Friedel-Crafts Alkylation

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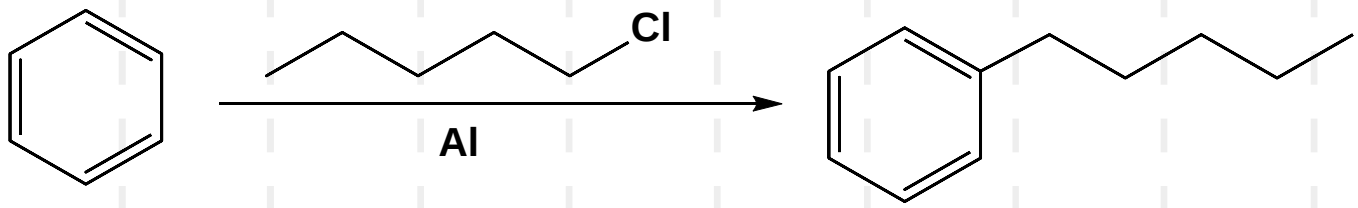
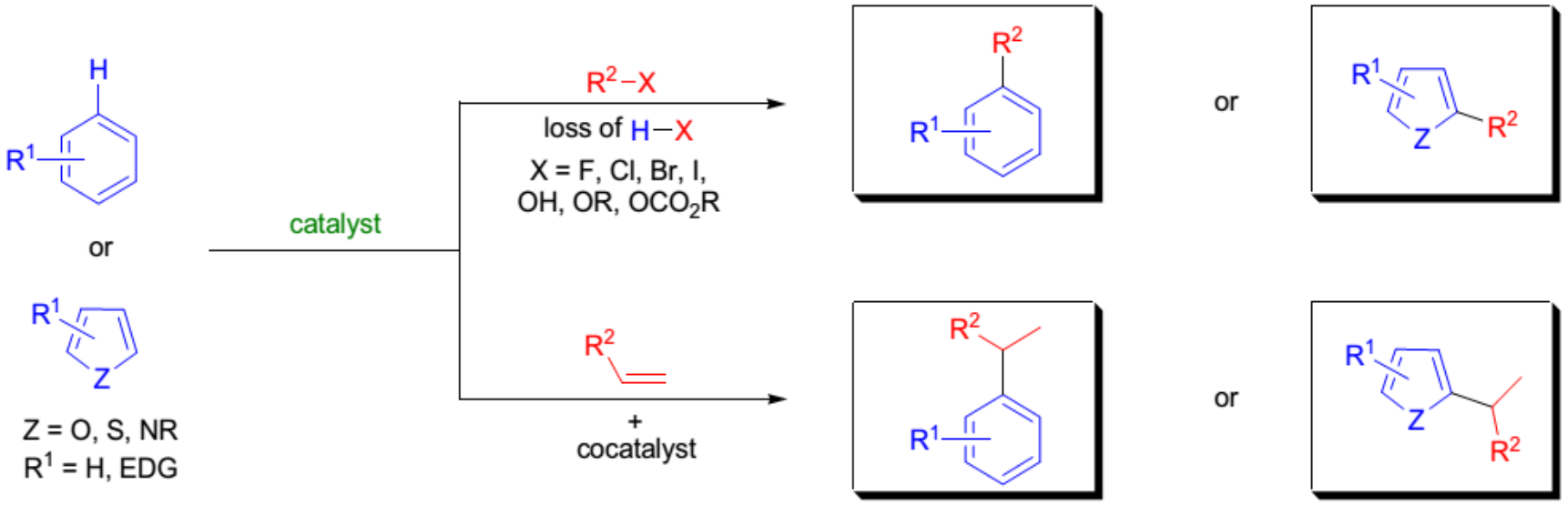
introduce

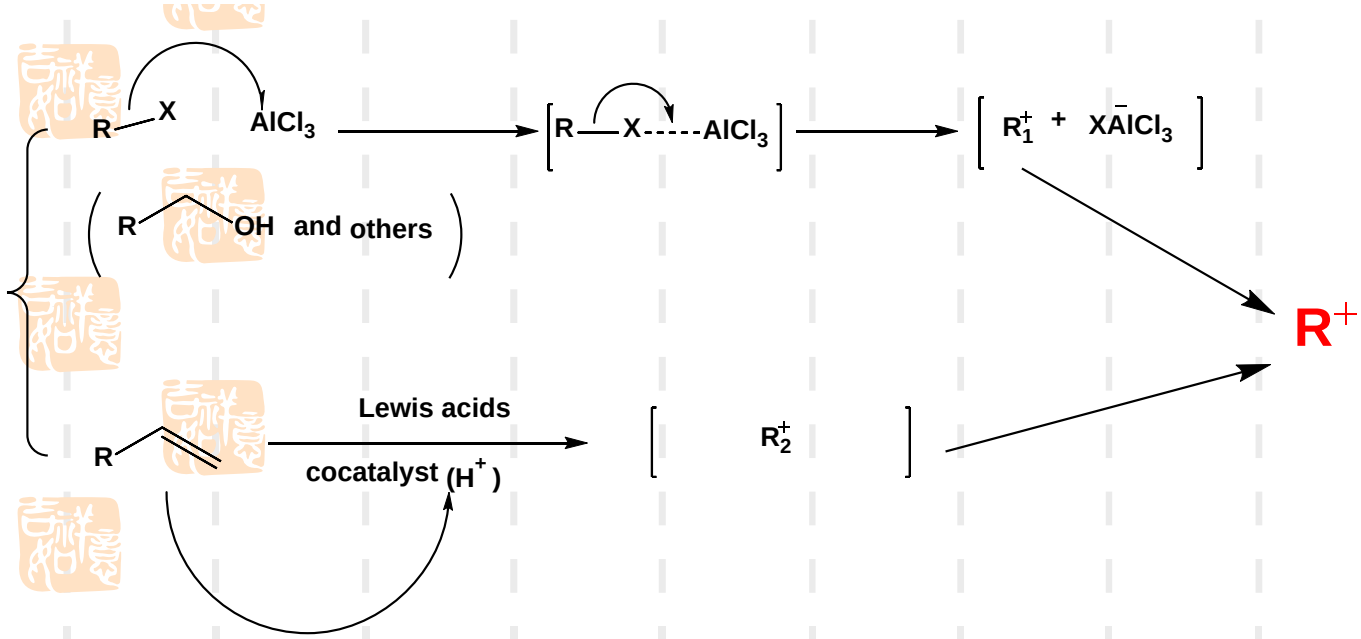
In 1877, C. Friedel and J.M. Crafts treated amyl chloride with thin aluminum strips in benzene and observed the formation of amylbenzene.

Since their discovery, the substitution of aromatic and aliphatic substrates with various alkylating agents (alkyl halides, alkenes, alkynes, alcohols, etc.) in the presence of catalytic amounts of Lewis acid is called the Friedel-Crafts alkylation.



introduce

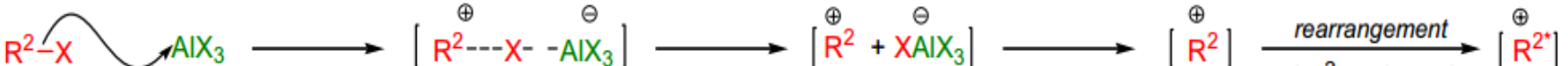

H
R1
or
R1
Z
Z = O, S, NR
R1 = H, EDG
catalyst
R2–X
loss of H–X
X = F, Cl, Br, I,
OH, OR, OCO2R
R2
+
cocatalyst
R2
R1
or
R1
Z
R2
R2
R1
or
R1
Z
R2

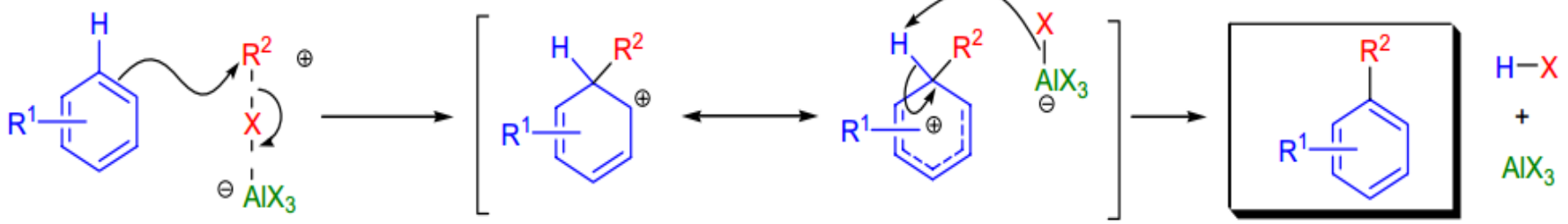

R
X
AlCl3
[R X----AlCl3]
[R1+ + XAlCl3]
R
OH and others
R+
R
Lewis acids
cocatalyst (H+)
[R2+]

introduce

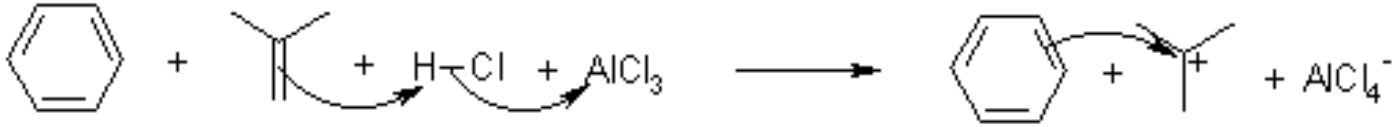
- The most widely employed catalysts are AlCl3 and BF3 for alkylations with alkyl halides. Becides, BeCl2, CdCl2, BF3, BBr3, GaCl3, AlBr3, FeCl3, TiCl4,SnCl4, SbCl5, lanthanide trihalides, and alkylaluminum halides (AlRX2).
- The reactivity of alkyl halides is the highest for alkyl fluorides and the lowest for alkyl iodides (F > Cl > Br > I).
- The branching of the alkyl group has a dramatic influence, since tertiary alkyl halides are the most reactive: tertiary>benzyl > secondary > primary.
- 1° and 2° alkyl groups tend to rearrange and therefore product mixtures are formed.
- If the aromatic substrate is substituted, electron-donating substituents are required, and electron-poor substrates do not undergo the alkylation.
- After the first alkyl group is introduced, the aromatic ring becomes more reactive and polyalkylation often occurs.
- The Friedel-Crafts alkylation reaction is reversible, and therefore alkyl groups that are already in the substrate may migrate, rearrange, or be removed under the reaction conditions.

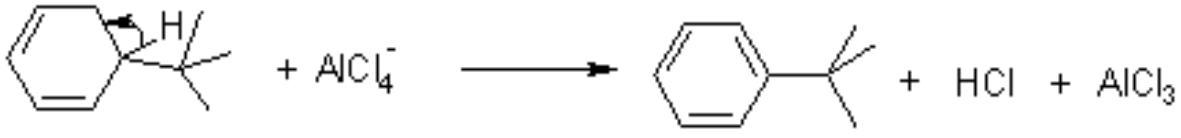
Mechanism



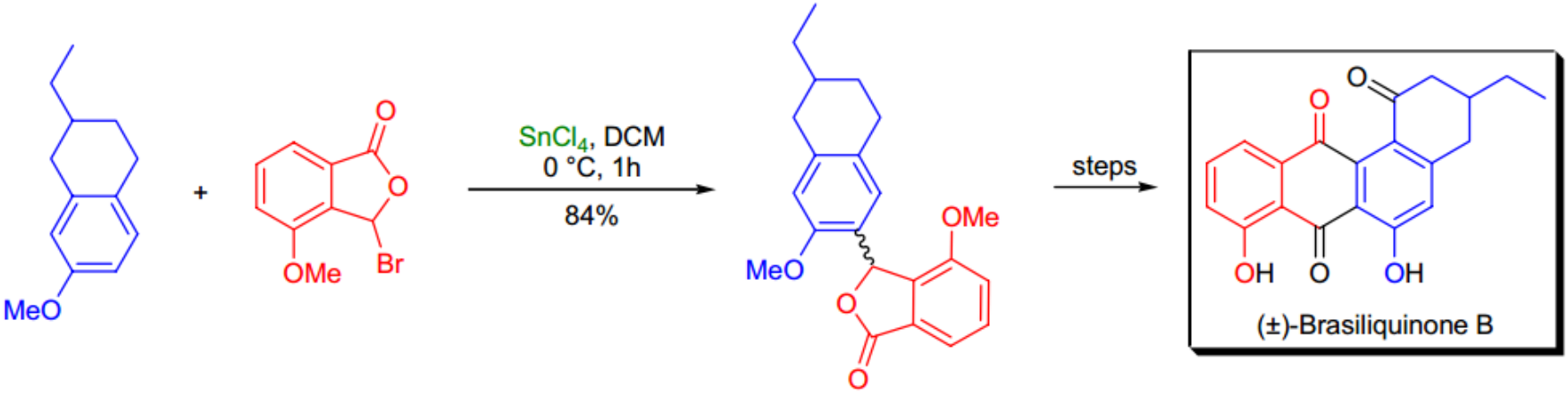


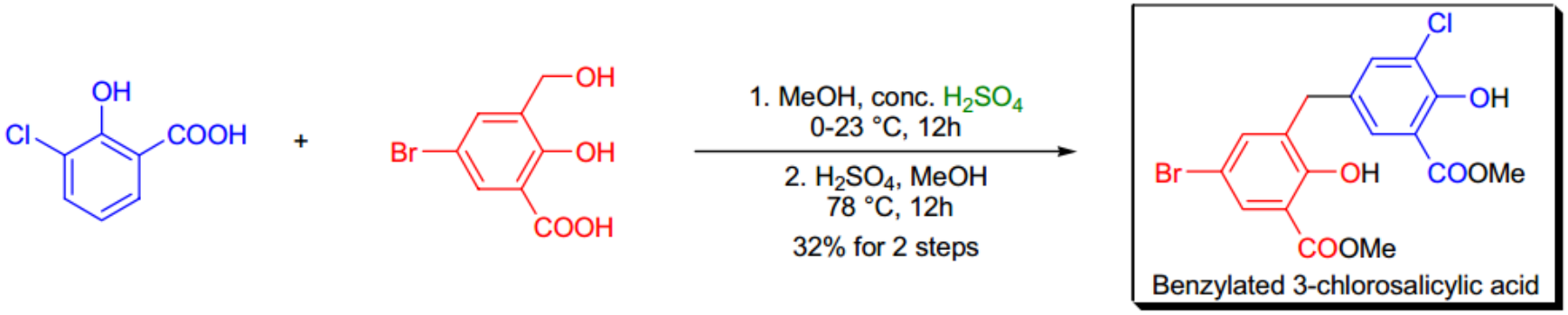
Using alkenes :





Synthetic Applications





Thanks for your attention!