An approach to glycerol dendrimers and pseudo-dendritic polyglycerols

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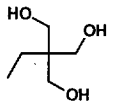
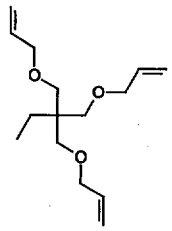
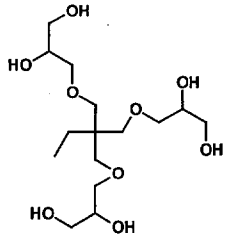
1) Structures of glycerol dendrimers [G-n] and allylated precursors [G-n.5]



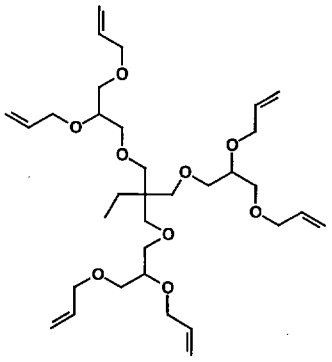
TMP = [G-0]



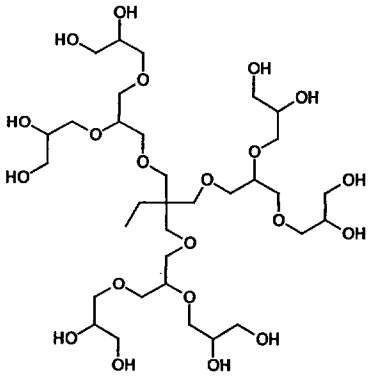
[G-0.5]



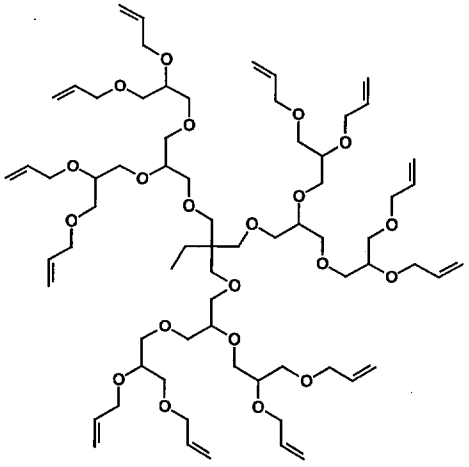
[G-1]



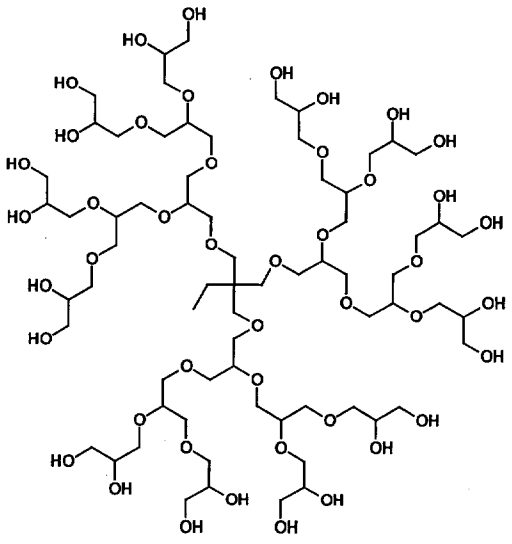
[G-1.5]



[G-2]



[G-2.5]



[G-3]

2) Experimental: general procedures

Allylation (adapted from ref. 14)

To a solution of the polyol (0.1 mol alcohol equivalents), tetrabutylammonium bromide (3.23 g, 0.01 mol) and sodium hydroxide (20 g, 0.50 mol) in 20 mL of distilled water, allylchloride (40.7 mL, 0.50 mol) was added over 22 h at 45°C under vigorous stirring. *CAUTION: Allylchloride is extremely toxic.* After addition of 100 mL of toluene, the organic phase was separated from the other phases, dried over $MgSO_4$, filtered and concentrated under vacuum. The crude was further purified by column chromatography (silica gel, petrolether/ethylacetate 10:1 to 1:1) to obtain a colorless oil. A tendency to slow polymerization has been observed in some cases. Oxygen should be excluded for long-term storage.

Dihydroxylation (adapted from ref. 15)

To a solution of the polyallyl ether (0.1 mol allyl equivalents), N-methylmorpholine-N-oxide (14.8 g, 0.11 mol) in acetone (50 mL), distilled water (50 mL) and t-butanol (10 mL), 2 mL of a 4 wt% OsO_4 solution in water was added. *CAUTION: Osmium tetroxide is extremely toxic.* Initially, an exothermic reaction was observed and cooling with a water bath became necessary in some cases. The mixture was stirred for 20 h at 25 °C, then all volatile compound were removed *in vacuo.* The high molecular weight polyglycerols ([G-3] dendrimer and pseudo-dendrimer) were further purified by dialysis in methanol using a benzylated cellulose membrane (MWCO 1000, Sigma). After concentration pale yellow oils were obtained.

3) Characterization data

[G-0.5]

^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.85 (m, 3H, C<u>H</u>=CH_2), 5.17 (m, 6H, CH=C<u>H_2</u>), 3.93 (d, 6H, $CH_2OC\underline{H_2}CH=CH_2$), 3.31 (s, 6H, $C(C\underline{H_2})_3$), 1.43 (q, 2H, $CH_3C\underline{H_2}$), 0.84 (t, 3H, C<u>H_3</u>); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 135.8 (3C, <u>C</u>H=CH_2), 116.5 (3C, CH=<u>C</u>H_2), 72.7 (3C, $\underline{C}H_2CH=CH_2$), 71.2 (3C, $C(\underline{C}H_2)_3$), 43.6 (1C, <u>C</u>$(CH_2)_4$), 23.5 (1C, $CH_3\underline{C}H_2$), 8.1 (1C, CH_3); IR(KBr): ν(cm^{-1}) = 3080 (C=CH), 1647 (C=C), 1094 (C-O-C), 991 ($CH=CH_2$), 922 ($CH=CH_2$).

[G-1]

^{1}H NMR (300 MHz, CD_3OD): δ = 4.9 (s, O<u>H</u>), 4.03 (m, 3H, C<u>H</u>OH), 3.86-3.53 (m, 12H), 3.46 (s, 6H, $C(C\underline{H_2})_3$), 1.50 (q, 2H, $C\underline{H_2}CH_3$), 0.97 (t, 3H, C<u>H_3</u>); ^{13}C NMR (75 MHz, CD_3OD): δ = 74.1 (3C, $CH_2O\underline{C}H_2$), 73.1 (3C, $C(\underline{C}H_2)_3$), 72.4 (3C, <u>C</u>HOH), 65.0 (3C, $\underline{C}H_2OH$), 44.8 (1C, <u>C</u>$(CH_2)_4$, 24.2 (1C, $\underline{C}H_2CH_3$), 8.3 (1C, <u>C</u>H_3); IR(KBr): ν(cm^{-1}) = 3448 (OH), 1654 (C-O-C), 1459 (C-OH), 1111 (C-OH); ESI-MS (4.3 kV) calcd. for $C_{15}H_{32}O_9$ 356.4 found 355.9 + Na.

[G-1.5]

^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.88 (m, 6H, C<u>H</u>=CH_2), 5.19 (m, 12H, CH=C<u>H_2</u>), 4.11 (d, 6H, $CHOC\underline{H_2}CH=CH_2$), 3.96 (d, 6H, $CH_2OC\underline{H_2}CH=CH_2$), 3.63 (m, 3H, $C(\underline{H})(CH_2)_2OCH_2$), 3.44 (m, 12H, $C\underline{H_2}CH(OR)C\underline{H_2}O$), 3.27 (s, 6H, $C(C\underline{H_2})_3$), 1.38 (q, 2H, $CH_3C\underline{H_2}$), 0.81 (t, 3H, C<u>H_3</u>); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 135.7 (3C, $CHOCH_2\underline{C}H=CH_2$), 135.2 (3C, $CH_2OCH_2\underline{C}H=CH_2$), 117.2 (3C, $CH_2OCH_2CH=\underline{C}H_2$), 117.0 (3C, $CHOCH_2CH=\underline{C}H_2$), 77.5 (3C, $CH_2\underline{C}(H)(OR)CH_2$), 72.8 (3C, $CH_2O\underline{C}H_2CH=CH_2$), 72.4 (3C, $\underline{C}H_2CH(OR)CH_2$), 72.2 (3C, $C(\underline{C}H_2)_3$), 71.8 (3C, $\underline{C}H_2OCH_2CH=CH_2$), 71.0 (3C, $CHO\underline{C}H_2CH=CH_2$), 43.7 (1C,

C(CH$_2$)$_4$), 23.4 (1C, CH$_2$CH$_3$), 8.1 (1C, CH$_2$CH$_3$); IR(KBr): ν(cm^{-1}) = 3080 (C=CH), 1647 (C=C), 1108 (C-O-C), 996 (C=CH$_2$), 923 (C=CH$_2$); MALDI-TOF MS calcd. for $C_{33}H_{56}O_9$ 596.8 found 596.9 + Li.

[G-2]

^{1}H NMR (300 MHz, CD_3OD): δ = 4.9 (s, OH), 3.86-3.59 (m, 45H), 3.44 (s, 6H, C(CH$_2$)$_3$), 1.50 (q, 2H, CH$_2$CH$_3$), 0.97 (t, 3H, CH$_3$); ^{13}C NMR (75 MHz, CD_3OD): δ = 80.0 (3C, (CH$_2$)$_2$C(H)OR), 74.1 (3C, CH$_2$OCH$_2$CH(OH)CH$_2$OH), 72.8-72.5 (12C, C(CH$_2$)$_3$, ROCH$_2$C(H)(OR)CH$_2$OR, CHOCH$_2$CH(OH)CH$_2$OH), 72.3 (6C, CHOH), 64.7 (6C, CH$_2$OH), 44.7 (1C, C(CH$_2$)$_4$, 24.2 (1C, CH$_2$CH$_3$), 8.3 (1C, CH$_3$); IR(KBr): ν(cm^{-1}) = 3448 (OH), 1654 (C-O-C), 1459 (C-OH), 1111 (C-OH); MALDI-TOF MS calcd. for $C_{33}H_{68}O_{21}$ 800.9 found 800.8 + Li.

[G-2.5]

^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.86 (m, 9H, CH=CH$_2$), 5.18 (m, 18H, CH=CH$_2$), 4.12 (d, 9H, CHOCH$_2$CH=CH$_2$), 3.96 (d, 9H, CH$_2$OCH$_2$CH=CH$_2$), 3.63-3.44 (m, 60H), 3.24 (s, 6H, C(CH$_2$)$_3$), 1.35 (q, 2H, CH$_3$CH$_2$), 0.80 (t, 3H, CH$_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 135.6 (6C, CHOCH$_2$CH=CH$_2$), 135.1 (6C, CH$_2$OCH$_2$CH=CH$_2$), 117.0 (12C, CH$_2$OCH$_2$CH=CH$_2$), 78.9 (3C), 77.4 (3C), 72.3 (24C), 70.6 (12C), 43.6 (1C, C(CH$_2$)$_4$), 23.4 (1C, CH$_2$CH$_3$), 8.1 (1C, CH$_2$CH$_3$); IR(KBr): ν(cm^{-1}) = 3080 (C=CH), 1647 (C=C), 1109 (C-O-C), 996 (C=CH$_2$), 923 (C=CH$_2$); MALDI-TOF MS calcd. for $C_{69}H_{116}O_{21}$ 1281.7 found 1280.8 + Li.

[G-3]

^{1}H NMR (300 MHz, CD_3OD): δ = 4.9 (s, O<u>H</u>), 3.84-3.53 (m, 105H), 3.42 (s, 6H, C(C<u>H</u>$_2$)$_3$), 1.49 (q, 2H, C<u>H</u>$_2$CH$_3$), 0.97 (t, 3H, C<u>H</u>$_3$); ^{13}C NMR (75 MHz, CD_3OD): δ = 80.2 (9C, $(CH_2)_2$<u>C</u>(H)OR), 74.3 (6C, CH_2O<u>C</u>$H_2CH(OH)CH_2OH$), 73.3-72.5 (36C, C$(CH_2)_3$, RO<u>C</u>H_2C(H)(OR)<u>C</u>H_2OR, CHO<u>C</u>H_2CH(OH)CH_2OH), 71.6 (3C, CHO<u>C</u>H_2CH(OR)CH_2OR) 64.8 (12C, <u>C</u>H_2OH), 44.9 (1C, <u>C</u>$(CH_2)_4$, 24.4 (1C, <u>C</u>H_2CH_3), 8.6 (1C, <u>C</u>H_3); IR(KBr): ν(cm^{-1}) = 3448 (OH), 1654 (C-O-C), 1459 (C-OH), 1111 (C-OH); MALDI-TOF MS calcd. for $C_{69}H_{140}O_{45}$ 1689.8 found 1689.4 + Li.

Allylated polyglycerol

^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.92 (m, C<u>H</u>=CH_2), 5.30 (d, CH=C<u>H</u>$_2$), 5.16 (m, CH=C<u>H</u>$_2$), 4.10 (d, C<u>H</u>$_2$CH=CH_2), 3.88-3.38 (m), 3.30 (s, C(C<u>H</u>$_2$)$_3$), 1.40 (q, CH_3C<u>H</u>$_2$), 0.85 (t,C<u>H</u>$_3$); ^{13}C NMR (75 MHz, CD_3OD): δ = 135.7 (CH_2OCH_2<u>C</u>H=CH_2), 135.2 (CH_2OCH_2<u>C</u>H=CH_2), 117.1 (CH_2OCH_2CH=<u>C</u>H_2), 79.0, 77.4, 72.3 (polyether backbone), 43.6, 23.4, 8.1 (TMP-core); IR(KBr): ν(cm^{-1}) = 3079 (C=CH), 1646 (C=C), 1105 (C-O-C), 996 (C=CH_2), 924 (C=CH_2);

Dihydroxylated polyglycerol 3 ("pseudo-dendrimer")

^{1}H NMR (300 MHz, CD_3OD): δ = 4.90 (s, O<u>H</u>), 3.92-3.38 (m), 3.22 (s, C(C<u>H</u>$_2$)$_3$), 1.35 (q, C<u>H</u>$_2$CH$_3$), 0.82 (t, C<u>H</u>$_3$); ^{13}C NMR (75 MHz, CD_3OD): δ = 80.4 ($(CH_2)_2$<u>C</u>(H)OR), 74.4 (CH_2O<u>C</u>$H_2CH(OH)CH_2OH$), 73.4-72.6 (C(<u>C</u>H_2)$_3$,ROCH_2C(H)(OR)<u>C</u>H_2OR, CHO<u>C</u>H_2CH-(OH)CH_2OH), 71.7 (CHO<u>C</u>H_2CH(OR)CH_2OR), 64.9 (<u>C</u>H_2OH), 43.6, 23.4, 8.1 (TMP-core); IR(KBr): ν(cm^{-1}) = 3374 (OH), 1652 (C-O-C), 1456 (C-OH).