

# Reproducing the Synthesis of MBIHC

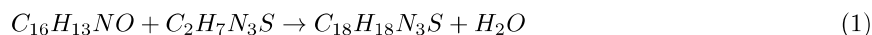
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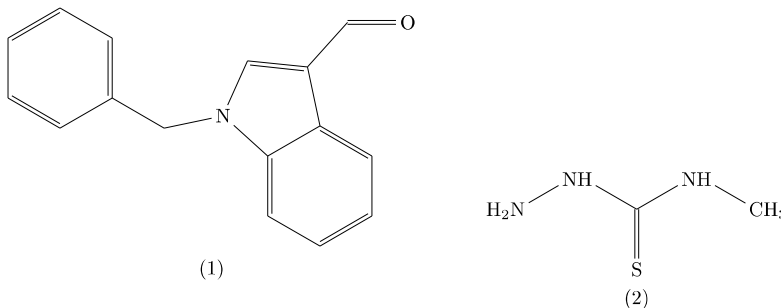
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## 1 Introduction

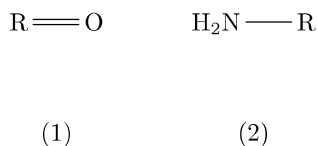
Synthesis of the (E)-2-((1-benzyl-1H-indol-3-yl)methylene)-N-methylhydrazine-1-carbothioamide ligand, henceforth referred to as **MBIHC**, was performed by a nucleophilic addition-elimination<sup>1</sup>. Reactants **N-benzylindole-3-carboxaldehyde (1)**, and **4-Methyl Thiosemicarbazide (2)** were reacted in a 1:1 ratio, with the molecular formula of the reaction:



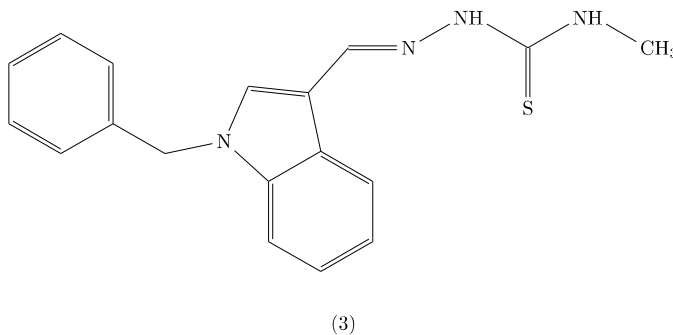
A structural formula of the reactants is elucidated below:



The mechanism of action of the synthesis of MBIHC can be conceptualized as the synthesis of a Schiff base.



Reactant (1) contains an aldehyde functional group, and reactant (2) contains an amine functional group. With nucleophilic addition-elimination, this enables the formation of the Schiff base MBIHC with structural formula **(3)**<sup>1</sup>:

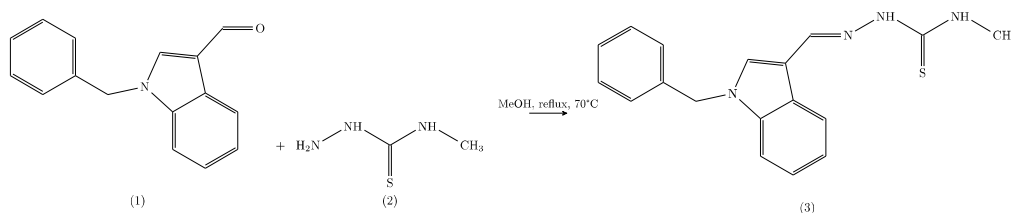


## 2 Methods

The reaction methods were reproduced as outlined by the original authors<sup>1</sup>. 50 mg (0.21 mmol) of reactant (1) was weighed on a calibrated balance, and dissolved to homogeneity in a 15 mL solution of methanol. Subsequently, 22.34 mg (0.21 mmol) of reactant (2) was added to the solution, and dissolved to homogeneity. 2-3 drops of glacial acetic acid were added to the reaction mixture. A round bottomed flask was used, heated under reflux at a 70°C paraffin bath for 20 hours.

Thin-layer chromatography was performed with a 15% ethyl acetate and 85% hexane mixture, and examined under short- and long-wave UV. Reactant (1) fluoresced clearly in purple, reactant (2) very weakly, and product (3) medium-yellow. Precise  $R_f$  values are not reported, due to inconsistencies between TLC readings, and further work must be done to optimize the analytical chemistry techniques used to characterize MBIHC. Product (3) was then isolated from the methanol solution, by vacuum distillation of the solution at 50°C. A rotary vane pump was used to provide a rough vacuum, an ethylene glycol condenser was used to re-collect the evaporated methanol, and the product remained a white-yellow solid stuck to the walls of the flask. The flask was then sealed to prevent contamination, and allowed to dry. Upon sufficient dryness, dissolving it in DCM, then precipitating with the help of hexane are the likely next steps, to enable the creation of crystallized MBIHC, for use in ligand-metal complexes. Further purification and analytical techniques are required to gauge the yield, as well as visual and physical characteristics of the compound. Crystallization is required to provide a crystallographic structure amenable to analysis via XRD, and so further analysis will require this sequence of steps to be undertaken.

A structural diagram of the above is provided for completeness and visual clarity.



The reaction's mechanism of action is an archetypal Schiff base formation. The aldehyde functional group in reactant (1), when in the presence of  $H^+$ , can be protonated at the oxygen to form an  $R\text{-CHO-}H^+$  intermediate, making the carbonyl carbon more electrophilic. The amine group in reactant (2) is nucleophilic, and attacks the electrophilic carbon atom of the carbonyl group in the aldehyde group in (1). This forms a carbinolamine intermediate where the nitrogen in the amine in (2) forms a single bond with the carbon atom in the aldehyde group of (1). Subsequently, under acidic conditions, the OH group is protonated and eliminated along with one hydrogen atom connected to the nitrogen in the amine group to form  $H_2O$  (water) as the leaving group, generating the  $C=N$  double bond characteristic of imines<sup>1</sup>.

## References

1. J. Singh, S. Gautam, M. B. Singh, P. Singh, U. Kumar, Chem. Biodiversity 2024, 21, e202401301. <https://doi.org/10.1002/cbdv.202401301>