gave IXb, m.p. 145–146°. (Found: C, 70·0; H, 5·0; Cl, 9·3; MeO, 7·5. $C_{23}H_{19}O_4Cl$ requires: C, 70·0; H, 4·9; Cl, 9·0; MeO, 7·9%), ν_{max} (KBr) 3485 (OH), 1690 cm^{-1} (C = O).

erythro,trans-3-(α-*Chloroanisyl*)-3-*hydroxy*-7-*methoxyflavanone* (VIIc)

Anhyd HCl was bubbled into a soln of IIIc (1g) in benzene–ether (3·5 :2; 55 ml) for 25 min. The volume of the soln was reduced (rotary evaporator) to about 3 ml and ether (20 ml) was added. Hexane (20 ml) was added to the warmed soln and on keeping the resulting mixture for 12 hr at room temp 1 g of white crystals, m.p. 134–139° (dec) separated which on recrystallization from benzene gave *chlorohydrin* VIIc (0·65 g), m.p. 139–142° (dec). (Found: C, 68·1; H, 5·1. $C_{24}H_{21}O_5Cl$ requires: C, 67·8; H, 5·0%);

ν_{max} ($CHCl_3$) 3460 (bonded OH), 2844 (OCH_3) and 1690 cm^{-1} (C=O), τ ($CDCl_3$) 2·08–2·8 (m, 6H, Ar–H), 3·07 (d, J=9c/s, 2H, Ar–H) 3·28–3·6 (m, 4H, Ar–H, 6-C–H and 8-C–H), 4·58 (s, 1H, α-H), 4·79 (s, 1H, 2-H), 5·47 (s, 1H, OH; not concentration dependent, exchanges with D_2O), 6·19 (s, 3H, OMe).

The chlorohydrin was not oxidized when treated with Jones's Reagent; a control, benzhydrol, at the same molar concentration, 0·05 *M* in acetone, required 0·5 ml chromic acid soln before the reaction mixture assumed a red colour. The chlorohydrin soln did not decolorize chromic acid soln (1 drop) even on standing for 20 min. In deuterated DMSO the signal of the α-H remained as a sharp singlet.

threo,cis-3-(*α-Chloroanisyl*)-*3-hydroxy-7-methoxyflavanone* (VIIIc)

Anhyd HCl was bubbled into a soln of IVc (4 g) in benzene–ether (2 : 1; 150 ml) for 45 min. After the soln had stood for 3·5 hr the solvent was removed (rotary evaporator) leaving a residual oil. The oil was dissolved in a hot mixture of hexane (100 ml) and benzene (25 ml) and the resulting soln on cooling deposited *chlorohydrin* VIIIc in white crystals (3·5 g; 80%), m.p. 126–127°. (Found: C, 67·95; H, 5·1. $C_{24}H_{21}O_5Cl$ requires: C, 67·8; H, 5·0%); ν_{max} ($CHCl_3$) 3460 (bonded OH), 2840 (OMe) and 1690 cm^{-1} (C=O), τ ($CDCl_3$) 2·2 (perturbed doublet, J = 9·5 c/s, 1H, 5-C–H), 2·34 (perturbed doublet, J = 9, 2H, Ar–H), 2·9 (s, 5H, Ar–H), 3·09 (d, J=9 c/s, 1H, Ar–H), 3·38 (pair of doublets, J=2 and J=9·5 c/s, 1H, 6-C–H; one doublet overlapping 8-C–H signal), 3·43 (perturbed doublet, J=2 c/s, 1H, 8-C–H) 4·56 (s, 1H, α-H), 4·77 (s, 1H, OH; not concentration dependent, exchanges with D_2O) and 6·27 (s, 6H, OMe).

When recrystallized from cyclohexane, this compound incorporates 0·5 mole of cyclohexane per mole of chlorohydrin to give crystals, m.p. 98–101°. (Found: C, 69·8; H, 5·9. $C_{27}H_{27}O_5Cl$ requires: C, 69·4; H, 5·8%). NMR spectrum shows a signal at τ 8·59 (6H) and the IR spectrum shows a strong absorption at 2930 cm^{-1}.

threo-cis-3-(*α-Chloroanisyl*)-*3-hydroxy-7-methoxyflavanone-α-d* (VIII'c)

In an expt similar to the preceding one, IV'c (2 g) gave chlorohydrin VIII'c in white crystals (Hexane), m.p. 124–126°. The IR and NMR spectra ($CHCl_3$) were essentially identical with those of the non-deuterated isomer except for the presence of weak absorptions at 945 and 971 cm^{-1} in the IR spectrum and the absence of the signal at τ 4·60 (which was thus assigned to the α-H) in the NMR spectrum.

erthro,cis-3-(*α-Chloroanisyl*)-*3-hydroxy-7-methoxyflavanone* (IXc)

In a reaction similar to that described above for the formation of chlorohydrin VIIIc, epoxide VIc (0·75 g) gave *chlorohydrin* IXc (0·7 g; 86%) in fine needles, m.p. 131–133°. (Found: C, 68·1; H, 5·25. $C_{24}H_{21}O_5Cl$ requires: C, 67·8; H, 5·0%); ν_{max} 3460 (bonded OH), 2840 (OMe), and 1690 cm^{-1} (C=O), τ ($CHCl_3$) 2·52 (d, J=9 c/s, 1H, 5-C–H), 2·81–3·55 (complex multiplet, 11H, Ar–H), 3·82 (s, 1H, 2-C–H), 4·58 (s, 1H, α-H), 6·17 (s, 3H, OMe_3), 6·22 (s, 1H, OH; concentration dependent) and 6·30 (s, 3H, OMe).

The chlorohydrin was not oxidized when treated with Jones's Reagent. In deuterated DMSO the α-H signal (τ 4·43) remains a sharp singlet.

erythro,cis-3-(*α-Chloroanisyl*)-*3-hydroxy-7-methoxyflavanone-α-d* (IX'c)

In an expt similar to the preceding one, VI'c (0·75 g) gave chlorohydrin IXc (0·65 g; 80%) in fine needles, m.p. 131–133°. The IR and NMR spectra were essentially identical with those of the non-deuterated isomer except for the presence of small absorptions at 969 and 949 cm^{-1} in the IR spectrum and the absence of a signal at τ 4·58 (which can thus be assigned to the α-H) in the NMR spectrum.

Treatment of cis,trans-3-*anisylideneflavanone epoxide* (Vb) *in alcohol solutions with hydrogen chloride*

(a) *With methanol and lithium chloride.* To a stirred soln of MeOH (50 ml) which had been saturated first with LiCl and then with dry HCl at 0° was added Vb (0·3 g) in MeOH (50 ml). The reaction mixture was stirred at 0° for 2 hr and then poured on to 500 ml of an ice-water mixture. The white solid which pptd was removed by filtration and washed thoroughly with water.

The product, 3-hydroxy-3-(β-methoxyanisyl)flavanone, was characterized by its IR and NMR spectra: ν_{max} 3490 (OH), 2740 and 2730 (OMe), and 1695 cm^{-1} (C=O), τ ($CDCl_3$) 2·14–3·48 (complex multiplet, 13H, Ar–H), 4·58 (s, 1H, 2-C–H), 5·96 (s, 1H, α-H), 6·58 (broad signal, 1H, OH), 6·36 (s, 3H, ArOMe), and 7·1 (s, 3H, OMe).

(b) *With propan-2-ol.* To a stirred saturated soln of (25 ml) of HCl in propan-2-ol (saturation was carried out with HCl at 0°) was added Vb (0·3 g) in propan-2-ol (40 ml). The soln was maintained at 0°

for 2 hr and then poured into an ice-water mixture. A white amorphous solid pptd which was removed by filtration and washed with water. An NMR spectrum of an aliquot of the solid, which showed that essentially only one component was present, had signals at τ 2·25–3·67 (complex multiplet, Ar–H), 4·64 (s, 1H), 5·22 (s, 1H) and 6·41 (s, 4H, OMe and possibly OH).

The amorphous solid was dissolved in hot hexane and on cooling the resulting soln a white solid (0·025 g) m.p. 140–142° was obtained. An additional solid (0·25 g), 115–155° was obtained on reducing the volume of the mother liquor. This solid was dissolved in $CDCl_3$ (0·5 ml) and allowed to stand for 1 hr. The soln assumed a yellow colour and evolved HCl. An NMR spectrum of this soln showed that in addition to the original compound, a second component was present to the extent of 25–30%. The chloroform soln was added to acetone (20 ml) and NaOH aq (10 ml; 10%) was added to the resulting mixture which was then vigorously shaken for 10 min. The solvent was removed from the upper organic layer and the residual solid was recrystallized from EtOH to give crystals of Vb (0·09 g) characterized by a comparison of its m.p. and IR spectrum with an authentic sample. The m.p. of the solid obtained initially (m.p. 140–142°) when determined 12 hr after isolation was 135–165° (dec).

Treatment of erythro,trans-3-(*α-chlorobenzyl*)-3-*hydroxyflavone* (VIIb) *with sodium iodide*

Sodium iodide (0·1 g) was added to a soln of VIIb in butan-2-one and the mixture was heated under reflux for 2 hr. The solvent was evaporated and the residue dissolved in ether. The ethereal soln was washed with water and dried (Na_2SO_4). Removal of the solvent gave a residual oil which crystallized from MeOH in fine needles of 2-phenyl-4-(4-methoxyphenyl)-2,3,4,5-tetrahydro-1-oxepin-3,5-dione (77 mg), m.p. 151–152°. A mixed m.p. determination with an authentic sample[4] showed no depression.

Cyclodehydrohalogenation of chlorohydrins with base

The chlorohydrins were dissolved in acetone and treated with NaOH aq. The epoxides formed were characterized (except in the case of VIc which is new) by mixed m.p. determinations with authentic samples and comparison of IR spectra (in most cases) with IR spectra of authentic samples.[1]

In a typical example a soln of VIIb (0·2 g) in acetone (10 ml) was shaken with NaOH aq (5 ml; 10%) for 10 min. The acetone layer was separated and the solvent removed. The solid residue which remained was recrystallized from EtOH to five IIIb (0·17 g), in needles, m.p. 176·7°.

In similar experiments chlorohydrin VIIIb (1·0 g) gave epoxide VIb (0·9 g), m.p. 145·5–146·5°; chlorohydrin IXb (0·1 g) gave epoxide IVb (0·08 g), m.p. 126–127°; chlorohydrin VIIc (0·3 g) gave epoxide IIIc (0·2 g), m.p. 145–147°; chlorohydrin VIIIc (2·0 g) gave cis,cis-3-*anisylidene*-7-*methoxyflavanone epoxide* (VIc; 1·6 g), m.p. 186–188°. (Found: C, 74·3; H, 5·3. $C_{24}H_{20}O_5$ requires: C, 74·2; H, 5·2%); chlorohydrin VIIIc (1·5 g) gave epoxide VIc (0·95 g), m.p. 184–185°; chlorohydrin IX (0·2 g) gave epoxide IVc (0·16 g), m.p. 165–166°.

Stability of trans,cis-*epoxide* IVb *and of* cis,cis-*epoxide* VIb *towards base*

A soln of IVb (0·1 g) in acetone (10 ml) was shaken with NaOH aq (5 ml; 10%) for 10 min (i.e. conditions used for cyclodehydrohalogenation of chlorohydrins). The acetone layer was separated and the solvent removed. The residual solid crystallized from EtOH in cubes of IVb (0·92 g), m.p. 126–127°. A mixed m.p. determination with starting material showed no depression. No trace of VIb was detected on TLC.

Treatment of VIb (0·1 g) by the same procedure yielded only the starting epoxide (0·082 g). No trace of IVb was detected on TLC.

REFERENCES

[1] Communication VI, D. D. Keane, W. I. O'Sullivan, E. M. Philbin, R. M. Simons and P. C. Teague, *Tetrahedron* **26**, 3533 (1970)

[2] For preliminary communication see J. R. Doherty, D. D. Keane, K. G. Marathe, E. M. Philbin, R. M. Simons and P. C. Teague, *Tetrahedron Letters* 441 (1968)

[3] See ref 3*a* in the preceding paper.

[4] J. R. Doherty, D. D. Keane, W. I. O'Sullivan, E. M. Philbin and P. C. Teague, *Chem. & Ind.* 586 (1969)

[5] L. J. Bellamy, "*The Infrared Spectra of Complex Molecules*" p. 96. Wiley, New York (1958)

[6] N. H. Cromwell, R. E. Bambury and R. P. Barkley, *J. Am. Chem. Soc.* **81**, 4294 (1959)

[7] R. E. Parker and N. S. Isaacs, *Chem. Revs* **59**, 737 (1959)

[8] [a] S. Winstein and H. J. Lucas, *J. Am. Chem. Soc.* **61**, 1576 (1939);
[b] J. E. Stevens, C. L. McCabe and J. C. Warner, *Ibid.* **70**, 2449, 4030 (1948);
[c] P. D. Bartlett, *Ibid.* **57**, 224 (1935)

[9] K. Freudenberg and L. Oehler, *Liebigs Ann* **483**, 140 (1930)

[10] H. H. Wasserman and N. E. Aubrey, *J. Am. Chem. Soc.* **78**, 1726 (1956)

[11] H. O. House and G. D. Ryerson, *Ibid.* **83**, 979 (1961)

[12] J. H. Brewster, *Ibid.* **78**, 4061 (1956)