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ORIGINAL PAPER

Base-free benzylation of 1,3-dicarbonyl compounds using sulfamic acid supported on silica by linker: a combined experimental and theoretical approach

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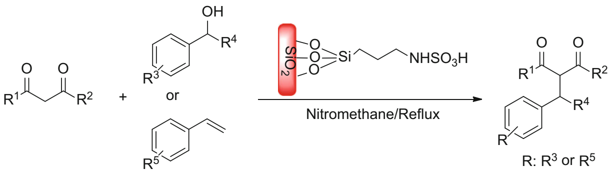
Abstract

Sulfamic acid stabilized on the surface of silica by the *n*-propyl organic group linker which is named silica-bonded *N*-propylsulfamic acid was applied as an efficient heterogeneous catalyst with good recyclability and reusability for direct benzylation of 1,3-dicarbonyl compounds using secondary aromatic alcohols or styrenes as alkylating agents in high yields and short reaction times. All the reactions were carried out in nitromethane as solvent under an air atmosphere. The catalyst showed reusable feature by six times without a significant loss in its activity.

Graphical abstract



Keywords Heterogeneous catalysis · Sulfamic acid · Alcohols · Styrenes · 1,3-Dicarbonyls

Introduction

The development of synthesis methods under the conditions in accordance with the framework of green chemistry is of great interest to chemists. One of the 12 principles of green chemistry is the use of catalytic reactants with higher selectivity. Therefore, using the biocompatible and green catalytic systems with the ability to recycle and reuse has been the focus of researchers. Heterogeneous catalysis has opened up a new window to chemists as a fundamental procedure from the standpoint of recovery, reusability, and product purification, especially in the production of fine chemicals.

Construction of carbon–carbon bond is among the important reactions in organic chemistry [1, 2]. One of the useful types of such reactions is the benzylation of 1,3-dicarbonyl compounds which leads to the generation of many bioactive structural motifs such as warfarin, reglitazar, and tipranavir [3, 4]. Traditionally, the alkylation of 1,3-dicarbonyl compounds is performed via the reaction of a 1,3-dicarbonyl with alkyl halides, phosphonates, carboxylates, or carbonates, mediated by a base. The common drawbacks associated with these methods, such as production of large amounts of by-products and their limited

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applications [5–10], has led to attempts to discover the alternative approaches.

As an eco-friendlier and atom-economical process, benzylation of 1,3-dicarbonyl compounds using secondary aromatic alcohols or styrenes as alkylating agents, without use of base, has been provided. In view of atom efficiency and avoiding waste, this route was superior to traditional methods, but the low reactivity of alcohols or styrenes towards the nucleophiles limited its use to the employment of a suitable catalyst. However, in the past several years, different types of catalysts including Lewis acidic metals such as $InCl_3$ [11], $Bi(OTf)_3$ [12], $Ln(OTf)_3$ (Ln = La, Yb, Sc, Hf) [13, 14], $FeCl_3$ [15–17], $Fe(ClO_4)_3$ [18], $InBr_3$ [19], homogeneous Brønsted acids such as *p*-toluenesulfonic acid [20], phosphotungstic acid (PWA) [21], $HClO_4$ [22], triflic acid [23], dodecylbenzenesulfonic acid [24], and heterogeneous Brønsted acids such as TfOH/SiO_2 [25], 12-tungstophosphoric acid supported on nano silica (NPW/SiO_2) [26], $NaHSO_4/SiO_2$ [27], H-montmorillonite [28], and $HClO_4/SiO_2$ [22], have been used for these transformations. Moreover, a ruthenium complex [29], trimethylsilyl trifluoromethanesulfonate (TMSOTf) [30], $B(C_6F_5)_3$ [31], and $BF_3.OEt_2$ [32], have also been previously examined for this transformation. Recently, Xu et al. has been reported an air-stable bis(isopropylcyclopentadienyl) zirconium perfluorooctanesulfonate for benzylation of 1,3-dicarbonyl derivatives with alcohols [33]. Undoubtedly, good progress has been made to date, but some common drawbacks, associated with these methods, such as air- or moisture-sensitive and failure in recovery of catalysts along with difficulty in preparation of them, long reaction time, expensive reagents, and strong acidic conditions are still highly demanded to develop much more convenient, prompt and recyclable system for the catalytic benzylation of 1,3-dicarbonyl compounds.

In this regard and in continuation of the research to develop new catalysts for organic transformations [34–43], we found that silica-bonded *N*-propylsulfamic acid (SBNPSA), which has been previously synthesized in our research lab, can effectively catalyst the benzylation of 1,3-dicarbonyl compounds with various secondary aromatic alcohols or styrenes as a reusable catalyst in short reaction times.

Results and discussion

SBNPSA was prepared according to our previously reported procedure [34]. Synthetic route and the structure of the catalyst are shown in Fig. 1.

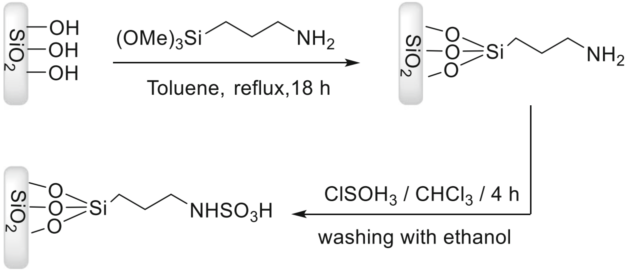
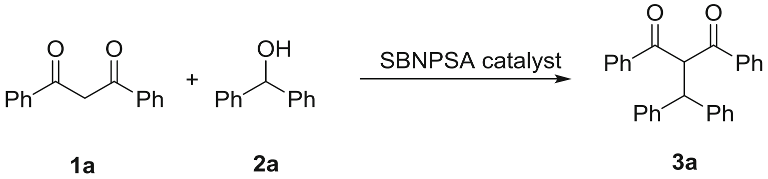


Fig. 1 Preparation of silica bonded *N*-propylsulfamic acid (SBNPSA)

Initially, the reaction between diphenylmethanol (1 mmol) and 1,3-diphenylpropane-1,3-dione (2 mmol) was carried out, as the model reaction, to establish the optimal reaction conditions. By employment of CH_2Cl_2 as the solvent and SBNPSA (60 mg, containing 0.02 mmol of H^+) as the catalyst under reflux conditions, the product **3a** was obtained in 70% yield (Table 1, entry1). The effect of some organic solvents such as EtOAc, CH_3CN, toluene, EtOH, and CH_3NO_2 was investigated and the best results were achieved with CH_3NO_2, affording the desired product in 95% yield within 15 min at reflux conditions (Table 1, entries 2–6). Reducing the reaction temperature to room temperature resulted in a sharp decline in efficiency (Table 1, entries 7–9). In the absence of the catalyst, the reaction did not proceed even after 2 h of reaction time (Table 1, entry 10). This showed that the catalyst is one prominent compound in this reaction. Further use of SBNPSA beyond the above-mentioned amount (0.07) did not show any further increase in the yield, whereas the lower use (0.05) resulted in poor yield (Table 1, entries 11 and 12). Therefore, 60 mg of SBNPSA was chosen as the most efficient amount in the rest of study. Under the standard reaction conditions, when diphenylmethanol was replaced by styrene, the same reaction was performed and the product **3b** was formed in 88% yield.

To demonstrate the generality of this method, we investigated the benzylation of 1,3-diketones with various secondary aromatic alcohols or styrenes in the presence of SBNPSA and the results are summarized in Table 2. According to the obtained data, the reaction of dibenzoylmethane, acetylacetone, benzoylacetone, ethyl acetoacetate, and isopropyl acetoacetate with benzhydrylic alcohols or styrene derivatives were converted into the corresponding products in good–excellent yields (85–97%; Table 2, entries 1–20). Various aromatic alcohols or styrenes having methyl, methoxy, chloro, and fluoro substitution group underwent smooth hydroalkylation with 1,3-diketones to afford the corresponding products in optimum conditions. Generally speaking, the electron-withdrawing groups on the phenyl ring of benzhydrylic alcohols or styrenes slightly benefited the yields (Table 2, entries 4, 5, 10, 11). Reaction of benzoylacetone and ethyl acetoacetate with unsymmetric benzhydrylic alcohols or styrenes gave two inseparable diastereomers (Products **3n**,

Table 1 Investigated conditions for the benzylation of diphenylmethanol with 1,3-diphenylpropane-1,3-dione using of SBNPSA as the catalyst



Entry	Catalyst/g	Solvent	Temp./°C	Time/min	Yield[a]/%
1	0.06	CH_2Cl_2	Reflux	25	70
2	0.06	EtOAc	Reflux	30	60
3	0.06	CH_3CN	Reflux	30	60
4	0.06	Toluene	Reflux	30	60
5	0.06	Ethanol	Reflux	60	25
6	0.06	CH_3NO_2	Reflux	15	95
7	0.06	CH_3NO_2	85	30	75
8	0.06	CH_3NO_2	60	40	40
9	0.06	CH_3NO_2	r.t.	120	20
10	–	CH_3NO_2	Reflux	120	–
11	0.07	CH_3NO_2	Reflux	15	95
12	0.05	CH_3NO_2	Reflux	15	80

Reaction conditions: **1a** (2.0 mmol), **2a** (1.0 mmol), 2.0 cm^3 solvent

[a] Isolated yields

3p, **3q**, and **3s**). In addition, the reaction of isopropyl acetoacetate with benzhydrol led to the corresponding product **3t** with excellent efficiency (Table 2, entry 20).

The efficacy of the presented method in the preparation of aryl-1,3-dione derivatives in comparison with some previously reported catalysts is illustrated in Table 3. The results showed that our method is superior in some circumstances such as catalyst amount, reaction time, or product yields.

Based on the results and according to the reported findings, the proposed mechanism for direct C–C bond coupling reaction of secondary benzylic alcohols with 1,3-dicarbonyl compounds in the presence of SBNSA is shown in Fig. 2. The mechanism of these reactions, catalyzed by Brønsted acids, was generally thought to involve the formation of a carbocation intermediate and subsequent S_N1 attack on the β-dicarbonyl compound to yield the addition product. Therefore, in this work, SBNPSA protonates the alcohol and carbocation intermediate **1** would rapidly be generated by loss of water. Then, the nucleophilic α-carbon of the β-diketone attacks the carbocation to form the product. Note that the β-diketone might be preferentially in an enol tautomeric at high temperature (100 °C). A mechanism very similar to the addition of β-diketones to alcohols is proposed as operative for SBNPSA catalyzed addition of β-diketones to styrenes (Fig. 3). Again, the crucial species is the carbocation intermediate 1, it attacks the β-diketone (or in enol form) to yield the addition product.

The reusability of SBNPSA was investigated in the model reaction. For each of the repeated reactions, the catalyst was recovered easily by simple filtration, washed exhaustively with warm ethanol and dried. The results showed that a significant loss in its activity was noticeable after reusing the catalyst six times (Fig. 4).

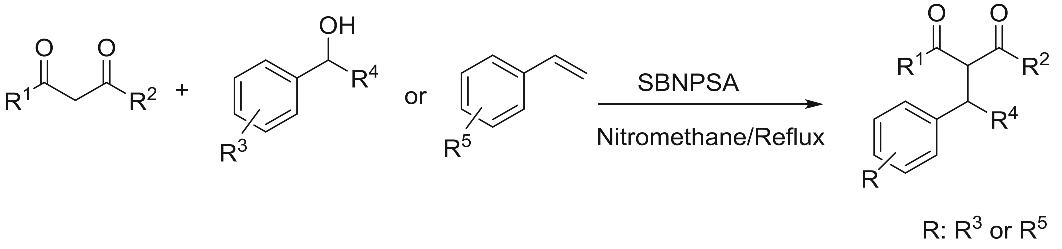
Conclusion

In summary, we have shown that silica-bonded *N*-propylsulfamic acid is an efficient solid acid catalyst for the direct coupling of secondary benzylic alcohols or styrene derivatives with 1,3- dicarbonyl compounds, resulting in the corresponding product in high yields and short reaction times. This method represents a simple, clean, and reusable alternative to the already established use of homogeneous acid catalyst.

Experimental

All chemicals were purchased from Merck or Fluka Chemical Companies. The ^1H and ^{13}C NMR was run on Bruker Avance (DRX 500 MHz and 400 MHz)

Table 2 Benzylation of 1,3-dicarbonyl compounds with benzyl alcohol or styrene derivatives in nitromethane under reflux conditions



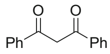
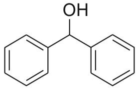
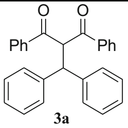
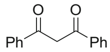
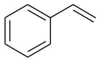
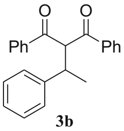
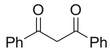
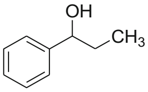
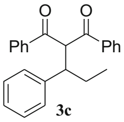
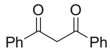
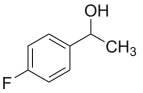
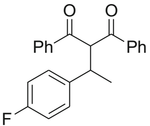
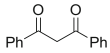
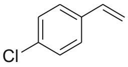
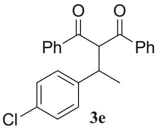
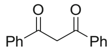
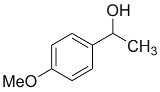
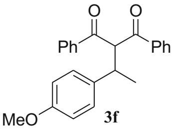
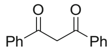
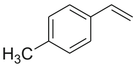
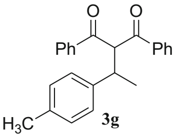
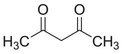
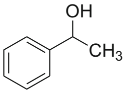
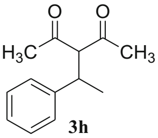
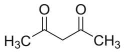
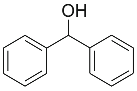
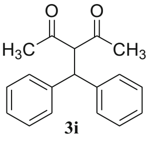
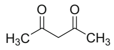
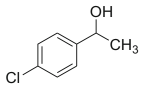
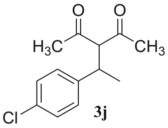
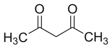
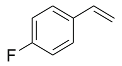
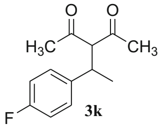
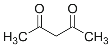
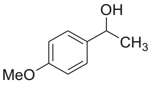
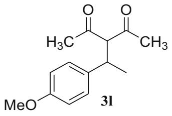
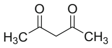
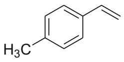
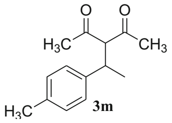
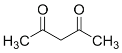
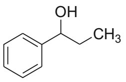
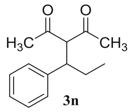
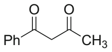
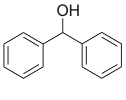
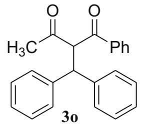
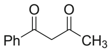
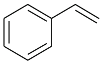
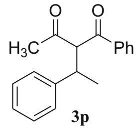
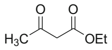
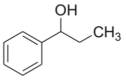
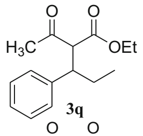
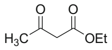
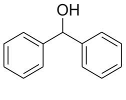
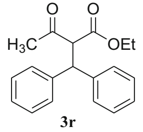
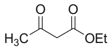
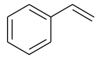
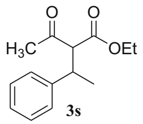
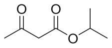
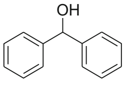
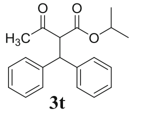
Entry	1,3-Dicarbonyl	Alcohol or styrene	Product	Time/min	Yield/%[a]	M.p. /°C
1			 3a	25	95	228–230 (227–229 [25])
2			 3b	25	88	124–126 (129–131 [29])
3			 3c	15	85	155–157 (154–156 [44])
4			 3d	15	97	111–113 (110–112 [29])
5			 3e	15	95	102–104 (107–109 [29])
6			 3f	20	85	105–107 [14]
7			 3g	20	85	105–108 (103–105 [25])
8			 3h	15	88	45–47 (43–45 [23])
9			 3i	15	92	115–118 (117–118 [22])

Table 2 continued

Entry	1,3-Dicarbonyl	Alcohol or styrene	Product	Time/min	Yield/%[a]	M.p. /°C
10			 3j	15	95	77–79 (77–79 [25])
11			 3k	15	95	58–60 (57–58 [29])
12			 3l	20	85	54–56 (53–55 [25])
13			 3m	20	88	58–60 (57–59 [25])
14			 3n	20	87	94–96 [38]
15			 3o	20	95	152–154 (150–152 [25])
16			 3p	25	85	82–84 (97–99 [25])
17			 3q	15	87	42–44 [38]
18			 3r	15	92	85–87 [44]
19			 3s	25	88	Oil [23]
20			 3t	25	85	89–91

Conditions: SBNPSA (60 mg, containing 0.02 mmol of $^{+}$H), β-dicarbonyl compound (2.0 mmol), alcohol or styrene (1.0 mmol), 2 cm^3 nitromethane in reflux conditions

[a] Isolated yield

Table 3 Comparison between efficiency of SBNPSA with some previously reported catalysts in the synthesis of product **3a**

Entry	Catalyst/mol%	Conditions	Time/h	Yield/%	References
1	PTSA (*p*-toluenesulfonic acid) (5)	CH_3NO_2 (100 °C)	0.5	83	[23]
2	$HClO_4$ (1)	Toluene (70 °C)	17	77	[22]
3	$HClO_4$–SiO_2 (1)	Solvent-free (70 °C)	17	99	[22]
4	TfOH–SiO_2 (3)	CH_3NO_2 (70 °C)	5	97	[25]
5	H_2SO_4 (5)	CH_3NO_2 (101 °C)	0.08	82	[45]
6	SBNPSA (2)	CH_3NO_2 (100 °C)	0.25	95	This work

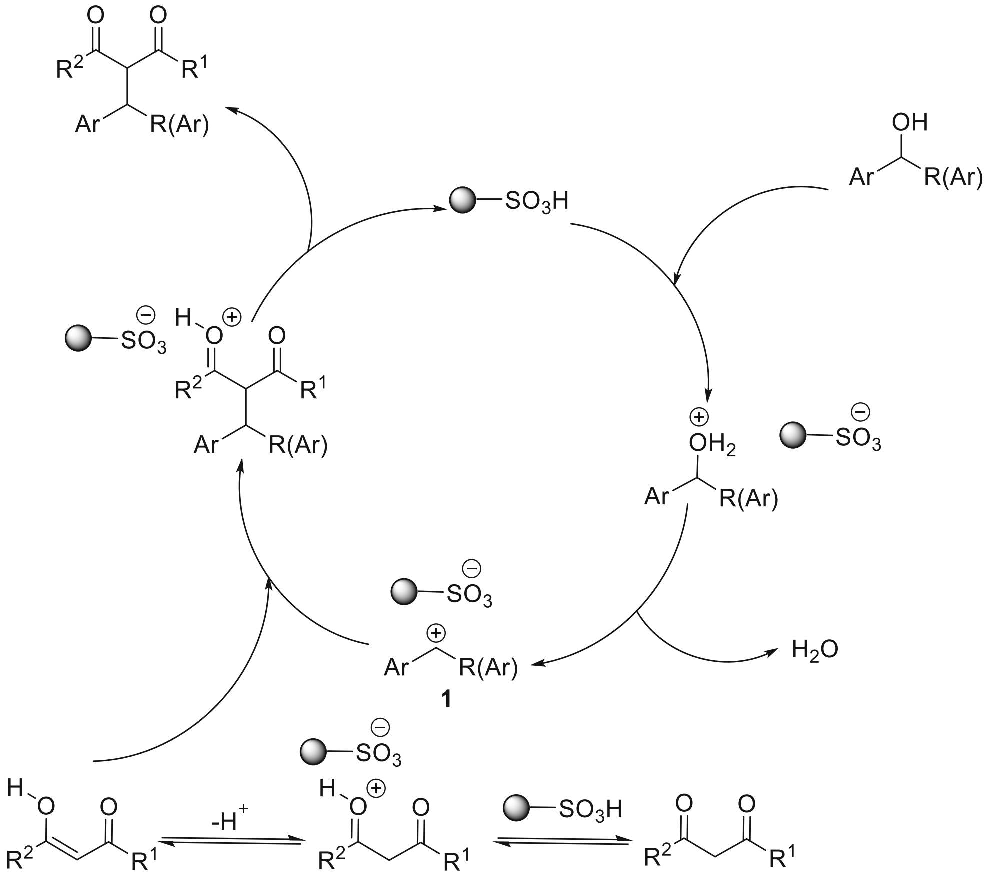


Fig. 2 Proposed mechanism of the SBNPSA-catalyzed addition of *β*-diketones to alcohols

instruments in $CDCl_3$. Results are reported in ppm, using TMS as an internal standard. IR spectra were obtained using a Shimadzu FT-IR 8300 spectrophotometer. Melting points were determined on a SMP1 Melting Point apparatus in open capillary tubes. Reaction progress was followed by TLC using silica gel SILG/UV 254 plates. Silica bonded *N*-propylsulfamic acid (SBNPSA) was prepared according to our previously reported procedure [34].

Geometric optimization of 1-phenyl-2-(1-phenylethyl)butane-1,3-dione (**3p**) performed with Minnesota functional at M06-2X/6-311 ++G(2d, p) level of theory [46–54]. Selection of basis set was done based on considering both polarization function and diffuse function to give more accurate results. There were no symmetric limitations for optimized compound (**3p**), and C1 symmetry selected for this compound. Finding global or local minima and then vibrational assignments were performed using frequency calculations at the same level of theory [46–54]. The GIAO method is one of the most usual methods for computing nuclear magnetic shielding tensors. The ^{13}C and ^{1}H NMR isotropic shielding values were obtained by GIAO approach using the optimized structure achieved by M06-2X/6-311 ++G(2d, p) method. The natural bond orbital technique applied for optimized

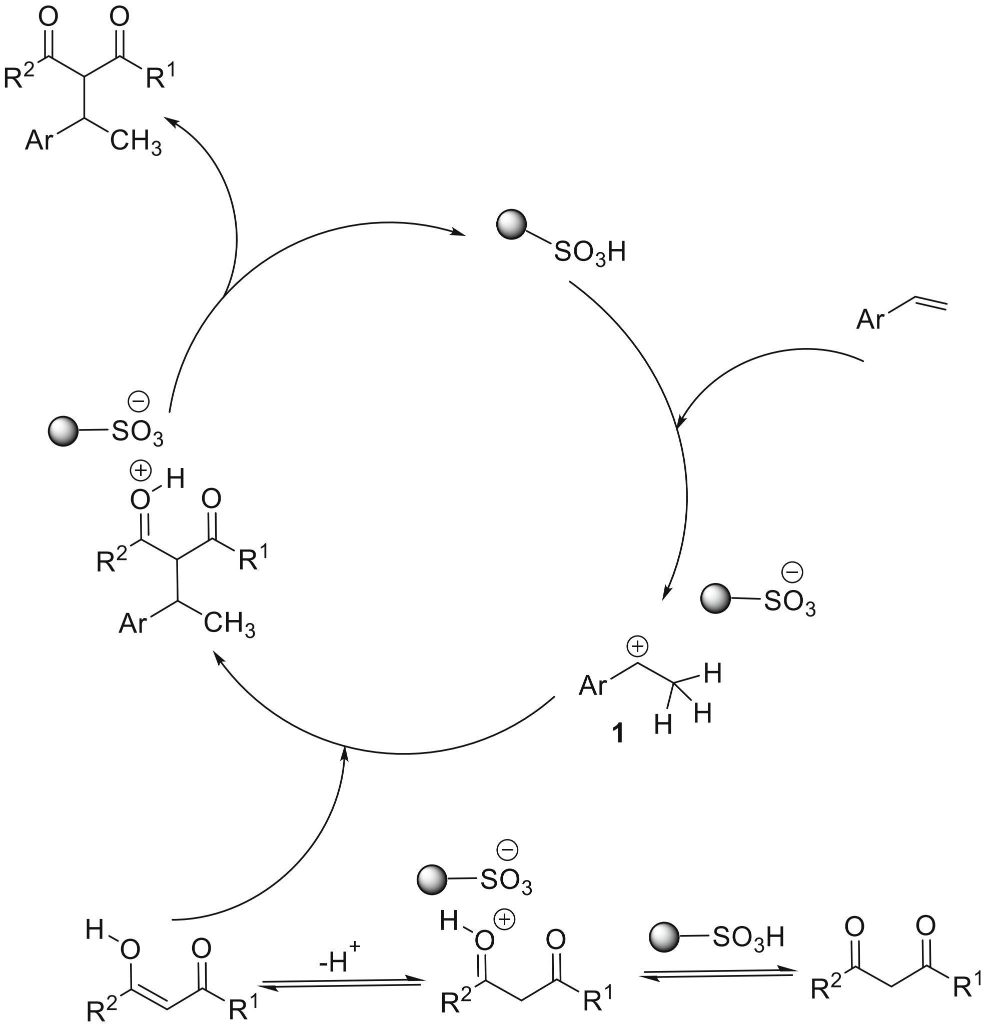


Fig. 3 Proposed mechanism of the SBNPSA-catalyzed addition of *β*-diketones to styrenes

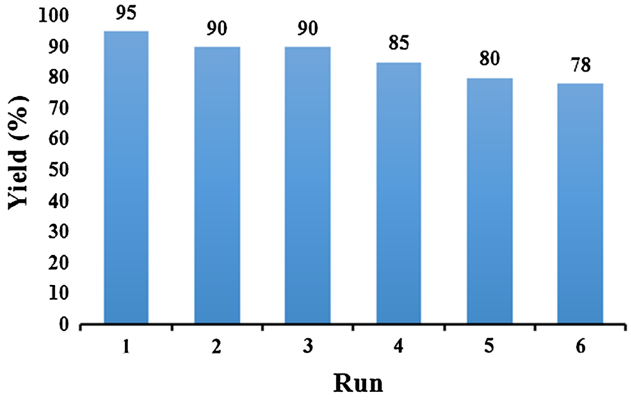


Fig. 4 Recyclability of SBNPSA in benzylation of 1,3-diphenylpropane-1,3-dione (2 mmol) with diphenylmethanol (1 mmol) in nitromethane under reflux conditions. Reaction time: 15 min

structures to find donor–acceptor interactions [55, 56]. Molecule building, viewing capabilities, setting up Gaussian jobs, and finally visualizing Gaussian results were done using Gauss View 5.0 [57]. Computations were performed by means of GAUSSIAN 09 package program [58] (see Supporting Information).

General procedure for direct benzylation of 1,3-dicarbonyl compounds using alcohols or styrenes as alkylating agents

To a mixture of 1,3-dicarbonyl compound (2 mmol), alcohol or styrene derivatives (1 mmol), and 0.6 g SBNPSA, was added 2 cm^3 nitromethane as solvent. The mixture was stirred under reflux conditions and the reaction was followed by TLC. After completion, the mixture was filtered, and the remaining was washed with warm ethanol to separate catalyst and nitromethane was removed under reduced pressure. Then, the crude products were recrystallized from mixture of dichloromethane and *n*-hexane. All the synthesized products were known and characterized by comparison of their spectral and physical data with those reported in literature.

Isopropyl 2-(diphenylmethyl)-3-oxobutanoate (3t, $C_{20}H_{22}O_3$) Yield 85%; white solid; m.p.: 89–91 °C; IR: = 708, 1102, 1175, 1418, 1571, 1654, 1700, 1715, 2984 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.25–7.06$ (m, 12H, Ar), 4.79–4.73 (m, 1H, $-CH(CH_3)_2$), 4.68 (d, 1H, $J = 12$ Hz, CH), 4.43 (d, 1H, $J = 12$ Hz, CO*CH*CO), 2.01 (s, 3H, CH_3CO), 0.94 (d, 3H, $J = 6.3$ Hz, $-CH_3$), 0.90 (d, 3H, $J = 6.3$ Hz, $-CH_3$) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 201.5$, 167.2, 141.6, 141.4, 128.8, 128.6, 127.8, 127.7, 126.9, 126.7, 68.8, 65.3, 50.7, 29.6, 20.8 ppm; MS (EI, 70 eV): m/z (%) = 310 (M^+, 1), 167 (100).

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