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Journal of Organometallic Chemistry 665 (2003) 250–257
Journal of Organometallic Chemistry
www.elsevier.com/locate/jorganchem

Air- and moisture-stable cationic (diphosphine)palladium(II) complexes as hydroamination catalysts X-ray crystal structures of two $[(diphosphine)Pd(NCMe)(OH_2)]^{2+}[OTf]_2^-$ complexes

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Received 29 September 2002; received in revised form 12 November 2002; accepted 12 November 2002

Abstract

A series of cationic (diphosphine)palladium(II) complexes have been prepared and fully characterized, including two crystal structures. These complexes were evaluated as catalysts for the hydroamination of acyclic alkenes. The reactivity of the catalysts is dependent on the nature of the diphosphine ligand and the substituents on the amine and alkene substrates.

Keywords: Palladium; Diphosphine; Hydroamination

1. Introduction

Generating no waste products, the addition of amine N–H bond across an olefin (hydroamination) is arguably one of the most efficient ways of accessing nitrogen-containing molecules from cheap, readily available starting materials (Scheme 1). Despite extensive studies over the last four decades, it remained a challenge in synthetic chemistry [1]. Uncatalysed reactions with unactivated olefins often require harsh reaction conditions. In addition, there is also the challenge of stereochemical control when the reaction involves unsymmetrical olefins. With conventional Michael acceptors (where R = electron-withdrawing group), the reaction tends to favour the anti-Markovnikov product, whereas the opposite regiomer, containing a stereogenic center, offers the more valuable product.

Previously, we reported the use of palladium catalysts for the hydroamination of cyclic olefins and applied them in the synthesis of α-amino-tetrahydrofuran and pyran rings [2]. In this paper, we report a class of dicationic palladium catalysts for the hydroamination of acyclic olefins under pH neutral conditions. Being well-defined, highly active, as well as relatively stable to air and moisture, we believe they offer significant advantages over other catalysts that have been reported recently in this area [3].

2. Result and discussion

Five diphosphine ligands were chosen in this study for their different steric and electronic characteristics. The (diphosphine)palladium(II) chlorides **1a**–**1e** were prepared simply by the reaction of the appropriate diphosphine ligands with $PdCl_2(NCMe)_2$ or $PdCl_2(cod)$ in dichloromethane. The dichloride complexes **1a**–**1e** were subsequently subjected to ligand exchange with silver trifluoromethanesulfonate in acetonitrile, furnishing dicationic (diphosphine)palladium(II) complexes **2a**–**2e**, in moderate to high yields [dppf = 1,1′-bis(diphenylphosphino)ferrocene (**a**); dppr = 1,1′-bis(diphenylphosphino)ruthenocene (**b**); dippf = 1,1′-bis(diisopropylphosphino)ferrocene (**c**); dppp = 1,3-bis(diphenylphos-

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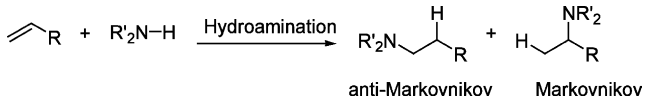
PII: S0022-328X(02)02138-1



Scheme 1. Hydroamination of an olefin.

phino)propane (**d**); BINAP = 1,1′-bis(diphenylphosphino)naphthalene (**e**)] (Scheme 2).

Freshly prepared samples of complexes **2a**–**2e** contain two coordinated acetonitrile solvent molecules in solution (integration of ^{1}H-NMR resonances). Once isolated, these triflate salts are somewhat hygroscopic, but may be stored indefinitely under nitrogen and handled briskly in air. Upon standing, one of the acetonitrile ligands is labile and is susceptible to displacement by a water molecule (through contact with atmospheric moisture), giving rise to crystalline mono–aqua complexes of the type $[(P_2)Pd(NCMe)(H_2O)]^{2+}[TfO]_2^-$. The molecular composition of the isolated crystals is supported by elemental analysis, and the requisite molecular weight is also observed in the ES–MS. Further evidence was provided by the crystal structures obtained of compounds **2c** and **2e** (Fig. 1). Each molecule contains water molecules in the asymmetric unit cell.

3. Catalytic studies

The hydroamination reaction between substituted anilines and styrenes were subsequently performed in the presence of these catalysts (Scheme 3) and the results are summarized in Table 1.

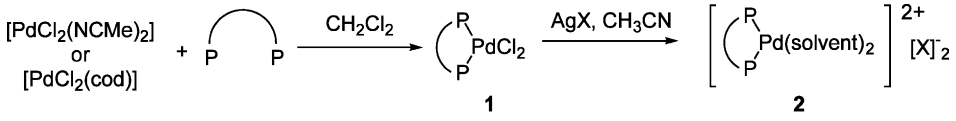
The reactions were carried out in thick-walled sealed Young tubes for convenience. In all cases, the addition was regiospecific — the branched product *N*-phenyl-*N*-(1-phenylethyl)amine was the only observed isomer. Unsurprisingly, the rate and turnover of the reactions are dependent on the diphosphine ligand employed. The most active complex is the complex **2a**, derived from the dppf ligand. At the optimal reaction temperature of 100 °C (entries 1–3), the catalytic loading can be reduced to as low as 0.25 mol% without any observable lost in catalytic activity or yield (entries 4 and 5). An increase in bite angle (**2b**) and electronic donating nature (**2c**) of the phosphine ligand led to the termination and decrease in reactivity, respectively (entries 6 and 7). The reaction catalysed by the less rigid diphosphine ligand (**2d**) is less efficient, leading to the formation of unidentifiable side products and a corresponding drop in yield (entry 8).

In comparison, the chiral complex (**2e**) offers moderate activity. Lowering the reaction temperature ensured a better yield at the expense of reactivity (entries 9 and 10). Interestingly, the ee of the product (70% *S*) is not dependent on the reaction temperature. We believe this compares favourably to a similar system previously reported [4]. Overall, the rate of the reaction decreases in the order: dppf > BINAP > dippf > dppe > dppr.

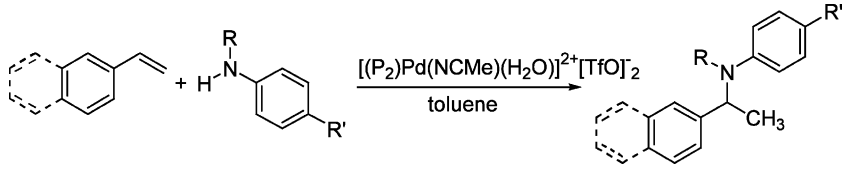
The system is also sensitive to changes in the steric and electronic character of the substrates. Substitution of aniline with electron-donating and -withdrawing groups led to retardation of the reaction, suggesting subtle counter-effects (entries 11 and 12). *N*-methyl aniline also reacted slower (entry 13). Vinyl naphthalene undergoes similar reactions (entries 14 and 15).

Palladium catalysts enabling the addition of ^{n}BuNH$_2$, piperidine and aniline to activated olefins (acrylic acid derivatives) have been described by Kawatsura and Hartwig [5], generated in situ from a mixture of $Pd(OAc)_2$ or $Pd(TFA)_2$ with PCP and PNP ligands. In comparison, the (diphosphine)palladium(II) complexes **2a**–**2d** can also catalyse these reactions in comparable activity. More interestingly, complex **2a** is also able to catalyse the addition of piperidine to the less activated methyl cinnamate (Table 2).

The addition of the amine is regiospecific, occurring at the β-position exclusively. Once again, the dppf-ligated complex **2a** appears to be the most active catalyst in the addition of piperidine to methylmethacrylate at



Scheme 2. Preparation of (diphosphine)palladium(II) complexes.



Scheme 3.

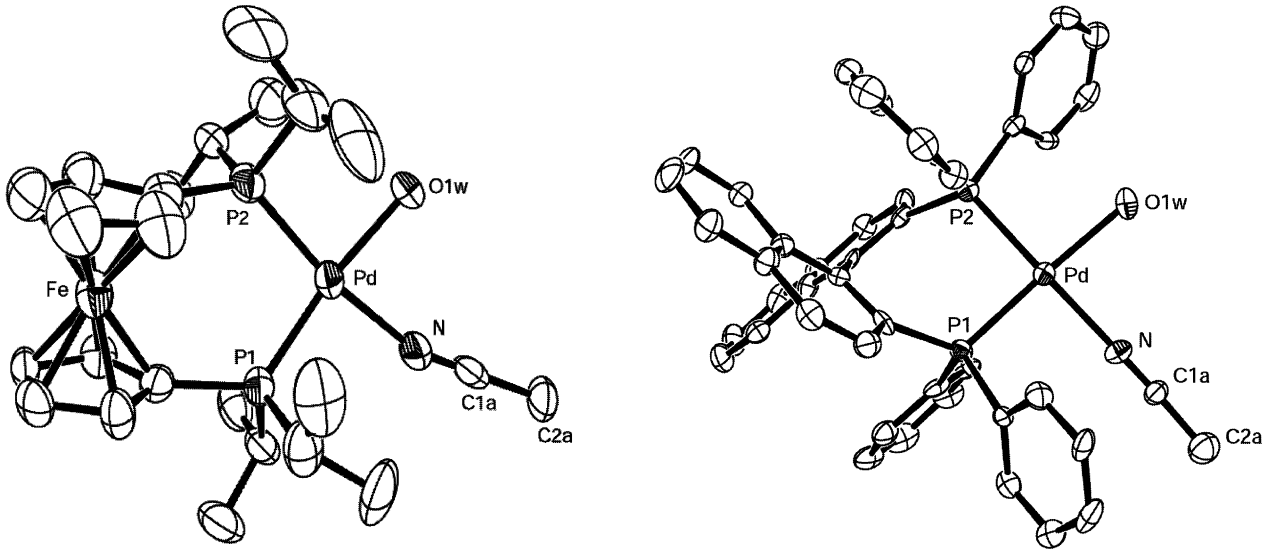


Fig. 1. ORTEP views of complexes **2c**·$2H_2O$ (left) and **2e**·$0.5H_2O$ (right) drawn with 50% thermal ellipsoids. Hydrogen atoms, solvent molecules and counterions are omitted for the sake of clarity.

room temperature (entries 1–4), where the loading can be reduced to 0.2 mol% (giving a yield of 76%).

Decreasing the nucleophilicity of amine requires higher reaction temperature, with a corresponding decrease in the reaction yield (entries 5–7). Methyl crotonate undergoes reaction with piperidine and pyrrolidine under ambient conditions to yield the Michael products (entries 8 and 10). Here, a more pronounced dependence of the yield on the ring size of the cyclic amine was observed (compared with entries 1 and 7). The addition of piperidine to the less activated cinnamate is comparatively slow (entry 9). Aniline can be similarly induced to undergo reaction with the methyl acrylate and acrylonitrile to give fairly good yields (entries 10 and 11).

In summary, we demonstrated that cationic diphosphinepalladium(II) complexes can catalyse hydroamination of different olefin substrates, including styrenes, acrylates, crotonates and methyl cinnamate (reported for the first time). Reactivity is found to be dependent on the diphosphine ligands, the nucleophilicity of the amine and the nature of the olefin.

Improvement in this and other combinations of olefins, amines and catalysts are currently under examination and will be reported in due course.

4. Experimental

All manipulations were performed using standard Schlenk techniques. Dichloromethane and acetonitrile were dried over CaH_2, distilled and stored under a nitrogen atmosphere. NMR spectra were recorded on a Bruker AVANCE 360 instrument (^1H at 360 MHz, ^{31}P at 145.8 MHz and ^{13}C at 90.6 MHz). The chemical shifts are reported in δ (ppm) referenced to residual protons and ^{13}C signals of deuterated chloroform or deuterated actonitrile as internal standard. ^{31}P-NMR spectra were referenced to H_3PO_4. The coupling constants are in Hertz (J Hz). Infrared spectra were recorded on a Perkin–Elmer 1600 FTIR spectrometer, either as Nujol mull between NaCl plates, or as KBr discs. Elemental analyses were carried out by Elemental Analysis Service, University of North London. Mass spectra (MS) were recorded using ES techniques by the EPSRC MS Services, Swansea, Wales. $(P_2)PdCl_2$ complexes were synthesized from bidentate ligand P_2 and $PdCl_2$(cod) or $PdCl_2(NCMe)_2$. All other compounds were used as received, unless otherwise specified.

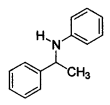
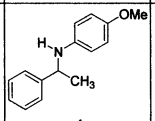
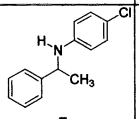
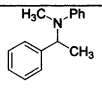
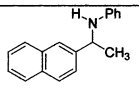
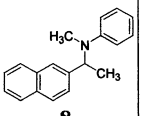
Suitable crystals were selected and data collected on a Bruker Nonius KappaCCD Area Detector at the window of a Bruker Nonius FR591 rotating anode ($\lambda_{Mo\–K_\alpha} = 0.71073$ Å) driven by COLLECT [7] and DENZO [8] software at 120 K. Structures were determined in SHELX-97 [9] and refined using SHELXL-97 [10] (Table 3).

4.1. Typical procedure for the synthesis of [(diphosphine)Pd(NCMe)(H_2O)]$(OTf)_2$ complexes

4.1.1. [(dppf)Pd(NCMe)(H_2O)]$(OTf)_2$ (**2a**)

A solution of AgOTf (0.17 g, 0.68 mmol) in 10 ml CH_3CN was added to a solution of (dppf)$PdCl_2$ (0.20 g, 0.27 mmol) in 20 ml CH_2Cl_2. The orange solution turned purple immediately followed the white precipitate of AgCl. The mixture was stirred at room temperature for at most 5 min, then it was filtered and evaporated to give a purple residue, which was recrystallized from CH_2Cl_2 to give 0.17 g purple solid. Yield = 61%. Anal. Calc. for $C_{38}H_{32}F_6NO_7P_2S_2FePd\cdot 4CH_2Cl_2$:

Table 1
Hydroamination between vinylarenes and substituted anilines

Entry	Catalyst	Product	S/C[a]	T/°C	Time/h	Yield[b]/%
1	**2a**	 **3**	50/1	60	21	25
2	**2a**		50/1	80	20	90
3	**2a**		50/1	100	18	92
4	**2a**		200/1	100	18	100
5	**2a**		400/1	100	18	100
6	**2b**		50/1	100	18	*Negligible*
7	**2c**		50/1	100	18	59
8	**2d**		50/1	100	18	11
9	**2e**		50/1	100	18	75[c]
10	**2e**		50/1	80	72	93[c]
11	**2a**	 **4**	50/1	100	18	85
12	**2a**	 **5**	50/1	100	18	39
13	**2a**	 **6**	50/1	100	18	78
14	**2a**	 **7**	50/1	100	18	100
15	**2a**	 **8**	50/1	100	18	47

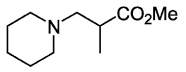
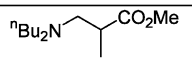
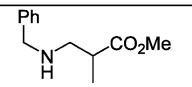
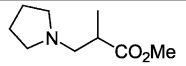
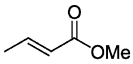
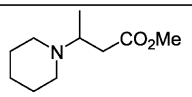
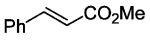
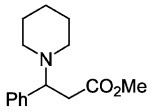
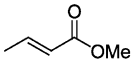
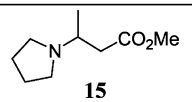
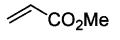
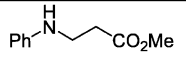
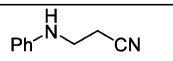
[a] Substrate/catalyst ratio.
[b] Isolated yields, reproducible to within ±3%.
[c] 70% ee (S), enantiopurity determined by chiral HPLC (Chiralcel OD-H column).

C, 37.15; H, 2.97; N, 1.03. Found: C, 37.87; H, 2.31; N, 1.48%. ES–MS (MeOH, 20 V): 725.1, 677.3, 661.1. ^{1}H-NMR (CD_3CN): $\delta = 7.72$–7.83 (m, 8H, Ph); 7.74 (t, 4H, $^2J_{HH} = 8.2$ Hz, Ph); 7.58 (t, 8H, $^2J_{HH} = 8.2$ Hz, Ph); 4.75 (s, 4H, Cp); 4.59 (s, 4H, Cp); 1.96 (s, 3H, NCCH_3). ^{31}P{^{1}H}-NMR (CD_3CN): $\delta = 43.8$. ^{13}C{^{1}H}-NMR (CD_3CN): $\delta = 134.8$, 134.8, 134.7, 134.4, 134.4, 130.5, 130.4, 130.3, 79.6, 79.5, 79.4, 77.4, 77.3, 77.2. IR (Nujol, cm^{-1}): 2326, 2298.

4.1.2. *[(dppr)Pd(NCMe)(H_2O)](OTf)$_2$ (**2b**)*

Yellow solid, yield = 99%. Anal. Calc. for $C_{38}H_{32}F_6NO_7P_2S_2PdRu \cdot 2CH_2Cl_2$: C, 40.63; H, 3.07; N, 1.18. Found: C, 39.92; H, 2.97; N, 1.12%. ES–MS

Table 2
Addition of amines to substituted acrylate, crotonate and cinnamate[a]

Entry	Catalyst	Alkene	Amine	Product	T/°C	Yield (%)
1	**2a**			 **9**	rt	88
2	**2b**				rt	69
3	**2c**				rt	86
4	**2d**				rt	61
5	**2a**		$^{n}Bu_2NH$	 **10**	100	32 44[b]
6	**2a**		$PhCH_2NH_2$	 **11**	100	37 50[b]
7	**2a**			 **12**	rt	80
8	**2a**			 **13**	rt	100
9	**2a**			 **14**	100	55
10	**2a**			 **15**	rt	62
11	**2a**		$PhNH_2$	 **16**	100	64
12	**2a**		$PhNH_2$	 **17**	100	78

[a] Reactions were performed with 2 mol% catalyst for 18 h (unoptimized). Uncatalysed reactions performed under the same reaction gave negligible yields [6].
[b] After 48 h.

(MeOH, 20 V): 764.1, 723.0, 706.7. ^{1}H-NMR (CD_3CN): $\delta = 7.78–7.84$ (m, 8H, Ph); 7.73 (t, 4H, $^2J_{HH} = 7.7$ Hz, Ph); 7.57 (t, 8H, $^2J_{HH} = 7.7$ Hz, Ph); 5.13 (s, 4H, Cp); 4.90 (s, 4H, Cp); 1.96 (s, 3H, NCCH_3). ^{31}P{^{1}H}-NMR (CD_3CN): $\delta = 39.9$. ^{13}C{^{1}H}-NMR (CD_3CN): $\delta =$ 134.6, 134.5, 134.4, 134.4, 134.3, 130.5, 130.4, 130.3, 81.6, 81.5, 81.4, 79.6, 79.5, 79.4. IR (Nujol, cm^{-1}): 2320, 2295.

Table 3
Crystallographic data for the **2c** and **2e**

Identification code	**2c**	**2e**
Formula	$[(C_{22}H_{36}FeP_2Pd)(NCMe)(H_2O)][CF_3SO_3]_2^- \cdot 2H_2O$	$[(C_{44}H_{32}P_2Pd)(NCMe)(H_2O)][CF_3SO_3]_2^- \cdot 0.5H_2O$
Crystal system	Monoclinic	Monoclinic
a (Å)	39.1915(9)	11.2625(4)
b (Å)	11.9660(3)	17.4583(9)
c (Å)	17.0622(5)	12.6295(7)
β (°)	111.748(2)	109.85
V (Å^3)	7432.0(3)	2335.7(2)
Z	8	2
Crystal	Block; Red	Block; Yellow
Crystal size (mm)	0.06 × 0.05 × 0.03	0.10 × 0.08 × 0.05
Absolute structure parameter		−0.04(2)
θ range (°); completeness (%)	2.96–25.03; 99.6	2.98–25.03; 99.8
Reflections collected	26 663	30 673
Independent reflections	6548 [$R_{int} = 0.1221$]	8129 [$R_{int} = 0.0963$]
Data/restraints/parameters	6548/0/458	8129/7/630
Goodness-of-fit on F^2	0.952	0.999
Final R indices [$I^2 > 2s(I^2)$]	$R_1 = 0.0772$, $wR_2 = 0.1488$	$R_1 = 0.0536$, $wR_2 = 0.0773$
R indices (all data)	$R_1 = 0.1633$, $wR_2 = 0.1807$	$R_1 = 0.0948$, $wR_2 = 0.0866$

4.1.3. *[(dippf)Pd(NCMe)(H$_2$O)](OTf)$_2$ (**2c**)*

Purple solid, which was recrystallized from CH_2Cl_2–ether to give purplish-red crystals suitable for X-ray analysis. Yield = 60%. Anal. Calc. for $C_{26}H_{41}F_6NO_7P_2S_2FePd \cdot 2H_2O \cdot 2CH_2Cl_2$: C, 30.92; H, 4.54; N, 1.29. Found: C, 31.63; H, 4.29; N, 0.90%. ES–MS (MeOH, 20 V): 585.2, 541.2, 525.1. ^{1}H-NMR (CD_3CN): 4.96 (s, 4H, Cp); 4.72 (s, 4H, Cp); 2.69 (m, 4H, ^{i}Pr); 1.96 (s, 3H, NCCH_3); 1.55 (dd, 12H, $^2J_{HH}$ = 7.0 Hz, $^3J_{PH}$ = 18.4 Hz, ^{i}Pr); 1.31 (dd, 12H, $^2J_{HH}$ = 6.8 Hz, $^3J_{PH}$ = 17.3 Hz, ^{i}Pr). ^{31}P{^{1}H}-NMR (CD_3CN): δ = 91.4. ^{13}C{^{1}H}-NMR (CD_3CN): δ = 77.4, 77.3, 77.2, 75.5, 75.4, 75.3, 30.6, 30.4, 30.3, 30.2, 20.5, 20.3. IR (Nujol, cm^{-1}): 2316, 2289.

4.1.4. *[(dppp)Pd(NCMe)(H$_2$O)](OTf)$_2$ (**2d**)*

Light-yellow solid, yield = 51%. Anal. Calc. for $C_{31}H_{30}F_6NO_7P_2S_2Pd \cdot 4CH_2Cl_2$: C, 34.58; H, 3.15; N, 1.15. Found: C, 34.11; H, 2.78; N, 1.33%. ES–MS (MeOH, 20 V): 577.1, 535.3, 518.2. ^{1}H-NMR (CD_3CN): δ = 7.57–7.67 (m, 12H, Ph); 7.49 (t, 8H, $^2J_{HH}$ = 7.2 Hz, Ph); 2.86 (td, 4H, $^2J_{HH}$ = 6.4 Hz, $^2J_{PH}$ = 1.8 Hz, PCH_2); 2.15–2.34 (m, 2H, PCH_2CH_2); 1.96 (s, 3H, NCCH_3). ^{31}P{^{1}H}-NMR (CD_3CN): δ = 12.3. ^{13}C{^{1}H}-NMR (CD_3CN): δ = 134.1, 134.0, 134.0, 130.6, 130.5, 130.4, 126.1, 125.4, 21.8, 21.6, 21.3, 18.9. IR (Nujol, cm^{-1}): 2324, 2297.

4.1.5. *[(R-BINAP)Pd(NCMe)(H$_2$O)](OTf)$_2$ (**2e**)*

Yellow crystal from recrystallization from CH_2Cl_2–Et_2O, yield = 97%. Anal. Calc. for $C_{48}H_{36}F_6NO_7P_2S_2Pd \cdot 0.5H_2O \cdot 2CH_2Cl_2$: C, 47.47; H, 3.27; N, 1.11. Found: C, 47.05; H, 3.02; N, 1.10%. ES–MS (MeOH, 20 V): 789.3, 746.3, 729.2. ^{1}H-NMR (CD_3CN): δ = 7.77–7.87 (m, 7H); 7.74 (d, 4H, J = 8.2 Hz); 7.65–7.70 (m, 6H); 7.52–7.62 (m, 5H); 7.21 (t, 2H, J = 8.6 Hz); 7.10 (t, 2H, J = 7.2 Hz); 6.91 (s, br, 4H); 6.67 (d, 2H, J = 8.6 Hz); 1.96 (s, 3H). ^{31}P{^{1}H}-NMR (CD_3CN): δ = 31.0 ppm. ^{13}C{1H}-NMR (CD_3CN): δ = 141.0, 136.0, 135.8, 135.7, 135.6, 135.5, 134.2, 133.9, 131.4, 131.3, 130.4, 130.3, 130.2, 129.8, 129.2, 128.8, 128.5, 128.4, 128.0, 127.4, 123.9, 120.3, 119.5, 118.8. IR (Nujol, cm^{-1}): 2318, 2291.

4.2. Typical reaction procedure for hydroamination

0.021 g (0.020 mmol) of complex **2a** was suspended in 0.5 ml of toluene in a thick-walled Young's tube. Freshly distilled styrene (0.17 ml, 1.50 mmol) and aniline (0.09 ml, 1.00 mmol) were added via syringe. The tube was sealed via a PTFE tap and the reaction mixture was stirred and heated in a thermostatic oil bath. After the appropriate reaction time (typically 18 h), the homogeneous red solution was subjected to column chromatography (silica gel: CH_2Cl_2–hexane, 2:1) to furnish the product, which was subsequently characterized by ^{1}H- and ^{13}C-NMR spectroscopy. Yield was calculated with respect to aniline (the limiting reagent).

4.2.1. *N-Phenyl-N-(1-phenylethyl)amine (**3**) [11]*

^{1}H-NMR ($CDCl_3$): δ = 7.38 (d, 2H, Ph, $^2J_{HH}$ = 6.8 Hz); 7.33 (t, 2H, Ph, $^2J_{HH}$ = 7.3 Hz); 7.25 (t, 1H, Ph, $^2J_{HH}$ = 7.3 Hz); 7.10 (t, 2H, Ph, $^2J_{HH}$ = 7.3 Hz); 6.65 (t, 1H, Ph, $^2J_{HH}$ = 7.3 Hz); 6.52 (d, 2H, Ph, $^2J_{HH}$ = 7.3 Hz); 4.40 (q, 1H, CHCH$_3$, $^2J_{HH}$ = 6.8 Hz); 3.94 (s, br, 1H, NH); 1.43 (d, 3H, CHCH_3, $^2J_{HH}$ = 6.8 Hz). ^{13}C{^{1}H}-NMR ($CDCl_3$): δ = 147.7, 145.6, 129.5, 129.0, 127.3, 126.2, 117.6, 113.7, 53.9, 25.5.

4.2.2. *N-(4-Methoxyphenyl)-N-(1-phenylethyl)amine (**4**) [12]*

^{1}H-NMR ($CDCl_3$): δ = 7.32–7.40 (m, 4H, Ph); 7.24 (t, 1H, Ph, $^2J_{HH}$ = 7.3 Hz); 6.71 (d, 2H, Ph, $^2J_{HH}$ = 9.1 Hz); 6.49 (d, 2H, Ph, $^2J_{HH}$ = 9.1 Hz); 4.45 (q, 1H, CHCH$_3$, $^2J_{HH}$ = 6.8 Hz); 3.91 (s, br, 1H, NH); 3.72 (s, 3H, OCH_3); 1.52 (d, 3H, CHCH_3, $^2J_{HH}$ = 6.8 Hz). ^{13}C{^{1}H}-NMR ($CDCl_3$): δ = 152.3, 145.9, 142.0, 129.0, 127.2, 126.3, 115.1, 114.9, 56.1, 54.6, 25.5.

4.2.3. N-(4-Chlorophenyl)-N-(1-phenylethyl)amine (**5**) [13]

^{1}H-NMR ($CDCl_3$): $\delta = 7.28–7.30$ (m, 4H, Ph); 7.21 (t, 1H, Ph, $^2J_{HH} = 6.8$ Hz); 6.99 (d, 2H, Ph, $^2J_{HH} = 8.6$ Hz); 6.38 (d, 2H, Ph, $^2J_{HH} = 8.6$ Hz); 4.40 (q, 1H, CHCH$_3$, $^2J_{HH} = 6.8$ Hz); 4.08 (s, br, 1H, NH); 1.54 (d, 3H, CHCH_3, $^2J_{HH} = 6.8$ Hz). ^{13}C{^{1}H}-NMR ($CDCl_3$): 144.9, 143.8, 128.1, 127.9, 126.2, 124.9, 120.9, 113.5, 52.7, 24.2.

4.2.4. N-Methyl-N-phenyl-N-(1-phenylethyl)amine (**6**) [14]

^{1}H-NMR ($CDCl_3$): $\delta = 7.35–7.38$ (m, 3H, Ph); 7.26–7.30 (m, 4H, Ph); 6.88 (d, 2H, Ph, $^2J_{HH} = 8.6$ Hz); 6.77 (t, 1H, Ph, $^2J_{HH} = 7.3$ Hz); 5.17 (q, 1H, CHCH$_3$, $^2J_{HH} = 6.8$ Hz); 2.73 (s, 3H, NCH_3); 1.59 (d, 3H, CHCH_3, $^2J_{HH} = 6.8$ Hz). ^{13}C{^{1}H}-NMR ($CDCl_3$): $\delta =$ 150.6, 143.2, 129.6, 128.8, 127.3, 127.2, 117.0, 113.5, 56.9, 32.3, 16.7.

4.2.5. N-[1-(2-Naphthyl)ethyl]-N-phenylamine (7) [15]

^{1}H-NMR ($CDCl_3$): $\delta = 7.82–7.86$ (m, 4H, naphthyl); 7.54 (d, 1H, naphthyl, $^2J_{HH} = 8.6$ Hz); 7.46–7.51 (m, 2H, naphthyl); 7.12 (t, 2H, Ph, $^2J_{HH} = 7.7$ Hz); 6.70 (t, 1H, Ph, $^2J_{HH} = 7.7$ Hz); 6.58 (d, 2H, Ph, $^2J_{HH} = 7.7$ Hz); 4.68 (q, 1H, CHCH$_3$, $^2J_{HH} = 6.5$ Hz); 4.16 (s, br, 1H, NH); 1.62 (d, 3H, CHCH_3, $^2J_{HH} = 6.5$ Hz). ^{13}C{^{1}H}-NMR ($CDCl_3$): $\delta = 147.7$, 143.2, 134.0, 133.2, 129.5, 128.9, 128.3, 128.1, 126.4, 125.9, 124.8, 124.7, 117.7, 113.8, 54.1, 25.5.

4.2.6. N-Methyl-N-[1-(2-naphthyl)ethyl]-N-phenylamine (**8**)

^{1}H-NMR ($CDCl_3$): $\delta = 7.78–7.86$ (m, 4H, naphthyl); 7.47–7.53 (m, 3H, naphthyl); 7.31 (t, 2H, Ph, $^2J_{HH} = 7.3$ Hz); 6.93 (d, 2H, Ph, $^2J_{HH} = 8.6$ Hz); 6.79 (t, 1H, Ph, $^2J_{HH} = 7.3$ Hz); 5.31 (q, 1H, CHCH_3, $^2J_{HH} = 6.8$ Hz); 2.72 (s, 3H, NCH_3); 1.68 (d, 2H, CHCH_3, $^2J_{HH} = 6.8$ Hz). ^{13}C{^{1}H}-NMR ($CDCl_3$): $\delta = 150.6$, 140.9, 133.8, 133.0, 129.7, 128.5, 128.4, 128.0, 126.5, 126.1, 125.3, 117.2, 113.5, 57.0, 32.3, 16.4.

4.2.7. 2-Methyl-3-piperidin-1-yl-propionic acid methyl ester (**9**) [16]

^{1}H-NMR ($CDCl_3$): $\delta = 3.67$ (s, 3H, COOCH_3); 2.64–2.73 (m, 1H, CHCH$_3$); 2.59 (dd, 1H, NCH_2CH, $^1J_{HH} =$ 8.6 Hz, $^2J_{HH} = 12.2$ Hz); 2.27–2.39 (m, 4H, piperidinyl); 2.26 (dd, 1H, NCH_2CH, $^1J_{HH} = 6.4$ Hz, $^2J_{HH} = 12.2$ Hz); 1.48–1.55 (m, 4H, piperidinyl); 1.34–1.41 (m, 2H, piperidinyl); 1.11 (d, 3H, CHCH_3, $^2J_{HH} = 6.8$ Hz). ^{13}C{^{1}H}-NMR ($CDCl_3$): $\delta = 177.7$, 63.2, 55.5, 52.4, 38.8, 26.9, 25.2, 16.6.

4.2.8. Methyl-3-(dibutylamino)-2-methylpropionate (**10**) [17]

^{1}H-NMR ($CDCl_3$): $\delta = 3.66$ (s, 3H, COOCH_3); 2.58–2.72 (m, 2H, NCH_2CH (1H) and NCH$_2CH$ (1H)); 2.28–2.42 (m, 5H, CH$_2CH_2$NCH_2CH$_2$ (4H) and NCH_2CH (1H)); 1.31–1.40 (m, 4H, CH_2CH$_2$NCH$_2CH_2$); 1.21–1.31 (m, 4H, CH_2CH$_3$); 1.11 (d, 3H, CHCH_3, $^2J_{HH} =$ 6.8 Hz); 0.89 (t, 6H, CH$_2CH_3$, $^2J_{HH} = 7.0$ Hz). ^{13}C{^{1}H}-NMR ($CDCl_3$): $\delta = 177.2$, 58.6, 54.6, 51.8, 39.4, 29.7, 20.9, 15.9, 14.5.

4.2.9. Methyl 3-(benzylamino)-2-methylpropanoate (**11**) [18]

^{1}H-NMR ($CDCl_3$): $\delta = 7.23–7.35$ (m, 5H, Ph); 3.79 (s, 2H, PhCH_2); 3.69 (s, 3H, COOCH_3); 2.85–2.92 (m, 1H, PhCH$_2$NCH_2); 2.63–2.73 (m, 2H, PhCH$_2$NCH_2 (1H), PhCH$_2$NCH$_2CH$ (1H)); 1.16 (d, 3H, CHCH_3, $^2J_{HH} = 6.8$ Hz). ^{13}C{^{1}H}-NMR ($CDCl_3$): $\delta = 176.4$, 140.4, 128.5, 128.1, 127.0, 53.8, 52.2, 51.7, 40.2, 15.4.

4.2.10. 2-Methyl-3-pyrrolindin-1-yl-propionic acid methyl ester (**12**) [19]

^{1}H-NMR ($CDCl_3$): $\delta = 3.66$ (s, 3H, COOCH_3); 2.76 (dd, 1H, NCH_2CH, $^1J_{HH} = 8.2$ Hz, $^2J_{HH} = 11.4$ Hz); 2.59–2.70 (m, 1H, NCH$_2CH$); 2.43–2.52 (m, 4H, pyrrolindinyl); 2.42 (dd, 1H, NCH_2CH, $^1J_{HH} = 6.2$ Hz, $^2J_{HH} = 11.4$ Hz); 1.71–1.75 (m, 4H, pyrrolindinyl); 1.16 (d, 3H, CHCH_3, $^2J_{HH} = 7.3$ Hz). ^{13}C{^{1}H}-NMR ($CDCl_3$): $\delta = 177.0$, 60.0, 54.6, 52.0, 40.0, 23.9, 16.2.

4.2.11. 3-Piperidin-1-yl-butyric acid methyl ester (**13**) [20]

^{1}H-NMR ($CDCl_3$): $\delta = 3.65$ (s, 3H, COOCH_3); 3.05–3.15 (m, 1H, NCH); 2.57 (dd, 1H, NCHCH_2, $^1J_{HH} = 5.6$ Hz, $^2J_{HH} = 14.1$ Hz); 2.43 (t, 2H, pyrrolindinyl, $^2J_{HH} =$ 5.5 Hz); 2.21 (dd, 1H, NCHCH_2, $^1J_{HH} = 8.6$ Hz, $^2J_{HH} = 14.1$ Hz); 1.50–1.56 (m, 4H, pyrrolindinyl); 1.36–1.42 (m, 4H, pyrrolindinyl); 1.03 (d, 3H, CHCH_3, $^2J_{HH} = 6.8$ Hz). ^{13}C{^{1}H}-NMR ($CDCl_3$): $\delta =$ 173.8, 57.4, 54.6, 51.9, 49.8, 38.2, 26.8, 25.2, 15.6.

4.2.12. 3-Phenyl-3-piperidino-propionic acid methyl ester (**14**) [21]

^{1}H-NMR ($CDCl_3$): $\delta = 7.21–7.34$ (m, 5H, Ph); 3.98 (t, 1H, PhCH, $^2J_{HH} = 7.7$ Hz); 3.59 (s, 3H, COOCH_3); 2.99 (dd, 1H, PhCHCH_2, $^1J_{HH} = 7.7$ Hz, $^2J_{HH} = 14.9$ Hz); 2.70 (dd, 1H, PhCHCH_2, $^1J_{HH} = 7.7$ Hz, $^2J_{HH} =$ 14.9 Hz); 2.36–2.42 (m, 2H, piperidinyl); 2.25–2.31 (m, 2H, piperidinyl); 1.43–1.58 (m, 4H, piperidinyl); 1.29–1.35 (m, 2H, piperidinyl). ^{13}C{^{1}H}-NMR ($CDCl_3$): $\delta =$ 173.0, 139.1, 128.7, 128.3, 127.7, 66.7, 51.9, 51.3, 38.3, 26.8, 24.9.

*4.2.13. 3-Pyrrolindin-1-yl-butyric acid methyl ester (**15**) [22]*

^{1}H-NMR ($CDCl_3$): $\delta = 3.67$ (s, 3H, COOCH_3); 2.84–2.93 (m, 1H, NCH); 2.68 (dd, 1H, NCHCH_2, $^1J_{HH} = 4.5$ Hz, $^2J_{HH} = 15.0$ Hz); 2.55–2.60 (m, 4H, pyrrolindinyl); 2.29 (dd, 1H, NCHCH_2, $^1J_{HH} = 8.6$ Hz, $^2J_{HH} = 15.0$ Hz); 1.75–1.79 (m, 4H, pyrrolindinyl); 1.15 (d, 3H, CHCH_3, $^2J_{HH} = 6.4$ Hz). ^{13}C{^{1}H}-NMR ($CDCl_3$): $\delta =$ 173.2, 55.9, 51.8, 51.1, 40.4, 23.7, 19.0.

*4.2.14. N-Phenyl-β-alanine methyl ester (**16**) [23]*

^{1}H-NMR ($CDCl_3$): $\delta = 7.19$ (t, 2H, Ph, $^2J_{HH} = 7.3$ Hz); 6.73 (t, 1H, Ph, $^2J_{HH} = 7.3$ Hz); 6.63 (d, 2H, Ph, $^2J_{HH} = 7.3$ Hz); 4.02 (s, br, 1H, NH); 3.70 (s, 3H, COOCH_3); 3.46 (t, 2H, NHCH_2, $^2J_{HH} = 6.4$ Hz); 2.64 (t, 2H, NHCH$_2CH_2$, $^2J_{HH} = 6.4$ Hz). ^{13}C{^{1}H}-NMR ($CDCl_3$): $\delta = 173.2$, 148.0, 129.7, 118.1, 113.4, 52.2, 39.8, 34.1.

*4.2.15. N-Phenyl-β-alanine nitrile (**17**) [24]*

^{1}H-NMR ($CDCl_3$): $\delta = 7.22$ (t, 2H, Ph, $^2J_{HH} = 7.3$ Hz); 6.79 (t, 1H, Ph, $^2J_{HH} = 7.3$ Hz); 6.62 (d, 2H, Ph, $^2J_{HH} = 7.3$ Hz); 3.99 (s, br, 1H, NH); 3.53 (m, 2H, NHCH_2); 2.64 (t, 2H, CH_2CN, $^2J_{HH} = 6.4$ Hz). ^{13}C{^{1}H}-NMR ($CDCl_3$): $\delta = 146.6$, 130.0, 119.0, 118.7, 113.5, 40.2, 18.5.

5. Supplementary material

Crystallographic data for the structural analysis have been deposited with the Cambridge Crystallographic Data Centre, CCDC nos. 193997 and 193998 for compounds **2c** and **2e**, respectively. Copies of this information may be obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk).

Acknowledgements

We thank the EPSRC for postdoctoral funding (ROPA award, Grant No.: GR/R50332/01) and Johnson Matthey, Plc. for the generous loan of palladium salts.

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