



Organic Preparations and Procedures International

The New Journal for Organic Synthesis

ISSN: 0030-4948 (Print) 1945-5453 (Online) Journal homepage: https://www.tandfonline.com/loi/uopp20

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To cite this article: Zakaria Benzekri, Sara Sibous, Houda Serrar, Said Boukhris, Amina Hassikou, Rachida Ghailane & Abdelaziz Souizi (2019): Efficient Synthesis of 1,4-Dihydropyrano[2,3c]pyrazoles Using Snail Shell as a Biodegradable and Reusable Catalyst, Organic Preparations and Procedures International, DOI: 10.1080/00304948.2019.1677991

To link to this article: https://doi.org/10.1080/00304948.2019.1677991



Published online: 05 Nov 2019.

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Efficient Synthesis of 1,4-Dihydropyrano[2,3c]pyrazoles Using Snail Shell as a Biodegradable and Reusable Catalyst

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The 4H-pyranopyrazoles are an important class of heterocyclic compounds due to their pharmacological and biological properties.¹ Compounds bearing the pyranopyrazole system have been found to have various biological activities, for instance antimicrobial,² anti-cancer³ and anti-inflammatory properties,⁴ analgesic activity,⁵ activity as hypoglycemic,³ hypotensive,⁶ and vasodilatory agents,⁷ inhibitory activity toward human Chk1 kinase,⁸ molluscicidal activity⁹ and antifungal properties.¹⁰ In addition, such heterocycles bearing 4H-pyran units are important precursors in the synthesis of a large family of medicinally useful compounds.¹¹

One-pot, multicomponent reactions (MCRs) are synthetically powerful, owing to their short reaction times, high efficiencies and unique selectivities.¹² They can form several chemical bonds simultaneously^{13–14} and have emerged as an efficient tool in organic and medicinal chemistry.^{15–16} They are well suited for the synthesis of valuable heterocyclic compounds.¹⁷

A number of synthetic approaches have been made for the synthesis of 1,4-dihydropyranopyrazoles using CAPB,¹⁸ CTACl,¹⁹ MDOs,²⁰ urea,²¹ amberlyst-A21,²² piperidine, ²³ [Dsim]AlCl₄,²⁴ isonicotinic acid,²⁵ EDDF,²⁶ triethylamine,²⁷ 1-butyl-3-methylimidazolium tetrafluoroborate,²⁸ Ba(OH)₂,²⁹ L-proline,³⁰ γ -alumina,³¹ per-6-amino- β -cyclodextrin,³² molecular sieves,³³ NaBr,³⁴ β -CD,³⁵ polystyrene supported p-toluenesulfonic acid,³⁶ ZrO₂-NPs,³⁷ NFS-PWA,³⁸ DES,³⁹ PPI⁴⁰ and Fe-CaOx/glutamic acid.⁴¹

Despite considerable progress, the need for the greener synthesis of biologically active molecules has emerged. The use of natural catalysts in organic synthesis offers many advantages in sustainable chemistry because the catalysts are inexpensive, readily available, non-toxic and show high selectivity.

In continuation of our interest in the development of synthetic methodologies for organic transformations,^{42–55} We now report on the use of snail shell, abundant in Morocco, as a natural catalyst. In the present work, we describe the synthesis of 1,4-dihydropyrano[2,3-c]pyrazoles using snail shell as a biocatalyst (*Scheme 1*).

Received June 1, 2018; in final form July 19, 2019.

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Scheme 1. Synthesis of 1,4-dihydropyrano[2,3-c]pyrazoles 5a-k in the presence of snail shell.

Snail shells are widely available as waste products in Morocco. Snail shells were collected, cleaned, and dried in an oven at 100 °C for 24h. The shells, thus obtained without resorting to expensive calcination, were crushed into a white soft powder. The latter material has been fully characterized by X-ray diffraction, by scanning electron microscopy, by FT-IR and by measuring the specific surface area.⁵²

To study the catalytic activity of the snail shell powder in the synthesis of dihydropyranopyrazoles, we began the process of optimization of reaction conditions. For this, we chose a four-component condensation reacting *p*-chloro benzaldehyde **1a**, malononitrile **2**, ethyl acetoacetate **3**, and hydrazine **4** as a model reaction. We used different solvents and various amounts of the catalyst at room temperature (*Scheme 1*). No product formation was observed when the mixture was stirred in ethanol in the absence of snail shell, even after 180 min (*Table 1*, entry 1).

We sought to find the effect of different solvents (MeOH, EtOH, CH₃CN, butanol, AcOEt, THF and DMF) for the four component coupling protocol (*Table 1*). The reaction using MeOH or EtOH gave the corresponding product **5a** (Ar = 4-ClC₆H₄) in high yields (*Table 1*, entries 10, 11). From the environmental point of view, EtOH was chosen as the reaction medium for all further reactions. Different masses of snail shell were then used at room temperature. From the results, it is clear that the best amount of catalyst for this reaction at 1 mmole scale in the given conditions is 0.05 g (*Table 1*, entry 11).

It is fundamental to examine the evolution turnover number (TON) and turnover frequency (TOF) as a function of the catalyst mass used, for the pilot reaction. *Table 1* presents these values.

The separation of the catalyst and isolation of the desired product from the reaction mixture is one of the most crucial aspects of organic synthesis. In our protocol, after completion of the reaction, the crude mixture was dissolved in EtOH (2 mL), and the catalyst was recovered by simple filtration, washed with ethanol and dried. For this purpose, the reusability of the catalyst was tested for the synthesis of **5a** applying the developed protocol. The catalyst was found to be reusable for at least ten cycles without any severe loss of activity (*Table 2*).

We also investigated the structural stability of the snail shell catalyst by comparing its FT-IR spectra before and after the synthesis of dihydropyrano[2,3-c]pyrazole **5a**. We could see that these spectra were nearly identical, indicating that the snail shell was structurally stable under the applied reaction conditions; and the spectra remained similar through ten catalytic cycles.

We examined the scope of our procedure, and the results are presented in *Table 3*. The condensation of aldehydes **1** with malononitrile **2**, ethyl acetoacetate **3**, and hydrazine provided the corresponding 1,4-dihydropyrano[2,3-c]pyrazoles **5a-k** with remarkable time savings (8-30 min), excellent yields (90-99%) and high purities.

Based on the obtained results and the literature survey, we suggest a mechanism for these reactions using our catalyst (*Scheme 2*).

Entry	Catalyst (g)	Solvent (1 mL)	Time (min) ^b	TON	TOF	Yield (%) ^c
1	_	EtOH	180			Trace
2	0.15	EtOH	10	64	376,47	96
3	0.15	MeOH	10	64.67	380.41	97
4	0.15	Butanol	10	48.67	286.29	73
5	0.15	THF	10	50.67	298.05	76
6	0.15	AcOEt	7	55.33	472.90	83
7	0.15	DMF	15	46	184	69
8	0.15	CH ₃ CN	10	56.67	333.35	85
9	0.02	MeOH	15	185	740	37
10	0.05	MeOH	15	196	784	98
11	0.05	EtOH	15	194	776	97
12	0.1	MeOH	15	97	388	97
13	0.1	EtOH	15	96	384	96
14	0.2	EtOH	15	47.5	190	95
15	0.25	EtOH	20	36	109.09	90

 Table 1

 Screening of the Reaction Conditions for the Synthesis of 5a^a

^aReaction conditions: p-chlorobenzaldehyde (1a, 1 mmol), malononitrile (2, 1 mmol), ethyl acetoacetate (3, 1 mmol) and hydrazine hydrate (4, 1 mmol), snail shell (50 mg), r.t.

^bTime reported in min monitored by thin layer chromatography (TLC).

^cIsolated yield.



Scheme 2. A plausible mechanism for the formation of 1,4-dihydropyrano[2,3-c]pyrazoles 5.

Given the well-documented ease of formation of pyrazolones,⁵⁹ it seems likely that pyrazolone **A** is easily formed by the condensation of hydrazine and ethyl acetoacetate. As previously known, aragonite is plentiful in our catalyst.⁵² Thus the carbonate ion in aragonite catalyzes the Knoevenagel condensation of malononitrile and an aldehyde (potentially activated by Ca^{2+} of the catalyst) to form arylidenemalononitrile as the

Run ^a	Yield $(\%)^{b}$
1	98
2	96
3	94
4	91
5	90
6	87
7	85
8	84
9	84
10	83

 Table 2

 Reusability of Snail Shell Biocatalyst for the Synthesis of Compound 5a

^aTypically, 48 mg of catalyst was recovered from an individual run.

^bIsolated yields.

Table 3Synthesis of Compounds 5a-k

					M.p (°C)	
Entry	Product	Ar	Time (min)	Yield %	Obs.	Lit.
1	5a	$4-ClC_6H_4$	15	98	244-246	244-246 ^{36,56}
2	5b	$2-ClC_6H_4$	20	92	144-146	144-146 ^{36,56}
3	5c	4-MeC ₆ H ₄	20	96	175-177	175-177 ³⁶
4	5d	4-MeOC ₆ H ₄	20	94	211-213	211-213 ³⁶
5	5e	$4-NO_2C_6H_4$	8	99	250-252	250-252 ^{56,57}
6	5 f	$2,4-Cl_2C_6H_3$	20	91	229-230	229-230 ⁵⁷
7	5g	C_6H_5	15	92	164-166	164-166 ³⁶
8	5h	2-furyl	30	90	176-178	176-178 ³⁶
9	5i	$3-NO_2C_6H_4$	10	96	213-215	214-216 ^{56,57}
10	5ј	$4-HOC_6H_4$	12	95	222-224	223-225 ⁵⁸
11	5k	$4-N(Me)_2C_6H_4$	15	96	167-169	168-169 ⁵⁸

^aIsolated yields.

intermediate **B**. Next, the Michael addition of the enolized pyrazolone to the arylidenmalononitrile is carried out to produce the intermediate **C**. Finally, the corresponding product is formed by tautomerization of the intermediate \mathbf{C} .⁶⁰

It is useful to compare the catalytic activity of our catalyst with those reported in the literature.^{39,40,58,61–65} We find that our catalytic system is noteworthy in terms of short time and high efficiency (*Table 4*).

In summary, a catalyst derived from snail shells proved to be extremely effective in the four-component synthesis of pyranopyrazole derivatives *via* the one-pot reaction of aromatic aldehydes, ethyl acetoacetate, hydrazine, and malononitrile. The merits for the presented methodology are its biodegradability, excellent product yields, short reaction times and ease of product isolation.

		Time	Yield
Catalyst	Conditions	(min)	(%)
SiO ₂ NPs ⁶¹	10 mol %, 5 mL H ₂ O, 80 °C	30-40	87-94
NH ₄ H ₂ PO ₄ /Al ₂ O ₃ ⁶²	0.03 g, 3 mL EtOH, reflux	15-20	74-91
Nano-CuFe ₂ O ₄ ⁶³	8 mol %, 5 mL H ₂ O, 60 °C	120-180	88-97
NMPs ⁶⁴	0.007 g, solvent-free, r.t	15-90	85-98
NMIL ⁶⁵	2 mg, H ₂ O, 60 °C	8-15	90-98
$Ca_{9.5} Mg_{0.5}(PO_4)_{5.5}F_{1.5}^{58}$	2 mol %, 8 mL H ₂ O-EtOH (1:1), 70 °C	40-150	73-91
DES ³⁹	5 mL, 80 °C	20	71-91
PPI ⁴⁰	20 mol%, 5 mL EtOH, reflux	5-40	52-96
Snail shell	0.05 g, 1 mL EtOH, r.t	8-30	90-99

 Table 4

 Comparison of Our Studies with Reported Works

Experimental Section

All the chemicals used were purchased from Sigma-Aldrich and were used as received. All products are known, and were identified by comparison of spectral and physical data with the literature. Melting points were taken on a KOFLER hot stage apparatus and are uncorrected. Powder X-ray diffraction (XRD) measurements were performed using a panalytical x'pert pro diffractometer. Scans were taken with a 2θ with an increment of 0.03° ranging from 10° to 90° using Cu K α radiation source generated at 45 kV and 40 mA. Please see our previous work⁵² for the complete physical characterization of the catalyst. Data are available from the corresponding author upon request. Elemental analyses were performed on a Perkin Elmer 2400 Serie II CHNS/O microanalyzer. FTIR spectra were recorded on an Equinox 55 spectrometer. ¹H NMR spectra were recorded on a Bruker 300-MHz spectrometer in DMSO-d₆.

Typical Procedure for the Preparation of Snail Shell Catalyst (Aragonite)

Snail shells, products from cuisine, were collected, cleaned, and dried at 100 °C for 24h. The shells obtained, without calcinations, were crushed into white soft powder. It is important to note that good activity was obtained without the costly process of calcination.

General Procedure for the Synthesis of 1,4-dihydropyrano[2,3-c]pyrazoles 5a-k

To a solution of aldehyde 1 (1 mmol), malononitrile 2 (1 mmol), ethyl acetoacetate 3 (1 mmol) and hydrazine hydrate 4 (1 mmol) in EtOH (1 mL), was added the snail shell catalyst (0.05 g). The mixture was then stirred at room temperature. The progress of the reaction was monitored by TLC (Solid phase: silica gel. Eluent: ethyl acetate:n-hexane, 2:8, v:v). After completion of the reaction, the crude mixture was dissolved in EtOH (2 mL), and the catalyst was recovered by filtration. The filtrate was cooled in ice water. The resulting solid precipitate was recrystallized from ethanol to give pure 1,4-dihydropyrano[2,3-c]pyrazoles **5a-k** in high yields. All products prepared are known compounds and identified by comparison of their ¹H NMR spectra and melting points with authentic samples reported in literature.^{36,56,57} In order to recover the catalyst, the filtrate was dried under

reduced pressure, and the recovered catalyst was washed with ethanol (2 mL) and reused after drying. Typically, 48 mg of catalyst was recovered from an individual run.

6-Amino-4-(4-chlorophenyl)-3-methyl-2,4-dihydropyrano[2,3-c]pyrazole-5carbonitrile (5a)

¹H NMR (300 MHz, DMSO-d₆) δ ppm 12.10 (s, 1H, NH), 7.20-7.22 (d, 2H, J = 8.40 Hz, Ar-H), 7.36-7.38 (d, 2H, J = 8.40 Hz, Ar-H), 6.79 (s, 2H, NH₂), 4.52 (s, 1H, CH), 1.76 (s, 3H, CH₃).

Anal. Calcd for $C_{14}H_{11}ClN_4O$: C, 58.62; H, 3.90; N, 19.53. Found: C, 58.62; H, 3.88; N, 19.56.

6-Amino-4-(2-chlorophenyl)-3-methyl-2,4-dihydropyrano[2,3-c]pyrazole-5carbonitrile (5b)

¹H NMR (300 MHz, DMSO-d₆): δ ppm 11.98 (s, 1H, NH), 7.16-7.24 (m, 1H, Ar-H), 7.28-7.34 (m, 2H, Ar-H), 7.40 (dd, 1H, J = 6.9, 0.9 Hz, Ar-H), 6.71 (s, 2H, NH₂), 5.06 (s, 1H, CH), 1.75 (s, 3H, CH₃).

Anal. Calcd for $C_{14}H_{11}CIN_4O$: C, 58.65; H, 3.87; N, 19.54. Found: C, 58.46; H, 3.79; N, 19.73.

6-Amino-3-methyl-4-(p-tolyl)-2,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (5c)

¹H NMR (300 MHz, DMSO-d₆): δ ppm 12.05 (s, 1H, NH), 6.98 (d, 2H, J = 8.4 Hz, Ar–H), 7.12 (d, 2H, J = 7.6 Hz, Ar–H), 6.79 (s, 2H, NH₂), 4.51 (s, 1H, CH), 2.24 (s, 3H, CH₃), 1.76 (s, 3H, CH₃).

Anal. Calcd for $C_{15}H_{14}N_4O$: Calculated. C 67.65, H 5.32, N 21.05; found C 67.64, H 5.30, N 21.03.

6-Amino-4-(4-methoxyphenyl)-3-methyl-2,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (5d)

¹H NMR (300 MHz, DMSO-d₆): δ ppm 12.06 (s, 1H, NH), 7.30-7.32 (d, 2H, J = 7.96 Hz, Ar-H), 7.76-7.78 (d, 2H, J = 8.67 Hz, Ar-H), 6.61 (s, 2H, NH₂), 4.51 (s, 1H, CH), 3.80 (s, 3H, OCH₃), 1.76 (s, 3H, CH₃).

Anal. Calcd for $C_{15}H_{14}N_4O_2$: C, 63.82; H, 5.00; N, 19.85. Found: C, 63.77; H, 5.07; N, 19.65.

6-Amino-3-methyl-4-(4-nitrophenyl)-2,4-dihydropyrano[2,3-c]pyrazole-5carbonitrile (5e)

¹H NMR (300 MHz, DMSO-d₆): δ ppm 11.69 (s, 1H, NH), 7.68-7.97 (d, 2H, J = 8.48 Hz, Ar-H), 8.21-8.23 (d, 2H, J = 8.48 Hz, Ar-H), 7.81 (s, 2H, NH₂), 4.74 (s, 1H, CH), 2.18 (s, 3H, CH₃).

Anal. Calcd for $C_{14}H_{11}N_5O_3$: C, 56.57; H, 3.73; N, 23.56. Found: C, 56.53; H, 3.75; N, 23.43.

6-Amino-4-(2,4-dichlorophenyl)-3-methyl-2,4-dihydropyrano[2,3-c]pyrazole-5carbonitrile (5f)

¹H NMR (300 MHz, DMSO-d₆): δ ppm 12.15 (s, 1H, NH), 7.20-7.89 (m, 3H, ArH), 6.98 (s, 2H, NH2), 5.03 (s, 1H, CH), 1.76 (s, 3H, CH₃).

Anal. Calcd for $C_{14}H_{10}Cl_2N_4O$: C, 52.36; H, 3.14; N, 17.45. Found: C, 52.02; H, 2.99; N, 17.38.

6-Amino-3-methyl-4-phenyl-2,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (5g)

¹H NMR (300 MHz, DMSO-d₆): *δ* ppm 11.95 (s, 1H, NH), 7.14-7.24 (m, 3H, Ph-H), 7.28-7.33 (m, 2H, Ph-H), 6.63 (s, 2H, NH₂), 4.57 (s, 1H, CH), 1.77 (s, 3H, CH₃).

Anal. Calcd for $C_{14}H_{12}N_4O$: C, 66.65; H, 4.79; N, 22.21. Found: C, 66.67; H, 4.75; N, 22.21.

6-Amino-4-(furan-2-yl)-3-methyl-2,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (5h)

¹H NMR (300 MHz, DMSO-d₆): δ ppm 12.14 (s, 1H, NH), 7.51 (s, 2H, NH₂), 6.15 (d, 1H, J = 3.0 Hz, furan-H), 6.37-6.39 (m, 1H, furan-H), 7.50 (t, 1H, J = 0.9 Hz, furan-H), 4.75 (s, 1H, CH), 1.95 (s, 3H, CH₃).

Anal. Calcd for $C_{12}H_{10}N_4O_2$: C, 59.50; H, 4.16; N, 23.13. Found: C, 59.70; H, 4.24; N, 23.32.

6-Amino-3-methyl-4-(3-nitrophenyl)-2,4-dihydropyrano[2,3-c]pyrazole-5carbonitrile (5i)

¹H NMR (300 MHz, DMSO-d₆): δ ppm 12.14 (1H, s, NH), 7.56 (t, 1H, J = 8.0 Hz, Ar-H), 7.61 (d, 1H, J = 7.6 Hz, Ar-H), 8.00-8.04 (m, 2H, Ar-H), 6.93 (s, 2H, NH₂), 4.61 (s, 1H, CH), 1.17 (s, 3H, CH₃).

Anal. Calcd for $C_{14}H_{11}N_5O_3$: C, 56.57; H, 3.73; N, 23.56. Found: C, 56.53; H, 3.75; N, 23.43.

6-Amino-4-(4-hydroxyphenyl)-3-methyl-2,4-dihydropyrano[2,3-c]pyrazole-5carbonitrile (5j)

¹H NMR (300 MHz, DMSO-d₆): δ ppm 12.10 (s, 1H, NH), 7.23-7.25 (d, 2H, J = 8.40 Hz, Ar–H), 7.34-7.39 (d, 2H, J = 8.40 Hz, Ar–H), 6.90 (s, 1H, OH), 6.78 (s, 2H, NH₂), 4.86 (s, 1H, CH), 1.83 (s, 3H, CH₃).

Anal. Calcd for $C_{14}H_{12}N_4O_2$: C, 62.65; H, 4.50; N, 20.87. Found: C, 62.70; H, 4.52; N, 20.88.

6-Amino-3-methyl-4-(4-N,N-dimethylanimophenyl)-2,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (5k)

¹H NMR (300 MHz, DMSO-d₆): δ ppm 11.87 (s, 1H, NH), 6.55 (d, 2H, J = 8.4 Hz, Ar-H), 6.93 (d, 2H, J = 8.4 Hz, Ar-H), 6.68 (s, 2H, NH₂), 4.55 (s, 1H, CH), 2.79 (s, 6H, CH₃), 1.81 (s, 3H, CH₃).

Anal. Calcd for $C_{16}H_{17}N_5O$: C, 65.10; H, 5.81; N, 23.70. Found: C, 65.11; H, 5.80; N, 23.72.

References

- 1. G. A. Nawwar, F. M. Abdelrazek and R. H. Swellam, Arch. Pharm., 324, 875 (1991).
- P. T. Mistry, N. R. Kamdar, D. D. Haveliwala and S. K. Patel, J. Heterocycl. Chem., 49, 349 (2012).
- J. L. Wang, D. Liu, Z. J. Zhang, S. Shan, X. Han, S. M. Srinivasula, C. M. Croce, E. S. Alnemri and Z Huang, *Proc. Natl. Acad. Sci.*, 97, 7124 (2000).
- 4. M. E. Zaki, H. A. Soliman, O. A. Hiekal and A. E. Rashad, Z Naturforsch C., 61, 1 (2006).
- 5. A. Mandour, E. El-Sawy, M. Ebaid and S. Hassan, Acta Pharm., 62, 15 (2012).
- M. E. Zaki, E. M. Morsy, F. M. Abdel-Motti and F. M. E. Abdel-Megeid, *Heterocycl. Commun.*, 10, 97 (2004).
- S. R. Mandha, S. Siliveri, M. Alla, V. R. Bommena, M. R. Bommineni and S. Balasubramanian, *Bioorg. Med. Chem. Lett.*, 22, 5272 (2012).
- N. Foloppe, L. M. Fisher, R. Howes, A. Potter, A. G. Robertson and A. E. Surgenor, *Bioorg. Med. Chem.*, 14, 4792 (2006).
- F. M. Abdelrazek, P. Metz, O. Kataeva, A. Jäger and S. F. El-Mahrouky, Arch. Pharm., 340, 543 (2007).
- M. Ramiz, I. Hafiz, S. Abdel, M. Reheim, A. M. Abdel and H. M. Gaber, J. Chin. Chem. Soc., 59, 72 (2012).
- E. S. El-Tamany, F. A. El-Shahed, B. H. Mohamed, H. El-Sayed, A. Fakher and H. M. Bellal, J. Serb. Chem. Soc., 64, 9 (1999).
- 12. A. Domling, Chem. Rev., 106, 17 (2006).
- 13. A. Dömling, W. Wang and K. Wang, Chem. Rev., 112, 3083 (2012).
- 14. Y. Han, Q. Wu, J. Sun and C. G. Yan, Tetrahedron, 68, 8539 (2012).
- 15. Tu, B. Jiang, Y. Zhang, R. Jia, J. Zhang, C. Yao and F. Shi, Org. Biomo. Chem., 5, 355 (2007).
- 16. J. P. Wan, S. F. Gan, G. L. Sun and Y. J. Pan, J. Org. Chem., 74, 2862 (2009).
- 17. P. A. Wender, S. T. Handy and D. L. Wright, Chem. Ind., 765, 767 (1997).
- 18. F. Tamaddon and M. Alizadeh, Tetrahedron Lett., 53, 3588 (2014).
- 19. M. Wu, Q. Feng, D. Wan and J. Ma, Synth. Commun., 43, 1721 (2013).
- 20. S. Muramulla and C. G. Zhao, Tetrahedron lett., 52, 3905 (2011).
- 21. G. Brahmachari and B. Banerjee, ACS Sustain. Chem. Eng., 2, 411 (2013).
- 22. M. Bihani, P. P. Bora, G. Bez and H. Askari, ACS Sustain. Chem. Eng., 1, 440 (2013).
- 23. G. Vasuki and K. Kumaravel, Tetrahedron Lett., 49, 5636 (2008).
- A. R. Moosavi-Zare, M. A. Zolfigol, E. Noroozizadeh, M. Tavasoli, V. Khakyzadeh and A. Zare, *New J. Chem.*, 37, 4089 (2013).
- M. A. Zolfigol, M. Tavasoli, A. R. Moosavi-Zare, P. Moosavi, H. G. Kruger, M. Shiri and V. Khakyzadeh, *RSC Adv.*, 3, 25681 (2013).
- 26. A. Thakur, M. Tripathi, U. C. Rajesh and D. S. Rawat, RSC Adv., 3, 18142 (2013).

- 27. Y. M. Litvinov, A. A. Shestopalov, L. A. Rodinovskaya and A. M. Shestopalov, J. Comb. Chem., 11, 914 (2009).
- 28. J. M. Khurana, B. Nand and S. Kumar, Synth. Commun., 41, 405 (2011).
- 29. S. H. S. Azzam and M. A. Pasha, Tetrahedron Lett., 53, 6834 (2012).
- H. Mecadon, M. R. Rohman, I. Kharbangar, B. M. Laloo, I. Kharkongor, M. Rajbangshi and B. L. Myrboh, *Tetrahedron Lett.*, 52, 3228 (2011).
- 31. H. Mecadon, M. R. Rohman, M. Rajbangshi and B. Myrboh, *Tetrahedron Lett*, **52**, 2523 (2011).
- 32. K. Kanagaraj and K. Pitchumani, Tetrahedron Lett., 51, 3312 (2010).
- J. B. Gujar, M. A. Chaudhari, D. S. Kawade and M. S. Shingare, *Tetrahedron Lett.*, 55, 6030 (2014).
- 34. M. N. Elinson, A. S. Dorofeev, F. M. Miloserdov and G. I. Nikishin, *Molec. Divers.*, **13**, 47 (2009).
- 35. Y. A. Tayade, S. A. Padvi, Y. B. Wagh and D. S. Dalal, Tetrahedron Lett., 56, 2441 (2015).
- M. A. Chaudhari, J. B. Gujar, D. S. Kawade, N. R. Jogdand and M. S. Shingare, *Cogent Chem.*, 1, 1063830 (2015).
- 37. A. Saha, S. Payra and S. Banerjee, Green Chem., 17, 2859 (2015).
- B. Maleki, H. Eshghi, M. Barghamadi, N. Nasiri, A. Khojastehnezhad, S. S. Ashrafi and O. Pourshiani, *Res. Chem. Intermed.*, 42, 3071 (2016).
- 39. M. R. Bhosle, L. D. Khillare, S. T. Dhumal and R. A. Mane, *Chin. Chem. Lett.*, **27**, 370 (2016).
- 40. H. Kiyani and M. Bamdad, Rev. Roum Chim., 62, 221 (2017).
- 41. K. K. Gangu, S. Maddila, S. N. Maddila and S. B. Jonnalagadda, RSC Adv., 7, 423 (2017).
- 42. Z. Benzekri, K. El Mejdoubi, S. Boukhris, B. Sallek, B. Lakhrissi and A. Souizi, *Synth. Commun.*, **46**, 442 (2016).
- 43. Z. Benzekri, H. Serrar, S. Boukhris, B. Sallek and A. Souizi, *Curr. Chem. Lett.*, **5**, 99 (2016).
- I. Bahammou, A. Esaady, S. Boukhris, R. Ghailane, N. Habbadi, A. Hassikou and A. Souizi, *Mediterr. J. Chem.*, 4, 615 (2016).
- 45. Z. Benzekri, H. Serrar, S. Sibous, S. Boukhris, A. Ouasri, A. Rhandour and A. Souizi, *Green Chem. Lett. Rev.*, **9**, 223 (2016).
- 46. Z. Benzekri, R. Benhdidou, S. Hamia, H. Serrar, S. Boukhris, B. Sallek, A. Hassikou and A. Souizi, *J. Mex. Chem. Soc.*, **61**, 217 (2017).
- Z. Benzekri, H. Serrar, S. Boukhris, A. Ouasri, A. Hassikou, A. Rhandour and A. Souizi, *Fr-Ukr. J. Chem.*, 5, 60 (2017).
- 48. S. Sibous, S. Boukhris, R. Ghailane, N. Habbadi, A. Hassikou and A. Souizi, *J. Turk. Chem. Soc.*, **4**, 1 (2017).
- 49. S. Sibous, T. Ghailane, H. Serrar, R. Ghailane, S. Boukhris and A. Souizi, *Mediterr. J. Chem.*, **6**, 53 (2017).

- Z. Benzekri, S. Hamia, R. Benhdidou, H. Serrar, S. Boukhris, A. Hassikou and A. Souizi, J. Mat. Environ. Sci., 8, 2986 (2017).
- 51. Z. Benzekri, H. Serrar, S. Boukhris and A. Souizi, J. Turk. Chem. Soc., 4, 775 (2017).
- 52. Z. Benzekri, H. Serrar, A. Zarguil, S. Boukhris and A. Souizi, Iran. J. Catal., 8, 1 (2018).
- 53. Y. Merroun, S. Chehab, T. Ghailane, S. Boukhris, R. Ghailane, N. Habbadi, A. Hassikou, B.Lakhrissi and A. Souizi, *J. Turk. Chem. Soc.*, **5**, 303 (2018).
- 54. S. Chehab, Y. Merroun, T. Ghailane, R. Ghailane, S. Boukhris and A. Souizi, *J. Turk. Chem. Soc.*, **5**, 355 (2018).
- S. Chehab, Y. Merroun, T. Ghailane, N. Habbadi, S. Boukhris, A. Hassikou, R. Ghailane, M. Akhazzane, A. Kerbal, A. Daich and A. Souizi, *Mediterr. J. Chem.*, 7, 56 (2018).
- 56. R. Ghorbani-Vaghei, J. Mahmoodi, A. Shahriari and Y. Maghbooli, *Appl. Organomet. Chem.*, **31**, e3816 (2017).
- 57. S. Y. Ebrahimipour, Z. R. Ranjabr, E. T. Kermani, B. P. Amiri, H. A. Rudbari, A. Saccá and F. Hoseinzade, *Transition Met Chem.*, **40**, 39 (2015).
- K. G. Patel, N. M. Misra, R. H. Vekariya and R. R. Shettigar, *Res. Chem. Intermed.*, 44, 289 (2018).
- 59. R. V. Antre, A. Cendilkumar, R. Nagarajan, D. Goli and R. J. Oswal, *J. Sci. Res.*, **4**, 183 (2012).
- 60. We thank a referee for pointing out an alternative possibility. In this, ethyl acetoacetate reacts directly with intermediate B, followed by double annulation. Future work may address further details of the mechanism.
- 61. B. Maleki and S. S. Ashrafi, RSC Adv., 4, 42873 (2014).
- 62. K. Pradhan, S. Paul and A. R. Das, Catal. Sci. Tech., 4, 822 (2014).
- 63. M. A. Zolfigol, R. Ayazi-Nasrabadi, S. Baghery, V. Khakyzadeh and S. Azizian, J. Mol. Catal. A Chem., 418, 54 (2016).
- 64. A. Pawar, A. Mane and R. Salunkhe, Chem. Sci. Rev. Lett., 7, 327 (2018).
- 65. L. Khazdooz, A. Zarei, T. Ahmadi, H. Aghaei, N. Nazempour, L. Golestanifar and N. Sheikhan, *Reac. Kinet. Mech. Cat.*, **122**, 229 (2017).