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Platinum-catalysed synthesis of trichloroamidines

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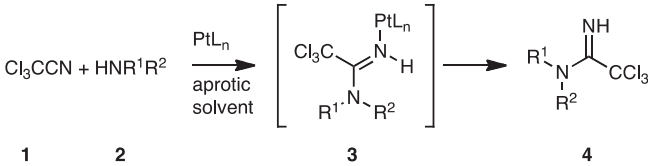
ABSTRACT

A mild platinum-catalysed method for the formation of free amidines from the reaction of amines and trichloroacetonitrile in nonpolar solvents has been developed. This protocol provides access to novel amidines that in some cases (**4b–d**) cannot be synthesised via the direct reaction of amines and halogenated nitriles.

Amidines are a useful class of compounds that have been exploited in a number of disparate fields including catalysis,[1,2] medicinal chemistry,[3] materials science[4] and as switchable solvents[5]/surfactants.[6] Traditional methods for the synthesis of amidines include nucleophilic addition of an amine to a protic or Lewis acid activated nitrile.[7,8] It has also been shown that nitriles that are activated by strong electron-withdrawing groups, such as trifluoro- or trichloroacetonitrile, will react directly with amines to form amidines.[9] This reaction is generally carried out in alcoholic or aqueous solvents and the product amidines are isolated as their corresponding hydrochloride salts. Additionally, tris(dimethylphosphinito)platinum hydride was shown to catalytically activate acetonitrile for the formation of a mixture of mono- and bis-amidines when reacted with *n*-propyl amine at 160 °C in DME.[10] Herein, we report the ability of simple platinum salts to catalytically activate trichloroacetonitrile towards the addition of amines for the formation of free amidines under mild conditions.

Our preliminary investigation was focused on the ability of simple platinum salts to activate trichloroacetonitrile **1** towards the addition of primary and secondary amines **2** in nonpolar solvents in order to form free amidines **4** directly (Scheme 1). It was envisaged that the platinum species would co-ordinate to the nitrile, thus activating it towards addition of the amine nucleophile to form an intermediate platinum bound amidine species **3**. The in situ formed trichloroamidine **3** would not be a strong ligand for the metal due to the electron-withdrawing nature of the halogens, and it would thus undergo ligand exchange with the starting material, leading to catalyst turnover. In contrast, it has been shown that more electron-rich platinum–amidine complexes can be synthesised and isolated via a two-step process.[11]

Thus, the addition of a range of primary and secondary amines to trichloroacetonitrile in the presence of platinum(II) chloride was used to assess the feasibility of this approach (Scheme 2). It was found that reaction of 2.2 equiv of trichloroacetonitrile with a primary or secondary amine in the presence of 10 mol % platinum(II) chloride in dichloromethane at room temperature afforded the desired amidines in good yields after isolation and purification.[12] For example, subjecting diethylamine to the reaction conditions gave amidine **4a** in 67% yield after isolation and purification. Secondary dialkylamines with longer alkyl chains gave the desired amidines **4b–d** as a mixture of geometric isomers in good yields. These results are in contrast to a previously reported uncatalysed process, which afforded the product of chlorine substitution.[10] Cyclic amines also gave the desired amidines **4e**,**f** in good yields. Additionally, the primary amines, benzylamine and *t*-butylamine, afforded amidines **4g** and **4h**, respectively. For benzylamidine **4g**, the double bond isomerised to form the more substituted imine. Unfortunately, no reaction was observed when the less nucleophilic amine aniline was used at room temperature. Control experiments in which the platinum species was omitted from the reaction mixture afforded the desired amidines **4a** and **4g** in significantly decreased yields under otherwise identical conditions.[13] Finally, trichloroacetonitrile was reacted with *N*-allylmethylamine under the standard conditions to afford allylamidine **4i** as a single geometric isomer, though the configuration of the isomer was not



Scheme 1. Proposed platinum-catalysed synthesis of halogenated amidines.

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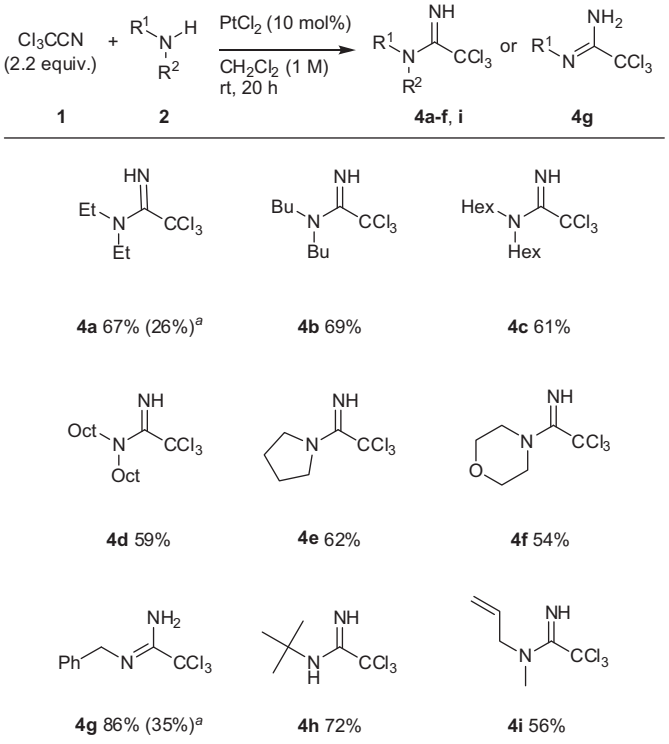

Scheme 2. Platinum-catalysed synthesis of trichloroacetamidine.

determined. Whilst it was hoped that [3,3]-sigmatropic rearrangement process catalysed by $PtCl_2$ would also occur to form a secondary amidine (multifaceted catalysis[14,15]) independent synthesis of allylamidine **4i** under basic conditions confirmed the structural assignment.

In conclusion, a platinum-catalysed method for the formation of amidines from the reaction of primary and secondary amines and trichloroacetonitrile in a nonpolar solvent has been developed. Importantly, this method allows for the direct catalytic synthesis of free amidines in nonpolar solvents at room temperature without the use of corrosive acids, strong bases or stoichiometric additives. We anticipate that this approach to amidine synthesis will find wide application due to its utility and operational simplicity. The further extension of this approach to less activated nitriles is currently in progress.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2013.06.062.

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12. Typical procedure for the synthesis of amidines **4**: A flame dried 5 mL microwave vial was charged with $PtCl_2$ (10 mol %), under nitrogen and evacuated under vacuum for ca. 10 min and backfilled with nitrogen prior to the addition of CH_2Cl_2. Trichloroacetonitrile (**1**, 2.2 equiv) and the primary or secondary amine **2** (1.0 equiv.) were added sequentially. The vessel was sealed and the reaction mixture allowed to stir at room temperature for 20 h. The crude reaction mixture was reduced in vacuo prior to purification by flash column chromatography (EtOAc/petroleum ether) on silica gel to afford the desired amidine **4**.
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