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Published on Web 08/29/2002

Steric Control of Organic Transformation by a Dendrimer Cage: Organocobalt Dendrimer Porphyrins as Novel Coenzyme B_{12} Mimics

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Received May 13, 2002

Abstract: Cobalt(II) complexes of poly(aryl ester) dendrimer porphyrins (*m*-[G*n*]TPP)Co^{II} and (*p*-[G*n*]TPP)-Co^{II} ($n = 0-3$) underwent AIBN-initiated alkylation (AIBN = 2,2′-azobis(isobutyronitrile)) at the metal center with propargyl alcohol in $CDCl_3$ at 60 °C, where the dendritic substituents did not affect the overall conversion rate but selectivity of the alkylation. With the largest (*m*-[G3]TPP)Co^{II}, a single organocobalt(III) species ($Co^{III}-C(=CH_2)CH_2OH$, **4**) was selectively formed in 91% yield, due to a steric protection of **4** by the large dendrimer cage from the access of another molecule of cobalt porphyrin species. In contrast, with other cobalt(II) porphyrins, isomerized compounds such as $Co^{III}-C(CH_3)=CHOH$ (**5**) and $Co^{III}-CH(CH_3)CHO$ (**6**) were formed in addition to **4**. A stereochemical investigation with (*m*-[G3]TPP)Co^{II} using AIBN-d_{12}, in place of nondeuterated AIBN, demonstrated that the alkylation (cobalt(III) hydride addition to propargyl alcohol) is selective to a trans adduct. Results also indicated that this addition step does not involve external activation of propargyl alcohol.

Introduction

Adenosylcobalamin or coenzyme B_{12} has attracted great attention, because of its interesting activity for selective transformation of organic substrates via homolytic dissociation of carbon−metal bonds.[1,2] Structural aspects of the natural holoenzymes[3] suggest a possible contribution of the protein matrix around the active site to the high selectivity of the transformation.[4] In this respect, several model studies related to coenzyme B_{12}, considering steric or site-isolation effects, have been investigated with group IX transition metal complexes of oximes, schiff bases, and porphyrins, and those embedded in physically organized media such as micelles and bilayer membranes.[5−7] However, compared with the natural systems, selectivities of such artificial coenzymes are not high, and further molecular design may be taken into consideration.

Here we report a novel artificial model of coenzyme B_{12}, having a cobalt(II) porphyrin functionality encapsulated within a radical-tolerant, large poly(aryl ester) dendrimer cage (*m*-[G3]-TPP)Co^{II} (Figure 1D), and we highlight its high potential for the steric control of AIBN-initiated transformation (AIBN = 2,2′-azobis(isobutyronitrile)) of alkynes.[7] Dendrimers are well-defined hyperbranched macromolecules with predictable three-dimensional shapes[8−10] and expected to possess an interesting

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(1) (a) *B_{12}*; Dolphin, D., Ed.; Wiley: New York, 1982; Vols. 1 and 2. (b) *Enzyme Mechanisms*; Page, M. I., Williams, A., Eds.; The Royal Society of Chemistry: London, 1987. (c) Frey, P. *Chem. Rev.* **1990**, *90*, 1343−1357. (d) Buckel, W.; Golding, B. T. *Chem. Soc. Rev.* **1996**, *25*, 329−338. (e) Stubbe, J.; van der Donk, W. A. *Chem. Rev.* **1998**, *98*, 705−762. (f) *Chemistry and Biochemistry of B_{12}*; Banerjee, R., Ed.; Wiley: New York, 1999.

(2) (a) Toraya, T.; Krodel, E.; Mildvan, A. S.; Abeles, R. H. *Biochemistry* **1979**, *18*, 417−426. (b) Halpern, J. *Science* **1985**, *227*, 869−875. (c) Halpern, J. *Bull. Soc. Chim. Fr.* **1988**, 187−191. (d) Zhao, Y.; Such, P.; Rétey, J. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 215−216. (e) Leutbecher, U.; Albracht, S. P. J.; Buckel, W. *FEBS Lett.* **1992**, *307*, 144−146. (f) Michel, C.; Albracht, S. P. J.; Buckel, W. *Eur. J. Biochem.* **1992**, *205*, 767−773. (g) Zhao, Y.; Abend, A.; Kunz, M.; Such, P.; Rétey, J. *Eur. J. Biochem.* **1994**, *225*, 891−896.

(3) (a) Mancia, F.; Smith, G. A.; Evans, P. R. *Biochemistry* **1999**, *38*, 7999−8005. (b) Masuda, J.; Shibata, N.; Morimoto, Y.; Toraya, T.; Yasuoka, N. *Structure* **2000**, *8*, 775−788.

(4) (a) Pratt, J. M. *Chem. Soc. Rev.* **1985**, *14*, 161−170. (b) Finke, R. G.; Schiraldi, D. A.; Mayer, B. J. *Coord. Chem. Rev.* **1984**, *54*, 1−22.

(5) Murakami, Y.; Kikuchi, J.; Hisaeda, Y.; Hayashida, O. *Chem. Rev.* **1996**, *96*, 721−758.

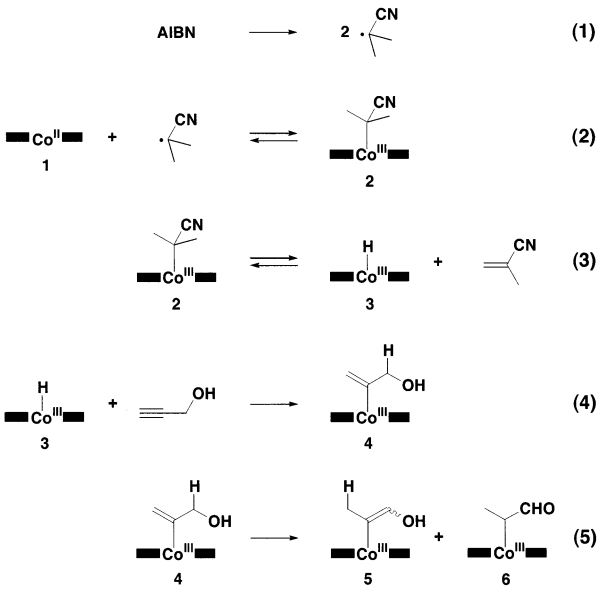
(6) (a) Rétey, J. *Helv. Chim. Acta* **1971**, *54*, 2747−2752. (b) Fendler, J. H.; Nome, F.; Woert, H. C. V. *J. Am. Chem. Soc.* **1974**, *96*, 6745−6753. (c) Nome, F.; Fendler, J. H. *J. Am. Chem. Soc.* **1977**, *99*, 1557−1564. (d) Flohr, H.; Panhorst, W.; Rétey, J. *Helv. Chim. Acta* **1978**, *61*, 1565−1587. (e) Murakami, Y.; Hisaeda, Y.; Ohno, T. *J. Coord. Chem.* **1990**, *21*, 13−22. (f) Murakami, Y.; Hisaeda, Y.; Ohno, Y. *Bioorg. Chem.* **1990**, *18*, 49−62. (g) Murakami, Y.; Hisaeda, Y.; Ohno, Y. *J. Chem. Soc., Perkin Trans. 2* **1991**, 405−416. (h) Wayland, B. B.; Poszmik, G.; Fryd, M. *Organometallics* **1992**, *11*, 3534−3542. (i) Breslow, R.; Duggan, P. J.; Light, J. P. *J. Am. Chem. Soc.* **1992**, *114*, 3982−3982. (j) Murakami, Y.; Hisaeda, Y.; Kohno, H.; Ohno, Y.; Nishioka, T. *J. Chem. Soc., Perkin Trans. 2* **1995**, 1175−1183. (k) Darbre, T.; Keese, R.; Siljegovic, V.; Wolleb-Gygi, A. *Helv. Chim. Acta* **1996**, *79*, 2100−2113. (l) Hisaeda, Y.; Ogawa, A.; Ohno, T.; Murakami, Y. *Inorg. Chim. Acta* **1998**, *273*, 299−309.

(7) (a) Gridnev, A. A.; Ittel, S. D.; Fryd, M.; Wayland, B. B. *J. Chem. Soc., Chem. Commun.* **1993**, 1010−1011. (b) Gridnev, A. A.; Ittel, S. D.; Fryd, M.; Wayland, B. B. *Organometallics* **1993**, *12*, 4871−4880. (c) Gridnev, A. A.; Ittel, S. D.; Wayland, B. B.; Fryd, M. *Organometallics* **1996**, *15*, 5116−5126.

(8) For selected reviews, see: (a) Zeng, F.; Zimmerman, S. C. *Chem. Rev.* **1997**, *97*, 1681−1712. (b) Bosman, A. W.; Janssen, H. M.; Meijer, E. W. *Chem. Rev.* **1999**, *99*, 1665−1688. (c) Vögtle, F.; Gerstermann, S.; Hesse, R.; Schwierz, H.; Windisch, B. *Prog. Polym. Sci.* **2000**, *25*, 987−1041. (d) Hecht, S.; Fréchet, J. M. J. *Angew. Chem., Int. Ed.* **2001**, *40*, 74−91. (e) Astruc, D.; Chardac, F. *Chem. Rev.* **2001**, *101*, 2991−3023.

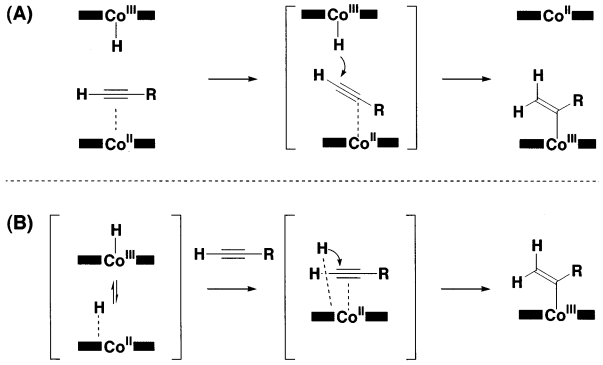
10.1021/ja020687i CCC: $22.00

potential as artificial substitutes for globular proteins.[9] Core−shell architectures of spherical dendrimers have also motivated exploration of the possibility of spatial reactivity control of active species encapsulated within such unique three-dimensional cages.[9,10] The AIBN-initiated alkylation of cobalt(II) porphyrin **1** with an alkyne such as propargyl alcohol (eqs 1−5)[7] involves the transient formation of an adduct (porphinato)Co^{III}-CMe_2CN (**2**; eq 2) with a tertiary radical originating from AIBN (eq 1), which immediately undergoes β-hydride abstraction to generate a (porphinato)$Co^{III}H$ (**3**)[11] with elimination of an unsaturated nitrile (eq 3). Subsequently, **3** undergoes addition



of propargyl alcohol to give **4** (eq 4), which gradually isomerizes to **5** and **6** (eq 5). Since the cobalt hydride addition to alkynes (eq 4), in most cases, is selective to trans adducts, a reaction mechanism involving two cobalt porphyrin molecules[7c] has been proposed by analogy to some related reactions,[12] where cobalt(III) hydride **3** reacts with activated alkynes through coordinative interaction with another cobalt porphyrin species (Scheme 1A). If this mechanism is really operative, use of a cobalt(II) porphyrin encapsulated within a large dendrimer cage such as (*m*-[G3]TPP)Co^{II} (Figure 1D) should result in considerable

Scheme 1



retardation of the reaction, since the access of two cobalt porphyrin centers must be sterically suppressed by the dendrimer cage.[9a,b] On the other hand, as for the isomerization of alkylated complex **4** (eq 5), an intramolecular 1,3-hydrogen shift mechanism has initially been considered a likely candidate (Scheme 2A).[7b] However, later, an alternative mechanism involving a cobalt(II) or a cobalt(III) hydride species (Scheme 2B) has been proposed to be more likely, since the isomerization is greatly suppressed when sterically encumbered mesitylporphyrin (TMP) is the ligand.[7c] Nevertheless, considering a large steric pressure of the mesityl moieties to the active center, the intramolecular 1,3-hydrogen shift mechanism (Scheme 2A) may not be excluded completely. From this point of view, studies with a large dendrimer cobalt(II) porphyrin such as (*m*-[G3]TPP)Co^{II} (Figure 1D) are interesting, since it possibly bears a larger space around the cobalt center than (TMP)Co^{II}, due to the dendritic growth of 1,3,5-trisubstituted aromatic building units.

In the present paper, we synthesized cobalt(II) complexes of meta- and para-substituted series of poly(aryl ester) dendrimer porphyrins, (*m*-[G*n*]TPP)Co^{II} and (*p*-[G*n*]TPP)Co^{II}, with different generation numbers ($n = 0-3$) (Figure 1) and investigated steric effects of the dendritic substituents on conversion rate and selectivity of the AIBN-initiated alkylation at the cobalt(II) center with propargyl alcohol.

Results and Discussion

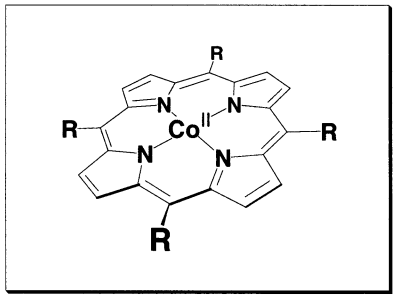
Synthesis of Dendrimer Cobalt(II) Porphyrins (*m*-[G*n*]-TPP)Co^{II} and (*p*-[G*n*]TPP)Co^{II} ($n = 1-3$) and Nondendritic References (*m*-[G0]TPP)Co^{II} and (*p*-[G0]TPP)Co^{II}. Free-base porphyrins, *m*-[G*n*]$TPPH_2$ and *p*-[G*n*]$TPPH_2$ ($n = 1-3$), were synthesized by DCC-mediated coupling of carboxylic acid-terminated poly(aryl ester) dendrons or 3,5-dimethoxybenzoic acid, in a manner similar to that reported by Suslick and coworkers.[10b] The yields were all satisfactorily high. In particular, *m*-[G3]$TPPH_2$ and *p*-[G3]$TPPH_2$, the largest homologues of the meta- and para-substituted series, were obtained in 79 and 93% yield, respectively. Nondendritic free-base porphyrins such as *m*-[G0]$TPPH_2$, *p*-[G0]$TPPH_2$, and $TMPH_2$ were synthesized by the condensation of pyrrole with the corresponding benzaldehyde derivatives.[10c] All the free-base porphyrins were unambiguously characterized by means of MALDI-TOF-MS spectrometry together with ^1H and ^{13}C NMR and electronic absorption spectroscopies. Cobalt(II) porphyrins, (*m*-[G*n*]TPP)Co^{II}, (*p*-[G*n*]-TPP)Co^{II} ($n = 0-3$) (Figure 1), and (TMP)Co^{II}, were prepared by the reaction of the corresponding free-base porphyrins with anhydrous $Co(OAc)_2$ in $CHCl_3$/EtOH, where complete metalation was confirmed by the disappearance of the characteristic

(9) (a) Jiang, D.-L.; Aida, T. *J. Chem. Soc., Chem. Commun.* **1996**, 1523−1524. (b) Collman, J. P.; Fu, L.; Zing, A.; Diederich, F. *J. Chem. Soc., Chem. Commun.* **1997**, 193−194. (c) Enomoto, M.; Aida, T. *J. Am. Chem. Soc.* **1999**, *121*, 874−875. (d) Enomoto, M.; Aida, T. *J. Am. Chem. Soc.* **2002**, *21*, 6099−6108.

(10) (a) Brunner, H. *J. Organomet. Chem.* **1995**, *500*, 39−46. (b) Bhyrappa, P.; Young, J. K.; Moore, J. S.; Suslick, K. S. *J. Am. Chem. Soc.* **1996**, *118*, 5708−5711. (c) Tomoyose, Y.; Jiang, D.-L.; Jin, R.-H.; Aida, T.; Yamashita, T.; Horie, K.; Yashima, E.; Okamoto, Y. *Macromolecules* **1996**, *29*, 5236−5238. (d) Rheiner, P. B.; Seebach, D. *Chem. Eur. J.* **1999**, *5*, 3221−3236. (e) Sellner, H.; Seebach, D. *Angew. Chem., Int. Ed.* **1999**, *38*, 1918−1920. (f) Habicher, T.; Diederich, F.; Gramlich, V. *Helv. Chim. Acta* **1999**, *82*, 1066−1095. (g) Kimura, M.; Sugihara, Y.; Muto, T.; Hanabusa, K.; Shirai, H.; Kobayashi, N. *Chem. Eur. J.* **1999**, *5*, 3495−3500. (h) Sen, A.; Suslick, K. S. *J. Am. Chem. Soc.* **2000**, *122*, 11565−11566. (i) Kimura, M.; Shiba, T.; Yamazaki, M.; Hanabusa, K.; Shirai, H.; Kobayashi, N. *J. Am. Chem. Soc.* **2001**, *123*, 5636−5642. (j) Kimata, S.; Aida, T. *Tetrahedron Lett.* **2001**, *42*, 4187−4190. (k) Hecht, S.; Fréchet, J. M. J. *J. Am. Chem. Soc.* **2001**, *123*, 6959−6960. (l) Weyermann, P.; Diederich, F. *Helv. Chim. Acta* **2002**, *85*, 599−617.

(11) For selected examples of hydridocobalt(III) porphyrin-mediated transformations, see: (a) Fukuzumi, S.; Noura, S. *J. Porphyrins Phthalocyanines* **1997**, *1*, 251−258. (b) Watanabe, J.; Setsune, J. *J. Organomet. Chem.* **1999**, *575*, 21−32.

(12) (a) Ogoshi, H.; Setsune, J.; Yoshida, Z. *J. Am. Chem. Soc.* **1977**, *99*, 3869−3870. (b) Zhang, X.-X.; Parks, G. F.; Wayland, B. B. *J. Am. Chem. Soc.* **1997**, *119*, 7938−7944.



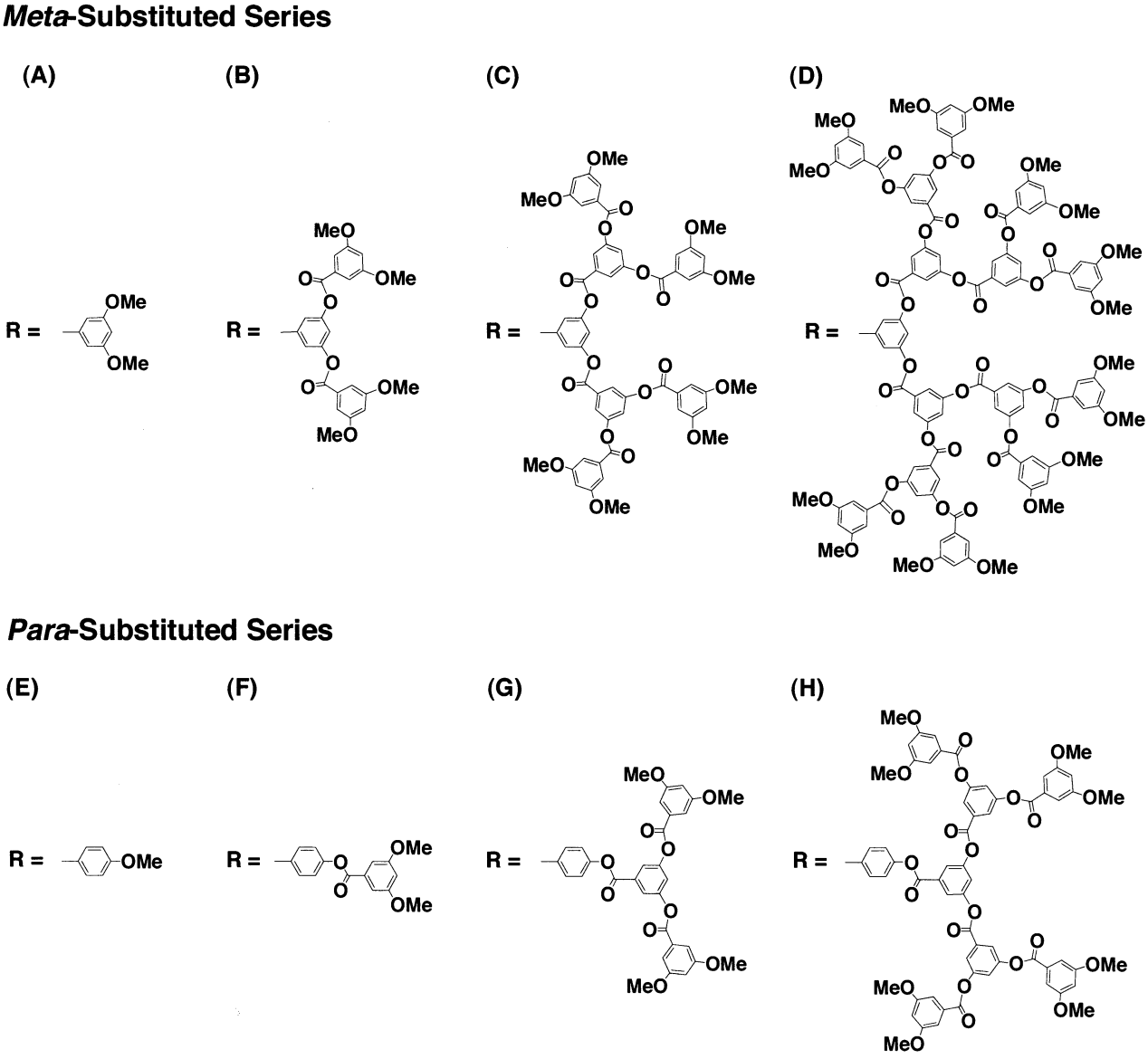


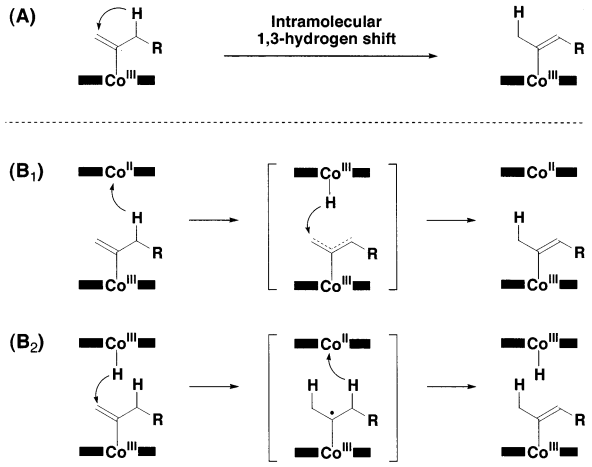
Figure 1. Schematic structures of cobalt(II) porphyrins: (A) (*m*-[G0]TPP)Co^{II}; (B) (*m*-[G1]TPP)Co^{II}; (C) (*m*-[G2]TPP)Co^{II}; (D) (*m*-[G3]TPP)Co^{II}; (E) (*p*-[G0]TPP)Co^{II}; (F) (*p*-[G1]TPP)Co^{II}; (G) (*p*-[G2]TPP)Co^{II}; (H) (*p*-[G3]TPP)Co^{II}.

free-base porphyrin fluorescence.[13] The products, isolated by chromatography on silica gel, showed a single molecular ion peak in MALDI-TOF-MS spectrometry (Figure 2) and characteristic absorption bands of cobalt(II) porphyrins in UV−vis spectroscopy.

AIBN-Initiated Alkylation of (*m*-[G3]TPP)Co^{II} with Propargyl Alcohol. We first investigated the alkylation of the largest (*m*-[G3]TPP)Co^{II} (Figure 1D). A CPK model study on (*m*-[G3]TPP)Co^{II} (Figure 3D) suggested that the four dendritic substituents are capable of forming a cage-like envelope around

(13) Sanders, J. K. M.; Bampos, N.; Clyde-Watson, Z.; Darling, S. L.; Hawley, J. C.; Kim, H.-J.; Mak, C. C.; Webb, S. J. In *The Porphyrin Handbook*; *Inorganic, Organometallic and Coordination Chemistry*; *Axial Coordination Chemistry of Metalloporphyrins*; Kadish, K. M., Smith, K. M., Guilard, R., Eds.; Academic Press: New York, 2000; Vol. 3, p 23.

Scheme 2



the cobalt(II) porphyrin focal core. For the alkylation of (*m*-[G3]TPP)Co^{II}, a $CDCl_3$ solution (0.5 mL) of a mixture of (*m*-[G3]TPP)Co^{II} (4.7 μmol), AIBN (40 μmol), and propargyl alcohol (450 μmol) was added to a NMR tube, which was then degassed and sealed. Upon heating at 60 °C, ^{1}H NMR spectroscopy of the mixture (Figure 4) clearly indicated that the cobalt(II) center within the large dendrimer cage is alkylated with propargyl alcohol. At the initial stage, the reaction mixture showed, e.g., a signal at δ 9.2 ppm (c) due to *p*-H of the meso-Ar groups at the porphyrin macrocycle, which gradually disappeared (●, Figure 5D) to give a new signal at δ 9.0 ppm (a′), assignable to pyrrole-β-H of diamagnetic cobalt(III) porphyrin species.[7] At the same time, a new set of signals appeared at δ −0.2 (*trans*-H), −1.9 (CH_2), and −2.4 (*cis*-H) ppm (see also Figure 7B), which are assigned to an allyl alcohol functionality at the axial position of (*m*-[G3]TPP)Co^{III}. As shown in Figure 5D, such a spectral change subsided in 200 min, where **4** (○) was obtained in 91% spectral yield. After heating for 240 min, degassed MeOH (1 mL) was added to the reaction mixture, whereupon a dark purple precipitate formed, which was isolated, washed with MeOH, and dried under reduced pressure at room temperature. When the residue, dissolved in $CHCl_3$, was subjected to preparative size-exclusion chromatography (SEC) equipped with a multichannel detector, a single, sharp chromatogram exhibiting a similar absorption spectral profile to that of (*m*-[G3]TPP)Co^{II} was observed as the major component with some very minor peaks. ^{1}H NMR spectroscopy in $CDCl_3$ (Figure 6) showed that this major fraction contains virtually a single organocobalt(III) species **4** with a clear signal at δ −1.2 (t, 1H) ppm due to the hydroxyl (OH) group of the axial allyl alcohol functionality. Quite interestingly, no signals characteristic of isomerized compounds[7] such as **5** and **6** were detected even upon prolonged heating.

Wayland and co-workers have reported that the cobalt(II) complex of mesitylporphyrin (TMP)Co^{II} is highly selectively alkylated by alkynes in the presence of AIBN.[7] For comparison, we investigated alkylation of (TMP)Co^{II} under the above-mentioned conditions with propargyl alcohol as alkylating agent, where **4** was observed in 75% yield in 220 min, but it gradually disappeared upon prolonged heating to furnish the spectral yield of 66% in 300 min. Isomerized compound **5** was formed in 3%, while compound **6** was not detected throughout the reaction. Although the selectivity is satisfactorily high, the yield of **4** is obviously lower than that in the alkylation of dendritic (*m*-[G3]-TPP)Co^{II} (91%), suggesting an interesting possibility that **4** derived from (*m*-[G3]TPP)Co^{II} is protected against thermal decomposition by the large dendrimer cage.

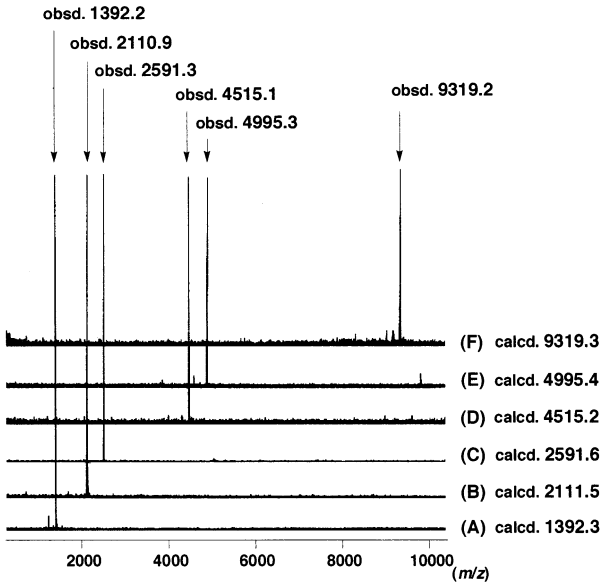


Figure 2. MALDI-TOF-MS spectra of dendrimer cobalt(II) porphyrins: (A) (*p*-[G1]TPP)Co^{II}; (B) (*m*-[G1]TPP)Co^{II}; (C) (*p*-[G2]TPP)Co^{II}; (D) (*m*-[G2]TPP)Co^{II}; (E) (*p*-[G3]TPP)Co^{II}; (F) (*m*-[G3]TPP)Co^{II}.

AIBN-Initiated Alkylation of (*m*-[Gn]TPP)Co^{II} (n = 0−2) with Propargyl Alcohol. To investigate effects of the generation number of the dendritic substituents on the alkylation, cobalt(II) porphyrin complexes, such as (*m*-[G0]TPP)Co^{II}, (*m*-[G1]-TPP)Co^{II}, and (*m*-[G2]TPP)Co^{II} (Figure 1A−C) with lower generation numbers than (*m*-[G3]TPP)Co^{II}, were heated at 60 °C in the presence of AIBN and propargyl alcohol under conditions identical to those given above. From the CPK models in Figure 3A−C, it is obvious that these cobalt(II) porphyrins have more open architectures than (*m*-[G3]TPP)Co^{II}, where the active centers of (*m*-[G0]TPP)Co^{II} and (*m*-[G1]TPP)Co^{II}, in particular, are totally exposed to external environments. From the time courses of the alkylation (Figure 5A−C), the conversion rates of (*m*-[G*n*]TPP)Co^{II} (n = 0−2) were almost comparable to one another and even slightly smaller than that of (*m*-[G3]-TPP)Co^{II} (Figure 5D). Although, in every case, the reaction gave compound **4** as the major product, it also afforded noticeable amounts of several organocobalt species including isomerized compounds **5** and **6**.

For example, in the case of nondendritic (*m*-[G0]TPP)Co^{II} (Figure 1A), the reaction mixture showed a set of ^{1}H NMR signals at δ −0.1 (*trans*-H), −1.8 (CH_2), and −2.3 (*cis*-H) ppm due to the axial allyl alcohol functionality of **4**, whose spectral yield was increased to 69% within the first 100 min and then decreased to 39% in the following 200 min (Figure 5A). The ^{1}H NMR spectrum of the reaction mixture in, e.g., 300 min (Figure 7A) showed another set of signals at δ −1.4 (q, vinyl-H) and −3.8 (d, J = 1.7 Hz, CH_3) ppm, assigned to isomerized compound **5**. In the ^{1}H NMR spectrum at a relatively early stage of the reaction (40−230 min), a set of signals due to isomerized compound **6** was also detected at δ −2.9 (m, CH) and −5.5 (d, J = 7.3 Hz, CH_3) ppm, which gradually disappeared in the latter stage. From these spectral change profiles, the yield of **5** was found to increase gradually with time to reach 11% in 300 min, while **6** was obtained in a maximum yield of 6% in 120 min.

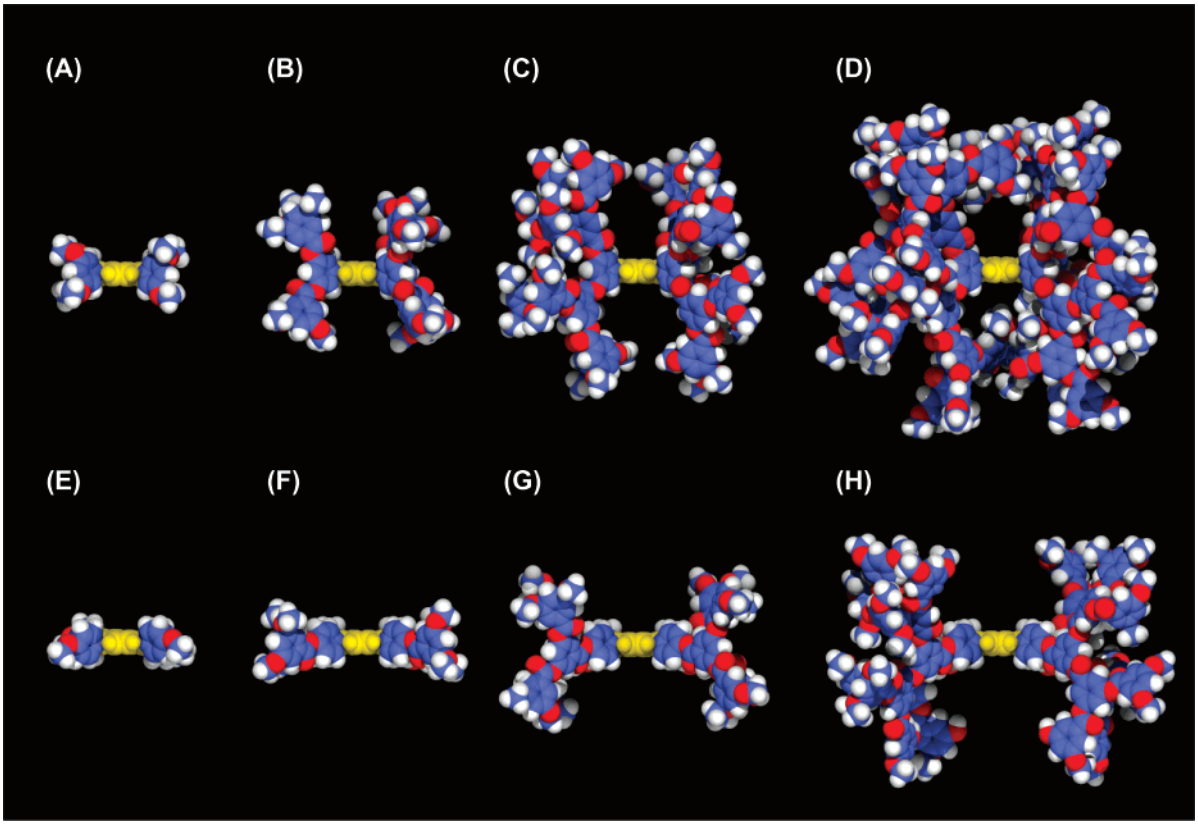


Figure 3. CPK models of cobalt(II) porphyrins: (A) (*m*-[G0]TPP)Co^{II}; (B) (*m*-[G1]TPP)Co^{II}; (C) (*m*-[G2]TPP)Co^{II}; (D) (*m*-[G3]TPP)Co^{II}; (E) (*p*-[G0]-TPP)Co^{II}; (F) (*p*-[G1]TPP)Co^{II}; (G) (*p*-[G2]TPP)Co^{II}; (H) (*p*-[G3]TPP)Co^{II}.

In addition to these signals, some unidentified signals (e.g., −0.3 (s) ppm, Figure 7A) also appeared in the latter stage, and the spectrum became rather complicated.

Alkylation of (*m*-[G2]TPP)Co^{II} (Figure 1C), a one-generation smaller homologue of (*m*-[G3]TPP)Co^{II}, proceeded rather selectively, where the yield of **4** was increased to 82% in 200 min and remained almost unchanged thereafter (Figure 5C). Nevertheless, similarly to the case of nondendritic (*m*-[G0]TPP)-Co^{II}, isomerized compounds **5** and **6** both formed in maximum yields of 5% (300 min) and 3% (80 min), respectively. On the other hand, the alkylation of (*m*-[G1]TPP)Co^{II} (Figure 1B) proceeded much less selectively than that of (*m*-[G3]TPP)Co^{II}, where **4**, once formed in 78% yield in 220 min, disappeared gradually to furnish 72% yield in 300 min (Figure 5B). In this case, isomerized compounds **5** and **6** were formed in 6% (300 min) and 9% (120 min) maximum yields, respectively. In both cases, **6** disappeared almost completely in the latter stage of the reaction.

AIBN-Initiated Alkylation of (*p*-[Gn]TPP)Co^{II} ($n = 0-3$) with Propargyl Alcohol. To obtain further insights into the structural effects of the dendritic substituents, alkylation of (*p*-[G*n*]TPP)Co^{II} ($n = 0-3$), which bear dendritic substituents at the para-positions of the meso-Ar groups (Figure 1E−H), was investigated under conditions identical to those for the alkylation of (*m*-[G*n*]TPP)Co^{II} ($n = 0-3$). CPK model studies (Figure 3E−H) suggested that the steric bulks of (*p*-[G*n*]TPP)Co^{II} ($n = 0-3$) are almost comparable to those of the corresponding one-generation lower compounds in the meta-substituted series. In the alkylation of (*p*-[G*n*]TPP)Co^{II} ($n = 0-3$), isomerized compounds **5** and **6** were detected, irrespective of the generation number of the dendritic substituents (Figure 5E−H). For example, in the case of (*p*-[G3]TPP)Co^{II} (Figure 1H), the largest homologue in this series, ^{1}H NMR spectroscopy of the reaction mixture (Figure 7D) clearly showed signals due to **5** at δ −1.4 (q, vinyl-H) and −3.8 (d, $J = 1.7$ Hz, CH_3) ppm. Although **6** was hardly detected throughout the reaction, the alkylation profile (Figure 5H) was quite similar to that of (*m*-[G2]TPP)-Co^{II} (Figure 1C), the second largest homologue in the meta-substituted series. On the other hand, the alkylation of nondendritic (*p*-[G0]TPP)Co^{II} (Figure 1E) was accompanied by the formation of considerable amounts of isomerized compounds **5** (17%, 300 min) and **6** (12%, 180 min) (Figure 5E; for ^{1}H NMR, see Figure 7C), while the maximum yield of **4** was only as low as 46% (130 min).

For comparison, the spectral yields of **4** and those of isomerization products (**5** + **6**) for the meta- and para-substituted series are summarized in Figure 8. As expected from the CPK models (Figure 3), the selectivities of the (*p*-[G*n*]TPP)Co^{II} series are virtually comparable to those observed for the alkylation of the corresponding one-generation lower compounds in the (*m*-[G*n*]TPP)Co^{II} series. Here, it is clear that the large dendritic cage of (*m*-[G3]TPP)Co^{II} is quite essential for achieving both high selectivity and high yield.

Mechanistic Aspects. As described in the Introduction, the cobalt(III) hydride addition to alkynes (eq 4) has been proposed to occur by the participation of another cobalt porphyrin molecule for the activation of alkynes (Scheme 1A). However, the alkylation of (*m*-[G3]TPP)Co^{II} actually takes place at its spatially encapsulated reaction center (Figure 5D), where the overall conversion rate shows no sign of retardation compared with those of the lower-generation homologues (Figure 5A−C). The two cobalt porphyrin centers of (*m*-[G3]TPP)Co must

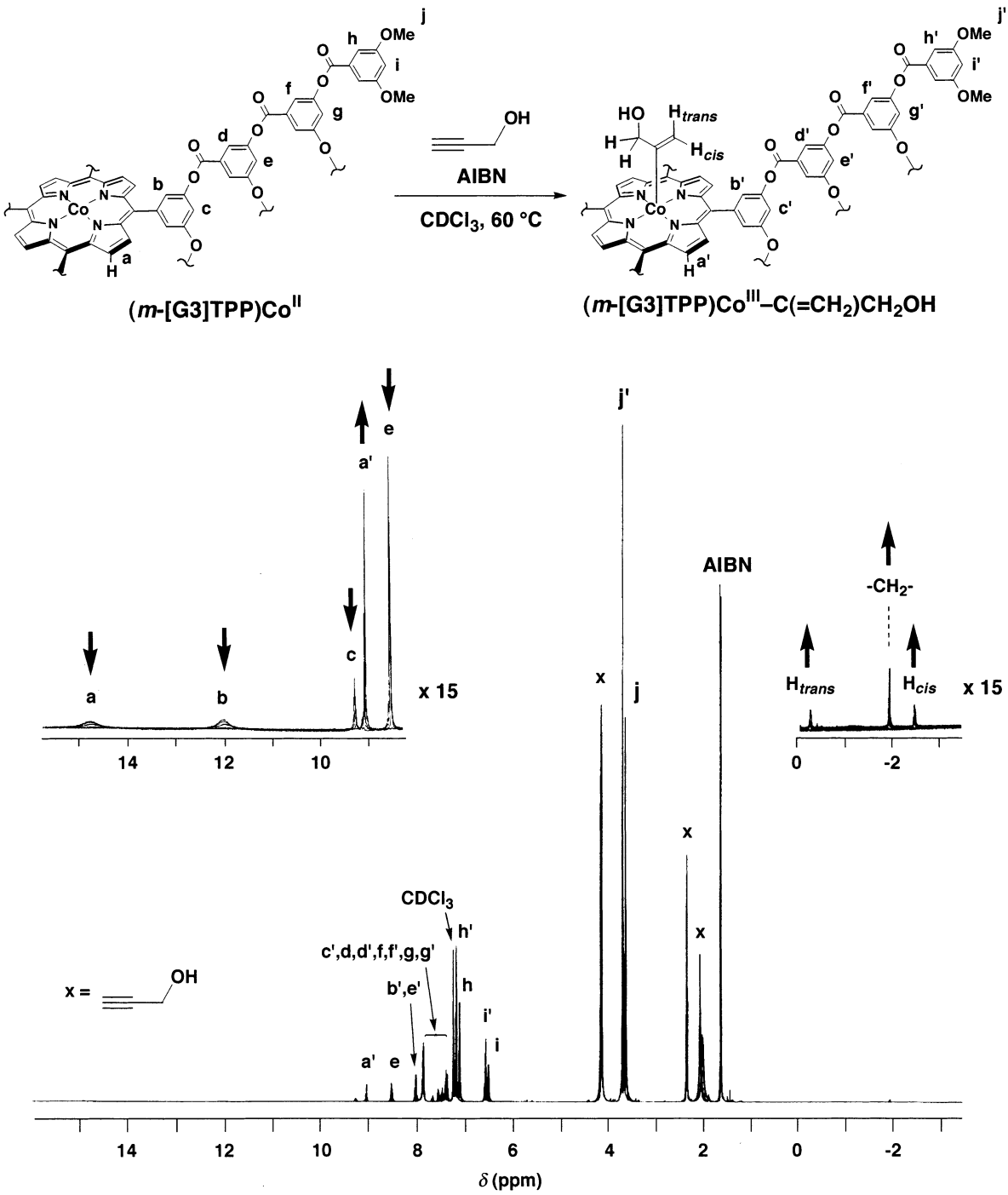


Figure 4. Reaction of (*m*-[G3]TPP)Co^{II} (4.7 μmol) with propargyl alcohol (450 μmol) in the presence of AIBN (40 μmol) in $CDCl_3$ (0.5 mL) at 60 °C. ^{1}H NMR spectral change profile over a period 300 min.

be hardly accessible to each other by the large dendritic cage. We and other groups have found similar size-exclusion phenomena in dioxygen binding of large dendrimer iron porphyrins, where the dioxygen adducts are highly stabilized by the steric protection against μ-oxo dimer formation.[9a,b] Furthermore, we have also reported that, in the axial coordination of dendrimer-appended imidazoles to dendrimer zinc porphyrins, the association constant drops discretely when their generation numbers both become high.[10c] Together with these related observations, the cobalt(III) hydride addition step (eq 4) most likely proceeds without external assistance for the activation of propargyl alcohol.

In relation to this mechanism, we examined the alkylation of (*m*-[G3]TPP)Co^{II} with propargyl alcohol by using deuterated AIBN-d_{12}, which allows investigation of the stereochemistry of the hydride addition step.[7c] As already described, when nondeuterated AIBN is the hydride source, the adduct **4** shows the *trans*-H signal of the axial allyl alcohol moiety at δ −0.2 ppm (Figure 9B). In sharp contrast, when AIBN-d_{12} was used, the corresponding signal was hardly detected, while relative intensities of the other signals remained virtually intact (Figure 9A). Furthermore, the doublet signal due to *cis*-H of **4** (Figure 9B) was observed as a singlet signal in Figure 9A. These spectral profiles demonstrate that the cobalt(III) hydride species (**3**)

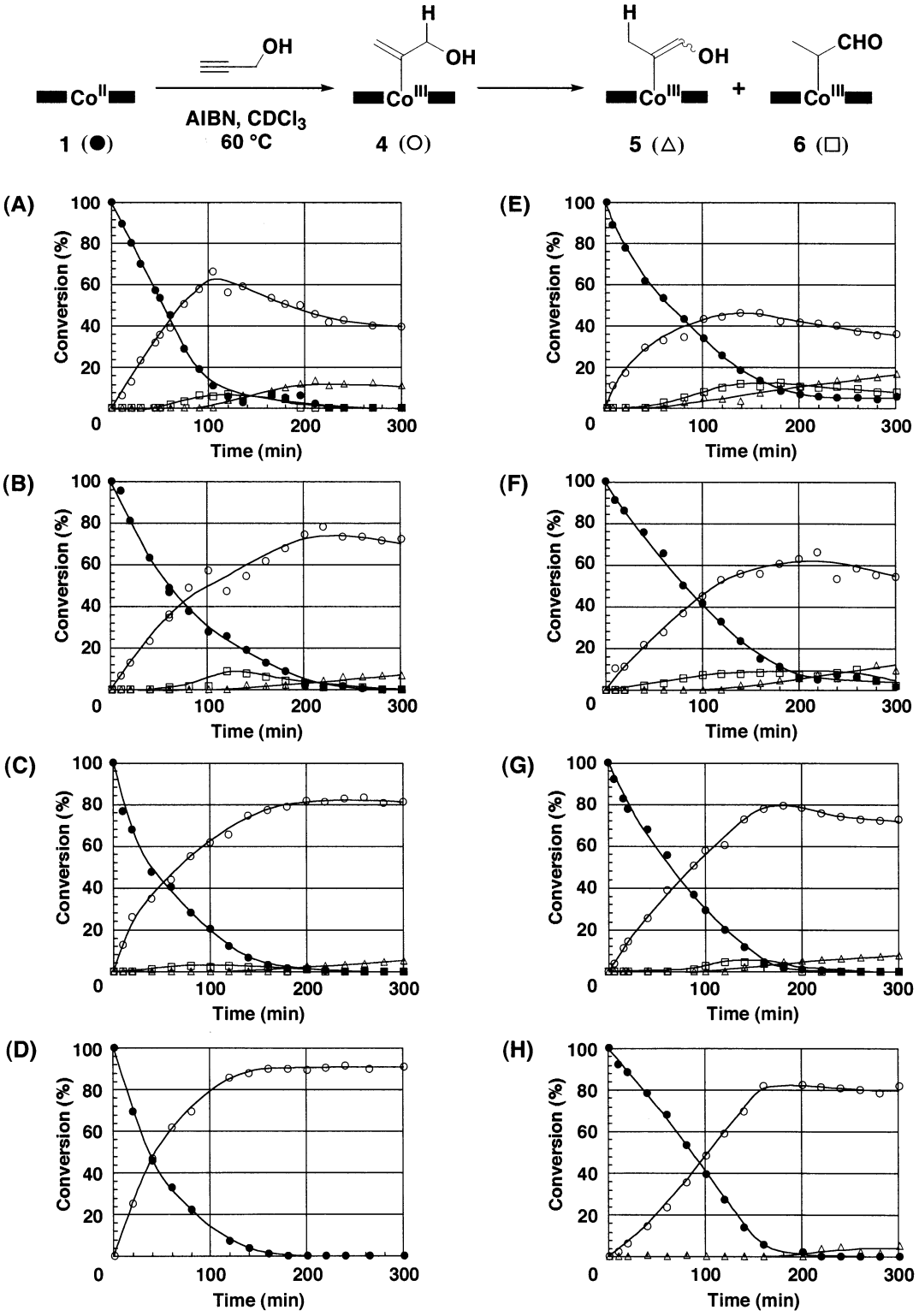


Figure 5. Time courses of the reaction of cobalt(II) porphyrins (4.7 μmol) with propargyl alcohol (450 μmol) in the presence of AIBN (40 μmol) in $CDCl_3$ (0.5 mL) at 60 °C: (A) (*m*-[G0]TPP)Co^{II}; (B) (*m*-[G1]TPP)Co^{II}; (C) (*m*-[G2]TPP)Co^{II}; (D) (*m*-[G3]TPP)Co^{II}; (E) (*p*-[G0]TPP)Co^{II}; (F) (*p*-[G1]TPP)Co^{II}; (G) (*p*-[G2]TPP)Co^{II}; (H) (*p*-[G3]TPP)Co^{II}.

undergoes trans-addition to propargyl alcohol.[7c] This is quite interesting, since the trans-selectivity has been considered an indication for the mechanism involving external activation of alkynes (Scheme 1A). Here, one may also have to consider that cobalt hydride species in porphyrin macrocycles are thermally dissociative. Chen and co-workers have suggested a rapid and reversible cobalt-to-ligand hydrogen migration,[7c] by analogy to the chemistry of hydridorhodium(III) phthalocyanines.[14] This possibility may account for the trans-selectivity of the hydride addition in the large dendrimer cage of (*m*-[G3]TPP)$Co^{III}H$, where external assistance cannot be expected for the activation of alkynes (Scheme 1B).

(14) Chen, M. J.; Nunez, L.; Ratheke J. W.; Rogers, R. D. *Organometallics* **1996**, *15*, 2338−2344.

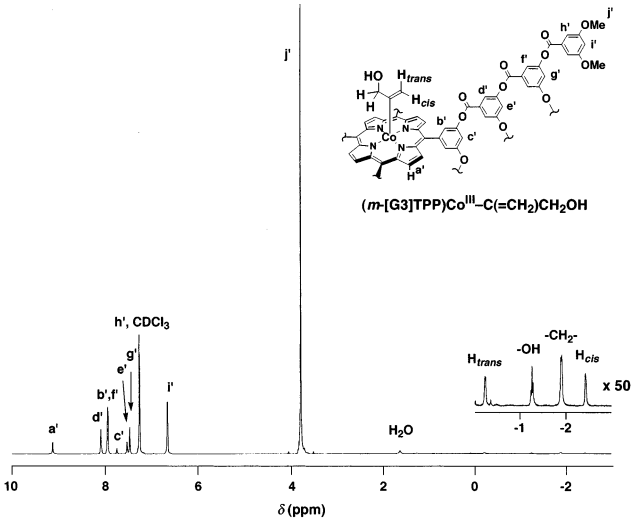


Figure 6. Reaction of (*m*-[G3]TPP)Co^{II} (4.7 μmol) with propargyl alcohol (450 μmol) in the presence of AIBN (40 μmol) in $CDCl_3$ (0.5 mL) at 60 °C. ^{1}H NMR spectral profile in $CDCl_3$ at 20 °C of a MeOH-insoluble part of the reaction mixture in 240 min (SEC-isolated fraction based on electronic absorption spectroscopy).

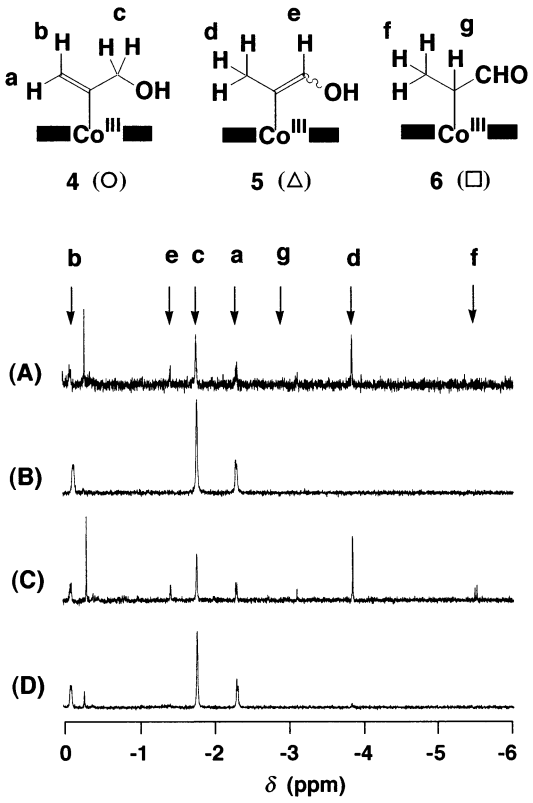


Figure 7. Reaction of cobalt(II) porphyrins (4.7 μmol) with propargyl alcohol (450 μmol) in the presence of AIBN (40 μmol) in $CDCl_3$ (0.5 mL) at 60 °C. ^{1}H NMR spectral profiles (δ −6 to 0 ppm, 60 °C) of the reaction mixtures in 300 min: (A) (*m*-[G0]TPP)Co^{II}; (B) (*m*-[G3]TPP)Co^{II}; (C) (*p*-[G0]TPP)Co^{II}; (D) (*p*-[G3]TPP)Co^{II}.

The mechanism involving two cobalt porphyrin molecules (Scheme 2B) has also been proposed for the isomerization of adduct **4** (eq 5). This possibility is quite reasonable, since the alkylation of the cobalt(II) center of large (*m*-[G3]TPP)Co^{II} is not accompanied by the isomerization of **4** (Figure 5D). Compound **4**, isolated from the reaction mixture with (*m*-[G3]-TPP)Co^{II}, also showed no sign of isomerization upon heating

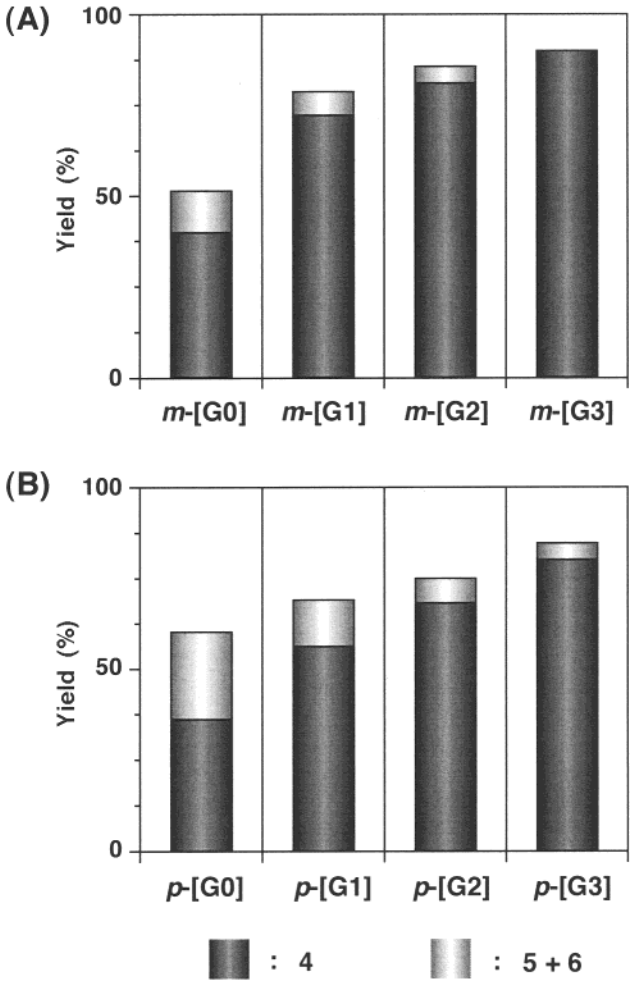


Figure 8. Reaction of cobalt(II) porphyrins (4.7 μmol) with propargyl alcohol (450 μmol) in the presence of AIBN (40 μmol) in $CDCl_3$ (0.5 mL) at 60 °C. ^{1}H NMR spectral yields (%) of nonisomerized **4** and isomerization products (**5** + **6**) in 300 min.

at 60 °C both in the absence and presence of AIBN. On the other hand, one might also consider that no isomerization activity of **4**, derived from (*m*-[G3]TPP)Co^{II}, is due to the steric suppression of the 1,3-hydrogen shift (Scheme 2A). However, the isomerization via this intramolecular process seems unlikely for the following consideration. Figure 8 shows that the selectivities of the alkylation of (*p*-[G3]TPP)Co^{II} and (*m*-[G2]-TPP)Co^{II} are almost comparable to each other. Their dendritic substituents are also comparable in size to each other, but the former has a larger interior space around the cobalt center than the latter (Figure 3C,H), since the dendrons are attached to the para-positions of the meso-Ar groups. If the isomerization of **4** takes place via the intramolecular 1,3-hydrogen shift (Scheme 2A), and if this process is sterically suppressed by the dendrimer cage, one can expect a higher probability of isomerization in the alkylation of (*p*-[G3]TPP)Co^{II} than that of (*m*-[G2]TPP)-Co^{II}. Therefore, once again, it is more likely that no isomerization with the largest (*m*-[G3]TPP)Co^{II} is due to the steric suppression of the mechanism in Scheme 2B, which requires two spatially encapsulated cobalt(II) centers to come in close proximity to each other.

Finally, it is interesting to note that the dendrimer cage does not affect the overall conversion rate but product selectivity (isomerization activity) in the alkylation of the cobalt(II) center.

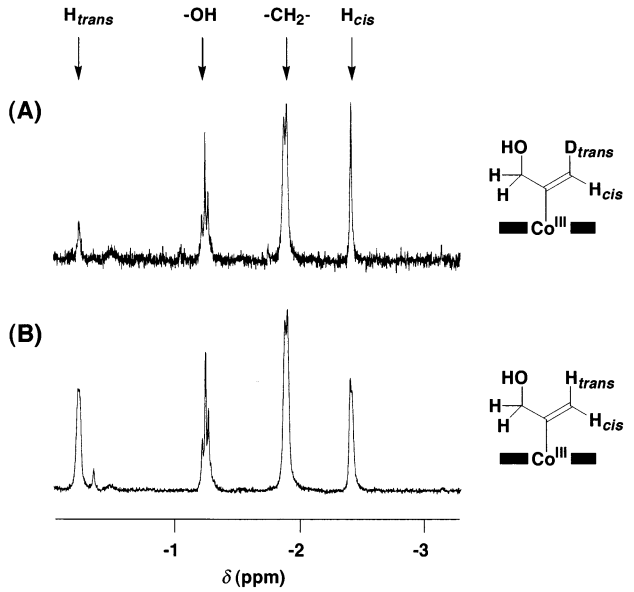


Figure 9. Azo-initiated reaction of (*m*-[G3]TPP)Co^{II} (4.7 μmol) and propargyl alcohol (450 μmol) in $CDCl_3$ (0.5 mL) at 60 °C. ^1H NMR spectral profiles (δ −3 to 0 ppm) in $CDCl_3$ at 20 °C of MeOH-insoluble parts of the reaction mixtures in 240 min with (A) AIBN-d_{12} (40 μmol) and (B) AIBN (40 μmol) (SEC-isolated fractions based on electronic absorption spectroscopy).

The dendrimer cage may serve as a molecular sieve to exclude large dendritic macromolecules but allow small molecules (propargyl alcohol and AIBN fragment) to have substantially a nonrestricted access to the interior active site.[10b,h,i,k]

Conclusion

By using a novel cobalt(II) porphyrin encapsulated by a radical-tolerant, large poly(aryl ester) dendritic cage ((*m*-[G3]-TPP)Co^{II}), we succeeded in demonstrating steric control of the AIBN-initiated alkylation of cobalt(II) porphyrin with an alkyne such as propargyl alcohol. Here, the dendritic cage sterically prohibits the access of two cobalt porphyrin molecules, thereby protecting the interior alkylated product (**4**) from subsequent isomerization. Although the alkylation has been proposed to involve additional cobalt porphyrin species for the activation of alkynes, the results with (*m*-[G3]TPP)Co^{II} also indicated that the reaction does not involve such an external activation of alkynes. Organic transformations involving free-radical species are of great importance both from biological and synthetic viewpoints.[1,2,5−7,15] In this sense, the present finding not only indicates the high potential of designer dendritic catalysts[9,10] but may also provide a new strategy toward precision organic synthesis involving free-radical species.

Experimental Section

General Methods. ^1H spectroscopies were performed in $CDCl_3$ using a JEOL type GSX-270 spectrometer operating at 270.05 MHz, where the chemical shifts were determined with respect to $CHCl_3$ (δ 7.24) as internal standard. ^{13}C NMR spectroscopies were performed in $CDCl_3$ using a JEOL type GSX-270 spectrometer and a JEOL type EXcalibur-500 spectrometer operating at 67.80 and 125.65 MHz, respectively, where the chemical shifts were determined with respect to $CDCl_3$ (δ 77.00) as internal standard. MALDI-TOF-MS spectra were recorded on a Bruker model Reflex III. Preparative size-exclusion chromatography (SEC) was performed at room temperature on a Japan Analytical Industry model LC-918 recycling preparative HPLC equipped with a JASCO model MD-1510 multichannel photodiode array detector, using $CHCl_3$ as eluent at a flow rate of 3.5 mL min^{-1}. The column set consisted of two Polystyragel columns (20 (i.d.) × 600 mm (L)) of JAIGEL-1H (exclusion limit 1 × 10^3)/JAIGEL-2H (5 × 10^3) or JAIGEL-2H/JAIGEL-3H (3 × 10^4). Electronic absorption spectra were recorded on a JASCO model V-570 spectrophotometer. Fluorescence spectra were recorded on a JASCO model FP-777W spectrofluorometer.

Materials. CH_2Cl_2 was washed successively with concentrated H_2SO_4, water, and aqueous $NaHCO_3$, dried over $CaCl_2$, and distilled over CaH_2 under Ar. Tetrahydrofuran (THF) was distilled under Ar over sodium benzophenone ketyl just before use. MeOH was distilled over Mg coupled with iodine under Ar. $CDCl_3$ was passed through alumina just before use. Propargyl alcohol was distilled before use. 4-(Dimethylamino)pyridinium 4-toluenesulfonate (DPTS) and 2′,2′,2′-trichloroethyl 3,5-dihydroxybenzoate were synthesized according to literature methods.[10b,16] 2,2′-Azobis(isobutyronitrile) (AIBN) was purchased from Wako Chemicals and used as received. Deuterium labeled AIBN-d_{12} was synthesized according to a literature method, using acetone-d_6 and D_2O, which were purchased from Merck.[17] 4-(Dimethylamino)pyridine (DMAP) and 1,3-dicyclohexylcarbodiimide (DCC) were purchased from Tokyo Chemical Industry and used as received. Anhydrous cobalt acetate ($Co(OAc)_2$) was purchased from Nakarai Chemicals and used as received.

(1) Synthesis of Nondendritic Porphyrin Free Bases and Cobalt(II) Complexes. 5,10,15,20-Tetrakis(4′-hydroxyphenyl)-21*H*,23*H*-porphine (T(*p*-[HO]Ar)PH_2), 5,10,15,20-tetrakis(3′,5′-dihydroxyphenyl)-21*H*,23*H*-porphine (T(*m*-$[HO]_2$Ar)PH_2), [5,10,15,20-tetrakis(4′-methoxyphenyl)-21*H*,23*H*-porphinato]cobalt(II) ((*p*-[G0]TPP)Co^{II}), [5,10,15,-20-tetrakis(3′,5′-dimethoxyphenyl)-21*H*,23*H*-porphinato]cobalt(II) ((*m*-[G0]TPP)Co^{II}), and [5,10,15,20-tetrakis(2′,4′,6′-trimethylphenyl)-21*H*,-23*H*-porphinato]cobalt(II) ((TMP)Co^{II}) were synthesized according to literature methods.[10c,13]

(2) Synthesis of Poly(aryl ester) Dendrons. [G*n*]poly(aryl ester)−CO_2H dendrons were prepared by a method with a slight modification of the reported procedure.[10b]

(i) Preparation of [G1]poly(aryl ester)−$CO_2CH_2CCl_3$ Dendron. To a distilled CH_2Cl_2 solution (220 mL) of a mixture of 3,5-dimethoxybenzoic acid (45.5 g, 250 mmol), 2′,2′,2′-trichloroethyl 3,5-dihydroxybenzoate (28.6 g, 100 mmol), and DPTS (8.24 g, 28 mmol) was added DCC (51.6 g, 250 mmol) under Ar at 0 °C. The reaction mixture was stirred overnight at room temperature, then filtered off from insoluble substances through Celite, washed with water (500 mL), and extracted with AcOEt and Et_2O. The combined extract was dried over anhydrous $MgSO_4$ and evaporated to dryness under reduced pressure at room temperature, and the residue was chromatographed on silica gel with CH_2Cl_2 as eluent, to give after evaporation 2′,2′,2′-trichloroethyl 3,5-bis(3′,5′-dimethoxybenzoyloxy)benzoate ([G1]poly-(aryl ester)−$CO_2CH_2CCl_3$ dendron) as white powder quantitatively (61.4 g). ^1H NMR (270.05 MHz; $CDCl_3$; 20 °C; ppm): δ 3.85 (s, 12H), 4.98 (s, 2H), 6.72 (t, 2H, J = 2.4 Hz), 7.32 (d, 4H, J = 2.4 Hz), 7.45 (t, 1H, J = 2.2 Hz), 7.89 (d, 2H, J = 2.2 Hz). ^{13}C NMR (67.80 MHz; $CDCl_3$; 20 °C; ppm): δ 55.7, 74.6, 94.6, 106.7, 107.7, 120.8, 121.5, 130.3, 130.8, 151.3, 160.6, 163.1, 164.2. MALDI-TOF-MS (dithranol) m/z $[M + Na]^+$. Calcd: 635.0. Found: 634.9.

(ii) Preparation of [G1]poly(aryl ester)−CO_2H Dendron. To a THF/AcOH solution (70/80 mL) of [G1]poly(aryl ester)−$CO_2CH_2CCl_3$ dendron (33.1 g, 54 mmol) was slowly added zinc powder (22.2 g) under Ar at 0 °C. The reaction mixture was vigorously stirred for 15 min at room temperature, then filtered off from insoluble substances

(15) (a) Pattenden, G. *Chem. Soc. Rev.* **1988**, *17*, 361−382. (b) Wayland, B. B.; Mukerjee, S.; Poszmik, G.; Woska, D. C.; Basickes, L.; Gridnev, A. A.; Fryd, M.; Ittel, S. D. *ACS Symp. Ser.* **1998**, *15*, 305−315. (c) Gridnev, A. A.; Ittel, S. D. *Chem. Rev.* **2001**, *101*, 3611−3660.

(16) Moore, J. S.; Stupp, S. I. *Macromolecules* **1990**, *23*, 65−70.

(17) Overberger, C. G.; Huang, P.-T.; Berenbaum, M. B. In *Organic Syntheses*; Wiley: New York, 1963; Collective Vol. 4, pp 66−67 and 274−275.

through Celite, and extracted with AcOEt and Et_2O. The combined extract was evaporated to dryness under reduced pressure at room temperature, and the residue dissolved in $CHCl_3$ was washed with water (1 L) and evaporated to dryness under reduced pressure at room temperature. The residue was dissolved in $CHCl_3$/2-PrOH (10%) and crystallized with hexane, to give 3,5-bis(3′,5′-dimethoxybenzoyloxy)-benzoic acid ([G1]poly(aryl ester)−CO_2H dendron) as white powder in 96% yield (25.0 g). ^{1}H NMR (270.05 MHz; $CDCl_3$; 20 °C; ppm): δ 3.85 (s, 48H), 6.72 (t, 8H, J = 2.4 Hz), 7.32 (d, 16H, J = 2.4 Hz), 7.45 (t, 4H, J = 2.4 Hz), 7.89 (d, 8H, J = 2.4 Hz). ^{13}C NMR (67.80 MHz; $CDCl_3$; 20 °C; ppm): δ 55.7, 106.8, 107.7, 121.0, 121.2, 130.5, 131.3, 151.2, 160.7, 164.2, 169.0. MALDI-TOF-MS (dithranol) m/z $[M + Na]^+$. Calcd: 505.1. Found: 505.5.

(iii) Preparation of [G2]poly(aryl ester)−$CO_2CH_2CCl_3$ Dendron. To a distilled CH_2Cl_2 solution (50 mL) of a mixture of [G1]poly(aryl ester)−CO_2H dendron (19.3 g, 40 mmol), 2′,2′,2′-trichloroethyl 3,5-dihydroxybenzoate (5.43 g, 19 mmol), and DPTS (1.35 g, 4.5 mmol) was added DCC (9.29 g, 45 mmol) under Ar at 0 °C. The reaction mixture was stirred overnight at room temperature, then filtered off from insoluble substances through Celite, washed with water (200 mL), and extracted with AcOEt and Et_2O. The combined extract was dried over anhydrous $MgSO_4$ and evaporated to dryness under reduced pressure at room temperature, and the residue was chromatographed on silica gel with CH_2Cl_2 as eluent, to give after evaporation 2′,2′,2′-trichloroethyl 3,5-bis[3′,5′-bis(3″,5″-dimethoxybenzoyloxy)benzoyloxy]-benzoate ([G2]poly(aryl ester)−$CO_2CH_2CCl_3$ dendron) as white powder in 98% yield (22.7 g). ^{1}H NMR (270.05 MHz; $CDCl_3$; 20 °C; ppm): δ 3.85 (s, 24H), 4.98 (s, 2H), 6.72 (t, 4H, J = 2.4 Hz), 7.32 (d, 8H, J = 2.4 Hz), 7.48 (t, 1H, J = 2.2 Hz), 7.50 (t, 2H, J = 2.2 Hz), 7.92 (d, 2H, J = 2.2 Hz), 7.99 (d, 4H, J = 2.2 Hz). ^{13}C NMR (125.65 MHz; $CDCl_3$; 20 °C; ppm): δ 55.7, 74.7, 94.6, 106.7, 107.6, 120.6, 120.9, 121.0, 121.5, 130.3, 130.7, 130.9, 150.9, 151.3, 160.5, 162.6, 162.8, 164.0. MALDI-TOF-MS (dithranol) m/z $[M + Na]^+$. Calcd: 1235.2. Found: 1235.0.

(iv) Preparation of [G2]poly(aryl ester)−CO_2H Dendron. To a THF/AcOH solution (50/45 mL) of [G2]poly(aryl ester)−$CO_2CH_2CCl_3$ dendron (34.0 g, 28 mmol) was slowly added zinc powder (13.5 g) under Ar at 0 °C. The reaction mixture was vigorously stirred for 10 min at 60 °C, then filtered off from insoluble substances through Celite, and extracted with AcOEt and Et_2O. The combined extract was evaporated to dryness under reduced pressure at room temperature, and the residue dissolved in $CHCl_3$ was washed with water (500 mL) and evaporated to dryness under reduced pressure at room temperature. The residue was dissolved in $CHCl_3$/2-PrOH (10%) and crystallized with hexane, to give 3,5-bis[3′,5′-bis(3″,5″-dimethoxybenzoyloxy)benzoyloxy]benzoic acid ([G2]poly(aryl ester)−CO_2H dendron) as white powder in 92% yield (28.0 g). ^{1}H NMR (270.05 MHz; $CDCl_3$; 20 °C; ppm): δ 3.85 (s, 24H), 6.72 (t, 4H, J = 2.4 Hz), 7.32 (d, 8H, J = 2.4 Hz), 7.49 (t, 1H, J = 2.2 Hz), 7.50 (t, 2H, J = 2.2 Hz), 7.91 (d, 2H, J = 2.2 Hz), 7.99 (d, 4H, J = 2.2 Hz). ^{13}C NMR (67.80 MHz; $CDCl_3$; 45 °C; ppm): δ 55.7, 106.9, 107.9, 120.8, 120.8, 121.0, 121.4, 130.6, 131.0, 131.6, 151.1, 151.5, 160.8, 162.7, 164.2, 168.7. MALDI-TOF-MS (dithranol) m/z $[M + Na]^+$. Calcd: 1105.2. Found: 1106.0.

(3) Synthesis of Dendrimer Porphyrins Free Bases. (i) Preparation of *p*-[G1]TPPH$_2$. To a distilled THF solution (5 mL) of a mixture of 3,5-dimethoxybenzoic acid (273 mg, 1.5 mmol), 5,10,15,20-tetrakis-(4′-hydroxyphenyl)-21*H*,23*H*-porphine (182 mg, 0.268 mmol), and DPTS (44.2 mg, 0.15 mmol) was added DCC (330 mg, 1.6 mmol) under Ar at room temperature. The reaction mixture was stirred overnight at room temperature and then evaporated to dryness under reduced pressure at room temperature, and the residue was chromatographed on silica gel with $CHCl_3$ as eluent. A fraction containing the desired product was isolated and evaporated to dryness under reduced pressure at room temperature, and the residue dissolved in $CHCl_3$ containing 2-PrOH (10%) was crystallized with hexane, to give 5,10,-15,20-tetrakis[4′-(3″,5″-dimethoxybenzoyloxy)phenyl]-21*H*,23*H*-porphine (*p*-[G1]TPPH$_2$) as a purple powder in 78% yield (278 mg). ^{1}H NMR (270.05 MHz; $CDCl_3$; 20 °C; ppm): δ −2.79 (s, 2H), 3.40 (s, 24H), 6.80 (t, 4H, J = 2.4 Hz), 7.52 (d, 8H, J = 2.4 Hz), 7.62 (d, 8H, J = 8.4 Hz), 8.28 (d, 8H, J = 8.4 Hz), 8.93 (s, 8H). ^{13}C NMR (125.65 MHz; $CDCl_3$; 45 °C; ppm): δ 55.8, 106.6, 107.9, 119.2, 119.9, 131.4, 135.2, 139.6, 150.8, 160.8, 164.8. MALDI-TOF-MS (dithranol) m/z $[M]^+$. Calcd: 1335.4. Found: 1335.2. UV−vis ($CHCl_3$; λ_{max} (nm)): 257, 309 (sh), 419, 515, 552, 590, 647.

(ii) Preparation of *p*-[G2]TPPH$_2$. To a distilled THF solution (5 mL) of a mixture of [G1]poly(aryl ester)−CO_2H dendron (724 mg, 1.50 mmol), 5,10,15,20-tetrakis(4′-hydroxyphenyl)-21*H*,23*H*-porphine (182 mg, 0.268 mmol), and DPTS (1.32 g, 4.5 mmol) was added DCC (330 mg, 1.6 mmol) under Ar at room temperature. The reaction mixture was stirred overnight at room temperature and then evaporated to dryness under reduced pressure at room temperature, and the residue was chromatographed on silica gel with $CHCl_3$ as eluent and subjected to SEC with $CHCl_3$ as eluent. A fraction containing the desired product was isolated and evaporated to dryness under reduced pressure at room temperature, and the residue dissolved in $CHCl_3$ containing 2-PrOH (10%) was crystallized with hexane, to give 5,10,15,20-tetrakis{4′-[3″,5″-bis(3‴,5‴-dimethoxybenzoyloxy)benzoyloxy]pheny l}-21*H*,-23*H*-porphine (*p*-[G2]TPPH$_2$) as a purple powder in 96% yield (654 mg). ^{1}H NMR (270.05 MHz; $CDCl_3$; 20 °C; ppm): δ −2.80 (s, 2H), 3.89 (s, 48H), 6.76 (t, 8H, J = 2.2 Hz), 7.38 (d, 16H, J = 2.2 Hz), 7.56 (t, 4H, J = 2.2 Hz), 7.65 (d, 8H, J = 8.1 Hz), 8.18 (d, 8H, J = 2.2 Hz), 8.28 (d, 8H, J = 8.1 Hz), 8.93 (s, 8H). ^{13}C NMR (125.65 MHz; $CDCl_3$; 45 °C; ppm): δ 55.8, 106.9, 107.9, 119.1, 119.8, 121.0, 121.2, 130.6, 131.9, 135.3, 139.8, 150.6, 151.5, 160.8, 163.4, 164.2. MALDI-TOF-MS (dithranol) m/z $[M + Na]^+$. Calcd: 2534.7. Found: 2534.6. UV−vis ($CHCl_3$; λ_{max} (nm)): 257, 307 (sh), 419, 515, 550, 590, 647.

(iii) Preparation of *p*-[G3]TPPH$_2$. To a distilled THF solution (2 mL) of a mixture of [G2]poly(aryl ester)−CO_2H dendron (812 mg, 0.75 mmol), 5,10,15,20-tetrakis(4′-hydroxyphenyl)-21*H*,23*H*-porphine (91 mg, 0.134 mmol), and DPTS (12.2 mg, 0.10 mmol) was added DCC (165 mg, 0.80 mmol) under Ar at room temperature. The reaction mixture was stirred for 90 min at room temperature and then evaporated to dryness under reduced pressure at room temperature. The residue was chromatographed on silica gel with $CHCl_3$ as eluent and subjected to SEC with $CHCl_3$ as eluent. A fraction containing the desired product was isolated and evaporated to dryness under reduced pressure at room temperature, and the residue dissolved in $CHCl_3$ containing 2-PrOH (10%) was crystallized with hexane, to give 5,10,15,20-tetrakis(4′-{3″,5″-bis[3‴,5‴-bis(3⁗,5⁗-dimethoxybenzoyloxy)benzoyloxy]-benzoyloxy}phenyl)-21*H*,23*H*-porphine (*p*-[G3]TPPH$_2$) as a purple powder in 93% yield (618 mg). ^{1}H NMR (270.05 MHz; $CDCl_3$; 20 °C; ppm): δ −2.81 (s, 2H), 3.86 (s, 96H), 6.73 (t, 16H, J = 2.4 Hz), 7.35 (d, 32H, J = 2.4 Hz), 7.53 (t, 8H, J = 2.2 Hz), 7.61 (t, 4H, J = 2.2 Hz), 7.65 (d, 8H, J = 8.5 Hz), 8.07 (d, 16H, J = 2.2 Hz), 8.28 (d, 8H, J = 8.5 Hz), 8.92 (s, 8H). ^{13}C NMR (125.65 MHz; $CDCl_3$; 45 °C; ppm): δ 55.8, 106.9, 107.9, 119.1, 119.7, 120.8, 121.1, 121.1, 121.5, 130.5, 131.0, 132.1, 135.3, 139.8, 150.5, 151.2, 151.5, 160.7, 162.7, 163.1, 164.1. MALDI-TOF-MS (dithranol) m/z $[M]^+$. Calcd: 4938.4. Found: 4938.5. UV−vis ($CHCl_3$; λ_{max} (nm)): 312 (sh), 419, 515, 550, 590, 647.

(iv) Preparation of *m*-[G1]TPPH$_2$. To a distilled THF solution (5 mL) of a mixture of 3,5-dimethoxybenzoic acid (1.63 g, 1.5 mmol), 5,10,15,20-tetrakis(3′,5′-dihydroxyphenyl)-21*H*,23*H*-porphine (100 mg, 0.134 mmol), and DPTS (44 mg, 0.15 mmol) was added DCC (330 mg, 1.6 mmol) under Ar at room temperature. The reaction mixture was stirred overnight at room temperature and then evaporated to dryness under reduced pressure at room temperature. The residue was chromatographed on silica gel with CH_2Cl_2 as eluent and then subjected to SEC with $CHCl_3$ as eluent. A fraction containing the desired product was isolated and evaporated to dryness under reduced pressure at room temperature, and the residue dissolved in $CHCl_3$/2-PrOH (10%) was

crystallized with hexane, to give 5,10,15,20-tetrakis[3′,5′-bis(3″,5″-dimethoxybenzoyloxy)phenyl]-21*H*,23*H*-porphine (*m*-[G1]TPPH$_2$) as a purple powder in 80% yield (221 mg). ^{1}H NMR (270.05 MHz; $CDCl_3$; 20 °C; ppm): δ −2.90 (s, 2H), 3.84 (s, 48H), 6.70 (t, 8H, J = 2.4 Hz), 7.41 (d, 16H, J = 2.4 Hz), 7.66 (t, 4H, J = 2.2 Hz), 8.04 (d, 8H, J = 2.2 Hz), 9.15 (s, 8H). ^{13}C NMR (125.65 MHz; $CDCl_3$; 45 °C; ppm): δ 55.7, 106.9, 107.8, 115.3, 118.3, 125.7, 131.1, 143.8, 149.8, 160.8, 164.7. MALDI-TOF-MS (dithranol) m/z $[M]^+$. Calcd: 2054.6. Found: 2053.9. UV−vis ($CHCl_3$; λ_{max} (nm)): 259, 310, 420, 515, 551, 589, 645.

(v) Preparation of *m*-[G2]TPPH$_2$. To a distilled THF solution (5 mL) of a mixture of [G1]poly(aryl ester)−CO_2H dendron (724 mg, 1.5 mmol), 5,10,15,20-tetrakis(3′,5′-dihydroxyphenyl)-21*H*,23*H*-porphine (100 mg, 0.134 mmol), and DPTS (1.32 g, 4.5 mmol) was added DCC (330 mg, 1.6 mmol) under Ar at room temperature. The reaction mixture was stirred overnight at room temperature and then evaporated to dryness under reduced pressure at room temperature. The residue was chromatographed on silica gel with CH_2Cl_2 as eluent and subjected to SEC with $CHCl_3$ as eluent. A fraction containing the desired product was isolated and evaporated to dryness under reduced pressure at room temperature, and the residue dissolved in $CHCl_3$/2-PrOH (10%) was crystallized with hexane, to give 5,10,15,20-tetrakis{3′,5′-bis[3″,5″-bis(3‴,5‴-dimethoxybenzoyloxy)benzoyloxy] phenyl}-21*H*,23*H*-porphine (*m*-[G2]TPPH$_2$) as a purple powder in 88% yield (523 mg). ^{1}H NMR (270.05 MHz; $CDCl_3$; 20 °C; ppm): δ −2.90 (s, 2H), 3.79 (s, 96H), 6.66 (t, 16H, J = 2.4 Hz), 7.28 (d, 32H, J = 2.4 Hz), 7.48 (t, 8H, J = 2.2 Hz), 7.70 (t, 4H, J = 2.2 Hz), 8.06 (m, 24H), 9.11 (s, 8H). ^{13}C NMR (125.65 MHz; $CDCl_3$; 45 °C; ppm): δ 55.7, 106.9, 107.7, 114.9, 118.0, 120.9, 121.2, 125.5, 130.5, 131.4, 143.9, 149.4, 151.4, 160.6, 163.0, 164.0. MALDI-TOF-MS (dithranol) m/z $[M + H]^+$. Calcd: 4458.1. Found: 4458.1. UV−vis ($CHCl_3$; λ_{max} (nm)): 256, 309 (sh), 420, 514, 548, 589, 647.

(vi) Preparation of *m*-[G3]TPPH$_2$. To a distilled THF solution (10 mL) of a mixture of [G2]poly(aryl ester)−CO_2H dendron (3.25 g, 3.0 mmol), 5,10,15,20-tetrakis(3′,5′-dihydroxyphenyl)-21*H*,23*H*-porphine (200 mg, 0.268 mmol), and DMAP (49 mg, 0.40 mmol) was added DCC (660 mg, 3.2 mmol) under Ar at room temperature. The reaction mixture was stirred for 45 min at room temperature and then evaporated to dryness under reduced pressure at room temperature. The residue was chromatographed on silica gel with CH_2Cl_2 as eluent and subjected to SEC with $CHCl_3$ as eluent. A fraction containing the desired product was isolated and evaporated to dryness under reduced pressure at room temperature, and the residue dissolved in $CHCl_3$/2-PrOH (10%) was crystallized with hexane, to give 5,10,15,20-tetrakis(3′,5′-bis{3″,5″-bis[3‴,5‴-bis(3⁗,5⁗-dimethoxybenzoyloxy)benzoyloxy]benzoyloxy}-phenyl)-21*H*,23*H*-porphine (*m*-[G3]TPPH$_2$) as a purple powder in 79% yield (3.12 g). ^{1}H NMR (270.05 MHz; $CDCl_3$; 20 °C; ppm): δ −2.90 (s, 2H), 3.75 (s, 192H), 6.62 (t, 32H, J = 2.2 Hz), 7.22 (d, 64H, J = 2.2 Hz), 7.43 (t, 16H, J = 2.2 Hz), 7.49 (t, 8H, J = 2.2 Hz), 7.73 (t, 4H, J = 2.2 Hz), 7.91 (m, 24H), 8.07 (d, 16H, J = 2.2 Hz), 9.11 (s, 8H). ^{13}C NMR (125.65 MHz; $CDCl_3$; 45 °C; ppm): δ 55.6, 106.7, 107.7, 114.9, 118.1, 120.7, 120.8, 120.9, 121.2, 125.6, 130.4, 130.8, 131.5, 143.8, 149.3, 151.0, 151.2, 160.5, 162.4, 162.7, 163.8. MALDI-TOF-MS (dithranol) m/z $[M]^+$. Calcd: 9262.3. Found: 9262.1. UV−vis ($CHCl_3$; λ_{max} (nm)): 312 (sh), 421, 516, 550, 589, 646.

(4) Synthesis of Cobalt(II) Porphyrin Complexes. General Procedure. To a $CHCl_3$ solution of a free-base porphyrin (1.3 mM) and a saturated EtOH solution of anhydrous Co(OAc)$_2$ were mixed at a 1:0.15 volume ratio, and the solution was stirred at room temperature until it became nonfluorescent. Then, the reaction mixture was evaporated to dryness under reduced pressure at room temperature, and the residue was chromatographed on silica gel with $CHCl_3$ as eluent, where a fraction containing the desired product was isolated and evaporated to dryness under reduced pressure at room temperature. The residue was dissolved in $CHCl_3$ and crystallized with 2-PrOH, to give a dendrimer porphyrin cobalt(II) complex as a dark purple powder.

(i) Preparation of (*p*-[G1]TPP)Co^{II}. Using *p*-[G1]TPPH$_2$ (20 mg, 15 μmol), {5,10,15,20-tetrakis[4′-bis(3″,5″-dimethoxybenzoyloxy)-phenyl]porphinato}cobalt(II) ((*p*-[G1]TPP)Co^{II}) was obtained in 72% yield (15 mg). ^{1}H NMR (270.05 MHz; $CDCl_3$; 20 °C; ppm): δ 4.33 (s, 24H), 7.16 (s, 4H), 8.33 (s, 8H), 9.81 (s, 8H), 13.20 (br s, 8H), 15.98 (br s, 8H). MALDI-TOF-MS (dithranol) m/z $[M]^+$. Calcd: 1392.3. Found: 1392.2. UV−vis ($CHCl_3$; λ_{max} (nm)): 259, 309 (sh), 412, 530.

(ii) Preparation of (*p*-[G2]TPP)Co^{II}. Using *p*-[G2]TPPH$_2$ (205 mg, 80.8 μmol), (5,10,15,20-tetrakis{4′-bis[3″,5″-bis(3‴,5‴-dimethoxybenzoyloxy)benzoyloxy]phenyl}porphinato)cobalt(II) ((*p*-[G2]TPP)Co^{II}) was obtained in 83% yield (173.9 mg). ^{1}H NMR (270.05 MHz; $CDCl_3$; 20 °C; ppm): δ 4.04 (s, 48H), 6.84 (s, 8H), 7.62 (s, 16H), 7.93 (s, 4H), 9.01 (d, 8H, J = 1.4 Hz), 9.84 (s, 8H), 13.18 (br s, 8H), 15.97 (br s, 8H). MALDI-TOF-MS (dithranol) m/z $[M]^+$. Calcd: 2591.6. Found: 2591.3. UV−vis ($CHCl_3$; λ_{max} (nm)): 260, 309 (sh), 412, 528.

(iii) Preparation of (*p*-[G3]TPP)Co^{II}. Using *p*-[G3]TPPH$_2$ (130 mg, 26.0 μmol), [5,10,15,20-tetrakis(4′-{3″,5″-bis[3‴,5‴-bis(3⁗,5⁗-dimethoxybenzoyloxy)benzoyloxy]benzoyloxy}phenyl)porphinato]cobalt-(II) ((*p*-[G3]TPP)Co^{II}) was obtained in 91% yield (120 mg). ^{1}H NMR (270.05 MHz; $CDCl_3$; 20 °C; ppm): δ 3.94 (s, 96H), 6.80 (t, 16H, J = 2.4 Hz), 7.49 (d, 32H, J = 2.4 Hz), 7.70 (t, 8H, J = 2.2 Hz), 7.98 (t, 4H, J = 1.9 Hz), 8.36 (d, 16H, J = 2.2 Hz), 9.01 (d, 8H, J = 1.9 Hz), 9.81 (s, 8H), 13.16 (br s, 8H), 15.91 (br s, 8H). MALDI-TOF-MS (dithranol) m/z $[M]^+$. Calcd: 4995.4. Found: 4995.3. UV−vis ($CHCl_3$; λ_{max} (nm)): 311 (sh), 412, 523.

(iv) Preparation of (*m*-[G1]TPP)Co^{II}. Using *m*-[G1]TPPH$_2$ (20.5 mg, 10 μmol), {5,10,15,20-tetrakis[3′,5′-bis(3″,5″-dimethoxybenzoyloxy)-phenyl]porphinato}cobalt(II) ((*m*-[G1]TPP)Co^{II}) was obtained quantitatively (21.5 mg). ^{1}H NMR (270.05 MHz; $CDCl_3$; 20 °C; ppm): δ 3.91 (s, 48H), 6.74 (s, 8H), 7.96 (s, 16H), 9.53 (s, 4H), 12.8 (br s, 8H), 15.9 (br s, 8H). MALDI-TOF-MS (dithranol) m/z $[M]^+$. Calcd: 2111.5. Found: 2110.9. UV−vis ($CHCl_3$; λ_{max} (nm)): 262, 308, 413, 528.

(v) Preparation of (*m*-[G2]TPP)Co^{II}. Using *m*-[G2]TPPH$_2$ (200 mg, 44.8 μmol), (5,10,15,20-tetrakis{3′,5′-bis[3″,5″-bis(3‴,5‴-dimethoxybenzoyloxy)-benzoyloxy]phenyl}porphinato)cobalt(II) ((*m*-[G2]TPP)Co^{II}) was obtained in 69% yield (140 mg). ^{1}H NMR (270.05 MHz; $CDCl_3$; 20 °C; ppm): δ 3.66 (s, 96H), 6.48 (s, 16H), 7.15 (s, 32H), 7.53 (s, 8H), 8.58 (s, 16H), 9.53 (s, 4H), 12.73 (br s, 8H), 15.86 (br s, 8H). MALDI-TOF-MS (dithranol) m/z $[M + H]^+$. Calcd: 4515.2. Found: 4515.1. UV−vis ($CHCl_3$; λ_{max} (nm)): 257, 311 (sh), 414, 527.

(vi) Preparation of (*m*-[G3]TPP)Co^{II}. Using *m*-[G3]TPPH$_2$ (648 mg, 70.0 μmol), [5,10,15,20-tetrakis(3′,5′-bis{3″,5″-bis[3‴,5‴-bis-(3⁗,5⁗-dimethoxybenzoyloxy)benzoyloxy]benzoyloxy}phenyl)-porphinato]cobalt(II) ((*m*-[G3]TPP)Co^{II}) was obtained in 91% yield (596 mg). ^{1}H NMR (270.05 MHz; $CDCl_3$; 20 °C; ppm): δ 3.68 (s, 192H), 6.54 (br s, 32H), 7.14 (br s, 64H), 7.39 (br s, 16H), 7.57 (br s, 8H), 7.90 (d, J = 1.4 Hz, 32H), 8.65 (br s, 16H), 9.60 (br s, 4H), 12.90 (br s, 8H), 15.89 (br s, 8H). MALDI-TOF-MS (dithranol) m/z $[M]^+$. Calcd: 9319.2. Found: 9319.3. UV−vis ($CHCl_3$; λ_{max} (nm)): 311 (sh), 413, 530.

(5) Reaction of Cobalt(II) Porphyrins with Propargyl Alcohol in the Presence of AIBN. As a typical example, a $CDCl_3$ solution (0.5 mL) of a mixture of [5,10,15,20-tetrakis(3′,5′-bis{3″,5″-bis[3‴,5‴-bis(3⁗,5⁗-dimethoxybenzoyloxy)benzoyloxy]benzoyloxy}phenyl)-porphinato]cobalt(II) ((*m*-[G3]TPP)Co^{II}, 43.7 mg, 4.7 μmol), propargyl alcohol (26.2 μL, 450 μmol), and AIBN (6.57 mg, 40 μmol) was transferred to a NMR tube. After three freeze−pump−thaw cycles, the NMR tube was sealed off under reduced pressure and subjected to ^{1}H NMR spectroscopy at 60 °C. Alkylation products were identified by analogy to the ^{1}H NMR spectral profiles reported in ref 7. After heating for 240 min, degassed MeOH (1 mL) was added to the reaction mixture, and the resulting dark purple precipitate was isolated, washed with degassed MeOH, and dried under reduced pressure at room temperature. Then, the residue was subjected to SEC with $CHCl_3$ as eluent, where a fraction containing the desired product was isolated and evaporated to dryness under reduced pressure at room temperature to give 2-(1-

hydroxy-2-propenyl)[5,10,15,20-tetrakis(3′,5′-bis{3″,5″-bis[3‴,5‴-bis-(3⁗,5⁗-dimethoxybenzoyloxy)benzoyloxy]benzoyloxy}phenyl)-porphinato]cobalt(III) ((*m*-[G3]TPP)Co^{III}−C(=CH_2)CH_2OH) as a dark purple powder. ^{1}H NMR (270.05 MHz; $CDCl_3$; 20 °C; ppm): δ −2.41 (br d, J = 2.7 Hz, 1H), −1.88 (d, J = 6.5 Hz, 2H), −1.24 (t, J = 6.5 Hz, 1H, OH), −0.22 (br d, J = 2.7 Hz, 1H), 3.76 (s, 192H), 6.62 (t, J = 2.2 Hz, 32H), 7.23 (d, J = 2.2 Hz, 64H), 7.44 (t, J = 2.2 Hz, 16H), 7.51 (t, J = 2.2 Hz, 8H), 7.73 (t, J = 2.2 Hz, 4H), 7.92 (br s, 32H), 8.07 (m, 24H), 9.10 (s, 8H). UV−vis ($CHCl_3$; λ_{max} (nm)): 310 (sh), 414, 531.

(6) Reaction of (*m*-[G3]TPP)Co^{II} with Propargyl Alcohol in the Presence of AIBN-d_{12}. The reaction was carried out with AIBN-d_{12} (7.05 mg, 40 μmol) under otherwise identical conditions to the above. A fraction containing cobalt porphyrin species was isolated from the reaction mixture by precipitation with degassed MeOH, followed by SEC with $CHCl_3$ as eluent, in a manner similar to the case using nondeuterated AIBN.

JA020687I