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Highly efficient Meinwald rearrangement reactions of epoxides catalyzed by copper tetrafluoroborate

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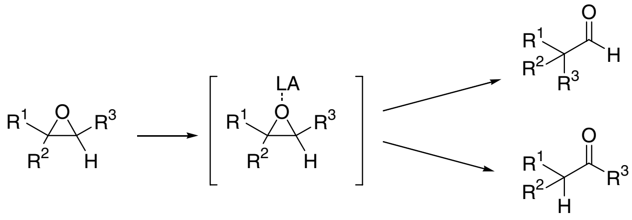
Abstract—Epoxides undergo a highly efficient and selective rearrangement in the presence of catalytic quantities of copper tetrafluoroborate to give carbonyl compounds in excellent yields. The low toxicity and ease of handling of this reagent make it an attractive alternative to the more corrosive Lewis acids frequently employed.

The rearrangement of epoxides to produce carbonyl compounds (the Meinwald rearrangement) has attracted considerable interest in recent years, given the efficiency of the rearrangement and the synthetic and industrial utility of this process (Scheme 1).[1] A number of factors have been identified as critical in determining the product distribution of this reaction, such as the migratory aptitude of the epoxide substituents, the Lewis acid catalyst utilized and the solvent employed.[2] Typically, if there is no structural bias, a mixture of products is produced due to the lack of regioselectivity in the ring opening process. Hence, there has been considerable interest in the development of Lewis acids that display enhanced selectivity and which are efficient in catalytic quantities.

The originally reported procedures utilizing boron trifluoride diethyletherate, lithium salts, magnesium bromide or methylaluminium bis(4-bromo-2,6-di-*tert*-butylphenoxide) (MABR)[3] have all proven to be useful, however, the reagents are typically employed in stoichiometric quantities. More recent protocols employing catalytic quantities of Lewis acids such as palladium salts, indium trichloride, iridium trichloride, bismuth salts and gallium salts have all proven to be efficient.[4] There remain, however, limitations to these protocols whether it be a lack of selectivity, the toxic or corrosive nature of the catalyst employed, the production of addition or polymeric products or the requirement to employ expensive rare metals. Recently, while investigating addition reactions to epoxides catalyzed by copper tetrafluoroborate ($Cu(BF_4)_2{\cdot}nH_2O$), we noted that epoxides underwent a highly efficient rearrangement process to produce carbonyl products. We were surprised to discover that there had only been one reported example of the use of copper(II) salts to catalyze epoxide rearrangement reactions[5,6] and this prompted us to initiate further studies in this area, the results of which are summarized in Table 1.



Scheme 1.

The rearrangement was found to be highly efficient at room temperature using 25 mol % quantities of $Cu(BF_4)_2{\cdot}nH_2O$ in a variety of solvents, although dry dichloromethane was the solvent of choice due to the short reaction times observed. The rearrangement of styrene oxide proceeded readily to give phenylacetaldehyde contaminated with small quantities of the suspected aldol product. This transformation is particularly noteworthy given the sensitivity of phenylacetaldehyde to acidic conditions and the difficulties encountered in previously reported procedures,[4d] and clearly demonstrates

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Keywords: Copper tetrafluoroborate; Lewis acid catalyst; Meinwald rearrangement.

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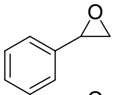
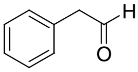
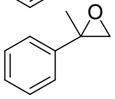
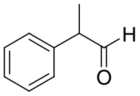
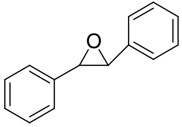
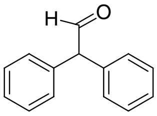
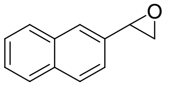
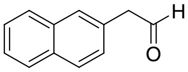
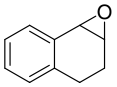
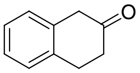
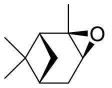
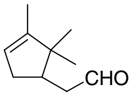
Table 1. Rearrangements of epoxides catalyzed by $Cu(BF_4)_2 \cdot nH_2O$

Entry	Epoxide[a]	Time	Product[b]	Yield[c] (%)
1		20 min		90
2[8a]		60 min		85
3[8b]		90 min		95[d]
4[8c]		15 min		90
5[8d]		5 h		89
6		20 min		88[e]

[a] All epoxides were used as supplied or were synthesized using published procedures (see Ref. 8).

[b] All reactions were carried out at room temperature in dichloromethane using 25 mol % of catalyst.

[c] All products gave satisfactory spectroscopic data.

[d] Carried out at reflux.

[e] >95% regioselectivity as determined by GC–MS analysis of the crude reaction mixture.

the benign nature of this catalyst. Similarly, α-methylstyrene oxide underwent efficient rearrangement to produce 2-phenylpropionaldehyde in high yield. The rearrangement of stilbene oxides has been used to demonstrate regioselectivity, since rearrangement can occur with either phenyl migration to produce diphenylacetaldehyde or with hydrogen migration to give deoxybenzoin. Under our conditions *trans*-stilbene oxide underwent regioselective rearrangement to produce diphenylacetaldehyde in excellent yield as the only product observed by ^1H NMR spectroscopy of the crude reaction mixture. Disappointingly, the rearrangement of cyclohexene oxide provided only trace amounts of cyclohexanone even after prolonged heating in chloroform, although the starting material was recovered unchanged in contrast to the previous reports where halohydrins are produced.[4b] However, dihydronaphthalene oxide did produce the expected tetralone in high yield on exposure to extended reaction times. The rearrangement of α-pinene oxide with this catalyst is particularly noteworthy given the number of potential products that can be formed during the rearrangement process. We were therefore gratified to observe that this substrate underwent a highly selective rearrangement to give campholenic aldehyde as the major product with ~95% selectivity by GC–MS in addition to small quantities of isomeric products.[7]

In conclusion, we have demonstrated that copper tetrafluoroborate is a highly efficient and effective reagent which catalyzes the Meinwald rearrangement of a range of epoxides to carbonyl compounds under mild reaction conditions. The benign nature of the catalyst in addition to its low cost and ease of use offers an attractive alternative to established methodologies.

Typical procedure: α-Methylstyrene oxide (127 mg, 0.95 mmol) was dissolved in dry dichloromethane (10 ml) at room temperature. Copper tetrafluoroborate (59.3 mg, 0.25 mmol) was added and the reaction was stirred at room temperature and monitored by TLC. Upon completion, the reaction mixture was diluted with dichloromethane (30 ml) and washed with water (4 × 40 ml). The organic phase was dried over magnesium sulfate and the solvent removed to give an oil that was purified by chromatography (petrol → 10% ethyl acetate:petrol) to give *2-phenylpropionaldehyde* (108 mg, 85%) as a colourless oil; ^1H NMR ($CDCl_3$; 400 MHz) $\delta = 9.62$ (1H, d, $J = 1.5$ Hz), 7.40–7.20 (5H, m), 3.55 (1H, dq, $J = 7$ and 1.5 Hz), 1.45 (3H, d, $J = 7$ Hz); ^{13}C NMR ($CDCl_3$; 100 MHz) $\delta = 201.9$, 137.7, 129.0, 128.5, 128.1, 52.9, 14.6; MS (EI) m/z 134, $(M)^+$; ν_{max} (film)/cm^{-1} (neat) 2978, 1718, 1494, 1452, 1020, 759 and 697.

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