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Efficiency of a tetraphosphine ligand in palladium catalysed allylic amination

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Abstract

A new tetraphosphine, the *cis*,*cis*,*cis*-1,2,3,4-tetrakis (diphenylphosphinomethyl)cyclopentane (Tedicyp), in combination with $[Pd(C_3H_5)Cl]_2$ affords a very efficient catalyst for allylic amination. A turnover number of 980 000 can be obtained for the addition of dipropylamine to allyl acetate in the presence of this catalyst. This complex is very stable and the reactions can be performed in water without loss of activity. © 2002 Published by Elsevier Science B.V.

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1. Introduction

Allylamines are fundamental building blocks in organic synthesis and their preparation is an important industrial goal (for a review on biaryl synthesis, see [1]). Palladium-catalysed allylic amination is one of the most powerful methods for the formation of allyl–nitrogen bonds (for reviews on allylic substitution reactions, see [2]). The classical method to perform this reaction is to employ palladium complexes associated with mono- [3] or diphosphine [4] ligands. Phosphine–amine [5] ligands have also been used successfully. Even if the catalysts formed by association of these ligands with palladium complexes are efficient in terms of yield of adduct, the efficiency in terms of ratio substrate/catalyst is low. In general 1–5% of these catalysts must be used. Decomposition of the catalyst is generally observed quite rapidly. A few years ago, Trost has reported that a diaminocyclohexane-*N*,*N*′-bis(2′-diphenylphosphinobenzoyl) ligand exhibits high allylic amination activity in the presence of 0.025% catalyst [6]. He had also observed that with a polystyrene–phosphine–palladium complex the reaction could be performed with as little as 0.018% catalyst (TON 3200) [7]. Nevertheless, very high values of ratio substrate/catalyst have not been reported for this reaction.

2. Experimental

2.1. General

All manipulations were carried out under an argon atmosphere using standard Schlenk techniques. THF was dried and distilled before use. The *cis*,*cis*,*cis*-1,2,3,4-tetrakis (diphenylphosphinomethyl) cyclopentane (Tedicyp)–Pd complex was prepared

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following a previously published procedure [9]. The products were characterised by NMR analysis in $CDCl_3$ with Bruker 200 and 300 MHz.

2.2. Catalytic procedures

2.2.1. Reactions performed in THF

As a typical experiment, allylic acetate was added to the adequate quantity of the complex THF solution previously prepared. After 10 min at ambient temperature, the amine was added and the mixture was stirred at adequate temperature until acetate disappearance checked by gas chromatography. A solution of NaOH was then added and the products were extracted with diethylether, dried over $MgSO_4$. After evaporation of the solvent, the product was distilled or filtered on silica gel.

2.2.2. Reactions performed in water

An adequate quantity of Tedicyp–Pd complex was prepared in THF, then the THF was removed in vacuo. The allylic acetate, the amine and distilled water were then added to the complex under argon. The mixture was stirred at the adequate temperature.

2.3. Allylation products with allyl acetate

Triallylamine (Table 1, entry 6): allyl acetate (0.25 ml, 2.32 mmol), Pd complex (2.32×10^{-3} μmol) and diallylamine (0.57 ml, 4.64 mmol). The progress of the reaction was monitored by GC and NMR, the product was obtained in 73% conversion.

N-Allyldioctylamine (Table 1, entry 9): allyl acetate (0.25 ml, 2.32 mmol), Pd complex (2.32×10^{-2} μmol) and dioctylamine (1.40 ml, 4.64 mmol). The mixture was purified by distillation (200 °C, 3 mm, Kugelrohr) to give the product in 93% (0.61 g) yield.

N-Allyldipropylamine (Table 2, entry 2): allyl acetate (0.25 ml, 2.32 mmol), Pd complex (2.32×10^{-3} μmol) and dipropylamine (0.63 ml, 4.64 mmol). The progress of the reaction was monitored by GC and NMR, the product was obtained in 68% conversion.

4-Allylmorpholine (Table 2, entry 10): allyl acetate (0.25 ml, 2.32 mmol), Pd complex (0.232 μmol) and morpholine (0.40 ml, 4.64 mmol). The progress of the reaction was monitored by GC and NMR, the product was obtained in 93% conversion.

1-Allylpyrrolidine (Table 2, entry 13): allyl acetate (0.25 ml, 2.32 mmol), Pd complex (0.232 μmol) and pyrrolidine (0.38 ml, 4.64 mmol). The progress of the reaction was monitored by GC and NMR, the product was obtained in 95% conversion. ^{1}H NMR δ 5.84 (ddt, 1H, J = 17.0, 10.2 and 6.6 Hz), 5.12 (d, 1H, J = 17.0 Hz), 5.02 (d, 1H, J = 10.2 Hz), 3.05 (d, 2H, J = 6.6 Hz), 2.5 (t, 4H, J = 6.6 Hz), 1.65 (m, 4H).

1-Allylpiperidine (Table 2, entry 14): allyl acetate (0.25 ml, 2.32 mmol), Pd complex (0.232 μmol) and piperidine (0.46 ml, 4.64 mmol). The progress of the reaction was monitored by GC and NMR, the product was obtained in 93% conversion. ^{1}H NMR δ 5.82 (ddt, 1H, J = 17.0, 10.2 and 6.8 Hz), 5.10 (d, 1H, J = 17.0 Hz), 5.05 (d, 1H, J = 10.2 Hz), 2.90 (d, 2H, J = 6.8 Hz), 2.3 (bs, 4H), 1.55 (m, 6H).

Table 1
Palladium catalysed allylic amination with allyl acetate: influence of the ligand (Scheme 1)[a]

Entry	Amine	Ligand	Ratio ligand/$[Pd(C_3H_5)Cl]_2$	Time (h)	Temperature (°C)	Ratio substrate/catalyst	Conversion (%)
1	Diallylamine	PPh_3	8	130	25	100000	5
2		dppm	4	130	25	100000	4
3		dppe	4	130	25	100000	7
4		dppb	4	130	25	100000	2
5		Tedicyp	2	130	25	100000	95
6		Tedicyp	2	90	55	1000000	73
7	Dioctylamine	PPh_3	8	48	55	100000	1
8		dppe	4	48	55	100000	3
9		Tedicyp	2	48	55	100000	93[b]
10		Tedicyp	2	24	55	1000000	17

[a] Conditions: catalyst THF; allyl acetate: 1 eq.; amine: 2 eq.
[b] Isolated yield.

Table 2
Tedicyp–Pd catalysed allylic amination of secondary amines with allyl acetate (Scheme 2)[a]

Entry	Amine	Time (h)	Temperature (°C)	Solvent	Ratio substrate/catalyst	Conversion (%)
1	Dipropylamine	20	25	THF	100000	99
2		72	25	THF	1000000	68
3		130	55	THF	5000000	14
4		20	25	H_2O	1000000	10
5		240	55	H_2O	1000000	98
6	Dioctylamine	48	55	THF	100000	99
7		24	55	THF	1000000	17
8		20	55	H_2O	10000	99[b]
9		20	55	H_2O	100000	80[b]
10	Morpholine	130	25	THF	10000	93
11		130	25	THF	100000	57
12		20	55	H_2O	100000	96[c]
13	Pyrrolidine	20	55	THF	10000	95
14	Piperidine	20	55	THF	10000	93
15	Diisopropylamine	72	25	THF	1000	81
16		72	25	THF	10000	19
17		20	25	H_2O	1000	97[c]
18	*N*-Methylaniline	72	25	THF	1000	78[d]
19		72	25	THF	10000	12

[a] Conditions: catalyst $[Pd(C_3H_5)Cl]_2$/Tedicyp = 1/2; 25 °C; 20 h; allyl acetate: 1 eq.; amine: 2 eq.
[b] Water saturated with NaCl.
[c] Allyl acetate: 2 eq.; amine: 1 eq.; K_2CO_3: 1 eq.
[d] Isolated yield.

N-Allyldiisopropylamine (Table 2, entry 15): allyl acetate (0.25 ml, 2.32 mmol), Pd complex (2.32 μmol) and diisopropylamine (0.65 ml, 4.64 mmol). The progress of the reaction was monitored by GC and NMR, the product was obtained in 81% conversion. ^{1}H NMR δ 5.83 (ddt, 1H, J = 17.2, 10.0 and 6.6 Hz), 5.12 (d, 1H, J = 17.2 Hz), 5.02 (d, 1H, J = 10.0 Hz), 3.2 (sept., 2H, J = 6.5 Hz), 3.04 (d, 2H, J = 6.6 Hz), 1.27 (d, 12H, J = 6.5 Hz).

N-Allyl-N-methylaniline (Table 2, entry 18): allyl acetate (0.25 ml, 2.32 mmol), Pd complex (2.32 μmol) and *N*-methylaniline (0.51 ml, 4.64 mmol). The mixture was purified by distillation (Kugelrohr) to give *N*-allyl-*N*-methylaniline in 78% (0.27 g) yield.

N-Allylbenzylamine and N,N-diallylbenzylamine (Table 3, entry 2): allyl acetate (0.25 ml, 2.32 mmol), Pd complex (2.32×10^{-2} μmol) and benzylamine (0.51 ml, 4.64 mmol). The mixture was purified by distillation (Kugelrohr) to give *N*-allylbenzylamine and *N,N*-diallylbenzylamine with a ratio (90/10) in 83% (0.29 g) yield.

N-Allylcyclohexylamine and N,N-diallylcyclohexylamine (Table 3, entry 4): allyl acetate (0.25 ml, 2.32 mmol), Pd complex (2.32 μmol) and cyclohexylamine (0.53 ml, 4.64 mmol). The progress of the reaction was monitored by GC and NMR, *N*-allylcyclohexylamine and *N,N*-diallylcyclohexylamine were obtained in 78% conversion (ratio 68/32). *N-Allylcyclohexylamine*: ^{1}H NMR δ 5.87–5.74 (ddt, 1H, J = 16.8, 10.2 and 6.3 Hz), 5.10 (d, 1H, J = 16.8 Hz), 5.05 (d, 1H, J = 10.2 Hz), 3.25 (d, 2H, J = 6.3 Hz), 2.50 (m, 1H), 2.0–1.0 (m, 10H); ^{13}C NMR δ 137.6, 116.9, 59.4, 53.3, 29.3, 26.8, 26.5. *N,N-Diallylcyclohexylamine*: ^{1}H NMR δ 5.87–5.74 (ddt, 2H, J = 16.8, 10.2 and 6.3 Hz), 5.10 (d, 2H, J = 16.8 Hz), 5.05 (d, 1H, J = 10.2 Hz), 3.15 (d, 4H, J = 6.3 Hz), 2.5 (m, 1H), 2.0–1.0 (m, 10H); ^{13}C NMR δ 137.6, 116.9, 59.4, 53.3, 29.3, 26.8, 26.5.

N-Allyl-(R)-phenylethylamine and N,N-diallyl-(R)-phenylethylamine (Table 3, entry 6): allyl acetate (0.25 ml, 2.32 mmol), Pd complex (2.32 μmol) and (*R*)-phenylethylamine (0.60 ml, 4.64 mmol). The mixture was purified by distillation (Kugelrohr) to give *N*-allyl-(*R*)-phenylethylamine and *N,N*-diallyl-(*R*)-phenylethylamine (ratio 76/24) in 94% (0.36 g) yield.

Table 3
Tedicyp–Pd catalysed allylic amination of primary amines with allyl acetate (Scheme 3)[a]

Entry	Amine	Time (h)	Temperature (°C)	Solvent	Ratio substrate/catalyst	Ratio **a**/**b** [b]	Conversion (%)
1	Benzylamine	48	55	THF	10000	85/15	97
2		72	55	THF	100000	90/10	83[c]
3		20	55	H_2O	100000	5/95	96[d]
4	Cyclohexylamine	20	25	Toluene	1000	68/32	78
5		20	25	H_2O	1000	1/99	100[d]
6	(*R*)-Phenylethylamine	20	25	THF	1000	76/24	94[c]
7		20	25	THF	10000	98/2	28
8		20	25	H_2O	1000	3/97	96[d]

[a] Conditions: catalyst $[Pd(C_3H_5)Cl]_2$/Tedicyp = 1/2; 25 °C; 20 h; allyl acetate: 1 eq.; amine: 2 eq.
[b] **a** correspond to the monoaddition product and **b** to the diaddition product (Scheme 3).
[c] Isolated yield.
[d] Allyl acetate: 2 eq.; amine: 1 eq.; K_2CO_3: 1 eq.

2.4. Allylation products with cinnamyl acetate

N,N-Dipropyl-3-phenylallylamine (Table 4, entry 1): cinnamyl acetate (1.30 g, 7.4 mmol), Pd complex (7.4 μmol) and dipropylamine (2.03 ml, 14.8 mmol), THF (20 ml). The residue was purified by column chromatography (ether/pentane: 3/7) to give *N,N*-dipropyl-3-phenylallylamine and *N,N*-dipropyl-1-phenylallyl amine (ratio 94/6) in 95% (1.52 g) yield. *N,N-Dipropyl-3-phenylallylamine*: ^{1}H NMR δ 7.35–7.15 (m, 5H), 6.43 (d, 1H, J = 15.9 Hz), 6.20 (dt, 1H, J = 15.9 and 6.6 Hz), 3.20 (d, 2H, J = 6.6 Hz), 2.35 (t, 4H, J = 7.4 Hz), 1.40 (tq, 4H, J = 7.4 and 7.4 Hz), 0.80 (t, 6H, J = 7.4 Hz); ^{13}C NMR δ 137.4, 131.9, 128.6, 128.2, 127.3, 126.3, 56.8, 56.0, 20.3, 12.0. *N,N-Dipropyl-1-phenylallylamine*: partial ^{1}H NMR spectra was obtained from the mixture. ^{1}H NMR δ 5.10 (d, 1H, J = 17.4 Hz), 5.05 (d, 1H, J = 10.0 Hz).

N,N-Diallyl-3-phenylallylamine (Table 4, entry 4): cinnamyl acetate (0.040 g, 0.23 mmol), Pd complex (0.023 μmol) and diallylamine (0.057 ml, 0.46 mmol). The residue was purified by column chromatography (ether/pentane: 3/7) to give *N,N*-diallyl-3-phenylallylamine and *N,N*-diallyl-1-phenylallylamine (ratio 99/1) in 98% (0.048 g) yield.

N,N-Dioctyl-3-phenylallylamine (Table 4, entry 6): cinnamyl acetate (0.040 g, 0.23 mmol), Pd complex (0.023 μmol) and dioctylamine (0.140 ml, 0.46 mmol). The residue was purified by column chromatography (ether/pentane: 1/4) to give the product in 98% (0.080 g) yield. ^{1}H NMR δ 7.45–7.20 (m, 5H), 6.52 (d, 1H, J = 15.9 Hz), 6.28 (dt, 1H, J = 15.9 and 6.3 Hz), 3.26 (d, 2H, J = 6.3 Hz), 2.47 (t, 4H, J = 7.0 Hz), 1.8–1.1 (m, 24H), 0.80 (m, 6H); ^{13}C NMR δ 137.3, 131.9, 128.4, 128.1, 127.1, 126.2, 56.7, 53.9, 31.8, 29.6, 29.3, 27.6, 27.0, 22.6, 14.0.

3-Morpholino-1-phenylprop-1-ene (Table 4, entry 8): cinnamyl acetate (0.040 g, 0.23 mmol), Pd complex (0.23 μmol) and morpholine (0.040 ml, 0.46 mmol). The residue was purified by column chromatography (ether/pentane: 3/7) to give 3-morpholino-1-phenylpropene and 3-morpholino-3-phenylpropene (ratio 86/14) in 95% (0.044 g) yield.

3-Pyrrolidino-1-phenylprop-1-ene (Table 4, entry 12): cinnamyl acetate (0.160 g, 0.92 mmol), Pd complex (4.6×10^{-2} μmol), K_2CO_3 (0.063 g, 0.46 mmol) and pyrrolidine (0.038 ml, 0.46 mmol). The residue was purified by column chromatography (ether/pentane: 3/7) to give 3-pyrrolidino-1-phenylpropene and 3-pyrrolidino-3-phenylpropene (ratio 84/16) in 95% (0.082 g) yield.

N,N-Dimethyl-3-phenylallylamine and N,N-dimethyl-1-phenylallylamine (Table 4, entry 13): cinnamyl acetate (0.040 g, 0.23 mmol), Pd complex (0.23 μmol) and a 2N solution of dimethylamine in methanol (0.23 ml, 0.46 mmol). The residue was purified by column chromatography (ether/pentane: 3/7) to give *N,N*-dimethyl-3-phenylallylamine and *N,N*-dimethyl-1-phenylallylamine (ratio 99/1) in 33% (0.013 g) yield.

N-Benzyl-3-phenylallylamine, N-benzyl-1-phenylallylamine and N-benzyl-di(3-phenylallyl)amine (Table 5, entry 1): cinnamyl acetate (0.040 g,

Table 4
Tedicyp–Pd catalysed allylic amination of secondary amines with substituted allyl acetates (Scheme 4)[a]

Entry	Allyl acetate	Amine	Time (h)	Temperature (°C)	Solvent	Ratio substrate/catalyst	Ratio **a**/**b**[b]	Conversion (%)
1	Cinnamyl acetate	Dipropylamine	24	25	THF	1000	94/6	95[c]
2			48	25	THF	10000	95/5	36
3		Diallylamine	130	25	THF	1000	95/5	85
4			40	25	H_2O	10000	99/1	98[c]
5			48	25	H_2O	100000	99/1	36
6		Dioctylamine	20	55	H_2O	10000	100/0	98[c]
7			20	25	H_2O	100000	100/0	18[d]
8		Morpholine	24	25	THF	1000	86/14	95[c]
9			24	25	THF	10000	84/16	44
10			20	25	H_2O	1000	83/17	96
11			20	25	H_2O	10000	85/15	62[e]
12		Pyrrolidine	20	25	H_2O	10000	84/16	95[c,e]
13		Dimethylamine	20	25	H_2O	1000	99/1	33[c,f]
14	*E*-Hex-2-en-1-yl acetate	Diethylamine	130	25	THF	100	100/0	95[c]
15			130	25	THF	1000	100/0	43
16		Dipropylamine	90	25	THF	1000	100/0	90[c]
17			20	25	H_2O	1000	99/1	85
18		Diallylamine	40	25	H_2O	1000	98/2	82[c]
19			20	25	H_2O	10000	99/1	50[e]
20		Dioctylamine	24	25	THF	100	100/0	95
21			48	25	THF	1000	100/0	80[c]
22			20	25	H_2O	1000	100/0	97[e]
23		Diisopropylamine	24	55	THF	1000	98/2	60[c]
24		Morpholine	24	55	THF	100	91/9	100
25			130	25	THF	1000	92/8	51
26			20	25	H_2O	1000	92/8	88[c,e]
27			20	25	H_2O	10000	88/12	62[e]
28		Pyrrolidine	24	25	THF	100	93/7	94[c]
29			48	55	THF	1000	94/6	49
30			20	25	H_2O	1000	95/5	95
31	3-Acetoxy-1,3-diphenylpropene	Morpholine	130	55	THF	100	–	65[c]
32		Dipropylamine	20	25	H_2O	100	–	45[c,e]

[a] Conditions: catalyst $[Pd(C_3H_5)Cl]_2$/Tedicyp = 1/2; 25 °C; 20 h; allyl acetate: 1 eq.; amine: 2 eq.
[b] Linear isomer corresponds to '**a**' and the branched isomer corresponds to '**b**' (Scheme 4).
[c] Isolated yield.
[d] Water saturated with NaCl.
[e] Allyl acetate: 2 eq.; amine: 1 eq.; K_2CO_3: 1 eq.
[f] Hydrolysis of the acetate is also observed.

Table 5
Tedicyp–Pd catalysed allylic amination (Scheme 5)[a]

Entry	Allyl acetate	Amine	Ratio substrate/catalyst	Ratio **a**/**b**/**c**[b]	Yield (%)
1	Cinnamyl acetate	Benzylamine	1000	95/1/4	96
2		Cyclohexylamine	1000	95/1/4	87
3	*E*-Hex-2-en-1-yl acetate	Cyclohexylamine	1000	62/38/0	82
4			100		94[c]

[a] Conditions: catalyst $[Pd(C_3H_5)Cl]_2$/Tedicyp = 1/2; 25 °C; H_2O; 20 h; allyl acetate: 1 eq.; amine: 2 eq.; isolated yield.
[b] Scheme 5.
[c] Allyl acetate: 2 eq.; amine: 1 eq.; K_2CO_3: 1 eq.

0.23 mmol), Pd complex (0.23 μmol) and benzylamine (0.051 ml, 0.46 mmol). The residue was purified by column chromatography (ether/pentane: 1/4) to give *N*-benzyl-3-phenylallylamine, *N*-benzyl-1-phenylallylamine and *N*-benzyl-di(3-phenylallyl)amine (ratio 95/4/1) in 96% (0.049 g), yield.

N-Cyclohexyl-3-phenylallylamine, N-cyclohexyl-1-phenylallylamine and N-cyclohexyl-di(3-phenylallyl)amine (Table 5, entry 2): cinnamyl acetate (0.040 g, 0.23 mmol), Pd complex (0.23 μmol) and cyclohexylamine (0.053 ml, 0.46 mmol). The residue was purified by column chromatography (ether/pentane: 3/7) to give *N*-cyclohexyl-3-phenylallylamine, *N*-cyclohexyl-1-phenylallylamine and *N*-cyclohexyldi(3-phenylallyl)amine (ratio 95/4/1) in 87% (0.044 g) yield.

2.5. Allylation products with E-hex-2-en-1-yl acetate

N-(E)-(Hex-2-en-1-yl)diethylamine (Table 4, entry 14): *E*-hex-2-en-1-yl acetate (0.099 g, 0.69 mmol), Pd complex (6.96 μmol) and diethylamine (0.14 ml, 1.38 mmol). The residue was purified by column chromatography (ether/pentane: 3/7) to give the product in 95% (0.102 g) yield.

N-(E)-(Hex-2-en-1-yl)dipropylamine (Table 4, entry 16): *E*-hex-2-en-1-yl acetate (0.33 g, 2.32 mmol), Pd complex (2.32 μmol) and dipropylamine (0.14 ml, 4.64 mmol). The residue was purified by column chromatography (ether/pentane: 3/7) to give the product in 90% (0.38 g) yield. ^{1}H NMR δ 5.50 (dt, 1H, $J = 15.4$ and 5.8 Hz), 5.40 (dt, 1H, $J = 15.4$ and 5.6 Hz), 3.00 (d, 2H, $J = 5.8$ Hz), 2.31 (t, 4H, $J = 7.6$ Hz), 1.95 (td, 2H, $J = 7.8$, 5.6 Hz), 1.35 (m, 6H), 0.80 (m, 9H).

N-(E)-(Hex-2-en-1-yl)diallylamine (Table 4, entry 18): *E*-hex-2-en-1-yl acetate (0.33 g, 2.32 mmol), Pd complex (2.32 μmol) and diallylamine (0.57 ml, 4.64 mmol). The residue was purified by column chromatography (ether/pentane: 3/7) to give *N*-(*E*)-(hex-2-en-1-yl)diallylamine and *N*-(hex-1-en-3-yl)diallylamine (ratio 98/2) in 82% (0.33 g) yield. *N-(E)-(Hex-2-en-1-yl)diallylamine*: ^{1}H NMR δ 5.72 (ddt, 2H, $J = 17.0$, 10.9 and 6.1 Hz), 5.45 (dt, 1H, $J = 15.9$ and 5.8 Hz), 5.40 (dt, 1H, $J = 15.9$ and 5.6 Hz), 5.00 (d, 2H, $J = 17.0$ Hz), 4.95 (d, 2H, $J = 10.9$ Hz), 3.09 (d, 4H, $J = 6.1$ Hz), 2.92 (d, 2H, $J = 5.8$ Hz), 1.92 (td, 2H, $J = 7.1$ and 5.6 Hz), 1.24 (qt, 2H, $J = 7.6$ and 7.1 Hz), 0.74 (t, 3H, $J = 7.6$ Hz); ^{13}C NMR δ 137.3, 134.8, 127.4, 116.5, 57.0, 52.3, 35.1, 23.0, 14.3. *N-(Hex-1-en-3-yl)diallylamine*: partial ^{1}H NMR spectra was obtained from the mixture. ^{1}H NMR δ 5.15 (dd, 1H, $J = 17.2$ and 1.5 Hz), 5.05 (dd, 1H, $J = 10.0$ and 1.5 Hz).

N-(E)-(Hex-2-en-1-yl)dioctylamine (Table 4, entry 21): *E*-hex-2-en-1-yl acetate (0.33 g, 2.32 mmol), Pd complex (2.32 μmol) and dioctylamine (1.40 ml, 4.64 mmol). The residue was purified by column chromatography (ether/pentane: 2/8) to give the product in 80% (0.60 g) yield. ^{1}H NMR δ 5.50 (dt, 1H, $J = 15.4$ and 5.8 Hz), 5.40 (dt, 1H, $J = 15.4$ and 5.6 Hz), 3.00 (d, 2H, $J = 5.8$ Hz), 2.31 (t, 4H, $J = 7.6$ Hz), 1.95 (td, 2H, $J = 7.8$ and 5.6 Hz), 1.35 (m, 26H), 0.80 (m, 9H); ^{13}C NMR δ 133.3, 127.4, 56.3, 53.7, 34.5, 31.9, 30.2, 29.6, 29.3, 27.6, 27.4, 26.9, 22.7, 14.1.

N-(E)-(Hex-2-en-1-yl)diisopropylamine (Table 4, entry 23): *E*-hex-2-en-1-yl acetate (0.33 g, 2.32 mmol), Pd complex (2.32 μmol) and diisopropylamine (0.65 ml, 4.64 mmol). The residue was purified by column chromatography (ether/pentane: 3/7) to give *N*-(*E*)-(hex-2-en-1-yl)diisopropylamine and *N*-(hex-1-en-3-yl)diisopropylamine (ratio 98/2) in 60% (0.26 g) yield. *N-(E)-(Hex-2-en-1-yl)diisopropylamine*: ^{1}H NMR δ 5.50 (dt, 1H, $J = 15.4$ and 5.8 Hz), 5.40 (dt, 1H, $J = 15.4$ and 5.6 Hz), 3.2 (sept., 2H, $J = 6.4$ Hz), 3.02 (d, 2H, $J = 5.8$ Hz), 1.95 (td, 2H, $J = 7.8$ and 5.6 Hz), 1.25 (d, 12H, $J = 6.4$ Hz), 0.80 (m, 9H). ^{13}C NMR δ 133.3, 127.4, 56.3, 48.6, 29.8, 29.2, 28.9, 20.8. *N-(Hex-1-en-3-yl)diisopropylamine*: partial ^{1}H NMR spectra was obtained from the mixture. ^{1}H NMR δ 5.15 (dd, 1H, $J = 17.2$ and 1.5 Hz), 5.05 (dd, 1H, $J = 10.0$ and 1.5 Hz).

(E)-1-Morpholinohex-2-ene (Table 4, entry 26): *E*-hex-2-en-1-yl acetate (0.198 g, 1.38 mmol), Pd complex (0.69 μmol), K_2CO_3 (0.095 g, 0.69 mmol) and morpholine (0.060 ml, 0.69 mmol). The residue was purified by column chromatography (ether/pentane: 3/7) to give (*E*)-1-morpholinohex-2-ene and 3-morpholinohex-1-ene (ratio 92/8) in 88% (0.101 g) yield.

(E)-1-Pyrrolidinohex-2-ene (Table 4, entry 28): *E*-hex-2-en-1-yl acetate (0.099 g, 0.69 mmol), Pd complex (6.96 μmol) and pyrrolidine (0.115 ml, 1.38 mmol). The residue was purified by column chromatography (ether/pentane: 3/7) to give (*E*)-1-pyrrolidinohex-2-ene and 3-pyrrolidinohex-1-ene (ratio 93/7) in 94% (0.99 g) yield. *(E)-1-Pyrrolidinohex-2-ene*: ^{1}H NMR δ 5.57 (dt, 1H, $J = 15.4$ and

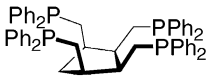
5.8 Hz), 5.45 (dt, 1H, J = 15.4 and 6.1 Hz), 3.10 (m, 6H), 2.60 (m, 4H), 1.90 (td, 2H, J = 7.3 and 6.1 Hz), 1.28 (tq, 2H, J = 7.3 and 7.3 Hz), 0.80 (t, 3H, J = 7.3 Hz). *3-Pyrrolidinohex-1-ene*: partial ^{1}H NMR spectra was obtained from the mixture. ^{1}H NMR δ 5.15 (dd, 1H, J = 17.2 and 1.5 Hz), 5.05 (dd, 1H, J = 10.0 and 1.5 Hz).

N-(E)-(Hex-2-en-1-yl)cyclohexylamine and N,N-di((E)-hex-2-en-1-yl)cyclohexylamine (Table 5, entry 3): (*E*)-hex-2-en-1-yl acetate (0.099 g, 0.69 mmol), Pd complex (0.69 μmol) and cyclohexylamine (0.16 ml, 1.38 mmol). The residue was purified by distillation (Kugelrohr) to give *N*-(*E*)-(hex-2-en-1-yl)cyclohexylamine and *N*-cyclohexyl-di((*E*)-hex-2-en-1-yl)amine (ratio 62/38) in 82% (0.10 g), yield. *N-(E)-(Hex-2-en-1-yl)cyclohexylamine*: ^{1}H NMR δ 5.61 (dt, 1H, J = 15.9 and 6.0 Hz), 5.46 (dt, 1H, J = 15.9 and 6.2 Hz), 3.17 (d, 2H, J = 6.0 Hz), 2.65 (m, 1H), 1.90 (td, 2H, J = 7.2 and 6.2 Hz), 1.8–1.5 (m, 10H), 1.30 (tq, 2H, J = 7.2 and 7.2 Hz), 0.80 (t, 3H, J = 7.2 Hz). *N-Cyclohexyl-di((E)-hex-2-en-1-yl)amine*: ^{1}H NMR δ 5.61 (dt, 2H, J = 15.9 and 6.0 Hz), 5.46 (dt, 2H, J = 15.9 and 6.2 Hz), 3.02 (d, 4H, J = 6.0 Hz), 2.52 (m, 1H), 1.90 (td, 4H, J = 7.2 and 6.2 Hz), 1.9–1.4 (m, 10H), 1.30 (tq, 4H, J = 7.2 and 7.2 Hz), 0.80 (t, 6H, J = 7.2 Hz).

2.6. Allylation products with 3-acetoxy-1,3-diphenylpropene

(E)-3-Morpholino-1,3-Diphenylprop-1-ene (Table 4, entry 31): 3-acetoxy-1,3-diphenylpropene (0.59 g, 2.32 mmol), Pd complex (23.2 μmol) and morpholine (0.40 ml, 4.64 mmol). The residue was purified by column chromatography (ether/pentane: 3/7) to give the product in 65% (0.42 g) yield. ^{1}H NMR δ 7.50–7.21 (m, 10H), 6.62 (d, 1H, J = 13.8 Hz), 6.45 (dd, 1H, J = 13.8 and 8.4 Hz), 4.50 (d, 1H, J = 8.4 Hz), 3.70 (t, 4H, J = 4.5 Hz), 2.35 (t, 4H, J = 4.5 Hz).

N,N-Dipropyl-1,3-diphenylallylamine (Table 4, entry 32): 3-acetoxy-1,3-diphenylpropene (1.18 g, 4.64 mmol), Pd complex (23.2 μmol), K_2CO_3 (0.32 g, 2.32 mmol) and dipropylamine (0.32 ml, 2.32 mmol). The residue was purified by column chromatography (ether/pentane: 3/7) to give the product in 45% (0.307 g) yield. ^{1}H NMR δ 7.50–7.21 (m, 10 H), 6.56 (d, 1H, J = 13.8 Hz), 6.35 (dd, 1H, J = 13.8 and 8.4 Hz), 4.44 (d, 1H, J = 8.4 Hz), 2.35 (t, 4H, J = 7.4 Hz), 1.35 (tq, 4H, J = 7.4 and 7.1 Hz), 0.80 (t, 6H, J = 7.1 Hz).



Tedicyp

Fig. 1.

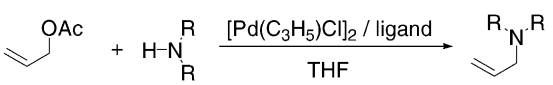
3. Results and discussion

3.1. Design of the ligand

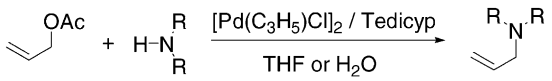
Our aim was to obtain very robust complexes capable of high turnover numbers in catalysis. In order to find such efficient palladium catalysts we have synthesised the new tetrapodal (for a review on the synthesis of polypodal diphenylphosphine ligands, see [8]) phosphine ligand, Tedicyp (Fig. 1) [9] in which the four diphenylphosphinoalkyl groups are stereospecifically bound to the same face of a cyclopentane ring. All four phosphines probably cannot bind at the same time to the same Pd centre, but the presence of these four phosphines close to the metal centre seems to increase the coordination of the ligand to the Pd complex and therefore increases the stability of the catalyst. Tedicyp was prepared in seven steps from the commercially available starting material himic anhydride.

3.2. Allylic amination: influence of the ligand

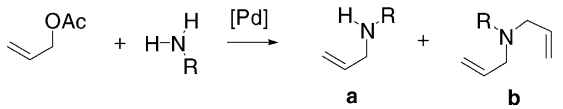
First we tried to evaluate the difference of efficiency for allylic amination between a classical monophosphine ligand: triphenylphosphine, diphosphine ligands such as bis(diphenylphosphino)methane (dppm), 1,2-bis(diphenylphosphino)ethane (dppe), 1,4-bis(diphenylphosphino)butane (dppb) and our tetraphosphine Tedicyp [10]. We observed that the addition of diallylamine to allyl acetate in the presence of 0.001% catalyst (ratio substrate/catalyst: 100 000), led to the addition product (Scheme 1) in 5% conversion when PPh_3 was used as ligand (entry 1, Table 1).



Scheme 1. Addition of secondary amines to allyl acetate.



Scheme 2. Addition of secondary amines to allyl acetate when Tedicyp was used as a ligand.



Scheme 3. Addition of primary amines to allyl acetate.

In the presence of dppm, dppe and dppb conversions of 4, 7 and 2% were obtained, respectively (entries 2–4). With Tedicyp conversion was 73% with a higher ratio substrate/catalyst: 1 000 000 (entry 6). A similar tendency was observed for the addition of dioctylamine to allyl acetate. In the presence of 0.001% catalyst, only 1 and 3% conversion were observed with PPh_3 and dppe (entries 7 and 8). With Tedicyp the conversion was 99% (entry 9).

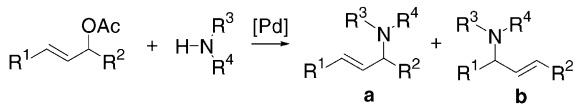
3.3. Addition of secondary amines to allyl acetate

Next we tried to evaluate the scope and limitations of Tedicyp–Pd complex for the addition of secondary amines to allyl acetate (Scheme 2, Table 2). We observed that the addition of dipropylamine to allyl acetate in the presence of 0.0001% catalyst, led to the addition product in 68% conversion (TON 680 000) when Tedicyp was used as ligand (entry 2). The addition rate was slightly decreased for the addition of morpholine, pyrrolidine or piperidine. With these amines, conversions of 93–95% are observed in the presence of 0.01% catalyst (entries 10, 13 and 14). With morpholine, a turnover number (TON) of 57 000 and a turnover frequency (TOF) of 1111 h^{-1} was obtained in the presence of 0.001% catalyst (entry 11). On the other hand, a significant steric effect was observed with the bulky diisopropylamine and *N*-methylaniline. In the presence of 0.1% catalyst only 81 and 78% conversions were obtained, respectively, after 3 days (entries 15 and 18).

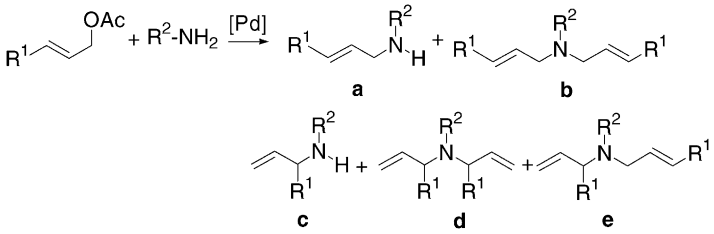
The complex formed by association of Tedicyp with $[PdCl(C_3H_5)]_2$ is a very efficient catalyst for allylic amination when the reactions are conducted in THF, so we could expect that if a small amount of this complex is soluble in a mixture amine–water some addition product should be observed when water is used as solvent (for a review on palladium catalysed reactions in aqueous medium, see [11]) [12]. Surprisingly, we observed that the reaction rate is in general slightly higher when water is used as solvent [13]. In water, a conversion of 98% was observed for the addition of dipropylamine to allyl acetate when a ratio substrate/catalyst of 1 000 000 was used (entry 5). The Tedicyp/$[PdCl(C_3H_5)]_2$ complex seems to be very water stable. A similar tendency was observed for the addition of morpholine or diisopropylamine to allyl acetate. In the case of morpholine, the conversion was 96% in water instead of 57% in THF in the presence of 0.001% catalyst (entry 12).

3.4. Addition of primary amines to allyl acetate

With primary amines, monoallylation and diallylation products can be obtained (Scheme 3). The ratio monoallylation/diallylation depends on the amine, on the ratio allyl acetate/amine, and on the ratio substrate/catalyst. When 2 eq. of amine is used the major product is the monoallylation adduct. For example, with benzylamine, the addition products are obtained in 83% yield and in 90% selectivity in favour of the monoaddition adduct in the presence of 0.001% catalyst (entry 2). A lower selectivity in favour of the monoaddition product is observed for the addition of cyclohexylamine or phenylethylamine (entries 4, 6 and 7). Good yields of diallylated products can be obtained by using an excess of allyl acetate. If 2 eq. of allyl acetate are used the diallylation product is obtained with a good selectivity. For example, with benzylamine the diaddition product was obtained in 95% selectivity and 96% yield in the presence of 0.001% catalyst (entry 3). Using similar conditions, the amination by cyclohexylamine and phenylethylamine also proceeded readily to give the corresponding diaddition products with very high selectivities (entries 5 and 8).



Scheme 4. Addition of secondary amines to substituted allyl acetates.



Scheme 5. Addition of primary amines to substituted allyl acetates.

3.5. Addition of secondary amines to substituted allyl acetates

With non-symmetrical allyl acetates the formation of two regioisomers is possible: the linear **a** and the branched **b** (Scheme 4). The regioselectivity in the product is determined by the nature of the amine, by the nature of the substituent on the π-allyl unit and by the nature of the ligand on palladium [6]. High regioselectivity was generally observed in which the amine bonds to the less substituted carbon. With dioctylamine a complete regio and stereoselectivity is obtained in favour of the *E* linear isomer for the addition to *E*-hex-2-en-1-yl acetate or cinnamyl acetate (entries 6, 7, 20–22). In the presence of diethylamine, dipropylamine or diallylamine good selectivities were also observed (entries 1–5 and 14–19). On the other hand with morpholine or pyrrolidine the regioselectivity is lower and 5–17% of the branched isomer are obtained (entries 8–12 and 24–30). In general high TONs were obtained for the amination of cinnamyl acetate or *E*-hex-2-en-1-yl acetate (350–36 000). Much lower TONs were observed in the course of the amination of hindered 3-acetoxy-1,3-diphenyl-1-propene (entries 31 and 32).

3.6. Addition of primary amines to substituted allyl acetates

The reaction of primary amines with substituted allyl acetates could led to five products: the linear mono and diallylated products **a** and **b**, the branched mono and diallylated products **c** and **d** and the linear/branched diallylation product **e** (Scheme 5). In all cases compounds **d** and **e** were not observed. For the addition of benzylamine and cyclohexylamine to cinnamyl acetate good selectivities in favour of the monoaddition linear isomer **a** were observed. The stereoselectivity in favour of the *E* isomer was complete (entries 1 and 2). *E*-hex-2-en-1-yl acetate in the presence of cyclohexylamine led to the same stereoselectivity, but to a lower regioselectivity: a large amount of diallylation product **b** was observed (entry 3). On the other hand, the reaction performed in the presence of an excess of allyl acetate (ratio allyl acetate/amine 2/1) led to product **b** in 93% selectivity (entry 4).

3.7. Reaction conditions

Substrate concentration is very important for this reaction. Most of the reactions run in THF have been performed using a ratio allyl acetate/amine of 1/2. We have observed that if the reaction is performed with an higher amine concentration the rate of the reaction increases. In the presence of 2, 4 and 8 eq. of amine the TONs after 40 min were, respectively, of 8100, 14 500 and 28 400 for the addition of dipropylamine to allylacetate with a ratio substrate/catalyst of 100 000. The catalyst concentration was kept constant. A similar effect is observed for the concentration of allyl acetate. If the concentration is doubled (ratio s/c of 100 000 and 200 000), TONs of 8100 and 17 000 were observed, respectively. These results seem to indicate that the reaction is first order in both substrates, so the higher the substrates concentration is, the faster the catalyst.

We have also examined the importance of the ratio palladium/Tedicyp for the catalysis. We observed that if the reaction is performed with ratios Pd-dimer/Tedicyp of 0.5, 1 and 2, the rate of the reaction decreases. The TONs after 40 min were,

respectively, 8100, 4000 and 1300 for the addition of dipropylamine to allylacetate with a ratio substrate/catalyst of 100 000. These results seem to indicate that the active palladium catalyst requires one tetraphosphine for one palladium centre.

4. Conclusion

The tetradentate ligand Tedicyp associated to a palladium complex provides a very efficient catalyst for allylic amination. This complex is thermally and water stable and less sensitive to poisoning than the complexes formed with simple phosphines such as triphenylphosphine or dppe. The catalyst remains active during several days and in general no deposition of the catalyst is observed during the course of the reaction. This stability probably comes from the presence of the four diphenylphosphinoalkyl groups stereospecifically bound to the same face of the cyclopentane ring which probably increases the coordination of the ligand to the metal and prevent precipitation of the catalyst. With allyl acetate the reaction can be performed in water with as little as 0.0001% catalyst without further optimisation of the reaction conditions. These results represent an inexpensive, efficient, and environmentally friendly synthesis. Further applications of this ligand will be reported in due course.

Acknowledgements

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