ELECTRONIC SUPPLEMENTARY INFORMATION (ESI)

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

Margaret A. Brimble* and Christina J. Bryant
Department of Chemistry, The University of Auckland, 23 Symonds St., Auckland, New Zealand.
E-mail: m.brimble@auckland.ac.nz; Fax: +64 9 3737599; tel: +64 9 3737599 ext 88259

Figure 2
Experimental Details

(3'E, 3S, 2''S, 5''S, 7''S)- (3'E, 3S, 2''S, 5''R, 7''S)- (3'Z, 3S, 2''S, 5''S, 7''S)- (3'Z, 3S, 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]-3H-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)-Meø), 1.30 (1.5H, d, J 6.2 Hz, ((E)-Meø and (Z)-Meø), 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), 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 (CH3, Meø), 23.1 (CH3, Meø), 24.0 (CH2, (Z)-C2'), 24.1 (CH2, (Z)-C5'), 29.7 (CH3, (E)-C2'), 30.2 (CH2, (E)-C5'), 30.2 (CH2, C8''ø), 30.5 (CH2, C8''ø), 32.2 (CH2, C3''ø), 32.6 (CH2, C3''ø), 34.6, 34.7 (CH2, C1'), 35.5

The symbol ‡ is used to denote the (3'E, 3S, 2''S, 5''S, 7''S) and (3'Z, 3S, 2''S, 5''R, 7''S) isomers.
The symbol ø is used to denote the (3'E, 3S, 2''S, 5''R, 7''S) and (3'Z, 3S, 2''S, 5''S, 7''S) isomers.
(CH2, C4''‡), 35.6 (CH2, C9''‡), 36.0 (CH2, C4''ø), 36.4 (CH2, C9''ø), 38.9 (CH2, C6'), 55.9 (CH3, OMe), 56.0 (CH3, 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, C24H32O6 requires 416.2193.

(3S, 2''S, 5''S, 7''S)- and (3S, 2''S, 5''R, 7''S)-5,7-Dimethoxy-3'-[6'-methyl-1''ø,6''ø-dioxaspiro[4.4]non-7''-yl]hex-1'-yl]-3H-isobenzofuran-1-one (1a) and (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; νmax (film)/cm⁻¹ 2929, 2856, 1755, 1614, 1462, 1337, 1217, 1158, 1104, 1030, 918, 837, 731, 690; δH (400 MHz, CDCl3) 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''ø), 4.07-4.12 (0.5H, m, H2''ø), 4.16-4.23 (0.5H, m, H2''ø), 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); δC (100 MHz, CDCl3) 21.1 (CH3, Me‡), 23.0 (CH3, Meø), 24.6 (CH2, C2'), 25.7, 25.9 (CH2,

The symbol ‡ is used to denote the (3S, 2''S, 5''R, 7''S) isomer. The symbol ø is used to denote the (3S, 2''S, 5''S, 7''S) isomer.
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; νmax (film)/cm⁻¹ 2966, 2932, 2248, 1755, 1613, 1494, 1461, 1338, 1217, 1158, 1056, 1030, 969, 918, 838, 731; δH (300 MHz, CDCl3)° 1.18 (1.5H, d, J 6.2 Hz, ((E)-Me‡ and (Z)-Meø), 1.26 (1.5H, d, J 6.2 Hz, ((E)-Meø and (Z)-Meø)), 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.
(3R, 2''S, 5''R, 7''S)- and (3R, 2''S, 5''S, 7''S)-5,7-Dimethoxy-3-[6'-methyl-1''',6'''-dioxaspiro[4.4]non-7''-yl]hex-1'-yl]-3H-isobenzofuran-1-one (1b) and (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; νmax (film)/cm−1 2931, 2857, 1755, 1613, 1494, 1462, 1337, 1217, 1159, 1054, 1030, 918, 837, 731, 690; δH (300 MHz, CDCl3) " 1.19 (1.5H, d, 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), 5.27 (1H, dd, J 8.5, 3.3 Hz, H3); δC (75.5 MHz, CDCl3) " 21.1 (CH3, Me‡), 22.6 (CH2, (Z)-C2'), 23.0 (CH3, Meø), 23.6 (CH2, (Z)-C5'), 27.8 (CH3, (E)-C2'), 28.8 (CH2, (E)-C5'), 30.1, 30.3, 30.6, 30.7 (CH2, C8''), 32.2 (CH2, C3''ø), 32.6 (CH2, C3''ø), 34.8 (CH2, C1'), 35.4 (CH2, C6''), 35.5 (CH2, C4''ø), 35.6 (CH2, C9''ø), 36.0 (CH2, C4''ø), 36.4 (CH2, C9''ø), 37.1 (CH2, C6''ø), 55.9 (CH3, OMe), 55.9 (CH3, OMe), 74.0 (CH, C2''ø), 75.8 (CH, C2''ø), 77.5 (CH, C7''ø), 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''ø), 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, C24H33O6 requires 417.2277.

The symbol † is used to denote the (3R, 2''S, 5''R, 7''S) isomer.
J 6.2 Hz, Me\(^{1}\)), 1.26 (1.5H, d, J 6.2 Hz, Me\(^{0}\)), 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); \(\delta\) (75.5 MHz, CDCl\(_3\)) \(^{\#}\) 21.1 (CH\(_3\), Me\(^{1}\)), 22.9 (CH\(_3\), Me\(^{0}\)), 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''\(^{‡}\)), 55.9 (CH\(_3\), OMe), 74.0 (CH, C2''\(^{‡}\)), 75.7 (CH, C2''ø), 78.0 (CH, C7''\(^{‡}\)), 79.9 (CH, C7''ø), 97.4 (CH, C6), 98.6 (CH, C4), 106.9 (quat, C7a), 114.2 (quat, C5''\(^{‡}\)), 114.7 (quat, C5''ø), 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 \(^{\#}\) is used to denote the (3\(R\), 2\(o\)S, 5\(S\), 7\(S\)) isomer.