Multicomponent Synthetic Reactions involving Aminopyrazole-Based Hetrocycles

---

[1]Rohit Kumar*, [2]Jitendra Kumar Chaurasiyaa, [3]Shachi Tiwaria

[1/2/3]Department of Humanities and Applied Science, Ashoka Institute of Technology and Management Pahariya Varanasi, India

[1]rohitjam786@gmail.com

https://doi.org/10.64882/ijrt.v14.iS1.1041

Abstract

Aminopyrazoles are important and versatile building blocks in heterocyclic chemistry and have been extensively employed in the synthesis of pyrazole-fused heterocyclic frameworks. Owing to the presence of multiple reactive sites, aminopyrazoles exhibit diverse chemical reactivity, making them particularly suitable substrates for multicomponent reactions (MCRs). These reactions provide efficient, atom-economical, and sustainable approaches for the rapid construction of structurally complex and functionalized aza-heterocycles. In recent years, the use of aminopyrazoles in MCRs has gained significant attention due to their ability to generate molecular diversity through one-pot processes while minimizing reaction steps, time, and waste. Pyrazole-containing compounds are widely recognized for their medicinal relevance, with reported biological activities including anticancer, antimicrobial, anti-inflammatory, and antiviral properties. Consequently, aminopyrazole-based MCRs have become an attractive strategy for the development of biologically relevant heterocyclic scaffolds. Although several reviews have focused on the synthesis and general applications of aminopyrazoles, a comprehensive review dedicated exclusively to their reactivity in multicomponent reactions has not been reported to date. This review presents a systematic and critical overview of the reactivity of aminopyrazoles in multicomponent reactions, covering various reaction types, mechanistic aspects, and synthetic outcomes. Recent developments, representative examples, and potential future directions in this rapidly evolving area are also highlighted, providing a valuable resource for researchers working in heterocyclic and medicinal chemistry.

Keywords: Multicomponent reactions; aminopyrazoles; pyrazole-fused heterocycles; aza-heterocycles; 1,3-binucleophiles; heterocyclic synthesis; fused heterocyclic systems; one-pot synthesis; green chemistry; medicinal chemistry.

Introduction

A pyrazole ring refers to a five-membered nitrogen-containing aromatic heterocycle, which occurs widely in natural products and synthetic compounds with important medical and agrochemical properties.[1] Biaryl compounds incorporating a pyrazole ring display diverse bioactivities such as anti-cancer, anti-inflammatory, antimicrobials, antimalarials, antivirals, neuroprotective, and metabolic disorders, establishing the relevance of the pyrazole ring in medical chemistry.[2] Several commercially available compounds incorporating the pyrazole

skeleton can be found in celecoxib (anti-inflammatory), rimonabant (antagonist of the CB1 receptor of cannabinoids and anti-obesity drug), fipronil (insecticide), and sildenafil (used in the treatment of sexual dysfunction). Besides the important roles in the various fields of medication, the compounds incorporating the pyrazole skeleton have attracted more attention in material science, especially in light-emitting diodes, semiconductors, solar cells, electroluminescent compounds, and liquid crystals. Additionally, pyrazole hybrids were found to be commonly used as chemosensors in the selective detection of heavy metal ions like Cu^{2+}, Ni^{2+}, Zn^{2+}, Hg^{2+}, Al^{3+}, Fe^{3+}, Cr^{3+}, and Ag^{+}; anions F^{-} and CN^{-}; and high-energy compounds like picric acid. Several natural compounds incorporating the pyrazole skeleton can be found in Figure 1 below, together with their applications as drugs and chemosensors. [3-9]

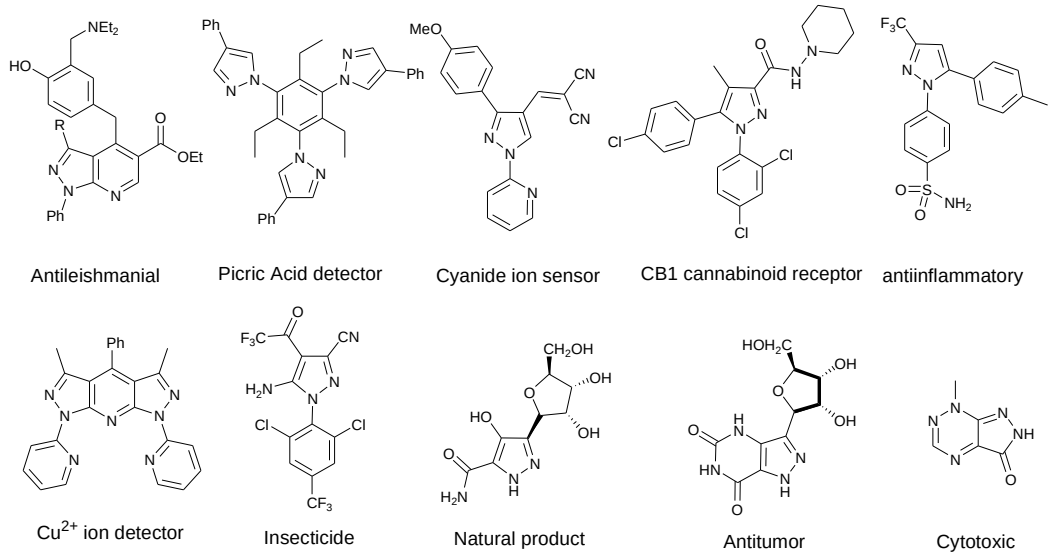


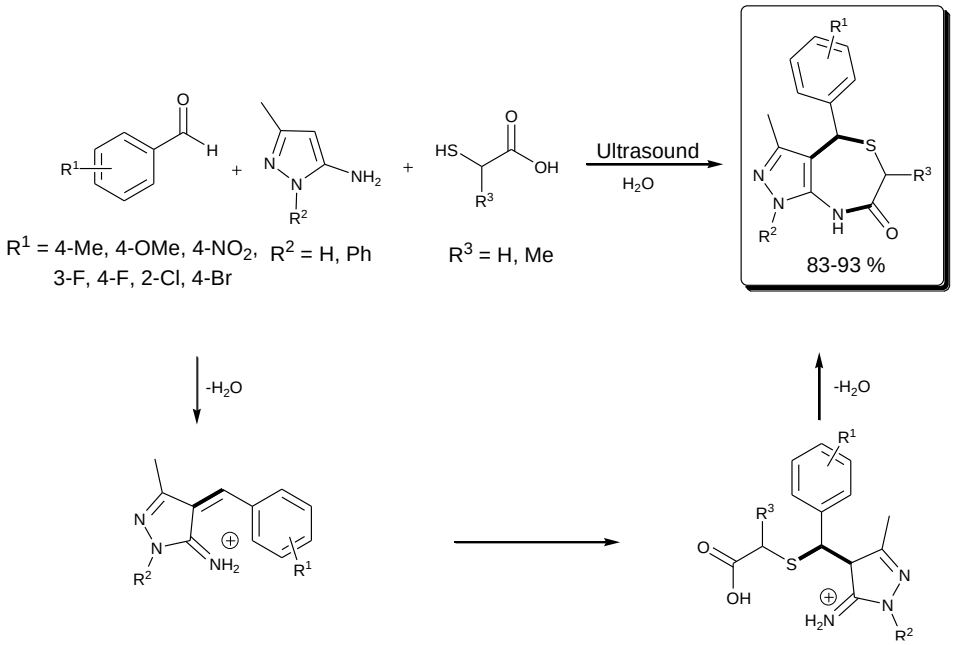
Figure 1. Typical examples of molecules containing the pyrazole nucleus

Aminopyrazoles are amino derivatives of pyrazoles and serve as versatile intermediates in the preparation of various pyrazole-fused heterocyclic compounds. Due to the presence of several active sites, aminopyrazoles serve as effective binucleophilic reagents and may take part in the reaction as an N, N- or C, N binucleophile. Multicomponent reactions (MCRs) involve the assembly of more than two reactants in a one-step process to provide the final compound containing appreciable contributions from all the reactants.[10] Multicomponent reactions are also termed as domino, tandem, or cascade reactions. These reactions have proven to be the best approach toward the creation of structural complexities in a one-step process. Multicomponent reactions achieve a lower number of synthetic steps; exhibit high atom economy; and demonstrate high efficiency in the formation of bonds. These were found to be more preferable to the classical multi-step methods. In fact, the use of MCRs has other attractive benefits, such as simplicity in operation, high yield of the final compound, and less production of waste. Due to the sustainable and green chemistry nature of the above-stated characteristics,[11] the application of multicomponent reactions has experienced growing interest in recent years. Owing to the importance of multicomponent reactions, the application of aminopyrazoles in synthesizing pyrazole-fused heterocycles has been extensively investigated. The current review targets the application of 1,3-binucleophilic properties of aminopyrazoles

in multicomponent reaction cascades[12]. Despite existing reviews for 5-aminopyrazoles and amino azoles, there has been a need for an independent review for the application of aminopyrazoles as 1,3-binucleophiles in multicomponent reaction cascades. As a result, this review begins by summarizing all existing literature between 2014 and the current time on aminopyrazoles working as N, N- and C, N-binucleophiles for the synthesis of different pyrazole fused heterocycles and in situ formed aminopyrazoles.[13]

Synthesis of Aminopyrazole Derivatives

Dandia et al. reported a one-pot, three-component synthesis of pyrazolo[3,4-e][1,4]thiazepines using ultrasonication through the reaction of aldehydes, 5-amino-3-methylpyrazole, and mercaptocarboxylic acids in an aqueous medium (Scheme 1). Mechanism was suggested to involve the initial condensation of the aminopyrazole component and the aldehyde component, followed by the addition of the mercaptocarboxylic acids component and the resulting cyclization to form the heterocyclic compound. A wide range of electronically distinct groups were tolerated in the reaction, providing the compounds in high yields (83-93%).[14] Biological studies of the compounds were conducted to find that several of the compounds had good antibacterial as well as antitubercular activity.

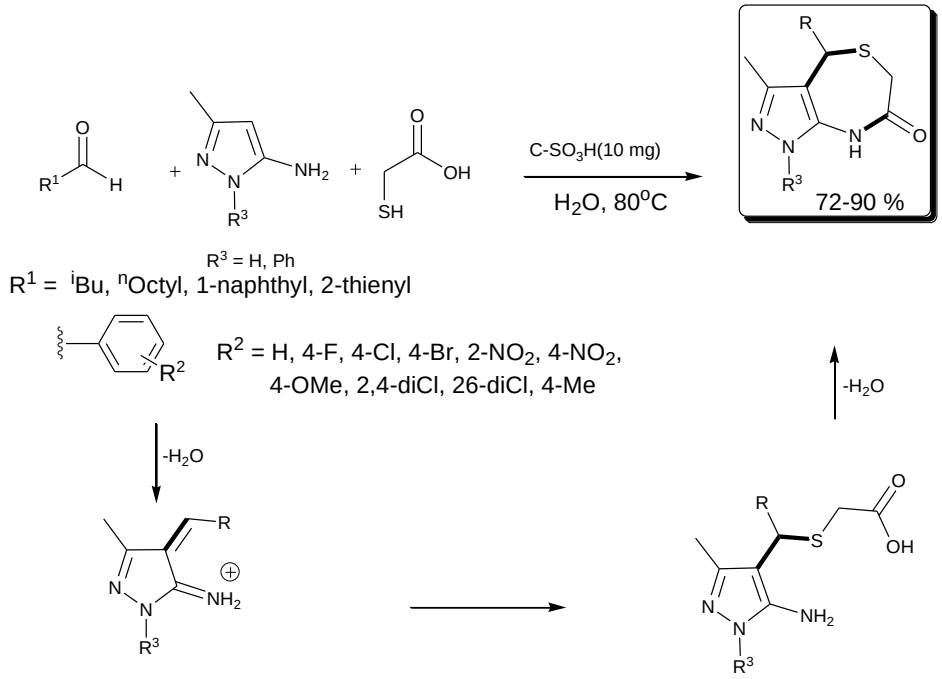


Scheme 1. One-Pot Formation of Pyrazolo-Fused Thiazepines.

Ref . A. Dandia, R. Singh, J. Joshi and S. Maheshwari, *Res. Chem. Intermed.*, 2015, 41, 4213-4226

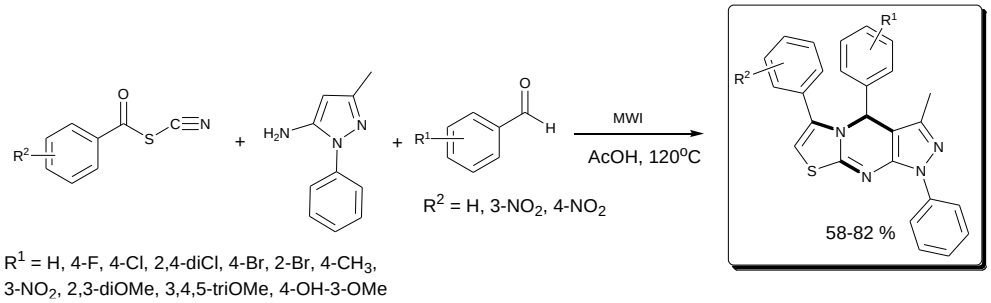
Zhang et al. published a solid acid-catalyzed three-component reaction of aminopyrazoles, aldehydes, and thioglycolic acid in aqueous media for the synthesis of 4,8-dihydro-1H-pyrazolo[3,4-e][1,4]thiazepin-7(6H)-one derivatives (Scheme 2)[15]. The reaction likely follows the mechanism in which the C-center of the aminopyrazole attacks the aldehyde carbonyl function in a nucleophilic addition reaction with the expulsion of water, forming an intermediate compound. Subsequent addition of the sulfur atom of the thioglycolic acid molecule, followed by the condensation of the carboxylic acid and the amine groups, results in

the final product formation. Various benzaldehydes were found to be satisfactory; however, heteroaromatic aldehydes like 2-thienylcarbaldehyde were more active. The effect of substituents in the benzaldehyde derivatives resulted in variable yields; electron-donating groups resulted in better yields of the final compound (with 4-OMe giving the maximum yield), whereas the presence of electron-withdrawing groups like 4-NO2 caused reduced yield of the final product. Overall, the reaction provided the desired products in good to excellent yields (72–90%).



Scheme 2. Three-component reaction in aqueous medium catalyzed by a solid acid.
Ref . F. Zhang, C. Li and C. Qi, *RSC Adv.*, 2016, **6**, 102924–102930

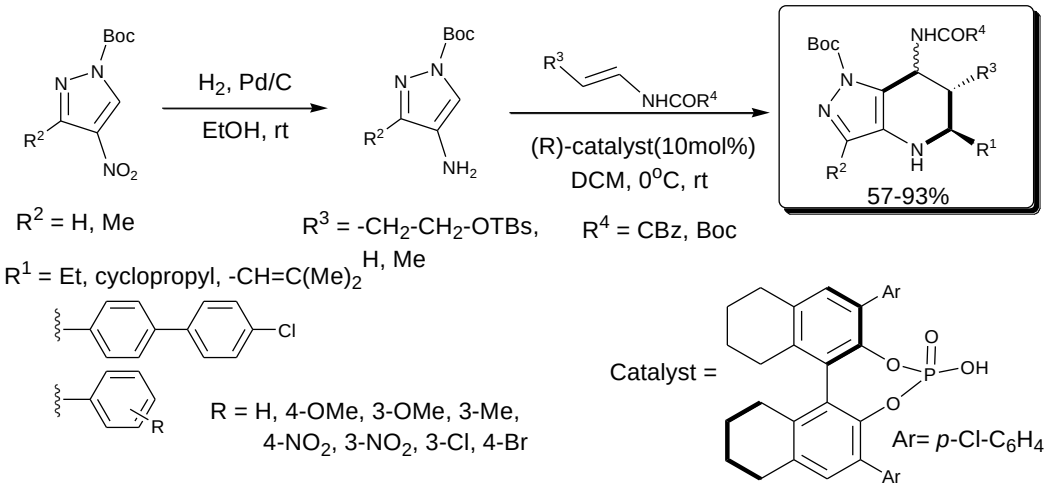
Hao et al. reported the microwave-assisted, three-component synthesis of pyrazolo[3,4-d]thiazolo[3,2-a]pyrimidine derivatives from aryl aldehydes, α-thiocyanate ketones, and 5-aminopyrazoles in acetic acid (Scheme 73). The reaction tolerated a wide range of substituents on the aromatic aldehyde, including sterically hindered ones such as 2-bromo and 2,6-dimethoxybenzaldehyde. Electron-withdrawing groups at the C-4 position enhanced product yields, while an –OMe group on the α-thiocyanate ketone led to complex mixtures. Using various substrates, the desired products were obtained in 58–82% yields. [16]



Scheme 3. Microwave-Promoted Three-Component Reaction in the Presence of Acetic Acid.

Ref . W. H. Hao, P. Zhou, F. Y. Wu, B. Jiang, S. J. Tu and G. Li, *Eur. J. Org. Chem.* 2016, 1968–1971

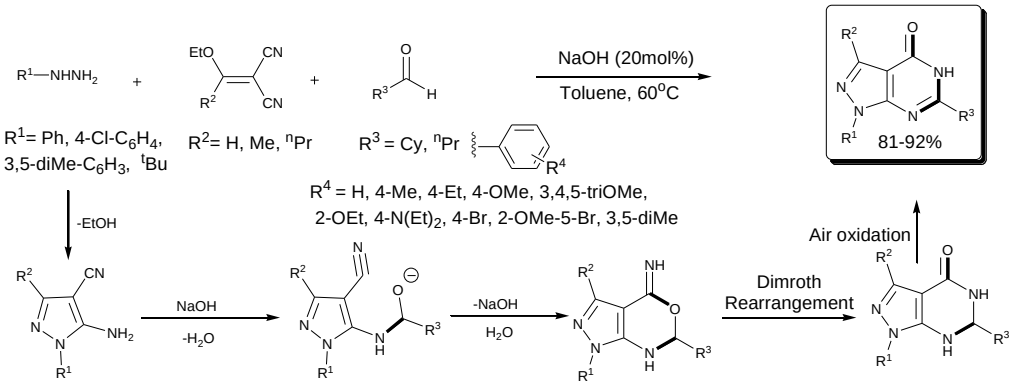
Brioche et al. communicated a chiral phosphoric acid-catalyzed, diastereo- and enantioselective synthesis of tetrahydropyrazolopyridines via the reaction of aminopyrazoles, aldehydes, and enecarbamates (Scheme 4). The in situ formation of aminopyrazoles was realized through the hydrogenation of the corresponding nitro derivatives using H_2 and Pd/C in ethanol under room temperature conditions.[17] Mechanistically, an imine was formed through condensation of the in situ aminopyrazoles with aldehydes, serving as an aza-diene precursor. The subsequent reaction with enecarbamates through a Povarov-type process furnished final tetrahydropyrazolopyridines in 57−93% yields.



Scheme 4. Three-Component Reaction Catalyzed by Chiral Phosphoric Acid.

Ref. J. Brioche, T. Courant, L. Alcaraz, M. Stocks, M. Fuber, J. Zhu and G. Masson, *Adv. Synth. Catal.*., 2014, **356**, 1719-1724

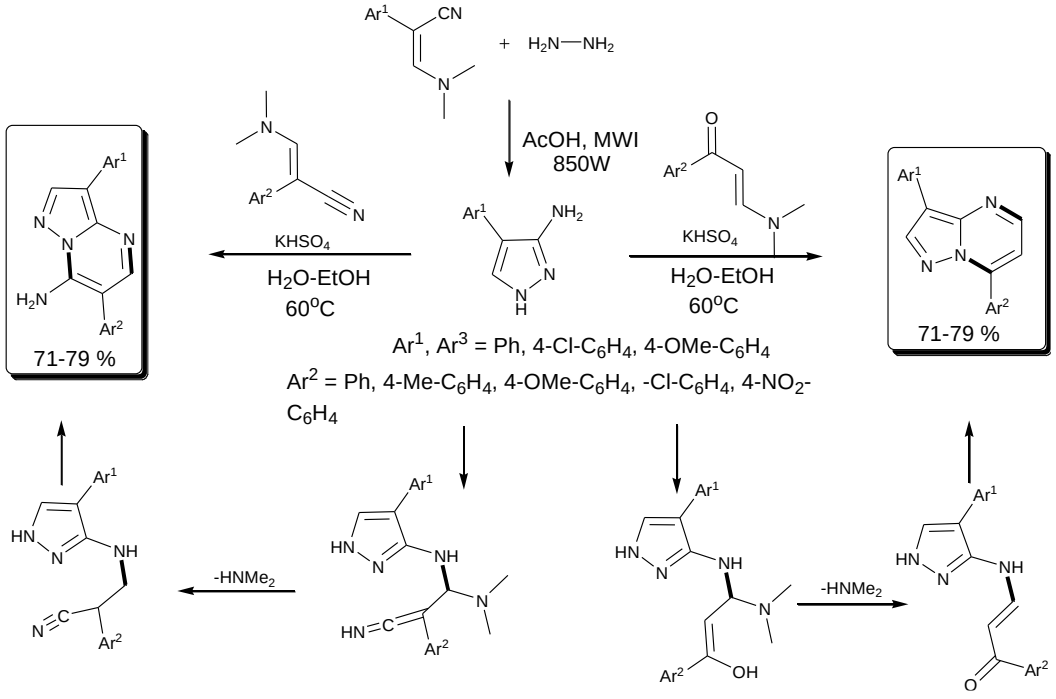
A one-pot three-component synthesis of pyrazolo[3,4-d]pyrimidinone derivatives using NaOH as the catalyst, by Liu et al., from the reaction of hydrazine, methylenemalononitrile, and aldehydes (Scheme 5), has been documented[18]. In this process, the in situ formation of the aminopyrazole from the reaction between the hydrazine and methylenemalononitrile followed by the reaction of the in situ formed compound with the aldehyde in the presence of NaOH and subsequent Dimroth rearrangement and air oxidation led to the formation of the desired product, while the reaction furnished the couple of products in 81 to 92% yields, and the presence.



Scheme 5. NaOH-catalysed three-component reaction

Ref. M. X. Liu, J. R. Li, K. Zhang and D. X. Shi, *Tetrahedron*, 2015, 71, 7658-7662

Devi et al. describe a three-component synthesis of 3,7-diarylpyrazolo[1,5-a]pyrimidines and 3,6-diarylpyrazolo[1,5-a]pyrimidine-7-amines by heating 3-dimethylamino-2-arylacrylonitrile, hydrazine, and formylated acetophenones or enaminonitriles at 60 °C with $KHSO_4$ in H_2O–ethanol (Scheme 6). First, the aminopyrazoles were formed in situ from 3-dimethylamino-2-arylacrylonitrile and hydrazine under microwave irradiation with AcOH.[19] These intermediates reacted with formylated acetophenones or enaminonitriles in a conjugate fashion to give the products. A range of substituents was tolerated, giving the products in yields of 71–79%.

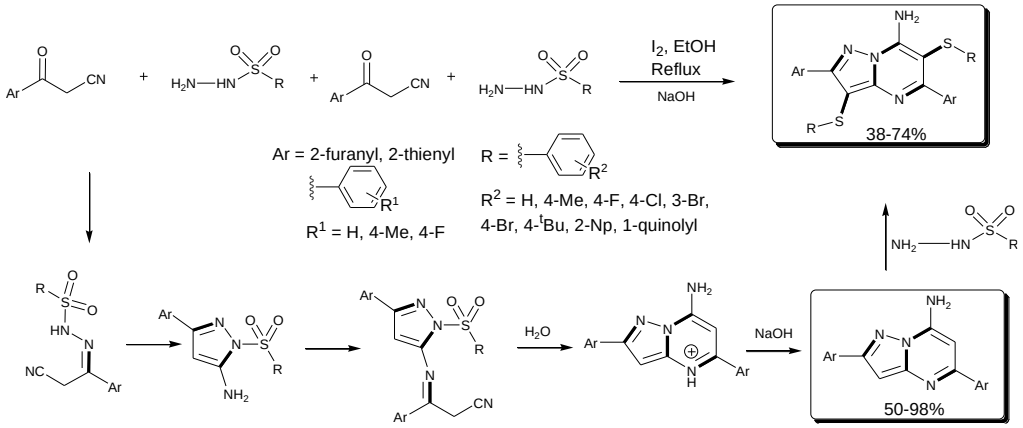


Scheme 6. $KHSO_4$-Catalyzed One-Pot Multicomponent Synthesis.

Ref. A. S. Devi, S. Kaping and J. N. Vishwakarma, *Mol. Divers.*, 2015, 19, 759-771

A multi-component approach for the synthesis of fully substituted pyrazolo[1,5-a]pyrimidines using iodine as a catalyst has been developed by Sun et al. (Scheme 7). In their approach, β-Ketonitrile reacts with sulfonyl hydrazide to form an aminopyrazole compound in

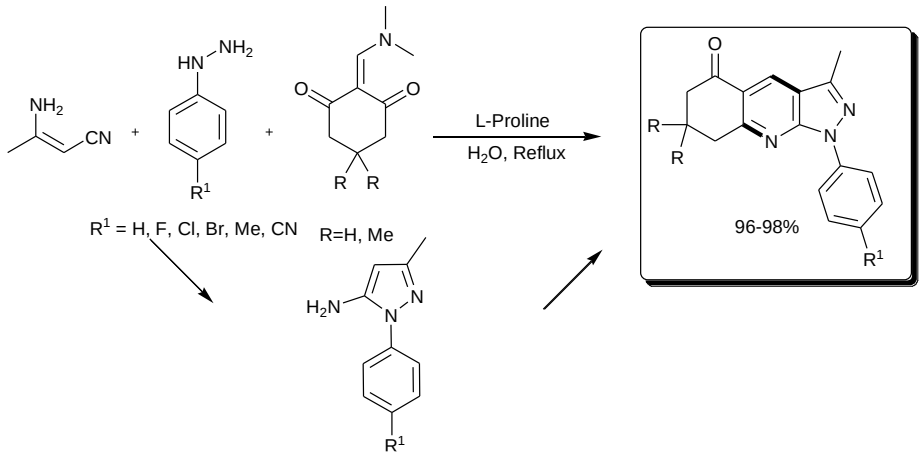
situ. A subsequent reaction with an additional equivalent of β-Ketonitrile in the presence of a base such as NaOH results in a fully functionalized pyrazolo[1,5-a] pyrimidine.[20] The compound then undergoes sulfenylation with an additional equivalent of sulfonyl hydrazide to produce the target molecule. The reaction promoted an excellent substituent effect, with electron-withdrawing groups facilitating increased yields. The desired compounds were obtained with moderate to good yields of 38 to 78%.



Scheme 7. I_2-catalyzed MCR for substituted pyrazolo[1,5-a]pyrimidines.

Ref. J. Sun, J. K. Qiu, B. Jiang, W. J. Hao, C. Guo, and S. J. Tu, *J. Org. Chem.*, 2016, 81, 3321-3328

Umesh et al. described a green one-pot multicomponent approach for the preparation of various pyrazolo[3,4-b]quinoline derivatives according to Scheme 8. In this method, in-situ prepared aminopyrazoles from the reaction of 3-aminocrotonitrile with arylhydrazine in water in the presence of L-proline further reacted with 2-((dimethylamino)methylene)cyclohexane-1,3-dione to yield the respective pyrazolo[3,4-b]quinolines in excellent yields ranging from 96 to 98%.[21]

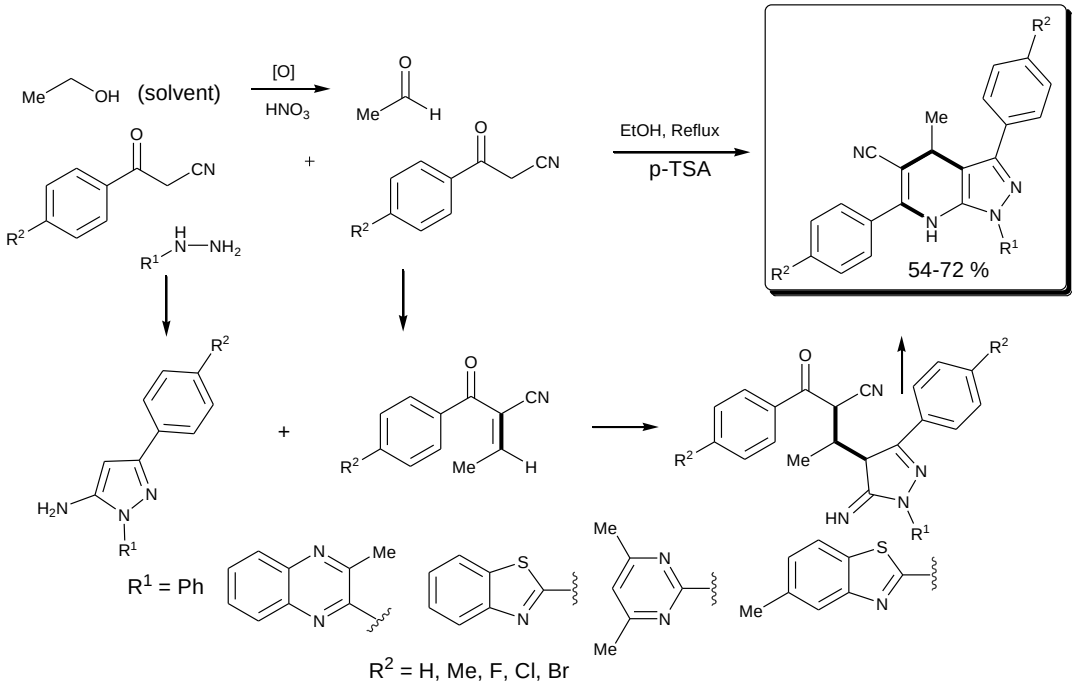


Scheme 8. H_2O-mediated multicomponent synthesis of pyrazolo[3,4-b]quinolone.

Ref. R. V.Sumesh, M. Muthu, A. I. Almansour, R. S. Kumar, N. Arumugam, S.Athimoolam, E. A. J. Y. Prabha, and R. R. Kumar, *ACS. Comb. Sci.*, 2016, 18, 262-270

Aggarwal et al. have also synthesized 4,7-dihydro-1H-pyrazolo[3,4-b]pyridine-5-nitrile compounds by a multicomponent reaction of 3-aryl-3-oxopropanonitriles (2.0 equiv.),

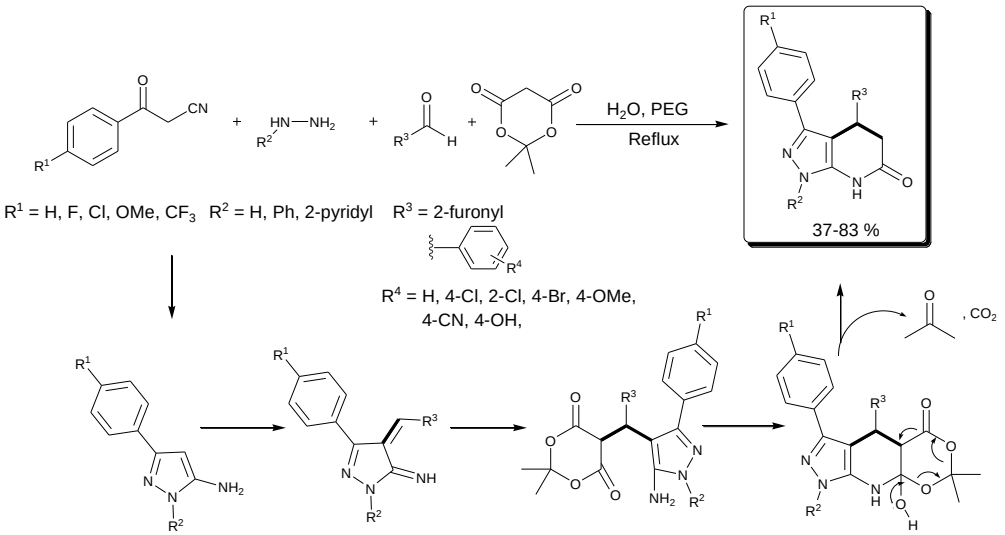
monosubstituted aryl and heteroarylhydrazines, and acetaldehyde derived in situ by the oxidation of the solvent itself (Scheme 9) in the presence of HNO_3.[22] The acetaldehyde was further used to react with one equivalent of 3-aryl-3-oxopropanitrile to yield a Knoevenagel adduct intermediate. The intermediate was further reacted with the in situ formed aminopyrazole, which was formed by the condensation of the hydrazine derivative and another equivalent of 3-aryl-3-oxopropanitrile. A wide variety of substrates was successfully employed, providing the products in 68 to 72% yields.



Scheme 9. Three-Component Reaction Utilizing the Solvent as a Reactant.

Ref . R. Aggarwal, G. Singh, S. Kumar, T. McCabe, I. Rozas, *ChemistrySelect*, 2016, 1, 5990 – 5994

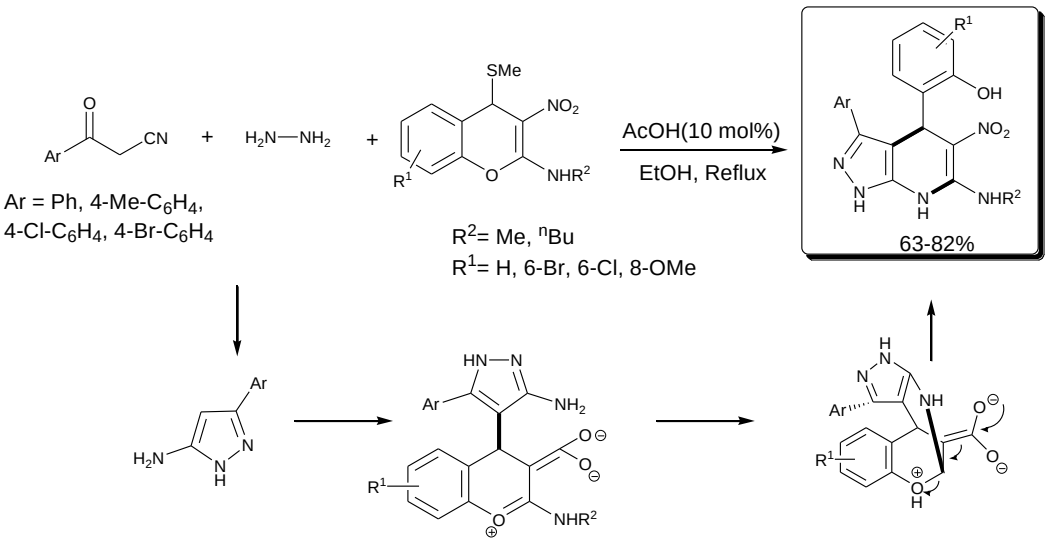
Zeng et al. described a multicomponent synthesis of the pyrazolo[3,4-b]pyridinones from the reaction of benzoyl acetonitrile, hydrazine, aldehydes, and Meldrum's acid in aqueous media (Scheme 10). Adding PEG2000 was shown to increase the efficacy considerably. It is hypothesized that the aminopyrazole is synthesized in situ from the reaction between the benzoyl acetonitrile and the hydrazine. Following a cyclical reaction involving the aldehydes and the subsequent inclusion of Meldrum's acid, the removal of acetone and carbon dioxide leads to the production of the target molecules. Electron-withdrawing groups 4-Cl, 4-F, and 4-CF3 on the benzoyl acetonitrile enhanced the yield. Furthermore, aldehydes containing electron-withdrawing groups gave enhanced yields. In contrast, the yield was lower in the case of the substituted aldehydes. A moderate to good range of 37% to 83% yield was obtained.[23] Additionally, some compounds gave encouraging anti-influenza virus activity.



Scheme 10. PEG-Mediated One-Pot Four-Component Synthesis.

Ref. L. Y. Zeng, T. Liu, J. Yang, Y. Yang, C. Cai, and S. Liu, *ACS Comb. Sci.*, 2017, 19, 437−446

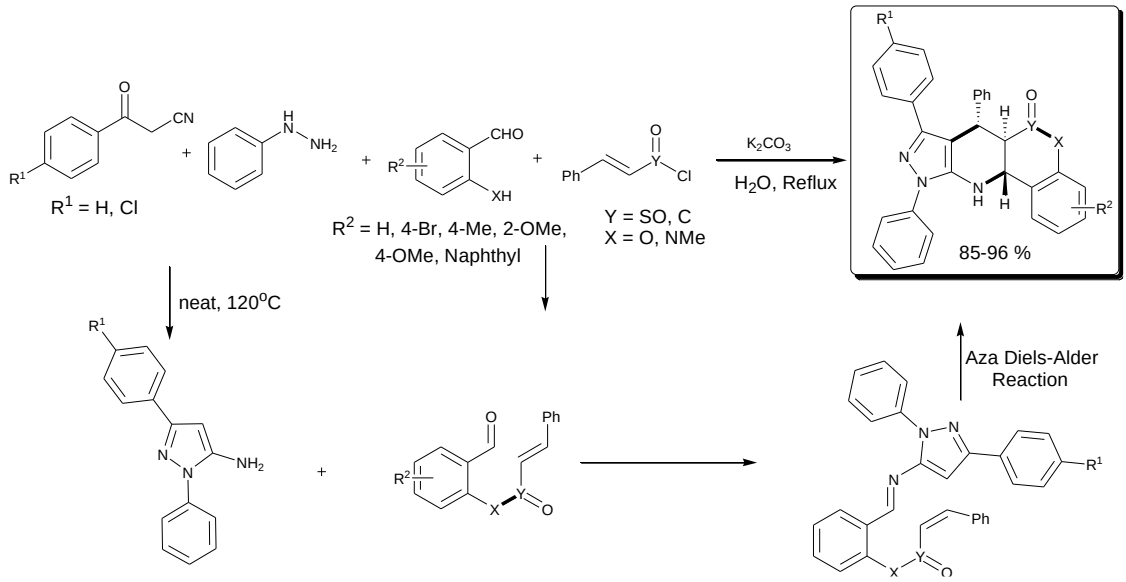
Rao et al. have described the three-component synthesis of pyrazolo[3,4-b]-4,7-dihydropyridine derivatives via the reaction between 3-oxo-3-phenylpropanenitriles, hydrazine, and 4-(methylthio)-4H-chromenes in ethanol using acetic acid as a catalyst (Scheme 11). The reaction is assumed to follow in situ formation of 5-aminopyrazole from 3-oxo-3-phenylpropanenitrile and hydrazine, which subsequently undergoes nucleophilic attack at the 4-(methylthio)-4H-chromene.[24] Elimination of the methylthio group followed by cyclization affords the desired pyrazolo[3,4-b]-4,7-dihydropyridine derivatives in good yields ranging from 63 to 82%.



Scheme 11. Three-component synthesis of pyrazolo[3,4-*b*]-4,7-dihydropyridine.

Ref. H. S. P. Rao, L. N. Adigopula and K. Ramadas, *ACS. Comb. Sci.*, 2017, 19, 279-285

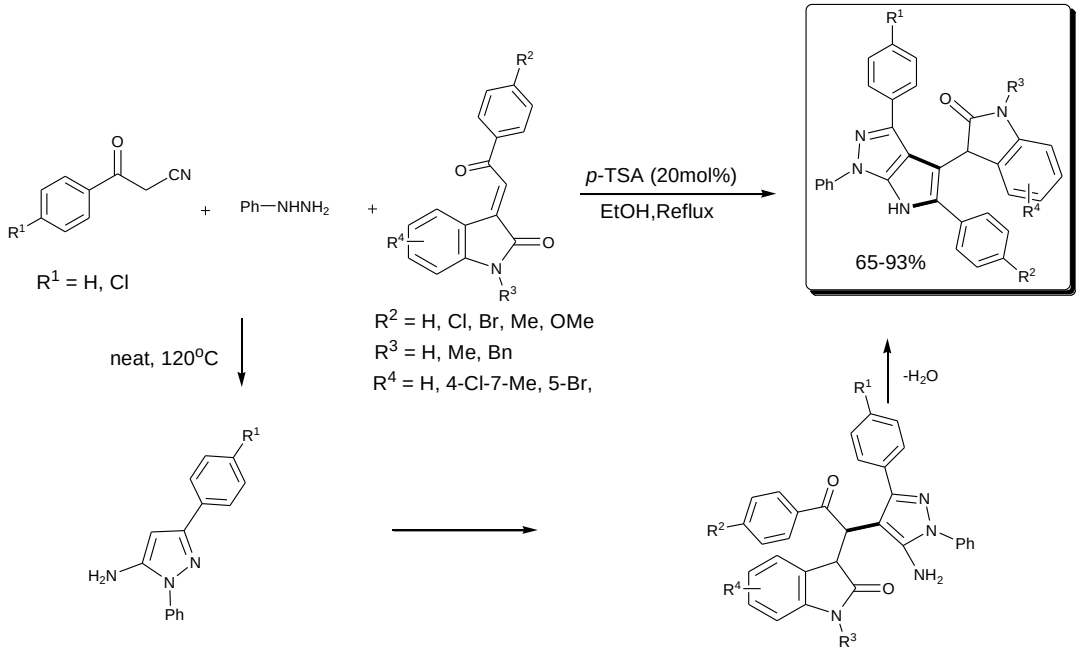
Nazeri et al. also synthesized pyrazolo-tetrahydropyridine derivatives by using benzoylacetonitrile derivatives, phenylhydrazine, salicylaldehydes, and styrene sulfonyl or cinnamoyl chlorides in an aqueous medium using potassium carbonate as the basic catalyst (Scheme 12). The process includes the in-situ preparation of aminopyrazoles from benzoylacetonitrile derivatives and phenylhydrazine by heating in the absence of solvents.[25] The resulting compounds are then treated with the adduct of salicylaldehydes and styrene sulfonyl or cinnamoyl chlorides, followed by an intramolecular aza Diels-Alder reaction to obtain the final compounds in an 85–96% yield.



Scheme 12. One-Pot Four-Component Reaction in Water.

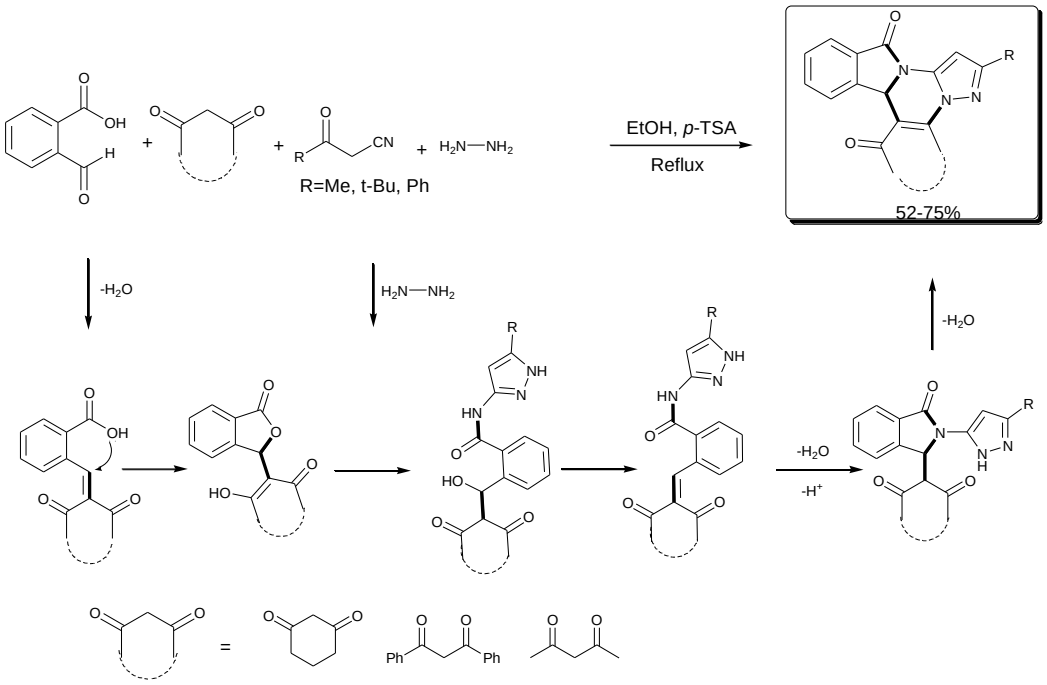
Ref . M. T. Nazeri, S. Javanbakht, A. Shaabani and H. R. Khavasi, *Chemistry Select* 2019, 4, 14271-14275

Similarly, this group also designed a three-component synthetic route for oxindole-fused pyrrolo[2,3-c]pyrazoles from benzoylacetonitriles, phenylhydrazine, and 3-phenacylideneoxindoles using ethanol as a solvent in the presence of p-TSA as a catalyst (Scheme 13).[26] The mechanism for this reaction is thought to involve the formation of an aminopyrazole from the reaction of benzoylacetonitrile and phenylhydrazine, followed by a Michael addition reaction between this aminopyrazole and 3-phenacylideneoxindoles, which is followed by intramolecular cyclization, leading to the formation of the desired products. Good to excellent.



Scheme 13. Multicomponent Reaction Promoted by p-TSA.
Ref. M. T. Nazeri, H. Farhid, S. Javanbakht, A. Shaabani and B. Notash, Synlett 2020, 31, 965-971.

Kouzehrash et al. designed a four-component reaction for the synthesis of N-fused heterocyclic compounds using p-TSA as an organocatalyst in ethanol (Scheme 14). The reaction requires the use of hydrazine hydrate, aldehydic acid, 3-oxoalkanonitriles, and different 1,3-dicarbonyl compounds. It proceeds through the in situ formation of aminopyrazole, which acts as the nucleophile to add to the condensate product of aldehyde acid and the 1,3-dicarbonyl compounds, followed by the elimination of water to yield the N-fused heterocyclic compounds.[27] The reaction showed notable steric consequences, where the least steric hindrance on the C-3 position of the aminopyrazole enhanced the product yield. In addition, the reaction used the cyclic 1,3-dicarbonyl compounds, which were highly acidic compared to the acyclic compounds, to increase the product yield. This reaction produced the N-fused heterocyclic compounds in moderate to good yields, between 52 and75%.



Scheme 14. *p*-TSA catalysed a component reaction.

Ref. M. A. Kouzehrash and A. Rahmati, *Tetrahedron*, 2020, **76**, 130923-130930

Conclusion

In this review, the application of aminopyrazoles as general 1,3-binucleophilic synthons for carrying out multicomponent syntheses for the formation of pyrazole-fused heterocycles is illustrated in Schemes 1-14. Aminopyrazoles, which can be used either before or concurrently in the course of syntheses, present the capability for acting as either an N, N- or a C, N-binucleophile for effective formation of diversified heterocycles. These methods described in this review point out the effectiveness, atom economy, functional group tolerance, and effective bond formation related to multicomponent syntheses. These syntheses occur in mild or green conditions in either aqueous or alcoholic media by using simple catalysts. These methods, therefore, prove the synthetic applications, biological potency, and interest in aminopyrazoles for future applications in green heterocyclic chemistry.

Acknowledgement

We are thankful to AITM Varanasi for providing the necessary facilities and support for the work. We also acknowledge the valuable discussions from our colleagues, which greatly contributed to the preparation of this review.

References

1. (a) J. V. Faria, P. F. Vegi, A. G. C. Miguita, M. S. d. Santos, N. Boechat and A. M. R. Bernardino, *Bioorg. Med. Chem.*, 2017, 25, 5891–5903.
(b) M. Lefoix, G. Mathis, T. Kleinmann, J. C. Truffert and U. Asseline, *J. Org. Chem.*, 2014, 79, 3221–3227.
(c) H. de Mello, A. Echevarria, A. M. Bernardino, M. C. Cavalheiro and L. L. Leon, *J. Med. Chem.*, 2004, 47, 5427–5432.

2. (a) M. F. Khan, M. M. Alam, G. Verma, W. Akhter, and M. Shaquiquzzaman, *Eur. J. Med. Chem.*, 2016, 120, 170–201. (b) F. E. Bennani, L. Doudach, Y. Cherrah, Y. Ramli, M. Ansar, and M. E. A. Faouzi, *Bioorg. Chem.*, 2020, 97, 103470.
3. (a) R. Aggarwal and S. Kumar, *Beilstein J. Org. Chem.*, 2018, 14, 203–242. (b) A. Shaabani, M. T. Nazeri, and R. Afshari, *Mol. Divers.*, 2019, 23, 751–807. (c) M. Marinozzi, G. Marcelli and A. Carotti, *Mini Rev. Med. Chem.*, 2015, 15, 272–299.
4. A. Dömling, W. Wang, and K. Wang, *Chem. Rev.*, 2012, 112, 3083–3135.
5. A. Tigreros and J. Portilla, *RSC Adv.*, 2020, 10, 19693–19712.
6. C.-H. Chen, F.-I. Wu, C.-F. Shu, C.-H. Chien and Y.-T. Tao, *J. Mater. Chem.*, 2004, 14, 1585–1589.
7. F. Zhang, C. Li and C. Qi, *RSC Adv.*, 2016, 6, 102924–102930.
8. H. S. P. Rao, L. N. Adigopula, and K. Ramadas, *ACS Comb. Sci.*, 2017, 19, 279–285.
9. H.-B. Fu and J.-N. Yao, *J. Am. Chem. Soc.*, 2001, 123, 1434–1439.
10. J. Brioche, T. Courant, L. Alcaraz, M. Stocks, M. Fuber, J. Zhu, and G. Masson, *Adv. Synth. Catal.*, 2014, 356, 1719–1724.
11. J. Burschka, A. Dualeh, F. Kessler, E. Baranoff, N.-L. C.-Ha, C. Yi, M. K. Nazeeruddin, and M. Grätzel, *J. Am. Chem. Soc.*, 2011, 133, 18042–18045.
12. J. Sun, J. K. Qiu, B. Jiang, W. J. Hao, C. Guo, and S. J. Tu, *J. Org. Chem.*, 2016, 81, 3321–3328.
13. L. Y. Zeng, T. Liu, J. Yang, Y. Yang, C. Cai, and S. Liu, *ACS Comb. Sci.*, 2017, 19, 437–446.
14. M. A. Kouzehrash and A. Rahmati, *Tetrahedron*, 2020, 76, 130923–130930.
15. M. T. Nazeri, H. Farhid, S. Javanbakht, A. Shaabani, and B. Notash, *Synlett*, 2020, 31, 965–971.
16. M. T. Nazeri, S. Javanbakht, A. Shaabani, and H. R. Khavasi, *ChemistrySelect*, 2019, 4, 14271–14275.
17. M. V. Murlykina, A. D. Morozova, I. M. Zviagin, Y. I. Sakhno, S. M. Desenko, and V. A. Chebanov, *Front. Chem.*, 2018, 6, 527.
18. M. X. Liu, J. R. Li, K. Zhang and D. X. Shi, *Tetrahedron*, 2015, 71, 7658–7662.
19. P.-T. Chou and Y. Chi, *Chem. Eur. J.*, 2007, 13, 380–395.
20. Preeti and K. N. Singh, *Org. Biomol. Chem.*, 2018, 16, 9084–9116.
21. R. Aggarwal, G. Singh, S. Kumar, T. McCabe, and I. Rozas, *ChemistrySelect*, 2016, 1, 5990–5994.
22. R. V. Sumesh, M. Muthu, A. I. Almansour, R. S. Kumar, N. Arumugam, S. Athimoolam, E. A. J. Y. Prabha, and R. R. Kumar, *ACS Comb. Sci.*, 2016, 18, 262–270.
23. S. Dandia, R. Singh, J. Joshi and S. Maheshwari, *Res. Chem. Intermed.*, 2015, 41, 4213–4226.
24. S. Devi, S. Kaping and J. N. Vishwakarma, *Mol. Divers.*, 2015, 19, 759–771.

25. U. M. Kauhanka and M. M. Kauhanka, *Liq. Cryst.*, 2006, 33, 121–127.
26. V. Kumar, K. Kaur, G. K. Gupta, and A. K. Sharma, *Eur. J. Med. Chem.*, 2013, 69, 735–753.
27. W. H. Hao, P. Zhou, F. Y. Wu, B. Jiang, S. J. Tu, and G. Li, *Eur. J. Org. Chem.*, 2016, 1968–1971.