Available online at www.sciencedirect.com
ScienceDirect
Journal of Molecular Catalysis A: Chemical 257 (2006) 78–88
JOURNAL OF MOLECULAR CATALYSIS A: CHEMICAL
www.elsevier.com/locate/molcata

A new approach to dendritic supported NIXANTPHOS-based hydroformylation catalysts

Stefan Ricken [a], Piotr W. Osinski [a], Peter Eilbracht [a,*], Rainer Haag [b,**]

[a] *Organische Chemie, Universität Dortmund, Otto-Hahn-Str. 6, 44227 Dortmund, Germany*
[b] *Freie Universität Berlin, Department of Chemistry, Takustrasse 3, D-14195 Berlin, Germany*

Available online 23 June 2006

Dedicated to Professor Bogdan Marciniec on the occasion of his 65th birthday.

Abstract

NIXANTHPHOS as an effective ligand in regioselective hydroformylation is modified at the nitrogen function and immobilized on soluble and solid polymer supports, such as dendrimers, polyglycerol and polyurethanes. The new ligands were tested in rhodium catalyzed regioselective hydroformylation and proved to be selective and reusable. Polymer supports require spacers between the ligand and the supporting units.

Keywords: Hydroformylation; Rhodium; Ligand; Support; Regioselectivity; XANTPHOS; Polyglycerol; Dendrimer

1. Introduction

Over the last few years catalysis saw various efforts to support metal complexes on soluble high-loading polymers and dendrimers as potential alternatives to insoluble solid-phase supports. This is because heterogenization of soluble metal complexes on solid supports often leads to mechanically sensitive systems with lower activity of the catalyst, which is less likely if the catalyst is supported on a soluble polymer and homogeneous conditions are maintained [1]. Soluble polymers may be easily separated from the reaction mixture via precipitation or membrane filtration [2]. Occasionally these systems are able to perform reactions in membrane flow reactors. The concept of soluble polymer support has been successfully employed in a wide variety of catalytic reactions [3].

For many years several groups have been investigating new applications of the hydroformylation reaction. This most important homogeneously catalysed reaction produces a mixture of linear and branched aldehydes from olefins, carbon monoxide, and hydrogen [4]. In order to achieve high selectivity towards the formation of one product, appropriate ligands have to be employed.

The phenoxazine-based ligand NIXANTPHOS (**1**) evolved from van Leeuwen's initial studies of xanthene-based diphosphine ligands [5] and proved to be a superior ligand with regard to its selectivity towards the linear aldehydes. Moreover, **1** has recently been successfully immobilized on silica [6] (**2**) and polystyrene (**3**) (Fig. 1) [7], providing, after metal complexation, a catalyst suitable for recycling by simple filtration.

On the other hand, soluble polymers with special ligands for asymmetric induction [8], water [9], and fluorous [10] solubility have been used in hydroformylation. Similarly catalysts on hyperbranched polyelectrolytes are under investigation [11]. Inspired by these achievements, we envisaged employing a soluble polymer support instead of a silica or polystyrene support in order to obtain a homogenous, highly active and selective hydroformylation catalyst that is recyclable via membrane filtration.

As a polymer support, dendritic polyglycerol was chosen (Fig. 2). This material is easily obtained from a controlled polymerization of glycidol [12]. In general, hyperbranched polymers, e.g., polyglycerol are excellent platforms for catalysts due to their easy accessibility and high degree of flexible functionality for the attachment of ligands [13].

* Corresponding author. Tel.: +49 231 7553858; fax: +49 7555363.
** Corresponding author.
E-mail addresses: peter.eilbracht@uni-dortmund.de (P. Eilbracht), haag@chemie.fu-berlin.de (R. Haag).

1381-1169/$ – see front matter © 2006 Elsevier B.V. All rights reserved.
doi:10.1016/j.molcata.2006.04.037

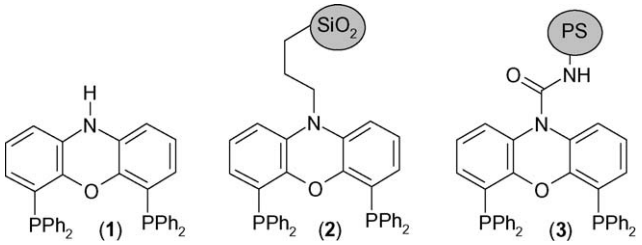


Fig. 1. Supported NIXANTPHOS structures.

2. Results and discussion

First, we wanted to evaluate different attachment routes by connecting the hydroxy groups of polyglycerol with the nitrogen anchor in the ligand. As expected, the phenoxazine nitrogen in **1** was found to be quite unreactive. Acylation of the nitrogen function with succinic anhydride failed despite the fact that many reaction conditions were tested. Alkylation of **1** with ethyl γ-bromobutyrate also failed to give the desired product.

With methyl acrylate and acrylonitrile, however, **1** reacts to give the corresponding products of a Michael addition **4** and **5** in good yields (60–80%) (Fig. 3). The TBS protected ligand **6** (Fig. 3) was prepared according to a modified literature procedure [14]. When **1** was reacted with allyl chloride, product **7** was formed with double bond isomerization in good yields (Fig. 3). The expected product of allylation rearranges under the basic conditions according to a well-known mechanism [15]. In another approach, **1** was reacted with activated ioscyanates, such as allylisocyanate to give the corresponding product **9** in 80% yield. The reaction with ethyl 6-isocyanatohexanoate, however, was very slow and after 1 week only 30% conversion was observed (product **8**, Fig. 3). The alkylation with 4-bromo-1-butene gave the expected product **11** in only 7% yield. Here no rearrangement was observed. Under the reductive conditions applied (NaH in DMF), NIXANTPHOS dimer **10** was the major product.

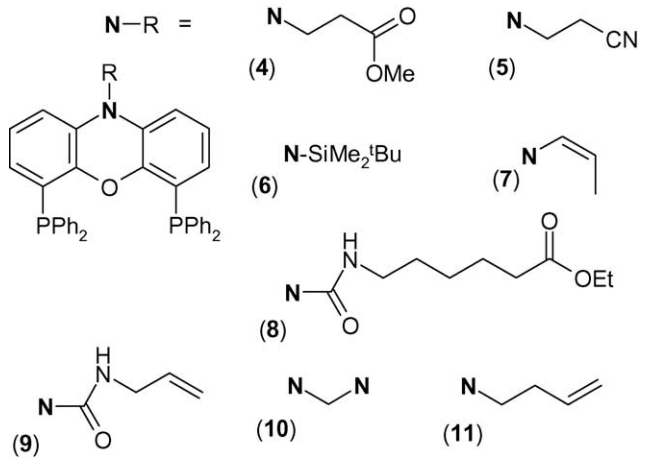


Fig. 3. *N*-Modified NIXANTPHOS structures.

The novel diphosphine ligands with different substituents at the phenoxazine nitrogen were tested in hydroformylation reaction of 1-octene (**A**) and *N*-allyl-phthalimide (**B**) as model substrates. Substrate (**B**) is easily obtained and can be used as a precursor for synthetically useful intermediates [16]. Highly regioselective hydroformylation of this substrate has not been reported yet.

First, the influence of the ligand amount was investigated (Tables 1 and 2). High selectivity towards linear aldehyde was obtained when at least a 3–5 M excess of ligand was used (entry 4). This is in accordance with the previously described suggestions to use 5–10 M excess of XANTPHOS and NIXANTPHOS ligands [6]. As expected *N*-allyl (**B**) gave a lower n/iso ratio.

Next, the series of *N*-modified NIXANTPHOS-based ligands was tested under optimal conditions to verify the influence of *N*-substitution on the hydroformylation selectivity (Tables 3 and 4). 1-Octene (**A**) converted in the presence of ligands **4** and **5** gave an increase in *n*-selectivity. Here the electron withdrawing substituents in the vicinity of the nitrogen seems to cause the higher selectivity. However besides electronic fac-

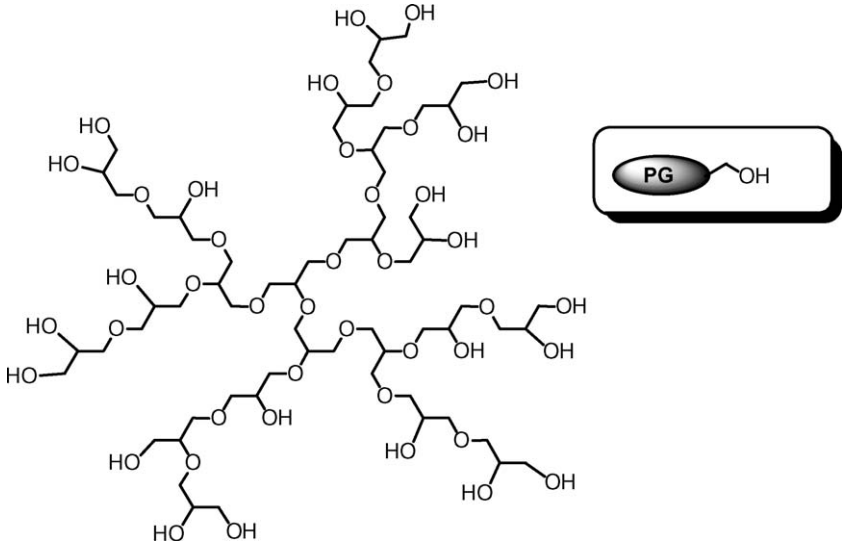


Fig. 2. Hyperbranched polyglycerol. The depicted structure presents only a small idealized fragment of the large polymer core.

Table 1
Results of hydroformylation of 1-octene (**A**)

Entry	Percent of **4**	Percent conversion[a]	*l*:*b*[a]
1	2.0	100	65:35
2	3.0	100	82:18
3	4.0	100	**97:3**
4	5.0	100	**98:2**
5	6.0	100	**98.3:1.7**
6	15.0	100	**98.4:1.6**

Conditions: 1 mol% $Rh(CO)_2acac$, CH_2Cl_2, 20 bar [CO–H_2 (1:1)], 20 h, 80 °C.
[a] Determined by ^1H NMR and GC.

Table 2
Results of hydroformylation of *N*-allyl-phthalimide (**B**)

Entry	mol% of **4**	Percent conversion[a]	*l*:*b*[a]
1	-	100	36:64
2	2.0	100	33:67
3	3.0	100	45:55
4	4.0	84	**78:22**
5	5.0	83	**78:22**
6	6.0	85	**78:22**

Conditions: 1 mol% $Rh(CO)_2acac$, CH_2Cl_2, 20 bar [CO–H_2 (1:1)], 20 h, 80 °C.
[a] Determined by ^1H NMR.

Table 3
Results of hydroformylation of 1-octene (**A**)

Entry	Ligand	Percent conversion[a]	*l*:*b*[a]
1	**1**	100	98.3:1.7
2	**4**	100	**>99:1**
3	**5**	100	**>99:1**
4	**6**	100	98.3:1.7
5	**8**	100	98.2:1.8
6	**9**	100	98.4:1.6
7	**10**	100	98.1:1.9

Conditions: 1 mol% $Rh(CO)_2acac$, 10 mol% ligand, CH_2Cl_2, 20 bar [CO–H_2 (1:1)], 20 h, 80 °C.
[a] Determined by ^1H NMR and GC.

tors other effects may be responsible for these observations (see below).

For *N*-allyl-phthalimide (**B**) the selectivity and activity of rhodium complexes slightly dropped in comparison to the parent ligand **1**, with the exception of ligand **6**. Here a distinct

Table 4
Results of hydroformylation of *N*-allyl-phthalimide (**B**)

Entry	Ligand	Percent conversion[a]	*l*:*b*[a]
1	**1**	100	80:20
2	**4**	83	78:22
3	**5**	100	80:20
4	**6**	100	**86:14**
5	**7**	83	78:22
6	**8**	88	79:21
7	**9**	77	79:21
8	**10**	95	80:20

Conditions: 1 mol% $Rh(CO)_2acac$, 5 mol% ligand, CH_2Cl_2, 20 bar [CO–H_2 (1:1)], 20 h, 80 °C.
[a] Determined by ^1H NMR.

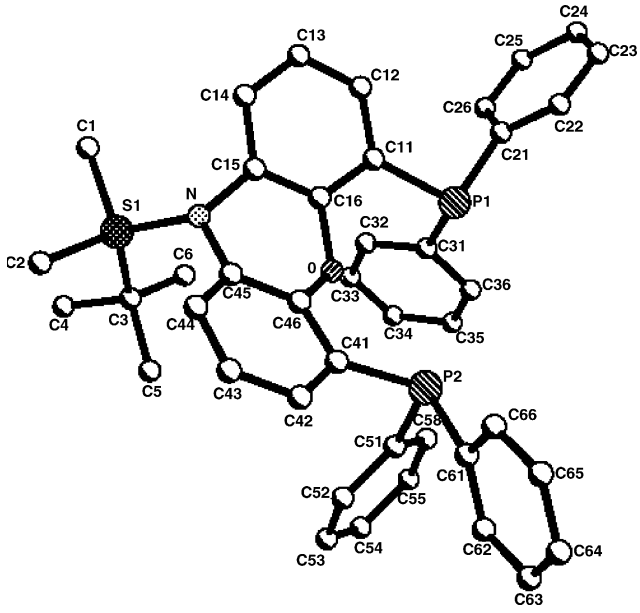


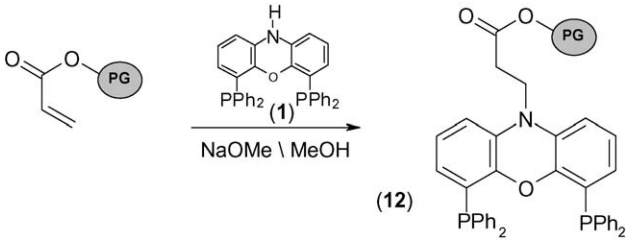
Fig. 4. X-ray structure of TBS-NIXANTPHOS (**6**).

enhancement of the formation of linear aldehyde was observed. In conclusion we can say that ligand effects clearly depend on the structure of different substrates, even though the ligand modifications appear to have a large distance to the phosphine units.

To explain the higher selectivity of ligand **6** (Table 4, entry 4), the X-ray structure of this ligand was determined (Fig. 4) [17]. It reveals the P–P distance to be 4.110 Å, thus a little higher than in XANTPHOS (4.080 Å) and the resulting wider bite angle in the corresponding chelate is supposed to effect the selectivity of the catalyst. In addition it was found that not only the bite angle influences the selectivity but also the rigidity of the ring system is important [18].

The conclusion that can be drawn from these results is that *N*-substitution in **1** may have a positive effect on the performance of the catalyst. Therefore, the modification of the *N*-functionality of NIXANTPHOS with dendrimeric structure support may not only provide immobilization but also improvement of selectivity control.

Having in mind the promising results from Michael addition of **1** to methyl acrylate, an analogous approach was employed in the immobilization reaction. The hydroxyl groups in polyglycerol were modified to acryloyl functionality by the reaction of polyglycerol with acryloyl chloride. Michael addition of **1** to this polymer provided the polymer supported ligand **12** (Scheme 1).



Scheme 1. Attachment of **1** to modified polyglycerol.

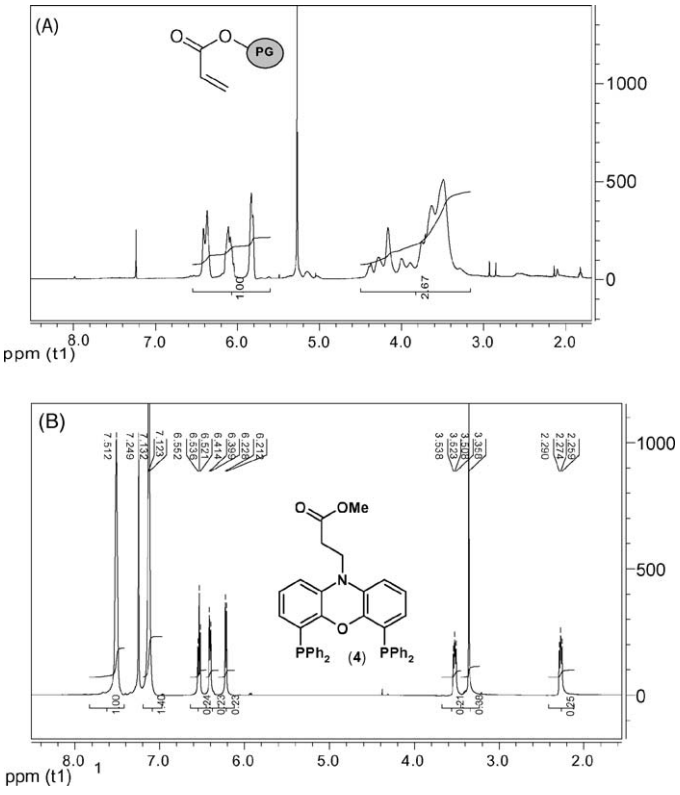


Fig. 5. ^{1}H NMR spectra (1.5–8.5 ppm region) of A: polyglycerol modified with acryloyl functionality; B: NIXANTPHOS attached to methyl acrylate (**4**).

The complex ^{1}H NMR spectra of **12** in comparison to the starting material (Fig. 5) clearly shows that the reaction proceeds with high conversion, as the vinyl signals disappear. It mainly consists of aromatic signals from phenoxazine core, broad singlets from diphenylphosphine portions, polyglycerol broad multiplets in the region 3.5–3.8 ppm, and two signals coming from the linking ethylene chain.

^{31}P NMR shows only one sharp signal in the phosphine region (Fig. 6A). ^{31}P NMR of the mixture of polymer supported ligand **12** and starting ligand **1** as internal standard shows two singlets, indicating there is no free ligand present in the polymer product **12**. The content of diphosphine attached in the polymeric material was calculated from the integration to be approximately 18% (w/w, Fig. 6B).

Disappointingly the polymer supported ligand **12** if mixed with rhodium precursor showed very poor activity and selectivity in the hydroformylation of *N*-allyl-phthalimide (**B**). The reaction performed under the conditions as described above resulted only in a 30–40% conversion and *l*:*b* ratio 38:62. When the supported ligand was heated with rhodium precursor for half an hour in order to generate the corresponding diphosphine–rhodium complex prior to hydroformylation the same *l*:*b* ratio was observed, but the conversion dropped to 20%. The same reaction performed in toluene gave better conversion (64%), but again with a low *l*:*b* ratio. Even with an excess of ligand (calculated to be 50 diphosphine portions to rhodium metal) no increase of selectivity could be achieved (conversion 40%, [*l*:*b*] 34:66).

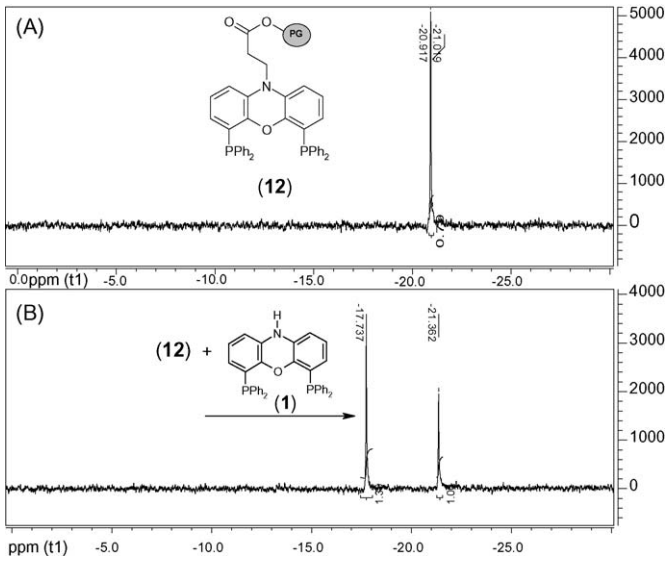


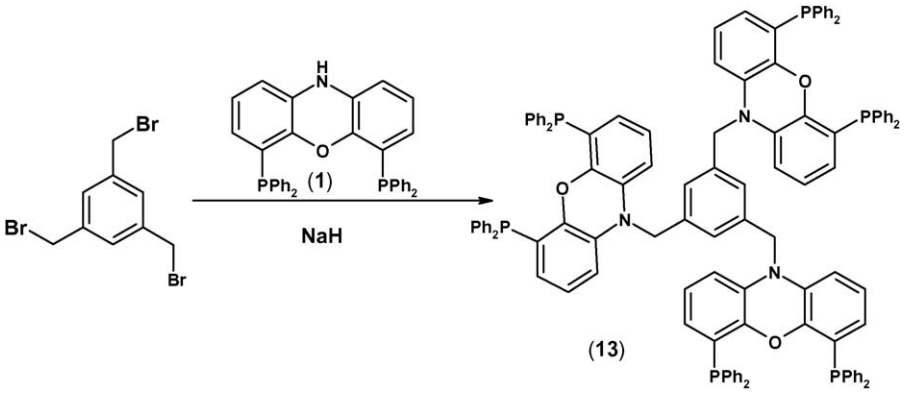
Fig. 6. ^{31}P NMR spectra (0 to −30 ppm region) of: A: NIXANTPHOS attached to polyglycerol (**12**); B: NIXANTPHOS attached to polyglycerol (20 mg) + **1** internal standard (5 mg).

If the rhodium precursor and NIXANTPHOS (**1**) are mixed in THF (in 1–5 M ratio) and the resulting diphosphine complex is attached to the polymeric material after standard work-up (dialysis purification) a crystalline powder was obtained in 88% yield. It dissolves well in dichloromethane, but upon testing the selectivity of hydroformylation, after 100% conversion, the disappointingly low *l*:*b* ratio for **B** was observed again (35:65 [*l*:*b*]). The same result was obtained when the polymer supported rhodium complex was mixed with an additional equivalent of rhodium precursor prior to the hydroformylation. It should be noted that low selectivity of polymer supported catalyst is not caused by the polymeric material present, since highly selective hydroformylation of terminally allylated polyglycerol has been recently achieved [19].

To compare these disappointing results with similar conversions using the solid polystyrene supported NIXANTPHOS **3** which was used before in hydrophosphinylation reaction [7], we repeated the synthesis of **3**. After stirring this polymeric ligand with 0.1 equiv $Rh(CO)_2(acac)$ and washing the polystyrene this catalyst was used in hydroformylation of octene (**A**) (100% conversion, 72:28 [*l*:*b*]) and *N*-allyl-phthalimide (**B**) (6% conversion, 43:57 [*l*:*b*]) resulting in a similar poor selectivity as compared to the soluble polymer supported ligand **12**.

In order to understand the low n selectivity of the polymer bound ligands we decided to use smaller dendrimer-based ligands. Therefore the model micro-dendritic ligand **13** was designed and synthesized via simple alkylation of **1** with 1,3,5-tris-bromomethyl-benzene [20] (Scheme 2). **13** consists of an aryl core and three NIXANTPHOS spheric ligands with a molecular mass of above 1700 g mol^{-1} which is large enough for purification by dialysis and use in membrane reactors. This nanofiltration technique is an attractive option for the separation of catalysts and products in homogeneous catalysis [21].

Ligand **13** gave excellent *n*-selectivities for the hydroformylation of 1-octene (**A**) (Table 5, entry 4) with a TOF of 5 h^{-1}



Scheme 2. Synthesis of micro-dendimeric NIXANTPHOS trimer **13**.

Table 5
Results of hydroformylation of 1-octene (**A**)

Entry	Percent of **13**	**P–P**	Percent conversion[a]	*l*:*b*[a]
1	1.0	3	100	60:40
2	1.7	5	100	64:36
3	2.0	6	100	76:24
4	**5.0**	**15**	100	**99:1**

Conditions: 1 mol% $Rh(CO)_2acac$, CH_2Cl_2, 20 bar [CO–H_2 (1:1)], 20 h, 80 °C.
[a] Determined by ^1H NMR and GC. **P–P**, number of diphosphine functions present in the reaction mixture.

[22]. As seen in Tables 5 and 6 hydroformylation of 1-octene (**A**) and *N*-allyl-phthalimide (**B**) with use of rhodium complex of **13** revealed that the molar ratio of 2:1 (**13**: rhodium) is not sufficient to achieve acceptable selectivity towards the formation of the linear aldehyde (entry 3). This ratio is equivalent to a 6 M excess of the NIXANTPHOS units and, according to the results presented in Table 1, should be sufficient to significantly enhancing the selectivity. A very good selectivity, comparable to other NIXANTPHOS-based ligands, was only obtained when at least a molar ratio of 3–5:1 (**13**: rhodium) was used. It should be noted that this enhancement of the selectivity was accompanied with a slight drop of activity of the catalyst (Table 6).

All results presented in Tables 1, 2, 5 and 6 clearly show that at least a three-fold excess of the ligand is required in order to achieve high selectivity, regardless of the amount of diphosphine functions present in a single ligand. Therefore presumably only one diphosphine unit per molecule can enhance the regioselectivity.

Indeed, Huges and Unruh [23] found that rhodium complexed with various rigid chelating diphosphines witnessed an increase

Table 6
Results of hydroformylation of *N*-allyl-phthalimide (**B**)

Entry	Percentage of **13**	**P–P**	% conversion[a]	*l*:*b*[a]
1	1.0	3	100	31:69
2	1.7	5	100	38:62
3	2.0	6	100	63:37
4	**3.0**	**9**	69	**76:24**
5	5.0	15	68	75:25

Conditions: 1 mol% $Rh(CO)_2acac$, CH_2Cl_2, 20 bar [CO–H_2 (1:1)], 20 h, 80 °C.
[a] Determined by ^1H NMR. **P–P**, number of diphosphine functions present in the reaction mixture.

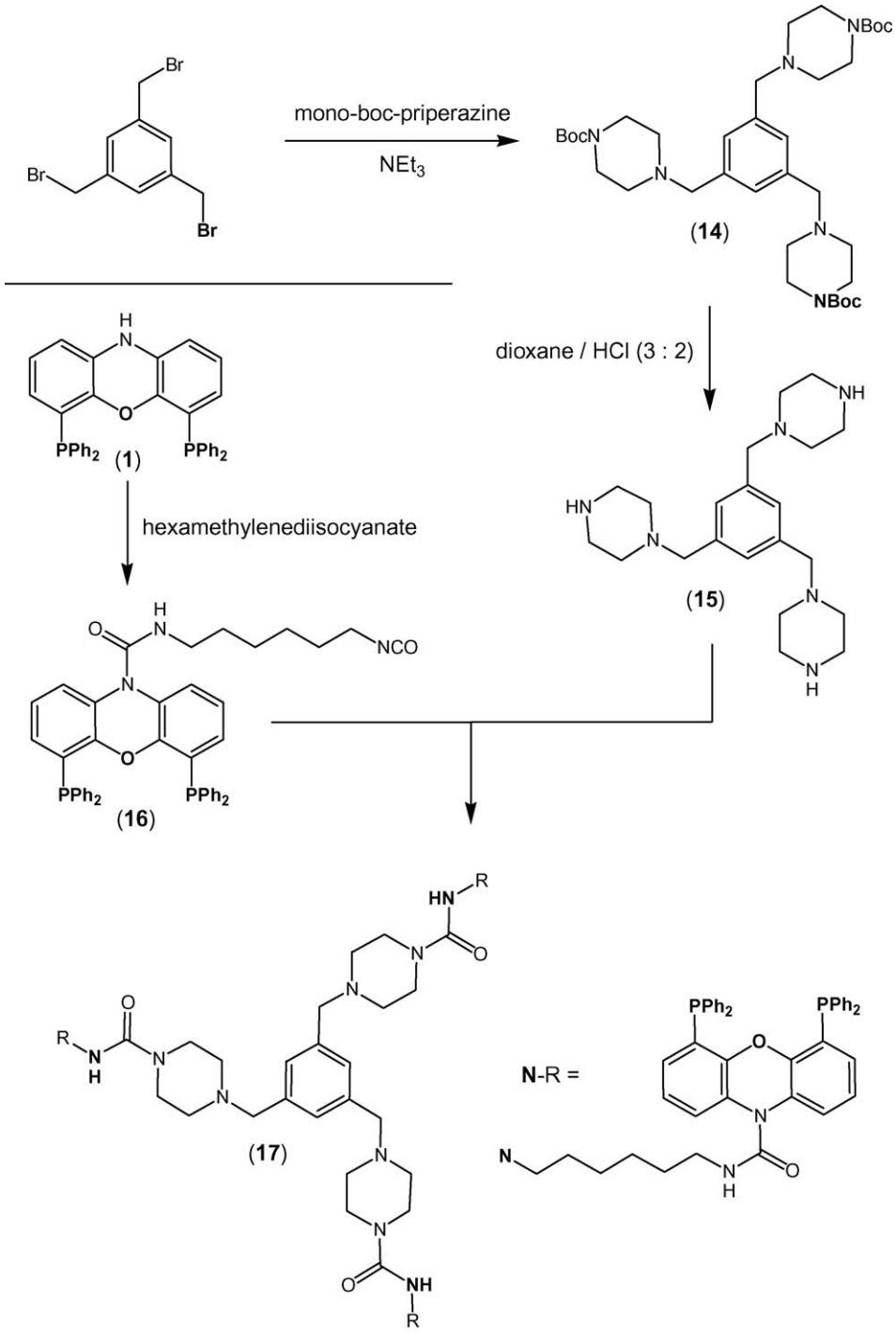
Fig. 7. Bridged dimeric species as proposed by Hughes and Unruh.

in *l*:*b* ratios when the ligand to rhodium ratio was 1.5:1 or higher. The complex that accounts for the increase in selectivity was proposed to be a dimeric rhodium complex in which two ligands are chelating one rhodium center, while another ligand is bridging two rhodium centers (Fig. 7). This complex was later observed by ^{31}P NMR [24].

The formation of higher valent complexes is, of course, not possible or very unlikely in the case of the rigid ligand **13**, when two or less equivalents of ligand were used. van Leeuween [25] has calculated that due to the rigid structure of the XANTPHOS-based ligands the presence of a binuclear species is very unlikely. Futhermore, a third phosphine ligand is readily replaced with carbon monoxide under an atmosphere of CO. Therefore, the optimal ligand to rhodium ratio of 2.2:1 was explained as a result of a dissociation equilibrium and thus dependent on the absolute concentration of the ligand. Our results do not fit in both models. Possibly only one NIXANTPHOS unit in the tris-NIXANTPHOS system **13** is active.

Following these interpretations, we expected that longer spacer units may increase the *n*-selectivity of the soluble polymer supported NIXANTPHOS ligand. A synthetic route of the micro-dendrimeric NIXANTPHOS **17** was therefore developed (Scheme 3). Starting from 1,3,5-tris-bromomethyl-benzene a nucleophilic substitution with mono BOC-protected piperazine [26] obtained **14** in quantitative yield. The following deprotection furnished the tris secondary amine core **15** in 90% yield. This was reacted with an isocyanate functionalized NIXANTPHOS ligand **16**, which was obtained by heating **1** with an excess of hexamethylene-diisocyanate. The resulting micro-dendimeric NIXANTPHOS **17** with hexamethylene spacers was purified by dialysis and yielded 33% as a yellow micro crystalline compound. Five mole percent of this ligand **17** gave an excellent *n*-selectivities for the hydroformylation of 1-octene (**A**) (92% conversion, 98.3:1.7 [*l*:*b*]) and *N*-allyl-phthalimide (**B**) (100% conversion, 80:20 [*l*:*b*]), like for **13**.

When compound **16** is reacted with polyglycerol attachment of the ligand readily occurs, however, due to small impuri-

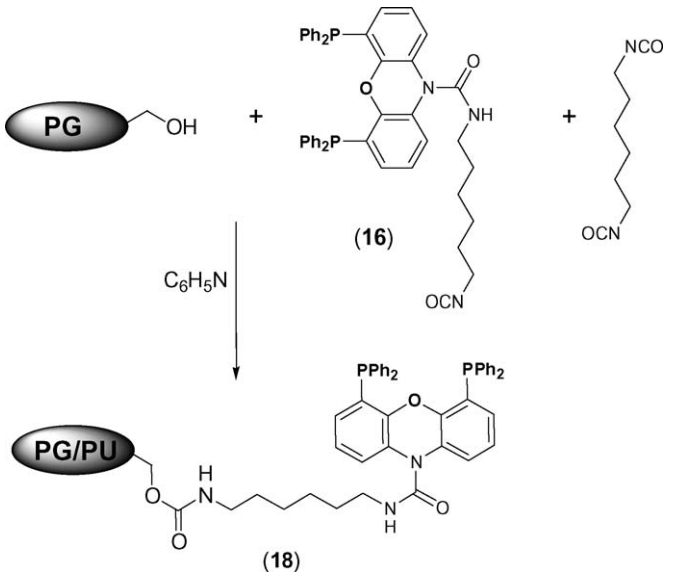


Scheme 3. Synthesis of micro-dendrimeric NIXANTPHOS **17** with a long spacer.

ties of unreacted hexamethylenediisocyanate the polyglycerol molecules (PG) are linked to form a higher molecular weight polyurethanes (PU) derivative (**18**) (Scheme 4).

The yellowish solid of **18** thus obtained was used in hydroformylation of 1-octene (**A**) (69% conversion, 96.8: 3.2 [*l*:*b*]). This shows that the long spacer increases the *n*-selectivity in comparison to compound **3** and **12**. The PG/PU NIXANTPHOS **18** is recyclable by simple filtration and this opens an convenient access to recyclabe supported ligands. Similarly by avoiding the diisocyanate impurity also soluble polymers are obtainable.

In conclusion, we have developed a practical route to synthesize a series of *N*-modified NIXANTPHOS-based ligands, and a straightforward procedure of immobilization NIXANTPHOS units on soluble polyglycerol and the corresponding urethanes. To our knowledge this is the first time this ligand has been covalently attached to polyglycerols. Extension of the scope of these ligands, including the most efficient ligands **4**, **5**, and **6**, are currently under investigation. As to be expected from the results with model micro-dendrimeric ligands **13**, the polymer supported catalyst **12** showed very poor selectivity together with



Scheme 4. Synthesis of polyurea NIXANTPHOS **18**.

rather low activity in hydroformylation reaction. To overcome this drawback a longer spacer was used. This allows a flexible cooperation of diphosphine portions in chelating the rhodium centers. Here the model micro-dendrimeric ligand **17** and the solid polyglycerol/polyurea-based ligand **18** both showed comparably good results regarding the *n*-selectivity in the hydroformylation of 1-octene (**A**).

3. Experimental

3.1. General remarks

Hyperbranched polyglycerol was prepared according to a published procedure [12] with a molecular weight of 8000 g mol^{-1} and analyzed by NMR and GPC. Dialysis (benzoylated cellulose tubing, Sigma, MWCO 1000) was performed in 1 L beaker charged with chloroform and stored over 24 h, and after one day solvent was exchanged.

4. Polystyrene supported NIXANTPHOS (3) [7]

Dry toluene (15 mL) was added to a mixture of polystyrene isocyanate resin (1.412 g, 2.4 mmol, novabiochem: 200–400 mesh, 1.7 mmol g^{-1}), and 4,6-bis(diphenylphosphino)phenoxazine **1** (0.653 g, 1.185 mmol). The suspension was stirred and heated at 115 °C overnight under Ar. To the resulting mixture was added anhydrous dipropylamine (0.5 mL, 3.56 mmol) in order to neutralize the unreacted isocyanate groups. The reaction mixture was stirred at room temperature for 1 h under Ar. After filtration, the collected resin (1.76 g) was rinsed with dichloromethane and dried under vacuum. The amount of recovered unreacted NIXANTPHOS was taken to calculate the loading of the resin. The supported ligand's loading was found to be 0.18 mmol g^{-1}.

The catalyst precursor (polystyrene-Nixantphos)Rh(acac) was prepared by stirring a suspension of 1 g of **3** (0.18 mmol) and 4.6 mg of $Rh(CO)_2(acac)$ (0.1 equiv, 0.018 mmol) in 5 mL of THF and 1 mL of Et_3N for 30 min. Next, the solvent was removed and the polystyrene was washed with toluene (2 × 10 mL) and dichlormethane (10 mL). Rhodium content: 1.8×10^{-5} mol g^{-1}.

5. Methyl 3-[10-(4,6-bis(diphenylphosphino))-phenoxazinyl]propionate (4)

To a stirred suspension of 2.5 g of **1** (4.54 mmol) and 8 mL of methyl acrylate (97 mmol, 21 equiv.) a solution of 0.2 g of NBu_4Br (0.62 mmol) and 40 mg of NaOMe (0.7 mmol, 16%) in 2 mL of methanol was added though a syringe. The mixture was heated and stirred under reflux for 2 h. After that TLC showed very little substrate left (cyclohexane–acetone (4:1)). Fifty millilitres of water was added and the mixture was extracted with 3 × 20 mL of DCM. The combined organic phases were dried over $MgSO_4$, filtered, evaporated, and dried with an oil pump. Crystallization (DCM\ethanol) yielded 1.81 g (62%) of pale yellow crystals, m.p. 204–205 °C.

^{1}H NMR (500 MHz, C_6D_6), δ: 2.27 (t, 2H, J = 7.5), 3.36 (s, 3H), 3.52 (t, 2H, J = 7.5), 6.22 (d, 2H, J = 8.0), 6.41 (d, 2H, J = 7.5), 6.54 (dd, 2H, J = 7.5, J = 8.0), 7.1 (bs, 12H), 7.5 (bs, 8H); ^{13}C NMR (125 MHz, C_6D_6), δ: 30.8 (CH_2), 41.2 (CH_2), 52.5 (CH_3), 113.2 (CH), 125.5 (CH), 127.2 (CH), 129.8 (m, CH), 134.1 (C), 135.7 (m, CH), 139.0 (C), 139.0 (C), 172.6 (C); ^{31}P NMR (81 MHz, C_6D_6), δ: −17.5; IR (KBr plate): ν (cm^{-1}) 694 (s), 744 (s), 1222 (s), 1279 (s), 1377 (s), 1417 (vs), 1462 (s), 1552 (s), 1577 (m), 1724 (s), 2949 (w), 2999 (w), 3051 (w), 3064 (w); MS(FAB + LR): m/z (%) = 638 (M)$^+$ (0.2); exact mass (FAB + HR): 637.1968 (M)$^+$ (calculated for $C_{40}H_{33}O_3NP_2$ 637.1936); elementary analysis: found C 74.8, H 5.2, N 2.1; $C_{42}H_{38}NO_3P_2$ requires C 75.3, H 5.2, N 2.2.

6. 3-[10-(4,6-bis(Diphenylphosphino))phenoxazinyl] propionitrile (5)

Prepared analogously as **5**, yield 77% of pale yellow seeds, m.p. 219–220 °C.

^{1}H NMR (500 MHz, C_6D_6), δ: 1.60 (t, 2H, J = 7.8), 3.02 (t, 2H, J = 7.8), 5.78 (d, 2H, J = 7.5), 6.42 (d, 2H, J = 7.5), 6.48 (t, 2H, J = 7.5), 7.1 (bs, 12H), 7.5 (bs, 8H); ^{13}C NMR (125 MHz, C_6D_6), δ: 14.3 (CH_2), 41.4 (CH_2), 113.0 (CH), 118.3 (C), 125.4 (CH), 127.8 (CH), 129.9 (m,CH), 133.1 (C), 135.7 (m, CH), 138.7 (C), 138.8 (C); ^{31}P NMR (81 MHz, C_6D_6), δ: −17.7; IR (KBr plate): ν (cm^{-1}) 696 (vs), 744 (s), 1227 (s), 1279 (s), 1381 (s), 1419 (vs), 1464 (s), 1554 (s), 1577 (m), 1612 (w), 2250 (w), 2360 (w), 2998 (w), 3014 (w), 3051 (m), 3066 (m); MS (FAB + LR): m/z (%) = 604 (M)$^+$ (22); exact mass (FAB + HR): 604.1837 (M)$^+$ (calculated for $C_{39}H_{30}ON_2P_2$ 604.1833).

7. 4,6-bis(Diphenylphosphino)-10-tertbutyldimethylsilyl-phenoxazine (6)

At 0 °C, 16 mL of *n*-butyllithium (2.5 M in hexanes, 39 mmol) was added dropwise to a stirred solution of 4.84 g of 10-(tertbutyldimethylsilyl)phenoxazine (16.3 mmol) and 5.9 mL of

TMEDA (39 mmol) in 250 mL of diethyl ether. The reaction mixture was slowly warmed to room temperature and stirred for 16 h. The maize yellow suspension was then cooled to 0 °C and a solution of 7.0 mL of chlorodiphenylphosphine (39 mmol) in 25 mL of hexanes was added dropwise. The reaction mixture decolorized and a light brown precipitate was formed. After stirring for 16 h at room temperature the reaction mixture was hydrolyzed with 50 mL of brine. The water layer was removed and the organic layer was dried over $MgSO_4$. The solvent was removed and the residue purified by chromatography (cyclohexane) followed by crystallization from DCM\ethanol. Yield 7.91 g (73%) of colorless crystals, m.p. 159–160 °C.

^{1}H NMR (500 MHz, C_6D_6), δ: 0.26 (s, 6H), 0.90 (s, 9H), 6.63 (d, 2H, J = 7.7), 6.71 (t, 2H, J = 7.7), 6.89 (d, 2H, J = 7.7), 7.1 (bs, 12H), 7.5 (bs, 8H); ^{13}C NMR (125 MHz, C_6D_6), δ: 0.9 (CH_3), 21.7 (C), 28.7 (CH3), 124.3 (CH), 125.0 (CH), 128.2 (C), 128.3 (C), 128.4 (C), 129.4 (CH), 129.8 (m, CH), 136.8 (m, CH), 138.4 (C), 139.0 (m, C); ^{31}P NMR (81 MHz, $CDCl_3$), δ: −16.6; IR (KBr plate): ν (cm^{-1}) 698 (vs), 746 (vs), 790 (vs), 836 (vs), 981 (vs), 1068 (s), 1215 (vs), 1288 (vs), 1407 (vs), 1432 (vs), 1570 (s), 2856 (s), 2927 (s), 2954 (s), 3047 (s), 3066 (s), 3066 (m); MS(FAB + LR): m/z (%) = 666 $(M)^+$ (20); exact mass (FAB + HR): 665.2425 $(M)^+$ (calcd for $C_{42}H_{41}ONSiP_2$ 665.2433); elementary analysis: found C 75.2, H 6.2, N 2.0; $C_{42}H_{41}NOP_2Si$ requires C 75.6, H 6.2, N 2.1.

8. *Z*-4,6-bis(Diphenylphosphino)-10-propenyl-phenoxazine (7)

A solution of 50 mg of **1** (0.09 mmol) and 5 mg of NaH (60% oil suspension, 10 equiv.) dissolved in 10 mL of DMF was heated to 70 °C for 1 h and then 7 mg (0.09 mmol) of allyl chloride dissolved in 1 mL of DMF was added though a syringe and the mixture was heated for an additional hour. 50 mL of water was added, the resulting mixture was extracted with 3 × 20 mL of ethyl acetate. Combined organic phases were dried on $MgSO_4$ and the solvent was removed. The residue was purified by chromatography (cyclohexane–ethyl acetate (10:1)) yield 41 mg (76%) of white plates, m.p. 175–176 °C.

^{1}H NMR (500 MHz, C_6D_6), δ: 1.31 (d, 3H, J = 6.5), 5.35 (d, 1H, J = 7.0), 5.40 (dq, 1H, J = 7.0; J = 6.5), 6.36 (d, 2H, J = 8.0), 6.45 (d, 2H, J = 7.0), 6.58 (dd, 2H, J = 7.0; J = 8.0), 7.1 (bs, 12H), 7.5 (bs, 8H); ^{13}C NMR (125 MHz, C_6D_6), δ: 13.6 (CH_3), 115.1 (CH), 125.2 (CH), 125.9 (CH), 127.2 (C), 127.4 (C), 127.8 (CH), 129.8 (m, CH), 131.1 (CH), 133.8 (C), 135.7 (m, CH), 139.0 (C), 139.0 (C), 139.1 (C); ^{31}P NMR (81 MHz, C_6D_6), δ: −17.6; IR (KBr plate): ν (cm^{-1}) 694 (vs), 742 (s), 773 (s), 1218 (s), 1282 (m), 1332 (s), 1396 (m), 1417 (vs), 1456 (vs), 1552 (m), 1577 (s), 1610 (m), 3012 (w), 3048 (m), 3066 (m); MS (FAB + LR): m/z (%) = 592 $(M)^+$ (17); exact mass (FAB + HR): 591.1858 $(M)^+$ (calculated for $C_{39}H_{31}ONP_2$ 591.1881).

9. Ethyl 6-[(4,6-bis(diphenylphosphino)phenoxazine-10-carbonyl)-amino]-hexanoate (8)

2.3 g of **1** (4.17 mmol) and ethyl 6-isocyanatohexanoate (6.26 mmol, 1.16 g, 1.12 mL, 1.5 equiv.) were mixed in toluene and heated under reflux for 5 days. The solvent was evaporated and the residue was purified by chromatography (cyclohexane–ethyl acetate (5:1)). Yield 1.4 g of substrate (61%) and 0.92 g (30%) of expected product, oil, after standing solidifies to give pale yellow microcrystalls, m.p. 75–76 °C.

^{1}H NMR (500 MHz, C_6D_6), δ: 1.06 (t, 3H, J = 7.0), 1.08 (m, 4H), 1.49 (tt, 2H, J = 7.5, J = 7.0), 2.12 (t, 2H, J = 7.3), 2.96 (dt, 2H, J = 6.0, J = 6.5), 4.05 (q, 2H, J = 7.0), 4.91 (t, 1H, J = 6.0), 6.79–6.89 (m, 4H), 7.1 (bs, 12H), 7.5 (bs, 8H), 7.68–7.69 (m, 2H); ^{13}C NMR (125 MHz, C_6D_6), δ: 15.6 (CH_3), 26.0 (CH_2), 27.7 (CH_2), 30.7 (CH_2), 35.3 (CH_2), 42.05 (CH_2), 61.3 (CH_2) 125.5 (CH), 126.1 (CH), 130.0 (m, CH), 131.6 (C), 131.7 (CH), 135.7 (m, CH), 138.6 (C), 155.2 (C), 174.1 (C); ^{31}P NMR (81 MHz, C_6D_6), δ: −17.2; IR (KBr plate): ν (cm^{-1}) 694 (vs), 742 (vs), 784 (s), 1025 (m), 1092 (m), 1224 (vs), 1252 (s), 1321 (s), 1413 (vs), 1432 (s), 1459 (s), 1506 (s), 1577 (m), 1687 (s), 1731 (vs), 2933 (m), 3050 (m), 3068 (m); MS (FAB + LR): m/z (%) = 737 $(MH)^+$ (100), 551 (85); exact mass (FAB + HR): 736.2628 $(M)^+$ (calculated for $C_{45}H_{42}O_4N_2P_2$ 736.2620).

10. 4,6-bis-Diphenylphosphanyl-phenoxazine-10-carboxylic acid allylamide (9)

0.5 g of **1** (0.906 mmol) and allylisocyanate (0.5 g, 6 mmol) were mixed in toluene and heated under reflux for 1 day under Ar. Next the reaction mixture was stirred at room temperature for 6 h, the solvent was evaporated and the residue was purified by chromatography (from cyclohexane–dichlormethane (1:1) to dichlormethane) followed by crystallization from DCM\ethanol. Yield 0.472 g (82%) of colorless crystals, m.p. 178–179 °C.

^{1}H NMR (500 MHz, $CDCl_3$), δ: 3.92 (t, 2H, J = 5.5), 5.15 (d v. d, 2H, J = 25.2 and 17.2), 5.40 (t, 2H, J = 5.5), 5.88 (m, 1H), 6.51 (d, 2H, J = 7.7), 6.99 (t, 2H, J = 8.0), 7.17–7.32 (bs, 20H), 7.51 (d, 2H, J = 8.0); ^{13}C NMR (125 MHz, $CDCl_3$), δ: 43.4 (CH_2), 116.3 (CH_2), 123.8 (CH), 124.8 (CH), 127.4 (C), 128.4 (m, CH), 129.0 (C), 130.6 (CH), 134.0 (m, CH), 134.5 (CH), 136.3 (C), 153.1 (C), 154.4 (C); ^{31}P NMR (81 MHz, $CDCl_3$), δ: −17.3; IR (KBr plate): ν (cm^{-1}) 737 (w), 908 (w), 1025 (m), 1093 (m), 1227 (m), 1259 (w), 1321 (m), 1414 (w), 1462 (m), 1504 (m), 1681 (m), 2925 (s), 2962 (s), 3055 (s), 3070 (s); MS (FAB + LR): m/z (%) = 635.5 $(M + H)^+$ (30), 551 (10); exact mass (FAB + HR): 634.1942 $(M)^+$ (90) (calculated for $C_{40}H_{32}O_2N_2P_2$ 634.1939).

11. bis-4,6-bis-Diphenylphosphanyl-10*H*-phenoxazine-methane (10)

A solution of 551 mg of **1** (1 mmol) and 200 mg of NaH (60% oil suspension, 10 equiv.) dissolved in 30 mL of abs. DMF was heated at 70 °C for 1 h, then 150 mg (1.1 mmol) of 4-bromo-1-butene dissolved in 1 mL of DMF was added though a syringe and the mixture was heated for 15 h. Thirty millilitre of water and 40 mL of ethyl acetate was added and the resulting mixture was extracted. The organic phase was evaporated

up to 10 mL and methanol was added. The formed crystals was filtered, evaporated, and dried with an oil pump. Yield 315 mg (57%) of **10** as pale yellow microcrystals, m.p. 178–179 °C.

^{1}H NMR (500 MHz, $CDCl_3$), δ: 5.38 (s, 2H), 6.13 (d, 4H, J = 6.2), 6.62–6.73 (m, 8H), 7.08–7.25 (bs, 40H); ^{13}C NMR (125 MHz, $CDCl_3$), δ: 59.4 (CH_2), 115.4 (CH), 123.7 (CH), 125.3 and 125.5 (C), 126.5 (CH), 128.1 (m, CH), 132.1 (C), 133.5 (CH), 133.6 (m, CH), 136.5 (C), 149.2 (C); ^{31}P NMR (81 MHz, $CDCl_3$), δ: −16.5; IR (KBr plate): ν (cm^{-1}) 694 (vs), 740 (s), 746 (s), 773 (s), 1093 (m), 1219 (s), 1242 (s), 1346 (s), 1417 (vs), 1464 (s), 1558 (m), 1577 (m), 1718 (s), 3047 (m), 3066 (m); MS (FAB + LR): m/z (%) = 1115.2 $(M+H)^+$ (2); 1114.2 $(M)^+$ (2); 564.1 (15); exact mass (FAB + HR): 1115.3245 $(M+H)^+$ (100) (calculated for $C_{73}H_{54}N_2O_2P_4$ 1114.3136).

The filtered solution was evaporated. The residue was purified by chromatography (cyclohexane–dichlormethane(1:1)) and gave the expected product **11** in 7% yield (42 mg).

12. 10-But-3-enyl-4,6-bis-diphenylphosphanyl-10*H*-phenoxazine (11)

^{1}H NMR (500 MHz, $CDCl_3$), δ: 2.45 (q, 2H, J = 7.2), 3.59 (t, 2H, J = 7.7), 5.19 (d v. d, 2H, J = 10.2 and 17.2), 5.89 (m, 1H), 6.02 (d, 2H, J = 6.7), 6.48 (d, 2H, J = 7.7), 6.68 (t, 2H, J = 7.7), 7.15–7.31 (bs, 20H); ^{13}C NMR (125 MHz, $CDCl_3$), δ: 29.1 (CH_2), 44.0 (CH_2), 111.8 (CH), 117.3 (CH_2), 123.7 (CH), 124.7 and 124.9 (C), 125.3 (CH), 128.1 (m, CH), 132.9 (C), 133.8 (CH), 133.9 (m, CH), 136.9 (C), 147.1 (C); ^{31}P NMR (81 MHz, $CDCl_3$), δ: −18.0; IR (KBr plate): ν (cm^{-1}) 694 (s), 746 (s), 918 (w), 1232 (m), 1278 (m), 1365 (w), 1417 (vs), 1464 (s), 1552 (m), 2854 (w), 2923 (w), 3049 (w), 3066 (w); MS (FAB + LR): m/z (%) = 605.4 $(M)^+$ (0.6).

13. Acryloyl modified polyglycerol

To an ice-cooled mixture of 0.4 g of polyglycerol (M = 8000, 5 mmol of free OH groups) and 0.9 mL of triethylamine (6.5 mmol) dissolved in 15 mL of DMF, 0.4 mL of acryloyl chloride (4.9 mmol) dissolved in 2 mL of DMF was added dropwise. The mixture was stirred overnight at room temperature. The solvent was evaporated with an oil pump and the residue dissolved in $CHCl_3$, filtered and put into a dialysis tube and kept in 1 L beaker filled with $CHCl_3$ under stirring. The solvent was replaced after one day and the dialysis tube was allowed to stand in the stirred solvent over night. The content of the tube was transferred to a flask and evaporated to leave 0.5 g (75%) of light brown gel. ^{1}H NMR (500 MHz, $CDCl_3$), δ: 3.0–4.6 (m, 8H), 5.76–5.90 (m, 1H), 6.02–6.18 (m, 1H), 6.30–6.48 (m, 1H).

14. Attaching of NIXANTPHOS (1) to polyglycerol (12)

To a stirred suspension of 1.0 g of **1** (181 mmol) and 0.31 g of acrylylated polyglycerol (2.3 mmol of vinyl functions) in 3 mL of methanol, a solution of 0.2 g of NBu_4Br (0.62 mmol) and 40 mg of NaOMe (0.7 mmol) in 2 mL of methanol was added through a syringe. The mixture was heated and stirred at reflux for 2 h. The solvent was evaporated, the residue was dissolved in $CHCl_3$ and filtered, placed into a dialysis tube, and kept in a 1 L beaker filled with $CHCl_3$ that was stirred. The solvent was replaced after 1 day, and again the dialysis tube was allowed to stand in the stirred solvent overnight. The content of the tube was transferred to a flask and evaporated to leave 0.56 g of **10**. ^{1}H NMR (500 MHz, $CDCl_3$), δ: 1.4–1.5 (m, 4.9H), 1.6–1.75 (m, 4.8H), 1.9–2.6 (m, 3.6H), 2.65–2.75 (m, 1.4H), 3.3–3.45 (m, 4.7H), 3.45–3.8 (m, 6.2H), 5.75–5.95 (m, 1.3H), 6.30–6.48 (m, 1H); ^{31}P NMR (81 MHz, $CDCl_3$), δ: −21.4.

15. Micro-dendrimeric NIXANTPHOS trimer (13)

Six-hundred milligram of NIXANTPHOS (1.09 mmol; 3.1 equiv.) and 26 mg of sodium hydride (1.09 mmol; 3.1 equiv.) was dissolved in 2 mL of DMF and stirred for 30 min at 70 °C. The mixture was cooled down and 126 mg of 1,3,5-tris-bromomethyl-benzene [27] (0.35 mmol, 1 equiv.) was added to the solution and stirred for 16 h at 90 °C in a sealed tube. The crude product was cleaned by dialysis in chloroform and heated in ethylacetate, filtered, and solvent was removed under reduced pressure.

Yield 335 mg (54%) of yellow microcrystals, m.p. 174–175 °C (dec.). ^{1}H NMR (500MHz, $CDCl_3$), δ: 4.71 (s, 6H), 6.04 (d, 6H, J = 7.7), 6.25 (d, 6H, J = 7.7), 6.53 (t, 6H, J = 7.7), 7.16–7.28 (bs, 63H); ^{13}C NMR (125MHz, $CDCl_3$), δ: 50.0 (CH_2), 112.7 (CH), 123.7 (CH), 125.7 (CH), 128.2 (CH), 133.6 (C), 134.0 (CH), 136.8 (C), 138.4 (C), 147.4 (C); ^{31}P NMR (81MHz, $CDCl_3$), δ: −17.9; IR (film): ν (cm^{-1}) = 3070 (m), 2925 (m), 2857 (w), 1654 (m), 1579 (m), 1556 (s), 1455 (vs), 1417 (vs), 1382 (s), 1249 (s), 1216 (s), 1093 (s), 908 (s), 740 (s); MS(FAB + LR): m/z (%) = 1768 $(M)^+$ (1); MS(ESI): m/z (%) = 1769 $(M+H)^+$ (0.4).

In the CH-COSY-NMR (Fig. 8) there are three interesting crosspeaks of the phenoxazine ring and the benzyl CH_2-group visible.

16. 1,3,5-tris-Boc-piperazinomethyl-benzene (14)

Three gram of 1,3,5-tris-bromomethyl-benzene acid (8.4 mmol), 5.5 g of boc-piperazine (29.5 mmol, 3.5 equiv.) and 4 mL of triethylamine were stirred in 50 mL dioxane at 80 °C for 3 h. The solvent was evaporated and 30 mL of dichloromethane was added. The formed solid was removed and the solution was extracted with 2 × 20 mL of a thinned HCl (pH 5) solution. The organic phases were dried on $MgSO_4$ and the solvent was removed. Yield 5.61 g (99%) of colorless crystals.

^{1}H NMR (500 MHz, $CDCl_3$), δ: 1.43 (s, 27H), 2.30–2.40 (12H), 3.36–3.44 (12H), 3.46 (s, 6H), 7.13 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$), δ: 28.4 (CH_3), 43.7 (CH_2 from CH-COSY), 52.8 (CH_2), 62.8 (CH_2), 79.5 (C), 128.7 (CH), 137.8 (C), 154.8 (C); IR (KBr plate): ν (cm^{-1}) 756 (m), 872 (m), 1007 (m), 1122 (s), 1171 (s), 1246 (s), 1366 (s), 1417 (s), 1456 (s), 1693 (s), 2808 (s), 2931 (s), 2976 (s), 3005 (m); MS(FAB + LR): m/z (%) = 673.2 $(M+H)^+$ (100); exact mass (FAB + HR): 673.4673 $(M+H)^+$ (calculated for $C_{36}H_{61}N_6O_6$ 673.4653).

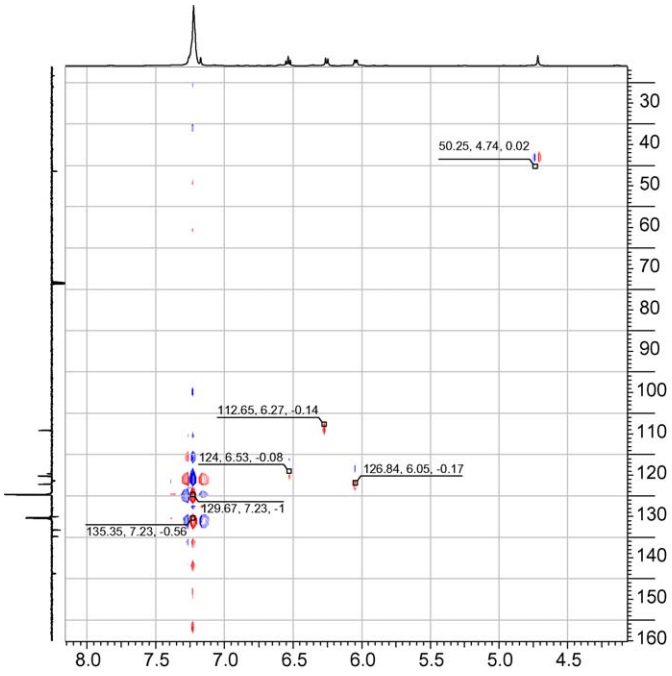


Fig. 8. CH-COSY-NMR of the micro-dendrimeric NIXANTPHOS trimer (**13**).

17. 1,3,5-tris-Piperazinomethyl-benzene (15)

5.61 g of 1,3,5-tris-boc-piperazinomethyl-benzene (**14**) (8.34 mmol) were stirred in 30 mL dioxane and 20 mL 3 molar HCl at room temperature for 1 day. The solvent was evaporated and a sodium hydroxide solution was added. The solution was extracted with 3 × 20 mL of chloroform. Combined organic phases were dried on $MgSO_4$ and the solvent was removed. Yielding 2.8 g of the 1,3,5-tris-piperazinomethyl-benzene as an oil (90%).

^{1}H NMR (400 MHz, MeOD), δ: 2.29–2.61 (12H), 2.76–2.92 (12H), 3.51 (s, 6H), 7.22 (s, 3H); ^{13}C NMR (100 MHz, MeOD), δ: 46.0 (CH_2), 54.5 (CH_2), 64.3 (CH_2), 131.1 (CH), 138.4 (C); IR (KBr plate): ν (cm^{-1}) 731 (vs), 796 (s), 1135 (vs), 1335 (s), 1362 (s), 1456 (vs), 1674 (vs), 2806 (vs), 2937 (vs), 3282 (w), 3452 (w); MS(FAB + LR): *m/z* (%) = 373.2 $(M+H)^+$ (5); exact mass (FAB + HR): 372.3021 $(M)^+$ (calculated for $C_{21}H_{36}N_6$ 372.3001).

18. Micro-dendrimeric NIXANTPHOS with a long spacer (17)

A solution of 551 mg of **1** (1 mmol) and 1.6 mL of hexamethylenediisocyanate (1.682 g, 10 mmol, 10 equiv.) dissolved in 5 mL of toluene was heated to reflux for 1 day. Next the solvent and hexamethylenediisocyanate was removed by bulb to bulb distillation. The crude product (**16**) was washed with dry heptane and analyzed by MS and NMR.

^{1}H NMR (500 MHz, $CDCl_3$), δ: 1.31–1.45 (4H), 1.52–1.65 (4H), 3.26–3.31 (4H), 5.35 (t, 3H, J = 5.5), 6.50 (d, 2H, J = 7.7), 6.98 (t, 2H, J = 7.7), 7.19–7.29 (20H), 7.49 (d, 2H, J = 7.7); ^{13}C NMR (125 MHz, $CDCl_3$), δ: 26.2 (CH_2), 26.3 (CH_2), 29.7 (CH_2), 31.1 (CH_2), 40.8 (CH_2), 42.8 (CH_2), 123.7 (CH), 124.6 (CH), 127.3 and 127.5 (C), 128.3 (CH), 128.4 (CH), 130.5 (CH), 133.9 (m, CH), 136.3 (C), 153.0 (C); 154.5 (C); 157.8 (C); ^{31}P NMR (81 MHz, $CDCl_3$), δ: −17.5; MS(FAB + LR): *m/z* (%) = 720.3 $(M+H)^+$ (65); exact mass (FAB + HR): 719.2476 $(M)^+$ (calculated for $C_{44}H_{39}N_3O_3P_2$ 719.2467).

A solution of 123 mg (0,33 mmol) 1,3,5-tris-piperazinomethyl-benzene (**15**) in 10 mL of dry dioxane was added and the mixture was stirred for 2 h at room temperature. The crude product was cleaned by dialysis in dichloromethane and yielded 275 mg (33%) of yellow microcrystals.

^{1}H NMR (500 MHz, $CDCl_3$), δ: 1.25–1.34 (12H), 1.43–1.54 (12H), 2.30–2.49 (12H), 3.13–3.26 (12H), 3.30–3.41 (12H), 3.45–3.55 (6H), 5.32–5.57 (3H), 6.33–6.62 (6H), 6.84–7.00 (6H), 7.00–7.41 (63H), 7.42–7.50 (6H); ^{13}C NMR (125 MHz, $CDCl_3$), δ: 26.0 (CH_2), 26.1 (CH_2), 29.5 (CH_2), 29.9 (CH_2), 40.3 (CH_2), 40.5 (CH_2), 43.5 (CH_2), 52.5 (CH_2), 62.5 (CH_2), 123.6 (CH), 124.4 (CH), 127.1 and 127.2 (C), 128.1 (CH), 128.4 (CH), 128.9 (C), 130.3 (CH), 133.7 (m, CH), 136.1 (C), 152.8 (C); 154.4 (C); 157.7 (C); ^{31}P NMR (81 MHz, $CDCl_3$), δ: −17.5; IR (KBr plate): ν (cm^{-1}) 704 (w), 740 (vw), 897 (s), 1265 (vw), 1416 (m), 1514 (s), 1645 (s), 1684 (s), 2305 (s), 2857 (s), 2937 (s), 2985 (s), 3053 (m); MS (ESI): *m/z* (%) = 2530.3 $(M)^+$ (100).

19. Polyurea NIXANTPHOS (18)

Eighty milligram of polyglycerol (M = 8000, 1 mmol of free OH groups) dissolved in 2 mL of pyridine and 420 mg of **16** (6.5 mmol), which remain traces of hexamethylenediisocyanate, dissolved in 3 mL of dry pyridine was stirred overnight at 80 °C. The solvent was evaporated with an oil pump and the received solid was washed with dichloromethane and dried with an oil pump to leave 171 mg of **18** as a yellowish solid.

20. General hydroformylation procedure

Fifty milligram of olefin (**A** or **B**), 1 mol% of $Rh(CO)_2acac$ and 5 mol% of diphosphine ligand were placed in an autoclave with a magnetic stirrer and dissolved in 4 mL of CH_2Cl_2. The autoclave was charged with 20 bar CO–H_2 (1:1) and heated at 80 °C. After 20 h the pressure was released and the crude reaction mixture was analyzed by NMR (and GC). Data of purified aldehydes:

Hydroformylation of **A**, linear product.

21. Nonanal

^{1}H NMR (500 MHz, $CDCl_3$), δ: 0.76–0.96 (m, 3H), 1.21–1.51 (m, 10H), 1.51–1.71 (m, 2H), 2.24–2.38 (m, 2H), 9.72 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$), δ: 15.4 (CH_3), 24.0 (CH_2), 26.1 (CH_2), 28.5 (CH_2), 30.5 (CH_2), 30.6 (CH_2), 33.2 (CH_2), 54.8 (CH_2), 201.2 (CH).

Hydroformylation of **A**, branched product.

22. 2-Methyl-octanal

^{1}H NMR (500 MHz, $CDCl_3$), δ: 0.76–0.96 (m, 3H), 1.06–1.20 (d, 3H, $J = 6.7$), 1.21–1.51 (m, 6H), 1.51–1.71 (m, 4H), 2.38–2.55 (m, 1H), 9.58 (d, 1H). ^{13}C NMR (125 MHz, $CDCl_3$), δ: 15.4 (CH_3), 18.8 (CH_3), 30.5 (CH_2), 30.6 (CH_2), 33.1 (CH_2), 35.0 (CH_2), 35.6 (CH_2), 40.9 (CH), 201.7 (CH).

Hydroformylation of **B**, linear product.

23. 4-Phthalimidylbutanal

^{1}H NMR (200 MHz, $CDCl_3$), δ: 1.98 (p, $J = 7.1$, 2H), 2.51 (dt, $J = 7.1$, $J = 1.2$, 2H), 3.70 (t, $J = 7.1$, 2H), 7.6–7.9 (m, 4H), 9.76 (t, $J = 1.2$, 1H); ^{13}C NMR (125 MHz, $CDCl_3$), δ: 21.1 ($CH_{2,}$), 37.0 ($CH_{2,}$), 41.0 (CH_2), 123.2 (CH), 131.9 (C), 133.9 (CH), 168.3 (C), 200.8 (CH).

Hydroformylation of **B**, branched product.

24. 2-Methyl-3-phthalimidylpropanal

^{1}H NMR (500 MHz, $CDCl_3$), δ: 1.16 (d, $J = 7.2$, 3H), 2.7–3.0 (m, 1H), 3.80 (dd, $J = 14.1$, $J = 6.5$, 1H), 4.02 (dd, $J = 14.1$, $J = 7.2$, 1H), 7.6–7.9 (m, 4H), 9.73 (d, $J = 1.6$, 1H).

References

[1] (a) A. Datta, K. Ebert, H. Plenio, Organometallics 22 (2003) 4685;
(b) H.-U. Blaser, A. Indolese, A. Schnyder, H. Steiner, M. Studer, J. Mol. Catal. A 173 (2001) 3.

[2] (a) I.F.J. Vankelecom, Chem. Rev. 102 (2002) 3779;
(b) C. Tzschucke, C. Markert, W. Bannwarth, S. Roller, A. Hebel, R. Haag, Angew. Chem. 114 (2002) 4136–4173;
C. Tzschucke, C. Markert, W. Bannwarth, S. Roller, A. Hebel, R. Haag, Angew. Chem. Int. Ed. 41 (2002) 3694–4001.

[3] (a) R. Haag, S. Roller, in: M.R. Buchmeiser (Ed.), Polymeric Materials in Organic Synthesis and Catalysis, Wiley-VCH, 2003;
(b) M. Benaglia, A. Puglisi, F. Cozzi, Chem. Rev. 103 (2003) 3401;
(c) R. Haag, S. Roller, Top. Curr. Chem. 242 (2004) 1.

[4] C. Claver, P.W.N.M. van Leeuwen, Rhodium Catalyzed Hydroformylation, Kluwer Academic Publishers, Dordrecht, The Netherlands, 2000.

[5] (a) L.A. van der Veen, M.D.K. Boele, F.R. Bregman, P.C.J. Kamer, P.W.N.M. van Leeuwen, K. Goubitz, J. Fraanje, H. Schenk, C. Bo, J. Am. Chem. Soc. 120 (1998) 11616;
(b) S. Gaemers, J.G. Sunley, PCT Int. Appl. 2004. WO 2004101488 A1. idem WO 2004101487 A1;
(c) J.F. Hartwig, J. Takaya, PCT Int. Appl. 2005. WO 2005077885 A1;
(d) D.F. Taber, H.Y. Li, U.S. Pat. Appl. 2005 US 2005288257 A1.

[6] (a) P.W.N.M. van Leeuwen, A.J. Sandee, J.N.H. Reek, P.C.J. Kamer, J. Mol. Calat. A 182–183 (2002) 107;
(b) A.J. Sandee, J.N.H. Reek, P.C.J. Kamer, P.W.N.M. van Leeuwen, J. Am. Chem. Soc. 123 (2001) 8468;
(c) A.J. Sandee, L.A. van der Veen, J.N.H. Reek, P.C.J. Kamer, M. Lutz, A.L. Spek, P.W.N.M. van Leeuwen, Angew. Chem. Int. Ed. 38 (1999) 3231.

[7] S. Deprèle, J.-L. Montchamp, Org. Lett. 6 (21) (2004) 3805.

[8] G. Parrinello, R. Deschenaux, J.K. Stille, J. Org. Chem. 51 (1986) 4189.

[9] (a) A.N. Ajjou, H. Alper, J. Am. Chem. Soc. 120 (1998) 1466;
(b) J. Chen, H. Alper, J. Am. Chem. Soc. 119 (1997) 893.

[10] W. Chen, L. Xu, J. Xiao, Chem. Commun. 10 (2000) 839.

[11] (a) E. Schwab, S. Mecking, J. Polym. Sci. Polym. Chem. 43 (2005) 4609;
(b) E. Schwab, S. Mecking, Organometallics 24 (2005) 3758.

[12] (a) R. Haag, A. Sunder, J.-F. Stumbé, J. Am. Chem. Soc. 122 (2000) 2954;
(b) A. Sunder, R. Hanselmann, H. Frey, R. Mülhaupt, Macromolecules 32 (1999) 4240–4246;
(c) A. Sunder, R. Mulhaupt, R. Haag, H. Frey, Macromolecules 33 (2000) 253.

[13] Modern Separation Techniques for the Efficient Workup in Organic Synthesis; C. Hajji, R. Haag, Topics in Organometallic Chemistry, L. Gade (Ed.), Hyperbranched Polymers as Platforms for Catalysts, Springer, in press.

[14] (a) Y. Antonio, P. Barrera, O. Contreras, F. Franco, E. Galeazzi, J. Garcia, R. Greenhouse, A. Guzman, E. Velarde, J.M. Muchowski, J. Org. Chem. 54 (1989) 2159;
(b) H.M. Petrassi, T. Klabunde, J. Sacchettini, J.W. Kelly, J. Am. Chem. Soc. 122 (2000) 2178;
(c) L.A. van der Veen, P.H. Keeven, G.C. Schoemaker, J.N.H. Reek, P.C.J. Kamer, P.W.N.M. van Leeuwen, M. Lutz, A.L. Spek, Organometallics 19 (2000) 872.

[15] (a) A.G.M. Barrett, M.A. Seefeld, Tetrahedron 49 (36) (1993) 7857;
(b) J.J. Eisch, J.H. Shah, J. Org. Chem. 56 (9) (1991) 2955.

[16] P. Köhling, A.M. Schmidt, P. Eilbracht, Org. Lett. 5 (18) (2003) 3213.

[17] P.W. Osinski, M. Schürmann, H. Preut, R. Haag, P. Eilbracht, Acta Cryst. E61 (2005) 3115–3116.

[18] P. Hofmann, unpublished results.

[19] F. Koc, M. Wyszogrodzka, P. Eilbracht, R. Haag, J. Org. Chem. 70 (2005) 2021.

[20] (a) Prepared in three steps from benzene-1,3,5-tricarboxylic acid in overall yield 83% S.M. Dimick, S.C. Powell, S.A. McMahon, D.N. Moothoo, J.H. Naismith, E.J. Toone, J. Am. Chem. Soc. 121 (1999) 10286–10296;
(b) Y. Yamagiwa, Y. Koreishi, S. Kiyozumi, M. Kobayashi, T. Kamikawa, M. Tsukino, H. Goi, M. Yamamoto, M. Munakata, Bull. Chem. Soc. Jpn. 69 (1996) 3317–3323;
(c) C.A. Ilioudis, D.A. Tocher, J.W. Steed, J. Am. Chem. Soc. 126 (2004) 12395–12402;
(d) One-pot transformation gave only 35% yield G. Bringmann, R.M. Pfeifer, C. Rummey, K. Hartner, M. Bruning, J. Org. Chem. 68 (2003) 6859–6863.

[21] (a) H.P. Dijkstra, G.P.M. van Klink, G. van Koten, Acc. Chem. Res. 35 (2002) 798;
(b) J.T. Scarpello, D. Nair, L.M. Freitas dos Santos, L.S. White, A.G. Livingston, J. Membr. Sci. 203 (2002) 71;
(c) J. Wöltinger, K. Drauz, A.S. Bommarius, Appl. Catal. A 221 (2001) 171.

[22] Turnover frequencies were calculated as (mol product) (mol catalyst)$-1\,h-1$ after 10% conversion. This value may increase with use of more effective stirring equipment.

[23] O.R. Huges, J.D. Unruh, J. Mol. Catal. 12 (1981) 71.

[24] O.R. Huges, D.A. Young, J. Am. Chem. Soc. 103 (1981) 6636.

[25] M. Kranenburg, Y.E.M. van der Burgt, P.C.J. Kamer, P.W.N.M. van Leeuwen, K. Goubitz, J. Fraanje, Organometallics 14 (1995) 3081.

[26] D. Boschi, A. Di Stilo, R. Fruttero, C. Medana, G. Sorba, A. Gasco, Arch. Pharm. (Weinheim) 327 (1994) 661–667.

[27] (a) Prepared in three steps from benzene-1,3,5-tricarboxylic acid in overall yield 83% S.M. Dimick, S.C. Powell, S.A. McMahon, D.N. Moothoo, J.H. Naismith, E.J. Toone, J. Am. Chem. Soc. 121 (1999) 10286–10296;
(b) Y. Yamagiwa, Y. Koreishi, S. Kiyozumi, M. Kobayashi, T. Kamikawa, M. Tsukino, H. Goi, M. Yamamoto, M. Munakata, Bull. Chem. Soc. Jpn. 69 (1996) 3317–3323;
(c) C.A. Ilioudis, D.A. Tocher, J.W. Steed, J. Am. Chem. Soc. 126 (2004) 12395–12402;
(d) One-pot transformation gave only 35% yield G. Bringmann, R.M. Pfeifer, C. Rummey, K. Hartner, M. Bruning, J. Org. Chem. 68 (2003) 6859–6863.