ALUMINA-AMMONIUM ACETATE AS AN EFFICIENT REAGENT FOR THE ONE-POT SYNTHESIS OF Cis-2,4,5-TRIARYLIMIDAZOLINES FROM AROMATIC ALDEHYDES

Babak Kaboudin* and Fariba Saadati

Department of Chemistry, Institute for Advanced Studies in Basic Sciences (IASBS), Gava Zang, Zanjan 45195-159, Iran
Fax: (+98) 241 4249023
E-mail: kaboudin@iasbs.ac.ir

Abstract – A simple, efficient, and new method has been developed for the synthesis of 2,4,5-triarylimidazolines from aldehydes through a one-pot reaction of aldehydes in the presence of alumina-ammonium acetate under solvent-free conditions using microwave irradiation. This method is easy, rapid, one-pot and good to high-yielding reaction for the synthesis of 2,4,5-triarylimidazolines.

2,4,5-Triarylimidazolines are good precursors for the synthesis of imidazoles and diarylethylenediamines that can be used as chiral ligands in asymmetric synthesis.¹ The most important method for the synthesis of 2,4,5-triarylimidazolines is the reaction of aromatic aldehydes with ammonia to give the diimine compounds, N,N'-bis(arylmethylidene)arylmethanediimines, and followed by heating with strong base to form triarylimidazolines (Scheme 1).² Recently, new methods have been reported for the synthesis of triarylimidazolines using of HMDS in the presence of Lewis acids such as ZnCl₂³ or without any catalyst under solvent-free conditions using microwave irradiation.⁴ The application of microwave energy to accelerate organic reactions is of increasing interest and offers several advantages over conventional techniques.⁵ As part of our efforts to explore the utility of mixture of alumina with ammonium acetate for the synthesis of organic compounds under microwave irradiation,⁶ we report a new method for the preparation of cis-triarylimidazolines from aldehydes in the presence of a mixture of alumina with ammonium acetate under solvent-free conditions using microwave irradiation. (Scheme 1, Table 1).

The reaction of benzaldehyde (1a), chosen as a model compound, was studied in the presence of a mixture of alumina with several ammonium salts. Initially, we carried out the reaction of benzaldehyde in
a mixture of alumina with ammonium acetate under microwave irradiation to afford the corresponding cis-2,4,5-triphenylimidazoline in 80% yield after 2 min. When this reaction was carried out in methanol for 3 h it afforded the corresponding cis-2,4,5-triphenylimidazoline in 10% yield. Ammonium formate (HCO$_2$NH$_4$) was not as effective as ammonium acetate and gave the required product in 35% yield under microwave irradiation. Other ammonium salts (NH$_4$Cl, NH$_4$Br, NH$_4$PF$_6$, NH$_4$I and NH$_4$NO$_3$) were not effective and did not give such product.

These results prompted us to extend this process to other aromatic aldehydes. Interestingly, aromatic aldehydes reacted smoothly in a mixture of alumina with ammonium acetate under microwave irradiation to produce the corresponding cis-triarylimidazolines in good to excellent yields (Table 1 and Scheme 2).

As shown in Table 1, substituted benzaldehydes in the presence of a mixture of alumina with ammonium acetate, afforded the desired products in good to high yields (2a-2h). Naphthalenecarbaldehydes also reacted in the presence of a mixture of alumina with ammonium acetate under microwave irradiation to give the desired compounds in good yields (2i, 2j). The reactions were clean with no tar formation and can be carried out in a one-step operation of aldehydes with ammonium acetate for the synthesis of cis-triarylimidazolines.

![Scheme 2](image-url)

Table 1. One-pot Synthesis of cis-triarylimidazolines from aldehydes in the presence of alumina-supported ammonium acetate under microwave irradiation.

<table>
<thead>
<tr>
<th>Product</th>
<th>Ar-</th>
<th>Time (min)</th>
<th>Yield (%)</th>
<th>Product</th>
<th>Ar-</th>
<th>Time (min)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2a</td>
<td>C$_6$H$_5$-$^4$a</td>
<td>2</td>
<td>80(85)</td>
<td>2f</td>
<td>p-BrC$_6$H$_4$-$^4$a</td>
<td>3</td>
<td>53(83)</td>
</tr>
<tr>
<td>2b</td>
<td>p-MeC$_6$H$_4$-$^4$a</td>
<td>3</td>
<td>79(82)</td>
<td>2g</td>
<td>m-O$_2$NC$_6$H$_4$-</td>
<td>2</td>
<td>75</td>
</tr>
<tr>
<td>2c</td>
<td>p-ClC$_6$H$_4$-$^4$a</td>
<td>2</td>
<td>78(83)</td>
<td>2h</td>
<td>o-ClC$_6$H$_4$-</td>
<td>4</td>
<td>56</td>
</tr>
<tr>
<td>2d</td>
<td>p-OMeC$_6$H$_4$-$^4$a</td>
<td>4</td>
<td>70(86)</td>
<td>2i</td>
<td>$\alpha$-Naphthyl</td>
<td>5</td>
<td>68</td>
</tr>
<tr>
<td>2e</td>
<td>$p$-(CH$_3$)$_2$CHC$_6$H$_4$-</td>
<td>5</td>
<td>72</td>
<td>2j</td>
<td>$\beta$-Naphthyl</td>
<td>4</td>
<td>76</td>
</tr>
</tbody>
</table>
In summary, simple work-up, low use of solvents, fast reaction rates, mild reaction conditions, good yields and the relatively clean reactions with no tar formation make this method an attractive and a useful contribution to present methodologies.

ACKNOWLEDGMENT
The Institute for Advanced Studies in Basic Sciences (IASBS) is thanked for supporting this work.

EXPERIMENTAL
General: All chemicals were commercial products and distilled or recrystallized before use. All melting points were obtained by a Buchi 510 and are uncorrected. A commercially available pulse microwave at 2450 MHz (900 W) was used in all experiments. IR spectra were determined using a FT-IR Brucker-Vector 22. NMR spectra were taken with a DMX-500 Bruker Avance instrument with the chemical shifts being reported as δ ppm and couplings expressed in Hertz. Silica gel column chromatography was carried out with Silica gel 100 (Merck No. 10184). Merck Silica-gel 60 F254 plates (No. 5744) were used for the preparative TLC. Aluminiumoxide 90 active acidic (activity stage I) was used for the reactions (Merck No. 1078).

Preparation of cis-Triarylimidazolines:
General Procedure: This solvent-free reaction is operationally simple. 10 Mmol of the reagent was prepared by the combination of ammonium acetate (0.77 g, 10 mmol, finely ground) and alumina (Al₂O₃, acidic, 2.5 g) in a mortar and pestle by grinding them together until a fine, homogeneous, powder was obtained (5-10 min). The aldehyde (9 mmol) was added to this reagent and the mixture was irradiated in a microwave for 2-5 min using 600 W. (A kitchen-type microwave instrument was used in all experiments). The mixture was then washed with 200 mL of EtOAc. The solvent was evaporated. Chromatography of the residue through a plug of silica gel with EtOAc/n-hexane (1:9 to 5:5) and evaporation of the solvent under reduced pressure gave the pure products in 53-90% yields. All products gave satisfactory spectral data in accord with the assigned structures and literature reports. 4a For new compounds spectral data are reported as following:

cis-2,4,5-Tris(p-isopropylphenyl)imidazoline (2e):
This imidazoline was prepared in the general way and had mp 222-224°C (ethanol). ¹H-NMR (CDCl₃/TMS-500 MHz): 1.05 (6H, d, J=6.8 Hz), 1.22 (6H, d, J=6.8 Hz), 1.26 (6H, d, J=6.8 Hz), 2.66 (2H, sep, J=6.8 Hz), 2.89 (1H, sep, J=6.9 Hz), 4.90 (2H, s), 6.57 (4H, d, J=7.9 Hz), 6.78 (4H, d, J=7.9 Hz), 7.46 (2H, d, J=8.1 Hz) 8.52 (2H, d, J=8.1 Hz), 10.93 (1H, br); ¹³C-NMR (CDCl₃/TMS-125.7 MHz): 23.53, 23.66, 23.73, 33.52, 34.03, 65.70, 120.75, 125.56, 127.03, 129.82, 130.66, 132.18, 148.23, 152.82, 165.06;
IR (KBr): 3220 (-NH), 1620 (C=N) cm\(^{-1}\); MS \(m/z\): 424 (M\(^+\)). Anal. Calcd for C\(_{30}\)H\(_{36}\)N\(_2\). C, 84.90; H, 8.49; N, 6.60. Found: C, 84.77; H, 8.41; N, 6.80.

**cis-2,4,5-Tris(m-nitrophenyl)imidazoline (2g):**

This imidazoline was prepared in the general way and had mp 130-142°C (ethanol). \(^1\)H-NMR, \(\delta_{\text{H}}\) (CD\(_3\)SOCD\(_3\), TMS): 5.82 (s, 2H), 7.32-7.45 (m, 4H), 7.81-7.89 (m, 5H), 8.44-8.53 (m, 3H), 8.89 (s, 1H); \(^{13}\)C-NMR, \(\delta_{\text{C}}\) (CDCl\(_3\), TMS): 61.04, 121.99, 122.29, 122.56, 126.07, 129.61, 130.75, 131.46, 134.20, 142.25, 147.50, 148.34, 162.97; IR (KBr): 3379 (-NH), 1610 (C=N) cm\(^{-1}\); MS \(m/z\): 433 (M\(^+\)). Anal. Calcd for C\(_{21}\)H\(_{15}\)N\(_5\)O\(_6\). C, 58.20; H, 3.46; N, 16.16. Found: C, 58.45; H, 3.66; N, 16.32.

**cis-2,4,5-Tris(o-chlorophenyl)imidazoline (2h):**

This imidazoline was prepared in the general way and had mp 132-134°C (ethanol). \(^1\)H-NMR, \(\delta_{\text{H}}\) (CD\(_3\)SOCD\(_3\), TMS): 6.04 (s, 2H), 6.94-7.01 (m, 4H), 7.09-7.26 (m, 4H), 7.36-7.48 (m, 3H), 7.97 (d, 1H, \(J=7.5\) Hz); \(^{13}\)C-NMR, \(\delta_{\text{C}}\) (CDCl\(_3\), TMS): 61.79, 123.26, 127.22, 128.26, 129.61, 130.41, 130.66, 130.98, 131.93, 132.03, 132.20, 132.81, 135.15, 164.88; IR (KBr): 3200 (-NH), 1610 (C=N) cm\(^{-1}\); MS \(m/z\): 400 (M\(^+\)). Anal. Calcd for C\(_{21}\)H\(_{15}\)N\(_2\)Cl\(_3\). C, 62.76; H, 3.74; N, 6.97. Found: C, 62.96; H, 3.98; N, 6.97.

**cis-2,4,5-Tris(\(\alpha\)-naphthyl)imidazoline (2i):**

This imidazoline was prepared in the general way and had mp 240-242°C (ethanol). \(^1\)H-NMR (CD\(_3\)SOCD\(_3\)/TMS-500 MHz): 6.39 (2H, s), 6.98-7.01 (3H, m), 7.09-7.27 (6H, m), 7.36 (2H, d, \(J=8.1\) Hz), 7.46-7.59 (6H, m), 7.76 (2H, d, \(J=8.2\) Hz), 7.92-7.97 (3H, m), 8.81 (1H, m); \(^{13}\)C-NMR (CD\(_3\)SOCD\(_3\)/TMS-125.7 MHz): 66.6, 125.3, 125.6, 126.0 127.1, 127.6, 127.7, 127.8, 128.1, 128.3, 129.0, 132.7, 132.8, 134.4, 138.4, 164.25; IR (KBr): 3412 (-NH), 1620 (C=N) cm\(^{-1}\); MS \(m/z\): 448 (M\(^+\)). Anal. Calcd for C\(_{33}\)H\(_{24}\)N\(_2\). C, 88.39; H, 5.36; N, 6.25. Found: C, 88.22; H, 5.45; N, 6.08.

**cis-2,4,5-Tris(\(\beta\)-naphthyl)imidazoline (2j):**

This imidazoline was prepared in the general way and had mp 208-209°C (ethanol). \(^1\)H-NMR (CD\(_3\)SOCD\(_3\)/TMS-500 MHz): 6.39 (2H, s), 6.92-7.03 (3H, m), 7.06-7.13 (2H, m), 7.14-7.23 (4H, m), 7.33 (2H, d, \(J=6.9\) Hz), 7.46-7.51 (3H, m), 7.55-7.59 (2H, m), 7.76 (2H, d, \(J=8.5\) Hz), 7.92-7.97 (3H, m), 8.82 (1H, m); \(^{13}\)C-NMR (CD\(_3\)SOCD\(_3\)/TMS-125.7 MHz): 65.16, 122.98, 124.31, 124.79, 124.86, 124.92, 125.19, 125.50, 126.40, 127.30, 127.36, 127.42, 128.09, 128.56, 130.57, 131.51, 132.85, 133.45, 165.73; IR (KBr): 3412 (-NH), 1620 (C=N) cm\(^{-1}\); MS \(m/z\): 448 (M\(^+\)). Anal. Calcd for C\(_{33}\)H\(_{24}\)N\(_2\). C, 88.39; H, 5.36; N, 6.25. Found: C, 88.18; H, 5.48; N, 5.98.

**REFERENCES**


