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A Novel Method for the *N*-Acylation of (4R, 5S)-1,5-Dimethyl-4-phenylimidazolidin-2-one

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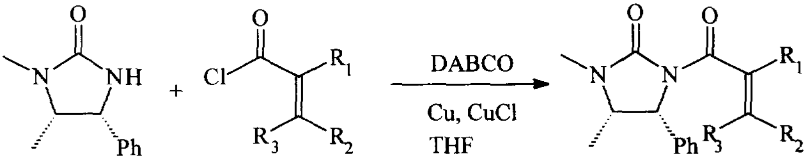
Abstract: An efficient synthesis of *N*-Acylimidazolidinones derived from α,β–unsaturated acid chlorides using DABCO as the base is described. Copyright © 1996 Published by Elsevier Science Ltd

N-Acylimidazolidinones have been used in various asymmetric catalytic studies due to their bidentate chelating properties.[1] In addition to this, these auxiliaries are readily prepared from low cost, naturally occurring starting materials, they are highly crystalline, facilitating purification and this allows for further kinetic resolution of the products. Also, the positioning of the bulky directing group is ideally situated in relation to the reactive site on the ring structure.

We have reported the efficiency of *N*-acylimidazolidinone auxiliaries as powerful face-selective dienophiles in Lewis acid catalysed Diels-Alder cycloaddition reactions.[2] However, difficulties which resulted in low yields, were encountered during the *N*-functionalisation of the title auxiliary with various α,β–unsaturated acyl chlorides according to published procedures.[3] Low yields were attributed to Michael-type additions taking place between the acyl chloride and the amide of the auxiliary, as well as polymerisation of the acyl chlorides themselves.

We now report a new route to *N*-acylimidazolidinones which is practical, economic and highly efficient. (Scheme 1).



Scheme 1

The successful preparation method requires the proper choice of base and the addition of CuCl and copper powder. The precise role of the copper remains to be established, but it is thought to prevent polymerisation of the α,β–unsaturated acid chlorides during the reaction and during workup.[3] The choice of base was 1,4-Diazabicyclo[2,2,2]octane (DABCO). This tertiary amine is a sufficiently strong base to abstract the amide proton of the auxiliary, but it is not able to cause epimerisation of the auxiliary's innate chiral centres.

Reaction conditions are thus simple, mild and favourable for the preparation of α,β–unsaturated imides in almost quantitative yields.(Table 1).

Table 1. Yields of Dienophiles obtained on *N*-Acylation of Imidazolidinone.

Dienophile [a]	Yield [%]
R_1, R_2, R_3=H	98
R_1, R_3=H, R_2=Me	96
R_1=Me, R_2, R_3=H	57
R_1=H, R_2, R_3=Me	95
R_1, R_3=H, R_2=Ph	98

[a] Dienophiles were characterised by ^1H and ^{13}C NMR spectroscopy and by GC/MS.

A typical reaction procedure is as follows: (4R, 5S)-1,5-dimethyl-4-phenylimidazolidin-2-one (0.30g, 1.58mmol) and DABCO (0.23g, 2.05mmol) were left to stir in anhydrous THF for 30 minutes at room temperature before Cu powder (0.10g, 1.58mmol) and CuCl (0.16g, 1.58mmol)) were added. The appropriate, freshly distilled acyl chloride (2eq, 3.16mmol) was then added slowly and the reaction mixture was left to stir overnight. The THF was removed under reduced pressure and purification was achieved by running a 2cm column using basic alumina and eluting with dichloromethane. Removal of the solvent under reduced pressure yielded the product as fine white crystals which were recrystallized from dichloromethane. A useful asset of this procedure is that there is no need for aqueous workup. Low yields obtained using methacryloyl chloride were attributed to the fact that polymerisation of the acyl chloride could not be prevented.

In conclusion, we have demonstrated a very simple and efficient procedure for the *N*-acylation of imidazolidinones and we expect that this will increase the use of these auxiliaries in further diastereoselective processes.

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