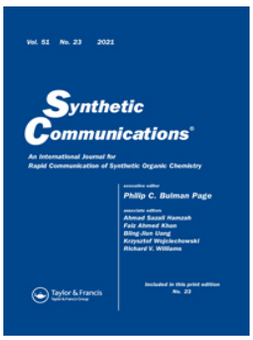


Taylor & Francis
Taylor & Francis Group

Synthetic Communications

An International Journal for Rapid Communication of Synthetic Organic Chemistry

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/lsyc20

A simple and efficient synthesis of imidazoquinoxalines and spiroquinoxalinones via pictect-spengler reaction using Wang resin

Simhachalam Gorle, Vaikunta Rao L, Chiranjeevi Y, Dhanunjaya Rao A. V, Ramamohan Mekala, Krishnaji Tadiparthi & Akula Raghunadh

To cite this article: Simhachalam Gorle, Vaikunta Rao L, Chiranjeevi Y, Dhanunjaya Rao A. V, Ramamohan Mekala, Krishnaji Tadiparthi & Akula Raghunadh (2021): A simple and efficient synthesis of imidazoquinoxalines and spiroquinoxalinones via pictect-spengler reaction using Wang resin, Synthetic Communications, DOI: 10.1080/00397911.2021.2015783

To link to this article: https://doi.org/10.1080/00397911.2021.2015783

SYNTHETIC COMMUNICATIONS®
https://doi.org/10.1080/00397911.2021.2015783

A simple and efficient synthesis of imidazoquinoxalines and spiroquinoxalinones via pictect-spengler reaction using Wang resin

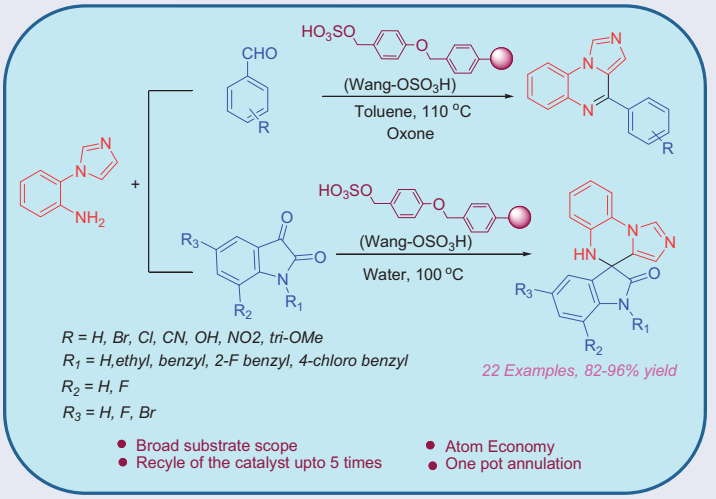
Simhachalam Gorle[a,b], Vaikunta Rao L[b], Chiranjeevi Y[a], Dhanunjaya Rao A. V[a], Ramamohan Mekala[a], Krishnaji Tadiparthi[c], and Akula Raghunadh[a]

[a]Technology Development Centre, Custom Pharmaceutical Services, Dr. Reddy's Laboratories Ltd, Hyderabad, India; [b]Department of Chemistry, GIS, GITAM (Deemed to be University), Visakhapatnam, India; [c]Department of Chemistry, CHRIST (Deemed to be University), Bangalore, India

ABSTRACT

An efficient approach for the synthesis of various imidazoquinoxalines and spiroquinoxalinones has been reported from 2-(1*H*-imidazol-1-yl) aniline and different aldehydes using Wang-OSO_3H as a reusable catalyst to get in good yields. The reaction condition has been optimized by screening in various solvents and a gram scale experiment has also demonstrated. Further, the substrate scope of the reaction has also been well demonstrated.

GRAPHICAL ABSTRACT



ARTICLE HISTORY
Received 19 September 2021

KEYWORDS
Wang-OSO_3H; imidazoquinoxaline; spiroquinoxalinones; recyclable catalyst

Introduction

Heterocyclic compounds are one of the most important scaffolds in the pharmaceutical and agro-industry. Especially, nitrogen-containing compounds possess the high

CONTACT Krishnaji Tadiparthi krishnaji.tadiparthi@christuniversity.in Department of Chemistry, CHRIST (Deemed to be University), Bangalore, India.

Supplemental data for this article can be accessed on the publisher's website.

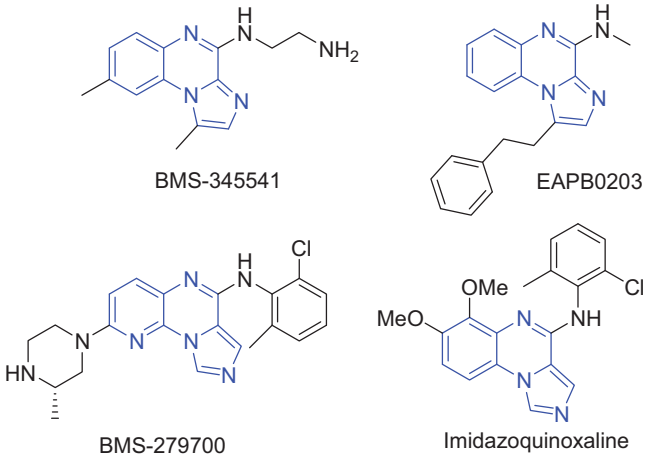


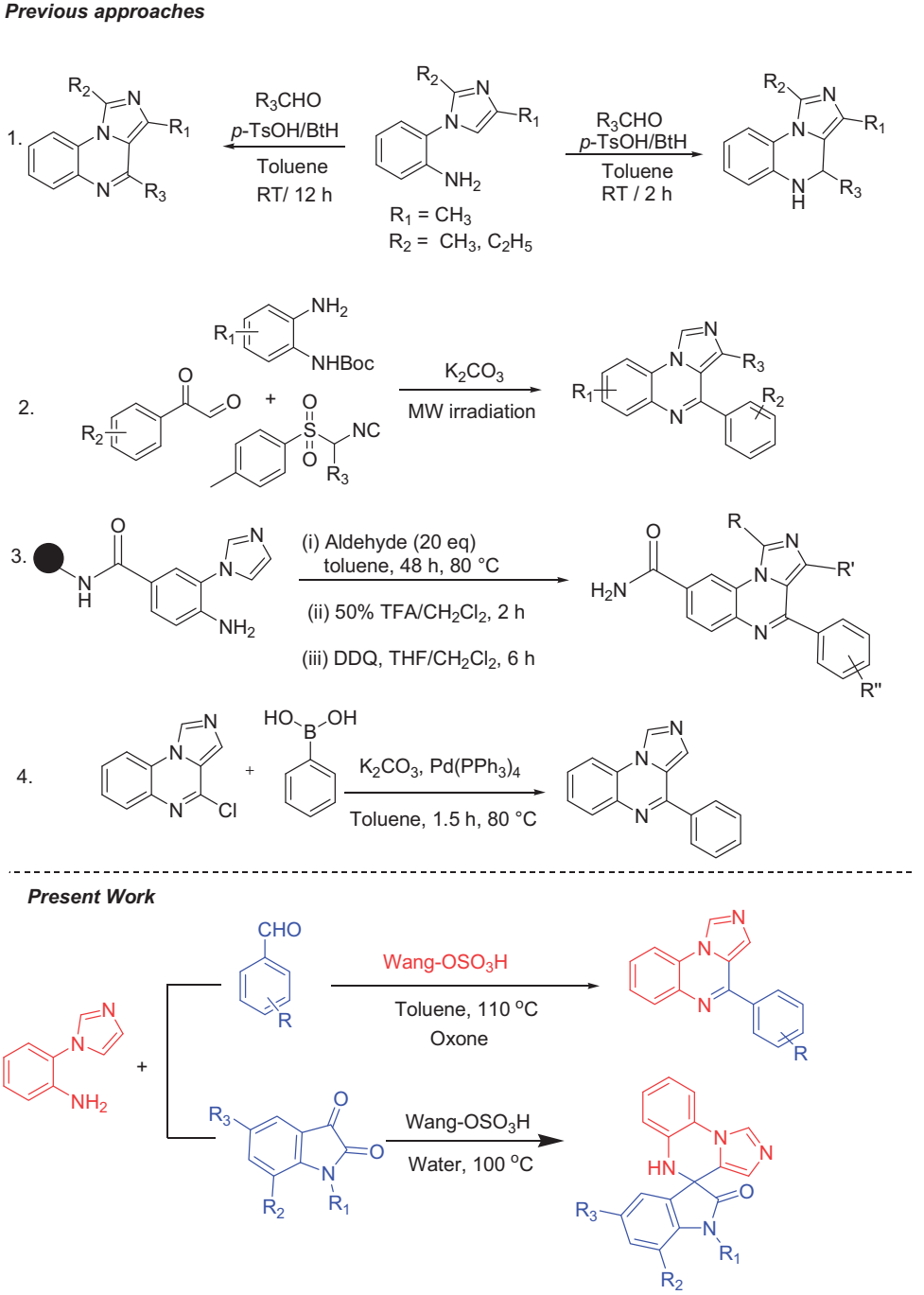
Figure 1. Some biologically important imidazoquinoxaline units.

biological activity and are found to be present in both natural products and synthetic drugs.[1,2] Noteworthy, most of the drugs were developed by fabricating the nitrogen-containing heterocyclic compounds in particular by using combinatorial synthesis. Among them, quinoxalines and imidazoquinoxalines are some of the important structural moieties having immense biological functions like antibacterial and anti-cancer. Because of having high biological importance, many synthetic chemists are attracted to the synthesis of these compounds (Figure 1).[3,4] For example the compound BMS-345541 has significant cytotoxicity on melanoma and is also a selective inhibitor of IκB kinase. Next, BMS-272900 is also an orally active inhibitor with anti-inflammatory activity. EAPB0203 exhibits important cytotoxicity *in vitro* on HTLV-I-infected CD4þ T-cell lines HuT102 and its amine derivative demonstrated significant activities against human melanoma cell line A375. Furthermore, imidazoquinoxaline scaffold was identified as an enzymatic inhibitor of Lck (IC50 = 2 nM) and having good potency against T-cell proliferation (IC50 = 0.67 μM).

Indeed, various synthetic methods have been developed to prepare different imidazoquinoxaline derivatives (Scheme 1),[5–8] but each method has its own limitation like low yields, expensive catalysts, harsh reaction conditions, and less substrate scope. To our delight, there are no reports on the synthesis of spiroquinoxalinones and hence we would like to explore more to prepare these novel compounds. Nevertheless, in continuation of our earlier affords for the synthesis of various heterocyclic compounds[9–11] herein we would like to report a unified approach for the synthesis of various imidazoquinoxalines and spiroquinoxalinones.

Results and discussion

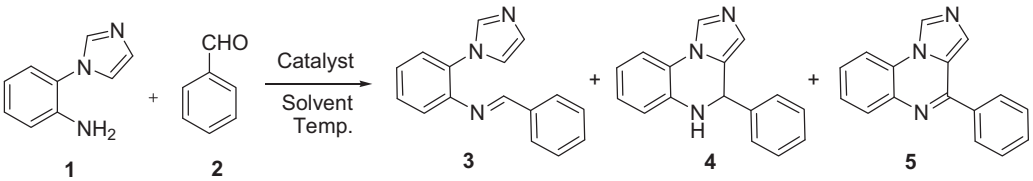
Initially, we commenced the reaction by taking 2-(1*H*-imidazol-1-yl)-aniline and benzaldehyde as model substrates. We have screened the reaction in various catalysts like $(n\text{-}Bu_3Sn)_2MoO_4$, β-cyclodextrin, and Wang-OSO_3H in different solvents like methanol and ethanol. In most of the cases, imine formation (**3**) was observed. Next, we have tried the same reaction in toluene as a solvent by using $(n\text{-}Bu_3Sn)_2MoO_4$ as a catalyst.



Scheme 1. Reported methods for the synthesis of imidazoquinoxalines

To our delight, we got the cyclized product (4) as a major product along with imine (3) as a byproduct under reflux conditions. Next, we have continued the reaction by adding the oxone as an oxidizing agent to get the quinoxaline (5) as a product in 50% yield.

Table 1. Optimization of reaction conditions.

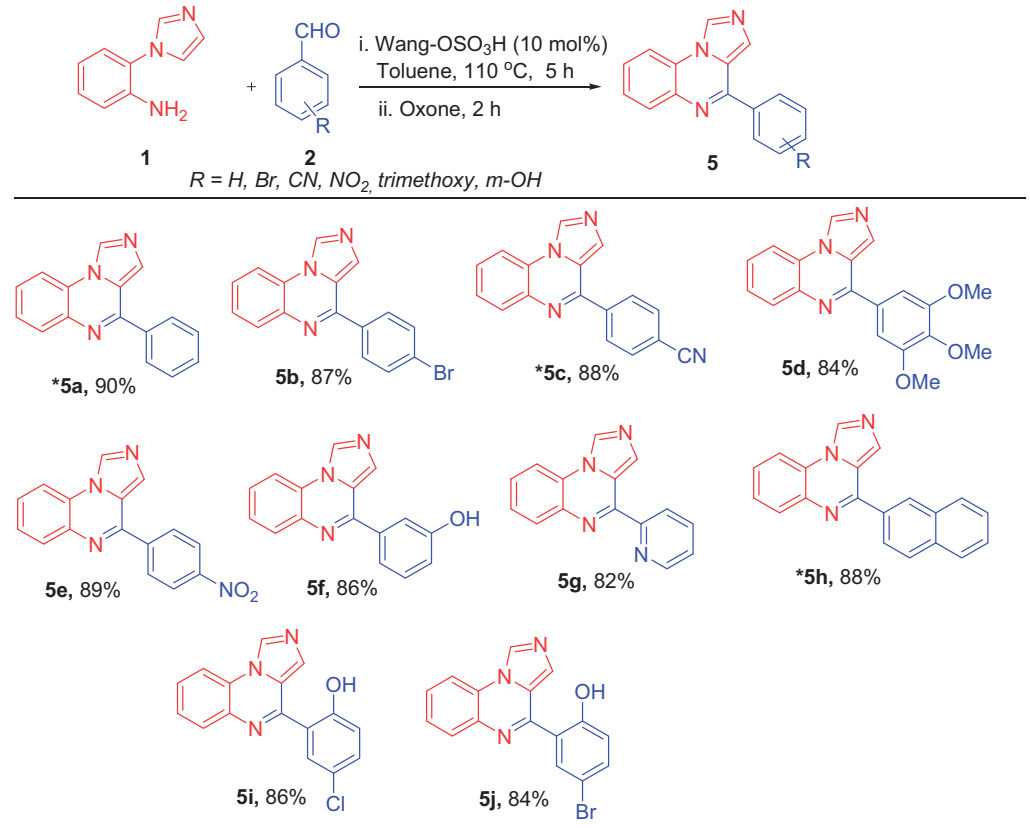


					Yield (%)		
Entry	Catalyst	Solvent	Temperature (°C)	Time (h)	3	4	5
1	$(n\text{-}Bu_3Sn)_2MoO_4$	Methanol	65	12	92	–	–
2	$(n\text{-}Bu_3Sn)_2MoO_4$	Ethanol	75	12	94	–	–
3	$(n\text{-}Bu_3Sn)_2MoO_4$	Toluene	110	15	20	30	50
4	β-Cyclodextrin	Ethanol	75	12	90	–	–
5	β-Cyclodextrin	Toluene	110	15	40	10	40
6	Wang-OSO_3H	Ethanol	75	12	95	–	–
7	Wang-OSO_3H	Toluene	110	5	–	–	87
8	TFA	Toluene	110	15	90	10	–
9	50% HCl	–	110	15	Trace	–	–
10	50% Acetic acid	–	110	5	–	–	85
11	Amberlite IR 120H	Toluene	110	10	–	–	45
12	Dowex 50WX2 H	Toluene	110	10	–	–	50

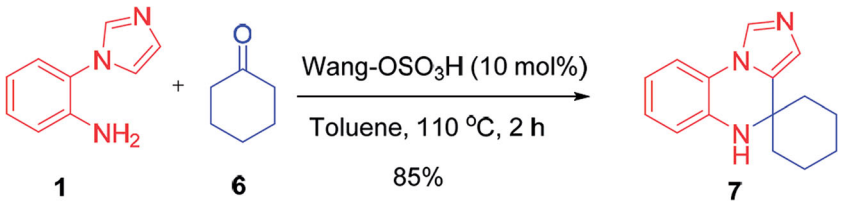
Table 2. Solvent screening in the presence of Wang-OSO_3H as a catalyst.

Entry	Solvent	Temperature (°C)	Catalyst (mole%)	Oxidant (eq.)	Yield (%)
1	Toluene	110	10	Oxone (2)	90
2	DMF	120	10	Oxone (2)	88
3	1,4-Dioxane	100	10	Oxone (2)	85
4	Water	100	10	Oxone (2)	83
5	O-Xylene	120	10	Oxone (2)	89
6	Toluene	110	10	PIDA (2)	85
7	Toluene	110	10	TBHP (2)	87
8	Toluene	110	10	Oxone (1)	80
9	Toluene	110	10	Oxone (1.5)	87
10	Toluene	110	5	Oxone (2)	70
11	Toluene	110	15	Oxone (2)	90

Furthermore, under similar reaction conditions, we have attempted the reaction by using Wang-OSO_3H resin as a catalyst in methanol and toluene. The best results were obtained in toluene under reflux conditions in an 87% yield. Next, we further screened the reaction in other catalysts like TFA, 50% HCl, Amberlite IR 120H, and Dowex 50WX2, but none of these were successful. But, the reaction in 50% acetic acid provided good yields. However, after comparing all the reaction conditions in terms of yields and environmental factors, we have chosen Wang-OSO_3H resin as a suitable catalyst for this reaction (Table 1). Moreover, in order to fine-tune the reaction, we further carried out the solvent screening using Wang-OSO_3H as a catalyst. Among all the solvents, a good yield was observed in toluene as a solvent. However, we further observed that increase in the equivalents of the catalyst will not make any difference in terms of yields. Moreover, we further performed the reaction in different oxidizing agents like PIDA, TBHP, and oxone. Among all, oxone was found to be the best for this reaction (Table 2).

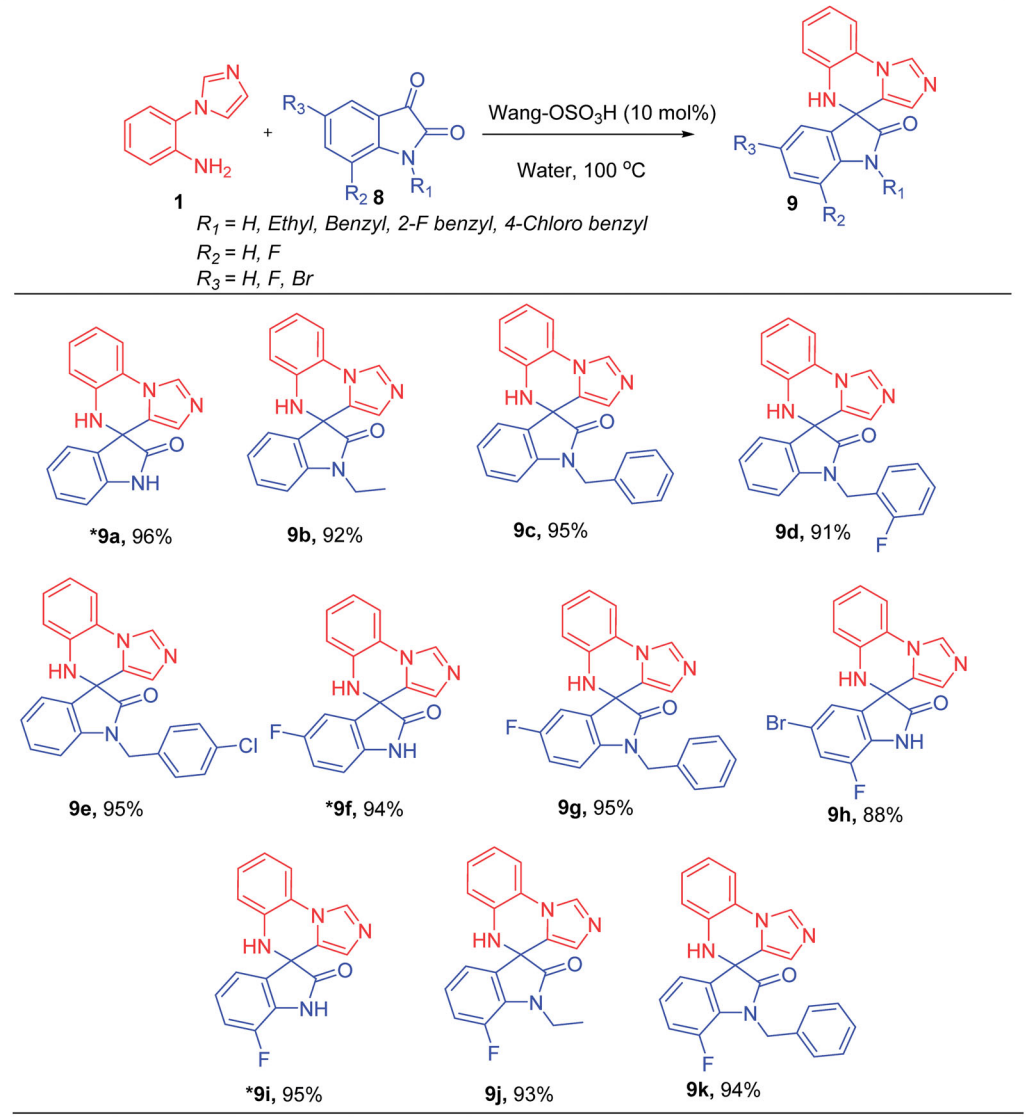


Scheme 2. Substrate scope of the reaction. *Experiments were conducted on gram scale



Scheme 3. Synthesis of spiroimidazo[1,5-a]-quinoxaline

Indeed, we have explored the substrate scope of the reaction with different aldehydes and to our delight, both electron-donating and withdrawing groups are compatible for this reaction to provide good yields. Notably, we could amenable to producing similar yields with pyridine aldehyde and napthaldehyde as well (Scheme 2). In order to apprehend this synthetic methodology, we have demonstrated the reaction by taking cyclohexanone (**6**) on a 10 g scale to provide its derivative in 85% yield (Scheme 3). Indeed, we have further synthesized different spiro compounds with various *N*-substituted isatins. Initially, we have carried out a reaction with 2-(1*H*-imidazol-1-yl)-aniline and isatine as model substrates, and the substrate scope of the reaction was carried out with different *N*-substituted isatins under



Scheme 4. Substrate scope of the reaction. *Experiments were conducted on gram scale.

the optimization conditions (Scheme 4). Moreover, the recyclability of the catalyst was also studied up to five times and observed without loss of its activity (Figure 2).

A possible mechanism for this reaction was also proposed. In the first step, Wang-OSO_3H act as ionic acid and activates the aldehyde by protonation. In the second step, the amine group of the 2-(1*H*-imidazol-1-yl) aniline react with activated aldehyde to form the Schiff base II *via* intermediate I by loss of water. In the third step, the Schiff base II intermediate undergoes intramolecular C–C bond formation and generates 2° carbocation ion III, which is aromatized to get the dihydroimidazoquinoxalines IV. In the final step, the oxidation of dihydroimidazoquinoxalines (IV) in presence of oxone results in the formation of imidazoquinoxalines V (Scheme 5).

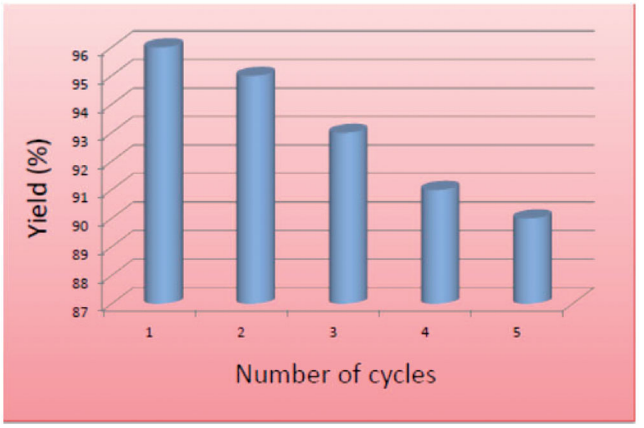
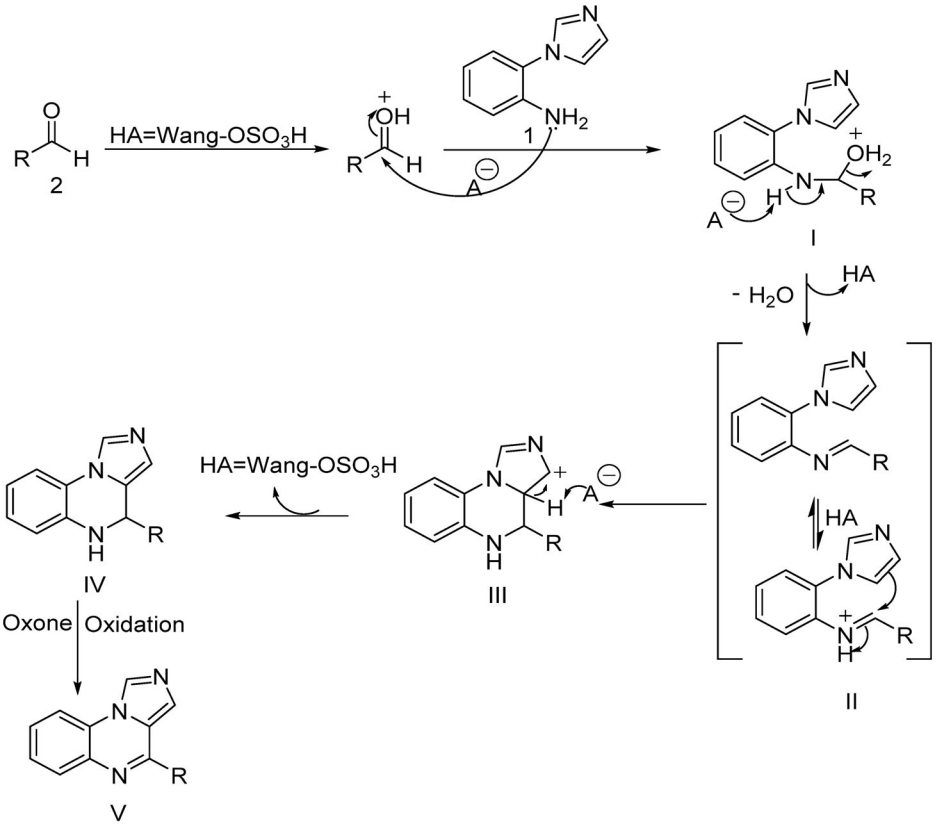


Figure 2. Recyclability of Wang resin.



Scheme 5. The possible mechanism for the preparation of imidazoquinoxline.

General information

All reagents were used as received and solvents from commercial sources without further purification or prepared as described in the literature. Reactions were monitored

by thin layer chromatography (TLC) on silica gel plates (60 F254), visualizing with ultraviolet light or ninhydrin charing. Chromatographic purification of products was carried out on silica gel (60–120 mesh). ^{1}H NMR and ^{13}C NMR spectra were determined in DMSO-d_6 solution by using 400 or 100 MHz spectrometers, respectively. Proton chemical shifts (δ) are relative to tetramethylsilane (TMS, δ = 0.00) as internal standard and expressed in ppm. Spin multiplicities are given as s (singlet), d (doublet), t (triplet) and m (multiplet) as well as b (broad). Coupling constants (*J*) are given in hertz. Melting points were determined using melting point B-540 apparatus. Mass spectra were recorded on an HP-5989A quadrapole mass spectrometer and uncorrected HRMS was determined using waters LCT premier XETOF ARE-047 apparatus.

General procedure for the synthesis of 4-phenylimidazo[1,5-a]quinoxaline (5)

To a solution of 2-(1*H*-imidazol-1-yl)aniline (3.14 mmol), in toluene (5 mL), aldehyde (3.45 mmol) and wang resin (10 mol%) were added sequentially. The reaction mass was stirred for 5 h at 110 °C. After completion of the reaction, the temperature was decreased to 50–60 °C and oxone (6.3 mmol) was added. Again, the temperature of the reaction mass was increased to 110 °C and stirred for 2 h. The catalyst was filtered and was washed with toluene (3 × 5 mL). The combined filtrate was concentrated under reduced pressure and the crude product was purified by column chromatography using silica gel (60–120 mesh) with methanol-DCM (1:9) as an eluent to afford the desired product (**5**).

General procedure for synthesis of 5′H-spiro[indoline-3,4′-Imidazo[1,2-a]quinoxalin]-2-one (9)

Isatin (3.45 mmol) and the wang resin (10 mol%) were added to the solution of 2-(1*H*-imidazol-1-yl)aniline (3.14 mmol) in water (5 mL). The reaction mass was stirred at 110 °C for 3 h. After completion of reaction, the reaction mass cooled to room temperature and diluted with a solution of methanol in ethyl acetate (1:9) to dissolve the precipitated product. The catalyst was removed by filtration and was washed with ethylacetate (3 × 5 mL). The combined filtrate was concentrated under reduced pressure and the crude product was purified by column chromatography using silica gel (60–120 mesh) with methanol and DCM (2:8) as an eluent to afford the desired product (**9**).

4-Bromo-2-(imidazo[1,5-a]quinoxalin-4-yl)phenol (5j)

Pale yellow solid; m.p: >250 °C, ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.56 (s, 1H), 9.38 (s, 1H), 8.45 (d, J = 8.4 Hz, 1H), 8.02–7.98 (m, 1H), 7.88–7.84 (m, 2H), 7.76–7.68 (m, 1H), 7.64–7.56 (m, 2H), 7.03 (d, J = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 156.3, 151.2, 134.2, 131.8, 131.5, 129.1 (2 C), 129.0, 128.5, 127.2, 124.3, 123.7, 122.3, 119.3, 115.5, 110.1; MS (ESI): *m/z* $[M+H]^+$ calcd for $C_{16}H_{11}BrN_3O$: 340.0085; found: 340.0085.

5′h-Spiro[cyclohexane-1,4′-imidazo[1,5-a]quinoxaline] (7)

White solid; m. p.: 180–181°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 (s, 1H), 7.45 (d, $J = 8.0$ Hz, 1H), 7.08–7.02 (m, 1H), 6.94 (s, 1H), 6.86–6.80 (m, 2H), 4.40 (s, 1H), 1.90–1.76 (m, 4H), 1.74–1.34 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 134.8, 133.2, 130.5, 126.4, 122.4, 122.2, 118.9, 116.1, 115.0, 52.0, 36.0 (2 C), 24.9, 21.4 (2 C); HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{15}H_{18}N_3$: 240.1501; found: 240.1497.

5h-Spiro[imidazo[1,5-a]quinoxaline-4,3′-indolin]-2′-one (9a)

Pale brown solid; m. p.: 177–178 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.42 (s, 1H), 8.53 (s, 1H), 7.73 (d, $J = 8.0$ Hz, 1H), 7.42–7.28 (m, 2H), 7.14 (s, 1H), 7.12–7.0 (m, 2H), 6.94 (d, $J = 8.0$ Hz, 1H), 6.85 (d, $J = 8.0$ Hz, 1H), 6.83–6.76 (m, 1H), 6.34 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 176.5, 142.5, 135.7, 132.9, 130.3, 129.8, 126.3, 125.5, 125.1, 123.8, 122.5, 121.5, 117.8, 115.3, 115.1, 110.1, 59.1; IR (KBr): 3237, 2676, 1726, 1618, 1486 cm^{-1}; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{17}H_{13}N_4O$: 289.1089; found: 289.1083.

Conclusions

In summary we have successfully demonstrated the synthesis of various imidazoquinoxalines and spiro-Imidazoquinoxalinones using Wang resin as a catalyst in good yields. It is an atom economic approach and the substrate scope of the reaction has been successfully executed and the recyclability of the catalyst has also been well performed. Finally, the possible reaction mechanism was also proposed.

Supporting information summary

The experimental section and additional information (^{1}H NMR, ^{13}C NMR and mass spectra for all compounds) are given in the supporting information.

Funding

The authors would like to thank Dr. Reddy's Laboratory, Hyderabad for providing facilities to carry out this work. One of the authors Dr. Krishnaji acknowledges CHRIST (Deemed to be University), Bangalore for funding Major Research Project [MRP # MRPDSC-1723].

References

[1] (a) Moarbess, G.; Deleuze-Masquefa, D. M. C.; Bonnard, V.; Gayraud-Paniagua, G. P. S.; Vidal, J. R.; Bressolle, F.; Pinguet, F.; Bonnet, P. A. *In Vitro* and *In Vivo* anti-Tumoral Activities of Imidazo[1,2-a]Quinoxaline, Imidazo[1,5-a]Quinoxaline, and Pyrazolo[1,5-a]Quinoxaline Derivatives. *Bioorg. Med. Chem.* **2008**, *16*, 6601–6610. DOI: 10.1016/j.bmc.2008.05.022. (b) Chen, P.; Norris, D.; Iwanowicz, E. J.; Spergel, S. H.; Lin, J.; Gu, H. H.; Shen, Z.; Wityak, J.; Lin, T. A.; Pang, S.; et al. Discovery and Initial SAR of Imidazoquinoxalines as Inhibitors of the Src-Family Kinase p56Lck. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 1361–1364. DOI: 10.1016/S0960-894X(02)00191-9.

[2] (a) Bakherad, M.; Keivanloo, A.; Samangooei, S. Synthesis of 1-Aryl-Substituted-4-Chloroimidazo[1,2-a]Quinoxalines Catalyzed by $PdCl_2$ in Water. *Tetrahedron Lett.* **2012**,

53, 1447–1449. DOI: 10.1016/j.tetlet.2012.01.028. (b) Mamedov, V. A.; Kalinin, A. A.; Balandina, A. A.; Kh.Rizvanov, I.; Latypov, S. K. An Efficient Method for the Synthesis of Imidazo[1,5-a]Quinoxalines from 3-Acylquinoxalinones and Benzylamines via a Novel Imidazoannulation. *Tetrahedron.* **2009**, *65*, 9412–9420. DOI: 10.1016/j.tet.2009.08.081. (c) Kalinin, A. A.; Voloshina, A. D.; Kulik, N. V.; Zobov, V. V.; Mamedov, V. A. Antimicrobial Activity of Imidazo[1,5-a]Quinoxaline Derivatives with Pyridinium Moiety. *Eur. J. Med. Chem.* **2013**, *66*, 345–354. DOI: 10.1016/j.ejmech.2013.05.038.

[3] (a) Sharma, S.; Kundu, B. Application of the Modified Pictet-Spengler Cyclization Reaction for the Preparation of an Imidazopyrazine Ring: Synthesis of New Pyrido- and Pyrimido-Imidazopyrazines. *J. Comb. Chem.* **2009**, *11*, 720–731. DOI: 10.1021/cc9000345. (b)Verma, A. K.; Jha, R. R.; Kasi Sankar, V.; Singh, R. P. Selective Synthesis of 4,5-Dihydroimidazo- and Imidazo[1,5-a]Quinoxalines via Modified Pictet–Spengler Reaction. *Tetrahedron. Lett.* **2013**, *54*, 5984–5990. DOI: 10.1016/j.tetlet.2013.08.052. (c) Sundaram, G. S. M.; Singh, B.; Venkatesh, C.; Ila, H.; Junjappa, H. Dipolar Cycloaddition of Ethyl Isocyanoacetate to 3-Chloro-2-(Methylthio)/2-(Methylsulfonyl)Quinoxalines: Highly Regio- and Chemoselective Synthesis of Substituted Imidazo[1,5-a]Quinoxaline-3-Carboxylates. *J. Org. Chem.* **2007**, *72*, 5020–5023. DOI: 10.1021/jo070590k.

[4] (a) Jacobsen, E. J.; Stelzer, L. S.; TenBrink, R. E.; Belonga, K. L.; Carter, D. B.; Im, H. K.; Im, W. B.; Sethy, V. H.; Tang, A. H.; VonVoigtlander, P. F.; et al. Piperazine Imidazo[1,5-a]Quinoxaline Ureas as High-Affinity GABAA Ligands of Dual Functionality. *J. Med. Chem.* **1999**, *42*, 1123–1144. DOI: 10.1021/jm9801307. (b) Varano, F.; Catarzi, D.; Colotta, V.; Cecchi, L.; Filacchioni, G.; Galli, A.; Costagli, C. Synthesis of a Set of Ethyl 1-Carbamoyl-3-Oxoquinoxaline-2-Carboxylates and of Their Constrained Analogue Imidazo. *Eur. J. Med. Chem.* **2001**, *36*, 203–209. DOI: 10.1016/s0223-5234(00)01203-4.

[5] (a) Xie, C.; Zhang, Z.; Li, D.; Gong, J.; Han, X.; Liu, X.; Ma, C. Dimethyl Sulfoxide Involved One-Pot Synthesis of Quinoxaline Derivatives. *J. Org. Chem.* **2017**, *82*, 3491–3499. DOI: 10.1021/acs.joc.6b02977. (b) Li, J.; Zhang, J.; Yang, H.; Gao, Z.; Jiang, G. A Green Aerobic Oxidative Synthesis of Pyrrolo[1,2-a]Quinoxalines from Simple Alcohols without Metals and Additives. *J. Org. Chem.* **2017**, *82*, 765–769. DOI: 10.1021/acs.joc.6b02501. (c) Sun, Q.; Liu, L.; Yang, Y.; Zha, Z.; Wang, Z. Unexpected Activated Carbon-Catalyzed Pyrrolo[1,2-a]Quinoxalines Synthesis in Water. *Chin. Chem. Lett.* **2019**, *30*, 1379–1382. DOI: 10.1016/j.cclet.2019.04.007.

[6] (a) Reeves, J. T.; Fandrick, D. R.; Tan, Z.; Song, J. J.; Lee, H.; Yee, N. K.; Senanayake, C. H. Copper-Catalyzed Annulation of 2-Formylazoles with o-Aminoiodoarenes. *J. Org. Chem.* **2010**, *75*, 992–994. DOI: 10.1021/jo9025644. (b) Biswas, S.; Batra, S. Retracted: Copper-Catalyzed Synthesis of Substituted Isoindolo[2,1-a]Quinoxalines and Isoindolo[2,1-a]Quinoxalin-6(5H)-Ones. *Eur. J. Org. Chem.* **2013**, *2013*, 4895–4902. DOI: 10.1002/ejoc.201300466. (c) Yuan, Q.; Ma, D. A One-Pot Coupling/Hydrolysis/Condensation Process to Pyrrolo[1,2-a]Quinoxaline. *J. Org. Chem.* **2008**, *73*, 5159–5162. DOI: 10.1021/jo8008098. (d) Cheeseman, G. W. H.; Tuck, B. The Synthesis of Pyrrolo[1,2-a]Quinoxalines from N-(2-Acylaminophenyl)Pyrroles. *J. Chem. Soc. C.* **1966**, *1966*, 852. DOI: 10.1039/j39660000852.

[7] (a) Preetam, A.; Nath, M. An Eco-Friendly Pictet–Spengler Approach to Pyrrolo- and Indolo[1,2-a]Quinoxalines Using p-Dodecylbenzenesulfonic Acid as an Efficient Brønsted Acid Catalyst. *RSC Adv.* **2015**, *5*, 21843–21853. DOI: 10.1039/C4RA16651E. (b) Jiang, G.; Wang, S.; Zhang, J.; Yu, J.; Zhang, Z.; Ji, F. Palladium-Catalyzed Primary Amine-Directed Decarboxylative Annulation of α-Oxocarboxylic Acids: Access to Indolo[1,2-a]Quinazolines. *Adv. Synth. Catal.* **2019**, *361*, 1798–1802. DOI: 10.1002/adsc.201900001. (c) An, Z.; Jiang, Y.; Guan, X.; Yan, R. Copper-Catalyzed Tandem Aerobic Oxidative Cyclization for the Synthesis of 4-Cyanoalkylpyrrolo[1,2-a]Quinoxalines from 1-(2-Aminophenyl)Pyrroles and Cyclobutanone Oxime Esters. *Chem. Commun.* **2018**, *54*, 10738–10741. DOI: 10.1039/c8cc06256k. (d) Huo, H.-R.; Tang, X.-Y.; Gong, Y.-F. *Synthesis* **2018**, *50*, 2727.

[8] (a) Huang, A.; Liu, F.; Zhan, C.; Liu, Y.; Ma, C. One-Pot Synthesis of Pyrrolo[1,2-a]Quinoxalines. *Org. Biomol. Chem.* **2011**, *9*, 7351–7357. DOI: 10.1039/c1ob05936j.

(b) Liu, H.; Zhou, F.; Luo, W.; Chen, Y.; Zhang, C.; Ma, C. Application of α-Amino Acids for the Transition-Metal-Free Synthesis of Pyrrolo[1,2-a]Quinoxalines. *Org. Biomol. Chem.* **2017**, *15*, 7157–7164. DOI: 10.1039/c7ob01688c. (c) Huang, A.; Chen, Y.; Zhou, Y.; Guo, W.; Wu, X.; Ma, C. An Efficient One-Pot Synthesis of Benzo[4,5]Imidazo[1,2-a]Quinoxalines via Copper-Catalyzed Process. *Org. Lett.* **2013**, *15*, 5480–5483. DOI: 10.1021/ol4026292. (d) Liu, H.; Duan, T.; Zhang, Z.; Xie, C.; Ma, C. One-Pot Synthesis of Pyrrolo[1,2-a]Quinoxaline Derivatives via a Copper-Catalyzed Aerobic Oxidative Domino Reaction. *Org. Lett.* **2015**, *17*, 2932–2935. DOI: 10.1021/acs.orglett.5b01167.

[9] (a) Murthy, V. N.; Satish, N. P.; Krishnaji, T.; Madhubabu, M. V.; Subba Rao, J.; Rao, L. V.; Raghunadh, A. Amberlite-15 Promoted an Unprecedented Aza Michael Rearrangement for One Pot Synthesis of Dihydroquinazolinone Compounds. *RSC Adv.* **2018**, *8*, 22331–22334. DOI: 10.1039/C8RA03308K. (b) Kumar, S. P.; Murthy, V. N.; Ganesh, K. R.; Rao, G. S.; Krishnaji, T.; Raghunadh, A. *ChemistrySelect.* **2018**, *24*, 6836. (c) Jaganmohan, C.; Kumar, K. P. V.; Reddy, G. S.; Mohanty, S.; Kumar, J.; Rao, B. V.; Krishnaji, T.; Raghunadh, A. De Novo Synthesis of 2,2-Bis (Dimethylamino)-3-Alkyl or Benzyl 2,3-Dihydroquinazolin-4(1H)-One Compounds. *Syn. Comm.* **2018**, *48*, 168–174. DOI: 10.1080/00397911.2017.1391291.

[10] (a) Krishnaji, T.; Murthy, V. N.; Raghunadh, A.; Rao, L. V. Simple and Efficient Amberlite 15-Catalyzed Synthesis of Dihydroquinazolinones. *Russ. J. Org. Chem.* **2020**, *56*, 1468–1475. DOI: 10.1134/S1070428020080199. (b) Raghunadh, A.; Krishnaji, T.; Suresh Babu, M.; Narayana Murthy, V.; Vaikunta Rao, L.; Syam Kumar, U. K. *SynOpen.* **2020**, *4*, 54.

[11] (a) Jaganmohan, C.; Vinay, K. P.; Venkateshwarlu, R.; Mohanty, S.; Kumar, J.; Venkateswara Rao, B.; Raghunadh, A.; Krishnaji, T. A Novel Approach for the Synthesis of Functionalized Hydroxylamino Derivative of Dihydroquinazolinones. *Synth. Commn.* **2020**, *50*, 2163–2170., DOI: 10.1080/00397911.2020.1768406. (b) Venkateshwarlu, R.; Murthy, V. N.; Krishnaji, T.; Nikumbh, S. P.; Jinkala, R.; Siddaiah, V.; Babu, M. V. M.; Rama Mohan, H.; Raghunadh, A. Base Mediated Spirocyclization of Quinazoline: One-Step Synthesis of Spiro-Isoindolinone Dihydroquinazolinones. *RSC Adv.* **2020**, *10*, 9486–9491. DOI: 10.1039/C9RA09567E.