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SOME REACTIONS OF SUBSTITUTED 2'-BENZYLOXY-CHALKONE EPOXIDES*

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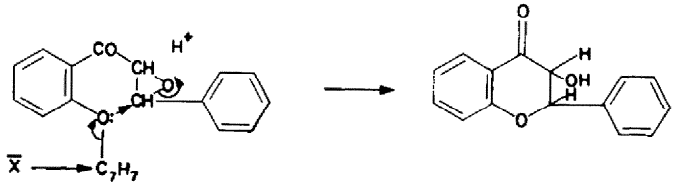
Abstract—The behaviour of 2'-benzyloxychalkone epoxides towards acid reagents depends on the presence of substituents in the styryl part as well as on the reaction conditions. Ethereal hydrogen chloride under various conditions has been generally used but acetic acid alone or in conjunction with hydrobromic acid have also been used in a few cases. Simple 2'-benzyloxy-(I) and 2'-benzyloxy-4'-methoxy-(XIV) chalkone epoxides give only dihydroflavonols II and XV respectively; whereas 2'-benzyloxy-4-methoxy-(XIX) and 2',4'-dibenzyloxy-4-methoxy-(III) chalkone epoxides give various products depending on the conditions. From the latter epoxide (III), chlorohydrin (VI), glycol monoacetate (IX), 1,2-diketone (IV), and isoflavones (VII and VIII) have been isolated.

Two polysubstituted 2'-benzyloxychalkone epoxides were recently found to be good substrates for the laboratory synthesis of natural isoflavones viz. formononetin and pseudobaptigenin.[1] They undergo rearrangement in the presence of boron trifluoride etherate to α-formyldesoxybenzoins and subsequent debenzylative cyclization either by catalytic hydrogenation or by treatment with hydrochloric acid–acetic acid mixture. This synthesis could be of biogenetic importance since chalkones are now known to be the biological precursors of isoflavones.[2] Bognar and Stefanovsky,[3] have reported that the action of (i) ethereal hydrogen chloride, (ii) halogen acids in acetic acid and (iii) iodic acid in acetone on the epoxide (I) gives good yields of the dihydroflavanol II. The mechanism is considered to consist of the simultaneous opening of the epoxide ring and formation of the pyranone ring as shown in formulae I and II. The action of these reagents on polysubstituted 2'-benzyloxychalkone epoxides has now been studied for two reasons. Firstly, it may be a good laboratory synthesis of dihydroflavonols and secondly, it was felt that dihydroflavonols like isoflavones could also arise in Nature from chalkone epoxides. Some novel results have been obtained and the results are reported in this paper.



I II

Reactions of 2',4'-Dibenzyloxy-4-methoxychalkone Epoxide (III)

This epoxide, chosen for the preliminary study, treated under different acidic conditions, yielded a variety of products, none of which was a dihydroflavonol.

* A preliminary note concerning this work was published in *Curr. Sci.* **33**, 48 (1964).

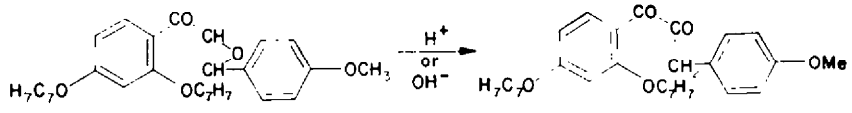
[1] S. K. Grover, A. C. Jain and T. R. Seshadri, *Ind. J. Chem.* **1**, 517 (1963).

[2] H. Grisebach and G. Brandner, [a] *Biochim. Biophys. Acta* **60**, 51 (1962); [b] *Experientia* **15**, 400 (1962).

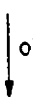
[3] R. Bognar and J. Stefanovsky, *Tetrahedron* **18**, 143 (1962).

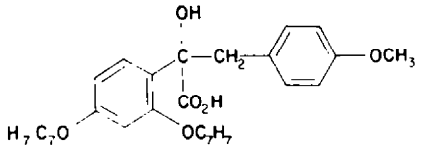
1. *Treatment with ethereal hydrogen chloride*

(i) *Formation of* 2,4-*dibenzyloxyphenyl*-4-*methoxybenzyl* 1,2-*diketone* (IV). When the epoxide (III) was dissolved in excess ether previously saturated with dry hydrogen chloride and kept at room temperature for 48 hr, a product (A) was obtained which contained no chlorine and gave no ferric reaction. The elemental analysis agreed with the molecular formula $C_{30}H_{28}O_5$ which meant that the two benzyloxy groups were intact and it was not a dihydroflavonol. The UV spectrum showed weak bands of decreasing intensity at 230, 280 and 315 mμ and the IR spectrum had two strong bands in the carbonyl region, one at 1720 cm^{-1} and the other at 1650 cm^{-1}. Such spectral characteristics seem to be shown by phenyl benzyl 1,2-diketones.[4] Hence it was considered that A has structure IV which was further supported by synthesis following the method of Baker and Robinson.[5] It consists in treating the chalkone epoxide (III) with sodium hydroxide solution when a mixture of two products is obtained. One is neutral and is the desired diketone (IV) identical with A; and the other is its rearranged product, 2,4-dibenzyloxyphenyl-4-methoxybenzyl glycollic acid (V), identical with the product obtained by alkali treatment of A.



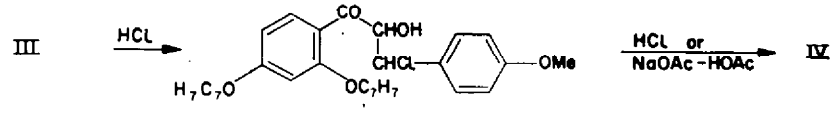
III IV





V

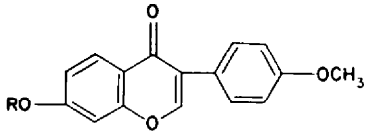
(ii) *Formation of chlorohydrin* (VI). The chalkone epoxide (III) when dissolved in the minimum of ether previously saturated with dry hydrogen chloride yielded the chlorohydrin B having structure VI by elemental analysis, and IR spectrum showing a hydroxyl band at 3600 cm^{-1} and a carbonyl band at 1665 cm^{-1} (cf. House[6]). Further the identity was established by converting it into the previously made diketone (IV).[5,6]



VI

[4] H. O. House, *J. Amer. Chem. Soc.* **76**, 1235 (1954).
[5] W. Baker and R. Robinson, *J. Chem. Soc.* 1798 (1932).
[6] H. O. House, *J. Amer. Chem. Soc.* **78**, 2298 (1956).

(iii) *Formation of isoflavone* (VII) *and diketone* (IV). Under conditions which encouraged 2′-debenzylation i.e. saturating an ether solution of III with dry hydrogen chloride at 0° for 4 hr and working up the product after keeping the reaction mixture at room temperature for 48 hr, a mixture of two products was obtained, and separated by fractional crystallization from methanol. The sparingly soluble product (C) which formed the minor fraction showed the characteristic UV spectrum of an isoflavone. Elemental analysis indicated that one benzyloxy group was intact and hence C was considered to be 7-*O*-benzylformononetin (VII). This identity was further established by direct comparison with an authentic sample prepared by benzylation of formononetin (VIII). The more soluble methanolic fraction formed the major part and proved to be identical with 1,2-diketone (IV) having the benzyl groups intact.



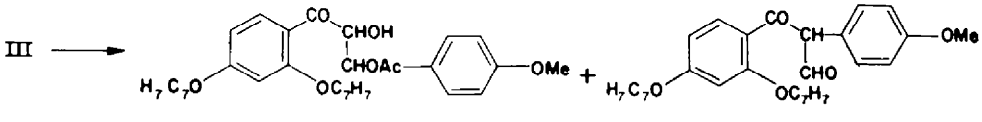
VII , R = C_7H_7
VIII , R = H

2. *Treatment with hydrobromic in acetic acid*

Formation of isoflavone (VII or VIII). Treatment of III with hydrobromic acid in acetic acid under two different conditions gave only the isoflavones. (i) Thus, a few drops of hydrobromic acid added to an acetic acid solution of III, yielded after keeping the solution at room temperature for a short period, 7-*O*-benzylformononetin (VII). (ii) Treatment with excess of hydrobromic acid for a longer period resulted in complete debenzylation and yielded formononetin (VIII).

3. *Treatment with glacial acetic acid*

Formation of glycol monoacetate (IX) *and α-formyl desoxybenzoin* (X). Boiling the chalkone epoxide (III) with glacial acetic acid yielded glycol monoacetate (IX) as a major product. This structure was supported by elemental analysis, UV and IR spectra and by its conversion into 1,2-diketone (IV). The mother liquor left after removal of glycol monoacetate gave a positive ferric reaction; it is probably due to the formation of α-formyldesoxybenzoin (X) in small amount.

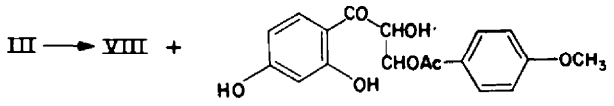


IX X

4. *Catalytic hydrogenation in acetic acid solution*

Formation of glycol monoacetate (XI) *and formononetin* (VIII). Catalytic debenzylation of III in acetic acid solution at room temperature yielded two products. The

minor product was identified as formononetin (VIII) and the major as glycol monoacetate (XI) having hydroxyls free in the benzoyl part. The structure XI is supported by elemental analysis, positive ferric reaction, ester and chelated carbonyl bands in the IR spectrum at 1725 cm^{-1} and 1625 cm^{-1} respectively.



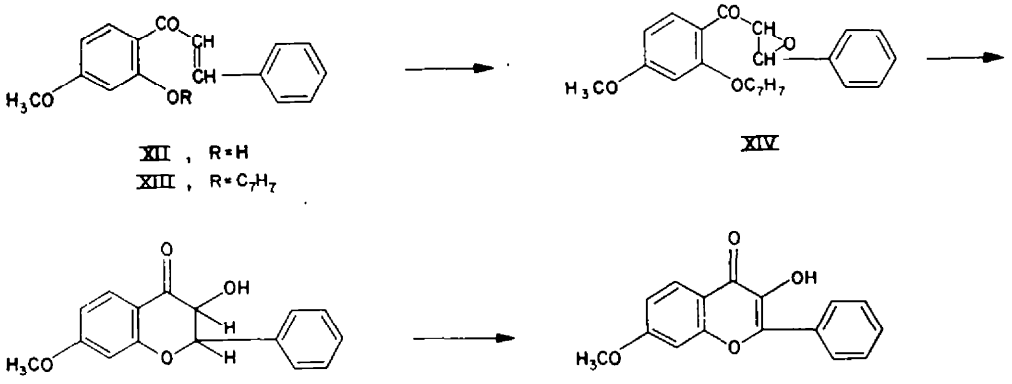
XI

Reactions of 2′-Benzyloxychalkone Epoxide (I)

The above results necessitated repeating the experiments of Bognar and Stefanovsky[3] who used the simple 2′-benzyloxychalkone epoxide (I). Their results were confirmed and good yields of dihydroflavonol (II) obtained as reported, but the m.p. of our dihydroflavonol (187–188°) did not agree with the one (178–180°) reported by these workers but agreed with the m.p. recorded earlier by Gripenberg.[7] In order to be sure as to its constitution, it was dehydrogenated to flavonol[8] with iodine in the presence of potassium acetate and acetic acid.[9] The behaviour of this simple chalkone epoxide showed that the substituents in chalkone epoxide markedly change the course of reaction. In order to know the effect of substitution in the two benzene rings, other chalkone epoxides were studied.

Reactions of 2′-Benzyloxy-4′-methoxychalkone Epoxide (XIV).

The chalkone epoxide (XIV) was prepared from 2′-hydroxy-4′-methoxychalkone (XII)[10] and subjected to the following varying conditions: (i) it was dissolved in the minimum of ethereal hydrogen chloride and the product worked up after 24 hr; (ii) it was kept in contact with excess ethereal hydrogen chloride at room temperature for 48 hr; (iii) it was treated with hydrobromic acid in acetic acid at room temperature



XII , R=H
XIII , R=C_7H_7

XIV

XV

XVI

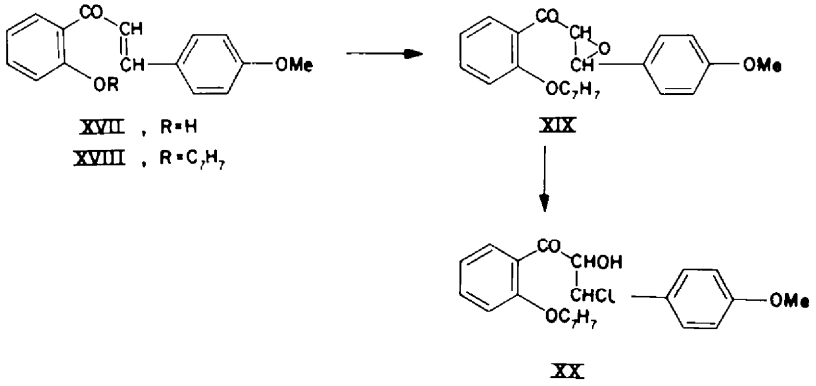
[7] J. Gripenberg, *Acta Chem. Scand.* **11**, 866 (1957).
[8] S. von Kostanecki and W. Szabranski, *Ber. Dtsch. Chem. Ges.* **37**, 2820 (1904).
[9] R. N. Goel, V. B. Mahesh and T. R. Seshadri, *Proc. Indian Acad. Sci.* **47A**, 184 (1958).
[10] T. Emilewiez and S. von Kostanecki, *Ber. Dtsch. Chem. Ges.* **32**, 311 (1899).

Under all these conditions, only 7-methoxydihydroflavonol[11] (XV) resulted in good yields. The structure (XV) has been confirmed by UV and IR spectral data and by dehydrogenation to the known flavonol (XVI).[12]

Since completion of the present work, Chopin and Durual[13] have published the reactions of 2′-benzyloxychalkone epoxides (I and XIV) with ethereal hydrogen chloride. They report similar results but have missed to refer to the work of Bognar *et al.*[3] and further they also report the low m.p. (176–177°) for dihydroflavonol (II). These results show conclusively that substitution in the benzoyl part of the chalkone epoxide does not hinder ring closure.

Reactions with 2′-Benzyloxy-4-methoxychalkone Epoxide (XIX)

This epoxide was prepared from XVII by benzylation and subsequent epoxidation as in the previous case. It was found to give chlorohydrin (XX) as readily as III with ethereal hydrogen chloride but did not yield dihydroflavonol even on prolonged treatment; chlorohydrin (XX) being the only product isolated. Thus it is clear that a *p*-methoxy group in the styryl part changes the course of reaction.



Reactions of 4,2′,4′-*Trimethoxychalkone Epoxide* (XXI)

Ring closure is prevented by effective protection of the 2′-hydroxyl group in the chalkone epoxide by methylation. Therefore, 4,2′,4′-trimethoxychalkone epoxide (XXI)[5] was reacted with ethereal hydrogen chloride under several conditions and also with glacial acetic acid. In the former case, the chlorohydrin (XXII) and in the latter case glycol monoacetate (XXIII) were formed as major products. The minor fraction which could not be crystallized in both the cases was considered to be α-formyl-desoxybenzoin (XXIV) because it gave a copper complex and positive ferric reaction.

Discussion of Results

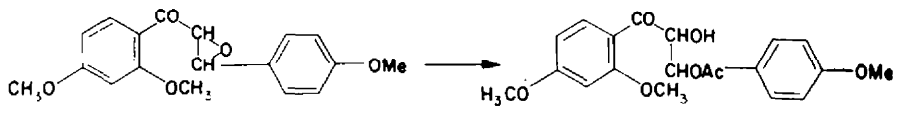
The results emphasize the influence of substituents on the reactions of chalkone epoxide. In the main there are two types.

(1) If the 4 position is substituted by a methoxyl group as in III, XIX and XXI,

[11] G. W. K. Cavill, F. M. Dean, A. McGookin, B. M. Marshall and A. Robertson, *J. Chem. Soc.* 4573 (1954).

[12] B. Krishnaswami and T. R. Seshadri, *Proc. Indian Acad. Sci.* **15A**, 437 (1942).

[13] J. Chopin and P. Durual, *C. R. Acad. Sci. Paris* **257**, 700 (1963).

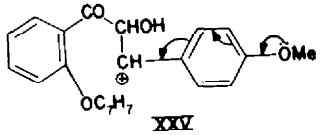


XXI XXIII

XXII XXIV

because of its influence as an electron source the formation of the intermediate carbonium ion (XXV) is favoured. In these cases, the debenzylation of the 2′-benzyloxy group is also inhibited and the carbonium ion tends to undergo the following reactions depending on the conditions: (i) it may accept nucleophiles such as chloride and acetate anions to give chlorohydrins such as VI, XX and XXII and glycol mono-acetates such as IX, XI and XXIII; (ii) it may give rise to 1,2-diketone such as IV; (iii) it may undergo rearrangement to yield α-formyldesoxybenzoins such as X and XXIV which could subsequently undergo debenzylative cyclization to give isoflavones such as VII and VIII.

(2) On the other hand, if the styryl part is unsubstituted as in chalkone epoxides I and XIV, by a concerted debenzylation in the 2′-position and the formation of carbonium ion, cyclization to pyranone ring is favoured to give dihydroflavonols such as II and XV exclusively.



XXV

EXPERIMENTAL

M.ps are uncorrected. Unless otherwise stated, UV spectra were measured in 95% ethanolic solution and IR spectra using Perkin-Elmer infracord spectrophotometer model 137 and KBr disc. The figures written in brackets after the maxima values in UV spectra represent log ϵ values. The light petroleum used had b.p. 40–60°.

1. *Reaction products of 2′,4′-dibenzyloxy-4-methoxychalkone epoxide*(III) *and their characterization*

(i) 2,4-*Dibenzyloxyphenyl* 4-*methoxybenzyl* 1,2-*diketone* (IV). The chalkone epoxide[1] (III, 0·5 g) was dissolved in dry ether (100 ml) previously saturated with dry HCl gas and left at room temp for 48 hr. The resulting solution was evaporated to dryness and methanol (10 ml) added to the oily residue. On cooling to 0°, a colourless solid separated which crystallized from methanol as colourless stout rectangular prisms (0·3 g), m.p. 106–107° alone or when mixed with an authentic sample of diketone (IV) (see below); it gave no colour with ethanolic ferric chloride; $\lambda_{max}^{methanol}$ 282 mμ(3·37) and 315 mμ(3·37); ν_{max}^{nujol} 1720 cm^{-1}, 1650 cm^{-1} (two different CO groups). (Found: C, 76·8; H, 5·6. $C_{30}H_{26}O_5$ requires: C, 77·2; H, 5·6%).

The diketone (IV, 0·3 g) was refluxed with ethanol (10 ml) and KOH (1·0 g in 5 ml water) for 2 hr.

Ethanol was distilled and water added to the residue. The solution was extracted with ether and the alkaline layer acidified when 2,4-dibenzyloxyphenyl-4-methoxybenzyl glycollic acid (V, ca 20 mg) separated. It crystallized from benzene–light petroleum mixture as colourless small prisms, m.p. and mixed m.p. with an authentic sample (see below) 146–147°. The ether extract on evaporation yielded the unchanged diketone (IV), m.p. 106–107°.

Authentic 1,2-*diketone* (IV) *and glycollic acid* (V). The chalkone epoxide (III, 1·0 g) was refluxed with ethanol (10 ml) and NaOH aq. (0·5 g/2 ml) for 2 hr. Ethanol was removed and water (50 ml) added to the residue. The alkaline solution was extracted with ether (ether extract A). The alkaline layer on acidification gave the glycollic acid (V) which crystallized from benzene–light petroleum mixture as colourless small prisms (0·4 g), m.p. 146–147°; λ_{max} 276 mμ(3·81) and 282 mμ(3·79); ν_{max} 3650, 3400, 2800 cm^{-1} (—OH), 1690, 1725 cm^{-1} (C=0). (Found: C, 73·5; H, 5·7. $C_{30}H_{28}O_6$ requires: C, 74·4; H, 5·8%).

The ether extract A on evaporation yielded the diketone (IV, 0·3 g), m.p. 106–107°.

(ii) 2,4-*Dibenzyloxyphenyl-β-chloro-α-hydroxy-β-4-methoxyphenyl ethyl ketone* (VI). The chalkone epoxide (III, 0·8 g) was dissolved in dry ether (10 ml) previously saturated with dry HCl gas at 0°. On shaking the resulting red solution at room temp for a few min, a white solid separated. It was filtered off, washed with dry ether and crystallized from benzene–light petroleum mixture when the chlorohydrin (VI) was obtained as colourless fine needles (0·45 g), m.p. 120–121°; it gave no colour with ethanolic ferric chloride; λ_{max} 270 mμ (3·56) and 305 mμ(3·39); ν_{max} 3600 cm^{-1} (—OH), 1665 cm^{-1} (C=O). (Found: C, 71·5; H, 5·6. $C_{30}H_{27}ClO_6$ requires: C, 71·6; H, 5·4%). The chlorohydrin was converted into 1,2-diketone (IV) in two ways: (a) The chlorohydrin (VI, 0·4 g) was dissolved in ethereal HCl (100 ml) and the solution left at room temp for 48 hr. The product was the diketone (IV, 0·1 g), m.p. and mixed m.p. 106–107°. (b) The chlorohydrin (VI, 0·5 g) was refluxed in acetic acid solution with fused sodium acetate (0·5 g) for 2 hr. Acetic acid was distilled and water added to the residue. The product gave diketone (IV, 50 mg), m.p. 106–107°.

(iii) *Diketone* (IV) *and* 7-*benzyloxy*-4'-*methoxyisoflavone* (VII). The chalkone epoxide (III, 0·2 g) was dissolved in dry ether (150 ml), cooled in ice and a current of dry HCl gas passed for 4 hr. After 48 hr at room temp, ether was evaporated and methanol added to the residue when a colourless solid separated on cooling. It was fractionally crystallized from methanol. The first fraction separated as colourless needles (30 mg), m.p. 180–182° alone or when mixed with an authentic sample of isoflavone (VII); it gave no colour with ethanolic ferric chloride. The methanolic mother liquor yielded the 1,2-diketone (IV, 80 mg), m.p. 106–107°.

Authentic 7-*benzyloxy*-4'-*methoxyisoflavone* (VII). 7-Hydroxy-4'-methoxyisoflavone (VIII, 0·1 g) was refluxed in acetone (50 ml) with benzyl chloride (0·1 ml), K_2CO_3 (2 g) and KI (0·1 g) for 5 hr. Acetone was distilled and water added to the residue. The benzyloxyisoflavone (VII) crystallized from ethyl acetate–ethanol mixture as colourless rhombohedral plates (100 mg), m.p. 180–182°; λ_{max} 248–262 mμ(3·99) and λ_{inflex} 305 mμ(3·56); ν_{max} 1640 cm^{-1} (C=O). (Found: C, 76·9; H, 5·2. $C_{22}H_{18}O_4$ requires: C, 77·1; H, 5·1%).

(iv) 7-*Hydroxy*-4'-*methoxyisoflavone* (VIII). A solution of the chalkone epoxide (III, 1 g) in glacial acetic acid (5 ml) was treated with HBr (60%, 2 ml) and the mixture kept at room temp for 24 hr. It was poured into water and the product collected, dried, washed repeatedly with light petroleum to remove benzyl bromide and crystallized from ethyl acetate–light petroleum mixture. Formononetin (VIII, 10 mg) was obtained as colourless small plates, m.p. and mixed m.p. 254–255°; broad band between 242–260 mμ and λ_{max} 249 mμ(4·39) and 300–303 mμ(3·96); ν_{max} 3600 cm^{-1} and 3225 cm^{-1}(—OH), 1640 cm^{-1} (> C=O).

(v) 7-*Benzyloxy*-4'-*methoxyisoflavone* (VII). The chalkone epoxide (III, 1 g) was dissolved in acetic acid (5 ml) and treated with HBr (0·5 ml) and the reaction worked up after 0·5 hr. From the resinous product, the isoflavone (VII, 20 mg) was obtained as a colourless solid, m.p. and mixed m.p. 180–182°.

(vi) 2,4-*Dibenzyloxyphenyl-β-acetoxy-α-hydroxy-β-4-methoxyphenyl ethyl ketone* (IX). The chalkone epoxide (III, 0·2 g) was dissolved in acetic acid (5 ml) and left at room temp for 24 hr. The product crystallized from methanol as colourless stout prisms (0·1 g), m.p. 134–135°; it gave no ferric reaction; $\lambda_{max}^{methanol}$ 272 mμ (4·02), 305 mμ(3·82), ν_{max} 3600 cm^{-1} (—OH), 1750 cm^{-1} (—OCOCH$_3$), 1665 cm^{-1} (>C=O). (Found: C, 72·8; H, 5·7. $C_{32}H_{30}O_7$ requires: C, 73·0; H, 5·7%). The methanolic mother liquor gave with ferric chloride a brown colour which is considered to be due to the α-formyldesoxybenzoin (X). The glycol monoacetate (IX, 0·5 g) was converted into

1,2-diketone (IV) with acetic acid (5 ml) and fused sodium acetate (0·5 g) just as in the case of chlorohydrin (VI).

(vii) 2,4-*Dihydroxyphenyl-β*-acetoxy-α-hydroxy-*β*-4-*methoxyphenyl ethyl ketone* (XI) and *formononetin* (VIII). The chalkone epoxide (III, 1 g) was dissolved in glacial acetic acid (20 ml), treated with Pd-C catalyst (5%, 0·5 g) and the mixture saturated with hydrogen at room temp. The catalyst was filtered off and the filtrate distilled to remove the solvent. The residue was dried over KOH *in vacuo* and treated with dry ether (30 ml) when formononetin (VIII) separated (50 mg), m.p. and mixed m.p. 254–255°. The residue of ethereal mother liquor was crystallized from ethyl acetate–light petroleum mixture when the glycol monoacetate (XI) separated as colourless needles (0·3 g), m.p. 104–106°; it gave wine red colour with ethanolic ferric chloride; λ_{max} 282 mμ (3·99) and 320 mμ (3·80); ν_{max}^{Nujol} 3600 cm^{-1} (—OH), 1735 cm^{-1} (—OCOCH$_3$) and 1640 cm^{-1} (>C=O). (Found: C, 59·4; H, 5·8. $C_{18}H_{16}O_7.1H_2O$ requires: C, 59·3; H, 5·5%).

2. *Reactions of 2′-benzyloxychalkone epoxide* (I)

2′-Benzyloxychalkone required for the preparation of the epoxide (I)[3] was prepared in better yields than reported earlier[3] as follows: An acetone solution (100 ml) of 2′-hydroxychalkone (3·3 g) was refluxed with benzyl chloride (7 ml), K_2CO_3 (21 g) and KI (10 g) for 16 hr. Acetone was distilled off and the residue steam distilled. The product crystallized from ethanol as light yellow long needles (3·8 g), m.p. 84–85° (lit.[3] 84·5–85·5°).

The dihydroflavonol (II) obtained from chalkone epoxide according to the various conditions reported earlier by Bognar and Stefanovsky[5] was obtained as colourless needles, m.p. 187–188° (lit.[13] 176–177°, lit.[3] 178–180°, lit.[7] 188°); λ_{max} 253 mμ (3·86), 320 mμ (3·45); ν_{max} 3620 cm^{-1} (OH), 1700 cm^{-1} (CO). It was dehydrogenated to flavonol as follows:

Dihydroflavonol (II, 100 mg) was refluxed in glacial acetic acid (15 ml) with anhydrous potassium acetate (0·5 g) and iodine (0·1 g) for 2 hr. Acetic acid was distilled and sulphurous acid (20 ml) added. The resulting mixture was extracted with ether; ether solution yielded flavonol after crystallization from ethyl acetate–light petroleum mixture as pale yellow needles (40 mg), m.p. 169–170° (lit.[8] 169–170°); violet red colour with ethanolic ferric chloride; ν_{max} 2900, 3335 cm^{-1} (OH), 1625 cm^{-1} (CO).

3. *Preparation and reactions of 2′-benzyloxy-4′-methoxychalkone epoxide* (XIV)

2′-Benzyloxy-4′-methoxychalkone (XIII). 2′-Hydroxy-4′-methoxychalkone[10] (XII, 4·5 g) was benzylated with benzyl chloride (4·2 ml), K_2CO_3 (12 g) and KI (4 g) in acetone medium as described previously. The product (XIII) crystallized from ethyl acetate–ethanol mixture as almost colourless tiny narrow rectangular plates (5 g), m.p. 105°; no ferric reaction. (Found: C, 79·8; H, 6·1. $C_{23}H_{20}O_3$ requires: C, 80·2; H, 5·9%).

2′-Benzyloxy-4′-methoxychalkone epoxide (XIV). The above chalkone (XIII, 4·0 g) dissolved in acetone (40 ml) and methanol (15 ml) was treated with NaOH aq. (8%, 6·6 ml) followed by H_2O_2 (30%, 5 ml). The solution was shaken and brought to the b.p. occasionally during 1 hr and then left overnight at room temp. Water was added until turbidity appeared and on keeping the epoxide separated. It was collected and crystallized from ethanol–ethyl acetate mixture yielding colourless long rectangular prisms (3·5 g), m.p. 87–88°; λ_{max} 234 mμ (4·30), 279 mμ (4·14) and 312 mμ (4·04); ν_{max} 1655 (CO), 1252 (epoxide C—O—C). (Found: C, 76·6; H, 6·0. $C_{23}H_{20}O_4$ requires: C, 76·7; H, 5·6%).

Reactions of the epoxide (XIV)

(i) *7-Methoxydihydroflavonol* (XV). The epoxide (XIV, 0·2 g) was dissolved in an ice cold solution of dry ethereal HCl (4 ml), shaken and left overnight at room temp. Ether was evaporated and the residue crystallized from ethyl acetate–light petroleum mixture when 7-methoxydihydroflavonol was obtained as colourless needles (0·1 g), m.p. 148–149° (lit.[11] 150°); no colour with ethanolic ferric chloride; λ_{max} 274 mμ (4·12), 311 mμ (3·82); ν_{max} 3575 cm^{-1} (—OH), 1690 cm^{-1} (C=O). (Found: C, 71·4; H, 5·2. $C_{16}H_{14}O_4$ requires: C, 71·1; H, 5·2%). It (XV, 100 mg) was dehydrogenated with anhydrous potassium acetate (0·5 g) and iodine (0·1 g) in acetic acid solution (15 ml). 7-Methoxyflavonol (XVI) crystallized from ethyl acetate–light petroleum mixture as colourless solid (50 mg), m.p. 175–176° (lit.[12] 177–178°); it gave a violet colour with ethanolic ferric chloride; λ_{max} 228, 253, 321, 340 mμ (4·22, 4·14, 4·18, 4·20 respectively); ν_{max} 3400 cm^{-1}, 2850 cm^{-1} (OH), 1625 cm^{-1} (chelated CO).

(ii) The above experiment when repeated with excess of ethereal HCl also gave 7-methoxydihydroflavonol, m.p. and mixed m.p. 148–149°.

(iii) The epoxide (0·5 g) was dissolved in boiling acetic acid (3·3 ml) and treated with HBr (65%, ca. 6 drops). The resulting solution after 0·5 hr at room temp gave 7-methoxydihydroflavonol (0·3 g), m.p. and mixed m.p. 148–149°.

4. *Preparation and reaction of 2′-benzyloxy-4-methoxychalkone epoxide* (XIX)

2′-Benzyloxy-4-methoxychalkone (XVIII). 2′-Hydroxy-4-methoxychalkone[14] (XVII; 5 g) was refluxed with acetone (100 ml), benzyl chloride (4·6 ml), KI (4 g) and K_2CO_3 (15 g) for 24 hr. The product crystallized from ethanol–ethyl acetate mixture as light yellow stout prisms (5·2 g), m.p. 116–117°; no ferric reaction. (Found: C, 80·2; H, 5·9. $C_{23}H_{20}O_3$ requires: C, 80·2; H, 5·9%).

2′-Benzyloxy-4-methoxychalkone epoxide (XIX). The above chalkone (4 g) was converted into its epoxide (XIX) using acetone (40 ml), methanol (15 ml), NaOH aq. (8%, 6 ml) and H_2O_2 (30%, 6 ml). It crystallized from ethanol–ethyl acetate mixture as aggregates of long rectangular prisms (4 g), m.p. 104–105°; λ_{max} 258 mμ (4·09), 313 mμ (3·69); ν_{max} 1665 cm^{-1} (CO), 1250 (C—O—C epoxide). (Found: C, 76·6; H, 5·7. $C_{23}H_{20}O_4$ requires: C, 76·7; H, 5·6%).

2-Benzyloxyphenyl-β-chloro-α-hydroxy-β-4-methoxyphenyl ethyl ketone (XX). A solution of the epoxide (XIX, 0·2 g) in the minimum quantity of ice-cold solution of ethereal HCl (3 ml) on shaking for a few min deposited a colourless compound. It crystallized from benzene–light petroleum mixture as colourless stout rectangular needles (0·1 g), m.p. 108–109°; ν_{max} 3600 cm^{-1} (OH), 1665 cm^{-1} (CO). (Found: C, 69·6; H, 5·2. $C_{23}H_{21}ClO_4$ requires: C, 69·6; H, 5·2%).

In another experiment, treatment of the epoxide (XIX) with excess ethereal HCl for 48 hr yielded a small amount of the chlorohydrin (XX), m.p. and mixed m.p. 108–109°. The major product was an oily liquid which could not be crystallized.

5. *Reactions of 2′,4′,4-trimethoxychalkone epoxide* (XXI)

(i) *2,4-Dimethoxyphenyl-β-acetoxy-α-hydroxy-β-4-methoxyphenyl ethyl ketone* (XXIII). An acetic acid solution of the chalkone epoxide[5] (XI, 0·4 g) was left overnight at room temp. Acetic acid was distilled, the residue extracted with ether and the ether solution extracted in turn with 5% NaOH aq. The residue from ether solution was crystallized from ethyl acetate–light petroleum mixture when the glycol monoacetate (XXIII) separated as colourless needles and rectangular plates (0·2 g), m.p. 131–132°; $\lambda_{max}^{Methanol}$ 272 mμ (4·09) and 305 mμ (3·91); ν_{max} 3600 cm^{-1} and 3000 cm^{-1} (—OH), 1750 cm^{-1} (ester carbonyl), 1665 cm^{-1} (C=O). (Found: C, 64·3; H, 6·0. $C_{20}H_{22}O_7$ requires: C, 64·2; H, 5·9%).

The alkaline solution on acidification yielded a noncrystallizable product giving positive ferric reaction and forming copper complex; it appeared to be α-formyldesoxybenzoin (XXIV).

(ii) *2,4-Dimethoxyphenyl-β-chloro-α-hydroxy-β-4-methoxyphenyl ethyl ketone* (XXII). The chalkone epoxide (XXI, 0·2 g) in dry ether (100 ml) was saturated with dry HCl gas at 0° and then left at room temp for 48 hr. The ether residue was crystallized from benzene–light petroleum mixture when the chlorohydrin (XXII) separated as aggregates of colourless prisms (60 mg), m.p. 123–124°; $\lambda_{max}^{methanol}$ 271 mμ (4·21), 305 mμ (4·04), ν_{max} 3600 cm^{-1} and 3000 cm^{-1} (—OH), 1650 cm^{-1} (C=O). (Found: C, 61·6; H, 5·7. $C_{18}H_{19}ClO_5$ requires: C, 61·6; H, 5·4%).

Note added in proof—The possible conversion of chalkone epoxides into isoflavones was recognised in 1932.[5] The idea, not then realized in the laboratory has been justified by our later work.[1]

[14] F. Herstein and S. von Kostanecki, *Ber. Dtsch. Chem. Ges.* **32**, 318 (1899).