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Aminimides as Potential CNS Acting Agents. III. Design, Synthesis and Receptor Binding of Aminimide Analogues of Dopamine, Serotonin, Morphine and Nicotine.

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Supplementary Information

Fig. S1. ^{1}H NMR spectra for **13** and **13a**.

Table S1. Crystal data including details of data collection, crystal structure determination and refinement of $C_{19}H_{22}N_2O_4.CH_3OH$ (**18**).

Table S2. Bond Angles [deg] for $C_{19}H_{22}N_2O_4.CH_3OH$ (**18**). Estimated standard deviations in the least significant figure are given in parentheses where applicable.

Table S3. Bond lengths [Å] for $C_{19}H_{22}N_2O_4.CH_3OH$ (**18**). Estimated standard deviations in the least significant figure are given in parentheses where applicable.

Table S4. Atomic coordinates and equivalent atomic temperature factor (Å^2) for $C_{19}H_{22}N_2O_4.CH_3OH$ (**18**). Estimated standard deviations in the least significant figure are represented in parentheses where applicable.

Table S5. Anistropic displacement parameters (Å)^2 for $C_{19}H_{22}N_2O_4.CH_3OH$ (**18**). Estimated standard deviations in the least significant figure are represented in parentheses where applicable.

Table S6. Torsional bond angles [deg] for $C_{19}H_{22}N_2O_4.CH_3OH$ (**18**). Estimated standard deviations in the least significant figure are given in parentheses where applicable.

Fig. S2. 300 MHz ^{1}H-^{1}H NOESY Spectrum of **19**, mixing time = 800 msec.

Table S7. ^{13}C NMR data for morphine and related compounds

Table S8. ^{1}H NMR data for morphine and related compounds

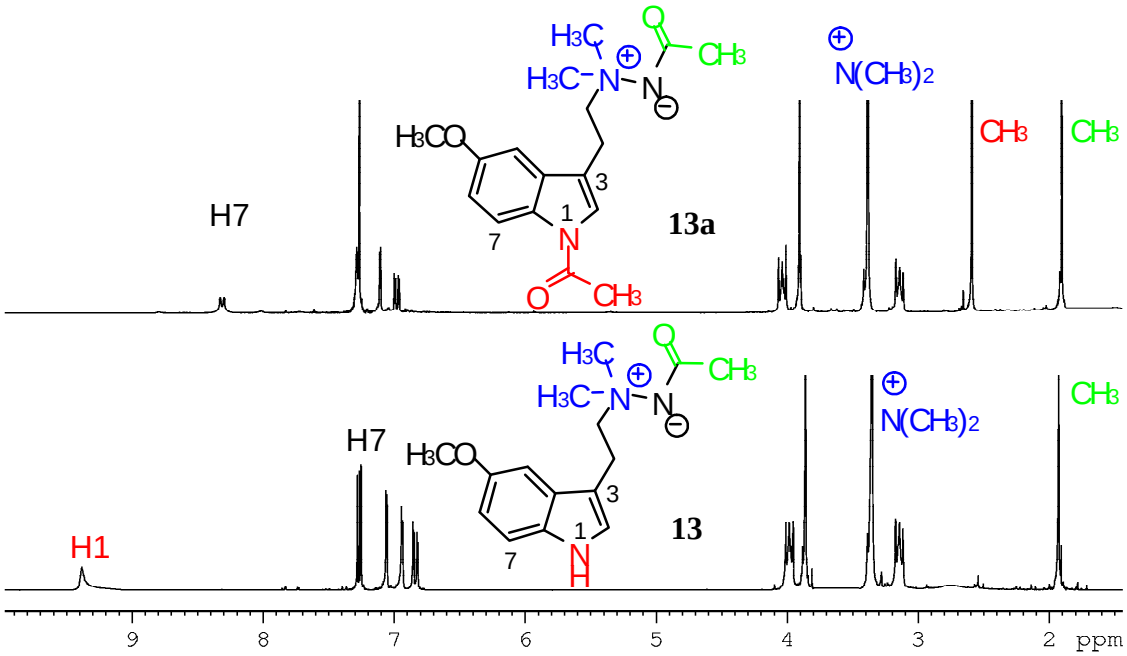

Fig. S1. ^{1}H NMR spectra for **13** and **13a**.

X-Ray Data for (5α,6α)-7,8-Didehydro-4,5-epoxy-17(*R*)-acetimidemethylmorphinan-3,6-diol (**18**)

Crystals of $C_{19}H_{22}N_2O_4.CH_3OH$ were grown by recrystallisation from methanol as colourless tabular crystals. A suitable crystal was coated in an inert viscous oil, mounted on a silica fibre, and promptly placed on a goniometer bathed in a cold stream of nitrogen at low temperature.

Crystallographic data were collected at 123(1) K, on an Enraf–Nonius Kappa CCD diffractometer system equipped with graphite monochromated Mo–Kα radiation using a combination of ϕ and ω rotations with 1˚ frames, a detector to crystal distance of 29 mm and a detector 2θ offset of -10˚ for the ϕ scans and 2˚ for the ω scans. Absorption corrections were not applied. The final unit cell determination, scaling of the data and corrections for Lorentz and polarisation effects were performed with Denzo-SMN.[1] The structure was solved by direct methods (SIR92[2]), expanded with the fourier technique (DIRDIF94[3]) and refined by the full matrix least-squares technique using the crystal structure analysis package teXsan4[4] on a Silicon Graphics Indy computer.

All non-hydrogen atoms were located in the initial solution and refined anisotropically. All hydrogen atoms of the aminimide molecule, and the hydroxy hydrogen of the methanol molecule, were observed during the course of the least-squares refinement and were included in the refinement at their calculated geometrically constrained positions. The hydrogen atoms of the methyl group of the methanol molecule were not observed, assigned or refined.

Crystallographic data are summarised in Table S1. Data including fractional atomic coordinates, anisotropic displacement parameters, interatomic bond distances and angles and bond torsion angles are given in Tables S2-S6.

[1] Otwinowski, Z.; Minor, W. In *Methods in Enzymology*; C. W. Carter and R. M. Sweet Jr., Ed.; Academic Press: San Diego, **1997**; Vol. 276, pp 307-326.
[2] Altomare, A.; Cascarono, G.; Giacovazzo, C.; Burla, M. C.; Polidori, G.; Camalli, M. *J. Appl. Cryst.* **1994**, *27*, 435.
[3]Beurskens, P. T.; Admirall, G.; Beurskens, G.; Bosman, W. P.; Garcia-Granda, S.; Gould, R. O.; Smits, J. M. M.; Smykalla, C. Crystallography Laboratory, Univ. of Nijmegen, Toorooveld, 6525, ED Nijmegen, The Netherlands,
[4] Corporation, M. S., teXsan: Single Crystal Structure Analysis Software, Program. The Woodlands, TX, Version 1.7, **1992-1997**.

Table S1. Crystal data including details of data collection, crystal structure determination and refinement of $C_{19}H_{22}N_2O_4.CH_3OH$ (**18**).

Empirical formula	$C_{20}H_{26}N_2O_5$
Mr g mol^{-1}	374.44
Temperature, K	173 (1)
Radiation	Mo Kα (graphite monochromator)
Wavelength, Å	0.7107
Crystal system	Monoclinic
Space group	P21
Unit cell dimensions	
a, Å	6.8431(2)
b, Å	17.7960(5)
c, Å	7.6101(2)
β, ˚	99.155(1)
Volume, Å^3	914.95
Z	2
ρ_C, g cm^{-3}	1.359
μ, cm^{-1}	0.098
F (000)	400
Crystal size (mm)	
±[0 1 0]	0.24
±[0 1 0]	0.22
±[0 1 0]	0.10
Detector aperture, mm	94 X 94
Data Images	360 exposures @ 40 sec.
Detector Position, mm	29
Detector Oscillation Angle, ˚	1.0
$2\theta_{max}$, ˚	-10.2
Decomposition	No decay correction was applied to data
Reflections collected	5002
No. of Unique Reflections	5002
R_{int}	0.01306
No. of Observed Reflections	4454 [$I>3\sigma(I)$]
Refinement method	Full-matrix least-squares on *F*
Data/Parameters	4454/243
Goodness-of-fit Indicator	2.74
Final *R* indicies [$I>3\sigma(I)$]	$R1$ = 0.0407, Rw = 0.0436
R indicies (all data)	$R1$ = 0.0490, $wR2$= 0.1028
Weighting scheme	$w = 1/\sigma^2(Fo)$
Extinction method	None
Maximum shift/e.s.d.	0.002
Max. and Min. residual electron density, e Å^3	0.28 and -0.33

Table S2. Bond Angles [deg] for $C_{19}H_{22}N_2O_4.CH_3OH$ (**18**). Estimated standard deviations in the least significant figure are given in parentheses where applicable.

Atom	Atom	Atom	[deg]	Atom	Atom	Atom	[deg]
C(3)	O(1)	H(23)	104.4	C(4)	O(2)	C(5)	106.7(1)
C(6)	O(3)	H(22)	101.0	C(20)	O(5)	H(21)	108.6
N(2)	N(1)	C(9)	113.3(1)	N(2)	N(1)	C(16)	104.2(1)
N(2)	N(1)	C(17)	108.5(1)	C(9)	N(1)	C(16)	108.6(1)
C(9)	N(1)	C(17)	112.6(1)	C(16)	N(1)	C(17)	109.3(1)
N(1)	N(2)	C(18)	116.1(1)	C(2)	C(1)	C(11)	120.3(1)
C(2)	C(1)	H(2)	120.1	C(11)	C(1)	H(2)	119.6
C(1)	C(2)	C(3)	122.2(1)	C(1)	C(2)	H(1)	118.7
C(3)	C(2)	H(1)	119.0	O(1)	C(3)	C(2)	124.1(1)
O(1)	C(3)	C(4)	119.7(1)	C(2)	C(3)	C(4)	116.1(1)
O(2)	C(4)	C(3)	126.4(1)	O(2)	C(4)	C(12)	112.1(1)
C(3)	C(4)	C(12)	121.4(1)	O(2)	C(5)	C(6)	108.7(1)
O(2)	C(5)	C(13)	106.7(1)	O(2)	C(5)	H(10)	110.1
C(6)	C(5)	C(13)	113.1(1)	C(6)	C(5)	H(10)	109.1
C(13)	C(5)	H(10)	109.2	O(3)	C(6)	C(5)	110.0(1)
O(3)	C(6)	C(7)	112.7(1)	O(3)	C(6)	C(7)	112.7(1)
O(3)	C(6)	H(9)	106.7	C(5)	C(6)	C(7)	113.6(1)
C(5)	C(6)	H(9)	107.3	C(7)	C(6)	H(9)	106.2
C(6)	C(7)	C(8)	120.4(1)	C(6)	C(7)	H(8)	119.7
C(8)	C(7)	H(8)	119.9(1)	C(7)	C(8)	C(14)	119.1(1)
C(7)	C(8)	H(7)	120.5	C(14)	C(8)	H(7)	120.4
N(1)	C(9)	C(10)	112.3(1)	N(1)	C(9)	C(14)	107.4(1)
N(1)	C(9)	H(5)	107.2	C(10)	C(9)	C(14)	114.3(1)
C(10)	C(9)	H(5)	107.9	C(14)	C(9)	H(5)	107.4
C(9)	C(10)	C(11)	115.0(1)	C(9)	C(10)	H(3)	108.2
C(9)	C(10)	H(4)	108.4	C(11)	C(10)	H(3)	107.7
C(11)	C(10)	H(4)	107.7	H(3)	C(10)	H(4)	109.7
C(1)	C(11)	C(10)	124.9(1)	C(1)	C(11)	C(12)	116.3(1)
C(10)	C(11)	C(12)	118.3(1)	C(4)	C(12)	C(11)	123.1(1)
C(4)	C(12)	C(13)	110.2(1)	C(11)	C(12)	C(13)	126.3(1)
C(5)	C(13)	C(12)	101.0(1)	C(5)	C(13)	C(14)	115.7(1)
C(5)	C(13)	C(15)	112.0(1)	C(12)	C(13)	C(14)	106.7(1)
C(12)	C(13)	C(15)	111.9(1)	C(14)	C(13)	C(15)	109.2(1)
C(8)	C(14)	C(9)	113.9(1)	C(8)	C(14)	C(13)	109.4(1)
C(8)	C(14)	H(6)	109.1	C(9)	C(14)	C(13)	107.4(1)
C(9)	C(14)	H(6)	109.3	C(13)	C(14)	H(6)	108.5
C(13)	C(15)	C(16)	112.7(1)	C(13)	C(15)	H(11)	108.9
C(13)	C(15)	H(12)	108.2	C(16)	C(15)	H(11)	109.0
C(16)	C(15)	H(12)	108.4	H(11)	C(15)	H(12)	109.6
N(1)	C(16)	C(15)	112.0(1)	N(1)	C(16)	H(13)	108.9
N(1)	C(16)	H(14)	109.0	C(15)	C(16)	H(13)	108.7
C(15)	C(16)	H(14)	108.4	H(13)	C(16)	H(14)	109.9
N(1)	C(17)	H(15)	109.6	N(1)	C(17)	H(16)	109.3
N(1)	C(17)	H(17)	108.8	H(15)	C(17)	H(16)	110.3
H(15)	C(17)	H(17)	109.4	H(16)	C917)	H(17)	109.3
O(4)	C(18)	N(2)	128.7(2)	O(4)	C(18)	N(2)	128.7(2)
O(4)	C(18)	C(19)	118.9(2)	N(2)	C(18)	C(19)	112.4(1)
C(18)	C(19)	H(24)	109.6	C(18)	C(19)	H(25)	109.3
C(18)	C(19)	H(26)	109.6	H(24)	C(19)	H(25)	109.4
H(24)	C(19)	H(26)	110.0	H(25)	C(19)	H(26)	109.0

Table S3. Bond lengths [Å] for $C_{19}H_{22}N_2O_4.CH_3OH$ (**18**). Estimated standard deviations in the least significant figure are given in parentheses where applicable.

Atom	Atom	Å	Atom	Atom	Å
O(1)	C(3)	1.462(2)	O(1)	H(23)	1.01
O(2)	C(4)	1.385(2)	O(2)	C(5)	1.480(2)
O(3)	C(6)	1.434(2)	O(3)	H(22)	1.03
O(4)	C(18)	1.250(2)	O(5)	C(20)	1.390(3)
O(5)	H(21)	1.09	N(1)	N(2)	1.482(2)
N(1)	C(9)	1.550(2)	N(1)	C(16)	1.507(2)
N(1)	C(17)	1.497(2)	N(2)	C(18)	1.324(2)
C(1)	C(2)	1.399(2)	C(1)	C(11)	1.395(2)
C(1)	H(2)	0.950	C(2)	C(3)	1.393(2)
C(2)	H(1)	0.950	C(3)	C(4)	1.382(2)
C(4)	C(12)	1.372(2)	C(5)	C(6)	1.534(2)
C(5)	C(13)	1.532(2)	C(5)	H(10)	0.950
C(6)	C(7)	1.496(2)	C(6)	H(9)	0.950
C(7)	C(8)	1.330(2)	C(7)	H(8)	0.950
C(8)	C(14)	1.506(2)	C(8)	H(7)	0.950
C(9)	C(10)	1.551(2)	C(9)	C(14)	1.534(2)
C(9)	H(5)	0.950	C(10)	C(11)	1.517(2)
C(10)	H(3)	0.950	C(10)	H(4)	0.950
C(11)	C(12)	1.374(2)	C(12)	C(13)	1.502(2)
C(13)	C(14)	1.542(2)	C(13)	C(15)	1.533(2)
C(14)	H(6)	0.950	C(15)	H(11)	0.940
C(15)	H(11)	0.940	C(15)	C(16)	1.513(2)
C(16)	H(13)	0.950	C(15)	H(12)	0.950
C(17)	H(15)	0.940	C(16)	H(14)	0.950
C(17)	H(17)	0.960	C(17)	H(16)	0.950
C(19)	H(24)	0.950	C(18)	C(19)	1.514(2)
C(19)	H(26)	0.950	C(19)	H(25)	0.960

Table S4. Atomic coordinates and equivalent atomic temperature factor ($Å^2$) for $C_{19}H_{22}N_2O_4.CH_3OH$ (**18**). Estimated standard deviations in the least significant figure are represented in parentheses where applicable.

	x	**y**	**Z**
O(1)	0.9300(1)	-0.0173	-0.28686(9)
O(2)	0.7562(1)	0.12890(6)	-0.0220(2)
O(3)	0.3635(1)	0.14178(6)	-0.3389(1)
O(4)	0.6619(1)	0.33519(6)	0.5279(1)
O(5)	0.4842(2)	0.36581(7)	0.8119(1)
N(1)	0.9494(1)	0.28548(6)	0.3352(1)
N(2)	0.8383(1)	0.35659(6)	0.2964(1)
C(1)	1.0529(1)	0.02939(7)	0.1930(1)
C(2)	1.0481(1)	-0.00869(7)	0.0315(1)
C(3)	0.9517(1)	0.02033(7)	-0.1292(1)
C(4)	0.8705(1)	0.09112(7)	-0.1219(1)
C(5)	0.6701(1)	0.19469(7)	-0.1821(1)
C(6)	0.4502(1)	0.17926(7)	-0.1784(1)
C(7)	0.4126(1)	0.13905(7)	-0.0144(1)
C(8)	0.501(1)	0.15817(7)	0.1443(1)
C(9)	0.8139(1)	0.21553(7)	0.3314(1)
C(10)	0.9339(1)	0.14149(7)	0.3638(1)
C(11)	0.9678(1)	0.10047(7)	0.1965(1)
C(12)	0.8897(1)	0.13078(7)	0.0345(1)
C(13)	0.7906(1)	0.20597(7)	0.0037(1)
C(14)	0.6690(1)	0.21763(7)	0.1556(1)
C(15)	0.9413(1)	0.26993(7)	0.0072(1)
C(16)	1.0702(1)	0.27863(7)	0.1869(1)
C(17)	1.0853(2)	0.29399(7)	0.5087(1)
C(18)	0.7065(2)	0.37245(7)	0.4007(1)
C(19)	0.5991(2)	0.44565(8)	0.3505(1)
C(20)	0.4072(1)	0.4378(1)	0.8192(2)
H(1)	1.1114	-0.0562	0.0320
H(2)	1.114	0.0069	0.3009
H(3)	0.8645	0.1085	0.4301
H(4)	1.0597	0.1528	0.4304
H(5)	0.7385	0.2212	0.4251
H(6)	0.6082	0.2655	0.1417
H(7)	0.4811	0.1349	0.2495
H(8)	0.3185	0.0996	-0.0240
H(9)	0.3862	0.2265	-0.1778
H(10)	0.6820	0.2382	-0.2520
H(11)	1.0228	0.2604	-0.0794
H(12)	0.8703	0.3157	-0.0206
H(13)	1.1485	0.3224	0.1849
H(14)	1.1531	0.2358	0.2077
H(15)	1.1558	0.2488	0.5365
H(16)	1.1740	0.3341	0.5001
H(17)	1.0082	0.3049	0.5999
H(21)	0.6153	0.3686	0.7467
H(22)	0.4635	0.0991	-0.3442
H(23)	1.0143	-0.0638	-0.2604
H(24)	0.6164	0.4784	0.4496
H(25)	0.4611	0.4357	0.3151
H(26)	0.6498	0.4682	0.2541

Table S5. Anistropic displacement parameters (Å)^2 for $C_{19}H_{22}N_2O_4.CH_3OH$ (**18**). Estimated standard deviations in the least significant figure are represented in parentheses where applicable.

	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
O(1)	0.0267(3)	0.0227(4)	0.0257(4)	0.0061(3)	-0.0005(3)	-0.0089(3)
O(2)	0.0287(4)	0.0207(4)	0.0158(3)	0.0088(3)	0.0009(3)	-0.0017(3)
O(3)	0.0325(4)	0.0303(5)	0.0317(4)	0.0017(3)	-0.0150(4)	0.0076(3)
O(4)	0.0704(6)	0.0228(4)	0.0416(4)	0.0134(4)	0.0372(4)	0.0106(4)
O(5)	0.1082(8)	0.0401(6)	0.0554(6)	0.0213(6)	0.474(6)	0.0036(5)
N(1)	0.0198(4)	0.0149(4)	0.0176(4)	0.0005(3)	0.0010(3)	-0.0007(3)
N(2)	0.0220(4)	0.0108(4)	0.0198(4)	0.0015(3)	0.0013(3)	0.0005(3)
C(1)	0.0215(5)	0.0171(5)	0.0222(5)	0.0017(4)	-0.0001(4)	0,0023(4)
C(2)	0.0183(4)	0.0139(5)	0.0317(5)	0.0028(4)	0.0030(4)	-0.0009(4)
C(3)	0.0162(4)	0.0174(5)	0.0224(5)	-0.0019(4)	0.0054(4)	-0.0045(4)
C(4)	0.0145(4)	0.0177(5)	0.0153(4)	0.0008(4)	0.0018(4)	0.0014(3)
C(5)	0.0239(5)	0.0141(5)	0.0170(4)	0.0021(4)	0.0022(4)	-0.0004(4)
C(6)	0.0196(4)	0.0186(5)	0.0252(5)	0.0038(4)	-0.0060(4)	-0.0034(40
C(7)	0.0147(4)	0.0191(5)	0.0359(5)	-0.0012(4)	0.0039(4)	-0.0031(4)
C(8)	0.0172(4)	0.0186(5)	0.0266(5)	-0.0010(4)	0.0088(4)	0.0012(4)
C(9)	0.0219(4)	0.0144(5)	0.0164(4)	-0.0005(4)	0.0054(4)	0.0009(4)
C(10)	0,0281(5)	0.0155(5)	0.0156(4)	0.0038(4)	0.0009(4)	0.0018(4)
C(11)	0.0169(4)	0.0152(5)	0.0172(4)	-0.0008(4)	0.0014(4)	0.0006(4)
C(12)	0.0125(4)	0.0126(4)	0.0201(4)	0.0005(3)	0.0051(4)	-0.0002(4)
C(13)	0.0148(4)	0.0123(4)	0.0148(4)	0.0008(3)	0.0026(4)	0.0008(3)
C(14)	0.0173(4)	0.0122(5)	0.0177(4)	0.0025(3)	0.0047(4)	0.0009(4)
C(15)	0.0198(4)	0.0167(5)	0.0197(5)	-0.0019(4)	0.0088(4)	-0.0004(4)
C(16)	0.0164(4)	0.0189(5)	0.0241(5)	-0.0012(4)	0.0036(4)	-0.0020(4)
C(17)	0.0348(6)	0.0248(6)	0.0208(5)	0.0020(4)	-0.0087(5)	-0.0043(4)
C(18)	0.0321(5)	0.0156(5)	0.0227(5)	-0.0003(4)	0.0076(4)	-0.0010(4)
C(19)	0.0325(5)	0.0209(6)	0.0332(6)	0.0072(5)	0.0084(5)	0.0015(4)
C(20)	0.0482(8)	0.0542(9)	0.070(1)	0.0195(7)	0.0081(7)	-0.0241(7)

Table S6. Torsional bond angles [deg] for $C_{19}H_{22}N_2O_4.CH_3OH$ (**18**). Estimated standard deviations in the least significant figure are given in parentheses where applicable.

(1)	(2)	(3)	(4)	[deg]	(1)	(2)	(3)	(4)	[deg]
O(1)	C(3)	C(2)	C(1)	-174.6(2)	O(1)	C(3)	C(4)	O(2)	3.3(2)
O(1)	C(3)	C(4)	C(12)	-179.9(1)	O(2)	C(4)	C(3)	C(2)	-175.0(1)
O(2)	C(4)	C(12)	C(11)	169.1(1)	O(2)	C(4)	C(12)	C(13)	-3.7(20
O(2)	C(5)	C(6)	O(3)	-39.7(2)	O(2)	C(5)	C(6)	C(7)	87.6(2)
O(2)	C(5)	C(13)	C(12)	-17.8(1)	O(2)	C(5)	C(13)	C(14)	-132.5(1)
O(2)	C(5)	C(13)	C(15)	101.5(1)	O(3)	C(6)	C(5)	C(13)	-158.0(1)
O(3)	C(6)	C(7)	C(8)	167.9(1)	O(4)	C(18)	N(2)	N(1)	-0.4(2)
N(1)	N(2)	C(18)	C(19)	-179.6(1)	N(1)	C(9)	C(10)	C(11)	-94.8(2)
N(1)	C(9)	C(14)	C(8)	-172.6(1)	N(1)	C(9)	C(14)	C(13)	66.7(1)
N(1)	C(16)	C(15)	C(13)	-52.6(2)	N(2)	N(1)	C(9)	C(10)	177.3(1)
N(2)	N(1)	C(9)	C(14)	50.9(1)	N(2)	N(1)	C(16)	C(15)	-64.2(2)
C(1)	C(2)	C(3)	C(4)	3.6(2)	C(1)	C(11)	C(10)	C(9)	-172.9(1)
C(1)	C(11)	C(12)	C(4)	8.4(2)	C(1)	C(11)	C(12)	C(13)	179.9(1)
C(2)	C(1)	C(11)	C(10)	169.4(2)	C(2)	C(1)	C(11)	C(12)	-2.8(2)
C(2)	C(3)	C(4)	C(12)	1.8(2)	C(3)	C(2)	C(1)	C(11)	-3.1(2)
C(3)	C(4)	O(2)	C(5)	168.7(1)	C(3)	C(4)	C(12)	C(11)	-8.2(2)
C(3)	C(4)	C(12)	C(13)	179.1(1)	C(4)	O(2)	C(5)	C(6)	-105.5(1)
C(4)	O(2)	C(5)	C(13)	16.7(2)	C(4)	C(12)	C(11)	C(10)	-164.4(1)
C(4)	C(12)	C(13)	C(5)	13.3(20)	C(40	C(12)	C(13)	C(14)	134.6(1)
C(4)	C(12)	C(13)	C(15)	-106.0(1)	C(5)	O(2)	C(4)	C(12)	-8.4(2)
C(5)	C(6)	C(7)	C(8)	42.0(2)	C(5)	C(13)	C(12)	C(11)	-159.1(1)
C(5)	C(13)	C(14)	C(8)	48.4(2)	C(5)	C(13)	C(14)	C(8)	48.4(2)
C(5)	C(13)	C(14)	C(9)	171.4(1)	C(5)	C(13)	C(15)	C(16)	-176.4(1)
C(6)	C(5)	C(13)	C(12)	101.7(1)	C(6)	C(5)	C(13)	C(14)	-13.0(2)
C(6)	C(5)	C(13)	C(15)	-139.1(1)	C96)	C(7)	C(8)	C(14)	-3.6(2)
C(7)	C(6)	C(5)	C(13)	-30.7(2)	C(7)	C(8)	C(14)	C(9)	-160.7(1)
C(7)	C(8)	C(14)	C(13)	-41.1(20	C(8)	C(14)	C(9)	C(10)	62.2(2)
C(8)	C(14)	C(13)	C(12)	-63.0(1)	C(8)	C(14)	C(13)	C(15)	175.9(1)
C(9)	N(1)	N(2)	C(18)	56.6(20	C(9)	N(1)	C(16)	C(15)	56.9(2)
C(9)	C(10)	C(11)	C(12)	-0.8(2)	C(9)	C(14)	C(13)	C(12)	60.0(1)
C(9)	C(14)	C(13)	C(15)	-61.1(1)	C(10)	C(9)	N(1)	C(16)	62.1(1)
C(10)	C(9)	N(1)	C(17)	-59.1(2)	C(10)	C(9)	C(14)	C(13)	-58.6(2)
C(10)	C(11)	C(12)	C(13)	7.1(2)	C(11)	C(10)	C(9)	C(14)	27.8(2)
C(11)	C(12)	C(13)	C(14)	-37.8(2)	C(11)	C(12)	C(13)	C(15)	81.6(2)
C(12)	C(13)	C(15)	C(16)	-63.8	C(14)	C(9)	N(1)	C(16)	-64.4(1)
C(14)	C(9)	N(1)	C(16)	-64.4	C(14)	C(9)	N(1)	C(17)	174.4(1)
C(15)	C(16)	N(1)	C(17)	-179.9(1)	C(16)	N(1)	N(2)	C(18)	174.4(1)
C(17)	N(1)	N(2)	C(18)	-69.2(2)					

Positive sign when looking from atom 2 to atom 3 a clockwise motion of atom 1 superimposes it on atom 3.

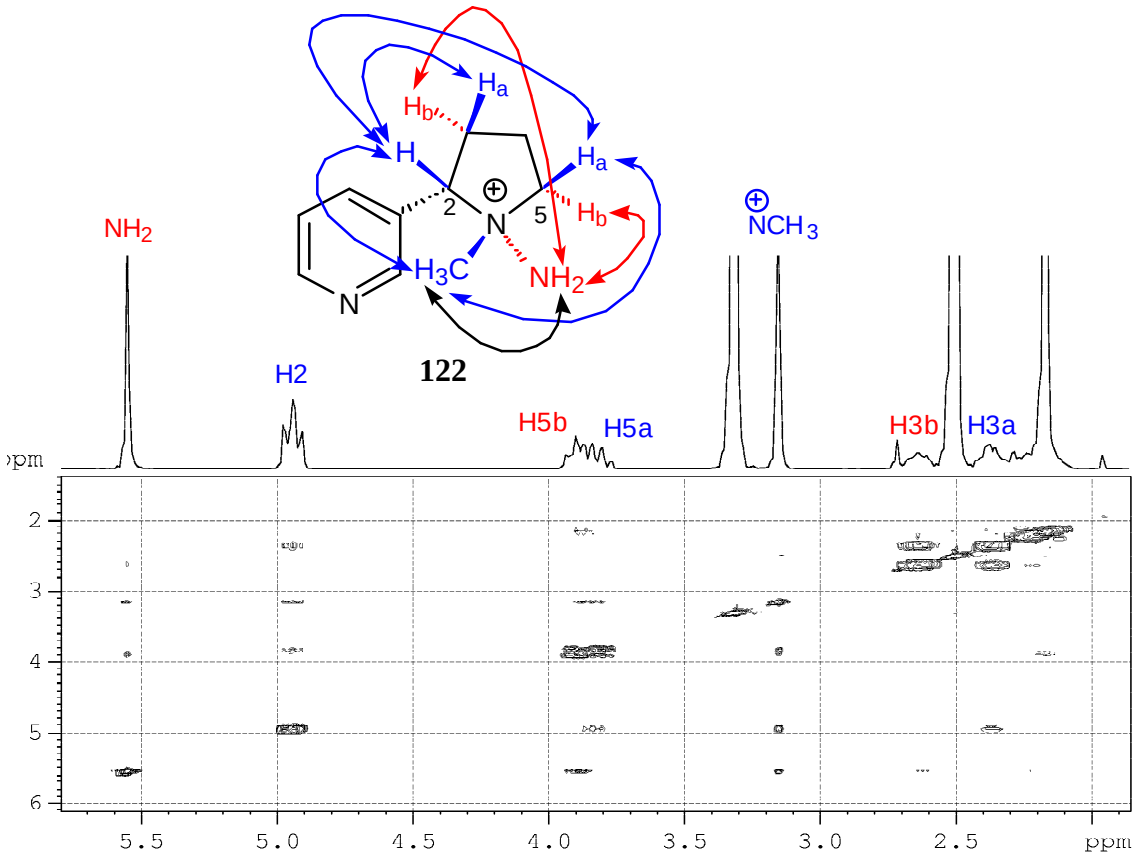

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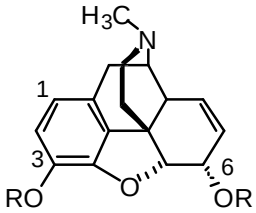
Fig. S2. 300 MHz ^{1}H-^{1}H NOESY spectrum of **19** in d_6-DMSO, mixing time = 800 msec.

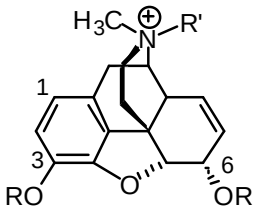
Table S7. ^{13}C NMR data for morphine and related compounds

	3	**15**	**16**	**17**	**18**
1	118.3	119.6	120.1	119.8	118.9
2	116.1	122.3	124.0	123.6	117.0
3	138.2	149.8	149.6	149.8	139.0
4	146.1	129.4	127.2	128.2	146.0
5	91.2	89.0	87.7	88.1	90.5
6	66.1	68.3	67.1	67.5	67.1
7	133.2	128.9	130.3	129.8	135.1
8	128.2	129.7	126.3	127.7	126.5
9	57.8	59.3	71.5	67.4	66.0
10	19.9	21.0	25.1	25.2	23.8
11	125.3	132.5	133.4	133.3	122.2
12	130.8	131.8	129.0	129.1	129.8
13	42.7	43.0	41.0	41.2	41.3
14	41.0	40.8	32.9	33.8	33.5
15	35.9	35.3	29.8	30.8	30.7
16	45.8	46.8	58.4	58.3	55.5
17	39.4	43.2	57.5	51.7	50.1
CH$_3$CO	-	-	-	23.9	23.8
CH$_3$**C**O	-	-	-	174.1	170.9
1'	-	132.5	129.8†	129.6	-
2', 6'	-	130.2	130.3	130.2	-
3', 5'	-	128.5	128.4	128.4	-
4'	-	133.3	133.6	133.5	-
CO	-	164.4	164.1	164.2	-
1"	-	132.5	129.7†	129.6	-
2", 6"	-	130.0	130.0	129.9	-
3", 5"	-	128.3	128.5	128.6	-
4"	-	133.0	133.1	133.1	-
CO	-	166.1	165.8	165.9	-
1"'	-	-	140.1	-	-
2"', 6"'	-	-	137.0	-	-
3"', 5"'	-	-	131.1	-	-
4"'	-	-	139.1	-	-
o-CH$_3$	-	-	23.4	-	-
p-CH$_3$	-	-	21.0	-	-



3 R = H

15 R = COPh



16 R = COPh R' = NH_2

17 R = COPh R' = $\overset{\ominus}{N}COCH_3$

18 R = H R' = $\overset{\ominus}{N}COCH_3$

[a] Spectra recorded in d_6-DMSO at 300 MHz; [b] Spectra recorded in $CDCl_3$ at 300 MHz; † These signals are interchangeable

Table S8. ^{1}H NMR data for morphine and related compounds

	3[a]	**15**[b]	**16**[b]	**17**[b]	**18**[a]
1	6.33 (d, *J* 8 Hz)	6.68 (d, *J* 8 Hz)	6.70 (d, *J* 8.5 Hz)	6.66 (d, *J* 8 Hz)	6.40 (d, *J* 8 Hz)
2	6.43 (d, *J* 8 Hz)	6.95 (d, *J* 8 Hz)	7.00 (d, *J* 8.5 Hz)	6.94 (d, *J* 8 Hz)	6.52 (d, *J* 8 Hz)
5	4.87 (dd, *J* 6 Hz)	5.27 (d, *J* 7 Hz)	5.33 (d, *J* 7 Hz)	5.29 (br d, *J* 7 Hz)	4.78 (br d, *J* 6 Hz)
6	4.09 (m)	5.44 (m, H6)	5.42 (dd, *J* 7, 2.5 Hz)	5.47 (m)	4.10 (br s)
7	5.52 (app dt, *J* , 12.5, 3 Hz)	5.82 (br app dt, *J* 10, 2 Hz)	5.86 (br app dt, *J* 10, 3 Hz)	5.80 (br app dt, *J* 9.5, 3 Hz)	5.57 (br d, *J* 9.5 Hz)
8	5.23 (app dt, *J* 11, 2.5 Hz)	5.54 (app dt, *J* 10, 2.5 Hz)	5.36 (d, *J* 10 Hz)	5.47 (m)	5.21 (app dt, *J* 10, 2.5 Hz)
9	3.23 (dd, *J* 6, 3 Hz)	3.50 (dd, *J* 5.5, 3.5 Hz)	4.78 (br s)	5.47 (m)	4.94-4.96 (m)
10ax	2.18 (dd, *J* 18.5, 6 Hz)	2.42 (dd, *J* 19, 5.5 Hz)	2.94 (dd, *J* 20.5, 6 Hz)	2.90 (dd, *J* 20.5, 6.5 Hz)	2.77 (dd, *J* 20.5, 7 Hz)
10eq	2.87 (d, *J* 18.5 Hz)	3.14 (d, *J* 19 Hz)	3.38 (d, *J* 20.5 Hz)	3.21 (d, *J* 20.5 Hz)	3.26 (d, *J* 20.5 Hz)
14	2.51 (m)	2.84 (app p, *J* 2.5 Hz)	4.20 (br s)	3.91 (app p, *J* 2.5 Hz)	3.60 (app p, *J* 2.5 Hz)
15ax	1.96 (app td, *J* 12.5, 5 Hz)	2.17 (ddd, *J* 13, 12.5, 3.5 Hz)	2.77 (app td, *J* 13, 4 Hz)	2.76 (app td, *J* 13, 4 Hz)	2.48 (app td, *J* 13, 4 Hz)
15eq	1.61 (br d, *J* 11 Hz)	2.00 (br dd, *J* 12.5, 1.5 Hz)	1.91 (br d, *J* 12 Hz)	1.91 (br d, 11.5 Hz)	1.61 (br d, *J* 11 Hz)
16ax	2.22 (app td, *J* 12, 3.5 Hz)	2.47 (app td, 12.5 Hz, 3.5 Hz)	3.17 (app td, *J* 12.5, 2.5 Hz)	2.92 (app td, *J* 12, 3 Hz)	2.90 (app td, *J* 13, 3.5 Hz)
16eq	2.44 (dd, *J* 12, 4 Hz)	2.72 (br dd, *J* 12.5, 3.5 Hz)	3.96 (br d, *J* 18 Hz)	3.80 (br d, *J* 12 Hz)	3.85 (br d, *J* 11.5 Hz)
17	2.29	2.52	3.95 (s)	3.57 (s)	3.45 (s)
CH_3CO	-	-	-	1.92 (s)	1.61 (s)
2', 6'	-	7.93 (app t, *J* 8, 1.5 Hz)	7.80 (d, *J* 7.5 Hz)	7.76 (d, *J* 8 Hz)	-
3', 5'	-	7.35 (app t, *J* 8 Hz)	7.31 (appt, *J* 7.5 Hz)	7.26 (app t, *J* 8 Hz)	-
4'	-	7.54 (td, *J* 8, 1.5 Hz)	7.53 (t, *J* 7.5 Hz)	7.47 (t, *J* 8 Hz)	-
2", 6"	-	8.01 (dd, *J* 7.5, 1.5 Hz)	7.98 (d, *J* 7 Hz)	7.92 (d, *J* 7.5 Hz)	-
3", 5"	-	7.25 (app t, *J* 7.5 Hz)	7.28 (app t, *J* 7 Hz)	7.21 (app t, *J* 7.5 Hz)	-
4"	-	7.45 (td, *J* 7.5, 1.5 Hz)	7.46 (t, *J* 7 Hz)	7.40 (t, *J* 7.5 Hz)	-
3"', 5"'	-	-	6.87 (s)	-	-
o-CH_3	-	-	2.70 (s)	-	-
p-CH_3	-	-	2.24 (s)	-	-
3-OH	8.71	-	-	-	-
6-OH	4.65 (dd, *J* 6, 1 Hz)		-	-	-
NH_2	-	-	6.64 (s)	-	-

[a] Spectra recorded in d_6-DMSO at 300 MHz; [b] Spectra recorded in $CDCl_3$ at 300 MHz.