Electronic supplementary information for **Light-MPEG-assisted organic synthesis**

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Electronic supplementary information 2 and 3 contain the NMR spectra of MPEG reagents and the products of reactions using supported reagents after MSPE (and washing with base in the case of ester 18), respectively.

General Experimental

All reactions were carried out in dry solvents. Diethyl ether, tetrahydrofuran, dichloromethane, and toluene were dried using a solvent drying system in which solvent is pushed from its storage container under low nitrogen pressure through two stainless steel columns containing activated alumina and copper. Anhydrous pyridine was purchased. ^{1}H and ^{13}C NMR spectra were obtained on an NMR spectrometer operating at 400 and 100 MHz respectively. All NMR *J* values are given in Hz and are uncorrected. CH_3, CH_2, CH, and C in the ^{13}C NMR spectra were assigned using DEPT. Infra-red (IR) spectra were obtained on a spectrophotometer with an attachment that uses a type IIa diamond as a single reflection element so that the IR spectrum of each compound (solid or liquid) could be directly detected without any sample preparation.

General Comments on synthesis and characterization of MPEG reagents

It is important to note that each type of MPEG-supported compound is comprised of functionally identical compounds with different MPEG chain lengths. Notional yields of MPEG-supported compounds are calculated based on the average MW of the starting MPEG-OH (i.e. 550) and assuming no change in the distribution of chain lengths. The loading of MPEG reagents was determined by microanalysis from percentage nitrogen or phosphorus. The purity of each MPEG-supported reagents was established by ^{1}H NMR spectroscopy comparing the integration of the methyl group of the MPEG to signals for the supported reagent, and from the absence of unexpected peaks in the ^{13}C NMR spectra. The large signal in the ^{1}H NMR spectra of supported reagents/scavengers corresponding to the ethylene groups of the MPEG chain is designated **MPEG** in the ^{1}H NMR spectra reported; the signals for the final ethylene unit linked to the supported reagent are often distinct and where this is the case, the integration is reported in the usual way with MPEG added by way of assignment. All signals in the ^{13}C NMR spectra of supported reagents/scavengers are reported in the usual way, and the large signal in each spectrum corresponding to the majority of ethylene groups of the MPEG chain is designated **MPEG**. Note that no designation is included for the few additional signals in the region 65-73 ppm in the ^{13}C NMR spectra that correspond to individual CH_2 groups in the MPEG that are not accidentally equivalent to others in the chain. For each type of supported compound the molecular ions appear as two series of peaks in the ESI-MS corresponding to $M + Na^+$ and $M + H^+$ with a difference of 44 amu between adjacent peaks in each series. One such series is reported for each type of compound with the 100% peak corresponding to the most intense peak in the series and all other intensities reported relative to it. For each type of supported reagent/scavenger, the HRMS is reported for the compound with twelve ethylene glycol units (n = 12).

General procedure for coupling of carboxylic acids with amines using ^{M}IIDQ

^{M}IIDQ (240 mg, 1.15 mmol g^{-1}, 0.28 mmol) in dry DCM (1 mL) was added to a stirred solution of (*S*)-Boc-valine **1** (0.2 mmol) and an amine (0.2 mmol) in dry DCM (1 mL) under argon and the mixture was stirred at 25 °C overnight. Solvent was removed under reduced pressure and the residue dissolved in ethyl acetate (1.5 mL). The resulting solution was filtered through a column of silica gel (3.5 g) eluting with ethyl acetate to give the amide **2**, **3** or **4** in the yields shown above after removal of solvent under reduced pressure.

2: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.85 (d, *J* = 6.6 Hz, 3H), 0.88 (d, *J* = 6.6 Hz, 3H), 1.33 (s, 9H), 2.05-2.07 (m, 1H), 3.86-3.93 (m, 1H), 4.31 (dd, *J* = 5.6 and 14.8 Hz, 1H), 4.34 (dd, *J* = 5.6 and 14.8 Hz, 1H), 5.14 (br d, *J* = 8.5 Hz 1H), 6.57 (br s, 1H), 7.16-7.25 (m, 5H); $[\alpha]_D$ –6.00 (*c* 1, $CHCl_3$). Agrees with literature.[1]

3: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.02 (d, J = 6.9 Hz, 3H), 1.03 (d, J = 6.9 Hz, 3H), 1.42 (s, 9H), 2.15-2.24 (m, 1H), 4.13-4.17 (m, 1H), 5.58 (br d, *J* = 8.5 Hz 1H), 7.01-7.07 (m, 1H), 7.18-7.31 (m, 2H), 7.47 (d, *J* = 7.7 Hz, 2H), 8.76 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 18.25 (CH_3), 19.40 (CH_3), 28.34 (CH_3), 30.80 (CH), 61.03 (CH), 80.22 (C), 120.22 (CH), 124.26 (CH), 128.83 (CH), 137.65 (C), 156.41 (CO), 170.50 (C); HRMS (ES+) 293.1855 (M + H^+, $C_{16}H_{25}N_2O_3$ requires 293.1865); IR (neat) ν: 3305, 2973, 1679, 1660, 1604, 1554, 1521, 1445, 1290, 1175 cm^{-1}. $[\alpha]_D$ –21.20 (*c* 1, EtOH); Literature contains no data.[2]

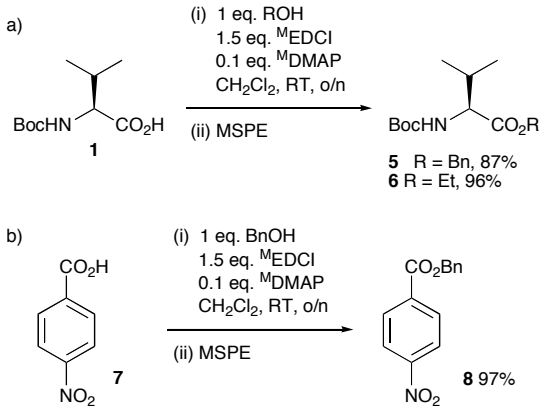
4: Alanine ethyl ester hydrochloride was stirred with excess triethylamine in DCM. The solvent and excess Et_3N were removed under reduced pressure and the residue used directly in the reaction. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.90 (d, *J* = 6.8 Hz, 3H), 0.95 (d, *J* = 6.8 Hz, 3H), 1.24 (t, *J* = 7.1 Hz, 3H), 1.37 (d, *J* = 7.2 Hz, 3H), 1.41 (s, 9H), 2.04-2.12 (m, 1H), 3.92-3.97 (m, 1H), 4.16 (q, *J* =

[1] Ramalingam, B.; Neuburger, M.; Pfaltz, A. *Synthesis* **2007**, 572-582.
[2] Voight, E, A.; Bodenstein, M. S.; Ikemoto, N.; Kress, M. H. *Tetrahedron Lett.* **2006**, *47*, 1717-1720.

7.1 Hz, 2H), 4.51-4.54 (m, 1H), 5.18 (br d, J = 8.5 Hz 1H), 6.65 (br d, J = 7.1 Hz 1H); $[\alpha]_D$ –8.30 (*c* 1, $CHCl_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.09 (CH_3), 17.73 (CH_3), 18.30 (CH_3), 19.17 (CH_3), 28.29 (CH_3), 31.07 (CH), 48.06 (CH), 59.77 (CH), 61.45 (CH_2), 79.81 (C), 155.83 (C), 171.10 (C), 172.67 (C), HRMS (ES+) 339.1886 (M + Na^+, $C_{15}H_{28}N_2O_5Na$ requires 339.1896); IR (neat) ν: 3329, 2954, 1728, 1684, 1652, 1519, 1464, 1298, 1159 cm^{-1}. Literature contains no data.[3]

[3] Shimagaki, M.; Koshiji, H.; Oishi, T. *Phosphorus and Sulfur* **1983**, *16*, 45-58.

General procedure for coupling of carboxylic acids with alcohols using ^{M}EDCI and ^{M}DMAP



^{M}EDCI (310 mg, 1.07 mmol g^{-1}, 0.33 mmol) was added to a stirred solution of the carboxylic acid **1** or **7** (0.2 mmol), the alcohol (0.2 mmol), and ^{M}DMAP (16 mg, 1.22 mmol g^{-1}, 0.02 mmol) in dry DCM (2 mL) under argon and the mixture was stirred at 25 °C overnight. Solvent was removed under reduced pressure and the residue dissolved in ethyl acetate (1.5 mL). The resulting solution was filtered through a column of silica gel (3.5 g) eluting with ethyl acetate to give the corresponding esters **5**, **6** or **8** in the yields shown above, following removal of solvent under reduced pressure.

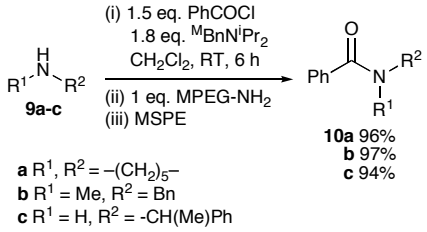
5: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.85 (d, J = 6.7 Hz, 3H), 0.94 (d, J = 6.7 Hz, 3H), 1.44 (s, 9H), 2.10-2.21 (m, 1H), 4.26-4.29 (m, 1H), 5.03 (br d, J = 8.5 Hz, 1H), 5.12 (d, J = 12.3 Hz, 1H), 5.20 (d, J = 12.3 Hz 1H), 7.30-7.40 (m, 5H); $[\alpha]_D$ +11.00 (*c* 1, $CHCl_3$). Agrees with literature.[4]

6: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.88 (d, J = 6.9 Hz, 3H), 0.94 (d, J = 6.9 Hz, 3H), 1.26 (t, J = 7.1 Hz, 3H), 1.43 (s, 9H), 2.09-2.14 (m, 1H), 4.14-4.24 (m, 3H), 5.18 (br d, J = 8.5 Hz 1H); $[\alpha]_D$ +43.00 (*c* 1, $CHCl_3$). ^{1}H NMR data agree with literature.[5]

8: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.41 (s, 2H), 7.36-7.47 (m, 5H), 8.24 (d, J = 9.1 Hz, 2H), 8.28 (d, J = 9.1 Hz, 2H). Agrees with literature.[6]

[4] Zeggaf, C.; Poncet, J.; Jouin, P.; Dufour, M. N.; Castro, B. *Tetrahedron*, **1989**, *45*, 5039-5050.
[5] Hayashida, O.; Sebo, L.; Rebek, J. *J. Org. Chem.* **2002**, *67*, 8291-8298.
[6] Hu, Y.; Pa, W.; Cui, W.; Wang, J. *Synth. Commun*. **1992**, *22*, 2763-2767.

General procedure for coupling of amines with acid chlorides using ^{M}BnN^{i}Pr$_2$ and MPEG-NH$_2$ as base and scavenger, respectively.



Benzoyl chloride (51 μL, 0.44 mmol) was added to a stirred solution of the amine **9a-c** (0.29 mmol) and ^{M}BnN^{i}Pr$_2$ (440 mg, 1.15 mmol g^{-1}, 0.53 mmol) in dry DCM (2 mL) under argon and the mixture was stirred at 25 °C for 6 h. MPEG-NH$_2$ (170 mg, 1.72 mmol g^{-1}, 0.29 mmol) was added and the reaction was continued overnight. Solvent was removed under reduced pressure and the residue dissolved in ethyl acetate (1.5 mL). The resulting solution was filtered through a column of silica gel (5 g) eluting with ethyl acetate to give the corresponding amides **10a-c** in the yields shown above, following removal of solvent under reduced pressure.

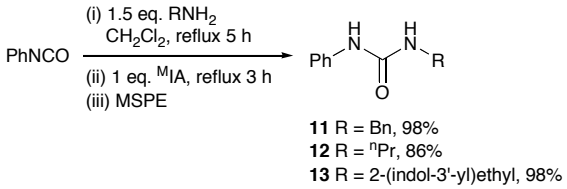
10a ^{1}H NMR (400 MHz, CDCl$_3$) δ: 1.42-1.58 (m, 2H), 1.59-1.75 (m, 4H), 3.27-3.42 (m, 2H), 3.56-85 (m, 2H), 7.38 (s, 5H). Agrees with literature.[7]

10b A 1:1 mixture of rotamers X and Y. ^{1}H NMR (400 MHz, CDCl$_3$) δ: 2.86 (s, 3H$^{X/Y}$), 3.03 (s, 3H$^{X/Y}$), 4.51 (s, 2H$^{X/Y}$), 4.76 (s, 2H$^{X/Y}$), 7.17-7.45 (m, 5H$^{X\&Y}$). Agrees with literature.[8]

10c ^{1}H NMR (400 MHz, CDCl$_3$) δ: 1.59 (d, J = 6.9 Hz, 3H), 5.29-5.37 (m, 1H), 6.43 (br d, J = 6.2 Hz) 7.25-7.46 (m, 8H), 7.75-7.77 (m, 2H). $[\alpha]_D$ –15.70 (*c* 1, CHCl$_3$). ^{1}H NMR data agree with literature.[9]

[7] Kita, Y.; Akai, S.; Ajimura, N.; Yoshigi, M.; Tsugoshi, T.; Yasuda, H.; Tamura, Y. *J.* Org. *Chem.* **1986**, *51*, 4150-4158.
[8] Maki, T.; Ishihara, K.; Yamamoto, H. *Org. Lett.* **2006**, *8*, 1431-1434.
[9] Qian, H.; Widenhoefer, R. A. *Org. Lett.* **2005**, *7*, 2635-2638.

General procedure for the use of ^{M}IA as a scavenger for nucleophiles.



11 R = Bn, 98%
12 R = ^{n}Pr, 86%
13 R = 2-(indol-3'-yl)ethyl, 98%

A mixture of phenyl isocyanate (22 μL, 0.22 mmol) and the amine (0.3 mmol) in dry DCM (1.3 mL) was stirred under argon at 60 °C (sealed reaction vessel) for 5 h. ^{M}IA (120 mg, 0.2 mmol) was then added and reaction continued for 3 h. Solvent was removed under reduced pressure and the residue dissolved in ethyl acetate (1.5 mL). The resulting solution was filtered through a column of silica gel (3.5 g) eluting with ethyl acetate, which gave the corresponding amides **11**-**13** in the yields shown above, following removal of solvent under reduced pressure.

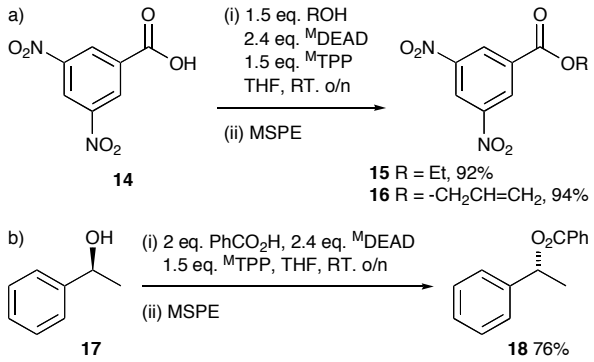
11: ^{1}H NMR (400 MHz, DMSO) δ: 4.31 (d, *J* = 5.8 Hz, 2H), 6.61 (t, *J* = 5.6 Hz, 1H), 6.90 (t, *J* = 7.3 Hz, 1H), 7.20-7.26 (m, 3H), 7.30-7.35 (m, 4H), 7.41 (d, *J* = 8.0 Hz, 2H), 8.56 (br s, 1H). Agrees with literature.[10]

12: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.77 (t, *J* = 7.4 Hz, 3H), 1.33-1.39 (m, 2H), 3.01-3.06 (m, 2H), 5.68 (t, *J* = 5.4 Hz, 1H), 6.89-6.93 (m, 1H), 7.12-7.20 (m, 4H), 7.51 (br s, 1H). Agrees with literature.[11]

13: ^{1}H NMR (400 MHz, DMSO) δ: 2.87 (t, *J* = 7.1 Hz, 2H), 3.39-3.44 (m, 2H), 6.13 (t, *J* = 5.7 Hz, 1H), 6.86-6.90 (m, 1H), 6.96-7.00 (m, 1H), 7.06-7.10 (m, 1H), 7.18-7.23 (m, 3H), 7.34-7.41 (m, 3H), 7.58 (d, *J* = 7.9 Hz, 1H), 8.48 (s, 1H), 10.84 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 25.62 (CH_2), 39.53 (CH_2), 111.35 (CH), 111.78 (C), 117.59 (CH), 118.22 (CH), 118.36 (CH), 120.90 (CH), 120.93 (CH), 122.73 (CH), 127.25 (C), 128.61 (CH), 136.31 (C), 140.61 (C), 155.23 (C); HRMS (ES+) 280.1439 (M + H^+, C17H18N3O requires 280.1450); IR (neat) ν: 3295, 1624, 1552, 1436, 1247, 739 cm^{-1}. Literature contains no data.[12]

[10] Gately, D. A.; Norton, J. R.; Goodson, P. A. *J. Am. Chem. Soc.* **1995**, *117*, 986-996.
[11] van Tilburg, E. W.; Windhorst, A. D.; Van der Mey, M.; Herscheid, J. D. M. *J. Label. Compd. Radiopharm*. **2006**, *49,* 321-330.
[12] Ho, B. T.; An, R.; Noel, M. B.; Tansey, L. W. *J. Med. Chem.* **1971**, *14*, 553-554.

General procedure for Mitsunobu reaction using ^{M}DEAD and ^{M}TPP.



Preparation of esters **15** and **16** from carboxylic acid **14** with alcohol in excess

^{M}DEAD (340 mg, 0.48 mmol) was added to a stirred solution of carboxylic acid **14** (43 mg, 0.20 mmol) in dry THF (1.3 mL) under argon and the mixture was stirred at RT for 20 min. A solution of ethanol or allyl alcohol (0.3 mmol) and ^{M}TPP (300 mg, 0.30 mmol) in THF (0.7 mL) was then added and the reaction was continued for 18 h. Solvent was removed under reduced pressure and the residue dissolved in ethyl acetate (1.5 mL). The resulting solution was filtered through a column of silica gel (7 g) eluting with ethyl acetate to give ester **15** or **16** in the yields shown above, following removal of solvent under reduced pressure.

15: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.48 (t, *J* = 7.1 Hz, 3H), 4.52 (q, *J* = 7.1 Hz, 2H), 9.16 (d, *J* = 2.1 Hz, 2H), 9.22 (d, J = 2.1Hz, 1H). Agrees with literature.[13]

16: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.95 (d, *J* = 6.0 Hz, 2H), 5.41 (dd, *J* = 0.9 and 10.4 Hz, 1H), 5.49 (dd, *J* = 1.1 and 17.2 Hz, 1H), 6.03-6.13 (m, 1H), 9.19 (d, *J* = 2.1 Hz, 2H), 9.24 (t, J = 2.1Hz, 1H). Agrees with literature.[14]

Preparation of ester **18** from alcohol **17** with carboxylic acid in excess

^{M}DEAD (340 mg, 0.48 mmol) was added to a stirred solution of benzoic acid (50 mg, 0.40 mmol), alcohol **17** (24 mg, 0.2 mmol), and ^{M}TPP (372 mg, 0.37 mmol) in dry THF (2 mL) at 0 °C under argon and the mixture was stirred at RT for 24 h. Solvent was removed under reduced pressure and the residue dissolved in ethyl acetate (1.5 mL). The resulting solution was filtered through a column of silica gel (7 g) using ethyl acetate, which resulted in a full separation of ester **18** and benzoic acid from the MPEG reagent. The crude product was dissolved in Et_2O (30 mL) and washed with a 1:1

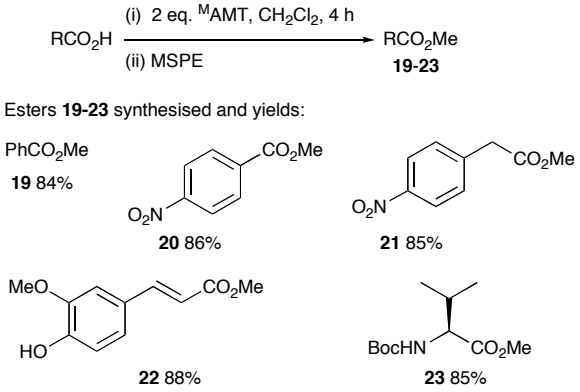
[13] Gallivan, J. P.; Schuster, G. B. *J. Org. Chem.* **1995**, *60,* 2423-2429.
[14] Dandapani, S.; Curran, D. P. *Tetrahedron,* **2002**, *58*, 3855-3864.

mixture of saturated aqueous sodium hydrogen carbonate and water (10 mL). Drying over $MgSO_4$ and removal of solvent under reduced pressure gave the ester **18** (33 mg, 76%).

18 ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.57 (d, J = 6.7 Hz, 3H), 6.03 (q, J = 6.7 Hz, 1H), 7.14-7.46 (m, 8H), 7.98 (d, J = 8.0 Hz, 2H); $[\alpha]_D$ −18. 2 (*c* 2, EtOH). Agrees with literature.[15]

[15] Kabuto, K.; Imuta, M.; Kempner, E. S. Ziffer, H. *J. Org. Chem.* **1978***, 43,* 23572361.

General procedure for the preparation of methyl esters using ^{M}AMT.



^{M}AMT (95% purity, 270 mg, 1.62 mmol g^{-1}, 0.41 mmol) in dry DCM (1 mL) was added to a stirred solution of the carboxylic acid (0.2 mmol) in dry DCM (3 mL) under argon and the mixture was stirred at 25 °C for 4 h. Solvent was removed under reduced pressure and the residue dissolved in ethyl acetate or DCM (1.5 mL). The resulting solution was filtered through a column of silica gel (3.5 g) eluting with ethyl acetate to give methyl esters **19**-**23** in the yields shown above, following removal of solvent under reduced pressure.

19: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.92 (s, 3H), 7.42-7.46 (m, 2H), 7.54-7.58 (m, 1H), 8.04 (d, *J* = 7.3 Hz 2H). Agrees with literature.[16]

20: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.98 (s, 3H), 8.21 (d, *J* = 9.0 Hz, 2H), 8.29 (d, *J* = 9.0 Hz, 2H). Agrees with literature.[17]

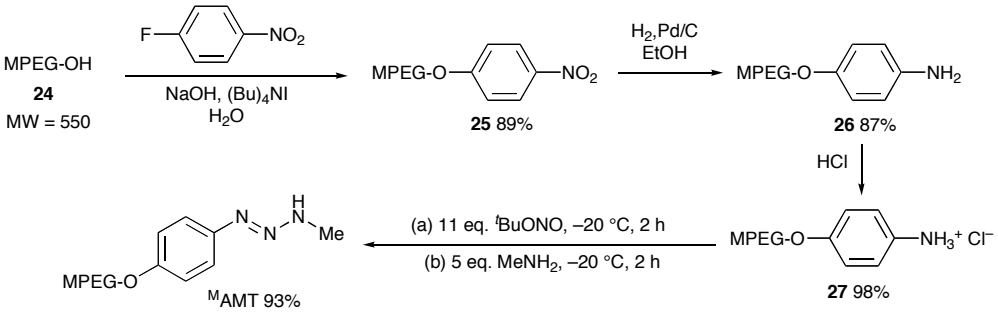
21: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.72 (s, 3H), 3.74 (s, 2H), 7.45 (d, *J* = 8.4 Hz, 2H), 8.19 (d, *J* = 8.4 Hz, 2H). Agrees with literature.[18]

22: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.79 (s, 3H), 3.91 (s, 3H), 6.00 (br s, 1H), 6.29 (d, *J* = 15.9 Hz, 1H), 6.91 (d, *J* = 8.2 Hz, 1H), 7.02 (s, 1H), 7.06 (d, *J* = 8.2 Hz, 1H), 7.62 (d, *J* = 15.9 Hz, 1H). Agrees with literature.[19]

23: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.87 (d, *J* = 6.9 Hz, 3H), 0.94 (d, *J* = 6.9 Hz, 3H), 1.43 (s, 9H), 2.05-2.15 (m, 1H), 3.72 (s, 3H), 4.19-4.23 (m, 1H), 5.02 (br d, *J* = 8.5 Hz, 1H). $[\alpha]_D$ +26.00 (*c* 1, $CHCl_3$). ^{1}H NMR data agree with literature.[20]

[16] Corio, P. L.; Dailey, B. P. *J. Am. Chem. Soc.* **1956**, *78*, 3043-3048.
[17] Maki, A. H.; Geske, D. H.; *J. Am. Chem. Soc*. **1961**, *83*, 1852-1853.
[18] Makosza, M.; Winiarski, J. *J. Org. Chem.* **1984**, *49*, 1494-1499.
[19] Tschesche, R.; Diederich, A.; Jha, H. C. *Phytochemistry* **1980**, *19*, 2783.

Preparation of ^{M}AMT



^{M}AMT was prepared as shown above.

4-(MPEGoxy)-nitrobenzene 25.

Adapting the procedure of Malkov *et al*,[21] a 28% aqueous solution of NaOH (3 mL) was slowly added dropwise to a mixture of *p*-fluoronitrobenzene (2.65 g, 18.8 mmol), MPEG-OH **24** (1.39 mL, 2.75 mmol), and tetrabutylammonium iodide (258 mg, 0.7 mmol) and the mixture was stirred at 45 °C for 28 h. After this time, water (40 mL) was added, and the mixture was extracted with CH_2Cl_2 (2 × 50 mL). The organic phase was dried over $MgSO_4$ and solvent removed under reduced pressure. The residue (~ 4.3 g) was dissolved in dichloromethane-ethyl acetate (1:1) and the resulting solution added to a column of silica gel (40 g) and eluted with the same solvent system to remove organic impurities. The eluent was then changed to a mixture of dichloromethane-methanol (30:1) to elute the product contaminated with the quaternary ammonium salt. Treatment with Et_2O (100 mL) induced precipitation of the quaternary ammonium salt, which was removed by filtration. Removal of solvent from the filtrate under reduced pressure gave the nitro compounds **25** as a yellow oil (1.63 g, 89%): R_f = 0.30 (CH_2Cl_2–MeOH, 30:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.35 (s, 3H), 3.50-3.71 (**MPEG**), 3.86 (t, J = 4.7 Hz, 2H, MPEG), 4.20 (t, J = 4.7 Hz, 2H, MPEG), 6.96 (d, J = 9.3 Hz, 2H), 8.16 (d, J = 9.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 58.92 (CH_3), 68.11 (CH_2), 69.26 (CH_2), 70.39 (CH_2), 70.44 (CH_2, **MPEG**), 70.51 (CH_2), 70.80 (CH_2), 71.80 (CH_2), 114.49 (CH), 125.74 (CH), 141.44 (C), 163.75 (C); MS (ESI+) *m/z* (%) for M + Na^+: 572 (30), 616 (70), 660 (100), 704 (100), 748 (80), 792 (50), 836 (20).; IR (neat) ν: 2870, 1593, 1514, 1452, 1340, 1263, 1109, 947, 850, 754 cm^{-1}.

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[20] Marcovici-Mizrahi, D.; Gottlieb, H. E.; Marks, V.; Nudelman A. *J. Org. Chem.* **1996**, *61,* 8402-8406.

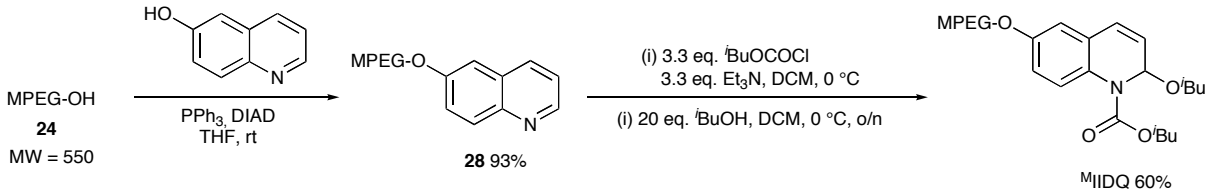
[21] Malkov, A. V.; Figlus, M.; Stoncius, S.; Kocovsky, P. *J. Org. Chem*. **2007**, *72*, 1315-1325.

4-(MPEGoxy)-aniline 26. Adapting the procedure of Ozeki *et al*,[22] a mixture of ether **25** (5.78 g, 8.61 mmol), and 10% palladium on activated carbon (500 mg, ~ 5 mol%) in absolute ethanol (75 ml) was stirred under a hydrogen atmosphere overnight. The mixture was filtered through Celite and Celite was additionally washed with MeOH (250 mL). Organic solutions were combined and the solvent removed under reduced pressure to afford aniline **24** (4.82 g, 87%) as an oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.37 (s, 3H), 3.45 (br s, 2H), 3.53-3.78 (**MPEG**), 3.80 (t, *J* = 4.8 Hz, 2H, MPEG), 4.04 (t, *J* = 4.8 Hz, 2H, MPEG), 6.62 (d, *J* = 8.7 Hz, 2H), 6.75 (d, *J* = 8.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 59.01 (CH_3), 69.85 (CH_2), 70.48 (CH_2), 70.52 (CH_2, **MPEG**), 70.57 (CH_2), 70.72 (CH_2), 71.88 (CH_2), 115.78 (CH), 116.40 (CH), 139.89 (C), 151.95 (C); MS (ESI+) *m/z* (%) for M + Na^+: 498 (23), 542 (65), 586 (92), 630 (100), 674 (83), 718 (71), 762 (46), 806 (18); IR (neat) ν: 2874, 1512, 1456, 1350, 1296, 1238, 1097, 908 cm^{-1}.

^{M}AMT. Aniline **26** (4.82 g, 7.52 mmol) was dissolved in THF (45 mL) and 1 M hydrochloric acid (45 mL) was added at RT. The resulting solution was stirred for 30 min, and the solvent removed under reduced pressure. The residue was dissolved in $CHCl_3$ (100 mL) and co-evaporated with toluene (150 mL) to afford the hydrochloride salt **27** as a purple oil (4.99 g, 98%). Adapting the procedure of Rademann *et al*,[23] *tert*-butyl nitrite (3.8 mL, 32 mmol) was slowly added (1 mL per 5 min) to a stirred solution of aniline salt **27** (2.09 g, 3.09 mmol) in dry THF (40 mL) under argon at –20 °C, and the resulting mixture was stirred at this temperature for 2 h. Methylamine (2 M solution in THF, 8 mL, 16 mmol) was then added and stirring at –20 °C continued for another 60 min. The purple solution was separated from insoluble impurities and the solvent removed under reduced pressure to afford **^{M}AMT** as a dark purple oil (95% purity by ^{1}H NMR spectroscopy, 2.01 g, 93%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.15 (br s, 3H), 3.34 (s, 3H), 3.42-3.88 (**MPEG**) 3.81 (t, *J* = 4.8 Hz, 2H MPEG), 4.09 (t, *J* = 4.8 Hz, 2H MPEG), 6.85 (d, *J* = 9.0 Hz, 2H), 7.31 (d, *J* = 9.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 31.11 (CH_3), 58.89 (CH_3), 67.52 (CH_2), 69.64 (CH_2), 70.35 (CH_2), 70.39 (CH_2, **MPEG**), 70.46 (CH_2), 70.66 (CH_2), 71.76 (CH_2), 114.74 (CH), 121.02 (br s, CH), 129.26 (C), 156.84; MS (ESI+) *m/z* (%) for M + Na^+: 540 (40), 584 (76), 628 (90), 672 (100), 716 (81), 760 (60), 804 (32), 848 (17); HRMS (ESI+) 694.4113 (M + H^+, n = 12, $C_{32}H_{60}N_3O_{13}$ requires 694.4126); IR (neat) ν: 2869, 1502, 1455, 1433, 1375, 1349, 1295, 1242, 1200, 1096, 947, 836 cm^{-1}. Loading = 1.62 mmol g^{-1} based on microanalysis: N, 6.81%.

[22] Ozeki, K.; Ichikawa, T.; Takehara, H.; Tanimura, K.; Sato, M.; Yaginuma, H. *Chem. Pharm. Bull*. **1989**, *37*, 1780-1787.
[23] Rademann, J.; Smerdka, J.; Jung, G.; Grosche, P.; Schmid, D. *Angew. Chem. Int. Ed*. **2001**, *40*, 381-385.

Preparation of ^{M}IIDQ



^{M}IIDQ was prepared as shown above.

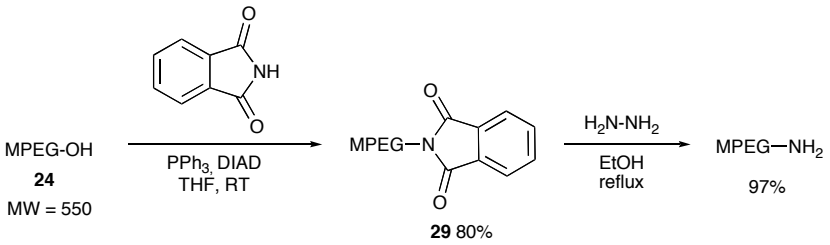
6-(MPEGoxy)-quinoline. Adapting the procedure of Malkov *et al*,[21] triphenylphosphine (3.92 g, 15.0 mmol), MPEG-OH **24** (6.02 mL, 11.9 mmol), and diisopropyl azodicarboxylate (2.96 mL, 15.0 mmol) were added consecutively to a stirred solution of 6-hydroxyquinoline (2.16 g, 14.9 mmol) in dry THF (28 mL) at 25 °C under argon. The resulting mixture was stirred at this temperature for 3h and the solvent was removed under reduced pressure. The residue (~ 15 g) was dissolved in dichloromethane-ethyl acetate (1:1) and the resulting solution added to a column of silica gel (100 g) and eluted with the same solvent system to remove organic impurities. The eluent was then changed to a mixture of dichloromethane-methanol (1:1) to give ether **28** (7.51 g, 93%) as a brown oil after evaporation of the solvent. R_f = 0.31 (CH_2Cl_2–MeOH, 30:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.31 (s, 3H), 3.47-3.71 (**MPEG**), 3.87 (t, J = 4.8 Hz, 2H MPEG), 4.19 (t, J = 4.8 Hz, 2H MPEG), 7.03 (d, J = 2.7 Hz, 1H), 7.27-7.30 (m, 1H), 7.34 (dd, J = 2.8 Hz, J = 9.2 Hz, 1H), 7.93 (d, J = 9.2 Hz, 1H), 7.98 (d, J = 8.4 Hz, 1H), 8.70 (dd, J = 1.7 Hz, J = 4.2, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 58.83 (CH_3), 67.48 (CH_2), 69.41 (CH_2), 70.29 (CH_2), 70.34 (CH_2, **MPEG**), 70.41 (CH_2), 70.67 (CH_2), 71.70 (CH_2), 105.79 (CH), 121.15 (CH), 122.35 (CH), 129.00 (C), 130.60 (CH), 134.61 (CH), 144.21 (C), 147.79 (CH), 156.66 (C); MS (ESI+) *m/z* (%) for M + Na^+: 534 (25), 578 (53), 622 (85), 666 (100), 710 (95), 754 (78), 798 (48), 842 (27), 886 (12); IR (neat) ν: 2868, 1622, 1597, 1500, 1456, 1379, 1350, 1325, 1228, 1099, 931, 835, 729 cm^{-1}.

^{M}IIDQ. Adapting the route of Valeur and Bradley,[24] *iso*-butyl chloroformate (0.60 mL, 4.62 mmol) was added to a stirred solution of ether **28** (0.95g, 1.40 mmol), and triethylamine (0.65 mL, 4.67 mmol) in dry DCM (12 mL) at 0 °C under argon, and the mixture was stirred at this temperature for 3 h. *Iso*-Butanol (2.65 mL, 29 mmol) was then added and stirring continued at 0 °C for another 18 h. The solvent was removed under reduced pressure and the residue treated with Et_2O (25 mL), and a solid removed by filtration. The filtrate was concentrated under reduced pressure (to ~ 2 mL) and added dropwise to hexane (50 mL). An orange oil separated out. Excess solvent was decanted off and the orange oil was washed with hexane (2 × 25 mL) to afford ^{M}IIDQ as a pale orange oil (0.72

[24] Valeur, E.; Bradley, M. *Chem. Commun*. **2005**, 1164-1166.

g, 60%): ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.73 (d, *J* = 6.7 Hz, 3H), 0.78 (d, *J* = 6.7 Hz, 3H), 0.94 (d, *J* = 6.7 Hz, 6H), 1.72 (nonet, *J* = 6.7 Hz, 1H), 1.91-2.03 (m, 1H), 3.28 (d, *J* = 6.7 Hz, 2H), 3.34 (s, 3H), 3.45-3.80 (**MPEG**), 3.81 (t, *J* = 4.9 Hz, 2H MPEG), 3.98-4.01 (m, 2H), 4.09 (t, *J* = 4.9 Hz, 2H MPEG), 6.04 (d, *J* = 5.4 Hz, 1H), 6.12 (dd, *J* = 5.4 Hz, *J* = 9.3 Hz, 1H), 6.63 (d, *J* = 9.4 Hz, 1H), 6.72 (d, *J* = 2.8 Hz, 1H), 6.81 (dd, *J* = 2.9 Hz, *J* = 8.9 Hz, 1H), 7.52 (d, *J* = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 19.09 (CH_3), 19.12 (CH_3), 19.22 (CH_3), 19.25 (CH_3), 27.76 (CH), 28.22 (CH), 58.90 (CH_3), 67.59 (CH_2), 69.91 (CH_2), 70.39 (CH_2), 70.46 (CH_2, **MPEG**), 70.51 (CH_2), 70.71 (CH_2), 71.82 (CH_2), 72.46 (CH_2), 73.66 (CH_2), 78.29 (CH), 111.63 (CH), 114.36 (CH), 124.33 (CH), 125.38 (CH), 126.62 (C), 127.20 (C), 127.48 (CH), 154.89 (C), 155.03 (C); MS (ESI+) *m/z* (%) for M + Na^+: 708 (36), 752 (78), 796 (100), 840 (96), 884 (89), 928 (64), 972 (36); HRMS (ESI+) 884.4985 (M + Na^+, n = 12, $C_{43}H_{75}NO_{16}Na$ requires 884.4984); IR (neat) ν: 2869, 1704, 1495, 1460, 1398, 1379, 1348, 1324, 1293, 1264, 1105, 1026, 944, 848, 765 cm^{-1}; Loading = 1.15 mmol g^{-1} based on microanalysis: N, 1.61%.

Preparation of MPEG-NH_2



MPEG-NH_2 was synthesized as shown above.

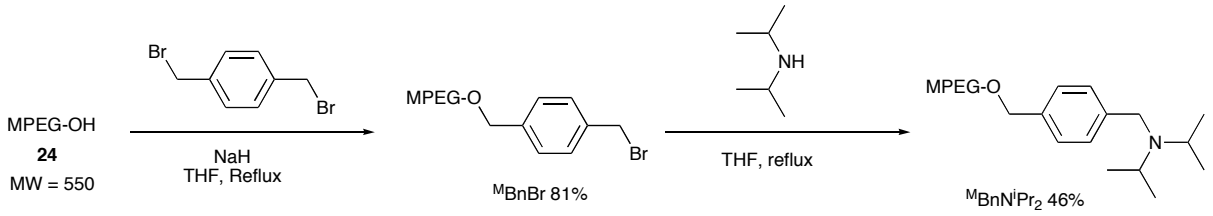
***N*-(MPEGoxy)-Phthalimide 29.** Adapting the procedure of Malkov *et al*,[21] triphenylphosphine (3.92 g, 15.0 mmol), MPEG-OH **24** (6.02 mL, 11.9 mmol), and diisopropyl azodicarboxylate (2.96 mL, 15.0 mmol) were added consecutively to a stirred solution of phthalimide (2.20 g, 15.0 mmol) in dry THF (28 mL) at 25 °C under argon. The resulting mixture was stirred at this temperature for 17 h and the solvent was removed under reduced pressure. The residue (~ 13.5 g) was dissolved in a mixture of dichloromethane and ethyl acetate (1:1) and the resulting solution filtered through a column of silica gel (100 g) to remove organic impurities. The column was washed next with a mixture of ethyl acetate and methanol (1:1) to elute product. After evaporation of the solvent, phthalimide **29** was obtained as a yellow oil (6.44 g, 80%): R_f = 0.37 (CH_2Cl_2–MeOH, 30:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.33 (s, 3H), 3.36-3.78 (**MPEG**), 3.69 (t, J = 5.8 Hz, 2H MPEG), 3.85 (t, J = 5.8 Hz, 2H MPEG), 7.66-7.70 (m, 2H), 7.79-7.81 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 37.07 (CH_2, CH_2-N of MPEG), 58.89 (CH_3), 67.73 (CH_2), 69.90 (CH_2), 70.41 (CH_2, **MPEG**), 71.77 (CH_2), 123.06 (CH), 131.96 (C), 133.76 (CH), 168.07 (C); MS (ESI+) *m/z* (%) for M + Na^+ 536 (35), 580 (75), 624 (100), 668 (99), 712 (81), 756 (59), 800 (34), 844 (18), 888 (7); IR (neat) ν: 2874, 1712, 1469, 1394, 1350, 1247, 1097 cm^{-1}.

MPEG-NH_2. Hydrazine (19 mL, 0.39 mol) was slowly added to a solution of phthalimide **29** (13.00 g, 19.1 mmol) in ethanol (200 mL), and the mixture was stirred at 90 °C for 3.5 h. The solvent was removed under reduced pressure and the residue extracted with DCM (3 × 100 mL). The DCM extracts were filtered and combined, and solvent was removed under reduced pressure. The resulting residue was dissolved in chloroform-toluene (1:1, 200 mL) and the solvent was removed under reduced pressure to afford amine MPEG-NH_2 as a pale brown oil (10.2 g, 97%); R_f = 0.14 (MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.72 (br s, 2H), 2.86 (t, J = 5.2 Hz, 2H), 3.37 (s, 3H), 3.44-3.82 (**MPEG**); ^{13}C NMR (100 Hz, $CDCl_3$) δ: 41.59 (CH_2, CH_2-N of MPEG), 58.87 (CH_3), 70.11 (CH_2), 70.34 (CH_2), 70.39 (CH_2, **MPEG**), 71.75 (CH_2), 73.20 (CH_2); MS (ESI+) *m/z* (%) for M + Na^+: 450 (29), 494 (62), 538 (95), 582 (100), 626 (97), 670 (71), 714 (46), 758 (24),

802 (10); HRMS (ESI+) 560.3646 ($M + H^+$, n = 12, $C_{25}H_{54}NO_{12}$ requires 560.3646); IR (neat) ν: 2872, 1456, 1350, 1300, 1247, 1101 cm^{-1}; Loading = 1.72 mmol g^{-1} based on microanalysis: N, 2.41%. ^1H NMR data agree with literature.[25]

[25] Jiang, L.; Chan, T. H. *Can. J. Chem.* **2005**, *83*, 693-701.

Preparation of ^{M}BnBr and ^{M}BnN^{i}Pr$_2$



^{M}BnBr and ^{M}BnN^{i}Pr$_2$ were prepared as shown above.

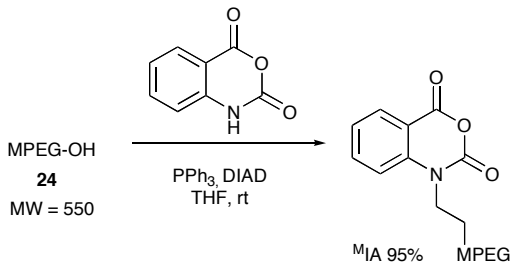
^{M}BnBr. Adapting the procedure of Chiu and Stoddart,[26] MPEG-OH **24** (0.92 mL, 1.82 mmol) was added dropwise (over 20 min) to a stirred suspension of α,α'-dibromo-*p*-xylene (2.40 g, 9.09 mmol), and sodium hydride (110 mg, 2.75 mmol, 60% suspension in mineral oil) in dry THF (10 mL) under argon and the mixture was stirred at RT overnight. The solvent was removed under reduced pressure and the mixture dispersed in ethyl acetate (50 mL). The resulting suspension was filtered (gravitational filtration using paper filter) and the solvent removed under reduced pressure. The residue (~ 3.3 g) was dissolved in ethyl acetate and the resulting solution added to a column of silica gel (40 g) and eluted with the same solvent to remove organic impurities. The eluent was then changed to a mixture of ethyl acetate-methanol (1:1) to give the ^{M}BnBr was obtained as a yellow oil (1.07 g, 81%) following removal of solvent under reduced pressure: R_f = 0.42 (CH_2Cl_2–MeOH, 20:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.35 (s, 3H), 3.42-3.80 (**MPEG**), 4.46 (s, 2H), 4.52 (s, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 33.24 (CH_2), 58.92 (CH_3), 69.46 (CH_2), 70.39 (CH_2), 70.45 (CH_2, **MPEG**), 70.51 (CH_2), 71.81 (CH_2), 72.63 (CH_2), 127.91 (CH), 128.97 (CH), 136.94 (C), 138.60 (C); MS (ESI+) *m/z* (%) for M(^{81}Br) + Na^+: 635 (83), 679 (100), 723 (75), 767 (58), 811 (33); IR (neat) ν: 2866, 1456, 1350, 1296, 1247, 1097, cm^{-1}.

^{M}BnN^{i}Pr$_2$. ^{M}BnBr (1.05 g, 1.43 mmol) was added to a stirred solution of diisopropylamine (2 mL, 14.3 mmol) in dry THF (10 mL) under argon, and the mixture was heated under reflux for 24 h. The mixture was quenched with saturated aqueous $NaHCO_3$ (5 mL), some of the solvent was removed under reduced pressure and the residue was extracted with DCM (5 × 20 mL). The combined organic extracts were dried over $MgSO_4$ and the solvent removed under reduced pressure. Chromatography on silica gel (50 g), eluting first with DCM-MeOH (50:1) to remove impurities and then changing to DCM-MeOH (10:1) to elute the product, gave ^{M}BnN^{i}Pr$_2$ as a yellow oil (0.50 g, 46%) after evaporation of solvent; R_f = 0.15 (CH_2Cl_2–MeOH, 20:1); ^{1}H NMR (400 MHz, $CDCl_3$)

[26] Chiu, S. H.; Stoddart, J. F. *J. Am. Chem. Soc*. **2002**, *124*, 4174-4175.

δ: 1.00 (d, J = 6.5 Hz, 12H), 2.99 (hept, J = 6.5 Hz, 2H), 3.37 (s, 3H), 3.44-3.82 (**MPEG** + CH_2N), 4.52 (s, 2H), 7.24 (d, *J* = 7.7 Hz, 2H), 7.33 (d, *J* = 7.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.71 (CH_3), 47.65 (CH), 48.60 (CH_2), 59.00 (CH_3), 69.26 (CH_2), 70.46 (CH_2), 70.50 (CH_2, **MPEG**), 70.60 (CH_2), 71.88 (CH_2), 73.18 (CH_2), 127.57 (CH), 127.80 (CH), 135.94 (C), 142.70 (C); MS (ESI+) *m/z* (%) for $M + H^+$: 632 (13), 676 (32), 720 (53), 764 (77), 808 (100), 852 (68), 896 (27), 940 (10); HRMS (ESI+) 764.5153 ($M + H^+$, n = 12, $C_{39}H_{74}NO_{13}$ requires 764.5160); IR (neat) ν: 2865, 1462, 1361, 1299, 1248, 1097, 945, 849 cm^{-1}; Loading = 1.15 mmol g^{-1} based on microanalysis: N, 1.61%.

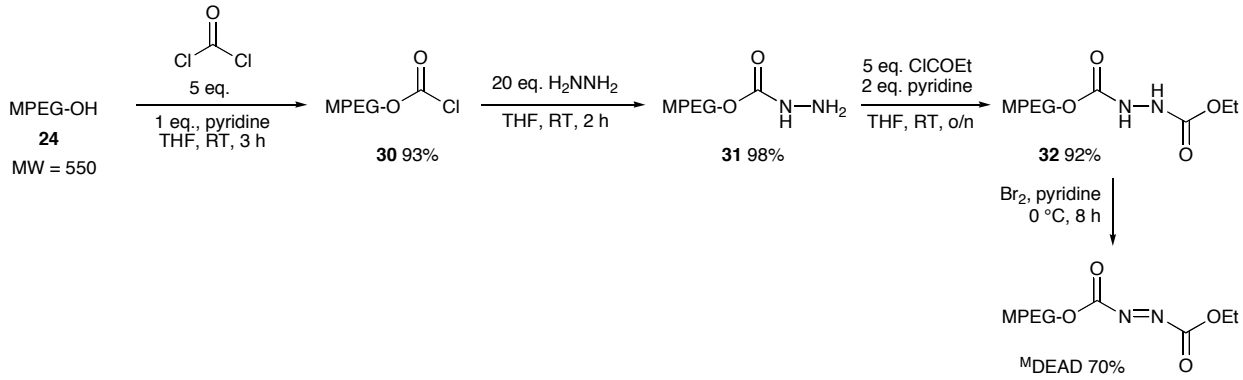
Preparation of ^{M}IA



^{M}IA was prepared in one step as shown above.

^{M}IA. Adapting the procedure of Malkov *et al*,[21] triphenylphosphine (0.98 g, 3.74 mmol), MPEG-OH **24** (1.51 mL, 2.98 mmol), and diisopropyl azodicarboxylate (0.74 mL, 3.75 mmol) were added consecutively to a stirred solution of isatoic anhydride (0.61 g, 3.74 mmol) in dry THF (7 mL) at 25 °C under argon. The resulting mixture was stirred at this temperature for 18 h and the solvent was removed under reduced pressure. The residue (~ 4 g) was dissolved in DCM-ethyl acetate (1:1) and the resulting solution added to a column of silica gel (30 g) and eluted with the same solvent system to remove organic impurities. The eluent was then changed to a mixture of DCM-methanol (1:1) to give ^{M}IA as a yellow oil (1.96 g, 95%) after removal of solvent under reduced pressure; R_f = 0.39 (CH_2Cl_2–MeOH, 30:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.34 (s, 3H), 3.39-3.77 (**MPEG**), 3.82 (t, *J* = 5.6 Hz, 2H MPEG), 4.24 (t, *J* = 5.6 Hz, 2H MPEG), 7.23-7.27 (m, 1H), 7.40 (d, *J* = 8.5 Hz, 1H), 7.68-7.73 (m, 1H), 8.09 (dd, *J* = 1.6 Hz, *J* = 7.8 Hz, 1H); ^{13}C NMR (100 Hz, $CDCl_3$) δ: 44.79 (CH_2, CH_2-N of MPEG), 58.90 (CH_3), 67.92 (CH_2), 70.40 (CH_2, **MPEG**), 70.44 (CH_2), 70.63 (CH_2), 71.75 (CH_2), 111.38 (C), 115.03 (CH), 123.83 (CH), 130.32 (CH), 136.87 (CH), 141.85 (C), 147.78 (C), 158.36 (C); MS (ESI+) *m/z* (%) for M + Na^+: 552 (28), 596 (61), 640 (100), 684 (98), 728 (92), 772 (64), 816 (45), 860 (28), 904 (13); HRMS (ESI+): 706.3644 (M + H^+ , n = 12, $C_{33}H_{56}NO_{15}$ requires 706.3649); IR (neat) ν: 2866, 1780, 1728, 1606, 1477, 1375, 1323, 1251, 1099, 1030 cm^{-1}; Loading = 1.74 mmol g^{-1} based on microanalysis: N, 2.43%.

Preparation of ^{M}DEAD



^{M}DEAD was prepared as shown above.

MPEGyl chloroformate 30. Adapting the procedure of Brimble and Lee,[27] MPEG-OH **24** (2.76 mL, 5.45 mmol), and dry pyridine (0.45 mL, 5.61 mmol) were added simultaneously (slow addition, 1 mL per 5 min) to a stirred solution of phosgene (20% solution in toluene, 14.4 mL, 27.4 mmol) in dry THF (15 mL) at RT, and the mixture was stirred for 3.5 h. Solvent was removed under reduced pressure and the product was extracted from the residue with diethyl ether (2 × 120 mL). The ethereal extracts were combined and filtered. Removal of the solvent from the filtrate under reduced pressure afforded the chloroformate **30** as an oil (3.09 g, 93%): ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.33 (s, 3H), 3.49-3.74 (**MPEG**), 4.40-4.42 (m, 2H MPEG); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 58.88 (CH_3), 68.12 (CH_2), 70.38 (CH_2), 70.44 (CH_2, **MPEG**), 70.53 (CH_2), 70.64 (CH_2), 71.80 (CH_2), 150.59 (CO); MS (ESI+) *m/z* (%) for M + Na^+: 469 (11), 513 (30), 557 (59), 601 (100), 645 (77), 689 (86), 733 (57), 777 (39), 822 (17), 866 (11); IR (neat) ν: 2867, 1775, 1447, 1349, 1297, 1247, 1099 cm^{-1}.

***N*-(MPEGoxycarbonyl)hydrazine 31.** Adapting the procedure of Brimble and Lee,[27] MPEGyl chloroformate **30** (0.63 g, 1.03 mmol) was slowly added to a solution of hydrazine hydrate (1 mL, 20.6 mmol) in dry THF (5 mL) at RT under argon, and the mixture was stirred for 2 h. The solvent was removed under reduced pressure, and the product extracted from the residue with toluene (2 × 40 mL). The organic extracts were combined and filtered. Removal of the solvent from the filtrate under reduced pressure gave the carbamate **31** as an oil (0.62 g, 98%); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.35 (s, 3H), 3.43-3.80 (**MPEG**), 4.23-4.25 (m, 2H MPEG), 6.26 (s br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 58.84 (CH_3), 64.30 (CH_2), 69.26 (CH_2), 70.33 (CH_2), 70.40 (CH_2, **MPEG**), 71.76 (CH_2), 158.47 (C); MS (ESI+) *m/z* (%) for M + Na^+: 465 (22), 509 (49), 553 (82), 597 (100), 641 (91), 685 (77), 729 (39), 773 (22) 817 (13); IR (neat) ν: 2852, 1715, 1349, 1252, 1097, 904 cm^{-1}.

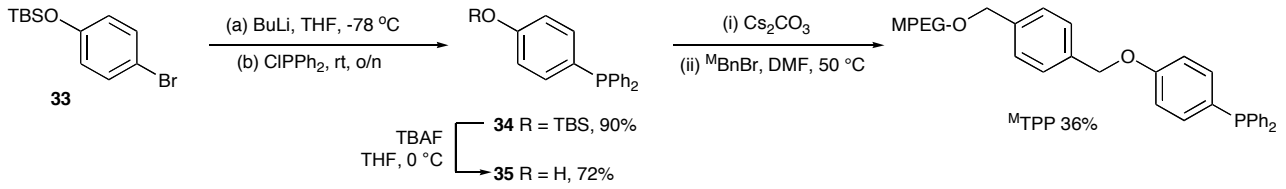
[27] Brimble, M. A.; Lee, C. K. Y. *Tetrahedron: Asymmetry* **1998**, *9*, 873-884.

***N*-(Ethoxycarbonyl)-*N′*-(MPEGoxycarbonyl)hydrazine 32.** Adapting the procedure of Brimble and Lee, ethyl chloroformate (2.1 mL, 21.96 mmol) was added to a stirred solution of MPEG-derivative **31** (2.69 g, 4.42 mmol) and pyridine (0.71 mL, 8.86 mmol) in THF (35 mL) at 25 °C, and the mixture was stirred at this temperature for 15 h. Solvent was removed under reduced pressure. The residue was twice dissolved in DCM-toluene (1:1, 60 mL) and the solvent removed under reduced pressure. The product was extracted from the resulting residue with diethyl ether (3 × 100 mL). The ethereal extracts were combined and filtered. Removal of the solvent from the filtrate under reduced pressure afforded the *bis*(carbamate) **32** as a yellow oil (2.75 g, 92%); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.23 (t, *J* = 7.1 Hz, 3H), 3.34 (s, 3H), 3.42-3.80 (**MPEG**), 4.15 (q, *J* = 7.1 Hz, 2H), 4.24-4.26 (m, 2H MPEG), 7.06 (s br, 1H), 7.28 (s br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.42 (CH_3), 58.91 (CH_3), 61.71 (CH_2), 64.72 (CH_2), 69.09 (CH_2), 70.34 (CH_2), 70.40 (CH_2), 70.46 (CH_2, **MPEG**), 70.54 (CH_2), 71.82 (CH_2), 156.60 (C); MS (ESI+) *m/z* (%) for M + Na^+: 537 (42), 581 (85), 625 (82), 669 (100), 713 (83), 757 (44), 801 (22), 845 (16), 889 (9); IR (neat) ν: 2868, 1729, 1348, 1218, 1097, 948 cm^{-1}.

^{M}DEAD. Adapting the procedure of Starr *et al.*,[28] a solution of bromine (115 μL, 2.24 mmol) in DCM (3 mL) was slowly added to a solution of *bis*(carbamate) **32** (2.00 g, 2.94 mmol) and dry pyridine (0.72 mL, 8.98 mmol) in dry DCM (17 mL) at 0 °C under argon, and the mixture was stirred at this temperature for 5 h. Another portion of bromine (37 μL, 0.72 mmol) was added and stirring was continued for 3 h. Solvent was removed under reduced pressure and the product was extracted from the resulting residue with diethyl ether (3 × 50 mL). The ethereal extracts were combined and filtered. Removal of the solvent from the filtrate under reduced pressure afforded the ^{M}DEAD as a yellow oil (1.42 g, 70%, 95% purity by ^{1}H NMR spectroscopy); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.41 (t, *J* = 7.1 Hz, 3H), 3.34 (s, 3H), 3.42-3.86 (**MPEG**), 4.48 (q, *J* = 7.1 Hz, 2H), 4.54-4.56 (m, 2H MPEG); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.94 (CH_3), 58.89 (CH_3), 65.36 (CH_2), 68.04 (CH_2), 68.32 (CH_2), 70.39 (CH_2), 70.44 (CH_2, **MPEG**), 70.52 (CH_2), 70.66 (CH_2), 71.81 (CH_2), 160.15 (C); MS (ESI+) *m/z* (%) for M + Na^+: 535 (34), 579 (72), 623 (100), 667 (95), 711 (85), 755 (42), 799 (23), 843 (11); HRMS (ESI+) 689.3693 (M + H^+ , n = 12, $C_{29}H_{57}N_2O_{16}$ requires 689.3708); IR (neat) ν: 2863, 1777, 1451, 1349, 1226, 1097, 1019, 947, 853 cm^{-1}; Loading = 1.40 mmol g^{-1} based on microanalysis: N, 3.91%.

[28] Starr, J. T.; Rai, G. S.; Dang, H.; McNelis, B. J. *Synth. Commun*. **1997**, *27*, 3197-3200.

Preparation of ^{M}TPP



^{M}TPP was prepared as shown above.

4-(*tert*-Butyldimethylsiloxy)phenyldiphenylphosphine 34. Following the procedure of Sieber *et al.*,[29] but conducting the reaction at a lower temperature, n-butyllithium (15 mL, 1.6 M in hexane, 24 mmol) was slowly added to a solution of 1-bromo-4-(*tert*-butyldimethylsiloxy)benzene **33** (6 g, 21 mmol) in dry THF at –78 °C under argon and the mixture was stirred for 10 min, followed by the addition of chlorodiphenylphosphine (4.8 mL, 26 mmol). The mixture was stirred at –78 °C for 2 h and then at RT overnight. Methanol (1 mL) was slowly added and the solvent removed under reduced pressure to afford a crude mixture. Chromatography on silica gel (200 g) eluting with petroleum ether-diethyl ether (20:1) gave the triarylphosphine **34** (7.40 g, 90%) as a solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.21 (s, 6H), 0.99 (s, 9H), 6.83 (d, J = 7.6 Hz, 2H), 7.20 (t, J = 7.5 Hz, 2H), 7.27-7.34 (m, 10H). Agrees with literature.[29]

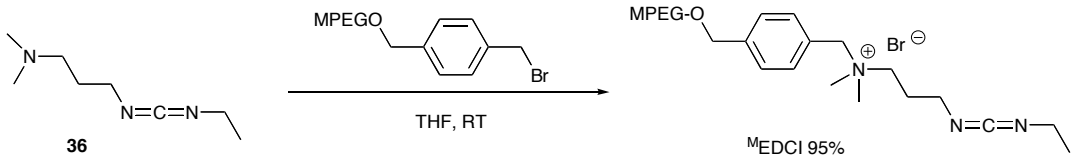
(4-Hydroxyphenyl)diphenylphosphine 35. Tetrabutylammonium fluoride in THF (1 M, 39 mmol) was added to a solution of triarylphosphine **34** (7.4 g, 18.9 mmol) in dryTHF (35 mL) at 0 °C and the mixture was then stirred at RT overnight. The solvent was evaporated to 70% of its original volume and the mixture added to a saturated aqueous solution of ammonium chloride (200 mL). The resulting solution was extracted with Et_2O (2 × 400 mL) and the combined organics concentrated to a volume of approximately 300 mL. The resulting solution was washed with brine (2 × 150 mL), dried over $MgSO_4$ and the solvent was removed under reduced pressure. Chromatography on silica gel (300 g) eluting with petroleum ether-diethyl ether (8:1 to 4:1) gave the phenol **35** as a solid (3.9 g, 72%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.21 (s, 6H), 0.99 (s, 9H), 6.83 (d, J = 7.6 Hz, 2H), 7.20 (t, J = 7.5 Hz, 2H), 7.27-7.34 (m, 10H). Agrees with literature.[29]

^{M}TPP. Adapting the procedure of Sieber *et al.*,[29] cesium carbonate (2.25 g, 6.9 mmol) was added to a stirred solution of phenol **35** (1.5 g, 5.40 mmol) in dry DMF (15 mL) (degassed 3 times by freezing under argon with liquid nitrogen and thawing under reduced pressure) under argon and the

[29] Sieber, F.; Wentworth, P.; Toker, J. D.; Wentworth, A. D.; Metz, W. A.; Reed, N. N.; Janda, K. D. *J. Org. Chem.* **1999**, *64,* 5188-5192.

mixture was stirred at 50 °C for 40 min. ^{M}BnBr (3.10 g, 4.2 mmol) was added in two portions 30 min apart. The resulting mixture was stirred at 50 °C for 17 h and then solvent was removed under reduced pressure. The residue was treated with DCM (200 mL), filtered to remove solid, and the solvent removed from the filtrate under reduced pressure. Chromatography on silica gel (120 g) eluting first with ethyl acetate to remove all unPEGylated impurities, and then with dichloromethane-methanol (30:1) gave ^{M}TPP contaminated with DMF, following removal of solvent. The residue (2.31 g) was dissolved in DCM (5 ml) and added to vigorously-stirred hexane (900 mL). ^{M}TPP separated from the hexane solution as a pale yellow oil (1.42 g, 36%); R_f = 0.23 (CH_2Cl_2–MeOH, 30:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.37 (s, 3H), 3.45-3.84 (**MPEG**), 4.57 (s, 2H), 5.04 (s, 2H), 6.95 (d, *J* = 7.9 Hz, 2H), 7.27-7.40 (m, 16H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 59.00 (CH_3), 69.47 (CH_2), 69.69 (CH_2), 70.48 (CH_2), 70.54 (CH_2, **MPEG**), 70.61 (CH_2), 71.90 (CH_2), 72.87 (CH_2), 115.04 (d, *J* = 8.1 Hz, CH), 127.52 (CH), 127.91 (CH), 128.37 (d, *J* = 6.8 Hz, CH), 128.44 (CH), 132.00 (d, *J* = 9.9 Hz, C), 133.82 (d, *J* = 19.2 Hz, CH), 135.54 (d, *J* = 21.3 Hz, CH), 136.01 (C), 137.78 (d, *J* = 10.7 Hz, C), 138.19 (C), 159.52 (C); ^{31}P NMR (162 MHz, $CDCl_3$) δ: –6.84; MS (ESI+) *m/z* (%) for M + Na^+: 787 (50), 831 (84), 875 (99), 919 (100), 963 (72); HRMS (ESI+) 941.4817 (M + H^+ , n = 12, $C_{51}H_{47}O_{14}P$ requires 941.4816); IR (neat) ν: 2866, 1593, 1567, 1496, 1435, 1349, 1284, 1243, 1094, 1027, 946, 827, 728, 698 cm^{-1}; Loading = 1.00 mmol g^{-1} based on microanalysis: P, 3.21%.

Preparation of ^{M}EDCI



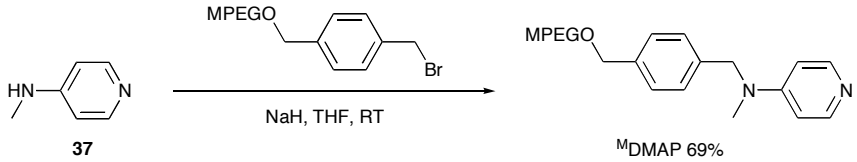
36 ^{M}EDCI 95%

^{M}EDCI was prepared in one step as shown above.

^{M}EDCI. Adapting the method of Jászay *et al.*,[30] ^{M}BnBr (2.1 g, 2.87 mmol) was added to a stirred solution of 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide **36** (2 mL, 11.4 mmol) in dry THF (20 mL) under argon and the mixture was stirred at RT for 16 h. The solvent was removed under reduced pressure, and the residue dissolved in DCM (6 mL). The resulting solution was added slowly to vigorously stirred hexane (700 mL). The mixture was left to stand for 5 min, and the solution decanted away from a dense yellow oil, which was dried under reduced pressure to afford ^{M}EDCI (2.40 g, 95%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.19 (t, *J* = 7.2 Hz, 3H), 2.00-2.11 (m, 2H), 3.22 (q, *J* = 7.2, 2H), 3.30 (s, 6H), 3.34 (s, 3H), 3.40-3.79 (**MPEG** + 2 × CH_2), 4.56 (s, 2H), 4.99 (s, 2H), 7.40 (d, *J* = 8.1 Hz, 2H), 7.62 (d, *J* = 8.1 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 16.65 (CH_3), 24.62 (CH_2), 41.22 (CH_2), 43.37 (CH_2), 49.93 (CH_3), 58.93 (CH_3), 61.51 (CH_2), 67.21 (CH_2), 69.94 (CH_2), 70.41 (CH_2), 70.46 (CH_2, **MPEG**), 70.55 (CH_2), 71.82 (CH_2), 72.36 (CH_2), 126.03 (C), 128.09 (CH), 133.16 (CH), 139.15 (C), 141.43 (C); MS (ESI+) *m/z* (%), M^+ of tetralkylammonium cations: 554 (8), 598 (25), 642 (55), 686 (82), 730 (100), 774 (98), 818 (82), 862 (55), 906 (33); HRMS (ESI+): 818.5385 (M^+ , n = 12, $C_{41}H_{76}N_3NO_{13}$ requires 818.5378); IR (neat) ν: 2870, 2125, 1452, 1348, 1059, 922 cm^{-1}. Loading = 1.07 mmol g^{-1} based on microanalysis: N, 4.48%.

[30] Jászay, Z. M.; Petneházy, I.; Töke, L.; Szajáni, B. *Synthesis*, **1988**, 397-399.

Preparation of ^{M}DMAP



^{M}DMAP. Adapting the route of Feng *et al.*,[31] 4-(methylamino)pyridine **37** (369 mg, 3.42 mmol) in dry THF (4 mL) was added to a stirred suspension of NaH [60% in mineral oil, 150 mg, 3.74 mmol, washed twice with hexane (10 mL) prior to the use] in dry THF (4 mL) at 0 °C under argon and the mixture was stirred at RT for 3.5 h. The mixture was cooled to 0 °C and ^{M}BnBr (0.5 g, 0.68 mmol) in THF (1 mL) was slowly added (0.5 mL per 5 min). Stirring at RT was continued for 12 h followed by the addition of methanol (2 mL) and evaporation of the solvent. Chromatography on silica gel (50 g) eluting with DCM-MeOH (10:1) afforded ^{M}DMAP as a pale brown oil (308 mg, 60%): R_f = 0.42 (CH_2Cl_2–MeOH, 20:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.04 (s, 3H), 3.34 (s, 3H), 3.39-3.79 (**MPEG**), 4.50 (s, 2H), 4.54 (s, 2H), 6.51 (d, *J* = 6.6 Hz, 2H), 7.10 (d, *J* = 8.1 Hz, 2H), 7.27 (d, *J* = 8.1 Hz, 2H); 8.17 (d, *J* = 6.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 37.72 (CH_3), 54.69 (CH_2), 58.91 (CH_3), 69.41 (CH_2), 70.38 (CH_2), 70.43 (CH_2, **MPEG**), 70.50 (CH_2), 71.79 (CH_2), 72.75 (CH_2), 106.74 (CH), 126.32 (CH), 128.15 (CH), 136.23 (C), 137.42 (C), 149.30 (CH), 153.86 (C); MS (ESI) *m/z* (%) for M + Na^+: 528 (18), 573 (24), 617 (53), 661 (90), 705 (100), 749 (93), 793 (81), 837 (57), 881 (35), 925 (16); HRMS (ESI+) for 771.4673 (M + H^+ , n = 12, $C_{39}H_{67}N_2O_{13}$ requires 771.4643); IR (neat) ν: 2866, 1597, 1516, 1454, 1388, 1348, 1298, 1095, 985, 931, 802 cm^{-1}. Loading = 1.22 mmol g^{-1} based on microanalysis: N, 3.42%.

[31] Feng, A. S.; Speer, D. V.; DiMagno, S. G.; Konings, M. S. Streitwieser, A. *J. Org. Chem.* **1992**, *57*, 2902-2909.