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Sonochemical synthesis of benzothiazolinone schiff based derivative & ADME prediction study

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INTRODUCTION & AIM

Benzothiazolines are heterocyclic compounds that have been developed over time because they have important biological properties, according to the literature [1], with the goal of extending these properties and creating derivatives with multiple biological properties and functions [2,3].
Schiff bases are also physiologically active molecules with a range of characteristics, and researchers have been interested in discovering methods to synthesis Schiff bases.
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.

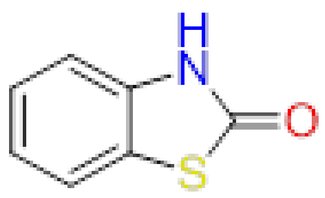


Fig.2-oxo-3H-benzothiazole

METHOD

Chemistry

To synthesize (E)-6-(((4-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 33 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 65%.

ADME study

The pharmacokinetical properties performed using SwissADME web [4] to investigate the of compound (1a).

RESULTS & DISCUSSION

Spectroscopic caracterisation

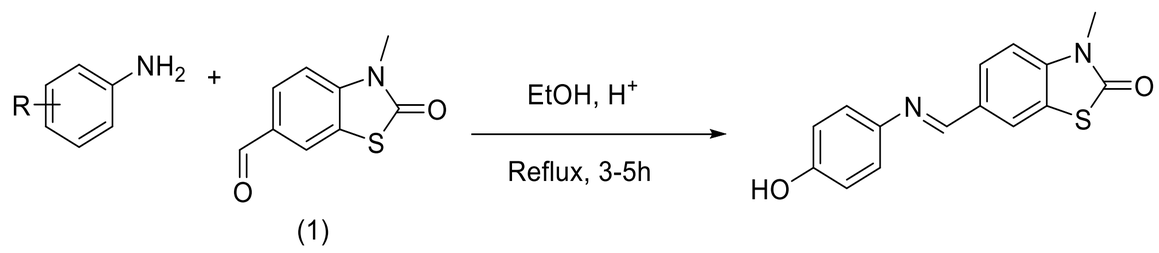
^{1}H NMR spectroscopy

The formation of the imine functionality in the derivative is confirmed by the appearance of the HC=N proton signals in the 8.58–8.77 ppm region, along with the disappearance of the CHO proton signal characteristic of the aldehyde group in compound (1), normally observed around 9.93 ppm. This comparison clearly indicates the successful conversion to the imine in the synthesized molecule (a).In the high-field region, the methyl group attached to the nitrogen atom appears as a singlet at 3.44–3.51 ppm, further supporting the proposed structure.

RMN ^{1}H(400 MHz, DMSO): δ, ppm (J, Hz): 9.54 s (1H, OH), 8.64 s (1H, HC=N), 8.23 d (1H, J 1.6 Hz, H-7), 7.94 dd (1H, H-5, J 8.4, 1.7 Hz), 7.46 d (1H, H-4, J 8.4 Hz), 7.28 – 7.20 m (2H, H-Ar), 6.90 – 6.81 m (2H, H-Ar), 3.49 s (3H, N–CH3).

13C NMR spectroscopy (101 MHz, DMSO): δ, ppm: 169.50, 156.69, 156.50, 142.97, 140.06, 132.44, 127.89, 122.91(2C), 122.58, 122.51, 116.20(2C), 111.90, 29.69.

FT-IR(KBr, *v*cm^{-1}): 1683.36 (C=O), 1617.47 (C=N) 3244.64 (O-H).



Schema.1. the reaction pathway.

ADME study

Parameter	Criteria	Observed Value
Molecular Weight	≤ 500 g/mol	284.33 g/mol
LogP (Consensus)	≤ 5.0	2.89
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.

According to Lipinski's Rule of Five [5] a widely used guideline for predicting whether a compound possesses the necessary physicochemical characteristics for oral activity, the analyzed molecule satisfies all the required criteria. Its compliance with these parameters suggests favorable absorption and permeability, highlighting the compound as a strong candidate for oral bioavailability and further drug development studies.

CONCLUSION

In summary, this study clearly demonstrates the effectiveness of using ethanol and an ultrasound-assisted method within a green chemistry framework for synthesizing the benzothiazolinone-based imine. This approach offers several advantages, including high yield, reduced reaction time, and easy recovery of the product in a pure form. The structure of the synthesized compound was confirmed through IR, ^{1}H NMR, and ^{13}C NMR spectroscopic analyses. Additionally, its pharmacokinetic properties were theoretically assessed. The findings highlight the compound's potential biological relevance and its suitability for further investigation.

FUTURE WORK / REFERENCES

[1] M. Erdogan et al., "Design, synthesis and biological evaluation of new benzoxazolone/benzothiazolone derivatives as multi-target agents against Alzheimer's disease," European Journal of Medicinal Chemistry, vol. 212, p. 113124, Feb. 2021, doi: 10.1016/j.ejmech.2020.113124.
[2] S. H. Ferreira, B. B. Lorenzetti, M. Devissaguet, D. Lesieur, and Y. Tsouderos, "S14080, a peripheral analgesic acting by release of an endogenous circulating opioid-like substance," British J Pharmacology, vol. 114, no. 2, pp. 303–308, Jan. 1995, doi: 10.1111/j.1476-5381.1995.tb13227.x.
[3] N. Dharmaraj, P. Viswanathamurthi, and K. Natarajan, "Ruthenium(II) complexes containing bidentate Schiff bases and their antifungal activity".
[4] A. Jarrahpour, et al., Molecules, vol. 12, no. 8, pp. 1720–1730, Aug. 2007, doi: 10.3390/12081720.[6]A. Daina, O. Michielin, and V. Zoete, "SwissADME: a free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules," Sci Rep, vol. 7, no. 1, p. 42717, Mar. 2017, doi: 10.1038/srep42717.
[5]C. A. Lipinski, F. Lombardo, B. W. Dominy, P. J. Feeney, Advanced Drug Delivery Reviews, 1997, 23, 3–25.