Reactive trityl derivatives: stabilised carbocation mass-tags for life sciences applications

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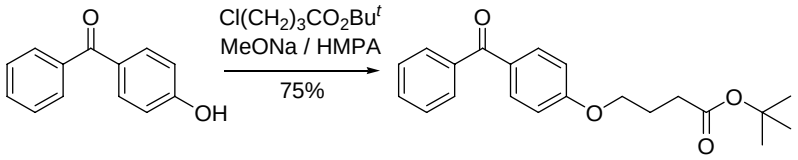
Supporting Information

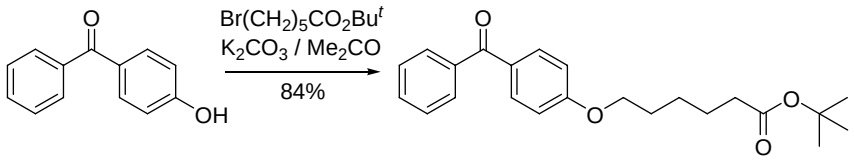
Experimental Section

Instrumentation. 500 MHz ^{1}H and 125.7 MHz ^{13}C NMR spectra were recorded on a Bruker DRX-500 spectrometer and referenced to $CDCl_3$ (7.25 ppm) and DMSO-d_6 (2.50 ppm). ^{1}H–^{13}C gradient-selected HMQC and HMBC spectra were obtained by using 2048 (t_2)×256 (t_1) complex point data sets, zero filled to 2048 (F_2)×1024 (F_1) points. The spectral widths were 13 ppm and 200 ppm for ^{1}H and ^{13}C dimensions, respectively. HMBC spectra were measured with 50 ms delay for evolution of long-range couplings. (MA)LDI-TOF mass spectra were obtained using a Voyager Elite Biospectrometry Research Station (PerSeptive Biosystems, Vestec Mass Spectrometry Products) in a positive ion mode. EI-TOF HRMS and ESI-TOF HRMS spectra in positive ion mode were obtained using Micromass LCT reflection TOF mass spectrometer. Analytical thin-layer chromatography was performed on the Kieselgel 60 F_{254} precoated aluminium plates (Merck), spots were visualised under UV light (254 nm). Column chromatography was performed on silica gel (Merck Kieselgel 60 0.040–0.063 mm).

Reagents and solvents. Reagents obtained from commercial suppliers were used as received. 4-Hydroxy-4′-methoxybenzophenone (**3**),[1] $Pd(PPh_3)_4$,[2] *tert*-butyl 6-bromohexanoate,[3] were prepared as described. Solvents were mainly HPLC grade and used without further purification unless otherwise noted. DCM was always used freshly distilled over CaH_2. THF was distilled over powdered $LiAlH_4$ or over sodium benzophenone ketyl and stored over 4Å molecular sieves under nitrogen. DMF was freshly distilled under reduced pressure.

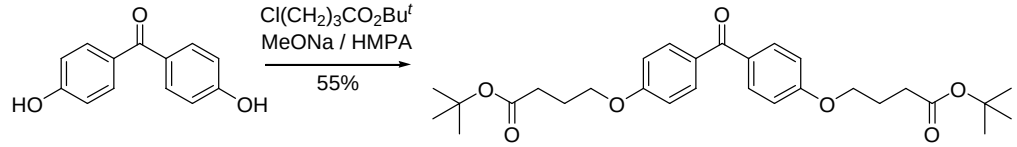


4-[3-(*tert*-Butyloxycarbonyl)propoxy]benzophenone (4a). A solution of sodium methoxide prepared from sodium (0.46 g, 20 mmol) and MeOH (50 mL), was added to the solution of 4-hydroxybenzophenone (3.96 g, 20 mmol) in MeOH (100 mL). The mixture was evaporated to dryness, coevaporated with *tert*-butanol (2×40 mL), the residue was dissolved in HMPA (30 mL) and *tert*-butyl 4-chlorobutyrate (4.0 g, 22 mmol) was added in one portion. The mixture was heated at 100ºC for 5 h, then cooled, diluted with water (300 mL) and extracted with EtOAc (2×200 mL). The combined organic layers were washed with water (5×100 mL), dried over Na_2SO_4, and evaporated. The residue was chromatographed on silica gel in 1→4% EtOAc in toluene to give the desired compound as white crystalline solid, mp 72ºC (EtOAc–hexane). Yield 5.10 g (75%). ESI-TOF HRMS: *m/z* = 341.1752 $[M+H]^+$, calc. for $[C_{21}H_{25}O_4]^+$ 341.1747. NMR (DMSO-d_6): 7.73 (d, 2H, *J* = 8.9 Hz, Ar*H*); 7.70–7.62 (m, 3H, Ar*H*); 7.54 (m, 2H, Ar*H*); 7.07 (d, 2H, *J* = 8.9 Hz, Ar*H*); 4.09 (t, 2H, *J* = 6.4 Hz, OCH_2); 2.38 (t, 2H, *J* = 7.3 Hz, COCH_2); 1.97 (m, 2H, $CH_2CH_2CH_2$); 1.40 (s, 9H, CH_3).

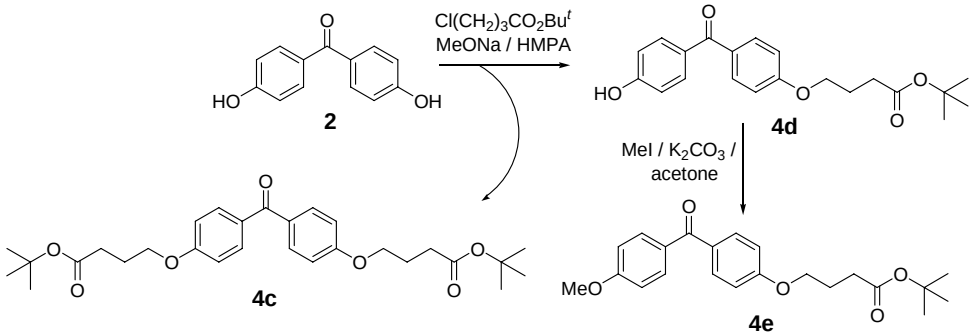


4-[5-(*tert*-Butyloxycarbonyl)pentyloxy]benzophenone (4b). To a solution of 4-hydroxybenzophenone (1.98 g, 10.0 mmol) in in dry acetone (80 mL) dry K_2CO_3 (14 g, 0.1 mol) and *tert*-butyl 6-bromohexanoate[4] (3.76 g, 15 mmol) were added, and the mixture was stirred for 48 h at ambient temperature, then filtered, and the solid was washed with acetone. The combined filtrate was evaporated, and the residue was dissolved in $CHCl_3$ (100 mL), filtered, and evaporated. The residue was chromatographed on silica gel in 0→6% EtOAc in toluene to give desired product (3.10 g, 84%) as a colourless oil. ESI-TOF HRMS: *m/z* = 369.2051 $[M+H]^+$, calc. for $[C_{23}H_{29}O_4]^+$ 369.2060. NMR (DMSO-d_6): 7.73 (d, 2H, *J* = 8.7 Hz, Ar*H*); 7.70–7.62 (m, 3H, Ar*H*); 7.54 (t, 2H, *J* = 7.6 Hz, Ar*H*); 7.06 (d, 2H, *J* = 8.7 Hz, Ar*H*); 4.07 (t, 2H, *J* =

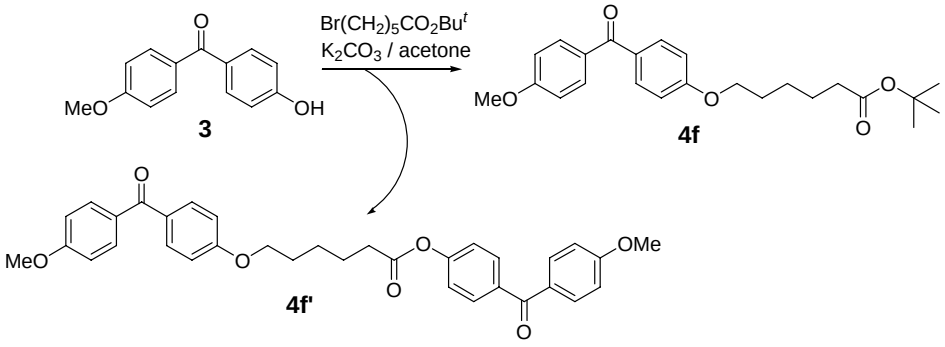
6.4 Hz, OCH_2); 2.21 (t, 2H, J = 7.4 Hz, COCH_2); 1.74 (m, 2H), 1.56 (m, 2H), 1.42 (m, 2H) (OCH$_2$CH_2CH_2CH_2); 1.39 (s, 9H, CH_3).



4,4′-Bis[3-(*tert*-butyloxycarbonyl)propoxy]benzophenone (4c). 4,4′-Dihydroxybenzophenone (4.24 g, 20 mmol) was alkylated as described in the procedure for **4a** using sodium (1.15 g, 50 mmol) and *tert*-butyl 4-chlorobutyrate (8.04 g, 45 mmol). The desired compound was purified by chromatography on silica gel in 2→5% EtOAc in toluene. Yield 5.49 g (55%), white crystalline solid, mp 92ºC (EtOAc–hexane). ESI-TOF HRMS: m/z = 499.2697 $[M+H]^+$, calc. for $[C_{29}H_{39}O_7]^+$ 499.2690. NMR (DMSO-d_6): 7.69 (d, 4H, J = 8.8 Hz, ArH); 7.05 (d, 2H, J = 8.8 Hz, ArH); 4.08 (t, 4H, J = 6.4 Hz, OCH_2); 2.38 (t, 4H, J = 7.3 Hz, COCH_2); 1.97 (m, 4H, CH$_2$CH_2CH$_2$); 1.41 (s, 18H, CH_3).

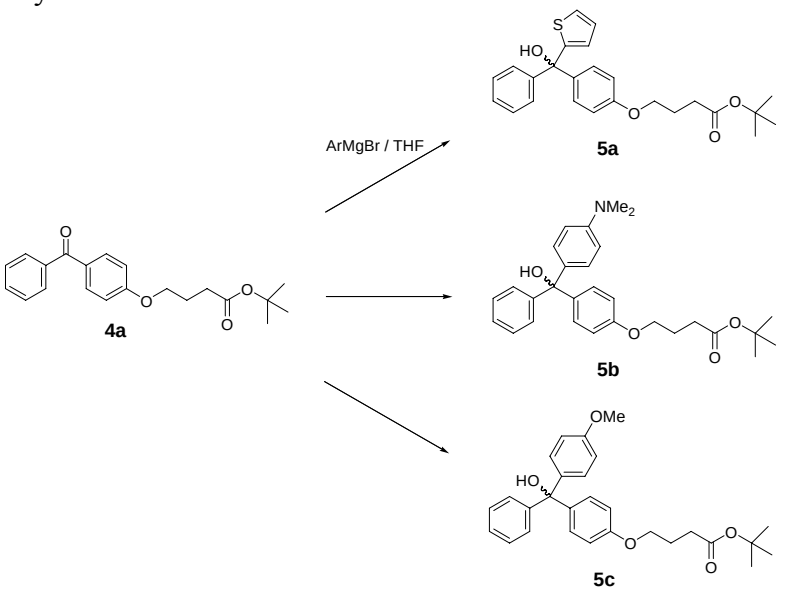


4-[3-(*tert*-Butyloxycarbonyl)propoxy]-4′-methoxybenzophenone (4e). 4,4'-Dihydroxybenzophenone (4.24 g, 20 mmol) was alkylated as described in the procedure for **2c** using sodium (1.15 g, 50 mmol) and *tert*-butyl 4-chlorobutyrate[2] (4.47 g, 25 mmol). The mixture was chromatographed on silica gel in 2→5→10→15% EtOAc in toluene to give 4,4'-bis[3-(*tert*-butyloxycarbonyl)propoxy]benzophenone **4c** (1.60 g, 16%) and **4-[3-(*tert*-butyloxycarbonyl)propoxy]-4′-hydroxybenzophenone (4d)** (3.14 g, 44%) as crystalline solid mp 122–124.5ºC (EtOAc). ESI-TOF HRMS: m/z = 357.1701 $[M+H]^+$, calc. for $[C_{21}H_{25}O_5]^+$ 357.1697. NMR (DMSO-d_6): 10.30 (br.s, 1H, OH), 7.67 (d, 2H, J = 8.8 Hz, ArH); 7.62 (d, 2H, J = 8.4 Hz, ArH); 7.04 (d, 2H, J = 8.8 Hz, ArH); 6.88 (d, 2H, J = 8.4 Hz, ArH); 4.08 (t, 2H, J = 6.3 Hz, OCH_2); 2.38 (t, 2H, J = 7.3 Hz, COCH_2); 2.01–1.93 (m, 2H, CH$_2$CH_2CH$_2$); 1.40 (s, 9H, CH_3). The latter compound was dissolved in acetone and methylated with MeI (3 eq) and K_2CO_3 (7 eq) at ambient temperature for 3 h. The solid was filtered and the solution was evaporated. The residue was dissolved in chloroform, and the solution was filtered and evaporated to give **4e** (3.18 g, 44% based on starting 4,4'-dihydroxybenzophenone), mp 76–78ºC (EtOAc–hexane). ESI-TOF HRMS: m/z = 371.1846 $[M+H]^+$, calc. for $[C_{22}H_{27}O_5]^+$ 371.1853. NMR (DMSO-d_6): 7.74–7.66 (m, 4H, ArH); 7.11–7.03 (m, 4H, ArH); 4.08 (t, 2H, J = 6.3 Hz, COCH_2); 3.86 (s, 3H, OCH_3); 2.38 (t, 2H, J = 7.3 Hz, COCH_2); 2.02–1.91 (m, 2H, CH$_2$CH_2CH$_2$); 1.41 (s, 9H, CH_3).



4-[5-(*tert*-Butyloxycarbonyl)pentyloxy]-4′-methoxybenzophenone (4f). To a solution of 4-hydroxy-4'-methoxybenzophenone (5.84 g, 25.6 mmol) in in dry acetone (250 mL) dry K_2CO_3 (17.7 g, 0.128 mol) and *tert*-butyl 6-bromohexanoate[4] (7.05 g, 28.1 mmol) were added, and the mixture was stirred for 96 h at ambient temperature, then filtered, and the solid was washed with acetone. The combined filtrate was evaporated, and the residue was dissolved in $CHCl_3$ (150 mL), filtered, and evaporated. The residue was chromatographed on silica gel in 0→20% EtOAc in toluene to give the desired product (1.99 g, 19.5%). ESI-TOF HRMS: *m/z* = 399.2175 $[M+H]^+$, calc. for $[C_{24}H_{31}O_5]^+$ 399.2166. NMR (DMSO-d_6): 7.70 (m, 4H, Ar*H*); 7.06 (m, 4H, Ar*H*); 4.06 (t, 2H, *J* = 6.4 Hz, OCH_2); 3.86 (s, 3H, OCH_3); 2.21 (t, 2H, *J* = 7.3 Hz, COCH_2); 1.75 (m, 2H), 1.56 (m, 2H), 1.42 (m, 2H) ($OCH_2CH_2CH_2CH_2$); 1.39 (s, 9H, CCH_3). **4-Methoxy-4′-[5-(4-methoxybenzoylphenoxycarbonyl)pentyloxy]benzophenone** (**4f'**) (22%) was isolated as a side product. NMR (DMSO-d_6): 7.78 (m, 8H, Ar*H*); 7.19 (d, 2H, *J* = 8.2 Hz, Ar*H*); 6.95 (m, 6H, Ar*H*); 4.07 (t, 2H, *J* = 6.1 Hz, OCH_2); 3.88; 3.87 (2s, 6H, OCH_3); 2.64 (t, 2H, *J* = 7.3 Hz, COCH_2); 1.88 (m, 4H, $OCH_2CH_2CH_2CH_2$); 1.64 (m, 2H, $OCH_2CH_2CH_2$).

General procedure for preparation of trirylmethanols 5. To a stirred solution of corresponding benzophenone (4.0 mmol) in dry THF (30 mL) the solution of arylmagnesium bromide (0.5 or 1.0 M, 5.0 mmol) was added in one portion under Ar, and the mixture was kept at ambient temperature overnight (monitoring by TLC in EtOAc–toluene 1:9). The reaction was diluted with water (200 mL) and 5% $NaHCO_3$ (100 mL), and extracted with EtOAc (2×100 mL). The organic phase was dried over Na_2SO_4, evaporated, and chromatographed on silica gel in appropriate solvent system.

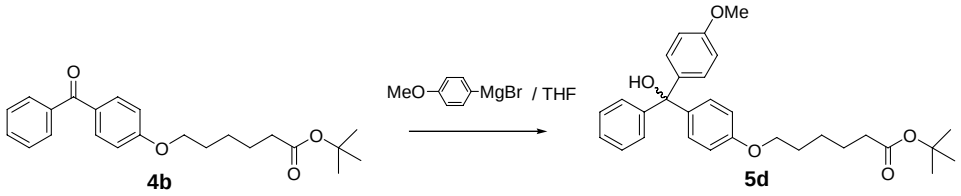


4-{4-[Hydroxy-(thiophen-2-yl)-phenyl-methyl]phenoxy}butanoic acid, *tert*-butyl ester (5a) was prepared from 4-[3-(*tert*-butyloxycarbonyl)propoxy]benzophenone **4a** (1.70 g; 5.0 mmol) in dry THF (50 mL) and 1.0 M 2-thienylmagnesium bromide (7.5 mL, 7.5 mmol). The title compound was chromatographed on silica gel in toluene with 1.0% of Et_3N; yellowish oil. Yield 1.55 g (72%). ESI-TOF HRMS: *m/z* = 407.1671 $[M–OH]^+$, calc. for $[C_{25}H_{27}O_3S]^+$ 407.1675. NMR (DMSO-d_6): 7.42 (m, 1H, H-5 (thiophene)); 7.33–7.21 (m, 5H, Ar*H* (phenyl)); 7.15 (d, 2H, *J* = 8.9 Hz, Ar*H* (phenyl)); 6.94 (m, 1H, H-4 (thiophene)); 6.84 (d, 2H, *J* = 8.9 Hz, Ar*H* (phenyl)); 6.67–6.62 (m, 2H, H-3 (thiophene), O*H*); 3.95 (t, 2H, *J* = 6.3 Hz, OCH_2); 2.35 (t, 2H, *J* = 7.3 Hz, COCH_2); 1.91 (m, 2H, $CH_2CH_2CH_2$), 1.39 (s, 9H, CCH_3).

4-{4-[Hydroxy-(4-dimethylaminophenyl)phenyl-methyl]phenoxy}butanoic acid, *tert*-butyl ester (5b) was prepared from **4a** (1.36 g; 4.0 mmol) in dry THF (30 mL) and 0.5 M 4-dimethylaminophenylmagnesium bromide (10.0 mL, 5.0 mmol). The compound was chromatographed on silica gel in same solvent system to give the desired compound as a pinkish oil. Yield 1.809 g (98%). ESI-TOF HRMS: *m/z* = 444.2537 $[M–OH]^+$, calc. for $[C_{29}H_{34}NO_3]^+$

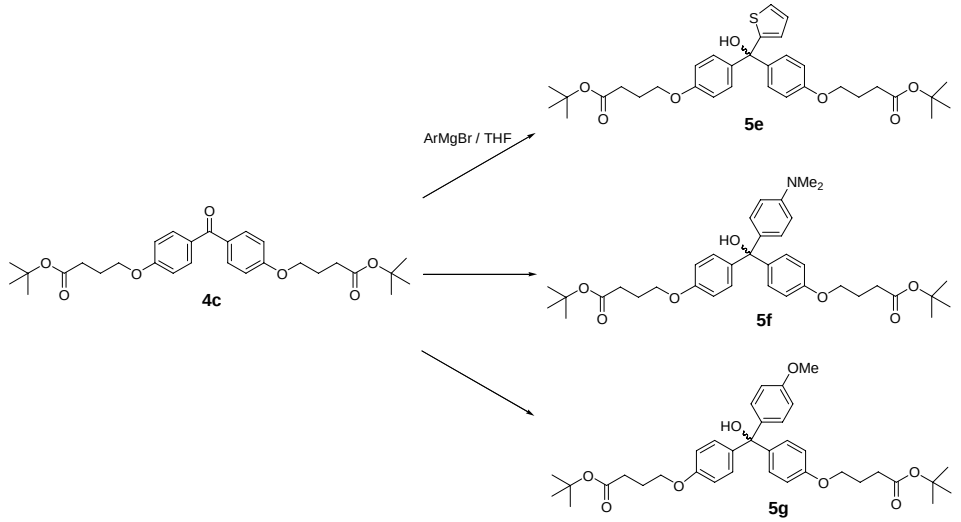
444.2533. NMR (DMSO-d_6): 7.26 (m, 2H, Ar*H*); 7.19 (m, 3H, Ar*H*); 7.07 (d, 2H, *J* = 8.8 Hz, Ar*H*); 6.96 (d, 2H, *J* = 8.8 Hz, Ar*H*); 6.81 (d, 2H, *J* = 8.8 Hz, Ar*H*); 6.62 (d, 2H, *J* = 8.8 Hz, Ar*H*); 6.02 (s, 1H, O*H*); 3.94 (t, 2H, *J* = 6.3 Hz, OCH_2); 2.86 (s, 6H, NCH_3); 2.35 (t, 2H, *J* = 7.3 Hz, COCH_2); 1.91 (m, 2H, $CH_2CH_2CH_2$), 1.40 (s, 9H, CCH_3).

4-[3-(*tert*-Butyloxycarbonyl)propoxy]-4′-methoxytritanol (5c) was prepared from **4a** (1.85 g; 5.0 mmol) in dry THF (30 mL) and 1 M phenylmagnesium bromide (7.0 mL, 7.0 mmol). The crude product was chromatographed on silica gel in 0→5% EtOAc in toluene with 0.5% of Et_3N to give the desired compound as a yellow oil. Yield 1.57 g (70%). ESI-TOF HRMS: *m/z* = 431.2214 $[M–OH]^+$, calc. for $[C_{28}H_{31}O_4]^+$ 431.2217. NMR (DMSO-d_6): 7.28 (m, 2H, Ar*H*); 7.20 (m, 3H, Ar*H*); 7.07 (m, 4H, Ar*H*); 6.83 (m, 4H, Ar*H*); 6.20 (s, 1H, O*H*); 3.94 (t, 2H, *J* = 6.2 Hz, OCH_2); 3.73 (s, 3H, OCH_3); 2.35 (t, 2H, *J* = 7.2 Hz, COCH_2); 1.91 (m, 2H, $CH_2CH_2CH_2$); 1.40 (s, 9H, CH_3).



4b 5d

6-{4-[Hydroxy-(4-methoxyphenyl)-phenyl-methyl]phenoxy}hexanoic acid, *tert*-butyl ester (5d) was prepared from 4-[5-(*tert*-butyloxycarbonyl)pentyloxy]benzophenone **4b** (1.84 g; 5.0 mmol) in dry THF (30 mL) and 1 M 4-methoxyphenylmagnesium bromide (7.0 mL, 7.0 mmol). The crude tritanol was chromatographed on silica gel in 0→5% EtOAc in toluene with 0.5% of Et_3N to give the desired compound as a colourless oil. Yield 1.597 g (67%). ESI-TOF HRMS: *m/z* = 459.2535 $[M–OH]^+$, calc. for $[C_{30}H_{35}O_4]^+$ 459.2530. NMR (DMSO-d_6): 7.26 (m, 2H, Ar*H*); 7.20 (m, 3H, Ar*H*); 7.07 (m, 4H, Ar*H*); 6.83 (m, 4H, Ar*H*); 6.17 (s, 1H, O*H*); 3.92 (t, 2H, *J* = 6.4 Hz, OCH_2); 3.73 (s, 3H, OCH_3); 2.20 (t, 2H, *J* = 7.3 Hz, COCH_2); 1.70 (m, 2H, OCH_2CH_2), 1.54 (m, 2H, $COCH_2CH_2$), 1.39 (m, 2H, $OCH_2CH_2CH_2$); 1.38 (s, 9H, CH_3).

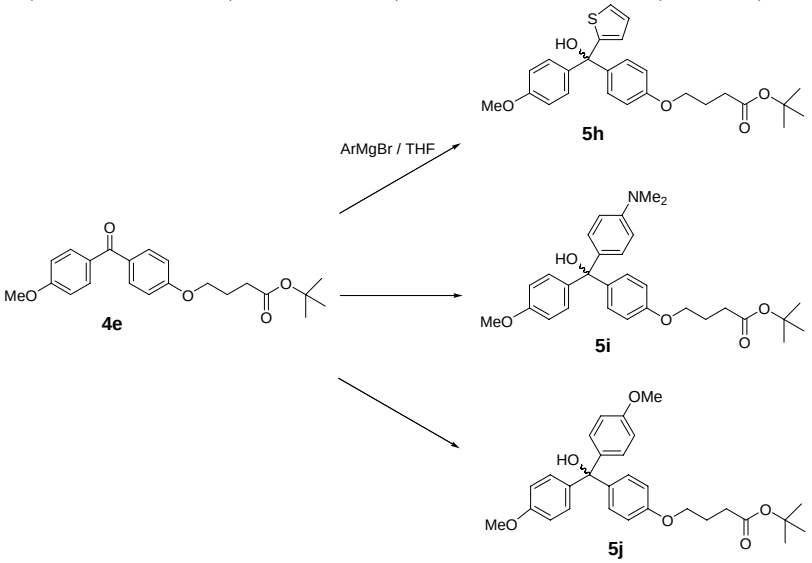


4c 5e 5f 5g

Thiophen-2-yl-bis{4-[3-(*tert*-butyloxycarbonyl)propoxy]phenyl}methanol (5e) was prepared from 4,4′-bis[3-(*tert*-butyloxycarboxy)propoxy]benzophenone **4c** (2.49 g; 5.0 mmol) in dry THF (50 mL) and 1.0 M 2-thienylmagnesium bromide (7.5 mL, 7.5 mmol). The crude tritanol was chromatographed on silica gel in toluene with 1.0% of Et_3N to give the desired compound as a violet oil. Yield 2.86 g (98%). ESI-TOF HRMS: *m/z* = 565.2611 $[M–OH]^+$, calc. for $[C_{33}H_{41}O_6S]^+$ 565.2618. NMR (DMSO-d_6): 7.40 (m, 1H, H-5 (thiophene)); 7.15 (d, 4H, *J* = 8.9 Hz, Ar*H* (phenyl)); 6.93 (m, 1H, H-4 (thiophene)); 6.83 (d, 4H, *J* = 8.9 Hz, Ar*H* (phenyl)); 6.61 (m, 1H, H-3 (thiophene)); 6.52 (s, 1H, O*H*); 3.94 (t, 4H, *J* = 6.3 Hz, OCH_2); 2.35 (t, 4H, *J* = 7.3 Hz, COCH_2); 1.91 (m, 4H, $CH_2CH_2CH_2$), 1.39 (s, 18H, CCH_3).

4-Dimethylaminophenyl-bis{4-[3-(*tert*-butyloxycarbonyl)propoxy]phenyl}methanol (5f) was prepared from **4c** (2.49 g; 5.0 mmol) in dry THF (50 mL) and 0.5 M 4-(*N*,*N*-dimethylamino)phenylmagnesium bromide (15 mL, 7.5 mmol). The tritanol was purified by chromatography on silica gel in toluene with 5% of EtOAc and 1% of Et_3N. Pale violet oil, yield 2.22 g (71%). ESI-TOF HRMS: *m/z* = 602.3477 $[M–OH]^+$, calc. for $[C_{37}H_{48}NO_6]^+$ 602.3476. NMR (DMSO-d_6): 7.06 (d, 4H, *J* = 8.7 Hz, Ar*H*); 6.94 (d, 2H, *J* = 8.8 Hz, Ar*H*); 6.80 (d, 4H, *J* = 8.7 Hz, Ar*H*); 6.61 (d, 2H, *J* = 8.8 Hz, Ar*H*); 5.91 (br.s, 1H, O*H*); 3.93 (t, 2H, *J* = 6.2 Hz, OCH_2); 2.85 (s, 6H, NCH_3); 2.34 (t, 4H, *J* = 7.2 Hz, COCH_2); 1.91 (m, 4H, $CH_2CH_2CH_2$), 1.40 (s, 18H, CCH_3).

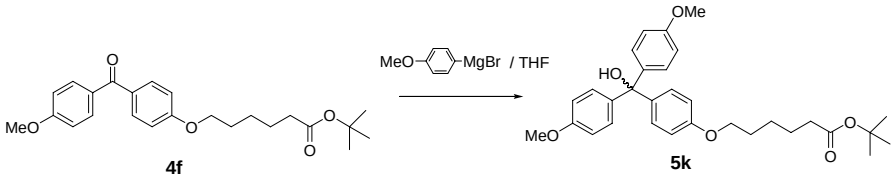
4-Methoxy-4′,4′′-bis[3-(*tert*-butyloxycarbonyl)propoxy]triphenylmethanol (5g) was prepared from 4c (2.49 g; 5.0 mmol) in dry THF (30 mL) and 1 M 4-methoxyphenylmagnesium bromide (7.0 mL, 7.0 mmol). The tritanol was chromatographed on silica gel in 3→7% EtOAc in toluene to give the desired compound as a colorless oil. Yield 1.88 g (62%). ESI-TOF HRMS: *m/z* = 589.3162 $[M–OH]^+$, calc. for $[C_{36}H_{45}O_7]^+$ 589.3160. NMR (DMSO-d_6): 7.10–7.04 (m, 6H, Ar*H* (phenyl)); 6.86–6.81 (m, 6H, Ar*H* (phenyl)); 6.07 (s, 1H, O*H*); 3.93 (m, 4H, OCH_2); 3.72 (s, 3H, OCH_3); 2.40–2.30 (m, 4H, COCH_2); 1.95-1.85 (m, 4H, $CH_2CH_2CH_2$), 1.40 (s, 18H, CCH_3).



4-{4-[Hydroxy-(thiophen-2-yl)-(4-methoxyphenyl)-methyl]phenoxy}butanoic acid, *tert*-butyl ester (5h) was prepared from 4-[3-(*tert*-butyloxycarbonyl)propoxy]-4′-methoxybenzophenone **4e** (1.85 g; 5.0 mmol) in dry THF (50 mL) and 1.0 M 2-thienylmagnesium bromide (7.5 mL, 7.5 mmol). The crude compound was chromatographed on silica gel in toluene with 1.0% of Et_3N to give the desired tritanol as a violet oil. Yield 1.33 g (58%). ESI-TOF HRMS: *m/z* = 565.2622 $[M–OH]^+$, calc. for $[C_{33}H_{41}O_6S]^+$ 565.2618. NMR (DMSO-d_6): 7.40 (m, 1H, H-5 (thiophene)); 7.15 (m, 4H, Ar*H* (phenyl)); 6.93 (m, 1H, H-4 (thiophene)); 6.84 (m, 4H, Ar*H* (phenyl)); 6.62 (m, 1H, H-3 (thiophene)); 6.52 (s, 1H, O*H*); 3.94 (t, 2H, *J* = 6.4 Hz, OCH_2); 3.73 (s, 3H, OCH_3); 2.35 (t, 2H, *J* = 7.3 Hz, COCH_2); 1.91 (m, 2H, $CH_2CH_2CH_2$), 1.39 (s, 9H, CCH_3).

4-{4-[Hydroxy-(4-dimethylaminophenyl)-(4-methoxyphenyl)-methyl]phenoxy}butanoic acid, *tert*-butyl ester (5i) was prepared from **4e** (1.48 g; 4.0 mmol) in dry THF (30 mL) and 0.5 M 4-dimethylaminophenylmagnesium bromide (10.0 mL, 5.0 mmol). The compound was chromatographed on silica gel in toluene with 1.0% of Et_3N. Colourless oil, yield 1.514 g (77%). ESI-TOF HRMS: *m/z* = 565.2622 $[M–OH]^+$, calc. for $[C_{30}H_{36}NO_4]^+$ 565.2618. NMR (DMSO-d_6): 7.07 (m, 4H, Ar*H*); 6.95 (d, 2H, *J* = 8.8 Hz, Ar*H*); 6.81 (m, 4H, Ar*H*); 6.62 (d, 2H, *J* = 8.8 Hz, Ar*H*); 5.91 (s, 1H, O*H*); 3.94 (t, 2H, *J* = 6.3 Hz, OCH_2); 3.72 (s, 3H, OCH_3); 2.85 (s, 6H, NCH_3); 2.35 (t, 2H, *J* = 7.3 Hz, COCH_2); 1.91 (m, 2H, $CH_2CH_2CH_2$), 1.40 (s, 9H, CCH_3).

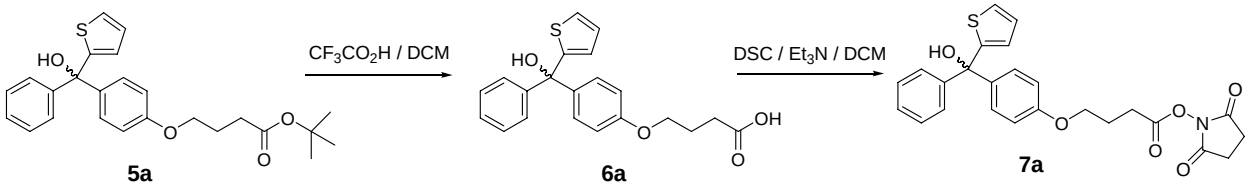
4-[3-(*tert*-Butyloxycarbonyl)propoxy]-4′,4″-dimethoxytritanol (5j) was prepared from **4e** (1.85 g; 5.0 mmol) in dry THF (30 mL) and 1 M 4-methoxyphenylmagnesium bromide (7.0 mL, 7.0 mmol); the purification was achieved using chromatography on silica gel in 3→7% EtOAc in toluene. The desired tritanol was obtained as a yellow oil, yield 1.79 g (75%). ESI-TOF HRMS: *m/z* = 461.2325 $[M–OH]^+$, calc. for $[C_{29}H_{33}O_5]^+$ 461.2323.



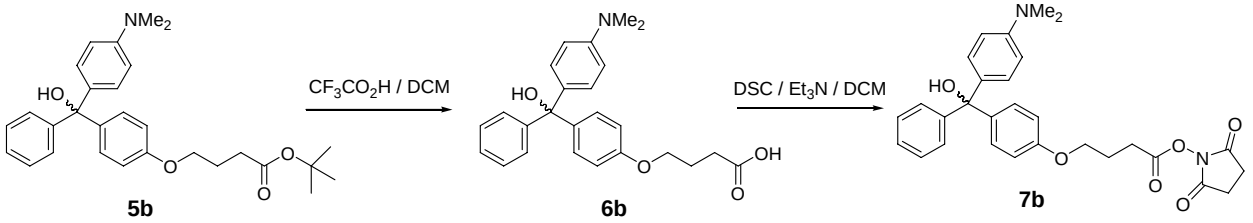
6-{4-[Hydroxy-bis(4-methoxyphenyl)methyl]phenoxy}hexanoic acid, *tert*-butyl ester (5k) was prepared from 4-[5-(*tert*-butyloxycarbonyl)pentyloxy]-4′-methoxybenzophenone **4f** (400 mg; 1.0 mmol) in dry THF (10 mL) and 1 M 4-methoxyphenylmagnesium bromide (1.2 mL, 1.2 mmol). The crude compound was chromatographed on silica gel in 0→15% EtOAc in toluene with 0.5% of Et_3N to give the desired tritanol as a colourless oil, yield 334 mg (66%). ESI-TOF HRMS: *m/z* = 489.2630 $[M–OH]^+$, calc. for $[C_{31}H_{37}O_5]^+$ 489.2636. NMR (DMSO-d_6): 7.06 (m, 6H, Ar*H*); 6.82 (m, 6H, Ar*H*); 6.07 (s, 1H, O*H*); 3.92 (t, 2H, *J* = 6.2 Hz, OCH_2); 3.72 (s, 6H, OCH_3); 2.20 (t, 2H, *J* = 7.3 Hz, COCH_2); 1.69 (m, 2H), 1.54 (m, 2H), 1.39 (m, 2H), ($OCH_2CH_2CH_2CH_2$); 1.37 (s, 9H, CCH_3).

General procedure for preparation of trityl acids 6. To a stirred solution of *tert*-butyl ester **5** (3 mmol) in dry DCM (5 mL) trifluoroacetic acid (5 mL) was added in one portion and the mixture was stirred at ambient temperature for 3 h, then evaporated, and co-evaporated with DCM (4×50 mL) to give free acid. These were used for the preparation of activated esters without additional purification. In some cases analytical samples of acids **6** were purified by column chromatography on silica gel (typically 20 to 40% acetone in toluene).

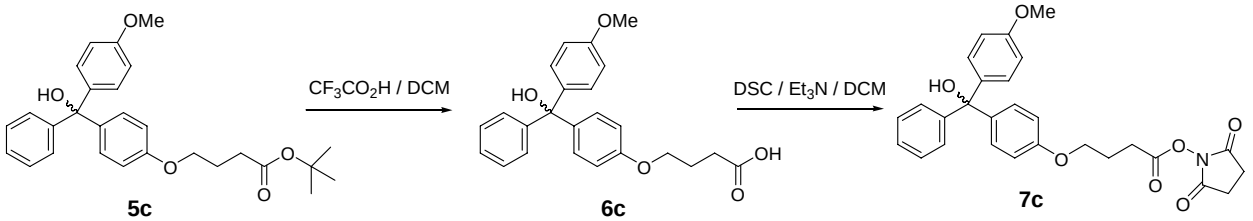
General procedure for preparation of N-oxysuccinimide activated esters 7. The acid **6** obtained from *tert*-butyl ester **5** (3 mmol) were dissolved in DCM (50 mL), triethylamine (0.92 mL, 6.6 mmol) and *N*,*N*-disuccinimidyl carbonate (1.27 g, 4.95 mmol) were added and the mixture was stirred overnight, then evaporated, dissolved in EtOAc (100 mL), washed with 5% $NaHCO_3$ (100 mL) and water (100 mL), dried over Na_2SO_4, and evaporated to give pure activated ester **7**. In some cases the latter was purified by column chromatography on silica gel (EtOAc in toluene).



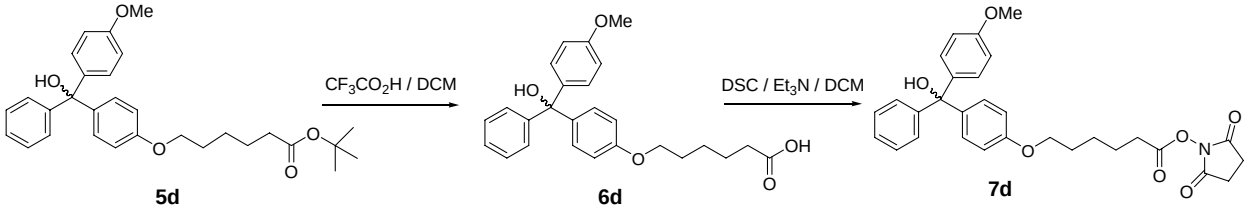
4-{4-[Hydroxy-(2-thienyl)-phenylmethyl]phenoxy}butanoic acid, *N*-succinimidyl ester (7a) was prepared from *tert*-butyl ester of 4-{4-[hydroxy-(2-thienyl)-phenylmethyl]phenoxy}butanoic acid **5a** (1.40 g; 3.3 mmol). The final compound purified by column chromatography (0→20% EtOAc in toluene). Yield 1.00 g (65%), pink amorphous solid. ESI-TOF HRMS: *m/z* = 448.1217 $[M–OH]^+$, calc. for $[C_{25}H_{22}NO_5S]^+$ 448.1213. NMR (DMSO-d_6): 7.42 (m, 1H, H-5 (thiophene)); 7.33–7.22 (m, 5H, Ar*H* (phenyl)); 7.16 (d, 2H, *J* = 8.9 Hz, Ar*H* (phenyl)); 6.94 (dd, 1H, $J_{4,5}$ = 4.8 Hz, $J_{3,4}$ = 3.6 Hz, H-4 (thiophene)); 6.87 (d, 2H, *J* = 8.9 Hz, Ar*H* (phenyl)); 6.65 (m, 2H, H-3 (thiophene), O*H*); 4.03 (t, 2H, *J* = 6.3 Hz, OCH_2); 2.84 (t, 2H, *J* = 7.4 Hz, COCH_2); 2.81 (s, 4H, $COCH_2CH_2CO$); 2.06 (m, 2H, $CH_2CH_2CH_2$).



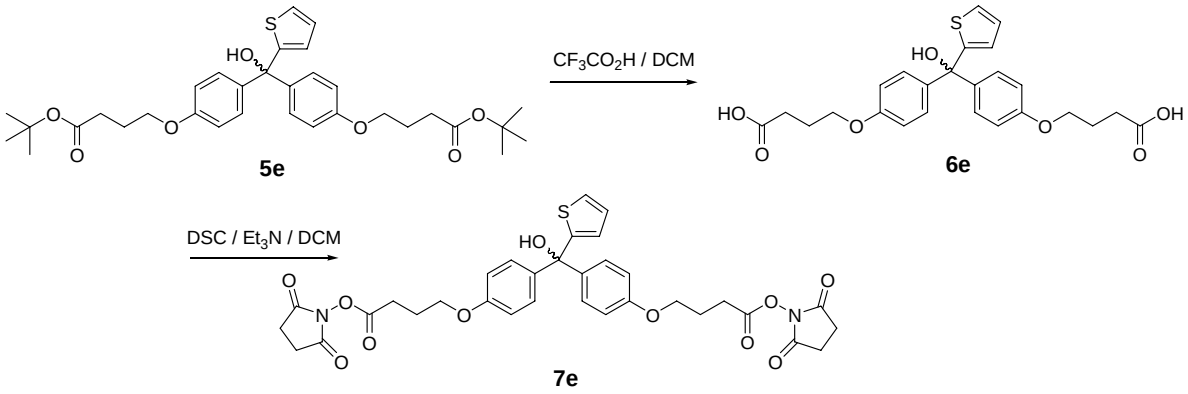
4-{4-[Hydroxy-(4-dimethylaminophenyl)-phenyl-methyl]phenoxy}butanoic acid, *N*-oxysuccinimide ester (7b) was prepared from *tert*-butyl 4-{4-[hydroxy-(4-dimethylaminophenyl)-phenyl-methyl]phenoxy}butanoate **5b** (923 mg; 2.0 mmol). Column chromatography: 5→10→15% EtOAc in toluene. Yield 458 mg (43%), pink amorphous solid. ESI-TOF HRMS: *m/z* = 485.2075 $[M–OH]^+$, calc. for $[C_{29}H_{29}N_2O_5]^+$ 485.2071. NMR (DMSO-d_6): 7.26 (m, 2H, Ar*H*); 7.19 (m, 3H, Ar*H*); 7.07 (d, 2H, *J* = 8.7 Hz, Ar*H*); 6.96 (d, 2H, *J* = 8.7 Hz, Ar*H*); 6.84 (d, 2H, *J* = 8.7 Hz, Ar*H*); 6.62 (d, 2H, *J* = 8.7 Hz, Ar*H*); 6.03 (s, 1H, O*H*); 4.02 (t, 2H, *J* = 6.3 Hz, OCH_2); 2.88–2.79 (m, 12H, NCH_3, $CH_2CH_2CH_2CO$, $COCH_2CH_2CO$); 2.06 (m, 2H, $CH_2CH_2CH_2$).



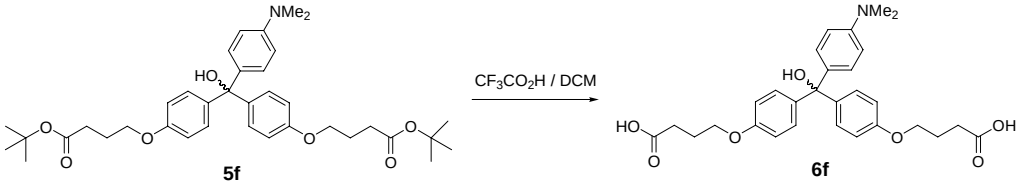
4-{4-[Hydroxy-(4-methoxyphenyl)-phenyl-methyl]phenoxy}butanoic acid, *N*-oxysuccinimide ester (7c) was prepared from 4-[3-(*tert*-butyloxycarbonyl)propoxy]-4′-methoxytritanol **5c** (1.12 g; 2.5 mmol). Column chromatography: 5→20% EtOAc in toluene. Yield 0.900 g (74%), white amorphous solid. ESI-TOF HRMS: *m/z* = 472.1751 $[M–OH]^+$, calc. for $[C_{28}H_{26}NO_6]^+$ 472.1755. NMR (DMSO-d_6): 7.28 (m, 2H, Ar*H*); 7.20 (m, 3H, Ar*H*); 7.08 (m, 4H, Ar*H*); 6.85 (m, 4H, Ar*H*); 6.20 (s, 1H, O*H*); 4.03 (t, 2H, *J* = 6.2 Hz, OCH_2); 3.73 (s, 3H, OCH_3); 2.84 (m, 6H, $OCOCH_2$, $COCH_2CH_2CO$); 2.06 (m, 2H, $CH_2CH_2CH_2$).



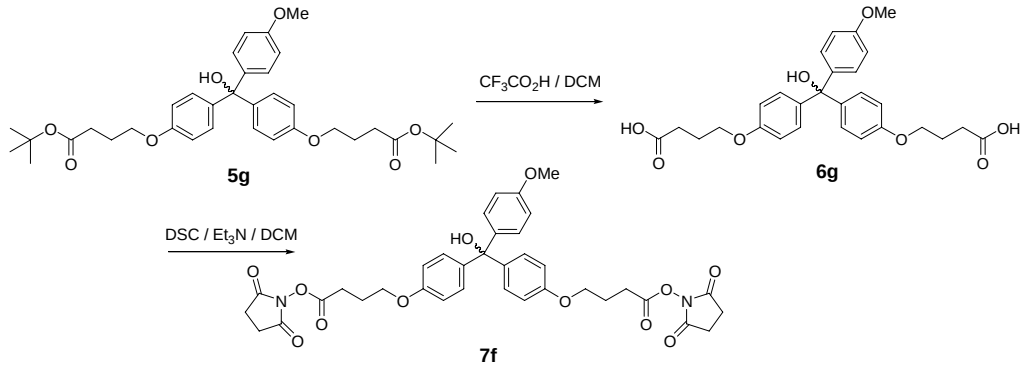
6-{4-[Hydroxy-(4-methoxyphenyl)-phenyl-methyl]phenoxy}hexanoic acid, *N*-oxysuccinimide ester (7d) was prepared from *tert*-butyl 6-{4-[hydroxy-(4-methoxyphenyl)-phenyl-methyl]phenoxy}hexanoate **5d** (953 mg; 2.0 mmol). Yield 743 mg (72%), white amorphous solid. ESI-TOF HRMS: *m/z* = 500.2075 $[M–OH]^+$, calc. for $[C_{30}H_{30}NO_6]^+$ 500.2068. NMR (DMSO-d_6): 7.26 (m, 2H, Ar*H*); 7.20 (m, 3H, Ar*H*); 7.07 (m, 4H, Ar*H*); 6.83 (m, 4H, Ar*H*); 6.17 (s, 1H, O*H*); 3.93 (t, 2H, *J* = 6.2 Hz, OCH_2); 3.73 (s, 3H, OCH_3); 2.81 (s, 4H, $COCH_2CH_2CO$); 2.69 (t, 2H, *J* = 7.2 Hz, $COCH_2$); 1.78–1.64 (m, 4H, $OCH_2CH_2CH_2CH_2$), 1.51 (m, 2H, $OCH_2CH_2CH_2$).



2-Thienyl-4′,4″-bis[3-(*N*-succinimidylcarbonyl)propoxy]triphenylmethanol (7e) was prepared from 2-thienyl-4′,4″-bis[3-(*tert*-butyloxycarbonyl)propoxy]triphenylmethanol **5e** (2.50 g; 4.29 mmol). The compound was purified by column chromatography (10→50% EtOAc in toluene). Yield 2.05 g (72%), pink amorphous solid. ESI-TOF HRMS: *m/z* = 647.1697 [M–OH]$^+$, calc. for $[C_{33}H_{31}N_2O_{10}S]^+$ 647.1694. NMR (DMSO-d_6): 7.41 (m, 1H, H-5 (thiophene)); 7.16 (d, 4H, *J* = 8.8 Hz, Ar*H*); 6.93 (dd, 1H, $J_{4,5}$ = 4.8 Hz, $J_{3,4}$ = 3.7 Hz, H-4 (thiophene)); 6.87 (d, 4H, *J* = 8.8 Hz, Ar*H*); 6.63 (m, 1H, H-3 (thiophene)); 6.54 (s, 1H, O*H*); 4.03 (t, 4H, *J* = 6.2 Hz, OCH_2); 2.87–2.78 (m, 12H, COCH_2, COCH_2CH_2CO); 2.07 (m, 4H, $CH_2CH_2CH_2$).

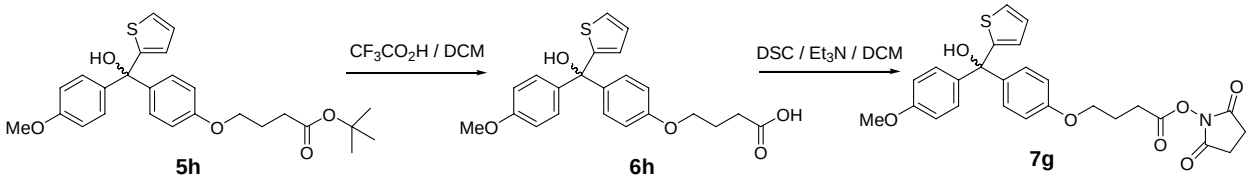


4-(*N*,*N*-Dimethylaminophenyl)-4′,4″-bis[3-carboxypropoxy]triphenylmethanol (6f). To a stirred solution of 4-(*N*,*N*-dimethylaminophenyl)-4′,4″-bis[3-(*tert*-butyloxycarbonyl)propoxy]-triphenylmethanol (1.55 g, 2.5 mmol) in dry DCM (5 mL) trifluoroacetic acid (5 mL) was added in one portion and the mixture was stirred at ambient temperature overnight (monitoring by TLC in EtOAc-toluene 1:4). The solution was evaporated to dryness, and co-evaporated with DCM (4×30 mL) to give acid **6f** as dark violet oil. Yield 1.23 g (97 %). ESI-TOF HRMS: *m/z* = 490.2220 [M–OH]$^+$, calc. for $[C_{29}H_{32}NO_6]^+$ 490.2224. NMR (DMSO-d_6): 7.49 (d, 2H, *J* = 9.6 Hz, Ar*H*); 7.33 (d, 4H, *J* = 8.9 Hz, Ar*H*); 7.27 (d, 2H, *J* = 9.6 Hz, Ar*H*); 7.21 (d, 4H, *J* = 8.9 Hz, Ar*H*); 4.18 (t, 4H, *J* = 6.4 Hz, OCH_2); 3.46 (s, 6H, NCH_3); 2.43 (t, 4H, *J* = 7.2 Hz, COCH_2); 2.01 (m, 4H, $CH_2CH_2CH_2$).

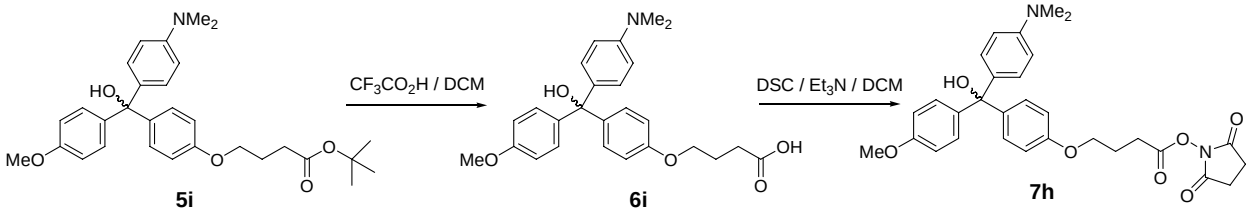


4-Methoxy-4′,4″-bis{[3-(*N*-succinimidyl)oxycarbonyl]propoxy}triphenylmethanol (7f) was prepared from 4,4′-bis[3-(*tert*-butyloxycarbonyl)propoxy]-4″-(4-methoxybenzoyl)tritanol 5g (1.21 g; 2.0 mmol) and purified by column chromatography (20→30% EtOAc in toluene). Yield 826 mg (78%), white amorphous solid. R_f 0.18 (toluene–EtOAc, 1:1). ESI-TOF HRMS: *m/z* = 671.2230 [M–OH]$^+$, calc. for $[C_{36}H_{35}N_2O_{11}]^+$ 671.2235. NMR (DMSO-d_6): 7.10–7.04 (m, 6H, Ar*H* (phenyl)); 6.88–6.81 (m, 6H, Ar*H* (phenyl)); 6.09 (s, 1H, O*H*); 4.03 (t, 4H, *J* = 5.3 Hz,

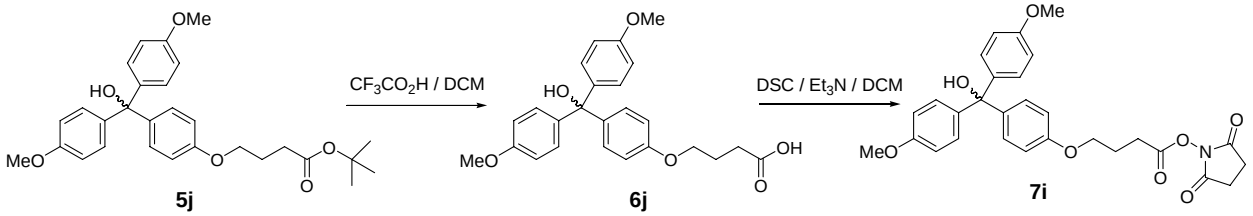
OCH_2); 3.73 (s, 3H, OCH_3); 2.87–2.77 (m, 12H, COCH_2CH_2CO, COCH_2); 2.11–2.03 (m, 4H, CH_2C$H_2$$CH_2$).



4-{4-[Hydroxy-(2-thienyl)-(4-methoxyphenyl)-methyl]phenoxy}butanoic acid, *N*-succinimidyl ester (7g) was prepared from *tert*-butyl ester of 4-{4-[hydroxy-(2-thienyl)-(4-methoxyphenyl)-phenoxy}butanoic acid **5h** (1.25 g; 2.75 mmol) and purified by column chromatography (0→20% EtOAc in toluene). Yield 1.06 g (78%), pink amorphous solid. ESI-TOF HRMS: *m/z* = 478.1315 $[M–OH]^+$, calc. for $[C_{26}H_{24}NO_6S]^+$ 478.1319. NMR (DMSO-d_6): 7.41 (m, 1H, H-5 (thiophene)); 7.19–7.13 (m, 4H, Ar*H* (phenyl)); 6.93 (dd, 1H, $J_{4,5}$ = 4.8 Hz, $J_{3,4}$ = 3.7 Hz, H-4 (thiophene)); 6.86 (m, 4H, Ar*H* (phenyl)); 6.62 (m, 1H, H-3 (thiophene)); 6.54 (s, 1H, O*H*); 4.03 (t, 2H, *J* = 6.2 Hz, OCH_2); 3.73 (s, 3H, OCH_3); 2.90–2.79 (m, 6H, COCH_2, COCH_2CH_2CO); 2.06 (m, 2H, CH_2C$H_2$$CH_2$).



4-{4-[Hydroxy-(4-dimethylaminophenyl)-(4-methoxyphenyl)-methyl]phenoxy}butanoic acid, *N*-oxysuccinimide ester (7h) was prepared from *tert*-butyl 4-{4-[hydroxy-(4-dimethylaminophenyl)-(4-methoxyphenyl)-methyl]phenoxy}butanoate **5i** (983 mg; 2.0 mmol) and purified by column chromatography (10→15% EtOAc in toluene). Yield 660 mg (62%), violet amorphous solid. ESI-TOF HRMS: *m/z* = 515.2181 $[M–OH]^+$, calc. for $[C_{30}H_{31}N_2O_6]^+$ 515.2177. NMR (DMSO-d_6): 7.07 (m, 4H, Ar*H*); 6.95 (d, 2H, *J* = 8.7 Hz, Ar*H*); 6.82 (m, 4H, Ar*H*); 6.62 (d, 2H, *J* = 8.7 Hz, Ar*H*); 5.92 (s, 1H, O*H*); 4.02 (t, 2H, *J* = 6.3 Hz, OCH_2); 3.72 (s, 3H, OCH_3); 2.88–2.79 (m, 12H, NCH_3, CH_2CH_2CH_2CO, COCH_2CH_2CO); 2.06 (m, 2H, CH_2C$H_2$$CH_2$).



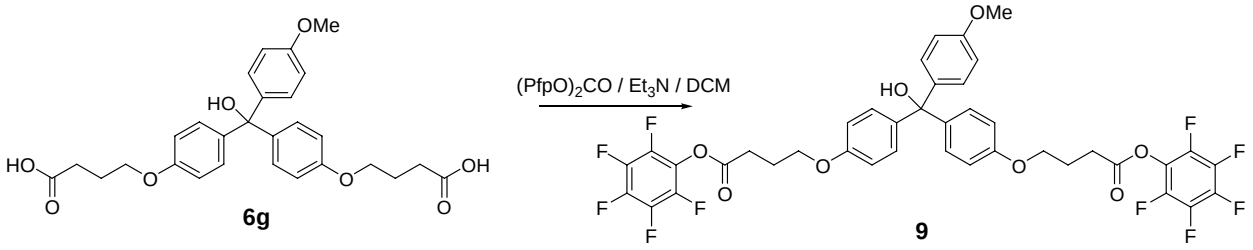
6-{4-[Hydroxy-bis(4-methoxyphenyl)methyl]phenoxy}hexanoic acid, *N*-oxysuccinimide ester (7i) was prepared from *tert*-butyl 6-{4-[hydroxy-bis(4-methoxyphenyl)methyl]phenoxy}hexanoate **5j** (253 mg; 0.5 mmol) and purified by column chromatography (10→25% EtOAc in toluene). Yield 240 mg (88%), white amorphous solid. ESI-TOF HRMS: *m/z* = 530.2175 $[M–OH]^+$, calc. for $[C_{31}H_{32}NO_7]^+$ 530.2173. NMR (DMSO-d_6): 7.06 (m, 6H, Ar*H*); 6.83 (m, 6H, Ar*H*); 6.07 (s, 1H, O*H*); 3.93 (t, 2H, *J* = 6.2 Hz, OCH_2); 3.72 (s, 3H, OCH_3); 2.80 (s, 4H, COCH_2CH_2CO); 2.69 (t, 2H, *J* = 7.3 Hz, CH_2CO_2); 1.70 (m, 4H, OCH_2CH_2CH_2CH_2); 1.50 (m, 2H, OCH_2CH_2CH_2).

General procedure for preparation of N-oxysulfosuccinimide activated esters.

A trityl acid (1.0 mmol), prepared as above, was dissolved in dry DMF (2.5 mL), then *N*-oxysulfosuccinimide sodium salt (250 mg, 1.17 mmol) and DCC (375 mg, 1.8 mmol) were added and the mixture was left under stirring overnight, then cooled to +4ºC and stirred for 2 h.

The precipitate formed was filtered off, and the solution was diluted with EtOAc (10 mL), cooled to +4ºC overnight, filtered, and diluted with dry Et_2O (200 mL). The mixture was kept at ambient temperature for 2-3 h and the desired compound was collected by filtration, washed with ether and dried *in vacuo*.

4-{4-[Hydroxy-bis(4-methoxyphenyl)methyl]phenoxy}butyric acid, *N*-oxysulfosuccinimide ester, sodium salt (8) was prepared using above procedure, 38% yield from the orthoester. ESI-TOF HRMS: *m/z* = 604.1262 $[M–OH]^+$, calc. for $[C_{29}H_{27}NNaO_{10}S]^+$ 604.1248. NMR (DMSO-d_6): 7.10-7.04 (m, 6H, Ar*H*); 6.88-6.80 (m, 6H, Ar*H*); 6.09 (s, 1H, O*H*); 4.02 (t, 2H, *J* = 6.3 Hz, OCH_2); 3.73 (s, 6H, OCH_3, C*H*); 2.91–2.79 (m, 4H, COCH_2, COCH_2CHCO); 2.10-2.02 (m, 2H, $CH_2CH_2CH_2$).

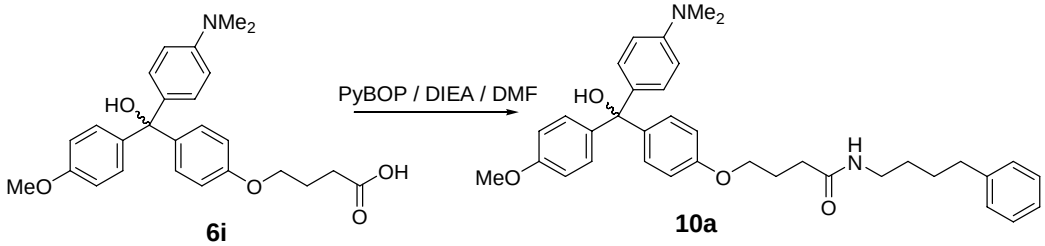


4,4′-Bis[3-(pentafluorophenyloxyacarbonyl)propoxy]-4′′-methoxy-tritanol (9). To a stirred solution of 4,4′-bis(3-carboxypropoxy)-4′′-methoxy-tritanol (742 mg; 1.5 mmol) in dry DCM (20 mL) triethylamine (0.28 mL, 2.0 mmol) pentafluorophenyl carbonate (1.97 g, 5.0 mmol) were added and the mixture was stirred overnight, then evaporated, coevaporated with DCM and chromatographed on silica gel (5→10% EtOAc in toluene). Yield 980 mg (79%), dark red oil R_f 0.25 (toluene–EtOAc, 3:1). ESI-TOF HRMS: *m/z* = 809.1595 $[M–OH]^+$, calc. for $[C_{40}H_{27}F_{10}O_7]^+$ 809.1592.

General procedure for preparation of amides 10.

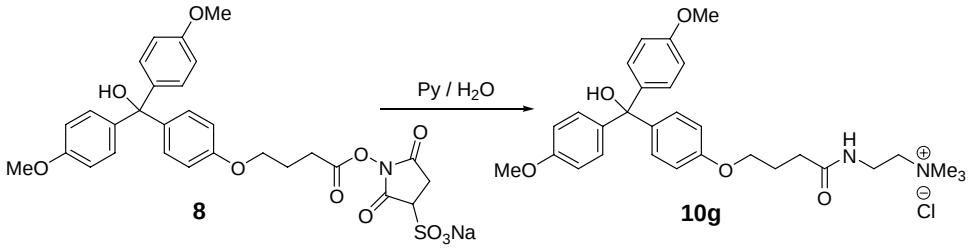
Succinimide activated ester (1 mmol) in DCM (20 mL) was treated with amine (2.5 mmol) for 3 h. The solution was then washed with water, 5% citric acid, dried, and evaporated. The residue was purified by column chromatography in appropriate solvent system. Yields are usually > 90%.

Examples of preparation of amides 10.

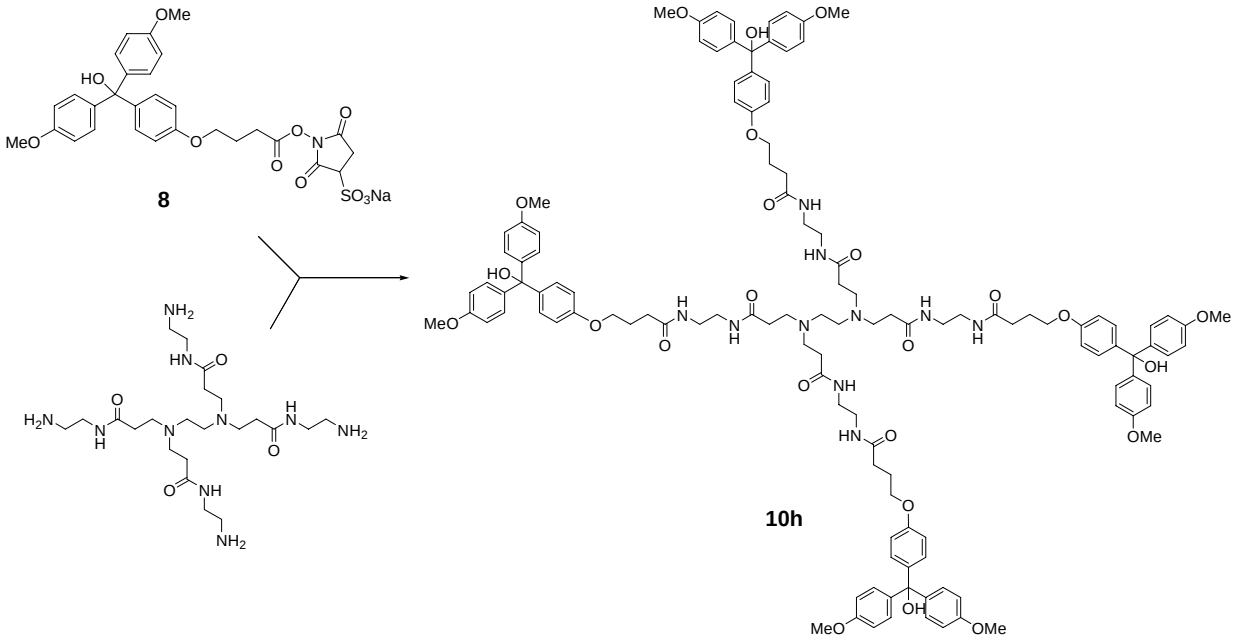


4-{4-[Hydroxy-(4-dimethylaminophenyl)-(4-methoxyphenyl)-methyl]phenoxy}butanoic acid, 4-phenylbutylamide (10f). To a stirred solution of 4-{4-[hydroxy-(4-dimethylaminophenyl)-(4-methoxyphenyl)-methyl]phenoxy}butanoic acid **6i** (245 mg, 0.56 mmol) in dry DMF (10 mL) *N*,*N*-diisopropylethylamine (145 μL, 0.84 mmol) and PyBOP (350 mg, 0.67 mmol) were subsequently added. The mixture was stirred 10 min at ambient temperature, and 4-phenylbutylamine (167 μL, 1.12 mmol) was added. The mixture was stirred then 1 h, diluted with EtOAc (200 mL), washed with water (4×100 mL), dried over Na_2SO_4, and chromatographed on silica gel in toluene with 10→15% of EtOAc and 0.5% Et_3N. The product was obtained as pale pink oil (275 mg), yield 86%. ESI-TOF HRMS: *m/z* = 549.3107 $[M–OH]^+$, calc. for $[C_{36}H_{41}N_2O_3]^+$ 549.3112. NMR (DMSO-d_6): 7.80 (m, 1H, N*H*); 7.30–7.10 (m, 5H, Ar*H*); 7.06 (m, 4H, Ar*H*); 6.95 (d, 2H, *J* = 8.8 Hz, Ar*H*); 6.80 (m, 4H, Ar*H*); 6.61 (d, 2H, *J* = 8.8 Hz, Ar*H*); 5.91 (s, 1H, O*H*); 3.91 (t, 2H, *J* = 6.3 Hz, OCH_2); 3.72 (s, 3H, OCH_3); 3.06 (m, 2H,

NCH_2); 2.85 (s, 6H, NCH_3); 2.55 (m, 2H, PhCH_2); 2.20 (t, 2H, J = 7.3 Hz, COCH_2); 1.91 (m, 2H, COCH$_2$CH_2), 1.54 (m, 2H, PhCH$_2$CH_2), 1.39 (m, 2H, NCH$_2$CH_2).

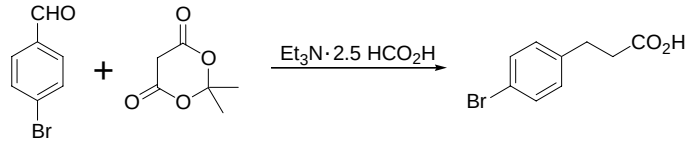


4-{3-[2-(Trimethylamino)ethylaminocarbonyl]propoxy}phenyl-4′,4″-dimethoxytritanol (10g). To a stirring solution of 2-aminoethyl-trimethylammonium chloride (69 mg, 0.5 mmol) in the mixture of pyridine (1 mL), acetonitrile (1 mL), and water (1 mL) 4-[3-(sulfosuccinimidooxycarbonyl)propoxy]phenyl-4′,4″-dimethoxytritanol, sodium salt, **8** (155 mg, 0.25 mmol) was added in one portion and the mixture was stirred for 6h, then diluted with $CHCl_3$ (50 mL), washed with water (100 mL), brine (100 mL), dried over Na_2SO_4, and evaporated to dryness. The residue was dissolved in acetone (2 mL) and precipitated in Et_2O to give pure 10b as white solid (95 mg, 70%). ESI-TOF HRMS: m/z = 490.2830 $[M–OH]^+$, calc. for $[C_{30}H_{38}N_2O_4]^+$ 490.2826. ^{1}H NMR (DMSO-d_6): 8.48 (m, 1H, NH); 7.21 (m, 2H, ArH); 7.06 (m, 4H, ArH); 6.90–6.80 (m, 6H, ArH); 6.09 (s, 1H, OH); 3.94 (m, 2H, OCH_2); 3.73 (s, 3H), 3.72 (s, 3H) (OCH_3); 3.48 (m, 2H, NHCH_2); 3.39 (m, 2H, NHCH$_2$CH_2); 3.11 (s, 9H, CCH_3); 2.29 (t, 2H, J = 7.2 Hz, COCH_2); 1.94 (m, 2H, COCH$_2$CH_2). ^{13}C NMR (DMSO-d_6): 172.26 (CO), 157.80 (2C, C4′,4″), 157.07 (C4), 140.57 (2C, C1′,1″), 136.21 (C1), 129.43 (2C, C2,6), 128.89 (4C, C2′,6′,2″,6″), 113.16 (2C, C3,5), 112.76 (4C, C3′,5′,3″,5″), 79.64 (Ar$_3$COH), 66.81, 55.06 (2C, 4′-OCH_3, 4″-OCH_3), 52.60, 33.10, 31.67, 29.64, 24.75.

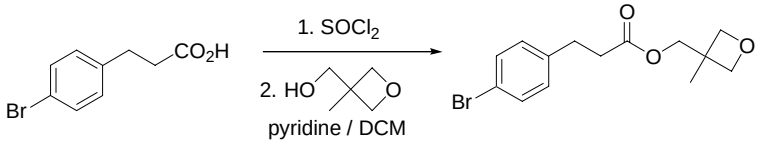


***N,N,N′,N′*-Tetrakis{2-[2-(4-{4-[bis(4-methoxyphenyl)hydroxymethyl]phenoxy}butyryl-amino)ethylaminocarbonyl]ethyl}ethylenediamine (10h).** To a stirring solution of *N,N,N',N'*-tetrakis[2-(2-aminoethylaminocarbonyl)ethyl]ethylenediamine (103 mg, 0.2 mmol) in the mixture of MeOH (1 mL), acetonitrile (1 mL), and water (1 mL) 4-[3-(sulfosuccinimidooxycarbonyl)propoxy]phenyl-4',4''-dimethoxytritanol, sodium salt, **8** (622 mg, 1.0 mmol) was added in one portion and the mixture was stirred for 6h, then diluted with $CHCl_3$ (50 mL), washed with water (2×100 mL), dried over Na_2SO_4, and evaporated to dryness. The residue was chromatographed on silica gel in 0→10% MeOH in Me_2CO to give 10h as white amorphous solid. Yield (326 mg, 76%). R_f 0.60 (acetone–MeOH, 1:1 + 0.5% Et_3N). ESI-TOF HRMS: m/z = 2116.0329 $[M–OH]^+$, calc. for $[C_{122}H_{143}N_{10}O_{23}]^+$ 2116.0322. ^{1}H NMR (DMSO-d_6): 7.92 (m, 4H,

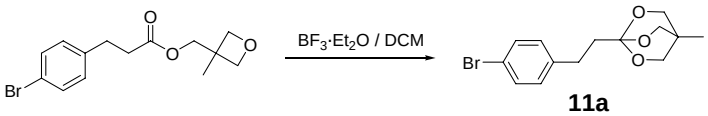
N*H*); 7.87 (m, 4H, N*H*); 7.20 (m, 8H, Ar*H*); 7.05 (m, 16H, Ar*H*); 6.88–6.78 (m, 24H, Ar*H*); 6.07 (br.s, 4H, O*H*); 3.91 (m, 8H, OCH_2); 3.71 (s, 24H, OCH_3); 3.07 (br.s, 16H, COCH_2CH_2N); 2.87 (s, 4H, NCH_2CH_2N); 2.61 (m, 8H, COCH_2); 2.19 (m, 16H, NHCH_2CH_2NH); 1.90 (m, 8H, OCH$_2$CH_2). ^{13}C NMR (DMSO-d_6): 171.79 (4C, CO), 171.56 (4C, CO), 157.92, 157.79, 157.28, 157.12, 140.58, 140.52, 136.27, 136.12, 129.46, 129.41, 128.89 (16C), 113.61, 113.26, 113.13, 112.74 (16C), 85.56, 79.64 (4C), 68.54, 66.90, 55.88, 55.03 (8C), 51.25, 50.95, 49.73, 38.45, 38.35, 33.51, 31.13, 31.82, 29.65, 24.91.



3-(4-Bromophenyl)propionic acid. 4-Bromobenzaldehyde (92.5 g, 0.50 mol) and Meldrum's acid (72.0 g, 0.50 mol) were dissolved in triethylamine–formic acid reagent[4] (1.5 L) and the mixture was refluxed for 20 h, then diluted with water (4 L) and acidified with 6N HCl (1 L) until pH reached 2. The precipitated solid was filtered off, washed with diluted HCl, and dissolved in 5% $NaHCO_3$. The aqueous salt solution was washed with ether (4x400 mL), filtered and acidified with diluted HCl. The resulting 3-(4-bromophenyl)propionic acid was filtered off and dried *in vacuo* over KOH and P_4O_{10}, yield 69.4 g (60 %). The compound was pure according to NMR. R_f 0.33 ($CHCl_3$–EtOAc, 9:1). An analytical sample was crystallyzed from toluene and showed mp 134ºC. NMR (DMSO-d_6): 9.52 (br. s, 1H, O*H*); 8.00 (d, 2H, J = 8.1 Hz, Ar*H*); 7.73 (d, 2H, J = 8.1 Hz, Ar*H*), 3.41 (t, 2H, J = 7.5 Hz, ArCH_2), 3.14 (t, 2H, J = 7.5 Hz, CH_2CO). The compound is also available from Aldrich.



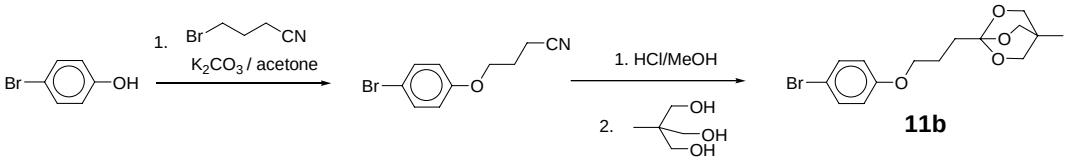
(3-Methyl-3-oxetanyl)methyl 3-(4-bromophenyl)propionate. 3-(4-Bromophenyl)propionic acid chloride was prepared in usual manner from 3-(4-bromophenyl)propionic acid (5.50 g, 24 mmol) and oxalyl chloride (4.2 ml, 50 mmol) in benzene (30 mL) with following evaporation. 3-Methyl-3-oxetanemethanol (2.30 ml, 23 mmol) and pyridine (3.8 mL, 48 mmol) were dissolved in DCM (50 mL) and crude 3-(4-bromophenyl)propionyl chloride in DCM (10 mL) was added dropwise within 30 min with stirring and cooling on a water bath. The mixture was stirred for 16 h, then diluted with $CHCl_3$ (200 mL), washed with water (2x200 mL), 5% $NaHCO_3$ (2x200 mL), 5% citric acid (3x100 mL) and 10% $NaHCO_3$ (100 mL), dried over Na_2SO_4, evaporated and chromatographed on silica gel in $CHCl_3$. Yield 5.90 g (82%). Colorless oil which solidifies upon storage, mp around 30ºC. R_f 0.20 (toluene–EtOAc, 9:1). NMR ($CDCl_3$): 7.39 (d, 2H, J = 8.2 Hz, Ar*H*); 7.07 (d, 2H, J = 8.2 Hz, Ar*H*); 4.44 (d, 2H, J = 6.0 Hz), 4.34 (d, 2H, J = 6.0 Hz) (CH_2OCH_2); 4.13 (s, 2H, CH_2OCO); 2.91 (t, 2H, J = 7.6 Hz, ArCH_2), 2.66 (t, 2H, J = 7.6 Hz, CH_2CO); 1.27 (s, 3H, CH_3).



11a

1-[2-(4-Bromophenyl)ethyl]-4-methyl-2,6,7-trioxabicyclo[2.2.2]octane (11a). 3-Methyl-3-oxetanyl)-methyl 3-(4-bromophenyl)propionate (31.32 g, 100 mmol) was dissolved in dry DCM (100 mL), cooled on NaCl–ice bath to -15ºC, and boron trifluoride diethyl etherate (3.1 mL, 25 mmol) was added in one portion. The mixture was stirred for 1h, then allowed to warm to room temperature, quenched with triethylamine (14 mL, 100 mmol) and diluted with diethyl ether (150 mL). The boron trifluoride–diethyl ether complex was filtered off, the solution was evaporated, and the residue was purified by flash chromatography on silica gel in toluene. Finally, the compound was crystallyzed from toluene–petroleum ether to give colorless needles (24.86 g,

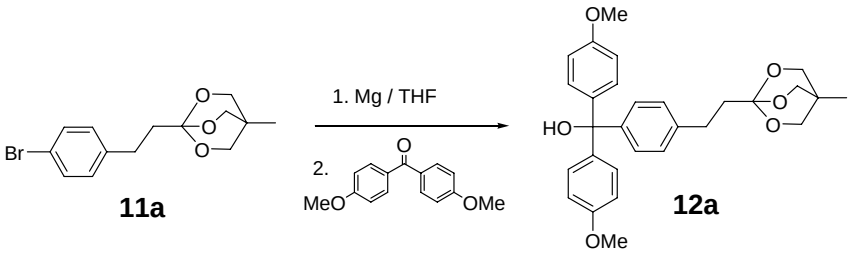
79%), mp 184ºC (toluene–petroleum ether). R_f 0.35 (toluene–EtOAc, 9:1). ESI-TOF HRMS: *m/z* = 313.0428 $[M+H]^+$, calc. for $[C_{14}H_{18}BrO_3]^+$ 313.0434. NMR (DMSO-d_6): 7.43 (d, 2H, *J* = 8.3 Hz, Ar*H*); 7.14 (d, 2H, *J* = 8.3 Hz, Ar*H*); 3.84 (s, 6H, CH_2O); 2.62 (m, 2H, ArCH_2); 1.82 (m, 2H, ArCH$_2$CH_2); 0.76 (s, 3H, CH_3).



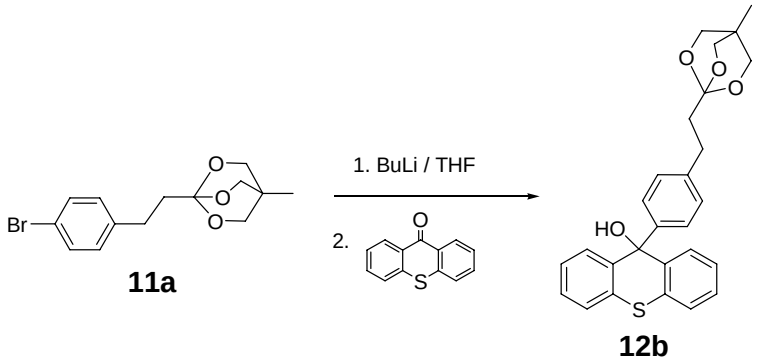
4-(4-Bromophenoxy)butyronitrile. To a solution of 4-bromophenol (17.3 g, 0.10 mol) in dry acetone (300 mL) dry K_2CO_3 (70 g, 0.5 mol) and 4-bromobutyronitrile (16.3 g, 0.11 mol) were added, and the mixture was refluxed for approximately 10h, until starting 4-bromophenol consumes (monitoring by TLC in $CHCl_3$). The mixture was cooled, filtered, and solid inorganic salts were washed with acetone. The combined filtrate was evaporated, and the residue was dissolved in $CHCl_3$ (100 mL), filtered again, and evaporated. The residue was triturated in petroleum ether, filtered, and dried *in vacuo* to give desired aryl alkyl ether (22.3 g, 93%) as colorless crystals, mp 62ºC, R_f 0.57 (toluene–EtOAc, 4:1). NMR (DMSO-d_6): 7.45 (d, 2H, *J* = 9.0 Hz, Ar*H*); 6.92 (d, 2H, *J* = 9.0 Hz, Ar*H*); 4.02 (t, 2H, *J* = 6.1 Hz, OCH_2); 2.64 (t, 2H, *J* = 7.1 Hz, CH_2CN); 2.01 (m, 2H, CH$_2$CH_2CH$_2$); NMR ($CDCl_3$): 7.37 (d, 2H, *J* = 8.9 Hz, Ar*H*); 6.77 (d, 2H, *J* = 8.9 Hz, Ar*H*); 4.03 (t, 2H, *J* = 5.7 Hz, OCH_2); 2.57 (t, 2H, *J* = 7.1 Hz, CH_2CN); 2.01 (m, 2H, CH$_2$CH_2CH$_2$).

1-[3-(4-Bromophenoxy)propyl]-4-methyl-2,6,7-trioxabicyclo[2.2.2]octane (11b). An ice cooled solution of 4-(4-bromophenoxy)butyronitrile (15.4 g, 64 mmol) in dry Et_2O (50 mL) and dry MeOH (2.6 mL, 64 mmol) was saturated with dry HCl within 3 h and then kept overnight at ambient temperature. The precipitate formed was filtered off, washed with Et_2O, and suspended in the mixture of Et_2O (70 mL) and MeOH (20 mL), then refluxed for 48 h and cooled. The solid was filtered off, the filtrate was evaporated, diluted with petroleum ether (100 mL) and filtered again. The filtrate was evaporated, dissolved in dry MeOH (30 mL), then 1,1,1-tris(hydrohymethyl)ethane (9.01 g, 75 mmol) and BF_3 etherate (0.15 mL, 1.1 mmol) were added. The mixture was stirred for 3 h, evaporated, and the residue was chromatographed on silica gel column in 0→5% EtOAc in toluene containing 1% Et_3N to yield the desired orthoester (6.13 g, 28%) as a colorless solid, mp 93ºC, R_f 0.55 (toluene–EtOAc, 4:1). ESI-TOF HRMS: *m/z* = 343.0548 $[M+H]^+$, calc. for $[C_{15}H_{20}BrO_4]^+$ 343.0539. NMR (DMSO-d_6): 7.41 (d, 2H, *J* = 8.9 Hz, Ar*H*); 6.87 (d, 2H, *J* = 8.9 Hz, Ar*H*); 3.94 (t, 2H, *J* = 6.3 Hz, ArOCH_2); 3.82 (s, 6H, OCH_2); 1.80–1.67 (m, 4H, OCH$_2$CH_2CH_2); 0.74 (s, 3H, CH_3).

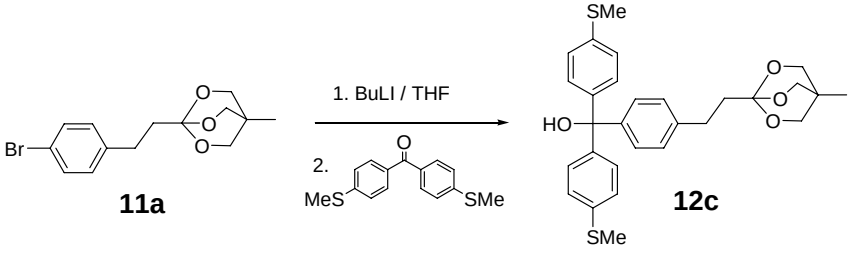
General procedure for preparation of tritanol orthoesters 12. To a stirred and coolled to -70ºC mixture of THF (20 mL) and 0.9 M BuLi in hexane (7.0 mL, 6.3 mmol) the solution of bromo orthoester **11a** or **11b** (5.0 mmol) in THF (50 mL) was added dropwise within 30 min. The mixture was then stirred for 30 min, and the solution of corresponding benzophenone (5.0 mmol) in THF (50 mL) was added dropwise within 30 min. The mixture was allowed to warm to room temperature and stirred overnight at ambient temperature. The solution was evaporated to dryness, the residue was dissolved in EtOAc (200 mL) with few drops of triethylamine, washed with 5% $NaHCO_3$ (2×200 mL), water (2×200 mL), dried over Na_2SO_4, and evaporated. The residue was dissolved in toluene containing 1% Et_3N (10 mL) and chromatographed on a silica gel column in appropriate solvent system. The desired product was triturated in petroleum ether filtered off and dried *in vacuo*.



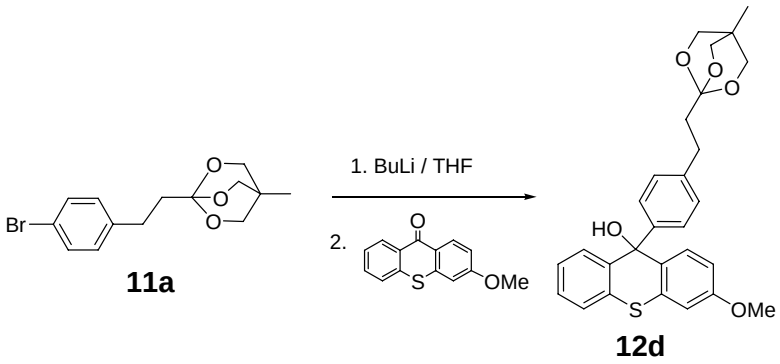
1-(2-{4-[Hydroxy-bis(4-methoxyphenyl)methyl]phenyl}ethyl)-4-methyl-2,6,7-trioxabicyclo-[2.2.2]octane (12a). **Method A.** Magnesium turnings (0.30 g, 12.5 mmol) was placed in a three-neck flask (250 mL) and activated by heating with a iodine crystal. The flask was then equipped with dropping funnel, reflux condenser, and argon inlet. THF (20 mL) was added to magnesium and 5–7 mL of the solution of 1-[2-(4-bromophenyl)ethyl]-4-methyl-2,6,7-trioxabicyclo[2.2.2]octane (3.13 g, 10 mmol) in THF (40 mL) was added. The mixture was heated under Ar near to boiling until a reaction started, then the remaining aryl bromide was added dropwise and the mixture was refluxed for 30 min. Using Ar pressure, the solution was filtered through glass wool in a 250 mL flask containing a solution of 4,4'-dimethoxybenzophenone (2.42 g, 10 mmol) in THF (40 mL). The mixture was refluxed for 2 h, then cooled, quenched with 5% $NaHCO_3$ (200 mL), and extracted with EtOAc (2x100 mL). The organic layer was separated, dried over Na_2SO_4, and evaporated. The residue was chromatographed on silica gel column (2→10% EtOAc in toluene containing 0.5% Et_3N). The resulting oil was triturated in petroleum ether to give the desired to give the desired tritanol (1.50 g, 31%) colorless crystals, mp 145ºC (dec.). R_f 0.44 (toluene–EtOAc, 1:1), R_f 0.14 (toluene–EtOAc, 9:1). ESI-TOF HRMS: *m/z* = 459.2175 $[M–OH]^+$, calc. for $[C_{29}H_{31}O_5]^+$ 459.2166. NMR (DMSO-d_6): 7.07 (m, 8H, Ar*H*); 6.83 (d, 4H, *J* = 8.8 Hz, Ar*H*); 6.11 (s, 1H, O*H*); 3.84 (s, 6H, CH_2O); 3.72 (s, 6H, OCH_3); 2.62 (m, 2H, $ArCH_2$); 1.81 (m, 2H, $ArCH_2CH_2$); 0.76 (s, 3H, CCH_3). **Method B.** Following the general procedure for compounds 12, tritanol **12a** was obtained in 85% yield.



3-[4-(9-Hydroxythioxanthen-9-yl)phenyl] propionic acid, *N*-oxysuccinimide ester (12b) was prepared from alkyl orthoester and thioxanthone. ESI-TOF HRMS: *m/z* = 429.1510 $[M–OH]^+$, calc. for $[C_{27}H_{25}O_3S]^+$ 429.1519. NMR (DMSO-d_6): 8.02 (d, 2H, *J* = 7.8 Hz, Ar*H* (thioxanthene)); 7.46–7.38 (m, 4H, Ar*H* (thioxanthene)); 7.35–7.28 (m, 2H, Ar*H* (thioxanthene)); 7.07 (d, 2H, *J* = 8.2 Hz, Ar*H* (phenyl)); 6.78 (m, 2H, Ar*H* (phenyl)); 5.75 (s, 1H, O*H*); 2.93–2.86 (m, 2H, $ArCH_2$); 2.85–2.74 (m, 6H, $ArCH_2CH_2$, $COCH_2CH_2CO$).

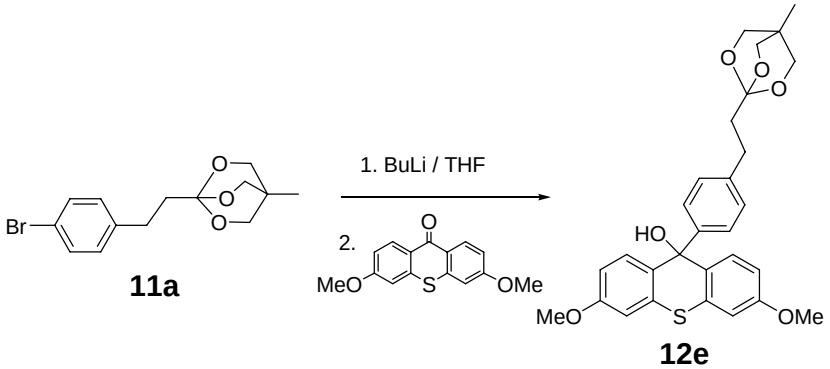


1-(2-{4-[Hydroxy-bis(4-methylthiophenyl)methyl]phenyl}ethyl)-4-methyl-2,6,7-trioxabicyclo[2.2.2]octane (12c) was prepared from 1-[2-(4-bromophenoxy)ethyl]-4-methyl-2,6,7-trioxabicyclo[2.2.2]octane (1.566 g, 5.0 mmol) and 4,4'-dimethylthiobenzophenone (1.372 g, 5.0 mmol). The compound was purified using stepwise gradient 2→2.5→3.5→4.0→4.5→5.0% Me_2CO in toluene containing 0.5% Et_3N. Yield 1.249 g (49.1%), amorphous solid. R_f 0.53 (toluene–EtOAc, 4:1). ESI-TOF HRMS: *m/z* = 491.1720 $[M–OH]^+$, calc. for $[C_{29}H_{31}O_3S_2]^+$ 491.1709. NMR (DMSO-d_6): 7.20–7.05 (m, 12H, Ar*H*); 6.30 (s, 1H, O*H*); 3.84 (s, 6H, CH_2O); 2.63 (m, 2H, $ArCH_2$); 2.44 (s, 6H, SCH_3); 1.81 (m, 2H, $ArCH_2CH_2$); 0.76 (s, 3H, CCH_3).



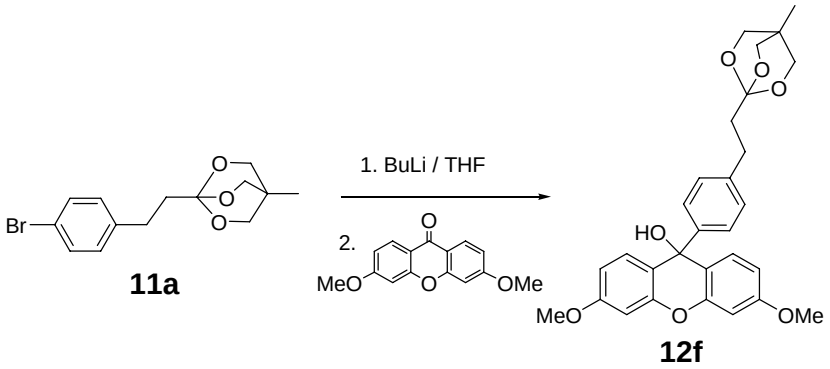
11a **12d**

1-{2-[4-(9-Hydroxy-3-methoxythioxanthen-9-yl)phenyl]ethyl}-4-methyl-2,6,7-trioxabicyclo-[2.2.2]octane (12d) was prepared from **11a** (845 mg, 2.70 mmol) and of 3-methoxythioxanthone[5] (653 g, 2.70 mmol). Purification in 10% acetone in toluene containing 0.5% Et_3N. Yield 1.14 g (94%), white amorphous solid. ESI-TOF HRMS: *m/z* = 459.1637 $[M–OH]^+$, calc. for $[C_{28}H_{27}O_4S]^+$ 459.1625. NMR (DMSO-d_6): 7.98 (d, 1H, *J* = 7.8 Hz, *H*–8 (thioxanthene)); 7.86 (d, 1H, *J* = 8.7 Hz, *H*–1 (thioxanthene)); 7.42–7.36 (m, 2H, *H*–5,7 (thioxanthene)); 7.29 (m, 1H, *H*–6 (thioxanthene)); 7.00–6.94 (m, 2H, ^4J = 2.6 Hz, *H*–2,4 (thioxanthene)); 6.93 (d, 2H, *J* = 8.0 Hz, Ar*H* (C_6H_4)); 6.77 (d, 2H, *J* = 8.0 Hz, Ar*H* (C_6H_4)); 6.63 (s, 1H, O*H*); 3.81 (s, 6H, OCH_2); 3.78 (s, 3H, OCH_3); 2.52 (m, 2H, $ArCH_2$); 1.71 (m, 2H, $ArCH_2CH_2$); 0.74 (s, 3H, CCH_3).

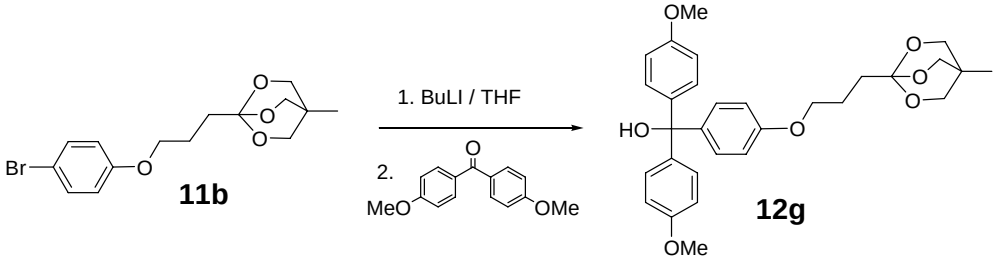


11a **12e**

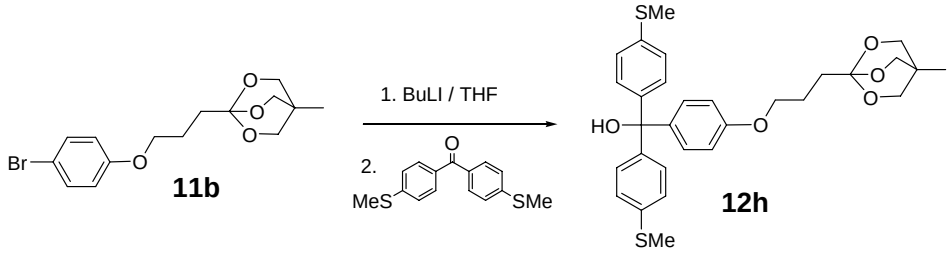
1-{2-[4-(9-Hydroxy-3,6-dimethoxythioxanthen-9-yl)phenyl]ethyl}-4-methyl-2,6,7-trioxa-bicyclo[2.2.2]octane (12e) was pepared from **11a** (313 mg, 1.00 mmol) and 3,6-dimethoxythioxanthone (272 mg, 1.00 mmol). The compound was chromatographed on silica gel in 10→15% acetone in toluene containing 0.5% Et_3N. Yield 415 mg (82%), white foam (from DCM). ESI-TOF HRMS: *m/z* = 489.1717 $[M–OH]^+$, calc. for $[C_{29}H_{29}O_5S]^+$ 489.1730. NMR (DMSO-d_6): 7.83 (d, 2H, *J* = 8.5 Hz, *H*–1,8 (thioxanthene)); 6.95 (m, 6H, *H*–2,4,5,7 (thioxanthene), Ar*H* (C_6H_4)); 6.79 (d, 2H, *J* = 7.8 Hz, Ar*H* (C_6H_4)); 6.53 (s, 1H, O*H*); 3.81 (s, 6H, OCH_2); 3.77 (s, 6H, OCH_3); 2.52 (m, 2H, $ArCH_2$); 1.71 (m, 2H, $ArCH_2CH_2$); 0.74 (s, 3H, CCH_3).



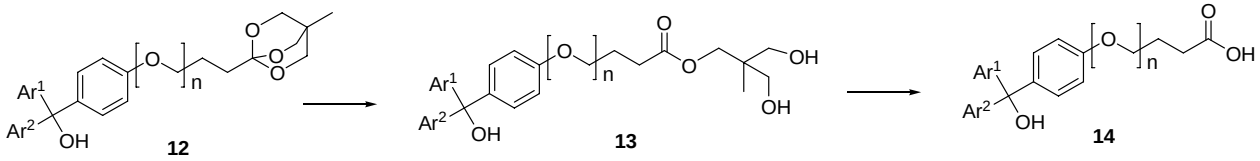
1-{2-[4-(9-Hydroxy-3,6-dimethoxyxanthen-9-yl)phenyl]ethyl}-4-methyl-2,6,7-trioxabicyclo-[2.2.2]octane (12f) was prepared from **11a** (5.86 g, 0.0187 mol) and 3,6-dimethoxyxanthone (4 g, 0.0187 mol). The compound was chromatographed on a silica gel. The column was eluted with 10% acetone in toluene containing 0.5% Et_3N. Yield 2.4 g, 31.3%. ESI-TOF HRMS: *m/z* = 473.1975 $[M–OH]^+$, calc. for $[C_{29}H_{29}O_6]^+$ 473.1959. ^1H NMR (200MHz, $CDCl_3$) δ 8.2 (d, *J* = 8.8 Hz, 1H), 7.4 (d, *J* = 8.4 Hz, 1H), 6.8 (m, 7H), 6.5 (m, 1H), 3.8 (m, 12H), 2.7 (m, 2H), 2 (m, 2H), 0.8 (s, 3H).



1-(3-{4-[Hydroxy-bis(4-methoxyphenyl)methyl]phenoxy}propyl)-4-methyl-2,6,7-trioxa-bicyclo[2.2.2]octane (12g) was prepared from 1-[3-(4-bromophenoxy)propyl]-4-methyl-2,6,7-trioxabicyclo[2.2.2]octane **11b** (1.716 g, 5.0 mmol) and 4,4'-dimethoxybenzophenone (1.211 g, 5.0 mmol). The trityl orthoester was purified on silica gel using stepwise gradient 5→10→15% EtOAc in toluene containing 1% Et_3N. The desired product was triturated in petroleum ether filtered off and dried *in vacuo*. Yield 720 mg (28%), colorless crystals, mp 132ºC (dec.). R_f 0.40 (toluene–EtOAc, 1:1). ESI-TOF HRMS: *m/z* = 489.2284 $[M–OH]^+$, calc. for $[C_{30}H_{33}O_6]^+$ 489.2272.



1-(3-{4-[Hydroxy-bis(4-methylthiophenyl)methyl]phenoxy}propyl)-4-methyl-2,6,7-trioxa-bicyclo[2.2.2]octane (12h) was prepared from **11b** (1.716 g, 5.0 mmol) and 4,4'-bis(methylthio)benzophenone (1.372 g, 5.0 mmol). The desired tritanol ortho ester was isolated by a column chromatography. The column was eluted with stepwise gradient 8→12→15% EtOAc in toluene containing 1% Et_3N. The isolated **12h** (810 mg, 1.5 mmol, 30% yield) was used in the next step without purification.

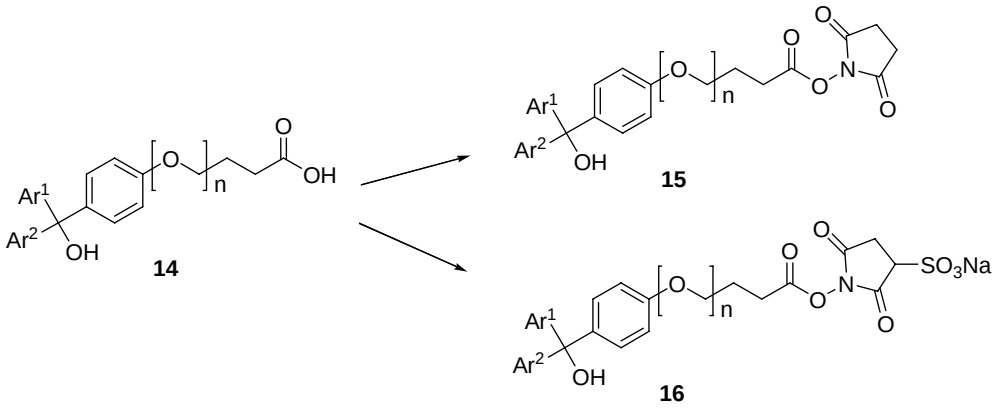


General procedure for preparation of tritanol acids 14. Orthoester **12** (5.0 mmol) was dissolved in the THF–water mixture (9:1, 10 mL), and trifluoroacetic acid (0.77 mL, 10 mmol) was added. After stirring for 10 min the mixture was evaporated and diluted with 10 % NaOH in ethanol–water (8:2, 30mL). The reaction mixture was refluxed for 30 min, cooled, and evaporated, the residue was diluted with water (50 mL), washed with Et_2O (2×50 mL), filtered, acidified with 5% oxalic acid, and extracted with ethyl acetate (3×50 mL). The solution was dried with Na_2SO_4, evaporated, and the residue was purified by column chromatography in an appropriate solvent system.

Intermediate diolesters isolated by chromatography:

3-{4-[Hydroxy-bis(4-methoxyphenyl)methyl]phenyl}propionic acid, 2-hydroxymethyl-2-methyl-3-hydroxypropyl ester (13a), colorless oil. ESI-TOF HRMS: *m/z* = 477.2261 $[M–OH]^+$, calc. for $[C_{29}H_{33}O_6]^+$ 477.2272. NMR (DMSO-d_6): 7.15–7.04 (m, 8H, Ar*H*); 6.83 (m, 4H, Ar*H*); 6.13 (s, 1H, CO*H*); 4.44 (t, 2H, *J* = 5.4 Hz, CH_2OH); 3.87 (s, 2H, CH_2OCO); 3.72 (s, 6H, OCH_3); 3.24 (m, 4H, CH_2OH); 2.83 (t, 2H, *J* = 7.6 Hz, $ArCH_2$); 2.61 (t, 2H, *J* = 7.6 Hz, $COCH_2$); 0.74 (s, 3H, CCH_3).

3-{4-[Hydroxy-bis(4-methylthiophenyl)methyl]phenyl}propionic acid 2-hydroxymethyl-2-methyl-3-hydroxypropyl ester (13c) was obtained as a colorless oil, yield 895 mg (85%). ESI-TOF HRMS: *m/z* = 509.1829 $[M–OH]^+$, calc. for $[C_{29}H_{33}O_4S_2]^+$ 509.1815. NMR (DMSO-d_6): 7.20–7.07 (m, 12H, Ar*H*); 6.32 (s, 1H, trityl O*H*); 4.43 (m, 2H, CH_2OH); 3.87 (s, 2H, CH_2OCO); 3.24 (m, 4H, CH_2OH); 2.84 (m, 2H, $ArCH_2$); 2.62 (m, 2H, CH_2CO); 2.44 (s, 6H, SCH_3); 0.74 (s, 3H, CCH_3).



Acids **14** were converted to the activated esters **15** and **16** using general procedures for corresponding esters **7** and **8**.

3-{4-[Hydroxy-bis(4-methoxyphenyl)methyl]phenyl}propionic acid, *N*-oxysuccinimide ester (15a) was prepared from **12a** (2.38 g, 5.0 mmol) and purified by column chromatography (10 to 40% EtOAc in toluene). Yield 2.05 g (86%), white amorphous solid. R_f 0.31 (toluene–EtOAc, 1:1). ESI-TOF HRMS: *m/z* = 472.1770 $[M–OH]^+$, calc. for $[C_{28}H_{26}NO_6]^+$ 472.1755. NMR (DMSO-d_6): 7.20 (d, 2H, *J* = 8.3 Hz, Ar*H*); 7.12–7.05 (m, 6H, Ar*H*); 6.83 (d, 4H, *J* = 9.0 Hz, Ar*H*); 6.15 (s, 1H, O*H*); 3.73 (s, 6H, OCH_3); 3.02–2.90 (m, 4H, $ArCH_2CH_2$); 2.81 (s, 4H, $COCH_2CH_2CO$).

3-{4-[Hydroxy-bis(4-methylthiophenyl)methyl]phenyl}propionic acid, *N*-oxysuccinimide ester (15c) 1-(2-{4-[Hydroxy-bis(4-methylthiophenyl)methyl]phenyl}ethyl)-4-methyl-2,6,7-

trioxabicyclo-[2.2.2]octane (1.08 g, 2.0 mmol) was dissolved in the THF–water mixture (19:1, 10mL), and trifluoroacetic acid (0.08 mL, 1 mmol) was added. After stirring for 10 min the mixture was evaporated, the residue was dissolved with EtOAc (200 mL), washed with 5% $NaHCO_3$ (100 mL) and water (2×100 mL), dried over Na_2SO_4, evaporated, and chromatographed on silica gel column in 10 → 40% Me_2CO in toluene to give **3-{4-[hydroxy-bis(4-methylthiophenyl)methyl]phenyl}propionic acid 2-hydroxymethyl-2-methyl-3-hydroxypropyl ester (13c)** as a colorless oil, yield 895 mg (85%). ESI-TOF HRMS: *m/z* = 509.1804 $[M–OH]^+$, calc. for $[C_{29}H_{33}O_4S_2]^+$ 509.1815. NMR (DMSO-d_6): 7.20–7.07 (m, 12H, Ar*H*); 6.32 (s, 1H, trityl O*H*); 4.43 (m, 2H, CH_2OH); 3.87 (s, 2H, CH_2OCO); 3.24 (m, 4H, CH_2OH); 2.84 (m, 2H, $ArCH_2$); 2.62 (m, 2H, CH_2CO); 2.44 (s, 6H, SCH_3); 0.74 (s, 3H, CCH_3). The ester was dissolved in 10% NaOH in ethanol–water (8:2, 10mL), stirred overnight, then evaporated, coevaporated with water (2×50 mL), dissolved in water (100 mL), washed with ether (2×100 mL), and then acidified with solid citric acid to pH 4. The reaction mixture was extracted with EtOAc (2×100 mL), the combined organic layers were washed with water (50 mL), dried over Na_2SO_4 and evaporated to dryness. The resulting **3-{4-[hydroxy-bis(4-methylthiophenyl)methyl]phenyl}propionic acid (14c)** was obtained as a colorless oil, 637 mg (88%). ESI-TOF HRMS: *m/z* = 407.1140 $[M–OH]^+$, calc. for $[C_{24}H_{23}O_2S_2]^+$ 407.1134. NMR (DMSO-d_6): 12.09 (s, 1H, CO_2H); 7.20–7.08 (m, 12H, Ar*H*); 6.32 (s, 1H, trityl O*H*); 2.81 (m, 2H, $ArCH_2$); 2.52 (m, 2H, CH_2CO); 2.44 (s, 6H, SCH_3). This was dissolved in anhydrous DCM (20 mL) and triethylamine (0.35 mL, 2.5 mmol) and *N*,*N*'-disuccinimidyl carbonate (512 g, 2.0 mmol) were added and the mixture was stirred until the reaction is complete (monitoring by TLC in toluene–EtOAc, 1:1), then evaporated, dissolved in EtOAc (200 mL), washed with 5% $NaHCO_3$ (100 mL) and water (100 mL), dried over Na_2SO_4, evaporated, and the residue was purified by column chromatography (5 to 10% EtOAc in toluene). Yield 542 mg (69%), white crystalline solid, mp 137ºC. R_f 0.36 (toluene–EtOAc, 4:1). ESI-TOF HRMS: *m/z* = 504.1282 $[M–OH]^+$, calc. for $[C_{28}H_{26}NO_4S_2]^+$ 504.1298. NMR (DMSO-d_6): 7.24–7.10 (m, 12H, Ar*H*); 6.34 (s, 1H, O*H*); 3.02–2.91 (m, 4H, $ArCH_2CH_2$); 2.81 (s, 4H, $COCH_2CH_2CO$); 2.45 (s, 6H, SCH_3).

3-[4-(9-Hydroxy-3-methoxythioxanthen-9-yl)phenyl] propionic acid, *N*-oxysuccinimide ester (15d). 1-{2-[4-(9-Hydroxy-3-methoxythioxanthen-9-yl)phenyl]ethyl}-4-methyl-2,6,7-trioxabicyclo[2.2.2]octane (1.14 g, 2.54 mmol) was dissolved in the THF–water mixture (4:1, 60 mL), and trifluoroacetic acid (290 μL, 3.82 mmol) was added. After stirring for 1 h the mixture was half evaporated, the residue was dissolved with EtOAc (100 mL), washed with 5% $NaHCO_3$ (100 mL) and water (2×100 mL), dried over Na_2SO_4 and evaporated. The residue was dissolved in EtOH (120 mL), and NaOH (1.22 g, 30.5 mmol) was added. The solution was stirred overnight at ambient temperature, filtered and evaporated. The residue was dissolved in water (100 mL), washed with EtOAc (50 mL), acidified with solid citric acid to pH 3, and extracted with EtOAc (3×50 mL). Combined organic layers were dried over Na_2SO_4 and evaporated to volume 30 mL. Triethylamine (1.76 mL, 13.7 mmol) and *N*,*N*′-disuccinimidyl carbonate (1.95 g, 7.60 mmol) were added and the mixture was stirred until the reaction is complete (monitoring by TLC), then dissolved in EtOAc (50 mL), washed with 5% $NaHCO_3$ (2×50 mL) and water (50 mL), dried over Na_2SO_4, evaporated, and the residue was purified by column chromatography (15% EtOAc in toluene). Yield 528 mg (45%), white amorphous solid. ESI-TOF HRMS: *m/z* = 472.1208 $[M–OH]^+$, calc. for $[C_{27}H_{22}NO_5S]^+$ 472.1213. NMR (DMSO-d_6): 7.99 (d, 1H, *J* = 7.8 Hz, Ar*H* (thioxanthene)); 7.87 (d, 1H, *J* = 8.7 Hz, *H*-1 (thioxanthene)); 7.39 (m, 2H, Ar*H* (thioxanthene)); 7.29 (m, 1H, Ar*H* (thioxanthene)); 7.07 (d, 2H, *J* = 8.2 Hz, Ar*H* (C_6H_4)); 7.00 (d, 1H, *J* = 2.5 Hz, *H*-4 (thioxanthene)); 6.96 (dd, 1H, *J* = 8.7 Hz, ^4J = 2.5 Hz, *H*-2 (thioxanthene)); 6.81 (d, 2H, *J* = 8.2 Hz, Ar*H* (C_6H_4)); 6.67 (s, 1H, O*H*); 3.79 (s, 3H, OCH_3); 2.90 (m, 2H, $ArCH_2$); 2.81 (m, 6H, $COCH_2$).

3-[4-(9-Hydroxy-3,6-dimethoxythioxanthen-9-yl)phenyl] propionic acid, *N*-oxysuccinimide ester (15e). 1-{2-[4-(9-Hydroxy-3,6-dimethoxythioxanthen-9-yl)phenyl]ethyl}-4-methyl-2,6,7-

trioxabicyclo[2.2.2]octane (253 mg, 0.50 mmol) was dissolved in the THF–water mixture (4:1, 20 mL), and trifluoroacetic acid (76 μL, 1.0 mmol) was added. After stirring for 1 h the mixture was half evaporated, the residue was dissolved with EtOAc (50 mL), washed with 5% $NaHCO_3$ (50 mL) and water (2×50 mL), dried over Na_2SO_4 and evaporated. The residue was dissolved in EtOH (40 mL), and NaOH (0.61 g, 15 mmol) was added. The solution was stirred overnight at ambient temperature, filtered and evaporated. The residue was dissolved in water (50 mL), washed with EtOAc (50 mL), acidified with solid citric acid to pH 3, and extracted with EtOAc (3×10 mL). Combined organic layers were dried over Na_2SO_4 and evaporated. Triethylamine (0.59 mL, 4.5 mmol) and *N*,*N*′-disuccinimidyl carbonate (256 mg, 1.0 mmol) were added and the mixture was stirred until the reaction is complete (monitoring by TLC), then dissolved in EtOAc (50 mL), washed with 5% $NaHCO_3$ (2×50 mL) and water (50 mL), dried over Na_2SO_4, evaporated, and the residue was purified by column chromatography (15→20% EtOAc in toluene). Yield 159 mg (61%), white amorphous solid. ESI-TOF HRMS: *m/z* = 502.1328 $[M–OH]^+$, calc. for $[C_{28}H_{24}NO_6S]^+$ 502.1319. NMR (DMSO-d_6): 7.84 (d, 2H, *J* = 8.2 Hz, *H*–1,8 (thioxanthene)); 7.06 (d, 2H, *J* = 8.2 Hz, Ar*H* (phenyl)); 6.98–6.92 (m, 4H, *H*–2,4,5,7 (thioxanthene)); 6.84 (d, 2H, *J* = 8.2 Hz, Ar*H* (phenyl)); 6.57 (s, 1H, O*H*); 3.78 (s, 6H, CH_3); 2.89 (m, 2H), 2.82 (m, 2H) (ArCH_2CH_2); 2.79 (br.s, 4H, COCH_2CH_2CO).

3-[4-(9-Hydroxy-3,6-dimethoxyxanthen-9-yl)phenyl] propionic acid, *N*-oxysuccinimide ester (15f). 2 g of starting material (4.07 mmol) was dissolved in the THF-water mixture (4:1, 60 mL), and trifluoroacetic acid (374 μL, 4.89 mmol) was added. After stirring for 1 h the mixture was half evaporated, the residue was dissolved with EtOAc (100 mL), washed with 5% $NaHCO_3$ (100 mL) and water (2×100 mL), dried over Na_2SO_4 and evaporated. The residue was dissolved in EtOH (120 mL), and NaOH (1.22 g, 30.5 mmol) was added. The solution was stirred overnight at ambient temperature, filtered and evaporated. The residue was dissolved in water (100 mL), washed with EtOAc (50 mL), acidified with solid citric acid to pH 3, and extracted with EtOAc (3×50 mL). Combined organic layers were dried over Na_2SO_4 and evaporated to volume 30 mL. Triethylamine (2.26 mL, 0.162 mol) and *N*,*N*′-disuccinimidyl carbonate (1.35 g, 5.27 mmol) were added and the mixture was stirred until the reaction is complete (monitoring by TLC), then dissolved in EtOAc (50 mL), washed with 5% $NaHCO_3$ (2×50 mL) and water (50 mL), dried over Na_2SO_4, evaporated, and the residue was purified by column chromatography (15% EtOAc in toluene). Yield 1.45 g, 71%. ESI-TOF HRMS: *m/z* = 486.1559 $[M–OH]^+$, calc. for $[C_{28}H_{24}NO_7]^+$ 486.1547. ^{1}H NMR (200MHz, $CDCl_3$) δ 7 (m, 8H), 6.5 (m, 2H), 3.6 (s, 6H), 2.8 (s, 4H), 2.7 (m, 2H).

4-{4-[Hydroxy-bis(4-methoxyphenyl)methyl]phenoxy}butanoic acid, *N*-oxysuccinimide ester (15g). 1-(3-{4-[Hydroxy-bis(4-methoxyphenyl)methyl]phenoxy}propyl)-4-methyl-2,6,7-trioxabicyclo-[2.2.2]octane (1.01 g, 2.0 mmol) was dissolved in the THF–water mixture (4:1, 50 mL), and trifluoroacetic acid (0.23 mL, 3 mmol) was added. After stirring for 1 h the mixture was half evaporated and diluted with EtOAc (200 mL), washed with water (100 mL), 5% $NaHCO_3$ (2×100 mL), evaporated. The resudue was dissolved in EtOH (100 mL), and NaOH (1.0 g, 25 mmol) was added and dossolved in the mixture. The solution was stirred overnight at ambient temperature, filtered and evaporated. The residue was dissolved in water (200 mL), washed with Et_2O (2×100 mL), acidified with solid citric acid to pH 3.5, and extracted with EtOAc (3×100 mL). A combined organic lauer was dried over Na_2SO_4 and evaporated to volume 20 mL. Triethylamine (0.7 mL, 5.0 mmol) and *N*,*N*′-disuccinimidyl carbonate (0.64 g, 2.5 mmol) were added and the mixture was stirred until the reaction is complete (monitoring by TLC in toluene–acetone, 2:1), then evaporated, dissolved in EtOAc (200 mL), washed with 5% $NaHCO_3$ (100 mL) and water (100 mL), dried with Na_2SO_4, evaporated, and the residue was purified by column chromatography (10 to 30% EtOAc in toluene). Yield 0.800 g (77%), white amorphous solid. R_f 0.30 (toluene–EtOAc, 1:1). ESI-TOF HRMS: *m/z* = 502.1848 $[M–OH]^+$, calc. for $[C_{29}H_{28}NO_7]^+$ 502.1860.

4-{4-[Hydroxy-bis(4-methylthiophenyl)methyl]phenoxy}butyric acid, *N*-oxysuccinimide ester (15h). To a stirred and coolled to -70ºC mixture of THF (40 mL) and 0.9M BuLi in hexane (11.1 mL, 10 mmol) the solution of 1-[3-(4-Bromophenoxy)propyl]-4-methyl-2,6,7-trioxabicyclo[2.2.2]octane (1.716 g, 5.0 mmol) in THF (50 mL) was added dropwise within 30 min. The mixture was left for 1h at -70ºC and the solution of 4,4′-bis(methylthio)benzophenone (1.372 g, 5.0 mmol) in THF (50 mL) was added dropwise within 30 min. The mixture was allowed to warm to room temperature and stirred overnight at ambient temperature. The solution was evaporated to dryness, the residue was dissolved in EtOAc (200 mL), washed with 5% $NaHCO_3$ (2×200 mL), water (2×200 mL), dried with Na_2SO_4, and evaporated. The residue was dissolved in toluene containing 1% Et_3N (10 mL) and the desired tritanol ortho ester was isolated by a column chromatography. The column was eluted with stepwise gradient 8→12→15% EtOAc in toluene containing 1% Et_3N. The isolated 1-(3-{4-[hydroxy-bis(4-methylthiophenyl)methyl]phenyl}propoxy)-4-methyl-2,6,7-trioxabicyclo[2.2.2]octane (810 mg, 1.5 mmol, 30% yield) was dissolved in the THF–water mixture (19:1, 10mL), and trifluoroacetic acid (0.08 mL, 1 mmol) was added. After stirring for 10 min the mixture was evaporated, the residue was dissolved with EtOAc (200 mL), washed with 5% $NaHCO_3$ (100 mL) and water (2×100 mL), dried over Na_2SO_4, evaporated, diluted with 10 % NaOH in ethanol–water (8:2, 10mL), stirred overnight, then evaporated, coevaporated with water (2×50 mL), dissolved in water (100 mL), washed with ether (2×100 mL), and then acidified with solid citric acid to pH 4. The reaction mixture was extracted with EtOAc (2x100 mL), the combined organic layers were washed with water (50 mL), dried over Na_2SO_4 and evaporated to dryness. The resulting acid was dissolved in dry DCM (30 mL). Triethylamine (0.7 mL, 5 mmol) and *N*,*N*'-disuccinimidyl carbonate (0.51 g, 2.0 mmol) were added and the mixture was stirred until the reaction is complete (monitoring by TLC in toluene–EtOAc, 1:1), then evaporated, dissolved in EtOAc (200 mL), washed with 5% $NaHCO_3$ (100 mL) and water (100 mL), dried with Na_2SO_4, evaporated, and the residue was purified by column chromatography (10 to 40% EtOAc in toluene). Yield 348 mg (42% from ortho ester), white amorphous solid. ESI-TOF HRMS: *m/z* = 534.1415 $[M–OH]^+$, calc. for $[C_{29}H_{28}NO_5S_2]^+$ 534.1403. NMR (DMSO-d_6): 7.18 (d, 4H, *J* = 8.5 Hz, Ar*H*); 7.12 (d, 4H, *J* = 8.5 Hz, Ar*H*); 7.07 (d, 2H, *J* = 8.9 Hz, Ar*H*); 6.87 (d, 2H, *J* = 8.9 Hz, Ar*H*); 6.27 (s, 1H, O*H*); 4.03 (t, 2H, *J* = 6.2 Hz, OCH_2); 2.87–2.79 (m, 6H, COCH_2, COCH_2CH_2CO); 2.45 (s, 6H, CH_3); 2.10–2.03 (m, 2H, $CH_2CH_2CH_2$).

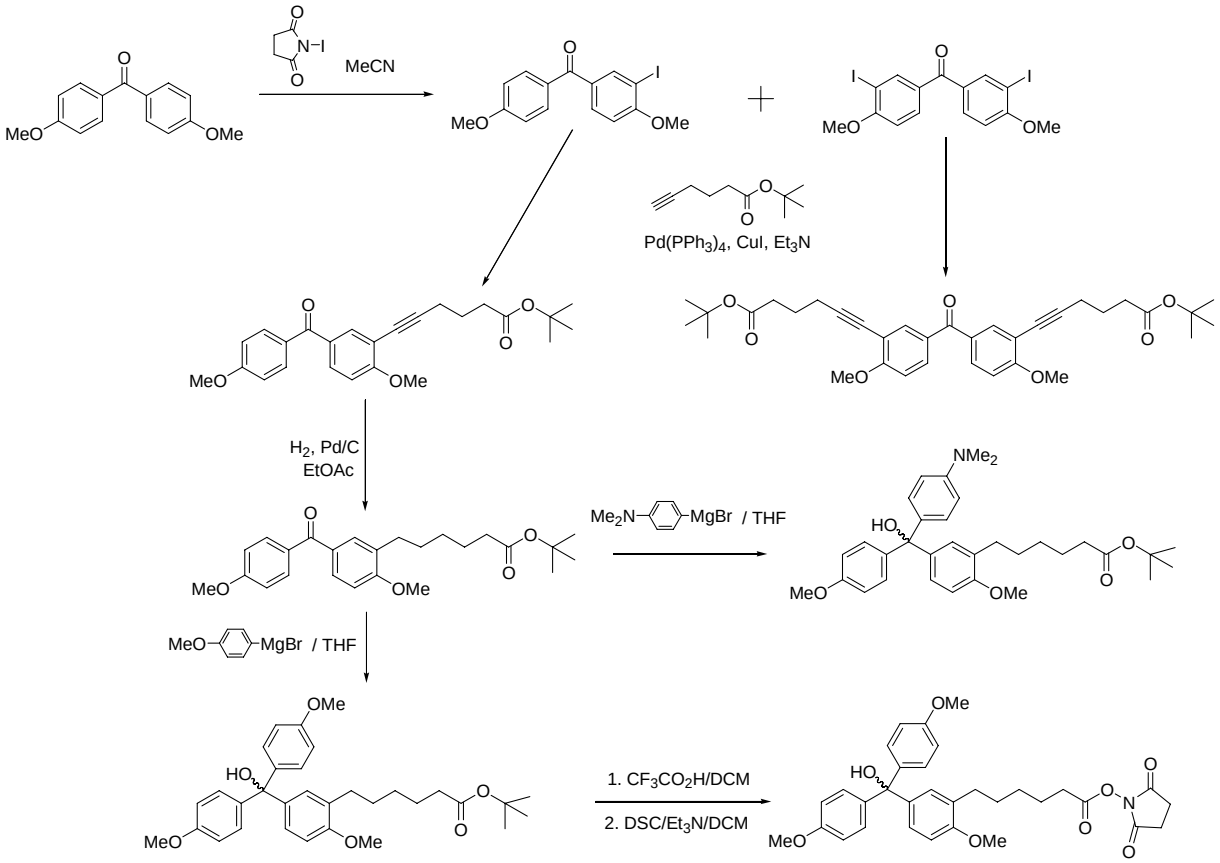
3-{4-[Hydroxy-bis(4-methoxyphenyl)methyl]phenyl}propionic acid, *N*-oxysulfosuccinimide ester, sodium salt (16a) was prepared from **14a** (0.96 g, 2.0 mmol) using the general procedure for oxysulfosuccinimide esters. Yield 793 mg (67%), brown solid, R_f 0.54 (*n*-propanol–EtOAc–water, 8:1:1).

3-{4-[Hydroxy-bis(4-methylthiophenyl)methyl]phenyl}propionic acid, *N*-oxysulfosuccinimide ester, sodium salt (16b) was prepared from **14c** (425 mg, 1.0 mmol). Yield 412 mg (66%), white solid, R_f 0.58 (*n*-propanol–EtOAc–water, 8:1:1). ESI-TOF HRMS: *m/z* = 606.0697 $[M–OH]^+$, calc. for $[C_{28}H_{25}NNaO_7S_3]^+$ 606.0685. NMR (DMSO-d_6): 7.24–7.08 (m, 12H, Ar*H*); 6.35 (s, 1H, O*H*); 3.94 (br., 1H, COC*H*S); 3.15 (br. s, 1H, COCH*H*CHS); 3.02–2.83 (m, 5H, ArCH_2CH_2, COC*H*HCHS); 2.45 (s, 6H, SCH_3).

***N,N′*-Bis(3-{4-[bis(4-methoxyphenyl)hydroxymethyl]phenyl}propionyl)ethylenediamine (17c).** The acid **14a** (200 mg, 0.51 mmol) and HATU were dissolved in DMF (5 mL), following DIEA (174 μL; 1.0 mmol) was added and the reaction mixture was left for 5 min at ambient temperature. After that this solution was added by one portion into the solution of ethylene diamine (16.7 μL; 0.25 mmol) in DMF (3 ml) and the reaction mixture was left for 1 h. TLC showed completion of the reaction (R_f 0.21; 30% acetone in PhMe + 0.5% Et_3N). The reaction was diluted with ethylacetate (150 mL), washed with water (2×100 mL) and brine (100 mL). Organic layer was dried over Na_2SO_4 and evaporated. The residue was separated by column chromatography. The target product was obtained as white solid. Yield 186 mg (92%). ESI-TOF HRMS: *m/z* = 791.3702 $[M–OH]^+$, calc. for $[C_{50}H_{51}N_2O_7]^+$ 791.3691. ^{1}H NMR (DMSO-d_6): 7.82

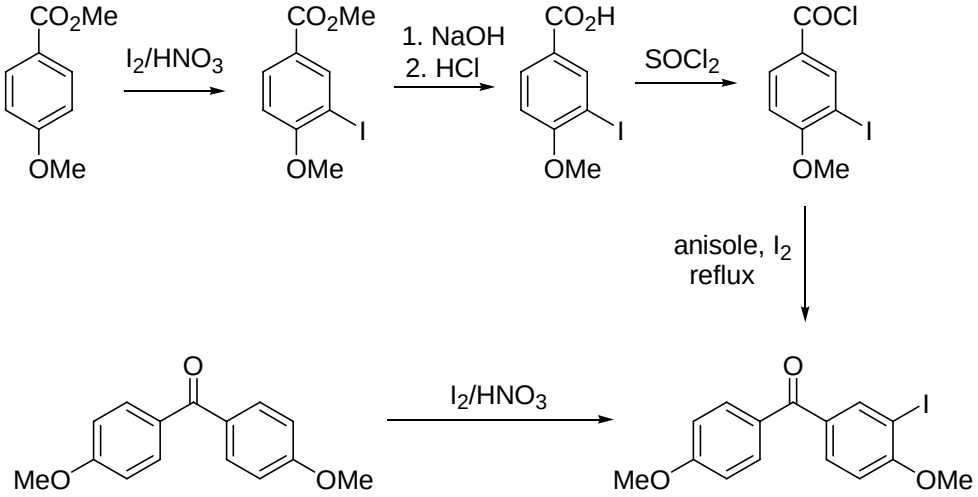
(m, 2H, N*H*); 7.09–7.05 (m, 16H, Ar*H*); 6.84–6.80 (m, 8H, Ar*H*); 6.12 (br.s, 2H, O*H*); 3.72 (s, 12H, OCH_3); 3.04 (m, 4H), 2.79 (m, 4H), 2.34 (m, 4H) (CH_2). ^{13}C NMR (DMSO-d_6): 171.50 (2C, CO), 157.83 (4C), 146.04 (2C), 140.41 (4C), 139.40 (2C), 128.92 (8C), 128.30, 128.21, 127.68 (2C), 127.26 (2C), 112.78 (8C), 79.82 (2C), 55.05 (4C), 38.37 (2C), 37.11, 37.03 (2C), 31.09, 30.67 (2C).

1,3,5-Tris[3-(2-{4-[bis(4-methoxyphenyl)hydroxymethyl]phenyl}ethylcarbonylamino)-propylaminocarbonyl]benzene (17d). A solution of activated ester **15a** (245 mg, 0.50 mmol) in DCM (300 mL) was added dropwise to a solution of 1,3-diaminopropane (7.40 g, 100 mmol) in DCM (300 mL) within 2 h and the mixture was stirred further for 2 h. The resulting solution was washed with water (15×100 mL), dried over Na_2SO_4 and evaporated. The residue was dissolved in DCM (10 mL) and trimesic chloride (26.5 mg, 0.1 mmol) was added in one portion. The mixture was stirred for 6 h, after that it diluted with ethyl acetate (200 mL) and successively washed with 5% $NaHCO_3$ (2×100 mL) and water (2×100 mL). The organic layer was dried over Na_2SO_4 and evaporated. The residue was cromatographed on silica gel (eluent PhMe–acetone 1:1 + 1% Et_3N) to give target product as white solid. Yield 132 mg (88%). R_f 0.44 (acetone + 0.5% Et_3N). ESI-TOF HRMS: *m/z* = 1483.6917 $[M–OH]^+$, calc. for $[C_{90}H_{95}N_6O_{14}]^+$ 1483.6901. ^{1}H NMR ([D$_6$]DMSO): 8.67 (t, 3H, *J* = 5.5 Hz, N*H*); 8.41 (s, 3H, Ar*H*); 7.84 (t, 3H, *J* = 5.6 Hz, N*H*); 7.13–7.04 (m, 24H, Ar*H*); 6.82 (d, 12H, *J* = 8.9 Hz, Ar*H*); 6.11 (br.s, 3H, O*H*); 3.26 (m, 6H), 3.10 (m, 6H) (NHCH_2); 2.78 (t, 6H, *J* = 7.6 Hz, ArCH_2); 2.36 (m, 6H, COCH_2); 1.65 (m, 6H, NHCH$_2$CH_2). ^{13}C NMR (DMSO-d_6): 171.35 (3C, CO), 165.49 (3C, CO), 157.82 (6C), 146.02 (2C), 140.40 (C), 139.44 (C), 135.07, 128.91 (12C), 128.40, 127.69 (C), 127.26 (C), 112.77 (12C), 79.81 (3C), 68.55, 55.88, 55.02 (6C), 45.73, 37.25, 37.09, 36.44, 32.13, 30.78, 29.65, 29.19.



4,4′-Dimethoxybenzophenone (2.42 g, 10 mmol) was iodinated with *N*-iodosuccinimide (2.24 g, 10 mmol) in boiling acetonitrile (200 mL) in the presence of trifluoroacetic acid (0.2 mL). After 5 h the mixture was cooled, evaporated, and neutralized with 5% $NaHCO_3$. The residue was dissolved in EtOAc (150 mL), washed with water (2×50 mL), dried over Na_2SO_4, evaporated and chromatographed in toluene. A sample (140 mg) of **3,3′-diiodo-4,4′-**

dimethoxybenzophenone was isolated. NMR (DMSO-d_6): 8.10 (d, 2H, $J_{2,6} = J_{2',6'} = 2.0$ Hz, Ar*H*); 7.74 (dd, 2H, $J_{2,6} = J_{2',6'} = 2.0$ Hz, $J_{5,6} = J_{5',6'} = 8.5$ Hz, Ar*H*); 7.15 (d, 2H, $J_{5,6} = J_{5',6'} = 8.5$ Hz, Ar*H*); 3.94 (s, 6H, OCH_3). The resulting mixture of 3-iodo-4,4'-dimethoxybenzophenone and 3,3'-diiodo-4,4'-dimethoxybenzophenone (3.55 g) was dissolved in DMF (100 mL) and *tert*-butyl 5-hexynoate (2.02 g, 12.0 mmol), triethylamine (3.34 mL, 24 mmol), $Pd(PPh_3)_4$ (925 mg, 0.8 mmol) and CuI (305 mg, 1.6 mmol) were added, and the reaction mixture was stirred for 24 h at room temperature. Then the mixture was diluted with EtOAc (400 mL), washed with 3% aqueous EDTA-$(NH_4)_2$ (5×200 mL) and water (2×200 mL), dried, and evaporated to dryness. The residue was chromatographed on a silica gel column (4.5×15 cm) in a 0→8% gradient of EtOAc in toluene to give **3-[5-(*tert*-butyloxycarbonyl)pent-1-ynyl]-4,4′-dimethoxybenzophenone (22a)** (2.12 g, 52%). ESI-TOF HRMS: *m/z* = 423.2175 $[M+H]^+$, calc. for $[C_{26}H_{31}O_5]^+$ 423.2166. NMR (DMSO-d_6): 7.72–7.67 (m, 3H, Ar*H*); 7.64 (d, 1H, $^4J = 2.3$ Hz, Ar*H*); 7.17 (d, 1H, $J = 8.7$ Hz, Ar*H*); 7.08 (d, 2H, $J = 9.0$ Hz, Ar*H*); 3.91 (s, 3H, OCH_3); 3.86 (s, 3H, OCH_3); 2.47 (t, 2H, $J = 7.0$ Hz, ≡CCH_2); 2.38 (t, 2H, $J = 7.4$ Hz, COCH_2); 1.75 (m, 2H, $CH_2CH_2CH_2$); 1.39 (s, 9H, CCH_3) and **3,3'-bis[5-(*tert*-butyloxycarbonyl)pent-1-ynyl]-4,4′-dimethoxybenzophenone** (1.26 g, 22%) NMR (DMSO-d_6): 7.67 (dd, 2H, $J = 8.7$ Hz, $^4J = 2.0$ Hz, Ar*H*); 7.64 (d, 2H, $^4J = 2.0$ Hz, Ar*H*); 7.18 (d, 2H, $J = 8.7$ Hz, Ar*H*); 3.91 (s, 6H, OCH_3); 2.47 (t, 4H, $J = 7.0$ Hz, ≡CCH_2); 2.37 (t, 4H, $J = 7.4$ Hz, COCH_2); 1.75 (m, 2H, $CH_2CH_2CH_2$); 1.39 (s, 18H, CCH_3) as colourless oils.



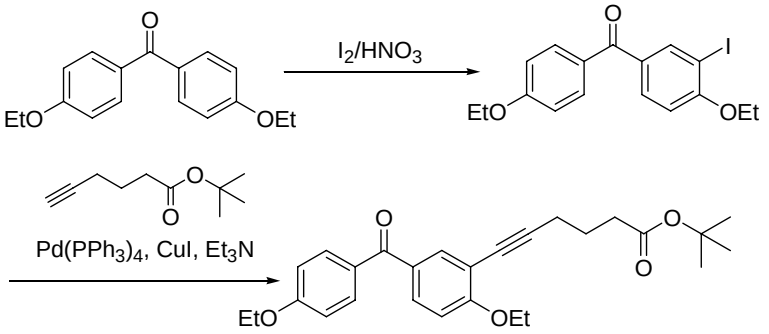
Methyl 3-iodo-4-methoxybenzoate. To a solution of methyl 4-methoxybenzoate (29.7 g, 0.18 mol) in CCl_4 (110 mL) iodine (22.7 g, 0.89 mol) was added and the mixture was stirred for 10 min. Nitric acid (58%, 50 mL) was added dropwise wiwhin 30 min and the mixture was refluxed for 3 h. The mixture was cooled to room temperature and precipitate formed was filtered off. The organic layer was separated, washed with 5% Na_2SO_3 (100 mL), dried over $CaCl_2$ and evaporated. The residue was combined with the precipitate and recrystallized twice from EtOH. Yield 30.4 g (58%).

3-Iodo-4-methoxybenzoyl chloride. Methyl 3-iodo-4-methoxybenzoate (29.2 g, 0.1 mol) was suspended in EtOH (150 mL), the solution of NaOH (4.4 g, 0.11 mol) was added in one portion. The mixture was stirred and heated at 40ºC overnight, then cooled, diluted with water (400 mL). 3-Iodo-4-methoxybenzoic acid was precipitated with conc. HCl, filtered off, washed with cold water, and dried over P_4O_{10}. The acid was suspended in $CHCl_3$ (150 mL), and $SOCl_2$ (9.5 mL, 0.13 mmol) was added. The mixture was stirred overnight, then evaporated and the residue was distilled under reduced pressure to give the desired acid chloride as a solid (mp ca. 50ºC, bp 145–150ºC/1 Torr). Yield 18.2 g (61%).

3-Iodo-4,4′-dimethoxybenzophenone (18). A. The mixture of 3-iodo-4-methoxybenzoyl chloride (14.8 g, 0.05 mol), anisole (11.0 mL, 0.1 mol) and iodine (0.5 g) was refluxed for 10 h, then cooled to 60ºC, diluted with iPrOH (200 mL), refluxed for 30 min, cooled and kept in

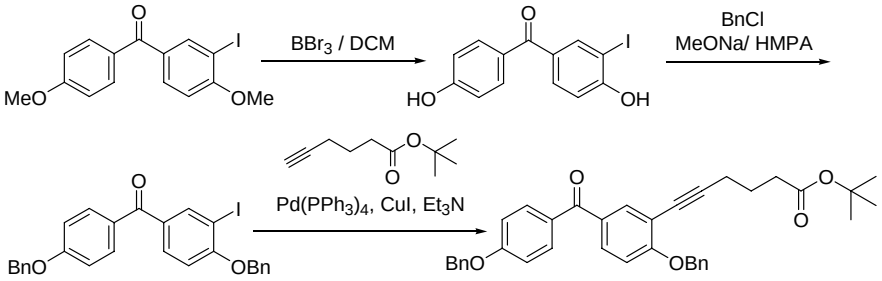
freezer overnight. The precipitate was filtered off, washed with cold iPrOH (10 mL), dried, and recrystallized from EtOH. Yield 10.4 (56.5%), off-white solid. ESI-TOF HRMS: *m/z* = 383.0139 $[M+H]^+$, calc. for $[C_{16}H_{16}IO_3]^+$ 383.0139. ^{1}H NMR (DMSO-d_6): 8.09 (d, $^4J_{2,6}$ = 2.0 Hz, 1H; H-2), 7.73 (dd, $J_{5,6}$ = 8.7 Hz, $^4J_{2,6}$ = 2.0 Hz, 1H; H-6), 7.70 (d, $J_{2',3'} = J_{5',6'}$ = 8.7 Hz, 2H; H-2',6'), 7.12 (d, $J_{5,6}$ = 8.7 Hz, 1H; H-5), 7.07 (d, $J_{2',3'} = J_{5',6'}$ = 8.7 Hz, 2H; H-3′,5′), 3.93 (s, 3H, 4-OCH_3), 3.86 (s, 3H, 4′-OCH_3). ^{13}C NMR (DMSO-d_6): 191.95 (CO), 162.80 (C-4′), 160.88 (C-4), 140.25 (C-2), 132.03 (C-6), 131.91 (2C, C-2′,6′), 131.85 (C-1), 129.55 (C-1′), 113.90 (2C, C-3′,5′), 110.90 (C-5), 86.15 (C-3), 56.87 (4-O*C*H$_3$), 55.57 (4′-O*C*H$_3$).

B. 4,4′-Dimethoxybenzophenone (18.1 g, 75 mmol) was dissolved in dioxane (70 mL) at 60ºC, iodine (9.9 g, 39 mmol) was added and the mixture was stirred for 15 min. Water (20 mL) was added, and 58% HNO_3 (41 mL) was added dropwise within 2 h. The mixture was stirred at 60ºC until iodine colouring disappears (ca. 6–7 h). The flask was evacuated to remove nitrogen oxides, the mixture was diluted with water (100 mL), cooled, and the precipitate was filtered off, washed with 5% $NaHCO_3$ and water. The solid was suspended in EtOH (200 mL), refluxed for 15 min, filtered hot, and cooled in freezer to 4ºC. The solid (16 g) was filtered off and dried. It contains (GLC) 75% of desired 3-iodo-4,4′-dimethoxybenzophenone, 24% of starting 4,4′-dimethoxybenzophenone and 0.7% of 3,3′-diiodo-4,4′-dimethoxybenzophenone. This was purified by column chromatography in toluene. Yield 11.2 g (40%).



3-Iodo-4,4′-diethoxybenzophenone (20). 4,4′-Diethoxybenzophenone was iodinated according to procedure for iodination of 4,4'-dimethoxybenzophenone. The resulting compound was purified by column chromatography in toluene. Yield 36%. ESI-TOF HRMS: *m/z* = 411.0441 $[M+H]^+$, calc. for $[C_{18}H_{20}IO_3]^+$ 411.0452. NMR (DMSO-d_6): 8.08 (d, 1H, $^4J_{2,6}$ = 2.0 Hz, H-2); 7.73–7.67 (m, 3H, H-2',6,6'); 7.10 (d, 1H, *J* = 8.7 Hz, H-5); 7.06 (d, 2H, *J* = 8.7 Hz, H-3',5'); 4.20 (q, 2H, *J* = 7.0 Hz), 4.13 (q, 2H, *J* = 7.0 Hz) (OCH_2); 1.40 (t, 3H, *J* = 7.0 Hz), 1.36 (t, 2H, *J* = 7.0 Hz) (CH_3).

3-[5-(*tert*-Butyloxycarbonyl)pent-1-ynyl]-4,4′-diethoxybenzophenone (22b). To a solution of 3-iodo-4,4′-diethoxybenzophenone (4.54 g, 11.5 mmol) and *tert*-butyl 5-hexynoate (2.14 g, 12.7 mmol) in DMF (50 mL) $Pd(PPh_3)_4$ (1.40 g, 1.22 mmol), CuI (465 mg, 2.44 mmol), Et_3N (3.2 mL, 23 mmol) were subsequently added. The mixture was stirred overnight under argon, then diluted with water (200 mL) and extracted with EtOAc (200 mL). The organic layer was washed with water (4×200 mL), 0.1 M solution $(NH_4)_2EDTA$ (4×200 mL) and dried over Na_2SO_4. The residue was chromatographed column in gradient of EtOAc in toluene (0→5%). Yield 4.53 g (90%), viscous yellowish oil. ESI-TOF HRMS: *m/z* = 451.2494 $[M+H]^+$, calc. for $[C_{28}H_{35}O_5]^+$ 451.2479. NMR (DMSO-d_6): 7.72–7.61 (m, 4H, H-2,2',6,6'); 7.15 (d, 1H, *J* = 8.7 Hz, H-5); 7.06 (d, 2H, *J* = 8.7 Hz, H-3',5'); 4.21–4.10 (m, 4H, OCH_2); 2.47 (t, 2H, *J* = 6.6 Hz), 2.42 (t, 2H, *J* = 7.6 Hz) (CH_2CH$_2$CH_2); 1.74 (m, 2H) (≡CH$_2$CH_2); 1.42–1.34 (m, 15H, CH_3).

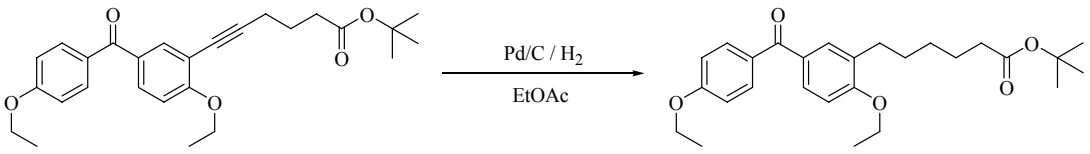


4,4′-Dihydroxy-3-iodobenzophenone (19). To a solution of 4,4′-dimethoxy-3-iodobenzophenone (6.0 g, 16.3 mmol) in DCM (100 mL) boron tribromide (4.6 mL, 49.0 mmol) was added in one portion. The mixture was stirred for 12 h. The progress of the reaction was monitored by TLC (30% EtOAc in toluene). Then the mixture was poured in water (200 mL) and the suspension was extracted with EtOAc (3×250 mL). The organic layer was dried with Na_2SO_4, evaporated, and the residue was coevaporated with MeOH (3×100 mL). Yield 5.5 g (99%), brownish solid. ESI-TOF HRMS: *m/z* = 354.9815 $[M+H]^+$, calc. for $[C_{14}H_{12}IO_3]^+$ 354.9826. NMR (DMSO-d_6): 11.18 (br.s, 1H, O*H*); 10.32 (br.s, 1H, O*H*); 8.01 (d, 1H, $^4J_{2,6}$ = 2.0 Hz, H-2); 7.63–7.55 (m, 3H, H-6,2',6'); 6.98 (d, 1H, *J* = 8.4 Hz, H-5); 6.88 (d, 2H, *J* = 8.4 Hz, H-3',5').

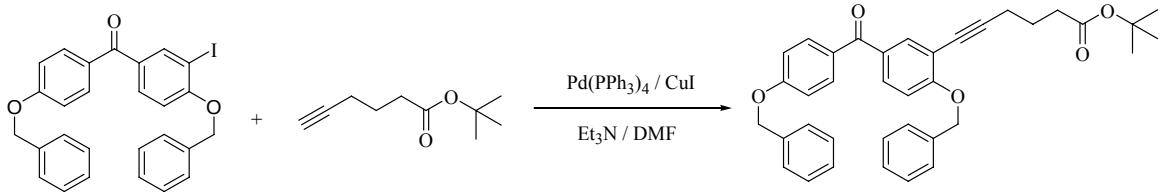
4,4′-Dibenzyloxy-3-iodobenzophenone (21). Sodium (0.46 g, 20 mmol) was dissolved in MeOH and the resulting solution of MeONa was added to a solution of 4,4'-dihydroxy-3-iodobenzophenone (3.40 g, 10 mmol) in methanol (50 mL). The mixture was evaporated to dryness, the residue was dissolved in HMPA (30 mL) and benzyl chloride (2.78 g, 22 mmol) was added in one portion. The mixture was heated at 80ºC for 5 h, then cooled, diluted with water (200 mL) and extracted with EtOAc (2×150 mL). The combined organic layers were washed with water (5×100 mL), dried over Na_2SO_4, and evaporated. The residue was chromatographed on silica gel in 0→3% EtOAc in toluene to give the desired benzophenone (4.10 g, 79%). ESI-TOF HRMS: *m/z* = 535.0752 $[M+H]^+$, calc. for $[C_{28}H_{24}IO_3]^+$ 535.0765. NMR (DMSO-d_6): 8.11 (d, 1H, $^4J_{2,6}$ = 1.9 Hz, H-2); 7.76–7.58 (m, 3H, H-2′,6,6′); 7.53 (m, 2H), 7.48 (m, 2H), 7.42 (m, 4H), 7.35 (m, 2H) (Ar*H* (phenyl)); 7.22 (d, 1H, *J* = 8.7 Hz, H-5); 7.17 (d, 2H, *J* = 8.7 Hz, H-3′,5′); 5.32 (s, 2H), 5.22 (s, 2H) (OCH_2).

3-[5-(*tert*-Butyloxycarbonyl)pent-1-ynyl]-4,4′-dibenzyloxybenzophenone (22c). To a solution of 3-iodo-4,4′-dibenzyloxybenzophenone (4.50 g, 8.65 mmol) and *tert*-butyl 5-hexynoate (1.60 g, 9.51 mmol) in DMF (50 mL) $Pd(PPh_3)_4$ (1.00 g, 0.86 mmol), CuI (330 mg, 1.783 mmol), Et_3N (2.4 mL, 17 mmol) were subsequently added. The mixture was stirred overnight under argon, then diluted with water (200 mL) and extracted with EtOAc (200 mL). The organic layer was washed with water (4×200 mL), 0.1 M solution $(NH_4)_2$EDTA (4×200 mL) and dried over Na_2SO_4. The residue was chromatographed column in gradient of EtOAc in toluene (0→10%). Yield 4.10 g (84%), viscous yellowish oil. ESI-TOF HRMS: *m/z* = 575.2805 $[M+H]^+$, calc. for $[C_{38}H_{39}O_5]^+$ 575.2792. NMR (DMSO-d_6): 7.75–7.65 (m, 4H, H-2,2′,6,6′); 7.49 (m, 4H), 7.41 (m, 4H), 7.35 (m, 2H) (Ar*H* (phenyl)); 7.26 (d, 1H, *J* = 8.9 Hz, H-5); 7.16 (d, 2H, *J* = 8.9 Hz, H-3′,5′); 5.30 (s, 2H), 5.22 (s, 2H) (OCH_2); 2.48 (t, 2H, *J* = 6.9 Hz), 2.35 (t, 2H, *J* = 7.3 Hz) ($CH_2CH_2CH_2$); 1.75 (m, 2H) (≡CH_2CH_2); 1.38 (m, 9H, CH_3).

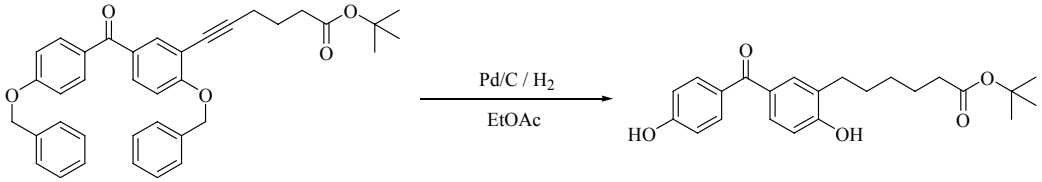
3-[5-(*tert*-Butyloxycarbonyl)pentyl]-4,4′-(1,1′,2,2′-[^{13}C])diethoxybenzophenone (23d). ESI-TOF HRMS: *m/z* = 459.2941 $[M+H]^+$, calc. for $[C_{24}{}^{13}C_4H_{39}O_5]^+$ 459.2926. NMR (DMSO-d_6): 7.67 (d, 2H, *J* = 8.7 Hz, H-2′,6′); 7.55 (dd, 1H, $^4J_{2,6}$ = 2.1 Hz, *J* = 8.3 Hz, H-6); 7.52 (d, 1H, *J* = 2.1 Hz, H-2); 7.05 (m, 3H, H-5,3′,5′); 4.13 (ddq, 4H, *J* = 6.8 Hz, $^1J_{H,C}$ = 145 Hz, $^2J_{H,C}$ = 2.5 Hz, OCH_2); 2.59 (t, 2H, *J* = 7.3 Hz, ArCH_2); 2.17 (t, 2H, *J* = 7.3 Hz, COCH_2); 1.59–1.45 (m, 7H, $COCH_2CH_2CH_2CH_2$, OCH_2CH_3 (3H)); 1.36 (s, 9H, CCH_3); 1.33–1.20 (m, 5H, $COCH_2CH_2CH_2$, OCH_2CH_3 (3H)).



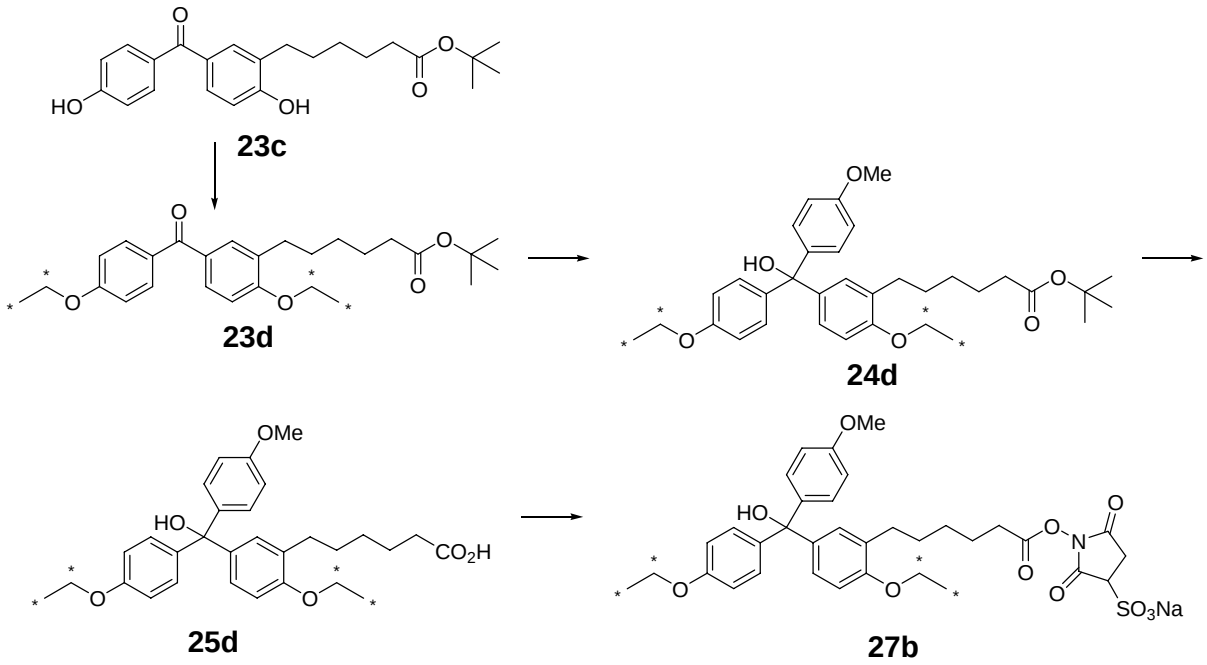
3-[5-(*tert*-Butyloxycarbonyl)pentyl]-4,4′-diethoxybenzophenone (23b). To a solution of 3-[5-(*tert*-butyloxycarbonyl)pent-1-ynyl]-4,4′-diethoxybenzophenone (2.27 g, 5.20 mmol) in EtOAc (100 mL) 10%Pd/C (500 mg) was added and the mixture was hydrogenated for 72 h at ambient pressure. The mixture was filtered, evaporated and the residue was chromatographed on silica gel (0 to 10% gradient of EtOAc in toluene) to give the desired compound as a viscous colourless oil (1.92 g, 84%). ESI-TOF HRMS: *m/z* = 455.2778 $[M+H]^+$, calc. for $[C_{28}H_{39}O_5]^+$ 455.2792. NMR (DMSO-d_6): 7.67 (d, 2H, J = 8.7 Hz, H-2′,6′); 7.55 (dd, 1H, $^4J_{2,6}$ = 2.1 Hz, J = 8.6 Hz, H-6); 7.52 (d, 1H, J = 2.1 Hz, H-2); 7.05 (d, 1H, J = 8.6 Hz, H-5); 7.04 (d, 2H, J = 8.7 Hz, H-3′,5′); 4.16–4.10 (m, 4H, OCH_2); 2.59 (t, 2H, J = 7.4 Hz, ArCH_2); 2.17 (t, 2H, J = 7.0 Hz, COCH_2); 1.53 (m, 4H, $COCH_2CH_2CH_2CH_2$); 1.39–1.34 (m, 15H, CH_3); 1.28 (m, 2H, $COCH_2CH_2CH_2$).



3-[5-(*tert*-Butyloxycarbonyl)pent-1-ynyl]-4,4′-dibenzyloxybenzophenone (22c). To a solution of 3-iodo-4,4′-dibenzyloxybenzophenone (4.50 g, 8.65 mmol) and *tert*-butyl 5-hexynoate (1.60 g, 9.51 mmol) in DMF (50 mL) $Pd(PPh_3)_4$ (1.00 g, 0.86 mmol), CuI (330 mg, 1.783 mmol), Et_3N (2.4 mL, 17 mmol) were subsequently added. The mixture was stirred overnight under argon, then diluted with water (200 mL) and extracted with EtOAc (200 mL). The organic layer was washed with water (4×200 mL), 0.1 M solution $(NH_4)_2EDTA$ (4×200 mL) and dried over Na_2SO_4. The residue was chromatographed column in gradient of EtOAc in toluene (0→10%). Yield 4.10 g (84%), viscous yellowish oil. ESI-TOF HRMS: *m/z* = 575.2788 $[M+H]^+$, calc. for $[C_{38}H_{39}O_5]^+$ 575.2792. NMR (DMSO-d_6): 7.75–7.65 (m, 4H, H-2,2′,6,6′); 7.49 (m, 4H), 7.41 (m, 4H), 7.35 (m, 2H) (Ar*H* (phenyl)); 7.26 (d, 1H, J = 8.9 Hz, H-5); 7.16 (d, 2H, J = 8.9 Hz, H-3′,5′); 5.30 (s, 2H), 5.22 (s, 2H) (OCH_2); 2.48 (t, 2H, J = 6.9 Hz), 2.35 (t, 2H, J = 7.3 Hz) ($CH_2CH_2CH_2$); 1.75 (m, 2H) ($\equiv CH_2CH_2$); 1.38 (m, 9H, CH_3).



3-[5-(*tert*-Butyloxycarbonyl)pentyl]-4,4′-dihydroxybenzophenone (23c). To a solution of 3-[5-(*tert*-butyloxycarbonyl)pent-1-ynyl]-4,4′-dibenzyloxybenzophenone (2.05 g, 3.66 mmol) in EtOAc (100 mL) 10%Pd/C (500 mg) was added and the mixture was hydrogenated for 72 h at ambient pressure. The mixture was filtered, evaporated and the residue was chromatographed on silica gel (0 to 10% gradient of EtOAc in toluene) to give the desired compound as a viscous colourless oil (1.03 g, 73%). ESI-TOF HRMS: *m/z* = 399.2177 $[M+H]^+$, calc. for $[C_{24}H_{31}O_5]^+$ 399.2166. NMR (DMSO-d_6): 10.22 (s, 1H), 10.14 (s, 1H) (O*H*); 7.59 (d, 2H, J = 8.8 Hz, H-2′,6′); 7.46 (d, 1H, J = 2.0 Hz, H-2); 7.41 (dd, 1H, $^4J_{2,6}$ = 2.0 Hz, J = 8.7 Hz, H-6); 6.87 (m, 3H, H-5,3′,5′); 2.55 (t, 2H, J = 7.6 Hz, ArCH_2); 2.16 (t, 2H, J = 7.3 Hz, COCH_2); 1.53 (m, 4H, $COCH_2CH_2CH_2CH_2$); 1.36 (m, 9H, CH_3); 1.30 (m, 2H, $COCH_2CH_2CH_2$).



3-[5-(*tert*-Butyloxycarbonyl)pentyl]-4,4′-(1,1′,2,2′-[^{13}C])-diethoxybenzophenone (23d). To a magnetically stirred solution of 3-[5-(*tert*-butyloxycarbonyl)pentyl]-4,4′-dihydroxybenzophenone (1.00 g, 2.6 mmol), [^{13}C]ethanol (400 mg) and triphenylphosphine (1.36 g, 5.20 mmol) in dry THF (30 mL) DIAD (2.46 ml, 8.1 mmol) was added dropwise within 15 min. The reaction mixture was heated to 40–45ºC until starting benzophenone is consumed according to TLC, then cooled to room temperature, diluted with EtOAc (250 mL), washed with washed with 3% citric acid (150 mL) and water (2×100 mL), dried over Na_2SO_4 and evaporated. The residue was purified by column chromatography on silica gel (elution 0→15% EtOAc in toluene). Yield (490 g, 42%), colourless oil. ESI-TOF HRMS: *m/z* = 459.2931 $[M+H]^+$, calc. for $[C_{24}{}^{13}C_4H_{39}O_5]^+$ 459.2926. NMR (DMSO-d_6): 7.68 (d, 2H, J = 8.7 Hz, H-2′,6′); 7.55 (dd, 1H, $^4J_{2,6}$ = 2.0 Hz, J = 8.2 Hz, H-6); 7.52 (d, 1H, J = 2.0 Hz, H-2); 7.07–7.02 (m, 3H, H-5, H-3′,5′); 4.13 (app. ddq, 4H, $^1J_{H,C}$ = 141.0 Hz, J = 6.8 Hz, $^2J_{H,C}$ = 2.5 Hz, [^{13}C]CH_2); 2.59 (t, 2H, J = 7.3 Hz, ArCH_2); 2.17 (t, 2H, J = 7.3 Hz, COCH_2); 1.58–1.45 (m, 7H, $COCH_2CH_2CH_2CH_2$, [^{13}C]CH_3); 1.36 (s, 9H, CH_3); 1.33–1.19 (m, 5H, $COCH_2CH_2CH_2$, [^{13}C]CH_3).

6-{2-(1,2-[^{13}C])Ethoxy-5-[hydroxy-(4-(1,2-[^{13}C])ethoxyphenyl)-(4-methoxyphenyl)-methyl]phenyl}hexanoic acid, *tert*-butyl ester (24d). To a stirred solution of 3-[5-(*tert*-butyloxycarbonyl)pentyl]-4,4′-(1,1′,2,2′-[^{13}C])-diethoxybenzophenone (470 mg; 1.06 mmol) in dry THF (10 mL) 0.5 M 4-methoxyphenylmagnesium bromide (2.53 mL, 1.27 mmol) was added in one portion under argon, and the mixture was stirred at ambient temperature overnight (monitoring by TLC in EtOAc–toluene 1:3). After the disappearance of the starting ketone the reaction was diluted with water (100 mL) and saturated aq. NH_4Cl (50 mL), and extracted with EtOAc (2×100 mL). The organic phase was dried over Na_2SO_4, evaporated, and chromatographed on silica gel in 0→6% EtOAc in toluene with 0.5% of Et_3N to give the desired compound as a colourless oil. Yield 351 g (60%). ESI-TOF HRMS: *m/z* = 503.3355 $[M–OH]^+$, calc. for $[C_{30}{}^{13}C_4H_{43}O_3]^+$ 503.3341. NMR (DMSO-d_6): 7.06 (m, 4H, ArH); 6.97 (d, 1H, ^4J = 2.1 Hz, ArH); 6.81 (m, 6H, ArH); 6.00 (s, 1H, OH); 3.98 (app. ddq, 4H, $^1J_{H,C}$ = 139.5 Hz, J = 6.9 Hz, $^2J_{H,C}$ = 2.5 Hz, [^{13}C]CH_2); 3.72 (s, 3H, OCH_3); 2.45 (t, 2H, J = 7.3 Hz, ArCH_2); 2.13 (t, 2H, J = 7.3 Hz, COCH_2); 1.50–1.40 (m, 7H, $COCH_2CH_2CH_2CH_2$, [^{13}C]CH_3); 1.37 (s, 9H, t-Bu); 1.25–1.13 (m, 5H, $COCH_2CH_2CH_2$, [^{13}C]CH_3).

6-{2-(1,2-[^{13}C])Ethoxy-5-[hydroxy-(4-(1,2-[^{13}C])ethoxyphenyl)-(4-methoxyphenyl)-methyl]-phenyl}hexanoic acid, sulphosuccinimide ester (27b). To a stirred solution of *tert*-butyl ester of 6-{2-(1,2-[^{13}C])ethoxy-5-[hydroxy-(4-(1,2-[^{13}C])ethoxyphenyl)-(4-methoxyphenyl)-methyl]phenyl}hexanoic acid (271 mg; 0.5 mmol) in dry DCM (1 mL) trifluoroacetic acid (1

mL) was added in one portion and the mixture was stirred at ambient temperature for 3 h, then evaporated, and co-evaporated with DCM (3×10 mL) to give the acid. The residue was chromatographed on silica gel in 0→25% acetone in toluene to give the desired compound as a yellowish oil, 30 mg (12% yield). It was dissolved in dry DMF (0.5 mL), then *N*-oxysulfosuccinimide sodium salt (13 mg, 0.06 mmol) and DCC (19 mg, 0.09 mmol) were added and the mixture was left under stirring overnight, then cooled to +4ºC and stirred for 2 h, and the precipitate formed was filtered off. The solution was diluted with EtOAc (6 mL), cooled to +4ºC overnight, filtered, and diluted with dry Et_2O (50 mL). The mixture was kept at ambient temperature for 2-3 h and the desired compound was collected by filtration, washed with ether and dried *in vacuo*. Yield 41 mg (98%), white solid. ESI-TOF HRMS: *m/z* = 544.2891 $[M–OH]^+$, calc. for $[C_{30}{}^{13}C_4H_{38}NO_5]^+$ 544.2879. NMR (DMSO-d_6): 7.05 (m, 4H, Ar*H*); 6.97 (d, 1H, ^4J = 2.0 Hz, Ar*H*); 6.81 (m, 6H, Ar*H*); 6.00 (s, 1H, O*H*); 3.98 (app. ddq, 4H, $^1J_{H,C}$ = 138.8 Hz, *J* = 6.9 Hz, $^2J_{H,C}$ = 2.0 Hz, [^{13}C]CH_2); 3.94 (br., 1H, COC*H*S); 3.72 (s, 3H, OCH_3); 3.15 (br. s, 1H, COCH*H*CHS); 2.86 (m, 1H, COC*H*HCHS); 2.45 (t, 2H, *J* = 7.3 Hz, ArCH_2); 2.15 (t, 2H, *J* = 7.3 Hz, COCH_2); 1.50–1.40 (m, 7H, $COCH_2CH_2CH_2CH_2$, [^{13}C]CH_3); 1.25–1.13 (m, 5H, $COCH_2CH_2CH_2$, [^{13}C]CH_3).

Amides **28a-h** were prepared using procedure similar to used for amides **10**. The compounds were chromatographed in 30% EtOAc in toluene + 0.5% Et_3N. The following compounds were obtained:

***N*-Octyl-6-{2-methoxy-5-[hydroxy-bis(4-methoxyphenyl)methyl]phenyl}hexanamide (28d)**, yellowish oil, yield 90%. ESI-TOF HRMS: *m/z* = 574.3535 $[M–OH]^+$, calc. for $[C_{36}H_{48}NO_5]^+$ 574.3527. NMR (DMSO-d_6): 7.65 (t, 1H, *J* = 5.4 Hz, N*H*); 7.06 (d, 4H, *J* = 8.9 Hz, Ar*H*, H-2',6'); 6.98 (d, 1H, ^4J = 2.3 Hz, Ar*H*, H-6); 6.85 (dd, 1H, *J* = 8.5 Hz, ^4J = 2.3 Hz, Ar*H*, H-4); 6.82 (d, 4H, *J* = 8.9 Hz, Ar*H*, H-3′,5′); 6.80 (m, 1H, H-3); 6.01 (s, 1H, O*H*); 3.74 (s, 3H), 3.72 (s, 6H) (OCH_3); 2.99 (m, 2H, NCH_2); 2.44 (t, 2H, *J* = 7.6 Hz, $COCH_2CH_2CH_2CH_2CH_2$), 1.99 (t, 2H, *J* = 7.3 Hz, COCH_2); 1.42 (m, 4H), 1.35 (m, 2H), 1.29–1.15 (m, 12H), ($COCH_2CH_2CH_2CH_2$, $NCH_2CH_2CH_2CH_2CH_2CH_2CH_2$); 0.85 (t, 3H, *J* = 6.9 Hz, CCH_3).

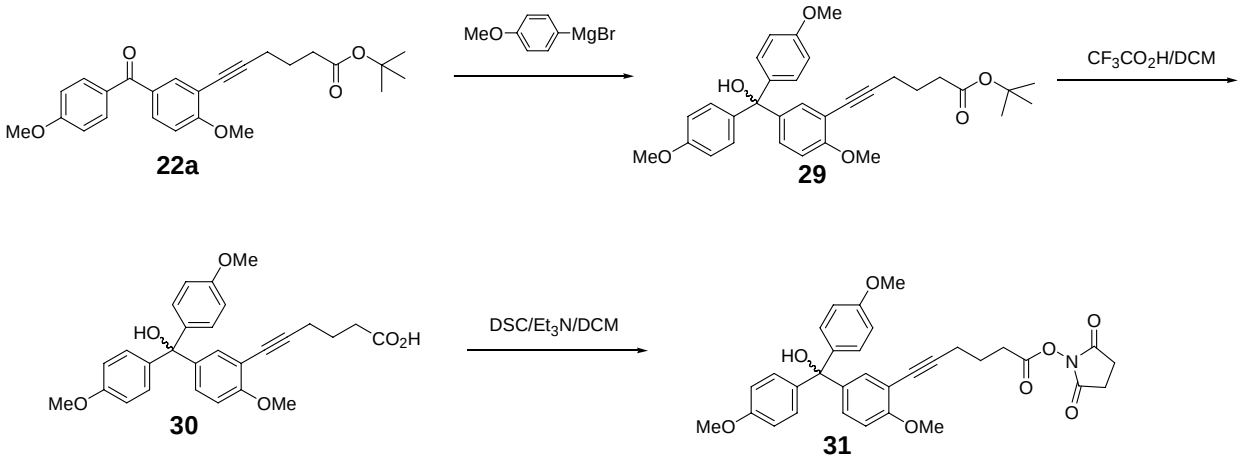
***N*-Nonyl-6-{2-methoxy-5-[hydroxy-bis(4-methoxyphenyl)methyl]phenyl}hexanamide (28e)**, yellowish oil, yield 96%. ESI-TOF HRMS: *m/z* = 588.3675 $[M–OH]^+$, calc. for $[C_{37}H_{50}NO_5]^+$ 588.3684. NMR (DMSO-d_6): 7.65 (t, 1H, *J* = 5.4 Hz, N*H*); 7.07 (d, 4H, *J* = 8.7 Hz, Ar*H*, H-2',6'); 6.98 (d, 1H, ^4J = 2.2 Hz, Ar*H*, H-6); 6.85 (dd, 1H, *J* = 8.5 Hz, ^4J = 2.2 Hz, Ar*H*, H-4); 6.82 (d, 4H, *J* = 8.7 Hz, Ar*H*, H-3′,5′); 6.80 (m, 1H, H-3); 6.02 (s, 1H, O*H*); 3.74 (s, 3H), 3.72 (s, 6H) (OCH_3); 2.99 (m, 2H, NCH_2); 2.44 (t, 2H, *J* = 7.6 Hz, $COCH_2CH_2CH_2CH_2CH_2$), 1.99 (t, 2H, *J* = 7.5 Hz, COCH_2); 1.44 (m, 4H), 1.35 (m, 2H), 1.29–1.15 (m, 14H), ($COCH_2CH_2CH_2CH_2$, $NCH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2$); 0.84 (t, 3H, *J* = 6.9 Hz, CCH_3).

***N*-Decyl-6-{2-methoxy-5-[hydroxy-bis(4-methoxyphenyl)methyl]phenyl}hexanamide (28f)**, yellowish oil, yield 100%. ESI-TOF HRMS: *m/z* = 602.3830 $[M–OH]^+$, calc. for $[C_{38}H_{52}NO_5]^+$ 602.3840. NMR (DMSO-d_6): 7.65 (t, 1H, *J* = 5.5 Hz, N*H*); 7.07 (d, 4H, *J* = 8.7 Hz, Ar*H*, H-2′,6′); 6.98 (d, 1H, ^4J = 2.1 Hz, Ar*H*, H-6); 6.86 (dd, 1H, *J* = 8.5 Hz, ^4J = 2.1 Hz, Ar*H*, H-4); 6.82 (d, 4H, *J* = 8.7 Hz, Ar*H*, H-3′,5′); 6.80 (m, 1H, H-3); 6.01 (s, 1H, O*H*); 3.74 (s, 3H), 3.72 (s, 6H) (OCH_3); 2.99 (m, 2H, NCH_2); 2.44 (t, 2H, *J* = 7.6 Hz, $COCH_2CH_2CH_2CH_2CH_2$), 1.99 (t, 2H, *J* = 7.3 Hz, COCH_2); 1.45 (m, 4H), 1.35 (m, 2H), 1.29–1.15 (m, 16H), ($COCH_2CH_2CH_2CH_2$, $NCH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2$); 0.84 (t, 3H, *J* = 6.9 Hz, CCH_3).

***N*-(2-Phenylethyl)-6-{2-methoxy-5-[hydroxy-bis(4-methoxyphenyl)methyl]phenyl}-hexanamide (28g)**, yellowish oil, 93% yield. ESI-TOF HRMS: *m/z* = 566.2909 $[M–OH]^+$, calc. for $[C_{36}H_{40}NO_5]^+$ 566.2901. NMR (DMSO-d_6): 7.78 (t, 1H, *J* = 5.5 Hz, N*H*); 7.26 (m, 2H, Ar*H*, H-3″,5″); 7.17 (m, 3H, Ar*H*, H-2″,4″,6″); 7.07 (d, 4H, *J* = 8.9 Hz, Ar*H*, H-2′,6′); 6.99 (d, 1H, ^4J = 2.1 Hz, Ar*H*, H-6); 6.86 (dd, 1H, *J* = 8.5 Hz, ^4J = 2.1 Hz, Ar*H*, H-4); 6.82 (d, 4H, *J* = 8.9 Hz, Ar*H*, H-3',5'); 6.80 (m, 1H, H-3); 6.02 (s, 1H, O*H*); 3.75 (s, 3H), 3.72 (s, 6H) (OCH_3); 3.24 (m, 2H, NCH_2); 2.68 (t, 2H, *J* = 7.3 Hz, $COCH_2CH_2CH_2CH_2CH_2$), 2.44 (t, 2H, *J* = 7.5 Hz,

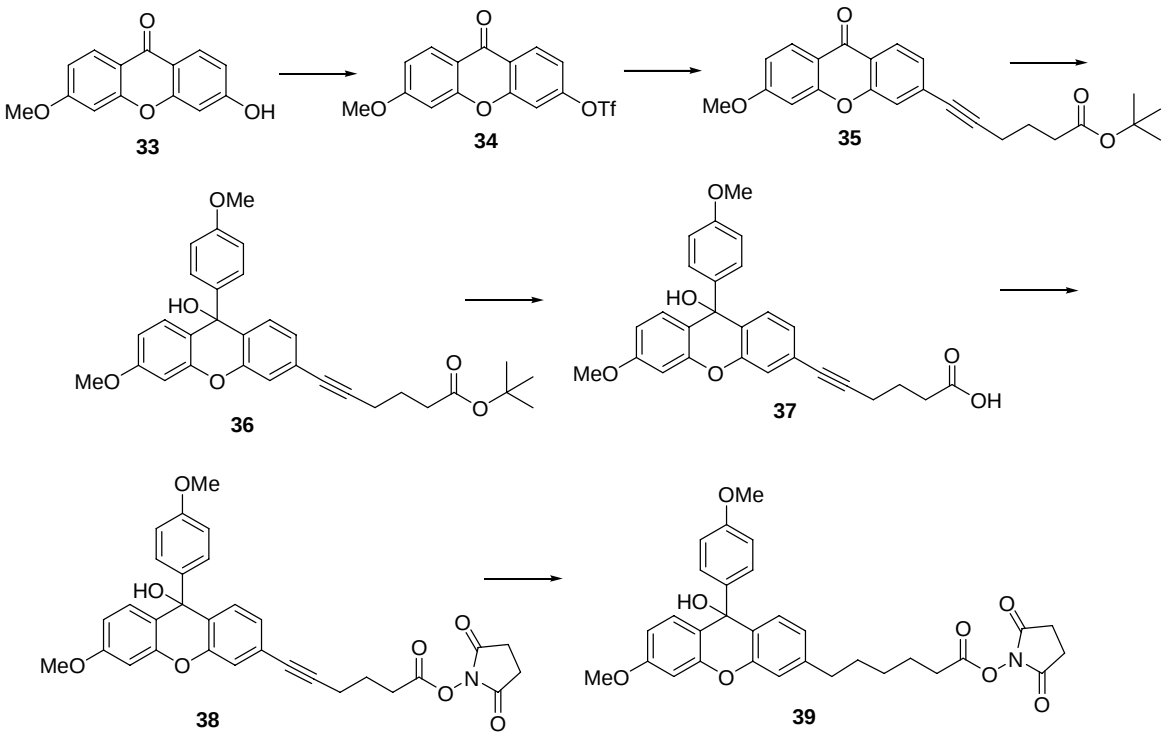
NCH_2CH_2); 1.99 (t, 2H, J = 7.4 Hz, $COCH_2$); 1.42 (m, 4H, $COCH_2CH_2CH_2CH_2$); 1.17 (m, 2H, $COCH_2CH_2CH_2$).

***N*-(3-Phenylpropyl)-6-{2-methoxy-5-[hydroxy-bis(4-methoxyphenyl)methyl]phenyl}-hexanamide (28h)**, yellowish oil 90% yield. ESI-TOF HRMS: *m/z* = 580.3043 $[M–OH]^+$, calc. for $[C_{37}H_{42}NO_5]^+$ 580.3057. NMR (DMSO-d_6): 7.73 (t, 1H, J = 5.5 Hz, N*H*); 7.26 (m, 2H, Ar*H*, H-3″,5″); 7.17 (m, 3H, Ar*H*, H-2″,4″,6″); 7.06 (d, 4H, J = 8.9 Hz, Ar*H*, H-2′,6′); 6.99 (d, 1H, ^4J = 2.0 Hz, Ar*H*, H-6); 6.85 (dd, 1H, J = 8.6 Hz, ^4J = 2.0 Hz, Ar*H*, H-4); 6.82 (d, 4H, J = 8.9 Hz, Ar*H*, H-3′,5′); 6.80 (d, 1H, J = 8.6 Hz, Ar*H*, H-3); 6.02 (s, 1H, O*H*); 3.73 (s, 3H), 3.72 (s, 6H) (OCH_3); 3.03 (m, 2H, NCH_2); 2.55 (t, 2H, J = 7.8 Hz, $COCH_2CH_2CH_2CH_2CH_2$), 2.45 (t, 2H, J = 7.4 Hz, $NCH_2CH_2CH_2$); 2.02 (t, 2H, J = 7.3 Hz, $COCH_2$); 1.67 (m, 2H, NCH_2CH_2); 1.45 (m, 4H, $COCH_2CH_2CH_2CH_2$); 1.21 (m, 2H, $COCH_2CH_2CH_2$).



6-{2-Methoxy-5-[hydroxy-bis(4-methoxyphenyl)methyl]phenyl}-5-hexynoic acid, *tert*-butyl ester (29). To a stirred solution 3-[5-(*tert*-butyloxycarbonyl)pent-1-ynyl]-4,4′-dimethoxy benzophenone (1.18 g; 2.88 mmol) in dry THF (20 mL) 0.9 M 4-methoxyphenylmagnesium bromide (5.8 mL, 4.0 mmol) was added in one portion under argon, and the mixture was kept at ambient temperature overnight (monitoring by TLC in EtOAc–toluene 1:3). The reaction was diluted with water (50 mL) and 5% citric acid (15 mL), and extracted with EtOAc (100 mL). The organic phase was dried over Na_2SO_4, evaporated, and chromatographed on silica gel in 0→5% EtOAc in toluene with 1% of Et_3N to give the desired compound as a colourless oil. Yield 516 mg (35%). ESI-TOF HRMS: *m/z* = 499.2474 $[M–OH]^+$, calc. for $[C_{32}H_{35}O_5]^+$ 499.2479. NMR (DMSO-d_6): 7.12 (d, 1H, ^4J = 2.1 Hz, Ar*H*); 7.09–7.02 (m, 5H, Ar*H*); 6.92 (d, 1H, J = 8.9 Hz, Ar*H*); 6.84 (d, 4H, J = 8.9 Hz, Ar*H*); 6.16 (s, 1H, O*H*); 3.78 (s, 3H), 3.73 (s, 6H) (OCH_3); 2.40 (t, 2H, J = 7.0 Hz, $\equiv CCH_2$); 2.33 (t, 2H, J = 7.5 Hz, $COCH_2$); 1.70 (m, 2H, $CH_2CH_2CH_2$); 1.39 (s, 9H, CCH_3).

6-{2-Methoxy-5-[hydroxy-bis(4-methoxyphenyl)methyl]phenyl}-5-hexynoic acid, *N*-oxysuccinimide ester (31). To a stirred solution of *tert*-butyl ester of 6-{2-methoxy-5-[hydroxy-bis(4-methoxyphenyl)methyl]phenyl}-5-hexynoic acid (516 mg; 1.0 mmol) in dry DCM (3.5 mL) trifluoroacetic acid (3.5 mL) was added in one portion and the mixture was stirred at ambient temperature for 5 h, then evaporated, and co-evaporated with DCM (4×20 mL) to give free acid. Product were dissolved in DCM (10 mL), and triethylamine (0.42 mL, 3.0 mmol) and *N*,*N*-disuccinimidyl carbonate (384 mg, 1.5 mmol) were added and the mixture was stirred overnight, then evaporated, dissolved in EtOAc (50 mL), washed with 5% $NaHCO_3$ (50 mL) and water (50 mL), dried over Na_2SO_4, evaporated, and the residue was purified by column chromatography (5→10% acetone in toluene). Yield 218 mg (39%), white amorphous solid. ESI-TOF HRMS: *m/z* = 540.2022 $[M–OH]^+$, calc. for $[C_{32}H_{30}NO_7]^+$ 540.2017. NMR (DMSO-d_6): 7.14 (d, 1H, ^4J = 2.1 Hz, Ar*H*); 7.09–7.02 (m, 5H, Ar*H*); 6.93 (d, 1H, J = 8.8 Hz, Ar*H*); 6.84 (d, 4H, J = 8.7 Hz, Ar*H*); 6.17 (s, 1H, O*H*); 3.79 (s, 3H), 3.73 (s, 6H) (OCH_3); 2.81 (m, 6H, $COCH_2$, $COCH_2CH_2CO$); 2.51 (t, 2H, J = 7.0 Hz, $\equiv CCH_2$); 1.86 (m, 2H, $CH_2CH_2CH_2$).



3-Methoxy-9-oxo-*9H*-xanthen-6-yl trifluoromethanesulfonate (34). To a ice cooled solution of 6-hydroxy-3-methoxy-*9H*-xanthen-9-one (0.70 g, 0.29 mmol) in dry pyridine (40 mL) trifluoromethanesulphonic anhydride (0.90 g, 0.32 mmol) was added dropwise within 1 h and the reaction was left overnight at room temperature, then poured into 5 % HCl (150 mL), and the product was extracted with dichloromethane (2×100 mL). The solution was dried over anhydrous sodium sulphate, filtered and concentrated in vacuo to give the desired product, 0.86 g (79.3 %). ESI-TOF HRMS: *m/z* = 375.0151 $[M+H]^+$, calc. for $[C_{15}H_{10}F_3O_6S]^+$ 375.0145. ^{1}H NMR (400MHz, $CDCl_3$) δ 8.43 (d, *J* = 8.8 Hz, 1H), 8.28 (d, *J* = 8.9 Hz, 1H), 7.45 (s, 1H), 7.30 ((d, *J* = 11.2 Hz, 1H), 7 (d, *J* = 11.3 Hz, 1H), 6.9 (s, 1H), 4 (s, 3H).

***tert*-Butyl 6-(3-methoxy-9-oxo-*9H*-xanthen-6-yl)hex-5-ynoate (35)** was prepared as described for ketones **22** from triflate **34** (0.864, 2.30 mmol), tert butyl 5-hexynoate (1.55 g, 9.23 mmol), $Pd(PPh_3)_2Cl_2$ (0.162 g, 0.230 mmol), CuI (0.0439 g, 0.230 mmol), and DIEA (1.61 mL, 9.2 mmol). The product was purified by column chromatography, hexane–ethyl acetate, gradient elution (7:1); yield 0.753 g (83 %). ESI-TOF HRMS: *m/z* = 393.1689 $[M+H]^+$, calc. for $[C_{24}H_{25}O_5]^+$ 393.1697. ^{1}H NMR (400MHz, $CDCl_3$) δ 8.2 (dd, *J* = 8.2, 8.9 Hz, 2H), 7.5 (s, 1H), 7 (dd, *J* = 8.8, 8.9 Hz, 2H), 6.9 (s, 1H), 4 (s, 3H), 2.6 (t, 2H), 2.4 (t, 2H), 1.9 (t, 2H), 1.5 (s, 9H).

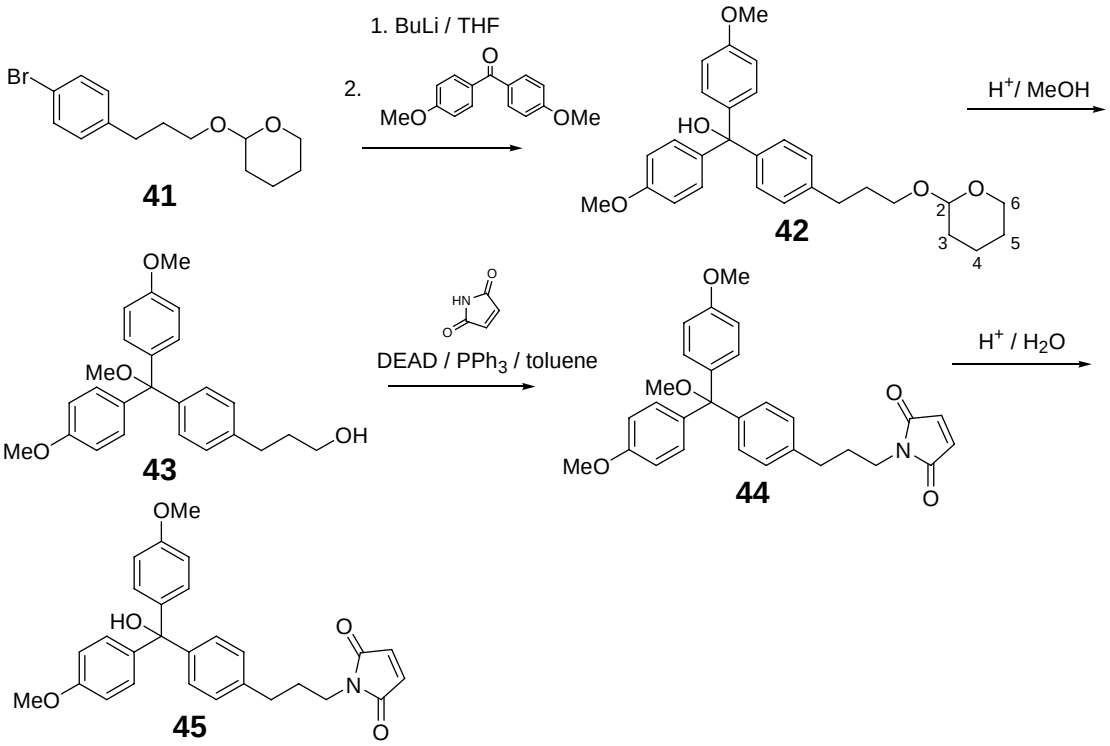
***tert*-Butyl 6-(9-hydroxy-3-methoxy-9-(4-methoxyphenyl)-*9H*-xanthen-6-yl)hex-5-ynoate (36)** was prepared from ketone **35** (0.720 g, 1.83 mmol) and 4-methoxyphenyl magnesium bromide (0.5 M solution in THF, 7.35 mL, 3.66 mmol) in THF (30 mL). After usual workup the product was purified by column chromatography, hexane–ethyl acetate (4:1), gradient elution; (0.52 g, 57 % yield). ESI-TOF HRMS: *m/z* = 483.2173 $[M–OH]^+$, calc. for $[C_{31}H_{31}O_5]^+$ 483.2166. ^{1}H NMR (400MHz, $CDCl_3$) δ 7.2 (m, 5H), 7.1 (d, *J* = 8.1 Hz, 2H), 7.4 (m, 1H), 6.6 (m, 2H), 3.8 (s, 3H), 3.78 (s, 3H), 2.5 (t, 2H), 2.4 (t, 2H), 1.9 (t, 2H), 1.4 (s, 9H).

6-(9-Hydroxy-3-methoxy-9-(4-methoxyphenyl)-*9H*-xanthen-6-yl)hex-5-ynoic acid (37) was prepared using general procedure for compounds **6** from ester 36 (0.520 g, 1.04 mmol). Yield 0.461 g (100 %).

6-(9-Hydroxy-3-methoxy-9-(4-methoxyphenyl)-*9H*-xanthen-6-yl)hex-5-ynoate-*N*-hydroxysuccinimide (38) was prepared using usual procedure from acid 37 (0.461, 1.04 mmol). Yield 0.561 g (100 %). ESI-TOF HRMS: *m/z* = 524.1702 $[M–OH]^+$, calc. for $[C_{31}H_{27}NO_7]^+$

524.1704. ^{1}H NMR (200MHz, $CDCl_3$) δ 7.2 (m, 4H), 7 (m, 2H), 6.7 (m, 2H), 6.5 (m, 2H), 3.8 (s, 3H), 3.7 (s, 3H), 2.8 (m, 6H), 2.5 (t, 2H), 2 (m, 2H).

6-(9-Hydroxy-3-methoxy-9-(4-methoxyphenyl)-9*H*-xanthen-6-yl)hexanoate-*N*-hydroxysuccinimide (39) was prepared by hydrogenation of compound **38** (0.275 g, 0.51 mmol) in EtOAc. Yield 0.277 g (100 %). ESI-TOF HRMS: *m/z* = 528.2020 $[M–OH]^+$, calc. for $[C_{31}H_{30}NO_7]^+$ 528.2017.



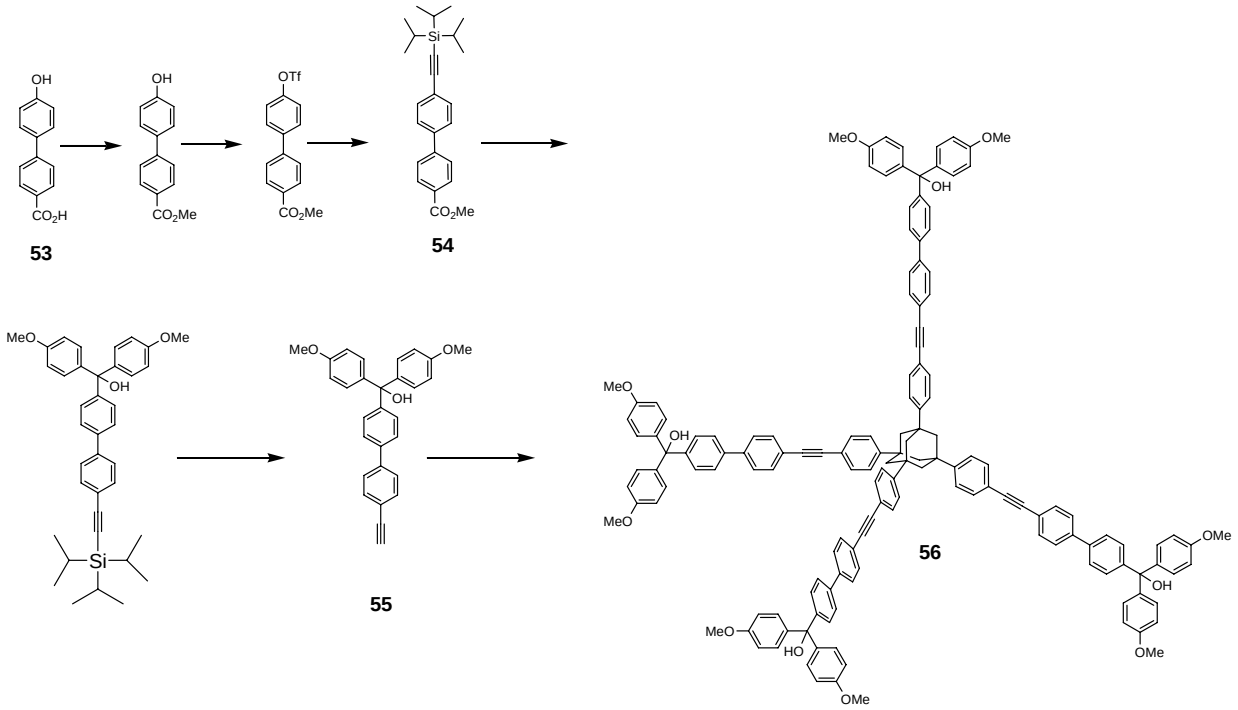
4-(3-{Tetrahydropyran-2-yloxy}propyl)-4′,4″-dimethoxytritanol (42). A solution of 1-bromo-4-(3-{2-tetrahydropyranyl}oxypropyl)benzene (2.99 g, 10 mmol) in dry Et_2O (15 mL) placed into a three-necked flask equipped with a septa and an argon inlet. n-BuLi (4 mL of 2.5 M solution in petroleum ether, 10 mmol) was introduced with a syringe. The mixture was kept at rt for one hour, and a solution of 4,4'-dimethoxybenzophenone (2.42 g, 10 mmol) in dry THF (70 mL) was added dropwise. After 24 hours of stirring the solution was half evaporated and poured into EtOAc (100 mL) and water (100 mL), organic layer was separated and washed with citric acid (5% in water, 2×100 mL), H_2O (2×100 mL), brine (100 mL), dried over Na_2SO_4 and evaporated. The residue was chromatographed on silica gel in 1% Et_3N + 2% EtOAc in PhMe. Yield 2.47 g (53%), colourless oil, R_f 0.20 (10% EtOAc in PhMe). ESI-TOF HRMS: *m/z* = 445.2379 $[M–OH]^+$, calc. for $[C_{29}H_{33}O_4]^+$ 445.2373. NMR (DMSO-d_6): 7.12–7.05 (m, 8H, Ar*H*); 6.83 (d, 4H, *J* = 8.7 Hz, Ar*H*); 6.12 (s, 1H, O*H*); 4.53 (m, 1H, *H*-2); 3.75–3.70 (m, 7H, OCH_3, *H*-6(1)); 3.63 (m, 1H, THPOCH_2 (1)); 3.41 (m, 1H, *H*-6(1)); 3.37–3.31 (m, 1H, THPOCH_2 (1)); 2.61 (m, 2H, ArCH_2); 1.80 (m, 2H, ArCH_2CH_2); 1.72 (m, 1H, *H*-5(1)); 1.60 (m, 1H, *H*-3(1)); 1.50–1.39 (m, 4H, *H*-3(1), *H*-4(2), *H*-5(1)).

4-(3-Hydroxypropyl)-4′,4″-dimethoxytritanol (43). A solution of 4-(3-{tetrahydropyran-2-yloxy}propyl)-4′,4″-dimethoxytritanol (2.29 g, 4.95 mmol) was dissolved in methanol (150 mL). *p*-Toluenesulphonic acid monohydrate (20 mg) was added in one portion and the solution was stirred for 48 hours. Solid K_2CO_3 (0.5 g) was added and the mixture was evaporated. The residue was twice co-evaporated with toluene (20 mL) and chromatographed on silica gel in 1% Et_3N and 3% to 10% Me_2CO in PhMe. Yield 0.696 g (37%), colourless oil, R_f 0.21 (10% Me_2CO and 1% Et_3N in PhMe). ESI-TOF HRMS: *m/z* = 361.1792 $[M–OH]^+$, calc. for $[C_{24}H_{25}O_3]^+$ 361.1798. NMR (DMSO-d_6): 7.27–7.19 (m, 6H, Ar*H*); 7.13 (d, 2H, *J* = 8.2 Hz, Ar*H*); 6.87 (d, 4H, *J* = 8.9

Hz, Ar*H*); 4.43 (t, 1H, *J* = 5.1 Hz, O*H*); 3.73 (s, 6H, ArOCH_3); 3.40 (m, 2H, CH_2OH); 2.91 (s, 3H, Ar_3COCH_3); 2.57 (m, 2H, ArCH_2); 1.69 (m, 2H, $ArCH_2CH_2$).

***N*-(3-{4-Methoxydi(4-methoxyphenyl)methylphenylpropyl)maleimide (44).** To a stirred solution of 4-(3-hydroxypropyl)-4′,4″-dimethoxytritanol (660 mg; 1.68 mmol) in toluene (10 mL) maleimide (179 mg, 1.85 mmol), PPh_3 (485 mg, 1.85 mmol) were added followed by DEAD (0.30 mL, 1.93 mmol). The mixture was kept at ambient temperature for 24 h (monitoring by TLC in EtOAc–toluene 1:9 + 1% Et_3N), evaporated and chromatographed on silica gel in 5% EtOAc + 1% Et_3N in toluene. R_f 0.40 (10% EtOAc in PhMe). Yield 657 mg (83%). ESI-TOF HRMS: *m/z* = 440.1861 $[M–OMe]^+$, calc. for $[C_{28}H_{26}NO_4]^+$ 440.1856. NMR (DMSO-d_6): 7.26–7.19 (m, 6H, Ar*H*); 7.12 (d, 2H, *J* = 8.2 Hz, Ar*H*); 6.91 (s, 2H, COC*H*=C*H*CO); 6.87 (d, 4H, *J* = 8.9 Hz, Ar*H*); 3.73 (s, 6H, ArOCH_3); 3.43 (m, 2H, NCH_2); 2.90 (s, 3H, Ar_3COCH_3); 2.52 (m, 2H, ArCH_2); 1.80 (m, 2H, $ArCH_2CH_2$).

***N*-(3-{4-Hydroxydi(4-methoxyphenyl)methylphenylpropyl)maleimide (45).** Trifluoroacetic acid (0.20 mL, 2.60 mmol) was added to a solution of *N*-(3-{4-methoxydi(4-methoxyphenyl)methylphenylpropyl)maleimide (614 mg. 1.304 mmol) in toluene (15 mL). The solution was stirred for 15 minutes and water (20 mL) was added. The mixture was quenched by addition of saturated aqueous $NaHCO_3$ solution. Organic layer separated was washed with saturated $NaHCO_3$ (20 mL), water (20 mL) and brine (20 mL), dried over Na_2SO_4 and evaporated. The residue was chromatographed on silica gel (10% to 15% EtOAc and 1% Et_3N in toluene). Yield 478 mg (80%) colourless oil. R_f 0.20 (10% EtOAc in PhMe). ESI-TOF HRMS: *m/z* = 440.1855 $[M–OH]^+$, calc. for $[C_{28}H_{26}NO_4]^+$ 440.1856. NMR (DMSO-d_6): 7.11–7.03 (m, 8H, Ar*H*); 6.96 (s, 2H, COC*H*=C*H*CO); 6.83 (d, 4H, *J* = 8.9 Hz, Ar*H*); 6.12 (s, 1H, O*H*); 3.72 (s, 6H, OCH_3); 3.43 (m, 2H, NCH_2); 2.53 (m, 2H, ArCH_2); 1.80 (m, 2H, $ArCH_2CH_2$).



4-Carbomethoxy-4′-hydroxybiphenyl. 4-Carboxy-4′-hydroxybiphenyl (2.14 g, 10 mmol) was suspended in MeOH (30 mL) and thionyl chloride (0.80 mL, 11mmol) was added dropwise. The mixture was stirred overnight, evaporated, and precipitated from THF in hexane. Yield 1.89 g (83%). NMR (DMSO-d_6): 9.71 (s, 1H, O*H*); 7.97 (d, 2H, *J* = 8.5 Hz, Ar*H*); 7.73 (d, 2H, *J* = 8.5 Hz, Ar*H*); 7.58 (d, 2H, *J* = 8.5 Hz, Ar*H*); 6.88 (d, 2H, *J* = 8.5 Hz, Ar*H*); 3.86 (s, 3H, OCH_3).

4-Carbomethoxy-4′-trifluoromethansulfonylbiphenyl. To a solution of 4-carbomethoxy-4′-hydroxybiphenyl (2.28 g, 10 mmol) in pyridine (10 mL) cooled to -20°C trifluoromethanesulfonic anhydride (1.85 mL, 11 mmol) was added dropwise within 30 min. The

mixture was allowed to warm to room temperature and left overnight, then diluted with EtOAc (150 mL), washed with water (100 mL), 5% citric acid (100 mL) and brine (100 mL), dried over Na_2SO_4 and evaporated. The residue (yellow oil) was dissolved in toluene and passed through silica gel to the desired compound as a white solid (3.38 g, 94%). NMR (DMSO-d_6): 8.05 (d, 2H, J = 8.2 Hz, Ar*H*); 7.93 (d, 2H, J = 8.8 Hz, Ar*H*); 7.86 (d, 2H, J = 8.2 Hz, Ar*H*); 7.62 (d, 2H, J = 8.8 Hz, Ar*H*); 3.88 (s, 3H, OCH_3).

Methyl 4-(4-triisopropylethynylphenyl)benzoate (54). To a solution of methyl 4-(4-trifluoromethanesulfonylphenyl)benzoate (720 mg, 2.0 mmol) and triisopropylsilylacetylene (490 μL, 2.2 mmol) in dry DMF (10 mL) $Pd(PPh_3)_4$ (115 mg, 0.1 mmol), CuI (10 mg, 0.05 mmol) and Et_3N (560 μL, 4.0 mmol) were added under Ar and the mixture was kept for 24 h at room temperature. The mixture was then diluted with EtOAc (100 mL), washed with 3% aqueous EDTA-$(NH_4)_2$ (3×100 mL) and water (2×50 mL), dried, and evaporated to dryness. The residue was chromatographed on a short silica gel column in toluene to give the title compound (438 mg, 56%) as white solid. ESI-TOF HRMS: *m/z* = 393.2250 $[M+H]^+$, calc. for $[C_{25}H_{33}O_2Si]^+$ 393.2244. NMR ($CDCl_3$): 8.09 (d, 2H, J = 8.4 Hz, Ar*H*); 7.63 (d, 2H, J = 8.4 Hz, Ar*H*); 7.56 (s, 4H, Ar*H*); 3.93 (s, 3H, OCH_3); 1.14 (s, 21H, Pr^i).

Bis(4-methoxyphenyl)-4-(4-triisopropylethynylphenyl)phenylmethanol. To a solution of methyl 4-(4-triisopropylethynylphenyl)benzoate (784 mg, 2.0 mmol) in THF (3 mL) 0.86 M 4-methoxyphenylmagnesium bromide in THF (11.6 mL, 10.0 mmol) was added in one portion and the mixture was refluxed for 3 h, then cooled, diluted with EtOAc (100 mL), washed with water (2×50 mL), 5% citric acid (2×50 mL), water (50 mL), dried over Na_2SO_4 and evaporated. The desired compound was isolated by column chromatography on silica gel (toluene + 1% Et_3N). Yield 192 mg (33%), white foam. NMR ($CDCl_3$): 7.51 (m, 6H, Ar*H*); 7.35 (d, 2H, J = 8.3 Hz, Ar*H*); 7.20 (d, 4H, J = 8.8 Hz, Ar*H*); 6.84 (d, 4H, J = 8.8 Hz, Ar*H*); 3.80 (s, 6H, OCH_3); 2.70 (s, 1H, O*H*); 1.14 (s, 21H, Pr^i).

Bis(4-methoxyphenyl)-4-(4-ethynylphenyl)phenylmethanol (55). To a solution of bis(4-methoxyphenyl)-4-(4-triisopropylethynylphenyl)phenylmethanol (180 mg, 0.31 mmol) in THF (10 mL) a solution of TBAF (113 mg, 0.47 mmol) in THF (2 mL) was added in one portion and the progress of the reaction was monitored by TLC (2% EtOAc in toluene). After 30 min the deprotection was complete. The reacton mixture was evaporated and the residue was purified by column chromatography on silica gel (toluene + 1% EtOAc + 1% Et_3N). Yield 136 mg (100%), white foam. ESI-TOF HRMS: *m/z* = 403.1688 $[M–OH]^+$, calc. for $[C_{29}H_{23}O_2]^+$ 403.1693. NMR ($CDCl_3$): 7.54 (s, 4H, Ar*H*); 7.52 (d, 2H, J = 8.4 Hz, Ar*H*); 7.36 (d, 2H, J = 8.4 Hz, Ar*H*); 7.20 (d, 4H, J = 8.8 Hz, Ar*H*); 6.84 (d, 4H, J = 8.8 Hz, Ar*H*); 3.80 (s, 6H, CH_3); 3.11 (s, 1H, ≡C*H*); 2.71 (s, 1H, O*H*).

1,3,5,7-Tetrakis[4-(4-{4-[4-bis(4-methoxyphenyl)hydroxymethyl]phenyl}phenyl-ethynyl)-phenyl]adamantan (56). To a solution of bis(4-methoxyphenyl)-4-(4-ethynylphenyl)phenylmethanol (122 mg, 0.29 mmol), tetra(4-iodophenyl)adamantane[6] (55 mg, 0.058 mmol) in DMF (4 mL) $Pd(PPh_3)_4$ (27 mg, 0.023 mmol), CuI (9.0 mg, 0.046 mmol) and Et_3N (60 μL, 0.46 mmol) were added and the solution was stirred for 24 h under Ar. The mixture was partitioned between water (50 mL) and EtOAc (50 mL), and the organic layer was washed with 0.1 M EDTA (3×30mL) and water (3×30mL), dried over Na_2SO_4 and chromatographed on silica gel in 5% acetone + 1 % Et_3N in toluene. Yield 107 mg (87%) yellowish foam, R_f 0.18 in 10% Me_2CO + 1% Et_3N in PhMe). ESI-TOF HRMS: *m/z* = 2095.8755 $[M–OH]^+$, calc. for $[C_{150}H_{119}O_{11}]^+$ 2095.8747. NMR ($CDCl_3$): 7.58 (s, 16H, Ar*H*); 7.54 (m, 16H, Ar*H*); 7.48 (d, 8H, J = 8.3 Hz, Ar*H*); 7.36 (d, 8H, J = 8.3 Hz, Ar*H*); 7.20 (d, 16H, J = 8.8 Hz, Ar*H*); 6.84 (d, 16H, J = 8.8 Hz, Ar*H*); 3.80 (s, 24H, CH_3); 2.71 (s, 4H, O*H*); 2.18 (br.s, 12H, CH_2).

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