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Microwave-Assisted from Synthesis of 2-Arylamino-2-Imidazolines on a Solid Support

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ABSTRACT: *An efficient synthesis of 2-arylamino-2-imidazolines from dimethyl N-aryldithioimidocarbonates and ethylenediamine on solid support under microwave irradiation has been developed. The reaction time has been reduced from hours to minutes with improved yields as compared to conventional heating. Their piperidin-4-ylmethyl and morpholin-4-ylmethyl derivatives were synthesized by treatment with formaldehyde and piperidine or morpholine.* © 2005 Wiley Periodicals, Inc. Heteroatom Chem 16:142–147, 2005; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.20081

INTRODUCTION

2-Arylamino-2-imidazoline compounds have an interesting chemistry [1,2], and they are effective pharmacophores in medicinal chemistry. The imidazolines class of drug interacting with adrenergic and imidazoline receptors is known to mediate a variety of biological actions including lowering blood pressure, sedation, anxiety reduction, analgesia, hypothermia, decreased salivary secretion, and mydriasis. Imidazoline I_2 receptors are widely distributed in the body and brain of different species including humans. Functionally, these receptors have been implicated in a variety of disease states such as psychiatric disorders, opiate withdrawal Parkinson's, and Alzheimer's disease as well as Huntington's chorea. Moreover, previous reports demonstrated that synthetic imidazolines act either as inhibitors of α_2-mediated events in platelets or inducers of platelet activation. The prototypical agents in the series of 2-arylamino-2-imidazolines are *clonidine* and *moxonidine* that contain aminoimidazoline structure, shown α_1 and α_2 adrenoceptor activities, and more specially *phentolamine*, which contains an imidazoline ring, is a known α_1-adrenergic antagonist [3–5].

Microwave-assisted organic synthesis has also received a great deal of recent attention due to shorter reaction times, minimization of reaction by-products, increased yields, and in many cases solvent-free conditions. The combination of solvent-free conditions and MW irradiation leads to large reductions in reaction times, enhancements in conversions, sometimes in selectivity, with several advantages of the eco-friendly approach. The short reaction times and expanded reaction range that is offered by microwave-assisted organic synthesis are suited to the increased demands in industry. In particular, there is a requirement in the pharmaceutical industry for a higher number of novel chemical entities to be produced, which requires chemists to employ a number of resources to reduce the time for the production of compounds [6–8].

The aim of this work is to demonstrate the advantages obtained by the use of microwave irradiation in the synthesis of 2-arylamino-2-imidazolines using the same precursors of the classical method. The present new method of the formation of 2-arylamino-2-imidazolines under microwave irradiation

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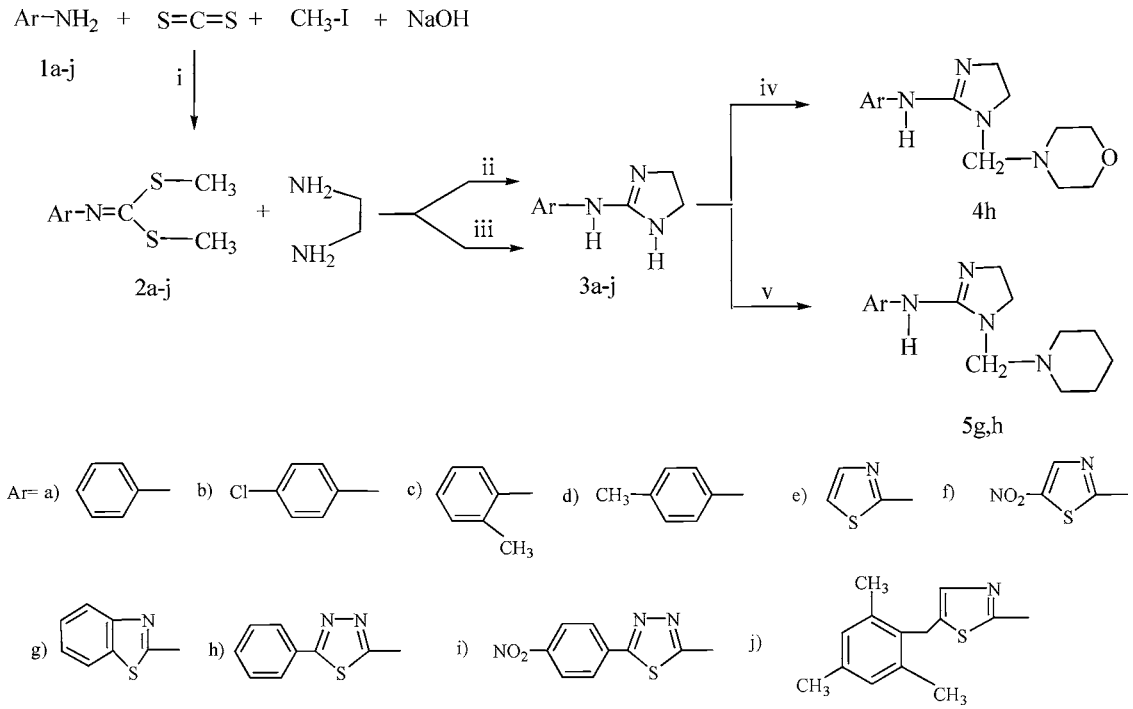
offers several advantages: faster reaction rates, fewer by-products, high yields, less expensive equipment, while the classical method of formation of 2-arylamino-2-imidazolines involves a long process.

RESULTS AND DISCUSSION

A number of methods to synthesize 2-arylamino-2-imidazolines from the corresponding aromatic amines have been reported in the literature. The most used methods in the last years are as follow: (a) Reaction of an aromatic amine with 2-methylthio-2-imidazoline in the presence of pyridine or toluene (reaction time 2–9 h) [9,10]; (b) a three-step protocol involving the conversion of an amine into the isothiocyanate, then treatment of the isothiocyanate with ethylenediamine followed by a cyclization using mercuric oxide or acetate to form the 2-arylamino-2-imidazoline (reaction time 2–5 h) [11,12]; (c) reaction of aromatic primary amine with an imidazoline sulfonic acid (reaction time 24–72 h) [13]; (d) reaction of 2-chloro-2-imidazoline with amine compounds (reaction time 2–12 h) [14,15]; (e) 2-arylamino-2-imidazolines such as *clonidine* and its derivatives were prepared by reaction of dimethyl *N*-aryldithioimidocarbonates with ethylenediamine (reaction time 8 h) [16–18]. In all these methods, yields of reaction are not very high and the reactions involve generally long process.

The synthetic route is depicted in Scheme 1. Dimethyl *N*-aryldithioimidocarbonates (**2a–j**) were synthesized from carbon disulfide, aromatic amine, and methyl iodide in the presence of concentrated aqueous NaOH. Synthesis of 2-arylamino-2-imidazolines **3a–j** carried out both by conventional heating and by microwave irradiation. Piperidine-4-yl methyl **5g,h** and morpholine-4-yl methyl **4h** derivatives were synthesized by treatment with piperidine or morpholine and formaldehyde for the first time. Elemental analysis, IR and ^{1}H NMR spectra of products clearly indicated formation of the products Table 1 shows yields and reaction time by the microwave irradiation and conventional methods.

Some methods for microwave-assisted solid support synthesis of substituted imidazoles and their derivatives are available in the literature [19,20], but not for of 2-arylamino-2-imidazolines. In this work, we report the microwave-assisted synthesis of several new 2-arylamino-2-imidazolines on silica gel as solid support. Silica gel is a very poor conductor of heat, but a very efficient microwave adsorbent, resulting in turn in a very rapid and homogeneous heating. Consequently, silica gel



SCHEME 1 (i) 0°C, DMF, (ii) microwave irradiation, 850 W, silica jel, (iii) DMF, 110°C, (iv) formaldehyde (35%), morpholine, room temperature, and (v) formaldehyde (35%), piperidine, room temperature.

TABLE 1 Time Required (min) and Yields (%) of 2-Arylamino-2-imidazolines Prepared

	Time		*Yield*	
	Thermal	*Microwave*	*Thermal*	*Microwave*
3a	450	3.0	63	82
3b	480	3.5	71	91
3c	420	3.0	65	87
3d	420	3.5	68	78
3e	510	3.5	51	69
3f	510	4.0	46	72
3g	480	3.5	66	79
3h	510	3.5	57	74
3i	540	4.5	44	68
3j	510	3.5	66	81

displays very strong specific microwave effects, with significant improvements in temperature homogeneity and heating rates, enabling faster reactions and less degradation of final products when compared to classical heating.

EXPERIMENTAL

Aromatic and heteroaromatic amines except **1h–j** were obtained from commercial sources. Melting points (uncorrected) were determined with a Gallenkamp apparatus. IR spectra were measured on a Mattson model FT-IR spectrometer, and ^{1}H spectra were measured on FX 90Q JEOL and 200 MHz Bruker AC instruments. Chemical shift values (δ) are reported in ppm relative to TMS. Elemental analysis results are within 0.4% of the calculated value.

General Procedure for **2a–j**

To a solution of aromatic (or heteroaromatic) amine (0.1 mol) in DMF (75 mL), aqueous 20 M sodium hydroxide (5.5 mL, 0.11 mol) was added with stirring at room temperature. After 10 min carbon disulfide (3.3 mL, *d*: 1.26 g cm^{-3}, 0.055 mol) was added and stirring was continued for 30 min. Then aqueous 20 M sodium hydroxide (3 mL, 0.06 mol) and carbon disulphide (1.8 mL, 0.0275 mol) were added. This operation was finally repeated 10 min later. After 30 min the reaction was placed in an ice bath, methyl iodide (12.5 mL, *d*: 2.28 g cm^{-3}, 0.2 mol) was added dropwise and stirring was continued for 2 h. The mixture was then poured into ice-cooled water and the precipitate thus obtained was filtered, washed with water, dried and recrystallized from ethanol.

Dimethyl N-(phenyl)dithioimidocarbonate **2a**. Yellow crystal, yield 64%, mp 92–93°C (ethanol); IR (KBr) υ_{max}: 2935 (aliphatic C—H stretching), 1597 (C=N stretching); 775 (SCH_3 stretching). ^{1}H-NMR ($CHCl_3$-*d*, 90 MHz): δ 2.62 (s, 6H, SCH_3), 7.4 (s, 5H, Ar-H). Anal. Calcd. for $C_9H_{11}NS_2$ (197): C, 54.78; H, 5.62; N, 7.10; S, 32.49. Found: C, 55.42; H, 5.79; N, 7.35; S, 31.53%.

Dimethyl N-(4-chlorophenyl)dithioimidocarbonate **2b**. Yellowish crystal, yield 71%, mp 110–112°C (ethanol); IR (KBr) υ_{max}: 2932 (aliphatic C—H stretching), 1617 (C=N stretching), 815 (SCH_3 stretching), 507 (C—CI). ^{1}H-NMR ($CHCl_3$-*d*, 200 MHz): δ 2.46 (s, 6H, SCH_3), 6.74–7.12 (m, 4H, Ar-H). Anal. Calcd. for $C_9H_{10}CINS_2$: (231): C, 46.64; H, 4.35; N, 6.04; S, 27.67. Found: C, 45.24; H, 4.50; N, 6.27; S, 28.56%.

Dimethyl N-(2-methylphenyl)dithioimidocarbonate **2c**. Orange powder, yield 67%, mp 152–153°C (ethanol), IR (KBr) υ_{max}: 2924 (aliphatic C—H stretching), 1532 (C=N stretching), 1090, 1070 (*o*-disubstituted benzene), 786 (SCH_3 stretching). ^{1}H-NMR ($CHCl_3$-*d*, 90 MHz): δ 2,29 (s, 3H, CH_3), 2.60 (s, 6H, SCH_3), 7.29–7.51 (m, 4H, Ar-H). Anal. calcd. for $C_{10}H_{13}NS_2$ (211): C, 56.83; H, 6.20; N, 6.63; S, 30.34. Found: C, 55.98; H, 6.17; N, 6.53; S, 30.42%.

Dimethyl N-(4-methylphenyl)dithioimidocarbonate **2d**. Light brown powder, yield 54%, mp 175–176°C (ethanol), IR (KBr) υ_{max}: 2921 aliphatic C—H stretching), 1537 (C=N stretching), 1100, 1030, and 820 (*p*-disubstituted benzene), 765 (SCH_3 stretching). ^{1}H-NMR ($CHCl_3$-*d*, 90 MHz): δ, 2.24 (s, 3H, CH_3), 2.50 (s, 6H, SCH_3), 7.21–7.44 (s, 4H, Ar-H). Anal. Calcd. for $C_{10}H_{13}NS_2$ (211): C, 56.83; H, 6.20; N, 6.63; S, 30.34. Found: C, 56.65; H, 6.38; N, 6.23; S, 30.57%.

Dimethyl N-(1,3-thiazole-2-yl)dithioimidocarbonates **2e**. Light brown powder, yield 61%, mp 194–195°C (ethanol), IR (KBr) υ_{max}: 3092 (aromatic C—H stretching), 2903 (aliphatic C—H stretching), 1640 (C=C stretching), 1550 (C=N stretching), 1530 (Ar-NO_2 asymmetric stretching) and 1350 (symmetric stretching), 827 (S—CH_3 stretching).^{1}H-NMR (DMSO-d_6, 90 MHz): δ 2.88 (s, 6H, SCH_3), 7.92 (d, 1H, thiazole ring proton). 8.18 (d, 1H, thiazole ring proton): Anal. Calcd. for $C_6H_8N_2S_3$ (204): C, 35.27; H, 3.95; N, 13.71; S, 47.08. Found: C, 35.59; H, 4.11; N, 13.44; S, 47.96%.

Dimethyl N-(5-nitro-1,3-thiazol-2-yl)-dithioimidocarbonates **2f**. Yellow powder, yield 59%, mp 174–175°C (ethanol), IR (KBr) υ_{max}: 3095 (aromatic C—H stretching), 2979–2930 (aliphatic C—H stretching), 1678 (C=C stretching), 1621 (C=N stretching),

1530 (Ar-NO_2 asymmetric stretching) and 1350 (symmetric stretching), 841 (S—CH_3 stretching). ^{1}H-NMR ($CHCl_3$-*d*, 90 MHz): δ: 2.65 (s, 6H, SCH_3), 8.36 (s, 1H, thiazole ring proton). Anal. Calcd. for $C_6H_7N_3O_2S_3$ (249): C, 28.90; H, 2.83; N, 16.85; S 38.58. Found: C, 28.39; H, 3.06; N, 15.34; S, 38.79%.

Dimethyl N-(1,3-benzothiazol-2-yl)dithioimidocarbonate **2g**. Yield 69%, yellowish powder, mp 101–102°C (ethanol); IR (KBr) υ_{max}: 2995 (aliphatic C—H stretching), 1592 (C=C stretching), 1510 (C=N stretching), 833 (S—CH_3 stretching). ^{1}H-NMR ($CHCl_3$-*d*, 90 MHz): δ 2.59 (s, 6H, SCH_3), 6.90–7.30 (m, 2H, Ar-H), 7.50–7.86 (2H, m, Ar-H). Anal. Calcd. for $C_{10}H_{10}N_2S_3$ (254): C, 47.21; H, 3.96; N, 11.01; S 37.81. Found: C, 48.39; H, 4.06; N, 11.34; S 38.77%.

Dimethyl N-(5-phenyl-[1,3,4]thiadiazol-2-yl)dithioimidocarbonate **2h**. Orange powder, yield 62%, mp 111–113°C (ethanol), IR (KBr) υ_{max}: 2968 (aliphatic C—H stretching), 1619 (C=C stretching), 1578 and 1537 (C=N stretching), 751 (S—CH_3 stretching). ^{1}H-NMR($CHCl_3$-*d*, 90 MHz) δ 2.64 (s, 6H, SCH_3), 7.47–7.99 (m, 5H, Ar-H), Anal. Calcd. for $C_{11}H_{11}N_3S_3$ (281): C, 46.95; H, 3.94; N, 14.93; S, 34.18. Found: C, 46.65; H, 3.38; N, 14.23; S, 34.37%.

Dimethyl N-{5-(4-nitrophenyl)[1,3,4]thiadiazol-2-yl}dithioimidocarbonates **2i**. Yield 55%; orange powder, mp 250–251°C (ethanol), IR (KBr) υ_{max}: 2930–2900 (aliphatic C—H stretching), 1633 (C=C stretching), 1592 (C=N stretching), 1510 (Ar-NO_2 asymmetric stretching) and 1349 (symmetric stretching), 846 (S—CH_3 stretching). ^{1}H-NMR ($CHCl_3$-*d*, 90 MHz) δ: 2.48 (s, 6H, SCH_3), 8.31–8.52 (m, 4H, Ar-H), Anal. Calcd. for $C_{11}H_{10}N_4O_2S_3$ (326): C, 40.48; H, 3.09; N, 17.16; S, 27.47. Found: C, 39.56; H, 3.32; N, 17.19; S, 28.09%.

Dimethyl N-[5-(2,4,6-trimethylbenzyl)-1,3-thiazole-2-yl]dithioimidocarbonates **2j**. Yield 74%, orange power, mp 91–92°C (ethanol), IR (KBr) υ_{max}: 2920 and 2855 (aliphatic C—H stretchings), 1612 (C=C stretching), 1523 (C=N stretching), 756 (S—CH_3 stretching). ^{1}H-NMR ($CHCl_3$-*d*, 90 MHz) δ: 2.26 (s, 9H, mesitylene CH_3), 2,58 (s, 6H, SCH_3), 3,92 (s, 2H, aliphatic CH_2), 6,21 (s, 1H, thiazole ring proton), 6.87–7.26 (m, 2H, Ar-H), Anal. Calcd. for $C_{16}H_{20}N_2S_3$ (336): C, 57.10; H, 5.99; N, 8.32; S, 28.58. Found: C, 58.12; H, 5.19; N, 8.45; S, 28.97%.

General Procedure for **3a–j**

Thermal Method. A solution of **2a–j** (0.04 mol) in DMF (15 mL) was added to a solution of ethylenediamine (5.4 mL, *d*: 0.897 g cm^{-3}, 0.08 mol) in DMF (15 mL) with stirring at room temperature. The reaction mixture was refluxed at 110°C for approximate 6–8 h, cooled, then added to ice-cold water. The resulting solid was washed with water, dried. The crude products were purified by crystallization from suitable solvents.

Microwave Irradiation Method. A mixture of **2a–j** (10 mmol) and ethylenediamine (0.7 mL, *d*: 0.897 g cm^{-3}, 10 mmol), was stirred a few minutes with 3 g of silica gel. The mixture was irradiated in a domestic microwave oven at 850 W for approximately 3.0–4.5 min. The temperature was measured at the end of MW irradiation. The temperatures were obtained around 140–145°C for all of the compounds. The mixture was allowed to cool, then the product was extracted with 4 × 25 mL methanol/ acetonitrile/chloroform (2/2/1) washed with distilled water (2 × 10 mL). The organic phase was separated, and the aqueous phase extracted with dichloromethane (2 × 5 mL). The combined organics were dried over anhydrous sodium sulfate, filtered. The solvents were removed by rotary evaporation. The crude products were purified by crystallization from suitable solvents.

N-(phenyl)-N-(4,5-dihydro-1H-imidazol-2-yl)-amine **3a**. White powder, mp 115–116°C (ethanol), IR (KBr) υ_{max}: 3277 (imidazoline N—H stretching), 3257 (N—H stretching), 1660 (C=N stretching), 1537 (N—H bending). ^{1}H NMR (DMSO-d_6, 200 MHz) δ: 3.48 (s, 1H, NH), 3.73 (s, 4H, imidazoline CH_2), 6.30 (broad peak, 1H, imidazoline NH), 7.12–8.20 (m, 5H, Ar-H). Anal. Calcd. for $C_9H_{11}N_3$ (161): C, 67.06; H, 6.88; N, 26.07. Found: C, 68.11; H, 7.24; N, 26.83%.

N-(4-Chlorophenyl)-N-(4,5-dihydro-1H-imidazol-2-yl)amine **3b**. White powder, mp 147–148°C (ethanol), IR (KBr) υ_{max}: 3284 (imidazoline N—H stretching), 3245 (N—H stretching), 1681 (C=N stretching), 1594 (N—H bending). ^{1}H NMR (DMSO-d_6, 200 MHz): δ 3.67 (s, 1H, NH), 3.76 (s, 4H, imidazoline CH_2), 6.24 (broad peak, 1H, imidazoline NH), 7.05–7.40 (m, 4H, Ar-H). Anal. Calcd. for $C_9H_{10}ClN_3$ (195): C, 55.25; H, 5.15; N, 21.48. Found: C, 56.13; H, 5.74; N, 22.05%.

N-(2-Methylphenyl)-N-(4,5-dihydro-1H-imidazol-2-yl)amine **3c**. Light brown powder, mp 188–191°C (THF), IR (KBr) υ_{max}: 3382 and 3252 (N—H stretching), 1660 (C=C stretching), 1523 (C=N stretching), 1498 (N—H bending); ^{1}H NMR (DMSO-d_6, 90 MHz): δ 2.01 (s, 1H, NH), 2.24 (s, 3H, CH_3), 3.74 (s, 4H,

imidazoline CH_2), 6.44 (broad peak, 1H, imidazoline NH), 7.71 (m, 4H, Ar-H), Anal. Calcd. for $C_{10}H_{13}N_3$ (175): C, 68.54; H, 7.48; N, 23.98; Found: C, 67.93; H, 7.96; N, 24.41.

N-(4-methylphenyl)-N-(4,5-dihydro-1H-imidazol-2-yl)amine **3d**. Light grey powder, mp 190–191°C (ethanol), IR (KBr) υ_{max}: 3364 (imidazoline N—H stretching), 3249 (N—H stretching), 1486 (N—H bending). ^{1}H NMR (DMSO-d_6, 90 MHz): δ 3.63 (s, 1H, NH), 2.38 (s, 3H, CH_3), 3.77 (s, 4H, imidazoline CH_2), 6.31 (broad peak, 1H, imidazoline NH), 7.71 (m, 4H, Ar-H), Anal. Calcd. for $C_{10}H_{13}N_3$ (175): C, 68.54; H, 7.48; N, 23.98; Found: C, 67.74; H, 7.36; N, 24.11%

N-(1,3-thiazol-2-yl)-N-(4,5-dihydro-1H-imidazol-2-yl)amine **3e**. Yellow powder, mp 245–246°C (ethanol), IR (KBr) υ_{max}: 3289 (imidazoline N—H stretching), 3219 (N—H stretching), 1609 (C=N stretching), 1531 (N—H bending). ^{1}H NMR (DMSO-d_6, 90 MHz): δ 3.69 (s, 4H, imidazoline CH_2), 7.21 (d, 1H, thiazole ring proton), 7.57 (d, 1H, thiazole ring proton), 8.48 (s, 2H, NH), Anal. Calcd. for $C_6H_8N_4S$ (168): C, 42.84; H, 4.79; N, 33.31; S,19.06. Found: C, 43.23; H, 4.55; N, 34.06; S, 19.37%.

N-(5-nitro-1,3-thiazol-2-yl)-N-(4,5-dihydro-1H-imidazol-2-yl)amine **3f**. White powder, mp 133–135°C (chloroform), IR (KBr) υ_{max}: 3358 and 3317 (N—H stretching), 1681 (C=C stretching), 1619 (C=N stretching), 1544 (Ar-NO_2 asymmetric stretching), 1465 (N—H bending) 1359 (Ar-NO_2 symmetric stretching), ^{1}H NMR (DMSO-d_6, 90 MHz): δ 3.66 (s, 4H, imidazoline CH_2), 8.19 (s, 2H, NH), 8.35 (s, 1H, thiazole ring proton), Anal. Calcd. for $C_6H_7N_5O_2S$ (213): C, 33.80; H, 3.31; N, 32.85; S, 15.04. Found: C, 34.19; H, 3.59; N, 33.21; S, 15.19%.

N-(1,3-Benzothiazol-2-yl)-N-(4,5-dihydro-1H-imidazol-2-yl)amine **3g**. White powder, mp 131–132°C (ethanol), IR (KBr) υ_{max}: 3281 (imidazoline N—H stretching), 3220 (N—H stretching), 1611 (C=N stretching), 1528 (N—H bending). ^{1}H NMR (DMSO-d_6, 200 MHz): δ 1.74 (s, 1H, NH), 3.78 (s, 4H, imidazoline CH_2), 7.09–7.64 (m, 4H, Ar-H), 8.01 (broad peak, 1H, imidazoline NH). Anal. Calcd. for $C_{10}H_{10}N_4S$ (218): C, 55.02; H, 4.62; N, 25.37; S, 14.69. Found: C, 55.63; H, 4.96; N, 26.41; S, 15.19%.

N-(5-Phenyl-[1,3,4]-thiadiazol-2-yl)-N-(4,5-dihydro-1H-imidazol-2-yl)amine **3h**. mp 192–194°C (toluene), IR (KBr) υ_{max}: 3317 and 3297 (N—H stretching), 1614 (C=C stretching), 1528 (C=N stretching), 1443 (N—H bending); ^{1}H NMR (DMSO-d_6, 90 MHz): δ 3.76 (s, 4H, imidazoline CH_2), 7.45 (s, 5H, Ar-H); 7.55 (s, 2H, NH). Anal. Calcd. for $C_{11}H_{11}N_5S$ (245): C, 53.86; H, 4.52; N, 28.56; S, 13.07. Found: C, 54.03; H, 4.66; N, 28.41; S, 13.65%.

N-[5-(4-nitrophenyl)-[1,3,4]-thiadiazole-2-yl]-N-(4,5-dihydro-1H-imidazol-2-yl)amine **3i**. Yellow powder, mp 239–240°C (ethanol), IR (KBr) υ_{max}: 3396 and 3218 (N—H stretching), 1626 (C=C stretching), 1538 (C=N stretching), 1508 (Ar-NO_2 asymmetric stretching), 1465 (N—H bending) 1350 (Ar-NO_2 symmetric stretching), ^{1}H NMR (DMSO-d_6, 90 MHz): δ 3.58 (s, 4H, imidazoline CH_2), 7.53–8.29 (m, 4H, Ar-H), 8.09 (s, 2H, NH) Anal. Calcd. for $C_{11}H_{10}N_6O_2S$ (290): C, 45.51; H, 3.47; N, 28.95; S, 11.05. Found: C, 45.11; H, 3.70; N, 28.56; S, 11.55%.

N-[5-(2,4,6-trimethylbenzyl)-1,3-thiazole-2-yl]-N-(4,5-dihydro-1H-imidazole-2-yl)amine **3j**. Light grey powder, mp 172–174°C (toluene), IR (KBr) υ_{max}: 3382 and 3372 (N—H stretching), 2923 (C—H stretching), 1626 (C=C stretching), 1532 (C=N stretching), 1471 (N—H bending). ^{1}H NMR (DMSO-d_6, 90 MHz) δ 2.15 (s, 2H, NH), 2.26 (s, 9H, 3 × CH_3), 3.66 (s, 4H, imidazoline CH_2), 3.91 (s, 2H, aliphatic CH_2), 5.76 (s, 1H, thiazole ring proton), 6.87 (m, 2H, Ar-H), Anal. Calcd. for $C_{16}H_{20}N_4S$ (300): C, 63.97; H, 6.71; N, 18.65; S, 10.67. Found: C, 63.85; H, 6.56; N, 18.34; S, 10.07%.

General Procedure for **4** *and* **5**

A solution of **3g,h** (0.01 mol) in methanol (20 mL) was stirred at room temperature for 2 h with aqueous formaldehyde (35%; 0.015 mol) and morpholine (0.9 mL, d: 1 g cm^{-3}, 0.01 mol or 1 mL, d: 0.86 g cm^{-3} for piperidine). The solvent was removed on a rotary evaporator. The residue was mixed with methanol, and the precipitate formed was filtered and then recrystallized from chloroform.

N-(5-Phenyl-[1,3,4]thiadiazol-2-yl)-N-[1-(morpholin-4-ylmethyl)-4,5-dihydro-1H-imidazol-2-yl]amine **4h**. Yellow crystal, yield 59%, mp 127–128°C (chloroform), IR (KBr) υ_{max}: 3305 (imidazoline N—H stretching), 1588 (C=N stretching), 1145 (C—N stretching), 1114 (cyclic ether C—O—C stretching), ^{1}H NMR ($CHCl_3$-d, 90 MHz) δ: 2.57–2.62 (s, 4H, morpholine ring CH_2—N—CH_2 protons), 3.64–3.74 (s, 8H, morpholine ring CH_2 protons and imidazoline ring protons), 4.11 (s, 2H, NCH_2N), 7.49–7.89 (m, 5H, Ar-H), 8.47 (broad peak, 1H, NH), Anal. Calcd. for $C_{16}H_{20}N_6OS$ (344): C, 55.79; H, 5.85; N, 24.40; S, 9.31. Found: C, 55.35; H, 4.86; N, 23.96; S, 8.79%.

N-(1,3-Benzothiazol-2-yl)-N-[1-(piperidin-4-ylmethyl)-4,5-dihydro-1H-imidazol-2-yl]amine **5g**. White crystal, yield 67%, mp 158–159°C (chloroform), IR (KBr) υ_{max} : 3297 (imidazoline N—H stretching), 1576 (C=N stretching), 1137 (C—N stretching), ^{1}H NMR ($CHCl_3$-*d*, 90 MHz) δ 1.49 (s, 6H, piperidine ring protons), 2.57–2.62 (s, 4H, piperidine CH_2—N—CH_2 protons) 3.62 (s, 4H, imidazoline ring protons), 4.10 (s, 2H, NCH_2N), 7.15–7.56 (4H, m, Ar-H), 8.78 (broad peak, 1H, NH), Anal. Calcd. for $C_{16}H_{21}N_5S$ (315): C, 60.92; H, 6.71; N, 22.20; S, 10.17. Found: C, 60.68; H, 6.54; N, 22.41; S,10.17%.

N-(5-Phenyl-[1,3,4]thiadiazol-2-yl)-N-[1-(piperidin-4-ylmethyl)-4,5-dihydro-1H-imidazol-2-yl]amine **5h**. White powder, yield 55%, mp 133–134°C (chloroform), IR (KBr) υ_{max}: 3234 (imidazoline N—H stretching), 1620 (C=N stretching), 1120 (C—N stretching). ^{1}H NMR ($CHCl_3$-*d*, 90 MHz) δ: (s, 6H, piperidine ring protons), 2.52 (s, 4H, piperidine CH_2—N—CH_2 protons), 3.64 (s, 4H, imidazoline ring protons), 4.08 (s, 2H, NCH_2N), 7.41–7.88 (5H, m, Ar-H), 8.34 (broad peak, 1H, N*H*), Anal. Calcd. for $C_{17}H_{22}N_6S$ (342): C, 59.62; H, 6.48; N, 24.54; S, 9.36. Found: C, 59.11; H, 6.87; N, 24.21; S, 9.60%.

CONCLUSION

In conclusion, we have described a rapid and highly efficient method for the synthesis of 2-arylamino-2-imidazolines starting from dimethyl *N*-aryldithioimidocarbonates on solid support microwave irradiation reaction conditions.

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