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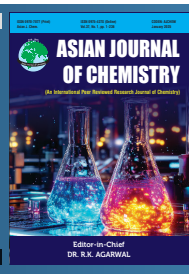

Green Synthesis of Naphthyridine Derivatives and their Cytochrome Activity against Human Microsomal P450 1A2: Comparative Studies on Organic and Aqueous Media

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In this work, the synthetic protocol of naphthyridine derivatives through one pot reaction using aqueous and organic solvents are reported. The cascade reaction of malononitrile dimer and aldehyde leads to the formation of 5,7-diamino-2-(dicyanomethyl)-4-(4-oxobutyl)-1,2,3,4-tetrahydro-1,6-naphthyridine-3,8-dicarbonitrile (**3**) in organic solvents in moderate yield. But the study shows the attractive features of using like elixir solvent 'water' as green solvent and ionic liquid as a catalyst to reduce chemical usage and environmentally malignant formation. The present investigation highlights to synthesize naphthyridine derivative **3** in a good yield using aqueous solvent in comparison to organic solvents because green solvents are highly eco-friendly approach, low cost and simple methodology. The structure of naphthyridine derivative **3** using water/catalyst was confirmed by spectral techniques, there are no changes with the spectral studies which were carried out in organic solvents but the yield was more in aqueous media when compared with naphthyridine derivatives in an organic solvent. The newly synthesized naphthyridine compound were evaluated for their cytochrome activity against Human Microsomal P450 1A2 enzyme, the results of molecular docking reveals that the compound perhaps chosen as clinical drug.

Keywords: Naphthyridine derivative, Malononitrile dimer, Green solvent, Cytochrome activity, Human Microsomal P450 1A2.

INTRODUCTION

The malononitrile dimer was excellent reactant intermediates and undergoes cascade reaction with aldehyde in presence of ethanol, results the naphthyridine derivatives [1]. Majority of naphthyridine derivatives are found to exhibit many medicinal applications such as antibiotic, antituberculosis, antifungal, anticancer, antimalarial, *etc.* [2,3]. Apart from the synthesis of naphthyridine derivative in organic solvents, we tried green chemistry methodology using water as a solvent and the catalyst called choline hydroxide, a metal-free compound, non-toxic, easily soluble in water and commercially available material, moreover, these reactions were found to require nitrogen temperature [4,5]. Literature survey reveals that naphthyridine compounds contain excellent biological properties. Herein, usually the reaction proceed organic media to obtain the naphthyridine product but the reaction proceeds between liquid ionic catalyst and intermediate to form the naphthyridine derivatives at nitrogen atmosphere. The inter-mediate such as malononitrile dimer [6,7] was prepared from aqueous NaOH and copper sulphate pentahydrate dissolved in malononitrile and the inorganic salt was removed by heating the mixture at 90 ºC to synthesize the crystals of intermediate.

Organic chemists typically employ water as their solvent of choice due to its abundance, low toxicity, low cost, high reaction rates and it also eliminates the requirement for many severe reaction conditions during the organic synthesis [8-10]. Insolubility of intermediates in water makes the reaction mixture difficult at some times, but the malononitrile dimer completely dissolves in water at 25 ºC stirring for a minute [6,11]. Herein, the development of new eco-friendly and efficient route to synthesize naphthyridine derivatives *via* greener approach in presence of water and catalyst are described [12,13]. So this article reports an on water-catalyst green synthetic methodology of naphthyridine derivatives with an aldehyde-malononitrile dimer moiety. In recent days, several researchers group reported the synthesis of organic compounds in aqueous reaction condition to synthesize highly efficient heterocycles in good

yield. The advantage of aqueous reaction is mild reaction condition, less toxic to environment, easy to work up in laboratory, safety and shorter reaction time with moderate to good yield.

This study describes the synthesis of 1,6-naphthyridine derivatives **3** using water/catalyst as a solvent. The elucidation of the synthesized compounds was confirmed by spectral analysis of ^{1}H, ^{13}C, FT-IR and UV visible spectrum. Moreover the molecular docking between synthesized naphthyridine derivative **3** with cytochrome activity against 2HI4, which is a human microsomal P450 1A2, a complex of α-naphthoflavone and the binding energy of 1.95 Å [14-17] was also carried out. This protein is present in human liver and it can actively participate in the cytochrome drug discoveries. The reported protein consist of P450 families 1, 2 and 3, for humans and mammals comes under family 1. They are three well characterized P450 monooxygenases such as 1A1, 1A2 and 1B1. Among the other proteins, the P450 1A2 plays a key role in many drugs discoveries such as lidocaine, olanzapine, tacrine, theophylline, flutamide and zolmitriptan.

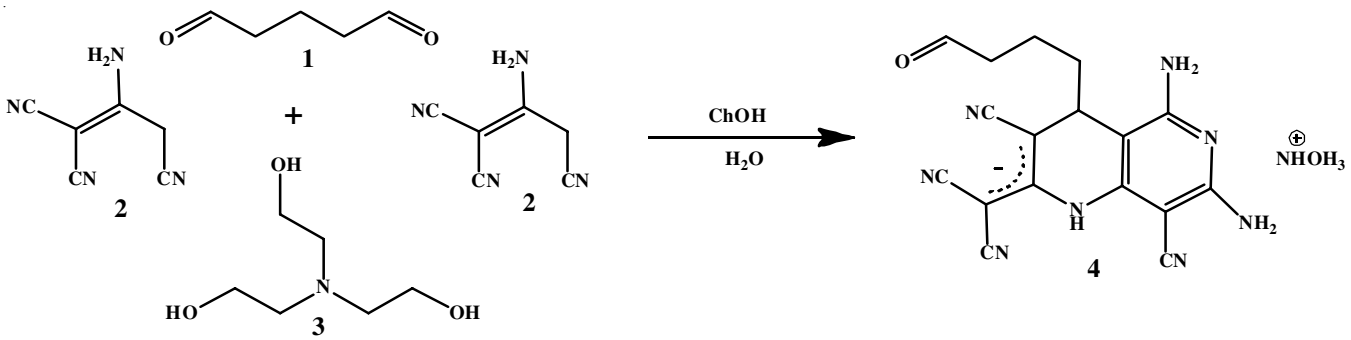
EXPERIMENTAL

The commercially available chemicals like glutaraldehyde, ethanol, triethanolamine and the catalyst choline hydroxide were purchased from Sigma-Aldrich and were used without further purification. The reaction was monitored by TLC (thin-layer chromatography) and the TLC plates were used are Merck TLC silica gel 60 F_{254}. nuclear magnetic resonance spectra were recorded on Bruker spectrometers (400 MHz for ^{1}H NMR, 125 MHz for ^{13}C NMR). The IR spectra were recorded in an FT-IR spectro-meter using KBr pellets and UV-vis region was observed in acetone as solvent.

Synthesis of 5,7-diamino-2-(dicyanomethyl)-4-(4-oxobutyl)-1,2,3,4-tetrahydro-1,6-naphthyridine-3,8-dicarbonitrile (4): A mixture of glutaraldehyde (**2**, 0.01 M, 1 g), malononitrile dimer (**1**, 0.02 M, 2.64 g), triethanolamine (**3**, 0.01 M, 1.49 g) stirred in 1 mL of H_2O followed by addition of choline hydroxide (ChOH) 1 mol%. The reaction stirred under N_2 conditions at 50 ºC for 8 h. The catalyst was separated and the naphthyridine derivative **4** was obtained with 95% yield (**Scheme-I**). M.P.: 210 ºC, Anal. calcd. (found) % for $C_{17}H_{10}N_8O$: C, 59.65 (59.62); H, 2.94 (2.90); N, 32.73 (32.71); O, 4.67 (4.63). IR (KBr, ν_{max}, cm^{-1}): 3255.91, 2201, 3062, 1593, 719. ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 1.53 (2H, tt, *J* = 7.5, 7.3 Hz), 1.73 (2H, td, *J* = 7.3, 6.7 Hz), 2.53 (2H, td, *J* = 7.5, 6.9 Hz), 3.17 (1H, td, *J* = 6.7, 4.6 Hz), 3.47 (1H, dd, *J* = 4.6, 1.9 Hz), 4.41 (1H, d, *J* = 6.0 Hz), 4.71 (1H, dd, *J* = 6.0, 1.9 Hz), 9.66 (1H, t, *J* = 6.9 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, δ ppm): 25.3 (1C, s), 32.2 (1C, s), 32.6 (1C, s), 43.4 (1C, s), 50.8 (1C, s), 51.8 (1C, s), 67.0 (1C, s), 112.0 (1C, s), 112.4 (1C, s), 112.9-113.0 (2C, 112.9 (s), 112.9 (s)), 115.2 (1C, s), 117.7 (1C, s), 133.8 (1C, s), 157.7 (1C, s), 160.1 (1C, s), 201.5 (1C, s).

Synthesis of 2-(5,7-diamino-3-(aminomethyl)-4-(2-chloro-4-oxobutyl)-8-cyano-1,2,3,4-tetrahydro-1,6-naphthyridin-2-yl)malononitrile (4a): A mixture of 3-chloro-glutaraldehyde (0.01 M, 1.34 g), malononitrile dimer (0.02 M, 2.64 g), triethanolamine (0.01 M, 1.49 g) stirred in 1 mL of H_2O followed by addition of choline hydroxide 1 mol%. The reaction stirred under N_2 conditions at 50 ºC for 9 h. The catalyst was separated and the naphthyridine derivative **4a** was obtained with 93% yield. M.P.: 225 ºC, Anal. calcd. (found) % for $C_{17}H_{19}N_8OCl$: C, 52.78 (52.75); H, 4.95 (4.92); Cl, 9.16 (9.14); N, 28.97 (28.91); O, 4.14 (4.12); IR (KBr, ν_{max}, cm^{-1}): 3258, 2212, 3067, 1585, 890, 735; ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 2.34-2.54 (3H, 2.41 (dtd, *J* = 4.6, 4.1, 1.9 Hz), 2.47 (dd, *J* = 8.6, 6.9 Hz)), 2.66 (2H, d, *J* = 4.1 Hz), 2.76-2.90 (3H, dd, *J* = 6.9, 6.4 Hz), 2.84 (td, *J* = 6.9, 4.6 Hz)), 4.18-4.32 (2H, 4.24 (dd, *J* = 6.4, 1.9 Hz), 4.25 (tt, *J* = 8.6, 6.4 Hz), 4.41 (1H, d, *J* = 6.4 Hz), 9.71 (1H, t, *J* = 6.9 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, δ ppm): 32.6 (1C, s), 35.6 (1C, s), 39.2 (1C, s), 42.6 (1C, s), 48.1 (1C, s), 51.8 (1C, s), 61.3 (1C, s), 67.0 (1C, s), 112.0 (1C, s), 112.4 (1C, s), 112.9-113.0 (2C, 112.9 (s), 112.9 (s)), 115.2 (1C, s), 133.8 (1C, s), 157.7 (1C, s), 160.1 (1C, s), 201.2 (1C, s).

Synthesis of 2-(5,7-diamino-3-(aminomethyl)-4-(2-bromo-4-oxobutyl)-8-cyano-1,2,3,4-tetrahydro-1,6-naphthyridin-2-yl)malononitrile (4b): A mixture of 3-bromo-glutaraldehyde (0.01 M, 1.79 g), malononitrile dimer (0.02 M, 2.64 g), triethanolamine (0.01 M, 1.49 g) stirred in 1 mL of H_2O followed by addition of choline hydroxide 1 mol%. The reaction stirred under N_2 conditions at 50 ºC for 8 h. The catalyst was separated and the naphthyridine derivative **4b** was obtained with 90% yield. M.P.: 220 ºC, Anal. calcd. (found) % for $C_{17}H_{19}N_8OBr$: C, 47.34 (47.31); H, 4.44 (4.43); Br, 18.53 (18.50); N, 25.98 (25.95); O, 3.71 (3.68); IR (KBr, ν_{max}, cm^{-1}): 3254.83, 2210, 3072, 1581, 654, 707; ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 2.38 (1H, dtd, *J* = 4.6, 4.1, 1.9 Hz), 2.52 (2H, dd, *J* = 8.5, 6.9 Hz), 2.66 (2H, d, *J* = 4.1 Hz), 2.72-2.90 (3H, 2.79 (dd, *J* = 6.9, 6.5 Hz), 2.83 (td, *J* = 6.9, 4.6 Hz)), 3.91 (1H,



Scheme-I: Synthesis of 5,7-diamino-2-(dicyanomethyl)-4-(4-oxobutyl)-1,2,3,4-tetrahydro-1,6-naphthyridine-3,8-dicarbonitrile (**4**)

tt, *J* = 8.5, 6.5 Hz), 4.25-4.46 (2H, 4.31 (dd, *J* = 6.4, 1.9 Hz), 4.41 (d, *J* = 6.4 Hz)), 9.72 (1H, t, *J* = 6.9 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, δ ppm): 32.6 (1C, s), 35.6 (1C, s), 39.2 (1C, s), 42.6 (1C, s), 48.1 (1C, s), 48.9 (1C, s), 51.8 (1C, s), 67.0 (1C, s), 112.0 (1C, s), 112.4 (1C, s), 112.9-113.0 (2C, 112.9 (s), 112.9 (s)), 115.2 (1C, s), 133.8 (1C, s), 157.7 (1C, s), 160.1 (1C, s), 201.2 (1C, s).

Synthesis of 2-(5,7-diamino-3-(aminomethyl)-8-cyano-4-(2-methoxy-4-oxobutyl)-1,2,3,4-tetrahydro-1,6-naphthyridin-2-yl)malononitrile (4c): A mixture of 3-methoxyglutaraldehyde (0.01 M, 1.30 g), malononitrile dimer (0.02 M, 2.64 g), triethanolamine (0.01 M, 1.49 g) stirred in 1 mL of H_2O followed by addition of choline hydroxide 1 mol%. The reaction stirred under N_2 conditions at 50 ºC for 10 h. The catalyst was separated and the naphthyridine derivative **4c** was obtained with 91% yield. M.P.: 240 ºC. Anal. calcd. (found) % for $C_{18}H_{22}N_8O_2$: C, 56.53 (56.50); H, 5.80 (5.75); N, 29.30 (29.27); O, 8.37 (8.34); IR (KBr) v max : 3246, 2816, 2229, 3080, 1575, 704; ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 1.92 (2H, dd, *J* = 10.1, 7.1 Hz), 2.38 (1H, dtd, *J* = 4.6, 4.1, 1.9 Hz), 2.58-2.71 (4H, 2.65 (dd, *J* = 6.9, 6.2 Hz), 2.65 (d, *J* = 4.1 Hz), 2.94 (1H, td, *J* = 7.1, 4.6 Hz), 3.23 (3H, s), 3.97 (1H, tt, *J* = 10.1, 6.2 Hz), 4.24 (1H, dd, *J* = 6.4, 1.9 Hz), 4.40 (1H, d, *J* = 6.4 Hz), 9.69 (1H, t, *J* = 6.9 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, δ ppm): 32.6 (1C, s), 35.6 (1C, s), 42.6 (1C, s), 48.1 (1C, s), 50.2 (1C, s), 51.8 (1C, s), 56.3 (1C, s), 67.0 (1C, s), 76.9 (1C, s), 112.0 (1C, s), 112.4 (1C, s), 112.9-113.0 (2C, 112.9 (s), 112.9 (s)), 115.2 (1C, s), 133.8 (1C, s), 157.7 (1C, s), 160.1 (1C, s), 201.2 (1C, s).

RESULTS AND DISCUSSION

In the present investigation, the reaction between glutaraldehyde and malononitrile dimer in presence of choline hydroxide (ChOH) in H_2O under nitrogen atmosphere at 50 ºC for 8 h was carried out. The expected product **4** was obtained in an excellent yield of 95% as shown in **Scheme-I**. We did not do the reaction in presence of water and catalyst at the first time, instead, we started to synthesis the naphthyridine compound in presence of ethanol and observed that the product formation is 75% of yield (entry 1). Then the reaction processed with acetone (entry 2) the product formed was 66% only. We have used water as a solvent (entry 3) in the absence of catalyst, but the yield was less (entry 4, 58%). Surprisingly, the expected yield obtained using ChOH catalyst in presence of water solvent (entry 6) the yield was 95% much better then catalyst with ethanol and acetone (entry 4 & 5). The same reaction (entry 6) was performed with room temperature, but the reaction took too much time to obtain product and the expected yield also less (entry 7) (Table-1). The reaction condition was monitored by TLC with pet. ether/ethyl acetate (4:1) as eluent and product was confirmed without column chromatography technique. The catalyst was separated and the product mixture was extracted by ethyl acetate: water 40:10 by concentrated in vacuum.

After developing a suitable reaction conditions, we used substituted glutaraldehyde with malononitrile dimer intermediate to obtain several naphthyridine derivatives **4a-c** in good yield with same reaction conditions and N_2 atmosphere at 50 ºC. Then, it can be further developed as larger scale by increasing the mole ratio for both aldehyde and intermediate hence comparative studies in organic and aqueous media have been studied successfully.

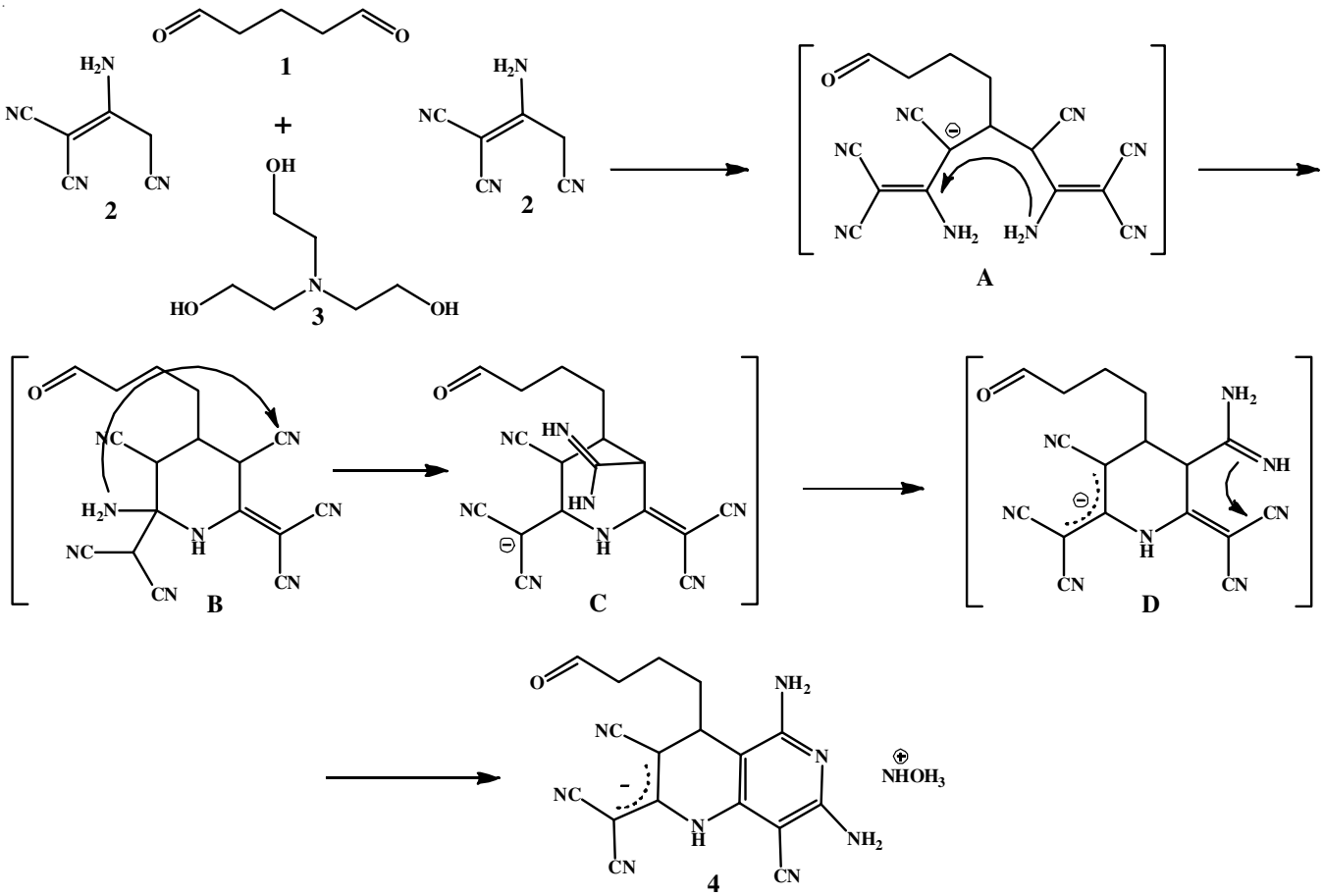
The FT-IR spectra of synthesized compound **4** was analyzed in absorption bands of hydroxyl group and NH-fragments appeared at ~3255.91 cm^{-1}. The strong intensive bands at 2201 are conjugated cyano groups. The peaks at ~3062 cm^{-1} correspond to the C-H stretching frequency, whereas the C=C bonds at around 1593 cm^{-1} are indicative of the aromatic area. And also the C-H bending vibration occurs at around 719 cm^{-1}. The UV-Vis absorption spectrum showed a significant adsorption band at 354 nm, which confirmed the formation of compound **4**.

In the ^{1}H NMR spectrum of compound **4** has a broad signal of hydroxyl protons at δ 1.92 ppm. Compound **4** showed the doublet of doublet at δ 1.53 and 2.53 ppm each for naphthyridine ring. The significant signals of doublet appeared in the region of 4.41 ppm. The appearance of triplet at δ 9.66 ppm due to –NH in pyridine ring confirmed the cyclization occurred. The ^{13}C NMR spectra for compound **4** has signals at C-atoms of second and fourth position of two pyridine rings which is naphthyridine ring at δ 160.1 and 157.7 ppm. The signals of C-atoms in fifth and third position are due to δ 67.0 ppm. The ^{13}C NMR signals of cyano group appears at the signals of δ 112-115.21 ppm. The other fragments of C-atoms at δ 67.0, 50.8, 43.4, 32.6, 32.2 and 25.3 ppm, respectively. All the results from spectral studies shows 5,7-diamino-2-(dicyanomethyl)-4-(4-oxobutyl)-1,2,3,4-tetrahydro-1,6-naphthyridine-3,8-dicarbonitrile derivatives **3** formed well with good yield from glutaraldehyde, malononitrile dimer in aqueous medium compared with organic medium.

Mechanism: The possible mechanism for the formation of 5,7-diamino-2-(dicyanomethyl)-4-(4-oxobutyl)-1,2,3,4-tetrahydro-1,6-naphthyridine-3,8-dicarbonitrile derivative **3** in **Scheme-II** by malononitrile dimer and glutaraldehyde was

TABLE-1
OPTIMIZATION OF THE SYNTHESIS OF NAPHTHYRIDINE DERIVATIVE

Entry	Catalyst (mol %)	Solvent	Temp. (ºC)	Time (h)	Yield (%)
1	–	Ethanol	50	12	75
2	–	Acetone	50	15	66
3	–	H_2O	50	11	58
4	ChOH	Ethanol	50	10	70
5	ChOH	Acetone	50	12	62
6	ChOH	H_2O	50	8	95
7	ChOH	H_2O	r.t	21	80



Scheme-II: Mechanism for the synthesis of 5,7-diamino-2-(dicyanomethyl)-4-(4-oxobutyl)-1,2,3,4-tetrahydro-1,6-naphthyridine-3,8-dicarbonitrile (**4**)

reviewed from **A** to **D** then to form a product . The three cyano group of malononitrile dimer **2** easily form an azaheterocyclic compound. The reaction mixture of glutaraldehyde, malononitrile dimer and few drops of triethanolamine in presence of catalyst/water under stirring at N_2 atmosphere at 50 ºC to form as adduct **A**, then the formation of **B** by addition of amino to imine group by electrophilic carbon atom. Compound **C** obtained by close proximity of the amino and cyano groups. At the end, compound **D** was formed by ring opening ring closure leads to formation of naphthyridine derivatives.

Molecular docking: The availability of suitable protein for the synthesized ligand, it can be easily accessed in protein bank. For molecular docking studies, the docking can be done in software such as Autodock and Molegro molecular viewer to generate conformation of binding affinities for the ligand molecule [18,19]. Also the molecular docking was used to predict small molecules, RNA, DNA, peptides and peptidomimetics. The ligand, compound **4** contains two pyridine ring and cyano groups. On molecular docking studies of naphthyridine derivative **4**, to find the cytochrome activity against human microsomal P450 1A2, the docking result of naphthyridine derivatives revealed that the highest binding energy range of (ΔG = -3.62 kcal/mol) and also amino acid residues at the binding sites. Usually selected protein (2HI4) was complexed with the α-naphthoflavone carries carbonyl and phenyl group, thus the phenyl group connecting with benzo(h)chromen-4-one moiety. The molecular docking analysis indicates the desired naphthyridine derivative **3** act as cytochrome activity.

Herein the MD simulations were also used for determining the dynamic behaviour of compound **4** with 2HI4, respectively. The human microsomal P450 1A2 (2HI4) considered as target protein can be docked with ligand the naphthyridine derivative of 5,7-diamino-2-(dicyanomethyl)-4-(4-oxobutyl)-1,2,3,4-tetrahydro-1,6-naphthyridine-3,8-dicarbonitrile **4**. Fig. 1 shows the binding mode of naphthyridine derivative **4** with 2HI4 protein shows intermolecular hydrogen bonding and Fig. 2 indicates

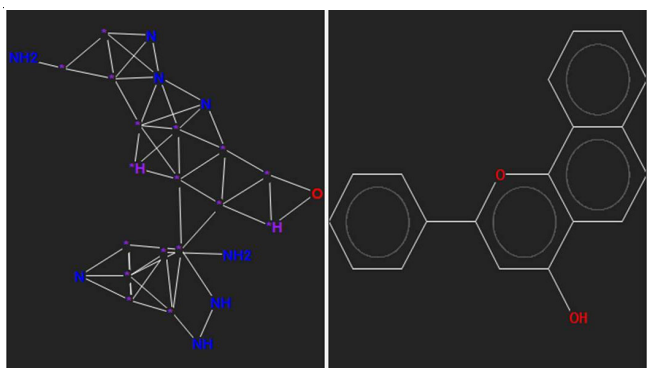


Fig. 1. Binding mode of naphthyridine derivative **3** with 2HI4 protein shows intermolecular hydrogen

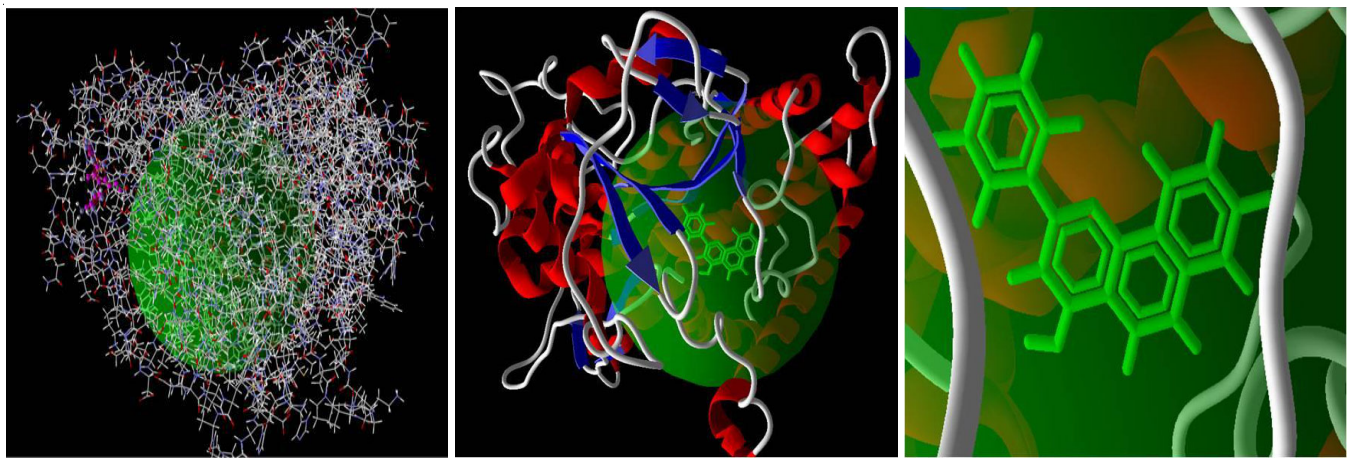


Fig. 2. Snapshot from molecular docking showing interaction of molecule **4** with human microsomal P450 1A2 (2HI4)

the structural image of molecular docking showing interaction of molecule **4** with human microsomal P450 1A2 (2HI4). Moreover, 16 aromatic carbons are detected as C-H interaction. The docking results revealed that the human microsomal P450 1A2 with ligand shares amino acid in C–H···π interaction. A structure based sequence alignment of 2HI4 protein docked with ligand in Fig. 2 shows that the molecules are active binding energies and protein active sites. The molecular docking results are encouraging as they are active in cytochrome activity against human microsomal P450 1A2 (2HI4) protein, respectively.

Conclusion

In summary, a one-pot eco-friendly reaction in water/choline hydroxide catalyst to synthesize 5,7-diamino-2-(dicyanomethyl)-4-(4-oxobutyl)-1,2,3,4-tetrahydro-1,6-naphthyridine-3,8-dicarbonitrile (**4**) with 95% yield have been achieved. As compared to organic solvents like ethanol and acetone, the greener solvent of water/catalyst form higher yield so this inexpensive methodology and greener synthesis approach with excellent yield and less reaction time. In addition, compound **4** on molecular docking studies show the cytochrome activity presents in human microsomal P450 1A2. Furthermore, the MD studies of compound **4** with 2HI4 the binding site scoring ΔG value of -3.62 kcal/mol. The use of water and ionic liquid as a catalyst in this innovative, eco-friendly and economical synthetic method holds the promise to transform the organic synthesis.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

REFERENCES

1. I.N. Bardasov, A.U. Alekseeva, V.A. Tafeenko and O.V. Ershov, *Synth. Commun.*, **49**, 3343 (2019); https://doi.org/10.1080/00397911.2019.1665184
2. T. Devadoss, V. Sowmya and R. Bastati, *ChemistrySelect*, **6**, 3610 (2021); https://doi.org/10.1002/slct.202004462
3. S.K. Srivastava, A. Jha, S.K. Agarwal, R. Mukherjee and A.C. Burman, *Anticancer. Agents Med. Chem.*, **7**, 685 (2007); https://doi.org/10.2174/187152007784111313
4. S.S. Choudhury, S. Jena, D.K. Sahoo, S. Shekh, R.K. Kar, A. Dhakad, K.H. Gowd and H.S. Biswal, *ACS Omega*, **6**, 19304 (2021); https://doi.org/10.1021/acsomega.1c02798
5. E. Mohamed, A. Abdelmajeid, M. Behalo, A. Abel-Maaboud and K. Hebaish, *Egypt. J. Chem.*, **65**, 651 (2022); https://doi.org/10.21608/ejchem.2021.95621.4488
6. R.A. Carboni, D.D. Coffman and E.G. Howard, *J. Am. Chem. Soc.*, **80**, 2838 (1958); https://doi.org/10.1021/ja01544a061
7. V.V. Dotsenko, S.G. Krivokolysko and A.M. Semenova, *Chem. Heterocycl. Compd.*, **54**, 989 (2018); https://doi.org/10.1007/s10593-018-2383-y
8. A. Ashraf, Z. Shafiq, K. Mahmood, M. Yaqub and W. Rauf, *RSC Adv.*, **10**, 5938 (2020); https://doi.org/10.1039/C9RA09148C
9. S. Banoth, S. Perugu and S. Boda, *J. Heterocycl. Chem.*, **55**, 709 (2018); https://doi.org/10.1002/jhet.3092
10. B.B. Feng, M.M. Zhang and X.S. Wang, *Polycycl. Aromat. Compd.*, **36**, 478 (2016); https://doi.org/10.1080/10406638.2015.1014969
11. E.C. Taylor and K.S. Hartke, *J. Am. Chem. Soc.*, **81**, 2452 (1959); https://doi.org/10.1021/ja01519a044
12. F.M. Abdelrazek, N.A.L. Kassab, N.H. Metwally and N.A. Sobhy, *Eur. J. Chem.*, **1**, 368 (2010); https://doi.org/10.5155/eurjchem.1.4.368-372.104
13. B. Sonyanaik, D. Ravi, P. Shyam and K. Kishore, Research Square, 2023, 1, 1-14; https://doi.org/10.21203/rs.3.rs-2453479/v1
14. A.F. Eweas, N.M. Khalifa, N.S. Ismail, M.A. Al-Omar and A.M.M. Soliman, *Med. Chem. Res.*, **23**, 76 (2014); https://doi.org/10.1007/s00044-013-0604-6
15. E.P. Gallagher, K.L. Kunze, P.L. Stapleton and D.L. Eaton, *Toxicol. Appl. Pharmacol.*, **141**, 595 (1996); https://doi.org/10.1006/taap.1996.0326
16. K.A. Usmani, T.M. Cho, R.L. Rose and E. Hodgson, *Drug Metab. Dispos.*, **34**, 1606 (2006); https://doi.org/10.1124/dmd.106.010439
17. E.P. Gallagher, L.C. Wienkers, P.L. Stapleton, K.L. Kunze and D.L. Eaton, *Cancer Res.*, **54**, 101 (1994).
18. S. Sansen, J.K. Yano, R.L. Reynald, G.A. Schoch, K.J. Griffin, C.D. Stout and E.F. Johnson, *J. Biol. Chem.*, **282**, 14348 (2007); https://doi.org/10.1074/jbc.M611692200
19. A.A. Walsh, G.D. Szklarz and E.E. Scatt, *Metabolism*, **288**, 12932 (2023).