

The Application of Microwaves in the Synthesis of Organophosphorus Compounds as Intermediates and Biologically Active Species

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The microwave (MW) technique has become an important tool in organophosphorus chemistry. In this lecture, the advantages of MWs in different reactions are surveyed allowing green chemical accomplishments. The first case is the MW-assisted direct esterification of phosphinic-¹ and phosphonic acids,² along with phosphoric ester-acids³ that all became more efficient in the presence of an ionic liquid catalyst. The O-alkylation of phosphonic acids and phosphoric ester-acid derivatives under MW irradiation is also a useful technique. A new field is the aminolysis of phosphinates and the alcoholysis of phosphinic amides.⁴ Alcoholyses and hydrolyses of P-esters were also investigated and optimized.⁵⁻⁷ MWs may substitute catalysts, in certain reactions, such as in the Kabachnik–Fields condensations of amines, aldehydes and >P(O)H reagents. The tandem phospho-Mannich reaction is a new protocol. A series of new α -aminophosphonate derivatives including acylated species were prepared that displayed significant anticancer activity on certain cell cultures.⁸⁻¹⁰ Another valuable finding of ours is that in the Hirao P–C coupling of >P(O)H reagents and bromoarenes applying Pd(OAc)₂ as the catalyst, the slight excess of the >P(O)H species may substitute the usual P-ligands in the tautomeric >POH form.^{11,12} Ni-catalyzed cases were also investigated involving an unexpected mechanism assuming a Ni(II) \rightarrow Ni(IV) transition.¹³ A halogene-free P-C coupling was also developed.¹⁴ The synthesis of α -hydroxyphosphonates and derivatives,¹⁵ as well as hydroxy-methylenebisphosphonates^{16,17} as biologically active substrates or drugs in the treatment of bone diseases will also be discussed. Flow chemical accomplishments of a few reactions mentioned above, e.g. esterifications, alcoholyses and hydrolyses are also presented. It is also the purpose of this paper to elucidate the scope and limitations of the MW tool.

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