SYNTHESIS OF NOVEL N-(2-CHLOROETHYL) SULFAMIDOPHOSPHONATES DERIVATIVES VIA KABACHNIK-FIELDS REACTION ASSISTED BY MICROWAVE IRRADIATIONS

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Introduction & Objectives:

In the recent years, the synthesis of phosphonates compounds and their derivatives has attracted much attention due to their potential biological activities with broad applications in several fields; they possess many properties such as: potent enzyme inhibitors, anticancer agents, herbicides and pesticides activities [1].

On the other hand, the synthesis and reactivity of sulfamides have stirred a major importance due to their interesting biological properties. The NH-SO_2-NH moiety is a bio-isostere of urea -NH-CO-NH, they represent a lower toxicity compared to the urea during their decomposition in the physiological medium [2].

According to the literature, the synthesis of bifunctional molecules containing phosphonates and sulfamides moiety generate a remarkable chemical and pharmacological properties such as: antibacterial, antiviral and anti-inflammatory agents [3].

The application of microwave (MW) in organic transformations has become more and more scientist's interest. [4]. They offers a cleaner and easier pathway compared to conventional methods, it has several advantages such as high temperature homogeneity, instantaneous and rapid heating, allowing the progress of reactions without solvent with a maximal efficiency.

In this contribution and in continuance of our attention toward developing novel biologically important phosphonates and sulfamides compounds. [5] We report a highly efficient one-pot, three-component condensation reaction for the synthesis of various *N*-(2-chloroethyl) sulfamidophosphonates derivatives *via* Kabachnik-filds reaction under microwave irradiation, catalyst and solvent-free conditions in good yields.

Methodology (Material and methods):

All reactions were monitored by TLC on silica Merck 60 F254 percolated aluminum plates and were developed by spraying with Ninhydrin solution. All reactions were carried out in the LG microwave Lightwave Oven MJ3281BCS, using 100 W of microwave power. Proton and carbon nuclear magnetic resonance (^{1}H, ^{13}C NMR) spectra were recorded on a Brücker spectrometer at 300 or 400 MHz. and 100 MHz, chemical shifts are reported in δ units (ppm) with TMS as reference. Infrared spectra were recorded on a SCHIMADZU FTIR 8000 spectrometer. Melting points were recorded on a Büchi B-545 apparatus in open capillary tubes.

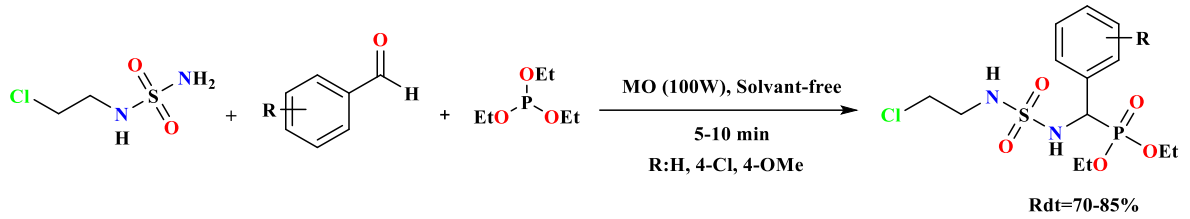
Procedure for synthesis of α-sulfamidophosphonate

A mixture of aldehydes (1 mmol), *N*-(2-chloroethyl) sulfamide (1 mmol) and triethylphosphite (1 mmol) was exposed to microwave irradiation for the appropriate time. After completion of the reaction (monitored by TLC), the reaction mixture was treated with *n*-

hexane/ diethyl ether (5:5), and was allowed to stand at 6 °C overnight. The product was finally filtered and dried.

Results and Discussion:

In our investigation program focused for the synthesis of novel phosphonates derivatives with very timely methods. A new *α*-sulfamidophosphonates were synthesized based on linear sulfonamide containing *N*-chloroethyl moiety, various aromatic aldehydes, and tri-ethylphosphite by a one-pot three component condensation under MW irradiation (100W) under solvent and catalyst-free conditions after 5-10 min, the reaction was completed with good yields (Scheme 1).



Schema 1. Synthesis of *N*-(2-chloroethyl) sulfamidophosphonates assisted by microwave irradiation

Structures of obtained compounds were confirmed by spectroscopic methods:

The ^{1}H NMR of *N*-(2-chloroethyl) sulfamidophosphonates with benzaldehyde derivative is characterized by the appearance of two triplets at 1.06 and 1.36 ppm which correspond to the two methyl groups ($J_{H\text{-}H}$ = 7.2 Hz) and the four protons of the two CH_2 groups resonate in the form of multiplets in the interval [3.60 – 4.18] ppm, the asymmetric carbon proton (*CH) resonates around 4.68 ppm in the form of a doublet split with two coupling constants ($J_{H\text{-}H}$ = 9.2 Hz and $J_{H\text{-}P}$ = 23.5 Hz). (**Fig 1**)

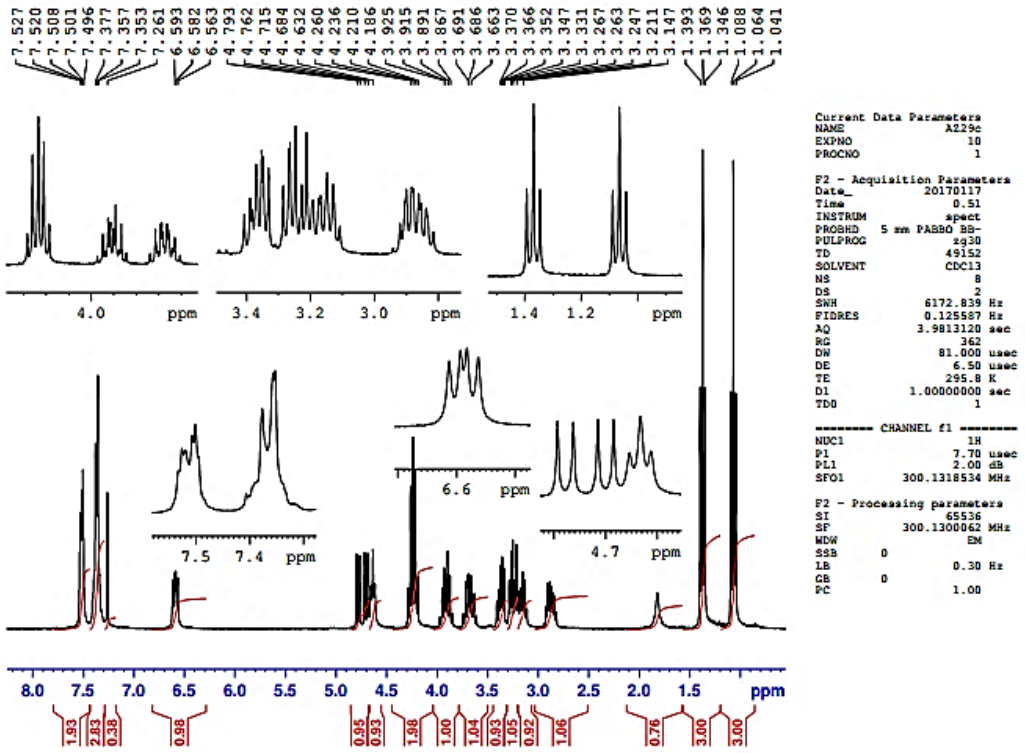


Fig 1. ^{1}H NMR spectrum of diethyl (((*N*-(2-chloroethyl) sulfamoyl) amino) (phenyl) methyl) phosphonate

In IR, the following absorption bands confirmed our structure:
Two bands at 3273 and 3153 cm^{-1} correspond to the two NH functions, two bands around 1325 cm^{-1} and 1151 cm^{-1} which characterize the SO_2 grouping and two bands around 1228 cm^{-1} and 1014 cm^{-1} attributed to the P=O group of phosphonate. (fig 2)

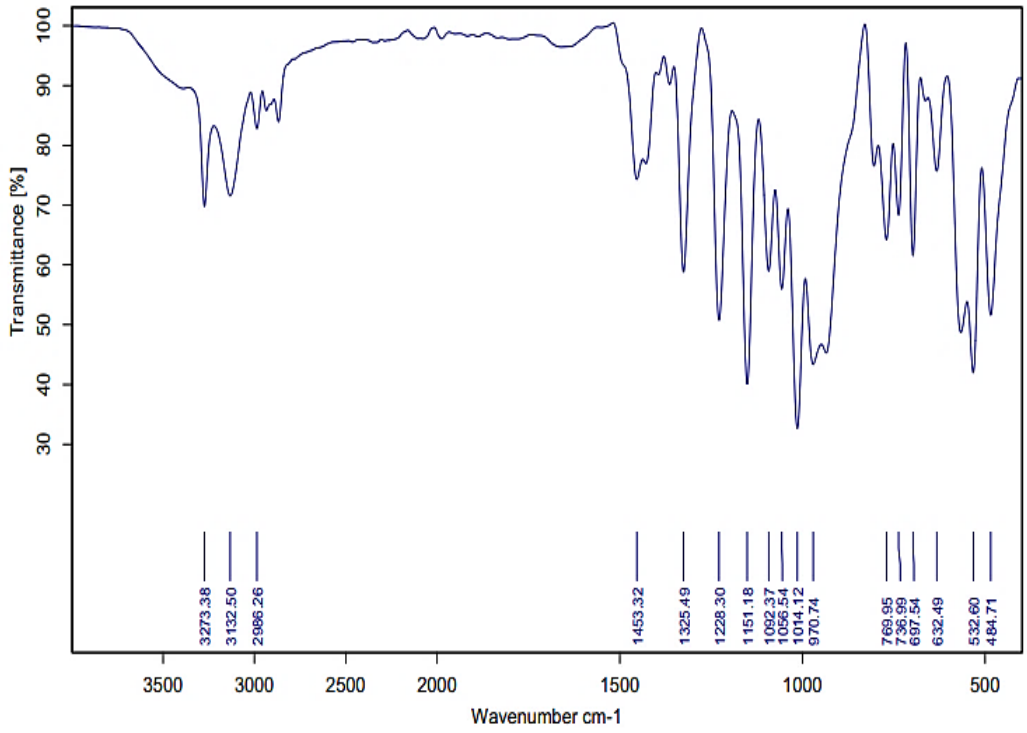


Fig 2. IR spectrum of diethyl (((*N*-(2-chloroethyl) sulfamoyl) amino) (phenyl) methyl) phosphonate

Conclusion:

In conclusion, we describe herein a successful strategy, efficient and convenient green synthesis of novel *N*-(2-chloroethyl) sulfamidophosphonates derivatives by one-pot reactions under MW irradiation, catalyst and solvent-free conditions. This new protocol represents an economically advantageous and environmentally benign process; it offers advantages like short reaction times, no use of solvent, facile isolation of products and high yields.

Keywords: Sulfamidophosphonates, Microwave irradiation, One pot, Kabachnik-filds reaction, Solvent-free conditions.

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