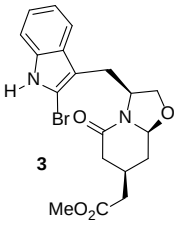
Studies on the Enantioselective Synthesis of *E*-Ethylidene-Bearing Spiro[indolizidine-1,3′-oxindole] Alkaloids

Nihan Yayik, Maria Pérez, Elies Molins, Joan Bosch, and Mercedes Amat*

Supporting Information Available



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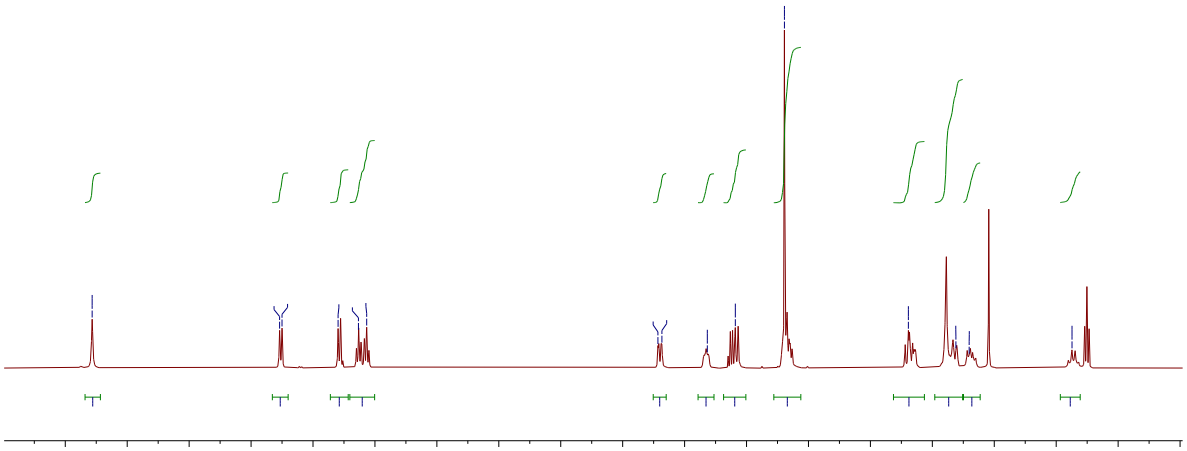

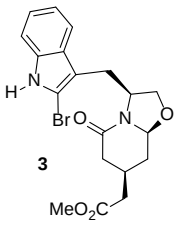

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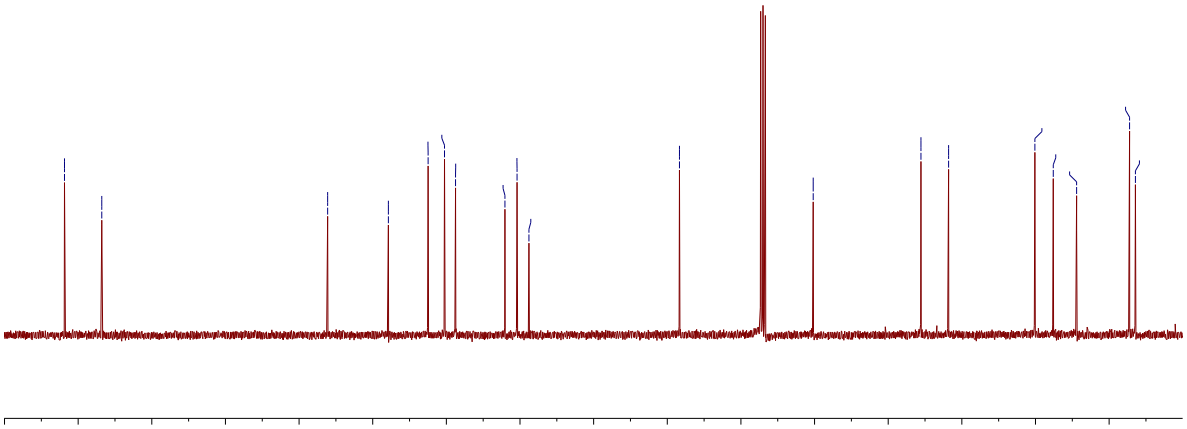

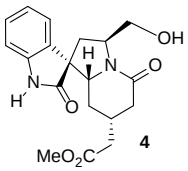

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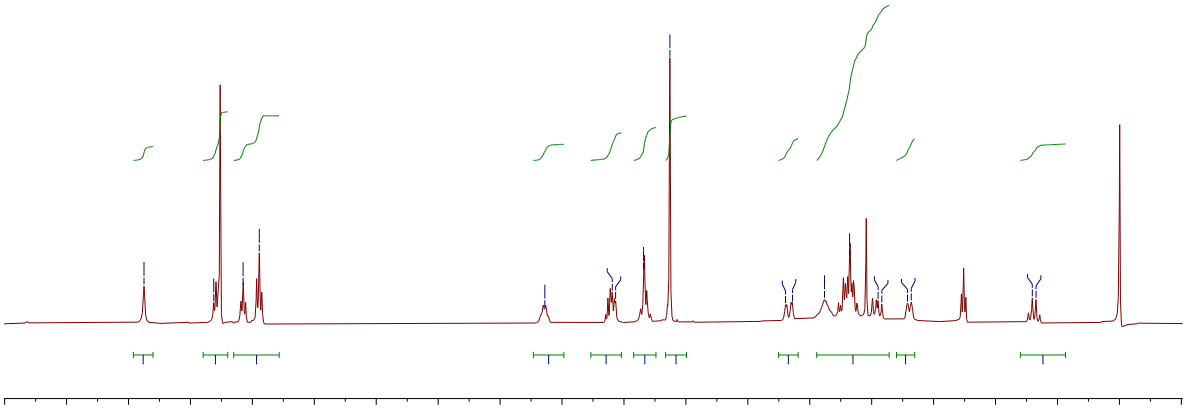

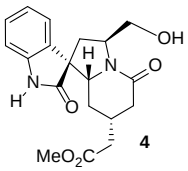

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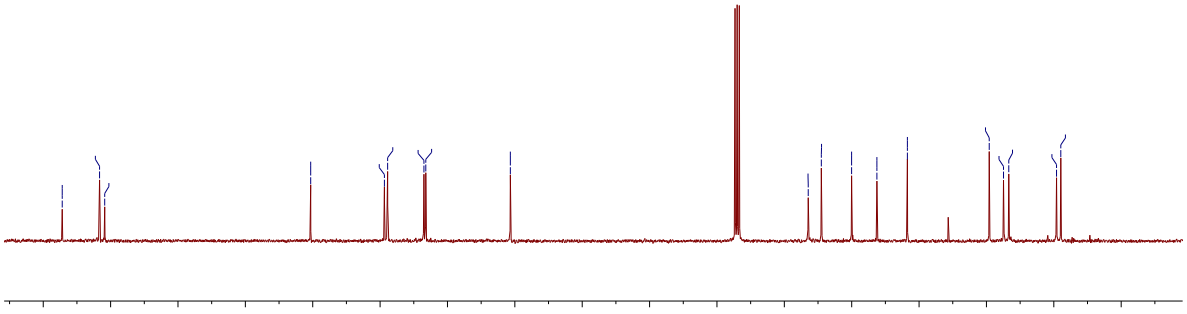

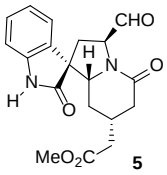

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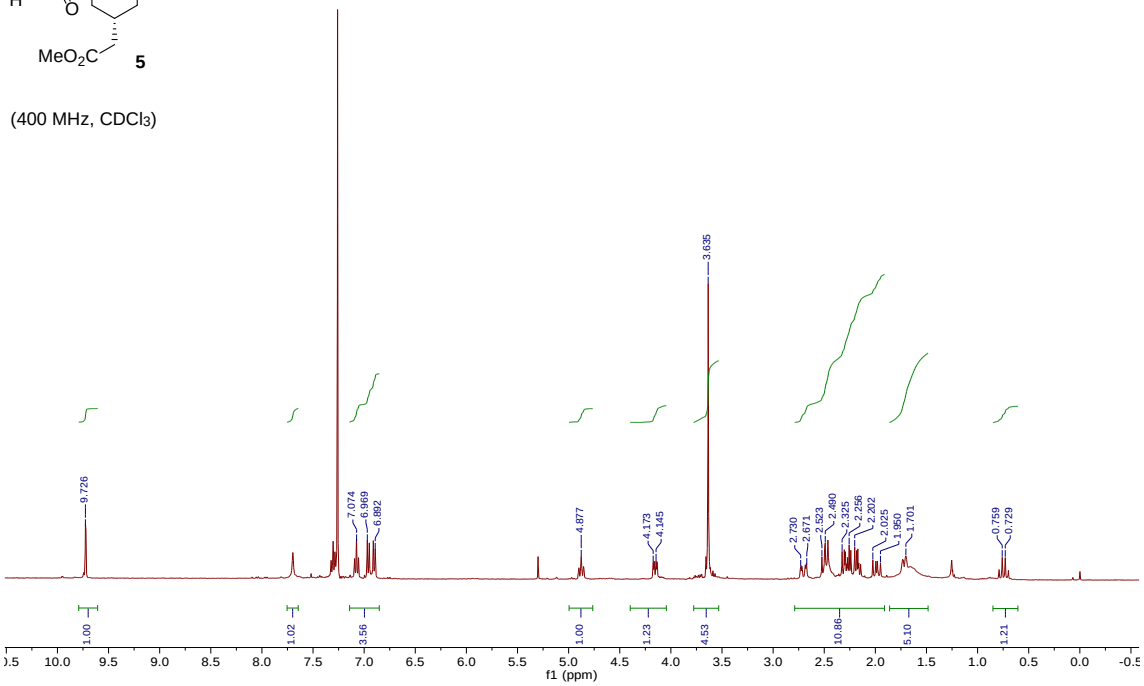

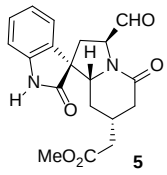

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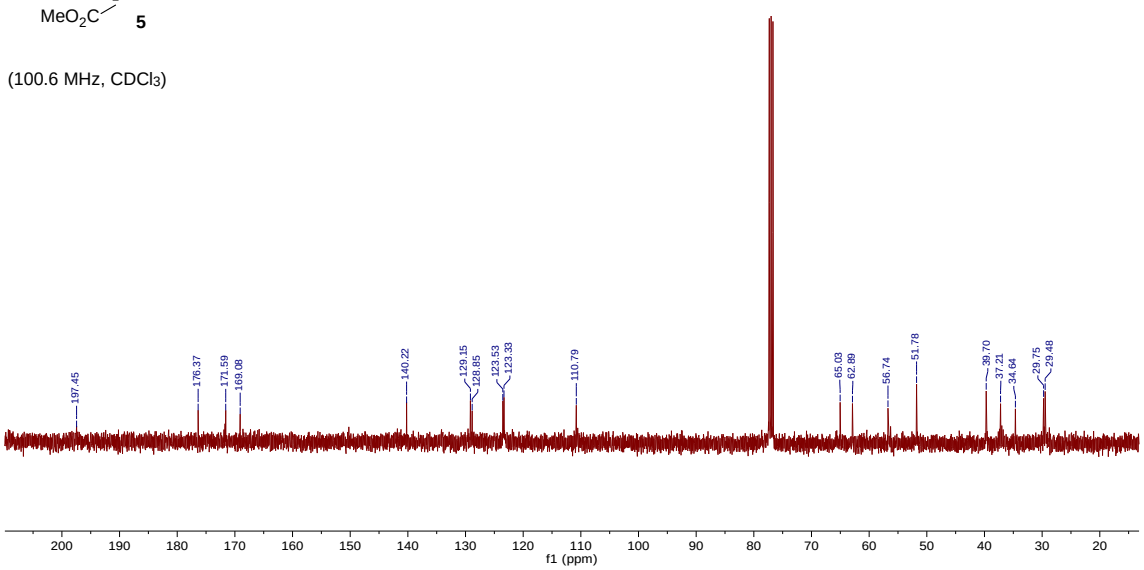

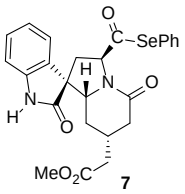

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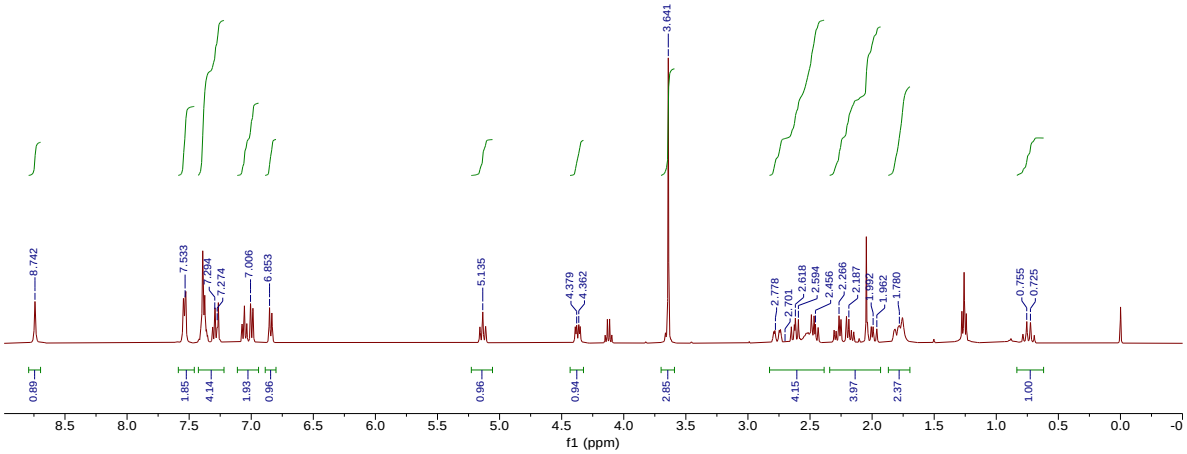

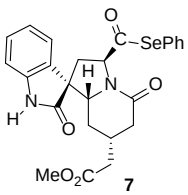

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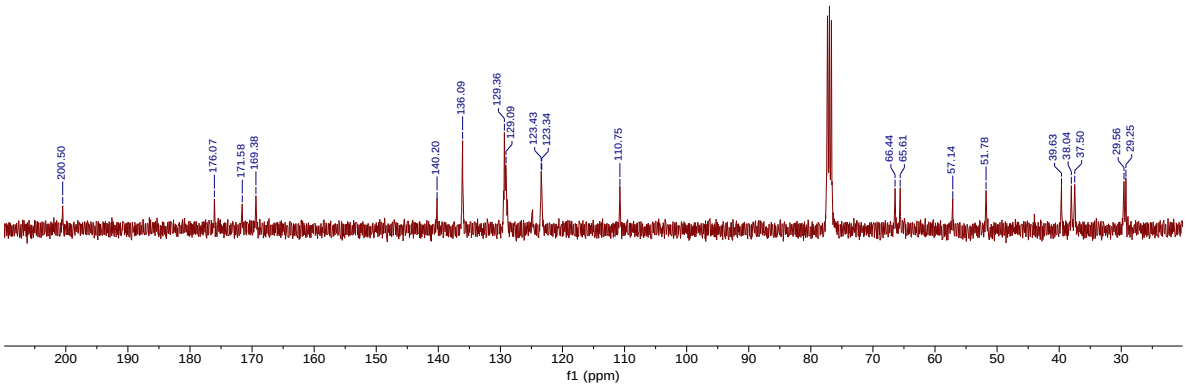

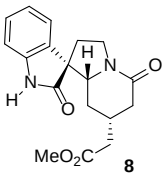

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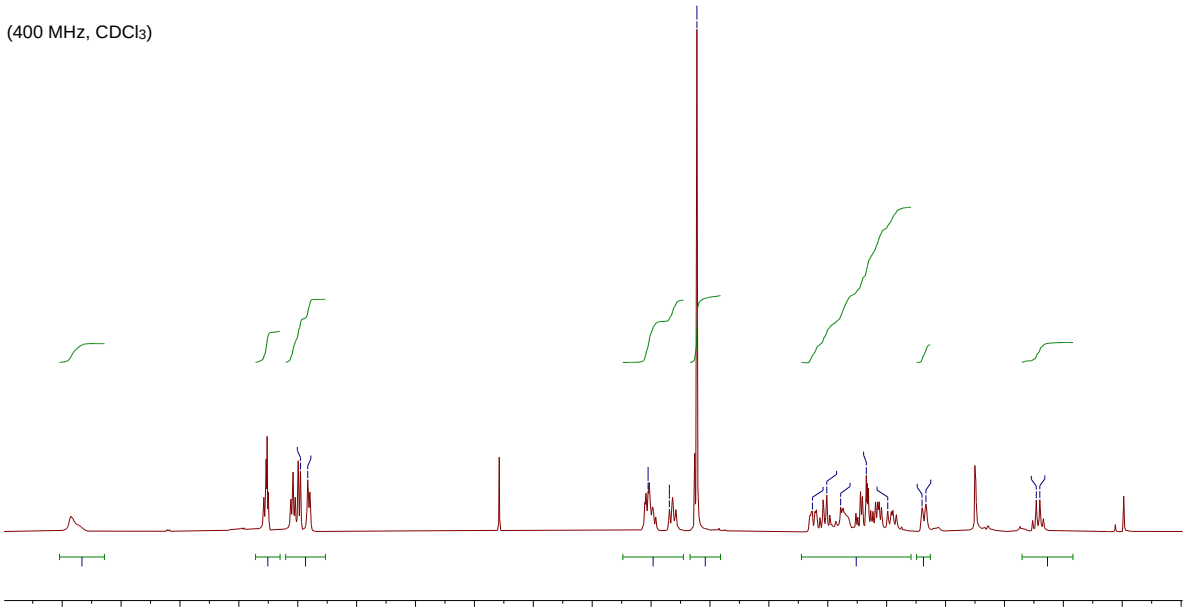
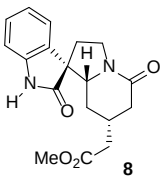
(400 MHz, $CDCl_3$)





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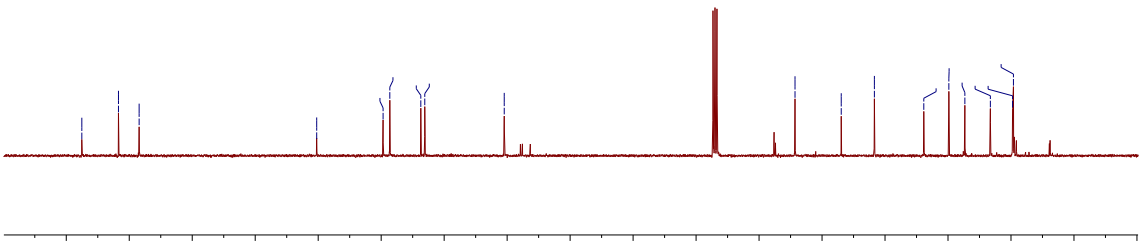
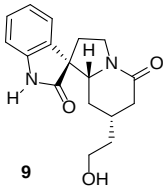
(100.6 MHz, $CDCl_3$)





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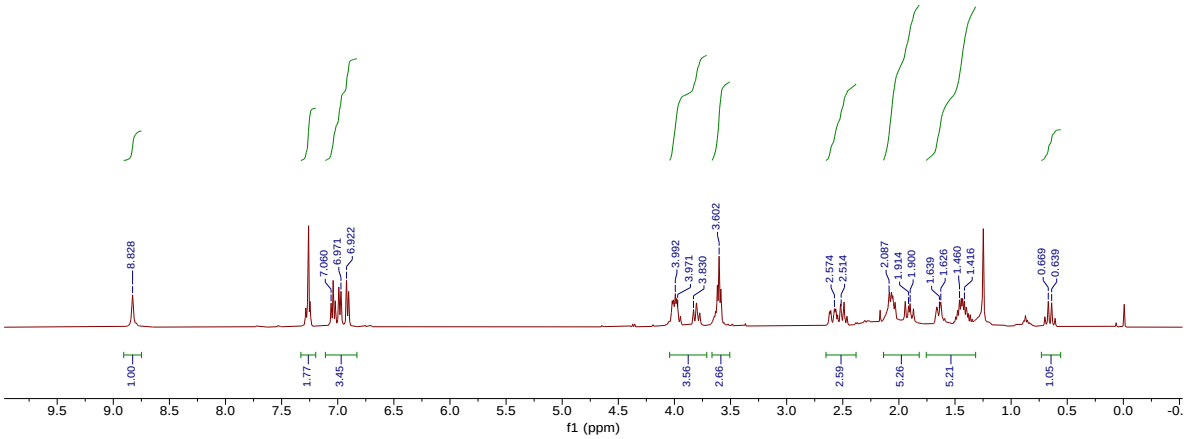
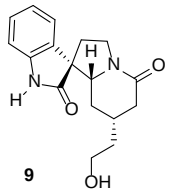
(400 MHz, $CDCl_3$)





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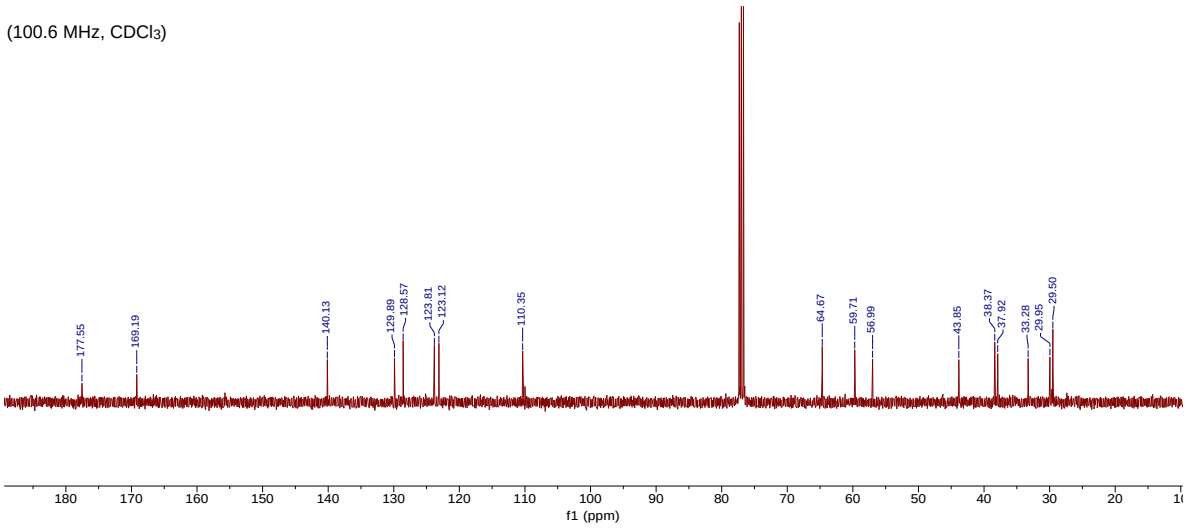
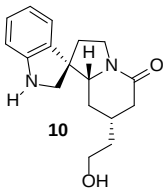
(100.6 MHz, $CDCl_3$)





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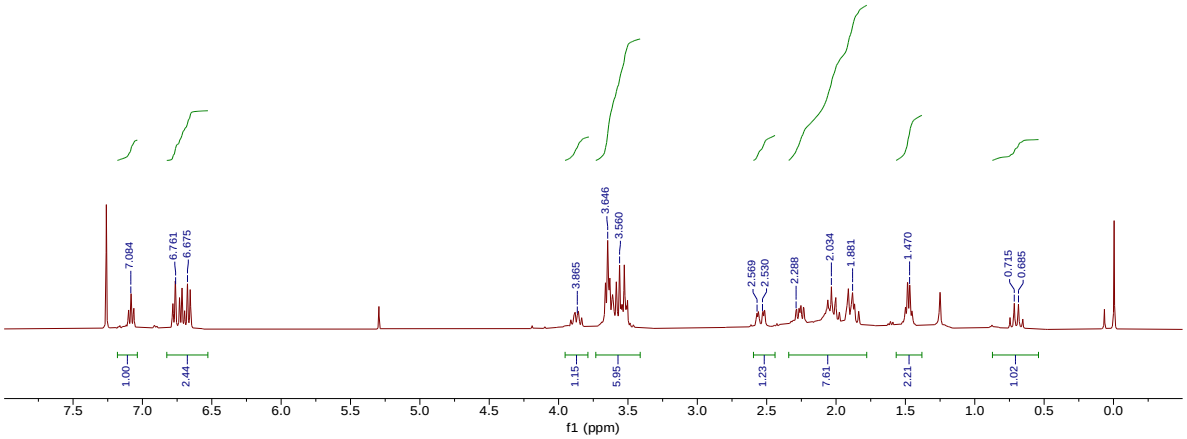
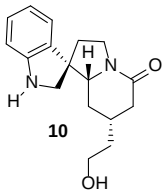
(400 MHz, $CDCl_3$)





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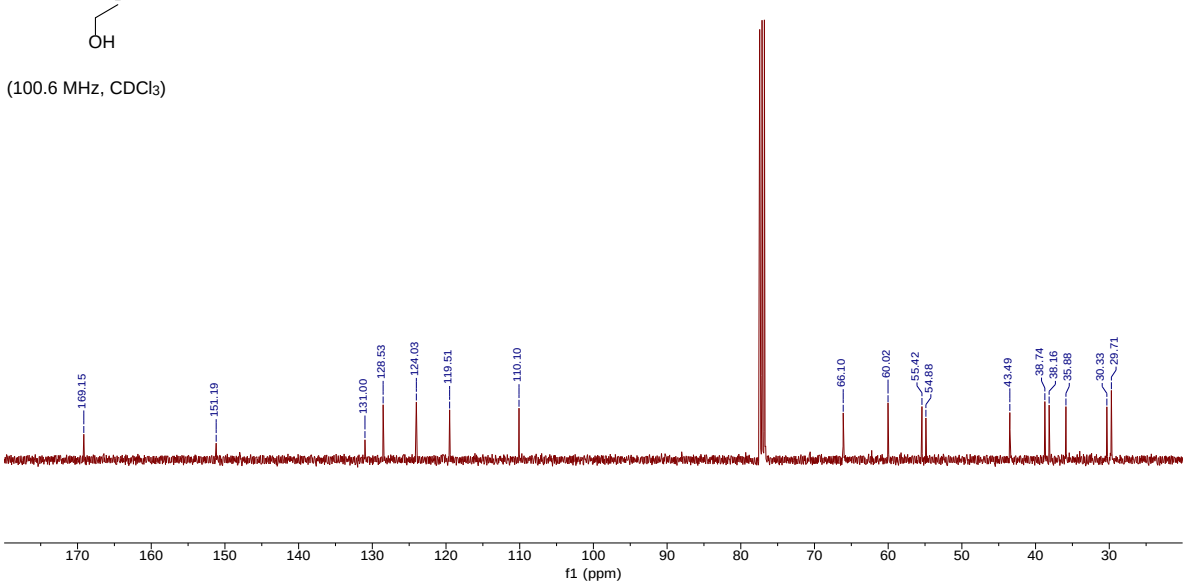
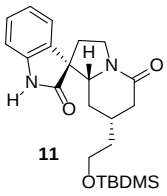
(100.6 MHz, $CDCl_3$)

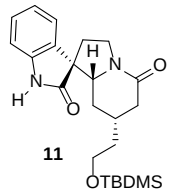




11

OTBDMS

(400 MHz, $CDCl_3$)



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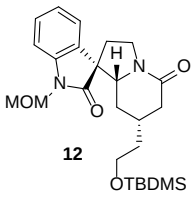
OTBDMS

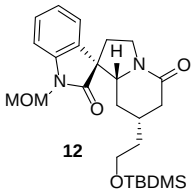
(100.6 MHz, $CDCl_3$)



12

OTBDMS

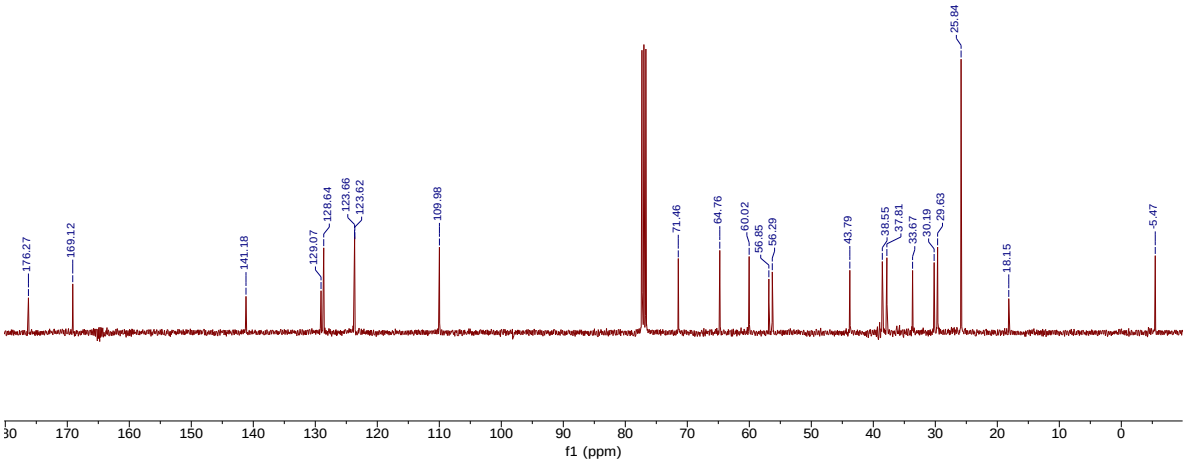
(400 MHz, $CDCl_3$)

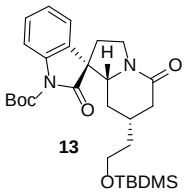


12

OTBDMS

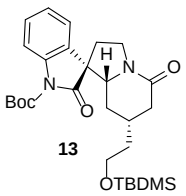
(100.6 MHz, $CDCl_3$)





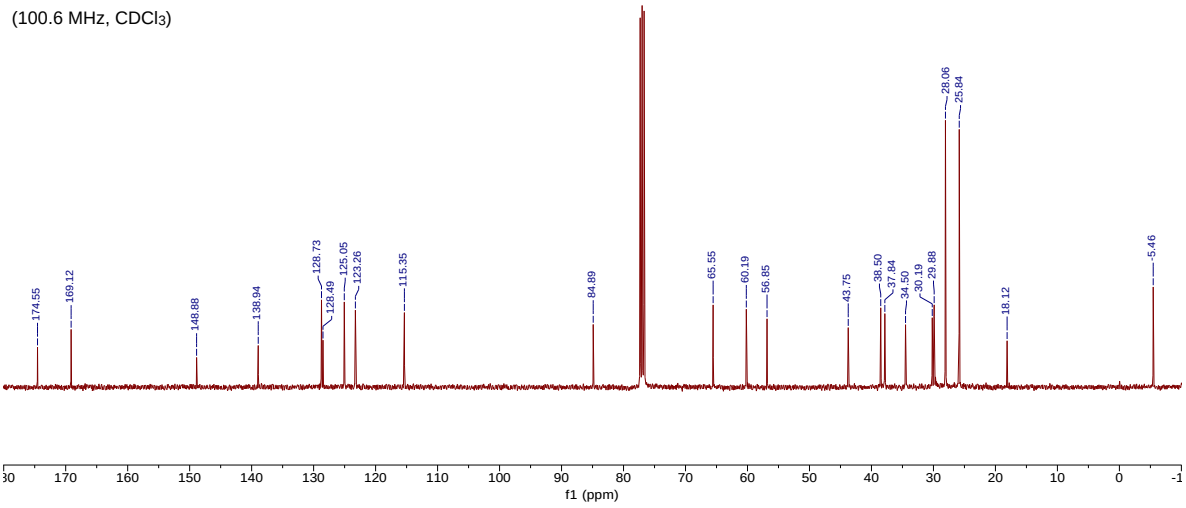
13

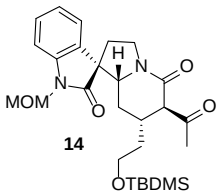
(400 MHz, $CDCl_3$)



13

(100.6 MHz, $CDCl_3$)





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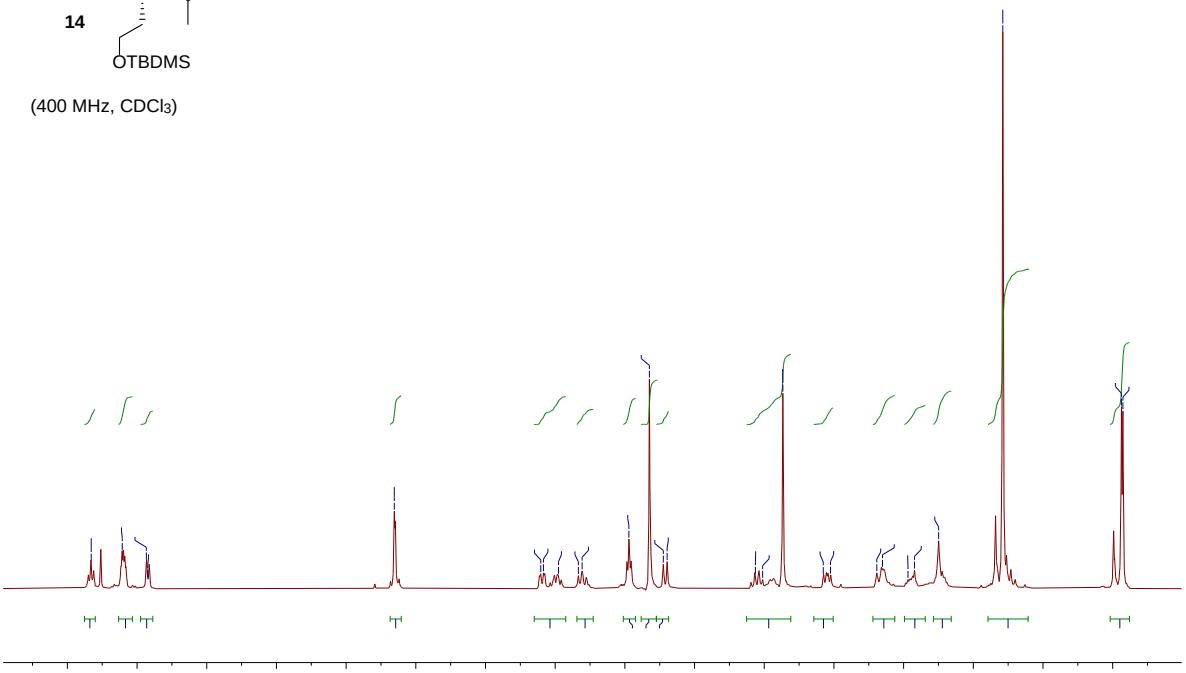
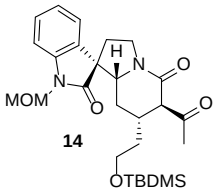
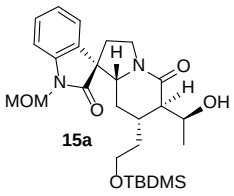
(400 MHz, $CDCl_3$)





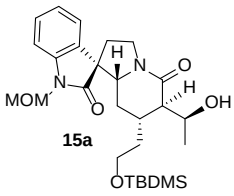
14

(100.6 MHz, $CDCl_3$)



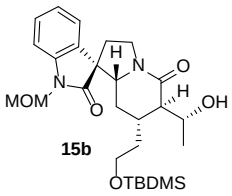
15a

(400 MHz, $CDCl_3$)



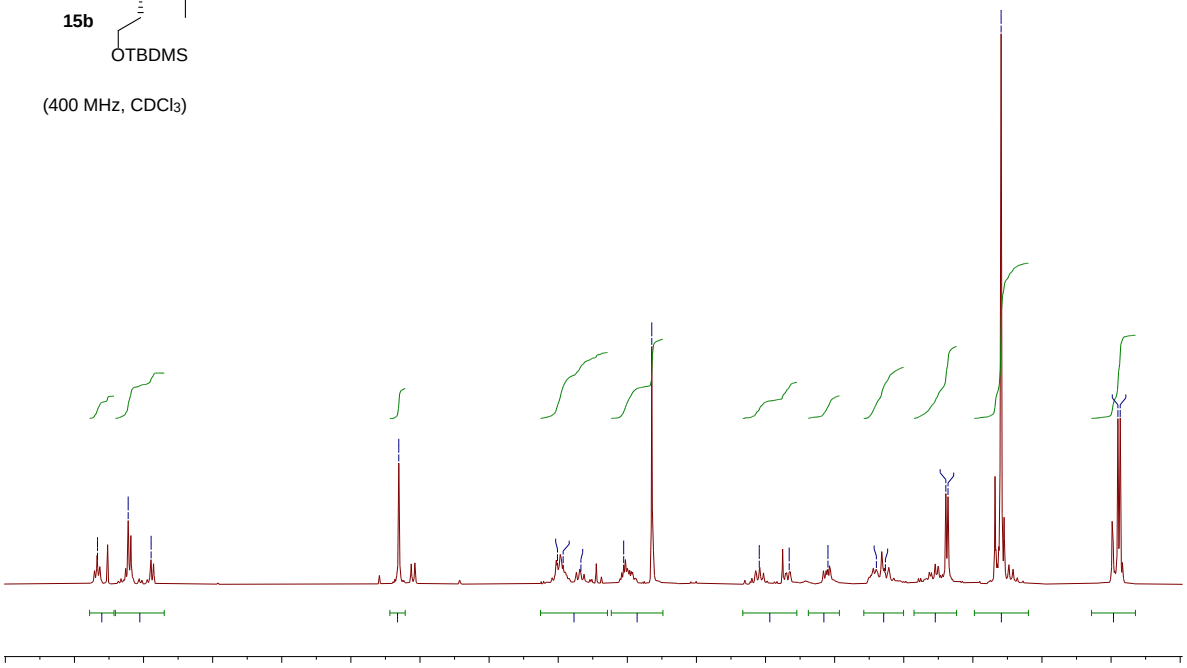
15a

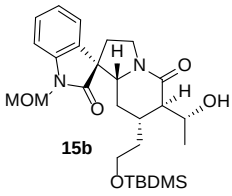
(100.6 MHz, $CDCl_3$)



15b

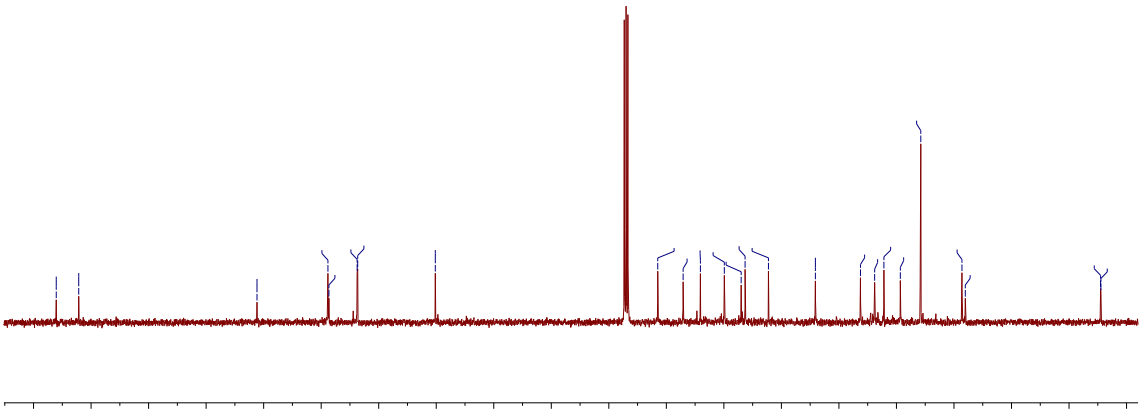
(400 MHz, $CDCl_3$)

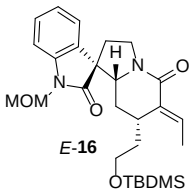




15b

(100.6 MHz, $CDCl_3$)

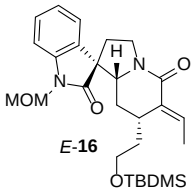




E-**16**

OTBDMS

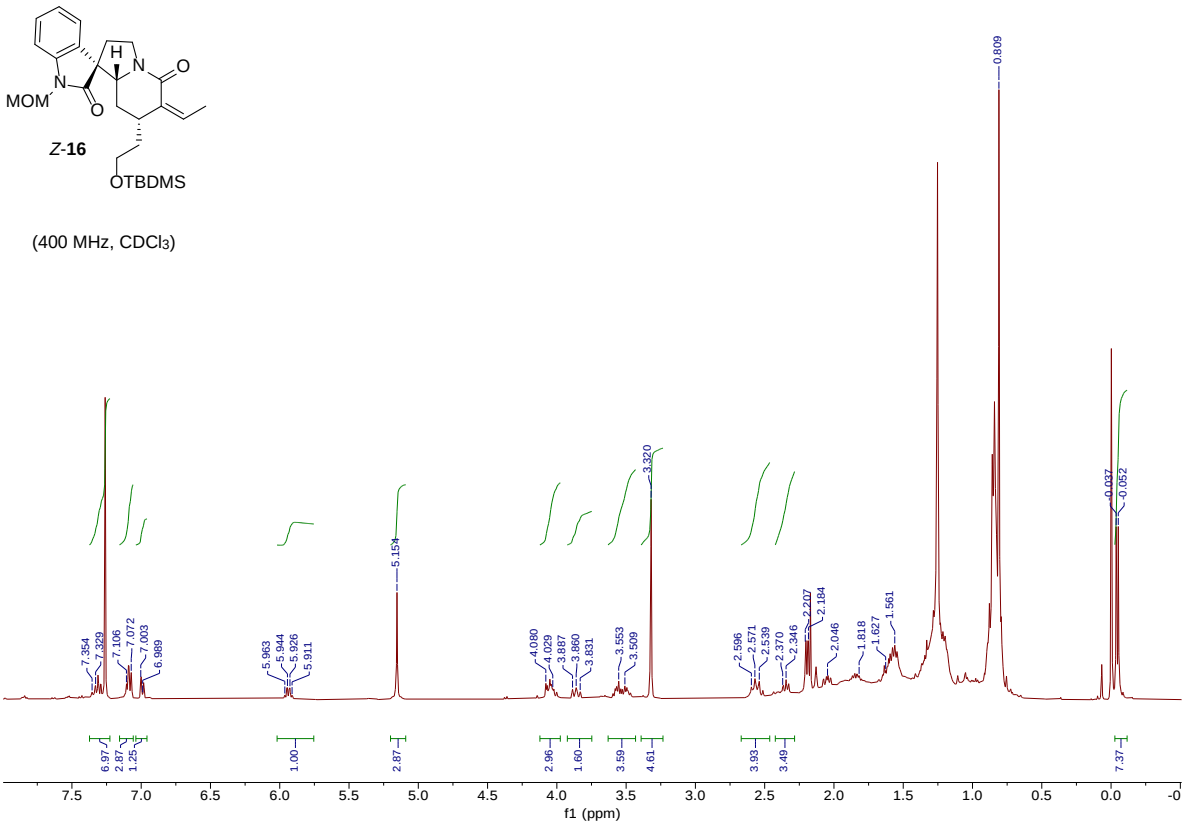
(500 MHz, $CDCl_3$)

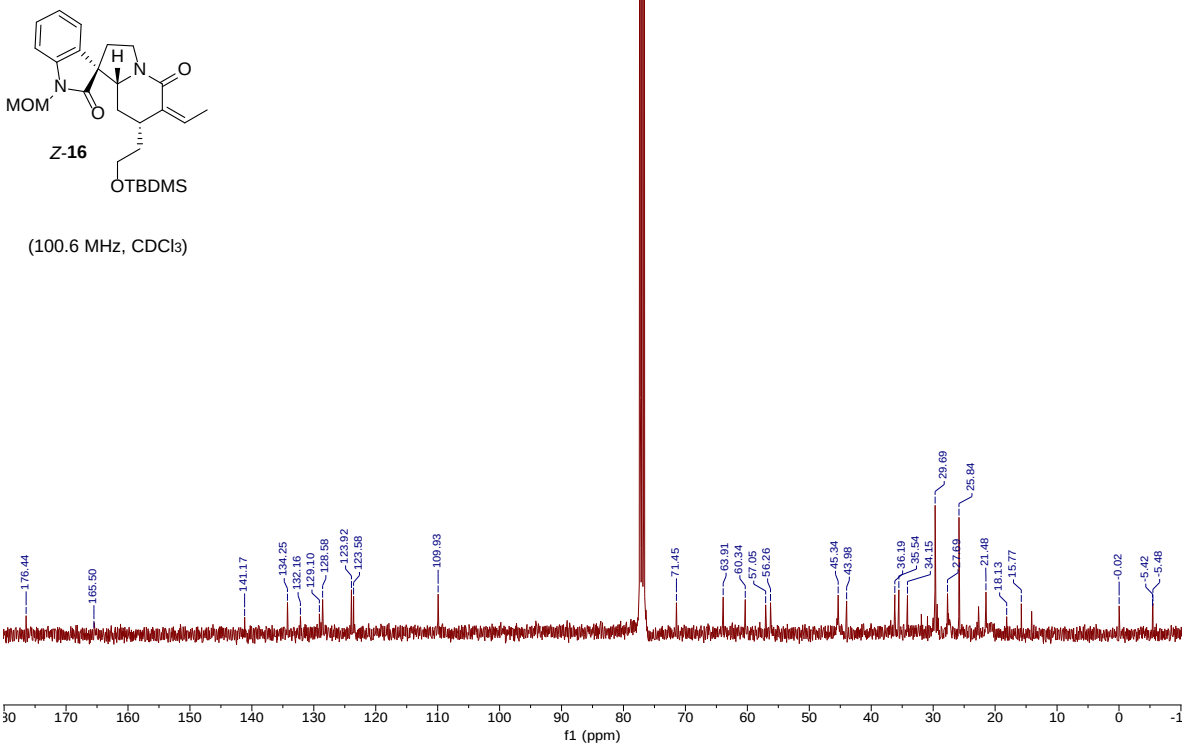


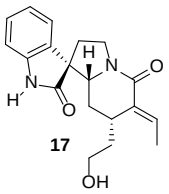
E-**16**

OTBDMS

125 MHz, $CDCl_3$)

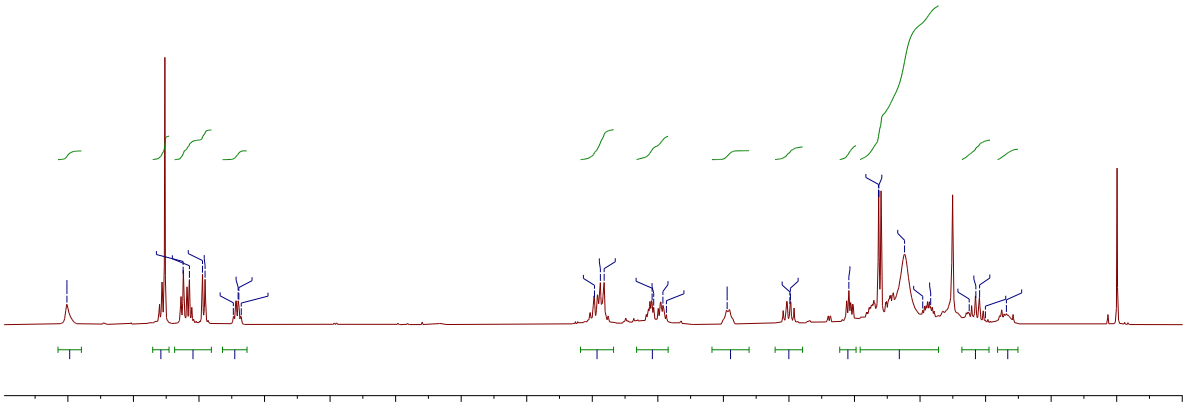

MOM
H
N
N
O
O
OTBDMS
Z-16
(400 MHz, CDCl3)
f1 (ppm)

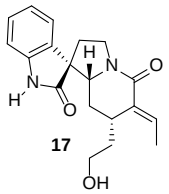

MOM
H
N
N
O
O
OTBDMS
Z-16
(100.6 MHz, CDCl3)
f1 (ppm)



17

(400 MHz, $CDCl_3$)





17

(100.6 MHz, $CDCl_3$)

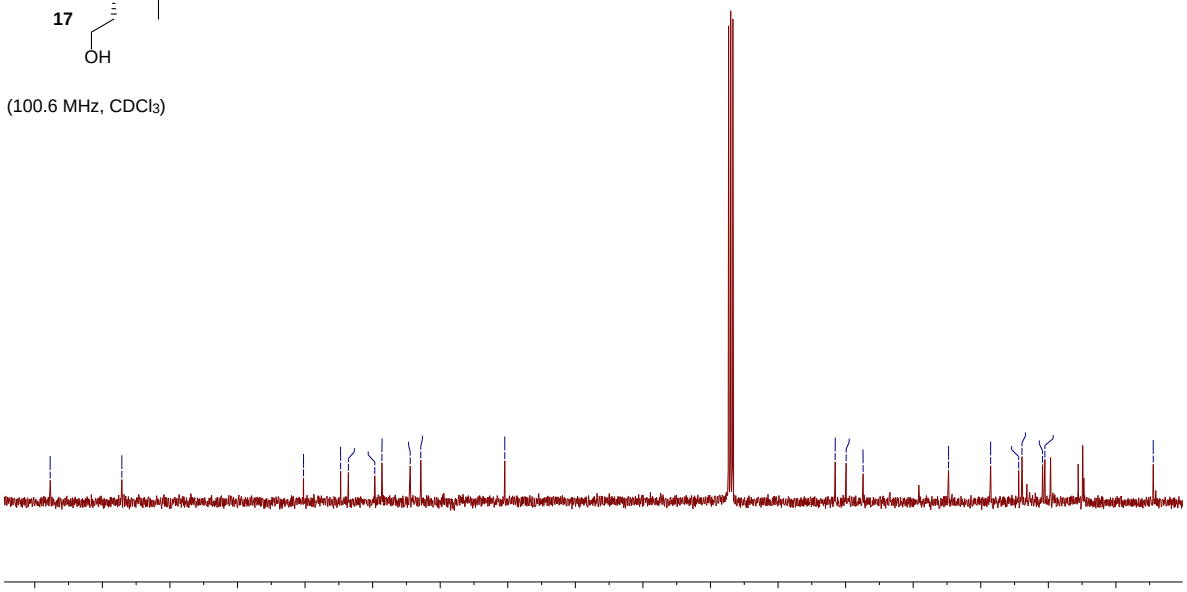
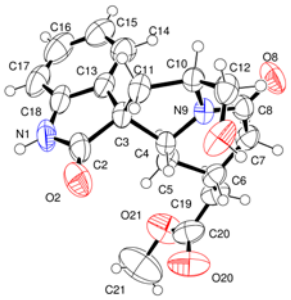


Table 1. Crystal data and structure refinement for **4**.



Identification code	Jb153	
Empirical formula	C19 H22 N2 O5	
Formula weight	358.38	
Temperature	294(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 6.6025(3) Å	α= 90°.
	b = 15.2412(6) Å	β= 90°.
	c = 17.8186(7) Å	γ = 90°.
Volume	1793.09(13) $Å^3$	
Z	4	
Density (calculated)	1.328 Mg/m^3	
Absorption coefficient	0.097 mm^{-1}	
F(000)	760	
Crystal size	0.280 x 0.180 x 0.150 mm^3	
Theta range for data collection	1.758 to 28.390°.	
Index ranges	-8<=h<=8, -20<=k<=20, -23<=l<=23	
Reflections collected	52832	
Independent reflections	4481 [R(int) = 0.0708]	
Completeness to theta = 25.242°	100.0 %	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4481 / 0 / 237	
Goodness-of-fit on F^2	1.013	
Final R indices [I>2sigma(I)]	R1 = 0.0525, wR2 = 0.1286	
R indices (all data)	R1 = 0.0823, wR2 = 0.1482	
Absolute structure parameter	-0.2(6)	
Largest diff. peak and hole	0.535 and -0.141 $e.Å^{-3}$	

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

	x	y	z	U(eq)
O(2)	3488(5)	4488(2)	7505(2)	82(1)
O(8)	9293(4)	3079(2)	4872(1)	76(1)
O(12)	5846(5)	2119(2)	6502(1)	71(1)
O(20)	826(5)	5303(3)	4440(2)	113(1)
O(21)	2376(5)	6549(2)	4207(2)	102(1)
N(1)	5352(6)	5768(2)	7481(2)	70(1)
N(9)	7348(4)	3712(2)	5747(1)	44(1)
C(2)	4936(7)	4923(3)	7303(2)	59(1)
C(3)	6638(5)	4602(2)	6782(2)	46(1)
C(4)	5776(5)	4308(2)	6013(2)	42(1)
C(5)	5299(6)	5015(2)	5441(2)	49(1)
C(6)	4924(5)	4596(2)	4679(2)	50(1)
C(7)	6822(5)	4112(2)	4436(2)	55(1)
C(8)	7895(5)	3592(2)	5030(2)	51(1)
C(10)	8383(5)	3268(2)	6368(2)	48(1)
C(11)	7613(6)	3759(2)	7065(2)	53(1)
C(12)	7919(6)	2294(2)	6383(2)	59(1)
C(13)	8001(5)	5389(2)	6737(2)	50(1)
C(14)	9801(6)	5530(2)	6368(2)	64(1)
C(15)	10702(7)	6359(3)	6398(3)	77(1)
C(16)	9780(9)	7023(3)	6795(3)	88(2)
C(17)	8001(9)	6895(3)	7184(3)	80(1)
C(18)	7136(7)	6063(2)	7155(2)	61(1)
C(19)	4297(6)	5283(3)	4092(2)	65(1)
C(20)	2316(7)	5699(3)	4261(2)	71(1)
C(21)	459(11)	7021(5)	4313(4)	149(3)

Table 3. Bond lengths [Å] and angles [°] for **4**.

O(2)-C(2)	1.218(5)
O(8)-C(8)	1.242(4)
O(12)-C(12)	1.411(5)
O(20)-C(20)	1.198(5)
O(21)-C(20)	1.299(6)
O(21)-C(21)	1.468(7)
N(1)-C(2)	1.355(5)
N(1)-C(18)	1.388(6)
N(9)-C(8)	1.340(4)
N(9)-C(4)	1.459(4)
N(9)-C(10)	1.467(4)
C(2)-C(3)	1.537(5)
C(3)-C(13)	1.501(5)
C(3)-C(11)	1.523(4)
C(3)-C(4)	1.551(4)
C(4)-C(5)	1.516(4)
C(5)-C(6)	1.522(4)
C(6)-C(7)	1.516(5)
C(6)-C(19)	1.536(5)
C(7)-C(8)	1.500(5)
C(10)-C(12)	1.515(5)
C(10)-C(11)	1.535(4)
C(13)-C(14)	1.375(5)
C(13)-C(18)	1.391(5)
C(14)-C(15)	1.398(5)
C(15)-C(16)	1.375(7)
C(16)-C(17)	1.378(7)
C(17)-C(18)	1.392(6)
C(19)-C(20)	1.485(6)
C(20)-O(21)-C(21)	116.9(4)
C(2)-N(1)-C(18)	112.4(3)
C(8)-N(9)-C(4)	125.9(3)
C(8)-N(9)-C(10)	122.1(3)
C(4)-N(9)-C(10)	111.9(2)
O(2)-C(2)-N(1)	127.4(4)
O(2)-C(2)-C(3)	125.4(3)

N(1)-C(2)-C(3)	107.2(3)
C(13)-C(3)-C(11)	116.0(3)
C(13)-C(3)-C(2)	102.5(3)
C(11)-C(3)-C(2)	112.2(3)
C(13)-C(3)-C(4)	113.8(2)
C(11)-C(3)-C(4)	101.7(2)
C(2)-C(3)-C(4)	110.9(3)
N(9)-C(4)-C(5)	111.8(2)
N(9)-C(4)-C(3)	101.9(2)
C(5)-C(4)-C(3)	117.7(2)
C(4)-C(5)-C(6)	109.6(3)
C(7)-C(6)-C(5)	108.9(3)
C(7)-C(6)-C(19)	111.1(3)
C(5)-C(6)-C(19)	111.4(3)
C(8)-C(7)-C(6)	116.5(3)
O(8)-C(8)-N(9)	120.2(3)
O(8)-C(8)-C(7)	121.6(3)
N(9)-C(8)-C(7)	118.2(3)
N(9)-C(10)-C(12)	111.8(3)
N(9)-C(10)-C(11)	103.4(2)
C(12)-C(10)-C(11)	113.4(3)
C(3)-C(11)-C(10)	106.5(2)
O(12)-C(12)-C(10)	112.6(3)
C(14)-C(13)-C(18)	119.7(3)
C(14)-C(13)-C(3)	132.0(3)
C(18)-C(13)-C(3)	108.4(3)
C(13)-C(14)-C(15)	119.4(4)
C(16)-C(15)-C(14)	119.7(5)
C(15)-C(16)-C(17)	122.1(4)
C(16)-C(17)-C(18)	117.4(4)
N(1)-C(18)-C(13)	109.5(3)
N(1)-C(18)-C(17)	128.8(4)
C(13)-C(18)-C(17)	121.6(4)
C(20)-C(19)-C(6)	113.0(3)
O(20)-C(20)-O(21)	123.2(5)
O(20)-C(20)-C(19)	124.2(4)
O(21)-C(20)-C(19)	112.6(4)

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

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(2)	88(2)	98(2)	60(2)	-3(2)	26(2)	7(2)
O(8)	80(2)	89(2)	59(2)	-8(1)	23(1)	25(2)
O(12)	104(2)	62(2)	48(1)	13(1)	-15(1)	-31(2)
O(20)	63(2)	127(3)	148(3)	35(3)	-2(2)	-19(2)
O(21)	89(2)	87(2)	129(3)	37(2)	18(2)	6(2)
N(1)	91(3)	69(2)	49(2)	-23(2)	-3(2)	27(2)
N(9)	56(2)	39(1)	37(1)	-4(1)	4(1)	-1(1)
C(2)	75(2)	65(2)	36(2)	-5(1)	3(2)	15(2)
C(3)	59(2)	43(2)	36(2)	-7(1)	-1(1)	4(2)
C(4)	49(2)	40(1)	37(1)	-5(1)	2(1)	-1(1)
C(5)	61(2)	44(2)	43(2)	0(1)	-7(1)	-3(2)
C(6)	54(2)	56(2)	40(2)	3(1)	-3(1)	-14(2)
C(7)	59(2)	71(2)	37(2)	-2(2)	4(1)	-13(2)
C(8)	53(2)	55(2)	45(2)	-8(1)	10(1)	-3(2)
C(10)	50(2)	47(2)	47(2)	-8(1)	-4(2)	5(1)
C(11)	74(2)	43(2)	43(2)	-4(1)	-8(2)	5(2)
C(12)	81(3)	43(2)	52(2)	-4(1)	-14(2)	12(2)
C(13)	64(2)	44(2)	43(2)	-7(1)	-14(2)	5(2)
C(14)	64(2)	51(2)	76(2)	-7(2)	-7(2)	-4(2)
C(15)	81(3)	66(2)	85(3)	1(2)	-20(2)	-17(2)
C(16)	115(4)	53(2)	95(3)	-6(2)	-40(3)	-13(3)
C(17)	114(4)	50(2)	77(3)	-23(2)	-36(3)	13(2)
C(18)	86(3)	51(2)	44(2)	-12(1)	-18(2)	15(2)
C(19)	62(2)	83(3)	50(2)	17(2)	-9(2)	-12(2)
C(20)	63(2)	91(3)	60(2)	24(2)	-15(2)	-16(2)
C(21)	124(5)	152(6)	171(7)	62(5)	36(5)	56(5)

Table 5. Hydrogen bonds for **4** [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(12)-H(12)...O(8)#1	0.82	1.86	2.671(3)	173.0
N(1)-H(1)...O(12)#2	0.86	2.07	2.854(4)	152.0
C(7)-H(7B)...O(20)#3	0.97	2.36	3.206(5)	145.4
C(12)-H(12A)...O(8)	0.97	2.52	3.083(5)	116.9

Symmetry transformations used to generate equivalent atoms:

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