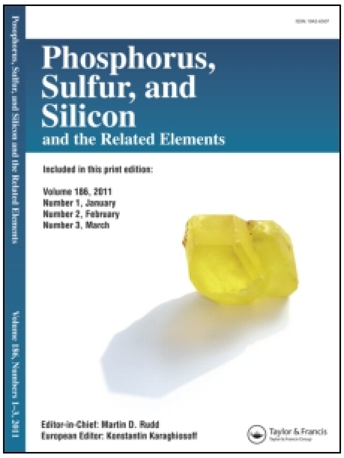

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Microwave Irradiation as a Useful Tool in Organophosphorus Syntheses

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Microwave Irradiation as a Useful Tool in Organophosphorus Syntheses

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Application of the microwave technique offers advantages in organophosphorus chemistry, such as in the Kabachnik–Fields reaction, in Diels–Alder cycloadditions, in an inverse Wittig-type reaction, and in fragmentation-related phosphorylations.

Keywords Diels–Alder reaction; fragmentation-related phosphorylation; inverse Wittig reaction; Kabachnik–Fields reaction; microwave

INTRODUCTION

In the last decade, microwave (MW)-assisted accomplishment of syntheses has become widespread.[1–3] MW-promoted reactions offer a number of advantages as compared to those carried out under traditional thermal heating. Such advantages are the much shorter reaction times and, in most cases, the selectivity.

There are reactions that do not take place upon heating, only upon MW irradiation. These days the application of the MW technique has attracted considerable industrial interest.[4,5] A typical accomplishment is when a MW-assisted reaction is carried out without the use of any solvent. This means an additional advantage from a green chemical point of view. The combination of the MW technique with a phase

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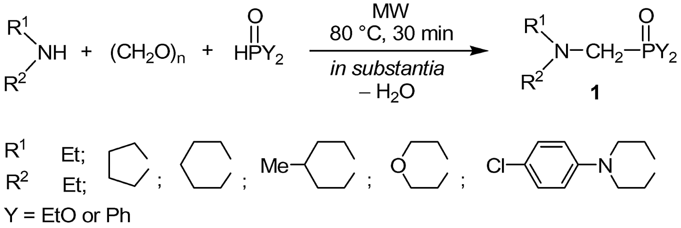
transfer catalytic method may also be beneficial.[6] In special cases, it was found that the phase transfer catalyst may be substituted by MW irradiation.[7,8] It has been a challenge for us to utilize the MW technique in organophosphorus chemistry. This field has not yet been studied in detail.

RESULTS AND DISCUSSION

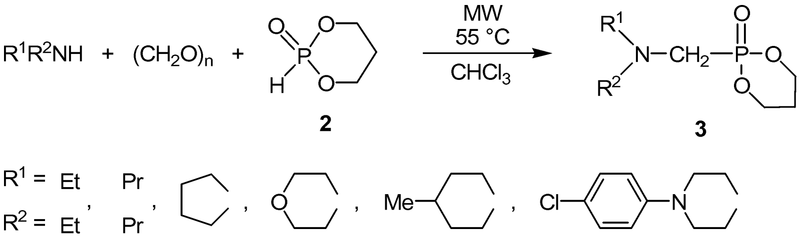
First, the Kabachnik–Fields (or phospha-Mannich) condensation of secondary amines including *N*-heterocycles, paraformaldehyde, and >P(O)H species that affords the corresponding α-aminomethylphosphonates and α-aminomethylphosphine oxides (**1**) was studied under MW and solventless conditions (Scheme 1).[9]



SCHEME 1

The products (**1**) were obtained efficiently and in a fast reaction.

A cyclic H-phosphonate, 1,3,2-dioxaphosphorine oxide **2** was also utilized in the phospha-Mannich reactions (Scheme 2).[10] In this case, the use of a solvent prevented the formation of by-products.

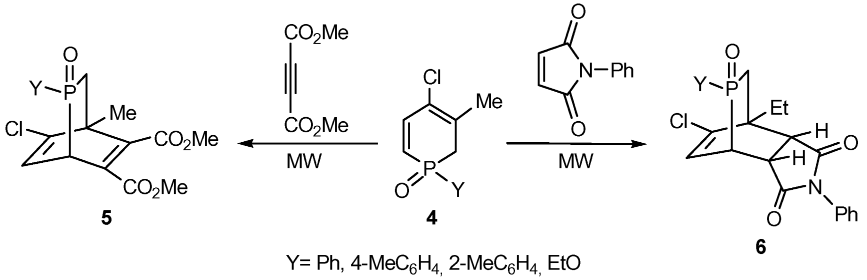


SCHEME 2

The corresponding α -aminomethyl-P(O)< derivatives (**1** and **3**) were obtained in 50%–90% yields. The products are important from the point of view potential biological activity.[11]

Further efforts to extend the scope of the phospha-Mannich reaction and to prove that no catalyst is needed to promote three-component condensations were also described.[12]

The Diels–Alder cycloaddition of 1,2-dihydrophosphinine oxides (**4**) with dienophiles, such as dimethyl acetylenedicarboxylate (DMAD) or *N*-phenylmaleimide, was highly promoted by MW irradiation at 110°C, again in a solvent-free accomplishment. Using three equivalents of DMAD, the reactions were complete in 30 min. As a comparison, under thermal conditions the reaction time was 16 h. The 2-phosphabicyclo[2.2.2]octadiene and the phosphabicyclo[2.2.2]octene oxides (**5** and **6**, respectively) were obtained in almost quantitative yields (Scheme 3).[13] No polymerization side-reactions of the components decreased the outcome.

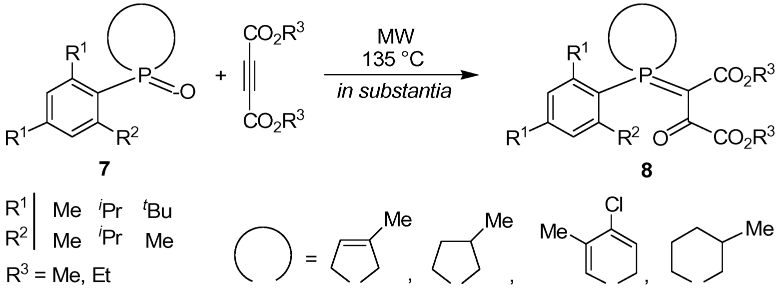


SCHEME 3

It was found that if the MW promoted cycloadditions are carried out in solvents, an onium salt additive may increase the rate of the reaction. The presence of ca. 4% of an onium salt, e.g., triethylbenzylammonium chloride, increased the energy uptake of the reaction medium.[14]

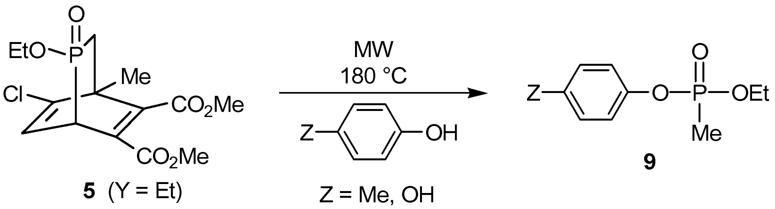
The inverse Wittig-type reaction of 1-(2,4,6-trialkylphenyl) cyclic phosphine oxides (**7**) and dialkyl acetylenedicarboxylate results in the formation of the corresponding β-oxophosphoranes (**8**).[15,16] The novel reaction is, however, rather slow, as the completion requires 10 days at 150°C. Application of MW without the use of any solvent brought a real breakthrough, as there was an 80-fold acceleration aside from the much better efficiency. Moreover, aryl derivatives otherwise unreactive under traditional heating could also be involved in the reaction under discussion (Scheme 4).[17]

Scheme 3 shows the MW-assisted synthesis of bridged P-heterocycles (**5** and **6**) that can undergo fragmentation on photolysis or on thermolysis. If there is an alcohol, phenol, or amine in the mixture, the low-coordinated methylenephosphine oxide [(YP(O)(CH_2)] ejected phosphorylates from the nucleophile.[18] The thermal conditions involve high



SCHEME 4

temperature (at around 230–240°C), at which the phosphorylations are not too efficient. To overcome this problem, the fragmentation-related phosphorylations were carried out under MW conditions. The MW-promoted fragmentation of the P-ethoxy–substituted precursor (**5**) in the presence of a fivefold excess of cresole or hydroquinone led to phosphonate **9** in a clear-cut and efficient reaction (Scheme 5).



SCHEME 5

Elaboration of possible extensions is in progress. It is also a task for us to investigate MW-assisted syntheses in ionic liquids. Phosphorus-containing imidazolium and onium salts form a representative group within ionic liquids.[19]

CONCLUSION

To summarize our results, the use of the MW technique offers advantages in organophosphorus syntheses. The benefits include fast, neat, and selective transformations with high yields under environmentally friendly conditions.

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