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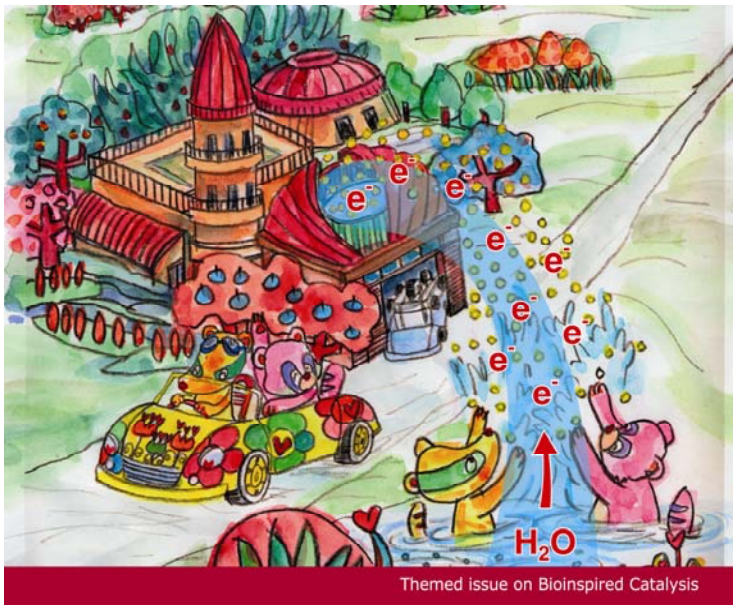

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Synthesis, characterization and catalytic function of a B_{12}-hyperbranched polymer†

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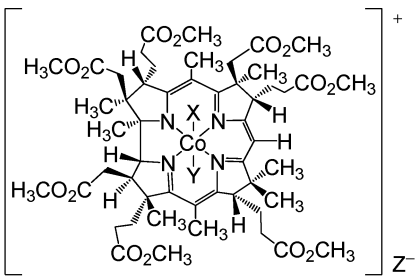
A new hybrid catalyst composed of a vitamin B_{12} derivative and a hyperbranched polymer (HBP) was synthesized and characterized by UV-vis and ESR spectroscopy as well as AFM. The B_{12}-HBP showed good properties as a homogenous catalyst. The covalently-immobilized B_{12} moieties were efficiently solvated and the cobalt centers were accessible for pyridine guests. The B_{12}-HBP showed high reactivity to 2-phenethylbromide and increased selectivity for reductive dimerization in the presence of TiO_2 with UV light irradiation.

Introduction

The catalytic function of vitamin B_{12} and coenzyme B_{12}, both *in vivo* and *in vitro*, has been the subject of much interest and numerous studies in these decades.[1-4] Vitamin B_{12} and derivatives can easily acquire oxidation states Co(III), Co(II) or Co(I), and each oxidation state has quite different ligand accepting abilities. The supernucleophilic Co(I) species has a high reactivity to organic halides to induce the oxidative addition of the alkylating agents to the metal center with dehalogenation. The resulting Co(III) alkyl complex induces the homolytic cobalt-carbon bond cleavage to form the Co(II) species and an alkyl radical. Due to their rich redox and coordination chemistry, vitamin B_{12} and derivatives are used as efficient homogenous catalysts in a number of chemical transformations[5,6] such as electron transfer reactions[7] and radical involved organic reactions.[8-10] We have been dealing with a hydrophobic vitamin B_{12}, heptamethyl cobyrinate perchlorate, [Cob(II)7C_1ester], which has ester groups in place of the peripheral amide moieties of vitamin B_{12} and succeeded in performing various electroorganic reactions (Chart 1).[11-14] In order to develop a good catalytic system, several methods for immobilization of vitamin B_{12} derivatives on a solid-phase support have been reported.[15-22] In some of these methods, organic polymers such as epoxy-polymer,[15-17] poly-L-lysin[18,19] and polypyrrole[20] are used as scaffolds which fix vitamin B_{12} derivatives on the surface of solid supports. However, to the best of our knowledge, methods for immobilization of a vitamin B_{12} derivative on a soluble polymer support have not been reported.

In recent years, the use of soluble polymers as catalyst supports has received increasing attention as an alternative to traditional solid phase synthesis.[23-26] Among soluble polymers, dendrimers are widely investigated as homogenous supports for catalytically active transition metal complexes.[27] The use of these monodisperse, nanosized supports offers some advantages such as good accessibility to catalytic centers and their ready removal from the products. Because the preparation of dendrimers requires tedious multistep syntheses and structural perfection is not always required, hyperbranched polymers (HBPs) are also used as homogenous supports.[28,29] The use of HBPs instead of dendrimers is justified by their similar properties and convenient preparation on large-scale in one-pot procedures. In a previous work, our interest in the immobilization of redox and coordination rich metal complexes on a soluble dendritic support has motivated us to prepare a new hybrid compound, B_{12}-HBP, composed of a vitamin B_{12} derivative and hyperbranched poly(ethyl methacrylate)s.[30] In this paper, we report a detailed synthesis and the characterization of the B_{12}-HBP hybrid catalyst and examine the catalytic activity for the dehalogenation of an organic halide.



Hydrophobic vitamin B_{12}

X = Y = CN, Z = none	$(CN)_2$Cob(III)7C_1ester (**1**)
X = CN, Y = H_2O, Z = ClO_4	[(CN)(H_2O)Cob(III)7C_1ester]ClO_4 (**2**)
X = Y = none, Z = ClO_4	[Cob(II)7C_1ester]ClO_4 (**3**)

Chart 1

Experimental

Materials

All solvents and chemicals used in the synthesis were of reagent grade and were used without further purification. [Cob(II)7C_1ester]ClO_4 (**3**) was synthesized by a previously reported method.[11] Bipyridyl ligands ($\mathbf{C_n py_2}$; n = 2, 4, 6, 8) were synthesized according to ref. 31. α-phenyl-*N*-*tert*-butylnitrone

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† Electronic supplementary information (ESI) available: Additional data of binding behavior of pyridine and bypyridyl guest. See DOI: 10.1039/b923924c

(PBN) was purchased from Aldrich and was used without further purification. TiO_2 powder (*P*-25; a mixture of rutile (20%) and anatase (80%) with a BET surface area of 50 $m^2\ g^{-1}$) was kindly supplied by Japan Aerosil.

General analyses and measurements

The UV-vis absorption spectra were measured on a Hitachi U-3300 spectrometer at room temperature. The IR spectra were recorded on a JASCO FT-IR 460 plus a KH spectrophotometer using KBr discs at room temperature. The ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance 500 spectrometer installed at the Center of Advanced Instrumental Analysis in Kyushu University, and the chemical shifts (in ppm) were referenced relative to the residual protic solvent peak. The MALDI-TOF-MS spectrum was obtained on a Bruker autoflex II using dithranol as a matrix. Elemental analyses were obtained from the Service Center of Elementary Analysis of Organic Compounds at Kyushu University. The ESR spectra were obtained on a Bruker EMX 8/2.7 spectrometer. The GC and GC-MS data were obtained using a Shimadzu GC-2010 and a GC-QP5050A equipped with a column J&W Scientific DB-1 (length 30 m; ID 0.25 mm; film 0.25 μm), respectively. Gel permeation chromatography was carried out on a Japan Analytical Industry Co., Ltd., LC-9201 apparatus combined with a UV-3702 attachment, using three connected columns, JAIGEL-4H, 3H and 2.5H, with $CHCl_3$ eluent. The cobalt contents of the B_{12}-HBPs were determined by a Shimadzu AA-6700 atomic absorption/flame emission spectrophotometer, and experimental errors are typically ± 0.05 wt%. The atomic force microscopy (AFM) image was acquired in air using a NanoScope IIIa. The sample was cast on mica and dried for 2 h under reduced pressure before AFM observation.

Synthesis of hyperbranched poly(ethyl methacrylate)s (4)

The photo-copolymerization in tetrahydrofuran solution of 2-(*N*,*N*-diethyldithiocarbamoyl)ethyl methacrylate (EMA-DC) and 2-hydroxyethylmethacrylate (HEMA) was carried out by irradiation with UV light at 30 ± 5 °C (100 W high-pressure mercury lamp). After polymerization, the hyperbranched polymer was precipitated in hexane. UV-vis (in CH_2Cl_2): [λ_{max}/nm] 250, 280. IR, ν/cm^{-1}: 1727 (ester C=O), 3437 (O–H). ^1H NMR ($CDCl_3$, 500 MHz): δ = 1.25, 1.29(-N(CH_2CH_3)$_2$), 3.57(-NCH_2CH_3), 3.76(-CH_2CH_2SC(S)N-), 3.81(-CH_2CH_2OH), 4.00(-CH_2CH_2SC(S)N-), 4.08(-CH_2CH_2OH), 4.17(-NCH_2CH_3). The signals of the methyl protons (-$CH_2C(CH_3)$-) were overlapped with those of the methylene protons of the main chains in the hyperbranched polymer (0.7-2.2 ppm). ^{13}C NMR ($CDCl_3$, 500 MHz): δ = 11.6, 12.6(-N(CH_2CH_3)$_2$), 17.6(-$CH_2C(CH_3)$-), 34.7(-CH_2SC(S)N-), 44.8(-$CH_2C(CH_3)$-), 46.9, 49.8(-N(CH_2CH_3)$_2$), 54.0(-$CH_2C(CH_3)$-), 60.2(-CH_2CH_2OH), 63.4(-C(O)OCH_2-), 66.8(-CH_2CH_2OH), 177.8, 177.8(-C(O)OCH_2-), 194.1(-SC(S)N-). Mw= 98400, Mw/Mn=7.69 determined by GPC-MALS (multiangle light scattering). Calcd. for $[C_{11}H_{19}NO_2S_2]_{251}$: C, 52.15; H, 7.47; N, 3.58. Found: C, 52.52; H, 7.55; N, 3.24. The content of hydroxy groups in **4** was determined to be 2.57 mmol g^{-1} by the following equation formula: 1/{(Mw of EMA-DC) + (Mw of HEMA)} because copolymerization proceeded with a 1 : 1 ratio of starting EMA-DC and HEMA which was confirmed by NMR and HPLC analysis.

Synthesis of $(CN)_2$Cob(III)6C_1ester (5)

Cyanocobalamin (2.00 g, 1.49 mmol) in 200 mL of methanol was mixed with 30 mL of cold conc. sulfuric acid and 100 mL of methanol. The solution was refluxed for 120 h in the dark under nitrogen atmosphere. The solution was concentrated, diluted with 100 mL of cold water, and neutralized with solid sodium carbonate (Na_2CO_3). After addition of 1.0 g of potassium cyanide, the reaction mixture was extracted with carbon tetrachloride (150 mL × 2) then dichloromethane (150 mL × 2). The carbon tetrachloride extract was the main product and was identified as $(CN)_2$Cob(III)7C_1ester **1** (1.29 g, 79%), consistent with the previous report.[11] Although hydrolysis of **1** by Na_2CO_3 afforded a mixture of partially hydrolyzed products, dicyanohexamethylcobyrinate, $(CN)_2$Cob(III)6C_1ester **5**, was selectively extracted with dichloromethane as a mixture of isomeric forms. The obtained dichloromethane extract was evaporated to dryness after drying over Na_2SO_4. The target product **5** was reprecipitated from chloroform upon the addition of n-hexane to afford a purple powder. The preparation of $(CN)_2$Cob(III)6C_1ester was previously reported, and the four propionic acid isomers were successfully isolated.[32] In this work, we used $(CN)_2$Cob(III)6C_1ester **5** as a mixture of isomeric forms for immobilization onto the hyperbranched polymer **4**. Yield: 168 mg (10%). MALDI-TOF-MS (dithranol matrix, *m*/*z*): $[M - CN]^+$, 1048.4, $[M - 2CN]^+$, 1022.3. UV-vis (in CH_2Cl_2): [λ_{max}/nm], 279, 316, 371, 423, 550, 589.

Syntheses of B_{12}-HBPs (dicyano form) (6a, 6b and 6c)

B_{12}-HBPs with different contents of B_{12}, **6a**, **6b** and **6c**, were synthesized. The typical procedure is described as follows. **6b**: To a solution of **4** (100 mg, 0.254 mmol of hydroxyl groups), **5** (273 mg, 0.254 mmol) and 4-dimethylaminopyridine (61 mg, 0.50 mmol) in 2.5 mL of dry CH_2Cl_2 was added *N*-(3-dimethylaminopropyl)-*N*′-ethylcarbodiimide hydrochloride (EDC) (195 mg, 1.02 mmol) under nitrogen atmosphere at 273 K. The solution was further stirred for 4 h at room temperature. The solution was then washed with H_2O (15 mL × 2), and the organic layer was extracted with CH_2Cl_2 (15 mL × 2). After drying over anhydrous Na_2SO_4, the CH_2Cl_2 extract was concentrated to dryness. The target product **6b** was separated from unreacted **5** by gel permeation chromatography (GPC) with $CHCl_3$ as eluant. The target product was reprecipitated from $CHCl_3$ upon addition of hexane to afford a purple powder. Yield: 190 mg. UV-vis (in CH_2Cl_2): [λ_{max}/nm], 280, 371, 422, 549, 589 (Fig. 1). IR, ν/cm^{-1}: 1729 (ester C=O), 3431 (O–H); ^1H NMR ($CDCl_3$, 500 MHz): δ = 1.3-(-N(CH_2CH_3)$_2$), 3.5-3.85(broad, -NCH_2CH_3, -CH_2CH_2SC(S)N-, -CH_2CH_2OH, C(O)OCH_3 of B_{12}), 4.00(-CH_2CH_2SC(S)N-), 4.1-4.5(broad, -CH_2CH_2OH, -NCH_2CH_3, -C(O)OCH_2CH_2OC(O)-), 5.55(C(10)-H of corrin). The content of B_{12} was determined based on the cobalt contents which were determined by atomic absorption spectrometry (0.47 mmol g^{-1}). Based on this value, the chemical formula was determined as follows. Calcd. for $[C_{11}H_{19}NO_2S_2]_{251}[C_6H_{10}O_3]_{156}[C_{59}H_{79}CoN_6O_{16}]_{95}$: C, 56.23; H, 7.02; N, 5.79. Found: C, 55.91; H, 6.81; N, 6.00.

6a. 0.1 equivalent mole of **5** to OH-groups of **4** was used. The content of B_{12}: 0.13 mmol g^{-1}. Calcd. for $[C_{11}H_{19}NO_2S_2]_{251}[C_6H_{10}O_3]_{236}[C_{59}H_{79}CoN_6O_{16}]_{15}$: C, 53.27; H, 7.34; N, 4.18. Found: C, 53.03; H, 7.32; N, 4.01.

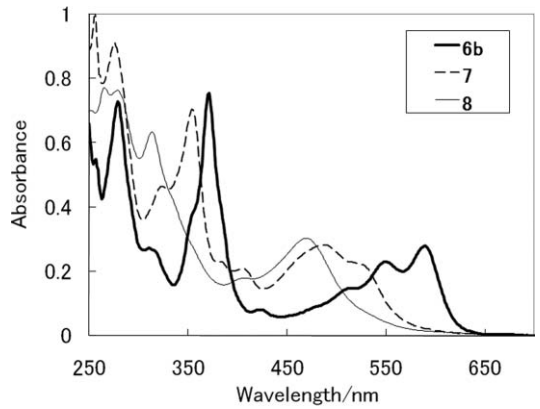


Fig. 1 UV-vis spectra of B_{12}-HBPs **6b**, **7** and **8** in CH_2Cl_2 ($[B_{12}] = 2.5 \times 10^{-5}$ M).

6c. 2 equivalent moles of **5** to OH-groups of **4** were used. The content of B_{12}: 0.46 mmol g^{-1}. Calcd. for $[C_{11}H_{19}NO_2S_2]_{251}[C_6H_{10}O_3]_{160}[C_{59}H_{79}CoN_6O_{16}]_{191}$: C, 56.14; H, 7.03; N, 5.74. Found: C, 56.62; H, 6.94; N, 6.17.

Synthesis of B_{12}-HBP (monocyano form) (7)

Compound **6b** (160 mg) was dissolved in 50 mL of CH_2Cl_2, and the resulting purple solution was treated with 40 mL of 30% aqueous perchloric acid. The orange CH_2Cl_2 layer was separated from the acidic aqueous layer and washed with distilled water. After drying over anhydrous Na_2SO_4, the organic layer was evaporated to dryness to obtain the target compound **7** in a nearly quantitative yield. UV-vis (in CH_2Cl_2): [λ_{max}/nm], 275, 354, 488 (Fig. 1).

Synthesis of B_{12}-HBP (Co(II) form) (8)

Compound **7** (170 mg) was dissolved in 10 mL of acetonitrile (CH_3CN), and 40 mL of distilled water and 50 mL of methanol were added to this solution. The solution was deoxygenated by bubbling nitrogen gas through it for 15 min at room temperature, and sodium tetrahydroborate (50 mg, 1.3 mmol) dissolved in 3 mL of methanol was added to the deoxygenated solution with vigorous stirring under nitrogen atmosphere. When the solution turned dark green, 3 mL of 60% aqueous perchloric acid was added carefully to decompose excess sodium tetrahydroborate. The resulting product was extracted with dichloromethane and washed with distilled water. After drying over anhydrous Na_2SO_4, the organic layer was evaporated to dryness. The residue was reprecipitated from $CHCl_3$ upon addition of n-hexane to afford a brown powder. Yield: 170 mg. UV-vis (in CH_2Cl_2): [λ_{max}/nm], 265, 314, 469. The content of B_{12} was determined based on the cobalt contents which were determined by atomic absorption spectrometry (0.47 mmol g^{-1}). Based on this value, the chemical formula was determined as follows. Calcd. for $[C_{11}H_{19}NO_2S_2]_{251}[C_6H_{10}O_3]_{156}[C_{57}H_{79}ClCoN_4O_{20}]_{95}$: C, 53.86; H, 6.86; N, 4.35. Found: C, 53.73; H, 7.12; N, 4.33.

Determination of binding constants

The affinity of **8** for pyridine and bipyridyl guests was measured by UV-vis titrations using similar reported procedures.[33] To a solution of **8** ($[B_{12}] = 8.2 \times 10^{-5}$ M) in CH_2Cl_2 was added a stock solution of pyridine (bipyridyl $\mathbf{C_npy_2}$) in CH_2Cl_2 at 298 K, and the change in the absorbance at 468 nm was monitored as exemplified for $\mathbf{C_4py_2}$. The binding constants (K) were calculated using a least-squares curve fitting for 1 : 1 binding between the B_{12} molecule and the pyridine unit. All binding constants were measured at least twice and errors were typically ±20%.

Catalytic debrominaton of 2-phenethylbromide

To a solution of 2-phenethylbromide (1.9×10^{-3} M) and B_{12}-HBP **8** ($[B_{12}] = 2.0 \times 10^{-5}$ M) in 25 mL of methanol was added 19 mg of TiO_2 powder, and nitrogen gas was bubbled for 20 min to degas oxygen. The solution was stirred for 8 h at room temperature under irradiation with 365 nm UV light (1.76 mW cm^{-2}). After the reaction, the TiO_2 was readily separated from the products by filtration. The products were analyzed by GC and GC-MS.

Results and discussion

Synthesis and characterization of B_{12}-HBP

Using the recent advanced technique for polymer syntheses,[34-36] the hyperbranched poly(ethyl methacrylate)s **4** was prepared from two monomers; the one (EMA-DC) offered branched polymeric backbones and the other (HEMA) offered an appropriate functional group for covalent immobilization of a vitamin B_{12} derivative as shown in Scheme 1.

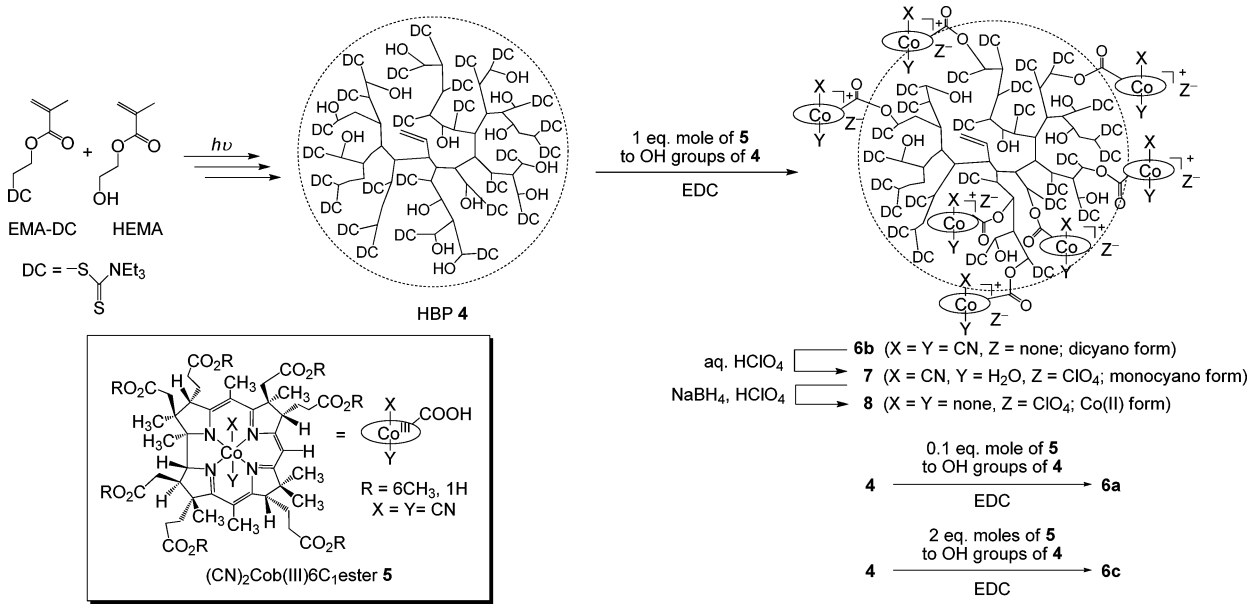
The vitamin B_{12} derivative having a carboxylic group (**5**) was covalently immobilized on **4**, which afforded the B_{12}-HBP hybrid compound as shown in Scheme 1. Polymer **4** was treated with **5** in the presence of EDC in CH_2Cl_2, and unreacted compound **5** was removed by GPC with $CHCl_3$. The target compound B_{12}-HBP was reprecipitated from $CHCl_3$ upon addition of hexane to afford a purple powder. The content of B_{12} in the hybrid compound was determined based on the cobalt amount quantified by atomic absorption spectrometry. Syntheses of B_{12}-HBP were carried out with 0.1, 1 and 2 equivalent moles of **5** to the hydroxyl groups of **4**, which afforded B_{12}-HBPs with different contents of B_{12}, *i.e.*, different degrees of esterification of the OH groups of **4** (α), **6a**, **6b** and **6c**, respectively, as shown in Table 1. Irrespective of the excess of **5**, only *ca.* 40% of the OH groups of **4** were esterified (**6c**), indicating the maximum of the modification ratio.

The UV-vis absorption spectra of B_{12}-HBPs in CH_2Cl_2 showed the typical shape for the monomeric vitamin B_{12} derivative **1** as exemplified for **6b** in Fig. 1. The absorbance intensities of B_{12}-HBPs were also in good agreement with those expected based on the contents of B_{12}, which were determined by atomic absorption

Table 1 Synthetic conditions and contents of B_{12} of B_{12}-HBPs

B_{12}-HBP	Molar ratio[a]	Form	Contents of B_{12}/ mmol g^{-1} [b]	α[c]
6a	0.1	Co(III), dicyano	0.13	5.9%
6b	1	Co(III), dicyano	0.47	38%
6c	2	Co(III), dicyano	0.46	36%
8[d]	—	Co(II)	0.47	39%

[a] Synthetic conditions; the molar ratio of **5** to OH groups of **4**. [b] The B_{12} contents in the B_{12}-HBP powder determined based on cobalt contents which were determined by atomic absorption spectrometry. [c] Degree of the esterification of OH groups of **4** with **5**. [d] Synthesized from **6b**.



Scheme 1 Syntheses of the B_{12}-HBP hybrid catalysts **6a-c**, **7** and **8**.

spectrometry. These results indicate that the modification procedure does not affect the intrinsic properties of the constituent B_{12} derivative and that the B_{12} moieties of the hybrid compound are sufficiently solvated with the solvent molecules in solution.

An axial ligand substitution and reduction of the cobalt centers in **6b** was performed using procedures similar to those reported for **1**.[11] Treatment of **6b** (dicyano form) with aqueous perchloric acid solution afforded the monocyano form of modified hyperbranched polymer (**7**), and a subsequent reduction with sodium tetrahydroborate afforded the Co(II) form of modified hyperbranched polymer (**8**).[37] The absorption spectra of **7** and **8** in CH_2Cl_2 showed the typical shape for the B_{12} derivatives **2** and **3**, respectively. The ESR spectra and the corresponding spin Hamiltonian parameters of **8** were also comparable to those of **3** as shown in Fig. 2a. These spectral data clearly indicate that the cobalt centers of B_{12}-HBP are accessible for reagents and solvents and that the desired ligand substitution and reduction of the cobalt centers were performed quantitatively.

The content of B_{12} in **8** was re-determined based on the cobalt amount quantified by atomic absorption spectrometry, which was almost equal to that in **6b** as shown in Table 1. The GPC diagram of **8** also revealed that immobilized B_{12} did not leach from the polymer support and that covalent bonds were maintained during these procedures. The AFM observation of **8** revealed spherical nanoparticles in the range from 3 to 5 nm as shown in Fig. 3. This indicates that the modified hyperbranched polymer **8** maintained the morphology derived from **4**. Accordingly, the B_{12}-HBP is a promising catalyst with respect to good accessibilities for substrates and enduring immobilization of the B_{12} catalyst on the stable support.

Binding behavior of pyridine and bypyridyl guests

The affinity of **8** for pyridine was measured by recording the UV-vis absorption spectrum of **8** in CH_2Cl_2 containing the ligand over a range of concentrations. The spectral change upon addition

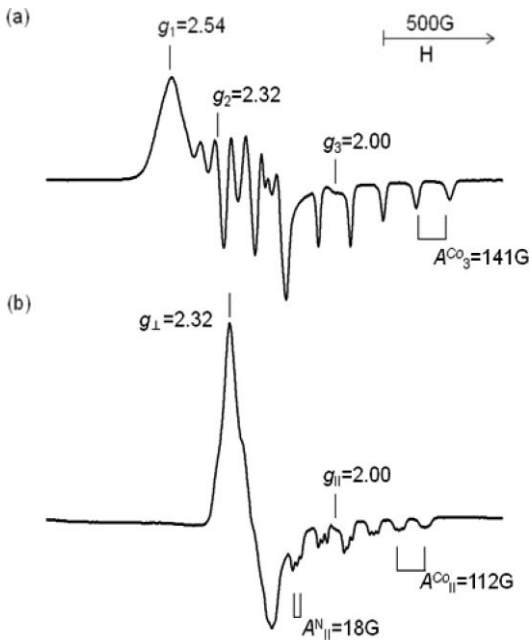


Fig. 2 ESR spectra of B_{12}-HBP **8** ($[B_{12}] = 2.0 \times 10^{-3}$ M) in the (a) absence and (b) presence of C_4py_2 (1.0×10^{-3} M) in CH_2Cl_2 at 77 K.

of pyridine is shown in Fig. S1.† A red shift was observed due to the binding of pyridine to the cobalt centers of **8**. A similar spectral change had been obtained for the binding of pyridine to the monomeric B_{12} derivative **3**, resulting in the formation of the 1 : 1 complex.[9] The pyridine binding data of **8** were found to fit well to a calculated curve in which one B_{12} unit bound one pyridine molecule with a single binding constant as shown in Table 2. The obtained binding constant of **8** for pyridine is comparable to or slightly smaller than that of **3**. This indicates that, in spite of some steric hindrance of the polymer support, the cobalt centers in the local environment of **8** are almost as accessible as those of **3** in

Table 2 Binding constants of B_{12}-HBP and monomeric B_{12} to pyridine in CH_2Cl_2 at 298 K[a]

Compound	$K/10^3$ M^{-1}
B_{12}-HBP **8**	4.7 ± 0.6[b]
[Cob(II)7C_1ester]ClO_4 **3**	5.8 ± 1.0

[a] Binding constants determined by using a binding model for the formation of the 1:1 complex between the B_{12} molecule and the pyridine. [b] Referring to the moles of binding sites (B_{12} units) of **8** rather than moles of B_{12}-HBP nanoparticles.

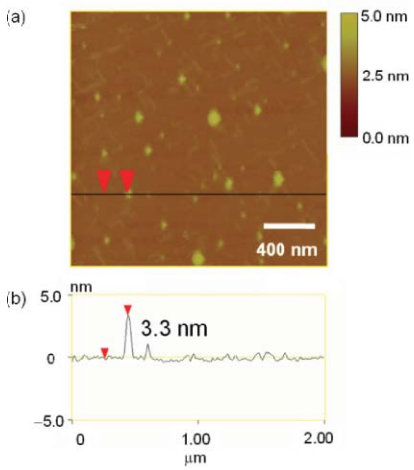


Fig. 3 AFM (a) image and (b) height profile of B_{12}-HBP **8**; the AFM tip was scanned along the black line.

the solution. Accordingly, substrate molecules can also access the cobalt centers of this homogenous catalyst.

The affinity of **8** for bipyridyl ligands (**$C_n$py$_2$**; $n = 2, 4, 6, 8$) was also measured in order to further investigate the local environment of **8**. These ligands were chosen to cover a range of interpyridyl distances. In each case, a red shift was observed due to coordination of a bipyridyl guest to cobalt centers in **8** as exemplified by the binding isotherm for **C_4py$_2$** in Fig. 4. A triplet nitrogen superfine coupling was also observed in the ESR spectrum of **8** in the presence of 0.5 equivalent moles of **C_4py$_2$** to B_{12} units in a frozen CH_2Cl_2 solution as shown in Fig. 2b, indicating the change from the 4-coordinated B_{12} complex to the 5-coordinated B_{12} complex in **8**. Each of the bipyridyl ligand binding data was found to fit well to a calculated curve in which one B_{12} unit of **8** bound one pyridine unit of **$C_n$py$_2$** with a single binding constant as exemplified in the inset of Fig. 4. The obtained binding constants of **8** for **$C_n$py$_2$** are shown in Fig. 5. All the binding constants of **8** for bipyridyl guests are larger than that for pyridine by a range of 6–10 times. This implies that both ends of the bipyridyl guests participate in the coordination to the cobalt centers and that all these bipyridyl guests can intercalate between pairs of B_{12} units in close proximity on the hyperbranched polymer support. The cobalt centers can readily get into positions of related interpyridyl distance with a local morphology change in **8** because the B_{12} units are covalently immobilized on the relatively flexible polymer backbone. Interestingly, the B_{12}-HBP **8** showed selectivity for bipyridyl guests. This implies that the B_{12} units are packed with a high density inside the hyperbranched polymer scaffold and that **C_4py$_2$** is the most suitable ligand to intercalate B_{12} units. A similar selective intercalation of Zn porphyrin dendrimers for bidentate ligands has been reported in a recent study on metallodendrimers aiming at a photochemical application.[33] In the present system, it should be noted that the effective organization of B_{12} has achieved a high local concentration of a catalytically active metal complex using a randomly branched polymeric scaffold.

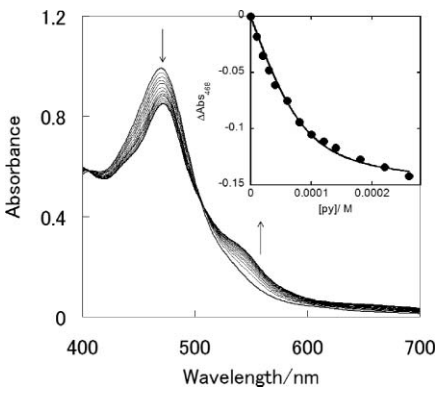


Fig. 4 Change in the absorbance of B_{12}-HBP **8** ($[B_{12}] = 8.2 \times 10^{-5}$ M) in CH_2Cl_2 upon addition of C_4py_2. Inset: binding isotherm of the data at 468 nm and fitted line as a binding constant equation. [py] is the total molarity of the binding sites of C_4py_2, which was calculated as twice the concentration of C_4py_2.

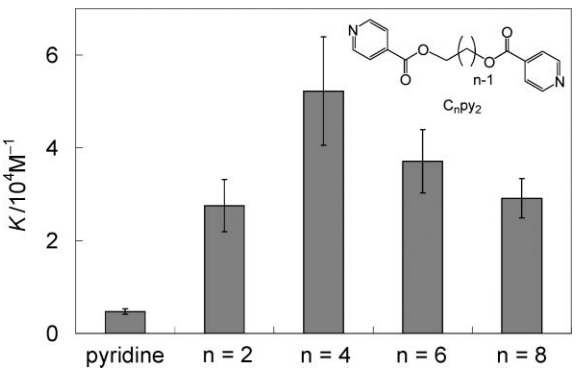


Fig. 5 Binding constants of B_{12}-HBP **8** with pyridine and bipyridyl guests ($C_n$py$_2$; $n = 2, 4, 6, 8$); referring to the moles of binding sites (B_{12} units) of **8** rather than moles of B_{12}-HBP nanoparticles.

Catalysis of B_{12}-hyperbranched polymer

The Co(I) species of vitamin B_{12} derivative is a strong nucleophile and reacts with various organic halides to give alkylated complexes with dehalogenation. In this section, we describe a new multi-component system constructed with B_{12}-HBP and titanium oxide (TiO_2) photosensitizer, which catalyzes an efficient reductive dehalogenation of organic halide as shown in Fig. 6. Recently, it has been demonstrated that the cobalt center of hydrophobic vitamin B_{12} can acquire the Co(I) oxidation state in the presence of TiO_2 with UV light irradiation.[38,39] The electron transfer from TiO_2 ($E_{red} = -0.5$ V *vs.* NHE, anatase-type) to the hydrophobic vitamin B_{12} **2** (Co(II)/Co(I) $= -0.3 \sim -0.4$ V *vs.* NHE) is thermodynamically favored. Thus, an efficient photoinduced electron transfer from TiO_2 to the cobalt center of B_{12}-HBP and a subsequent reaction

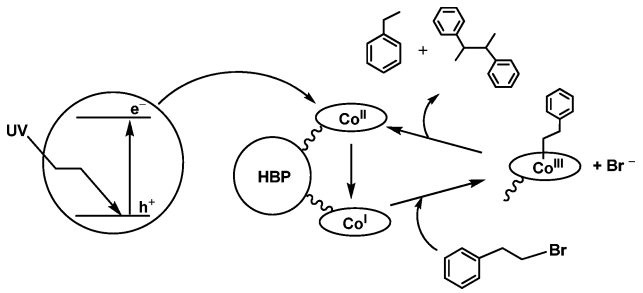


Fig. 6 Schematic representation of the debromination system catalyzed by B_{12}-HBP.

of the Co(I) species with organic halides are expected as shown in Fig. 6.

First, we examined the formation of the Co(I) species of B_{12}-HBP **8** by UV-vis spectroscopy. The absorption spectrum of **8** (Co(II) form) in methanol containing TiO_2 is shown in Fig. 7 (solid line). After the subsequent UV light irradiation, the characteristic strong absorption at 390 nm indicative of the Co(I) species was observed as shown in Fig. 7 (broken line). This result suggests that an effective reduction of the cobalt center in **8** proceeds by the expected photoinduced electron transfer from TiO_2.

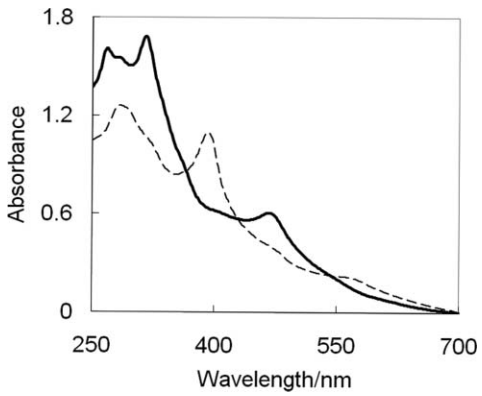


Fig. 7 UV-vis spectra of B_{12}-HBP **8** (6.0×10^{-5} M) in methanol (solid line) containing TiO_2 (*P*-25, 0.10 mg) and after irradiation with UV light (20 min, broken line).

We then examined the catalytic activity of B_{12}-HBP to an organic halide. A series of debrominations of phenethylbromide was carried out as summarized in Table 3. The B_{12}-HBP **8** showed high reactivity to the organic halide and a quantitative debromination proceeded (entry 1 in Table 3). It is obvious that the B_{12} moieties of **8** catalyzed the debromination because the debromination did not proceed in the presence of only the hyperbranched polymer (entry 5 in Table 3). The turnover number based on the B_{12} content in **8** is *ca.* 100, and the reactivity of **8** is comparable with or slightly larger than that of the hydrophobic vitamin B_{12} (entry 3 in Table 3). This result implies that catalytic processes at the cobalt center of **8** are not hindered by the polymeric support, consistent with the accessibility of solvent molecules, reagents or pyridyl ligands into the cobalt center of B_{12}-HBP as described above. Interestingly, in the B_{12}-HBP system, 2,3-diphenylbutane (1 : 1 mixture of racemic and *meso*) was obtained in 31% yield as well as ethylbenzene in 56% yield (entry 1 in Table 3). In contrast, 2,3-diphenylbutane was obtained only in 2% yield in the monomeric B_{12} system (entry 3 in Table 3). The increased selectivity of **8** for the homocoupling reaction results from covalent immobilization of B_{12} onto the HBP because a mixture of the monomeric vitamin B_{12} derivative **3** and the HBP **4** did not afford such an increased yield of 2,3-diphenylbutane (entry 4 in Table 3).

Table 3 Catalytic debromination of 2-phenethylbromide catalyzed by B_{12}-HBP[a]

Entry	Compound	Conversion [b](%)	Product yield [b](%)	
			Ethylbenzene	2,3-Diphenylbutane
1	B_{12}-HBP **8**	100	56	31
2	B_{12}-HBP **8**[c]	100	27	1
3	B_{12} **3** only	92	84	2
4	B_{12} **3**, HBP **4**[d]	91	70	4
5	HBP **4**[d,e]	0	0	0
6	B_{12}-HBP **6a**[f]	97	82	10

[a] Conditions: $[B_{12}] = 2.0 \times 10^{-5}$ M, [2-phenethylbromide] $= 1.9 \times 10^{-3}$ M, solvent: 25 mL methanol under N_2, reaction time 8 h. [b] Conversions were estimated by the recovery of 2-phenethylbromide. Yields were based on the initial concentration of the 2-phenethylbromide. [c] In the presence of PBN (0.1 M). [d] Unmodified HBP (4.0 mg L^{-1}) was used. [e] Reaction time 24 h. [f] Reaction time 14 h.

Mechanistic aspects of the catalytic processes

The debromination of 2-phenethylbromide was also carried out upon addition of a spin-trapping reagent, α-phenyl-*N*-(*t*-butyl)nitrone (PBN). Upon addition of PBN, the formation of the products was somewhat inhibited (entry 2 in Table 3), and the corresponding PBN spin adduct was observed by ESR spectroscopy; $g = 2.01$, $A_N = 15.0$ G, $A_H = 4.3$ G (10^4 G = 1 Tesla). This result indicates that a radical species is generated as an intermediate under the present conditions.

In order to determine the source of the hydrogen in the produced ethylbenzene, the debrominations of 2-phenethylbromide were carried out in CD_3OD and CH_3OD as shown in Table 4. The incorporation of deuterium ion did not occur in the reaction in CH_3OD. In contrast, 80% of the deuterium was incorporated into ethylbenzene in the reaction in CD_3OD. Therefore, ethylbenzene was mainly produced directly from a radical intermediate.

We also examined the influence of B_{12}-modification degrees (α values in Table 1) on the catalysis of B_{12}-HBP. The debromination of 2-phenethylbromide using B_{12}-HBP **6a** gave a poor yield of 2,3-diphenylbutane (entry 6 in Table 3). Only 6% of the OH groups of HBP are esterified with B_{12} in **6a**, and the local concentration of B_{12} in **6a** is expected to be lower than that in **8**. Thus, this result implies that the local concentration of B_{12} in B_{12}-HBP may reflect the selectivity for the dimerization. The formation of 2,3-diphenylbutane can be ascribed to the coupling reaction of two

Table 4 Deuterium atom incorporation ratio from solvent[a]

Entry	Compound	Solvent	D-atom incorporation ratio of ethylbenzene-d_1 (%)[b]
1	B_{12}-HBP **8**	CD_3OD	80
2	B_{12}-HBP **8**	CH_3OD	< 1

[a] Conditions: $[B_{12}]=2.0 \times 10^{-5}$ M, [2-phenethylbromide] $= 1.9 \times 10^{-3}$ M, TiO_2 19 mg, solvent: 25 mL methanol under N_2, reaction time 30 h. [b] Determined by GC-MS.

benzyl radicals because of the lack of diastereoselectivity observed in the product.

A proposed mechanism of the B_{12}-HBP mediated reaction is shown in Fig. 6 and Fig. 8. The reaction is initiated by the photochemical reduction of Co(II) to the Co(I) state. The resulting supernucleophile Co(I) species reacts with 2-phenethylbromide to form the cobalt-phenethyl complex. The Co–C bond of the complex then homolytically cleaves to form the corresponding radical upon UV light irradiation.[40] The resulting radical **9** and rearrangement radical **10** can abstract hydrogen from the solvent to form ethylbenzene. The benzyl radical **10** can also couple to form 2,3-diphenylbutane. It is expected that this radical coupling is close to a diffusion-controlled reaction ($k_d \sim 10^9$ M^{-1} s^{-1} at room temperature) and that the yield of 2,3-diphenylbutane is largely dependent on the forming benzyl radical concentration (*i.e.*, a rate of $10^9 \times [\mathbf{10}]^2$ for the formation of 2,3-diphenylbutane from the benzyl radical).[9] In the monomeric B_{12} system, hydrogen abstraction can proceed prior to the radical coupling to give a poor yield of 2,3-diphenylbutane. In contrast, in the B_{12}-HBP system, the benzyl radical coupling can be enhanced because of the high local concentration of B_{12} units in **8** as described above. Effective pre-organization of catalytic amounts of B_{12} on the nano-sized scaffold could lead to production of the benzyl radical in high concentration, promoting the intermolecular C–C bond formation.

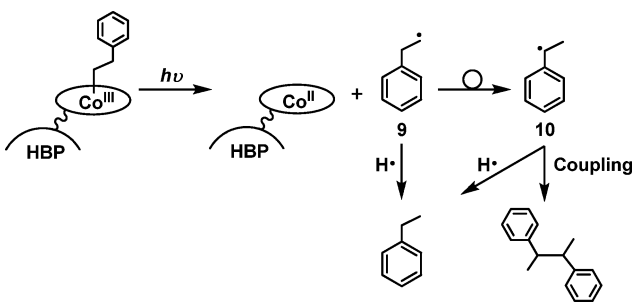


Fig. 8 Proposed mechanism for generation of dehalogenatd products.

The present system is likely to show a positive correlation between the cobalt density in the nano-sized catalyst and the selectivity for the intermolecular coupling. Such effect dependent on the density of metal centers in the nano-material is somewhat similar to "dendritic effects" reported in the catalysis of metallodendrimers. Indeed, the coupling reaction of organic radicals has been reported to be involved in the atom-transfer radical addition catalyzed by nickelated carbosilane dendrimers in the pioneering work on dendritic effects.[41,42] It has been demonstrated that a proximity effect between the peripheral Ni active sites can lead to the irreversible formation of inactive sites and the coupling of two transient radicals. In the present work, we have demonstrated a new synergetic nano-material that achieves the C–C bond formation in the combination of a redox and coordination rich metal complex and a randomly branched polymeric scaffold without a decrease in catalytic activity on a substrate.

Conclusions

In the present paper, a new hybrid catalyst composed of a vitamin B_{12} derivative and a hyperbranched polymer (HBP) was synthesized and characterized by UV-vis and ESR spectroscopy as well as AFM. The B_{12}-HBP showed good properties for use as a homogenous catalyst; the covalently-immobilized B_{12} moieties were efficiently solvated and the cobalt centers were accessible for pyridine guests. The B_{12}-HBP showed a high reactivity to 2-phenethylbromide and increased selectivity for reductive dimerization in the presence of TiO_2 with UV light irradiation. These results provide new insight into the effective organization of small amounts of catalytically active metal complexes to explore new catalytic reactions. The present system would be applicable to radical reactions such as intramolecular coupling.

Acknowledgements

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