Versatile and sustainable heterogenous *N*-methylation of various amines by methanol over a Pt/C catalyst

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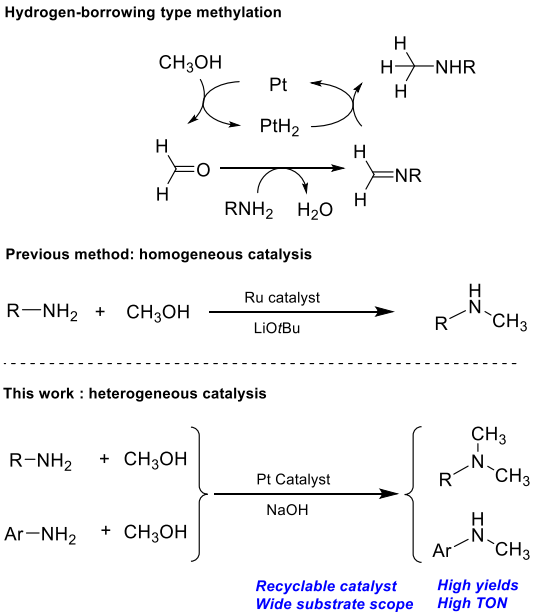
Abstract: We report a versatile and selective heterogeneous catalytic method for *N*-methylation by methanol under oxidant-free conditions using carbon-supported Pt catalyst (Pt/C) with NaOH. The reaction proceeds through the hydrogen-borrowing mechanism. This catalytic system is effective for various aliphatic, aryl and heterocyclic amines. It is noteworthy that the process promotes selective *N*,*N*-dimethylation for aliphatic amines and *N*-monomethylation for aromatic amines. The system shows high tolerance to various functional groups with wide substrate scope (36 examples; up to 98% isolated yield).

Keywords: Methylation, Heterogeneous Pt catalyst, Borrowing Hydrogen.

1. Introduction

The *N*-methylation of amines is one of the most important sustainable transformations in the synthesis of fine chemicals, pharmaceuticals, agrochemicals as well as biologically active natural products.[1] In the conventional methods, reactive and toxic methyl halides, formaldehyde, etc. are generally used as methylating agents.[2] Thus the development of sustainable methylation protocols using green methylating agents is strongly desired and is of significant importance. In this regard, much attention has been paid to the direct *N*-methylation of amines by employing methanol as a sustainable methylating agent. [1-5] The reactions are driven by hydrogen-borrowing mechanism where the catalyst dehydrogenates methanol to formaldehyde, which condenses with the amine to form an imine, and finally, the process is completed with the reduction of the imine to amine by borrowed hydrogen at the first step.[4,5] However, most of the previous works employ homogeneous catalytic system with additives, where the catalysts are not reusable and isolation of the products are difficult. We report herein a highly versatile heterogeneous catalytic scheme comprised of a carbon-supported Pt catalyst (Pt/C) for direct *N*-methylation of various primary amines by employing methanol as a methylating agent.



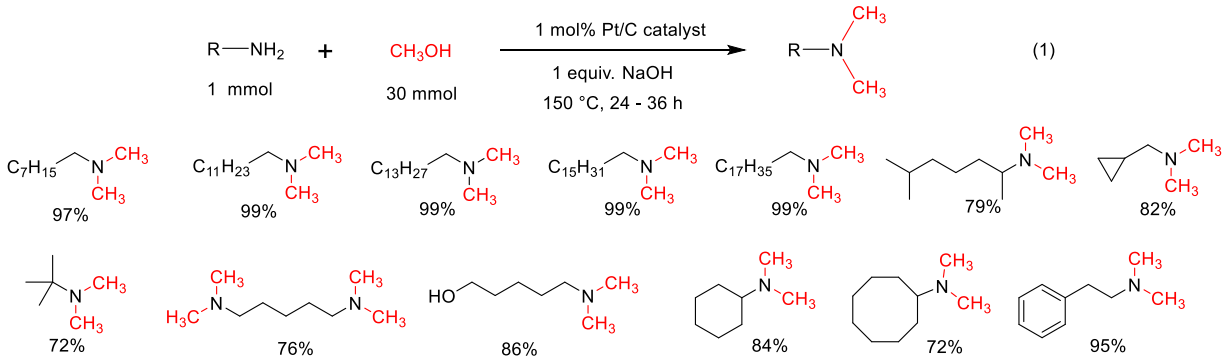
Scheme 1. *N*-Methylation of various amines by methanol.

2. Experimental

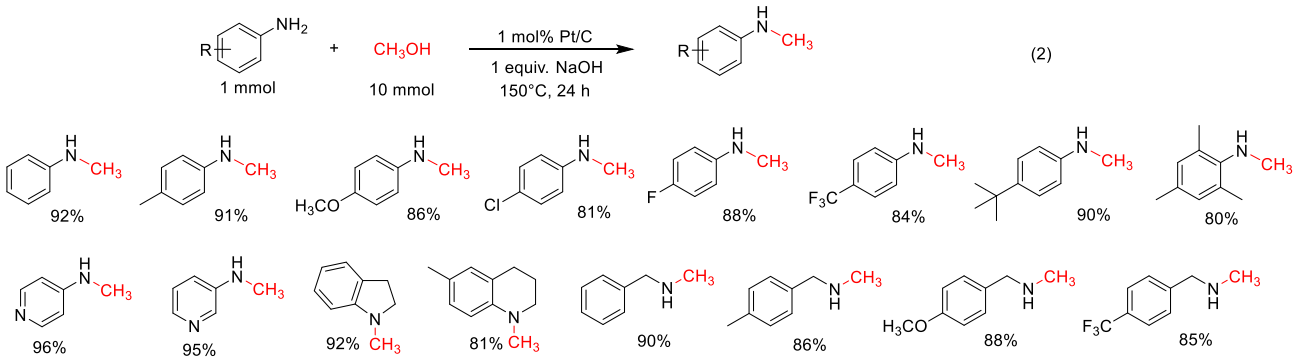
The catalyst was prepared by impregnating a support with an aqueous HNO_3 solution containing $Pt(NH_3)_2(NO_3)_2$ followed by reduction with H_2 at 300 °C. For a typical reaction, methanol (30.0 mmol) was injected to the reduced catalyst inside the glass tube through a septum inlet. Subsequently, the septum was tentatively removed under air, and 1.0 mmol of substrate (amine), NaOH (1.0 mmol), *n*-dodecane (0.25 mmol) and a magnetic stirrer bar were put in the tube. The tube was then inserted in a stainless autoclave (28 cm^3) and the resulting mixture was heated at 150 °C and stirred for 24 to 36 h under N_2 atmosphere as in eqn. (1). After completion of the reaction, the catalyst was separated and the products were isolated by column chromatography. The products were characterized by GC, GCMS, ^{1}H NMR and ^{13}C NMR analyses.

3. Results and discussion

Various supported Pt catalysts were screened for *N*-methylation of the model substrate *n*-octylamine as in eqn. (1). It was found that Pt/C showed the highest yield for *N*,*N*-dimethyloctylamine synthesis among various metal-loaded carbon catalysts (Rh/C, Ir/C, Ru/C, Pd/C, Re/C, Ag/C, Cu/C, Ni/C and Co/C). Pt/C gave 97% yield after the reaction time of 36 h. As shown in the Scheme 2 & 3, the method is effective for dimethylation of various aliphatic amines and mono methylation of aryl and heterocyclic amines respectively. This catalytic system was reusable at least 4 times without significant loss in the activity for these reactions. It was also shown that the system is effective for gram scale synthesis. This simple and heterogeneous catalytic system serves as a highly versatile *N*-methylation method by employing methanol as a methylating agent.



Scheme 2. Selective *N*,*N*-dimethylation of various aliphatic amines.



Scheme 3. Selective *N*-monomethylation of various aromatic amines.

4. Conclusions

We have established a general heterogeneous catalytic method for the *N*-methylation of aliphatic and aromatic amines using methanol as a sustainable C1 source. This simple process has several advantages compared to the conventional system as well as to the previous homogeneous catalytic methods employing the hydrogen borrowing mechanism. This reaction proceeds with high selectivity to give *N*,*N*-dimethylamine for aliphatic amines and *N*-monomethylamine for aromatic amines. The catalytic system also offers additional benefits: 1) catalyst reusability, 2) wide substrate scope, 3) high tolerance to various functional groups, 4) high TON and 5) easy catalyst/product separation.

References

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