Microwave irradiation and DMC: a potent combination for the synthesis of 2-arylamino-3-tritylsulfanyl-propionic ethyl ester

Stephanie Amarillis E. Santo, Luiz S. Longo Jr., Adriana Karla C. Amorim Reis*

Instituto de Ciências Ambientais, Químicas e Farmacêuticas – Universidade Federal de São Paulo
Rua Prof. Artur Riedel, 275, Diadema, SP, Brazil, CEP 09972-270
*e-mail corresponding author: adriana.amorim@unifesp.br

Keywords: HIV-Protease, Microwave, Coupling Reactions

INTRODUCTION

HIV-1 protease (HIV-1-PR) has a critical role in the life cycle of HIV-1. In order to reduce the overall viral replication, an attractive alternative is to improve the pharmacological properties, pharmacokinetic and safety profiles of the potential therapeutic anti-proteases drugs (PAs), such as Nelfinavir (II) (antiretroviral drug).

This work reports our preliminary results obtained in the synthesis of N-(1-hydroxy-3-mercaptopropan-2-yl)aryl-amides (I) via the coupling reaction of N-(1-hydroxy-3-mercaptopropan-2-yl)aryl-amides with benzoic acid derivatives using classical as well green solvents.

RESULTS AND DISCUSSION

The 2-arylamino-3-tritylsulfanyl-propionic ethyl esters (VI) were prepared following the reaction pathway showed in Scheme 1.

Scheme 1

Several benzoic esters derivatives (VI) were obtained from the coupling reaction between IV and benzoic derivatives acids using DCC as coupling reagent and CH₂Cl₂ or dimethylcarbonate (DMC) as solvents, under microwave irradiation. The results obtained for these reactions are summarized in Table 1.

Table 1. Results of the coupling reactions for N-(1-hydroxy-3-mercaptopropan-2-yl)aryl-amides IV with benzoic acid derivatives V using DCC and MW irradiation.

<table>
<thead>
<tr>
<th>Entry</th>
<th>(R)</th>
<th>Solvent (% yield)</th>
<th>CH₂Cl₂</th>
<th>DMC</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>H</td>
<td>63</td>
<td>66</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>O-OMe</td>
<td>70</td>
<td>51</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>M-OMe</td>
<td>79</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>P-OMe</td>
<td>77</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>O-NO₂</td>
<td>62</td>
<td>55</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>M-NO₂</td>
<td>20</td>
<td>47</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>P-NO₂</td>
<td>49</td>
<td>66</td>
<td></td>
</tr>
</tbody>
</table>

All compounds were obtained in 20-78% yields in CH₂Cl₂ and 30-66% in DMC, being characterized by NMR and LC-MS techniques.

CONCLUSION

We demonstrated that the compounds VI can be efficiently prepared by DCC-mediated coupling reaction of amines and acids in green solvent DMC, using MW irradiation. From our results, it is possible to conclude that DMC is a potential substitute for dichloromethane in amide-forming reactions using common amide coupling reagent, DCC.

ACKNOWLEDGEMENTS

We are grateful to CNPq, Fapesp and Capes.

REFERENCES

2 Padrige, W. M. Ad. Drug Deli. Re. 1995, 15, 5