Synthesis of Triarylmethanes and Diarylalkanes using Iodine Reagent

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Abstract: A first synthetic utility of NaICl₂ for preparation of triarylmethanes and diarylalkanes is described. In the presence of aqueous solution of NaICl₂, the reaction of arenes with aromatic aldehydes gives corresponding triarylmethane regioselectively, in moderate to good yields. The method also useful for the preparation of diarylalkane derivatives by using aliphatic aldehydes.

Key words: Triarylmethane, diarylalkane, sodium dichloroiodate

During the last three decades, Diaminotriphenylmethane¹⁻³ (DTM) compounds have received considerable attention because of their applications in various displays such as in the biological and analytical fields where these compounds are used as dyes for detection of hydrogen peroxide in medical diagnostic kits and biotechnology process control⁴⁻⁵. Where as in the field of medicinal these compounds are used as antifungal⁶⁻⁸ anti-tubercular,⁹ anti-infective, and antimicrobial agents.¹⁰ Different methods have been reported for the preparation of the 4,4’-diaminotriphenylmethane compounds such as from 4,4’-diaminodiphenylmethanes and amines,
by condensation of amines and anilines in acid medium\textsuperscript{11} using zeolites\textsuperscript{12} metal catalyst\textsuperscript{13-15} or clay-mediated by microwave.\textsuperscript{16} Most of these protocols, however, suffer from drawbacks, namely long reaction times and use of corrosive acids or toxic metallic compounds that result in generation of waste streams, complicated workup procedures, by-products and consequently, low yields. Thus despite of the availability of variety of well known methods, the development of new general synthetic protocols for DTM is still an active field.

Our group has been working extensively on the development of novel methodologies under mild conditions using iodine reagents. We observed that in the presence of aqueous sodium dichloroiodate solution \textit{N,N}-dimethylaniline and aromatic or aliphatic aldehydes, converted into either 4,4'-arylmethylene-bis-\textit{(N,N}-dimethylaniline) or 4,4'-alkylmethylene-bis-\textit{(N,N}-dimethylaniline) (Scheme 1).

\textbf{Scheme 1.} Reaction of aryl and alkyl aldehydes with \textit{N,N}-dimethylaniline in presence of \textit{NaICl}_2

Herein, we report efficient and versatile methodology for synthesizing diaminotriphenylmethanes as well as diaminodiphenylalkanes by using aqueous sodium dichloroiodate.

Initially we selected benzaldehyde as a model substrate. Exposure of aqueous solution of sodium dichloroiodate in presence of \textit{N}, \textit{N}-dimethylaniline at reflux temperature resulted in the
formation of 4,4’-(Phenylmethylene)bis(N, N-dimethylaniline). It was observed that under similar reaction conditions but at room temperature slower reaction rate was observed.

During reaction it was observed that N, N-dimethylaniline reacted with para-formaldehyde at reflux temperature in presence of aqueous solution of sodium dichloiodate and resulted in the formation of 4,4’-methylene-bis(N, N-dimethylaniline) and thus provided an interesting rout for synthesis of diphenylmethane compounds (Scheme 2).

Scheme 2. Reaction of paraformaldehyde with N,N-dimethylaniline in presence of NaICl₂

Next to evaluate scope of this new method, these conditions were applied to variety of aromatic and aliphatic aldehydes and the results are presented in Table 1. The results clearly indicate that this method is suitable for electron withdrawing and donating substituted aromatic substrates (Table 1, entries 2-6). In each case, good to excellent yields of the desired 4,4’-arylmethylene-bis-(N,N-dimethylaniline) products were isolated. Heterocyclic aromatic aldehyde compounds were also suitable for this transformation (Table 1, entries 7-9). A lowered reaction rate was observed in case of aliphatic aldehydes (Table 1, entries 11, 12). Further investigations indicated
that α, β-unsaturated aldehydes are also suitable for this reaction (Table 1, entry 13) without affecting the double bond.

**Table 1.** Reaction of \(N,N\)-dimethylaniline with aldehydes in presence of aqueous NaI\(_2\).\(^a\)

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<table>
<thead>
<tr>
<th>Entry</th>
<th>R-CHO</th>
<th>Product</th>
<th>Time (hr)</th>
<th>% Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(\text{CHO})</td>
<td>(</td>
<td>\text{H}_2\text{C}-\text{N}</td>
<td>\text{NCH}_3) (\text{CHO})</td>
</tr>
<tr>
<td>2</td>
<td>(\text{F-CHO})</td>
<td></td>
<td>5</td>
<td>70</td>
</tr>
<tr>
<td>3</td>
<td>(\text{Cl-CHO})</td>
<td></td>
<td>5</td>
<td>68</td>
</tr>
<tr>
<td>4</td>
<td>(\text{O}_2\text{N-CHO})</td>
<td></td>
<td>3</td>
<td>78</td>
</tr>
<tr>
<td>5</td>
<td>(\text{CHO})</td>
<td></td>
<td>6</td>
<td>65</td>
</tr>
<tr>
<td>6</td>
<td>(\text{CHO})</td>
<td></td>
<td>6</td>
<td>65</td>
</tr>
</tbody>
</table>
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The plausible mechanism for this reaction can be proposed in scheme 3, in which the C-C coupling may be due to activation of the carbonyl group of the aldehyde by NaICl₂.
Scheme 2. Plausible reaction mechanism

In conclusion, a new reaction system using NaICl₂ for C-C coupling has been developed, which is capable of converting various aldehydes into corresponding triphenyl and diphenyl compounds. The developed method is mild and gives moderate to good yields of product for both aliphatic and aromatic substrates.

**General Experimental Methods: Synthesis of Lucomalachite green (Table 1, entry 1):**

Benzaldehyde (1 equiv), *N*, *N*-dimethylaniline (2 equiv) and aqueous NaICl₂ (2 M, 10 ml, 0.5 equiv) was reflux in round bottom flask for 3-6 hrs. After completion of reaction (TLC), the reaction mixture was quenched in water (10 mL) and further diluted with dichloromethane (30 mL). The organic layer was separated and washed successively with 10% aqueous solution of Na₂S₂O₃ (2 x 20 mL), 10% aqueous solution of NaHCO₃ (2 x 15 mL), and finally with H₂O (2 x 20 mL). Then organic layer was dried over anhydrous Na₂SO₄ and concentrated under reduced pressure to give crude product. Pure DTM as a green solid was obtained after silica gel column chromatography (EtOAc: hexane, 1: 9)

4,4’-(phenylmethylene)bis(N,N-dimethylaniline) (Table 1, entry 1): m.p. 92-93°C; ¹H NMR (CDCl₃): δ 2.93 (s, 12H), 5.40 (s, 1H ), 6.66-7.25 (m, 13H,); IR (KBr, cm⁻¹): 3075, 1611, 1532,
1459, 1347; $^{13}$C NMR (CDCl$_3$): δ 148.91, 145.41, 132.81, 129.98, 129.86, 129.32, 128.02, 112.54, 112.41, 55.04, 40.79, 40.65

$4,4'$-(cyclohexylphenylmethylene)bis(N,N-dimethylaniline) (Table 1, entry 10): m.p. 150-152°C; $^1$H NMR (CDCl$_3$): δ 1.27-1.52(m, 10H), 2.35(m, 1H), 2.95(s, 12H), 4.19(d, 1H), 6.61(d, 4H), 7.25(d, 4H); IR (KBr, cm$^{-1}$): 3061, 2926, 1611, 1532, 1440, 1347; $^{13}$C NMR (CDCl$_3$): δ 14.83, 133.90, 128.66, 128.54, 113.13, 112.99, 54.03, 41.61, 41.05, 32.35, 29.79, 25.57.

$4,4'$-(3-methylbutane-1,1-diyl)bis(N,N-dimethylaniline) (Table 1, entry 11): liquid >250°C; $^1$H NMR (CDCl$_3$): δ 0.97 (t, 6H), 1.45(m, 1H), 1.89(t, 2H), 2.80(s, 12H), 3.95(d, 1H), 6.69(d, 4H), 7.15(d, 4H); IR (KBr, cm$^{-1}$): 3070, 2915, 1465, 1375, 800; $^{13}$C NMR (CDCl$_3$): δ 149.05, 148.86, 134.76, 130.62, 129.50, 129.40, 128.40, 128.31, 113.26, 113.13, 46.85, 45.51, 43.30, 41.19, 41.06, 41.00, 40.93, 39.96, 29.77, 25.57, 22.81.

$4,4'$-(propane-1,1-diyl)bis(N,N-dimethylaniline) (Table 1, entry 12): B.P. 51-52°C; $^1$H NMR (CDCl$_3$): δ 0.90(t, 3H), 1.95(m, 2H), 2.80(s, 12H), 3.90(t, 1H), 6.68(d, 4H), 7.15(d, 4H); IR (KBr, cm$^{-1}$): 3070, 2980, 1462, 1370, 802; $^{13}$CNMR(CDCl$_3$): δ 149.04, 130.33, 129.46, 129.35, 113.10, 112.96, 49.04, 41.14, 41, 40.88, 40.72 , 39.88, 12.04

(E)-$4,4'$-(3-phenylprop-2-ene-1,1-diyl)bis(N,N-dimethylaniline) (Table 1, entry 13): $^1$H NMR (CDCl$_3$): δ 2.95(s, 12H), 4.80(d, 1H), 6.60 (d, 1H), 6.80(d, 1H), 7.10(m, 8H), 7.21-7.60(m, 5H); IR (KBr, cm$^{-1}$): 3065, 2924, 1611, 1470, 1532, 801; $^{13}$CNMR(CDCl$_3$): δ 144.09, 136.34, 134.74, 130.08, 129.92, 128.48, 127.08, 116.78, 113.09, 52.79, 40.78

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Supporting Information Available: Experimental procedures as well as spectral data of selected compounds are given. This material is available free of charge via the Internet at http://pubs.acs.org.

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