INTERNATIONAL JOURNAL OF PHARMACEUTICAL, CHEMICAL AND BIOLOGICAL SCIENCES

Available online at www.ijpcbs.com

Research Article

ONE-POT NEDA CATALYZED KNOVENAGEL CONDENSATION UNDER ULTRASONIC IRRADIATION IN SOLVENT-FREE MEDIUM

Sayyed Hussain[1], Shivaji Jadhav[1]*, Megha Rai[2] and Mazahar Farooqui[2, 3]

[1]Sir Sayyed College, Aurangabad – 431001, Maharashtra, India.
[2]Dr. Rafiq Zakaria College for Women, Aurangabad, Maharashtra, India.
[3]Post Graduate and Research Centre, Maulana Azad College, Aurangabad, Maharashtra, India.

ABSTRACT

Herein we wish to report an efficient, eco-friendly and cleaner method for rapid knovenagel condensation of substituted 2-chloroquinoline-3-carbaldehyde with ethyl cynoacetate under ultrasonic irradiation in solvent-free medium by using N-ethyl diisopropyl amine (NEDA) as catalyst within short time period (14-20 min.) at room temperature. The overall progress of reaction was monitored by TLC and formation of compound III(a-h) was confirmed by physical constants and spectroscopic studies. Compared with traditional method, this method is more convenient and reaction can be carried out in higher yield, shorter reaction time and milder condition, without generation of pollution and safer to analyst. From these features present methods can be correlated for safer and efficient synthesis of other products.

Keywords: Knovenagel condensation, NEDA, Ultrasonic irradiation, Solvent-free medium.

INTRODUCTION

Now-a-days it is an innovation to design and develop green procedures that are both environmentally desirable and economically acceptable. Most of organic solvent used in industry are toxic and costly, to overcome these issues, most of the chemist are interested to develop solvent-free reactions. New strategies have recently been developed which contribute to green and safer synthesis, such as use of ultrasound irradiation is one of the promising experimental techniques recently introduced in chemical synthesis[1-4].

By using ultrasound irradiation hydrolysis of dimethyl sulphide and iodine was reported by Rechards and Looms in 1927[5]. Recently Han and Boudjouk reported a significant increase in the yields and rates of Reformatsky reaction under ultra-sonication[6]. Several compounds of quinolones have been screened for biological activity such as bactericidal[7], antitumor[8], anti-inflammatory[9], antimalarial[10] etc. Among quinolones, 2-chloroquinoline-3-carbaldehydes are one of the key intermediates for various functional group interconversions[11-12]. Recently α-hydroxyphosphonates, α-acetoloxy phosphonates derived from the 2-chloroquinoline-3-carbaldehydes showed good antibacterial activity[13].Knovenagel condensation have been extensively studied by using various catalyst such as Betonite[14], Ammonium acetate[15], KF-Al_2O_3 under ultrasound irradiation[16] etc.

In view of research to develop newer environmentally benign methods[17-20] for chemical transformation, we decide to investigate use of NEDA as a catalyst for Knovenagel condensation reaction.

EXPERIMENTAL

General procedure for the preparation of ethyl 3-(2-chloro-substituted-quinolin-3-yl)-2-cyanoacrylate

In 50 ml conical flask 2-chloro-substituted-quinoline-3-carbaldehyde (10 mmol), ethyl cynoacetate (10 mmol) and NEDA (0.2 mmol) were mixed and irradiated under ultrasonic waves at room temperature for 14-20 minutes, The progress of reaction monitored on TLC. After completion of reaction, solid product obtained was washed with distilled water. The product was filtered, dried and recrystallized from ethanol.

Melting points were obtained using capillary method and are uncorrected. The purity of the compoundIII(a-h) was checked using TLC technique, carried out on precoated silica gel 60 F254 on aluminium plates (Merck), spots were visualized under UV cabinet.

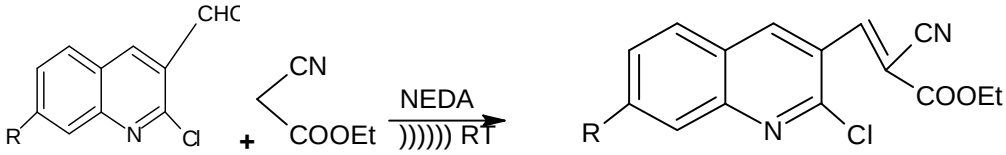
RESULTS AND DISCUSSION

In order to find out suitable catalyst for the synthesis of quinoline derivatives via knovenagel condensation, the reaction of 2-chloro-sustituted-quinoline-3-carbaldehyde with ethyl cynoacetate under ultrasound irradiation, was chosen as a model to get ethyl 3-(2-chloro-substituted-quinolin-3-yl)-2-cyanoacrylate and its beheviour was studied on the presence of NEDA as catalyst.

The melting points, sonication time, percentage of yield of the synthesized compound are given in table1.

Comp.	R	Sonication time in min.	% yield	Melting point In ^{0}C
III a	8-CH_3	14	89	162-164
III b	H	18	85	160-162
III c	6-OCH_3	15	88	144-146
III d	7- OCH_3	15	84	155-157
III e	6-CH_3	17	87	150-152
III f	7-CH_3	19	89	146-148
III g	6-C_2H_5	20	82	168-170
III h	7-C_2H_5	15	91	165-167

REACTION SCHEME



I **II** **III(a-h)**

Spectroscopic studies

The synthesized compounds were subjected to their spectroscopic studies, the outcomes of all compounds are relatively similar and representative spectra of compound IIIa are described below:

IR: Characteristic IR (KBr) Bands found at752 cm^{-1}(C-Cl), 1619cm^{-1}(C=N), 2260cm^{-1}(CN),1737 cm^{-1}(-COO- of ester),3058cm^{-1}(Ar-H).

NMR: 1.86 δ (t 3H),2.3 (d 3H), 3.7δ (q 2H), 6.8δ (s 1H), 7.5-8.4 δ (m 4H).

MASS (m/z): 301, 190, 177, 142, 102 (100%)

CONCLUSION

In summary, we have developed an efficient method for NEDA catalyzed Knovenagel condensation of 2-chloro-substituted-quinoline-3-carbaldehyde with ethyl cynoacetate under ultrasonic irradiation in solvent-free medium at room temperature. This new strategy has several advantages, such as excellent yield, Short reaction time, low cost, solvent removal, minimized environmental hazard, simplified procedures. Finally it is in agreement with green chemistry protocols.

ACKNOWLEDGEMENT

Author is greatly thankful to P.D.Lab, OCPL, Aurangabad for the technicalsupport provided for carrying out this research work.

REFERENCES

1. Mason TJ and Lorimer JP. Sonochemistry, Ellis Horwood, Chicheste., 1988.
2. Boudjouk P and Suslick KS. Ultrasounds, its chemical, physical and biological effects, VCH, Weinheim. 1988:165.
3. Suslick KS. Handbook of heterogeneous catalysis, Wiley-VCH, New York. 1997;3:1350.
4. Torok B and Molnar A. Akademiai kiado, Budapest (Hungarian). 1997;82:281.
5. Rechards WT and Looms AL. J Am Chem Soc. 1927;49:3086.
6. Han BH and Boudjouk P. J Org chem. 1982;47:5030.
7. Patel HV and Vyas kv. Ind J Chem. 1990;29B:836.
8. Sukhova NM, Lidak M and Zidermane A. Khim Farm Zh. 1989;23:1226.

9. Dillard RD, Pavey DE and Benslay DN. J Med Chem. 1973;16:251.
10. Craig JC and Person PE. J med Chem. 1971;14:1221.
11. Meth-Cohn O. Heterocycles. 1993;35:539.
12. Rajendran SP and Manonmoni M. Org Prep Proced Int. 1994;26:383.
13. Pokalwar RU, Hangarge RV, Mhaske PV and Shingare MS. Arkivock, 2006;Xi:196.
14. Lonphy A and Song SJ. J Chem Soci. Perkin trans. 2001;1:1220.
15. Mitra AK, De A and Karchaudhari NV. Synth Commun. 1999;29(16):2731.
16. Wang SX and Li JT. ultrason sonochem. 2002;9(3):159.
17. Zhau S, Wang X and Zhang L. RSC Adv. 2013;29:11691.
18. Qing Liu, Hangmei ai and Zhen Li. Ultrasonic Sonochemistr., 2011;18(2):477.
19. Mallouk S, Bougrin K, Laghzizil A and Benhind R. Molecules. 2010;15(2):813.
20. Mondal J, Modakj A and Bhaumik A. J Mol Cat A: chemical. 2011;335(1-2):236.