


 Cite this: *RSC Adv.*, 2025, 15, 19069

Green protocol for the synthesis of 2-amino-4*H*-chromene-3-carbonitrile derivatives utilizing pyridine-2-carboxylic acid as a rapid catalyst†

 Smitkumar D. Vankar,  ‡ Hardi M. Makwana  ‡ and Mayank G. Sharma  *

This study investigates the green synthesis of 2-amino-4*H*-chromene-3-carbonitrile derivatives using pyridine-2-carboxylic acid (P2CA) as a sustainable and rapid catalyst. The reaction employs a one-pot multicomponent approach, combining various substituted aldehydes, malononitrile, and dimesone in a water–EtOH (1 : 1) solvent mixture under reflux conditions. Optimization of the reaction conditions revealed that P2CA (15 mol%) facilitated high yields of up to 98% in short reaction times while adhering to green chemistry principles. Control experiments, mechanistic studies and plausible mechanisms demonstrated the catalyst's dual acid–base behaviour, which drives the formation of intermediates and the selective generation of products. The process showed significant green metrics, including a high Atom Economy (AE) (99.36%) and a low *E*-factor (16.68), confirming its greenness with EcoScale of 82 (>75, excellent synthesis). Furthermore, gram-scale synthesis validated the method's scalability and potential for industrial applications, instilling confidence in its practicality and widespread use. The catalyst's recyclability was established, with consistent performance observed over four cycles. A comparative analysis with previously reported catalysts highlighted P2CA's competitive efficiency and industrial applicability. This work underscores the utility of P2CA as a versatile and sustainable catalyst, contributing to the development of eco-efficient methodologies for synthesizing 4*H*-chromene derivatives. The potential impact of this research is inspiring as it paves the way for more sustainable chemical synthesis practices.

 Received 18th April 2025
 Accepted 27th May 2025

DOI: 10.1039/d5ra02718g

rsc.li/rsc-advances

1 Introduction

Green chemistry and sustainable techniques are crucial, not only in chemical processes but also for the future. These approaches, which aim at reduce waste, minimize environmental impact, and promote resource efficiency,^{1,2} are paving the way for a more sustainable and eco-friendly chemical industry. By using renewable feedstocks, eco-friendly reaction conditions, and recyclable catalysts, we are developing more environmentally friendly chemical processes.³ The green metrics for measuring sustainability have played a pivotal role in driving resource efficiency and waste minimization over the past 25 years,⁴ such as *E*-Factor,⁵ Atom Economy (AE),⁶ Product Mass Intensity (PMI),⁷ Reaction Mass Efficiency (RME),⁸ Effective Mass Yield,⁹ and Carbon Efficiency.¹⁰ Catalysis, including biocatalysis and rapid catalysis, has been instrumental in waste reduction and the development of green processes.⁴ The

chemical industries are transitioning from an unsustainable linear economy based on fossil resources to a sustainable circular economy, focusing on renewable resources and eco-friendly technologies.¹⁴ This shift, which is at the core of our research, is not just essential for addressing global environmental challenges; it is a beacon of hope for ensuring sustainable development in the chemical sector. Thus, the central objective of our research is to develop a sustainable and environmentally benign catalytic system.

Chromene derivatives exhibit a wide range of pharmacological activities (Fig. 1), including anticancer,^{11,12} antioxidant,¹² antibacterial,¹³ anticonvulsant,¹⁴ anti-inflammatory¹⁵ and anti-tubercular¹⁶ properties. These compounds are abundant in nature and have gained significant interest in drug discovery due to their diverse biological applications and mild adverse effects.^{17,18} The chromene nucleus, consisting of an oxine ring fused with a phenyl ring, serves as an important scaffold for designing therapeutic and diagnostic agents.¹⁷ Structure-activity relationship studies have revealed that specific substitutions on the chromene nucleus can enhance its pharmacological activities.^{18,19} Various synthetic strategies, including microwave-assisted and catalyst-based approaches, have been developed to produce their antioxidant properties particularly,

Department of Chemical Sciences, School of Science, GSFC University, Fertilizer Nagar, Vadodara, Gujarat-391750, India. E-mail: mayanksharma.oc@gmail.com; mayank.sharma@gsfcuniversity.ac.in

† Electronic supplementary information (ESI) available. See DOI: <https://doi.org/10.1039/d5ra02718g>

‡ Both authors have the same contribution.



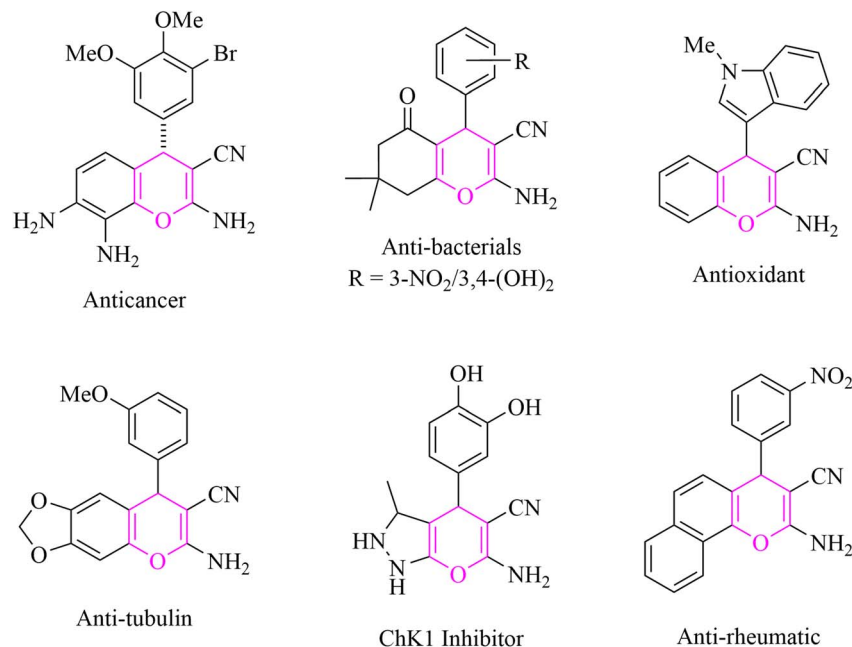


Fig. 1 Bioactive pyran derivatives.

which have made them promising candidates for chemopreventive and chemotherapeutic applications.²⁰

A wide array of catalysts and synthetic protocols for 4*H*-chromene derivatives synthesis have been reported in the literature. However, a lot of them were not viable on a large scale or were not industrially available. Also, sustainability and green chemistry always need new developments in the domain. So, here, we synthesized the chromene derivatives with the green protocol as per mild reaction conditions, with good green metrics of the reaction. Here, we explored the catalytic efficiency of a versatile moiety, P2CA, in the synthesis of 4*H*-chromenes. Catalyst has a crucial role in synthetic transformation; it speeds up the reaction as well as modulates the selectivity of the reaction. P2CA is also reported as a catalyst with a metal salt or complex for some reactions.²¹ Here, we report the catalytic efficiency of P2CA without any use of metal salt or complex and expand its utility towards MCRs with significant impact. We measured the efficiency of the catalyst by calculating the green metrics and confirmed the industrial readiness of the catalyst by performing the gram-scale reaction.

2 Results and discussions

2.1 Catalytic activity studies

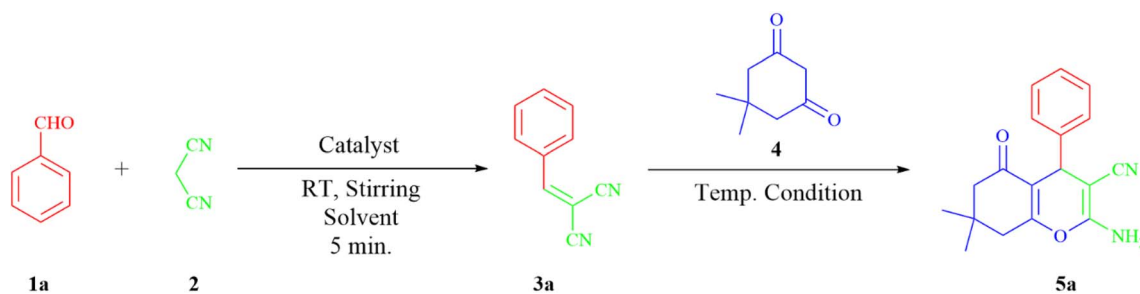
In our initial stage to synthesize 2-amino-4*H*-chromene-3-carbonitrile derivatives, the model reaction of 3 mmol benzaldehyde **1a**, 3 mmol malononitrile **2**, and 3 mmol dimedone **4** was carried out in different reaction conditions, as mentioned in Table 1. The reactions were investigated using different catalysts and amounts of catalysts, different temperatures, and two green solvents, water and ethanol. This comprehensive study, which involved systematic testing of various conditions, allowed us to identify the most effective conditions for the reaction. This

process, crucial in the development of green chemistry techniques, was significantly influenced by the role of P2CA as a catalyst, a critical factor in the success of our research.

From a green chemistry perspective, we first attempted to synthesize the compounds under catalyst-free conditions using water, ethanol, and a mixture of water and ethanol as solvents (entries 1–6). However, these conditions did not yield satisfactory results. We then sought an effective and efficient catalyst that aligns with green chemistry principles. We conducted the model reaction in the presence of P2CA at room temperature and reflux temperature (entries 7–12). While we observed an incomplete reaction at room temperature, we achieved considerable results with reflux temperature. The reaction medium was initially water, but the product was sticky, so we proceeded with neat ethanol, resulting in a single spot on the TLC in 40 minutes. This experiment highlighted the potential of P2CA as a catalyst in green chemistry, a finding that could significantly impact future research in the field.

Meanwhile, we noticed precipitates fall out during the reaction, so we added an equal amount of water in EtOH and got the product to fall out quickly in 20 min (entry 12). To reduce the time, we performed the reaction by increasing the catalytic load to 15 mol%; we obtained the highest yield of the product (entry 13). We also performed the reaction by increasing the water in the reaction medium. Still, the same issue persisted, as the product exhibited stickiness. However, in the case of lowering the water part in the reaction medium, the reaction proceeded with clean kinetics and high selectivity. Even so, the time was relatively longer than the water:EtOH (1:1) ratio, so we proceeded accordingly (entry 14). After analyzing the results, P2CA was proved to be an efficient catalyst for synthesizing the desired products in water:EtOH (1:1) as a reaction medium. We found P2CA (15 mol%) the best candidate for reaction transformation.



Table 1 Screening of solvent, mol% of catalyst and temperature effect on the model reaction^a

Entry	Catalyst	Catalytic load (mol%)	Solvent	Temp.	Time (minutes)	Consumption of dimedone ^b
1	—	—	Water	RT	180	NIL
2	—	—	EtOH	RT	180	NIL
3	—	—	Water : EtOH (1 : 1)	RT	180	NIL
4	—	—	Water	60 °C	120	NIL
5	—	—	EtOH	60 °C	120	Incomplete
6	—	—	Water : EtOH (1 : 1)	60 °C	120	Incomplete
7	P2CA	10	Water	RT	90	Incomplete
8	P2CA	10	EtOH	RT	90	Incomplete
9	P2CA	10	Water : EtOH (1 : 1)	RT	90	Incomplete
10	P2CA	10	Water	60 °C	60	Incomplete
11	P2CA	10	EtOH	60 °C	40	100%
12	P2CA	10	Water : EtOH (1 : 1)	60 °C	20	100%
13	P2CA	15	Water : EtOH (1 : 1)	60°C	10	100%
14	P2CA	15	Water : EtOH (1 : 4)	60 °C	35	100%
15	P2CA	15	Water : EtOH (4 : 1)	60 °C	20	100%
16	P2CA	20	Water : EtOH (1 : 1)	60 °C	10	100%
17	CH ₃ COOH	15	Water : EtOH (1 : 1)	Reflux	90	Incomplete
18	Conc. HCl	15	Water : EtOH (1 : 1)	Reflux	90	Incomplete

^a 3 mmol benzaldehyde **1a**, 3 mmol malononitrile **2** and 3 mmol dimedone **4**. ^b Monitored by TLC.

In conclusion, our study demonstrates the potential of P2CA as a versatile and efficient catalyst in the synthesis of 2-amino-4*H*-chromene-3-carbonitrile derivatives. The dual behaviour of the catalyst as an acid and a base,^{22–24} its easy workup procedure, and its recyclability make it a promising candidate for green chemistry applications. The use of a water–EtOH mixture as a reaction medium significantly reduced the reaction time and facilitated the isolation of the product. These findings contribute to the development of sustainable and efficient synthetic methods in green chemistry.

2.2 Substrate scope for the synthesis of 2-amino-4*H*-chromene-3-carbonitriles

To illustrate the diversity of the substrate scope (Fig. 2) and the broad applicability of the catalytic reaction, various substituted aldehydes were examined, and reactions were carried out (Table 2, 5(a–j)). All of the substituted aldehydes resulted in 2-amino-4*H*-chromene-3-carbonitriles, forming excellent yields.

After synthesizing a library of 4*H*-chromenes by substituted aldehydes, malononitrile and dimedone, we also performed some control experiments to understand the mechanism and reactivity change by varying the reactant's equivalents. Initially, a control experiment was conducted, in which 1 eq. of

salicylaldehyde was reacted with 1 eq. of malononitrile (Scheme 1, reaction a) to form 2-imino-2*H*-chromene-3-carbonitrile (C1), which fall out during the reaction and isolated, which was previously not isolated by Bahuguna *et al.*²⁹ To the resulting product, separate charging of 1 eq. of dimedone and isatin resulted in the 4*H*-chromene product (C2 and C3). However, when 2 eq. of malononitrile was used in the reaction with 1 mmol salicylaldehyde, an exciting product 2-(2-amino-3-cyano-4*H*-chromen-4-yl)malononitrile (C4) was formed (Scheme 1, reaction b). For the further study of the reactivity and mechanism of the reaction, we carried out the reaction with a two-aldehyde group containing moiety (isophthalaldehyde) in equal equivalents of the reactant (Scheme 1, reaction c, C5). However, multiple spots were observed in TLC in 60 min, with the protocol, due to uncontrolled reaction on both aldehyde groups. To resolve this, we took 1 eq. of the isophthalaldehyde and two equivalents of malononitrile and dimedone each (Scheme 1, reaction d, C6). Surprisingly, single spot TLC was observed in 30 min. and the two 4*H*-chromene ring-containing products were formed. From the control experiments, we came to know about the change in reactivity of the catalyst due to the change in equivalents of the reactants used in the reaction. All the control experiments confirmed the formation of an intermediate formed during the catalytic cycle.



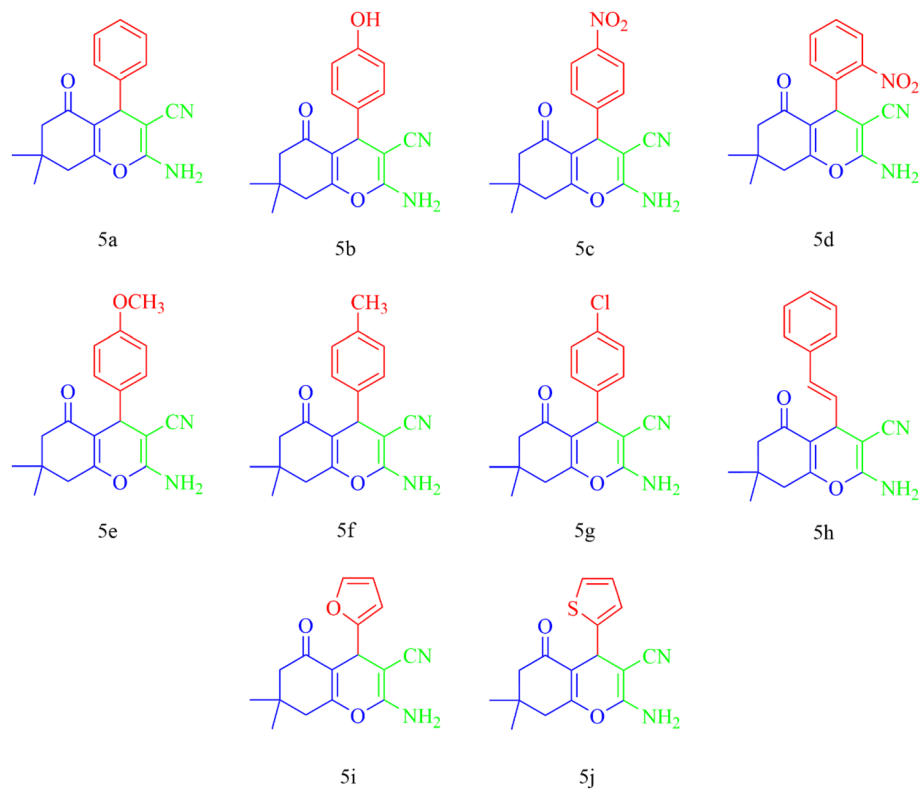
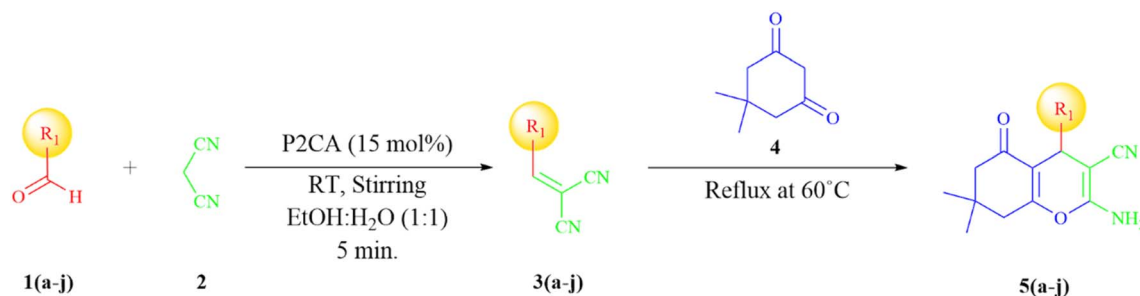


Fig. 2 Substrate scope for the synthesis of 2-amino-4H-chromene-3-carbonitrile derivatives.

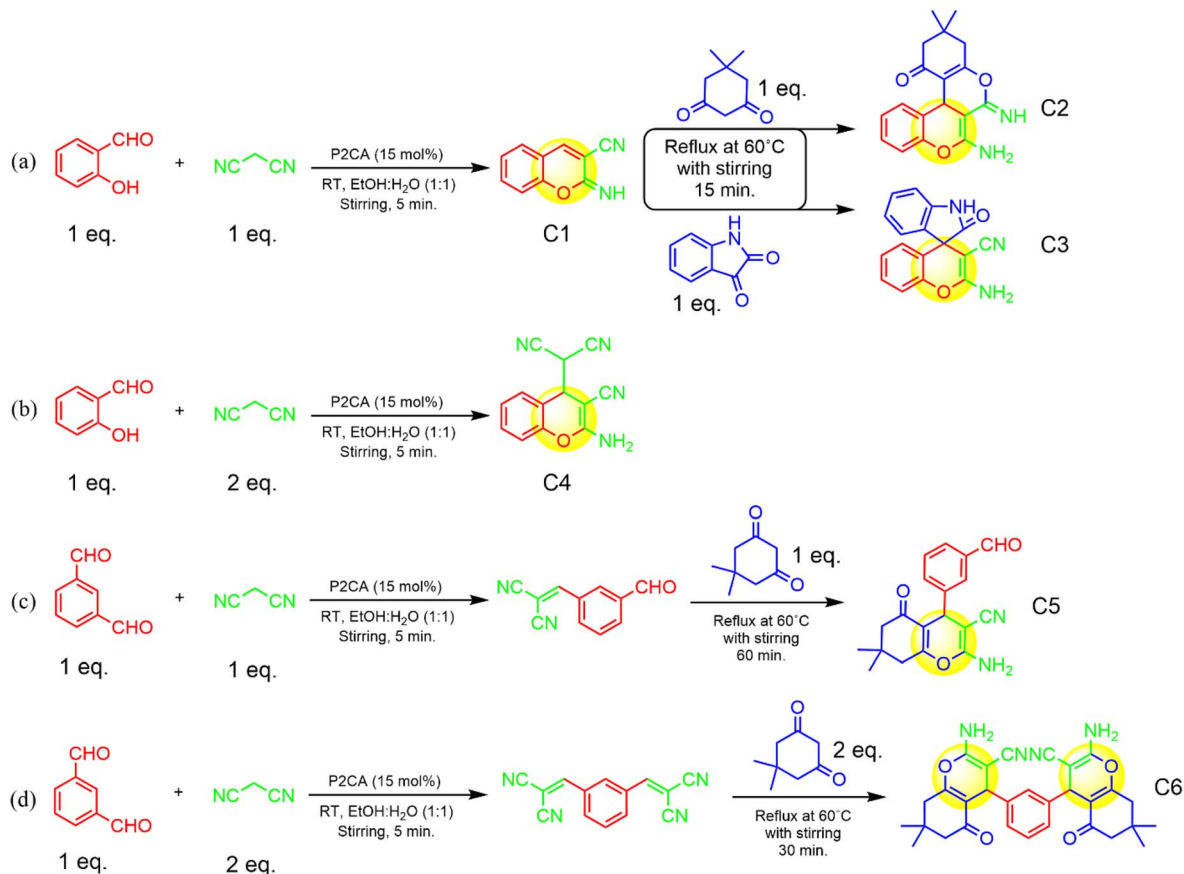
Table 2 P2CA catalysed one-pot synthesis of 2-amino-4H-chromene-3-carbonitriles^a



Sr. no.	Product	R ₁	Time (min)	% yield	M.P./Lit. (°C)
1	5a	C ₆ H ₅	10	98	228–230/230–232 ²⁵
2	5b	4-OHC ₆ H ₄	15	92	207–208/206–208 ²⁶
3	5c	4-NO ₂ C ₆ H ₄	08	95	178–180/179–180 ²⁷
4	5d	2-NO ₂ C ₆ H ₄	08	93	230–232/231–233 ²⁷
5	5e	4-OCH ₃ C ₆ H ₄	12	97	201–202/200–202 ²⁸
6	5f	4-CH ₃ C ₆ H ₄	12	97	218–220/217–219 ²⁸
7	5g	4-ClC ₆ H ₄	07	98	215–217/214–216 ²⁸
8	5h	CHCHC ₆ H ₅	15	96	181–182/181–183 ²⁵
9	5i	C ₄ H ₃ O	05	92	225–227/224–226 ²⁵
10	5j	C ₄ H ₃ S	05	99	178–181

^a 3 mmol substituted aldehydes **1(a–j)**, 3 mmol malononitrile **2**, 3 mmol dimedone **4** and 15 mol% P2CA as catalyst.





Scheme 1 Control experiments performed using different equivalents of reactants for the synthesis of 4H-chromenes.

2.3 Plausible mechanism

Scheme 2 represents the catalytic cycle and the plausible mechanism of the reaction. In brief, aldehyde [II], in the presence of P2CA, grabs the hydrogen from P2CA [I] and generates the electrophilic center (Cation) [III]. Simultaneously, malononitrile [IV] loses its most acidic hydrogen to the nitrogen atom of the P2CA and attacks the electrophilic center at [III] to form adduct [VI], which on dehydration followed by the attacked of dimedone to produce [XI], which is later converted to [XII]. [XII] on cyclization followed by two hydrogen losses to form the final product structure [XV].^{30–34}

2.4 Green metrics

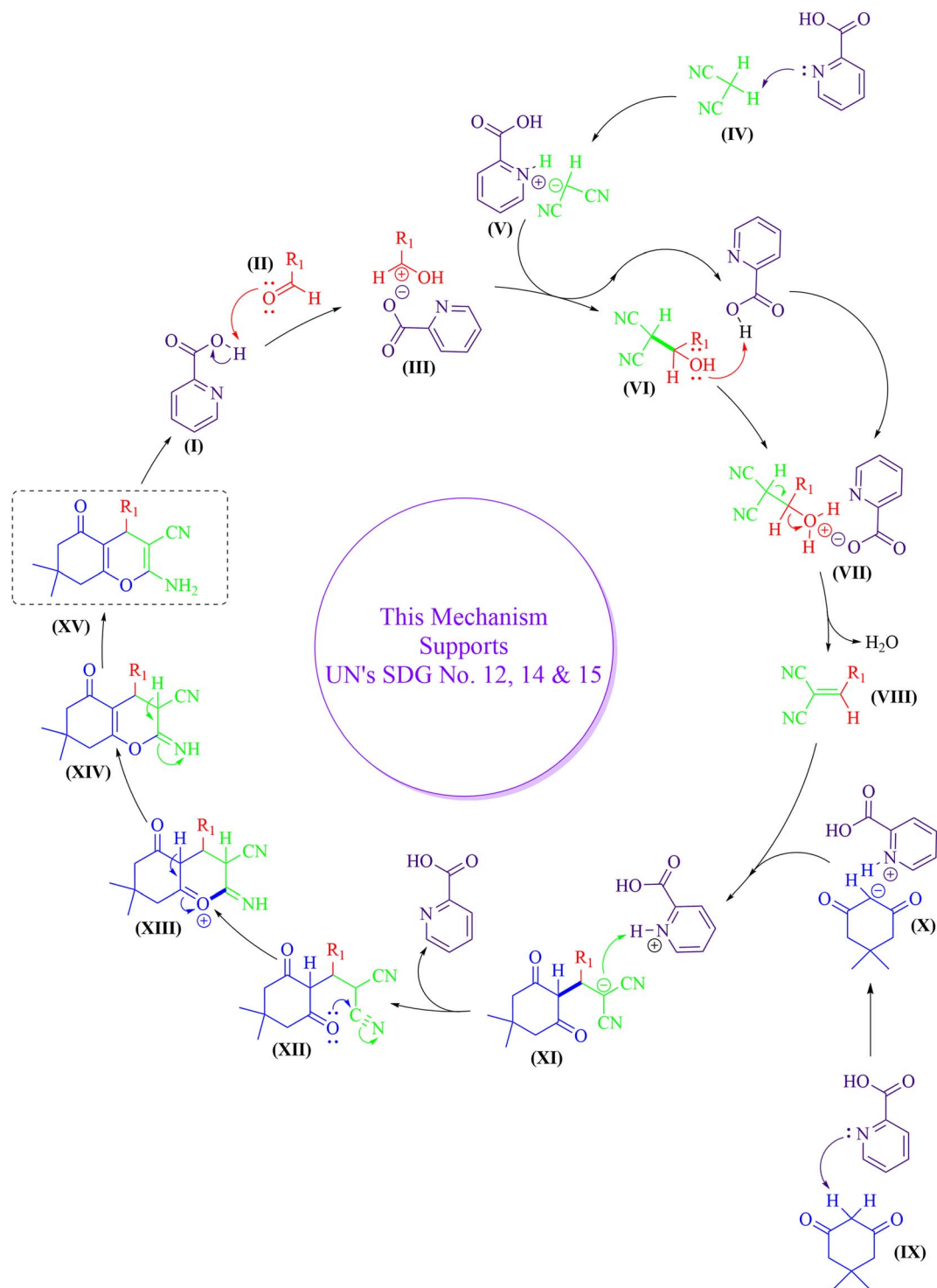
Because all of the reactions catalysed by P2CA have been performed under green conditions, the least waste was generated during this multicomponent reaction. To support this, we have measured our protocol with some green metrics (Fig. 3 and 4). The Atom Economy (AE) focuses on the maximum number of atoms of reactants appearing in the product,^{35,36} and the *E*-factor highlights the waste minimization and resource efficiency for chemicals, mainly those manufactured in the fine chemicals industry.⁴ AE determines the theoretical efficiency, while Reaction Mass Efficiency (RME) gives the observed value and allows a direct comparison between different reaction types. Process Mass Intensity (PMI) is based on waste intensity.

As such, AE gives the theoretical maximum efficiency of reactant utilization, while RME gives the observed. Comparison of RME and AE gives a new metric, Optimum Efficiency (OE).³⁷ Here, the ideal value for the *E*-factor is considered Zero, while the actual/ideal PMI is *E*-factor + 1. The ideal value of the AE factor is 100%, which means that all starting material is converted into a product, while a higher value of RME signifies the cleanliness of the reaction.

2.5 Reusability study and EcoScale

Finally, we performed recyclability studies (Fig. 5) to check the catalyst's catalytic potential. After each cycle, the catalyst was recovered from the water by rota-evaporator and then used for the next cycle. We tested the reusability of P2CA for the synthesis of 5g. For this, 3 mmol 4-chlorobenzaldehyde 1g and 3 mmol malononitrile 2 were added with 15 mol% of P2CA as a catalyst and 2 mL of each EtOH and water and stirred for 5 min on a magnetic stirrer at RT. After charging 3 mmol of dimedone 4, the reaction mixture was stirred and refluxed on rota-mantle at 60 °C temp. Then, after reaction completion, crude product was poured in 10 mL of water to afford the precipitates. We separated the precipitated product by simple filtration. The collected mother liquor was heated at 60 °C in rota-evaporator under reduced pressure to recover P2CA. The catalyst was authenticated after each cycle *via* IR spectroscopy.





Scheme 2 Plausible mechanism for the synthesis of 4H-chromenes via P2CA, supporting UN SDG 12 (responsible consumption and production), SDG 14 (life below water), and SDG 15 (life on land).

The catalyst was successfully recovered up to the 4th cycle without any significant loss in catalytic activity, and more than 90% yield was obtained.

The EcoScale is a semi-quantitative tool designed to assess the environmental sustainability of synthetic methods by evaluating their impact based on six key criteria: yield, chemical cost, safety, technical setup, reaction conditions, and workup/

purification methods (Table 3). This tool aids in determining whether a synthetic process aligns with the principles of green chemistry, promoting the adoption of more environmentally friendly practices.^{38,39}

$$\text{EcoScale} = 100 - \text{sum of individual penalties}$$



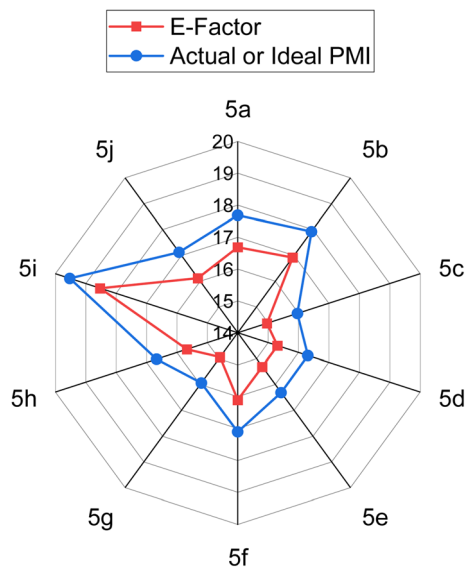


Fig. 3 E-factor & PMI.

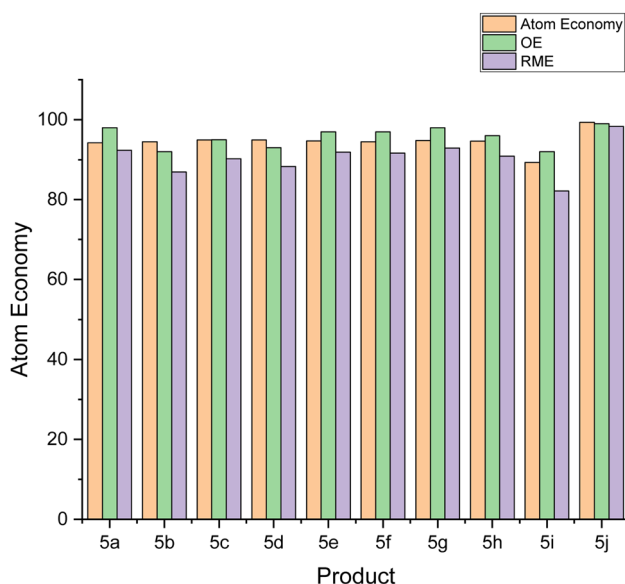


Fig. 4 AE, OE & RME.

$$\text{EcoScale} = 100 - 18 = 82 (>75, \text{excellent synthesis})$$

An ideal reaction has the EcoScale value of 100. Eco-scale from 0 to 100 using the following scores: >75, excellent; >50, acceptable; and <50, inadequate. The EcoScale score for a particular preparation of the product in a high purity state (>98%) is calculated by lowering the maximum value of 100 by any applicable penalty points.

2.6 Gram-scale reaction & comparison of catalyst

Looking at the industry point of view, we performed a model gram-scale reaction to show the industrial potential of the P2CA catalyst (Scheme 3). We performed our model reaction with 10 mmol of each benzaldehyde, malonitrile and dimedone,

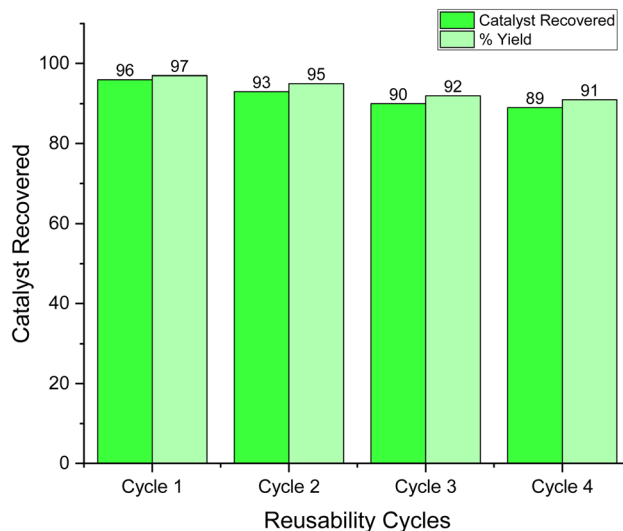


Fig. 5 Recovery & reusability of catalyst.

using a 15 mol% the catalyst. We got a 98% yield for the gram-scale response, similar to that for the small-scale one. Hence, we could confirm the industrial potential of the P2CA catalyzed under green and sustainable conditions.

Only a few reports are available in the literature on the synthesis of 4*H*-chromenes using dimedone, which is catalysed by various heterogeneous and homogeneous catalysts. We have compared the activity of the P2CA with some earlier catalysts reported in the literature (Table 4), which revealed that our catalyst is more efficient and equally good in some cases. In addition to this, our catalyst is homogeneous, non-metal, readily available, and industrially viable.

Compared with other reported catalysts, P2CA proved to be highly efficient for the synthesis of 4*H*-chromene derivatives. Additionally, calculations of various green metrics, EcoScale and reusability study confirmed P2CA as an ideal catalyst, offering rapid and efficient synthesis while minimizing environmental impact.

3 Experimental section

3.1 General experimental information

All chemicals used in this study were purchased from commercially available sources and used without further purification. The progress of the reaction was monitored by silica gel 60 F₂₅₄ (Merck) coated TLC plates. Melting points were determined by the open capillary tube method, which was uncorrected. IR spectra were recorded using Instrument Spectrum Two, PKI. ¹H NMR and ¹³C NMR spectral analyses were recorded using a BRUKER AVANCE III 400 MHz FT-NMR spectrometer.

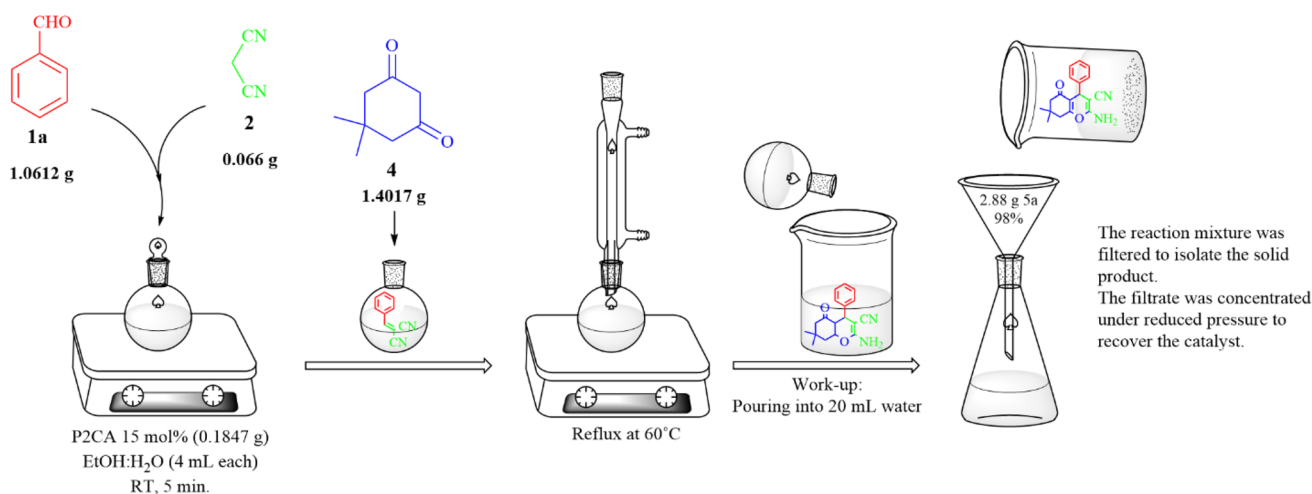
3.2 General procedure for synthesis

To a 100 mL round-bottom flask, 3 mmol aldehydes **1(a–j)** and 3 mmol malonitrile **2** were added with 15 mol% of pyridine-2-carboxylic acid as catalyst and 2 mL of each EtOH and water and stirred for 5 min on a magnetic stirrer at RT. Then 3 mmol of dimedone **4** was added, and the reaction mixture was stirred



Table 3 EcoScale (E-Score)

Sr. no.	Parameter	Value	Penalty point
1	Yield	100–98/2	1
2	Price of reaction components (to obtain 10 mmol of end product)	Inexpensive (<\$10)	0
3	Safety (reactants)	T (toxic) 5 + 5 + 5	15
4	Technical setup	Common setup	0
5	Temperature, time	Heating, <1 h	2
6	Workup and purification	Simple filtration	0
Total penalty points			18



Scheme 3 Gram-scale reaction of 5a.

Table 4 Comparison of catalytic potential of P2CA

Entry no.	Reaction conditions	Temp. (°C)	Time (min)	% yield	Literature
1	rGO@Fe ₃ O ₄ -ZrCp ₂ Cl ₂ , PEG-400	100 °C	60	80	40
2	SO ₃ H/NH ₂ NH ₂ /GPTMS/Fe ₃ O ₄ , H ₂ O/EtOH (1 : 1)	Reflux	15	95	41
3	Fe ₃ O ₄ @GO- <i>N</i> -(pyridin-4-amine), H ₂ O	Reflux	30	94	42
4	NH ₄ Al(SO ₄) ₂ ·12H ₂ O (Alum), EtOH	80 °C	120	92	43
5	PPI, H ₂ O	Reflux	15	95	44
6	Fe ₃ O ₄ @SiO ₂ /DABCO, H ₂ O	Reflux	25	90	45
7	Fe ₃ O ₄ @MCM-41@Zr-piperazine-MNPs, EtOH : H ₂ O (3 : 7)	Reflux	40	75	46
8	PIL-SBMn(III), water	80 °C	15	94	28
9	Fe ₃ O ₄ @SiO ₂ -guanidine-PAA, H ₂ O	70 °C	35	96	47
10	Fe ₃ O ₄ @Ph-SO ₃ H, H ₂ O, US	RT	25	95	48
11	MMWCNTs-D-(CH ₂) ₄ -SO ₃ H, EtOH	Reflux	15	93	49
12	H ₅ BW ₁₂ O ₄₀ , EtOH/H ₂ O	Reflux	60	98	50
13	GO-Trp, EtOH : H ₂ O (1 : 1)	RT	25	96	51
14	Piperazine-GO, EtOH : H ₂ O (1 : 1)	50 °C	15	95	52
15	P2CA, EtOH : H₂O (1 : 1)	Reflux	10	98	This work

and refluxed on rota-mantle at 60 °C temperature. Reaction kinetics was measured using TLC. After the reaction completion, the reaction mixture was cooled to room temperature and poured into 10 mL of water. The precipitated product was separated by gravitational filtration. The crude product was washed with EtOH/acetone (1 mL).

3.3 Catalyst reusability protocol

After completion of the reaction and subsequent work-up, the collected filtrate was concentrated under reduced pressure at 60 °C in rota-evaporator to recover the catalyst. The recovered catalyst was then directly reused in the next reaction cycle without further purification.



3.4 Gram-scale reaction procedure

A 100 mL round-bottom flask was charged with 10 mmol benzaldehyde **1a**, and 10 mmol malononitrile **2**, along with P2CA, 15 mol% as the catalyst. To this mixture, 4 mL each of ethanol and water were added as the reaction medium. The resulting mixture was stirred at room temperature for 5 minutes using a magnetic stirrer. Subsequently, 10 mmol dimedone **4**, was introduced to the reaction mixture, and the contents were refluxed on a rota-mantle at 60 °C. The progress of the reaction was monitored by TLC.

Upon completion, the reaction mixture was allowed to cool to room temperature and poured into 20 mL of water to facilitate product precipitation. The solid product was isolated by gravitational filtration and washed with a small volume (2 mL) of ethanol to remove residual impurities. The purified product was then dried under ambient conditions.

4 Conclusion

This study demonstrates the successful application of pyridine-2-carboxylic acid (P2CA) as an efficient, sustainable, and rapid catalyst for synthesizing 2-amino-4*H*-chromene-3-carbonitrile derivatives. By optimizing reaction conditions, including solvent composition, catalyst loading, and temperature, we established a highly efficient one-pot multicomponent protocol. The water–ethanol (1 : 1) solvent system proved ideal, yielding excellent product efficiencies while adhering to green chemistry principles.

The catalytic system achieved good green metrics, such as high Atom Economy (AE), low *E*-factor, favorable Reaction Mass Efficiency (RME), and excellent EcoScale underscoring its green chemistry profile. Comparative studies revealed P2CA's performance as competitive with existing catalysts while offering advantages such as simplicity, cost-effectiveness, and recyclability. Its consistent performance over four cycles further highlights its practical utility, providing reassurance and confidence in its application. Gram-scale synthesis confirmed the scalability of this method, demonstrating industrial applicability and reinforcing its potential to replace traditional, less sustainable processes. This work not only contributes to advancing green and sustainable methodologies in organic synthesis but also stands as a testament to the potential of research to make a significant contribution to the field, offering an environmentally responsible approach.

Abbreviations

P2CA	Pyridine-2-carboxylic acid
AE	Atom economy
PMI	Product mass intensity
RME	Reaction mass efficiency
OE	Optimum efficiency
EtOH	Ethanol
TLC	Thin layer chromatography
RT	Room temperature
IR	Infra red

Data availability

The data that support the findings of this study are available in the ESI of this article.†

Author contributions

Smitkumar D. Vankar: conceptualization; methodology; investigation; data curation; formal analysis; visualization; writing – original draft; writing – review & editing. Hardi M. Makwana: conceptualization; methodology; investigation; data curation; formal analysis; visualization; writing – original draft; writing – review & editing. Mayank G. Sharma: supervision; project administration.

Conflicts of interest

There is no conflict of interest to declare.

Acknowledgements

We wish to extend our heartfelt gratitude to Shri P. K. Taneja, IAS (Retd.), our esteemed President, whose unwavering support has been instrumental in our pursuits. We are deeply thankful to our Provost, Prof. (Dr) G. R. Sinha, for his guidance and vision. Our sincere appreciation also goes to Dr K. S. Kumar, our Head of Department, for fostering an enriching academic environment. Additionally, we recognize the management of GSFC University for providing outstanding facilities that have greatly enhanced our research capabilities. Also, we are grateful to GSFC University for providing us with financial assistance under SEED GRANT (File No. SF-06). SDV and HMM dedicate this work to their beloved parents, whose unwavering support and sacrifices have been the cornerstone of their journey. They are offering this work with deep gratitude.

References

- 1 K. D. Patil, *Curr. Opin. Chem. Eng.*, 2014, **2**, 1–7.
- 2 J. Colberg, K. Kuok (Mimi) Hii and S. G. Koenig, *Org. Process Res. Dev.*, 2022, **26**, 2176–2178.
- 3 R. Varma, *Appl. Sci.*, 2014, **4**, 493–497.
- 4 R. A. Sheldon, *Green Chem.*, 2017, **19**, 18–43.
- 5 F. Roschangar, R. A. Sheldon and C. H. Senanayake, *Green Chem.*, 2015, **17**, 752–768.
- 6 R. Hudson, D. Leaman, K. E. Kawamura, K. N. Esdale, S. Glaisher, A. Bishop and J. L. Katz, *J. Chem. Educ.*, 2016, **93**, 691–694.
- 7 C. Jimenez-Gonzalez, C. S. Ponder, Q. B. Broxterman and J. B. Manley, *Org. Process Res. Dev.*, 2011, **15**, 912–917.
- 8 K. Budzinski, M. Blewis, P. Dahlin, D. D'Aquila, J. Esparza, J. Gavin, S. V. Ho, C. Hutchens, D. Kahn, S. G. Koenig, R. Kottmeier, J. Millard, M. Snyder, B. Stanard and L. Sun, *New Biotechnol.*, 2019, **49**, 37–42.
- 9 A. D. Curzons, D. N. Mortimer, D. J. C. Constable and V. L. Cunningham, *Green Chem.*, 2001, **3**, 1–6.



- 10 D. J. C. Constable, A. D. Curzons and V. L. Cunningham, *Green Chem.*, 2002, **4**, 521–527.
- 11 T. C. Braga, M. M. Silva, E. O. O. Nascimento, E. C. Dantas da Silva, Y. de Freitas Rego, M. Mandal, Z. Alves de Souza, A. L. Tasca Góis Ruiz, J. Ernesto de Carvalho, F. T. Martins, I. M. Figueiredo, T. Mendonça de Aquino, C. Moreira da Silva, B. Mandal, G. Brahmachari, J. C. Caldas Santos and Â. de Fátima, *Eur. J. Med. Chem. Rep.*, 2022, **4**, 100030.
- 12 P. Anaikutti, M. Selvaraj, J. Prabhakaran, T. Pooventhiran, T. C. Jeyakumar, R. Thomas and P. Makam, *J. Mol. Struct.*, 2022, **1266**, 133464.
- 13 M. Mirza-Aghayan, M. Mohammadi and R. Boukherroub, *J. Heterocycl. Chem.*, 2022, **59**, 1102–1115.
- 14 P. Andreeva-Gateva, J. Tchekalarova, V. Angelova, S. Marchev, Y. Voynikov, N. Vassilev, M. Vlaskovska and S. Surcheva, *Clin. Ther.*, 2017, **39**, e78–e79.
- 15 Y. Kakumu, M. T. Thi Nguyen and T. Mitsunaga, *Phytochemistry*, 2022, **202**, 113322.
- 16 G. A. Khan, G. A. Naikoo, J. A. War, I. A. Sheikh, U. J. Pandit, I. Khan, A. K. Harit and R. Das, *J. Heterocycl. Chem.*, 2018, **55**, 699–708.
- 17 M. K. Katiyar, G. K. Dhakad, S. Arora, S. Bhagat, T. Arora and R. Kumar, *J. Mol. Struct.*, 2022, **1263**, 133012.
- 18 A. Chaudhary, K. Singh, N. Verma, S. Kumar, D. Kumar and P. P. Sharma, *Mini-Rev. Med. Chem.*, 2022, **22**, 2736–2751.
- 19 N. Thomas and S. M. Zachariah, *Asian J. Pharm. Clin. Res.*, 2013, **6**, 11–15.
- 20 N. F. L. Machado and M. P. M. Marques, *Curr. Bioact. Compd.*, 2010, **6**, 76–89.
- 21 P. Saisaha, J. J. Dong, T. G. Meinds, J. W. de Boer, R. Hage, F. Mecozzi, J. B. Kasper and W. R. Browne, *ACS Catal.*, 2016, **6**, 3486–3495.
- 22 D. S. Baptista, M. F. M. Piedade and C. V. Esteves, *Cryst.*, 2023, **13**, 392.
- 23 B. García, S. Ibeas and J. M. Leal, *J. Phys. Org. Chem.*, 1996, **9**, 593–597.
- 24 A. I. Lytkin, V. G. Badelin, O. N. Krutova, E. Yu. Tyunina and P. D. Krutov, *Russ. J. Gen. Chem.*, 2019, **89**, 2235–2238.
- 25 M. Mashhadinezhad, M. Mamaghani, M. Rassa and F. Shirini, *ChemistrySelect*, 2019, **4**, 4920–4932.
- 26 H. Zhi, C. Lü, Q. Zhang and J. Luo, *Chem. Commun.*, 2009, 2878.
- 27 D. Fang, H.-B. Zhang and Z.-L. Liu, *J. Heterocycl. Chem.*, 2010, **47**, 63–67.
- 28 M. Mashhoori, R. Sandaroods and A. Zeraatkar Moghaddam, *ChemistrySelect*, 2020, **5**, 7148–7154.
- 29 A. Bahuguna, P. Choudhary, T. Chhabra and V. Krishnan, *ACS Omega*, 2018, **3**, 12163–12178.
- 30 M. G. Sharma, R. M. Vala and H. M. Patel, *RSC Adv.*, 2020, **10**, 35499–35504.
- 31 S. D. Vankar, H. M. Makwana and M. G. Sharma, *ChemistrySelect*, 2024, **9**, e202402376.
- 32 D. M. Patel and H. M. Patel, *ACS Sustain. Chem. Eng.*, 2019, **7**, 18667–18676.
- 33 M. G. Sharma, P. Juhee, P. Divyang M., V. Raturajsinh M., S. Raghunandankumar, G. Vivek K., G. Ramesh L., D. Anuradha and H. M. and Patel, *Polycyclic Aromat. Compd.*, 2021, **41**, 1495–1505.
- 34 D. M. Patel, R. M. Vala, M. G. Sharma, D. P. Rajani and H. M. Patel, *ChemistrySelect*, 2019, **4**, 1031–1041.
- 35 B. Trost, *Science*, 1991, **254**, 1471–1477.
- 36 B. M. Trost, *Acc. Chem. Res.*, 2002, **35**, 695–705.
- 37 C. R. McElroy, A. Constantinou, L. C. Jones, L. Summerton and J. H. Clark, *Green Chem.*, 2015, **17**, 3111–3121.
- 38 A. P. Dicks, H. Andrei and K. J. and Koroluk, *Green Chem. Lett. Rev.*, 2018, **11**, 29–35.
- 39 K. Van Aken, L. Strekowski and L. Patiny, *Beilstein J. Org. Chem.*, 2006, **2**, 3.
- 40 S. Momeni and R. Ghorbani-Vaghei, *RSC Adv.*, 2024, **14**, 21608–21622.
- 41 F. Kalantari, H. Esmailipour, H. Ahankar, A. Ramazani, H. Aghahosseini, O. Kaszubowski and K. Ślepokura, *ACS Omega*, 2023, **8**, 25780–25798.
- 42 D. Azarifar and M. Khaleghi-Abbasabadi, *Res. Chem. Intermed.*, 2019, **45**, 199–222.
- 43 A. A. Mohammadi, M. R. Asghariganjeh and A. Hadadzahmatkesh, *Arabian J. Chem.*, 2017, **10**, S2213–S2216.
- 44 H. Kiyani and F. Ghorbani, *J. Saudi Chem. Soc.*, 2014, **18**, 689–701.
- 45 J. Davarpanah, A. R. Kiasat, S. Noorizadeh and M. Ghahremani, *J. Mol. Catal. A:Chem.*, 2013, **376**, 78–89.
- 46 R. Pourhasan-Kisomi, F. Shirini and M. Golshekan, *Appl. Organomet. Chem.*, 2018, **32**, e4371.
- 47 P. Mohammadi and H. Sheibani, *Mater. Chem. Phys.*, 2019, **228**, 140–146.
- 48 D. Elhamifar, Z. Ramazani, M. Norouzi and R. Mirbagheri, *J. Colloid Interface Sci.*, 2018, **511**, 392–401.
- 49 F. Adibian, A. R. Pournali, B. Maleki, M. Baghayeri and A. Amiri, *Polyhedron*, 2020, **175**, 114179.
- 50 M. M. Heravi, M. Mirzaei, S. Y. S. Beheshtiha, V. Zadsirjan, F. Mashayekh Ameli and M. Bazargan, *Appl. Organomet. Chem.*, 2018, **32**, e4479.
- 51 L. Amiri-Zirtol and S. Khabnadideh, *Sci. Rep.*, 2024, **14**, 6957.
- 52 A. Khazaei, R. Jahanshahi, S. Sobhani, J. Skibsted and J. M. Sansano, *Green Chem.*, 2020, **22**, 4604–4616.

