Appl. Sci. **2015**, *5*, 380-401; doi:10.3390/app5030380

OPEN ACCESS

applied sciences

ISSN 2076-3417

www.mdpi.com/journal/applsci

Review

Synthetic Applications of the Parkins Nitrile Hydration Catalyst [PtH{$(PMe_2O)_2H$}(PMe_2OH)]: A Review

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Academic Editor: Thomas J. J. Müller

Received: 11 July 2015 / Accepted: 13 August 2015 / Published: 18 August 2015

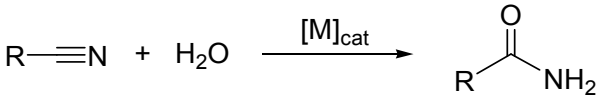
Abstract: The air-stable hydride-platinum(II) complex [PtH{$(PMe_2O)_2H$}(PMe_2OH)], reported by Parkins and co-workers in 1995, is the most versatile catalyst currently available for the hydration of C≡N bonds. It features remarkable activity under relatively mild conditions and exceptionally high functional group compatibility, facts that have allowed the implementation of this complex in the synthesis of a large number of structurally complex, biologically active molecules and natural products. In this contribution, synthetic applications of the Parkins catalyst are reviewed.

Keywords: homogeneous catalysis; hydration reactions; platinum; amides; nitriles; organic synthesis

1. Introduction

The selective transformation of a functional group within a complex molecule to generate target compounds is a very important issue in organic synthesis. Although this is not a trivial task, the use of homogeneous metal catalysts allows, in many cases, to reach compounds with remarkable levels of selectivity. Indeed, the field of homogeneous catalysis is currently so widespread that, in the literature, it is difficult to find advanced syntheses not using metal catalysts at some stage [1–3]. One of the organic transformations in which metal catalysts have played a key role is the hydration of nitriles (Scheme 1),

a process of great relevance in view of the broad industrial, synthetic, biological, and pharmacological applications of corresponding primary amide products [4–6].



Scheme 1. The catalytic hydration of nitriles.

The conversion of nitriles into amides by conventional acid/base strategies usually requires harsh conditions and remains impractical for most purposes due to yield and selectivity issues, since these classical methods are frequently unable to control the over-hydrolysis of the primary amide product [7,8]. The use of transition metal complexes (mainly of Groups 8–12) as catalysts under neutral and mild conditions has allowed researchers to overcome these traditional barriers, and a large number of selective catalysts for the nitrile hydration process have seen the light during the last two decades [9–15]. Among them, the commercially available hydride-platinum(II) complex [PtH{(PMe$_2$O)$_2$H}(PMe$_2$OH)] (**1**), first described by Ghaffar and Parkins in 1995 [16,17], has achieved great success among organic chemists because of its outstanding activity and selectivity and its exquisite compatibility with other functional groups (Figure 1). As a matter of fact, this platinum complex has found applications in the synthesis of a huge number of natural products and biologically active molecules of elaborate structure, making it the most widely used catalyst to date for the hydration of C≡N bonds.

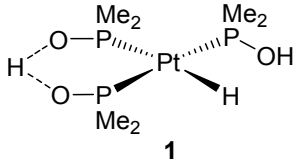


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Figure 1. Structure of the nitrile hydration catalyst [PtH{(PMe$_2$O)$_2$H}(PMe$_2$OH)] (**1**).

This article intends to provide a comprehensive account on the chemistry and synthetic applications of [PtH{(PMe$_2$O)$_2$H}(PMe$_2$OH)] (**1**). The literature and patented works published up to July 2015 are covered.

2. Preparation of Complex [PtH{(PMe$_2$O)$_2$H}(PMe$_2$OH)], First Catalytic Studies and Mechanism of Action

The synthesis of complex [PtH{(PMe$_2$O)$_2$H}(PMe$_2$OH)] (**1**) involves the reaction of the platinum(0) precursor [Pt(PPh$_3$)$_4$] with an excess (five equiv.) of dimethylphosphine oxide Me$_2$P(=O)H, which tautomerizes *in situ* into the phosphinite ligand Me$_2$POH, in toluene under inert atmosphere. The reaction proceeds at room temperature, and the complex precipitates directly in the medium, thus making its isolation easy by simple filtration (isolated yields are usually in the range 75%–80%) [16–19]. In their first studies, Parkins and Ghaffar demonstrated the ability of **1** to selectively hydrate different model nitrile substrates, such as benzonitrile, acetonitrile, acrylonitrile, or 3-cyanopyridine, employing water, aqueous ethanol, or aqueous THF as the reaction medium at 70–90 °C [16–18]. The remarkable activity

of [PtH{(PMe$_2$O)$_2$H}(PMe$_2$OH)] (**1**) was readily evidenced in these seminal works, with reported turnover frequencies exceeding 1400 h^{-1} and turnover numbers of up to 77,000. Remarkably, contrary to other metal catalysts reported in the literature, complex **1** was able to operate under neutral conditions. The studies by Parkins and Ghaffar also showed that the size of the substituents on the phosphorus ligand is key to achieving good catalytic activity, the performances of the related complex [PtH{(PPh$_2$O)$_2$H}(PPh$_2$OH)] containing a bulkier phosphinito ligand being significantly lower in comparison to those of **1** (an additional example has been recently described [20]). Further evidence of the synthetic potential of complex [PtH{(PMe$_2$O)$_2$H}(PMe$_2$OH)] (**1**) was given by de Vries and co-workers, who reported excellent yields and chemoselectivities in the hydration of a variety of sterically hindered tertiary nitriles and nitriles containing acid- or base-sensitive functional groups (some representative examples are shown in Figure 2) [21].

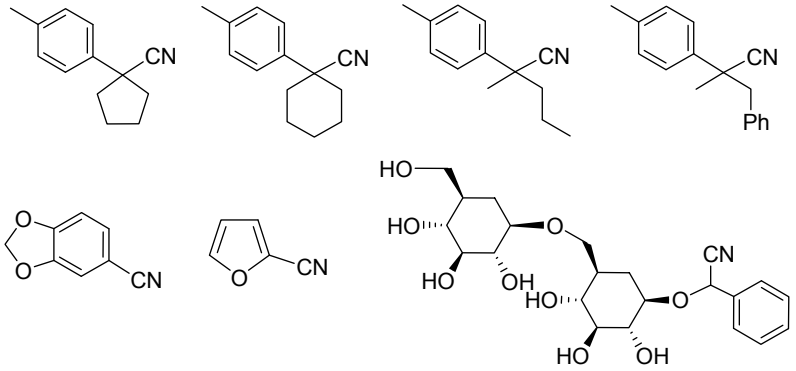
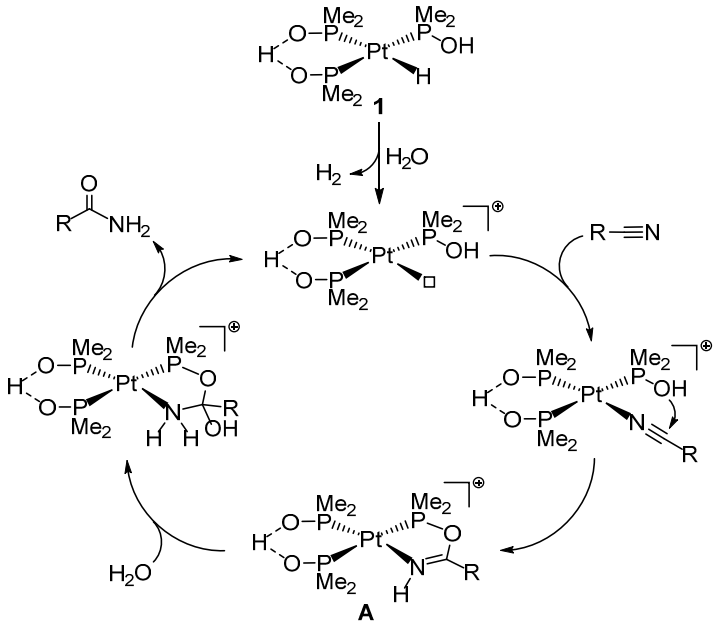


Figure 2. Examples of nitriles that complex **1** is able to hydrate.

Concerning its mechanism of action, Ghaffar and Parkins proposed that in aqueous medium, protonation of the hydride ligand of **1** by water readily takes place, generating a vacant coordination site on the metal for substrate binding, with concomitant dihydrogen extrusion (Scheme 2) [16–18].

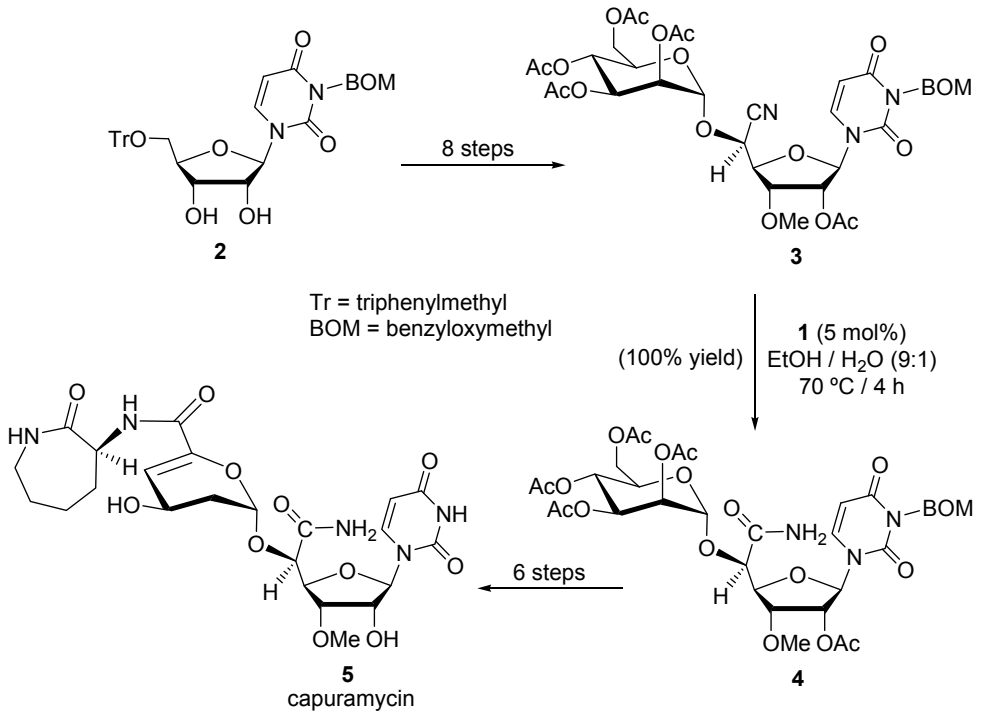


Scheme 2. Proposed mechanism for the catalytic hydration of nitriles with complex **1**.

Then, an intramolecular nucleophilic attack of the OH group of the PMe_2OH ligand on the coordinated nitrile takes place, affording the five-membered metallacyclic intermediate **A**. Further hydrolysis of this metallacycle generates the amide product and regenerates the active platinum species [16–18].

3. Application of Complex [PtH{$(PMe_2O)_2H$}(PMe_2OH)] in the Total Synthesis of Natural Products

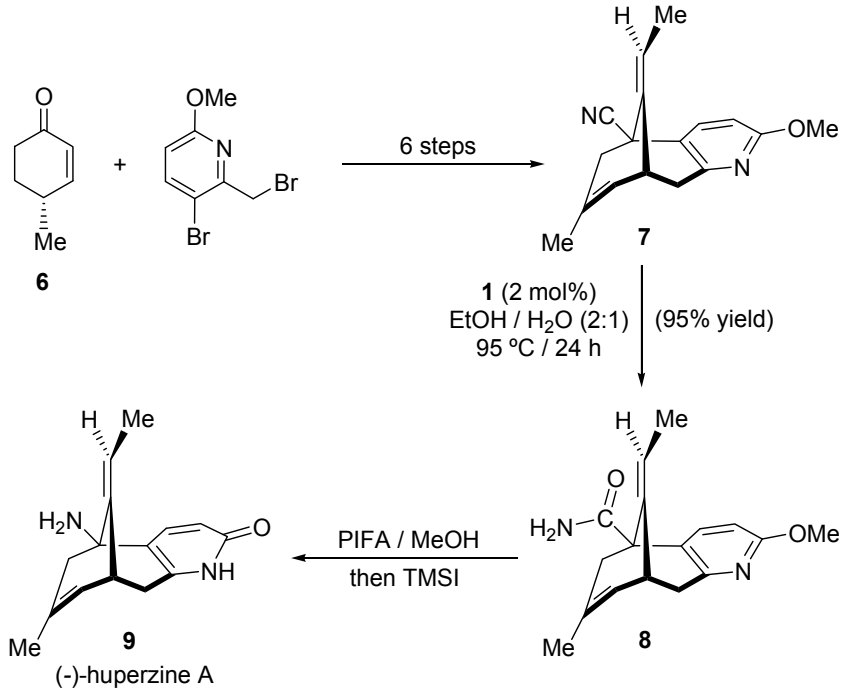
Capuramycin (**5**), a nucleoside antibiotic isolated from the culture filtrate of *Streptomyces griseus* 446-S3 [22], and its congeners are considered to be important lead molecules for the development of new drugs for *Mycobacterium tuberculosis* infections [23]. Accordingly, remarkable efforts have been devoted to establish convergent synthetic routes to access **5** that allow the preparation of analogues for SAR (structure-activity relationship) studies [24]. In this context, in 2009, Kurosu and co-workers described a concise synthesis of capuramycin (**5**), starting from the partially protected uridine **2** (15 steps), in which the primary amide unit was conveniently generated by the hydration of the C≡N unit of intermediate **3** using [PtH{$(PMe_2O)_2H$}(PMe_2OH)] (**1**) (Scheme 3) [25]. The hydration reaction, performed in aqueous ethanol at 70 °C, with 5 mol% of **1**, allowed the quantitative conversion of **3** to the corresponding amide **4**.



Scheme 3. The Parkins catalyst in the synthesis of capuramycin.

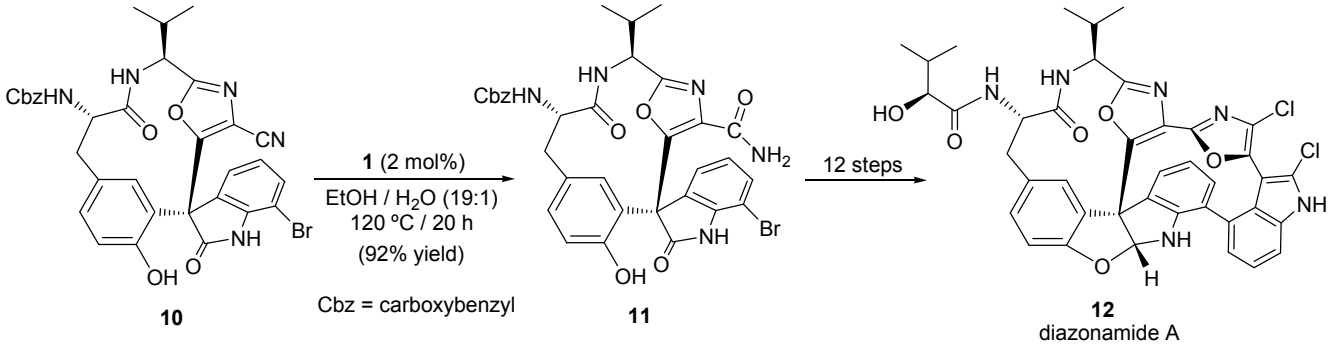
(−)-Huperzine A (**9**) is a tricyclic alkaloid produced by the Chinese herb *Hupercia serrata* [26], with intense contemporary interest in clinical application for treating neurodegenerative diseases [27–29]. Several total syntheses of **9** have been reported [27–29]. In one of the most recent and scalable (eight steps starting from (*R*)-4-methyl-cyclohex-2-ene-1-one (**6**); 35%–45% overall yield), complex **1** was employed to promote the high-yield conversion of advanced nitrile intermediate **7** into amide **8** in aqueous ethanol (Scheme 4) [30]. From **8**, Hoffmann's rearrangement of the amide group by means of

[bis(trifluoroacetoxy)iodo]benzene (PIFA), followed by *in situ* deprotection of the pyridone unit with iodotrimethylsilane (TMSI), delivered the desired alkaloid.



Scheme 4. The Parkins catalyst in the synthesis of (−)-huperzine A.

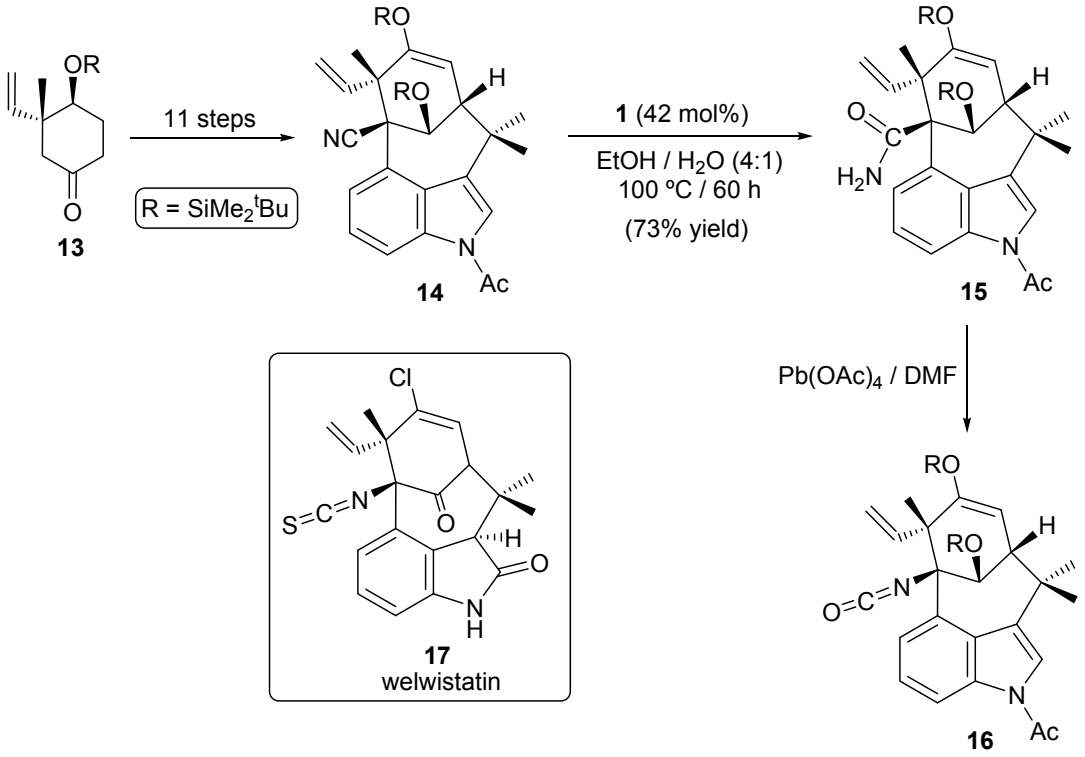
The selective hydration of nitrile **10** to generate primary amide **11**, an advanced intermediate for the Nicolaou's synthesis of the marine natural product diazonamide A (**12**) [31,32], using [PtH{(PMe2O)2H}(PMe2OH)] (**1**) was described by Sammakia and co-workers (Scheme 5) [33]. The reaction proceeded cleanly in aqueous ethanol at 120 °C with a catalyst loading of only 2 mol%, delivering **11** in 92% isolated yield.



Scheme 5. Synthesis of an amide intermediate for the preparation of diazonamide A.

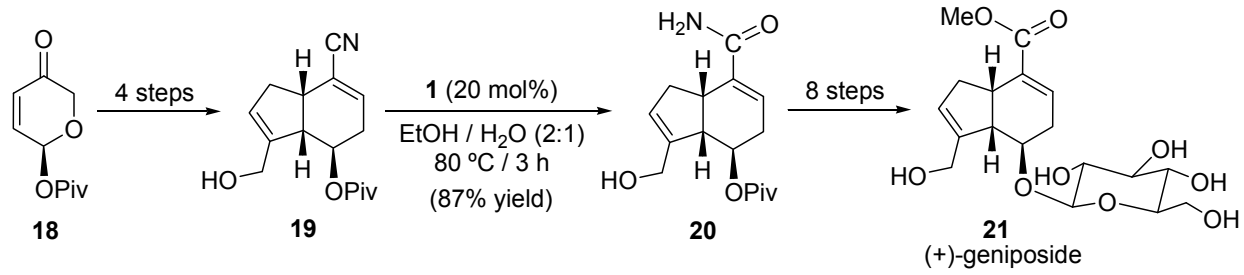
The welwitindolinones are a fascinating group of structurally unique metabolites isolated from blue-green algae that contain 3,4-bridged or spiro-cyclobutaneoxindole moieties [34,35]. Due to their challenging structures and their broad spectrum of biological activities, these compounds have attracted the attention of synthetic chemists for some time, although their complexity has prevented the completion of total syntheses for most of them thus far [36]. In an approach to welwitindolinone C isothiocyanate (welwistatin **17**), Funk and co-workers have described the preparation of the related

indole isocyanate derivative **16** starting from the vinylcyclohexanone **13** after 13 steps (Scheme 6) [37]. In this synthesis, the Parkins catalyst was employed to hydrate the encumbered nitrile **14**. A high loading of complex **1** (42 mol%) was, in this case, required to generate the bridgehead primary amide **15** in high yield (73%). In the presence of $Pb(OAc)_4$, amide **15** evolved into the final isocyanate **16** through the Baumgarten variant of the Hoffmann rearrangement.



Scheme 6. Funk's approach to the synthesis of welwistatin.

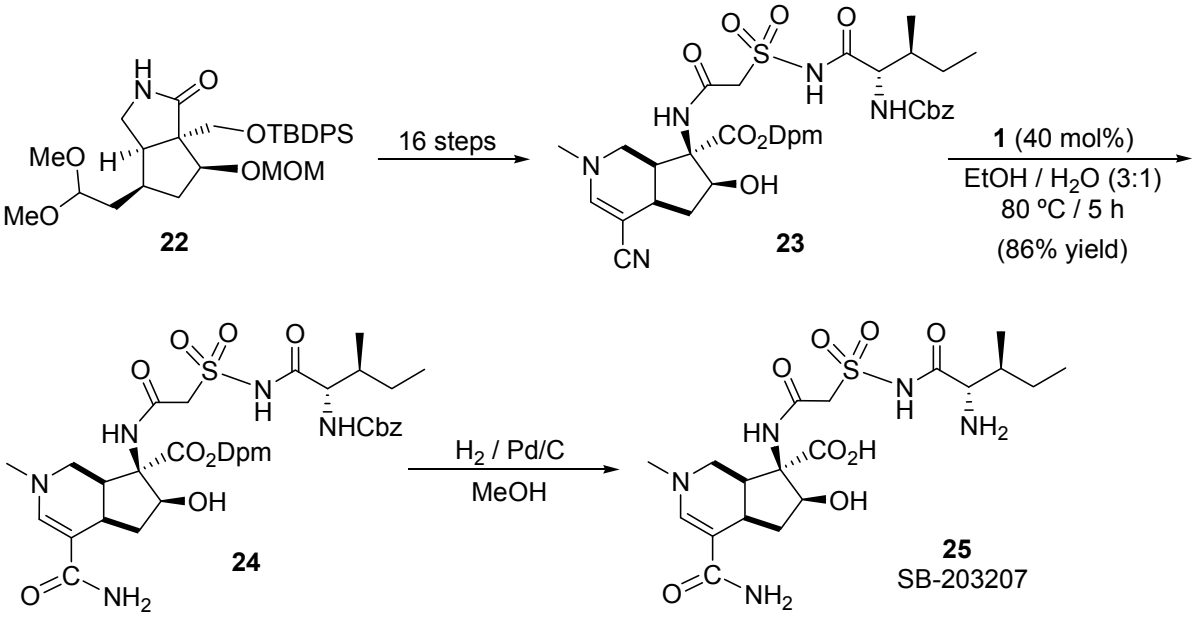
In 2009, Jones and Krische developed a total synthesis of (+)-geniposide (**21**), an iridoid β-glucoside of natural origin with anti-tumor and anti-inflammatory activity, starting from pivalate-protected lactol **18** (Scheme 7) [38]. During this synthesis the conversion of nitrile intermediate **19** into amide **20** was successfully accomplished in 87% yield using 20 mol% of the platinum complex [PtH{$(PMe_2O)_2H$}(PMe_2OH)] (**1**).



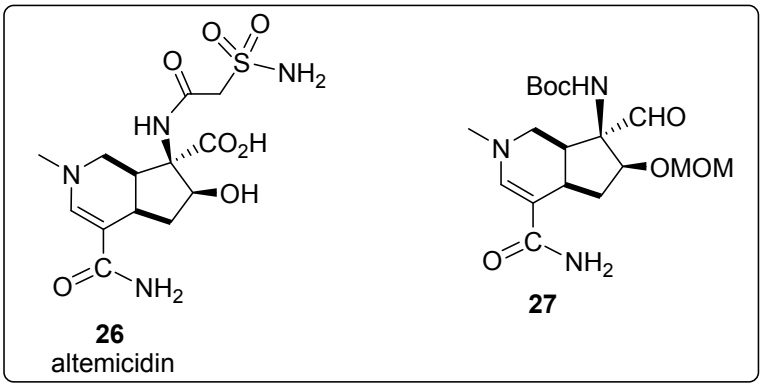
Scheme 7. The hydration step in total synthesis of (+)-geniposide.

SB-203207 (**25**), an alkaloid isolated from a *Streptomices* species by researchers in the SmithKline Beecham group, was found to show marked isoleucyl tRNA synthetase inhibition activity [39,40]. Very recently, Kan and co-workers described a total synthesis of this compound starting from lactam **22**, in

which the primary amide unit was generated by catalytic hydration of nitrile intermediate **23** with complex **1** (Scheme 8) [41]. As in the two previous cases, a high loading of **1** was needed to obtain the corresponding amide product **24** in high yield. SB-203207 can also be accessed by acylation of the sulfonamide unit of naturally occurring altemicidin (**26** in Scheme 8) [42]. In this context, the stereoselective synthesis of a key intermediate for altemicidin, *i.e.* amide **27** (see Scheme 8), was accomplished by Kan and Fukuyama employing [PtH{$(PMe_2O)_2H$}(PMe_2OH)] (**1**) [43]. Compound **27** was obtained in quantitative yield by the hydration of the corresponding nitrile in aqueous ethanol at 75 °C for 12 h with 28 mol% of **1**.

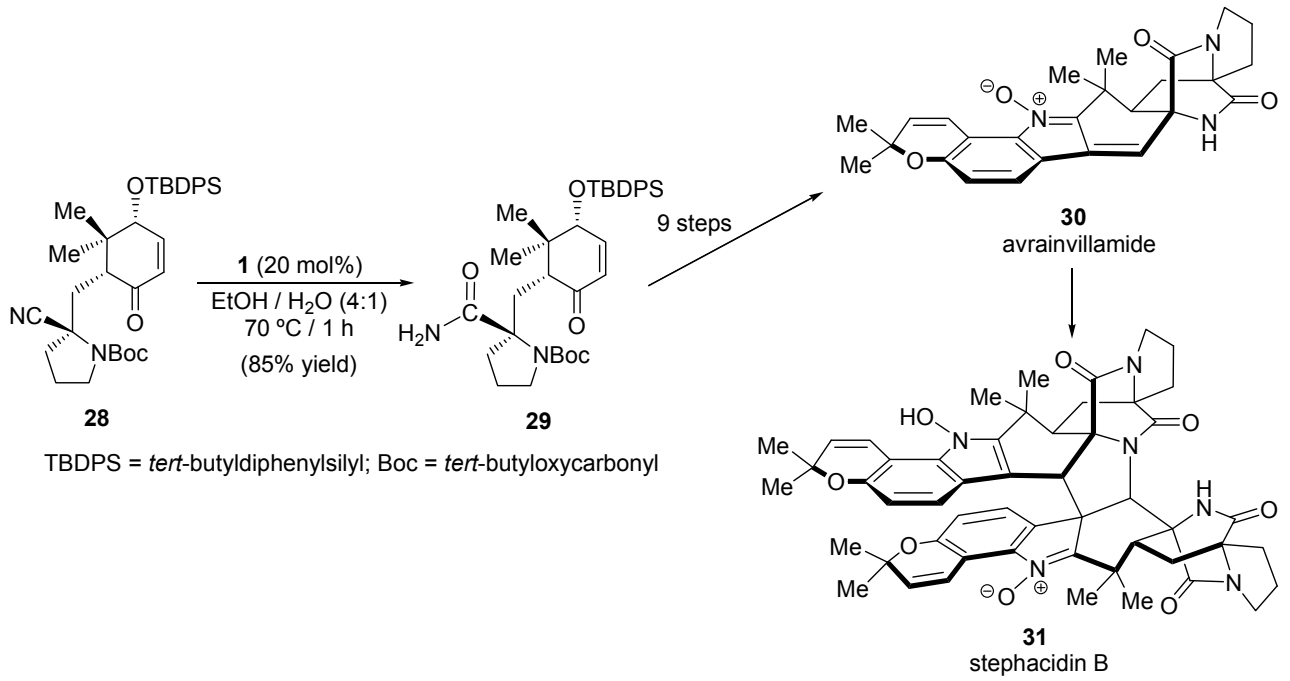


MOM = methoxymethyl ether; TBDPS = *tert*-butyldiphenylsilyl; Cbz = carboxybenzyl; Dpm = 1,2-diphenylmaleyl; Boc = *tert*-butyloxycarbonyl



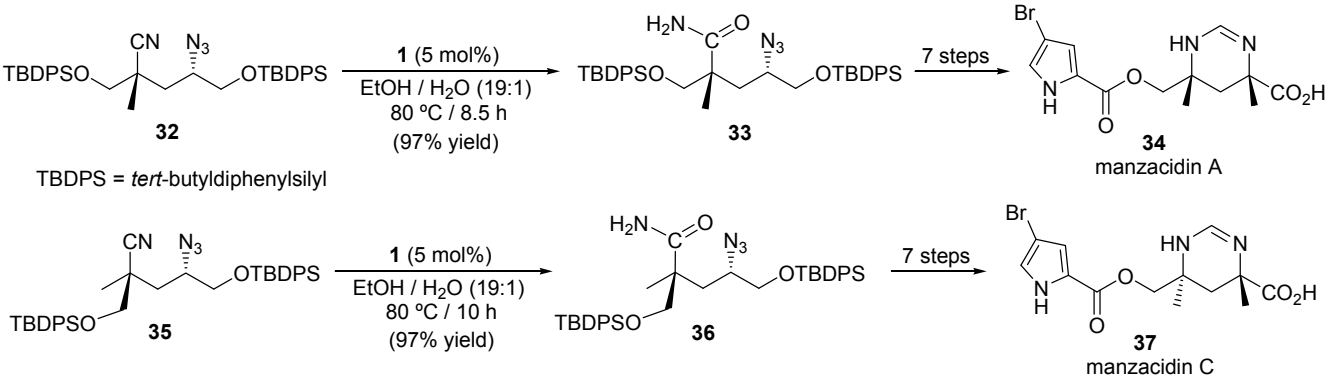
Scheme 8. The Parkins catalyst in the synthesis of alkaloid SB-203207.

In a synthetic approach toward the cytotoxic indole alkaloid avrainvillamide (**30**) and its dimeric form stephacidin B (**31**) [44], Myers and co-workers used [PtH{$(PMe_2O)_2H$}(PMe_2OH)] (**1**) to synthesize primary amide intermediate **29** by the hydration of nitrile **28** (Scheme 9) [45,46]. The reaction proceeded cleanly in aqueous ethanol at 70 °C and with 20 mol% of **1**, affording **29** in 85% isolated yield.



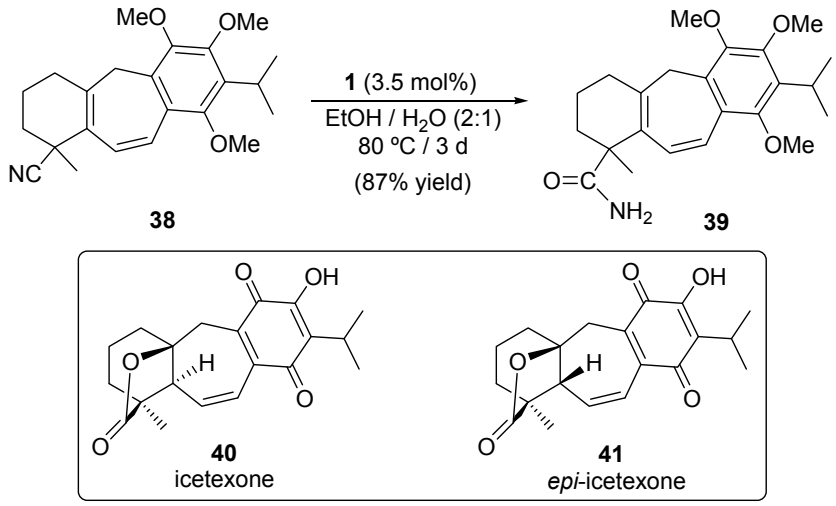
Scheme 9. The Parkins catalyst in the synthesis of avrainvillamide and stephacidin B.

The manzacidins are a family of marine natural products featuring a tetrahydropyrimidine carboxylic acid and an ester-linked bromopyrrole unit. This class of alkaloids has attracted significant attention due to their biological activities and unusual structure. Consequently, many groups have described the enantio- and diastereoselective synthesis of some of them [47]. In this context, Deng and co-workers reported synthetic routes to manzacidin A (**34**) [48,49] and manzacidin C (**37**) [50] involving a nitrile hydration step promoted by complex [PtH{(PMe2O)2H}(PMe2OH)] (**1**) (Scheme 10). In particular, **1** was used to transform the diasteromeric nitriles **32** and **35** into the corresponding primary amide intermediates **33** and **36**, respectively. As shown in the scheme, almost quantitative yields were achieved in both cases, performing the reactions at 80 °C with low catalyst loading (5 mol%).



Scheme 10. Hydration steps in the syntheses of manzacidins developed by Deng.

In the context of their synthetic studies on the icetaxane family of diterpenoids, the hydration of nitrile **38** by complex **1** was successfully employed by Sarpong and co-workers to prepare primary amide **39**, from which the formal synthesis of icetexone (**40**) and *epi*-icetexone (**41**) could be completed (Scheme 11) [51,52].



Scheme 11. Structure of icetexone and *epi*-icetexone, and synthesis of one intermediate.

The marine natural product psymberin (**42** in Figure 3) has attracted a great deal of attention since its discovery in 2004 due to its complex architecture, biological properties, and paucity in nature. This interest has resulted in a large number of synthetic investigations and the development of analogous molecules [53]. The Parkins catalyst [PtH{$(PMe_2O)_2H$}(PMe_2OH)] (**1**) has been involved in some of these studies [54–59]. In particular, in the first total synthesis of this compound, De Brabender and co-workers employed **1** to synthesize advanced amide intermediate **43** from the corresponding nitrile [54,55,57]. The same group also described the synthesis of different psymberin analogues from primary amide **44**, which was also accessed though a nitrile hydration reaction promoted by **1** [56,57].

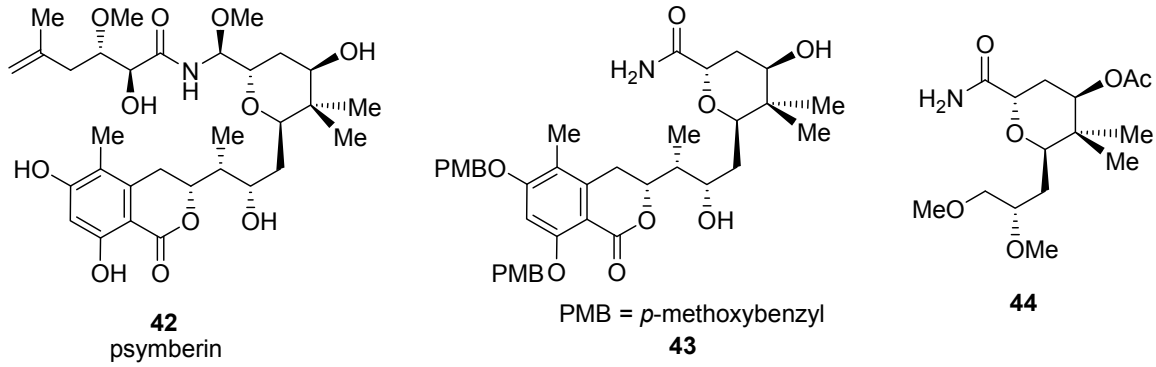
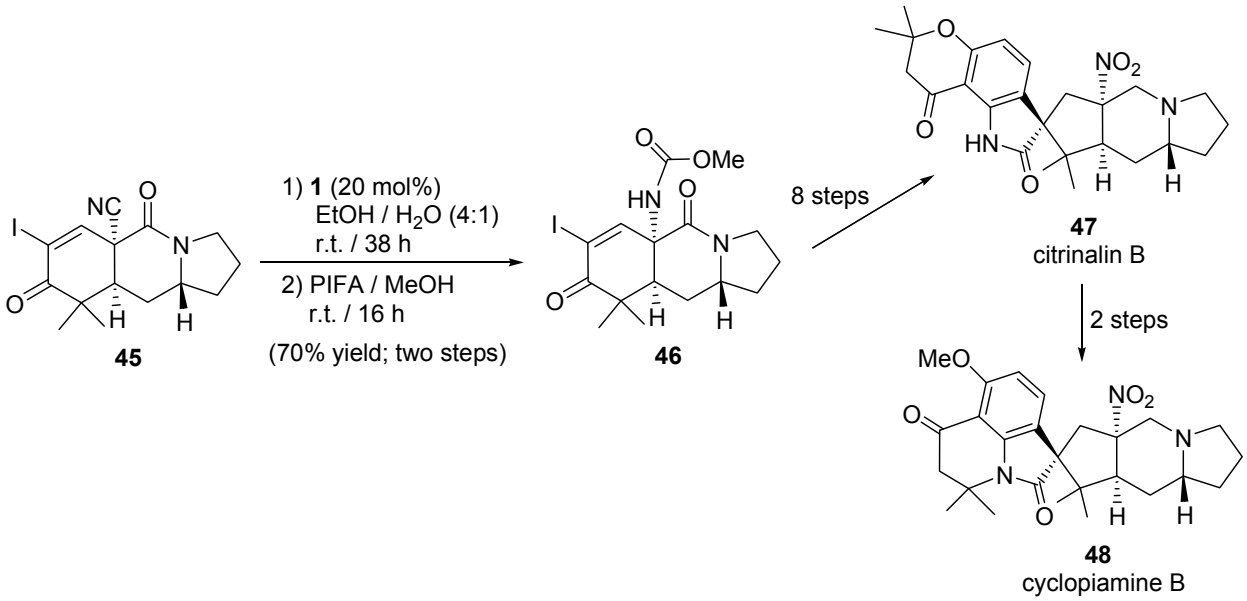


Figure 3. Structure of psymberin and amides **43**–**44**.

The total syntheses of the prenylated indole alkaloids citrinalin B (**47**) and cyclopiamine (**48**) has been recently accomplished for the first time by Mercado-Marin, García-Reinada, and co-workers (Scheme 12) [60]. In their work, the key carbamate intermediate **46** was generated through a two-step sequence from tricyclic nitrile **45** via initial hydration of the C≡N catalyzed by complex [PtH{$(PMe_2O)_2H$}(PMe_2OH)] (**1**), followed by Hofmann rearrangement of the resulting carboxamide (not isolated) promoted by PIFA in MeOH.



Scheme 12. The Parkins catalyst in the total synthesis of citrinalin B and cyclopiamine B.

In an independent work, Sarpong and co-workers reported the preparation of the related 17-hydroxy-citrinalin B (**50**), as well as those of the alkaloids stephacidin A (**51**) and notoamide I (**52**), using carbamate **49** as a common intermediate (Figure 4) [61]. As in the previous case, formation of **49** was accomplished through a hydration/Hofmann rearrangement sequence from the corresponding nitrile, the hydration step being again promoted by the Parkins platinum catalyst **1**.

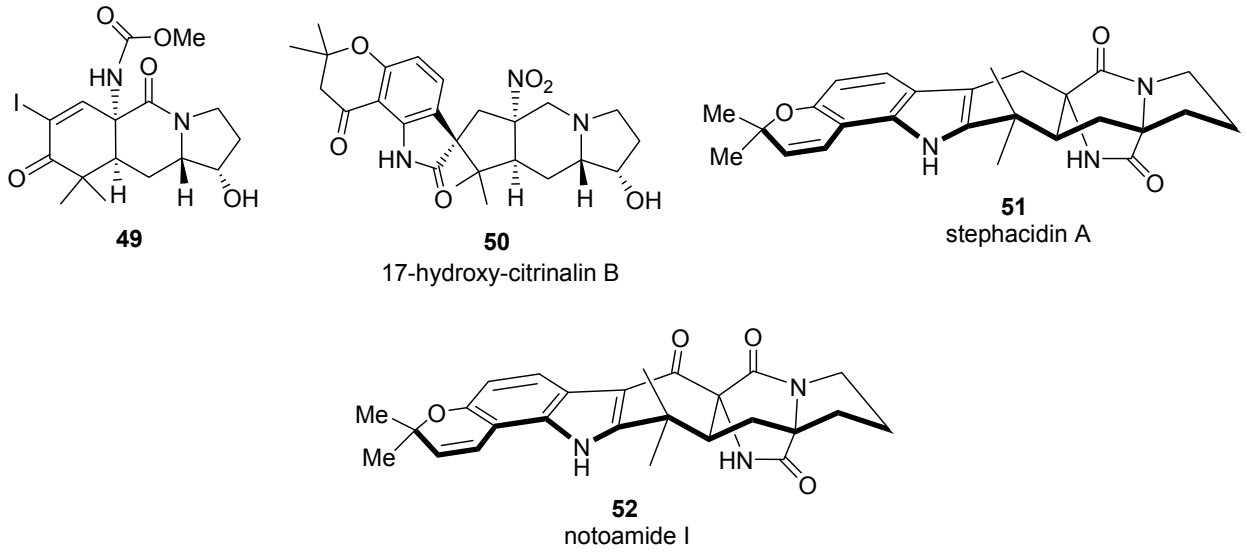
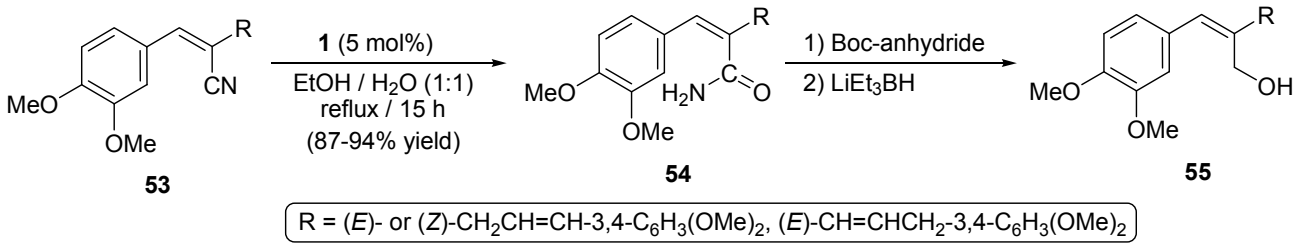


Figure 4. Structure of the carbamate **49** and the alkaloids **50**–**52**.

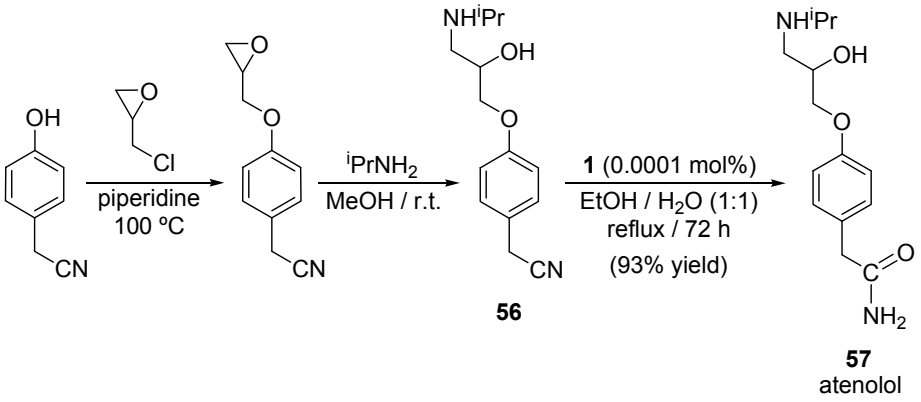
Finally, Fleming and co-workers reported the preparation of a series of morinol-type lignans **55** starting from α,β-unsaturated nitriles **53** (Scheme 13) [62]. The selective transformation of the alkenenitrile unit of **53** into the allylic alcohol one involved an initial hydration step, catalyzed by complex [PtH{$(PMe_2O)_2H$}(PMe_2OH)] (**1**), followed by an acylation/reduction of the resulting amides **54**.



Scheme 13. Synthetic route to morinol-type lignans.

4. Application of Complex [PtH{(PMe$_2$O)$_2$H}(PMe$_2$OH)] in the Synthesis of Other Biologically Active Molecules and Pharmaceutical Compounds

One of the first synthetic applications of complex [PtH{(PMe$_2$O)$_2$H}(PMe$_2$OH)] (**1**) was in the preparation of atenolol (**57**), a drug belonging to the group of β-blockers which contains a primary amide group and is commonly employed in the treatment of hypertension [63]. In particular, **1** had no difficulty in promoting the final hydration step of the nitrile intermediate **56**. Thus, as shown in Scheme 14, performing the reaction in a refluxing ethanol/water (1:1 *v/v)* mixture, and using a very low catalyst loading of 0.0001 mol%, atenolol could be selectively obtained in 93% yield [64].

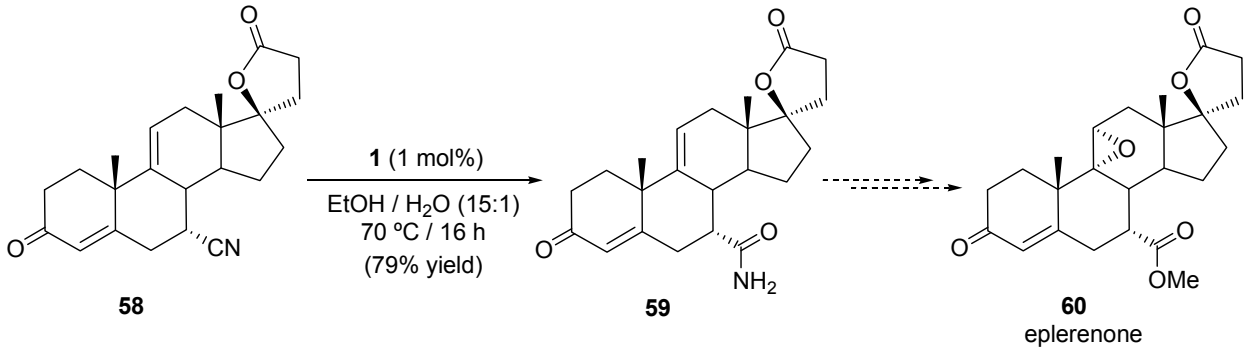


Scheme 14. Application of the Parkins catalyst in the synthesis of atenolol.

The steroidal compound eplerenone (**60**) is an orally-active aldosterone antagonist featuring a canrenone-type structure that is also used for the treatment of hypertension and heart failure [65,66]. The synthesis of **60** has been the subject of several patents. In one of them, the Parkins catalyst was successfully employed to transform the advanced intermediate 7α-cyano-9(11)$^{\Delta}$-canrenone **58** into 7α-carbamoyl-9(11)$^{\Delta}$-canrenone **59** (Scheme 15) [67]. Conversion of the amide unit of **59** to the corresponding carboxylic acid, followed by esterification, or direct alcoholysis of the amide to the ester, completed the synthesis of **60**.

Antagonists of the kappa opioid receptor have great therapeutic potential for the treatment of a range of central nervous system diseases and disorders, including, for example, schizophrenia, depression, and anxiety [68–70]. Quite recently, 8-azabicyclo[3.2.1]octan-3-yloxy-benzamides, as exemplified by **61** in Figure 5, were identified by Brugel and co-workers as potent and selective kappa opioid receptor antagonists [71]. In an additional SAR study, the same authors synthesized a large number of related compounds, such as **62** and **63**, in which the benzamide unit was generated by hydration of the

corresponding nitrile with the Parkins catalyst [72]. Reactions were performed in an EtOH/water (6:1 *v/v*) mixture at 80 °C, but no details on the yields, metal loadings, and reaction times were given in the document. The preparation of the structurally related azabicyclooctane derivatives **64** using **1** was also described, and their receptor binding affinity for kappa, mu, and delta opioid receptors was evaluated [73].



Scheme 15. The Parkins catalyst in the synthesis of the aldosterone antagonist eplerenone.

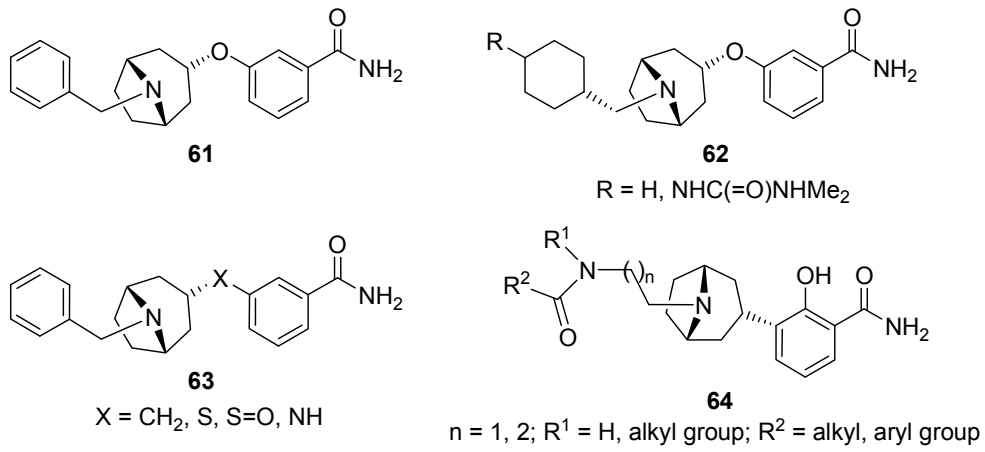
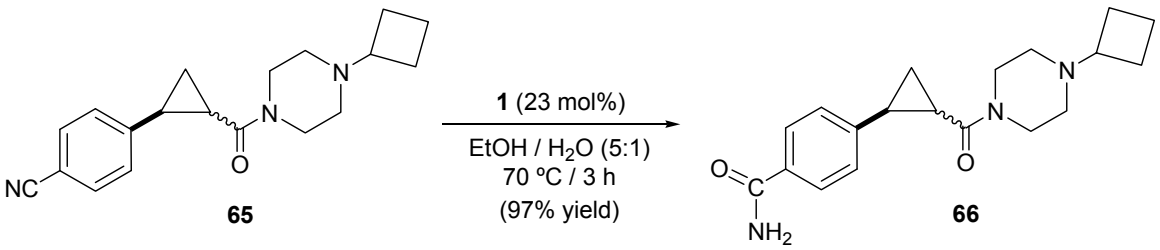


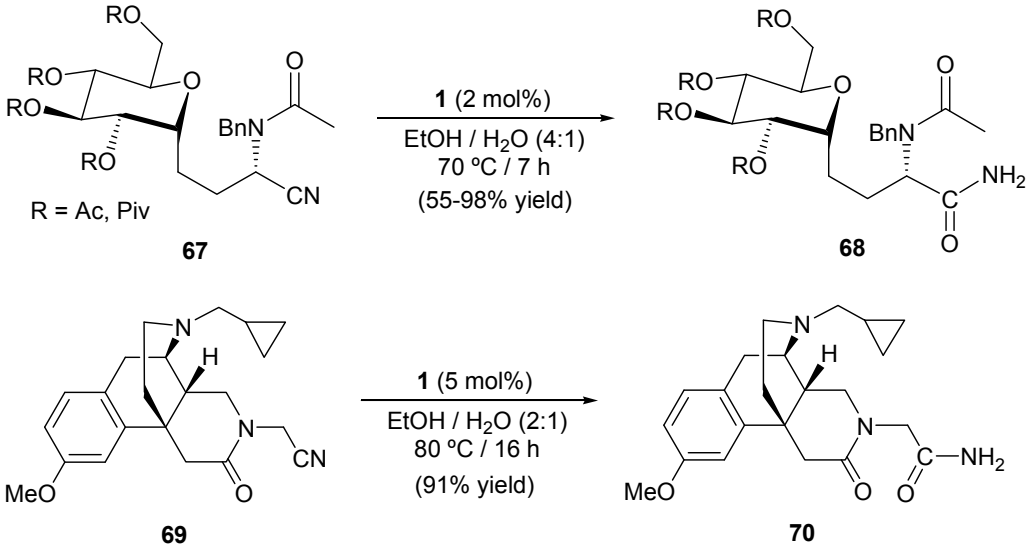
Figure 5. Structure of the opioid receptor antagonists **61-64**.

In a patented work directed to the identification of novel histamine H3 receptor ligands, Brugel and co-workers also employed complex [PtH{(PMe2O)2H}(PMe2OH)] (**1**) to promote the high yield conversion of the racemic cyclopropyl-substituted benzamide **65** into primary amide **66** (Scheme 16) [74]. It is of note that when the same reaction was carried out employing an excess of KOH as the promoter, **66** was obtained in a much lower yield (69% *vs.* 97%).



Scheme 16. Catalytic synthesis of a cyclopropyl-substituted benzamide using **1**.

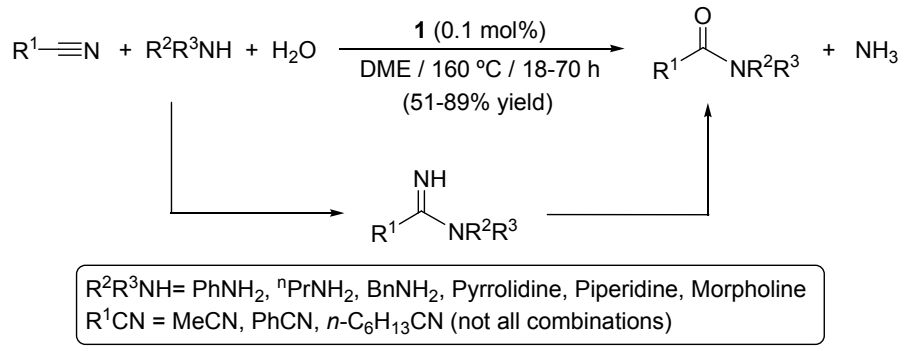
In addition, hydration with the Parkins catalyst **1** was also successfully employed to transform the acetate- and pivaloate-protected aminonitrile glycoside **67** and the morphinan derivative **69** into the corresponding primary amides **68** and **70**, respectively (Scheme 17) [75,76].



Scheme 17. Catalytic hydration of the biologically active nitriles **67** and **69**.

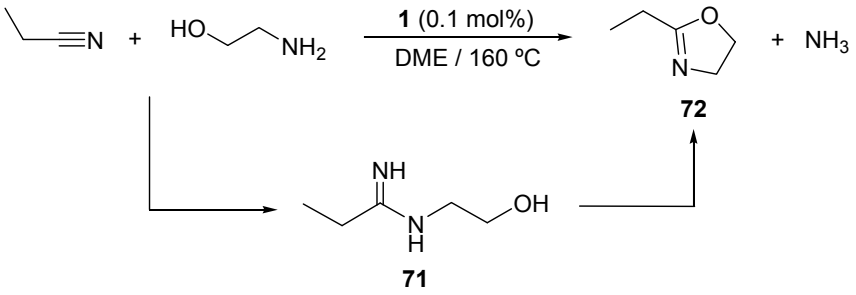
5. Other Synthetic Applications of Complex [PtH{(PMe$_2$O)$_2$H}(PMe$_2$OH)]

The synthetic utility of the Parkins catalyst [PtH{(PMe$_2$O)$_2$H}(PMe$_2$OH)] (**1**) is not restricted to the catalytic hydration of nitriles. Using this complex, other amide-bond forming reactions could be developed. In this context, de Vries and co-workers found that **1** efficiently catalyzes the direct conversion of unactivated nitriles to *N*-substituted amides by reaction with both primary and secondary amines in the presence of water (Scheme 18) [77]. A mechanism involving the initial formation of an amidine intermediate, which subsequently hydrolyzes into the amide, was proposed. Indeed, when the reactions were performed in the absence of water, the corresponding amidines could be isolated.



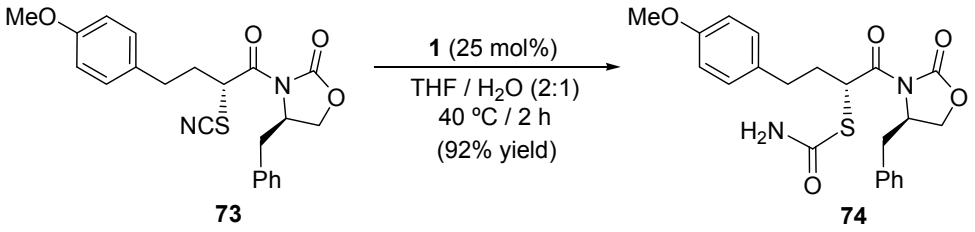
Scheme 18. Hydrolytic amidation of nitriles catalyzed by [PtH{(PMe$_2$O)$_2$H}(PMe$_2$OH)] (**1**).

An interesting extension of this amidation process is the quantitative formation of 2-ethyl-2-oxazoline **72** from the reaction of propionitrile with 2-aminoethanol via ring-closure of the intermediate amidine **71** (Scheme 19) [77].



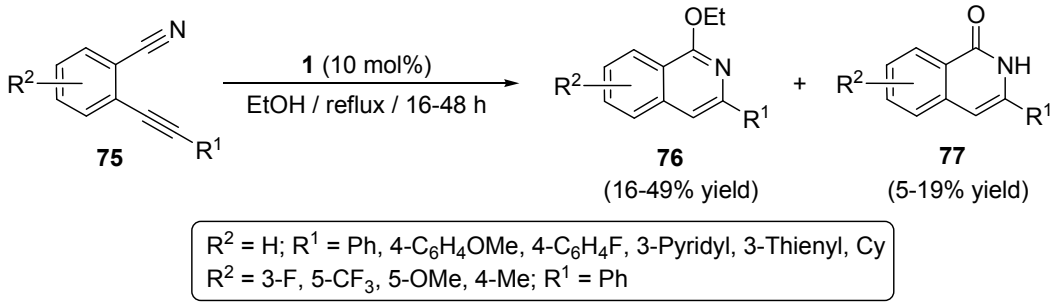
Scheme 19. Catalytic synthesis of 2-ethyl-2-oxazoline.

Although scarcely explored, the ability of complex **1** to promote the hydration of thiocyanates was also demonstrated [78,79]. As a representative example, treatment of the optically active thiocyanate **73** with 25 mol% of **1** in a THF/H_2O mixture led to the high-yield formation of thiocarbamate **74** (Scheme 20). Remarkably, in marked contrast with the use of classical acidic hydrolysis conditions, which induced the complete racemization at the stereogenic carbonyl α-carbon, the reaction proceeded without loss of chirality.



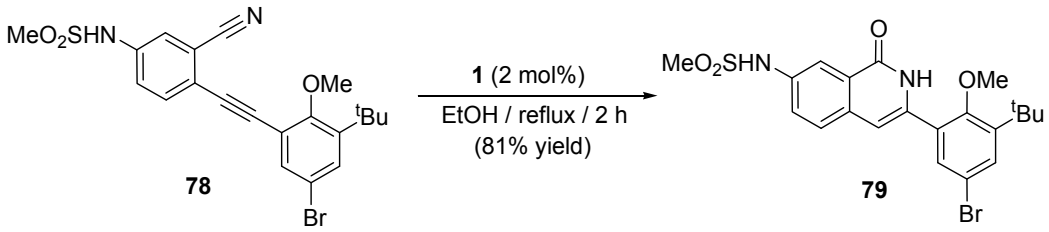
Scheme 20. Catalytic hydration of an optically active thiocyanate.

On the other hand, in the presence of catalytic amounts of [PtH{$(PMe_2O)_2H$}(PMe_2OH)] (**1**), separable mixtures of 1-ethoxyisoquinolines **76** and isoquinolones **77** were synthesized by intramolecular 6-*endo-dig* cyclization of *ortho*-alkynylbenzonitriles **75** in ethanol (Scheme 21) [80]. In these reactions the Parkins catalyst activates not only the nitrile unit, but also the alkyne moiety of the substrates. The use of other alcohols, such as methanol, *iso*-propanol, or cyclopentanol, also led to mixtures of the corresponding 1-alkoxyisoquinolines and isoquinolones **77**.



Scheme 21. Platinum-catalyzed intramolecular cyclization of *ortho*-alkynylbenzonitriles.

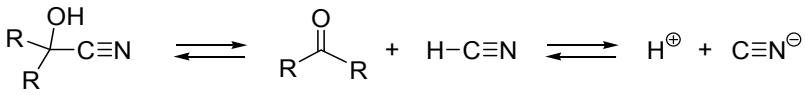
In an independent patented work, a more selective transformation of *ortho*-alkynylbenzonitrile **78** was observed [81]. Thus, as shown in Scheme 22, the treatment of this substrate with 2 mol% of platinum complex **1** in refluxing methanol resulted in the exclusive formation of isoquinolone **79**.



Scheme 22. Selective synthesis of isoquinolone **79** using complex **1**.

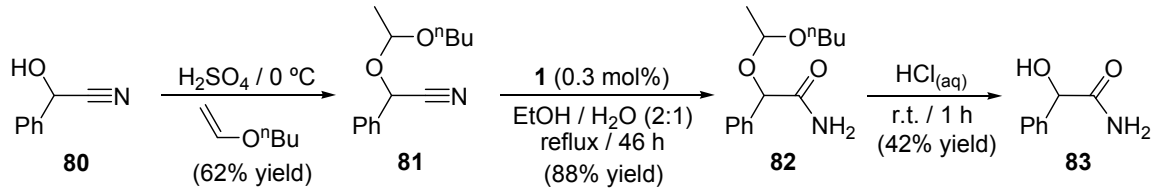
6. Limitations

Despite the broad scope shown by complex [PtH{(PMe$_2$O)$_2$H}(PMe$_2$OH)] (**1**), a major limitation was encountered when studying its application for the catalytic hydration of cyanohydrins, *i.e.* α-hydroxynitriles. Unfortunately, the hydration rates for these substrates were very low in comparison to those observed with other nitriles, and only a few turnovers could be achieved [82,83]. The poor reactivity observed was ascribed to the low stability of the cyanohydrin substrates, which slowly equilibrate in solution with HCN and the corresponding aldehyde or ketone (Scheme 23), and the irreversible coordination of the cyanide anion to platinum leads to the deactivation of the catalyst. In fact, most of the nitrile hydration catalysts reported to date are poisoned by cyanide and, therefore, with some notable exceptions [84–89], are inoperative with this particular class of nitriles.



Scheme 23. Equilibrium between a cyanohydrin and the corresponding aldehyde/ketone and hydrogen cyanide.

Although with only one example, Parkins and co-workers showed that this limitation can be circumvented, protecting the OH group of the cyanohydrin prior to the hydration reaction [90]. Thus, as shown in Scheme 24, mandelamide (**83**) was accessible from mandelonitrile (**80**) by the hydration of the corresponding mixed acetal **81** and the subsequent removal of the α-butoxyethoxy protecting group in the resulting amide **82** with dilute acid. In this context, we must also stress that the ability of complex **1** to promote the selective conversion of cyanohydrin acetates into α-acetoxy amides has also been demonstrated [91].



Scheme 24. Access to mandelamide from mandelonitrile using the Parkins catalyst.

In addition to cyanohydrins, other nitriles mentioned in the literature for which complex [PtH{(PMe$_2$O)$_2$H}(PMe$_2$OH)] (**1**) proved ineffective were **84** and **85** (Figure 6). In the case of **84**, the treatment with **1** in an EtOH/H$_2$O mixture at 70 °C resulted in the decyanation of the substrate and

generation of the corresponding aldimine [92]. For the malonodinitrile **85**, although its monohydration using **1** was possible, the reaction yield was very low in comparison to that achieved employing the more classical KF-Al_2O_3 system [93].

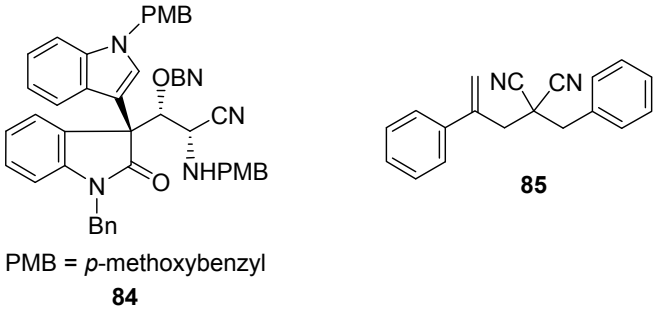


Figure 6. Structure of the nitriles **84** and **85**.

7. Conclusions

In summary, in this paper we have tried to summarize, in a comprehensive manner, all the synthetic processes in which the commercially available phosphinito-platinum(II) complex [PtH{$(PMe_2O)_2H$}(PMe_2OH)] (**1**) has been involved to date. Although tens of nitrile hydration catalysts are currently known, none has achieved nearly the same success of compex **1**. From the examples shown along the manuscript, it is easy to realize the extraordinary synthetic usefulness of this complex, which is capable of promoting the selective hydration of C≡N units in densely functionalized molecules of very high structural complexity due to its exceptionally high functional group compatibility. The high synthetic versatility of the primary amide −C(=O)NH_2 function, along with its presence in a multitude of natural products and biological active molecules already known, and certainly in many others waiting to be discovered, allow us to presume an increase in the use of **1** in the near future. In short, the Parkins catalyst [PtH{$(PMe_2O)_2H$}(PMe_2OH)] (**1**) is called to occupy a preferred position within the toolbox of synthetic organic chemists.

Acknowledgments

The author thanks the Ministerio de Economía y Competitividad (MINECO) of Spain (projects CTQ2013-40591-P and CTQ2014-51912-REDC) and the Gobierno del Principado de Asturias (project GRUPIN14-006) for financial support.

Conflicts of Interest

The author declares no conflict of interest.

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