Appendix I

List of publications

1) Sulfonated Graphene-Oxide as Metal-Free Efficient Carbocatalyst for the Synthesis of 3-Methyl-4-(hetero)arylmethyleneisoxazole-5(4H)-ones and Substituted pyrazole

Puja Basak, **Sourav Dey** and Pranab Ghosh.

ChemistrySelect, 2020, 5, 626.

2) A Green Synthetic Approach Towards One Pot Multicomponent Synthesis of Hexahydroquinoline and 9-Arylhexahydroacridine-1, 8-dione Derivatives Catalyzed by Sulphonated Rice Husk

Sourav Dey, Puja Basak and Pranab Ghosh.

ChemistrySelect, 2020, 5, 15209.

3) Convenient one-pot synthesis of 1,2,4-oxadiazoles and 2,4,6-triarylpyridines using graphene oxide (GO) as a metal-free catalyst: Importance of dual catalytic activity

Puja Basak, **Sourav Dey** and Pranab Ghosh.

RSC Advances, 2021, 11, 32106.

4) A design for convenient and greener root towards one pot multi-component synthesis of substituted pyrano-dichromeno-dione and chromeno-pyrido-pyrimidinone derivatives using rice husk based heterogeneous catalyst

Sourav Dey, Puja Basak, Subhajit Sarkar and Pranab Ghosh.

Asian Journal of Green Chemistry, 2020, 6, 24-39.

5) A a collective laboratory studies on one pot multi-component synthesis of a few varieties of heterocyclic compounds following greener approach using rice husk based greener catalyst

Sourav Dey, Puja Basak and Pranab Ghosh.

Chemistry Select (communicated, Manuscript No.-slct 202203405).

Appendix II

Seminar and Symposium Attended

- Science Academic Lecture Workshop On " Frontiers in Chemical and Material Sciences: Theory and Practice (February 8-10, 2018)
- International Seminar on "Frontiers in Chemistry 2018"(August 27, 2018)
- National Seminar on "Frontiers in Chemistry-2019"(May 22,2019)
- International Seminar on International Year of the Periodic Table of Chemical Elements-2019 (November 22-23,2019**;Poster presented**)
- National Seminar on Frontiers in Chemistry-2020 (5^{th} March, **Poster presented)**

- International Webinar about "Drug discovery Development and Vaccinatiom"(September 13,2020)

BIBLIOGRAPHY

I.7 References of Chapter I.

[1] R. Cammack et al.; Oxford Dictionary of Biochemistry and Molecular Biology (2nd Ed). Oxford University Press, **2006**, 74.

[2] Anonymous; Larousse de poche (in french), Les Editions Francaises Inc., **1994**, 8.

[3]Online Etymology Dictionary (website): http://www.etymonline.com, **2013**.

[4] G. Bernard, A Dromard; Book of etymology and medical terminology: Lexicon etymology (in French). Livretd'etymologieet de terminologiemedicale: Lexiqued'etymologie, **2011**, 1.

[5] Dictionary of Food Science and Technology (2nd Ed). International

[6] M. Keane, T. O. Marie; Miller-Keane Encyclopedia and Dictionary of Medicine, Nursing and Allied Health (7th Ed). Saunders, **2005**, 62.

[7] D. H. Williams, M. J. Stone, P. R. Hauck, S. K. Rahman, *J. Nat. Prod*. **1989**, 52.

[8] H. W. Kim, S. Y. Choi, H. S. Jang, B. Ryu, S. H. Sung, H. Yang, *Sci. Rep*. **2019**, 9.

[9] M. F. Holick. *N Engl J Med*. **2007**, 357.

[10] S. Chambial, S. Dwivedi, K. K. Shukla, P. J. John, P. Sharma, *Ind J Clin Biochem*. **2013**, 28..

[12] B. Aksel, *Oslo: The Norwegian Academy of Science and Letters*, **2010**, 11.

[13] N. Dudareva, E. Pichersky, *Plant Physiology*, **2000**, 122.

[14] P. Karlovsky, *Secondary Metabolites in Soil Ecology, Part II Bacterial Metabolites, Springer*, **2008**, 93.

[15] Š. Elga, *Natural, Exact, and Applied Sciences*, **2013**, 2.

[16] D. A. Clare, H. E. Swaisgood, *Journal of dairy science*, **2000**, 83.

[17] A. Keizo, O. Motoko, *Bioactive Compounds in Meat*. *Meat Biotechnology, Springer*, **2008**, 231.

[18] H. Rainer, *Bioactive Egg Compounds*. *Springer-Verlag Berlin Heidelberg*, **2007**, 309.

[19] P. Anne, K. Hannu, *Advances in food and nutrition research*, **2003**, 47.

[20] S. Arseniyadis, J. Cossy, *Modern Tools for the Synthesis of Complex Bioactive Molecules*, **2012**, 581.

[21] T. Corrado, *Bioactive compounds from natural sources:natural products as lead compounds in drug discovery*, **2012**, 622.

[22] S. P. Berit, *Oslo*: *The Norwegian Academy of Science and Letters*, **2010**, 23.

[23] T. Corrado, Bioactive compounds from natural sources: isolation, characterization and biological properties.London;New York: Taylor & Francis, **2001**, 693.

[24] A. V. Iosub, S. Moravcik, C. K. Wallentin, J. Berman, *Org.Lett*., **2019**, 21.

[25] B. V. Rokade, J. R. Prabhu, *J*. *Org*. *Chem*., **2012**,77.

[26] M. Orlandi, F. Tosi, M. Bonsignore, M. Benaglia, *Org*. *Lett*., **2015**, 17.

[27] X. J. Quan, Z. H. Ren, Y. Y. Wang, Z. H. Guan, *Org.Lett*., **2014**, 16.

[28] B. Das, C. R. Reddy, D. N. Kumar, M. Krishnaiah, R. Narender, *Synlett*, **2010**.

[29] A. Debache, R. Boulcina, A. Belfaitah, S. Rhouati, B. Carboni, *Synlett*, **2008**.

[30] S. A. Siddiqui, U. C. Narkhede, S. S. Palimkar, T. Daniel, R. J. Lahoti, K. V. Srinivasan, *Tetrahedron*, **2005**, 61.

[31] T. Sugino, K. Tanaka, *Chem. Lett*., **2001**.

[32] H. Chung, J. Kim, G. A. Gonzalez-Montiel, P. H. Y. Cheong, H. G. Lee, *Org.Lett*., **2021**, 23.

[33] Z. Wang, T. Song, Y. Yang, *Synlett*., **2019**, 30.

II.9 References of Chapter II.

[1] N. Soltani, A. Bahrami, M. I. Pech-Canul, L. A. Gonzàlez, *Chem. Eng. J.* **2015**, 264.

[2] M. J. Jeon, S. S. Kim, J. K. Jeon, S. H. Park, J. M. Kim, J. M. Sohn, S. H. Lee, Y. K. Park. *Nanoscale Res. Lett.* **2012**, 7.

[3] S. B. Qadri, M. A. Imam, A. W. Fliflet, B. B. Rath, R. Goswami, J. D. Caldwell, *J. Appl. Phys.* **2012**, 111.

[4] L. Wang, X. Wang, B. Zou, X. Ma, Y. Qu, C. Rong, Y. Li, Y. Su, Z. Wang. *Bioresour. Technol.* **2011**, 102.

[5] A. Loupy, *C. R. Chim*. **2004**, 7.

[6] D. D. Someshwar, G. P. Vedavati, T. J. Yeon. *Tetrahedron Lett*. **2012**, 53.

[7] R. B. NasirBaig , R. S. Varma. *Green Chem*. **2013**, 15.

[8] S. Maddila, K. K. Gangu, S. N. Maddila, S. B. Jonnalagadda. *Mol. Divers*.**2017**, 21.

[9] S. N. Maddila, S. Maddila, W. E. Van Zyl, S. B. Jonnalagadda. *Res.Chem.Intermed*. **2016**, 42.

[10] S. N. Maddila, S. Maddila, W. E. Van Zyl, S. B. Jonnalagadda. *Curr. Org. Chem*. **2016**, 20.

[11] V. Polshettiwar, R. S. Varma. *Chem. Soc. Rev*. **2008**, 37.

[12]S. Maddila, R. Pagadala, S. B. Jonnalagadda. *Lett. Org. Chem*. **2013**, 10.

[13] M. M. Ghorab, M. S. Alsaid , M. S. Al-Dosari, F.A. Ragab, A. A. Al-Mishari, A. N. Almoqbil. *Acta Pharm.* **2016**, 66.

[14] X. Q. Deng, M. X. Song, Y. Zheng , Z. S. Quan. *Eur. J. Med. Chem.* **2014**, 73.

[15] I. Briguglio, R. Loddo, E. Laurini, M. Fermeglia, S. Piras, P. Corona , P. Giunchedi, E. Gavini, G. Sanna, G. Giliberti, C. Ibba , P. Farci P, P. La Colla, S. Pricl, A. Carta. *Eur. J. Med. Chem*. **2015**, 105.

[16]D. Nardi , R. Pozzi, L. Degen, M. J. Magistretti. *J. Med. Chem*. **1970**, 13.

[17] D. Dube, M. Bloun, C. Brideau, C. C. Chan, S. Desmarais. *Bioorg. Med. Chem. Lett*. **1998**, 8.

[18] A. Nayyar, A. Malde, R. Jain, E. Coutinho. *Bioorg. Med. Chem*. **2006**, 14.

[19] Meneses Santos Rde, P. R. Barros, J. H. Bortoluzzi, M. R. Meneghetti, Y. K. da Silva, A. E. da Silva, M. S. da Silva, M. S. Alexandre-Moreira. *Bioorg. Med. Chem.* **2015**, 23.

[20] F. Zare, A. Abi, R. Moosavi-Zare , M. H. Beyzavi, M. A. Zolfigol. *J. Mol. Liq.* **2013**, 178.

[21] M. R. Aly, M. M. Ibrahim, A. M. Okael, Y. A. Gherbawy. *Bioorg. Khim.* **2014**, 40.

[22] D. W. Wang, H. Y. Lin, R. J. Cao, T. Chen, F. X. Wu, G. F. Hao, Q. Chen, W. C. Yang, G. F. Yang. *J. Agric. Food* Chem. **2015**, 63.

[23] M. R. Aly, M. M. Ibrahim, A. M. Okael, Y. A. Gherbawy. *Bioorg. Khim*. **2014**, 40.

[24] M. Abaszadeh, M. Seifi, A. Asadipour. *Res. Chem. Intermed*. **2015**, 41.

[25] B. Amirheidari, M. Seifi, M. Abaszadeh. *Res. Chem. Intermed.* **2016**, 42.

[26] M. Suarez, Y. Verdecia, E. Ochoa, N. Martin, R. Martinez, M. Quinteiro, C. Seoane, J. L. Soto, H. Novoa, N. Blaton, O. M. Peeters, C,De. Ranter. *J. Heterocyc. Chem.* **2003**, 37.

[27] A. Siddekha, S. H. S. Azzam, M. A. Pasha. *Syn. Commun*. **2014**, 44.

[28] S. Moloi, S. Maddila, S. B. Jonnalagadda. *Res. Chem. Intermed*. **2017**, 43.

[29] D. Azarifar, Y. Abbasi, O. Badalkhani. *Appl Organometal Chem.* **2018**, 32.

[30] K. Y. Foo, B. H. Hameed. *Bioresour. Technol*. **2011**, 102.

[31] R. Breslow, D. C. Riseout. *J. Am. Chem. Soc*. **1980**, 102.

[32] J. H. Li, G. D. Yasay, S. T. Kan, C. J. Ohnmacht, D. A. Trainor, A. D. Boney, T. J. Heppner, M. T. Nelson. *Arzneimittelforschung*. **1996**, 46.

[33] K.J. Prabahar, V.T. Ramakrishnan, D. Sastikumar, D. Selladurai, V. Masilamani. *Indian J. Pure Appl. Phys*. **1991**, 29.

[34] P. Shanmugasundaram, K. J. Prabahar, V.T. Ramakrishnan. *J. Heterocyclic Chem*. **1993**, 30.

[35] H. Mohan, N. Srividya, P. Ramamurthy, J. P. Mittal. *J. Chem. Soc. Faraday Trans*. **1996**, 92.

[36] J. Sivaraman, K. Subramanian, D. Velmurugan, E. Subramanian, P. S. Shanmugasunda-ram. *Acta Crystallogr*. **1996**, C52.

[37] M. Abdollahi-Alibeik, A. Rezaeipoor-Anari. *J. Magn. Magn. Mater*. **2016**, 398.

[38] A. Tadjarodi, A. Azad, M. G. Dekamin, S. Afshar, R. Hejazi, A. Mollahosseini, *J. Nanostruct.* **2015**, 5.

[39] L. S. Gadekar, S. S. Katkar, S. R. Mane, B. R. Arbad, M. K. Lande. *Bull. Kor. Chem. Soc*. **2009**, 30.

[40] M. Saha, A. K. Pal. *Tetrahedron Lett*. **2011**, 52.

[41] M. G. Dehbalaei, N. Foroughifar, H. Pasdar, A. Khajeh-Amiri. *New J. Chem*. **2018**, 42.

[42] F. Rashedian, D. Saberi, K. Niknam. *J. Chin. Chem*. Soc. **2010**, 57.

[43] Y. B. Shen, G.W. Wang. *Arkivoc.* **2008**, 16.

[44]A. Davoodnia, M. Khashi, N. Tavakoli-Hoseini. *Chin. J. Catal*. **2013**, 34.

[45] S. Rahmani, A. Amoozadeh. *J. Nanostruct*. **2014**, 4.

[46] H. A. Soliman, A.Y. Mubarak, A. El-Merakabi, S. A. Elmorsy. *Chem. Sci. Trans*. **2014**, 3.

[47] M. T ajbakhsh, H. Alinezhad, M. Norouzi, S. Baghery, M. Akbari . *J. Mol. Liq*. **2013**, 177.

[48] B. S. Samer, V.T. Kamble. *J. Chem. Pharm. Res*. **2015**, 7.

[49] S. Ko, C. F. Yao. *Tetrahedron.* **2006,** 62.

[50] A. Kumar, R. M. Maurya. *Tetrahedron*. **2007**, 63.

[51] S. B. Sapkal, K. F. Shelke, B. B. Shingate, M. S. Shingare. *Tetrahedron Lett*. **2009**, 50.

[52]H. Mierzace, A. Isadyar, A. Davoodnia, H. J. Eshghi. *Appl*. *Chem*. *Res*. **2014**, 8.

[53] S. Gholap, N. Gunjal. *Iran. J. Catal*. **2016**, 6.

[54] M. S. Vahdat, F. Chekin, M. Hatami, M. Khavarpour, S. Baghery, Z. Roshan-Kouhi. *Chin. J. Catal*. **2013**, 34.

[55] S. U. Tekale,V. P. Pagore, S. S. Kauthale, R. P. Pawar. *Chin*. *Chem*. *Lett*. **2014**, 25.

[56] R. Tafer, R. Boulcina, B. Carboni, A. Debache. *J*. *Chin*. *Chem*. *Soc*. **2012**, 59.

[57] D. Touhamia, Z. Zhua, W. S. Balanb, J. Janaunb, S. Haywooda, S. Zeina. *Journal of Environmental Chemical Engineering*. **2017**, 5.

[58] C. Li, B. Knierim, C. Manisseri, R. Arora, H. V. Scheller, M. Auer, K. P. Vogel, B. A. Simmons, S. Singh. *Bioresour*.*Technol*. **2010**, 101.

[59] M. Seddighi, F. Shirini, M. Mamaghani, *RSC Adv*. **2013**,3.

[59] L. Dobbin, *Journal of Chemical Education*, **1934**, 11.

[60] D. R. Boyd, N. D. Sharma, P. L. Loke, J. F. Malone, W. C. McRoberts, J. T. G. Hamilton, *Organic & Biomolecular Chemistry*, **2007**, 5.

[61] S. Cretton, L. Breant, L. Pourrez, C. Ambuehl, L. Marcourt, S. N. Ebrahimi, M. Hamburger, R. Perozzo, S. Karimou, M. Kaiser, M. Cuendet, P. Christen, *Journal of Natural Products*, **2014**, 77.

[62] S. Jain, V. Chandra, P. Kumar Jain, K. Pathak, D. Pathak, A. Vaidya, *Arabian Journal of Chemistry*, **2016**,12.

[63] A. Marella, O. P. Tanwar, R. Saha, M. R. Ali, S. Srivastava, M. Akhter, M. Shaquiquzzaman, M. M. Alam, *Saudi Pharmaceutical Journal*, **2013**, 21.

[64] O. Afzal, S. Kumar, M. R. Haider, M. R. Ali, R. Kumar, M. Jaggi, S. Bawa, *European Journal of Medicinal Chemistry*, **2015**, 97.

[65] M. C. Mandewale, U. C. Patil, S. V. Shedge, U. R. Dappadwad, R. S. Yamgar, *Journal of Basic and Applied Sciences*, **2017**, 6.

[66] J. B. Bharate, R. A. Vishwakarma, S. B. Bharate, *RSC Advances*, **2015**, 5.

[67] R.S. Keri, S.A. Patil, *Biomedicine & Pharmacotherapy*, **2014**, 68.

[68] S. Mukherjee, M. Pal, *Drug Discovery Today*, **2013**, 18.

[69] Y.Q. Hu, C. Gao, S. Zhang, L. Xu, Z. Xu, L.-S. Feng, X. Wu, F. Zhao, *European Journal of Medicinal Chemistry*, **2017**, 139.

[70] R. I. Khusnutdinov, A. R. Bayguzina, U. M. Dzhemilev, *Journal of Organometallic Chemistry*, **2014**, 768.

[71] H. Saggadi, D. Luart, N. Thiebault, I. Polaert, L. Estel, C. Len, *Catalysis Communications*, **2014**, 44.

[72] M.Y. Li, H.W. Xu, W. Fan, Q. Ye, X. Wang, B. Jiang, S.L. Wang, S.J. Tu, *Tetrahedron*, **2014**, 70.

[73] Y. Yu, M.S. Tu, B. Jiang, S.L. Wang, S.J. Tu, *Tetrahedron Letters*. **2012**, 53.

[74] M. Nasr-Esfahani, S.J. Hoseini, M. Montazerozohori, R. Mehrabi, H. Nasrabadi, *Journal of Molecular Catalysis A: Chemical*. **2014**, 382, 99-105.

[75] A. Khazaei, A.R. Moosavi-Zare, H. Afshar-Hezarkhani, V. Khakyzadeh, *RSC Advances*. **2014**, 4.

[76] G.M. Ziarani, S. Asadi, A. Badiei, S. Mousavi, P. Gholamzadeh, *Research on Chemical Intermediates*. **2015**, 41.

[77] Z. Arabpoor, H.R. Shaterian, *RSC Advances*. **2016**, 6.

[78] D. Patil, D. Chandam, A. Mulik, S. Jagdale, P. Patil, M. Deshmukh, *Journal of Saudi Chemical Society*. **2017**, 21.

[79] N.G. Khaligh, *Chinese Journal of Catalysis*. **2014**, 35, 1036-1042.

[80] N.A. Liberto, J.B. Simões, S. de Paiva Silva, C.J. da Silva, L.V. Modolo, Â. de Fátima, L.M. Silva, M. Derita, S. Zacchino, O.M.P. Zuñiga, G.P. Romanelli, S.A. Fernandes, , *Bioorganic & Medicinal Chemistry*. **2017**, 25.

[81] S. Sheik Mansoor, K. Aswin, K. Logaiya, S.P.N. Sudhan, *Arabian Journal of Chemistry*. **2017**, 10.

[82] A. Davoodnia, M. Khashi, N. Tavakoli-Hoseini, *Chinese Journal of Catalysis*. **2013**, 34.

[83] A. Khojastehnezhad, F. Moeinpour, A. Davoodnia, *Chinese Chemical Letters*. **2011**, 22.

[84] B. Paplal, S. Nagaraju, P. Veerabhadraiah, K. Sujatha, S. Kanvah, B. Vijaya Kumar, D. Kashinath, *RSC Advances*. **2014**, 4.

[85] A.A. Abdelhamid, O.A.A. Allah, A.H.A. Tamam, *Journal of Heterocyclic Chemistry*, **2017**, 54.

[86] A. Alizadeh, A. Rezvanian, *Comptes Rendus Chimie*, **2014**, 17.

[87] E. Schur, J. Bernstein, L. S. Price, R. Guo, S. L. Price, S. H. Lapidus, P. W. Stephens, *Crystal Growth & Design*, **2019**, 19.

[88] C. Grabe, H. Caro, *Berichte der Deutschen Chemischen Gesellschaft*. **1870**, 3.

[89] V. A. Byvaltsev, L. A. Bardonova, N. R. Onaka, R. A. Polkin, S. V. Ochkal, V. V. Shepelev, M. A. Aliyev and A. A. Potapov, *Front. Oncol*.**2019**, 9.

[90] M. Gensicka-Kowalewska, G. Cholewiński and K. Dzierzbicka, *RSC Adv*. **2017**, 7.

[91] P. Prasher and M. Sharma, *Med. Chem. Commun*. **2018**, 9.

[92] M. R. Galdino-Pitta, M. G. R. Pitta, M. C. A. Lima, L. S. Galdino and R. I. Pitta, *Mini Rev Med Chem*. **2013**, 13.

[93] S. Mirrett, *Infection Control & Hospital Epidemiology*. **1982**, 3.

[94] C. D. Geddes, *Dyes and Pigments*. **2000**, 45.

[95] C. Wang, J. Fu, K. Yao, K. Xue, K. Xu and X. Pang, *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*. **2018**, 199.

[96] X. Liu, T. N. V. Karsili, A. L. Sobolewski, W. Domcke, *J. Phys. Chem. B*. **2015**, 119.

[97] P. Qin, S. Paek, M. I. Dar, N. Pellet, J. Ko, M. Grätzel, M. K. Nazeeruddin, *J. Am. Chem. Soc*. **2014**, 136.

[98] K. A. Margrey and D. A. Nicewicz, *Acc. Chem. Res*., **2016**, 49.

[99] N. A. Romero, K. A. Margrey, N. E. Tay, D. A. Nicewicz, *Science*. **2015**, 349.

[100] A. V. Dubrovskiy, R. C. Larock, *J. Org. Chem*. **2012**, 77.

[101] P. Belmont, T. Belhadj, *Org. Lett*. **2005**, 7.

[102] Y. Kitahara, T. Mizuno and A. Kubo, *Tetrahedron*. **2004**, 60.

[103] J. Zhang, Y. Chen, X. Chen, X. Zheng, W. Cao, J. Chen and M. Zhang, *Tetrahedron*. **2014**, 70.

[104] X. D. Han, Y.-L. Zhao, J. Meng, C. Q. Ren, Q. Liu, *J. Org. Chem*. **2012**, 77.

[105] F. D. Popp, *J. Org. Chem*. **1962**, 27.

[106] Z. Guan, S. Wiechmann, M. Drafz, E. Hübner and A. Schmidt, *Org. Biomol. Chem*. **2013**, 11.

[107] M. Bobin, A. Kwast, Z. Wróbel, *Tetrahedron*. **2007**, 63.

[108] Y. Kuninobu, T. Tatsuzaki, T. Matsuki, K. Takai, *J. Org. Chem*. **2011**, 76.

[109] A. Bernthsen, *Justus Liebigs Annalen der Chemie*. **1884**, 224.

[110] A. Bernthsen, *Ann*. **1878**, 192.

[111] E. Delfourne, C. Roubin, J. Bastide, *J. Org. Chem*. **2000**, 65.

[112] M. G. Ferlin, C. Marzano, G. Chiarelotto, F. Baccichetti, F. Bordin, *Eur. J. Med. Chem.* **2000**, 39.

[113] J. Antonini, P. Polucci, A. Magnano, S. Martelli, *J. Med. Chem*. **2001**, 44.

[114] B. Stefanska, M. M. Bontemps-Gracz, I. Antonini, S. Martelli, M. Arciemiuk, A. Piwkowska, D. Rogacka, E. Borowski, *Bioorg. Med. Chem.* **2005**, 13.

[115] B. D. Gooch, P. A. Beal, *J. Am. Chem. Soc*. **2004**, 126.

[116] R. A. Janis, P. J. Silver, G. J. Triggle, *Adv. Drug Res*. 1987, 16.

[117] N. K. Ladani, D. C. Mungra , M. P. Patel, R. G. Patel. *Chinese Chemical Letters*. **2011**, 22.

[118] M. Demeunynck, F. Charmantray, A. Martelli, *Current Pharmaceutical Design*. **2001**, 17.

[119] M. B. Mazzucco, L. B. Talarico, S. Vatansever, A. C. Carro, M. L. Fascio, N. B. D'Accorso, C. C. García, *Journal of Biomedical Science*. **2015**, 22.

[120] S. Girault, P. Grellier, A. Berecibar, L. Maes, E. Mouray, P. Lemière, M. Debreu, E. Davioud-Charvet, C. Sergheraert. *J. Med. Chem*. **2000**, 43.

[121] R. Popielarz, S. Hu, D. C. Neckers, *Journal of Photochemistry and Photobiology A*. **1997**, 110.

[122] J. R. Sunkara, M. Rallabhandi, S. Prasangi, M. Palla, *Chem Sci Trans*. **2016**, 5.

[123] S. Sudha and M. A. Pasha, *Scientific World Journal*, A Facile Synthesis of N-H- and N-Substituted Acridine-1,8-diones under Sonic Condition, Volume **2013**, Article ID 930787, 6 pages,DOI: http://dx.doi.org/10.1155/2013/930787

[124] A. Amoozadeh, S. Rahmani, M. Bitaraf, F. B. Abadi and E. Tabrizian, *New J.Chem*. **2016**, 40.

[125] A. Zhu, R. Liu, C. Du and L. Li, *RSC Adv*. **2017**, 7.

[126] A. Djemoui, M. R. Ouahrani, A. Naouri, L. Souli, S. Rahmani L. M. Boualem, *Heterocyclic Letters*. **2018**, 8.

[127] M. Nasr-Esfahani, M. Montazerozohori, T. Abdizadeh, *C. R. Chimie*.**2015**, 18.

[128] A. Naouri, A. Djemoui, M. R. Ouahrani, M. B. Lahrech, N. Lemouari, D. H. A. Rocha, H. Albuquerque, R. F. Mendes, F. A. A. Paz, L. A. Helguero, K. Bachari, O. Talhi, A. M. S. Silvae, *Journal of Molecular Structure*. **2020**, 1217, https://doi.org/10.1016/j.molstruc.2020.128325

[129] M. Mazloumi, F. Shirini, Introduction of a new catalyst containing an ionic liquid bridge on nanoporous Na+ - montmorillonite for the synthesis of hexahydroquinolines and 1,8-dioxo-decahydroacridines via Hantzsch condensation, *Journal of Molecular Structure*, **2020**, doi: https:// doi.org/10.1016/j.molstruc.2020.128326.

[130] S. M. Vahdat, M. Akbari, *Oriental Journal of Chemistry*, **2011**,27.

[131] S. Chandrasekhar, Y. S. Rao, L. Sreelakshmi, B. Mahipal, C. R. Reddy, *Synthesis*. **2008**,11.

[132] M. Kidwai, D. Bhatnagar, *Chemical Papers*. **2010**, 64.

[133] M. S. Mirhosseyni, F. Nemati, A. Elhampour, *Journal of the Iranian Chemical Society*. **2017**,14.

[134] B. Malekia, A. V. Mofrada, R. Tayebeea, A. Khojastehnezhad, H. Alinezhad, E. Rezaei Seresht, *Russian Journal of General Chemistry*. **2017**, 87, 2922–2929.

[135] B. Maleki, R. Tayebee, M. Kermanian, S. S. Ashrafi, *J. Mex. Chem. Soc*. **2013**,57.

III.9 References of Chapter III.

[1] K. C. Fylaktakidou, D. J. Hadjipavlou-Litinas, K. E. Litinas, D. N. Nicolaides, *Curr*. *Pharm*. *Des*. **2004**, 10.

[2] J. Grover J, S. M. Jachak, *RSC Adv*. **2015**, 5.

[3] A. Thakur, R. Singla, V. Jaitak, *Eur*. *J*. *Med*. *Chem*. **2015**, 101.

[4] Y. Q. Hu, Z. Xu, S. Zhang, X. Wu, J. W. Ding, Z.S. Lv, L. S. Feng, *Eur*. *J*. *Med*. *Chem*. **2017**, 136.

[5] M. Z. Hassan, H. Osman, M. A. Ali, M. J. Ahsan, *Eur*. *J*. *Med*. *Chem*. **2016**, 123.

[6] X. L. Hu, Z. Xu, M. L. Liu, L. S. Feng, G. D. Zhang, *Curr*. *Top*. *Med*. *Chem*. **2017**, 17.

[7] E. M. Beccalli, A. Contini, P. Trimarco, *Tetrahedron Lett*. **2004**, 45.

[8] Y. Zhou, X. Zhang, S. Yang, Y. Li, Z. Qing, J. Zheng, J. Li, R. Yan, *Anal*. *Chem*. **2017**, 89.

[9] M. J. Jeon, S. S. Kim, J. K. Jeon, S. H. Park, J. M. Kim, J. M. Sohn, S. H. Lee, Y. K. Park, *Nanoscale Res. Lett.* **2012**, 7.

[10] N. Soltani, A. Bahrami, M. I. Pech-Canul, L. A. Gonzàlez, *Chem. Eng. J.* **2015**, 264.

[11] L. Wang, X. Wang, B. Zou, X. Ma, Y. Qu, C. Rong, Y. Li, Y. Su, Z. Wang, *Bioresour. Technol.* **2011**, 102.

[12] M. S. A. El-Gaby, M A. Zahran, M. M. F. Ismail, Y. A. Ammar, *Farmaco* **2000**, 55.

[13] V. Raj, J. Lee, *Trontiers in Chemistry*, **2020**, 8.

[14] A. Goel, V. J. Ram, *Tetrahedron*, **2009**, 65.

[15] W. D. Seo, J. Y. Kim, H. W. Ryu, J. H. Kim, S. I. Han, J. E. Ra, K. H. Seo, K. C. Jang, J. H. Lee, *J. Funct. Foods* **2013**, 5.

[16] M. Iranshahi, F. Kalategi, A. Sahebkar, A. Sardashti, B. Schneider, *Pharm. Boil.* **2010**, 48.

[17] Y. Bai, D. Li, T. Zhou, N. Qin, Z. Li, Z. Yu, H. Hua, *J. Funct. Foods* **2016**, 20.

[18] A. Sakunpak, K. Matsunami, H. Otsuka, P. Panichayupakaranant, *Food Chem*. **2013**, 139.

[19] W. W. Peng, Y. Q. Zheng, Y. S. Chen, S. M. Zhao, C. J. Ji, N. H. Tan, *J. Asian Nat. Prod. Res*. **2013**, 15.

[20] K. R. Joshi, H. P. Devkota, S. Yahara, *Nat. Prod. Commun*. **2013**, 8.

[21] M. Naseri, H. Monsef-Esfehani, S. Saeidnia, D. Dastan, A. Gohari, *Asian J. Chem.* **2013**, 25.

[22] S. Sukumaran, S. Kiruba, M. Mahesh, S. Nisha, P. Z. Miller, C. Ben, *Asian Pac. J. Trop. Med*. **2011**, 4.

[23] A. Kicel, M. Wolbis, Chem. Nat. Compd. **2012**, 48.

[24] S. Wang, F. Tang, Y. Yue, X. Yao, Q. Wei, J. Yu, *J. AOAC Int*. **2013**, 96.

[25] S. S. S. A. Aziz, M. A. Sukari, M. Rahmani, M. Kitajima, N. Aimi, N. J. Ahpandi, *Malays. J. Anal. Sci*. ***2010***, 14.

[26] J. Joselin, T. S. S. Brintha, A. R. Florence, S. Jeeva, *Asian Pac. J. Trop. Dis.* **2012**, 2.

[27] P. H. Nguyen, B. T. Zhao, O. Kim, J. H. Lee, J. S. Choi, B. S. Min, M. H. Woo, *J. Nat. Med*. **2016**, 70.

[28] V. Petrul'ová-Poracká, M. Repcak, M. Vilkova, J. Imrich, *Food Chem*. **2013**, 141.

[29] J. Sun, Y. D. Yue, F. Tang, X. F. Guo, *J. Asian Nat. Prod. Res*. **2010**, 12.

[30] J. Y. Cho, T. L. Hwang, T. H. Chang, Y. P. Lim, P. J. Sung, T. H. Lee, J. J. Chen, *Food Chem*. **2012**, 135.

[31] M. N. Erichsen, T. H. V. Huynh, B. Abrahamsen, J. F. Bastlund, C. Bundgaard, O. Monrad, A. B. Jensen, C. W. Nielsen, K. Frydenvang, A. A. Jensen, L. Bunch, *J. Med. Chem*. **2010**, 53.

[32] A. Berg, K. Reiber, H. Dorfelt, G. Walther, B. Schlegel, U. J. Grafe, *Antibiot*. **2000**, 53.

[33] K. Otoguro, K. Shiomi, Y. Yamaguchi, N. Arai, T. Sunazuka, R. Masuma, Y. Iwai, S. Omura, *J. Antibiot*. **2000**, 53.

[34] Z. Q. Xu, M. G. Hollingshead, S. Borgel, C. Elder, A. Khilevich, M. T. Flavin, *Bioorg. Med. Chem. Lett*. **1999**, 133.

[35] E. R. Almeida, *Open Nat. Prod. J*. **2009**, 2.

[36] M. Makino , Y. Fujimoto, *Phytochemistry*.**1999**, 50.

[37] S. Ray, H. K. Majumder, A. K. Chakraborty, S. Mukhopadhyay, *J. Nat. Prod*. **1996**, 59.

[38] W. Schmidt, L. Beerhues, *FEBS Lett*. **1997**, 420.

[39] Y. L. Lin, C. C. Shen, Y. J. Huang, Y. Y. Chang, *J. Nat. Prod*. **2005**, 68.

[40] N. Thomas, S. M. Zachariah, *Asian J. Pharm. Clin. Res*. **2013**, 6.

[41] G. Brahmachari, S. K. Jash, *Rec. Pat. Biotechnol*. **2014**, 8.

[42] C. D. Hufford, B. O. Oguntimein, D. V. Engen, D. Muthard, J. Clardy, *J. Am. Chem. Soc*. **1980**, 102.

[43] E. Herrera, C. Barbas, *J. Physiol. Biochem*. **2001**, 57.

[44] V. Fuendjiep, A. E. Nkengfack, Z. T.Fomum, B. L. Sondengam, B. Bodo, *J. Nat. Prod*. **1998**, 61.

[45] C. Ito, M. Itoigawa, Y. Mishina, V. C. Filho, F. Enjo, H. Tokuda, H. Nishino, H. Furukawa, *J. Nat. Prod*. **2003**, 66.

[46] J. Wandji, Z. T. Fomum, F. Tillequin, F. Libot, M. Koch, *J. Nat. Prod*. **1995**, 58.

[47] M. N. Erichsen, T. H. V. Huynh, B. Abrahamsen, J. F. Bastlund, C. Bundgaard, O. Monrad, A. B. Jensen, C. W. Nielsen, K. Frydenvang, A. A. Jensen, L. Bunch, *J. Med. Chem*. **2010**, 53.

[48] P. K. Paliwal, S. R. Jetti, S. Jain, *Med. Chem. Res*. **2013**, 22.

[49] S. Bhavanarushi, V. Kanakaiah, E. Yakaiah, V. Saddanapu, A. Addlagatta, V. J. Rani, *Med. Chem. Res*. **2013**, 22.

[50] A. G. E Amr, A. M. Mohamed, S. F. Mohamed, N. A. Abdel-Hafez, A. E. F. G. Hammam, *Bioorg. Med. Chem*. **2006**, 14.

[51] D. Olmedo, R. Sancho, L. M. Bedoya, J. L. López-Pérez, E. Del Olmo, E. Muñoz, J. Alcami, M. P. Gupta, A. S. Feliciano, *Molecules.* **2012**, 17.

[52] A. S. Al-Ayed, *Int. J. Org. Chem*. **2011**, 1.

[53] A. A. Al-Amiery, Y. K. Al-Majedy, A. A. H. Kadhum, A. B. Mohamad, *Sci. Rep*. **2015**, 5.

[54] L. Z. Chen, W. W. Sun, L. Bo, J. Q. Wang, C. Xiu, W. J. Tang, J. B. Shi, H. P. Zhou, X. H. Liu, *Eur. J. Med. Chem*. **2017**, 138.

[55] P. Anand, B. Singh, N. Singh, *Bioorg. Med. Chem*. **2012**, 20.

[56] M. J. Matos, F. Mura, S. Vazquez-Rodriguez, F. Borges, L. Santana, E. Uriarte, C. Olea-Azar, *Molecules.* **2015**, 20.

[57] M. M. Abdou, *Arab. J. Chem*. **2017**, 10.

[58] M. D. J Wijayabandara, M. I. Choudhary, A. Adhikari, *P. Ann. Sci. Sess. Fac. Med. Sci*. **2015**, 2.

[59] S. Akoudad, S. K. Darweesh, M. J. Leening, P. J. Koudstaal, A. Hofman, A. Van Der Lugt, B. H. Stricker, M. A. Ikram, M. W. Vernooij, *Stroke*. **2014**, 45.

[60] R. S. Keri, B. S. Sasidhar, B. M. Nagaraja, M. A. Santos, *Eur. J. Med. Chem.* **2015**, 100.

[61] M. Z. Hassan, H. Osman, M. A. Ali, M. J. Ahsan, M. J. Ahsan, *Eur. J. Med. Chem*. 2016, 123.

[62] S. Emami, S. Dadashpour, *Eur. J. Med. Chem*. **2015**, 102.

[63] S. F. Razavi, M. Khoobi, H. Nadri, A. Sakhteman, A. Moradi, S. Emami, A. Foroumadi, A. Shafiee, *Eur. J. Med. Chem*. **2013**, 64.

[64] A. Shaabani, R. Ghadari, S. Ghasemi, M. Pedarpour, A. H. Rezayan, A. Sarvary, S. W. Ng, *J. Comb. Chem*. **2009**, 11.

[65] D. Rajguru, B S. Keshwal, S. Jain, *Chin. Chem. Lett*. **2013**, 24.

[66] J. M. Khurana, B. Nand, P. Saluja, *Tetrahedron*.**2010**, 66.

[67] A. T. Khan, M. Lal, S. Ali, Md. M. Khan, *Tetrahedron Lett*. **2011**, 52, 5327–5332.

[68] M. Bihani, P. P. Bora, G. Bez, H. Askari, *C. R. Chimie*. **2013**,16.

[69] Z. Chen, Q. Zhu, W. Su, *Tetrahedron Lett*. **2011**, 52.

[70] K. Pradhan, S. Paul, A. R. Das, *Tetrahedron Lett*. **2013**, 54.

[71] M. G. Dekamin, M. Eslami, A. Maleki, *Tetrahedron*. **2013**, 69.

[72] G. Brahmachari, S. Laskar, *J. Heteroclyclic Chem*. **2014**, 51.

[73] J. F. Swinbourne, H. J. Hunt, G. Klinkert, *Adv Heterocycl Chem*. **1987**, 23.

[74] O. V. Koval'chukova, N. I. Mordovina, N. E. Kuz'mina, S. V. Nikitin, B. E. ZaItsev, S. B. Strashnova , K. K. Palkina, *Crystallogr Rep*.**2004**, 49.

[75] M. V. R. Reddy, B. Akula, S. C. Cosenza, S. Athuluridivakar, M. R. Mallireddigari, V. R. Pallela, V. K. Billa, D. R. C. V. Subbaiah, E. V. Bharathi, R. V. Carpio, A. Padgaonkar, S. J. Baker, E. P. Reddy, *J. Med. Chem*., **2014**, 57.

[76] J. A. Palop, D. Plano, E. Moreno, C. Sanmartín, *ARKIVOC*, **2014**, 2.

[77] K. M. Khokhani, R. M. Gol, T. T. Khatri, P. K. Patel, *Chem. Biol. Interface*., **2014**, 4..

[78] N. R. Mohamed, M. M. Abdelhalim, Y. A. Khadrawyd, G. A. Elmegeed, O. M. E. Abdel-Salam, *Steroids*, **2012**, 77.

[79] D. A. DeGoey, D. A. Betebenner, D. J. Grampovnik, D. Liu, J. K. Pratt, M. D. Tufano, W. He, P. Krishnan, T. J. Pilot-Matias, K. C. Marsh, A. Molla, D. J. Kempf, C. J. Maring, *Bioorg. Med. Chem. Lett*., **2013**, 23.

[80] N. L. Colbry, E. F. Elslager, L. M. Werbel, *J. Med. Chem*., **1985**, 28.

[81] J. B. Smaill, G. W. Rewcastle, J. A. Loo, K. D. Greis, O. H. Chan, E. L. Reyner, E. Lipka, H. D. H. Showalter, P. W. Vincent, W. L. Elliott, W. A. Denny, *J. Med. Chem*., **2000**, 43.

[82] L. Weia, S. V. Malhotra, *Med. Chem. Commun*., **2012**, 3.

[83] H. Daub, K. Specht, A. Ullrich, *Nat. Rev. Drug Discov*., **2004**, 3, 1001-1010.

[84] A. M. Mohamed, W. A. El-Sayed, M. A. Alsharari, H. R. M. Al-Qalawi, M. O. Germoush, *Arch. Pharm. Res*., **2013**, 36.

[85] S. M. Rajesh, R. S. Kumar, L. A. Libertsen, S. Perumal, P. Yogeeswari, D. Sriram, *Bioorg. Med. Chem. Lett*., **2011**, 21.

[86] B. U. Khan,. *J. Autism. Dev. Disord*., **1997**, 27.

[87] P. Molina, E. Aller, , A. Lorengo, P. L. Cremadis, I. Rioja, A. Ubeda, , M. C. Terencio, M. J. Alcaraz, *J. Med. Chem*., **2001**, 44.

[88] L. M. Oppegard, K. R. Streck, J. D. Rosen, H. A. Schwanz, K. Drlica, R. J. Kerns, H. Hiasa, *Antimicrob. Agents Chemother*., **2010**, 54.

[89] C. Jadhav, A. Nipate, A. Chate, C. Gill, *ACS Omega*. **2021**, 6.

[90] K. Yang, J. Xiang, G. Bao, Q. Dang, X. Bai, *ACS Com*. *Sci*. **2013**, 15.

[91] M. Mohssenimehra, M. Mamaghania, F. Shirinia, M. Sheykhana, F. A. Moghaddamb, *Chinese Chemical Letters*. 2014, http://dx.doi.org/10.1016/j.cclet.2014.04.025

[92] M. Adib, M. H. Sayahi, H. Ziyadi, H. R. Bijanzadehb, L. Zhuc, *Tetrahedron*, **2007**, 63.

[93] K. C. Majumdar, S. Ponra, D. Ghosh, *Synthesis*. **2011**, 7.

[94] S. Abdolmohammadi , S. Balalaie, *International Journal of Organic Chemistry*, **2012**, 2.

[95] M. Kidwai, A. Jain, S. Bhardwaj, *Mol Divers*. **2012**, 16.

[96] M. Khalaj, M. Taherkhani, M. Kalhor, *New J*. *Chem*. **2021**, 45.

[97] G. Brahmachari, I. Karmakara, K. Nurjamala, *ACS Sustainable Chem*. *Eng*.**2018**, 6.

[98] N. Hassanloie, N. N. Pesyan, G. Sheykhaghaei, *Appl .Organometal*. *Chem*. **2019**, 34.

[99] M. Seddighi, F. Shirini, M. Mamaghani, *RSC Adv*. **2013**, 3.

[100] S. Dey, P. Basak, P. Ghosh. *Chemistry Select*. **2020**, 5.

IV.13 References of Chapter IV.

[1] Y. Zhou, X. Zhang, S. Yang, Y. Li, Z. Qing, J. Zheng, J. Li, R. Yang, Anal. Chem. **2017**, 89.

[2] K. C. Fylaktakidou, D. J. Hadjipavlou-Litina, K. E. Litinas, D. N. Nicolaides, *Curr*. *Pharm*. *Des*. **2004**, 10.

[3] X. L. Hu, Z. Xu, M. L. Liu, L. S. Feng, G. D. Zhang, *Curr. Top. Med. Chem*. **2017**, 17.

[4] J. Grover, S. M. Jachak, *RSC Adv*. **2015**, 5.

[5] Y. Q. Hu, Z. Xu, S. Zhang, X. Wu, J. W. Ding, Z. S. Lv, L. S. *Feng*, *Eur. J. Med. Chem*. **2017**, 136.

[6] M. Z. Hassan, H. Osman, M. A. Ali, M. J. Ahsan, *Eur. J. Med. Chem*. **2016**, 123.

[7] A. Thakur, R. Singla, V. Jaitak, *Eur. J. Med. Chem*. **2015**, 101.

[8] E.M. Beccalli, A. Contini, P. Trimarco, *Tetrahedron Lett*. **2004**, 45.

[9] V. L. Gein, V. V. Mishunin, E. P. Tsyplyakova, O. V. Vinokurova, M. I. Vakhrin, *Pharm Chem J*. **2009**, 43.

[10] E. S. Pereyaslavskaya, V. A. Potemkin, E. V. Bartashevich, *Pharm Chem J*. **2008**, 42.

[11] H. L. Wang, C. X. Wei, X. Q. Deng, F. L. Li, Z. S. Quan, *Arch Pharm*. **2009**, 342.

[12] Xi-Cun W, Ying W, Yu-Xia D, Zhang Z, Zheng-Jun Q. Heterocycles. **2011**, 83.

[13] Z. Li-Yan , C. Chun, *J Comb Chem*. **2010**, 12, 35.

[14] V. L. Gein, L. F. Gein, E. P. Tsyplyakova, O. S. Panova. *Russ J Org Chem*. **2007**, 43.

[15] C. Raju, K. Madhaiyan, R. Uma, R. Sridhar, S. Ramakrishna. *RSC Adv*. **2012**, 2.

[16] L. Tuan-Jie, Y. Chang-Sheng, Y. Chen-Xia, W. Xiang-Shan, T. Shu-Jiang, *Synth Commun*, **2012**, 42.

[17] G. V. Ramin, T. S. Zahra, A. Mostafa, K. N. Rahman, *Mol Divers*. **2013**, 17.

[18] S. Maddila, R. Pagadala, S. B. Jonnalagadda. *Lett. Org. Chem.* 2013, 10.

[19] M. M. Ghorab, M. S. Alsaid , M. S. Al-Dosari, F.A. Ragab, A. A. Al-Mishari, A. N. Almoqbil. *Acta Pharm.* **2016**, 66.

[20] I. Briguglio, R. Loddo, E. Laurini, M. Fermeglia, S. Piras, P. Corona , P. Giunchedi, E. Gavini, G. Sanna, G. Giliberti, C. Ibba , P. Farci , P. La Colla, S. Pricl, A. Carta. *Eur. J. Med. Chem*. **2015**, 105.

[21] D. Dube, M. Bloun, C. Brideau, C. C. Chan, S. Desmarais. *Bioorg. Med. Chem. Lett*. **1998**, 8.

[22] D. Nardi , R. Pozzi, L. Degen, M. J. Magistretti. *J. Med. Chem*. **1970**, 13.

[23] X. Q. Deng, M. X. Song, Y. Zheng , Z. S. Quan. *Eur. J. Med. Chem.* **2014**, 73.

[24] A. Nayyar, A. Malde, R. Jain, E. Coutinho. *Bioorg. Med. Chem*. **2006**, 14.

[25] Meneses Santos Rde, P. R. Barros, J. H. Bortoluzzi, M. R. Meneghetti, Y. K. da Silva, A..E. da Silva, M. S. da Silva, M. S. Alexandre-Moreira. *Bioorg. Med. Chem.* **2015**, 23.

[26] F. Zare, A. Abi, R. Moosavi-Zare , M. H. Beyzavi, M. A. Zolfigol. *J. Mol. Liq,* **2013**, 178.

[27] M. R. Aly, M. M. Ibrahim, A. M. Okael, Y. A. Gherbawy. *Bioorg. Khim.* **2014**, 40.

[28] D. W. Wang, H. Y. Lin, R. J. Cao, T. Chen, F. X. Wu, G. F. Hao, Q. Chen, W. C. Yang, G. F. Yang. *J. Agric. Food* Chem. **2015**, 63.

[29] M. R. Aly, M. M. Ibrahim, A. M. Okael, Y. A. Gherbawy. *Bioorg. Khim*. **2014**, 40.

[30] M. Abaszadeh, M. Seifi, A. Asadipour. *Res. Chem. Intermed*. **2015**, 41.

[31] B. Amirheidari, M. Seifi, M. Abaszadeh. *Res. Chem. Intermed.* **2016**, 42.

[32] S. S. Mansoor, K. Aswin, K. Logaiya, P. N. Sudhan, S. Malik, *Res. Chem. Intermed*, **2014**, 40.

[33] S. R. Sarda, W. N. Jadhav, M. G. Soni, S. K. Wasmatkar, S. A. Dake, P. G. Ingole, R. P. Pawar, *Chem. Bio. Interface*, **2013**, 3.

[34] W. Xiang-Shan, S. Da-Qing, T. Shu-Jing, Synth. Commun. **2002**, 32.

[35] H. Xueyuan, Z. Xinying, F. Xuesen, Q. Guirong, L. Yanzhen, *J. Chem. Res*. **2005**, 3.

[36] E. M. Beccalli, A. Contini, P. Trimarco, *Tetrahedron Lett*. **2004**, 45.

[37] M. J. Jeon, S. S. Kim, J. K. Jeon, S. H. Park, J. M. Kim, J. M. Sohn, S. H. Lee, Y. K. Park. *Nanoscale Res. Lett.* **2012**, 7.

[38] N. Soltani, A. Bahrami, M. I. Pech-Canul, L. A. Gonzàlez, *Chem. Eng. J.* **2015**, 264.

[39] Goswami, J. D. Caldwell, *J. Appl. Phys.* **2012**, 111.

[40] A. Hantzsch, *Chem. Ber*. **1881**, 14.

[41] G. Swarnalatha, G. Prasanthi, N Sirisha, C. M Chetty, *Int. J. Chem. Tech. Res*. **2011**, 3.

[42] C. A. Kontogiorgis, D. J. H. Litina, *Bio. Med. Chem. Lett*, **2004**, 14.

[43] G. W. Rewcastle, G. J. Atwell, D. Chambers, B. C. Baguley, W. A. Denny, *J. Med. Chem*. **1986**, 29.

[44] E. A. Tanifum, A. Y. Kots, B. K. Choi, F. Murad, S. R. Gilbertson, *Bioorg. Med. Chem. Lett*. **2009**, 19.

[45] M. B. El-Ashmawy, M. A. El-Sherbeny, N. S. El-Gohary, *Med. Chem. Res*. **2013**, 22.

[46] S. Girault, P. Grellier, A. Berecibar, L. Maes, E. Mouray, P. Lemière, M.A. Debreu, E. DavioudCharvet, C. Sergheraert, *J. Med. Chem*. **2000**, 43.

[47] S. Samai, G. C. Nandi, S. Chowdhury, M. S. Singh, *Tetrahedron*, **2011**, 67.

[48] W. A. Denny, G. J. Atwell, B. C. Baguley, L. P. G. Wakelin, *J. Med. Chem*. **1985**, 28.

[49] Z. Nofal, M. El-Zahar, and A. El-Karim, *Molecules*, **2000**, 5.

[50] C. A. Kontogiorgis, D. J. Hadjipavlou-Litina, *Journal of Medicinal Chemistry*, **2005**, 48, 6400–8.

[51] T. Ojala, S. Remes, P. Haansuu, H. Vuorela, R. Hiltunen, K. Haahtela, and P. Vuorela, *Journal of Ethnopharmacology*, **2000**, 73.

[52] A. A. H. Kadhum, A. A. Al-Amiery, A. Y. Musa, A. B. Mohamad, *International Journal of Molecular Sciences*, **2011**, 12.

[53] S. Lee, K. Sivakumar, W. S. Shin, F. Xie, Q. Wang, *Bioorganic & Medicinal Chemistry Letters*, **2006**, 16.

[54] T. Nasr, S. Bondock, M. Youns, *European Journal of Medicinal Chemistry*, **2014**, 76.

[55] B. Zeynizadeh, S. Rahmani, E. Eghbali, *Polyhedron*, **2017**, 168.

[56] M. Gilanizadeh, B. Zeynizadeh, *Res Chem Intermed*, **2019**, 45.

[57] M. Kidwai, S. Kukreja, S. Rastogi, K. Singhal, N. K. Mishra, *Indian J. Chem*, **2004**, 53B.

[58] H. Saffarian, F. Karimi, M. Yarie, M. A. Zolfigol, *Journal of Molecular Structure*, **2020**, 1224,.

[59] A. Shaabani, S. Shaabani, M. Seyyedhamzeh, M. H. Sangachin, F. Hajishaabanha, *Res Chem Intermed*, **2016**, 42.

[60] D. I. Brahmbhatt, U. R. Pandya, G. B. Raolji, *Heterocyclic Communications*, **2004**, 10.

[61] M. Seddighi, F. Shirini, M. Mamaghani, *RSC Adv*. **2013**, 3.

[62] D. J. Cooonnoly, D. Cusack, T. P. O'Sullivan, P. J. Guiry, Tetrahedrom, **2005**, 61.

[63] G. S. Jedhe, D. Paul, R. G. Gonnade, M. K. Santra, E. Hamel, T. L. Nguyen, G. J. Sanjayan, *Bioorg. Med. Chem. Lett*. **2013**, 23.

[64] L. Wu, *RSC Adv*. **2015**, 5.

[65] A. M. Dougherty, H. Guo, G. Westby, Y. Liu, E. Simsek, J. T. Guo, A. Mehta, P. Norton, B. Gu, T. Block, A. Cuconati, *Antimicrob. Agents. Chemother*. **2007**, 51.

[66] S. B. Wang, X. Q. Deng, Y. Zheng, Y. P. Yuan, Z. S. Quan, L. P. Guan, *Eur. J. Med. Chem*. **2012**, 56.

[67] K. Pegklidou, C. Koukoulitsa, I. Nicolaou, V. J. Demopoulos, *Bioorg. Med. Chem*., **2010,** 18.

[68] C. G. Dave, R. D. Shah, *Molecules*. **2002**, 7.

[69] M. Hussein, O. M. Ahmed, *Bioorg. Med. Chem*. **2010**, 18.

[70] P. Verhaeghe, N. Azas, M. Gasquet, S. Hutter, C. Ducros, M. Laget, S. Rault, P. Rathelot, P. Vanelle, *Bioorganic & Medicinal Chemistry Letters*, **2008**, 18.

[71] L. F. Kuyper, D. P. Baccanari, M. L. Jones, R. N. Hunter, R. L. Tansik, S. S. Joyner, C. Boytos, S. K. Rudolph, V. Knick, H. R. Wilson, J. M. Caddell, H. S. Friedman, J. C. W. Comley, J. N. Stables, *Journal of Medicinal Chemistry*, **1996**, 39.

[72] V. Alagarsamy, V. R. Solomon, R. V. Sheorey, R. Jayakumar, *Chemical Biology & Drug Design,* **2009**, 73.

[73] H. Georgey, N. Abdel-Gawad, S. Abbas, *Molecules*, **2008**, 13.

[74] M. A. H. Ismail, S. Barker, D. A. Abau El Ella, K. A. M. Abouzid, R. A. Toubar, M. H. J. Todd, *Medicinal Chemistry*, **2006**, 49.

[75] M. S. Malamas, J. Millen, *Journal of Medicinal Chemistry*, **1991**, 34.

[76] M. Decker, European Journal of Medicinal Chemistry, **2005**, 40.

[77] D. Giardin, D. Martarelli, G. Sagratini, P. Angeli, D. Ballinari, U. Gulini, C. Melchiorre, E. Poggesi, P. Pompei, *Journal of Medicinal Chemistry*, **2009**, 52.

[78] A. Gangjee, M. Kothare, R. L. Kisliuk, *Journal of Heterocyclic Chemistry*, **2000**, 37.

[79] A. Levitzky, *Accounts of Chemical Research*, **2003**, 36.

[80] S. F. Basha, T. N. Prasad, V. B. Gudise, V. S. Kumar, N. Mulakayala, S. Anwar, An efficient, multicomponent, green protocol to access 4, 7-dihydrotetrazolo [1,5-a] pyrimidines and 5,6,7,9-tetrahydrotetrazolo[5,1-b]quinazolin-8(4H)-ones using PEG-400 under microwave irradiation, Synthetic Communications, DOI: 10.1080/00397911.2019.1659973.

[81] S. F. Basha, T. N. Prasad, V. B. Gudise, V. S. Kumar, N. Mulakayala, S. Anwar, An efficient, multicomponent, green protocol to access 4, 7-dihydrotetrazolo [1,5-a] pyrimidines and 5,6,7,9-

tetrahydrotetrazolo[5,1-b]quinazolin-8(4H)-ones using PEG-400 under microwave irradiation, Synthetic Communications, DOI: 10.1080/00397911.2019.1659973

[82] R. Ghorbani-Vaghei, S. Alavinia, N. Sarmast, *Appl Organometal Chem*. 2017;e4038. DOI: https://doi.org/10.1002/aoc.4038.

[83] C. Raju, K. Madhaiyan, R. Uma, R. Sridhar, S. Ramakrishnab, *RSC Advances*, **2012**, 2.

[84] L. Zeng, C. Cai, *J. Comb. Chem*. **2010**, 12.

[85] L. Zeng, C. Cai, *J. Comb. Chem*. **2010**, 12.

[86] A. Hassankhani, B. Gholipour, S. Rostamnia, E. Zarenezhad, N. Nouruzi, T. Kavetskyy, R. Khalilov, M. Shokouhimeh, *Appl Organomet Chem*. **2021**, 35.

[87] P. Kour, V. P. Singh, B. Khajuria, T. Singh, A. Kumar, *Tetrahedron Letters*, **2017**, 58.

[88] R. A. Janis, P. J. Silver, G. J. Triggle, Adv. Drug Res. **1987**, 16.

[89] B. Gabriele, R. Mancuso, G. Salerno, G. Ruffolo, P. Plastina, J. Org. Chem. **2007**, 72.

[90] G. Roma, M. D. Braccio, G. Grossi, F. Mattioli, M. Ghia, Eur. J. Med. Chem. **2000**, 35.

[91] D. Doube, M. Blouin, C. Brideau, C. Chan, S. Desmarais, D. Eithier, J. P. Falgueyret, R. W. Friesen, M. Girrard, Y. Girard, J. Guay, P. Tagari, R. N. Young, *Bioorg. Med. Chem. Lett*. **1998**, 8.

[92] R. D. Larsen, E. G. Corley, A. O. King, J. D. Carroll, P. Davis, T. R. Verhoeven, P. J. Reider, M. Labelle, J. Y. Gauthier, Y. B. Xiang, R. J. Zamboni, *J. Org. Chem*. **1996**, 61.

[93] M. P. Maguire, K. R. Sheets, K. McVety, A. P. Spada, A. Zilberstein, *J. Med. Chem.* **1994**, 37.

[94] A. Zarghia, I. Sabakhib, V. Topuzyanc, Z. Hajimahdid, B. Daraie, *Ijpr*, **2014**, 13.

[95] S. Ray , M. Brown, A. Bhaumik, A. Dutta, C. Mukhopadhyay, *Green Chem*., **2013**,15.

[96] S. Wang , S. Guo, M. Gao, J. Li, Y. Duan, *E-Journal of Chemistry*., **2006**, 3.

[97] X. Hua, X. Zhanga, X. Fana, G. Qu, Y. Li, *Journal of Chemical Research* **2005**.

[98] S. Tu, S. Yan, X. Cao, S. Wu, X. Zhang, W. Hao, Z. Han, F. Shi, *Journal of Organometallic Chemistry*, **2009**, 694.

[99] Z. Karimi-Jaberi, M. Azadi, *Res Chem Intermed.*, **2015**, 41.

[100] X. Wang, D. Shi, S. Tu, *Synthetic Communications*, **2002**, 32.

[101] J. Safari, S. H. Banitaba, S. D. Khalili, *Chin. J. Catal*., **2011**, 32.

[102] S. Dey, P. Basak, P. Ghosh. *ChemistrySelect*, **2020**, 5.

Index

Catalysis

A Green Synthetic Approach Towards One Pot Multi Component Synthesis of Hexahydroquinoline and 9-Arylhexahydroacridine-1,8-dione Derivatives Catalyzed by Sulphonated Rice Husk

Sourav Dey, Puja Basak, and Pranab Ghosh*[a]

An efficient, straight forward, eco-friendly procedure for the synthesis of biologically active hexahydroquinoline derivatives and hexahydroacridine-1,8-diones has been designed using a novel bio-degradable heterogeneous catalyst, sulphonated rice-husk (SRH). SRH provides high density of acid groups making it different from conventional solid acids containing single acid groups. We report an efficient protocol for the synthesis of hexahydroquinolines and hexahydroacridine-1,8-diones using this carbon based acid catalyst (SRH) in solvent free and greener solvent respectively. Moreover, operational simplicity, greener reaction condition, reusability of the catalyst, excellent yield (upto 98%) are the fundamental features of this protocol. The metal free catalyst was characterised using different spectroscopic techniques FTIR, SEM, EDX, Powder XRD, ICP-AES.

1. Introduction

Over the past decade, green chemistry has emerged as an important environmental aspect to reduce the use of toxic and hazardous reagents in synthetic and industrial chemistry. In recent years industrial usage of agricultural wastage has received much interest due to economical and environmental reasons. Rice husk is a major agricultural by-product in south Asian countries that can be a promising feedstock of industrial use.[1,2] Rice husk (RH) contains cellulose, hemicelluloses, lignin, ash like other lignocellulosic material and the features like high silica content, high porosity, light weight and high external surface area turn it a good catalyst support for many industrial synthesis [3,4]. The use of eco-friendly catalysts and selected green solvents are of being promising demand in recent years for the synthesis of organic compounds.[5] In terms of green chemistry, the development of efficient multi-component reactions (MCRs) has attracted much consideration regarding the use of heterogeneous catalyst.[2–3] One-pot MCRs are energy saving processes that eliminates the multiple steps and increases the productivity with high level of structural diversity.[5–10] MCRs are convergent in nature and an important toolbox of green chemistry to synthesize different biologically active heterocyclic compounds. A large variety of MCRs are catalyzed by homogeneous and heterogeneous acid catalyst. However, solid acid catalyst have gained attention due to their heterogeneous nature and are favoured over homogeneous one as they can be easily separated from the reaction system.

Quinolines are ubiquitous in nature and they represent a wide variety of pharmaceutical (Figure 1and agrochemical products.[11] Substituted quinolines exhibit diverse biological activities and they are found to be major building blocks in various natural products.[12] Quinoline posseses considerable interest due to their biological activity including antibacterial, antifungal, antioxidant, anticancer, anticonvulsant, and antiviral activity.[12–16] Substituted quinolines and tetrahydroquinolines (THQ) are a class of heterocycles that serve as chemotherapeutic agents also.[17–19] Many heterocyclic,[25] compounds containing the quinoline nucleus display anti-inflammatory activity and they serve as antagonist inhibitors.[20]

Many heterocyclic,[25] compounds containing the quinoline nucleus display anti-inflammatory activity and they serve as antagonist inhibitors.[20] Quinolines with 1,4-Dihydropyridine (DHP) nucleus have been found efficient in cardiovascular diseases as calcium channel blockers.[21,22] Along with these, this heterocyclic moiety have vast application in agricultural field also.[23] Many recent research works are carried on this unique heterocyclic motif due to its diverse biological activity.[24–25]

Several homogeneous and heterogeneous catalysts have been employed for the synthesis of substituted hexahydroquinolines derivatives. Among them, the synthesis using nano-ZnO/ultrasound nano-Fe_3O_4,[26] AcOH,[27] K_2CO_3,[28] triethylamine,[29] $Fe_{3-x}Ti_xO_4$@SPDETATSA (N-(3-silyl propyl) diethylene triamine N,N′,N″-tri-sulfonic acid immobilized on $Fe_{3-x}Ti_xO_4$magnetic nanoparticles[30] are noteworthy to mention. Acridine derivatives containing keto functional groups are found to be good anti-malarial agents and substituted hexahydroacridine-1,8-dione being resemble to dihydropyridine molecule can act as a K-channel openers in urinary-bladder smooth muscle.[31,32] These acridinediones were also

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found to act as laser dyes due to electron delocalization and exhibit fluorescence and laser activity.[33,34] The effectiveness of lasing is dependent upon the substituents at C-9 and N-10 of the acridine chromophore. Apart from the above applications, acridinediones also possess other important photo-physical and electrochemical properties.[35] Acridine dyes can bind with photo damaged nucleic acids which have increasing interest as mutagens in micro-organisms.[36] The usefulness of acridines have led to the development of numerous methods of their synthesis by the three component Hantzsch condensation of aldehydes with β-diketones and ammonium acetate or appropriate primary amines. Many procedures describe the synthesis of acridinedione derivatives by cyclocondensation between dimedone and aldehyde and primary amine in the presence of heat in organic solvents with a varity of catalysts such as Fe_3O_4@B-MCM-41,[37] SO_4 2/TiO_2NPs,[38] Scolecite,[39] Pd nanoparticle,[40] MNPsN-propyl-benzoguanamine-SO_3H,[41] silica bonded N-propyl sulfamic acid[42], CH_3SO_3H,[43] tetrabutylammonium hexatungstate,[44] nano TiO_2,[45] $SiO_2/ZnCl_2$,[46] protic pyridinium ionic liquid,[47] $CsCO_3$,[48] ceric ammonium nitrate,[49] organocatalysts,[50] Ni nanoparticles,[51] MgO,[52] thiamine hydrochloride,[53] SnO_2,[54] La_2O_3/TFE (2,2,2-trifluoroethanol),[55] $Cd(NO_3)_2$.$4H_2O$.[56] However, many protocols suffer from some limitations such as harsh reaction conditions, costly and non recyclable catalyst, and tedious purification, use of toxic reagents and generation of hazardous wastes. By eliminating the drawbacks of previous methods, it is important to find out new greener protocols for the synthesis of substituted quinolines and hexahydroacridine-1,8-dione. Eco-friendly heterogeneous solid acid catalysts have gained much attention over homogeneous catalysts owing to its easy separation process. Amongst them carbon-based sulphonated catalysts are most promising because of the presence of different acidic functional groups and large carbon framework. Owing to the low price and simple preparation, biomass waste (RH) is extensively used in several field as mentioned above. With increasing demand in green chemistry, the use of heterogeneous solid acid catalyst has attracted the researchers regarding environmental issues. An ideal solid acid catalyst should be the one which have excellent stability, high porosity, active acidic sites, low cost and hydrophobic surfaces. Among them carbon-based acidic catalysts are most promising as they can be extensively prepared from biomass material (RH). However, RH based alkaline catalyst and solid acid catalyst under MW irradiation has been reported previously.[57,58] Herein, we report a conventional heating technique for the preparation of sulphonated RH (SRH) and characterisation as well. We report the use of this novel green catalyst SRH for feasible synthesis of hexahydroquinoline and hexahydroacridine-1,8-diones derivatives in one-pot strategy.)

2. Results and discussion

The prepared catalyst was characterised by FTIR spectroscopy, scanning electron microscopy (SEM), powder X-ray diffraction (XRD) and ICP-AES for quantifying weight percentage of sulphur and other elements. The comparison of FTIR, SEM image and XRD pattern of RH and SRH strongly supports the synthesis of the sulphonated catalyst through a completely new method. The comparison of SEM images of RH and SRH shows that a molecular aggregation occurs in SRH resulted from the incorporation of $-SO_3H$ functional group into the skeleton of rice husk material (Figure 2). EDX analysis of sulphonated rice husk and rice husk showed a measurable difference in the weight percentage of the elements especially carbon, slicon, sulphur and oxygen (Figure 2).

The newly appearing band with a peak 1098 cm^{-1} represents the symmetric and asymmetric streatching of S=O bonds of $-SO_3H$ (sulphonic acid).The the new broad band at 3342 cm^{-1} along with the band at 1098 cm^{-1} both confirmly denoting the incorporation of $-SO_3H$ groups in SRH after sulphonation of rice husk (Figure 3). The powder XRD analysis shows characteristics peaks at $2\theta = 20.82°$, 22.28°, 26.67° in which a broad peak at around 20° is due to the carbon composed aromatic sheets which are oriented in a random manner (Figure 4).[58]

ICP-AES analysis showed that weight percentage sulphur is 1% to that of total weight of all the elements present. To make surety in broad aspect all the results and graphs were thoroughly viewd and compared with other sulphonated materials such as sulphonated rice husk ash,[59] CBSC (carbon-based sulphonated catalyst)[57] which confirmly showed that SRH was morphologically and compositionally different from those reported sulphonated catalysts. Detailed informations are attached into the supporting information for further support.

Initially, the reaction was first started with benzaldehyde (1 mmol), malononitrile (1 mmol), ammonium acetate (1.2 mmol) and 5,5-dimethylecyclohex-1,3-dione (1 mmol) were

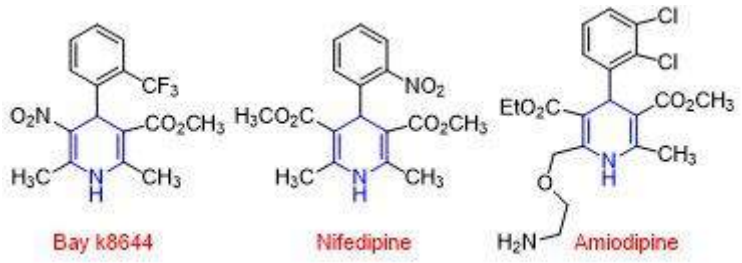

Figure 1. Some examples of biologically active drugs.

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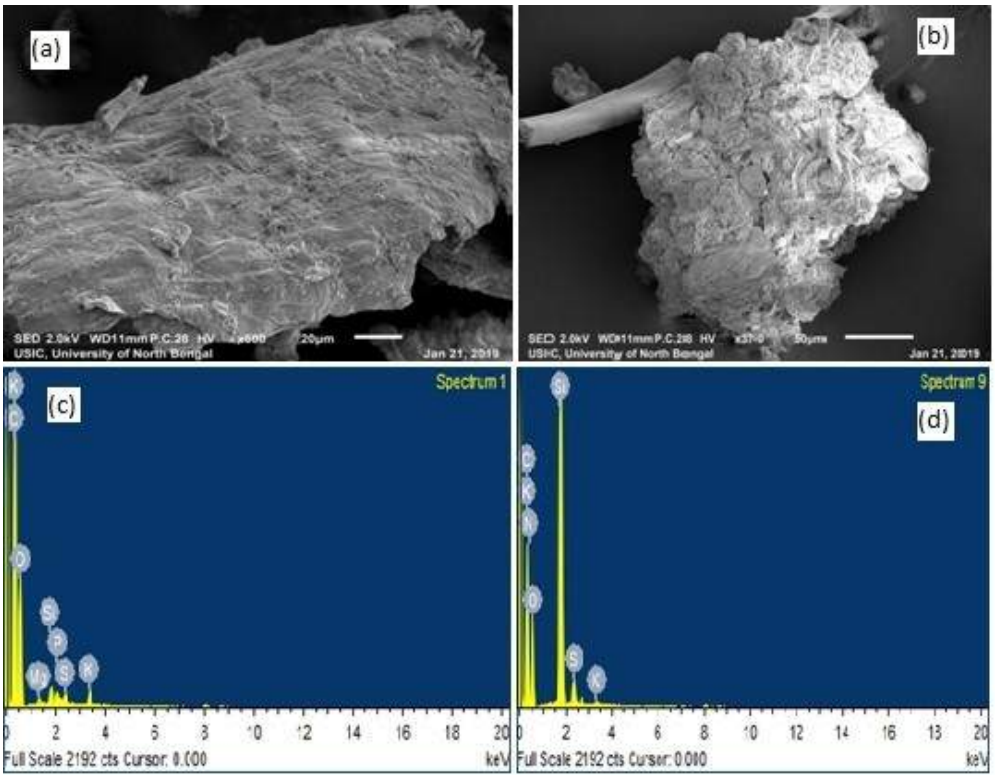

Figure 2. (a) SEM image of rice husk(RH) (b) SEM image of sulphonatrice husk (SRH) (c)EDX of RH (d) EDX of SRH.

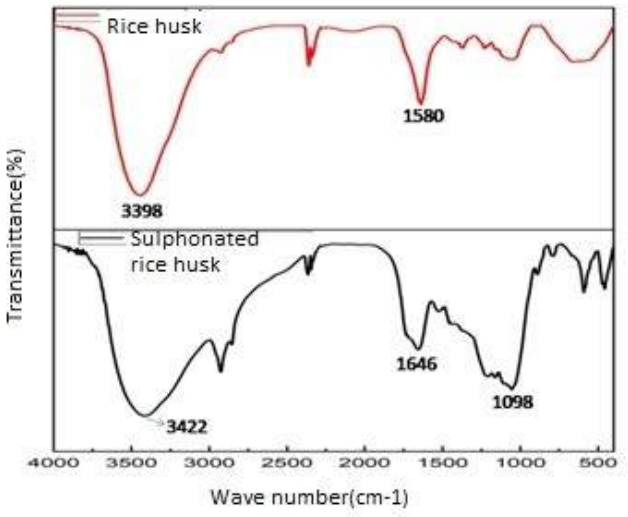

Figure 3. FTIR of RH and SRH.

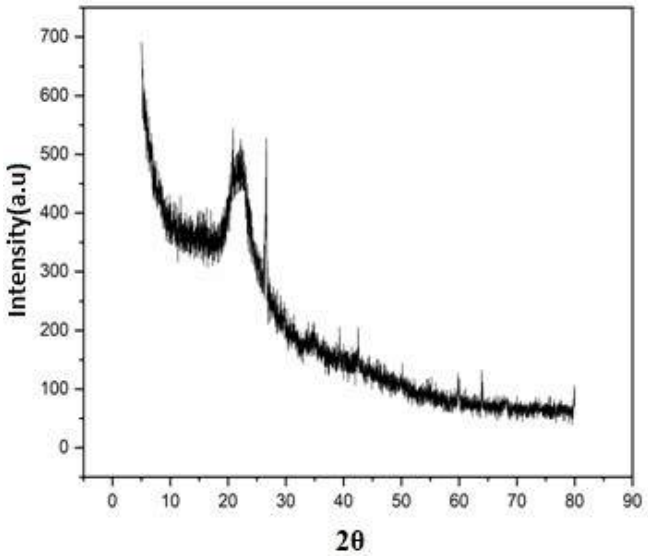

Figure 4. Powder XRD plot of SRH.

taken in a 25 mL RB with 100 mg of catalyst. For screening the reaction p-tolualdehyde (0.5 mmol), ammonium acetate (0.8 mmol) and 5,5-dimethylecyclohex-1,3-dione (1 mmol) were taken in a 25 mL RB.. However, in absence of catalyst the formation of the corresponding product was diminished (Table 1,entry 10). Excellent yield was observed in presence of 100 mg of SRH catalyst in ethanol solvent at 80 °C temperature (Table 1, entry 1).With decreasing the amount of catalyst, the yield of the product decreases slightly in ethanol. From the optimized condition it is clear that SRH catalyst is proved to be suitable for the conversion of hexahydroquinoline with excellent yield in short reaction time. The amount of the catalyst and time of the reaction was further checked to find out the optimized condition of the reaction. It was observed that the best result was obtained at 70 °C temperature using 60 mg of

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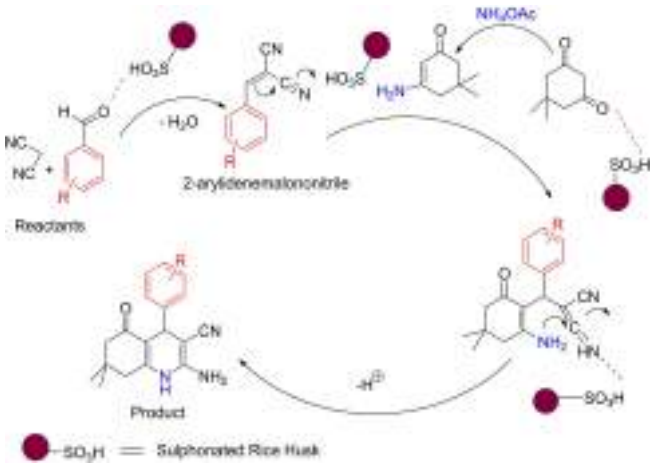

Figure 5. The plausible mechanism for the synthesis of hexahydroquinoline.

Table 1. Optimisation of the reaction condition for the synthesis of substituted 5-oxo-1,4,5,6,7,8-hexahydroquinolines.[a]

Entry	Catalyst (mg)	Solvent	Temperature (°C)	Time (min)	Yield (%)[b]
1	100	Ethanol	80	40	96
2	80	Ethanol	80	30	96
3	70	Ethanol	80	30	94
4	50	Ethanol	80	30	85
5	40	Ethanol	80	30	78
6	40	Ethanol	100	30	80
7	30	Neat	50	120	80
8	30	Neat	50	90	70
9	20	Neat	60	60	64
10	None	Neat	80	120	30
11	80	Neat	70	40	96
12	80	Neat	70	30	96
13	60	Neat	70	20	96
14	60	Neat	60	20	92
15	80	Methanol	80	30	94

[a] Reaction of p-toluealdehyde (1mmol), malononitrile (1mmol), 5,5-dimethyl-cyclohexane-1,3-dione (1mmol), ammonium acetate (1.2 mmol), [b] tableIsolated yield after purification through column chromatography.

catalyst SRH under neat reaction contion (Table 1, entry 13). The effectiveness of SRH over other acid catalyst was established as it requires very short reaction time under solvent free condition and easily seperable from the reaction mixture (Table 2, entry 11). The progress of the reaction was monitored by thin layer chromatography (TLC) and the pure product was separated by column chromatography with petroleum ether/ethyl acetate (v/v ratio70/30) mixture. Role of methanol has also been observed(table 1,entry 15) showing that product yield is quite closer to that of ethanol but methanol is considered as toxic alcohol so it should be avoided in greener aspect of reaction. From the optimized condition it is clear that SRH catalyst is proved to be suitable for the conversion of hexahydroquinoline with excellent yield in short reaction time. The amount of the catalyst and time of the reaction was further checked to find out the optimized condition of the reaction. It was observed that the best result was obtained at 70 °C

Table 2. Comparison of efficiency of the catalyst for the synthesis of substituted 5-oxo-1,4,5,6,7,8-hexahydroquinolines.[a]

Entry	Catalyst	Solvent	Temperature (°C)	Time (min)	Yield (%)[b]
1	PTSA(60mg)	Ethanol	80	30	93
2	PEG-400(5mL)	–	80	40	80
3	PEG-200(5mL)	–	80	60	70
4	Glycerol (5mL)	–	80	60	72
5	H_2SO_4 (5mL)	Ethanol	70	30	85
6	AcOH (5mL)	–	80	30	80
7	$HClO_4$ (5mL)	–	70	30	90
8	K_2CO_3 (60mg)	Neat	80	30	94
9	Et_3N(5mL)	–	80	30	95
10	Fe_3O_4 (60 mg)	Neat	80	30	91
11	SRH (60mg)	Neat	70	20	96

[a] Reaction of p-toluealdehyde (1mmol), malononitrile (1mmol), 5,5-dimethyl-cyclohexane-1,3-dione (1mmol), ammonium acetate (1.2 mmol), [b] Isolated yield after purification through column chromatography.

temperature using 60 mg of catalyst SRH under neat reaction contion (Table 1, entry 13). Few controlled experiments were carried out to compare our prepared catalyst (SRH) with some conventional solid and liquid acid catalyst (Table 2). It was observed from the results that most of the acid catalyst showed good activity in ethanol solvent. However, some base catalyst was also employed and they exerted the corresponding product with high yield in 30 minutes (Table 2, entry 8–9). The effectiveness of SRH over other acid catalyst was established as it requires very short reaction time under solvent free condition and easily seperable from the reaction mixture (Table 2, entry 11). The progress of the reaction was monitored by thin layer chromatography (TLC) and the pure product was separated by column chromatography with petroleum ether/ethyl acetate (v/v ratio70/30) mixture.

The generality of the reaction was also observed with a variety of aromatic and heterocyclic aldehydes (Scheme 1). There is no significant difference in the yield of the desired product with electron donating and electron withdrawing substituents at *ortho*, *meta* and *para* position of the aromatic aldehyde. The target compounds (5a–5q) are successively synthesized using SRH as efficient catalyst under neat reaction condition and short reaction time.

2.1. Mechanism

A plausible SRH catalyzed synthesis of hexahydroquinoline is established by considering the acidic behaviour of the catalyst (Figure5). At very first step of the reaction, protonation occurs at aldehyde oxygen of aromatic aldehyde followed by the Knoevenagel condensation of malononitrile and aromatic aldehyde. After that, Michael addition reaction occurs between 5,5-dimethylecyclohex-1,3-dione and 2-arylidenemalononitrile, resulting a intermediate. However, this intermediate rapidly

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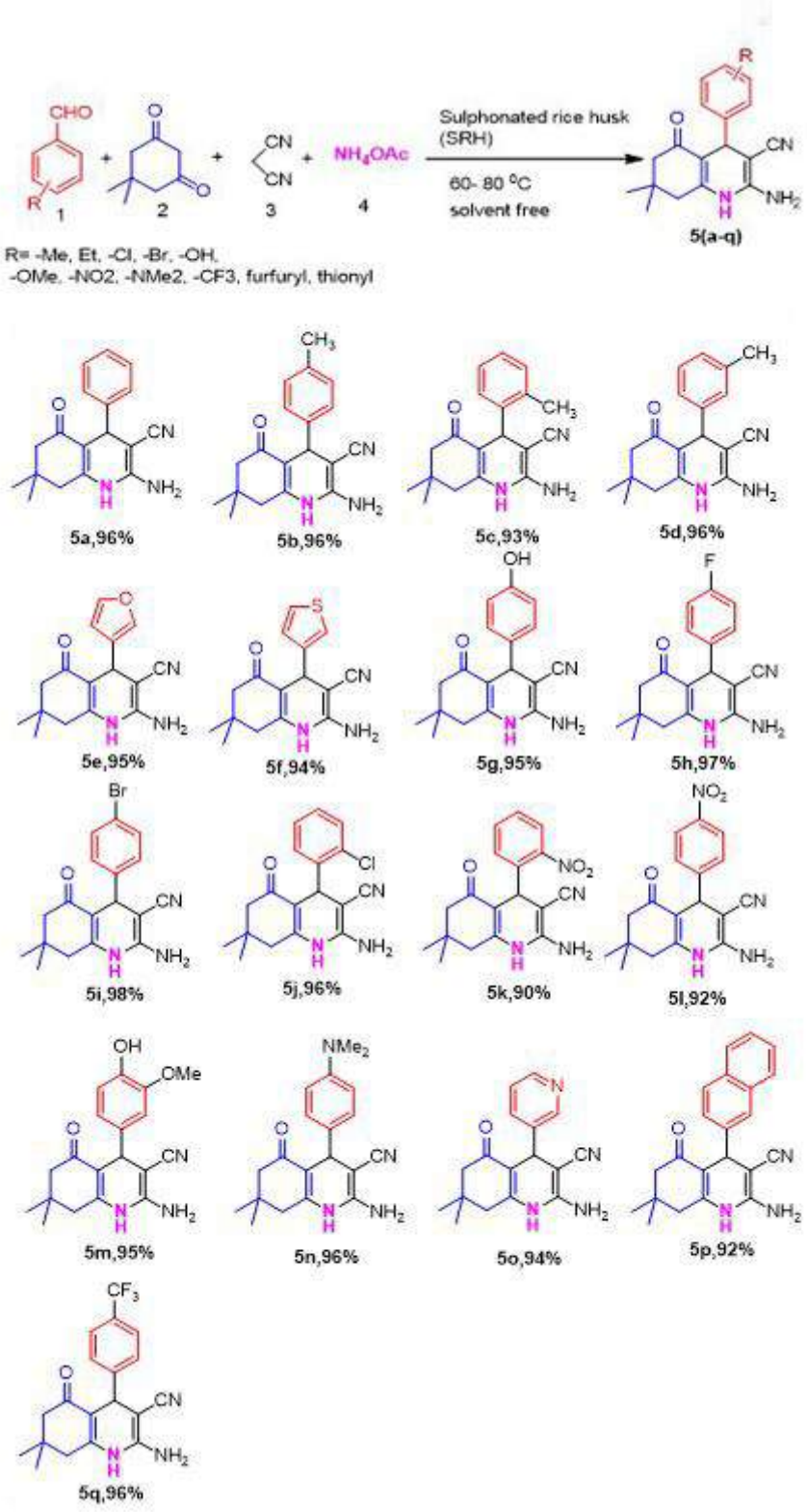

Scheme 1. Synthesis of substituted 5-oxo-1,4,5,6,7,8-hexahydroquinoline derivatives using sulphonated rice husk[a] [a] Reaction of aromatic aldehyde (1mmol), malononitrile (1mmol), 5,5-dimethyl-cyclohexane-1,3-dione (1mmol), ammonium acetate (1.2 mmol) and SRH (60 mg). The yields are isolated through column chromatography.

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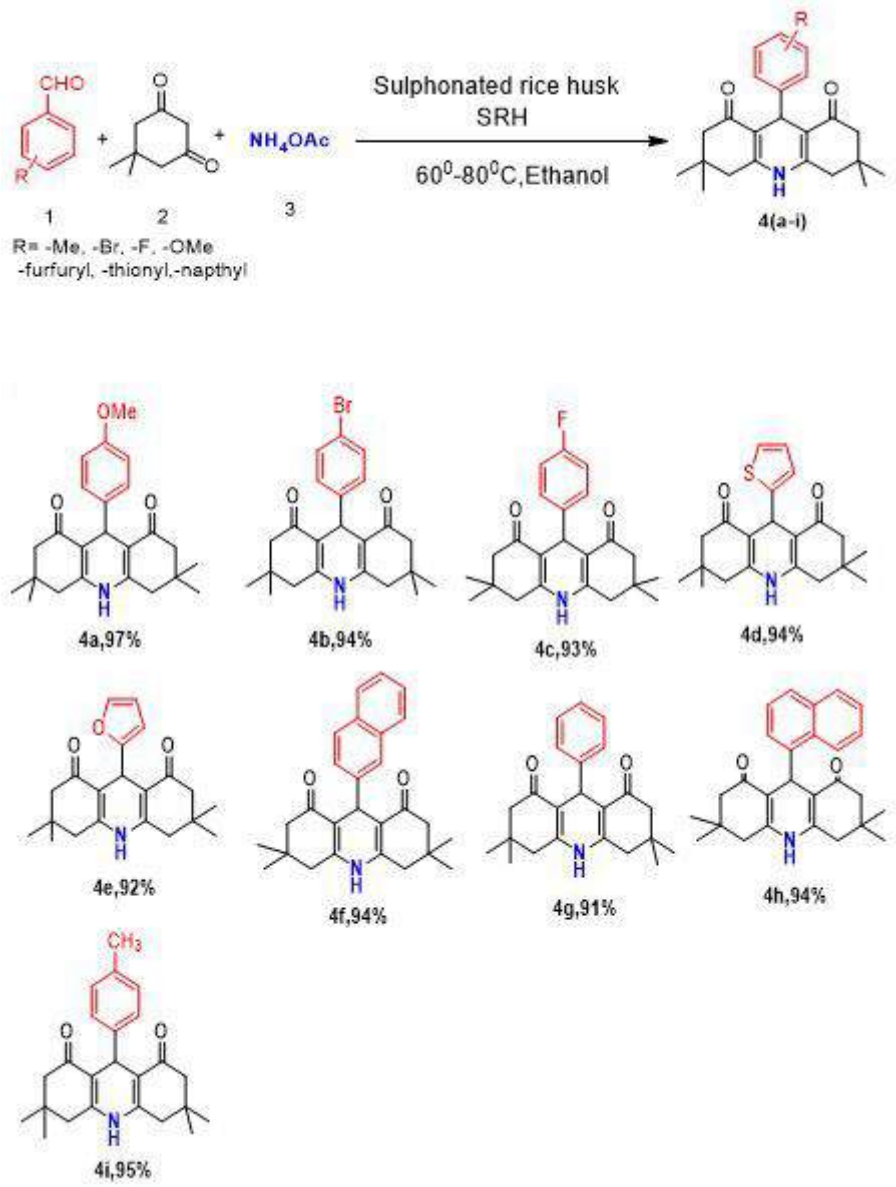

Scheme 2. Synthesis of substituted 9-arylhexahydroacridine-1,8-dione derivatives using sulphonated rice husk[a] [a] Reaction of aromatic aldehyde (1mmol), 5,5-dimethyl-cyclohexane-1,3-dione (2mmol), ammonium acetate (1.2 mmol) and SRH (50 mg). The yields are isolated through recrystalisation.

undergoes in cyclization and exters the target hexahydroquinoline product.

First, the reaction was started with Anisaldehyde (1 mmol), ammonium acetate (1.2 mmol) and 5,5-dimethylecyclohex-1,3-dione (2 mmol) and the catalyst (SRH) in a 25 mL RB. Optimisation reaction was carried out with taking anisaldehyde and excellent yield was observed in presence of 40 mg of SRH catalyst in ethanol solvent at 60 °C temperature (Table 3, entry 7) with reaction time of 50 minutes. With decreasing the amount of catalyst, the yield of the product decreases slightly in ethanol. However, in absence of catalyst the formation of the product was diminished (Table 3, entry 13). The performance of the reaction is almost similar in methanol solvent but for greener aspect ethanol is is considered as more safer solvent than methanol to get the maximum yield. (Table3, entry 7 & 8). From the optimized condition it is clear that SRH catalyst is proved to be suitable for the conversion of hexahydroacridine-1,8-dione with excellent yield in short reaction time. The amount of the catalyst and time of the reaction was checked to find out the optimized condition of the reaction. It was observed that the best result was obtained at 60 °C temperature using minimum amount of catalyst SRH (40 mg) in ethanol (Table 3, entry 7).The progress of the reaction was monitored continuously by thin layer chromatography (TLC) and the pure product was separated only by recrystalisation procedure in ethyl acetate and petroleum ether (1 : 1)

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Table 3. Optimisation of the reaction condition for the synthesis of hexahydroacridine-1,8-dione [a]

Entry	Catalyst (mg)	Solvent	Temperature (°C)	Time (min)	Yield (%)[b]
1	90	Ethanol	80	120	97
2	80	Ethanol	80	90	97
3	70	Ethanol	80	70	97
4	60	Ethanol	80	60	97
5	50	Ethanol	70	60	95
6	40	Ethanol	70	60	95
7	40	Ethanol	60	50	95
8	40	methanol	60	60	94
9	40	Neat	60	50	84
10	40	Neat	80	90	86
11	40	Ethanol/H_2O (3:1)	70	60	62
12	40	Methanol/H_2O (3:1)	70	60	58
13	None	Ethanol	70	120	20

[a] Reaction of anisaldehyde (1mmol), 5,5-dimethyl-cyclohexane-1,3-dione (2mmol), ammonium acetate (1.2 mmol). [b] Isolated yield after purification through recrystalisation procedure.

2.2. Mechanism

A plausible SRH catalyzed synthesis of hexahydroacridine-1,8-dione are established considering the acidic behaviour of the catalyst (Figure 6). At very first step of the reaction, protonation occurs at aldehyde oxygen of aromatic aldehyde followed by Hantzsch condensation of aldehydes with β-diketones and ammonium acetate. Intermediates are produced in situ rapidly undergo cyclization and exters the targeted hexahydroacridine-1,8-dione product.

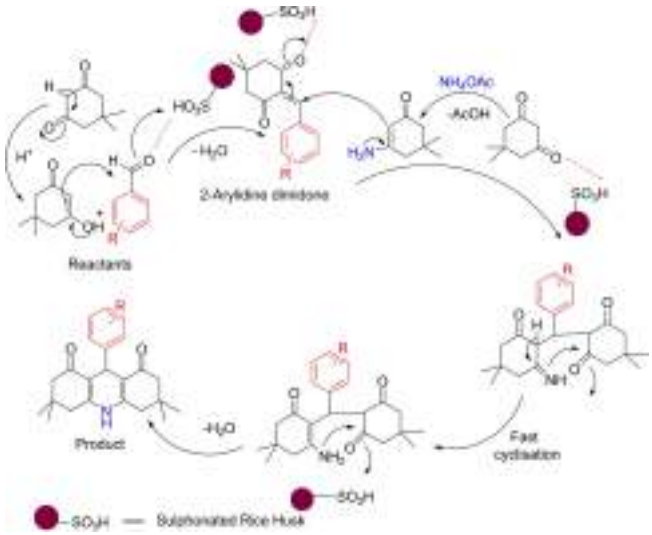

Figure 6. The plausible mechanism for the synthesis of hexahydroacridine-1,8-dione.

2.3. Catalyst Recyclability Experiment

To check the recyclability of the catalyst, a model reaction between benzaldehyde(1.6 mmol), malononitrile(1.6 mmol), ammonium acetate(1.92 mmol) and 5,5-dimethylecyclohex-1,3-dione(1 mmol) in presence of 100 mg of sulphonated rice husk was carried out under optimised reaction condition. After successful completion of the each reaction step, ethyl acetate (10 ml) and water was added to the reaction mixture. The supernatant liquid (ethyl acetate extract) was decanted off and this process was repeated thrice. The catalyst was then filtered and washed with water and acetone repeatedly and dried under vaccum. The recovered catalyst weight was measured after every recovery step and the next reaction was repeated in required proportion of the reactants to that of weight of the recovered catalyst. The temperature and time of the reaction were kept constant in this regard. Amount of catalyst, aldehyde, reaction time,temperature and yield percentage of the product have been shown in table 4 (entry 1–7) The catalyst can easily be separated from the reaction mixture by simple filtration and was found to retain its acidic property, even after 7th run (Figure 8). This was further supported by comparing the FTIR spectra of fresh SRH catalyst and recovered catalyst after successive reactions (Figure 7).

3. Conclusion

In conclusion, a simple and greener methodology for the synthesis of variety of hexahydroquinolines and hexahydroacridine-1,8-dione from commercially available aldehydes has been established. We have introduced a new cheap and green heterogeneous catalyst SRH (Sulphonated rice husk) for the synthesis of substituted 5-oxo-1,4,5,6,7,8-hexahydroquinoline and 9-Arylhexahydroacridine-1,8-dione derivatives with excellent yield. This heterogeneous catalyst is found to be highly efficient for the synthesis of hexahydroquinoline and hexahydroacridine-1,8-dione in short reaction time. The catalyst is highly recyclable upto 7th run and has profound effect to catalyze a wide range of acid-catalysed reactions.

Table 4. Table for the amount of recovered catatyst with isolated product yield[a]

Entry	Catalyst (mg)	Aldehyde (x mmol)	Temperature (°C)	Time (min)	Yield (%)[b]
1	100	1.6 mmol	70	20	96
2	80	1.3 mmol	70	20	94
3	60	1.0 mmol	70	20	90
4	50	0.8 mmol	70	20	87
5	40	0.6 mmol	70	20	82
6	30	0.5 mmol	70	20	76
7	20	0.3 mmol	70	20	71

[a] Reaction of benzaldehyde (x mmol), malononitrile (x mmol), 5,5-dimethyl-cyclohexane-1,3-dione (2x mmol), ammonium acetate (1.2x mmol), [b] Isolated yield after purification through recrystalisation.

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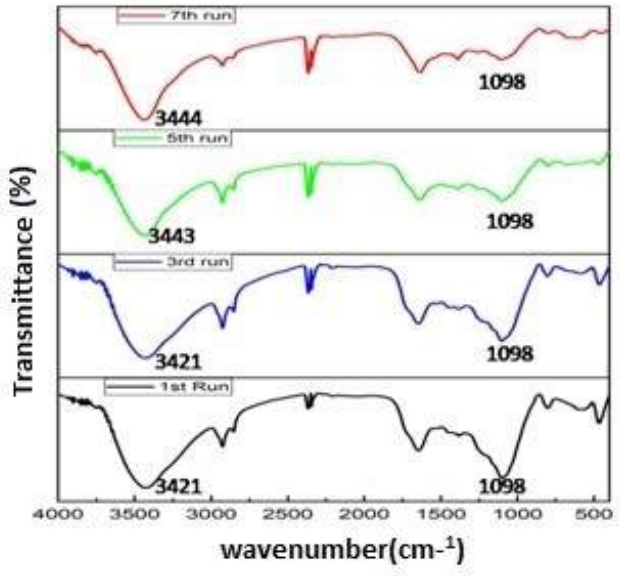

Figure 7. FTIR spectra of reused catalysts after 1st, 3rd, 5th and 7th run.

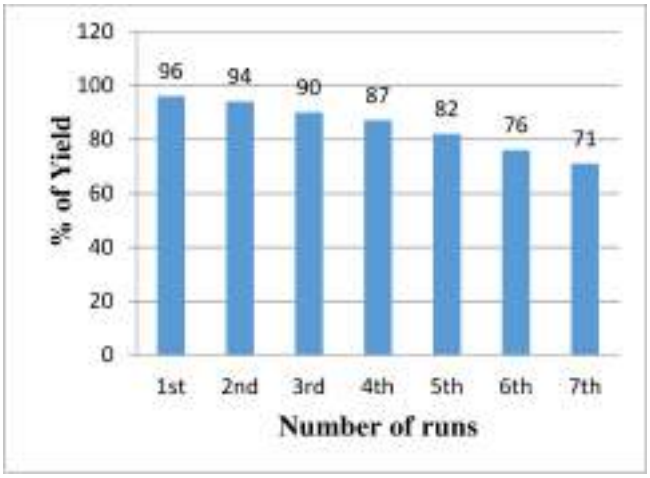

Figure 8. Recyclability experiment.

Supporting Inforamation Summary

Supporting information data are provided in electronic supporting information include experimental details, ^{1}H NMR, ^{13}C NMR spectra of all the synthesized compounds (5a-5p), (4a-4h) and EDX & ICP-AES data of the prepared catalyst.

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Conflict of Interest

The authors declare no conflict of interest.

Keywords: Sulphonated rice husk · Greener catalyst · Hexahydroquinoline · hexahydroacridine-1,8-diones · Multicomponent reaction

[1] N. Soltani, A. Bahrami, M. I. Pech-Canul, L. A. Gonzàlez, *Chem. Eng. J.* **2015**, *264*, 899–935.
[2] M. J. Jeon, S. S. Kim, J. K. Jeon, S. H. Park, J. M. Kim, J. M. Sohn, S. H. Lee, Y. K. Park, *Nanoscale Res. Lett.* **2012**, *7*, 18.
[3] S. B. Qadri, M. A. Imam, A. W. Fliflet, B. B. Rath, R. Goswami, J. D. Caldwell, *J. Appl. Phys.* **2012**, *111*, 1–5.
[4] L. Wang, X. Wang, B. Zou, X. Ma, Y. Qu, C. Rong, Y. Li, Y. Su, Z. Wang, *Bioresour. Technol.* **2011**, *102*, 8220–8224.
[5] A. Loupy, *C. R. Chim.* **2004**, *7*, 103–112.
[6] D. D. Someshwar, G. P. Vedavati, T. J. Yeon, *Tetrahedron Lett.* **2012**, *53*, 4376–4380.
[7] R. B. NasirBaig, R. S. Varma, *Green Chem.* **2013**, *15*, 1839–1843.
[8] S. Maddila, K. K. Gangu, S. N. Maddila, S. B. Jonnalagadda, *Mol. Diversity* **2017**, *21*, 247–255.
[9] S. N. Maddila, S. Maddila, W. E. Van Zyl, S. B. Jonnalagadda, *Res. Chem. Intermed.* **2016**, *42*, 2553–2566.
[10] S. N. Maddila, S. Maddila, W. E. Van Zyl, S. B. Jonnalagadda, *Curr. Org. Chem.* **2016**, *20*, 2125–2133.
[11] V. Polshettiwar, R. S. Varma, *Chem. Soc. Rev.* **2008**, *37*, 1546–1557.
[12] S. Maddila, R. Pagadala, S. B. Jonnalagadda, *Lett. Org. Chem.* **2013**, *10*, 693–714.
[13] M. M. Ghorab, M. S. Alsaid, M. S. Al-Dosari, F. A. Ragab, A. A. Al-Mishari, A. N. Almoqbil, *Acta Pharm.* **2016**, *66*, 155–171.
[14] X. Q. Deng, M. X. Song, Y. Zheng, Z. S. Quan, *Eur. J. Med. Chem.* **2014**, *73*, 217–224.
[15] I. Briguglio, R. Loddo, E. Laurini, M. Fermeglia, S. Piras, P. Corona, P. Giunchedi, E. Gavini, G. Sanna, G. Giliberti, C. Ibba, P. Farci, P. La Colla, S. Pricl, A. Carta, *Eur. J. Med. Chem.* **2015**, *105*, 63–79.
[16] D. Nardi, R. Pozzi, L. Degen, M. J. Magistretti, *J. Med. Chem.* **1970**, *13*, 380–383.
[17] D. Dube, M. Bloun, C. Brideau, C. C. Chan, S. Desmarais, *Bioorg. Med. Chem. Lett.* **1998**, *8*, 1255–1260.
[18] A. Nayyar, A. Malde, R. Jain, E. Coutinho, *Bioorg. Med. Chem.* **2006**, *14*, 847–856.
[19] Meneses Santos Rde, P. R. Barros, J. H. Bortoluzzi, M. R. Meneghetti, Y. K. da Silva, A. E. da Silva, M. S. da Silva, M. S. Alexandre-Moreira, *Bioorg. Med. Chem.* **2015**, *23*, 4390.
[20] F. Zare, A. Abi, R. Moosavi-Zare, M. H. Beyzavi, M. A. Zolfigol, *J. Mol. Liq.* **2013**, *178*, 113.
[21] M. R. Aly, M. M. Ibrahim, A. M. Okael, Y. A. Gherbawy, *Bioorg. Khim.* **2014**, *40*, 234.
[22] D. W. Wang, H. Y. Lin, R. J. Cao, T. Chen, F. X. Wu, G. F. Hao, Q. Chen, W. C. Yang, G. F. Yang, *J. Agric. Food Chem.* **2015**, *63*, 5587–5596.
[23] M. R. Aly, M. M. Ibrahim, A. M. Okael, Y. A. Gherbawy, *Bioorg. Khim.* **2014**, *40*, 234–247.
[24] M. Abaszadeh, M. Seifi, A. Asadipour , *Res. Chem. Intermed.* **2015**, *41*, 5229–5238.
[25] B. Amirheidari, M. Seifi, M. Abaszadeh, *Res. Chem. Intermed.* **2016**, *42*, 3413–3423.
[26] M. Suarez, Y. Verdecia, E. Ochoa, N. Martin, R. Martinez, M. Quinteiro, C. Seoane, J. L. Soto, H. Novoa, N. Blaton, O. M. Peeters, C. De Ranter, *J. Heterocyc. Chem.* **2003**, *37*, 735–742.
[27] A. Siddekha, S. H. S. Azzam, M. A. Pasha, *Syn. Commun.* **2014**, *44*, 424–432.
[28] S. Moloi, S. Maddila, S. B. Jonnalagadda, *Res. Chem. Intermed.* **2017**, *43*, 6233–6243.
[29] D. Azarifar, Y. Abbasi, O. Badalkhani, *Appl. Organomet. Chem.* **2018**, *32*, 3939.
[30] K. Y. Foo, B. H. Hameed, *Bioresour. Technol.* **2011**, *102*, 9814–9817.
[31] R. Breslow, D. C. Riseout, *J. Am. Chem. Soc.* **1980**, *102*, 7816–7817.
[32] J. H. Li, G. D. Yasay, S. T. Kan, C. J. Ohnmacht, D. A. Trainor, A. D. Boney, T. J. Heppner, M. T. Nelson, *Arzneimittelforschung.* **1996**, *46*, 525.
[33] K. J. Prabahar, V. T. Ramakrishnan, D. Sastikumar, D. Selladurai, V. Masilamani , *Indian J. Pure Appl. Phys.* **1991**, *29*, 382.
[34] P. Shanmugasundaram, K. J. Prabahar, V. T. Ramakrishnan , *J. Heterocycl. Chem.* **1993**, *30*, 1003–1007.

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[35] H. Mohan, N. Srividya, P. Ramamurthy, J. P. Mittal, *J. Chem. Soc. Faraday Trans.* **1996**, *92*, 2353–2359.
[36] J. Sivaraman, K. Subramanian, D. Velmurugan, E. Subramanian, P. S. Shanmugasunda-ram, *Acta Crystallogr.* **1996**, *C52*, 481–483.
[37] M. Abdollahi-Alibeik, A. Rezaeipoor-Anari, *J. Magn. Magn. Mater.* **2016**, *398*, 205–214.
[38] A. Tadjarodi, A. Azad, M. G. Dekamin, S. Afshar, R. Hejazi, A. Mollahosseini, *J. Nanostruct.* **2015**, *5*, 327–335.
[39] L. S. Gadekar, S. S. Katkar, S. R. Mane, B. R. Arbad, M. K. Lande, *Bull. Kor. Chem. Soc.* **2009**, *30*, 2532–2534.
[40] M. Saha, A. K. Pal, *Tetrahedron Lett.* **2011**, *52*, 4872–4877.
[41] M. G. Dehbalaei, N. Foroughifar, H. Pasdar, A. Khajeh-Amiri, *New J. Chem.* **2018**, *42*, 327–335.
[42] F. Rashedian, D. Saberi, K. Niknam, *J. Chin. Chem. Soc.* **2010**, *57*, 998–1006.
[43] Y. B. Shen, G. W. Wang, *Arkivoc* **2008**, *16*, 1–8.
[44] A. Davoodnia, M. Khashi, N. Tavakoli-Hoseini, *Chin. J. Catal.* **2013**, 34, 1173–1178.
[45] S. Rahmani, A. Amoozadeh, *J. Nanostruct.* **2014**, *4*, 91–98.
[46] H. A. Soliman, A. Y. Mubarak, A. El-Merakabi, S. A. Elmorsy, *Chem. Sci. Trans.* **2014**, *3*, 819–825.
[47] M. Tajbakhsh, H. Alinezhad, M. Norouzi, S. Baghery, M. Akbari, *J. Mol. Liq.* **2013**, *177*, 44–48.
[48] B. S. Samer, V. T. Kamble, *J. Chem. Pharm. Res.* **2015**, *7*, 356–361.
[49] S. Ko, C. F. Yao, *Tetrahedron* **2006**, *62*, 7293–7299.
[50] A. Kumar, R. M. Maurya, *Tetrahedron* **2007**, *63*, 1946–1952.
[51] S. B. Sapkal, K. F. Shelke, B. B. Shingate, M. S. Shingare, *Tetrahedron Lett.* **2009**, *50*, 1754–1756.
[52] H. Mierzace, A. Isadyar, A. Davoodnia, H. J. Eshghi, *Appl. Chem. Res.* **2014**, *8*, 57–63.
[53] S. Gholap, N. Gunjal, *Iran. J. Catal.* **2016**, *6*, 147–152.
[54] M. S. Vahdat, F. Chekin, M. Hatami, M. Khavarpour, S. Baghery, Z. Roshan-Kouhi, *Chin. J. Catal.* **2013**, *34*, 758–763.
[55] S. U. Tekale, V. P. Pagore, S. S. Kauthale, R. P. Pawar, *Chin. Chem. Lett.* **2014**, *25*, 1149–1152.
[56] R. Tafer, R. Boulcina, B. Carboni, A. Debache, *J. Chin. Chem. Soc.* **2012**, *59*, 1555–1560.
[57] D. Touhamia, Z. Zhua, W. S. Balanb, J. Janaunb, S. Haywooda, S. Zeina, *J. Environ. Chem. Eng.* **2017**, *5*, 2388–2394.
[58] C. Li, B. Knierim, C. Manisseri, R. Arora, H. V. Scheller, M. Auer, K. P. Vogel, B. A. Simmons, S. Singh, *Bioresour. Technol.* **2010**, *101*, 4900–4906.
[59] M. Seddighi, F. Shirini, M. Mamaghani, *RSC Adv.* **2013**, *3*, 24046–24053.

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