New approach of side chain *N*-acylation and *C*-oxidation reactions of CF_3-containing 7-amino-8-methylquinolines

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INTRODUCTION

Compounds containing the –CO–N(R)–CO– function have shown a variety of important pharmacological properties, particularly acting as anticonvulsants.[1] On the other hand, quinoline ring systems deserve special interest.[2] We can also highlight that the class of five-membered heterocycles as oxazolidinones, pyrrolidin-2,5-diones and thiophenes derivatives attract considerable attention due to the broad range of pharmacological properties and their chemical applications.[3] So, considering the great biological importance and employment of amino-heterocycles as starting material for the synthesis of new heterocycles, the purpose of this work is to report the results of an investigation of the chemical behavior of 7-amino-8-methylquinolines in side chain *N*-acylation and *C*-oxidation reactions.

RESULTS AND DISCUSSION

N-Acylation reactions carried out with the compounds **1a-d** allowed us to obtain the (*N*-acetyl)acetamide- (**3a-d**) instead of the *N*-acetylamino-quinoline (**2a-d**) derivatives (Figure 1).[4,5] When the compounds **1a-d** were treated with trifluoroacetic anhydride only monotrifluoracetyl substituted quinolines (**4a-d**) were isolated. Figure 2 outlines the synthesis of tri-heterocyclic systems from reactions of **1d** with: *i*) (2-bromoethyl) chloroformate; *ii)* phthalic anhydride; *iii*) succinic acid dichloride. *C*-Oxidation of the compound **3d** leading to product **10d** in 79 % yield (Figure 3), with potential use as a block precursor to promote the synthesis of other poliheterocyclic systems from reactions with several nucleophiles.

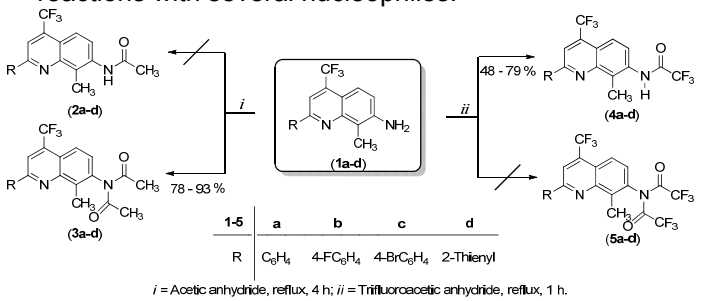

Figure 1. *N*-Acylation reactions.

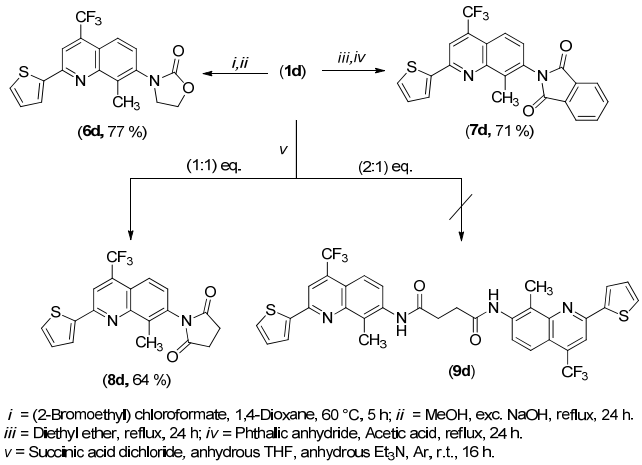

Figure 2. Synthesis of tri-heterocyclic systems.

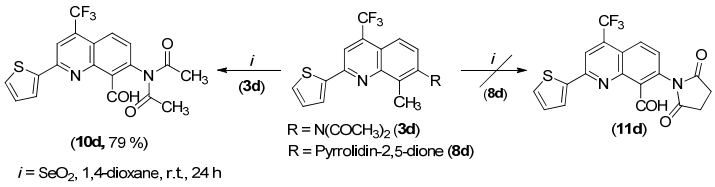

Figure 3. *C*-Oxidation reactions.

CONCLUSION

We demonstrated the versatility of the 7-amino-8-methylquinolines (**1**) as blocks precursors to promote the synthesis of CF_3- and heteroaryl-substituted heterocycles by simple, highly efficient and inexpensive routes. Furthermore, the possibility of *C*-oxidation of the compound **3d** containing two acetyl groups attached to the nitrogen atom in β-position to the CH_3 substituent.

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