HETEROCYCLES, Vol. 65, No. 2, 2005, pp. 353 - 357
Received, 17th August, 2004, Accepted, 8th December, 2004, Published online, 10th December, 2004

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

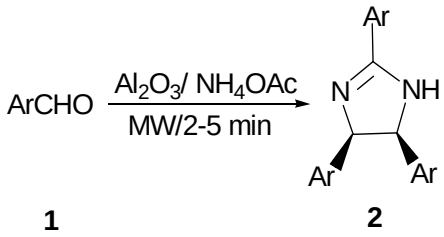
Abstract – A simple, efficient, and new method has been developed for the synthesis of 2,4,5-triarylimidazolines from aldehydes through a one-pot reaction of aldehydes in the presence of alumina-ammonium acetate under solvent–free conditions using microwave irradiation. This method is easy, rapid, one-pot 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)arylmethanediamines, 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 $ZnCl_2$ [3] 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 irradation,[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_2NH_4) was not as effective as ammonium acetate and gave the required product in 35% yield under microwave irradiation. Other ammonium salts (NH_4Cl, NH_4Br, NH_4PF_6, NH_4I and NH_4NO_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

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

Product **2**	Ar- **1**	Time (min)	Yield (%)	Product **2**	Ar- **1**	Time (min)	Yield (%)
a	C_6H_5-[4a]	2	80(85)	**f**	*p*-BrC_6H_4-[4a]	3	53(83)
b	*p*-MeC_6H_4-[4a]	3	79(82)	**g**	*m*-$O_2NC_6H_4$-	2	75
c	*p*-ClC_6H_4-[4a]	2	78(83)	**h**	*o*-ClC_6H_4-	4	56
d	*p*-$MeOC_6H_4$-[4a]	4	70(86)	**i**	α-Naphthyl	5	68
e	*p*-$(CH_3)_2CHC_6H_4$-	5	72	**j**	β-Naphthyl	4	76

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 (Al_2O_3, 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). ^{1}H-NMR ($CDCl_3$/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); ^{13}C-NMR ($CDCl_3$/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, δ_H (CD_3SOCD_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, δ_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 $C_{21}H_{15}N_5O_6$. 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, δ_H (CD_3SOCD_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, δ_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 $C_{21}H_{15}N_2Cl_3$. C, 62.76; H, 3.74; N, 6.97. Found: C, 62.96; H, 3.98; N, 6.97.

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

This imidazoline was prepared in the general way and had mp 240-242° C (ethanol). ^{1}H-NMR (CD_3SOCD_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_3SOCD_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): 3140 (-NH), 1590 (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(β-naphthyl)imidazoline (2j)**:

This imidazoline was prepared in the general way and had mp 208-209°C (ethanol). ^{1}H-NMR (CD_3SOCD_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_3SOCD_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

1. a) E. J. Corey and M. J. Grogan, *Org. Lett*., 1999, **1**, 157; b) T. Isobe, K. Fukuda, Y. Araki, and T. Ishikawa, *Chem. Commun*., 2001, 243; c) M. Anastassiadou, G. Baziard-Mouysset, and M. Payard, *Synthesis*, 2000, 1814; d) E. J. Corey and H. C. Huang, *Tetrahedron Lett*., 1989, **30**, 5235; e) E. J.

Corey, R. Imwinkelried, S. Pikul, and Y. B. Xing, *J. Am. Chem. Soc*., 1989, **111**, 5493; f) E. J. Corey and S. S. Kim, *J. Am. Chem. Soc.*, 1990, **112**, 4976; g) E. J. Corey, N. Imai, S. Pikul, and Y. B. Xing, *Tetrahedron Lett*., 1991, **32**, 7517; h) D. A. Evans and S. G. Nelson, *J. Am. Chem. Soc*., 1997, **119**, 6452.

2. a) A. Furth, *Monatsh. Chem*., 1906, **27**, 839; b) K. Saigo, N. Kubota, S. Takebayashi, and M. Hasegawa, *Bull. Chem. Soc. Jpn*., 1986, **59**, 931; c) E. J. Corey and F. N. M. Kuhnle, *Tetrahedron Lett*., 1997, **38**, 8631; d) M. L. Larter, M. Phillips, F. Ortega, G. Aguirre, R. Somanathan, and P. J. Walsh, *Tetrahedron Lett*., 1998, **39**, 4785; e) E. A. Mistryukov, *Medeleev Commun.*, 2001, **11**, 29; f) N. A. Lozinskaya, V. V. Tsybezova, M. V. Proskurnina, and N. S. Zefirov, *Russian Chemical Bulletin,* 2003, **52**, 674.
3. a) K. Nishiyama, M. Saito, and M. Oba, *Bull. Chem. Soc. Jpn*., 1988, **61**, 609; b) S. V. Grigor'ev, *Zh. Obshch. Khim*., 2001, **71**,163; *Russ. J. Gen. Chem., (Engl. Transl.)* 2001, **71**, 149.
4. a) H. Uchida, T. Shimizu, P. Y. Reddy, S. Nakamura, and T. Toru, *Synthesis,* 2003, 1236; b) H. Uchida, H. Tanikoshi, S. Nakamura, P. Y. Reddy, and T. Toru, *Synlett,* 2003, 1117.
5. a) S. Caddick. *Tetrahedron,* 1995, **51**, 10403; b) A. Zlotorzynsky, *Critical Reviews in Analytical Chemistry,* 1995, **25**, 43; c) R. S. Varma, *Green Chemistry,* 1999, **1**, 43; d) P. Lidstrom, J. Tierney, B. Wathey, and J. Westman, *Tetrahedron,* 2001, **57**, 9225; e) L. Perreux and A. Loupy, *Tetrahedron*, 2001, **57**, 9199.
6. a) B. Kaboudin, *Tetrahedron Lett*., 2002, **43**, 8713; b) B. Kaboudin and H. Norouzi, *Tetrahedron Lett*., 2004, **45**, 1283.