Supporting Information

Analogs of Thiolactomycin as Potential Antimalarial Agents

Simon M. Jones,[a,†] Jonathan E. Urch,[b,†] Marcel Kaiser,[c] Reto Brun,[c] John L. Harwood,[b] Colin Berry,[b] Ian H. Gilbert.[a,*]

a. Welsh School of Pharmacy, Cardiff University, Redwood Building, King Edward VII Avenue, Cardiff, CF10 3XF, UK.

b. Cardiff School of Biosciences, Biomedical Building, Museum Avenue, Cardiff, CF10 3US, UK.

c. Swiss Tropical Institute, Socinstrasse 57, CH-4002 Basel, Switzerland.

* Corresponding Author: Tel: +44 29 2087 5800; Fax: +44 29 2087 4149;

E-mail: gilbertih@cf.ac.uk

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Analytical Data

Cyclisation, general procedure A for compounds 6a, 6b, 6c, 6d

Potassium hydroxide (2.5 equiv) in water (20 ml) was added to the bromide **5** (1.0 equiv) at 0°C. The resulting solution was then vigorously stirred at ambient temperature for 15h. The aqueous layer was washed with diethyl ether (2 x 30 ml) and acidified to ph 1 with the addition of 2M HCl (~20 ml). The aqueous layer was then extracted with diethyl ether (3 x 40 ml) and the combined organic solutions washed with brine (100 ml), then dried over magnesium sulfate and the solvent removed in vacuo. The crude residue was purified by flash column chromatography (5-30% ethyl acetate in hexanes). The coupling constants (*J*) are in Hz.

3-Ethyl-4-hydroxy-5-methyl-2,5-dihydro-2-furanone (6a)

As described in procedure A, starting from **5a** (2.00 g, 8.47 mmol) and potassium hydroxide (1.18 g, 21.18 mmol), **6a** was obtained as a colourless solid (0.40 g, 33%); mp 44-46°C, δ_H (acetone-d_6) 1.02 (3H, t, J = 7.4, 2'-CH_3), 1.42 (3H, d, J = 6.6, CH_3), 2.18 (2H, q, J = 7.4, 1'-CH_2) and 4.78 (1H, q, J = 6.6, 5-CH); δ_C (acetone-d_6) 13.4 (2'-CH_3), 15.6 (6-CH_3), 18.7 (1'-CH_2), 74.6 (5-CH), 102.9 (3-C), 175.7 (4-C) and 175.8 (2-CO); MS (ES^-) *m/z* 141.0 ($M-H,^-$ 100%).

5-Hexyl-4-hydroxy-3,5-dimethyl-2,5-dihydro-2-furanone (6b)

As described in procedure A, starting from **5b** (1.14 g, 3.72 mmol) and potassium hydroxide (0.52 g, 9.31 mmol), **6b** was obtained as a colourless solid (72 mg, 9%), mp 52-54°C, δ_H 0.90 (3H, t, J = 7.0, 6''-CH_3), 1.29 (8H, m, 4 x CH_2), 1.52 (3H, s, CH_3), 1.77 (3H, s, CH_3) and 1.81 (2H, t, J = 6.9, 1''-CH_2); δ_C 6.2 (CH_3), 14.4 (CH_3), 22.9, 23.3 (both CH_2), 23.5 (CH_3), 29.5, 32.0, 36.7 (all CH_2), 85.3 (5-C), 96.2 (3-C), 178.0 (4-C) and 179.5 (CO); MS (ES^-) *m/z* 211.0 ($M-H,^-$ 100%); HRMS (ES^-) $(M-H)^-$ $C_{12}H_{19}O_3$ requires 211.1334, found 211.1337. Anal. ($C_{12}H_{20}O_3$) C, H, N.

5-Decyl-3-ethyl-4-hydroxy-5-methyl-2,5-dihydro-2-furanone (6c)

As described in procedure A, starting from **5c** (320 mg, 1.15 mmol) and potassium hydroxide (160 mg, 2.89 mmol), **6c** was obtained as a colourless oil (40 mg, 13%), δ_H 0.92 (3H, t, J = 7.0, 10''-CH_3), 1.09 (3H, t, J = 7.4, 2'-CH_3), 1.28 (16H, m, 8 x CH_2), 1.52 (3H, s, CH_3), 1.83-1.84 (2H, m, CH_2) and 2.22-2.32 (2H, m, 1''-CH_2); δ_C 13.3 (10''-CH_3), 14.5 (2'-CH_3), 23.1, 23.3, 23.5, 29.7, 30.0, 30.7, 32.3 and 36.7 (all CH_2), 84.8 5-C), 102.4 (3-C), 177.2 (4-C) and 178.7 (2-C); MS (ES^-) *m/z* 281.0 (M – H^- 100%); HRMS (ES^+) $(M + NH_4)^+$ $C_{17}H_{34}O_3N$ requires 300.2533, found 300.2536.

3-Butyl-5-decyl-4-hydroxy-5-methyl-2(*5H*)-furanone (6d)

As described in procedure A, starting from **5d** (600 mg, 1.48 mmol) and potassium hydroxide (200 mg, 3.71 mmol), **6d** was obtained as a pale yellow oil (52 mg, 12%), δ_H 0.89-0.96 (6H, m, 15-CH_3 and 4'-CH_3), 1.24-1.28 (18H, m, 9 x CH_2), 1.30-1.36 (2H, m, CH_2), 1.53 (3H, s, CH_3), 1.77-1.84 (2H, m, 6-CH_2) and 2.27 (2H, t, J = 6.9, 1'-CH_2); δ_C 14.3 (15-CH_3), 14.5 (4'-CH_3), 21.1, 22.8, 22.9, 23.1, 23.4, 23.6, 29.7, 29.9, 30.0, 30.6, 30.8, 32.3, 36.7 (all CH_2), 85.0 (5-C), 101.1 (3-C), 177.7 (4-C) and 181.2 (2-CO); MS (ES^-) *m/z* 309.1 (M-H^- 100%); HRMS (ES^+) $(M + H)^+$ $C_{19}H_{35}O_3$ requires 311.2581, found 311.2573.

Alkylation, general procedure B for compounds 15, 16, 17, 18

Lithium bis (trimethylsilyl)amide (1.0 M solution in THF, 2.0 equiv) was added dropwise to a stirred solution of thiolactone **14** (1.0 equiv) in dry THF (6 ml) at -78°C. After stirring for 0.5 h at -78°C, the halide (1.0 equiv) was added dropwise. After stirring for a further 0.5 h, the mixture was allowed to warm to ambient temperature and stirred overnight. The reaction was quenched with the addition of saturated aqueous ammonium chloride (~10 ml) and the organic layer separated. The aqueous layer was extracted with diethyl ether (3 x 10 ml). The organic layers were washed with water (3 x 20 ml) and brine (40 ml), dried over anhydrous magnesium sulfate and the solvent

removed in vacuo. The crude residue was purified by flash column chromatography (0 to 30% gradient of ethyl acetate in hexanes).

5-Hexadecyl-4-hydroxy-5-methyl-3-propyl-2(5H)-thiophenone (15)

As described in procedure B, starting from **14b** (300 mg, 1.74 mmol), lithium bis (trimethylsilyl)amide (3.48 ml, 3.48 mmol) and 1-iododecane (530 mg, 1.74 mmol), **15** was obtained as a colourless solid (103 mg, 15%); mp 55-56°C, δ_H 0.91-0.98 (6H, m, 2 x CH_3), 1.31 (26H, m, 13 x CH_2), 1.49-1.57 (4H, m, 2 x CH_2), 1.72 (3H, s, CH_3), 1.88-1.94 (2H, m, CH_2), 2.21-2.26 (2H, m, CH_2) and 7.63 (1H, OH); δ_C 14.1, 14.4 (both CH_3), 21.7, 23.1, 25.0, 25.5, 26.6, 29.7, 29.7, 29.8, 29.9, 29.9, 30.0, 30.0, 30.1, 32.3, 38.9, 57.7 (5-C), 115.5 (3-C), 179.5 (4-C) and 196.3 (CO); MS (ES^-) *m/z* 395.2 (M – H,$^-$ 100%); HRMS (ES^-) $(M - H)^-$ $C_{24}H_{43}O_2S$ requires 395.2984, found 395.2977. Anal. ($C_{24}H_{44}O_2S$) C, H, N.

3-Benzyl-5-hexadecyl-4-hydroxy-5-methyl-2(5H)-thiophenone (16)

As described in procedure B, starting from **14c** (100 mg, 0.45 mmol), lithium bis (trimethylsilyl)amide (0.90 ml, 0.90 mmol) and 1-bromohexadecane (130 mg, 0.45 mmol), **16** was obtained as a pale yellow solid (42 mg, 21%); mp 44-45°C, δ_H 0.94 (3H, t, J = 6.6, CH_3), 1.32 (28H, m, 14 x CH_2), 1.68 (3H, s, CH_3), 1.85-1.91 (2H, m, CH_2), 3.60 (2H, s, CH_2Ph) and 7.21-7.34 (5H, m, ArCH); δ_C 14.5 (CH_3), 23.1, 25.5, 26.3, 29.1, 29.4, 29.8, 29.9, 29.9, 30.0, 30.1, 30.1, 32.0, 32.3, 38.8, 41.7 (5-C), 58.3 (CH_2Ph), 114.2 (3-C), 126.9 (ArC), 128.8 (ArCH), 129.1 (ArCH), 138.5 (ArC), 181.5 (4-C) and 197.2 (CO); MS (ES^-) *m/z* 443.1 (M - H,$^-$ 100%); HRMS (ES^-) $(M - H)^-$ $C_{28}H_{43}O_2S$ requires 443.2985, found 443.2984. Anal. ($C_{28}H_{44}O_2S.0.1H_2O$) C, H, N.

3-Ethyl-5-{2-[2-(hexyloxy)ethoxy]ethyl}-4-hydroxy-5-methyl-2,5-dihydro-2thiophenone (17).

As described in procedure B, starting from **14a** (300 mg, 1.74 mmol), lithium bis (trimethylsilyl)amide (3.78 ml, 3.78 mmol) and 1-(2-(2-bromoethoxy)ethoxy)hexane (470 mg, 1.74 mmol), **17** was obtained as a colourless oil (60 mg, 10%), δ_H 0.94 (3H, t, J = 6.8, 17-CH_3), 1.07 (3H, t, J = 7.4, 2'-CH_3), 1.31-1.45 (8H, m, 4 x CH_2), 1.62 (2H, q, J = 6.8, CH_2), 1.76 (3H, s, CH_3), 2.21-2.29 (2H, m, 6-CH_2), 3.53 (2H, t, J = 6.6, 12-CH_2), 3.67 (2H, t, J = 4.0, CH_2), 3.72-3.79 (4H, m, 2 x CH_2) and 7.32 (1H, brs, OH); δ_C 12.9 (CH_3), 14.4 (CH_3), 16.7, 22.9, 25.0, 26.1, 29.9, 32.0 (all CH_2), 37.9 (CH_2), 54.6 (5-C), 67.9, 69.5, 71.1, 72.1 (all CH_2), 117.1 (3-C), 180.0 (4-C) and 194.1 (CO); MS (ES^-) *m/z* 329.0 (M – H,$^-$ 100%); HRMS (ES^-) (M – H)$^-$ $C_{17}H_{29}O_4S$ requires 329.1787, found 329.1780. Anal. ($C_{17}H_{30}O_4S.0.5H_2O$) C, H, N.

5-(6-{[tert-butyl(dimethyl)silyl]oxy}hexyl)-4-hydroxy-5-methyl-3-propyl-2(5H)-thiophenone (18)

As described in procedure B, starting from **14b** (300 mg, 1.74 mmol), lithium bis (trimethylsilyl)amide (5.54 ml, 5.54 mmol) and (6-bromohexyloxy)(*tert*-butyl)dimethylsilane (810 mg, 1.74 mmol), **18** was obtained as a colourless oil (0.20 g, 20%), δ_H ($CDCl_3$) 0.10 (6H, s, $Si(CH_3)_2$), 0.94 (12H, m, $C(CH_3)_3$ and CH_3), 1.38-1.36 (4H, m, 2 x CH_2), 1.45-1.55 (6H, m, 3 x CH_2), 1.72 (3H, s, CH_3), 2.24 (2H, t, J = 7.4, CH_2), 3.66 (2H, t, J = 6.5, 11-CH_2) and 8.60 (1H, br s, OH); δ_C –4.8 ($Si(CH_3)_2$), 14.1, 18.8, 21.8, 25.0, 25.4, 25.9, 26.4, 26.6, 29.6, 32.8, 33.1, 38.7, 58.0 (5-C), 63.6 (11-CH_2), 115.5 (3-C), 178.3 (4-C) and 196.8 (CO). MS (ES^+) m/z 409.2 (M+H,$^+$ 100%); HRMS (ES^+) $(M+NH_4)^+$ $C_{20}H_{42}O_3SNSi$ requires 404.2649, found 404.2651.

Alkylation, general procedure C for compounds 21a, 21b/22a, 21c/22b, 21d, 21e, 22c, 22d, 22e

Thiophenone **20** (1.0 equiv) was added portionwise to a stirred suspension of sodium hydride (1.2 eqiuv) in dry THF (10 ml) at ambient temperature. After stirring for 0.5 h, the halide (1.1 equiv) was added dropwise. The resulting solution was then heated to reflux and stirred for 15-20 h. The

reaction was allowed to cool and quenched with the addition of aqueous saturated ammonium chloride (10 ml). The organic layer was separated and the aqueous layer extracted with diethyl ether (3 x 10 ml). The organic layers were washed with water (2 x 20 ml) and brine (2 x 20 ml), dried over anhydrous magnesium sulfate and the solvent removed in *vacuo*. The crude residue was purified by flash column chromatography (0-20% ethyl acetate in hexanes).

3-Allyl-3,5-dimethyltetrahydro-2,4-thiophenedione (21a).

As described in procedure C, starting from **20a** (400 mg, 2.77 mmol), sodium hydride (130 mg, 3.33 mmol) and allyl bromide (0.26 ml, 3.00 mmol), **21a** was obtained as a mixture of diastereoisomers (3:1) (310 mg, 61%), δ_H 1.27 and 1.31 (3H, s, CH_3), 1.60 and 1.64 (3H, d, J = 7.1, 5-CH_3), 2.44 and 2.51 (2H, d, J = 7.2, 1'-CH_2), 4.24 and 4.36 (1H, q, J = 7.1, 5-CH), 5.08-5.18 (2H, m, 3'-CH_2) and 5.54-5.73 (1H, m, 2'-CH); δ_C 17.7and 17.9 (CH_3), 20.1 and 23.0 (CH_3), 40.3 and 42.7 (CH_2), 49.3 and 50.4 (3-C), 57.6 and 57.8 (5-CH), 120.4 and 120.8, 130.9 and 131.9, 203.8 and 204.1 (4-CO) and 210.9 and 211.2 (2-CO).

3-Allyl-5-decyl-3,5-dimethyl-2,4(3H, 5H)-thiophenedione (21b) and 4-(Allyloxy)-5-decyl-3,5-dimethyl-2(5H)-thiophenone (22a).

As described in procedure C, starting from **20b** (140 mg, 0.49 mmol), sodium hydride (23 mg, 0.59 mmol) and allyl bromide (0.04 ml, 0.54 mmol), **21b** was obtained as a mixture of diastereoisomers (4:1) (50 mg, 61%); δ_H 0.93 (3H, t, J = 6.8, 15-CH_3), 1.30-1.40 (19H, m, 8 x CH_2 and CH_3), 1.63 and 1.71 (3H, s, CH_3), 1.81-2.03 (2H, m, CH_2), 2.51 (2H, d, J = 7.2, 1'-CH_2), 5.12-5.17 (2H, m, 3'-CH_2) and 5.60-5.74 (1H, m, 2'-CH_2); δ_C 14.5 (15-CH_3), 22.6, 23.0, 24.2, 25.8 and 26.0, 26.6, 28.6, 29.6 and 29.7, 29.9 and 30.0, 32.3 and 32.6, 40.1, 41.3 and 41.8, 42.5, 58.5 and 58.8, 65.3 and 65.5, 120.5 and 120.6, 131.9 and 132.0, 205.0 (CO), 214.9 (CO); MS (ES^+) *m*/*z* 347.2 (M + $Na,^+$ 100%); HRMS (ES^+) $(M + NH_4)^+$ $C_{19}H_{36}O_2NS$ requires 342.2461, found 342.2462.

Following column chromatography (0-20% ethyl acetate in hexanes) compound **22a** was isolated as a pale yellow oil (15 mg, 10%), δ_H 0.97 (3H, t, J = 6.8, 15-CH_3), 1.34 (16H, m, 8 x CH_2), 1.69 (3H, s, CH_3), 1.85-1.91 (2H, m, CH_2), 2.04 (3H, s, CH_3), 4.91-4.93 (2H, dd, J = 5.2 and 1.5, 1'-CH_2), 5.40-5.43 (1H, dd, J = 10.5 and 1.2, 3'-CH_A), 5.46-5.52 (1H, dd, J = 17.3 and 1.2, 3'-CH_B) and 6.01-6.14 (1H, m, 2'-CH); δ_C 10.1 (CH_3), 14.5 (CH_3), 23.1, 25.6 (both CH_2), 27.0 (CH_3), 29.7, 29.8, 30.0, 32.0, 32.3 (all CH_2), 57.8 (5-C), 72.9 (1'-CH_2), 112.1 (3-C), 132.9 (2'-CH), 179.8 (4-C) and 196.3 (2-CO); MS (ES^+) *m/z* 347.2 (M + Na,$^+$ 60%); HRMS (ES^+) $(M + H)^+$ $C_{19}H_{33}O_2S$ requires 325.2201, found 325.2202.

3-Allyl-5-decyl-5-methyl-3-propyl-2,4(3H, 5H)-thiophenedione (21c) and 4-(allyloxy)-5-methyl-3-propyl-2,5-dihydro-2-thiophenone (22b).

As described in procedure C, starting from **20c** (400 mg, 1.28 mmol), sodium hydride (61 mg, 1.53 mmol) and allyl bromide (0.12 ml, 1.40 mmol), **21c** was obtained as a pale yellow oil (63 mg, 14%), δ_H 0.89-0.95 (6H, m, 2 x CH_3), 1.30 (18H, m, 9 x CH_2), 1.61 (3H, s, CH_3), 1.73-1.78 (2H, m, CH_2), 1.86-1.94 (2H, m, CH_2), 2.48-2.54 (2H, m, CH_2), 5.10-5.17 (2H, m, CH_2) and 5.61-5.77 (1H, m, CH); δ_C 14.5 (CH_3), 14.6 (CH_3), 18.4, 23.0, 25.6 (CH_3), 26.3, 29.7, 29.7, 29.8, 29.9, 30.0, 32.3, 39.3, 40.8, 42.1, 63.4, 65.2, 120.4, 131.8 (CH), 204.9 (CO) and 214.8 (CO); MS $(ES)^+$ *m/z* 375.2 (M + Na,$^+$ 70%) HRMS (ES^+) $(M + Na)^+$ $C_{21}H_{36}O_2NaS$ requires 375.2328, found 375.2334.

Following column chromatography, compound **22b** was isolated as a colourless oil (12 mg, 3%), δ_H 0.84 (3H, t, J = 6.7, CH_3), 0.89 (3H, t, J = 7.3, CH_3), 1.20 (16H, m, 8 x CH_2), 1.38-1.48 (2H, m, CH_2), 1.56 (3H, s, CH_3), 1.71-1.78 (2H, m, CH_2), 2.30 (2H, t, J = 7.5, CH_2), 4.71-4.73 (2H, m, O-CH_2), 5.26-5.39 (2H, m, CH_2) and 5.88-6.01 (1H, m, CH); δ_C 14.2, 14.5 (both CH_3), 23.1, 23.7 (both CH_2), 25.5 (CH_3), 26.3, 27.2, 29.7, 29.8, 29.9, 32.3, 39.4 (all CH_2), 57.8 (5-C), 72.7 (OCH_2), 117.5 (3-C), 118.5 (CH_2), 132.8 (CH), 179.6 (4-C) and 196.2 (2-CO); MS $(ES)^+$ *m/z* 375.2 (M + Na,$^+$ 60%); HRMS (ES^+) $(M + H)^+$ $C_{21}H_{37}O_2S$ requires 353.2509, found 353.2508.

3-(3,7-Dimethyl-2,6-octadienyl)-5-methyl-3-propyl-2,4(3H, 5H)-thiophenedione (21d)

As described in procedure C, starting from **20c** (130 mg, 1.74 mmol), sodium hydride (83 mg, 2.09 mmol) and geranyl bromide (0.41 ml, 1.91 mmol), **21d** was obtained as a mixture of diastereoisomers (120 mg, 23%), δ_H 0.90 (3H, t, J = 7.2, CH_3), 1.08-1.45 (2H, m, CH_2), 1.60-1.61 (3H, m, CH_3), 1.62-1.63 (3H, m, CH_3), 1.64-1.65 (3H, m, CH_3), 1.69-1.71 (3H, m, CH_3), 1.74-1.81 (2H, m, CH_2), 1.95-2.13 (4H, m, 2 x CH_2), 2.44-2.53 (2H, m, CH_2), 4.08 and 4.16 (1H, q, J = 7.1, 5-CH) and 5.06-5.11 (2H, m, 2 x CH); δ_C 14.6 and 14.7 (CH_3), 16.4 and 16.5, 17.6 and 18.0, 18.1 and 18.2, 26.0 and 26.1, 26.7 and 26.8, 36.0, 38.0 and 38.4, 40.1 and 40.2, 40.6, 51.1 and 51.2, 62.7 and 62.9, 116.4 and 117.5 (CH), 124.2 and 124.3 (CH), 132.0 and 132.2 (C), 140.5 and 141.3 (C), 204.1and 204.2 (CO) and 213.0 and 213.3 (CO); MS (ES^+) *m/z* 331.1 (M + $Na,^+$ 100%); HRMS (EI^+) $C_{18}H_{28}O_2S$ requires 308.1805, found 308.1808. Anal. ($C_{18}H_{28}O_2S.0.15H_2O$) C, H, N.

5-Decyl-3-[(2Z)3,7-dimethyl-2,6-octadienyl]-5-methyl-3-propyl-2,4(3H,5H) thiophenedione (21e)

As described in procedure C, starting from **20d** (63 mg, 0.20 mmol), sodium hydride (9 mg, 2.09 mmol) and geranyl bromide (0.04 ml, 1.91 mmol), **21e** was obtained as a colourless oil (22 mg, 24%), δ_H 0.89-0.95 (6H, m, 2 x CH_3), 1.30 (18H, m, 9 x CH_2), 1.58 (3H, s, CH_3), 1.61 (3H, s, CH_3), 1.63 (3H, s, CH_3), 1.72 (3H, s, CH_3), 1.75-1.90 (2H, m, CH_2), 1.97-2.09 (4H, m, 2 x CH_2), 2.46-2.58 (2H, m, CH_2) and 5.03-5.12 (2H, m, CH_2); δ_C 14.5 (CH_3), 14.7 (CH_3), 16.5, 18.0, 18.6, 23.1, 25.6, 25.8, 26.1, 26.7, 29.7, 29.9, 29.9, 30.0, 30.2, 32.3, 36.9, 39.6, 40.2, 40.9, 63.8, 65.3, 117.6 (CH), 124.3 (CH), 132.0 (C), 140.5 (C), 205.7 (CO) and 213.2 (CO); MS (ES^+) *m/z* 487.0 (M + $K,^+$ 100%); HRMS (ES^+) $(M + NH_4)^+$ $C_{28}H_{52}O_2NS$ requires 466.3713, found 466.3713.

5-Decyl-5-methyl-4-phenoxy-3-propyl-2(5H)-thiophenone (22c)

As described in procedure C, starting from **20d** (230 mg, 0.73 mmol), sodium hydride (35 mg, 0.88 mmol) and benzyl bromide (0.10 ml, 0.80 mmol), **22c** was obtained as a colourless oil (43 mg, 14%), δ_H 0.93 (3H, t, J = 7.4, CH_3), 1.01 (3H, t, J = 7.4, CH_3), 1.29 (16H, m, 8 x CH_2), 1.55-1.63 (2H, m, CH_2), 1.66 (3H, s, CH_3), 1.81-1.88 (2H, m, CH_2), 2.49 (2H, t, J = 7.8, CH_2), 5.36 (2H, s, OCH_2) and 7.41-7.51 (5H, m, 5 x ArCH); δ_C 14.3 and 14.5 (both CH_3), 23.1, 23.9 (both CH_2), 25.6 (CH_3), 27.2, 29.7, 29.8, 29.9, 30.0, 32.0, 32.3, 39.4 (all CH_2), 57.8 (5-C), 74.0 (OCH_2), 117.5 (3-C), 127.8, 129.0, 129.2 (all ArCH), 136.3 (ArC), 179.7 (4-C) and 196.2 (2-CO); MS (ES^+) *m/z* 425.1 (M + $Na,^+$ 55%); HRMS (ES^+) $(M + H)^+$ $C_{25}H_{39}O_2S$ requires 403.2665, found 403.2660.

4-Methoxy-5-methyl-3-propyl-2,5-dihydro-2-thiophenone (22d)

As described in procedure C, starting from **20c** (800 mg, 4.65 mmol), sodium hydride (220 mg, 5.58 mmol) and iodomethane (0.34 ml, 5.11 mmol), **22d** was obtained as a colourless oil (40 mg, 5%), δ_H 0.88 (3H, t, J = 7.3, 3'-CH_3), 1.35-1.51 (2H, m, 2'-CH_2), 1.58 (3H, d, J = 6.9, 6-CH_3), 2.23 (2H, t, J = 7.4, 1'-CH_2), 3.97 (3H, s, OCH_3) and 4.21 (1H, q, J = 6.9, 5-CH); δ_C 14.2 (CH_3), 20.5 (CH_2), 22.4 (CH_2), 25.7 (CH_3), 41.7 (5-CH), 58.4 (OCH_3), 119.7 (3-C), 179.3 (4-C) and 195.8 (2-CO); MS (ES^+) *m/z* 209.0 (M+$Na,^+$ 30%); HRMS (ES^+) $(M + H)^+$ $C_9H_{15}O_2S$ requires 187.0787, found 187.0788.

4-[(6-{[tert-Butyl(dimethyl)silyl]oxy}hexyl)oxy]-5-methyl-3-propyl-2(5H)-thiophenone (22e)

As described in procedure C, starting from **20c** (300 mg, 1.74 mmol), sodium hydride (83 mg, 2.09 mmol) and bromide (0.41 ml, 2.09 mmol), **22e** was obtained as a colourless oil (67 mg, 10%), δ_H 0.10 (6H, s, $Si(CH_3)_2$), 0.94 (9H, s, $(CH_3)_3$), 1.44-1.62 (6H, m, 3 x CH_2), 1.64 (3H, d, J = 7.0, 6-CH_3), 1.77-1.82 (2H, m, CH_2), 2.28 (2H, t, J = 7.6, CH_2), 3.67 (2H, t, J = 6.2, OCH_2), 4.14 (1H, q, J = 7.0, 5-CH) and 4.24-4.31 (2H, m, OCH_2); δ_C 0.0 $Si(CH_3)_2$, 12.8 (CH_3), 17.3, 19.2, 20.9, 24.4,

24.4, 24.5, 24.9, 28.8, 31.6, 40.5, 61.9 (OCH_2), 69.7 (OCH_2), 118.5 (3-C), 177.6 (4-C) and 194.5 (CO); MS (ES^+) *m/z* 425.0 (M + K,$^+$ 100%); HRMS (ES^+) $(M + Na)^+$ $C_{20}H_{38}O_3NaSiS$ requires 409.2196, found 409.2209.

Microanalytical data

Compd	Formula	Calc%			Found%		
		C	H	N	C	H	N
6b	$C_{12}H_{20}O_3$	67.9	9.5	-	67.5	9.7	-
13	$C_{16}H_{27}O_3N$	68.3	9.7	5.0	68.0	9.7	4.9
15	$C_{24}H_{44}O_2S$	72.7	11.3	-	72.7	11.2	-
16	$C_{28}H_{44}O_2S.0.1H_2O$	75.3	9.9	-	75.0	10.0	-
17	$C_{17}H_{30}O_4S.0.5H_2O$	60.1	9.2	-	60.4	9.2	-
19	$C_{14}H_{24}O_3S.0.05H_2O$	61.5	8.9	-	61.1	8.9	-
21d	$C_{18}H_{28}O_2S.0.15H_2O$	69.5	9.2	-	69.2	9.2	-
22f	$C_{14}H_{24}O_3S$	61.7	8.9	-	61.5	9.1	-