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Microwave-Assisted Dry Synthesis of 2-Amino-1H-imidazoles Supported by a Natural Clay

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ABSTRACT

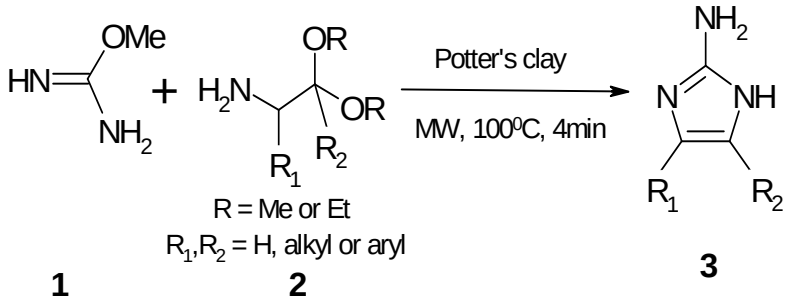
A new and efficient solid natural clay supported microwave-assisted protocol for the preparation of 2-amino-imidazole was developed. Starting from cheap commodities O-methyl-iso-urea and acetals or ketals of α–amino carbonyl compounds the desired product is isolated through a very simple work-up in a good yield. Use of solid acid clay catalyst instead of strong mineral acids under solvent-free condition is a major significance of this method. This new procedure overcomes several technical and environmental problems of the traditional approaches to this molecule and is therefore very attractive for large-scale preparation.

Key Words: 2-aminoimidazoles,O-methyl-iso-urea, acetals or ketals of α–amino carbonyl compounds, natural kaolinite clay, microwave assisted reactions.

INTRODUCTION

2-Aminoimidazoles constitute an important class of heterocyclesbecause they are found in many pharmacologicallyactive substances [1]and in various marine metabolites [2], someof which are potent antagonists of serotonergic and histaminergicreceptors [3a]. The unsubstituted 2-aminoimidazole is the major starting material for the synthesis of azomycin and its homologs having potent antibacterial and antiprotozoal activities [3b,3c]. It is also used as the substrate for the synthesis of misonidazole, which play important role as drugs in chemotherapy [3d]. Because of these interesting biologicalproperties and synthetic utility, numerous synthetic routes to 2-aminoimidazoleshave been reported [4]. Among them, however, only a fewdescribe the direct synthesis of unsubstituted 2-aminoimidazoles. Probably the most popular and the earliest method involves the condensation of α-aminocarbonylcompounds with cyanamide or isothioureas [4b, 4f].However, this reaction is strongly pH-sensitive and can lead to the self- condensation of α-aminoaldehydes or ketones resulting in the formation of symmetrical pyrazines [4g, 4h].Another procedure is the cyclocondensation of aldehydes andguanidine nitrate using sodium cyanide and supportedaluminum oxide [4c], which provides 2-aminoimidazoles with identical substituents on positions 4 and 5 of the ringstructure. Ohta and co-workers performed the synthesis of

polysubstituted 2-aminoimidazoles via functionalization of the imidazole ring [5]. Other general applicable strategies involve the reaction of α-diketones with guanidine [6], the reaction of α -halo ketones with *N*-acetylguanidine [7], and the iminophosphoranemediated cyclization of α-azido esters [8]. An alternative strategy for the synthesis of 2-aminoimidazoles involves the formation of imidazo[1,2-*a*]pyrimidines, followed by cleavage of the pyrimidine ring upon treatment with strong nucleophiles as hydrazine or amines [9 – 13]. Among these methodologies, the latter procedure appears to be the most straightforward and avoidsthe need for reduction or ring cleavage. However thismethodology requires long reaction times for both steps ofthe reaction, and the yields of the substituted *N*-(1H-imidazol-2-yl)acetamidesobtained vary with the substrate used. In addition this procedure though yields only *N*-1-unsubstituted 2-aminoimidazoles, on the contrary, when the corresponding *N*-1-substituted imidazo[1,2-*a*]pyrimidinium salt should be cleaved, this would result in the formation of *N*-1-substituted 2-aminoimidazoles [14]. Work by Denis S. Ermolat'v*et.al*. for the synthesis of polysubstituted 2 aminoimidazolesinvolves harsh treatment usingconcentrated HBr or polyphosphoric acid at 140^0C [15, 3c]. Thusfinding an improved procedure that is viable for librarysynthesis will be desirable.



Scheme1. Microwave-assisted synthesis of 2-amino-1H-imidazoles

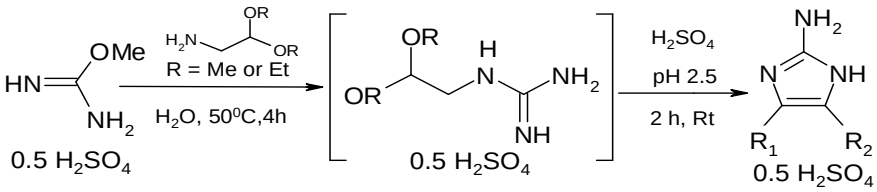
Microwave-assisted organic synthesis (MAOS) in conjunction with solid clay catalysts, a growingarea in synthetic organic chemistry, is based on the empiricalobservation that some reactions proceed faster and result inhigher yields under microwave irradiation than under conventionalheating [16]. In particular, the clay catalysts make the reaction process more convenient, economical, environmentally benign, and act as both Bronsted and Lewis acids in their natural and ion-exchanged forms, enabling them to function as efficient catalysts for various transformations [17]. Montmorillonite clays have been used as catalysts for a number of organic reactions and offer several advantages over classical acids: strong acidity, noncorrosive properties, recyclability, low cost, mild reaction conditions, high yields and selectivity, and the ease of setup and workup [18]. Our present aim is to make it convenient to use locally available traditional potter's clay of Assam, India as catalysts in organic synthesis. Recently, in one of our works, characterization of this potter's clay using XRD, SEM-EDXRA, thermal analysis, FT-IR spectra and elemental analysis revealed it to be an iron rich clay with kaolinite as the major component [19]. The potent catalytic activity of this clay is already eatablished by the synthesis of a diverse set of imidazolinones and pyrimidinones using this natural clay [19]. Although MAOS has been applied to the synthesis of various heterocyclic compounds, to our knowledge, this technique has not been applied to the synthesis of 2-aminoimidazoles **3** via the reaction of O-methyl-iso-urea with acetalsor ketals of α–amino carbonyl compounds. Hilmar Weinmann*et. al.* reported similar work but this suffers from the use of concentrated H_2SO_4 for maintenance of very high pH along with long reaction time and low yield rather it is a two-step process getting only 2-aminoimidazole [20]. We therefore investigated the use of microwave irradiation supported by the kaolinite natural clay to promote and activate this synthetic strategy and as a

result, we now wish to present an ameliorated, rapid, high yielding and convenient one-pot single-step protocol for the synthesis of a considerable number of 2-amino-1H-imidazoles**3** (Scheme 1), applying microwave irradiation supported by a traditional potter's clay without using any solvent.

MATERIALS AND METHODS

Experimental

For comparison purposes, we began our investigation by carrying out the synthesis of simple unsubstituted 2-aminoimidazoleusing the conventional procedure described by Hilmar Weinmann*et.al*.[20].(Scheme 2). Keeping in mind the strong acidic behaviour of clays, we have tried to replace H_2SO_4 used in the second step by the mentioned natural clay in this



Scheme 2.Two-step conventional synthesis of 2-aminoimidazole

conventional method. Satisfactory results were obtained resulting a good amount of 2-aminoimidazole. One crucial point regarding the yield of the final product is the time gap between the two steps. We were to wait for a considerable time for the reaction mixture to cool down to the room temperature for addition of H_2SO_4 in the second step. It was observed that unfortunately with increase in the time gap between the two steps the amount of yield of the final product decreased disappointingly, probably which is due to the question of stability of the intermediate product. This led us to investigate the protocol in a one-pot single-step manner to overcome this obstacle. Initially the reaction was done by mixing 1mmol of O-methyl-isourea, 1mmol of 2-aminoacetaldehyde-acetal and 0.5g of the clay at 50^0C by conventional heating but only a trace amount of the product was obtained. So the reaction was repeated by irradiating the reaction mixture together in a Microwave reactor.

Table1. Investigation of the Condensation under Conventional Heating and Microwave Irradiation Conditions[a]

Entry	Condition	Amount of clay used(g)	Temp. (^{0}C)	Time(min)	Yield(%)[b]		
					1st cycle	2nd cycle	3rd cycle
1	Reflux in water bath	0.5	50	5 -10	12	12	11
2	Reflux/MW	0.0	50	10	0.0	-	-
3	MW	0.5	50	5	55	54	53
4		0.5	80	10	82	82	81
5		1.0	100	10	94	94	93
6		1.0	150	10	94.5	94	94
7		1.5	150	15	94	93	94

*[a]All reactions were carried out on a 1 mmol scale of O-methyl-isourea with 1 mmol of 2-aminoacetaldehyde-acetal (R_1, R_2 = H, R = Me in substrate **1**) without solvent. [b]Isolated yield after recrystallization ethanol*

However, contrary to the reaction under conventional heating conditions, we found that at 80^0C ceiling temperature the reaction was much faster as monitored by TLC (Table 1, entry 4). A further experiment performed at 100^0C improved substantially the yield of 2-amino-1H-

imidazole and the reaction was completed within 10 min. Finally the optimum amount of the product (94%) was obtained when the temperature was increased to 100^0C (entry 5, table1). Necessity of the clay support is revealed by the fact that no yield was obtained when the reaction was carried out without using the clay (entry 2, table 1). No considerable increase in in the amount of product was observed with further increase in the amount of clay, temperature or reaction time.The recyclability of the clay was investigated by reusing it for three subsequent cycles and its activity was almost intact (**Table 1**).

All chemical reagents were obtained from either Aldrich or Merck and were used without further purification. Melting points were determined using an Electrothermal 9200 digital melting point apparatus and are uncorrected. The microwave-assisted reactions were performed using a CEM Mars X microwave oven equipped with an EST-300 plus temperature probe as sensor. Ramp time was 5 min for all the reactions. Analytical TLC was carried out on precoated plates (Merck silica gel 60, F254) and visualized with UV light or iodine chamber. Flash column chromatograph was performed with silica (Merck, 70–230 mesh). ^{1}H and ^{13}C NMR spectra were measured at 298 K on either a Bruker AMX500 or a Bruker ACF 300 Fourier transform spectrometer and calibrated using residual undeuterated solvent as an internal reference. The following abbreviations were used to explain the multiplicities: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet). The number of protons (*n*) for a given resonance was indicated as *n*H. Mass spectra were performed on Finnigan MAT 95/XL-T spectrometer under electron impact (EI).

Microwave Experiments

A multimode Milestone MicroSYNTH microwave reactor (Laboratory Microwave Systems) was used in the standard configuration as delivered, including proprietary software. Reaction temperatures were monitored by an IR sensor on the outside wall of the reaction vial and a fiber optic sensor inside the reaction vial. All experiments were carried out in sealed microwave process vials (15, 50 mL). After completion of the reaction, the vial was cooled to 25 °C via air jet cooling before opening.

General Procedure for the Synthesis of 2-Amino-1*H*-imidazoles, 2a-2s

1mmol of O-methyl-iso-urea, 1mmol of the acetal or ketal of the α–aminocarbonyl compound were mixed thoroughly with 1g of the clay in a glass mortar. The mixture was transferred to a 20 mL microwave vial and was degassed by passing nitrogen gas through it properly by shaking for 2-3 min. The vial was sealed and exposed to microwave irradiation in Milestone MicroSYNTH multi-mode microwave reactor at 150 W maximum power and a ceiling temperature 100°C for the appropriate time required (TLC monitored). After the mixture was cooled with an air flow for 15 min, it was diluted with H_2O (50 mL), extracted with CH_2Cl_2 (2 × 150 mL), and the combined organic extracts were dried (Na_2SO_4). The solvent was removed under reduced pressure and the residue was subjected to column chromatography on silica gel using 15-20% MeOH-DCM as the eluent.

4-Phenyl-1*H*-imidazol-2-ylamine, 2o

Purification by column chromatography [silica gel, 15% MeOH-DCM] afforded the product **2o** (72 mg, 91%) as an amorphous solid. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 10.46 (br, 1H), 7.58 (d, *J* = 7.5 Hz, 2H), 7.26 (t, *J* = 7.4 Hz, 2H), 7.08 (t, *J* = 7.5 Hz, 1H), 6.97 (s, 1H), 5.33 (br, 2H). ^{13}C NMR (300 MHz, DMSO-*d*6): δ = 150.7, 134.8, 134.1, 128.7 (×2), 125.4, 123.7 (×2), 110.8. DEPT-135 NMR (75 MHz, DMSO-d_6) δ 128.7 (×2), 125.4, 123.7 (×2), 110.8. HRMS (EI): $C_9H_9N_3$calcd 159.0796, found 159.0788.

5-(4-Methoxyphenyl)-1*H*-imidazol-2-ylamine, 2d
Purification by column chromatography [silica gel, 20% MeOH-DCM] afforded the product **2d** (0.75 g, 79%) as an amorphous solid. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 10.27 (br, 1H), 7.50 (br, 2H), 6.85 (d, *J* = 8.2 Hz, 2H), 6.83 (s, 1H), 5.20 (br 2H). ^{13}C NMR (75 MHz, DMSO-d_6): δ = 157.4, 150.5, 128.0, 124.9 (×2), 114.1, 55.3. HRMS (EI): $C_{10}H_{11}N_3O$ calcd 189.0902, found 189.0899.

4-(4-Chlorophenyl)-1*H*-imidazol-2-ylamine, 2f
Purification by column chromatography [silica gel, 15% MeOH-DCM] afforded the product **2f** (0.85 g, 88%) as an amorphous solid. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 10.29 (br, 1H), 7.60 (d, *J* = 8.5 Hz, 2H), 7.31 (d, *J* = 8.5 Hz, 2H), 7.04 (s, 1H), 5.37 (br, 2H). ^{13}C NMR (75 MHz, DMSO-d_6): δ = 150.8, 134.0, 129.5, 128.6 (×2), 125.3 (×2), 110.6. HRMS (EI): $C_9H_8ClN_3$calcd 193.0403, found 193.0400.

4-(4-Bromophenyl)-1*H*-imidazol-2-ylamine, 2e
Purification by column chromatography [silica gel, 15% MeOH-DCM] afforded the product **2e** (1.04 g, 87%) as an amorphous solid. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 10.56 (br, 1H), 7.54 (d, *J* = 7.9 Hz, 2H), 7.44 (d, *J* = 7.8 Hz, 2H), 7.06 (s, 1H), 5.40 (br 2H). ^{13}C NMR (75 MHz, DMSO-d_6): δ = 150.8, 134.3, 133.5, 131.5 (×2), 125.7 (×2), 117.8, 110.7. HRMS (EI): $C_9H_8BrN_3$calcd 236.9902, found 236.9911.

4-(*p*-Tolyl)-1*H*-imidazol-2-ylamine, 2k
Purification by column chromatography [silica gel, 15% MeOH-DCM] afforded the product **2k** (0.69 g, 80%) as an amorphous solid. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 10.14 (br, 1H), 7.48 (d, *J* = 7.6 Hz, 2H), 7.08 (d, *J* = 7.6 Hz, 2H), 6.91 (s, 1H), 5.36 (br, 2H), 2.26 (s, 3H). ^{13}C NMR (75 MHz, DMSO-d_6): δ = 150.6, 134.2, 134.1, 129.2 (×2), 123.7 (×2), 110.2, 21.1. HRMS (EI): $C_{10}H_{11}N_3$calcd 173.0953, found 173.0956.

4-(4-Nitrophenyl)-1*H*-imidazol-2-amine, 2g
Purification by column chromatography [silica gel, 20% MeOH-DCM] afforded the product **2g** (0.92 g, 90%) as an amorphous solid. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 10.80 (br, 1H), 8.12 (d, *J* = 9.0 Hz, 2H), 7.81 (d, *J* = 9.0 Hz, 2H), 7.37 (s, 1H), 5.59 (s, 2H). ^{13}C NMR (75 MHz, DMSO-d_6): δ = 151.9, 144.2, 142.0, 133.2 (br), 124.4 (x2), 123.8 (x2), 115.4 (br). HRMS (EI): $C_9H_8N_4O_2$calcd 204.0647, found 204.0648.

5-(4-Chlorophenyl)-4-phenyl-1*H*-imidazol-2-amine, 2n
Purification by column chromatography [silica gel, 5% MeOH-DCM] afforded the product **2n** (92 mg, 68%) as an amorphous solid. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 10.95 (br, 1H), 8.16 (m, 1H), 7.65–7.13 (m, 8H), 5.40 (s, 2H). ^{13}C NMR (75 MHz, DMSO-d_6): δ = 159.5, 150.8, 133.3, 131.0, 130.5, 129.0, 128.8 (×2), 128.6 (×2), 127.4 (×2), 127.2 (×2), 126.7. HRMS (EI): $C_{15}H_{12}ClN_3$calcd 269.0720, found 269.0715.

4-(4-Chlorophenyl)-5-(4-fluorophenyl)-1*H*-imidazol-2-amine, 2p
Purification by column chromatography [silica gel, 5% MeOH-DCM] afforded the product **2p** (120 mg, 83%) as an amorphous solid. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 11.18 (br, 1H), 7.75–7.02 (m, 8H), 5.54 (s, 2H). ^{13}C NMR (75 MHz, DMSO-d_6): δ = 164.5, 161.3, 161.1, 151.2, 138.2, 131.6, 130.7, 129.6 (×4), 129.1 (×2), 128.9 (×2), 112.3, 111.9, 109.3, 109.0, 104.6, 101.7, 101.3, 101.0. HRMS (EI): $C_{15}H_{11}ClFN_3$calcd 287.0626, found 287.0631.

4-(4-Chlorophenyl)-5-(4-(trifluoromethyl)phenyl)-1*H*-imidazol-2-amine, 2q
Purification by column chromatography [silica gel, 10% MeOH-DCM] afforded the product **2q** (160 mg, 95%) as an amorphous solid. ^{1}H NMR (300 MHz, DMSO-*d*6): δ = 11.08 (br, 1H), 7.63 (d, *J* = 7.6 Hz, 2H), 7.58 (d, *J* = 7.6 Hz, 2H), 7.40 (br, 4H), 5.50 (br, 2H). ^{13}C NMR (75 MHz, DMSO-*d*6): δ = 151.4, 137.4 (×2), 129.3 (×2), 128.9 (×2), 127.1 (×2), 126.5, 126.1, 125.6, 123.0, 104.6. HRMS (EI): C16H11ClF3N3 calcd 337.0594, found 337.0581.

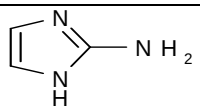
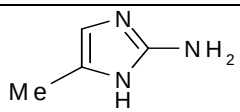
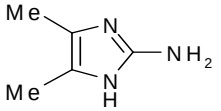
5-(4-Chlorophenyl)-4-*p*-tolyl-1*H*-imidazol-2-amine, 2r
Purification by column chromatography [silica gel, 10% MeOH-DCM] afforded the product **2r**(133 mg, 94%) as an amorphous solid. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 11.01 (br, 1H), 7.40 (d, *J* = 8.2 Hz, 2H), 7.31 (d, *J* = 8.2 Hz, 2H), 7.27 (d, *J* = 8.2 Hz, 2H), 7.14 (d, *J* = 8.2 Hz, 2H), 5.46 (br, 2H), 2.29 (s, 3H). ^{13}C NMR (75 MHz, DMSO-d_6): δ = 150.4, 136.2, 133.5, 130.5 (×2), 129.5 (×2), 129.3, 128.7, 128.5 (×2), 127.5, 127.4, 21.2. HRMS (EI): $C_{16}H_{14}ClN_3$calcd 283.0876, found 283.0877.

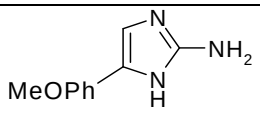
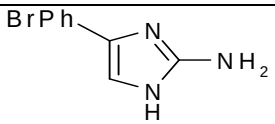
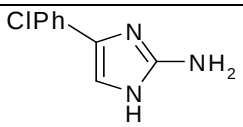
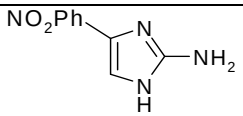
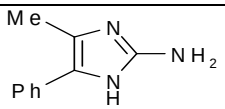
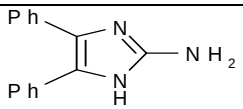
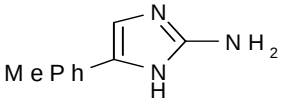
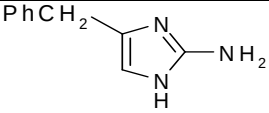
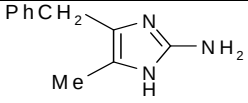
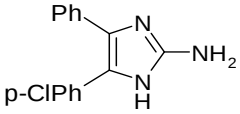
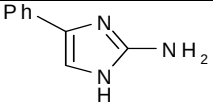
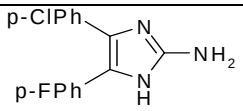
5-(4-Methoxyphenyl)-4-phenyl-1*H*-imidazol-2-amine, 2s
Purification by column chromatography [silica gel, 10% MeOH-DCM] afforded the product **2s** (110 mg, 83%) as an amorphous solid. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 10.77 (br, 1H), 7.91–6.86 (m, 9H), 5.24 (s, 2H), 3.75 (s, 3H). ^{13}C NMR (75 MHz, DMSO-d_6): δ = 159.5, 158.2, 150.2, 129.9, 129.0 (×2), 128.8 (×2), 128.6 (×2), 126.8, 126.0, 115.3, 114.1 (×2), 55.4. HRMS (EI): $C_{16}H_{15}N_3O$ calcd 265.1215, found 265.1216.

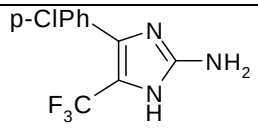
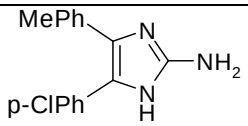
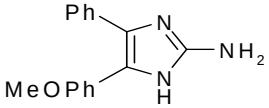
RESULTS AND DISCUSSION

To illustrate the generality of this microwave condition, the reaction was carried out between O-methyl-iso-urea and various acetals or ketals of α–amino carbonyl compounds and we were pleased to observe that the cyclization always proceeded, sometimes with difficulties, to furnish both unsubstituted and substituted *2-amino-1H-imidazoles* in satisfactory yields ranging from 55-95% (**Table 2**). All reactions were carried out on a 1 mmol scale at a ceiling temperature of 100^0C, applying microwave irradiation at 150W maximum power (Table 2). The reactions proceeded smoothly with a very low amount of the starting material left and the products 2a–s were purified by column chromatography using 15-20% MeOH in CH_2Cl_2 as the eluent. The reaction times varied from 5 to 20 min depending on the nature of substituent R_1 and R_2 in the substrate **1** (**Table 2**)**.**

Table 2: Microwave-assisted synthesis of 2-amino-1H-imidazoles[a]

Entry	R_1	R_2	Product(s),3	Time(min)	Yield(%)[b]
2a	H	H		10	94
2b	H	Me		15	92
2c	Me	Me		20	85

2d	H	p-MeOPh		20	79
2e	p-BrPh	H		7	87
2f	p-ClPh	H		6	88
2g	p-NO_2Ph	H		5	90
2h	Me	Ph		25	57
2j	Ph	Ph		30	50
2k	H	p-MePh		20	80
2l	CH_2Ph	H		10	85
2m	CH_2Ph	Me		20	52
2n	Ph	p-ClPh		23	68
2o	Ph	H		20	91
2p	p-ClPh	p-FPh		28	83

2q	p-ClPh	F_3C		25	95
2r	MePh	p-ClPh		15	94
2s	Ph	MeOPh		20	83

[a]*All reactions were performed on a 1-mmol scale in dry conditions.*
All the microwave experiments were performed at a ceiling temperature of 100^{0}C and 150W maximum power.
[b]*All yields are isolated yields.*

It was found that acetals bearing electron donating substituents, for example, p-methoxyphenyl and p-tolyl (Table 2, entries 2d and 2k), require up to 20 min to drive the cyclization to completion. On the contrary, the cyclization of the acetals or ketals bearing electron withdrawing substituents was completed within 5 min (Table 2, entries 2e, 2f, and 2g). Importantly, the nitro function remained intact upon irradiation for the product 4-(4-Nitrophenyl)-1H-imidazol-2-amine, (Table 2, entry 2g) and we have not observed any trace of by-products.

With these results in hand, we developed an elegant onepot, single-step, microwave-assisted protocol for the synthesis of unsubstituted 2-aminoimidazoles along with 4-, 5-, and 4,5-substituted 2-aminoimidazoles starting from readily available O-methyl-iso-urea **1** and acetals or ketals of α–amino carbonyl compounds **2** (Table 2). Upon completion, the reaction mixture was diluted with water and extracted with dichloromethane. Side products could easily be removed by washing the organic phase with water, resulting in nearly pure compounds. The residual clay was washed twice with acetone and distilled water and recycled to use in the subsequent reactions. The yields varied from good to excellent, although in some cases lowered yields were observed (Table 2, entries 2h, 2j and 2m) probably due to the steric constraints of the two bulky substituents R_1 and R_2 without significant electronic effectin the acetal or ketal**2**. Interestingly, applying conventional heating conditions, longer total reaction times (up to 2-4 h) were necessary, resulting in lower yields due to significant decomposition of the starting compounds. Moreover, since the preparation of 2-aminoimidazole **3**under conventional conditions involves the exposure of the intermediatesto strong acids at elevated temperature (Scheme 1), sensitive R_1, R_2 substituents as p-nitrophenyl and *p*-methoxyphenyl are not tolerated. Heterocyclization reaction of acetals and ketals of α-aminocarbonyl compounds are hardly known due to their high reactivity. Nevertheless, we were able to generate the corresponding unsubstituted 2-aminoimidazoles along with 4-, 5-, and 4,5-substituted 2-aminoimidazoles in high yields by applying our microwave-assisted protocol.

CONCLUSION

In conclusion, we have developed a simple and practical procedure for the preparation of 2-aminoimidazole and its differentky substituted homologs. We have investigated the cyclization of O-methyl-iso-urea and various acetals or ketals of α–amino carbonyl compounds and found microwave irradiation supported by a natural kaolinite clay to be very effective in this

regard.The merits of this method are that (a) it is a very simple, one-pot, rapid, high yielding process, (b) natural potter's clay is cheap and available as compared to other catalysts, (c) the method is environmentally benign as it does not require any solvent. Equimolar amounts of the substrates and reagents used typically, avoiding waste and providing very simple experimental and workup procedure. Because of its simplicity, generality, efficacy, cost-effectiveness, environment friendly nature and recyclability of the clay, this method is expected to have wide applicability for the synthesis of 2-aminoimidazole containing alkaloids.

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