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Published in:
Tetrahedron Letters

DOI:
[10.1016/S0040-4039\(00\)00181-7](https://doi.org/10.1016/S0040-4039(00)00181-7)

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Document Version
Publisher's PDF, also known as Version of record

Publication date:
2000

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Cobley, C. J., Heuvel, M. V. D., Abbadi, A., & Vries, J. G. D. (2000). Platinum catalysed hydrolytic amidation of unactivated nitriles. *Tetrahedron Letters*, 41(14). [https://doi.org/10.1016/S0040-4039\(00\)00181-7](https://doi.org/10.1016/S0040-4039(00)00181-7)

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Pergamon

Tetrahedron Letters 41 (2000) 2467–2470

TETRAHEDRON
LETTERS

Platinum catalysed hydrolytic amidation of unactivated nitriles

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Received 5 January 2000; accepted 25 January 2000

Abstract

The platinum(II) complex, [(Me₂PO·H·OPMe₂)PtH(PMe₂OH)], efficiently catalyses the direct conversion of unactivated nitriles to *N*-substituted amides with both primary and secondary amines. Possible mechanisms for this reaction are discussed and evidence for initial amidine formation is reported. Isolated yields vary from 51–89%. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: homogeneous catalysis; nitriles; amides; platinum compounds.

The preparation of amides is one of the most important synthetic transformations in organic synthesis. Most syntheses are based on the reaction between an activated carboxylic acid and an amine or ammonia.^{1–3} So far, few methods have been found to make the amide bond catalytically without the aid of stoichiometric activating agents.^{4,5} For this reason we have turned our attention to the use of nitriles as they are intrinsically more reactive than carboxylic acids. We were triggered by the work of Ghaffar and Parkins who used tris-dimethylphosphinito platinum hydride (**1**) as a catalyst for the selective hydration of nitriles to the amides (Scheme 1).⁶ Most impressive are the high turnover numbers (up to 50 000) and the rate of the reaction (1 485 mol/mol.h) achieved for the hydrolysis of acrylonitrile.

Scheme 1.

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It occurred to us that in view of the fact that the reaction is not retarded by the presence of pyridines, use of nucleophiles other than water, such as amines, should proceed equally well (Scheme 2). *N*-Substituted amides have previously been prepared from nitriles and amines, however these methods lack generality and require severe reaction conditions such as extremely high temperatures⁷ or catalysts such as strong acids⁸ and strong bases.⁹ Hence, the reaction of acetonitrile with propylamine and water in DME at 160°C in an autoclave, catalysed by 0.1 mol% of tris-dimethylphosphinite platinum hydride (**1**), gave the amide in 57% isolated yield after 24 h. The reaction is very fast initially and could also be performed with catalyst amounts as low as 0.02 mol%. However, build-up of ammonia pressure occurs and this may well be the reason that the reaction slows down appreciably afterwards. In addition, some black material precipitates at the end of the reaction which suggests that catalyst decomposition also plays a role.

Scheme 2.

We investigated the scope of this new reaction to some extent (Table 1) and found it to work equally well for both primary and secondary amines. All experiments were performed with unactivated alkylnitriles; benzonitrile gave only benzamide in these reactions. In the case of succinonitrile, the use of two equivalents of primary amine (entries 11 and 12) resulted in the formation of bisamides.

Table 1
Platinum catalysed hydrolytic amidation of nitriles

Entry	Nitrile	Amine	Time (h)	Isolated Yield of <i>N</i> -subst. Amide (%)
1	CH ₃ CN	<i>n</i> -Pr-NH ₂	24	57
2	CH ₃ CN	C ₆ H ₅ CH ₂ NH ₂	24	73
3	CH ₃ CN	C ₆ H ₅ NH ₂	70	63
4 ^a	CH ₃ CN	Pyrrolidine	39	66
5	CH ₃ CN	Piperidine	24	62
6	CH ₃ CN	Morpholine	60	60
7	C ₆ H ₅ CN	<i>n</i> -Pr-NH ₂	24	0
8	<i>n</i> -Hex-CN	<i>n</i> -Pr-NH ₂	18	63
9	<i>n</i> -Hex-CN	C ₆ H ₅ CH ₂ NH ₂	18	83
10	<i>n</i> -Hex-CN	Pyrrolidine	18	71
11	Succinonitrile	<i>n</i> -Pr-NH ₂	18	51 ^b
12	Succinonitrile	C ₆ H ₅ CH ₂ NH ₂	18	61 ^b
13	Succinonitrile	Pyrrolidine	18	89 ^b

^a This experiment was performed using only 0.023 mol% of catalyst **1**.

^b Resulted in the formation of the *N*-substituted *bis*amide.

The mechanism of the reaction is still unclear (Scheme 3). It is possible that the nitrile is rapidly hydrolysed to the amide, which then goes on to react further with the alkylamines. Indeed, in each case, the only observable side product was the unsubstituted amide, the result of nitrile hydrolysis. However,

it is also conceivable that the substituted amines react initially with the nitrile to form amidines, which then further hydrolyse to the amides.

Scheme 3.

Metal-catalysed formation of amidines¹⁰ from the reaction between nitriles and amines has previously been reported and indeed, for reactions performed in the absence of water, amidines have been detected. Specifically, when *n*-propylamine is reacted with acetonitrile the major products formed are the mono- and bisamidines, **2** and **3** (Scheme 4).¹¹ This seems to strongly support the latter mechanism.

Scheme 4.

An interesting extension to this finding results when 2-amino-ethanol is reacted with propionitrile. The initial formation of amidine **4** occurs,¹¹ which subsequently undergoes ring-closure to form the final product, 2-ethyl-2-oxazoline **5**; no other products being visible by GC analysis (Scheme 5).

Scheme 5.

In summary, we have found that the platinum(II) complex **1** acts as an efficient homogeneous catalyst for the direct conversion of nitriles to *N*-substituted amides.

Typical experimental procedure: the amine (0.110 mol), nitrile (0.121 mol) and water (0.220 mol) were dissolved in 10 ml of dimethoxyethane in an autoclave. Catalyst **1** (0.110 mmol, 0.1 mol%) was added and the mixture was heated under N₂ for the time given in Table 1. After cooling, the mixture was dried over Na₂SO₄ and concentrated by rotary evaporation. The crude product was purified by spinning band distillation for acetamides or by column chromatography (CH₂Cl₂/2% MeOH/1% NEt₃) for the remainder.¹²

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11. Observed by GC-MS analysis using a Cp sil 8 CB-MS, 30 m×0.25 mm Df=1.0 µm, injection temp.: 250°C, column temperature program: 5 min at 50°C (rate 7.5°C/min) 28 min at 250°C (rate 25°C/min) 30 min at 280°C, split: 1:50, flow: He 1.2 ml/min, injection volume: 1.0 µl.
12. All products are known compounds that show satisfactory GC-MS and NMR spectral data.