

Effect on Cycloaddition Reactions of Aqueous Micellar Systems Formed by Amphiphilic Imidazolium Ionic Liquids [†]

Jésica B. Soffietti, Claudia G. Adam * and Claudia D. Della Rosa *

IQAL (UNL-CONICET), Laboratorio Físicoquímica Orgánica, Facultad de Ingeniería Química, Universidad Nacional del Litoral, Santa Fe 3000, Argentina; jsoffietti@fiq.unl.edu.ar

* Correspondence: cadam@fiq.unl.edu.ar (C.G.A.); cdellaro@fiq.unl.edu.ar (C.D.D.R.);

Fax: +54-342-4571-162 (C.G.A. & C.D.D.R.)

† Presented at the 24th International Electronic Conference on Synthetic Organic Chemistry, 15 November–15 December 2020; Available online: <https://ecsoc-24.sciforum.net/>.

Abstract: The micellar effect on Diels–Alder (DA) reaction 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 [C₁₂mim]. These ILs can act as surfactants forming micelles in aqueous solution. The reactive system studied consists of nitrofurane and isoprene which allows obtaining benzofuran through green synthetic strategies. 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

Citation: Soffietti, J.B.; Adam, C.G.; Della Rosa, C.D. Effect on Cycloaddition Reactions of Aqueous Micellar Systems formed by Amphiphilic Imidazolium Ionic Liquids. *Chem. Proc.* **2021**, *3*, 142. <https://doi.org/10.3390/ecsoc-24-08338>

Published: 14 November 2020

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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 [C₁₂mim] 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].

Compounds with biological activity in nature generally include heterocycles, and for this reason it is attempted to reproduce them in synthetic form, among others for pharmacological, agrochemical, etc. [5,6]. In this regard, preliminary studies carried out on the feasibility of using dienophile aromatic rings in cycloaddition reactions concluded on the potential advantages that this strategy offers for the synthesis of these systems. Studies involving aromatic pentaheterocyclic compounds (pyrrole, furan, thiophene and selenophene derivatives), mono- and disubstituted (one of the substituents is always the nitro group) in Diels–Alder (DA) reactions with normal electron demand allowed to obtain the corresponding indoles, benzofurans, benzothiophenes and benzoselenophenes—relevant structures because of the biological interest they possess—[7].

The media of development of the polar DA reactions has been shown to be decisive, so considering the need to replace conventional solvents and develop more benign working conditions arise as potential substitutes Ionic Liquids (ILs) or systems formed by them. In this sense an interesting media for the development of reactions in the framework of Green Chemistry are the ILs with amphiphilic character.

The purpose of this research is to study the impact of a micellar reaction media on a polar DA reaction using 2-nitrofuran as dienophile and isoprene as counterpart. This reaction was taken as the model system because it generates 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 [8].

In this direction our general objective is to deepen to study as optimize cycloaddition reactions taking advantage of specific behaviour observed in ILs or systems formed by them. In particular, a micellar medium was prepared using *N,N*-dodecylmethylimidazolium bromide ([DoMIm][Br]) which is synthesized in our laboratory. In addition, it has been shown that the presence of the dialquylimidazolium 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 [DoMIm][Br] in a reference cycloaddition DA reaction was analyzed (Figure 1).

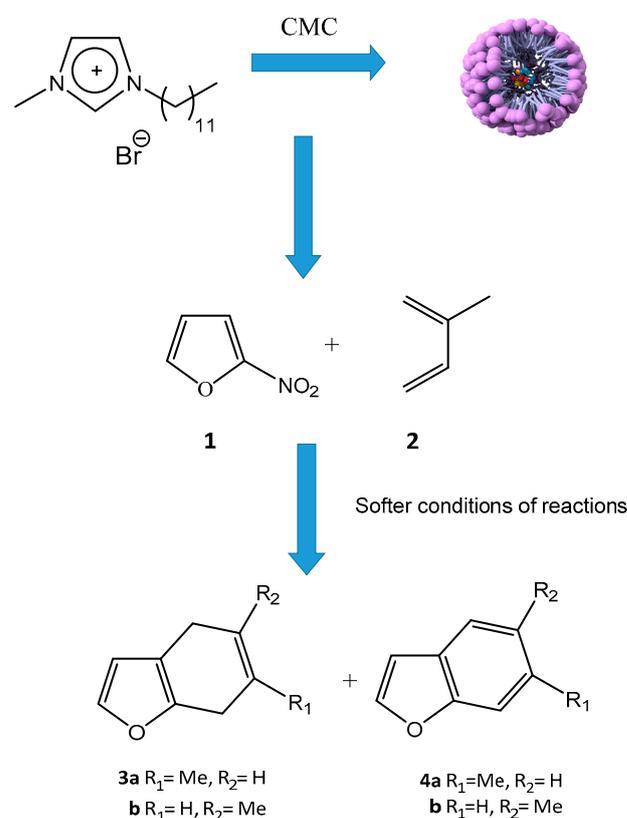


Figure 1. Diels–Alder reaction in a micellar solution of *N,N*-dodecylmethylimidazolium bromide ([DoMIm][Br]).

Cycloaddition reactions were carried out in a glass reactor equipped with magnetic stirring. Variables such as diene:dienophile ratio and temperature among the most important were optimized and [DoMIm][Br] were used at a critical micellar concentration (CMC) of 1×10^{-2} M.

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

Table 1. Diels–Alder (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 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%

^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 and 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.

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.

Funding: This research was supported by CAI+D 2016 PIC 50420150100023LI at Universidad Nacional del Litoral, Santa Fe, Argentina and Convocatoria Investigación Orientada 2016-2010-035-16 Ministerio de Ciencia, Tecnología e Innovación Productiva de la provincia de Santa Fe (ASaCTel).

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: <https://www.mdpi.com/ethics>.

Conflicts of Interest: The authors declare no conflict of interest.

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