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Short Communication

Nimesulide Based 1,2,4,5-Tetra Substituted Imidazole Derivative: Synthesis and Characterisation

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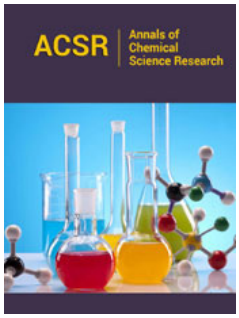

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Chemical Abstract

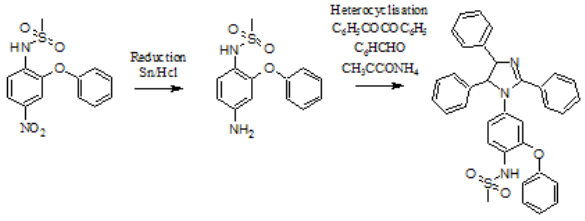
Nimesulide a preferential "cyclooxygenase-2 inhibitor" is one of the well-known non-steroidal anti-inflammatory drugs that has been utilized to treat pain and other inflammatory diseases. Nimesulide was withdrawn from the market due to its hepatotoxicity which could be due to the presence of nitro group. Imidazoles represent an important class of bioactive molecules that shows a wide range of pharmacological activities besides anti-inflammatory activity. In our strategy to develop safer and potential anti-inflammatory molecules, we have decided to combine some of the structural features of nimesulide and imidazole in a single molecule. We have described the design and synthesis of nimesulide based 1,2,4,5-tetra substituted imidazole of potential biological significance via chemical modifications of a commonly used anti-inflammatory agent nimesulide. This derivative was prepared from nimesulide via a two-step process involving regio selective reduction of nimesulide followed by hetero cyclisation of reduced nimesulide in very 81 % yield. The title compound nimesulide based 1,2,4,5-tetra substituted imidazole was synthesized in very good yield by reaction of benzil, benzaldehyde, ammonium acetate, and N-(4-amino-2-phenoxy phenyl) methane sulphonamide in acetic acid using multi-component strategy and molecular modification. The structure of the synthesized compound was confirmed by IR and H1 NMR spectral analysis.

Keywords: Nimesulide; Nimesulide based 1,2,4,5-tetra substituted imidazole; Molecular modification

Introduction

Nimesulide a preferential "cyclooxygenase-2 inhibitor" is one of the well-known non-steroidal anti-inflammatory drugs that have been utilized to treat pain and other inflammatory diseases. Nimesulide was withdrawn from the market due to its hepatotoxicity which was due to the presence of nitro group(toxicophore) [1,2]. Imidazoles represent an important class of bioactive molecules that shows a wide range of pharmacological activities besides anti-inflammatory activity. In our strategy to develop safer and potential anti-inflammatory molecules, we have decided to modify the toxicophore and integrate some of the structural features of nimesulide and imidazole in a single molecule. Because of their common anti-inflammatory properties and our interest in nimesulide derivatives as potential anti-inflammatory agents, we decided to prepare a compound having structural features of both compounds. We estimated that a combination of structural features of imidazole with nimesulide in a single molecule would provide novel agents possessing potent pharmacological activities. We report the synthesis nimesulide based 1,2,4,5 -tetra substituted imidazole as hybrid molecule derived from nimesulide in very 81% yield from nimesulide via reducing its nitro group followed by hetero cyclisation using multicomponent strategy [3,4].

Synthetic scheme:



Synthesis of Nimesulide based 1,2,4,5-tetra substituted Imidazole

Materials and Methods

Synthetic procedure

0.016 moles of reduced nimesulide, 0.005 moles of benzil, 0.005 moles of benzaldehyde, 0.012moles of ammonium Acetate, 0.174 moles of acetic acid were taken in a clean, dry round bottom flask fitted with a reflux condenser along with condenser pipes. The reaction mixture was heated on a magnetic stirrer at 970 RPM with a hot plate to reflux at 120 °C for about 6 hours. The progress of the reaction was monitored using ascending TLC technique. Excess acetic acid was distilled off and the reaction mixture was quenched into 100mL of ice-cold water [5,6]. Crude 1,2,4,5 tetra substituted imidazole separated out as solid which was filtered at suction, washed with sodium bisulfite wash, cold water, dried, and recrystallized from suitable recrystallization technique.

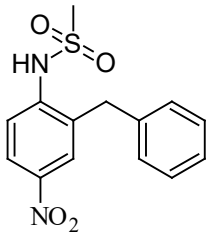
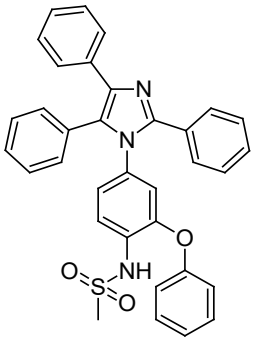
Results and Discussions

Computational data of the title compound using Chem sketch, Mol inspiration, Pro Tox-II and Swiss ADME (Table 1 & 2).

Table 1: Table of characterization.

Physical state	Amorphous solid
Color	Yellow
Physical constant	M.P:167 °C
Theoretical yield	2 Gms
Practical yield	1.62 Gms
Percentage of yield	81
Recrystallizing solvent	Chloroform
Mobile phase for TLC:	Chloroform and Ethyl acetate in the ratio 2:1
R_f value	0.86
Molecular formula	$C_{34}H_{27}N_3O_3S$
Molecular weight:	557.66
IR- spectral data	2970,1444 (CH_3); 1346(S=O); 1160(Ether); 968,765,694,835 (Benzene ring); 1346(C-N). ^{1}H-NMR spectral data ($CDCl_3$): 0.98 (CH_3), 7.48 (Ar-H).
Elemental data:	C (73-23%) H (4.88%) N (7.54%) O (8.61%) S (5.75%)

Table 2: Table of computational data.

	Nimesulide	Nimesulide Based 1,2,4,5- Imidazole Derivative
Structure		
Molar refractivity	76.32 ± 0.4 cm^3	164.97 ± 0.5 cm^3
Molar volume	212.3 ± 3.0 cm^3	454.0 ± 7.0 cm^3
Parachor	595.9 ± 4.0 cm^3	1204.7 ± 8.0 cm^3
Index of refraction	1.638 ± 0.02	1.646 ± 0.05
Polarizability	30.25 ± 0.5 10^{-24} cm^3	65.40 ± 0.5 $10^{-24}cm^3$
RDBE	11	25

Log P	-0.62	5.69
Log S	-4.38	-12.85
TPSA	109.60	73.23
Number of rotatable bonds	5	8
Number of hydrogen bond acceptors	7	6
Number of hydrogen bond donors	1	1
GPCR ligand score	-0.15	0.10
Ion channel modulatory score	-0.01	-0.24
Nuclear receptor ligand score	-0.17	-0.10
Protease inhibitory score	-0.11	-0.13
Enzyme inhibitory score	-0.12	-0.03
Number of heavy atoms	21	41
Number of aromatic heavy atoms	12	35
Class of solubility	Moderately soluble	Insoluble
GI absorption	High	Low
BBB Permeability	No	No
Lipinski rule	Yes; 0 violation	No
Ghose filter	Yes	No
Veber rule	Yes	Yes
Egan rule	Yes	No
Muegge rule	Yes	No
Bioavailability score	0.55	0.17

Conclusion

In conclusion, we have described the design and synthesis of nimesulide based 1,2,4,5- tetra substituted imidazole of potential biological significance via chemical modifications of a commonly used anti-inflammatory agent nimesulide. It was prepared from Nimesulide via a two-step process involving reduction of nimesulide followed by hetero cyclisation of reduced nimesulide in very 81% yield. Moreover, because of the lack of nitro group in the final molecule, it is expected to be free from the side effects of nimesulide such as hepatotoxicity which is due to nitro group. Overall, the present nimesulide-based imidazole framework appeared to be a useful template for the design and identification of novel and potential anti-inflammatory agents.

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References

1. John H Gajewski (1965) Molecular Modification in Drug Design. Clinical Chemistry 11(5): 612.
2. Sandhya P, Jyoti M, Geetha Rani DP, Padmavathi VG, Sarbani P (2007) Chemical Modifications of Nimesulide. J Braz Chem Soc 18(2): 384-390.
3. Ghodsi MZ, Zeinab D, Monireh SN, Alireza B (2015) One-pot synthesis of 1,2,4,5-tetra substituted Imidazoles using sulfonic acid functionalized silica (SiO2-Pr-SO3H). Arabian Journal of Chemistry 8(5): 692-697.
4. Nascimento MVPS, Munhoz ACM, Theindl LC, Mohr ETB, Saleh N, et al. (2018) A novel tetrasubstituted imidazole as a prototype for the development of anti-inflammatory drugs. Inflammation 41(4): 1334-1348.
5. Banerjee P, Eckert OA, Schrey AK, Preissner R (2018) ProTox-II: a webserver for the prediction of toxicity of chemicals. Nucleic Acids Res 46(W1): W257-W263.
6. Antoine Daina, Olivier Michielin, Vincent Zoete (2017) Swiss ADME: a free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules 7: 42717.