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Intermolecular Hydride Transfer Reactions. V. Acid Induced Redox Reaction of 4-Phenylflav-3-ene

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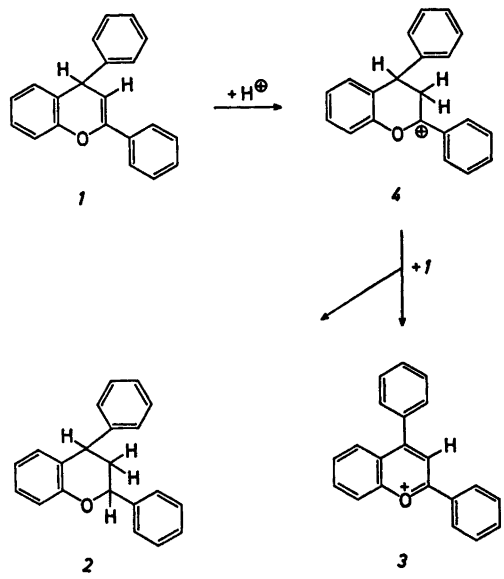
4-Phenylflav-3-ene was found to undergo intermolecular hydride transfer reaction in perchloric or trifluoroacetic acid. The main product besides the 4-phenylflavylium cation was *trans*-1-(*o*-hydroxyphenyl)-1,3-diphenylprop-1-ene. Traces of 4-phenylflavanes were also formed. A reaction mechanism accounting for these products was proposed.

2-Flavenes undergo intermolecular hydride transfer in acid solution to yield equimolar mixtures of the flavylium salt and the flavane. Thus the reaction of 4-phenylflav-2-ene (*1*) with trifluoroacetic acid (TFA) was found to be nearly quantitative and gave both *cis*- and *trans*-4-phenylflavanes (*2*) in 10:1 ratio besides the 4-phenylflavylium salt (*3*).[1] The course of the reaction (Scheme 1) was assumed to proceed through the intermediate formation of the carbonium ion *4*, formed by protonation of *1* at C-3. Subsequent hydride transfer from unprotonated *1* to the carbonium ion would account for the formation of the products. 4-Alkyl- and 3,4-dialkyl substituted 3-chromenes [2] as well as their thio-analogues [3] undergo similar intermolecular hydride transfer reactions in acidic solutions.

The present work deals with the behaviour of 4-phenylflav-3-ene (*5*) in acidic solutions. The reaction of this compound with perchloric-acetic acid mixture led to the formation of 4-phenylflavylium perchlorate (*3*), the yield of which approximates 50 % which is consistent with an acid-induced disproportionation of *5*. Examination of the reaction mixture by TLC and GLC showed the presence of 4-phenylflavanes (*2*) using authentic samples previously prepared.[1] The other main reaction product (about 35 %) which was isolated by preparative TLC afforded an acetyl derivative on treatment with acetic anhydride in pyridine. Its ^{1}H NMR spectrum in deuteriochloroform exhibited a doublet at δ 3.38 (2 H, J 8 Hz), a triplet at δ 6.55 (1 H, J 8 Hz) and a multiplet at δ 7.0 – 7.3 (14 H). The ^{1}H NMR spectrum of the acetate was similar to that of the parent compound except for a slight upfield shift of the olefinic proton triplet and a



Scheme 1.

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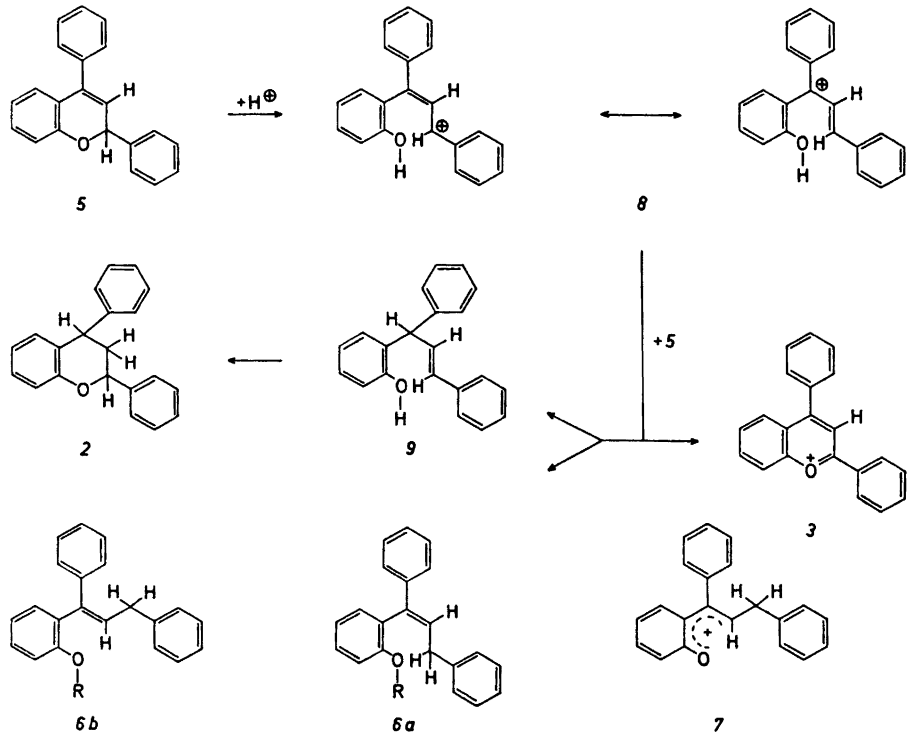


Scheme 2.

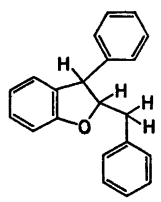
down-field shift of the methylene doublet, besides a singlet at δ 1.92 (3 H) for the acetate group. On the basis of these data, the structure of the parent compound was suggested to be either the *cis*- or the *trans*-1-(*o*-hydroxyphenyl)-1,3-diphenylprop-1-ene (*6a* or *b*, R = H) given in Scheme 2. The structure was further confirmed by mass spectrometry. The spectrum of *6a* or *b* (R = H) showed a base peak at *m/e* 286 which corresponds to its molecular ion, and a fragmentation pattern explainable on the basis of the proposed structure. The molecular ion in the mass spectrum of the acetate *6a* or *b* ($R = CH_3CO$) appeared at *m/e* 328 (relative abundance 41 %). The base peak which appeared at *m/e* 285 corresponds to the resonance-stabilised cation *7* shown in Scheme 2. Its formation from the molecular ion is supported by the presence of a metastable peak at *m** 247.5.

4-Phenylflav-3-ene (*5*) was also found to undergo disproportionation in trifluoroacetic acid (TFA). The oxidation product was isolated in 94 % yield as the perchlorate salt *3* by addition of perchloric acid to the reaction mixture after removal of TFA. The phenolic compound *6* was isolated in 64 % yield by preparative TLC. The mentioned yields were calculated according to the stoichiometry of a disproportionation reaction of *5*. The ^1H NMR spectrum of the reaction mixture showed signals due to the flavylium cation *3*, and the phenolic compound *6a* or *b* (R = H). The ^1H NMR spectrum carried out about 10 min after addition of drops of TFA to a solution of *5* in deuteriochloroform, apart from the signals of the flavylium cation showed two doublets centered at δ 3.63 (J 8 Hz) and 3.38 (J 8 Hz). The spectrum of the same solution after 24 h revealed the disappearence of the low-field doublet with increasing intensity of the other one. These two doublets may be assigned to *6a* (R = H) and *6b* (R = H), respectively, since the methylene protons of these two isomers are expected to give doublets of nearly the same coupling constant but with different chemical

shifts. It seems likely that the observed process is isomerisation of *6a* (R=H) to the more stable *6b* (R=H) with the benzyl and *o*-hydroxyphenyl groups *trans* oriented. Hence the isolated phenolic compound should be the *trans* isomer *6b* (R=H).

4-Phenylflavanes (*2*) were also formed in the above reaction as minor products, the detection of which was evident by GLC. The failure of their identification by ^{1}H NMR is probably due to their relatively low concentration in the reaction mixture.

A probable reaction mechanism which accounts for the observed products *3*, *6* (R=H) and *2* (Scheme 2) involves initial protonation of the heteroatom of *5* and subsequent ring opening to the carbonium ion *8*. A hydride transfer from unprotonated *5* to this carbonium ion would lead to the flavylium cation *3*. The carbonium ion *8* offers two sites for the transferred hydride ion. Attack at the secondary carbon would result in the formation of the phenolic compound *6* (R=H). Meanwhile hydride transfer to the tertiary carbon should give *9*, ring closure of which may explain the observed formation of 4-phenylflavanes (*2*). Moreover *9*, the precursor of *2*, can be considered to arise by a shift of the double bond of the phenolic compound *6* (R=H). This is supported by the formation of *trans*-4-phenylflavane (*2*) on boiling *6b* with TFA. The isomerisation is similar to that reported for the conversion of 1-(*o*-hydroxyphenyl)-3-phenylprop-1-ene into flavane in boiling acid.[4] Such an acid catalysed isomerisation probably involves the dihydrobenzofuran intermediate *10* (Scheme 3 A).



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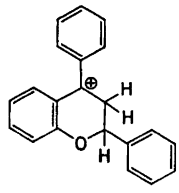

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A $6b \rightleftharpoons 10 \rightleftharpoons 9 \rightarrow 2$

B $5 \xrightarrow{H^+} 11 \xrightarrow{+5} 2+3$

Scheme 3.

With respect to the formation of the carbonium ion *8*, it should be mentioned that the acid catalysed reaction of 2,2-diphenylchromene with 1,1-diphenylethylene to yield 2,2-diphenyl-4-(2,2-diphenylvinyl)chromane was shown to proceed through an intermediate carbonium ion formed by fission of the chromene ring. Attack of this carbonium ion on the double bond of the olefin leads to a new cation which subsequently cyclises to the chromane derivative.[5] Moreover the conversion of certain isoflavenes into indenes under acid conditions, was assumed to take place by fission of the heterocyclic ring.[6]

Alternatively, the 4-phenylflavanes (*2*) may also be formed *via* the cyclic carbonium ion *11* produced by protonation of the double bond in *5* (Scheme 3 B). This reaction path is similar to the mechanism proposed for the acid-induced disproportionation of 4-alkyl- and 3,4-dialkyl substituted 3-chromenes.[3] It should be pointed out that disproportionation reactions proceeding *via* acyclic carbonium ion intermediate like *8* which gave rise to the unsaturated phenolic derivative *6* further susceptible to cyclisation, were not discussed before. It seems likely that fission of the heterocyclic ring should be more favoured in the 2-substituted 3-chromenes. As indicated from our results, a facile ring opening may be attributed to the benzylic group attached to ring oxygen of *5*.

EXPERIMENTAL

The ^{1}H NMR spectra were recorded on a Varian A-60A instrument with TMS as internal standard. A Perkin Elmer F11 instrument equipped with an OV-17 column was used for GLC analysis. Mass spectra were recorded on a AEI MS902 instrument. TLC was performed on silica plates using hexane, ethyl acetate baths.

Reaction of 4-phenylflav-3-ene (5)[7] *with perchloric acid.* To a mixture of perchloric acid (70 %) and acetic acid (1:10; 15 ml), 4-phenylflav-3-ene (*5*, 0.5 g) was added and the reaction mixture was stirred at 20 °C for 72 h. On addition of ether (100 ml), 4-phenylflavylium perchlorate (*3*), m.p. 222 °C[1] precipitated and was collected by filtration (0.3 g; 90 % yield). ^{1}H NMR spectrum of *3* in TFA: δ 8.58 (s, 1 H), 7.7–8.4, (m, 14 H). The ethereal solution was washed with water, 10 % $NaHCO_3$ and dried ($MgSO_4$). GLC and TLC analysis of this solution showed the presence of 4-phenylflavanes (*2*) besides traces of unreacted *5*. The ether was evaporated and the residue gave after pre-

parative TLC (hexane: ethyl acetate 10:1), *trans*-1-(*o*-hydroxyphenyl)-1,3-diphenylprop-1-ene (*6b*, R=H) (0.18 g; 72 % yield) as an oil. Molecular weight by MS: obs. 286.1356. Calc. for $C_{21}H_{18}O$: 286.1358. ^{1}H NMR ($CDCl_3$): δ 3.38 (d, 2 H, J 8.0 Hz), 6.55 (t, 1 H, J 8.0 Hz), 7.0–7.3 (m, 14 H).

trans-*1-(o-Acetoxyphenyl)-1,3-diphenylprop-1-ene* (6b, *R=CH$_3$CO*): A solution of *trans-1-*(*o*-hydroxyphenyl)-1,3-diphenylprop-1-ene (*6b*, R=H) (0.20 g) in pyridine (12 ml) was treated with acetic anhydride (1 ml) and kept overnight at room temperature. The reaction mixture was poured into water, extracted with ether and the ethereal solution washed successively with 10 % HCl, 10 % $NaHCO_3$, dried ($MgSO_4$) and evaporated. From the residue the pure acetate was obtained as an oil by preparative TLC (hexane: ethyl acetate 7:1). Molecular weight by MS: obs. 328.1468, calc. for $C_{23}H_{20}O_2$ 328.1463. ^{1}H NMR ($CDCl_3$) δ 1.92 (s, 3 H), 3.43 (d, 2 H, J 8.0 Hz), 6.36 (t, 1 H, J 8.0 Hz), 7.0–7.5 (m, 14 H).

Reaction of 4-phenylflav-3-ene (5) with TFA. A solution of 4-phenylflav-3-ene (*5*) (0.5 g) in TFA (10 ml) was stirred at 20 °C for 48 h, evaporated and the residue dissolved in chloroform. GLC analysis showed the presence of 4-phenylflavanes (*2*) besides traces of unreacted *5*. On addition of a mixture of perchloric acid (70 %) and acetic acid (1:10, 15 ml), followed by ether (100 ml) and then keeping overnight, 4-phenylflavylium perchlorate (*3*), m.p. 222 °C, was obtained in 94 % yield (0.32 g). The residue from the ethereal solution obtained after washing with 10 % $NaHCO_3$, drying ($MgSO_4$) and evaporation gave by preparative TLC (hexane:ethyl acetate 10:1), the *trans*-1-(*o*-hydroxyphenyl)-1,3-diphenylprop-1-ene (*6b*, R=H) (0.15 g, 64 %).

Reaction of trans-*1-(o-hydroxyphenyl)-1,3-diphenylprop-1-ene* (6b, *R=H) with TFA.* A solution of *trans*-1-(*o*-hydroxyphenyl)-1,3-diphenylprop-1-ene (0.1 g) in TFA (5 ml) was refluxed for 2 h, poured into water and extracted with ether. The ethereal solution after washing with 10 % $NaHCO_3$, drying ($MgSO_4$) was analysed by GLC. The *trans*-4-phenylflavane (*2*) was identified by comparison with authentic sample previously prepared.[1] Traces of *cis*-4-phenylflavane [1] (*2*) could not be detected.

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