

Proceeding Paper

Comparative Study of the Effects of Aqueous Micellar Media Formed by Amphiphilic Ionic Liquids and Conventional Surfactants on Reactions of Synthetic Interest [†]

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Abstract: For polar Diels-Alder (DA) reactions one of the most relevant aspects is its dependence on the reaction media so in this work the objective is to analyze the effect of aqueous micellar systems on the synthesis of compounds of biological interest. Based on the system formed by isoprene and 2-nitrofurane, the experiments were carried out in micellar media formed by amphiphilic ionic liquid (*N,N*-dodecylmethylimidazolium bromide) and by conventional surfactants (SDS and CTAB). In this sense, there are few studies that involve DA reactions in micro-heterogeneous systems. The challenge is to have the knowledge about the behavior of ILs in order to take advantage of all their potentialities in order to replace a toxic molecular solvent with ILs that allows developing a methodology framed within the concepts of Green Chemistry.

Keywords: ionic liquids; amphiphilic; micelles; Diels-Alder

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1. Introduction

The development of high-efficiency synthetic methodologies that can be used in the construction of carbogenic and heterogenic skeletons corresponding to compounds with high pharmacological and/or biological applicability represents a unique attraction of chemistry organic. In this direction it can be thought that the incorporation into synthesis schemes of a series of cycloaddition reactions makes it possible to achieve a broad development and great potential, especially for its “economy in stages” [1].

Due to the synthetic applicability of cycloaddition reactions there is a continuing interest in their exploration and in the study of simple strategies for the synthesis of very diverse molecules.

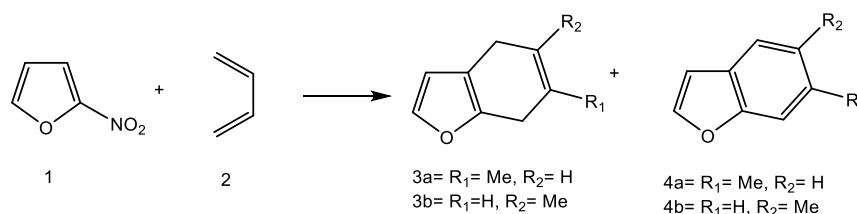
The exploration of new, more environmentally friendly reaction conditions such as the use of non-conventional solvents will, among others, reduce or eliminate the use of organic solvents and optimize the consumption of all reagents used in reactions.

Given our experience in cycloaddition reactions of the Diels-Alder type (DA) we have extended our studies developed in molecular solvents to ionic liquids (LIs) [2]. The DA reaction is of great value in organic synthesis and is a key step in the construction of compounds containing six-membered rings. Studies have appeared reporting beneficial effects of micellar systems on the yield of DA reactions [3]. Solubilization of the DA reaction partners in the micelles could offer a solution for improving the otherwise limited solubility of diene and dienophile in water. In this sense, we have started studies of these reactions in ILs with amphiphilic character of the type: Crnim. For the maleic anhydride/isoprene reactive pair in these micellar systems good yields at room temperature

and 24/48 h were obtained [4]. Due to these results, it is of interest to expand these reaction media to other systems such as 2-nitrofuran and isoprene. In this direction, there are few works involving DA cycloaddition reactions in micro-heterogeneous systems. In this regard and for comparative purposes, the objective is to analyze the effect of aqueous micellar systems formed by *N,N*-dodecylmethylimidazolium bromide [DoMIm](Br) in a polar DA reaction taken as a reference, as well as in aqueous micellar systems formed by conventional surfactants such as sodium dodecyl sulphate (SDS) and hexadecyltrimethylammonium bromide (CTAB).

2. Results and Discussion

LIIs are 'more than an ionic solvent', their role within a physico-chemical system is far from passive, leaving behind the traditional thinking of 'dissolving solutes' or 'homogenizing' a reaction medium. That is why our working group has long been committed to developing experiences with aqueous reaction media in which micelles are generated from ILs with an amphiphilic character. The reaction under study is a polar Diels-Alder cycloaddition, which is taken as a reactive model for its synthetic relevance. The reactive pair consists of isoprene 1 and 2-nitrofuran 2 (Scheme 1).



Scheme 1. Diels-Alder reaction in micellar solution.

This system was put to react in different micellar aqueous media generated with LIIs amphiphilic *N,N*-dodecylmethylimidazolium bromide ([DoMIm][Br]) and conventional surfactants as sodium dodecyl sulfate (SDS) and cetyltrimethylammonium bromide (CTAB) for comparative purposes. (Figure 1).

For ([DoMIm][Br]), it was possible to determine the value of the CMC in the specially formed systems when the counterion is Br⁻ concluding that the organization in micelles depends not only on the length of the alkyl chain but also on the conrail, therefore an appropriate combination between the two variables is required [5].

General procedure for the Diels-Alder reactions.

The temperature, the length of the reaction, and the diene/dienophile ratio are indicated in Table 1. The micellar medium concentration employed were: SDS and CTAB (Critical Micellar Concentration CMC), [DoMIm][Br] values slightly higher than CMC were used. The Diels-Alder reaction were carried out in a glass reactor with magnetic stirring. After the reaction time was completed, the cycloadducts were extracted with ethyl acetate and purified using classical column chromatography using alumina as stationary phase and hexane-ethyl acetate mixtures as eluent [6]. The reaction products were analyzed by spectroscopic methods.

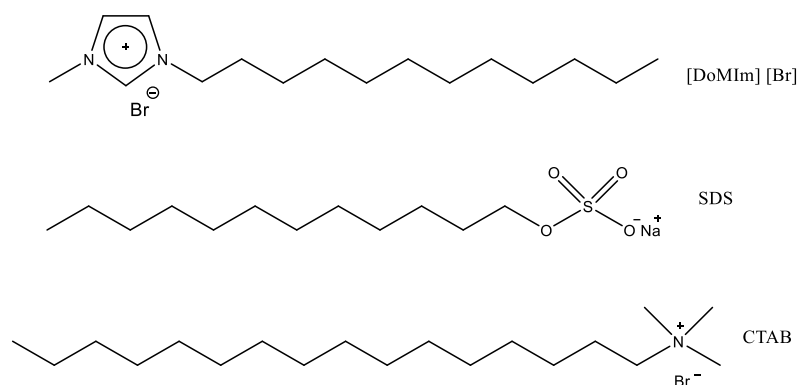


Figure 1. Micelle-forming surfactants used.

Table 1. Comparison of DA reaction in different aqueous micellar media.

Reaction Media	Diene/Dienophile Ratio	Conditions	Products	Yield %
[DoMIm][Br]/H ₂ O ^a	4:1	120°C/48 h	3a,b; 4a,b	32%
[DoMIm][Br]/H ₂ O ^a	4:1	90°C/48 h	3a,b; 4a,b	15%
[DoMIm][Br]/H ₂ O ^a	6:1	90°C/72 h	3a,b; 4a,b	20%
SDS/ H ₂ O ^b	4:1	120°C/48 h	3a,b; 4a,b	20%
SDS/ H ₂ O ^b	4:1	90°C/48 h	3a,b; 4a,b	15%
SDS/ H ₂ O ^b	6:1	90°C/72 h	3a,b; 4a,b	33%
CTAB/ H ₂ O ^b	4:1	120°C/48 h	3a,b; 4a,b	20%
CTAB/ H ₂ O ^b	4:1	120°C/72 h	3a,b; 4a,b	22%
CTAB/ H ₂ O ^b	6:1	90°C/48 h	3a,b; 4a,b	12%

^a values slightly higher than CMC (Critical Micellar Concentration); ^b CMC.

3. Conclusions

The results obtained so far indicate that the micellar system of [DoMIm][Br] produces approximately the same yields as those obtained through the use of micellar systems of traditional surfactants. These conditions are far softer than traditional thermals [6].

Decision-making to replace traditional solvents with others is a critical point of control. The challenge is to have the finished knowledge about the behavior of an LI to be able to take advantage of all its potentialities in order to replace a toxic molecular solvent with an LI that allows to develop a methodology framed within the concepts of the Green Chemistry.

Author Contributions: J.B.S.: Doctoral student responsible for the synthesis of dienophiles and to carrying out the Diels–Alder reactions using different experimental conditions. C.G.A.: Researcher responsible for the synthesis of ionic liquids, design of experiences and evaluation of results. C.D.D.R.: Researcher responsible for the design of cycloaddition reactions in aqueous media, synthesis of dienophiles and evaluation of results. All authors have read and agreed to the published version of the manuscript.

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