Plasma fetal bile acids 7α-hydroxy-3-oxochol-4-en-24-oic acid and 3-oxachola-4,6-dien-24-oic acid indicate the severity of liver cirrhosis

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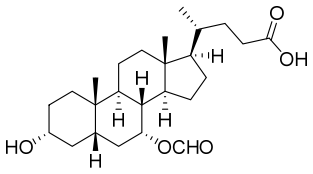
Supplementary Materials

Supplementary spectral data

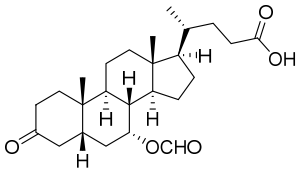
Compound 4 (Fig. 4)



(*R*)-4-((3*R*,5*S*,7*R*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-7-(formyloxy)-3-hydroxy-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)pentanoic acid (4).

Prepared according to the procedure b. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, *J*=1.0 Hz, 1H), 5.02 (d, *J*=3.2 Hz, 1H), 3.50 (td, *J*=11.0, 5.5 Hz, 1H), 2.40 (ddd, *J*=15.4, 10.1, 5.2 Hz, 1H), 2.26 (ddd, *J*=15.9, 9.6, 6.6 Hz, 1H), 2.17 (s, 2H), 2.07–1.94 (m, 3H), 1.83 (tdd, *J*=13.7, 7.4, 3.6 Hz, 3H), 1.72–1.40 (under water peak, m, 7H), 1.40–1.23 (m, 6H), 1.22–0.97 (m, 4H), 0.96–0.91 (m, 4H), 0.90–0.78 (m, 1H), 0.66 (s, 2H).

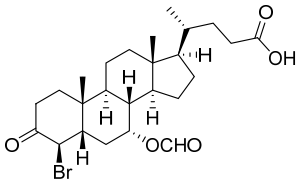
Compound 5 (Fig. 4)



(*R*)-4-((5*R*,7*R*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-7-(formyloxy)-10,13-dimethyl-3-oxohexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)pentanoic acid (5).

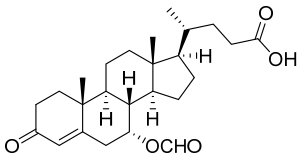
Prepared according to the procedure c. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, *J*=1.0 Hz, 1H), 5.12 (d, *J*=3.2 Hz, 1H), 3.02 (dd, *J*=15.2, 13.8 Hz, 1H), 2.46–2.32 (m, 2H), 2.32–2.24 (m, 1H), 2.24–2.16 (m, 1H), 2.15–2.06 (m, 2H), 2.04–1.92 (m, 3H), 1.91–1.77 (m, 3H), 1.73–1.65 (m, 3H), 1.60–1.52 (m, 2H), 1.51–1.30 (m, 7H), 1.29–1.23 (m, 1H), 1.22–1.07 (m, 2H), 1.04 (s, 2H), 0.95 (d, *J*=6.5 Hz, 2H), 0.70 (s, 2H).

Compound 6 (Fig. 4)



(*R*)-4-((4*R*,5*S*,7*R*,8*S*,9*S*,10*R*,13*R*,14*S*,17*R*)-4-bromo-7-(formyloxy)-10,13-dimethyl-3-oxohexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)pentanoic acid (6). Prepared according to the procedure d. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, *J*=4.7 Hz, 1H), 5.34 (d, *J*=11.8 Hz, 1H), 5.17 (d, *J*=3.2 Hz, 1H), 2.65–2.49 (m, 2H), 2.41 (ddd, *J*=15.4, 10.0, 5.2 Hz, 1H), 2.27 (ddd, *J*=17.8, 9.6, 6.6 Hz, 1H), 2.21–2.13 (m, 2H), 2.09–2.01 (m, 1H), 2.01–1.93 (m, 2H), 1.93–1.70 (m, 3H), 1.61–1.50 (m, 2H), 1.50–1.31 (m, 5H), 1.30–1.22 (m, 1H), 1.22–1.12 (m, 2H), 1.11 (s, 2H), 0.98-0.91 (m, 3H), 0.70 (s, 2H).

Compound 7 (Fig. 4)



(*R*)-4-((7*R*,8*S*,9*S*,10*R*,13*R*,14*S*,17*R*)-7-(formyloxy)-10,13-dimethyl-3-oxo-2,3,6,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)pentanoic acid (7). Prepared according to the procedure e. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, *J*=3.8 Hz, 1H), 5.17 (s, 1H), 2.68–2.50 (m, 1H), 2.50–2.33 (m, 2H), 2.33–2.19 (m, 2H), 2.20–1.99 (m, 3H), 1.93–1.67 (m, 4H), 1.64–1.42 (m, 5H), 1.39–1.07 (m, 9H), 1.01–0.87 (m, 3H), 0.79–0.65 (m, 2H).

UPLC-TQMS characteristics of 16 free and conjugated bile acids

Supplementary Table S1. Details of the ultraperformance liquid chromatography-triple quadrupole mass spectrometry assay for 15 free and conjugated bile acids

Bile acid	Retention Time (min)	MRM transition	Cone voltage (V)	Collision energy (eV)
Lithocholic acid (LCA)	0.90	375.25 > 375.25	60	32
Deoxycholic acid (DCA)	0.83	391.25 > 391.25	60	16
Glycolithocholic acid (GLCA)	0.82	432.25 > 74.00	60	35
Chenodeoxycholic acid (CDCA)	0.80	391.25 > 391.25	60	16
Taurolithocholic acid (TLCA)	0.71	482.25 > 80.00	60	60
Glycodeoxycholic acid (GDCA)	0.70	448.25 > 74.00	60	35
Glycochenodeoxycholic acid (GCDCA)	0.67	448.25 > 74.00	60	35
Cholic acid (CA)	0.66	407.25 > 343.25	60	34
Ursodeoxycholic acid (UDCA)	0.66	391.25 > 391.25	60	16
Taurodeoxycholic acid (TDCA)	0.60	498.25 > 80.00	60	60
Taurochenodeoxycholic acid (TCDCA)	0.57	498.25 > 80.00	60	60
Glycocholic acid (GCA)	0.55	464.25 > 74.00	60	34
Taurocholic acid (TCA)	0.46	514.25 > 80.00	60	64
Tauroursodeoxycholic acid (TUDCA)	0.44	498.25 > 80.00	60	60
Glycoursodeoxycholic acid (GUDCA)	0.52	448.25 > 74.00	60	35

Primary bile acids (CA and CDCA) and their glycine and taurine conjugates are shaded green.