Supporting Information

Synthetic Studies of Neoclerodane Diterpenes from *Salvia divinorum*: Role of the Furan in Affinity for Opioid Receptors

Denise S. Simpson, Kimberly M. Lovell, Anthony Lozama, Nina Han, Victor W. Day, Christina M. Dersch, Richard B. Rothman, and Thomas E. Prisinzano[*]

Contents of Supporting Information

(2*S*,4a*R*,6a*R*,7*R*,9*S*,10a*S*,10b*R*)-methyl 9-acetoxy-6a,10b-dimethyl-4,10-dioxo-2-(phenylcarbamoyl)dodecahydro-1H-benzo[f]isochromene-7-carboxylate (5). Compound **5** was synthesized from **4** using Procedure A and aniline to afford 0.1891g (47.4%) as a white solid, mp 136 – 140 ºC; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.54 (dd, *J* = 1.0, 8.6, 2H), 7.38 – 7.31 (m, 2H), 7.18 – 7.13 (m, 1H), 5.18 (dd, *J* = 8.2, 11.9, 1H), 5.03 (dd, *J* = 6.1, 11.0, 1H), 3.72 (s, 3H), 2.77 (ddd, *J* = 5.3, 13.1, 16.8, 2H), 2.36 – 2.25 (m, 2H), 2.19 (d, *J* = 9.4, 4H), 2.15 – 2.03 (m, 2H), 1.82 – 1.74 (m, 1H), 1.72 – 1.60 (m, 2H), 1.60 – 1.51 (m, 1H), 1.42 (s, 3H), 1.11 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.62, 171.68, 170.29, 169.85, 167.32, 136.77, 129.27, 125.16, 120.18, 76.01, 74.84, 63.96, 53.49, 52.15, 51.21, 42.00, 39.18, 37.92, 35.52, 30.87, 20.73, 18.19, 16.44, 15.59. HRMS (*m/z*): [M+Na] calcd for $C_{26}H_{31}NO_8Na$, 508.1948; found, 508.1970. HPLC t_R = 5.568 min; purity = 98.23%.

(2*S*,4a*R*,6a*R*,7*R*,9*S*,10a*S*,10b*R*)-methyl 9-acetoxy-2-(indoline-1-carbonyl)-6a,10b-dimethyl-4,10-dioxododecahydro-1H-benzo[f]isochromene-7-carboxylate (6). Compound **6** was synthesized from **4** using Procedure A and indoline to afford 0.0866g (34.1%) as a white solid, mp 146 – 149 ºC; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.21 – 8.16 (m, 1H), 7.22 (t, *J* = 7.0, 2H), 7.11 – 7.04 (m, 1H), 5.22 (t, *J* = 7.8, 1H), 5.19 – 5.11 (m, 1H), 4.34 – 4.26 (m, 1H), 4.08 – 4.00 (m, *J* = 7.3, 9.5, 1H), 3.73 (s, 3H), 3.23 (t, *J* = 8.5, 2H), 2.77 (dd, *J* = 6.1, 10.7, 1H), 2.54 (dd, *J* = 8.3, 13.5, 1H), 2.43 (dd, *J* = 3.2, 11.6, 1H), 2.33 – 2.26 (m, 2H), 2.16 (s, 3H), 2.11 (dd, *J* = 3.2, 13.9, 1H), 1.92 (dd, *J* = 7.3, 13.5, 1H), 1.75 (dd, *J* = 3.1, 12.9, 1H), 1.72 – 1.54 (m, 3H), 1.42 (s, 3H), 1.07 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 202.44, 171.81, 171.30, 169.98, 166.93, 142.42, 131.61, 127.76, 124.92, 124.88, 117.53, 75.12, 73.58, 64.74, 53.33, 52.12, 49.15, 47.75, 42.15, 37.83, 37.50, 35.28, 30.80, 28.21,

20.74, 18.31, 17.17, 16.12. HRMS (*m/z*): [M+H] calcd for $C_{28}H_{34}NO_8$, 512.2285; found, 512.2294. HPLC t_R = 6.680 min; purity = 98.00%.

(2*S*,4a*R*,6a*R*,7*R*,9*S*,10a*S*,10b*R*)-methyl 9-acetoxy-2-(cyclohexylcarbamoyl)-6a,10b-dimethyl-4,10-dioxododecahydro-1H-benzo[f]isochromene-7-carboxylate (7). Compound **7** was synthesized from **4** using Procedure A and cyclohexylamine to afford 0.0525g (21.0%) as a white solid, mp 141 – 145 ºC; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.26 (d, *J* = 8.3, 1H), 5.16 (dd, *J* = 8.0, 12.1, 1H), 4.86 (dd, *J* = 6.1, 10.8, 1H), 3.81 – 3.69 (m, 4H), 2.77 – 2.66 (m, 2H), 2.35 – 2.20 (m, 2H), 2.17 (d, *J* = 3.8, 4H), 2.13 – 2.06 (m, 1H), 2.06 – 2.00 (m, 1H), 1.88 (t, *J* = 15.0, 2H), 1.81 – 1.69 (m, 4H), 1.66 – 1.47 (m, 4H), 1.44 – 1.22 (m, 7H), 1.10 (d, *J* = 8.9, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.56, 171.68, 170.65, 169.80, 168.32, 76.01, 74.83, 64.07, 53.54, 52.09, 51.11, 48.38, 42.01, 39.35, 37.98, 35.46, 33.17, 32.99, 30.92, 25.50, 24.99, 24.97, 20.69, 18.20, 16.41, 15.65. HRMS (*m/z*): [M+H] calcd for $C_{26}H_{38}NO_8$, 492.2598; found, 492.2597. HPLC t_R = 5.793 min; purity = 98.29%.

(2*S*,4a*R*,6a*R*,7*R*,9*S*,10a*S*,10b*R*)-methyl 9-acetoxy-2-(cyclopentylcarbamoyl)-6a,10b-dimethyl-4,10-dioxododecahydro-1H-benzo[f]isochromene-7-carboxylate (8). Compound **8** was synthesized from **4** using Procedure A and cyclopentylamine to afford 0.0580g (24.4%) as a white solid, mp 188 – 190 ºC; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.30 (d, *J* = 7.6, 1H), 5.16 (dd, *J* = 7.9, 12.1, 1H), 4.86 (dd, *J* = 6.1, 10.8, 1H), 4.19 (dd, *J* = 7.2, 14.4, 1H), 3.72 (s, 3H), 2.77 – 2.66 (m, 2H), 2.35 – 2.20 (m, 2H), 2.17 (s, 4H), 2.10 (dd, *J* = 3.2, 14.0, 1H), 2.00 (m, 3H), 1.78 (d, *J* = 13.1, 1H), 1.73 – 1.49 (m, 7H), 1.44 – 1.30 (m, 5H), 1.09 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.55, 171.69, 170.63, 169.82, 168.82, 76.03,

74.84, 64.12, 53.59, 52.12, 51.17, 51.14, 42.03, 39.34, 38.01, 35.48, 33.15, 33.05, 30.94, 23.88, 23.87, 20.71, 18.22, 16.43, 15.64. HRMS (*m/z*): [M+H] calcd for $C_{25}H_{36}NO_8$, 478.2441; found, 478.2422. HPLC t_R = 5.098 min; purity = 95.33%.

(*2S*,4a*R*,6a*R*,7*R*,9*S*,10a*S*,10b*R*)-methyl 9-acetoxy-6a,10b-dimethyl-4,10-dioxo-2-(pyridin-3-ylcarbamoyl)dodecahydro-1H-benzo[f]isochromene-7-carboxylate (9). Compound **9** was synthesized from **4** using Procedure A and 3-aminopyridine to afford 0.0870g (36.7%) as a white solid, mp 148 – 150 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.15 (s, 1H), 8.60 (s, 1H), 8.26 (d, *J* = 4.1, 1H), 8.06 (d, *J* = 8.5, 1H), 7.20 (dd, *J* = 8.2, 4.7, 1H), 5.11 (dd, *J* = 11.6, 8.4, 1H), 4.99 (dd, *J* = 10.8, 6.2, 1H), 3.63 (s, 3H), 3.01 (s, 1H), 2.79 – 2.50 (m, 2H), 2.28 – 2.13 (m, 3H), 2.09 (S, 3H), 1.71 – 1.42 (m, 4H), 1.27 (s, 3H), 0.99 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.09, 171.80, 170.83, 170.07, 168.64, 145.65, 141.80, 134.52, 128.03, 123.96, 76.15, 75.09, 63.62, 53.35, 52.11, 50.79, 42.04, 39.00, 37.88, 35.44, 31.10, 30.91, 20.76, 16.44, 15.56. HRMS (*m/z*): [M+H] calcd for $C_{25}H_{31}N_2O_8$, 487.2080; found, 487.2068. HPLC t_R = 8.904 min; purity = 98.10%.

(2*S*,4a*R*,6a*R*,7*R*,9*S*,10a*S*,10b*R*)-methyl 9-acetoxy-2-(2-methoxyphenylcarbamoyl)-6a,10b-dimethyl-4,10-dioxododecahydro-1H-benzo[f]isochromene-7-carboxylate (10). Compound **10** was synthesized from **4** using procedure A and *o*-anisidine to afford 0.0472 g (38.4%) as a white solid, mp 127 – 128 ºC; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.66 (s, 1H), 8.30 (dd, *J* = 1.6, 8.0, 1H), 7.12 – 7.06 (m, 1H), 6.96 (dd, *J* = 4.5, 11.1, 1H), 6.89 (dd, *J* = 1.2, 8.2, 1H), 5.17 (dd, *J* = 8.2, 11.8, 1H), 5.03 (dd, *J* = 6.5, 10.3, 1H), 3.88 (s, 3H), 3.72 (s, 3H), 2.81 – 2.71 (m, 2H), 2.34 – 2.28 (m, 2H), 2.17 (s, 3H), 2.15 – 2.07 (m, 2H), 1.82 –

1.71 (m, 2H), 1.71 – 1.62 (m, 1H), 1.61 – 1.51 (m, 2H), 1.42 (s, 3H), 1.11 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.69, 171.77, 170.37, 169.88, 167.35, 148.58, 126.64, 124.84, 121.19, 120.19, 110.22, 77.48, 76.20, 74.95, 64.35, 55.96, 53.64, 52.19, 51.05, 42.13, 39.28, 38.02, 35.69, 20.79, 18.37, 16.48, 16.01. HRMS (*m/z*): [M+Na] calcd for $C_{27}H_{33}NO_8Na$, 538.2055; found, 538.2053. HPLC t_R = 6.932 min; purity = 98.38%.

(2*S*,4a*R*,6a*R*,7*R*,9*S*,10a*S*,10b*R*)-methyl 9-acetoxy-2-(3-methoxyphenylcarbamoyl)-6a,10b-dimethyl-4,10-dioxododecahydro-1H-benzo[f]isochromene-7-carboxylate (11). Compound **11** was synthesized from **4** using procedure A and *m*-anisidine to afford 0.0361 g (29.7%) as a white solid, mp 122 – 124 ºC; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.68 – 8.65 (m, 1H), 8.32 – 8.28 (m, 1H), 7.11 – 7.07 (m, 1H), 6.99 – 6.95 (m, 2H), 5.19 – 5.13 (m, 2H), 5.05 – 5.01 (m, 1H), 3.88 (s, 3H), 3.72 (s, 3H), 2.85 – 2.67 (m, 5H), 2.38 – 2.30 (m, 2H), 2.17 (s, 3H), 1.72 – 1.62 (m, 3H), 1.43 (s, 3H), 1.11 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.35, 171.85, 171.02, 168.98, 167.31, 148.72, 126.84, 124.62, 121.19, 120.97, 119.97, 110.00, 77.48, 75.97, 74.73, 64.13, 55.74, 53.42, 51.97, 50.83, 41.91, 39.06, 35.47, 20.57, 18.15, 16.25, 15.79. HRMS (*m/z*): [M+H] calcd for $C_{27}H_{34}NO_8$, 516.2216; found, 516.2234. HPLC t_R = 6.003 min; purity = 95.39%.

(2*S*,4a*R*,6a*R*,7*R*,9*S*,10a*S*,10b*R*)-methyl 9-acetoxy-2-(4-methoxyphenylcarbamoyl)-6a,10b-dimethyl-4,10-dioxododecahydro-1H-benzo[f]isochromene-7-carboxylate (12). Compound **12** was synthesized from **4** using procedure A and *p*-anisidine to afford 0.0813 g (32.4%) as a white solid, mp 147 – 150 ºC; ^{1}H NMR (300 MHz, acetone-d_6) δ 9.22 (s, 1H), 7.60 (d, *J* = 9.1, 2H), 6.88 (d, *J* = 9.1, 2H), 5.27 (dd, *J* = 12.5, 7.5, 1H), 5.05 (dd, *J* = 10.8,

6.4, 1H), 3.76 (s, 3H), 3.68 (s, 3H), 3.03 (dd, *J* = 13.2, 3.5, 1H), 2.52 (dd, *J* = 13.5, 6.4, 1H), 2.32 (ddd, *J* = 10.9, 7.7, 3.7, 2H), 2.25 – 2.13 (m, 1H), 2.09 (s, 3H), 2.07 – 1.99 (m, 2H), 1.66 (dtd, *J* = 18.3, 11.4, 5.0, 4H), 1.36 (s, 3H), 1.07 (s, 3H). ^{13}C NMR (75 MHz, acetone-d_6) δ 203.50, 172.70, 170.90, 169.91, 168.71, 157.35, 132.41, 122.40 (2C), 114.72 (2C), 76.65, 76.02, 63.39, 55.71, 53.50, 52.02, 50.82, 42.62, 39.97, 38.46, 36.02, 31.63, 20.60, 19.10, 16.55, 15.77. HRMS (*m/z*): [M+H] calcd for $C_{27}H_{34}NO_9$, 516.2155; found, 516.2227. HPLC t_R = 13.023 min; purity = 98.80%.

(*2S*,4a*R*,6a*R*,7*R*,9*S*,10a*S*,10b*R*)-methyl 9-acetoxy-2-(3,5-dimethoxyphenyl-carbamoyl)-6a,10b-dimethyl-4,10-dioxododecahydro-1H-benzo[f]isochromene-7-carboxylate (13). Compound **13** was synthesized from **4** using procedure A and 3,5-dimethoxyaniline to afford 0.0364 g (18.3%) as a white solid, mp 130 – 133 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.24 (s, 1H), 6.81 (t, *J* = 6.0, 2H), 6.27 (t, *J* = 1.9, 1H), 5.17 (dd, *J* = 11.5, 8.5, 1H), 4.99 (dd, *J* = 10.9, 6.1, 1H), 3.79 (s, 6H), 3.72 (s, 3H), 2.81 – 2.64 (m, 2H), 2.34 – 2.19 (m, 3H), 2.16 (s, 3H), 2.04 (td, *J* = 13.1, 2.6, 2H), 1.81 – 1.49 (m, 4H), 1.38 (s, 3H), 1.08 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.81, 171.77, 170.49, 169.91, 167.60, 161.23 (2C), 138.73, 98.57 (2C), 97.64, 76.09, 74.95, 63.79, 55.59 (2C), 53.41, 52.08, 50.98, 42.01, 39.05, 37.89, 35.48, 30.94, 20.75, 18.24, 16.44, 15.59. HRMS (*m/z*): [M+H] calcd for $C_{28}H_{36}NO_{10}$, 546.2339; found, 546.2321. HPLC t_R = 6.388 min; purity = 98.30%.

(2*S*,4a*R*,6a*R*,7*R*,9*S*,10a*S*,10b*R*)-methyl 9-acetoxy-2-(2,5-dimethoxyphenylcarbamoyl)-6a,10b-dimethyl-4,10-dioxododecahydro-1H-benzo[f]isochromene-7-carboxylate (14). Compound **14** was synthesized from **4** using procedure A and 2,5-dimethoxyaniline to

afford 0.034 g (26.8%) as a white solid, mp 119 – 121 ºC; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.68 (s, 1H), 8.04 (d, *J* = 3.0, 1H), 6.62 (dd, *J* = 3.0, 8.9, 1H), 5.16 (dd, *J* = 8.2, 11.8, 1H), 5.02 (dd, *J* = 6.4, 10.3, 1H), 3.84 (s, 3H), 3.78 (s, 3H), 3.72 (s, 3H), 2.82 – 2.71 (m, 3H), 2.37 – 2.28 (m, 2H), 2.18 (d, *J* = 9.6, 4H), 2.15 – 2.04 (m, 3H), 1.81 – 1.69 (m, 3H), 1.42 (s, 3H), 1.11 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.47, 171.55, 170.06, 169.68, 167.19, 153.70, 142.54, 127.01, 110.78, 109.58, 106.03, 77.22, 75.94, 74.74, 64.12, 56.22, 55.80, 53.44, 51.98, 50.87, 41.92, 39.08, 37.82, 35.47, 20.57, 18.14, 16.26, 15.74. HRMS (*m/z*): [M+Na] calcd for $C_{28}H_{35}NO_{10}Na$, 568.2161; found, 568.2164. HPLC t_R = 7.896 min; purity = 99.38%.

(2*S*,4a*R*,6a*R*,7*R*,9*S*,10a*S*,10b*R*)-methyl 9-acetoxy-2-(3,4-dimethoxyphenylcarbamoyl)-6a,10b-dimethyl-4,10-dioxododecahydro-1H-benzo[f]isochromene-7-carboxylate (15). Compound **15** was synthesized from **4** using procedure A and 3,4-dimethoxyaniline to afford 0.0632 g (48.5%) as a white solid, mp 124 – 126 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (s, 1H), 6.98 (dd, *J* = 2.4, 8.6, 1H), 6.84 (d, *J* = 8.7, 1H), 5.19 (dd, *J* = 8.4, 11.7, 1H), 5.04 (dd, *J* = 6.1, 11.0, 1H), 3.90 (s, 3H), 3.89 (s, 3H), 3.74 (s, 3H), 2.80 (d, *J* = 6.1, 1H), 2.74 (d, *J* = 5.0, 1H), 2.32 (dd, *J* = 4.3, 7.6, 2H), 2.19 (s, 3H), 2.17 – 2.05 (m, 2H), 1.81 (d, *J* = 13.0, 1H), 1.75 – 1.59 (m, 4H), 1.56 (d, *J* = 10.0, 1H), 1.46 (d, *J* = 12.3, 3H), 1.18 – 1.09 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.42, 171.52, 170.15, 169.70, 166.98, 149.07, 146.29, 122.79, 112.01, 111.24, 104.73, 76.71, 76.64, 74.74, 63.94, 56.08, 55.97, 52.00, 51.17, 50.38, 41.91, 39.17, 37.85, 35.42, 20.57, 18.11, 16.32, 15.47. HRMS (*m/z*): [M+Na] calcd for $C_{28}H_{35}NO_{10}Na$, 568.2161; found, 568.2154. HPLC t_R = 4.645 min; purity = 98.44%.

(2*S*,4a*R*,6a*R*,7*R*,9*S*,10a*S*,10b*R*)-methyl 9-acetoxy-2-(2,4-dimethoxyphenylcarbamoyl)-6a,10b-dimethyl-4,10-dioxododecahydro-1H-benzo[f]isochromene-7-carboxylate (16). Compound **16** was synthesized from **4** using procedure A and 2,4-dimethoxyaniline to afford 0.0244 g (18.4%) as a white solid, mp 121 – 123 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (s, 1H), 8.17 (d, *J* = 9.6, 1H), 6.49 (d, *J* = 6.8, 2H), 5.18 (dd, *J* = 8.4, 11.6, 1H), 5.03 (dd, *J* = 6.5, 10.1, 1H), 3.87 (s, 3H), 3.82 (s, 3H), 3.73 (s, 3H), 2.84 – 2.70 (m, 2H), 2.32 (dd, *J* = 4.4, 7.8, 2H), 2.19 (s, 3H), 2.12 (d, *J* = 9.5, 2H), 1.85 – 1.66 (m, 3H), 1.63 – 1.53 (m, 2H), 1.44 (s, 3H), 1.12 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.63, 174.11, 171.43, 169.99, 168.79, 160.07, 156.40, 141.81, 121.26, 120.01, 103.92, 98.68, 75.96, 74.70, 64.23, 55.76, 55.54, 53.35, 51.97, 50.81, 41.87, 39.16, 37.98, 35.46, 20.57, 18.09, 16.26, 15.80. HRMS (*m/z*): [M+Na] calcd for $C_{28}H_{35}NO_{10}Na$, 568.2161; found, 568.2175. HPLC t_R = 6.468 min; purity = 98.92%.

(2*S*,4a*R*,6a*R*,7*R*,9*S*,10a*S*,10b*R*)-methyl 9-acetoxy-2-(2-bromophenylcarbamoyl)-6a,10b-dimethyl-4,10-dioxododecahydro-1H-benzo[f]isochromene-7-carboxylate (17). Compound **17** was synthesized from **4** using procedure A and *o*-bromoaniline to afford 0.0382 g (18.5%) as a white solid, mp 125 – 128 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.62 (s, 1H), 8.18 (d, *J* = 11.7, 1H), 7.48 (d, *J* = 8.0, 1H), 7.24 (dd, *J* = 15.3, 7.3, 1H), 6.97 (t, *J* = 7.8, 1H), 5.15 – 5.04 (m, 1H), 4.99 (dd, *J* = 10.5, 6.3, 1H), 3.64 (s, 3H), 2.79 – 2.59 (m, 2H), 2.36 – 2.13 (m, 3H), 2.06 (s, 3H), 2.01 (t, *J* = 10.2, 2H), 1.82 – 1.41 (m, 4H), 1.35 (s, 3H), 1.03 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.71, 171.72, 169.86, 169.78, 167.76, 134.79, 132.61, 128.59, 126.19, 122.22, 114.45, 76.10, 74.93, 64.06, 53.52, 52.13, 51.11, 42.07,

39.22, 37.94, 35.64, 30.95, 20.74, 18.31, 16.44, 15.75. HRMS (*m/z*): [M+NH_4] calcd for $C_{26}H_{34}BrN_2O_8$, 581.1498; found, 581.1492. HPLC t_R 8.011= min; purity = 95.03%.

(*2S*,4a*R*,6a*R*,7*R*,9*S*,10a*S*,10b*R*)-methyl 9-acetoxy-2-(3-bromophenylcarbamoyl)-6a,10b-dimethyl-4,10-dioxododecahydro-1H-benzo[f]isochromene-7-carboxylate (18). Compound **18** was synthesized from **4** using procedure A and *m*-bromoaniline to afford 0.0600 g (29.1%) as a white solid, mp 145 – 148 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.46 (s, 1H), 7.80 (s, 1H), 7.49 (d, *J* = 8.0, 1H), 7.32 – 7.12 (m, 2H), 5.25 – 5.08 (m, 1H), 5.01 (dd, *J* = 6.1, 10.8, 1H), 3.71 (s, 3H), 2.83 – 2.61 (m, 2H), 2.38 – 2.11 (m, 6H), 2.11 – 1.87 (m, 2H), 1.82 – 1.44 (m, 4H), 1.38 (s, 3H), 1.08 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.79, 171.72, 170.52, 169.92, 167.80, 138.39, 130.54, 128.05, 123.31, 122.72, 118.88, 76.09, 74.93, 63.80, 53.44, 52.11, 51.02, 42.00, 39.05, 37.91, 35.50, 30.92, 20.75, 18.26, 16.44, 15.59. HRMS (*m/z*): [M+Na] calcd for $C_{26}H_{30}BrNO_8Na$, 586.1052; found, 586.1050. HPLC t_R = 9.178 min; purity = 100%.

(*2S*,4a*R*,6a*R*,7*R*,9*S*,10a*S*,10b*R*)-methyl 9-acetoxy-2-(4-bromophenylcarbamoyl)-6a,10b-dimethyl-4,10-dioxododecahydro-1H-benzo[f]isochromene-7-carboxylate (19). Compound 19 was synthesized from 4 using procedure A and *p*-bromoaniline to afford 0.0486 g (23.6%) as a white solid, mp 159 – 162 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.41 (s, 1H), 7.53 – 7.37 (m, 4H), 5.25 – 5.09 (m, 1H), 5.00 (dd, *J* = 6.1, 11.0, 1H), 3.73 (d, *J* = 12.6, 3H), 2.83 – 2.60 (m, 2H), 2.38 – 2.11 (m, 6H), 2.02 (t, *J* = 14.3, 2H), 1.76 (d, *J* = 12.3, 1H), 1.71 – 1.43 (m, 3H), 1.37 (s, 3H), 1.08 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.79, 171.69, 170.43, 169.94, 167.65, 136.16, 132.21, 121.96, 117.80, 76.08, 74.96, 63.81, 53.47, 52.12, 51.06, 42.00, 39.05, 37.92, 35.48,

30.91, 20.74, 18.24, 16.44, 15.54. HRMS (*m/z*): [M+NH_4] calcd for $C_{26}H_{34}BrN_2O_8$, 581.1498; found, 581.1497. HPLC t_R = 8.672 min; purity = 100%.

(*2S*,4a*R*,6a*R*,7*R*,9*S*,10a*S*,10b*R*)-methyl 9-acetoxy-6a,10b-dimethyl-4,10-dioxo-2-(pyrrolidine-1-carbonyl)dodecahydro-1H-benzo[f]isochromene-7-carboxylate (22).

Compound **22** was synthesized from **4** using procedure A and pyrrolidine to afford 0.0640 g (56.6%) as a white solid, mp 234 – 236 ºC (dec.); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.19 – 5.03 (m, 2H), 3.67 (s, 3H), 3.59 (dd, *J* = 11.7, 5.0, 1H), 3.52 – 3.29 (m, 3H), 2.76 (dd, *J* = 10.7, 6.0, 1H), 2.44 – 2.30 (m, 3H), 2.30 – 2.18 (m, 2H), 2.14 (s, 3H), 1.93 (dd, *J* = 12.7, 6.3, 2H), 1.89 – 1.51 (m, 7H), 1.33 (s, 3H), 1.02 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.43, 171.82, 171.39, 169.88, 167.47, 75.11, 73.26, 64.47, 53.25, 51.98, 49.19, 46.53, 46.50, 42.10, 37.80, 37.68, 35.16, 30.84, 26.16, 24.05, 20.68, 18.27, 16.90, 16.10. HRMS (*m/z*): [M+Na] calcd for $C_{24}H_{33}NO_8Na$, 486.2104; found, 486.2095. HPLC t_R = 7.314 min; purity = 98.67%.

(*2S*,4a*R*,6a*R*,7*R*,9*S*,10a*S*,10b*R*)-methyl 9-acetoxy-2-(4-bromopiperidine-1-carbonyl)-6a,10b-dimethyl-4,10-dioxododecahydro-1H-benzo[f]isochromene-7-carboxylate (24).

Compound **24** was synthesized from **4** using procedure A and 4-bromopiperidine hydrochloride to afford 0.1770 g (64.5%) as a white solid, mp 198 – 201 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.36 – 5.25 (m, 1H), 5.24 – 5.12 (m, 1H), 4.42 (dd, *J* = 31.6, 27.9, 1H), 3.95 – 3.82 (m, 1H), 3.81 – 3.63 (m, 4H), 3.61 – 3.33 (m, 2H), 2.82 (dd, *J* = 12.2, 4.4, 1H), 2.49 – 2.22 (m, 5H), 2.21 – 2.11 (m, 4H), 2.10 – 1.92 (m, 4H), 1.89 – 1.53 (m, 4H), 1.41 – 1.33 (m, 3H), 1.06 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.35, 171.73, 171.07, 169.73, 167.34,

74.98, 71.34, 64.28, 53.07, 51.93, 49.00, 44.04, 43.10, 41.96, 39.92, 37.65, 36.06, 35.52, 35.06, 30.75, 21.08, 20.63, 18.21, 16.93, 16.04. HRMS (*m/z*): [M+H] calcd for $C_{25}H_{35}BrNO_8$, 556.1546; found, 556.1539. HPLC t_R = 15.039 min; purity = 98.40%.

(*2S*,4a*R*,6a*R*,7*R*,9*S*,10a*S*,10b*R*)-methyl 9-acetoxy-6a,10b-dimethyl-4,10-dioxo-2-((*R*)-tetrahydrofuran-3-ylcarbamoyl)dodecahydro-1H-benzo[f]isochromene-7-carboxylate (25). Compound **25** was synthesized from **4** using procedure A and *R*-(+)-3-aminotetrahydrofuran toluene-4-sulfonate to afford 0.1490 g (63.9%) as a white solid, mp 134 – 137 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.86 (d, *J* = 9.7, 1H), 5.13 (dd, *J* = 11.7, 8.3, 1H), 4.84 (dt, *J* = 12.4, 6.2, 1H), 4.44 (td, *J* = 10.2, 5.3, 1H), 3.92 – 3.80 (m, 2H), 3.80 – 3.70 (m, 2H), 3.65 (d, *J* = 12.3, 3H), 3.59 (dd, *J* = 9.5, 2.7, 1H), 2.72 (dd, *J* = 12.1, 4.7, 1H), 2.62 (dd, *J* = 13.7, 5.9, 1H), 2.31 – 2.15 (m, 4H), 2.15 – 2.08 (m, 3H), 1.86 – 1.66 (m, 3H), 1.51 (ddd, *J* = 14.3, 13.0, 8.0, 3H), 1.32 (s, 3H), 1.03 (s, *J* = 11.3, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.70, 171.65, 170.51, 169.76, 169.25, 76.01, 74.83, 73.22, 66.96, 63.71, 53.40, 52.01, 50.99, 50.23, 41.93, 39.31, 37.89, 35.37, 32.84, 30.86, 20.64, 18.13, 16.36, 15.33. HRMS (*m/z*): [M+H] calcd for $C_{24}H_{34}NO_9$, 480.2234; found, 480.2226. HPLC t_R = 10.948 min; purity = 95.30%.

(*2S*,4a*R*,6a*R*,7*R*,9*S*,10a*S*,10b*R*)-methyl 9-acetoxy-6a,10b-dimethyl-4,10-dioxo-2-(((*R*)-tetrahydrofuran-2-yl)methylcarbamoyl)dodecahydro-1H-benzo[f]iso-chromene-7-carboxylate (26). Compound **26** was synthesized from **4** using procedure A and *R*-(-)-tetrahydrofurfurylamine to afford 0.1660 g (69.2%) as a white solid, mp 111 – 113 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.86 (t, *J* = 5.6, 1H), 5.18 (dd, *J* = 11.7, 8.3, 1H), 4.92 (dd, *J* =

10.4, 6.3, 1H), 4.02 – 3.78 (m, 2H), 3.78 – 3.66 (m, 4H), 3.61 – 3.45 (m, 1H), 3.26 – 3.07 (m, 1H), 2.77 (dt, *J* = 13.9, 6.9, 1H), 2.64 (dd, *J* = 13.8, 6.3, 1H), 2.35 – 2.21 (m, 3H), 2.16 (s, 3H), 2.13 – 2.03 (m, 2H), 2.02 – 1.82 (m, 3H), 1.81 – 1.70 (m, 1H), 1.67 – 1.46 (m, 4H), 1.37 (s, 3H), 1.09 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.73, 171.68, 170.51, 169.72, 169.60, 77.36, 75.85, 74.81, 68.10, 63.81, 53.30, 51.95, 50.71, 43.24, 41.90, 39.11, 37.84, 35.33, 30.83, 28.82, 25.80, 20.62, 18.15, 16.29, 15.65. HRMS (*m/z*): [M+H] calcd for $C_{25}H_{36}NO_9$, 494.2390; found, 494.2383. HPLC t_R = 9.580 min; purity = 98.10%.

(*2S*,4a*R*,6a*R*,7*R*,9*S*,10a*S*,10b*R*)-methyl 9-acetoxy-6a,10b-dimethyl-4,10-dioxo-2-(((*S*)-tetrahydrofuran-2-yl)methylcarbamoyl)dodecahydro-1H-benzo[f]iso-chromene-7-carboxylate (27). Compound **27** was synthesized from **4** using procedure A and (*S*)-(+)-tetrahydrofurfurylamine to afford 0.1470 g (61.3%) as a white solid, mp 99 – 101 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.82 (t, *J* = 5.5, 1H), 5.14 (dd, *J* = 11.4, 8.5, 1H), 4.87 (dd, *J* = 10.9, 6.0, 1H), 3.99 – 3.86 (m, 1H), 3.81 (dd, *J* = 14.6, 6.8, 1H), 3.75 – 3.63 (m, 4H), 3.58 – 3.40 (m, 1H), 3.20 – 3.03 (m, 1H), 2.69 (ddd, *J* = 19.7, 12.7, 5.4, 2H), 2.32 – 2.22 (m, 2H), 2.13 (s, 3H), 2.03 (dd, *J* = 14.2, 7.5, 3H), 1.90 (ddt, *J* = 26.7, 13.6, 6.7, 3H), 1.74 (d, *J* = 10.1, 1H), 1.64 – 1.43 (m, 4H), 1.31 (d, *J* = 15.3, 3H), 1.06 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.71, 171.72, 170.44, 169.77, 169.65, 77.47, 75.99, 74.86, 68.20, 63.87, 53.43, 52.02, 50.97, 43.16, 42.00, 39.42, 37.95, 35.44, 30.91, 28.78, 25.90, 20.67, 18.18, 16.38, 15.53. HRMS (*m/z*): [M+H] calcd for $C_{25}H_{36}NO_9$, 494.2390; found, 494.2378. HPLC t_R = 9.114 min; purity = 99.20%.

(*2S*,4a*R*,6a*R*,7*R*,9*S*,10a*S*,10b*R*)-2-((3a*S*,4*R*,6a*S*)-hexahydro-2*H*-cyclopenta[b]furan-4-yl)

7-methyl 9-acetoxy-6a,10b-dimethyl-4,10-dioxododecahydro-1*H*-benzo[f]isochromene-2,7-dicarboxylate (28). Compound **28** was synthesized from **4** using procedure A and (3a*R*,4*R*,6a*S*)-hexahydro-2*H*-cyclopenta[b]furan-4-ol[56] to afford 0.1820 g (72.4%) as a white solid, mp 229 – 231 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.21 – 4.90 (m, 3H), 4.37 (t, *J* = 6.0, 1H), 3.97 – 3.81 (m, 1H), 3.72 (s, 3H), 3.58 (dd, *J* = 15.4, 7.8, 1H), 2.99 – 2.83 (m, 1H), 2.77 (dd, *J* = 10.6, 6.0, 1H), 2.58 (dd, *J* = 13.4, 7.0, 1H), 2.37 – 2.02 (m, 8H), 1.98 – 1.47 (m, 10H), 1.37 (s, 3H), 1.08 (s, 3H).^{13}C NMR (75 MHz, $CDCl_3$) δ 201.97, 171.59, 170.08, 169.89, 169.79, 83.33, 77.66, 75.04, 74.07, 69.15, 64.31, 53.47, 52.06, 50.18, 44.80, 42.14, 39.10, 37.95, 35.34, 30.80, 29.03, 28.79, 27.65, 20.66, 18.26, 16.25, 15.84. HRMS (*m/z*): [M+H] calcd for $C_{27}H_{37}O_{10}$, 521.2387; found, 521.2388. HPLC t_R = 5.704 min; purity = 95.70%.

(*2S*,4a*R*,6a*R*,7*R*,9*S*,10a*S*,10b*R*)-7-methyl 2-((*R*)-tetrahydrofuran-3-yl) 9-acetoxy-6a,10b-dimethyl-4,10-dioxododecahydro-1*H*-benzo[f]isochromene-2,7-dicarboxylate (29). Compound **29** was synthesized from **4** using procedure A and (*R*)-(-)-3-hydroxytetrahydrofuran to afford 0.1820 g (40.6%) as a white solid, mp 161 – 163 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.39 – 5.31 (m, 1H), 5.20 – 5.11 (m, 1H), 4.97 (dd, *J* = 10.1, 7.0, 1H), 3.97 – 3.80 (m, 4H), 3.72 (s, 3H), 2.74 (dt, *J* = 12.9, 5.9, 1H), 2.59 (dd, *J* = 13.4, 7.0, 1H), 2.37 – 2.26 (m, 2H), 2.24 – 2.08 (m, 7H), 2.07 – 1.99 (m, 1H), 1.78 (dd, *J* = 12.5, 3.3, 1H), 1.67 – 1.47 (m, 3H), 1.37 (s, 3H), 1.09 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.94, 171.67, 170.14, 170.08, 170.06, 77.55, 77.23, 76.91, 75.12, 74.00, 73.17, 67.21, 64.42, 53.58, 52.20, 52.19, 50.41, 42.19, 35.47, 32.66, 20.80, 18.30, 16.33, 15.80. HRMS (*m/z*): [M+Na] calcd for $C_{24}H_{32}O_{10}Na$, 503.1893; found, 503.1898. HPLC t_R = 4.304 min; purity =

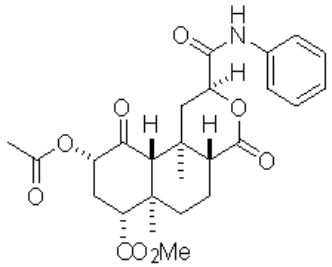
96.10 %.

(*2S*,4a*R*,6a*R*,7*R*,9*S*,10a*S*,10b*R*)-7-methyl 2-((*S*)-tetrahydrofuran-3-yl) 9-acetoxy-6a,10b-dimethyl-4,10-dioxododecahydro-1*H*-benzo[f]isochromene-2,7-dicarboxylate (30).

Compound **30** was synthesized from **4** using procedure A and (*S*)-(+)-3-hydroxytetrahydrofuran to afford 0.1110 g (47.4%) as a white solid, mp 159 – 161 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.28 (dd, *J* = 6.0, 4.5, 1H), 5.13 (dd, *J* = 11.3, 8.6, 1H), 4.92 (dd, *J* = 9.7, 7.1, 1H), 3.96 – 3.73 (m, 4H), 3.64 (d, *J* = 19.7, 3H), 2.74 (dd, *J* = 11.7, 5.0, 1H), 2.52 (dd, *J* = 13.5, 7.0, 1H), 2.31 – 1.85 (m, 10H), 1.81 – 1.43 (m, 4H), 1.37 (s, 3H), 1.10 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.00, 171.63, 170.12, 170.00, 169.92, 76.75, 74.96, 73.89, 72.73, 66.99, 64.08, 53.29, 52.01, 50.11, 42.02, 38.79, 37.83, 35.31, 32.77, 30.78, 20.65, 18.19, 16.25, 15.87. HRMS (*m/z*): [M+H] calcd for $C_{24}H_{33}O_{10}$, 481.2074; found, 481.2072. HPLC t_R = 9.502 min; purity = 98.40%.

DAD1 A, Sig=209,4 Ref=360,100 (KIM\KML-2-151000001.D)

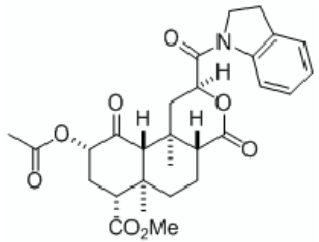
pump: Agilent 1100 series quaternary pump
column: Phenomenex Luna C-18, 5 micron, 10 x 250 mm
sample size: 100 microliters
sample concentration: 2.3 mg/mL
mobile phase: 60% acetonitrile - 40% water
flow rate: 5 mL/min
purity: 98.23%



5

DAD1 A, Sig=209,4 Ref=360,100 (KIM\KML-1-267000001.D)

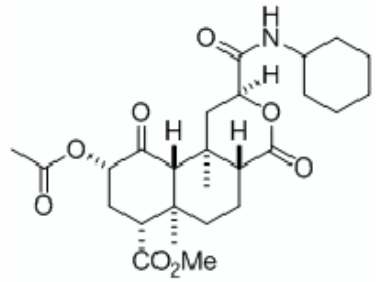
pump: Agilent 1100 series quaternary pump
column: Phenomenex Luna C-18, 5 micron, 10 x 250 mm
sample size: 100 microliters
sample concentration: 1.2 mg/mL
mobile phase: 60% acetonitrile - 40% water
flow rate: 5 mL/min
purity: 98.00%



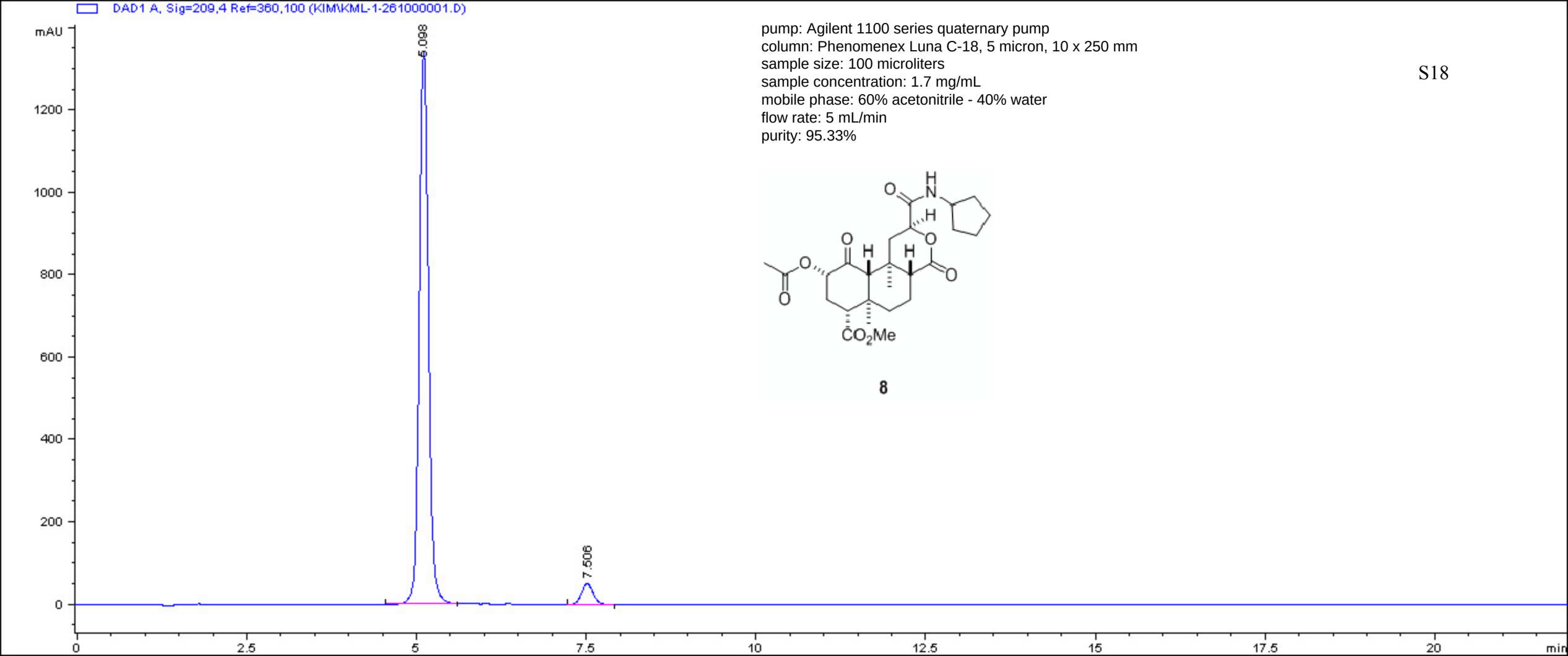
6

DAD1 A, Sig=209,4 Ref=360,100 (KIM\KML-1-263000001.D)

pump: Agilent 1100 series quaternary pump
column: Phenomenex Luna C-18, 5 micron, 10 x 250 mm
sample size: 100 microliters
sample concentration: 2.4 mg/mL
mobile phase: 60% acetonitrile - 40% water
flow rate: 5 mL/min
purity: 98.29%



7

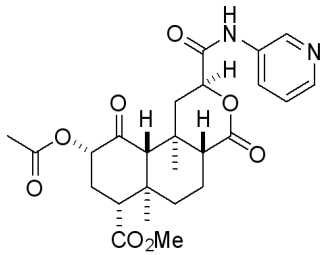


pump: Agilent 1100 series quaternary pump
column: Phenomenex Luna C-18, 5 micron, 10 x 250 mm
sample size: 100 microliters
sample concentration: 1.7 mg/mL
mobile phase: 60% acetonitrile - 40% water
flow rate: 5 mL/min
purity: 95.33%

8

DAD1 C, Sig=254,8 Ref=360,100 (DENISE\DS-2-44000002.D)

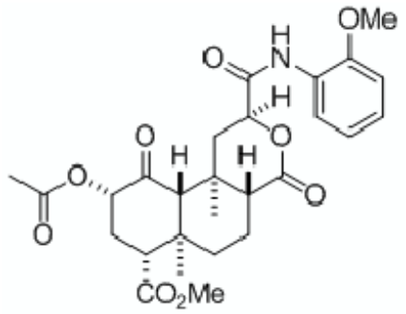
pump: Agilent 1100 series quaternary pump
column: Phenomenex Luna C-18, 5 micron, 10 x 250 mm
sample size: 100 microliters
sample concentration: 1.1 mg/mL
mobile phase: 60% acetonitrile - 40% water
flow rate: 2 mL/min
purity: 98.1%



9

DAD1 A, Sig=209,4 Ref=360,100 (AL\AL-1-57B000019.D)

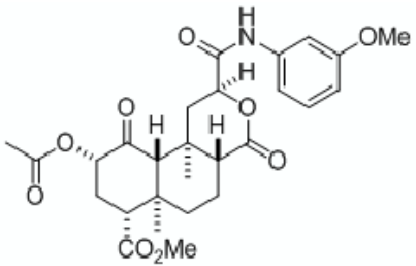
pump: Agilent 1100 series quaternary pump
column: Phenomenex Luna C-18, 5 micron, 10 x 250 mm
sample size: 100 microliters
sample concentration: 0.5 mg/mL
mobile phase: 60% acetonitrile - 40% water
flow rate: 5 mL/min
purity: 98.38%



10

DAD1 A, Sig=209,4 Ref=360,100 (AL\AL-1-249000005.D)

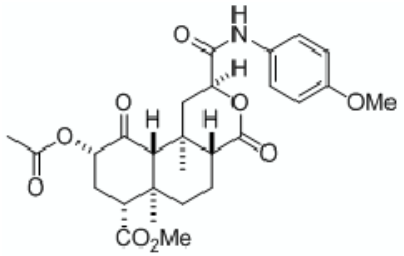
pump: Agilent 1100 series quaternary pump
column: Phenomenex Luna C-18, 5 micron, 10 x 250 mm
sample size: 100 microliters
sample concentration: 0.7 mg/mL
mobile phase: 60% acetonitrile - 40% water
flow rate: 5 mL/min
purity: 95.39%



11

DAD1 C, Sig=254,8 Ref=360,100 (DENISE\NH-1-29000001.D)

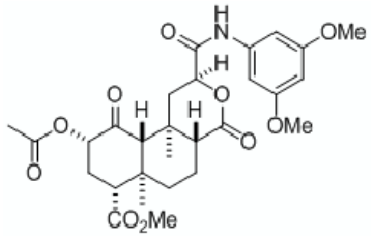
pump: Agilent 1100 series quaternary pump
column: Phenomenex Luna C-18, 5 micron, 10 x 250 mm
sample size: 100 microliters
sample concentration: 1.8 mg/mL
mobile phase: 60% acetonitrile - 40% water
flow rate: 2 mL/min
purity: 98.8%



12

DAD1 C, Sig=254,8 Ref=360,100 (DENISE\NH-1-31000001.D)

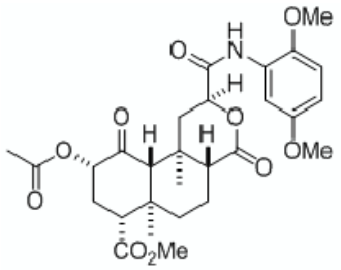
pump: Agilent 1100 series quaternary pump
column: Phenomenex Luna C-18, 5 micron, 10 x 250 mm
sample size: 100 microliters
sample concentration: 0.9 mg/mL
mobile phase: 60% acetonitrile - 40% water
flow rate: 5 mL/min
purity: 98.3%



13

DAD1 A, Sig=209,4 Ref=360,100 (AL\AL-1-113000005.D)

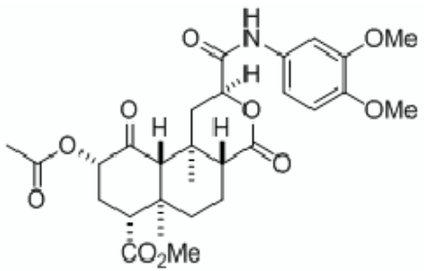
pump: Agilent 1100 series quaternary pump
column: Phenomenex Luna C-18, 5 micron, 10 x 250 mm
sample size: 100 microliters
sample concentration: 0.5 mg/mL
mobile phase: 60% acetonitrile - 40% water
flow rate: 5 mL/min
purity: 99.38%



14

DAD1 A, Sig=209,4 Ref=360,100 (AL\AL-1-109000018.D)

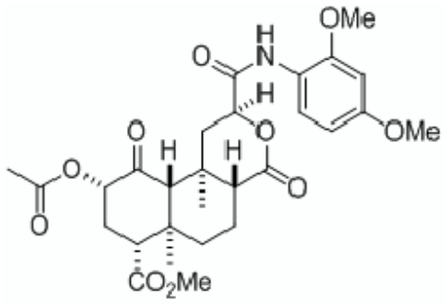
pump: Agilent 1100 series quaternary pump
column: Phenomenex Luna C-18, 5 micron, 10 x 250 mm
sample size: 100 microliters
sample concentration: 0.7 mg/mL
mobile phase: 60% acetonitrile - 40% water
flow rate: 5 mL/min
purity: 98.44%



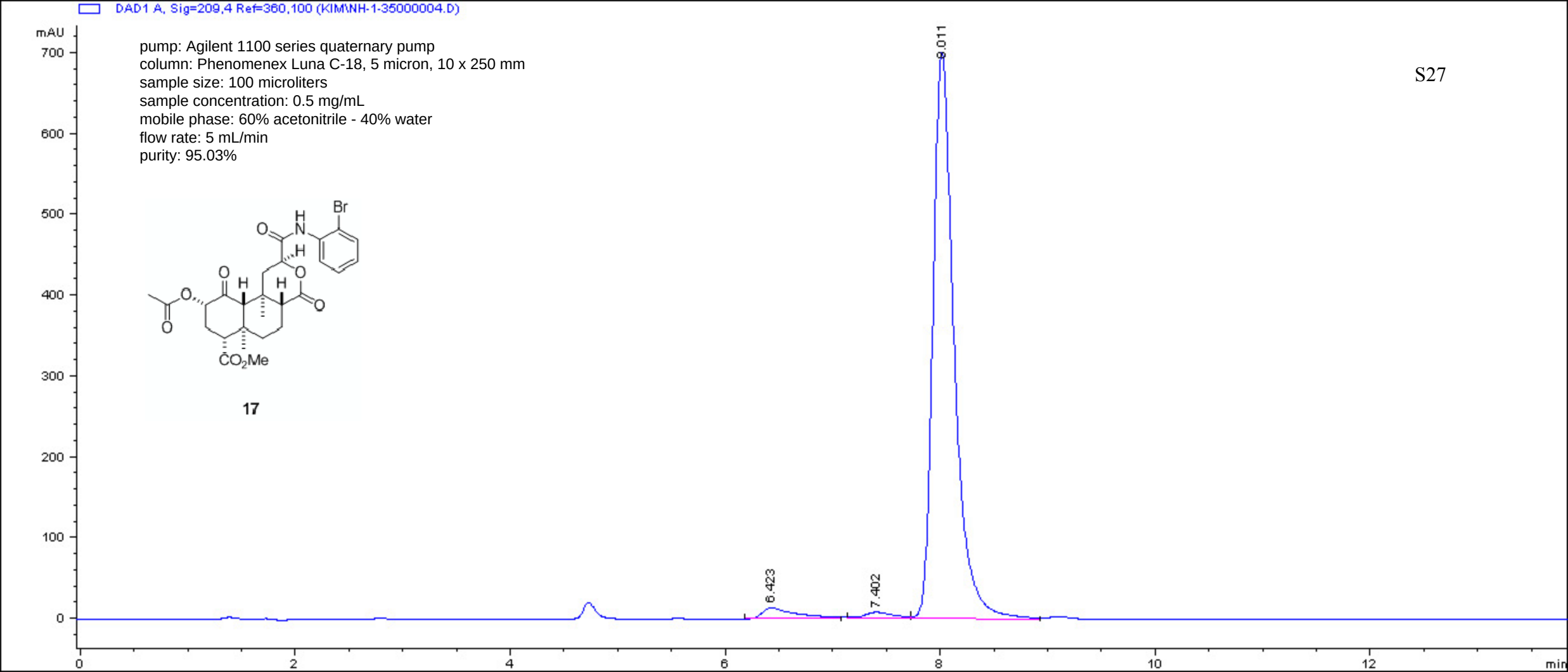
15

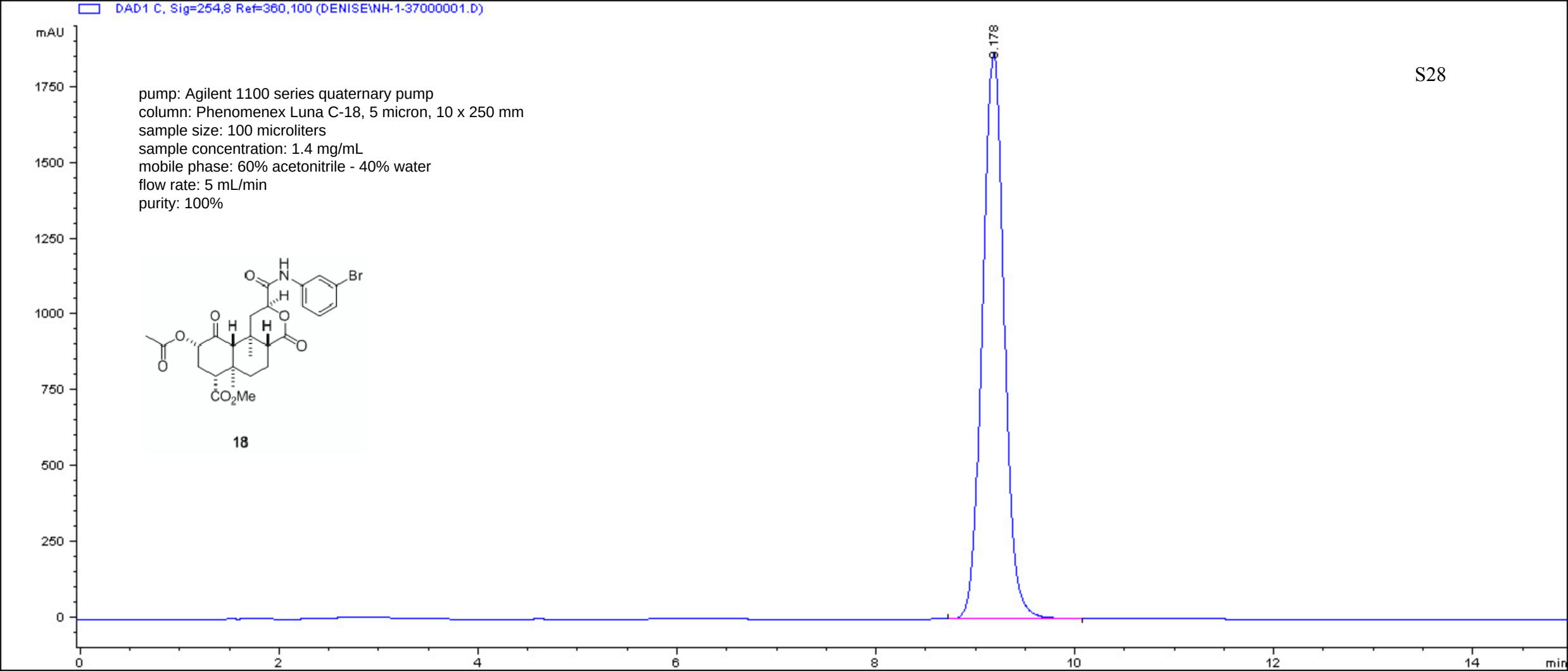
DAD1 A, Sig=209,4 Ref=360,100 (AL\AL-1-117000009.D)

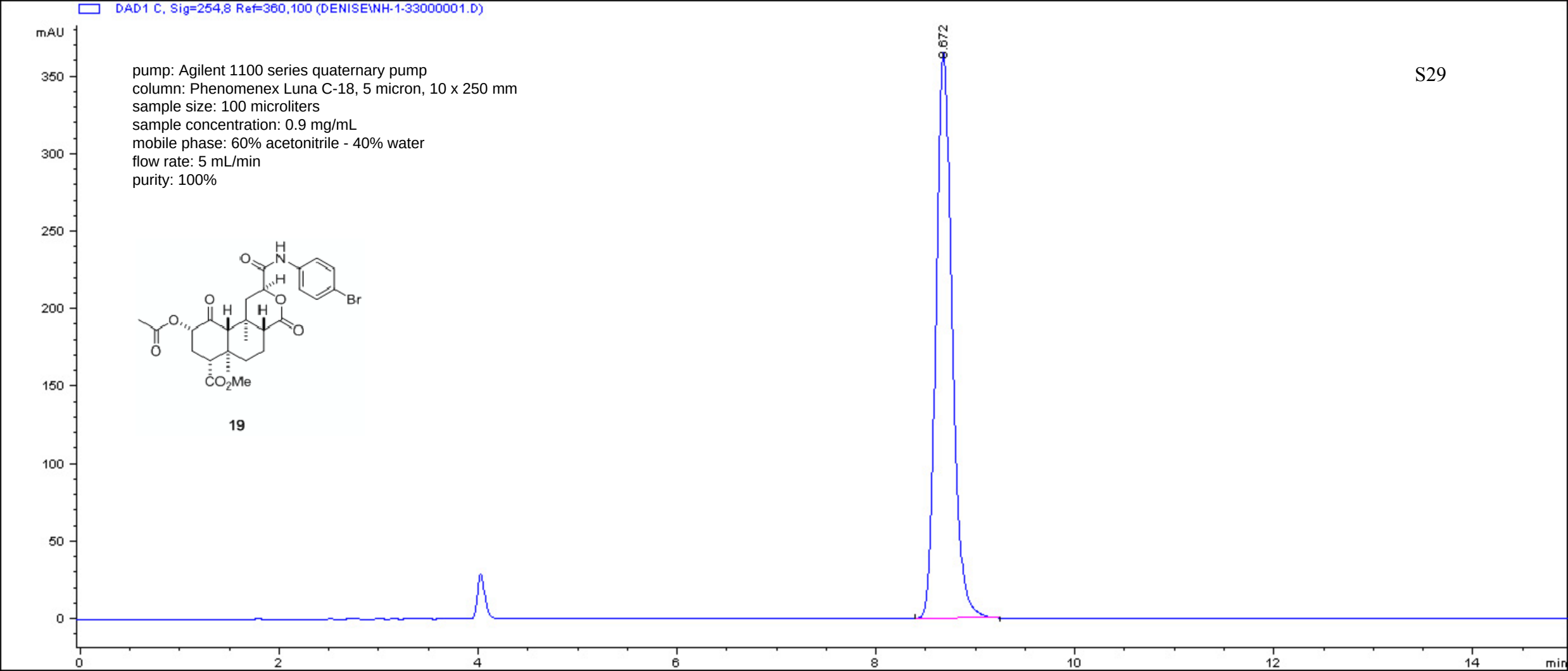
pump: Agilent 1100 series quaternary pump
column: Phenomenex Luna C-18, 5 micron, 10 x 250 mm
sample size: 100 microliters
sample concentration: 0.5 mg/mL
mobile phase: 60% acetonitrile - 40% water
flow rate: 5 mL/min
purity: 98.92%



16

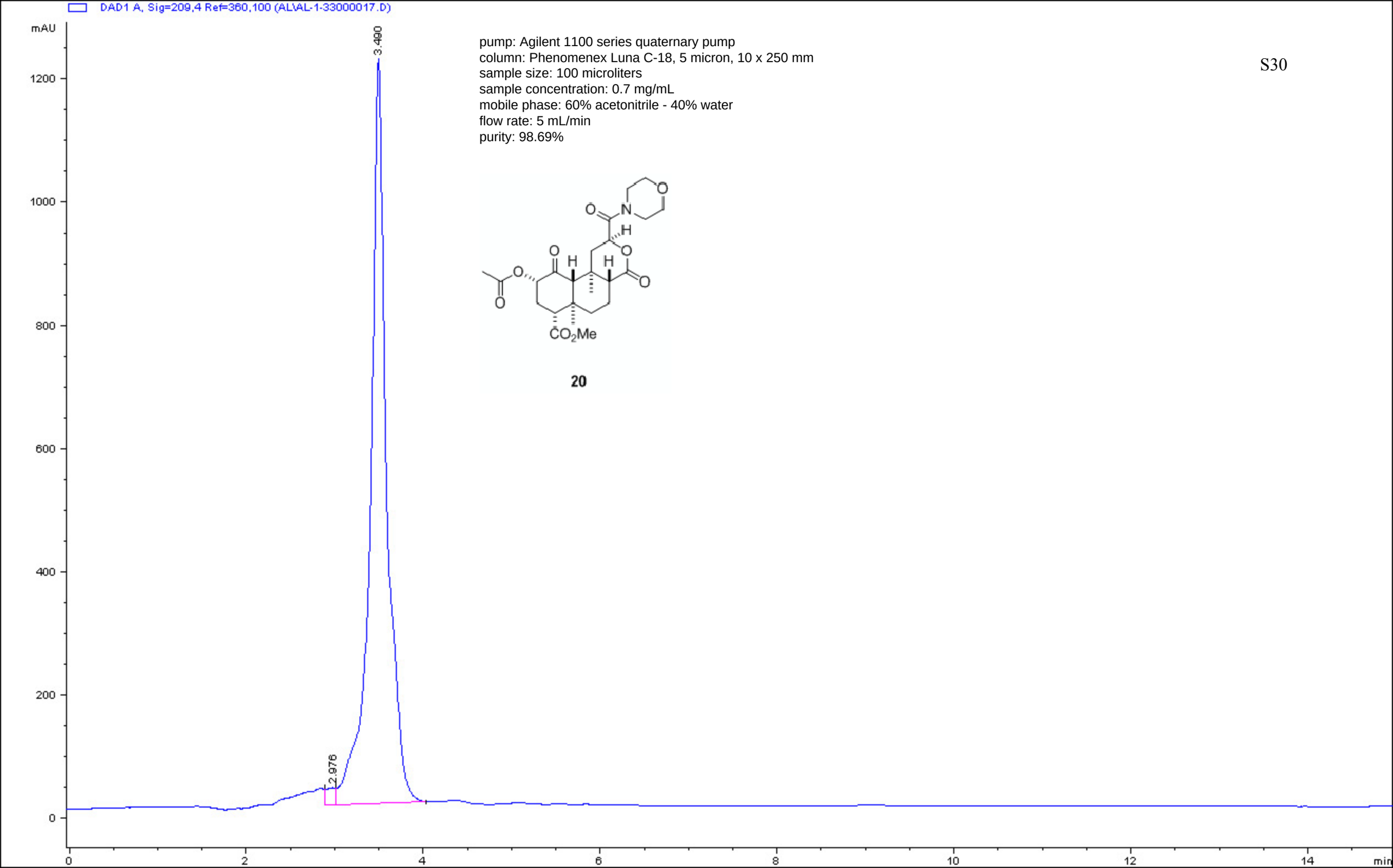

DAD1 A, Sig=209,4 Ref=360,100 (KIM\NH-1-35000004.D)
mAU
700
600
500
400
300
200
100
0
pump: Agilent 1100 series quaternary pump
column: Phenomenex Luna C-18, 5 micron, 10 x 250 mm
sample size: 100 microliters
sample concentration: 0.5 mg/mL
mobile phase: 60% acetonitrile - 40% water
flow rate: 5 mL/min
purity: 95.03%
Br
H
N
O
H
O
O
H
H
O
O
O
O
O
CO2Me
17
6.423
7.402
8.011
0
2
4
6
8
10
12
min


DAD1 C, Sig=254,8 Ref=360,100 (DENISE\NH-1-37000001.D)
mAU
1750
1500
1250
1000
750
500
250
0
9.178
0
2
4
6
8
10
12
14
min
pump: Agilent 1100 series quaternary pump
column: Phenomenex Luna C-18, 5 micron, 10 x 250 mm
sample size: 100 microliters
sample concentration: 1.4 mg/mL
mobile phase: 60% acetonitrile - 40% water
flow rate: 5 mL/min
purity: 100%
18



pump: Agilent 1100 series quaternary pump
column: Phenomenex Luna C-18, 5 micron, 10 x 250 mm
sample size: 100 microliters
sample concentration: 0.9 mg/mL
mobile phase: 60% acetonitrile - 40% water
flow rate: 5 mL/min
purity: 100%

19

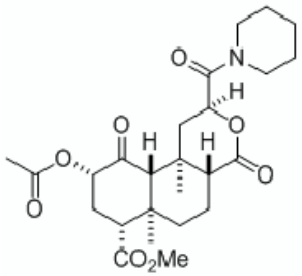


pump: Agilent 1100 series quaternary pump
column: Phenomenex Luna C-18, 5 micron, 10 x 250 mm
sample size: 100 microliters
sample concentration: 0.7 mg/mL
mobile phase: 60% acetonitrile - 40% water
flow rate: 5 mL/min
purity: 98.69%

20

DAD1 A, Sig=209,4 Ref=360,100 (DENISE\DS-1-243000008.D)

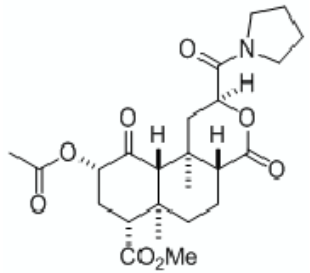
pump: Agilent 1100 series quaternary pump
column: Phenomenex Luna C-18, 5 micron, 10 x 250 mm
sample size: 100 microliters
sample concentration: 1.1 mg/mL
mobile phase: 60% acetonitrile - 40% water
flow rate: 2.5 mL/min
purity: 97.04%



21

DAD1 A, Sig=209,4 Ref=360,100 (DENISE\DS-1-242000009.D)

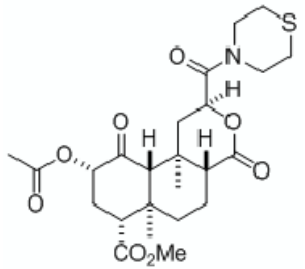
pump: Agilent 1100 series quaternary pump
column: Phenomenex Luna C-18, 5 micron, 10 x 250 mm
sample size: 100 microliters
sample concentration: 1.1 mg/mL
mobile phase: 60% acetonitrile - 40% water
flow rate: 2.5 mL/min
purity: 98.67%



22

DAD1 A, Sig=209,4 Ref=360,100 (DENISE\DS-3-224000004.D)

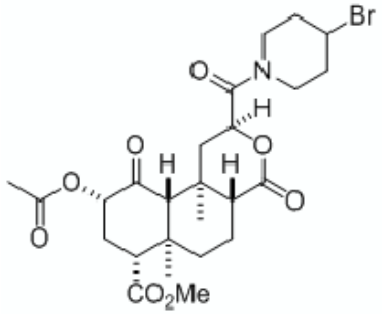
pump: Agilent 1100 series quaternary pump
column: Phenomenex Luna C18, 5 micron, 10 x 250 mm
sample size: 100 microliter
sample concentration: 2.1 mg/mL
mobile phase: 60% acetonitrile - 40% water
flow rate: 2 mL/min
purity: 98.4%



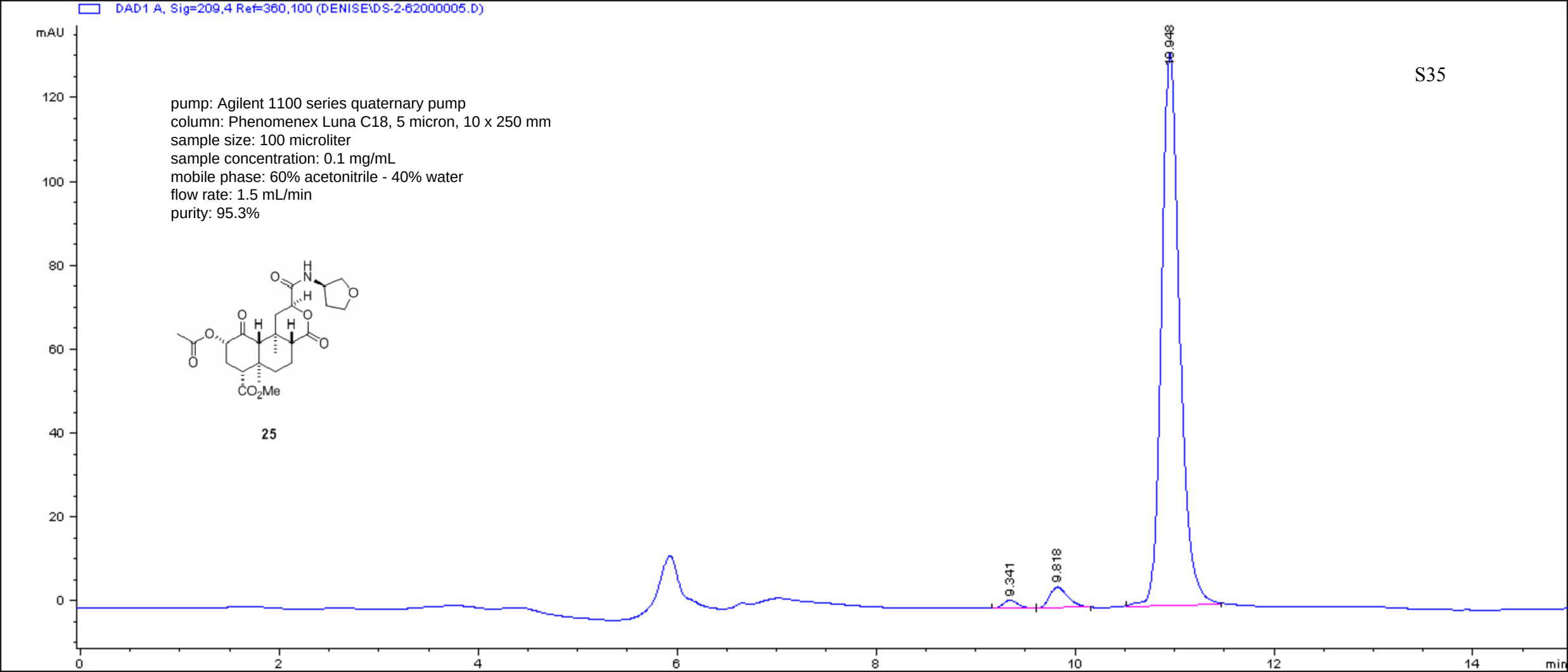
23

DAD1 A, Sig=209,4 Ref=360,100 (DENISE\DS-3-220000002.D)

pump: Agilent 1100 series quaternary pump
column: Phenomenex Luna C-18, 5 micron, 10 x 250 mm
sample size: 100 microliters
sample concentration: 1.5 mg/mL
mobile phase: 60% acetonitrile - 40% water
flow rate: 2 mL/min
purity: 98.4%



24

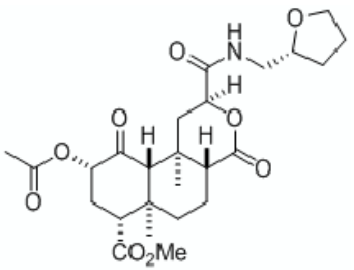


pump: Agilent 1100 series quaternary pump
column: Phenomenex Luna C18, 5 micron, 10 x 250 mm
sample size: 100 microliter
sample concentration: 0.1 mg/mL
mobile phase: 60% acetonitrile - 40% water
flow rate: 1.5 mL/min
purity: 95.3%

25

DAD1 A, Sig=209,4 Ref=360,100 (DENISE\DS-1-291000004.D)

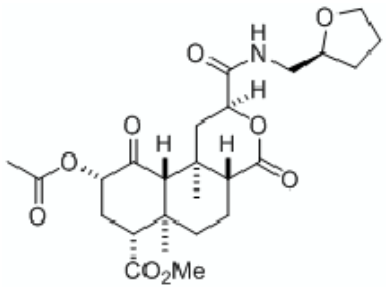
pump: Agilent 1100 series quaternary pump
column: Phenomenex Luna C-18, 5 micron, 10 x 250 mm
sample size: 100 microliters
sample concentration: 1.5 mg/mL
mobile phase: 60% acetonitrile - 40% water
flow rate: 2 mL/min
purity: 98.1%



26

DAD1 A, Sig=209,4 Ref=360,100 (DENISE\DS-1-292000002.D)

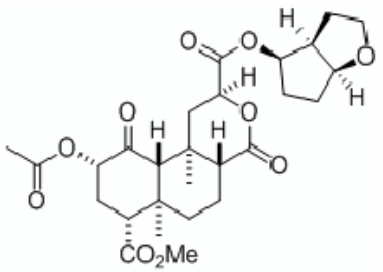
pump: Agilent 1100 series quaternary pump
column: Phenomenex Luna C-18, 5 micron, 10 x 250 mm
sample size: 100 microliters
sample concentration: 1.9 mg/mL
mobile phase: 60% acetonitrile - 40% water
flow rate: 2 mL/min
purity: 99.2%



27

DAD1 A, Sig=209,4 Ref=360,100 (DENISE\DS-2-98000002.D)

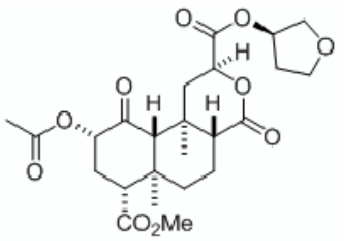
pump: Agilent 1100 series quaternary pump
column: Phenomenex Luna C-18, 5 micron, 10 x 250 mm
sample size: 100 microliters
sample concentration: 0.8 mg/mL
mobile phase: 60% acetonitrile - 40% water
flow rate: 5 mL/min
purity: 95.70%



28

DAD1 A, Sig=209,4 Ref=360,100 (DENISE\DS-3-145000007.D)

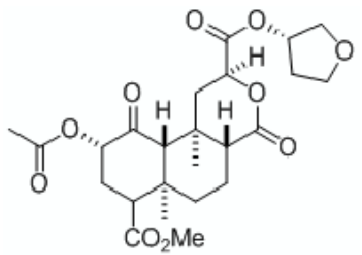
pump: Agilent 1100 series quaternary pump
column: Phenomenex Luna C-18, 5 micron, 10 x 250 mm
sample size: 100 microliters
sample concentration: 3.0 mg/mL
mobile phase: 60% acetonitrile - 40% water
flow rate: 5 mL/min
purity: 97.10%



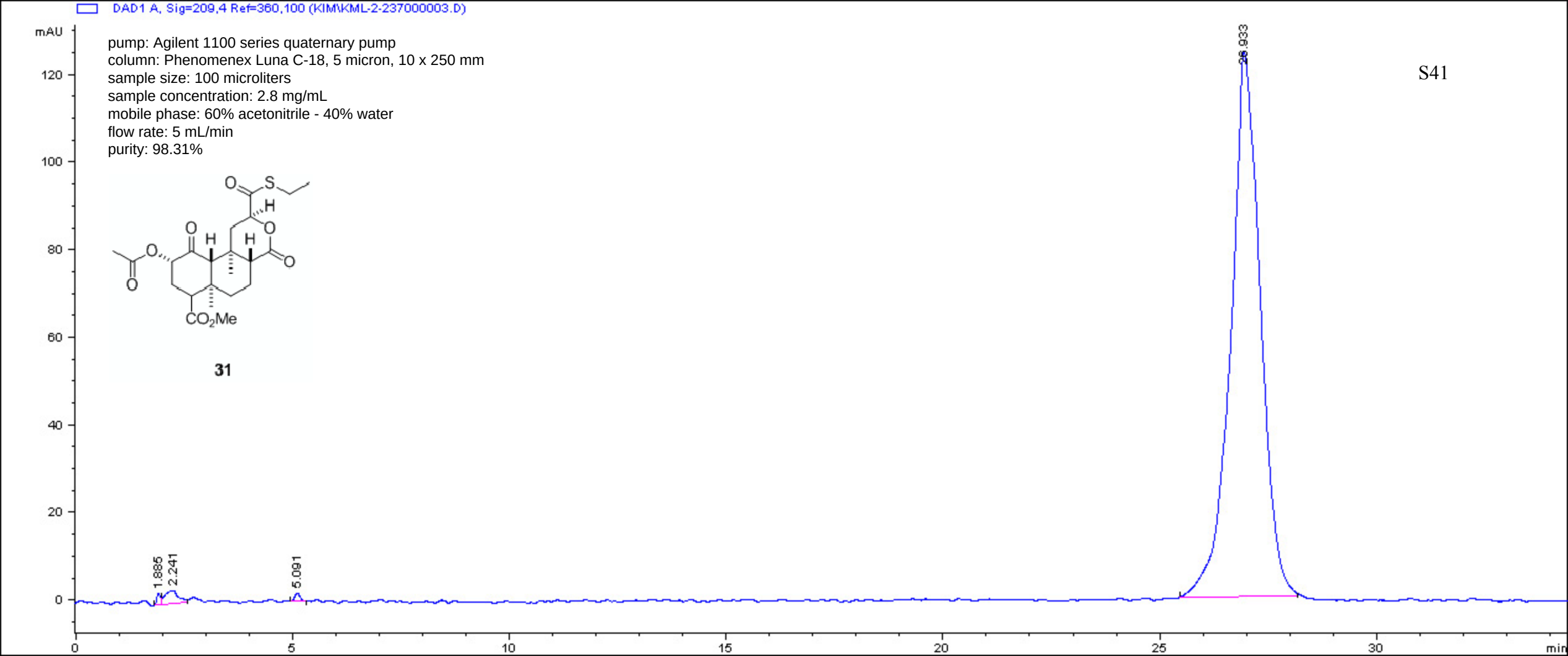
29

DAD1 A, Sig=209,4 Ref=360,100 (DENISE\DS-1-293000004.D)

pump: Agilent 1100 series quaternary pump
column: Phenomenex Luna C18, 5 micron, 10 x 250 mm
sample size: 100 microliter
sample concentration: 0.3 mg/mL
mobile phase: 60% acetonitrile - 40% water
flow rate: 3 mL/min
purity: 98.4%

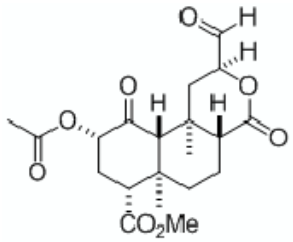


30

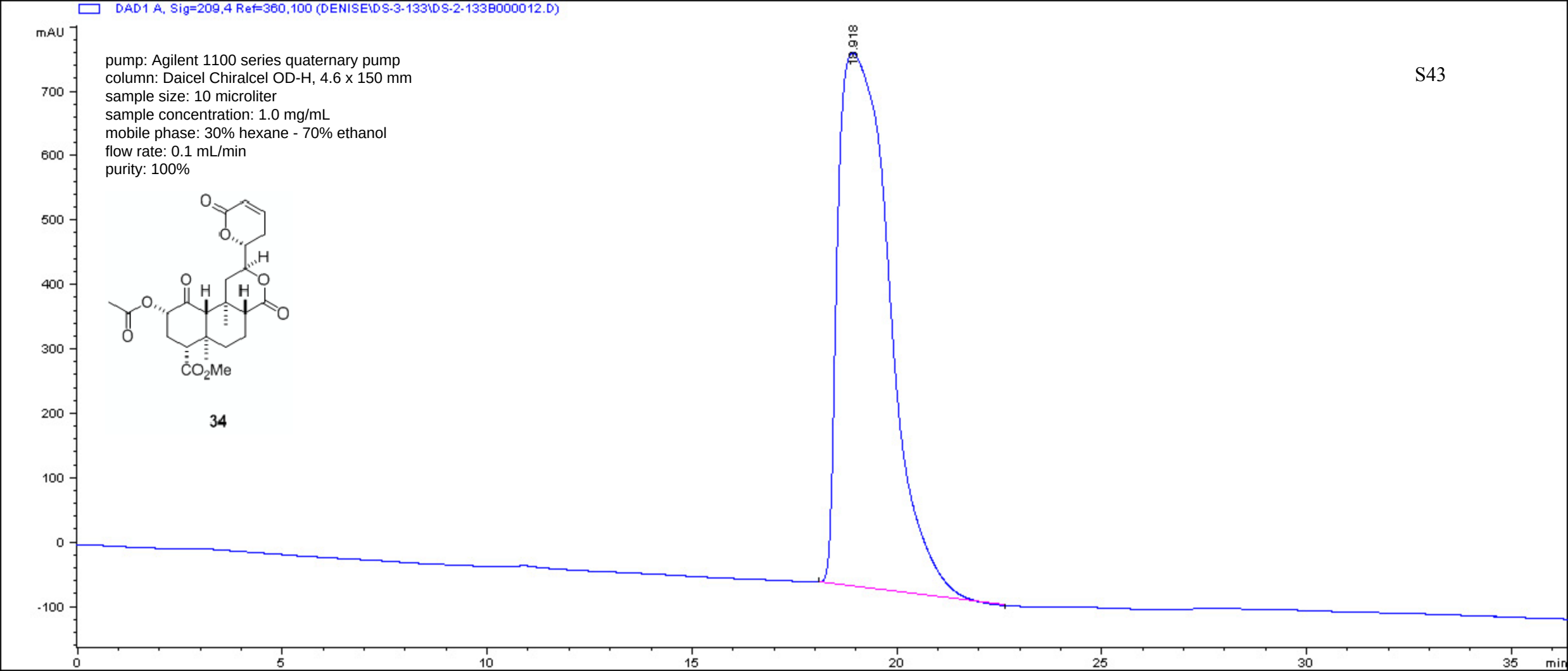

DAD1 A, Sig=209,4 Ref=360,100 (KIM\KML-2-237000003.D)
mAU
pump: Agilent 1100 series quaternary pump
column: Phenomenex Luna C-18, 5 micron, 10 x 250 mm
sample size: 100 microliters
sample concentration: 2.8 mg/mL
mobile phase: 60% acetonitrile - 40% water
flow rate: 5 mL/min
purity: 98.31%
31
S41
1.885
2.241
5.091
26.933
min

DAD1 A, Sig=209,4 Ref=360,100 (KIM\KML-ALDEHYDE003.D)

pump: Agilent 1100 series quaternary pump
column: Phenomenex Luna C-18, 5 micron, 10 x 250 mm
sample size: 100 microliters
sample concentration: 3.0 mg/mL
mobile phase: 60% acetonitrile - 40% water
flow rate: 5 mL/min
purity: 95.63%



32

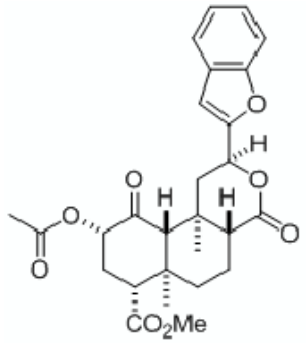


pump: Agilent 1100 series quaternary pump
column: Daicel Chiralcel OD-H, 4.6 x 150 mm
sample size: 10 microliter
sample concentration: 1.0 mg/mL
mobile phase: 30% hexane - 70% ethanol
flow rate: 0.1 mL/min
purity: 100%

34

DAD1 C, Sig=254,8 Ref=360,100 (DENISE\DS-3-73000001.D)

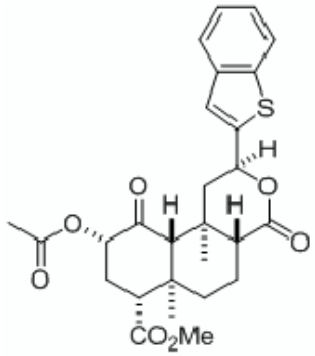
pump: Agilent 1100 series quaternary pump
column: Phenomenex Luna C-18, 5 micron, 10 x 250 mm
sample size: 100 microliters
sample concentration: 0.7 mg/mL
mobile phase: 60% acetonitrile - 40% water
flow rate: 5 mL/min
purity: 98.1%



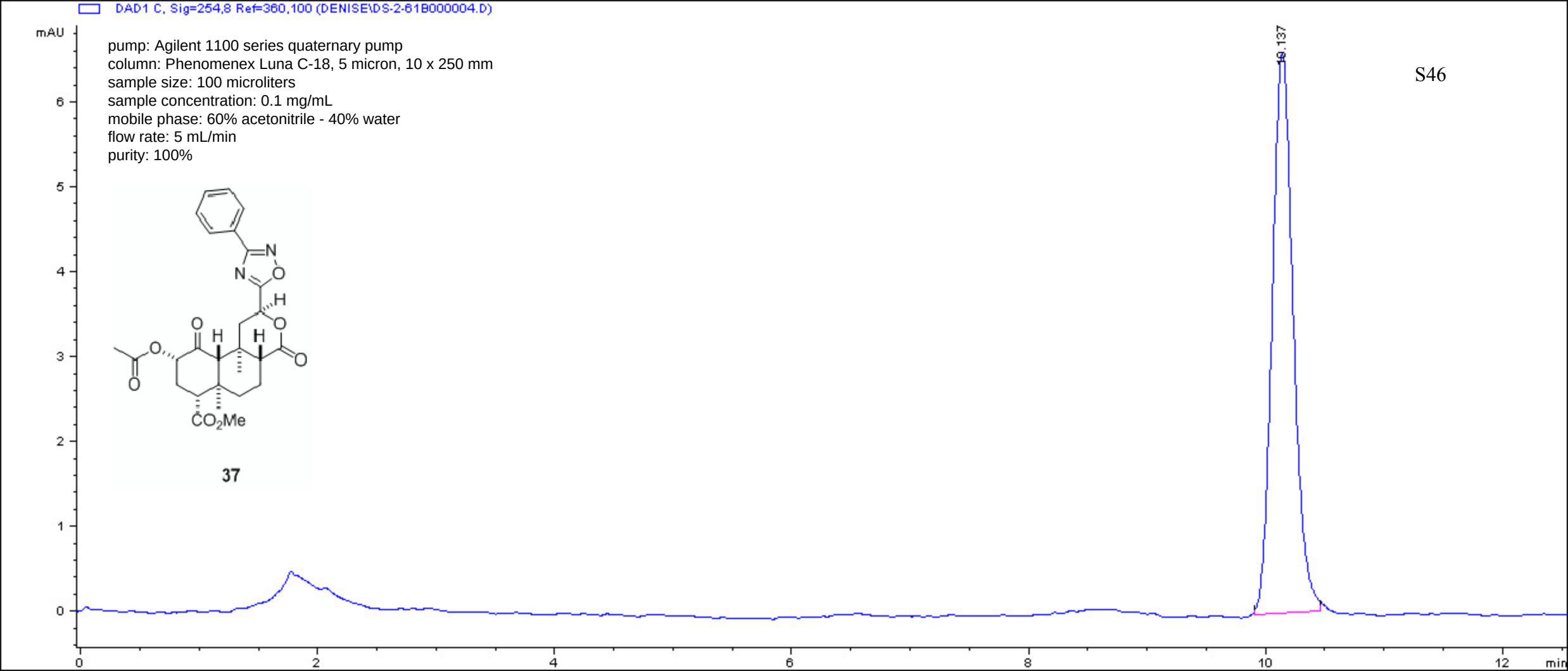
35

DAD1 C, Sig=254,8 Ref=360,100 (DENISE\DS-2-84A000001.D)

pump: Agilent 1100 series quaternary pump
column: Phenomenex Luna C-18, 5 micron, 10 x 250 mm
sample size: 100 microliters
sample concentration: 0.7 mg/mL
mobile phase: 60% acetonitrile - 40% water
flow rate: 5 mL/min
purity: 100%



36


DAD1 C, Sig=254,8 Ref=360,100 (DENISE\DS-2-61B000004.D)
mAU
pump: Agilent 1100 series quaternary pump
column: Phenomenex Luna C-18, 5 micron, 10 x 250 mm
sample size: 100 microliters
sample concentration: 0.1 mg/mL
mobile phase: 60% acetonitrile - 40% water
flow rate: 5 mL/min
purity: 100%
10.137
37
min