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A novel synthetic method for 2-arylmethyl substituted imidazolines and imidazoles from 2-aryl-1,1-dibromoethenes

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Abstract—Various 2-arylmethylimidazolines were prepared by treating readily available 2-aryl-1,1-dibromoethenes with ethylenediamine under mild conditions and further converted into the corresponding imidazoles smoothly with Swern oxidation.

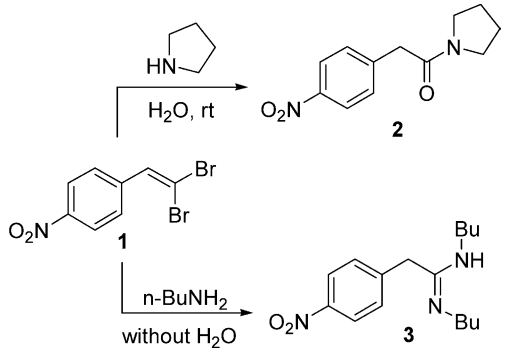
1. Introduction

1,1-Dihaloalkenes, efficiently prepared from the corresponding aldehydes are useful intermediates in organic synthesis. They have been used as alkynyl precursors,[1] monomers of AB_2 type polymers,[2] and for the synthesis of conjugated dienes or enynes.[3] They also have been effective intermediates for the stereoselective formation of either *E*- or *Z*-alkenes via transition metal-catalyzed coupling reactions.[4] Recently, we and others have found that 2-aryl-1,1-dibromoethenes reacted with secondary or primary amines under mild conditions to give the substitution products such as **2** (Scheme 1).[3c,5] We have also shown that the reaction of 2-(4-nitrophenyl)-1,1-dibromoethene **1** with $BuNH_2$ gave amidine **3** quantitatively in the absence of water and the reaction with ethylenediamine gave a good yield of the corresponding imidazoline.[5a]

There has been considerable attention on the synthesis of imidazolines and imidazoles[6] because of their diverse biological and pharmacological activities.[7] A novel and efficient methodology for the preparation of imidazoline[8] and imidazole derivatives[9] would provide synthetic chemists with a valuable tool and versatility. Although several synthetic methods have been developed for 2-substituted imidazolines and imidazoles, there is still a need for a method employing mild reaction conditions and readily available reagents. Because the reaction of 2-aryl-1,1-dibromoethenes with ethylenediamine can provide another mild and efficient alternative to the known synthetic methods of 2-arylmethyl substituted imidazolines and imidazoles, we have systematically investigated the reactions of various 2-aryl-1,1-dibromoethenes and report the results as follows.

2. Results and discussion

First, the formation of imidazolines from aryl dibromoethenes with ethylenediamine as a reaction solvent was examined at room temperature (Table 1). The required aryl dibromoethenes were efficiently prepared from the corresponding aryl aldehydes with different substituents in 73–99% yield as described in the previous work.[5a] Both the rate and the yield of the imidazoline formation reactions depend much on the electronic properties of the substituents on the aryl group. Aryl dibromoethenes with an electron-withdrawing substituent produced the corresponding imidazolines at a faster rate and in better yield than those with an electron-donating group. To our satisfaction, the



Scheme 1. The substitution reactions of 2-(4-nitrophenyl)-1,1-dibromoethene **1** with amines.[5a]

Keywords: Aryl-1,1-dibromoethene; Imidazoline; Swern oxidation; Imidazole.

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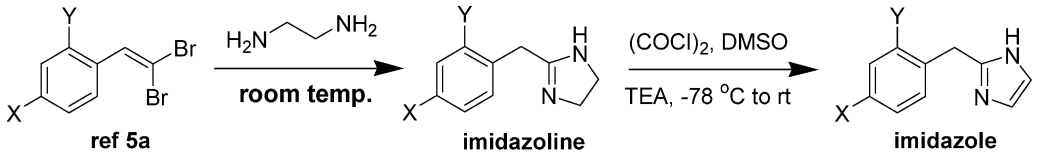
Table 1. Synthesis of 2-arylmethyl substituted imidazolines and imidazoles from 2-aryl-1,1-dibromoethenes



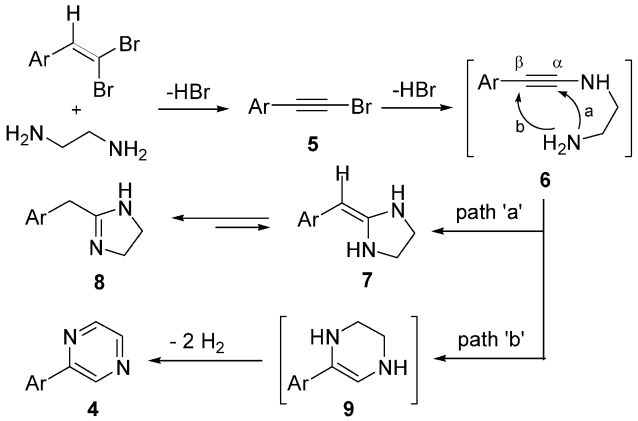
Entry	X	Y	Imidazoline		Imidazole	
			Time (h)	Yield[a] (%)	Time (h)	Yield[a] (%)
1	NO_2	H	0.5	81	2.5	75
2	H	NO_2	0.5	90	2.5	73
3	CN	H	1	93	2.5	66
4	CF_3	H	1	95	2.5	58
5	H	CF_3	5	93	2.5	74
6	Cl	H	3	95	2.5	58
7	H	Cl	6	95	2.5	68
8	H	H	15	75	2.5	84
9	Me	H	36	63[b]	2.5	89
10	H	Me	48	92	2.5	67
11	MeO	H	80	70[b,c]	2.5	53
12	H	MeO	84	55	2.5	75

[a] Isolated yield.
[b] Corresponding pyrazines **4** were obtained additionally in 13–15% yield (Scheme 2).
[c] The crude yield.

reaction of *o*-nitrophenyl dibromoethene with ethylenediamine gave a high yield of the corresponding imidazoline (entry 2). Its reaction with pyrrolidine in the previous report gave a poor yield (20%) of 2-(*o*-nitrophenyl)acetamide because of other unknown side products.[5a] Although the *p*-cyano group is tolerated under the reaction conditions (entry 3), the *o*-cyano group seemed to react to give the unidentified side products and no desired product was isolated (not shown). For the slow-reacting aryl dibromoethenes, the reaction rate could be increased by raising the reaction temperature up to 50 °C and the reactions were finished less than 30 min. However, the yields of the corresponding imidazolines were not improved. It is also notable that the reaction rate of aryl dibromoethenes with an *ortho* substituent is slower compared to that with a *para* substituent probably because of the steric hindrance from the *ortho* substituent. It was interesting to find that aryl dibromoethenes with a *para* electron-donating substituent on the aryl group produced the corresponding pyrazines **4** (Scheme 2) in 15% (Ar=4-methylphenyl) and 13% (Ar=4-methoxyphenyl) yield, respectively, in addition to the expected imidazolines (entries 9 and 11).[10] Only trace amount of the corresponding pyrazines was detected with aryl dibromoethenes having an electron-donating group at an *ortho* position, probably because of the steric hindrance in the reaction intermediate. The same reactions with alkyl dibromoethenes prepared from octanal and cyclohexane carboxaldehyde were very slow. No reaction occurred after 24 h and undesired products were noticeable after 40 h with no expected imidazoline detected. The reaction of **1** with *N*-methylethylenediamine yielded the corresponding *N*-methyl imidazoline in 65% yield together with a small amount of unknown by-products.[11]

Next, we have tested several oxidation methods to convert imidazoline into imidazole with dehydrogenation catalysts or reagents such as Pd, DDQ or MnO_2[12–15] and found that the Swern oxidation reaction[16] gave a reasonable yield of the desired imidazoles (Table 1). For entry 11, the crude imidazoline product was not purified and used directly for the dehydrogenation reaction because a significant decrease in the yield was observed after unsuccessful purification of the crude imidazoline with silica gel column chromatography. Thus, a better yield of the imidazole product was obtained using the crude imidazoline in the Swern oxidation. An oxidation reaction of 2-(4-nitrophenyl)methylimidazole with MnO_2 resulted in the further oxidation at the benzylic position to give 2-(4-nitrobenzoyl)imidazoline in about 20% yield and other unidentified products (not shown). No dehydrogenation reaction was successful with Pd catalyst or DDQ at room temperature.

A plausible explanation for the reaction results of aryl dibromoethenes with ethylenediamine is shown in Scheme 2. The dehydrobromination reaction occurs to give alkynyl bromide **5** under the reaction conditions. A similar dehydrobromination mechanism for the formation of



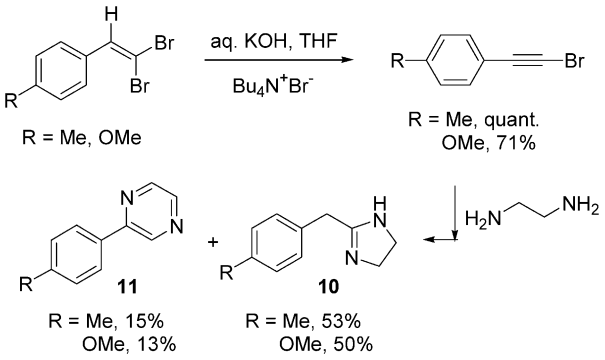
Scheme 2. A probable mechanism for the formation of imidazoline and pyrazine.

alkynyl halide was proposed with quaternary ammonium hydroxide.[17] A substitution reaction of **5** with ethylenediamine would result in ynamine **6**[18] that can undergo an addition reaction to the triple bond in either way, path 'a' or 'b'. A 6-*endo* mode of cyclization via path 'b' yields tetrahydropyrazine **9** while a 5-*exo* type of ring closure via path 'a' produces imidazoline **8** after equilibration with the initial addition intermediate **7**.[19] A similar ynamine intermediate was suggested for the formation of imidazolines from the reaction of ynamine of aziridine with primary amines.[8a] In situ air oxidation of **9** would give the more stable product, pyrazine **4**.

We have tested the possible involvement of alkynyl bromide as a reaction intermediate by an independent reaction of alkynyl bromide with ethylenediamine (Scheme 3). The required alkynyl bromides were prepared separately according to the literature.[20] Treatment of alkynyl bromides having an electron-donating group with ethylenediamine gave a mixture of imidazoline **10** and pyrazine **11** as products. Heating the reaction mixture to 50 °C or under reflux increased the yield of each product by about 5%. It was worthy to note that no significant amount of pyrazine was detected from alkynyl bromides with an electron-withdrawing group or an *ortho* substituent (not shown). Presumably, the electron-withdrawing group makes the α-carbon attached to the amine more electrophilic to the incoming amine and the *ortho* substituent seems to increase steric hindrance for the nucleophilic attack at the β-carbon by the amine (Scheme 2). Another thing to note is the facile oxidation of partially saturated pyrazine **9** to fully unsaturated pyrazine **4**. We could not isolate or even detect **9** in the reaction mixture at all. In contrast, no autoxidation product of partially saturated imidazole **7** or **8** was observed in either reaction, that is, one-step or two-step reaction (Schemes 2 or 3).

3. Conclusion

We have established that a novel transformation of aryl dibromoethenes into the corresponding 2-arylmethyl substituted imidazolines can be done efficiently under mild conditions and the selective oxidation of the imidazoline ring is possible to give the corresponding imidazole with the Swern oxidation in the presence of the reactive benzylic group. The methods described in the present study would be a good and mild way to prepare pharmaceutically important imidazoline and imidazole derivatives.



Scheme 3. Independent synthesis of imidazoline and pyrazine from alkynyl bromide.

4. Experimental

4.1. General

Materials were obtained from commercial suppliers and used without further purification. For anhydrous solvents, dichloromethane was distilled from calcium hydride immediately prior to use. THF and 1,4-dioxane were distilled from sodium/benzophenone ketyl. All glassware, syringes, needles, and magnetic bars used in moisture-sensitive reactions were oven-dried at 120 °C for at least 4 h and stored in desiccators until use. Upon workup, solvent was removed with a rotary evaporator and then with a high vacuum pump. Reactions were monitored with TLC. Commercially available TLC plates (silica gel, 5–25 μm) were visualized under UV light (254 or 365 nm) and then with a molybdophosphoric acid or ninhydrin stain. The R_f values of aryl dibromoethenes and imidazolines were measured with hexane/EtOAc (4:1) and CH_2Cl_2/MeOH (4:1), respectively. For pyrazines and imidazoles, pure EtOAc was used for measurement of the R_f value, unless stated otherwise. Flash column chromatography was carried out on Kieselgel 60 (Merck). ^1H and ^{13}C NMR spectra were measured at 300 and 75 MHz, respectively, in $CDCl_3$ unless stated otherwise and data were reported as follows in ppm (δ) from the internal standard (TMS, 0.0 ppm); chemical shift (multiplicity, integration, coupling constant (J) in Hz).

4.2. General procedure for synthesis of 2-arylmethylimidazoline

To a solution of ethylenediamine (5 mL) was added aryl dibromoethene (0.50 mmol) at room temperature. After stirring for the indicated time in Table 1, the resulting mixture was concentrated under reduced pressure to remove excess ethylenediamine. An aq ammonia (20 mL) solution was added to the residue and the resulting mixture was extracted with chloroform (3×10 mL). The combined organic layers were dried over anhydrous $MgSO_4$ and concentrated under reduced pressure to give the crude residue. The crude product was chromatographed on silica gel and elution with ethyl acetate afforded the corresponding pyrazine, if any. Further elution with a solution of dichloromethane, ethanol and triethylamine (7:2:1) yielded the corresponding pure imidazoline.

4.2.1. 2-(4-Nitrophenyl)methylimidazoline. Yield (83 mg, 81%); violet solid; mp 135–137 °C; R_f 0.49; ^1H NMR δ 3.62 (s, 4H), 3.69 (s, 2H), 7.47 (d, 2H, J=8.7 Hz), 8.19 (d, 2H, J=8.7 Hz); ^{13}C NMR δ 36.3, 50.5 (br), 124.3, 130.2, 144.3, 147.4, 165.0; HRMS (CI) calcd for $C_{10}H_{12}N_3O_2$ 206.0929 (M^++1), found 206.0925.

4.2.2. 2-(2-Nitrophenyl)methylimidazoline. Yield (92 mg, 90%); pale yellowish solid; mp 118–120 °C; R_f 0.48; ^1H NMR δ 3.58 (s, 4H), 3.86 (s, 2H), 4.54 (br s, 1H), 7.44 (ddd, 1H, J=8.3, 7.3, 1.1 Hz), 7.52 (dd, 1H, J=8.3, 1.1 Hz), 7.60 (ddd, 1H, J=8.3, 7.3, 1.1 Hz), 8.01 (dd, 1H, J=8.3, 1.1 Hz); ^{13}C NMR δ 33.4, 49.9 (br), 125.0, 128.2, 131.5,

132.8, 133.5, 148.9, 165.0; HRMS (EI) calcd for $C_{10}H_{11}N_3O_2$ 205.0851, found 205.0854. Anal. Calcd for $C_{10}H_{11}N_3O_2$: C, 58.53; H, 5.40; N, 20.48. Found: C, 58.52; H, 5.50; N, 20.48.

4.2.3. 2-(4-Cyanophenyl)methylimidazoline. Yield (86 mg, 93%); pale yellowish solid; mp 172–174 °C; R_f 0.48; ^{1}H NMR δ 3.61 (br s, 4H), 3.64 (s, 2H), 7.41 (d, 2H, J=8.3 Hz), 7.63 (d, 2H, J=8.3 Hz); ^{13}C NMR δ 33.5, 47.4 (br), 108.3, 116.1, 127.1, 129.9, 139.1, 162.3; HRMS (CI) calcd for $C_{11}H_{12}N_3$ 186.1031 (M^++1), found 186.1034.

4.2.4. 2-(4-Trifluoromethylphenyl)methylimidazoline. Yield (108 mg, 95%); pale yellowish solid; mp 100–102 °C; R_f 0.48; ^{1}H NMR δ 3.61 (br s, 4H), 3.66 (s, 2H), 7.41 (d, 2H, J=8.2 Hz), 7.60 (d, 2H, J=8.2 Hz); ^{13}C NMR 35.7, 49.7, 124.0 (q, J=270.0 Hz), 125.5 (q, J=3.8 Hz), 129.1, 129.2 (q, J=32.1 Hz), 140.1 (q, J=1.2 Hz), 165.4; HRMS (CI) calcd for $C_{11}H_{12}N_2F_3$ 229.0952 (M^++1), found 229.0952.

4.2.5. 2-(2-Trifluoromethylphenyl)methylimidazoline. Yield (106 mg, 93%); pale yellowish solid; mp 87–89 °C; R_f 0.48; ^{1}H NMR δ 3.59 (br s, 4H), 3.77 (s, 2H), 7.36–7.39 (m, 1H), 7.51–7.53 (m, 2H), 7.66 (d, 1H, J=7.7 Hz); ^{13}C NMR δ 32.3, 49.7 (br), 124.2 (q, J=271.4 Hz), 125.7 (q, J=5.6 Hz), 126.9, 128.3 (q, J=29.6 Hz), 131.2, 131.9, 134.6 (q, J=1.2 Hz), 165.1; HRMS (CI) calcd for $C_{11}H_{12}N_2F_3$ 229.0952 (M^++1), found 229.0957. Anal. Calcd for $C_{11}H_{11}N_2F_3$: C, 57.89; H, 4.86; N, 12.28. Found: C, 57.82; H, 4.97; N, 11.95.

4.2.6. 2-(4-Chlorophenyl)methylimidazoline. Yield (92 mg, 95%); pale yellowish solid; mp 138–140 °C; R_f 0.47; ^{1}H NMR δ 3.60 (s, 6H), 7.22 (d, 2H, J=8.3 Hz), 7.30 (d, 2H, J=8.3 Hz); ^{13}C NMR (acetone-d_6) δ 35.6, 50.6 (br), 129.0, 131.5, 132.5, 137.2, 167.2; HRMS (CI) calcd for $C_{10}H_{12}N_2Cl$ 195.0689 (M^++1), found 195.0690. Anal. Calcd for $C_{10}H_{11}N_2Cl$: C, 61.70; H, 5.70; N, 14.39. Found: C, 61.76; H, 5.77; N, 14.17.

4.2.7. 2-(2-Chlorophenyl)methylimidazoline. Yield (92 mg, 95%); yellowish solid; mp 132–134 °C; R_f 0.48; ^{1}H NMR δ 3.59 (br s, 4H), 3.75 (s, 2H), 7.19–7.25 (m, 2H), 7.35–7.40 (m, 2H); ^{13}C NMR δ 33.7, 49.9 (br), 127.2, 128.5, 129.5, 131.0, 134.0, 134.2, 165.3; HRMS (CI) calcd for $C_{10}H_{12}N_2Cl$ 195.0689 (M^++1), found 195.0689. Anal. Calcd for $C_{10}H_{11}N_2Cl$: C, 61.70; H, 5.70; N, 14.39. Found: C, 62.00; H, 5.78; N, 14.40.

4.2.8. 2-Benzylimidazoline. Yield (59 mg, 75%); light brown oil; R_f 0.49; ^{1}H NMR δ 3.59 (br s, 4H), 3.71 (s, 2H), 6.73 (br s, 1H), 7.22–7.37 (m, 5H); ^{13}C NMR δ 35.0, 48.3, 127.1, 128.7, 128.9, 135.1, 167.3; HRMS (CI) calcd for $C_{10}H_{13}N_2$ 161.1079 (M^++1), found 161.1079.

4.2.9. 2-(4-Methylphenyl)methylimidazoline. Yield (55 mg, 63%); pale yellowish solid; mp 172–174 °C; R_f 0.52; ^{1}H NMR δ 2.34 (s, 3H), 3.96 (br s, 4H), 4.18 (s, 2H), 7.18 (d, 2H, J=8.2 Hz), 7.29 (d, 2H, J=8.2 Hz); ^{13}C NMR 21.1, 32.0, 44.6, 128.9, 129.6, 129.9, 138.0, 170.8; HRMS (CI) calcd for $C_{11}H_{15}N_2$ 175.1235 (M^++1), found 175.1236.

4.2.10. 2-(2-Methylphenyl)methylimidazoline. Yield (80 mg, 92%); yellowish solid; mp 77–79 °C; R_f 0.53; ^{1}H NMR δ 2.33 (s, 3H), 3.58 (br s, 4H), 3.63 (s, 2H), 7.18–7.19 (m, 4H); ^{13}C NMR δ 19.4, 34.1, 49.8, 126.2, 127.3, 130.0, 130.4, 134.4, 137.0, 166.0; HRMS (CI) calcd for $C_{11}H_{15}N_2$ 175.1235 (M^++1), found 175.1236. Anal. Calcd for $C_{11}H_{14}N_2$: C, 75.82; H, 8.10; N, 16.80. Found: C, 75.43; H, 8.13; N, 16.23.

4.2.11. 2-(2-Methoxyphenyl)methylimidazoline. Yield (52 mg, 55%); pale yellowish oil; R_f 0.51; ^{1}H NMR δ 3.46 (br s, 1H), 3.55 (br s, 4H), 3.62 (s, 2H), 3.87 (s, 3H), 6.88–6.96 (m, 2H), 7.23–7.28 (m, 2H); ^{13}C NMR δ 30.5, 50.1 (br), 55.4, 110.5, 120.9, 124.6, 128.3, 130.7, 157.0, 166.9; HRMS (CI) calcd for $C_{11}H_{15}N_2O$ 191.1184 (M^++1), found 191.1183.

4.2.12. 2-(4-Methylphenyl)pyrazine. Yield (13 mg, 15%); yellow solid; mp 125–127 °C; R_f 0.54; ^{1}H NMR δ 2.43 (s, 3H), 7.33 (d, 2H, J=8.0 Hz), 7.92 (d, 2H, J=8.0 Hz), 8.48 (d, 1H, J=2.6 Hz), 8.61 (dd, 1H, J=2.6, 1.6 Hz), 9.01 (d, 1H, J=1.6 Hz); ^{13}C NMR δ 21.4, 126.8, 129.8, 133.6, 140.1, 142.0, 142.6, 144.1, 152.9; HRMS (CI) calcd for $C_{11}H_{11}N_2$ 171.0922 (M^++1), found 171.0923. Anal. Calcd for $C_{11}H_{10}N_2$: C, 77.62; H, 5.92; N, 16.46. Found: C, 78.00; H, 6.11; N, 16.35.

4.2.13. 2-(4-Methoxyphenyl)pyrazine. Yield (12 mg, 13%); pale yellowish solid; mp 104–105 °C; R_f 0.50; ^{1}H NMR δ 3.88 (s, 3H), 7.04 (d, 2H, J=8.6 Hz), 7.99 (d, 2H, J=8.6 Hz), 8.44 (d, 1H, J=2.6 Hz), 8.59 (m, 1H), 8.98 (m, 1H); ^{13}C NMR δ 55.4, 114.5, 128.3, 128.9, 141.6, 142.1, 144.0, 152.5, 161.2; HRMS (CI) calcd for $C_{11}H_{11}N_2O$ 187.0871 (M^++1), found 187.0873. Anal. Calcd for $C_{11}H_{10}N_2O$: C, 70.95; H, 5.41; N, 15.04. Found: C, 71.07; H, 5.51; N, 15.02.

4.3. General procedure for synthesis of 2-arylmethylimidazole

To a solution of CH_2Cl_2 (20 mL) and DMSO (0.17 mL, 1.25 mmol) was added oxalyl chloride (1.25 mL of 2 M solution in CH_2Cl_2, 1.25 mmol) at −78 °C under N_2 atmosphere. After stirring for 20 min, a solution of the purified or crude imidazoline (0.50 mmol) in CH_2Cl_2 (15 mL) was added to the reaction mixture. After stirring for 50 min, TEA (0.71 mL, 2.5 mmol) was added and then the reaction mixture was warmed to room temperature. After stirring for 50 min, an aq ammonia solution (20 mL) was added and the resulting mixture was extracted with $CHCl_3$ (3×10 mL). The combined organic layers were washed with brine (2×20 mL), dried with anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was eluted with ethyl acetate only to give the corresponding imidazoles with silica gel column chromatography.

4.3.1. 2-(4-Nitrophenyl)methylimidazole. Yield (62 mg, 75%); pale yellowish solid; mp 190 °C; R_f 0.11; ^{1}H NMR δ 4.23 (s, 2H), 7.02 (s, 2H), 7.42 (d, 2H, J=8.8 Hz), 8.19 (d, 2H, J=8.8 Hz); ^{13}C NMR (methanol-d_4) δ 32.6, 120.7, 122.5, 128.5, 144.6, 144.7, 146.1; HRMS (CI) calcd for $C_{10}H_{10}N_3O_2$ 204.0773 (M^++1), found 204.0773.

4.3.2. 2-(2-Nitrophenyl)methylimidazole. Yield (67 mg, 73%); pale yellowish solid; mp 125–126 °C; R_f 0.13; ^{1}H NMR δ 4.35 (s, 2H), 6.97 (br s, 2H), 7.39–7.44 (m, 1H), 7.58–7.60 (m, 2H), 7.97 (d, 1H, J=7.9 Hz); ^{13}C NMR (methanol-d_4) δ 29.7, 120.0, 123.1, 126.5, 130.5, 131.0, 131.7, 143.4, 147.3; HRMS (EI) calcd for $C_{10}H_9N_3O_2$ 203.0695, found 203.0697. Anal. Calcd for $C_{10}H_9N_3O_2$: C, 59.11; H, 4.46; N, 20.68. Found: C, 59.25; H, 4.50; N, 20.70.

4.3.3. 2-(4-Cyanophenyl)methylimidazole. Yield (56 mg, 66%); white solid; mp 150–151 °C; R_f 0.10; ^{1}H NMR (acetone-d_6) δ 4.16 (s, 2H), 6.96 (s, 2H), 7.48 (d, 2H, J=8.2 Hz), 7.69 (d, 2H, J=8.2 Hz); ^{13}C NMR δ (acetone-d_6) δ 35.2, 111.0, 119.4, 130.5, 133.0, 145.4, 146.0; HRMS (CI) calcd for $C_{11}H_{10}N_3$ 184.0875 ($M^+ + 1$), found 184.0879. Anal. Calcd for $C_{11}H_9N_3$: C, 72.11; H, 4.95; N, 22.94. Found: C, 72.01; H, 5.07; N, 22.55.

4.3.4. 2-(4-Trifluoromethylphenyl)methylimidazole. Yield (62 mg, 58%); white solid; mp 124–125 °C; R_f 0.11; ^{1}H NMR δ 4.19 (s, 2H), 7.00 (s, 2H), 7.37 (d, 2H, J=8.1 Hz), 7.59 (d, 2H, J=8.1 Hz); ^{13}C NMR (acetone-d_6) δ 35.0, 125.4 (q, J=270.0 Hz), 126.0 (q, J=3.8 Hz), 128.9 (q, J=32.3 Hz), 130.1 (br), 144.4, 146.5; HRMS (CI) calcd for $C_{11}H_{10}N_2F_3$ 227.0796 ($M^+ + 1$), found 227.0794.

4.3.5. 2-(2-Trifluoromethylphenyl)methylimidazole. Yield (78 mg, 74%); white solid; mp 148–149 °C; R_f 0.15; ^{1}H NMR δ 4.26 (s, 2H), 6.95 (s, 2H), 7.34 (t, 1H, J=7.9 Hz), 7.35 (d, 1H, J=7.9 Hz), 7.47 (t, 1H, J=7.9 Hz), 7.65 (d, 1H, J=7.9 Hz); ^{13}C NMR δ 31.2, 121.9 (br), 124.4 (q, J=272.0 Hz), 125.9 (q, J=5.6 Hz), 126.8, 128.2 (q, J=29.6 Hz), 131.2, 132.1, 136.2, 145.6; HRMS (CI) calcd for $C_{11}H_{10}N_2F_3$ 227.0796 ($M^+ + 1$), found 227.0800.

4.3.6. 2-(4-Chlorophenyl)methylimidazole. Yield (53 mg, 58%); light yellowish solid; mp 158–159 °C; R_f 0.11; ^{1}H NMR δ 4.10 (s, 2H), 7.00 (br s, 2H), 7.19 (d, 2H, J=8.5 Hz), 7.31 (d, 2H, J=8.5 Hz); ^{13}C NMR (methanol-d_4) δ 31.7, 119.9, 126.9, 128.4, 130.7, 135.2, 145.0; HRMS (CI) calcd for $C_{10}H_{10}N_2Cl$ 193.0532 ($M^+ + 1$), found 193.0534. Anal. Calcd for $C_{10}H_9N_2Cl$: C, 62.35; H, 4.71; N, 14.54. Found: C, 62.26; H, 4.81; N, 14.11.

4.3.7. 2-(2-Chlorophenyl)methylimidazole. Yield (62 mg, 68%); light yellowish solid; mp 123–124 °C; R_f 0.13; ^{1}H NMR δ 4.24 (s, 2H), 6.96 (br s, 2H), 7.19–7.24 (m, 2H), 7.30–7.33 (m, 1H), 7.37–7.41 (m, 1H); ^{13}C NMR δ 32.6, 121.8, 127.2, 128.3, 129.5, 130.8, 133.7, 135.5, 145.7; HRMS (EI) calcd for $C_{10}H_9N_2Cl$ 192.0454, found 192.0454. Anal. Calcd for $C_{10}H_9N_2Cl$: C, 62.35; H, 4.71; N, 14.54. Found: C, 62.59; H, 4.84; N, 14.52.

4.3.8. 2-Benzylimidazole. Yield (50 mg, 84%); brown solid; mp 120–121 °C; R_f 0.13; ^{1}H NMR (methanol-d_4) δ 4.06 (s, 2H), 6.97 (br s, 2H), 7.20–7.31 (m, 5H); ^{13}C NMR (methanol-d_4) δ 33.0, 120.4, 125.8, 127.6, 127.8, 137.0, 146.5; HRMS (CI) calcd for $C_{10}H_{11}N_2$ 159.0922 ($M^+ + 1$), found 159.0919. Anal. Calcd for $C_{10}H_{10}N_2$: C, 75.92; H, 6.37; N, 17.71. Found: C, 76.29; H, 6.73; N, 17.29.

4.3.9. 2-(4-Methylphenyl)methylimidazole. Yield (70 mg, 89%); pale yellowish solid; mp 106–107 °C; R_f 0.10; ^{1}H NMR δ 2.34 (s, 3H), 4.09 (s, 2H), 6.95 (br s, 2H), 7.14 (br s, 4H); ^{13}C NMR (methanol-d_4) δ 21.0, 34.6, 122.3, 129.4, 130.2, 135.9, 137.4, 148.5; HRMS (CI) calcd for $C_{11}H_{13}N_2$ 173.1079 ($M^+ + 1$), found 173.1079. Anal. Calcd for $C_{11}H_{12}N_2$: C, 76.71; H, 7.02; N, 16.27. Found: C, 76.76; H, 7.11; N, 16.23.

4.3.10. 2-(2-Methylphenyl)methylimidazole. Yield (53 mg, 67%); brown solid; mp 146–147 °C; R_f 0.11; ^{1}H NMR δ 2.23 (s, 3H), 4.13 (s, 2H), 6.95 (br s, 2H), 7.20 (br s, 4H); ^{13}C NMR (methanol-d_4) δ 17.5, 31.1, 120.3 (br), 125.1, 125.9, 128.2, 129.2, 135.1, 135.5, 145.9; HRMS (CI) calcd for $C_{11}H_{13}N_2$ 173.1079 ($M^+ + 1$), found 173.1078. Anal. Calcd for $C_{11}H_{12}N_2$: C, 76.71; H, 7.02; N, 16.27. Found: C, 76.68; H, 7.10; N, 16.29.

4.3.11. 2-(4-Methoxyphenyl)methylimidazole. Yield (35 mg, 53%); brown solid; mp 124–125 °C; R_f 0.13; ^{1}H NMR (acetone-d_6) δ 3.74 (s, 3H), 3.95 (s, 2H), 6.82 (d, 2H, J=8.8 Hz), 6.89 (br s, 2H), 7.16 (d, 2H, J=8.8 Hz); ^{13}C NMR (methanol-d_4) δ 34.3, 55.7, 115.0, 122.4 (br), 130.5, 131.1, 148.8, 160.0; HRMS (CI) calcd for $C_{11}H_{13}N_2O$ 189.1028 ($M^+ + 1$), found 189.1029. Anal. Calcd for $C_{11}H_{12}N_2O$: C, 70.19; H, 6.43; N, 14.88. Found: C, 70.11; H, 6.67; N, 14.66.

4.3.12. 2-(2-Methoxyphenyl)methylimidazole. Yield (39 mg, 75%); white solid; mp 122–124 °C; R_f 0.11; ^{1}H NMR (methanol-d_4) δ 3.78 (s, 3H), 4.03 (s, 2H), 6.84 (ddd, 1H, J=8.7, 7.5, 1.1 Hz), 6.91 (dd, 1H, J=7.5, 1.1 Hz), 7.04 (dd, 1H, J=7.5, 1.7 Hz), 7.19 (ddd, 1H, J=8.7, 7.5, 1.7 Hz); ^{13}C NMR δ 29.6, 55.8, 111.5, 121.6, 122.2, 127.1, 129.3, 130.9, 148.2, 158.5; HRMS (CI) calcd for $C_{11}H_{13}N_2O$ 189.1028 ($M^+ + 1$), found 189.1030. Anal. Calcd for $C_{11}H_{12}N_2O$: C, 70.19; H, 6.43; N, 14.88. Found: C, 70.35; H, 6.50; N, 15.00.

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11. The reaction was much cleaner in a mixed solvent system (4:1 CH_2Cl_2:*N*-methylethylenediamine) to give the desired product: sticky violet oil; R_f 0.55 (17:2:1 CH_2Cl_2:EtOH:TEA); ^{1}H NMR δ 2.73 (s, 3H), 3.31 (t, 2H, J=9.4 Hz), 3.69 (s, 2H), 3.71 (t, 2H, J=9.4 Hz), 7.46 (d, 2H, J=8.7 Hz), 8.19 (d, 2H, J=8.7 Hz); ^{13}C NMR δ 33.9, 41.1 52.2, 53.0, 123.5, 129.5, 143.6, 147.6, 165.0; MS (EI) *m*/*z* (%): 219 (M^+, 56) 218 (100), 172 (30), 136 (18), 83 (6).
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