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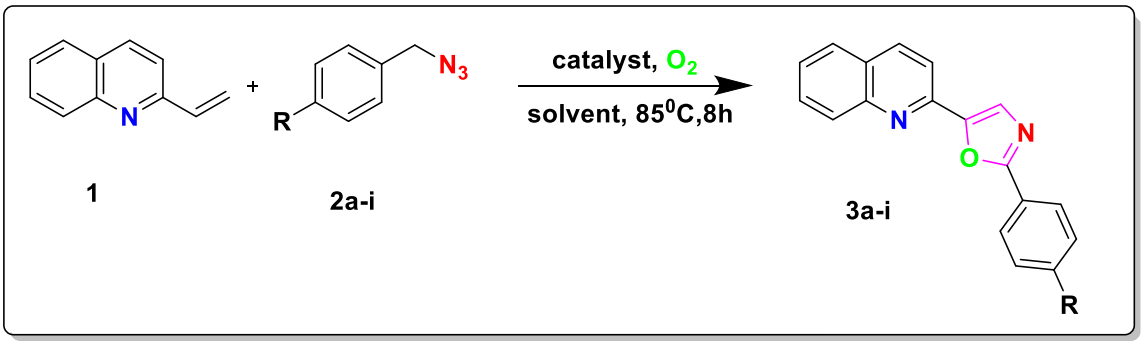
Facile Synthesis and Characterization of series of different 2,5 disubstituted 5-(quinolin-2-yl)-oxazoles

SrikanthPodishetty[1], Jagadeesh Kumar Ega[1*]
[1*]Department of Chemistry, Chaitanya (Deemed to be University), Himayatnagar, Moinabad, Ranga Reddy, Hyderabad – 500075, (TG)
***E-mail:** jkjagadeeshkumare@gmail.com*

ABSTRACT

An efficient method to 2,5-disubstituted oxazoles**3a-i** is developed *via* a 1,3-dipolar cycloaddition/ring-cleavage/1,2-Hmigration/denitrogenation/Cu-catalysed aerobic oxidative dehydrogenative cyclization. The desired products can beattained from readily available 2-vinylquinoline **1** and diverseazides**2a-i**using air as the oxidant beneath conditions, and it offers an attractive substitute method for the synthesis of oxazole derivatives which are further confirmed by spectral analysis.



Scheme I Synthesis of 5-(quinolin-2-yl)-2-substituted oxazoles 3a-i

KEYWORDSOxazole,1,3-dipolar cycloaddition, 2-vinylquinoline, azide.

INTRODUCTION

Nitrogen heterocycles embody the core structure of many drugentrants with a broad spectrum of pharmaceutical and therapeutic outlooks [1–6].The biological budding of quinoline spinoffs has beenreported previously [7-8].

Peptides play crucial and diverse biological roles as signalling and regulatory molecules in numerousphysiological and pathological processes, such as immunity, stress, growth, homeostasis,reproduction, and other cell functions [9]. Synthesis, bio-specificity, and efficacyprofile in people, peptides provide a stand for the design of novel therapeutic drugs [10-12].

A systematic search for peptidomimetics asoxazole-based peptides [13-14]. Oxazoles are an important class of 5-membered N,O-heterocyclic compoundswith numerous applications, from medicines to agrochemical products. The presence of oxazolemoieties in natural peptides confers stability and electronic dispersal to the peptide chain, therebyqualifying peptide–protein gratitude and DNA/RNA–peptide interactions [15].

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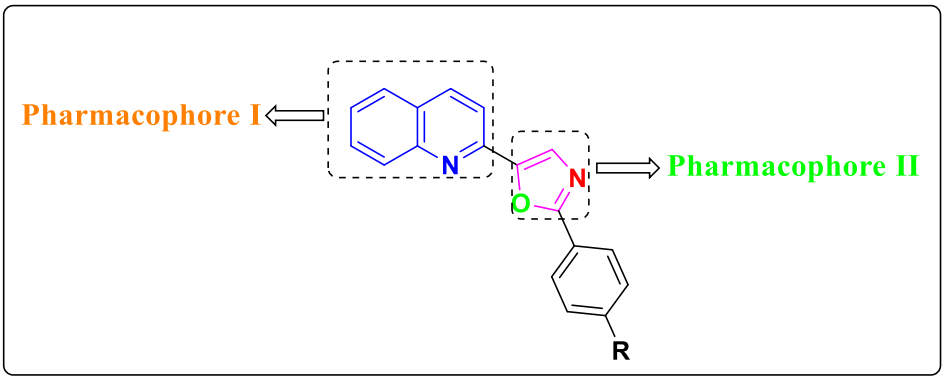
Furthermore, oxazolesshow anti-bacterial [16-17], anti-viral [18], anti-malarial [19], and anti-algal properties [20]. Herein, we design, synthesis and characterization of target is shown below.



Designed Target 3a-i

EXPERIMENTAL SECTION

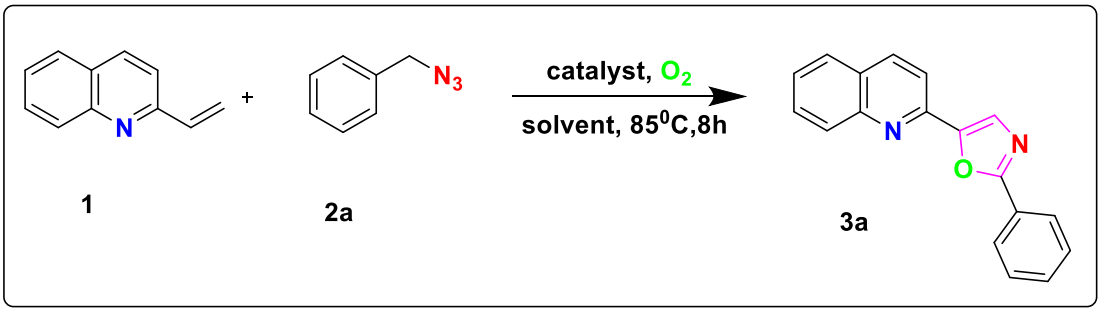
Material and Methods

All the commercially available chemicals and reagents were further used without purification. The purity of the compounds was analyzed by TLC using Merck 60F254 silica gel plates. The ^{1}H &$^{13}CNMR$ spectra recorded with a Mercury Plus spectrometer had chemical shifts that were referenced to TMS. ESI mass spectra were obtained using a Shimadzu QP5050A quadrupole-based mass spectrometer. Elemental analyses were performed on Carlo Ebra 106 and Perkin Elmer Model 240 analyzers.Synthesis of 5-(quinolin-2-yl)-2-substituted oxazoles designed targets 3a-iare depicted in Schem I.

RESULTS AND DISCUSSIONS

We initiated our research on the model reaction of 2-vinylquinoline (1)with benzyl azide (2a) under different reaction conditions (Table 1).Under an atmosphere of air, the 2,5-disubstituted oxazole (3a) treatment of a 1: 1.2 mixture of 1 and 2a with 10 mol % CuCl in toluene at 80^{o}C for 8 h. It is worth noting that 1 equiv. of the CuCl was sufficient to promote the reaction[21]effectively, and the yield of 3a

Table 1 Optimization of reaction conditions[a]



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Entry	Catalyst	Solvent	Yield (%)[b] of 3a
1	CuCl (10 mol %)	toluene	70
2	CuBr (10 mol %)	toluene	68
3	CuI (10 mol %)	toluene	64
4	none	toluene	0
5	CuCl (1 equiv.)	toluene	80

Reaction conditions: 2-vinylquinoline**1** (0.5 mmol, 1 equiv.), benzyl azide**2a** (0.6 mmol, 1.2 equiv), catalyst (0.05 mmol, 10 mol %), solvent (3.0mL), 80 °C, 8 h under air. [b]Isolatedyield of pure product based on **1**. [c]CuCl (0.5 mmol, 1 equiv.) wasused.

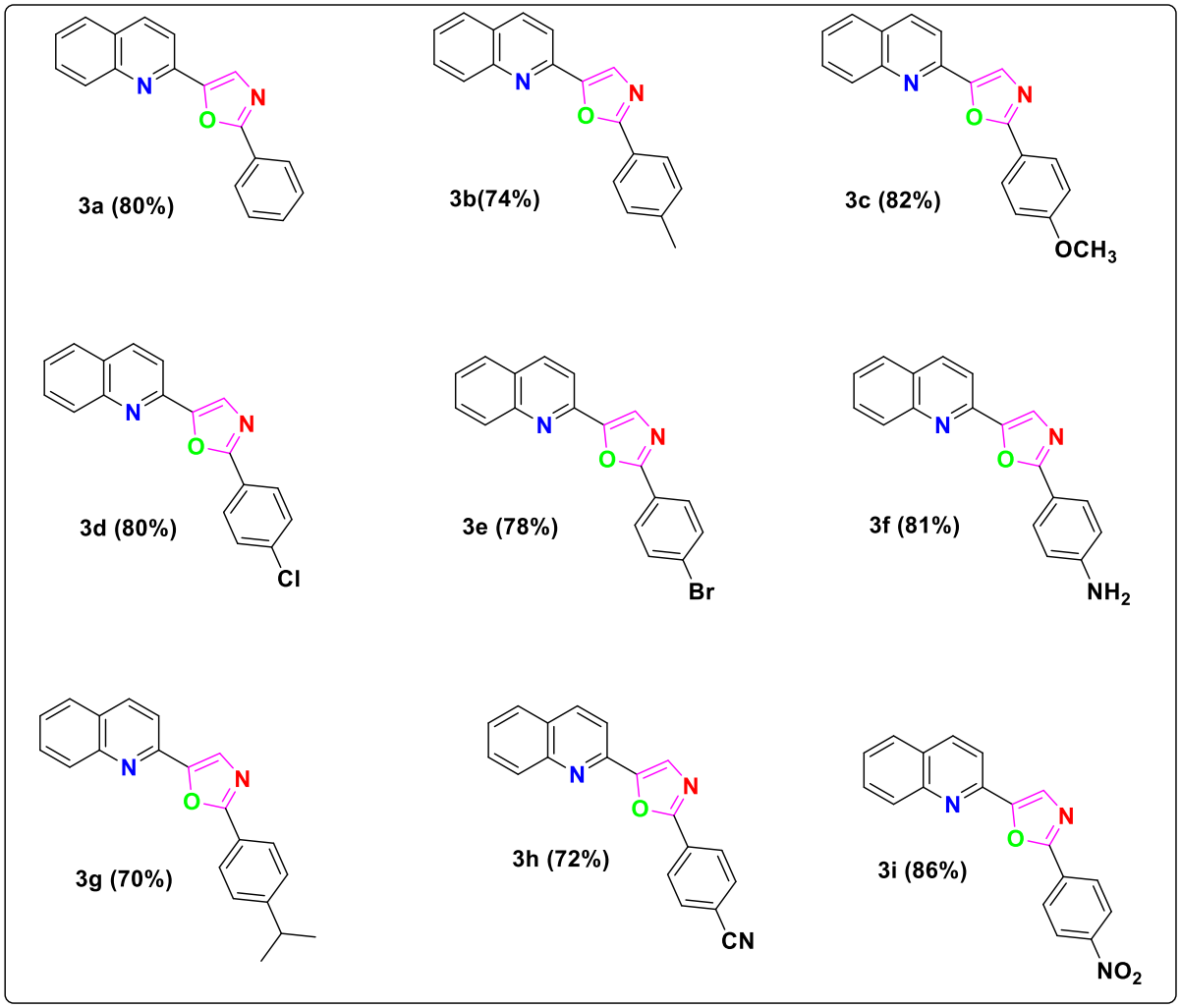

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Table 2: Names, MFand ESIof Compounds 3a-3i

Entry	Name	MF	ESI
3a	2-phenyl-5-(quinolin-2-yl)oxazole	$C_{18}H_{12}N_2O$	272
3b	5-(quinolin-2-yl)-2-(p-tolyl)oxazole	$C_{19}H_{14}N_2O$	286
3c	2-(4-methoxyphenyl)-5-(quinolin-2-yl)oxazole	$C_{19}H_{14}N_2O_2$	302.
3d	2-(4-chlorophenyl)-5-(quinolin-2-yl)oxazole	$C_{18}H_{11}ClN_2O$	306
3e	2-(4-bromophenyl)-5-(quinolin-2-yl)oxazole	$C_{18}H_{11}BrN_2O$	350
3f	4-(5-(quinolin-2-yl)oxazol-2-yl)aniline	$C_{18}H_{13}N_3O$	287
3g	2-(4-isopropylphenyl)-5-(quinolin-2-yl)oxazole	$C_{21}H_{18}N_2O$	314
3h	4-(5-(quinolin-2-yl)oxazol-2-yl)benzonitrile	$C_{19}H_{11}N_3O$	297
3i	2-(4-nitrophenyl)-5-(quinolin-2-yl)oxazole	$C_{18}H_{11}N_3O_3$	317

Table 3: ^{1}H &^{13}CNMR data of titled compounds 3a-3i

Entry	^{1}H NMR (400 MHz, DMSO) (δppm)	^{13}CNMR (100 MHz, DMSO) (δ, ppm)
3a	8.27 (s, 1H), 8.06 (s, 1H), 7.68 (dd, *J* = 27.2, 7.5 Hz, 4H), 7.59 (s, 1H), 7.44 (d, *J* = 6.4 Hz, 3H), 7.37 (d, *J* = 9.0 Hz, 1H), 7.25 (s, 1H).	160.89,156.40,149.76,148.77,137.95,134.56 (2C),131.28,130.12,129.77,129.12(2C),127. 81(2C),127.17(2C),125.47,113.94.
3b	8.24 (s, 1H), 8.05 (s, 1H), 7.74 (s, 2H), 7.64 – 7.41 (m, 4H), 7.36 – 7.17 (m, 3H), 2.37 (s, 3H).	160.89,156.40,149.76,148.77,141.07,137.95, 134.56(2C),130.10,129.77,129.37(2C),129.0 4,127.16(2C), 125.47(2C), 113.94, 21.12.
3c	8.25 (s, 1H), 8.06 (s, 1H), 7.75 – 7.57 (m, 5H), 7.46 (s, 1H), 7.23 (s, 1H), 7.05 (s, 2H), 3.82 (s, 3H)	162.01,160.89,156.40,149.76,148.77,137.95, 134.56(2C),130.10, 129.77(2C), 127.24(2C), 125.47(2C), 124.97, 114.52, 113.94, 56.03.
3d	8.25 (s, 1H), 8.06 (s, 1H), 7.71 (d, *J* = 12.4 Hz, 2H), 7.58 (s, 1H), 7.53 (s, 2H), 7.44 (s, 3H), 7.20 (s, 1H).	160.89,156.40,149.76,148.77,137.95,136.29, 134.56(2C),132.42,130.10,129.77(2C),129.1 5, 128.32, 127.17(2C), 125.47(2C).
3e	8.25 (s, 1H), 8.06 (s, 1H), 7.71 (d, *J* = 12.4 Hz, 2H), 7.58 (s, 1H), 7.53 (s, 2H), 7.45 (s, 3H), 7.20 (s, 1H).	160.89,156.40,149.76,148.77,137.95,134.56, 132.65,130.42,130.10,129.77,129.57(2C),12 7.17(2C), 125.47(2C), 124.76, 113.94.
3f	8.25 (s, 1H), 8.05 (s, 1H), 7.75 (s, 2H), 7.61 (s, 1H), 7.43 (s, 1H), 7.39 (s, 2H), 7.26 (s, 1H), 6.71 (s, 2H), 3.92 (s, 2H).	160.89,156.40,154.90,149.76,148.77,137.95, 134.56,130.10,129.77(2C),127.83,127.17(2 C),125.47(2C), 119.34, 116.07, 113.94.
3g	8.27 (s, 1H), 8.04 (s, 1H), 7.75 (s, 2H), 7.62 (d, *J* = 30.1 Hz, 3H), 7.43 (s, 3H), 7.26 (s, 1H), 3.10 (s, 1H), 1.33 (s, 6H).	160.89,156.40,149.76,148.77,146.88,137.95, 134.56(2C),130.13,129.77(2C),127.60(2C),1 27.17(2C),125.55(2C),113.94,34.19,23.37 (2C).
3h	8.25 (s, 1H), 8.06 (s, 1H), 7.84 (d, *J* = 7.5 Hz, 2H), 7.78 – 7.70 (m, 4H), 7.58 (s, 1H), 7.43 (s, 1H), 7.25 (s, 1H).	160.89,156.40,149.76,148.77,137.95,134.56 (2C)132.45,131.46(2C), 130.10, 129.77(2C), 127.16(2C), 125.47,119.12,113.94, 111.40.
3i	8.29 (d, *J* = 21.0 Hz, 3H), 8.08 (s, 1H), 7.92 (s, 2H), 7.83 – 7.67 (m, 2H), 7.60 (d, *J* = 8.9 Hz, 1H), 7.45 (d, *J* = 15.0 Hz, 1H), 7.24 (s, 1H).	160.89,156.40,149.76,148.77,137.95,136.29, 134.56(2C),132.42,130.10,129.77(2C),129.1 5, 128.32, 127.17(2C), 125.47(2C).

CONCLUSION

Herein, we have described the synthesis of 2,5-disubstituted oxazoles 3a-iwith promising yields, that functions*via* azide-2-vinylquinoline 1,3-dipolar cycloaddition/ring cleavage/1,2-*H* migration/denitrogenation, followed by Cu-catalysed aerobic oxidative dehydrogenative cyclization of the resulting imines. The use of naturally abundant air as an oxidant as well as an oxygen source.

REFERENCES

[1] V. Spano, M. Barreca, V. Cilibrasi, et al., Evaluation of fused pyrrolothiazole systems as correctors of mutant CFTR protein, *Molecules.*, 26,**2021,**1275.
[2] G. Li Petri, V. Spano, R. Spatola, et al., Bioactive pyrrole-based compounds with target selectivity, *Eur. J. Med. Chem*., 208 **,2020,** 112783.
[3] M. Barreca, A. Stathis, P. Barraja, F. Bertoni, An overview on anti-tubulin agents for the treatment of lymphoma patients, *Pharmacol. Ther*., 211,**2020,** 107552.
[4] V. Spano, A. Montalbano, A. Carbone, P. Scudieri, L.J.V. Galietta, P. Barraja, An overview on chemical structures as ΔF508-CFTR correctors, *Eur. J. Med. Chem*., 180 **2019,** 430–448.
[5] I. Frasson, V. Span_o, S. Di Martino, et al., Synthesis and photocytotoxic activity of [1,2,3]triazolo[4,5-h][1,6]naphthyridines and [1,3]oxazolo[5,4-h][1,6]naphthyridines, *Eur.J. Med. Chem*.,162,**2019,** 176–193.
[6] S.A. Everett, M.A. Naylor, P. Barraja, *et al*., Controlling the rates of reductivelyactivated elimination from the (indol-3-yl)methyl position of indolequinones,*J Chem Soc Perkin Trans.*, 2,**2001,** 843–860.
[7] S. Kumar, S. Bawa, H. Gupta, Biological activities of quinoline derivatives,*Mini Rev. Med. Chem.*, 9,**2009,** 1648–1654.
[8] S. Bawa, S. Kumar, S. Drabu, R. Kumar, Structural modifications of quinolinebased antimalarial agents: recent developments, *J. Pharm. Bioallied Sci.*, 2**(2010)** 64–71.
[9] Sun, L. Peptide-based drug development. Mod. Chem. Appl.,**2013**, 1, 1–2.
[10] Fosgerau, K.; Homann, T. Peptide therapeutics: Current status and future directions. *Drug Discov. Today*.,**2015**, 20, 122–128.
[11]Vlieghe, P.; Lisowski, V.; Martinez, J.; Khrestchatisky, M. Synthetic therapeutic peptides: Science and market.*Drug Discov. Today*.,**2010**, 15, 40–56.
[12] Craik, D.J.; Fairlie, D.P.; Liras, S.; Price, D. The future of peptide-based drugs. *Chem. Biol. Drug Des*.,**2013**, 81,136–147.
[13]Murru, S.; Dooley, C.T.; Nefzi, A. Parallel synthesis of bis-oxazole peptidomimetics. *Tetrahedron Lett*.,**2013**,54, 7062–7064.
[14]Pelay-Gimeno, M.; Glas, A.; Koch, O.; Grossmann, T.N. Structure-based design of inhibitors of protein–proteininteractions: Nimicking peptide binding epitopes. *Angew. Chem. Int. Ed*.,**2015**, 54, 8896–8927.
[15] Roy, R.S.; Kelleher, N.L.; Milne, J.C.;Walsh, C.T. In vivo processing and antibiotic activity of microcin B17analogs with varying ring content and altered bisheterocyclic sites. *Chem. Biol*.,**1999**, 6, 305–318.
[16] Oku, N.; Adachi, K.; Matsuda, S.; Kasai, H.; Takatsuki, A.; Shizuri, Y. Ariakemicins A and B, novelpolyketide-peptide antibiotics from a marine gliding bacterium of the genus Rapidithrix. *Org. Lett*.,**2008**, 10,2481–2484.
[17] Wada, H.; Williams, H.E.; Moody, C.J. Total synthesis of the posttranslationally modified polyazole peptideantibiotic plantazolicin A. *Angew. Chem. Int. Ed*.,**2015**, 54, 15147–15151.

[18]Kehraus, S.; König, G.M.; Wright, A.D.; Woerheide, G. Leucamide A: A new cytotoxic heptapeptide from theAustralian sponge Leucettamicroraphis. *J. Org. Chem.*,**2002**, 67, 4989–4992.
[19] Linington, R.G.; González, J.; Urena, L.-D.; Romero, L.I.; Ortega-Barría, E.; Gerwick, W.H. Venturamides Aand B: Antimalarial constituents of the panamanian marine Cyanobacterium Oscillatoria sp. *J. Nat. Prod.*,**2007**, 70, 397–401.
[20] Todorova, A.K.; Juettner, F.; Linden, A.; Pluess, T.; von Philipsborn,W.Nostocyclamide: A new macrocyclic,thiazole-containing allelochemical from Nostoc sp.31 (cyanobacteria) *J. Org. Chem.*,**1995**, 60, 7891–7895.
[21] Jiu-ling Li, Ying-chun Wang, Wei-ze Li, Heng-shan Wang, Dong-liang Moand Ying-ming Pan, *Chemcomm.,* 2013, 1-3.