

Photolabile Dendrimers using o-Nitrobenzyl Ether Linkages

Mario Smet,[†] Li-Xin Liao, Wim Dehaen,[†] and Dominic V. McGrath*

Department of Chemistry, The University of Arizona, Tucson, AZ 85721

mcgrath@u.arizona.edu

SUPPORTING INFORMATION

Materials and Methods. NMR spectra were acquired on commercial instrumentation and chemical shifts are reported in ppm (δ) referenced to internal residual solvent protons (^1H) or the carbon signal of the deuterated solvents (^{13}C). All chemicals were purchased from commercial suppliers and used as received unless otherwise specified. All reactions were conducted in oven-dried glassware under an inert atmosphere (N_2). Acetone was stored over freshly activated 3Å molecular sieves. Other solvents such as ethyl acetate, dichloromethane, and hexane were used as received. Dendritic bromides $[\text{G}-n]\text{Br}$ ($n = 1-3$) were prepared according to the literature.¹ Flash chromatography using silica (Natland International Corp., silica gel 200-400 Mesh) was performed by the method of Still et al.² Thin-layer chromatography (TLC) was performed on precoated TLC plates (Silica Gel HLO, F-254, Scientific Adsorbants, Inc., or Merck).

4-{3',5'-Bis(benzyloxy)benzyloxy}-5-methoxy-2-nitrophenylethan-1-ol (2a). To a solution of $[\text{G}-1]\text{Br}$ (1.08 g, 2.82 mmol), alcohol **1** (0.40 g, 1.88 mmol) and 18-Crown-6 (50 mg, 0.19 mmol) in acetone (15 mL), K_2CO_3 (0.39 g, 2.8 mmol) was added and the resulting suspension was stirred at reflux temperature for 24 h, protected from light. The reaction mixture was then allowed to cool to room temperature and evaporated in vacuum. To the residue, CH_2Cl_2 (45 mL) was added and the resulting suspension was washed with water (ca. 50 mL). The organic layer was separated, dried over MgSO_4 and evaporated in vacuum. The title compound **2a** (0.85 g, 86%) was obtained after column chromatography (SiO_2 , 20:1 CH_2Cl_2 - Et_2O) as a pale yellow oil: ^1H NMR (250 MHz, CDCl_3) δ 7.57 (s, 1H), 7.41-7.30 (m, 10H), 7.29 (s, 1H), 6.68 (d, $J = 2.2$ Hz, 2H), 6.56 (t, $J = 2.2$ Hz, 1H), 5.51 (q, $J = 6.3$ Hz, 1H), 5.09 (s, 2H), 5.01 (s, 4H), 3.96 (s, 3H), 2.5-2.3 (s, br, 1H), 1.52 (d, $J = 6.3$ Hz, 3H); ^{13}C NMR (62.5 MHz, CDCl_3) δ 160.19, 154.19, 146.46, 139.34, 138.09, 137.20, 136.61, 128.54, 127.99, 127.50, 109.73, 108.68, 106.31, 101.77, 70.99, 70.06, 65.69, 56.31, 24.22; MS (FAB) m/z 515.1 (M^+ , 1.8%, $\text{C}_{30}\text{H}_{29}\text{NO}_7$ requires 515.2).

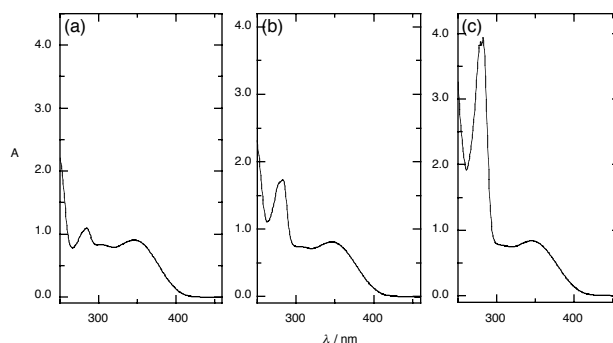


Figure S1. Absorption spectra for dendrons (a) **2a**, (b) **2b**, and (c) **2c** in CHCl_3 solution.

4-{3',5'-Bis[3'',5''-bis(benzyloxy)benzyloxy]benzyloxy}-5-methoxy-2-nitrophenylethan-1-ol (2b). Following the procedure for **2a**, $[\text{G}-2]\text{Br}$ (2.00 g, 2.48 mmol), alcohol **1** (0.53 g, 2.5 mmol), 18-Crown-6 (50 mg, 0.19 mmol) and K_2CO_3 (0.56 g, 4.0 mmol) in acetone (18 mL) yielded, after purification by column chromatography (SiO_2 , 9:1 CH_2Cl_2 - EtOAc) alcohol **2b** (1.9 g, 83%) as a pale yellow oil: ^1H NMR (250 MHz, CDCl_3) δ 7.57 (s, 1H), 7.42-7.30 (m, 20H), 7.28 (s, 1H), 6.66-6.65 (m, 6H), 6.56-6.54 (m, 3H), 5.49 (q, $J = 6.3$ Hz, 1H), 5.09 (s, 2H), 5.01 (s, 8H), 4.96 (s, 4H), 3.94 (s, 3H), 2.36-2.31 (s, br, 1H), 1.52 (d, $J = 6.3$ Hz, 3H); ^1H NMR (250 MHz, CDCl_3) δ 7.57 (s, 1H), 7.41-7.29 (m, 20H), 7.27 (s, 1H), 6.654-6.650 (m 2H), 6.55 (t, $J = 2.2$ Hz, 2H), 6.54 (t, $J = 2.2$ Hz, 1H), 4.49 (q, $J = 6.3$ Hz, 1H), 5.09 (s, 2H), 5.01 (s, 8H), 4.96 (s, 4H), 3.95 (s, 3H), 1.52 (d $J = 6.3$ Hz, 3H); ^{13}C NMR (62.5 MHz, CDCl_3) δ 160.08, 154.16, 146.40, 139.30, 139.09, 138.11, 137.28, 136.67, 128.54, 127.97, 127.52, 109.68, 108.68, 106.25, 101.79, 101.54, 70.92, 70.04, 69.94, 65.68, 56.31, 24.20; MS (FAB) m/z 939.7 (M^+ , 4%, $\text{C}_{58}\text{H}_{53}\text{NO}_{11}$ requires 939.4).

4-{3',5'-Bis[3'',5''-bis[3''',5'''-bis(benzyloxy)benzyloxy]benzyloxy}-5-methoxy-2-nitrophenylethan-1-ol (2c). Following the procedure for **2a**, $[\text{G}-3]\text{Br}$ (2.00 g, 2.48 mmol), alcohol **1** (1.21 g, 0.732 mmol), 18-Crown-6 (50 mg, 0.19 mmol) and K_2CO_3 (0.21 g, 1.5 mmol) in acetone (12 mL) yielded, after purification by column chromatography (SiO_2 , 20:1 CH_2Cl_2 - Et_2O) alcohol

[†] Current address: Katholieke Universiteit Leuven, Heverlee, Belgium.

(1) Hawker, C.J.; Fréchet, J.M.J. *J. Am. Chem. Soc.* **1990**, *112*, 7638.

(2) Still, W.C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

2c (0.55 g, 42%) as a pale yellow oil: ^1H NMR (250 MHz, CDCl_3) δ 7.55 (s, 1H), 7.42-7.22 (m, 41H), 6.67-6.64 (m, 16H), 6.56-6.53 (m, 7H), 7.46 (q, $J = 6.3$ Hz, 1H), 5.06 (s, 2H), 5.00 (s, 16H), 4.94 (s, 4H), 4.93 (s, 8H), 3.98 (s, 3H), 2.33-2.25 (s, br, 1H); ^{13}C NMR (62.5 MHz, CDCl_3) δ 160.11, 160.00, 154.18, 146.42, 139.33, 139.14, 138.17, 137.28, 136.71, 128.55, 128.33, 127.98, 127.53, 109.73, 108.68, 106.35, 101.81, 101.56, 70.92, 70.05, 69.94, 65.70, 56.31, 24.19; MS (FAB) m/z 1789.4 (M+H, 1%, $\text{C}_{114}\text{H}_{101}\text{NO}_{19}$ requires 1789.7).

G1-dendrimer 3a. A solution of alcohol **2a** (0.56 g, 1.1 mmol) and DMAP (0.16 g, 1.3 mmol) in benzene (15 mL), was refluxed for 1 h under Dean-Stark conditions. The solution was cooled down and to the stirred solution, 1,3,5-benzenetricarbonyl trichloride (87 mg, 0.33 mmol) was added on which a precipitate formed. Dry chloroform (ca. 10 mL) was added to restore homogeneity after which the clear solution was left for 15 h. The reaction mixture was evaporated in vacuum and the dendrimer **3a** (0.35 g, 62%) was obtained as a pale yellow glass (mixture of diastereomers): ^1H NMR (500 MHz, CDCl_3 , 25 °C, CHCl_3) δ = 8.91-8.88 (m, 3H), 7.60-7.58 (3 x s, 3H), 7.40-7.27 (m, 30H), 7.11-7.09 (3 x s, 3H), 6.73-6.70 (m, 3H), 6.70-6.64 (m, 6H), 6.56-6.55 (m, 3H), 5.13-5.04 (m, 6H), 5.02-4.99 (3 x s, 12H), 3.92-3.89 (3 x s, 9H), 1.78-1.74 (m, 9H); MS (FAB) m/z 1703.2 (M+H, 1%, $\text{C}_{99}\text{H}_{87}\text{N}_3\text{O}_{24}$ requires 1703.6).

G2-dendrimer 3b. To a solution of alcohol **2b** (0.48 g, 0.51 mmol) and DMAP (62 mg, 0.51 mmol) in CH_2Cl_2 (16 mL) was added 1,3,5-benzenetricarbonyl trichloride (41 mg, 0.15 mmol) and the resulting clear solution was left at room temperature for 24 h. The reaction mixture was evaporated in vacuum and after column chromatography (SiO_2 , 35:1 CH_2Cl_2 - Et_2O) **3b** (0.19 g, 43%) was obtained as a pale yellow glass (mixture of diastereomers): ^1H NMR (500 MHz, CDCl_3 , 25 °C, CHCl_3) δ = 8.89-8.87 (m, 3H), 7.62-7.60 (3 x s, 3H), 7.39-7.26 (m, 60H), 7.11-7.09 (3 x s, 3H), 6.74-6.69 (m, 3H), 6.66-6.62 (m, 18H), 6.55-6.51 (m, 9H), 5.10-5.02 (m, 6H), 5.00-4.98 (3 x s, 24H), 4.94-4.92 (3 x s, 12H), 3.90-3.88 (3 x s, 9H), 1.77-1.73 (m, 9H); MS (FAB) m/z 2977.1 (M+H, 0.2%, $\text{C}_{183}\text{H}_{159}\text{N}_3\text{O}_{36}$ requires 2977.1).

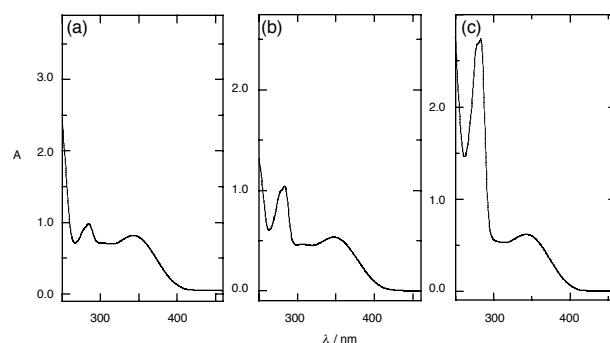


Figure S2. Absorption spectra for dendrimers (a) **3a**, (b) **3b**, and (c) **3c** in CHCl_3 solution.

G3-dendrimer 3c. A solution of alcohol **2c** (0.55 g, 0.31 mmol) and DMAP (49 mg, 4.0 mmol) in benzene (10 mL), was refluxed for 1 h under Dean-Stark conditions. The solution was cooled down and to the stirred solution, 1,3,5-benzenetricarbonyl trichloride (25 mg, 0.094 mmol) was added on which a precipitate formed. Dry chloroform (ca. 2 mL) was added to restore homogeneity after which the clear solution was left for 24 h. The reaction mixture was evaporated in vacuum and the dendrimer **3c** (0.26 g, 50%) was obtained as a pale yellow glass after column chromatography (SiO_2 , 35:1 CH_2Cl_2 - Et_2O) as a mixture of diastereomers: ^1H NMR (500 MHz, CDCl_3 , 25 °C, CHCl_3) δ = 8.94-8.92 (m, 3H), 7.63-7.61 (m, 3H), 7.43-7.28 (m, 120), 7.13-7.11 (m, 3H), 6.78-6.74 (m, 3H), 6.70-6.63 (m, 42H), 6.58-6.55 (m, 21H), 5.03-4.91 (m, 90H), 3.91-3.87 (m, 9H), 1.80-1.76 (m, 9H); MS (MALDI) m/z 5549.7 (M+Na, $\text{C}_{351}\text{H}_{303}\text{N}_3\text{O}_{60}\text{Na}$ requires 5546.1)

General Procedure for Photolyses. Photolyses were performed under argon at RT on CHCl_3 (**3a-c**) solutions with dendrimer concentrations that resulted in an optical density of 0.5 to 1.0 at the ca. 345 nm band (approx. 40 μM). The prepared samples were irradiated for successive intervals using a Spectroline 36-380 miniature UV quartz pencil lamp (365 nm). Photolyses of **3a-3c** are shown in Figure S3.

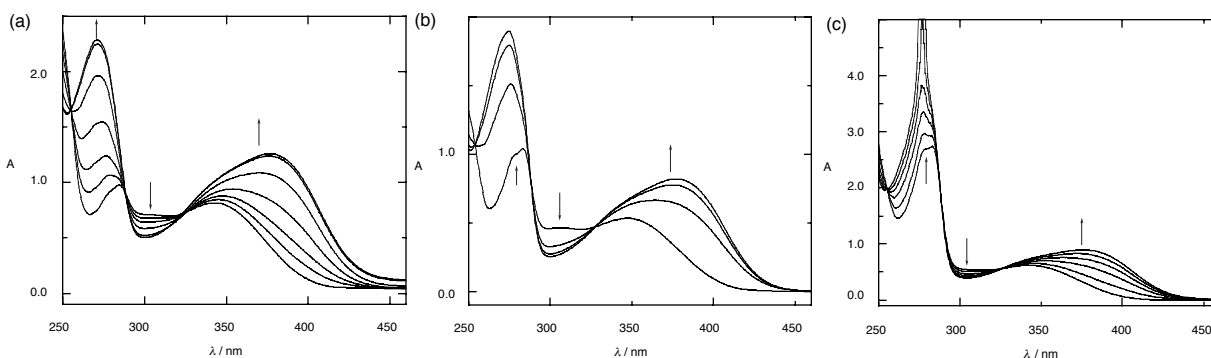


Figure S3. Photolysis experiments on (a) dendrimer **3a** irradiated for 0, 3, 6, 12, 24, 45, and 57 minutes, (b) dendrimer **3b** irradiated for 0, 3, 6, and 12 minutes, and (c) dendrimer **3c** irradiated for 0, 2, 5, 8, 11, and 17 minutes, all monitored by absorption spectroscopy.