AN ECO-FRIENDLY ONE-POT SYNTHESIS OF 4,4′-(ARYLMETHYLENE)BIS(1H-PYRAZOL-5-OLS) USING $[Et_3NH][HSO_4]$ AS A RECYCLABLE CATALYST

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ABSTRACT

A simple and efficient procedure for synthesis of 4,4′-(arylmethylene)bis(1H-pyrazol-5-ols) by one-pot three-component condensation of aromatic aldehydes, ethyl acetoacetate, and phenylhydrazine/hydrazine hydrate under solvent-free conditions in the presence of $[Et_3NH][HSO_4]$ as catalyst is described. The present protocol offers several advantages such as using a reusable and cost-effective ionic liquid, high yields, simple procedure, easy work-up and eco-friendly reaction conditions.

Keywords: 4,4′-(Arylmethylene)bis(1H-pyrazol-5-ols); $[Et_3NH][HSO_4]$; Solvent-free; Multicomponent reaction

INTRODUCTION

4,4′-(Arylmethylene)bis(1H-pyrazol-5-ols) are applied as fungicides[1], pesticides[2] and dyestuffs[3]. The condensation of aldehydes with two equivalents of 3-methyl-1-phenyl-5- pyrazolone is a conventional chemical approach to 4,4′-(arylmethylene)bis(1H-pyrazol-5-ols). Many catalysts have been used for this transformation such as xanthan sulfuric acid[4], phosphomolybdic acid[5], silica sulfuric acid[6], 3-aminopropylated silica gel[7], sodium dodecyl sulfate[8], $[Cu(3,4\text{-tmtppa})](MeSO_4)_4$ [9], PEG-SO_3H[10], cellulose sulfuric acid[11], lithium hydroxide monohydrate[12], 1,3,5-tris(hydrogensulfato) benzene[13], sulfuric acid ([3-(3-silicapropyl)sulfanyl]propyl)ester[14], ethylenediammonium diacetate[15], $[Sipmim]HSO_4$ [16], TEBA[17], ceric ammonium nitrate[18], silica-bonded S-sulfonic acid[19], 2-hydroxyethylammonium acetate[20], 1,3-disulfonic acid imidazolium tetrachloroaluminate[21] and 1-sulfopyridinium chloride[22]. Catalyst-free protocol and the electrocatalytic procedure were also applied to the preparation of 4,4'-(arylmethylene)bis(1H-pyrazol-5-ols)[23-26]. All of the aforementioned procedures include two main steps: (1) 3-methyl-1-phenyl-5-pyrazolone should be synthesized from phenylhydrazine and ethyl acetoacetate firstly[27], and (2) then 3-methyl-1-phenyl-5-pyrazolone reacted with aldehydes. Even though, 4,4′-(arylmethylene)bis(1H-pyrazol-5-ols) could be synthesized by these methods, most of the methods suffer from limitations such as long reaction time, use of expensive catalysts, the requirement of special apparatus, tedious work-up procedures and noncompliance with green chemistry protocols. Therefore, finding an efficient and eco-friendly protocol for the preparation of 4,4′-(arylmethylene)bis(1H-pyrazol-5-ols) is of obvious importance.

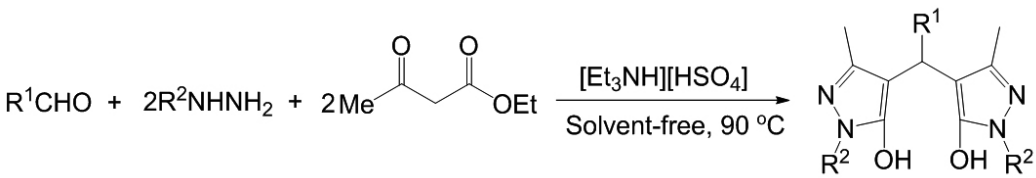
In green chemistry, elimination of volatile organic solvents in organic synthesis is a most important goal. Solvent-free conditions makes synthesis simpler, save energy, and prevent solvent waste, hazards, and toxicity[28-29]. Ionic liquids have been widely used as environmentally benign reaction media and catalysts in organic synthesis because of their unique properties of nonvolatility, nonflammability, and recyclability[30-31]. Recently, the use of acidic ionic liquid $[Et_3NH][HSO_4]$ has received considerable attention as a cheap and easily available reagent in organic reactions [32-37]. In continuation of our work on the application of acidic ionic liquid for development of useful synthetic methodologies[37-38], we report herein, an alternative protocol for the one-pot three-component synthesis of 4,4′-(arylmethylene)bis(1H-pyrazol-5-ols) derivatives starting directly from aldehydes, phenylhydrazine/hydrazine hydrate and ethyl acetoacetate using $[Et_3NH][HSO_4]$ as an efficient, cost-effective and recyclable catalyst under solvent-free conditions (Scheme 1).

EXPERIMENTAL

Material and instruments

Melting points were determined on a X-4 micro melting point apparatus and are uncorrected. FT-IR spectra were obtained as KBr pellets on a Nexus 470 spectrophotometer. ^{1}H NMR spectra were recorded on a Bruker Avance III 400 with TMS as internal standard. All chemicals were commercial products. $[Et_3NH][HSO_4]$, $[Et_3NH][H_2PO_4]$, $[BPy][HSO_4]$ and $[BPy][H_2PO_4]$ were prepared according to the literature method[32,38-39].

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



Scheme 1. $[Et_3NH][HSO_4]$ catalyzed synthesis of 4,4′-(arylmethylene)bis(1H-pyrazol-5-ols)

A mixture of aldehyde (5 mmol), ethyl acetoacetate (10 mmol), phenylhydrazine (10 mmol), and $[Et_3NH][HSO_4]$ (0.5 mmol) was stirred at 90 °C under solvent-free conditions. The progress of the reaction was monitored by TLC using EtOAc/petroleum ether (1/2) as eluent. During the reaction process, a solid product spontaneously formed. After completion of the reaction, the reaction mixture was cooled to room temperature. The resulting solid was recrystallized by using ethanol (95%) to afford the pure product. The filtrate containing catalyst was evaporated under reduced pressure to give the catalyst which was used for the next run under similar reaction conditions. All the products are known and were identified by comparison of their physical and spectroscopic data with those of authentic samples. The spectral data of products are given below:

4,4′-(Phenylmethylene)bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (Table 2, entry 1): ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 2.32 (s, 6H, $2CH_3$), 4.96 (s, 1H, CH), 7.17-7.30 (m, 7H, ArH), 7.44 (t, *J*=7.6 Hz, 4H, ArH), 7.71 (d, *J*=8.0 Hz, 4H, ArH). IR (KBr) ν: 3358, 3061, 2965, 2582, 1596, 1495, 1414, 1272, 1074, 792, 734, 689 cm^{-1}.

4,4′-[(4-Methylphenyl)methylene]-bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (Table 2, entry 2): ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 2.24 (s, 3H, CH_3), 2.30 (s, 6H, $2CH_3$), 4.90 (s, 1H, CH), 7.09 (d, *J*=8.4 Hz, 2H, ArH), 7.13 (d, *J*=8.0 Hz, 2H, ArH), 7.24 (t, *J*=7.2 Hz, 2H, ArH), 7.44 (t, *J*=7.6 Hz, 4H, ArH), 7.70 (d, *J*=7.6 Hz, 4H, ArH). IR (KBr) ν: 3413, 3051, 2928, 1604, 1581, 1507, 1414, 1299, 806, 752, 695 cm^{-1}.

4,4′-[(4-Methoxyphenyl)methylene]-bis(3-methyl-1-phenyl-1H-pyrazol-

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5-ol) (Table 2, entry 3): ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 2.32 (s, 6H, $2CH_3$), 3.72 (s, 3H, CH_3O), 4.93 (s, 1H, CH), 6.87 (d, *J*=8.8 Hz, 2H, ArH), 7.18 (d, *J*=8.4 Hz, 2H, ArH), 7.23-7.31 (m, 2H, ArH), 7.45-7.49 (m, 4H, ArH), 7.72-7.73 (m, 4H, ArH). IR (KBr) ν: 3437, 3068, 2918, 2559, 1606, 1584, 1510, 1411, 1378, 1039, 801, 755 cm^{-1}.

4,4′-[(4-Flurophenyl)methylene]-bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (Table 2, entry 4): ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 2.32 (s, 6H, $2CH_3$), 4.96 (s, 1H, CH), 7.09 (t, *J*=8.0 Hz, 2H, ArH), 7.24-7.32 (m, 4H, ArH), 7.45 (t, *J*=7.6 Hz, 4H, ArH), 7.72 (d, *J*=8.0 Hz, 4H, ArH). IR (KBr) ν: 3445, 3080, 288, 1590, 1495, 1401, 1380, 1308, 1121, 902, 842, 788, 690 cm^{-1}.

4,4′-[(3-Methoxyphenyl)methylene]-bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (Table 2, entry 5): ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 2.42 (s, 6H, $2CH_3$), 3.51 (s, 3H, CH_3O), 4.71 (s, 1H, CH), 6.55 (d, *J*=8.8 Hz, 2H, ArH), 6.66-6.72 (m, 2H, ArH), 7.89 (m, 1H, ArH), 7.32-7.45 (m, 4H, ArH), 7.73 (m, 4H, ArH). IR (KBr) ν: 3428, 3085, 2920, 1580, 1508, 1410, 1133, 1025, 804, 685 cm^{-1}.

4,4′-[(3-Nitrophenyl)methylene]bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (Table 2, entry 6): ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 2.30 (s, 6H, $2CH_3$), 4.95 (s, 1H, CH), 7.2 (t, *J*=7.2 Hz, 2H, ArH), 7.37 (t, *J*=8.0 Hz, 2H, ArH), 7.44 (t, *J*=8.8 Hz, 2H, ArH), 7.67 (d, *J*=8.0 Hz, 4H, ArH), 8.07 (d, *J*=6.4 Hz, 4H, ArH). IR (KBr) ν: 3078, 2918, 1599, 1523, 1502, 1346, 1269, 1093, 758, 734, 696 cm^{-1}.

4,4′-[4-Hydroxy-3-methoxyphenyl)methylene]-bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (Table 2, entry 7): ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 2.33 (s, 6H, $2CH_3$), 3.69 (s, 3H, CH_3O), 4.87 (s, 1H, CH), 6.71-6.74 (m, 2H, ArH), 6.88-6.89 (m, 1H, ArH), 7.24-7.26 (m, 2H, ArH), 7.43-7.47 (m, 4H, ArH), 7.72-7.74 (m, 4H, ArH), 8.81 (s, 1H, OH). IR (KBr) ν: 3213, 3071, 2561, 1609, 1507, 1422, 1264, 1131, 1044, 816, 789, 760, 693 cm^{-1}.

4,4′-[(2-Chlorophenyl)methylene]-bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (Table 2, entry 8): ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 2.29 (s, 6H, $2CH_3$), 5.14 (s, 1H, CH), 7.22-7.33 (m, 4H, ArH), 7.41 (d, *J*=8.0 Hz, 1H, ArH), 7.46 (t, *J*=7.6 Hz, 4H, ArH), 7.70 (d, *J*=8.0 Hz, 4H, ArH), 7.80 (d, *J*=7.2 Hz, 1H, ArH). IR (KBr) ν: 3435, 3066, 2916, 1615, 1562, 1503, 1404, 1374, 1310, 839, 752, 695 cm^{-1}.

4,4′-[(4-Chlorophenyl)methylene]-bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (Table 2, entry 9): ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 2.30 (s, 6H, $2CH_3$), 4.98 (s, 1H, CH), 7.22-7.28 (m, 4H, ArH), 7.35 (d, *J*=8.4 Hz, 2H, ArH), 7.44 (t, *J*=8.0 Hz, 4H, ArH), 7.71 (d, *J*=8.0 Hz, 4H, ArH). IR (KBr) ν: 3432, 3068, 2924, 1601, 1496, 1412, 1296, 1196, 1094, 1019, 835, 752, 691 cm^{-1}.

4,4′-[(4-Bromophenyl)methylene]bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (Table 2, entry 10): ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 2.32 (s, 6H, $2CH_3$), 4.95 (s, 1H, CH), 7.19-7.27 (m, 4H, ArH), 7.42-7.48 (m, 6H, ArH), 7.70 (d, *J*=8.0 Hz, 4H, ArH). IR (KBr) ν: 3422, 3066, 2922, 2546, 1598, 1484, 1407, 1293, 1013, 809, 747, 687 cm^{-1}.

4,4′-[(2,4-Dichlorophenyl)methylene]bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (Table 2, entry 11): ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 2.28 (s, 6H, $2CH_3$), 5.09 (s, 1H, CH), 7.25 (t, *J*=7.2 Hz, 2H, ArH), 7.40-7.46 (m, 5H, ArH), 7.56 (d, *J*=2.0 Hz, 1H, ArH), 7.69 (d, *J*=8.0 Hz, 4H, ArH), 7.75 (d, *J*=8.4 Hz, 1H, ArH). IR (KBr) ν: 3425, 3060, 2919, 1595, 1573, 1498, 1471, 1380, 1295, 1105, 843, 754, 690 cm^{-1}.

4,4′-[(4-Nitrophenyl)methylene]-bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (Table 2, entry 12): ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 2.28 (s, 6H, $2CH_3$), 5.06 (s, 1H, CH), 7.18 (t, 2H, *J*=7.2 Hz, ArH), 7.38 (t, *J*=7.2 Hz, 4H, ArH), 7.45 (d, *J*=8.4 Hz, 2H, ArH), 7.64 (d, *J*=8.0 Hz, 4H, ArH), 8.10 (d, *J*=8.8 Hz, 2H, ArH). IR (KBr) ν: 3423, 3071, 2925, 1599, 1518, 1502, 1348, 1299, 835, 759, 693 cm^{-1}.

4,4′-[(2-Hydroxyphenyl)methylene]-bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (Table 2, entry 13): ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 2.28 (s, 6H, $2CH_3$), 5.16 (s, 1H, CH), 6.70-6.74 (m, 2H, ArH), 6.96 (t, *J*=7.2 Hz, 1H, ArH), 7.22 (t, *J*=7.2 Hz, 2H, ArH), 7.42 (t, *J*=8.0 Hz, 4H, ArH), 7.57 (d, *J*=7.2 Hz, 1H, ArH), 7.71 (d, *J*=7.8 Hz, 4H, ArH). IR (KBr) ν: 3427, 3066, 2928, 2832, 1603, 1578, 1501, 1454, 1372, 1231, 754, 690 cm^{-1}.

4,4′-[(4-Hydroxyphenyl)methylene]bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (Table 2, entry 14): ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 2.30 (s, 6H, $2CH_3$), 4.84 (s, 1H, CH), 6.66 (d, *J*=8.8 Hz, 2H, ArH), 7.04 (d, *J*=8.8 Hz, 2H, ArH), 7.22-7.26 (t, *J*=7.2 Hz, 2H, ArH), 7.44 (t, *J*=8.0 Hz, 4H, ArH), 7.71 (d, *J*=8.0 Hz, 4H, ArH), 9.16 (s, 1H, OH). IR (KBr) ν: 3413, 3158, 2969, 1597, 1502, 1427, 1275, 819, 756, 692 cm^{-1}.

4,4′-[(2-Methoxyphenyl)methylene]-bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) (Table 2, entry 15): ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 2.26 (s, 6H, $2CH_3$), 3.79 (s, 3H, OCH_3), 5.18 (s, 1H, CH), 6.82-6.93 (m, 2H, ArH), 7.11-7.24 (m, 3H, ArH), 7.41 (t, *J*=7.2 Hz, 4H, ArH), 7.60 (d, *J*=7.6 Hz, 1H, ArH), 7.67-7.70 (m, 4H, ArH). IR (KBr) ν: 3427, 3062, 2922, 1598, 1575, 1497, 1241, 756 cm^{-1}.

4,4′-(Phenylmethylene)bis(3-methyl-1H-pyrazol-5-ol) (Table 2, entry 16): ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 2.07 (s, 6H, $2CH_3$), 4.82 (s, 1H, CH), 7.09-7.14 (m, 3H, ArH), 7.19-7.22 (m, 2H, ArH). IR (KBr) ν: 3296, 2971, 1612, 1522, 1494, 1380, 1049, 825, 778, 717 cm^{-1}.

4,4′-[(3-Nitrophenyl)methylene]bis(3-methyl-1H-pyrazol-5-ol) (Table 2, entry 17): ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 2.11 (s, 6H, CH_3), 4.99 (s, 1H, CH), 7.54-7.57 (m, 2H, ArH), 7.96 (s, 1H, ArH), 8.03 (s, 1H, ArH). IR (KBr): 3419, 2961, 1599, 1447, 1390, 1182, 837, 795, 764 cm^{-1}.

4,4′-[(4-Chlorophenyl)methylene]bis(3-methyl-1H-pyrazol-5-ol) (Table 2, entry 18): ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 2.08 (s, 6H, CH_3), 4.82 (s, 1H, CH), 7.12 (s, 2H, ArH), 7.27 (m, 2H, ArH). IR (KBr): 3437, 1614, 1488, 1388, 1094, 757 cm^{-1}.

4,4′-[(4-Hydroxyphenyl)methylene]bis(3-methyl-1H-pyrazol-5-ol) (Table 2, entry 19): ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 2.06 (s, 6H, CH_3), 4.71 (s, 1H, CH), 6.58 (d, *J*=8.4 Hz, 2H, ArH), 6.90 (d, *J*=8.4 Hz, 2H, ArH), 9.04(s, 1H). IR (KBr): 3266, 1561, 1514, 1466, 1400, 1174, 872, 786, 731 cm^{-1}.

RESULTS AND DISCUSSION

In order to optimize the reaction conditions, the reaction of phenylhydrazine, ethyl acetoacetate and 2,4-dichlorobenzaldehyde was selected as a model reaction. The reactions catalyzed by various ionic liquids were carried out under solvent-free conditions at 50 °C. The product was obtained in 65%, 31%, 42% and 31% yield, respectively (Table 1, entries 1-4). The results clearly showed that $[Et_3NH][HSO_4]$ was an effective catalyst for this condensation.

Then the reaction temperature was examined and 90 °C was found to be the optimum temperature. Reducing the temperature from 90 °C led to a longer reaction time. Raising the reaction temperature from 90 to 100 °C did not increase the yield and also did not improve the reaction rate. We also evaluated the amount of catalyst required for this transformation using 5 mol% and we obtained 69% yield. Maximum yield (86%) was obtained when the reaction was carried out with 10 mol% of the catalyst. Any further increase of catalyst loading does not affect the yield (Table 1, entry 12). So, the optimum amount of $[Et_3NH][HSO_4]$ was found to be 10 mol% relative to reactants. The catalyst plays a crucial role in the reaction. The condensation reaction gave very low yield in the absence of catalyst (Table 1, entry 10).

To compare the efficiency as well as capacity of the solvent-free conditions with respect to solution conditions, various solvents were examined. The results showed that reactions in solvents take more time and also the yields are low compared to the solvent-free conditions (Table 1, entries 13-18). Water has been identified as an ideal solvent because it is abundant, inexpensive, non-flammable and environmentally benign [40,41]. However, when the reaction was carried out in water, the expected product was obtained only in 18% yield after 2 h. This may be explained due to the decreased diffusion of the reactant molecules in the presence of the solvent. Considering the importance of green chemistry, the solvent-free reaction conditions are the advantageous aspect of the present method, since it avoids the use of environmental hazardous and toxic solvents.

In order to establish the generality, the catalyst was successfully applied to the reaction by using different aromatic aldehydes with a wide range of ortho-, meta- and para-substitutions under the optimized reaction conditions. The results are summarized in Table 2. It is clear from this table that, high product yields were obtained with aromatic aldehydes containing electron-donating and electron-withdrawing substituents. Furthermore, the reaction is compatible in the presence of various functional groups such as -Cl, $-OCH_3$, $-NO_2$ and -OH. When changing phenylhydrazine into hydrazine hydrate, a similar result was given; the reaction gave the corresponding compounds in good yields.

The possibility of recycling the catalyst was examined using the reaction of benzaldehyde, ethyl acetoacetate, and hydrazine hydrate under the optimized reaction conditions. After completion of the reaction, the reaction mixture was cooled to room temperature. The resulting solid was purified by recrystallization from ethanol (95%). The filtrate (consisting of ethanol, acidic ionic liquid and some other residual reactants or by-products) was further evaporated under reduced pressure to dryness and the resulting catalyst was reused directly for the next run without any further treatment. As can be seen from Table 3, the catalyst was reused for successive reaction at least six times without any appreciable loss of catalytic activity.

Table 1 Effect of different reaction conditions on ionic liquids catalyzed synthesis of 4,4′-(arylmethylene)bis(1H-pyrazol-5-ols) [a]

Entry	Catalyst	Solvent	Temperature (°C)	Catalyst loading (mol%)	Time (min)	Yield[b] (%)
1	$[Et_3NH][HSO_4]$	Solvent-free	50	10	180	65
2	$[Et_3NH][H_2PO_4]$	Solvent-free	50	10	180	31
3	[BPy][HSO_4]	Solvent-free	50	10	180	42
4	[BPy][H_2PO_4]	Solvent-free	50	10	180	31
5	$[Et_3NH][HSO_4]$	Solvent-free	60	10	160	80
6	$[Et_3NH][HSO_4]$	Solvent-free	70	10	90	85
7	$[Et_3NH][HSO_4]$	Solvent-free	80	10	55	85
8	$[Et_3NH][HSO_4]$	Solvent-free	90	10	35	86
9	$[Et_3NH][HSO_4]$	Solvent-free	100	10	35	86
10	No catalyst	Solvent-free	90	0	210	7
11	$[Et_3NH][HSO_4]$	Solvent-free	90	5	35	69
12	$[Et_3NH][HSO_4]$	Solvent-free	90	20	35	86
13	$[Et_3NH][HSO_4]$	THF	Reflux	10	120	trace
14	$[Et_3NH][HSO_4]$	CH_3CN	Reflux	10	120	trace
15	$[Et_3NH][HSO_4]$	$CHCl_3$	Reflux	10	120	34
16	$[Et_3NH][HSO_4]$	C_6H_6	Reflux	10	120	33
17	$[Et_3NH][HSO_4]$	C_2H_5OH	Reflux	10	120	15
18	$[Et_3NH][HSO_4]$	H_2O	Reflux	10	120	18

[a] Reaction condition: 2,4-dichlorobenzaldehyde (5 mmol), ethyl acetoacetate (10 mmol), phenylhydrazine (10 mmol), solvent (10 mL).
[b] Isolated yield.

Table 2 $[Et_3NH][HSO_4]$ catalyzed synthesis of 4,4′-(arylmethylene)bis (1H-pyrazol-5-ols) [a]

Entry	R^1	R^2	Time (min)	Yield [b] (%)	Mp. (°C)	
					Found	Reported
1	C_6H_5	C_6H_5	45	90	171-172	170-172[6]
2	4-$CH_3C_6H_4$	C_6H_5	30	92	201-203	201-203[13]
3	4-$CH_3OC_6H_4$	C_6H_5	30	97	172-174	173-175[24]
4	4-FC_6H_4	C_6H_5	30	83	181-183	182-184[13]
5	3-$CH_3OC_6H_4$	C_6H_5	35	90	181-183	180-182[5]
6	3-$NO_2C_6H_4$	C_6H_5	25	82	151-153	149-150[8]
7	4-HO-3-$MeOC_6H_3$	C_6H_5	30	93	195-197	196-197[17]
8	2-ClC_6H_4	C_6H_5	30	90	236-238	235-237[13]
9	4-ClC_6H_4	C_6H_5	30	87	215-216	213-215[21]
10	4-BrC_6H_4	C_6H_5	25	91	201-203	183-185[13]
11	2,4-$Cl_2C_6H_3$	C_6H_5	35	86	227-229	227-229[13]
12	4-$NO_2C_6H_4$	C_6H_5	45	79	217-219	219-220[9]
13	2-HOC_6H_4	C_6H_5	30	90	222-224	218-220[5]
14	4-HOC_6H_4	C_6H_5	30	97	161-163	154-157[13]
15	2-$CH_3OC_6H_4$	C_6H_5	45	92	210-211	211-214[13]
16	C_6H_5	H	30	93	229-231	230-232[8]
17	3-$NO_2C_6H_4$	H	20	87	272-274	271-272[8]
18	4-ClC_6H_4	H	25	88	223-225	224-226[8]
19	4-HOC_6H_4	H	20	84	263-265	262-264[8]

[a] Reaction condition: aldehyde (5 mmol), ethyl acetoacetate (10 mmol), phenylhydrazine/ hydrazine hydrate (10 mmol), $[Et_3NH][HSO_4]$ (0.5 mmol) at 90 °C under solvent-free conditions.
[b] Isolated yield.

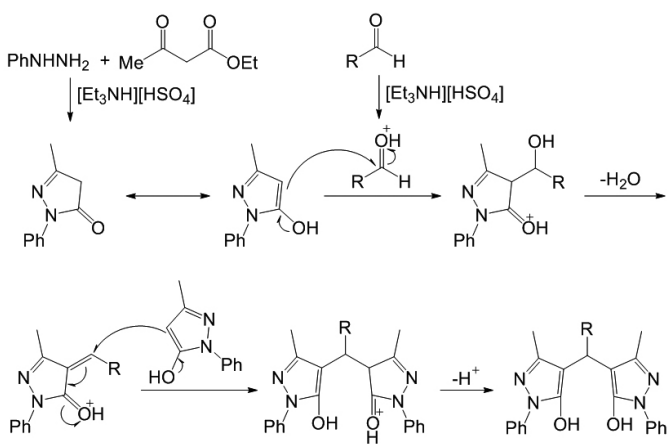
Table 3 Recycling of the $[Et_3NH][HSO_4]$ [a]

Run	Time (min)	Yield[b] (%)
1	30	92
2	30	92
3	30	91
4	30	93
5	30	92
6	30	87
7	30	88

[a] Reaction condition: benzaldehyde (5 mmol), ethyl acetoacetate (10 mmol), hydrazine hydrate (10 mmol), $[Et_3NH][HSO_4]$ (0.5 mmol) at 90 °C under solvent-free conditions.

[b] Isolated yield.

To reveal the mechanism of this reaction, we performed several control experiments. In the first series of experiments, ethyl acetoacetate treated with phenylhydrazine under solvent-free conditions at 90 °C for 40 min gave 3-methyl-1-phenyl-5-pyrazolone in 87% yield in the presence of 10 mol% of $[Et_3NH][HSO_4]$. The same reaction, carried out for 270 min in the absence of $[Et_3NH][HSO_4]$, only gave 3-methyl-1-phenyl-5-pyrazolone in 79% yield. Therefore $[Et_3NH][HSO_4]$ has catalytic role in this first step. In the second series of experiments, 2,4-dichlorobenzaldehyde and 3-methyl-1-phenyl-5-pyrazolone treated with 10 mol% of $[Et_3NH][HSO_4]$ under solvent-free conditions at 90 °C for 30 min provided 4,4′-[(2,4-dichlorophenyl)methylene] bis(3-methyl-1-phenyl-1H-pyrazol-5-ol) in 88% yield. The same reaction, carried out for 210 min in the absence of $[Et_3NH][HSO_4]$, only gave the product in 9% yield. Therefore $[Et_3NH][HSO_4]$ also has catalytic role in this second step. Finally, it was demonstrated that the three component condensation of 2,4-dichlorobenzaldehyde, ethyl acetoacetate, and phenylhydrazine could be performed with $[Et_3NH][HSO_4]$ affording the corresponding product in 86% yield in 35 min (Table 1, entry 8). However, the condensation reaction only gave 7% yield for 210 min in the absence of catalyst (Table 1, entry 10). With these results in hand, possible mechanism for the $[Et_3NH][HSO_4]$ catalyzed synthesis of 4,4′-(arylmethylene)bis(1H-pyrazol-5-ols) has been proposed in Scheme 2. The first step involves $[Et_3NH][HSO_4]$ catalyzed synthesis of 3-methyl-1-phenyl-5-pyrazolone by the condensation of phenylhydrazine with ethyl acetoacetate. Aldehyde is activated by the proton from $[Et_3NH][HSO_4]$. Next, the carbonyl carbon is attacked by the nucleophilic 3-methyl-1-phenyl-5-pyrazolone to form the Knoevenagel products. The subsequent addition of these fragments to 3-methyl-1-phenyl-5-pyrazolone, gives the 4,4′-(arylmethylene) bis(1H-pyrazol-5-ols) derivatives.



Scheme 2. Plausible mechanism for the synthesis of 4,4′-(arylmethylene) bis(1H-pyrazol-5-ols) catalyzed by $[Et_3NH][HSO_4]$

CONCLUSION

In summary, this paper describes a convenient and efficient process for the solvent-free synthesis of 4,4′-(arylmethylene)bis(1H-pyrazol-5-ols) through the three-component coupling of aldehydes, ethyl acetoacetate and phenylhydrazine/hydrazine hydrate using $[Et_3NH][HSO_4]$ as a recyclable catalyst. High yields of products, short reaction time, easily available and cheap catalyst, simple experimental and isolation procedures, eco-friendly reaction conditions make this methodology a valid contribution to the existing processes in the field of 4,4′-(arylmethylene)bis(1H-pyrazol-5-ols) derivatives synthesis.

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