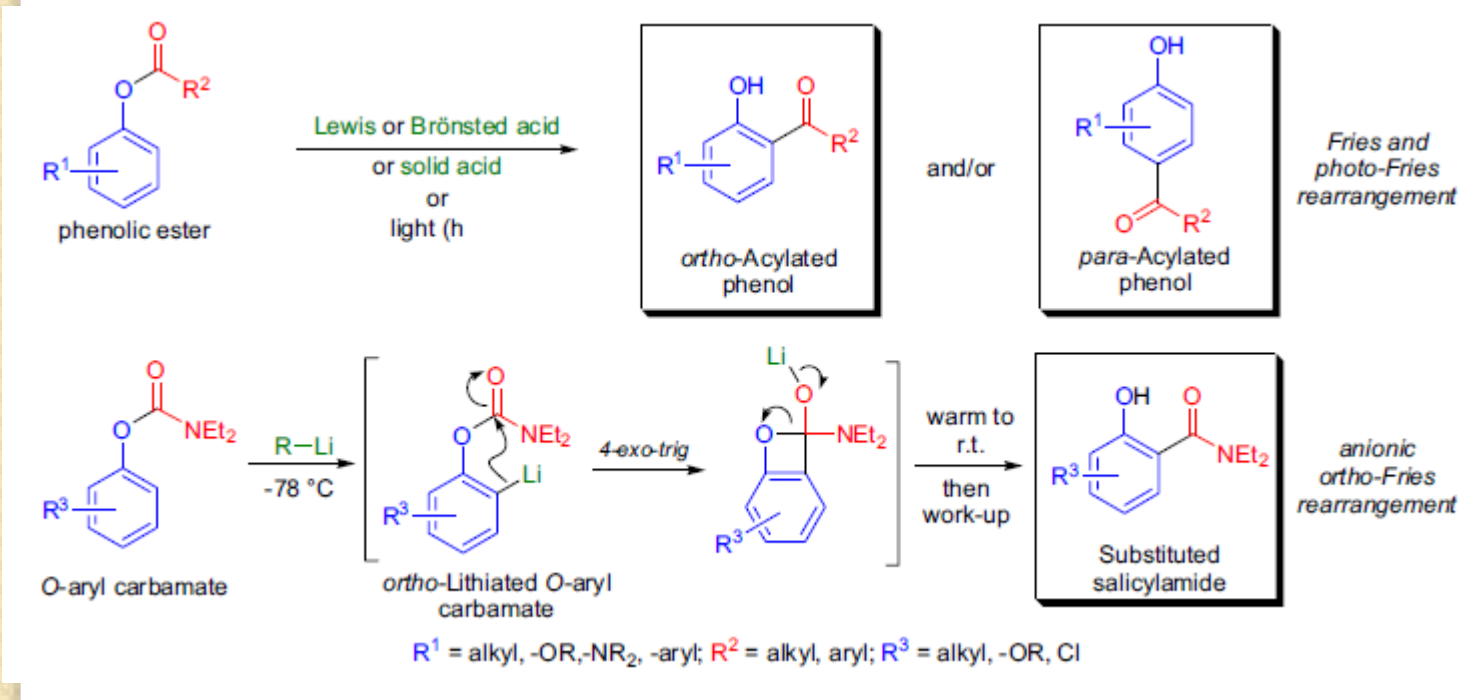
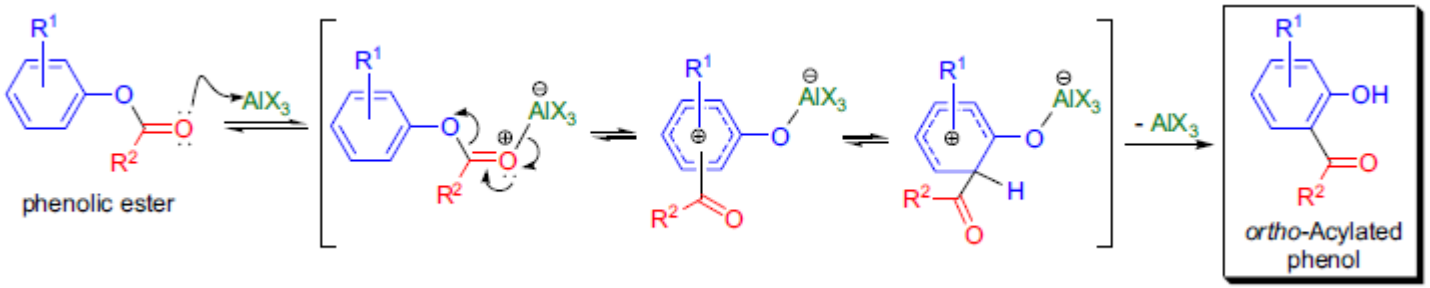
# FRIES-, PHOTO-FRIES, AND ANIONIC ORTHO-FRIES REARRANGEMENT

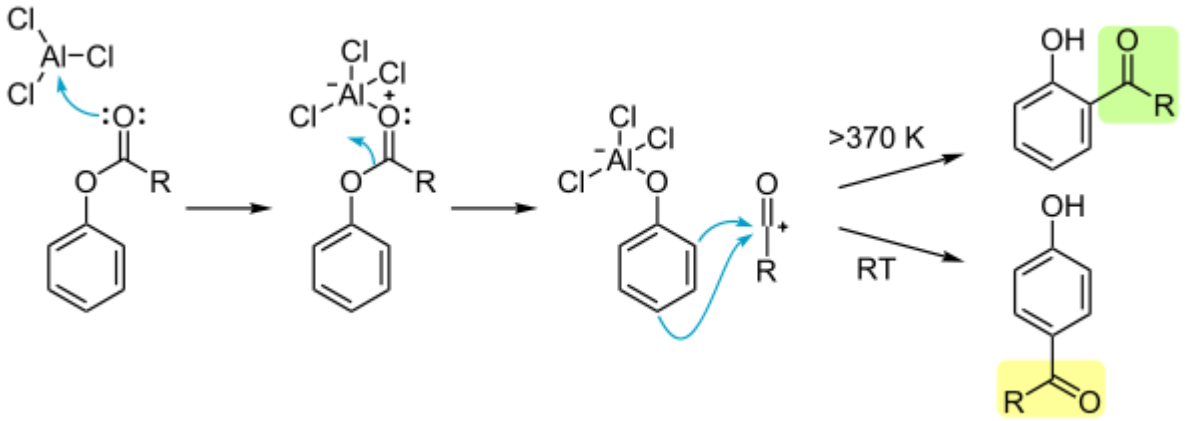


**Mechanism:**

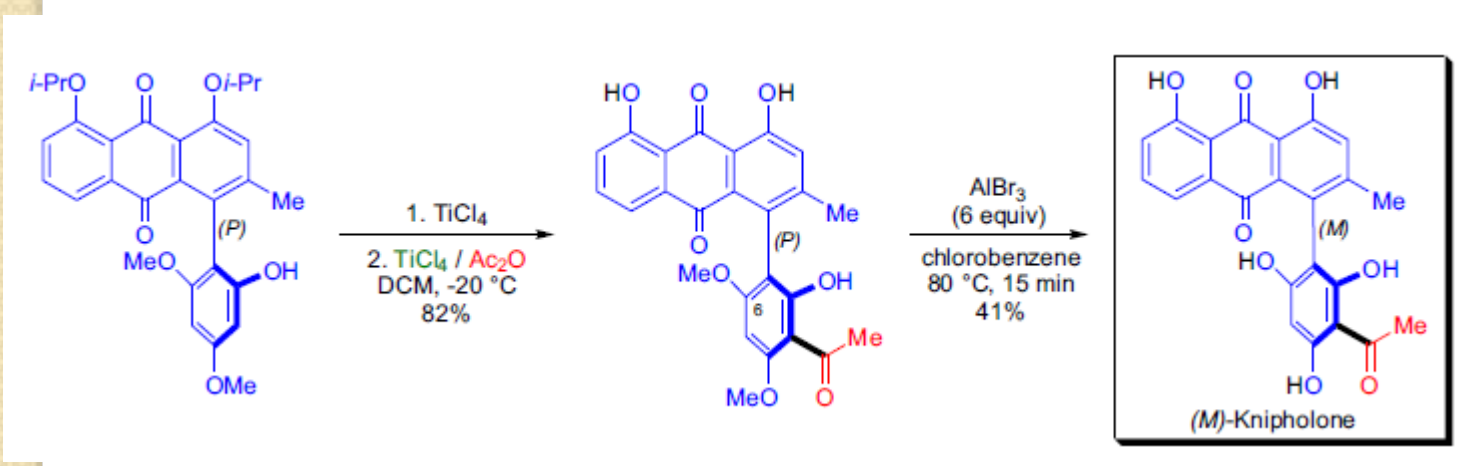
The *Fries rearrangement* proceeds *via* ionic intermediates but the exact mechanistic pathway (whether it is inter- or intramolecular) is still under debate. There are many reports in the literature that present evidence to support either of the pathways, but it appears that the exact route depends on the structure of the substrates and the reaction conditions. The scheme depicts the formation of an *ortho*-acylated phenol from a substituted phenolic ester in the presence of aluminum trihalide catalyst. The *photo-Fries rearrangement* proceeds *via* radical intermediates.



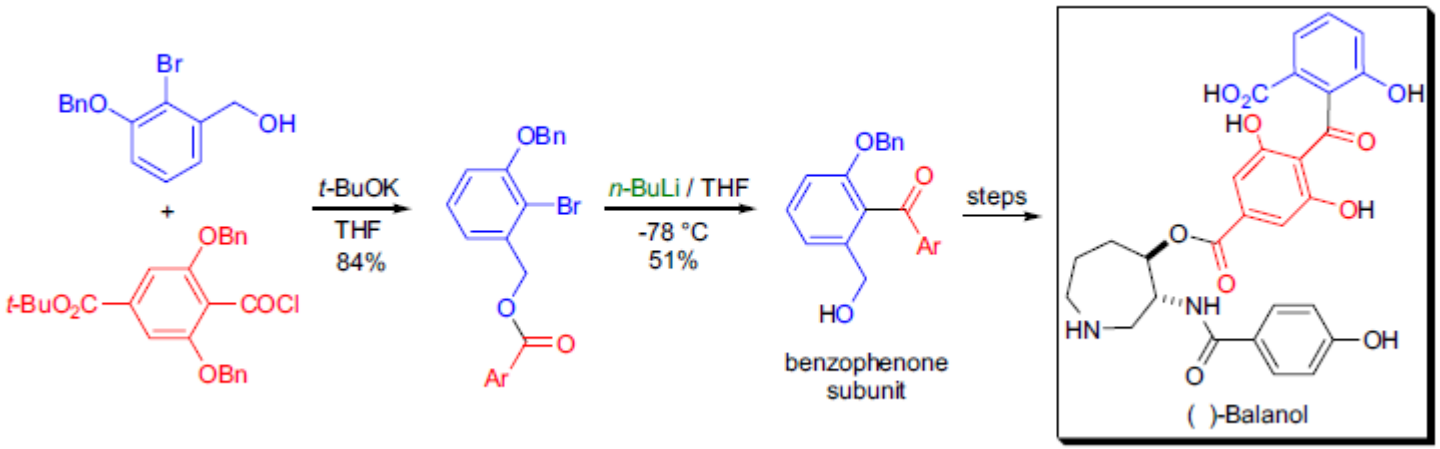

**Mechanism of Fries rearrangement (from Wikipedia)**



The first atropo-enantioselective total synthesis of a phenylanthraquinone natural product (*M*)-knipholone was reported by G. Bringmann et al.51 In the late stages of the synthesis, an acetyl group had to be introduced under mild conditions. The advanced substituted anthraquinone intermediate was first deprotected with TiCl4 and then acylated with Ac2O in the presence of TiCl4. A spontaneous *Fries-rearrangement* took place to afford the *ortho*-acylated product in high yield. The natural product was obtained by a mono *O*-demethylation at C6 with AlBr3.



The total synthesis of the potent protein kinase C inhibitor (–)-balanol was accomplished by J.W. Lampe and coworkers. They took advantage of the *anionic homo-Fries rearrangement* to prepare the sterically congested benzophenone subunit. To this end, 2-bromo-3-benzyloxy benzyl alcohol was first acylated with a 1,3,5-trisubstituted benzoyl chloride to obtain the ester precursor in 84% yield. Next, the ester was treated with *n*-BuLi at -78 ° C to perform a metal-halogen exchange. The resulting aryllithium rapidly underwent the *anionic homo-Fries rearrangement* to afford the desired tetra *ortho*-substituted benzophenone in 51% yield.



Research in the laboratory of P. Magnus showed that the macrocyclic skeleton of diazonamide could be synthesized with the use of *macrolactonization* followed by a *photo-Fries rearrangement*.53 First, the aromatic carboxylic acid and the phenol were coupled with EDCI to form the macrolactone (phenolic ester), which was then exposed to light at high-dilution to cleanly afford the macrocyclic *ortho*-acylated phenol skeleton of diazonamide.