Supporting Information
for

Approach to the Synthesis of Antitumor Quassinoids from Labdane Diterpenes: An Efficient Synthesis of a Picrasane Related Intermediate

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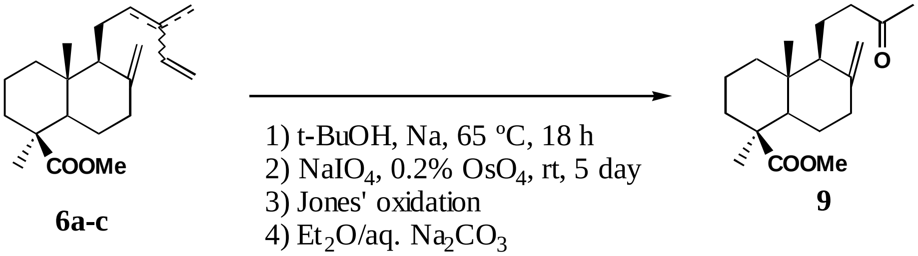
All compounds reported in this experimental section were isolated as oils. The purity of these was established on the basis of their ^{1}H NMR spectra, which revealed the presence of more than 95% of the corresponding compound.

(1’*R*,3’*R*,4a’*S*,5’*S*,8a’*S*)-4-[3’,4’,4a’,5’,6’,7’,8’,8a’-Octahydro-2’(1’H)-methylene-5’β-methoxycarbonyl-5’α,8a’β-dimethylnaphtyl]-2-butanone (9).



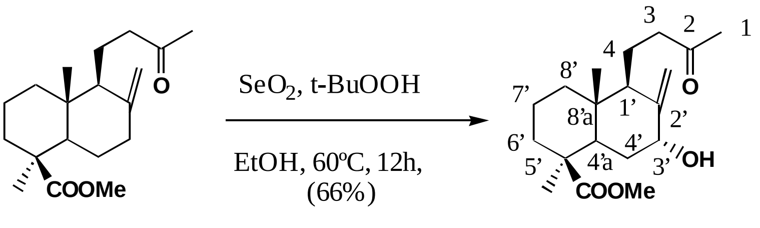
6a-c **9**

To a magnetically stirred solution of the mixture of **6a-c** (70.2 g, 222.31 mmol) in *t*-BuOH (1000 mL), an excess of Na (50 g, 2.17 mol) was slowly added within 3 h at room temperature. The resulting viscous mixture was further stirred at 60 ºC for 24 h. After filtration of the mixture, hexane (500 mL) was added to the filtrate and the resulting solution was washed with brine (3 x 200 mL). The organic phase was dried over anhydrous sodium sulfate and evaporated to give a crude (62.4 g) principally formed by **7** and **8** (ratio 2:8, 88%), which was reacted without further purification.

A 0.2 % aq. OsO_4 solution (43 mL) was added to a solution of the above crude (17.0 g, 53.6 mmol) in *t*-BuOH (195 mL) and H_2O (82 mL) and the mixture was stirred for 15 min. Then $NaIO_4$ (40.5 g, 189.34 mmol) was added and the mixture was further stirred at room temperature for 5 days. After filtration, the solvent was evaporated and the residue was fractionated into *t*-BuOMe (150 mL)-H_2O (40 mL). The organic phase was successively washed with 10 % aq. K_2CO_3 (2 x 50 mL) and brine (2 x 50 mL), dried over anhydrous sodium sulfate and evaporated to give a crude (16.26 g).

A 2M solution of Jones’ reagent (8 mL) was added slowly to a stirred solution of the latter crude (16.26 g) in acetone (75 mL) until orange colour permanence, and the mixture was further stirred at room temperature for 3 h. Then it was poured into H_2O-ice (150 mL) and extracted with Et_2O (4 x 50 mL). The organic phase was successively washed with sat. solution of Na_2CO_3 (3 x 50 mL) and brine (2 x 50 mL), dried over anhydrous sodium sulfate and evaporated to give **9** as a colourless oil (11.5 g, 70%). Compound **9** had identical spectroscopic properties to those reported in the literature.

(1’*R*,3’*R*,4a’*S*,5’*S*,8a’*S*)-4-[3’,4’,4a’,5’,6’,7’,8’,8a’-Octahydro-2’(1’H)-methylene-3’α-hydroxy-5’β-methoxycarbonyl-5’α,8a’β-dimethylnaphtyll]-2-butanone (10).

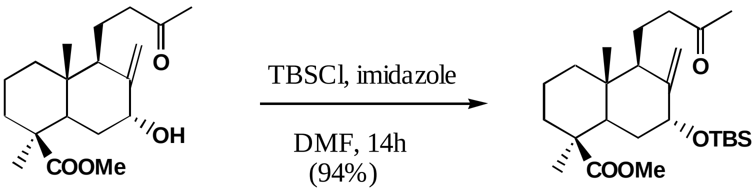


9 **10**

A mixture of methylketone **9** (1.99 g, 6.51 mmol) and SeO$_2$ (960 mg, 8.45 mmol) in EtOH (15 mL) was heated at 60 ^{o}C for 10 h. The solvent was evaporated and the residue was fractionated into *t*-BuOMe (30 mL) and water (20 mL). The organic extract was washed with water, dried over anhydrous sodium sulfate and evaporated to yield **10** as a colourless oil (1.40 g, 66%).

$[\alpha]_D^{25^{o}}$: +11^{o} (*c* 0.05, CHCl$_3$); **IR** (film, cm^{-1}) ν_{max}: 3414, 3079, 2931, 2874, 2853, 1720, 1648, 1456, 1442, 1379, 1362, 1310, 1251, 1197, 1152, 1095, 1052, 976, 902, 754, 664; **^{1}H NMR** (CDCl$_3$, 300 MHz) δ 0.49 (s, 3H, Me-8a’), 1.10 (ddd, *J* = 17.5, 13.3, 4.0 Hz, 1H, H-8’α), 1.17 (s, 3H, Me-5’), 2.07 (dd, *J* = 5.8, 3.1 Hz, 1H, H-1’), 2.10 (s, 3H, H-1), 2.17 (bd, *J* = 17.7 Hz, 1H, H-8’β), 2.30 (ddd, *J* = 17.6, 9.0, 6.7 Hz, 1H, H-3A), 2.55 (ddd, *J* = 17.6, 9.5, 4.7 Hz, 1H, H-3B), 3.61 (s, 3H, 5’-COO$\underline{\text{CH}}_3$), 4.39 (t, *J* = 3.0 Hz, 1H, H-3’), 4.57 (s, 1H, =$\underline{\text{CH}}_2$), 5.06 (s, 1H, =$\underline{\text{CH’}}_2$); **^{13}C NMR** (CDCl$_3$, 75 MHz) δ 209.3 (C-2), 177.7 (-$\underline{\text{C}}$OOCH$_3$), 148.9 (C-2´), 109.1 (=$\underline{\text{CH}}_2$), 73.7 (C-3´), 51.2 (C-4a´), 49.1 (-COO$\underline{\text{CH}}_3$), 48.5 (C-1´), 43.9 (C-5´), 42.5 (C-3), 40.3 (C-8a´), 38.7 (C-8´), 38.1 (C-6´), 32.6 (C-4´), 29.9 (C-1), 28.6 (Me-5´), 19.9 (C-7´), 17.3 (C-4), 11.5 (Me-8a´); **FAB HRMS** calcd for C$_{19}$H$_{30}$O$_4$Na 345.2042, found 345.2040.

(1’*R*,3’*R*,4a’*S*,5’*S*,8a’*S*)-4-[3’α-(*tert*-Butyldimethylsilyl)oxy-3’,4’,4a’,5’,6’,7’,8’,8a’-octahydro-2’(1’H)-methylene-5’β-methoxycarbonyl-5’α,8a’β-dimethylnaphthyl]-2-butanone (11).



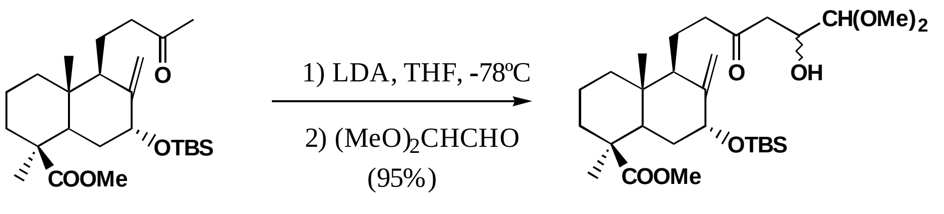
10 **11**

To a solution of alcohol **10** (1.65 g, 5.12 mmol) in DMF (15 ml) at room temperature was added imidazole (377 mg, 5.63 mmol) and *tert*-butyldimethylsilyl chloride (1.15 g, 7.68 mmol). After being stirred for 14 h the mixture was extracted with *t*-BuOMe (3 x 20 mL). The organic phase was successively washed with aqueous HCl (1.2 M) (3 x 20 mL), water (3 x 20 mL) and dried over anhydrous sodium sulfate and evaporated to yield **11** as a colourless oil (2.10 g, 94%).

$[\alpha]_D^{25^{o}}$: +4^{o} (*c* 0.06, CHCl$_3$); **IR** (film, cm^{-1}) ν_{max} 2949, 2932, 2884, 2855, 1723, 1647, 1464, 1440, 1412, 1383, 1358, 1252, 1223, 1197, 1151, 1069, 990, 943, 901, 867, 837, 776, 727, 677, 634; **^{1}H NMR** (CDCl$_3$, 300 MHz) δ 0.00 (s, 3H, Me-Si-$\underline{\text{CH}}_3$), 0.05 (s, 3H, Me-Si-$\underline{\text{CH}}_3$), 0.48 (s, 3H, Me-8a’), 0.87 (s, 9H, ($\underline{\text{CH}}_3$)$_3$C-Si), 1.10 (ddd, *J* = 17.5, 13.2, 4.2 Hz, 1H, H-8’α), 1.12 (s, 3H, Me-5’), 2.10 (s, 3H, H-1), 2.16 (bd, *J* = 15.0 Hz, 1H, H-1’), 2.26 (ddd, *J* = 15.2, 9.0, 6.7 Hz, 1H, H-3A), 2.51 (ddd, *J* = 14.0, 9.0, 4.7 Hz, 1H, H-3B), 3.61 (s, 3H, 5’-COO$\underline{\text{CH}}_3$), 4.29 (d, *J* = 2.9 Hz, 1H, H-3’), 4.46 (s, 1H, =$\underline{\text{CH}}_2$), 4.93 (s, 1H, =$\underline{\text{CH’}}_2$); **^{13}C NMR** (CDCl$_3$, 75 MHz) δ 209.1 (C-2), 177.9 (-$\underline{\text{C}}$OOCH$_3$), 149.8 (C-2´), 107.3 (=$\underline{\text{CH}}_2$), 74.2 (C-3´), 51.2 (C-4a´), 49.3 (-COO$\underline{\text{CH}}_3$), 48.6 (C-1´), 43.9 (C-5´), 42.5 (C-3), 40.2 (C-8a´), 39.0 (C-8´), 38.2 (C-6´), 34.3 (C-4´), 30.0 (C-1), 28.7 (Me-5'), 25.8 (3C, ($\underline{\text{CH}}_3$)$_3$C-Si), 20.1 (C-7´), 18.1 ((CH$_3$)$_3\underline{\text{C}}$-Si), 17.3

(C-4), 11.7 (Me-8a'), -4.5 (Me-Si-$\underline{CH}_3$), -4.9 (Me-Si-$\underline{CH}_3$); **FAB HRMS** calcd for $C_{25}H_{44}O_4SiNa$ 459.2899, found 459.2906.

[(1'*R*,3'*R*,4a'*S*,5'*S*,8a'*S*,2*R*(*S*)]-6-[3'α-(*tert*-Butyldimethylsilyl)oxy-3',4',4a',5',6',7',8',8a'-octahydro-2'(1'H)-methylene-5'β-methoxycarbonyl-5'α,8a'β-dimethylnaphthyl]-2-hydroxy-4-oxo-hexanal dimethylacetal (12).

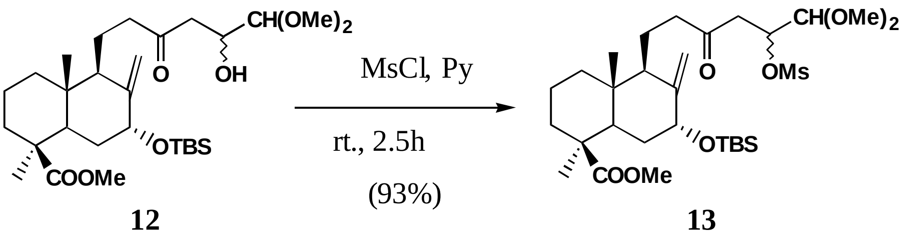


11 **12**

To a solution of LDA (*n*-BuLi (2.5 M in hexane, 18.77 mmol, 7.5 mL) and *i*-Pr_2NH (22.53 mmol, 3.16 mL)) in THF (25 mL) at –78°C was added **11** (2.73 g, 6.26 mmol) disolved in THF (25 ml). After being stirred for 30 min a solution of glyoxal 1,1-dimethyl acetal (9.40 mmol) (45% in *t*-BuOMe) (Fluka, ref. 50707) was added and the reaction was stirred at this temperature for another 30 min. The mixture was extracted with *t*-BuOMe (3 x 30 mL), and the combined organic phases were washed with aqueous HCl (1.2 M) (3 x 30 mL) and water (3 x 30 mL), dried over anhydrous sodium sulfate and evaporated to give a residue which was chromatographed (4:6 hexane/*t*-BuOMe, silica gel) to yield **12** as a colourless oil (3.21 g, 95%).

$[\alpha]_D^{25°}$: -2.3° (*c* 0.1, $CHCl_3$); **IR** (film, cm^{-1}) ν_{max}: 3490, 3472, 3440, 3077, 2950, 2934, 2890, 2856, 1723, 1648, 1465, 1443, 1409, 1383, 1362, 1336, 1252, 1223, 1196, 1149, 1070, 988, 942, 901, 866, 836, 814, 775, 674; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ -0.01 (s, 3H, Me-Si-$\underline{CH}_3$), 0.04 (s, 3H, Me-Si-$\underline{CH}_3$), 0.47 (s, 3H, Me-8a'), 0.87 (s, 9H, $(\underline{CH}_3)_3$C-Si), 1.11 (s, 3H, Me-5'), 1.47-1.54 (m, 2H), 1.76-1.98 (m, 6H), 2.09-2.28 (m, 3H), 2.56-2.82 (m, 2H), 4.09 (q, *J* = 4.2 Hz, 1H, H-2), 3.44 (s, 6H, CH(O$\underline{CH}_3$)$_2$), 3.59 (s, 3H, 5'-COO$\underline{CH}_3$), 4.23 (d, *J* = 5.2 Hz, 1H, H-1), 4.28 (t, *J* = 2.3 Hz, 1H, H-3'), 4.45 (s, 1H, =$\underline{CH}_2$), 4.91 (s, 1H, =$\underline{CH'}_2$); **^{13}C NMR** ($CDCl_3$, 75 MHz) *δ* 212.5 (C-4), 179.3 (-$\underline{C}OOCH_3$), 151.0 (C-2´), 107.4 (=$\underline{CH}_2$), 106.10 (C-1), 74.1 (C-3´), 68.1 (C-2), 55.4 (C-4a´), 51.2 (-COO$\underline{CH}_3$), 49.3 (O$\underline{CH}_3$), 49.3 (O$\underline{CH}_3$), 48.6 (C-1´), 43.9 (C-5), 42.5 (C-3), 41.5 (C-5´), 40.3 (C-8a´), 39.0 (C-8´), 38.1 (C-6´), 34.2 (C-4´), 28.7 (Me-5'), 26.0 ($(\underline{CH}_3)_3$C-Si), 25.8 ($(\underline{CH}_3)_3$C-Si), 25.3 ($(\underline{CH}_3)_3$C-Si), 20.1 (C-7´), 18.1 ($(CH_3)_3\underline{C}$-Si), 17.0 (C-6), 11.7 (Me-8a'), -4.4 (Me-Si-$\underline{CH}_3$), -4.9 (Me-Si-$\underline{CH}_3$); **FAB HRMS** calcd for $C_{29}H_{52}O_7SiNa$ 563.3384, found 563.3380.

[(1’*R*,3’*R*,4a’*S*,5’*S*,8a’*S*,2*R*(*S*)]-6-[3’α-(*tert*-Butyldimethylsilyl)oxy-3’,4’,4a’,5’,6’,7’,8’,8a’-octahydro-2’(1’H)-methylene-5’β-methoxycarbonyl-5’α,8a’β-dimethylnaphthyl]-2-(mesyl)oxy-4-oxo-hexanal dimethylacetal (13).

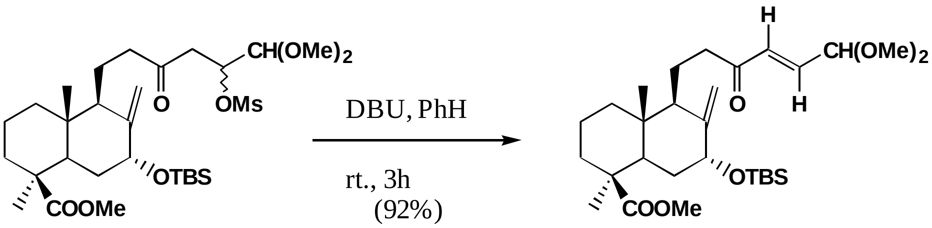


12 **13**

To a solution of alcohol **12** (456 mg, 0.84 mmol) in pyridine (6.1 mL) at 0^{o}C was added slowly MsCl (0.7 mL). After being stirred at room temperature for 2.5 h the mixture was fractionated into *t*-BuOMe (25 mL) – water (25 mL), and the organic phase was successively washed with aqueous HCl (1.2 M) (3 x 30 mL) and water (3 x 30 mL), dried over anhydrous sodium sulfate and evaporated to yield **13** as a colourless oil (490 mg, 94%).

IR (film, cm^{-1}) ν_{max} 3076, 2951, 2934, 2887, 2854, 1796, 1722, 1647, 1466, 1447, 1410, 1359, 1252, 1223, 1195, 1176, 1150, 1073, 983, 962, 866, 837, 776, 757, 677, 632; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 0.01 (s, 3H, Me-Si-$\underline{CH}_3$), 0.06 (s, 3H, Me-Si-$\underline{CH}_3$), 0.48 (s, 3H, Me-8a'), 0.88 (s, 9H, $(\underline{CH}_3)_3$C-Si), 1.13 (s, 3H, Me-5'), 1.04-1.16 (m, 1H, H-8'α), 1.46-1.55 (m, 2H), 1.76-2.00 (m, 6H), 2.11 (bd, *J* = 12.3 Hz, 1H, H-1'), 2.16-2.21 (m, 1H, H-5A), 2.49-2.62 (m, 1H, H-5B), 2.84 (dd, *J* = 18.4, 3.0 Hz, 1H, H-3A), 2.89 (dd, *J* = 18.4, 9.5 Hz, 1H, H-3B), 3.11 (s, 3H, 2-$OSO_2\underline{CH}_3$), 3.46 (s, 3H, $CH(O\underline{CH}_3)_2$), 3.53 (s, 3H, $CH(O\underline{CH}_3)_2$), 3.69 (s, 3H, 5'-$COO\underline{CH}_3$), 4.29 (t, *J* = 1.5 Hz, 1H, H-3'), 4.44 (s, 1H, =$\underline{CH}_2$), 4.59 (d, *J* = 3.3 Hz, 1H, H-1), 4.93 (s, 1H, =$\underline{CH'}_2$), 4.96-5.03 (m, 1H, H-2); **^{13}C NMR** ($CDCl_3$, 75 MHz)δ 207.6 (C-4), 178.0 (-$\underline{C}OOCH_3$), 149.5 (C-2´), 107.3 (=$\underline{CH}_2$), 104.8 (C-1), 76.9 (C-2), 74.0 (C-3´), 56.9 (C-4a´), 52.6 ($OSO_2\underline{CH}_3$), 51.2 (-$COO\underline{CH}_3$), 49.3 ($CH(O\underline{CH}_3)_2$), 49.1 ($CH(O\underline{CH}_3)_2$), 48.5 (C-1´), 43.8 (C-5´), 42.1 (C-5), 40.6 (C-3), 40.2 (C-8a´), 39.0 (C-8´), 38.2 (C-6´), 34.2 (C-4´), 28.7 (Me-5'), 25.9 ($(\underline{CH}_3)_3$C-Si), 25.8 ($(\underline{CH}_3)_3$C-Si), 25.8 ($(\underline{CH}_3)_3$C-Si), 20.0 (C-7´), 18.1 ($(CH_3)_3\underline{C}$-Si), 17.0 (C-6), 11.6 (Me-8a'), -4.4 (Me-Si-$\underline{CH}_3$), -4.9 (Me-Si-$\underline{CH}_3$); **FAB HRMS** calcd for $C_{30}H_{54}SO_9SiNa$ 641.3148, found 641.3155.

(1’*R*,3’*R*,4a’*S*,5’*S*,8a’*S*)-6-[3’α-(*tert*-Butyldimethylsilyl)oxy-3’,4’,4a’,5’,6’,7’,8’,8a’-octahydro-2’(1’H)-methylene-5’β-methoxycarbonyl-5’α,8a’β-dimethylnaphthyl]-2-en-4-oxo-hexanal dimethylacetal (14).

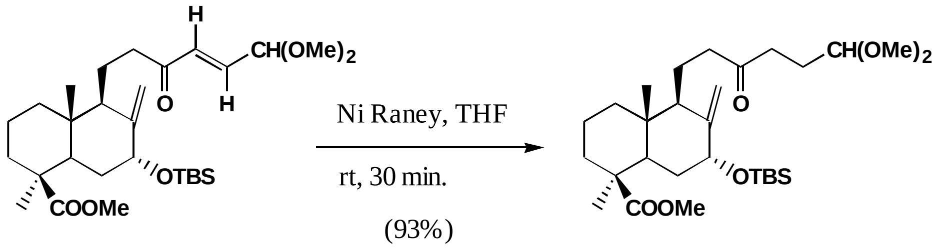


13 **14**

To a solution of **13** (560 mg, 0.90 mmol) in benzene (10 mL) at room temperature was slowly added DBU (280 mg, 1.80 mmol) and the mixture was stirred at room temperature for 3 h. Then, it was diluted with benzene (20 mL), washed with aqueous HCl (1.2 M) (3 x 30 mL) and water (3 x 30 mL), and dried over anhydrous sodium sulfate and evaporated to give a residue which after column chromatography (7:3 hexane/*t*-BuOMe, silica gel) afforded **14** as a colourless oil (435 mg, 92%).

$[\alpha]_D^{25^o}$: -2.0^o (*c* 0.09, CHCl$_3$); **IR** (film, cm^{-1}) ν_{max} 2932, 2887, 2855, 1793, 1725, 1702, 1682, 1645, 1544, 1465, 1443, 1409, 1382, 1359, 1300, 1252, 1222, 1195, 1150, 1129, 1066, 988, 953, 942, 903, 865, 836, 814, 776, 677; **^{1}H NMR** (CDCl$_3$, 400 MHz) δ-0.01 (s, 3H, Me-Si-CH$_3$), 0.04 (s, 3H, Me-Si-CH$_3$), 0.47 (s, 3H, Me-8a’), 0.86 (s, 9H, (CH$_3$)$_3$C-Si), 1.12 (s, 3H, Me-5’), 1.13 (ddd, *J* = 17.4, 13.4, 4.1 Hz, 1H, H-8’α), 1.48-1.55 (m, 2H), 1.77-1.98 (m, 6H), 2.15 (bd, *J* = 12.1 Hz, 1H, H-1’), 2.40 (ddd, *J* = 15.6, 9.2, 6.6 Hz, 1H, H-5A), 2.67 (ddd, *J* = 14.0, 9.1, 4.6 Hz, 1H, H-5B), 3.32 (s, 6H, CH(OCH$_3$)$_2$), 3.59 (s, 3H, 5’-COOCH$_3$), 4.28 (t, *J* = 2.9 Hz, 1H, H-3’), 4.47 (s, 1H, =CH$_2$), 4.92 (s, 1H, =CH’$_2$), 4.93 (dd, *J* = 4.1, 1.3 Hz, 1H, H-1), 6.31 (dd, *J* = 16.1, 1.3 Hz, 1H, H-3), 6.54 (dd, *J* = 16.1, 4.1 Hz, 1H, H-2); **^{13}C NMR** (CDCl$_3$, 75 MHz) δ 200.3 (C-4), 178.0 (COOCH$_3$), 149.7 (C-2´), 139.7 (C-3), 132.1 (C-2), 107.3 (=CH$_2$), 101.0 (C-1), 74.1 (C-3´), 52.9 (C-1´), 51.18 (C-4a´), 49.3 (2C, CH(OCH$_3$)$_2$), 48.5 (COOCH$_3$), 43.8 (C-5´), 40.0 (C-8a´), 39.5 (C-5), 38.9 (C-8´), 38.1 (C-6´), 34.2 (C-4´), 28.7 (Me-5'), 25.8 (3C, (CH$_3$)$_3$C-Si), 20.0 (C-7´), 18.1 ((CH$_3$)$_3$C-Si), 17.2 (C-6), 11.6 (Me-8a'), -4.4 (Me-Si-CH$_3$), -4.9 (Me-Si-CH$_3$); **FAB HRMS** calcd for $C_{29}H_{50}O_6SiNa$ 545.3265, found *m/z* 545.3274.

(1’*R*,3’*R*,4a’*S*,5’*S*,8a’*S*)-6-[3’α-(*tert*-Butyldimethylsilyl)oxy-3’,4’,4a’,5’,6’,7’,8’,8a’-octahydro-2’(1’H)-methylene-5’β-methoxycarbonyl-5’α,8a’β-dimethylnaphthyl]-4-oxo-hexanal dimethylacetal (15).



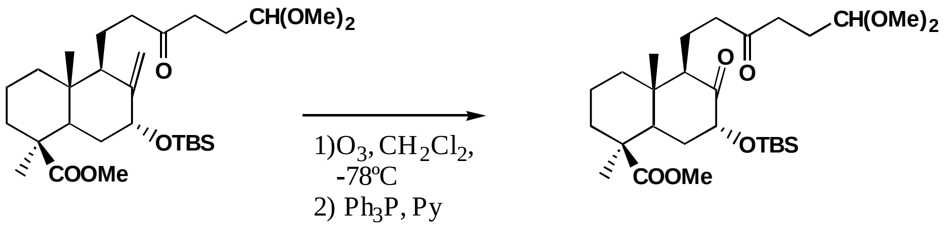
14 **15**

To a solution of **14** (423 mg, 0.81 mmol) in THF (25 mL) at room temperature was added wet Raney Ni (824 mg). After being stirred for 30 min the mixture was filtered through SiO$_2$ and the solvent was evaporated to yield **15** as a colourless oil (399 mg, 94%).

IR (film, cm^{-1}) ν_{max} 3077, 2950, 2933, 2889, 2855, 1723, 1647, 1466, 1440, 1411, 1383, 1362, 1252, 1223, 1195, 1150, 1128, 1068, 989, 939, 901, 867, 837, 814, 776, 678, 655, 627; **^{1}H NMR** (CDCl$_3$, 300 MHz) δ-0.04 (s, 3H, Me-Si-CH$_3$), 0.06 (s, 3H, Me-Si-CH$_3$), 0.47 (s, 3H, Me-8a'), 0.87 (s, 9H, (CH$_3$)$_3$C-Si), 1.12 (s, 3H, Me-5'), 1.49-1.54 (m, 2H), 1.81-1.96 (m, 6H), 2.09 (bs, 1H, H-1'), 3.33 (s, 6H, CH(OCH$_3$)$_2$), 3.60 (s, 3H, 5'-COOCH$_3$), 4.28 (t, *J* = 3.0 Hz, 1H, H-3'), 4.35 (t, *J* = 5.6 Hz, 1H, H-1), 4.46 (s, 1H,

$=\underline{CH}_2$), 4.91 (s, 1H, $=\underline{CH'}_2$); **^{13}C NMR** ($CDCl_3$, 75 MHz) δ 210.5 (C-4), 178.0 (-$\underline{C}OOCH_3$), 149.8 (C-2), 107.3 ($=\underline{CH}_2$), 103.9 (C-1), 74.2 (C-3´), 53.3 (C-1´), 51.2 (C-4a´), 49.3 (-$COO\underline{CH}_3$), 48.6 ($CH(O\underline{CH}_3)_2$), 48.3 ($CH(O\underline{CH}_3)_2$), 43.9 (C-5´), 41.6 (C-5), 40.2 (C-8a´), 39.0 (C-8´), 38.2 (C-6´), 37.4 (C-3), 34.3 (C-4´), 28.7 (Me-5'), 26.6 (C-2), 25.8 (3C, $(\underline{CH}_3)_3C$-Si), 20.1 (C-7´), 18.1 ($(CH_3)_3\underline{C}$-Si), 17.3 (C-6), 11.7 (Me-8a'), -4.5 (Me-Si-$\underline{CH}_3$), -4.9 (Me-Si-$\underline{CH}_3$); **FAB HRMS** calcd for $C_{29}H_{52}O_6SiNa$ 547.3435, found 547.3431.

(1'*R*,3'*R*,4a'*S*,5'*S*,8a'*S*)-6-[3'α-(*tert*-Butyldimethylsilyl)oxy-3',4',4a',5',6',7',8',8a'-octahydro-5'β-methoxycarbonyl-5'α,8a'β-dimethyl-2'(1'H)-naphthalenone-yl]-4-oxo-hexanal dimethylacetal (16).

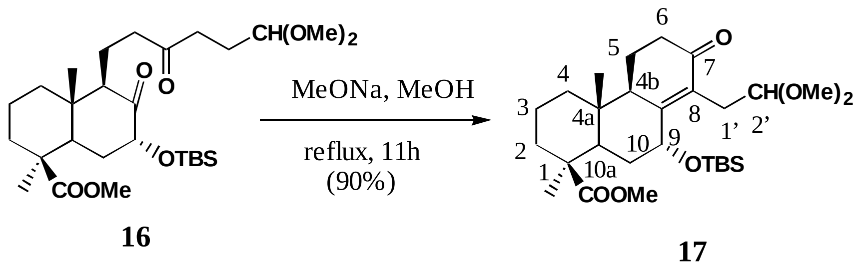


15 **16**

A solution of **15** (1.125 g, 2.14 mmol) in CH_2Cl_2 (40 mL) at –78°C was treated with ozone for 35 min and with Ar for 5 min. Then, triphenylphosphine (674 mg, 2.60 mmol) was added and the resulting mixture was stirred at room temperature for 4 h. The solvent was evaporated and the residue was chromatographed (3:2 hexane/*t*-BuOMe, silica gel) to yield **16** as a colourless oil (1.03 mg, 91%).

$[\alpha]_D^{25^\circ}$: -14° (*c* 0.1, $CHCl_3$); **IR** (film, cm^{-1}) ν_{max} 2950, 2899, 2855, 1721, 1651, 1464, 1439, 1407, 1385, 1363, 1334, 1306, 1254, 1221, 1150, 1120, 1081, 1008, 982, 942, 865, 835, 778, 756, 666; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 0.00 (s, 3H, Me-Si-$\underline{CH}_3$), 0.07 (s, 3H, Me-Si-$\underline{CH}_3$), 0.49 (s, 3H, Me-8a'), 0.89 (s, 9H, $(\underline{CH}_3)_3C$-Si), 1.10 (ddd, *J* = 17.4, 13.4, 4.1 Hz, 1H, H-8'α), 1.18 (s, 3H, Me-5'), 1.31 (dd, *J* = 11.9, 4.3 Hz, 1H, H-4a'), 1.52-1.66 (m, 3H), 1.71-1.87 (m, 6H), 2.03-2.15 (m, 2H), 2.16-2.33 (m, 2H), 2.36-2.70 (m, 2H), 2.89 (dd, *J* = 11.2, 2.9 Hz, 1H ,H-1'), 3.29 (s, 6H, $CH(O\underline{CH}_3)_2$), 3.60 (s, 3H, 5'-$COO\underline{CH}_3$), 3.99 (bs, 1H, H-3'), 4.32 (t, *J* = 5.3 Hz, 1H, H-1); **^{13}C NMR** ($CDCl_3$, 75 MHz) δ 211.6 (C-2´), 209.9 (C-4), 177.4 (-$\underline{C}OOCH_3$), 103.8 (C-1), 75.4 (C-3´), 56.7 (C-1´), 53.2 ($CH(O\underline{CH}_3)_2$), 53.1 ($CH(O\underline{CH}_3)_2$), 51.4 (C-4a´), 47.7 (-$COO\underline{CH}_3$), 44.1 (C-5), 43.9 (C-8a´), 41.4 (C-5), 39.5 (C-8´), 38.0 (C-6´), 37.3 (C-3), 34.2 (C-4´), 28.7 (Me-5'), 26.5 (C-2), 25.7 (3C, $(\underline{CH}_3)_3C$-Si), 19.9 (C-7´), 18.0 ($(CH_3)_3\underline{C}$-Si), 15.7 (C-6), 12.4 (Me-8a'), -4.8 (Me-Si-$\underline{CH}_3$), -4.8 (Me-Si-$\underline{CH}_3$); **FAB HRMS** calcd for $C_{28}H_{50}O_7SiNa$ 549.3220, found 549.3223.

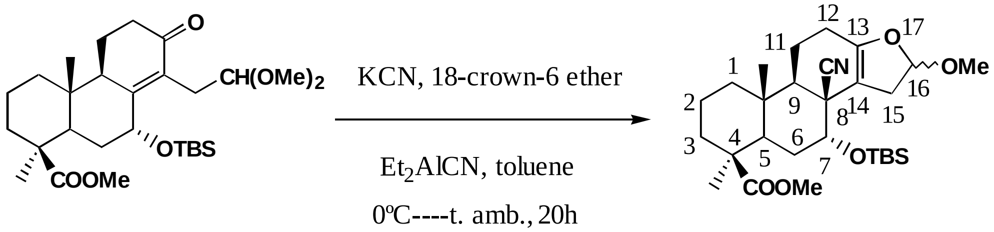
(1*S*,4a*S*,4b*R*,9*R*,10a*S*)-[9’α-(*tert*-Butyldimethylsilyl)oxy]-1,2,3,4,4a,4b,5,6,7,9,10,10a-dodecahydro-1β-methoxycarbonyl-8-(2’,2’-dimethoxyethyl)-1α,4aβ-dimethylphenanthren-7-one (17).



MeONa-MeOH (Na (850 mg):MeOH (25 mL)) was added to a solution of **16** (1.771 g, 3.367 mmol) in MeOH (25 mL) and the mixture was heated under reflux for 11 h. After being cooled to room temperature, the mixture was fractionated into *t*-BuOMe (40 mL) – water (50 mL). The organic phase was washed with water (3 x 40 mL), dried over anhydrous sodium sulfate and evaporated to give a crude product which was chromatographed (6:4 hexane/*t*-BuOMe, silica gel) to yield **17** as a colourless oil (1.55 g, 91%).

$[\alpha]_D^{25^\circ}$: -1.4° (*c* 0.14, $CHCl_3$); **IR** (film, cm^{-1}) ν_{max}: 2951, 2932, 2897, 2854, 2833, 1725, 1673, 1626, 1465, 1439, 1380, 1360, 1343, 1305, 1290, 1252, 1226, 1212, 1203, 1188, 1149, 1125, 1071, 1025, 982, 941, 866, 833, 810, 775, 673; **^{1}H NMR** ($CDCl_3$, 300 MHz) δ -0.05 (s, 3H, Me-Si-$\underline{CH}_3$), 0.05 (s, 3H, Me-Si-$\underline{CH}_3$), 0.60 (s, 3H, Me-4a), 0.85 (s, 9H, $(\underline{CH}_3)_3$C-Si), 0.85-0.92 (m, 1H, H-10a), 1.06 (ddd, *J* = 16.5, 13.0, 3.5 Hz, 1H, H-4α), 1.16 (s, 3H, Me-1), 1.26 (m, 1H), 1.51-58 (m, 1H, H-3β), 1.73-1.85 (m, 2H), 1.91-2.07 (m, 3H), 2.17 (m, 1H, H-5), 2.23 (m, 1H), 2.36-2.48 (m, 3H), 2.66 (t, *J* = 6.8 Hz, 1H, H-4β), 2.89 (dd, *J* = 13.2, 2.9 Hz, 1H, H-4b), 3.28 (s, 3H, $CH(O\underline{CH}_3)_2$), 3.39 (s, 3H, $CH(O\underline{CH}_3)_2$), 3.59 (s, 3H, 1-$COO\underline{CH}_3$), 4.23 (dd, *J* = 5.1, 3.0 Hz, 1H, H-2’), 4. 90 (bs, 1H, H-9); **^{13}C NMR** ($CDCl_3$, 75 MHz) δ 200.3 (C-7), 177.9 (-$\underline{C}OOCH_3$), 160.1 (C-8), 128.9 (C-8a), 105.1 (C-2ʹ), 67.2 (C-9), 55.3 (C-4b), 53.7 ($CH(O\underline{CH}_3)_2$), 53.2 ($CH(O\underline{CH}_3)_2$), 51.2 (C-10a), 48.0 (-$COO\underline{CH}_3$), 43.8 (C-1), 41.6 (C-4a), 39.2 (C-4), 38.1 (C-2), 36.0 (C-6), 32.7 (C-10), 29.8 (C-1ʹ), 28.6 (Me-1), 26.2 ($(\underline{CH}_3)_3$C-Si), 25.9 ($(\underline{CH}_3)_3$C-Si), 25.8 ($(\underline{CH}_3)_3$C-Si), 19.8 (C-3), 19.6 (C-5), 18.0 ($(CH_3)_3\underline{C}$-Si), 13.1 (Me-4a), -4.5 (Me-Si-$\underline{CH}_3$), -4.5 (Me-Si-$\underline{CH}_3$); **FAB HRMS** calcd for $C_{28}H_{48}O_6SiNa$ 531.3107, found 531.3110.

(4*S*,5*S*,7*R*,8*R*,9*R*,10*S*,16*R*)-7α-[(*tert*-Butyldimethylsilyl)oxy]-8β-cyano-1,2,3,4,5,6,7,8,9,10,11,12,15,16-tetradecahydro-4β-methoxycarbonyl-16β-methoxy-17-oxa-cyclopenta[a]-4α,10β-dimethylphenanthrene (18a) and (4*S*,5*S*,7*R*,8*R*,9*R*,10*S*,16*S*)-7α-[(*tert*-butyldimethylsilyl)oxy]-8β-cyano-1,2,3,4,5,6,7,8,9,10,11,12,15,16-tetradecahydro-4β-methoxycarbonyl-16α-methoxy-17-oxa-cyclopenta[a]-4α,10β-dimethylphenanthrene (18b)



17

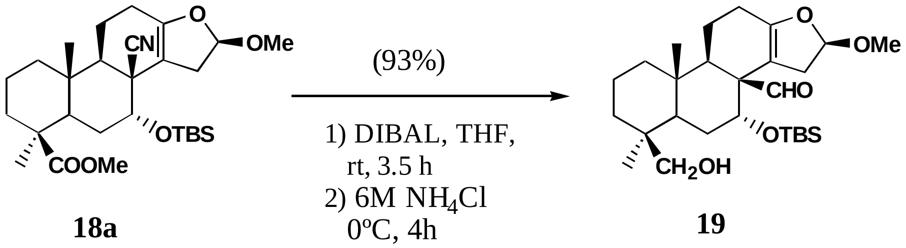
18a 16β–OMe
18b 16α–OMe

To a solution of **17** (500 mg, 0.984 mmol), 18-crown-6-ether (130 mg, 1.075 mmol) and KCN (649 mg, 9.84 mmol) in a 1:1 mixture of toluene-benzene (14 mL) at 0°C was added Et_2AlCN (1.0 M in toluene, 2.95 mmol). The reaction was stirred at room temperature for 20 h. Then, the solution was cooled to 0°C and an aqueous NaOH solution (1 M, 15 mL) was added. The resulting mixture was fractionated into *t*-BuOMe (25 mL) – water (25 mL). The organic phase was washed with water (3 x 3 0 mL), dried over anhydrous sodium sulfate and evaporated to afford a residue which was chromatographed (9:1 hexane/*t*-BuOMe, silica gel) to yield **18a** (0.738 g, 75%) and **18b** (0.118 g, 12%) as colourless oils.

18a: $[\alpha]_D^{25^\circ}$: +171° (*c* 0.1, $CHCl_3$); **IR** (film, cm^{-1}) ν_{max} 2951, 2929, 2854, 1725, 1465, 1445, 1409, 1384, 1363, 1343, 1329, 1310, 1290, 1253, 1228, 1151, 1099, 1068, 1036, 1018, 983, 948, 913, 869, 835, 809, 774, 720, 678; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ -0.005 (s, 3H, Me-Si-$\underline{CH_3}$), 0.06 (s, 3H, Me-Si-$\underline{CH_3}$), 0.57 (s, 3H, Me-10), 0.85 (s, 9H, $(\underline{CH_3})_3$C-Si), 1.03 (d, *J* = 3.9 Hz, 1H, H-5), 1.09 (ddd, *J* = 11.3, 7.0, 3.9 Hz, 1H, H-1α), 1.15 (s, 3H, Me-4), 1.40 (ddd, *J* = 14.9, 11.6, 3.4 Hz, 1H, H-11α), 1.45-1.50 (m, 1H), 1.51-1.53 (m, 1H), 1.55-1.57 (m, 1H), 1.58-1.60 (m, 1H, H-12β), 1.63 (bd, *J* = 13.5 Hz, 1H, H-6β), 1.77 (qt, *J* = 13.4, 3.4 Hz, 1H, H-2β), 1.84-1.91 (m, 1H, H-1β), 2.04 (dd, *J* = 10.9, 3.2 Hz, 1H, H-6), 2.20 (bd, *J* = 13.48 Hz, 1H, H-11α), 2.34-2.40 (m, 2H), 2.73 (d, *J* = 3.7 Hz, 1H, H-15A), 2.74 (d, *J* = 3.7 Hz, 1H, H-15B), 3.28 (s, 3H, 16-O$\underline{CH_3}$), 3.61 (s, 3H, 4-COO$\underline{CH_3}$), 4.46 (t, *J* = 2.0 Hz, 1H, H-7), 5.14 (dd, *J* = 3.7, 2.6 Hz, 1H, H-16); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 177.9 (-$\underline{C}OOCH_3$), 137.5 (C-20), 128.1 (C-14), 120.2 (C-13), 103.7 (C-16), 75.4 (C-8), 67.3 (C-7), 54.8 (C-17), 51.4 (-COO$\underline{CH_3}$), 48.2 (C-9), 44.4 (C-5), 43.7 (C-4), 40.3 (C-10), 38.5 (C-1), 38.1 (C-3), 34.6 (C-12), 34.0 (C-6), 33.0 (C-15), 28.7 (C-18), 25.8 (3C, $(\underline{CH_3})_3$C-Si), 19.6 (C-2), 18.4 (C-11), 18.0 ($(CH_3)_3\underline{C}$-Si), 12.0 (C-19), -4.6 (Me-Si-$\underline{CH_3}$), -4.7 (Me-Si-$\underline{CH_3}$); **FAB HRMS** calcd for $C_{28}H_{45}NO_5SiNa$ 526.2962, found 526.2964.

18b: $[\alpha]_D^{25°}$: -7.3° (*c* 0.11, $CHCl_3$); **IR** (film, cm^{-1}) ν_{max} 2951, 2929, 2854, 1725, 1465, 1445, 1409, 1384, 1363, 1343, 1329, 1310, 1290, 1253, 1228, 1151, 1099, 1068, 1036, 1018, 983, 948, 913, 869, 835, 809, 774, 720, 678; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ -0.05 (s, 3H, Me-Si-$\underline{CH_3}$), 0.06 (s, 3H, Me-Si-$\underline{CH_3}$), 0.58 (s, 3H, Me-10), 0.85 (s, 9H, $(\underline{CH_3})_3$C-Si), 1.03 (d, *J* = 3.9 Hz, 1H, H-5), 1.09 (ddd, *J* = 13.2, 9.5, 3.8 Hz, 1H, H-1α), 1.14 (s, 3H, Me-4), 1.24-1.30 (m, 1H), 1.35 (ddd, *J* = 15.0, 11.9, 3.6 Hz, 1H, H-11α), 1.49 (dt, *J* = 13.8, 3.3 Hz, 1H, H-12β), 1.61-1.66 (m, 1H), 1.78 (qt, *J* = 13.7, 3.4 Hz, 1H, H-2β), 1.82-1.91 (m, 2H), 2.02 (dd, *J* = 11.0, 3.2 Hz, 1H, H-6), 2.20 (bd, *J* = 13.1 Hz, 1H, H-9), 2.32 (bd, *J* = 7.48 Hz, 1H, H-11β), 2.33-2.38 (m, 2H), 2.65 (dt, *J* = 16.7, 2.6 Hz, 1H, H-15A), 2.93 (ddd, *J* = 16.7, 5.7, 1.8 Hz, 1H, H-15B), 3.48 (s, 3H, 16-O$\underline{CH_3}$), 3.62 (s, 3H, 4-COO$\underline{CH_3}$), 4.38 (t, *J* = 2.0 Hz, 1H, H-7), 5.16 (dd, *J* = 5.7, 2.3 Hz, 1H, H-16); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 177.7 (-$\underline{C}OOCH_3$), 136.8 (C-20), 128.5 (C-14), 120.6 (C-13), 105.0 (C-16), 73.2 (C-8), 67.2 (C-7), 55.6 (C-17), 51.4 (-COO$\underline{CH_3}$), 48.2 (C-9), 44.7 (C-5), 43.6 (C-4), 40.1 (C-10), 38.5 (C-1), 38.1 (C-3), 34.7 (C-6), 34.6 (C-12), 32.9 (C-15), 28.7 (C-18), 26.0 ($(\underline{CH_3})_3$C-Si), 25.7 ($(\underline{CH_3})_3$C-Si), 25.7 ($(\underline{CH_3})_3$C-Si), 19.5 (C-2), 18.4 (C-11), 18.4 ($(CH_3)_3\underline{C}$-Si), 11.9 (C-19), -4.3 (Me-Si-$\underline{CH_3}$), -4.4 (Me-Si-$\underline{CH_3}$); **FAB HRMS** calcd for $C_{28}H_{45}NO_5SiNa$ 526.2962, found 526.2965.

(4*S*,5*S*,7*R*,8*R*,9*R*,10*S*,16*R*)-7α-[(*tert*-Butyldimethylsilyl)oxy]-1,2,3,4,5,6,7,8,9,10,11,12,15,16-tetradecahydro-4β-hydroxymethyl-16β-methoxy-17-oxa-cyclopenta[a]-4α,10β-dimethylphenanthren-8-al (19).

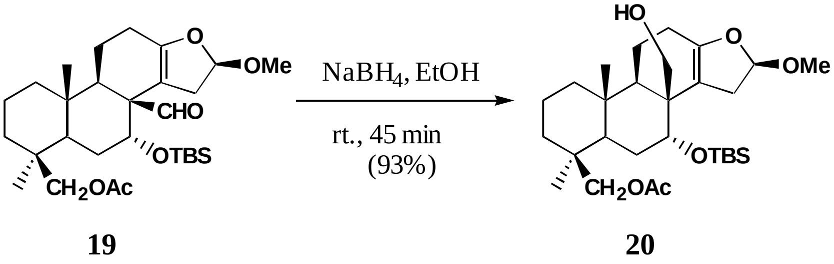


To a solution of **18a** (385 mg, 0.765 mmol) in THF (8 mL) at 0°C was added DIBAL (1 M in hexane, 1.68 mmol) and the mixture was stirred at room temperature for 3.5 h. Then, the solution was cooled to 0°C and an aqueous NH_4Cl solution (6 M, 15 mL) was added, and the resulting mixture was further stirred for 6 h. It was fractionated into *t*-BuOMe (30 mL) – water (30 mL), and the organic phase was washed with water (3 x 30 mL), dried over anhydrous sodium sulfate and evaporated to yield **19** as a colourless oil (340 mg, 93%):

$[\alpha]_D^{25°}$: +36° (*c* 0.14, $CHCl_3$); **IR** (film, cm^{-1}) ν_{max} 3581, 3469, 2927, 2855, 1733, 1657, 1465, 1447, 1405, 1365, 1252, 1213, 1098, 1062, 1030, 963, 871, 834, 809, 774; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 0.04 (s, 3H, Me-Si-$\underline{CH_3}$), 0.07 (s, 3H, Me-Si-$\underline{CH_3}$), 0.60 (s, 3H, Me-10), 0.87 (s, 9H, $(\underline{CH_3})_3$C-Si), 1.07 (ddd, *J* = 17.6, 12.2, 5.80 Hz, 1H, H-1α), 1.24 (s, 3H, Me-4), 1.34-1.60 (m, 2H), 1.71-1.78 (m, 4H), 1.81-1.90 (m, 3H), 2.27-2.37 (m, 2H), 2.48 (d, *J* = 14.8 Hz, 1H, H-15A), 2.75 (d. *J* = 14.8 Hz, 1H, H-15B), 3.28 (s, 3H, 16-O$\underline{CH_3}$), 3.39 (d, *J* = 10.8 Hz, 1H, 4-$\underline{CH_2}$OH-A), 3.76 (d, *J* = 10.8 Hz, 1H, 4-$\underline{CH_2}$OH-B), 4.49 (bs, 1H, H-7), 5.14 (d, *J* = 5.3 Hz, 1H, H-16), 9.45 (s, 1H, 8-C$\underline{H}$O).

^{13}**C NMR** had not been recorded due to the instability of the compound; **FAB HRMS** calcd for $C_{27}H_{46}O_5SiNa$ 501.3015, found 501.3012.

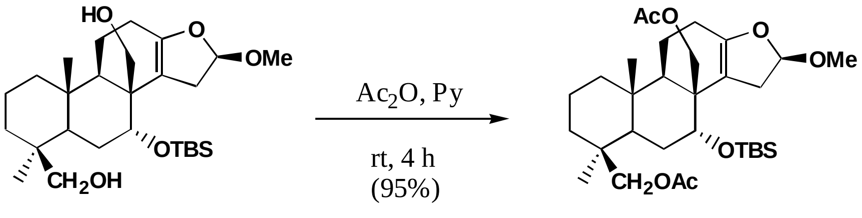
(4*S*,5*S*,7*R*,8*R*,9*R*,10*S*,16*R*)-7α-[(*tert*-Butyldimethylsilyl)oxy]-1,2,3,4,5,6,7,8,9,10,11,12,15,16-tetradecahydro-16β-methoxy-17-oxa-cyclopenta[a]-4β,8β-dihydroxymethyl-4α,10β-dimethylphenanthrene (20).



To a solution of **19** (280 mg, 0.58 mmol) in EtOH (7 mL) at 0°C was added $NaBH_4$ (85 mg, 2.23 mmol) and the mixture was stirred at room temperature for 30 min. Then, the solution was cooled to 0°C and water (1 mL) was added. The resulting mixture was stirred for 5 min and fractionated into *t*-BuOMe (20 mL) – water (20 mL). The organic phase was washed with water (3 x 30 mL), dried over anhydrous sodium sulfate and evaporated to yield **20** as a colourless oil (262 mg, 93%).

$[\alpha]_D^{25^\circ}$: -26° (*c* 0.35, $CHCl_3$); **IR** (film, cm^{-1}) ν_{max} 3433, 2949, 2926, 2853, 1713, 1660, 1466, 1446, 1364, 1252, 1214, 1153, 1069, 1032, 980, 922, 871, 834, 808, 773, 699, 673; ^{1}**H NMR** ($CDCl_3$, 300 MHz) δ 0.05 (s, 3H, Me-Si-$\underline{CH_3}$), 0.08 (s, 3H, Me-Si-$\underline{CH_3}$), 0.66 (s, 3H, Me-10), 0.88 (s, 9H, $(\underline{CH_3})_3$C-Si), 0.96 (s, 3H, Me-4), 0.99-1.31 (m, 4H), 1.39-1.50 (m, 2H), 1.58 (bd, *J* = 13.8 Hz, 1H, H-2α), 1.65-1.73 (m, 1H), 1.79-1.92 (m, 2H), 2.18 (m, 1H), 2.35 (m, 1H), 2.59 (ddd, *J* = 14.6, 8.0, 2.9 Hz, 1H, H-15A), 2.69 (d, *J* = 14.6 Hz, 1H, H-15B), 3.27 (s, 3H, 16-O$\underline{CH_3}$), 3.39 (d, *J* = 11.3 Hz, 1H, 4-$\underline{CH_2}$OH-A), 3.41 (d, *J* = 10.8 Hz, 1H, 8-$\underline{CH_2}$OH-A), 3.50 (d, *J* = 11.3 Hz, 1H, 4-$\underline{CH_2}$OH-B), 3.78 (d, *J* = 10.8 Hz, 1H, 8-$\underline{CH_2}$OH-B), 4.46 (t, *J* = 2.8 Hz, 1H, H-7), 5.05 (d, *J* = 5.0 Hz, 1H, H-16); ^{13}**C NMR** ($CDCl_3$, 75 MHz) δ 134.6 (C-14), 131.2 (C-13), 102.6 (C-16), 82.7 (C-8), 67.5 (C-7), 66.7 (4-$\underline{CH_2}$OH), 65.7 (C-20), 53.8 (C-17), 47.8 (C-9), 45.6 (C-5), 38.8 (C-10), 38.4 (C-1), 38.1 (C-4), 35.8 (C-3), 35.8 (C-6), 31.5 (C-12), 30.3 (C-15), 27.0 (C-18), 25.9 (3C, $(\underline{CH_3})_3$C-Si), 19.2 (C-2), 18.7 (C-11), 18.1 ($(CH_3)_3\underline{C}$-Si), 14.4 (C-19), -4.5 (Me-Si-$\underline{CH_3}$), -4.6 (Me-Si-$\underline{CH_3}$); **FAB HRMS** calcd for $C_{27}H_{48}O_5SiNa$ 503.3164, found 503.3168.

(4*S*,5*S*,7*R*,8*R*,9*R*,10*S*,16*R*)-4β,8β-Di(acetoxymethyl)-7α-[(*tert*-butyldimethylsilyl)oxy]-1,2,3,4,5,6,7,8,9,10,11,12,15,16-tetradecahydro-16β-methoxy-17-oxacyclopenta[a]-4α,10β-dimethylphenanthrene (21).

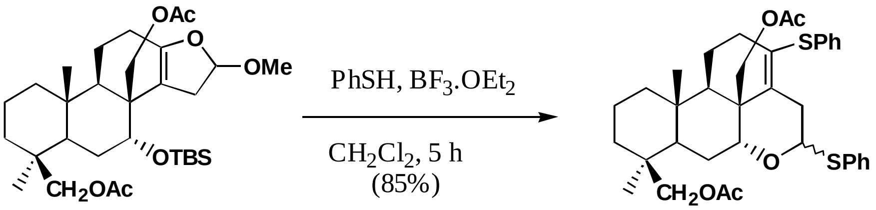


20 **21**

A mixture of **20** (280 mg, 0.58 mmol), pyridine (5 mL) and Ac_2O (1.5 mL) was stirred at room temperature for 4 h. The reaction mixture was poured into an ice bath and extracted with *t*-BuOMe (3 x 20 mL). The organic phase was successively washed with 1.2 M HCl (3 x 20 mL), 5% aqueous $NaHCO_3$ (3 x 30 mL), water (3 x 30 mL), and dried over anhydrous sodium sulfate. After evaporating the solvent, **21** was obtained as a colourless oil (314 g, 95%):

$[\alpha]_D^{25^o}$: +51° (*c* 0.21, $CHCl_3$); **IR** (film, cm^{-1}) ν_{max} 2949, 2930, 2855, 1741, 1649, 1467, 1368, 1341, 1235, 1153, 1085, 1026, 965, 924, 869, 835, 809, 774, 757; **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 0.02 (s, 3H, Me-Si-$\underline{CH_3}$), 0.05 (s, 3H, Me-Si-$\underline{CH_3}$), 0.68 (s, 3H, Me-10), 0.84 (s, 9H, $(\underline{CH_3})_3$C-Si), 0.91 (s, 3H, Me-4), 1.07 (ddd, *J* = 16.9, 13.0, 4.4 Hz, 1H, H-1α), 1.15-1.25 (m, 2H), 1.31 (dd, *J* = 14.7, 3.4 Hz, 1H, H-5), 1.41-1.89 (m, 6H), 2.01 (s, 3H, 4-$CH_2OCO\underline{CH_3}$), 2.07 (s, 3H, 8-$CH_2OCO\underline{CH_3}$), 2.03-2.22 (m, 2H), 2.34 (t, *J* = 7.8 Hz, 1H, H-11β), 2.59 (ddd, *J* = 14.4, 7.8, 3.0 Hz, 1H, H-15A), 2.66 (d, *J* = 14.4 Hz, 1H, H-15B), 3.23 (s, 3H, 16-O$\underline{CH_3}$), 3.86 (d, *J* = 11.0 Hz, 1H, 4-$\underline{CH_2}$OAc-A), 3.90 (d, *J* = 11.7 Hz, 1H, 8-$\underline{CH_2}$OAc-A), 4.09 (d, *J* = 11.7 Hz, 1H, 8-$\underline{CH_2}$OAc-B), 4.18 (d, *J* = 11.0 Hz, 1H, 4-$\underline{CH_2}$OAc-B), 4.45 (t, *J* = 2.6 Hz, 1H, H-7), 5.04 (d, *J* = 4.2 Hz, 1H, H-16); **^{13}C NMR** ($CDCl_3$, 75 MHz) δ 171.3 (-$CH_2O\underline{C}OCH_3$), 171.0 (-$CH_2O\underline{C}OCH_3$), 134.9 (C-14), 130.9 (C-13), 102.8 (C-16), 80.7 (C-8), 68.3 ($\underline{CH_2}$OAc), 67.4 (C-7), 67.2 (C-20), 53.9 (C-17), 47.8 (C-9), 45.63 (C-5), 38.77 (C-10), 38.15 (C-1), 36.57 (C-4), 36.49 (C-3), 35.75 (C-6), 31.4 (C-12), 31.0 (C-15), 27.5 (C-18), 25.8 (3C, $(\underline{CH_3})_3$C-Si), 21.1 (-$CH_2OCO\underline{CH_3}$), 21.0 (-$CH_2OCO\underline{CH_3}$), 19.2 (C-2), 18.6 (C-11), 18.0 ($(CH_3)_3\underline{C}$-Si), 14.3 (C-19), -4.5 (Me-Si-$\underline{CH_3}$), -4.6 (Me-Si-$\underline{CH_3}$); **FAB HRMS** calcd for $C_{31}H_{52}O_7SiNa$ 587.3380, found 587.3380.

(4*S*,5*S*,7*R*,8*R*,9*R*,10*S*,16*R*)-4β,20-Di(acetoxymethyl)-13,16β-di(phenylthio)-21-norpicras-13-ene (22a) and (4*S*,5*S*,7*R*,8*R*,9*R*,10*S*,16*S*)-4β,20-di(acetoxymethyl)-13,16α-di(phenylthio)-21-norpicras-13-ene (22b).



21

22a 16β-SPh
22b 16α-SPh

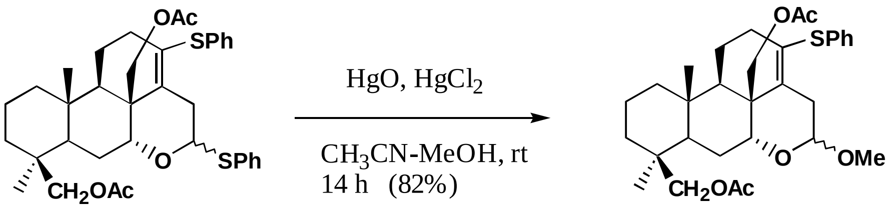
To a solution of **21** (85 mg, 0.150 mmol) in CH_2Cl_2 (5 mL) at 0°C was added thiophenol (42 mg, 0.375 mmmol) and $BF_3{\cdot}OEt_2$ (0.15 mL, 0.173 mmol) and the mixture was stirred at room temperature for 5 h. Then, the solution was cooled to 0°C and an 5% aqueous $NaHCO_3$ solution was added until neutralization. The resulting mixture was vigorously stirred for 15 min and then fractionated into *t*-BuOMe (30 mL) – water (30 mL). The organic phase was washed with water (3 x 30 mL), dried over anhydrous sodium sulfate and evaporated to give a crude product which was chromatographed (3:2 hexane/*t*-BuOMe, silica gel) to yield **22a** (51 mg, 55%) and **22b** (28 m g, 30%) as colourless oils:

22a: $[\alpha]_D^{25°}$: +2.3° (*c* 0.1, $CHCl_3$); **IR** (film, cm^{-1}) ν_{max} 3040, 2930, 2867, 1737, 1471, 1452, 1440, 1373, 1235, 1130, 1095, 1031, 982, 752, 693, 665; **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 0.73 (s, 3H, Me-10), 0.90 (s, 3H, Me-4), 0.92 (m, 1H, H-1α), 1.06-1.23 (m, 1H, H-9), 1.29 (m, 1H, H-5), 1.40 (dd, *J* = 14.5, 5.8 Hz, 1H, H-15A), 1.49-1.60 (m, 2H), 1.68 (dd, *J* = 14.5, 5.8 Hz, 1H, H-15B), 1.71 (m, 1H, H-6A), 1.75 (m, 1H, H-6B), 1.92-2.09 (m, 1H, H-12A), 2.02 (s, 3H, 4-$CH_2OCO\underline{CH_3}$), 2.09 (s, 3H, 8-$CH_2OCO\underline{CH_3}$), 2.13 (m, 1H, H-9), 2.17 (m, 1H), 2.40 (m, 1H, H-11β), 2.68 (ddd, *J* = 11.0, 7.8, 3.0 Hz, 1H, H-12β), 3.82 (d, *J* = 12.0 Hz, 1H, C4-$\underline{CH_2}$OAc-A), 3.83 (d, *J* = 12.0 Hz, 1H, C4-$\underline{CH_2}$OAc-B), 4.10 (bs, 1H, H-7), 4.20 (d, *J* = 11.4 Hz, 1H, C8-$\underline{CH_2}$OAc-A), 4.25 (d, *J* = 11.4 Hz, 1H, C8-$\underline{CH_2}$OAc-B), 4.40 (dt, *J* = 6.3, 2.2 Hz, 1H, H-16), 7.27-7.35 (m, 6H), 7.44-7.52 (m, 4H); **^{13}C NMR** ($CDCl_3$, 75 MHz) δ 171.3 ($CH_2O\underline{C}OCH_3$), 171.0 ($CH_2O\underline{C}OCH_3$), 137.8 (C_6H_5-1´), 136.5 (C-14), 134.7 (C_6H_5-1´´), 131.3 (C-13), 129.1 (C_6H_5-3´), 128.8 (C_6H_5-3´´), 128.7 (C_6H_5-2´), 128.5 (C_6H_5-2´´), 128.3 (C_6H_5-4´), 128.0 (C_6H_5-4´´), 81.5 (C-8), 72.9 (C-16), 66.9 ($\underline{CH_2}$OAc), 63.7 (C-20), 49.9 (C-7), 49.3 (C-9), 48.6 (C-15), 48.3 (C-4), 47.3 (C-5), 38.5 (C-10), 38.2 (C-1), 36.3 (C-3), 35.8 (C-6), 27.3 (C-18), 27.0 (C-12), 21.1 ($CH_2OCO\underline{CH_3}$), 21.0 ($CH_2OCO\underline{CH_3}$), 19.3 (C-11), 18.6 (C-2), 14.9 (C-19); **FAB HRMS** calcd for $C_{36}H_{44}O_5S_2Na$ 643.2528, found *m/z* 643.2528.

22b: $[\alpha]_D^{25°}$: +1.2° (*c* 0.05, $CHCl_3$); **IR** (film, cm^{-1}) ν_{max} 3050, 2928, 2854, 1737, 1580, 1474, 1440, 1389, 1371, 1330, 1237, 1154, 1113, 1088, 1031, 982, 916, 749, 693, 666; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 0.78 (s, 3H, Me-10), 0.92 (s, 3H, Me-4), 0.75-0.98 (m, 2H), 1.24-1.37 (m, 2H), 1.48-1.79 (m, 4H), 1.82-1.98 (m, 2H), 2.02 (s, 3H, 4-$CH_2OCO\underline{CH_3}$), 2.06 (s, 3H, 8-$CH_2OCO\underline{CH_3}$), 1.99-2.10 (m, 2H), 2.45 (dd, *J* = 15.2, 9.4

Hz, 1H, H-11β), 2.71 (m, 1H, H-12β), 3.68 (d, *J* = 12.0 Hz, 1H, 4-$\underline{CH}_2$OAc-A), 3.71 (d, *J* = 12.0 Hz, 1H, 4-$\underline{CH}_2$OAc-B), 3.83 (d, *J* = 10.9 Hz, 1H, 8-$\underline{CH}_2$OAc-A), 4.17 (d, *J* = 10.9 Hz, 1H, 8-$\underline{CH}_2$OAc-B), 4.30 (s, 1H, H-7), 4.64 (dd, *J* = 9.4, 5.9 Hz, 1H, H-16), 7.25-7.35 (m, 6H), 7.42-7.44 (m, 2H), 7.46-7.49 (m, 2H); ^{13}**C NMR** ($CDCl_3$, 75 MHz) δ 173.1 ($CH_2O\underline{C}OCH_3$), 170.5 ($CH_2O\underline{C}OCH_3$), 140.2 (C-14), 135.4 (C_6H_5-1´), 134.1 (C_6H_5-1´´), 132.7 (C_6H_5-3´), 132.4 (C-13), 129.1 (C_6H_5-3´´), 129.05, 129.0 (C_6H_5-2´), 128.5 (C_6H_5-4´), 128.1 (C_6H_5-2´´), 128.0 (C_6H_5-4´´), 72.0 (C-8), 69.5 ($\underline{CH_2}$OAc), 66.9 (C-20), 60.0 (C-16), 49.1 (C-7), 48.6 (C-9), 47.8 (C-4), 47.0 (C-5), 39.9 (C-10), 38.6 (C-1), 36.1 (C-3), 34.7 (C-6), 32.4 (C-15), 27.3 (C-18), 27.1 (C-12), 21.0 (2C, $CH_2OCO\underline{CH_3}$), 18.6 (C-2), 16.1 (C-11), 15.6 (C-19); **FAB HRMS** calcd for $C_{36}H_{44}O_5S_2Na$ 643.2528, found *m/z* 643.2526.

(4*S*,5*S*,7*R*,8*R*,9*R*,10*S*,16*R*)-4β,20-Di(acetoxymethyl)-16-methoxy-13-phenylthio-21-norpicras-13-ene (23).



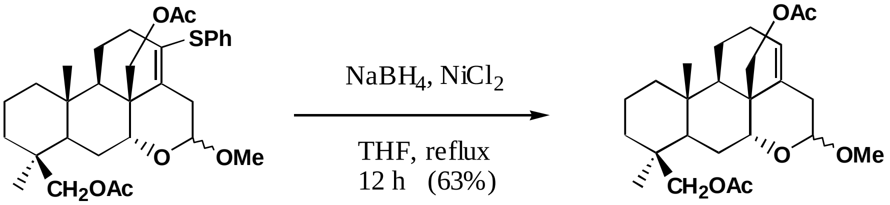
22a-b **23**

HgO (200 mg, 0.92 mmol) and $HgCl_2$ (160 mg, 0.57 mmol) were added to a solution of **22-ab** (85 mg, 0.137 mmol) in acetonitrile (2 mL) – MeOH (2 mL) and the mixture was stirred at room temperature for 14 h. The mixture was filtered and washed with *t*-BuOMe (3 x 15 mL). After evaporating the solvent, the residue was disolved in *t*-BuOMe (50 mL) and the solution was successively washed with 10% aqueous potassium iodide (3 x 30 mL) and brine (3 x 30 mL). The organic phase was dried over anhydrous sodium sulfate and evaporated to give a residue which after column chromatography (1:1 hexane/*t*-BuOMe, silica gel) gave **23** (61 mg, 82%) as a colourless oil.

IR (film, cm^{-1}) ν_{max} 3030, 2930, 2860, 1735, 1469, 1435, 1240, 1130, 1090, 1040, 950, 740; **FAB HRMS** calcd for $C_{31}H_{42}O_6SNa$ *m/z* 565.2599, found *m/z* 565.2601; ^{1}**H NMR** (CD_3COCD_3, 300 MHz) δ 0.79 (s, 9H, Me-10, Me-4), 0.92 (s, 3H, Me-4), 1.94 (s, 3H, AcO), 1.97 (s, 3H, AcO), 2.02 (s, 3H, AcO), 2.03 (s, 3H, AcO), 2.76 (d, *J* = 15.2 Hz, 1H), 2.81 (ddd, *J*= 15.2, 5.9, 3.5 Hz, 1H), 2.97 (s, 3H, MeO), 3.22 (s, 3H, MeO), 3.75 (d, *J* = 11.1 Hz, 1H, CH_2-OAc), 3.83 (d, *J* = 11.1 Hz, 1H, CH_2-OAc), 4.00 (d, *J* = 11.6 Hz, 1H, CH_2-OAc), 4.04 (d, *J* = 11.6 Hz, 1H, CH_2-OAc), 4.05 (d, *J* = 11.6 Hz, 1H, CH_2-OAc), 4.16 (d, *J* = 11.6 Hz, 1H, CH_2-OAc), 4.21 (bs, 1H, H-7), 4.25 (d, *J* = 11.1 Hz, 1H, CH_2-OAc), 4.27 (d, *J* = 11.1 Hz, 1H, CH_2-OAc), 4.31 (dd, *J* = 4.0, 1.9 Hz, 1H, H-16), 5.13 (d, *J* = 5.1 Hz, 1H, H-16), 7.05-7.60 (m, 10H, SPh); ^{13}**C NMR** (CD_3COCD_3, 75 MHz) δ 170.9* ($CH_2O\underline{C}OCH_3$), 170.8 ($CH_2O\underline{C}OCH_3$), 170.7 ($CH_2O\underline{C}OCH_3$), 136.4 (C-14), 136.2 (C-14), 135.9 (C_6H_5-1´), 133.8 (C_6H_5-3´), 133.3 (C_6H_5-3´), 131.1 (C-13), 131.0 (C-13), 129.8 (C_6H_5-2´), 129.4 (C_6H_5-2´), 128.1 (C_6H_5-

4´), 126.2 (C_6H_5-4´), 104.5 (C-16), 103.7 (C-16), 81.5 (C-8), 81.0 (C-8), 66.8 ($\underline{C}H_2$-OAc), 66.7 ($\underline{C}H_2$-OAc), 66.6 ($\underline{C}H_2$-OAc), 55.1 ($O\underline{C}H_3$), 53.7 ($O\underline{C}H_3$), 50.2$^{\#}$ (C-7), 49.8$^{\#}$ (C-7), 49.6$^{\#}$ (C-9), 49.5$^{\#}$ (C-9), 48.7$^{\#}$ (C-5), 47.4$^{\#}$ (C-5), 39.3 (C-4), 38.9 (C-4), 38.6* (C-1), 37.3* (C-10), 36.8 (C-3), 36.7 (C-3), 36.3 (C-6), 36.0 (C-6), 31.7 (C-15), 30.2 (C-15), 27.7 (C-18), 27.6 (C-10), 27.5 (C-12), 26.8 (C-12), 20.8 ($OCO\underline{C}H_3$), 20.7* ($OCO\underline{C}H_3$), 20.6 ($OCO\underline{C}H_3$), 20.3 (C-11), 19.3 (C-11), 19.0* (C-2), 15.1 (C-19), 14.9 (C-19) (* overlapped signals for two stereoisomers; $^{\#}$ interchangeable signals); **FAB HRMS** calcd for $C_{31}H_{42}O_6SNa$ 565.2600, found 565.2602.

(4*S*,5*S*,7*R*,8*R*,9*R*,10*S*,16*R*)-4β,20-Di(acetoxymethyl)-16-methoxy-21-norpicras-13-ene (24).



23 **24**

$NaBH_4$ (8 mg, 0.21 mmol) and $NiCl_2$ (12 mg, 0.093 mmol) were added to a solution of **23** (40 mg, 0.073 mmol) in THF (5mL) and the mixture was refluxed for 12 h. Then it was filtered through a short silica gel column (5 g), washing with t-BuOMe, and concentrated to give **24** (20 mg, 63%) as a colourless oil.

IR (film, cm^{-1}) ν_{max} 2960, 2855, 1735, 1670, 1475, 1435, 1230, 1120, 1070, 1035, 935, 810; ^{1}**H NMR** (CD_3COCD_3, 300 MHz) δ 0.76 (s, 3H, Me-10), 0.77 (s, 3H, Me-10), 0.98 (s, 3H, Me-4), 1.00 (s, 3H, Me-4), 1.10-1.95 (m, 12H), 2.06 (9H, AcO), 2.07 (s, 3H, AcO), 2.10-2.30 (m, 2H), 2.39-2.57 (m, 4H), 2.90 (d, *J* = 13.7, 6.3 Hz, 2H), 3.33 (s, 3H, MeO), 3.41 (s, 3H, MeO), 3.88 (d, *J* = 11.8 Hz, 1H), 3.89 (d, *J* = 11.8 Hz, 1H), 3.93 (d, *J* = 11.1 Hz,1H), 3.97 (d, *J* = 11.1 Hz, 1H), 4.12 (d, *J* = 11.1 Hz, 1H), 4.17 (d, *J* = 11.1 Hz, 1H), 4.18 (d, *J* = 11.8 Hz, 1H), 4.24 (bs, 2H, H-7), 4.26 (d, *J* = 11.8 Hz, 1H), 5.07(dd, *J* = 6.3, 3.2 Hz, 2H, H-16), 5.08 (bs, 2H, H-1 3). ^{13}**C NMR** (CD_3COCD_3, 75 MHz) δ 171.3* ($O\underline{C}OCH_3$), 171.2* ($O\underline{C}OCH_3$), 125.3* (C-13), 123.4 (C-14), 104.4 (C-16), 103.1 (C-16), 80.8 (C-8), 68.3 ($\underline{C}H_2OAc$), 66.9* ($\underline{C}H_2OAc$), 66.6 ($\underline{C}H_2OAc$), 55.9* (OCH_3), 51.8 (C-7), 51.7 (C-7), 49.4* (C-9), 47.3 (C-5), 47.2 (C-5), 39.4 (C-4), 39.0 (C-4), 38.5 (C-1), 38.4 (C-1), 37.1* (C-10), 36.4 (C-3)$^{*\#}$, 36.2$^{\#}$ (C-6), 36.1$^{\#}$ (C-6), 31.8 (C-15), 31.3 (C-15), 27.6* (C-18), 22.5 (C-12), 22.3 (C-12), 21.0* ($OCO\underline{C}H_3$), 19.1 (C-11), 18.6 (C-11), 18.6* (C-2), 15.1* (C-19) (* overlapped signals for two stereoisomers; $^{\#}$ interchangeable signals); **FAB HRMS** calcd for $C_{25}H_{38}O_6SNa$ 457.2566, found 457.2566.