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Effect on Cycloaddition Reactions of Aqueous Micellar Systems formed by Amphiphilic Imidazolium Ionic Liquids †

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Abstract: The micellar effect on a Diels-Alder reaction (DA) was analyzed taking advantage of the property presented by Ionic Liquids (ILs) based on 1-alkyl-3-methylimidazolium cations by having amphiphilic character when the alkyl group is a long hydrocarbon chain -12 carbon atoms [C_{12}mim]-. These ILs can act as surfactants forming micelles in aqueous solution. The reactive system studied consists of nitrofuran and isoprene which allows obtaining benzofuran through green synthetic strategie. These "new microheterogeneous systems" would allow a better solubilization of non-polar substrates and to adopt reaction conditions softer than the traditional thermal.

Keywords: Ionic Liquids; Imidazolium cation; Diels-Alder; micelles

1. Introduction

In recent years, chemists have tried to adapt chemical reactions to meet the principles of Green Chemistry [1]. In this direction our challenge is to take advantage of specific behaviors observed in Ionic Liquids (ILs) and transform them into a benefit on a particular reactive process [2]. An interesting medium for the development of reactions in the framework of Green Chemistry are the ILs with amphiphilic character. In this sense, ILs based on 1-alkyl-3-methylimidazolium cations specifically with a 12-carbon hydrocarbon chain [C_{12}mim] form micelles in aqueous solution. These microheterogeneous "new systems" would allow, in addition to better solubilization of non-polar substrates, to adopt softer reaction conditions [3,4].

In particular, for the polar Diels-Alder (DA) reaction one of the most relevant aspect is its dependence on the solvent. Generally, in this type of reactions, little polar organic compounds are involved. This is an inconvenience because molecular solvents are required as a reaction medium, which are highly polluting and toxic. In this direction and as an alternative to traditional solvents, the ILs with amphiphilic character arise. These characteristics cause the organization of this type of ILs in micelles in aqueous solution. In this way, new surfactants to the traditional ones are presented expanding the spectrum of applications such as micellar catalysis, solubilization, protein folding and drug transport, etc.

In this sense, our objective is to analyze the effect of the micellar medium on a DA cycloaddition reaction taken as a reference, the reaction of 2-nitrofuran and isoprene was taken as the model system because they generate benzofurans which are precursors of agrochemicals.

2. Results and Discussion

Preliminary studies have shown that 2-nitrofuran acts as a dienophile in thermal DA reactions with normal electron demand by using conventional reaction media [5].

In order to optimize an aqueous reaction medium by implementing micellar systems, *N*,*N*-dodecylmethylimidazolium bromide ([DoMIm][Br]) was worked on, its synthesis was carried out in our work group following the methodology reported [6].

In addition, it has been shown that the presence of the dialquilimidazolium group as well as polar head and counter in various ILs allows the formation of micelles. In this sense, the effect of aqueous micellar systems formed by *N*,*N*-dodecylmethylimidazolium bromide [DoMIm][Br] in a reference cycloaddition DA reaction was analyzed.

In this work, the reactive system tested consists of 2-nitrofuran and 2-methyl-1,3-butadiene (isoprene); this cycloaddition reaction generates adducts which are precursors of agrochemicals.

Cycloaddition reactions were carried out in a glass reactor equiped with magnetic stirring. Variables such as diene:dienophile ratio and temperature among the most important were optimized.

1 mmol of 2-nitrofuran, 4 mmol of isoprene and [DoMIm][Br] were used at a critical micellar concentration (CMC) of 1×10^{-2} M. The reactions were developed at different temperatures (90 y 120 °C) during 48 hours (Table 1).

After the reaction time was over, the products were extracted with ethyl acetate and purified using classical column chromatography using silica gel as stationary phase and hexane-ethyl acetate mixtures as eluent. The reaction products were analyzed be spectroscopic methods.

The results obtained were compared with those of thermal cycloaddition reactions performed with conventional media (Table 1) [5]. These conditions are softer than traditional thermals reported.

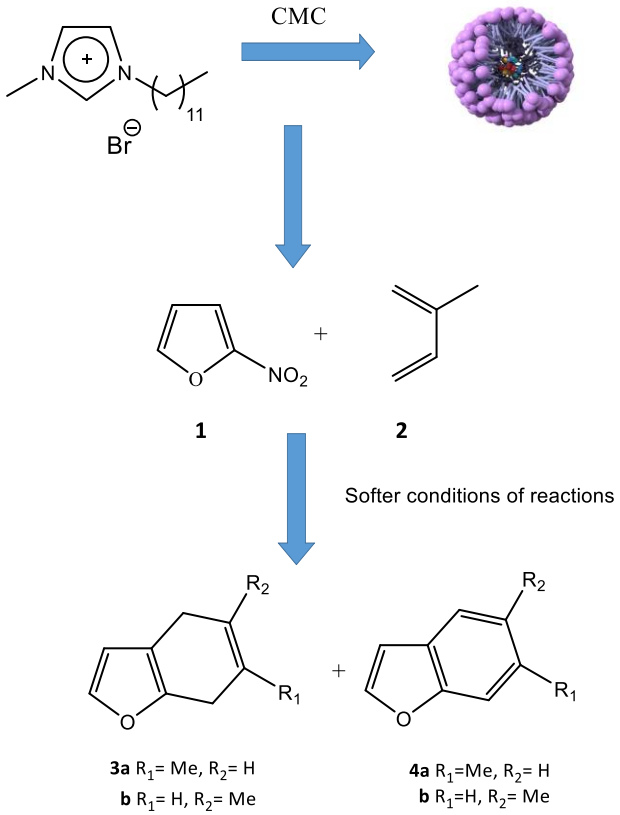

Figure 1. Diels-Alder reaction in a micellar solution of [DoMIm][Br].

Table 1. DA reactions of 2-nitrofuran with isoprene.

Reaction Media	Diene/Dienophile Ratio	Conditions	Products	Yield %
Benzene anh.	12:1	200 °C/72 h	3a,b; 4a,b	38%
Benzene anh.	12:1	150 °C/72 h	3a,b; 4a, b	30%
[DoMIm][Br]/H_2O[a]	4:1	120 °C/48 h	3a,b; 4a,b	32%
[DoMIm][Br]/H_2O[a]	4:1	90 °C/48 h	3a,b; 4a,b	15%

[a] CMC: Critical Micellar Concentration.

3. Conclusions

The micellar system selected as a reaction medium turned out to be potentially effective since, although the yields obtained in the working conditions are slightly less than those reported when using molecular solvents, very high temperatures, high excess of diene. The synergy achieved with micelles derived from ILs and the DA reaction leads to the development of reaction conditions framed within the principles of Green Chemistry.

These micro-heterogeneous "new systems" would allow for better solubilization of non-polar substrates, adopt softer reaction conditions.

In addition, the results obtained will contribute to a better understanding of the effects of the environment in these reactions of utmost synthetic importance.

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