A Platinum Open Access Journal for Organic Chemistry

Paper

Free to Authors and Readers | DOAJ Seal | *Arkivoc* **2023** (viii) 202312167

Serendipitous synthesis of 2,3-dihydroquinazolin-4(1*H*)-ones in $ZnCl_2$/urea deep eutectic solvent

Gobind Kumar,[a] Lungisani Khubone, [a] Pule Seboletswe,[a] Neha Manhas,[c] Talent Makhanya,[c] Gaurav Bhargava,[b] and Parvesh Singh,*[a]

[a]*School of Chemistry and Physics, University of KwaZulu Natal, P/Bag X54001, Westville, Durban 4000, South Africa*

[b]*Department of chemical sciences, I. K. Gujral Punjab Technical University Kapurthala, Punjab-144603, India*

[c]*Department of Chemistry, ML Sultan Campus, Durban University of Technology, Durban-4000, South Africa*

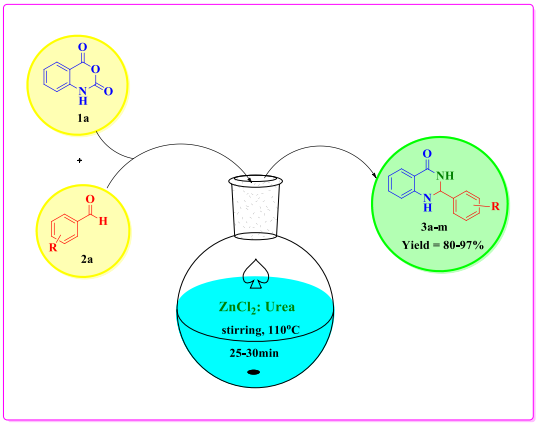
Email: singhp4@ukzn.ac.za

Received mm-dd-yyyy **Accepted** mm-dd-yyyy **Published on line** mm-dd-yyyy

Dates to be inserted by editorial office

Abstract

A green, sustainable, and efficient one-pot, synthetic strategy for the synthesis of 2,3-dihydroquinazolin-4(1*H*)-ones (DHQs) was developed. The $ZnCl_2$/urea used as a deep eutectic solvent (DES) not only efficiently promoted the condensation between isatoic anhydride and benzaldehyde but unexpectedly acted as a nitrogen source (like ammonia) *in situ* to afford DHQs in excellent yields. This approach offers remarkable advantages, involving the triple role of DES in the synthesis of DHQs, atom-economical, green organocatalysts, metal-free conditions, cost-effectiveness, and tolerance to a range of functional groups.



Keywords: Deep eutectic solvent, 2,3-dihydroquinazolinone, green chemistry, heterocyclic compounds, solvent-free

Cite as *Arkivoc* **2023** (viii) 202312167

DOI: https://doi.org/10.24820/ark.5550190.p012.167

Introduction

Among the major limitations of organic solvents are their flammability, volatility, toxicity, high cost, and environmental impact.[1] Nowadays, the most demanding and active area of research is developing atom-economic, environment-friendly, and green methods for organic transformations.[2-5] In the past decade, ionic liquids (ILs) have attracted much attention due to their promising properties: non-flammability, stability, eco-friendliness, low volatility, and recyclability.[6] Unfortunately, ILs have some impediments like a lack of biocompatibility, difficult purification, high air/moisture sensitivity, and expensive and complicated synthetic process.[7]

To overcome the aforementioned issues, recently researchers worldwide have paid substantial attention to deep eutectic solvents (DESs). These DESs combine hydrogen bond donors such as urea, and ammonium acetate, and hydrogen bond acceptors such as choline chloride or zinc chloride in precise molar ratios to generate relatively low boiling solvents.[8-10] DESs are greener and more sustainable alternatives to ILs[11] and serve as excellent solvents in organic synthesis towing to their tremendous properties such as excellent catalytic action, cost-effectiveness, biodegradability, use without additional purification, non-toxicity, and non-volatility.[12-14] As a result, DESs find a lot of applications in many organic conversions like Paal-Knorr reaction,[15] Perkin reaction,[16] Hantzsch reaction,[17] Biginelli reaction,[18] Diels-Alder reaction[19], etc.

Heterocyclic compounds have displayed incredible applications in the chemical and pharmaceutical industries.[20-22] Among various nitrogen heterocycles, 2,3-dihydroquinazolin-4(1*H*)-ones (DHQs) have shown immense potential in various sectors, particularly in the medicinal field. The heterocycles bearing DHQ as a core of their structure or a structural unit have been reported to exhibit various biological activities such as anticancer,[23] antimalarial,[24] antiviral,[25] antitubercular,[26] antibacterial,[27] etc. For instance, quinethazone and fenquizone are DHQ-based antihypertensive drugs[28] (**Figure 1**).

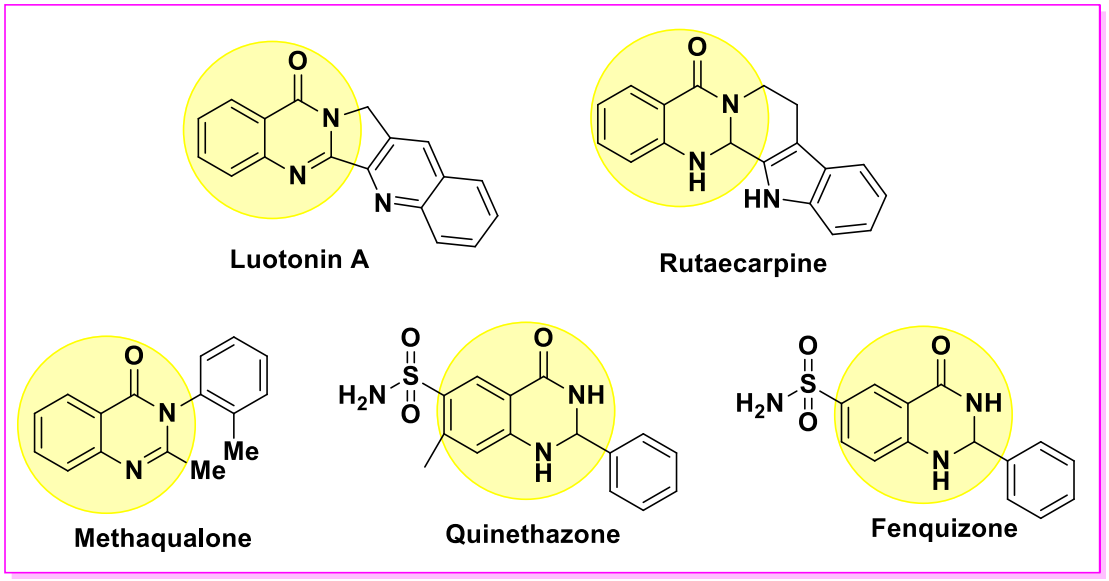


Figure 1. DHQ core structure in some important drugs.

Accordingly, various reaction methods targeting the synthesis of diversely substituted DHQs have been reported in the literature. One of the commonly used methods involves a three-component reaction between isatoic anhydride, ammonium acetate (a nitrogen source), and aldehyde[29, 30] that has been carried out using different BrØnsted/Lewis acids catalysts such as citric acid,[31] β-CD-SO_3H,[32-34] cellulose-H_3BO_3, Sc $(OTf)_3$,[35]

p-TSA,[36] and acetic acid[37], etc. However, all of these reactions suffer from different limitations including acidic environment, prolonged reaction times, use of sophisticated catalysts prepared in multiple steps, moderate yields, and cumbersome work-up/purification procedures.[38,39] In 2019, Solorzano and coworkers[40] also employed the same three-component reaction protocol between isatoic anhydride, benzaldehyde, and ammonium acetate or different aromatic amines (as a nitrogen source) for the synthesis of DHQs, using $ZnCl_2$/urea as a DES at 110 °C (**Figure 2**).

In continuation with our research interests in the synthesis of nitrogen heterocycles coupled with the incredible medicinal significance of DHQs, we explored the reaction between isatoic anhydride and different benzaldehydes in $ZnCl_2$/urea DES that serendipitously led to the formation of DHQs disclosing an unprecedented role of DES in synthesizing this class of heterocyclic compounds. The present demonstrates a triple role of DES as a green solvent, an eco-friendly catalyst that promotes condensation, and a substrate that can donate nitrogen to the product making it a relatively easier and cost-effective protocol for the synthesis of DHQs. A plausible mechanism showing the generation of ammonia from DES that eventually acts as a nitrogen source in the formation of DHQs in these reactions is also proposed. To the best of our knowledge, this is the first report in which the urea in DES has been proposed to release ammonia that subsequently acts as a nitrogen source in this reaction. Also, our reaction procedure demonstrated that the reaction can proceed without ammonium acetate as opposed to the previously published work[37]. However, the reaction remains a three-component reaction based on the components contributed by the reactants.

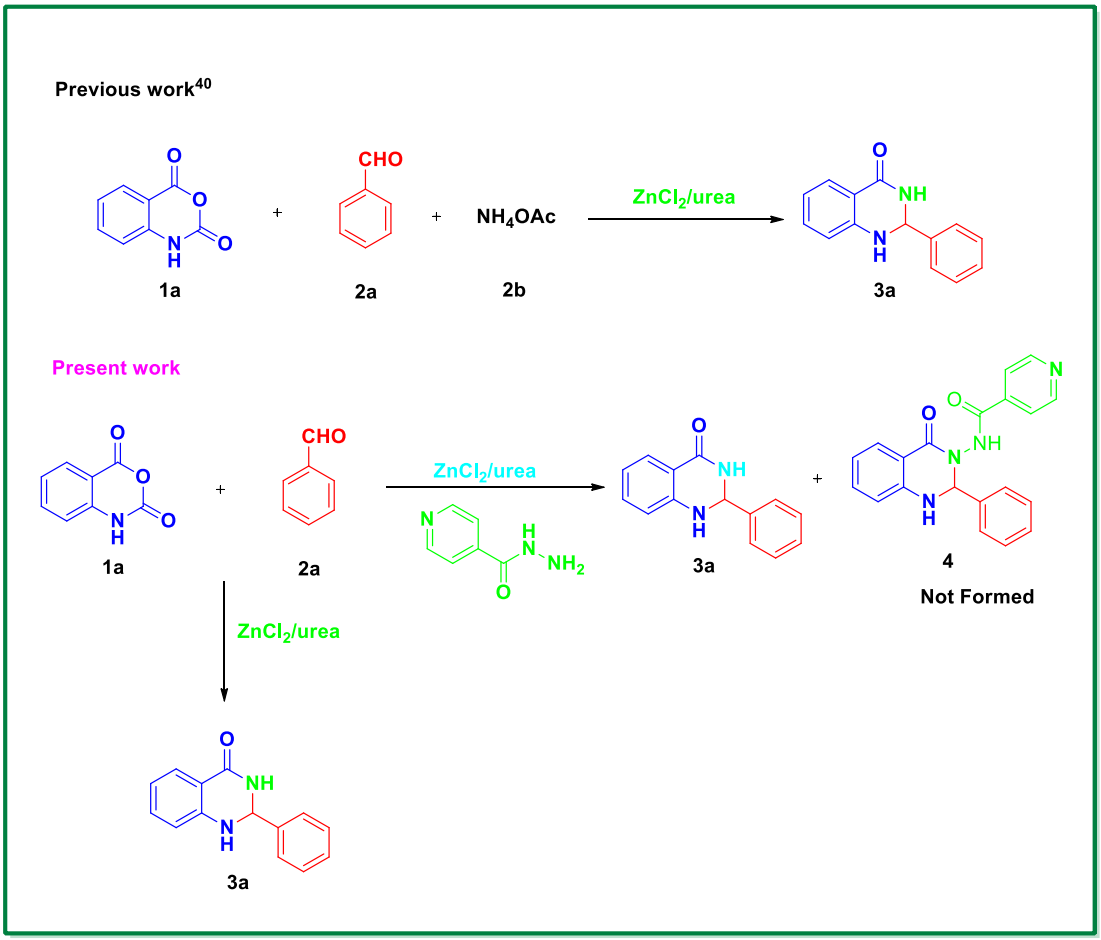
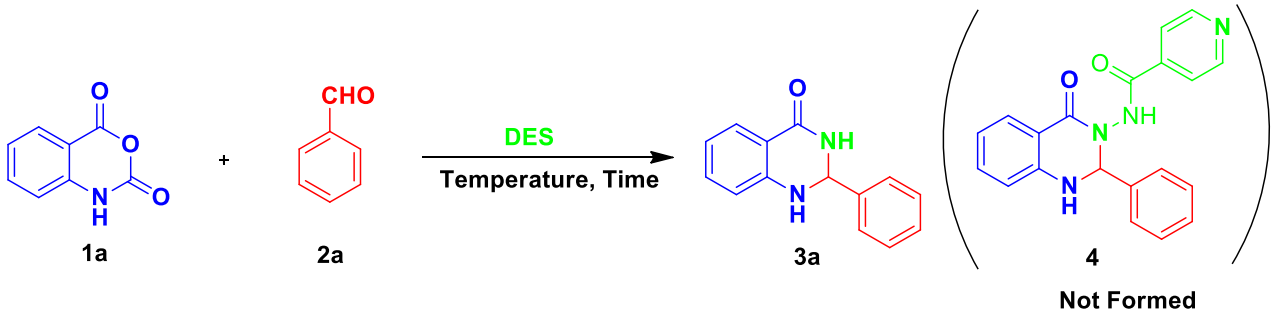


Figure 2. Present and past reactions towards DHQs synthesis.

Results and Discussion

We initiated our study by heating an equimolar mixture of isatoic anhydride, isonicotinic acid hydrazide (isoniazid), and benzaldehyde in $ZnCl_2$/urea DES at 110 °C for 35 min (Table 1, entry 1) with the aim to synthesising a new molecular hybrid of DHQ and isoniazid (**4**). The monitoring of the reaction by thin-layer chromatography (TLC) indicated the formation of a UV-fluorescent spot which was separated using column chromatography. Surprisingly, the initial proton NMR analysis of the isolated compound ruled out the formation of the expected product (**4**) based on the absence of proton resonances of isoniazid and prompted us to characterize the structure of this unknown compound. The subsequent detailed NMR analysis of the compound interestingly indicated the serendipitous obtention of 2-phenyl DHQ (**3a**) as reported previously,[41-43] and prompted us to explore the scope of this reaction further in the synthesis of DHQ derivatives. We were subsequently curious to know which substrate acts as a nitrogen source in the reaction. To accomplish this, we refluxed the same starting materials in ethanol which again offered the same product **3a** as confirmed by TLC and NMR spectroscopy, however, extended the reaction time led to a decrease in the yield (Table 1, entry 2). To confirm whether isoniazid or DES played the role of the nitrogen source, further reaction optimization was conducted without isoniazid (Table 1, entry 3). Delightfully, the reaction proceeded in 25 minutes with an improved yield (95%) of **3a**. Hence, these studies confirmed that the isoniazid did not play any role in the reaction but somehow negatively impacted the reaction outcome in terms of reaction time and product yield (Table 1, entries 1–3). The reaction was also performed using only urea in different moles of urea (3.5 mmol and 1 mmol) and afforded the unreacted starting materials without any traces of the product (TLC-based) (Table 1, entries 4 and 5). The same reaction outcome was observed when this reaction was carried out in refluxing ethanol for 2.5 h (Table 1, entry 6). These results led us to believe that urea alone is ineffective in catalyzing this reaction. Similarly, the reaction carried out using Lewis acid catalyst, $ZnCl_2$ (1 mmol) in ethanol, or under solvent-free conditions also did not produce the desired product (Table 1, entries 7 and 8) ruling out their individual role in the conversion to a product.

Table 1. Optimization of protocols for the synthesis of DHQ.



Entry	DES (molar ratio)	Solvent (mL)	Temperature (°C)	Time (min)	Yield (%)[a]
1	$ZnCl_2$/Urea (1:3.5)	-	110	35	88[b]

2	$ZnCl_2$/Urea (1:3.5)	EtOH	80	60	72[c]
3	$ZnCl_2$/Urea (1:3.5)	-	110	25	95
4	Urea (3.5mmol)	-	110	25	0
5	Urea (1mmol)	-	110	25	0
6	Urea (1mmol)	EtOH	80	150	0
7	$ZnCl_2$ (1mmol)	EtOH	80	150	0[d]
8	$ZnCl_2$ (1mmol)	-	110	25	0[d]
9	Choline chloride/Urea (1:2)	-	110	25	0
10	Choline chloride (1mmol)	-	110	25	0[d]
11	$AlCl_3$ (1mmol)	-	110	25	0[d]

[a]Isolated yield.

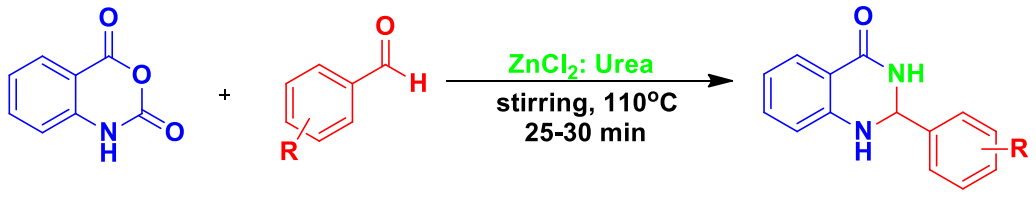
[b]Reaction protocols: **1a** (1mmol), **2a** (1mmol), isoniazid (1mmol), 8 g of DES ($ZnCl_2$/Urea (1:3.5) at 110 °C.

[c]Reaction protocols: **1a** (1mmol), **2a** (1mmol), isoniazid (1mmol), 8 g of DES ($ZnCl_2$/Urea (1:3.5) and ethanol at 80 °C.

[c]Reaction protocols: **1a** (1mmol), **2a** (1mmol), urea (1mmol), $ZnCl_2$ (1mmol), ethanol, reflux.

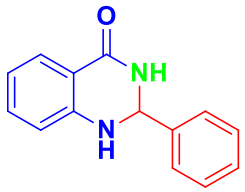
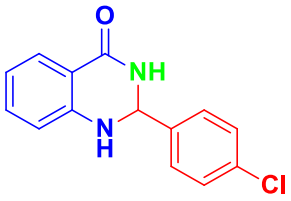
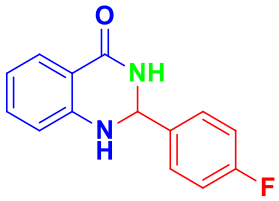
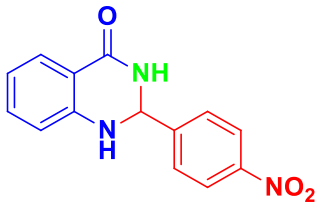
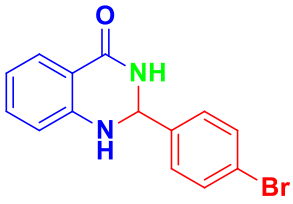
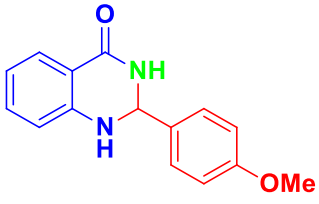
The use of another DES system choline chloride (ChCl) and urea (ChCl/urea) in catalyzing the reaction of **1a** and **2a** was unsuccessful (Table 1, entry 9). Finally, the Lewis acid capacity of ChCl and $AlCl_3$ to catalyze this reaction also did not lead to the product **3a** (Table 1, entries 10 and 11). Based on these optimization studies, the reaction conditions employing $ZnCl_2$/urea DES (Table 1 entry 3) were proven to be the best choice and were subsequently used for further derivatization of **3a.** The results are depicted in Table 2.

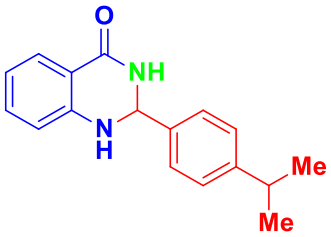
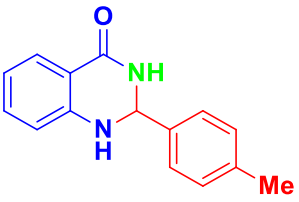
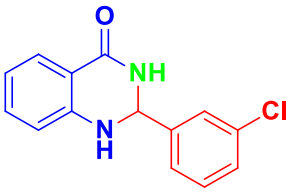
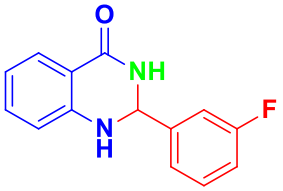
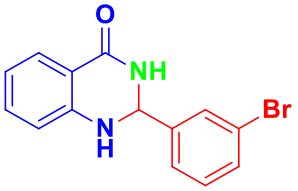
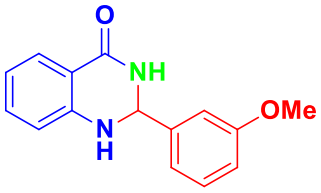
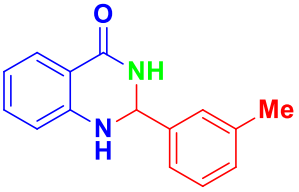
Table 2. Synthesis of DHQ & its derivatives.



1a **2a** **3**

Entry	R	Product	Yield (%)[a]	Measured mp (°C)	Reported[Ref] mp (°C)

1	Ph	 **3a**	95	214-216	216-218[43,50]
2	4-(Cl)-C_6H_4	 **3b**	92	204-206	205-206[43,44]
3	4-(F)-C_6H_4	 **3c**	96	200-201	203-204[43]
4	4-(NO_2)-C_6H_4	 **3d**	90	>300	>300[45,46]
5	4-(Br)-C_6H_4	 **3e**	94	195-196	196-198[47]
6	4-(OMe)-C_6H_4	 **3f**	91	183-185	181-183[43]

7	4-(*iso*-Propyl)-C_6H_4	 **3g**	96	161-164	162-163[47]
8	4-(Me)-C_6H_4	 **3h**	80	221-222	224-225[47,48,50]
9	3-(Cl)-C_6H_4	 **3i**	94	184-186	185-187[43,44]
10	3-(F)-C_6H_4	 **3j**	97	263-266	264-266[43]
11	3-(Br)-C_6H_4	 **3k**	92	228-230	227-228[48]
12	3-(OMe)-C_6H_4	 **3l**	88	147-149	148-150[44]
13	3-(Me)-C_6H_4		94	206-207	206-207[48]

3m

[a]Isolated yield.
[R]Reference.

Different aldehydes bearing electron-withdrawing or electron-donating groups were coupled with isatoic anhydride to get deeper insights into their reactivity. Worth of note, the electronic factors did not play much role as both aldehydes bearing electron-donating and electron-withdrawing groups reacted smoothly with isatoic anhydride under the optimized conditions offering the corresponding DHQs in good to high yield (80-97%). The mechanistic pathway depicting the significance of DES in the synthesis of DHQs is outlined in **Figure 3**.[40, 49]

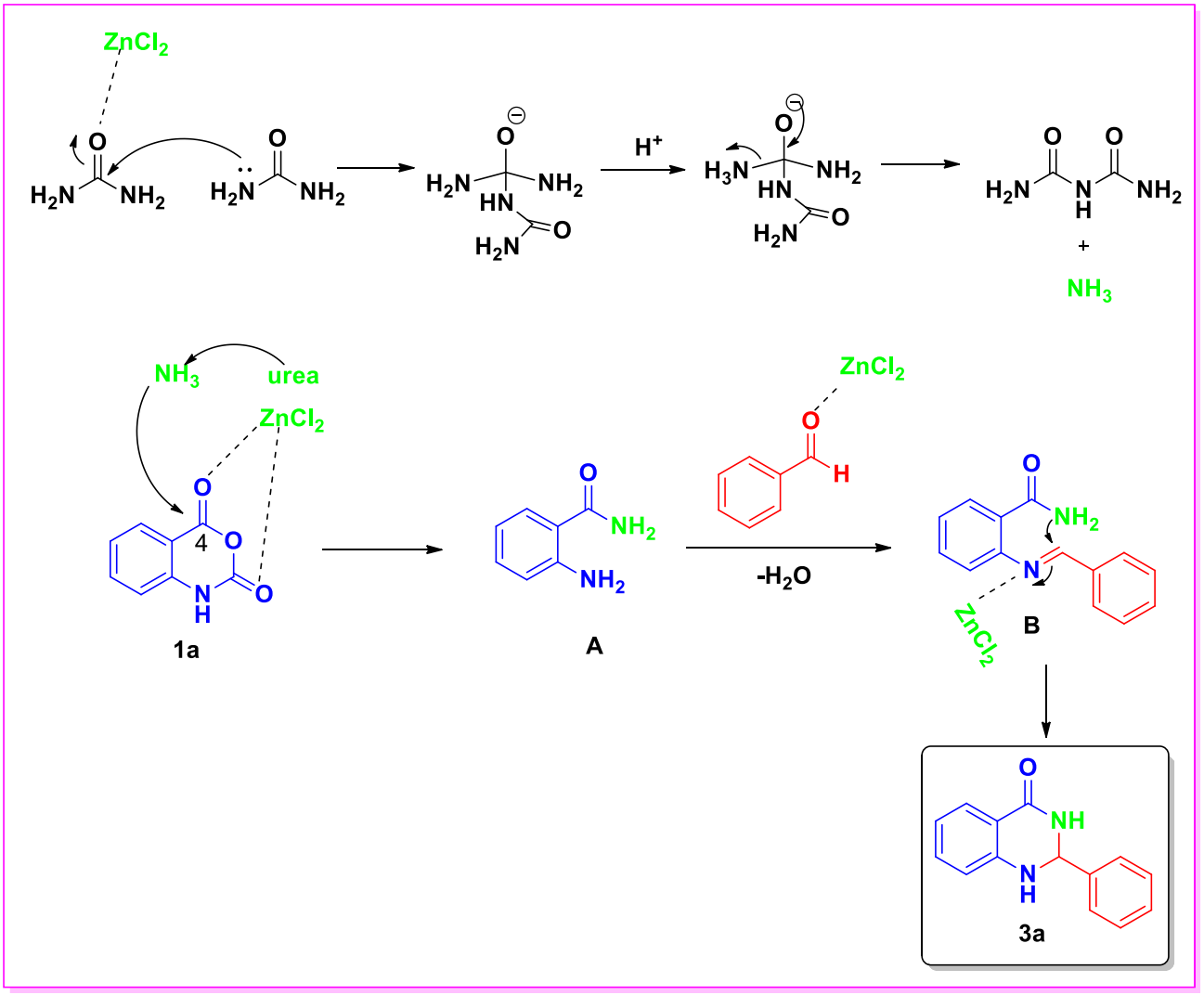


Figure 3. A proposed mechanism for the synthesis of DHQ.

The reaction is initiated by in-situ-generated ammonia from urea in a deep eutectic solvent (Figure 3). The generation of ammonia vapors in the reaction was confirmed by using litmus paper test (color changes from red to blue). The $ZnCl_2$ component facilitates the nucleophilic addition of ammonia to carbonyl carbon at the C-4 position of isatoic anhydride **1a**, followed by decarboxylation to yield anthranilamide **A** as an intermediate.

The Schiff base **B** is subsequently formed when the amino group of **A** attack the carbonyl carbon of the aldehyde, which has been activated by the eutectic mixture. In the final step, the activated azomethinic group is attacked by the nitrogen of the amide, resulting in the desired DHQ derivative.

Conclusions

An accidental three-component reaction in DES offered 2,3-dihydroquinazolines in excellent yields. The method employed was found to be atom-economical, cost-effective, green, and eco-friendly. Moreover, DES in this method played a triple role as a nitrogen source, catalyst, and solvent. The reaction conditions showed a wide range of tolerance abilities to varyingly substituted aldehydes bearing both electron-donating and electron-withdrawing groups.

Experimental Section

General. All chemicals were purchased from commercial sources (Acros, Spectrochem, Merck, and Aldrich). ^{1}H and ^{13}C NMR spectra were recorded on Bruker spectrometer using a 600 MHz spectrometer. TLCs Kieselgel-60 F-254 used to monitor the reaction were procured from Merck. Melting points were recorded using the melting point apparatus. Prominence-i (LC-2030C 3D) and PerkinElmer FT-IR Spectrometer were used to perform the LC-MS and IR spectral analysis of the compounds, respectively.

Preparation of DES. The DES was prepared as per the reported method.[40] The $ZnCl_2$ and urea (1:3.5) were taken in a test tube and heated at 80 °C until the solid phase converted into a transparent liquid and used further without any purification.

General procedure for the synthesis of DHQ. A mixture of isatoic anhydride (**1a**) and benzaldehyde (**2a**) was dissolved in $ZnCl_2$/urea deep eutectic solvent for 25 min, and the reaction progress was monitored using TLC. After completion of the reaction, water was added to the reaction mixture. Solid precipitate obtained filtered out and purified by using recrystallization in ethanol. Compounds **3a**, **3c**, **3f**, **3g**, **3j**, and **3m** were characterized with NMR spectroscopy, remaining derivatives were confirmed with IR spectra, LCMS and melting points also verified with literature.

2-Phenyl-2,3-dihydroquinazolin-4(1*H*)-one (3a).[11] (CAS Registry Number: 954-91-6) IR (ATR): 1608, 1653, 3067, 3166, 3299 cm^{-1}. ^{1}HNMR (600 MHz, DMSO-d6): 5.75 (s, 1H), 6.66-6.69 (t, *J* 15.03 Hz, *J* 7.42 Hz, 1H), 6.74-6.75 (d, *J* 8.02 Hz, 1H), 7.11 (s, 1H), 7.23-7.26 (dd, *J* 7.15 Hz, *J* 1.02 Hz, 1H), 7.33-7.40 (m, 3H), 7.49-7.50 (d, *J* 7.30 Hz, 2H), 7.61-7.62 (d, *J* 7.30 Hz, 1H), 8.29 (s, 1H); ^{13}C NMR (APT) (150 MHz, DMSO-d6): 67.0, 114.8, 115.4, 117.5, 127.3, 127.8, 128.7, 128.8, 133.7, 142.1, 148.3, and 164.3. MS *m/z* 225 (M+1).

2-(4-Chlorophenyl)-2,3-dihydroquinazolin-4(1*H*)-one (3b).[11] (CAS Registry Number:13165-11-2) IR (ATR): 1609, 1651, 3058, 3190, 3311 cm^{-1}. MS *m/z* 258.05 (M+1); Anal. Calc. for $C_{14}H_{11}ClN_2O$: 258.05; found: 259.

2-(4-Fluorophenyl)-2,3-dihydroquinazolin-4(1*H*)-one (3c).[11] (CAS Registry Number:359605-44-0) IR (ATR): 1603, 1648, 3040, 3175, 3302 cm^{-1}. ^{1}HNMR (600 MHz, DMSO-d6): 5.78 (s, 1H), 6.67-6.70 (t, *J* 14.77 Hz, *J* 7.50 Hz, 1H), 6.74-6.75 (d, *J* 7.94 Hz, 1H), 7.10 (s, 1H), 7.21-7.26 (m, 3H), 7.53-7.55 (dd, *J* 14.11 Hz, *J* 3.39 Hz, 2H), 7.61-7.62 (d, *J* 7.80 Hz, 1H), 8.29 (s, 1H); ^{13}C NMR (APT) (150 MHz, DMSO-d6): 66.4, 114.9, 115.4, 115.6, 117.7, 127.8, 129.4, 129.5, 133.8, 138.3, 148.2, 161.7, 163.3, and 164.0. MS *m/z* 243 (M+1).

2-(4-Nitrophenyl)-2,3-dihydroquinazolin-4(1*H*)-one (3d).[11] (CAS Registry Number:26029-31-2) IR (ATR): 1604, 1640, 3030, 3162, 3290 cm^{-1}. MS *m/z* 270 (M+1).

2-(4-Bromophenyl)-2,3-dihydroquinazolin-4(1*H*)-one (3e).[11] (CAS Registry Number:358386-50-2) IR (ATR): 1603, 1644, 3012, 3191, 3290 cm^{-1}. MS *m/z* 303 (M+1).

2-(4-Methoxyphenyl)-2,3-dihydroquinazolin-4(1*H*)-one (3f).[11] (CAS Registry Number:61195-16-2) IR (ATR): 1611, 1648, 2991, 3177, 3304 cm^{-1}. ^{1}HNMR (600 MHz, DMSO-d6): 3.75 (s, 3H), 5.71 (s, 1H), 6.66-6.69 (t, *J* 14.79 Hz, *J* 7.39 Hz, 1H), 6.73-6.75 (d, *J* 8.08 Hz, 1H), 6.94-6.95 (d, *J* 8.62 Hz, 2H), 7.01 (s, 1H), 7.23-7.25 (t, *J* 7.60 Hz, *J* 7.26 Hz, 1H), 7.41-7.43 (d, *J* 8.62 Hz, 2H), 7.60-7.62 (d, *J* 7.67 Hz, 1H), 8.19 (s, 1H); ^{13}C NMR (APT) (150 MHz, DMSO-d6): 55.6, 66.7, 114.1, 114.9, 115.4, 11.5, 127.8, 128.6, 134.2, 134.8, 148.4, 159.9, 164.1. MS *m/z* 255 (M+1).

2-(4-Isopropylphenyl)-2,3-dihydroquinazolin-4(1*H*)-one (3g).[11] (CAS Registry Number:83800-96-8) IR (ATR): 1607, 1654, 2948, 3196, 3298 cm^{-1}. ^{1}HNMR (600 MHz, DMSO-d6): 1.18 (d, *J* 6.99 Hz, 6H), 2.85 (septet, 7H), 5.7 (s, 1H), 6.66-6.68 (t, *J* 15.02 Hz, *J* 7.36 Hz, 1H), 6.73-6.74 (d, *J* 7.66 Hz, 1H), 7.07 (s, 1H), 7.22-7.27 (m, 3H), 7.41-7.43 (d, *J* 7.95 Hz, 2H), 7.61-7.62 (d, *J* 7.82 Hz, 1H), 8.24 (s, 1H); ^{13}C NMR (APT) (150 MHz, DMSO-d6): 24.3, 33.7, 67.0, 114.8, 115.4, 117.5, 126.7, 127.4, 127.8, 133.7, 139.5, 148.4, 149.2, and 164.1. MS *m/z* 267 (M+1).

2-(p-tolyl)-2,3-dihydroquinazolin-4(1*H*)-one (3h).[11] (CAS Registry Number:13324-79-3) IR (ATR): 1600, 1654, 3045, 3198, 3302 cm^{-1}. MS *m/z* 239 (M+1).

2-(3-Chlorophenyl)-2,3-dihydroquinazolin-4(1*H*)-one (3i).[11] (CAS Registry Number:83800-92-4) IR (ATR): 1612, 1643, 3028, 3181, 3290 cm^{-1}. . MS *m/z* 243 (M+1).

2-(3-Fluorophenyl)-2,3-dihydroquinazolin-4(1*H*)-one (3j).[11] (CAS Registry Number:386242-54-2) IR (ATR): 1609, 1648, 3178, 3284, 3345 cm^{-1}. ^{1}HNMR (600 MHz, DMSO-d6): 5.79 (s, 1H), 6.67-6.70 (t, *J* 14.85 Hz, *J* 7.68 Hz, 1H), 6.76-6.77 (d, *J* 8.30 Hz, 1H), 7.16-7.34 (m, 5H), 7.41-7.45 (dd, *J* 7.81 Hz, 1H), 7.60 (d, *J* 7.46 Hz, 1H), 8.42 (s, 1H); ^{13}C NMR (APT) (150 MHz, DMSO-d6): 66.1, 113.9, 114.1, 11.9, 115.5, 115.6, 117.7, 123.2, 127.8, 130.8, 130.84, 133.8, 145.3, 147.9, 161.7, 163.3, and 163.88$. MS *m/z* 243 (M+1).

2-(3-Bromophenyl)-2,3-dihydroquinazolin-4(1*H*)-one (3k).[11] (CAS Registry Number:304451-29-4) IR (ATR): 1609, 1646, 3033, 3199, 3281 cm^{-1}. MS *m/z* 303 (M+1).

2-(3-Methoxyphenyl)-2,3-dihydroquinazolin-4(1*H*)-one (3l).[11] (CAS Registry Number:198068-91-6) IR (ATR): 1606, 1643, 2911, 3060, 3200 cm^{-1} MS *m/z* 255 (M+1).

2-(m-tolyl)-2,3-dihydroquinazolin-4(1*H*)-one (3m).[11] (CAS Registry Number:83800-93-5) IR (ATR): 1612, 1645, 3030, 3183, 3299 cm^{-1}. ^{1}HNMR (600 MHz, DMSO-d6): 2.31 (s, 3H), 5.71 (s, 1H), 6.66-6.68 (t, *J* 14.84 Hz, *J* 7.42 Hz, 1H), 6.73-6.75 (d, *J* 7.81 Hz, 1H), 7.07 (s, 1H), 7.16 (d, *J* 4.15 Hz, 1H), 7.22-7.28 (m, 3H), 7.60 (d, *J* 8.04 Hz, 1H), 8.24 (s, 1H); 13C NMR (APT) (150 MHz, DMSO-d6): 21.5, 67.1, 114.8, 117.5, 124.4, 127.8, 127.95, 128.7, 129.5, 133.7, 137.8, 141.9, 148.3, and 164.0. MS *m/z* 239 (M+1).

Acknowledgements

PS gratefully acknowledges the National Research Foundation (SA) for a Competitive grant for rated researchers (Grant Number: SRUG2204092857). NM acknowledges the National Research Foundation (SA) for the PDF fellowship (PSTD2204214150).

Supplementary Material

Provided as a separate file

References

1. Qiu, X.; Zhou, M.; Zhu, Z.; Qi, *J*.; Wang, Y.; Yang, J. *Sep. Puri. Tech.* **2022**, 297, 121498.
https://doi.org/10.1016/j.seppur.2022.121498
2. Sheldon, R. A. *G. Chem.* **2005**, 7 (5), 267-278.
https://doi.org/10.1039/b418069k
3. Andrade, C. K.; Alves, L. M. *Curr. Org. Chem*. **2005**, *9*, 195.
https://doi.org/10.2174/1385272053369178
4. Kumar, G.; Bhargava, G.; Kumar, Y.; Kumar, R. *J. Chem. Sci.* **2022**, 134 (2), 44.
https://doi.org/10.1007/s12039-022-02039-z
5. Kumar, G.; Singh, P.; Bhargava, G.; Gill, B. S.; Rajput, J. K.; Kumar, R. *J. Sul. Chem.* **2023**, 1-11.
6. Dinodia, M. *Curr. Org. Syn.* **2022**, 19 (4), 543-557.
https://doi.org/10.2174/1570179419666220107160725
7. Hansen, B. B.; Spittle, S.; Chen, B.; Poe, D.; Zhang, Y.; Klein, J. M.; Horton, A.; Adhikari, L.; Zelovich, T.; Doherty, B. W. *Chem. Rev.* **2020**, 121 (3), 1232-1285.
https://doi.org/10.1021/acs.chemrev.0c00385
8. Santana-Mayor, Á.; Rodríguez-Ramos, R.; Herrera-Herrera, A. V.; Socas-Rodríguez, B.; Rodríguez-Delgado, M. Á. *T. Tren. Ana. Chem.* **2021**, 134, 116108.
https://doi.org/10.1016/j.trac.2020.116108
9. Alonso, D. A.; Baeza, A.; Chinchilla, R.; Guillena, G.; Pastor, I. M.; Ramón, D. J. *E. J. Org. Chem.* **2016**, 2016 (4), 612-632.
https://doi.org/10.1002/ejoc.201501197
10. Lomba, L.; Ribate, M.; Sangüesa, E.; Concha, J.; Garralaga, M.; Errazquin, D.; García, C. B.; Giner, B. *App. Sci.* **2021**, 11 (21), 10061.
https://doi.org/10.3390/app112110061
11. Kumar, G.; Seboletswe, P.; Manhas, N.; Singh, P.; Bhargava, G.; Rajput, J. K.; Kumar, R. *J. Het. Chem.* **2023**.
12. Perna, F. M.; Vitale, P.; Capriati, V. *Curr. Op. G. Sus. Chem.* **2020**, 21, 27-33.
https://doi.org/10.1016/j.cogsc.2019.09.004
13. Smith, E. L.; Abbott, A. P.; Ryder, K. S. *Chem. Rev.* **2014**, 114 (21), 11060-11082.
https://doi.org/10.1021/cr300162p
14. Zhang, Q.; Vigier, K. D. O.; Royer, S.; Jérôme, F. *Chem. Soc. Rev.* **2012**, 41 (21), 7108-7146.
https://doi.org/10.1039/c2cs35178a
15. Handy, S.; Lavender, K. *T. L.* **2013**, 54 (33), 4377-4379.
https://doi.org/10.1016/j.tetlet.2013.05.122
16. Pawar, P. M.; Jarag, K. J.; Shankarling, G. S. *G. Chem.* **2011**, 13 (8), 2130-2134.
https://doi.org/10.1039/c0gc00712a
17. Kumar, G.; Bhargava, G.; Kumar, R. *Poly. Arom. Comp.* **2022**, 1-14.
https://doi.org/10.1039/D3MD00012E
18. Shaibuna, M.; Kuniyil, M. J. K.; Sreekumar, K. *N. J. Chem.* **2021**, 45 (44), 20765-20775.
https://doi.org/10.1039/D1NJ03879F
19. Wang, A.; Zheng, X.; Zhao, Z.; Li, C.; Zheng, X. *Prog. Chem.* **2014**, 26 (05), 784.
20. Saini, M. S.; Kumar, A.; Dwivedi, J.; Singh, R. *Int. J. Pharm. Sci. Res*. **2013**, 4 (3), 66-77.
21. Mermer, A.; Keles, T.; Sirin, Y. *B. Chem.* **2021**, 114, 105076.
https://doi.org/10.1016/j.bioorg.2021.105076
22. Halimehjani, A. Z.; Namboothiri, I. N.; Hooshmand, S. E. *RSC Adv.* **2014**, 4 (89), 48022-48084.
https://doi.org/10.1039/C4RA08828J

23. Ravez, S.; Castillo-Aguilera, O.; Depreux, P.; Goossens, L. *Exp. Op. ther. Pat.* **2015**, 25 (7), 789-804. https://doi.org/10.1517/13543776.2015.1039512
24. Rojas-Aguirre, Y.; Hernández-Luis, F.; Mendoza-Martínez, C.; Sotomayor, C. P.; Aguilar, L. F.; Villena, F.; Castillo, I.; Hernández, D. J.; Suwalsky, M. *Biochem. Biophys. Act. Biomem.* **2012**, 1818 (3), 738-746. https://doi.org/10.1016/j.bbamem.2011.11.026
25. Karan, R.; Agarwal, P.; Sinha, M.; Mahato, N. *Chem. Eng.* **2021**, 5 (4), 73. https://doi.org/10.3390/chemengineering5040073
26. Dutta, A.; Sarma, D. *Tub.* **2020**, 124, 101986. https://doi.org/10.1016/j.tube.2020.101986
27. Li, Z.; Zhao, L.; Bian, Y.; Li, Y.; Qu, J.; Song, F. *Curr. Topi. Med. Chem.* **2022**, 22 (12), 1035-1044. https://doi.org/10.2174/1568026622666220307144015
28. Azizi, N.; Shirdel, F. *Res. Chem. Int.* **2017**, 43, 3873-3882. https://doi.org/10.1007/s11164-016-2849-4
29. Abbas, S. Y.; El-Bayouki, K. A.; Basyouni, W. M. *Syn. Comm.* **2016**, 46 (12), 993-1035. https://doi.org/10.1080/00397911.2016.1177087
30. Tashrifi, Z.; Mohammadi-Khanaposhtani, M.; Biglar, M.; Larijani, B.; Mahdavi, M. Curr. Org. Chem. **2019**, 23 (10), 1090-1130. https://doi.org/10.2174/1385272823666190701142930
31. Ghorbani-Choghamarani, A.; Taghipour, T. *Lett. Org. Chem.* **2011**, 8 (7), 470-476. https://doi.org/10.2174/157017811796505025
32. Ramesh, K.; Karnakar, K.; Satish, G.; Reddy, K. H. V.; Nageswar, Y. *T. L.* **2012**, 53 (45), 6095-6099. https://doi.org/10.1016/j.tetlet.2012.08.141
33. Mitra, B.; Pariyar, G. C.; Ghosh, P. *RSC adv.* **2021**, 11 (3), 1271-1281. https://doi.org/10.1039/D0RA09562A
34. Wu, J.; Du, X.; Ma, J.; Zhang, Y.; Shi, Q.; Luo, L.; Song, B.; Yang, S.; Hu, D. *G. Chem.* **2014**, 16 (6), 3210-3217. https://doi.org/10.1039/C3GC42400F
35. Deng, T.; Wang, H.; Cai, C. *J. Flu. Chem.* **2015**, 169, 72-77. https://doi.org/10.1016/j.jfluchem.2014.11.008
36. Saffar-Teluri, A.; Bolouk, S. *Mon. f. Chemi. Chem. Mont.* **2010**, 141, 1113-1115. https://doi.org/10.1007/s00706-010-0376-3
37. Karimi-Jaberi, Z.; Arjmandi, R. *Mon. f. Chemi. Chem. Mont.* **2011**, 142, 631-635. https://doi.org/10.1007/s00706-011-0494-6
38. Roopan, S. M.; Nawaz Khan, F.; Jin, J. S.; Senthil Kumar, R. *Res. Chem. Int.* **2011**, 37, 919-927. https://doi.org/10.1007/s11164-011-0301-3
39. Surpur, M. P.; Singh, P. R.; Patil, S. B.; Samant, S. D. *Syn. Comm*. **2007**, 37 (12), 1965-1970. https://doi.org/10.1080/00397910701354699
40. Peña-Solórzano, D.; Guilombo, C. E. G.; Ochoa-Puentes, C. *Sus. Chem. Pharm*. **2019**, 14, 100167. https://doi.org/10.1016/j.scp.2019.100167
41. Chandra Pariyar, G.; Mitra, B.; Mukherjee, S.; Ghosh, P. *Chem. Sel.* **2020**, 5 (1), 104-108. https://doi.org/10.1002/slct.201903937
42. Rueping, M.; Antonchick, A. P.; Sugiono, E.; Grenader, K. *Ang. Chem. Int. Ed.* **2009**, 48 (5), 908-910. https://doi.org/10.1002/anie.200804770
43. Safari, J.; Gandomi-Ravandi, S. *J. Mol. Cat. A. Chem*. **2014**, 390, 1-6. https://doi.org/10.1016/j.molcata.2014.02.013

44. Borase, P. N.; Thale, P. B.; Shankarling, G. *RSC adv.* **2016**, 6 (67), 63078-63083.
https://doi.org/10.1039/C6RA15574J
45. Qiao, R. Z.; Xu, B. L.; Wang, Y. H. *Chin. Chem. Lett.* **2007**, 18 (6), 656-658.
https://doi.org/10.1016/j.cclet.2007.04.036
46. Wu, S. J.; Zhao, Z. Q.; Gao, J. S.; Chen, B. H.; Chen, G. F. *Res. Chem. Int.* **2019**, 45, 2327-2339.
https://doi.org/10.1007/s11164-018-03732-w
47. Yashwantrao, G.; Jejurkar, V. P.; Kshatriya, R.; Saha, S. *ACS Sus. Chem. Eng.* **2019**, 7 (15), 13551-13558.
https://doi.org/10.1021/acssuschemeng.9b03199
48. Xie, Z.-B.; Zhang, S.-G.; Jiang, G.-F.; Sun, D.-Z.; Le, Z.-G. *G. Chem. Lett. Rev.* **2015**, 8 (3-4), 95-98.
https://doi.org/10.1080/17518253.2015.1109145
49. Sahoo, S.; Pal, S. *T. J. Org. Chem.* **2021**, 86 (24), 18067-18080.
https://doi.org/10.1021/acs.joc.1c02343
50. Keikhosravi, N; Dehghan-Ghahfarokhi, E; Abdollahi, S; Piramoon, M; Javad Ghasemian-Yadegari, M; Rezaeinasab, R. *J. Med. Chem. Sci*. **2022,** 308-314.