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덴드리틱 벤질 클로라이드의 효율적인 합성

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Facile Synthesis of Dendritic Benzyl Chlorides from Their Alcohols with Methanesulfonyl Chloride/Et_3N

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초록 : 덴드리틱 벤질 알코올을 트리에틸아민과 메탄술포닐클로라이드와 반응시켜서, 덴드리틱 벤질 클로라이드의 효율적인 합성이 이루어졌다. 이 반응은 히드록시기의 메실화 반응과 염소화 반응의 2단계 반응으로 이루어지는데, 중간체의 분리없이 한 반응 용기내에서 반응이 진행되는 경제적인 방법이다.

Abstract : A successful rapid synthesis of dendritic benzyl chlorides from dendritic benzyl alcohols using methanesulfonyl chloride/Et_3N as activating agents was described. In this method, each dendritic benzyl chloride can be prepared in one pot: no isolation of intermediate mesylated dendrons is required. The key steps in the syntheses of dendritic benzyl chlorides were the mesylation of the hydroxymethyl group followed by the chlorination by *in-situ* generated triethylammonium chloride.

Keywords : benzylic alcohol, chlorination.

Introduction

Dendrimers represent a novel type of polymeric material that has generated much interest in diverse areas due to their unique structure and properties, and have served as functional objects in nanotechnology and nanoscience.[1] Dendrimers are prepared by repetition of a given set of reactions using either divergent or convergent strategies. The two most widely studied dendrimer families are the Fréchet-type polyether and the Tomalia-type PAMAM dendrimers.[2,3] The convergent approach to dendrimer synthesis introduced by Fréchet and co-workers revolutionized the synthetic approaches to monodisperse dendrimers.[3] An effective convergent synthesis requires a monomer that can undergo the activation and coupling steps in high yield. In addition, the coupling step must be very efficient to enable complete reaction. In this viewpoint, the dendritic benzylic alcohols and halides are key intermediates in synthesis of the Fréchet-type poly(aryl ether) dendrimers. In addition, the focal benzylic halide functionality has applied in many fields. In continuation with our research for the synthesis of dendrimers,[4] there is still a demand to develop a simple, convenient, and efficient method to approach dendritic benzyl chlorides. Here, we present a successful rapid synthesis of dendritic benzyl chlorides from dendritic benzyl alcohols using methanesulfonyl chloride/Et_3N as activating agents (Scheme 1). In our method, each dendritic benzyl chloride can be prepared in one pot: no isolation of intermediate mesylated dendrons is required. The key steps in the syntheses of dendritic benzyl chlorides were the mesylation of the

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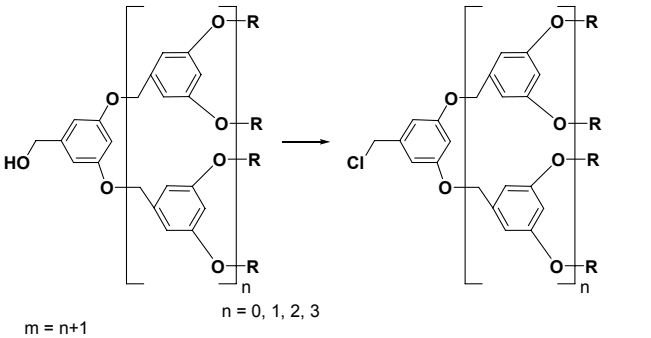


Scheme 1.

hydroxymethyl group followed by the chlorination by *in-situ* generated triethylammonium chloride. Furthermore, the purification of every dendritic molecule requires only solvent extraction.

Experimental

^{1}H-NMR spectra were recorded on a 300 MHz NMR spectrometer using the residual proton resonance of the solvent as the internal standard. Chemical shifts are reported in parts per million(ppm). When peak multiplicities are given, the following abbreviations are used: s, singlet; d, doublet; t, triplet; m, multiplet; br, broad. ^{13}C-NMR spectra were proton decoupled and recorded on a 75 MHz NMR spectrometer using the carbon signal of the deuterated solvent as the internal standard. EI and FAB mass spectra were obtained from Korea Basic Science Institute(KBSI) in Daegu. Analytical thin layer chromatography was performed on silica plates with F_{254} indicator and the visualization was accomplished by UV lamp or using an iodine chamber. All chemicals were obtained from commercial sources and used as received, unless otherwise mentioned.

General Procedure for the Chlorination of Dendritic Benzyl Alcohols. Triethylamine(3.3 mmol) was added to a solution of dendritic benzyl alcohols(3 mmol) and methanesulfonyl chloride (3.3 mmol) in solvent(see Table 1) in an ice bath and the resulting mixture was stirred for 2 h at room temperature and then additional time(see Table 1) with heating. The reaction mixture was poured into brine(100 mL) and extracted with CH_2Cl_2 or EtOAc. The extract was washed with saturated Na_2CO_3 aqueous solution, dried over Na_2SO_4, and filtered and the filtrate was concentrated to provide the analytical pure product.

Compound 6-D1. A brownish solid; 100% yield; 32-34 ℃. IR 2941, 2839, 1600, 1462, 1208, 1157, 1066, 837, 715 cm^{-1}; ^{1}H-NMR($CDCl_3$) δ 3.80(s, 6H), 4.52(s, 2H), 6.41(s, 1H), 6.54(d, J=1.1 Hz, 2H); ^{13}C-NMR($CDCl_3$) δ 160.9, 139.5, 106.4, 100.4, 55.3, 46.3; MS(EI): m/z 151[M^+-Cl], 186[M^+], 188[M^++2]; HRMS(EI) Calcd for $C_9H_{11}ClO_2$: 186.0448. Found: 186.0448[M^+], 188.0420[M^++2].

Compound 6-D2. A brownish solid; 100% yield; m.p. 96-98 ℃. IR 2939, 2839, 1598, 1460, 1206, 1155, 1053, 834, 712 cm^{-1}; ^{1}H-NMR($CDCl_3$) δ 3.8(s, 12H), 4.51(s, 2H), 4.98

Table 1. Synthesis of Dendritic Benzyl Chlorides

Entry	SM[a]	Solvent[b]	Temperature[c]	Reaction period[d]	Product	Yield(%)[e]
1	**1-D1**	DMF(0.5M)	r.t./50 ℃	2 h/1.5 h	**6-D1**	quant
2	**1-D2**	DMF(0.5M)	r.t./50 ℃	2 h/1.5 h	**6-D2**	quant
3	**1-D3**	DMF(0.5M)	r.t./50 ℃	2 h/1.5 h	**6-D3**	quant
4	**2-D1**	CH_2Cl_2(0.1M)	r.t./reflux	2 h/14 h	**7-D1**	quant
5	**2-D1**	DMF(0.1M)	r.t./50 ℃	2 h/2 h	**7-D1**	99
6	**2-D2**	DMF(0.5M)	r.t./50 ℃	2 h/1.5 h	**7-D2**	99
7	**2-D3**	DMF(0.1M)	r.t./50 ℃	2 h/2 h	**7-D3**	98
8	**3-D1**	CH_2Cl_2(0.1M)	r.t./reflux	2 h/15 h	**8-D1**	96
9	**3-D2**	CH_2Cl_2(0.1M)	r.t./reflux	2 h/17 h	**8-D2**	99
10	**3-D3**	CH_2Cl_2(0.1M)	r.t./reflux	2 h/19 h	**8-D3**	99
11	**4-D1**	CH_2Cl_2(0.1M)	r.t./reflux	2 h/14 h	**9-D1**	99
12	**4-D2**	CH_2Cl_2(0.1M)	r.t./reflux	2 h/16 h	**9-D2**	quant
13	**4-D3**	CH_2Cl_2(0.1M)	r.t./reflux	2 h/18 h	**9-D3**	quant
14	**5-D1**	DMF(0.5M)	r.t./50 ℃	2 h/2 h	**10-D1**	99

[a]SM means starting material. [b]Parenthesis is molar concentration of starting substrate. [c,d]First one is for mesylation step and second one is for chlorination step. [e]Isolated yield and quant means quantitative yield.

(s, 4H), 6.42(m, 2H), 6.57(m, 5H), 6.63(d, J=1.7 Hz, 2H); ^{13}C-NMR($CDCl_3$) δ 161.0, 160.0, 139.5, 139.0, 107.7, 105.2, 102.1, 100.0, 70.1, 55.4, 46.3; MS(FAB): m/z 151.34, 423.02[M^+-Cl], 459.01 [M^+]; HRMS(FAB) Calcd for $C_{25}H_{27}ClO_6$: 458.1496. Found: 459.1574[M^++H].

Compound 6-D3. A brownish gum; 100% yield; IR 2939, 2839, 1598, 1460, 1206, 1155, 1053, 834, 712 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 3.79(s, 24H), 4.51(s, 2H), 4.98(s, 12H), 6.41(m, 4H), 6.57(m, 11H), 6.61(m, 2H), 6.66(m, 4H); ^{13}C-NMR($CDCl_3$) δ 161.0, 160.1, 160.0, 139.5, 139.1, 139.0, 107.6, 106.4, 105.2, 102.0, 101.6, 99.9, 70.04, 69.97, 55.3, 46.3; MS(FAB): m/z 967.33[M^+-Cl], 1002.21[M^+]; HRMS(FAB) Calcd for $C_{57}H_{59}ClO_{14}$: 1002.3593. Found: 1003.3672[M^++H].

Compound 7-D1. A yellowish oil; 99% yield; IR 2935, 2879, 2097, 1597, 1454, 1298, 1171, 1063, 837, 715 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 2.04(quin, J=6.4 Hz, 4H), 3.51(t, J=6.6 Hz, 4H), 4.04(t, J=5.9 Hz, 4H), 4.50(s, 2H), 6.41(s, 1H), 6.54(d, J=1.9 Hz, 2H); ^{13}C-NMR($CDCl_3$) δ 160.0, 139.6, 107.2, 101.4, 64.6, 48.1, 46.2, 28.7; MS(FAB): m/z 324.95[M^+]; HRMS (FAB) Calcd for $C_{13}H_{17}ClN_6O_2$: 324.1102. Found: 325.1180 [M^++H].

Compound 7-D2. A yellowish oil; 99% yield; IR 2935, 2879, 2097, 1597, 1452, 1298, 1169, 1059, 835, 715 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 2.05(quin, J=6.2 Hz, 8H), 3.52(t, J=6.6 Hz, 8H), 4.04(t, J=5.9 Hz, 8H), 4.52(s, 2H), 4.97(s, 4H), 6.42(m, 2H), 6.55-6.57(m, 5H), 6.63(m, 2H); ^{13}C-NMR($CDCl_3$) δ 160.0, 159.9, 139.5, 139.0, 107.6, 105.9, 102.0, 100.9, 69.9, 64.6, 48.1, 46.2, 28.7; MS(FAB): m/z 735.0[M^+]; HRMS(FAB) Calcd for $C_{33}H_{39}ClN_{12}O_6$: 734.2804. Found: 735.2882[M^++H].

Compound 7-D3. A yellowish oil; 98% yield; IR 2935, 2879, 2097, 1597, 1452, 1298, 1169, 1059, 835, 715 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 2.04(quin, J = 6.2 Hz, 16H), 3.50(t, J = 6.6 Hz, 16H), 4.03(t, J=5.8 Hz, 16H), 4.51(s, 2H), 4.97(s, 12H), 6.41 (m, 4H), 6.57-6.58(m, 11H), 6.63(m, 2H), 6.67(m, 4H); ^{13}C-NMR ($CDCl_3$) δ 160.0, 159.9, 139.5, 139.1, 139.0, 107.6, 106.4, 105.9, 102.0, 101.6, 100.8, 70.0, 69.9, 64.5, 48.1, 46.2, 28.7; MS(FAB): m/z 1527.5 [M^+-N_2], 1555.2[M^+]; HRMS(FAB) Calcd for $C_{73}H_{83}ClN_{24}O_{14}$: 1554.6209. Found: 1555.6287[M^++H].

Compound 8-D1. A yellowish oil; 96% yield; IR 2920, 2875, 1597, 1450, 1298, 1178, 1070, 851, 715 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 3.38(s, 6H), 3.55-3.56(m, 4H), 3.64-3.73 (m, 12H), 3.84(t, J=4.7 Hz, 4H), 4.10(t, J=4.7 Hz, 4H), 4.48 (s, 2H), 6.44(s, 1H), 6.54(d, J=1.7 Hz, 2H); ^{13}C-NMR ($CDCl_3$) δ 159.7, 139.1, 107.1, 101.3, 71.6, 70.5, 70.3, 70.2, 69.3, 67.2, 58.7, 46.0; MS (FAB): m/z 322.06, 393.15, 451.02[M^+]; HRMS (FAB) Calcd for $C_{21}H_{35}ClO_8$: 450.2020. Found: 451.2099 [M^+ + H].

Compound 8-D2. A yellowish oil; 99% yield; IR 2920, 2875, 1597, 1450, 1298, 1175, 1070, 849, 715 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 3.37(s, 12H), 3.54-3.56(m, 8H), 3.64-3.73(m, 24H), 3.84(t, J=4.7 Hz, 8H), 4.11(t, J=4.7 Hz, 8H), 4.50 (s, 2H), 4.95(s, 4H), 6.44(m, 2H), 6.53(m, 1H), 6.57(m, 4H), 6.60(m, 2H); ^{13}C-NMR($CDCl_3$) δ 159.9, 159.8, 139.3, 138.7, 107.4, 105.8, 101.8, 100.9, 71.7, 70.6, 70.43, 70.35, 69.8, 69.4, 67.3, 58.8, 46.1; MS(FAB): m/z 829.28, 987.27[M^+]; HRMS (FAB) Calcd for $C_{49}H_{75}ClO_{18}$: 986.4642. Found: 987.4720 [M^++H].

Compound 8-D3. A yellowish oil; 99% yield; IR 2920, 2875, 1597, 1450, 1298, 1175, 1070, 847, 715 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 3.37(s, 24H), 3.52-3.55(m, 16H), 3.63-3.73(m, 48H), 3.84(t, J=4.5 Hz, 16H), 4.10(t, J=4.5 Hz, 16H), 4.51 (s, 2H), 4.95(s, 8H), 4.96(s, 4H), 6.44(m, 4H), 6.54(m, 2H), 6.58(m, 9H), 6.62(m, 2H), 6.65(m, 4H); ^{13}C-NMR($CDCl_3$) δ 159.95, 159.89, 139.4, 138.9, 107.5, 106.3, 105.9, 101.8, 101.5, 101.0, 71.8, 70.7, 70.5, 70.4, 69.91, 69.86, 69.5, 67.3, 58.9, 46.2; MS(FAB): m/z 2059.7[M^+].

Compound 9-D1. A yellowish oil; 99% yield; IR 2871, 2106, 1597, 1448, 1298, 1176, 1070, 848, 715 cm^{-1}; ^{1}H-NMR($CDCl_3$) δ 3.38(t, J=4.9 Hz, 4H), 3.65-3.71(m, 20H), 3.84(t, J=4.7 Hz, 4H), 4.11(t, J=4.7 Hz, 4H), 4.49(s, 2H), 6.44(m, 1H), 6.54(m, 2H); ^{13}C-NMR($CDCl_3$) δ 159.8, 139.1, 107.1, 101.3, 70.5, 70.4, 69.7, 67.3, 67.3, 50.4, 46.0; MS (FAB): m/z 560.03[M^+]; HRMS(FAB) Calcd for $C_{23}H_{37}ClN_6O_8$: 560.2361. Found: 561.2440[M^++H].

Compound 9-D2. A yellowish oil; 100% yield; IR 2871, 2106, 1597, 1448, 1298, 1175, 1068, 844, 715 cm^{-1}; ^{1}H-NMR($CDCl_3$) δ 3.37(t, J=4.9 Hz, 8H), 3.65-3.71(m, 40H), 3.84(t, J = 4.6 Hz, 8H), 4.11(t, J = 4.6 Hz, 8H), 4.50(s, 2H), 4.95 (s, 4H), 6.45(m, 2H), 6.53(m, 1H), 6.58 (m, 4H), 6.60 (m, 2H); ^{13}C-NMR($CDCl_3$) δ 159.9, 159.8, 139.4, 138.7, 107.4, 105.8, 101.8, 100.9, 70.6, 70.5, 69.8, 69.4, 67.3, 50.4, 46.1; MS(FAB): m/z 1178.6[M^+-N_2], 1206.6[M^+]; HRMS(FAB) Calcd for $C_{53}H_{79}ClN_{12}O_{18}$: 1206.5324. Found: 1207.5402 [M^+ + H].

Compound 9-D3. A yellowish oil; 100% yield; IR 2871, 2106, 1597, 1448, 1298, 1175, 1068, 842, 715 cm^{-1}; ^{1}H-NMR($CDCl_3$) δ 3.36(t, J=4.8 Hz, 16H), 3.66-3.71(m, 80H), 3.84(t, J=4.4 Hz, 16H), 4.11(t, J=4.5 Hz, 16H), 4.51(s, 2H), 4.95(s, 12H), 6.44(m, 4H), 6.54(m, 2H), 6.58(m, 9H), 6.63 (m, 2H), 6.66(m, 4H); ^{13}C-NMR($CDCl_3$) δ 159.9, 139.4, 138.9, 107.5, 106.3, 105.9, 101.8, 101.4, 101.0, 70.6, 70.5, 69.9, 69.5, 67.3, 50.5, 46.2; MS(FAB): m/z 1143.5, 2472.7[M^+-N_2], 2500.9[M^+].

Compound 10-D1. A yellowish oil; 99% yield; IR 3252, 2873, 2113, 1597, 1449, 1297, 1175, 1070, 845, 715 cm^{-1}; ^{1}H-NMR($CDCl_3$) δ 2.43(t, J=2.4 Hz, 2H), 3.66-3.74(m, 24H), 3.84(t, J=4.8 Hz, 4H), 4.10(t, J=4.8 Hz, 4H), 4.19

(d, J=2.3 Hz, 4H), 4.49(s, 2H), 6.44(t, J=2.2 Hz, 1H), 6.54 (d, J=2.1 Hz, 2H); ^{13}C-NMR($CDCl_3$) δ 160.0, 139.4, 107.4, 101.6, 79.7, 74.8, 70.8, 70.6, 70.4, 69.6, 69.1, 67.6, 58.4, 46.3; MS(FAB): *m/z* 154.3, 551.4[M^+-Cl], 586.2[M^+]; HRMS (FAB) Calcd for $C_{29}H_{43}ClO_{10}$: 586.2545. Found: 587.2623 [M^++H].

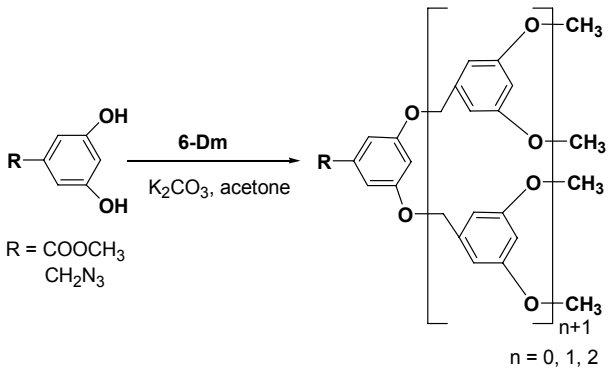
Results and Discussion

In the syntheses of classical benzyl ether dendrimers, the conversion of the hydroxymethyl moiety to the bromomethyl functionality is achieved using triphenylphosphine and carbontetrabromide(or *N*-bromosuccinimide).[3(a)] However, this methodology often had drawback to occur the aromatic ring bromination, since the reagents above could generate bromonium ions.[5] Several methods have been reported to avoid the most difficult step of the bromination in the Fréchet process. Utilization of the Mitsunobu reaction and of the solid support system was developed.[6,7] They are, however, still tedious to prepare the high-quality dendrimer in a practical scale. Thionyl chloride also is the attractive reagent for the chlorination of benzyl alcohols due to the short reaction time, low reaction temperature, and low price.[8] The utilization of thionyl chloride as a chlorination agent of benzyl alcohols was reported and demonstrated that benzyl chloride is sufficient for the synthesis of aryl ether dendrimers.[9] But thionyl chloride is moisture sensitive compound and should be distillated before their use in reaction.

In order to optimize the reaction conditions, we first examined the solvent effect in the presence of methanesulfonyl chloride (MsCl) and Et_3N at room temperature for the conversion of 3,5-dimethoxybenzyl alcohol **1-D1** as a model compound to 3,5-dimethoxybenzyl chloride. From the reactions of **1-D1** in THF or EtOAc(0.1 M) in the presence of MsCl and Et_3N at room temperature, the only mesylated product was obtained. The disappearance of **1-D1** and the appearance of mesylated product were observed from TLC analysis of the reaction mixture. The reactions of **1-D1** in CH_2Cl_2 or DMF (0.1 M) in the presence of MsCl and Et_3N at room temperature provided the mesylated product as well as chlorinated product **7-D1** which was detected by TLC runs of the reaction mixture. As the reaction time increased, the generation of chlorinated product **7-D1** was increased gradually which is possible by the chlorination of the mesylated product by the generated triethylammonium chloride. It was observed that the mesylation reaction was finished within 2 h but the chlorination reaction was taken long time at room temperature. For completion of the chlorination reaction in one-pot within short time, the reaction mixture was heated. We found that the reaction conducted from CH_2Cl_2 was finished after 15 h under reflux and one from DMF was completed within 2 h at 50 ℃. Eventually, the differences of reactivity in the chlorination step could be caused by the reaction concentration and the solubility of the *in-situ* generated triethylammonium chloride due to solvents as well as temperature.

With this basic result, we began our study by establishing the validity of the chemistry in the synthesis of dendritic benzyl chlorides, as shown in Scheme 1. Considering the polarity of reactant and product, the solvent used in reaction was selected to reduce the isolation problem of product. CH_2Cl_2 was used for polar substrates and DMF was used for nonpolar one. The reaction conditions including solvents, temperature, and time was summarized in Table 1, together with the isolated yields of the dendritic benzyl chlorides. When the chlorination was carried out in CH_2Cl_2, the molar concentration of reaction mixture was diluted (0.1 M) to increase the amount of soluble $Et_3N \cdot HCl$. On the other hand, when the chlorination was carried out in DMF, the molar concentration of reaction mixture was concentrated (0.5 M) to decrease the reaction period. The purification of the resulting compounds was achieved by normal aqueous work-up. The structures of the dendritic benzyl chlorides were confirmed by ^{1}H-and ^{13}C-NMR spectroscopy, IR spectroscopy, and mass spectra. Therefore we found the optimized conditions for the quantitative conversion of the focal benzylic alcohol functionality to the focal benzylic chloride in dendrons without any problems. This process can be achieved by the conversion of the hydroxyl group into the mesylated group followed by *in-situ* chlorination reaction. This method is general and can be easily applied for the conversion of benzylic and allylic alcohols to their halides. The mesylation of alcohols with methanesulfonyl chloride is powerful tool in organic synthetic transformations and often known to provide the chloride compound instead of the mesylated compound in case of benzylic alcohols.[10] To the best of our knowledge, this is the first systematic investigation to synthesize dendritic benzyl chloride from their alcohol.

The synthetic utilities of dendritic benzyl chloride in dendron chemistry are further demonstrated by the facile syntheses of dendritic benzoate and dendritic benzyl azide (Scheme 2). In the formers, 3,5-dihydroxybenzoate was reacted with dendritic benzyl chlorides in the presence of potassium carbonate to provide a generation higher dendritic benzoates which were reduced into dendritic benzyl alcohols. In the latters, a generation higher dendritic benzyl azides were obtained in excellent yields from the reactions of 3,5-dihydroxybenzyl azide with dendritic benzyl chlorides



Scheme 2.

in the presence of potassium carbonate.[4(d)] In both cases, the key synthetic step involves O-benzylations of dihydroxyphenyl ring with dendritic benzyl chlorides, which were easily synthesized from dendritic benzyl alcohols using methanesulfonyl chloride/Et_3N presented here.

Conclusions

We have developed a one-pot synthesis method for dendritic benzyl chlorides from their alcohols in the presence of methanesulfonyl chloride and triethylamine. This process can be achieved by the conversion of the hydroxyl group into the mesylated group followed by the chlorination by *in-situ* generated triethylammonium chloride. Furthermore, the purification of every dendritic molecule requires only solvent extraction.

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References

1. (a) A. C. Grimsdale and K. Müllen, *Angew. Chem. Int. Ed.,* **44**, 5592 (2005). (b) D. A. Tomalia, *Prog. Polym. Sci.,* **30**, 294 (2005).
2. (a) D. A. Tomalia, H. Baker, J. Dewald, M. Hall, G. Kallos, S. Martin, J. Roeck, J. Ryder, and P. Smith, *Polym. J.,* **17**, 117 (1985). (b) D. A. Tomalia, A. M. Naylor, and W. A. Goddard III, *Angew. Chem., Int. Ed. Engl.,* **29**, 138 (1990).
3. (a) C. J. Hawker and J. M. J. Fréchet, *J. Am. Chem. Soc.,* **112**, 7638 (1990). (b) C. J. Hawker and J. M. J. Fréchet, *J. Chem. Soc., Chem. Commun.,* 1010 (1990). (c) S. M. Grayson and J. M. J. Fréchet, *Chem. Rev.,* **101**, 3819 (2001).
4. (a) J. W. Lee and B. K. Kim, *Bull. Korean Chem. Soc.,* **26**, 658 (2005). (b) J. W. Lee, B. K. Kim, and S. H. Jin, *Bull. Korean Chem. Soc.,* **26**, 715 (2005). (c) J. W. Lee, B. K. Kim, and S. H. Jin, *Bull. Korean Chem. Soc.,* **26**, 833 (2005). (d) J. W. Lee, B. K. Kim, J. H. Kim, W. S. Shin, and S. H. Jin, *Bull. Korean Chem. Soc.,* **26**, 1790 (2005). (e) J. W. Lee and B. K. Kim, *Synthesis,* 615 (2006). (f) J. W. Lee, J. H. Kim, B. K. Kim, W. S. Shin, and S. H. Jin, *Tetrahedron,* **62**, 894 (2006). (g) J. W. Lee, B. K. Kim, J. H. Kim, W. S. Shin, and S. H. Jin, *J. Org. Chem.,* **71**, 4988 (2006).
5. A. Nantalaksakul, R. R. Dasari, T.-S. Ahn, R. Al-Kaysi, C. J. Bardeen, and S. Thayumanavan, *Org. Lett.,* **8**, 2981 (2006).
6. B. Forier and W. Dehaen, *Tetrahedron,* **55**, 9829 (1999).
7. A. Basso, B. Evans, N. Pegg, and M. Bradley, *Chem. Commun.*, 697 (2001).
8. F. C. Whitmore, F. A. Karnatz, and A. H. Popkin, *J. Am. Chem. Soc.*, **60**, 2540 (1938).
9. (a) V. S. K. Balagurusamy, G. Ungar, V. Percec, and G. Johansson, *J. Am. Chem. Soc.*, **119**, 1539 (1997). (b) V. Percec, W.-D. Cho, P. E. Mosier, G. Ungar, and D. J. P. Yeardley, *J. Am. Chem. Soc.,* **120**, 11061 (1998). (c) V. Percec, W.-D. Cho, G. Ungar, and D. J. P. Yeardley, *J. Am. Chem. Soc.,* **123**, 1302 (2001). (d) V. Percec, C. M. Mitchell, W.-D. Cho, S. Uchida, M. Glodde, G. Ungar, X. Zeng, Y. Liu, V. S. K. Balagurusamy, and P. A. Heiney, *J. Am. Chem. Soc.,* **126**, 6078 (2004). (e) M. Tanaka, Y. Higuchi, N. Adachi, Y. Shibutani, S. A. Ahmed, S. Kado, M. Nakamura, and K. Kimura, *Tetrahedron,* **61**, 8159 (2005). (f) N. Yamazaki, I. Washio, Y. Shibasaki, and M. Ueda, *Org. Lett.,* **8**, 2321 (2006).
10. (a) Y. Sawada, H. Kayakiri, Y. Abe, T. Mizutani, N. Inamura, M. Asano, C. Hatori, I. Aramori, T. Oku, and H. Tanaka, *J. Med. Chem.,* **47**, 2853 (2004). (b) K. Tanaka, M. Katsurada, F. Ohno, Y. Shiga, M. Oda, M. Miyagi, J. Takehara, and K. Okano, *J. Org. Chem.,* **65**, 432 (2000). (c) F. Mazzini, A. Mandoli, P. Salvadori, T. Netscher, and T. Rosenau, *Eur. J. Org. Chem.,* 4864 (2004).