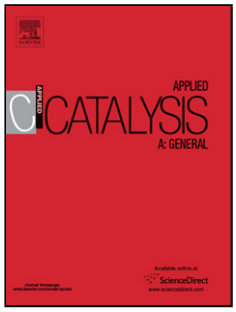

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A modular approach for multicomponent synthesis of amidines using modified Scolecite

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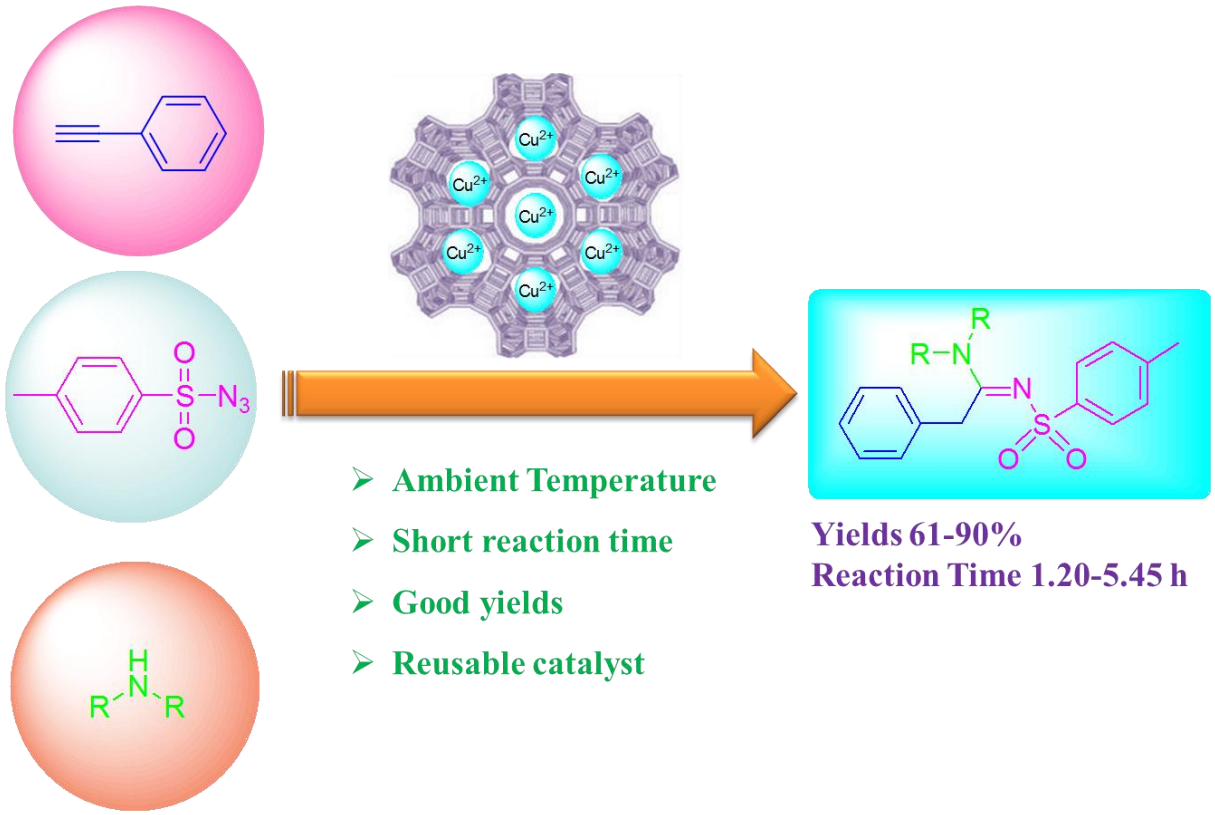
Highlights:

- Copper exchanged Scolecite(Cu-Scolecite)was prepared by ion exchange method.
- Thecatalytic activity of Cu-Scolecite was evaluated for multi-component synthesis of amidines.
- High yields with easy recovery and reusability of catalyst were observed.

Graphical Abstract



Abstract

Copper exchanged Scolecite was successfully synthesized and used as an efficient, mild and recyclable catalyst for promoting multi-component synthesis of amidines from 4-toluenesulfonyl azide, phenyl acetylene and variety of substituted amines in THF at ambient temperature in good yields within short reaction time.

Keywords: Scolecite, *N*- Sulfonyl amidines, Multi-component synthesis, Reusability.

1. Introduction

Scolecite is a subclass of zeolites, which is crystalline, fibrous aggregation of an aluminum silicate that occurs in nature and manufactured by synthetic methods [1]. They have orderly pore structure within aluminosilicate framework which comprises interchangeable alkali and alkaline earth metal cations accompanied by water [2]. By virtue of their Lewis and Bronsted acidic sites, Scolecites have been extensively used as heterogeneous catalyst in the preparation of polyhydroquinolines by Hantzsch synthesis [3] and 3, 4 dihydropyrimidin-2(1H)-ones (DHPMs) by Biginelli reaction [4]. They have also been successfully employed in the synthesis of bioactive benzimidazoles and 2, 4, 5-triarylimidazoles [5, 6]. In addition, Scolecites are widely used as adsorbents for removal of heavy and toxic metal from waste water [2].

A unique characteristic feature of zeolites is their micropores of molecular size, which give them adsorption and ion exchange characteristic properties of paramount importance. These properties enable the introduction of transition metal cations in the porous framework of zeolites. Zeolites render a unique ligand system, which provides multiple types for coordination of the cation, thus providing active sites for catalyzing a variety of reactions. It is now well established that cation-exchanged zeolites offer unique and high catalytic activity for a wide variety of important reactions. The cation exchanged zeolites have been widely used in the study of new applications related to process intensification [7], green chemistry [8], hybrid materials [9], medicine [10], animal food [11], optical and electrical based applications [12], reactions [13], sensing [14] and nanotechnology [15]. The Scolecites, like zeolites, also possess micropores that can be exchanged with transition metals. The scrutiny of the literature reveals that there are scarce reports on transition metal exchanged Scolecites [16]. To tap the barely exploited potential of transition metal exchanged Scolecites in catalysis, we sought to exchange alkali

metal ions in the Scolecite network by copper envisioning that such process could lead to a new composite with interesting catalytic properties.

Amidines are structural motifs in numerous natural products and biologically active molecules [17]. They have fascinating chemical properties and have profound applications in medicinal chemistry, synthetic chemistry, supramolecular chemistry, and coordination chemistry [17a, 18-20]. *N*-Sulfonyl amidines constitute an important class of amidines that has received much attention due to their wide range of pharmaceutical and biological properties [17], and also serves as useful synthetic intermediates [21] as well as efficient coordinating ligands [20]. Consequently, the construction of these molecules represents a significant area in organic synthesis. A plethora of distinct protocols have been developed for the synthesis of *N*-sulfonyl amidines. Some of the most prominent methods include Cu-catalyzed multi-component coupling of terminal alkyne, sulfonyl azide and amine [22], oxidative dehydrogenation of a tertiary amine followed by 1, 3-dipolar cycloaddition of sulfonyl azide [23], chlorophosphite-mediated Beckmann ligation of oximes and *p*-toluenesulfonyl azide [24], palladium catalyzed sulfonyl ynamide rearrangement in the presence of an amine [25], aerobic oxidative three-component coupling of a terminal alkyne, secondary amine and sulfonamide [22e], NaI-catalyzed condensation of sulfonamide and formamide [26], and direct condensation of sulfonamide derivatives with *N*, *N*-dimethylformamide dimethyl acetal (DMF-DMA) [27]. Amongst these, Cu-catalyzed multi-component coupling between *p*-toluenesulfonyl azide, phenyl acetylene and amines represents most elegant protocol due to wide substrate scope, mild reaction conditions, and potential synthetic utility. A variety of catalytic systems have been reported to improve the efficiency of this protocol [22]. However, there is a still scope for improvement especially toward developing a green procedure using heterogeneous catalyst.

In continuation of our studies related to heterogeneous catalysis [28-29], we report herein synthesis of modified Scolecite and its application in the synthesis of *N*-sulfonyl amidines.

2. Experimental

2.1. *General remarks*

Infrared spectra were recorded on a Perkin-Elmer FTIR spectrometer. X-Ray Diffraction (XRD) pattern was taken by using Brucker D2 Phaser. Elemental analyses were performed on EURO EA3000 vectro model. Surface area and pore volume were determined by N_2-physisorption using the Quantachrome Nova Station instrument. Surface areas were calculated by using the BET model with micro- and macropores described by Barrett-Joyner-Halenda (BJH) model. The thermal gravimetric analysis (TGA) curves were obtained using the instrument TA SDT Q600 in the presence of static air at a linear heating rate of 10 °C min^{-1} from 25 °C to 1000 °C. Copper loadings were determined by Atomic Absorption Spectroscopy (AAS) using a VARIAN Spectra AA-20 instrument. SEM was recorded using JSM-6701F, Japan. The elemental composition of materials was analyzed by an energy-dispersive X-ray spectra (EDS) attached to the field emission scanning electron microscope (FE-SEM, Model Hitachi S 4800, Japan). ^{1}H NMR and ^{13}C NMR spectra were recorded on a Brucker AC (300 MHz for ^{1}H NMR and 75 MHz for ^{13}C NMR) spectrometer using $CDCl_3$ as solvent and tetramethylsilane (TMS) as an internal standard. Chemical shifts (δ) are expressed in parts per million (ppm) values with tetramethylsilane (TMS) as the internal reference and coupling constants are expressed in hertz (Hz). Mass spectra were recorded on a Shimadzu QP2010 GCMS and all other chemicals (Spectrochem) were used as received. Melting points were determined in an open capillary and are uncorrected. All reactions were carried out under air atmosphere in dried glasswares. X-ray diffraction data of compound **4e** was collected at T = 298 and 293 K on a Bruker APEXII CCD and Crys Alis PRO Oxford diffractometer with graphite monochromated Mo Ka (k = 0.71073 A °) radiation. Table 4 shows

the unit cell parameters and other crystallographic details. Table 5 shows specified hydrogen bonding in packing diagram of **4e**. The determination of cell refinement and data reduction were performed with program SAINT and Crys Alis PRO [30]. The structure was solved using the direct methods of program SHELXS97 and refined anisotropically by full-matix least-square on F^2 was carried out with the program SHELXL97 [31].

2.2. Preparation of Cu-Scolecite

Scolecite (10 g) was exchanged three times with 1M aqueous $Cu(NO_3)_2$ solution. Each exchange was performed at 80 ^{0}C for 24 h. Following exchange, the material was separated by gently decanting mother liquor and the blue colored solid was thoroughly washed with deionized water and dried overnight at 373 K to give Cu-Scolecite.

2.3. General procedure for the synthesis of N-sulfonyl amidine

A mixture of phenyl acetylene (1 mmol), *p*-toluenesulfonyl azide (1 mmol), amine (1.2 mmol) and Cu-Scolecite (150 mg) in THF (5 mL) were added to a dried round bottom flask. The reaction mixture was magnetically stirred at ambient temperature and progress was monitored by thin layer chromatography (TLC). After completion of reaction, the reaction mixture was filtered to isolate insoluble Cu-Scolecite. The evaporation of solvent in vacuuo afforded crude product which was purified by column chromatography over silica gel using petroleum ether/ethyl acetate (85:15 *v*/*v*).

2.4. Spectroscopic data

N^1, *N*^{1}-Diisopropyl-2-phenyl-*N*^{2}-tosylacetamidine (Table 3, product entry **4a**): White solid; mp 146-147 °C (lit., 147.5-148.5 °C)[22d]; IR (KBr): υ = 2973, 1541, 1457, 1375, 1263,

1137, 1084, 802, 755, 716, 546 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.89 (d, J = 6.6 Hz, 6H), 1.40 (d, J = 6.9 Hz, 6H), 2.40 (s, 3H), 3.46 (t, 1H), 4.02 (q, 1H), 4.42 (s, 2H), 7.19-7.32 (m, 7H), 7.84 (d, J = 8.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): 19.8, 21.4, 38.7, 48.0, 50.3, 126.2, 126.7, 127.9, 128.8, 129.0, 134.9, 141.5, 163.4; MS (EI): *m/z* 373 $(M+H)^+$; Anal. Calcd. for $C_{21}H_{28}N_2O_2S$ (372.524): C, 71.17; H, 8.63; N, 7.02. Found: C, 71.21; H, 8.69; N, 6.90.

N^1, N^1-Dimethyl-2-phenyl-N^2-tosylacetamidine (Table 3, product entry **4b**): Colourless solid; mp 127 °C (lit., 126.5-128.0 °C)[32]; IR (KBr): υ = 3054, 3037, 2945, 2920, 2299, 1938, 1856, 1750, 1625, 1579, 518, 494 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.37 (s, 3H), 2.56 (s, 8H), 7.27-7.34 (m, 5H), 7.45 (d, J = 7.5 Hz, 2H), 7.61 (d, J = 7.7 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): 21.4, 21.8, 40.7, 63.3, 124.4, 127.5, 128.4, 129.1, 130.0, 136.2, 140.4, 142.4, 144.2, 164.2; MS (EI): *m/z* 317 $(M+H)^+$; Anal. Calcd. for $C_{17}H_{20}N_2O_2S$ (316.417): C, 64.53; H, 6.37; N, 8.85. Found: C, 64.01; H, 6.89; N, 8.32.

N^1, N^1-Diethyl-2-phenyl-N^2-tosylacetamidine (Table 3, product entry **4c**): White solid; mp 138 °C (lit., 136-139 °C)[22a]; IR (KBr): υ = 2980, 1552, 1471, 1363, 1274, 1142, 1076, 827, 593 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.97 (t, 3H), 1.17 (t, 3H), 2.38 (s, 3H), 3.23 (q, 2H), 3.52 (q, 2H), 4.40 (s, 2H), 7.11-7.30 (m, 7H), 7.79 (d, J = 8.1 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): 11.9, 13.4, 21.4, 22.4, 36.5, 43.2, 43.3, 126.2, 126.7, 127.8, 128.8, 128.9, 141.3, 141.6, 164.5; MS (EI): *m/z* 345 $(M+H)^+$; Anal. Calcd. for $C_{19}H_{24}N_2O_2S$ (344.471): C, 66.25; H, 7.02; N, 8.13. Found: C, 66.02; H, 7.18; N, 7.69.

N^1, N^1-Dibutyl-2-phenyl-N^2-tosylacetamidine (Table 3, product entry **4d**): White solid; mp 65 °C (lit., 66-67 °C)[22e]; IR (KBr): υ = 3066, 3016, 2965, 2927, 2852, 1584, 1542, 1469, 1477, 1371, 1286, 1264, 1192, 1172, 1134, 1088, 1025, 950, 902, 844, 813, 722, 692, 652, 592, 539, 506 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.80-0.90 (m, 6H), 1.12-1.38 (m, 8H), 2.39 (s,

3H), 3.12 (t, 2H), 3.42 (t, 2H), 4.40 (s, 2H), 7.14-7.30 (m, 7H), 7.79 (d, J = 8.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): 13.5, 13.6, 19.9, 20.2, 21.3, 28.7, 30.4, 36.9, 48.7, 49.0, 126.2, 126.7, 127.9, 128.8, 128.9, 134.5, 141.5, 141.5, 164.6; MS (EI): *m/z* 401 $(M+H)^+$; Anal. Calcd. for $C_{23}H_{32}N_2O_2S$ (400.577): C, 68.96; H, 8.05; N, 6.99. Found: C, 68.38; H, 8.23; N, 7.06.

N^1, N^1-Dipropyl-2-phenyl-N^2-tosylacetamidine (Table 3, product entry **4e**): White solid; mp 86 °C(lit., 84-85 °C)[22e]; IR (KBr): υ = 2965, 2929, 2879, 1539, 1471, 1377, 1252, 1132, 1090, 954, 853, 691, 597 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.77 (t, 3H), 0.87 (t, 3H), 1.25-1.49 (m, 2H), 1.58-1.66 (m, 2H), 2.39 (s, 3H), 3.10 (t, 2H), 3.38-3.43 (m, 2H), 4.40 (s, 2H), 7.23 (m, 7H), 7.78 (d, J = 8.1 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): 11.0, 11.4, 20.0, 21.4, 21.6, 36.8, 50.6, 50.8, 126.1, 126.7, 127.9, 128.8, 128.9, 134.5, 141.6, 164.8; MS (EI): *m/z* 373 $(M+H)^+$; Anal. Calcd. for $C_{21}H_{28}N_2O_2S$ (372.524): C, 67.71; H, 7.58; N, 7.52. Found: C, 67.89; H, 7.46; N, 7.71.

N^1, N^1-Dinonyl-2-phenyl-N^2-tosylacetamidine (Table 3, product entry **4f**)[22b]: colorless solid; mp 91 °C; IR (KBr): υ = 3032, 2956, 2937, 2845, 1725, 1606, 1555, 1496, 1468, 1458, 1369, 1388, 1276, 1155, 1087, 1016, 965, 886, 767, 745, 689, 594, 587, 545 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.77-0.85 (m, 6H), 1.16-1.49 (m, 28H), 2.32 (s, 3H), 3.01 (t, 2H), 3.34 (t, 2H), 4.41 (s, 2H), 7.09-7.19 (m, 7H), 7.81 (d, J = 7.7 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): 14.4, 21.1, 22.4, 26.4, 26.9, 28.3, 29.0, 29.6, 31.4, 31.8, 36.5, 48.9, 49.5, 125.8, 126.5, 127.7, 128.7, 128.9, 133.7, 141.5, 141.7, 164.7; MS (EI): *m/z* 541 $(M+H)^+$; Anal. Calcd. for $C_{33}H_{52}N_2O_2S$ (540.843): C, 73.28; H, 9.69; N, 5.18. Found: C, 73.25; H, 9.72; N, 5.16.

N^1, N^1-Diphenyl-2-phenyl-N^2-tosylacetamidine (Table 3, product entry **4g**)[22c]: White solid; mp 147 °C; IR (KBr): υ = 3068, 3015, 2915, 1587, 1519, 1427, 1387, 1137, 1078, 979, 819, 750, 673, 546, 529 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.31 (s, 3H), 4.27 (s, 2H), 6.89 (d,

J = 3.5 Hz, 4H), 7.17-7.27 (m, 13H), 7.55 (d, J = 8.0 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): 21.1, 37.3, 126.1, 126.8, 128.4, 128.5, 128.9, 129.3, 134.4, 140.0, 141.8, 164.7; MS (EI): *m/z* 441 $(M+H)^+$; Anal. Calcd. for $C_{27}H_{24}N_2O_2S$ (440.556): C, 73.61; H, 5.49; N, 6.36. Found: C, 73.64; H, 7.51; N, 6.34.

N^1-Methyl-*N*^{1}-phenyl-*N*^{2}-(4-methylbenzensulfonyl)-2-phenylacetamidine (Table 3, product entry **4h**): White solid; mp 132 °C (lit., 131.5-133.5 °C)[22d]; IR (KBr): υ = 3055, 1525, 1459, 1288, 1142, 1070, 754, 710, 676, 542 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.26 (s, 3H), 3.29 (s, 3H), 4.20 (s, 2H), 6.65-6.75 (m, 4H), 7.00-7.25 (m, 3H), 7.27-7.36 (m, 5H), 7.86 (d, J = 7.8 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): 20.4, 35.7, 41.4, 126.5, 126.7, 127.3, 128.1, 128.6, 129.0, 129.4, 133.9, 141.2, 142.1, 142.5, 166.2; MS (EI): *m/z* 379 $(M+H)^+$; Anal. Calcd. for $C_{22}H_{22}N_2O_2S$ (378.487): C, 69.81; H, 5.86; N, 7.40. Found: C, 69.69; H, 5.68; N, 7.32.

N^1-Benzyl-*N*^{2}-(4-methylbenzenesulfonyl)-2-phenylacetamidine (Table 3, product entry **4i**): White solid; mp 112 °C (lit., 110-111 °C)[22d]; IR (KBr): υ = 3301, 3027, 2909, 1587, 1565, 1267, 1132, 1067, 720, 780, 658 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.40 (s, 3H), 4.32 (s, 2H), 4.41 (d, J = 5.6 Hz, 2H), 5.52 (s, 1H), 7.07 (m, 2H), 7.20-7.40 (m, 10H), 7.70 (d, J = 8.1 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): 20.1, 39.6, 44.1, 126.1, 127.3, 127.9, 128.2, 128.7, 129.2, 129.6, 130.1, 131.6, 135.9, 139.2, 141.4, 165.7; MS (EI): *m/z* 379 $(M+H)^+$; Anal. Calcd. for $C_{22}H_{22}N_2O_2S$ (378.487): C, 69.81; H, 5.86; N, 7.40. Found: C, 69.62; H, 5.54; N, 7.63.

N^1-Isopropyl-*N*^{2}-(4-methylbenzensulfonyl)-2-phenylacetamidine (Table 3, product entry **4j**): White solid; mp 112 °C (lit., 110-111 °C)[22d]; IR (KBr): υ = 3305, 2999, 1566, 1261, 1163, 1070, 722, 689, 557, 522 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.95 (d, J = 6.5 Hz, 6H), 2.35 (s, 3H), 4.02 (m, 1H), 4.25 (s, 2H), 5.25 (s, 1H), 7.09 (d, J = 7.8 Hz, 2H), 7.20 (d, J = 8.1 Hz, 2H), 7.35-7.46 (m, 3H), 7.82 (d, J = 7.8 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): 21.1, 21.6, 39.2, 42.8,

126.2, 127.6, 129.1, 129.4, 130.0, 133.4, 140.6, 141.7, 165.6; MS (EI): *m/z* 331 $(M+H)^+$; Anal. Calcd. for $C_{18}H_{22}N_2O_2S$ (330.444): C, 65.42; H, 6.71; N, 8.48. Found: C, 65.19; H, 6.39; N, 8.70.

N^1-4-Fluro benzyl-*N*^{2}-(4-methylbenzensulfonyl)-2-phenylacetamidine (Table 3, product entry **4k**): White solid; mp 91 °C; IR (KBr): υ = 3383, 2924, 1602, 1513, 1226, 1158, 1074, 845, 770, 697, 542 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.27 (s, 3H), 2.42 (s, 4H), 5.45 (s, 1H), 6.89-7.06 (m, 3H), 7.20-7.35 (m, 6H), 7.75 (s, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): 21.4, 39.6, 45.1, 115.3 (d, $^2J_{C-F}$ = 21 Hz), 126.3, 128.1, 128.6, 128.9, 129.1, 130.0, 139.3, 140.4, 142.3, 143.3, 160.5 (d, $^1J_{C-F}$ = 244 Hz), 166.4; MS (EI): *m/z* 397 $(M+H)^+$; Anal. Calcd. for $C_{22}H_{21}FN_2O_2S$ (396.477): C, 65.65; H, 5.34; N, 7.07. Found: C, 65.87; H, 5.23; N, 7.15.

N^1, *N*^{1}-Dicyclohexyl-2-phenyl-*N*^{2}-tosylacetamidine (Table 3, product entry **4l**): White solid; mp 160 °C; IR (KBr): υ = 2934, 2861, 1542, 1450, 1392, 1268, 1192, 1140, 1084, 947, 785, 694, 547 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 0.96-1.73 (m, 20H), 2.41 (s, 3H), 2.96 (s, 1H), 3.59 (t, 1H), 4.41 (s, 2H), 7.27 (t, 7H), 7.87 (d, J = 7.5 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): 21.4, 24.9, 28.5, 30.2, 39.3, 58.6, 126.2, 126.7, 128.2, 128.7, 128.9, 135.3, 141.5, 141.6, 163.7; MS (EI): *m/z* 453 $(M+H)^+$; Anal. Calcd. for $C_{27}H_{36}N_2O_2S$ (452.651): C, 71.64; H, 8.02; N, 6.19. Found: C, 71.51; H, 8.15; N, 6.41.

3. Result and Discussion

Our initial efforts were directed toward the synthesis of modified Scolecite acronymed as Cu-Scolecite. The Cu^{2+} ions were entrapped into Scolecite matrix ($Ca_8[Al_{16}Si_{24}O_{80}]\cdot 24H_2O$) *via* heating mixture of $Cu(NO_3)_2$ and Scolecite following standard ion exchange technique. The Ca^{+2} ions in Scolecite were replaced by Cu^{+2} ions with the equilibrium established as

$$Ca^{2+}_{(s)} + Cu^{2+}_{(aq.)} \rightleftharpoons Ca^{2+}_{(aq.)} + Cu^{2+}_{(s)}$$

The resultant Cu-Scolecite was characterized by FTIR spectroscopy. The FTIR spectrum displayed internal and external silanol group characteristic bands at 3740 and 3725 cm^{-1}. In addition, bands at 1652 cm^{-1} (bending mode of water), 1105 and 987 cm^{-1} (antisymmetric stretching modes of alumino-silicate tetrahedral), 719 cm^{-1} (symmetric stretching vibrations of Al-Si-O bonds) and 504 cm^{-1} (liberation mode of water) were observed. A weak diagnostic peak at 820 cm^{-1} attributed to the formation of Si-O-Cu bond confirmed entrapment of Cu in the Scolecite framework. This is further supported by the fact that the peak at 1013 cm^{-1} (asymmetric stretching vibrations of Si-Al-O group) of pristine Scolecite is shifted to 1019 cm^{-1} in Cu-Scolecite revealing the interaction of the Scolecite network with the Cu atoms. The quantification of Cu in modified Scolecite was done by energy Dispersive X-Ray (EDX) spectroscopy. The analysis revealed the presence of 1.76 wt % of Cu.

The Cu-Scolecite had a BET surface area of around 3.710 m^2/g with a micropore volume of about 0.014 mL/g, which is less in comparison with the parent Scolecite (13.638 m^2/g, 0.051 mL/g, respectively). The minute decrease in surface area is due to sorption of copper ions through the pores of Scolecite.

The powder XRD pattern of Cu-Scolecite is shown in the fig. 1. All the reflections in the powder XRD pattern of Cu-Scolecite are successfully indexed to monoclinic structure of Scolecite with space group C1c1 [33] except one line marked by asterisk in the fig. 1 appearing at $2\theta = 12.80°$. This line, in our view, is because of 220 hkl reflection from Cu-exchanged phase of Scolecite. As the cationic radius of Cu^{2+} is smaller than the Ca^{2+}, if there is any cation exchange in Scolecite, the position of 220 reflection has to be shifted towards higher 2θ values.

However, in the present study, the peak is shifted towards lower 2θ values which can be rationalized on the basis that although the ionic size of Cu^{2+} is smaller, it may have strong hydration sphere which would expand the channel size in greater strength as compared to Ca^{2+} analogue. The similar results have been observed for Mg^{2+} exchanged Scolecite. It is evident from XRD results that Ca in the channels of Scolecite is exchanged by Cu, although partially but significantly. We have further indexed the powder XRD pattern to obtain the information regarding unit cell parameters from the model-less Le bail fitting, which were found to be nearly similar to that of natural Scolecite analogue.

The SEM images of Scolecite and Cu-Scolecite are shown in the fig. 2. The SEM image of modified Scolecite reveals that particles are irregular in size and comparatively less spherical but not aggregated. The particle size of Scolecite is about 2-8 μm and that of Cu-Scolecite is about 8-15 μm respectively.

The thermal profile of Cu-Scolecite was studied by TGA and is shown in fig. 3. The thermogram shows that the initial weight loss due to dehydration does not occur in single step but is step wise. This is in contrast to the recently reported thermal behavior of pure Scolecite, which shows two step dehydration mechanism in the 100-250 °C and from 250-400 °C [34]. The Cu-Scolecite shows three step dehydration mechanism plausibly due to the slight alteration of the channel cation composition. These channel cations have crucial impact on the dehydration profile as they are directly interacting with the water molecules present in the channels. Thus, the altered TGA profile of Cu-Scolecite can be taken as additional evidence that the Cu is exchanged partially in the Scolecite channels. The initial weight loss of 5.3% can be attributed to the loss of approximately 10 molecules from the channels of Scolecite. The further weight loss of 2.4% suggests that the four more molecules are expelled from the channels of Scolecite. The third step

of water loss occurs at a slightly elevated temperature and eliminates 10 more water molecules from channels of Scolecite, thus leaving behind the dehydrated form of Cu-Scolecite.

In order to evaluate the catalytic activity of Cu-Scolecite in the synthesis of *N*-sulfonyl amidines, the multi-component reaction of phenyl acetylene (**1**), 4-toluenesulfonyl azide (**2**) and diisopropyl amine (**3**) was chosen as model reaction in order to optimize different parameters. Initial studies to examine the effect of catalyst loading were carried out on model reaction between **1** (1mmol), **2** (1 mmol) and **3** (1.2 mmol) in THF (5 mL) using different quantities of Cu-Scolecite at ambient temperature. We observed that the amount of catalyst had a significant impact on the reaction course. When the quantity of Cu-Scolecite was increased from 50 mg (1.39 mol %) to 150 mg (4.17 mol%), the yield of corresponding product N^1, N^1-diisopropyl-2-phenyl-N^2-tosylacetamidine (**4a**) elevated significantly (from 50% to 90%; Table 1, entries 1−3). The further increase in catalyst quantity beyond 150 mg did not have a profound influence on yield of the product (Table 1, entry 4).

Subsequently, the solvent effect on the reaction was examined. An array of solvents was employed for this purpose. The model reaction afforded moderate yields in polar protic solvents such as ethanol and methanol (Table 2, entries 1-2). Better yields were achieved in polar aprotic solvents like DCM and THF (Table 2, entries 3-4) while lower yields were acquired in non-polar solvents such as toluene, chloroform and 1, 4-dioxane (Table 2, entries 5-7). Among all the screened solvents, THF was found to furnish excellent yield of product in short reaction time (Table 2, entry 4).

After the optimization of reaction conditions, the generality of the protocol was studied by reacting structurally diverse amines with 4-toluenesulfonyl azide and phenyl acetylene. The results are summarized in Table 3. In all cases, the reactions proceeded smoothly affording the

corresponding *N*-sulfonyl amidines in a short reaction time. The reactions were clean and high yielding without any side products. In general, aliphatic secondary amines (Table 3, entry a-f) offered better yields of corresponding products than aromatic secondary amines (Table 3, entry g, h). The aliphatic primary amines (Table 3, entry i-k) also reacted efficiently providing the desired products in relatively good yields. Moreover, alicyclic amine such as dicyclohexyl amine also furnished high yield of anticipated product highlighting the general applicability of the protocol (Table 3, entry l). The use of heterogeneous catalyst and the choice of a low-boiling solvent such as THF greatly simplified and speed-up the isolation procedure. Indeed, it was only necessary to filter off the spent solid at the end of the reaction, wash it with a few portions of THF, and evaporate the resulting filtrate to obtain a final product.

The molecular structure of all products **4a-l** were elucidated from the FTIR, ^{1}H and ^{13}C NMR spectroscopy as well as mass spectrometry as described for **4e.** The mass spectrum of **4e** displayed the molecular ion peak at m/z = 373 ($M+H^{+}$)**,** which is in agreement with the proposed structure. The FTIR spectrum of **4e** displayed C=N stretching band at 1539 cm^{-1} and coupled vibration bands of sulfonyl group at 1377, 1132 cm^{-1} indicating the most significant functional groups of the product. The ^{1}HNMR spectrum of **4e** exhibit two sharp singlets at δ 2.39 ppm and 4.40 ppm for methyl and methylene groups attached to phenyl rings. The propyl group could be readily recognized on the basis of two triplets at δ 0. 87 and 3.10 ppm and a multiplet at 3.40 ppm. The nine aromatic protons appeared as multiplets in the region δ 7.10-7.80 ppm. The proton decoupled ^{13}C NMR spectrum of **4e** displayed 16 distinct signals which are in agreement with the proposed structure. The final confirmation for the formation of product was derived from X-ray analysis as shown in the fig. 4 and the packing arrangement of molecules was shown in the fig. 5. The C=N bond of *N*-sulfonyl amidines has E configuration.

A plausible mechanism for the formation of sulfonyl amidines is shown in Scheme 2. The initial interaction between alkyne and Cu-Scolecite forms copper acetylide intermediate (I). The reaction of sulfonyl azide with (I) generates copper-triazolyl intermediate (II) that eliminates nitrogen to form ketenimine intermediate (III). Further nucleophilic attack of amine on (III) furnishes the desired *N*-sulfonyl amidine.[22e]

The heterogeneity of Cu-Scolecite was assessed by leaching studies and hot filtration test. Initially, leaching of Cu from Cu-Scolecite was investigated using atomic absorption spectroscopy (AAS). There was negligible leaching of the copper (0.0038%) as evidenced by AAS indicating that most of copper ions were held strongly in the Scolecite matrix. Using the same amount of copper (in the form of copper nitrate) as that leached out, the model reaction could not be initiated even after prolonged reaction time (12h). The heterogeneity of Cu-Scolecite was also investigated by hot filtration test for the stated model reaction. After 50 % completion of the reaction (gas chromatography), the Cu-Scolecite was removed by simple hot-filtration method and the filtrate (without the catalyst) was subjected to further reaction under the optimized reaction conditions. There was no further increase in the yield of product even after 3 hours. These results suggest that the catalysis take place exclusively under heterogeneous conditions.

Reusability is representative characteristic of heterogeneous catalysts to determine their dynamic lifespan. The reusability of the Cu-Scolecite was tested by repeating model reaction for the synthesis of **4a** (Fig. 6). After accomplishment of the reaction, the catalyst was recovered by simple filtration, washed thoroughly with THF and then dried under vacuum. The catalyst showed a substantial recyclability as the corresponding yields started at 90% and reached 70% at the seventh run. The reduction in conversion observed on successive recycles is due to attrition

during filtration that disallowed quantitative recovery of the catalyst. It was also observed from FTIR studies that there is no change in the nature of catalyst even after seventh cycle.

To show the merit of Cu-Scolecite in comparison with other reported catalysts, we have summarized some of previous reports for the preparation of N^1, N^1-diisopropyl-2-phenyl-N^2-tosylacetamidine in Table 6. The comparison of results clearly proves that Cu-Scolecite is a good catalyst in terms of reaction time and yields of product than the other reported catalysts.

4. Conclusion

In summary, a simple, efficient and facile protocol for the synthesis of *N*-sulfonyl amidines using Cu-Scolecite has been described. The notable features of this novel procedure are mild reaction conditions, higher yields, and simplicity in operation and reusable catalyst.

Supplementary material for X-ray analysis

Crystallographic data for the structural analyses of compound **4e** has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 1039420. A copy of this information may be obtained free of charge from the Director, CCDC, 12 Union Road, Cambridge, CBZ 1EZ, UK (fax: +44 1223 336 033; e-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk).

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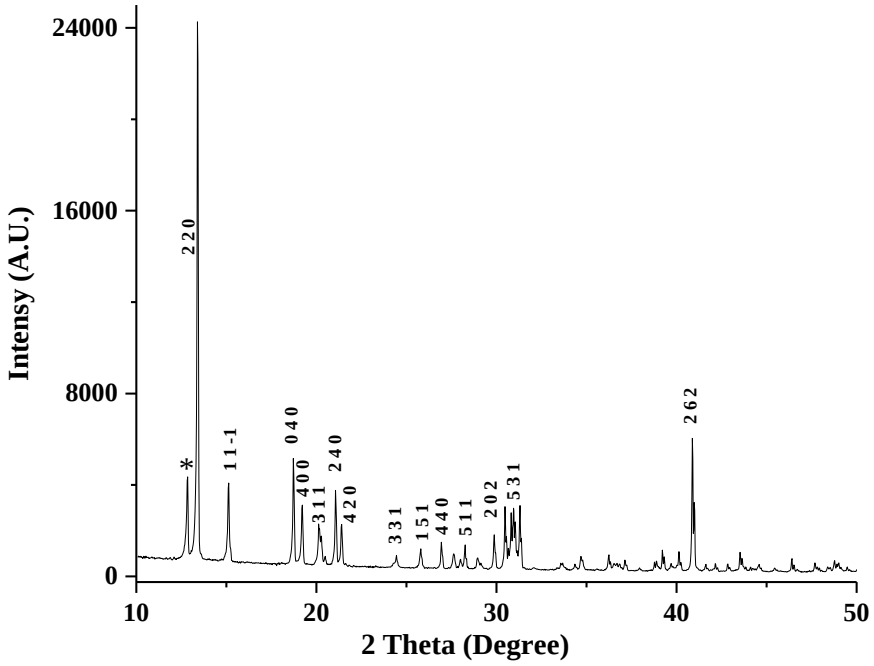


Fig. 1: XRD of Cu-Scolecite

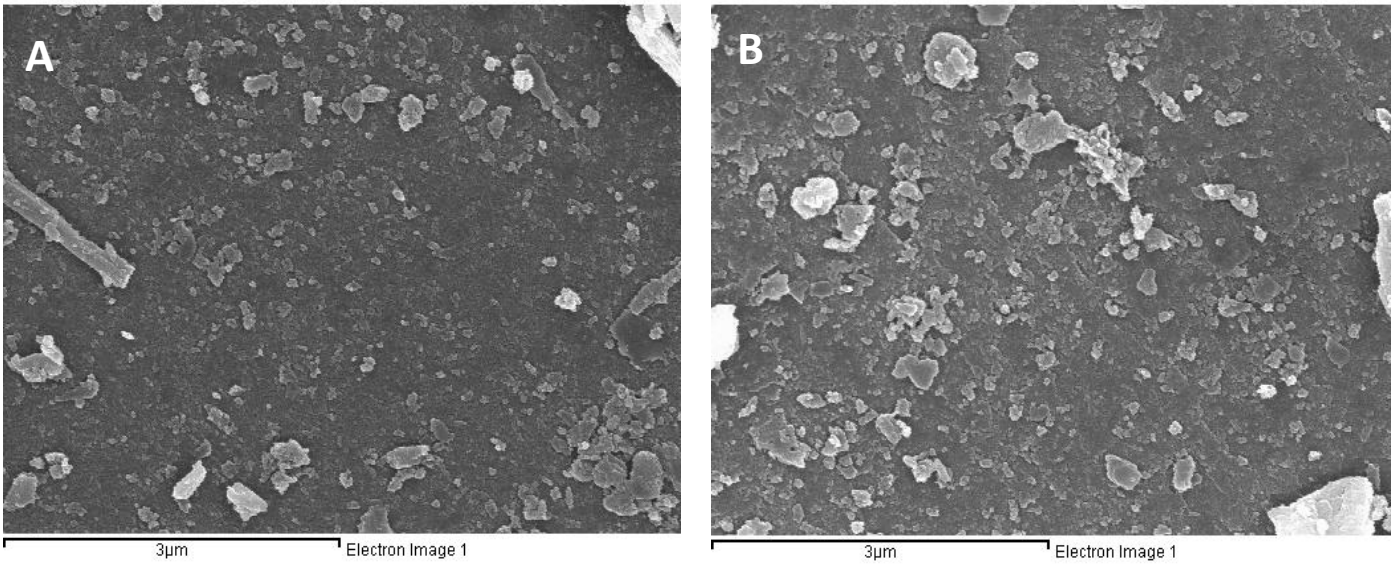


Fig.2: Scanning electron micrographs of (A) Scolecite and (B) Cu-Scolecite

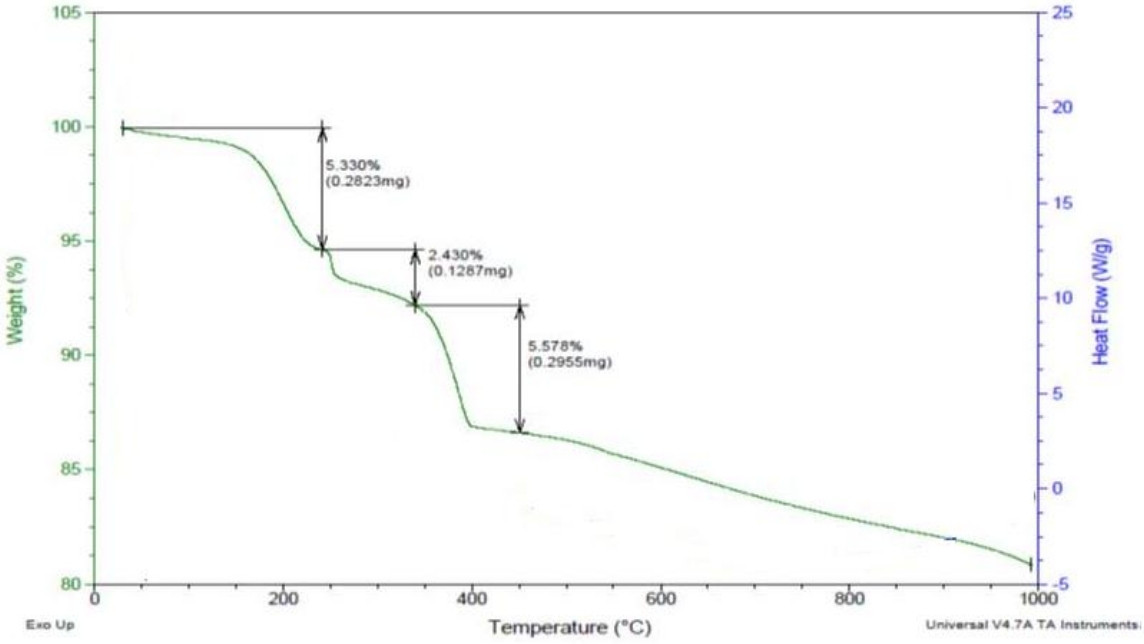


Fig. 3: TGA curve of Cu-Scolecite

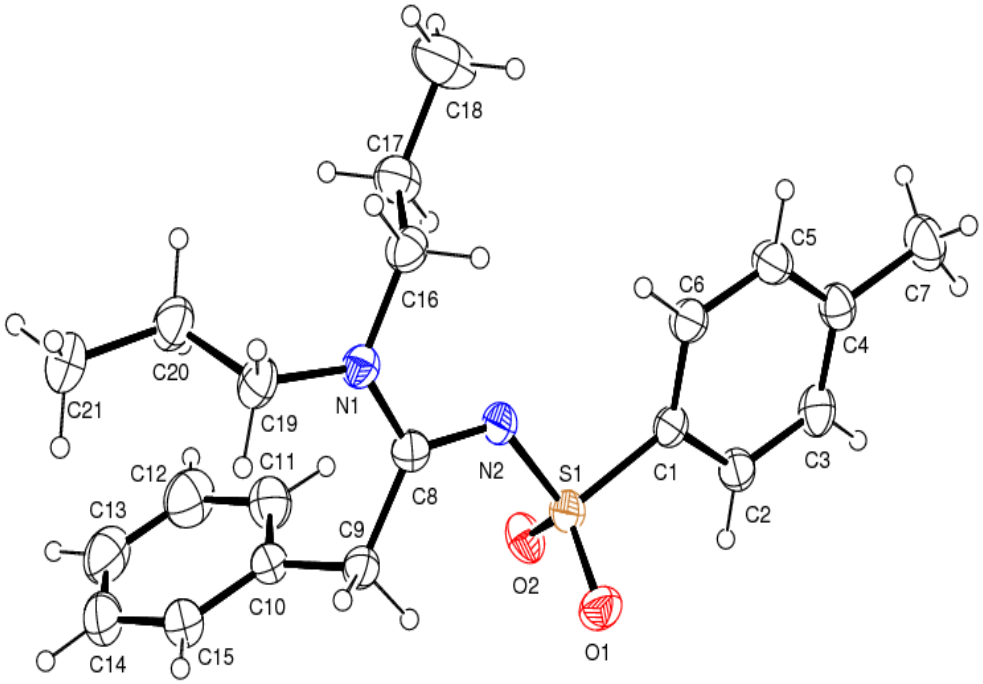


Fig. 4: Single crystal structure of N^1, N^1-dipropyl-2-phenyl-N^2-tosylacetamidine (4e)

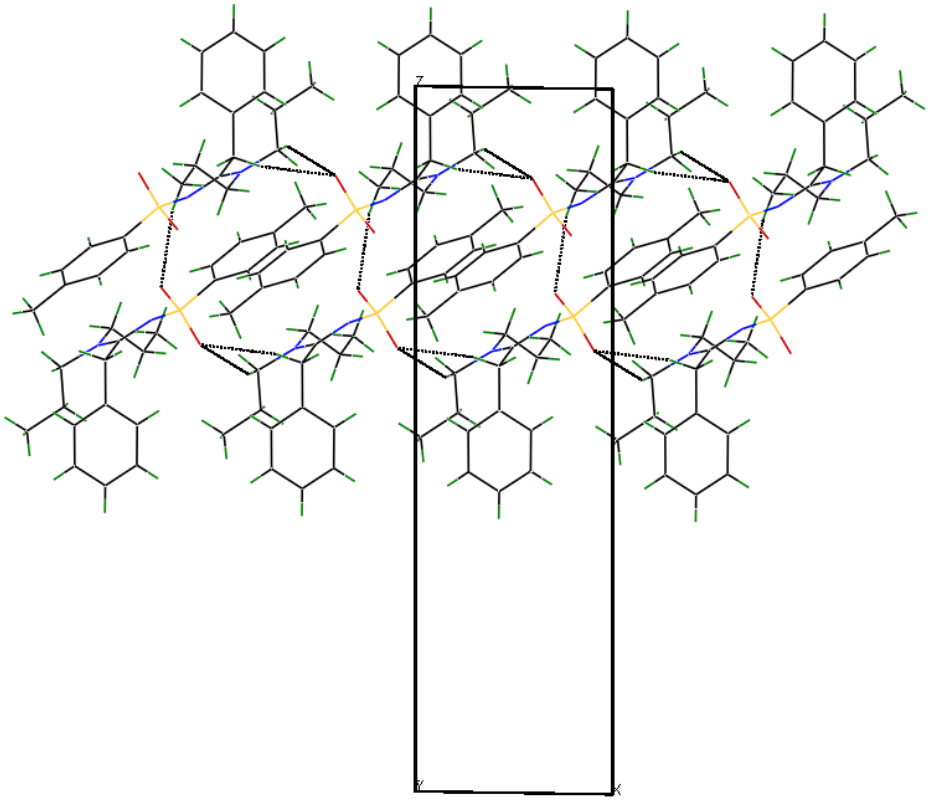


Fig.5: The packing diagram of 4e compound, viewed down Y axis. The packing arrangement of molecules viewed along the b axis. The dashed lines show intermolecular C–H…O hydrogen bonds.

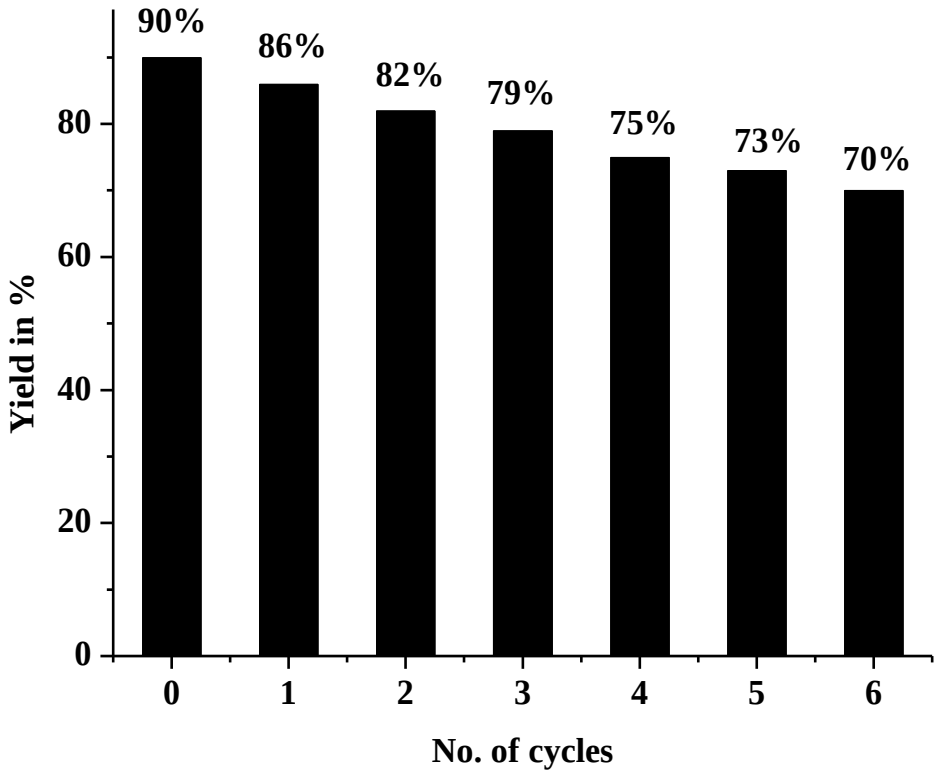
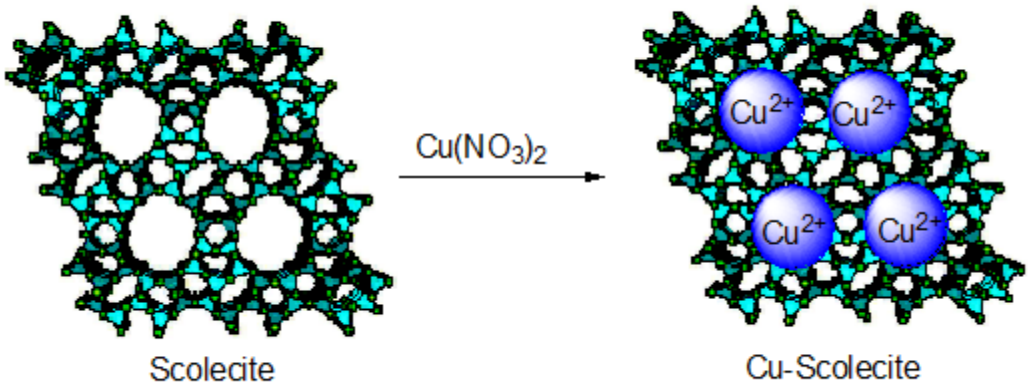
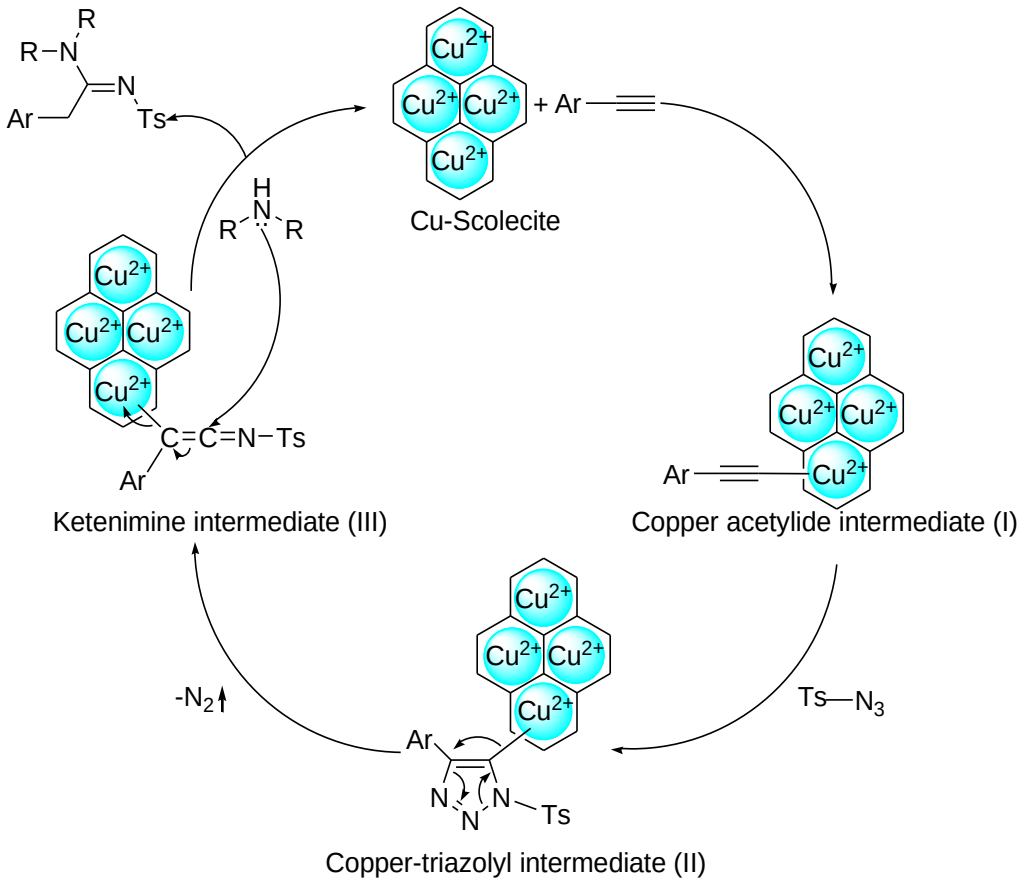


Fig. 6: Reusability of Cu-Scolecite in synthesis of *N*-sulfonyl amidines

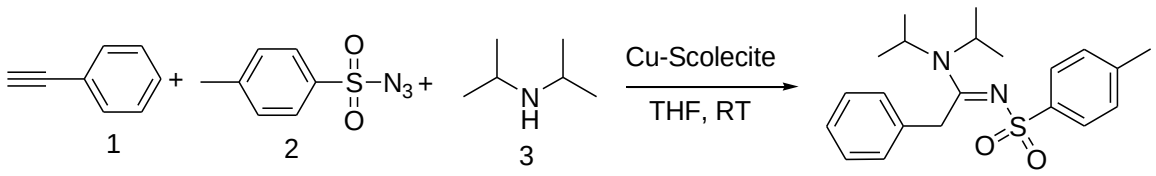


Scheme 1: Synthesis of Cu-Scolecite by ion exchange process



Scheme 2: A plausible mechanism for the formation of *N*-sulfonyl amidines

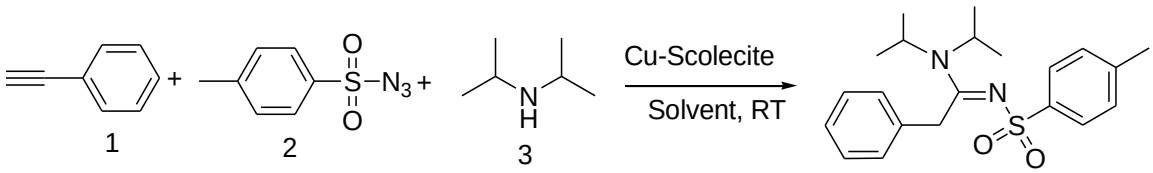
Table 1. Optimization of reaction conditions in synthesis of *N*-sulfonyl amidines [a,b]



Entry	Catalyst (mg)	Time (h)	Yield[b] (%)
1	50 (0.013 mmol)	4	50
2	100 (0.027 mmol)	3	65
3	150 (0.041 mmol)	**1.20**	**90**
4	200 (0.055 mmol)	1.20	91

[a]Reaction condition: Phenyl acetylene (1 mmol), 4-toluenesulfonyl azide (1 mmol), di-isopropyl amine (1.2 mmol), THF (5 mL)
[b] Isolated yields after chromatography.

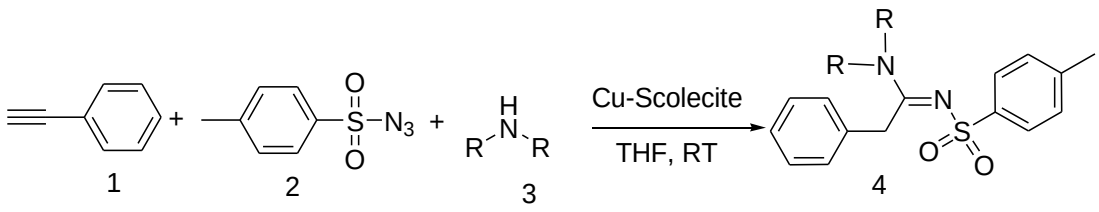
Table 2. Solvent optimization for the synthesis of *N*-sulfonyl amidines [a,b]

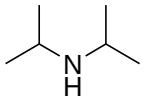
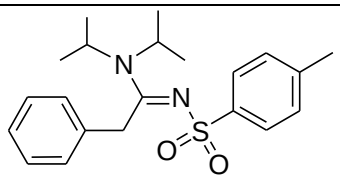
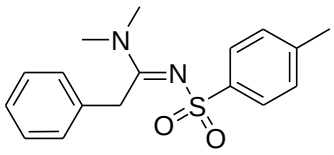
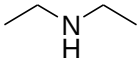
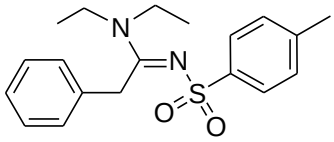
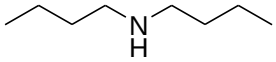
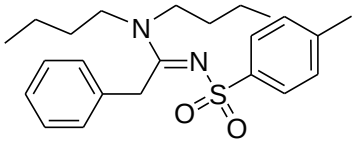
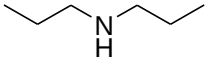
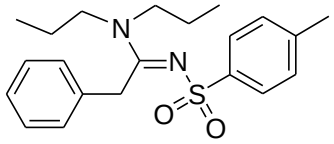


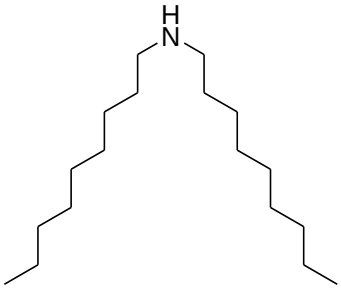
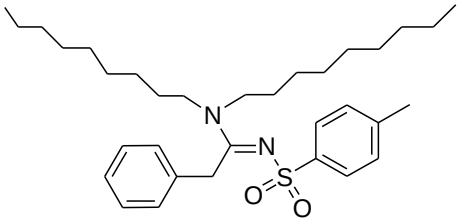
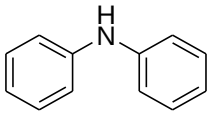
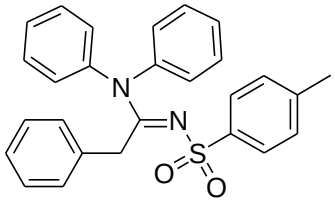
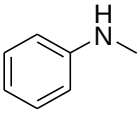
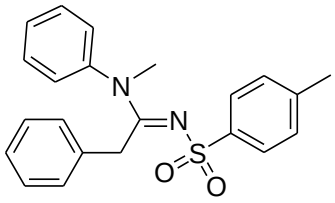
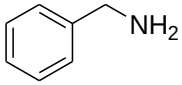
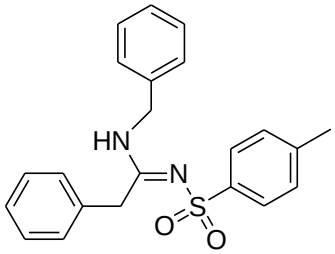
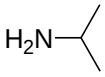
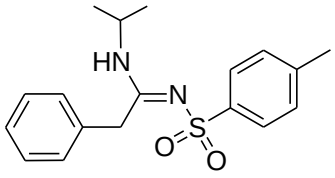
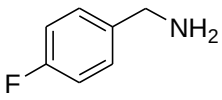
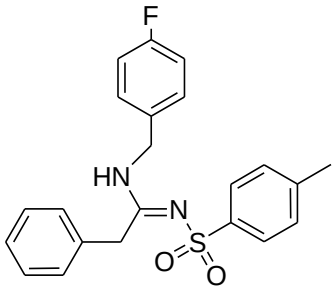
Entry	Solvent	Time (h)	Yield[b] (%)
1	Ethanol	4	60
2	Methanol	4	58
3	DCM	5	70
4	**THF**	**1.20**	**90**
5	Toluene	5	44
6	$CHCl_3$	4	40
7	1, 4-Dioxane	10	25

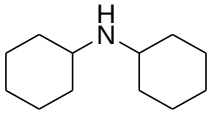
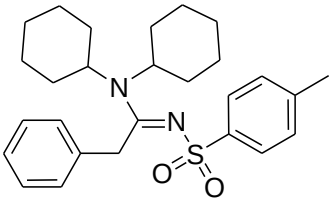
[a]Reaction condition: Phenyl acetylene (1 mmol), 4-toluenesulfonyl azide (1 mmol), di-isopropyl amine (1.2 mmol), THF (5 mL)
[b] Isolated yields after chromatography.

Table 3. Cu-Scolecite catalyzed synthesis of *N*-sulfonyl amidines [a,b]



Entry	Amine (3)	Product (4)	Time (h)	Yield[b] (%)
a			1.20	90
b			2.45	85
c			2.30	80
d			3.00	87
e			2.30	80

f			3.05	78
g			5.45	61
h			5.30	81
i			2.30	70
j			2.00	78
k			2.50	84

l			2.15	87

[a]Reaction condition: Phenyl acetylene (1 mmol), 4-toluenesulfonyl azide (1 mmol), amines (1.2 mmol), THF (5 mL)
[b] Isolated yields after chromatography

Table 4. Crystal data and structure refinement for **4e**

Identification code	**4e**	
Empirical formula	$C_{21}H_{28}N_2O_2S$	
Formula weight	372.51	
Temperature	293(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1/n$	
Unit cell dimensions	a = 6.6844(4) Å	a= 90°.
	b = 12.5711(9) Å	b= 90.879(5)°.
	c = 23.9102(16) Å	g = 90°.
Volume	2008.9(2) $Å^3$	
Z	4	
Density (calculated)	1.232 Mg/m^3	
Absorption coefficient	0.178 mm^{-1}	
F(000)	800	
Crystal size	0.350 x 0.350 x 0.300 mm^3	
Theta range for data collection	2.351 to 24.997°.	
Index ranges	-7<=h<=7, -14<=k<=14, -28<=l<=28	
Reflections collected	25195	
Independent reflections	3515 [R(int) = 0.0832]	
Completeness to theta = 24.997°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9499 and 0.9421	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3515 / 0 / 236	
Goodness-of-fit on F^2	1.034	
Final R indices [I>2sigma(I)]	R1 = 0.0455, wR2 = 0.1039	
R indices (all data)	R1 = 0.1079, wR2 = 0.1303	
Extinction coefficient	0.0048(10)	
Largest diff. peak and hole	0.205 and -0.258 $e.Å^{-3}$	
CCDC number	1039420	

Table 5. Hydrogen-bond geometry (A°, °) of **4e**

Specified hydrogen bonds (with esds except fixed and riding H)

D-H	H...A	D...A	<(DHA)	
0.97	2.58	3.530(3)	165.8	C9-H9A...O2_$1
0.97	2.54	3.221(3)	127.1	C9-H9B...O1
0.97	2.56	3.038(3)	110.5	C9-H9B...S1
0.97	2.64	3.131(4)	111.4	C17-H17C...N2
0.97	2.65	3.473(3)	142.5	C19-H19D...O2_$1

Table 6. Comparison of different catalyst for synthesis of **4a**

Sr. No.	Catalyst	Quantity	Temp (°C)	Time (h)	Yield (%)	Ref.
1	MOF−Cu_2I_2($BTTP_4$)	2.4 mol%	RT	2	88	22c
2	CuI	10 mol%	RT	2	89	22d
3	$Cu(OTf)_2$	5 mol%	70°C	15	98	22e
4	CuI	10 mol%	RT	2	82	22f
5	CuI	10 mol%	RT	12	89	22g
6	Cu-Scolecite	4.17 mol%	RT	1.20	90	This work