Supplementary Material (ESI) for Chemical Communications

ELECTRONIC SUPPLEMENTARY INFORMATION (ESI)

Synthesis of the Spiroacetal-Containing Anti-*Helicobacter Pylori* Agents CJ-12,954 and CJ-13,014

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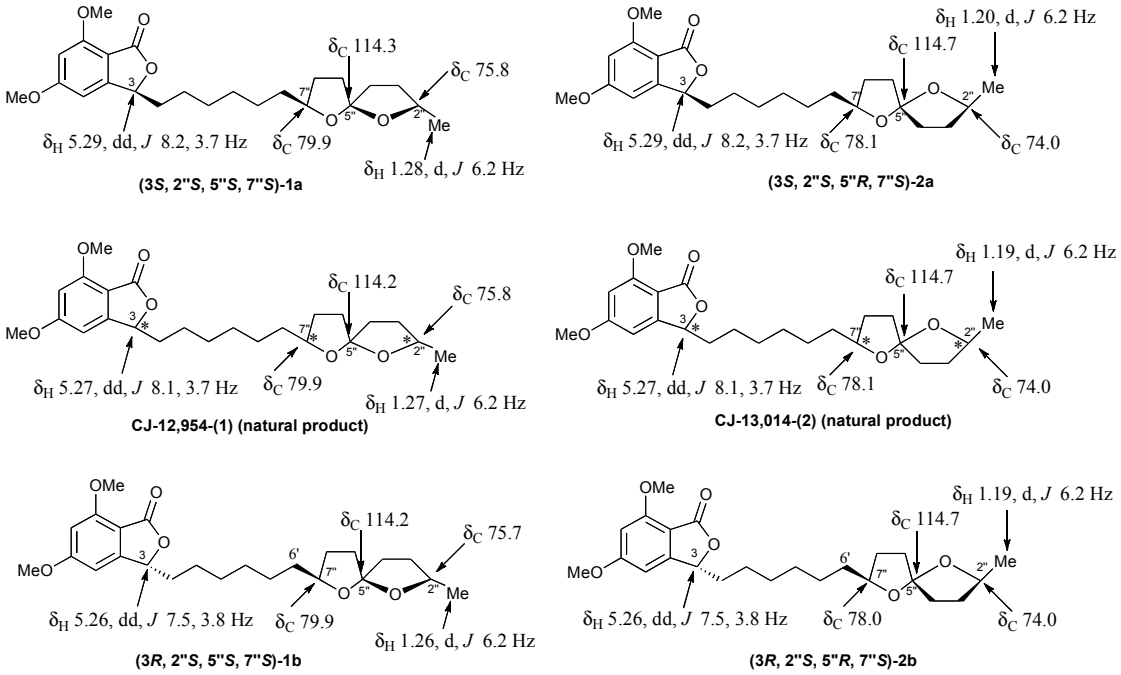
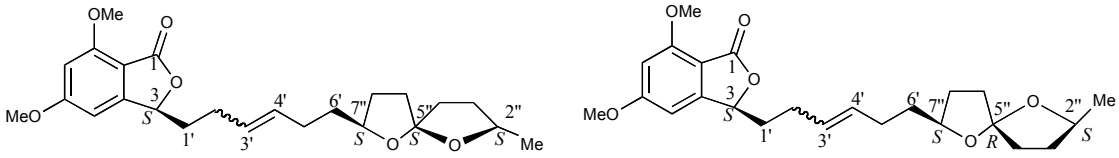


Figure 2

Experimental Details

(3'*E*, 3*S*, 2''*S*, 5''*S*, 7''*S*)- (3'*E*, 3*S*, 2''*S*, 5''*R*, 7''*S*)- (3'*Z*, 3*S*, 2''*S*, 5''*S*, 7''*S*)- (3'*Z*, 3*S*, 2''*S*, 5''*R*, 7''*S*)- 5,7-Dimethoxy-3-[6'-(2''-methyl-1'',6''dioxaspiro[4.4]non-7''-yl)hex-3'-en-1'-yl]-3*H*-isobenzofuran-1-one [precursors to (1a) and (2a)]

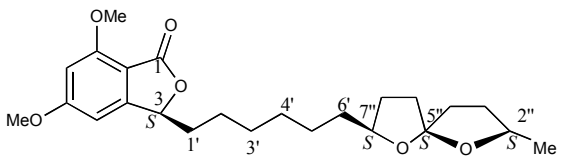


To a solution of sulfones **6** and **7** (30 mg, 0.08 mmol, 1:1) in tetrahydrofuran (1 mL), under an atmosphere of nitrogen at -78 °C, was added potassium hexamethyldisilazide (0.20 mL, 0.5M in toluene, 0.10 mmol) dropwise. The mixture was stirred for 20 min at -78 °C then a solution of aldehyde **5a** (19 mg, 0.08 mmol) in tetrahydrofuran (1 mL) added. The mixture was stirred for 1.5 h at -78 °C then 1 h at rt. Diethyl ether (10 mL) was added followed by saturated aqueous sodium chloride (10 mL). The layers were separated and the aqueous layer washed with diethyl ether (2 x 10 mL). The combined organic layers were dried over potassium carbonate and the solvent removed under reduced pressure. The crude oil was purified by flash column chromatography using hexane-diethyl ether (1:1) as eluent to afford the *title compounds* (28 mg, 84%) as a colourless oil and as a 1:1 mixture of diastereomers; ν_{max} (film)/cm^{-1} 2971, 2248, 2091, 1743, 1614, 1458, 1337, 1217, 1158, 1028, 910, 837, 730; δ_H (300 MHz, $CDCl_3$)[#] 1.19 (1.5H, d, *J* 6.2 Hz, ((*E*)-Me[‡] and (*Z*)-Me[‡]), 1.30 (1.5H, d, *J* 6.2 Hz, ((*E*)-Me[ø] and (*Z*)-Me[ø]), 1.40-1.52 (2H, m, H6'), 1.69-1.81 (3H, m, H3'', H8''A), 1.83-1.91 (1H, m, H8''B), 1.95-2.17 (6H, m, H1', H4'', H9''), 2.27-2.48 (4H, m, (*E*)-H2' and (*Z*)-H2', (*E*)-H5' and (*Z*)-H5'), 3.89 (3H, s, OMe), 3.89-3.99 (2H, m, H7''), 3.95 (3H, s, OMe), 4.01-4.10 (1H, m, H2''[ø]), 4.13-4.20 (1H, m, H2''[‡]), 5.28, 5.35 (each 1H, each dd, *J* 8.5, 3.1 Hz, H3), 5.50-5.62 (2H, m, (*E*)-H3' and (*Z*)-H3', (*E*)-H4' and (*Z*)-H4'), 6.40-6.42 (1H, m, H6), 6.42-6.43 (1H, m, H4); δ_C (75.5 MHz, $CDCl_3$)[#] 21.1 (CH_3, Me[‡]), 23.1 (CH_3, Me[ø]), 24.0 (CH_2, (Z)-C2'), 24.1 (CH_2, (Z)-C5'), 29.7 (CH_3, (E)-C2'), 30.2 (CH_2, (E)-C5'), 30.2 (CH_2, C8''[‡]), 30.5 (CH_2, C8''[ø]), 32.2 (CH_2, C3''[‡]), 32.6 (CH_2, C3''[ø]), 34.6, 34.7 (CH_2, C1'), 35.5

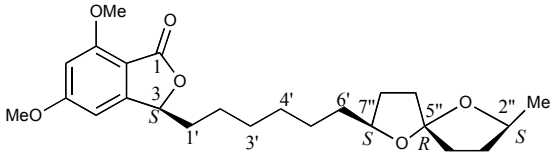
[#] The symbol [‡] is used to denote the (3'*E*, 3*S*, 2''*S*, 5''*R*, 7''*S*) and (3'*Z*, 3*S*, 2''*S*, 5''*R*, 7''*S*) isomers.
The symbol [ø] is used to denote the (3'*E*, 3*S*, 2''*S*, 5''*S*, 7''*S*) and (3'*Z*, 3*S*, 2''*S*, 5''*S*, 7''*S*) isomers.

(CH_2, C4"‡), 35.6 (CH_2, C9"‡), 36.0 (CH_2, C4"ø), 36.4 (CH_2, C9"ø), 38.9 (CH_2, C6'), 55.9 (CH_3, OMe), 56.0 (CH_3, OMe), 74.1, 75.9, 76.0 (CH, C2"), 77.2, 78.5, 78.6 (CH, C7"), 79.2 (CH, C3), 97.4 (CH, C6), 98.9 (CH, C4), 106.8 (quat, C7a), 114.4 (quat, C5"ø), 114.9 (quat, C5"‡), 123.4, 123.6 (CH, C3'), 126.1, 126.3 (CH, C4'), 154.7 (quat, C3a), 159.7 (quat, C7), 166.7 (quat, C5), 166.8 (quat, C1); *m/z* (EI+) (MH+, 96%), 399 (38), 305 (12), 219 (7), 193 (12), 154 (100), 85 (9); HRMS (EI+): Found M^+, 416.2183, $C_{24}H_{32}O_6$ requires 416.2193.

(3*S*, 2"*S*, 5"*S*, 7"*S*)- and (3*S*, 2"*S*, 5"*R*, 7"*S*)-5,7-Dimethoxy-3-[6'-(2"-methyl-1",6"-dioxaspiro[4.4]non-7"-yl)hex-1'-yl]-3*H*-isobenzofuran-1-one (1a) and (2a)



1a



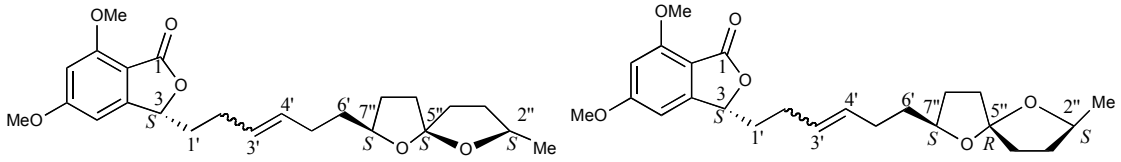
2a

To a solution of the above alkenes (2 mg, 0.01 mmol) in tetrahydrofuran:methanol (1:1, 2.0 mL) was added potassium carbonate (2 mg, 0.01 mmol) and platinum(IV) oxide (1 mg, catalytic) and the mixture stirred under a hydrogen atmosphere for 4 h. The mixture was filtered through a pad of silica and Celite® and the solvent removed under reduced pressure. The clear oil was purified by flash column chromatography using dichloromethane-acetone (99:1-95:5) as eluent to afford the *title compounds* **1a** and **2a** (1.7 mg, 85%) as a clear colourless oil and as a 1:1 mixture of diastereomers; ν_{max} (film)/cm^{-1} 2929, 2856, 1755, 1614, 1462, 1337, 1217, 1158, 1104, 1030, 918, 837, 731, 690; δ_H (400 MHz, $CDCl_3$)[#] 1.20 (1.5H, d, *J* 6.2 Hz, Me‡), 1.28 (1.5H, d, *J* 6.2 Hz, Meø), 1.25-1.35 (4H, m, H3', H5'), 1.39-1.49 (4H, m, H2', H4'), 1.61-1.73 (3H, m, H6', H8"A), 1.83-1.91 (1H, m, H8"B), 1.92-1.97 (2H, m, H3"), 2.00-2.07 (4H, m, H4", H9"), 2.09-2.14 (2H, m, H1'), 3.89 (3H, s, OMe), 3.90-3.92 (0.5H, m, H7"ø), 3.94 (3H, s, OMe), 3.99-4.04 (0.5H, m, H7"‡), 4.07-4.12 (0.5H, m, H2"ø), 4.16-4.23 (0.5H, m, H2"‡), 5.29 (1H, dd, *J* 8.2, 3.6 Hz, H3), 6.40 (1H, d, *J* 1.7 Hz, H6), 6.41 (1H, d, *J* 1.7 Hz, H4); δ_C (100 MHz, $CDCl_3$)[#] 21.1 (CH_3, Me‡), 23.0 (CH_3, Meø), 24.6 (CH_2, C2'), 25.7, 25.9 (CH_2,

[#] The symbol ‡ is used to denote the (3*S*, 2"*S*, 5"*R*, 7"*S*) isomer.
The symbol ø is used to denote the (3*S*, 2"*S*, 5"*S*, 7"*S*) isomer.

C5'), 29.3, 29.4 (CH_2, C3'), 29.7 (CH_2, C4'), 30.2 (CH_2, C8"‡), 30.7 (CH_2, C8"^{ø}), 32.2 (CH_2, C3"‡), 32.6 (CH_2, C3"^{ø}), 34.8 (CH_2, C1'), 35.6 (CH_2, C6'‡), 35.7 (CH_2, C4"‡), 36.1 (CH_2, C4"^{ø}), 36.5 (CH_2, C9"), 37.3 (CH_2, C6'^{ø}), 55.9 (CH_3, OMe), 56.0 (CH_3, OMe), 74.0 (CH, C2"‡), 75.8 (CH, C2"^{ø}), 78.1 (CH, C7"‡), 79.9 (CH, C7"^{ø}), 79.9 (CH, C3), 97.3 (CH, C6), 98.6 (CH, C4), 106.9 (quat, C7a), 114.3 (quat, C5"^{ø}), 114.7 (quat, C5"‡), 155.2 (quat, C3a), 159.6 (quat, C7), 166.6 (quat, C5), 168.6 (quat, C1); *m/z* (EI+) 418 (M^+, 3%), 361 (26), 320 (24), 278 (9), 207 (16), 193 (35), 141 (100), 112 (13), 85 (24), 55 (9); HRMS (EI+): Found MH^+, 418.2340, $C_{24}H_{35}O_6$ requires 418.2355.

(3'*E*, 3*R*, 2"*S*, 5"*S*, 7"*S*)- (3'*E*, 3*R*, 2"*S*, 5"*R*, 7"*S*)- (3'*Z*, 3*R*, 2"*S*, 5"*S*, 7"*S*)- (3'*Z*, 3*R*, 2"*S*, 5"*R*, 7"*S*)- 5,7-Dimethoxy-3-[6'-(2"-methyl-1",6"-dioxaspiro[4.4]non-7"-yl)hex-3'-en-1'-yl]-3*H*-isobenzofuran-1-one [precursors to (1b) and (2b)]

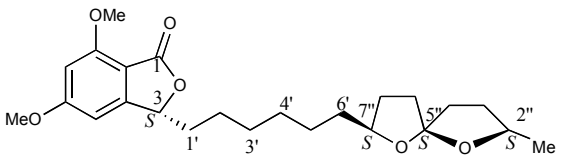


To a solution of sulfones **6** and **7** (70 mg, 0.18 mmol, 1:1) in tetrahydrofuran (2 mL) under an atmosphere of nitrogen at -78 °C was added potassium hexamethyldisilazide (0.46 mL, 0.5M in toluene, 0.23 mmol) and stirred for 20 min. A solution of aldehyde **5b** (45 mg, 0.18 mmol) in tetrahydrofuran (2 mL) was added to the mixture and then stirred at -78 °C for 1 h, before being warmed to rt and stirred for 1 h. Saturated aqueous sodium chloride (10 mL) was added to the mixture, followed by diethyl ether (20 mL), and the layers separated. The aqueous layer was extracted with diethyl ether (2 x 20 mL), and the combined organic extracts were dried over potassium carbonate and the solvent removed under reduced pressure. The crude oil was purified by flash column chromatography using dichloromethane-methanol (99:1), then hexane-diethyl ether (1:1) as eluent to afford the *title compounds* (57 mg, 76%) as a clear colourless oil and as a 1:1 mixture of diastereomers; ν_{max} (film)/cm^{-1} 2966, 2932, 2248, 1755, 1613, 1494, 1461, 1338, 1217, 1158, 1056, 1030, 969, 918, 838, 731; δ_H (300 MHz, $CDCl_3$)[#] 1.18 (1.5H, d, *J* 6.2 Hz, ((*E*)-Me‡ and (*Z*)-Me‡), 1.26 (1.5H, d, *J* 6.2 Hz, ((*E*)-Me^{ø} and (*Z*)-Me^{ø}), 1.41-1.49 (2H,

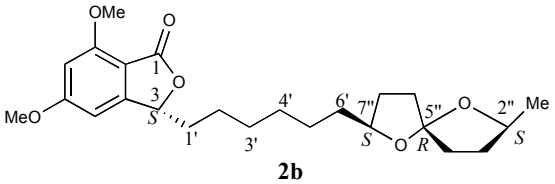
[#] The symbol ‡ is used to denote the (3'*E*, 3*R*, 2"*S*, 5"*R*, 7"*S*) and (3'*Z*, 3*R*, 2"*S*, 5"*R*, 7"*S*) isomers.
The symbol ^{ø} is used to denote the (3'*E*, 3*R*, 2"*S*, 5"*S*, 7"*S*) and (3'*Z*, 3*R*, 2"*S*, 5"*S*, 7"*S*) isomers.

m, H6'), 1.51-1.65 (1H, m, H8"A), 1.67 (3H, m, H8"B, H3"), 1.94-2.11 (8H, m, H1', H4", H5', H9"), 2.13-2.24 (2H, m, (*E*)-H2' and (*Z*)-H2'), 3.87 (3H, s, OMe), 3.87-3.89 (1H, m, H7"^{ø}), 3.92 (3H, s, OMe), 3.92-3.98 (1H, m, H7"‡), 4.00-4.08 (1H, m, H2"^{ø}), 4.09-4.21 (1H, m, H2"‡), 5.27 (1H, dd, *J* 8.5, 3.3 Hz, H3), 5.35-5.53 (2H, m, (*E*)-H3' and (*Z*)-H3', (*E*)-H4' and (*Z*)-H4'), 6.39 (2H, s, H4, H6); δ_C (75.5 MHz, $CDCl_3$)[#] 21.1 (CH_3, Me‡), 22.6 (CH_2, (Z)-C2'), 23.0 (CH_3, Me^{ø}), 23.6 (CH_2, (Z)-C5'), 27.8 (CH_3, (E)-C2'), 28.8 (CH_2, (E)-C5'), 30.1, 30.3, 30.6, 30.7 (CH_2, C8"), 32.2 (CH_2, C3"‡), 32.6 (CH_2, C3"^{ø}), 34.8 (CH_2, C1'), 35.4 (CH_2, C6'‡), 35.5 (CH_2, C4"‡), 35.6 (CH_2, C9"‡), 36.0 (CH_2, C4"^{ø}), 36.4 (CH_2, C9"^{ø}), 37.1 (CH_2, C6'^{ø}), 55.9 (CH_3, OMe), 55.9 (CH_3, OMe), 74.0 (CH, C2"‡), 75.8 (CH, C2"^{ø}), 77.5 (CH, C7"‡), 79.1 (CH, C7"^{ø}), 79.2 (CH, C3), 97.4 (CH, C6), 98.7 (CH, C4), 106.9 (quat, C7a), 114.3 (quat, C5"^{ø}), 114.7 (quat, C5"‡), 128.2, 128.4 (CH, C3'), 131.5, 131.7 (CH, C4'), 155.1 (quat, C3a), 159.6 (quat, C7), 166.6 (quat, C5), 168.4 (quat, C1); *m/z* (FAB+) (MH+, 96%), 399 (38), 305 (12), 219 (7), 193 (12), 154 (100), 85 (9); HRMS (FAB+): Found MH^+, 417.2268, $C_{24}H_{33}O_6$ requires 417.2277.

(3*R*, 2"*S*, 5"*R*, 7"*S*)- and (3*R*, 2"*S*, 5"*S*, 7"*S*)-5,7-Dimethoxy-3-[6'-(2"-methyl-1",6"-dioxaspiro[4.4]non-7"-yl)hex-1'-yl]-3*H*-isobenzofuran-1-one (1b) and (2b)



1b



2b

To a solution of the above alkenes (20 mg, 0.48 mmol) in tetrahydrofuran:methanol (1:1, 4 mL) was added potassium carbonate (25 mg, 0.18 mmol) and platinum(IV) oxide (2 mg) and the mixture stirred under an atmosphere of hydrogen for 4 h. The mixture was filtered through a pad of silica and Celite® and the solvent removed under reduced pressure to afford the *title compounds* **1b** and (**2b** (18 mg, 90%) as a colourless oil and as a 1:1 mixture of diastereomers; ν_{max} (film)/cm^{-1} 2931, 2857, 1755, 1613, 1494, 1462, 1337, 1217, 1159, 1054, 1030, 918, 837, 731, 690; δ_H (300 MHz, $CDCl_3$)[#] 1.19 (1.5H, d,

[#] The symbol [‡] is used to denote the (3*R*, 2"*S*, 5"*R*, 7"*S*) isomer.

J 6.2 Hz, Me‡), 1.26 (1.5H, d, *J* 6.2 Hz, Me^{ø}), 1.23-1.36 (4H, m, H3', H5'), 1.38-1.49 (6H, m, H2', H4', H6'), 1.62-1.72 (2H, m, H1'A, H8"A), 1.88-1.90 (1H, m, H8"B), 1.92-1.97 (2H, m, H3"), 1.99-2.05 (3H, m, H4"A, H9"), 2.09-2.14 (2H, m, H1'B, H4"B), 3.87 (3H, s, OMe), 3.88-3.90 (0.5H, m, H7"^{ø}), 3.92 (3H, s, OMe), 3.96-4.03 (0.5H, m, H7"‡), 4.05-4.08 (0.5H, m, H2"^{ø}), 4.11-4.21 (0.5H, m, H2"‡), 5.26 (1H, dd, *J* 7.5, 3.8 Hz, H3), 6.38 (1H, s, H6), 6.41 (1H, s, H4); δ_C (75.5 MHz, $CDCl_3$)$^{\#}$ 21.1 (CH_3, Me‡), 22.9 (CH_3, Me^{ø}), 24.5, 24.6 (CH_2, C2'), 25.6, 25.9 (CH_2, C5'), 29.2, 29.4 (CH_2, C3'), 29.6 (CH_2, C4'), 30.2 (CH_2, C8"‡), 30.7 (CH_2, C8"^{ø}), 32.2 (CH_2, C3"‡), 32.6 (CH_2, C3"^{ø}), 34.8 (CH_2, C1'), 35.6 (CH_2, C6'‡), 35.7 (CH_2, C4"‡), 36.1 (CH_2, C4"^{ø}), 36.4 (CH_2, C9"), 37.3 (CH_2, C6'^{ø}), 55.9 (CH_3, OMe), 55.9 (CH_3, OMe), 74.0 (CH, C2"‡), 75.7 (CH, C2"^{ø}), 78.0 (CH, C7"‡), 79.9 (CH, C7"^{ø}), 79.9 (CH, C3), 97.4 (CH, C6), 98.6 (CH, C4), 106.9 (quat, C7a), 114.2 (quat, C5"^{ø}), 114.7 (quat, C5"‡), 155.1 (quat, C3a), 159.6 (quat, C7), 166.6 (quat, C5), 168.4 (quat, C1); *m/z* (FAB+) 419 (MH^+, 81%), 361 (5), 320 (6), 207 (7), 193 (10), 154 (100), 120 (12), 111 (11) (9); HRMS (FAB+): Found MH^+, 419.2446, $C_{24}H_{35}O_6$ requires 419.2434.

The symbol ^{ø} is used to denote the (3*R*, 2"*S*, 5"*S*, 7"*S*) isomer.