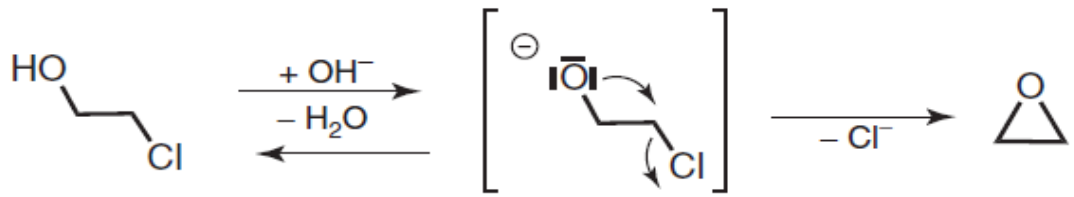
Synthesis of Oxiranes

In general, oxiranes can be synthesized according to three (broadly defined) principles, namely (a) by cyclization of C_2-moieties bearing an anionic oxygen and a leaving group in β-position, (b) by transfer of an oxygen to an olefin ("epoxidation"), and (c) by addition of a C_1-fragment to a carbonyl substrate.

(1) Cyclodehydrohalogenation of β-halogeno alcohols

β-Halo alcohols are deprotonated by bases (e.g., hydroxides or alcoholates) followed by intramolecular displacement of the halogen as rate-determining step according to the mechanism of a 1,3-elimination of HCl:

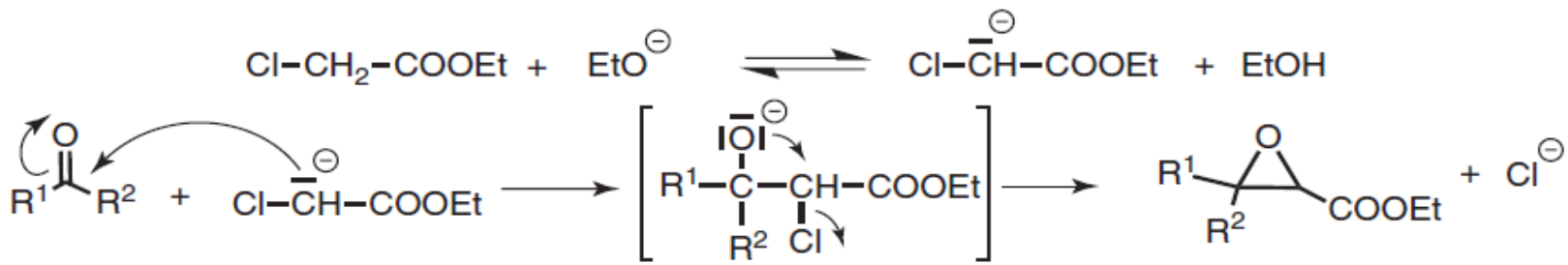


In spite of the ring strain in the product and the considerable activation enthalpy, the reaction occurs rapidly at room temperature owing to favorable entropy. The activation entropy is affected only by the loss of the degree of freedom of the internal rotation in the 2-chloroalkoxide ion because of the monomolecular rate-determining step.

Oxirane was first prepared by Wurtz (1859) by the action of sodium hydroxide on 2-chloroethanol.

(2) Darzens reaction (glycidic ester synthesis)

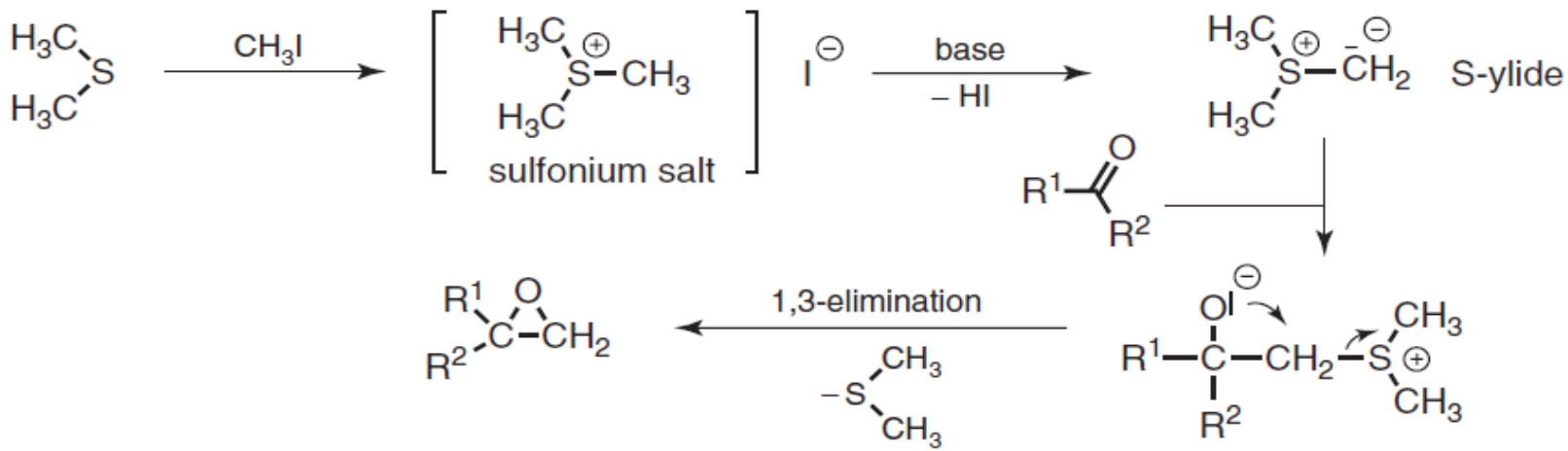
The reaction of α-halo esters with carbonyl compounds in the presence of sodium alkoxides leads to (2-alkoxycarbonyl) oxiranes (DARZENS, 1904), known as *glycidic esters*. Primarily, the α-halo ester is deprotonated by the base to the corresponding ester enolate, which adds to the carbonyl compounds in the rate-determining step. Finally, the halogen atom is substituted intramolecularly, for example:



The reaction of diazoacetamides with aldehydes in the presence of chiral Ti(O*i*Pr)$_4$/(*R*)-BINOL (1,1′-bis-2-naphthol) catalyst leads to trans-(2-amidocarbonyl)oxiranes with high stereoselectivities (>95% *ee*) and thus can be regarded as an asymmetric catalytic *Darzens reaction* [11].

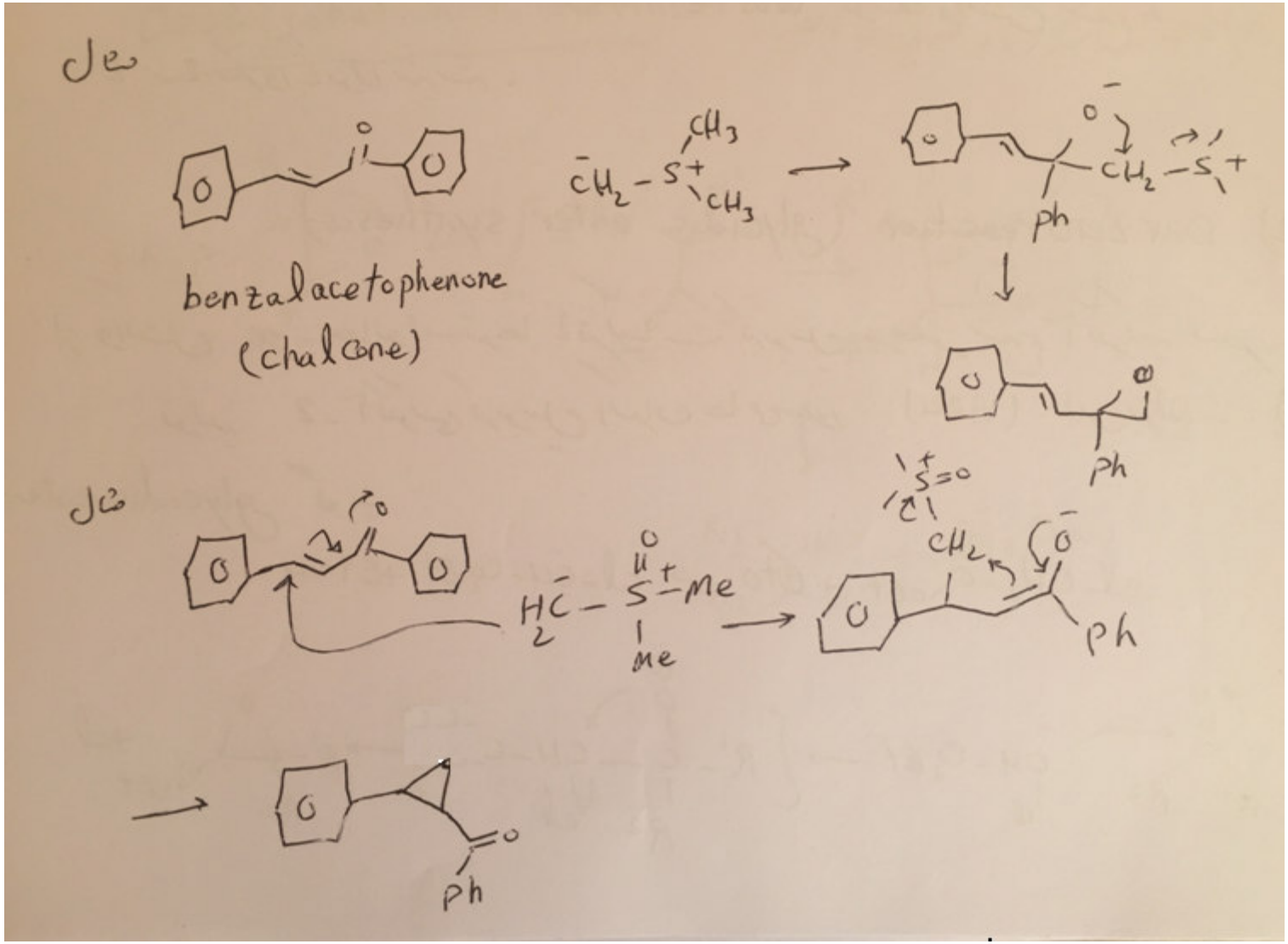
(3) Corey synthesis

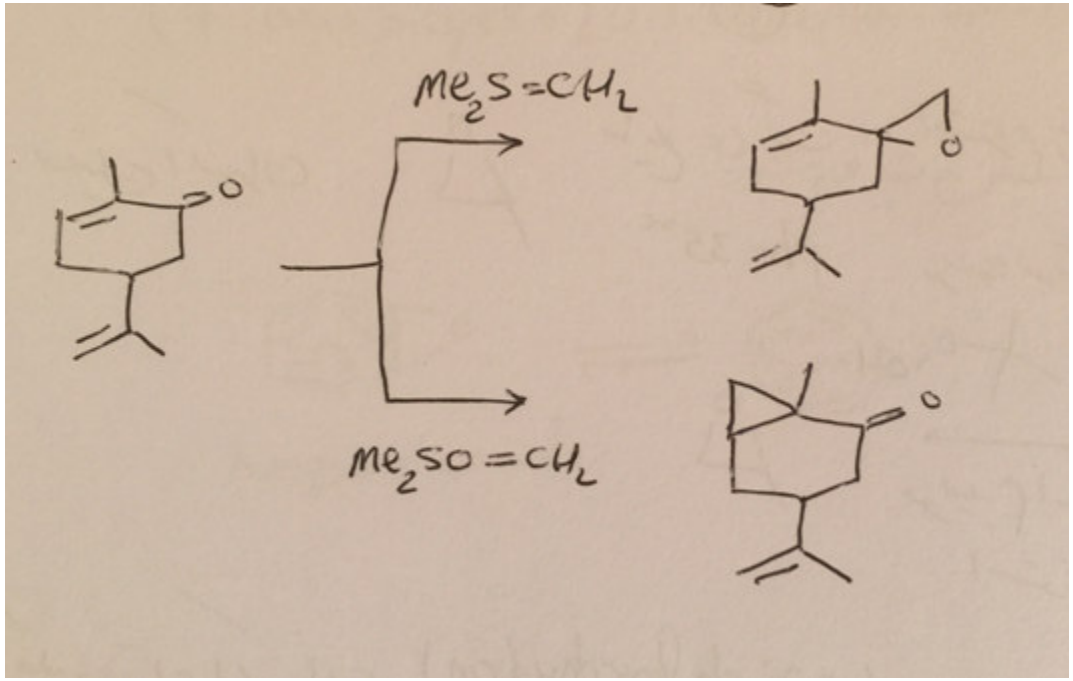
S-Ylides derived from trialkylsulfonium or trialkylsulfoxonium halides react as nucleophiles with aldehydes or ketones to give oxiranes [12]:



This process follows the mechanistic pattern of a 1,3-elimination and formally corresponds to a (1 + 2)-cycloaddition of the ylidic (carbene-like) CH_2 group to the carbonyl group. It should be mentioned that α, β-unsaturated ketones like benzalacetophenone react with sulfonium ylides to give oxiranes, but with sulfoxonium ylides to give cyclopropanes [13].

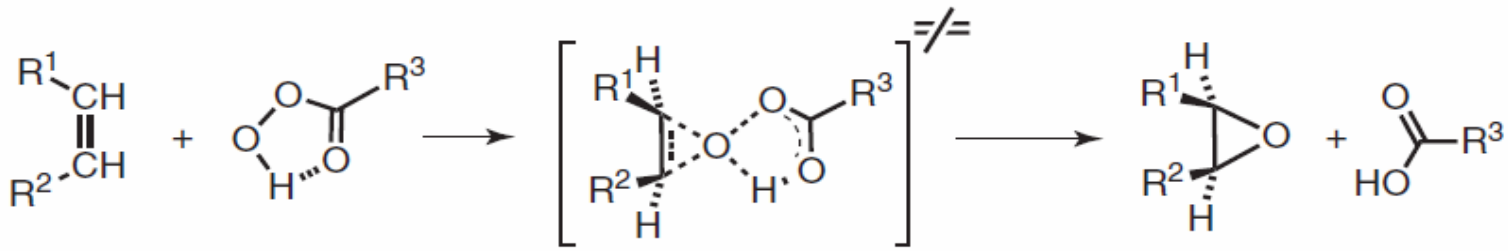
Examples:

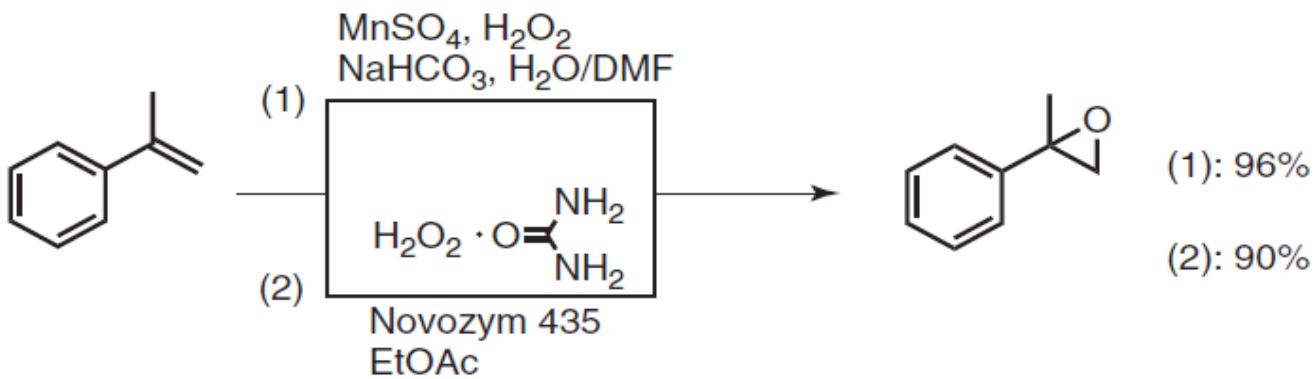



Me2S=CH2
Me2SO=CH2

(4) Epoxidation of alkenes

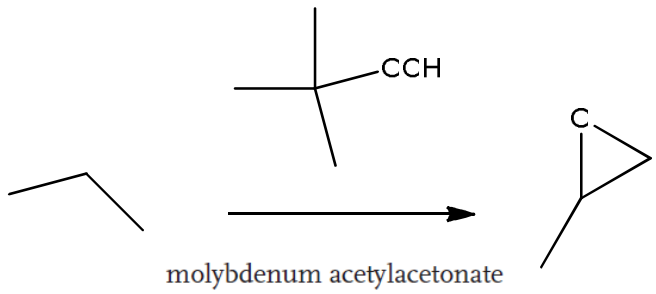
For the addition of oxygen to a C=C double bond, reactive (electrophilic) oxygen has to be produced in situ by means of an activator from a stable oxygen donor. Activation of oxygen can be accomplished (1) by O–O bond transformation like in the classical percarboxylic acid – carboxylic acid system (see (a)) or (2) by interaction of O_2, peroxides, or H_2O_2 with transition metals



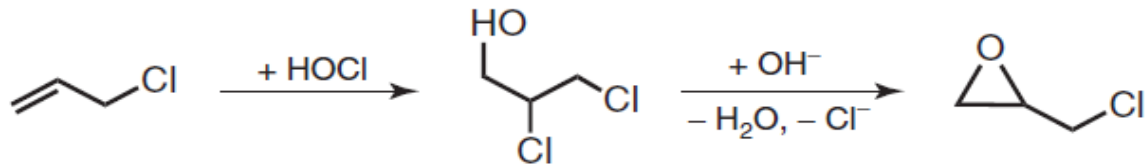

MnSO4, H2O2
NaHCO3, H2O/DMF
(1)
H2O2 · O=C(NH2)2
(2)
Novozym 435
EtOAc
O
(1): 96%
(2): 90%

D **Oxirane** (ethylene oxide), a colorless, water-soluble, very poisonous gas of bp 10.5 °C, is produced on an industrial scale by direct air oxidation of ethene in the presence of a silver catalyst. Oxirane is important as an intermediate in the petrochemical industry. The annual production worldwide is estimated to be more than 7 million tonnes.

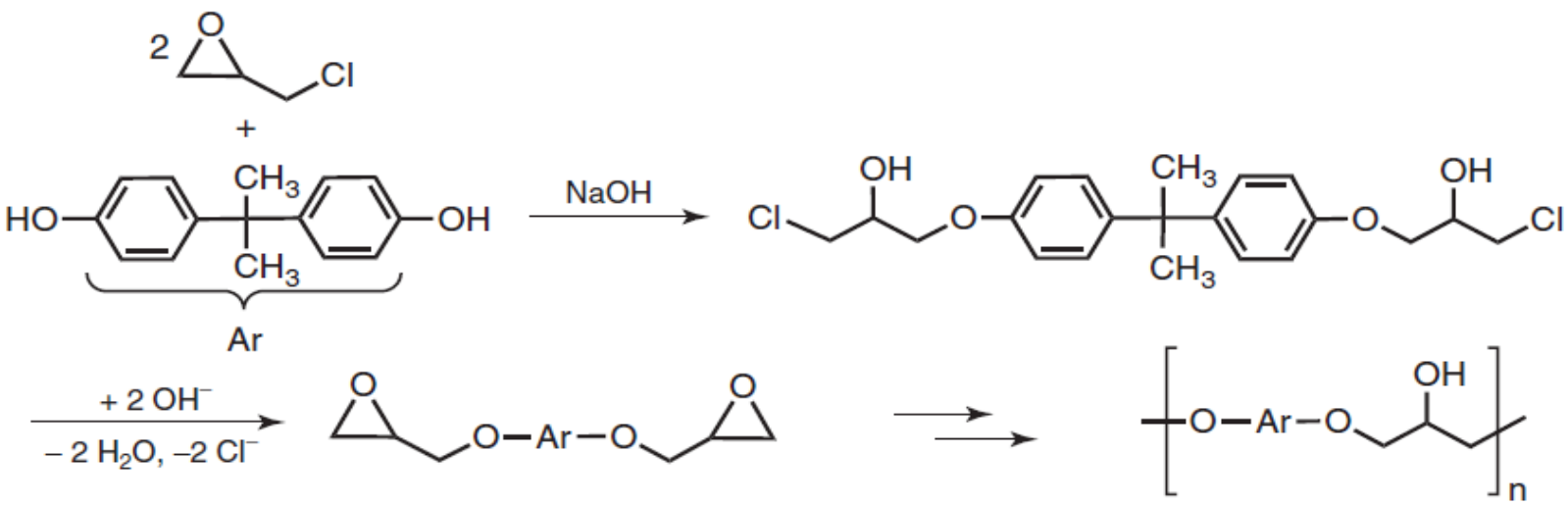
Methyloxirane (propylene oxide) is a colorless, water-miscible liquid, bp 35 °C. It is obtained commercially from propene and *tert*-butyl hydroperoxide in the presence of molybdenum acetylacetonate [25].



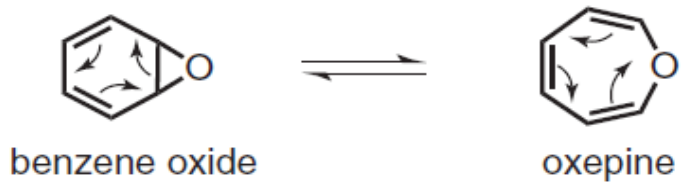
(Chloromethyl)oxirane (epichlorohydrin) is prepared from allyl chloride as follows:



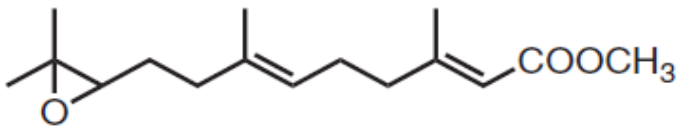
Epichlorohydrin is the starting material for epoxy resins. When used in excess, for example, with bis-2,2-(4-hydroxyphenyl)propane, the so-called bisphenol A, in the presence of sodium hydroxide, it reacts to give linear polymers with oxirane end-groups.



Benzene oxide (7-oxabicyclo[4.1.0]hepta-2,4-diene) was obtained in an equilibrium mixture with the valence isomer oxepine (see p. 529):



Benzene dioxide and benzene trioxide are also known [27]. Arene oxides are crucial intermediates in the carcinogenic action of benzo[a]pyrene and other polycondensed arenes [28]. Oxiranes are found relatively rarely in nature. An example of an oxirane in a natural product is, however, juvenile hormone (**1**) of the sphinx moth.



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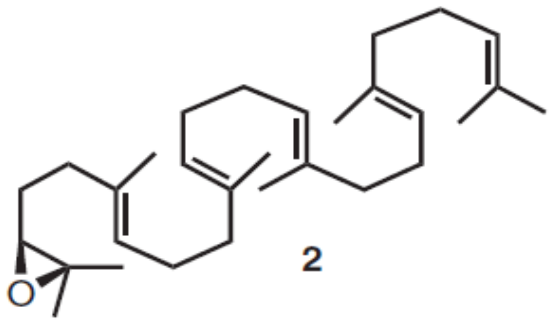

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