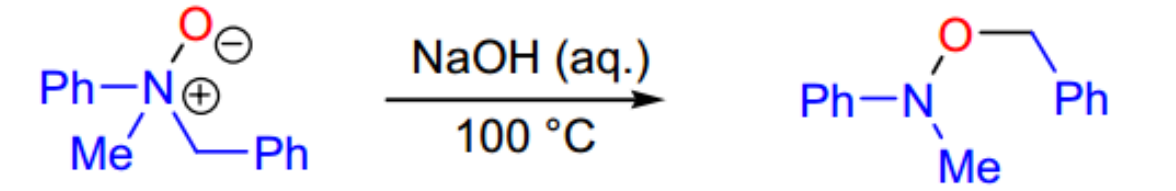
MEISENHEIMER REARRANGEMENT

Meisenheimer (1919):

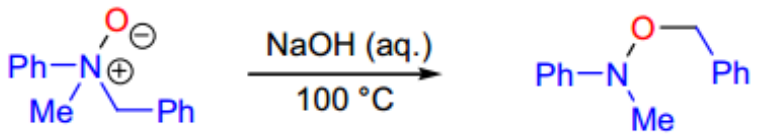


N-benzyl-*N*-methyl aniline-*N*-oxide

O-benzyl-*N*-methyl-*N*-phenylhydroxylamine

MEISENHEIMER REARRANGEMENT

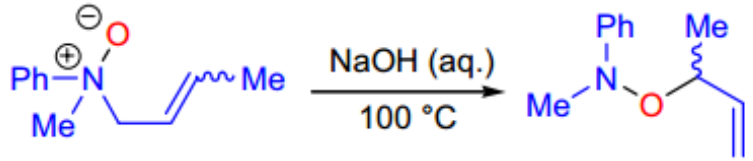
Meisenheimer (1919):



N-benzyl-*N*-methyl aniline-*N*-oxide

O-benzyl-*N*-methyl-*N*-phenylhydroxylamine

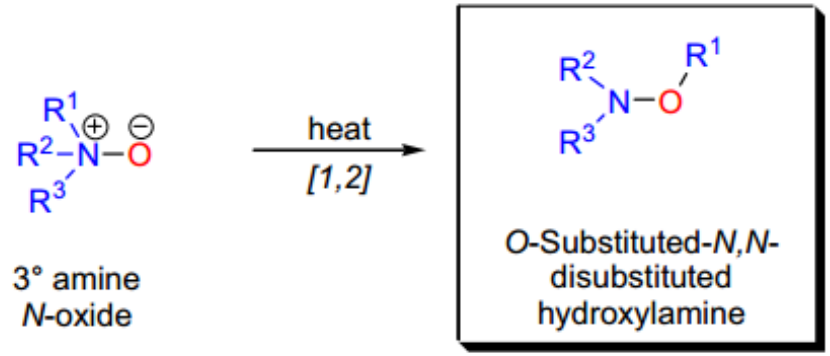
Cope and Kleinschmidt (1944):



N-crotyl-*N*-methyl aniline-*N*-oxide

N-Methyl-*O*-(1-methyl-allyl)-*N*-phenyl-hydroxylamine

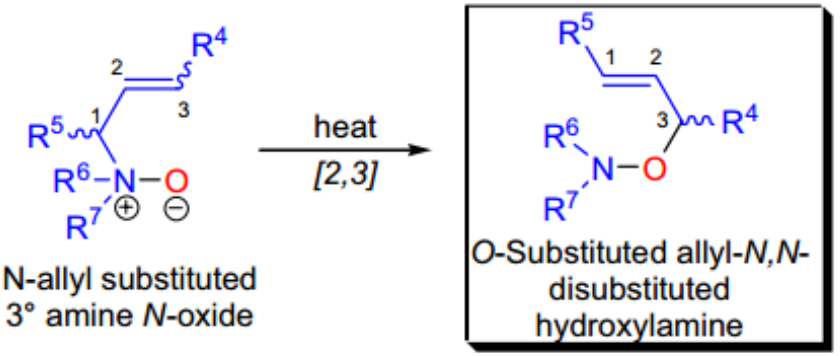
[1,2]-Meisenheimer rearrangement in acyclic systems:



3° amine *N*-oxide

O-Substituted-*N*,*N*-disubstituted hydroxylamine

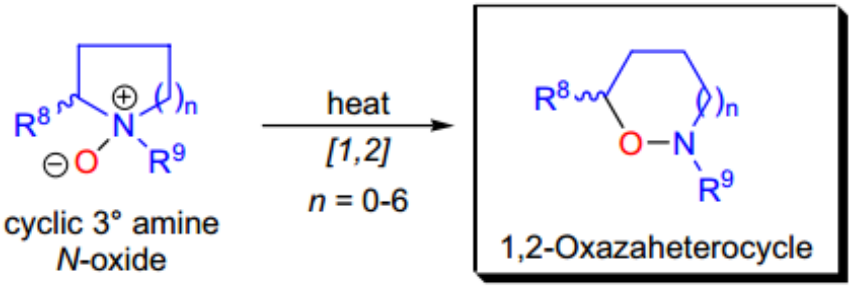
[2,3]-Meisenheimer rearrangement in acyclic systems:



N-allyl substituted 3° amine *N*-oxide

O-Substituted allyl-*N*,*N*-disubstituted hydroxylamine

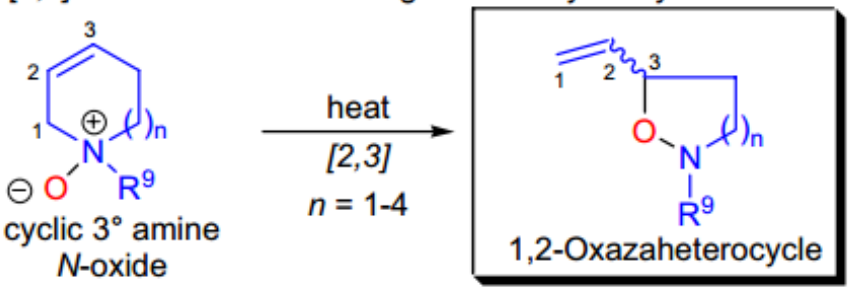
[1,2]-Meisenheimer rearrangement in cyclic systems:



cyclic 3° amine *N*-oxide

1,2-Oxazaheterocycle

[2,3]-Meisenheimer rearrangement in cyclic systems:

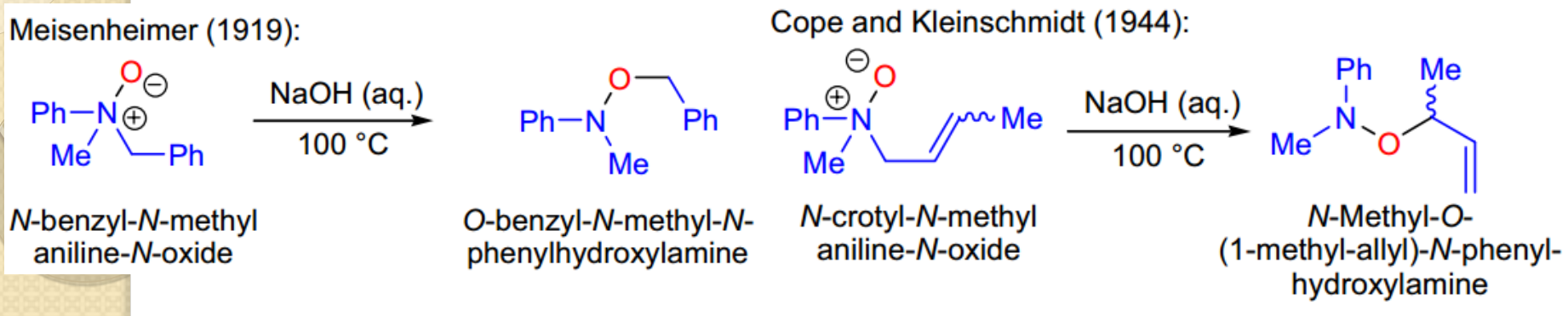


cyclic 3° amine *N*-oxide

1,2-Oxazaheterocycle

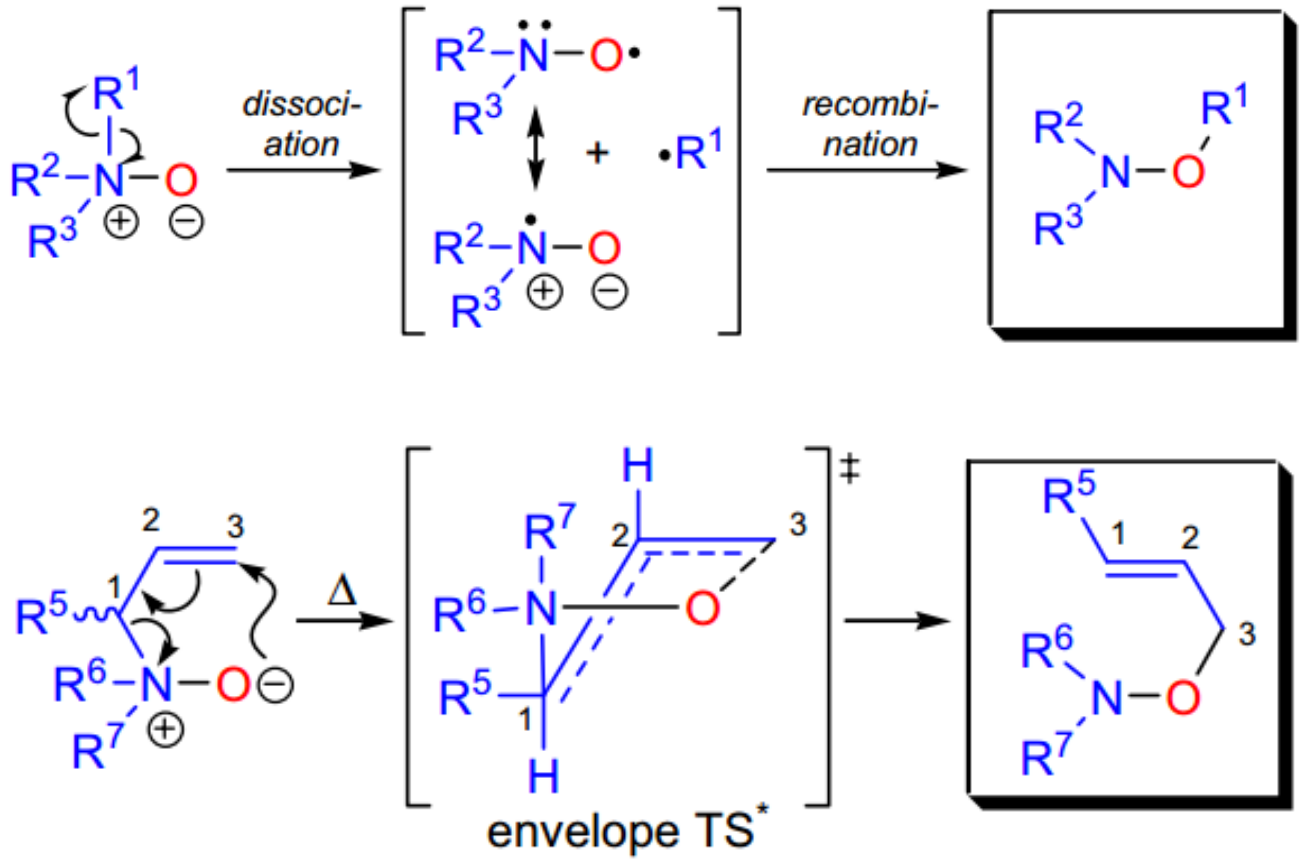
R^1 = CH_2Ph, $CHPh_2$, CH_2Ar, allyl; R^{2-3} = alkyl with no β-hydrogen, aryl; R^{4-5} = H, alkyl, aryl; R^{6-7} = alkyl with no β-hydrogen, aryl; R^8 = alkenyl, aryl; R^9 = alkyl with no β-hydrogen

MEISENHEIMER REARRANGEMENT

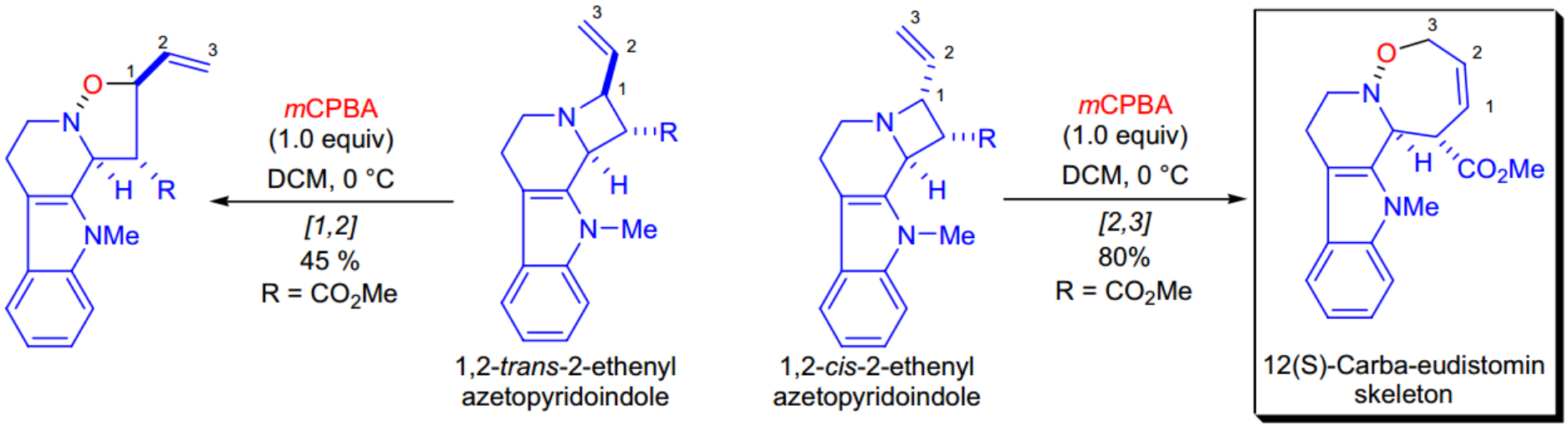


- the [1,2]-shift occurs when one of the substituents is capable of stabilizing radicals (R1 = benzyl, diphenylmethyl, etc.), during the [1,2]-shift, the stereocenter on the migrating group suffers extensive racemization;
- the [2,3]-shift is common when one of the substituents is allylic, the [2,3]-shift usually takes place much faster than the [1,2]-shift and the transfer of chirality of the migrating group is possible;
- when any of the groups are alkyl groups that have a hydrogen atom at their β-position, the Cope elimination becomes competitive;

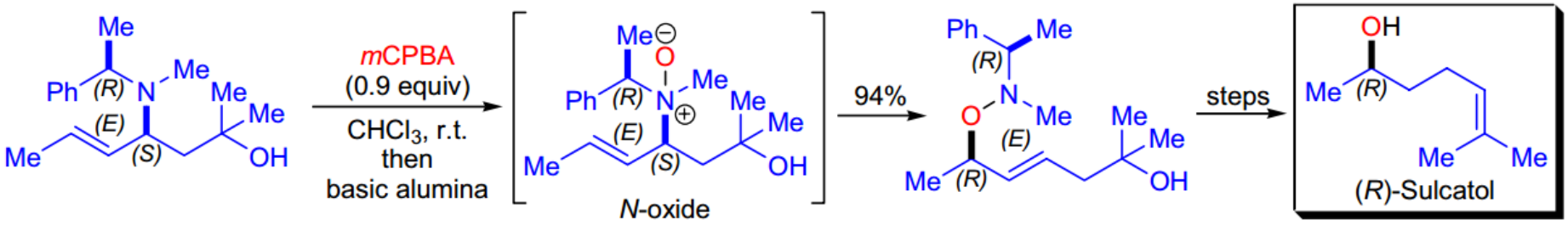
Mechanism



A new route to the 12(S)carba-eudistomin skeleton was developed by T. Kurihara et al.[22] The key substrate for this new route was a 1,2-*cis*-2-ethenylazetopyridoindole, which was readily oxidized at 0 °C to afford the corresponding *N*-oxide. This *N*-oxide spontaneously underwent a *[2,3]-Meisenheimer rearrangement* to afford the desired oxazepine derivative. Interestingly, when the 1,2-*trans*-2-ethenylazetopyridoindole was subjected to identical conditions, the *[1,2]-Meisenheimer rearrangement* occurred exclusively and gave rise to an isoxazolidine derivative.



The natural product (*R*)-sulcatol is a male-produced aggregation pheromone of the ambrosia beetle. This insect can devastate entire forests when its population is out of control.[21] Various studies revealed that different species respond to the compound in different enantiomeric excess. The asymmetric synthesis of (*R*)-sulcatol was accomplished in the laboratory of S.G. Davies using a *stereospecific [2,3]-Meisenheimer rearrangement* as the key step. The treatment of the allylic amine substrate with *m*CPBA followed by the filtration of the reaction mixture through deactivated basic alumina afforded the desired hydroxylamine as a single diastereomer.



The *[1,2]-Meisenheimer rearrangement* and a *Heck cyclization* were the key steps in T. Kurihara's synthesis of magallanesine.[24] The azetidine was exposed to H_2O_2, and the resulting azetidine *N*-oxide was refluxed in THF to afford the desired azocine derivative. Other usual oxidants such as *m*CPBA or MMPP gave rise to complex mixtures.