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SUPPLEMENTARY MATERIAL TO

Synthesis, crystal structure and local anti-inflammatory activity of the L-phenylalanine methyl ester derivative of dexamethasone-derived cortienic acid

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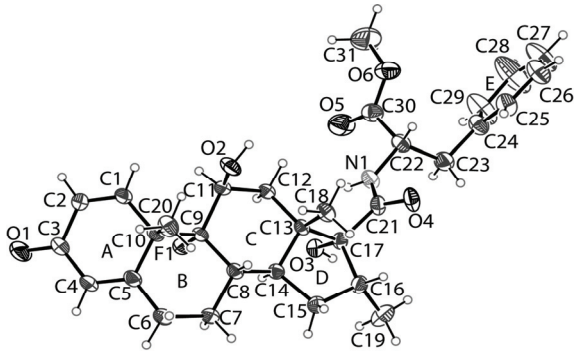

Fig. S-1. Structure of DF with atomic labelling.

PHYSICAL AND SPECTRAL DATA FOR DF

Yield: 83.5 %; m.p.: 119.3–122.0 °C; IR (ATR, cm^{-1}): 1269.02 (ester C–O stretching), 1658.36 (amide C=O stretching), 1670.71 (C_3=O stretching), 1718.18 (ester C=O stretching), 3407.79 (N–H stretching); ^{1}H-NMR (400 MHz, DMSO-d_6, δ / ppm): 0.75 (3H, *d*, J = 7.2 Hz, CH_3 at C16), 0.91 (3H, *s*, H18), 1.05–1.41 (3H, *m*, H6, H12, H15), 1.48 (3H, *s*, H19), 1.61 (1H, *m*, H6), 1.74 (1H,

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m, H15), 1.90–2.10 (2H, *m*, H14, H12), 2.22–2.40 (2H, *m*, H7, H8), 2.61 (1H, *m*, H7), 2.92 (1H, *m*, H16), 3.05 (2H, *d*, *J* = 6.4 Hz, C**H**$_2$C$_6$H$_5$), 3.61 (3H, *s*, OCH$_3$), 4.08 (1H, *m*, H11), 4.54 (1H, *q*, *J* = 7.6 Hz, NH–C**H**), 6.01 (1H, *s*, H4), 6.22 (1H, *dd*, *J* = 1.6 Hz, *J* = 10.2 Hz, H2), 7.18–7.31 (5H, *m*, Ar-H), 7.44 (1H, *d*, *J* = 7.6 Hz, H1); ^{13}C-NMR (100 MHz, DMSO-d_6, δ / ppm): 15.26 (CH$_3$ at C16), 17.11 (C18), 23.40 (*d*, *J* = 5 Hz, C19), 27.76 (C15), 32.27 (C7), 33.79 (C6), 34.28 (*d*, *J* = 19 Hz, C8), 35.21 (C16), 35.71 (C12), 37.20 (**C**H$_2$C$_6$H$_5$), 43.58 (C14), 48.39 (C13), 48.53 (*d, J* = 22 Hz, C10), 52.25 (OCH$_3$), 53.65 (NH–CH), 71.12 (*d, J* = 37 Hz C11), 86.88 (C17), 102.07 (*d, J* = 175 Hz C9), 124.51 (C4), 127.06 (C4′), 128.75 (C3′), 129.41 (C2), 129.56 (C2′), 137.45 (C1′), 157.17 (C1), 167.82 (C=O, ester), 172.25 (C20), 172.82 (C5), 185.86 (C3); MS $[M+H]^+$: calcd. for C$_{31}$H$_{38}$FNO$_6$: 540.27560. Observed: 540.27426; UV-Vis (CH$_3$OH) (λ_{max} / nm): 239.

TABLE S-I. Experimental details; crystal data

Chemical formula	C$_{31}$H$_{38}$FNO$_6$
Mr	539.62
Crystal system, space group	Orthorhombic, $P2_12_12_1$
Temperature, K	293
a, *b*, *c* / Å	8.2969 (3), 18.9358 (8), 20.0904 (6)
V / Å^3	3156.4 (2)
Z	4
Radiation type	MoK_α
μ / mm^{-1}	0.08
Crystal size, mm^3	0.18×0.02×0.02
Data collection	
No. of measured, independent and observed ($I > 2\sigma(I)$) reflections	18785, 7284, 5651
R_{int}	0.024
(sin $\theta/\lambda)_{max}$ / Å^{-1}	0.683
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, *S*	0.044, 0.104, 0.984
No. of reflections	7284
No. of parameters	368
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$, $\Delta\rho_{min}$ / e Å^{-3}	0.16, –0.16

TABLE S-II. Selected bond lengths and angles (standard uncertainties (s.u.) are given in parentheses)

Bond	Bond length, Å	Bond	Bond length, Å
F1–C9	1.4237(17)	C9–C10	1.567(2)
N1–C21	1.339(2)	C10–C20	1.557(2)
N1–C22	1.447(2)	C11–C12	1.534(2)
O1–C3	1.222(2)	C12–C13	1.518(2)
O2–C11	1.413(2)	C13–C14	1.535(2)
O3–C17	1.4250(18)	C13–C18	1.543(2)
O4–C21	1.2239(19)	C13–C17	1.558(2)
O5–C30	1.188(2)	C14–C15	1.534(2)
O6–C30	1.318(2)	C15–C16	1.553(2)
O6–C31	1.451(3)	C16–C19	1.507(3)
C1–C2	1.320(2)	C16–C17	1.552(2)
C1–C10	1.494(3)	C17–C21	1.533(2)
C2–C3	1.460(3)	C22–C30	1.509(3)
C3–C4	1.442(3)	C22–C23	1.535(3)
C4–C5	1.325(3)	C23–C24	1.510(3)
C5–C6	1.489(3)	C24–C25	1.365(3)
C5–C10	1.520(2)	C24–C29	1.373(3)
C6–C7	1.532(3)	C25–C26	1.369(3)
C7–C8	1.530(2)	C26–C27	1.352(3)
C8–C14	1.518(2)	C27–C28	1.346(4)
C8–C9	1.533(2)	C28–C29	1.387(4)
C9–C11	1.549(2)		
Bond	Bond angle, °	Bond	Bond angle, °
C21–N1–C22	124.21(15)	C12–C13–C17	115.57(12)
C30–O6–C31	116.7(2)	C14–C13–C17	98.60(12)
C2–C1–C10	124.69(16)	C18–C13–C17	110.42(13)
C1–C2–C3	120.84(18)	C8–C14–C15	119.64(13)
O1–C3–C4	122.51(18)	C15–C16–C17	104.70(13)
O1–C3–C2	120.41(19)	O3–C17–C21	109.16(13)
C4–C3–C2	117.07(16)	O3–C17–C16	111.96(13)
C5–C4–C3	123.20(16)	C21–C17–C16	113.84(13)
C4–C5–C6	122.84(16)	O3–C17–C13	106.41(12)
C4–C5–C10	121.88(17)	C21–C17–C13	113.13(13)
C6–C5–C10	115.24(15)	C16–C17–C13	101.98(12)
C5–C6–C7	111.33(15)	O4–C21–N1	122.89(16)
C8–C7–C6	114.64(15)	O4–C21–C17	123.17(15)
C14–C8–C7	110.49(14)	N1–C21–C17	113.89(14)
C14–C8–C9	109.16(13)	N1–C22–C30	107.47(15)
C7–C8–C9	110.34(13)	N1–C22–C23	111.22(15)
F1–C9–C8	106.19(12)	C30–C22–C23	109.67(15)
F1–C9–C11	101.99(12)	C24–C23–C22	113.24(16)
C8–C9–C11	115.62(13)	C25–C24–C29	117.02(19)
F1–C9–C10	104.00(12)	C25–C24–C23	120.87(18)
C8–C9–C10	112.26(13)	C29–C24–C23	122.01(18)

TABLE S-II. Continued

Bond	Bond angle, °	Bond	Bond angle, °
C11–C9–C10	115.04(13)	C24–C25–C26	122.02(19)
C1–C10–C5	112.26(14)	C27–C26–C25	119.7(2)
C1–C10–C20	107.72(15)	C28–C27–C26	120.3(2)
C5–C10–C20	108.39(15)	C27–C28–C29	119.7(3)
C1–C10–C9	109.69(14)	C24–C29–C28	121.1(2)
C5–C10–C9	105.52(13)	O5–C30–O6	124.7(2)
C20–C10–C9	113.34(14)	O5–C30–C22	123.84(19)
O2–C11–C12	114.16(13)	O6–C30–C22	111.41(18)
O2–C11–C9	108.02(13)	C8–C14–C13	114.35(13)
C12–C11–C9	112.51(13)	C15–C14–C13	103.68(12)
C13–C12–C11	113.65(13)	C14–C15–C16	105.00(13)
C12–C13–C14	108.88(12)	C19–C16–C15	114.11(17)
C12–C13–C18	110.47(14)	C19–C16–C17	115.34(15)
C14–C13–C18	112.43(13)		

TABLE S-III. Hydrogen bond geometry of DF

D–H···A	Symmetry code	D–H	H···A	D···A	D–H···A
O2–H2O···O4	$-1/2+x$, $1/2-y$, $-z$	0.84(2)	1.97(2)	2.791(2)	165(2)
O3–H3O···O1	$1-x$, $-1/2+y$, $1/2-z$	0.76(2)	2.00(2)	2.750(2)	167(2)
C29–H29···F1	$1-x$, $-1/2+y$, $1/2-z$	0.93	2.52	3.376(3)	154
N1–H1N···O3		0.86(2)	2.114(18)	2.587(2)	114(2)
N1–H1N···O5		0.86(2)	2.415(18)	2.716(2)	101(1)
C14–H14···F1		0.980(1)	2.46	2.851(2)	103
C14–H14···O3		0.98	2.31	2.736(2)	105
C12–H12A···O3		0.97	2.40	2.832(2)	107
C18–H18C···O2		0.96	2.44	3.043(2)	120
C16–H16···O4		0.98	2.56	2.953(2)	104
C20–H20A···O2		0.96	2.32	2.921(2)	120