ORIGINAL ARTICLE

A C G publications

*Org. Commun.*17:4 (2024) 241-248

organic communications

Synthesis of β-enaminoesters from β-ketoesters and amines by solvent-drop grinding approach in PEG 400

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(Received September 25 2024; Revised December 18, 2024; Accepted December 21, 2024)

Abstract: An effective catalytic system for the synthesis of β-enaminoesters from β-ketoesters under mechanochemical conditions using mortar and pestle in recyclable PEG 400 as solvent-drop approach was developed. This method has a number of benefits, including shorter reaction times, use of inexpensive recyclable solvent cum catalyst system, compatible reaction conditions, and high product yields.

Keywords: Amines; β-ketoesters; β-enaminoesters; grinding; PEG 400; mechanochemical catalysis.

1. Introduction

β-Enamino esters are helpful links in the synthesis of nitrogen-containing compounds.[1] Additionally, they are important ingredients in many pharmaceuticals and naturally occurring compounds that have biological significance.[2] The synthesis and use of β-enamino ester derivatives have long piqued the interest of organic synthesis due to their value as versatile building blocks and bioactive leads.

The synthesis of β-enaminoesters has been reported using a variety of techniques, including tosyl imines, imidoyl halides, adding enamines or ketimines to activated carboxylic acid derivatives, adding an ester or amide enolate to a nitrile, and directly condensation of β-ketoesters with amines.[3-22] Although the majority of the protocols include a wealth of documentation, some of their shortcomings include their wide applicability, harsh reaction conditions, and small chemical yields. Consequently, it is imperative to develop a better catalyst for the synthesis of β-enaminoesters.

Synthetic chemistry researchers are constantly inventing novel catalysts and reagents to carry out chemical reactions. Because they are simple to use and have cheap production costs, solvent-free based synthetic procedures have become more and more common in the synthesis of pharmacologically relevant heterocyclic compounds.[23-25] On the other hand, the mechanochemical technique has gained popularity because to its little impact on the environment and affordability.[26-29] Mechanical grinding has emerged as a key tool in the synthetic organic chemistry paradigm due to its ease of use, distinct reaction profile, and potential for larger-scale application with the right experimental setup.[30-31]

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Thearticlewaspublishedby ACG Publications
http://www.acgpubs.org/journal/organic-communications © October-December 2024 EISSN:1307-6175
DOI: http://doi.org/10.25135/acg.oc.178.2409.3334
Available online: December 30, 2024

One such component that is receiving increasing attention is the use of alternative reaction media, which circumvents the problems associated with many of the traditional volatile organic solvents. Over time, a variety of suitable and environmentally friendly alternative reaction media have been studied, such as supercritical fluids, ionic liquids, and polyethylene glycol.[32-34]Inspired by the work of Tanemura, we have explored the possibility of PEG-400 in solvent-drop grinding.[35] According to the report, using the solvent-drop grinding (SDG) technique, a few drops of solvent were added to increase the rate of co-crystallization.

According to this perspective, polyethylene glycol (PEG) acts as a green solvent and a replacement for reaction media. PEG has been studied as a solvent for chemical synthesis for more than 20 years.[36-39] Because PEG is benign, non-toxic, biodegradable, and biocompatible, it is frequently preferred over hazardous organic solvents in organic synthesis. PEG has been used as a solvent in several reactions related to the synthesis of heterocyclic molecules, oxidations and reductions, the formation of heteroatom-heteroatom bonds, and the formation of carbon-carbon and heteroatom-heteroatom bonds.[40-43] As a follow-up to our work on C-C and C-heteroatom bond formation reactions,[44-47] we have used a mechanochemical method to manufacture β-enaminoesters in moderate to good yields.

2. Experimental

All the chemicals and solvents employed in the synthesis were supplied by Sigma Aldrich, Merck, Loba, SRL and Spectrochem and used without purification. The melting points were measured by open capillary method and uncorrected. The reaction mixtures were irradiated by a 100W tungsten lamp (Philips India Ltd). The IR spectrums (NaCl) were recorded on a Nicolet Fourier Transform spectrometer. The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AV-300 instrument. As internal standards served TMS (δ 0.00) for ^{1}H NMR and $CDCl_3$ (δ 77.0) for ^{13}C NMR spectroscopy *J* values are given in Hz. The multiplicities of the signals in the ^{1}H NMR spectra are abbreviated by s (singlet), d (doublet), t (triplet), q (quarted), m (multiplet), br (broad) and combinations thereof. Thin-layer chromatography (TLC) was performed on GF-25U (Anal. Tech.) plates and silica gel glass-backed plates. All the chemical reactions were carried out in dried glassware.

2.1. Chemistry

2.1.1. General Experimental Procedure

A mortar and pestle was used to grind the amine (1.5 mmol), β-ketoester (1 mmol) in PEG 400 (1 mL) added drop-wise for the allotted amount of time at ambient temperature (see Table 2).Following the conclusion of the reaction, which was observed by thin-layer chromatography, the mixture was diluted with anhydrous diethyl ether and allowed to stir for fifteen minutes. Subsequently, the layers were allowed to separate, and the ether layer was decanted. The mother liquor (PEG) was set aside for subsequent runs, and this procedure was performed twice to provide the crude products in diethyl ether. Following solvent evaporation, the crude product was refined using column chromatography on silica gel with 1:1 petroleum ether/ethyl acetate to produce the pure corresponding β-enaminoester. All of the compounds synthesized are known.

2.1.2. Spectroscopic Data of Compounds

*(Z)-Methyl 3-(phenylamino)but-2-enoate (**I**)*: Yellow liquid. IR: ν = 1492, 1599, 1655, 2926, 3264 cm^{-1}; ^{1}H-NMR δ = 10.35 (s, 1H), 7.26-7.34 (m, 2H), 7.08-7.18 (m, 3H), 4.70 (s, 1H), 3.69 (s, 3H), 2.00 (s, 3H); ^{13}C-NMR δ = 170.7, 159.1, 139.3, 129.0, 125.0, 124.5, 85.6, 50.2, 20.3; Mass: *m/z*: 175 (M^+)

*(Z)-Ethyl 3-(p-tolylamino)but-2-enoate (**II**)*: Yellow liquid. IR: ν = 1135, 1320, 1480, 1580, 1615, 2950, 3210 cm^{-1}; ^{1}H-NMR δ = 10.32 (s, 1H), 7.10-7.13 (m, 2H), 6.95-6.98 (m, 2H), 4.67 (s, 1H), 4.14 (q, 2H, *J* = 7.2 Hz), 2.32 (s, 3H), 1.94 (s, 3H), 1.28 (t, 3H, *J* = 7.2 Hz). ^{13}C-NMR δ = 170.3, 159.3, 136.6, 134.7, 129.5, 124.6, 85.3, 58.6, 20.8, 20.1, 14.5; Mass: *m/z*: 219 (M^+)

*(Z)-Methyl 3-(p-tolylamino)but-2-enoate (**III**)*: Yellow oily liquid. IR: ν = 1105, 1321, 1470, 1585, 1605, 3045 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 10.25 (s, 1H, NH), 7.13-6.96 (m, 4H, aromatic CH), 4.67 (s, 1H), 3.74 (s, 3H, OCH_3), 2.33 (s, 3H, CH_3), 1.95 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 170.7 (C=O), 159.6, 136.6, 134.9, 129.6, 124.8, 84.9, 50.2 (OCH_3), 20.8 (CH_3), 20.2 (CH_3). GC-MS (*m/z*): 205.1

*(Z)-Ethyl 3-(4-methoxyphenylamino)but-2-enoate **(IV)***: Yellow liquid. ^{1}H-NMR δ = 10.15 (s, 1H), 6.97-7.00 (m, 2H), 6.80-6.83 (m, 2H), 4.62 (s, 1H), 4.07-4.14 (q, 2H, *J* = 7.0 Hz), 3.75 (s, 3H), 1.85 (s, 3H), 1.24 (t, 3H, *J* = 7.0 Hz); ^{13}C-NMR δ = 170.3, 159.7, 157.2, 131.9, 126.5, 113.9, 84.5, 58.4, 55.1, 19.9, 14.4

*(Z)-Ethyl 3-(4-bromophenylamino)but-2-enoate **(V)***: Yellow liquid. ^{1}H-NMR δ = 10.34 (s, 1H), 7.34-7.37 (m, 2H), 6.88-6.89 (m, 2H), 4.67 (s, 1H), 4.06-4.13 (q, 2H, *J* = 7.2 Hz), 1.93 (s, 3H), 1.23 (t, 3H, *J* = 7.2 Hz); ^{13}C-NMR δ = 170.2, 158.0, 138.4, 132.0, 125.5, 117.7, 87.0, 58.8, 20.1, 14.5

*(Z)-Ethyl 3-(4-nitrophenylamino)but-2-enoate **(VI)***: Yellow liquid.^{1}H NMR (400 MHz, TMS, $CDCl_3$) δ (ppm): 10.96 (s, 1H, NH), 8.24 (d, 2H, 2H, 2 x ArH), 7.15 (d, 2H, 2H, 2 x ArH), 4.90 (s, 1H, 2-CH), 4.25 (m, 2H, 5-CH_2), 2.26 (s, 3H, 4-CH_3), 1.34 (m, 3H,6-CH_3). ^{13}C NMR (100 MHz, TMS, $CDCl_3$) δ (ppm): 167.23(C-1), 162.04(C-3), 152.25(C-1'), 139.05(C-4'), 122.65(C-3', C-5'), 119.14(C-2', C-6'), 84.46(C-2), 61.57(C-5), 21.26(C-4), 14.45(C-6)

*(Z)-Methyl 3-((4-nitrophenyl)amino)but-2-enoate (**VII**)*: Yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$): =δ 10.88 (s, 1H, N-H), 8.20-8.18 (d, *J*=8, 2H, aromatic H), 8.14–8.12 (d, *J*=8, 1H, aromatic H), 4.89 (s, 1H, C-H), 3.71 (s, 3H, -OCH_3), 2.22 (s, 3H, -CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): = δ 170.38, 155.93, 145.75, 125.34, 120.76,; 91.09, 50.78, 21.02. HRMS (ESI) Exact mass calculated for $C_{11}H_{13}N_2O_4^+$ [M+ H^+] = 237.0870, found 237.0881

(*Z*)-Ethyl 3-(benzylamino)but-2-enoate *(**VIII**)*: Yellow liquid. ^{1}H NMR (400 MHz, TMS, $CDCl_3$) δ (ppm): 10.31 (s, 1H, NH), 7.13 (m, 2H, 2 x ArH), 6.98 (m, 3H, 3 x ArH), 4.69 (s, 1H,2- CH), 4.18 (m, 4H,5 and 1'-CH2), 1.93 (s, 3H,4-CH_3), 1.27 (m, 3H,6-CH_3). ^{13}C NMR (100 MHz, TMS, $CDCl_3$) δ (ppm): 170.66(C-1), 162.82(C-3), 138.85(C-2'), 128.81(C-4',C-6'), 127.46(C-3',C7'), 126.82(C-5'), 83.21(C-2), 58.51(C-5), 46.86(C-1'), 24.15(C-4), 14.73(C-6)

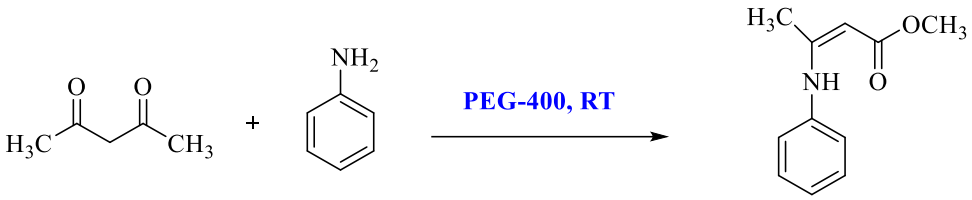
*(Z)-Methyl 3-(benzylamino)but-2-enoate (**IX**)*: Yellow liquid. ^{1}H NMR (400 MHz, TMS, $CDCl_3$) δ (ppm): 8.94 (s, 1H, NH), 7.32-7.26 (m, 2H, 2 x ArH), 7.23 (m, 3H, 3 x ArH), 4.53 (s, 1H, 3-CH), 4.42 (m, 2H, 1'-CH2), 3.63 (s, 3H, 1-CH_3), 1.93 (s, 3H, 5-CH_3). ^{13}C NMR (100 MHz, TMS, $CDCl_3$) δ (ppm): 170.61(C-1), 161.71(C-3), 138.48(C-2'), 128.62(C-4', C-8'), 127.21(C-5'), 126.53(C-3', C-7'), 82.72(C-2), 50.12(C-5), 46.82(C-1'), 19.46(C-4)

*Ethyl 2-(phenylamino)cyclopent-1-enecarboxylate (**X**):* Light yellow liquid. IR: ν = 1150, 1745, 3315, cm^{-1}; ^{1}H NMR (400 MHz, TMS, $CDCl_3$) δ (ppm):9.65 (s, 1H), 7.24-7.30 (m, 2H), 6.99-7.05 (m, 3H) , 4.21 (q, 2H, *J* = 7.2 Hz), 2.79 (t, 2H, *J* = 7.2 Hz), 2.58 (t, 2H, *J* = 7.2 Hz), 1.86 (m, 2H), 1.32 (t, 3H, *J* = 7.2 Hz); ^{13}C NMR (100 MHz, TMS, $CDCl_3$) δ (ppm): 168.4, 160.3, 140.6, 129.1, 123.0, 120.6, 97.6, 58.9, 33.6, 28.7, 21.7, 14.6; Mass: *m/z*: 231 (M^+)

3. Results and Discussion

Initially, a methodical investigation was carried out to evaluate the role of grinding for the reaction between aniline and methylacetoacetate in various solvent conditions at room temperature (Scheme 1).

Synthesis of β-enaminoestersβ-ketoesters and amines



Scheme 1. Mechanochemical synthesis of β-enaminoesters

The reaction mixture is stirred at room temperature as specified in Table 1; the reaction has not been successful in water (Table 1, entry 6) and in negligible amounts in neat conditions (Table 1, entry 1). To accelerate the same reaction, we have conducted the reaction in methanol using for 1 h, the reaction had 68% of yield (Table 1, entry 4). In addition, the reaction is carried out in chloroform and acetonitrile to check the productivity, and the results are disclosed in Table 1 (entries 2 and 3). To our satisfaction, the use of the grinding method in PEG 400 directed an increase in the yield of the target product (**I**, entry 5, Table 1).

Table 1. Scope of the reaction using different solvents

Entry	Solvent	Time	Yield[a] %
1	Neat	120 min.	12
2	$CHCl_3$	60 min.	45
3	CH_3CN	60 min.	71
4	MeOH	60 min.	68
5	**PEG400**	**45min.**	**88**
6	H_2O	60 min.	NR

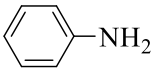
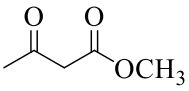
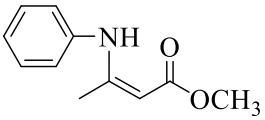
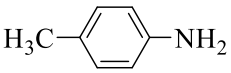
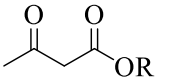
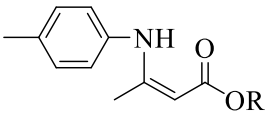
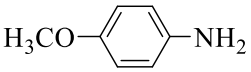
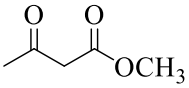
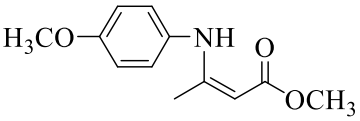
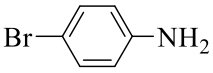
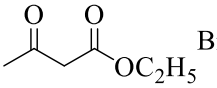
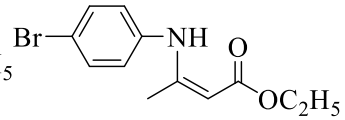
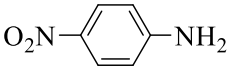
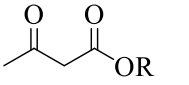
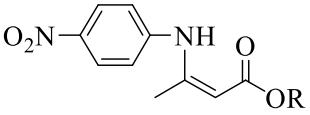
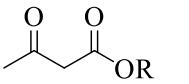
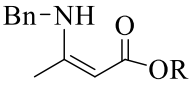
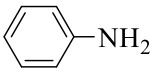
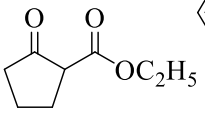
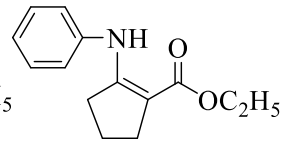
[a]Isolatedyeields; NR: No reaction

The technique proved effective for primary aromatic amines, as demonstrated by the data shown in Table 2. For example, it was easy to convert methyl and ethyl acetoacetates into the appropriate β-enaminoesters. The present method has many notable advantages over the ones outlined, two of which are moderate to good yields and rapid reaction times. Generally speaking, amines with both electron-withdrawing and electron-donating groups produced comparable yields of desired products (**II-VII**, Table 2). Benzyl amine also reacted well with methyl and ethyl β-ketoesters to result in the corresponding products with good yields (**VIII-IX**, Table 2). Even with cyclic β-ketoesters, moderate product yield was obtained (58%, **X**, Table 2).

In terms of chemoselectivity, the approach worked well. In all cases, no interaction with the ester was detected to yield the corresponding amide; instead, the amine reacts exclusively with the ketone of the β-ketoesters (**I-IX**, Table 2). Intramolecular hydrogen bonding ensured the (*Z*)-selectivity in the β-ketoester-derived products. This stereostructure was confirmed by the separated products' ^{1}H NMR spectra studies. The -NH-group's proton was found between 8.0 and 10.9 ppm. Nevertheless, the ^{1}H NMR spectra of the β-enaminones obtained from cyclic diketone (**X**, Table 2) showed signals for the non-hydrogen bound proton of the -NH- group in the range of δ 4.5-6.5, indicating the (*E*)-configuration.

For the synthesis of desired product on the control reaction of aniline and methyl acetoacetate under the optimized reaction conditions, the separation of the products and the reaction medium were investigated. The yield dropped after five runs, but we were happy to find out that the reaction medium could be successfully recycled for a maximum of five cycles with little loss of activity (88, 87, 87, 85 and 85% respectively).

Table 2. Synthesis of β-enaminoesters from β-ketoesters and amines

Entry	Amine	Ketoester R = CH_3/C_2H_5	Product		Time (min)	Yield[a, ref] (%)
1				(**I**)	45	88[18]
2				R=C_2H_5 (**II**)	45	81[18]
3				R = CH_3 (**III**)	45	82[19]
4				(**IV**)	45	91[21]
5				(**V**)	60	74[18]
6				R=C_2H_5 (**VI**)	60	67[18]
7				R = CH_3 (**VII**)	60	68[21]
8				R=C_2H_5 (**VIII**)	45	80[18]
9				R = CH_3 (**IX**)	45	85[21]
10				(**X**)	60	58[10]

[a]Yields of pure isolated products

Based upon the present results and earlier reports, possible reaction mechanism is proposed for the PEG catalyzed synthesis of β-ketoenamines (Figure 1). In the first step, the presence of active hydroxyl group on PEG binds with the carbonyl oxygen of β-keto ester and a subsequent addition of aniline in step 2 forms an intermediate as shown in Figure 1. In step 3, the elimination of water molecule from intermediate from step 2 yields the desired enamino ester**.**

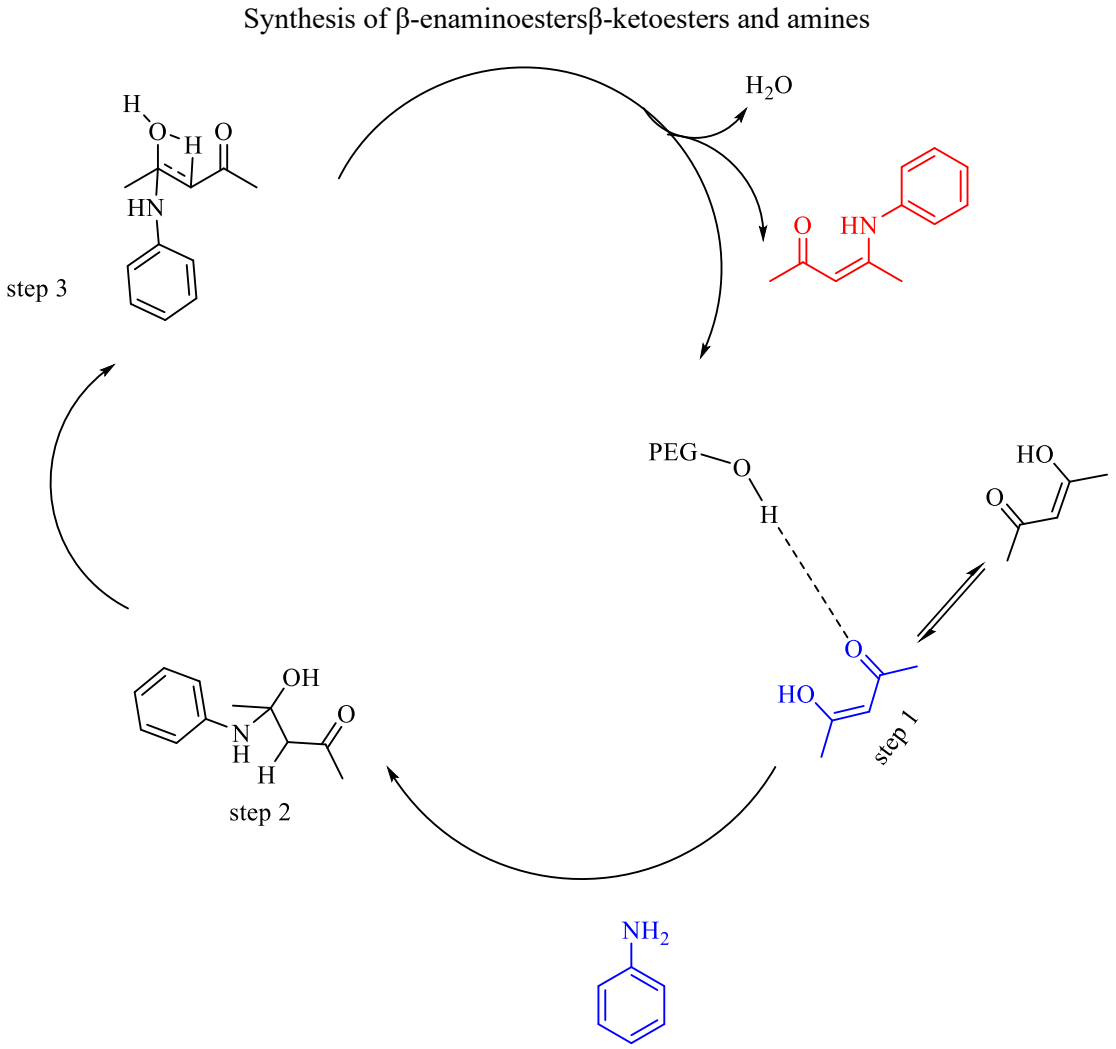


Figure 1. Proposed mechanism

4. Conclusion

As a result, we have developed a novel methodology for the synthesis of β-enaminoesters using mortar and pestle *via* mechanochemical/grinding approach. The key appealing aspects of this method include the use of a cheap and widely accessible reusable solvent (PEG 400) in solvent-drop technique, experimental simplicity, amicable to aromatic and benzyl amines, a straightforward work-up procedure, recyclable and reused for minimum five times and a quick response.

Conflict of Interests

The authors declare no conflict of interest either of a financial or personal nature.

Supporting Information

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References

[1] Ying, H.; Jing, S.; Yan, S.; Hong, G.; Chaoguo, Y. Development of domino reactions with *β*-enamino esters as key intermediates. *Chin. J. Org. Chem.***2012**, *32(09*), 1577-1586.

[2] Salaheldin, A. M.; Al-Sheikh, M. A. β-Enamino esters in heterocyclic synthesis: Synthesis of pyrazoloneand pyridinone derivatives. *Molecules***2010**, *15(6)*, 4359-4368.

[3] Zhang, Z-H.; Hu, J-Y. Cobalt(II) chloride-mediated synthesis of beta-enamino compounds under solvent-free conditions. *J. Braz. Chem. Soc.***2006**, *17(7)*, 1447-1451.

[4] Waghmare, S. R. NH_4Cl Catalyzed synthesis of β-amino esters. *Results in Chemistry***2020**, *2*, 100036.

[5] Zhang, Z-H.; Yin, L.; Wang, Y-M. A general and efficient method for the preparation of β-enamino ketones and esters catalyzed by indium tribromide. *Adv. Synth. Catal.***2006**, *348(1-2)*, 184-190.

[6] Xin, D.; Burgess, K. A chemoselective route to β-enamino esters and thioesters. *Org. Lett.* **2014**, *16(8)*, 2108-2110.

[7] Feng, C. L.; Chu, N. N.; Zhang, S. G.; Cai, J.; Chen, J-Q.; Hu H-Y.; Ji, M. Solvent-free synthesis of β-enamino ketones and esters catalysed by recyclable iron(III) triflate. *Chem. Pap.* **2014**, *68*, 1097-1103.

[8] Kim, S-H.; Bae, S.; Ko, E. B.; Park, G. Y.; Lee, E.; Hwang, H. J.; Im, C. Y.; Song, M. Silica gel-mediated synthesis of β-enamino esters and its application for the synthesis of indeno 4-hydroxypyridin-2(1*H*)-ones. *Bull. Korean Chem. Soc.***2019**, *40(3*), 262-269.

[9] Brandt, C. A.; da Silva, A. C. M. P.; Pancote, C. G.; Brito, C. L.; da Silveira, M. A. B. Efficient synthetic method for β-enamino esters using ultrasound. *Synthesis***2004**, *10*, 1557-1559.

[10] Lin, J.; Zhang, L-F. $ZrCl_4$-Catalyzed efficient synthesis of enaminones and enamino esters under solvent-free conditions. *Monatshefte Chem.***2007**, *138(1*), 77-81.

[11] Chen, X. M.; Li, X. S.; Chan, A. S. C. Highly efficient synthesis of β-amino esters via Mannich-type reaction under solvent-free conditions using $ZnCl_2$ catalyst. *Chin. Chem. Lett.* **2009**, *20*, 407-410.

[12] Shekhar, A.; Pathak, D. D. Zeolite (ZSM-5) as a highly efficient and heterogeneous catalyst for the synthesis of β-enaminones and β-enamino esters. *E-J. Chem.* **2011**, *8(4*), 1632-1637.

[13] Xu, F.; Lv, H-X.; Wang, J-P.; Lian, Y-P.; Wang, J-J. A mild method for the synthesis of β-enaminones and β-enamino esters using KH_2PO_4 as catalyst. *J. Chem. Res.* **2008**, 707-710.

[14] Zhang, M.; Abdukader, A.; Fu, Y.; Zhu, C. Efficient synthesis of β-enaminones and β-enaminoesters catalyzed by gold (I)/silver (I) under solvent-free conditions. *Molecules* **2012**, *17*, 2812-2822.

[15] Guizzetti, S.; Benaglia, M.; Bonsignore, M.; Raimondi, L. Triclorosilane-mediated stereoselectivesynthesis of β-amino esters and their conversion to highly enantiomerically enriched β-lactams. *Org. Biomol. Chem.* **2011**, *9*, 739-743.

[16] Chen, H-Y.; Patkar, L. N.; Ueng, S-H.; Lin, C-C.; Lee, S-Y. Synthesis of β-amino esters by regioselective amination of allyl bromides with aryl and alkyl amines synthesis of β-amino esters. *Synlett* **2005**, *13*, 2035-2038.

[17] Kamble, V. T.; Joshi, N. S.; Atkore, S. T. Cyanuric chloride catalyzed rapid conversion of β-ketoesters into β-enaminoesters under mild and solvent-free conditions. *J. Iranian Chem. Soc.* **2011**, *8*, 616-621.

[18] Varala, R.; Nuvula, S.; Adapa, S. R. Efficient synthetic method for β-enamino esters catalyzed by $Yb(OTf)_3$ under solvent-free conditions. *Australian J. Chem.***2006**, *59 (12)*, 921-924.

[19] Bartoli, G.; Bosco, M.; Lacatelli, M.; Marcantoni, E.; Melchiorre, P.; Sambri, L. $Zn(ClO_4)_2{\cdot}6H_2O$ as a powerful catalyst for the conversion of β-ketoesters into enamino esters. *Synlett* **2004**, *2*, 239-242.

[20] Wang, Y.; Zhang, C.; Li, S.; Liu, L.; Feng, X. Recent advances in transition metal catalyzed synthesis of *β*-enaminones and *β*-enaminoesters. *ChemistrySelect* **2022**, *7(13)*, e202103345.

[21] Dutta, S.; Kumar, P.; Sharma, S.; Yadav, S.; Priyanka, Dixit, R.; Srivastava, A.; Sharma, R. K. A versatile core-shell hetero-nanostructure catalysed chemo-selective synthesis of β-enamino carbonyl compounds. *RSC Sustain.***2023**, *1*, 975-986.

[22] Bachute, A.; Dobhal, B. S. Tetrabutylammonium bromide (TBAB)-catalyzed rapid conversion of β-ketoesters into β-enaminoesters under solvent-free conditions. *South Afr. J. Chem.* **2024**,*78*, 24-26.

[23] Tanaka, K.; Toda, F. Solvent-free organic synthesis. *Chem. Rev.* **2000**, *100(3)*, 1025-1074.

[24] Lei, L.; Zhou,Y. Solvent-free or less-solvent solid state reactions. *Progres. Chem.***2020**, *32(8)*,1158-1171.

[25] Zangade,S.; Patil, P. A review on solvent-free methods in organic synthesis.*Curr. Org. Chem.***2019**, *23(21)*, 2295-2318.
[26] Wang, G-W. Mechanochemical organic synthesis. *Chem. Soc. Rev.***2013**, *42*, 7668-7700.
[27] Jean-Louis, D.; Tomislav, F. Mechanochemistry: A force of synthesis. *ACS Cent. Sci.* **2017**, *3(1)*, 13-19.
[28] Kishore, K.; Sinha, M.K.; Singh, A.; Archana, R.; Gupta, M.K.; Korkmaz, M. E. A comprehensive review on the grinding process: Advancements, applications and challenges. *Proceed.Institution Mechanical Engineer. Part C: J. Mechan. Engineer. Sci.***2022**, *236(22)*, 10923-10952.
[29] Leonardi, M.; Villacampa, M.; Menéndez, J. C. Multicomponent mechanochemical synthesis. *Chem. Sci.***2018**, *9*, 2042-2064.
[30] Ardila-Fierro, K. J.; Hernandez, J. G. Sustainability assessment of mechanochemistry by using the twelve principles of green chemistry. *ChemSusChem* **2021**, *14*, 2145-2162.
[31] Friščić, T.; Mottillo, C.; Titi, H. M. Mechanochemistry for synthesis. *Angew. Chem. Int. Ed. Engl*. **2020**, *59(3)*, 1018-1029.
[32] Winterton, N. The green solvent: a critical perspective. *Clean Technol. Environ. Policy.***2021**, *23(9)*, 2499- 2522.
[33] Sheldon, R. A. Green solvents for sustainable organic synthesis: state of the art. *Green Chem.* **2005**,*7*, 267-278.
[34] Andrade, C. K. Z.; Alves L. M. Environmentally benign solvents in organic synthesis: current topics. *Curr. Org. Chem.***2005,** 9, 195-218.
[35] Tanemura, K. Acceleration under solvent-drop grinding: Synthesis of bis(indolyl)methanes using small amounts of organic solvents or ionic liquids. *Tetrahedron Lett.***2021**, *82*,153391.
[36] Soni, J. P.; Nusrat, S.; Sethiya, A.; Agarwal, S. Polyethylene glycol: A promising approach for sustainable organic synthesis. *J. Mol. Liq.* **2020**,*315*, 113766.
[37] Hoffmann, M. M. Polyethylene glycol as a green chemical solvent. *Curr. Opin. Colloid In.* **2022**,*57*, 101537.
[38] Liwei, X.; Fucai, D.; Zheng, L.; Xuemin, J.; Jie, K.; Guangxian, L. Polyethylene glycol: A new mediumfor green organic synthesis. *Chin. J. Org. Chem*. **2019**, *39(3)*, 648-660.
[39] Kardooni, R.; Kiasat, A. R. Polyethylene glycol as a green and biocompatible reaction media for the catalyst free synthesis of organic compounds. *Curr. Org. Chem*. **2020**,*24*, 1275-1314.
[40] Qadir, M.; Yaseen, A.; Shah, W. A. PEG-400 catalysed selective C-Se cross dehydrogenative coupling: An ultrasonication-assisted green strategy. *Results Chem.***2023**,*5*, 100944.
[41] Yaseen, A.; Waseem, M. A.; Qadir, M.; Dar, P. A.; Hijazi, S.; Hussain, M. A.; Shah, W. A. PEG-400 catalyzed N-C, O-C & C-S bond formations: A robust sonication promoted synthesis of benzo[*d*]oxazole (3*H*)-thione & benzo[*d*]thiazole-2(3*H*)-thione hybrids. *Anal. Chem. Lett.***2022**,*12(3)*, 302-309.
[42] Lim, H. Y.; Dolzhenko, A. V. Polyethylene glycol as a green medium for the microwave-assisted synthesis of guanamines. *ChemistrySelect* **2023**, *8(29)*, e202302106 and references cited thereinPulagama, M.; Bollikolla, H. B. PEG 400-Catalyzed *C3* & *O*-alkylation reactions of 4-hydroxycoumarin-A study. *Curr. Chem. Lett.***2025**, *14*, 10.5267/j.ccl.2024.8.004
[44] Kokane, B. D.; Varala, R.; Patil, S. G. $Zn(OAc)_2 \cdot 2H_2O$: An efficient catalyst for the one-pot synthesis of 2-substituted benzothiazoles. *Org. Commun*. **2022**, *15*, 378-385.
[45] Kokane, B. D.; Patil, S. G. Ammonium acetate as a dual reagent-catalyst role in efficient synthesis of 2,4,6-trisubstituted 1,3,5-triazines from aldehydes.*Caribbean J. Sci. Tech.***2022**, *10(2)*, 42-46.
[46] Mukhedkar, S. S.; Kokane, B. D.; Deshmukh, J. H.; Anjanikar, S. S. Three-component $Zn(OAc)_2$-catalyzed one pot synthesis of mono and disubstituted pyrimidine derivatives. *J. Sci. Tech.* **2024**, *9(4)*, 1-7.
[47] Kokane, B. D.; Varala, R.; Patil, S. G. $Zn(OAc)_2 \bullet 2H_2O$-catalyzed efficient synthesis of 5-Substituted 1*H*-tetrazoles. *Curr. Chem. Lett*. **2023**, *12*, 509-518.