## 78. 4-*Pyrones. Part V.*[1] *Some Reactions of Flavanone and its* 5,6-*Benzo-derivative.*

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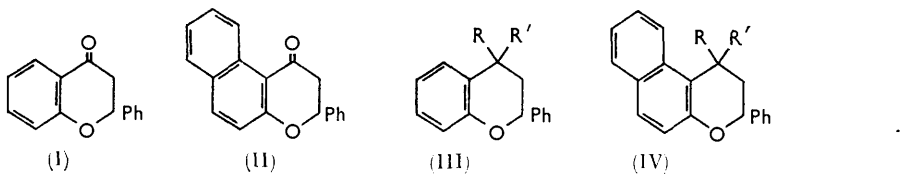
Flavanones are stable towards alkylamines but give the normal carbonyl reactions with carbonyl reagents. With Grignard reagents, they give either 4-substituted flavan-4-ols or 4,4-disubstituted flavans. The mechanism of this reaction is discussed.

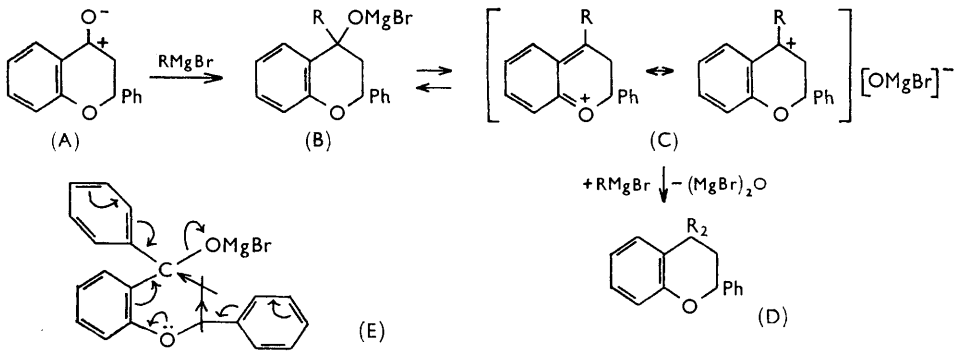
Continuing our study on the 4-pyrones, we proceeded to the study of hydrogenated pyrones. Flavanones gave no reaction with alkylamines but gave the normal reactions with carbonyl reagents.



(I) (II) (III) (IV)

(a) R = R′ = Ph (b) R = R′ = *p*-$C_6H_4$·OMe
(c) R = R′ = *p*-$C_6H_4$Me (d) R = R′ = $CH_2Ph$
(e) R = Me, R′ = OH (f) R = Et, R′ = OH
(g) R = Ph, R′ = OH

With Grignard reagents, flavanones afforded 4,4-diaryl- or -dibenzyl-flavans (Table 1) and 4-alkylflavan-4-ols (Table 2) in the presence of an excess of the reagent. The reaction is presumed to proceed according to the following scheme:



(A) (B) (C) (D) (E)

[1] Part IV, *J.*, 1963, 4647.

Evidence in favour of this mechanism is sought as follows. Reaction of flavanone (I) and 5,6-benzoflavanone (II) with one equivalent of phenylmagnesium bromide afforded 4,4-phenylflavan-4-ol (IIIg) and 4-phenyl-5,6-benzoflavan-4-ol (IVg) (cf. Table 2). The bromomagnesium derivatives from the isolated flavanols (IIIg) or (IVg) (cf. Table 3) reacted with one equivalent of phenylmagnesium bromide to afford 4,4-diphenylflavan (IIIa) (compound D, R = Ph) or 4,4-diphenyl-5,6-benzoflavan (IVa), respectively. Such a reaction should proceed by way of a carbonium ion (C), the ease of formation and stability of which, due to electron shifts (cf. structure E), may be compared with those of the triarylmethyl ion.[2]

It was noted that the formation of 4,4-disubstituted flavans (D) depends on the ease of formation and the extent of ionisation of both the carbonium ion (C) and the Grignard reagent. Thus, whilst the 4-phenylflavan-4-ol bromomagnesium derivative (B; R = Ph) reacted with phenylmagnesium bromide to give 4,4-diphenylflavan, 4-phenylflavan-4-ol (111 g.) was recovered unchanged when reacted with an excess of weakly ionised ethylmagnesium bromide. The less-readily ionisable 4-alkylflavan-4-ol bromomagnesium derivatives (B; R = alkyl) did not react with excess of the reagent to give the doubly substituted compounds, nor did 4-ethyl-5,6-benzoflavan-4-ol (IVf) bromomagnesium derivative react with phenylmagnesium bromide, but ionisation of this compound was, however, shown by its change from the isomer melting at 127° to the isomer melting at 140°.[3]

The method of Koelsch and Anthes [4] for the preparation of 5,6-benzoflavanone gave a poor or no yield. We modified this method as described in the experimental. 5,6-Benzoflavanone was changed to 5,6-benzoflavone by the action of N-bromosuccinimide.

## Experimental

Light petroleum had boiling point 70—80° unless otherwise stated.

*Preparation of 5,6-Benzoflavan-4-one.*—To a solution of 1-cinnamoyl-2-methoxynaphthalene (10 g.) in dry carbon disulphide (150 c.c.) heated to reflux, anhydrous aluminium chloride (7·5 g.) was added in small portions, with stirring, over ½ hr. Reflux was continued for 10 hr. more. The residual solid, left after the evaporation of the solvent, was refrigerated overnight under glacial acetic acid. The solution was filtered and the solid was crystallised from light petroleum as colourless crystals, m. p. 116° (Found: C, 83·1; H, 5·3. Calc. for $C_{19}H_{14}O_2$: C, 83·2; H, 5·2%). The compound gave an *oxime*, m. p. 156° (from ethanol) (Found: C, 79·1; H, 5·2; N, 4·7. $C_{19}H_{15}NO_2$ requires C, 78·9; H, 5·2; N, 4·8%), a *phenylhydrazone*, m. p. 204° (from ethanol) (Found: C, 82·1; H, 5·5; N, 7·7. $C_{25}H_{20}N_2O$ requires C, 82·4; H, 5·5; N, 7·7%), a 2,4-*dinitrophenylhydrazone*, m. p. 298° (from benzene) (Found: C, 66·4; H, 4·1; N, 11·9. $C_{25}H_{18}N_4O_5$ requires C, 66·7; H, 4·0; N, 12·3%), and *bis*-5,6-*benzoflavanone hydrazone*, m. p. 262° (from chloroform) (Found: C, 83·5; H, 5·2; N, 5·3. $C_{38}H_{28}N_2O_2$ requires C, 83·2; H, 5·1; N, 5·1%).

*Preparation of 5,6-Benzoflavone.*—A mixture of 5,6-benzoflavanone (0·5 g.) and *N*-bromosuccinimide (0·4 g.) in carbon tetrachloride (25 c.c.) was refluxed for 3 hr., cooled, and filtered. On concentration of the filtrate, a solid separated (0·3 g.), m. p. and mixed m. p.[5] 145° (from carbon tetrachloride).

*Treatment of 5,6-Benzoflavanone with Methylamine.*—When 5,6-benzoflavanone was boiled with methylamine in dilute ethanol, it was quantitatively recovered unchanged, m. p. and mixed m. p. 116° (from light petroleum).

*Flavanone.*—It was prepared according to the literature,[6] and gave a *semicarbazone*, m. p. 202° (from ethanol) (Found: C, 68·1; H, 5·1; N, 15·2. $C_{16}H_{15}N_3O_2$ requires C, 68·3; H, 5·3; N, 15·0%) and an *oxime*, m. p. 169° (from ethanol) (Found: N, 5·8. $C_{15}H_{15}NO_2$ requires N, 5·8%).

[2] Elkaschef and Ahmad, *J.*, 1960, 2272.
[3] Karrer, Yen, and Reichstein, *Helv. Chim. Acta*, 1930, **13**, 1308.
[4] Koelsch and Anthes, *J. Org. Chem.*, 1941, **6**, 558.
[5] Menon and Venkataraman, *J.*, 1931, 2591.
[6] Pongraez and Spiess, *Ber.*, 1924, **57**, 1517.

*Action of Grignard Reagents on Flavanones.*—To a solution of the Grignard reagent in dry ether (50 c.c.) a solution of the flavanone [2·24 g. of (I) or 2·7 g. of (II)] in dry benzene was added. The mixture was left overnight, refluxed for 4 hr., and decomposed with dilute hydrochloric acid and ice. The combined ethereal layer and the ethereal extract of the aqueous layer were washed with water and dried ($Na_2SO_4$). The residue remaining after evaporation of the solvent, was crystallised from the appropriate solvent to give 4,4-disubstituted flavans (Table 1) or 4-substituted flavan-4-ols (Table 2).

TABLE 1.

4,4-Disubstituted flavans.

| | | | | | Found (%) | | | Reqd. (%) | |
|---|---|---|---|---|---|---|---|---|---|
| Halide | Flavonone | Product | M. p. | Solvent | C | H | Formula | C | H |
| PhBr (3·2 c.c.) ..... | (I) | (IIIa) (0·5 g.) | 118° | Light pet.* | 89·0 | 6·1 | $C_{27}H_{22}O$ | 89·5 | 6·1 |
| $PhCH_2Br$ (5·1 g.) ..... | (I) | (IIId) (0·4 g.) | 53 | Ethanol | 89·4 | 6·6 | $C_{29}H_{26}O$ | 89·2 | 6·7 |
| PhBr (3·2 c.c.) ..... | (II) | (IVa) (1·6 g.) | 170 | ,, | 90·1 | 5·4 | $C_{31}H_{24}O$ | 90·3 | 5·8 |
| *p*-MeO·$C_6H_4Br$ (5·6 g.) | (II) | (IVb) (1·8 g.) | 156 | ,, | 84·2 | 5·8 | $C_{33}H_{28}O_3$ | 83·9 | 5·9 |
| *p*-Me·$C_6H_4Br$ (4 c.c.) ... | (II) | (IVc) (1·4 g.) | 148 | ,, | 90·0 | 5·9 | $C_{33}H_{28}O$ | 90·0 | 6·4 |
| $PhCH_2Br$ (5·1 g.) ..... | (II) | (IVd) (1·6 g.) | 168 | ,, | 89·9 | 6·2 | $C_{33}H_{28}O$ | 90·0 | 6·4 |

* B. p. 40—60°.

*Treatment of the Bromomagnesium Derivatives of the Flavan-4-ols with Grignard Reagents.*—To the bromomagnesium derivative, prepared by the reaction of flavanol with an equivalent amount of ethyl- or methyl-magnesium halide in ether–benzene, the Grignard reagent was added.

TABLE 2.

4-Substituted flavan-4-ols.

| | | | | | Found (%) | | | Reqd. (%) | |
|---|---|---|---|---|---|---|---|---|---|
| Halide | Flavanone | Product | M. p. | Solvent | C | H | Formula | C | H |
| PhBr (1·6 c.c.) ... | (I) | (IIIg) (0·5 g.) | 83° | Light pet.* | 83·9 | 6·0 | $C_{21}H_{18}O_2$ | 83·4 | 6·0 |
| MeI (1·85 g.) ... | (I) | (IIIe) (0·9 g.) | 86 | Light pet.* | 79·5 | 6·6 | $C_{16}H_{16}O_2$ | 80·0 | 6·7 |
| PhBr (1·5 c.c.) ... | (II) | (IVg) (2·7 g.) | 108 | Ethanol | 85·0 | 5·7 | $C_{25}H_{20}O_2$ | 85·3 | 5·7 |
| MeI (1·9 g.) ..... | (II) | (IVe) | 138 | Light pet.† | 82·7 | 6·3 | $C_{20}H_{18}O_2$ | 82·7 | 6·2 |
| EtBr (3·3 g.) ... | (II) | (IVf) (0·7 g.) | 127 | Ethanol | 82·9 | 6·6 | $C_{21}H_{20}O_2$ | 82·9 | 6·6 |

* B. p. 40—60°. † B. p. 70—80°.

TABLE 3.

Products from reaction of 4-substituted flavan-4-ols with Grignard reagents.

| Halide | Flavanol | Product | M. p. | Solvent |
|---|---|---|---|---|
| PhBr (1·6 c.c.) | (IVg) (1·2 g.) | (IVa) (0·5 g.) | 170° * | Ethanol |
| PhBr (1·1 c.c.) | (IVf) † (1·2 g.) | (IVf) ‡ (0·5 g.) | 140 | Methanol |
| PhBr (1·1 c.c.) | (IIIg) (0·5 g.) | (IIIa) (0·4 g.) | 118 * | Light petroleum (b. p. 40—60°) |
| EtBr (in excess) | (IIIg) (0·5 g.) | (IIIg) (0·4 g.) | 83 * | ,, ,, |

* Mixed m. p. † M. p. 127°. ‡ Found: C, 82·9; H, 6·6. Calc. for $C_{21}H_{20}O_2$: C, 82·9; H, 6·6%.

After the necessary reflux the mixture was worked up as usual and the product (Table 3) was crystallised from the appropriate solvent.

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