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HYDROGEN BONDING IN ORGANIC SYNTHESIS: EVIDENCE FOR THE ROLE OF HYDROGEN BONDING IN REACTIONS OF FLUORENE PROMOTED BY FLUORIDE ION

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Fluoride ion activated fluorene is readily alkylated by methyl iodide and oxidised by molecular oxygen but does not undergo H-D exchange with D_2O under the same conditions.

In recent years a number of organic reactions have been reported where hydrogen bonding has been claimed to play an important role[1]. Typically, H-bonding through the hydrogen of a protic molecule will result in an overall transfer of electron density from the proton acceptor atom to the proton donor atom resulting in an increase in nucleophilic character of the latter.[2] The fluoride ion is a popular choice as an H-bond proton acceptor (electron donor) as it is known to be capable of forming a number of strong H-bonds.[3] A large number of reactions that are normally base-assisted have been promoted by the fluoride ion and it has been suggested that many of these reactions involve a hydrogen bonded anionic complex as the reactive intermediate rather than the simple organic anion.[4] As part of our studies on the use of fluorides in organic synthesis[5] we wish to report preliminary results from experiments on the behaviour of the carbon acid fluorene on activation by fluoride. Little is known of the reactions of carbon acids in the presence of fluoride apart from Michael addition reactions.[4] We have successfully demonstrated not only that fluoride activates fluorene towards alkylation and autoxidation but also that the reaction apparently occurs via an H-bonded complex.

When tetraethylammonium fluoride dihydrate (TEAF.$2H_2O$) is added to a solution of fluorene in CH_3CN, we can envisage two possible equilibria

$$F(H_2O)_2^- + RH \rightleftharpoons R^- + HF + 2H_2O \qquad (1)$$

$$F(H_2O)_2^- + RH \rightleftharpoons R\text{-}H...F(H_2O)^- + H_2O \qquad (2)$$

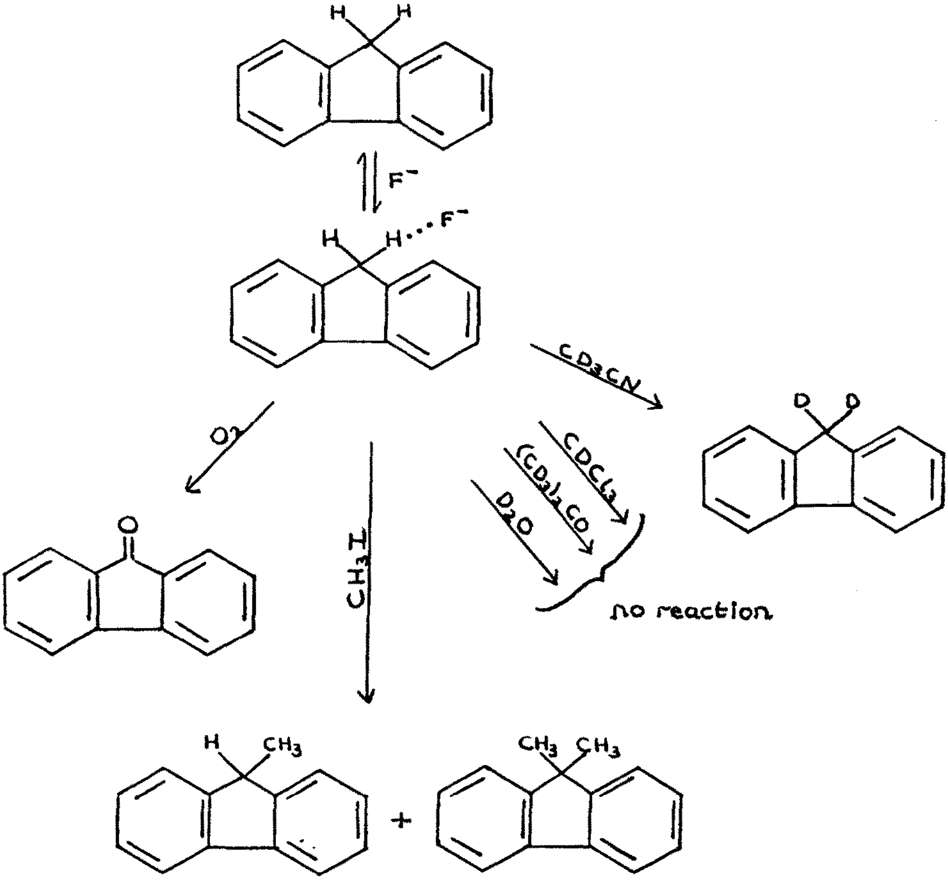
where $R\text{-}H...F(H_2O)^-$ represents an H-bonded complex of fluorene. Addition of fluorene to TEAF.$2H_2O$ in CH_3CN under an argon atmosphere results in the formation of a yellow-orange solution which rapidly turns purple in colour. The solution is stable at this stage, although decolourises under the action of water. The visible spectrum of this solution shows a weak band at 378 nm and a very intense band at 550 nm. The higher energy band is very similar in position to that reported for the carbanion but the 550 nm band does not correspond to bands due to the carbanion or oxidation products.[6]

In the presence of oxygen, TEAF.$2H_2O$ readily catalyses the oxidation of fluorene to fluorenone. This reaction is typically base-catalysed although it is interesting to note that the F^- catalysed reaction occurs under mild conditions.[7] Alkylation of fluorene can also be achieved using fluoride activation, and by running the reaction in the presence of a dessicant[8] the efficiency of the reaction is comparable to those employing more conventional soluble bases.[9] These reaction characteristics are consistent with a species that possesses carbanion character but they do not allow us to distinguish between the equilibria (1) and (2).

Water can behave as an electrophile towards carbanions and will protonate the fluorene anion. Water is also a powerful H-bond proton donor, and a complex such as $R\text{-}H...F(H_2O)^-$ containing a relatively weak $R\text{-}H...F^-$ H-bond and a coordinatively unsaturated F^- is likely to undergo rapid decomposition in water. Quenching a CH_3CN solution of fluorene-TEAF.$2H_2O$ with a large excess of D_2O results in no measurable increase in deuterium content above natural abundance. Quenching the same solution with CH_3I results in the formation of alkylated products. It is interesting to note that addition of fluorene to a dilute solution of TEAF.$2H_2O$ in CD_3CN results in rapid H-D exchange of the fluorene methylene hydrogens. This exchange does not occur with $CDCl_3$ or $(CD_3)_2CO$ solutions of TEAF.$2H_2O$. Water, chloroform and acetone (via the enol form) are certainly more powerful H-bond proton donors than fluorene or acetonitrile and presumably would destroy a fluorene-F^- complex before H-D exchange could take place. Rapid H-D exchange between H-bonded complexes (fluorene-F^- and $CD_3CN\text{-}F^-$) is consistent with the known rapid H-H exchange between such species.[9] We believe that our observations are consistent with the interaction of fluorene and F^- producing an H-bonded complex with carbanion character as the reactive intermediate in such systems (eqn. 2) rather than the simple carbanion (eqn. 1).

Fluorene (2 mmol) and TEAF.$2H_2O$ (2 mmol) were stirred together in dry CH_3CN under an oxygen atmosphere at room temperature for 24 hours. The resulting solution was poured into a large volume of water and extracted with CCl_4 to give a 54% yield of fluorenone (confirmed by n.m.r. and i.r.) along with unreacted fluorene. Slow addition of an excess of CH_3I to a refluxing solution of fluorene (2.4 mmol) and TEAF.$2H_2O$ (4.8 mmol) in CH_3CN over anhydrous KF[8] (argon atmosphere) resulted in the formation of a 24% yield of 9-methylfluorene and a 12% yield of 9,9-dimethylfluorene (confirmed by n.m.r.). For comparative studies on the behaviour of different electrophiles toward TEAF.$2H_2O$-fluorene the following procedure was used. A freshly dried CH_3CN solution containing equimolar quantities of TEAF.$2H_2O$ and fluorene was divided into two equal portions. The first portion was quenched with excess D_2O in CH_3CN while the second was quenched with excess CH_3I in CH_3CN. In both cases work-up involved precipitation of salts with ether followed by drying with anhydrous $MgSO_4$ and removal of the solvent by evaporation. ^2H N.m.r. of the first portion showed no increase in ^2H content in the fluorene above natural abundance. ^1H N.m.r. of the second portion showed the presence of both mono- and di-alkylated products (ca. 4% in total). Experiments using $(CD_3)_2CO$ or $CDCl_3$ as the source of deuterium failed to give any n.m.r. evidence for H-D exchange with fluorene whereas use of CD_3CN resulted in a 100% incorporation of deuterium at both 9-positions by n.m.r.

Our reaction observations are summarised in the figure below.



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