Supporting Information

Synthetic studies of callyspongiolide: Synthesis of macrolactone core of the molecule

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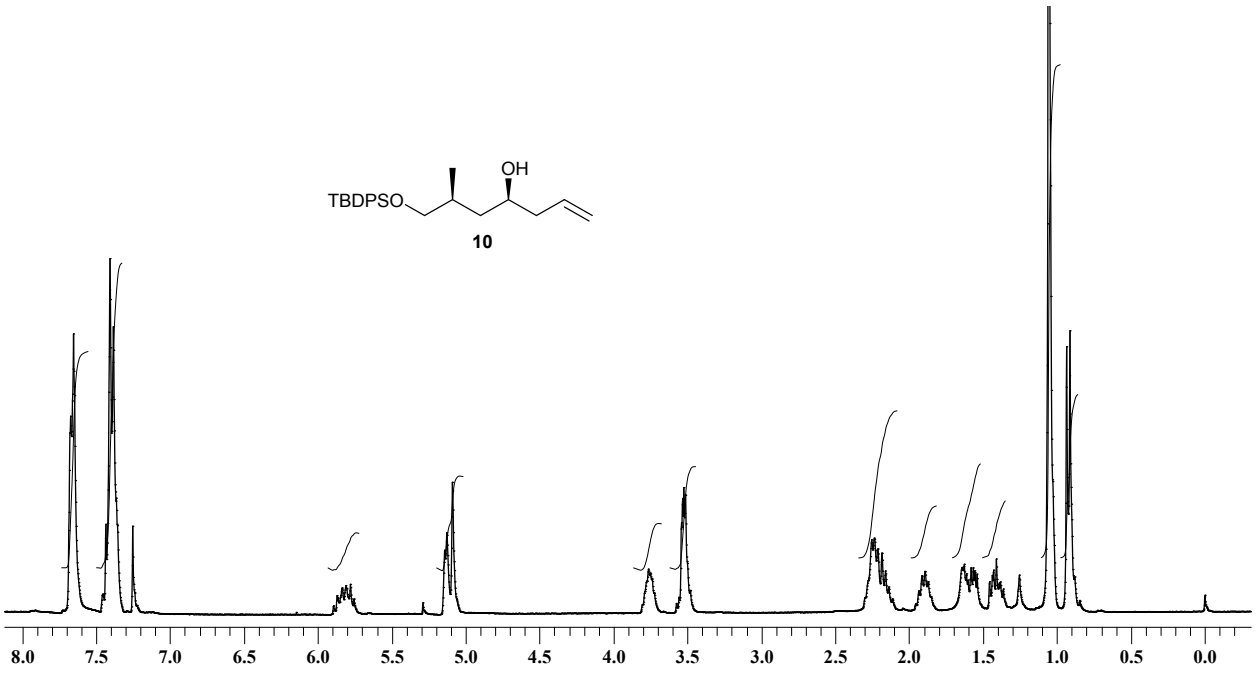
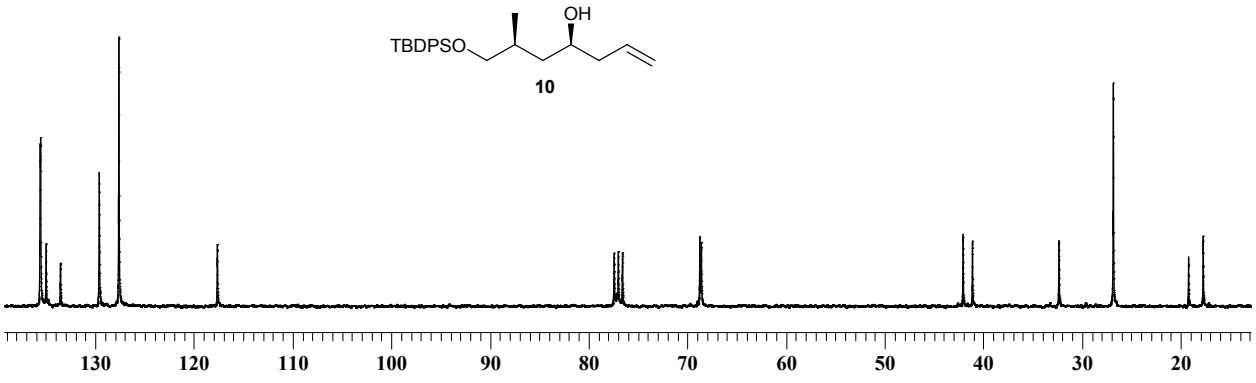
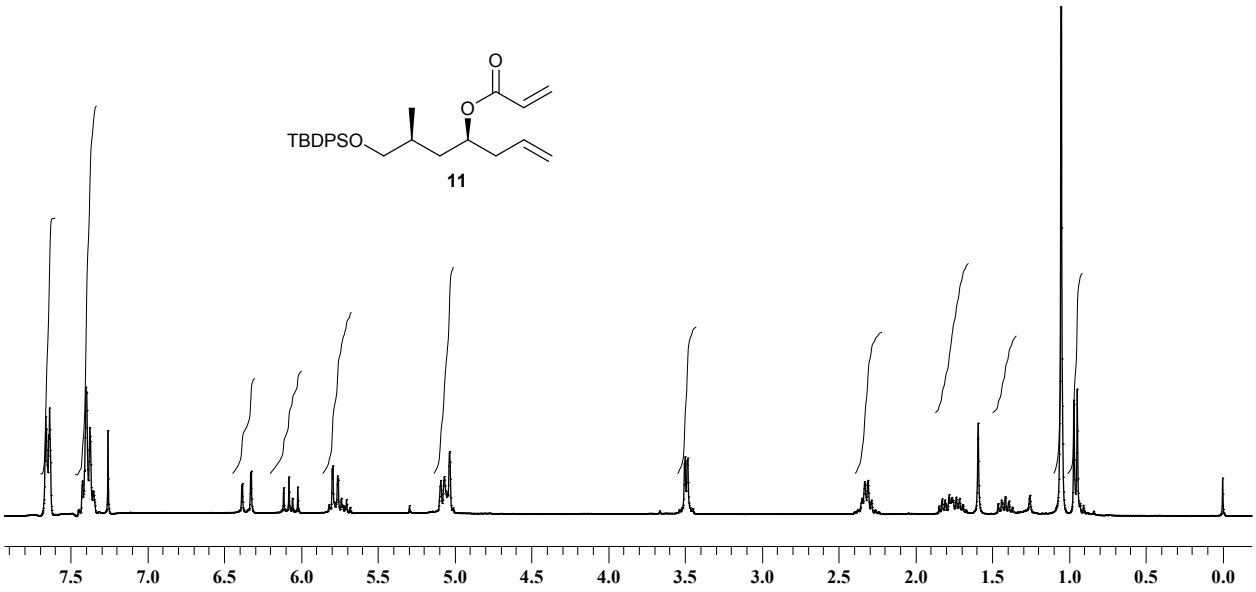


^{1}H NMR SPECTRUM OF COMPOUND 10 (300 MHz, $CDCl_3$)



^{13}C NMR SPECTRUM OF COMPOUND 10 (75 MHz, $CDCl_3$)



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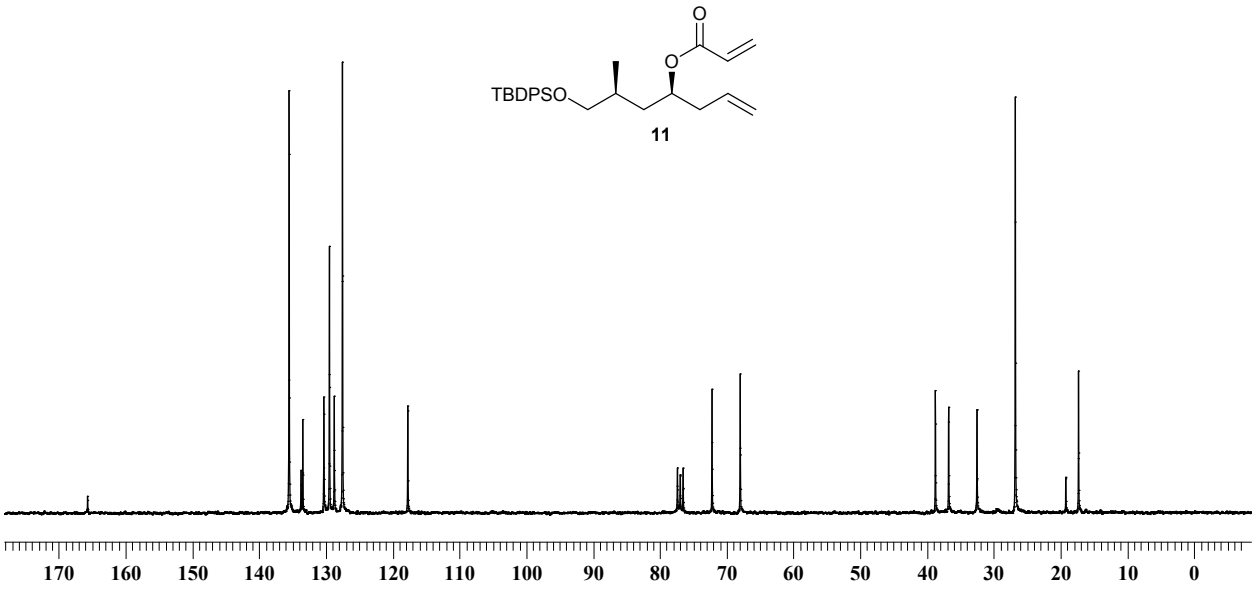

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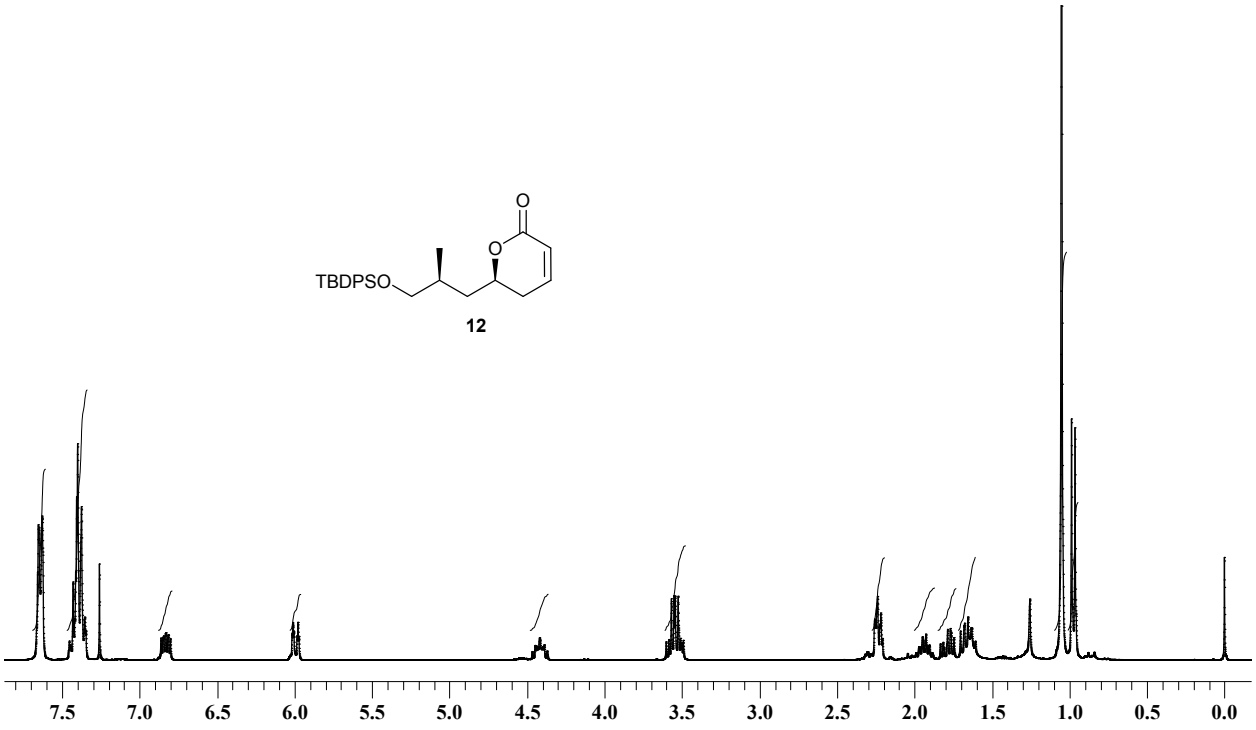

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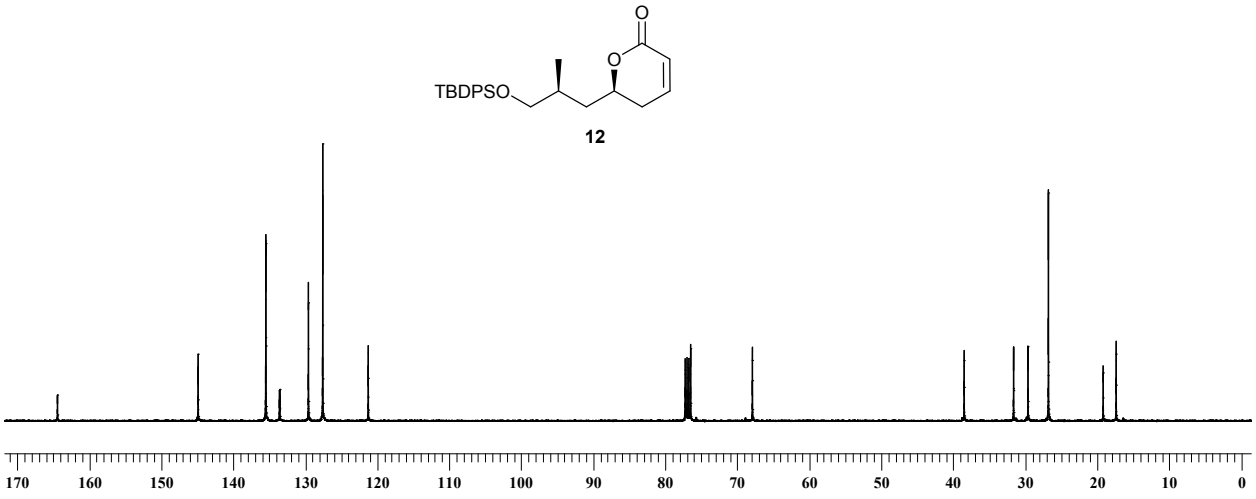

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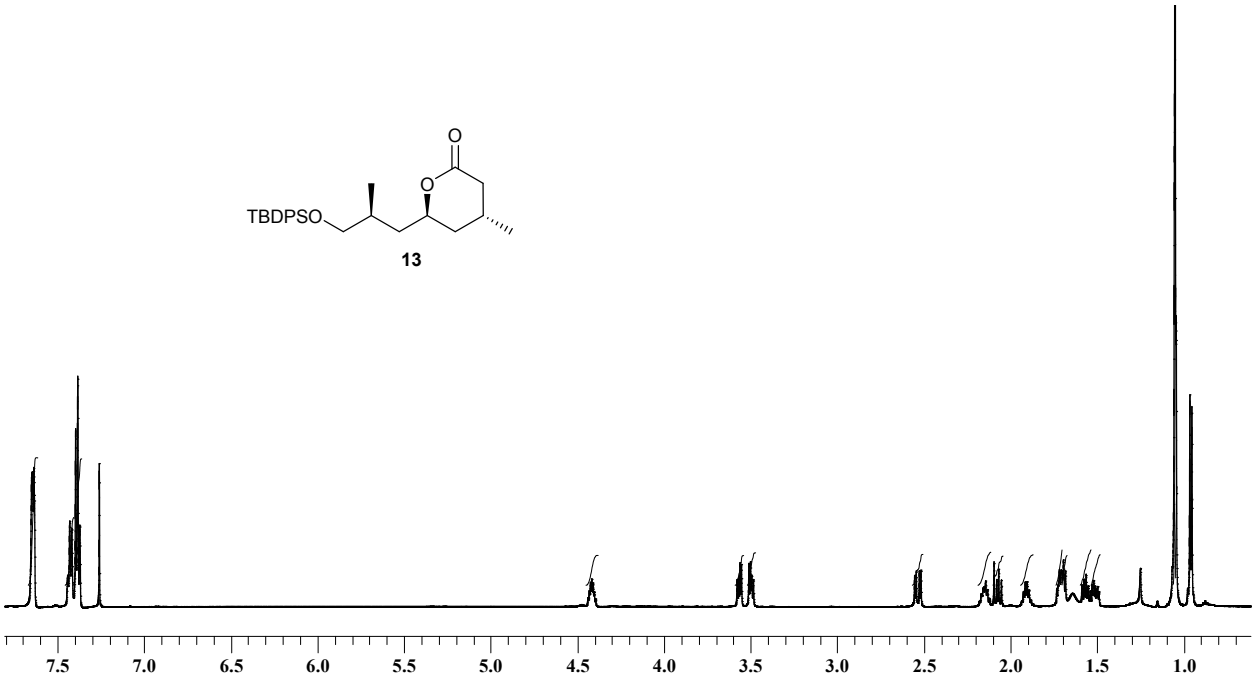

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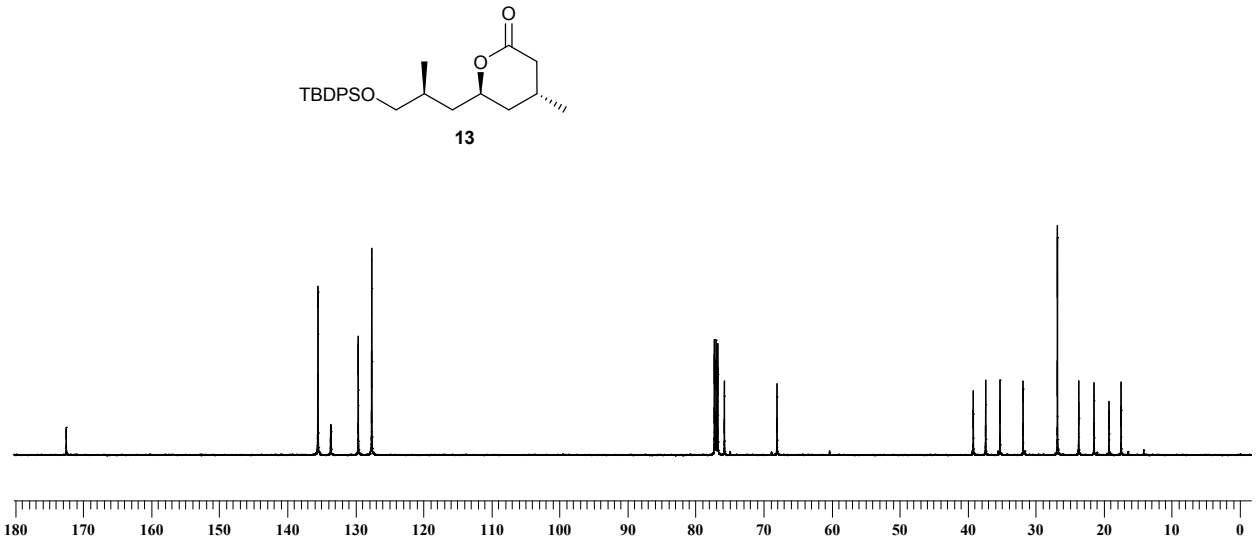
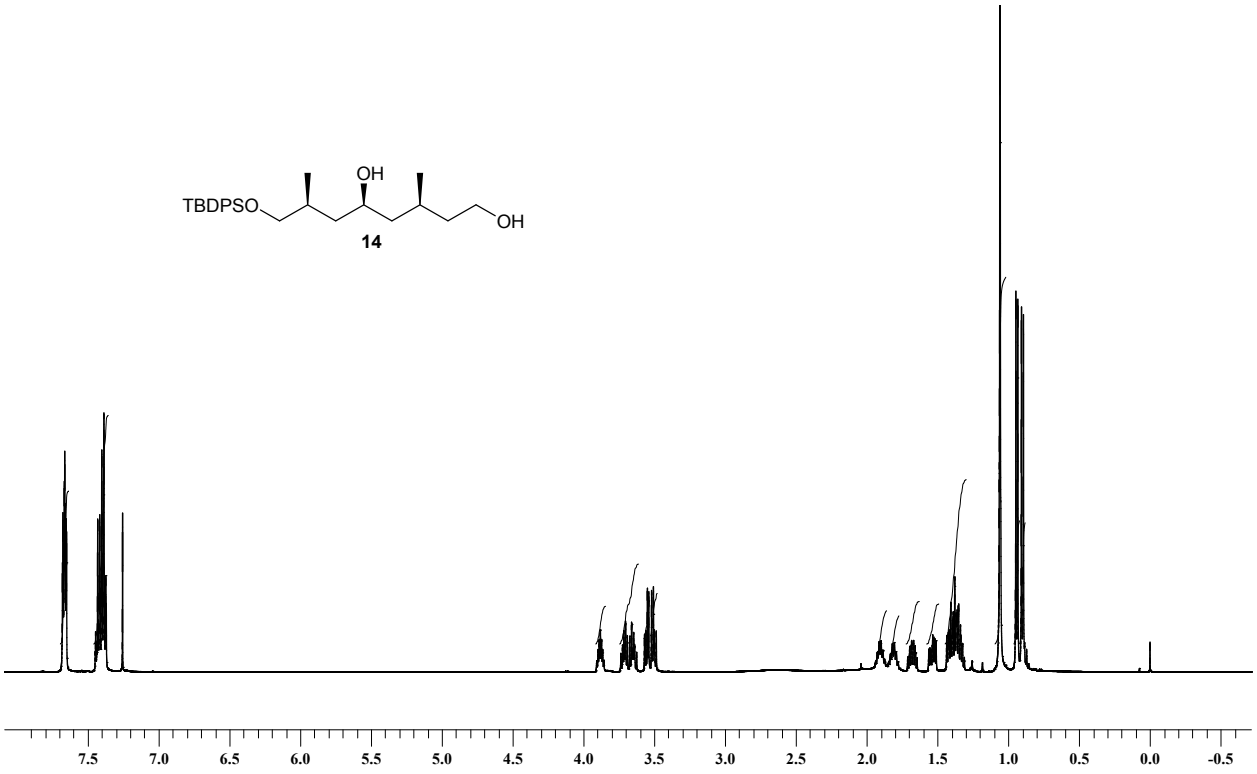


^{13}C NMR SPECTRUM OF COMPOUND 13 (125 MHz, $CDCl_3$)



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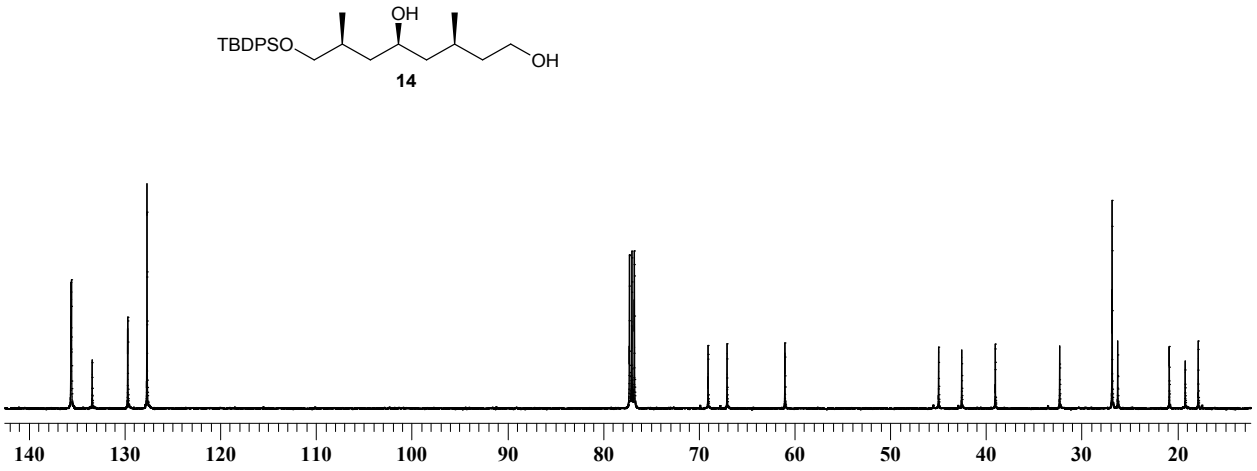

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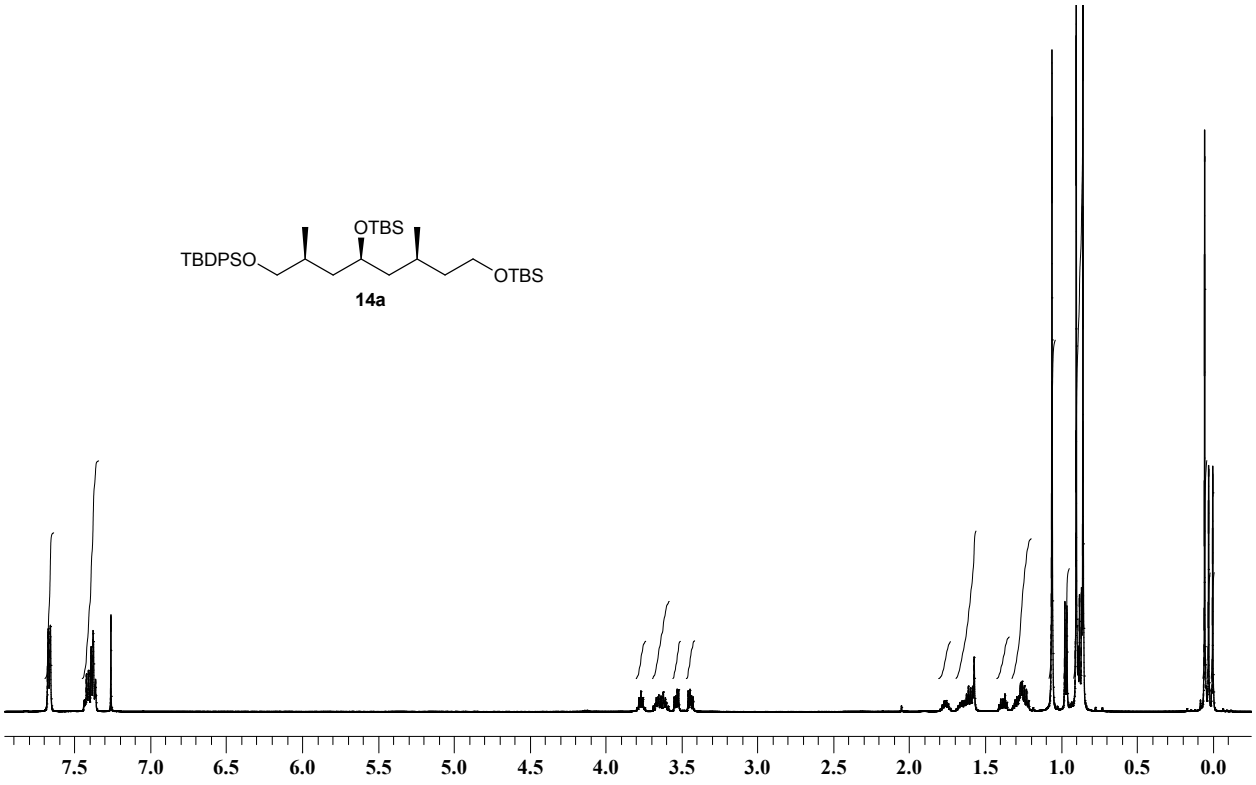

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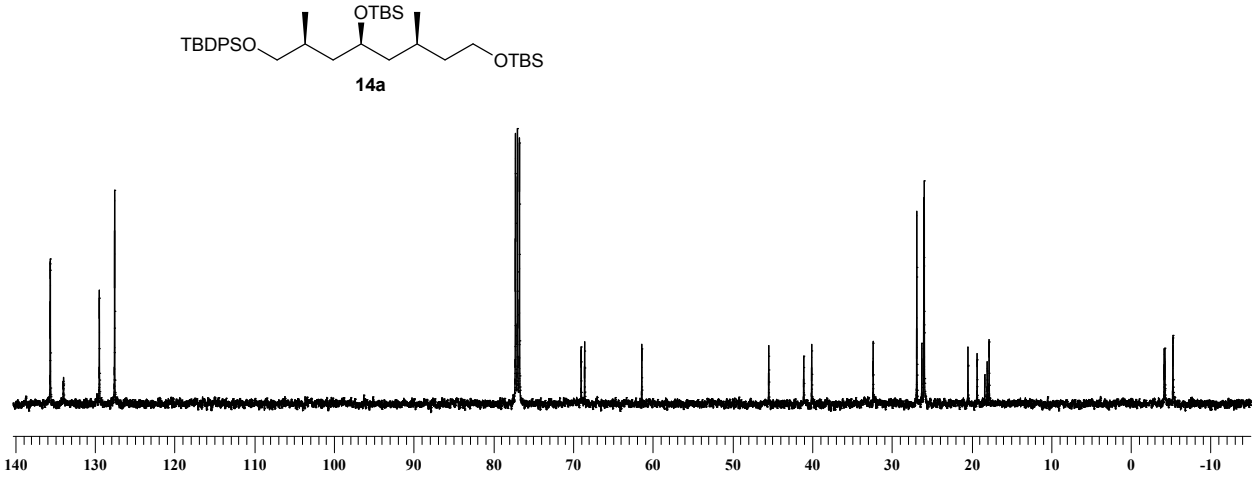
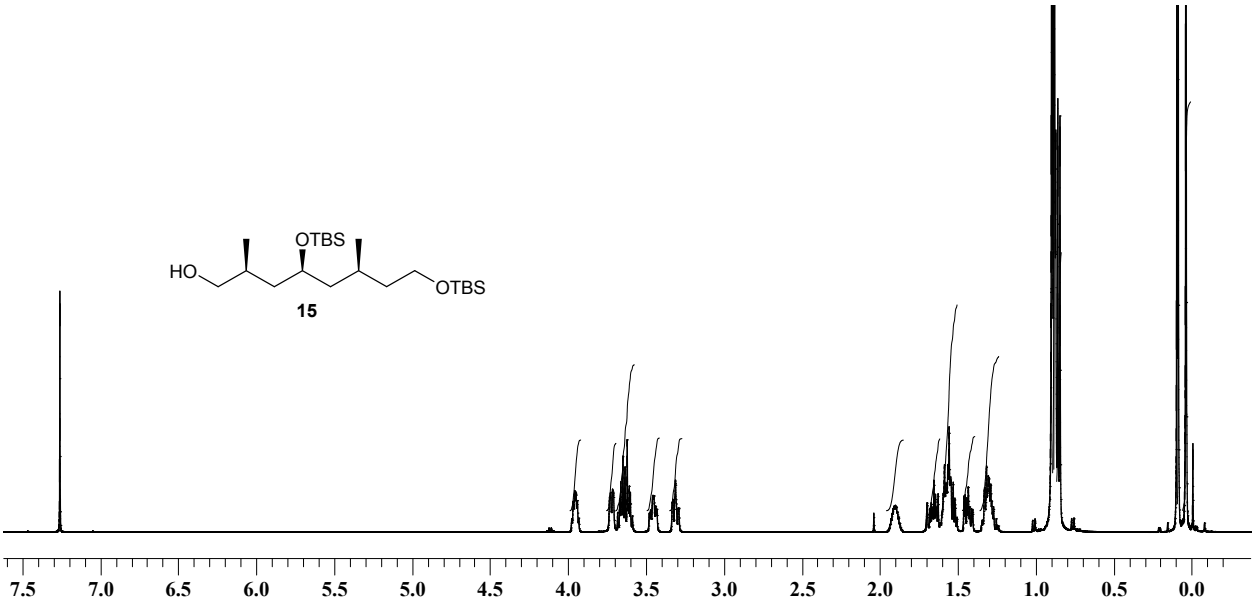


^{13}C NMR SPECTRUM OF COMPOUND 14a (125 MHz, $CDCl_3$)



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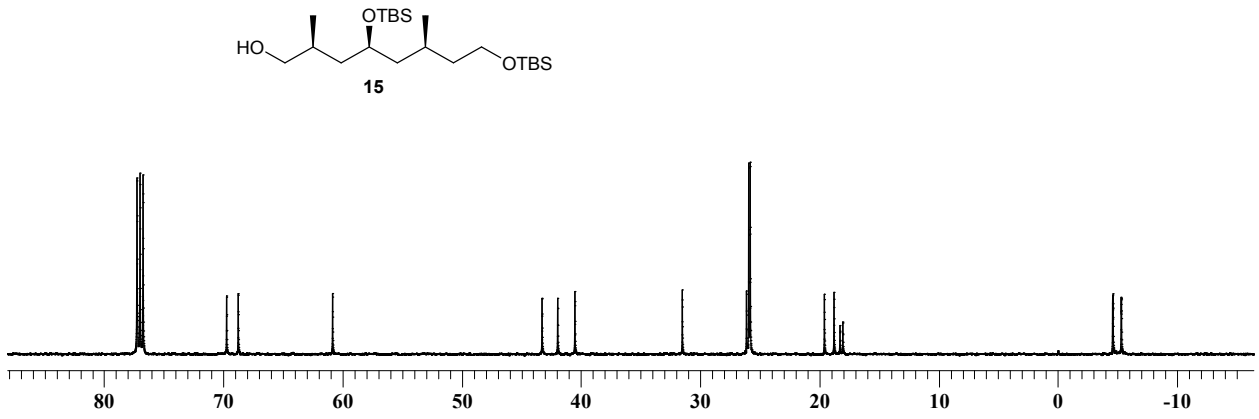

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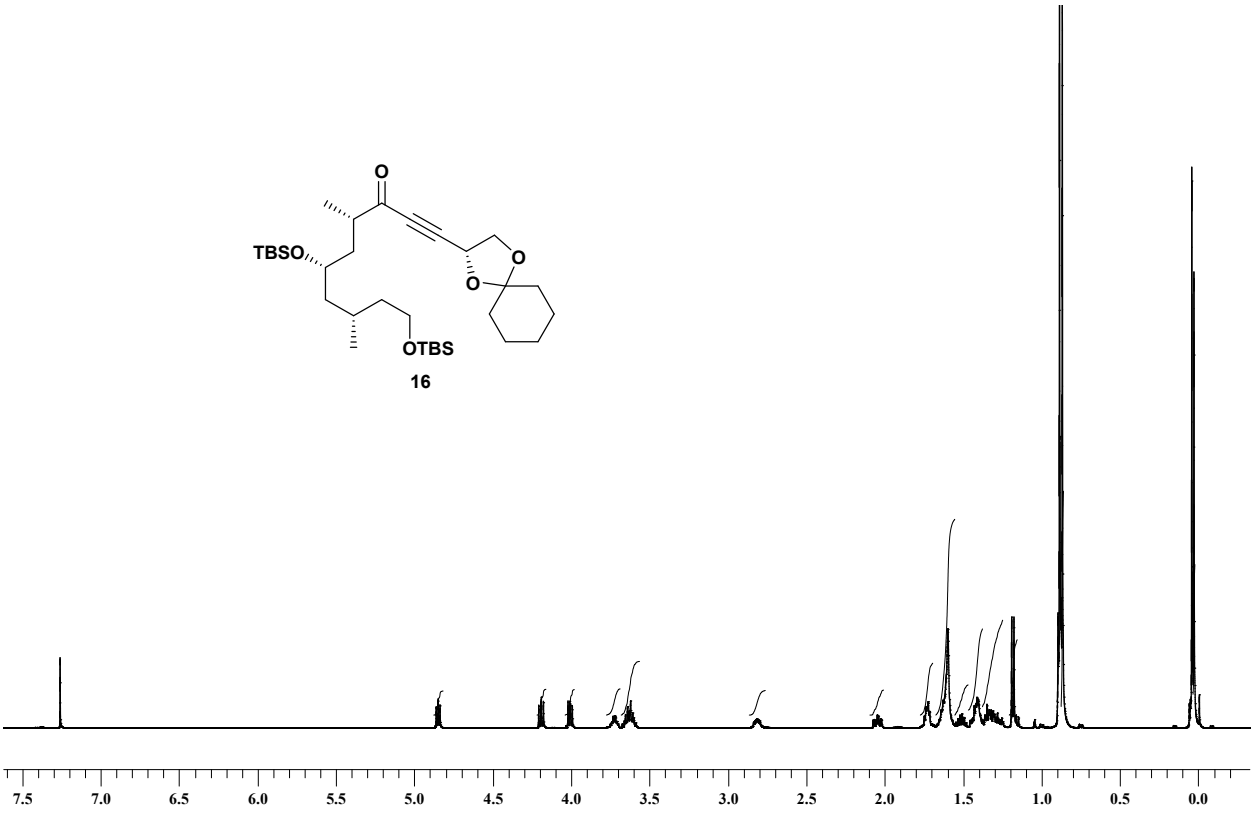

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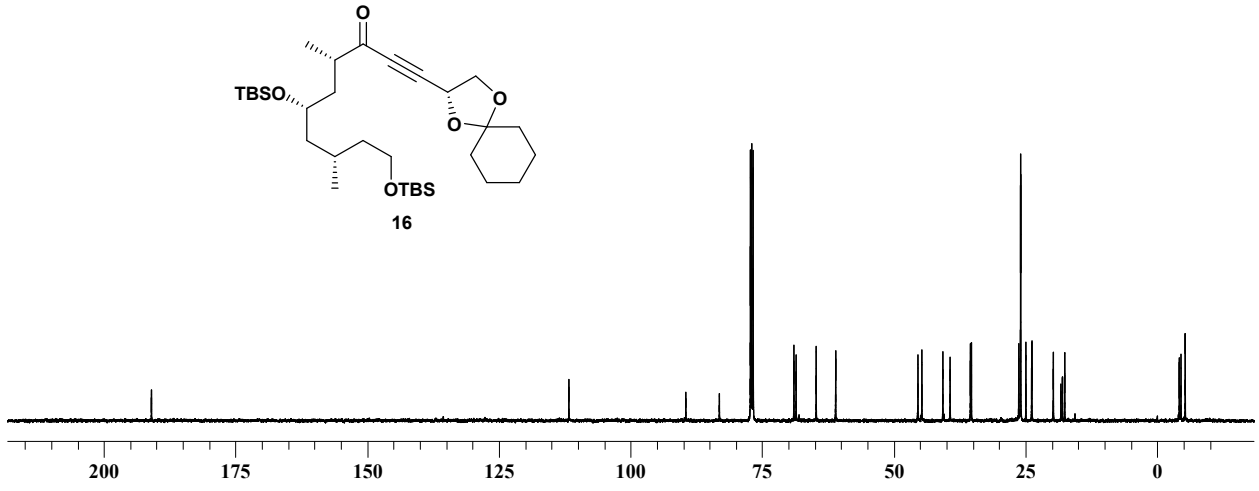

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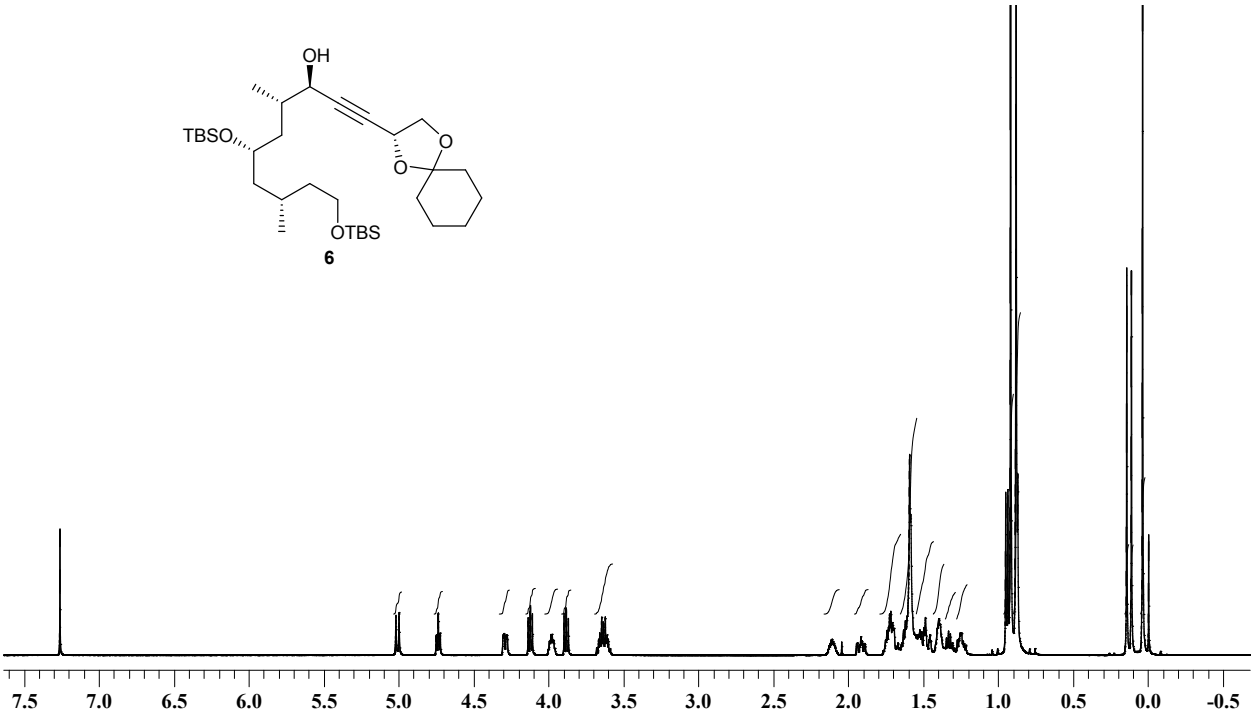

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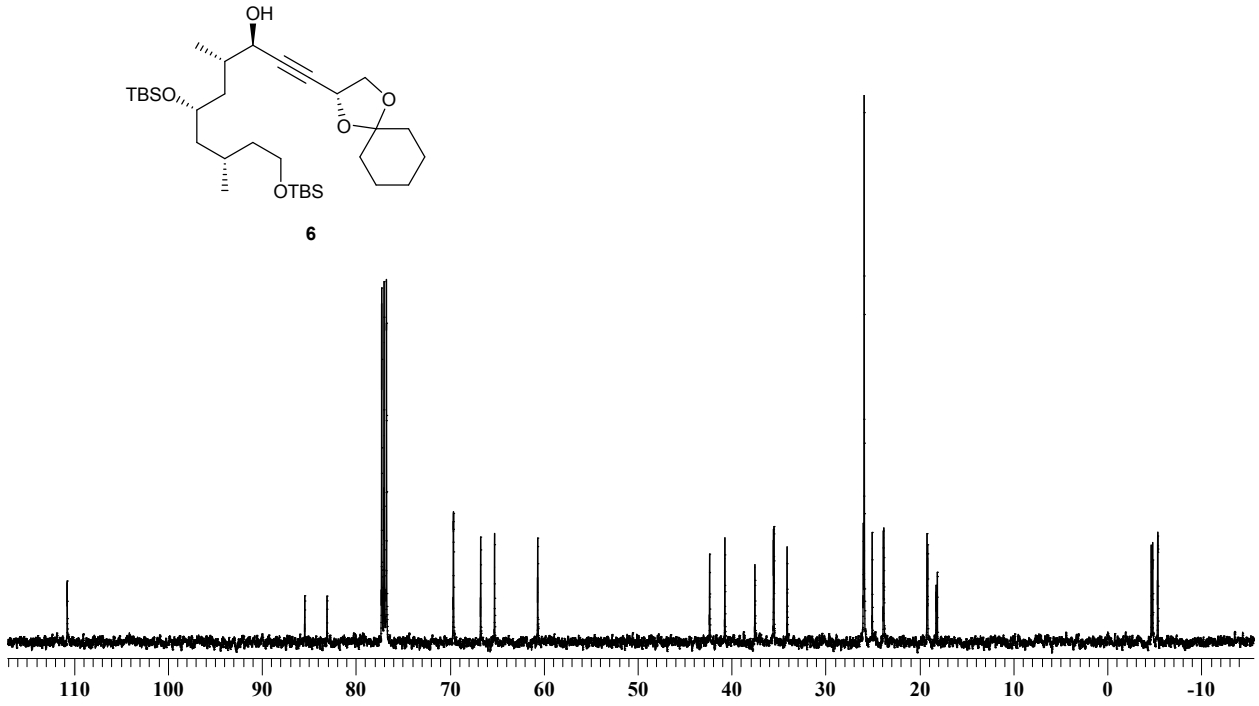

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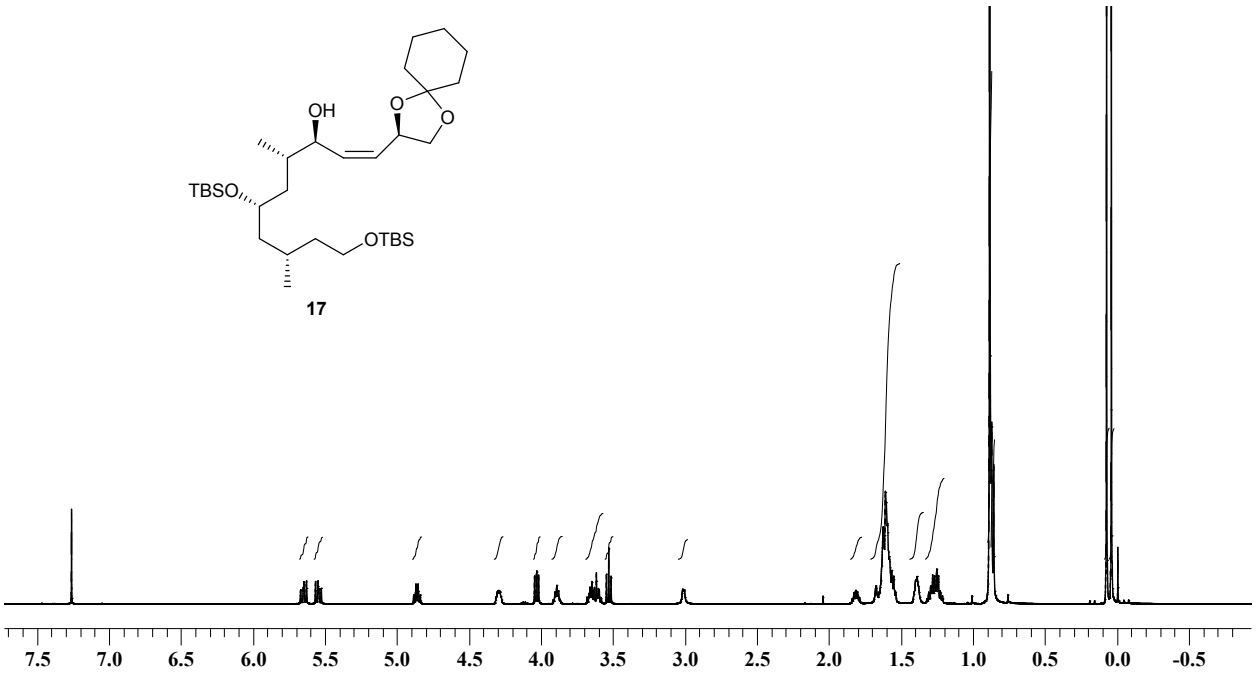

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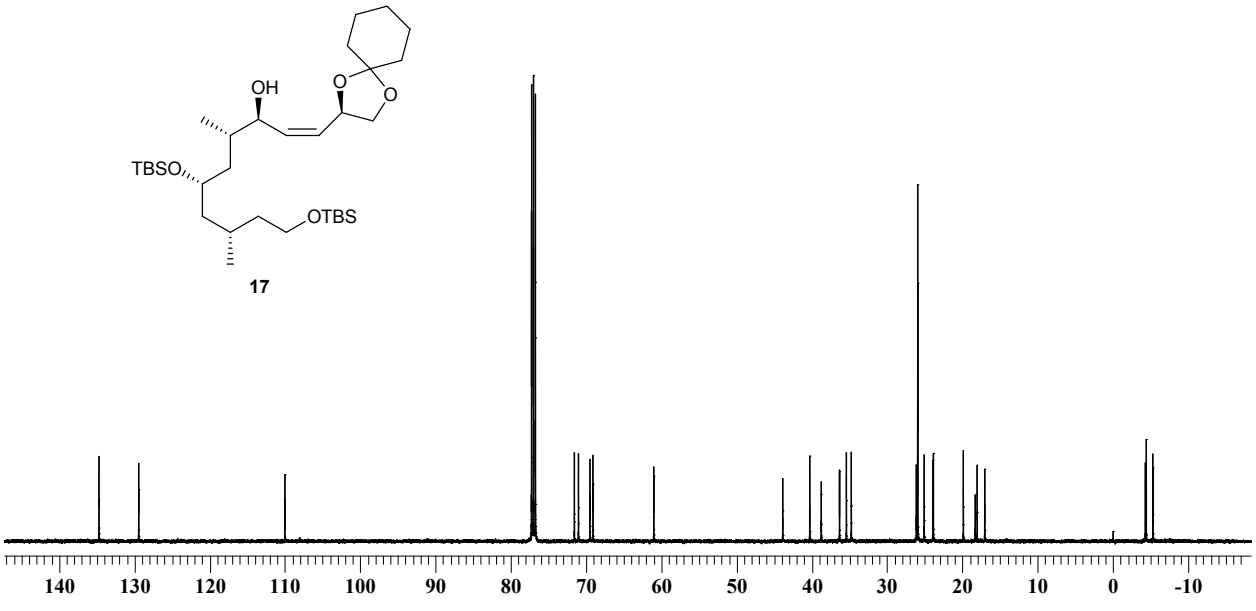

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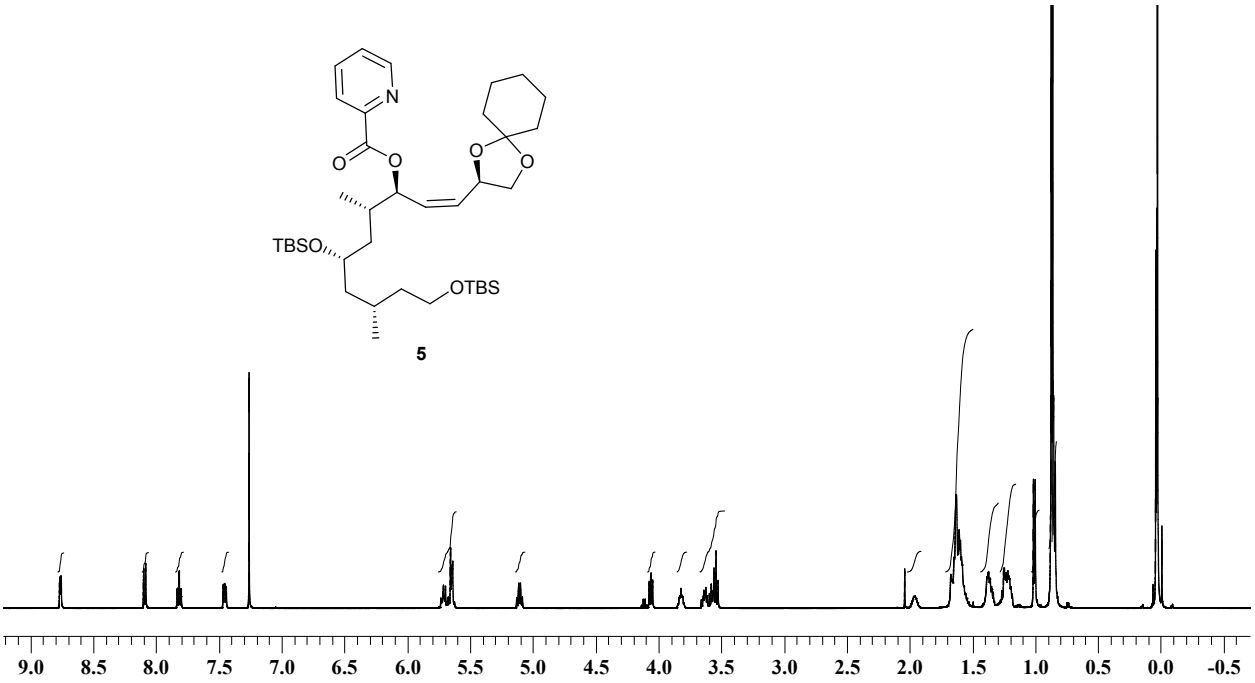

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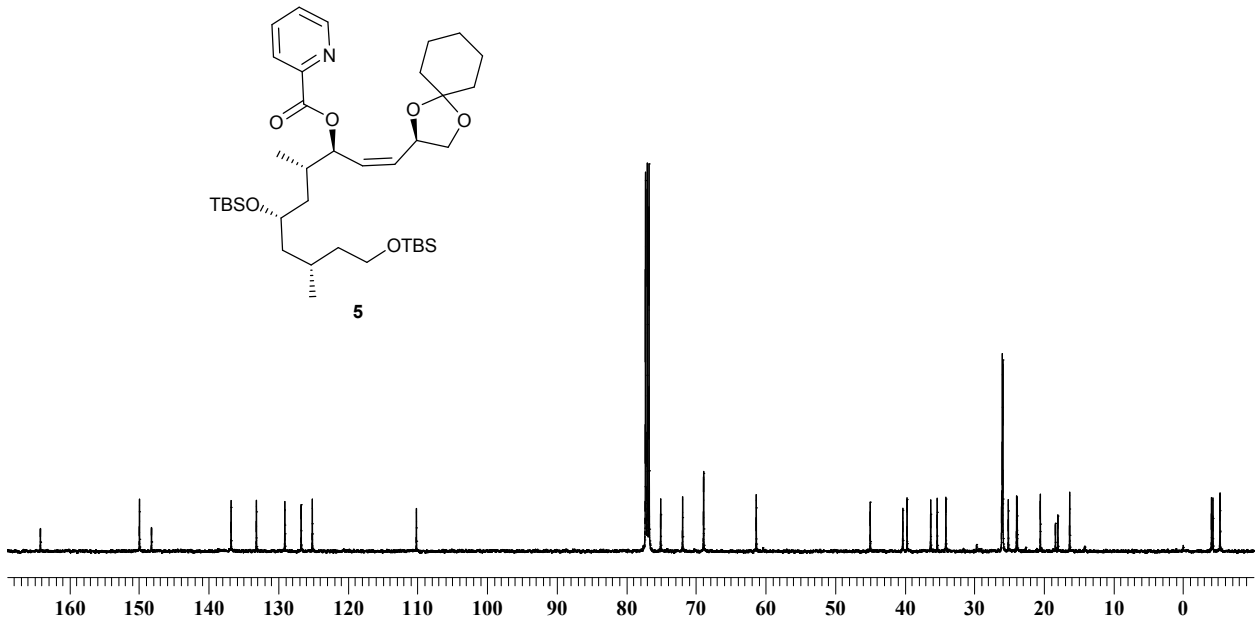
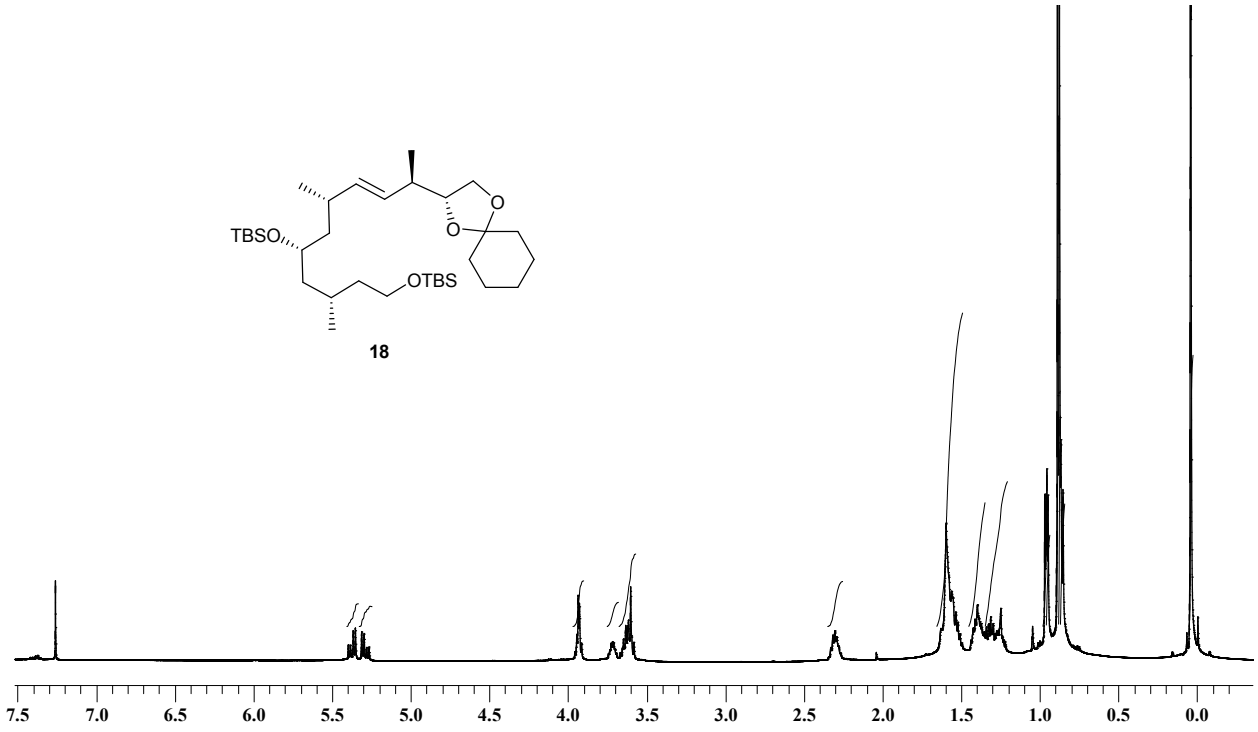
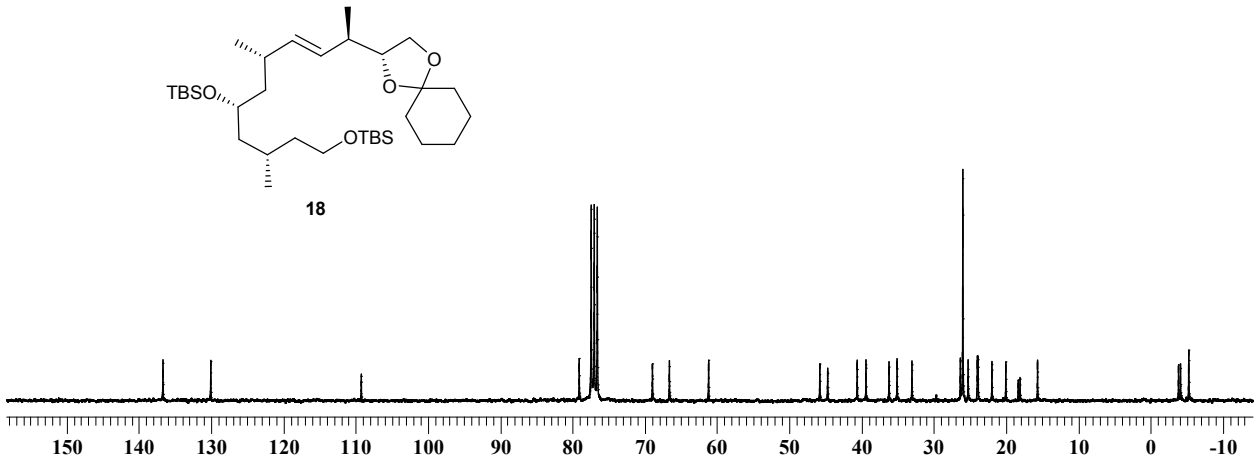


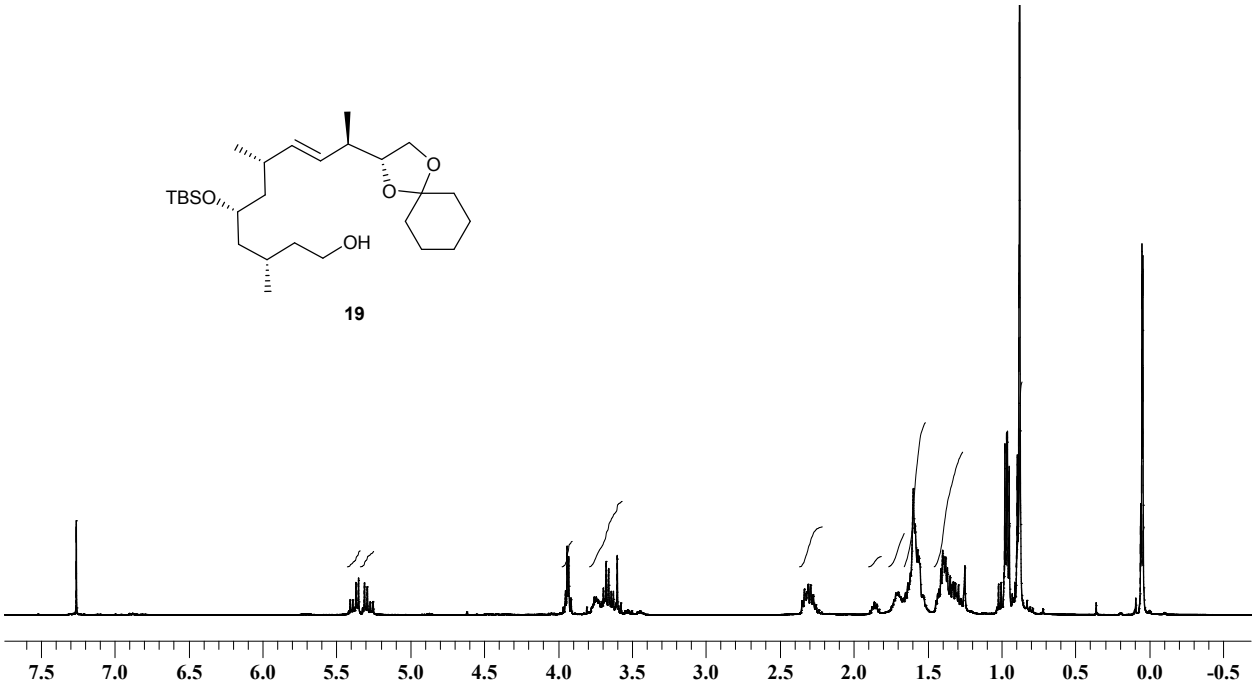
^{13}C NMR SPECTRUM OF COMPOUND 5 (125 MHz, $CDCl_3$)



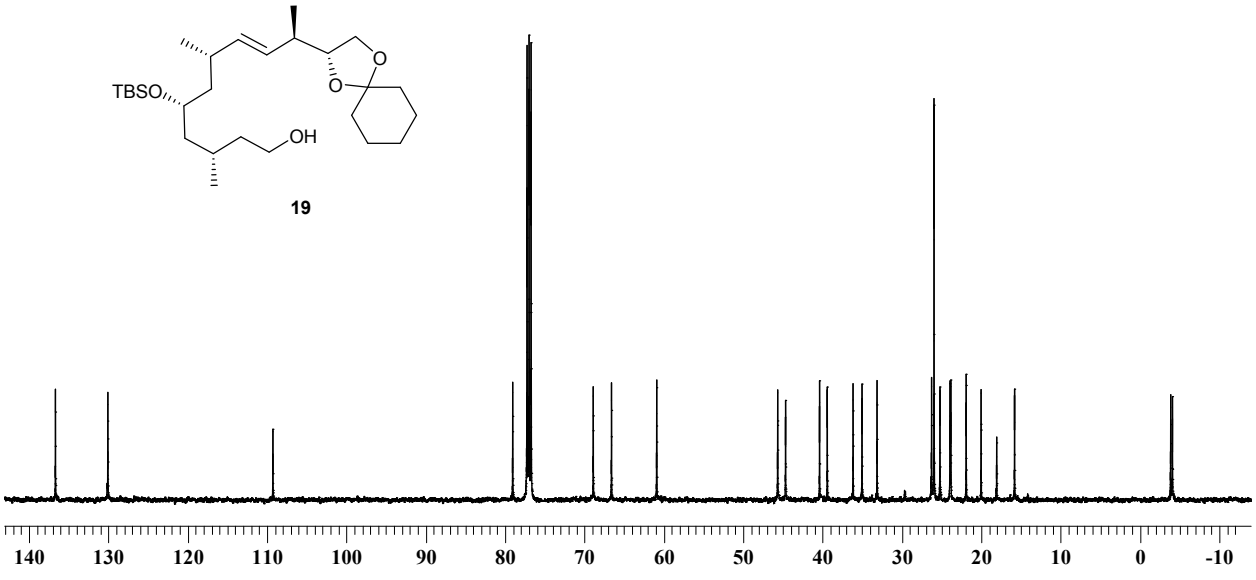
^{1}H NMR SPECTRUM OF COMPOUND 18 (500 MHz, $CDCl_3$)



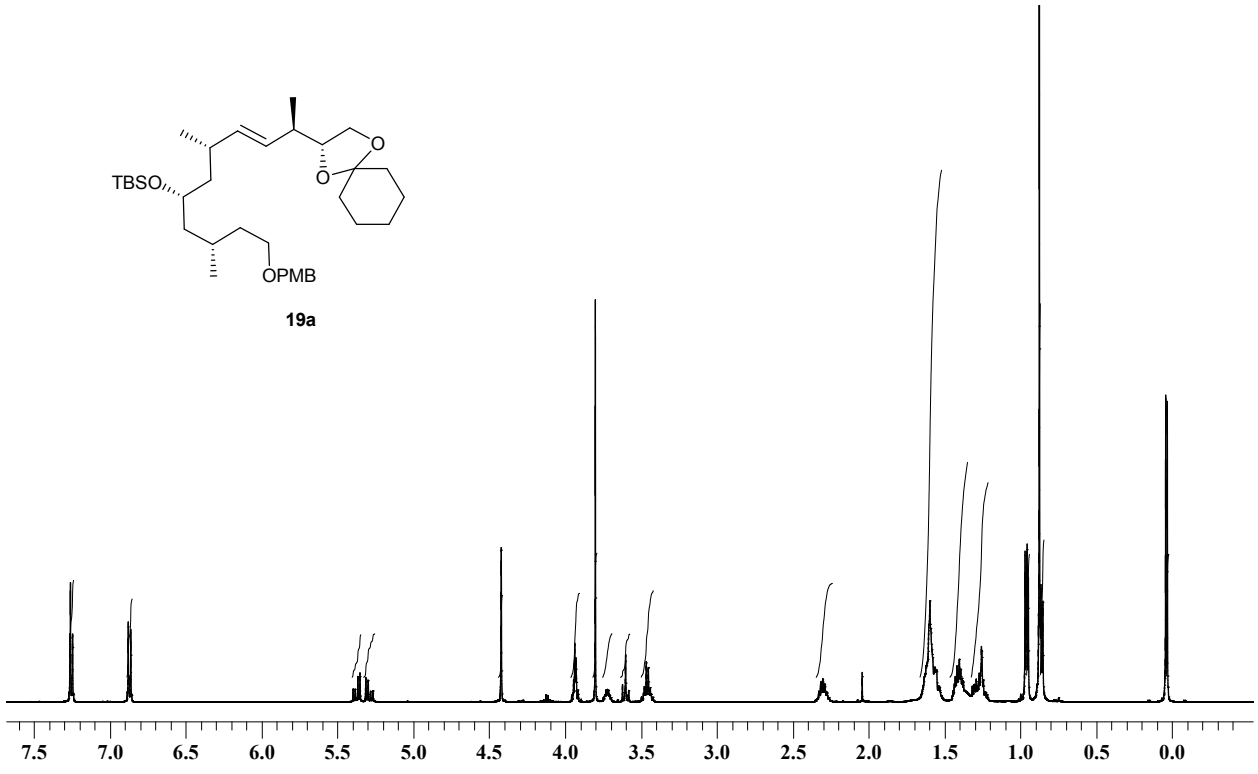
^{13}C NMR SPECTRUM OF COMPOUND 18 (125 MHz, $CDCl_3$)



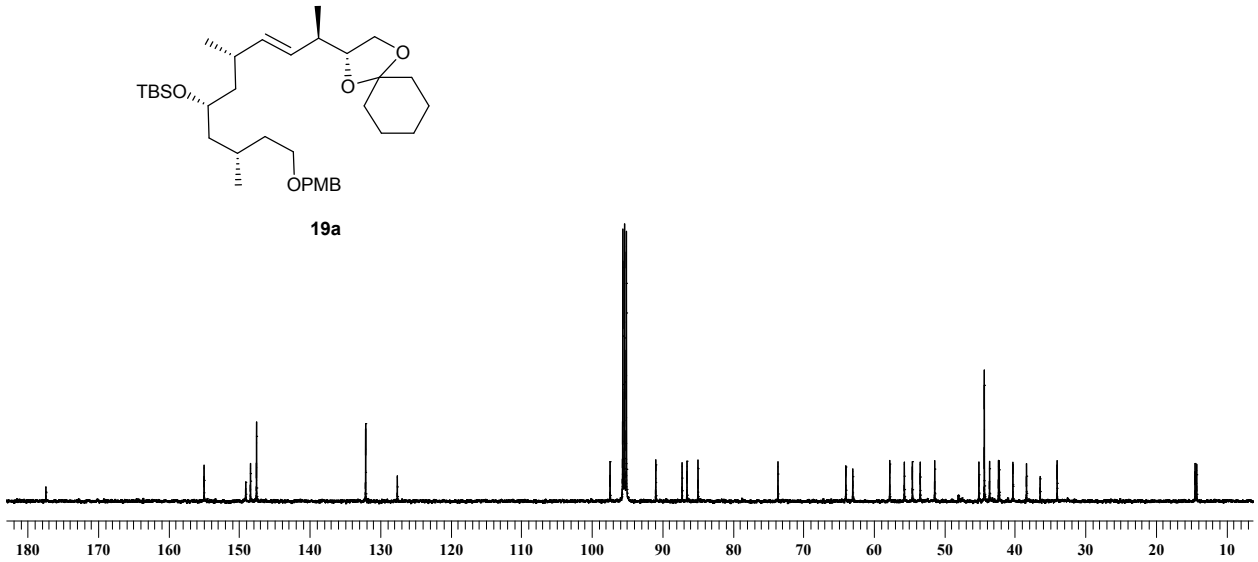
^{1}H NMR SPECTRUM OF COMPOUND 19 (400 MHz, $CDCl_3$)



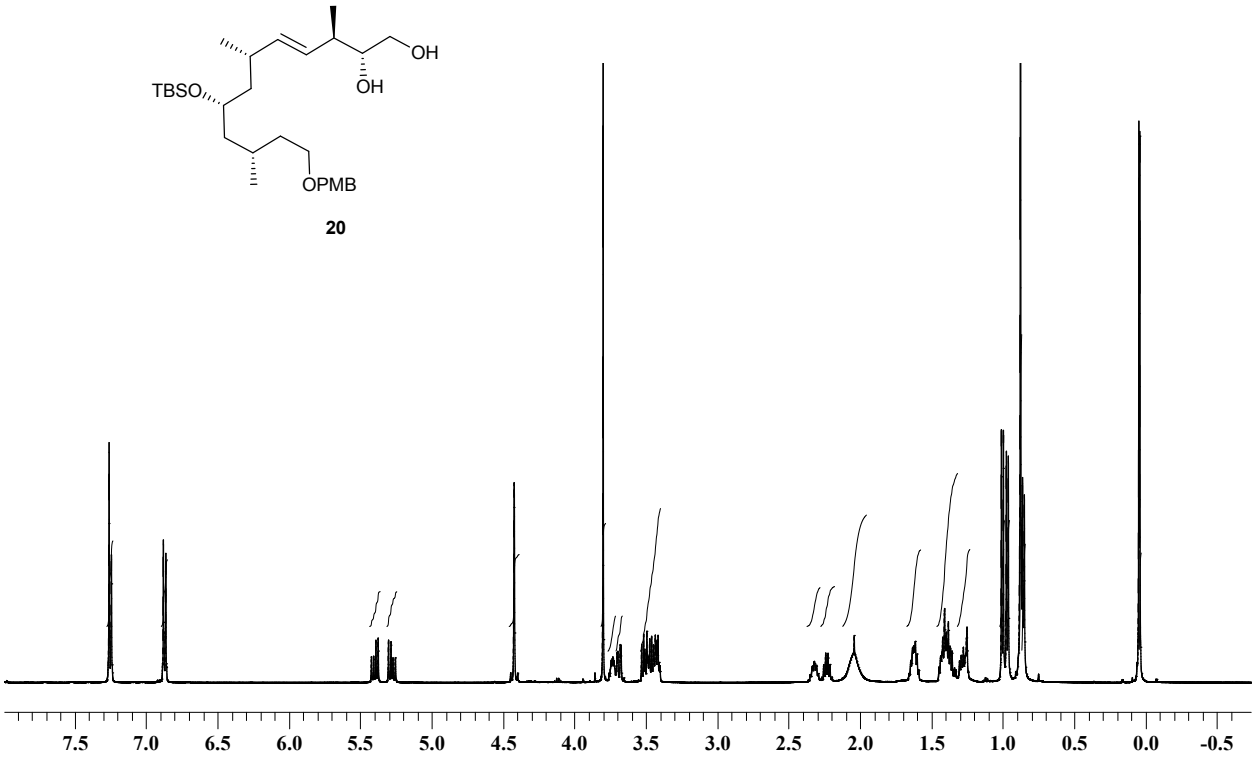
^{13}C NMR SPECTRUM OF COMPOUND 19 (125 MHz, $CDCl_3$)



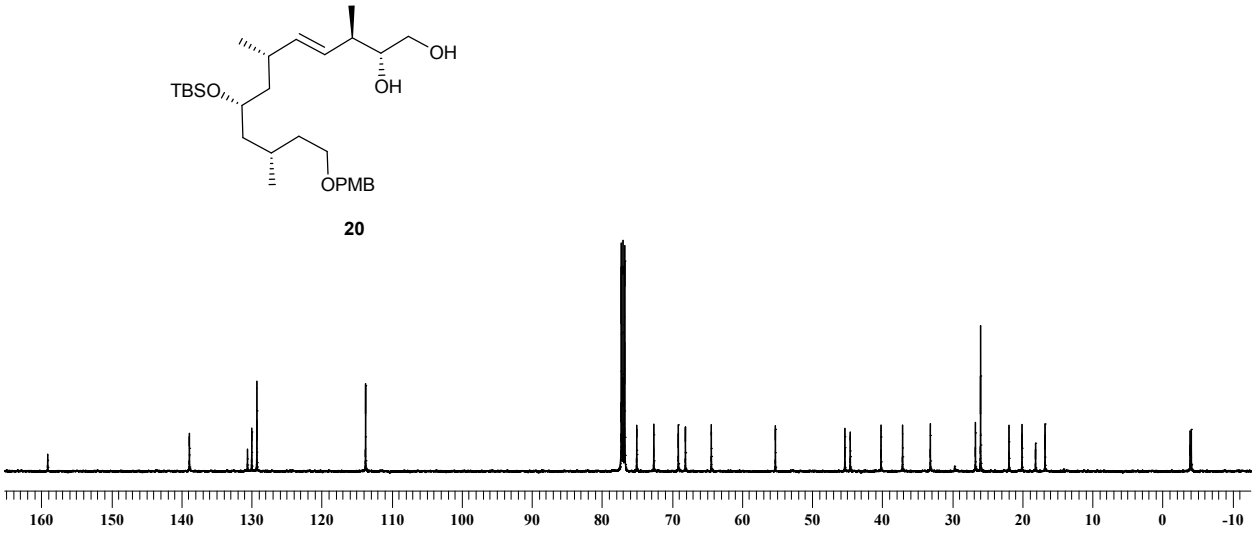
^{1}H NMR SPECTRUM OF COMPOUND 19a (500 MHz, $CDCl_3$)



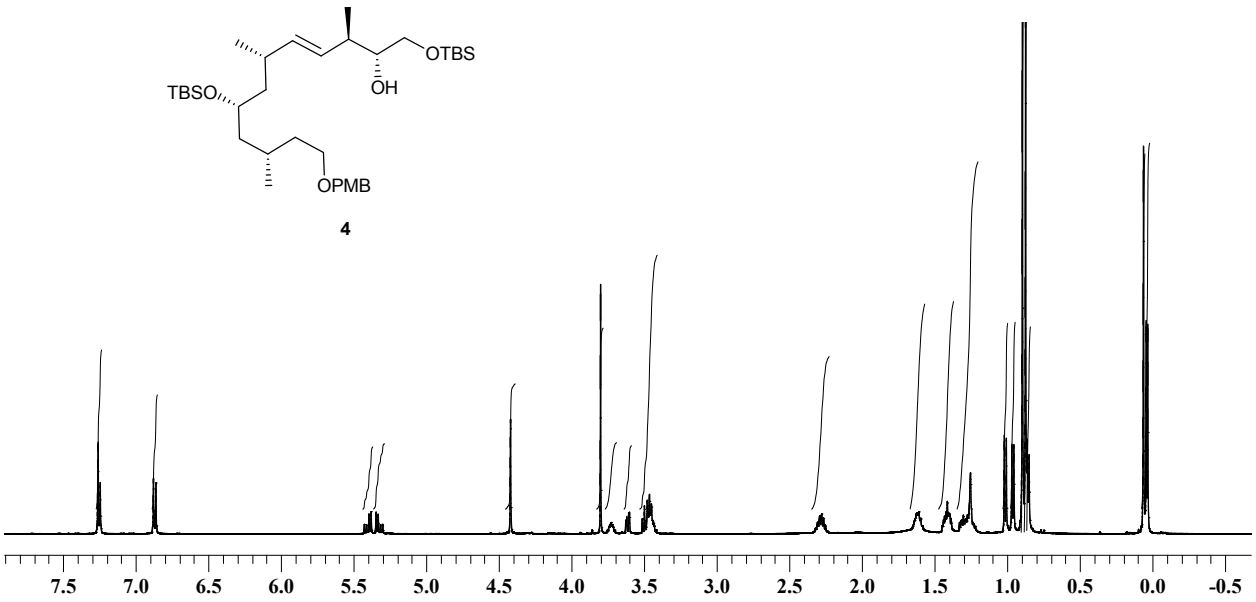
^{13}C NMR SPECTRUM OF COMPOUND 19a (125 MHz, $CDCl_3$)



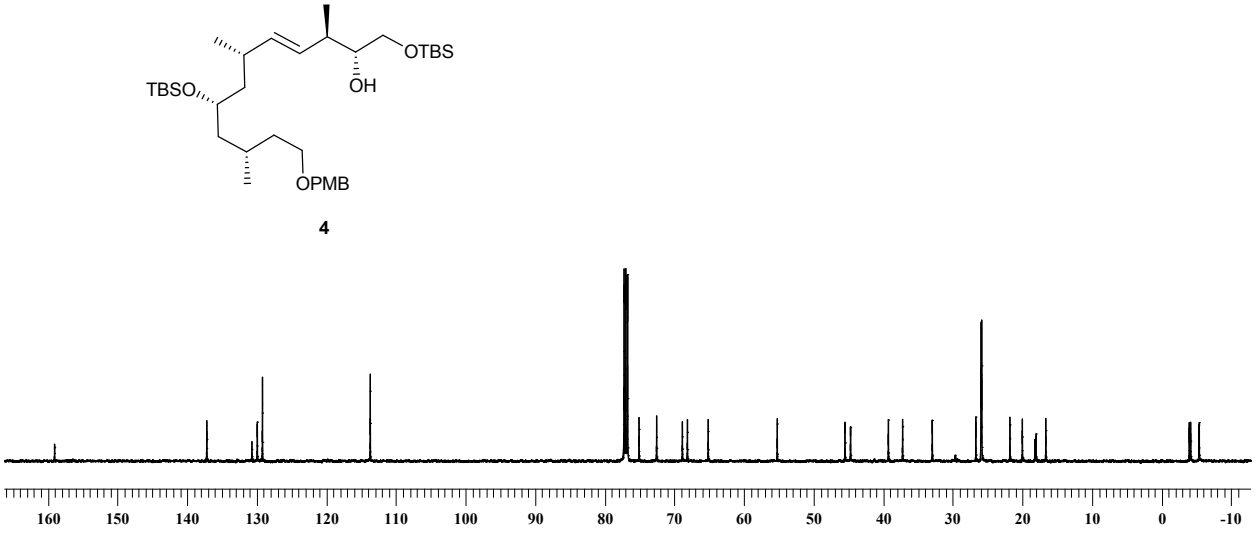
^{1}H NMR SPECTRUM OF COMPOUND 20 (500 MHz, $CDCl_3$)



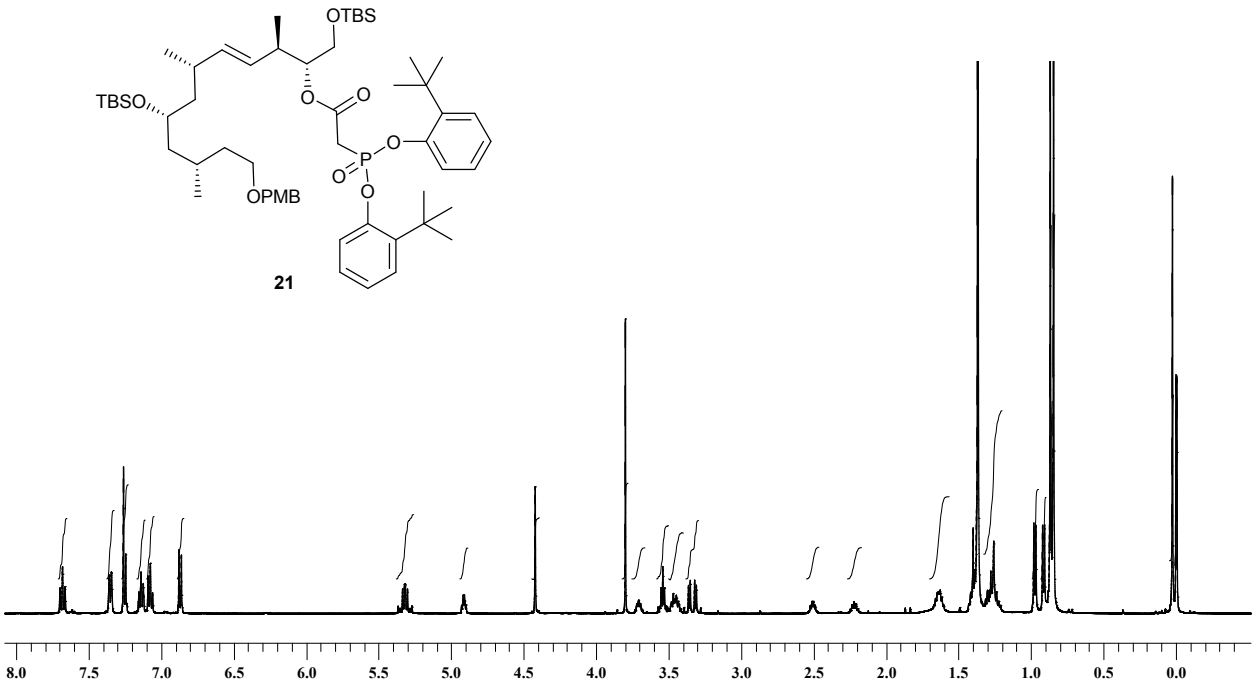
^{13}C NMR SPECTRUM OF COMPOUND 20 (125 MHz, $CDCl_3$)



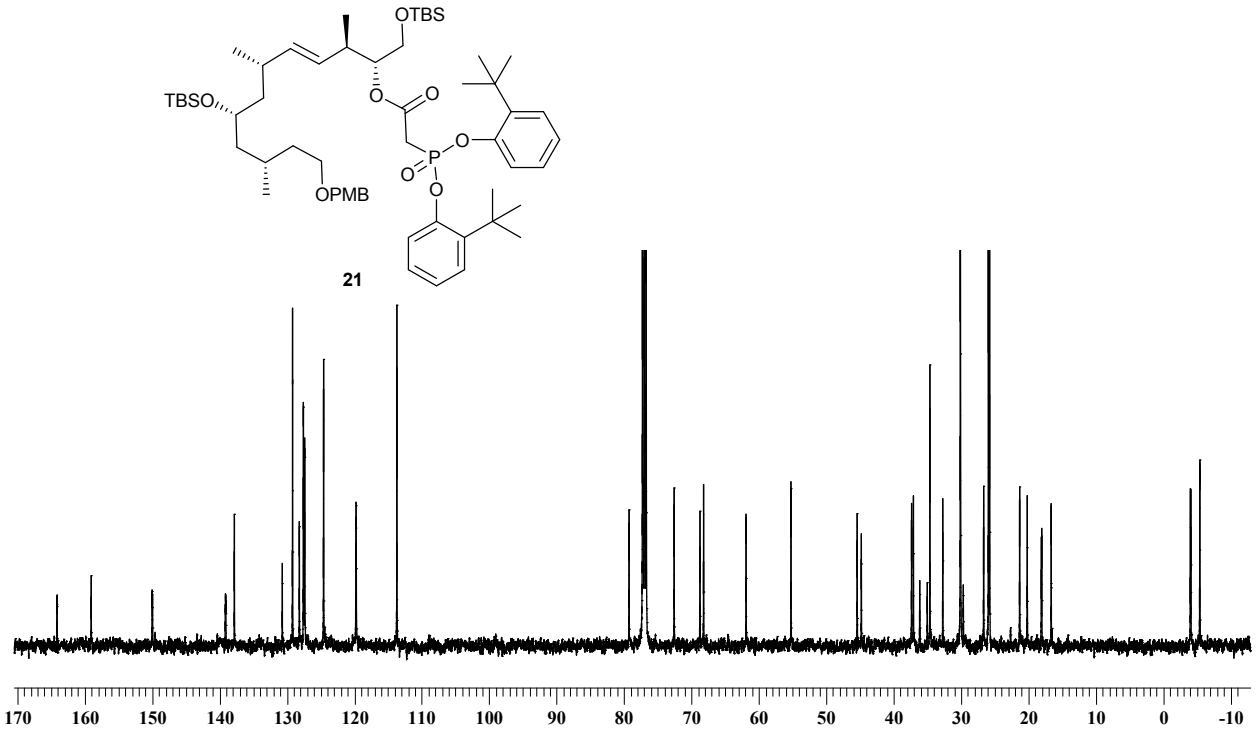
^{1}H NMR SPECTRUM OF COMPOUND 4 (500 MHz, $CDCl_3$)



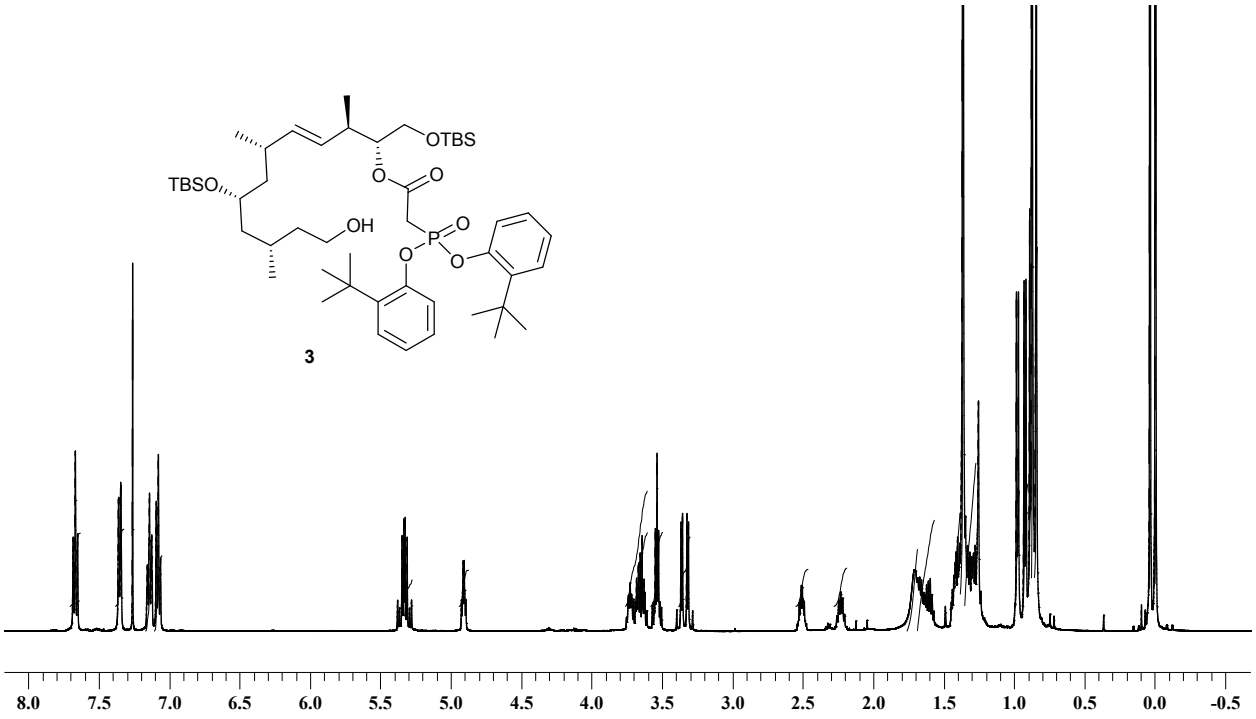
^{13}C NMR SPECTRUM OF COMPOUND 4 (125 MHz, $CDCl_3$)



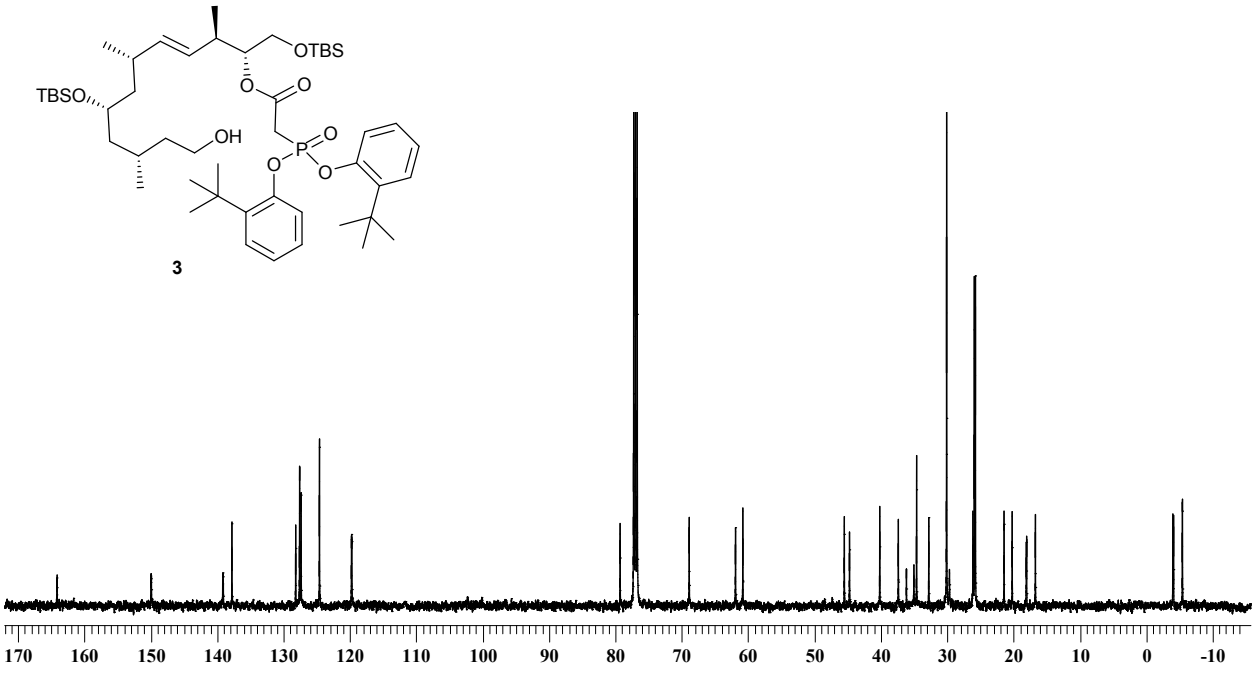
^{1}H NMR SPECTRUM OF COMPOUND 21 (500 MHz, $CDCl_3$)



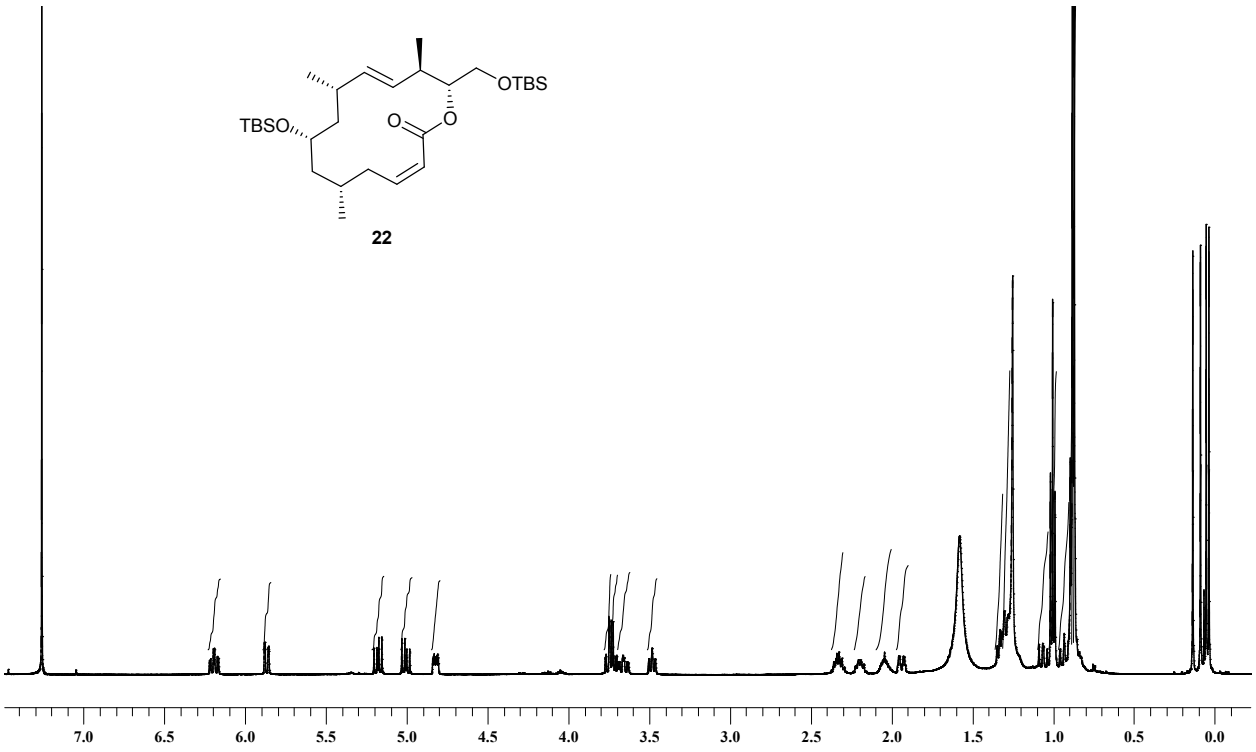
^{13}C NMR SPECTRUM OF COMPOUND 21 (125 MHz, $CDCl_3$)



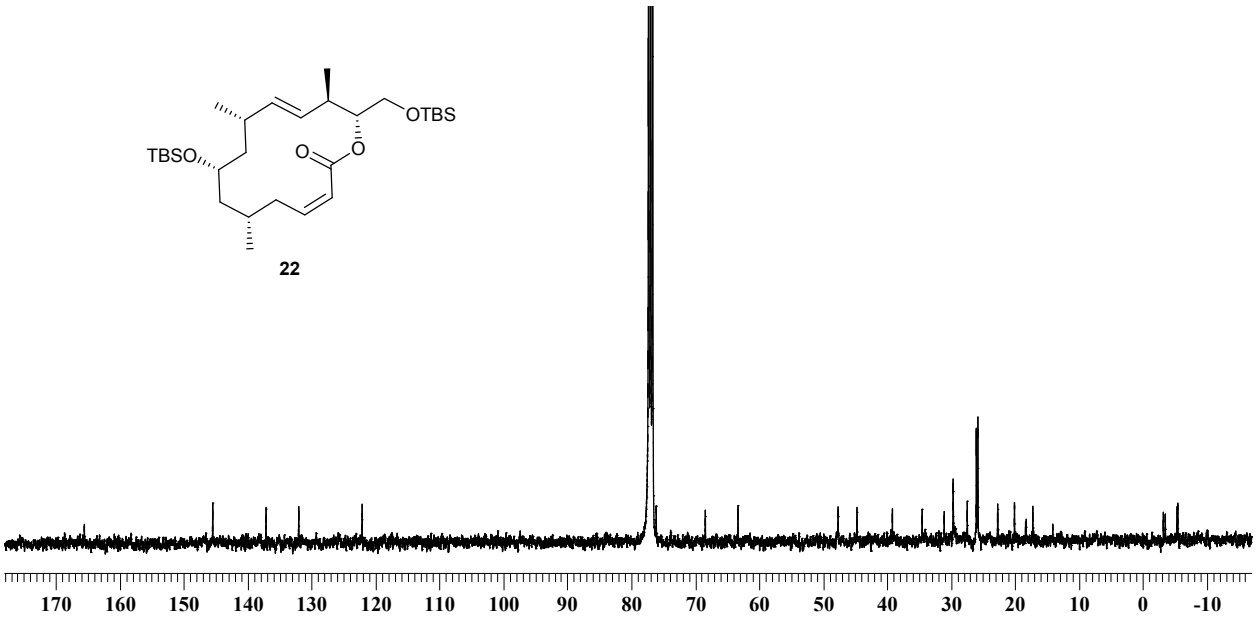
^{1}H NMR SPECTRUM OF COMPOUND 3 (500 MHz, $CDCl_3$)



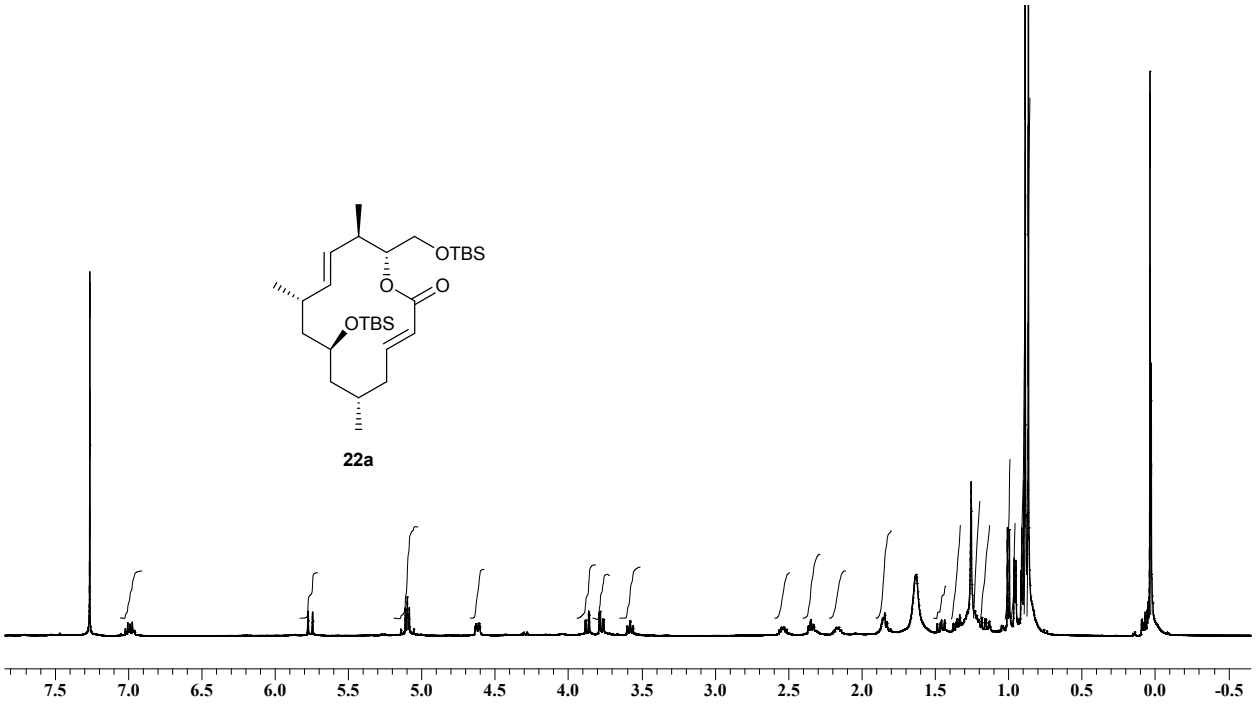
^{13}C NMR SPECTRUM OF COMPOUND 3 (125 MHz, $CDCl_3$)



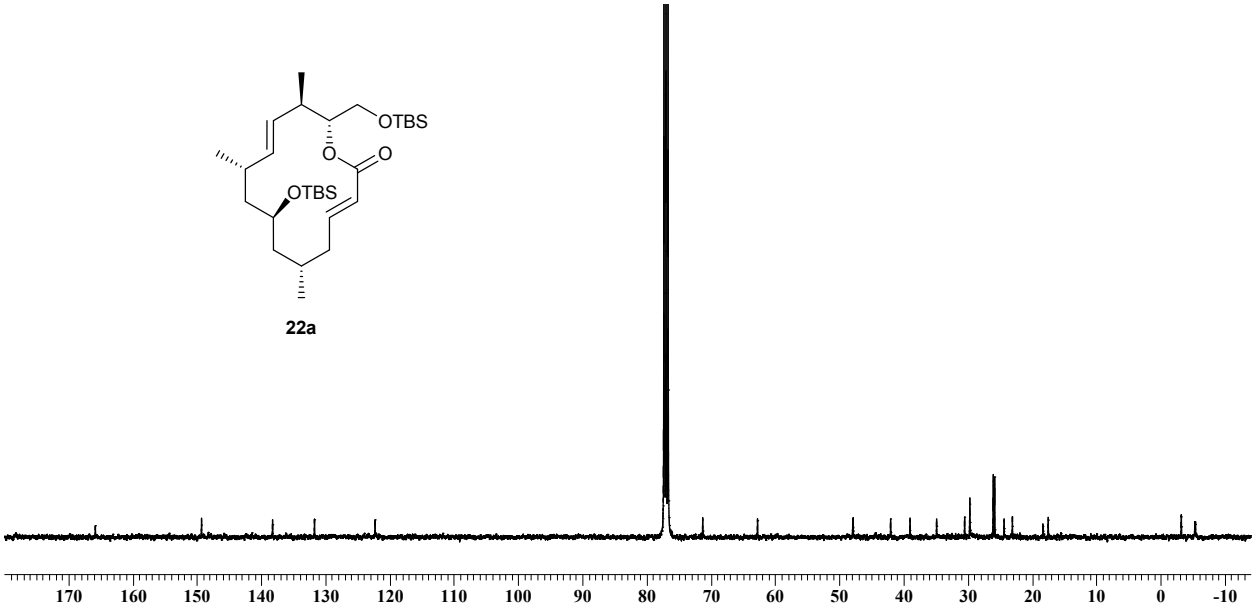
^{1}H NMR SPECTRUM OF COMPOUND 22 (500 MHz, $CDCl_3$)



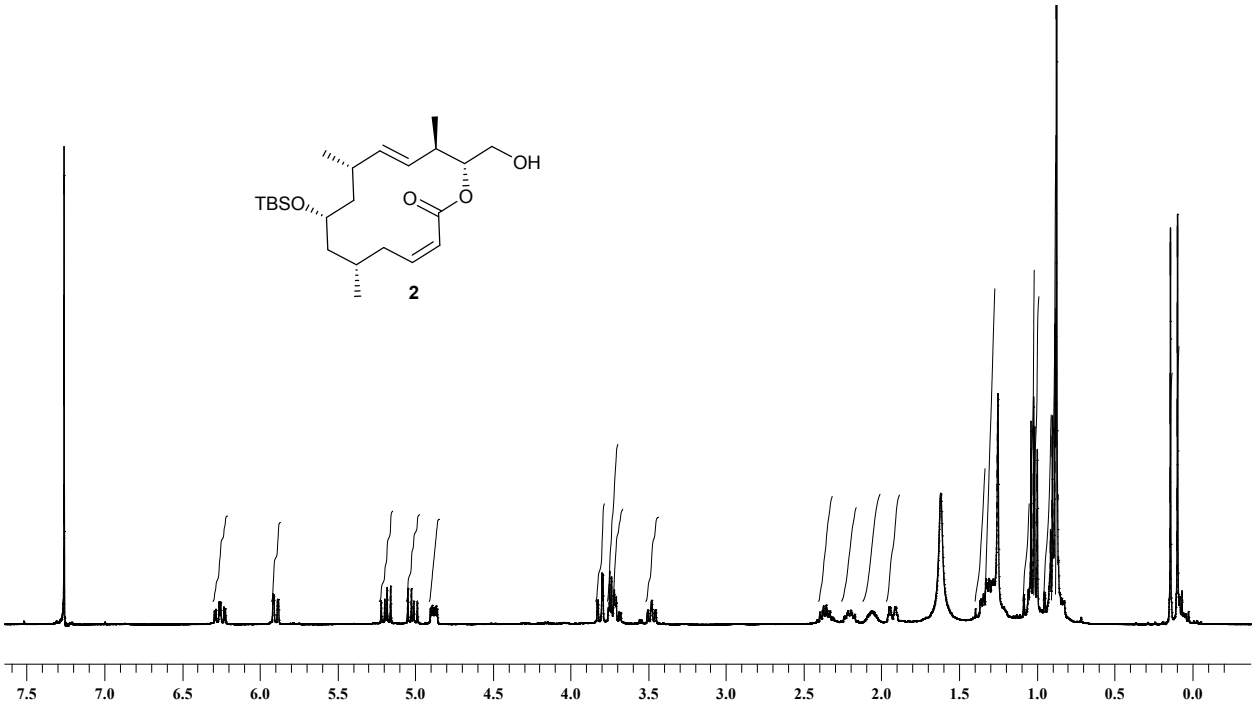
^{13}C NMR SPECTRUM OF COMPOUND 22 (100 MHz, $CDCl_3$)



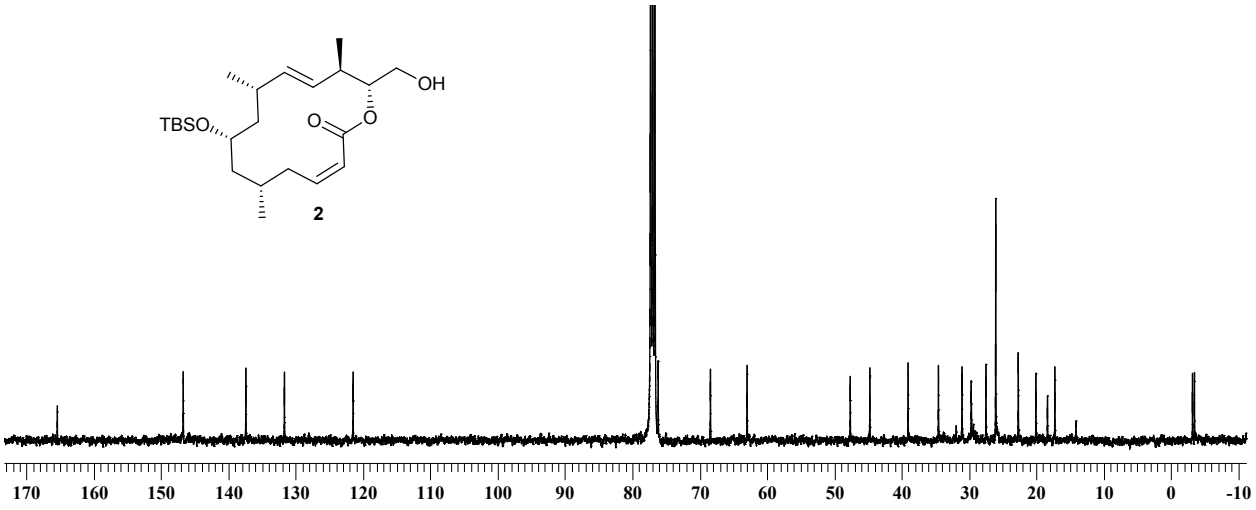
^{1}H NMR SPECTRUM OF COMPOUND 22a (500 MHz, $CDCl_3$)



^{1}3C NMR SPECTRUM OF COMPOUND 22a (400 MHz, $CDCl_3$)



^{1}H NMR SPECTRUM OF COMPOUND 2 (400 MHz, $CDCl_3$)



^{13}C NMR SPECTRUM OF COMPOUND 2 (100 MHz, $CDCl_3$)

NOE studies of compound 13:

The structure of **13** was derived by extensive NMR experiments including 2-D Double Quantum Filtered Correlation Spectroscopy (DQF-COSY) and Nuclear Overhauser Effect Spectroscopy (NOESY) experiments. The resonances in the 4.42 ppm, in **13** due to 5-H, which is distinctive and thus very useful in initiating the resonance assignments. It was interesting to note a medium intensity NOE, 2-H′/5-H, indicating the presence of a boat conformation for the six membered lactone ring. The intra-ring ^{1}H-^{1}H coupling constants, $^{3}J_{2\text{-H}'/3\text{-H}} = 9.6$, $^{3}J_{2\text{-H}/3\text{-H}} = 5.6$ and $^{3}J_{4\text{-H}'/5\text{-H}} = 4.1$Hz and the NOE correlations 2-H′/ 5-H, 3-H/ 4-H, 4-H/ 6-H, 3-CH_3/5-H and 5-H/7-CH_3 are consistent with this observation with boat conformation of six-membered ring. In addition, the NOE 3-CH_3/5-H, confirms that these protons are on the same side of the lactone ring. The energy minimized structure adequately supports the proposed structure of **13**.

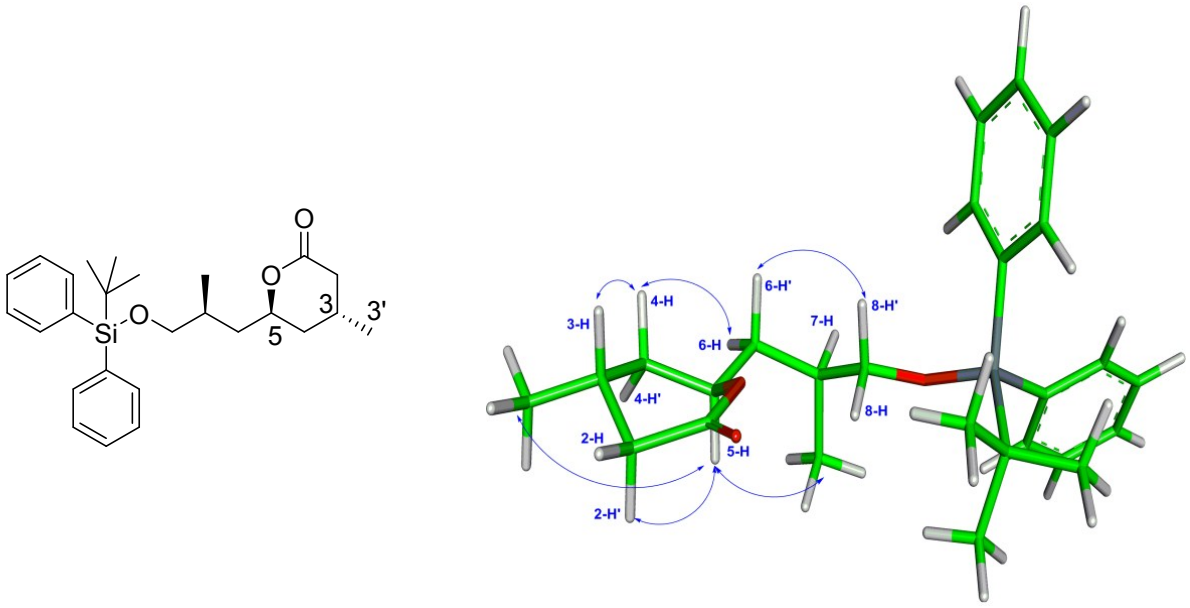
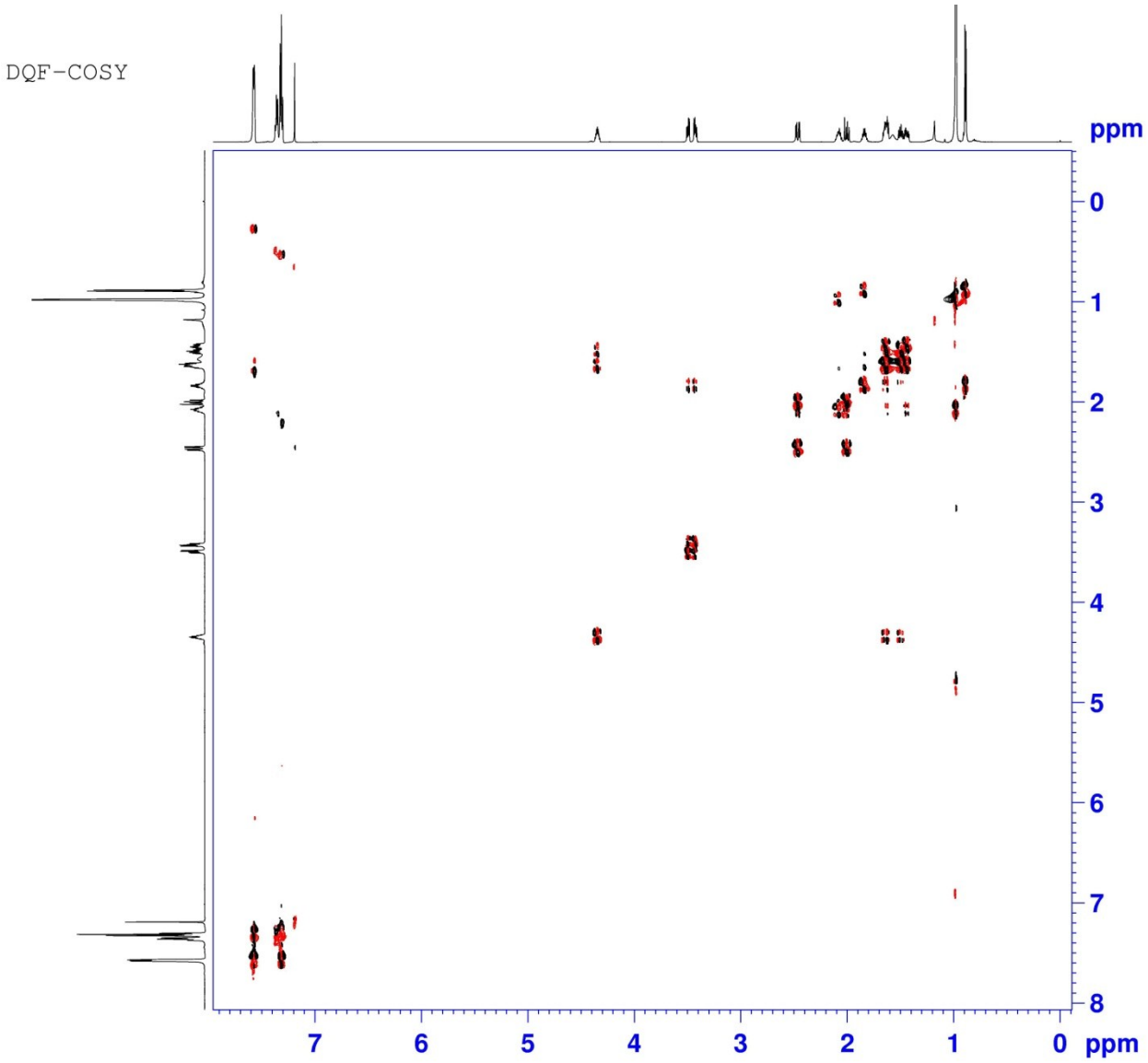
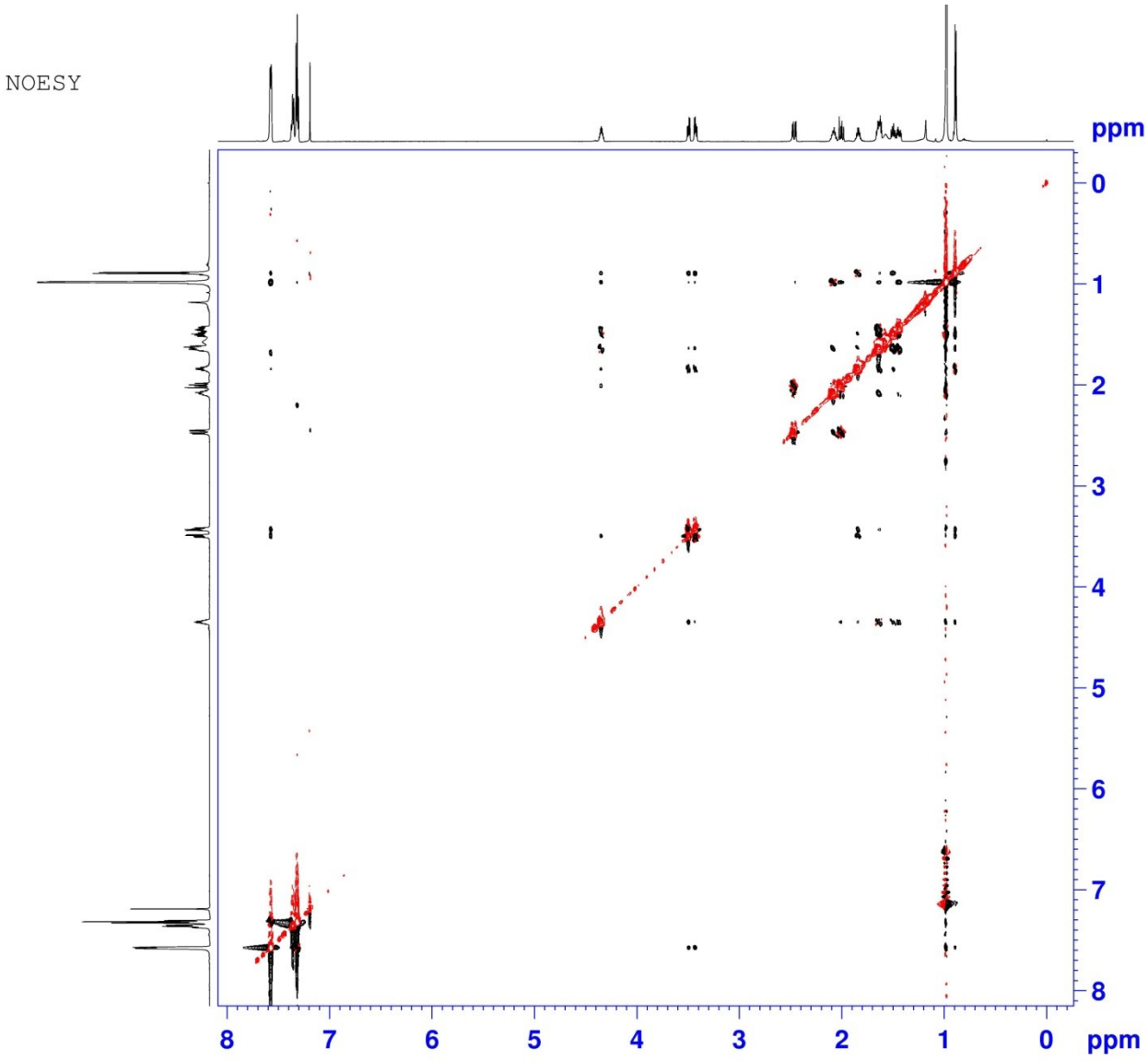


Figure 1: Energy minimized structure of **13** along with the characteristic NOE correlations



DQF-COSY spectrum of compound 13 (600 MHz, $CDCl_3$, 298 K)



NOESY spectrum of compound 13 (600 MHz, $CDCl_3$, 298 K)

Detailed NMR studies of compounds 22: The structures of compounds **22** were derived by extensive NMR experiments including 2-D Double Quantum Filtered Correlation Spectroscopy (DQF-COSY), Total Correlation Spectroscopy (TOCSY), Nuclear Overhauser Effect Spectroscopy (NOESY) and Heteronuclear-Single Quantum correlation (HSQC) experiments. The resonances in the 5.0 - 6.2 ppm, arising from two pairs of olefinic protons, are distinctive and thus very useful in initiating the resonance assignments. The protons at 5.00 ppm (dd) and 5.17 ppm (dd) are due to 10-H and 11-H (displaying a distinct *trans* $^{3}J_{10\text{-H}/11\text{-H}}$ = 15.2 Hz) coupling. The other pair of olefinic protons 2-H and 3-H appear at 5.87 ppm (dd) and 6.19 ppm(dt) respectively. A value of $^{3}J_{2\text{-H}/3\text{-H}}$ = 12.0 Hz is consistent with a *cis* olefinic bond (the minor compound **22a** with *trans* C2-C3 olefinic bond has $^{3}J_{2\text{-H}/3\text{-H}}$ = 15.8 Hz). Interestingly the 14 membered macrocycle is very rigid as reflected by the presence of large number of medium range NOE correlations and several distinctive vicinal couplings (^{3}J > 9 Hz or <4 Hz) that could be derived from the complex ^{1}H spectrum. Large coupling constants, $^{3}J_{10\text{-H}/11\text{-H}}$ = 15.2 Hz, and The NOE correlations 9-H/11-H, 10-H/12-H and 11-H/13-H, 7-H/9-H, 6-Hb/8-Hb, 9-H/11-H, 4-Ha/7-H and 3-H/5-CH_3 the large coupling constants ($^{3}J_{2\text{-H}/3\text{-H}}$ = 12.0, $^{3}J_{3\text{-H}/4\text{-Ha}}$ = 12.0, $^{3}J_{9\text{-H}/10\text{-H}}$ = 9.5, $^{3}J_{10\text{-H}/11\text{-H}}$ = 15.2, $^{3}J_{11\text{-H}/12\text{-H}}$ = 10.0, $^{3}J_{12\text{-H}/13\text{-H}}$ = 10.0 Hz) and small couplings ($^{3}J_{3\text{-H}/4\text{-Hb}}$ = 4.0, $^{3}J_{13\text{-H}/14\text{-Ha}}$ = 5.2, $^{3}J_{13\text{-H}/14\text{-Ha}}$ = 2.5 Hz) support the deduced minimum energy structure (Figure **1**). The energy minimized structure adequately supports the proposed structure of **22**.

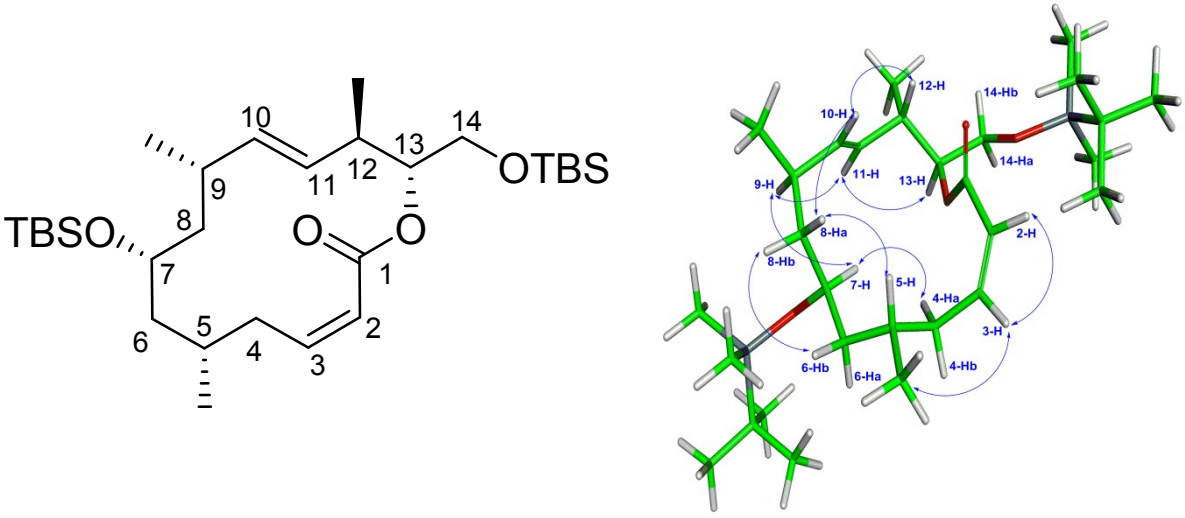
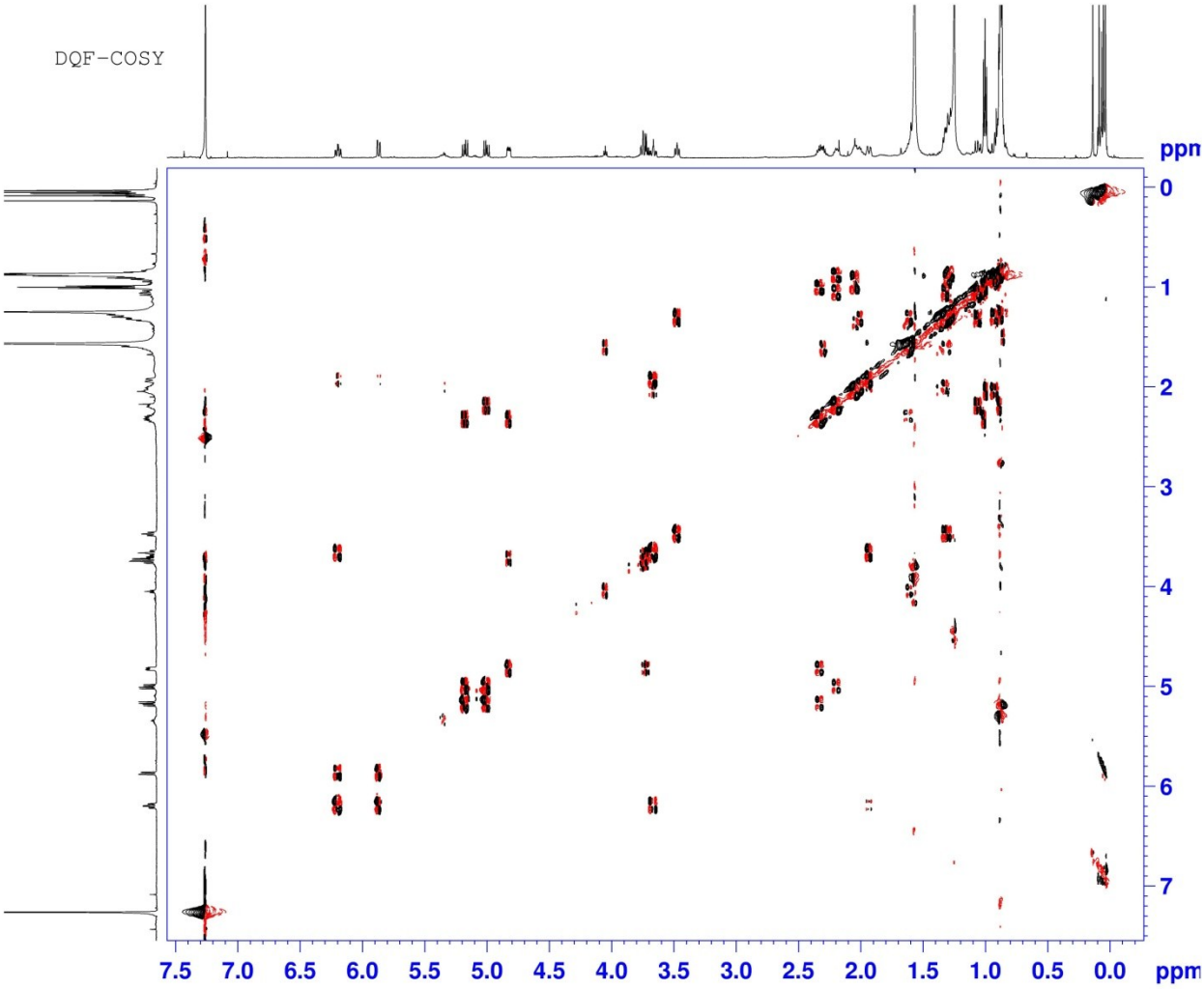


Figure**2:** Energy minimized structure of **22** along with the characteristic NOE correlations

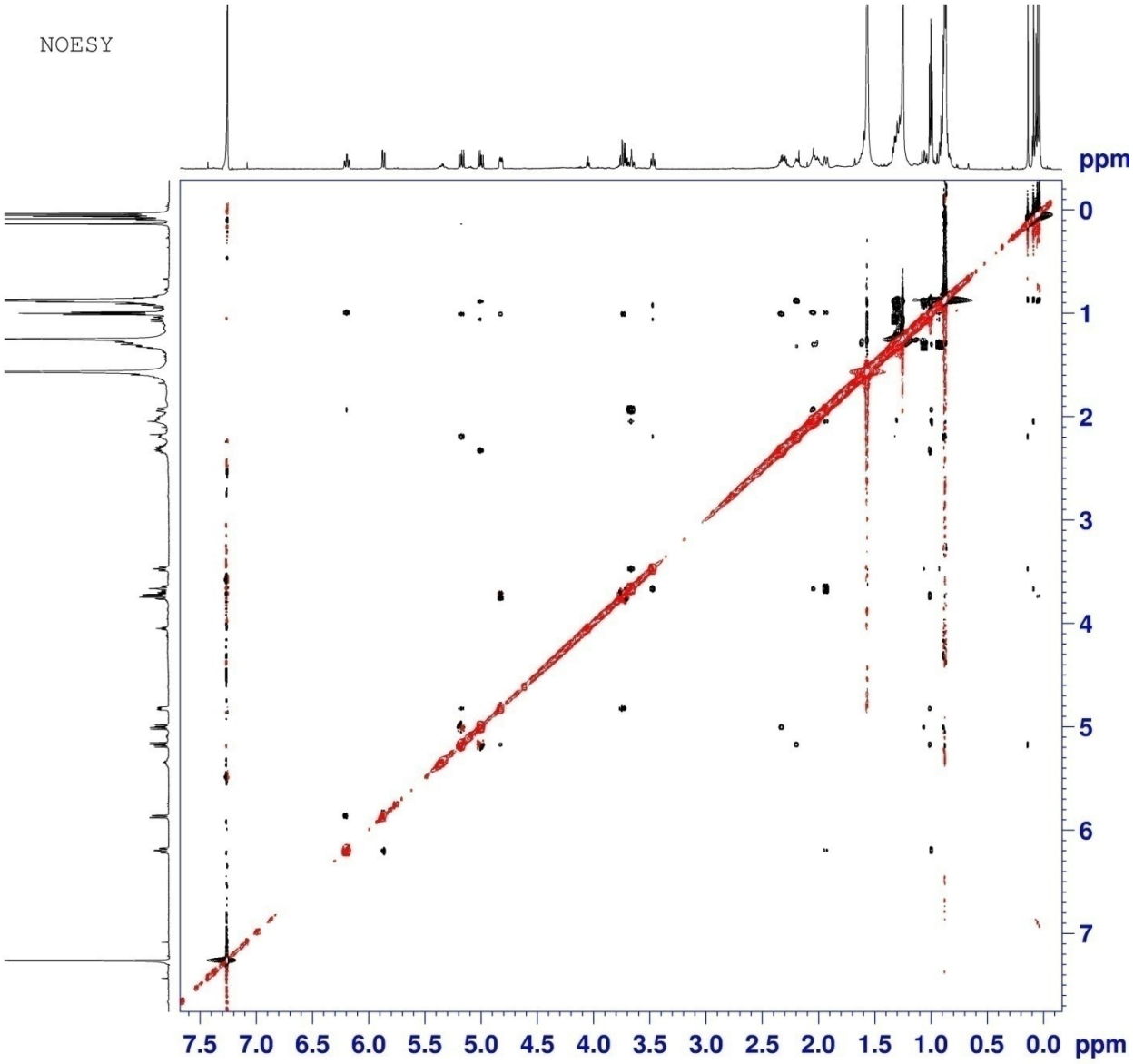
Table 1: ^{1}H chemical shifts (δ) and coupling constants (*J*) of compound **22**

No	**δ (ppm)**	**Multiplicity**	***J* values (Hz)**
2-H	5.87	dd	$^{3}J_{2\text{-H}/3\text{-H}} = 12.0$ $^{3}J_{2\text{-H}/4\text{-Hb}} = 2.5$
3-H	6.19	td	$^{3}J_{2\text{-H}/3\text{-H}} = 12.0$ $^{3}J_{3\text{-H}/4\text{-Ha}} = 12.0$ $^{3}J_{3\text{-H}/4\text{-Hb}} = 4.0$
4-Ha	3.67	ddd	$^{3}J_{3\text{-H}/4\text{-Ha}} = 12.0$ $^{2}J_{4\text{-Ha}/4\text{-Hb}} = 15.0$ $^{3}J_{4\text{-H}/5\text{-H}} = 4.0$
4-Hb	1.93	dq	$^{3}J_{3\text{-H}/4\text{-Hb}} = 12.0$ $^{2}J_{4\text{-Ha}/4\text{-Hb}} = 15.0$ $^{3}J_{4\text{-H}/5\text{-H}} = 12.0$
5-H	2.04	m	---------
5-CH_3	0.99	d	$^{3}J_{5\text{-H}/5\text{-CH3}} = 7.5$
6-Ha	1.32	m	---------
6-Hb	0.92	m	---------
7-H	3.47	td	$^{3}J_{6\text{-Hb}/7\text{-H}} = 10.0$ $^{3}J_{7\text{-H}/8\text{-Ha}} = 2.2$ $^{3}J_{7\text{-H}/8\text{-Hb}} = 10.0$

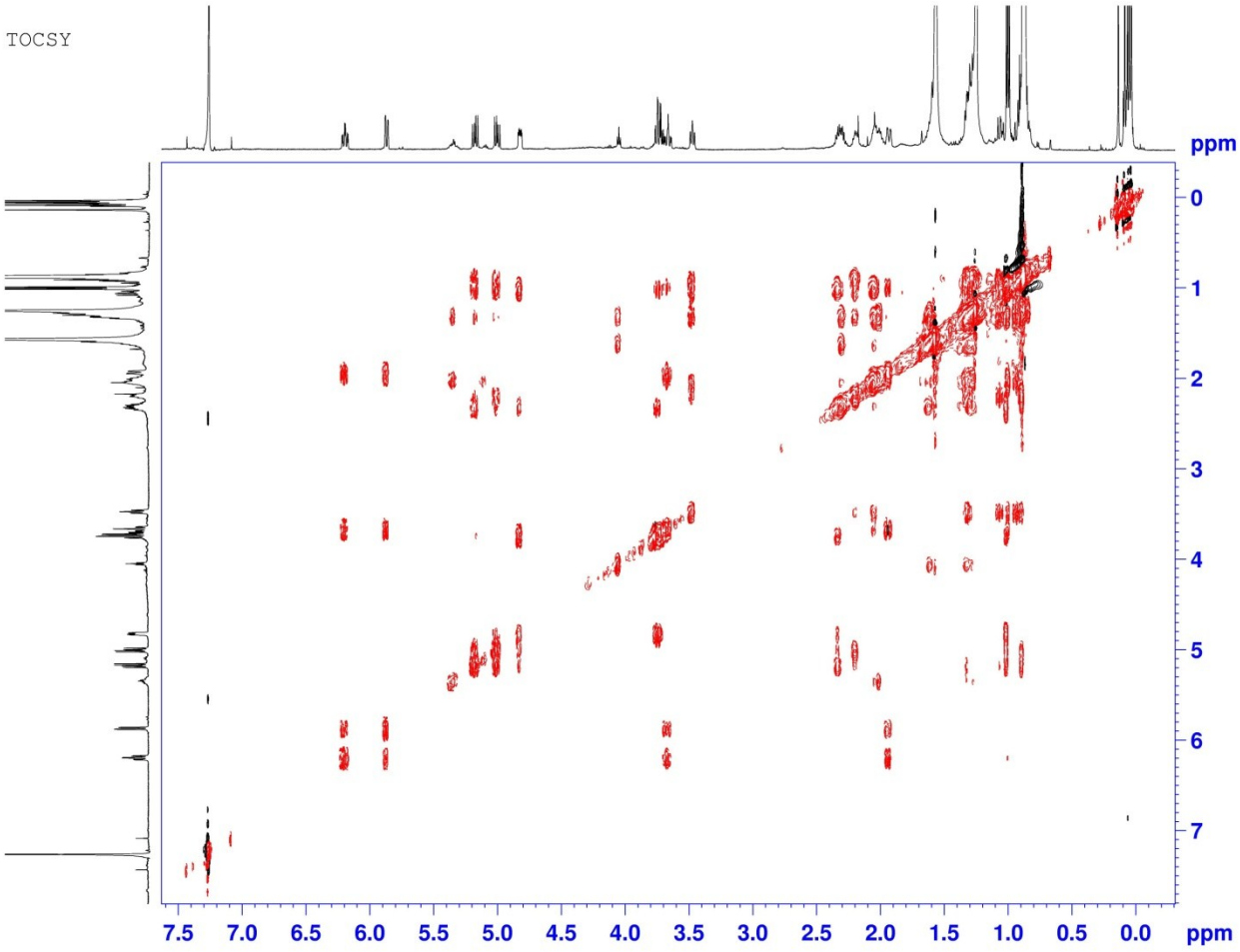
8-Ha	1.05	m	---------
8-Hb	1.32	m	---------
9-H	2.18	m	---------
9-CH_3	0.88	d	$^3J_{9\text{-H/9-CH3}} = 7.5$
10-H	5.00	dd	$^3J_{9\text{-H/10-H}} = 9.5$ $^3J_{10\text{-H/11-H}} = 15.2$
11-H	5.17	dd	$^3J_{10\text{-H/11-H}} = 15.2$ $^3J_{11\text{-H/12-H}} = 10.0$
12-H	2.33	tq	$^3J_{11\text{-H/12-H}} = 10.0$ $^3J_{12\text{-H/13-H}} = 10.0$ $^3J_{12\text{-H/12-CH3}} = 7.0$
12-CH_3	1.00	d	$^3J_{12\text{-H/12-CH3}} = 7.0$
13-H	4.82	ddd	$^3J_{12\text{-H/13-H}} = 10.0$ $^3J_{13\text{-H/14-Ha}} = 5.2$ $^3J_{13\text{-H/14-Hb}} = 2.5$
14Ha	3.74	dd	$^3J_{13\text{-H/14-Ha}} = 5.2$ $^2J_{14\text{-Ha/14-Hb}} = 11.6$
14Hb	3.72	dd	$^3J_{13\text{-H/14-Hb}} = 2.5$ $^2J_{14\text{-Ha/14-Hb}} = 11.6$



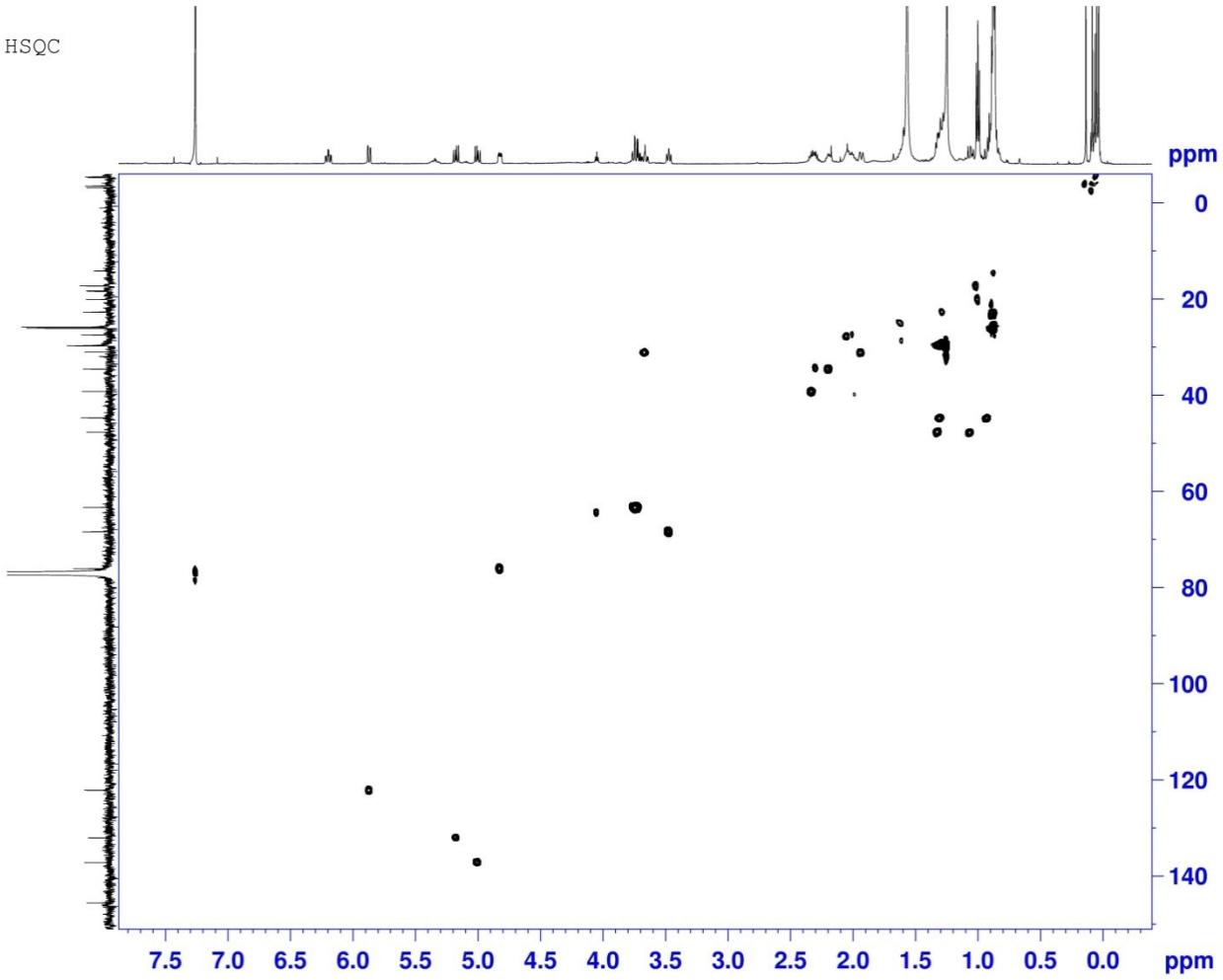
DQF-COSY spectrum of compound 22 (600 MHz, $CDCl_3$, 298 K)



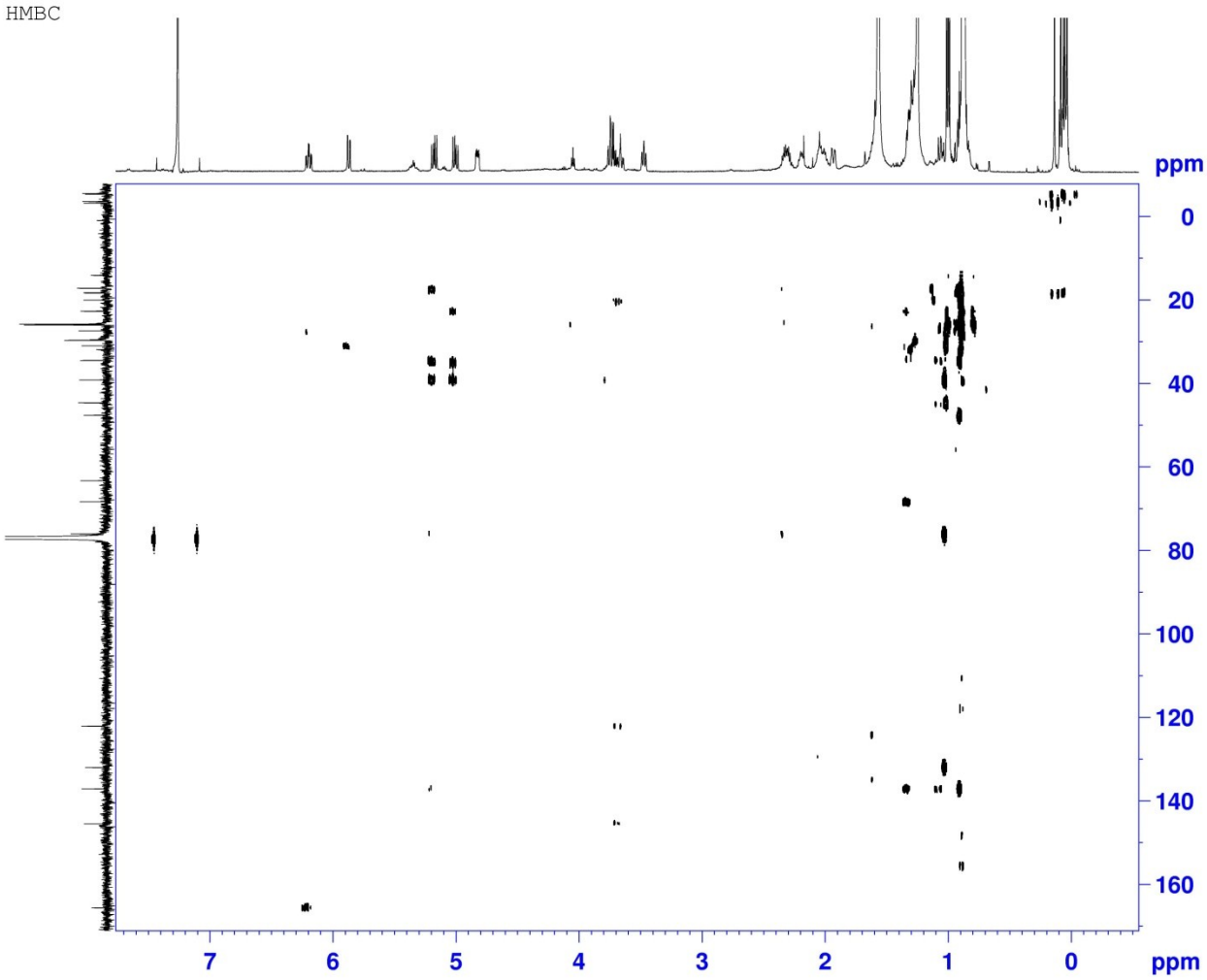
NOESY spectrum of compound 22 (600 MHz, $CDCl_3$, 298 K)



TOCSY spectrum of compound 22 (600 MHz, $CDCl_3$, 298 K)



HSQC spectrum of compound 22 (600 MHz, $CDCl_3$, 298 K)



HMBC spectrum of compound 22 (600 MHz, $CDCl_3$, 298 K)