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

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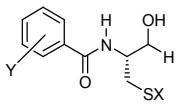
INTRODUCTION

HIV-1 protease (HIV-1-PR) has a critical role in the life cycle of HIV-1.[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).[2,3]

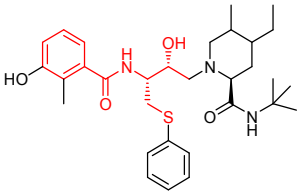
This work reports our preliminary results obtained in the synthesis of *N*-(1-hydroxy-3-mercaptopropan-2-yl-arylamides (**I**) *via* the coupling reaction of N-(1-hydroxy-3-mercaptopropan-2-yl)aryl-amides with benzoic acid derivatives using classical as well green solvents.



(**I**)

X = H e NO

Y = o-MeO, m-MeO e p-MeO, H, o-NO_2, m-NO_2 e p-NO_2



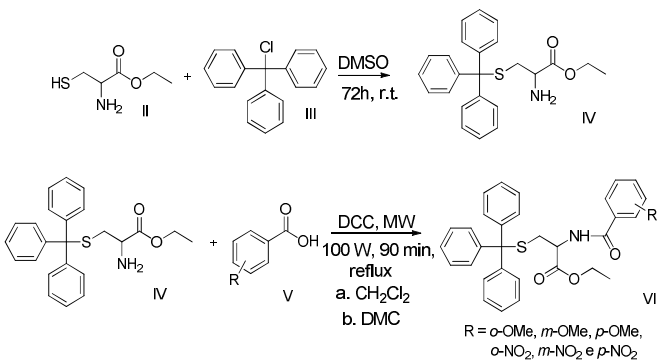
(**II**)

Nelfinavir

RESULTS AND DISCUSSION

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

Scheme 1



Protection of *L*-cysteine ethanoate (**II**) with trityl chloride (**III**) in DMSO led to **IV** in 74 % yield after 4 days.[4]

Several benzoic esters derivatives (**VI**) were obtained from the coupling reaction between **IV** and benzoic derivatives acids using DCC as coupling reagent and CH_2Cl_2 or dimethylcarbonate (DMC) as solvents, under microwave irradiation.[5] 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.

Entry	(R)	Solvent(% yeald)	
		CH_2Cl_2	DMC
1	H	63	66
2	*o*-OMe	70	51
3	*m*-OMe	79	30
4	*p*-OMe	77	50
5	*o*-NO_2	62	55
6	*m*-NO_2	20	47
7	*p*-NO_2	49	66

All compounds were obtained in 20-78% yields in CH_2Cl_2 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.

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