SMILES REARRANGEMENT
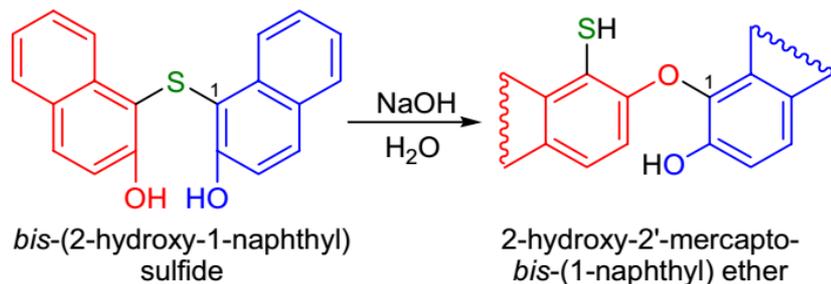
Henriques & Hinsberg (1894 & 1914):

bis-(2-hydroxy-1-naphthyl) sulfide → 2-hydroxy-2'-mercapto-*bis*-(1-naphthyl) ether

Smiles (1930-1936):

2-(2-nitro-benzenesulfonyl)-*N*-phenyl-benzamide → 2-[(2-nitro-phenyl)-phenyl-carbamoyl]-benzenesulfinate
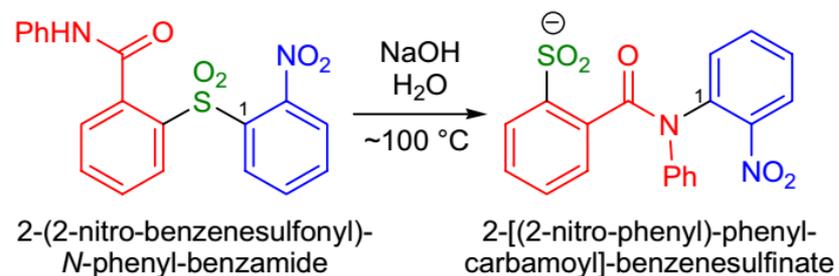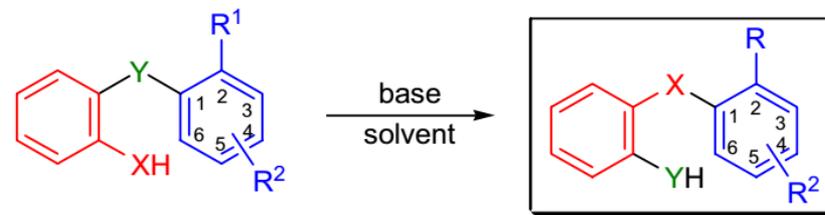
Smiles rearrangement (general equation):
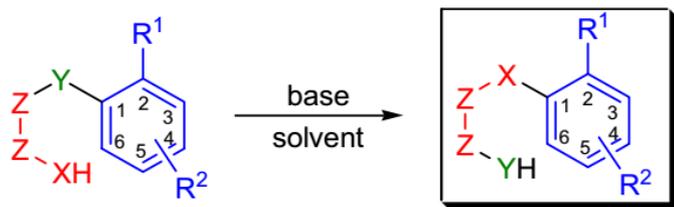
Smiles rearrangement of biaryl systems:

XH = NHCOR, CONH₂, SO₂NH₂, OH, NH₂, SH, SO₂H, CH₃ (*Smiles-Truce rearrangement*); Z = sp² or sp³ hybridized substituted- or unsubstituted carbon, C=O, sp³ nitrogen; Y = S, O, SO₂, S=O, CO₂, SO₃, I⁺, P⁺; R¹ = EWG = NO₂, SO₂R, Cl; R² = alkyl, halogen, NO₂, acyl; <u>base:</u> NaOH, KOH, RONa, RLi, K₂CO₃/DMSO

Mechanism and Features

reactive conformation   transition state
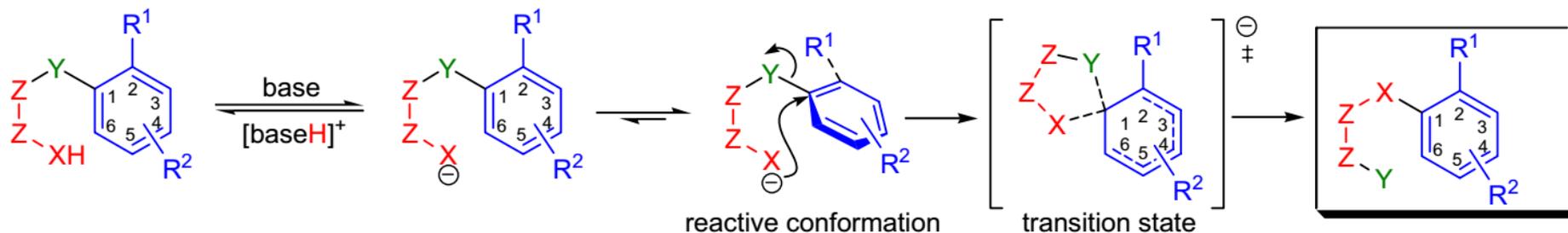
1) the aromatic ring needs to be activated by electron-withdrawing groups at the ortho- or para positions (e.g. NO2, SO2R); electron-withdrawing groups in the meta position usually do not activate the aromatic ring sufficiently; if there is more than one activating group (when R2=EWG), the rate of the rearrangement increases; in the absence of activating groups or when R1 and R2 are electron-donating, the rearrangement is slow or does not occur;

2) besides substituted benzene rings, the aromatic ring can also be heteroaromatic such as pyridine or pyrimidine;

3) the nucleophilicity of the XH group and the ability of the Y group to function as a good leaving group are two factors that are interconnected and their combined effect have a dramatic influence on the rate of the rearrangement;

4) when XH=NH2, usually no base is required and Y does not have to be a good leaving group for the reaction to take place;

5) the more stabilization of the negative charge is possible on Y, the faster the reaction will proceed (e.g., Y = SO2 > SO > S);
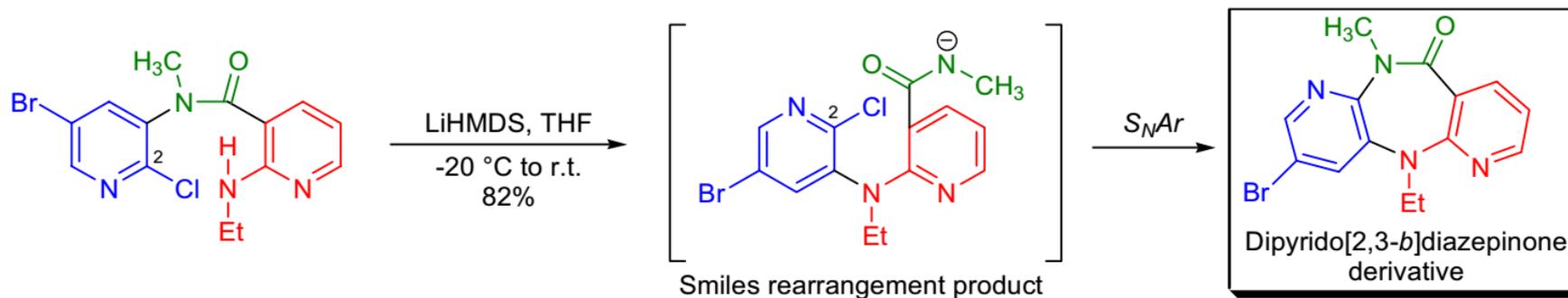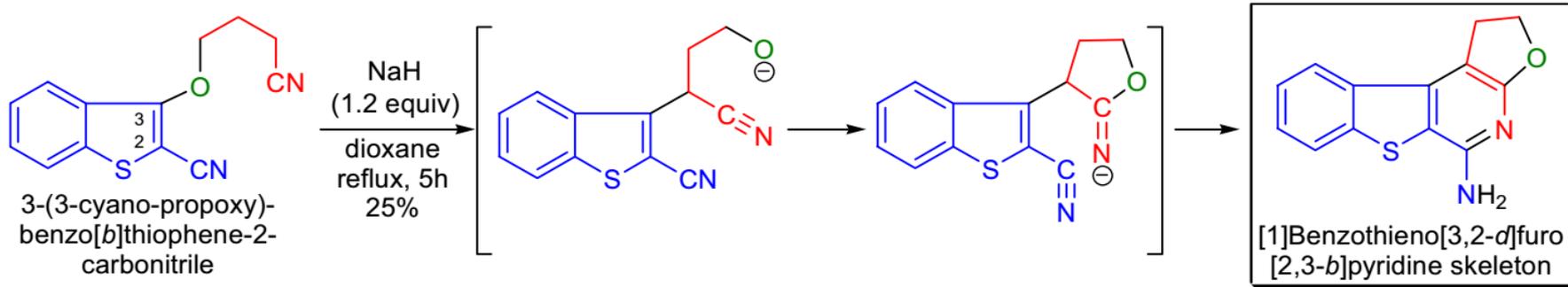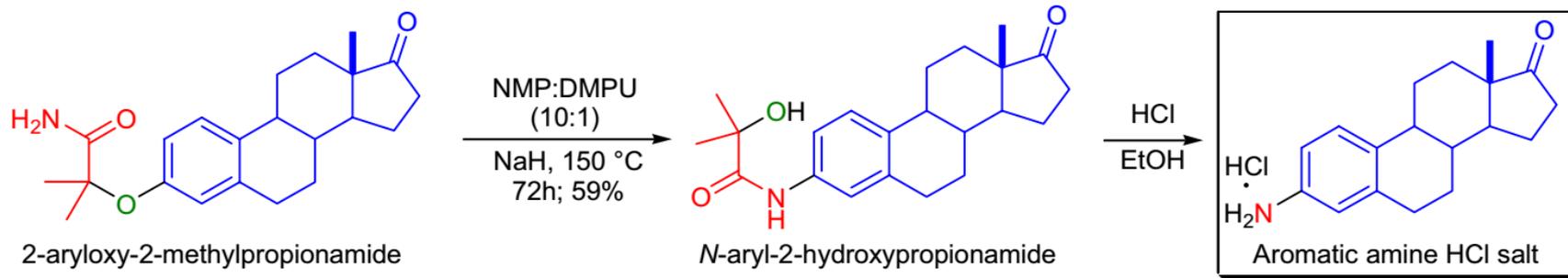
Features

Smiles rearrangement of biaryl systems:
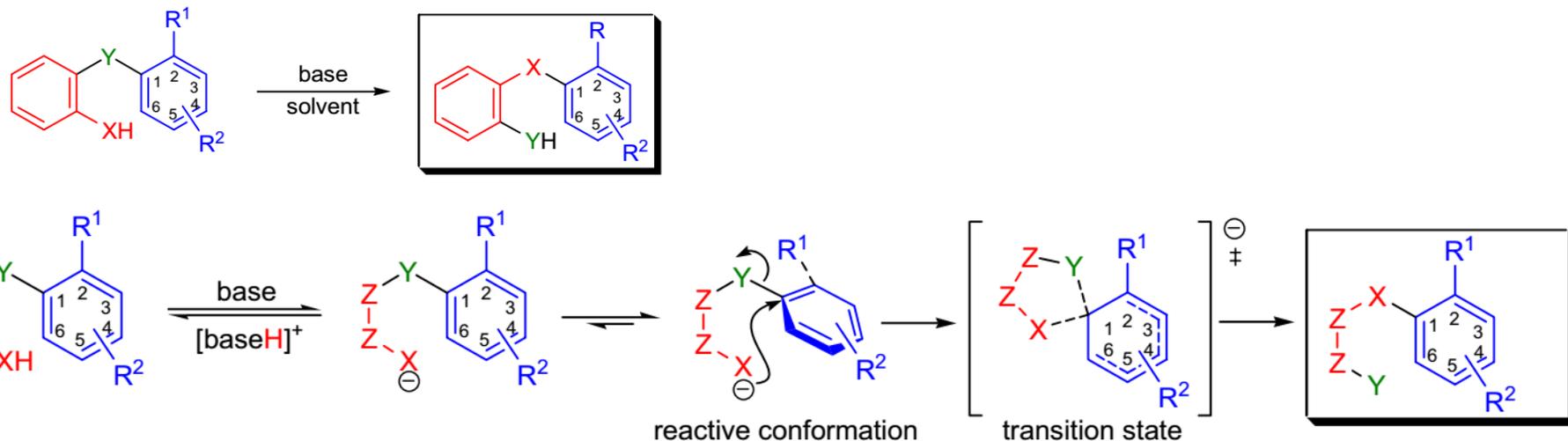
6) when the Z groups are part of an aromatic ring (e.g.,biaryl systems), electron-withdrawing substituents on this second ring tend to accelerate the reaction;

7) substituents at the 6-position of the second ring (ortho to Y) also accelerate the reaction because it forces the substrate to be predominantly in the reactive conformation, where the migrating ring is perpendicular to the plane of the other aromatic ring;

8) when the Y and the XH groups have very similar negative charge stabilizing abilities, the Smiles rearrangement becomes a reversible process.

Applications

2-aryloxy-2-methylpropionamide → (NMP:DMPU (10:1), NaH, 150 °C, 72h; 59%) → *N*-aryl-2-hydroxypropionamide → (HCl, EtOH) → Aromatic amine HCl salt

3-(3-cyano-propoxy)-benzo[*b*]thiophene-2-carbonitrile → (NaH (1.2 equiv), dioxane reflux, 5h, 25%) → [intermediates] → [1]Benzothieno[3,2-*d*]furo[2,3-*b*]pyridine skeleton

(LiHMDS, THF, -20 °C to r.t., 82%) → Smiles rearrangement product → (S$_N$Ar) → Dipyrido[2,3-*b*]diazepinone derivative

Smiles-Truce rearrangement

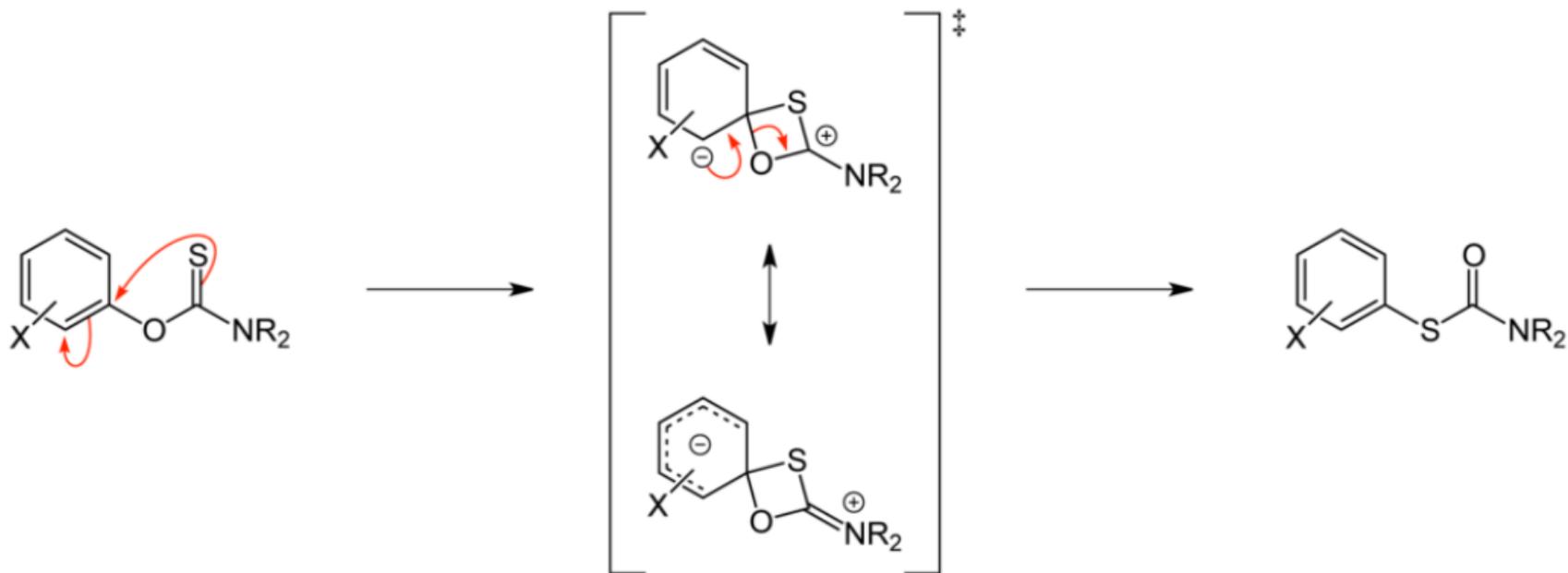9) in the presence of a strong base, when Y=SO2 and XH=CH3, no activating group is necessary and the process is called Smiles-Truce rearrangement
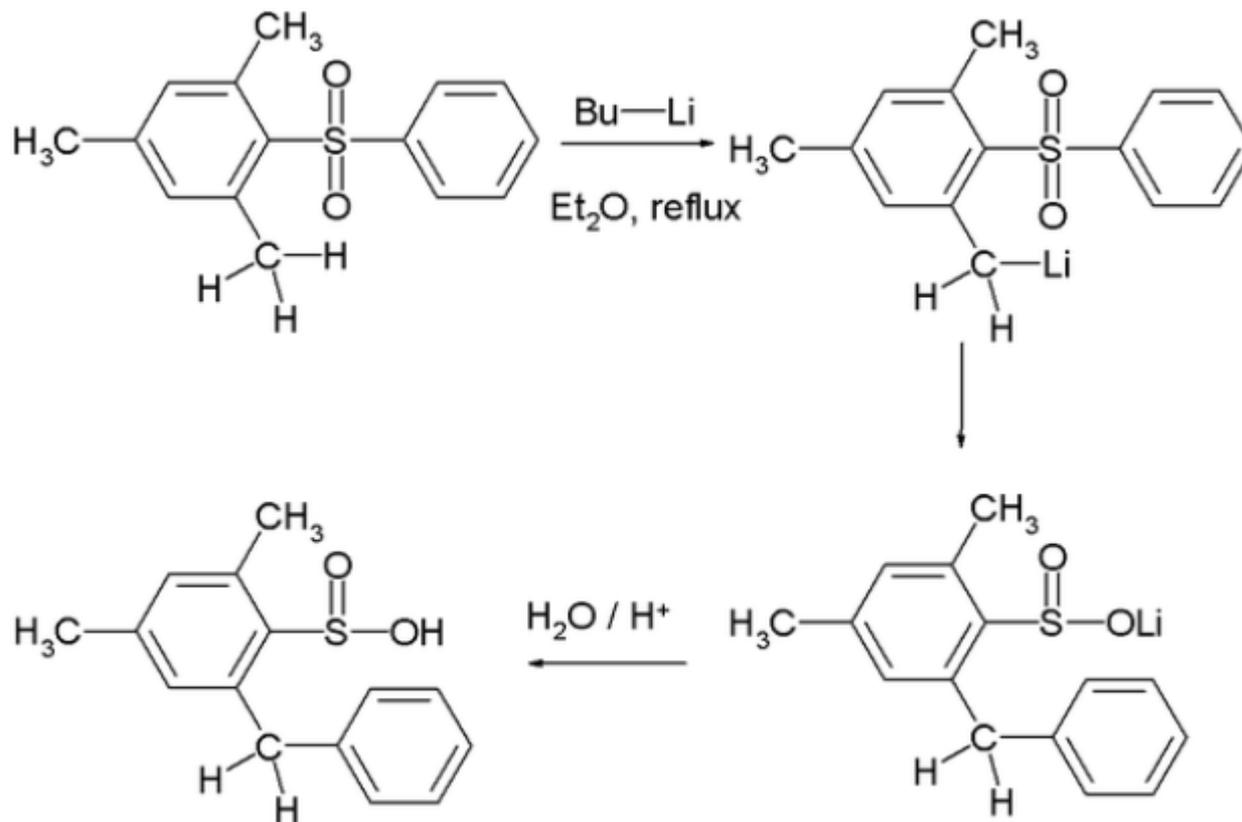
Chapman rearrangement
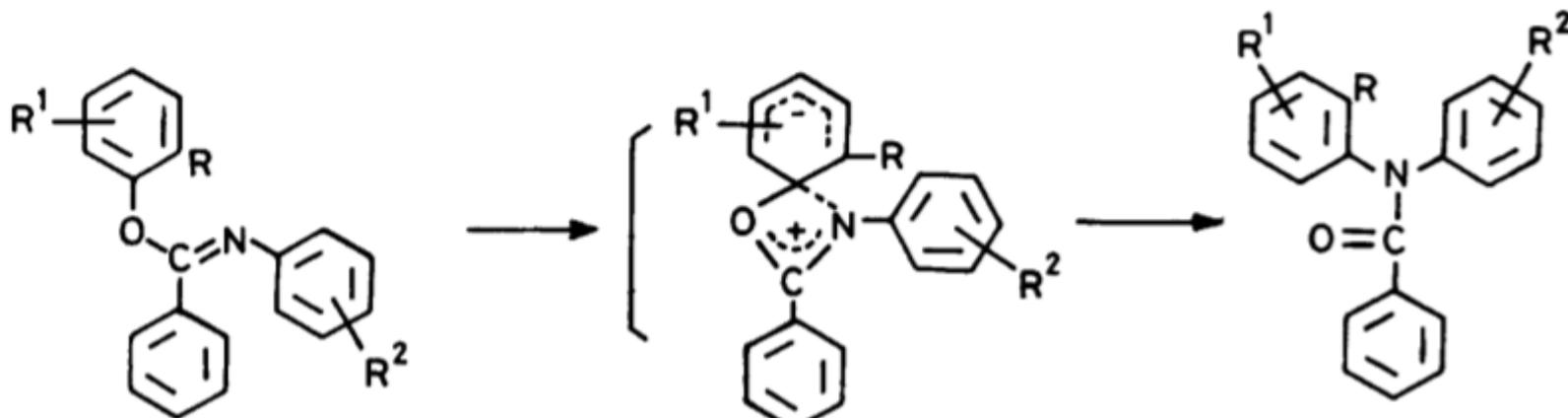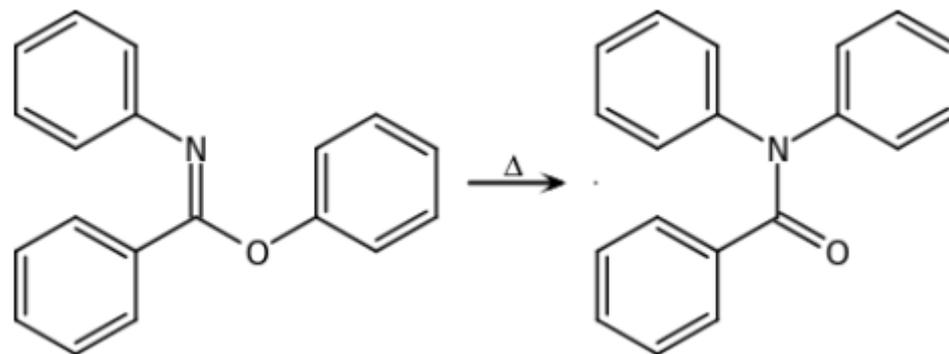
Newman–Kwart rearrangement

Hayashi rearrangement