

Synthesis, *In Vitro* and *In Vivo* Antimalarial Assessment of Sulfide, Sulfone and Vinyl Amide Substituted 1,2,4-Trioxanes prepared via Thiol-Olefin Co-Oxygenation (TOCO) of Allylic Alcohols

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Supporting Information

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8-(4-Chloro-phenylsulfanylmethyl)-8-methyl-6,7,10-trioxa-spiro-[4.5]decane (16).

(White powder, 78%). Mpt. 56-58 °C. ν_{\max} (CHCl₃)/cm⁻¹ 814.0, 965.5, 1007.2, 1094.3, 1329.2, 1386.0, 1454.2, 1473.1, 2870.5, 2961.4, 3014.4. ¹H NMR (400MHz, CDCl₃, 25 °C) δ_{H} 1.15 (s, 3H, CH₃), 1.62-1.89 (m, 8H, cyclopentyl), 3.50 (bs, 2H, SCH₂), 3.60 (d, 1H, J = 11.6 Hz, CH₂O), 3.84 (d, 1H, J = 11.6 Hz, CH₂O), 7.27 (d, 2H, J = 8.6 Hz, Ar), 7.37 (d, 2H, J = 8.4 Hz, Ar). ¹³C NMR (100MHz, CDCl₃), δ_{C} 20.4, 25.0, 37.4, 43.7, 66.6, 79.3, 114.6, 129.4, 131.0, 132.5, 136.1. MS (ES+) [M + Na]⁺ (100) 337.1 HRMS calculated for 337.0641 C₁₆H₂₁O₃NaSCl, found 337.0648. Elemental analysis C: 56.91, H: 5.92 (required values C: 57.22, H: 6.08).

3-(4-Chloro-phenylsufanylmethyl)-3-methyl-1, 2,3-trioxa-spiro [5.11] heptadecane (17).

(White powder, 50%). Mpt. 68-70 °C. ν_{\max} (CHCl₃)/cm⁻¹ 1007.2, 1090.5, 1442.8, 1473.1, 2855.3, 2923.5, 3014.4. ¹H NMR (400MHz, CDCl₃) δ_{H} 1.13 (s, 3H, CH₃), 1.25-1.48 (m, 18H, cyclododecanyl), 1.49-1.75 (m, 2H, cyclododecanyl), 1.80-2.15 (m, 2H, cyclododecanyl), 3.50 (bs, 2H, SCH₂), 3.72 (bs, 2H, CH₂O), 7.24 (d, 2H, J = 8.4 Hz, Ar), 7.35 (d, 2H, J = 8.6 Hz, Ar). ¹³C NMR (100MHz, CDCl₃), δ_{C} 19.3, 20.3, 22.6, 24.6, 26.0, 31.8, 38.5, 64.0, 78.8, 106.3, 129.0, 130.5, 132.0, 135.6. MS (ES+) [2M + Na]⁺ (100) 847.36. HRMS calculated for 847.3576 C₂₀H₂₅O₃NaSCl, found 847.3549. Elemental analysis C: 63.88, H: 8.04 (required values C: 63.98, H: 8.05).

6'-{[(4-Chlorophenyl)thio]methyl}-6'-methylspiro[tricyclo[3.3.1.1^{3,7}]decane-2,3'-[1,2,4]trioxane] (18)

(Colourless oil, 70%). ν_{\max} (neat)/cm⁻¹ 809.5, 918.3, 1006.1, 1064.6, 1089.7, 1106.5, 1290.5, 1374.1, 1449.4, 1474.5, 2847.5, 2906.0. ¹H NMR (400MHz, CDCl₃, -20 °C) δ_{H} 1.13 (s, 3H, CH₃), 1.51-1.72 (m, 6H, adamantyl), 1.80 (bs, 4H, adamantyl), 1.87-2.08 (m, 4H, adamantyl), 3.49 (d, 1H, J = 13.1 Hz, SCH₂), 3.61 (d, 1H, J = 13.1 Hz, SCH₂), 3.68 (d, 1H, J = 12.0 Hz, OCH₂), 3.82(d, 1H, J = 12.0 Hz, OCH₂), 7.24 (d, 2H, J = 8.7 Hz, Ar), 7.34 (d, 2H, J = 8.6 Hz, Ar). ¹³C NMR (100MHz, CDCl₃), δ_{C} 20.6, 27.5, 33.4, 33.7, 33.8, 37.6, 63.7, 79.2, 104.7, 129.4, 131.0, 132.4, 136.0. MS (ES+) [M + Na]⁺ (100) 403/405, [2M + Na]⁺ 783/785/786. HRMS calculated for 403.1111 C₂₀H₂₅O₃NaSCl, found 403.1126.

3-(4-Chloro-phenylsulfanylmethyl)-3-phenyl-1,2,3-trioxa-spiro[5.5]-undecane (19).

(White powder, 80%). Mpt. 56-58 °C. ν_{\max} (CHCl₃)/cm⁻¹ 817.8, 923.8, 1090.5, 1442.8, 1473.1, 2855.3, 2931.1, 3014.4. ¹H NMR (400MHz, CDCl₃) δ_{H} 1.35-2.30 (m, 10H, cyclohexyl), 3.64-3.82 (m, 2H, SCH₂), 3.85-4.30 (m, 2H, CH₂O), 7.14 (m, 4H, Ar), 7.31(m, 5H, Ar). ¹³C NMR (100MHz, CDCl₃), δ_{C} 22.6, 25.9, 33.7, 39.8, 63.9, 81.4, 103.2, 128.9, 129.5, 129.7, 131.3, 131.6, 134.0, 135.8. MS (ES+) [M + Na]⁺ (100) 413.1/415.1, [2M + Na]⁺ 803.2. HRMS calculated for 413.0954 C₂₁H₂₃O₃NaSCl, found 413.0939. Elemental analysis C: 64.53, H: 5.96 (required values C: 64.52, H: 5.93).

3-(4-Chloro-phenylsufanylmethyl)-3-phenyl-1, 2,3-trioxa-spiro [5.11] heptadecane (20).

(White powder, 46%). Mpt. 76-78 °C. ¹H NMR (400MHz, CDCl₃) δ_{H} 1.13-1.52 (m, 18H, cyclododecanyl), 1.61-1.78 (m, 2H, cyclododecanyl), 1.90-2.20 (m, 2H, cyclododecanyl), 3.75 (bs, 1H, CH₂O), 3.95 (bs, 1H, CH₂O), 4.15 (bs, 2H, SCH₂), 7.11-7.19 (m, 4H, Ar), 7.24-7.37 (m,

5H, Ar). ^{13}C NMR (100MHz, CDCl_3), δ_{C} 18.7, 19.2, 21.8, 22.0, 22.4, 22.4, 22.6, 24.3, 24.7, 24.8, 26.1, 40.4, 64.3, 107.1, 125.0, 128.5, 128.8, 131.0. MS (ES+) $[\text{M} + \text{Na}]^+$ (100) 497.2, $[\text{2M} + \text{Na}]^+$ 973.4. HRMS calculated for 497.1893 $\text{C}_{27}\text{H}_{35}\text{O}_3\text{NaS}$, found 497.1894. Elemental analysis C: 68.53, H: 7.78 (required values C: 68.48, H: 8.00).

3-Phenyl-3-phenylsulfanylmethyl-1,2,5-trioxa-spiro[5.5]undecane (21).

(White powder, 68%). ^1H NMR (250 MHz, CDCl_3) δ_{H} 1.28- 2.21 (m, 10H, cyclohexyl), 3.78 (bs, 2H, CH_2S), 4.19 (bs, 2H, CH_2O), 7.02-7.45 (m, 10H, Ar). ^{13}C NMR (100MHz, CDCl_3) δ_{C} 22.2, 23.7, 24.0, 25.4, 63.5, 73.0, 102.7, 125.09, 125.30, 127.4, 128.7, 129.2, 143.8. MS (ES+) m/z 379.1 $[\text{M}^+ + \text{Na}]$. HRMS m/z calculated for $\text{C}_{21}\text{H}_{24}\text{O}_3\text{SNa}$ $[\text{M}^+ + \text{Na}]$ 379.1336 found, 379.1344. Elemental analysis C: 70.37, H: 6.66 (required values, C: 70.76, H: 6.79).

3-Phenyl-3-phenylsulfanyl-1,2,5-trioxa-spiro[4.5]decane (22).

(White powder, 54%). ^1H NMR (250MHz, CDCl_3) δ_{H} 1.34-2.32 (m, 8H, cyclopentyl); 3.81 (bs 2H, CH_2S), 4.22 (bs, 2H, CH_2O), 7.08-7.56 (m, 10H, Ar). ^{13}C NMR (100MHz, CDCl_3) δ_{C} 22.6, 23.2, 24.1, 25.3, 25.7, 63.5, 73.0, 102.6, 125.9, 128.4, 129.6, 143.0. MS (ES+) m/z 265.5 $[\text{M}^+ + \text{Na}]$. Elemental analysis: C: 69.97, H: 6.32 (required values, C: 70.15, H: 6.48).

3-Methyl-3-phenylsulfanylmethyl-1,2,5-trioxa-spiro[5.5]undecane (23).

(White powder, 53%). Mp 45-46°C. ν_{max} (CHCl_3)/ cm^{-1} 689, 735, 945, 1095, 1158, 1311, 1481, 1711, 3020 ^1H NMR (400 MHz, CDCl_3) δ_{H} 0.88 (s, 3H, CH_3), 1.55 (bm, 10H, cyclohexyl), 3.50 (bs, 2H, CH_2S), 3.77 (bs, 2H, CH_2O), 7.27 (t, $J = 7.7$ Hz, 2H, Ar), 7.34 (t, $J = 7.7$ Hz, 1H, Ar), 7.48 (d, $J = 7.6$ Hz, 2H, Ar). MS (ES+) m/z 317.2 $[\text{M} + \text{Na}]^+$ (33). HRMS m/z calculated for $\text{C}_{16}\text{H}_{22}\text{O}_3\text{SNa}$ $[\text{M}^+ + \text{Na}]$ 317.1187 found, 317.1179. Elemental analysis C: 65.29, H: 7.71 (required values, C: 65.27, H: 7.53).

7-Methyl-7-phenylsulfanylmethyl-5,6,9-trioxa-spiro[3.5]nonane (24).

(Colourless oil, 61%). ^1H NMR (400 MHz, CDCl_3) δ_{H} 1.31 (s, 3H, CH_3), 1.76 (bm, 2H, cyclobutyl), 2.20 (bm, 4H, cyclobutyl), 3.10 (bs, 2H, CH_2S), 3.55 (d, $J = 11.7$, 1H, OCH_2), 3.75 (d, $J = 11.7$ Hz, 1H, OCH_2), 7.34 (m, 5H, Ar). ^{13}C NMR (100 MHz, CDCl_3) δ_{C} 11.0, 20.3, 37.2, 41.0, 73.1, 79.7, 104.7, 126.56, 128.0, 129.3, 133.0. MS (ES+) m/z 289.1 $[\text{M} + \text{Na}]^+$ (89), 305.1 $[\text{M} + \text{K}]^+$ (100). HRMS m/z calcd for $\text{C}_{14}\text{H}_{18}\text{O}_3\text{SNa}$ $[\text{M}^+ + \text{Na}]$ 289.0874 found, 289.0877. Elemental analysis C: 63.01, H: 6.55 (required values; C: 63.13 H: 6.81).

6'-Methyl-6'-[(phenylthio)methyl]spiro[tricyclo[3.3.1.1^{3,7}]decane-2,3'-[1,2,4]trioxane] (25).

(Colourless oil, 42%). ν_{max} (CHCl_3)/ cm^{-1} 1598, 1795, 2860, 2913, 3062. ^1H NMR (400 MHz, CDCl_3) δ_{H} 1.15 (s, 3H, CH_3), 1.75 (bm, 14H, adamantyl), 2.60 (bs, 2H, CH_2S), 3.60 (bs, 2H, OCH_2), 7.16 (t, $J = 7.4$ Hz, 1H, Ar), 7.26 (t, $J = 7.4$ Hz, 2H, Ar), 7.42 (d, $J = 7.7$ Hz, 2H, Ar). ^{13}C NMR (100 MHz, CDCl_3) δ_{C} 20.6, 27.8, 33.2, 33.7, 37.6, 39.5, 73.0, 79.3, 104.7, 126.3, 128.8, 135.9. MS (ES+) m/z 369.15 $[\text{M} + \text{Na}]^+$ (100), 370.15 $[\text{M} + 1 + \text{Na}]^+$ (21), 385.13 $[\text{M} + \text{K}]^+$ (12). HRMS m/z calculated for $\text{C}_{20}\text{H}_{26}\text{O}_3\text{SNa}$ $[\text{M}^+ + \text{Na}]$ 369.1489 found, 369.1500. Elemental analysis C: 67.87, H: 6.19 (required values; C: 67.78 H: 6.14).

9-*Tert*-butyl-3-(4-chloro-phenylsulfanylmethyl)-3-methyl-1,2,5-trioxa-spiro[5.5]undecane (26).

(Off-white solid, 80%). Mp 77-78°C. ¹H NMR (400 MHz, CDCl₃) δ_H, 0.85 (s, 9H, CH₃), 1.05 (bm, 1H, CH), 1.14, (bs, 3H, CH₃), 1.36 (bm, 4H, cyclohexyl), 1.68 (bs, 4H, cyclohexyl), 3.50 (bs, 2H, CH₂S), 3.75 (bs, 2H, OCH₂), 7.25-7.34 (m, 4H, Ar). ¹³C NMR (100 MHz, CDCl₃) δ_C 20.6, 23.4, 28.2, 32.7, 34.5, 38.7, 48.0, 64.2, 79.3, 102.7, 129.7, 132.3, 136.0, 138.9. MS (ES+) m/z 407.14 [M + Na]⁺ (100), 423.13 [M + K]⁺ (18). HRMS m/z calculated for C₂₀H₂₉O₃SClNa [M⁺ + Na] 407.1424 found, 407.1442. Elemental analysis C: 62.42, H: 7.58 (required values; C: 62.40, H: 7.59).

3-Methyl-3-phenylsulfanylmethyl-1,2,5-trioxa-spiro[5.11]heptadecane (27).

(White powder, 68%). Mp 89°C. ¹H NMR (400 MHz, CDCl₃) δ_H 1.31 (bm, 22H, cyclododecanyl), 1.48 (s, 3H, CH₃), 3.53 (bs, 2H, CH₂S), 3.75 (bs, 2H, OCH₂), 7.17 (t, J = 7.5 Hz, 1H, Ar), 7.26 (t, J = 7.5 Hz, 2H, Ar), 7.43 (d, J = 7.6 Hz, 2H, Ar). MS (ES+) m/z 401.1 [M + Na]⁺ (100), 417.1 [M + K]⁺ (24), 779.3 [2M + Na]⁺ (13). HRMS m/z calculated for C₂₂H₃₄O₃SNa [M⁺ + Na] 401.2126 found, 401.2130. Elemental analysis C: 70.17, H: 9.27 (required values; C: 69.8 H: 9.05).

3-Methyl-3-(naphthalen-2-ylsulfanylmethyl)-1,2,5-trioxa-spiro[5.11]heptadecane (28).

(Pale yellow foam, 64%). ¹H NMR (400 MHz, CDCl₃) δ_H 1.28 (bm, 20H, cyclododecanyl), 1.53 (s, 3H, CH₃), 1.72 (bm, 2H, cyclododecanyl), 2.50 (bs, 2H, CH₂S), 4.10 (bs, 2H, OCH₂), 7.45-7.66 (bm, 7H, Ar). ¹³C NMR (100 MHz, CDCl₃) δ_C 19.8, 22.8, 24.7, 25.1, 33.9, 40.8, 68.2, 72.4, 113.7, 126.6, 127.9, 128.8, 130.1, 131.9, 134.0, 134.7. MS (ES+) m/z 451.30 [M + Na]⁺ (56), 468.20 [M + K]⁺ (10). HRMS m/z calculated for C₂₆H₃₆O₃SNa [M⁺ + Na] 451.2283 found, 451.2296.

6'-((4-Chlorophenylthio)methyl)-6'-methyltetrahydro-1H-spiro[pentalene-2,3'-[1,2,4]trioxan]-5(3H)-one (29).

(White powder, 65%). Mp 84.3°C. ¹H NMR (400 MHz, CDCl₃) δ_H 1.60 (s, 3H, CH₃), 1.76 (bm, 2H, bicyclooctanyl), 2.15 (bm, 4H, bicyclooctanyl), 2.50 (m, 4H, bicyclooctanyl), 2.89 (bs, 2H, CH₂S), 3.61 (bs, 2H, OCH₂), 7.26-7.34 (m, 4H, Ar). ¹³C NMR (100 MHz, CDCl₃) δ_C 20.4, 36.8, 37.8, 38.7, 44.5, 66.8, 79.5, 108.9, 128.9, 129.4, 131.0, 132.6, 133.6. MS (ES+) m/z 391 [M + Na]⁺ (100), 407 [M + K]⁺ (17). HRMS m/z calculated for C₁₈H₂₁O₄SClNa [M⁺ + Na] 391.0747 found, 391.0757. Elemental analysis C: 58.59, H: 5.75 (required values; C: 58.61, H: 5.74).

3-Methyl-3-phenylsulfanylmethyl-1,2,5-trioxa-spiro[5.5]undecan-9-one (30).

(Orange residue, 25%). ¹H NMR (400 MHz, CDCl₃) δ_H 1.35 (s, 3H, CH₃); 2.04 (bm, 4H, -oxocyclohexyl), 2.43 (bm, 4H, oxocyclohexyl), 3.57 (bs, 2H, CH₂S), 3.85 (bs, 2H, OCH₂), 7.23 (m, 5H, Ar). ¹³C NMR (100 MHz, CDCl₃) δ_C 20.6, 36.8, 36.9, 38.6, 74.3, 80.0, 101.1, 126.7, 129.4, 130.0, 137.1, 210.0. MS (ES+) m/z 331 [M + Na]⁺ (100), 347 [M + K]⁺ (53), 363 [M + CH₃OH + Na]⁺ (78). HRMS m/z calculated for C₁₆H₂₀O₄SNa [M⁺ + Na] 331.0980 found, 331.0985. Elemental analysis C: 62.05, H: 6.58 (required values; C: 62.31 H: 6.54).

3-(4-Chloro-benzenesulfonylmethyl)-3-methyl-1, 2,3-trioxa-spiro [5.5]undecane (32).

(White solid, 80%). Mpt. 60-62 °C. ν_{\max} (CHCl₃)/cm⁻¹ 825.4, 916.3, 1090.5, 1147.3, 1279.9, 1321.6, 1389.8, 1446.6, 1473.1, 1579.2, 2855.3, 2938.7, 3014.4. ¹H NMR (400MHz, CDCl₃) δ_{H} 1.30-1.59 (m, 11H, cyclohexyl/CH₃), 1.60-1.94 (m, 2H, cyclohexyl), 3.67-3.91 (m, 4H, SO₂CH₂/CH₂O), 7.58 (d, 2H, J = 8.8 Hz, Ar), 7.90 (d, 2H, J = 8.7 Hz, Ar). ¹³C NMR (100MHz, CDCl₃) δ_{C} 14.6, 20.3, 22.4, 25.7, 56.8, 60.8, 65.1, 73.7, 102.9, 130.0, 139.9, 140.7. MS (ES+) [M + Na]⁺ (100) 383.1/385.1, [2M + Na]⁺ 743.2/745.2. HRMS calculated for 383.0696 C₁₆H₂₁O₅NaSCL, found 383.0699. Elemental analysis C: 59.57, H: 5.46 (required values C: 59.64, H: 5.48).

6'-{[(4-Chlorophenyl)sulfonyl]methyl}-6'-methylspiro[tricyclo[3.3.1.1^{3,7}]decane-2,3'-[1,2,4]trioxane] (34)

(White powder, 80%). Mpt. 94-96 °C. ν_{\max} (CHCl₃)/cm⁻¹ 820.0, 918.4, 1008.7, 1082.5, 1107.1, 1148.1, 1316.2, 1377.7, 1451.5, 1472.0, 1578.6, 2046.7, 2912.3, 3010.7. ¹H NMR (400MHz, CDCl₃) δ_{H} 1.50 (bs, 3H, CH₃), 1.62 (m, 8H, adamantyl), 1.80 (bd, 4H, J = 10.65Hz, adamantyl), 1.98 (bd, 2H, J = 11.12Hz, adamantyl), 3.68-3.96 (m, 4H, SO₂CH₂/CH₂O), 7.95 (d, 2H, J = 8.4 Hz, Ar), 7.95 (d, 2H, J = 8.4 Hz, Ar). ¹³C NMR (100MHz, CDCl₃) δ_{C} 20.3, 27.3, 33.1, 33.4, 37.3, 59.1, 60.7, 64.6, 104.8, 129.8, 139.8, 140.6. MS (ES+) [M + Na]⁺ (100) 435/437, [2M + Na]⁺ (8%) 847/850. HRMS calculated for 435.1009 C₂₀H₂₅O₅NaSCL, found 435.0988. Elemental analysis C: 57.18, H: 5.94 (required values C: 58.17, H: 6.10)

3-(4-Chloro-benzenesulfonylmethyl)-3-phenyl-1,2,5-trioxa-spiro[5.5]-undecane (35).

(White powder, 77%). Mpt. 134-136 °C. ν_{\max} (CHCl₃)/cm⁻¹ 1084.7, 1151.6, 1273.6, 1324.7, 1391.6, 1446.7, 1474.2, 1580.4, 2852.6, 2931.3, 3010.0. ¹H NMR (400MHz, CDCl₃) δ_{H} 1.44-1.76 (m, 8H, cyclohexyl), 1.80-2.20 (m, 2H, cyclohexyl), 4.18 (bs, 2H, CH₂O), 4.36 (bs, 2H, SO₂CH₂), 7.17 (bs, 2H, Ar), 7.21-7.31 (m, 5H, Ar), 7.47 (d, 2H, J = 8.4 Hz, Ar). ¹³C NMR (100MHz, CDCl₃) δ_{C} 22.2, 25.4, 28.1, 34.6, 59.2, 63.8, 78.5, 103.0, 125.50, 128.5, 129.0, 129.3, 138.9, 139.7. MS (ES+) [M + Na]⁺ (100) 455.1/447.1, [2M + Na]⁺ 867.2/869.2. HRMS calculated for 445.0852 C₂₁H₂₃NO₅NaSCL, found 445.0868. Elemental analysis C: 59.28, H: 5.84 (required values C: 59.64, H: 5.48)

3-(4-Chloro-benzenesulfonylmethyl)-3-phenyl-1,2,5-trioxa-spiro[5.11]-heptadecane (36).

(White powder, 79%). Mpt. 114-116 °C. ν_{\max} (CHCl₃)/cm⁻¹ 1088.7, 1147.7, 1316.8, 1391.6, 1446.7, 1474.2, 1580.4, 2852.6, 2923.4, 3010.0. ¹H NMR (400MHz, CDCl₃) δ_{H} 1.10-1.45 (m, 16H, cyclododecanyl), 1.46-1.74 (m, 2H, cyclododecanyl), 1.80-2.15 (m, 2H, cyclododecanyl), 2.50 (m, 2H, cyclododecanyl), 4.04-4.37 (m, 4H, CH₂O/SO₂CH₂), 7.16 (bs, 2H, Ar), 7.23-7.33 (m, 5H, Ar), 7.50 (d, 2H, J = 8.3 Hz, Ar). ¹³C NMR (100MHz, CDCl₃) δ_{C} 19.5, 23.0, 25.2, 26.3, 30.1, 40.8, 59.7, 65.0, 66.2, 107.4, 123.9, 125.9, 127.1, 127.9, 137.5, 138.3. MS (ES+) [M + Na]⁺ (100) 529.2/531.2, [2M + Na]⁺ 1035.4/1037.4, HRMS calculated for C₂₇H₃₅NO₅NaSCL 529.1791, found 529.1796. Elemental analysis C: 63.56, H: 6.71 (required values C: 63.95, H: 6.96)

3-Benzenesulfonylmethyl-3-methyl-1,2,5-trioxa-spiro[5.5]undecane (37).

(White powder, 75%). Mpt. 88-89°C. ¹H NMR (400 MHz, CDCl₃) δ_{H} 1.38 (s, 3H, CH₃), 1.50 (bm, 10H, cyclohexyl), 3.80 (bs, 2H, OCH₂), 3.97 (bs, 2H, CH₂SO₂), 7.57 (t, J = 7.8 Hz, 2H), 7.65 (t, J = 7.8 Hz, 1H), 7.96 (d, J = 7.0 Hz, 2H). ¹³C NMR (100 MHz, CDCl₃) 20.5, 22.5, 22.6, 25.8, 43.1, 64.9, 128.2, 129.5, 134.0, 141.5. MS (ES+) m/z 349.2 [M + Na]⁺ (100), 365.2 [M +

K^+ (7), 675.4 $[2M + Na]^+$ (98). HRMS m/z calculated for $C_{16}H_{22}O_5SNa$ $[M + Na]^+$ 349.1086 found, 349.1072. Elemental analysis C: 59.00, H: 6.83 (required values; C: 58.88 H: 6.79).

7-Benzenesulfonylmethyl-7-methyl-5,6,9-trioxa-spiro[3.5]nonane (38).

(White powder, 91%). Mpt. 96-97°C. 1H NMR (400 MHz, $CDCl_3$) δ_H 1.44 (s, 3H, CH_3), 1.76 (m, 2H, cyclobutyl), 2.24 (m, 4H, cyclobutyl), 3.61 (bs, 2H, OCH_2), 4.06 (bs, 2H, CH_2SO_2), 7.57 (t, $J = 7.4$ Hz, 2H, Ar), 7.66 (t, $J = 7.4$ Hz, 1H, Ar), 7.96 (d, $J = 8.2$ Hz, 2H, Ar). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 11.9, 20.2, 31.0, 66.3, 105.0, 108.8, 128.2, 129.6, 134.1, 141.4. MS (ES+) m/z 321.1 $[M + Na]^+$ (100), 337.3 $[M + K]^+$ (5). HRMS m/z calculated for $C_{14}H_{18}O_5SNa$ $[M + Na]^+$ 321.0773 found, 321.0771. Elemental analysis C: 56.50, H: 6.09 (required values; C: 56.36 H: 6.08).

6'-Methyl-6'-(phenylsulfonyl)methyl]spiro[tricyclo[3.3.1.1^{3,7}]decane-2,3'-[1,2,4]trioxane] (39).

(Off-white solid, 56%). Mpt. 126-127°C. 1H NMR (400 MHz, $CDCl_3$) δ_H 1.46 (s, 3H, CH_3) 1.53-2.05 (m, 14H, adamantyl), 3.66 (bd, $J = 12.1$ Hz, 1H, OCH_2), 3.76 (d, $J = 12.1$ Hz, 1H, OCH_2), 3.92 (bs, 2H, CH_2SO_2), 7.55 - 7.64 (m, 3H, Ar), 7.96 (d, $J = 7.1$ Hz, 2H, Ar). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 20.4, 27.4, 33.2, 33.6, 33.8, 37.4, 59.2, 64.5, 104.9, 128.3, 129.5, 133.9, 141.5. MS (ES+) m/z 401.1 $[M + Na]^+$ (100). HRMS m/z calculated for $C_{20}H_{26}O_5SNa$ $[M + Na]^+$ 401.1399 found, 401.1379. Elemental analysis C: 63.45, H: 6.95: (required values; C: 63.47 H: 6.92).

3-Benzenesulfonylmethyl-9-tert-butyl-3-methyl-1,2,5-trioxa-spiro[5.5]undecane (40).

(Off-white solid, 92%). Mpt. 154°C. 1H NMR (400 MHz, $CDCl_3$) δ_H 0.82 (bm, 4H, cyclohexyl), 0.90 (m, 1H, cyclohexyl), 1.27 (bm, 4H, cyclohexyl), 1.46 (s, 3H, CH_3), 3.73 (bs, 2H, OCH_2), 3.81 (bs, 2H, CH_2SO_2), 7.53-7.91 (m, 4H, Ar). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 14.5, 20.3, 23.5, 27.9, 32.0, 32.6, 47.5, 65.5, 103.0, 129.4, 130.1, 135.0, 139.7. MS (ES+) m/z 439.13 $[M + Na]^+$ (100), 455.11 $[M + K]^+$ (10). HRMS m/z calculated for $C_{20}H_{29}O_5SCiNa$ $[M^+ + Na]$ 439.1322 found, 439.1344. Elemental analysis C: 57.53, H: 6.89 (required values; C: 57.60 H: 7.00).

3-Benzenesulfonylmethyl-3-methyl-1,2,5-trioxa-spiro[5.5]undecan-9-one (41).

(Pale orange solid, 82%). Mpt 96°C. 1H NMR (400 MHz, $CDCl_3$) δ_H 1.26 (s, 3H, CH_3), 2.01 (bm, 4H, cyclohexyl), 2.40 (bm, 4H, cyclohexyl), 3.82 (bs, 2H, OCH_2), 4.12 (bs, 2H, CH_2SO_2), 7.58 (t, $J = 7.2$ Hz, 2H, Ar), 7.67 (t, $J = 7.5$ Hz, 1H, Ar), 7.98 (d, $J = 7.2$ Hz, 2H, Ar). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 20.2, 29.7, 36.2, 36.4, 65.3, 127.9, 128.3, 129.4, 133.7, 133.8, 141.0. MS (ES+) m/z 363.19 $[M + Na]^+$ (100), 379.17 $[M + K]^+$ (49), 395.23 $[M + Na + CH_3OH]^+$ (55), 411.21 $[M + K + CH_3OH]^+$ (25). HRMS m/z calculated for $C_{16}H_{20}O_6SNa$ $[M + Na]^+$ 363.0878 found, 363.0867. Elemental analysis C: 57.00, H: 5.82 (required values; C: 56.76 H: 5.92).

3-Benzenesulfonylmethyl-3-methyl-1,2,5-trioxa-spiro[5.11]heptadecane (42).

(White powder, 93%). Mpt. 123-124°C. 1H NMR (400 MHz, $CDCl_3$) δ_H 1.32 (bm, 22H, cyclododecanyl), 1.55 (s, 3H, CH_3), 3.68 (bs, 2H, OCH_2), 3.94 (bs, 2H, CH_2SO_2), 7.57 (t, $J = 7.3$ Hz, 2H, Ar), 7.65 (t, $J = 7.4$ Hz, 1H, Ar), 7.96 (d, $J = 7.3$ Hz, 2H, Ar). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 19.0, 19.7, 20.4, 22.1, 22.7, 26.4, 56.3, 107.0, 128.2, 129.5, 134.0, 141.5. MS (ES+)

m/z 433.2 [M + Na]⁺ (100), 449.2 [M + K]⁺ (5). HRMS m/z calculated for C₂₂H₃₄O₅Na [M⁺ + Na] 433.2025 found, 433.2032.

3-Methyl-1,2,5-trioxa-spiro[5.5]undecane-3-carbaldehyde (50).

(White powder, 72%). ¹H NMR (400MHz, CDCl₃) δ_H 1.09 (s, 3H, CH₃), 1.37-1.60 (m, 8H, cyclohexyl), 1.95-2.05 (m, 1H, cyclohexyl), 2.16-2.25 (m, 1H, cyclohexyl), 3.82 (d, 1H, J = 11.6 Hz, CH₂O), 4.10 (d, 1H, J = 11.6 Hz, CH₂O), 9.88 (d, 1H, J = 2.1 Hz, CHO). ¹³C NMR (400MHz, CDCl₃), δ_C 16.7, 22.7, 28.5, 34.7, 61.9, 84.6, 102.8, 203.2. MS (ES⁺) [M - H₂O + Na]⁺ (100) 205.1, [2M - H₂O + Na]⁺ 378.2. HRMS calculated for 205.0841 C₁₀H₁₆O₃Na, found 205.0841.

3-Methyl-1,2,5-trioxa-spiro[5.11]heptadecane-3-carbaldehyde (51).

(White powder, 58%). ¹H NMR (400MHz, CDCl₃) δ_H 1.10 (s, 3H, CH₃), 1.20-1.80 (m, 20H, cyclododecanyl), 2.10 (bs, 2H, cyclododecanyl) 3.76 (d, 1H, J = 11.6 Hz, CH₂O), 3.90 (d, 1H, J = 11.6 Hz, CH₂O), 9.88 (d, 1H, J = 2.2 Hz, CHO). ¹³C NMR (400MHz, CDCl₃), δ_C 18.8, 19.0, 19.9, 22.7, 26.4, 62.2, 84.4, 106.8, 203.5. MS (ES⁺) [M + CH₃OH + Na]⁺ (100) 339.2, HRMS calculated for 307.1885 C₁₆H₂₈O₄Na, found 307.1879.

6'-Methylspiro[tricyclo[3.3.1.1^{3,7}]decane-2,3'-[1,2,4]trioxane]-6'-carbaldehyde (52).

(White powder, 78%). ¹H NMR (400MHz, CDCl₃) δ_H 1.05 (s, 3H, CH₃), 1.46-2.34 (m, 14H, adamantyl), 3.78 (d, 1H, J = 11.6 Hz, CH₂O), 4.10 (d, 1H, J = 11.6 Hz, CH₂O), 9.90 (s, 1H, CHO). ¹³C NMR (400MHz, CDCl₃), δ_C 16.7, 27.4, 33.6, 36.7, 37.5, 61.6, 84.5, 104.9, 203.5. MS (ES⁺) [M + CH₃OH + Na]⁺ (100) 307.2. HRMS calculated for 275.1259 C₁₄H₂₀O₄Na, found 275.1242.

3-Phenyl-1,2,5-trioxa-spiro[5.5]undecane-3-paraldehyde (53).

(White powder, 64%). ¹H NMR (400MHz, CDCl₃) δ_H 1.38-1.75 (m, 8H, cyclohexyl), 2.01-2.10 (m, 1H, cyclohexyl), 2.20-2.29 (m, 1H, cyclohexyl), 4.01 (d, 1H, J = 11.7 Hz, CH₂), 4.51 (d, 1H, J = 11.7 Hz, CH₂) 7.25 (dd, 2H, J = 8.1 Hz, Ar), 7.32-7.42 (m, 3H, Ar), 9.80 (s, 1H, CHO). ¹³C NMR (100MHz, CDCl₃), δ_C 22.5, 25.8, 34.8, 61.8, 87.6, 103.3, 125.2, 128.7, 129.5, 132.7, 199.4.

3-Phenyl-1,2,5-trioxa-spiro[5.11]heptadecane-3-carbaldehyde (54).

(White powder, 70%). ¹H NMR (400MHz, CDCl₃) δ_H 1.20-1.60 (m, 16H, cyclododecanyl), 1.66-1.75 (m, 2H, cyclododecanyl), 2.08-2.17 (m, 2H, cyclododecanyl), 2.43-2.48 (m, 2H, cyclododecanyl), 3.97 (d, 1H, J = 11.8 Hz, CH₂O), 4.53 (d, 1H, J = 11.6 Hz, CH₂O) 7.39 (d, 2H, J = 8.7 Hz, Ar), 7.34-7.41 (m, 3H, Ar), 9.8 (s, 1H, CHO). ¹³C NMR (400MHz, CDCl₃), δ_C 22.1, 23.0, 24.6, 25.2, 26.4, 40.8, 62.0, 87.4, 107.3, 125.2, 129.7, 134.0, 135.5, 199.4.

6'-Methyl-6'-[(Z)-2-phenylvinyl]spiro[tricyclo[3.3.1.1^{3,7}]decane-2,3'-[1,2,4]trioxane] (61).

(Colourless oil, 62%). ¹H NMR (400 MHz, CDCl₃) δ_H 7.30 (m, 5H, Ar), 6.70 (d, J=12.80 Hz, trans olefin -C=CH), 6.28 (d, J=12.80 Hz, trans olefin -C=CH) 3.90 (bs, 1H, -OCH₂), 3.71 (bs, 1H, -OCH₂), 1.75 (m, 14H, adamantyl), 1.26 (s, 3H, CH₃). ¹³C NMR (100 MHz, CDCl₃) δ_C 21.1, 27.2, 33.5, 37.3, 37.9, 76.7, 77.3, 110.5, 124.9, 126.7, 127.9, 128.6, 129.0, 133.7 MS (ES⁺) m/z

349.2 $[M + Na]^+$ (100), 365.2 $[M + K]^+$ (20). HRMS m/z calculated for $C_{21}H_{26}O_3Na$ $[M + Na]^+$ 349.1780 found, 349.1763.

3-Phenyl-3-(2-phenylvinyl)-1,2,5-trioxa-spiro[5.5]undecane (62).

(White foam, 74%). 1H NMR (250 MHz, $CDCl_3$) δ_H 1.25-2.20 (m, 10H, cyclohexyl), 3.88 (bs, 1H, CH_2O), 4.07 (d, $J = 11.9$ Hz, 1H, CH_2O), 6.38 (bd, $J = 12.0$ Hz, 1H, CH), 6.81 (bd, $J = 12.0$ Hz, 1H, CH), 7.02-7.55 (m, 10H, Ar). ^{13}C NMR (100MHz, $CDCl_3$) δ_C 22.8, 25.9, 83.12, 102.9, 127.0, 127.3, 127.9, 128.1, 128.5, 128.9, 129.0, 129.3, 132.1, 132.4, 134.1, 137.0. MS (ES+) m/z 359.1 $[M^+ + Na]$.

(*E/Z*)-*N,N*-Diethyl-3-(8-methyl-6,7,10-trioxa-spiro[4.5]dec-8-yl)-acrylamide (64).

Major fraction (*trans*-isomer):

(Colourless oil, 34%). ν_{max} (neat)/ cm^{-1} 970.6, 1092.6, 1140.7, 1187.0, 1261.7, 1427.0, 1442.7, 1619.8, 1659.1, 2860.5, 2931.3, 2970.6. 1H NMR (400MHz, $CDCl_3$) δ_H 1.13-1.30 (m, 9H, CH_3), 1.50-2.93 (m, 8H, cyclopentyl), 3.35-3.53 (m, 4H, NCH_2), 3.85 (bs, 2H, CH_2O), 6.65 (bs, 1H, CH), 6.85 (bs, 1H, CH). ^{13}C NMR (100MHz, $CDCl_3$) δ_C 13.5, 15.3, 41.3, 42.7, 67.9, 79.0, 114.6, 122.9, 144.3, 166.0. MS (ES+), $[M + Na]^+$ (100) 306.2. HRMS calculated for 306.1681 $C_{15}H_{25}NO_4Na$, found 306.1669. Elemental analysis C: 63.84, H: 8.89, N: 4.75 (required values; C: 63.58 H: 8.89 N: 4.94).

Minor fraction (*cis*-isomer):

(Colourless oil, 9%). ν_{max} (neat)/ cm^{-1} 974.6, 1096.5, 1143.7, 1191.0, 1265.7, 1430.9, 1621.7, 2868.3, 2923.4, 2962.7. 1H NMR (400MHz, $CDCl_3$) δ_H 1.12-1.37 (m, 9H, CH_3), 1.58-1.90 (m, 8H, cyclopentyl), 3.35-3.52 (m, 4H, NCH_2), 3.74 (d, 1H, $J = 11.2$ Hz, CH_2O), 4.30 (d, 1H, $J = 11.1$ Hz, CH_2O), 6.14 (d, 1H, $J = 12.8$ Hz, CH), 6.28 (d, 1H, $J = 12.8$ Hz, CH). ^{13}C NMR (100MHz, $CDCl_3$) δ_C 13.1, 14.4, 39.8, 43.1, 67.8, 81.0, 114.5, 123.8, 141.8, 167.2. MS (ES+), $[M + Na]^+$ (100) 306.2. HRMS calculated for 306.1681 $C_{15}H_{25}NO_4Na$, found 306.1669. Elemental analysis C: 63.84, H: 9.22, N: 4.44 (required values; C: 63.58 H: 8.89 N: 4.75).

(*2E/Z*)-*N,N*-diethyl-3-(6'-methylspiro[tricyclo[3.3.1.1^{3,7}]decane-2,3'-[1,2,4]trioxan]-6'-yl)acrylamide (65).

Major fraction (*trans*-isomer):

(Colourless oil, 40%) ν_{max} (neat)/ cm^{-1} 923.4, 970.6, 990.3, 1072.9, 1088.7, 1139.8, 1297.2, 1375.9, 1430.9, 1454.5, 1619.8, 1659.1, 2852.6, 2923.4, 2970.6. 1H NMR (400MHz, $CDCl_3$) δ_H 1.12-1.23 (m, 9H, CH_3), 1.50-1.75 (m, 6H, adamantyl), 1.80-2.05 (m, 6H, adamantyl), 3.23-3.55 (m, 4H, NCH_2), 3.85 (bs, 2H, CH_2O), 6.66 (d, 1H, $J = 15.4$ Hz, CH), 6.89 (d, 1H, $J = 15.4$ Hz, CH). ^{13}C NMR (100MHz, $CDCl_3$) δ_C 14.0, 15.8, 28.0, 34.2, 38.0, 41.8, 43.3, 61.3, 65.4, 79.4, 105.2, 128.7, 149.1, 166.1. MS (ES+) $[M + Na]^+$ (100) 372.2, $[2M + Na]$ (30%) 721.5. HRMS calculated for 372.2151 $C_{20}H_{31}NO_4Na$, found 372.2145. Elemental analysis C: 68.55, H: 8.88, N: 4.12 (required values; C: 68.74 H: 8.94 N: 4.01).

Minor fraction (*cis*-isomer):

(Colourless oil, 7%). ^1H NMR (400MHz, CDCl_3) δ_{H} 1.10-1.35 (m, 6H, CH_3), 1.35 (bs, 3H, adamantyl), 1.50-2.20 (m, 14H, adamantyl), 3.29-3.53 (m, 4H, NCH_2), 3.80 (d, 1H, $J = 10.5$ Hz OCH_2), 4.12 (d, 1H, $J = 12.0$ Hz, OCH_2), 5.52 (d, 1H, $J = 13.1$ Hz, CH), 6.07 (d, 1H, $J = 13.1$ Hz, CH). ^{13}C NMR (100MHz, CDCl_3) δ_{C} 13.0, 14.3, 27.5, 33.7, 37.6, 39.5, 43.0, 64.8, 80.7, 104.4, 124.0, 141.6, 167.4. MS (ES+) $[\text{M} + \text{Na}]^+$ (100) 372.2, $[2\text{M} + \text{Na}]$ (30%) 721.5. HRMS calculated for 372.2151 $\text{C}_{20}\text{H}_{31}\text{NO}_4\text{Na}$, found 372.2145. Elemental analysis C: 68.70, H: 8.58, N: 4.25 (required values; C: 68.74, H: 8.94, N: 4.01).

(E)-3-(3-Methyl-1,2,5-trioxa-spiro[5.5]undec-3-yl)-acrylic acid methyl ester (67).

(Colourless oil, 61%). ν_{max} (neat)/ cm^{-1} 864.0, 975.8, 1094.8, 1164.5, 1197.3, 1275.2, 1308.0, 1439.2, 1660.6, 1722.2, 2854.9, 2936.9. ^1H NMR (400MHz, CDCl_3) δ_{H} 1.20 (bs, 3H, CH_3) 1.30-1.79 (m, 8H, cyclohexyl), 1.80-2.30 (m, 2H, cyclohexyl), 3.65-4.10 (m, 5H, $\text{CH}_2\text{O}/\text{CH}_3\text{O}$), 6.14 (bs, 1H, CH), 7.14 (bs, 1H, CH). ^{13}C NMR (100MHz, CDCl_3) δ_{C} 21.4, 22.6, 25.8, 34.5, 52.1, 65.2, 78.9, 102.8, 122.2, 149.3, 167.0. MS (ES+) $[\text{M} + \text{Na}]^+$ (100) 279, HRMS calculated for 279.1208 $\text{C}_{13}\text{H}_{20}\text{O}_5\text{Na}$, found 279.1201. Elemental analysis C: 60.60, H: 7.77 (required values; C: 60.92 H: 7.87).

Methyl (2E)-3-(6'-methylspiro[tricyclo[3.3.1.1^{3,7}]decane-2,3'-[1,2,4]trioxan]-6'-yl)acrylate (68).

(Colourless oil, 72%). ν_{max} (neat)/ cm^{-1} 864.8, 975.6, 1094.3, 1211.1, 1265.4, 1308.7, 1375.7, 1434.8, 1450.6, 1656.5, 1722.2, 2856.4, 2919.4. ^1H NMR (400MHz, CDCl_3) δ_{H} 1.24 (bs, 3H, CH_3), 1.45-1.75 (m, 9H, adamantyl), 1.77-2.20 (m, 5H, adamantyl), 3.65-4.08 (m, 5H, $\text{CH}_2\text{O}/\text{CH}_3\text{O}$), 6.15 (bs, 1H, CH), 7.15 (bs, 1H, CH). ^{13}C NMR (100MHz, CDCl_3) δ_{C} 21.4, 27.5, 33.7, 37.5, 39.6, 52.1, 78.7, 104.8, 122.2, 149.4, 167.0. MS (ES+) m/z , 308.3695 $[\text{M} + \text{Na}]^+$ (100) 331.2 MS (ES+) $[\text{M} + \text{Na}]^+$ (100) 331.0. HRMS calculated for 331.1521 $\text{C}_{17}\text{H}_{24}\text{O}_5\text{Na}$, found 331.1522. Elemental analysis C: 66.40, H: 7.47 (required values; C: 66.21 H: 7.84).

(E)-3-(8-Methyl-6,7,10-trioxa-spiro[4.5]dec-8-yl)-acrylic acid ethyl ester (69).

(Colourless oil, 78%). ν_{max} (neat)/ cm^{-1} 1454.4, 1655.1, 1714.0, 2878.0, 2978.2. ^1H NMR (400MHz, CDCl_3) δ_{H} 1.20 (bs, 3H, CH_3), 1.32 (t, 3H, $J = 7.0$ Hz, CH_3), 1.60-1.90 (m, 8H, cyclopentyl), 3.82 (bs, 2H, CH_2O), 4.22 (q, 2H, $J = 7.0$ Hz, CH_2O), 6.10 (bs, 1H, CH), 7.14 (bs, 1H, CH). ^{13}C NMR (100MHz, CDCl_3) δ_{C} 14.6, 25.1, 32.2, 37.4, 60.9, 67.8, 78.8, 114.7, 122.8, 148.6, 166.5 MS (ES+) $[\text{M} + \text{Na}]^+$ (100) 279.1. HRMS calculated for 279.1208 $\text{C}_{13}\text{H}_{20}\text{O}_5\text{Na}$, found 279.1222. Elemental analysis C: 60.40, H: 7.64 (required values; C: 60.72 H: 7.87).

(E)-3-(3-Methyl-1,2,5-trioxa-spiro[5.5]undec-3-yl)-acrylic acid ethyl ester (70).

(Colourless oil, 66%). ν_{max} (neat)/ cm^{-1} 1655.1, 1718.5, 2858.9, 2913.3. ^1H NMR (400MHz, CDCl_3) δ_{H} 1.30 (t, 6H, $J = 7.0$ Hz, CH_3), 1.36-1.48 (m, 2H, CH_2), 1.50-1.72 (m, 6H, CH_2), 1.80-2.22 (m, 2H, CH_2), 3.80 (bs, 2H, CH_2O), 4.25 (q, 2H, $J = 7.2$ Hz, CH_2O), 6.10 (bs, 1H, CH), 7.04 (bs, 1H, CH). ^{13}C NMR (100MHz, CDCl_3) δ_{C} 14.6, 21.6, 22.6, 25.9, 34.7, 61.0, 65.3, 78.9, 102.9, 128.9, 144.1, 166.5. MS (ES+) $[\text{M} + \text{Na}]^+$ (100) 293.1, HRMS calculated for $\text{C}_{14}\text{H}_{22}\text{O}_5\text{Na}$ 293.1365, found 293.1372. Elemental analysis C: 60.53, H: 7.91 (required values; C: 62.20 H: 8.20).

Ethyl (2E)-3-(6'-methylspiro[tricyclo[3.3.1.1^{3,7}]decane-2,3'-[1,2,4]trioxan]-6'-yl)acrylate (71).

(Colourless oil, 89%). ν_{\max} (neat)/ cm^{-1} 1655.1, 1714.0, 2849.8, 2922.3. ^1H NMR (400MHz, CDCl_3) δ_{H} 1.30 (t, 6H, $J = 7.2$ Hz, CH_3), 1.55-1.74 (m, 8H, adamantyl), 1.83 (bs, 2H, adamantyl), 1.88-2.12 (m, 4H, adamantyl), 3.79 (bs, 2H, CH_2O), 4.22 (q, 2H, $J = 7.0$ Hz, CH_2O), 6.10 (bs, 1H, CH), 7.10 (bs, 1H, CH). ^{13}C NMR (100MHz, CDCl_3) δ_{C} 14.6, 27.5, 33.6, 37.5, 39.7, 47.4, 60.7, 64.8, 78.7, 104.9, 122.6, 144.1, 166.5. MS (ES+) $[\text{M} + \text{Na}]^+$ (100) 345.1, and $[2\text{M} + \text{Na}]^+$ 667.2 HRMS calculated for 345.1678 $\text{C}_{18}\text{H}_{26}\text{O}_5\text{Na}$, found 345.1682. Elemental analysis C: 67.23, H: 7.90 (required values; C: 67.06 H: 8.13).

(E)-3-(3-Phenyl-1,2,5-trioxa-spiro[5.5]undec-3-yl)-acrylic acid ethyl ester (72).

(Colourless oil, 59%). ^1H NMR (400MHz, CDCl_3) δ_{H} 1.26 (t, 3H, $J = 7.21$ Hz, CH_3), 1.36-1.47 (m, 2H, cyclohexyl), 1.48-1.64 (m, 6H, cyclohexyl), 1.63-1.98 (m, 2H, cyclohexyl), 4.12 (d, 1H, $J = 12.1$ Hz, OCH_2), 4.18 (q, 2H, $J = 7.1$ Hz, CH_2), 4.25 (d, 1H, $J = 12.1$ Hz, OCH_2), 6.12 (bs, 1H, CH), 7.14(bs, 1H, CH), 7.25-7.42 (m, 5H, Ar). ^{13}C NMR (100MHz, CDCl_3) δ_{C} 14.6, 22.7, 22.7, 25.9, 60.8, 82.3, 103.2, 123.9, 126.1, 129.0, 138.7, 147.2, 148.0, 166.3. MS (ES+) $[\text{M} + \text{Na}]^+$ (100) 355.1, and $[2\text{M} + \text{Na}]^+$ 687.2 HRMS calculated for 355.1521 $\text{C}_{19}\text{H}_{24}\text{O}_5\text{Na}$, found 355.1504. Elemental analysis C: 68.46, H: 7.23 (required values; C: 68.66 H: 7.28).

(E)-3-(3-Phenyl-1,2,5-trioxa-spiro[5.11]heptadec-3-yl)-acrylic acid ethyl ester (73).

(Colourless oil, 44%). ν_{\max} (neat)/ cm^{-1} 1655.1, 1714.0, 2849.8, 2931.3, 3012.8. ^1H NMR (400MHz, CDCl_3) δ_{H} 1.28 (t, 3H, $J = 7.0$ Hz, 1.30-1.50 (m, 18H, dodecanyl), 1.56-1.89 (m, 4H, dodecanyl), 4.15 (d, 2H, $J = 12.2$ Hz, CH_2O), 4.21 (q, 2H, $J = 7.0$ Hz, CH_2), 6.10 (bs, 1H, CH), 7.18 (bs, 1H, CH), 7.30-7.42 (m, 5H, Ar). ^{13}C NMR (100MHz, CDCl_3) δ_{C} 14.2, 19.3, 22.4, 26.1, 29.7, 60.7, 64.1, 81.7, 107.0, 123.7, 126., 128.7, 132.1, 132.2, 138.4, 147.0, 147.6, 166.1. MS (ES+) $[\text{M} + \text{Na}]^+$ (100) 439.0 and $[2\text{M} + \text{Na}]^+$ 855.1. HRMS calculated for 439.2460 $\text{C}_{25}\text{H}_{36}\text{O}_5\text{Na}$, found 439.24379. Elemental analysis C: 72.14, H: 8.65 (required values; C: 72.08 H: 8.71)

(2E)-3-(6'-Methylspiro[tricyclo[3.3.1.1^{3,7}]decane-2,3'-[1,2,4]trioxan]-6'-yl)acrylic acid (75).

(White powder, 64%). ^1H NMR (400MHz, CDCl_3) δ_{H} 1.19-1.40 (bs, 3H, CH_3), 1.55-1.74 (m, 8H, adamantyl), 1.84 (bs, 2H, adamantyl), 1.85-2.09 (m, 4H, adamantyl), 3.08 (bs, 2H, OCH_2), 6.14 (d, 1H, $J = 15.8$ Hz, CH), 7.20 (bs, 1H, CH). ^{13}C NMR (100MHz, CDCl_3) δ_{C} 21.6, 27.9, 33.8, 37.5, 39.7, 47.4, 78.8, 105.0, 121.8, 151.4, 171.6. MS (ES-) $[\text{M} - \text{H}]^-$ (100) 293.2. HRMS calculated for 293.1389 $\text{C}_{16}\text{H}_{21}\text{O}_5$, found 293.1403.

(E)-3-(3-Phenyl-1,2,5-trioxa-spiro[5.5]undec-3-yl)-acrylic acid (76).

(White powder, 84%). ^1H NMR (400MHz, CDCl_3) δ_{H} 1.36- 1.49 (m, 2H, cyclohexyl), 1.50-1.63 (m, 6H, cyclohexyl), 1.64-1.99 (m, 2H, cyclohexyl), 4.13 (d, 1H, $J = 12.1$ Hz, OCH_2), 4.27 (d, 1H, $J = 12.1$ Hz, OCH_2) 6.15 (bs, 1H, CH), 7.25 (bs, 1H, CH), 7.30 (m, 5H, Ar). ^{13}C NMR

(100MHz, CDCl₃) δ_C 22.7, 25.9, 29.9, 74.5, 82.3, 103.4, 123.1, 126.1, 129.2, 138.3, 150.0, 171.6. MS (ES-) [M - H]⁻ (100) 303.1, HRMS calculated for 303.1232 C₁₇H₁₉O₅, found 303.1222.

(E)-3-(8-Methyl-6,7,10-trioxa-spiro[4.5]dec-8-yl)-N-(2-morpholin-4-yl-ethyl)-acrylamide (79).

(White powder, 81%). Mpt. 118-120 °C. ν_{\max} (CHCl₃)/cm⁻¹ 1505.7, 1605.7, 1637.0, 1668.7, 2813.6, 2858.9, 2958.5, 3003.8, 3284.5. ¹H NMR (400MHz, CDCl₃) δ_H 1.21 (bs, 3H, CH₃), 1.62-1.98 (m, 8H, cyclopentyl), 2.47 (t, 4H, J = 4.4 Hz, NCH₂), 2.52 (q, 2H, J = 6.0 Hz, CH₂N), 3.45 (q, 2H, J = 6.1 Hz, NHCH₂), 3.72 (t, 4H, J = 4.7 Hz, CH₂O), 3.82 (d, 2H, J = 10.9 Hz, CH₂O), 6.10 (bs, 2H, CH/NH), 6.91 (bs, 1H, CH). ¹³C NMR (100MHz, CDCl₃) δ_C 22.0, 23.8, 36.1, 53.74, 57.3, 67.3, 67.9, 78.9, 114.7, 124.7, 144.1, 165.5. MS (ES+) [M + Na]⁺ (100) 363.1, [2M + Na]⁺ 703.2 HRMS calculated for 363.1896 C₁₇H₂₈N₂O₅Na, found 363.1904. Elemental analysis C: 60.22, H: 8.48, N: 8.44 (required values C: 59.98, H: 8.29, N: 8.23)

(E)-N-(2-Diethylamino-ethyl)-3-(8-methyl-6,7,10-trioxa-spiro[4.5]dec-8-yl)-acrylamide (80).

(Colourless oil, 77%). ν_{\max} (neat)/cm⁻¹ 1537.4, 1637.0, 1673.2, 1709.4, 2813.6, 2867.9, 2958.5, 3302.6. ¹H NMR (400MHz, CDCl₃) δ_H 1.03 (t, 3H, J = 7.2 Hz, CH₃), 1.08 (t, 6H, J = 7.0 Hz, CH₃), 1.61-1.89 (m, 8H, cyclopentyl), 2.57 (q, 4H, J = 7.2 Hz, NCH₂), 2.66 (t, 2H, J = 7.2 Hz, CH₂N), 3.43 (q, 2H, J = 6.1 Hz, NHCH₂), 3.81 (bs, 2H, CH₂O), 6.08 (bs, 1H, CH), 6.61 (bs, 1H, NH), 6.85 (bs, 1H, CH). ¹³C NMR (100MHz, CDCl₃) δ_C 11.3, 14.7, 36.8, 38.5, 46.9, 51.6, 52.1, 67.6, 78.5, 114.3, 124.6, 156.8, 165.3. MS (ES+) [M + H]⁺ (50) 327.1, [M + Na]⁺ (100) 349.1, HRMS calculated for 349.2103 C₁₇H₃₀N₂O₄Na, found 349.2102. Elemental analysis C: 62.22, H: 9.48, N: 8.34 (required values C: 62.55, H: 9.26, N: 8.58)

(2E)-3-(6'-methylspiro[tricyclo[3.3.1.1^{3,7}]decane-2,3'-[1,2,4]trioxan]-6'-yl)-1-(morpholin-4-yl)prop-2-en-1-one (81).

(White powder, 80%). Mpt. 128-138 °C. ν_{\max} (CHCl₃)/cm⁻¹ 1433.2, 1446.8, 1614.3, 1655.1, 2849.8, 2913.2. ¹H NMR (400MHz, CDCl₃) δ_H 1.33 (bs, 3H, CH₃), 1.56-1.72 (m, 8H, adamantyl), 1.84 (bs, 2H, adamantyl), 1.88-2.10 (bs, 4H, adamantyl), 3.59 (bs, 2H, NCH₂), 3.68 (bs, 6H, NCH₂/CH₂N), 3.80 (bs, 2H, OCH₂), 6.53 (d, 1H, J = 13.9 Hz, CH), 6.81 (d, 1H, J = 13.9 Hz, CH). ¹³C NMR (100MHz, CDCl₃) δ_C 21.5, 27.2, 33.4, 37.2, 42.5, 46.4, 64.5, 66.8, 78.6, 104.5, 124.6, 157.0, 166.0. MS (ES+) [M + Na]⁺ (100) 386.0 and [2M + Na]⁺ 749.1. HRMS calculated for 386.1943 C₂₀H₂₉NNaO₅, found 386.1933. Elemental analysis C: 66.28, H: 8.27, N: 3.66 (required values C: 66.09, H: 8.04, N: 3.85)

(2E)-3-(6'-methylspiro[tricyclo[3.3.1.1^{3,7}]decane-2,3'-[1,2,4]trioxan]-6'-yl)-N-[2-(morpholin-4-yl)ethyl]acrylamide (82).

(White powder, 78%). Mpt. 96-98 °C. ν_{\max} (CHCl₃)/cm⁻¹ 1528.3, 1641.5, 1673.2, 1704.9, 2804.5, 2849.0, 2931.3, 3357.0. ¹H NMR (400MHz, CDCl₃) δ_H 1.40 (bs, 3H, CH₃), 1.58-1.74 (m, 8H, adamantyl), 1.83 (bs, 2H, adamantyl), 1.89-2.01 (m, 4H, adamantyl) 2.42-2.50 (m, 6H, NCH₂/CH₂N) 3.44 (q, 2H, J = 6.1 Hz, NHCH₂), 3.67-3.75 (m, 4H, CH₂O), 3.80 (bs, 2H, OCH₂), 6.10 (bs, 1H, CH), 6.28 (bs, 1H, NH), 6.87 (bs, 1H, CH). ¹³C NMR (100MHz, CDCl₃) δ_C 27.5, 33.8, 36.2, 37.5, 53.8, 57.4, 57.9, 67.3, 78.8, 104.8, 124.6, 157.0, 166.0. MS (ES+) [M + Na]⁺

(100) 429.1 and $[2M + Na]^+$ 835.1. HRMS calculated for 429.2365 $C_{22}H_{34}NNaO_5$, found 429.2351. Elemental analysis C: 64.96, H: 8.76, N: 7.12 (required values C: 65.00, H: 8.43, N: 6.89).

(2E)-N-[2-(diethylamino)ethyl]-3-(6'-methylspiro[tricyclo[3.3.1.1^{3,7}]]decane-2,3'-[1,2,4]trioxan]-6'-yl)acrylamide (83).

(White powder, 84%). Mpt. 84-86 °C. ν_{max} ($CHCl_3$)/ cm^{-1} 1532.8, 1637.0, 1668.7, 2849.0, 2931.3, 2994.7, 3257.4. 1H NMR (400MHz, $CDCl_3$) δ_H 1.09 (t, 3H, J = 7.0 Hz, CH_3), 1.16 (t, 6H, J = 7.2 Hz, CH_3), 1.56-1.72 (m, 8H, adamantyl), 1.83 (bs, 2H, adamantyl), 1.88-2.01 (m, 4H, adamantyl), 2.74-2.94 (m, 6H, NCH_2/CH_2N), 3.51 (q, 2H, J = 6.1 Hz, $NHCH_2$), 3.80 (bs, 2H, OCH_2), 6.13 (d, 1H, J = 14.8 Hz, CH), 6.90 (bs, 1H, CH), 7.10 (bs, 1H, NH). ^{13}C NMR (100MHz, $CDCl_3$), δ_C 10.9, 27.1, 27.5, 33.8, 36.7, 37.5, 47.5, 52.2, 78.8, 104.8, 124.6, 157.2, 166.0 MS (ES+) $[M + H]^+$ (100) 393.1. HRMS calculated for 393.2753 $C_{22}H_{37}O_4N_2$, found 393.2757. Elemental analysis C: 66.98, H: 9.46, N: 7.34 (required values C: 67.32, H: 9.24, N: 7.14).

(E)-1-Morpholin-4-yl-3-(3-phenyl-1,2,5-trioxa-spiro[5.5]undec-3-yl)-propenone (84).

(White powder, 86%). Mpt. 110-112 °C. ν_{max} ($CHCl_3$)/ cm^{-1} 1428.7, 1614.3, 1655.1, 2849.8, 2931.3, 3003.8. 1H NMR (400MHz, $CDCl_3$, -20 °C) δ_H 1.37-1.49 (m, 2H, cyclohexyl), 1.51-1.62 (m, 6H, cyclohexyl), 1.64-1.99 (m, 2H, cyclohexyl), 3.55 (bs, 2H, NCH_2), 3.67 (bs, 6H, CH_2O/NCH_2), 4.10 (d, 1H, J = 12.0 Hz, OCH_2), 4.27 (d, 1H, J = 12.0 Hz, OCH_2), 6.51 (d, 1H, J = 15.5 Hz, CH), 6.96 (d, 1H, J = 15.5 Hz, CH), 7.29-7.44 (m, 5H, Ar). ^{13}C NMR (100MHz, $CDCl_3$), δ_C 22.7, 25.8, 42.8, 46.7, 61.9, 64.6, 67.1, 82.7, 103.2, 122.7, 125.66, 129.0, 139.0, 144.1, 165.5. MS (ES+) $[M + Na]^+$ (100) 396.0, and $[2M + Na]^+$ 769.0 HRMS calculated for 396.1787 $C_{21}H_{27}O_5NNa$, found 396.1780. Elemental analysis C: 67.88, H: 7.31, N: 3.76 (required values C: 67.54, H: 7.29, N: 3.75).

(E)-N-(2-Morpholin-4-yl-ethyl)-3-(3-phenyl-1,2,5-trioxa-spiro[5.5]undec-3-yl)-acrylamide (85).

(Yellow oil, 83%). ν_{max} (neat)/ cm^{-1} 1259.4, 1446.2, 1539.6, 1639.0, 1710.8, 2814.3, 2843.4, 2936.8, 3310.4. 1H NMR (400MHz, $CDCl_3$) δ_H 1.38-1.49 (m, 2H, cyclohexyl), 1.50-1.63 (m, 6H, cyclohexyl), 1.64-1.92 (m, 2H, cyclohexyl), 2.38-2.55 (m, 6H, CH_2), 3.43 (q, 2H, J = 5.7 Hz, $NHCH_2$), 3.70 (t, 4H, J = 4.7 Hz, CH_2O), 4.20 (d, 1H, J = 12.2 Hz, OCH_2), 4.26 (d, 1H, J = 12.2 Hz, OCH_2), 6.08 (bs, 1H, CH), 6.21 (bs, 1H, NH), 7.10 (bs, 1H, CH), 7.29-7.44 (m, 5H, Ar). ^{13}C NMR (100MHz, $CDCl_3$), δ_C 22.7, 25.8, 36.2, 37.6, 53.8, 57.9, 67.3, 82.5, 103.2, 126.5, 129.0, 139.2, 142.9, 165.3. MS (ES+) $[M + Na]^+$ (100) 439.0. HRMS calculated for 439.2209 $C_{23}H_{32}O_5N_2Na$, found, 439.2202. Elemental analysis C: 66.22, H: 7.42, N: 68.34 (required values C: 66.32, H: 7.56, N: 6.58)