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RESEARCH PAPER

Sulfuric Acid ([3-(3-Silicapropyl)sulfanyl]propyl)ester as a Recyclable Catalyst for the Synthesis of 4,4'-(Arylmethylene)bis(1*H*-pyrazol-5-ols)

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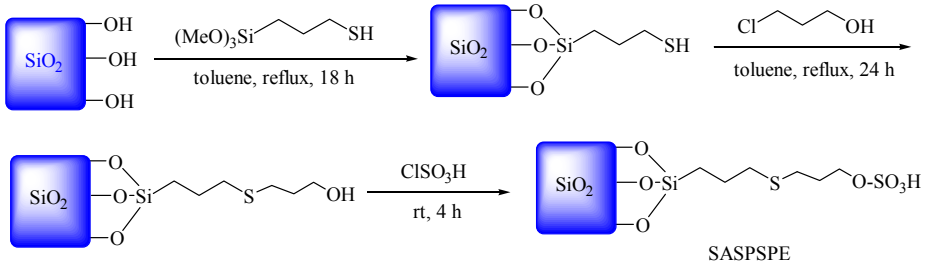
Abstract: Sulfuric acid ([3-(3-silicapropyl)sulfanyl]propyl)ester is employed as a recyclable catalyst for the condensation reaction between aromatic aldehydes and 3-methyl-l-phenyl-5-pyrazolone. This condensation reaction was performed in ethanol under refluxing conditions giving 4,4'-alkylmethylene-bis(3-methyl-5-pyrazolones) in 74-90% yields. The heterogeneous catalyst was recycled and used in eleven runs for the reaction between benzaldehyde and 3-methyl-l-phenyl-5-pyrazolone without losing catalytic activity.

Key words: sulfuric acid ([3-(3-silicapropyl)sulfanyl]propyl)ester; silica-bonded *N*-propyl sulfamic acid; 3-methyl-l-phenyl-5-pyrazolone; aldehydes

The development of heterogeneous catalysts for organic synthesis has become a major area of research. The potential advantages of these materials over homogeneous systems (simplified recovery, reusability, and the potential for incorporation in continuous reactors and microreactors) could lead to novel, environmentally benign chemical procedures for academia and industry [1,2]. The application of solid acids in organic transformations is important because they have many advantages including ease of handling, decreased reactor and plant corrosion problems, and their disposal is more environmentally friendly [3–21].

Several types of solid sulfonic acid functionalized silica (both amorphous and ordered) have been synthesized and applied as alternatives to traditional sulfonic acid resins and homogeneous acids for catalyzing chemical transformations [3–8]. In continuation of our studies into the design and application of solid acid catalysts in organic transformations [7–21], we thus describe the application of sulfuric acid ([3-(3-silicapropyl)sulfanyl]propyl)ester (SASPSPE) as recyclable catalyst for the synthesis of 4,4'-alkylmethylene-bis(3-methyl-5-pyrazolones) (Scheme 1).

Pyrazoles are an important class of bio-active drug targets in the pharmaceutical industry as they are the core structure of numerous biologically active compounds [22–24]. For example; they exhibit anti-anxiety, antipyretic, analgesic and anti-inflammatory properties. 2,4-Dihydro-3*H*-pyrazol-3-one



Scheme 1. Preparation of sulfuric acid ([3-(3-silicapropyl)sulfanyl]propyl)ester (SASPSPE).

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derivatives including 4,4'-(arylmethylene)bis(3-methyl-1-phenyl-1*H*-pyrazol-5-ols) have a broad spectrum of approved biological activity and are used as anti-inflammatory [25], antipyretic [26], gastric secretion stimulatory [27], antidepressant [28], antibacterial [29] and antifilarial agents [30]. Moreover, the corresponding 4,4'-(arylmethylene)bis(1*H*-pyrazol-5-ols) are applied as fungicides [31], pesticides [32], insecticides [33], and dyestuffs [34–36], and as chelating and extraction reagents for different metal ions [37,38]. The conventional chemical approach to 4,4'-(arylmethylene)bis(3-methyl-1-phenyl-pyrazol-5-ols) involves the successive Knoevenagel synthesis of the corresponding arylidenepyrazolones and its base-promoted Michael reaction as well as the one-pot tandem Knoevenagel-Michael reaction of arylaldehydes with two equivalents of 5-methyl-2-phenyl-2,4-dihydro-3*H*-pyrazol-3-one performed under various reaction conditions [39,40]. The first set of procedures is concerned with the catalysis of the components with piperidine in ethanolic solution [41,42]. The second set of methods involves the non-catalyzed tandem Knoevenagel-Michael reaction under neutral conditions in either ethanol [43] or benzene [44] solutions. Although the corresponding 4,4'-(arylmethylene)bis(1*H*-pyrazol-5-ols) are obtained in reliable 70%–90% yields, the reaction requires 3–12 h of initial reflux and a further 24 h under ambient temperature to reach completion. Recently, sodium dodecyl sulfate [45], an electrocatalytic procedure [46], CAN [47], and silica-bonded *S*-sulfonic acid [17] were reported for the synthesis of 4,4'-(arylmethylene)bis(3-methyl-1-phenyl-1*H*-pyrazol-5-ols). However, most of these methods suffer from at least one limitation that may include moderate yields, long reaction times, harsh reaction conditions, or tedious workup procedures.

1 Experimental

1.1 Catalyst preparation

1.1.1 3-(3-Silicapropylthio)-1-propanol

3-Chloro-1-propanol (5 mmol, 0.473 g) was added to a magnetically stirred mixture of 3-mercaptopropylsilica (10 g) in toluene (30 ml) and then a few drops of triethyl amine was added and the resulting mixture was refluxed for 24 h. The mixture was filtered and the solid was washed with ethanol (20 ml × 3) and then dried in an oven. 3-(3-Silicapropylthio)-1-propanol was obtained as a cream powder (10.3 g).

1.1.2 SASPSPE

To a mixture of 3-(3-silicapropylthio)-1-propanol (5 g) in chloroform (20 ml), chlorosulfonic acid (0.19 g, 1.65 ml) was added dropwise at 0 °C over 2 h. After the addition was complete the mixture was stirred for 2 h until HCl gas evolution was stopped. Then, the mixture was filtered and washed with ethanol (30 ml) and dried at room temperature to obtain SASPSPE as a cream powder (5.13 g). The sulfur content of the samples by conventional elemental analysis was 15.51% [7].

1.2 General procedure for the synthesis of 4,4'-(arylmethylene)bis(1*H*-pyrazol-5-ols)

A mixture of aromatic aldehyde (1 mmol), 5-methyl-2-phenyl-2,4-dihydro-3*H*-pyrazol-3-one (2 mmol), and SASPSPE (0.1 g) in ethanol (10 ml) were added to a flask and heated under reflux for an appropriate time. After completion of the reaction, as indicated by thin layer chromatography (TLC, silica gel SILG/UV 254 plates), the reaction mixture was washed with warm ethanol (30 ml × 3). After cooling, the crude products were precipitated. The crude products were purified by recrystallization from ethanol (95%). The recovered catalyst was washed with diethyl ether, dried, and reused in subsequent runs.

The infrared (IR) spectra were obtained on a Shimadzu IR-435. The ^{1}H NMR was carried out on a Bruker Avance (300 MHz or DRX 500 MHz) or Bruker Ultrashield (400 MHz). Melting points were determined using a Melting Point SMP1 apparatus in open capillary tubes and are uncorrected. All the products were characterized by comparing their spectral (IR, ^{1}H NMR), TLC, and physical data with those reported in the literature [34–48]

4,4'-(Phenylmethylene)bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (3a). White cream solid; recrystallized from ethanol; mp 170–172 °C (171–172 °C [45]). IR (KBr, cm^{-1}): 3400 (br), 3080 (w), 2900 (w), 1593 (s), 1494 (vs), 1410 (s), 1275 (s), 1020 (m), 730 (vs), 690 (s). ^{1}H NMR (300 MHz, DMSO-d$_6$): δ 2.32 (6H, s), 4.96 (1H, s), 7.17–7.27 (7H, m), 7.44 (4H, t, J = 7.72 Hz), 7.71 (4H, d, J = 7.91 Hz), 13.96 (2H, br, OH). ^{13}C NMR (75 MHz, DMSO-d$_6$): δ 33.13, 120.52, 125.55, 125.88, 127.17, 128.12, 128.90, 142.22, 146.29.

4,4'-[(4-Methylphenyl)methylene]bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (3b). White solid; recrystallized from ethanol; mp 202–204 °C (203 °C [40]). IR (KBr, cm^{-1}): 3440 (br), 3075 (w), 2830 (w), 1590 (s), 1495 (vs), 1408 (s), 1294 (s), 1020 (m), 800 (m), 744 (vs), 688 (s). ^{1}H NMR (300 MHz, DMSO-d$_6$): δ 2.24 (3H, s), 2.30 (6H, s), 4.90 (1H, s), 7.07 (2H, d, J = 8.29 Hz), 7.13 (2H, d, J = 8.10 Hz), 7.24 (2H, t, J = 7.35 Hz), 7.44 (4H, t, J = 7.72 Hz), 7.70 (4H, d, J = 7.91 Hz), 13.93 (2H, br, OH). ^{13}C NMR (75 MHz, DMSO-d$_6$): δ 18.55, 32.39, 114.85, 120.47, 125.49, 128.08, 128.89, 132.27, 137.39, 146.18, 155.49.

4,4'-[(4-isopropylphenyl)methylene]bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (3c). White cream solid; recrystallized from ethanol; mp 132–134 °C. IR (KBr, cm^{-1}): 3435 (br), 3080 (w), 2920 (w), 2830 (w), 1590 (s), 1495 (vs), 1408 (s), 1380 (m), 1365 (m), 1294 (s), 1020 (m), 779 (m), 744 (s), 688 (s). ^{1}H NMR (500 MHz, DMSO-d$_6$): δ 1.16 (6H, d, J = 6.9 Hz), 2.31

(6H, s), 2.79–2.85 (1H, m), 4.90 (1H, s), 7.13 (2H, d, J = 8.2 Hz), 7.18 (2H, d, J = 8.1 Hz), 7.23 (2H, t, J = 7.25 Hz), 7.43 (4H, t, J = 7.3 Hz), 7.72 (4H, d, J = 7.9 Hz), 12.30 (1H, br, OH), 14.03 (1H, s, OH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 12.51, 24.78, 33.70, 33.84, 121.39, 126.40, 126.93, 127.93, 129.77, 140.57, 146.72, 147.14. Anal. Calcd for $C_{30}H_{30}N_4O_2$ (%): C, 75.29; H, 6.32; N, 11.71. Found: C, 75.12; H, 6.35; N, 11.54.

4,4'-[(3,4,5-Trimethoxyphenyl)methylene]bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (3d). White cream solid; recrystallized from ethanol; mp 195–197 °C. IR (KBr, cm^{-1}): 3447 (br), 3085 (w), 2885 (w), 1585 (s), 1490 (vs), 1443 (s), 1410 (s), 1318 (m), 1262 (m), 1122 (m), 898 (m), 850 (s), 790 (vs), 690 (s). ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.33 (6H, s), 3.62 (3H, s), 3.69 (6H, s), 4.85 (1H, s), 6.69 (2H, s), 7.24 (2H, t, J = 7.25 Hz), 7.43 (4H, t, J = 7.81 Hz), 7.71 (4H, d, J = 7.91 Hz), 14.29 (1H, s, OH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 12.61, 34.76, 56.70, 60.80, 105.81, 121.59, 126.45, 129.78, 136.86, 138.29, 139.62, 147.03, 153.42. Anal. Calcd for $C_{30}H_{30}N_4O_5$ (%): C, 68.42; H, 5.74; N, 10.64. Found: C, 68.19; H, 5.59; N, 10.38.

4,4'-[(2-Hydroxyphenyl)methylene]bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (3e). White solid; recrystallized from ethanol; mp 227–229 °C (230–231 °C [46]). IR (KBr, cm^{-1}): 3400 (br), 3060 (w), 2920 (w), 2830 (w), 1605 (s), 1575 (s), 1455 (vs), 1225 (m), 750 (s), 690 (s). ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.28 (6H, s), 5.16 (1H, s), 6.70 (1H, t, J = 7.5 Hz), 6.74 (1H, d, J = 7.5 Hz), 6.96 (1H, t, J = 7.0 Hz), 7.22 (2H, t, J = 7.3 Hz), 7.42 (4H, t, J = 7.9 Hz), 7.57 (1H, d, J = 7.2 Hz), 7.71 (4H, d, J = 7.8 Hz). ^{13}C NMR (125 MHz, DMSO-d_6): δ 12.73, 28.15, 115.66, 119.42, 121.37, 126.18, 127.65, 129.71, 147.16, 154.68.

4,4'-[(2-Bromophenyl)methylene]bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (3f). White cream solid; recrystallized from ethanol; mp 198–200 °C. IR (KBr, cm^{-1}): 3440 (br), 3060 (w), 2920 (w), 1605 (s), 1560 (s), 1495 (vs), 1395 (m), 1365 (m), 1300 (m), 830 (m), 744 (s), 690 (s). ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.31 (6H, s), 5.10 (1H, s), 7.13 (1H, t, J = 7.25 Hz), 7.23 (2H, t, J = 7.0 Hz), 7.33 (1H, t, J = 7.3 Hz), 7.42 (4H, t, J = 7.9 Hz), 7.56 (1H, d, J = 7.8 Hz), 7.71 (4H, d, J = 7.9 Hz), 7.86 (1H, m), 12.68 (1H, br, OH), 13.92 (1H, s, OH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 13.08, 35.21, 121.49, 123.54, 126.43, 128.30, 129.16, 129.76, 131.44, 133.64, 138.21, 146.78. Anal. Calcd for $C_{27}H_{23}BrN_4O_2$ (%): C, 62.92; H, 4.50; Br, 15.50; N, 10.87. Found: C, 62.74; H, 4.54; N, 10.70.

4,4'-[(4-Chlorophenyl)methylene]bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (3g). White solid; recrystallized from ethanol; mp 215–217 °C (210 °C [40]). IR (KBr, cm^{-1}): 3430 (br), 3085 (w), 2920 (w), 1595 (s), 1490 (vs), 1410 (s), 1290 (m), 804 (m), 742 (s), 690 (s). ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.30 (6H, s), 4.98 (1H, s) 7.22–7.28 (4H, m), 7.35 (2H, d, J = 8.48 Hz), 7.44 (4H, t, J =7.91 Hz), 7.71 (4H, d, J = 7.91 Hz), 13.90 (2H, br, OH). ^{13}C NMR (75 MHz, DMSO-d_6): δ 32.56, 120.54, 125.62, 128.00, 128.90, 129.13, 130.56, 137.18, 141.14, 146.23.

4,4'-[(2-Chlorophenyl)methylene]bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (3h). White solid; recrystallized from ethanol; mp 235–237 °C (236–237 °C [45]). IR (KBr, cm^{-1}): 3450 (br), 3070 (w), 2910 (w), 1610 (m), 1555 (s), 1495 (vs), 1395 (m), 1360 (m), 1300 (s), 835 (m), 740 (s), 690 (s). ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.29 (6H, s), 5.14 (1H, s), 7.22–7.33 (4H, m), 7.40 (1H, d, J = 7.82 Hz), 7.44 (4H, t, J = 7.57 Hz), 7.70 (4H, d, J = 7.57 Hz), 7.80 (1H, d, J = 7.06 Hz), 13.92 (2H, br, OH). ^{13}C NMR (100 MHz, DMSO-d_6): δ 32.41, 120.67, 123.62, 126.92, 128.05, 128.93, 129.45, 130.32, 135.94, 137.36, 140.60, 141.18.

4,4'-[(4-Flurophenyl)methylene]bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (3i). White solid; recrystallized from ethanol; mp 181–183 °C (182 °C [40]). IR (KBr, cm^{-1}): 3445 (br), 3080 (w), 2882 (w), 1590 (s), 1495 (vs), 1401 (m), 1380 (s), 1308 (m), 1121 (m), 902 (s), 842 (m), 788 (s), 690 (s). ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.31 (6H, s), 4.95 (1H, s), 7.09 (2H, t, J = 8.75 Hz), 7.22-7.28 (4H, m), 7.43 (4H, t, J = 7.65 Hz), 7.70 (4H, d, J = 7.90 Hz), 12.48 (1H, br, OH), 13.91 (1H, s, OH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 12.43, 33.32, 115.51, 115.68, 121.42, 126.45, 129.74, 129.78, 129.85, 129.92, 139.07, 147.11, 162.50.

4,4'-[(4-Nitrophenyl)methylene]bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (3j). Yellow solid; recrystallized from ethanol; mp 225–227 °C (224–226 °C [45]). IR (KBr, cm^{-1}): 3440 (br), 3090 (w), 2920 (w), 1595 (s), 1495 (vs), 1410 (s), 1340 (m), 744 (s), 689 (s). ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.28 (6H, s), 5.06 (1H, s), 7.18 (2H, t, J = 7.06 Hz), 7.38 (4H, t, J = 7.31 Hz), 7.45 (2H, d, J = 8.32 Hz), 7.64 (4H, d, J = 7.82 Hz), 8.10 (2H, d, J = 8.58 Hz), 13.81 (2H, br, OH). ^{13}C NMR (100MHz, DMSO-d_6): δ 34.45, 121.91, 124.65, 127.03, 129.92, 130.25, 147.20, 147.58, 151.63.

4,4'-[(3-Nitrophenyl)methylene]bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (3k). Pale yellow solid; recrystallized from ethanol; mp 151–153 $_o$C (149–150 °C [45]). IR (KBr, cm^{-1}): 3420 (br), 3085 (w), 2910 (w), 1595 (s), 1495 (vs), 1340 (s), 758 (m), 735 (s), 692 (s), 598 (m). ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.35 (6H, s), 5.14 (1H, s), 7.26 (2H, t, J = 7.31 Hz), 7.45 (4H, t, J = 7.57 Hz), 7.60 (1H, t, J = 8.32 Hz), 7.68–7.74 (5H, m), 8.06–8.10 (2H, m), 13.91 (2H, br, OH). ^{13}C NMR (100MHz, DMSO-d_6): δ 32.80, 120.63, 121.21, 121.70, 125.78, 125.81, 128.98, 129.71, 134.34, 137.39, 144.56, 146.30, 147.72.

4,4'-[(4-Cyanophenyl)methylene]bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (3l). Yellow solid; recrystallized from ethanol; mp 210–212 °C, (210–212 °C [17]). IR (KBr, cm^{-1}): 3420 (br), 3090 (w), 2921 (w), 2230 (m), 1595 (s), 1495 (vs), 1410 (s), 1290 (m), 810 (m), 750 (s), 690 (s). ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.33 (6H, s), 5.07 (1H, s), 7.25 (2H, t, J = 7.31 Hz), 7.42–7.46 (6H, m), 7.40 (4H, d, J = 7.82 Hz), 7.76 (2H, d, J = 8.32 Hz), 13.89 (2H, br, OH). ^{13}C NMR (100 MHz, DMSO-d_6): δ 33.23, 119.00, 120.61, 125.57, 128.38, 128.94, 133.36, 142.59, 148.15.

4,4'-[(2-Naphthyl)methylene]bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (**3m**). White solid; recrystallized from ethanol; mp 206–208 °C. IR (KBr, cm^{-1}): 3410 (br), 3030 (w), 1590 (s), 1490 (vs), 1392 (s), 1360 (m), 1280 (m), 1020 (m), 810 (m), 780 (m), 740 (s), 690 (s); ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.36 (6H, s), 5.14 (1H, s), 7.24 (2H, t, J = 6.9 Hz), 7.41–7.45 (7H, m), 7.71–7.73 (5H, m), 7.81–7.85 (3H, m), 12.41 (1H, br, OH), 13.93 (1H, s, OH); ^{13}C NMR (125 MHz, DMSO-d_6): δ 12.50, 34.22, 121.46, 125.80, 126.30, 126.83, 127.36, 128.16, 128.52, 128.59, 129.79, 132.54, 133.73, 140.55, 147.19. Anal. Calcd for $C_{31}H_{26}N_4O_2$ (%): C, 76.52; H, 5.39; N, 11.51; Found: C, 76.35; H, 5.30; N, 11.46.

4,4'-[(3-Pyridyl)methylene]bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (**3n**). White cream solid; recrystallized from ethanol; mp 238–240 °C. IR (KBr, cm^{-1}): 3410 (br), 3050 (w), 2900 (w), 1595 (s), 1490 (vs), 1410 (s), 1345 (m), 1280 (m), 1020 (m), 850 (m), 790 (m), 745 (s), 695 (s); ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.34 (6H, s), 5.05 (1H, s), 7.23 (2H, t, J = 7.1 Hz), 7.34 (1H, t, J = 6.0 Hz), 7.43 (4H, t, J = 7.5 Hz), 7.71–7.73 (5H, m), 8.41 (1H, d, J = 3.6 Hz), 8.51 (1H, s), 12.10 (1H, br, OH), 14.12 (1H, br, OH); ^{13}C NMR (125 MHz, DMSO-d_6): δ 12.54, 31.96, 104.68, 121.45, 124.22, 126.44, 129.76, 136.16, 138.25, 138.91, 147.04, 147.61, 149.32. Anal. Calcd for $C_{26}H_{23}N_5O_2$ (%): C, 71.38; H, 5.30; N, 16.01; Found C, 71.20; H, 5.25; N, 15.87.

4,4'-[(2-Thienyl)methylene]bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (**3o**). White cream solid; recrystallized from ethanol; mp 181–183 °C (181–183 °C [17]). IR (KBr, cm^{-1}): 3420 (br), 3080 (w), 2920 (w), 1595 (s), 1490 (vs), 1410 (s), 1284 (s), 779 (vs), 690 (s). ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.32 (6H, s), 5.13 (1H, s), 6.75–6.77 (1H, m), 6.90–6.92 (1H, m), 7.24–7.30 (3H, m), 7.45 (4H, t, J = 7.82 Hz), 7.71 (4H, d, J = 7.82 Hz) 14.01 (2H, br, OH). ^{13}C NMR (100MHz, DMSO-d_6): δ 29.43, 120.58, 124.05, 124.15, 126.75, 128.94, 132.99, 134.13, 147.73.

4,4'-[(2-Furyl)methylene]bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (**3p**). White cream solid; recrystallized from ethanol; mp 189–191 °C (181–183 °C [47]). IR (KBr, cm^{-1}): 3420 (br), 3080 (w), 2920 (w), 1595 (s), 1490 (vs), 1410 (s), 1284 (s), 779 (vs), 690 (s). ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.31 (6H, s), 4.99 (1H, s), 6.12-6.14 (1H, m), 6.34-6.36 (1H, m), 7.25 (2H, t, J = 6.0 Hz), 7.43–7.51 (5H, m), 7.71 (4H, d, J = 8.0 Hz), 12.46 (1H, br, OH), 13.85 (1H, s, OH). ^{13}C NMR (100MHz, DMSO-d_6): δ 28.22, 106.11, 109.88, 110.34, 120.43, 120.55, 125.60, 128.91, 131.92, 141.54.

1,3-Diphenylene-4,4'-(methylene)bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (**4a**). White cream solid; recrystallized from ethanol; mp 191–192 °C (190–194 °C [48]). IR (KBr, cm^{-1}): 3405 (br), 3015 (w), 1599 (s), 1402 (vs), 1279 (vs), 1025 (m), 788 (m), 753 (vs), 683 (vs). ^{1}H NMP (400 MHz, DMSO-d_6): δ 2.25 (12H, s), 4.86 (2H, s), 7.07–7.67 (24H, m), 12.45 (2H, br, OH) 14.08 (2H, s, OH). ^{13}C NMP (100 125MHz, DMSO-d_6): δ 18.54, 33.34, 120.70, 125.87, 126.68, 128.82, 134.52, 142.40, 149.89, 154.26.

1,4-Diphenylene-4,4'-(methylene)bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (**4b**). White cream solid; recrystallized from ethanol; mp 214–216 °C (218–220 °C [48]). IR (KBr, cm^{-1}): 3410 (br), 3020 (w), 1590 (s), 1490 (vs), 1410 (s), 1350 (s), 1290 (s), 1120 (s), 1020 (m), 850 (m), 745 (vs), 690 (s). ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.29 (12H, s), 5.05 (2H, s), 7.17 (4H, s), 7.22 (4H, t, J = 7.1 Hz), 7.41 (8H, t, J = 7.8 Hz), 7.69 (8H, d, J = 7.9 Hz), 12.41 (2H, br, OH) 14.11 (2H, s, OH). ^{13}C NMR (125MHz, DMSO-d_6): δ 12.51, 33.69, 121.50, 127.84, 129.72, 140.93, 147.07, 155.01. Anal. Calcd for $C_{48}H_{42}N_8O_4$ (%): C, 72.52; H, 5.32; N, 14.09. Found: C, 72.35; H, 5.29; N, 13.85.

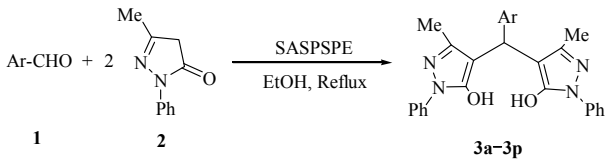
2 Results and discussion

To study the effect of catalyst loading on the condensation reaction of aromatic aldehydes with 3-methyl-l-phenyl-5-pyrazolone the reaction between benzaldehyde and 5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one was chosen as the model reaction (Table 1). The results show clearly that SASPSPE is an effective catalyst for this condensation and in the absence of SASPSPE the condensation reaction gave a very low yield after 24 h. The optimal amount of SASPSPE was 0.1 g (3.4 mol%) per 1 mmol of aldehyde in refluxing ethanol. Although the lower catalyst loading of 0.05 g of SASPSPE accomplished this condensation, 0.1 g SASPSPE per 1 mmol of aldehyde was optimum in terms of the reaction time and the isolated yield. Also, the model reaction was examined using optimum amounts and at room temperature, and we obtained a GC yield of 55% for the corresponding product (Table 1, entry 11). In addition, the result of this condensation in the presence

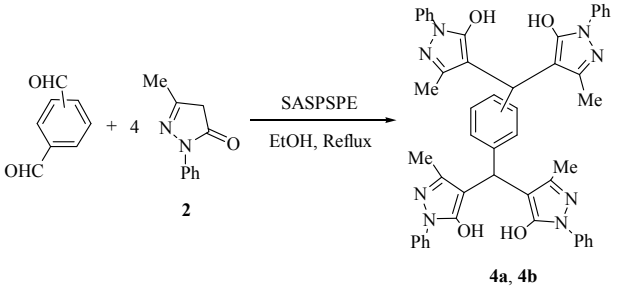
Table 1 Condensation reaction of benzaldehyde with 5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one in the presence of different amounts of catalysts

Entry	Catalyst	Catalyst loading	Time (h)	Yield[a] (%)
1	no catalyst	—	24	<10
2	SASPSPE	0.05 g (0.017 mmol)	6.5	70
3	SASPSPE	0.07 g (0.023 mmol)	5.0	78
4	SASPSPE	0.1 g (0.034 mmol)	3.0	90
5	SASPSPE	0.15 g (0.051 mmol)	3.0	89
6	SBNPSA	0.2 g (0.068 mmol)	4.0	90
7	H_2SO_4	0.2 mmol	4.0	44[c]
8	H_2SO_4	1.0 mmol	3.0	44[c]
9	H_2SO_4	4.0 mmol	1.2	45[c]
10	H_2SO_4	10.0 mmol	0.7	47[c]
11	SASPSPE	0.1 g (0.034 mmol)	15.0	55[d]

Reaction conditions: benzaldehyde 1 mmol, 5-methyl-2-phenyl-2,4-dihydro-3*H*-pyrazol-3-one 2 mmol, EtOH 10 ml, reflux conditions. [a]Isolated yield. [b]Silica-bonded *N*-propyl-sulfamic acid (SBNPSA) [8]. [c]The same yield was obtained for the by-product. [d]GC yield of the conversion at room temperature.



Scheme 2. The condensation of aromatic aldehydes with 3-methyl-l-phenyl-5-pyrazolone upon catalysis by SASPSPE.



Scheme 3. The condensation of terephthaldehyde with 3-methyl-l-phenyl-5-pyrazolone catalyzed by SASPSPE.

of commercially available sulfuric acid is shown in Table 1.

Therefore, we employed optimized conditions for the condensation reaction of various aryl aldehydes with 3-methyl-l-phenyl-5-pyrazolone to give the corresponding 4,4'-(arylmethylene)bis(3-methyl-1-phenyl-1H-pyrazol-5-ols) (Scheme 2).

As shown in Table 2, both the aromatic and heteroaromatic aldehydes react with 3-methyl-l-phenyl-5-pyrazolone to afford 4,4'-(arylmethylene)-bis-(3-methyl-1-phenyl-1*H*-pyrazol-5-ols) in excellent yields. On the other hand, benzaldehydes with electron-donating or electron-withdrawing groups, i.e. methyl, iso-propyl, and 3,4,5-trimethoxybenzaldehyde (Table 2, entries 2–4) or 4-nitro, 3-nitro, and 4-cyano-benzaldehyde (Table 2, entries 10–12) condense into the corresponding 4,4'-(arylmethylene)-bis-(3-methyl-1-phenyl-1*H*-pyrazol-5-ols) **3b**–**3d** and **3j**–**3l** in high yields. The acid sensitive substrates 3-pyridine carbaldehyde, thiophene-2-carbaldehyde, and furfural (Table 2, entries 14–16) were converted into the corresponding products **3n**, **3o**, and **3p** in 84%, 74%, and 75% yields, respectively. 2-Naphthyl carbaldehyde was converted into the corresponding product **3m** in 88% yield (Table 2, entry 13). Cinnamyl aldehyde was reacted with 3-methyl-1-phenyl-5-pyrazolone under the optimized conditions but gave a mixture of products.

The practical synthetic efficiency of this reaction was highlighted by the reaction of terephthaldehyde and isophthaldehyde with 3-methyl-1-phenyl-5-pyrazolone to give structurally complex pyrazol-5-ol derivatives (**4a** and **4b**, Scheme 3).

The possibility of recycling the catalyst SASPSPE was examined using the reaction of benzaldehyde and 5-methyl-2-phenyl-2,4-dihydro-3*H*-pyrazol-3-one under the optimized conditions. Upon completion, the reaction mixture was washed with warm ethanol (30 ml × 3). The recovered catalyst was washed with diethyl ether, dried, and reused for subsequent runs. The recycled catalyst was reused eleven times without any additional treatment. No observation of any appreciable loss in the catalytic activity of SASPSPE was observed (Fig. 1).

Table 2 Preparation of 4,4'-(arylmethylene)-bis-(3-methyl-1-phenyl-1*H*-pyrazol-5-ols) derivatives catalyzed by SASPSPE in ethanol under reflux conditions

Entry	Ar (**1**)	Product	Time (h)	Yield[a] (%)	mp (°C)
1	C_6H_5-	**3a**	3.0	90	170–172 (171–172 [45])
2	4-Me-C_6H_4-	**3b**	2.3	89	202–204 (203 [40])
3	4-*iso*-Pr-C_6H_4-	**3c**	3.5	88	132–134
4	3,4,5-$(MeO)_3$-C_6H_2-	**3d**	3.3	89	195–197
5	2-HO-C_6H_4-	**3e**	3.5	83	227–229 (230–231 [46])
6	2-Br-C_6H_4-	**3f**	2.6	78	198–200
7	4-Cl-C_6H_4-	**3g**	2.2	85	215–217 (210 [40])
8	2-Cl-C_6H_4-	**3h**	2.4	77	235–237 (236–237 [45])
9	4-F-C_6H_4-	**3i**	2.5	86	181–183 (182 [40])
10	4-O_2N-C_6H_4-	**3j**	2.0	88	225–227 (224–226 [45])
11	3-O_2N-C_6H_4-	**3k**	2.3	87	151–153 (149–150 [45])
12	4-(CN)-C_6H_4-	**3l**	2.1	89	210–212 (210–212 [17])
13	2-$C_{10}H_7$-	**3m**	3.0	88	206–208
14	3-pyridyl-	**3n**	3.0	84	238–240
15	2-thienyl-	**3o**	4.0	74	181–183 (181–183 [17])
16	2-furyl-	**3p**	4.0	75	189–191 (189–190 [47])
17	3-OHC-C_6H_4-	**4a**	4.0	82	191–192 (190–194 [48])
18	4-OHC-C_6H_4-	**4b**	4.0	86	214–216 (218–220 [48])

Reaction conditions: aromatic aldehyde 1 mmol, 5-methyl-2-phenyl-2,4-dihydro-3*H*-pyrazol-3-one 2 mmol, catalyst SASPSPE 0.1 g, EtOH 10 ml, reflux conditions. [a]Isolated yield.

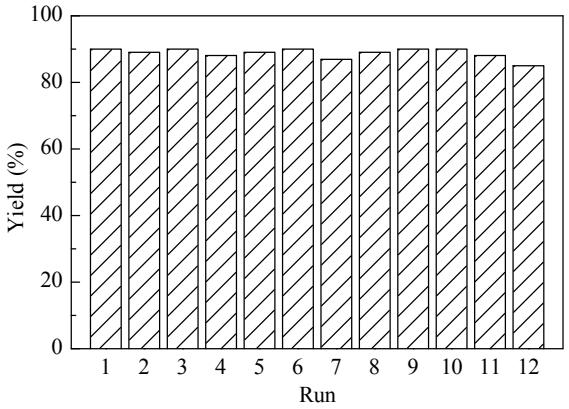


Fig. 1. Recyclability of SASPSPE as a catalyst in the condensation reaction between benzaldehyde (1 mmol) and 5-methyl-2-phenyl-2,4-dihydro-3*H*-pyrazol-3-one (2 mmol) in the presence of 0.1 g of SASPSPE in refluxing ethanol. Reaction time 3 h.

3 Conclusions

We prepared new 4,4'-(arylmethylene)-bis-(3-methyl-1-phenyl-1*H*-pyrazol-5-ols) by a tandem condensation reaction between aromatic aldehydes and two equivalents of 5-methyl-2-phenyl-2,4-dihydro-3*H*-pyrazol-3-one in the presence of sulfuric acid ([3-(3-silicapropyl)sulfanyl]propyl) ester in refluxing ethanol.

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