

Article

Montmorillonite K10-catalyzed solvent-free conversion of furfural into cyclopentenones

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Abstract:

A simple and eco-friendly Montmorillonite K10 (MK10) catalyzed method for the synthesis of cyclopentenone derivatives from biomass-produced furfural has been developed. The versatility of this protocol is that the reactions were carried out in solvent free condition and in short reaction time under heterogeneous catalysis. Montmorillonite K10 is a material most explored as heterogeneous catalyst since it is inexpensive and environmentally friendly.

Keywords: heterogeneous catalysis; Montmorillonite, furfural; cyclopentenones

1. Introduction

In the last years, the use of the heterogeneous catalysis has become a promising field in chemical synthesis, especially in industrial applications [1]. From an economic point of view, the tendency to use heterogeneous acid catalysis in the industrial field derives from their intrinsic stability, ease of recovery, separation and recycling minimizing waste contamination. On the other hand, the use of toxic and dangerous solvents in the chemical industry is considered a major risk for the environment and human health of workers [2-6], so that the necessity for clean processes, in which energy, waste and costs are reduced, is of general concern [7].

Different studies have promoted the use of alternative methods or “green” solvents [8], principally water [8-15], ionic liquids [16-20], deep eutectic solvents [21-24] or bio-solvents [25-30], but the use of solvent free condition [31-35] is certainly the best choice to conduct eco-sustainable chemical procedures. A solvent-free reaction may be carried out using the reactants alone or incorporating them in solid supports simplifying the experimental and work-up procedures lowering considerably environmental impact. These would be particularly important in the industrial manufactures where, in the last decades, the use of microwave heating among others [37-40], was proposed in solvent-free chemical processes catalyzed by solid Lewis acids as useful method for increasing the reaction rate, simplifying the work-up and improving yield [41-44].

The Pollution Prevention Act of 1990 was enacted to increase interest in source reduction or pollution prevention and encourage design of environmentally benign processes and products.

Lowering the environmental impact of the industrial activities is particularly important for the pharmaceutical industry very often indicated as the principal source of environmental pollution [46]. Anyhow, since the development of novel synthetic methods to produce potential drug compounds has always an important research area, in recent years, very important has become the use of renewable sources or waste material as start product to obtain useful pharmaceutical synthons. [47-49]. In this context, furfural is important biomass compound derived and used to synthesize different bio-products [50]. The cyclization rearrangement can be realized by different Lewis acids as metallic compounds [51], triflate [52-54], metal chloride [55] in ionic liquids [56] or using green media as water [57] or deep eutectic solvents [58].

The use of solid supports in the organic synthesis have attracted the attention of chemists for their extremely versatile properties, thermal stability and their low cost.

Recyclable heterogeneous catalysts have been extensively experimented, but their activities are generally lower than those of homogeneous catalysts because of the lower exposure degree of active site to the reactants. Lanthanide chloride immobilized on silica as $\text{ErCl}_3 \cdot 6\text{H}_2\text{O}$ [59-60] was proposed for the synthesis of diaminocyclopent-2-enones from furfural, but the procedure involved the use of organic solvents to obtain a selectivity above 83%. Recently, metal-organic framework (MOF) showed higher activity than homogeneous catalyst, but the system condition under which the reaction occurs, such the use organic solvent under N_2 atmosphere, was crucial in determining the course of the performance [61].

MK10 is one of the most interesting clay catalysts [62-63] because over other solid support offers several advantages [64]. It may act as a general Brønsted or Lewis acid and it is considered an inexpensive green catalyst [65] since it prevents waste, it is reusable and safe to handle. In fact, MK10 can be simply recovered by filtration and employed in one-pot synthesis under solvent-free conditions and MW or ultrasound irradiation [66].

Considering the stability and catalytic activity of MK10 and our experience in developing eco-friendly reactions for the synthesis of pharmaceutical compounds [67-73], we decided to test the MK10 as catalyst in the cyclization of the furfural for synthesizing bifunctionalized cyclopentenones. The catalytic process showed high conversion and selectivity under MW irradiation. It is scalable and can be considered an environmental promising route for production of bio-compounds in pharmaceutical industry.

2. Results

In initial experiment, we choose morpholine as amine substrate to added to 2-furaldehyde to obtain selectively *trans*-4, 5-dimorpholinocyclopent-2-enone. The results for development and optimization of the cyclization rearrangement of furfural and morpholine studies are displayed in Table 1.

The effect of MK10 on the system furfural/morpholine was investigated performing the reaction at room temperature (Table 1, entries 1) using 10 wt% of MK10 respect to furfural. The corresponding *trans*-4, 5-dimorpholinocyclopent-2-enone was produced in 55% yield in 2 h. The GC-MS analysis showed the presence of 2,4-dimorpholinecyclopent-2-enone as by-product (45% yield).

Although the complete conversion of furfural at room temperature was observed, the evidence that the system could work better was recorded when the same reaction

was performed higher temperatures, observing total conversion with a better selectivity in only 35 minutes (Table 1, entries 2 and 3).

Table 1. Optimization of the reaction conditions.^a

The reaction scheme shows furfural (furan-2-carbaldehyde) reacting with morpholine in the presence of MK10 catalyst to produce trans-4,5-dimorpholinocyclopent-2-enone. The product is a cyclopent-2-enone ring with two morpholine groups attached at the 4 and 5 positions in a trans configuration.

Entry	MK10 wt (%) ^b	Temp (°C)	Time (min)	Conversion (%) ^b	Selectivity (%) ^d
1	10	rt	120	99.9	55.0
2	10	60	35	99.9	61.1
3	10	80	35	99.9	65.3
4	20	80	35	99.9	75.0
5	20	100	20	99.9	78.3
6	-	100	20	60.0	49.0
7 ^s	20	80	5	99.9	99.9
8^e	20	60	5	99.9	99.9
9 ^s	20	60	10	99.9	99.9

^a General reaction conditions: furfural (1 mmol) and morpholine (2 mmol) were stirred for 5-120 min at different temperatures and different wt (%) of MK10. ^b wt % respect to furfural. ^c Percent conversion calculated from GC/MS data of conversion of furfural. ^d Yield (%) of *trans*-4,5-dimorpholinocyclopent-2-enone obtained, calculated from GC/MS. By-product obtained is constituted by 2,4-dimorpholinocyclopent-2-enone. ^e Reaction mixture under MW irradiation.

We observed a better conversion with higher selectivity of desired product when the amount of catalyst was improved at 20 wt% at 80 °C (Table 1, entry 4), and comparable selectivity was achieved increasing the temperature (Table 1, entry 5). In the same reaction conditions, but in the absence of catalyst, no complete conversion of furfural and a poor selectivity was observed (Table 1, entry 6). Based on our previous experiences in developing eco-friendly and selective procedures [55,56], we tested the microwave activation of the reaction, finding that the microwave irradiation at 60 °C gave the best results in terms of reaction rate and product yield (Table 1, entries 7-9). Surprisingly, we obtained the desired product in 99% yield in only 5 minutes at 60 °C (Table 1, entry 8).

Furthermore, we have evaluated the recyclability of the heterogeneous catalyst in the reaction model system. The final reaction mixture, including MK10 and product, was treated with ethyl acetate; the catalyst was separated from the solution by filtration, washed with ethyl acetate (3 mL) for four times and dried in oven. Afterward, the combined organic phases were concentrated under vacuum and the crude product was analyzed by GCMS. The recovered catalyst was used directly for the next run adding new fresh reagents. Thus, the second reaction mixture was subjected again to the above-described procedure and further reaction cycle was repeated using the previously recycled MK10.

The MK10 can be recovered and reused for three consecutive cycles in the synthesis of 4,5-*trans*-dimorpholinocyclopent-2-enone furnishing high yields in every single cycle (Figure 1). The recycling showed the true heterogeneous catalytic nature for rearrangement reaction and the stable structure of MK10.

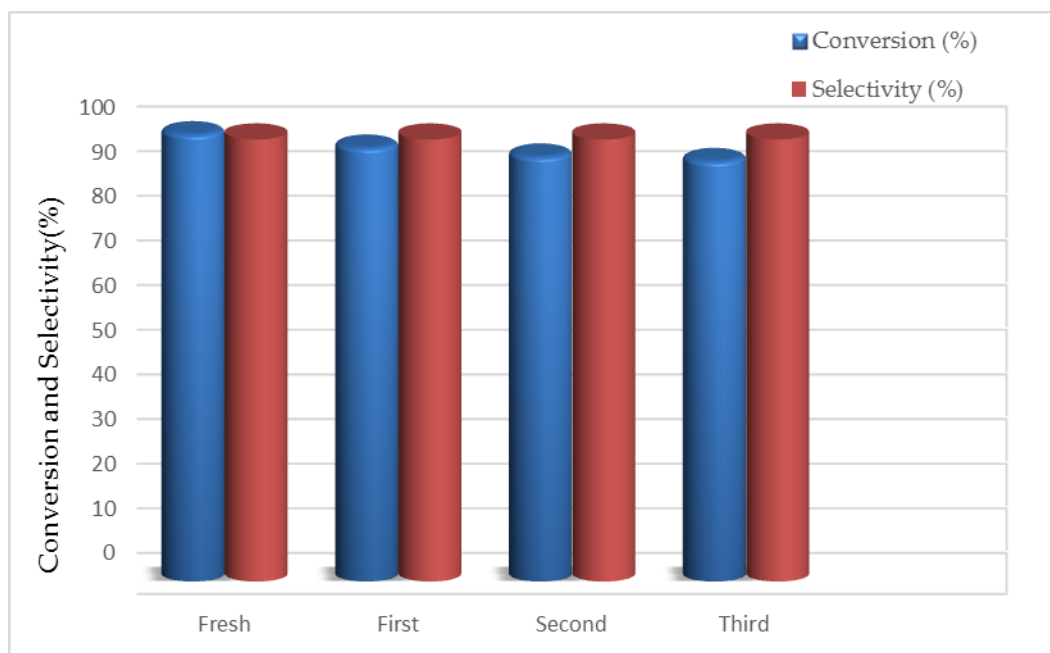
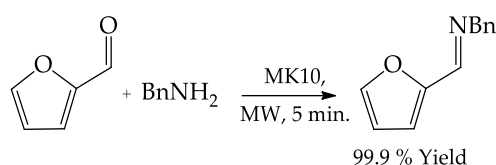


Figure 1. Cycling performance of MK10 in synthesis of 4,5-*trans*-dimorpholinocyclopent-2-enone under MW irradiation.

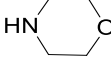
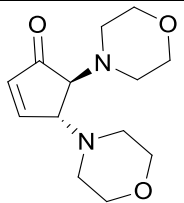

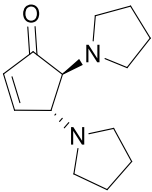

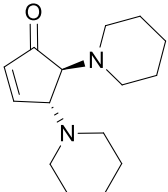
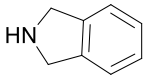
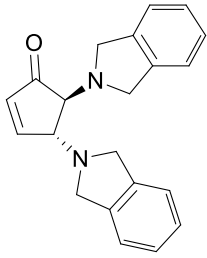
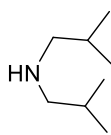
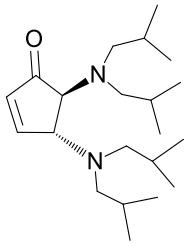
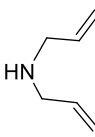
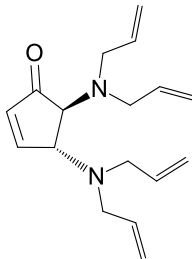
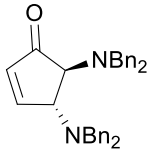
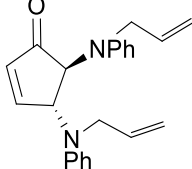
Then, to demonstrate the potential applicability of this eco-friendly procedure, the model reaction was carried out in a scale of 10 mmol of furfural and 20 mmol of morpholine using the respective amount of MK10. The reaction was completed in 10 min with 98% isolated yield after simple extraction with ethyl acetate.

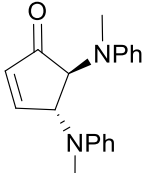
At this point, the experimental procedure was applied to different amines to obtain the the desired 4,5-diaminocyclopenten-2-enones and the quantitative yields superior to 90% were obtained in all cases (Table 2). The reaction gave those excellent results after the above reported simple workup with alicyclic (Table 2, entries 2-4), aliphatic (Table 2, entries 5-7) as well as with aromatic secondary amines (Table 2, entries 8-9); whereas, in the case of primary aliphatic amines, the corresponding imine was observed as the only product (Scheme 1).



Scheme 1. Reaction of furfural with BnNH₂

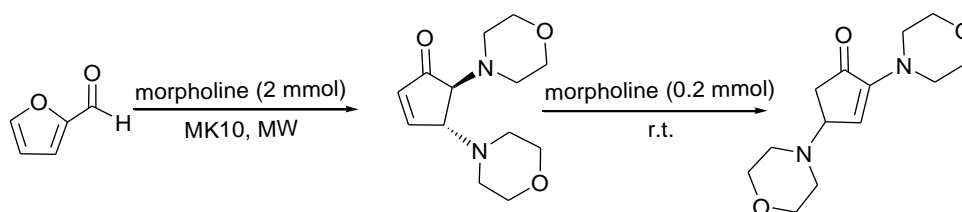
Table 2. Synthesis of bifunctionalized cyclopentenones.^a

Entry	Amine	Product	Conversion (%)	Selectivity (%)	Yield (%) ^b
1			99.9	99.9	95.0
2			95.9	99.7	96.6
3			99.9	99.7	99.6
4			91.0	99.3	90.8
5			97.8	99.0	94.8
6			96.8	99.0	94.1
7	HNBN_2		90.6	99.0	98.3
8	AllylNHPh		99.7	99.8	97.8

9	CH ₃ NHPh		99.9	99.6	95.6
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^aGeneral reaction conditions: 1 mmol of furfural and 2 mmol of amine are added to 20% mw to furfural of MK10. The mixture conducted in a Syntos 3000 microwave oven (Anton-Paar) at 60°C for 5 min. ^bPercent yield calculated from GC/MS data.

The 2,4-diamino cyclopent-2-enone, by-product observed in the cyclization reaction of furfural, is performed at room temperature or in the absence of a catalyst (Table 1, entries 1 and 6) after long time reaction. As previously observed [57,58], the conversion of 4,5-diamino cyclopentenone to 2,4-diamino cyclopentenone, performed in the presence of an excess of amine. To investigation the catalytic activity of MK10 and its selectivity, we tested the performance of 4,5-*trans*-dimorpholinocyclopent-2-enone in the presence of a small amount of morpholine to obtain the 2,4-dimorpholinocyclopent-2-enone (Scheme 2).



Scheme 2. Synthesis of 2,4-dimorpholinocyclopent-2-enone.

Adding amine (0.2 mmol) to the reaction mixture at room temperature without microwave irradiation, we observed that the product 4,5-dimorpholinocyclopentenone is converted into the respective 2,4-cyclopentenone derivative after only one hour. The mechanism of reaction is proposed by Lewis and Mulquiney [74].

3. Materials and Methods

3.1. General Methods

All chemicals and solvents were purchased from common commercial sources and were used as received without any further purification. Montmorillonite K10 clay obtained from Aldrich, has the following chemical composition (wt%) SiO₂: 67.6; Al₂O₃: 14.6; Fe₂O₃: 2.9; MgO: 1.8.

All reactions were monitored by GC-MS. The GC-MS Shimadzu workstation was constituted by a GC 2010 (equipped with a 30 m-QUADREX 007-5MS capillary column, operating in the “split” mode, 1 mL min⁻¹ flow of He as carrier gas).

Proton nuclear magnetic resonance (¹H-NMR) spectra were recorded on a Bruker spectrometer at 300 MHz. Chemical shifts are reported in δ units (ppm) with tetramethylsilane (TMS) as reference (δ 0.00). All coupling constants (*J*) are reported in Hertz. Multiplicity is indicated by one or more of the following: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet). Carbon nuclear magnetic resonance (¹³C-NMR) spectra were recorded on a Bruker at 75 MHz. Chemical shifts are reported in δ units (ppm) relative to CDCl₃ (δ 77.0).

MW-assisted reactions were performed on a Synthos 3000 instrument from Anton Paar, equipped with a 4 × 24MG5 Rotor and an IR probe used for external temperature control.

3.2. General Experimental Procedure for Microwave-Assisted Cyclization rearrangement of furfural and amines.

The morpholine (2 mmol) was added to a stirred solution of furfural (1 mmol) and MK10 (20 mg). The resulting mixture was reacted for 5 min in a Synthos 3000 microwave instrument, fixed on the temperature value of 60 °C (IR Limit). After completion of the reaction (monitored by GCMS), the MK10 was separated from the reaction mixture by filtration and washed with ethyl acetate (3 mL) for four times. The products were isolated after evaporation of the solvent to afford compounds in 90-99 % yields. Spectral data were in accordance with the literature [57].

The reaction of morpholine with furfural was scaled up to grams using 20 mmol of furfural and 40 mmol of morpholine with amount corresponding of MK10. After completion of the reaction and separation of MK10, the product were obtained with a yield of 97%.

3.3. General protocol for the synthesis of 2,4-dimorpholinecyclopent-2-enones.

After performed the 4,5-trans-dimorpholinocyclopent-2-enone as the reported procedure, to reaction mixture we added 0,2 mmol of morpholine and kept at room temperature for further 1 hour. After completion, ethyl acetate was added (3 mL), the catalyst was filtrate and the product isolate after evaporation of the solvent to afford 2,4-dimorpholinecyclopent-2-enone in 99 % yields. Spectral data were in accordance with the literature [57].

3.4. Catalyst recycling

After completion of the reaction (monitored by GCMS), the MK10 was separated from the reaction mixture by a rapid filtration and washed with ethyl acetate (3 mL) for four times and dried in a oven.

The MK10 obtained is further evaluated in the cyclization reaction of furfural and morpholine. As shown in Fig. 1, after 4 runs, the selectivity still retains above 99%, and the conversion is only slightly decreased.

4. Conclusions

An effective procedure for the synthesis of *trans*-4,5-diamino-cyclopent-2-enones has been developed. The reaction showed high conversion and selectivity.

The use of MK10 under MW irradiation is a valuable method of heterogeneous catalyst respect to the previously reported procedure: the performance don't allows the use of solvent, the reaction times are very short and a greater selectivity in the rearrangement process, thus avoiding the formation of by-products.

Moreover, other advantages of this method are the use of a heterogeneous catalysts recycling and stable after next run. MK10 was reused for three consecutive cycles without any significant loss in catalytic activity in the synthesis of *trans*-4,5-dimorpholine-cyclopent-2-enone.

Supplementary Materials: The following are available online at www.mdpi.com/link.

Author Contributions: M.N. and A.P. conceived and designed the experiments; S.B. and P.C. performed the experiments; A.D.N., M.L.D.G. and M.O. analyzed the data; A.D.N. and A.P. contributed reagents/materials/analysis tools; M.N., M.L.D.G. and A.P. wrote the paper.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Thomas, J. M.; Raja, R.; Lewis, D. W. Single-site heterogeneous catalysts. *Angew. Chem. Int. Ed.* **2005**, *44*, 6456. DOI:10.1002/ANIE.200462473.

2. Ballini, R.; Bosica, G.; Carloni, L.; Maggi, R.; Sartori, G. Zeolite HSZ-360 as a new reusable catalyst for the direct acetylation of alcohols and phenols under solventless conditions. *Tetrahedron Lett.* **1998**, *39*, 6049–6052.
3. Procopio, A.; De Luca, G.; Nardi, M.; Oliverio, M.; Paonessa, R. General MW-assisted grafting of MCM-41: Study of the dependence on time dielectric heating and solvent. *Green Chem.*, **2009**, *11*, 770–773. DOI: 10.1039/B820417A.
4. Procopio, A.; Cravotto, G.; Oliverio, M.; Costanzo, P.; Nardi, M.; Paonessa, R. An Eco-Sustainable Erbium(III)-Catalysed Method for Formation/Cleavage of O-tert-butoxy carbonates. *Green Chem.*, **2011**, *13*, 436–443. DOI: 10.1039/C0GC00728E.
5. Oliverio, M.; Costanzo, P.; Macario, A.; De Luca, G.; Nardi, M.; Procopio, A. A Bifunctional Heterogeneous Catalyst Erbium-Based: A Cooperative Route Towards C-C Bond Formation. *Molecules*, **2014**, *19*, 10218–10229. DOI:10.3390/molecules190710218.
6. Procopio, A.; Das, G.; Nardi, M.; Oliverio, M.; Pasqua, L.; A Mesoporous Er(III)-MCM-41 Catalyst for the Cyanosilylation of Aldehydes and Ketones under Solvent-free Conditions. *ChemSusChem*, **2008**, *1*, 916–919. DOI: 10.1002/cssc.200800183.
7. K. Mikami, *Green Reaction Media in Organic Synthesis*, Blackwell, 2005.
8. W. M. Nelso, *Green Solvents for Chemistry Perspectives and Practice*, Oxford University Press, **2004**.
9. Lindström, U.M. Stereoselective Organic Reactions in Water. *Chem. Rev.* **2002**, *10*, 2751–2772.
10. Procopio, A.; Gaspari, M.; Nardi, M.; Oliverio, M.; Tagarelli, A.; Sindona, G. Simple and efficient MW-assisted cleavage of acetals and ketals in pure water. *Tetrahedron Lett.* **2007**, *48*, 8623–8627.
11. Procopio, A.; Gaspari, M.; Nardi, M.; Oliverio, M.; Rosati, O. Highly efficient and versatile chemoselective addition of amines to epoxides in water catalyzed by erbium(III) triflate *Tetrahedron Lett.* **2008**, *49*, 2289–2293.
12. Simon, M.O.; Li, C.J. Green chemistry oriented organic synthesis in water. *Chem. Soc. Rev.* **2012**, *41*, 1415–1427.
13. Oliverio, M.; Costanzo, P.; Paonessa, R.; Nardi, M.; Procopio, A. Catalyst-free tosylation of lipophilic alcohols in water *RSC Advances*, **2013**, *3*(8), 2548–2552.
14. Nardi, M.; Herrera Cano, N.; Costanzo, P.; Oliverio, M.; Sindona, G.; Procopio, A. Aqueous MW eco-friendly protocol for amino group protection. *RSC Adv.* **2015**, *5*, 18751–18760.
15. Nardi, M.; Di Gioia, M.L.; Costanzo, P.; De Nino, A.; Maiuolo, L.; Oliverio, M.; Olivito, F.; Procopio, A. Selective acetylation of small biomolecules and their derivatives catalyzed by Er(OTf)₃. *Catalysts*, **2017**, *7*, 269–282.
16. Abbott, A.P.; Davies, D.L.; Capper, G.; Rasheed, R.K.; Tambyrajah, V. Ionic Liquids and Their Use As solvents. U.S. Patent, 7,183,433, 27 February 2007.
17. Di Gioia, M.L.; Barattucci, A.; Bonaccorsi, P.; Leggio, A.; Minuti, L.; Romio, E.; Temperini, A.; Siciliano, C. Deprotection/reprotection of the amino group in α -amino acids and peptides. A one-pot procedure in [Bmim][BF₄] ionic liquid. *RSC Adv.* **2014**, *4*, 2678–2686.
18. Efficient organocatalyst supported on a simple ionic liquid as a recoverable system for the asymmetric diels-alder reaction in the presence of water *ChemCatChem* **2015**, *7*(5), 830–835.
19. Di Gioia, M.L.; Gagliardi, A.; Leggio, A.; Leotta, V.; Romio, E.; Liguori, A. N-Urethane protection of amines and amino acids in an ionic liquid. *RSC Adv.* **2015**, *5*, 63407–63420.
20. Di Gioia, M.L.; Costanzo, P.; De Nino, A.; Maiuolo, L.; Nardi, M.; Olivito, F.; Procopio, A. Simple and efficient Fmoc removal in ionic liquid. *RSC Adv.* **2017**, *7*, 36482–36491.
21. 2Abbott, A.P.; Capper, G.; Davies, D.L.; Rasheed, R.K.; Tambyrajah, V. Novel solvent properties of choline chloride/urea mixtures. *Chem. Commun.* **2003**, 70–71.
22. Gorke, J.T.; Srien, F.; Kazlauskas, R.J. Hydrolase-catalyzed biotransformations in deep eutectic solvents. *Chem. Commun.* **2008**, *10*, 1235–1237.
23. Smith, E.L.; Abbott, A.P.; Ryder, K.S. Deep Eutectic Solvents (DESs) and their applications *Chem. Rev.* **2014**, *114*, 11060–11082;
24. Paiva, A.; Craveiro, R.; Aroso, I.; Martins, M.; Reis, R.L.; Duarte, A.R.C. Natural deep eutectic solvents—Solvents for the 21st century. *ACS Sustainable Chem. Eng.* **2014**, *2*, 1063–1071.
25. Virot, M.; Tomao, V.; Ginies, C.; Chemat, F. Total lipid extraction of food using d-limonene as an alternative to n-hexane. *Chromatographia* **2008**, *68*, 311–313.
26. Lapkin, A.; Plucinski, P.K.; Cutler, M. Comparative assessment of technologies for extraction of artemisinin. *J. Nat. Prod.* **2006**, *69*, 1653–1664.

27. Pereira, C. S. M.; Silva, V. M. T. M.; Rodrigues, A. E. Ethyl lactate as a solvent: Properties, applications and production processes. *Green Chem.*, **2011**, *13*, 2658-2671.
28. García, J. I.; García-Marín, H.; Pires, E. Glycerol based solvents: synthesis, properties and applications. *Green Chem.*, **2014**, *16*, 1007-1033
29. Nardi, M.; Oliverio, M.; Costanzo, P.; Sindona, G.; Procopio, A. Eco-friendly stereoselective reduction of α,β -unsaturated carbonyl compounds by $\text{Er}(\text{OTf})_3/\text{NaBH}_4$ in 2-MeTHF. *Tetrahedron* **2015**, *71*, 1132-1135.
30. Nardi, M.; Herrera Cano, N.; De Nino, A.; Di Gioia, M.L.; Maiuolo, L.; Oliverio, M.; Santiago, A.; Sorrentino, D.; Procopio, A. An eco-friendly tandem tosylation/Ferrier *N*-glycosylation of amines catalyzed by $\text{Er}(\text{OTf})_3$ in 2-MeTHF. *Tetrahedron Lett.* **2017**, *58*, 1721-1726.
31. Ješelnik, M.; S. Varma, R.; Polanca, S.; Kocevar M. Catalyst-free reactions under solvent-free conditions: microwave-assisted synthesis of heterocyclic hydrazones below the melting points of neat reactants *Chem. Commun.*, **2001**, 1716-1717
32. Procopio, A.; Dalpozzo, R.; De Nino, A.; Maiuolo, L.; Nardi, M.; Russo, B. Synthesis of Acetonides from Epoxides Catalyzed by Erbium(III) Triflate *Adv. Synth. Catal.* **2005**, *347*, 1447 - 1450.
33. Procopio, A.; De Nino, A.; Nardi, M.; Oliverio, M.; Paonessa, R.; Pasceri, R. A New Microwave-Assisted Organocatalytic Solvent-Free Synthesis of Optically Enriched Michael Adducts *Synlett* **2010**, *12*, 1849-1853.
34. Procopio, A.; Costanzo, P.; Curini, M.; Nardi, M.; Oliverio, M.; Paonessa, R. An Eco-Sustainable Erbium(III) Triflate Catalyzed Formation and Cleavage of *tert*-Butyl Ethers *Synthesis*, **2011**, 73-78.
35. Oliverio, M.; Costanzo, P.; Nardi, M.; Calandruccio, C.; Salerno, R.; Procopio, A. Tunable microwave-assisted method for the solvent-free and catalyst-free peracetylation of natural products. *Beilstein. J. Org. Chem.* **2016**, *12*, 2222-2233.
36. Maiuolo, L.; Merino, P.; Algieri, V.; Nardi, M.; Di Gioia, M.L.; Russo, B.; Delso, I.; Tallarida, M.A.; De Nino, A. Nitrones and nucleobase-containing spiro-isoxazolidines derived from isatin and indanone: Solvent-free microwave-assisted stereoselective synthesis and theoretical calculations *RSC Adv.* **2017**, *7*, 48980-48988.
37. T. J. Mason Sonochemistry: current uses and future prospects in the chemical and processing industries *Phil. Trans. R. Soc. Lond. A*, **1999**, *357*, 355-369.
38. Kappe, O. Controlled microwave heating in modern organic synthesis. *Angew. Chem. Int. Ed.* **2004**, *43*, 6250-6284;
39. Desai, KR. *Green Chemistry Microwave Synthesis 1st ed.*; Himalaya Publication House: New Delhi, India, **2005**; 20.
40. Cravotto, G.; Cintas P. The combined use of microwaves and ultrasound: improved tools in process chemistry and organic synthesis *Chem. Eur. J.* **2007**, *13*, 1902 - 1909
41. De Nino, A.; Maiuolo, L.; Merino, P.; Nardi, M.; Procopio, A.; Roca-López, D.; Russo, B.; Algieri, V. Efficient organocatalyst supported on a simple ionic liquid as a recoverable system for the asymmetric diels-alder reaction in the presence of water, *ChemCatChem*, **2015**, *7*, 5, 830-835
42. Bortolini, O.; D'Agostino, M.; De Nino, A.; Maiuolo, L.; Nardi, M.; Sindona, G. Solvent-free, microwave assisted 1,3-cycloaddition of nitrones with vinyl nucleobases for the synthesis of N,O-nucleosides *Tetrahedron*, **2008**, *64*(35), 8078-8081
43. Procopio, A.; Gaspari, M.; Nardi, M.; Oliverio, M.; Romeo, R. MW-assisted $\text{Er}(\text{OTf})_3$ -catalyzed mild cleavage of isopropylidene acetals in Tricky substrates *Tetrahedron Letters*, **2008**, *49*(12), 1961-1964.
44. Oliverio, M.; Nardi, M.; Cariati, L.; Vitale, E.; Bonacci, S.; Procopio, A. "on Water" MW-Assisted Synthesis of Hydroxytyrosol Fatty Esters *ACS Sustainable Chem. Eng.* **2016**, *4*, 661-665
45. Maiuolo, L.; De Nino, A.; Algieri, V.; Nardi, M. Microwave-assisted 1,3-dipolar cyclo-addition: Recent advances in synthesis of isoxazolidines *Mini-Reviews in Organic Chemistry* **2017**, *14*(2), 136-142.
46. Summerton, L.; Sneddon, H.F.; Jones, L.C.; Clark, J.H *Green and Sustainable Medicinal Chemistry: Methods, Tools and Strategies for the 21st Century Pharmaceutical Industry* Royal Society of Chemistry **2016**.
47. Nardi, M.; Bonacci, S.; De Luca, G.; Maiuolo, J.; Oliverio, M.; Sindona, G.; Procopio, A. Biomimetic synthesis and antioxidant evaluation of 3,4-DHPEA-EDA

- [2-(3,4-hydroxyphenyl) ethyl (3S,4E)-4-formyl-3-(2-oxoethyl)hex-4-enoate], *Food Chemistry*, **2014**, *162*, 89-93.
48. Nardi, M.; Bonacci, S.; Cariati, L.; Costanzo, P.; Oliverio, M.; Sindona, G.; Procopio, A. Synthesis and antioxidant evaluation of lipophilic oleuropein aglycone derivatives *Food and Function*, **2017**, *8*, 12, 4684-4692
49. Costanzo, P.; Calandruccio, C.; Di Gioia, M.L.; Nardi, M.; Oliverio, M.; Procopio, A. First multicomponent reaction exploiting glycerol carbonate synthesis, *Journal of Cleaner Production*, **2018**, *202*, 504-509
50. Li, G.; Li, N.; Zheng, M.; Li, S.; Wang, A.; Cong, Y.; Wang, X.; Zhang, T. Industrially scalable and cost-effective synthesis of 1,3-cyclopentanediol with furfuryl alcohol from lignocellulose, *Green Chem.*, **2016**, *18*, 3607-3613.
51. Griffiths, K.; Kumar, P.; Mattock, J.D.; Abdul-Sada, A.; Pitak, M.B.; Coles, S.J.; Navarro, O.; Vargas, A.; Kostakis, G.E. Efficient Ni²⁺/Ln³⁺ electrocyclicization catalysts for the synthesis of trans-4,5-diaminocyclopent-2-enones from 2-furaldehyde and primary or secondary amines, *Inorg. Chem.*, **2016**, *55*, 6988-6994.
52. Li, S.W.; Batey, R.A. Mild lanthanide (III) catalyzed formation of 4,5-diaminocyclopent-2-enones from 2-furaldehyde and secondary amines: a domino condensation/ring-opening/electrocyclization process, *Chem. Commun.* **2007**, 3759-3761.
53. Gomes, R.F.A.; Esteves, N.R.; Coelho, J.A.S.; Afonso, C.A.M. Copper (II) triflate as a reusable catalyst for the synthesis of trans-4,5-diamino-cyclopent-2-enones in water, *J. Org. Chem.* **2018**, *83*, 7509-7513.
54. Nunes, J.P.M.; Afonso, C.A.M.; Caddick, S. Synthesis of 2,4-bifunctionalised cyclopentenones from 2-furaldehyde, *RSC Adv.* **2013**, *3*, 14975-14978.
55. Procopio, A.; Costanzo, P.; Curini, M.; Nardi, M.; Oliverio, M.; Sindona, G. Erbium(III) Chloride in Ethyl Lactate as a Smart Ecofriendly System for Efficient and Rapid Stereoselective Synthesis of trans-4,5-Diaminocyclopent-2-enones. *ACS Sustain Chem Eng.* **2013**, *1*, 541-544.
56. Ramesh, D.; Reddy, T.S.; Narasimhulu, M.; Rajaram, S.; Suryakiran, N.; Mahesh, K.C.; Venkateswarlu, Y. Efficient and rapid stereoselective synthesis of trans-4,5-diaminocyclopent-2-enones by acidic ionic liquid under solvent-free conditions, *Chem. Lett.* **2009**, *38*, 586-587.
57. Nardi, M.; Costanzo, P.; De Nino, A.; Di Gioia, M.L.; Olivito, F.; Sindona, G.; Procopio, A. Water excellent solvent for the synthesis of bifunctionalized cyclopentenones from furfural, *Green Chem.*, **2017**, *19*, 5403-5411.
58. Di Gioia, M.L.; Nardi, M.; Costanzo, P.; De Nino, A.; Maiuolo, L.; Oliverio, M.; Procopio, A. Biorenewable Deep Eutectic Solvent for Selective and Scalable Conversion of Furfural into Cyclopentenone Derivatives *Molecules*, **2018**, *23*, 8, 1891-1905.
59. Estevão, M.S.; Afonso, C.A.M. Synthesis of trans-4,5-diaminocyclopent-2-enones from furfural catalyzed by Er(III) immobilized on silica, *Tetrahedron Letters* **2017**, *58*, 302-304
60. Estevão, M.S.; Martins, R.J.V.; Afonso, C.A.M. Synthesis of trans-4,5-bis-dibenzylaminocyclopent-2-enone from furfural catalyzed by ErCl₃·6H₂O, *J. Chem. Educ.* **2017**, *94*, 1587-1589.
61. Deng, Q.; Wang, R. Heterogeneous MOF catalysts for the synthesis of trans-4,5-diaminocyclopent-2-enones from furfural and secondary amines *Catalysis Communication*, **2019**, *120*, 11-16.
62. Bhattacharyya, K. G.; Gupta, S. S. Adsorption of a few heavy metals on natural and modified kaolinite and montmorillonite: A review *Adv. Colloid Interface Sci.* **2008**, *140*, 114-131.
63. Kaur, N.; Kishore, D. Montmorillonite: an efficient, heterogeneous and green catalyst for organic synthesis. *J. Chem. Pharm. Res.* **2012**, *4*, 991-1015.
64. Kumar, B.S.; Dhakshinamoorthy, A.; Pitchumani, K. K10 montmorillonite clays as environmentally benign catalysts for organic reactions. *Catal. Sci. Technol.*, **2014**, *4*, 2378-2396.
65. Hechelski, M.; Ghinet, A.; Brice Louvel, B.; Dufrenoy, P.; Rigo, B.; Dai'ch, A.; Waterlot, C. From Conventional Lewis Acids to Heterogeneous Montmorillonite K10: Eco-Friendly Plant-Based Catalysts Used as Green Lewis Acids *ChemSusChem* **2018**, *11*, 1249 - 1277
66. Li, J.-T., Xing, C.-Y., Li, T.-S., An efficient and environmentally friendly method for synthesis of arylmethylenemalononitrile catalyzed by Montmorillonite K10-ZnCl₂ under ultrasound irradiation. *J. Chem. Technol. Biotechnol.* **2004**, *79*, 1275-1278.
67. Nardi, M.; Cozza, A.; Maiuolo, L.; Oliverio, M.; Procopio, A. 1,5-Benzoheteroazepines through eco-friendly general condensation reactions *Tetrahedron Letters*, **2011**, *52* (38), 4827-4834.

68. Nardi, M.; Cozza, A.; De Nino, A.; Oliverio, M.; Procopio, A. One-pot synthesis of dibenzo[b,e][1,4]diazepin-1-ones. *Synthesis* **2012**, *44*, 800–804.
69. Oliverio, M.; Costanzo, P.; Nardi, M.; Rivalta, I.; Procopio, A. Facile ecofriendly synthesis of monastrol and its structural isomers via biginelli reaction. *ACS Sustain. Chem. Eng.* **2014**, *2*, 1228–1233
70. Herrera Cano, N.; Uranga, J.G.; Nardi, M.; Procopio, A.; Wunderlin, D.A.; Santiago, A.N. Selective and eco-friendly procedures for the synthesis of benzimidazole derivatives. The role of the Er(OTf)₃ catalyst in the reaction selectivity, *Beilstein J. Org. Chem.* **2016**, *12*, 2410–2419.
71. De Nino, A.; Maiuolo, L.; Nardi, M.; Pasceri, R.; Procopio, A.; Russo, B. Development of one-pot three component reaction for the synthesis of N'-aryl-N-cyanoformamidines, essential precursors of formamidine pesticides family *Arabian Journal of Chemistry*, **2016**, *9*, 1, 32-37
72. Costanzo, P.; Bonacci, S.; Cariati, L.; Nardi, M.; Oliverio, M.; Procopio, A. Simple and efficient sustainable semi-synthesis of oleacein [2-(3,4-hydroxyphenyl) ethyl (3S,4E)-4-formyl-3-(2-oxoethyl)hex-4-enoate] as potential additive for edible oils *Food Chemistry*, **2018**, *245*, 410-414.
73. Paonessa, R.; Nardi, M.; Di Gioia, M.L.; Olivito, F.; Oliverio, M., Procopio, A. Eco-friendly synthesis of lipophilic EGCG derivatives and antitumor and antioxidant evaluation *Natural product communications*, **2018**, *9*, 1117-1122
74. K. G. Lewis and C. E. Mulquiney, Aspects of the formation and use of stenhose salts and related compounds, *Tetrahedron*, **1977**, *33*, 463-475.