

Diels–Alder reaction using a dendritic copper(II) triflate-catalyst: a positive dendritic effect on the chemical yield

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Abstract—A series of dendritic ligands with a 2,2'-bipyridine core was synthesized through the coupling of 4,4'-dihydroxy-2,2'-bipyridine with poly(arylether) dendron in fair yields. The corresponding copper(II) trifluoromethanesulfonate (triflate) dendrimers were applied as a Lewis acid catalyst to the Diels–Alder reaction. A positive dendritic effect on the chemical yields of adducts was observed.

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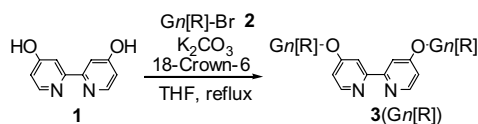
Dendrimers are fascinating molecules due to their unique physical and chemical properties caused by their well-defined hyperbranched frameworks.¹ From the perspective of their character, immobilization of functional or catalytic sites on dendrimers is one of the important goals. In particular, dendritic catalysts have received considerable attention due to the possibility of catalyst recovery using membrane or nanofiltration techniques² and due to the alteration of catalyst solubility by peripheral modification.³

Depending on the location of the catalytic sites, organometallic dendrimers with catalytic sites at the core or at the periphery have been described.⁴ In the case of core-catalyzed dendrimers, it is expected that the specific nanoenvironment of the catalytic core site created by the dendritic structure could modulate its catalytic behaviors such as its reactivity and selectivity. Previously, several examples of a positive dendritic effect, which means that the reactivity or the selectivity is enhanced by increasing the generation of the dendrimer, have been reported by us⁵ and by other groups.⁶ We wish to report herein the simple preparation of dendritic ligands with a 2,2'-bipyridine core, Lewis acid-catalyzed Diels–Alder reaction by employing the corresponding copper(II) trifluoromethanesulfonate (triflate) dendri-

mers, and the positive dendritic effect on the chemical yields of the Diels–Alder adducts.

2,2'-Bipyridine core dendrimers **3**(Gn[R]) were synthesized as follows (Table 1).⁷ To a solution of 4,4'-dihydroxy-2,2'-bipyridine^{7a} and poly(arylether) dendritic benzyl bromide **2**⁸ (structural formulas of Gn[R] are shown in Figure 1) in tetrahydrofuran (THF) was added potassium carbonate and a catalytic amount of 18-crown-6 under an argon atmosphere. After refluxing for 12 h with stirring, the reaction mixture was filtered with Celite, and the filtrate was concentrated in vacuo and then purified by column chromatography on silica gel. The second- and third-generation dendrimers **3** were obtained in fair yields (entries 2–5).⁹ However the first-generation **3** was obtained in poor yield (entry 1), probably due to the nucleophilic attack of the nitrogen of

Table 1. Preparation 2,2'-bipyridine core dendrimers **3**(Gn[R])



Entry	R	Gn	Yield (%)
1	Me	G1	8
2	Me	G2	86
3	Me	G3	86
4	Bn	G2	80
5	Bn	G3	85

Keywords: Dendrimer; Lewis acid catalyst; Diels–Alder reaction; Dendritic effect.

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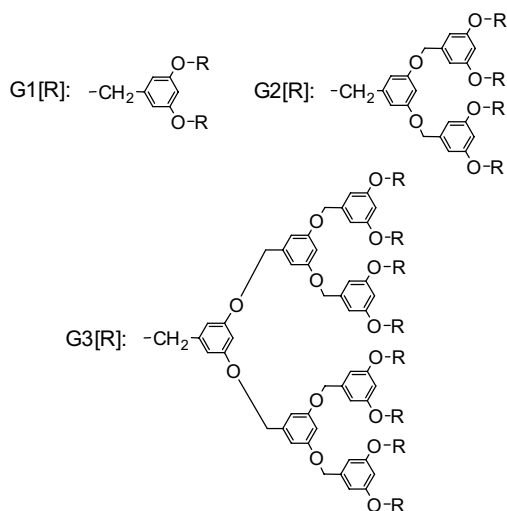
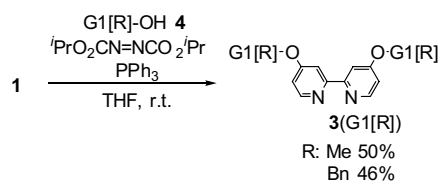


Figure 1. Structural formulas of $G_n[R]$ dendrons ($n = 1-3$).

bipyridine on **2** owing to the small size of $G1[Me]$ -dendron.

In the case of the preparation the first-generation **3**, it was found that **1** was coupled with dendritic benzyl alcohol **4** under Mitsunobu conditions¹⁰ to provide $3(G1[R])$ in moderate yields (Scheme 1).



Scheme 1. Preparation of 2,2'-bipyridine core dendrimers $3(G1[R])$.

We examined the utility of the dendrimer $3(G_n[R])$ as a dendritic ligand by performing copper(II) triflate-catalyzed Diels–Alder reaction (Table 2).^{11,12} First, by employing 10 mol % $3(G2[Me])\text{-Cu}(\text{OTf})_2$ catalyst, a Diels–Alder reaction of cyclopentadiene with various dienophiles proceeded at room temperature to afford the corresponding adducts in excellent yields (entries 1–3). In these reactions, the *endo/exo* ratios were almost similar to those previously reported.¹¹

On the other hand, stirring a dichloromethane solution of cyclopentadiene and various dienophiles at room temperature in the presence of 10 mol % $\text{Cu}(\text{OTf})_2$, which was not immobilized on the dendrimer, the corresponding Diels–Alder adduct was not obtained entirely to promote the polymerization of cyclopentadiene. Furthermore, even by employing the modified $\text{Cu}(\text{OTf})_2$ catalyst, which was coordinated by non-dendritic 4,4'-dimethoxy-2,2'-bipyridine ($=3(G0[Me])$), the corresponding Diels–Alder adduct was obtained in only 1% yield. Thus, the immobilization of $\text{Cu}(\text{OTf})_2$ on the dendrimer is effective for the modulation of its Lewis acidity.

Table 2. Diels–Alder reaction by employing $3(G2[Me])\text{-Cu}(\text{OTf})_2$ catalyst

Diene		Dienophile		Adduct	
Entry	Diene	Dienophile	Adduct	Yield ^a (%)	<i>endo:exo</i> ^b
1	Cyclopentadiene	Maleic anhydride	<i>endo</i> -Adduct	95	91:9
2	Cyclopentadiene	Acrylonitrile	<i>endo</i> -Adduct	88	93:7
3	Cyclopentadiene	Maleic anhydride	<i>endo</i> -Adduct	96	81:19
4	Cyclohexadiene	Maleic anhydride	<i>endo</i> -Adduct	91	100:0
5	Cyclopentadiene	Maleic anhydride	<i>endo</i> -Adduct	56	100:0
6	Cyclohexadiene	Maleic anhydride	<i>endo</i> -Adduct	76	—
7	Cyclohexadiene	Maleic anhydride	<i>endo</i> -Adduct	86	—

^a Isolated yield.

^b Determined by ¹H NMR spectra.¹³

Encouraged by these results, we applied the dendritic $3(G2[Me])\text{-Cu}(\text{OTf})_2$ catalyst to other dienes, only the corresponding Diels–Alder reaction proceeded smoothly also in these cases (entries 4–7). However, in the case of entry 5, the chemical yield of the adduct was rather low (56% yield).

We subsequently performed this Diels–Alder reaction with substrates in Table 2, entry 5 using 10 mol % various generation dendritic catalysts $3(G_n[R])\text{-Cu}(\text{OTf})_2$, which were carried out for 16 h (Table 3). In both cases

Table 3. Dendritic effect on chemical yields of adducts

Entry	R	G_n	Yield ^a (%)
1	Me	G1	5
2	Me	G2	56
3	Me	G3	80
4	Bn	G1	77
5	Bn	G2	87
6	Bn	G3	94

^a Isolated yield.

of 3(Gn[Me]) and 3(Gn[Bn]), the chemical yield of an adduct was enhanced by increasing the generation of the dendritic Cu(OTf)₂ catalyst. This relationship between the generation of the dendritic catalyst and the chemical yield is one of the positive dendritic effects.^{5,6,14}

On the other hand, the negative dendritic effect in the Diels–Alder reaction caused by employing the dendritic bis(oxazoline)-Cu(OTf)₂ catalyst has previously been reported by the other group.¹⁵ They reported that the reason of their negative dendritic effect was due to the steric hindrance of its bulky dendritic skeleton. We assume that our profound dendritic effect is probably derived from the increase of the Lewis acidity due to the distorted bipyridine skeleton of the 3-Cu(OTf)₂ complex by the steric repulsion of the dendritic wedges,¹⁶ thus affording better chemical yield with increasing the generation of the dendrimer.^{6c} Exactly, by the comparison of the chemical yields in the same generation, 3(Gn[Bn]), which possesses bulkier groups at its periphery, affords better chemical yields than 3(Gn[Me]) in all generations.

We are currently trying to apply this dendritic ligand to other catalytic conversions and to apply these catalytic processes to a continuous-flow membrane reactor by nanofiltration. The results will be reported in due course.

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References and notes

- (a) *Dendrimers and Other Dendritic Polymers*; Fréchet, J. M. J., Tomalia, D. A., Eds.; John Wiley & Sons: New York, 2001; (b) Newkome, G. R.; Moorefield, C. N.; Vogtle, F. *Dendrimers and Dendrons*; Wiley-VCH: Weinheim, 2001.
- (a) Dijkstra, H. P.; van Klink, G. P. M.; van Koten, G. *Acc. Chem. Res.* **2002**, *35*, 798–810; (b) van Heerbeek, R.; Kamer, P. C. J.; van Leeuwen, P. W. N. M.; Reek, J. N. H. *Chem. Rev.* **2002**, *102*, 3717–3756.
- (a) Grayson, S. M.; Fréchet, J. M. J. *Chem. Rev.* **2001**, *101*, 3819–3867; (b) Astruc, D.; Chardac, F. *Chem. Rev.* **2001**, *101*, 2991–3023.
- (a) Kreiter, R.; Kleij, A. W.; Gebbink, R. J. M. K.; van Koten, G. *Top. Curr. Chem.* **2001**, *217*, 163–199; (b) Oosterom, G. E.; Reek, J. N. H.; Kamer, P. C. J.; van Leeuwen, P. W. N. M. *Angew. Chem., Int. Ed.* **2001**, *40*, 1828–1849.
- (a) Fujita, K.; Muraki, T.; Sakurai, T.; Oishi, A.; Taguchi, Y. *Chem. Lett.* **2005**, *34*, 1180–1181; (b) Muraki, T.; Fujita, K.; Oishi, A.; Taguchi, Y. *Polym. J.* **2005**, *37*, 847–853.
- (a) Helms, B.; Liang, C. O.; Hawker, C. J.; Fréchet, J. M. J. *Macromolecules* **2005**, *38*, 5411–5415; (b) Fujihara, T.; Obora, Y.; Tokunaga, M.; Sato, H.; Tsuji, Y. *Chem. Commun.* **2005**, 4526–4528; (c) Fan, G.-H.; Chen, Y.-M.; Chen, X.-M.; Jiang, D.-Z.; Xi, F.; Chan, A. S. C. *Chem. Commun.* **2000**, 789–790; (d) Bhyrappa, P.; Young, J. K.; Moore, J. S.; Suslick, K. S. *J. Am. Chem. Soc.* **1996**, *118*, 5708–5711.
- Previously reported 2,2'-bipyridine core dendrimers: (a) Hong, Y.-R.; Gorman, C. B. *J. Org. Chem.* **2003**, *68*, 9019–9025; (b) Tyson, D. S.; Luman, C. R.; Castellano, F. N. *Inorg. Chem.* **2002**, *41*, 3578–3586; (c) Issberner, J.; Vogtle, F.; Cola, L. D.; Balzani, V. *Chem. Eur. J.* **1997**, *3*, 706–712.
- (a) Tomoyose, Y.; Jiang, D.-L.; Jin, R.-H.; Aida, T.; Yamashita, T.; Horie, K.; Yashima, E.; Okamoto, Y. *Macromolecules* **1996**, *29*, 5236–5238; (b) Hawker, C. J.; Fréchet, J. M. J. *J. Am. Chem. Soc.* **1990**, *112*, 7638–7647.
- Selected data*: 3(G2[Me]) white powder; mp 151.5–152.5 °C; $\nu_{\max}(\text{CH}_2\text{Cl}_2)/\text{cm}^{-1}$ 3001, 2937, 2838, 1597, 1458, 1374, 1296, 1230, 1204, 1155, 1055, 833; δ_{H} (500 MHz; CDCl₃; Me₄Si) 3.79 (24H, s, OCH₃), 4.99 (8H, s, outer-CH₂), 5.15 (4H, s, inner-CH₂), 6.41 (4H, t, *J* 2.2, *ArH*), 6.59–6.57 (10H, m, *ArH*), 6.69 (4H, d, *J* 2.2, *ArH*), 6.88 (2H, dd, *J* 5.6 and 2.7, 5,5'-bipyridine-*H*), 8.06 (2H, d, *J* 2.7, 3,3'-bipyridine-*H*), 8.47 (2H, d, *J* 5.6, 6,6'-bipyridine-*H*); δ_{C} (125 MHz; CDCl₃; Me₄Si) 55.3, 69.7, 70.1, 100.0, 101.9, 105.2, 106.4, 107.1, 111.4, 138.2, 139.0, 150.2, 157.8, 160.1, 161.0, 165.7; *m/z* (FAB) 1033.5 ([*(M+H)*]⁺ C₆₀H₆₁N₂O₁₄ requires 1033.4); Anal. Calcd for C₆₀H₆₀N₂O₁₄: C, 69.75; H, 5.85; N, 2.71. Found: C, 69.74; H, 6.03; N, 2.60.
- (a) Freeman, A. W.; Christoffels, L. A. J.; Fréchet, J. M. J. *J. Org. Chem.* **2000**, *65*, 7612–7617; (b) Forier, B.; Dahan, W. *Tetrahedron* **1999**, *55*, 9829–9846.
- Previously reported Cu(OTf)₂-catalyzed Diels–Alder reaction: (a) Hertweck, C. *J. Pract. Chem.* **2000**, *342*, 316–321; (b) Sagasser, I.; Helmchen, G. *Tetrahedron Lett.* **1998**, *39*, 261–264; (c) Brunel, J. M.; Campo, B. D.; Buono, G. *Tetrahedron Lett.* **1998**, *39*, 9663–9666; (d) Carbone, P.; Desimoni, G.; Faita, G.; Filippone, S.; Righetti, P. *Tetrahedron* **1998**, *54*, 6099–6110; (e) Evans, D. A.; Miller, S. J.; Lectka, T. *J. Am. Chem. Soc.* **1993**, *115*, 6460–6461.
- General procedure: The dendritic Lewis acid catalyst was prepared by treatment of Cu(OTf)₂ (0.03 mmol) with 3(G2[Me]) (0.03 mmol) at room temperature in dry dichloromethane (1.5 mL) for 2 h under an argon atmosphere. To the resulting bluish green solution of the catalyst was added a mixture of diene (1.5 mmol) and dienophile (0.3 mmol) in dry dichloromethane (1.5 mL) at 0 °C under an argon atmosphere. The resulting mixture was stirred for 2–16 h at room temperature (monitored by TLC). It was then quenched with water and was subjected to the usual extractive workup with dichloromethane. The residual oil obtained after evaporation of dichloromethane, which was dried over magnesium sulfate, was purified by column chromatography on silica gel to give the corresponding Diels–Alder adducts.
- Narasaka, K.; Iwasawa, N.; Inoue, M.; Yamada, T.; Nakashima, M.; Sugimori, J. *J. Am. Chem. Soc.* **1989**, *111*, 5340–5345.
- Previously reported positive dendritic effects caused by the periphery-catalyzed dendrimers: (a) Benito, J. M.; de Jesus, E.; de la Mata, F. J.; Flores, J. C.; Gomez, R. *Chem. Commun.* **2005**, 5217–5219; (b) Delort, E.; Darbre, T.; Raymond, J.-L. *J. Am. Chem. Soc.* **2004**, *126*, 15642–15643; (c) Ribourdouille, Y.; Engel, G. D.; Richard-Plouet, M.; Gade, L. H. *Chem. Commun.* **2003**, 1228–1229; (d) Dahan, A.; Portnoy, M. *Org. Lett.* **2003**, *5*, 1197–1200;

- (e) Mizugaki, T.; Murata, M.; Ooe, M.; Ebitani, K.; Kaneda, K. *Chem. Commun.* **2002**, 52–53.
15. (a) Chow, H.-F.; Mak, C. C. *J. Org. Chem.* **1997**, *62*, 5116–5127; (b) Mak, C. C.; Chow, H.-F. *Macromolecules* **1997**, *30*, 1228–1230.
16. It has been reported that the Lewis acid complex having a distorted skeleton afforded a better Lewis acidity: (a) Brunner, H.; Bluchel, C.; Doyle, M. P. *J. Organomet. Chem.* **1997**, *541*, 89–95; (b) Koide, Y.; Bott, S. G.; Barron, A. R. *Organometallics* **1996**, *15*, 5514–5518.