



DIVERSE METHODS FOR THE SYNTHESIS OF IMINES

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Abstract: Imines are versatile starting compounds for the preparation of many nitrogen-containing organic compounds. Diverse methods for the synthesis of imines are discussed. This reaction takes place through a condensation of aldehydes or ketones with primary amines. It is found that acidic catalysts and solid surfaces are good stimulant for the preparation of imines. This reaction also proceeds in the absence of any catalyst.

Introduction: Synthesis of Schiff bases (imines) is a very important reaction because diverse nitrogen-containing organic compounds are prepared from them by several chemical manipulations. Imines are prepared by reacting primary amines with aldehydes/ketones. Depending upon their structures of the reactants, a number of procedures are adopted for the preparation of the imines. In this paper, we describe various concise methods for the preparation of imines.

Results and Discussion:

(a): Preparation of imines by acid-catalyzed reaction: Perhaps acid-catalyzed dehydration method is one of the widely studied reactions for the preparation of imines from aldehydes/ketones and primary amines. For example, benzaldehyde and aniline reacted in benzene solution in the presence of catalytic amounts of para-toulenesulfonic acid using a Dean-Stark water separator at reflux temperature. The yield of the reaction was very high. On removal of benzene, imine was isolated from this reaction directly. There were no other products formed [1].

The above reaction was applied successfully for almost all stable primary amines and aldehydes/ketones. However, with relatively unstable aldehydes derived from sugars, this reaction produced low yield of the imine at high temperature, possibly due to the decomposition, self condensation and rearrangement [2].

(b): Preparation of imines at room temperature and in the absence of any acid catalyst: Optically active imine was obtained by reaction with glyceraldehydes acetonide and primary

amine at room temperature in the absence of acidic catalyst and in water solution [2]. A spontaneous reaction took place between the reactive carbonyl group and primary amine and further dehydration produced the product. The success of this reaction proved that elimination/dehydration can occur even the media has enough water. The highly unstable 1, 2 amino alcohol intermediate eliminated water for stabilization. The imine was isolated with organic solvent through extraction method.

(c): Preparation of imines at room temperature in the presence of Montmorillonite clay: Montmorillonite has acidic properties. This solid was used for the preparation of imines by reaction of aldehydes/keones and primary amines without using any organic solvent or water. Carbonyl compounds and primary amines were added to this clay and mixed them thoroughly. The solid mass was kept at room temperature for 2-3h. Dichloromethane was added to the solid reaction mixture, it was then filtered and evaporated to afford the imine in excellent yield [3].

(d): Preparation of imines at room temperature in the presence of molecular sieves: Some clays have acidic or basic properties and as a result, they catalyzed imine formation. Molecular sieves in powdered form was found to be a good surface for the preparation of imines starting from aldehydes/ketones and primary amines. The commercially available molecular sieves are neutral, yet they produced imines successfully [4].

(e): Preparation of imines at room temperature by grinding in a mortar-pestle: Imine was also prepared by grinding equimolar proportion of aldehyde/ketone and primary amines at room temperature without any catalyst, surface or solvent. It appeared that the grinding of these reactants by mortar pestle produced sufficient interaction among the reagents. Because of the exothermic nature of the reaction and enough friction among these molecules in concentrated forms was a perfect choice for imine production.

Steric Hindrance and Electronic Distribution: The rate of imine formation depends on the conditions of the experiments as well as the steric and electronic factors present in the structure of the starting compounds. Since this reaction is an example of a nucleophilic addition of the amines to aldehydes/ketones, the factors that increase the nucleophilic power of the amines is expected to accelerate the course of the reaction. Electron donating group present in the amines favor the formation of imines and electron withdrawing group retard the formation of amines. Sterically hindered amines produce imines at a slower rate compared to non-sterically hindered amines. In contrast, electron withdrawing groups in aldehydes and ketones may favor the formation of imines. The lower charge density at the carbonyl groups favors the formation of the imines. Some exceptions of these general trends may be explained using more advanced explanations. Nevertheless, preparation of imines by various methods is a very useful method because these are widely accepted as the building blocks for the preparation of versatile organic compounds of interests. However, some imines are not stable even at room temperature for a prolonged period of time. These imines should be used as soon as they were prepared. Optically active imines may undergo racemisation. It has been found that imines are relatively stable at basic media. In acidic situation, imines may undergo decomposition. This is an interesting observation because mild acidity helps to form imines and strong acidic condition may cleave the imine bond.

Curriculum Development: Because of the simplicity and availability of the starting compounds, undergraduate students were able to prepare diverse imines within 2h. It is obvious that this method is extremely appealing to students and scientists working at the research laboratory. The instructors and students captured a number of subjects while performing this reaction because of the wide application of imines in chemistry. For examples, they know about the types of functional groups present in molecules, nucleophilic reaction and subsequent dehydration, preparation and characterization of imines following IR

Spectroscopy. The disappearance of the carbonyl band indicated the completion of the reaction. New band formation for the C=N bond indicated the formation of imines. The presence of carbonyl and imine band together indicated incomplete reaction. The reaction can be also be monitored by Thin layer chromatography using ethyl acetate and hexanes as the solvent (20: 80).

The imines are very versatile intermediates for the preparation of many compounds. For example, reduction of the C=N bond by sodium borohydride/sodium cyanoborohydride produces secondary amino compounds. Reductive dimerization of imines with metal to diamino compounds is also possible. Cycloaddition reaction of the imine with acid chloride in the presence of a tertiary base produces diverse beta lactams.

Conclusion: Several simple methods for the preparation of imines are described here. Depending upon the structure of the primary amines and aldehydes/ketones, an exact preparative method can be chosen.

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