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Green synthesis of benzothiazolinone Schiff base derivative ADME prediction study

Yasser Bouchebcheb [1*], Aya Alem[1] , Dalila Fedaoui[1], Messaoud Liachaa[1]

•[1]Laboratory of Synthesis and Organic Biocatalysis (LSBO), Department of chemistry, Faculty of Science, University of Badji Mokhtar Annaba - Algeria.BP 12 – 23200 Sidi-Ammar

INTRODUCTION & AIM

Benzothiazolines are a class of heterocyclic compounds known for their diverse biological properties, as reported in the literature [1-2]. These properties have motivated extensive research to synthesize derivatives with enhanced and multiple biological activities.

Similarly, Schiff bases are well documented for their significant biological activity and diverse applications [3-5]. They remain a focus of research for the development of novel biologically active compounds.

Our objective was to create a Schiff base benzothiazolinone derivative with a high yield and quick turnaround time using green chemistry. IR, ^{1}HNMR, and ^{13}C NMR spectroscopy were used to establish the derivative's structure after it was theoretically examined using the SwissADME webservice based on Lipinski's rule of five.

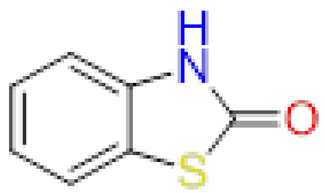


Fig.2-oxo-3H-benzothiazole

METHOD

Chemistry

To synthesize (E)-6-(((5-chloro-2-hydroxyphenyl)imino)methyl)-3-methylbenzo[d]thiazol-2(3H)-one Schiff Base, amine (1 equiv) and 6-carbaldehyde (1 equiv) are reacted using EtOH as solvent. The reaction takes place at 80°C under ultrasonic irradiation for 32 min. After monitoring the progress of the reaction by TLC, the mixture is allowed to cool, resulting in the formation of a precipitate. The solid is then filtered on filter paper and washed with a little water. This method has a number of advantages: it's easy to set up, enables direct recovery of the pure product, requires a short reaction time and, above all, offers high yields 54% .

ADME study

The pharmacokinetical properties performed using SwissADME web [6] to investigate the of compound (1a).

RESULTS & DISCUSSION

Spectroscopic caracterisation

^{1}H NMR spectroscopy

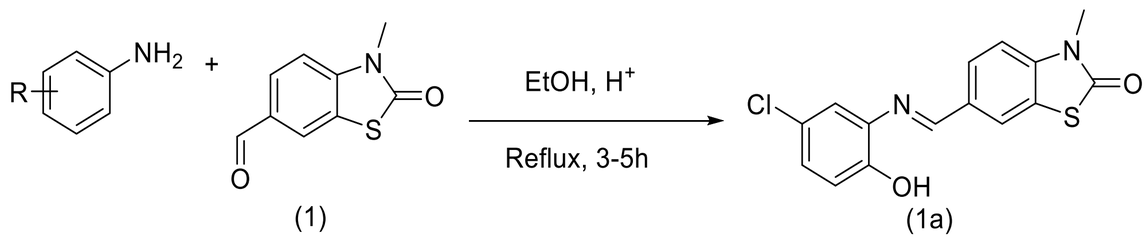
The creation of the imine function for the derivative is confirmed by the arrival of the HC=N proton signals in the 8.58-8.77 ppm region and the absence of the CHO proton signal, which is indicative of the aldehyde function of the aldehyde (1) at about 9.93 ppm in comparison to the synthesized molecule (a).

In the strong fields, the methyl group attached to the nitrogen atom is visible as a singlet at 3.44–3.51 ppm.

RMN ^{1}H(400 MHz, DMSO): δ, ppm (J, Hz): 9.22 (1H, s, OH); 8.72 (1H, d, J = 1.5 Hz, HC=N); 8.38 (1H, d, J = 1.8 Hz, H-7); 7.99 (1H, dd, J = 8.4, 1.8 Hz, H-5); 7.42 (1H, dd, J = 8.5, 2.6 Hz, H-4); 7.11 (1H, dd, J = 8.6, 2.5 Hz, H-Ar); 6.91 (1H, d, J = 8.6 Hz, H-Ar); 3.46 (3H, s, N–CH3).

13C NMR spectroscopy (101 MHz, DMSO): δ, ppm: 169.41 (**C**=O); 159.89 (N=**C**); 150.82; 140.58; 139.19; 132.03; 128.99; 127.08; 123.43; 123.23; 122.42; 119.08; 117.77; 111.77 (carbones aromatiques); 29.83 (**C**H_3-N).

FT-IR(KBr, *v*cm^{-1}): 1668.31 (C=O), 1570.31 (C=N), 3411.97 (O-H).



Schema.1. the reaction pathway.

ADME study

Parameter	Criteria	Observed Value
Molecular Weight	≤ 500 g/mol	318.39 g/mol
LogP (Consensus)	≤ 5.0	4.22
Hydrogen Bond Donors (HBD)	≤ 5	1
Hydrogen Bond Acceptors (HBA)	≤ 10	3
Topological Polar Surface Area (TPSA)	≤ 140 Å² (bonus criterion)	82.83 Å²

Table. Lipinski Rule of Five Analysis results.

Using Lipinski's Rule of Five [7], a guideline that assesses a compound's potential as an orally active drug based on properties, it was founf that the compound obey the rule , making it a promising candidate for oral bioavailability.

CONCLUSION

In conclusion, this study effectively illustrates the use of EtOH and an ultrasound-assisted method in a green chemistry approach to the synthesis of the imine benzothiazolinone derivative. This approach not only produces a high yield and a quicker reaction time, but it also makes it easier to recover the product in a pure form. The synthetic derivative's structure was verified using IR, ^{1}H NMR, and ^{13}C NMR spectroscopy methods. Furthermore, pharmacokinetic properties were theoretically analyzed. The results demonstrate the synthetic compound's possible biological significance and appropriateness for additional research.

FUTURE WORK / REFERENCES

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