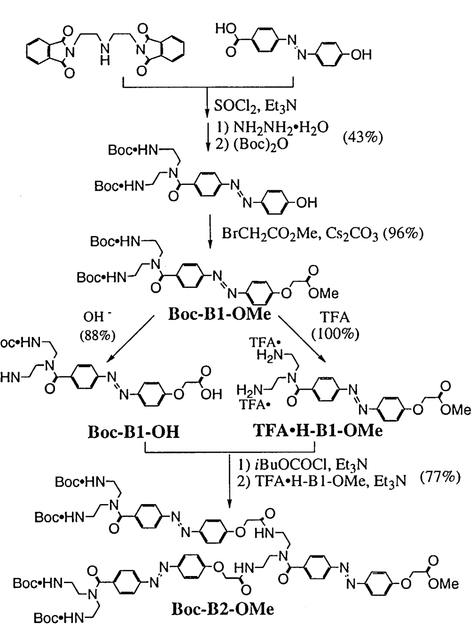
Syntheses and Characterization of Photochromic Dendrimers Including a 1,3-Alternate Calix[4]arene as a Core and Azobenzene Moieties as Branches

Takeshi Nagasaki,* Seizo Tamagaki, and Kenji Ogino
Department of Bioapplied Chemistry, Faculty of Engineering, Osaka City University, Sugimoto 3-3-138, Sumiyoshi-ku, Osaka 558

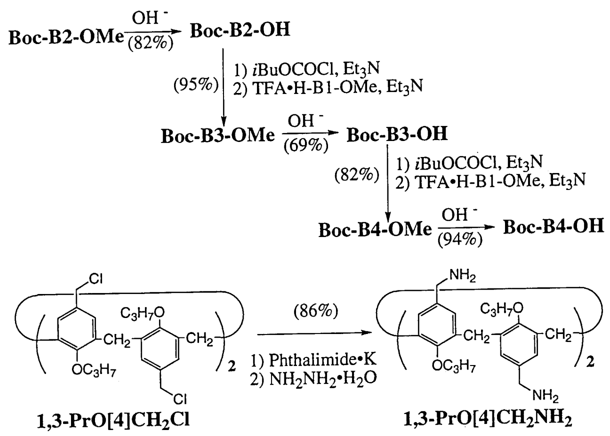
(Received February 19, 1997; CL-970119)

The first photochromic dendrimers which involve a 1,3-alternate conformer of a calix[4]arene as a core and azobenzene skeletons as branches have been synthesized and characterized. Photochemical properties of the photochromic dendrimers are described.

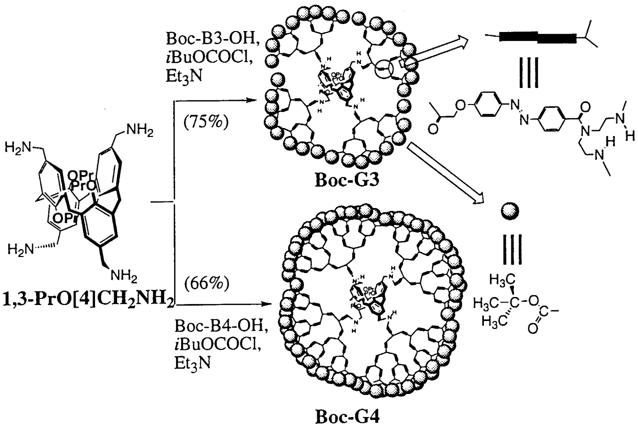
Dendritic molecules are receiving growing attention for constructing nanostructural materials.[1] Outstanding features of dendrimers are a highly branched structure, a mono-dispersed molecular-weight, a globular and symmetrical conformation, and a high density of peripheral functionalities, *etc.* Therefore, it is expected that a dendritic polymer has quite different properties compared to well-known linear polymers reported to date. Although many linear and photochromic polymers[2] have been investigated, to the best of our knowledge, the photochromism of globular polymers has hardly been exploited so far. In this communication, we report the syntheses and chracterization of the first photochromic dendrimers consisting of the 1,3-alternate conformer of a calix[4]arene derivative as a core, and the azobenzene-based diamino carboxylic acid as a branched building block. Recently, Mckervey and co-workers[3] reported the first calix[4]arene-bound dendritic molecules which adopt a cone conformation. On the other hand, the fixed 1,3-alternate conformer used here is suitable to decrease crowded repulsions at the periphery since the 1,3-alternate conformer has a pseudo-tetrahedral structure.



Scheme 1.



Scheme 2.



Scheme 3.

As shown in Scheme 1, the protected 4-[*N,N*-bis(2-amioethyl)amino]carbonyl-4'-carboxymethoxyazobenzene is prepared as a diamino carboxylic acid which allows standard peptide synthesis conditions for chain elongation. Treatment of 4-carboxyl-4'-hydroxyazobenzene with thionyl chloride was followed by the reaction with diphthaloyldiethylenetriamine to give an amide derivative.[4] After removal of phthaloyl groups by hydrazine hydrate, two amino groups were repeatedly protected with $(Boc)_2O$ to give 4-[*N,N*-bis(2-tert-butoxycarbonylamino-ethyl)amino]carbonyl-4'-hydroxyazobenzene. Finally, alkylation of the hydroxyl group with methyl bromoacetate and Cs_2CO_3 afforded the desired diamino carboxylic acid derivative (Boc-B1-OMe) in which both amino- and carboxyl-terminals were protected by Boc and methyl groups, respectively. Then, amide bond formation was achieved by isobutylchloroformate mediated mixed anhydride method from N-Boc derivatives (Boc-B1-OH) and the methyl ester (H-B1-OMe) to give the fully protected second-generation branch (Boc-B2-OMe). Repetitive hydrolysis of the carboxyl terminal followed by amide couplings with H-B1-OMe generated third- and forth-generation branches (Boc-B3-OMe and Boc-B4-OMe, respectively) as shown in Scheme 2. Furthermore, dendrimers covered with protected amino groups (Boc-G3 and Boc-G4) were obtained by hydrolysis of carboxyl terminals of Boc-B3-OMe and Boc-B4-OMe followed by the coupling with 1,3-alternate-5,11,17,23-tetrakis(amino-methyl)-25,26,27,28-tetrapropoxycalix[4]arene (1,3-PrO[4]CH_2NH_2) which is derived from corresponding chloromethyl derivative[5] (Scheme 2 and 3). In coupling reaction between the core tetraamine and acid-baranch molecules 1.2 equivalent of mixed anhydride were treated against one amino group. Gel permeation-chromatography was amazingly efficient for purification because of enormous difference of molecular weight between desired dendrimer and impurities. The reactions of high generation steps proceed smoothly in the dark, that is, trans-isomers of the azobenzene skeletons are more favorable than cis-isomers with respect to steric hindrance. Each compound was identified on the basis of elemental analyses, IR, NMR, and mass spectral evidences.[6] Interestingly, in ^{1}H-NMR spectra the slow rotation around the amide bond neighboring the azobenzene causes the splitting of peaks which are shielded or deshielded by the ring current of the azobenzene even at high temperature (130 ℃) as given in reference.

The theoretical molecular weights of Boc-G3 and Boc-G4 are computed to be 14200 and 29161, respectively. Since these compounds contain protonizable azo groups, one can estimate the relative molecular masses by matrix assisted laser desorption ionization time-of-flight mass spectrometry (MALDI- TOF-MS)[7] in acidic media. For Boc-G3, m/z = 14201, which corresponds to $[\text{Boc-G3}\bullet\text{H}]^+$, 7101 ($[\text{Boc-G3+2H}]^{2+}$), 4734 ($[\text{Boc-G3+3H}]^{3+}$), 3551 ($[\text{Boc-G3+4H}]^{4+}$), and 2841 ($[\text{Boc-G3+5H}]^{5+}$) were observed. Similarly we could detect m/z peaks for Boc-G4. These values are in good accord with the theoretical relative molecular masses.

Photochromic properties due to the isomerism of azobenzene moieties was estimated with irradiation of UV light or visible light and standing in the dark.[8] Both dendrimers (Boc-G3 and Boc-G4) showed the typical switching behavior of an azobenzene. The intense absorption of trans azobenzene at 347 nm decreased on irradiation at 365 nm light while the absorption at 441 nm due to cis form increased. Irradiation with UV light (365 nm) yields a 20/80 mixture of trans/cis conformer in the case of Boc-G3, whereas an equilibrium with 35/65 ratio of trans/cis is achieved for Boc-G4 in THF.[9] Compared to Boc-G3, Boc-G4 shows the small conversion between cis and trans forms. This can be attributed to increased steric repulsions in the higher generation branches. By irradiation at 436 nm, the content of trans azobenzenes was recovered. These conversions were reproducible upon further irradiation cycle, although spectra were slightly different from the initial one. The decrease in absorption at 347 nm was ca. 5% in twenty cycles. The half-life of thermal cis-to-trans isomerization at 38 ℃ were 240 and 200 min for Boc-G3 and Boc-G4, respectively.

These observations indicate that the particle size of globular molecules which include azobenzene skeletons might be controllable by irradiation with UV or visible light and the dark adaptation. The regulation of particle sizes and the development of drug delivery systems by using such photoresposive dendrimers are now in progress in our laboratory.

T. N. thanks Kazuo Harada for comments on the manuscript and acknowledges a Grant-in-aid for Encouragement of Young Scientists, No. 08780547 from the Ministry of Education, Science, Sports and Culture, Japan and a partial financial support of Arakawa Award in Synthetic Chemistry, Japan.

References and Notes

1 G. R. Newkome, C. N. Moorefield, and F. Vögtle, *Dendritic Molecules*, VCH, Weinheim (1996); S. C. Zimmerman, F. Zeng, D. E. C. Reichert, and S. V. Kolotuchin, *Science*, **271**, 1095(1996); R. Sadamoto, N. Tomioka, and T. Aida, *J. Am. Chem. Soc.*, **118**, 3978 (1996); K. Aoi, K. Itoh, and M. Okada, *Macromolecules*, **28**, 5391 (1995); J. M. J. Fréchet, *Science*, **263**, 1710 (11994); T. Nagasaki, O. Kimura, M. Ukon, S. Arimori, I. Hamachi, and S. Shinkai, *J. Chem. Soc., Perkin Trans. 1*, **1994**, 75.; D. A. Tomalia and H. D. Drust,*Top. Curr. Chem.*, **165**, 193 (1993).

2 For a comprehensive references, see, F. Ciardelli, O. Pieroni, A. Fissi, C. Carlini, and A. Altomare, *Brit. Poly. J.*, **21**, 97 (1989).

3 G. Ferguson, J. F. Gallagher, M. A. McKervey, and E. Madigan, *J. Chem. Soc., Perkin Trans. 1*, **1996**, 599.

4 C. Y. Ng, R. J. Motekaitis, and A. E. Martell, *Inor. Chem.*, **18**, 2982 (1979).

5 A. Ikeda, T. Nagasaki, K. Araki, and S. Shinkai, *Tetrahedron*, **48**, 1059 (1992); A. Ikeda and S. Shinkai, *J. Am. Chem. Soc.*, **113**, 7335 (1991).

6 Selected data for ***Boc-G4***; mp 167-171 ℃; ν_{max}(KBr)/cm^{-1} 3600-2800 (NH and COOH), 1730-1640 (C=O), and 1142 (C-O-C); δ(DMSO-d6; 130 ℃, 400 MHz): 0.74 (3 H, t, J=7.6 Hz, CH_3), 1.39 and 1.41 (576 H, s x 2, ^{t}Bu), 1.40 (8 H, m, $\underline{CH_2}CH_3$), 3.11-3.66(496 H, m, N CH_2CH_2N, ArCH_2Ar, and $\underline{CH_2}CH_2CH_3$), 4.60 and 4.97 (112 H, sx2, OCH_2 of 2nd-4th generations), 4.64 (2 H, s, OCH_2 of 1st generation), 6.15 and 8.15 (64 H, s(br) x 2, NH of urethane), 6.92 (8 H, s, Ar-H of core), 7.06-7.16 (120 H, m, *ortho* Ar-H to OH) , 7.72-7.98 (388 H, m, *meta* Ar-H to OH, *meta* and *ortho* Ar-H to C=O, and NH of amide), 8.33 (28 H, s(br), NH of amide); MALDI-TOF-MS m/z 29162 ($[\text{Boc-G4+H}]^+$), 14581 ($[\text{Boc-G4+2H}]^{2+}$), 9721($[\text{Boc-G4+3H}]^{3+}$), 7291 ($[\text{Boc-G4+4H}]^{4+}$), and 5833 ($[\text{Boc-G4+5H}]^{5+}$) (Found: C, 61.74; H, 6.21; N, 14.36%. Calcd for $C_{1504}H_{1832}N_{304}O_{312}$: C, 61.95; H, 6.33; N, 14.60%).

7 B. T. Chait and S. B. H. Kent, *Science*, **257**, 1885 (1992).

8 The irradiations of 365 and 436 nm were performed with the 150 W high pressure mercury lamp and the 500 W tungsten lamp, respectively.

9 W. R. Brode, J. H. Gould, and G. M. Wyman, *J. Am. Chem. Soc.*, **74**, 4641 (1952).