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FLUORIDE ION CATALYSED MICHAEL REACTIONS

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A study of the relative efficiencies of different sources of F^- in catalysing the Michael reaction of nitroethane to 3-buten-2-one reveals that KF or CsF supported on alumina are the best reagents.

In recent years the fluoride ion has been successfully applied to a wide range of typically base assisted reactions.[1)] Fluoride catalysed Michael reactions have proven to be especially popular and an appreciable number of successful reactions of this type have been reported. A variety of sources of F^- have been used in these reactions including alcoholic solutions of KF[2)], heterogenous KF and CsF-aprotic solvent systems[3)], tetraalkylammonium fluorides[4)] and KF-18-crown-6.[5)] Current interest in the concept of utilising the enhanced reactivity of inorganic reagents impregnated on inorganic support materials has prompted us to investigate the relative efficiency of supported metal fluorides in Michael reactions as part of a general study programme in this area.[6,7)]

We chose the Michael reaction of nitroethane and 3-buten-2-one (Eq. 1) as a model system for our study.

$$CH_3CH_2NO_2 \;+\; CH_3COCH = CH_2 \xrightarrow{F^-} CH_3COCH_2CH_2CH(NO_2)CH_3 \qquad (1)$$

We have already shown that F^- is a very useful catalyst for this type of reaction as part of a general reaction scheme for the preparation of 1,4-diketones.[7)] After considering various methods for monitoring the progress of this reaction we decided that gas chromatrography was the most convenient and reliable technique - the results obtained were reproducible to within + 20% and are presented in graphical form in Fig. 1.

The observed order of reactivities and times required for 100% reaction are: CsF-alumina (1-3 minutes depending on loading and efficiency of drying) > KF-alumina (3-5 min) > CsF in ethanol (13 min) > wet CsF (15 min) > reagent grade CsF (30 min) $\approx$ dry CsF (30 min) > dry alumina (60 min) > KF-18-crown-6 (85 min) > KF (1750 min). The supported fluorides are clearly the most reactive sources of F^- tested. Supported KF is considerably more reactive than KF-18-crown-6 which was previously regarded as the best KF source for Michael reactions.[5)] We have found that alumina is the best support material for enhancing the reactivity of the fluorides in agreement with the recently reported observations of Ando et al.[8)] Our previous experience with the properties of potassium permanganate on silica[6)] taught us that the best results are obtained by achieving optimum surface dispersion (monolayer formation) of the salt which requires efficient drying of the reagent. Thermogravimetric analysis of the supported fluorides shows that forcing conditions (e.g. 150°C for 24h under reduced pressure) are required to remove the bulk of the physisorbed water. Inefficiently dried reagents are certainly less effective in catalysing the Michael reaction than those described here. Variations in reaction rate on changing the loading of the fluoride by more than a factor of 10 are small compared to the reported increase in reaction rates for non-catalytic reactions on increasing the fluoride loading.[8)] The reactivity of the reagent having the highest fluoride loading (1 mole CsF/100 g alumina) is surprising as the concentration of salt molecules (<u>ca</u>. 40/nm^2) is clearly too high for monolayer formation. It is possible that the excess fluoride is essentially redundant although it may be that small fluoride clusters within the pores of the support are themselves very reactive.

The high reactivity of CsF in ethanol is rather surprising as F^- will suffer a loss in local electron density through strong hydrogen bonding to ethanol and would therefore be expected to be a weaker base. The best analogy for this observation is probably the known reaction behaviour of F^- -carboxylic acid systems which act as excellent sources of the carboxylate ion but not of F^-.[9)] It is quite possible therefore, that the reactive nucleophilic site in CsF-ethanol is the oxygen atom (Eq. 2). Traces of water also seem to improve the reactivity of unsupported CsF and this may be due to activation of surface

$$F^- \quad + \quad CH_3CH_2OH \quad \rightarrow \quad \overset{\delta-}{F}{}^-.(..H\text{-}\overset{\delta-}{O}{}^-\text{-}CH_2CH_3)_x \qquad (2)$$

water by F^-...HOH hydrogen bonding. Similarly, well dried alumina containing only traces of water is quite reactive which is again likely to be due to surface activation.

The supported fluoride reagents were prepared by slow evaporation with thorough mixing of mixtures of the fluoride and neutral alumina (BDH reagent, 90Å pore diameter, 100-130 m^2/g surface area) in water. The resulting solids were dried at temperatures up to 200°C under reduced pressure. Reactions were carried out by stirring a solution of nitroethane (0.25 mol) and 3-buten-2-one (0.0125 mol) in 30 cm^3 dry acetonitrile (or ethanol in one case) over the source of the fluoride (0.025 mol equiv. F^-) at room temperature. 0.5 cm^3 samples were withdrawn at regular intervals, rapidly quenched in a mixture of ether and

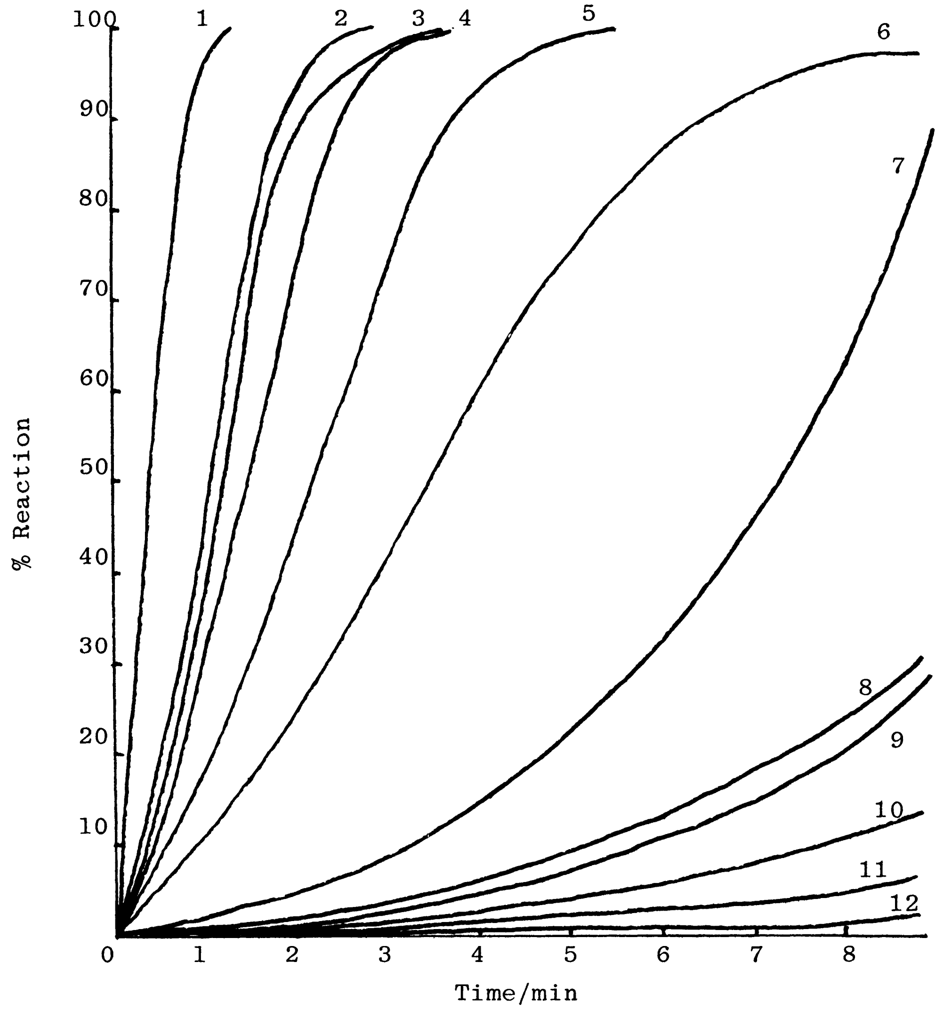

Fig.1.

1. CsF-alumina, 8 molecules/nm^2. 2. CsF-alumina, 2.5 molecules/nm^2.
3. KF-alumina, 8 molecules/nm^2. 4. CsF-alumina, 40 molecules/nm^2.
5. KF-alumina, 2.5 molecules/nm^2. 6. CsF dissolved in ethanol.
7. CsF + trace of water. 8. CsF (reagent grade). 9. CsF dried at 200°C.
10. Alumina dried at 200°C. 11. KF-18-crown-6. 12. KF dried at 200°C.

dichloromethane, and injected into the G.C. Reaction was allowed to continue until no change in the peak area ratio of product to excess nitroethane was observed. Long-term variations in this ratio could be attributed to further F^- catalysed reactions such as oxidative dimerisation of the nitroethane to 2,3-dinitrobutane.

In conclusion, we have shown that KF or CsF supported on alumina are remarkably efficient reagents for catalysing a typical Michael reaction. The reagent should be well dried and a loading of about 2.5 molecules/nm^2 is adequate.

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