Supporting information for:

A Mild Deprotection Strategy for Allyl Protecting Groups and its Implications in Sequence Specific Dendrimer Synthesis

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Experimental Details

¹H-NMR spectra were recorded on a 400 MHz NMR spectrometer using the residual proton resonance of the solvent as 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; q, quartet; qd, quartet of doublet; dd, doublet of doublet; m, multiplet; b, broad. ¹³C-NMR spectra were proton decoupled and recorded on a 400 MHz NMR spectrometer using the carbon signal of the deuterated solvent as the internal standard. Mass spectra were obtained at the Coordinated Instrumentation Facility of Tulane University. Flash chromatography was performed with EM science 37-75 μm silica gel. Analytical thin layer chromatography was performed on EM science silica gel plates with F-254 indicator and the visualization was

accomplished by UV lamp or using the cerium molybdic acid stain mixture. THF was distilled over Na/Ph₂CO ketyl. All other chemicals obtained from commercial sources were used without further purification, unless otherwise mentioned. The purity of compounds reported here were judged to be >95% using ¹H NMR and ¹³C NMR.

General procedure for aryl allyl ether synthesis: A mixture of phenol (1.0 equiv), allylbromide (1.5 equiv), K₂CO₃ (2.0 equiv), and acetone was heated to reflux and stirred vigorously under nitrogen for 12 hours. The reaction mixture was allowed to cool and evaporated to dryness. The residue was partitioned between water and CH₂Cl₂. The organic layer was separated, the aqueous layer extracted with CH₂Cl₂, the combined organic layer dried over anhydrous Na₂SO₄, and concentrated in vacuo. The crude mixture was purified by silica gel column chromatography. All compounds were obtained in 85-90% yield.

General procedure for alkyl allyl ether synthesis: To NaH (2.0 equiv, 60% dispersion in mineral oil) in dry THF was added alcohol (1.0 equiv) in dry THF at 0 °C. The mixture was stirred for 15 min and allylbromide (1.2 equiv) was added dropwise to this solution. The reaction mixture was allowed to stir at room temperature for 12 hours. The reaction mixture was poured into water and extracted with ether. The organic layer was washed with water, brine and dried over anhydrous Na₂SO₄. The organic layer was concentrated in vacuo and the residue was purified by silica gel column chromatography. All compounds were obtained in 80-85% yield.

General procedure for the synthesis of alloc protected amines: To a solution of amine (1.0 equiv) in dry dichloromethane was added pyridine (2.0 equiv) at 0 °C. The mixture was stirred for 10 min. Allyl chloroformate (1.2 equiv) was added dropwise and

the mixture was allowed to stir at room temperature overnight. Water was added to the reaction mixture, organic layer was separated and the aqueous layer extracted with CH₂Cl₂. The organic layer was washed with dilute HCl, water and brine solution. It was dried over Na₂SO₄. The resultant mixture was concentrated in vacuo and purified by silica gel column chromatography. All compounds were obtained in 90-95% yield.

1-Naphthyl allyl ether (1): ¹H NMR (400 MHz, CDCl₃): δ 8.32-8.30 (m, 1H), 7.80-7.78 (m, 1H), 7.50-7.34 (m, 4H), 6.81 (d, *J*= 7.6 Hz, 1H), 6.23-6.13 (m, 1H), 5.52 (qd, *J*=1.6, 17.2 Hz, 1H), 5.34 (qd, *J*=1.6, 10.4 Hz, 1H), 4.73-4.71 (m, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 154.2, 134.4, 133.2, 127.3, 126.3, 125.7, 125.1, 122.0, 120.2, 117.2, 104.9, 68.7.

4-Methoxyphenyl allyl ether (2): ¹H NMR (400 MHz, CDCl₃): δ 6.85 (d, *J*=6.0 Hz, 2H), 6.83 (d, *J*=5.6 Hz, 2H), 6.12-6.02 (m, 1H), 5.43 (qd, *J*=1.6, 17.2 Hz, 1H), 5.29 (qd, *J*=1.6, 10.4 Hz, 1H), 4.49-4.47 (m, 2H), 3.75 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 153.6, 152.5, 133.4, 117.0, 115.4, 114.3, 69.1, 55.2.

4-*tert*-butylphenyl allyl ether (3):^{12a} ¹H NMR (400 MHz, CDCl₃): δ 7.30 (d, *J*=9.2 Hz, 2H), 6.85 (d, *J*= 9.2 Hz, 2H), 6.10-6.01 (m, 1H), 5.41 (qd, *J*=1.6, 17.2 Hz, 1H), 5.27 (qd, *J*=1.6, 10.4 Hz, 1H), 4.52-4.50 (m, 2H), 1.29 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ 156.2, 143.1, 133.5, 125.9, 117.0, 114.04, 114.02, 68.4, 33.8, 31.41.

4-Cyanophenyl allyl ether (4):¹⁰ ¹H NMR (400 MHz, CDCl₃): δ 7.58 (d, *J*=9.2 Hz, 2H), 6.96 (d, *J*=9.2 Hz, 2H), 6.08-5.98 (m, 1H), 5.42 (qd, *J*=1.6, 17.2 Hz, 1H), 5.33 (qd, *J*=1.6, 10.4 Hz, 1H), 4.60-4.58 (m, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 161.6, 133.7, 131.8, 118.9, 118.2, 115.2, 103.7, 68.7.

3-Allyloxy benzaldehyde (5): ^1H NMR (400 MHz, CDCl_3): δ 9.76 (s, 1H), 7.27-7.19 (m, 3H), 7.01-6.98 (m, 1H), 5.92-5.82 (m, 1H), 5.25 (qd, $J=1.6, 17.2$ Hz, 1H), 5.11 (qd, $J=1.6, 10.4$ Hz, 1H), 4.38-4.36 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3): δ 191.5, 158.5, 137.2, 132.2, 129.5, 122.8, 121.3, 117.3, 112.7, 68.2.

Methyl-3-allyloxy-4-nitro-benzoate (6): ^1H NMR (400 MHz, CDCl_3): δ 7.81 (d, $J=8.4$ Hz, 1H), 7.71 (d, $J=1.2$ Hz, 1H), 7.60 (dd, $J=8.4$ Hz, 1.6 Hz, 1H), 6.06-5.97 (m, 1H), 5.48 (qd, $J=1.6, 17.2$ Hz, 1H), 5.33 (qd, $J=1.6, 10.4$ Hz, 1H), 4.73-4.71 (m, 2H), 3.93 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 165.0, 151.2, 142.4, 134.6, 131.1, 125.1, 121.3, 118.5, 115.7, 70.0, 52.7. GC/MS m/z (r.i.) 237 (M^+ , 13), 220 (100), 190 (41), 158 (47), 131 (30), 102 (35), 91 (48), 77 (40), 63 (20), 51 (31).

Ethyl-3-benzyloxy-5-allyloxy-benzoate (7): ^1H NMR (400 MHz, CDCl_3): δ 7.44-7.21 (m, 7H), 6.73 (t, $J=2.4$ Hz, 1H), 6.08-5.98 (m, 1H), 5.35 (qd, $J=1.6, 17.2$ Hz, 1H), 5.29 (qd, $J=1.6, 10.4$ Hz, 1H), 5.06 (s, 2H), 4.54-4.52 (m, 2H), 4.34 (q, $J=7.2$ Hz, 2H), 1.37 (t, $J=7.2$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 166.2, 159.6, 159.4, 136.4, 132.7, 132.2, 128.5, 128.0, 127.5, 117.8, 108.1, 106.8, 70.1, 68.9, 61.0, 14.2. GC/MS m/z (r.i.) 312 (M^+ , 42), 267 (9), 221(39), 91 (100), 65 (20).

O, O'-diallyl-3-hydroxybenzyl alcohol (8): ^1H NMR (400 MHz, CDCl_3): δ 7.26-7.22 (m, 1H), 6.93-6.91 (m, 2H), 6.85-6.82 (m, 1H), 6.10-5.90 (m, 2H), 5.42 (qd, $J=1.6, 17.2$ Hz, 1H), 5.31 (qd, $J=1.6, 10.4$ Hz, 1H), 5.28 (qd, $J=1.6, 17.2$ Hz, 1H), 5.21 (qd, $J=1.6, 10.4$ Hz, 1H), 4.55-4.53 (m, 2H), 4.5 (s, 2H), 4.03-4.01 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3): δ 158.5, 139.7, 134.5, 133.1, 129.1, 119.7, 117.2, 116.7, 113.6, 113.5, 71.6, 70.8, 68.3.

Allyl-1-hexadecyl ether (9): ^1H NMR (400 MHz, CDCl_3): δ 5.97-5.87 (m, 1H), 5.26 (qd, $J=1.6, 17.2$ Hz, 1H), 5.16 (qd, $J=1.6, 10.4$ Hz, 1H), 3.97-3.95 (m, 2H), 3.42 (t, $J=6.8$ Hz, 2H), 1.62-1.25 (m, 28H), 0.88 (t, $J=6.8$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 135.0, 116.3, 71.6, 70.3, 31.9, 29.74, 29.68, 29.64, 29.58, 29.48, 29.35, 26.1, 22.6, 14.0.

N-(Allyloxycarbonyl)-4-*tert*-butylaniline (11): ^1H NMR (400 MHz, CDCl_3): δ 7.34-7.28 (m, 4H), 6.58 (bs, NH), 6.02-5.92 (m, 1H), 5.36 (qd, $J=1.6, 17.2$ Hz, 1H), 5.26 (qd, $J=1.6, 10.4$ Hz, 1H), 4.67-4.65 (m, 2H), 1.3 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 153.1, 146.3, 135.1, 132.4, 125.7, 118.5, 118.0, 65.6, 34.1, 31.2.

N-(Allyloxycarbonyl)-dodecyl amine (12): ^1H NMR (400 MHz, CDCl_3): δ 5.97-5.87 (m, 1H), 5.30 (qd, $J=1.6, 17.2$ Hz, 1H), 5.21 (qd, $J=1.6, 10.4$ Hz, 1H), 4.56-4.55 (m, 2H), 3.17 (t, $J=6.8$ Hz, 2H), 1.50-1.25 (m, 20H), 0.88 (t, $J=6.8$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 156.1, 132.9, 117.3, 65.2, 40.9, 31.8, 29.8, 29.54, 29.52, 29.48, 29.45, 29.23, 29.19, 26.64, 22.57, 13.9.

Ethyl-3-benzyloxy-5-hydroxy-benzoate (7a): ^1H NMR (400 MHz, CDCl_3): δ 7.38-7.21 (m, 7H), 6.70 (t, $J=2.4$ Hz, 1H), 4.98 (s, 2H), 4.32 (q, $J=6.8$ Hz, 2H), 1.33 (t, $J=7.2$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 166.9, 159.7, 157.3, 136.3, 131.9, 128.4, 127.9, 127.5, 109.5, 107.7, 107.2, 70.08, 61.3, 14.11. GC/MS m/z (r.i.) 273 (M^+ , 4), 227 (4), 136 (2), 108 (4), 91 (100), 65 (22), 51 (9).

Methyl-3-benzyloxy-5-hydroxy-benzoate (7b): ^1H NMR (400 MHz, CDCl_3): δ 7.42-7.19 (m, 7H), 6.69 (t, $J=2.4$ Hz, 1H), 5.04 (s, 2H), 3.89 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 167.1, 159.9, 156.9, 136.35, 131.82, 128.58, 128.09, 127.5, 109.5, 107.9, 107.4, 70.21, 52.43. GC/MS m/z (r.i.) 258 (M^+ , 5), 136 (7), 108 (14), 91 (100), 65 (25), 51 (9).

3-Hydroxy-allyl benzyl ether (10): ^1H NMR (400 MHz, CDCl_3): δ 7.19-7.15 (t, $J=7.2$ Hz, 1H), 6.87-6.82 (m, 2H), 6.74 (dd, $J=2.4$ Hz, 1H), 5.98-5.88 (m, 1H), 5.30 (qd, $J=1.6$, 17.2 Hz, 1H), 5.21 (qd, $J=1.6$, 10.4 Hz, 1H), 4.48 (s, 2H), 5.06 (s, 2H), 4.04-4.02 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3): δ 155.9, 139.3, 134.1, 129.5, 119.9, 117.8, 114.8, 114.7, 71.7, 71.0.

Synthesis of Ethyl-3-allyloxy-5-hydroxy-benzoate (13): This compound was synthesized from 3,5-dihydroxybenzoic acid. 3,5-dihydroxy benzoic acid was converted to the ethyl-3,5-dihydroxybenzoate using ethanol and H_2SO_4 under refluxing conditions. Further, the ethyl-3,5-dihydroxybenzoate was treated with allyl bromide in the presence of K_2CO_3 to obtain the mono protected ethyl-3-allyloxy-5-hydroxybenzoate **13**. ^1H NMR (400 MHz, CDCl_3): δ 7.18-7.16 (m, 2H), 6.63 (t, $J=2.4$ Hz, 1H), 6.09-5.99 (m, 1H), 5.43 (qd, $J=1.6$, 17.2 Hz, 1H), 5.31 (qd, $J=1.6$, 10.4 Hz, 1H), 4.56-4.54 (m, 2H), 4.36 (q, $J=7.2$ Hz, 2H), 1.38 (t, $J=7.2$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 167.07, 159.6, 157.0, 132.6, 131.9, 117.9, 109.4, 107.7, 107.2, 68.9, 61.5, 14.1.

Synthesis of 3-Allyloxy-5-hydroxybenzyl alcohol (18):^{1 3} Ethyl-3-allyloxy-5-hydroxybenzoate was reduced with lithium aluminum hydride to afford the product **18**. ^1H NMR (400 MHz, CDCl_3): δ 6.51 (bs, 1H), 6.46 (bs, 1H), 6.35 (t, $J=2.4$ Hz, 1H), 6.08-5.99 (m, 1H), 5.40 (qd, $J=1.6$, 17.2 Hz, 1H), 5.28 (qd, $J=1.6$, 10.4 Hz, 1H), 5.09 (s, 1H), 4.61 (d, $J=6.0$ Hz, 2H), 4.52-4.50 (m, 2H), 1.76 (t, $J=6.4$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 159.8, 157.0, 142.8, 132.9, 117.8, 106.6, 105.5, 101.5, 68.8, 64.8.

3-(4-tert-butylbenzyloxy)-5-(3-methylbenzyloxy)-benzyl alcohol (17) : ^1H NMR (400 MHz, CDCl_3): δ 7.36-7.06 (m, 8H), 6.55-6.49 (m, 3H), 4.88 (s, 4H), 4.47 (s, 2H), 2.29 (s, 3H), 1.28 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3): δ 159.96, 159.91, 150.7, 143.3,

137.9, 136.5, 133.6, 128.5, 128.2, 128.1, 127.3, 125.3, 124.4, 105.35, 105.34, 100.9, 69.8,
69.6, 64.7, 34.3, 31.1, 21.2. GC/MS m/z (r.i.) 390 (M^+ , 2), 147 (29), 132 (15), 117 (22),
105 (100), 77 (11), 64 (2).