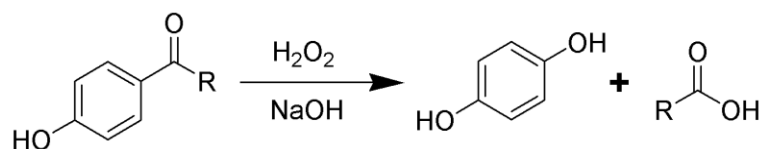


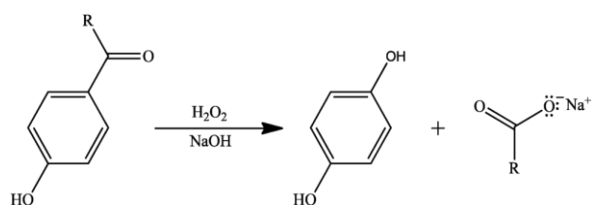
B.SC Sem – IV CHEMISTRY HONOURS
Paper ; CC – 10
Unit : Rearrangement Reaction

Dakin Rearrangement

The **Dakin oxidation** (or **Dakin reaction**) is an organic redox reaction in which an ortho- or para-hydroxylated phenyl aldehyde (2-hydroxybenzaldehyde or 4-hydroxybenzaldehyde) or ketone reacts with hydrogen peroxide in base to form a benzenediol and a carboxylate. Overall, the carbonyl group is oxidized, and the hydrogen peroxide is reduced.

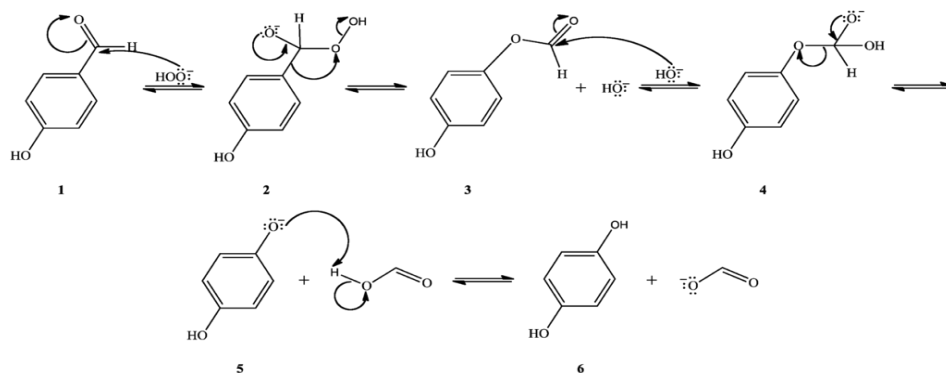


The Dakin oxidation, which is closely related to the Baeyer-Villiger oxidation.

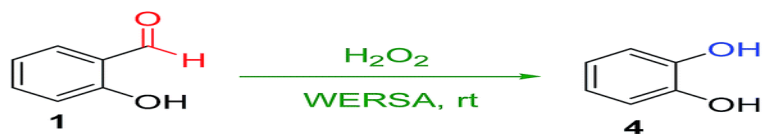


Mechanism :

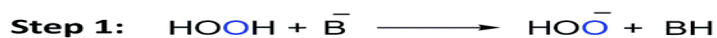
The Dakin oxidation starts with nucleophilic addition of a hydroperoxide anion to the carbonyl carbon, forming a tetrahedral intermediate (2). The intermediate collapses, causing [1,2]-aryl migration, hydroxide elimination, and formation of a phenyl ester (3). The phenyl ester is subsequently hydrolyzed: nucleophilic addition of hydroxide from solution to the ester carbonyl carbon forms a second tetrahedral intermediate (4), which collapses, eliminating a phenoxide and forming a carboxylic acid (5). Finally, the phenoxide extracts the acidic hydrogen from the carboxylic acid, yielding the collected products (6).^{[1][2]}



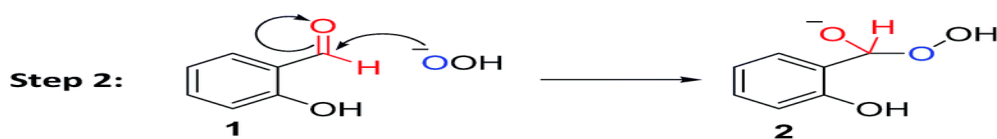
Step wise Mechanism :



Mechanism:



Base source is **WERSA**
Base = B^-

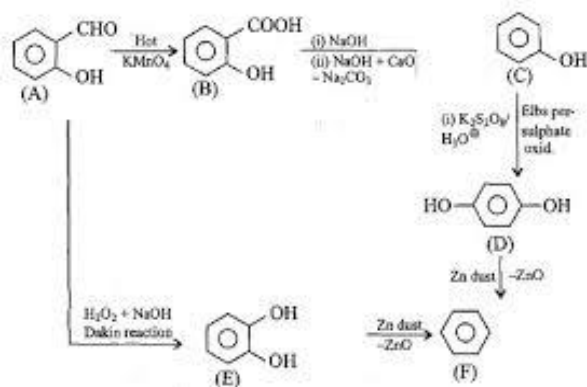
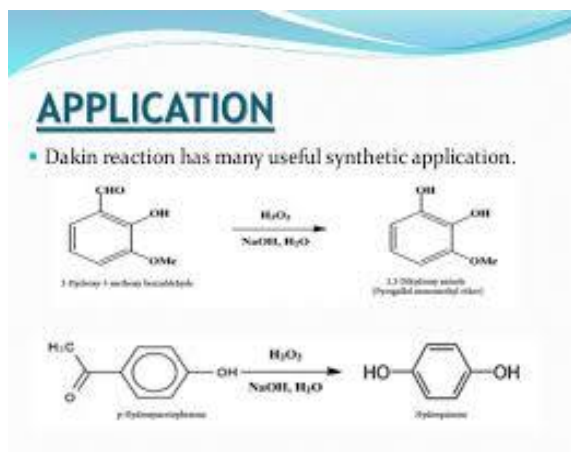


Factors affecting reaction kinetics

The Dakin oxidation has two rate-limiting steps: nucleophilic addition of hydroperoxide to the carbonyl carbon and [1,2]-aryl migration. Therefore, the overall rate of oxidation is dependent on the nucleophilicity of hydroperoxide, the electrophilicity of the carbonyl carbon, and the speed of [1,2]-aryl migration. The alkyl substituents on the carbonyl carbon, the relative positions of the hydroxyl and carbonyl groups on the aryl ring, the presence of other functional groups on the ring, and the reaction mixture pH are four factors that affect these rate-limiting steps.

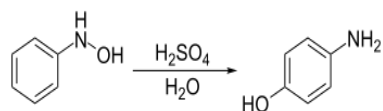
Alkyl substituents

In general, phenyl aldehydes are more reactive than phenyl ketones because the ketone carbonyl carbon is less electrophilic than the aldehyde carbonyl carbon. The difference can be mitigated by increasing the temperature of the reaction mixture.



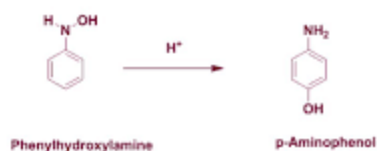
Bamberger rearrangement :

The **Bamberger rearrangement** is the chemical reaction of phenylhydroxylamines with strong aqueous acid, which will rearrange to give 4-aminophenols. It is named for the German chemist Eugen Bamberger .



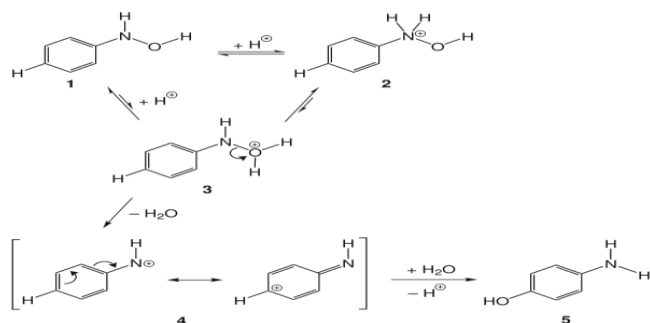
The starting phenylhydroxylamines are typically synthesized by the transfer hydrogenation of nitrobenzenes using rhodium or zinc catalysts.

Bamberger Rearrangement

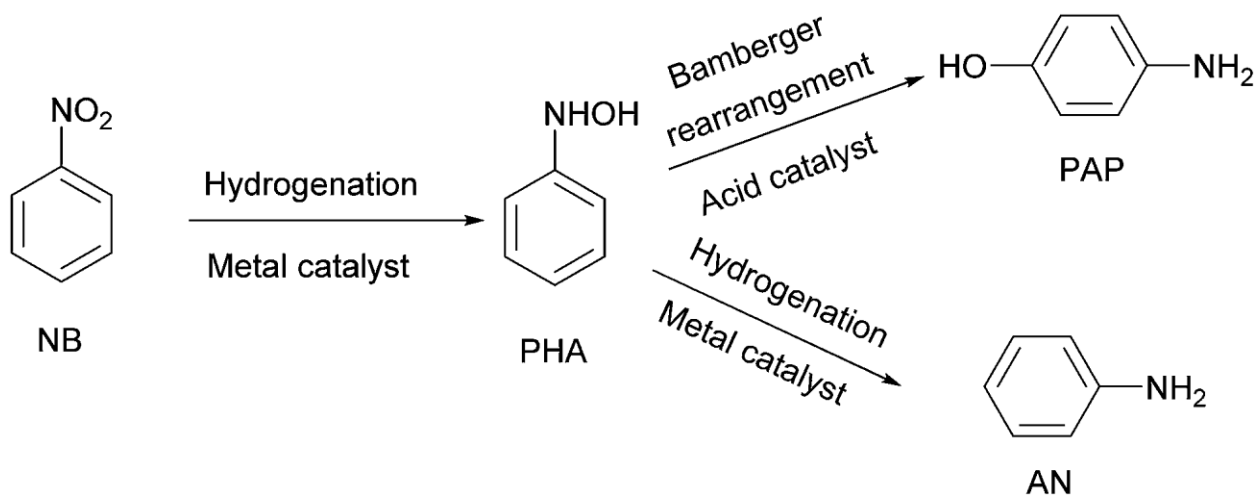


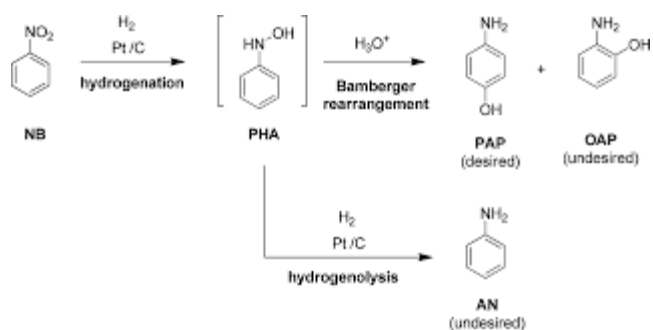
Reaction mechanism

The mechanism of the Bamberger rearrangement proceeds from the monoprotection of N-phenylhydroxylamine **1**. N-protonation **2** is favored, but unproductive. O-protonation **3** can form the nitrenium ion **4**, which can react with nucleophiles (H_2O) to form the desired 4-aminophenol **5**.



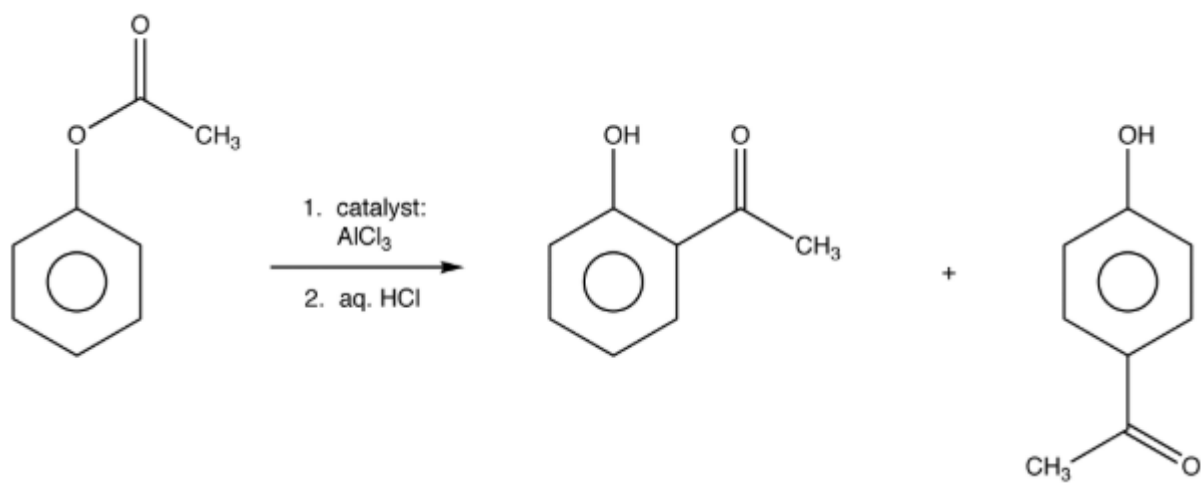
Application



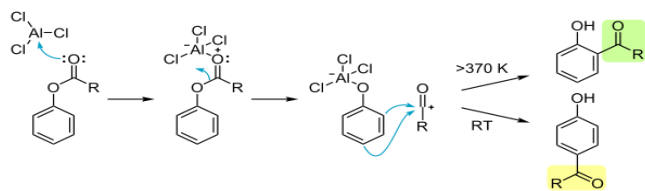


The **Fries rearrangement**, named for the German chemist Karl Theophil Fries, is a rearrangement reaction of a phenolic ester to a hydroxy aryl ketone by catalysis of Lewis acids.

It involves migration of an acyl group of phenol ester to the aryl ring. The reaction is ortho and para selective and one of the two products can be favoured by changing reaction conditions, such as temperature and solvent.



□ Despite many efforts, a definitive reaction mechanism for the Fries rearrangement has not been determined. Evidence for inter- and intramolecular mechanisms have been obtained by crossover experiments with mixed reactants. The Reaction progress is not dependent on solvent or substrate. A widely accepted mechanism involves a carbocation intermediate.



In the first reaction step a Lewis acid for instance aluminium chloride AlCl_3 co-ordinates to the carbonyl oxygen atom of the acyl group. This oxygen atom is more electron rich than the phenolic oxygen atom and is the preferred Lewis base. This interaction polarizes the bond between the acyl residue and the phenolic oxygen atom and the aluminium chloride group rearranges to the phenolic oxygen atom. This generates a free acylium carbocation which reacts in a classical electrophilic aromatic substitution with the aromatic ring. The abstracted proton is released as hydrochloric acid where the chlorine is derived from aluminium chloride. The orientation of the substitution reaction is temperature dependent. A low reaction temperature favors para substitution and with high temperatures the ortho product prevails, this can be rationalised as exhibiting classic Thermodynamic versus kinetic reaction control as the ortho product can form a more stable bidentate complex with the Aluminium. Formation of the ortho product is also favoured in non-polar solvents; as the solvent polarity increases, the ratio of the para product also increases.

Scope

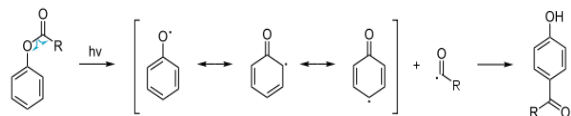
Phenols react to form esters instead of hydroxyarylketones when reacted with acyl halides under Friedel-Crafts acylation conditions. Therefore, this reaction is of industrial importance for the synthesis of hydroxyarylketones, which are important intermediates for several pharmaceuticals. As an alternative to aluminium chloride, other Lewis acids such as boron trifluoride and bismuth triflate or strong protic acids such as hydrogen fluoride and methanesulfonic acid can also be used. In order to avoid the use of these corrosive and environmentally unfriendly catalysts altogether research into alternative heterogeneous catalysts is actively pursued.

Limits

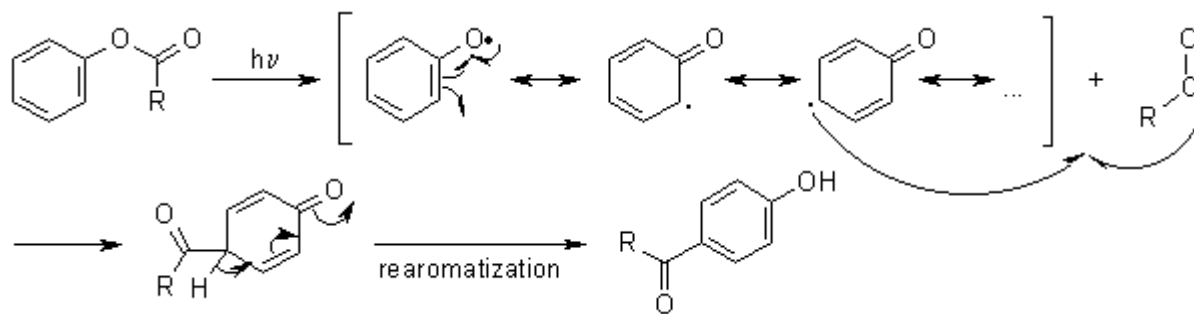
In all instances only esters can be used with stable acyl components that can withstand the harsh conditions of the Fries rearrangement. If the aromatic or the acyl component is heavily substituted then the chemical yield will drop due to steric constraints. Deactivating meta-directing groups on the benzene group will also have an adverse effect as can be expected for a Friedel-Crafts acylation.

Photo-Fries rearrangement

In addition to the ordinary thermal phenyl ester reaction a photochemical variant is possible. The **photo-Fries rearrangement** can likewise give and products. that involves a radical reaction mechanism. This reaction is also possible with deactivating substituents on the aromatic group. Because the yields are low this procedure is not used in commercial production. However, photo-Fries rearrangement may occur naturally, for example when a plastic bottle made of polycarbonate (PC) is exposed to the sun, particularly to UV light at a wavelength of about 310 nm, if the plastic has been heated to 40° Celsius or above (as might occur in a car with windows closed on a hot summer day). In this case, photolysis of the ester groups would lead to leaching of phthalate from the plastic.



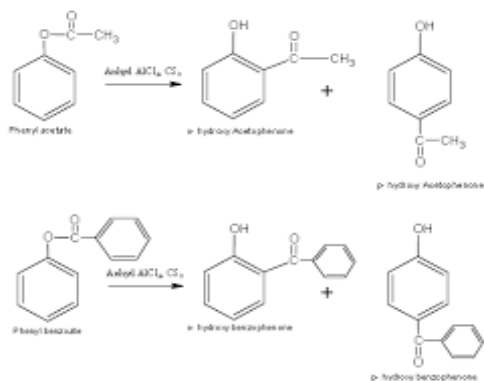
Alternative Mechanism :



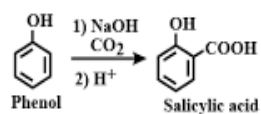
Anionic Fries rearrangement

In the anionic Fries rearrangement ortho-metalation of aryl esters, carbamates and carbonates with a strong base results in a rearrangement to give ortho-carbonyl species.

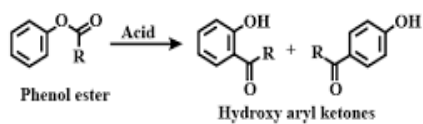
Application

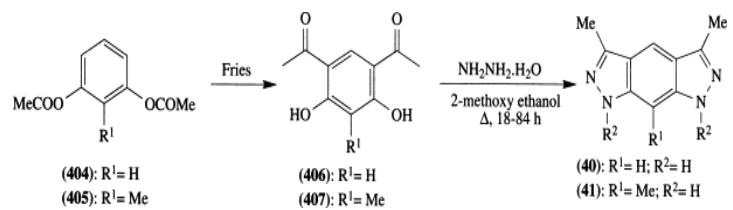


Kolbe-Schmitt Reaction



Fries Rearrangement reaction





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