Supplementary Information

Synthesis and evaluation of analogs of tetracyclic *Ganoderma* alkaloids as inhibitors of the enzyme α-glucosidase

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Table S1. Crystal data and structure refinement for **13** at 298 K and 80 K.

Variable /Temperature	298(2) K	80(2) K
Empirical formula	$C_{17}H_{15}NO_3$	$C_{17}H_{15}NO_3$
Formula weight	281.30	281.30
Crystal system	Monoclinic	Monoclinic
Space group, Z	P 2_1/n, 4	
Unit cell dimensions a, b, c (Å) α, β,γ (°)	a= 8.0988(4) α= 90 b= 18.4631(7) β= 110.4210(10) c= 9.7483(3) γ= 90	a= 8.1853(2) α= 90 b= 17.5919(5) β= 109.8720(10) c=9.6213(3) γ= 90
Cell volume ($Å^3$)	1366.05(10)	1302.92(6)
Density (calcd., g/cm^3)	1.368	1.434
Absorption coef. (mm^{-1})	0.094	0.099
F(000)	592	592
Crystal size (mm^3)	0.669 x 0.157 x 0.144	0.200x0.200x0.200
θ range for data collection (°)	2.902 to 26.371	2.832 to 26.448
Reflections collected	25141	46326
Independent reflections	2784 [R(int) = 0.0552]	2673 [R(int) = 0.0287]
Refinement method	Full-matrix least-squares on F2	
Data / restraints / parameters	2784 / 0 / 241	2673 / 0 / 191
Goodness-of-fit on F2	1.113	1.048
Final R indices [I >2sigma(I)]	R1 = 0.0804, wR2 = 0.2240	R1 = 0.0350, wR2 = 0.0991
R indices (all data)	R1 = 0.1327, wR2 = 0.3157	R1 = 0.0367, wR2 = 0.1007
CCDC deposition number	2501682	2501681

Table S2. Bond lengths [Å] for **13** at 298 K.

C(1)-C(2B)	1.319(13)
C(1)-C(18)	1.387(5)
C(1)-C(2A)	1.59(2)
C(1)-H(1)	0.9300
C(5)-O(6)	1.387(5)
C(5)-C(18)	1.388(5)
C(5)-C(4A)	1.392(19)
C(5)-C(4B)	1.413(15)
O(6)-C(7)	1.428(4)
C(7)-C(8)	1.501(4)
C(7)-H(7A)	0.9700
C(7)-H(7B)	0.9700
C(8)-C(9)	1.375(4)
C(8)-C(17)	1.389(4)
C(9)-C(10)	1.394(4)
C(9)-H(9)	0.9300
C(10)-C(15)	1.392(4)
C(10)-C(11)	1.478(4)
C(11)-O(19)	1.214(4)
C(11)-C(12)	1.491(5)
C(12)-C(13)	1.499(6)
C(12)-H(12A)	0.9700
C(12)-H(12B)	0.9700
C(13)-C(14)	1.510(5)
C(13)-H(13A)	0.9700
C(13)-H(13B)	0.9700
C(14)-C(15)	1.493(4)
C(14)-H(14A)	0.9700
C(14)-H(14B)	0.9700
C(15)-N(16)	1.350(4)
N(16)-C(17)	1.340(4)
C(17)-C(18)	1.474(4)
O(20A)-C(21A)	1.35(3)
O(20A)-C(2A)	1.38(3)

C(21A)-H(21D)	0.9600
C(21A)-H(21E)	0.9600
C(21A)-H(21F)	0.9600
O(20B)-C(21B)	1.361(17)
O(20B)-C(2B)	1.41(2)
C(21B)-H(21A)	0.9600
C(21B)-H(21B)	0.9600
C(21B)-H(21C)	0.9600
C(2A)-C(3A)	1.39(2)
C(3A)-C(4A)	1.36(2)
C(3A)-H(3A)	0.9300
C(4A)-H(4A)	0.9300
C(2B)-C(3B)	1.381(12)
C(3B)-C(4B)	1.378(16)
C(3B)-H(3B)	0.9300
C(4B)-H(4B)	0.9300

Table S3. Bond angles [°] for **13** at 298 K.

C(2B)-C(1)-C(18)	130.8(12)
C(18)-C(1)-C(2A)	105.7(12)
C(18)-C(1)-H(1)	127.2
C(2A)-C(1)-H(1)	127.2
O(6)-C(5)-C(18)	121.0(3)
O(6)-C(5)-C(4A)	101.1(14)
C(18)-C(5)-C(4A)	137.5(14)
O(6)-C(5)-C(4B)	127.7(11)
C(18)-C(5)-C(4B)	111.2(11)
C(5)-O(6)-C(7)	115.2(3)
O(6)-C(7)-C(8)	111.7(3)
O(6)-C(7)-H(7A)	109.3
C(8)-C(7)-H(7A)	109.3
O(6)-C(7)-H(7B)	109.3
C(8)-C(7)-H(7B)	109.3
H(7A)-C(7)-H(7B)	107.9
C(9)-C(8)-C(17)	118.1(3)
C(9)-C(8)-C(7)	123.4(3)
C(17)-C(8)-C(7)	118.3(3)
C(8)-C(9)-C(10)	119.5(3)
C(8)-C(9)-H(9)	120.2
C(10)-C(9)-H(9)	120.2
C(15)-C(10)-C(9)	118.7(3)
C(15)-C(10)-C(11)	121.2(3)
C(9)-C(10)-C(11)	120.1(3)
O(19)-C(11)-C(10)	121.3(3)
O(19)-C(11)-C(12)	121.3(3)
C(10)-C(11)-C(12)	117.5(3)
C(11)-C(12)-C(13)	113.6(3)
C(11)-C(12)-H(12A)	108.8
C(13)-C(12)-H(12A)	108.8
C(11)-C(12)-H(12B)	108.8
C(13)-C(12)-H(12B)	108.8
H(12A)-C(12)-H(12B)	107.7

C(12)-C(13)-C(14)	111.4(3)
C(12)-C(13)-H(13A)	109.4
C(14)-C(13)-H(13A)	109.4
C(12)-C(13)-H(13B)	109.4
C(14)-C(13)-H(13B)	109.4
H(13A)-C(13)-H(13B)	108.0
C(15)-C(14)-C(13)	112.1(3)
C(15)-C(14)-H(14A)	109.2
C(13)-C(14)-H(14A)	109.2
C(15)-C(14)-H(14B)	109.2
C(13)-C(14)-H(14B)	109.2
H(14A)-C(14)-H(14B)	107.9
N(16)-C(15)-C(10)	122.1(3)
N(16)-C(15)-C(14)	117.2(3)
C(10)-C(15)-C(14)	120.7(3)
C(17)-N(16)-C(15)	117.9(2)
N(16)-C(17)-C(8)	123.5(3)
N(16)-C(17)-C(18)	118.6(3)
C(8)-C(17)-C(18)	117.9(3)
C(1)-C(18)-C(5)	118.8(3)
C(1)-C(18)-C(17)	122.6(3)
C(5)-C(18)-C(17)	118.6(3)
C(21A)-O(20A)-C(2A)	121.6(19)
O(20A)-C(21A)-H(21D)	109.5
O(20A)-C(21A)-H(21E)	109.5
H(21D)-C(21A)-H(21E)	109.5
O(20A)-C(21A)-H(21F)	109.5
H(21D)-C(21A)-H(21F)	109.5
H(21E)-C(21A)-H(21F)	109.5
C(21B)-O(20B)-C(2B)	118.9(13)
O(20B)-C(21B)-H(21A)	109.5
O(20B)-C(21B)-H(21B)	109.5
H(21A)-C(21B)-H(21B)	109.5
O(20B)-C(21B)-H(21C)	109.5
H(21A)-C(21B)-H(21C)	109.5
H(21B)-C(21B)-H(21C)	109.5

O(20A)-C(2A)-C(3A)	117(2)
O(20A)-C(2A)-C(1)	115(2)
C(3A)-C(2A)-C(1)	128.7(14)
C(4A)-C(3A)-C(2A)	121.8(14)
C(4A)-C(3A)-H(3A)	119.1
C(2A)-C(3A)-H(3A)	119.1
C(3A)-C(4A)-C(5)	107.1(13)
C(3A)-C(4A)-H(4A)	126.5
C(5)-C(4A)-H(4A)	126.5
C(1)-C(2B)-C(3B)	111.9(12)
C(1)-C(2B)-O(20B)	123(2)
C(3B)-C(2B)-O(20B)	124.6(15)
C(4B)-C(3B)-C(2B)	120.2(10)
C(4B)-C(3B)-H(3B)	119.9
C(2B)-C(3B)-H(3B)	119.9
C(3B)-C(4B)-C(5)	127.1(11)
C(3B)-C(4B)-H(4B)	116.5
C(5)-C(4B)-H(4B)	116.5

Table S4. Torsion angles [°] for **13** at 298 K.

C(18)-C(5)-O(6)-C(7)	-31.9(5)
C(4A)-C(5)-O(6)-C(7)	154.3(8)
C(4B)-C(5)-O(6)-C(7)	151.4(7)
C(5)-O(6)-C(7)-C(8)	48.4(4)
O(6)-C(7)-C(8)-C(9)	147.8(3)
O(6)-C(7)-C(8)-C(17)	-37.3(4)
C(17)-C(8)-C(9)-C(10)	-2.3(5)
C(7)-C(8)-C(9)-C(10)	172.7(3)
C(8)-C(9)-C(10)-C(15)	-0.2(4)
C(8)-C(9)-C(10)-C(11)	-179.3(3)
C(15)-C(10)-C(11)-O(19)	178.0(3)
C(9)-C(10)-C(11)-O(19)	-2.8(5)
C(15)-C(10)-C(11)-C(12)	-1.7(5)
C(9)-C(10)-C(11)-C(12)	177.4(3)
O(19)-C(11)-C(12)-C(13)	154.3(4)
C(10)-C(11)-C(12)-C(13)	-26.0(4)
C(11)-C(12)-C(13)-C(14)	52.9(4)
C(12)-C(13)-C(14)-C(15)	-52.1(4)
C(9)-C(10)-C(15)-N(16)	2.7(4)
C(11)-C(10)-C(15)-N(16)	-178.2(3)
C(9)-C(10)-C(15)-C(14)	-177.4(3)
C(11)-C(10)-C(15)-C(14)	1.7(4)
C(13)-C(14)-C(15)-N(16)	-154.6(3)
C(13)-C(14)-C(15)-C(10)	25.5(4)
C(10)-C(15)-N(16)-C(17)	-2.4(4)
C(14)-C(15)-N(16)-C(17)	177.7(3)
C(15)-N(16)-C(17)-C(8)	-0.2(4)
C(15)-N(16)-C(17)-C(18)	178.7(2)
C(9)-C(8)-C(17)-N(16)	2.6(5)
C(7)-C(8)-C(17)-N(16)	-172.6(3)
C(9)-C(8)-C(17)-C(18)	-176.3(3)
C(7)-C(8)-C(17)-C(18)	8.4(4)
C(2B)-C(1)-C(18)-C(5)	1.9(9)
C(2A)-C(1)-C(18)-C(5)	-0.4(8)

C(2B)-C(1)-C(18)-C(17)	-176.9(7)
C(2A)-C(1)-C(18)-C(17)	-179.1(7)
O(6)-C(5)-C(18)-C(1)	-177.6(3)
C(4A)-C(5)-C(18)-C(1)	-6.6(13)
C(4B)-C(5)-C(18)-C(1)	-0.4(7)
O(6)-C(5)-C(18)-C(17)	1.2(5)
C(4A)-C(5)-C(18)-C(17)	172.1(12)
C(4B)-C(5)-C(18)-C(17)	178.4(6)
N(16)-C(17)-C(18)-C(1)	10.1(5)
C(8)-C(17)-C(18)-C(1)	-170.9(3)
N(16)-C(17)-C(18)-C(5)	-168.6(3)
C(8)-C(17)-C(18)-C(5)	10.4(4)
C(21A)-O(20A)-C(2A)-C(3A)	-174(2)
C(21A)-O(20A)-C(2A)-C(1)	10(3)
C(18)-C(1)-C(2A)-O(20A)	-178.1(11)
C(18)-C(1)-C(2A)-C(3A)	6(2)
O(20A)-C(2A)-C(3A)-C(4A)	178.4(15)
C(1)-C(2A)-C(3A)-C(4A)	-6(3)
C(2A)-C(3A)-C(4A)-C(5)	0(2)
O(6)-C(5)-C(4A)-C(3A)	179.2(12)
C(18)-C(5)-C(4A)-C(3A)	7(2)
C(18)-C(1)-C(2B)-C(3B)	-2.0(14)
C(18)-C(1)-C(2B)-O(20B)	177.0(9)
C(21B)-O(20B)-C(2B)-C(1)	149.2(14)
C(21B)-O(20B)-C(2B)-C(3B)	-32(2)
C(1)-C(2B)-C(3B)-C(4B)	0.8(17)
O(20B)-C(2B)-C(3B)-C(4B)	-178.2(11)
C(2B)-C(3B)-C(4B)-C(5)	0.4(19)
O(6)-C(5)-C(4B)-C(3B)	176.4(8)
C(18)-C(5)-C(4B)-C(3B)	-0.6(14)

Table S5. Hydrogen bonds for **13** [Å and °] at 298 K.

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
C(7)-H(7B)...O(19)#1	0.97	2.47	3.381(4)	156.9
C(21B^b)-H(21B^b)...O(19)#2	0.96	2.56	3.490(11)	163.1
C(3A^a)-H(3A^a)...O(6)#3	0.93	2.34	3.18(2)	149.7

Symmetry transformations used to generate equivalent atoms:

#1 -x+2,-y+1,-z+2 #2 -x+1,-y+1,-z+1 #3 x-1/2,-y+3/2,z-1/2

Table S6. Bond lengths [Å] for **13** at 80 K.

C(2)-O(20)	1.3716(14)
C(2)-C(1)	1.3927(15)
C(2)-C(3)	1.3953(16)
C(1)-C(18)	1.3970(15)
C(1)-H(1)	0.9500
C(3)-C(4)	1.3913(17)
C(3)-H(3)	0.9500
C(4)-C(5)	1.3868(16)
C(4)-H(4)	0.9500
C(5)-O(6)	1.3821(13)
C(5)-C(18)	1.4063(15)
O(6)-C(7)	1.4431(13)
C(7)-C(8)	1.5067(15)
C(7)-H(7A)	0.9900
C(7)-H(7B)	0.9900
C(8)-C(9)	1.3796(15)
C(8)-C(17)	1.4048(15)
C(9)-C(10)	1.3973(15)
C(9)-H(9)	0.9500
C(10)-C(15)	1.4053(15)
C(10)-C(11)	1.4897(15)
C(11)-O(19)	1.2210(14)
C(11)-C(12)	1.5121(15)
C(12)-C(13)	1.5269(15)
C(12)-H(12A)	0.9900
C(12)-H(12B)	0.9900
C(13)-C(14)	1.5252(15)
C(13)-H(13A)	0.9900
C(13)-H(13B)	0.9900
C(14)-C(15)	1.5087(14)
C(14)-H(14A)	0.9900
C(14)-H(14B)	0.9900
C(15)-N(16)	1.3414(14)
N(16)-C(17)	1.3460(14)

C(17)-C(18)	1.4732(15)
O(20)-C(21)	1.4270(14)
C(21)-H(21A)	0.9800
C(21)-H(21B)	0.9800
C(21)-H(21C)	0.9800

Table S7. Bond angles [°] for **13** at 80 K.

O(20)-C(2)-C(1)	116.06(10)
O(20)-C(2)-C(3)	124.04(10)
C(1)-C(2)-C(3)	119.90(10)
C(2)-C(1)-C(18)	120.48(10)
C(2)-C(1)-H(1)	119.8
C(18)-C(1)-H(1)	119.8
C(4)-C(3)-C(2)	119.94(10)
C(4)-C(3)-H(3)	120.0
C(2)-C(3)-H(3)	120.0
C(5)-C(4)-C(3)	120.33(10)
C(5)-C(4)-H(4)	119.8
C(3)-C(4)-H(4)	119.8
O(6)-C(5)-C(4)	118.25(10)
O(6)-C(5)-C(18)	121.43(10)
C(4)-C(5)-C(18)	120.20(10)
C(5)-O(6)-C(7)	113.95(8)
O(6)-C(7)-C(8)	111.68(9)
O(6)-C(7)-H(7A)	109.3
C(8)-C(7)-H(7A)	109.3
O(6)-C(7)-H(7B)	109.3
C(8)-C(7)-H(7B)	109.3
H(7A)-C(7)-H(7B)	107.9
C(9)-C(8)-C(17)	118.51(10)
C(9)-C(8)-C(7)	123.06(10)
C(17)-C(8)-C(7)	118.28(10)
C(8)-C(9)-C(10)	118.98(10)
C(8)-C(9)-H(9)	120.5
C(10)-C(9)-H(9)	120.5
C(9)-C(10)-C(15)	118.74(10)
C(9)-C(10)-C(11)	120.13(10)
C(15)-C(10)-C(11)	121.11(10)
O(19)-C(11)-C(10)	121.24(10)
O(19)-C(11)-C(12)	121.31(10)
C(10)-C(11)-C(12)	117.45(9)

C(11)-C(12)-C(13)	112.46(9)
C(11)-C(12)-H(12A)	109.1
C(13)-C(12)-H(12A)	109.1
C(11)-C(12)-H(12B)	109.1
C(13)-C(12)-H(12B)	109.1
H(12A)-C(12)-H(12B)	107.8
C(14)-C(13)-C(12)	110.12(9)
C(14)-C(13)-H(13A)	109.6
C(12)-C(13)-H(13A)	109.6
C(14)-C(13)-H(13B)	109.6
C(12)-C(13)-H(13B)	109.6
H(13A)-C(13)-H(13B)	108.2
C(15)-C(14)-C(13)	110.75(9)
C(15)-C(14)-H(14A)	109.5
C(13)-C(14)-H(14A)	109.5
C(15)-C(14)-H(14B)	109.5
C(13)-C(14)-H(14B)	109.5
H(14A)-C(14)-H(14B)	108.1
N(16)-C(15)-C(10)	122.60(10)
N(16)-C(15)-C(14)	116.84(9)
C(10)-C(15)-C(14)	120.54(9)
C(15)-N(16)-C(17)	117.83(9)
N(16)-C(17)-C(8)	123.21(10)
N(16)-C(17)-C(18)	118.83(10)
C(8)-C(17)-C(18)	117.95(10)
C(1)-C(18)-C(5)	119.13(10)
C(1)-C(18)-C(17)	122.81(10)
C(5)-C(18)-C(17)	118.06(10)
C(2)-O(20)-C(21)	117.14(9)
O(20)-C(21)-H(21A)	109.5
O(20)-C(21)-H(21B)	109.5
H(21A)-C(21)-H(21B)	109.5
O(20)-C(21)-H(21C)	109.5
H(21A)-C(21)-H(21C)	109.5
H(21B)-C(21)-H(21C)	109.5

Table S8. Torsion angles [°] for **13** at 80 K.

O(20)-C(2)-C(1)-C(18)	-179.10(10)
C(3)-C(2)-C(1)-C(18)	1.37(17)
O(20)-C(2)-C(3)-C(4)	-179.34(11)
C(1)-C(2)-C(3)-C(4)	0.15(16)
C(2)-C(3)-C(4)-C(5)	-1.66(17)
C(3)-C(4)-C(5)-O(6)	177.77(10)
C(3)-C(4)-C(5)-C(18)	1.65(16)
C(4)-C(5)-O(6)-C(7)	148.10(10)
C(18)-C(5)-O(6)-C(7)	-35.83(13)
C(5)-O(6)-C(7)-C(8)	50.43(12)
O(6)-C(7)-C(8)-C(9)	148.29(10)
O(6)-C(7)-C(8)-C(17)	-36.33(13)
C(17)-C(8)-C(9)-C(10)	-2.22(15)
C(7)-C(8)-C(9)-C(10)	173.15(10)
C(8)-C(9)-C(10)-C(15)	-0.70(15)
C(8)-C(9)-C(10)-C(11)	-179.23(10)
C(9)-C(10)-C(11)-O(19)	-6.87(16)
C(15)-C(10)-C(11)-O(19)	174.64(10)
C(9)-C(10)-C(11)-C(12)	173.07(9)
C(15)-C(10)-C(11)-C(12)	-5.42(15)
O(19)-C(11)-C(12)-C(13)	155.40(11)
C(10)-C(11)-C(12)-C(13)	-24.54(13)
C(11)-C(12)-C(13)-C(14)	55.66(12)
C(12)-C(13)-C(14)-C(15)	-56.88(12)
C(9)-C(10)-C(15)-N(16)	3.36(16)
C(11)-C(10)-C(15)-N(16)	-178.12(9)
C(9)-C(10)-C(15)-C(14)	-175.00(9)
C(11)-C(10)-C(15)-C(14)	3.51(15)
C(13)-C(14)-C(15)-N(16)	-150.47(9)
C(13)-C(14)-C(15)-C(10)	27.99(13)
C(10)-C(15)-N(16)-C(17)	-2.79(15)
C(14)-C(15)-N(16)-C(17)	175.63(9)
C(15)-N(16)-C(17)-C(8)	-0.38(15)
C(15)-N(16)-C(17)-C(18)	-179.04(9)

C(9)-C(8)-C(17)-N(16)	2.90(16)
C(7)-C(8)-C(17)-N(16)	-172.69(10)
C(9)-C(8)-C(17)-C(18)	-178.43(9)
C(7)-C(8)-C(17)-C(18)	5.98(14)
C(2)-C(1)-C(18)-C(5)	-1.37(16)
C(2)-C(1)-C(18)-C(17)	178.60(10)
O(6)-C(5)-C(18)-C(1)	-176.13(9)
C(4)-C(5)-C(18)-C(1)	-0.14(16)
O(6)-C(5)-C(18)-C(17)	3.90(15)
C(4)-C(5)-C(18)-C(17)	179.89(9)
N(16)-C(17)-C(18)-C(1)	9.94(16)
C(8)-C(17)-C(18)-C(1)	-168.79(10)
N(16)-C(17)-C(18)-C(5)	-170.09(9)
C(8)-C(17)-C(18)-C(5)	11.17(15)
C(1)-C(2)-O(20)-C(21)	153.66(10)
C(3)-C(2)-O(20)-C(21)	-26.83(16)

Table S9. Hydrogen bonds for **13** [Å and °] at 80 K.

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
C(1)-H(1)...O(20)#1	0.95	2.57	3.4612(14)	155.6
C(3)-H(3)...O(6)#2	0.95	2.51	3.3321(14)	145.3
C(7)-H(7B)...O(19)#3	0.99	2.46	3.3829(14)	154.4
C(9)-H(9)...O(19)#3	0.99	2.57	3.3960(10)	144.9
C(21)-H(21A)...N(16)#1	0.98	2.68	3.5882(15)	154.1
C(21)-H(21C)...O(19)#4	0.98	2.40	3.3770(15)	176.4

Symmetry transformations used to generate equivalent atoms:

#1 -x+1,-y+1,-z #2 x-1/2,-y+3/2,z-1/2 #3 -x+2,-y+1,-z+2

#4 -x+1,-y+1,-z+1

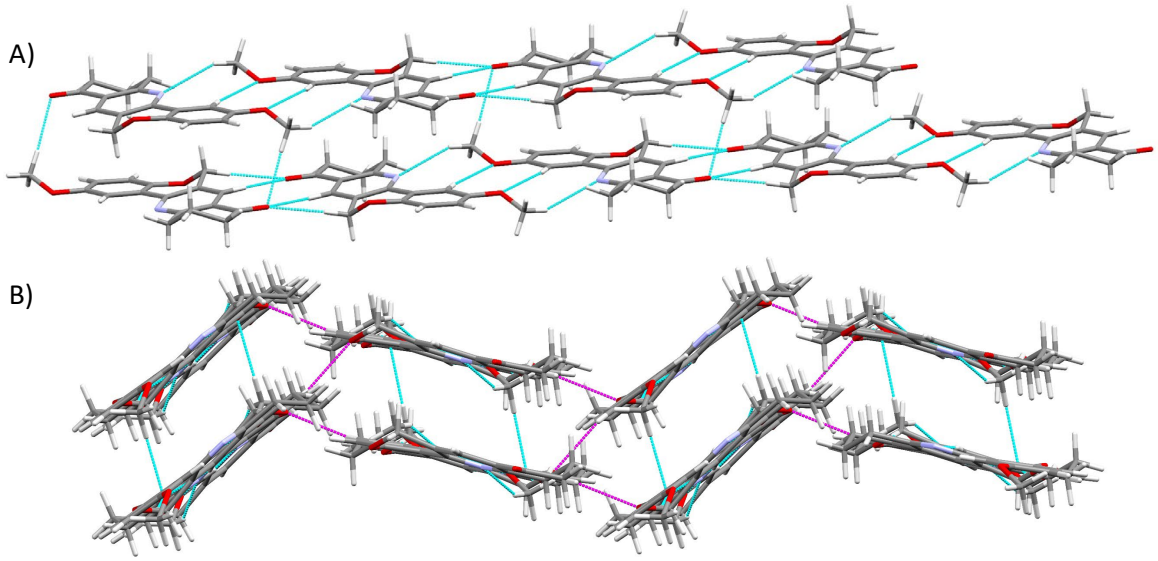


Figure S1. Structure of compound **13** at 80 K. A) 1D chains formed between neighbouring molecules through C9-H9…O19 (-x+2,-y+1,-z+2) and C7-H7B…O19 (-x+2,-y+1,-z+2) hydrogen bonds, alternated with C1-H1…O20 (-x+1,-y+1,-z) and C21-H21A…N16 (-x+1,-y+1,-z) interactions. The hydrogen bonds are depicted as cyan lines. B) The inter-chain connections (shifted in the [101] direction take place via C21-H21C…O(19) (-x+1,-y+1,-z+1) hydrogen bonds (cyan) and zig-zag C3-H3…O6 (x-1/2,-y+3/2,z-1) interactions (magenta).

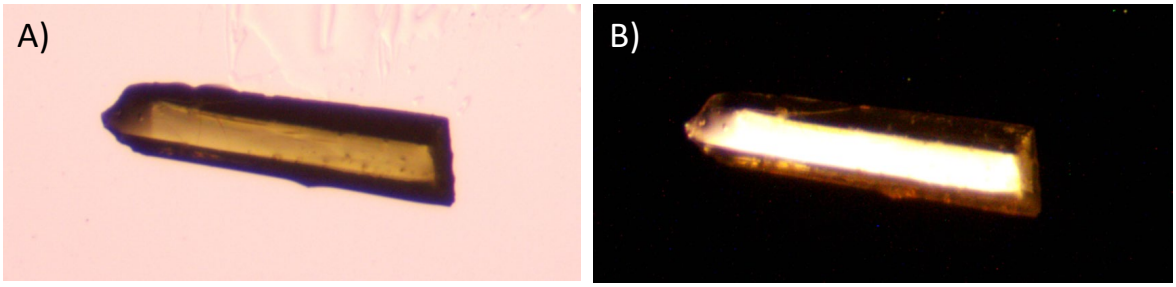
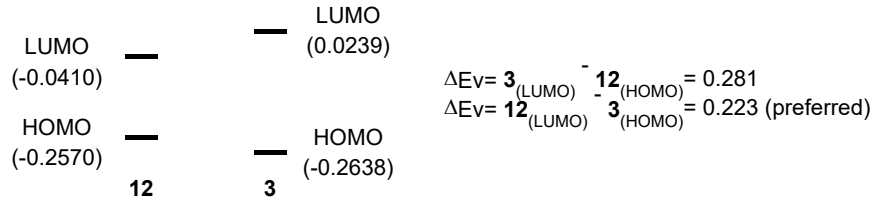


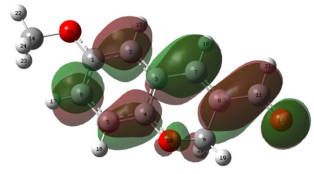
Figure S2. Stereoscopic view of the yellow crystal of compound **13** used in the single crystal X-ray diffraction measurements (4× objective), under white (A) and polarized (B) light, where birefringence was observed.

Computational Methods with full list of authors in the Gaussian 09

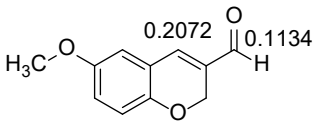
Conformational searches for the reactants, the transition structures (TSs) and the products were run to locate the global minima at the M062X/6-31G* level of theory. Initially, a large number of geometries were generated using the conformational search module of Hyperchem with the MM+ method.[1] Selected structures were then successively reoptimized at the M062X/6-31G* and M062X/6-311G** levels of theory.[2] Geometries for all structures were fully optimized and normal mode analysis was used to confirm the nature of the stationary points and to evaluate the thermochemical properties. Reported thermochemical properties include zero-point energies (ZPEs) without scaling and were calculated at 1 atm and 298.15 K. The molecular orbitals of the reactants were calculated to analyze the frontier orbital interactions. Intrinsic reaction coordinate (IRCs) calculations were run to verify the connectivity between reactants, TSs and products. To examine the more important interactions in the TSs we performed natural bond orbital calculations and Wiberg bond indexes (WBIs) were analyzsed. To interpret the presence of hydrogen bonds and the energy value, Second Order Perturbation analysis was carried out of the transition state at different theory levels theories. Free energies in solution were computed on the structures optimized in the gas phase at the B3LYP/6-31G* and M062X/6-311G** levels of theory with the polarizsable continuum model (PCM)[3] using methanol as solvent and Solvation Model based on Density (SMD)[4] to observe the differences between the models ($\varepsilon_{toluene}$= 2.37). Atomic charges were obtained from single-point calculations at the M062x/6-311g** level. Mulliken and Natural Population Analyses (NPA) were performed for all optimized structures (reactants and transition states) involved in both 1,2- and 1,4-addition pathways.Charge variations (Δq) were computed as the difference between the transition state and the corresponding reactant, $\Delta q = q(TS) - q(reactant)$.

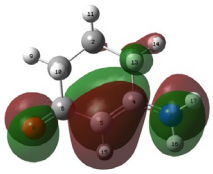
Shapes and energies of FMOs of the reactants



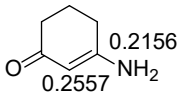


12_LUMO





3_HOMO



Natural Population Analysis of carbonyl and b-carbon in reagents and transition state.

Pathway	Atom	Method	q(reactant)	q(TS)	Δq	Comment
1,2-addition	C(carbonyl)	NPA	−0.219	−0.342	−0.123	Significant charge increase upon nucleophilic attack
1,4-addition	C(β)	NPA	−0.205	−0.210	−0.005	Minimal charge change

The data indicate that the carbonyl carbon in the 1,2-transition state undergoes a more pronounced charge increase ($\Delta q \approx -0.12$ e) than the β-carbon in the 1,4-transition state ($\Delta q \approx -0.01$ e), consistent with stronger electron transfer from the nucleophile to the carbonyl group. This analysis supports the kinetic preference for 1,2-addition, in agreement with the lower activation barrier obtained from transition-state energy calculations.

Full reaction coordinate diagrams

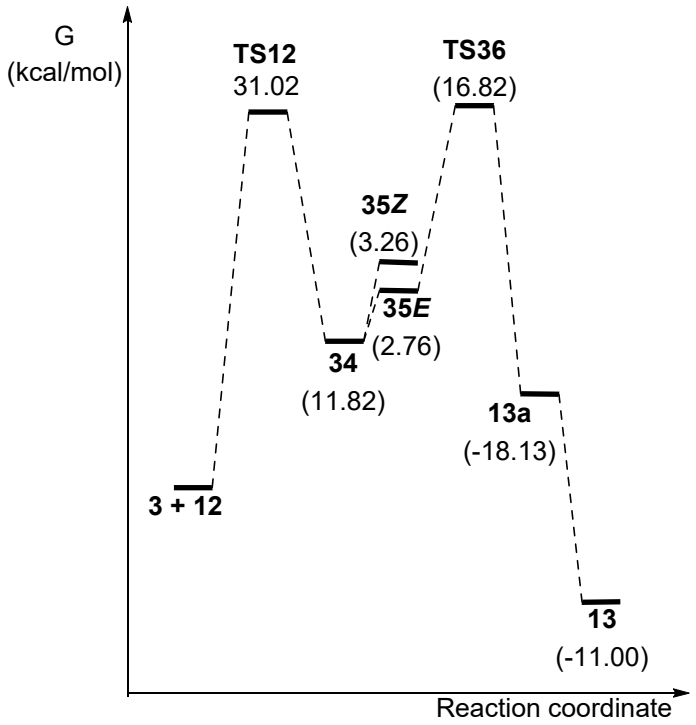


Figure S3. Formation of **13**. Free energies are in kcal mol^{-1}.

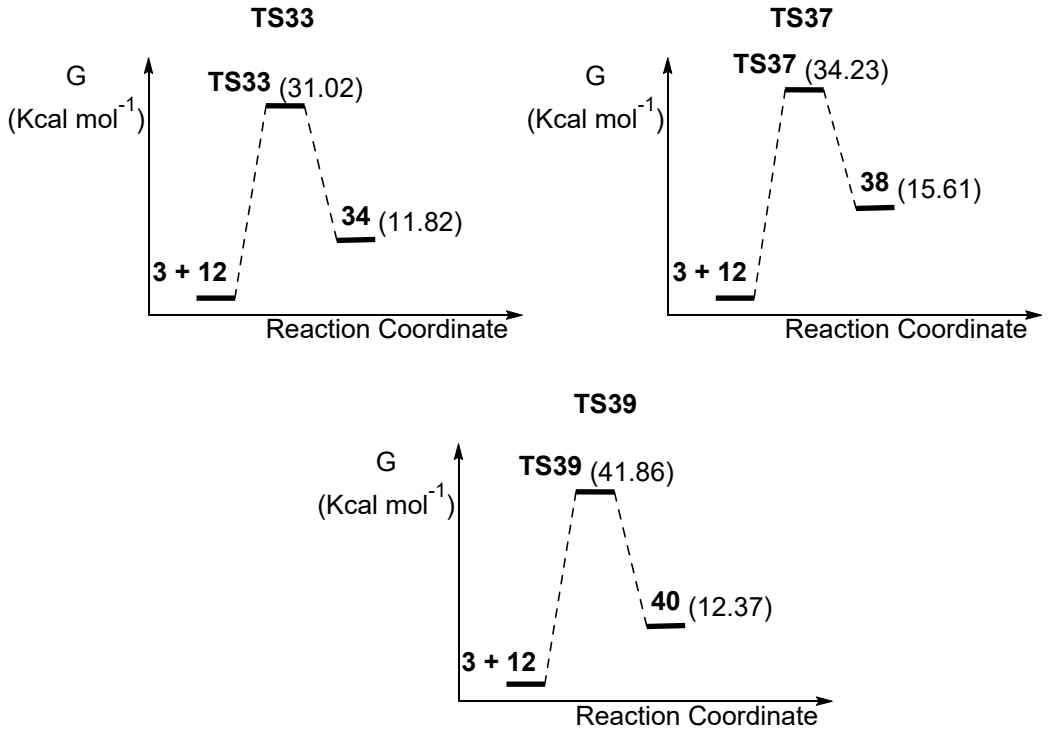
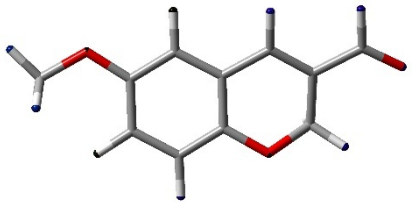


Figure S4. Representative reaction coordinate diagrams of **TS32**, **TS37** and **TS39**. Energies are in Kcal mol^{-1}.

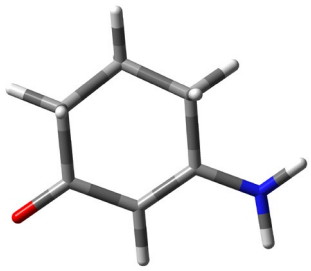
Cartesian coordinates, absolute energies including zero-points energy corrections, and free energies in solution (in Hartrees) of all stationary points reported in this paper and values of the imaginary frequencies in all transition states

 **12**	M062X/6-31G* Energy + ZPE in Toluene: -650.379607 M062X /6-31G* Free Energy in Toluene: -650.417852 M062X/6-311G** Energy + ZPE in Toluene: -650.553015 M062X/6-311G** Free Energy in Toluene: -650.591232

0 1

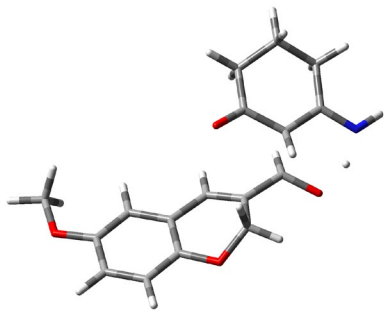
C	-2.37270700	-0.36611500	0.00309900
C	-1.17522300	-1.07806700	-0.02974100
C	0.04511500	-0.41245100	-0.08626600
C	0.06764600	0.99414400	-0.11717400
C	-1.12246100	1.70100400	-0.10683000
C	-2.34212900	1.02891500	-0.04546300
C	1.32368300	-1.10258500	-0.17142600
C	2.45657500	-0.40928600	0.01074500
C	2.37912000	1.05166100	0.35624200
O	1.24035200	1.67545100	-0.23693600
C	3.76609000	-1.06591300	-0.06348300
O	4.81303800	-0.49264100	0.12283300
O	-3.50582600	-1.11059200	0.07472200
C	-4.73977600	-0.42028600	0.13602000
H	-1.20927800	-2.16150300	-0.00947400
H	-1.08979400	2.78272600	-0.15035100
H	-3.25612400	1.60737200	-0.03106900
H	1.34237200	-2.16571000	-0.39599900
H	3.25153700	1.58298800	-0.02021500

H	2.33838300	1.18135900	1.44650600
H	3.73641100	-2.14708900	-0.29839000
H	-5.51061400	-1.18642500	0.19361600
H	-4.79609600	0.21519000	1.02588600
H	-4.90290100	0.18722800	-0.75979000

 **3**	M062X/6-31G* Energy + ZPE in Toluene: -363.734127 M062X /6-31G* Free Energy in Toluene: -363.765577 M062X/6-311G** Energy + ZPE in Toluene: -363.841080 M062X/6-311G** Free Energy in Toluene: -363.872756

0 1

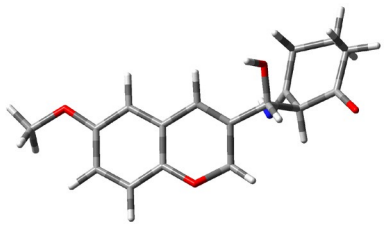
C	-1.39031800	0.94844000	0.24323400
C	-0.21127900	1.70636500	-0.35800800
C	1.10499800	1.14494200	0.17111500
C	1.17202600	-0.35261200	0.01477700
C	0.04753000	-1.11517600	-0.07995100
C	-1.28778200	-0.55289200	0.01733700
N	2.42094700	-0.87543500	-0.02878900
O	-2.29315400	-1.24102000	-0.04001300
H	-2.34680000	1.28218500	-0.16171000
H	-1.41981900	1.10820600	1.32847500
H	-0.28057900	2.77159200	-0.12825300
H	-0.23101900	1.60364800	-1.44711700
H	1.21399500	1.37897400	1.23740900
H	1.95831900	1.59471000	-0.34418800
H	0.11910500	-2.19154500	-0.19959700
H	2.55390600	-1.87302100	0.02748900
H	3.22044600	-0.29294400	0.15810000

 **TS33**	M062X/6-31G* Energy + ZPE in Toluene: -1014.086138 M062X /6-31G* Free Energy in Toluene: -1014.135302 M062X/6-311G** Energy + ZPE in Toluene: -1014.365779 M062X/6-311G** Free Energy in Toluene: -1014.414552 Imaginary frecuencies: 1 (-1013.46)

0 1

N	4.52834900	-1.19961700	-0.43130900
C	2.67541500	-0.16243500	0.52664700
C	3.98113100	-0.07201300	-0.05730100
C	1.98248100	1.05978800	0.97566500
C	2.50453400	2.37241800	0.42732500
O	1.02202200	1.00776600	1.71525300
C	4.03393000	2.39704800	0.45344400
C	4.59414500	1.25985800	-0.39680500
H	3.64011100	-1.88044700	-0.80695200
H	5.37267400	-1.11435900	-0.98942000
H	2.50694300	-1.02741500	1.16100800
H	2.15205300	2.46788100	-0.60853000
H	2.06456800	3.18201100	1.00962100
H	4.40641600	3.35263800	0.08113500
H	4.38207800	2.29200200	1.48532600
H	5.68059100	1.18005200	-0.30954300
H	4.37197600	1.44745600	-1.45583600
O	2.39777600	-2.09162700	-1.18931600
C	1.76365100	-0.97825700	-1.00418200
C	0.37500000	-1.03175300	-0.48884500
C	-0.57414100	-0.18643100	-0.90279600
C	-1.92472000	-0.30467000	-0.36099000

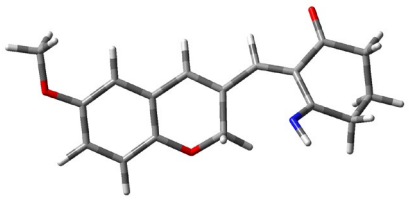
C	-2.24112100	-1.47497900	0.33557900
O	-1.32178600	-2.46897400	0.49059100
C	0.03337500	-2.03158300	0.58025100
C	-2.90882000	0.67215400	-0.55917000
C	-4.19379500	0.47920900	-0.06422300
C	-4.50025000	-0.70296600	0.61816400
C	-3.53224200	-1.67353000	0.81467700
O	-5.21217400	1.37069100	-0.19637800
C	-4.93362900	2.58048200	-0.87235600
H	1.90277800	-0.17853000	-1.75007700
H	-0.36980100	0.57668700	-1.64895500
H	0.64861700	-2.92460500	0.48139500
H	0.20453200	-1.57426800	1.56586100
H	-2.64222100	1.56881500	-1.10421800
H	-5.50810000	-0.83602700	0.99221400
H	-3.76163400	-2.59349400	1.33849300
H	-5.85799500	3.15489000	-0.85726900
H	-4.14729300	3.14905400	-0.36496400
H	-4.64109400	2.39809500	-1.91182200

 **34**	M062X/6-31G* Energy + ZPE in Toluene: -1014.115397 M062X /6-31G* Free Energy in Toluene: -1014.163682 M062X/6-311G** Energy + ZPE in Toluene: -1014.396485 M062X/6-311G** Free Energy in Toluene: -1014.445149

0 1

N	1.56995200	-0.70576000	2.06023500
C	2.75157400	0.48194200	0.36771400
C	2.37528600	-0.80114800	1.08427200
C	4.19254900	0.54352200	-0.14283400
C	4.88408200	-0.75662300	-0.48301100
O	4.71417200	1.61798300	-0.31008500
C	4.52545800	-1.89763400	0.47030800
C	3.00501100	-2.06953400	0.56973800
O	2.09227100	-0.24092500	-1.81511300
C	1.82843500	0.75817800	-0.84834300
C	0.38260500	0.82013700	-0.44449100
C	-0.54792200	-0.04015800	-0.86252100
C	-1.92868800	0.11906700	-0.40518100
C	-2.27994600	1.33705300	0.20128000
O	-1.35591200	2.33198000	0.34092800
C	-0.01802100	1.88459400	0.54487500
C	-2.90581100	-0.85197700	-0.58633600
C	-4.22134200	-0.62863900	-0.17710600
C	-4.56321100	0.58930100	0.40843400
C	-3.58530400	1.56795200	0.59459500
O	-5.09245500	-1.64925800	-0.39809300
C	-6.44065500	-1.44753700	-0.02280000
H	1.37393500	-1.62991300	2.45123600

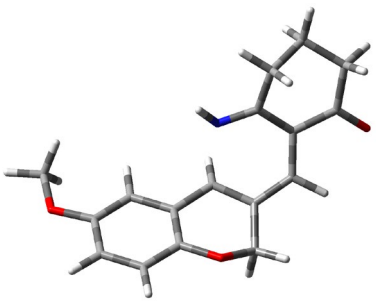
H	2.61797000	1.31412400	1.06277400
H	4.54334400	-1.01363800	-1.49308200
H	5.95733800	-0.56738700	-0.52303600
H	4.97893900	-2.82443000	0.11460500
H	4.93652000	-1.69682300	1.46461500
H	2.74263200	-2.90153800	1.22668700
H	2.60070700	-2.27041900	-0.42823300
H	1.61209700	-0.01554500	-2.61947100
H	2.12881400	1.74500300	-1.22811300
H	-0.30914700	-0.85942500	-1.53209700
H	0.09255800	1.48737800	1.56366800
H	0.60679300	2.77415100	0.44712800
H	-2.66034300	-1.79768600	-1.05672800
H	-5.57606000	0.79209400	0.72912400
H	-3.83678900	2.52051600	1.04503400
H	-6.96857500	-2.36150200	-0.28868700
H	-6.53522300	-1.27824300	1.05478700
H	-6.88437200	-0.60562300	-0.56449900

 **35*E***	M062X/6-31G* Energy + ZPE in Toluene: -937.736768 M062X /6-31G* Free Energy in Toluene: -937.783636 M062X/6-311G** Energy + ZPE in Toluene: -937.984587 M062X/6-311G** Free Energy in Toluene: -938.0317804

0 1

O	3.61124400	2.66416600	-0.45374300
C	2.80214900	0.50500200	0.13796200
C	3.86765800	1.50913600	-0.19843800
C	3.23484000	-0.77357100	0.75609400
C	4.58294300	-1.34327200	0.34094000
N	2.49192100	-1.30372500	1.64478500
C	5.31318200	-0.47557500	-0.68032600
C	5.28751600	0.98376000	-0.22859800
C	1.52339100	0.87996200	-0.09440200
C	0.27690800	0.14229700	-0.04911900
C	-0.88019700	0.83886300	-0.09414600
C	-2.15847800	0.15199600	-0.10452300
C	-2.14469900	-1.20305300	-0.44866800
O	-0.97363600	-1.82712800	-0.73406300
C	0.16006400	-1.36562400	0.00891800
C	-3.38012300	0.80397700	0.12402700
C	-4.57100200	0.09954900	0.00864600
C	-4.54229200	-1.25444200	-0.35374400
C	-3.34175100	-1.90143000	-0.58404100
O	-5.80500200	0.62846800	0.21309400
C	-5.87807300	1.99844900	0.55721700
H	5.19239900	-1.44061200	1.24569400
H	4.41868000	-2.35365600	-0.04441300

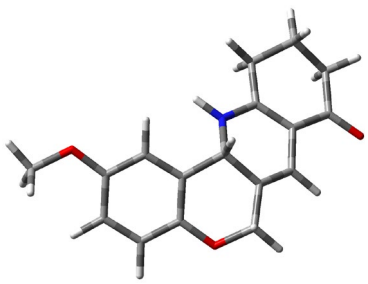
H	2.91825400	-2.16863400	1.98797700
H	6.34129000	-0.82183300	-0.79670600
H	4.83009400	-0.56091600	-1.65861400
H	5.87170500	1.64078700	-0.87356500
H	5.69455200	1.06554500	0.78758400
H	1.41128200	1.91625500	-0.40898400
H	-0.87065100	1.92385100	-0.13822700
H	1.01505300	-1.85103900	-0.45421100
H	0.08120500	-1.70997800	1.04517100
H	-3.36464000	1.85530800	0.38304500
H	-5.48512400	-1.77990600	-0.44678100
H	-3.31353900	-2.94533900	-0.87198600
H	-6.93679300	2.22632400	0.66506000
H	-5.36861300	2.19970300	1.50535900
H	-5.45166900	2.63002000	-0.22898800

 **36**	M062X/6-31G* Energy + ZPE in Toluene: -937.712020 M062X /6-31G* Free Energy in Toluene: -937.757174 M062X/6-311G** Energy + ZPE in Toluene: -937.959657 M062X/6-311G** Free Energy in Toluene: -938.004977 Imaginary frecuencies: 1 (-397.00)

0 1

C	0.29811100	0.26171100	-0.70085000
O	-4.57002700	1.07241100	-1.26200000
C	-4.07461900	0.20231800	-0.57044400
C	-2.60965700	0.11313000	-0.38299700
C	-1.89184300	1.27678400	-0.66994400
C	-2.03222500	-0.91879300	0.46781700
N	-0.76780000	-1.16671200	0.50386700
C	-0.50928200	1.38999400	-0.56385800
C	0.19378900	2.67545000	-0.19734200
O	1.17822500	2.44274900	0.81735900
C	2.05651100	1.44885700	0.52139800
C	1.68810400	0.35738900	-0.27253800
C	2.61890100	-0.65694300	-0.54678600
C	3.90166400	-0.58146100	-0.02385400
C	4.25120000	0.50753700	0.78843500
C	3.34171700	1.51244400	1.05813100
O	4.87858400	-1.50096600	-0.23208200
C	4.55727300	-2.61620100	-1.04105100
C	-4.97453200	-0.78810800	0.14598200
C	-4.25429200	-2.04043200	0.62415400
C	-2.99362800	-1.64697300	1.39117800
H	0.04313200	-0.50206200	-1.42006700

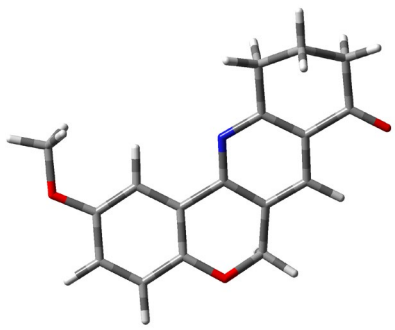
H	-2.49151100	2.16785300	-0.84620400
H	-0.49060300	-1.72000800	1.31587100
H	0.70339600	3.11538100	-1.06544200
H	-0.49312900	3.40957800	0.21867500
H	2.30137300	-1.49247400	-1.15839500
H	5.25677300	0.54544000	1.18986400
H	3.60980200	2.35942600	1.67786300
H	4.27449100	-2.30716300	-2.05275800
H	3.74799200	-3.20706500	-0.59981900
H	5.45878400	-3.22355500	-1.09099400
H	-5.81314200	-1.01229600	-0.51514400
H	-5.38384300	-0.24800500	1.00919000
H	-4.90968900	-2.63516100	1.26342000
H	-3.97796100	-2.66552600	-0.23079900
H	-3.26229500	-0.98532200	2.22265400
H	-2.49638200	-2.52583000	1.80421600

 **13a**	M062X/6-31G* Energy + ZPE in Toluene: -937.768235 M062X /6-31G* Free Energy in Toluene: -937.813727 M062X/6-311G** Energy + ZPE in Toluene: -938.015094 M062X/6-311G** Free Energy in Toluene: -938.060671

0 1

C	3.60873700	-0.76765400	0.03018400
C	2.29974000	-0.78031200	0.50475400
C	1.46502200	0.32341000	0.36515700
C	1.97267100	1.48623600	-0.22846200
C	3.28011200	1.50073500	-0.70251600
C	4.09833300	0.38403300	-0.58775000
C	0.02522500	0.26030400	0.84874700
C	-0.71600700	1.52342300	0.47995300
C	0.13426700	2.74629200	0.52325300
O	1.24230300	2.62706300	-0.37707900
O	4.32391500	-1.90825500	0.21739700
C	5.66630600	-1.91795000	-0.23055000
C	-2.01037200	1.49342900	0.15789100
C	-1.99915900	-0.92468400	0.04880300
N	-0.67046900	-0.89301400	0.26707900
C	-2.61089500	-2.26251600	-0.26069100
C	-4.08941800	-2.27870600	0.12312800
C	-4.82060700	-1.10641000	-0.52312800
C	-2.73654200	0.23643700	0.04871500
C	-4.16291700	0.23644200	-0.24921200
O	-4.81072800	1.26762000	-0.31938700
H	1.94928700	-1.68376300	0.99457700

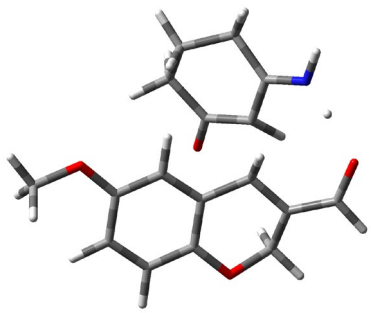
H	3.64862300	2.40933500	-1.16345000
H	5.10978100	0.43050400	-0.96797600
H	0.04355200	0.14944100	1.94632000
H	0.53671500	2.90697800	1.53356800
H	-0.41952300	3.63052500	0.21294700
H	6.06029200	-2.90079200	0.02062900
H	5.72691200	-1.77208600	-1.31387900
H	6.26115800	-1.15123900	0.27612000
H	-2.54958500	2.40517700	-0.07839400
H	-0.17568300	-1.77366200	0.26594500
H	-2.06079000	-3.04705100	0.26537300
H	-2.50118900	-2.45185300	-1.33514700
H	-4.17723600	-2.21146600	1.21147100
H	-4.54013300	-3.22467100	-0.18359100
H	-5.85996000	-1.03971600	-0.19790800
H	-4.82981700	-1.23104100	-1.61325300

 **13**	M062X/6-31G* Energy + ZPE in Toluene: -936.625866 M062X /6-31G* Free Energy in Toluene: -936.669995 M062X/6-311G** Energy + ZPE in Toluene: -936.864878 M062X/6-311G** Free Energy in Toluene: -936.908996

0 1

C	-3.71302700	0.71090600	-0.00178000
C	-2.33584400	0.78964700	-0.14500300
C	-1.55496000	-0.36929100	-0.03876100
C	-2.16316800	-1.60030700	0.21557400
C	-3.54694900	-1.67266900	0.37233900
C	-4.31286800	-0.52882600	0.26275200
C	-0.08575700	-0.32517400	-0.09488900
C	0.59465000	-1.54962000	-0.19346100
C	-0.23336100	-2.79017500	-0.38148100
O	-1.43556000	-2.74242500	0.38058200
O	-4.55903700	1.76851000	-0.09346100
C	-3.98248800	3.04224400	-0.31289200
C	1.97267600	-1.52770700	-0.17314400
C	1.86899200	0.87307000	-0.01630800
N	0.53471100	0.85156600	-0.00977600
C	2.53325400	2.22272500	0.06928400
C	3.93414300	2.12789300	0.66958100
C	4.77150700	1.10101700	-0.09144800
C	2.63279700	-0.30021000	-0.09019600
C	4.12568300	-0.26571900	-0.09487900
O	4.77278300	-1.28802900	-0.12344300

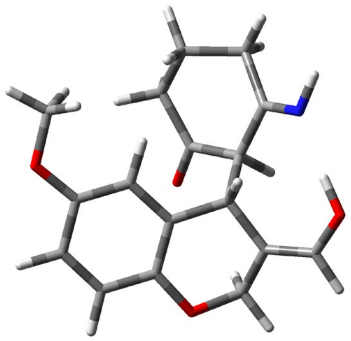
H	-1.82672600	1.72667400	-0.32564600
H	-4.00109900	-2.63383500	0.57993700
H	-5.38989400	-0.56638000	0.37418700
H	0.30301400	-3.67960200	-0.05420700
H	-0.49431100	-2.90428000	-1.44247500
H	-4.81039300	3.74782200	-0.34338100
H	-3.30435900	3.31574000	0.50177500
H	-3.44250600	3.07758500	-1.26447600
H	2.55828700	-2.43959500	-0.23352800
H	1.88789000	2.88347400	0.65014200
H	2.59438800	2.64075000	-0.94321300
H	3.86142200	1.83221500	1.72104800
H	4.42265900	3.10340700	0.63957500
H	5.78020900	0.99571400	0.30938500
H	4.86128100	1.40807200	-1.14183500

 **TS37**	M062X/6-31G* Energy + ZPE in Toluene: -1014.082463 M062X /6-31G* Free Energy in Toluene: -1014.129771 M062X/6-311G** Energy + ZPE in Toluene: -1014.362467 M062X/6-311G** Free Energy in Toluene: -1014.409449 Imaginary frequencies: 1 (-536.20)

0 1

C	-1.64489400	-1.93703200	-0.24502200
C	-0.92396100	-0.74899700	-0.55847800
C	0.53829200	-0.84252800	-0.32703600
C	-2.95005800	-2.12052700	-0.68766400
O	-3.65798200	-1.26828800	-1.29341400
C	-1.03780800	-2.80336000	0.80876600
O	0.34236200	-3.09873900	0.54336000
C	1.08959800	-2.02320600	0.19968800
C	1.39646100	0.18423000	-0.71081100
C	2.77383400	0.08201400	-0.56523100
C	3.31517600	-1.09524000	-0.04218500
C	2.47177100	-2.13511200	0.32634500
O	3.50237300	1.16381000	-0.95707700
C	4.90999600	1.06988200	-0.85344400
H	-1.20055200	-0.26577000	-1.49293000
H	-3.40999700	-3.09998000	-0.47563900
H	-1.54364100	-3.76611300	0.88481600
H	-1.07167900	-2.30626700	1.79011100
H	0.99003600	1.08484700	-1.15426200
H	4.38296600	-1.21506300	0.08400300
H	2.87653500	-3.05734500	0.72538400

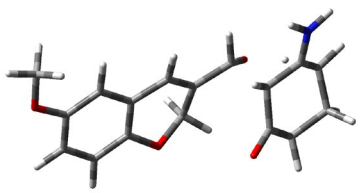
H	5.30233300	0.25621300	-1.47228700
H	5.22658200	0.92426800	0.18456100
H	5.30382700	2.01719700	-1.21727600
N	-3.17374400	1.27727800	-1.11016000
C	-1.64987500	0.70275900	0.60347100
C	-2.26211700	1.67043700	-0.26704400
C	-0.62200100	1.15617500	1.56108100
C	0.00680800	2.52997200	1.38330600
C	-0.36634100	3.26807000	0.09811000
C	-1.85267000	3.11397700	-0.22427600
O	-0.27635200	0.44360700	2.48131100
H	-3.42116800	0.23178200	-1.19582300
H	-3.60851800	1.95637700	-1.72219200
H	-2.34957500	0.00721200	1.04807400
H	1.08897300	2.40839900	1.47673100
H	-0.31931300	3.11089800	2.25396100
H	-0.13189200	4.32904900	0.20127600
H	0.22302000	2.90144100	-0.74359200
H	-2.44731400	3.58322400	0.56977200
H	-2.11088100	3.60647100	-1.16446200

 **38**	M062X/6-31G* Energy + ZPE in Toluene: -1014.111770 M062X /6-31G* Free Energy in Toluene: -1014.158689 M062X/6-311G** Energy + ZPE in Toluene: -1014.372202 M062X/6-311G** Free Energy in Toluene: -1014.439124

0 1

N	-2.70972700	1.55104800	-1.23923500
C	-1.36626700	0.70658600	0.55422200
C	-1.95365500	1.84624600	-0.26176100
C	-0.29314500	1.10203600	1.57321500
C	0.37875400	2.46310800	1.49745800
C	-0.06437300	3.33314300	0.32507700
C	-1.58475700	3.24522000	0.15248700
O	-0.01219000	0.33108300	2.45614900
C	-1.82577200	-1.71295700	-0.13232400
C	-0.94883200	-0.51419500	-0.36581600
C	0.50672200	-0.91543400	-0.23622300
C	-2.97845800	-1.91889800	-0.77512800
O	-3.56164700	-1.10002200	-1.66735700
C	-1.32322900	-2.63490100	0.92848700
O	-0.00937700	-3.12222900	0.62962200
C	0.87881200	-2.17106100	0.23265400
C	1.50120500	-0.01361700	-0.64106900
C	2.84494700	-0.35116900	-0.57515400
C	3.20724400	-1.62200200	-0.11170300
C	2.23511600	-2.51616400	0.28402800
O	3.86714100	0.46926700	-0.94132500

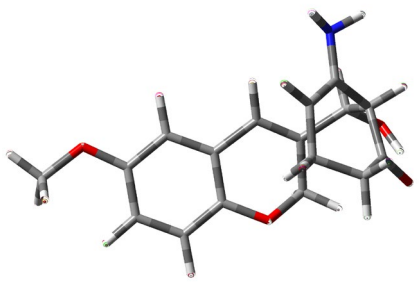
C	3.52976100	1.77543500	-1.35928100
H	-3.07283400	2.38225000	-1.70569800
H	-2.18787900	0.34790500	1.18459900
H	1.45707500	2.28239000	1.50060500
H	0.14489000	2.96229900	2.44425000
H	0.23273800	4.36865600	0.49860000
H	0.42206200	3.01374900	-0.60210500
H	-2.06849900	3.47037100	1.11101200
H	-1.95518600	3.95685400	-0.58773500
H	-1.08821500	-0.17399000	-1.39418600
H	-3.55519000	-2.82441900	-0.60241800
H	-3.21134300	-0.18208700	-1.59466500
H	-1.95446700	-3.51642900	1.03624300
H	-1.26694500	-2.10972700	1.89193100
H	1.18731700	0.95075000	-1.02451500
H	4.25856200	-1.88032900	-0.06977800
H	2.49992900	-3.50244900	0.64589000
H	3.00258100	2.32197000	-0.56902600
H	2.91674900	1.76295300	-2.26694300
H	4.47090000	2.27889600	-1.57315000

 **TS39**	M062X/6-31G* Energy + ZPE in Toluene: -1014.082167 M062X /6-31G* Free Energy in Toluene: -1014.130008 M062X/6-311G** Energy + ZPE in Toluene: -1014.350851 M062X/6-311G** Free Energy in Toluene: -1014.397291 Imaginary Frecuencies: 1 (-1193.11)

0 1

O	-1.70547200	-1.05754300	-2.00074400
C	-2.41909500	0.75504400	-0.67060200
C	-2.48671600	-0.66324900	-1.16784000
C	-3.68829400	1.34985500	-0.31064200
C	-4.58097900	0.50622200	0.41419500
N	-3.82852400	2.67025800	-0.36124100
C	-4.83244700	-0.87042600	-0.20042800
C	-3.51124900	-1.57163500	-0.52086700
H	-1.77312000	1.36381000	-1.30069600
H	-3.69672400	0.30735300	1.31801500
H	-5.46937300	1.00531600	0.79940600
H	-4.66107900	3.11585700	-0.00516000
H	-3.08795600	3.25861000	-0.71401200
H	-5.40480200	-1.47765700	0.50257000
H	-5.43649200	-0.77453100	-1.10785100
H	-3.64315700	-2.44492800	-1.15991300
H	-3.06621700	-1.89602100	0.42548700
O	-2.40377100	0.13808900	1.81772300
C	-1.64480600	0.73104400	0.91799800
C	-0.29427900	0.10304700	0.70049800
C	0.78184000	0.80143900	0.32848400
C	2.07557300	0.13365200	0.20212200
C	2.08243200	-1.26384900	0.19836600

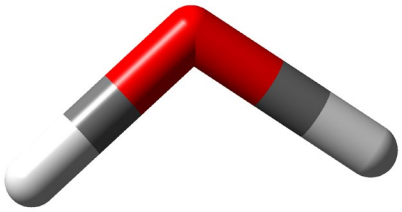
O	0.92291200	-1.97058000	0.30099800
C	-0.11619500	-1.34951700	1.05500000
C	3.27841400	0.83127200	0.03567400
C	4.47130200	0.13669100	-0.13683300
C	4.46066400	-1.26148400	-0.15300900
C	3.27465500	-1.95652000	0.01425000
O	5.68819100	0.72256200	-0.30240000
C	5.73534100	2.13464900	-0.31743300
H	-1.51771500	1.82313500	1.04647400
H	0.72063800	1.86596500	0.11764300
H	0.10322500	-1.44131500	2.12858200
H	-1.01203200	-1.93052900	0.85190200
H	3.25099000	1.91384200	0.03951300
H	5.39948400	-1.78276800	-0.29508700
H	3.25402900	-3.03944000	-0.00238700
H	6.77922500	2.40069900	-0.47395100
H	5.13376300	2.54698600	-1.13443700
H	5.39514300	2.55617400	0.63439400

 **40**	M062X/6-31G* Energy + ZPE in Toluene: -1014.112000 M062X /6-31G* Free Energy in Toluene: -1014.160743 M062X/6-311G** Energy + ZPE in Toluene: -1014.382604 M062X/6-311G** Free Energy in Toluene: -1014.431905

0 1

C	-3.85214900	0.32506800	-0.16003100
C	-2.64265200	0.73028100	-0.72589600
C	-1.48968100	-0.02785800	-0.56266500
C	-1.55573600	-1.21775200	0.18316800
C	-2.74931100	-1.61624800	0.75637800
C	-3.90379700	-0.85084300	0.58785800
O	-4.91539300	1.14241600	-0.38615900
C	-6.14753700	0.79313400	0.21364500
C	-0.18058200	0.37902600	-1.07236600
C	0.82951600	-0.49582100	-1.07380400
C	0.53522000	-1.91167400	-0.63644200
O	-0.42637600	-1.95048200	0.41707900
C	2.22904000	-0.12662600	-1.50344300
O	2.91739000	-1.21825200	-2.07406500
C	3.04838900	0.50490800	-0.32509100
C	3.20353600	-0.50586400	0.80484900
C	2.80135300	-0.10317600	2.19557300
C	1.57540300	0.81276400	2.19633000
C	1.77026900	1.95939300	1.24166600
C	2.45320200	1.82310700	0.10002000
N	2.53655200	2.81404800	-0.88679300
O	3.65399400	-1.60771500	0.56164000

H	-2.61554000	1.65586100	-1.29008200
H	-2.77172400	-2.52828000	1.34059300
H	-4.82698400	-1.18700300	1.04014700
H	-6.85118900	1.57496000	-0.06627200
H	-6.51540100	-0.16963800	-0.15590600
H	-6.06434100	0.75827000	1.30504600
H	-0.04353400	1.39964300	-1.41849400
H	1.41568400	-2.41786700	-0.24609600
H	0.16120900	-2.49385100	-1.49077000
H	2.15986200	0.64544600	-2.27216600
H	3.33290800	-1.70710600	-1.35081400
H	4.05447500	0.66548700	-0.73545500
H	3.65610400	0.44643800	2.61011400
H	2.66042600	-1.01049700	2.78427300
H	1.40962600	1.18770500	3.20782500
H	0.68642400	0.22791100	1.92736000
H	1.30919900	2.91518400	1.47280700
H	2.27156500	3.73473700	-0.56045800
H	3.43154900	2.84561100	-1.36055300

 **H_2O**	M062X/6-31G* Energy + ZPE in Toluene: -76.390672 M062X /6-31G* Free Energy in Toluene: -76.408963 M062X/6-311G** Energy + ZPE in Toluene: -76.390672 M062X/6-311G** Free Energy in Toluene: -76.408963

0 1

O	0.00000000	0.11846900	0.00000000
H	0.76240900	-0.47387600	0.00000000
H	-0.76240900	-0.47387600	0.00000000

 **H_2**	M062X/6-31G* Energy + ZPE in Toluene: -1.152740 M062X /6-31G* Free Energy in Toluene: -1.164204 M062X/6-311G** Energy + ZPE in Toluene: -1.157734 M062X/6-311G** Free Energy in Toluene: -1.169209

0 1

H	0.00000000	0.00000000	0.36838700
H	0.00000000	0.00000000	-0.36838700

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