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LETTERS

Synthesis and Catalytic Application of Amino Acid Based Dendritic Macromolecules

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Abstract: The use of amino acid based dendrimers as molecular scaffolds for the attachment of catalytically active organometallic Ni "pincer" complexes, *via* a urea functionality, is described; the dendrimer catalysts have comparable activity to their mononuclear (NCN)NiX analogues.

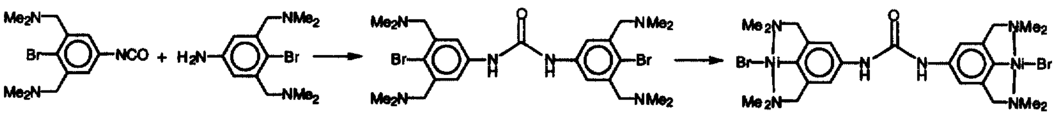
Keywords: Dendrimer; Catalysis; Macromolecules; Nickel and compounds

Dendrimer research is currently a blossoming area of macromolecular science. These tree–like molecules typically eminate from a central core and are usually produced in a step–wise manner by a repetitive reaction sequence. Hence, these materials have a well–defined size, molecular weight, internal connectivity and a specific number of end–groups.[1] We are interested in the use of dendrimers as inert frameworks for the attachment of catalytically active transition metal (TM) complexes[2,3] and in the investigation of molecular sensor technology (*i.e.*, nanoprobe devices).[4]

In this communication, we disclose our efforts directed towards the synthesis of novel dendrimers which contain catalytically active TM fragments on the dendritic exterior.[2] In addition, the active species has been designed to be linked to macromolecules or other substrates *via* a urea functionality. This fragment will allow the resulting TM complex to be used in a variety of applications which involve H–bonding.[5] These characteristics can facilitate the attachment, *via* H–bonding, of molecules (*e.g.*, a catalyst or free ligand)[6] to polar surfaces, supports or other functionalized materials.[1,5] An obvious further objective of this work is to evaluate the performance of a polar dendrimer in catalysis and to thus compare this activity with our previously investigated (comparatively non-polar) carbosilane analogues.[2,3]

The fragment used to coordinate the active metal atom to the dendrimer is the functionalized 1,3-bis[(dimethylamino)methyl]benzene or NCN. This unit contains a formal aryl carbanion in addition to two N donor atoms.[6] Diamagnetic nickel(II) complexes of the general formula (NCN)NiX (*e.g.*, X = Br; Table 1) are highly active catalysts for the addition of polyhalogenated alkanes to olefins (Kharasch addition).[2-3, 6-8] We have used the facile formation of a urea functionality as the means to link two pincer ligands. This is accomplished by

Scheme 1



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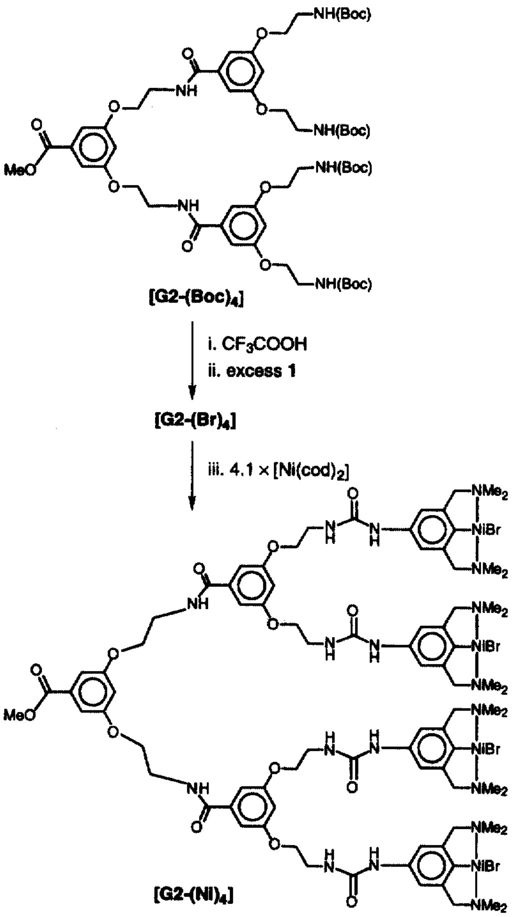
the condensation of isocyanato derivative **1**[2] with the substituted aniline **2**[9] to give the urea bis–pincer **3**, in excellent yield (95%; Scheme 1).[10] Insertion of two Ni atoms into the C–Br bonds of **3** is readily accomplished by treatment of this amine with two equiv of [Ni(cod)$_2$] to yield catalyst **4** (91%; Scheme 1).[11]

Scheme 2



Having succeeded with forming the model complex **4**, the incorporation of the ligand array into an amino acid based dendrimer[12] was carried out *via* similar formation of a urea linkage. The dendrimer precursors can be made in high yield[12] and are distinctly different from our previously studied examples of dendrimer catalysts (*i.e.*, carbosilanes[2,3,7,13]). Notably, these contrasts include higher polarity of the dendrimer unit and the presence of numerous amide bonds within the dendritic backbone. Treatment of an MeCN solution of the trifluoroacetate salt of dendrimer **[G2–Boc)$_4$]** (formed by the deprotection of the amines by CF_3COOH: Scheme 2) with a three fold excess of **1** affords the substituted dendrimer **[G2–(Br)$_4$]**.[14] This pincer-appended molecule was then treated with [Ni(cod)$_2$] to form the desired dendrimer catalyst [G2–(Ni)$_4$] in 93% yield (Scheme 2).[15]

The final objective is to evaluate this material as a Kharasch addition catalyst. We have previously demonstrated that small dendritic molecules, *i.e.*, < 25 Å in diameter (less than the approximate dimension estimated for **[G2–(Ni)$_4$]**)[15], can be effectively recovered using modern ultrafiltration membrane technology.[3,17] The results of the addition of CCl_4 to methyl methacrylate (MMA) catalyzed by complex **4** or dendrimer **[G2–(Ni)$_4$]** are summarized in the Table 1. The data obtained earlier with other complexes and dendrimer catalysts are also included. These results clearly show that complex **4** and **[G2–(Ni)$_4$]** are effective catalysts for the Kharasch addition and hence the presence of polar functional groups does not adversely influence catalytic performance. Also, the activity per metal site is of the same order of magnitude as the related mononuclear (*i.e.*, (NCN)NiBr[9,18]), carbosilane dendrimer[2,3,7] or polymer supported complexes (Table 1).[7,19]

Table 1[a]

Compound	TN[b]	Reference
4	187	This work
[G2-(Ni)$_4$]	114	This work
(NCN)NiBr	234	2, 18
carbosilane Ni$_4$	118	3
carbamate Ni$_4$	190	2
(NCN)NiBr] PS[c]	249	19

[a] All data were obtained (GC and/or NMR) from degassed solutions consisting of 12 mL CH_2Cl_2, 2.0 mL dodecane (internal standard), 3.0 mL MMA (28 mmol), 10.0 mL CCl_4 (104 mmol) and a concentration of 0.016 mmol of Ni (1.8 mol%). [b] TN refers to the turnover number per Ni site per h. [c] PS = Polysiloxane Supported.

This work has shown that novel amino acid based dendrimers[12] can be used as effective molecular frameworks for the attachment of TM complexes.[2,3,7] The synthesis of "pincer" ligands or organometallic catalysts[6] which contain a urea functionality, will allow these compounds to be evaluated as candidates for the self-assembly of new materials *via* H–bonding.[1,5] As is obvious from the depiction of **[G2–(Ni)$_4$]** in Scheme 2, this compound (or its metal-free precursor **[G2–(Br)$_4$]**) could be used as a dendron (*i.e.*, as a dendritic "wedge") in the convergent synthesis[1,20] of larger functionalized macromolecules. We are currently investigating these possibilities.

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10 Compound **3**. Synthesis: To an MeCN solution of **2** (0.57 g, 2.0 mmol), was added **1** (0.77 g; 2.0 mmol) and 1.05 mL (6.0 mmol) of $EtN(i\text{–}Pr)_2$ at RT. The clear solution was heated to reflux temperature under an N_2 atmosphere for 48 h. Volatiles were then removed *in vacuo* and the residual light brown material was dissolved in warm MeOH. Addition of Et_2O caused the product to precipitate, residual liquid was then decanted off and the remaining white powder was dried under vacuum (Yield 1.14 g; 95%). NMR ($CDCl_3$, 298 K): ^1H (200 MHz): δ 8.15 (s, N*H*), 7.48 (s, Ar*H*), 3.59 (s, CH_2), 3.22 (s, H_2O), 2.32 (s, CH_3); $^{13}C\{^1H\}$: δ 153.1 (*C*=O), 138.3, 138.0, 120.9, 120.1 (Ar*C*'s), 63.5 (NCH_2), 45.3 (CH_3). Anal. Calc. (Found) for $C_{25}H_{38}N_6Br_2O \cdot H_2O$: C 48.71 (48.42); H 6.54 (7.20); N 13.63 (13.86). The presence of water in crystalline samples of **3** was confirmed by NMR (*vide supra*).

11 Compound **4**. Synthesis: $[Ni(cod)_2]$ (0.50 mmol) was suspended in THF and cooled to -60 °C. Compound **3** (0.25 mmol) was then added and the mixture was allowed to warm to RT. After 2 h, the color had changed from light yellow to orange and all volatile components were then removed *in vacuo*. The crude

material was recrystallized from dry MeOH at -20 °C and then dried under high vacuum to give **4** as a yellow solid (yield: 0.163 g, 91%). NMR: ^{1}H (CD_3OD, 300 MHz): δ 7.18 (s, Ar*H*), 4.64 (s, br, N*H*), 3.47 (s, NCH_2), 2.54 (s, CH_3); $^{13}C\{^1H\}$ (CD_3OD, 75 MHz): δ 162.5 (*C*=O), 148.3, 138.8, 136.8, 122.4 (Ar*C*'s), 64.3 (NCH_2), 45.3 (CH_3). Anal. Calc. (Found) for $C_{27}H_{38}N_6Br_2Ni_2O{\cdot}2H_2O$: C 39.94 (39.16); H 5.34 (5.65)

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14 Compound **[G2–(Br)$_4$]**. Synthesis: A sample of **[G2–(Boc)$_4$]** (0.60 mmol, see Scheme 2[12]) was dissolved in a mixture of CF_3COOH (5 mL) and CH_2Cl_2 (5 mL) and stirred at RT for 20 min. Solvent was then evaporated to yield a clear oil that was subsequently dissolved in water and lyophilized. A sample of the resulting white powder (0.17 mmol, 0.20 g) was dissolved in MeCN and **1** was added (2.1 mmol) followed by EtN(*i*–Pr)$_2$ (4.8 mmol). The salts were then dissolved and the mixture was heated (reflux) and stirred for 24 h. Volatiles were then removed (*vacuo*) and the light brown solid washed with dry MeOH and CH_2Cl_2. The resulting off-white solid was then dried *in vacuo* (yield 0.26 g, 79%). NMR: ^{1}H (DMSO–d_6, 300 MHz): δ 8.80 (br, N*H*), 8.18 (br, N*H*C[O]), 7.91 (s, Ar*H*), 7.15 (s, Ar*H*), 7.08 (s, Ar*H*), 6.83 (s, Ar*H*), 6.72 (s, Ar*H*), 4.49 (m, OCH_2), 4.19 (m, OCH_2), 3.81 (s, OCH_3), 3.60 (m, NCH_2), 3.16 (m, N*H*), 2.83 (s, $ArCH_2$), 1.20 (s, NCH_3); $^{13}C\{^1H\}$ (DMSO–d_6, 75 MHz): δ 166.1, 160.0, 159.2 (*C*=O), 139.7, 136.8, 132.2, 132.1, 108.0, 106.9, 106.4, 105.2 (Ar*C*'s), 66.8, 65.0 (OCH_2), 60.2 ($ArCH_2$), 53.8 (OCH_3), 42.7, 42.1 (NCH_2), 18.3 (NCH_3) . Anal. Calc. (Found) for $C_{86}H_{118}N_{18}Br_4O_{14}{\cdot}4H_2O$: C 51.14 (51.15); H 6.29 (6.42); N 12.48 (12.32); O 14.26 (14.32).

15 Compound **[G2–(Ni)$_4$]**. Synthesis: To a THF suspension of [Ni(cod)$_2$] (0.062 mmol) at -60 °C, was added **[G2–(Br)$_4$]** (0.016 mmol) and the mixture slowly raised to RT. After 2 h of stirring, the solution changed color from yellow to orange and then all volatiles were removed (vacuo). The residue was dissolved in dry MeOH and recrystallized at -20 °C. The resulting yellow solid was dried under high vacuum (yield 0.032 g, 93%). NMR: ^{1}H (CD_3OD, 300 MHz): δ 7.08 (s, 1H, Ar*H*), 7.04 (s, 2H, Ar*H*), 6.74 (s, 2H, Ar*H*), 6.65 (s, 4H, Ar*H*), 6.57 (s, 8H, Ar*H*), 4.40 (br, N*H*), 4.06 (s, 16H, $ArCH_2$), 3.85 (m, 4H, OCH_2), 3.77 (m, 8H, OCH_2), 3.58 (m, 4H, NCH_2), 3.41 (s, 3H, OCH_3), 3.29 (m, 8H, NCH_2), 2.86 (s, 48H, NCH_3); $^{13}C\{^1H\}$ (CD_3OD, 75 MHz): δ 163.8, 159.8, 159.1 (*C*=O), 143.5, 140.7, 138.6, 135.3, 132.2, 120.3, 113.5, 112.8 (Ar*C*'s), 71.1 ($ArCH_2$), 66.0, 64.3 (OCH_2), 53.4 (OCH_3), 50.8, 50.2 (NCH_2), 43.8 (NCH_3). A reproducible combustion analysis could not be obtained, probably due to the high MW and oxygen sensitivity of this compound.

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