

## Experimental Section

**General.** Dichloromethane was distilled from calcium hydride. Diethyl ether was distilled from sodium benzophenone ketyl. THF was distilled from sodium benzophenone ketyl, stirred over LAH, degassed by several (3-5) freeze-pump-thaw cycles, and then distilled by vacuum transfer before use. DMF was degassed by three freeze-pump-thaw cycles. 2-Benzyloxyethanol was obtained from Aldrich and distilled from calcium hydride. Ethylene oxide was distilled by vacuum transfer from calcium hydride three times and used immediately. Amberlite IR-120(+) acidic ion exchange resin was washed with 1N HCl, then thoroughly washed with distilled water until negative to AgNO<sub>3</sub> test (for presence of Cl<sup>-</sup>), washed with ethanol, followed by diethyl ether and dried under vacuum. Phosphonitrilic chloride trimer was obtained from Fluka and used without further purification. Methylisocyanate polystyrene HL (200-400 mesh), 2% DVB resin was obtained from Novabiochem. Diphenyl (4-hydroxyphenyl)phosphine was prepared as described in ref. 14. All other reagents were obtained from Aldrich and used without further purification. <sup>1</sup>H and <sup>13</sup>C NMR spectra were obtained on either a Bruker DRX-400 or a Bruker DRX-500. Chemical shifts are reported as  $\delta$  values relative to CHCl<sub>3</sub> (7.26 ppm for <sup>1</sup>H, 77.0 for <sup>13</sup>C). <sup>31</sup>P NMR spectra were obtained on a Bruker DRX-400 and chemical shifts are reported relative to an external standard of phosphoric acid at 0 ppm. Mass spectra were performed on a PerSeptive Biosystems Voyager mass spectrometer. Concentrated in vacuo as used in the experimental section refers to rotary evaporation using a Büchi rotavapor.

**Polyethylene glycol monobenzyl ether MW 600 (3a).** To a suspension of potassium hydride (580 mg, 14.5 mmol, 1.06 eq.) in degassed THF (125 mL) was added 2-benzyloxyethanol **2** (2.09 g, 13.7 mmol, 1 eq) and stirred for 4 h. The solution was degassed by three freeze-pump-thaw cycles, then ethylene oxide (7.84 g, 178 mmol, 13 eq.) was introduced and stirred at ambient temperature for 24 h. The reaction was quenched by the addition of Amberlite IR-120(+) resin (20 g) and stirred until the reaction was no longer basic by litmus. Filtration from the resin and concentration afforded the product monobenzyl PEG **3a** as an oil (8.93 g, 90%): <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  7.32-7.22 (m, 5H), 4.53 (s, 2H), 3.75-3.5 (m, 64H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  138.1, 128.2, 127.6, 127.5, 73.1, 72.4, 70.5, 70.2, 69.3, 67.8, 61.5.

**Polyethylene glycol monobenzyl ether MW 1000 (3b).** To a suspension of potassium hydride (605 mg, 15.9 mmol, 1.06 eq.) in degassed THF (125 mL) was added 2-benzyloxyethanol **2** (2.28 g, 15 mmol, 1 eq) and stirred for 4 h. The solution was degassed by three freeze-pump-thaw cycles, then ethylene oxide (15.31 g, 347 mmol, 23 eq.) was introduced and stirred at ambient temperature for 24 h. The reaction was quenched by the addition of Amberlite IR-120(+) resin (20 g) and stirred until the reaction was no longer basic by litmus. Filtration from the resin directly into diethyl ether (1L) at 0° afforded the product monobenzyl PEG **3b** as a white powder (13.67 g, 78%) with an additional lower MW fraction collected from the ethereal filtrate (3.2 g, total 96%): <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  7.32-7.22 (m, 5H), 4.54 (s, 2H), 3.75-3.45 (m, 105H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  138.1, 128.1, 127.5, 127.4, 73.0, 72.3, 70.4, 70.2, 69.3, 61.5.

**Polyethylene glycol monobenzyl ether MW 2000 (3c).** To a suspension of potassium hydride (320 mg, 8 mmol, 1.02 eq.) in degassed THF (125 mL) was added 2-benzyloxyethanol **2** (1.18 g, 7.8 mmol, 1 eq) and stirred for 4 h. The solution was degassed by three freeze-pump-thaw cycles, then ethylene oxide (14.88 g, 337 mmol, 43 eq.) was then introduced and stirred at ambient temperature for 24 h. The reaction was quenched by the addition of Amberlite IR-120(+) resin (10 g) and stirred until the reaction was no longer basic by litmus. Filtration from the resin directly into diethyl ether (1L) at 0°

afforded the product monobenzyl PEG **3c** as a white powder (15.54 g, 97%):  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.35-7.25 (m, 5H), 4.55 (s, 2H), 3.81-3.45 (m, 190H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  138.0, 128.1, 127.6, 127.4, 73.0, 72.3, 70.3, 70.2, 69.2, 61.5.

**$\text{P}_3\text{N}_3((\text{OCH}_2\text{CH}_2)_n\text{OBn})_6$  MW 3,500 (4a).** To a suspension of potassium hydride (587 mg, 14.6 mmol, 6.6 eq.) in THF (50 mL) was added **3a** (8.8 g, 14.6 mmol, 6.6 eq) in THF (100 mL) and stirred at ambient temperature for 4 h. Phosphonitrilic chloride trimer (767 mg, 2.21 mmol, 1 eq.) in THF (10 mL) was then introduced and stirred at ambient temperature overnight. Methylisocyanate polystyrene resin (3.5 g, 1 mmol/g) was added to the stirred solution and stirred an additional 4 h. The reaction was then filtered under argon into a flask containing Amberlite IR-120(+) (10 g) and stirred until the reaction was no longer basic by litmus. Filtration and concentration afforded the pure MW 3,500 **4a** star as an oil (7.88 g, 95%):  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.30-7.23 (m, 30H), 4.52 (s, 12H), 4.01 (bs, 12H), 3.8-3.4 (m, 550H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  138.2, 128.3, 127.7, 127.5, 73.1, 70.5, 69.4;  $^{31}\text{P}$  NMR (200 MHz,  $\text{CDCl}_3$ )  $\delta$  18.09 (s).

**$\text{P}_3\text{N}_3((\text{OCH}_2\text{CH}_2)_n\text{OBn})_6$  MW 6,000 (4b).** To a suspension of potassium hydride (900 mg, 22.4 mmol, 7.3 eq.) in THF (50 mL) was added **3b** (22.1 g, 20.1 mmol, 6.6 eq) in THF (100 mL) and stirred at ambient temperature for 5 h. Phosphonitrilic chloride trimer (1.06 g, 3.05 mmol, 1 eq.) in THF (10 mL) was then introduced and stirred at ambient temperature for 12h. Methylisocyanate polystyrene resin (4 g, 1 mmol/g) was then added to the stirred solution and stirred an additional 4 h. The reaction was then filtered under argon into a flask containing Amberlite IR-120(+) (15 g) and stirred until the reaction was no longer basic by litmus. Filtration from the resin into diethyl ether (1L) at  $0^\circ$  afforded the pure MW 6,000 star **4b** as a white powder (20.29 g, 99%):  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.34-7.25 (m, 30H), 4.54 (s, 12H), 4.01 (bs, 12H), 3.78 (t,  $J=4.7$  Hz, 12H), 3.62 (m, 550H), 3.44 (t,  $J=4.8$  Hz, 12H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  138.0, 128.1, 127.5, 127.3, 72.9, 70.5, 69.2;  $^{31}\text{P}$  NMR (200 MHz,  $\text{CDCl}_3$ )  $\delta$  18.2 (s).

**$\text{P}_3\text{N}_3((\text{OCH}_2\text{CH}_2)_n\text{OBn})_6$  MW 12,000 (4c).** To a suspension of potassium hydride (234 mg, 5.83 mmol, 7.3 eq.) in THF (125 mL) was added **3c** (12.22 g, 5.81 mmol, 7.3 eq) in THF (50 mL) and stirred at ambient temperature for 4 h. Phosphonitrilic chloride trimer (277 mg, 0.796 mmol, 1 eq.) in THF (10 mL) was then introduced and stirred at ambient temperature overnight. The reaction was quenched by the addition of Amberlite IR120(+) acidic ion exchange resin (10 g) and stirred until neutral by litmus, filtered from the resin and precipitated from pentane (900 ml) at  $0^\circ$  C to afford the crude polymer (12.41 g). The crude product was taken up in THF (100 mL), deprotonated with KH (110 mg, 2.74 mmol), treated with methylisocyanate polystyrene resin (3 g) and stirred for 4h to remove unreacted monobenzyl PEG. The reaction was then filtered under argon into a flask containing Amberlite IR-120(+) (5 g) and stirred until the reaction was no longer basic by litmus. Filtration into diethyl ether (800 mL) at  $0^\circ$  afforded the pure MW 12,000 star **4c** as a white powder (8.91 g, 93%):  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.35-7.28 (m, 30H), 4.55 (s, 12H), 4.01 (bs, 12H), 3.80 (t,  $J=4.6$  Hz, 12H), 3.73-3.57 (m, 1176H), 3.44 (t,  $J=4.6$  Hz, 12H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  138.1, 128.2, 127.5, 127.3, 73.0, 70.4, 69.3;  $^{31}\text{P}$  NMR (200 MHz,  $\text{CDCl}_3$ )  $\delta$  18.54 (s).

**$\text{P}_3\text{N}_3((\text{OCH}_2\text{CH}_2)_n\text{OH})_6$  MW 6,000 (1b).** **4b** (8.16 g, 1.4 mmol) was dissolved in 4:1-EtOAc: $\text{CH}_2\text{Cl}_2$  (100 mL). 10 % Pd/C (810 mg) was added and the reaction was agitated under a hydrogen atmosphere at 55 psi until  $\text{H}_2$  uptake ceased (3 h). Filtration through celite and concentration provided a clear oil which was taken up in THF (50 mL) and precipitated from diethyl ether (1 L) at  $0^\circ$  C to give the product **4b** as a white powder (7.06 g, 95%):  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  4.04 (bs, 12H), 3.76 (t,  $J=4.8$

Hz, 12H), 3.72-3.52 (m, 540H), 3.48 (t, J=4.8 Hz, 12H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  72.4, 70.5, 70.3, 61.6;  $^{31}\text{P}$  NMR (200 MHz,  $\text{CDCl}_3$ )  $\delta$  18.3 (s).

**$\text{P}_3\text{N}_3((\text{OCH}_2\text{CH}_2)_n\text{OH})_6$  MW 12,000 (1c).** **4c** (7.12 g, 0.6 mmol) was dissolved in 4:1-EtOAc: $\text{CH}_2\text{Cl}_2$  (100 mL). 10 % Pd/C (890 mg) was added and the reaction was agitated under a hydrogen atmosphere at 55 psi until  $\text{H}_2$  uptake ceased (3 h). Filtration through celite and concentration provided a clear oil which was taken up in THF (50 mL) and precipitated from diethyl ether (500 mL) at  $0^\circ\text{C}$  to give the product **1c** as a white powder (6.72 g, 98%):  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  4.04 (bs, 12H), 3.76 (t, J=4.75 Hz, 12H), 3.73-3.52 (m, 1100H), 3.48 (t, J=4.7 Hz, 12H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  72.5, 70.5, 70.3, 61.7;  $^{31}\text{P}$  NMR (200 MHz,  $\text{CDCl}_3$ )  $\delta$  18.3 (s).

**$\text{P}_3\text{N}_3((\text{OCH}_2\text{CH}_2)_n\text{OSO}_2\text{CH}_3)_6$  (7).** To a solution of **1b** (6.6g, 1.1 mmol, 1 eq.) in  $\text{CH}_2\text{Cl}_2$  (100 mL) was added triethylamine (12.5 mL, 80 mmol, 12 eq.) and cooled to  $0^\circ$ . Methanesulfonyl chloride (3.8 mL, 48 mmol, 7.3 eq.) was added via syringe pump at 0.2 mL/minute and stirred for 14 h. The reaction was then poured into isopropanol (500 mL), concentrated to approximately 100 mL, and filtered. The precipitate was washed with cold isopropanol (2x 75 mL) and diethyl ether (2x 100 mL). The tan powder was then taken up in benzene (200 mL) and decolorizing carbon (4 g) added, stirred for 2h, then filtered through celite. The resulting light yellow solution was then concentrated, taken up in THF (50 mL) and precipitated into diethyl ether at  $0^\circ$ . Filtration and drying afforded the product **7** as a off white powder (6.55 g, 92%):  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  4.35 (t, J=4.4 Hz, 12H), 4.01 (s, 12H), 3.74 (t, J=4.75 Hz, 12H), 3.65-3.47 (bm, 560H), 3.06 (s, 18H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  70.5, 69.9, 69.2, 68.9, 37.7;  $^{31}\text{P}$  NMR (200 MHz,  $\text{CDCl}_3$ )  $\delta$  18.07 (s).

**$\text{P}_3\text{N}_3((\text{OCH}_2\text{CH}_2)_n\text{OC}_6\text{H}_4\text{P}(\text{Ph})_2)_6$  (8).** A solution of diphenyl (4-hydroxyphenyl)phosphine (351 mg, 1.26 mmol, 1.5 eq.), **7** (896 mg, 0.84 mmol, 1.0 eq.) and cesium carbonate (438 mg, 1.34 mmol, 1.6 eq.) in degassed DMF (35 mL) was heated to  $65^\circ$  and stirred for 18 h. The dark brown solution was cooled to ambient temperature and Amberlite IR-120(+) (6g) added and stirred for 2h. The solution was filtered, concentrated to approx. 5 mL, and precipitated from diethyl ether (500 mL) at  $0^\circ$ . The precipitate was filtered, washed with cold isopropanol (25 mL) and diethyl ether (2x50 mL) and dried to give the product phosphine **8** as a white solid (1.03 g, 91%):  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.35-7.10 (m, 72H), 6.84 (d, J=5.5 Hz, 12H), 4.14 (s, 12H), 4.00 (s, 12H), 3.79 (m, 12H), 3.75-3.45 (bm, 550H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  159.4, 137.6, 135.4, 135.2, 133.2, 133.0, 128.2, 114.6, 70.3, 69.7, 69.4, 67.1, 64.9;  $^{31}\text{P}$  NMR (200 MHz,  $\text{CDCl}_3$ )  $\delta$  18.3, -6.65.

**General procedure for Mitsunobu etherifications:** Phenol (0.1 mmol) was added to **8** (0.12 mmol, 0.78 mmol/g) in  $\text{CH}_2\text{Cl}_2$  (0.6 mL) and stirred for 20 minutes. The alcohol (0.1 mmol) and DEAD (0.11 mmol) were added and the reaction stirred at room temperature (times shown in table 2). Upon completion, the reaction was concentrated, precipitated from cold diethyl ether (10-20 mL) to recover the PEG-star phosphine oxide, and the ethereal solution concentrated. Chromatography (95:5:hexane-ethyl acetate) afforded the product ethers (yields shown in table 2) which were identical to authentic samples.

**Regeneration of phosphine 8** PEG-star phosphine oxide (366 mg, 0.28 mmol, 1.0 eq.) was dissolved in THF (5 mL) and cooled to  $0^\circ$ . Freshly prepared alane<sup>14</sup> (1.94 mL, 0.95 M, 1.84 mmol, 6.6 eq.) was added dropwise and the solution was refluxed for 0.5 h, then cooled to ambient temperature. MeOH (3 mL) was added and the solution filtered through Celite, then concentrated *in vacuo*. The residue was taken up in 10 mL THF and precipitated into 100 mL diethyl ether at  $0^\circ$ , filtered, and dried to give a white solid (294 mg, 80%). Spectral properties were identical to **8**.

Weight percent solubilities of PEG diol, **1b**, **1c**, **4b**, and **4c**

<u>Solvent</u>	PEG <u>1K</u>	Star <b>4b</b> <u>6K Bn</u>	Star <b>1b</b> <u>6K OH</u>	PEG <u>2K</u>	Star <b>4c</b> <u>12K Bn</u>	Star <b>1c</b> <u>12K OH</u>
CH <sub>2</sub> Cl <sub>2</sub>	75%	77%	74%	60%	62%	59%
CHCl <sub>3</sub>	69%	70%	69%	54%	53%	52%
H <sub>2</sub> O	84%	85%	85%	63%	66%	66%
6:4-EtOH:H <sub>2</sub> O	85%	82%	84%	62%	62%	64%
C <sub>6</sub> H <sub>6</sub>	68%	65%	63%	36%	46%	45%
1,4-dioxane	67%	60%	63%	27%	24%	25%
MeOH	80%	82%	79%	60%	63%	59%

<u>Solvent</u>	PEG <u>4.6K</u>	PEG <u>6K</u>	PEG <u>8K</u>	PEG <u>12K</u>
CH <sub>2</sub> Cl <sub>2</sub>	53%	52%	53%	51%
CHCl <sub>3</sub>	53%	45%	40%	45%
H <sub>2</sub> O	51%	54%	42%	52%
6:4-EtOH:H <sub>2</sub> O	50%	49%	49%	48%
C <sub>6</sub> H <sub>6</sub>	8%	7%	7%	5%
1,4-dioxane	2%	1%	1%	1%
MeOH	6%	4%	2%	1%

Values are expressed as weight % solubility (weight PEG/weight saturated soln)