

Newer developments in the microwave-assisted synthesis of potentially biologically active organophosphorus compounds

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ABSTRACT:

The microwave (MW) technique has become an important tool in organophosphorus chemistry. In this paper, the advantages of MWs in different reactions are surveyed allowing green chemical accomplishments. The first case is the MW-assisted direct esterification of phosphinic and phosphonic acids to phosphinates and phosphonates, respectively. These reactions do not take place on conventional heating. The higher enthalpy of activation may be overcome only by MW activation. It was also observed that the esterifications became more efficient in the presence of an ionic liquid catalyst. The phase transfer catalyzed (PTC) O-alkylation of phosphonic acids under MW irradiation is another option for the esterification. The opposite reaction, the acidic hydrolysis of the above mentioned P-esters were carried out under optimized conditions both on conventional heating, and on MW irradiation. Both steps of the hydrolysis of phosphonates were characterized by pseudo first order rate constants. The second step was found to be the rate determining. MWs may substitute

catalysts, such as in the Kabachnik–Fields condensations of amines (even carboxylic acid amides), aldehydes and $>P(O)H$ reagents to afford α -aminophosphonic derivatives. 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 via its tautomeric $>POH$ form. The products, arylphosphonates and arylphosphine oxides were obtained in good yields. Pd- and Ni-catalyzed cases are of interest, on the one hand, from the point of view of the nature of the catalysts that were found to be of type “ $P2Pd(0)$ ” and “ $P2Ni(0)$ ”, respectively, on the basis of experiments and theoretical calculations.

On the other hand, the Ni-catalyzed variation was found to take place via a new mechanism assuming a $Ni(II) \rightarrow Ni(IV)$ transition instead of the generally assumed $Ni(0) \rightarrow Ni(II)$ protocol. The Pudovik reaction of aldehydes and $>P(O)H$ reagents may be performed under MW irradiation or simply thermally to furnish α -hydroxyphosphonates of potential biological activity. Dronic acid derivatives used as drugs against osteoporosis were obtained by the optimized reaction of the corresponding substituted acetic acids with phosphorus trichloride/phosphorous acid in methanesulfonic acid/sulfolane. A few reactions mentioned above, e.g. esterifications, as well as alcoholyses were also performed under optimized MW-assisted flow chemical accomplishments. These variations were more efficient than the batch realizations.

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