

Synthesis of 4,4'-(Arylmethylene)bis(1H-pyrazol-5-ols) Using Silica-bonded Ionic Liquid as Recyclable Catalyst

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Abstract

4,4'-(Arylmethylene)bis(1*H*-pyrazol-5-ols) were synthesized in the presence of *N*-(3-silicapropyl)-*N*-methyl imidazolium hydrogen sulfate ([Sipmim]HSO₄) as a recyclable solid acid catalyst from the reaction between aldehydes and 3-methyl-1-phenyl-5-pyrazolone in refluxing ethanol. [Sipmim]HSO₄ showed much the same efficiency when used in consecutive reaction runs.

Keywords: *N*-(3-Silicapropyl)-*N*-methyl imidazolium hydrogen sulfate, catalyst, bis(1*H*-pyrazol-5-ols), synthesis

1. Introduction

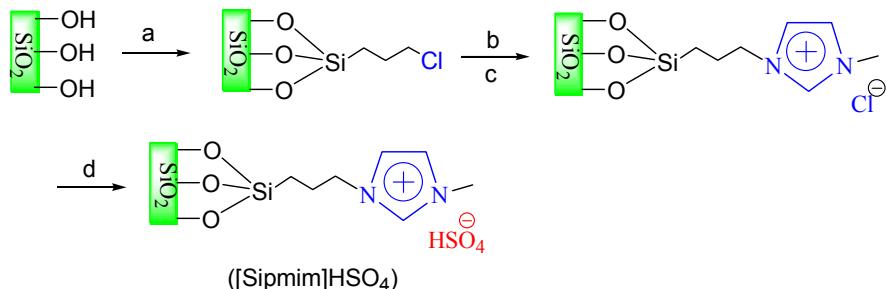
In the recent years, ionic liquids were used as solvents due to their particular properties, such as the ability to dissolve many organic and inorganic substances and undetectable vapor pressure (Wasserscheid & Welton, 2007). In addition, Brønsted acidic task-specific ionic liquids (BAILS), such as those possessing HSO₄⁻ as a counter anion find a broad application in organic synthesis, acting as both solvents and catalysts. Keim and co-workers reported the synthesis of 1-butyl-3-methylimidazolium hydrogensulfate ([bmim]HSO₄) (Keim et al., 2000). In addition, in the year of 2002 ([bmim]HSO₄) was used as a catalyst in the Friedel-Crafts alkylation (Wasserscheid et al., 2002). The other applications of these acidic ionic liquids such as acetalization and thioacetalization of carbonyl compounds (Gupta et al., 2007), Fischer indole synthesis (Xu et al., 2007), acetylation of alcohols and phenols (Wang et al., 2008), preparation of azides from alcohols (Hajipour et al., 2009), selective nitration of phenols (Tajik et al., 2009), synthesis of 1,8-dioxo-octahydroxanthenes (Niknam & Damya, 2009), formylation of alcohols (Niknam et al., 2009), synthesis of polysubstituted quinolines (Tajik et al., 2011), have been proceeded with very good yields and selectivities. Recently, immobilization of acidic ionic liquids on solid supports has been designed and it can offer important advantages in handling, separation and reuse procedures. Based on economic criteria, it is desirable to minimize the amount of ionic liquid utilized in a potential process. Immobilized acidic ionic liquids have been used as novel solid catalysts, e.g., for esterification, nitration reactions (Qiao et al., 2006), acetal formation (Sugimura et al., 2007), and Baeyer-Villiger reaction (Chrobok et al., 2009).

The pyrazolones and bis-pyrazolones were paid much attention for their various biological activities such as selective COX-2 inhibitory (Cho et al., 2004), antitumor (Park et al., 2005; Clark et al., 2004), cytokine inhibitors (Clark et al., 2005). Bis-pyrazolones can be used as antidepressant (Bailey et al., 1985), gastric secretion stimulatory (Rosiere & Grossman, 1951), antibacterial (Mahajan et al., 1991) and antifilarial agents (Chauhan et al., 1993). Moreover, 4,4'-(arylmethylene)bis(1*H*-pyrazol-5-ols) are applied as pesticides (Londershausen, 1996), fungicides (Singh & Singh, 1991) and dyestuffs (Hamama, 2001).

In recent years, different reagents were applied for the synthesis of 4,4'-(arylmethylene)bis(3-methyl-1-phenyl-pyrazol-5-ols) derivatives, some of them including condensation reaction between arylaldehydes and two equivalents of 5-methyl-2-phenyl-2,4-dihydro-3*H*-pyrazol-3-one (Li et al., 1998; Singh & Singh, 1984; Pavlov et al., 1998; Buzykin & Lonshchakova, 1971; Wang et al., 2005; Elinson et al., 2008; Sujatha et al., 2009; Niknam et al., 2010; Niknam & Mirzaee, 2011; Mosaddegh et al., 2010; Zang et al., 2011; Tayebi et al., 2011).

Herein, we prepared [Sipmim]HSO₄ according to previously reported procedure (Chrobok et al., 2009) (Scheme

1) and used as heterogeneous solid acid catalyst for the synthesis of 4,4'-alkylmethylene-bis(3-methyl-5-pyrazolones).



a) (MeO)₃Si-(CH₂)₃-Cl, toluene(dry), Et₃N, reflux, 48 h; b) N-Methyl Imidazole, toluene (dry), 24 h, reflux;
c) Dry under vaccum (50 °C), 4 h; d) CH₂Cl₂ (dry, H₂SO₄ (97%), 48 h, reflux

Scheme 1. Preparation of *N*-(3-silicapropyl)-*N*-methyl imidazolium hydrogen sulfate ([Sipmim]HSO₄)

2. Method

General: Chemicals were purchased from Merck and Fluka. IR spectra were run on a Shimadzu Infra Red Spectroscopy FT-IR-8000. The ¹H and ¹³C NMR was run on Bruker Avance (DRX 500 MHz and 400 MHz) instruments in DMSO-d₆. Results are reported in ppm. Melting points were recorded on a SMP1 Melting Point apparatus in open capillary tubes and are uncorrected. Reaction progress was followed by TLC using silica gel SILG/UV 254 plates. 3-Chloropropyl silica, *N*-(3-silicapropyl)-*N*-methyl imidazolium chloride ([Sipmim]Cl), and *N*-(3-silicapropyl)-*N*-methyl imidazolium hydrogen sulfate ([Sipmim]HSO₄) were prepared according to previously reported procedure (Chrobok et al., 2009).

2.1 Catalyst Preparation

2.1.1 Preparation of *N*-(3-silicapropyl)-*N*-methyl imidazolium Hydrogen Sulfate ([Sipmim]HSO₄)

Into the three-necked round bottom flask equipped with stirrer, ice bath condenser, and thermometer *N*-(3-silicapropyl)-*N*-methyl imidazolium chloride ([Sipmim]Cl) (3.0 g) was suspended in dry CH₂Cl₂ (20 mL). During vigorous stirring, concentrated H₂SO₄ (97 %) (2.9 mmol) was added drop by drop at 0 °C. Then the mixture was warm up to the room temperature, and was refluxing for 48 h. When the formed HCl was completely distilled off the condenser the solution was cooled and the CH₂Cl₂ was removed under vacuum. To remove any water from the reaction mixture 10 mL of benzene was added to the crude ionic liquid and stirred for 3 h with magnetic stirrer at 50 °C. Formed azeotrope was distilled off yielding [Sipmim]HSO₄. Elemental analysis showed the S content to be 1.77 %. According to S content the number of H⁺ sites of [Sipmim]HSO₄ is 0.55 mmol/g.

2.2 General Procedure for the Synthesis of 4,4'-(arylmethylene)bis(1*H*-pyrazol-5-ols)

A round bottom flask contains 6 mL of ethanol was heated in an oil bath. When the temperature was reached to above 70 °C, aromatic aldehyde (1 mmol), 5-methyl-2-phenyl-2,4-dihydro-3*H*-pyrazol-3-one (2 mmol) and [Sipmim]HSO₄ (0.15 g, equal to 0.083 mmol of H⁺) were added to a flask and heated under reflux conditions. After completion of the reaction, as indicated by TLC, the reaction mixture was filtered. The remaining was washed with warm ethanol (3 × 30 mL) in order to separate heterogeneous catalyst. After cooling the crude products were precipitated. The crude products were purified by recrystallization from ethanol (95 %). The recovered catalyst was dried and reused for subsequent runs.

All the products were characterized by comparison of their ¹H NMR and ¹³C NMR spectroscopic data and their melting points with reported values (Li et al., 1998; Singh & Singh, 1984; Wang et al., 2005; Elinson et al., 2008; Sujatha et al., 2009; Niknam et al., 2010; Niknam & Mirzaee, 2011; Mosaddegh et al., 2010; Tayebi et al., 2011).

4,4'-(Phenylmethylene)bis(3-methyl-1-phenyl-1*H*-pyrazol-5-ol) (Table 2, entry 1). White cream solid; mp 170-172 °C, [Lit.: (Wang et al., 2005) 171-172 °C]; δ_H (300 MHz; DMSO-d₆; Me₄Si) 2.32 (6H, s, 2 × CH₃), 4.96 (1H, s, CH), 7.17-7.27 (7H, m, Ar), 7.44 (4H, t, *J* 7.7 Ar), 7.71 (4H, d, *J* 7.9 Ar), 13.96 (2H, br, OH). δ_C (75 MHz; DMSO-d₆; Me₄Si) 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-1*H*-pyrazol-5-ol) (Table 2, entry 2). White solid;

mp 202-204 °C, [Lit.: (Li et al., 1998) 203 °C]; δ_H (300 MHz; DMSO-d₆; Me₄Si) 2.24 (3H, s, CH₃), 2.30 (6H, s, 2 × CH₃), 4.90 (1H, s, CH), 7.07 (2H, d, *J* 8.3 Ar), 7.13 (2H, d, *J* 8.1 Ar), 7.24 (2H, t, *J* 7.4 Ar), 7.44 (4H, t, *J* 7.7 Ar), 7.70 (4H, d, *J* 7.9 Ar), 13.93 (2H, br, OH). δ_C (75 MHz; DMSO-d₆; Me₄Si) 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-Benzoyloxyphenyl)methylene]bis(3-methyl-1-phenyl-1H-pyrazol-5-ol* (**Table 2, entry 3**): White solid; mp 210-212 °C [Lit.: (Li et al., 1998) 214 °C]; δ_H (400 MHz, DMSO-d₆; Me₄Si) 2.32 (6H, s, 2 × CH₃), 4.91 (1H, s, CH), 5.06 (2H, s, CH₂O), 6.93 (2H, d, *J* 8.8 Ar), 7.18 (2H, d, *J* 8.8 Ar), 7.25 (2H, t, *J* 7.2 Ar), 7.31 (1H, t, *J* 7.0 Ar), 7.38 (2H, t, *J* 7.2 Ar), 7.43-7.47 (6H, m, Ar), 7.72 (4H, d, *J* 8.0 Ar), 13.97 (1H, br, OH). δ_C (100 MHz, DMSO-d₆; Me₄Si) 12.10, 32.85, 69.63, 114.86, 120.97, 126.00, 128.09, 128.23, 128.67, 128.89, 129.39, 134.83, 137.72, 146.69, 157.11. Anal. Calcd for C₃₈H₃₀N₄O₃: C, 75.26; H, 5.57; N, 10.33. Found: C, 75.09; H, 5.49; N, 10.18.

4,4'-[*(4-Acetamido-N-phenyl)methylene]bis(3-methyl-1-phenyl-1H-pyrazol-5-ol* (**Table 2, entry 4**): White cream solid; mp 251-253 °C; ν_{max} (KBr)/cm⁻¹ 3405, 3150, 3025, 2910, 1660, 1598, 1570, 1518, 1485, 1410, 1370, 1318, 1275, 1120, 902, 779, 760, 690; δ_H (400 MHz, DMSO-d₆; Me₄Si) 2.02 (3H, s, CH₃CO), 2.32 (6H, s, 2 × CH₃), 4.92 (1H, s, CH), 7.18 (2H, d, *J* 8.4 Ar), 7.25 (2H, t, *J* 7.2 Ar), 7.43-7.47 (6H, m, Ar), 7.72 (4H, d, *J* 7.6 Ar), 9.88 (1H, s, NH), 13.91 (1H, br, OH). δ_C (100 MHz, DMSO-d₆; Me₄Si) 12.11, 24.31, 24.36, 39.08, 119.38, 119.48, 120.99, 126.06, 127.86, 129.40, 137.11, 137.63, 137.73, 146.74, 168.43, 168.52. Anal. Calcd for C₂₉H₂₇N₅O₃: C, 70.57; H, 5.51; N, 14.19. Found: C, 70.41; H, 5.42; N, 14.03.

4,4'-[*(5-Bromo-2-hydroxy-phenyl)methylene]bis(3-methyl-1-phenyl-1H-pyrazol-5-ol* (**Table 2, entry 5**): White cream solid; mp 266-268 °C; ν_{max} (KBr)/cm⁻¹ 3405, 3080, 2910, 1620, 1598, 1570, 1495, 1405, 1375, 1275, 1102, 899, 805, 790, 745, 690; δ_H (400 MHz, DMSO-d₆; Me₄Si) 2.30 (6H, s, 2 × CH₃), 5.13 (1H, s, CH), 6.74 (1H, d, *J* 8.4 Ar), 7.17 (1H, d, *J* 6.8 Ar), 7.25-7.28 (2H, m, Ar), 7.46 (4H, t, *J* 7.4 Ar), 7.66-7.72 (5H, m, Ar). δ_C (100 MHz, DMSO-d₆; Me₄Si) 12.19, 27.91, 110.28, 117.40, 121.14, 126.21, 129.43, 130.06, 131.61, 146.74, 153.87. Anal. Calcd for C₂₇H₂₃BrN₄O₃: C, 61.03; H, 4.36; Br, 15.04; N, 10.54. Found: C, 60.84; H, 4.29; N, 10.38.

4,4'-[*(2-Bromophenyl)methylene]bis(3-methyl-1-phenyl-1H-pyrazol-5-ol* (**Table 2, entry 6**): White cream solid; mp 198-200 °C, [Lit.: (Tayebi et al., 2011) 198-200 °C]; ν_{max} (KBr)/cm⁻¹ 3440, 3060, 2920, 1605, 1560, 1495, 1395, 1365, 1300, 830, 744, 690; δ_H (500 MHz; DMSO-d₆; Me₄Si) 2.31 (6H, s, 2 × CH₃), 5.10 (1H, s, CH), 7.13 (1H, t, *J* 7.3 Ar), 7.23 (2H, t, *J* 7.0 Ar), 7.33 (1H, t, *J* 7.3 Ar), 7.42 (4H, t, *J* 7.9 Ar), 7.56 (1H, d, *J* 7.8 Ar), 7.71 (4H, d, *J* 7.9 Ar), 7.86 (1H, m, Ar), 12.68 (1H, br, OH), 13.92 (1H, s, OH). δ_C (125 MHz; DMSO-d₆; Me₄Si) 13.08, 35.21, 121.49, 123.54, 126.43, 128.30, 129.16, 129.76, 131.44, 133.64, 138.21, 146.78. Elemental analysis: for C₂₇H₂₃BrN₄O₂: 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* (**Table 2, entry 7**): White solid; mp 215-217 °C, [Lit.: (Li et al., 1998) 210 °C]; δ_H (300 MHz; DMSO-d₆; Me₄Si) 2.30 (6H, s, 2 × CH₃), 4.98 (1H, s, CH) 7.22-7.28 (4H, m, Ar), 7.35 (2H, d, *J* 8.5 Ar), 7.44 (4H, t, *J* 7.9 Ar), 7.71 (4H, d, *J* 7.9 Ar), 13.90 (2H, br, OH). δ_C (75 MHz; DMSO-d₆; Me₄Si) 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* (**Table 2, entry 8**): White solid; mp 235-237 °C, [Lit.: (Wang et al., 2005) 236-237 °C]; δ_H (400 MHz; DMSO-d₆; Me₄Si) 2.29 (6H, s, 2 × CH₃), 5.14 (1H, s, CH), 7.22-7.33 (4H, m, Ar), 7.40 (1H, d, *J* 7.8 Ar), 7.44 (4H, t, *J* 7.6 Ar), 7.70 (4H, d, *J* 7.6 Ar), 7.80 (1H, d, *J* 7.1 Ar), 13.92 (2H, br, OH). δ_C (125 MHz; DMSO-d₆; Me₄Si) 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-Fluorophenyl)methylene]bis(3-methyl-1-phenyl-1H-pyrazol-5-ol* (**Table 2, entry 9**): White solid; mp 181-183 °C [Lit.: (Li et al., 1998) 182 °C]; δ_H (500 MHz; DMSO-d₆; Me₄Si) 2.31 (6H, s, 2 × CH₃), 4.95 (1H, s, CH), 7.09 (2H, t, *J* 8.8 Ar), 7.22-7.28 (4H, m, Ar), 7.43 (4H, t, *J* 7.7 Ar), 7.70 (4H, d, *J* 7.9 Ar), 12.48 (1H, br, OH), 13.91 (1H, s, OH). δ_C (125 MHz; DMSO-d₆; Me₄Si) 32.41, 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* (**Table 2, entry 10**): Yellow solid; mp 228-230 °C, [Lit.: (Wang et al., 2005) 230-232 °C]; δ_H (400 MHz; DMSO-d₆; Me₄Si) 2.28 (6H, s, 2 × CH₃), 5.06 (1H, s, CH), 7.18 (2H, t, *J* 7.1 Ar), 7.38 (4H, t, *J* 7.31 Ar), 7.45 (2H, d, *J* 8.3 Ar), 7.64 (4H, d, *J* 7.8 Ar), 8.10 (2H, d, *J* 8.6 Ar), 13.81 (2H, br, OH). δ_C (100 MHz; DMSO-d₆; Me₄Si) 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* (**Table 2, entry 11**): Pale yellow

solid; mp 151-153 °C, [Lit.: (Wang et al., 2005) 149-150 °C]; δ_H (400 MHz; DMSO-d₆; Me₄Si) 2.35 (6H, s, 2 × CH₃), 5.14 (1H, s, CH), 7.26 (2H, t, *J* 7.3 Ar), 7.45 (4H, t, *J* 7.6 Ar), 7.60 (1H, t, *J* 8.3 Ar), 7.68-7.74 (5H, m, Ar), 8.06-8.10 (2H, m, Ar), 13.91 (2H, br, OH). δ_C (100 MHz; DMSO-d₆; Me₄Si) 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) (Table 2, entry 12). Yellow solid; mp 210-212 °C, [Lit.: (Niknam et al., 2010) 210-212 °C]; δ_H (400 MHz; DMSO-d₆; Me₄Si) 2.33 (6H, s, 2 × CH₃), 5.07 (1H, s, CH), 7.25 (2H, t, *J* 7.3 Ar), 7.42-7.46 (6H, m, Ar), 7.40 (4H, d, *J* 7.8 Ar), 7.76 (2H, d, *J* 8.3 Ar), 13.89 (2H, br, OH). δ_C (100 MHz; DMSO-d₆; Me₄Si) 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) (Table 2, entry 13). White solid; mp 206-208 °C, [Lit.: (Niknam & Mirzaee, 2011) 206-208 °C]; δ_H (500 MHz; DMSO-d₆; Me₄Si) 2.36 (6H, s, 2 × CH₃), 5.14 (1H, s, CH), 7.24 (2H, t, *J* 6.9 Ar), 7.41-7.45 (7H, m, Ar), 7.71-7.73 (5H, m, Ar), 7.81-7.85 (3H, m, Ar), 12.41 (1H, br, OH), 13.93 (1H, s, OH). δ_C (125 MHz; DMSO-d₆; Me₄Si) 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.

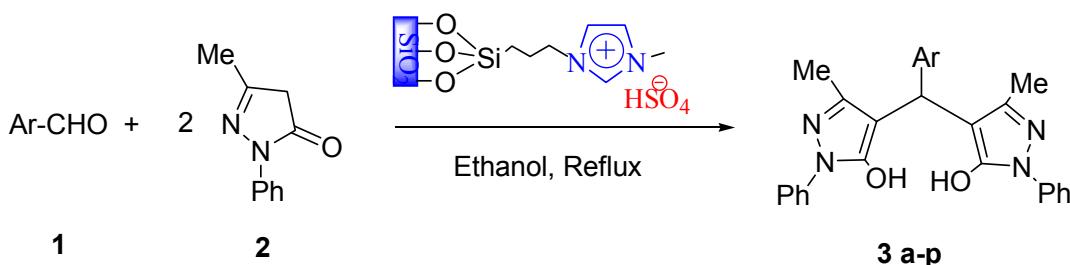
4,4'-(3-Pyridyl)methylene]bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (Table 2, entry 14). White cream solid; mp 238-240 °C; [Lit.: (Niknam & Mirzaee, 2011) 238-240 °C]; δ_H (500 MHz; DMSO-d₆; Me₄Si) 2.34 (6H, s, 2 × CH₃), 5.05 (1H, s, CH), 7.23 (2H, t, *J* 7.1 Ar), 7.34 (1H, t, *J* 6.0 Ar), 7.43 (4H, t, *J* 7.5 Ar), 7.71-7.73 (5H, m, Ar), 8.41 (1H, d, *J* 3.6 Ar), 8.51 (1H, s, Ar), 12.10 (1H, br, OH), 14.12 (1H, br, OH). δ_C (125 MHz; DMSO-d₆; Me₄Si) 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.

4,4'-(2-Thienyl)methylene]bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (Table 2, entry 15). White cream solid; mp 181-183 °C, [Lit.: (Niknam et al., 2010) 181-183 °C]; δ_H (400 MHz; DMSO-d₆; Me₄Si) 2.32 (6H, s, 2 × CH₃), 5.13 (1H, s, CH), 6.75-6.77 (1H, m, Ar), 6.90-6.92 (1H, m, Ar), 7.24-7.30 (3H, m, Ar), 7.45 (4H, t, *J* 7.8 Ar), 7.71 (4H, d, *J* 7.82 Ar) 14.01 (2H, br, OH). δ_C (100 MHz; DMSO-d₆; Me₄Si) 29.43, 120.58, 124.05, 124.15, 126.75, 128.94, 132.99, 134.13, 147.73.

4,4'-(Methylene)bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (Table 2, entry 16): White cream solid; mp 225-227 °C, [Lit.: Wang et al., 2005) 227-229 °C]; δ_H (400 MHz; DMSO-d₆; Me₄Si) 2.22 (6H, s, 2 × CH₃), 3.24 (2H, s, CH₂), 7.18-7.26 (2H, m, Ar), 7.38-7.50 (4H, m, Ar), 7.65-7.75 (4H, m, Ar), 12.00 (1H, br, OH), 13.17 (1H, br, OH). δ_C (100 MHz; DMSO-d₆; Me₄Si) 14.69, 18.16, 120.17, 125.69, 128.92, 136.68, 142.41.

3. Results

In continuation of our studies towards the preparation and applications of heterogeneous solid acid catalysts (Niknam et al., 2010; Niknam et al., 2011; Tayebi et al., 2011; Nouri Sefat et al., 2011; Niknam et al., 2010; Niknam & Saberi, 2009; Niknam et al., 2010; Niknam et al., 2010), herein we wish to report an efficient procedure for the synthesis of 4,4'-(arylmethylene)bis(3-methyl-1-phenyl-pyrazol-5-ols) via condensation reaction between aldehydes and 5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one in the presence of [Sipmim]HSO₄ as solid acid catalyst (Scheme 2).



Scheme 2. The condensation of aromatic aldehydes with 3-methyl-1-phenyl-5-pyrazolone catalyzed by [Sipmim]HSO₄

The FT-IR spectra of [Sipmim]HSO₄ was shown in Figure 1. The IR spectrum shows the overlap asymmetric and symmetric stretching bands of SO₂ with Si-O-Si stretching bands in the silica functionalized alkyl-sulfuric acid. The spectrum also shows a broad OH stretching absorption around 3600 to 2600 cm⁻¹.

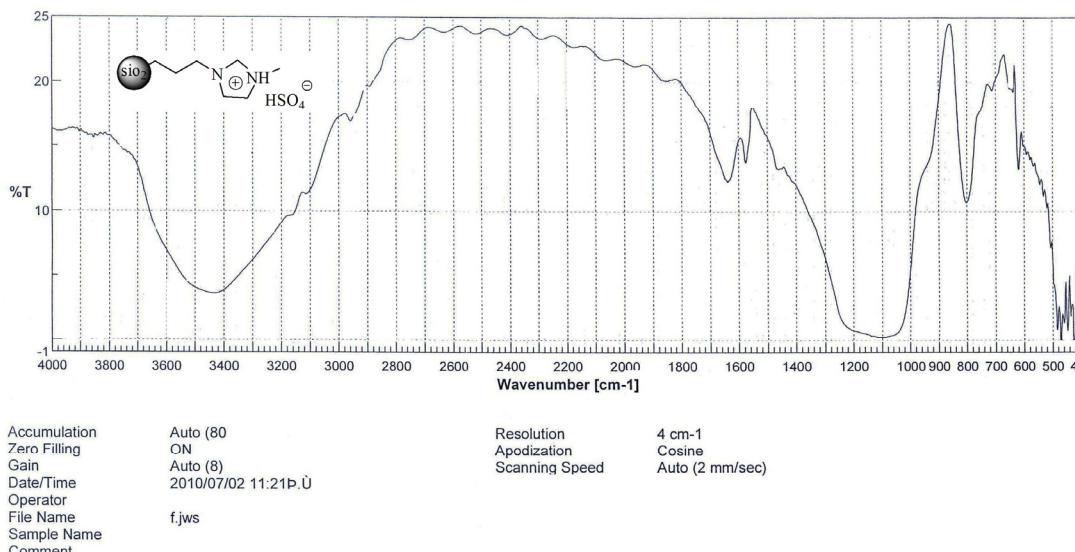


Figure 1. FT-IR of [Sipmim]HSO₄

The thermogravimetric analysis (TGA) curve of [Sipmim]HSO₄ shows the mass loss of organic materials as they decompose upon heating (Figure 2). The weight loss below 125 °C corresponds to desorption of physically adsorbed solvent and surface hydroxyl groups. The weight loss centered at higher temperature of about 9 % between 150 and 500 °C should be attributed to the thermal decomposition of organic groups.

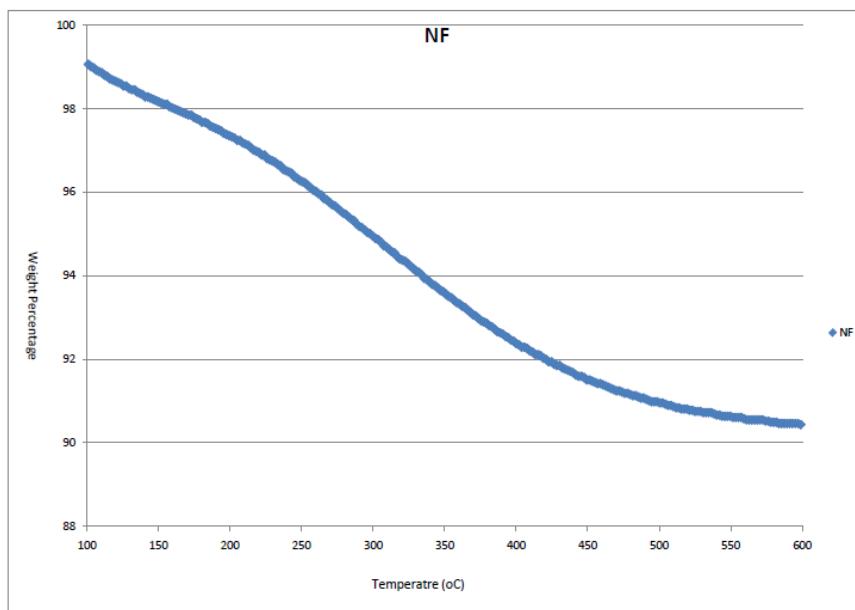


Figure 2. TGA of [Sipmim]HSO₄

The BET surface area using nitrogen adsorption isotherms at the temperature of liquid nitrogen which gave the results of $a_{s,BET}$ 1.11 m² g⁻¹ and the total pore volume 0.1737 cm³ g⁻¹ (see supplementary material).

Initial studies were carried out on the condensation reaction between 4-chlorobenzaldehyde and

3-methyl-1-phenyl-5-pyrazolone in the presence of catalytic amounts of [Sipmim]HSO₄ as a model reaction (Table 1). A blank experiment without catalyst gave very low yield after 24 h. The optimal amount of [Sipmim]HSO₄ was 0.15 g (equal to 0.083 mmol of H⁺) per 1 mmol of aldehyde in refluxing ethanol.

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

Entry	Catalyst	Catalyst loading (g)	Time (min)	Yield % ^b
1	No catalyst	-	24 h	<10
2	[Sipmim]HSO ₄	0.05 (0.027 mmol of H ⁺)	130	81
3	[Sipmim]HSO ₄	0.07 (0.038 mmol of H ⁺)	90	84
4	[Sipmim]HSO ₄	0.15 (0.083 mmol of H ⁺)	60	90
5	[Sipmim]HSO ₄	0.20 (0.11 mmol of H ⁺)	60	90

^aReaction conditions: 4-chlorobenzaldehyde (1 mmol), 5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (2 mmol), ethanol (6 ml) reflux conditions. ^bIsolated yield.

Using the optimized conditions, the catalytic efficiency of [Sipmim]HSO₄ was also observed for other substituted aromatic aldehydes (Scheme 2 and Table 2).

Table 2. Preparation of 4,4'-(arylmethylene)-bis-(3-methyl-1-phenyl-1*H*-pyrazol-5-ols) derivatives catalyzed by [Sipmim]HSO₄ in ethanol under refluxing conditions ^a

Entry	Ar (1)	Product	Time (h)	Yield% ^b	Mp (°C)	Lit. mp (°C)
1	C ₆ H ₅ -	3a	2.0	89	170-172	171-172 (Wang et al., 2005)
2	4-Me-C ₆ H ₄ -	3b	2.2	88	202-204	203 (Li et al., 1998)
3	4-C ₆ H ₅ CH ₂ O-C ₆ H ₄ -	3c	3.5	77	210-212	214 (Li et al., 1998)
4	4-MeCONH-C ₆ H ₄ -	3d	4.5	86	251-253	-
5	5-Br-2-(OH)-C ₆ H ₃ -	3e	3.5	87	266-268	-
6	2-Br-C ₆ H ₄ -	3f	2.5	81	198-200	198-200 (Tayebi et al., 2011)
7	4-Cl-C ₆ H ₄ -	3g	1.0	90	215-217	210 (Li et al., 1998)
8	2-Cl-C ₆ H ₄ -	3h	1.25	83	235-237	236-237 (Wang et al., 2005)
9	4-F-C ₆ H ₄ -	3i	1.15	87	181-183	182 (Li et al., 1998)
10	4-O ₂ N-C ₆ H ₄ -	3j	2.0	88	228-230	230-232 (Wang et al., 2005)
11	3-O ₂ N-C ₆ H ₄ -	3k	1.75	89	151-153	149-150 (Wang et al., 2005)
12	4-(CN)-C ₆ H ₄ -	3l	1.0	87	210-212	210-212 (Niknam et al., 2010)
13	2-C ₁₀ H ₇ -	3m	3.0	90	206-208	206-208 (Niknam & Mirzaee, 2011)
14	3-Pyridyl-	3n	3.0	82	238-240	238-240 (Niknam & Mirzaee, 2011)
15	2-Thienyl-	3o	3.0	80	181-183	181-183 (Niknam et al., 2010)
16	H-	3p	2.0	82	225-227	227-229 (Wang et al., 2005)

^aReaction conditions: aromatic aldehyde (1 mmol), 5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (2 mmol), catalyst [Sipmim]HSO₄ (0.15 g), ethanol (6 mL), reflux conditions. ^bIsolated yield.

As shown in Table 2, a series of benzaldehydes including electron-donating or electron-withdrawing groups, i.e. methyl, benzyloxy, and acetamido-benzaldehyde (Table 2, entries 2-4) or 4-nitro, 3-nitro, and

4-cyano-benzaldehyde (Table 2, entries 10-12), were condensed into the corresponding 4,4-(arylmethylene)-bis-(3-methyl-1-phenyl-1*H*-pyrazol-5-ols) **3b-3d** and **3j-3l** in very good yields. 2-Naphthyl carbaldehyde was treated with 5-methyl-2-phenyl-2,4-dihydro-3*H*-pyrazol-3-one gave into corresponding product **3m** in 90% yield (Table 2, entry 13). Heteroaromatic aldehydes such as 3-pyridine carbaldehyde and thiophene-2-carbaldehyde (Table 2, entries 14,15) were reacted with 5-methyl-2-phenyl-2,4-dihydro-3*H*-pyrazol-3-one gave the corresponding products **3n**, **3o** in 82% and 80% yield respectively. Formaldehyde was converted into the corresponding product **3p** in 82% yield (Table 2, entry 16).

The condensation reaction between 4-chlorobenzaldehyde and 5-methyl-2-phenyl-2,4-dihydro-3*H*-pyrazol-3-one was examined for the possibility of recycling [Sipmim]HSO₄ under the optimized conditions. After completion, the reaction mixture was washed with warm ethanol (3 × 30 mL). The recovered catalyst was washed with diethyl ether, dried and reused for subsequent runs. [Sipmim]HSO₄ showed much the same efficiency when used in six consecutive reactions runs (Figure 3).

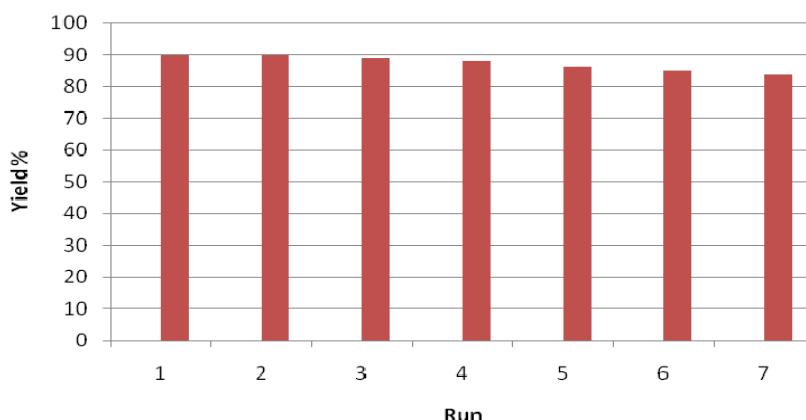


Figure 3. Recyclability of [Sipmim]HSO₄ as catalyst in the condensation reaction of 4-chlorobenzaldehyde (1 mmol) and 5-methyl-2-phenyl-2,4-dihydro-3*H*-pyrazol-3-one (2 mmol) in the presence of 0.15 g of [Sipmim]HSO₄ in refluxing ethanol. Reaction time = 1.0 h

In conclusion, the synthesis of bis-pyrazolones *via* three-component condensation reaction of aldehydes with two equivalents of 5-methyl-2-phenyl-2,4-dihydro-3*H*-pyrazol-3-one using [Sipmim]HSO₄ as heterogeneous acid catalyst in refluxing ethanol, and also recovery and reusability of the catalyst, high yields, and clean work-up makes this method practical.

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