

Intermolecular Hydride Transfer Reactions. II. Reinvestigation of the Reaction between Flavylum Perchlorate and Dimethylaniline

EILIF TERJE ØSTENSEN

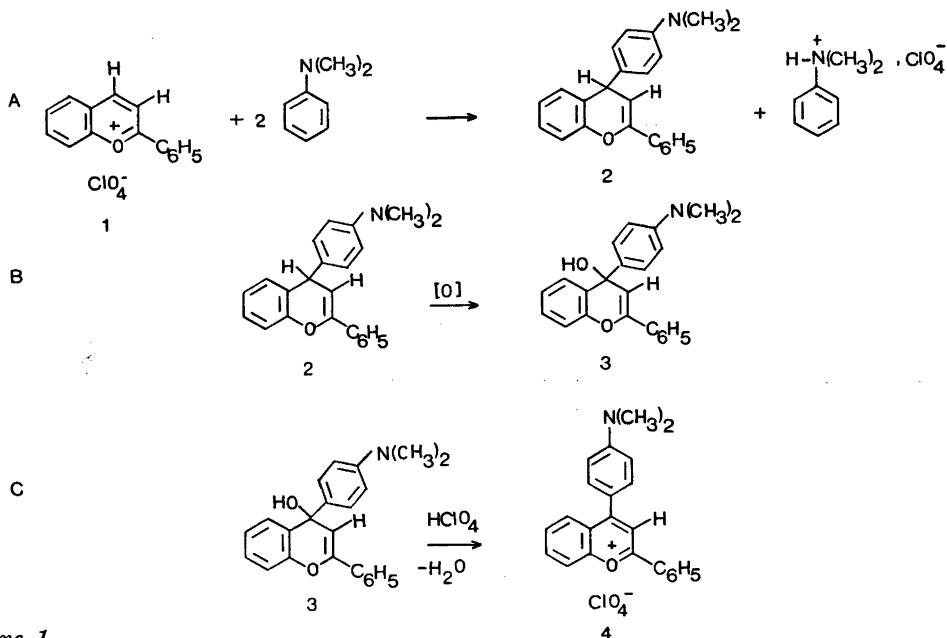
Organic Chemistry Laboratories, The Norwegian Institute of Technology, University of Trondheim, N-7034 Trondheim-NTH, Norway

Reaction of flavylum perchlorate with dimethylaniline in ether solution produced 4-(*p*-dimethylaminophenyl)flav-2-ene. Intermolecular hydride transfer between the 4-substituted flavene and unreacted flavylum salt with formation of 4-(*p*-dimethylaminophenyl)flavylium perchlorate and the parent flav-2-ene was observed. In addition, 3-(flav-2-ene-4-yl)-2-methoxyflavane was formed when the reaction was carried out in methanol solution.

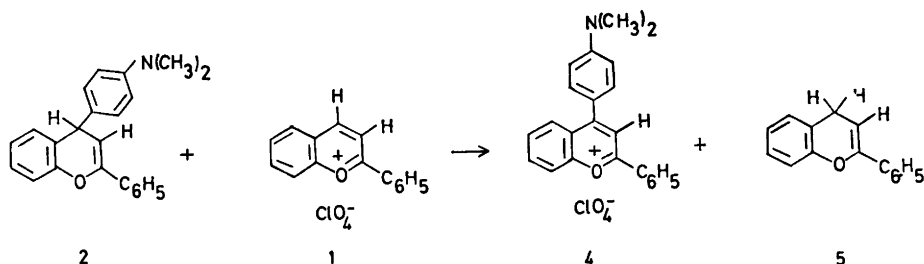
Recently the reactions of 2,6-dimethoxycarbonylpyrylium perchlorate with dimethylaniline, anisole, and toluene have been studied

and it was shown that the 2,6-dimethoxycarbonyl-4*H*-pyran-yl group was introduced into the *para* position of these benzene derivatives.¹ The 4*H*-pyran-yl group was further oxidized to the corresponding pyrylium cation by an intermolecular hydride transfer reaction. The 2,6-dimethoxycarbonylpyrylium cation acted as hydride acceptor and was reduced to the 2,6-dimethoxycarbonyl-4*H*-pyran in this process.

The present work deals with the nature of the reaction between flavylum perchlorate (*I*) and dimethylaniline (DMA). This reaction



Scheme 1.



Scheme 2.

was first studied by Shriner and Shotton whose conclusions are summarized in Scheme 1.³

Addition of flavylium perchlorate (1) to an ether solution of DMA produced the flavene derivative 2 and the hydrop perchlorate salt of DMA (step A). The flavene 2 was further oxidized by air to the carbinol 3 (step B). The carbinol 3 yielded with perchloric acid the flavylium salt 4 (step C). The reaction which was carried out in presence of air, gave a mixture of the products mentioned above. The evidence supporting the conclusion that carbinol 3 is an intermediate in the oxidation of the flavene 2 to the flavylium salt 4 was based on the following observations. A dark coloured precipitate was collected from the reaction mixture of 1 with DMA in ether solution. The flavene 2 was isolated from the filtrate. The dark coloured material was treated with 5% sodium carbonate and ether. The flavylium perchlorate 4 was obtained by filtration of this mixture and furthermore the carbinol 3 was isolated from the ether soluble fraction.

It is not clear whether the isolated carbinol 3 resulted from air oxidation of 2 or from reaction of flavylium salt 4, present in the coloured material, with sodium carbonate solution. The transformation of 4 to the carbinol 3 with base has been demonstrated by Shriner and Shotton.³

In addition to the sequence proposed by Shriner and Shotton (Scheme 1), the flavylium salt 4 could arise by a second possible route. An intermolecular hydride transfer reaction between unreacted flavylium salt 1 and flavene 2 would result in the formation of 4 and the parent flav-2-ene (5) (Scheme 2).

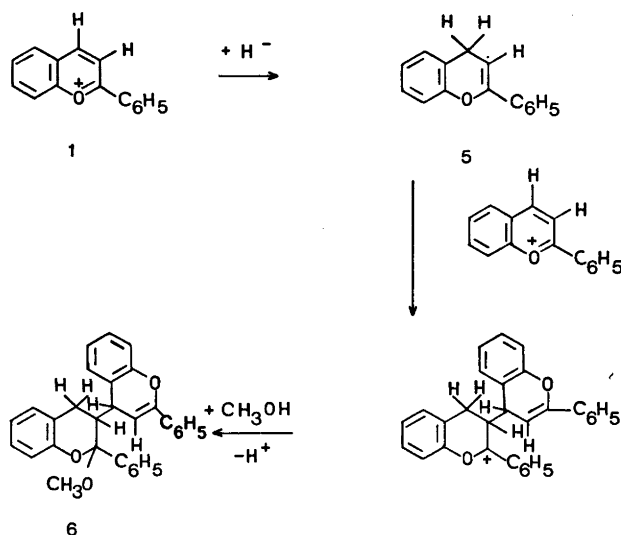
In search of the reduction product 5, flavylium perchlorate (1) was reacted with DMA in ether. The ether insoluble material

was removed by filtration. Gas chromatography and ^1H NMR analysis of the filtrate verified the formation of flavenes 2 and 5. The latter two flavenes were synthesized by alternative procedures for purposes of identification. Compound 5 was not reported by Shriner and Shotton. The intermolecular hydride transfer reaction depicted in Scheme 2 was further demonstrated in a separate experiment.

Equimolecular amounts of the flavene 2 and flavylium perchlorate were allowed to react for 24 h in acetonitrile solution. Treatment with ether yielded a crystalline product, which was identified as the flavylium salt 4 (80%). The ethereal solution consisted mainly of flavene 5 with traces of unreacted 2 as shown by GLC and ^1H NMR analysis. These results suggest that the formation of 4 from the reaction of 1 with DMA proceed *via* the steps shown in Schemes 1A and 2.

The reaction of flavylium perchlorate 1 with DMA has also been investigated by Blackburn *et al.*³ using methanol as solvent. The flavylium salt 4 reportedly precipitated from the reaction mixture. The constituents of the remaining solution were not commented on. On repeating this reaction it was verified that the main component in the precipitated material was the flavylium salt 4. However, careful extraction of the collected solide material with ether resulted in the isolation of the flavane derivative 6 (m.p. 202°C) (Scheme 3). The remaining methanol solution was examined by GLC and ^1H NMR analysis. First of all the substitution product 2 and the flavene 5 could be identified. Furthermore resonances at δ 5.2 (doublet, J 4.5 Hz) in the ^1H NMR spectrum could, as shown below, be attributed to the diastereomers of the isolated flavane derivative 6.

Reynolds *et al.*⁴ have reported that reduction



Scheme 3.

of the flavylium cation (1) with sodium borohydride in methanol resulted in formation of the flavane derivative 6.

The reaction sequences used to explain the formation of 6 were similar to those depicted in Scheme 3. While the borohydride reduction of 1 yielded the parent flav-2-ene (5) the redox reaction depicted in Scheme 2 explains the formation of this compound in the reaction of 1 with DMA.

The reaction sequence in Scheme 3 is supposed to yield four stereoisomers provided a selective addition to the double bond of flavene (5). Repetition of the reduction of 1 with sodium borohydride in methanol resulted in the isolation of the isomers (m.p. 203 °C) reported by Reynolds *et al.*⁴ and in addition their methanol soluble diastereomers (m.p. 163 °C).

¹H NMR resonance signals of the β -flavenyl proton of the methanol soluble isomers (m.p. 163 °C) showed up as a doublet at δ 5.2 ($J = 4.5$ Hz) consistent with signals observed by ¹H NMR analysis of the methanol fraction from the reaction of 1 with DMA as mentioned above. Signals at δ 3.0 (s, 3 H and m, 4 H) were also compatible.

The observations described in this paper do not rule out the possibility of a reaction path in which air oxidation plays an important part in formation of 4 from flavene 2. However, it seems possible that the main path is through

the intermolecular hydride transfer process depicted in Scheme 2.

It should be pointed out that Shriner and Shotton² reported that addition of acid to an air oxidized solution of flavene 2 resulted in the formation of the flavylium salt 4.

EXPERIMENTAL

¹H NMR spectra were recorded on a Varian A-60A instrument. A Perkin-Elmer F11 instrument equipped with an OV-17 column was used for the GLC analysis. The mass spectra were run on a AEI MS902 with a PDP11 computer.

Flavylium perchlorate and dimethylaniline in ether. Flavylium perchlorate⁵ (7.65 g, 0.0025 mol) was added to a solution of dimethylaniline (6.05 g, 0.05 mol) in ether with vigorous stirring. After 3 h the insoluble material was collected. Crystallization from methanol yielded 1.9 g of 4-(*p*-dimethylaminophenyl)flavylium perchlorate (4) m.p. 246 °C. ¹H NMR spectrum in TFA: δ 3.63 [s, N(CH₃)₂], 7.5–8.7 (m, 14 arom. H).

The filtrate was evaporated and the residual oil was examined by GLC and ¹H NMR spectroscopy. Flav-2-ene (5) and 4-(*p*-dimethylaminophenyl)flav-2-ene (2) were identified together with unreacted dimethylaniline.

Flav-2-ene (5) which was synthesized by the reduction of flavylium perchlorate with lithium-aluminum hydride⁶ and 4-(*p*-dimethylaminophenyl)flav-2-ene (2) synthesized from flavylium perchlorate and *p*-dimethylaminophenyl lithium,² were used as reference substances.

^1H NMR spectrum of flav-2-ene (5) in CDCl_3 : δ 3.5 (d, 2 H_4), 5.4 (t, H_3 , $J_{3,4}$ 4 Hz) 6.8–7.8 (m, 9 arom. H). ^1H NMR spectrum of 4-(*p*-dimethylaminophenyl)flav-2-ene (2) in CDCl_3 : δ 2.88 [s, $\text{N}(\text{CH}_3)_2$], 4.72 (d, H_4 , $J_{3,4}$ 4.5 Hz), 5.58 (d, H_3) 6.6–7.9; (m, 13 arom. H).

Flavylium perchlorate and 4-(p-dimethylaminophenyl)flav-2-ene (2) in acetonitrile. To a solution of flavylium perchlorate (0.306 g, 0.001 mol) in acetonitrile (10 ml) was added 4-(*p*-dimethylaminophenyl)flav-2-ene (2) (0.327 g, 0.001 mol) with stirring. After 24 h ether was added and the precipitated material was collected by filtration. Crystallization from methanol yielded 4-(*p*-dimethylaminophenyl)flavylium perchlorate (4), m.p. 248°C (83%). The filtrate was evaporated and GLC and ^1H NMR analyses of the residual oil showed almost pure flavene (5). The product was contaminated with 4-(*p*-dimethylaminophenyl)flav-2-ene (2).

Flavylium perchlorate and dimethylaniline in methanol. To a solution of dimethylaniline (1.21 g, 0.01 mol) in methanol (50 ml) was added flavylium perchlorate (3.06 g, 0.01 mol) with stirring. After 12 h at 25°C the reaction mixture was filtered. The collected solid material was triturated with 250 ml ether and filtered. This yielded 0.68 g of 4-(*p*-dimethylaminophenyl)flavylium perchlorate (4), m.p. 248°C. Evaporation of the ether fraction yielded 0.25 g of 3-(flav-2-ene-4-yl)-2-methoxyflavene (6) m.p. 202°C.

The remaining methanol solution from above was concentrated and the residual oil was examined by GLC and ^1H NMR spectroscopy. Flav-2-ene (5), 4-(*p*-dimethylaminophenyl)flav-2-ene (2) and diastereomers of the 3-(flav-2-ene-4-yl)-2-methoxyflavanes (6) were identified from comparison with authentic samples.

Diastereomers of 3-(flav-2-ene-4-yl)-2-methoxyflavane (6). A suspension of flavylium perchlorate (5.0 g, 0.016 mol) in methanol (100 ml) was stirred and sodium borohydride (1 g) was added in small portions. After 0.5 h, 2.2 g of a white solid was collected (m.p. 203°C). ^1H NMR spectrum in CDCl_3 : δ 2.90 (s, OCH_3), 2.0–2.7 (m, 2 H, methylene), 2.9–3.6 (m, 2 H, methine), 4.68 (doublet; H_{β} -flavenyl, $J_{\beta,\gamma}$ 6 Hz), 6.5–7.9 (m, 18 arom. H). The filtrate was concentrated and diluted with water. The precipitated material was collected and after fractionated crystallization a white crystalline compound was obtained (m.p. 163°C). Molecular weight by MS: Found 446.1887. Calc. for $\text{C}_{31}\text{H}_{28}\text{O}_3$: 446.1882. ^1H NMR spectrum in CDCl_3 : (δ): 3.0 (s, OCH_3), 2.4–2.8 (m, 2 H, methylene), 3.1–3.5 (m, 2 H, methine) 5.15 (d. H_{β} -flavenyl, $J_{\beta,\gamma}$ 4.5 Hz), 6.6–7.9 (m, 18 arom. H).

Acknowledgement. A grant from The Norwegian Institute of Technology, University of Trondheim, is gratefully acknowledged.

REFERENCES

1. Østensen, E. T. *Acta Chem. Scand. B* 28 (1974) 1107. Part I.
2. Shriner, R. L. and Shotton, J. A. *J. Amer. Chem. Soc.* 74 (1952) 3622.
3. Blackburn, M., Sankey, G. B., Robertson, A. and Whalley, W. B. *J. Chem. Soc.* (1957) 1573.
4. Reynolds, G. A. and VanAllan, J. A. *J. Org. Chem.* 32 (1967) 3616.
5. Wizinger, R. and v. Tobel, H. *Helv. Chim. Acta* 40 (1957) 1305.
6. Freudenberg, K. and Weinges, K. *Justus Liebigs Ann. Chem.* 590 (1954) 148.

Received January 17, 1975.