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Microwave-assisted condensation of two potential antibacterial pharmacophores (sulfonamide and oxazolidinone)

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INTRODUCTION & AIM

A microwave serves as an energy source to activate a chemical reaction through a process known as microwave-assisted heating, resulting in shorter reaction times and potentially higher yields compared to conventional heating methods. Additionally, microwave heating can offer more uniform heating throughout the reaction mixture, reducing the likelihood of localized overheating or side reactions [1-2].

The microwave-assisted condensation of two potential antibacterial pharmacophores, namely sulfonamide and oxazolidinone [3-6], involves the utilization of irradiation to expedite the condensation reaction between these two compounds. This innovative approach facilitates the rapid and efficient formation of a new compound endowed with enhanced antibacterial properties. By judiciously applying microwave energy, this method optimizes the reaction conditions, resulting in higher yields, reduced reaction times, and improved efficiency [7]. This technique holds significant promise for the swift synthesis of antibacterial agents, thus paving the way for new applications in pharmaceutical research and drug development. In our study, our synthesis approach involves developing a new compound incorporating both oxazolidinone and sulfonamide groups. Initially, we introduced oxazolidinone into a reactor with chloro-acetyl chloride under microwave irradiation, followed by the addition of sulfonamide in situ. The desired product is obtained after recrystallization in dichloromethane.

Microwaves act as electric fields and generally heat any material containing mobile electric charges, such as polar molecules in a solvent or conductive ions in a solid. However, the magnetic field component of the waves is not involved [8].

Microwaves are capable of heating targeted compounds without heating the entire oven, which saves energy **(** figure 1**)**. In theory, they can also provide more uniform heating. However, due to the design of microwave ovens and the non-uniform absorption of heated objects, the electric field is generally not uniform and overheated zones are observed. objects, the electric field is generally not uniform and overheated zones are observed.

Figure 1: chemical laboratory microwave

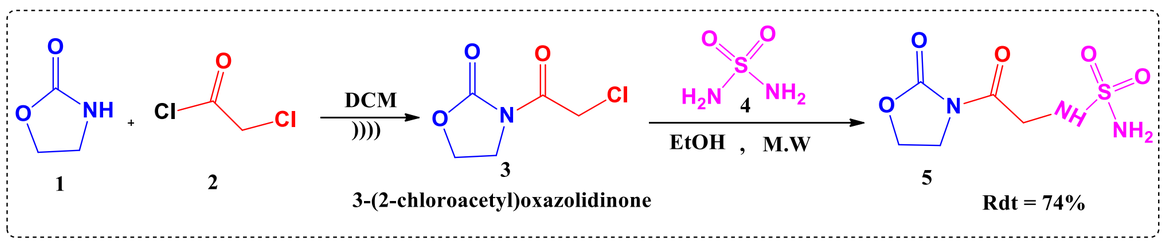
The use of microwaves as an energy source in chemical reactions offers advantages in terms of efficiency, control, and speed.

METHOD

General procedure for the synthesis of derivative oxazolidinone-sulfonamide:

Acylation of oxazolidin-2-one **1** by one equivalent of chloro-acetyl chloride **2** in the presence of two equivalents of triethylamine in dichloromethane and under ultrasonic irradiation leads to 3-(2-chloroacetyl)oxazolidinone **3**. The TLC shows a rapid evolution of the reaction, after a few minutes oxazolidinone is totally consumed with the appearance of a less polar product revealed by ninhydrin. The synthesized product is recovered directly by purification on a silica gel column, and the desired product is recovered as a solid.

In a microwave reactor, one equivalent 3-(2-chloroacetyl)oxazolidinone **3** prepared previously and one equivalent of a commercial sulfonamide **4** are placed in minimal ethanol. The reaction mixture is exposed to microwave irradiation for 15 min. The evolution of the reaction is followed by ccm, showing the appearance of a new, more polar product compared with its precursor, which is revealed with ninhydrin. Recrystallization in dichloromethane was necessary to purify the new product **5**. The final product was obtained as a white powder in good yield **(scheme 1)**.



Scheme 1; Synthesis of oxazolidinone-sulfonamide

RESULTS & DISCUSSION

Generally speaking, before microwave irradiation, the sample is prepared by mixing all the reagents, possibly in the presence of a catalyst, or by adsorption on the insoluble mineral support. At the end of the reaction, the desired product is recovered by simple extraction with a suitable solvent, followed by filtration to remove the solid support.

Our approach revolves around the preparation of a new compound containing both oxazolidinone and sulfonamide units.

The reaction sequence is carried out in two steps: first, acylation of oxazolidinone by chloro-acetyl chloride in the presence of TEA using ultrasonic irradiation, then, in a second step, condensation of a commercial sulfonamide on the acyl oxazolidinone prepared previously in the minimum amount of solvent and under the effect of the microwave. The final product was obtained as a white powder after recrystallization in DCM.

The structures of the synthesized compounds are confirmed by elemental analysis IR and ^{1}H and ^{13}C NMR spectral data.

Data Availability Statement;

3-(2-chloroacetyl)oxazolidinone (3):

Powder; yield: 70 %; 1H NMR ($CDCl_3$): δ = 4.21 (s, 2H, CO-CH_2-Cl), 4.05 (t, *J* = 5.4 Hz, 2H, CH_2-CH_2-N-cyc), 4.40 (t, *J* = 5.4 Hz, 2H, -O-CH_2-CH_2-cyc) ppm. IR (KBr): v = 1717.20 and 1761.14 (C=O) cm-1. ^{13}C NMR ($CDCl_3$) δ = 168.50, 153.11, 62.7, 44.11, 41.70. Anal. Calcd for C5H6ClNO3 (163.00 g/mol): C, 36.72; H, 3.70; Cl, 21.68; N, 08.56; O, 29.35. Found: C, 61.02; H, 3.78; Cl, 21.75; N, 08.80; O, 29.40 %.

Oxazolidinone-sulfonamide (5):

Powder; yield: 75 %;1H NMR (DMSO): δ= 2.00 (s, 2H,NH_2), 3.54 (d, *J* = 7.1 Hz, 2H, CH_2-N), 4.05 (t, *J* = 5.4 Hz, 2H, CH_2-CH_2-N-cyc), 4.40 (t, *J* = 5.4 Hz, 2H, -O-CH_2-CH_2-cyc). 7.74-7.70 (t, *J* = 5.4 Hz, 1H,CH_2-NH-SO_2) ppm. IR (KBr): v =1355.20 and 1164.60 (SO_2), 1735.06 and 1560.06 (C=O), 3243.44 and 3333.39 (NH) and (NH_2) cm-1. ^{13}C NMR (DMSO) δ = 168.90, 153.10, 62.7, 45.11, 39,40.Anal. Calcd for C5H9O5N3S (223.03g/mol): C, 26.90; H, 4.06; N, 18.83; O, 35.84; S, 14.37 Found: C, 27.07; H, 4.09; N, 18.91; O, 35.99; S, 14.41%.

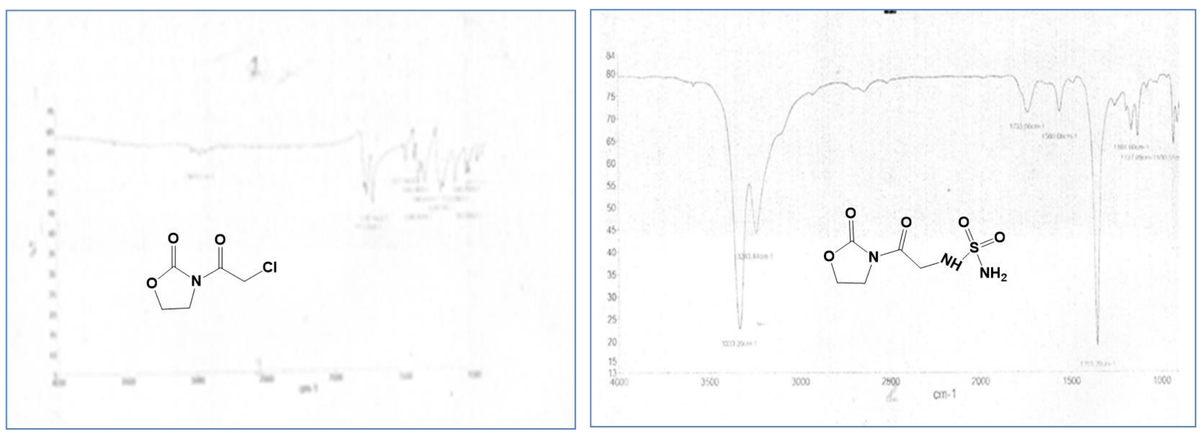


Figure 2; I.R Spectrum

CONCLUSION

Coupling solvent-free reaction techniques with microwave irradiation is proving to be an impressively efficient, clean, safe and economical process. Considerable improvements and simplifications in operating procedures have been achieved compared with conventional methods. In most cases, this results in significantly reduced reaction times, higher purity of end products and increased yields.

FUTURE WORK / REFERENCES

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