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Al_2O_3 Supported KF: An Efficient Mediator in the Epoxidation of Electron Deficient Alkenes with t-BuOOH[#]

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Abstract: KF-Al_2O_3 is discovered to promote epoxidation of electron deficient alkenes. Functional groups that are labile to aqueous basic conditions survive. The steric demand for the reaction is higher than that for alkaline H_2O_2.

Fluoride salts are useful bases that facilitate a variety of synthetic reactions such as alkylations and arylations, esterifications and transesterifications, intermolecular condensations including Michael, aldol, and Knoevenagel, intramolecular cyclizations including carbocycle, lactone, and other heterocycle forming reactions, eliminations comprising dehydrohalogenations and dehydrations, and a host of other important transformations[1].

Clark, Miller, and their coworkers[2-4] favored appreciably enhanced nucleophilicity of protic organic compounds, e.g. phenols and carboxylic acids, arising from strong hydrogen bonds formation with the fluoride ion; the nucleophilic substitution proceeding with *"hydrogen bond assistance"*. The poor solubility of alkali metal fluorides in common solvents, however, restricted their broad application in organic synthesis. In partial solution to this problem, the reactions were carried out at high temperatures with preformed hydrogen-bonded complexes or in a high boiling solvent such as dimethylformamide.

Reagents supported on organic and inorganic solids are attractive alternatives as these offer advantages in (a) simple workup and products' purification, (b) enhanced or reduced reactivity of functional groups, and (c) offering selectivity that may be different from that in solution. Ando and Yamawaki[5] found KF supported on celite more efficient than unsupported KF in alkylations of protic compounds. In another study, Ando and coworkers[6] adsorbed several alkali metal fluorides on alumina and compared their activity in promoting alkylaton of phenols and alcohols. Although CsF-Al_2O_3 was discovered to be the most effective, KF-Al_2O_3 was preferred for its nonhygroscopic nature and its relatively much lower cost. Optimization of reagent preparation and elucidation of the active species were investigated[7]. This lead to much enhanced research activity and KF-Al_2O_3 witnessed improved larger usage for almost all the

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[#] *Dedicated to the sweet memory of a soul who died of cancer on October 12, 1994.*

reactions that were performed earlier with unsupported fluoride salts[8]. We became interested in the KF-Al_2O_3 reagent and reasoned that it may be suitable for epoxidation of electron deffìcient alkenes when used in combination with anhydrous *t* -BuOOH, a reaction that we were interested in inconnection with another ongoing synthetic endeavour.

True to our expectations, a good range of olefins reacted smoothly. The examples are collected in Table[9]. The following points may be discerned: (a) acyclic enones such as chalcone and dibenzalacetone reacted extremely rapid to provide near quantitative yields of the epoxy products, (b) β-unsubstituted cyclic enones such as 2-cyclohexen-1-one and R-(-)-carvone reacted at moderate rate to provide high yields of the products. Carvone reacted relatively much slower, possibly due to the steric interference of the isopropenyl substituent, (c) β-substituted cyclic enones are much less reactive, e.g. isophorone and testosterone did not participate in the reaction and were recovered unchanged even afer 20 hrs of stirring. 3-Methyl-2-cyclopenten-1-one, however, reacted to the extent of ~ 65% conversion[10] after a reaction time of 20 hrs. Cyclopentenone substrate is somewhat special for its near planar geometry which may, at least partially, be contributing to the reaction. Isophorone situation suffers further from steric interactions due to the *gem* dimethyl group, and (d) β, β-disubstituted acyclic enones such as that at entry 8 did not react. Acyclic and cyclic α, β-unsaturated esters did not react either.

Success of the reaction with cyclopentenone is remarkable. This material is notorious for base catalyzed self condensation of aldol-type. No aldol products were noticed in the present study. The acetate derived from testosterone was although unreceptive to epoxidation but did retain the acetoxy function in the recoverd material. Survival of the acetoxy group is indicative of the fact that the present procedure is suitable for systems having base-labile groups that would otherwise not survive the existing methods of treatment with alkaline H_2O_2 under conditions related to those of Trost[11] and Payne[12]. While the reaction with chalcone gave only the *trans* product, the reaction with cinnamaldehyde (not shown) furnished a mixture of *trans* and *cis* oxides (ratio 3:1), showing that the reaction with at least cinnamaldehyde is not stereoselective. This result is at variance from those achieved with alkaline H_2O_2 [13-14].

Hydrogen bond assisted 1,4-addition of t-butylperoxy anion followed by attack of the resultant enolate on the peroxy oxygen accounts for product formation. In an experiment with chalcone when t-BuOOH was replaced by MeI, chalcone was recovered unchanged. Absence of PhCH(F)CH(Me)COPh negates the halohydrin pathway that may be conceived arising from conjugate addition of fluoride ion and quench of the enolate with t-BuOOH.

In a typical procedure, the reacting olefin (2 mmol) dissolved in carefully dried acetonitrile (1 ml) was added to a stirred suspension of KF-Al_2O_3[15] (0.475g, 3 mmol of KF) in acetonitrile (6 ml) containing dichloroethane solution of t-BuOOH (1.7 ml, 4 mmol of t-BuOOH)[16]. The resultant was stirred at room temperature and monitored for completion. Simple filtration and evaporation of the volatiles furnished the product(s) which, if necessary, could be filtered through a silica gel or alumina column.

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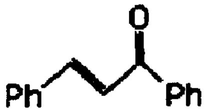
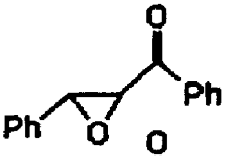
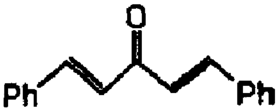
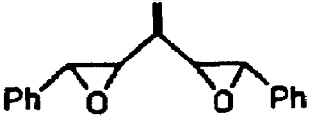
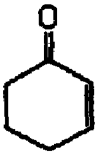
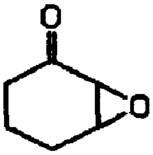
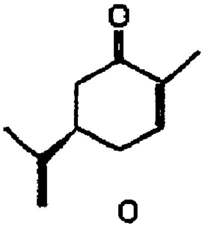
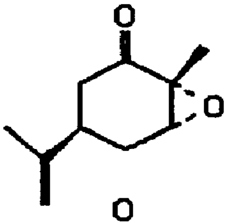
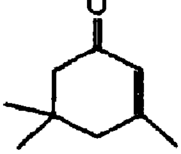
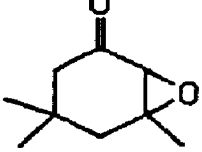
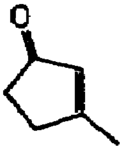
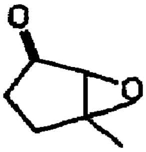
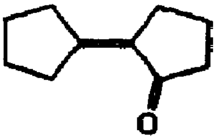
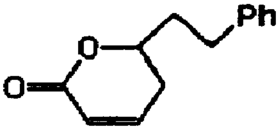
Table

entry	substrate	product	rxn time	yield
1.			10 min	Quant.
2.			10 min	Quant.
3.			1 h	85
4.			10 h	85
5.			20 h	no rxn
6.	Testosterone	Testosterone	20 h	no rxn
7.			20 h	65
8.			20 h	no rxn
9.	Methyl cinnamate		15 h	no rxn
10.			20 h	no rxn

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8. For aldol reaction, see Lin, Y.; Gong, C.; Han, A. *Xiangton Daxue Ziran Kexue Xuebao* **1991**, *14*, 82; *Chem. Abstr.* **1993**, *118*, 59890y: For Knoevenagel reaction, see Nakano, Y.; Niki S.; kinouchi, S.; Miyamae, H.; Igarashi, M. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 2934: For Michael reactions, see Laszlo, P.; Pennetreau, P. *Tetrahedron Lett.* **1985**, *26*, 2645. For a review, see Liao L.; Guo, Q. *Huaxue Shiji* **1990**, *12*, 118; *Chem. Abstr.* **1990**, *113*, 190449a.
9. All the products prepared in this study exhibited satisfactory ^{1}H nmr, ir, and mass spectral data.
10. The extent of conversion was computed from ^{1}H nmr spectral signals.
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15. Anhydrous KF was dissolved in distilled water (100 mls) and mixed with alumina (neutral, 100g). The water was removed at 45-50°C on a rotovap under reduced pressure and dried further at 75°C for 30h in a vacuum drying oven. The free flowing material thus obtained was used throughout this study.
16. Sharpless, K.B.; Verhoeven, T.R. *Aldrichimia Acta* **1979**, *12*, 63; Direct use of 70% aqueous t-BuOOH was also found effective as it did oxidize carvone. In comparision, the effectiveness was inferior to the use of anhydrous t-BuOOH. With 70% t-BuOOH, side products (not characterised) were also noticed.

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