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A kinetic study on the activating power of lithium ions on the porphyrin metallation by lanthanides and on a microwave specific effect

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Abstract

A kinetic study of the lithium ion activating effect on porphyrin metallation has been investigated using monohydroxy-tritolyl porphyrin and the lanthanides erbium and gadolinium in dimethylacetamide. The powerful, concentration-dependent, catalytic effect of lithium, observed in both cases with classical heating was considerably enhanced under microwave irradiation at the same temperature thus underscoring a specific microwave effect. ***To cite this article: R. Faure et al., C. R. Chimie 12 (2009).***

Résumé

Une étude cinétique de l'effet activateur des ions lithium sur la métallation de la monohydroxy-tritolyl porphyrine par des sels de lanthanides comme l'erbium et le gadolinium a été réalisée dans le diméthylacétamide. L'effet catalytique important du lithium, observé dans les deux cas par chauffage classique, est considérablement augmenté par l'utilisation de l'activation micro ondes à la même température. Ceci met en évidence un effet particulier micro ondes. ***Pour citer cet article : R. Faure et al., C. R. Chimie 12 (2009).***

Keywords: Porphyrins; Lanthanides; Lithium ions; Metallation; Microwaves; Kinetics

Mots-clés : Porphyrines ; Lanthanides ; Ions lithium ; Métallation ; Micro ondes ; Cinétique

1. Introduction

Lanthanide elements have found high technological interest because of their photophysical properties. Particularly important are their applications in Medical Sciences as contrast agents in NMR imaging, especially gadolinium, beginning in the early 1980s, and more recently for optical imaging of cells.

Metalloporphyrins have been extensively studied in many fields such as non-linear optics, photoelectronic conversion, and since their discovery in 1974, the lanthanide porphyrin complexes have found a growing interest. They can find applications in nuclear magnetic

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resonance contrast [1,2] or recently as a redox active tumour selective agent for the treatment of cancer [3,4]. They can also serve in polymer light emitting diodes [5] or as catalysts for polymerisation reactions [6]. Erbium and gadolinium porphyrin complexes were first synthesised by Horroks and Wong [7] and by Radzki and Giannotti [8]. All these syntheses involve long reaction times (8–18 h) at elevated temperature in high boiling solvents such as trichlorobenzene. Evaporation of the solvents and the separation are generally tedious and time consuming.

In a previous paper [9] we reported the activating effect of lithium ions on the metallation of tetraphenylporphyrin by Cu^{2+} in dichloromethane as a solvent. The enhancement of the reaction rate was considerable – more than 500-fold – in a Li^+ saturated solution. We anticipated that this activating effect would also happen in a more polar solvent such as dimethylacetamide in which much higher concentration in Li^+ could be reached.

Moreover, as it could be anticipated from the previously assumed mechanism (i.e. deformation of the porphyrin ring due to the binding of lithium ion to the macrocycle) a possible microwave specific effect could be noticed. Accordingly, when a polar species is formed as a transition state one can expect that microwave activation enhances the reaction rate [10]. This second effect added to the intrinsic catalytic effect of lithium ions, could lead to a dramatic reduction in the reaction time from several hours to a few minutes.

2. Experimental

2.1. Materials

DMA, LiCl, $Gd(acac)_3$ and $Er(acac)_3$ were obtained from Aldrich and used as received.

5-Parahydroxyphenyl 10,15,20-tritolylporphyrin (TTPOH) was synthesised according to the Little method [11] and purified on silica gel column using a $CHCl_3$ petroleum ether gradient and then by preparative thin layer chromatography. The course of the reaction was monitored on a Lambda 25 Perkin Elmer UV–vis Spectrophotometer. Reactions were activated by using a Synthewave 402 Prolabo microwave apparatus.

2.2. Kinetic studies

A stock solution of porphyrin was made at 7.4×10^{-4} mol L^{-1} and to five samples (10 mL) was added $Er(acac)_3$ or $Gd(acac)_3$ at a concentration of 2×10^{-3} mol L^{-1} in dimethylacetamide. In each sample the required quantities of lithium ions were introduced from a stock solution in DMA (0.118 mol L^{-1}). The actual concentration in monohydroxytetratolylporphyrin was monitored by UV–vis spectroscopy at 514 and 552 nm. Reactions were run under pseudo-first order kinetic conditions, with the lanthanide metal ion in a large excess over the free base porphyrin.

2.3. Classical heating

The five samples were immersed in an oil bath thermostated at 150 ± 1 °C, removed at increasing times and then quickly cooled and analysed by UV–vis spectrophotometry.

2.4. Microwave heating

Each sample was put in the reactor and activated for the stipulated time at a constant power input. In all cases the final temperature was 150 °C and verified by measuring it at the end of the experiment with a thermometer. After removing the reactor, the solution was quickly cooled and analysed by UV–vis spectrophotometry.

3. Results and discussion

3.1. Influence of the lithium ions

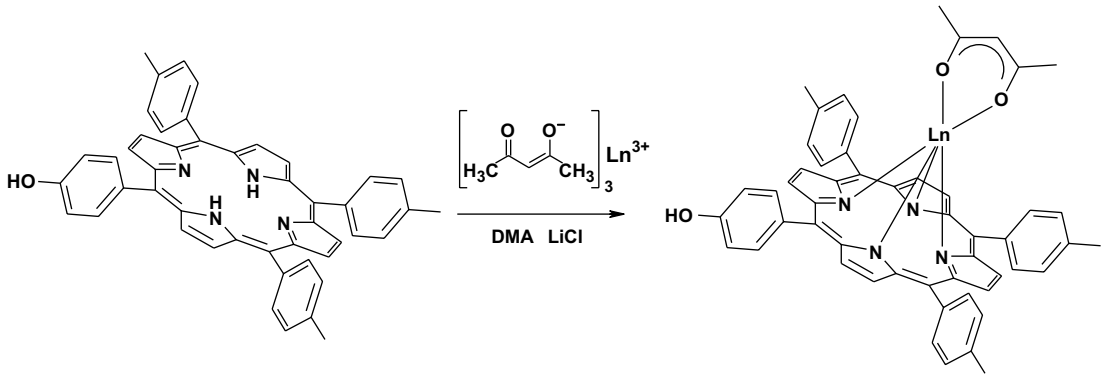
The great enhancement of the rate of porphyrin metallation by Cu^{2+} in the presence of Li^+ observed previously in dichloromethane [9] encouraged us to extend the method to lanthanide ions which are much more difficult to bind to porphyrins. The use of dimethylacetamide as a solvent permitted us to reach larger values of Li^+, up to 25 mM.

In these series of experiments the metallation reaction of the porphyrin by erbium (Scheme 1) was conducted in the presence of increasing quantities of lithium ions. Two methods of activation were used for comparison: microwave activation and classical heating.

In the case of microwave irradiation, the reaction time was fixed at 2 min which is sufficient to reach a significant reaction. The power input was maintained constant at 165 W during the reaction time. In all cases the final temperature never exceeded 150 ± 1 °C (Fig. 1).

When classical heating was employed the temperature was the same and the reaction time was 1 h in order to have a comparable yield.

The percentages of complex formed as a function of lithium concentration are plotted in Fig. 2 for



Scheme 1. Metallation reaction of hydroxy porphyrin by lanthanide acetyl acetonate.

microwave irradiation and for classical heating. During microwave irradiation complex formation is hardly detectable in the absence of Li^+ in contrast to experiments conducted under classical heating. It should be recalled that in this case the reaction time is only 2 min instead of 1 h for classical heating. When lithium is added, in the two cases we observe a linear relationship between the percentage of complex formed and the lithium concentration. The slope of the straight line is steeper in the case of the microwave activation by approximately 2-fold. So the catalytic effect of lithium is much more pronounced in the case of microwave activation. It should be noted that classical heating needs a much longer reaction time (30×) in order to reach the same yield.

These results demonstrate a considerable effect of both the lithium ions and the microwave activation on the metallation rate and yield.

3.2. Kinetics

The metallation of TTPOH was then studied at a constant concentration in LiCl in order to determine the rate constant of the reaction with the modes of activation: microwave and classical heating.

For comparison the temperature conditions were the same with classical heating and microwave activation. The oil bath was maintained at 150 ± 1 °C and the power input of the microwave reaction was chosen as to reach 150 °C (Fig. 1).

The rate of the formation of metallated porphyrin is first order with respect to porphyrin concentration at constant concentration of Li^+ and $Er(acac)_3$.

$$d[LTTPOH]/dt = -d[TTPOH]/dt = k_a[TTPOH]$$

where k_a is the apparent first order rate constant involving the metal concentration (30-fold that of the porphyrin) that could be considered constant and [TTPOH] is the actual porphyrin concentration which is proportional to $(A - A_\infty)$ values. So the plot of ln[TTPOH] versus t gives a straight line with the slope giving k_a.

3.2.1. Erbium

Erbium metallation was conducted in the presence of a constant lithium concentration (2.7 mM) in order

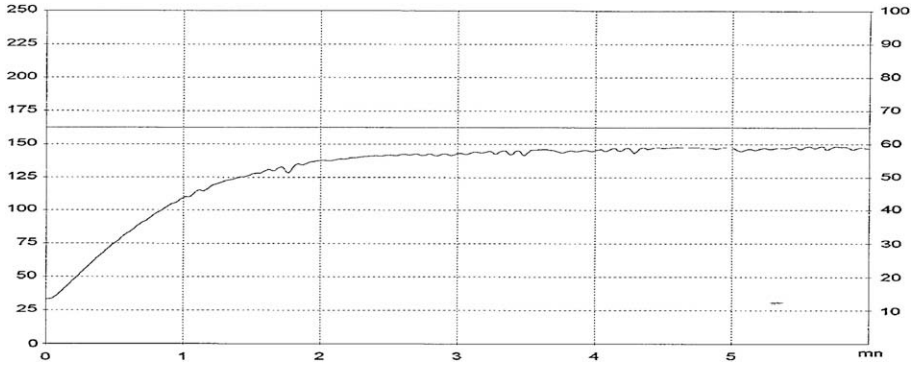


Fig. 1. Evolution of temperature inside the reaction vessel during microwave irradiation.

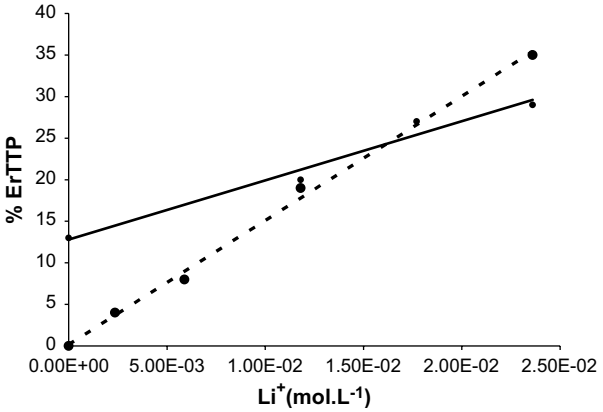


Fig. 2. Yield of erbium porphyrin complex as a function of [Li^+] added: (- - -) microwave activation, (—) classical heating.

to have sufficient reaction time (10 min) for a kinetic study (Fig. 3).

Linear relationship is observed for the plot of ln[TTPOH] versus time in the case of classical heating as well as for microwave activation.

The k_a value obtained for microwave activation, $1.25 \times 10^{-3}\ s^{-1}$, was ca. 35-fold the value for classical heating, $3.5 \times 10^{-5}\ s^{-1}$ that is a considerable enhancement of the reaction rate. It is to be noticed that the experimental conditions, temperature and pressure, are the same.

3.2.2. Gadolinium

In the case of gadolinium we increased the lithium concentration to 5.4 mM in order to have reaction times comparable to the previous experiments. As for erbium the k_a for microwave irradiation ($1.2 \times 10^{-2}\ s^{-1}$) was higher than for classical heating ($8.8 \times 10^{-4}\ s^{-1}$) but only by 14-fold (Fig. 4).

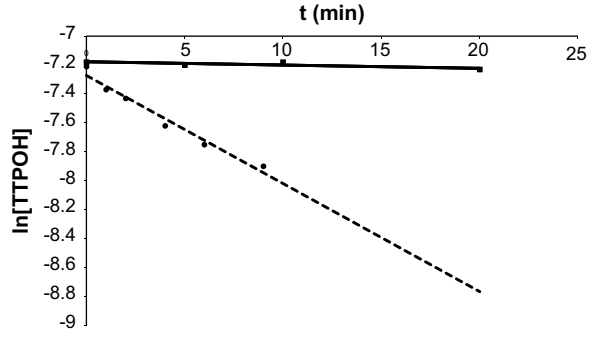


Fig. 3. Evolution of ln[TTPOH] as a function of time for erbium: (- - -) microwave activation, (—) classical heating.

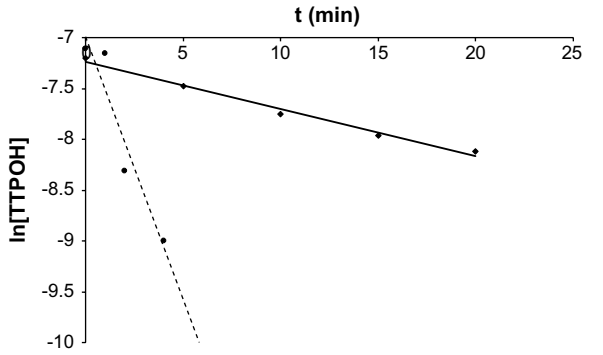


Fig. 4. Evolution of ln[TTPOH] as a function of time for gadolinium: (- - -) microwave irradiation, (—) classical heating.

Microwave irradiation exerts a strong effect on the rate constant when compared to classical heating in the same conditions of temperature and pressure. This effect is more pronounced for erbium (35-fold) than for gadolinium (14-fold). This observation could be explained by the higher hardness of Er^{3+} [12]. In this case the transition state of metallation reaction would be more polar and it has been shown previously [10] that the more polar the transition state, the more important is the microwave effect. These new findings are in accordance with the thermodynamic explanation of the so-called microwave effect.

4. Conclusion

In this study we have demonstrated for the first time a strong kinetic effect of lithium ions on the metallation of porphyrins by lanthanides in a polar solvent. This effect is concentration-dependent, which confirms the mechanism proposed previously concerning a bending of the macrocycle by the lithium ions that favors lanthanide insertion.

Moreover we clearly show in this study a specific influence of the microwave irradiation which enhances the reaction in the same carefully controlled experimental conditions.

In conclusion, we propose here an expeditious synthesis of lanthanide complexes of porphyrins with good yields obtained within 3 min, thanks to microwave irradiation, instead of 10 h for classical heating in high temperature boiling solvents which, in addition, are tedious to evaporate.

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