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Efficient, green and solvent-free synthesis of tetrasubstituted imidazoles using $SbCl_3/SiO_2$ as heterogeneous catalyst

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Abstract. Antimony trichloride absorbed on silica gel ($SbCl_3/SiO_2$) efficiently catalyses the four-component cyclocondensation of 1,2-diketone, aldehyde, ammonium acetate, and primary amine under solvent-free conditions to afford the corresponding tetrasubstituted imidazoles in high yields. The main merit of this study is introducing a novel catalyst to successful synthesis of a wide range of 1,2,4,5-tetrasubstituted imidazoles for the first time. The proposed method involves features such as simplicity, generality, fairly good efficiency, and reusability of the catalyst.

Keywords. Imidazole; solvent-free conditions; four-component reaction; heterogeneous catalyst; Lewis acid.

1. Introduction

Imidazoles and their derivatives are important compounds that are found in nature and also in biological and chemical systems.[1] They play a major role in pharmacology, for instance histidine, histamine, and biotin.[2] These aromatic hetrocyclic compounds operate as active parts in drugs like Losartan and eprosartan.[3] The substituted imidazoles perform various biological activities such as anti-inflammatory,[4] antiallergic[5] and analgesic activities.[6] Trisubstituted imidazole derivatives are used as organic materials, for example, to resist composition on textile, fluorescent whiteners on textile, optical materials, and photographic materials.[7] In addition, these compounds are employed in agriculture e.g., herbicides, pesticides, fungicides,[8] and plant growth regulators.[9] Therefore, the synthesis of these imidazole derivatives has attracted much attention in organic synthesis. Different methods have been developed to synthesize imidazole derivatives. The synthesis of 1,2,4,5-tetrasubstituted imidazoles are carried out by four-component condensation of an aldehyde, 1,2-diketone, primary amine and ammonium acetate. Recently, some modification has been carried out in the presence of molecular iodine,[10] silica-bonded propylpiperazine N-sulphamic acid (SBPPSA),[11] microwave irradiation,[12] silica gel-$NaHSO_4$,[13] $FeCl_3.6H_2O$,[14] silica-supported Wells–Dawson acid,[15] heteropoly-acids,[16] ionic liquids,[17] DABCO,[18] sodium benzenesulphinate,[19] solid acid nano-catalyst,[20] $HClO_4$-SiO_2,[21] organocatalysis,[22] MCM-41 or p-TsOH,[23] $ZrCl_4$,[24] mercaptopropylsilica (MPS),[25] $BF_3.SiO_2$,[26] and sulphonated carbon/silica functionalized Lewis acids.[27] In addition, they can also be obtained by hetero-cope rearrangement,[28] condensation of imines and acid chlorides,[29] and from diazocarbonyls by N–H insertion reactions of primary ureas.[30]

Antimony (III) chloride has received considerable attention due to its accessibility as inexpensive reagent and easier handling as compared to other metal halides.[31,32] It has emerged as an efficient catalyst in promoting various organic transformations.[33–42] Due to the high toxicity of $SbCl_3$,[43] supported antimony (III) chloride has recently received considerable importance. Recently, use of silica-supported antimony (III) chloride not only because it enables eco-friendly green protocols but also due to the recyclability of the heterogeneous catalyst enhanced reaction rates, the operational simplicity, improved activity, make $SbCl_3/SiO_2$ as an attractive alternative to conventional individual reagents.[44,45] Despite the use of various solid heterogeneous catalysts in literature, silica-supported heterogeneous Lewis acid catalysts, like $SbCl_3/SiO_2$, have not yet been explored with regard to the synthesis of imidazoles. In this paper, we report a simple and

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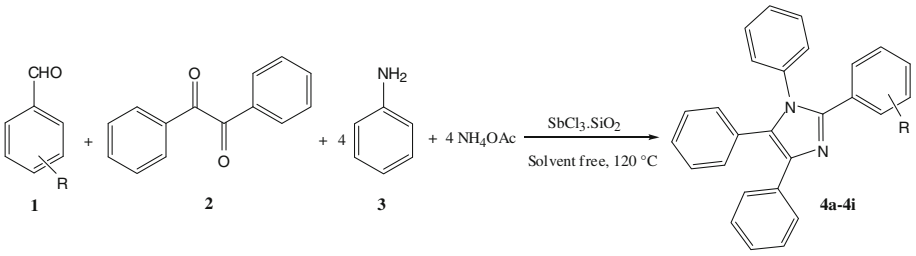
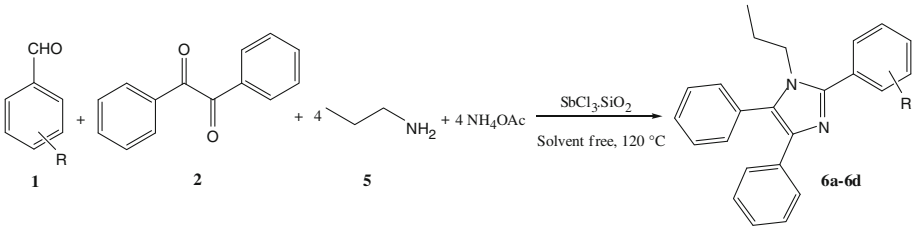


Scheme 1. Synthesize 1,2,4,5-tetrasubstituted imidazoles in the presence of aromatic amine.



Scheme 2. Synthesize 1,2,4,5-tetrasubstituted imidazoles in the presence of aliphatic amine.

efficient method to synthesize 1,2,4,5-tetrasubstituted imidazoles using silica-supported antimony trichloride ($SbCl_3/SiO_2$) as a novel heterogeneous catalyst under solvent-free conditions (schemes 1, 2).

2. Experimental

2.1 *Materials and instruments*

Chemical reagents in high purity were purchased from the Merck Chemical Company. All materials were of commercial reagent grade. Melting points were determined in an open capillary using an Electrothermal Mk3 apparatus. Infrared (IR) spectra were recorded using a Perkin-Elmer FTIR 550 spectrometer. ^{1}H NMR and ^{13}C NMR spectra were recorded in DMSO-d_6 using Bruker DRX-400 spectrometer at 400 and 100 MHz, respectively. The elemental analyses (C, H, N) were obtained from a Carlo ERBA Model EA 1108 analyzer carried out on Perkin-Elmer 240c analyzer. UV spectra were recorded on a Hitachi 200–20 spectrophotometer using spectrophotometric grade chloroform (Baker). Transmission electron microscopy (TEM) was performed with a jeol JEM–2100UHR, operated at 200 KV.

2.2 *Typical procedure for synthesis of silica-supported antimony (III) chloride catalyst*

A mixture of 1 g antimony trichloride ($SbCl_3$), 6 g SiO_2 and 15 mL dried dichloromethane solvent were stirred at room temperature for 120 min. HCl gas evolved from the reaction vessel immediately. The solvent was then removed on a rotary evaporator under reduced pressure to afford white powder of silica-supported antimony (III) chloride (6.44 g). It was applied in the next stage.

2.3 *General procedure for solvent-free synthesis of 1,2,4,5-tetrasubstituted imidazoles by use of $SbCl_3/SiO_2$ catalyst*

In a 50 mL round bottom flask mixture of benzil (1 mmol), ammonium acetate (4 mmol), benzaldehyde (1 mmol) and primary amine (4 mmol) in the presence of 0.1 g $SbCl_3/SiO_2$ catalyst was stirred at 120°C for appropriated time. The progress of the reaction was monitored by TLC. After cooling, the reaction mixture was dissolved in acetone and filtered. The filtrate was concentrated on a rotary evaporator under reduced pressure and the solid product obtained was washed with water and recrystallized from acetone–water. Pure products were obtained in excellent yields.

2.4 *Spectral data*

2.4a *1,2,4,5-Tetraphenyl-1H-imidazole ($C_{27}H_{20}N_2$, **4a**)*: White powder; m.p. 216–218°C; R_f (petroleum ether:ethylacetate): 7:3 (v/v) = 0.71; FTIR (KBr) ν_{max}: 3055 (=C-H aromatic), 1599 (C=C aromatic), 1496 (C=N) cm^{-1}; U.V (CH_3OH) λ_{max}: 286 nm; ^{1}H NMR (400 MHz, DMSO-d_6)δ: 7.16–7.49 (m, 20H, H–Ar) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ: 128.63,

128.70, 130.05, 130.85, 131.02, 131.55, 132.53, 132.67, 132.92, 133.87, 134.26, 134.81, 135.41, 136.23, 137.11, 138.40, 139.54 ppm; Anal. Calcd. for $C_{27}H_{20}N_2$: C 87.07, H 5.41, N 7.52; found: C 87.09, H 5.40, N 6.51%.

2.4b *1,4,5-Triphenyl-2-p-tolyl-1H-imidazole($C_{28}H_{22}N_2$, **4b**)*: Yellow needle solid; m.p. 186–188°C; R_f (petroleum ether:ethylacetate): 7:3 (v/v) = 0.8; FTIR (KBr) ν_{max}: 3047 (=C–H aromatic), 1598 (C=C aromatic), 1493 (C=N) cm^{-1}; U.V (CH_3OH) λ_{max}: 274 nm; ^1H NMR (400 MHz, DMSO-d_6)δ: 2.25 (s, 3H, CH_3), 7.07 (d, J = 8Hz, 2H, H-Ar), 7.08–7.45 (m, 15H, H-Ar), 7.46 (d, J = 8 Hz, 2H, H-Ar) ppm; ^{13}C NMR (100 MHz, DMSO-d_6)δ: 21.20, 126.83, 126.84, 128.03, 128.61, 128.83, 128.90, 129.13, 129.59, 130.92, 131.54, 131.59, 134.92, 137.19, 138.29, 146.61 ppm; Anal. Calcd. for $C_{28}H_{22}N_2$: C 87.02, H 5.72, N 7.27; found: C 87.01, H 5.74, N 7.25%.

2.4c *2-(4-Chlorophenyl)-1,4,5-triphenyl-1H-imidazole ($C_{27}H_{19}ClN_2$, **4c**)*: Cream crystal; m.p. 160–163°C; R_f (petroleum ether:ethylacetate): 7:3 (v/v) = 0.57; FTIR (KBr) ν_{max}: 3050 (=C-H aromatic), 1601 (C=C aromatic), 1505 (C=N), 1065 (C–Cl) cm^{-1}; U.V (CH_3OH) λ_{max}: 296 nm; ^1H NMR (400 MHz, DMSO-d_6)δ: 7.15–7.36 (m, 17H, H-Ar), 7.47 (d, J = 7.4 Hz, 2H, H-Ar) ppm; ^{13}C NMR (100 MHz, DMSO-d_6)δ: 127.30, 127.50, 127.70, 128.0, 128.20, 129.31, 129.70, 129.85, 130.10, 131.54, 132.69, 133.60, 133.68, 145.0, 149.72 ppm; Anal. Calcd. for $C_{27}H_{19}ClN_2$: C 79.70, H 4.71, N 6.88; found: C 79.72, H 4.70, N 6.87%.

2.4d *2-(3,5-Dimethoxyphenyl)-1,4,5-triphenyl-1H-imidazole ($C_{29}H_{24}N_2O_2$, **4d**)*: White powder; m.p. 163–165°C; R_f (petroleum ether:ethylacetate): 7:3 (v/v) = 0.62; FTIR (KBr) ν_{max}: 3057 (=C-H aromatic), 1598 (C=C aromatic), 1498 (C=N), 1159 (C–O–Ar) cm^{-1}; U.V (CH_3OH) λ_{max}: 293 nm; ^1H NMR (DMSO-d_6, 400 MHz) δ: 3.56 (s, 6H, OCH_3), 6.41 (s, 1H, Ar), 6.51 (s, 2H, Ar), 7.15–7.47 (m, 15H, Ar) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 55.5, 100.9, 106.7, 126.8, 126.9, 128.6, 129.9, 129.3, 129.6, 130.8, 131.6, 131.9, 132.4, 134.8, 137.2, 137.2, 146.7, 160 ppm; Anal. Calcd. for $C_{27}H_{20}N_2O$ (388): C 80.07, H 5.96, N 6.87, O 7.03; found: C 80.05, H 5.95, N 6.84, O 7.04%.

2.4e *2-(1,4,5-Triphenyl-1H-imidazol-2-yl)phenol ($C_{27}H_{20}N_2O$, **4e**)*: White powder; m.p. 252–254°C; R_f (petroleum ether:ethylacetate): 7:3 (v/v) = 0.91; FTIR (KBr) ν_{max}: 3448 (OH), 3061 (=C–H aromatic), 1590 (C=C aromatic), 1485 (C=N), 1254 (Ar–O) cm^{-1}; U.V (CH_3OH) λ_{max}: 320 nm; ^1H NMR (400 MHz, DMSO-d_6)δ: 6.54 (t, J = 8.0 1H, H–Ar), 6.65 (d, 1H, H-Ar), 6.93 (d, 1H, H–Ar), 7.16–7.43 (m, 16H, H-Ar), 12.57 (s, 1H, OH) ppm; ^{13}C NMR (100 MHz, DMSO-d_6)δ: 115.30, 122.51, 124.61, 125.48, 126.92, 127.35, 128.90, 129.35, 130.47, 131.74, 135.65, 136.24, 137.61, 139.66, 145.82, 155.72 ppm; Anal. Calcd for $C_{27}H_{20}N_2O$: C 83.48, H 5.19, N, 7.21; found: C 83.46, H 5.20, N 7.22%.

2.4f *4-(1,4,5-Triphenyl-1H-imidazol-2-yl)phenol ($C_{27}H_{20}N_2O$, **4f**)*: White powder; m.p. 282–285°C; R_f (petroleum ether:ethylacetate): 7:3 (v/v) = 0.90; FTIR (KBr) ν_{max}: 3452 (OH), 3057 (=C–H aromatic), 1604 (C=C aromatic), 1578 (C=N), 1230 (Ar–O) cm^{-1}; U.V (CH_3OH) λ_{max}: 330 nm; ^1H NMR (DMSO-d_6, 400 MHz) δ: 6.87–6.91 (d, J = 8 Hz, 2H), 7.15–7.49 (m, 15H), 7.61–7.65 (d, J = 8.2 Hz) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 115.3, 119.8, 125.3, 126.0, 126.7, 127.9, 128.2, 128.5, 128.6, 129.3, 131.6, 131.8, 135.3, 137.3, 146.6, 159.3 ppm; Anal. Calcd. for $C_{27}H_{20}N_2O$ (388): C, 83.48; H, 5.19; N, 7.21; found: C, 83.44; H, 5.11; N, 7.09%.

2.4g *2-(3,4-Dimethoxyphenyl)-1,4,5-triphenyl-1H-imidazole ($C_{29}H_{24}N_2O_2$, **4g**)*: White powder; m.p. 178–180°C; R_f (petroleum ether:ethylacetate): 7:3 (v/v) = 0.62; FTIR (KBr) ν_{max}: 3057 (=C-H aromatic), 1597 (C=C aromatic), 1494 (C=N), 1154 (C-O-Ar) cm^{-1}; U.V (CH_3OH) λ_{max}: 293 nm; ^1H NMR (400 MHz, DMSO-d_6)δ: 3.56 (s, 6H, $2CH_3$), 6.41 (d, J = 8.8 Hz, 1H, H–Ar), 6.51 (d, J = 7.2 Hz, 2H, H-Ar), 7.15–7.47 (m, 15H, H-Ar) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ: 55.57, 55.60, 115.18, 124.55, 127.18, 128.53, 128.61, 129.09, 129.19, 129.20, 129.36, 130.10, 131.15, 132.30, 132.48, 136.50, 136.55, 136.61, 140.49, 145.29 ppm; MS (70eV) m/z (%): 432 (M^+, 55), 417 (50), 402 (44), 77 (32); Anal. Calcd. for $C_{29}H_{24}N_2$: C 87.80, H 5.60, N 6.60; found: C 87.82, H 5.58, N 6.61%.

2.4h *2-(4-Methoxyphenyl)-1,4,5-triphenyl-1H-imidazole ($C_{28}H_{22}N_2O$, **4h**)*: Milky crystal; m.p. 177–180°C; R_f (petroleum ether:ethylacetate): 7:3 (v/v) = 0.63; FTIR (KBr) ν_{max}: 3058 (C–H aromatic), 1606 (C=C aromatic), 1526 (C=N), 1250 (C–O–Ar) cm^{-1}; U.V (CH_3OH) λ_{max}: 289 nm; ^1H NMR (400 MHz, DMSO-d_6)δ: 3.24 (s, 3H, CH_3), 6.83 (d, J = 7.4 Hz, 2H, H–Ar), 7.23–7.41 (m, 15H, H-Ar), 7.47 (d, J = 7.4 Hz, 2H, H–Ar) ppm; ^{13}C NMR (100 MHz,

DMSO-d_6) δ: 55.57, 114.07, 123.30, 126.83, 128.60, 128.77, 128.89, 129.12, 129.16, 129.24, 130.12, 131.10, 131.29, 131.59, 135.0, 137.07, 137.27, 146.49, 160.0 ppm; Anal. Calcd. for $C_{28}H_{22}N_2O$: C 87.30, H 5.16, N 7.54; found: C 87.33, H 5.15, N 7.52%.

2.4i *2-(4-Bromophenyl)-1,4,5-triphenyl-1H-imidazole ($C_{27}H_{19}BrN_2$, **4i**)*: White powder; m.p. 165–168°C; R_f (petroleum ether:ethylacetate): 7:3 (v/v) = 0.71; FTIR (KBr) υ: 3056 (=CH), 1597 (C=C aromatic), 1495 (C=N), 1072 (C-Br) cm^{-1}; UV-vis (EtOH) λ_{max}: 292 nm; ^{1}H NMR (400 MHz, DMSO-d_6)δ: 7.40–7.12 (m, 17H, Ar), 7.94 (d, 2H, Ar) ppm; ^{13}C NMR (100 MHz, DMSO-d_6)δ: 123.0, 124.4, 125.2, 126.0, 127.4, 128.1, 128.3, 128.4, 128.5, 128.6, 128.9, 129.1, 129.2, 129.4, 129.6, 130.3, 131.0, 132.6, 133.2, 136.1, 136.3, 139.7, 144.6, 147.0 ppm; Anal. Calcd. for $C_{27}H_{19}BrN_2$: C 71.85, H 4.24, N 6.26; found: C 71.32, H 4.16, N 6.21%.

2.4j *2,4,5-Triphenyl-1-propyl-1H-imidazole($C_{24}H_{22}N_2$, **6a**)*: Milky solid; m.p. 87–89°C; R_f (petroleum ether:ethylacetate): 7:3 (v/v) = 0.55; UV-vis (EtOH) λ_{max}: 284 nm; FTIR (KBr) υ: 3057 (=C-H aromatic), 1601 (C=C aromatic), 1472 (C=N) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6)δ: 0.48 (t, J = 6.8 Hz, 3H, CH_3), 1.3 (m, 2H, CH_2), 3.9 (t, J = 7.2 Hz, 2H, CH_2), 7.1–7.8 (m, 15H, CH-Ar) ppm; ^{13}C NMR (100 MHz, DMSO-d_6)δ: 11.07, 23.56, 46.32, 126.55, 128.50, 129.12, 129.17, 129.33, 129.62, 130.27, 131.30, 131.56, 131.78, 135.17, 137.0, 147.20 ppm; Anal. Calcd. for $C_{24}H_{22}N_2$: C 85.49, H 6.68, N 8.87; found: C 85.51, H 6.65, N 8.92%.

2.4k *2-(4-Chlorophenyl)-4,5-diphenyl-1-propyl-1H-imidazole ($C_{24}H_{21}N_2Cl$, **6b**)*: White powder; m.p. 85–87°C, R_f (petroleum ether:ethylacetate): 7:3 (v/v) = 0.46; UV-vis (EtOH) λ_{max}: 294 nm; FTIR (KBr) υ: 3050 (=CH), 1601 (C=C), 1489 (C=N), 1074 (C-Cl) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6)δ: 0.51 (t, J = 6.8 Hz, 3H, CH_3), 1.27 (m, 2H, CH_2), 3.85–3.87 (t, J = 6.7 Hz, 2H, CH_2), 7.11–7.55 (m, 10H, CH-Ar), 7.6 (d, J = 8 Hz, 2H, Ar), 7.75 (d, J = 8 Hz, 2H, Ar) ppm; ^{13}C NMR (100 MHz, DMSO-d_6)δ: 11.08, 23.54, 46.39, 126.55, 126.66, 128.53, 129.24, 129.43, 129.65, 130.52, 130.65, 130.89, 131.29, 131.30, 133.96, 137.15, 145.98 ppm; MS (70eV) m/z (%): 435 (M^+, 55), 432 (53), 417 (50), 402 (44), 77 (32); Anal. Calcd. for $C_{24}H_{22}N_2$: C 77.30, H 5.68, N 7.51; found: C 77.32, H 5.69, N 7.48%.

2.4l *2-(4-Methylphenyl)-4,5-diphenyl-1-propyl-1H-imidazole ($C_{25}H_{24}N_2$, **6c**)*: Yellow needles; m. p. 78–83°C; R_f (petroleum ether:ethylacetate): 7:3 (v/v) = 0.57; UV-vis (EtOH) λ_{max}: 294 nm; IR (KBr): υ 3063 (=CH), 1603 (C=C), 1451 (C=N) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6)δ: 0.47 (t, J = 6.8 Hz, 3H, CH_3), 1.30 (m, J = 6.8 Hz, 2H, CH_2), 2.36 (s, 3H, CH_3), 3.82 (t, J = 6.0 Hz, 2H, CH_2), 7.10–7.35 (m, 12H, Ar), 7.50 (d, J = 8 Hz, 2H, Ar) ppm; ^{13}C NMR (100 MHz, DMSO-d_6)δ: 11.07, 21.36, 23.56, 46.30, 125.64, 126.49, 126.54, 128.47, 128.96, 129.05, 129.28, 129.60, 129.68, 130.12, 131.65, 135.25, 136.88, 138.63, 147.26 ppm; MS (70eV) m/z (%): 352 (M^+, 70), 323 (52), 309 (59), 295 (46), 15 (37); Anal. Calcd. for $C_{25}H_{24}N_2$: C 85.19, H 6.86, N 7.95; found: C 85.17, H 9.21, N 7.55%.

2.4m *2-(4-Methoxyphenyl)-4,5-diphenyl-1-propyl-1H-imidazole ($C_{25}H_{24}N_2O$, **6d**)*: White powder; m.p.76–80°C; R_f (petroleum ether:ethylacetate): 7:3 (v/v) = 0.72; UV-vis (EtOH) λ_{max}: 305 nm; IR (KBr) υ: 3050 (=CH), 1500 (C=C), 1498 (C=N), 1243 (C-O) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6)δ: 0.47 (t, J = 6.8 Hz, 3H, CH_3), 1.33 (m, J = 6.8 Hz, 2H, CH_2), 2.36 (s, 3H, CH_3), 3.81 (t, J = 7.2 Hz, 2H, CH_2), 7.10–7.30 (m, 12H, Ar), 7.46 (d, J = 8 Hz, 2H, Ar) ppm; ^{13}C NMR (100 MHz, DMSO-d_6)δ: 21.15, 61.46, 127.08, 129.64, 133.57, 138.01, 157.97, 174.82 ppm; MS (70eV) m/z (%): 368 (M^+, 59), 337 (52), 323 (59), 309 (48), 234 (46), 31 (30); Anal. Calcd for $C_{25}H_{24}N_2O$: C 81.49, H 6.56, N 7.60, O 4.74; found: C 81.46, H 6.55, N 7.61, O 4.73%.

3. Results and discussion

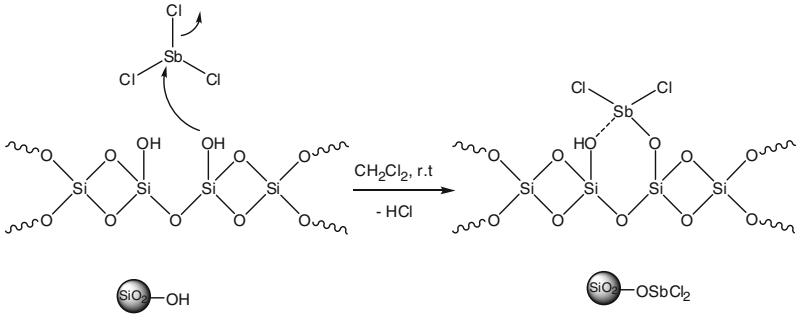
To synthesize tetrasubstituted imidazoles, we carried out the reactions of benzil, aliphatic and aromatic amines and ammonium acetate with various aromatic aldehydes carrying either electron-releasing or electron-withdrawing substituent under solvent-free conditions. To study their feasibility, the reaction of benzaldehyde, aniline, benzil and ammonium acetate was selected as a model reaction. To explore the scope and generality of the present method, various aldehydes and amines were examined in model reaction. The results show that the nature of the functional group on the aromatic ring of the aldehyde exerted a strong influence on the time and the reaction yield. Aldehydes with electron-withdrawing groups afford more pure products compared with electron-donor groups in higher yields and fewer times (table 1). In addition, the results

Table 1. Catalytic synthesize 1,2,4,5-tetrasubstituted imidazoles under solvent-free conditions.

Entry	R	Amine	Product	Time (min)	Yield (%)	M.p. (°C) Found	M.p. (°C) Refs.
1	H	$PhNH_2$	**4a**	25	93	216–218	26
2	4-Me	$PhNH_2$	**4b**	28	90	187–188	46
3	4-Cl	$PhNH_2$	**4c**	15	95	160–163	46
4	3,5-$(OMe)_2$	$PhNH_2$	**4d**	31	78	163–165	–
5	2-OH	$PhNH_2$	**4e**	30	75	254–256	10
6	4-OH	$PhNH_2$	**4f**	30	58	282–285	26
7	3,4-$(OMe)_2$	$PhNH_2$	**4g**	33	80	178–180	–
8	4-OMe	$PhNH_2$	**4h**	28	87	182–184	10
9	4-Br	$PhNH_2$	**4i**	12	93	165–168	–
10	H	n-$PrNH_2$	**6a**	20	94	87–89	–
11	4-Cl	n-$PrNH_2$	**6b**	13	95	85–87	–
12	4-Me	n-$PrNH_2$	**6c**	25	91	78–83	–
13	4-OMe	n-$PrNH_2$	**6d**	25	89	76–80	–

Table 2. Comparison of catalysts efficiency.

Entry	Catalyst (g)	Time (min)	Yield (%)
1	0.6 mmol $SbCl_3$ and 0.1 g SiO_2	25	22
2	0.1 g $SbCl_3/SiO_2$	25	93



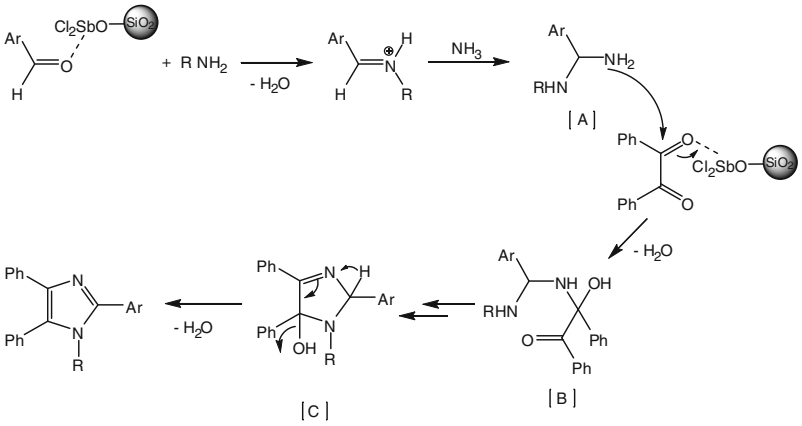
Scheme 3. Synthesis of highly active catalyst ($SbCl_3/SiO_2$).

showed that the reaction worked well in the presence of aliphatic amine and the yield of product was higher than aromatic ones. The reason is that the aliphatic amines are stronger bases and they have more nucleophilic strength rather than aromatic amines. The structures of products were characterized by ^1H NMR, ^{13}C NMR, CHN, MS spectral analysis, and also by comparison with authentic samples.

Lewis acid site on silica-supported antimony (III) chloride ($SbCl_3/SiO_2$) acts as a highly efficient acid catalyst, in the synthesis of imidazole derivatives. This eco-friendly and green catalyst was found to be a heterogeneous acid catalyst that could be easily separated from the reaction mixture only by filtration. In this paper, a systematic study was carried out to evaluate the impact of supported catalyst and the efficiency of $SbCl_3/SiO_2$ in a model reaction (table 2). Furthermore, the physical mixture of silica and antimony (III) chloride (0.6 mmol $SbCl_3$ and 0.1 g SiO_2) exhibited a moderated level of activity, which was lower than the silica supported antimony (III) chloride. $SbCl_3/SiO_2$ catalyses the reaction superior compared with the physical mixture of $SbCl_3$ and SiO_2. This reveals that the high catalytic activity of $SbCl_3/SiO_2$ is due to an excellent dispersion of $SbCl_3$ over high surface area silica support. The results indicated that dispersed $SbCl_3$ coordinates with surface hydroxyl groups leading to formation -O–Sb–Cl as stable Lewis acid sites under the reaction conditions (SiO_2–$OSbCl_2$). Therefore, the efficiency of $SbCl_3/SiO_2$ can be explained by better synergetic effects of $SbCl_3$ with SiO_2 due to the existence of multiple Lewis acids in catalyst (scheme 3).

Table 3. Optimization of amount of catalyst for the preparation of **4a**.

Entry	Catalyst (g)	Time (min)	Yield (%)
1	0.02	5	23
2	0.04	5	41
3	0.06	5	64
4	0.08	5	75
5	0.09	5	81
6	0.1	5	93
7	0.11	5	93



Scheme 4. Plausible mechanism for the formation of tetrasubstituted imidazoles in the presence of $SbCl_3/SiO_2$ catalyst.

In the rest of our studies, the effect of amount of active species $SbCl_3$ for the synthesis product **4a** was investigated with various molar ratios of $SbCl_3/SiO_2$. The best result was obtained at 0.44 mmol (0.1 g) of $SbCl_3/SiO_2$, as shown in table 3. The use of smaller amounts of the catalyst gave a low yield and the more amounts could not enhance the yield of product. A mechanism for the catalytic activity of $SbCl_3/SiO_2$ in the synthesis of tetrasubstituted imidazoles may be postulated as shown in scheme 4. Based on this mechanism, $SbCl_3/SiO_2$ is a green and effective catalyst for the formation of imidazoles, so that it can activate the carbonyl group of aldehyde to facilities formation of diamine intermediate [A]. This intermediate then condenses with activated benzil to form imidazol-5-ol intermediate [C], which it converts to tetrasubstituted imidazoles by elimination of water.

4. Conclusions

Silica-supported antimony trichloride is introduced as a heterogeneous Lewis acid catalyst for the synthesis of a variety of 1,2,4,5-tetrasubstituted imidazoles. This catalyst provides an improved protocol in terms of reaction time and yield when compared with the other catalysts. The proposed method involves features such as simplicity, fairly good efficiency, minimal waste generation, reusability and excellent activity of catalyst. These features make this procedure a valuable contribution to the existing processes in the field of imidazole compounds synthesis.

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