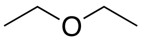
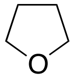
CHEM 203

Topics Discussed on Nov. 16

Ethers: acyclic and cyclic

diethyl ether: a
typical acyclic ether

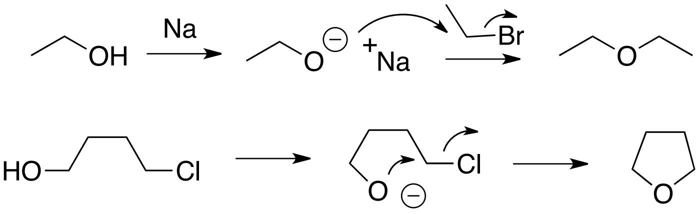




tetrahydrofuran (THF):
a typical cyclic ether

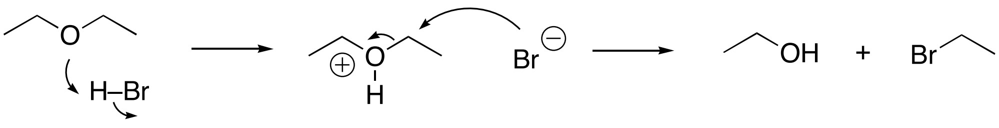
Poor reactivity of ethers and consequent use thereof as solvents for many organic reactions

The Williamson reaction: synthesis of ethers via the S_N2 alkylation of a metal alkoxide with an appropriate alkyl halide:



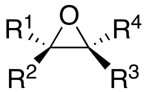
Cleavage of ethers with H–X resulting in formation of a molecule of alcohol and one of alkyl halide; e.g.:

via:



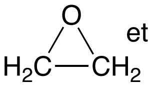
Epoxides or oxiranes: cyclic ethers in which the oxygen atom is part of a three membered ring:

a generic epoxide (oxirane):

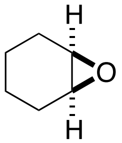


Enhanced reactivity of epoxides due to angle strain

Nomenclature of epoxides: attaching the term "oxide" to the name of the corresponding alkene:

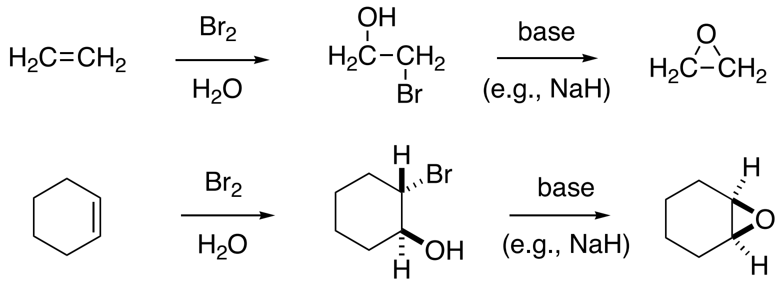


ethylene oxide



cyclohexene oxide

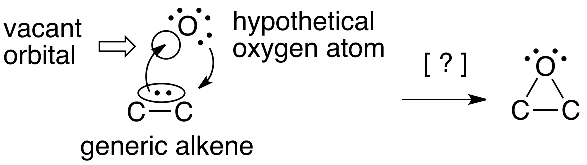
Preparation of epoxides by cyclization of halohydrins. Examples:



The base-promoted cyclization of halohydrins as an intramolecular variant of the Williamson reaction, which is itself a special case of S_N2 reaction

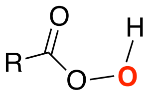
Direct conversion of olefins into epoxides by formal reaction with an "oxygen atom"

note: the electronic configuration of O shown in this diagram is not necessarily in the most favorable one



Peroxycarboxylic acids (formula below) as reagents that behave as formal carriers of "oxygen atoms" in epoxide-forming reactions

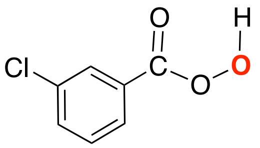
R = any alkyl group



the O atom that is transferable to an alkene is shown in **red**

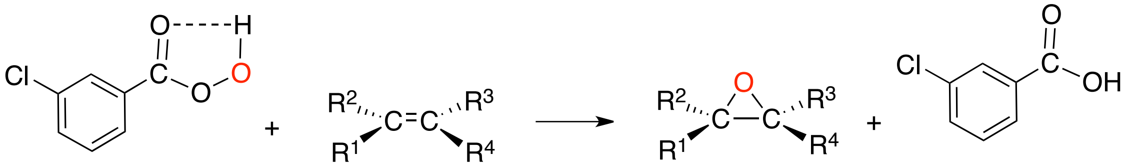
a peroxycarboxylic acid

Meta-chloroperoxybenzoic acid (MCPBA) as an especially convenient peroxyacid reagent for olefin epoxidation:



meta-chloroperoxybenzoic acid

The epoxidation reaction of alkenes: their conversion into epoxides, e.g., by reaction with MCPBA



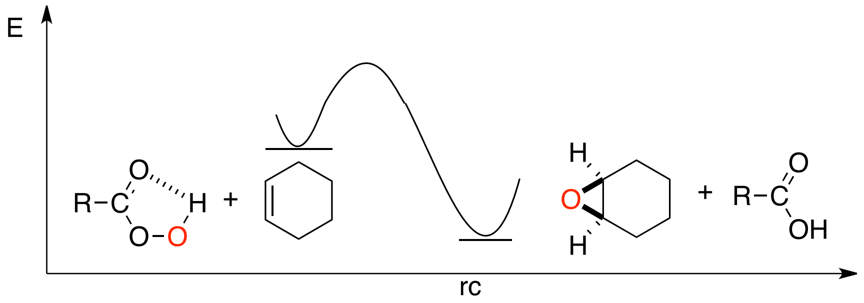
MCPBA
red: transferable O atom

a generic alkene

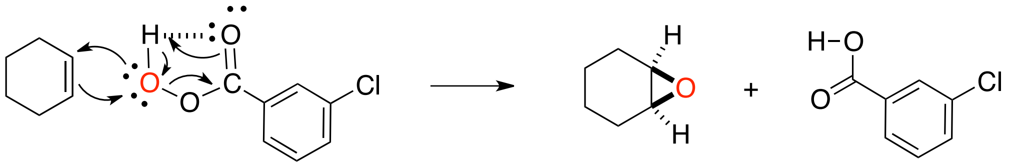
an epoxide

meta-chlorobenzoic acid: largely inert

Concerted mechanism of peroxyacid epoxidation of alkenes: the epoxide forms in a single kinetic step though a mechanism that involves no radical or ionic intermediates:



Presumed mechanism of peroxyacid epoxidation of olefins; e.g., with MCPBA:

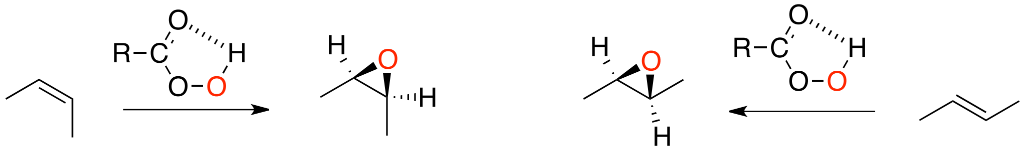


meta-chloroperoxybenzoic acid (MCPBA)

meta-chlorobenzoic acid

Strictly syn course of the epoxidation of alkenes with peroxyacid reagents: both C–O bonds form from the same face of the olefinic π system

Retention of olefin geometry during epoxidation reactions; e.g.:



Principle: **more reactive, basic** nucleophiles (= conjugate bases of acids with pKa >10; such as Grignard reagents, acetylide ions, etc.), induce nucleophilic opening of epoxides through S_N2-type reactions *despite the poor leaving group abilities of the epoxide oxygen* (now departing as an alkoxide). These reactions are driven by release of strain. Examples: