



# A Review on Synthesis of Benzophenone Imine by Benzonitrile

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**Abstract:** In the Buchwald-Hartwig amination, benzophenone imine is a valuable ammonia analogue and a significant precursor for the synthesizing of N-protected primary amines. The traditional synthesis of benzophenone imine, on the other hand, necessitates the use of stoichiometric concentrations of metal reagents or high-pressure conditions. To improve the prospective applicability of benzophenone imine, researcher present a simple method for producing it. The reaction was performed by adding benzonitrile in phenyl-magnesium bromide solution, by refluxing it for about 12 hours. Finally, methanol (anhydrous) has been added that results in liquid form of prepared compound. The TLC of finally yielded compound was done for its efficacy.

**Key words:** Benzophenone imine, Benzonitrile, Grignard reagent, TLC.

## **Introduction:**

Imines play a very important role in the field of medicinal and pharmaceutical chemistry, synthesis of Benzophenone imine by using a benzonitrile and grignard reagent, the reaction is air and moisture sensitive, the conventional synthesis of benzophenone imine requires stoichiometric amounts of metal reagents or high-pressure conditions {Scheme (2)}, so we report the best appropriate method to synthesis the benzophenone imine. These advantages have led to the development of various C–N bond-forming reactions. Using ammonia as a nitrogen source in performing animation is a fundamental transformation that directly affords primary amines. {Scheme (1)}

The need of Imines play a vital role in pharmaceutical & medicinal chemistry but it also useful in polymer industries for the preparation of carbon fibers i.e. the project is mainly based upon the appropriate and convenient method for the synthesis of Benzophenone imine.

Conventional preparation methods for benzophenone imine, however, have several drawbacks that limit their potential utility, for example the addition of phenylmagnesium bromide to benzonitrile. All the reactions were performed in oven dried glassware.

Benzonitrile, Tetrahydrofuran, silica gel and methanol were purchased from commercial source. Flash silica gel column chromatography was performed with Kanto Chemical silica gel 60N (spherical neutral, particle size 40–50  $\mu\text{m}$ ).

Chemical Name : Benzophenone imine

I U P A C Name : Diphenylmethane imine

Chemical Formula :  $\text{C}_{13}\text{H}_{11}\text{N}$

Molecular Weight : 181.238 g/mole

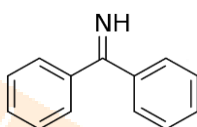
Boiling point : 151-153°/ 10mm

Solubility : Insoluble in water

Density : 1.08

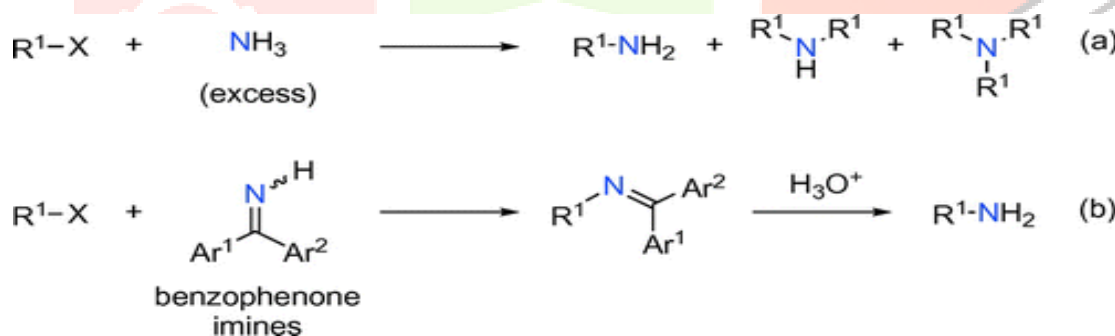
Reflective index : 1.6180

Storage and Sensitivity : Ambient temperature



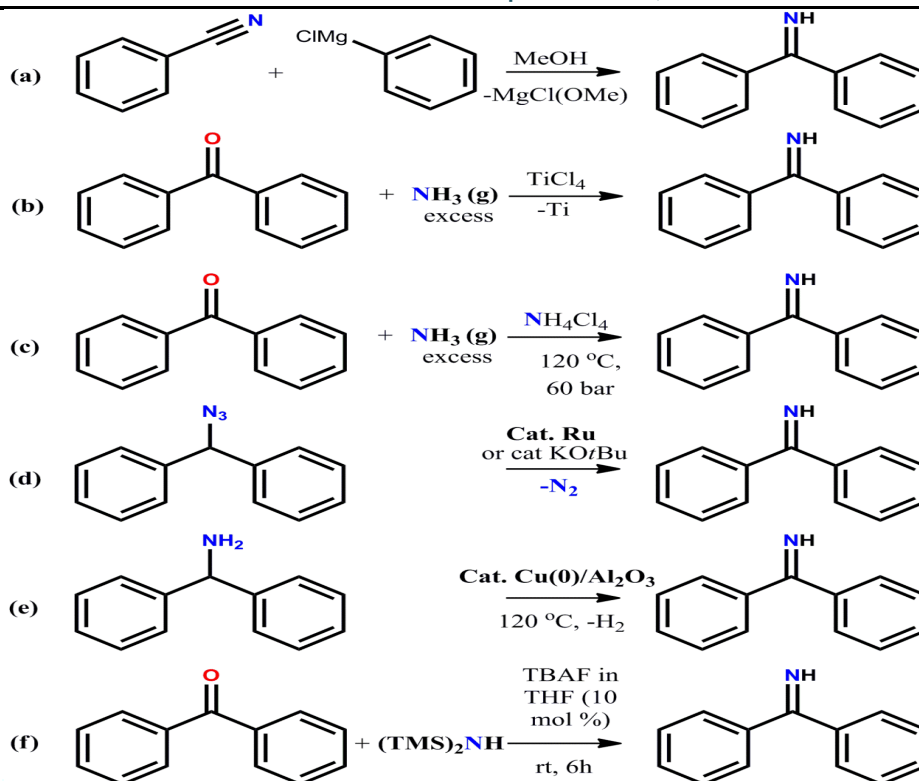
**Fig. 1 Structure of Benzophenone imine**

Nitrogen-containing compounds are more commonly abundant in natural products and pharmaceuticals, and approximately 90% of the top best-selling small molecular drugs contained nitrogen atoms, with 25% of these drugs containing unprotected primary amine moieties.



**Fig.2 Scheme 1. Synthetic routes to primary amines.**

Benzophenone Imine, one the most frequently used N-unsubstituted ketimines, is well-established ammonia equivalent in Buchwald-Hartwig amination reaction. Useful in preparation of nitrile ylide dimers. Benzophenone imine act as an ammonia surrogate, and the starting material for the synthesis of aniline. It is also an important organic synthesis intermediate for the formation of Glycine Schiff base which is the starting material of non amino acid derivatives synthesis. It recently used as a substrate for C-H functionalization reactions.



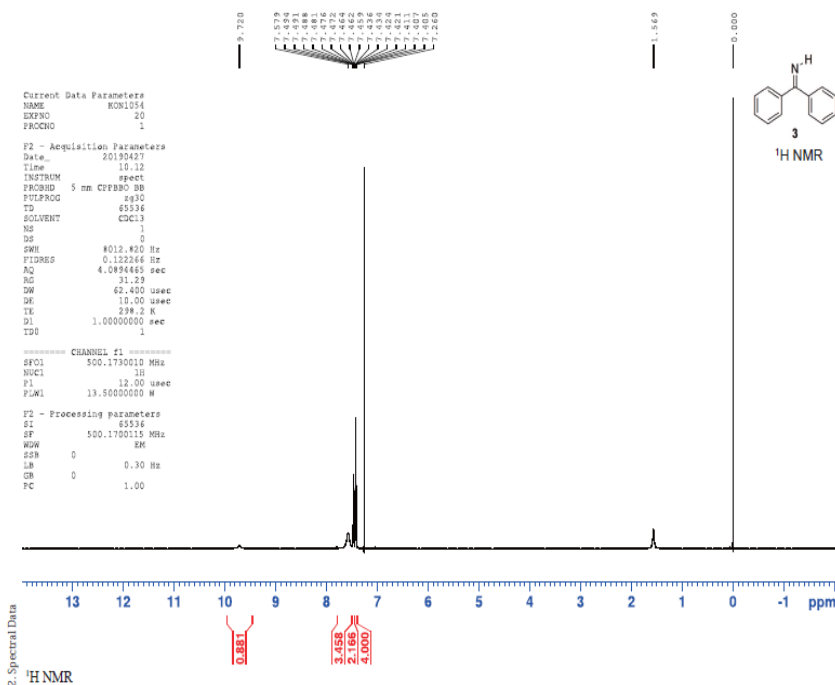
**Fig.3 Scheme 2: Other methods to synthesis Benzophenone imine**

#### NMR DATA:

NMR spectra were acquired on 500 MHz Bruker Avance III spectrometers.  $^1\text{H}$  and  $^{13}\text{C}\{^1\text{H}\}$  NMR chemical shifts are reported in parts per million and referenced to tetramethylsilane or residual solvent peaks as internal standards (tetramethylsilane at 0 ppm for  $^1\text{H}$  and  $\text{CDCl}_3$  at 77.0 ppm for  $^{13}\text{C}\{^1\text{H}\}$ ). Coupling constants are reported in hertz. The following abbreviations are used: s=singlet, d=doublet, t=triplet, q=quartet, m= multiplet, br=broad.

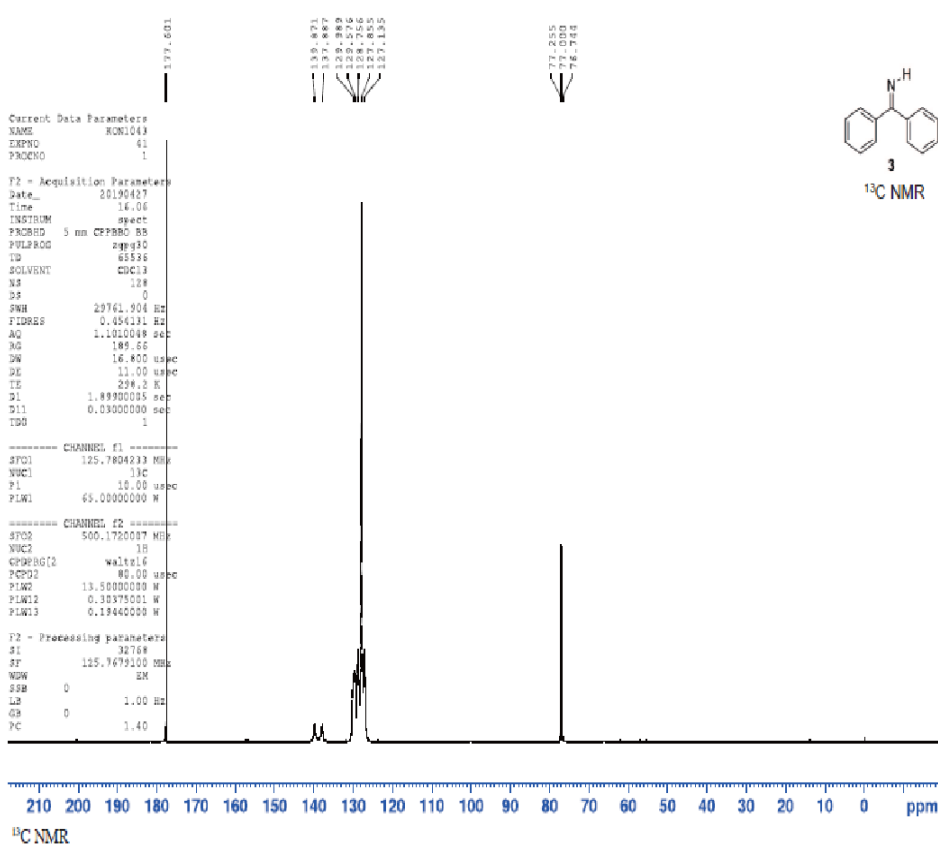
$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  9.72 (br s, 1H), 7.58 (br s, 4H), 7.49–7.46 (m, 2H), 7.44–7.41 (m, 4H).

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  177.60, 139.87, 137.89, 129.99, 129.58, 128.76, 127.86 (overlapped), 127.14.



S6

Fig. 4 <sup>1</sup>H NMR DATA



## Experimental Section

- All of the reactions were performed in flame-dried or oven-dried glassware under an nitrogen atmosphere unless otherwise noted.
- Reagents, catalysts, and solvents were obtained from commercial sources and used as received unless otherwise stated. Flash silica gel column chromatography was performed with Kanto Chemical silica gel 60N (spherical neutral, particle size 40–50 $\mu$ m).
- NMR spectra were acquired on 500 MHz Bruker Avance III spectrometers.  $^1\text{H}$  and  $^{13}\text{C}$  {1H} NMR chemical shifts are reported in parts per million and referenced to tetramethylsilane or residual solvent peaks as internal standards(tetramethylsilane) at 0 ppm for  $^1\text{H}$  and  $\text{CDCl}_3$  at 77.0 ppm for  $^{13}\text{C}$  {1H}).
- Coupling constants are reported in hertz.The following abbreviations are used: s=singlet, d=doublet,t=triplet, q= quartet, m=multiplet, br=broad.Benzonitrile was purchased from SPECTROCHEM PVT.LTD, MUMBAI (INDIA).THF was purchased from MICHELCHEMICAL.PVT .LTD MUMBAI (INDAI).

### 1. Solvent purification

Tetrahydrofuran and Diethyl ether are used as a solvent the AR grade solvents are stored over calcium chloride overnight, decanted and refluxed over sodium containing benzophenone which give a blue purple solution of disodium benzophenone complex, then these were distilled from this mixture under nitrogen atmosphere and stored over sodium wire or molecular sieves. Special case was taken, to keep these ethers away from a hot plate or flame to avoid ready ignition of their vapours.

### 2. Preparation of Grignard reagent

- For the success of the Grignard reaction, it is essential that all glassware that is clean and dry.
- Fit a 250 ml of two neck round bottom flask with a condenser.
- The bottom fitting of the condenser should be connected to a hose that supplies water, and the top fitting on the condenser should be outletted to a drain hose.
- The apparatus should be held in place by two clamps affixed to a ring stand, and a heating mantle should be placed under the round bottomed flask, then add 0.58g of magnesium turnings after activation and then fixed on apparatus and put on magnetic stirrer then add iodine, the pink fumes are formed in the round bottom flask, then add distilled Tetrahydrofuran (THF) the solution turns orange in colour.
- After 5 minutes add 2ml of bromobenzene the reaction was exothermic in nature the colour changes to light green and after 10 minutes it becomes deep blue and then colourless indicates magnesium starts reacting and the reaction becomes exothermic, of each sample after checking the TLC, collect all the sample solution in a 500mg round bottom flask and remove out solvent by distillation process. And crystalline solid form of compound is form.(3)

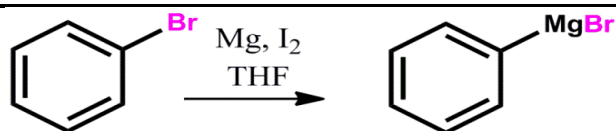


Fig.6 Synthesis of Phenyl magnesium bromide

### 3. Synthesis of Benzophenone imine

- Add 2.06 ml of benzonitrile in phenylmagnesium bromide solution the colour change to pale yellow within 30 minutes.
- Then allow the reaction for the reflux for 12 hours, the butter yellow like solution formed. The stirred mixture is cooled to room temperature, and the Grignard-nitrile complex is decomposed by careful addition of 120 ml.
- Add 3 moles of anhydrous methanol and then filter the solution. This yields a liquid form of compound as filtrate and a salt of methyl magnesium-bromide residue then proceeds the liquid filtrate form of compound for thin layer chromatography to check the purity of the compound.
- It gives two spots, and then proceeds for column chromatography along with pet. ether as solvent, to yield the corresponding compound.

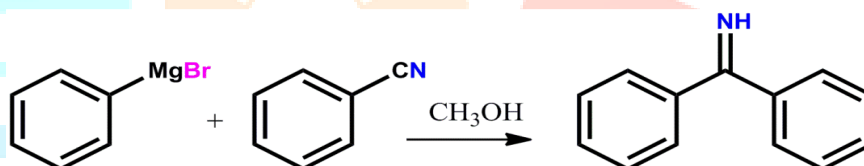


Fig.7 Synthesis of Benzophenone Imine

### Outcomes of the reaction of Benzonitrile & Grignard reagent in presence of N<sub>2</sub>, Ar but not O<sub>2</sub> gas

The reaction of benzonitrile and grignard reagent are air and moisture sensitive, so chemist perform this reaction in presence of argon and nitrogen gas atmosphere because it does not take part in reaction, But restrict the use of oxygen gas atmosphere because most grignard reaction occurs in solvent such as anhydrous diethyl ether or THF(1), because the oxygen in this solvent stabilizes the magnesium reagents. The reagent may also react with oxygen present in atmosphere. This will cause insert an oxygen atom in between carbon base and magnesium halide group. Usually, the side reaction may be limited by the volatile solvent vapour displacing air by above reaction mixture. However, the chemist use N<sub>2</sub>&Ar gas atmosphere.

### Conclusion

It is conclude from above reaction that we have developed a convenient method for the synthesis of Benzophenone Imine. The reaction is performed by simply mixing commercially purchased benzonitrile and laboratory prepared Grignard reagent basically (phenylmagnesium bromide) in presence of methanol to give formation of a desired compound benzophenone imine. Note: The reaction is perform in presence

of nitrogen atmosphere, because the reaction is air and moisture sensitive. Another mentioned methods for the synthesis of benzophenone imine is quite tough and requires ambient temperature & pressure and also requires standard laboratory setup, A preliminary mechanistic study of the reaction and its application to one-pot benzophenone imine synthesis/Buchwald–Hartwig amination were also realized. Although the present reaction is totally based upon the synthesis of Benzophenone Imine, is generally used as nitrogen source and can be used further for the synthesis of Nitrogenated compounds, Therefore, we hope that this work will contribute to the future development of carbon fiber polymers and cross coupling reactions.

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