

Supporting Information

SYNTHESIS AND BIOLOGICAL ACTIVITIES OF ACETAL ANALOGS AT POSITION 3 OF 10-METHYL-APLOG-1, A POTENTIAL ANTI-CANCER LEAD DERIVED FROM DEBROMOAPLYSIATOXIN

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I. Growth Inhibitory Activity of **1**, **2**, and **16** against 39 Human Cancer Cell Lines

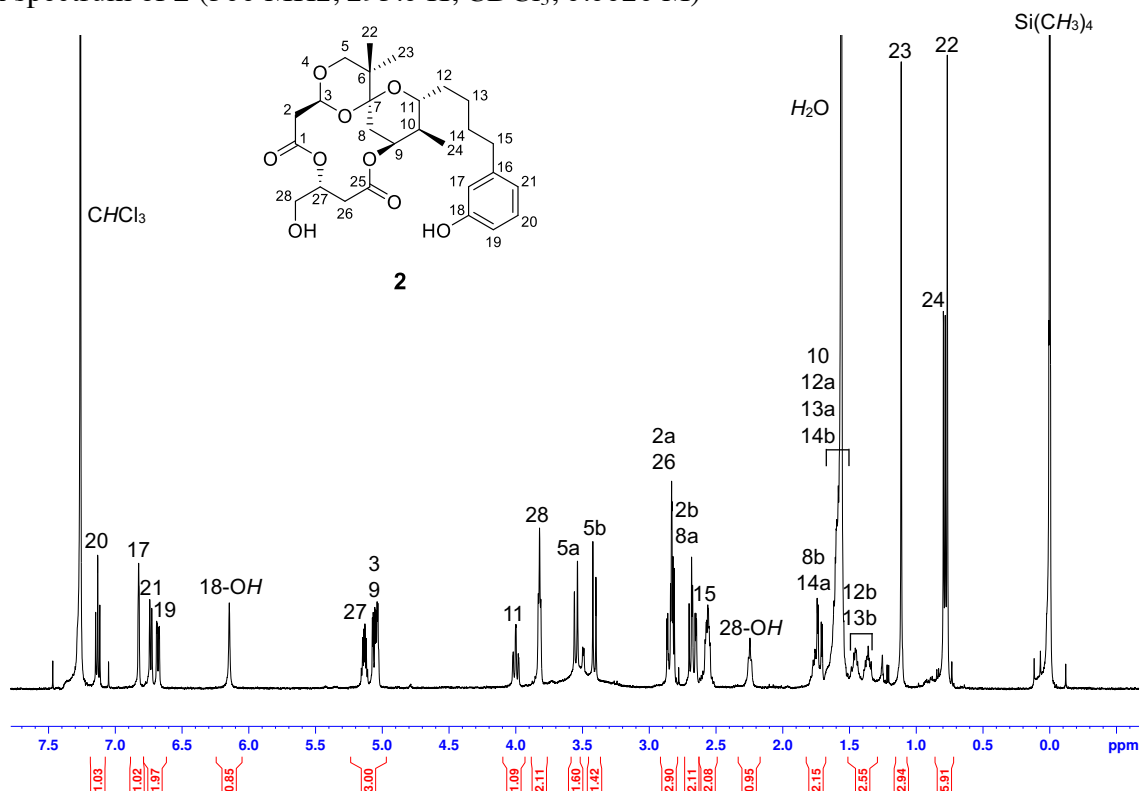
This assay was performed by Screening Committee of Anticancer Drugs supported by Grant-in-Aid for Scientific Research on Innovative Areas “Platform of Advanced Animal Model Support” (No. 16H06276) from the Japanese government (Monbukagakusho: MEXT).

Cancer cell line		log GI ₅₀ (M)		
		1 ^a	2	16
Breast	HBC-4	-7.48	-6.26	-5.88
	BSY-1	-4.91	> -5.00	-4.74
	HBC-5	-4.82	> -5.00	-4.59
	MCF-7	-4.84	-5.01	-4.59
	MDA-MB-231	-6.90	-5.10	-4.95
CNS	U251	-4.79	> -5.00	-4.69
	SF-268	-4.83	> -5.00	-4.72
	SF-295	-4.98	-5.50	-4.96
	SF-539	-4.88	-5.51	-4.95
	SNB-75	-4.92	> -5.00	-4.76
	SNB-78	-6.05	> -5.00	-4.60
Colon	HCC2998	-6.47	-5.56	-5.17
	KM-12	-4.82	> -5.00	-4.71
	HT-29	-4.81	> -5.00	-4.70
	HCT-15	-4.87	-5.26	-4.79
	HCT-116	-4.89	> -5.00	-4.70
Lung	NCI-H23	-4.87	> -5.00	-4.71
	NCI-H226	-6.15	-5.31	-4.80
	NCI-H522	-4.86	> -5.00	-4.66
	NCI-H460	-7.07	-6.12	-5.69
	A549	-6.01	-5.40	-5.20
	DMS273	-4.88	> -5.00	-4.90
	DMS114	-5.05	> -5.00	-4.74
Melanoma	LOX-IMVI	-6.21	> -5.00	-4.75
Ovarian	OVCAR-3	-4.88	> -5.00	-4.66
	OVCAR-4	-4.77	> -5.00	-4.52
	OVCAR-5	-4.92	> -5.00	-4.91
	OVCAR-8	-4.75	> -5.00	-4.47
	SK-OV-3	-4.88	> -5.00	-4.69
Renal	RXF-631L	-4.84	> -5.00	-4.64
	ACHN	-4.94	> -5.00	-4.78
Stmach	St-4	-6.24	-5.96	-5.33
	MKN1	-4.87	> -5.00	-4.84
	MKN-B	-4.80	> -5.00	-4.69
	MKN-A	-4.82	> -5.00	-4.76
	MKN45	-4.97	-6.00	-5.62
	MKN74	-4.68	-5.08	-4.86
Prostate	DU-145	-4.82	> -5.00	-4.61
	PC-3	-4.94	-5.13	-4.83

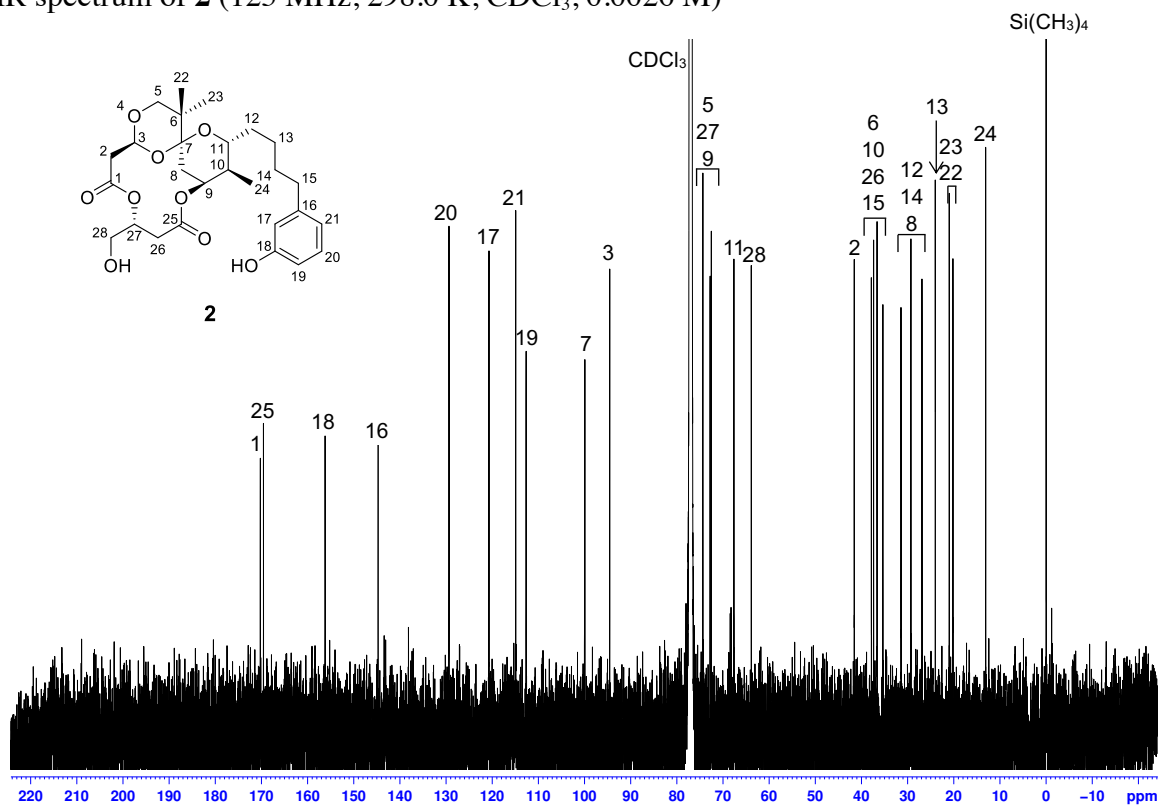
^aM. Kikumori, R. C. Yanagita, H. Tokuda, N. Suzuki, H. Nagai, K. Suenaga, and K. Irie, *J. Med. Chem.*, 2012, **55**, 5614.

II. ^1H , ^{13}C , and 2-D NMR Spectra of **2**, **16**, **14**, and **15**

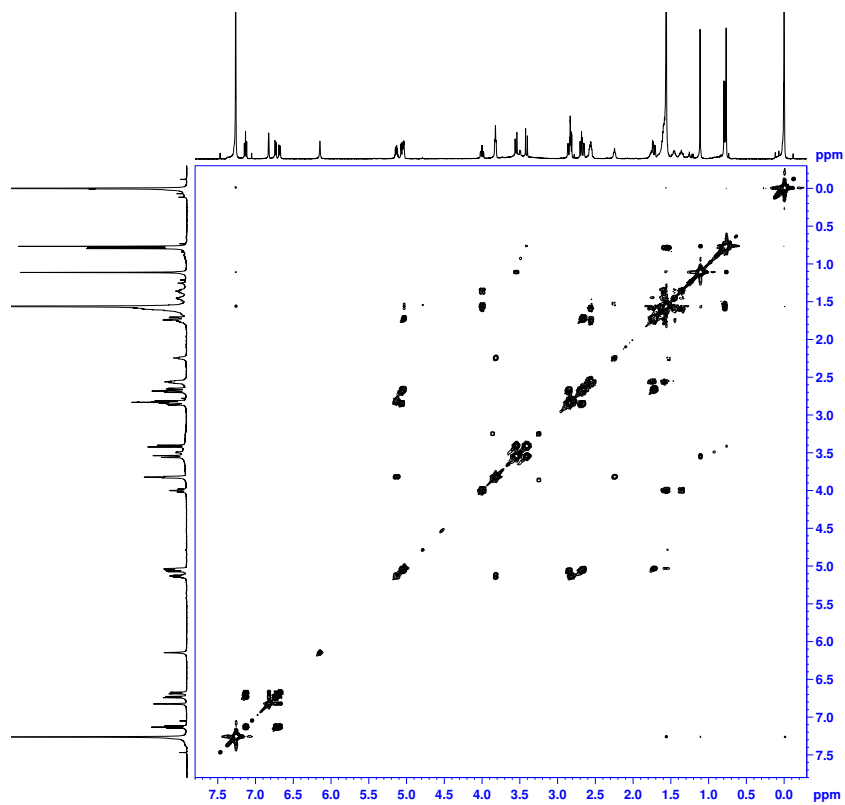
^1H NMR spectrum of **2** (500 MHz, 295.0 K, CDCl_3 , 0.0026 M)



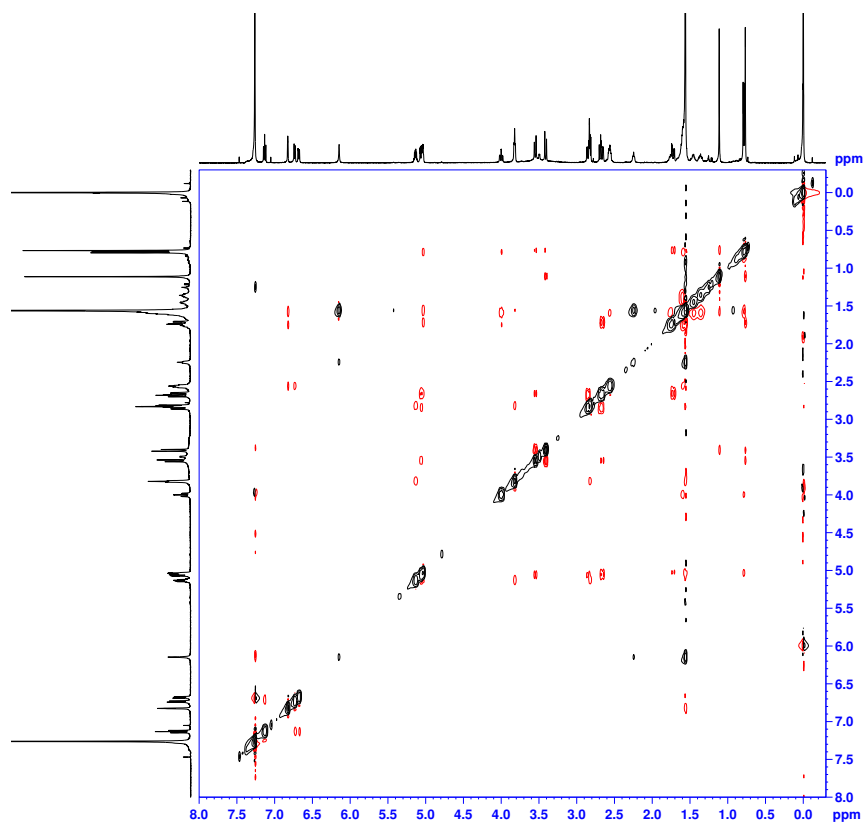
^{13}C NMR spectrum of **2** (125 MHz, 298.0 K, CDCl_3 , 0.0026 M)



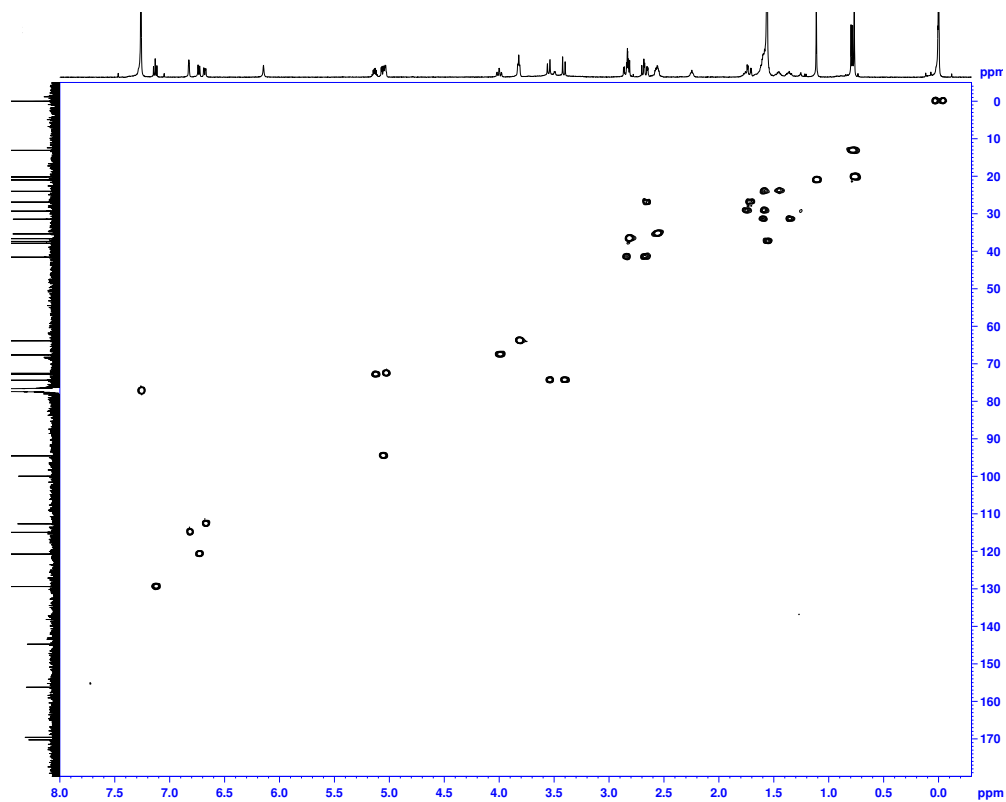
COSY spectrum of **2** (500 MHz, 295.0 K, CDCl₃, 0.0026 M)



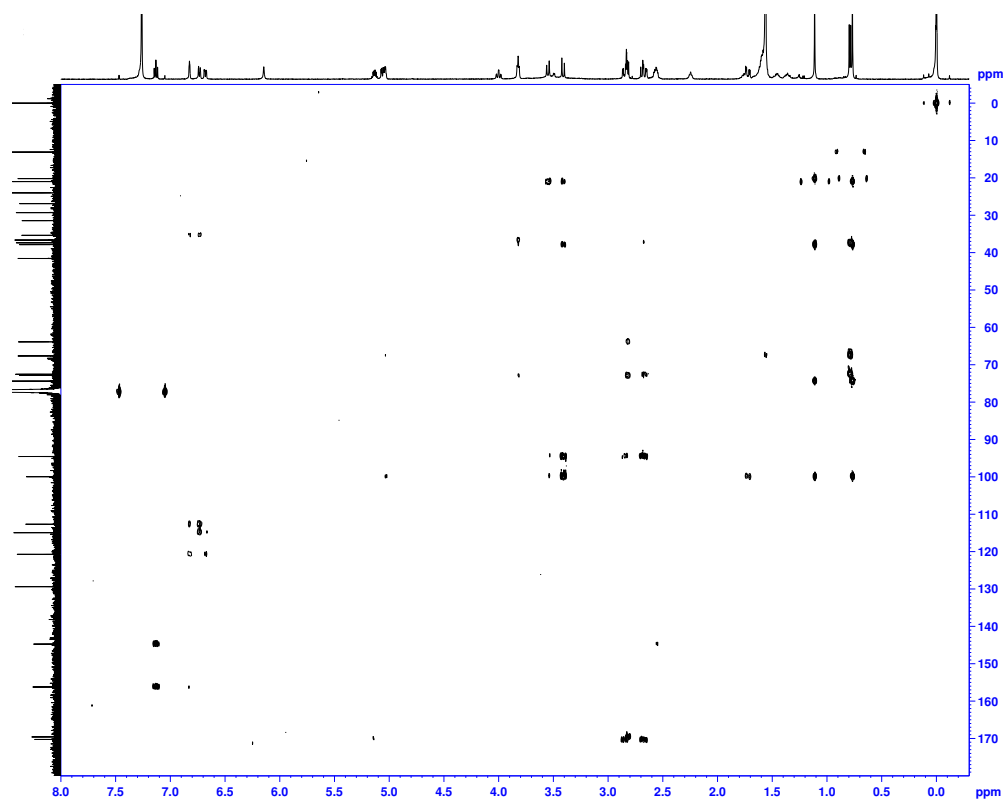
NOESY spectrum of **2** (500 MHz, 295.0 K, CDCl₃, 0.0026 M)



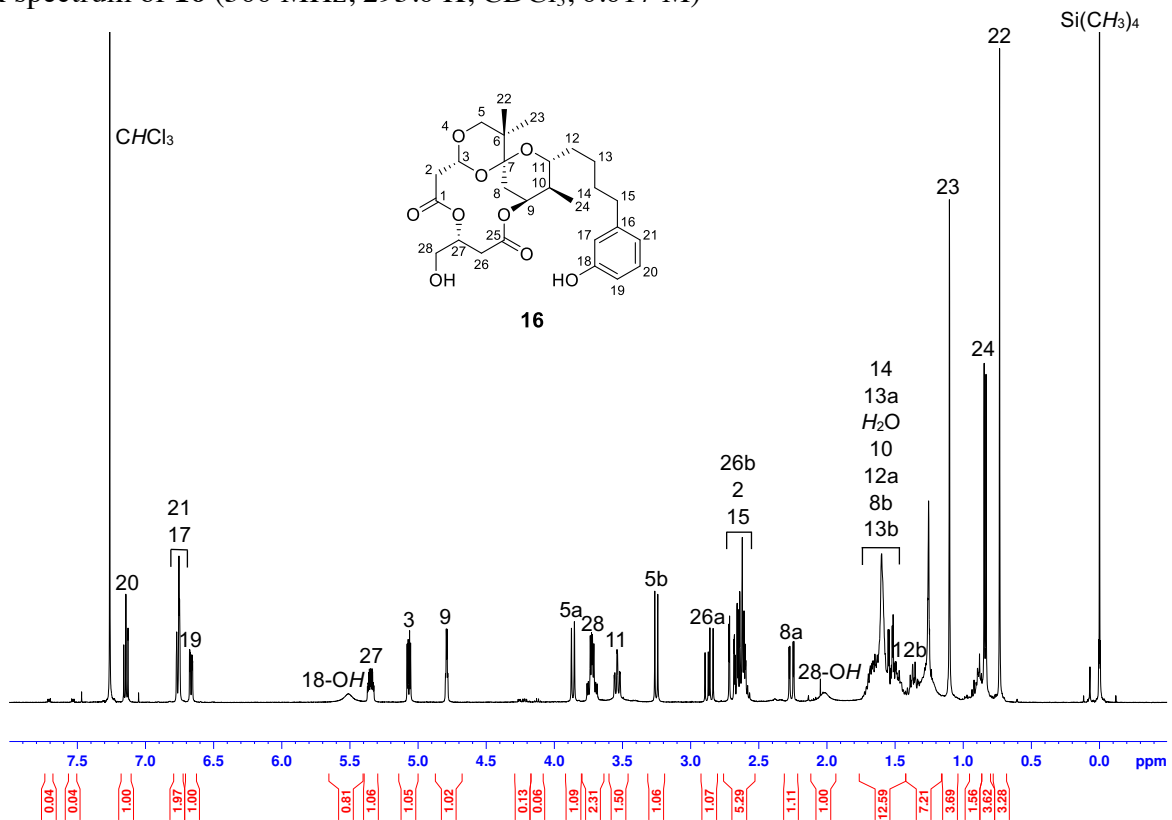
HSQC spectrum of **2** (^1H : 500 MHz, 295.0 K, CDCl_3 , 0.0026 M)



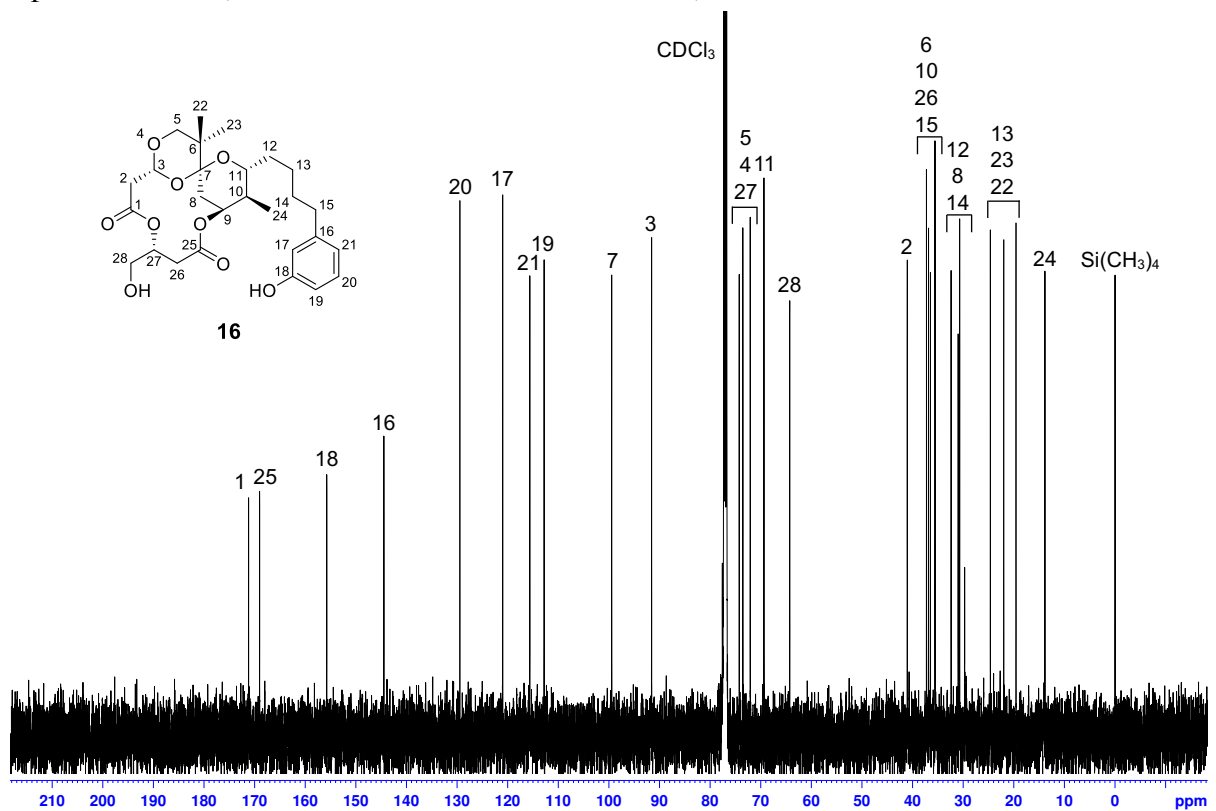
HMBC spectrum of **2** (^1H : 500 MHz, 296.0 K, CDCl_3 , 0.0026 M)



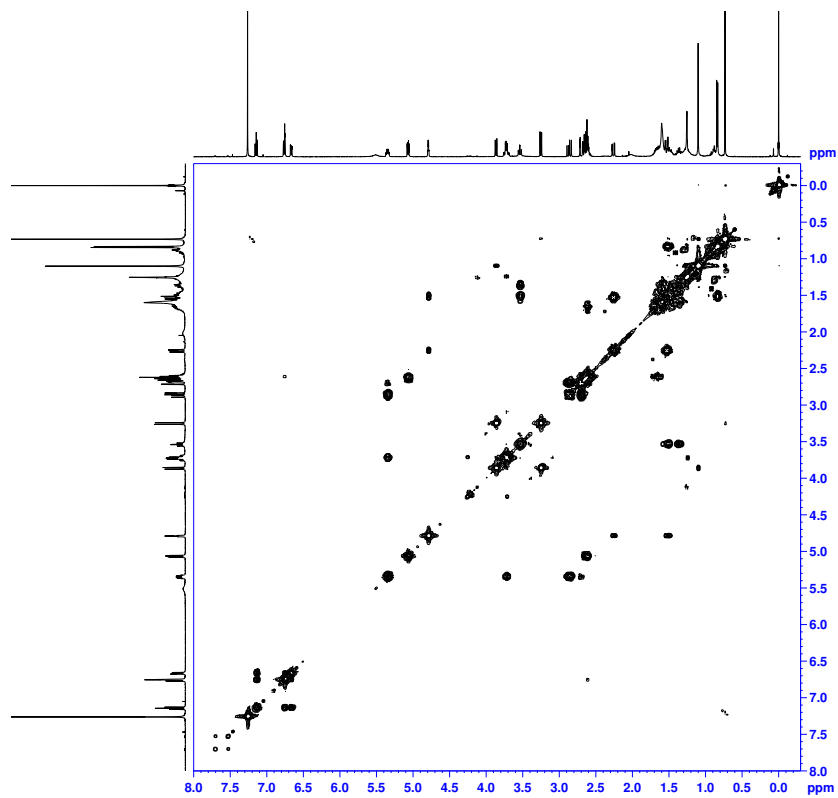
^1H NMR spectrum of **16** (500 MHz, 295.0 K, CDCl_3 , 0.017 M)



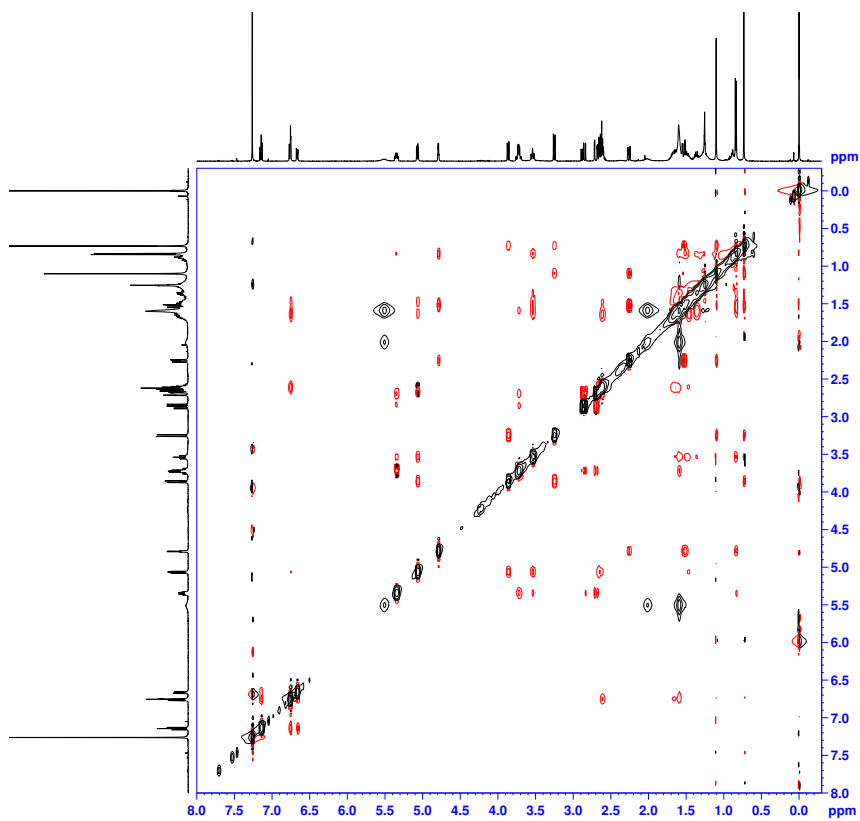
^{13}C NMR spectrum of **16** (125 MHz, 296.0 K, CDCl_3 , 0.017 M)



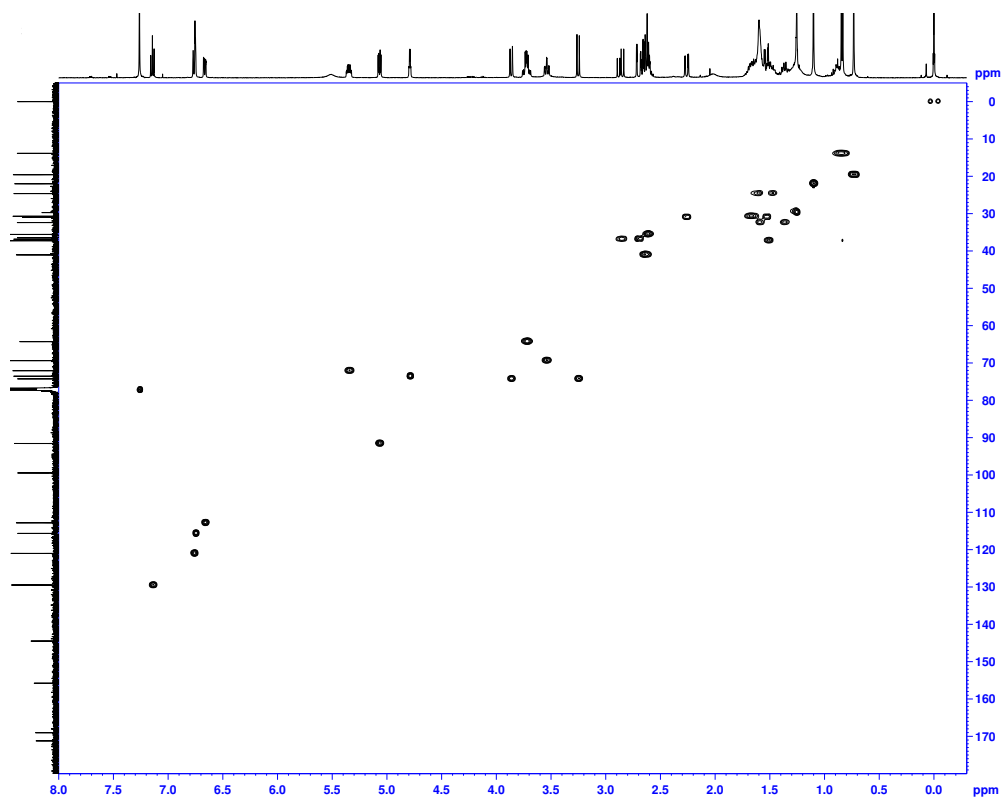
COSY spectrum of **16** (500 MHz, 295.0 K, CDCl₃, 0.017 M)



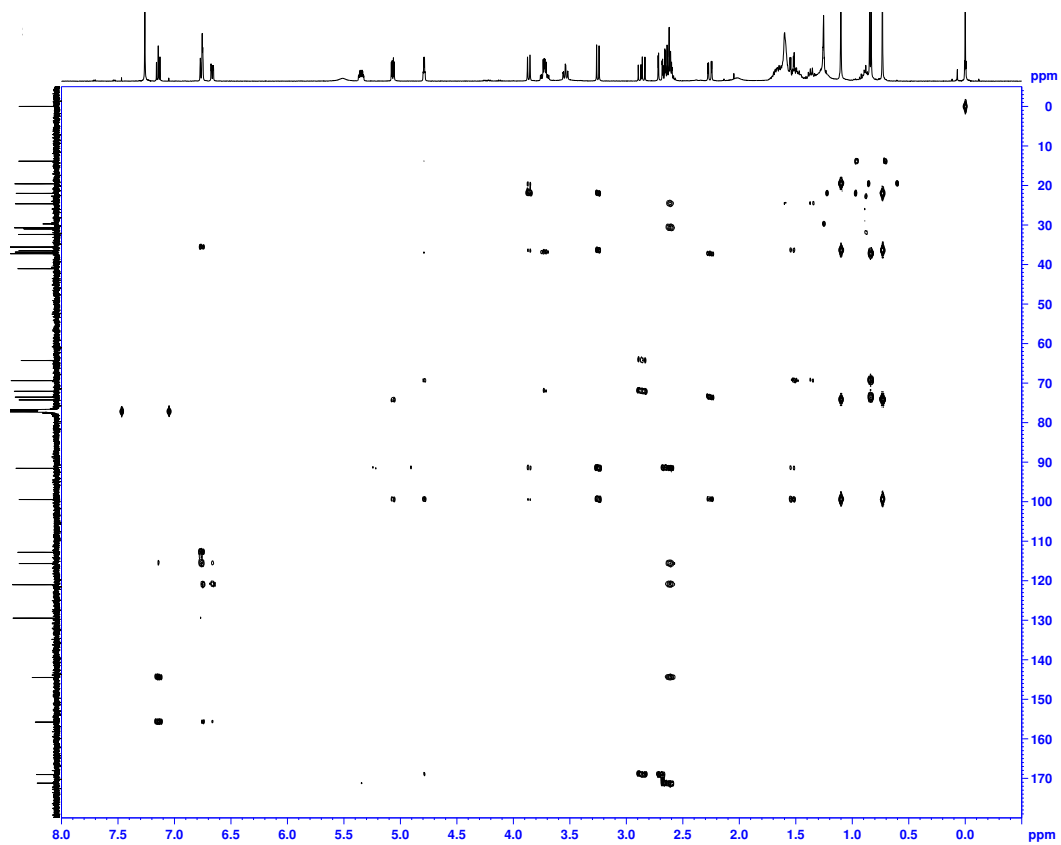
NOESY spectrum of **16** (500 MHz, 295.0 K, CDCl₃, 0.017 M)



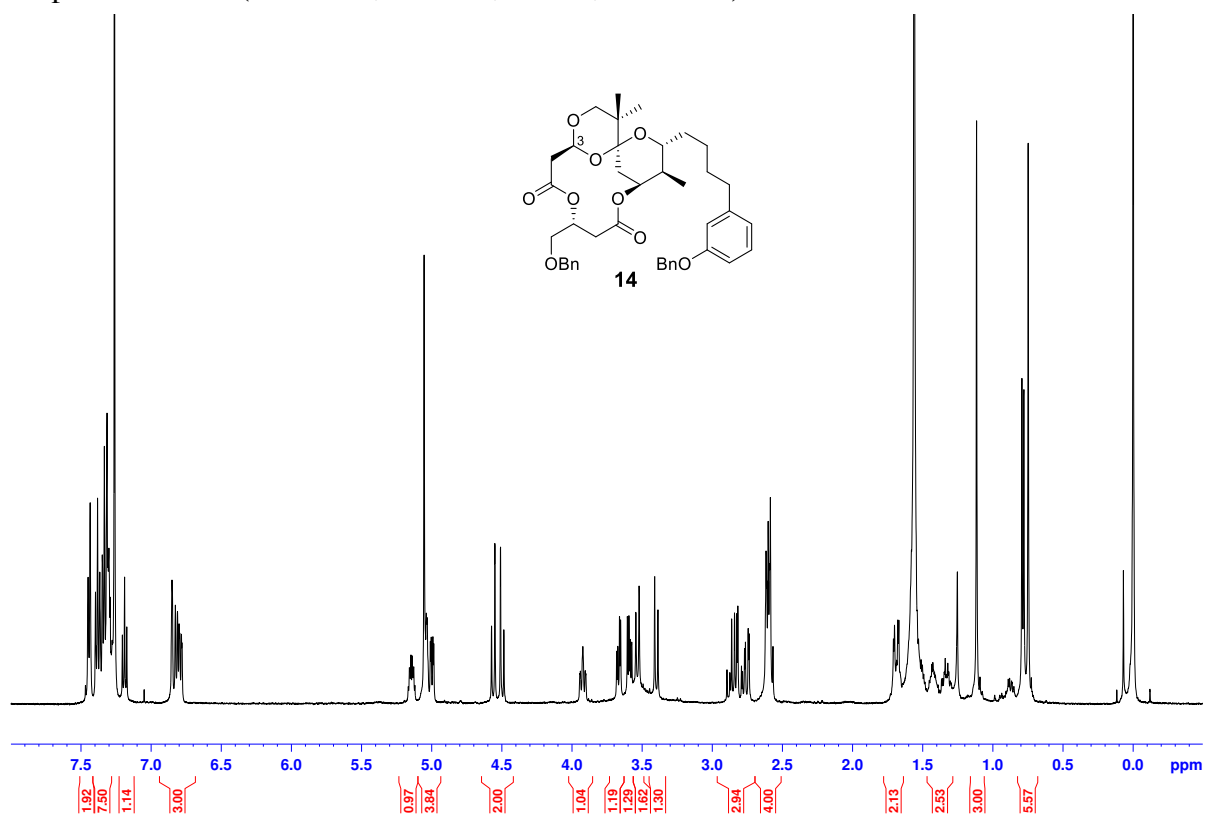
HSQC spectrum of **16** (^1H : 500 MHz, 298.0 K, CDCl_3 , 0.017 M)



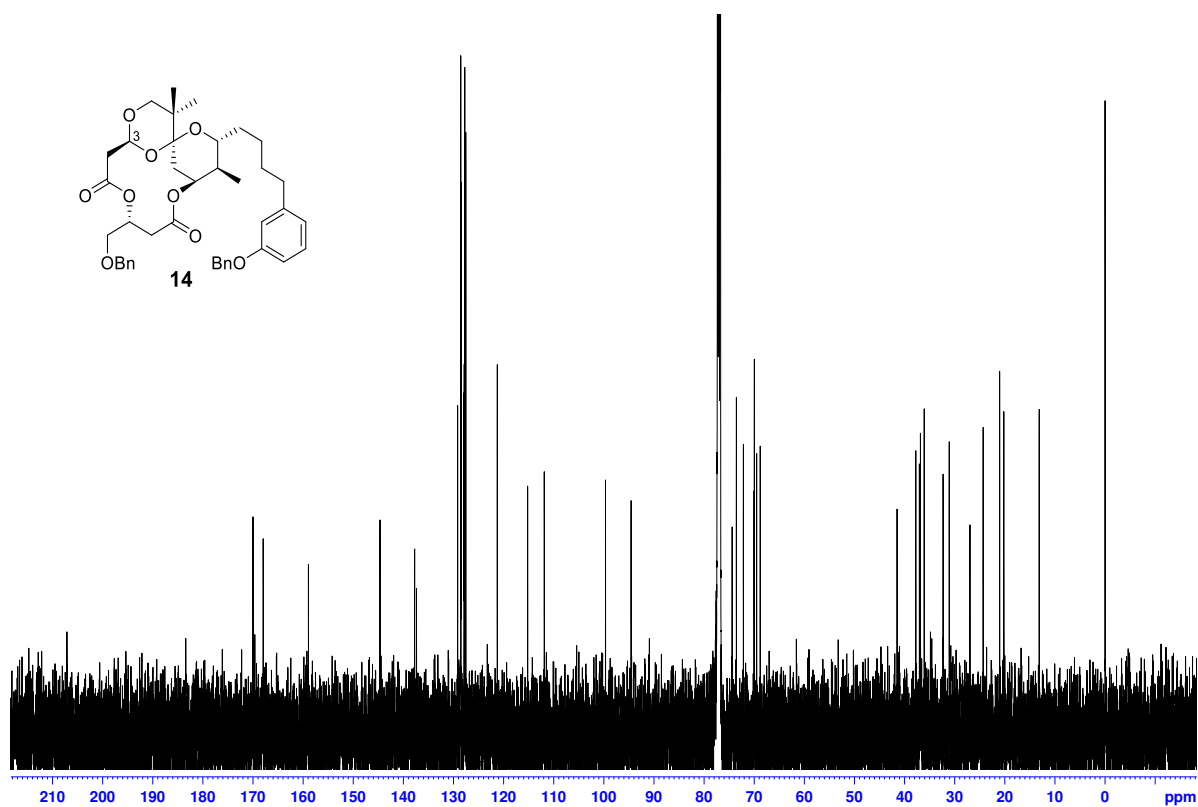
HMBC spectrum of **16** (^1H : 500 MHz, 296.0 K, CDCl_3 , 0.017 M)



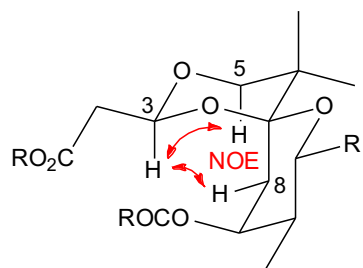
^1H NMR spectrum of **14** (500 MHz, 295.0 K, CDCl_3 , 0.0034 M)



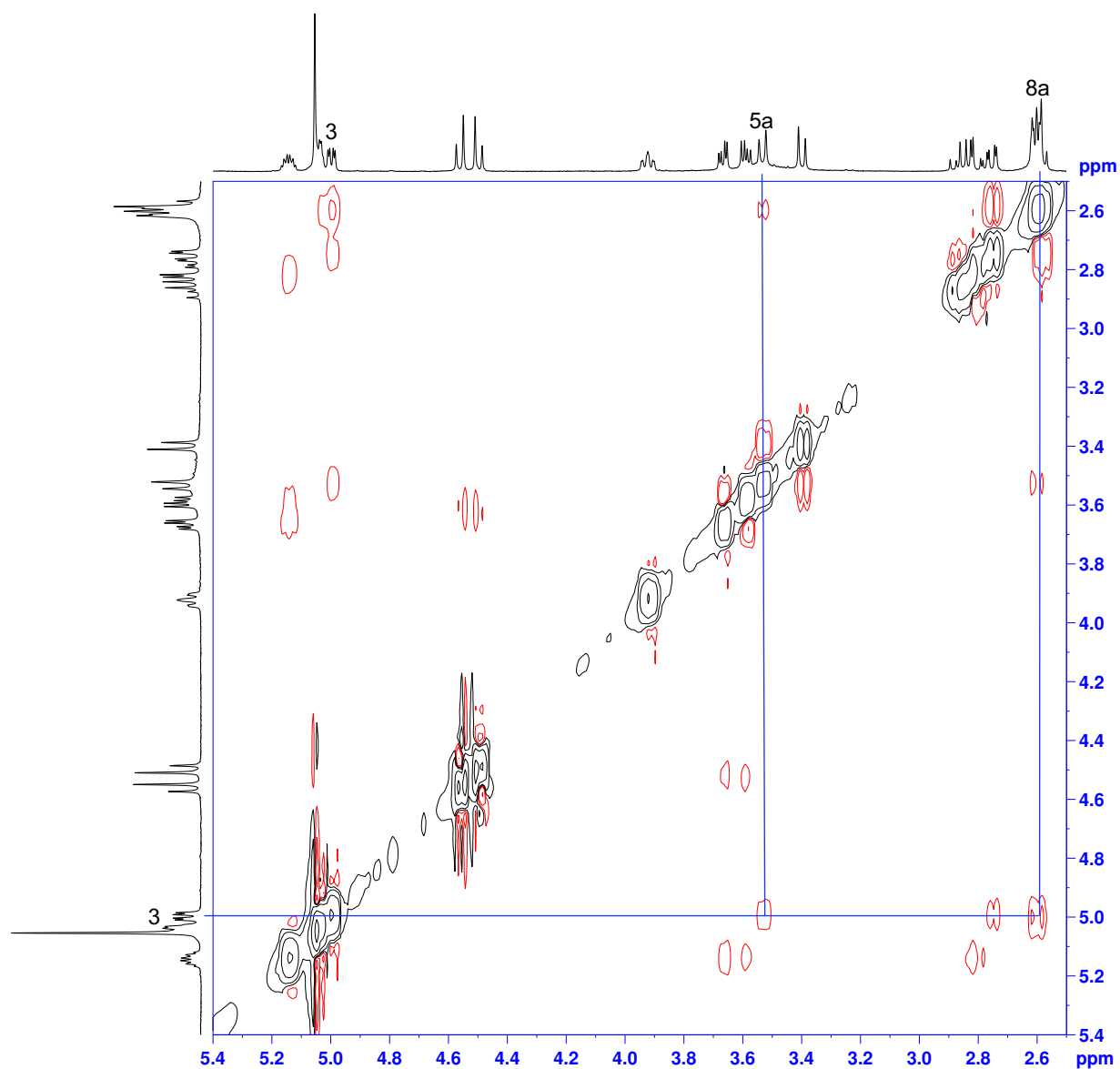
^{13}C NMR spectrum of **14** (125 MHz, 297.0 K, CDCl_3 , 0.0034 M)



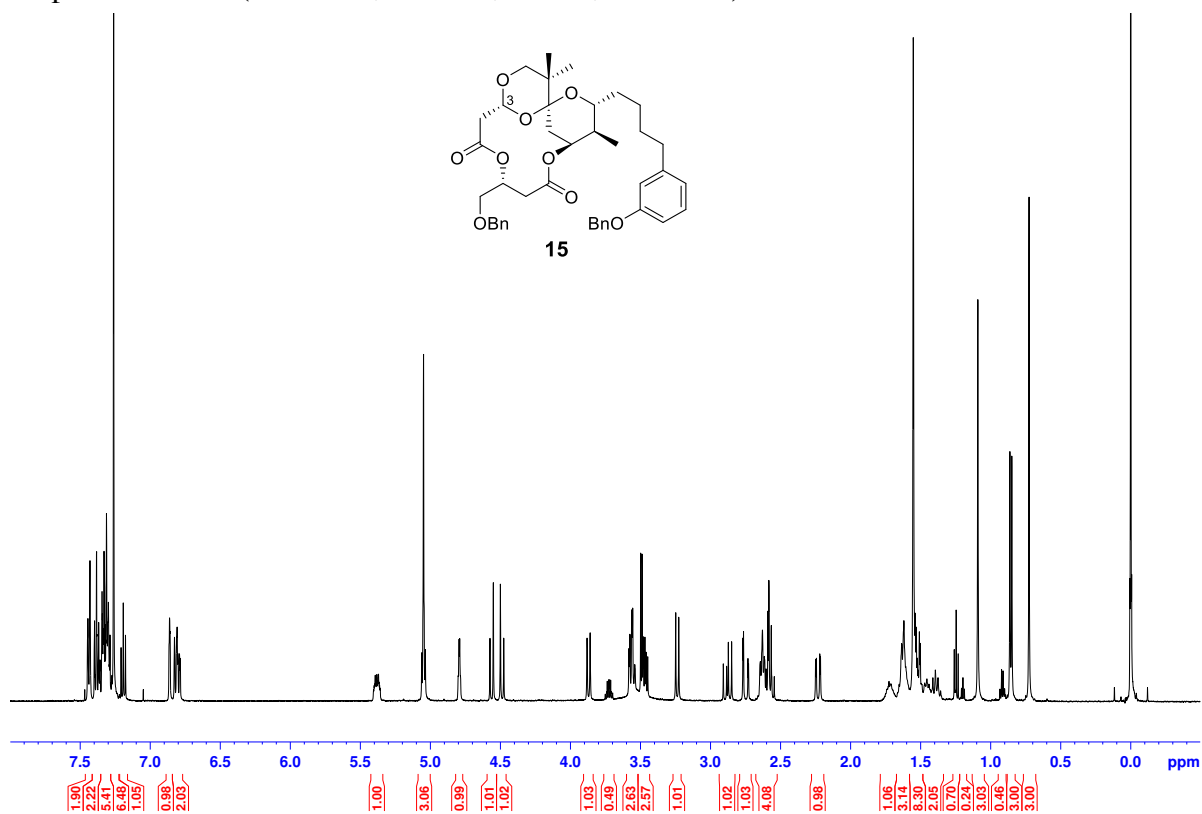
NOESY spectrum of **14** (500 MHz, 295.0 K, CDCl₃, 0.0034 M)



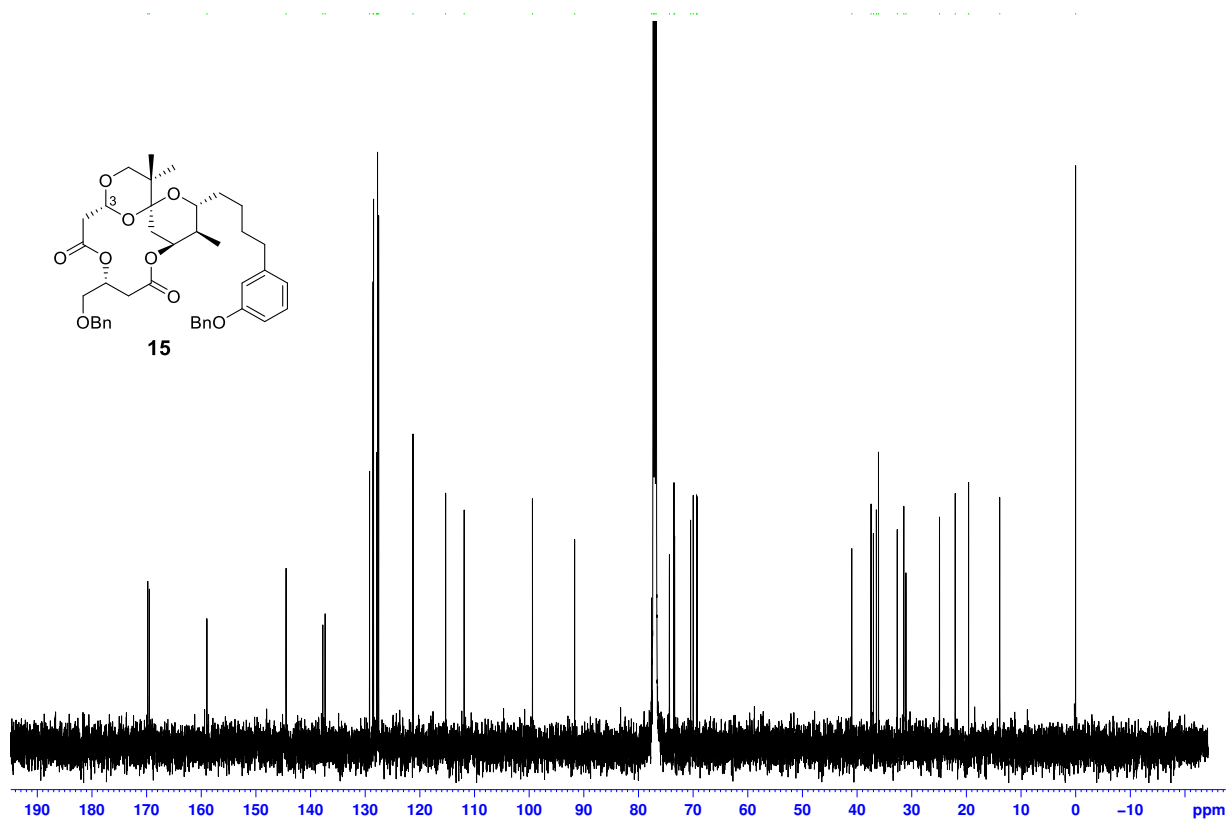
14



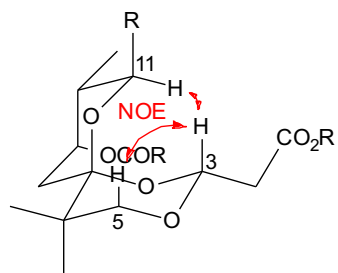
^1H NMR spectrum of **15** (500 MHz, 295.0 K, CDCl_3 , 0.0076 M)



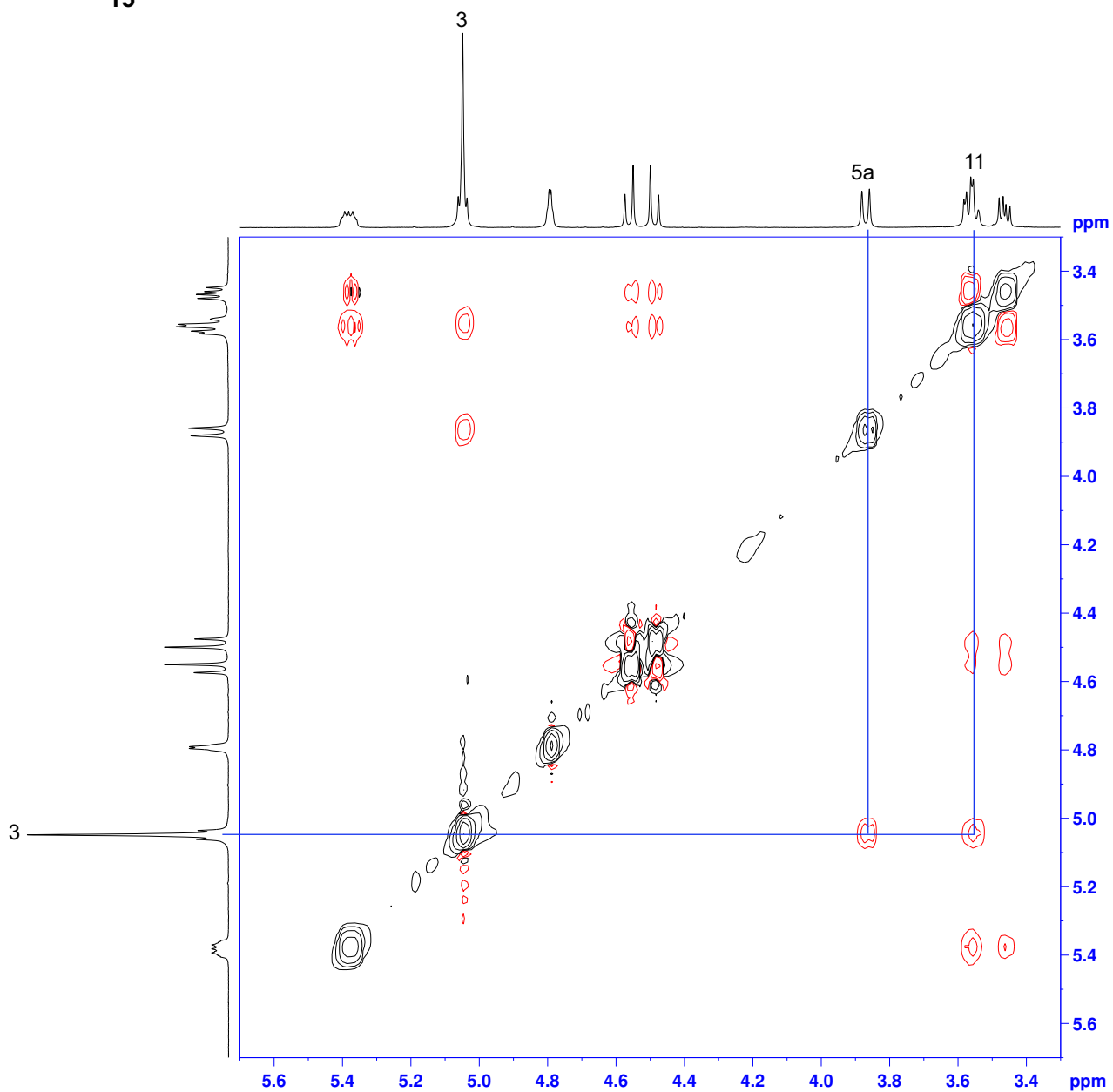
^{13}C NMR spectrum of **15** (125 MHz, 297.0 K, CDCl_3 , 0.0076 M)



NOESY spectrum of **15** (500 MHz, 295.0 K, CDCl₃, 0.010 M)

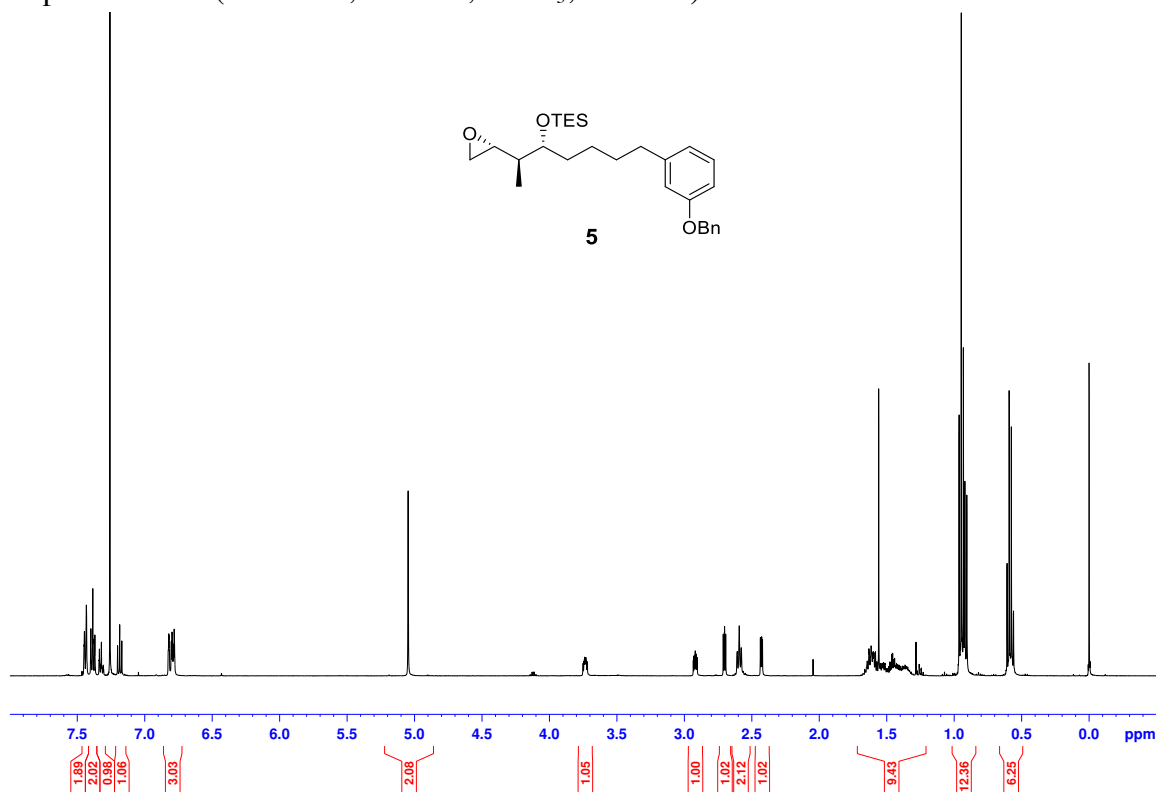


15

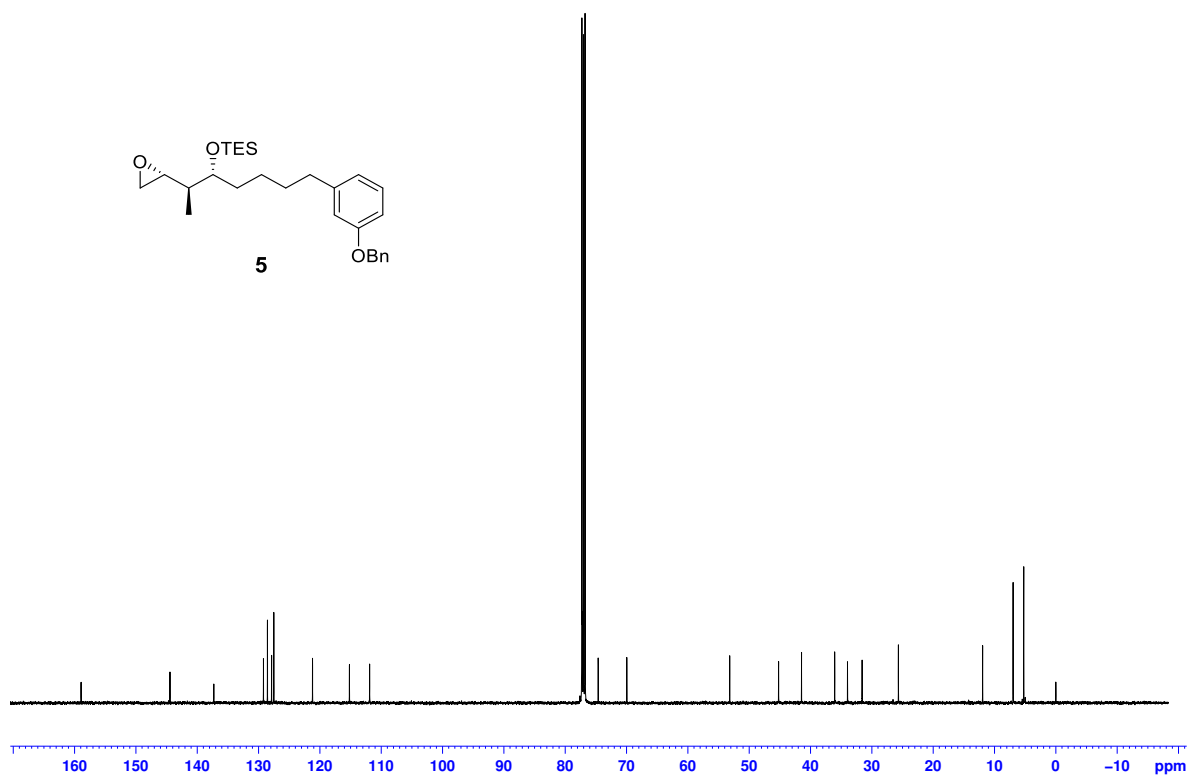


III. ^1H and ^{13}C NMR Spectra of Other Intermediates

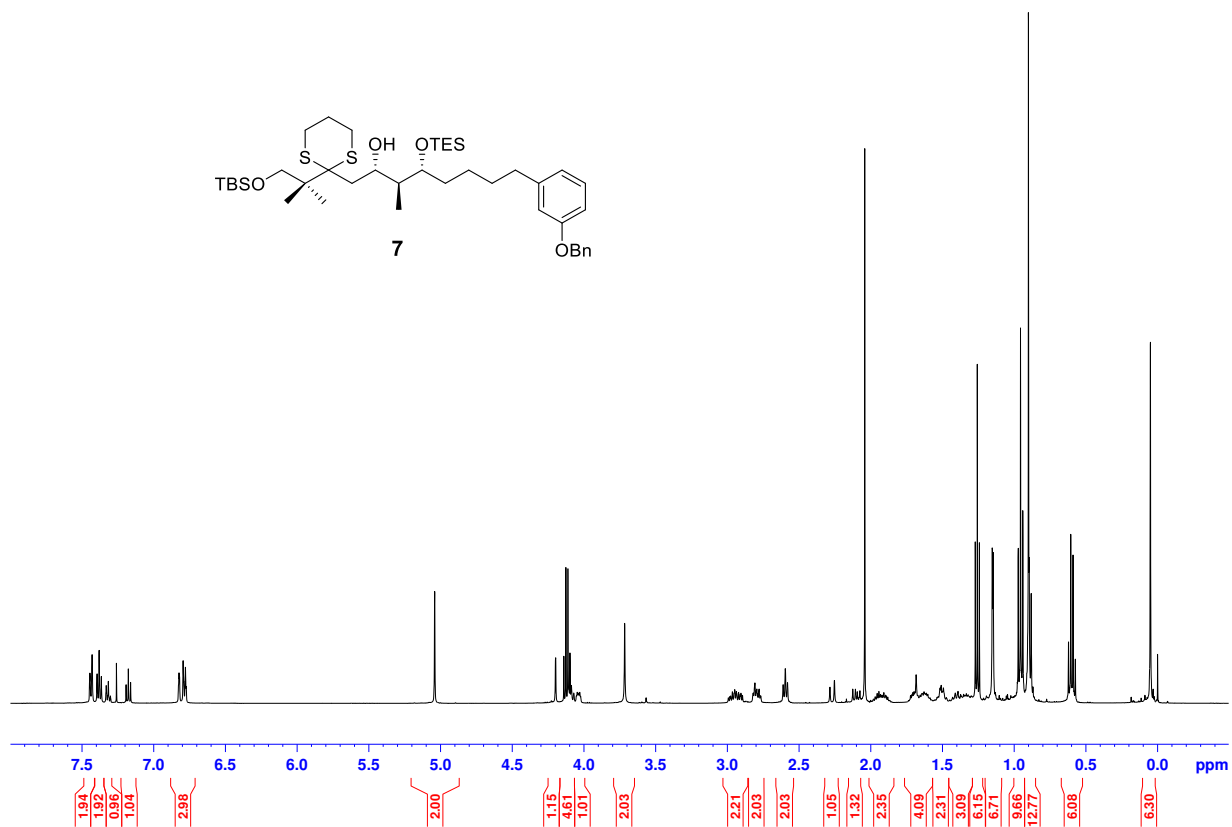
^1H NMR spectrum of **5** (500 MHz, 295.0 K, CDCl_3 , 0.043 M)



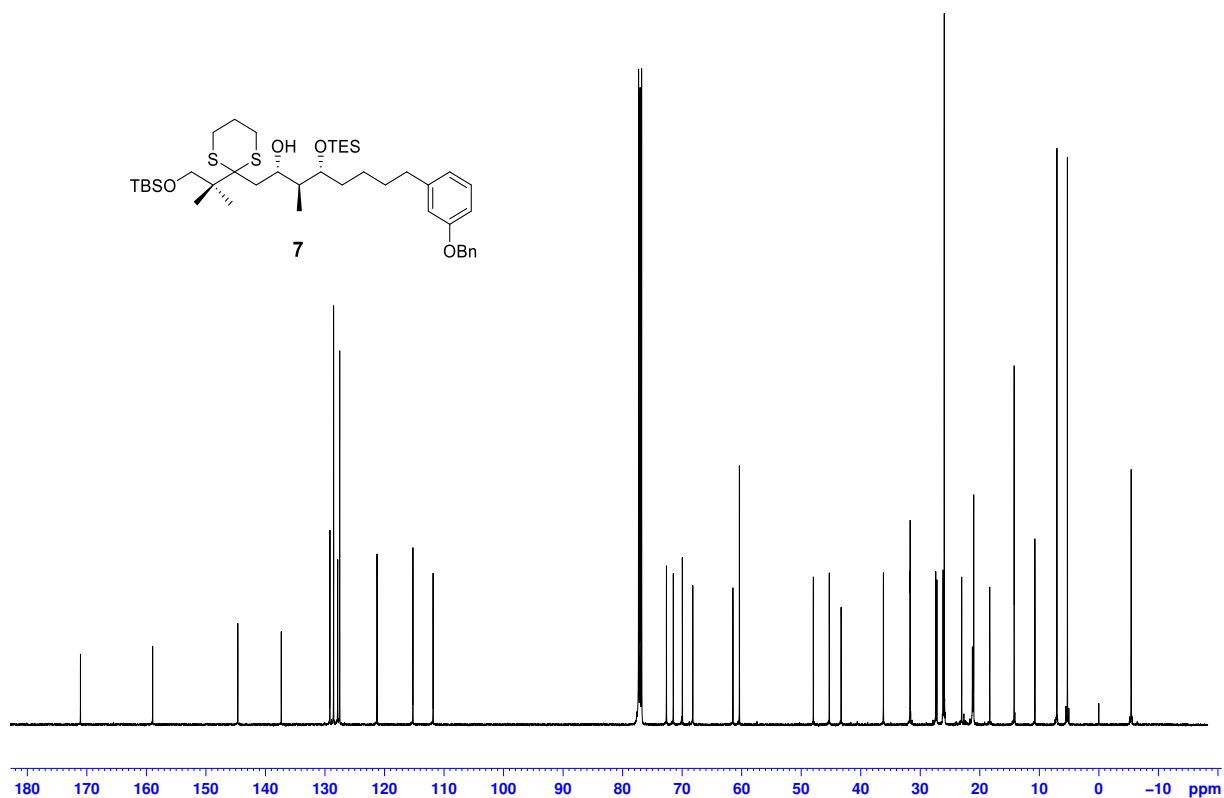
^{13}C NMR spectrum of **5** (125 MHz, 297.0 K, CDCl_3 , 0.043 M)



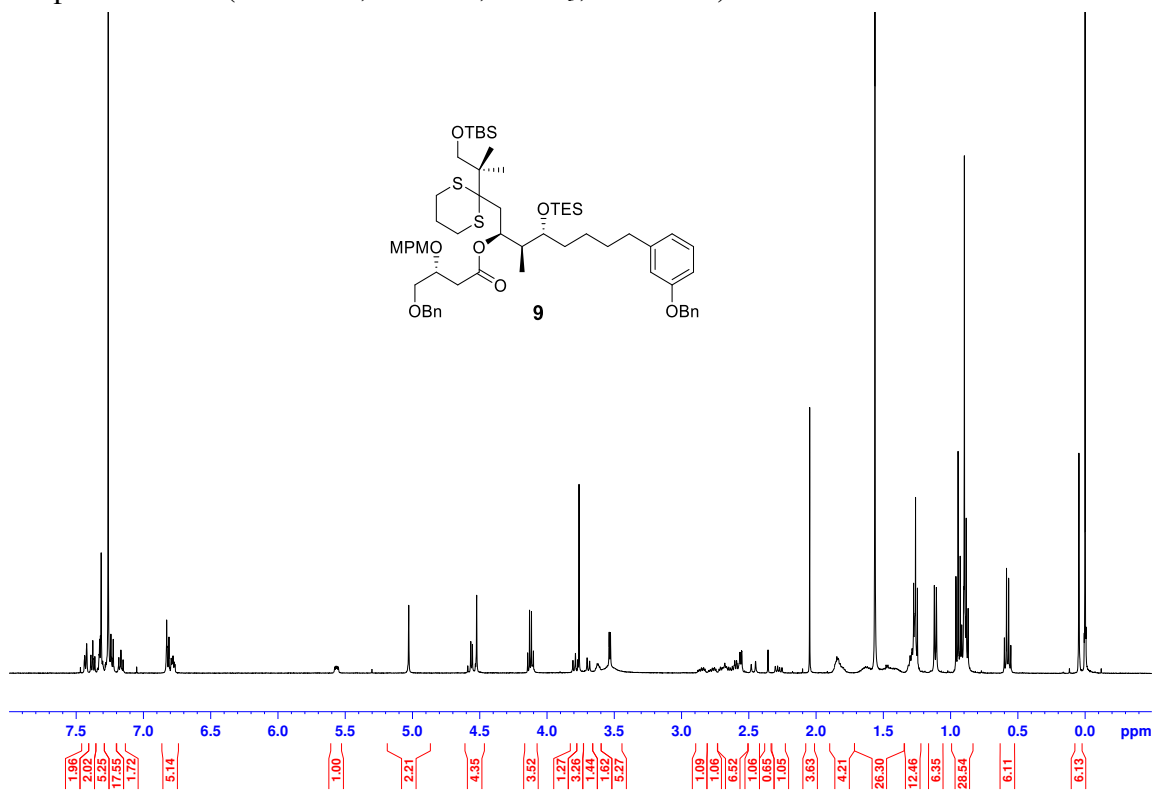
^1H NMR spectrum of **7** (500 MHz, 295.0 K, CDCl_3 , 0.022 M)



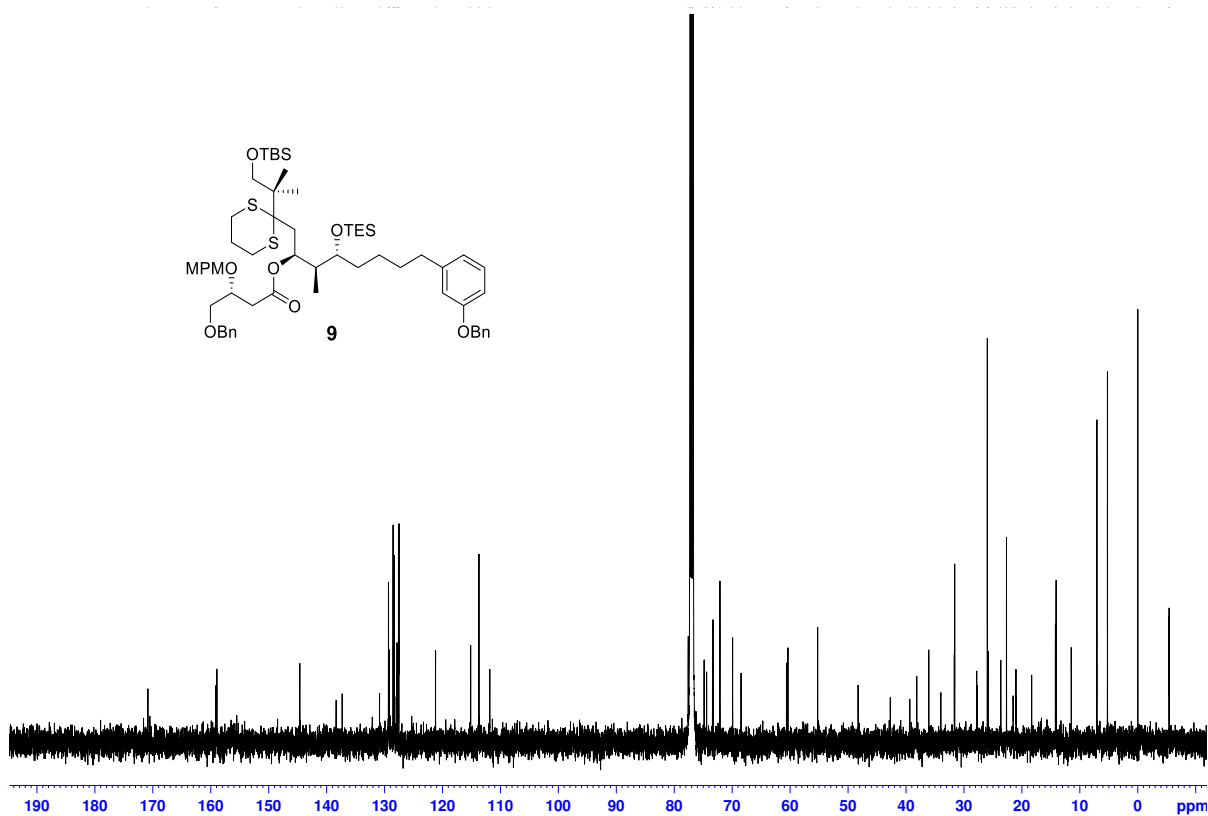
^{13}C NMR spectrum of **7** (125 MHz, 296.0 K, CDCl_3 , 0.022 M)



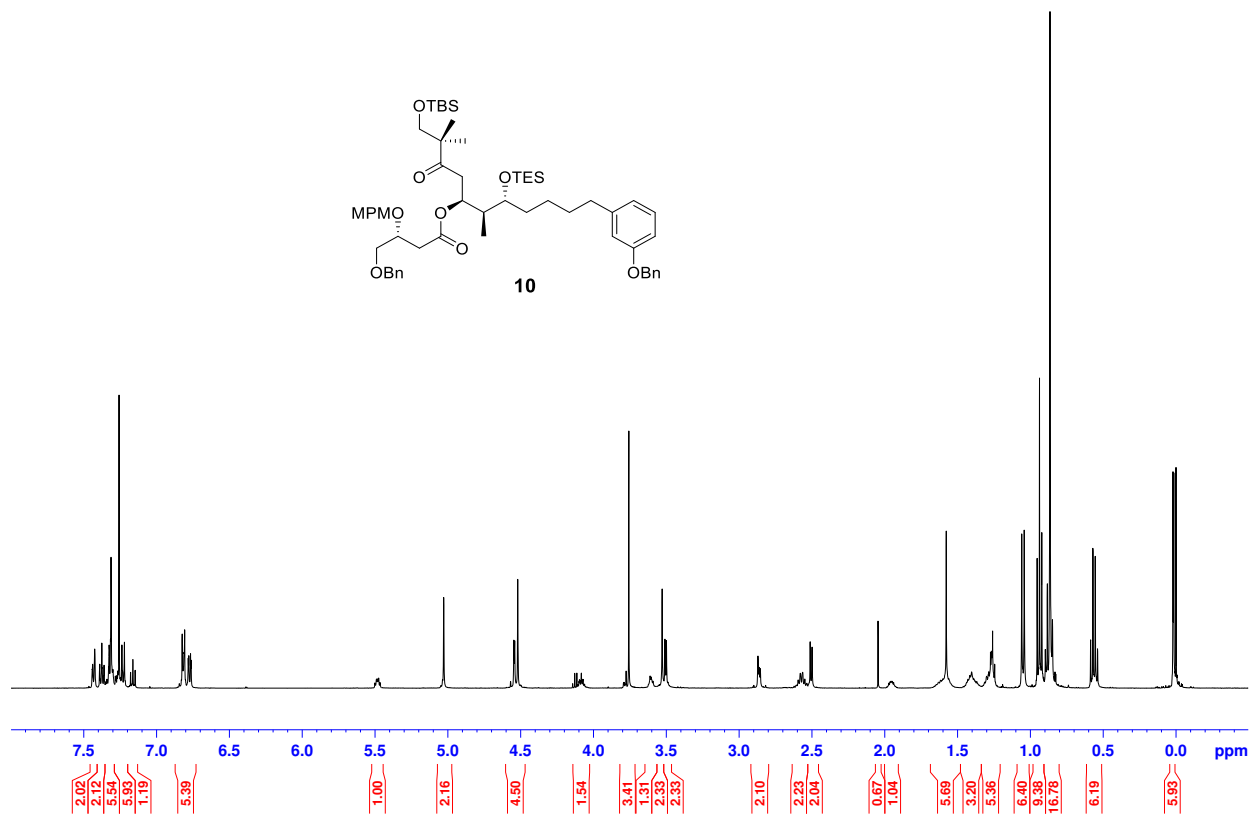
^1H NMR spectrum of **9** (500 MHz, 295.0 K, CDCl_3 , 0.0063 M)



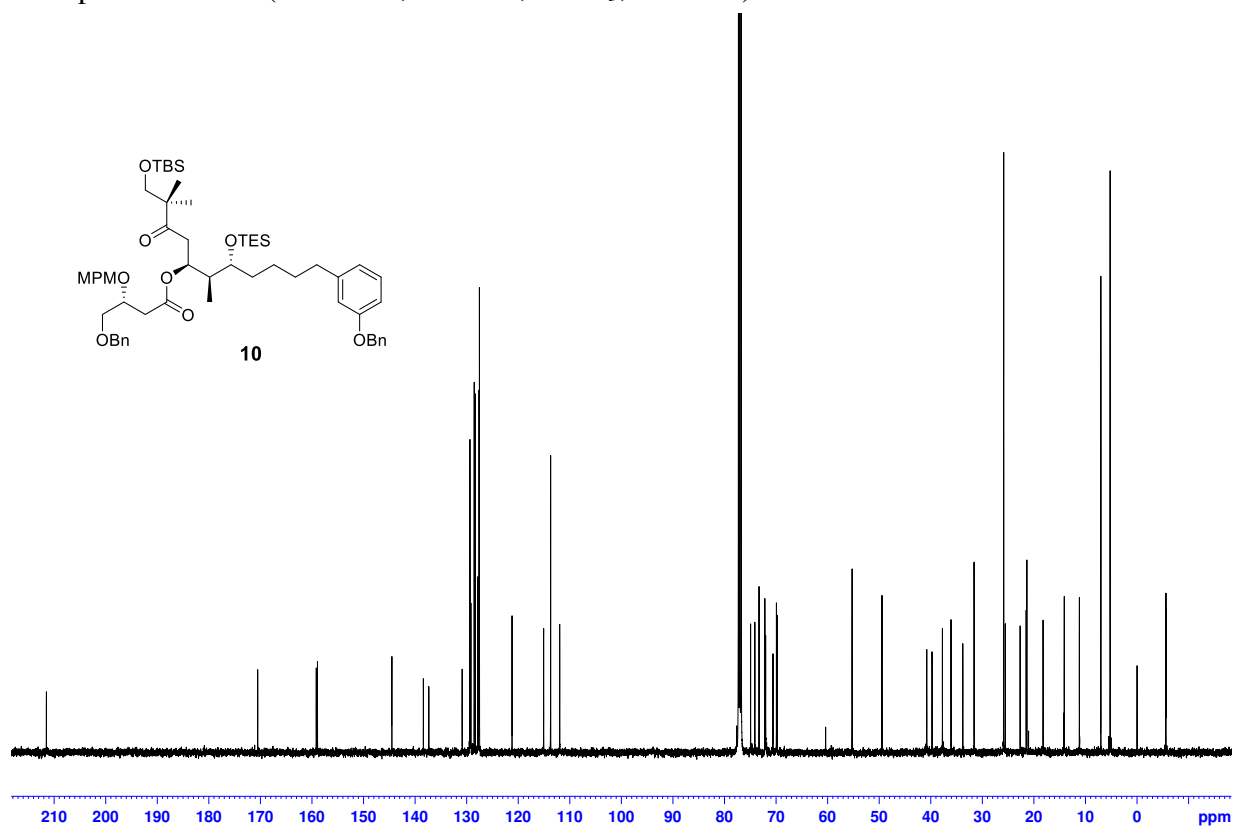
^{13}C NMR spectrum of **9** (125 MHz, 296.0 K, CDCl_3 , 0.0063 M)



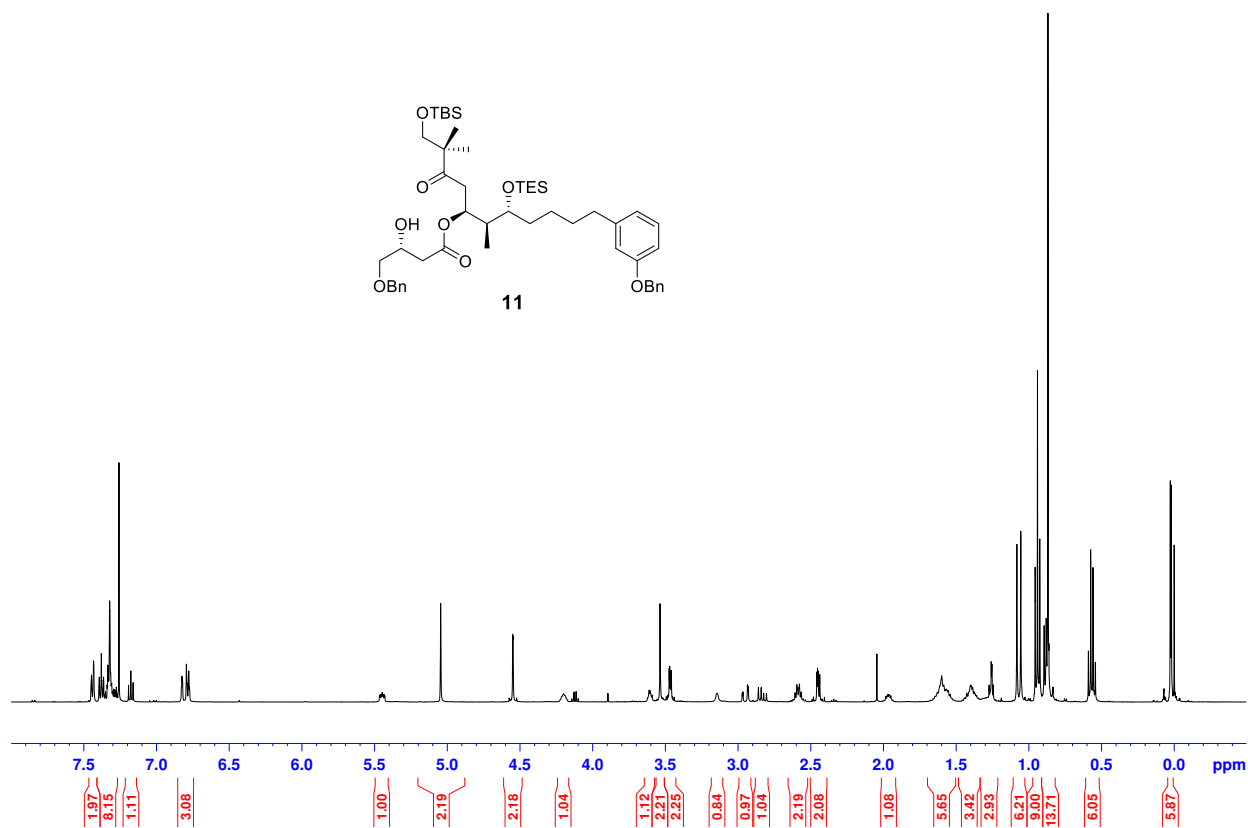
^1H NMR spectrum of **10** (500 MHz, 295.0 K, CDCl_3 , 0.032 M)



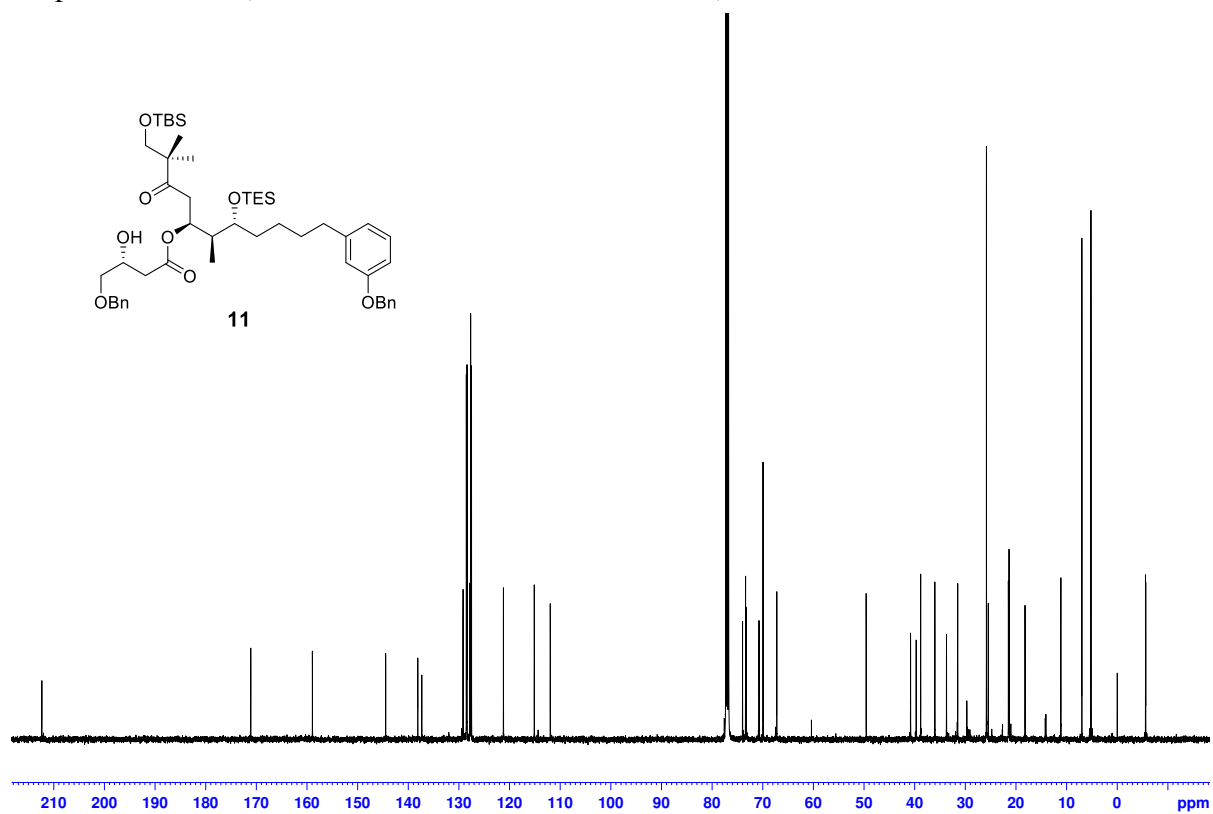
^{13}C NMR spectrum of **10** (125 MHz, 297.0 K, CDCl_3 , 0.032 M)



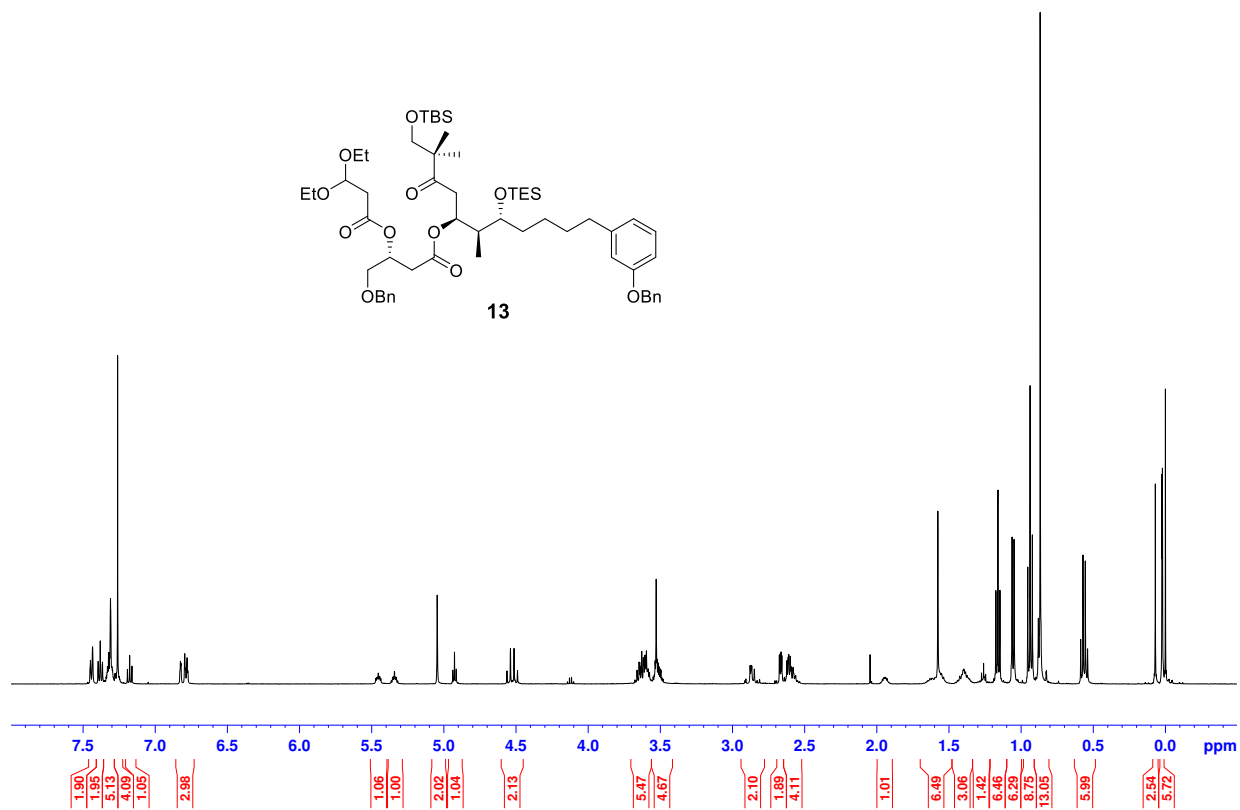
^1H NMR spectrum of **11** (500 MHz, 295.0 K, CDCl_3 , 0.037 M)



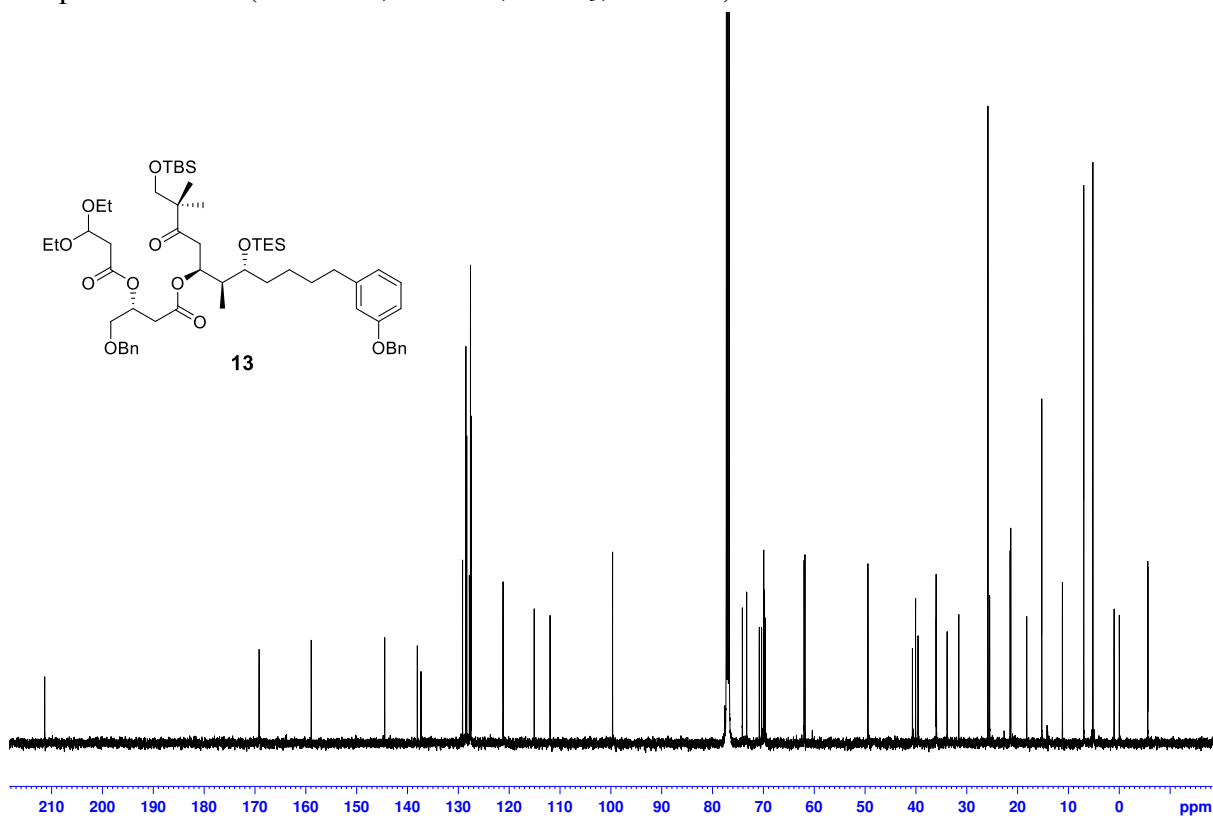
^{13}C NMR spectrum of **11** (125 MHz, 296.0 K, CDCl_3 , 0.037 M)



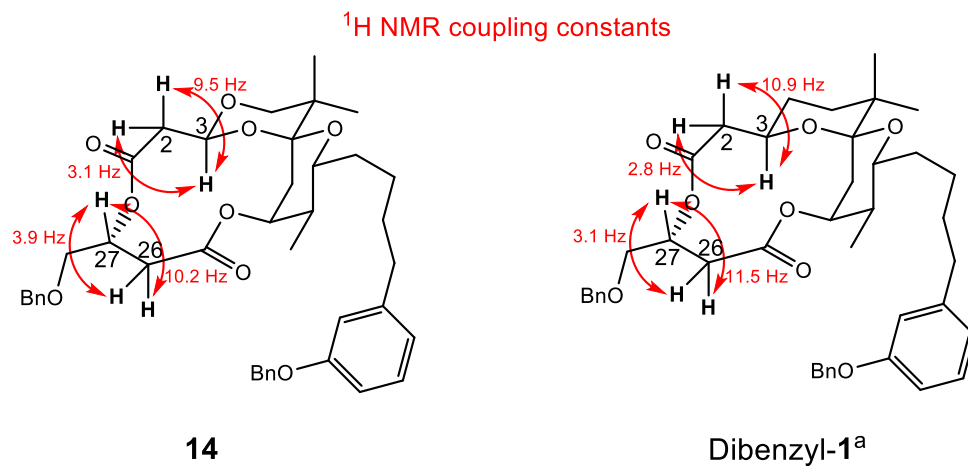
^1H NMR spectrum of **13** (500 MHz, 295.0 K, CDCl_3 , 0.029 M)



^{13}C NMR spectrum of **13** (125 MHz, 296.0 K, CDCl_3 , 0.029 M)



IV. ^1H NMR Coupling Constants of **14** and Dibenzyl-**1**



^aM. Kikumori, R. C. Yanagita, and K. Irie, *Tetrahedron*, 2014, **70**, 9776.