SOLVENT FREE GREENER APPROACH TO SYNTHESIZE 4,5-DIPHENYL-1*H*-IMIDAZOL TETRAZOLO[1,5-a]QUINOLINES

Amol H. Kategaonkar*[1], Manohar K. Jopale[1], Santosh S. Katkar[2], Arun M. Bhagare[3], Balasaheb P. Pagar[4]

[1]Department of Chemistry, G.M.D. Arts, B.W. Com. and Sci. College, Sinnar, Nashik, (MS)
[2]Department of Chemistry, MSS's Arts, Com. and Sci. College, Ambad, Jalna, (MS)
[3]Department of Chemistry, Arts, Sci. and Com. College, Ozar (Mig), Nashik, (MS)
[4]Department of Chemistry, KSKW Arts, Sci. & Com. College, CIDCO Nashik, (MS)
**Email: amol.kategaonkar@gmail.com*

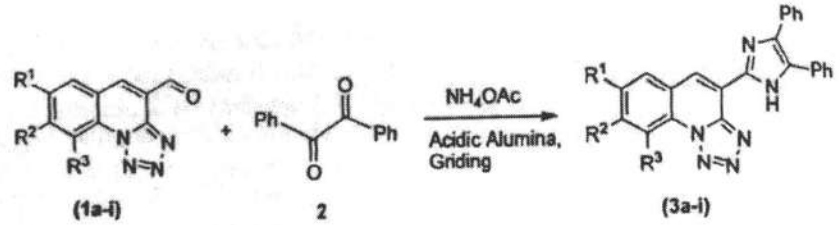
Abstract

To avoid toxicity and volatile nature of many organic solvents used in organic reactions have posed a serious threat to the environment. Therefore we have planned to highly convenient, green and recyclable heterogeneous catalysis for the synthesis of some 4,5-diphenyl-1H-imidazol derivatives in good yields by treating various tetrazolo [1,5-a] quinolines with benzil and ammonium acetate on acidic alumina under grinding condition.

***Keywords:** Solvent-free reaction, Greener reaction, 4,5-diphenyl imidazole, tetrazolo[1,5-a]quinoline, 1,5-hydrogen shift*

Introduction: Quinolines have been associated with broad spectrum of biological activities.[1-6] The fusion of quinoline to the tetrazole ring is known to increase the biological activity. The tetrazole group which is considered as analogues to carboxylic group as a pharmacore possesses wide range of biological activities. Several substituted tetrazoles have been shown to possess anticonvulsant,[7] anti-inflammatory,[8] CNS dispersant,[9] antimicrobial,[10] anti-AIDS[11] and antifertility agents.[12]

In nature fused heterocyclic compounds are common and used as drugs to treat a wide variety of diseases.[13] The fused-ring heterocycles have generally similar properties to those of the simple heterocycles and they are found to possess wide variety of biological activities.[14-18] The imidazoles are common components of a large number of natural products and pharmacologically active molecules.[19] The prevalence and prominence of this moiety makes a method, which expedites their preparation highly valuable. The biological importance of the imidazole ring system has made it a common structure in numerous synthetic compounds, such as fungicides,[20] herbicides,[21] plant growth regulators[22] and therapeutic agents.[23] In recent years, substituted imidazoles are substantially used in ionic liquids,[24] that have been given a new approach to 'Green Chemistry'. Now a days lot of organic reactions tried under solvent free conditions. Some reactions also show higher yields and greater selectivity.[25] Multicomponent reactions including many reagents which give a single product, draws much attention of the chemists.[26] Many classical reactions have been modified using green methods.[27]The present work deals with the solvent-free greener approach to synthesize the title compounds in regards to develop our ongoing research work.[28]

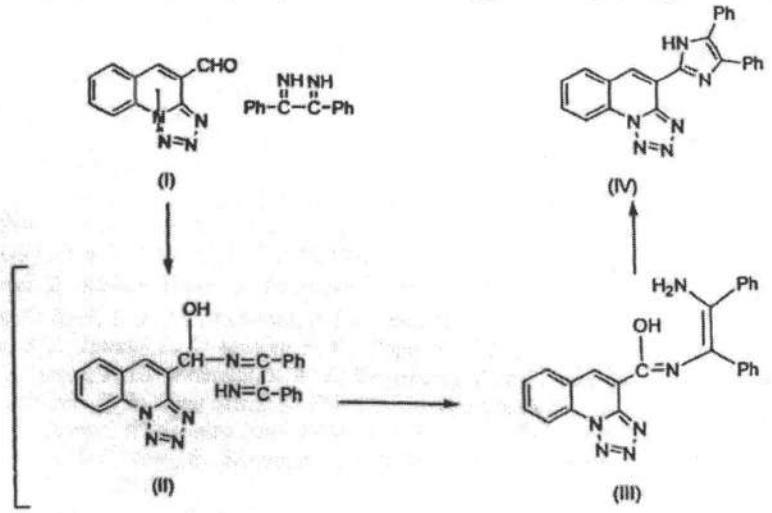


(1a-i) 2 (3a-i)

a) $R^1 = R^2 = R^3 = H$; b) $R^2 = R^3 = H$; $R^1 = Me$;
c) $R^1 = R^3 = H$; $R^2 = Me$; d) $R^1 = R^2 = H$; $R^3 = Me$;
e) $R^2 = R^3 = H$; $R^1 = OMe$; f) $R^1 = R^3 = H$; $R^2 = OMe$;
g) $R^1 = R^2 = H$; $R^3 = OMe$; h) $R^2 = R^3 = H$; $R^1 = OEt$;
i) $R^1 = R^2 = H$; $R^3 = Et$.

Scheme 1 Synthesis of new 4,5-diphenyl-1*H*-imidazol derivatives (**3a-i**).

A plausible mechanism (Scheme 2) underlying the formation of the imidazole, initially formed benzildiimine having nucleophilic activity would attack the aldehyde function of (I) giving rise to an intermediate (II), latter undergoing a 1,5-hydrogen shifts to give the intermediate (III). Further (III) cyclise to 4-(4,5-diphenyl-1*H*-imidazol-2-yl)tetrazolo[1,5-a]quinoline (IV).



(I) (II) (III) (IV)

Experimental: All chemicals and solvents were purchased from Merck (Darmstadt, Germany), Spectrochem (Mumbai, India), Lancaster (Ward Hill, MA, USA) and S. D. Fine-chem. (India). Melting points were determined in open capillaries on Kumar's melting point apparatus (India) and are uncorrected. IR spectra were recorded on JASCO FT-IR 4100, Japan using KBr discs. ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker DRK-300 and NMR

10. *Ko, O. H.; Kang, H. R.; Yoo, J. C.; Kim G. S.; Hong, S. S. Yakhak Hoechi 1992, 36, 150.*

11. *Dereu, N.; Evers, M.; Poujade C.; Soler, F. PCT Int. Appl. WO 9426725 1994. (CA 95:214297p)*

12. *Singh, H.; Bhutani, K. K.; Malhotra, R. K.; Paul, D. Experientia 1978, 34, 557; Singh, H.; Bhutani, K. K.; Malhotra R. K.; Paul, D. J. Chem. Soc. Perkin Trans-1 1979, 3166.*

13. *Wade, L. G. In Organic Chemistry: Fused Heterocyclic Compounds, 5th Ed.; Pearson Education (Singapore) Pte. Ltd: Delhi, 706, 2004.*

14. *Preston, P. N. In Benzimidazoles and Congeneric Tricyclic Compounds, Wiley Interscience: New York; 2, 531, 1980.*

15. *Grimmett, M. R. In Comprehensive Heterocyclic Chemistry, Pregamon Press: Oxford, Vol. 5, 457, 1984.*

16. *Weissberger, A. In The Chemistry of Heterocyclic Compounds, Wiley Interscience: New York, Part I, 247.*

17. *Preston, P. N. Chem. Rev. 1974, 74, 279.*

18. *Bradon, D. L.; Binder, R.G.; Betes, A.H.; Montague, C. J. Agric. Food Chem. 1994, 42, 1588.*

19. *Greenlee, W. J.; Siegl, P. K. S. Ann. Rep. Med. Chem. 1992, 27, 59; Hodges, J. C.; Hamby, J. M.; Blankley, C. J. Future Drugs 1992, 17, 575; Shilcrat, S. C.; Mokhallalati, M. K.; Fortunak, J. M. D.; Pridgen, L. N. J. Org. Chem. 1997, 62, 8449-8454; Meanwell, N. A.; Romine, J. L.; Seiler, S. M. Future Drugs 1994, 19, 361; Rizzi, J. P.; Nagel, A. A.; Rosen, T.; McLean, S.; Seeger, T. J. Med. Chem. 1990, 33, 2721; Shapiro, G.; Gomez-Lor, B. J. Org. Chem. 1994, 59, 5524; Adams, J. L.; Boehm, J. C.; Kassis, S.; Goycki, P. D.; Webb, E. F.; Hall, R.; Sorenson, M.; Lee, J. C.; Ayrton, A.; Griswold, D. E.; Gallagher, T. F. Bioorg. Med. Chem. Lett. 1998, 8, 3111.*

20. *Faulkner, D. J. Nat. Prod. Rep. 2000, 17, 1; Lewis, J. R. Nat. Prod. Rep. 2002, 19, 223; Jin, Z.; Li, Z.; Huang, R. Nat. Prod. Rep. 2002, 19, 454; Ho, J. Z.; Mohareb, R. M.; Ahn, J. H.; Sim, T. B.; Rapoport, H. J. Org. Chem. 2003, 68, 109.*

21. *Maier, T.; Schmierer, R.; Bauer, K.; Bieringer, H.; Buerstell, H.; Sachse, B. Canadian Patent 1201716 1986. (CA.86:148200); Maier, T.; Schmierer, R.; Bauer, K.; Bieringer, H.; Buerstell, H.; Sachse, B. US Patent 4820335 1989. (CA 89:19494).*

22. *Schmierer, R.; Mildenberger, H.; Buerstell, H. German Patent 3614364 1987. (CA 88:37838).*

23. *Heeres, J.; Back, L. J. J. ; Mostmans, J. H.; Vancutsem, J. J. Med. Chem. 1979, 22 1003; Dyer, R. L.; Ellames, G. J.; Hamill, B. J.; Manley, P. W.; Pope, A. M. S. J. Med. Chem. 1983, 26, 442; Lo, Y. S.; Nolan, J. C.; Maren, T. H.; Welstead Jr. W. J.; Gripshover, D. F.; Shamblee, D. A. J. Med. Chem. 1992, 35, 4790; Lednicer, D. In Drug Based on Five Membered Heterocycles in Strategies for Organic Drug Synthesis and Design, Wiley, New York 1998, 8, 185; Adams, J. L.; Boehm, J. C.; Gallagher, T. F.; Kassis, S.; Webb, E. F.; Hall, R.; Sorenson, M.; Garigipati, R.; Griswold, D. E.; Lee, J. C. Bioorg. Med. Chem. Lett. 2001, 11, 2867.*

24. *Wasserscheid, P.; Keim, W. Angew. Chem. In. Ed. Eng. 2000, 39, 3772.*

25. *Girijesh, K.V.; Keshav, R; Rajiv, K.V.; Patibha, D.; Singh, M.S. Tetrahedron 2011, 67, 3698.*

26. *Ahmad, S; Mozhdeh, S; Ali, M; Fatemeh, H. Tetrahedron 2010, 66, 4040.*

27. *Ryabukhin, S.V.; Andrey, S.P.; Bondarenko, S.S.; Ostapchuk, E.N.; Oleksnde, O.G.; Oleg, V.S.; Andrey, A.T. Tedtrahedron Letters, 2010, 51, 4229.*

28. *Kategaonkar, A. H.; Sadaphal, S. A.; Shelke, K. F., Shingate, B. B.; Shingare, M. S. Ukranica Bioorg. Acta 2009, 1, 3-7; Kategaonkar, A. H.; Pokalwar, R. U.; Sonar, S. S.; Gawali, V. U.; Shingate, B. B.; Shingare, M. S. Eur. J. Med. Chem. 2010, 45, 1128; v. Kategaonkar, A. H.; Pokalwar, R. U.;*

Sadaphal, S. A.; Shinde, P.V.; Shingate, B. B.; Shingare, M. S. Heteroatom Chemistry 2009, 20, 436; Shinde, P.V.; Kategaonkar, A.H.; Shingate, B. B.; Shingare, M.S. Tetrahedron Letters 2011, 52, 2889. Shinde, P.V.; Kategaonkar, A.H.; Shingate, B. B.; Shingare, Chin Chem Lett. 2011, 22, 915; Shinde, P.V.; Kategaonkar, A.H.; Shingate, B. B.; Shingare, 2011, Beilstein J. Org. Chem. 2011, 7, 53.

29. Kategaonkar, A. H.; Sapkal, S. B.; Madje, B. R.; Shingate, B. B.; Shingare, M. S. Chem Het Comp. 2010, 46, 754.

Spectrometer AC200. Mass spectra were recorded on Single-Quadrupole Mass Detector 3100, Waters. Elemental analyses were performed on CHNS analyzer Flash 1112, Thermo Finnigan. The progress of the reactions was monitored by TLC on Merck silica plates. Results are presented as, chemical shift δ in ppm, multiplicity, *J* values in Hertz (Hz), number of protons, proton's position. Multiplicities are shown as the abbreviations: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet). Solvents were commercially available materials of reagent grade.

General procedure for the synthesis of 4-(4,5-diphenyl-1*H*-imidazol-2-yl)tetrazolo[1,5-a]quinoline derivatives (3a-i): A mixture of tetrazolo[1,5-a]quinoline-4-carbaldehyde **1**, benzil **2** and ammonium acetate in the molar ratio of (1:2:4) was grinded over acidic alumina in mortar pestle. The catalyst was reactivated, each time, before use. The progress of the reaction was monitored on TLC. After completion of reaction, reaction mixture was poured on crushed ice. The solid obtained was extracted with CH_2Cl_2 (2×50 mL) and washed with water (2×10 mL), brine (2×20 mL). Thus separated organic layer, dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure. The obtained crude product was purified by column chromatography on silica gel by CH_2Cl_2: MeOH (8:2) as an eluent.

4-(4,5-diphenyl-1*H*-imidazol-2-yl)tetrazolo[1,5-a]quinoline (3a). ^{1}H NMR (DMSO-d_6, 400 MHz, δ ppm): 7.28-7.58 (m, 10H, Ar-H), 7.85 (t, 1H, J = 7.6 Hz, Ar-H), 7.97 (t, 1H, J = 7.6 Hz, Ar-H), 8.38 (d, 1H, J = 8 Hz, Ar-H), 8.66 (d, 1H, J = 8 Hz, Ar-H), 8.87 (s, 1H, Ar-H), 12.66 (s, 1H, NH).

Acknowledgement: The authors would like to thank the Principal, G.M.D. Arts, B.W. Commerce and Science College, Sinnar, Nashik for constant encouragement and providing necessary facilities. AHK also wish to express his gratitude to Director, BCUD, Savitribai Phule Pune University, Pune for providing the financial support in form of Minor Research Project to carry out the present work.

References:

1. *Atwell G. J.; Baguley B. C.; Denny W. A. J. Med. Chem. 1989, 32, 396.*
2. *Kuo S. C.; Lee H. Z.; Juang J. P.; Lin Y. T.; Wu T. S.; Chang J. J.; Lednicer D.; Paull K. D.; Lin C. M.; Hamel E.; Lee K. H. J. Med. Chem. 1993, 36, 1146.*
3. *Xia Y.; Yang Z. Y.; Xia P.; Bastow K. F.; Tachibana Y.; Kuo S. C.; Hamel E.; Hackl T.; Lee K. H. J. Med. Chem. 1998, 41, 1155.*
4. *Chen Y. L.; Chen I. L.; Tzeng C. C.; Wang T. C. Helv. Chim. Acta 2000, 83, 989.*
5. *El-Subbagh, H. I.; Abu-Zaid, S. M.; Mahran, M. A.; Badria, F. A.; Alofaid, A. M. J. Med. Chem. 2000, 43, 2915.*
6. *Gupta, R.; Gupta, A. K.; Paul S. Ind. J. Chem. 2000, 39B, 847.*
7. *Shekarchi, M.; Marvasti, M. B.; Sharifzadeh M.; Shafiee, A. Iran J. Pharm. Res. 2005, 1, 33.*
8. *Kumar P.; Knaus, E. E. Drug Des. Discov. 1994, 11, 15.*
9. *Shukla J. S.; Saxena, S. Indian Drugs 1980, 18, 15.*