# Use of Dimethyl Carbonate (DMC) as Methylating Agent under Microwave Irradiation-A Green Chemical Approach

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***Abstract*—A new method for N-methylation of aromatic diamines using environmentally safe and less toxic methylation reagent dimethyl carbonate (DMC) has been developed. The effects of various functional groups on the aromatic ring have been investigated. This method provides the desired product in high yields with high purity under microwave irradiation.**

***Index terms* – Atom economy, Conventional, Environmental benign, Methylation, Microwave irradiation, optimization, and selectivity.**

## I. INTRODUCTION

The increasing local global concern for environmental pollution offers incentive to explore new green materials for safeguarding the environment. Green materials have been used to design benign synthetic processes to eliminate or minimize pollution at the source, as well as in the remediation of a variety of existing environmental pollution problems. Dimethyl carbonate (DMC) is a versatile and environmentally innocuous material for chemical industries [1]. It has been successfully used to introduce a methyl group at the α - position of arylacetonitrile and methyl aryl acetate [2]. It has also been used for selectively monomethylation of primary aromatic amines [3].

N-Methylation of indoles with methyl iodide [4], in the presence of base such as NaH [5], is classical method to form N-methylated indole derivative. However, use of these methods has several disadvantages. Methyl iodide has very low boiling point ($40^0$C) causing air emission problem, and it is also a suspected carcinogen. Dimethyl sulphate is also highly toxic (LD 50 orally in rats is 440 mg/kg). The byproduct generated by these methylating agents can cause waste disposal problems. In view of these disadvantages, an alternate methylating agent and an efficient process for large-scale manufacturing is highly desirable.

On the other hand, DMC is a nontoxic, environmentally safe reagent that can be used as a "green substitute" for toxic reagent used in conventional methylation reaction. Synthesis of N-dimethyl aniline from aniline using DMC as a green reagent and onium salt, as a catalyst has been reported by Shivarkar *et al.* [6]. N-Methylation of nitrogen containing heterocyclic compounds with DMC has also been successfully carried out [7]. Selva *et al.* [8] reported mono N-methylation of functionalized anilines with alkyl methyl carbonates. Mechanism of selective mono N-methylation of aniline has been recently reported [9]. Functional group containing N-oxide was used in controlling the outcome of N-alkylated reaction [10]. Dimethyl carbonate mediated mono N-methylation of aniline has been reported by Esakkidurai and Pitchumani [11]. Selva and Tundo [12] carried out selective N-methylation of primary aliphatic amines with DMC in presence of alkali cation.

As a part of our ongoing studies towards the application of microwave irradiation (MWI) has been under taken as it is an established methodology for eco-friendly procedure, takes short reaction time as compared to conventional heating, ease of work-up after reaction and the reduction in usual thermal degradation and better selectivity . Looking to an urgent need of green techniques and reagents under present day conditions, N-methylation of aromatic diamines has been carried out using dimethyl carbonate under microwave irradiation.

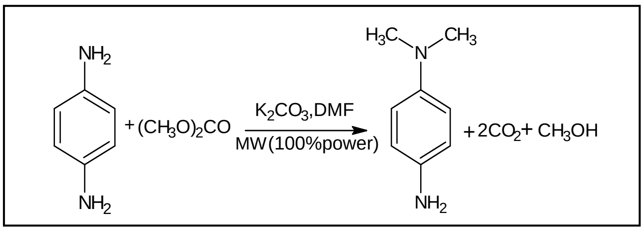

Fig. 1. N-Methylation of p-phenylenediamine using DMC

## II. RESULTS AND DISCUSSION

The reaction between p-phenylenediamine and DMC in dimethylformamide (DMF) in the presence of a base was accomplished by heating for 13 minutes, which is shown in fig. 1. The desired N-methylated product was obtained, which was separated by column chromatography.

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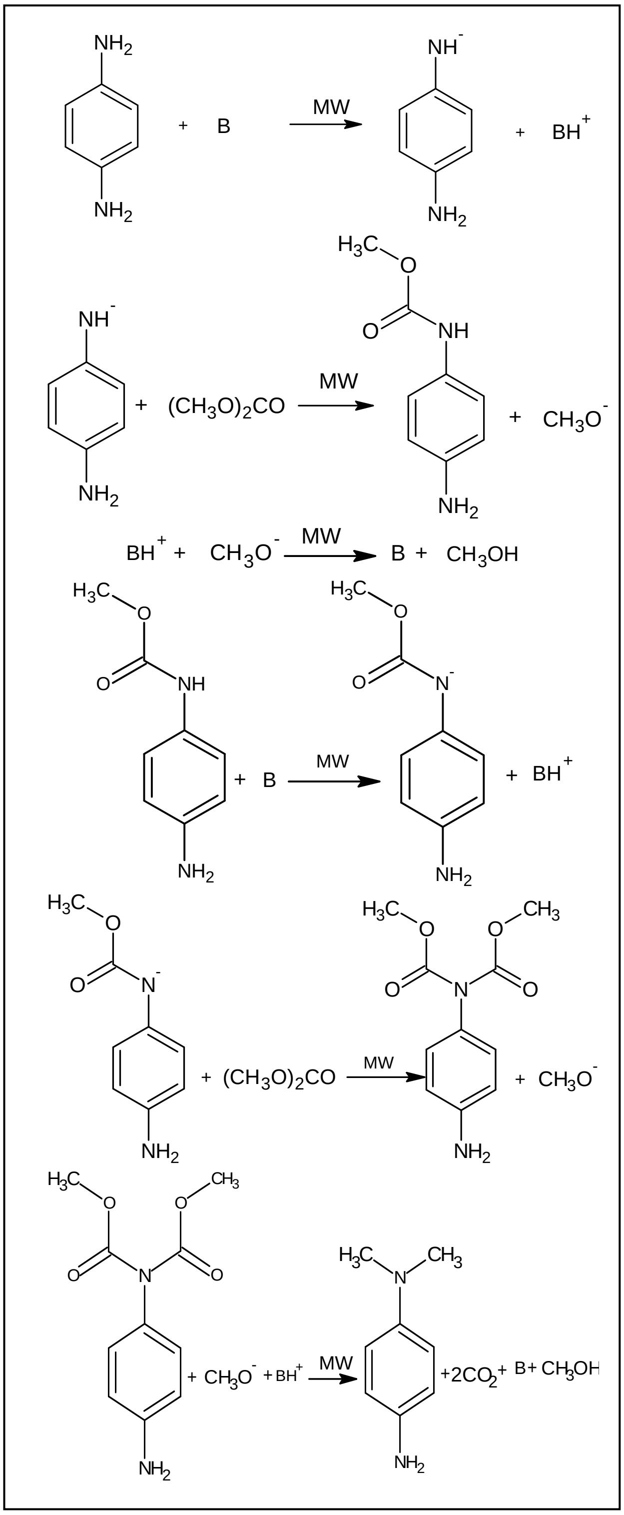

Fig. 2 Mechanism of N-methylation of p-phenylenediamine

The tentative mechanism of this reaction is shown in fig. 2. Optimization studies on the stoichiometry of DMC (table I) led to conclusion that 2.0-3.0 equivalent of DMC with the substrate would work best for this reaction. Lower quantities of DMC results in longer reaction times while higher quantities of DMC drop the boiling point of the reaction mixture; thus again prolonging the reaction time. This process of N-methylation using DMC and potassium carbonate proved highly scalable. Next, our attention was focused on the scope and utility of this reaction. The substituent effects were examined on p-phenylenediamines which is shown in Fig.3. As can be seen from table II, several electron withdrawing functional groups were used. There is not much difference in reaction times and yields with the change in functional groups on the nucleus. All substrates provide high yields of N-methylated products by this method.

**Table – I: Optimization of DMC stoichiometry**

| Ratio (mol)DMC/ p-Phenylenediamine | Reaction time (min) | Yield (%) |
|---|---|---|
| 0.7 | 21 | 75 |
| 1.1 | 19 | 96 |
| 2.2 | 15 | 97.4 |
| 2.5 | 13 | 97.7 |

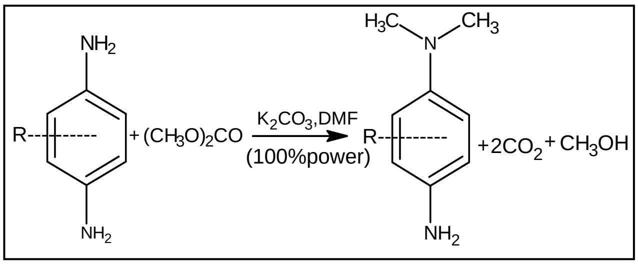

Fig. 3 Substituent effects on p-phenylenediamine system

**Table II. Electron withdrawing effects on p-phenylenediamines**

| Substituent (R) | Reaction time(min) | N-Methylation product yield (%) |
|---|---|---|
| 2a | 20 | 97 |
| 2b | 19 | 96 |
| 2c | 21 | 95 |
| 2d | 21 | 95.5 |

2a = CN, 2b = $NO_2$, 2c = CHO, 2d = $COOCH_3$

To investigate the selectivity between N- and O-methylation, the reaction 2, 5-diaminobenzoic acids and DMC was studied (Table III).The selectivity between esterification and N-methylation was not high. However, the esterification was slightly faster than N-methylation. The reaction of 2, 5-diaminopropionic acid with DMC in the presence of potassium carbonate (in DMF) afforded 91 % of N- and O-dimethylated product after 19 min, together with 30% of only O-methylated product. Similar results were obtained with 2, 5-diaminophenylacetic acid, which of as 87% of the dimethylated product along with 22% O-methylated product.

**Table III. Selectivity between N-and O-methylation**

| Substituent (R) | Reaction time(min) | Product yield (%) |
|---|---|---|
| 2e | 16 | N-O-dimethylation (85)<br>O-methylation (83) |
| 2f | 18 | N-O-dimethylation (91)<br>O-methylation (30) |

2e = COOH, 2f = $CH_2CH_2COOH$

## II. EXPERIMENTAL SECTION

$^1$H NMR spectra was recorded in Bruker AC (400MHz) spectrophotometer using TMS as an internal standard. IR spectra were obtained on Perkin-Elmer infrared spectrophotometer. The melting points were determined by the electrothermal method in open capillary tubes and are uncorrected. The mass spectra were recorded on Perkin-Elmer auto system XL (GC-MC) mass spectrometer. All reactions were carried out in a microwave oven model, Kenstar-OM-26EGO.

## III. GENERAL PROCEDURE

p-Phenylenediamines (2.0 g), anhy $K_2$ $CO_3$ (1.0 g) and DMC (2.5 ml) in DMF (14ml) were taken in 100 ml Erlenmeyer flask. The reaction mixture was exposed to MWI at 100% power level for the required time period .The progress of reaction was monitored by TLC. After completion of reaction, mixture was cooled at room temperature and product was isolated with help of column chromatography over silica gel.

**Spectral Data of Synthesized Compounds**

| Compound | IR (Cm$^{-1}$ ) | $^1$H NMR ( δ ) |
|---|---|---|
| 2a | 3115(N-H str.), 3075(C-H str. aromatic), 2200(CN) 2922, 2890 (asy of sym. Str.) | 6.2-6.7(dd,2H,AsH), 6.8 (S,1H,As-H),1.5 (S,2H,-$NH_2$ ) |
| 2b | 3110(N-H str.), 3081(C-H str. Aromatic), 1350-1550(-$NO_2$), 2930-2891(asym of sym.str) | 6.0-6.59dd,2H,Ar-H), 6.9(S,1H,Ar-H),1.6(s,6h,-$CH_3$ ), 3.8(s,2H,-$NH_2$ ) |
| 2c | 3105(N-H str.), 3080(C-H str. Aromatic), 2825-2720(-CHO), 1700(C=O str.), 2935-2890(asy of sym.str.) | 6.1-6.4(dd, 2H, As-H), 6.9(S, 1H, As-H)1.4(s, 6H, -$CH_3$ ), 3.9(S,2H,-$NH_2$ ), 3.5(S,1H,-CHO) |
| 2d | 3100(-N-H str), 3070(C-H str. aromatic), 2925, 2895(assy, symetric $CH_3$ str) 810 (As-H bend,1,4-disub) 1735(C=O str) | 6.0-6.5(dd, 2H, As-H), 2.60(s, 6H, $CH_3$ ), 3.8(s, 2H –$NH_2$ ), 2.1(s,3H,$COOCH_3$ ) |
| 2e | 1700(-C=O-str), 3360(-N-Hstr.), 3300(-O-Hstr.), 3070(C-Hstr.) 2920-2890(assy, s-$CH_3$ str) 810(As-bend,1,4-disub) | 4.9(s,1H,-OH), 6.1-6.4(dd, 2H, As-H), 6.9(s, 1H, As-H) ), 1.4(s, 6H,-$CH_3$ ), 3.9(s, 2H,-$NH_2$ )11.10(s –COOH) |
| 2f | 3100(N-H str.) , 3070(C-H str. aromatic) 2925, 2895(assy, symmetric $CH_3$ str), 815(As-H bend, 1, 4-disub) 1701(C=O str.), 3301(O-H) | 6.0-6.5(d d, 2HAs-H), 6.9(s, 1H, As-H), 1.6(s, 1H, $CH_3$), 3.8(s, 2H, -$NH_2$ ), 2.5(t, 2H, ph-$CH_2$ ), 5.0(s, 1H, -OH) 2.0(t, 2H, -$CH_2$ –COOH) |

## IV. CONCLUSION

Methylation with dimethyl carbonate (DMC) has been found to be an effective method to prepare N-methylated derivative in high yield and purity. This method also provides an efficient way to synthesize N-methyl p-phenylenediamine carboxylic acid methyl ester from 2, 5-diaminobenzoic acid in one pot**.**

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