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Journal of Molecular Catalysis A: Chemical 227 (2005) 197–207
JOURNAL OF MOLECULAR CATALYSIS A: CHEMICAL
www.elsevier.com/locate/molcata

PAMAM dendrimer-palladium complex catalyzed synthesis of five-, six- or seven membered ring lactones and lactams by cyclocarbonylation methodology

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Received 15 July 2004; received in revised form 18 October 2004; accepted 18 October 2004

Abstract

Palladium complexes immobilized onto generations 0–3 PAMAM dendrimers supported on silica, in the presence of 1,4-bis(diphenylphosphino)butane, were used as catalysts for the cyclocarbonylation of 2-allylphenols, 2-allylaniline, 2-vinylphenol and 2-vinylaniline affording five-, six- or seven membered ring lactones and lactams. Good conversions were realized using the catalytic system, and the catalyst was recycled 3–5 times. The influence of the spacer chain was investigated, as well as the solvent and the CO/H_2 ratio, on the selectivity and the recyclability of the cyclocarbonylation reactions.

Keywords: PAMAM palladium dendrimer; Cyclocarbonylation reaction; Silica-immobilized catalysts

1. Introduction

Cyclocarbonylation chemistry is widely used in organic synthesis and represents a useful method for the preparation of a variety of cyclic compounds [1–4]. Transition metals and their complexes functioning as catalysts for carbonylation reactions usually promote the introduction of a carbonyl moiety into an organic molecule. Among the most interesting and synthetically useful carbonylation reactions is the cyclocarbonylation of unsaturated alcohols and amines [5–7]. These transformations provide convenient and effective strategies for the synthesis of lactams and lactones, which have potential applications in the area of pharmaceuticals [8,9].

In 1996, Alper and co-workers described the regioselective cyclocarbonylation of 2-allylphenol derivatives, using palladium acetate [$Pd(OAc)_2$] and 1,4-bis(diphenylphosphino)butane (dppb) as a homogenous catalytic system, for the synthesis of five-, six- or seven-membered ring lactones. They found that the selectivity of the process was dependent on the solvent, and the ratio of CO/H_2 [10]. This catalytic system has been validated for the synthesis of a large variety of molecules, such as bis-lactones and estrone derivatives [11,12].

To our knowledge, very few examples of heterogeneous catalysts have been reported in the literature for this kind of reaction. For example, palladium-montmorillonite is an effective catalyst for the cyclocarbonylation reactions of allylphenols, affording seven membered ring lactones as the principal products [13]. Palladium on activated carbon (Pd/C) has also been used as a heterogeneous system for the same reaction, and it has been observed that the regioselectivity differs in some cases from the homogeneous system and depends on the reaction conditions, CO/H_2, and the solvent [14].

The use of metallo-dendrimers having a metal incorporated at the core or on the surface of the dendrimer, has great potential in catalytic processes [15–23]. Such dendritic catalysts are considered as the interface between homogeneous and heterogeneous catalysis [24]. In addition, they can also

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doi:10.1016/j.molcata.2004.10.024

be separated easily from the resulting reaction product mixtures by simple filtration [25] thus allowing the catalyst to be re-used. Using PAMAM-(polyaminoamido) dendrimers supported on silica, with their globular shape, make them more suitable for recycling than other soluble polymer-supported catalysts. They can be easily removed from the reaction mixture by membrane or nanofiltration techniques because of their large size compared to the products.

Several groups have prepared systems that are functionalized with phosphine ligands at the periphery of the dendrimers. Reetz et al. [26] used commercially available DAB-dendr$(NH_2)_2$ dendrimer as a source of dendrimer-$N(CH_2PPh_2)_2$ groups. The latter function acts as bidentate ligands when complexed with Pd(tmeda)Me_2. The dendrimer catalyst has been used for the coupling of bromobenzene and styrene to form stilbene [26]. The same reaction has also been investigated using several palladium dendrimer catalysts with a PAMAM backbone supported on silica gel [27,28].

The hydroformylation of styrene was realized using a bis-diphenylphosphine terminated PAMAM-dendrimer supported on SiO_2, complexed to $Rh[(CO)_2Cl]_2$ [29,30]. A solid phase and biomimetic approach to obtain dendrimer ligands attached onto polystyrene beads was also described [31]. The rhodium complexes of these dendrimers were excellent catalysts for the hydroformylation of several olefins. These advantages prompted us to investigate the possibility of using a palladium dendrimer catalyst for the cyclocarbonylation reactions.

Herein, we report cyclocarbonylation reactions using catalytic quantities of palladium complexes immobilized onto silica in the presence of dppb.

2. Experimental

2.1. General experimental procedure for the cyclocarbonylation of allylphenols

To a 50 ml stainless steel autoclave, equipped with a glass liner and a magnetic stirring bar, were charged allylphenol (1 mmol), toluene (5 ml), dppb (0.04 mmol) and 25 mg of the Pd-dendritic catalyst. The autoclave was flushed several times with CO, then pressurized with 500 psi of CO and 100 of H_2 (P_{total} = 600 psi). The reaction mixture was heated in an oil bath to 120 °C for 48 h. After cooling, the reaction mixture was filtered and washed with toluene. The solvent was evaporated under vacuum. The lactones and lactams were separated, purified by using preparative TLC, with hexane and ethyl acetate as eluants, and characterized by ^{1}H NMR spectroscopy. Conversions and regioselectivities were determined by GC and ^{1}H NMR spectroscopy.

The following lactones and lactams are known compounds and have spectral data in according to the literature data [10]: **2a**, **2b**, **2c**, **2d**, **2e**, **3a**, **3b**, **3c**, **3d**, **3e**, **4a**, **4b**, **4c**, and **4d**.

3. Results and discussion

3.1. Preparation of PAMAM-SiO_2 dendrimers

Commercial aminopropylsilica gel with aminopropyl groups (0.9 mmol/g ± 0.1) was used to prepare generations 0–3 of polyaminoamido (PAMAM) dendrimers (Fig. 1), following a literature procedure [29].

3.2. Preparation of phosphonated PAMAM-SiO_2 dendrimers

Phosphonation of PAMAM-SiO_2 dendrimers was achieved with diphenylphosphinomethanol, prepared in situ from paraformaldehyde and diphenylphosphine, and resulted in the double phosphinomethylation of each terminal amine group. The detailed preparation was described before [29] and based on the procedure by Reetz et al. [26]. The resulting phosphonylated dendrimers were characterized by ^{31}P solid state NMR spectra. For example, in the ^{31}P NMR spectrum of generation G0 there is a sharp signal at $\delta = -27.4$ ppm due to the metal free dendrimers. The ^{31}P solid state NMR spectra for the various generations compared well with the published value of ($\delta = -28.0$ ppm) for the homogeneous polyaminophosphonated dendrimer [26,29].

3.3. Complexation of the phosphino-PAMAM dendrimer supported on SiO_2 with Pd

The phosphonated dendrimers were complexed to Pd using $Pd(PhCN)_2Cl_2$ according to literature procedures [32,33]. The palladium complex is coordinated to the dendrimer on silica by simply stirring the phosphonylated dendrimers with one equivalent of dichlorobis(benzonitrile)palladium(II) in degassed toluene. The resulting complexed dendrimers (see Fig. 1) were characterized by ^{31}P solid state NMR—e.g. the G0 dendrimer complex gave a sharp signal at δ = +11.2 ppm (compared quite well with the published value of +8.3 ppm) [26] (Table 1).

The palladium content of the various generations was measured by ICP. The results are summarized in Table 2. We observed that the degree of complexation increases significantly with dendrimer for G0, and G1-C2, and decreases for G2-C2 and G3-C2. These findings are believed to be due to incomplete phosphonation reactions arising from steric crowding and ultimately resulting in the threshold of dendrimer growth being reached [29,34].

3.4. Catalytic cyclocarbonylation reaction of unsaturated alcohols and amines with PAMAM-dendrimer-Pd complexes

The catalytic activity of the palladium-complexed PPh_2-PAMAM-SiO_2 dendrimers (generations 0–3) was investigated for the cyclocarbonylation reaction of 2-allylphenols **1a**–**1c**, 2-allylaniline **1d**, 2-vinylaniline **1e** and 2-vinylphenol

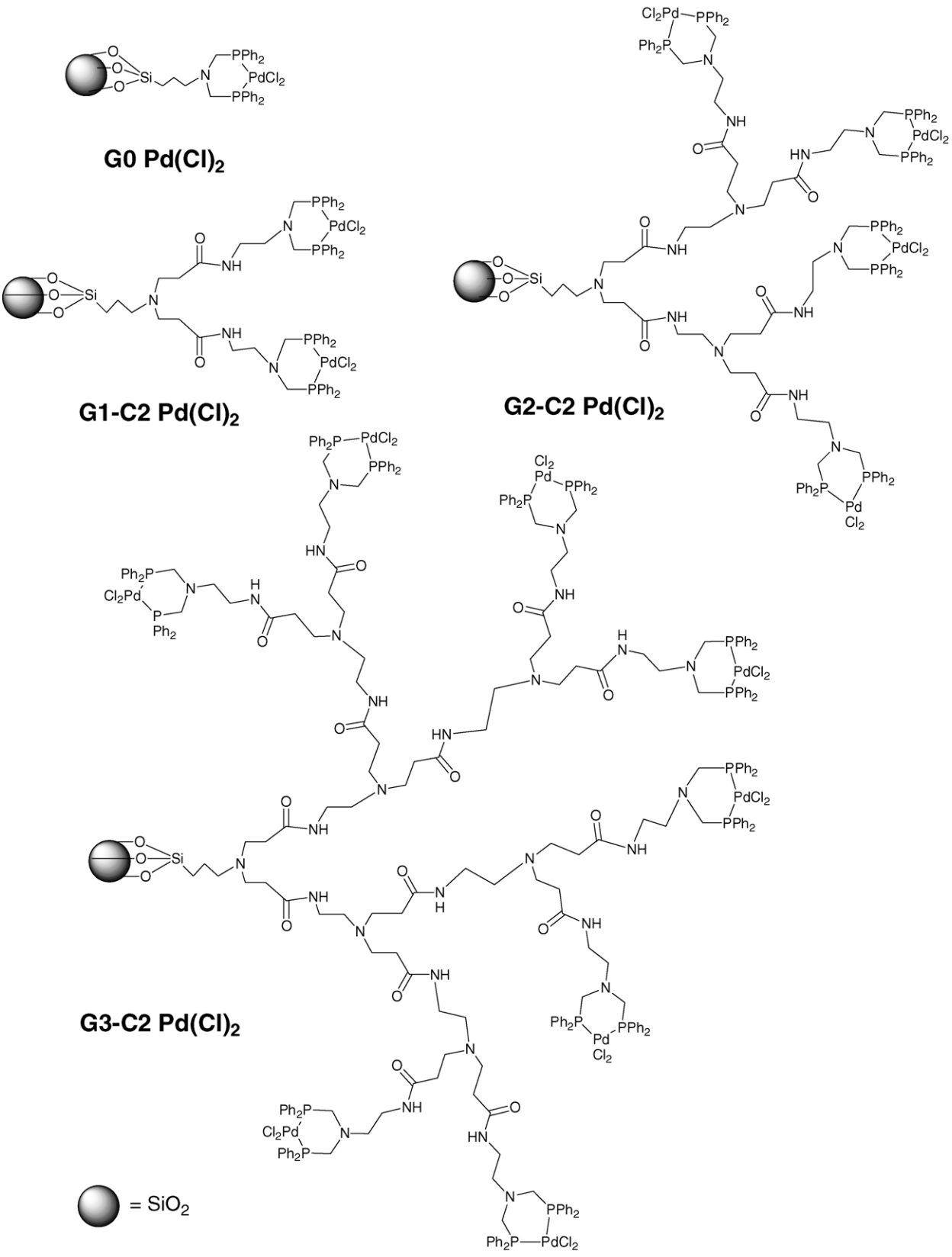


Fig. 1. G0 to G3-C2 Pd dendrimers.

Table 1
^{31}P solid state NMR and the phosphorus content of the various generations

Generation	^{31}P solid state NMR δ (ppm)	mmol PPh_2/g SiO_2[a]
G0-C2	−27.4	0.332
G1-C2	−27.1	0.338
G2-C2	−26.6	0.343
G3-C2	−26.1	0.292

[a] Determined by ^{31}P solid state NMR of the mixture of dendrimer and internal standard ($PhCH_3P^+Br^-$).

1′a (Scheme 1 and Scheme 2) and the results are summarized in Tables 3–10. Treatment of 1 mmol of a substrate with a 5:1 mixture of carbon monoxide and hydrogen (600 psi total pressure), at 120 °C for 48 h, with Pd-complexed-PPh_2-PAMAM-SiO_2 dendrimers (25 mg), in the presence of 0.04 mmol of dppb, affords the corresponding lactones and lactams **2**–**4** (Scheme 1, 2). The product ratio was determined by ^{1}H NMR and by GC analysis.

Different generations of Pd-dendrimer complexes were inactive catalysts for the cyclocarbonylation reaction in the absence of dppb, and starting material was recovered. The key to success of this reaction is the presence of dppb, and this is likely due to the ability of dppb to coordinate to palladium through one or two phosphorus atoms. In the dppb complexes the phenyl groups can bend away from the remaining two coordination sites [10,35,36]. Flexible backbones also impose low-energy barriers for the variation of the P–Pd–P angle and Pd–P distances. Moreover, theoretical calculations [37–43] indicate that such flexibility may enhance migration reactions.

For the homogenous catalytic system, other bidentate phosphine ligands such as 1,2-bis(diphenylphosphino)ethane (dppe) and 1,3-bis(diphenylphosphino)propane (dppp), or monodentate phosphine ligands such as triphenylphosphine and tricyclohexylphosphine, have been used for this reaction, but dppb was found to be the most effective [10], perhaps because CO insertion into a Pd–C bond is faster for palladium dppb complexes [44,45].

Using generation G0 for the cyclocarbonylation of 2-allylphenols **1a**–**1c**, and 2-allylaniline **1d** afforded **2**–**4** in 90–100% conversions (70–85% yields) (Table 3). We observed that the cyclocarbonylation could be recycled 3–4 times. These reactions were highly solvent dependent. When toluene was used as the solvent the seven-membered ring lactone was the major product with, for example, 95% regioselectivity for compound **1b** using a 5/1 mixture of CO/H_2 (entry 5, Table 3). However, using dichloromethane and a 1/5 mixture of CO/H_2 afforded the five-membered ring lactone as the major product (e.g., 74% **1b**) (entry 13, Table 3). In contrast, using either dichloromethane or toluene and a 5/1 mixture of CO/H_2 in reaction with **1d** gave the seven-membered ring lactam in only 56% selectivity (entry 21, Table 3). But when a 1/2 mixture of CO/H_2 was used for the reaction with 1d, there was 45% conversion with 50% selectivity for the six-membered ring lactam (entry 24, Table 3).

When generation G1-C2 was used as the catalyst for the cyclocarbonylation of 2-allylphenols and 2-allylaniline, we achieved 86% selectivity for the seven-membered ring lactone **4b**, in toluene and with a 5/1 mixture of CO/H_2 (entry 7, Table 4). Using dichloromethane, with a 1/5 mixture of CO/H_2, afforded 76% selectivity for the five-membered ring lactone **2c** (entry 16, Table 4). In the case of 2-allylaniline, there was 60% selectivity for the seven-membered ring lactam **4d** (entry 19, Table 4). The six-membered ring lactam was observed as the major product using a 1/2 mixture of CO/H_2 in dichloromethane and G1-C2/dppb as the catalyst system (entry 22, Table 4).

We then evaluated the G2-C2 Pd-dendrimer complex as the catalyst, using a 5/1 mixture of CO/H_2 and toluene in the presence of G2-C2 and dppb, the seven-membered ring lactone, **4c**, was obtained in 91% regioselectivity (Table 5, entries 1–3), accompanied by 7–10% of an isomerization product. Using dichloromethane as the solvent in the presence of G2-C2 and dppb, gave the five-membered ring lactone as the major product (Table 5, entries 4-6). As shown in Table 5, in the case of the cyclocarbonylation of allylaniline in dichloromethane with a 5/1 mixture of CO/H_2, using the G2-C2/dppb as catalyst system, gave the seven-membered ring lactams in reasonably good selectivity (entries 11-13, Table 5).

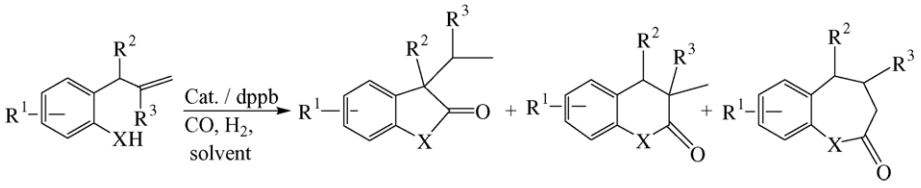
The next higher generation complex G3-C2, afforded the seven-membered ring products **4a**–**4c** by reaction of **1a**–**1c** (entries 1, 5 and 8, Table 6) in toluene with a 5/1 mixture of CO/H_2 accompanied by 7-30% of an isomerization product (entries 3–4, 8–10 and 13–14, Table 6). Modest selectivity was observed for the seven membered ring lactam **1d**, when dichloromethane was employed as the solvent, and G3-C2/dppb as the catalytic system, with different ratios of carbon monoxide and hydrogen (entries 15–17, Table 6). The results contrast with G2-C2, but are in accord with G0 and G1-C2 dendrimers.

The cyclocarbonylation reactions of other substrates, such as 2-vinylaniline **1e** and 2-vinyphenol **1′a**, were also investigated (Scheme 2). When equal amounts of carbon monoxide

Table 2
^{31}P solid state NMR and Pd content of the complexed dendrimers

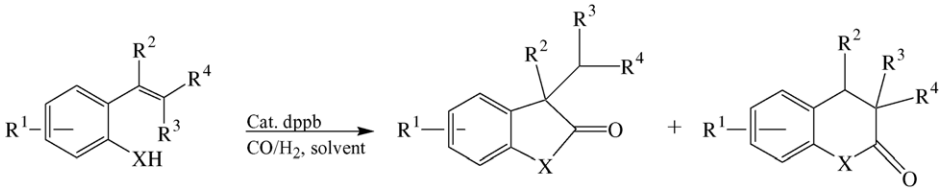
Generation	^{31}P solid state NMR δ (ppm)	Percentage Pd[a]	g Pd/g SiO_2	μmol Pd/25 mg
G0-C2	11.2	5.47	0.0547	12.85
G1-C2	14.5	8.75	0.0875	20.55
G2-C2	18.8	5.46	0.0546	12.82
G3-C2	20.7	2.11	0.0211	4.95

[a] Determined by inductively coupled plasma (ICP).



1a: $R^1 = R^2 = R^3 = H$; X = O — **2** — **3** — **4**
1b: R^1= 6-CH_3 ; $R^2 = R^3 = H$; X = O
1c: R^1= 4-Cl ; $R^2 = R^3 = H$; X = O
1d:$R^1 = R^2 = R^3 = H$; X = NH

Scheme 1.



1e: $R^1 = R^4 = R^3 = H$; $R^2 = CH_3$; X = NH — **2** — **3**
1'a: $R^1 = R^3 = R^2 = H$; $R^4 = CH_3$; X = O

Scheme 2.

Table 3
Cyclocarbonylation of 2-allylphenols and 2-allylaniline by G0/dppb/CO/H_2[a]

Entry	Cycle	Sub.	Solvent	P_{CO} (psi)	P_{H_2} (psi)	Conversion (%)	Product distribution (%)		
							2	**3**	**4**
1	1	**1a**	Toluene	500	100	100 (85)[b]	10	12	78
2	2	**1a**	Toluene	500	100	98 (74)[b]	9	15	76
3	3	**1a**	Toluene	500	100	94	6	18	76
4	4	**1a**	Toluene	500	100	94	3	10	87
5	1	**1b**	Toluene	500	100	100	2	3	95
6	2	**1b**	Toluene	500	100	98	4	6	90
7	3	**1b**	Toluene	500	100	94	6	7	87
8	1	**1c**	Toluene	500	100	98 (78)[b]	18	20	62
9	2	**1c**	Toluene	500	100	95	8	11	81
10	3	**1c**	Toluene	500	100	Traces	–	–	–
11	1	**1a**	CH_2Cl_2	500	100	100 (83)[b]	62	30	8
12	1	**1b**	CH_2Cl_2	500	100	100	51	24	25
13	1	**1b**	CH_2Cl_2	100	500	100	74	26	0
14	2	**1b**	CH_2Cl_2	200	400	75 (20)[c]	52	34	14
15	3	**1b**	CH_2Cl_2	300	300	50 (10)[c]	35	60	5
16	1	**1c**	CH_2Cl_2	500	100	94	52	36	12
17	1	**1a**	Toluene	100	500	100	33	26	41
18	2	**1a**	Toluene	200	400	100	28	41	31
19	3	**1a**	Toluene	300	300	97	16	36	48
20	4	**1a**	Toluene	400	200	60	0	12	88
21	1	**1d**	CH_2Cl_2	500	100	97 (70)[b]	11	33	56
22	2	**1d**	CH_2Cl_2	400	200	96	16	30	54
23	3	**1d**	CH_2Cl_2	300	300	61	10	44	46
24	4	**1d**	CH_2Cl_2	200	400	45	15	50	35
25	1	**1d**	Toluene	500	100	93	4	24	72

[a] Reaction conditions: catalyst (25 mg); dppb (0.04 mmol); substrate (1.0 mmol); solvent (5 mL), reaction time (48 h), temperature (120 °C).
[b] Isolated yield.
[c] Isomerization product. The ratio of 2:3:4 was determined by GC and ^{1}H NMR spectroscopy.

Table 4
Cyclocarbonylation of 2-allylphenols and 2-allylaniline by G1-C2/dppb/CO/H_2[a]

Entry	Cycle	Sub.	Solvent	P_{CO} (psi)	P_{H_2} (psi)	Conversion (%)	Product distribution (%)		
							2	**3**	**4**
1	1	**1a**	Toluene	500	100	100	14	12	74
2	2	**1a**	Toluene	500	100	98 (75)[c]	17	16	67
3	3	**1a**	Toluene	500	100	96	20	16	64
4	4	**1a**	Toluene	500	100	Traces	–		
5	1	**1b**	Toluene	500	100	100 (80)[c]	3	18	79
6	2	**1b**	Toluene	500	100	97	1	14	85
7	3	**1b**	Toluene	500	100	75	0	14	86
8	4	**1b**	Toluene	500	100	Traces	–		
9	1	**1a**	CH_2Cl_2	500	100	100	44	34	22
10	2	**1a**	CH_2Cl_2	100	500	100	62	35	3
11	3	**1a**	CH_2Cl_2	200	400	46 (5)[b]	20	58	22
12	1	**1b**	CH_2Cl_2	500	100	100	40	51	9
13	2	**1b**	CH_2Cl_2	100	500	91 (7)[b] (63)[c]	73	27	0
14	3	**1b**	CH_2Cl_2	200	400	Traces	–		
15	1	**1c**	CH_2Cl_2	500	100	94 (6)[b]	44	40	16
16	2	**1c**	CH_2Cl_2	100	500	90 (10)[b]	76	24	0
17	3	**1c**	CH_2Cl_2	200	400	40 (10)[b]	9	90	1
18	1	**1b**	Toluene	500	100	Traces	–		
19	1	**1d**	CH_2Cl_2	500	100	95	10	30	60
20	2	**1d**	CH_2Cl_2	400	200	99	13	31	56
21	3	**1d**	CH_2Cl_2	300	300	99	15	31	56
22	4	**1d**	CH_2Cl_2	200	400	55	18	47	35
23	1	**1d**	Toluene	500	100	98	2	31	67

[a] Reaction conditions: catalyst (25 mg); dppb (0.04 mmol); substrate (1.0 mmol); solvent (5 mL), reaction time (48 h), temperature (120 °C). The ratio of 2:3:4 was determined by GC and ^{1}H NMR spectroscopy.
[b] Isomerization product.
[c] Isolated yield.

and hydrogen were used, together with dichloromethane as the solvent and various generations of dendrimer Pd complexes (G0, G1-C2 and G2-C2) as the catalysts, in the presence of dppb, the six-membered ring lactam was obtained as the principal product (entry 3, Table 7; entry 8 Tables 8 and 9). In contrast, using G3-C2/dppb as the catalyst, under the same reaction conditions, gave the five-membered ring lactam as the major compound (entry 8, Table 10).

Reaction of vinylphenol **1′a** with the G0/dppb catalyst in dichloromethane, and with different ratios of CO/H_2, afforded the five-membered ring lactone **2a** in 70–98% conversion (entries 6–9, Table 7). Using a 5/1 mixture of CO/H_2 and

Table 5
Cyclocarbonylation of 2-allylphenols and 2-allylaniline by G2-C2/dppb/CO/H_2[a]

Entry	Cycle	Sub.	Solvent	P_{CO} (psi)	P_{H_2} (psi)	Conversion (%)	Product distribution (%)		
							2	**3**	**4**
1	1	**1c**	Toluene	500	100	90 (8)[b]	0	9	91
2	2	**1c**	Toluene	500	100	40 (7)[b]	0	10	90
3	3	**1c**	Toluene	500	100	20 (10)[b]	0	8	92
4	1	**1c**	CH_2Cl_2	500	100	95 (5)[b] (80)[c]	16	24	60
5	1	**1b**	CH_2Cl_2	500	100	90	3	18	79
6	1	**1a**	CH_2Cl_2	500	100	91	3	18	79
7	1	**1a**	Toluene	500	100	96	1	9	90
8	2	**1a**	Toluene	500	100	50	0	8	92
9	3	**1a**	Toluene	500	100	Traces		–	
10	1	**1b**	Toluene	500	100	100	0	7	93
11	1	**1d**	CH_2Cl_2	500	100	97	0	7	93
12	2	**1d**	CH_2Cl_2	400	200	98	0	7	93
13	3	**1d**	CH_2Cl_2	300	300	80	0	7	93
14	1	**1d**	Toluene	500	100	70	7	26	67

[a] Reaction conditions: catalyst (25 mg); dppb (0.04 mmol); substrate (1.0 mmol); solvent (5 mL), reaction time (48 h), temperature (120 °C). The ratio of 2:3:4 was determined by GC and ^{1}H NMR spectroscopy.
[b] Isomerization product.
[c] Isolated yield.

Table 6
Cyclocarbonylation of 2-allylphenols and 2-allylaniline by G3-C2/dppb/CO/H_2[a]

Entry	Cycle	Sub.	Solvent	P_{CO} (psi)	P_{H_2} (psi)	Conversion (%)	Product distribution (%)		
							2	**3**	**4**
1	1	**1a**	Toluene	500	100	90	2	10	88
2	2	**1a**	CH_2Cl_2	500	100	95	48	31	21
3	3	**1a**	CH_2Cl_2	400	200	60 (21)[b]	9	29	62
4	4	**1a**	CH_2Cl_2	300	300	30 (30)[b]	0	39	61
5	1	**1b**	Toluene	500	100	97	2	10	85
6	2	**1b**	Toluene	500	100	65	0	8	92
7	3	**1b**	Toluene	500	100	Traces		–	
8	1	**1c**	Toluene	500	100	90 (9)[b]	5	10	85
9	2	**1c**	Toluene	500	100	87 (10)[b]	3	9	88
10	3	**1c**	Toluene	500	100	53 (20)[b]	2	12	86
11	4	**1c**	Toluene	500	100	Traces		–	
12	1	**1b**	CH_2Cl_2	500	100	100	37	36	27
13	1	**1a**	CH_2Cl_2	500	100	90 (10)[b]	25	42	33
14	1	**1c**	CH_2Cl_2	500	100	90 (7)[b]	37	36	27
15	1	**1d**	CH_2Cl_2	500	100	96	13	28	59
16	2	**1d**	CH_2Cl_2	400	200	98	15	34	51
17	3	**1d**	CH_2Cl_2	300	300	95	10	32	58
18	1	**1d**	Toluene	500	100	55	5	30	65

[a] Reaction conditions: catalyst (50 mg); dppb (0.04 mmol); substrate (1.0 mmol); reaction time (48 h); solvent (5 mL). The ratio of 2:3:4 was determined by GC and ^{1}H NMR spectroscopy.
[b] Isomerization product.

Table 7
Cyclocarbonylation of 2-vinylaniline and 2-vinylphenol by G0/dppb/CO/H_2[a]

Entry	Cycle	Sub.	Solvent	P_{CO} (psi)	P_{H_2} (psi)	Conversion (%)	Product distribution (%)	
							2	**3**
1	1	**1e**	CH_2Cl_2	500	100	40	3	97
2	2	**1e**	CH_2Cl_2	400	200	85	2	98
3	3	**1e**	CH_2Cl_2	300	300	97	2	98
4	4	**1e**	CH_2Cl_2	200	400	96	4	96
5	5	**1e**	CH_2Cl_2	100	500	95	20	80
6	1	**1′a**	CH_2Cl_2	500	100	97	84	16
7	2	**1′a**	CH_2Cl_2	400	200	98	86	14
8	3	**1′a**	CH_2Cl_2	300	300	90	90	10
9	4	**1′a**	CH_2Cl_2	200	400	70	97	3
10	1	**1′a**	Toluene	500	100	45	0	100
11	1	**1e**	Toluene	500	100	99	84	16

[a] Reaction conditions: catalyst (25 mg); dppb (0.04 mmol); substrate (1.0 mmol); solvent (5 mL), reaction time (48 h), temperature (120 °C). The ratio of 2:3 was determined by GC and ^{1}H NMR spectroscopy.

Table 8
Cyclocarbonylation of 2-vinylaniline and 2-vinylphenol by G1-C2/dppb/CO/H_2[a]

Entry	Cycle	Sub.	Solvent	P_{CO} (psi)	P_{H_2} (psi)	Conversion (%)	Product distribution (%)	
							2	**3**
1	1	**1′a**	CH_2Cl_2	500	100	96	87	13
2	2	**1′a**	CH_2Cl_2	500	100	90	78	22
3	3	**1′a**	CH_2Cl_2	500	100	86	74	26
4	4	**1′a**	CH_2Cl_2	500	100	52	69	31
5	5	**1′a**	CH_2Cl_2	500	100	20	61	39
6	1	**1e**	CH_2Cl_2	500	100	85	15	85
7	2	**1e**	CH_2Cl_2	400	200	90	2	98
8	3	**1e**	CH_2Cl_2	300	300	70	2	98
9	4	**1e**	CH_2Cl_2	200	400	Traces	–	–
10	1	**1e**	Toluene	500	100	35	10	90

[a] Reaction conditions: catalyst (25 mg); dppb (0.04 mmol); substrate (1.0 mmol); solvent (5 mL), reaction time (48 h), temperature (120 °C). The ratio of 2:3 was determined by GC and ^{1}H NMR spectroscopy.

Table 9
Cyclocarbonylation of 2-vinylaniline and 2-vinylphenol by G2-C2/dppb/CO/H_2[a]

Entry	Cycle	Sub.	Solvent	P_{CO} (psi)	P_{H_2} (psi)	Conversion (%)	Product distribution (%)	
							2	**3**
1	1	**1′a**	CH_2Cl_2	500	100	100	88	12
2	2	**1′a**	CH_2Cl_2	500	100	100	90	10
3	3	**1′a**	CH_2Cl_2	500	100	90	80	20
4	4	**1′a**	CH_2Cl_2	500	100	85	75	25
5	5	**1′a**	CH_2Cl_2	500	100	40	71	29
6	1	**1e**	CH_2Cl_2	500	100	66	6	94
7	2	**1e**	CH_2Cl_2	400	200	73	2	98
8	3	**1e**	CH_2Cl_2	300	300	91	2	98
9	1	**1e**	Toluene	500	100	30	5	95

[a] Reaction conditions: catalyst (25 mg); dppb (0.04 mmol); substrate (1.0 mmol); solvent (5 mL),reaction time (48 h), temperature (120 °C). The ratio of 2:3 was determined by GC and ^{1}H NMR spectroscopy.

G0/dppb in toluene, afforded the five-membered ring lactam **2e** in 84% yield (entry 11, Table 7).

When the reaction was conducted with a 1/1 mixture of CO/H_2, in dichloromethane, and G0-C2/dppb, the six-membered ring lactam was formed in 97% yield (entry 3; Table 7). However, use of **1′a**, as the reactant under the same conditions gave the five-membered ring lactone (**1′a**) as the principal product.

The six-membered ring lactone was obtained as the sole product (**3a**) in 45% yield, when 5/1: CO/H_2 was used in toluene (entry 10, Table 7). In contrast, treatment of **1e** in toluene with a 5/1 mixture of carbon monoxide and hydrogen in the presence of G0/dppb as the catalytic system, resulted in 99% conversion to the five-membered ring lactam **2e** in 84% selectivity (entry 11; Table 7).

Use of G1-C2/dppb as the catalytic system for the cyclocarbonylation of 2-vinylaniline (**1e**) and 2-vinylphenol (**1′a**), resulted in better conversions and good selectivities (Table 8). For example, use of a 2/1 or 1/1 mixture of carbon monoxide and hydrogen in dichloromethane, gave the six-membered ring lactam **3e** in 98% selectivity (entries 7 and 8, Table 8). The conversion decreases when using a 5/1 mixture of CO/H_2 in toluene, with G1-C2 in the presence of dppb (entry 10, Table 8). Use of **1′a** as the reactant in dichloromethane, with G1-C2 in the presence of dppb, and a 5/1 mixture of carbon monoxide and hydrogen, afforded **2a** in 87% selectivity (entry 1, Table 8). Treatment of **1e** in dichloromethane with a 5/1 mixture of carbon monoxide and hydrogen, and using the G2-C2 dendrimer complex and dppb resulted in 66% conversion, with 94% selectivity for the six-membered ring lactam **3e** (Table 9, entry 6).

Good conversion, with 98% selectivity, resulted for the cyclocarbonylation of **1e** with a 1/1 mixture of CO/H_2 in dichloromethane, and G1-C2/dppb as catalytic system (Table 9, entry 8). The regioselectivity for the five-membered ring lactone was 95–90% when **1′a** was used as the reactant in dichloromethane (Table 9, entries 1–4).

The selectivity observed for the six membered ring lactone and lactam was comparable to that using the generation G3-C2 in the presence of dppb, for the cyclocarbonylation of 2-vinylaniline **1e** and 2-vinylphenol **1′a** with the use of previous generations G0 to G2-C2 (Table 10). For example, **1e** can be carbonylated in dichloromethane using a 5/1 mixture of carbon monoxide and hydrogen to form the five-membered ring lactam as the dominant product (Table 10, entry 6). Use of a 2/1 mixture of CO/H_2 in dichloromethane with

Table 10
Cyclocarbonylation of 2-vinylaniline and 2-vinylphenol by G3-C2/dppb/CO/H_2[a]

Entry	Cycle	Sub.	Solvent	P_{CO} (psi)	P_{H_2} (psi)	Conversion (%)	Product distribution (%)	
							2	**3**
1	1	**1′a**	CH_2Cl_2	500	100	100	93	7
2	2	**1′a**	CH_2Cl_2	500	100	98	86	14
3	3	**1′a**	CH_2Cl_2	500	100	60	75	25
4	4	**1′a**	CH_2Cl_2	500	100	47	77	23
5	5	**1′a**	CH_2Cl_2	500	100	20	80	20
6	1	**1e**	CH_2Cl_2	500	100	60	2	98
7	2	**1e**	CH_2Cl_2	400	200	85	56	44
8	3	**1e**	CH_2Cl_2	300	300	65	95	5
9	4	**1e**	CH_2Cl_2	200	400	35	95	5

[a] Reaction conditions: catalyst (50 mg); dppb (0.04 mmol); substrate (1.0 mmol); solvent (5 mL), reaction time (48 h), temperature (120 °C). The ratio of 2:3 was determined by GC and ^{1}H NMR spectroscopy.

G3-C2/dppb as the catalytic system gave 85% conversion, with reduced regioselectivity (56%) for the five-membered ring lactam (Table 10, entry 7). When **1′a** was used as the reactant in dichloromethane, with 5/1 mixture of carbon monoxide and hydrogen, good regioselectivity resulted for the five-membered ring lactone **2a**, (Table 10, entries 1, 2).

3.5. Influence of the space length

In order to determine the effect of the length of the spacer group on the activity and recyclablity of the dendrimer palladium complex for the cyclocarbonylation reaction, third generation G3-C6 palladium-complexed PPh_2-PAMAM-

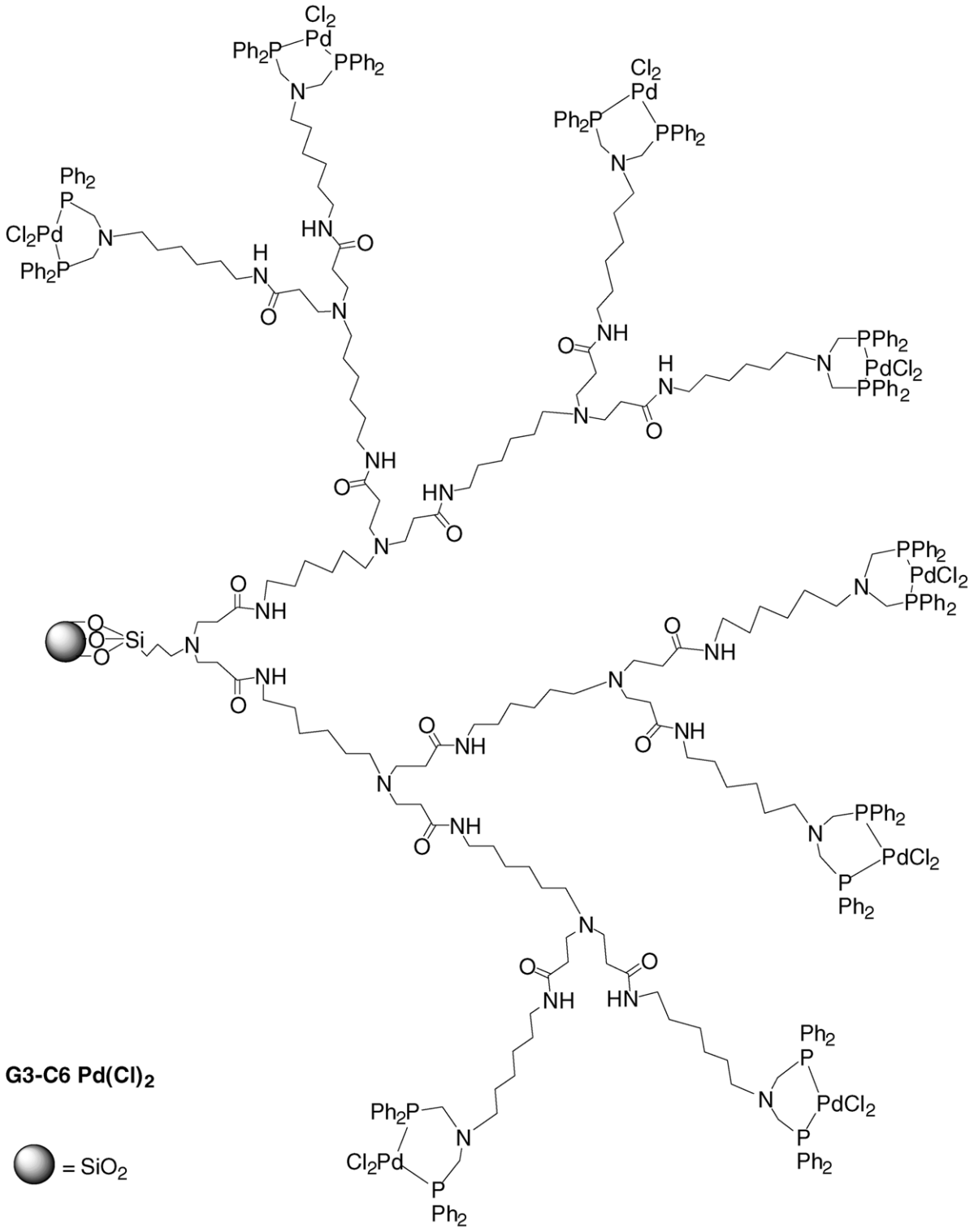


Fig. 2. The proposed structure of the 3rd generation C6-PPh_2-PAMAM-SiO_2.

Table 11
Cyclocarbonylation of 2-allylphenols by G3-C6/dppb/CO/H_2[a]

Entry	Cycle	Sub.	Solvent	P_{CO} (psi)	P_{H_2} (psi)	Conversion (%)	Product distribution (%)		
							2	**3**	**4**
1	1	**1c**	Toluene	500	100	94 (5)[b]	10	9	81
2	2	**1c**	Toluene	500	100	95 (5)[b]	7	10	83
3	3	**1c**	Toluene	500	100	95 (5)[b]	7	14	79
4	4	**1c**	Toluene	500	100	97 (3)[b]	8	21	71
5	5	**1c**	Toluene	500	100	96 (3)[b]	3	13	84
6	6	**1c**	Toluene	500	100	90 (10)[b]	5	20	75
7	7	**1c**	Toluene	500	100	90 (8)[b]	1	15	84
8	1	**1c**	CH_2Cl_2	500	100	94 (6)[b]	42	44	14
9	1	**1a**	Toluene	500	100	100	8	12	80
10	2	**1a**	Toluene	500	100	99	22	25	53
11	3	**1a**	Toluene	500	100	99	10	15	75
12	4	**1a**	Toluene	500	100	98	2	10	88
13	5	**1a**	Toluene	500	100	71	2	7	91
14	6	**1a**	Toluene	500	100	57	2	6	92
15	7	**1a**	Toluene	500	100	35	2	5	93

[a] Reaction conditions: catalyst (25 mg); dppb (0.04 mmol); substrate (1.0 mmol); solvent (5 mL), reaction time (48 h), temperature (120 °C).
[b] Isomerization product. The ratio of 2:3:4 was determined by GC and ^{1}H NMR spectroscopy.

Table 12
Cyclocarbonylation of 2-vinylaniline and 2-vinylphenol by G3-C6/dppb/CO/H_2[a]

Entry	Cycle	Sub.	Solvent	P_{CO} (psi)	P_{H_2} (psi)	Conversion (%)	Product distribution (%)	
							2	**3**
1	1	**1e**	CH_2Cl_2	500	100	40	3	97
2	2	**1e**	CH_2Cl_2	400	200	85	2	98
3	3	**1e**	CH_2Cl_2	300	300	97	2	98
4	4	**1e**	CH_2Cl_2	200	400	96	4	96
5	5	**1e**	CH_2Cl_2	100	500	95	20	80
6	1	**1′a**	CH_2Cl_2	500	100	97	84	16
7	2	**1′a**	CH_2Cl_2	400	200	98	86	14
8	3	**1′a**	CH_2Cl_2	300	300	90	90	10
9	4	**1′a**	CH_2Cl_2	200	400	70	97	3
10	1	**1′a**	Toluene	500	100	45	0	100
11	1	**1e**	Toluene	500	100	99	84	16

[a] Reaction conditions: catalyst (25 mg); dppb (0.04 mmol); substrate (1.0 mmol); solvent (5 mL), reaction time (48 h), temperature (120 °C). The ratio of 2:3 was determined by GC and ^{1}H NMR spectroscopy.

SiO_2 dendrimers were prepared according to the literature (see Fig. 2) [46]. The ethylenediamine linker was substituted by 1,6-diaminohexane. The resulting complexed dendrimer was characterized by ^{31}P solid state NMR (complexed $\delta = +26.9$ ppm, uncomplexed $\delta = -28.7$ ppm), and the ICP analysis shows 5.49% palladium.

High conversions (90–97%) occurred when generation G3-C6/dppb was employed for the cyclocarbonylation of 2-allylphenol at 600 psi pressure ($CO/H_2 = 5/1$) and 120 °C for 48 h. Furthermore, **1a** and **1c**, could be recycled up two times (Table 11). Using toluene as the solvent and a 5/1 mixture of CO/H_2 gave the seven-membered ring lactone, **4c**, in 84% selectivity (entries 5 and 7, Table 11). Dichloromethane gave 94% conversion but poor selectivity (entry 8, Table 11).

We found that the use of generation G3-C6 as the catalyst for the cyclocarbonylation of 2-vinylaniline **1e** and 2-vinylphenol **1′a**, in toluene or dichloromethane, gave selectivities comparable to those of the previous generations with the C2 spacer group (Scheme 2; Table 12). No cyclocarbonylation reaction has been observed without any additional dppb.

4. Conclusion

We can conclude that generations 0–3 of complexes with either a C2 or C6 linker, in the presence of dppb, catalyze the cyclocarbonylation of 2-allylphenols, 2-allylaniline, 2-vinylaniline and 2-vinylphenol, affording lactones and lactams often in good yields and selectivities. The regioselectivity obtained for the cyclocarbonylation reactions using different generations of Pd-PPh_2-PAMAM-SiO_2 dendrimer as a heterogeneous catalytic system is, in some cases different and superior to the homogeneous system and depends on the reaction conditions (CO/H_2 ratio and solvent). The heterogeneous system also has the advantages of easy separation and re-use of the catalyst (recycling three to seven times).

Acknowledgements

We are grateful to The Natural Sciences and Engineering Research Council for support of this research. We also thank Dr. Glenn Facey for recording the solid state NMR spectra.

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