chemistry proceedings

MDPI

Proceeding Paper

Development of Easy and Practical Access of Novel Imidazo[2,1-b]thiazole Derivatives †

Djamila Benzenine [1,2,*], Fatima Belhadj [1,3], Zahira Kibou [1,2], M. Pilar Vázquez-Tato [4], Julio A. Seijas [4] and Noureddine Choukchou-Braham [1]

[1] Laboratoire de Catalyse et Synthèse en Chimie Organique, Faculté des Sciences, Université de Tlemcen, B.P. 119, Tlemcen 13000, Algeria; zahira_kibou@yahoo.fr (Z.K.); fbelhadj88@yahoo.fr (F.B.); nbchoukchou@yahoo.fr (N.C.B.)
[2] Faculté des Sciences et de la Technologie, Université de Ain Témouchent, B.P. 284, Ain Témouchent 46000, Algeria
[3] Faculté de Médecine, Université Oran 1, B.P. 1510 El Menaouar, Oran 31000, Algeria
[4] Departamento de Química Orgánica, Facultad de Ciencias, Universidad of Santiago De Compostela, Alfonso X elSabio, 27002 Lugo, Spain
* Correspondence: benzeninedjamila@gmail.com
† Presented at the 26th International Electronic Conference on Synthetic Organic Chemistry; Available online: https://ecsoc-26.sciforum.net.

Abstract: The scientific discoveries exposed the privileged skeleton of the imidazo[2,1-*b*]thiazole heterocycles for the development of pharmacological compounds. Imidazo[2,1-*b*]thiazoles showed interesting potency against a bord range of biological activities such as antibacterial, antifungal, antiviral, anti-inflammatory, antihypertensive, anticancer and antioxidant, also used as drug that has significant immunomodulatory properties (Levamisole). Encouraged by these bioactivities, we report herein a new, easy and efficient procedure for the preparation of imidazo[2,1-*b*]thiazole derivatives under green chemistry conditions.

Keywords: Imidazo[2,1-b]thiazoles; Hetrocycles; Green Chemistry

Citation: Benzenine, D.; Belhadj, F.; Kibou, Z.; Vázquez-Tato, P.; Seijas, J.A.; Choukchou-Braham, N. Development of Easy and Practical Access of Novel Imidazo[2,1-b]thiazole Derivatives. **2022**, *4*, x. https://doi.org/10.3390/xxxxx

Academic Editor(s):

Published: 15 November 2022

1. Introduction

Heterocyclic compounds with atoms of nitrogen, and sulfur constitute a class of interesting products with attractive biological and chemical properties [1,2]. Imidazo[2,1-b]thiazoles (Figure 1) which is a substantial heterocycle have a great of interest in many fields, especially in medicinal chemistry due to their large spectrum of bioactivities, such as anti-inflammatory [1], antimicrobial [2], antioxidant [3], antitumor [6,7], and antitubercular activities [4].

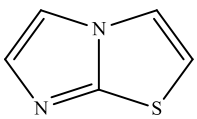


Figure 1. structure of imidazo[2,1-b]thiazole skeleton.

Levamisole, which is an imidazo[2,1-b]thiazole moiety-containing component, is a drug with significant immunomodulatory properties [5] in addition to its anthelmintic activity [6] (Figure 2).

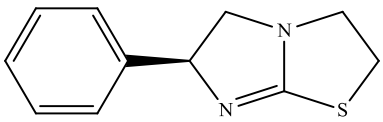


Figure 2. structure of Levamisole.

Considering their high pharmaceutical benefits, the development of new strategies for the synthesis of imidazo[2,1-b]thiazole derivatives attracted the attention of researchers for a long time ago [11–15].

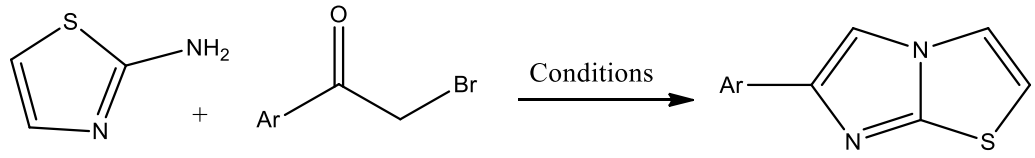
In order to set up synthetic strategies sustainable and ecofriendly, the development of green synthetic protocols have gained importance lately. Therefore, attempts are being made to promote a catalytic protocol that is ecological and environmentally safe for the synthesis of imidazo[2,1-b]thiazoles [7].

In the light of this, we describe here a facile and practical aluminum catalyst synthesis of imidazo[2,1-b]thiazole derivatives.

2. Results and Discussion

In the continuation of our interest in the synthesis of heterocycles with biological importance [17–26], the preparation of the title compounds was deemed of interest. Thus, we describe here a new and practical method for the synthesis of new imidazo[2,1-b]thiazole derivatives from 2-aminothiazole and 2-bromoketones under refluxed ethanol firstly without catalyst , then catalysed by basic alumina in the same reaction conditions (Table 1).

Table 1. Synthesis of imidazo[2,1-b]thiazoles.



Product	1	2	3
Ar	Ph	4-MeC_6H_4	4-$OMeC_6H_4$
Yield	80 [a]; 67 [b]	91 [a]; 76 [b]	88 [a]; 80 [b]
Reference	[27–30]	[27–29]	[27–30]

Reaction conditions: [a] 2-aminothiazole (0.01 mol and α-bromoketones (0.01 mol); [b] 2-aminothiazole (0.01 mol) and α-bromoketones (0.01 mol), Al_2O_3 (30% w/w).

3. Experimental Procedure

Experimental procedure for the synthesis of imidazo[2,1-b]thiazoles without catalyst

A mixture of 2-aminothiazole (0.01 mol) and α-bromoketones (0.01 mol) was refluxed in ethanol. After completion of the reaction, as indicated by TLC (8–12 h), the crude product was cooled to room temperature and washed several times with diethylether and ethanol. The product was filtered to give the corresponding imidazo[2,1-b]thiazoles**.**

Experimental procedure for the synthesis of imidazo[2,1-b]thiazoles with Al_2O_3

A mixture of 2-aminothiazole (0.01 mol) and α-bromoketones (0.01 mol), a catalytic amount of Al_2O_3 (30% w/w) was added and the mixture was refluxed in ethanol (10 mL). After completion of the reaction, as indicated by TLC (6–8 h), the residue was cooled to room temperature and washed several times with diethylether and ethanol. The product was filtered to give the corresponding imidazo[2,1-b]thiazoles**.**

Product **3:** Yield: [a] 80%; [b] 88%; white solid; m.p. 256 °C; IR (KBr): 3000, 1678, 1635, 1245; ^{1}H NMR (91 MHz, $(CD_3)_2SO$): δ 9.54 (s, 1H), 7.92-7.00 (m, 6H), 3.80 (s,1H); HRMS (ESI) calcd for $C_{12}H_{10}N_2OS$ $[M+H]^+$ 230,29; found 231.

4. Conclusion

In summary, a new simple and easily synthesized imidazo[2,1-b]thiazole derivatives, was designed and synthesized based on condensation of two components in a single reaction under green chemistry conditions. The structure of prepared heterocycles was characterized by NMR, FTIR and ESI-MS spectroscopy. This strategy includes some merits like simplicity, high yields, benign reaction conditions and ecofriendly process which reflect the activity of the catalyst.

Acknowledgments: The authors wish to thank Directorate General for Scientific Research and Technological Development (DGRSDT), the University of Tlemcen and the University of Ain Témouchent for the financial support. We also thank the Ministerio de Economía, Industria y Competitividad (Spain) for financial support.

References

1. Dincel, E.D.; Gürsoy, E.; Yilmaz-Ozden, T.; Ulusoy-Güzeldemirci, N., Antioxidant activity of novel imidazo [2, 1-b] thiazole derivatives: Design, synthesis, biological evaluation, molecular docking study and in silico ADME prediction. *Bioorganic chemistry* **2020**, *103*, 104220.
2. Dincel, E.D.; Hasbal-Celikok, G.; Yilmaz-Ozden, T.; Ulusoy-Güzeldemirci, N., Design, biological evaluation, molecular docking study and in silico ADME prediction of novel imidazo [2, 1-b] thiazole derivatives as a novel class of α-glucosidase inhibitors. *Journal of Molecular Structure* **2021**, *1245*, 131260.
3. Andreani, A.; Leoni, A.; Locatelli, A.; Morigi, R.; Rambaldi, M.; Cervellati, R.; Greco, E.; Kondratyuk, T.P.; Park, E.-J.; Huang, K.J.E. j. o. m. c., Chemopreventive and antioxidant activity of 6-substituted imidazo [2, 1-b] thiazoles. **2013**, *68*, 412–421.
4. Moraski, G.C.; Seeger, N.; Miller, P.A.; Oliver, A.G.; Boshoff, H.I.; Cho, S.; Mulugeta, S.; Anderson, J.R.; Franzblau, S.G.; Miller, M.J.J.A.I.D., Arrival of imidazo [2, 1-b] thiazole-5-carboxamides: Potent anti-tuberculosis agents that target QcrB. **2016,** *2* (6), 393-398.
5. Dincel, E.D.; Hasbal-Celikok, G.; Yilmaz-Ozden, T.; Ulusoy-Güzeldemirci, N.J.J. o. M. S., Design, synthesis, biological evaluation, molecular docking, and dynamic simulation study of novel imidazo [2, 1-b] thiazole derivatives as potent antioxidant agents. **2022**, *1258*, 132673.
6. Ewida, M.A.; Ewida, H.A.; Ahmed, M.S.; Allam, H.A.; ElBagary, R.I.; George, R.F.; Georgey, H.H.; El‐Subbagh, H.I.J.A. d. P., Nanomolar potency of imidazo [2, 1‐b] thiazole analogs as indoleamine 2, 3‐dioxygenase inhibitors. **2021,** *354* (11), 2100202.
7. Geedkar, D.; Kumar, A.; Sharma, P.J.J. o. H. C., Multiwalled carbon nanotubes crowned with nickel‐ferrite magnetic nanoparticles assisted heterogeneous catalytic strategy for the synthesis of benzo [d] imidazo [2, 1‐b] thiazole scaffolds. **2020,** *57* (12), 4331-4347.

.