Dendritic Bis(oxazoline)copper(II) Catalysts. 2.[1] Synthesis, Reactivity, and Substrate Selectivity

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Received February 28, 1997[⊗]

A series of dendritic bis(oxazoline) ligands **1**−**4** were synthesized to evaluate the effects of the degree of branching of a dendritic sector on both the reactivity and selectivity of their corresponding copper(II) complex-catalyzed Diels−Alder reaction between cyclopentadiene and a crotonyl imide. Kinetic studies unveiled a two-step mechanism of the Diels−Alder reaction, in which a reversible binding of the dienophile to the copper complex was followed by a rate-determining reaction between the resulting dienophile−catalyst complex with the diene. Furthermore, two interesting features emerged: first, the formation constant of the dienophile−catalyst complex decreased gradually on going from the lower to higher generations, and secondly, while the Diels−Alder reaction rate constant remained essentially the same from the zeroth to second generation catalysts, it dropped abruptly for the third generation one. These observations were rationalized as a consequence of a folding-back of the dendritic sectors toward the catalytic unit at the third generation, so that increase in steric size impeded both the reactivity and binding profiles of the catalytic system. This behavior was reminiscent of related phenomena observed by others from solvatomatic, photophysical, and viscosity studies. In line with this reasoning, a slight but noticeable substrate selectivity was observed for the third generation catalyst, which was absence for the lower ones, in competitive kinetic studies involving two dienophiles of different steric sizes.

Introduction

The design of catalyst systems to mimic enzyme functions has been a topic of current interest. Enzyme molecules, in contrast to man-made catalysts, are unique not only for their high substrate- and enantioselectivities but also for their efficiency in catalyzing reactions with extremely fast turnover rates. It is well documented that the supremacy of enzyme catalysts lies in their well-defined three dimensional structures. The creation of an active site within a large enzyme molecule provides the requisite geometry which holds the reacting partners in close proximity, thereby facilitating their union at extremely fast rates, while the size and shape of this catalytic pocket control the substrate- and enantioselectivity of enzymatic transformation.

Recent progress in various areas in host−guest chemistry have enabled chemists to design receptor or host molecules approaching enzyme−substrate binding efficiency.[2] When a catalytic center is assembled into a receptor molecule, an artificial enzyme model is produced. A number of successful enzyme models have been reported which are invariably small molecules with considerably sophisticated internal structures.[3] On the other hand, polymer chemists have long been engaging in efforts to incorporate catalytic unit(s) into a polymer structure, in hope that a properly fabricated polymer chain may impart onto the catalytic sectors higher reactivity and selectivity.[4] Obviously, the additional advantage of using polymer-supported catalysts is the ready recoverability of the catalyst system, which often simplifies product separation.

Enzyme molecules are unique in that they are homogenous, monodisperse macromolecular catalysts with well-defined three-dimensional topology in sharp contrast to the heterogeneous, polydisperse polymer-supported catalysts. Their well-defined three-dimensional structures combined with their monodispersity allow enzyme molecules to exert powerful substrate- and enantioselective control. While enzyme molecules are designed by nature and synthesized *in vivo* with high efficiency, it is extremely difficult, if not impossible, for chemists to prepare monodisperse and structurally defined polymer catalysts.

Recent success in reactions promoted by soluble polymer-bound catalysts,[5] especially in light of their improved reactivity and selectivity, has prompted us to look into the similar uses of soluble dendritic catalysts. An attractive feature of dendrimers is that they can be prepared with controllable topology and with specific functionalities located at predetermined positions within the dendritic matrix.[6] Furthermore, dendrimers can also be specifically engineered with certain physical and chemical properties so as to allow possibilities in fine-tuning of catalytic activity and selectivity. As a result, the idea of incorporating catalytic centers into a dendritic structure to produce catalytic dendrimers with high

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⊗ Abstract published in *Advance ACS Abstracts,* June 15, 1997.

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S0022-3263(97)00383-6 CCC: $14.00

reactivity and selectivity has been one of the long-standing goals in dendrimer chemistry.

At the outset of the present work, only a few catalytic dendrimers were known.[7−12] They were assembled by either one or two approaches. The first involved the attachment of a dendritic sector(s) to a single catalytic moiety followed by the study of its influence on catalyst reactivity and selectivity. The second approach entailed the deployment of multiple catalytic units onto a dendritic matrix and the subsequent scrutiny for signs of cooperativity among these catalytic units. Notwithstanding the dissimilarity of these two approaches, both of them address the singular issues in catalytic chemistry, namely, reactivity and selectivity.

Some years ago Brunner[7] reported the preparation of a series of low generation chiral dendrimers containing a catalytic diphos rhodium complex unit. Interestingly, the resulting catalytic dendrimers not only preserve their catalytic activity but display enhanced reactivity. However, the structure−reactivity issue was not pursued in detail. Ford[8] was first to capitalize on the "multiple catalytic centers" concept and designed a series of polyether-based catalytic dendrimers terminated with multiple quaternary ammonium ions which were capable of promoting unimolecular decarboxylation of 6-nitrobenzisoxazole-3-carboxylate. Positive cooperative reactivity was observed for the higher generation catalysts which was not present in lower generation analogs. Shortly afterward, DuBois[9] and van Koten[10] described the properties of two different series of multicenter dendritic catalysts but were unable to detect any positive cooperativity in them. On the other hand, the substrate selectivity issue was addressed by Moore in a study of a number of dendritic porphyrin-based catalysts.[11] It was noted that substrate selectivity was higher for the higher generation dendritic catalysts. All these developments suggested that dendritic catalysts rivaled polymer-support catalysts in terms of manipulability of their physical, chemical, and topological properties and had the potential to become an alternative type of insoluble or soluble catalysts.

Until recently there were few studies on the effect of a dendritic sector on the reactivity and selectivity of single-center catalytic systems. Earlier we disclosed[1] the synthesis of a series of dendritic bis(oxazoline) ligand **1**−**4** and demonstrated that the reactivity and substrate binding profile of their corresponding metal complex-catalyzed Diels−Alder reaction were strongly dependent upon the size of the dendritic sector in a manner that the substrate binding ability deteriorated with increasing size of the dendritic fragment, and that a sudden change of catalyst conformation and reactivity occurred from the second to the third generation. These initial findings provided the foundations of the work described in this paper. Reported herein are additional findings on the substrate selectivity of this novel series of dendritic catalysts, together with the full details of their synthesis. Our experimental results showed that the substrate selectivity was again higher for the third generation dendritic catalyst, whereas the first generation analog exhibited indistinguishable substrate selectivity as that of a nondendritic compound, an observation that is in line with the sudden change of dendrimer conformation at the third generation reported earlier by us.[1]

Results and Discussions

1. Synthesis. The catalytic moiety chosen for this study is a bis(oxazoline) ligand, metal complexes[12] of which are a well established class of catalysts capable of promoting reactions such as cyclopropanation of olefins and the Diels−Alder reaction. The dendritic fragments employed to modulate the reactivity and properties of the catalytic core are the known polyether dendritic sectors **5**−**8**.[13] Two approaches were regarded to be viable for anchoring the dendritic units onto the catalytic moiety (Scheme 1). One involved the direct coupling of a pivotal bis(oxazolinyl) dibromide **9** to two equiv of dendritic phenol [Gn]-OH **5**−**8**. Alternatively, one could first attach the dendritic phenol to a bis(hydroxyethyl)amido dibromide **10** and subsequently cyclize the diamide to the desired bis(oxazoline). Demurred at the likelihood of self *N*-alkylation in a molecule such as **9**, we decided to take the latter approach.

The synthetic operation entailed the initial preparation of the central core **10** and the attachment to it of the various generation dendritic sectors **5**−**8**. Construction of the core began with the readily available 4-(benzyloxy)-benzyl alcohol **11** (Scheme 2). Treatment of the alcohol with concentrated hydrobromic acid in glacial acetic acid afforded the corresponding benzyl bromide **12** as a white solid in 64% yield. Di-*C*-alkylation of diethyl malonate with 2.1 mol equiv of bromide **12** (NaH, THF) furnished the diester **13** as an oil in 74% yield. Alkaline hydrolysis of **13** in aqueous ethanol resulted in the formation of a separable mixture of the decarboxylated monoacid **14** (27%) and the desired diacid **15** (65%). However, prolonged heating of the reaction mixture led to the predominant formation of the decarboxylation product **14**. Conversion of diacid **15** to the corresponding diacyl chloride with oxalyl chloride in DMF, followed by quenching with excess 2-ethanolamine gave diamide **16** as a white solid in 69% yield. At this point the benzyl protective groups were dismantled by hydrogenolysis to give bisphenol **17**, which was then *O*-alkylated to give dibromide **10** in a combined yield of 69% by reaction with excess 1,3-dibromopropane in the presence of anhydrous K_2CO_3 in acetone.

The structures of the compounds in Scheme 2 were characterized by NMR and MS techniques. Thus, for the diester **13**, the unique ^{1}H-NMR resonance signal of the oxygenated benzylic protons at δ 5.03 together with the singlet at δ 3.15 ascribable to the benzylic protons adjacent to the quaternary carbon confirmed its structure. The ^{1}H-NMR spectrum of monoacid **14** gave a set of complex resonance signals at δ 2.50−3.10 while that of the symmetric diacid **15** exhibited a simple singlet at δ 3.22 diagnosed as the benzylic protons adjacent to the quaternary carbon. The structural identity of diamide **16** was established by its ^{1}H-NMR spectrum which showed two characteristic quartets at δ 3.31 and 3.56

(7) Brunner, H. *J. Organomet. Chem.* **1995**, *500*, 39−46.
(8) Lee, J.-J.; Ford, W. T.; Moore, J. A.; Li, Y. *Macromolecules* **1994**, *27*, 4632−4634.
(9) Miedaner, A.; Curtis, C. J.; Barkley, R. M.; DuBois, D. L. *Inorg. Chem.* **1994**, *33*, 5482−5490.
(10) Knapen, J. W. J.; van der Made, A. W.; de Wilde, J. C.; van Leeuwen, P. W. N. M.; Wijkens, P.; Grove, D. M.; van Koten, G. *Nature* **1994**, *372*, 659−663.
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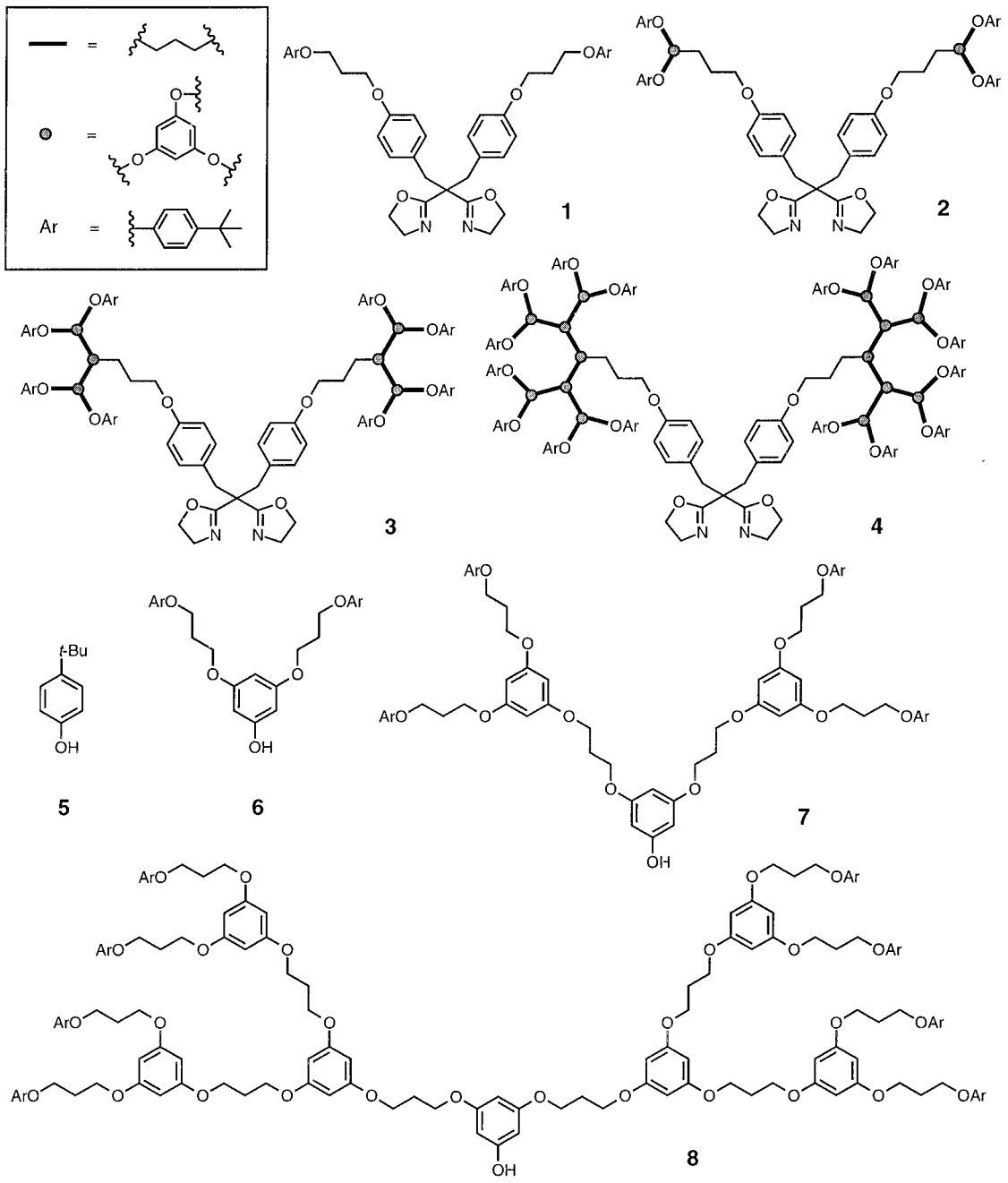
(12) For a review, see Pfaltz, A. *Acc. Chem. Res.* **1993**, *26*, 339−345.
(13) Chow, H.-F.; Chan, I. Y.-K.; Mak, C. C.; Ng, M.-K. *Tetrahedron* **1996**, *52*, 4277−4290.

Chart 1

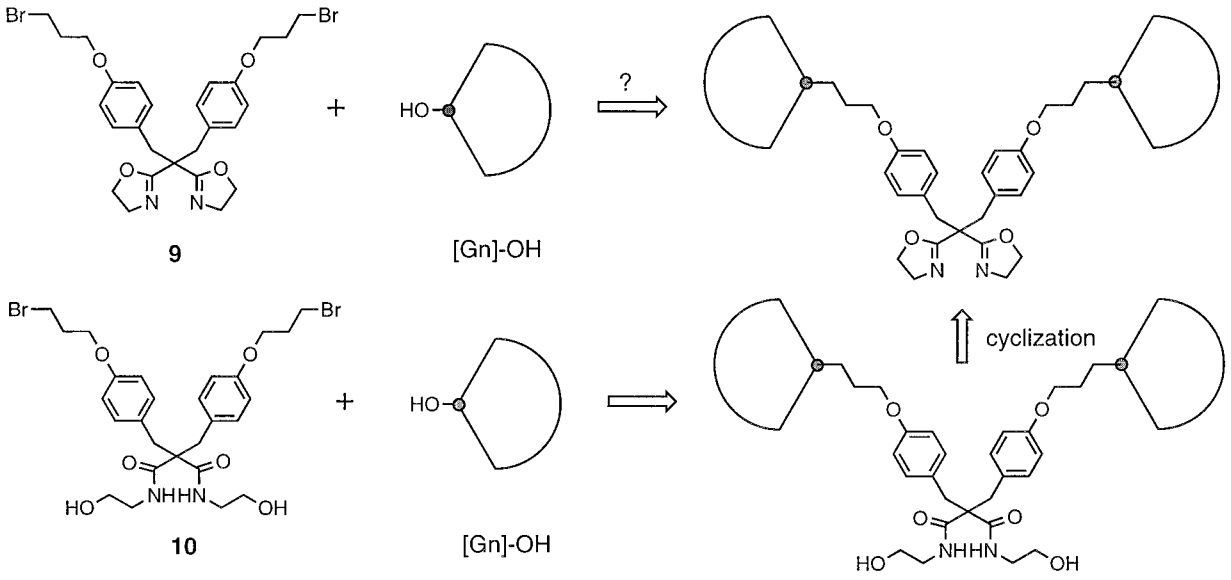


attributable to the methylene protons adjacent to the nitrogen atom and hydroxyl group, respectively. The presence of a triplet at δ 7.69 provided evidence for the presence of the nitrogen-bonded hydrogen. The successful deprotection of the benzyl groups from **16** was readily confirmed by the absence of the signal for the oxygenated benzylic proton at δ 5.00 and the signal for the corresponding benzylic carbon at δ 69.9 in the ^{1}H- and ^{13}C-NMR spectra, respectively, which were present in those of compound **15**. For diamide **10**, its structure was supported by a distinct quintet at δ 2.29 for the central methylene protons of the three-carbon linker. Mass spectra data provided additional evidence for the molecular identities of all the aforementioned compounds.

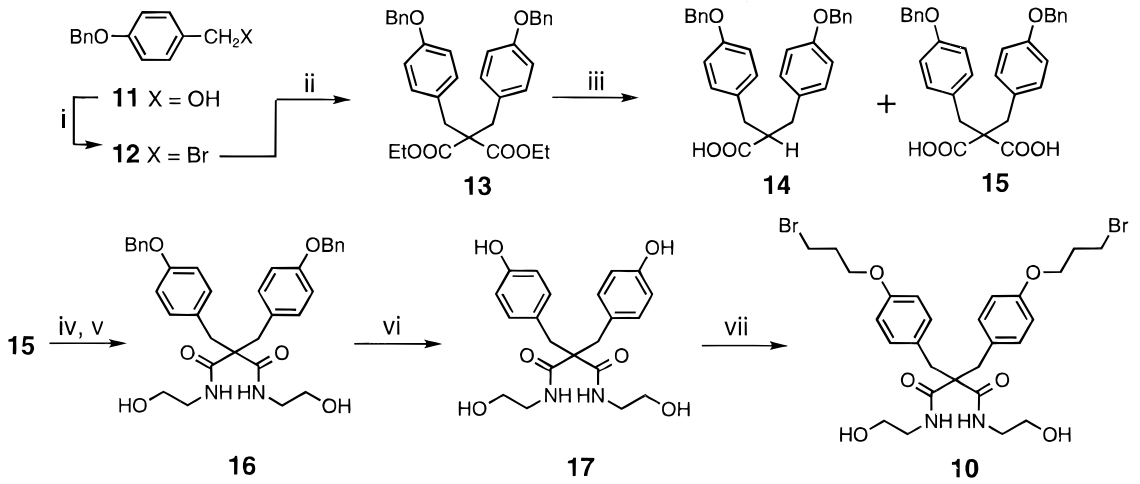
With both the catalytic core **10** and the dendritic fragments **5**−**8** on hand, the stage was set for the assemblage of the catalytic core onto the various dendritic sectors (Scheme 3). Reaction of 4-*tert*-butylphenol **5** with dibromide **10** gave the diol **18** in 60% yield. Conversion of the diol **18** into the dibromide **22** using carbon tetrabromide/triphenylphosphine followed by intramolecular cyclization of **22** in the presence of NaOH in EtOH/THF afforded the bis(oxazoline) dendrimer G0 **1** as a pale yellow liquid in 43% overall yield from **10**. In a similar manner, coupling of the higher generation polyether dendritic sectors **2**−**4** onto **10** followed by bromination/cyclization furnished the higher generation dendritic ligands **2**−**4** in 46, 25, and 27% overall yields from **10**, respectively.

It should be noted that the bromination and cyclization steps of the above reaction sequence take place at the site of the catalytic core against a landscape of dendritic sectors which expands with each upward generation. Therefore, the appraisal of the success of these reactions by NMR methods was not expected to be easy at high generations, owing to the disproportionality in intensity of the relevant signals. Fortunately, the methylene protons at the reaction site displayed triplets at measur-

Scheme 1. Preparation of Dendritic Bis(oxazoline) Ligands



Scheme 2[a]

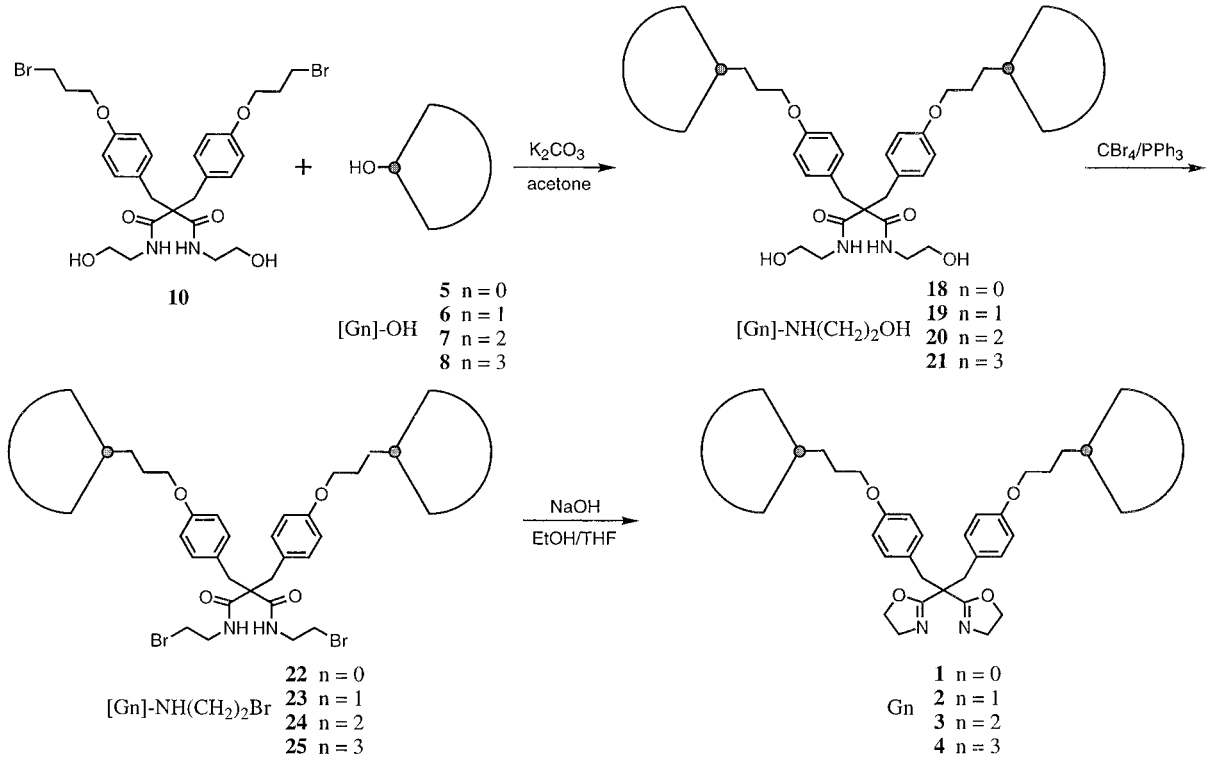


[a] (i) HBr, HOAc; (ii) NaH (2 eq), diethyl malonate, THF; (iii) NaOH, H_2O/EtOH; (iv) DMF, $(COCl)_2$; (v) ethanolamine; (vi) H_2, 10% Pd-C; (vii) 1,3-dibromopropane, K_2CO_3, acetone.

ably different chemical shift values for the series of diols [Gn]-$NHCH_2CH_2OH$ (δ ~3.6), dibromides [Gn]-$NHCH_2CH_2Br$ (δ ~3.3) and bis(oxazoline) Gn (δ ~4.2, CH_2O), which were not obscured by the ^{1}H-NMR signals arising from the dendritic sectors. In addition, the diols **18**−**21**, dibromides **22**−**25**, and bis(oxazoline)s **1**−**4** all displayed significantly different TLC mobilities so that monitoring of the progress of the reactions could be carried out with ease. The *tert*-butyl groups on the surface sector served as markers for the dendrimer generation of these molecules. Therefore, by focusing on the relative intensities of the *tert*-butyl signals at δ ~1.3 and the oxygenated methylene signal at δ ~3.6 of compounds **18**−**21**, one could ascertain whether two dendritic sectors had been incorporated. For example, experimental integration ratios for these two signals for the diols **18**−**21** (from the zeroth to third generation) of 4.5:1, 8.1:1, 20.7:1, and 36.0:1, respectively, indeed closely matched the theoretical values of 4.5:1, 9:1, 18:1, and 36:1. The successful conversions of the above dendritic diols [Gn]-$NH(CH_2)_2OH$ to the corresponding dibromides [Gn]-$NH(CH_2)_2Br$ were substantiated by the appearance of the distinctive ^{1}H-NMR resonance triplet centered at about δ 3.3 for the methylene protons adjacent to the bromine atoms which were not present in the precursors. In addition, the unique ^{13}C-NMR resonance signals at about δ 31.2 for all the dibromides **22**−**25** was also diagnostic of the carbons adjacent to the bromine atoms.

Upon cyclization to the bis(oxazoline) dendritic ligands **1**−**4**, Gn (n = 0−3), an appreciable downfield shift (from δ 3.5 to δ 3.8) of the triplet signals due to the methylene protons adjacent to the nitrogen atom together with the disappearance of the triplets for the nitrogen-bonded hydrogens were noted. A comparison of the ^{1}H-NMR spectra of dendritic ligands **1**−**4** of different generations showed that the intensities of ^{1}H signals due to the catalytic core decreased gradually with respect to those of the signals arising from the dendritic sectors toward the higher generation ligands. Infrared spectroscopy offered little information since the spectra were overwhelmed by the signals arising from the polyether dendritic sectors. Nevertheless the stretching frequencies at about 1660 cm^{-1} in the IR spectra of G0 **1** and G1 **2** were consistent with the presence of oxazoline C=N bond although this signal could not be observed for the higher generation dendrimers. Additional evidence for the formation of the bis(oxazoline) dendrimers was secured from their satisfactory mass spectra. Thus,

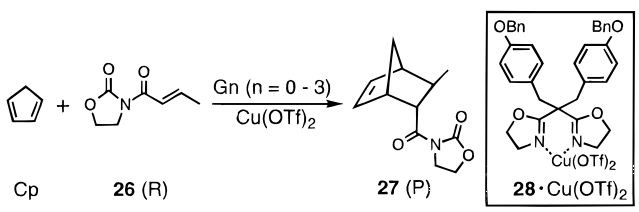
Scheme 3. Schematic Diagram Showing the Synthetic Transformations of the Various Dendritic Sectors 5−8 to the Corresponding Bis(oxazoline) Dendritic Ligands 1−4



dendrimers **1**−**4** showed ions at 747 (M + H^+), 1460 (M + H^+), 2883 (M^+), and 5731 (M^+), respectively, which corresponded to their molecular ion peaks within experimental error.

2. Kinetics and Mechanism of the Dendritic-Complex-Catalyzed Diels−Alder Reaction. Attachment of dendritic sectors to a catalytic center will invariably affect the polarity and steric environment around its vicinity. As a result, its catalytic reactivity and selectivity can be modulated. The successful preparation of the novel series of dendritic ligands **1**−**4** having a single catalytic unit embedded in a dendritic matrix of different sizes provided us the opportunity to probe the microenvironment around the catalytic center, to identify the role of the dendritic sector in this type of single site dendritic catalyst, and to examine their practical usefulness in catalytic chemistry.

Although the bis(oxazoline)copper(II) complex-catalyzed Diels−Alder reaction had been known for some time, little effort was devoted to elucidate the mechanism of this reaction.[14] Hence, the kinetics and mechanism of the Diels−Alder reaction in our study were investigated prior to the study of the effect of dendrimerization on the properties of the catalytic bis(oxazoline) center.



The educts for the Diels−Alder reaction were cyclopentadiene (Cp) and crotonyl imide **26** (R). The dendritic copper(II) catalysts were prepared by stirring a 1:1 mixture of individual dendritic ligand (Gn) and copper(II) triflate in anhydrous dichloromethane under nitrogen until complete dissolution of the solid inorganic copper reagent. The reaction was monitored by UV spectroscopy to ensure complete complexation as all the copper(II) dendritic complexes gave UV spectra with a λ_{max} at approximately 720 nm. As expected, dendritic ligands of higher generations (G2 and G3) required longer time (3−5 h) for complete complexation than did ligands of lower generations (1.5 h). The reaction was conducted by mixing a preformed solution of a ligand−copper(II) triflate complex, Cp, and R in anhydrous dichloromethane, and the resulting solution was stirred at 25.0 ± 0.1 °C. The kinetics were followed by taking aliquots at specified time intervals for gas chromatographic analysis. The starting materials and adduct **27** (P) all possessed different retention times allowing easy assay of their relative concentrations at any particular time interval.

The rate law of the reaction was studied by employing pseudo-order kinetics technique on a nondendritic bis(oxazoline)copper complex **28**·$Cu(OTf)_2$. The pseudo-order conditions were satisfied by keeping concentrations of all but one of the components constant. This condition was automatically fulfilled by the catalyst component because it was continuously regenerated and therefore remained constant during the reaction. The concentrations of the other components were maintained essentially constant by using a large excess of the reagents. Only the initial kinetic data of the reaction with less than 15% product conversion were taken into consideration.

The kinetic results are summarized in Figure 1. It was found that the initial rate of the reaction d[P]/dt was directly proportional to [**28**·$Cu(OTf)_2$] and to [Cp], while a plot of 1/[R] *vs* 1(d[P]/dt) gave a straight line not passing

(14) For discussions on plausible mechanisms: see (a) Evans, D. A.; Miller, S. J.; Lectka, T. *J. Am. Chem. Soc.* **1993**, *115*, 6460−6461. (b) Evans, D. A.; Murry, J. A.; Norcross, R. D.; Miller, S. J. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 798−800.

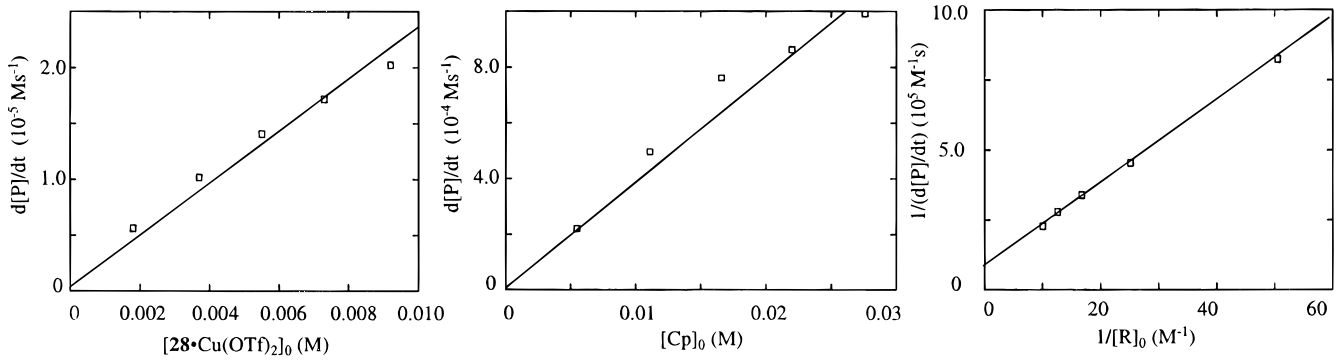


Figure 1. Initial rate of product (P) formation *vs* [**28**·Cu(OTf)$_2$]$_0$ ([R]$_0$ = 0.0843 M, [Cp]$_0$ = 1.52 M) (left). Initial rate of (P) formation *vs* [Cp]$_0$ ([R]$_0$ = 0.32 M, [**28**·Cu(OTf)$_2$]$_0$ = 5.0 mM) (middle). Plot of 1/{d[P]/dt} *vs* 1/[R]$_0$ ([Cp]$_0$ = 2.39 M, [**28**·Cu(OTf)$_2$]$_0$ = 1.22 mM) (right).

through the origin. Hence the rate equation of the Diels–Alder reaction has the form:

$$\frac{d[P]}{dt} = \frac{k_1 k_2 [\mathbf{28}\cdot Cu(OTf)_2][R][Cp]}{k_{-1} + k_1[R]} \quad (1)$$

The rate law is consistent with the mechanism shown in Scheme 4. The copper-containing catalyst **28**·Cu(OTf)$_2$ first forms a 1:1 complex with the dienophile (R). The ligand–dienophile complex **28**·Cu(OTf)$_2$–R can either react with an incoming Cp molecule to form the Diels–Alder adduct (P) with the liberation of a free catalyst **28**·Cu(OTf)$_2$, or dissociate to regenerate the free catalyst and the dienophile.

Applying steady state approximation on the catalyst–dienophile complex **28**·Cu(OTf)$_2$–R, eq 2 can be obtained,[15] where subscript 0 denotes the initial concentrations of the reactants.

$$\frac{d[P]}{dt} = \frac{k_1 k_2 [\mathbf{28}\cdot Cu(OTf)_2]_0[R][Cp]}{k_{-1} + k_1[R] + k_2[Cp]} \quad (2)$$

If the rate of the Diels–Alder reaction between **28**·Cu(OTf)$_2$–R and Cp is slow compared to both the rates of formation and the decomplexation of the **28**·Cu(OTf)$_2$–R complex, *i.e.*, $k_{-1} \gg k_2$[Cp] and k_1[R] $\gg k_2$[Cp], we have

$$\frac{d[P]}{dt} = \frac{k_1 k_2 [\mathbf{28}\cdot Cu(OTf)_2]_0[R][Cp]}{k_{-1} + k_1[R] + k_2[Cp]} \cong \frac{k_1 k_2 [\mathbf{28}\cdot Cu(OTf)_2]_0[R][Cp]}{k_{-1} + k_1[R]} \quad (3)$$

Thus, the initial rate of the reaction becomes:

$$\frac{d[P]}{dt} = v_{init} = \frac{k_1 k_2 [\mathbf{28}\cdot Cu(OTf)_2]_0[R][Cp]}{k_{-1} + k_1[R]} \rightarrow \frac{k_1 k_2 [\mathbf{28}\cdot Cu(OTf)_2]_0[R]_0[Cp]_0}{k_{-1} + k_1[R]_0} \quad (4)$$

Equation 4 is the modified Michaelis–Menten equation for enzyme kinetics and is equivalent to the experimental rate law expressed by eq 1. The binding constant ($K_c = k_1/k_{-1}$) of the bis(oxazoline)copper(II)–dienophile complex and the rate constant k_2 of the Diels–Alder reaction could readily be extrapolated from the Lineweaver–Burk plot,[16] data of which was obtainable by measuring the initial rates of the reaction at different dienophile concentrations [R]$_0$.

Scheme 4. Proposed Mechanism of the Diels–Alder Reaction

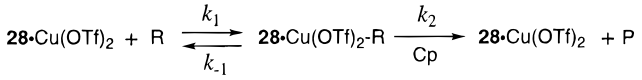


Table 1. K_c and k_2 Values of the Diels–Alder Reactions

catalyst	K_c (M^{-1})	$10^3 k_2$ (M^{-1} s^{-1})
G0·Cu(OTf)$_2$	10.4 ± 0.2	3.3 ± 0.1
G1·Cu(OTf)$_2$	9.8 ± 1.1	3.3 ± 0.3
G2·Cu(OTf)$_2$	7.8 ± 1.1	3.2 ± 0.4
G3·Cu(OTf)$_2$	5.7 ± 0.5	1.9 ± 0.2

The effect of the various dendritic fragments on the catalytic reactivity and binding capability was addressed by looking at the binding and rate constants of the various dendritic ligand–copper(II) complex-catalyzed reactions (Table 1 and Figure 2). In comparing the binding constants (K_c) and the rate constants (k_2) of the different dendrimer-catalyzed reactions, two important findings were noteworthy. First, the binding constant decreased with increasing dendrimer generation. The destablization could be attributed to an increased distortion of the catalyst–dienophile complex (Gn·Cu(OTf)$_2$–R) from its optimal geometry as a result of the increasing steric repulsion between the two large dendritic sectors at the higher generations. Secondly, the rate constant k_2 for the Diels–Alder reaction remained essentially constant from the zeroth to the second generation catalysts, but dropped suddenly at the third generation. This rate-determining process involved the Diels–Alder reaction between the catalyst–dienophile complex and Cp, and the rate should be controlled by the steric accessibility of the catalytic cavity. The sudden drop of k_2 for the G3 catalyst can be ascribed to a sudden change of the steric environment around the catalytic cavity from the second to the third generation. We postulated that the catalytic core which was essentially open to the surroundings at G0–G2 became partially buried in the interior of the dendritic matrix at G3. For the lower generation catalytic dendrimers, the two dendritic sectors are capable of disposing themselves in such a way so as to avoid steric repulsion between them and to allow the catalytic core to be exposed to the surroundings. Con-

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(16) Segel, I. H. *Enzyme Kinetics*; John Wiley & Sons, Inc.: New York, 1975; p 46.

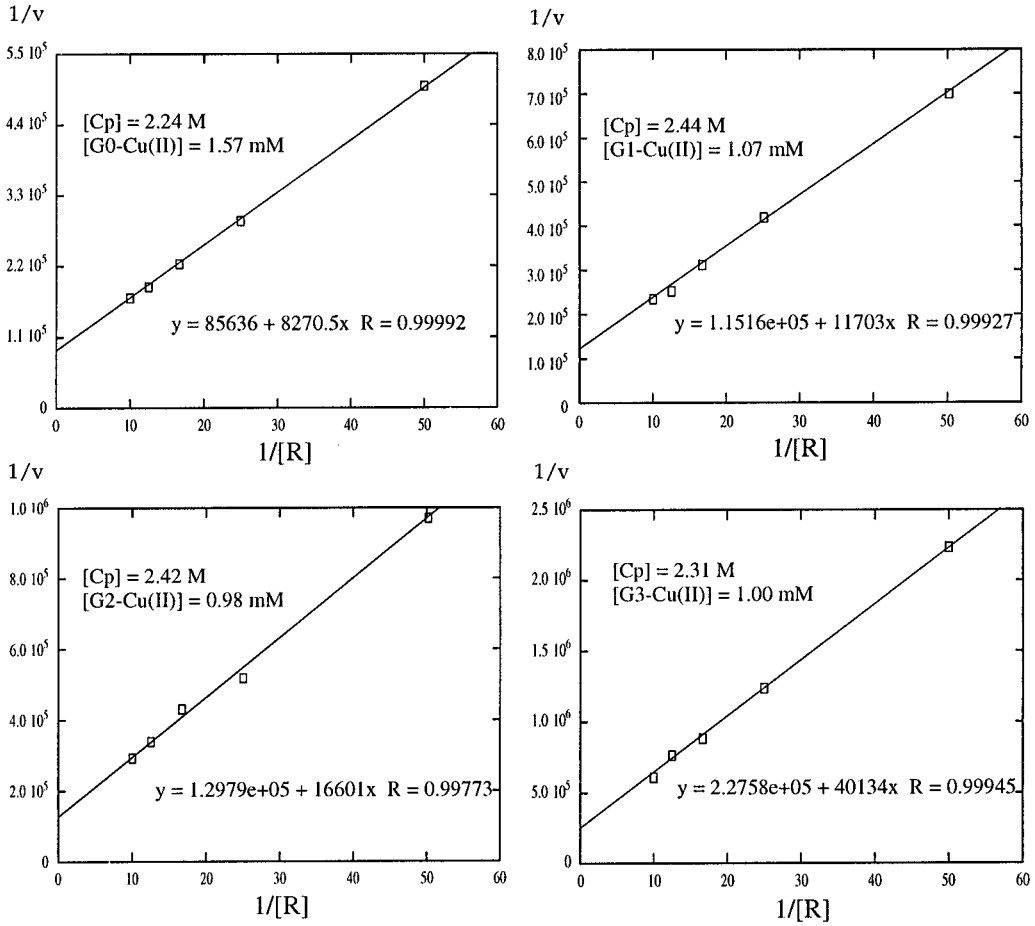

Figure 2. Linewaver−Burk plot for G0- (top left), G1- (top right), G2- (bottom left), and G3- (bottom right) copper(II)-catalyzed Diels−Alder reaction of Cp and crotonyl imide **26** (R).

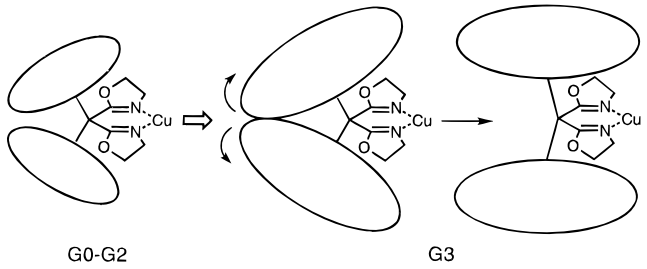

Figure 3. Transition from an exposed to a partially buried active site from lower generation to the third generation dendrizyme.

sequently, k_2 was insensitive to the dendrimer generation in these cases. However, for the third generation analog, the steric repulsion between the two large dendritic sectors might be so severe that one or both of them has to move toward the catalytic core to relieve the steric strain, resulting in a decrease of steric accessibility around the reaction center (Figure 3).

Changes in the physical properties of dendrimers across generations have been interpreted as a consequence of a change of conformation in them. For examples, the encapsulation of hydrophilic metal ions by large hydrophobic dendritic sectors was used to explain the unexpected solubility of higher generation dendritic rhodium phosphine complexes in nonpolar solvents such as pentane.[7] Such unusual solubility, however, was not observed for the analogous dendritic complexes of lower generations. It was proposed that the hydrophobic sectors of the higher generation dendrimers, in order to avoid the steric repulsion between them, folded backward and acted as an envelope for the hydrophilic metal center. Similarly, inward folding of chain ends toward the center with increasing generation number was also detected by rotational-echo double-resonance NMR study.[17] The sudden transition from an extended to a globular structure from the third to the fourth generation of a series of polyether-based dendrimers has also been inferred from a solvatochromatic investigation.[18] In another study of a family of carboxylate-terminated starburst dendrimers, the occurrence of a structural change between the third and fourth generations was also demonstrated by photoinduced electron transfer measurements.[19] Fréchet and co-workers further noted that the intrinsic viscosity profile of low-generation polyether dendrimers increased with molecular weight but that of the higher generation counterparts showed a reverse trend.[20] Such behaviors were again interpreted by a conformational change from an extended configuration to a globular one. The kinetic results obtained in our study therefore served to demonstrate that profound effects on the reactivity of a metal complex can be brought about by a conformational change on the dendritic sectors of its ligands.

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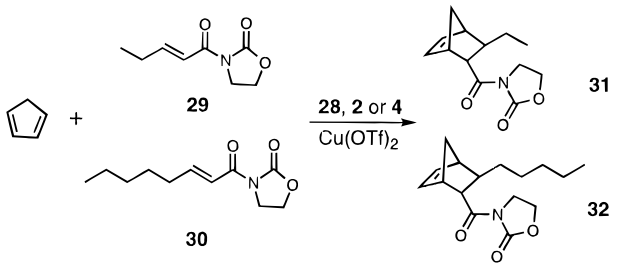
Table 2. Initial Velocities of Diels−Alder Adduct Formation Promoted by Different Catalysts (all rates normalized to 1 mM of catalyst concentration)

catalyst	10^4d[**31**]/dt (M/s)	10^4d[**32**]/dt (M/s)	k_{rel}
28·Cu(OTf)$_2$ (non-dendritic)	2.33 ± 0.04	2.21 ± 0.04	1.05 ± 0.03
G1·Cu(OTf)$_2$	1.93 ± 0.04	1.80 ± 0.04	1.07 ± 0.03
G3·Cu(OTf)$_2$	0.67 ± 0.01	0.57 ± 0.01	1.18 ± 0.03

The kinetic data indicated that under saturated kinetic conditions, when nearly all catalysts are dienophile bound (*i.e.* [Gn·Cu(OTf)$_2$−R]/[Gn·Cu(OTf)$_2$] ≥ 10^2, or when [R] = [Gn·Cu(OTf)$_2$−R]/([Gn·Cu(OTf)$_2$] × K_c) ≈ 10 M), there is little reactivity difference among the zeroth to the second generation catalysts. It should be pointed out, however, that under ordinary nonsaturated kinetic conditions (*i.e.* [R] ≤ 10^0 M), because of the decreasing binding constant, a gradual decrease of reactivity should be observed on going from the zeroth to the second generation dendritic catalyst.

3. Substrate Selectivity. The encapsulation of a catalytic functionality within a dendritic matrix may provide the key for successful substrate control of a catalytic reaction. Dendritic catalysts of different generations may therefore display differential substrate selectivity in competitive experiments. Dienophiles **29** and **30** of slightly different steric sizes were chosen to probe these effects in our study. Under the reaction conditions, a 1:1 molar ratio mixture of dienophiles **29** and **30** was allowed to react with a large excess of Cp in the presence of a catalytic amount (20 mol %) of a copper catalyst formed by complexation of individual ligands **1**−**4** with Cu(OTf)$_2$. On the basis of the kinetic study described earlier, the third generation catalyst G3·Cu(OTf)$_2$, due to its presumably partially folded structure around the catalytic center, would be the starting point to exhibit discernible selectivity toward the two substrates **29** and **30**. For comparison purpose, the nondendritic complex **28**·Cu(OTf)$_2$ and the first generation catalyst G1·Cu(OTf)$_2$ were also employed in the selectivity study. The initial velocities for the formation of the respective Diels−Alder adducts **31** and **32** with these three catalysts are tabulated in Table 2.



Examination of the kinetic profile showed that the smaller unsaturated imide **29**, as expected, reacted faster than the bulkier analogue **30** in all three catalysts studied. Since all competitive experiments were conducted under nonsaturated kinetic conditions, the lower generation catalyst, as anticipated, promoted a faster turnover rate than the higher generation one. Nevertheless, a significantly large rate retardation was noted for the Diels−Alder reactions promoted by the third generation dendritic catalyst. The nondendritic bis(oxazoline) **28**·Cu(OTf)$_2$ and G1·Cu(OTf)$_2$ catalysts displayed similar reactivity patterns toward the two different dienophiles, suggesting that they possessed intrinsically the same level of substrate selectivity. On the other hand, a notable difference of the rates of formation of the two Diels−Alder adducts was observed for the reaction catalyzed by the third generation complex. The higher substrate selectivity brought about by the third generation catalyst can be put into better perspective if one compares the ratio of the initial velocities (k_{rel}) for the formation of the two Diels−Alder adducts. For the nondendritic **28**·Cu(OTf)$_2$ and the G1·Cu(OTf)$_2$ catalysts, the ratio of the initial velocities for the formation of **31** to **32** was 1.05 and 1.07, respectively, whereas the corresponding value for the G3·Cu(OTf)$_2$ catalyst was 1.18. These figures are consistent with our notion that the partially folded G3 dendritic sectors imposed significant steric crowding around the catalytic site. As a result, the Diels−Alder reaction involving the bulkier dienophile **30** reacted with Cp at a slower rate than the less hindered competitor **29**, whereas in the absence of shielding caused by the folding back of the dendritic sectors in lower generation ligands, such discrimination was negligible.

4. Conclusions. This paper reported the synthesis, reactivity, and substrate selectivity of a new class of bis(oxazoline)-based dendritic catalyst. From both kinetic and substrate selectivity studies, it was deduced that a sudden change of dendrimer conformation occurred from the second to the third generation. Furthermore, we have shown here that enhanced substrate selectivity can be realized with this class of dendritic catalysts, in a manner similar to the results reported earlier by Moore on dendritic porphyrin catalysts.[11] Even though the observed substrate selectivity enhancement for the third generation catalyst was not significantly high to warrant its practical usefulness in synthesis, we believe that dendritic catalysts with much better substrate selectivity and reactivity could be designed by carefully choosing suitable dendritic sectors with proper disposition around the catalytic center.

Experimental Section

1. Synthesis. The particulars on the analytical instruments employed in the present study were previously described.[21] Unless otherwise stated, all chemicals were purchased from commercial suppliers and used without further purification. The molecular mass reported in each case is the most abundant molecular isotopic peak for the compound.

4-(Benzyloxy)benzyl Bromide (12). To a stirred solution of 4-(benzyloxy)benzyl alcohol (**11**) (48.0 g, 0.22 mol) in acetic acid (150 mL) at 0 °C was added a solution of hydrobromic acid (100 mL, 48% in acetic acid). A white precipitate formed immediately, and the mixture was poured into ice−water. The white solid was suction filtered, washed with water, and redissolved in ethyl acetate (400 mL). The organic layer was washed with brine, dried (Na_2SO_4), and filtered. The filtrate was concentrated to about 100 mL, and the bromide **12** (40.0 g, 64%) crystallized out as a white solid: mp 78−80 °C (lit.[22] mp 81−82 °C); R_f 0.45 (hexane/ethyl acetate = 5/1); ^{1}H-NMR ($CDCl_3$) δ 4.49 (s, 2 H), 5.05 (s, 2 H), 6.93 (d, J = 8.7 Hz, 2 H), 7.31 (d, J = 8.7 Hz, 2 H), 7.34−7.50 (m, 5 H).

Diethyl 2,2-Bis((4-benzyloxy)benzyl)malonate (13). To a suspension of sodium hydride (1.50 g, 62.3 mmol) in dry THF (150 mL) at 0 °C was added dropwise a solution of diethyl malonate (2.75 g, 17.2 mmol) in dry THF (15 mL) over 15 min. The resulting mixture was warmed to 20 °C and stirred for a further 15 min. (4-Benzyloxy)benzyl bromide (**12**) (10.0 g, 36.1

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mmol) was added and the mixture heated under reflux for 2 h. Water was added carefully into the reaction mixture and excess THF removed under reduced pressure. The residue was taken up in ethyl acetate, washed with brine, dried (Na_2SO_4), and filtered. Concentration of the filtrate followed by flash chromatography on silica gel (hexane/ethyl acetate = 8/1) provided the product **13** (7.0 g, 74%) as a pale yellow syrup: R_f 0.35 (hexane/ethyl acetate = 5/1); IR (film) cm^{-1} 1730, 1244; ^{1}H-NMR ($CDCl_3$) δ 1.16 (t, J = 7.1 Hz, 6 H), 3.15 (s, 4 H), 4.09 (q, J = 7.1 Hz, 4 H), 5.03 (s, 4 H), 6.88 (d, J = 8.7 Hz, 4 H), 7.09 (d, J = 8.7 Hz, 4 H), 7.20−7.45 (m, 10 H); ^{13}C-NMR ($CDCl_3$) δ 13.8, 38.2, 60.3, 61.0, 69.8, 114.4, 127.3, 127.8, 128.4, 131.0, 136.9, 157.6, 171.0; MS (EI, m/z) 552 (M^+, 4), 308 (18), 197 (28), 91 (100), 65 (24). Anal. Calcd for $C_{35}H_{36}O_6$: C, 76.06; H, 6.57. Found: C, 75.81; H, 6.69.

2,2-Bis(4-(benzyloxy)benzyl) Malonic Acid (15). A mixture of the diester **13** (5.8 g, 10.5 mmol) and aqueous sodium hydroxide (35 mL, 4.0 M) in ethanol (100 mL) was stirred at 90 °C for 1 d. The mixture was cooled to 0 °C and acidified with concentrated HCl to pH 2. The mixture was extracted with ethyl acetate (3 × 100 mL), and the combined organic layers were washed with brine, dried (Na_2SO_4), and filtered. Concentration of the filtrate followed by flash chromatography on silica gel (hexane/ethyl acetate/ethanol = 2/1/1) afforded the diacid **15** (3.4 g, 65%) as a white solid: mp 168−170 °C; R_f 0.44 (hexane/ethyl acetate/ethanol = 2/1/1); IR (film) cm^{-1} 3441, 1731; ^{1}H-NMR (acetone-d_6, COOH not observed) δ 3.22 (s, 4 H), 5.08 (s, 4 H), 6.93 (d, J = 8.8 Hz, 4 H), 7.20 (d, J = 8.8 Hz, 4 H), 7.30−7.55 (m, 10 H); ^{13}C-NMR (acetone-d_6) δ 40.7, 61.2, 70.4, 115.4, 128.5, 129.3, 129.4, 131.8, 138.4, 158.9, 174.1; MS (FAB, m/z) 496 (M^+, 35). Anal. Calcd for $C_{31}H_{28}O_6$: C, 74.98; H, 5.68. Found: C, 75.20; H, 5.70. The monoacid **14** was obtained in 27% yield as a white solid: mp 138−140 °C; R_f 0.78 (hexane/ethyl acetate/ethanol = 2/1/1); IR (film) cm^{-1} 3441, 1703; ^{1}H-NMR (acetone-d_6, COOH not observed) δ 2.50−3.10 (m, 5 H), 5.05 (s, 4 H), 6.90 (d, J = 8.7 Hz, 4 H), 7.13 (d, J = 8.6 Hz, 4 H), 7.25−7.50 (m, 10 H); MS (EI, m/z) 452 (M^+, 3), 161 (28), 131 (45), 117 (74), 91 (100). Anal. Calcd for $C_{30}H_{28}O_4$: C, 79.62; H, 6.24. Found: C, 79.47; H, 6.17.

***N,N′*-Bis(2-hydroxyethyl)-2,2-bis(4-(benzyloxy)benzyl)-1,3-propanediamide (16).** Oxalyl chloride (1.6 mL) was added dropwise to a stirred solution of DMF (1.4 mL) in dry dichloromethane (10 mL) at 0 °C over 5 min. A solution of the diacid **15** (2.5 g, 5.0 mmol) in dry dichloromethane (20 mL) was added in one portion. After stirring for 30 min, a solution of 2-aminoethanol (2 mL) in acetonitrile (20 mL) was added to the solution at 0 °C. After 30 min, the reaction mixture was filtered and the filtrate concentrated under reduced pressure. The residue was purified by flash chromatography (hexane/ethyl acetate/ethanol = 4/2/1) to give the diamide **16** (2.0 g, 69%) as a white solid: mp 134−136 °C; R_f 0.35 (hexane/ethyl acetate/ethanol = 4/2/1); IR (film) cm^{-1} 3346, 1660; ^{1}H-NMR ($CDCl_3$) δ 2.76 (t, J = 4.3 Hz, 2 H), 3.25 (s, 4 H), 3.31 (q, J = 5.3 Hz, 4 H), 3.56 (q, J = 4.3 Hz, 4 H), 5.00 (s, 4 H), 6.85 (d, J = 8.7 Hz, 4 H), 7.07 (d, J = 8.7 Hz, 4 H), 7.30−7.42 (m, 10 H), 7.69 (t, J = 5.5 Hz, 2 H); ^{13}C-NMR ($CDCl_3$) δ 42.4, 42.6, 59.4, 61.6, 69.9, 114.6, 127.4, 127.8, 128.4, 128.5, 130.5, 136.9, 157.7, 173.4; MS (FAB, m/z) 583 (M + H^+, 100). Anal. Calcd for $C_{35}H_{38}N_2O_6$: C, 72.14; H, 6.57; N, 4.81. Found: C, 72.06; H, 6.54; N, 4.79.

***N,N′*-Bis(2-hydroxyethyl)-2,2-bis(4-hydroxybenzyl)-1,3-propanediamide (17).** A suspension of the dibenzyl ether **16** (1.0 g, 1.71 mmol) and 10% palladium-on-charcoal (100 mg) in absolute ethanol (30 mL) was stirred under an atmospheric pressure of hydrogen at room temperature. After 3 h, the suspension was filtered through a pad of Celite and the filtrate concentrated. The residue was recrystallized from ethyl acetate−chloroform (1/1) to give the diphenol **17** (0.55 g, 88%) as a white solid: mp 199−200 °C; R_f 0.42 (ethyl acetate/ethanol = 5/1); IR (KBr) cm^{-1} 3500−2800, 1661; ^{1}H-NMR (methanol-d_4) δ 3.39 (s, 4 H), 3.44 (t, J = 6.0 Hz, 4 H), 3.69 (t, J = 6.0 Hz, 4 H), 4.80−5.05 (br s, 6 H), 6.83 (d, J = 8.6 Hz, 4 H), 7.17 (d, J = 8.6 Hz, 4 H); ^{13}C-NMR (acetone-d_6) δ 42.9, 43.7, 61.0, 61.4, 115.9, 128.7, 131.6, 157.1, 174.8; MS (FAB, m/z) 403 (M + H^+, 40). Anal. Calcd for $C_{21}H_{26}N_2O_6$: C, 62.67; H, 6.51; N, 6.96. Found: C, 62.56; H, 6.54; N, 6.89.

***N,N′*-Bis(2-hydroxyethyl)-2,2-bis[4-(3-bromopropoxy)-benzyl]-1,3-propanediamide (10).** A mixture of the diphenol **17** (0.20 g, 0.50 mmol), 1,3-dibromopropane (3.00 g, 15.0 mmol), and anhydrous potassium carbonate (0.20 g, 1.45 mmol) in acetone (50 mL) was heated under reflux for 3 d. Upon cooling to room temperature, the reaction mixture was filtered through a pad of Celite. The filtrate was concentrated and the residue purified by flash chromatography on silica gel (hexane/ethyl acetate = 1/5 gradient to ethyl acetate) to afford the dibromide **10** (0.25 g, 78%) as a white solid: mp 121−122 °C; R_f 0.45 (ethyl acetate); IR (film) cm^{-1} 3344, 1660; ^{1}H-NMR ($CDCl_3$) δ 2.29 (quin, J = 6.1 Hz, 4 H), 2.83 (br s, 2 H), 3.26 (s, 4 H), 3.34 (q, J = 5.0 Hz, 4 H), 3.50−3.65 (m, 8 H), 4.05 (t, J = 5.8 Hz, 4 H), 6.79 (d, J = 8.7 Hz, 4 H), 7.08 (d, J =8.6 Hz, 4 H), 7.73 (t, J = 5.2 Hz, 2 H); ^{13}C-NMR ($CDCl_3$) δ 29.8, 32.2, 42.4, 42.6, 59.4, 61.4, 65.3, 114.2, 128.5, 130.4, 157.6, 173.3; MS (FAB, m/z) 645 (M + H^+, 54); HRMS calcd for $C_{27}H_{37}N_2O_6{}^{79}Br^{81}Br$ 645.0998, found 645.0986. Anal. Calcd for $C_{27}H_{36}N_2O_6Br_2$: C, 50.33; H, 5.63; N, 4.35. Found: C, 50.86; H, 5.70; N, 4.37.

General Procedure for Synthesis of Dendritic *N,N′*-Bis(2-hydroxyethyl)diamides ([Gn]-NH(CH$_2$)$_2$OH, n = 0 to 3) 18−21. A mixture of dibromide **10** (1.0 mol equiv), 4-*tert*-butylphenol or dendritic phenol [Gn]-OH[13] (2.3 mol equiv), and potassium carbonate (3.5 mol equiv) in acetone was heated under reflux. The reaction time required was 3 d for n = 0−2 and 5 d for n = 3, respectively. The reaction mixture was filtered through a pad of silica gel to remove the inorganic materials. The filtrate was concentrated and the crude oily substance purified as described in the following text.

[G0]-NH(CH$_2$)$_2$OH 18. This was prepared from 4-*tert*-butylphenol and purified by flash chromatography on silica gel (hexane/ethyl acetate = 1/3) to give [G0]-NH(CH$_2$)$_2$OH **18** (60%) as a white foam: R_f 0.15 (hexane/ethyl acetate = 1/3); IR (film) cm^{-1} 3600−3100, 1660; ^{1}H-NMR ($CDCl_3$) δ 1.28 (s, 18 H), 2.19 (quin, J = 6.0 Hz, 4 H), 2.84 (br s, 2 H), 3.23 (br s, 4 H), 3.30 (q, J = 4.9 Hz, 4 H), 3.57 (t, J = 4.6 Hz, 4 H), 4.07 (t, J = 6.1 Hz, 4 H), 4.10 (t, J = 6.1 Hz, 4 H), 6.76 (d, J = 8.6 Hz, 4 H), 6.83 (d, J = 8.8 Hz, 4 H), 7.05 (d, J = 8.6 Hz, 4 H), 7.28 (d, J = 8.8 Hz, 4 H), 7.77 (t, J = 5.4 Hz, 2 H); ^{13}C-NMR ($CDCl_3$) δ 29.4, 31.5, 34.0, 42.5, 42.9, 59.5, 61.8, 64.5, 64.6, 114.1, 114.4, 126.2, 128.4, 130.6, 143.5, 156.6, 158.1, 173.4; MS (FAB, m/z) 783 (M^+, 28). Anal. Calcd for $C_{47}H_{62}N_2O_8$: C, 72.10; H, 7.98; N, 3.58. Found: C, 72.29; H, 8.05; N, 3.51.

[G1]-NH(CH$_2$)$_2$OH 19. This was prepared from [G1]-OH **6**[13] and purified by flash chromatography on silica gel (hexane/ethyl acetate = 1/2) to yield [G1]-NH(CH$_2$)$_2$OH **19** (65%) as a white foam; R_f 0.15 (hexane/ethyl acetate = 1/2); IR (film) cm^{-1} 3600−3100, 1667; ^{1}H-NMR ($CDCl_3$) δ 1.29 (s, 36 H), 2.21 (quin, J = 6.1 Hz, 12 H), 2.52 (br s, 2 H), 3.24 (s, 4 H), 3.32 (q, J = 5.1 Hz, 4 H), 3.59 (br s, 4 H), 4.08 (t, J = 5.8 Hz, 12 H), 4.11 (t, J = 5.9 Hz, 12 H), 6.09 (s, 6 H), 6.79 (d, J = 8.7 Hz, 4 H), 6.84 (d, J = 8.9 Hz, 8 H), 7.06 (d, J = 8.7 Hz, 4 H), 7.29 (d, J = 8.9 Hz, 8 H), 7.63 (t, J = 5.6 Hz, 2 H); ^{13}C-NMR ($CDCl_3$) δ 29.3, 31.4, 33.9, 42.4, 42.8, 59.4, 61.7, 64.4, 64.6, 94.4, 114.1, 114.4, 126.2, 128.5, 130.6, 143.5, 156.7, 158.0, 160.9, 173.5; MS (FAB, m/z) 1495 (M^+, 5). Anal. Calcd for $C_{91}H_{118}N_2O_{16}$: C, 73.06; H, 7.95; N, 1.87. Found: C, 72.76; H, 8.11; N, 1.74.

[G2]-NH(CH$_2$)$_2$OH 20. This was prepared from [G2]-OH **7**[13] and purified by flash chromatography on silica gel (hexane/ethyl acetate = 1/2) to afford [G2]-NH(CH$_2$)$_2$OH **20** (50%) as a white foam: R_f 0.29 (hexane/ethyl acetate = 1/2); IR (film) cm^{-1} 3600−3100; ^{1}H-NMR ($CDCl_3$) δ (s, 72 H), 2.23 (quin, J = 6.0 Hz, 28 H), 3.22 (br s, 4 H), 3.27−3.33 (m, 4 H), 3.52−3.62 (m, 4 H), 4.07−4.13 (m, 56 H), 6.08 (s, 18 H), 6.78 (d, J = 8.7 Hz, 4 H), 6.84 (d, J = 8.8 Hz, 16 H), 7.05 (d, J = 8.6 Hz, 4 H), 7.28 (d, J = 8.8 Hz, 16 H), 7.61 (t, J = 5.4 Hz, 2 H); ^{13}C-NMR ($CDCl_3$) δ 29.3, 31.5, 34.0, 42.5, 43.2, 59.4, 62.0, 64.4, 64.6, 94.2, 114.0, 114.4, 126.2, 128.3, 130.5, 143.4, 156.6, 158.0, 160.7, 173.4; MS (FAB, m/z) 2924 (M^+, 12). Anal. Calcd for $C_{179}H_{230}N_2O_{32}$: C, 73.59; H, 7.93; N, 0.96. Found: C, 73.43; H, 7.96; N, 0.90.

[G3]-NH(CH$_2$)$_2$OH 21. This was prepared from [G3]-OH **8**[13] and purified by flash chromatography on silica gel (hexane/ethyl acetate = 2/1 gradient to 1/1) to give [G3]-NH(CH$_2$)$_2$OH **21** (46%) as a white foam; R_f 0.15 (hexane/ethyl acetate = 3/2);

IR (film) cm^{-1} 3500−3150; ^{1}H-NMR ($CDCl_3$) δ 1.28 (s, 144 H), 2.22 (quin, J = 5.9 Hz, 60 H), 2.45 (br s, 2 H), 3.20 (br s, 4 H), 3.28 (q, J = 4.0 Hz, 4 H), 3.56 (t, J = 4.8 Hz, 4 H), 3.98−4.18 (m, 120 H), 6.08 (s, 42 H), 6.76 (d, J = 8.6 Hz, 4 H), 6.83 (d, J = 8.9 Hz, 32 H), 7.04 (d, J = 8.6 Hz, 4 H), 7.27 (d, J = 8.8 Hz, 32 H), 7.62 (t, J = 5.5 Hz, 2 H); ^{13}C-NMR ($CDCl_3$) δ 29.3, 29.4, 31.5, 34.0, 42.5, 43.3, 59.4, 61.9, 64.5, 64.6, 94.4, 114.1, 114.4, 126.2, 128.3, 130.5, 143.4, 156.6, 158.0, 160.8, 173.3. Anal. Calcd for $C_{355}H_{454}N_2O_{64}$: C, 73.85; H, 7.93; N, 0.49. Found: C, 73.48; H, 8.11; N, 0.47.

General Procedure for Synthesis of Dendritic *N,N′*-Bis(2-bromoethyl)diamides ([Gn]-NH(CH$_2$)$_2$Br, *n* = 0 to 3) 22−25. Carbon tetrabromide (5.0 mol equiv) was added to a solution of individual dendritic *N,N′*-bis(2-hydroxyethyl)-diamide [Gn]-NHCH$_2$CH$_2$OH (1.0 mol equiv) and triphenylphosphine (5.0 mol equiv) in dry THF under nitrogen at 0 °C. The reaction mixture was then stirred at room temperature for 3 h. The mixture was concentrated under reduced pressure, and triphenylphosphine oxide was precipitated by addition of a solvent mixture of hexane−ethyl acetate (5/1). The mixture was filtered through a pad of silica gel, and the filter cake thoroughly washed with the aforementioned solvent mixture. The combined filtrates were concentrated, and the residue was purified as described in the following text.

[G0]-NH(CH$_2$)$_2$Br 22. This was prepared from [G0]-NH(CH$_2$)$_2$OH **18** and purified by flash chromatography on silica gel (hexane/ethyl acetate = 3/1) to give [G0]-NH(CH$_2$)$_2$-Br **22** (75%) as a white solid: mp 120−121 °C; R_f 0.37 (hexane/ethyl acetate = 2/1); IR (film) cm^{-1} 3303, 1667; ^{1}H-NMR ($CDCl_3$) δ 1.29 (s, 18 H), 2.22 (quin, J = 6.0 Hz, 4 H), 3.25 (s, 4 H), 3.32 (t, J = 6.0 Hz, 4 H), 3.58 (q, J = 5.9 Hz, 4 H), 4.09 (t, J = 5.9 Hz, 4 H), 4.14 (t, J = 6.0 Hz, 4 H), 6.78 (d, J = 8.6 Hz, 4 H), 6.85 (d, J = 8.9 Hz, 4 H), 7.05 (d, J = 8.6 Hz, 4 H), 7.29 (d, J = 8.8 Hz, 4 H), 7.58 (t, J = 5.5 Hz, 2 H); ^{13}C-NMR ($CDCl_3$) δ 29.5, 31.3, 31.5, 34.1, 41.4, 43.1, 59.4, 64.5, 64.7, 114.1, 114.6, 126.2, 128.2, 130.6, 143.6, 156.7, 158.2, 172.6; MS (FAB, *m/z*) 909 (M + H$^+$, 36). Anal. Calcd for $C_{47}H_{60}N_2O_6$-Br_2: C, 62.12; H, 6.65; N, 3.08. Found: C, 62.12; H, 6.70; N 3.06.

[G1]-NH(CH$_2$)$_2$Br 23. This was prepared from [G1]-NH(CH$_2$)$_2$OH **19** and purified by flash chromatography on silica gel (hexane/ethyl acetate = 2/1) to give [G1]-NH(CH$_2$)$_2$-Br **23** (80%) as a white foam; R_f 0.30 (hexane/ethyl acetate = 2/1); IR (film) cm^{-1} 3347, 1668; ^{1}H-NMR ($CDCl_3$) δ 1.29 (s, 36 H), 2.20 (quin, J = 6.0 Hz, 12 H), 3.24 (s, 4 H), 3.29 (t, J = 6.0 Hz, 4 H), 3.55 (q, J = 5.9 Hz, 4 H), 4.08 (t, J = 5.8 Hz, 12 H), 4.10 (t, J = 5.9 Hz, 12 H), 6.09 (s, 6 H), 6.77 (d, J = 8.7 Hz, 4 H), 6.83 (d, J = 8.8 Hz, 8 H), 7.04 (d, J = 8.7 Hz, 4 H), 7.28 (d, J = 8.8 Hz, 8 H), 7.67 (t, J = 5.7 Hz, 2 H); ^{13}C-NMR ($CDCl_3$) δ 29.4, 31.2, 31.5, 34.0, 41.4, 43.1, 59.3, 64.5, 64.7, 94.4, 114.1, 114.5, 126.1, 128.2, 130.5, 143.4, 156.6, 158.0, 160.8, 172.5; MS (FAB, *m/z*) 1621 (M + H$^+$, 10). Anal. Calcd for $C_{91}H_{116}N_2O_{14}Br_2$: C, 67.40; H, 7.21; N, 1.73. Found: C, 67.44; H, 7.17; N, 1.72.

[G2]-NH(CH$_2$)$_2$Br 24. This was prepared from [G2]-NH(CH$_2$)$_2$OH **20** and purified by flash chromatography on silica gel (hexane/ethyl acetate = 3/2) to give [G2]-NH(CH$_2$)$_2$-Br **24** (85%) as a white foam; R_f 0.21 (hexane/ethyl acetate = 3/2); IR (film) cm^{-1} 3379; ^{1}H-NMR ($CDCl_3$) δ 1.28 (s, 72 H), 2.20 (quin, J = 5.9 Hz, 28 H), 3.23 (s, 4 H), 3.29 (t, J = 5.7 Hz, 4 H), 3.55 (q, J = 5.9 Hz, 4 H), 4.07−4.13 (m, 56 H), 6.08 (s, 18 H), 6.77 (d, J = 8.7 Hz, 4 H), 6.83 (d, J = 8.8 Hz, 16 H), 7.03 (d, J = 8.6 Hz, 4 H), 7.28 (d, J = 8.8 Hz, 16 H), 7.58 (t, J = 5.3 Hz, 2 H); ^{13}C-NMR ($CDCl_3$) δ 29.4, 31.2, 31.5, 34.0, 41.4, 43.2, 59.3, 64.5, 64.6, 64.7, 94.4, 114.1, 114.5, 126.2, 128.2, 128.3, 130.5, 143.5, 156.6, 158.1, 160.8, 172.5; MS (FAB, *m/z*) 3044 (M + H$^+$, 4). Anal. Calcd for $C_{179}H_{228}N_2O_{30}Br_2$: C, 70.55; H, 7.54; N, 0.92. Found: C, 70.34; H, 7.81; N, 0.71.

[G3]-NH(CH$_2$)$_2$Br 25. This was prepared from [G3]-NH(CH$_2$)$_2$OH **21** and purified by flash chromatography on silica gel (hexane/ethyl acetate = 3/1 gradient to 1/1) to provide [G3]-NH(CH$_2$)$_2$Br **25** (79%) as a white foam: R_f 0.50 (hexane/ethyl acetate = 5/2); IR (film) cm^{-1} 3500−3300; ^{1}H-NMR ($CDCl_3$) δ 1.28 (s, 144 H), 2.15−2.25 (m, 60 H), 3.21 (s, 4 H), 3.28 (t, J = 5.8 Hz, 4 H), 3.54 (q, J = 5.7 Hz, 4 H), 3.90−4.20 (m, 120 H), 6.09 (s, 42 H), 6.76 (d, J = 8.4 Hz, 4 H), 6.83 (d, J = 8.5 Hz, 32 H), 7.03 (d, J = 8.4 Hz, 4 H), 7.28 (d, J = 8.5 Hz, 32 H), 7.63 (t, J = 5.4 Hz, 2 H); ^{13}C-NMR ($CDCl_3$) δ 29.3, 31.2, 31.5, 34.0, 41.4, 43.3, 53.9, 64.5, 64.6, 94.3, 114.1, 114.5, 126.1, 128.2, 128.3, 130.4, 143.4, 156.6, 158.0, 160.8, 172.5. Anal. Calcd for $C_{355}H_{452}N_2O_{62}Br_2$: C, 72.28; H, 7.72; N, 0.47. Found: C, 72.30; H, 7.81; N 0.46.

General Procedure for Synthesis of Dendritic Bis(oxazoline)s (Gn, *n* = 0−3) 1−4. To a solution of *N,N′*-bis-(2-bromoethyl)diamide [Gn]-NHCH$_2$CH$_2$Br (0.1 mmol) in a solvent mixture of EtOH−THF (10 mL, 1/1) was added sodium hydroxide solution (10.0 mol equiv, 1 M). The mixture was stirred under reflux for 8 h and quenched with water (10 mL). The aqueous phase was extracted with ethyl acetate (3 × 20 mL), and the combined organic layers were washed with brine, dried (Na_2SO_4), and filtered. Concentration of the filtrate gave a crude pale yellow oily substance. The crude product was then purified as described in the following text.

Bis(oxazoline) 28. To a solution of the dialcohol **16** (3.00 g, 5.16 mmol) and triphenylphosphine (4.10 g, 15.7 mmol) in dry THF (25 mL) was added carbon tetrabromide (5.20 g, 15.7 mmol) under nitrogen at 0 °C. The reaction mixture was stirred at room temperature for 3 h. Concentration of the mixture to near-dryness followed by addition of a solvent mixture of hexane−ethyl acetate (5/1) effectively precipitated most of the triphenylphosphine oxide. The mixture was filtered through a pad of silica gel and washed with the aforementioned solvent mixture. The combined filtrates were evaporated under reduced pressure to give a pale yellow oil. The crude product was then purified by flash chromatography (hexane/ethyl acetate = 3/1) to give the corresponding dibromide (3.0 g, 82%) as a white solid, mp 127−129 °C; R_f 0.30 (hexane/ethyl acetate = 2/1); IR (film) cm^{-1} 3346, 1667; ^{1}H-NMR ($CDCl_3$) δ 3.26 (s, 4 H), 3.29 (t, J = 4.1 Hz, 4 H), 3.57 (q, J = 5.9 Hz, 4 H), 5.01 (s, 4 H), 6.85 (d, J = 8.6 Hz, 4 H), 7.07 (d, J = 8.6 Hz, 4 H), 7.30−7.50 (m, 10 H), 7.68 (t, J = 5.6 Hz, 2 H); ^{13}C-NMR ($CDCl_3$) δ 31.3, 41.4, 43.1, 59.3, 70.0, 114.8, 127.4, 127.9, 128.4, 128.5, 130.5, 137.0, 157.9, 172.5; MS (L-SIMS, *m/z*) 709 (M + H$^+$, 100). Anal. Calcd for $C_{35}H_{36}N_2O_4$-Br_2: C, 59.34; H, 5.12; N, 3.95. Found: C, 59.22; H, 5.12; N, 3.95. To a solution of this dibromide (2.30 g, 3.25 mmol) in EtOH−THF (40 mL, 3/1) was added sodium hydroxide solution (25 mL, 0.5 M). The mixture was stirred under reflux for 12 h and poured into water (20 mL). The aqueous phase was extracted with ethyl acetate (3 × 40 mL), and the combined organic layers were washed with brine, dried (Na_2SO_4), and filtered. Concentration of the filtrate gave a crude pale yellow oily substance which was then purified by flash chromatography (hexane/ethyl acetate = 1/2 gradient to ethyl acetate) to give the bis(oxazoline) **28** (3.0 g, 82%) as a white solid: mp 160−162 °C; R_f 0.29 (hexane/ethyl acetate = 1/3); IR (film) cm^{-1} 1659; ^{1}H-NMR ($CDCl_3$) δ 3.23 (s, 4 H), 3.79 (t, J = 9.5 Hz, 4 H), 4.21 (t, J = 9.5 Hz, 4 H), 5.03 (s, 4 H), 6.88 (d, J = 8.7 Hz, 4 H), 7.14 (d, J = 8.6 Hz, 4 H), 7.30−7.50 (m, 10 H); ^{13}C-NMR ($CDCl_3$) δ 38.9, 48.7, 54.2, 67.3, 69.9, 114.4, 127.4, 127.9, 128.5, 129.1, 131.2, 137.1, 157.6, 167.4; MS (EI, *m/z*) 546 (M$^+$, 0.1), 348 (50), 155 (9), 91 (70), 57 (100). Anal. Calcd for $C_{35}H_{34}N_2O_4$: C, 76.90; H, 6.27; N, 5.12. Found: C, 76.68; H, 6.26; N, 5.05.

Dendritic Bis(oxazoline) G0 1. This was prepared from [G0]-NH(CH$_2$)$_2$Br **22** and purified by flash chromatography on silica gel (hexane/ethyl acetate = 2/1 gradient to ethyl acetate) to afford G0 **1** (96%) as a colorless oil: R_f 0.30 (hexane/ethyl acetate = 1/3); IR (film) cm^{-1} 1658; ^{1}H-NMR ($CDCl_3$) δ 1.29 (s, 18 H), 2.22 (quin, J = 6.0 Hz, 4 H), 3.22 (s, 4 H), 3.78 (t, J = 9.5 Hz, 4 H), 4.11 (t, J = 6.0 Hz, 4 H), 4.12 (t, J = 6.1 Hz, 4 H), 4.19 (t, J = 9.6 Hz, 4 H), 6.80 (d, J = 8.7 Hz, 4 H), 6.84 (d, J = 8.9 Hz, 4 H), 7.12 (d, J = 8.6 Hz, 4 H), 7.29 (d, J = 8.7 Hz, 4 H); ^{13}C-NMR ($CDCl_3$) δ 29.4, 31.4, 32.9, 39.0, 48.7, 54.2, 64.4, 67.2, 114.0, 126.1, 128.8, 131.1, 143.3, 156.5, 157.7, 167.3; MS (FAB, *m/z*) 747 (M + H$^+$, 95); HRMS calcd for $C_{47}H_{59}N_2O_6$ 747.4365, found 747.4370. Anal. Calcd for $C_{47}H_{58}N_2O_6$: C, 75.57; H, 7.83; N, 3.75. Found: C, 75.77; H, 8.14; N, 3.28.

Dendritic Bis(oxazoline) G1 2. This was prepared from [G1]-NH(CH$_2$)$_2$Br **23** and purified by flash chromatography on silica gel (hexane/ethyl acetate = 2/1 gradient to ethyl acetate) to afford G1 **2** (89%) as a white foam: R_f 0.35 (hexane/ethyl

acetate = 1/3); IR (film) cm^{-1} 1660; ^{1}H-NMR ($CDCl_3$) δ 1.29 (s, 36 H), 2.21 (quin, J = 5.9 Hz, 12 H), 3.22 (br s, 4 H), 3.78 (t, J = 9.6 Hz, 4 H), 4.09 (t, J = 5.5 Hz, 12 H), 4.11 (t, J = 5.8 Hz, 12 H), 4.20 (t, J = 9.5 Hz, 4 H), 6.10 (s, 6 H), 6.81 (d, J = 8.4 Hz, 4 H), 6.84 (d, J = 8.8 Hz, 8 H), 7.12 (d, J = 8.5 Hz, 4 H), 7.28 (d, J = 8.8 Hz, 8 H); ^{13}C-NMR ($CDCl_3$) δ 29.4, 31.5, 34.0, 39.2, 48.9, 54.2, 64.5, 64.7, 67.3, 94.3, 114.1, 126.1, 129.0, 131.2, 143.4, 156.6, 157.8, 160.8, 167.4; MS (FAB, *m/z*) 1460 (M + H^+, 100). Anal. Calcd for $C_{91}H_{114}N_2O_{14}$: C, 74.87; H, 7.87; N, 1.92. Found: C, 74.87; H, 7.86; N, 1.82.

Dendritic Bis(oxazoline) G2 3. This was prepared from [G2]-NH$(CH_2)_2$Br **24** and purified by flash chromatography on silica gel (hexane/ethyl acetate = 2/1 gradient to ethyl acetate) to afford G2 **3** (58%) as a white foam: R_f 0.40 (hexane/ethyl acetate = 1/3); IR (film) cm^{-1} 1667; ^{1}H-NMR ($CDCl_3$) δ 1.28 (s, 72 H), 2.20 (quin, J = 6.0 Hz, 28 H), 3.21 (s, 4 H), 3.77 (t, J = 9.5 Hz, 4 H), 3.95−4.05 (m, 56 H), 4.18 (t, J = 8.9 Hz, 4 H), 6.08 (s, 12 H), 6.09 (s, 6 H), 6.80 (d, J = 8.5 Hz, 4 H), 6.83 (d, J 8.9 Hz, 16 H), 7.12 (d, J = 8.7 Hz, 4 H), 7.28 (d, J = 8.9 Hz, 16 H); ^{13}C-NMR ($CDCl_3$) δ 29.4, 31.5, 34.0, 39.3, 49.0, 54.3, 64.6, 64.7, 67.3, 94.5, 114.1, 126.2, 129.1, 131.2, 143.5, 156.7, 157.8, 160.8, 167.4; MS (MALDI, *m/z*) 2883 (M^+, 48). Anal. Calcd for $C_{179}H_{226}N_2O_{30}$: C, 74.50; H, 7.89; N, 0.97. Found: C, 74.75; H, 8.04; N, 0.94.

Dendritic Bis(oxazoline) G3 4. This was prepared from [G3]-NH$(CH_2)_2$Br **25** and purified by flash chromatography on silica gel (hexane/ethyl acetate = 2/1 gradient to ethyl acetate) to give G3 **4** (78%) as a white foam: R_f 0.15 (hexane/ethyl acetate = 1/1); ^{1}H-NMR ($CDCl_3$) δ 1.28 (s, 144 H), 2.20 (quin, J = 5.3 Hz, 60 H), 3.21 (s, 4 H), 3.76 (t, J = 9.7 Hz, 4 H), 3.95−4.12 (m, 120 H), 4.17 (t, J = 9.3 Hz, 4 H), 6.08 (s, 42 H), 6.80 (d, J = 8.7 Hz, 4 H), 6.83 (d, J = 8.8 Hz, 32 H), 7.12 (d, J = 8.7 Hz, 4 H), 7.27 (d, J = 8.8 Hz, 32 H); ^{13}C-NMR ($CDCl_3$) δ 29.3, 31.4, 33.9, 39.2, 48.9, 54.2, 64.4, 64.5, 67.2, 94.3, 114.0, 126.1, 128.9, 131.1, 143.3, 156.6, 157.7, 158.0, 160.7, 167.3; MS (MALDI, *m/z*) 5731 (M^+, 19). Anal. Calcd for $C_{355}H_{450}N_2O_{62}$: C, 74.32; H, 7.91; N, 0.49. Found: C, 74.50; H, 8.15; N, 0.46.

General Procedure for the Alkenoylation of 2-Oxazolidinone. To a solution of 2-oxazolidinone in anhydrous THF (∼0.5 M) at −78 °C was added *n*-butyllithium (1.0 mol equiv in hexane solution). After 15 min, freshly distilled alkenoyl chloride (1.1 mol equiv) was added. The mixture was stirred at −78 °C for 30 min and at 0 °C for 15 min. The reaction was quenched with excess saturated ammonium chloride solution and the solvent evaporated under reduced pressure. The resulting slurry was diluted with dichloromethane and washed with brine. The organic layer was dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The product was purified by flash chromatography on silica gel to afford the desired *N*-alkenoyl-2-oxazolidinone.

3-((2*E*)-Pentenoyl)-2-oxazolidinone (29). 2-Oxazolidinone was acylated with (*E*)-2-pentenoyl chloride[23] according to the general procedure detailed above and purified by flash chromatography on silica gel (hexane/ethyl acetate = 4/1) to afford the title compound **29** (22%) as an oil: R_f 0.29 (hexane/ethyl acetate = 2/1); IR (film) cm^{-1} 1778, 1682, 1634; ^{1}H-NMR ($CDCl_3$) δ 1.11 (t, J = 7.4 Hz, 3 H), 2.20−2.40 (m, 2 H), 4.08 (t, J = 8.1 Hz, 2 H), 4.44 (t, J = 8.0 Hz, 2 H), 7.15−7.35 (m, 2 H); ^{13}C-NMR ($CDCl_3$) δ 11.9, 25.4, 42.4, 61.8, 118.8, 152.3, 153.3, 165.0; MS (EI, *m/z*) 169 (M^+, 10), 140 (7), 84 (100), 82 (100), 55 (85). HRMS calcd for $C_8H_{12}NO_3$ 170.0812, found 170.0821.

3-((2*E*)-Octenoyl)-2-oxazolidinone (30). 2-Oxazolidinone was acylated with (*E*)-2-octenoyl chloride[23] according to the general procedure detailed above and purified by flash chromatography on silica gel (hexane/ethyl acetate = 3/1) to afford the title compound **30** (88%) as a white solid: mp 38−39 °C; R_f 0.23 (hexane/ethyl acetate = 3/1); IR (film) cm^{-1} 1789, 1770, 1682, 1634; ^{1}H-NMR ($CDCl_3$) δ 0.89 (t, J = 6.7 Hz, 3 H), 1.25−1.40 (m, 4 H), 1.49 (quin, J = 7.1 Hz, 2 H), 2.28 (dt, J = 5.5, 7.3 Hz, 2 H), 4.06 (t, J = 8.2 Hz, 2 H), 4.43 (t, J = 8.1 Hz, 2 H), 7.10−7.20 (m, 2 H); ^{13}C-NMR ($CDCl_3$) δ 13.7, 22.1, 27.5, 31.0, 32.3, 42.4, 61.8, 119.7, 151.3, 153.3, 165.0; MS (EI, *m/z*) 211 (M^+, 7), 168 (11), 155 (13), 142 (9), 124 (75), 88 (74), 81 (79), 68 (79), 55 (100). Anal. Calcd for $C_{11}H_{17}NO_3$: C, 62.54; H, 8.11; N, 6.63. Found: C, 62.15; H, 8.06; N, 6.37.

General Procedure for Preparation of Authentic Samples of Diels−Alder Cycloadduct. A mixture of preformed G0·Cu(II) complex (0.03−0.05 mol equiv) (see experimental of kinetic section described below), *N*-alkenoyl-2-oxazolidinone (1.0 mol equiv), and cyclopentadiene (10 mol equiv) in anhydrous CH_2Cl_2 was stirred at room temperature for 1 d. The mixture was filtered through a pad of silica gel and washed with CH_2Cl_2. The combined filtrates were concentrated, and the residue was purified as described in the following text. Cycloadduct **27** was prepared according to literature method.[24]

3-((3′-Ethylbicyclo[2.2.1]hept-5′-en-2′-yl)carbonyl)-1,3-oxazolidin-2-one (31). This was prepared from 3-((2*E*)-pentenoyl)-2-oxazolidinone (**29**) and purified by flash chromatography on silica gel (hexane/ethyl acetate = 4/1) to afford cycloadduct **31** (83%) as a white solid: mp 56−58 °C; R_f 0.30 (hexane/ethyl acetate = 4/1); IR (film) cm^{-1} 1777, 1697; ^{1}H-NMR ($CDCl_3$) δ 0.92 (t, J = 7.4 Hz, 3 H), 1.42−2.00 (m, 5 H), 2.66 (br s, 1 H), 3.27 (br s, 1 H), 3.59 (t, J = 3.9 Hz, 1 H), 3.90−4.10 (m, 2 H), 4.42 (t, J = 8.1 Hz, 2 H), 5.79 (dd, J = 2.7, 5.6 Hz, 1 H), 6.37 (dd, J = 3.2, 5.4 Hz, 1 H); MS (EI, *m/z*) 235 (M^+, 12), 170 (100), 149 (22), 128 (26), 83 (100), 66 (100). Anal. Calcd for $C_{13}H_{17}NO_3$: C, 62.36; H, 7.28; N, 5.95. Found: C, 62.19; H, 7.28; N, 5.62.

3-((3′-Pentylbicyclo[2.2.1]hept-5′-en-2′-yl)carbonyl)-1,3-oxazolidin-2-one (32). This was prepared from 3-((2*E*)-octenoyl)-2-oxazolidinone (**30**) and purified by flash chromatography on silica gel (hexane/ethyl acetate = 5/1) to afford cycloadduct **32** (84%) as a colorless oil: R_f 0.40 (hexane/ethyl acetate = 4/1); IR (film) cm^{-1} 1778, 1698; ^{1}H-NMR ($CDCl_3$) δ 0.80−2.05 (m, 14 H), 2.64 (br s, 1 H), 3.26 (br s, 1 H), 3.58 (dd, J = 3.5, 4.4 Hz, 1 H), 3.90−4.10 (m, 2 H), 4.41 (t, J = 8.2 Hz, 2 H), 5.78 (dd, J = 2.8, 5.7 Hz, 1 H), 6.35 (dd, J = 3.2, 5.8 Hz, 1 H); MS (EI, *m/z*) 277 (M^+, 6), 211 (72), 170 (6), 125 (10), 91 (21), 66 (100). HRMS calcd for $C_{16}H_{24}NO_3$ 278.1751, found 278.1746.

2. Kinetic Experiments. Unless otherwise indicated, anhydrous dichloromethane was the solvent used in the kinetic experiments as well as in preparing the stock solutions. All reactions were stirred at 25.0 ± 0.1 °C in a temperature control water bath and reactions monitored by taking aliquots (2 μL) at recorded time and analyzed by gas chromatography. For each aliquot, the integrated area under the dienophile (R) or Diels−Alder cycloadduct (P) was corrected according to their sensitivity ratio and such ratio was determined by injecting a sample of known concentration of R and P. The percent conversion for each reaction was evaluated according to the areas of dienophile and Diels−Alder adduct. GC conditions: injector temperature, 220 °C; detector temperature, 250 °C, FID detector, 180 °C isothermal oven, 50 mL/min carrier gas flow rate; retention times, dienophile **26** (R) = 4.3 min; Diels−Alder cycloadduct **27** (P) = 11.5 min.

Establishment of the Rate Equation of the Diels−Alder Reaction Using Bis(oxazoline)copper(II) Complex 28 as the Model Catalyst. (a) Variation of Cp Concentration. A stock metal complex solution (A) was prepared by charging a 25.00 mL volumetric flask with bis(oxazoline) **28** (0.150 g, 0.28 mmol) and $Cu(OTf)_2$ (0.100 g, 0.27 mmol) and diluting to the mark. The resulting mixture was stirred vigorously until the complete dissolution of the solid $Cu(OTf)_2$. A 5.00 mL stock solution (B) of dienophile **26** (0.703 M) was prepared by proper weighing. To five reaction tubes were charged 0.50 mL of each of these two stock solutions. To another five 10.00 mL volumetric flasks were charged 40, 80, 120, 160, and 200 mg of freshly distilled Cp, respectively, and diluted to the mark. From each of these volumetric flasks, 0.10 mL was pipetted into the reaction mixtures inside the five reaction tubes prepared above. The resulting mixtures were stirred at 25.0 ± 0.1 °C and aliquots taken at recorded

(23) Lauk, U. H.; Skrabal, P.; Zollinger, H. *Helv. Chim. Acta* **1985**, *68*, 1406−1426.

(24) Narasaka, K.; Iwasawa, N.; Inoue, M.; Yamada, T.; Nakashima, M.; Sugimori, J. *J. Am. Chem. Soc.* **1989**, *111*, 5340−5345.

time and analyzed by gas chromatography as described in the general conditions.

(b) Variation of Metal Complex Concentration. A stock solution (C) containing dienophile **26** and Cp was prepared by charging a 2.00 mL volumetric flask with **26** (0.157 g, 1.01 mmol) and Cp (1.20 g, 18.2 mmol) and diluting to the mark. To five reaction tubes were charged 1.00, 0.80, 0.60, 0.40 and 0.20 mL, respectively, of the stock metal complex solution (A) and the last four tubes topped to 1.00 mL with CH_2Cl_2. To each of these reaction tubes were then charged 0.20 mL of the stock solution (C) prepared above. The resulting mixtures were stirred at 25.0 ± 0.1 °C and aliquots taken at recorded time and analyzed by gas chromatography as described in the general conditions.

(c) Variation of Dienophile Concentration. A 3.00 mL stock solution (D) of Cp (7.17 M) and a 2.00 mL stock solution (E) of dienophile **26** (0.30 M) were prepared by proper weighing. By proper dilution from the stock metal complex solution (A), a 3.00 mL diluted stock metal complex solution (0.00367 M) was prepared and 0.50 mL of it pipetted into five reaction tubes followed by charging with 0.50, 0.40, 0.30, 0.20, and 0.10 mL, respectively, of the stock dienophile solution (E) and the last 4 tubes all topped to 1.00 mL with CH_2Cl_2. Then 0.50 mL of the stock Cp solution (D) was added into each of the above reaction mixtures. The resulting mixtures were stirred at 25.0 ± 0.1 °C and aliquots taken at recorded time and analyzed by gas chromatography as described in the general conditions.

Kinetic Experiments for Various Generation Dendritic-Cu(II) Complexes. (a) Variation of Dienophile Concentration for G0−Cu(II) Complex. A stock metal complex solution was prepared by charging a 10.00 mL volumetric flask with G0 dendrimer **1** (41.0 mg, 0.055 mmol), $Cu(OTf)_2$ (17.0 mg, 0.047 mmol) and diluting to the mark. The resulting mixture was stirred vigorously until the complete dissolution of the solid $Cu(OTf)_2$. A 3.00 mL stock solution of Cp (7.27 M) and a 2.00 mL stock solution of dienophile **103** (0.30 M) were prepared by proper weighing. To each of five reaction tubes were charged 0.50 mL of the stock metal complex solution followed by charging with 0.50, 0.40, 0.30, 0.20, and 0.10 mL, respectively, of the stock dienophile solution and the last 4 tubes all topped to 1.00 mL. Then 0.50 mL of the stock Cp solution was added into each of the above reaction mixtures. The resulting mixtures were stirred at 25.0 ± 0.1 °C and aliquots taken at recorded time and analyzed by gas chromatography as described in the general conditions.

(b) Variation of Dienophile Concentration for G1−Cu(II) Complex. The kinetic experiment was set up as described above except the stock metal complex solution (F) was prepared from G1 dendrimer **2** (0.0048 M). The reaction mixtures were stirred at 25.0 ± 0.1 °C and aliquots taken at recorded time and analyzed by gas chromatography as detailed in the general conditions.

(c) Variation of Dienophile Concentration for G2−Cu(II) Complex. The kinetic experiment was set up as described in section a except the stock metal complex solution was prepared from G2 dendrimer **3** (0.00294 M). The reaction mixtures were stirred at 25.0 ± 0.1 °C and aliquots taken at recorded time and analyzed by gas chromatography as detailed in the general conditions.

(d) Variation of Dienophile Concentration for G3−Cu(II) Complex. The kinetic experiment was set up as described in section (a) except the stock metal complex solution (G) prepared from G3 dendrimer **4** (0.0030 M). The reaction mixtures were stirred at 25.0 ± 0.1 °C and aliquots taken at recorded time and analyzed by gas chromatography as detailed in the general conditions.

Competitive Experiments with Two Dienophiles. (a) Substrate Selectivity for Bis(oxazoline)−Cu(II) Complex 28·Cu(OTf)$_2$. A metal complex solution (0.0018 M) was prepared by diluting one-sixth of the stock metal complex solution (A) (0.011 M) prepared above. A 1.00 mL stock Cp solution (7.73 M) and a 10.00 mL stock solution containing both dienophile **29** and **30** (0.03 M each) were prepared by proper weighing. To a reaction tube was charged 0.30 mL of the metal complex solution and 0.10 mL of each of the stock Cp and dienophile solutions. The reaction mixture was stirred at 25.0 ± 0.1 °C, and aliquots were taken (0.001 mL) at recorded time and analyzed by gas chromatography. For each aliquot, the integrated area under any dienophiles (R) or Diels−Alder adducts (P) were corrected according to their respective sensitivity ratios and these two ratios determined by injecting samples with known concentration of R and P. GC conditions: injector temperature, 220 °C; detector temperature, 250 °C, FID detector, 180 °C isothermal oven, 35 mL/min carrier gas flow rate; retention times, dienophile **29** = 3.1 min; dienophile **30** = 7.5 min; Diels−Alder cycloadduct **31** = 8.3 min; Diels−Alder cycloadduct **32** = 20.4 min.

(b) Substrate Selectivity for G1−Cu(II) Complex. The kinetic experiment was set up as described above except the G1 metal complex solution (0.00193 M) was prepared by diluting two-fifths of the stock metal complex (F) (0.0048 M) prepared above. The reaction mixture was stirred at 25.0 ± 0.1 °C, and aliquots were taken (0.001 mL) at recorded time and analyzed by gas chromatography as described above.

(c) Substrate Selectivity for G3−Cu(II) Complex. The kinetic experiment was set up as described above except the G3 metal complex solution (0.002 M) prepared by diluting two-third of the stock metal complex (G) (0.003 M) prepared above. The reaction mixture was stirred at 25.0 ± 0.1 °C, and aliquots were taken (0.001 mL) at recorded time and analyzed by gas chromatography as described above.

Acknowledgment. The authors wish to thank Dr. T. L. Chan for helpful discussions, and the Research Grants Council, Hong Kong, for the financial support (Ref No.: CUHK466/95P).

JO970383S