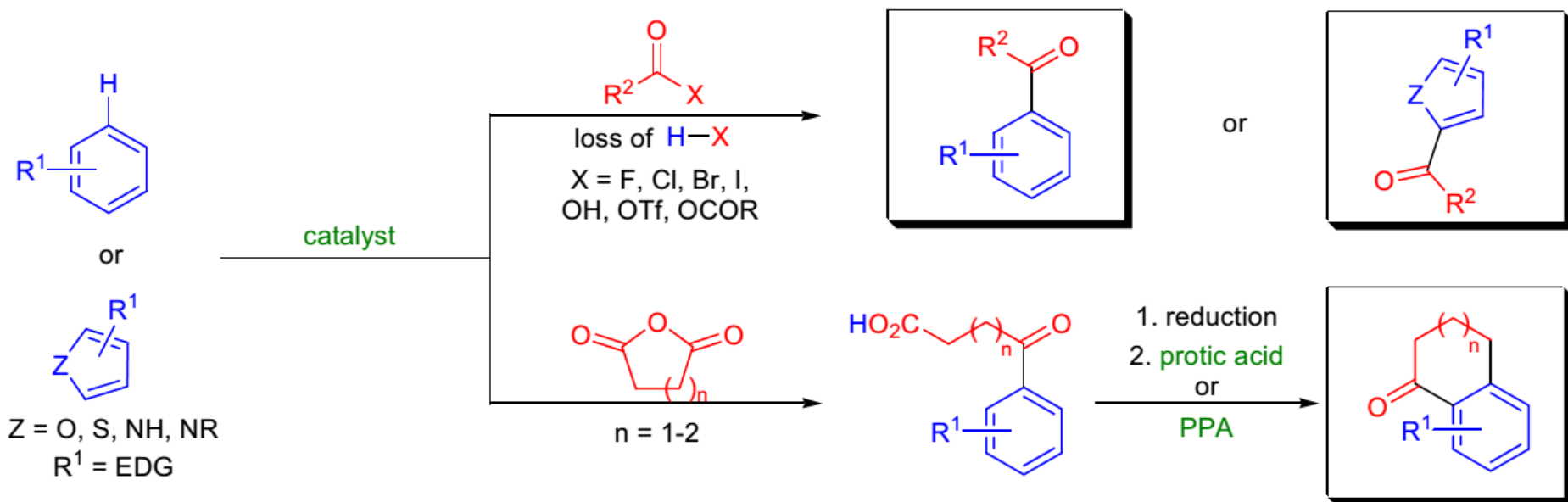


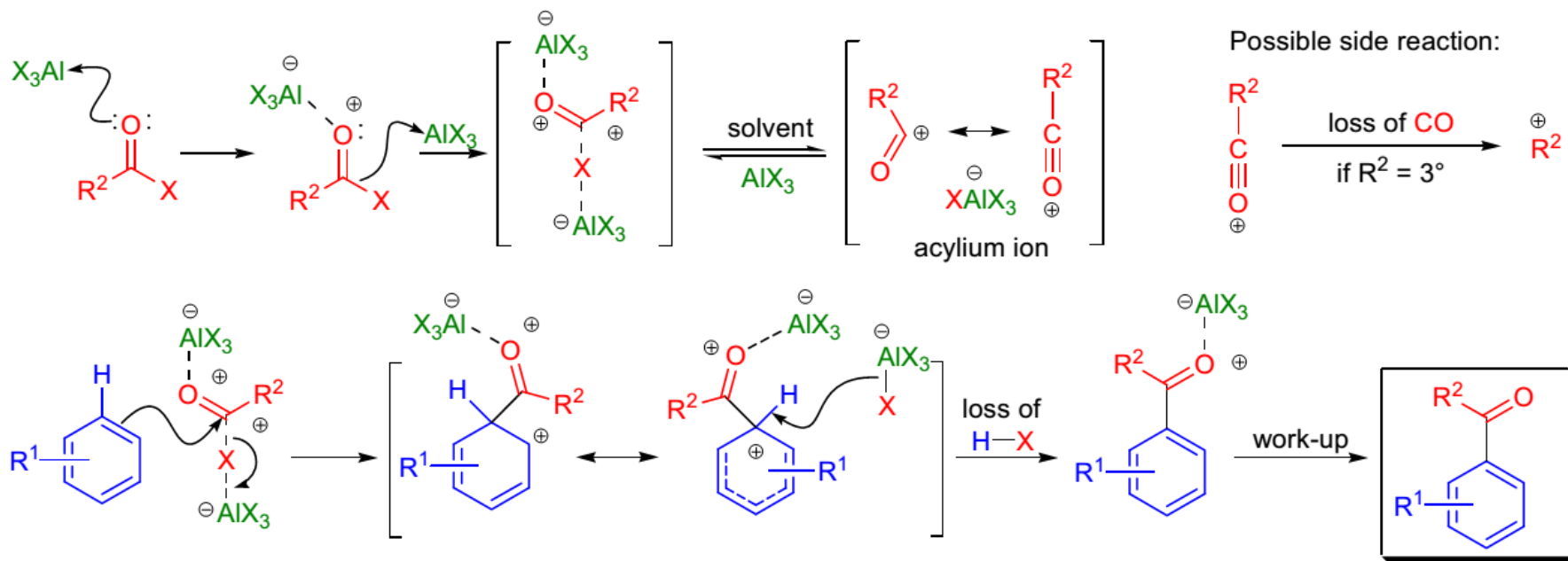
FRIEDEL-CRAFTS ACYLATION



General features

1) substrates that undergo the Friedel-Crafts alkylation are also easily acylated and in most cases electron-rich substrates ($R_1 = -OH, -NR_2, \text{alkyl}, \text{etc.}$) are needed to obtain the desired ketone in good yield; **2)** aromatic substrates with strongly electron-withdrawing groups ($R_1 = -NO_2, -CX_3, \text{etc.}$) and **certain heteroaromatic compounds (e.g., quinolines, pyridines) do not undergo the acylation at all, and they may be used as solvents (these unreactive substrates, however, are efficiently acylated by the Minisci reaction)**; **3)** acylating agents besides acyl halides are: aromatic and aliphatic carboxylic acids, anhydrides, ketenes and esters, as well as polyfunctional acylating agents (oxalyl halides); **4)** acyl iodides are usually the most reactive, while acyl fluorides are the least reactive ($I > Br > Cl > F$); **5)** unlike in the alkylations, Friedel-Crafts acylations require substantial amounts of catalyst (**slightly more than one equivalent**), since the acylating agent itself coordinates one equivalent of Lewis acid, and therefore excess is needed to observe catalysis; **6)** most often used catalysts are: AlX_3 , lanthanide triflates, zeolites, protic acids (e.g., H_2SO_4, H_3PO_4), $FeCl_3, ZnCl_2, PPA$; **7)** in the case of very reactive acylating agents (e.g., acyloxy triflates) or very electron-rich substrates there is **little or no catalyst** required; **8)** **no polyacylated products are observed**, since, after the introduction of the first acyl group, the substrate becomes deactivated; **9)** **rearrangement of the acylating agent under the reaction conditions is rarely observed** and this feature allows the preparation of straight chain alkylated aromatic compounds in a two-step process (acylation followed by reduction); **10)** unprotected Lewis basic functional groups (e.g., amines) are poor substrates, since the acylation will preferentially take place on these functional groups instead of the aromatic ring; **11)** the intramolecular Friedel-Crafts acylation is well-suited for the closure of 5-, 6- and 7-membered rings with a tendency for **the formation of the 6-membered ring**. One drawback of the Friedel-Crafts acylation is that the Lewis acid catalyst usually cannot be recovered at the end of the reaction, since it is destroyed in the work-up step. However, recent studies showed that the use of **heterogeneous catalysts (mainly zeolites)** makes this important reaction more feasible on an industrial scale.

Mechanism



Examples

