Supporting Information for the Paper (Note)

Solution-phase and Solid-phase Syntheses of Enzyme Inhibitor RK-682 and Antibiotic Agglomerins

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General remarks: Microwave irradiations were carried out in sealed vials (W_{max} 1200, temperature messured with fiber-optical sensor). Melting points are uncorrected. Optical rotations were recorded at 589 nm. IR spectra were recorded on an FT-IR spectrophotometer equipped with an ATR sampling unit. NMR spectra were recorded under conditions as indicated and chemical shifts are given in ppm downfield from tetramethylsilane as internal standard. Mass spectra were recorded under EI (70 eV) conditions. The trityl resin (FLUKA) was 100–200 mesh, cross-linked with 1% DVB, loading 1.7 mmol/g.

(5*R*)-RK-682 (1). ν_{max} (ATR)/cm^{-1} 3329 (br), 2916, 2847, 1750, 1663, 1604, 1047; ^{1}H NMR (300 MHz, DMSO-d$_3$) δ 0.85 (t, J = 6.8 Hz, 3 H), 1.10–1.35 (m, 24 H), 1.40–1.58 (m, 2 H), 2.73 (t, J = 7.4 Hz, 2 H), 3.65 (dd, J = 12.3, 3.6 Hz, 1 H), 3.75 (dd, J = 12.3, 2.6 Hz, 1 H), 4.60–4.68 (m, 1 H), 6.08 (br, 2 H); *m/z* (EI) 368 (7) [M$^+$], 350 (5), 337 (5), 319 (5), 185 (15), 172 (45), 154 (10), 43 (100); HR-MS: Found 368.25630. Calcd for $C_{21}H_{36}O_5$ 368.25627.

(4*R*)-4-Benzoxycarbonyl-2,2-dimethyl-1,3-dioxolane (4). A solution of **3** (0.73 mL, 5.0 mmol) in dry benzyl alcohol (7 mL) was treated with dibutyltin oxide (124 mg, 0.5 mmol) and the mixture was placed in the microwave cavity. With an irradiation of initially 600 W a T-ramp from room temperature to 120 °C was passed through within 2 min and the end temperature was maintained for a further 30 min. After cooling to room temperature, sat. aqueous $NaHCO_3$ (10 mL) was added and the resulting mixture was extracted with ethyl acetate (3 × 50 mL). The combined organic phases were filtered over celite and the filtrate was dried and concentrated. After removal of the excess benzyl alcohol in a kugelrohr apparatus, the remainder was purified by column chromatography (CC) on silica gel 60 to leave 980 mg (83%) of **4** as a colorless oil; R_f 0.38 (hexane/ethyl acetate 4:1); $[\alpha]_D^{25}$ 14.3 (c 1.0, dioxane) [lit[1] 14.1 (c 1.2, dioxane)]; ν_{max} (ATR)/cm^{-1} 1756, 1733, 1382, 1372, 1187, 1098; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.37 (s, 3 H), 1.46 (s, 3 H), 4.08 (dd, J = 8.6, 5.1 Hz, 1 H), 4.20 (dd, J = 8.6, 7.1 Hz, 1 H) 4.60 (dd, J = 7.1, 5.1 Hz, 1 H), 5.17 (d, J = 5.2 Hz, 2 H), 7.29–7.36 (m, 5 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.5, 25.9, 66.9, 67.3, 74.1, 111.4, 128.3, 128.5, 128.6, 135.4, 171.0.

(2*R*)-Benzyl 2,3-dihydroxypropanoate (5). A solution of **4** (1.9 g, 8.0 mmol) in THF (20 mL) was treated with aqueous 1M HCl (32 mL, 4 equiv.) and the mixture was left stirring overnight. The THF was distilled off, the residue was neutralized with sat. $NaHCO_3$ and the resulting aqueous phase was then extracted with ethyl acetate / 10% isopropanol (3 × 50 mL). The combined organic phases were washed with brine (20 mL), dried and evaporated to leave crude **5** (1.34 g, 85%) which was used as such for the next step.

Benzyl (2*R*)-2-hydroxy-3-triphenylmethoxypropanoate (6). A stirred solution of crude **5** (1.25 g, 6.4 mmol) in CH_2Cl_2 was kept at 0 °C and treated with NEt_3 (1.2 mL, 9.2 mmol), 4-(dimethylamino)pyridine (DMAP, 40 mg, 0.32 mmol) and Ph_3CCl (2.55 g, 9.2 mmol). After having stirred for a further 8 h at room temperature the reaction was quenched with water. The organic phase was separated and the aqueous one

was extracted with diethyl ether (3 × 30 mL). The combined organic phases were dried and concentrated in vacuo, the remainder was purified by CC. Yield: 2.3 g (80%) of white solid **6** (Found: C, 79.26; H, 6.06. $C_{29}H_{26}O_4$ requires C, 79.43; H, 5.98%); mp 95–97 °C; R_f 0.28 (hexane/ethyl acetate 4:1); $[\alpha]_D^{25}$ 9.9 (*c* 0.5, $CHCl_3$); ν_{max} (ATR)/cm^{-1} 3516 (br), 1735, 1117, 1095; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.41 (dd, *J* = 10.4, 2.9 Hz, 1 H), 3.57 (dd, *J* = 9.5, 2.9 Hz, 1 H), 4.35 (dt, *J* = 7.7, 2.9 Hz, 1 H), 5.20 (d, *J* = 12.4, 1 H), 5.33 (d, *J* = 12.4, 1 H), 7.23–7.47 (m, 20 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 65.2, 67.3, 70.7, 86.3, 126.9, 127.7, 128.3, 128.4, 128.5, 134.9, 143.5, 173.0; *m/z* (EI) 438 (10) [M$^+$], 347 (10), 243 (100), 183 (10), 165 (60), 105 (50), 91 (100).

(5*R*)-3-Hexadecanoyl-5-(triphenylmethoxy)methyl-[5*H*]furan-2,4-dione (9). ν_{max} (ATR)/cm^{-1} 3326 (br), 2923, 2851, 1770, 1695, 1605; ^{1}H NMR (300 MHz, DMSO-d_6) δ 0.83 (t, *J* = 6.7 Hz, 3 H), 1.10–1.35 (m, 24 H), 1.41–1.58 (m, 2 H), 2.73–2.89 (m, 2 H), 3.25 (dd, *J* = 10.3, 3.7 Hz, 1 H), 3.37 (dd, *J* = 10.3, 2.4 Hz, 1 H), 4.72–4.89 (m, 1 H), 7.15–7.35 (m, 15 H), 8.30 (br, 1 H); *m/z* (EI) 610 (10) [M$^+$], 533 (10), 243 (100).

3-Decanoyl-5-(triphenylmethoxy)methyl-[5*H*]furan-2,4-dione (10a). 230 mg (88%) from *rac*-**8** (185 mg, 0.5 mmol), decanoic acid (95 mg, 0.55 mmol), DCC (125 mg, 0.60 mmol), DMAP (20 mg) and NEt_3 (76 µL, 0.55 mmol) as a yellow oil by the method described for the synthesis of **9** from **8**; (Found: C, 77.58; H, 7.36. $C_{34}H_{38}O_5$ requires C, 77.54; H, 7.27%); ν_{max} (ATR)/cm^{-1} 3326 (br), 2925, 1770, 1698, 1600; ^{1}H NMR (300 MHz, DMSO-d_6) δ 0.86 (t, *J* = 6.8 Hz, 3 H), 1.10–1.35 (m, 12 H), 1.52–1.68 (m, 2 H), 2.82–2.93 (m, 2 H), 3.33–3.42 (m, 1 H), 3.47–3.55 (m, 1 H), 4.65–4.84 (m, 1 H), 7.11–7.36 (m, 15 H); ^{13}C NMR (75 MHz, CD_3OD) δ 14.6, 23.8, 26.1, 27.2, 30.3, 30.5, 30.7, 33.1, 35.0, 63.0, 82.6, 87.9, 101.1, 128.4, 129.0, 129.8, 144.7, 173.7, 194.8, 196.5; *m/z* (EI) 526 (10) [M$^+$], 449 (20), 267 (5), 259 (50), 243 (100).

3-[(5'*Z*)-Dodecenoyl]-5-(triphenylmethoxy)methyl-[5*H*]furan-2,4-dione (10b). 135 mg (56%) from *rac*-**8** (160 mg, 0.43 mmol), (5*Z*)-dodecenoic acid (109 µL, 0.50 mmol), DCC (114 mg, 0.55 mmol), DMAP (20 mg) and NEt_3 (69 µL, 0.50 mmol) as a yellow oil (Found: C, 78.18; H, 7.36. $C_{36}H_{40}O_5$ requires C, 78.23; H, 7.29%); ν_{max} (ATR)/cm^{-1} 3324 (br), 2926, 1770, 1695, 1601; ^{1}H NMR (300 MHz, DMSO-d_6) δ 0.88 (t, *J* = 6.8 Hz, 3 H), 1.20–1.35 (m, 10 H), 1.52–1.62 (m, 2 H), 1.87–2.15 (m, 4 H), 2.85–2.96 (m, 2 H), 3.42–3.46 (m, 1 H), 3.48–3.62 (m, 1 H), 4.71–4.84 (m, 1 H), 5.25–5.43 (m, 2 H),

7.11–7.36 (m, 15 H); *m/z* (EI) 552 (5) [M$^+$], 475 (5), 243 (100), 165(75), 55 (45), 41 (70); HR-MS: Found 552.28746. Calcd for $C_{36}H_{40}O_5$ 552.28755.

3-Dodecanoyl-5-(triphenylmethoxy)methyl-[5*H*]furan-2,4-dione (10c). 250 mg (91%) from *rac*-**8** (185 mg, 0.5 mmol), dodecanoic acid (111 mg, 0.55 mmol), DCC (125 mg, 0.60 mmol), DMAP (20 mg) and NEt_3 (76 μL, 0.55 mmol) as a yellow oil (Found: C, 78.08; H, 7.76. $C_{36}H_{42}O_5$ requires C, 77.95; H, 7.63%); ν_{max} (ATR)/cm^{-1} 3328 (br), 2923, 1769, 1693, 1602; ^{1}H NMR (300 MHz, DMSO-d$_6$) δ 0.87 (t, *J* = 6.8 Hz, 3 H), 1.10–1.35 (m, 16 H), 1.52–1.68 (m, 2 H), 2.78–2.93 (m, 2 H), 3.31–3.42 (m, 1 H), 3.44–3.58 (m, 1 H), 4.65–4.89 (m, 1 H), 7.15–7.35 (m, 15 H).

3-Decanoyl-5-hydroxymethyl-[5*H*]furan-2,4-dione (11a). 70 mg (56%) as a yellowish oil from **10a** (230 mg, 0.44 mmol) (Found: C, 63.49; H, 8.58. $C_{15}H_{24}O_5$ requires C, 63.36; H, 8.51%); ν_{max} (ATR)/cm^{-1} 3323 (br), 3228 (br), 2915, 2847, 1754, 1662, 1603; ^{1}H NMR (300 MHz, CD_3OD) δ 0.88 (t, *J* = 7.0 Hz, 3 H), 1.21–1.35 (m, 12 H), 1.59–1.73 (m, 2 H), 2.88 (t, *J* = 7.4 Hz, 2 H), 3.88 (dd, *J* = 12.6, 2.9 Hz, 1 H), 3.95 (dd, *J* = 12.6, 2.6 Hz, 1 H), 4.66-4.76 (m, 1 H); ^{13}C NMR (75 MHz, CD_3OD) δ 14.6, 23.8, 26.5, 30.5, 30.6, 30.7, 33.1, 61.4, 82.5, 101.2, 173.9, 195.9, 196.2; *m/z* (EI) 284 (5) [M$^+$], 266 (5), 253 (10), 235 (10), 185 (30), 172 (100); HR-MS: Found 284.16240. Calcd for $C_{15}H_{24}O_5$ 284.16237.

3-[(5'*Z*)-Dodecenoyl]-5-hydroxymethyl-[5*H*]furan-2,4-dione (11b). 47 mg (62 %) as a colorless viscous oil from **10b** (135 mg, 0.24 mmol) (Found: C, 65.61; H, 8.46. $C_{17}H_{26}O_5$ requires C, 65.78; H, 8.44%); ν_{max} (ATR)/cm^{-1} 3346 (br), 3255 (br), 2922, 2852, 1743, 1660, 1605; ^{1}H NMR (300 MHz, CD_3OD) δ 0.90 (t, *J* = 6.8 Hz, 3 H), 1.25–1.39 (m, 8 H), 1.65–1.79 (m, 2 H), 1.98-2.20 (m, 4 H), 2.89 (t, *J* = 7.4 Hz, 2 H), 3.88 (dd, *J* = 12.6, 2.3 Hz, 1 H), 3.96 (dd, *J* = 12.6, 1.9 Hz, 1 H), 4.65-4.82 (m, 1 H) 5.31-5.48 (m, 2 H); ^{13}C NMR (75 MHz, CD_3OD) δ 14.6, 23.8, 26.4, 27.9, 28.3, 30.1, 30.9, 33.1, 61.2, 85.2, 101.6, 130.0, 132.2, 173.4, 195.6, 195.8; *m/z* (EI) 310 (5) [M$^+$], 292 (10), 274 (5), 185 (10), 172 (65), 154 (25), 142 (15), 67 (30), 55 (35), 41 (100); HR-MS: Found 310.17800. Calcd for $C_{17}H_{26}O_5$ 310.17802.

3-Dodecanoyl-5-hydroxymethyl-[5*H*]furan-2,4-dione (11c). 95 mg (75%) as a yellowish oil from **10c** (250 mg, 0.45 mmol) (Found: C, 65.25; H, 9.11. $C_{17}H_{28}O_5$ requires C, 65.36; H, 9.03%); ν_{max} (ATR)/cm^{-1} 3327 (br), 3231 (br), 2914, 2847, 1748, 1661, 1602; ^{1}H NMR (300 MHz, CD_3OD) δ 0.88 (t, *J* = 6.9 Hz, 3 H), 1.21–1.35 (m, 16 H), 1.60–1.71 (m, 2 H), 2.88 (t, *J* = 7.4 Hz, 2 H), 3.89 (dd, *J* = 12.7, 1.8 Hz, 1 H),

3.97 (dd, J = 12.7, 2.1 Hz, 1 H), 4.68-4.79 (m, 1 H); m/z (EI) 312 (10) [M^+], 281 (5), 264 (5), 247 (5), 185 (25), 173 (35), 43 (95), 41 (100); HR-MS: Found 312.19370. Calcd for $C_{17}H_{28}O_5$ 312.19367.

Agglomerin A (2a).[2] 46 mg (60%) as a white solid from **11a** (90 mg, 0.3 mmol), DMAP (15 mg), methanesulfonyl chloride (48 μL, 0.6 mmol), and NEt_3 (0.16 mL, 1.2 mmol); mp 112–114 °C (lit[2c] 113–115 °C); R_f 0.32 ($CHCl_3$/MeOH 10:1); ν_{max} (ATR)/cm^{-1} 3381 (br), 2922, 1724, 1619, 1471; ^{1}H NMR (300 MHz, CD_3Cl_3/CD_3OD 10:1) δ 0.81 (t, J = 6.3 Hz, 3 H), 1.11–1.32 (m, 14 H), 1.40–1.61 (m, 2 H), 2.75 (m, 2 H), 4.85 (s, 1 H), 5.14 (s, 1 H); m/z (EI) 266 (10) [M^+], 167 (20), 154 (65), 139 (15), 98 (15), 84 (15), 69 (20), 55 (25), 41 (100); HR-MS: Found 266.15180. Calcd for $C_{15}H_{22}O_4$ 266.15181.

Agglomerin B (2b).[2] 30 mg (69 %) as a white solid from **11b** (47 mg, 0.16 mmol), DMAP (10 mg), methanesulfonyl chloride (26 μL, 0.32 mmol), and NEt_3 (0.90 mL, 0.64 mmol); mp 86–88°C (lit[2c] 85-88 °C); R_f 0.32 ($CHCl_3$/MeOH 10:1); ν_{max} (ATR)/cm^{-1} 3363 (br), 2924, 1733, 1620, 1468; ^{1}H NMR (300 MHz, CD_3Cl_3/CD_3OD 10:1) δ 0.81 (t, J = 6.3 Hz, 3 H), 1.11–1.32 (m, 14 H), 1.47–1.62 (m, 2 H), 1.85–2.07 (m, 4 H), 2.68–2.82 (m, 2 H), 4.83 (s, 1 H), 5.14 (s, 1 H), 5.20–5.39 (m, 2 H); ESI-MS: Found 292.18. Calcd for $C_{17}H_{24}O_4$ 292.17.

(4*R*)-4-(2'-Trimethylsilylethoxycarbonyl)-2,2-dimethyl-1,3-dioxolane (13). **12** (0.58 g, 4.0 mmol) was prepared from **4** by hydrogenolysis and dissolved in dry THF (20 mL) under an atmosphere of argon. *O*-trimethylsilylethyl-N,N'-dicyclohexylisourea (1.6 g, 5.0 mmol) was added and the resulting mixture was heated at 50 °C overnight. The precipitated dicyclohexylurea was removed by filtration over a short plug of celite and the filtrate was evaporated. The remainder was purified by CC on silica gel to leave 0.74 g (74%) of **13** (Found: C, 53.58; H, 8.89. $C_{11}H_{22}O_4Si$ requires C, 53.62; H, 9.00%); R_f 0.43 (hexane/ethyl acetate 6:1); $[\alpha]_D^{25}$ 7.6 (c 0.98, dioxane); ν_{max} (ATR)/cm^{-1} 1756, 1729, 1249, 1102, 856, 835; ^{1}H NMR (300 MHz, $CDCl_3$) δ –0.02 (s, 9 H), 0.89–1.01 (m, 2 H), 1.33 and 1.42 (s, 3 H), 4.08 (dd, J = 8.6, 5.5 Hz, 1 H), 4.20 (dd, J = 8.6, 5.1 Hz, 1 H), 4.2–4.4 (m, 2 H), 4.60 (dd, J = 5.5, 5.1 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ –1.6, 17.3, 25.5, 25.8, 63.6, 67.2, 74.1, 111.1, 171.2.

(2*R*)-2,3-Dihydroxypropanoic acid β–trimethylsilylethyl ester (14). A solution of **13** (496 mg, 2.0 mmol) in MeOH (4 mL) was treated with aqueous 1M HCl (2.5 mL, 1.25 equiv.) and the mixture was left stirring overnight. The volatiles were distilled off, the residue was neutralized with sat. $NaHCO_3$ and the resulting aqueous phase was extracted with ethyl acetate / 10% isopropanol (3 × 50 mL). The combined

organic phases were washed with brine (20 mL), dried and evaporated to leave crude **14** (292 mg, 70%) which was used as such for the next step.

References

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