**Supplemental material**

**Structure-activity relationship of atorvastatin derivatives for metabolic activation by hydrolases**

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**Abbreviations**

hCESs: human carboxylesterases; HPLC: high-performance liquid chromatography; IR: infrared; mp: melting point; NMR: nuclear magnetic resonance; TMS: tetramethylsilane

Table S1. Summarize points of structure-activity relationship

|  |  |  |  |
| --- | --- | --- | --- |
| Property | hCESs | Results | Discussion |
| Carbon chain | 1b | increased from **2j** to **2a** | steric hindrance |
| 1c |
| 2 | nealy equal |
| Three carbon atoms | 1b | **2m** < **2c** < **2k** | steric hindrance |
| 1c |
| 2 |
| Carbon atom adjacent to the ester oxygen atom | 1b | **2o** < **2m** < **2b** | steric hindrance |
| 1c |
| 2 |
| Similar structure | 1b | **2l** < **2k**, **2n** < **2m** | steric hindrance |
| 1c |
| 2 | **2l** < **2k**, **2n** ≤ **2m** |
| Methylene adjacent to the ester oxygen atom | 1b | **2m** < **2p**, **2o** < **2q** | steric hindrance |
| 1c |
| 2 |
| Fluorine-containing | 1b | **2b** < **2r**, **2m** < **2s** | electron density |
| 1c | **2r** < **2b**, **2m** < **2s** |
| 2 | **2b** < **2r**, **2m** < **2s** |
| Aromatic | 1b | **2v** is the highest | steric hindrance |
| 1c |
| 2 | increased from **2t** to **2x** | electron density |
| Thioester | 1b | **5b** < **2b**, **2m** < **5m** | balance of steric hindrance and electron density |
| 1c |
| 2 | **5b** ≤ **2b**, **5m** ≤ **2m** |
| Amide | 1b | barely hydrolyzed | rarely substrate |
| 1c |
| 2 |

This table presents the notable points in Figure 2.

**Characterization of Synthesized Atorvastatin Derivatives**

Column chromatography was performed using silica gel 60 (0.040–0.063 mm, 230–400 mesh ASTM) (Merck, Darmstadt, Germany). Melting points (mp) were measured using a Micro melting point apparatus (Yanaco, Kyoto, Japan), and are uncorrected. Infrared (IR) spectra were recorded on a FT-720 (Horiba, Kyoto, Japan). 1H- and 13C-nuclear magnetic resonance (NMR) spectra were obtained on an AscendTM 400 (Bruker, MA, USA). 1H-NMR spectra were recorded in CDCl3 as a solvent on a 400 MHz spectrometer using tetramethylsilane (TMS) (0.00 ppm) as an internal standard. 13C-NMR spectra were recorded in CDCl3 as a solvent on a 100 MHz spectrometer using the central peak of CDCl3 (77.0 ppm) as an internal standard. The high-performance liquid chromatography (HPLC) analyses were done using an LCsolution (Shimadzu, Kyoto, Japan). The characterization of the newly synthesized atorvastatin derivatives is described below.

**Propyl (3*R*,5*R*)-7-(2-(4-fluorophenyl)-5-isopropyl-3-phenyl-4-(phenylcarbamoyl)-1*H*- pyrrol-1-yl)-3,5-dihydroxyheptanoate (2c)** Colorless solid; mp 80–81°C; IR max (KBr) cm–1: 3392, 1720, 1660; 1H-NMR (400 MHz, CDCl3) : 7.23–7.13 (m, 9H), 7.06 (d, 2H, *J* = 7.6 Hz), 7.03–6.95 (m, 3H), 6.86 (br s, 1H), 4.20–4.04 (m, 4H), 3.99–3.89 (m, 1H), 3.80–3.68 (m, 2H), 3.68–3.51 (m, 2H), 2.41 (d, 2H, *J* = 6.0 Hz), 1.75–1.58 (m, 4H), 1.54 (d, 6H, *J* = 6.8 Hz), 1.50–1.42 (m, 1H), 1.29-1.23 (m, 1H), 0.94 (t, 3H, *J* = 7.2 Hz); 13C-NMR (100 MHz, CDCl3) : 172.8, 164.8, 162.3 (d, 1*J*C–F = 246.2 Hz), 141.6, 138.4, 134.7, 133.2 (d, 3*J*C–F = 8.1 Hz), 130.5, 128.75, 128.68, 128.37 (d, 4*J*C–F = 4.0 Hz), 128.35, 126.6, 123.5, 121.8, 119.6, 115.4 (d, 2*J*C–F = 21.3 Hz), 115.3, 69.7, 69.0, 66.6, 41.8, 41.30, 41.27, 39.1, 26.1, 21.9, 21.8, 21.7, 10.3; HPLC (Method 3): *t*R = 19.4 min.

**Pentyl (3*R*,5*R*)-7-(2-(4-fluorophenyl)-5-isopropyl-3-phenyl-4-(phenylcarbamoyl)-1*H*- pyrrol-1-yl)-3,5-dihydroxyheptanoate (2e)** Pale yellow solid; mp 41–44°C; IR max (KBr) cm–1: 3407, 1731, 1648; 1H-NMR (400 MHz, CDCl3) : 7.22–7.13 (m, 9H), 7.06 (d, 2H, *J* = 8.0 Hz), 7.02–6.96 (m, 3H), 6.87 (br s, 1H), 4.19–4.08 (m, 4H), 3.98–3.90 (m, 1H), 3.78–3.71 (m, 2H), 3.65 (br s, 1H), 3.61–3.54 (m, 1H), 2.40 (d, 2H, *J* = 6.0 Hz), 1.74–1.58 (m, 4H), 1.54 (d, 6H, *J* = 7.2 Hz), 1.52–1.42 (m, 1H), 1.39–1.22 (m, 5H), 0.90 (t, 3H, *J* = 7.0 Hz); 13C-NMR (100 MHz, CDCl3) : 172.7, 164.8, 162.3 (d, 1*J*C–F = 246.2 Hz), 141.6, 138.4, 134.7, 133.2 (d, 3*J*C–F = 8.1 Hz), 130.5, 128.8, 128.7, 128.4 (d, 4*J*C–F = 4.3 Hz), 128.3, 126.6, 123.5, 121.9, 119.6, 115.4 (d, 2*J*C–F = 21.4 Hz), 115.3, 69.6, 69.0, 65.2, 41.8, 41.3, 39.1, 28.2, 28.0, 26.2, 22.3, 21.8, 21.7, 13.9; HPLC (Method 3): *t*R = 27.8 min.

**Hexyl (3*R*,5*R*)-7-(2-(4-fluorophenyl)-5-isopropyl-3-phenyl-4-(phenylcarbamoyl)-1*H*- pyrrol-1-yl)-3,5-dihydroxyheptanoate (2f)** Colorless oil; IR max (KBr) cm–1: 3409, 1731, 1664; 1H-NMR (400 MHz, CDCl3) : 7.21–7.13 (m, 9H), 7.06 (d, 2H, *J* = 7.6 Hz), 7.02–6.96 (m, 3H), 6.88 (br s, 1H), 4.18–4.08 (m, 4H), 3.98–3.90 (m, 1H), 3.86–3.67 (m, 3H), 3.61–3.54 (m, 1H), 2.40 (d, 2H, *J* = 6.0 Hz), 1.74–1.59 (m, 4H), 1.54 (d, 6H, *J* = 7.2 Hz), 1.49–1.43 (m, 1H), 1.37–1.24 (m, 7H), 0.89 (t, 3H, *J* = 7.0 Hz); 13C-NMR (100 MHz, CDCl3) : 172.4, 164.6, 162.0 (d, 1*J*C–F = 246.3 Hz), 141.2, 138.1, 134.4, 132.9 (d, 3*J*C–F = 8.0 Hz), 130.2, 128.5, 128.4, 128.10, 128.06, 126.3, 123.3, 121.6, 119.4, 115.1 (d, 2*J*C–F = 21.2 Hz), 115.0, 69.3, 68.7, 64.9, 41.6, 41.1, 41.0, 38.8, 31.1, 28.2, 25.9, 25.2, 22.2, 21.5, 21.4, 13.7; HPLC (Method 3): *t*R = 32.6 min.

**Heptyl (3*R*,5*R*)-7-(2-(4-fluorophenyl)-5-isopropyl-3-phenyl-4-(phenylcarbamoyl)-1*H*- pyrrol-1-yl)-3,5-dihydroxyheptanoate (2g)** Colorless solid; mp 66–68°C; IR max (KBr) cm–1: 3353, 1733, 1654; 1H-NMR (400 MHz, CDCl3) : 7.22–7.12 (m, 9H), 7.06 (d, 2H, *J* = 8.0 Hz), 7.02–6.96 (m, 3H), 6.88 (br s, 1H), 4.19–4.07 (m, 4H), 3.97–3.90 (m, 1H), 3.79–3.71 (m, 3H), 3.61–3.54 (m, 1H), 2.40 (d, 2H, *J* = 6.0 Hz), 1.74–1.59 (m, 4H), 1.54 (d, 6H, *J* = 7.2 Hz), 1.49–1.43 (m, 1H), 1.37–1.20 (m, 9H), 0.88 (t, 3H, *J* = 7.0 Hz); 13C-NMR (100 MHz, CDCl3) : 172.7, 164.9, 162.3 (d, 1*J*C–F = 246.3 Hz), 141.5, 138.4, 134.7, 133.2 (d, 3*J*C–F = 8.0 Hz), 130.5, 128.8, 128.7, 128.39, 128.35, 126.6, 123.6, 121.9, 119.6, 115.4 (d, 2*J*C–F = 21.3 Hz), 115.3, 69.6, 69.0, 65.1, 41.8, 41.4, 41.3, 39.1, 31.7, 28.9, 28.5, 26.2, 25.8, 22.6, 21.8, 21.7, 14.1; HPLC (Method 3): *t*R = 37.2 min.

**Nonyl (3*R*,5*R*)-7-(2-(4-fluorophenyl)-5-isopropyl-3-phenyl-4-(phenylcarbamoyl)-1*H*- pyrrol-1-yl)-3,5-dihydroxyheptanoate (2i)** Colorless solid; mp 62–63°C; IR max (KBr) cm–1: 3372, 1731, 1654; 1H-NMR (400 MHz, CDCl3) : 7.23–7.12 (m, 9H), 7.06 (d, 2H, *J* = 7.6 Hz), 7.03–6.95 (m, 3H), 6.87 (br s, 1H), 4.20–4.05 (m, 4H), 3.98–3.90 (m, 1H), 3.79–3.71 (m, 2H), 3.67 (br s, 1H), 3.61–3.54 (m, 1H), 2.40 (d, 2H, *J* = 6.0 Hz), 1.75–1.57 (m, 4H), 1.54 (d, 6H, *J* = 6.8 Hz), 1.49–1.43 (m, 1H), 1.37–1.22 (m, 13H), 0.88 (t, 3H, *J* = 6.4 Hz); 13C-NMR (100 MHz, CDCl3) : 172.8, 164.8, 162.3 (d, 1*J*C–F = 246.2 Hz), 141.5, 138.4, 134.7, 133.2 (d, 3*J*C–F = 8.0 Hz), 130.5, 128.75, 128.68, 128.39, 128.35, 126.6, 123.5, 121.8, 119.6, 115.4 (d, 2*J*C–F = 21.2 Hz), 115.3, 69.7, 69.0, 65.2, 41.8, 41.3, 39.1, 31.8, 29.5, 29.2, 28.5, 26.1, 25.9, 22.7, 21.8, 21.7, 14.1; HPLC (Method 3): *t*R = 48.5 min.

**Isopropyl (3*R*,5*R*)-7-(2-(4-fluorophenyl)-5-isopropyl-3-phenyl-4-(phenylcarbamoyl)- 1*H*-pyrrol-1-yl)-3,5-dihydroxyheptanoate (2m)** Colorless solid; mp 63–65°C; IR max (KBr) cm–1: 3392, 1724, 1660; 1H-NMR (400 MHz, CDCl3) : 7.23–7.12 (m, 9H), 7.06 (d, 2H, *J* = 7.6 Hz), 7.03–6.95 (m, 3H), 6.86 (br s, 1H), 5.10–4.98 (m, 1H), 4.20–4.04 (m, 2H), 4.01–3.89 (m, 1H), 3.80–3.69 (m, 2H), 3.65 (br s, 1H), 3.62–3.53 (m, 1H), 2.37 (d, 2H, *J* = 6.0 Hz), 1.76–1.58 (m, 2H), 1.54 (d, 6H, *J* = 6.8 Hz), 1.49–1.41 (m, 1H), 1.30–1.19 (m, 7H); 13C-NMR (100 MHz, CDCl3) : 172.3, 164.8, 162.3 (d, 1*J*C–F = 246.2 Hz), 141.6, 138.4, 134.7, 133.2 (d, 3*J*C–F = 8.1 Hz), 130.5, 128.75, 128.68, 128.39, 128.35, 126.6, 123.5, 121.8, 119.6, 115.4 (d, 2*J*C–F = 21.2 Hz), 115.3, 69.7, 69.1, 68.6, 41.8, 41.5, 41.3, 39.1, 26.1, 21.79, 21.77, 21.6; HPLC (Method 3): *t*R = 18.4 min.

***tert*-Butyl (3*R*,5*R*)-7-(2-(4-fluorophenyl)-5-isopropyl-3-phenyl-4-(phenylcarbamoyl)- 1*H*-pyrrol-1-yl)-3,5-dihydroxyheptanoate (2o)** Colorless solid; mp 147–148°C; IR max (KBr) cm–1: 3397, 1714, 1646; 1H-NMR (400 MHz, CDCl3) : 7.21–7.13 (m, 9H), 7.06 (d, 2H, *J* = 7.6 Hz), 7.02–6.96 (m, 3H), 6.86 (br s, 1H), 4.15–4.07 (m, 2H), 3.97–3.89 (m, 1H), 3.81 (br s, 1H), 3.76–3.71 (m, 2H), 3.61–3.54 (m, 1H), 2.31 (d, 2H, *J* = 6.0 Hz), 1.73–1.59 (m, 2H), 1.53 (d, 6H, *J* = 6.8 Hz), 1.49–1.40 (m, 10H), 1.30–1.21 (m, 1H); 13C-NMR (100 MHz, CDCl3) : 172.1, 164.8, 162.2 (d, 1*J*C–F = 246.1 Hz), 141.5, 138.4, 134.6, 133.2 (d, 3*J*C–F = 8.1 Hz), 130.5, 128.7, 128.6, 128.39, 128.34, 126.5, 123.5, 121.8, 119.6, 115.3 (d, 2*J*C–F = 21.2 Hz), 115.2, 81.8, 69.7, 69.2, 42.2, 41.7, 41.3, 39.0, 28.0, 26.1, 21.7, 21.6; HPLC (Method 3): *t*R = 21.0 min.

**Isobutyl (3*R*,5*R*)-7-(2-(4-fluorophenyl)-5-isopropyl-3-phenyl-4-(phenylcarbamoyl)-　1*H*-pyrrol-1-yl)-3,5-dihydroxyheptanoate (2p)** Colorless needles; mp 155–156°C; IR max (KBr) cm–1: 3392, 1722, 1660; 1H-NMR (400 MHz, CDCl3) : 7.22–7.13 (m, 9H), 7.06 (d, 2H, *J*=7.6 Hz), 7.02–6.96 (m, 3H), 6.87 (br s, 1H), 4.20–4.08 (m, 2H), 3.98–3.91 (m, 1H), 3.89 (d, 2H, *J*=6.4 Hz), 3.78–3.71 (m, 2H), 3.68 (br s, 1H), 3.61–3.54 (m, 1H), 2.42 (d, 2H, *J*=6.0 Hz), 1.98–1.88 (m, 1H), 1.72–1.58 (m, 2H), 1.54 (d, 6H, *J*=7.2 Hz), 1.50–1.43 (m, 1H), 1.30–1.24 (m, 1H), 1.54 (d, 6H, *J*=7.2 Hz); 13C-NMR (100 MHz, CDCl3) : 172.7, 164.9, 162.3 (d, 1*J*C–F=246.4 Hz), 141.5, 138.4, 134.7, 133.2 (d, 3*J*C–F=8.0 Hz), 130.5, 128.75, 128.67, 128.37, 128.34, 126.6, 123.5, 121.8, 119.6, 115.4 (d, 2*J*C–F=21.4 Hz), 115.3, 71.0, 69.6, 69.0, 41.8, 41.3, 39.1, 27.6, 26.1, 21.8, 21.7, 19.0; HPLC (Method 3): *t*R = 23.7 min.

**Neopentyl (3*R*,5*R*)-7-(2-(4-fluorophenyl)-5-isopropyl-3-phenyl-4-(phenylcarbamoyl)-　1*H*-pyrrol-1-yl)-3,5-dihydroxyheptanoate (2q)** Colorless solid; mp 165–167°C; IR max (KBr) cm–1: 3396, 3334, 1725, 1660; 1H-NMR (400 MHz, CDCl3) : 7.22–7.13 (m, 9H), 7.06 (d, 2H, *J*=7.6 Hz), 7.02–6.96 (m, 3H), 6.86 (br s, 1H), 4.21–4.07 (m, 2H), 3.99–3.89 (m, 1H), 3.81 (s, 2H), 3.79–3.63 (m, 3H), 3.61–3.52 (m, 1H), 2.44 (d, 2H, *J*=6.0 Hz), 1.75–1.57 (m, 2H), 1.54 (d, 6H, *J*=7.2 Hz), 1.50–1.44 (m, 1H), 1.31–1.24 (m, 1H), 0.93 (s, 9H); 13C-NMR (100 MHz, CDCl3) : 172.8, 164.8, 162.3 (d, 1*J*C–F=246.3 Hz), 141.5, 138.4, 134.7, 133.2 (d, 3*J*C–F=8.0 Hz), 130.5, 128.8, 128.7, 128.4, 126.6, 123.5, 121.8, 119.6, 115.4 (d, 2*J*C–F=21.1 Hz), 115.3, 74.2, 69.7, 69.0, 41.8, 41.31, 41.27, 39.1, 31.3, 26.4, 26.1, 21.8, 21.7; HPLC (Method 3): *t*R = 27.2 min.

**2,2,2-Trifluoroethyl (3*R*,5*R*)-7-(2-(4-fluorophenyl)-5-isopropyl-3-phenyl-4- (phenylcarbamoyl)-1*H*-pyrrol-1-yl)-3,5-dihydroxyheptanoate (2r)** Colorless solid; mp 54–58°C; IR max (KBr) cm–1: 3403, 1756, 1646; 1H-NMR (400 MHz, CDCl3) : 7.22–7.13 (m, 9H), 7.05 (d, 2H, *J* = 8.0 Hz), 7.03–6.96 (m, 3H), 6.85 (br s, 1H), 4.56–4.42 (m, 2H), 4.24–4.16 (m, 1H), 4.15–4.07 (m, 1H), 3.99–3.91 (m, 1H), 3.78–3.71 (m, 1H), 3.60–3.53 (m, 1H), 3.40 (br s, 1H), 3.29 (br s, 1H), 2.59–2.48 (m, 2H), 1.73–1.57 (m, 2H), 1.54–1.45 (m, 7H), 1.32–1.27 (m, 1H); 13C-NMR (100 MHz, CDCl3) : 170.7, 164.8, 162.2 (d, 1*J*C–F = 247.0 Hz), 141.5, 138.3, 134.5, 133.1 (d, 3*J*C–F = 8.0 Hz), 130.4, 128.7, 128.6, 128.37, 128.33 (d, 4*J*C–F = 4.0 Hz), 126.6, 123.5, 122.7 (d, 1*J*C–F = 275.3 Hz), 121.9, 119.6, 115.4 (d, 2*J*C–F = 21.2 Hz), 115.3, 69.6, 68.6, 60.4 (q, 2*J*C–F = 36.6 Hz), 41.6, 41.16, 41.11, 39.1, 26.1, 21.8, 21.6; HPLC (Method 3): *t*R = 19.8 min.

**1,1,1,3,3,3-Hexafluoropropan-2-yl (3*R*,5*R*)-7-(2-(4-fluorophenyl)-5-isopropyl-3-phenyl-4-(phenylcarbamoyl)-1*H*-pyrrol-1-yl)-3,5-dihydroxyheptanoate (2s)** Colorless solid; mp 59–61°C; IR max (KBr) cm–1: 3401, 1779, 1646; 1H-NMR (400 MHz, CDCl3) : 7.22–7.13 (m, 9H), 7.06–6.96 (m, 5H), 6.85 (br s, 1H), 5.80–5.72 (m, 1H), 4.26–4.20 (m, 1H), 4.14–4.07 (m, 1H), 3.99–3.92 (m, 1H), 3.77–3.71 (m, 1H), 3.60–3.53 (m, 1H), 3.27 (br s, 1H), 3.01 (br s, 1H), 2.70–2.57 (m, 2H), 1.74–1.60 (m, 2H), 1.56–1.47 (m, 7H), 1.35–1.31 (m, 1H); 13C-NMR (100 MHz, CDCl3) : 168.8, 164.7, 162.2 (d, 1*J*C–F = 246.6 Hz), 141.5, 138.3, 134.5, 133.1 (d, 3*J*C–F = 8.0 Hz), 130.4, 128.7, 128.6, 128.3, 128.2 (d, 3*J*C–F = 3.5 Hz), 126.6, 123.6, 121.9, 120.2 (d, 1*J*C–F = 282.7 Hz), 119.6, 115.5 (d, 2*J*C–F = 21.3 Hz), 115.4, 69.5, 68.4, 66.5 (m, 2*J*C–F = 34.7 Hz), 41.6, 41.08, 41.05, 39.1, 26.1, 21.8, 21.6; HPLC (Method 3): *t*R = 28.8 min.

**4-Tolyl (3*R*,5*R*)-7-(2-(4-fluorophenyl)-5-isopropyl-3-phenyl-4-(phenylcarbamoyl)- 1*H*-pyrrol-1-yl)-3,5-dihydroxyheptanoate (2u)** Colorless solid; mp 68–69°C; IR max (KBr) cm–1: 3406, 1751, 1662; 1H-NMR (400 MHz, CDCl3) : 7.23–7.12 (m, 11H), 7.06 (d, 2H, *J* = 7.6 Hz), 7.03–6.91 (m, 5H), 6.87 (br s, 1H), 4.31–4.21 (m, 1H), 4.18–4.08 (m, 1H), 4.00–3.90 (m, 1H), 3.81–3.72 (m, 1H), 3.65–3.46 (m, 3H), 2.72–2.60 (m, 2H), 2.34 (s, 3H), 1.77–1.60 (m, 2H), 1.60–1.49 (m, 7H), 1.38–1.32 (m, 1H); 13C-NMR (100 MHz, CDCl3) : 171.3, 164.9, 162.3 (d, 1*J*C–F = 246.2 Hz), 147.9, 141.5, 138.3, 136.0, 134.6, 133.2 (d, 3*J*C–F = 8.0 Hz), 130.5, 130.1, 128.8, 128.7, 128.4, 126.6, 123.6, 121.8, 121.0, 119.6, 115.5 (d, 2*J*C–F = 21.1 Hz), 115.3, 69.6, 68.9, 41.8, 41.6, 41.3, 39.1, 26.2, 21.8, 21.7, 20.9; HPLC (Method 3): *t*R = 23.4 min.

**4-Chlorophenyl (3*R*,5*R*)-7-(2-(4-fluorophenyl)-5-isopropyl-3-phenyl- 4-(phenylcarbamoyl)-1*H*-pyrrol-1-yl)-3,5-dihydroxyheptanoate (2x)** Colorless solid; mp 142–143°C; IR max (KBr) cm–1: 3383, 1745, 1664; 1H-NMR (400 MHz, CDCl3) : 7.37–7.32 (m, 2H), 7.23–7.12 (m, 9H), 7.06 (d, 2H, *J* = 8.0 Hz), 7.04–6.96 (m, 5H), 6.87 (br s, 1H), 4.31–4.22 (m, 1H), 4.18–4.08 (m, 1H), 4.01–3.91 (m, 1H), 3.81–3.72 (m, 1H), 3.63–3.50 (m, 2H), 3.43 (br s, 1H), 2.73–2.60 (m, 2H), 1.76–1.59 (m, 2H), 1.59–1.49 (m, 7H), 1.38–1.31 (m, 1H); 13C-NMR (100 MHz, CDCl3) : 170.8, 164.9, 162.3 (d, 1*J*C–F = 246.4 Hz), 148.6, 141.5, 138.3, 134.6, 133.2 (d, 3*J*C–F = 8.1 Hz), 131.6, 130.5, 129.6, 128.74, 128.71, 128.39, 128.36 (d, 4*J*C–F = 4.7 Hz), 126.6, 123.6, 122.8, 121.9, 119.7, 115.5 (d, 2*J*C–F = 21.4 Hz), 115.4, 69.6, 68.8, 41.8, 41.6, 41.2, 39.1, 26.2, 21.8, 21.7; HPLC (Method 3): *t*R = 25.9 min.

**4-Bromophenyl (3*R*,5*R*)-7-(2-(4-fluorophenyl)-5-isopropyl-3-phenyl- 4-(phenylcarbamoyl)-1*H*-pyrrol-1-yl)-3,5-dihydroxyheptanoate (2y)** Colorless solid; mp 151–152°C; IR max (KBr) cm–1: 3381, 1745, 1666; 1H-NMR (400 MHz, CDCl3) : 7.52–7.47 (m, 2H), 7.22–7.12 (m, 9H), 7.06 (d, 2H, *J* = 7.6 Hz), 7.03–6.93 (m, 5H), 6.87 (br s, 1H), 4.30–4.21 (m, 1H), 4.17–4.08 (m, 1H), 4.01–3.91 (m, 1H), 3.80–3.72 (m, 1H), 3.62–3.51 (m, 2H), 3.45 (br s, 1H), 2.72–2.59 (m, 2H), 1.76–1.60 (m, 2H), 1.59–1.49 (m, 7H), 1.37–1.31 (m, 1H); 13C-NMR (100 MHz, CDCl3) : 170.7, 164.9, 162.3 (d, 1*J*C–F = 246.3 Hz), 149.2, 141.5, 138.3, 134.6, 133.2 (d, 3*J*C–F = 8.0 Hz), 132.6, 130.5, 128.8, 128.7, 128.39, 128.37 (d, 4*J*C–F = 5.0 Hz), 126.6, 123.6, 123.2, 121.9, 119.7, 119.3, 115.5 (d, 2*J*C–F = 21.3 Hz), 115.4, 69.6, 68.8, 41.8, 41.7, 41.2, 39.1, 26.2, 21.9, 21.7; HPLC (Method 3): *t*R = 27.0 min.

***S*-Ethyl (3*R*,5*R*)-7-(2-(4-fluorophenyl)-5-isopropyl-3-phenyl-4-(phenylcarbamoyl)- 1*H*-pyrrol-1-yl)-3,5-dihydroxyheptanethioate (5b)** Colorless solid; mp 95–97°C; IR max (KBr) cm–1: 3401, 1670, 1652; 1H-NMR (400 MHz, CDCl3) : 7.22–7.14 (m, 9H), 7.06 (d, 2H, *J* = 7.6 Hz), 7.03–6.96 (m, 3H), 6.86 (br s, 1H), 4.24–4.18 (m, 1H), 4.15–4.07 (m, 1H), 3.97–3.90 (m, 1H), 3.76–3.70 (m, 1H), 3.60–3.53 (m, 1H), 3.48 (br s, 2H), 2.90 (q, 2H, *J* = 7.5 Hz), 2.65 (d, 2H, *J* = 6.0 Hz), 1.73–1.57 (m, 2H), 1.54 (d, 6H, *J* = 7.2 Hz), 1.50–1.42 (m, 1H), 1.29–1.24 (m, 4H); 13C-NMR (100 MHz, CDCl3) : 199.5, 164.8, 162.3 (d, 1*J*C–F = 246.3 Hz), 141.5, 138.4, 134.6, 133.2 (d, 3*J*C–F = 8.0 Hz), 130.5, 128.74, 128.68, 128.36, 128.33, 126.6, 123.5, 121.9, 119.6, 115.4 (d, 2*J*C–F = 21.3 Hz), 115.3, 69.63, 69.62, 50.6, 41.8, 41.3, 39.1, 26.2, 23.5, 21.8, 21.7, 14.6; HPLC (Method 3): *t*R = 19.8 min.

***S*-Isopropyl (3*R*,5*R*)-7-(2-(4-fluorophenyl)-5-isopropyl-3-phenyl-4-(phenylcarbamoyl)- 1*H*-pyrrol-1-yl)-3,5-dihydroxyheptanethioate (5m)** Colorless solid; mp 63–65°C; IR max (KBr) cm–1: 3397, 1677, 1658; 1H-NMR (400 MHz, CDCl3) : 7.22–7.12 (m, 9H), 7.06 (d, 2H, *J* = 8.0 Hz), 7.02–6.96 (m, 3H), 6.88 (br s, 1H), 4.23–4.15 (m, 1H), 4.14–4.06 (m, 1H), 3.96–3.89 (m, 1H), 3.76–3.61 (m, 4H), 3.60–3.53 (m, 1H), 2.66–2.57 (m, 2H), 1.72–1.57 (m, 2H), 1.53 (d, 6H, *J* = 7.2 Hz), 1.49–1.41 (m, 1H), 1.30 (d, 6H, *J* = 6.8 Hz), 1.27–1.23 (m, 1H); 13C-NMR (100 MHz, CDCl3) : 199.4, 164.9, 162.3 (d, 1*J*C–F = 246.2 Hz), 141.5, 138.3, 134.6, 133.2 (d, 3*J*C–F = 8.1 Hz), 130.5, 128.8, 128.7, 128.4, 128.3, 126.6, 123.6, 121.9, 119.7, 115.4 (d, 2*J*C–F = 21.4 Hz), 115.3, 69.6, 69.5, 50.6, 41.8, 41.3, 39.1, 35.0, 26.2, 22.9, 22.8, 21.8, 21.7; HPLC (Method 3): *t*R = 24.5 min.

**1-((3*R*,5*R*)-3,5-Dihydroxy-7-(methylamino)-7-oxoheptyl)-5-(4-fluorophenyl)-2-isopropyl-*N*,4-diphenyl-1*H*-pyrrole-3-carboxamide (6a)** Pale yellow solid; mp 82–85°C; IR max (KBr) cm–1: 3401, 1652, 1646; 1H-NMR (400 MHz, CDCl3) : 7.21–7.12 (m, 9H), 7.06 (d, 2H, *J* = 8.0 Hz), 7.02–6.97 (m, 3H), 6.89 (br s, 1H), 5.86–5.85 (m, 1H), 4.75 (br s, 1H), 4.14–4.06 (m, 2H), 3.97–3.89 (m, 1H), 3.81 (br s, 1H), 3.76–3.70 (m, 1H), 3.58–3.51 (m, 1H), 2.78 (d, 3H, *J* = 4.8 Hz), 2.23–2.21 (m, 2H), 1.72–1.56 (m, 2H), 1.52 (d, 6H, *J* = 7.2 Hz), 1.47–1.37 (m, 1H), 1.18–1.14 (m, 1H); 13C-NMR (100 MHz, CDCl3) : 172.6, 165.0, 162.2 (d, 1*J*C–F = 245.9 Hz), 141.4, 138.2, 134.5, 133.2 (d, 3*J*C–F = 8.0 Hz), 130.4, 128.77, 128.70, 128.36, 128.33, 126.5, 123.6, 121.8, 119.7, 115.4 (d, 2*J*C–F = 21.3 Hz), 115.3, 69.7, 69.5, 41.98, 41.93, 41.2, 39.1, 26.16, 26.13, 21.8, 21.7; HPLC (Method 2): *t*R = 14.5 min.

**1-((3*R*,5*R*)-7-(Ethylamino)-3,5-dihydroxy-7-oxoheptyl)-5-(4-fluorophenyl)-2-isopropyl-*N*,4-diphenyl-1*H*-pyrrole-3-carboxamide (6b)** Colorless solid; mp 74–77°C; IR max (KBr) cm–1: 3413, 1652, 1646; 1H-NMR (400 MHz, CDCl3) : 7.21–7.13 (m, 9H), 7.06 (d, 2H, *J* = 7.6 Hz), 7.02–6.96 (m, 3H), 6.88 (br s, 1H), 5.76 (br t, 1H), 4.77 (br s, 1H), 4.14–4.07 (m, 2H), 3.97–3.89 (m, 1H), 3.83 (br s, 1H), 3.77–3.70 (m, 1H), 3.59–3.51 (m, 1H), 3.30–3.23 (m, 2H), 2.21 (d, 2H, *J* = 5.6 Hz), 1.72–1.56 (m, 2H), 1.53 (d, 6H, *J* = 7.2 Hz), 1.47–1.37 (m, 1H), 1.20–1.11 (m, 4H); 13C-NMR (100 MHz, CDCl3) : 171.8, 164.9, 162.2 (d, 1*J*C–F = 246.0 Hz), 141.4, 138.3, 134.6, 133.2 (d, 3*J*C–F = 8.0 Hz), 130.4, 128.7, 128.6, 128.39, 128.35, 126.5, 123.6, 121.8, 119.6, 115.4 (d, 2*J*C–F = 21.3 Hz), 115.3, 69.7, 69.5, 42.0, 41.9, 41.3, 39.1, 34.3, 26.1, 21.8, 21.7, 14.7; HPLC (Method 2): *t*R = 19.1 min.

**1-((3*R*,5*R*)-3,5-Dihydroxy-7-oxo-7-(phenylamino)heptyl)-5-(4-fluorophenyl)-2-isopropyl-*N*,4-diphenyl-1H-pyrrole-3-carboxamide (6v)** Colorless solid; mp 187–188°C; IR max (KBr) cm–1: 3409, 3299, 1652, 1637; 1H-NMR (400 MHz, CDCl3) : 8.11 (br s, 1H), 7.47–7.45 (m, 2H), 7.31–7.27 (m. 2H), 7.19–7.08 (m, 10H), 7.06 (d, 2H, *J* = 7.6 Hz), 7.02–6.96 (m, 3H), 6.94 (br s, 1H), 4.53 (br s, 1H), 4.21–4.15 (m, 1H), 4.13–4.06 (m, 1H), 3.98–3.90 (m, 1H), 3.76–3.70 (m, 1H), 3.60 (br s, 1H), 3.57–3.49 (m, 1H), 2.45–2.35 (m, 2H), 1.71–1.57 (m, 2H), 1.51 (d, 6H, *J* = 7.2 Hz), 1.49–1.43 (m, 1H), 1.26–1.19 (m, 1H); 13C-NMR (100 MHz, CDCl3) : 170.3, 165.3, 162.3 (d, 1*J*C–F = 246.5 Hz), 141.2, 138.1, 137.5, 134.5, 133.2 (d, 3*J*C–F = 8.1 Hz), 130.4, 129.0, 128.8, 128.7, 128.4, 128.3 (d, 4*J*C–F = 3.4 Hz), 126.6, 124.6, 123.9, 121.9, 120.1, 119.9, 115.517 (d, 2*J*C–F = 21.3 Hz), 115.516, 69.8, 69.5, 43.5, 41.8, 41.2, 39.2, 26.2, 22.0, 21.8; HPLC (Method 3): *t*R = 17.5 min.