Journal of the Iranian Chemical Society
https://doi.org/10.1007/s13738-018-1424-x

ORIGINAL PAPER

Silica-bonded DABCO hydrogen sulfate ((SB-DABCO)HSO_4): a new dual-interphase catalyst for the diversity-oriented pseudo-five-component synthesis of bis(pyrazolyl)methanes and novel 4-[bis(pyrazolyl) methane]phenylmethylene-bis(indole)s

Mohsen Shekouhy[1] · **Reza Kordnezhadian**[1] · **Ali Khalafi-Nezhad**[1]

Received: 19 December 2017 / Accepted: 31 May 2018

Abstract
Silica bonded *n*-propyl-4-aza-1-azoniabicyclo[*2.2.2*]octane hydrogen sulfate ((SB-DABCO)HSO_4) was prepared as a new interphase dual-catalyst and was successfully applied for the diversity-oriented synthesis of bis(pyrazolyl)methanes via a one-pot pseudo-five-component condensation reaction. This approach provides a versatile range of available substrates and high diversity of desired products. Moreover, ((SB-DABCO)HSO_4) was successfully applied for the synthesis of some novel [bis(pyrazolyl)methane]-bis(indole)s as more complex molecules.

Keywords Interphase catalyst · Silica bonded *n*-propyl-4-aza-1-azoniabicyclo[*2.2.2*]octane Hydrogen sulfate · Bis(pyrazolyl)methane · Pseudo-five-component reaction · Pyrazolone · Indole

Introduction

Nowadays, environmental care is one of the worldwide increasing worries of human society and in the evolution towards a sustainable development; catalysis is one of the most important tools available to introducing more clear, efficient and benign chemical processes. The use of catalyzed systems instead of stoichiometric reagents will provide ideal conditions for the application of more benign reaction media, minimizing the waste and undesired by-products and the reduction of energy consumption. To gain a practical and benign catalytic system, the covalent anchoring of soluble acid or base catalysts to a heterogeneous recyclable support in such a way as to preserve its catalytic activity is an important challenge in green catalysis [1, 2] and their usefulness by means of sustainable chemistry has been studied several times [3, 4]. The immobilization of catalytic systems onto a large surface area solid carrier such as SiO_2 using organic species as connectors to create new organic–inorganic hybrids (interphase) is a practical and frequently used pathway for the preparation of efficient heterogeneous catalysts [5–12]. An interphase defines as a region in a material in which the molecules of a stationary (organic–inorganic hybrid catalyst) and mobile component (solvent and reactants) reach each other. To overcome the steric effects of the catalyst surface, active sites will be connected to the surface of the heterogeneous support with a flexible organic group that provides sufficient mobility of the reactive centers [13].

Between various kinds of nitrogen heterocycles, pyrazole and its derivatives occupied a special position. They are the main backbone of numerous biological active compounds and have been used as drug targets in the pharmaceutical industries [14–20]. In addition, their derivatives such as 4,4′-(arylmethylene)bis(3-methyl-1-phenyl-1*H*-pyrazol-5-ol)s have a broad spectrum of approved biological activity, being used as anti-inflammatory [21], antipyretic [22], gastric secretion stimulatory [23], anti-depressant [24], antibacterial [25] and anti-filarial agents [26].

One useful strategy to gain a versatile library of biologically active compounds is the diversity-oriented synthesis [27–29]. This approach provides a widespread spectrum of synthesized compounds with diverse substitution profiles using simple starting materials. In this context, multicomponent reactions (MCRs) are of increasing importance due to their high efficiency for delivering molecular diversity [30].

✉ Ali Khalafi-Nezhad
khalafi@chem.susc.ac.ir

[1] Department of Chemistry, College of Sciences, Shiraz University, Shiraz 71454, Iran

Published online: 25 June 2018

More recently, a new pseudo-five-component strategy for the synthesis of bis(pyrazolyl)methanes via a one-pot condensation reaction of aryl aldehydes (1 equivalent), phenylhydrazine (2 equivalents) and ethyl acetoacetate (2 equivalents) has been reported and immediately attracted some research groups to introduce more efficient catalytic systems and reaction conditions to improve its efficiency for the diversity-oriented synthesis of titled compounds [31–37]. However, most of the reported catalysts as well as reaction conditions suffer from some drawbacks such as harsh reaction conditions [35], no reusability of catalyst [32], tedious work up [37], application of hazardous solvents and reagents [37], very low diversity of available starting materials [31, 32, 35, 36] and need to the special instruments [33] *etc*.

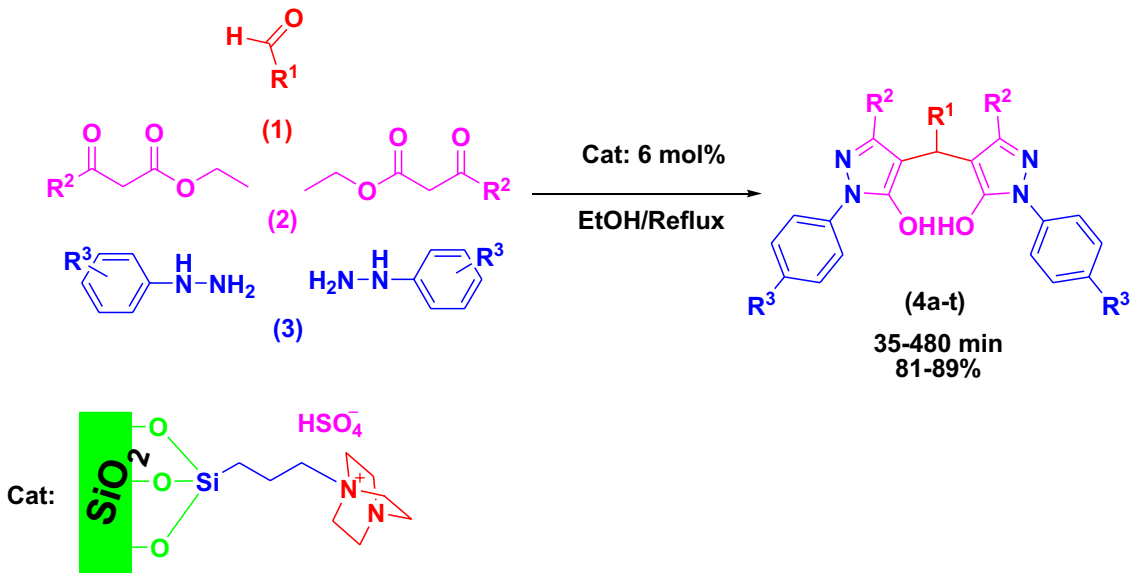
Considering above facts about the various therapeutic activities of 4,4′-(arylmethylene)bis(1*H*-pyrazol-5-ol)s and unique advantages of interphase catalysts and in continuation of our works on introducing more efficient and environmentally benign catalytic systems and methods for the fine chemical synthesis [38–53], we herein report silica-bonded *n*-propyl-4-aza-1-azoniabicyclo[*2.2.2*]octane hydrogen sulfate ((SB-DABCO)HSO_4) as a new, highly efficient and reusable dual-interphase catalyst for the diversity-oriented one-pot pseudo-five-component synthesis of bis(pyrazolyl) methanes. (Scheme 1).

Experimental

All applied solvents and reagents are commercially available and purchased from Merck, Sigma-Aldrich, Fluka or Acros companies. A Büchi B-545 apparatus was applied for the melting point determination. All known compounds were identified by comparison of their melting points and ^{1}H NMR data with those in the authentic samples. The ^{1}H NMR (400 and 250 MHz) and ^{13}C NMR (100 and 62.5 MHz) were run on Bruker Avance DPX-400 and Bruker Avance DPX-250 FT-NMR spectrometers. Chemical shifts are given as δ values against tetramethylsilane as an internal standard and J values are given in Hz. TG analysis was done using a METTLER TOLEDO TG analysis instrument at an air flow of 3 mL min^{-1} and temperature ramp of 2 °C min^{-1}. The temperature programmed desorption (TPD) of CO_2 was done using a self-made TG instrument. Mass spectra were recorded with the Agilent 7000 Series Triple Quad-MS apparatus. The microanalysis was performed on a Perkin-Elmer 240-B microanalyzer. The BET surface area measurements were performed on a Micrometric ASAP 2020 (USA) instrument.

The preparation of silica-bonded *n*-propyl-4-aza-1-azoniabicyclo[*2.2.2*]octane chloride (SB-DABCO)

DABCO (0.56 g, 5 mmol) was added to a 50 mL round-bottom flask contained the suspension of 3-chloropropyl silica (1 g) in dried acetone (30 mL) and obtained mixture was



Scheme 1 The one-pot pseudo-five-component synthesis of bis(pyrazolyl)methanes in the presence of silica-bonded DABCO hydrogen sulfate ((SB-DABCO)HSO_4)

vigorously stirred for 36 h at reflux conditions. The reaction mixture was cooled to room temperature and obtained solids were filtered and washed [acetone (10 mL, two times)]. The resulting solid was dried under vacuum at 50 °C for 4 h to give SB-DABCO as a white powder (1.158 g) [54].

The preparation of silica-bonded *n*-propyl-4-aza-1-azoniabicyclo[*2.2.2*]octane hydrogen sulfate ((SB-DABCO)HSO_4)

At 0 °C, the solution of H_2SO_4 (3 mL, 98%) in CH_2Cl_2 (20 mL) was added dropwise to a 50 mL round-bottom flask contained the suspension of silica-bonded *n*-propyl-4-aza-1-azoniabicyclo[*2.2.2*]octane chloride (SB-DABCO) (1 g) in dried CH_2Cl_2 (20 mL) and the addition continued for 30 min. During this time, the mixture was stirred vigorously and it continued for 12 h. The reaction mixture was filtered and washed with methanol (20 mL, three times). The resulting solid was dried under reduced pressure at 50 °C for 4 h to give ((SB-DABCO)HSO_4) as a white powder (1.107 g).

The general procedure for the preparation of bis(pyrazolyl)methanes

The catalyst ((SB-DABCO)HSO_4) (6 mol%, 0.07 g) was added to a 25 mL round-bottom flask contained a solution of hydrazine derivative (2 mmol) and β-keto ester (2 mmol) in ethanol (10 mL) and resulting mixture was stirred at reflux conditions for 10 min. After this time, aldehyde (1 mmol) was added to the reaction mixture and stirring was continued at reflux conditions and the completion of the reaction was monitored by TLC. After completion, insoluble catalyst was separated by a simple filtration, and the filtrate was stand at room temperature for 12 h, during this time pure crystals of desired products were formed. The separated catalyst was washed with CH_2Cl_2 (20 mL), dried under vacuum at 50 °C (12 h) and reused.

The general procedure for the preparation of 4-[bis(pyrazolyl)methane] phenylmethylene-bis(indole)s

To a mixture of hydrazine derivative (2 mmol), β-keto ester (2 mmol) and 4-(di(1*H*-indol-3-yl)methyl)benzaldehyde (1 mmol) and ethanol (10 mL) in a three-neck round-bottom flask, catalyst ((SB-DABCO)HSO_4) (6 mol%, 0.07 g) was added and the resulting mixture was stirred under the nitrogen atmosphere at reflux temperature. After completion of the reaction as indicated by TLC, insoluble catalyst was separated with a simple filtration and the filtrate was stand at room temperature for 12 h, during this time pure crystals of desired product were formed. The separated catalyst was washed with CH_2Cl_2 (20 mL), dried under vacuum at 50 °C (12 h) and reused.

Selected spectral data

4,4′-(Phenylmethylene) bis(1-phenyl-3-propyl-1*H*-pyrazol-5-ol) (4g)

White solid, υ_{max}: 3620, 3050, 2980, 1665, 1610, 1460 cm^{-1}. ^1H NMR (400 MHz, DMSO d_6): δ 0.91 (t, $J = 7.5$ Hz, 6H), 1.58 (m, 4H), 2.36 (t, $J = 7.5$ Hz, 4H), 5.67 (s, 1H), 7.19 (d, $J = 8.0$ Hz, 2H), 7.28 (t, $J = 8.0$ Hz, 1H), 7.34 (t, $J = 8.0$ Hz, 1H), 7.49 (t, $J = 8.3$ Hz, 2H), 7.60 (t, $J = 8.3$ Hz, 4H), 7.68 (d, $J = 8.3$ Hz, 4H), 10.60 (s, 1H), 10.81 (s, 1H), ^{13}C NMR (100 MHz, DMSO d_6): δ 13.1, 21.9, 33.1, 35.9, 118.9, 122.5, 126.3, 128.7, 129.0, 129.4, 137.7, 138.0, 153.6, 154.7. MS (*m*/*z*): 492 (M^+).

4,4′-(Phenylmethylene) bis(3-propyl-1-*p*-tolyl-1*H*-pyrazol-5-ol) (4 h)

White solid, υ_{max}: 3610, 3070, 2950, 1675, 1605, 1460, 850 cm^{-1}. ^1H NMR (400 MHz, DMSO d_6): δ 0.90 (t, $J = 7.8$ Hz, 6H), 1.54 (m, 4H), 2.35–2.39 (m, 10 H), 5.45 (s, 1H), 7.28–7.31 (m, 3H), 7.38 (t, $J = 8.5$ Hz, 2H), 7.41 (d, $J = 8.3$ Hz, 4H), 7.53 (d, $J = 8.3$ Hz, 4H), 10.62 (s, 1H), 10.89 (s, 1H), ^{13}C NMR (100 MHz, DMSO d_6): δ 13.4, 21.1, 22.8, 32.4, 36.0, 119.7, 125.1, 125.4, 128.5, 129.1, 129.7, 134.3, 135.8, 154.0, 154.7.

4,4′-(Phenylmethylene) bis(1-(4-methoxyphenyl)-3-propyl-1*H*-pyrazol-5-ol) (4i)

White solid, υ_{max}: 3610, 3070, 2960, 1675, 1610, 1470, 1150 cm^{-1}. ^1H NMR (400 MHz, DMSO d_6): δ 0.91 (t, $J = 7.5$ Hz, 6H), 1.55 (m, 4H), 2.34 (t, $J = 7.5$ Hz, 4H), 3.81 (s, 6H), 5.49 (s, 1H), 6.91 (d, $J = 8.4$ Hz, 4H), 7.23–7.27 (m, 3H), 7.36 (t, $J = 8.4$ Hz, 2H), 7.61 (d, $J = 8.6$ Hz, 4H), 10.52 (s, 1H), 10.95 (s, 1H), ^{13}C NMR (100 MHz, DMSO d_6): δ 13.3, 22.8, 32.7, 36.5, 55.9, 112.7, 115.0, 119.3, 125.5, 128.7, 129.0, 129.9, 153.8, 154.3, 158.3.

4,4′-(Phenylmethylene) bis(3-phenyl-1-*p*-tolyl-1*H*-pyrazol-5-ol) (4j)

White solid, υ_{max}: 3640, 3050, 2970, 1670, 1600, 1460, 810 cm^{-1}. ^1H NMR (400 MHz, DMSO d_6): δ 2.36 (s, 6H), 5.46 (s, 1H), 7.21–7.26 (m, 3H), 7.40–7.45 (m, 8H), 7.51–7.56 (m, 8H), 7.83 (d, $J = 8.3$, 4H), 10.93 (s, 1H), 11.31, (s, 1H), ^{13}C NMR (100 MHz, DMSO d_6): δ 21.4, 36.1, 117.5, 125.3, 125.7, 127.3, 128.1, 128.5, 129.3, 129.5, 129.9, 132.9, 133.9, 135.6, 138.3, 150.1, 152.5.

4,4′-((4-Chlorophenyl)methylene) bis(1,3-diphenyl-1*H*-pyrazol-5-ol) (4k)

White solid, υ_{max}: 3650, 3040, 2950, 1670, 1620, 1450, 840, 650 $cm^{-1.}$ ^1H NMR (400 MHz, DMSO d_6): δ (ppm) 5.48 (s, 1H), 7.16 (d, $J = 8.0$ Hz, 2H), 7.35 (d, $J = 8.0$ Hz, 2H), 7.41–7.49 (m, 4H), 7.51–7.58 (m, 8H), 7.64 (d, $J = 8.3$ Hz, 4H), 7.81 (d, $J = 8.5$ Hz, 4H), 10.59 (s, 1H), 10.90 (s, 1H), ^{13}C NMR (100 MHz, DMSO d_6): δ (ppm) 34.9, 117.8, 122.6, 126.1, 127.8, 128.1, 129.0, 129.3, 130.1, 131.2, 133.6, 136.0, 137.1, 150.9.

4,4′-((4-Bromophenyl)methylene) bis(1-(4-methoxyphenyl)-3-propyl-1*H*-pyrazol-5-ol) (4l)

White solid, υ_{max}: 3650, 3050, 2940, 1670, 1610, 1460, 1430, 1250, 630 $cm^{-1.}$ ^1H NMR (400 MHz, DMSO d_6): δ (ppm) 0.91 (t, $J = 7.6$ Hz, 6H), 1.68 (m, 4H), 2.51 (t, $J = 7.6$ Hz, 4H), 3.87 (s, 6H), 5.54 (s, 1H), 6.97 (d, $J = 8.3$ Hz, 4H), 7.16 (d, $J = 8.5$ Hz, 2H), 7.58 (d, $J = 8.3$ Hz, 4H), 7.79 (d, $J = 8.5$ Hz, 2H), 10.91 (s, 1H), 11.61 (s, 1H), ^{13}C NMR (100 MHz, DMSO d_6): δ (ppm) 14.01, 23.01, 33.1, 36.6, 55.5, 112.7, 115.1, 119.3, 120.4, 129.9, 131.1, 131.4, 154.0, 154.6, 158.3.

4,4′-(*p*-Tolylmethylene) bis(3-propyl-1-*p*-tolyl-1*H*-pyrazol-5-ol) (4m)

White solid, υ_{max}: 3660, 3030, 2920, 1670, 1610, 1460, 1430, 650 $cm^{-1.}$ ^1H NMR (400 MHz, DMSO d_6): δ (ppm) 0.90 (t, $J = 7.6$ Hz, 6H), 1.63 (m, 4H), 2.38 (t, $J = 7.6$ Hz, 4H), 2.33 (s, 6H), 2.37 (s, 3H), 5.49 (s, 1H), 7.11–7.16 (m, 4H), 7.38 (d, $J = 8.5$ Hz, 4H), 7.48 (d, $J = 8.5$ Hz, 4H), 10.93 (s, 1H), 11.31 (s, 1H), ^{13}C NMR (100 MHz, DMSO d_6): δ (ppm) 13.9, 21.4, 21.5, 23.0, 32.7, 36.4, 119.3, 125.1, 128.9, 129.2, 129.7, 133.9, 135.0, 135.3, 135.8, 153.7, 154.9.

4,4′-(Furan-2-ylmethylene) bis(3-propyl-1-*p*-tolyl-1*H*-pyrazol-5-ol) (4n)

White solid, υ_{max}: 3650, 3050, 2970, 1670, 1610, 1465, 1420, 850 $cm^{-1.}$ ^1H NMR (400 MHz, DMSO d_6): δ (ppm) 0.89 (t, $J = 7.5$ Hz, 6H), 1.61 (m, 4H), 2.29 (s, 6H), 2.41 (t, $J = 7.5$ Hz, 4H), 5.51 (s, 1H), 6.12 (d, $J = 8.7$ Hz, 1H), 6.38 (t, $J = 8.7$ Hz, 1H), 7.39 (d, $J = 8.0$ Hz, 4H), 7.51–7.53 (m, 5H), 10.81 (s, 1H), 11.02 (s, 1H), ^{13}C NMR (100 MHz, DMSO d_6): δ (ppm) 13.4, 21.4, 22.8, 27.1, 31.6, 106.5, 109.1, 119.5, 125.1, 129.3, 134.5, 135.6, 142.7, 152.5, 154.6, 155.1.

4,4′-(*p*-Tolylmethylene) bis(3-phenyl-1-*p*-tolyl-1*H*-pyrazol-5-ol) (4o)

White solid, υ_{max}: 3610, 3050, 2960, 1670, 1600, 1470 $cm^{-1.}$ ^1H NMR (400 MHz, DMSO d_6): δ (ppm) 2.35 (s, 6H), 2.39 (s, 3H), 5.41 (s, 1H), 7.11–7.14 (m, 4H), 7.41–7.43 (m, 6H), 7.49–7.56 (m, 8H), 7.81 (d, $J = 8.3$ Hz, 4H), 10.61 (s, 1H), 10.94 (s, 1H), ^{13}C NMR (100 MHz, DMSO d_6): δ (ppm) 21.1, 21.4, 35.6, 117.9, 125.3, 127.6, 128.3, 128.5, 128.9, 129.1, 129.5, 133.0, 134.3, 135.2, 135.4, 135.9, 150.0, 152.6.

4,4′-((4-Nitrophenyl)methylene) bis(3-phenyl-1-*p*-tolyl-1*H*-pyrazol-5-ol) (4p)

White solid, υ_{max}: 3600, 3070, 2960, 1670, 1590, 1470, 750 $cm^{-1.}$ ^1H NMR (400 MHz, DMSO d_6): δ (ppm) 2.36 (s, 6H), 5.46 (s, 1H), 7.41–7.49 (m, 8H), 7.50–7.63 (m, 8H), 7.81 (d, $J = 8.1$ Hz, 4H), 8.16 (d, $J = 8.1$ Hz, 2H), 10.6 (s, 1H), 10.9 (s, 1H), ^{13}C NMR (100 MHz, DMSO d_6): δ (ppm) 21.4, 35.6, 117.9, 124.0, 125.5, 127.1, 128.3, 129.0, 129.5, 132.7, 133.0, 134.1, 136.1, 144.7, 144.9, 150.1, 152.9.

4,4′-((3-Nitrophenyl)methylene) bis(1-(4-methoxyphenyl)-3-propyl-1*H*-pyrazol-5-ol) (4q)

White solid, υ_{max}: 3620, 3040, 2950, 1665, 1595, 1470 $cm^{-1.}$ ^1H NMR (400 MHz, DMSO d_6): δ (ppm) 0.90 (t, $J = 7.8$, 6H), 1.67 (m, 4H), 2.55 (t, $J = 7.8$ Hz, 4H), 3.85 (s, 3H), 5.46 (s, 1H), 6.97 (d, $J = 8.3$ Hz, 4H), 7.51–7.68 (m, 6H), 7.93 (t, $J = 8.5$ Hz, 1H), 8.12 (s, 1H), 10.61 (s, 1H), 10.93 (s, 1H), ^{13}C NMR (100 MHz, DMSO d_6): δ (ppm) 13.9, 23.0, 32.1, 35.6, 56.1, 112.6, 114.6, 119.2, 121.1, 125.3, 129.5, 129.7, 135.3, 139.1, 147.7, 153.6, 154.5, 158.3.

4,4′-((4-Isopropylphenyl)methylene) bis(1-(4-methoxyphenyl)-3-propyl-1*H*-pyrazol-5-ol) (4r)

White solid, υ_{max}: 3610, 3050, 2950, 1670, 1610, 1465 $cm^{-1.}$ ^1H NMR (400 MHz, DMSO d_6): δ (ppm) 0.91 (t, $J = 7.5$ Hz, 6H), 1.23 (d, $J = 7.5$ Hz, 6H), 1.68 (m, 4H), 2.46 (t, $J = 7.5$ Hz, 4H), 2.89 (m, 1H), 3.76 (s, 6H), 5.46 (s, 1H), 6.98 (d, $J = 8.3$ Hz, 4H), 7.14–7.18 (m, 4H), 7.48 (d, $J = 8.3$ Hz, 4H), 10.64 (s, 1H), 10. 96 (s, 1H), ^{13}C NMR (100 MHz, DMSO d_6): δ (ppm) 13.8, 23.0, 23.4, 32.3, 33.1, 36.0, 55.4, 112.5, 114.4, 119.4, 126.3, 128.8, 129.6, 135.0, 145.9, 153.1, 154.7, 158.4.

4,4′-((4-Isopropylphenyl)methylene) bis(1-(4-methoxyphenyl)-3-phenyl-1*H*-pyrazol-5-ol) (4s)

White solid, υ_{max}: 3610, 3030, 2990, 1670, 1610, 1470, 655 $cm^{-1.}$ ^1H NMR (400 MHz, DMSO d_6): δ (ppm) 1.23

(d, $J = 7.5$ Hz, 6H), 2.89 (m, 1H), 3.81 (s, 6H), 5.47 (s, 1H), 6.93 (d, $J = 8.6$ Hz, 4H), 7.16–7.21 (m, 4H), 7.39 (t, $J = 8.6$ Hz, 2H), 7.50–7.58 (m, 8H), 7.81 (d, $J = 8.6$ Hz, 4H), 10.91 (s, 1H), 11.12 (s, 1H), ^{13}C NMR (100 MHz, DMSO d_6): δ (ppm) 23.4, 33.6, 35.1, 55.9, 112.5, 114.8, 117.9, 126.0, 127.9, 128.6, 129.1, 129.7, 133.0, 135.2, 145.6, 149.8, 152.5, 158.3.

4,4′-((3-Methoxyphenyl)methylene) bis(1-(4-methoxyphenyl)-3-phenyl-1*H*-pyrazol-5-ol) (4t)

White solid, υ_{max}: 3610, 3030, 2990, 1670, 1610, 1250, 870, 780, 690 cm$^{-1.}$ ^{1}H NMR (400 MHz, DMSO d_6): δ (ppm) 3.76 (s, 6H), 3.79 (s, 3H), 5.47 (s, 1H), 6.79 6.81 (m, 2H), 6.98–7.06 (m, 5H), 7.19 (t, $J = 8.5$ Hz, 1H), 7.39 (t, $J = 8.5$ Hz, 2H), 7.51–7.63 (m, 8H), 7.81 (d, $J = 8.5$ Hz, 4H), 10.63 (s, 1H), 10.91 (s, 1H), ^{13}C NMR (100 MHz, DMSO d_6): δ (ppm) 35.6, 55.9, 60.1, 111.3, 112.5, 113.0, 114.9, 117.9, 121.3, 127.6, 128.4, 129.3, 129.5, 129.8, 133.0, 139.2, 149.9, 152.7, 158.3, 160.1.

4,4′-((4-(Di(1*H*-indol-3-yl)methyl)phenyl)methylene) bis(3-methyl-1-phenyl-1*H*-pyrazol-5-ol) (6a)

Pink solid, m.p. >300 °C. ^{1}H NMR (250 MHz, DMSO d_6): δ (ppm) 2.31 (s, 6H), 4.88 (s, 1H), 5.83 (s, 1H), 6.68 (s, 2H), 7.13–7.98 (m, 22H), 9.31 (s, 2H), 10.67 (s, 1H), 10.90 (s, 1H), ^{13}C NMR (62.5 MHz, DMSO d_6): δ (ppm) 14.5, 36.7, 53.9, 111.0, 133.3, 118.8, 119.3, 119.8, 122.0, 122.5, 123.7, 126.9, 127.8, 128.8, 129.3, 129.9, 134.5, 135.1, 136.1, 136.9, 146.6, 154.5.

4,4′-((4-(Di(1*H*-indol-3-yl)methyl)phenyl)methylene) bis(3-methyl-1-p-tolyl-1*H*-pyrazol-5-ol) (6b)

Pink solid, m.p. > 300 °C. ^{1}H NMR (250 MHz, DMSO d_6): δ (ppm) 2.31 (s, 6H), 3.19 (s, 6H), 4.85 (s, 1H), 5.91 (s, 1H), 6.64 (s, 2H), 7.15–7.92 (m, 20H), 9.42 (br, 2H), 10.67 (s, 1H), 10.90 (s, 1H), ^{13}C NMR (62.5 MHz, DMSO d_6): δ (ppm) 14.5, 22.1, 35.6, 53.5, 111.0, 112.7, 119.0, 119.3, 119.8, 122.0, 12.4, 125.0, 127.8, 128.9, 129.2, 129.9, 135.1, 135.6, 135.9, 136.3, 136.7, 147.0, 154.1.

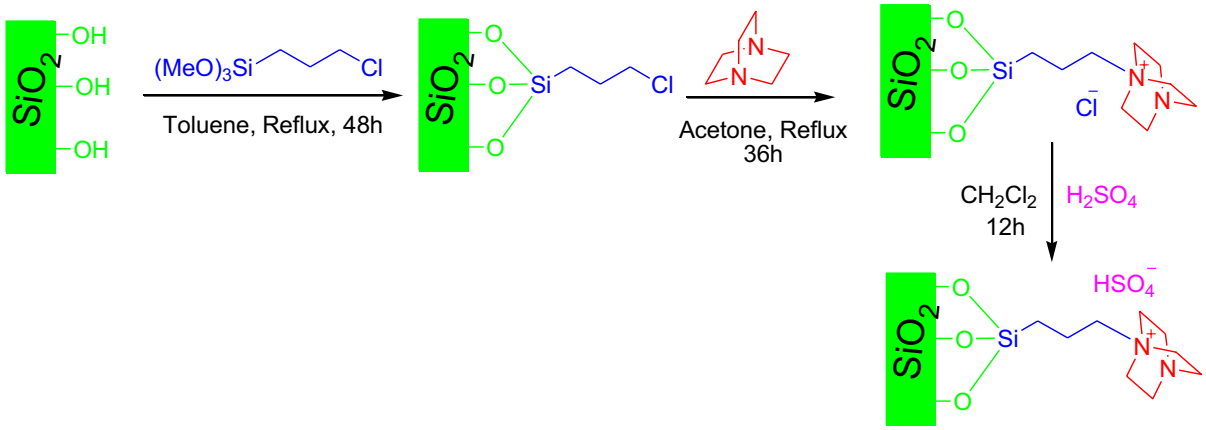
4,4′-((4-(Di(1*H*-indol-3-yl)methyl)phenyl)methylene) bis(1-(4-methoxyphenyl)-3-methyl-1*H*-pyrazol-5-ol) (6c)

Pink solid, m.p. > 300 °C. ^{1}H NMR (250 MHz, DMSO d_6): δ (ppm) 2.33 (s, 6H), 3.41 (s, 6H), 4.81 (s, 1H), 5.90 (s, 1H), 6.66 (s, 2H), 6.91–7.84 (m, 20H), 9.50 (br, 2H), 10.51 (s, 1H), 10.87 (s, 1H), ^{13}C NMR (62.5 MHz, DMSO d_6): δ (ppm) 14.1, 36.3, 55.5, 56.1, 111.0, 112.6, 112.9, 115.0, 118.5, 119.3, 119.8, 122.0, 123.1, 126.5, 129.0, 129.5, 130.1, 135.3, 136.4, 147.2, 153.8, 159.0.

Results and discussions

In the first step, SB-DABCO was prepared using a reported procedure [54] and then was treated with H_2SO_4 to afford silica-bonded *n*-propyl-4-aza-1-azoniabicyclo[*2.2.2*]octane hydrogen sulfate ((SB-DABCO)HSO_4) as a white powder (Scheme 2).

The catalyst structure was studied with IR spectroscopy (Fig. 1). There are seven characteristic peaks in the spectrum of ((SB-DABCO)HSO_4). The acid O–H stretching at 3700–3200 cm^{-1} as a broad band, sp^3 C–H stretching at 2990 cm^{-1}, C–N$^+$ stretching at 1620 cm^{-1}, CH_2 bending at 1460 cm^{-1}, Si–C stretching at 1215 cm^{-1}, Si–O stretching



Scheme 2 The preparation of silica-bonded *n*-propyl-4-aza-1-azoniabicyclo[*2.2.2*]octane hydrogen sulfate ((SB-DABCO)HSO_4)

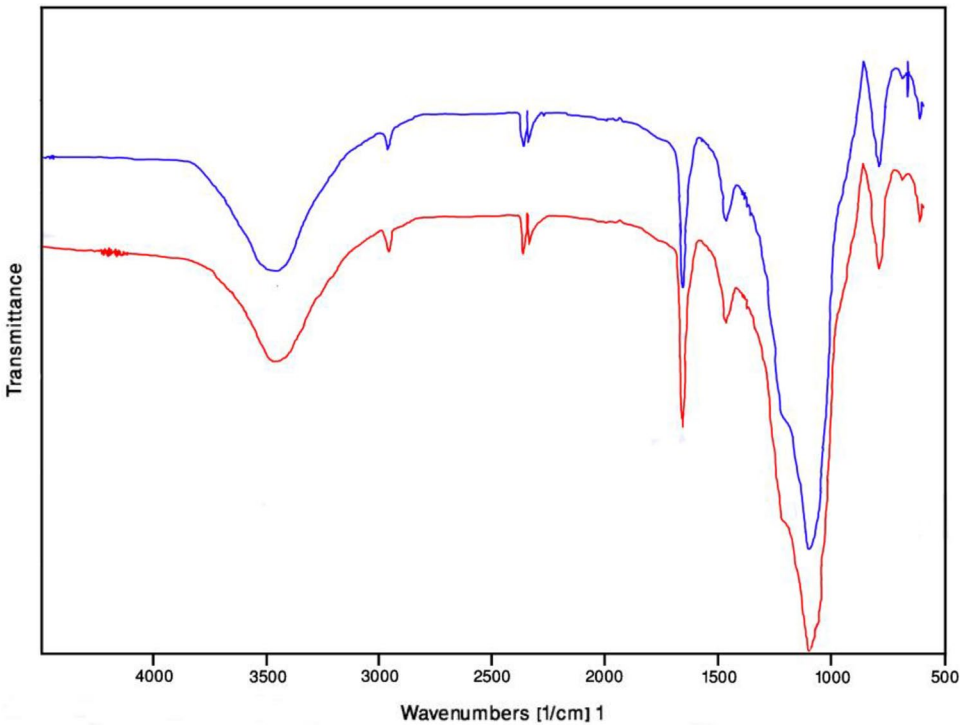


Fig. 1 The IR spectra of freshly synthesized silica-bonded *n*-propyl-4-aza-1-azoniabicyclo[2.2.2]octane hydrogen sulfate ((SB-DABCO)HSO_4) (blue line) and recovered ((SB-DABCO)HSO_4) after eighth reuse (red line)

at 1110–1090 cm^{-1} as a broad bond and S–O stretching at 870 cm^{-1}.

In another study, the loading level of HSO_4^- has been determined (using an acid–base titrimetric method) to be at around 1.10 mmol g^{-1}, which is in good agreement with thermal gravimetric analysis (TGA) as well as elemental analysis results. Nitrogen and sulfur content of the silica-bonded *n*-propyl-4-aza-1-azoniabicyclo[*2.2.2*]octane hydrogen sulfate ((SB-DABCO)HSO_4) were 2.91% and 3.48%, respectively, by conventional elemental analysis. The thermal stability of ((SB-DABCO)HSO_4) was also investigated and obtained results are demonstrated in Fig. 2.

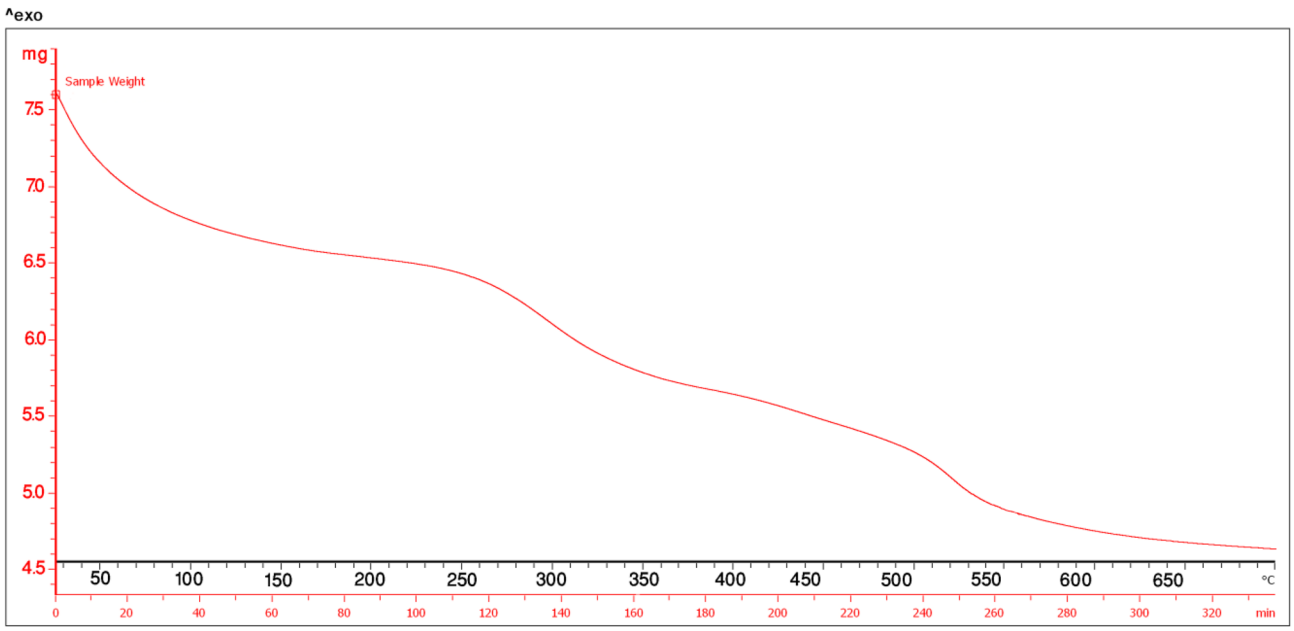


Fig. 2 The TG analysis of silica-bonded *n*-propyl-4-aza-1-azoniabicyclo[2.2.2]octane hydrogen sulfate ((SB-DABCO)HSO_4)

The 9.2% weight lost at around 90 °C can be related to desorption of water vapor and other volatile organic compounds which have been adsorbed on the catalyst. Following the thermogram, the decrease observed in the slope of the diagram, starting at around 270 °C can be related to the loss of the covalently bounded organic groups. Based on the obtained results from the thermogram, the amount of organic moiety was about 25% against solid support. Considering obtained data from TGA and elemental analysis the empirical formula of this catalyst can be calculated as $SiO_2{\cdot}0.087(C_9H_{18}N_2\text{-}HSO_4){\cdot}0.44H_2O$.

The basicity of 3-chloropropyl silica (SiPrCl) and silica-bonded *n*-propyl-4-aza-1-azoniabicyclo[2.2.2]octane hydrogen sulfate ((SB-DABCO)HSO_4) was also compared by the temperature programmed desorption (TPD) of CO_2 using a TGA method. The desorption temperature and amount of CO_2 desorbed are considered as indexes of base strength and total number of base sites, respectively. Fig. 3 shows only one major weight loss occurred over SiPrCl at the range of 220–260 °C, but there are two major weight losses in the case of ((SB-DABCO)HSO_4), the first occurred between 240 and 270 °C and the second occurred between 310 and 350 °C. This is obviously known that TPD could be used to evaluate the relative strength of basic sites. Fig. 3 indicates that the ((SB-DABCO)HSO_4) can be considered as a basic catalyst as well as an acid catalyst at the same time according to desorption temperature and intensity of CO_2 adsorbed.

The N_2 adsorption–desorption isotherm and pore size distribution of the ((SB-DABCO)HSO_4) are presented in Fig. 4. As it is clear from Fig. 4, the ((SB-DABCO)HSO_4) shows a lower BET surface area and average pore size (272.10 $m^2\ g^{-1}$ and 3.5 nm, respectively) compared with silica gel (550 $m^2\ g^{-1}$ and 6 nm, respectively). These results confirmed the immobilization of (DABCO)HSO_4 on the surface of silica gel. The narrow pore size distribution of (SB-DABCO)HSO_4 confirms the uniform immobilization of (DABCO)HSO_4 on the surface of silica gel.

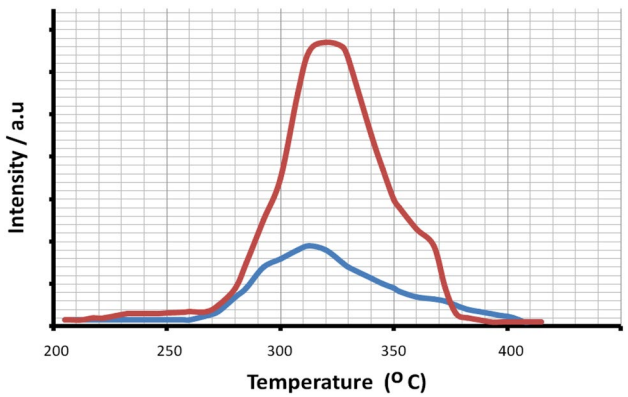


Fig. 3 The CO_2-TPD plots of SiPrCl (blue) and (SB-DABCO)HSO_4 (red)

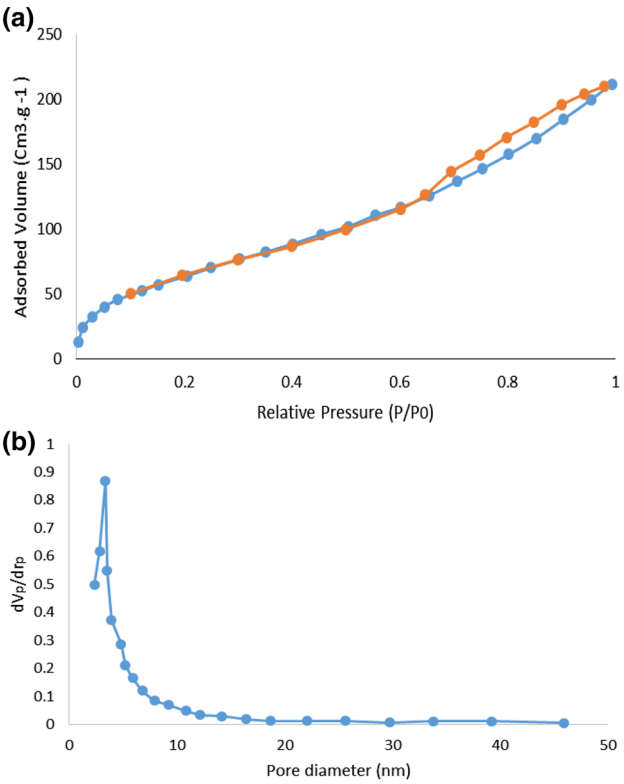
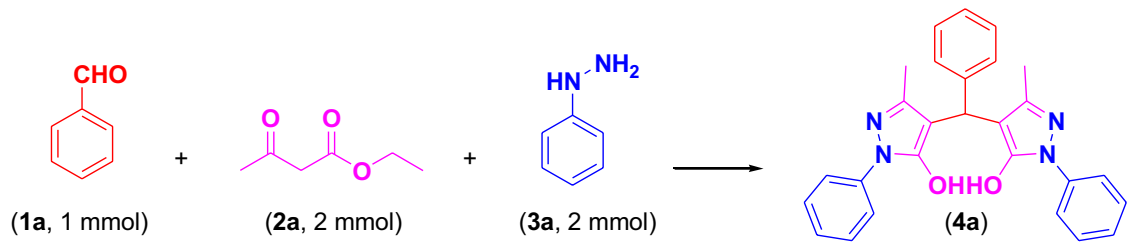


Fig. 4 The nitrogen adsorption–desorption isotherms (**a**) and the pore size distribution (**b**) of (SB-DABCO)HSO_4

In the next step, one-pot pseudo-five-component condensation reaction of phenylhydrazines (2 equivalents), β-ketoesters (2 equivalents) and aldehydes (1 equivalent) for the preparation of bis(pyrazolyl)methanes was investigated in the presence of ((SB-DABCO)HSO_4) as a new interphase dual-catalyst. To find the best reaction conditions, the one-pot condensation of benzaldehyde (**1a**) (1 mmol, 0.10 g), ethyl acetoacetate (**2a**) (2 mmol, 0.26 g) and phenylhydrazine (**3a**) (2 mmol, 0.21 g) in the presence of ((SB-DABCO)HSO_4) was selected as a model reaction (Scheme 3).

The reaction was examined in the presence of different molar ratios of ((SB-DABCO)HSO_4) in various solvents at different temperatures and obtained results are summarized in Table 1.

As it is indicated in Table 1, the best results (maximum yield and shortest reaction time) were obtained in the presence of 6 mol% of the catalyst in ethanol as a solvent at reflux temperature. Under these conditions, the corresponding product (**4a**) was obtained in 86% yield within 40 min (Table 1, entry 4). The model reaction was also examined in the presence of ((SB-DABCO)HSO_4) at various temperatures and in several solvents including $CHCl_3$, CH_3CN, EtOAc, H_2O, CH_2Cl_2, THF, DMF, DMSO and PEG 200 (Table 1, entries 11–19). As it is clear from Table 1, ethanol was the best solvent for this reaction. Besides, the model



Scheme 3 The one-pot condensation of benzaldehyde (**1a**) (1 mmol, 0.10 g), ethyl acetoacetate (**2a**) (2 mmol, 0.26 g) and phenylhydrazine (**3a**) (2 mmol, 0.21) in the presence of ((SB-DABCO)HSO_4)

Table 1 The one-pot condensation of benzaldehyde (**1a**) (1 mmol, 0.10 g), ethyl acetoacetate (**2a**) (2 mmol, 0.26 g) and phenylhydrazine (**3a**) (2 mmol, 0.21) in the presence of ((SB-DABCO)HSO_4) under different conditions

Entry	Solvent (5 mL)	Catalyst (mol%)	Temp. (°C)	Time (min)	Yield (%)[a]
1	EtOH	3	Reflux	120	41
2	EtOH	4	Reflux	120	45
3	EtOH	5	Reflux	70	86
4	EtOH	6	Reflux	40	86
5	EtOH	7	Reflux	40	85
6	EtOH	8	Reflux	40	86
7	EtOH	–	Reflux	120	Trace
8	EtOH	6	r.t	120	–
9	EtOH	6	40	120	39
10	EtOH	6	60	40	79
11	CH_3Cl	6	Reflux	120	40
12	CH_3CN	6	Reflux	120	55
13	EtOAc	6	Reflux	120	35
14	H_2O	6	80	120	25
15	CH_2Cl_2	6	Reflux	120	28
16	THF	6	Reflux	120	Trace
17	DMF	6	80	120	46
18	DMSO	6	80	120	52
19	PEG 200	6	80	120	70

[a]Isolated pure products

reaction was examined without the catalyst and only trace amounts of desired product were obtained even after a long time (Table 1, entry 7). This observation establishes the crucial catalytic role of ((SB-DABCO)HSO_4) as a new interphase catalyst for the expedition of the one-pot pseudo-five-component synthesis of bis(pyrazolyl)methanes.

With optimized conditions in hand and to probe the efficiency and the scope of our method, a broad range of structurally diverse aldehydes (**1**) were condensed with β-ketoesters (**2**) and hydrazines (**3**) to furnish the corresponding bis(pyrazolyl)methanes in high yields and in relatively short reaction times (Scheme 1) and obtained results are summarized in Table 2.

As it is shown in Table 2, various β-ketoesters, phenylhydrazines and aryl aldehydes were successfully condensed and desired products were obtained in short times and with good yields. Moreover, acid-sensitive aldehydes such as furfural and thiophene-2-carbaldehyde have been successfully applied without the formation of any by-products (Table 2, entries 4 and 14).

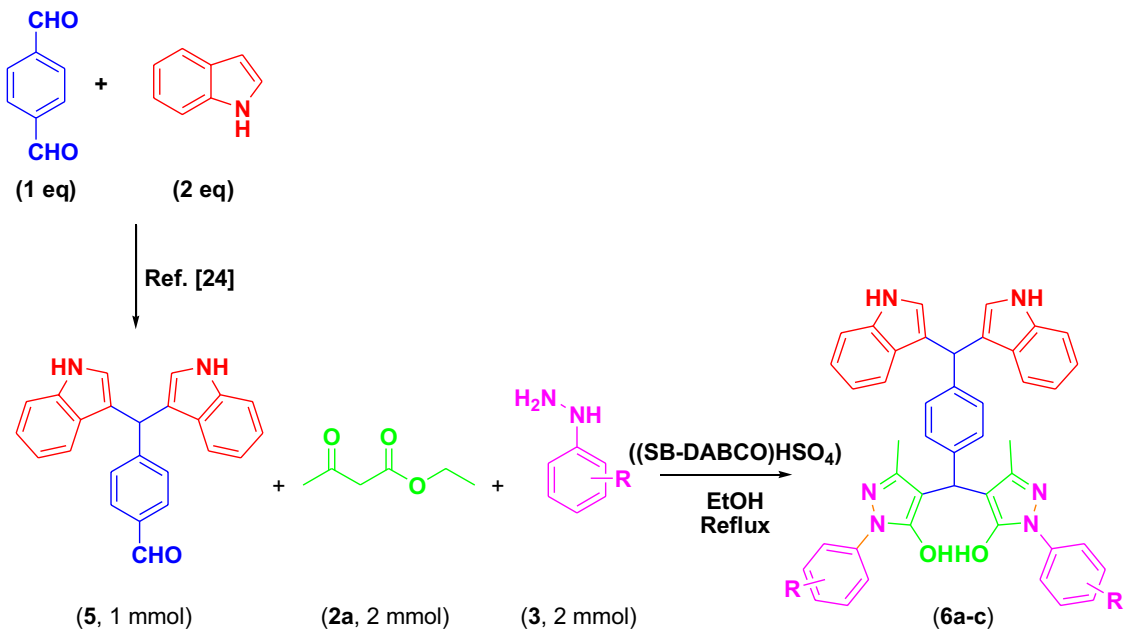
Indole derivatives are important class of biologically active compounds and have been frequently studied due to their unique and extensive biological activities [57]. Bis(indolyl)methanes are one of the most important group of indole derivatives which are found and isolated from some natural sources [58]. These compounds have shown some different pharmaceutical activities such as anticancer [59], antihyperglycemic, antiviral and antimicrobial properties [60] and are known as a promoter of estrogen metabolism [61]. The resultant pharmacological interest in compounds, which belong to the pyrazole, indole, bis(pyrazolyl)methane and bis(indolyl)methane families, has led us to apply our presented method for the synthesis of some novel 4-[bis(pyrazolyl)methane]phenylmethylene-bis(indole)s. For this, 4-(di(1*H*-indole-3-yl)methyl)benzaldehyde (**7**) was prepared via the condensation of indole with terephthalaldehyde using a reported procedure [62] and was condensed with ethyl acetoacetate (**2a**) and hydrazines (**3**) under the optimized conditions and nitrogen atmosphere (Scheme 4) and desired products were successfully obtained in good yields after short times.

Although the detailed mechanism of this reaction is still not completely clear, the formation of bis(pyrazolyl) methanes via a one-pot pseudo-five-component condensation reaction between aldehydes (**1**), β-ketoesters (**2**) and hydrazines (**3**) could be explained by the reaction sequences in Scheme 5. In the first step, a condensation of hydrazines (**3**) with β-ketoesters (**2**) is proposed to give the intermediate (**5**). After this, the tandem Knoevenagel–Michael reaction of intermediate (**5**) with aldehydes (**1**) leads to the formation of desired products (**4**). Based on this mechanism, ((SB-DABCO)HSO_4) is an effective bifunctional catalyst (acid as well as base). Based on our suggestion, ((SB-DABCO)HSO_4) serves two catalytic

Table 2 The one-pot multicomponent synthesis of bis(pyrazolyl)methanes in the presence of ((SB-DABCO)HSO_4) as a new interphase catalyst

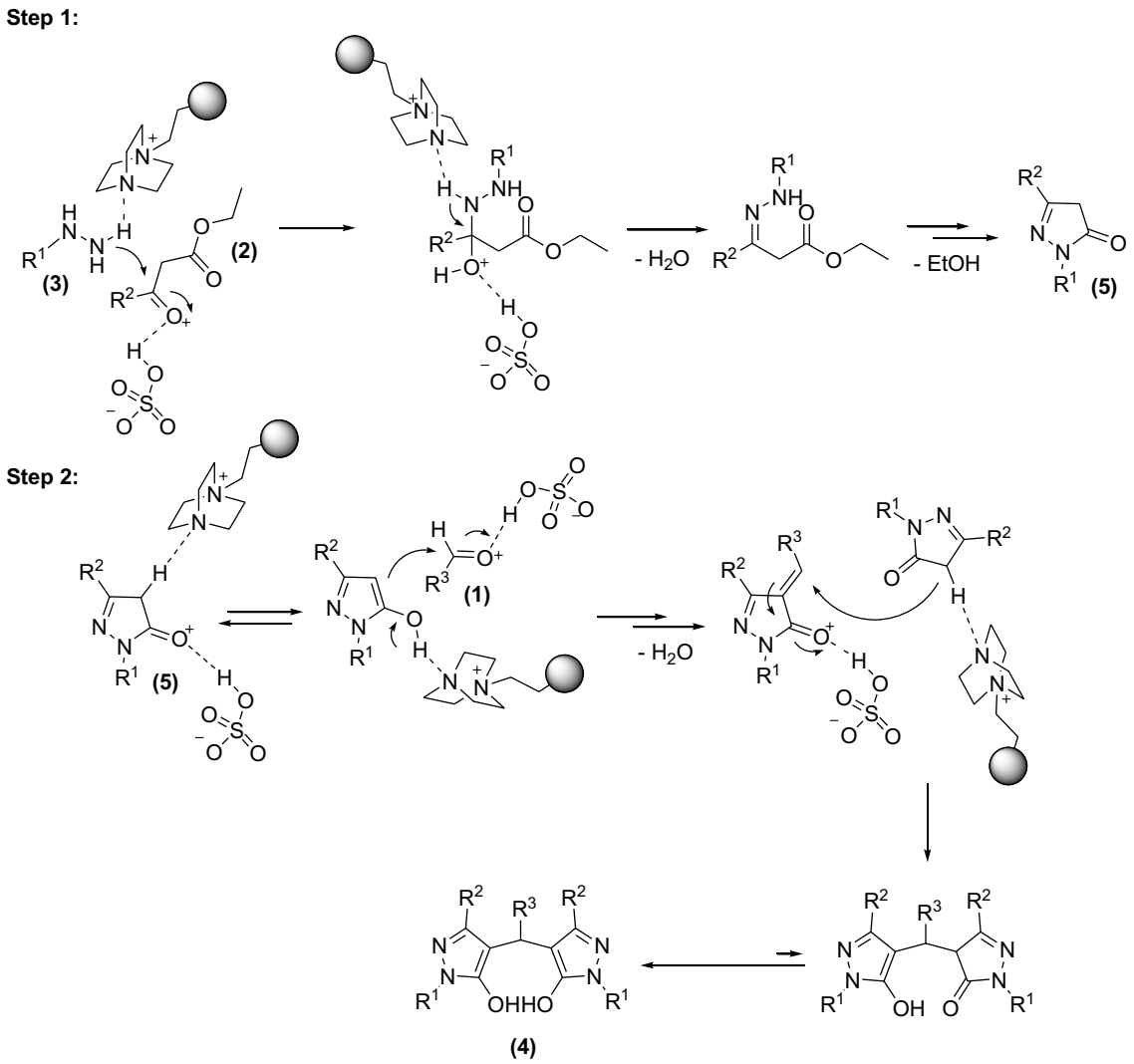
Entry	R^1	R^2	R^3	Product	Time (min)	Yield (%)[a]	M.P. (°C)
1	Ph	CH_3	H	**4a**	40	86	170–172 (171–172) [55]
2	4-Cl-Ph	CH_3	H	**4b**	40	88	211–213 (207–209) [55]
3	4-OEt-Ph	CH_3	H	**4c**	100	83	183–184 (185–188) [56]
4	2-Thionyl	CH_3	H	**4d**	120	87	193–195 (190–192) [56]
5	3-Br-Ph	CH_3	H	**4e**	50	85	171–173 (172–175) [56]
6	4-Me-Ph	CH_3	H	**4f**	70	87	202–204 (200–202) [56]
7	Ph	$CH_3CH_2CH_2$	H	**4g**	45	86	189–191
8	Ph	$CH_3CH_2CH_2$	4-Me	**4h**	40	87	205–207
9	Ph	$CH_3CH_2CH_2$	4-OMe	**4i**	40	89	211–213
10	Ph	Ph	4-Me	**4j**	360	83	252–254
11	4-Cl-Ph	Ph	H	**4k**	480	85	274–276
12	4-Br-Ph	$CH_3CH_2CH_2$	4-OMe	**4l**	50	85	261–263
13	4-Me-Ph	$CH_3CH_2CH_2$	4-Me	**4m**	110	83	245–247
14	2-Furyl	$CH_3CH_2CH_2$	4-Me	**4n**	100	86	233–235
15	4-Me-Ph	Ph	4-Me	**4o**	480	82	249–251
16	4-NO_2-Ph	Ph	4-Me	**4p**	360	87	> 300
17	3-NO_2-Ph	$CH_3CH_2CH_2$	4-OMe	**4q**	35	85	> 300
18	4-$CH(CH_3)_2$Ph	$CH_3CH_2CH_2$	4-OMe	**4r**	100	87	255–257
19	4-$CH(CH_3)_2$Ph	Ph	4-OMe	**4s**	480	81	265–267
20	3-OMe-Ph	Ph	4-OMe	**4t**	480	82	284–287

[a]Isolated yield



R	H (**6a**)	CH_3 (**6b**)	OCH_3 (**6c**)
Time (min)	80	60	50
Yield(%)	83	89	89

Scheme 4 The synthesis of some novel 4-[bis(pyrazolyl)methane]phenylmethylene-bis(indole)s in the presence of ((SB-DABCO)HSO_4)



Scheme 5 The proposed mechanism for the synthesis of bis(pyrazolyl)methanes in the presence of ((SB-DABCO)HSO_4)

functions: first, to electrophilically activate the aldehydes and carbonyl group of β-ketoesters through the interaction between positively charged hydrogen of HSO_4^- and the carbonyl oxygen, and second, to enhance the nucleophilicity of the hydrazines and intermediate (**5**) through the interaction between C_α-H with nitrogen of DABCO-like part of the catalyst.

To corroborate the suggested mechanism, a benchmark reaction in two steps was carried out. In this regard, ethyl acetoacetate (**2a**, 2 mmol, 0.26 g) was treated with phenylhydrazine (**3a**, 2 mmol, 0.21 g) under optimized conditions and the completion of the reaction was followed by TLC. It is found that ethyl acetoacetate was converted to corresponding pyrazolone (3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one) under applied conditions. In the next step, benzaldehyde (**1a**, 1 mmol, 0.10 g) was added to the reaction mixture and resulted mixture was stirred under the optimized conditions and finally it has been found that all pyrazolones are converted to the corresponding bis(pyrazolyl)methane (**4a**).

To examine the possibility of recycling the catalyst, the model reaction was run in the presence of recovered catalyst and obtained results are summarized in Fig. 5. Upon completion of reaction, insoluble catalyst was separated by simple filtration, washed with CH_2Cl_2 and dried at 50 °C under reduced pressure for 12 h. The filtrate was stand at room temperature for 12 h and during this time pure crystals of desired product were formed. The recovered catalyst was reused ten times in the condensation reaction of benzaldehyde (**1a**, 1 mmol, 0.10 g), ethyl acetoacetate (**2a**, 2 mmol, 0.28 g) and phenylhydrazine (**3a**, 2 mmol, 0.21 g) and smooth loss of catalytic activity was observed from the eighth time of reuse (Fig. 4). Moreover, the IR spectrum of recovered catalyst after the eighth time of reuse was compared with the IR spectrum of freshly synthesized catalyst

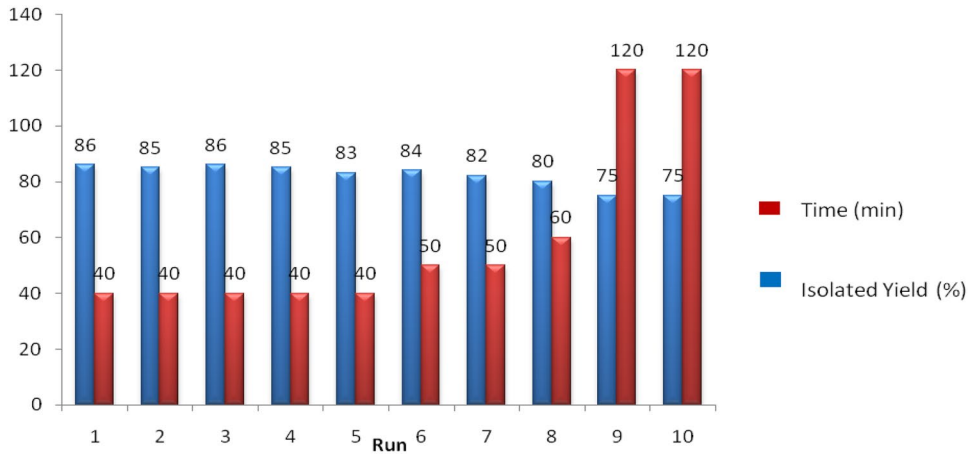


Fig. 5 The catalytic activity of ((SB-DABCO)HSO_4) in ten cycles for the one-pot reaction of benzaldehyde (**1a**, 1 mmol, 0.10 g), ethyl acetoacetate (**2a**, 2 mmol, 0.28 g) and phenylhydrazine (**3a**, 2 mmol, 0.21 g)

(Fig. 1). As it is clear from Fig. 1, there are no differences between the two IR spectra, so it is expressible that the catalyst structure is stable under the applied conditions even after the eighth time of reuse.

Conclusions

In summary, an efficient protocol for the one-pot synthesis of bis(pyrazolyl)methane derivatives via a multicomponent reaction of β-ketoesters (2 equivalents), phenylhydrazines (2 equivalents) and aryl aldehydes (1 equivalent) has been described using silica-bonded *n*-propyl-4-aza-1-azoniabicyclo[*2.2.2*]octane hydrogen sulfate ((SB-DABCO)HSO_4) as a recoverable and heterogeneous interphase catalyst. Mild reaction conditions, versatile range of available substrates and high diversity of products, operational simplicity, enhanced rates and high isolated yields of pure products are significant advantages of the protocol described here. This easy removal and reusability of the catalyst makes this method a better choice for chemical industries. Moreover, some novel 4-[bis(pyrazolyl)methane]phenylmethylene-bis(indole)s as more complex molecules were synthesized successfully.

Acknowledgements We gratefully appreciate the Shiraz University Research Councils for the financial support of this work.

References

1. R. Schlögl, Angew. Chem. Int. Ed. **54**, 3465–3520 (2015)
2. J.R.H. Ross, *Heterogeneous catalysis* (Fundamentals and Applications, Elsevier, Amsterdam, 2012)
3. C.M. Friend, B. Xu, Acc. Chem. Res. **50**, 517–521 (2017)
4. M. Boronat, P. Concepción, Catal. Today **285**, 166–178 (2017)
5. M. Sheykhan, L. Mamani, A. Ebrahimi, A. Heydari, J. Mol. Catal. A: Chem. **335**, 253–261 (2011)
6. B. Karimi, M. Ghoreishi-Nezhad, Clark JH. Org. Lett. **7**, 625–628 (2005)
7. B. Karimi, M. Khalkhali, J. Mol. Catal. A Chem. **232**, 113–117 (2005)
8. B. Karimi, A. Zamani, J.H. Clark, Organometallics **24**, 4695–4698 (2005)
9. B. Karimi, L. Ma'Mani, Org. Lett. **6**, 4813–4815 (2004)
10. R. Gupta, S. Paul, R. Gupta, J. Mol. Catal. A Chem. **266**, 1–2 (2007)
11. K. Niknam, A. Piran, Z. Karimi, J. Iran. Chem. Soc. **13**, 859–871 (2016)
12. K. Niknam, N. Borazjani, Monatsh. Chem. **147**, 1129–1135 (2016)
13. R. Noyori, M. Aoki, K. Sato, (2003) Chem. Commun., pp. 1977–1986
14. E. McDonald, K. Jones, P.A. Brough, M.J. Drysdale, P. Workman, Curr. Top. Med. Chem. **6**, 1193–1203 (2006)
15. J. Elguero, in *Comprehensive Heterocyclic Chemistry*, ed. by A.R. Katritzky, C.W. Rees, E.F.V. Scriven (Oxford, Pergamon, 1996)
16. J. Elguero, P. Goya, N. Jagerovic, A.M.S. Silva, Targets Heterocycl. Syst. **6**, 52–98 (2002)
17. J. Elguero, P. Goya, N. Jagerovic, A.M.S. Silva, in *Targets in Heterocyclic Systems*, ed. by O.A. Attanasi, D. Spinelli (Italian Society of Chemistry, Roma, 2002)
18. Y.R. Huang, J.A. Katzenellenbogen, Org. Lett. **2**, 2833–2836 (2000)
19. K.Y. Lee, J.M. Kim, J.N. Kim, Tetrahedron Lett. **44**, 6737–6740 (2003)
20. H. Nakagawa, R. Ohyama, A. Kimata, T. Suzuki, N. Miyata, Bioorg. Med. Chem. Lett. **16**, 5939–5942 (2006)
21. S. Sugiura, S. Ohno, O. Ohtani, K. Izumi, T. Kitamikado, H. Asai, K. Kato, J. Med. Chem. **20**, 80–85 (1977)
22. L.C. Behr, R. Fusco, C.H. Jarboe, in *The Chemistry of Heterocyclic Compounds, Pyrazoles, Pyrazolines, Pyrazolidines, Indazoles and Condensed Rings*, ed. by A. Weissberger (Interscience, New York, 1967)
23. C.E. Rosiere, M.I. Grossman, Science **113**, 651–659 (1951)
24. D.M. Bailey, P.E. Hansen, A.G. Hlavac, E.R. Baizman, J. Pearl, A.F. Defelice, M.E. Feigenson, J. Med. Chem. **28**, 256–260 (1985)
25. R.N. Mahajan, F.H. Havaldar, P.S. Fernandes, J. Indian Chem. Soc. **68**, 245–246 (1991)
26. P.M.S. Chauhan, S. Singh, R.K. Chatterjee, Indian J Chem Sect B **32**, 858–863 (1993)
27. C.J. O'Connor, H.S.G. Beckmanna, D.R. Spring, Chem. Soc. Rev. **41**, 4444–4456 (2012)

28. H.S.G. Beckmann, F. Nie, C.E. Hagerman, H. Johansson, Y.S. Tan, D. Wilcke, D.R. Spring, Nat. Chem. **5**, 861–867 (2013)
29. J.J. Ciardiello, W.R.J.D. Galloway, C.J. O'Connor, H.F. Sore, J.E. Stokes, Y. Wu, D.R. Spring, Tetrahedron **72**, 3567–3578 (2016)
30. E. Ruijter, R. Scheffelaar, R.V.A. Orru, Angew. Chem. Int. Ed. **50**, 6234–6246 (2011)
31. Sh. Tayebi, K. Niknam, Iran. J. Catal. **2**, 69–74 (2012)
32. E. Soleimani, S. Ghorbani, M. Taran, A. Sarvary, C. R. Chim. **15**, 955–961 (2012)
33. A. Hasaninejed, M.R. Kazerooni, A. Zare, ACS Sustain. Chem. Eng. **1**, 679–684 (2013)
34. J. Safaei-Ghomi, B. Khojastehbakht-Koopaei, H. Shahbazi-Alavi, RSC Adv. **4**, 46106–46113 (2014)
35. F. Shirini, M. Seddighi, M. Mazloumi, M. Makhsous, M. Abedini, J. Mol. Liq. **208**, 291–297 (2015)
36. N.G. Khaligh, S.B.A. Hamid, S.J. Titinchi, Chin. Chem. Lett. **27**, 104–108 (2016)
37. R. Jahanshahi, B. Akhlaghinia, Chem. Pap. **71**, 1351–1364 (2017)
38. M. Shekouhy, A. Khalafi-Nezhad, Green Chem. **17**, 4815–4829 (2015)
39. H.R. Safaei, M. Safaei, M. Shekouhy, RSC Adv. **5**, 6797–6806 (2015)
40. M. Shekouhy, A. Moaddeli, A. Khalafi-Nezhad, Res. Chem. Intermed. **42**, 3805–3827 (2016)
41. A. Khalafi-Nezhad, M. Shekouhy, H. Sharghi, J. Aboonajmi, A. Zare, RSC Adv. **6**, 67281–67289 (2016)
42. M. Shekouhy, A. Moaddeli, A. Khalafi-Nezhad, J. Ind. Eng. Chem. **50**, 41–49 (2017)
43. H.R. Safaei, M. Shekouhy, S. Rahmanpur, A. Shirinfeshan, Green Chem. **14**, 1696–1704 (2012)
44. A. Hasaninejad, M. Shekouhy, A. Zare, Catal. Sci. Technol. **2**, 201–214 (2012)
45. A. Hasaninejad, A. Zare, M. Shekouhy, J. Ameri-Rad, Green Chem. **13**, 958–964 (2011)
46. A. Hasaninejad, A. Zare, M. Shekouhy, Tetrahedron **67**, 390–400 (2011)
47. H.R. Safaei, M. Shekouhy, A. Shirinfeshan, S. Rahmanpur, Mol. Divers. **16**, 669–683 (2012)
48. A. Khalafi-Nezhad, S. Mohammadi, RSC Adv. **3**, 4362–4371 (2013)
49. A. Khalafi-Nezhad, S. Mohammadi, Synthesis **44**, 1725–1735 (2012)
50. A. Hasaninejad, M. Shekouhy, M.R. Mohammadizadeh, A. Zare, RSC Adv. **2**, 6174–6177 (2012)
51. H.R. Safaei, M. Shekouhy, V. Shafiee, M. Davoodi, J. Mol. Liq. **180**, 139–144 (2013)
52. H.R. Safaei, M. Davoodi, M. Shekouhy, Synth. Commun. **43**, 2178–2190 (2013)
53. H.R. Safaei, M. Shekouhy, S. Khademi, V. Rahmanian, M. Safae, J. Ind. Eng. Chem. **20**, 3019–3024 (2014)
54. A. Hasaninejad, M. Shekouhy, N. Golzar, A. Zare, M.M. Doroodmand, Appl. Catal. A Gen. **402**, 11–22 (2011)
55. W. Wang, S.X. Wang, X.Y. Qin, J.T. Li, Synth. Commun. **3**, 1263–1269 (2005)
56. A. Hasaninejad, A. Zare, M. Shekouhy, N. Golzar, Org. Prep. Proced. Int. **43**, 131–137 (2011)
57. R.J. Sundberg, *The Chemistry of Indole* (Academic Press, New York, 1996)
58. R. Bell, S. Carmeli, N. Sar, A. Vibrindole, J. Nat. Prod. **57**, 1587–1590 (1994)
59. C. Hong, G.L. Firestone, L.F. Bjeldance, Biochem. Pharmacol. **63**, 1085–1097 (2002)
60. L. Povszsz, G.P. Katakin, S. Foleat, B. Malkovics, Acta Phys. Acad. Sci. Hung. **29**, 299–312 (1996)
61. M.A. Zeligs, J. Med. Food **1**, 67–82 (1998)
62. A. Hasaninejad, A. Zare, H. Sharghi, K. Niknam, M. Shekouhy, ARKIVOC **xiv**:39–50 (2007)