Ultrasound-assisted synthesis of glycoporphyrin conjugates bearing carbamate and thiocarbamate linkers.

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INTRODUCTION

Since porphyrins have been used as anticancer agents in photodynamic therapy numerous studies were dedicated to the synthesis of more efficient photosensitizers. In this field some molecules have already been elaborated through convergent synthesis strategies, specially bearing ether[1], ester[2] and triazole[3,4] linkers. Nevertheless this type of linkage could not be considered ideal for the synthesis of glycoporphyrins since deglycosylation process and decreasing of biological activity[5] have already been associated with the nature of these linkers. There are only few examples of ultrasound-assisted porphyrin synthesis. On the other hand, it is reported that this energy input method can increase the selectivity and reduce reaction time. In order to access a new method to bind porphyrins to carbohydrates we investigated the synthesis of carbamate and thiocarbamate derivates by conventional and ultrasound-assisted methods.

RESULTS AND DISCUSSION

Two new porphyrin glycoconjugates (**3** and **4**) were synthesized by conventional and ultrasound-assisted methods (Scheme 1). We were able to access one reaction condition to obtain only the thiocarbamate conjugate and another one to access only the carbamate derivate. Under ultrasound condition the reaction time was drastically reduced and the ratio between carbamate and thiocarbamate derivates was enhanced from 1.4 to 5.0 (Table 1).

Table 1. Product yield obtained by conventional and ultrasound-assisted methods.

Compound	3	4	Ratio 4:3
Conventional method 1	19 %	0	-
Conventional method 2	23 %	33 %	1.4
Conventional method 3	0	49 %	-
Ultrasound-assisted	8 %	40 %	5.0

CONCLUSION

It was found that both carbamate and thiocarbamate porphyrins can be synthesized together from hydroxyphenylporphyrin **1** and glycosyl isothiocyanate **2**. The reaction condition was mandatory to the reaction selectivity.

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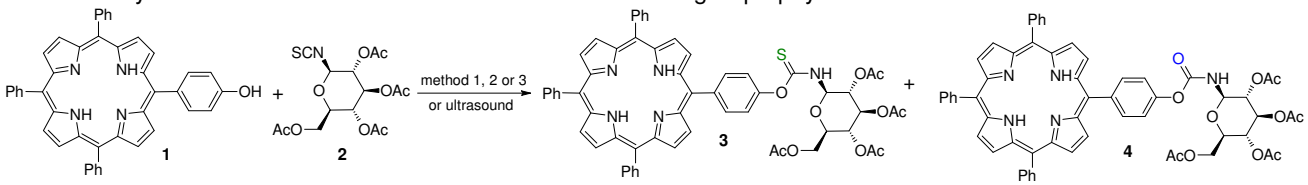
Scheme 1. Synthesis of thiocarbamate derivate **3** and carbamate glicoporphyrin derivate **4**.



Method 1: 60º C, 48 h; **Method 2:** triethylamine, 60º C, 48 h; **Method 3:** triethylamine, NaOH, 60º C, 48 h; **Ultrasound-assisted method**: triethylamine, 42 kHz, 1 h.