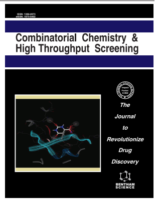
Combinatorial Chemistry & High Throughput Screening, 2018, 21, 19-25

RESEARCH ARTICLE



Citrus Juice: Green and Natural Catalyst for the Solvent-free Silica Supported Synthesis of *β*-Enaminones using Grindstone Technique

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Abstract: ***Aim and Objective***: Citrus Juice as an efficient, cost-effective and green catalyst employed for one-pot synthesis of various β-substituted enaminones through the reaction of β-dicarbonyl compounds with different primary amines in a solvent-free conditions on silica gel as solid surface using grindstone technique in high yields and short reaction times. The presented procedure is operationally simple, practical and green.

Material and Methods: The wide application of this procedure is demonstrated by the use of various substituted amines to react with β-dicarbonyl compounds. The method was successfully applied for primary amines (15 entries) and the related enaminones were well synthesized in good to excellent yields. Melting points were measured on an Electro thermal 9100 apparatus. 1HNMR and 13C NMR spectra were recorded on a FTNMR BRUKER DRX 500 Avence spectrometer. Chemical shifts were given in ppm from TMS as internal references and CDCl3 was used as the solvent as well. The IR spectra were recorded on a Perkin Elmer FT-IR GX instrument. The chemicals used in this work were purchased from Merck and Fluka chemical companies.

Results: Grinding synthesis of citrus juice catalyzed enamination of 1,3-dicarbonyls (acetylacetone, methyl and ethyl- 3-oxobutanoate) with various primary amines (aromatic and aliphatic) under solvent-free silica supported conditions was examined and studied (15 entries) and the obtained enaminones were well synthesized in good to excellent yields. Furthermore, the effect of various catalysts on the yield and reaction time for grinding synthesis of 3-phenylamino- but- 2- enoic acid ethyl ester (1) by this method has evaluated as well.

Conclusion: a novel, efficient and green protocol for the grinding synthesis of enaminones using citrus juice as natural catalyst has been presented. This methodology is user friendly, green and low cost procedure under mild reaction condition with faster reaction rates. The citrus juice is inexpensive and non-toxic which makes the process convenient, more economic and benign. Furthermore, applying grindstone technique in solvent-free conditions, use of silica gel as a solid and heterogeneous surface in reaction, high yields of products, cleaner reaction profiles, and availability of the reagents makes this method a better choice for synthetic chemists.

ARTICLE HISTORY

Received: November 17, 2016
Revised: May 2, 2017
Accepted: November 29, 2017

DOI:
10.2174/1386207321666180102115733

Keywords: Citrus juice, silica, *β*-enaminone, solvent-free, grinding, green catalyst.

1. INTRODUCTION

The enaminones are a very important class of organic compounds with stable structural motifs due to their occurrence in versatile building blocks for the synthesis of important heterocyclic compounds, nitrogen containing compounds, natural products, pharmaceutical drugs with antiepileptic, anticonvulsant and antitumor properties [1-3].

The synthesis of enaminones and enamino esters has been reported through the condensation reactions of carbonyl compounds with primary and secondary amines with various acid catalysts like $Yb(OTf)_3$ [4], $Zn(O_4Cl)_2$ [5, 6], $InBr_3$ [7], $CoCl_2$ [8], $LiHSO_4{\cdot}SiO_2$ [9a]. Recently, the hydrolysate of bovine tendons for the multigram scale synthesis of coumarins and chromenes, as well as in the three-component reaction for chromene synthesis has been reported [9b]. Furthermore, non-conventional methods such as microwave and ultrasound are reported as well [10-12]. However, most of these techniques involved harsh reaction conditions, expensive and harmful reagents, organic solvents, use of moisture sensitive metal triflates and tedious workup [4, 5a]. Therefore, the development of rapid and eco-friendly approaches has crucial importance in the synthesis of these compounds.

On the other hand, the application of catalysts prepared from renewable sources like biodiesel has afforded importance in organic synthesis. Biodiesel has become beguiling nowadays for its environmental benefits and it seems an opposite alternative fuels for future. It is made from renewable biological sources such as vegetable oils and animal fats. It is biodegradable and nontoxic and has low emission profiles and environmentally beneficial as well

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[5b]. Also, it is widely acknowledged that there is a growing need for more environmentally acceptable processes in the chemical industry. This trend towards what has become known as ‘Green Chemistry’ or ‘Sustainable Technology’ necessitates a paradigm shift from traditional concepts of process efficiency, that focus largely on chemical yield, to one that assigns economic value to eliminating waste at source and avoiding the use of toxic and/or hazardous substances [5c].

Due to acidic nature, citrus juice as a natural catalyst has been found to be a suitable replacement for different homogeneous acid catalysts that is well compatible with a so-called green process as well [13].

2. MATERIALS AND METHODS

Melting points were measured on an Electro thermal 9100 apparatus. ^{1}HNMR and ^{13}C NMR spectra were recorded on a FTNMR BRUKER DRX 500 Avence spectrometer. Chemical shifts were given in ppm from TMS as internal references and $CDCl_3$ was used as the solvent as well. The IR spectra were recorded on a Perkin Elmer FT-IR GX instrument. The chemicals used in this work were purchased from Merck and Fluka chemical companies.

2.1. Nutritional Properties of Citrus Juice

Mineral content, moisture content and ash [14d,15], vitamin A [16], vitamin C [17] and pH value [18] were determined by the methods described in the relevant references.

2.2. Preparation of Citrus Juice from the Fruits of Citrus

The citrus juice prepared from fresh fruits was extracted mechanically and centrifuged using Centrifuge (JENUS TDL-4) and the clear portion of the juices was applied as a catalyst in the reactions.

2.3. Typical Procedure

In a typical experiment (entry **11**), 5 drops (0.25 mL) citrus juice and 1 g silica gel (200- 400 mesh) was ground together in a mortar using pestle for 2 min. To this mixture, acetylacetone (3 mmol) and aniline (4 mmol) were then added and grinding was continued at room temperature for the time presented in Table **1** to complete the reaction (monitored by TLC, n-hexane/ chloroform, 3/1). After completing the reaction, the product was extracted with CH_2Cl_2 (2×15 mL) and silica gel filtered off. The organic layer after washing with water was dried over $MgSO_4$, filtered and the solvent was evaporated under vacuum to afford the product **11**. Solid products recrystallized from di-isopropyl ether and oil products were purified column chromatography using hexane and ethyl acetate (3:1) as an eluent. All isolated products were characterized by melting points (solids), IR, ^{1}HNMR and ^{13}CNMR spectrometric data and were compared with the literature [19].

3-Phenylamino- but- 2- enoic acid ethyl ester (1): Oil (Oil) [19b], IR (neat, cm^{-1}): 3435, 3016, 2951,1642, 1513, 1291, 1128, 1089, 979, 758; ^{1}H NMR (500 MHz, $CDCl_3$): δ= 1.21 (t, *J*= 7.3 Hz, 3H), 1.96 (s, 3H), 4.19 (q, *J*= 7.3 Hz, 2H), 4.66 (s, 1H), 6.69-7.31 (m, 5H arom.), 11.41 (s, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$): δ= 16.1 (CH_2CH_3), 19.8 (CH_3), 59.1 (CH_2), 92.8 (=CH), 122.6 (CH), 125.0 (CH), 127.2 (CH) , 135.7 (qC), 157.5 (N-C=), 185.6 (O=C).

3-Benzylamino- but- 2- enoic acid ethyl ester (2): Oil (Oil) [19b], IR (neat, cm^{-1}): 3286, 3077, 2963, 1661, 1612, 1517, 1221, 1179, 1148, 1075, 931, 751; ^{1}H NMR (500 MHz, $CDCl_3$): δ= 1.18 (t, *J*= 7.3 Hz, 3H), 1.91 (s, 3H), 4.18 (q, *J*= 7.3 Hz, 2H), 4.30 (d, *J*= 6.4 Hz, 2H), 4.52 (s, 1H), 7.07-7.32 (m, 5H arom.),11.18 (s, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$): δ= 14.8 (CH_2CH_3), 18.1 (CH_3), 45.9 ($PhCH_2$), 57.1 (CH_2), 82.0 (=CH), 127.2 (CH), 125.9 (CH), 128.5 (CH), 138.4 (qC), 161.1 (N-C=), 171.8 (O=C).

3-(1-Phenylethanamino)-but- 2- enoic acid ethyl ester (3): Oil (Oil) [19a], IR (neat, cm^{-1}): 3229, 3014, 2991, 1680, 1619, 1539, 1225, 1181, 1163, 1058, 989, 742; ^{1}H NMR (500 MHz, $CDCl_3$): δ= 1.23 (s, 3H), 1.36 (t, *J*= 7.3 Hz, 3H), 2.12 (d, *J*= 4.7 Hz, 3H), 4.05 (m, 1H), 4.22 (q, *J*= 7.3 Hz, 2H), 4.62 (s, 1H), 7.15-7.46 (m, 5H arom.), 11.10 (s, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$): δ= 14.1 (CH_2CH_3), 18.5 (CH_3), 22.5 (CH_3CH), 56.5 (CH_2CH_3), 61.1 ($CHCH_3$), 82.3 (=CH), 116.1 (CH), 125.5 (CH), 128.4(CH), 129.0 (qC) , 162.8 (N-C=), 171.1 (O=C).

3-Allylamino- but- 2- enoic acid ethyl ester (4): Oil (Oil) [19c], IR (neat, cm^{-1}): 3294, 3069, 2971, 1663, 1619, 1511, 1275, 1161, 1055, 958, 753; ^{1}H NMR (500 MHz, $CDCl_3$): δ= 1.21 (t, *J*= 7.3 Hz, 3H), 3.68 (s, 3H), 3.84-3.89 (m, 2H), 4.18 (q, *J*= 7.3 Hz, 2H), 4.89 (s, 1H), 5.15-5.29 (m, 2H), 5.83-5.95 (m, 1H), 8.64 (s, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$): δ= 14.0 (CH_2CH_3), 24.7 (CH_3), 49.4 (CH_2C=), 61.8 (CH_2CH_3), 81.8 (=CH), 117.2 (=CH_2), 135.6 (=CH-CH_2), 161.1 (N-C=), 171.6 (O=C).

3-Methylamino- but- 2- enoic acid ethyl ester (5): Oil (Oil) [19c], IR (neat, cm^{-1}): 3286, 3044, 2981, 1648, 1612, 1531, 1275, 1151, 1141, 1096, 948, 799; ^{1}H NMR (500 MHz, $CDCl_3$): δ= 1.22 (t, *J*= 7.3 Hz, 3H), 1.93 (s, 3H), 2.85 (d, *J*= 7.4 Hz, 3H), 4.12 (q, *J*= 7.3 Hz, 2H), 4.59 (s, 1H), 11.85 (s, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$): δ=14.0 (CH_2CH_3), 18.5 (CH_3), 46.1 (NCH_3), 57.5 (CH_2CH_3), 81.2 (=CH), 161.8 (N-C=), 172.0 (O=C).

3-(Pyrimidin-2-ylamino)but- 2- enoic acid methyl ester (6): m.p. 163-165°C (161-163°C) [19c], IR (KBr, cm^{-1}): 3329, 3168, 2774, 2681, 1649, 1559, 1578, 1478, 1357, 1223, 803; ^{1}H NMR (500 MHz, $CDCl_3$): δ= 1.80 (s, 3H), 3.78 (s, 3H), 4.65 (s, 1H), 5.51(br. s, NH), 6.58-6.60 (2H arom., t, *J*= 8.7 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ= 20.39 (CH_3), 52.59 (OCH_3), 84.2 (=CH), 111.4 (CH), 157.0 (CH), 158.2 (CH), 139.8 (qC), 185.1 (N-C=), 185.4 (O=C).

3-(2-Methyl-phenylamino)- but- 2- enoic acid methyl ester (7): m.p. 27-30°C (26-27°C) [19c]; IR (KBr, cm^{-1}): 3435, 2691, 1641, 1599, 1439, 1275, 1139, 875, 798; ^{1}H NMR (500 MHz, $CDCl_3$): δ= 1.32 (s, 3H), 1.85 (s, 3H), 3.49 (s, 3H), 4.69 (s, 1H), 6.77-7.16 (m, 4H arom.), 10.49 (s, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$): δ= 14.9 (CH_2CH_3), 18.9 (CH_3), 51.2 ($PhCH_3$), 84.1 (=CH), 123.1 (CH), 126.1 (CH), 127.0 (CH), 131.1 (CH), 135.8 (qC), 136.2 (CH_3-C arom.), 160.6 (N-C=), 170.2 (O=C).

3-(4-Bromo-phenylamino)- but- 2- enoic acid methyl ester (8): m.p. 120-122°C (121-123°C) [19c]; IR (KBr, cm^{-}

^{1}): 3449, 3336, 3106, 1628, 1584, 1496, 1334, 1257, 1124, 1063, 744; ^{1}H NMR (500 MHz, $CDCl_3$): δ= 1.99 (t, *J*= 7.2 Hz, 3H), 3.63 (s, 3H), 4.73 (s, 1H, CH), 6.96 (d, *J*= 8.7 Hz, 2H), 7.43 (d, *J*= 8.7 Hz, 2H), 10.34 (s, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$): δ= 19.7 (CH_3), 51.5 (OCH_3), 84.8 (=CH), 116.5 (C-Br), 133.4 (CH), 137.7 (CH), 137.7 (qC), 160.4 (N-C=), 170.7 (O=C).

4-(2,4-Dinitrophenylamino)-3-penten-2-one (9): m.p. 173-175°C (170-172°C) [19a]; IR (KBr, cm^{-1}): 3183, 3012, 2954, 1654, 1623, 1567, 1484, 1263, 1165, 1003, 830; ^{1}H NMR (500 MHz, $CDCl_3$): δ= 2.07 (s, 3H, CH_3), 2.40 (s, 3H, CH_3), 5.62 (s, 1H, vinyl), 8.28-9.04 (m, 3H arom.), 13.26 (s, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$): δ= 23.9 (CH_3), 29.2 ($COCH_3$), 97.8 (=CH), 126.4 (CH), 126.9 (CH), 128.5 (CH), 130.9 (CH), 131.3 (CH), 147.6 (qC), 162.3 (N-C=), 197.2 (O=C).

4-Methylamino-3-penten-2-one (10): m.p. 35-38°C (31-33°C) [19a]; IR (KBr, cm^{-1}): 3264, 3088, 2980, 1655, 1635, 1566, 1281, 1155, 1067, 974, 789; ^{1}H NMR (500 MHz, $CDCl_3$): δ= 1.92 (s, 3H), 1.97 (s, 3H), 2.85 (d, *J*= 5.6 Hz, 3H), 11.84 (s, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$): δ= 18.8 (CH_3), 28. (NCH_3), 29.1 ($OCCH_3$), 94.9 (=CH), 163.1 (N-C=), 192.4 (O=C).

4-Phenylamino-3-penten-2-one (11): m.p. 46-48°C (49-50°C) [19b]; IR (KBr, cm^{-1}): 3437, 3371, 3009, 2996, 1651, 1529, 1350, 1321, 1168, 736; ^{1}H NMR (500 MHz, $CDCl_3$): δ= 1.80 (s, 3H), 2.30 (s, 3H), 3.65 (s, 1H), 6.29-7.05 (m, 5H arom.), 9.89 (s, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$): δ= 19.1 (CH_3), 28.9 ($OCCH_3$), 96.4 (=CH), 124.1 (CH), 125.7 (CH), 128.3 (CH), 139.1 (qC), 159.3 (N-C=), 195.7 (O=C).

4-(4-Nitro-phenylamino)-3-penten-2-one (12): m.p. 136-138°C (137-139°C) [19d]; IR (KBr, cm^{-1}): 3489, 3369, 3005, 2995, 1666, 1615, 1350, 1280, 1193, 1114, 840, 786; ^{1}H NMR (500 MHz, $CDCl_3$): δ= 2.15 (s, 3H), 2.20 (s, 3H), 4.48 (s, 1H), 7.20 (d, 2H arom., *J*= 8.6 Hz), 8.20 (d, 2H arom., *J*= 8.7 Hz), 12.78 (s, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$): δ= 20.5 (CH_3), 29.6 ($COCH_3$) , 101.2 (=CH), 120.3 (CH), 121.8 (CH), 125.1 (CH), 128.3 (CH), 143.5 (qC), 145.3 (O-C arom.), 157.0 (N-C=), 197.9 (O=C).

4-(3,4-Dimethyl-phenylamino)-3-penten-2-one (13): m.p. 97-99°C (95-9°C) [19d]; IR (KBr, cm^{-1}): 3485, 3365, 3125, 2990, 1649, 1643, 1496, 1348, 1321, 1128, 856, 767; ^{1}H NMR (500 MHz, $CDCl_3$): δ= 1.69 (s, 3H), 2.05 (s, 3H), 2.37 (s, 3H), 2.39 (s, 3H), 3.49 (s, 1H), 6.40-7.53 (m, 3H arom.), 9.85 (s, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$): δ= 17.6 ($PhCH_3$), 18.2 ($PhCH_3$), 19.3 (CH_3), 28.5 ($COCH_3$), 98.7 (=CH), 123.5 (CH), 126.9 (CH), 128.1 (CH), 131.0 (CH_3-C arom.), 131.8 (CH_3-C arom.), 136.7 (qC), 158.8 (N-C=), 197.5 (O=C).

4-(4-Chloro-phenylamino)-3-penten-2-one (14): m.p. 59-61°C (61-64) [19d]; IR (KBr, cm^{-1}): 3479, 3386, 3201, 3011, 2994, 1620, 1495, 1288, 1182, 1089, 831; ^{1}H NMR (500 MHz, $CDCl_3$): δ= 1.94 (s, 3H), 2.33 (s, 3H), 3.88 (s, 1H), 6.62 (d, 2H arom., *J*= 8.7), 7.12 (d, 2H arom., *J*= 8.8), 10.03 (s, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$): δ= 18.5 (CH_3), 23.8 ($COCH_3$), 96.3 (=CH), 123.0 (CH), 124.1 (CH), 125.9 (CH), 135.1 (CH), 135.9 (C-Cl), 141.8 (qC), 158.3 (N-C=), 196.6 (O=C).

4- Benzylamino-3-penten-2-one (15): Oil (Oil) [19a], IR (neat,cm^{-1}): 3281, 3046, 2980, 1643, 1608, 1535, 1256, 1141, 1125, 1068, 969, 790; ^{1}H NMR (500 MHz, $CDCl_3$): δ= 1.83 (s, 3H), 2.05 (s, 3H), 4.36 (d, 2H), 4.97 (s, 1H), 6.83-7.25 (m, 5H, arom.), 11.17 (s, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$): δ= 18.5 (CH_3), 22.8 (COCH3), 57.7 (CH_2), 80.6 (=CH), 123.7 (CH), 125.1 (CH), 127.5 (CH), 136.4 (qC), 162.2 (N-C=), 191.8 (O=C).

3. RESULTS AND DISCUSSIONS

In continuation of our efforts on this methodology, here we report grinding synthesis of *β*-amino-*α*,*β*-unsaturated esters and ketones applying citrus juice as an efficient acidic catalyst on silica gel as support in a simplified, rapid way and generally without the use of any solvent in excellent yields [14a-c]. Proximate nutritional composition of citrus juice has been evaluated and is shown in Table **1**. The citrus juice acts as the effective acid catalyst by activating the carbonyl group of the *β*-dicarbonyl compound in this reaction (Scheme **1**).

The nutritional composition of applied citrus juices is presented in Table **1**. The moisture content of lime (90.8%) is higher than that of other juices (88.3-90.2%). The orange juice has higher ash, pH, phosphorus, potassium and vitamin C contents, with values of 0.4%, 3.8, 17 mg/100 g, 200 mg/100 g and 50 mg/100 g respectively. However, in applying lime juice with the lowest pH (2.3), the products were obtained in the highest yields.

The juice of lime contains citric acid (5% - 8%) and ascorbic acid (the main components of the juice) and acts as the effective acid catalyst by activating the carbonyl group of the dicarbonyl compound in this reaction. The juice is highly soluble in water and thus acts as a homogeneous catalyst in aqueous systems as well. However, dicarbonyl compounds are less soluble in water only and thus using the pure citrus juice also acts as a green solvent better than the water. Citric acid (2-hydroxy-1,2,3-propanetricarboxylic acid) is a weak tricarboxylic acid that is naturally concentrated in citrus fruits. Among fruits, citric acid is most concentrated in lemon and lime, comprising as much as 8% of the dry fruit weight. Lime has a slightly higher acid content (on average) than lemon do about 6% for lime, compared to 4.5% for lemon. The composition of acids in the two also differs. The acid in lemon juice is almost entirely citric acid, which also makes up most of the acid in lime. However, lime includes about 10% each of succinic acid and malic acid which has an effect on their flavor [14d]. Here, we only emphasize minor differences and advantages that are due to the use of various citrus juices with different acidic identities (pH values). The reaction is carried out in a solvent-free and open reaction system, and the key step is the NH_2 attack on the carbonyl group in dicarbonyl compound. This increases with the increase in acidic identity of citrus juice (lime, pH= 2.3) on the surface of silica along increase in polarity of C=O.

Due to acidic nature, aqueous citrus juice as a natural and green catalyst has been found to be a suitable replacement for various homogeneous acid solutions. In this regard, we examined various concentrations of HCl (pH= 1.5, 2, 2.5, 3, 3.5 and 4) on silica for the reaction entry **1** under the same conditions and the yields obtained 95, 94, 94, 91, 90 and

87% respectively. These values show that there is no notable difference in use of similar acid solutions. In fact, the main advantage of the desired method is applying an eco-friendly and economic process for the synthesis of enaminones using citrus juice as natural, clean and green catalyst instead of the polluting and toxic materials such as common acid solutions. Reaction times (grinding time) in all reactions have been optimized to obtain the highest yields as well (Table **2**).

The scope of application of the presented method is demonstrated by using the various substituted aromatic and aliphatic amines to react with beta dicarbonyls. The aliphatic amines (entries 2-5, 10, 15) also worked well to form the products in high yields.

Also, as shown in Table **2**, the yields obtained for lime were higher whereas the reaction times were shorter than those by other juices. These observations can be attributed to the more acidic identity of the lime juice (pH= 2.3).

As mentioned above, the wide application of this procedure is demonstrated by the use of various substituted amines to react with *β*-dicarbonyl compounds. The method was successfully applied for primary amines (15 entries) and the related enaminones were well synthesized in good to excellent yields.

In order to generalize the above catalytic protocol, enamination of 1,3-dicarbonyls with various amines was studied as depicted in Table **2**. When 1,3-dicarbonyl compounds were reacted with an aryl amine with an electron donating substituent such as CH_3, the corresponding products were obtained in excellent yields (entries 13). However, in the presence of an electron withdrawing group, such as NO_2, moderate yield of the product was obtained (entries 9, 12). Further when diverse aliphatic amines were studied, high yields of products were obtained as well (entries 2-5, 10 and 15).

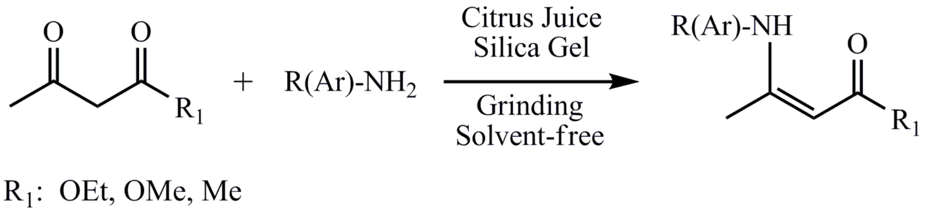
In addition to the mild conditions of the method and its high results, another notable case is the simplicity of product isolation that offers a significant advantage. A comparison of efficiency of this method with various catalysts employed for the synthesis of **1** was carried out (Table **3**). Slightly higher isolated yield was found in this procedure compared to other methods.

CONCLUSION

In summary, a novel, efficient and green protocol for the grinding synthesis of enaminones using citrus juice as natural catalyst has been presented. This methodology is user friendly, green and low cost procedure under mild reaction condition with faster reaction rates. The citrus juice is inexpensive and non-toxic which makes the process convenient, more economic and benign. Furthermore, applying grindstone technique in solvent-free conditions, use of silica gel as a solid and heterogeneous surface in reaction, high yields of products, cleaner reaction profiles, and availability of the reagents makes this method a better choice for synthetic chemists.

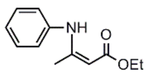
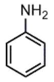
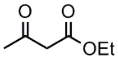
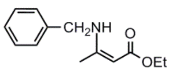
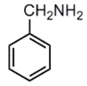
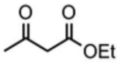
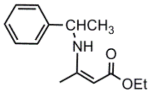
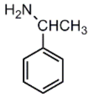
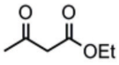
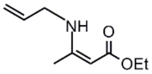
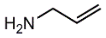
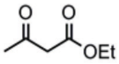
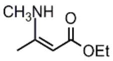
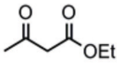
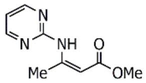
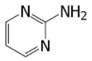
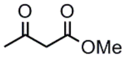
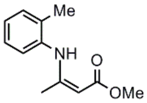
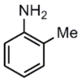
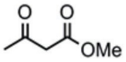
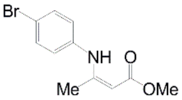
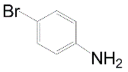
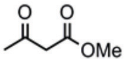
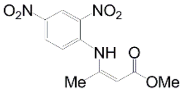
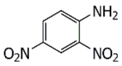
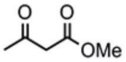
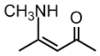
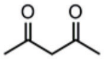
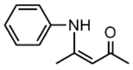
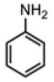
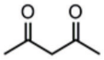
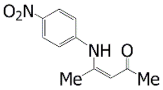
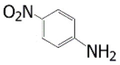
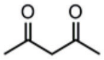
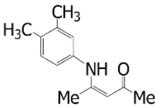
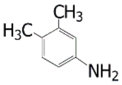
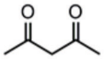
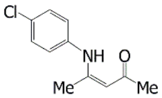
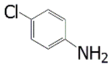
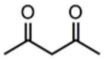
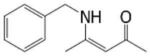
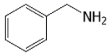
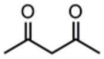
Table 1. Proximate nutritional composition of citrus juice.

Citrus Juice	Lime	Lemon	Orange	Grapefruit
Moisture (g/100 g)	90.8	90.59	88.3	90.2
Ash (g/100 g)	0.3	0.2	0.4	0.2
pH	2.3	2.6	3.8	3.4
Calcium (mg/100 g)	14	2	11	9
Phosphorus (mg/100 g)	13	6	17	15
Sodium (mg/100 g)	2	0.8	1	0.9
Potassium (mg/100 g)	117	124	200	162
Vitamin A (IU)	50	200	3	440
Vitamin C (mg/100 g)	30	46	50	38



Scheme 1. Citrus juice catalyzed grinding synthesis of enaminones (**1-15**) under solvent-free conditions on silica.

Table 2. The yields and reaction times for citrus juice catalyzed solvent-free silica supported grinding synthesis of enaminones.

Reaction Time, min Lemon /Lime Orange /Grapefruit	Yield*, % Lemon /Lime Orange/Grapefruit	Product	Amine	Dicarbonyl Compound	Entry
15/10 20/15	92/95 90/90				1
20/15 20/20	92/96 91/90				2
20/10 15/15	90/94 89/91				3
15/10 20/20	91/94 87/90				4
15/10 20/15	92/96 90/91		CH_3NH_2		5
15/10 20/15	91/94 90/89				6
15/10 20/20	92/94 88/90				7
15/10 15/15	92/95 91/93				8
15/10 20/20	86/89 84/85				9
15/10 15/15	89/95 87/91		CH_3NH_2		10
15/10 20/20	90/92 87/90				11
15/10 20/15	90/91 88/89				12
15/10 15/20	94/96 92/94				13
20/15 20/20	90/94 89/91				14
15/15 20/15	92/96 93/90				15

* Isolated Yields.

Table 3. Effect of various catalysts on the synthesis of enaminone (1) by grinding method.[a]

Entry	Catalyst	Catalyst loading	Time (min)	Yield (%)
1	SiO_2	1g	45	58
2	Lime/SiO_2	5 drops/1g	10	95
3	Al_2O_3(acidic)	1g	25	79
4	Al_2O_3(neutral)	1g	45	62
5	Lime/Al_2O_3(neutral)	5 drops/1g	30	86
6	nano-Alumina	0.005g	30	73
7	nano-Fe_3O_4	0.005g	30	71
8	$ZnCl_2$	1g	25	67

[a] In all reactions, at first, *β*-dicarbonyl compound and solid catalyst were ground together in a mortar using pestle for 2 min and then amine was added to the mixture and grinding was continued.

CONSENT FOR PUBLICATION

Not applicable.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

ACKNOWLEDGEMENTS

The authors thank Roodsar Payam Noor University for financial support.

SUPPLEMENTARY MATERIAL

Supplementary material is available on the publisher's website along with the published article.

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