Supporting Information

Discovery Of Potent, Non-Systemic Apical Sodium-Codependent Bile Acid Transporter

Inhibitors (Part I)

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Table 1. Crystal data and structure refinement for compound **34a**.

Identification code	mcr1195/RT/P4	
Empirical formula	C ₂₂ H ₂₈ O ₃ S	
Formula weight	372.50	
Temperature	298(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P2 ₁ /c	
Unit cell dimensions	a = 16.7307(9) Å	$\alpha = 90^\circ$.
	b = 14.4865(10) Å	$\beta = 116.950(5)^\circ$.
	c = 18.4491(10) Å	$\gamma = 90^\circ$.
Volume	3985.9(4) Å ³	
Z	8	
Density (calculated)	1.241 Mg/m ³	
Absorption coefficient	1.581 mm ⁻¹	
F(000)	1600	
Crystal size	0.50 x 0.30 x 0.20 mm ³	
Theta range for data collection	2.96 to 55.99°	
Index ranges	-1 ≤ h ≤ 17, -1 ≤ k ≤ 15, -19 ≤ l ≤ 18	
Reflections collected	6663	
Independent reflections	5188 [R(int) = 0.0273]	
Completeness to theta = 55.99°	99.9 %	
Absorption correction	None	
Max. and min. transmission	0.7427 and 0.5053	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	5188 / 0 / 478	
Goodness-of-fit on F ²	1.040	
Final R indices [I > 2sigma(I)]	R1 = 0.0464, wR2 = 0.1129	
R indices (all data)	R1 = 0.0614, wR2 = 0.1223	
Largest diff. peak and hole	0.184 and -0.362 e.Å ⁻³	

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for **34a**. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	$U(\text{eq})$
S(1)	9240(1)	4218(1)	2456(1)	49(1)
O(1)	8887(2)	3634(2)	2871(1)	70(1)
O(2)	9727(1)	3765(1)	2077(1)	58(1)
O(3)	9433(1)	6939(1)	2426(1)	46(1)
C(1)	9926(2)	5049(2)	3173(2)	45(1)
C(2)	10552(2)	5697(2)	2996(2)	38(1)
C(3)	10016(2)	6343(2)	2268(2)	36(1)
C(4)	9444(2)	5853(2)	1441(1)	35(1)
C(5)	8502(2)	5607(2)	1319(2)	36(1)
C(6)	7752(2)	6091(2)	781(2)	44(1)
C(7)	6894(2)	5851(2)	649(2)	50(1)
C(8)	6762(2)	5116(2)	1047(2)	52(1)
C(9)	7481(2)	4622(2)	1591(2)	50(1)
C(10)	8342(2)	4868(2)	1724(2)	41(1)
C(11)	11265(2)	5161(2)	2847(2)	42(1)
C(12)	11899(2)	4547(2)	3537(2)	51(1)
C(13)	12538(2)	4011(2)	3332(2)	63(1)
C(14)	13212(2)	3459(3)	4042(2)	76(1)
C(15)	11025(2)	6286(2)	3777(2)	50(1)
C(16)	11748(2)	6944(2)	3816(2)	63(1)
C(17)	9414(2)	6384(2)	719(2)	38(1)
C(18)	9479(2)	7330(2)	695(2)	59(1)
C(19)	9461(2)	7777(3)	27(2)	77(1)
C(20)	9361(2)	7284(3)	-637(2)	76(1)
C(21)	9301(2)	6349(3)	-630(2)	71(1)
C(22)	9318(2)	5900(2)	40(2)	53(1)
S(2)	15327(1)	472(1)	3200(1)	43(1)
O(1')	15488(1)	144(2)	3993(1)	57(1)
O(2')	15009(1)	-199(1)	2549(1)	52(1)
O(3')	15408(1)	2918(1)	2464(1)	49(1)
C(1')	14559(2)	1397(2)	2964(2)	40(1)

C(2')	14131(2)	1864(2)	2120(2)	35(1)
C(3')	14855(2)	2249(2)	1895(2)	38(1)
C(4')	15491(2)	1525(2)	1812(2)	36(1)
C(5')	16342(2)	1426(2)	2617(2)	37(1)
C(6')	17153(2)	1818(2)	2739(2)	48(1)
C(7')	17900(2)	1772(2)	3490(2)	57(1)
C(8')	17867(2)	1329(2)	4129(2)	58(1)
C(9')	17083(2)	929(2)	4037(2)	51(1)
C(10')	16325(2)	979(2)	3279(2)	40(1)
C(11')	13502(2)	1201(2)	1449(2)	44(1)
C(12')	12691(2)	849(3)	1532(2)	65(1)
C(13')	12178(3)	104(3)	919(2)	86(1)
C(14')	12591(3)	-794(3)	1137(3)	81(1)
C(14A)	11566(13)	-486(15)	878(10)	91(8)
C(15')	13596(2)	2687(2)	2211(2)	47(1)
C(16')	13087(2)	3277(2)	1457(2)	61(1)
C(17')	15673(2)	1715(2)	1088(2)	39(1)
C(18')	15728(2)	982(2)	633(2)	47(1)
C(19')	15862(2)	1127(2)	-47(2)	54(1)
C(20')	15945(2)	2001(2)	-283(2)	54(1)
C(21')	15886(2)	2737(2)	160(2)	55(1)
C(22')	15751(2)	2604(2)	839(2)	51(1)

Table 3. Bond lengths [Å] and angles [°] for **34a**.

S(1)-O(1)	1.436(2)
S(1)-O(2)	1.450(2)
S(1)-C(10)	1.769(3)
S(1)-C(1)	1.773(3)
O(3)-C(3)	1.429(3)
C(1)-C(2)	1.547(4)
C(2)-C(3)	1.546(4)
C(2)-C(15)	1.548(4)
C(2)-C(11)	1.550(4)
C(3)-C(4)	1.557(3)
C(4)-C(17)	1.518(4)
C(4)-C(5)	1.530(4)
C(5)-C(6)	1.386(4)
C(5)-C(10)	1.398(4)
C(6)-C(7)	1.387(4)
C(7)-C(8)	1.366(4)
C(8)-C(9)	1.369(4)
C(9)-C(10)	1.394(4)
C(11)-C(12)	1.521(4)
C(12)-C(13)	1.502(4)
C(13)-C(14)	1.514(4)
C(15)-C(16)	1.516(4)
C(17)-C(18)	1.378(4)
C(17)-C(22)	1.380(4)
C(18)-C(19)	1.381(4)
C(19)-C(20)	1.362(5)
C(20)-C(21)	1.359(5)
C(21)-C(22)	1.385(4)
S(2)-O(1')	1.4413(19)
S(2)-O(2')	1.446(2)
S(2)-C(1')	1.769(3)
S(2)-C(10')	1.769(3)
O(3')-C(3')	1.419(3)
C(1')-C(2')	1.544(4)

C(2')-C(11')	1.544(4)
C(2')-C(15')	1.544(4)
C(2')-C(3')	1.551(4)
C(3')-C(4')	1.550(4)
C(4')-C(17')	1.524(4)
C(4')-C(5')	1.528(4)
C(5')-C(6')	1.392(4)
C(5')-C(10')	1.394(4)
C(6')-C(7')	1.385(4)
C(7')-C(8')	1.367(4)
C(8')-C(9')	1.371(4)
C(9')-C(10')	1.401(4)
C(11')-C(12')	1.520(4)
C(12')-C(13')	1.516(5)
C(13')-C(14A)	1.310(14)
C(13')-C(14')	1.442(6)
C(15')-C(16')	1.522(4)
C(17')-C(18')	1.382(4)
C(17')-C(22')	1.393(4)
C(18')-C(19')	1.387(4)
C(19')-C(20')	1.366(4)
C(20')-C(21')	1.374(4)
C(21')-C(22')	1.384(4)

O(1)-S(1)-O(2)	116.63(14)
O(1)-S(1)-C(10)	108.02(13)
O(2)-S(1)-C(10)	109.98(13)
O(1)-S(1)-C(1)	106.56(14)
O(2)-S(1)-C(1)	110.62(13)
C(10)-S(1)-C(1)	104.27(13)
C(2)-C(1)-S(1)	121.73(19)
C(3)-C(2)-C(1)	111.7(2)
C(3)-C(2)-C(15)	109.0(2)
C(1)-C(2)-C(15)	104.3(2)
C(3)-C(2)-C(11)	109.8(2)
C(1)-C(2)-C(11)	112.5(2)

C(15)-C(2)-C(11)	109.4(2)
O(3)-C(3)-C(2)	111.7(2)
O(3)-C(3)-C(4)	107.6(2)
C(2)-C(3)-C(4)	115.6(2)
C(17)-C(4)-C(5)	111.5(2)
C(17)-C(4)-C(3)	112.9(2)
C(5)-C(4)-C(3)	112.7(2)
C(6)-C(5)-C(10)	116.1(2)
C(6)-C(5)-C(4)	121.7(2)
C(10)-C(5)-C(4)	122.2(2)
C(5)-C(6)-C(7)	121.8(3)
C(8)-C(7)-C(6)	120.5(3)
C(7)-C(8)-C(9)	119.9(3)
C(8)-C(9)-C(10)	119.4(3)
C(9)-C(10)-C(5)	122.3(3)
C(9)-C(10)-S(1)	116.8(2)
C(5)-C(10)-S(1)	121.0(2)
C(12)-C(11)-C(2)	116.5(2)
C(13)-C(12)-C(11)	113.4(2)
C(12)-C(13)-C(14)	113.0(3)
C(16)-C(15)-C(2)	116.9(2)
C(18)-C(17)-C(22)	117.0(3)
C(18)-C(17)-C(4)	124.1(3)
C(22)-C(17)-C(4)	118.9(3)
C(17)-C(18)-C(19)	121.7(3)
C(20)-C(19)-C(18)	120.1(4)
C(21)-C(20)-C(19)	119.6(3)
C(20)-C(21)-C(22)	120.3(4)
C(17)-C(22)-C(21)	121.3(3)
O(1')-S(2)-O(2')	116.74(12)
O(1')-S(2)-C(1')	106.29(13)
O(2')-S(2)-C(1')	110.59(12)
O(1')-S(2)-C(10')	108.53(13)
O(2')-S(2)-C(10')	109.03(13)
C(1')-S(2)-C(10')	105.00(13)
C(2')-C(1')-S(2)	122.25(19)

C(11')-C(2')-C(15')	110.4(2)
C(11')-C(2')-C(1')	111.8(2)
C(15')-C(2')-C(1')	104.8(2)
C(11')-C(2')-C(3')	109.9(2)
C(15')-C(2')-C(3')	108.2(2)
C(1')-C(2')-C(3')	111.5(2)
O(3')-C(3')-C(4')	106.8(2)
O(3')-C(3')-C(2')	111.9(2)
C(4')-C(3')-C(2')	115.9(2)
C(17')-C(4')-C(5')	113.6(2)
C(17')-C(4')-C(3')	112.5(2)
C(5')-C(4')-C(3')	110.2(2)
C(6')-C(5')-C(10')	117.0(2)
C(6')-C(5')-C(4')	122.0(2)
C(10')-C(5')-C(4')	121.0(2)
C(7')-C(6')-C(5')	121.0(3)
C(8')-C(7')-C(6')	121.0(3)
C(7')-C(8')-C(9')	120.2(3)
C(8')-C(9')-C(10')	118.9(3)
C(5')-C(10')-C(9')	122.0(3)
C(5')-C(10')-S(2)	120.9(2)
C(9')-C(10')-S(2)	117.0(2)
C(12')-C(11')-C(2')	116.3(2)
C(13')-C(12')-C(11')	113.2(3)
C(14A)-C(13')-C(14')	71.9(12)
C(14A)-C(13')-C(12')	132.2(9)
C(14')-C(13')-C(12')	113.4(3)
C(16')-C(15')-C(2')	116.5(2)
C(18')-C(17')-C(22')	118.0(2)
C(18')-C(17')-C(4')	119.2(2)
C(22')-C(17')-C(4')	122.8(2)
C(17')-C(18')-C(19')	121.0(3)
C(20')-C(19')-C(18')	120.6(3)
C(19')-C(20')-C(21')	119.0(3)
C(20')-C(21')-C(22')	121.0(3)
C(21')-C(22')-C(17')	120.3(3)

Table 4. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for **34a**. The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
S(1)	45(1)	43(1)	58(1)	12(1)	22(1)	0(1)
O(1)	64(2)	65(1)	80(2)	29(1)	32(1)	-7(1)
O(2)	57(1)	43(1)	74(1)	1(1)	31(1)	3(1)
O(3)	41(1)	43(1)	49(1)	-8(1)	16(1)	4(1)
C(1)	43(2)	53(2)	39(2)	9(1)	18(1)	5(1)
C(2)	33(2)	45(2)	32(1)	2(1)	12(1)	2(1)
C(3)	34(2)	37(1)	36(2)	-1(1)	14(1)	-1(1)
C(4)	33(1)	37(1)	32(1)	1(1)	12(1)	2(1)
C(5)	36(2)	40(2)	32(1)	-4(1)	15(1)	-2(1)
C(6)	38(2)	49(2)	40(2)	1(1)	13(1)	1(1)
C(7)	33(2)	62(2)	45(2)	-5(2)	9(1)	3(2)
C(8)	37(2)	69(2)	52(2)	-18(2)	20(2)	-11(2)
C(9)	43(2)	51(2)	57(2)	-4(2)	24(2)	-9(2)
C(10)	37(2)	40(2)	44(2)	-3(1)	17(1)	-3(1)
C(11)	36(2)	49(2)	39(2)	2(1)	17(1)	4(1)
C(12)	42(2)	54(2)	52(2)	5(2)	17(2)	10(1)
C(13)	52(2)	74(2)	57(2)	1(2)	19(2)	18(2)
C(14)	62(2)	75(2)	87(3)	17(2)	28(2)	26(2)
C(15)	45(2)	60(2)	37(2)	-6(1)	11(1)	9(2)
C(16)	50(2)	60(2)	55(2)	-10(2)	3(2)	-3(2)
C(17)	29(1)	47(2)	35(2)	2(1)	13(1)	2(1)
C(18)	71(2)	54(2)	42(2)	6(2)	15(2)	-10(2)
C(19)	78(3)	75(2)	59(2)	23(2)	14(2)	-22(2)
C(20)	52(2)	120(4)	54(2)	35(2)	24(2)	-1(2)
C(21)	68(2)	106(3)	49(2)	10(2)	37(2)	21(2)
C(22)	49(2)	65(2)	47(2)	2(2)	24(2)	10(2)
S(2)	45(1)	38(1)	39(1)	8(1)	14(1)	0(1)
O(1')	59(1)	64(1)	44(1)	24(1)	19(1)	4(1)
O(2')	62(1)	33(1)	54(1)	2(1)	19(1)	-5(1)
O(3')	40(1)	33(1)	65(1)	-7(1)	16(1)	1(1)

C(1')	37(2)	44(2)	35(1)	0(1)	13(1)	-1(1)
C(2')	35(1)	39(2)	30(1)	1(1)	13(1)	2(1)
C(3')	39(2)	38(2)	34(1)	3(1)	13(1)	3(1)
C(4')	35(2)	35(1)	37(1)	-1(1)	15(1)	-1(1)
C(5')	40(2)	31(1)	40(2)	-1(1)	18(1)	8(1)
C(6')	42(2)	53(2)	52(2)	1(2)	25(2)	5(1)
C(7')	35(2)	64(2)	65(2)	-3(2)	17(2)	0(2)
C(8')	37(2)	69(2)	50(2)	2(2)	6(2)	9(2)
C(9')	45(2)	53(2)	42(2)	9(1)	10(2)	9(2)
C(10')	36(2)	39(2)	38(2)	3(1)	11(1)	5(1)
C(11')	41(2)	52(2)	32(2)	1(1)	10(1)	-3(1)
C(12')	53(2)	76(2)	57(2)	-3(2)	15(2)	-22(2)
C(13')	69(3)	85(3)	74(2)	-3(2)	8(2)	-31(2)
C(14')	89(4)	69(3)	79(3)	-15(3)	34(3)	-10(3)
C(14A)	89(14)	141(19)	60(11)	-38(12)	49(11)	-96(14)
C(15')	40(2)	49(2)	52(2)	3(1)	20(1)	6(1)
C(16')	46(2)	58(2)	72(2)	14(2)	19(2)	15(2)
C(17')	36(2)	44(2)	35(2)	3(1)	15(1)	-3(1)
C(18')	48(2)	47(2)	46(2)	-2(1)	22(1)	0(1)
C(19')	48(2)	71(2)	43(2)	-10(2)	21(2)	0(2)
C(20')	45(2)	78(2)	39(2)	9(2)	19(1)	5(2)
C(21')	60(2)	58(2)	49(2)	12(2)	26(2)	-1(2)
C(22')	62(2)	48(2)	45(2)	1(1)	27(2)	-1(2)

Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^{-3}$) for 34a.

	x	y	z	U(eq)
H(3B)	9666	7449	2562	70
H(1A)	9531	5440	3294	54
H(1B)	10300	4717	3669	54
H(3A)	10451	6735	2196	43
H(4A)	9745	5267	1460	42
H(6A)	7826	6591	501	53
H(7A)	6405	6193	287	60
H(8A)	6184	4952	948	63
H(9A)	7396	4127	1869	60
H(11A)	10955	4779	2367	50
H(11B)	11621	5605	2726	50
H(12A)	12241	4928	4010	61
H(12B)	11548	4117	3679	61
H(13A)	12857	4437	3149	75
H(13B)	12199	3594	2886	75
H(14A)	13603	3133	3877	115
H(14B)	12902	3025	4217	115
H(14C)	13560	3869	4482	115
H(15A)	10571	6643	3842	60
H(15B)	11290	5870	4237	60
H(16A)	11991	7270	4324	94
H(16B)	11494	7378	3376	94
H(16C)	12216	6602	3774	94
H(18A)	9535	7677	1140	71
H(19A)	9518	8416	30	93
H(20A)	9333	7585	-1093	91
H(21A)	9249	6008	-1077	85
H(22A)	9262	5261	31	64
H(3'B)	15162	3424	2346	73
H(1'A)	14069	1179	3064	48

H(1'B)	14860	1879	3360	48
H(3'A)	14541	2560	1368	46
H(4'A)	15179	930	1708	43
H(6'A)	17193	2114	2309	57
H(7'A)	18433	2048	3560	69
H(8'A)	18376	1298	4628	69
H(9'A)	17056	629	4471	61
H(11C)	13291	1514	930	53
H(11D)	13851	672	1436	53
H(12C)	12889	605	2076	78
H(12D)	12291	1362	1463	78
H(13C)	12134	276	400	103
H(13D)	11581	72	867	103
H(14D)	12236	-1234	728	121
H(14E)	12628	-977	1651	121
H(14F)	13182	-769	1176	121
H(14G)	11367	-843	388	137
H(14H)	11066	-158	876	137
H(14I)	11816	-891	1340	137
H(15C)	13169	2449	2385	56
H(15D)	14010	3083	2641	56
H(16D)	12781	3765	1581	92
H(16E)	12659	2901	1028	92
H(16F)	13502	3537	1285	92
H(18B)	15673	383	786	56
H(19B)	15896	624	-345	64
H(20B)	16039	2096	-737	65
H(21B)	15939	3334	1	66
H(22B)	15712	3111	1131	61