was removed by filtration, and the solvent evaporated under reduced pressure. The crude residue was chromatographed on silica gel (CH_2Cl_2 : MeOH, 9 : 1) to give the pure *N,N*-dimethylhexylamine (0.36 g, 95%) (entry 1): ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.88 (t, 3H, J=6.4 Hz), 1.39 (m, 8H), 2.20 (s, 6H), 2.23 (t, 2H, J=7.3 Hz); IR (neat) 3400, 2950, 2800, 1490, 1050 cm^{-1}; MS m/z (relative intensity) (EI, 70 eV) 129 (M^+, 63), 59 (4), 58 (100), 42 (5).

***N,N*-Dimethyl-3-cyclohexenylmethylamine.** (entry 3) ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.07 (m, 6H), 2.11 (m, 1H), 2.83 (s, 6H), 2.92 (d, 2H, J=6.8 Hz), 5.68 (brs, 2H); IR (neat) 3623, 2960, 2570, 1730, 1690, 1265 cm^{-1}; MS m/z (relative intensity) (EI, 70 eV) 139 (M^+, 3), 79 (2), 77 (1), 59 (4), 58 (100); Anal. Calcd for $C_9H_{17}N$: C, 77.63; H, 12.31; N, 10.06. Found: C, 77.54; H, 12.70; N, 10.05.

***N,N*-Dimethyl-*p*-carbomethoxybenzylamine.** (entry 10) ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.24 (s, 6H), 3.47 (s, 2H), 3.91 (s, 2H), 7.38 (d, 2H, J=7.8 Hz), 7.99 (d, 2H, J=8.06 Hz); IR (neat) 2976, 2817, 1720, 1435, 757 cm^{-1}; MS m/z (relative intensity) (EI, 70 eV) 193 (M^+, 46), 192 (30), 149 (10), 89 (6), 58 (100); Anal. Calcd for $C_{11}H_{15}NO_2$: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.78; H, 8.07; N, 6.76.

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References

1. (a) Shaw, K. T.; Luly, J. R.; Rapoport, H. *J. Org. Chem.* **1985**, *50*, 4515. (b) Ojima, I.; Kato, K.; Nakahashi, K.; Fuchikami, T, T.; Fujita, M. *J. Org. Chem.* **1989**, *54*, 4511. (c) Askin, D.; Wallace, M. A.; Vacca, J. P.; Reamer, R. A.; Volante, R. P.; Shinkai, I. *J. Org. Chem.* **1992**, *57*, 2771.
2. (a) Cohen, N.; Lopresti, R. J.; Neukom, C.; Saucy, G. *J. Org. Chem.* **1980**, *45*, 582. (b) Payne, N. C.; Stephan, D. W. *Inorg. Chem.* **1982**, *21*, 182. (c) Togni, A.; Venanzi, L. M. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 497.
3. (a) Niall, H. D.; Keutmann, H. T.; Copp, D. H.; Potts, J. T., Jr. *Proc. Nat. Acad. Sci. U. S.* **1969**, *64*, 771. (b) Hermodson, M. A.; Ericsson, L. H.; Titani, K.; Neurath, H.; Walsh, K. A. *Biochemistry* **1972**, *11*, 4493.
4. (a) Dhaon, M. K.; Olsen, R. K.; Ramasamy, K. *J. Org. Chem.* **1982**, *47*, 1062. (b) Becker, M. M.; Wang, J. C. *Nature* **1984**, *309*, 682.
5. (a) Borch, R. F.; Durst, H. D. *J. Am. Chem. Soc.* **1969**, *91*, 3996. (b) Borch, R. F.; Berstein, M. D.; Durst, H. D. *J. Am. Chem. Soc.* **1971**, *93*, 2897. (c) Hutchins, R. O.; Markowitz, M. *J. Org. Chem.* **1981**, *46*, 3571. (d) Kim, S.; Oh, C. H.; Ko, J. S.; Ahn, K. H.; Kim, Y. J. *J. Org. Chem.* **1985**, *50*, 1927.
6. Pelter, C. A.; Rasser, R. M.; Mills, S. *J. Chem. Soc., Perkin Trans.* **1984**, 717.
7. Abdel-Magid, A. F.; Carson, K. G.; Harris, B. D.; Maryanoff, C. A.; Shah, R. D. *J. Org. Chem.* **1996**, *61*, 3849.
8. Yoon, N. M.; Kim, E. G.; Son, H. S.; Choi, J. *Synth. Commun.* **1993**, *23*, 1595.
9. Bhattacharyya, S. *J. Org. Chem.* **1995**, *60*, 4928.

An Efficient Synthesis of Ethylenimine Dendrimer

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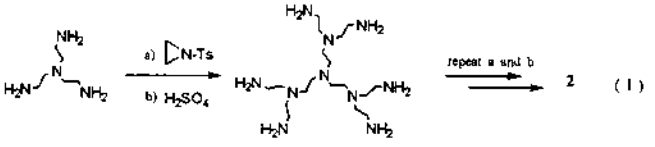
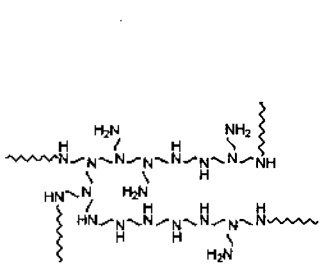
Because of their potential in cancer chemotherapy,[1] siderophores,[2] immobilization of enzyme,[3] gene delivery,[4] anion-exchange chromatography,[5] and skeleton of artificial enzyme,[6] poly(ethylenimine) (**1**)[7] derivatives have received a great deal of attention from synthetic chemists. Amongst them, ethylenimine dendrimer (**2**) is our recent interest because various biomimetic functional molecules can be designed by attaching appropriate chemical moieties to it. Dendrimer with hydrophilic exteriors and hydrophobic interiors like **2** may be regarded as covalently bonded assemblies of amphiles such as micells[8] or vesicles[9] possessing well-defined structures.

We used **2** for the study of biomimetic catalyst in our previous publication.[10] For further application of **2**, we need to improve the synthetic procedure because it was not easy to get enough amount of **2** by the known procedure.[11] Tomalia *et al.* synthesized **2** as shown in equation 1. They used *N*-(*p*-toluenesulfonyl)aziridine (Ts-aziridine) as a repeating unit. However, the deprotection of *p*-toluenesulfonyl (Ts) group with H_2SO_4 was inefficient due to the complex procedure and low yield (~30%) in each deprotection step.

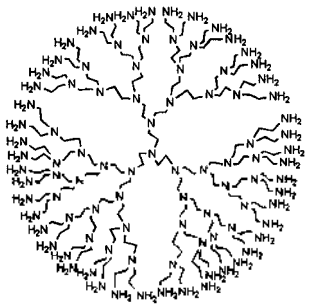


(1)

In this paper, we report an efficient procedure for the synthesis of dendrimer **2**. The key step for this synthesis is deprotection. If we can use the *N*-benzyloxycarbonylaziridine (Cbz-aziridine) (**4**) as a repeating unit, the deprotection procedure will be more efficient and simpler than otherwise because the Cbz can be removed by catalytic hydrogenolysis. **4** was synthesized from β-aminoethylsulfuric acid as shown in equation 2. The reaction of **4** with benzylamine was examined in order to establish the reaction conditions. The



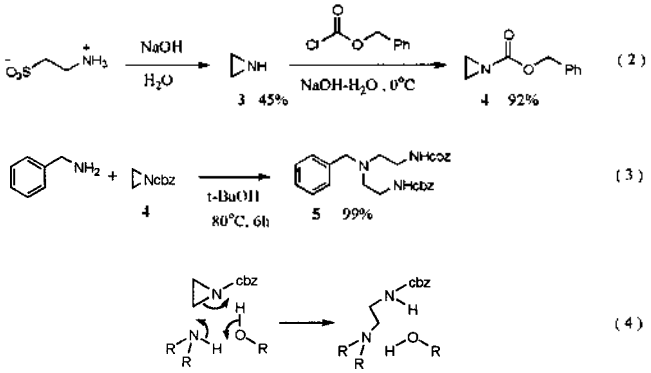
Poly(ethylenimine) (**1**)



Ethylenimine Dendrimer (**2**)

reaction of **4** with benzylamine in CH_3CN-toluene (2 : 1) was found to be very slow (3 days at 80 °C).[12] This condition is not practical for the synthesis of 2. When CH_3CN-toluene (2 : 1) was replaced by EtOH, the reaction was completed within 12 hr at rt. However, we detected several side products simultaneously which resulted from the attack of EtOH as a nucleophile. These observations indicate that non-nucleophilic protic solvent is crucial for the acceleration of this reaction as shown in equation 4. Upon using *t*-BuOH instead of EtOH as a solvent, the reaction time was reduced to 6 hr from 3 days at 80 °C in the reaction of **4** with benzylamine and any side-products were not detected. Thus, this condition was applied to the reaction of **4** with tris(2-aminoethyl)amine (Scheme 1). Under this condition, the product **7** was obtained in high yield (96%) as expected after short column chromatography (SiO_2, hexane-ethyl acetate=1 : 1) to remove the excess of Cbz-aziridine. Cbz group of **7** was removed easily by catalytic hydrogenolysis (H_2, 40 psi, Pd/C) to give **9**. However, the reaction of **9** with **4** is not practical due to the low solubility of **9** in *t*-BuOH and its slow reaction rate. Thus, Ts-aziridine (**6**) instead of Cbz-aziridine (**4**) was used for the next sequential steps.

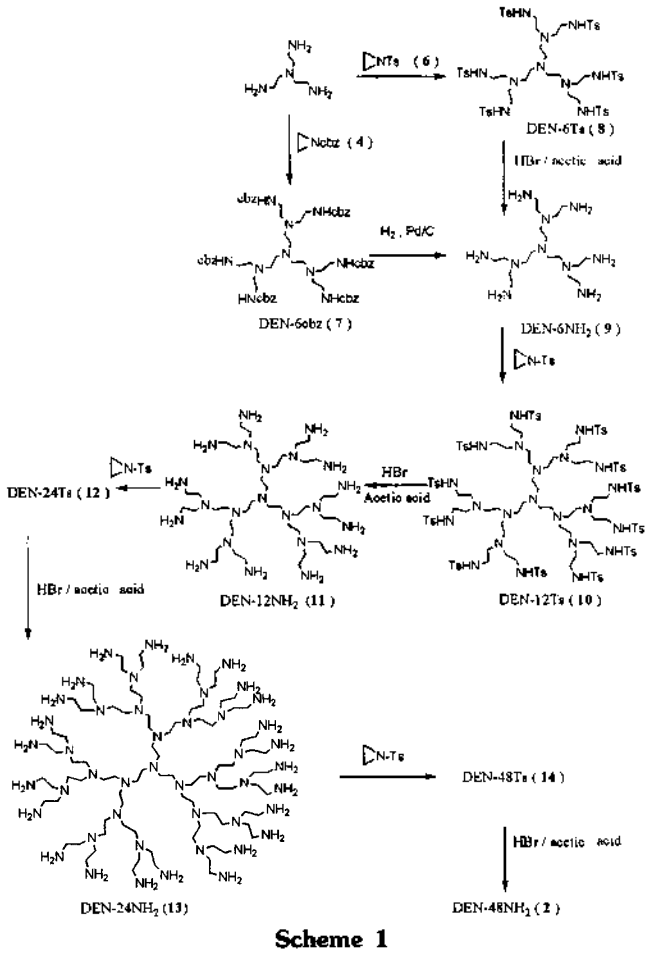
In case of Ts-aziridine,[13] EtOH was used as solvent because the reaction was completed within a day at rt without any side reaction. However, it was necessary to improve the detosylation procedure due to the reason mentioned above. Fortunately, we could remove Ts group easily with HBr/AcOH. A solution of **9** in HBr/AcOH was stirred overnight at 90 °C, and the resulting solid was characterized as HBr salt of detosylated dendrimer 10 by ^{1}H NMR and



elemental analysis. The ^{1}H NMR spectrum of this solid showed completion of detosylation by disappearance of aromatic protons of Ts group. After neutralization of the HBr salt to pH 10 with NaOH, it was used in the next step without further purification. This detosylation procedure is simple and efficient (yields are more than 80% in each step) and can be applied to all of the next detosylation steps. Of course, **9** also could be prepared from **8** under the same condition.

The reaction condition and purification procedure of *N*-alkylation, the reactions of Ts-aziridine with amines (**9**, **11**, and **13**), were also improved. Tomalia *et al.*[11] used EtOH as a solvent in the reaction of *N*-alkylation. In that case, syrup was coated on the surface of reaction flask during the reaction. This syrup can contain the intermediates which are insoluble in EtOH, and thus make the reaction difficult to complete. Thus, EtOH was replaced by EtOH-THF (3 : 1) which can rule out the formation of the syrup. After completion of the reaction, the excess of Ts-aziridine was removed by the following procedure. The reaction mixture was concentrated and the resulting syrup was dissolved in CH_2Cl_2-EtOH (1 : 1) followed by evaporation of CH_2Cl_2 to give *N*-alkylated product (DEN-Ts) as a syrup in EtOH. By simple repetition of the *N*-alkylation with Ts-aziridine and the detosylation with HBr/AcOH as shown in Scheme 1, **2** was synthesized efficiently from core amine (overall yield: 35%).

The precursor **13** of dendrimer **2** was examined by ^{1}H NMR, GPC, and elemental analyses. The ratio of signal integration of aromatic protons (7.24-7.62 ppm) to ethylene protons (2.24-2.64 ppm) in ^{1}H NMR (DMSO-d_6) spectrum was in agreement with the theoretical value within 10%



Scheme 1

error. GPC analysis showed the molecular weight distributions of M_w/M_n=1.06 for **13**, meaning that the defect of dendrimer **2** is not serious. In HBr salts of **2**, **9**, **11**, and **13** the numbers of HBr designated by "n" were determined by acid-base titration (n=61 for **2**, 6 for **9**, 14 for **11**, and 30 for **13**) and elemental analysis (n=63 for **2**, 6 for **9**, 15 for **11**, and 31 for **13**). A preparation of higher generation than **2** was not tried because CPK model of the higher generation is forbidden due to starburst dense packing as described and predicted by de Gennes and others.[15,16]

It is noteworthy that *t*-BuOH as a non-nucleophilic solvent is crucial for the acceleration of the reaction of Cbz-aziridine with amine although Cbz-aziridine was found to be not suitable for the synthesis of **2** due to the low solubility of polyamine in *t*-BuOH and slow reaction. For the synthesis of **2**, the procedure of detosylation was improved by using HBr/AcOH which was found to be much more efficient than H_2SO_4 due to the simple procedure and high yield. Establishment of this synthetic procedure will stimulate the study of molecular recognition using ethylenimine dendrimer.

Experimental

General. GPC analysis was done using Waters 440, styragel HR5E4E2 column, and adjustable UV/vis detctor, using THF. Acid-base titration was performed using Mettler Toledo 320 pH Meter. Melting points were obtained on a Mel-Temp melting point apparatus. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker 500 MHz and 125.8 MHz. Elemental analyses were performed using Fisons EAGER 200.

***N*-Benzyloxycarbonylaziridine (4).**[12] For the preparation of aziridine, the known procedure[14] was modified. A solution of *β*-aminoethylsulfuric acid (564 g, 4 mole) and 40% of NaOH (704 g of NaOH in 1056 mL of water) was distilled until 100 mL of distillate is collected as quickly as possible under atmosphere. This distillate was redistilled through a wrapped 10 inch Vigreux column and the distillate boiling at 50-100 °C was collected (yield: 41-45%). This aqueous aziridine was used for the next step without further purification. After determination of content of aziridine by ^{1}H NMR, the aqueous aziridine (0.46 mole) was saturated with KOH (220 g). To the aqueous aziridine was added benzylchloroformate (68 mL, 0.48 mole) in Et_2O (100 mL) dropwise with vigorous stirring at 0 °C. After completion of the addition, the reaction mixture was stirred for 2 hr at 0 °C. The reaction mixture was extracted with Et_2O, concentrated and chromatographed (SiO_2, hexane-ethyl acetate=10 : 1) to give 66.8 g (82%) as colorless oil. ^{1}H NMR ($CDCl_3$) δ 2.21 (s, 4H), 5.21 (s, 2H), 7.34 (s, 5H). ^{13}C NMR ($CDCl_3$) δ 25.39, 67.72, 127.71.

DEN-6cbz (7). A solution of tris(2-aminoethyl)amine (1.46 g, 10 mmole) and *N*-benzyloxycarbonylaziridine (12.74 g, 72 mmole) in anhydrous *t*-BuOH (50 mL) was refluxed for 16 hr under N_2. After concentration, the residue was chromatographed (SiO_2, hexane : ethyl acetate=1 : 1) to give **7** (11.6 g, 96%, thick oil).; ^{1}H NMR (acetone-d_6) δ 2.55 (t, 24H), 3.17 (m, 12H), 5.04 (s, 3H), 7.33 (m, 30H); ^{13}C NMR (acetone-d_6) δ 40.0, 40.1, 55.0, 66.6, 128.6, 128.8, 129.2, 138.5, 157.5; Mass (FAB): m/z 1208.

***N*-(*p*-toluenesulfonyl)aziridine (6).** **6** was synthesized according to the reference.[17] To a stirred suspention of TsCl (80.3 g, 0.42 mole) in pyridine (80 mL) cooled to −40 °C was added dropwise a solution (cooled to 0 °C) of 2-aminoethanol (12.2 g, 0.2 mole) in pyridine (30 mL). After the addition was completed, the temperature was maintained for 1 hr at 0 °C. Crushed ice was added, the solid was filtered, washed with H_2O and dissolved in $CHCl_3$ (100 mL), and this solution was washed 3x with H_2O, dried (Na_2SO_4) and concentrated. This solid was dissolved in hot CCl_4 (150 mL), and recrystalized on cooling to give 2-(tosylamino) ethyl *p*-touenesulfonate (55 g, 75%), mp 87-88 °C. (lit.[17a] 86-87 °C). This ditosylate (228 g, 0.61 mole) was suspended in toluene (2 L). To this vigoriously stirred mixture was added a solution of KOH (156 g, 2.8 mole) in H_2O (800 mL) whin 1 hr. The stirring was maintained for 2 hr, the organic layer washed 3x with H_2O, dried (Na_2SO_4), and evaporated to give **6** (110 g, 99%) as a white solid. This Ts-aziridine was used for following step without further purification, mp 63 °C (lit.[17b] 63-64 °C). ^{1}H NMR ($CDCl_3$) δ 2.36 (s, 2H), 2.46 (s, 3H), 7.4 and 7.9 (m, 4H).

DEN-6Ts (8). **8** was synthesized according to the reference.[11] A solution of tris(2-aminoethyl)amine (3.5 g, 0.024 mole) and Ts-aziridine (28.55 g, 0.145 mole) in EtOH (50 mL, 95%) was stirred with mechanical stirrer for 2 hr. After adding another 50 mL of EtOH to the resulting solid mass and stirring overnight at 25 °C, the white solid are isolated by filtration, washed with 2× 100 mL EtOH and 2× 150 mL Et_2O to give **8** (24.8 g, 87%). ^{1}H NMR (DMSO-d_6) δ 2.12 (t, 6H), 2.19 (t, 12H), 2.33 (s, 18H), 2.65 (t, 12H), 7.33 (d, 12H), 7.37 (br, s, 6H), 7.64 (d, 12H).

DEN-6NH$_2$ (9). From DEN-6cbz (7): To a solution of **7** (10 g, 8.28 mole) in MeOH (40 mL) was added Pd/C (10%, 1 g) and the reaction mixture was shaked for 16 hr under H_2 (40 psi). After filtration, MeOH was evaporated to give **9** (3.25 g, 98%, pale yellow thick oil). ^{1}H NMR (D_2O) δ 2.52 (br, s, 12H), 2.61 (t, 12H), 2.86 (t, 12H); ^{13}C NMR (D_2O) δ 49.9, 50.6, 51.4, 52.3. **From DEN-6Ts(8):** A solution of **6** (12 g, 8.65 mmole) and phenol (0.5 g, 5.3 mmole) in 30% HBr/AcOH (200 mL) was refluxed for 24 hr. The reaction mixture was filtered and the resulting pale redish solid was placed in EtOH (50 mL). After refluxing for 1 hr, the solution was filtered and the resulting solid was washed with 2× 50 mL of Et_2O to give **9** (6.73 g, 84%, as white solid); ^{1}H NMR (D_2O) δ 2.79 (t, 6H), 3.00 (m, 12H), 3.34 (m, 18H). Anal. Calc. for $C_{18}H_{48}N_{10}\cdot 6HBr\cdot 2H_2O$: C, 23.33; H, 6.26; N, 15.12. Found C, 23.55; H, 6.40; N, 14.93.

DEN-12Ts (10). A solution of **9** (2 g, 4.96 mole) and *N*-(*p*-toluenesulonyl)aziridine (**6**) (12.3 g, 62.5 mmloe) in EtOH (60 mL)-THF (20 mL) was stirred for overnight at rt. After concentration, the residue was dissolved in CH_2Cl_2 (40 mL)-EtOH (40 mL). CH_2Cl_2 was evaporated to form a syrup and ethanol was stripped. For the removal of excess of Ts-aziridine, the last procedure was repeated once more and the resulting syrup was dissolved in CH_2Cl_2, washed with H_2O, dried (Na_2SO_4) and concentrated to yield 12.6 g (92%) of **10**. ^{1}H NMR ($CDCl_3$), δ 2.36 (br, s, 36H), 2.37-2.62 (m, 60H), 6.48 (s, 12H), 7.22 (d, 24H), 7.73 (d, 24H); Anal. Calc. for $C_{126}H_{180}N_{22}O_{24}S_{12}\cdot 3H_2O$: C, 53.58; H, 6.59; N, 10.91; O, 15.31. Found C, 53.64; H, 6.57; N, 10.37; O, 15.56.

DEN-12NH$_2$ (11). A solution of **10** (23 g, 8.15 mmole) and phenol (1.0 g, 10.9 mmole) in 30% HBr/AcOH

(150 mL) was refluxed for 24 hr. The reaction mixture was filtered and the resulting pale redish solid was placed in EtOH (100 mL). After refluxing for 1 hr, EtOH was removed by filtration and washed with Et_2O to give **11** (15 g, 83%, as white solid); ^1H NMR (D_2O) δ 3.00 (t, 12H), 3.03 (m, 6H), 3.13 (t, 24H), 3.16 (t, 12H), 3.27-3.39 (m, 24H), 3.41-3.51 (m, 6H), Anal. Calc. for $C_{42}H_{103}N_{22}\cdot 15HBr\cdot 5H_2O$: C, 22.70; H, 5.77; N, 13.87. Found C, 23.18; H, 5.79; N, 13.42.

DEN-24Ts (12). A solution of **11** (15 g, 6.76 mmole) in H_2O (30 mL) was basified with 4 N NaOH to pH 10 and diluted with EtOH (120 mL). *N*-(*p*-toluenesulfonyl)aziridine (32 g, 162.2 mmole) was added to the above solution and stirred overnight at rt. After the solvent was stripped, the resulting syrup was dissolved in CH_2Cl_2 (100 mL) and washed with sat'd Na_2CO_3. The organic layer was concentrated and the residue was dissolved in EtOH (100 mL)-THF (50 mL). *N*-(*p*-toluenesulfonyl)aziridine (4 g, 20.3 mmole) were added to above solution and stirred for overnight at rt. The reaction mixture was concentrated and dissolved in CH_2Cl_2 (50 mL)-EtOH (100 mL). CH_2Cl_2 was evaporated to form syrup and EtOH was stripped. To remove excess of Ts-aziridine, the last procedure was repeated once more The resulting syrup was dissolved in CH_2Cl_2 and washed with H_2O and concentrated to give **12** (31.7 g, 87%, amorphous solid); ^1H NMR (DMSO-d_6) δ 2.29 (br, s, 213H), 2.64 (br, s, 48H), 7.28 (br, s, 72H), 7.62 (br, s, 48H); Anal. Calc. for $C_{258}H_{372}N_{46}O_{48}S_{24}\cdot 6H_2O$: C, 51.12; H, 6.35; N, 10.60; O, 14.52. Found C, 51.65; H, 6.41; N, 10.28; O, 14.40.

DEN-24NH$_2$ (13). Following the procedure described for the preparation of **10, 12** (29.0 g, 6.83 mmole) was deprotected to DEN-24N**H**$_2$ (**13**) (18.5 g, 81%). ^1H NMR (D_2O) δ 2.98 (br, s, 24H), 3.10 (m, 66H), 3.19-3.50 (m, 90H); Anal. Calc. for $C_{60}H_{228}N_{46}\cdot 31HBr\cdot 8H_2O$: C, 16.95; H, 6.48; N, 15.16; O, 3.39. Found C, 17.17; H, 6.39; N, 14.99; O, 3.36.

DEN-48Ts (14). **13** (16 g, 3.77 mmole) was converted to **14** (32.4 g, 87%) by the same procedure for the preparation of **10**; ^1H NMR (DMSO-d_6) δ 2.26 (br, s, 390H), 2.60 (br, s, 96H), 7.24 (br, s, 134H), 7.60 (br, s, 96H). Anal. Calc. for $C_{522}H_{756}N_{94}O_{96}S_{48}\cdot 9H_2O$: C, 54.10; H, 6.70; N, 11.38; O, 14.53. Found C, 53.98; H, 6.64; N, 11.10; O, 14.52.

DEN-48NH$_2$ (2). By the same procedure described for preparation of **10, 14** (27 g, 2.74 mmole) was converted to **2** (22.8 g, 80%) using 30% HBr/AcOH (200 mL) and phenol (2.0 g); ^1H NMR (D_2O); δ 2.95 (br, s, 48H), 3.13 (br, s, 124H), 3.21-3.60 (m, 200H); Anal. Calcd for $C_{2232}H_{468}N_{1316}\cdot 63HBr\cdot 12H_2O$: C, 23.91; H, 5.95; N, 14.09. Found C, 24.17; H, 6.14; N, 13.88.

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References

1. (a) Poter, C. W.; Bergeron, R. J.; Stolowich, N. *J. Cancer Res.* **1982**, *42*, 4072. (b) Poter, C. W.; Bergeron, R. *J. Science* **1983**, *219*, 1083.
2. (a) Perterson, T.; Falk, K. E.; Leong, S. A.; Kelin, M. P.; Neilands, J. B. *J. Am. Chem. Soc.* **1980**, *102*, 7715. (b) Eng-Wilmot, D. L.; van der Helmn, D. *J. Am. Chem. Soc.* **1980**, *102*, 7719.
3. Chuang, C. L.; Wang, Y. J.; Lan, H. L. *Analytica Chimica Acta* **1997**, *353*, 37.
4. (a) Zanta, M. A.; Boussif, O.; Adif, A.; Behr, J. P. *Bioconjugate Chem.* **1997**, *8*, 839. (b) Boletta, A.; Benigni, A.; Lutz, J.; Remuzzi, G.; Soria, M. R.; Monaco, L. *Gean Theraphy* **1997**, *4*, 808.
5. McNeff, C.; Carr, P. W. *Anal. Chem.* **1995**, *67*, 3886.
6. Suh, J.; Lee, S. H.; Zoh, K. D. *J. Am. Chem. Soc.* **1992**, *114*, 7916.
7. (a) *Ethyleneimine and Other aziridines*, Academic press: New York, 1969. (b) Tomalia, D. A.; Naylor, A. M.; Goddard, III, W. A. *Angew. Chem. Int. Engl. Ed.* **1990**, *138*, 175.
8. (a) Tomalia, D. A.; Hall, B. M.; Hedstrand, D. M. *Macromolecules* **1987**, *20*, 1167. (b) Bunton, C. A.; Nome, F.; Quina, F. H.; Romsted, L. S. *Acc. Chem. Res.* **1991**, *24*. 357.
9. (a)Fendler, J. H. *Membrane Mimetic Chemistry*, Wiley-Interscience: New york, 1997. (b) Bunton, C. A.; Nome, F.; Qunia, F. H.; Romsted, L. S. *Acc. Chem. Res.* **1991**, *24*, 357.
10. Suh, J.; Hah, S. S.; Lee, S. H. *Bioorg. Chem.* **1997**, *25*, 63.
11. Tomalia, D. A.; Dewalt, J. R. U.S. Patent 4631339 1986.
12. Zinic, M.; Alihodzic, S.; Skaric, V. *J. Chem. Soc., Perkin Trans. 1* **1993**, 21.
13. Dietrich, B.; Hoseini, M. W.; Lehn, J.-M.; Session, R. B. *Helv. Chim. Acta.* **1985**, *68*, 289.
14. Allen, C. F. H.; Spangler, F. W.; Webster, E. R. *Organic Synthesis*, IV, 433.
15. Tomalia, D. A.; Berry, V.; Hall, B. M.; Hedstrand, D. M. *Macromolecules* **1987**, *20*, 1164.
16. de Gennes, P. G.; Hervet, H. *J. Phys. Lett.* (paris) **1983**, *44*, 351.)
17. (a) Hope, D. B.; Horncastle, K. C. *J. Chem. Soc., Chem. Com.* **1966**, 1098. (b) Martin, A. E.; Ford, T. M.; Bullkowski, J. E. *J. Org. Chem.* **1982**, *47*, 412.