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Supporting Information

for

Towards Organo-Click Chemistry: Development of Organocatalytic Multicomponent Reactions Through Combinations of Aldol, Wittig, Knoevenagel, Michael, Diels-Alder and Huisgen Cycloaddition Reactions

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General Methods. The ^{1}H NMR and ^{13}C NMR spectra were recorded at 400 MHz and 100 MHz, respectively. The chemical shifts are reported in ppm downfield to TMS (δ = 0) for ^{1}H NMR and relative to the central $CDCl_3$ resonance (δ = 77.0) for ^{13}C NMR. *In the ^{13}C NMR spectra, the nature of the carbons (C, CH, CH_2 or CH_3) was determined by recording the DEPT-135 experiment, and is given in parentheses.* The coupling constants *J* are given in Hz. Flash chromatography (FC) was performed using silica gel Merck 60 (particle size 0.040-0.063 mm). High-resolution mass spectra were recorded on an IonSpec FTMS mass spectrometer with a DHB-matrix. Electrospray ionization (ESI) mass spectrometry was performed on an API 100 Perkin-Elmer SCIEX single quadrupole mass spectrometer. The enantiomeric excess (*ee*) of the products were determined by HPLC using Daciel chiralcel OD-H or Daciel chiralpak AS or Daciel chiralpak AD columns with *i*-PrOH/hexane as eluent. HPLC was carried out using a Hitachi organizer consisting of a D-2500 Chromato-Integrator, a L-4000 UV-Detector, and a L-6200A

Intelligent Pump. For thin-layer chromatography (TLC), silica gel plates Merck 60 F254 were used and compounds were visualized by irradiation with UV light and/or by treatment with a solution of *p*-anisaldehyde (23 mL), conc. H_2SO_4 (35 mL), acetic acid (10 mL), and ethanol (900 mL) followed by heating.

Materials. All solvents and commercially available chemicals were used as received. 1,5-Dioxa-spiro[5.5]undecane-2,4-dione and 7-isopropyl-10-methyl-1,5-dioxa-spiro[5.5]undecane-2,4-diones are prepared cyclizing corresponding cyclohexanone and (-)-menthone with malonic acid in acetic anhydride under catalysis of concentrated H_2SO_4 or *p*-TSA at 20 to 50 °C for 5-10 h, aqueous work-up and recrystalisation with petroleum ether furnished spiro[5.5]undecane-2,4-diones. Catalyst 4-benzyl-1-methyl-imidazolidine-2-carboxylic acid (*dr* = 2:1),[1] $4\text{-}N_3C_6H_4CHO$,[2] and 4-[(2,3,4,6-tetra-O-acetyl-D-glucopyranosyl)oxy]benzaldehyde[3] are prepared according to literature procedures.

General Experimental Procedures for the Organo-Click Reactions:

Pyrrolidine Catalyzed A/K/DA and K/M Reactions in One Pot: In an ordinary glass vial equipped with a magnetic stirring bar, to 1.0 mmol of the aldehyde, 0.5 mmol of Meldrum's acid and 1.0 mmol of acetone was added 0.5 mL of solvent, and then the catalyst pyrrolidine (0.15 mmol) was added and the reaction mixture was stirred at 40 °C for the time indicated in Tables 1 and 2. The crude reaction mixture was directly loaded on silica gel column without aqueous work-up and pure domino K/A/DA and K/M products were obtained by flash column chromatography (silica gel, mixture of hexane/ethyl acetate).

Amino acids Catalyzed W/K/DA Reactions in One Pot: For the synthesis of antioxidants **6**, all reactants 1-(triphenylphosphanylidene)-propan-2-one (0.5 mmol), aldehyde (1.3 mmol), 1,5-dioxa-spiro[5.5]undecane-2,4-dione (0.5 mmol) and L-proline or glycine (0.1 mmol) in ethanol (1.0 mL) was taken in an ordinary glass vial equipped with a magnetic stirring bar and stirred at 65 °C for the time indicated in Tables 3-6. The crude reaction mixture was directly loaded on silica gel column without aqueous work-up and pure

domino antioxidant products were obtained by flash column chromatography (silica gel, mixture of hexane/ethyl acetate).

L-Proline/Cu^{I}-Catalyzed W/K/DA/HC Reactions in One Pot: For the synthesis of spirotrione-triazoles **8**, reactants 1-(triphenylphosphanylidene)-propan-2-one (0.25 mmol), 4-prop-2-ynyloxy-benzaldehyde (0.6 mmol), 1,3-cyclic diketone (0.25 mmol) and L-proline (0.05 mmol) in ethanol (0.5 mL) was taken in an ordinary glass vial equipped with a magnetic stirring bar and stirred at 65 °C for the time indicated in Table 7. $CuSO_4$ (0.25 mmol), Cu wire (3 mg), and azide (1.2 mmol) were added to the crude reaction mixture and stirred at room temperature for the time indicated in Table 7. The crude reaction mixture was directly loaded on silica gel column without aqueous work-up and pure spirotrione-triazoles **8** were obtained by flash column chromatography (silica gel, mixture of hexane/ethyl acetate).

L-DMTC Catalyzed AFCDA Reactions in One Pot: Aldehyde, Ar^1-CHO (0.5 mmol) and 1-(triphenylphosphanylidene)-propan-2-one (0.5 mmol) in benzene (0.2 mL) was stirred at 65° C for 1 h then L-DMTC (0.1 mmol), aldehyde, Ar^2-CHO (0.5 mmol), Meldrum's acid (0.5 mmol) and methanol (1.0 mL) was added and stirred at 25° C for the time indicated in Table 8. The crude reaction mixture was treated with saturated aqueous ammonium chloride solution, the layers were separated, and the organic layer was extracted three to four times with dichloromethane, dried with anhydrous Na_2SO_4, and evaporated. The pure AFCDA products were obtained by flash column chromatography (silica gel, mixture of hexane/ethyl acetate). Enantiomeric excesses (ee) and NMR of pure AFCDA products were compared with our previous report of ATCDA products.[4]

Imidazolidine Catalyzed ATCM Reactions in One Pot: Aldehyde (0.5 mmol) and 1-(triphenylphosphanylidene)-propan-2-one (0.5 mmol) in benzene (0.2 mL) was stirred at 65° C for 1 h then 4-benzyl-1-methyl-imidazolidine-2-carboxylic acid (0.05 mmol) and diethyl malonate or dibenzyl malonate (0.5 mL) was added and stirred at 25° C for the time indicated in Scheme 6. The pure ATCM products were obtained by FC directly from crude reaction mixture and NMR and ee's of the ATCM products were compared with literature values, which are obtained from two-component reactions.[5]

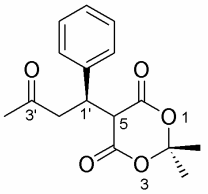
(7b,11b)-3,3-Dimethyl-7,11-diphenyl-2,4-dioxa-spiro[5.5]undecane-1,5,9-trione (4a). Purified by FC using EtOAc/hexane and isolated as light yellow colored solid. Note the product contains a plane of symmetry. ^{1}H NMR ($CDCl_3$) δ 7.38 – 7.20 (10H, m, Ph-*H*), 4.01 (2H, dd, *J* = 14.4, 4.4 Hz, H-7 & 11), 3.72 (2H, t, *J* = 14.4 Hz), 2.65 (2H, ddd, *J* = 14.4, 4.4, 1.2 Hz), 0.55 (6H, s, 2 x *tert*-CH_3); ^{13}C NMR ($CDCl_3$, DEPT) δ 207.5 (C, C=O), 168.1 (C, O=C-O), 165.2 (C, O-C=O), 137.0 (2 x C), 129.2 (4 x CH), 128.6 (2 x CH), 128.4 (4 x CH), 106.3 (C, O-*C*-O), 60.5 (C, C-6), 50.0 (2 x CH), 42.8 (2 x CH_2), 28.3 (2 x CH_3); HRMS (MALDI-FTMS) m/z 401.1352 (M + Na^+), calcd for $C_{23}H_{22}O_5\,Na^+$ 401.1359.

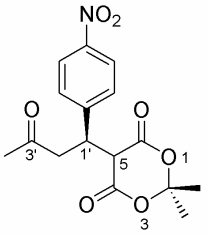
(7b,11b)-3,3-Dimethyl-7,11-(di 4-nitrophenyl)-2,4-dioxa-spiro[5.5]undecane-1,5,9-trione (4b). Purified by FC using EtOAc/hexane and isolated as a white solid and it has a plane of symmetry. ^{1}H NMR ($CDCl_3$) δ 8.24 (4H, td, *J* = 8.8, 2.0 Hz), 7.45 (4H, td, *J* = 8.8, 2.0 Hz) [Aromatic-*H*]; 4.15 (2H, dd, *J* = 14.4, 4.0 Hz), 3.72 (2H, t, *J* = 14.8 Hz), 2.70 (2H, dd, *J* = 14.8, 4.0 Hz), 0.63 (6H, s, 2 x *tert*-CH_3); ^{13}C NMR ($CDCl_3$, DEPT) δ 204.6 (C, C=O), 167.3 (C, O=C-O), 164.6 (C, O=C-O), 148.1 (2 x C), 143.5 (2 x C), 129.7 (4 x CH), 124.4 (4 x CH), 106.8 (C, O-C-O), 59.5 (C, C-6), 49.8 (2 x CH), 42.3 (2 x CH_2), 28.7 (2 x CH_3); ESI m/z 467.10 (M – H), calcd for $C_{23}H_{20}O_9N_2$ 468.1168.

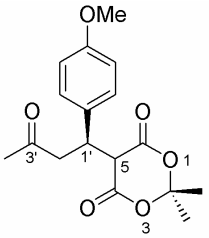
(7b,11b)-3,3-Dimethyl-7,11-(di 4-methoxyphenyl)-2,4-dioxa-spiro[5.5]undecane-1,5,9-trione (4c). Purified by FC using EtOAc/hexane and isolated as a white solid and it has a plane of symmetry. ^{1}H NMR ($CDCl_3$) δ 7.15 (4H, d, *J* = 8.8 Hz), 6.85 (4H, d, *J* = 8.8 Hz) [Aromatic-*H*]; 3.95 (2H, dd, *J* = 14.4, 4.4 Hz), 3.76 (6H, s, 2 x OCH_3), 3.65 (2H, t, *J* = 14.8 Hz), 2.59 (2H, dd, *J* = 14.8, 4.0 Hz), 0.65 (6H, s, 2 x *tert*-CH_3); ^{13}C NMR ($CDCl_3$, DEPT) δ 207.6 (C, C=O), 168.3 (C, O=C-O), 165.3 (C, O=C-O), 159.5 (2 x C), 129.4 (4 x CH), 129.1 (2 x C), 114.3 (4 x CH), 106.1 (C, O-C-O), 60.8 (C, C-6), 55.2 (2 x CH_3,

O*C*H_3), 49.1 (2 x CH), 43.0 (2 x CH_2), 28.3 (2 x CH_3); HRMS (MALDI-FTMS) m/z 461.1568 (M + Na^+), calcd for $C_{25}H_{26}O_7\,Na^+$ 461.1571.

(7b,11b)-3,3-Dimethyl-7,11-(di 4-cyanophenyl)-2,4-dioxa-spiro[5.5]undecane-1,5,9-trione (4f). Purified by FC using EtOAc/hexane and isolated as a white solid and it has a plane of symmetry. ^{1}H NMR ($CDCl_3$) δ 7.68 (4H, d, *J* = 8.4 Hz), 7.37 (4H, d, *J* = 8.4 Hz) [Aromatic-*H*]; 4.07 (2H, dd, *J* = 14.4, 4.4 Hz), 3.68 (2H, t, *J* = 14.8 Hz), 2.67 (2H, dd, *J* = 14.4, 4.4 Hz), 0.63 (6H, s, 2 x *tert*-C*H*$_3$).

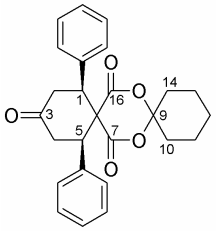
2,2-Dimethyl-5-(3-oxo-1-phenyl-butyl)-[1,3]dioxane-4,6-dione (7a): 
Purified by FC using EtOAc/hexane and isolated as a solid. ^{1}H NMR ($CDCl_3$) δ 7.35 – 7.20 (5H, m, Ph-*H*), 4.26 (1H, m, H-1'), 4.20 (1H, d, *J* = 3.6 Hz, H-5), 3.70 (1H, dd, *J* = 18.8, 10.0 Hz), 3.05 (1H, dd, *J* = 18.8, 5.2 Hz), 2.20 (3H, s, C*H*$_3$, COC*H*$_3$), 1.67 (3H, s, *tert*-C*H*$_3$), 1.32 (3H, s, *tert*-C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT) δ 207.8 (C, C=O), 165.3 (C, O=C-O), 165.1 (C, O=C-O), 139.6 (C), 128.70 (2 x CH), 128.66 (2 x CH), 127.7 (CH), 105.2 (C, O-C-O), 48.9 (CH), 45.3 (CH_2), 39.5 (CH), 30.3 (CH_3), 28.0 (CH_3), 27.7 (CH_3).

2,2-Dimethyl-5-[3-oxo-1-(4-nitrophenyl)-butyl]-[1,3]dioxane-4,6-dione (7b): 
Purified by FC using EtOAc/hexane and isolated as a light yellow color solid. ^{1}H NMR ($CDCl_3$) δ 8.13 (2H, td, *J* = 8.8, 2.0 Hz), 7.59 (2H, td, *J* = 8.8, 2.0 Hz) [Ar-*H*]; 4.39 (1H, m, H-1'), 4.34 (1H, d, *J* = 3.2 Hz, H-5), 3.68 (1H, dd, *J* = 18.8, 9.6 Hz), 3.12 (1H, dd, *J* = 18.8, 5.6 Hz), 2.22 (3H, s, C*H*$_3$, COC*H*$_3$), 1.75 (3H, s, *tert*-C*H*$_3$), 1.60 (3H, s, *tert*-C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT) δ 207.3 (C, C=O), 164.8 (C, O=C-O), 164.3 (C, O=C-O), 147.2 (C), 147.1 (C), 130.2 (2 x CH), 123.7 (2 x CH), 105.3 (C, O-C-O), 48.7 (CH), 44.8 (CH_2), 38.4 (CH), 30.2 (CH_3), 28.0 (CH_3), 27.2 (CH_3).

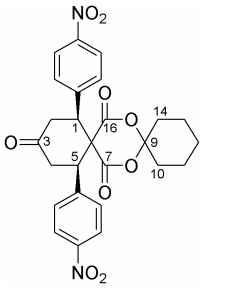
2,2-Dimethyl-5-[3-oxo-1-(4-methoxyphenyl)-butyl]-[1,3]dioxane-4,6-dione (7c): 
Purified by FC using EtOAc/hexane and isolated as a light yellow color solid. ^{1}H NMR ($CDCl_3$) δ 7.25 (2H, td, *J* = 9.2, 2.4 Hz), 6.81 (2H, td, *J* = 8.8, 2.0 Hz) [Ar-*H*];

4.22 (1H, m, H-1'), 4.19 (1H, d, *J* = 3.6 Hz, H-5), 3.77 (3H, s, OC*H*$_3$), 3.70 (1H, dd, *J* = 18.8, 10.4 Hz), 3.01 (1H, dd, *J* = 18.8, 4.8 Hz), 2.20 (3H, s, C*H*$_3$, COC*H*$_3$), 1.67 (3H, s, *tert*-C*H*$_3$), 1.35 (3H, s, *tert*-C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT) δ 208.3 (C, C=O), 165.7 (C, O=C-O), 165.5 (C, O=C-O), 159.2 (C), 131.8 (C), 130.1 (2 x CH), 114.2 (2 x CH), 105.4 (C, O-C-O), 55.4 (CH_3, O*C*H$_3$), 49.3 (CH), 45.9 (CH_2), 39.1 (CH), 30.6 (CH_3), 28.3 (CH_3), 28.1 (CH_3).

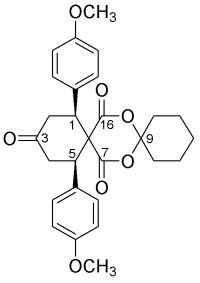
(1b,5b)-1,5-Bis-phenyl-8,15-dioxa-dispiro[5.2.5.2]hexadecane-3,7,16-trione (6a). Purified by FC using EtOAc/hexane and isolated as a white solid. Note the product contains a plane of symmetry. ^{1}H NMR ($CDCl_3$) δ 7.35 – 7.21 (10H, m, Ph-*H*), 4.01 (2H, dd, *J* = 14.4, 4.4 Hz, H-1 & 5), 3.73 (2H, t, *J* = 15.2 Hz), 2.64 (2H, dd, *J* = 14.8, 4.4 Hz), 1.30 – 1.10 (6H, m), 0.48 (4H, br s); ^{13}C NMR ($CDCl_3$, DEPT) δ 207.6 (C, C=O), 168.3 (C, O=C-O), 165.4 (C, O-C=O), 137.1 (2 x C), 129.0 (4 x CH), 128.5 (2 x CH), 128.3 (4 x CH), 106.7 (C, O-*C*-O), 61.0 (C, C-6), 50.0 (2 x CH), 42.8 (2 x CH_2), 37.2 (2 x CH_2), 23.5 (CH_2), 21.6 (2 x CH_2); ESI m/z 417.20 (M – H), calcd for $C_{26}H_{26}O_5$ 418.1780.



(1b,5b)-1,5-Bis-(4-nitrophenyl)-8,15-dioxa-dispiro[5.2.5.2]hexadecane-3,7,16-trione (6b). Purified by FC using EtOAc/hexane and isolated as a light yellow color solid. Note the product contains a plane of symmetry. ^{1}H NMR ($CDCl_3$) δ 8.20 (4H, d, *J* = 8.8 Hz), 7.42 (4H, d, *J* = 8.8 Hz) [Ar-*H*]; 4.13 (2H, dd, *J* = 14.4, 4.4 Hz, H-1 & 5), 3.70 (2H, t, *J* = 14.8 Hz), 2.68 (2H, dd, *J* = 14.8, 4.4 Hz), 1.40 – 1.15 (6H, m), 0.52 (4H, br s); ^{13}C NMR ($CDCl_3$, DEPT) δ 204.7 (C, C=O), 167.6 (C, O=C-O), 164.8 (C, O-C=O), 148.0 (2 x C), 143.7 (2 x C), 129.6 (4 x CH), 124.2 (4 x CH), 107.4 (C, O-*C*-O), 60.0 (C, C-6), 49.8 (2 x CH), 42.3 (2 x CH_2), 37.6 (2 x CH_2), 23.3 (CH_2), 21.5 (2 x CH_2); ESI m/z 507.20 (M – H), calcd for $C_{26}H_{24}O_9N_2$ 508.1481.

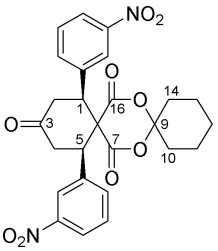


(1b,5b)-1,5-Bis-(4-methoxyphenyl)-8,15-dioxa-dispiro[5.2.5.2]hexadecane-3,7,16-trione (6c). Purified by FC using

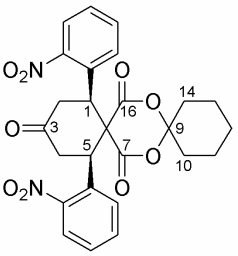


EtOAc/hexane and isolated as a light yellow color solid. Note the product contains a plane of symmetry. ^{1}H NMR ($CDCl_3$) δ 7.07 (4H, br d, *J* = 8.4 Hz), 6.77 (4H, br d, *J* = 8.4 Hz) [Ar-*H*]; 3.87 (2H, dd, *J* = 14.4, 4.4 Hz, H-1 & 5), 3.69 (6H, s, 2 x OCH_3), 3.59 (2H, t, *J* = 14.4 Hz), 2.52 (2H, dd, *J* = 14.8, 4.4 Hz), 1.30 – 1.00 (6H, m), 0.52 (4H, br s); ^{13}C NMR ($CDCl_3$, DEPT) δ 207.8 (C, C=O), 168.6 (C, O=C-O), 165.6 (C, O-C=O), 159.5 (2 x C), 143.2 (2 x C), 129.4 (4 x CH), 114.2 (4 x CH), 106.6 (C, O-*C*-O), 61.4 (C, C-6), 55.2 (2 x CH_3, OCH_3), 49.2 (2 x CH), 43.1 (2 x CH_2), 37.2 (2 x CH_2), 23.5 (CH_2), 21.6 (2 x CH_2); HRMS (MALDI-FTMS) m/z 501.1868 (M + Na^+), calcd for $C_{28}H_{30}O_7$ Na^+ 501.1884.

(1b,5b)-1,5-Bis-(3-nitrophenyl)-8,15-dioxa-dispiro[5.2.5.2]hexadecane-3,7,16-trione (6d). Purified by FC using EtOAc/hexane and isolated as a light yellow color solid. Note the product contains a plane of symmetry. ^{1}H NMR ($CDCl_3$) δ 8.21 (2H, br d, *J* = 7.2 Hz), 8.11 (2H, br s), 7.64 – 7.56 (4H, m) [Ar-*H*]; 4.18 (2H, dd, *J* = 14.4, 4.4 Hz, H-1 & 5), 3.76 (2H, t, *J* = 14.8 Hz), 2.73 (2H, dd, *J* = 14.8, 4.4 Hz), 1.40 – 1.15 (6H, m), 0.53 (4H, br s); ^{13}C NMR ($CDCl_3$, DEPT) δ 204.8 (C, C=O), 167.6 (C, O=C-O), 164.7 (C, O-C=O), 148.5 (2 x C), 138.9 (2 x C), 134.6 (2 x CH), 130.3 (2 x CH), 123.8 (2 x CH), 123.2 (2 x CH), 107.2 (C, O-*C*-O), 60.3 (C, C-6), 49.5 (2 x CH), 42.4 (2 x CH_2), 37.6 (2 x CH_2), 23.2 (CH_2), 21.4 (2 x CH_2); ESI m/z 507.20 (M – H), calcd for $C_{26}H_{24}O_9N_2$ 508.1481.

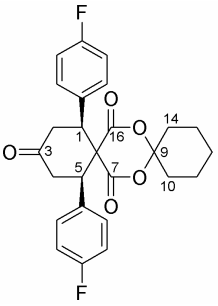


(1b,5b)-1,5-Bis-(2-nitrophenyl)-8,15-dioxa-dispiro[5.2.5.2]hexadecane-3,7,16-trione (6e). Purified by FC using EtOAc/hexane and isolated as a light yellow color solid. Note the product contains a plane of symmetry. ^{1}H NMR ($CDCl_3$) δ 7.76 (2H, br d, *J* = 8.0 Hz), 7.68 – 7.53 (4H, m), 7.52 – 7.44 (2H, m) [Ar-*H*]; 4.77 (2H, br d, *J* = 12.8 Hz, H-1 & 5), 3.57 (2H, br t, *J* = 13.6 Hz), 2.88 (2H, br d, *J* = 15.6 Hz), 1.40 – 1.00 (6H, m), 0.64 (4H, br s); ^{13}C NMR ($CDCl_3$, DEPT) δ 204.3 (C, C=O), 167.2 (C, O=C-O), 166.1 (C, O-C=O), 150.6 (2 x C), 132.8 (2 x CH), 130.8 (2 x C), 129.5 (2 x CH), 128.7 (2 x CH), 125.3 (2 x CH), 107.2 (C, O-*C*-O), 59.1

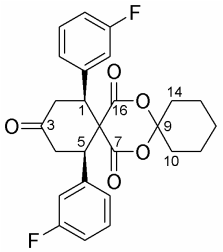


(C, C-6), 43.1 (2 x CH), 42.7 (2 x CH_2), 37.4 (2 x CH_2), 23.3 (CH_2), 21.4 (2 x CH_2); HRMS (MALDI-FTMS) m/z 531.1393 ($M + Na^+$), calcd for $C_{26}H_{24}N_2O_9Na^+$ 531.1374.

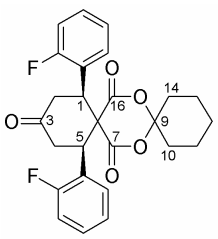
(1b,5b)-1,5-Bis-(4-fluorophenyl)-8,15-dioxa-dispiro[5.2.5.2]hexadecane-3,7,16-trione (6f). Purified by FC using EtOAc/hexane and isolated as a white solid. Note the product contains a plane of symmetry. ^{1}H NMR ($CDCl_3$) δ 7.22 (2H, br d, *J* = 8.8 Hz), 7.21 (2H, br d, *J* = 8.8 Hz), 7.04 (2H, br d, *J* = 8.8 Hz), 7.02 (2H, br d, *J* = 8.8 Hz), 3.99 (2H, dd, *J* = 14.4, 4.4 Hz, H-1 & 5), 3.65 (2H, t, *J* = 14.8 Hz), 2.62 (2H, dd, *J* = 14.8, 4.4 Hz), 1.27 (4H, m), 1.19 (2H, m), 0.60 (4H, m); ^{13}C NMR ($CDCl_3$, DEPT) δ 206.7 (C, C=O), 168.3 (C, O=C-O), 165.3 (C, O-C=O), 163.9 (C, Ph-F), 161.4 (C, Ph-F), 132.96 (C), 132.93 (C), 130.16 (2 x CH), 130.09 (2 x CH), 116.1 (2 x CH), 115.8 (2 x CH), 106.9 (C, O-*C*-O), 61.1 (C, C-6), 49.2 (2 x CH), 42.9 (2 x CH_2), 37.4 (2 x CH_2), 23.5 (CH_2), 21.6 (2 x CH_2); HRMS (MALDI-FTMS) m/z 477.1484 ($M + Na^+$), calcd for $C_{26}H_{24}F_2O_5Na^+$ 477.1484.



(1b,5b)-1,5-Bis-(3-fluorophenyl)-8,15-dioxa-dispiro[5.2.5.2]hexadecane-3,7,16-trione (6g). Purified by FC using EtOAc/hexane and isolated as a white solid. Note the product contains a plane of symmetry. ^{1}H NMR ($CDCl_3$) δ 7.32 (1H, t, *J* = 8.0 Hz), 7.31 (1H, t, *J* = 8.0 Hz) [H-5' & 5'']; 7.07 – 6.90 (6H, m), 4.0 (2H, dd, *J* = 14.4, 4.4 Hz, H-1 & 5), 3.66 (2H, t, *J* = 14.4 Hz), 2.65 (2H, dd, *J* = 15.2, 4.4 Hz), 1.28 (4H, m), 1.18 (2H, m), 0.60 (4H, m); ^{13}C NMR ($CDCl_3$, DEPT) δ 206.3 (C, C=O), 168.0 (C, O=C-O), 165.1 (C, O-C=O), 164.1 (C, Ph-F), 161.7 (C, Ph-F), 139.44 (C), 139.37 (C), 130.74(CH), 130.65 (CH), 124.20 (CH), 124.17 (CH), 115.77 (CH), 115.55 (2 x CH), 115.33 (CH), 107.0 (C, O-*C*-O), 60.5 (C, C-6), 49.67 (CH), 49.66 (CH), 42.6 (2 x CH_2), 37.4 (2 x CH_2), 23.5 (CH_2), 21.5 (2 x CH_2); HRMS (MALDI-FTMS) m/z 477.1479 ($M + Na^+$), calcd for $C_{26}H_{24}F_2O_5Na^+$ 477.1484.

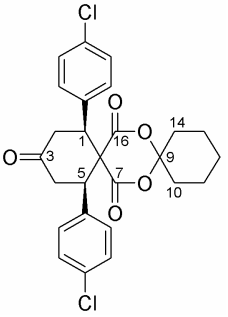


(1b,5b)-1,5-Bis-(2-fluorophenyl)-8,15-dioxa-dispiro[5.2.5.2]hexadecane-3,7,16-trione (6h). Purified by FC using EtOAc/hexane and isolated as a white solid. Note the product

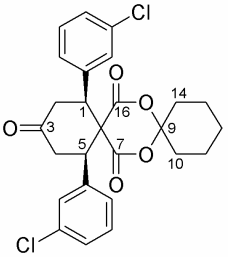


contains a plane of symmetry. ^{1}H NMR ($CDCl_3$) δ 7.35 (2H, br t, *J* = 7.6 Hz), 7.32 – 7.24 (2H, m), 7.14 (2H, br t, *J* = 8.0 Hz), 7.06 (2H, m), 4.48 (2H, dd, *J* = 14.4, 4.4 Hz, H-1 & 5), 3.68 (2H, t, *J* = 14.4 Hz), 2.62 (2H, dd, *J* = 15.2, 4.8 Hz), 1.40 – 1.0 (6H, m), 0.74 (4H, t, *J* = 6.0 Hz); ^{13}C NMR ($CDCl_3$, DEPT) δ 206.2 (C, C=O), 166.7 (C, O=C-O), 165.9 (C, O-C=O), 161.3 (C, Ph-F), 158.8 (C, Ph-F), 130.22 (CH), 130.14 (CH), 129.2 (2 x C), 124.66 (CH), 124.62 (CH), 124.56 (CH), 124.43 (CH), 116.52 (CH), 116.29 (CH), 106.7 (C, O-*C*-O), 58.5 (C, C-6), 43.0 (2 x CH), 42.2 (2 x CH_2), 37.5 (2 x CH_2), 23.6 (CH_2), 21.6 (2 x CH_2); HRMS (MALDI-FTMS) m/z 477.1485 (M + Na^+), calcd for $C_{26}H_{24}F_2O_5\ Na^+$ 477.1484.

(1b,5b)-1,5-Bis-(4-chlorophenyl)-8,15-dioxa-dispiro[5.2.5.2]hexadecane-3,7,16-trione (6i). Purified by FC using EtOAc/hexane and isolated as a light yellow color solid. Note the product contains a plane of symmetry. ^{1}H NMR ($CDCl_3$) δ 7.31 (4H, td, *J* = 8.4, 2.0 Hz), 7.16 (4H, td, *J* = 8.4, 2.0 Hz), 3.97 (2H, dd, *J* = 14.4, 4.4 Hz, H-1 & 5), 3.64 (2H, t, *J* = 14.8 Hz), 2.62 (2H, dd, *J* = 14.8, 4.4 Hz), 1.28 (4H, m), 1.18 (2H, m), 0.60 (4H, br s); ^{13}C NMR ($CDCl_3$, DEPT) δ 206.4 (C, C=O), 168.2 (C, O=C-O), 165.2 (C, O-C=O), 135.4 (2 x C), 134.6 (2 x C), 129.7 (4 x CH), 129.2 (4 x CH), 107.0 (C, O-*C*-O), 60.8 (C, C-6), 49.4 (2 x CH), 42.7 (2 x CH_2), 37.4 (2 x CH_2), 23.5 (CH_2), 21.6 (2 x CH_2); HRMS (MALDI-FTMS) m/z 509.0878 (M + Na^+), calcd for $C_{26}H_{24}Cl_2O_5\ Na^+$ 509.0893.

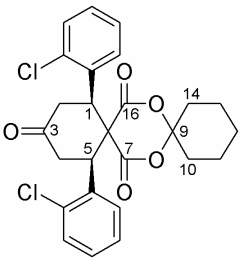


(1b,5b)-1,5-Bis-(3-chlorophenyl)-8,15-dioxa-dispiro[5.2.5.2]hexadecane-3,7,16-trione (6j). Purified by FC using EtOAc/hexane and isolated as a light yellow color solid. Note the product contains a plane of symmetry. ^{1}H NMR ($CDCl_3$) δ 7.31 – 7.26 (4H, m), 7.23 (2H, br s), 7.15 – 7.09 (2H, m) [Ar-*H*]; 3.96 (2H, dd, *J* = 14.4, 4.4 Hz, H-1 & 5), 3.65 (2H, t, *J* = 14.8 Hz), 2.64 (2H, dd, *J* = 15.2, 4.4 Hz), 1.40 – 1.20 (4H, m), 1.20 – 1.10 (2H, m), 0.62 (4H, t, *J* = 5.6 Hz); ^{13}C NMR ($CDCl_3$, DEPT) δ 206.2 (C, C=O), 167.9 (C, O=C-O), 165.0 (C, O-C=O), 139.0 (2 x C), 135.1 (2 x C), 130.4 (2 x CH), 128.9 (2 x CH), 128.4 (2 x CH), 126.7 (2 x

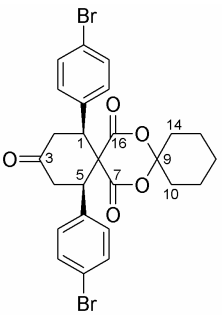


CH), 107.1 (C, O-*C*-O), 60.5 (C, C-6), 49.6 (2 x CH), 42.6 (2 x CH_2), 37.4 (2 x CH_2), 23.5 (CH_2), 21.5 (2 x CH_2); HRMS (MALDI-FTMS) m/z 509.0884 ($M + Na^+$), calcd for $C_{26}H_{24}Cl_2O_5Na^+$ 509.0893.

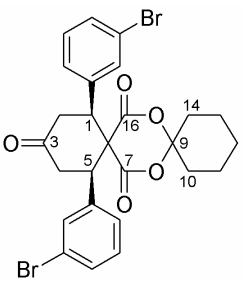
(1b,5b)-1,5-Bis-(2-chlorophenyl)-8,15-dioxa-dispiro[5.2.5.2]hexadecane-3,7,16-trione (6k). Purified by FC using EtOAc/hexane and isolated as a light yellow color solid. Note the product contains a plane of symmetry. ^{1}H NMR ($CDCl_3$) δ 7.48 – 7.38 (4H, m), 7.30 – 7.18 (4H, m) [Ar-*H*]; 4.80 (2H, dd, *J* = 14.4, 4.4 Hz, H-1 & 5), 3.52 (2H, t, *J* = 15.2 Hz), 2.63 (2H, dd, *J* = 15.2, 4.4 Hz), 1.40 – 1.10 (6H, m), 0.84 (4H, br s); ^{13}C NMR ($CDCl_3$, DEPT) δ 205.9 (C, C=O), 166.7 (C, O=C-O), 165.8 (C, O-C=O), 135.3 (2 x C), 134.5 (2 x C), 130.7 (2 x CH), 129.5 (2 x CH), 128.5 (2 x CH), 127.2 (2 x CH), 106.9 (C, O-*C*-O), 57.4 (C, C-6), 44.9 (2 x CH), 43.9 (2 x CH_2), 37.5 (2 x CH_2), 23.6 (CH_2), 21.6 (2 x CH_2); HRMS (MALDI-FTMS) m/z 509.0875 ($M + Na^+$), calcd for $C_{26}H_{24}Cl_2O_5Na^+$ 509.0893.



(1b,5b)-1,5-Bis-(4-bromophenyl)-8,15-dioxa-dispiro[5.2.5.2]hexadecane-3,7,16-trione (6l). Purified by FC using EtOAc/hexane and isolated as a light yellow color solid. Note the product contains a plane of symmetry. ^{1}H NMR ($CDCl_3$) δ 7.46 (4H, td, *J* = 8.4, 1.6 Hz), 7.10 (4H, td, *J* = 8.4, 1.6 Hz) [Ar-*H*]; 3.95 (2H, dd, *J* = 14.4, 4.4 Hz, H-1 & 5), 3.64 (2H, t, *J* = 14.4 Hz), 2.62 (2H, dd, *J* = 15.2, 4.8 Hz), 1.40 – 1.15 (6H, m), 0.59 (4H, br s); ^{13}C NMR ($CDCl_3$, DEPT) δ 206.4 (C, C=O), 168.1 (C, O=C-O), 165.2 (C, O-C=O), 136.0 (2 x C), 132.22 (2 x CH), 132.17 (2 x CH), 130.0 (4 x CH), 122.7 (2 x C), 107.0 (C, O-*C*-O), 60.7 (C, C-6), 49.5 (2 x CH), 42.6 (2 x CH_2), 37.5 (2 x CH_2), 23.5 (CH_2), 21.7 (2 x CH_2); HRMS (MALDI-FTMS) m/z 596.9877 ($M + Na^+$), calcd for $C_{26}H_{24}Br_2O_5Na^+$ 596.9883.

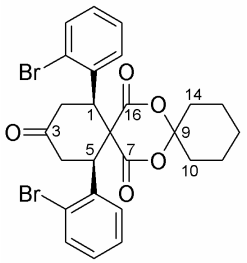


(1b,5b)-1,5-Bis-(3-bromophenyl)-8,15-dioxa-dispiro[5.2.5.2]hexadecane-3,7,16-trione (6m). Purified by FC using EtOAc/hexane and isolated as a light yellow color solid. Note the product contains a plane of symmetry. ^{1}H NMR ($CDCl_3$) δ 7.44 (2H, br d, *J* = 8.0 Hz), 7.38

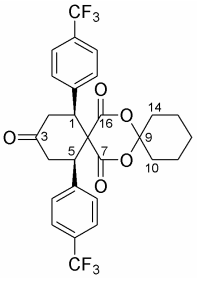


(2H, br s), 7.21 (2H, br t, *J* = 7.6 Hz), 7.15 (2H, br d, *J* = 8.0 Hz) [Ar-*H*]; 3.95 (2H, dd, *J* = 14.4, 4.4 Hz, H-1 & 5), 3.64 (2H, t, *J* = 14.4 Hz), 2.63 (2H, dd, *J* = 14.8, 4.4 Hz), 1.40 – 1.15 (6H, m), 0.62 (4H, t, *J* = 6.0 Hz); ^{13}C NMR ($CDCl_3$, DEPT) δ 206.1 (C, C=O), 167.9 (C, O=C-O), 165.0 (C, O-C=O), 139.2 (2 x C), 131.8 (2 x CH), 131.2 (2 x CH), 130.6 (2 x CH), 127.1 (2 x CH), 123.1 (2 x C), 107.1 (C, O-*C*-O), 60.5 (C, C-6), 49.5 (2 x CH), 42.5 (2 x CH_2), 37.4 (2 x CH_2), 23.5 (CH_2), 21.5 (2 x CH_2); HRMS (MALDI-FTMS) m/z 596.9872 (M + Na^+), calcd for $C_{26}H_{24}Br_2O_5$ Na^+ 596.9883.

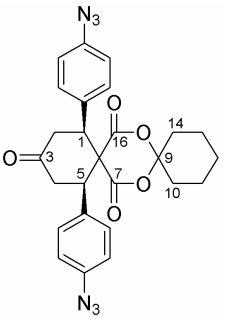
(1b,5b)-1,5-Bis-(2-bromophenyl)-8,15-dioxa-dispiro[5.2.5.2]hexadecane-3,7,16-trione (6n). Purified by FC using EtOAc/hexane and isolated as a light yellow color solid. Note the product contains a plane of symmetry. ^{1}H NMR ($CDCl_3$) δ 7.60 (2H, br d, *J* = 8.0 Hz), 7.43 (2H, br d, *J* = 7.6 Hz), 7.31 (2H, br t, *J* = 8.0 Hz), 7.14 (2H, br t, *J* = 7.6 Hz) [Ar-*H*]; 4.77 (2H, dd, *J* = 14.0, 4.4 Hz, H-1 & 5), 3.48 (2H, t, *J* = 14.8 Hz), 2.66 (2H, dd, *J* = 15.6, 4.4 Hz), 1.50 – 1.15 (6H, m), 0.87 (4H, m); ^{13}C NMR ($CDCl_3$, DEPT) δ 205.8 (C, C=O), 166.8 (C, O=C-O), 165.6 (C, O-C=O), 137.1 (2 x C), 134.2 (2 x CH), 129.7 (2 x CH), 128.5 (2 x CH), 127.9 (2 x CH), 125.3 (2 x C), 107.0 (C, O-*C*-O), 57.3 (C, C-6), 47.8 (2 x CH), 44.0 (2 x CH_2), 37.5 (2 x CH_2), 23.6 (CH_2), 21.7 (2 x CH_2); HRMS (MALDI-FTMS) m/z 596.9895 (M + Na^+), calcd for $C_{26}H_{24}Br_2O_5$ Na^+ 596.9883.



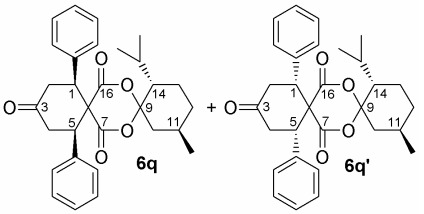
(1b,5b)-1,5-Bis-(4-trifluoromethylphenyl)-8,15-dioxa-dispiro[5.2.5.2]hexadecane-3,7,16-trione (6o). Purified by FC using EtOAc/hexane and isolated as a light yellow color solid. Note the product contains a plane of symmetry. ^{1}H NMR ($CDCl_3$) δ 7.62 (4H, d, *J* = 7.6 Hz), 7.38 (4H, d, *J* = 8.0 Hz) [Ar-*H*]; 4.11 (2H, dd, *J* = 14.4, 4.0 Hz, H-1 & 5), 3.74 (2H, t, *J* = 14.4 Hz), 2.69 (2H, dd, *J* = 14.8, 4.0 Hz), 1.22 (6H, m), 0.47 (4H, br s); ^{13}C NMR ($CDCl_3$, DEPT) δ 205.8 (C, C=O), 167.9 (C, O=C-O), 165.0 (C, O-C=O), 140.8 (2 x C), 128.9 (4 x CH), 126.10 (2 x CH), 126.04 (2 x CH), 126.0 (2 x C), 124.9 (C), 122.2 (C), 107.1 (C, O-*C*-O), 60.6 (C, C-6), 49.8 (2 x CH), 42.4 (2 x CH_2), 37.4 (2 x CH_2), 23.4 (CH_2), 21.5 (2 x CH_2); ESI m/z 553.20 (M – H), calcd for $C_{28}H_{24}O_5F_6$ 554.1527.



(1b,5b)-1,5-Bis-(4-azidophenyl)-8,15-dioxa-dispiro[5.2.5.2]hexadecane-3,7,16-trione (6p). Purified by FC using EtOAc/hexane and isolated as a yellow color solid. Note the product contains a plane of symmetry. IR (Neat): 2930, 2104 (N=N=N), 1720 (C=O), 1603, 1505, 1282 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.21 (4H, td, *J* = 8.8, 2.8 Hz), 6.98 (4H, td, *J* = 8.4, 2.0 Hz) [Ar-*H*]; 3.97 (2H, dd, *J* = 14.4, 4.4 Hz, H-1 & 5), 3.65 (2H, t, *J* = 14.4 Hz), 2.61 (2H, dd, *J* = 15.2, 4.8 Hz), 1.33 – 1.15 (6H, m), 0.61 (4H, br s); ^{13}C NMR ($CDCl_3$, DEPT) δ 206.9 (C, C=O), 168.3 (C, O=C-O), 165.3 (C, O-C=O), 140.5 (2 x C), 133.6 (2 x C), 129.8 (4 x CH), 119.5 (4 x CH), 106.9 (C, O-*C*-O), 61.0 (C, C-6), 49.4 (2 x CH), 42.8 (2 x CH_2), 37.5 (2 x CH_2), 23.5 (CH_2), 21.6 (2 x CH_2); ESI m/z 499.20 (M – H), calcd for $C_{26}H_{24}O_5N_6$ 500.1808.

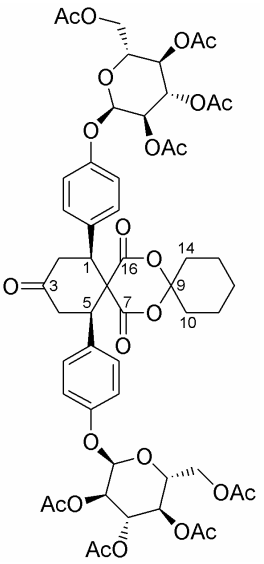


(1*R*,5*S*,11*R*,14*S*)-14-Isopropyl-11-methyl-1,5-bis-phenyl-8,15-dioxa-dispiro[5.2.5.2]hexadecane-3,7,16-trione (6q) and (1*S*,5*R*,11*R*,14*S*)-14-Isopropyl-11-methyl-1,5-bis-phenyl-8,15-dioxa-dispiro[5.2.5.2]hexadecane-3,7,16-trione (6q'). Purified by FC using EtOAc/hexane and isolated as a white solid. ^1H NMR ($CDCl_3$, 1:1 diastereomers) δ 7.39 – 7.17 (20H, m) [Ar-*H*]; 4.20 – 3.92 (4H, m), 3.82 (1H, t, *J* = 14.8 Hz), 3.74 (2H, AB q, *J* = 14.4 Hz), 3.63 (1H, t, *J* = 14.4 Hz), 2.62 – 2.37 (4H, m), 1.60 – 0.90 (10H, m), 0.72 – 0.52 (4H, m), 0.50 (3H, d, *J* = 6.8 Hz, *sec*-CH_3), 0.42 (3H, d, *J* = 7.2 Hz, *sec*-CH_3), 0.41 (3H, d, *J* = 7.0 Hz, *sec*-CH_3), 0.38 (3H, d, *J* = 6.4 Hz, *sec*-CH_3), 0.34 (3H, d, *J* = 6.8 Hz, *sec*-CH_3), 0.26 (1H, m), 0.07 (3H, d, *J* = 6.8 Hz, *sec*-CH_3), -0.06 (1H, m), -0.56 (1H, ddd, *J* = 14.0, 3.6, 2.0 Hz), -0.61 (1H, ddd, *J* = 14.0, 3.6, 2.0 Hz); ^{13}C NMR ($CDCl_3$, DEPT, 1:1 diastereomers) δ 207.3 (C, C=O), 207.2 (C, C=O), 169.6 (C, O=C-O), 168.5 (C, O-C=O), 166.9 (C, O=C-O), 165.6 (C, O-C=O), 138.2 (C), 138.1 (C), 136.9 (C), 136.7 (C), 129.3 (16 x CH), 129.1 (CH), 129.0 (CH), 128.6 (CH), 128.3 (CH), 109.7 (C, O-*C*-O), 109.6 (C, O-*C*-O), 60.7 (C, C-6), 60.5 (C, C-6), 52.8 (CH), 52.6 (CH), 49.3 (CH), 49.1 (CH), 48.9 (CH), 48.8 (CH), 48.2 (CH_2), 47.7 (CH_2), 44.1 (CH_2), 43.5 (2 x CH_2), 43.45 (CH_2), 33.3 (2 x CH_2), 28.6 (CH), 28.5 (CH), 24.0 (CH_3), 23.8 (CH_3), 23.3

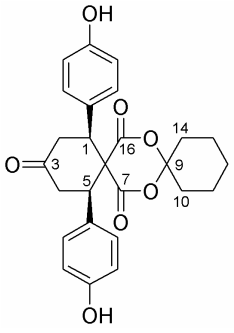


(CH), 22.8 (CH), 22.3 (CH_2), 22.05 (CH_2), 20.9 (CH_3), 20.8 (CH_3), 19.2 (CH_3), 18.3 (CH_3); HRMS (MALDI-FTMS) m/z 497.2287 (M + Na^+), calcd for $C_{30}H_{34}O_5$ Na^+ 497.2298.

(1b,5b)-1,5-Bis-[4-(2,3,4,6-tetra-O-acetyl-D-glucopyranosyl)oxy-phenyl]-8,15-dioxa-dispiro[5.2.5.2]hexadecane-3,7,16-trione (6r). Purified by FC using EtOAc/hexane and isolated as a light yellow color solid. Note the product contains a plane of symmetry. ^{1}H NMR ($CDCl_3$) δ 7.15 (4H, br d, *J* = 8.0 Hz), 6.94 (4H, br d, *J* = 8.0 Hz) [Ar-*H*]; 5.32 – 5.20 (4H, m), 5.14 (2H, br t, *J* = 9.6 Hz), 5.03 (2H, br d, *J* = 7.6 Hz), 4.29 (1H, dd, *J* = 5.6, 3.6 Hz), 4.26 (1H, dd, *J* = 5.2, 3.6 Hz), 4.12 (2H, br d, *J* = 11.6 Hz), 3.95 (2H, br dd, *J* = 14.4, 4.4 Hz, H-1 & 5), 3.85 (2H, m), 3.64 (2H, t, *J* = 14.4 Hz), 2.60 (2H, br d, *J* = 14.4 Hz), 2.08 (2 x CH_3, br s, COC*H*$_3$), 2.04 (2 x CH_3, br s, COC*H*$_3$), 2.03 (4 x CH_3, br s, COC*H*$_3$), 1.32 – 1.15 (6H, m), 0.58 (4H, m); ^{13}C NMR ($CDCl_3$, DEPT) δ 207.0 (C, C=O), 170.3 (2 x C, O*C*OCH3), 170.0 (2 x C, O*C*OCH3), 169.2 (2 x C, O*C*OCH3), 169.03 (C, O*C*OCH3), 169.01 (C, O*C*OCH3), 168.4 (C, O-C=O), 165.3 (C, O=C-O), 156.7 (2 x C), 131.8 (2 x C), 129.53 (2 x CH), 129.51 (2 x CH), 117.24 (2 x CH), 117.20 (2 x CH), 106.7 (C, O-*C*-O), 98.65 (CH), 98.62 (CH), 72.4 (2 x CH), 72.0 (2 x CH), 70.9 (2 x CH), 68.0 (2 x CH), 61.7 (2 x CH_2), 61.2 (C, C-6), 49.20 (CH, C-1), 49.14 (CH, C-5), 42.8 (2 x CH_2), 37.3 (2 x CH_2), 23.4 (CH_2), 21.6 (2 x CH_2), 20.5 (2 x CH_3, OCO*C*H3), 20.4 (6 x CH_3, OCO*C*H3); HRMS (MALDI-FTMS) m/z 1133.3469 (M + Na^+), calcd for $C_{54}H_{62}O_{25}$ Na^+ 1133.3472.

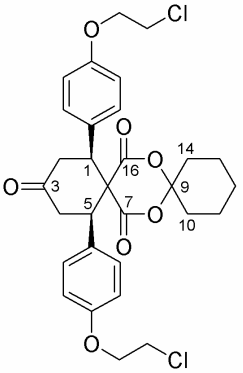


(1b,5b)-1,5-Bis-(4-hydroxyphenyl)-8,15-dioxa-dispiro[5.2.5.2]hexadecane-3,7,16-trione (6s). Purified by FC using EtOAc/hexane and isolated as a light brown color solid. Note the product contains a plane of symmetry. ^{1}H NMR (CD_3COCD_3) δ 8.53 (2H, s, Ph-O*H*), 7.03 (4H, td, *J* = 8.4, 1.6 Hz), 6.80 (4H, td, *J* = 8.4, 1.6 Hz) [Ar-*H*]; 3.92 (2H, dd, *J* = 14.4, 4.4 Hz, H-1 & 5), 3.55 (2H, t, *J* = 14.4 Hz), 2.45 (2H, dd, *J* = 15.2, 4.8 Hz), 1.21 (6H, m),

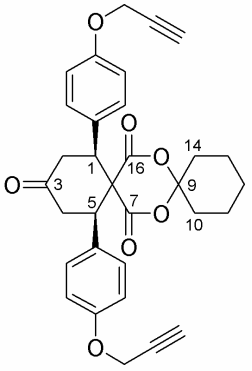


0.67 (4H, br s); ^{13}C NMR (CD_3COCD_3, DEPT) δ 206.8 (C, C=O), 168.8 (C, O=C-O), 165.8 (C, O-C=O), 158.0 (2 x C), 130.0 (4 x CH), 129.1 (2 x C), 116.0 (4 x CH), 106.4 (C, O-*C*-O), 62.0 (C, C-6), 49.5 (2 x CH), 43.4 (2 x CH_2), 37.6 (2 x CH_2), 23.8 (CH_2), 22.2 (2 x CH_2); HRMS (MALDI-FTMS) m/z 473.1572 (M + Na^+), calcd for $C_{26}H_{26}O_7$ Na^+ 473.1571.

(1b,5b)-1,5-Bis-[4-(2-chloro-ethoxy)-phenyl]-8,15-dioxa-dispiro[5.2.5.2]hexadecane-3,7,16-trione (6t). Purified by FC using EtOAc/hexane and isolated as a light yellow color solid. Note the product contains a plane of symmetry. ^{1}H NMR ($CDCl_3$) δ 7.15 (4H, d, *J* = 8.8 Hz), 6.86 (4H, d, *J* = 8.8 Hz) [Ar-*H*]; 4.20 (4H, t, *J* = 5.6 Hz) & 3.78 (4H, t, *J* = 5.6 Hz) [2 x -OC*H*$_2$C*H*$_2$Cl]; 3.94 (2H, dd, *J* = 14.4, 4.0 Hz, H-1 & 5), 3.65 (2H, t, *J* = 14.4 Hz), 2.59 (2H, dd, *J* = 14.8, 4.0 Hz), 1.31-1.15 (6H, m), 0.56 (4H, br s); ^{13}C NMR ($CDCl_3$, DEPT) δ 207.6 (C, C=O), 168.5 (C, O=C-O), 165.5 (C, O-C=O), 158.2 (2 x C), 129.9 (2 x C), 129.5 (4 x CH), 115.0 (4 x CH), 106.7 (C, O-*C*-O), 68.0 (2 x CH_2), 61.3 (C, C-6), 49.1 (2 x CH), 43.0 (2 x CH_2), 41.6 (2 x CH_2), 37.3 (2 x CH_2), 23.5 (CH_2), 21.6 (2 x CH_2); HRMS (MALDI-FTMS) m/z 575.1598 (M + H^+), calcd for $C_{30}H_{32}Cl_2O_7$ H^+ 575.1598.

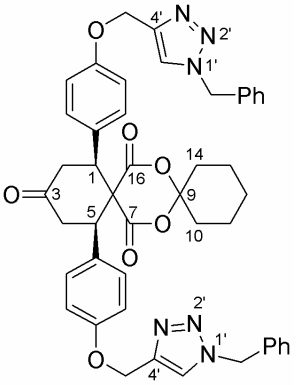


(1b,5b)-1,5-Bis-(4-prop-2-ynyloxy-phenyl)-8,15-dioxa-dispiro[5.2.5.2]hexadecane-3,7,16-trione (6u). Purified by FC using EtOAc/hexane and isolated as a white solid. Note the product contains a plane of symmetry. ^{1}H NMR ($CDCl_3$) δ 7.16 (4H, td, *J* = 8.8, 2.0 Hz), 6.91 (4H, td, *J* = 8.8, 2.0 Hz) [Ar-*H*]; 4.64 (4H, d, *J* = 2.4 Hz) [2 x –OC*H*$_2$C≡CH]; 3.94 (2H, dd, *J* = 14.4, 4.0 Hz, H-1 & 5), 3.65 (2H, t, *J* = 14.8 Hz), 2.59 (2H, dd, *J* = 15.2, 4.4 Hz), 2.47 (2H, t, *J* = 2.4 Hz) [2 x –OCH$_2$C≡C*H*]; 1.30-1.15 (6H, m), 0.58 (4H, br s); ^{13}C NMR ($CDCl_3$, DEPT) δ 207.7 (C, C=O), 168.6 (C, O=C-O), 165.5 (C, O-C=O), 157.4 (2 x C), 130.1 (2 x C), 129.4 (4 x CH), 115.3 (4 x CH), 106.8 (C, O-*C*-O), 78.0 (2 x C, –OCH$_2$*C*≡CH), 75.6 (2 x CH, –OCH$_2$C≡*C*H), 61.4 (C, C-6), 55.7 (2 x CH_2,

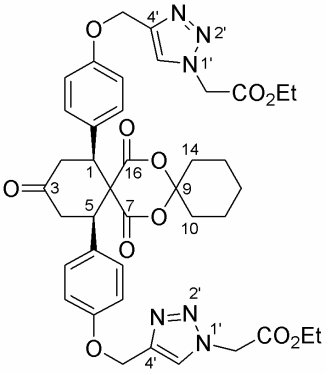


–O*C*H$_2$C≡CH), 49.2 (2 x CH), 43.0 (2 x CH$_2$), 37.4 (2 x CH$_2$), 23.6 (CH$_2$), 21.7 (2 x CH$_2$); HRMS (MALDI-FTMS) m/z 527.2058 (M + H$^+$), calcd for $C_{32}H_{30}O_7$ H$^+$ 527.2064.

(1b,5b)-1,5-Bis-[4-(1-benzyl-1*H*-[1,2,3]triazol-4-ylmethoxy)-phenyl]-8,15-dioxa-dispiro[5.2.5.2]hexadecane-3,7,16-trione (8a). Purified by FC using EtOAc/hexane and isolated as a white solid. Note the product contains a plane of symmetry. ^{1}H NMR ($CDCl_3$) δ 7.53 (2H, br s, [1,2,3]triazole-*H*), 7.40-7.34 (6H, m, Ph-*H*), 7.27 (4H, m, Ph-*H*), 7.13 (4H, br d, *J* = 8.8 Hz), 6.90 (4H, br d, *J* = 8.8 Hz) [Ar-*H*]; 5.53 (4H, s, 2 x –NC*H*$_2$Ph), 5.10 (4H, s, 2 x –OC*H*$_2$–), 3.92 (2H, dd, *J* = 14.4, 4.0 Hz, H-1 & 5), 3.63 (2H, t, *J* = 14.8 Hz), 2.57 (2H, dd, *J* = 15.2, 4.4 Hz), 1.30-1.14 (6H, m), 0.55 (4H, br s); ^{13}C NMR ($CDCl_3$, DEPT) δ 207.7 (C, C=O), 168.6 (C, O=C-O), 165.6 (C, O-C=O), 158.2 (2 x C), 144.0 (2 x C), 134.3 (2 x C), 129.9 (2 x C), 129.5 (4 x CH), 129.1 (4 x CH), 128.8 (2 x CH), 128.1 (4 x CH), 122.6 (2 x CH), 115.1 (4 x CH), 106.7 (C, O-*C*-O), 62.0 (2 x CH$_2$, –N*C*H$_2$Ph), 61.3 (C, C-6), 54.2 (2 x CH$_2$, –O*C*H$_2$–), 49.2 (2 x CH), 43.1 (2 x CH$_2$), 37.3 (2 x CH$_2$), 23.6 (CH$_2$), 21.6 (2 x CH$_2$); HRMS (MALDI-FTMS) m/z 793.3334 (M + H$^+$), calcd for $C_{46}H_{44}N_6O_7$ H$^+$ 793.3344.

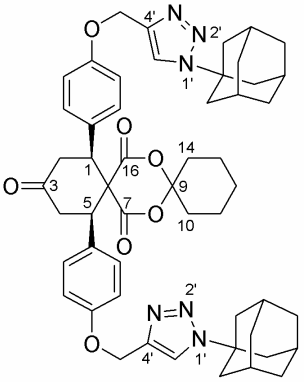


(1b,5b)-1,5-Bis-[4-(1-ethoxycarbonylmethyl-1*H*-[1,2,3]triazol-4-ylmethoxy)-phenyl]-8,15-dioxa-dispiro[5.2.5.2]hexadecane-3,7,16-trione (8b). Purified by FC using EtOAc/hexane and isolated as a white solid. Note the product contains a plane of symmetry. ^{1}H NMR ($CDCl_3$) δ 7.78 (2H, br s, [1,2,3]triazole-*H*), 7.15 (4H, br d, *J* = 8.8 Hz), 6.93 (4H, br d, *J* = 8.8 Hz) [Ar-*H*]; 5.17 (4H, s, 2 x –NC*H*$_2$CO$_2$Et), 5.16 (4H, s, 2 x –OC*H*$_2$–), 4.26 (4H, q, *J* = 6.8 Hz, 2 x CO$_2$C*H*$_2$CH$_3$), 3.94 (2H, dd, *J* = 14.4, 4.0 Hz, H-1 & 5), 3.65 (2H, t, *J* = 14.8 Hz), 2.58 (2H, dd, *J* = 15.2, 4.4 Hz), 1.30 (6H, t, *J* = 6.8 Hz, 2 x CO$_2$CH$_2$C*H*$_3$), 1.30-1.14 (6H, m), 0.59 (4H, br s); ^{13}C NMR ($CDCl_3$, DEPT) δ 207.8 (C, C=O), 168.6 (C, O=C-O), 166.1 (2

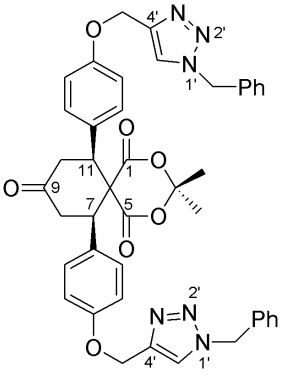


x C, O=C-O), 165.6 (C, O-C=O), 158.2 (2 x C), 144.0 (2 x C), 129.9 (2 x C), 129.5 (4 x CH), 124.1 (2 x CH), 115.1 (4 x CH), 106.8 (C, O-*C*-O), 62.4 (2 x CH_2, $-NCH_2CO_2Et$), 61.8 (2 x CH_2, $-OCH_2-$), 61.3 (C, C-6), 50.8 (2 x CH_2, $CO_2CH_2CH_3$), 49.2 (2 x CH), 43.1 (2 x CH_2), 37.3 (2 x CH_2), 23.6 (CH_2), 21.6 (2 x CH_2), 13.9 (2 x CH_3, $CO_2CH_2CH_3$); HRMS (ESI-TOF) m/z 785.3128 ($M + H^+$), calcd for $C_{40}H_{44}N_6O_{11}$ H^+ 785.3141.

(1b,5b)-1,5-Bis-[4-(1-adamantan-1-yl-1*H*-[1,2,3]triazol-4-ylmethoxy)-phenyl]-8,15-dioxa-dispiro[5.2.5.2]hexadecane-3,7,16-trione (8c). Purified by FC using EtOAc/hexane and isolated as a white solid. Note the product contains a plane of symmetry. ^{1}H NMR ($CDCl_3$) δ 7.70 (2H, br s, [1,2,3]triazole-*H*), 7.16 (4H, br d, *J* = 8.4 Hz), 6.96 (4H, br d, *J* = 8.4 Hz) [Ar-*H*]; 5.14 (4H, s, 2 x $-OCH_2-$), 3.95 (2H, dd, *J* = 14.4, 4.0 Hz, H-1 & 5), 3.66 (2H, t, *J* = 14.8 Hz), 2.60 (2H, dd, *J* = 15.2, 4.4 Hz), 2.25 (17H, br s), 1.80 (13H, m), 1.30-1.14 (6H, m), 0.59 (4H, br s); ^{13}C NMR ($CDCl_3$, DEPT) δ 207.8 (C, C=O), 168.6 (C, O=C-O), 165.5 (C, O-C=O), 158.4 (2 x C), 142.4 (2 x C), 129.7 (2 x C), 129.5 (4 x CH), 119.1 (2 x CH), 115.0 (4 x CH), 106.7 (C, O-*C*-O), 62.3 (2 x CH_2, $-OCH_2-$), 61.3 (C, C-6), 59.6 (2 x C), 49.2 (2 x CH), 43.1 (2 x CH_2), 42.8 (6 x CH_2), 37.3 (2 x CH_2), 35.7 (6 x CH_2), 29.3 (6 x CH), 23.5 (CH_2), 21.6 (2 x CH_2); HRMS (ESI-TOF) m/z 881.4585 ($M + H^+$), calcd for $C_{52}H_{60}N_6O_7$ H^+ 881.4596.

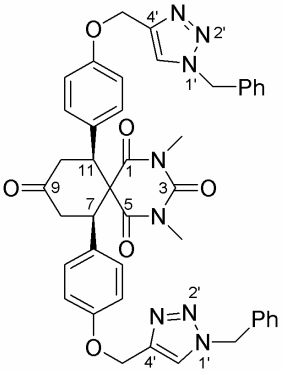


(7b,11b)-7,11-Bis-[4-(1-benzyl-1*H*-[1,2,3]triazol-4-ylmethoxy)-phenyl]-3,3-dimethyl-2,4-dioxa-spiro[5.5]undecane-1,5,9-trione (8d). Purified by FC using EtOAc/hexane and isolated as a white solid. Note the product contains a plane of symmetry. ^{1}H NMR ($CDCl_3$) δ 7.53 (2H, br s, [1,2,3]triazole-*H*), 7.40-7.34 (6H, m, Ph-*H*), 7.27 (4H, m, Ph-*H*), 7.13 (4H, br d, *J* = 8.8 Hz), 6.91 (4H, br d, *J* = 8.8 Hz) [Ar-*H*]; 5.52 (4H, s, 2 x $-NCH_2Ph$), 5.11 (4H, s, 2 x $-OCH_2-$), 3.92 (2H, dd, *J* = 14.8, 4.0 Hz, H-1 & 5), 3.63 (2H, t, *J* = 14.8 Hz), 2.57 (2H, dd, *J* = 15.2, 4.4 Hz), 0.57 (6H,

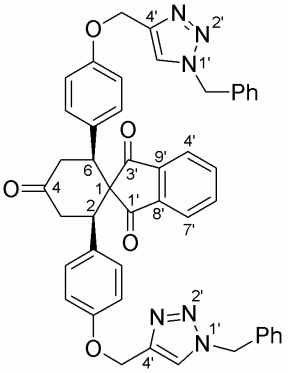


s, 2 x CH_3); ^{13}C NMR ($CDCl_3$, DEPT) δ 207.6 (C, C=O), 168.3 (C, O=C-O), 165.3 (C, O-C=O), 158.2 (2 x C), 143.9 (2 x C), 134.2 (2 x C), 129.7 (2 x C), 129.5 (4 x CH), 129.1 (4 x CH), 128.8 (2 x CH), 128.0 (4 x CH), 122.6 (2 x CH), 115.2 (4 x CH), 106.2 (C, O-*C*-O), 61.9 (2 x CH_2, –N*C*H_2Ph), 60.7 (C, C-6), 54.2 (2 x CH_2, –O*C*H_2–), 49.1 (2 x CH), 43.0 (2 x CH_2), 28.4 (2 x CH_3); HRMS (MALDI-FTMS) m/z 753.3021 (M + H^+), calcd for $C_{43}H_{40}N_6O_7$ H^+ 753.3031.

(7b,11b)-7,11-Bis-[4-(1-benzyl-1*H*-[1,2,3]triazol-4-ylmethoxy)-phenyl]-2,4-dimethyl-2,4-diaza-spiro[5.5]undecane-1,3,5,9-tetraone (8e). Purified by FC using EtOAc/hexane and isolated as a white solid. Note the product contains a plane of symmetry. ^{1}H NMR ($CDCl_3$) δ 7.49 (2H, br s, [1,2,3]triazole-*H*), 7.40-7.34 (6H, m, Ph-*H*), 7.27 (4H, m, Ph-*H*), 6.97 (4H, td, *J* = 8.8, 2.0 Hz), 6.82 (4H, td, *J* = 8.8, 2.0 Hz) [Ar-*H*]; 5.53 (4H, s, 2 x –N*C*H_2Ph), 5.12 (4H, s, 2 x –O*C*H_2–), 3.93 (2H, dd, *J* = 14.8, 4.0 Hz, H-1 & 5), 3.65 (2H, t, *J* = 14.8 Hz), 2.98 (3H, s, –N*C*H_3), 2.85 (3H, s, –N*C*H_3), 2.56 (2H, dd, *J* = 15.2, 4.4 Hz); ^{13}C NMR ($CDCl_3$, DEPT) δ 208.2 (C, C=O), 170.7 (C, O=C-N), 168.9 (C, N-C=O), 157.9 (C, N-C=O), 149.6 (2 x C), 144.1 (2 x C), 134.3 (2 x C), 129.6 (2 x C), 129.1 (4 x CH), 128.7 (2 x CH), 128.5 (4 x CH), 128.0 (4 x CH), 122.5 (2 x CH), 114.8 (4 x CH), 61.8 (2 x CH_2, –N*C*H_2Ph), 61.2 (C, C-6), 54.1 (2 x CH_2, –O*C*H_2–), 49.5 (2 x CH), 43.0 (2 x CH_2), 28.3 (CH_3), 27.8 (CH_3); HRMS (ESI-TOF) m/z 765.3146 (M + H^+), calcd for $C_{43}H_{40}N_8O_6$ H^+ 765.3143.

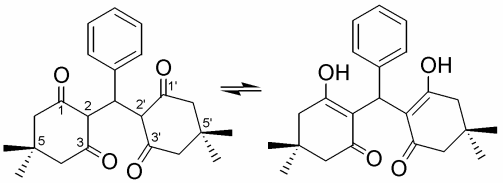


(2b,6b)-2,6-Bis-[4-(1-benzyl-1*H*-[1,2,3]triazol-4-ylmethoxy)-phenyl]-spiro[cyclohexane-1,2'-indan]-1',3',4-trione (8f). Purified by FC using EtOAc/hexane and isolated as a white solid. Note the product contains a plane of symmetry. ^{1}H NMR ($CDCl_3$) δ 7.64 (1 H, m), 7.48 (1 H, m), 7.43 (2 H, m), 7.42 (2H, br s, [1,2,3]triazole-*H*), 7.35-7.33 (6H, m, Ph-*H*), 7.23 (4H, m, Ph-*H*), 6.92 (4H, br d, *J* = 8.8 Hz), 6.58 (4H, br d, *J* = 8.8 Hz) [Ar-*H*]; 5.48 (4H, s, 2 x

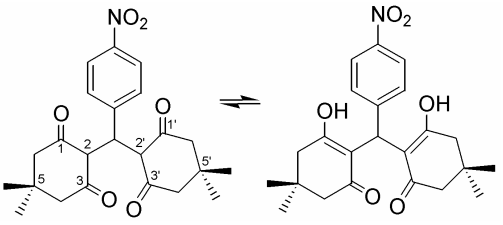


–NCH_2Ph), 4.91 (4H, s, 2 x –OCH_2–), 3.73 (4H, m), 2.58 (2H, d, *J* = 12.0 Hz); ^{13}C NMR ($CDCl_3$, DEPT) δ 208.4 (C, C=O), 203.6 (C, C=O), 202.1 (C, C=O), 157.3 (2 x C), 144.0 (2 x C), 142.6 (C, C-8'), 141.9 (C, C-9'), 135.45 (CH, C-7'), 135.37 (CH, C-6'), 134.3 (2 x C), 130.2 (2 x C), 129.1 (4 x CH), 129.0 (4 x CH), 128.7 (2 x CH), 128.0 (4 x CH), 122.5 (2 x CH), 122.3 (CH, C-5'), 122.0 (CH, C-4'), 114.3 (4 x CH), 62.2 (C, C-1 or C-2'), 61.7 (2 x CH_2, –NCH_2Ph), 54.1 (2 x CH_2, –OCH_2–), 47.8 (2 x CH), 43.6 (2 x CH_2); HRMS (ESI-TOF) m/z 755.2956 (M + H^+), calcd for $C_{46}H_{38}N_6O_5$ H^+ 755.2976.

2,2'-Phenylmethylene-bis-[5,5-dimethyl-1,3-cyclohexanedione] (13a). Purified by FC using EtOAc/hexane and isolated as semi solid. ^{1}H NMR ($CDCl_3$) δ 11.95 (2H, br s, 2 x O*H*), 7.26 (2H, m), 7.17 (1H, br t, *J* = 6.8 Hz), 7.10 (2H, br d, *J* = 8.0 Hz) [Ph-*H*]; 5.54 (1H, s, C*H*Ph), 2.38 (8H, m, 4 x CH_2), 1.23 (6H, s, 2 x *tert*-CH_3), 1.10 (6H, s, 2 x *tert*-CH_3); ^{13}C NMR ($CDCl_3$, DEPT) δ 190.4 (C, C=O), 189.3 (C, C=O), 138.0 (C), 128.2 (2 x CH), 126.7 (2 x CH), 125.8 (CH), 115.5 (C, C-2 and 2'), 47.0 (2 x CH_2), 46.4 (2 x CH_2), 32.7 (CH), 31.3 (2 x C), 29.6 (2 x CH_3), 27.3 (2 x CH_3); HRMS (ESI-TOF) m/z 369.2063 (M + H^+), calcd for $C_{23}H_{28}O_4$ H^+ 369.206.



2,2'-[(4-Nitrophenyl)methylene]-bis-[5,5-dimethyl-1,3-cyclohexanedione] (13b). Purified by FC using EtOAc/hexane and isolated as semi solid. ^{1}H NMR ($CDCl_3$) δ 12.0 (2H, br s, 2 x O*H*), 8.26 (2H, d, *J* = 8.8 Hz), 7.38 (2H, d, *J* = 8.0 Hz) [Ar-*H*]; 5.68 (1H, s, C*H*Ar), 2.55 (8H, m, 4 x CH_2), 1.36 (6H, s, 2 x *tert*-CH_3), 1.24 (6H, s, 2 x *tert*-CH_3); ^{13}C NMR ($CDCl_3$, DEPT) δ 190.9 (C, C=O), 189.5 (C, C=O), 146.5 (C), 146.0 (C), 127.6 (2 x CH), 123.4 (2 x CH), 114.8 (C, C-2 and 2'), 46.9 (2 x CH_2), 46.3 (2 x CH_2), 33.1 (CH), 31.4 (2 x C), 29.4 (2 x CH_3), 27.3 (2 x CH_3); HRMS (MALDI-FTMS) m/z 414.1916 (M + H^+), calcd for $C_{23}H_{27}NO_6$ H^+ 414.1911.



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