

Supporting Information for

Potent Antitumor Mimetics of Annonaceous Acetogenins Embedded with an Aromatic Moiety in the Left Hydrocarbon Chain Part

Qicai Xiao,[†] Yongqiang Liu,[#] Yatao Qiu,[†] Guangbiao Zhou,[#] Chan Mao,[‡] Zheng Li,^Φ Zhu-Jun Yao,^{‡*} Sheng Jiang^{†*}

[†]Laboratory of Regenerative Biology, Guangzhou Institute of Biomedicine and Health, Chinese Academy of Sciences, Guangzhou 510530, China

[#]Laboratory of Molecular Carcinogenesis and Targeted Therapy for Cancer, State Key Laboratory of Biomembrane and Membrane Biotechnology, Institute of Zoology, Chinese Academy of Sciences, Beijing, 100101, China

[‡]School of Chemistry and Chemical Engineering, Nanjing National Laboratory of Microstructures, Nanjing University, 22 Hankou Road, Nanjing 210093, China

^ΦDepartment of Radiology, the Methodist Hospital Research Institute, Houston TX 77030, USA

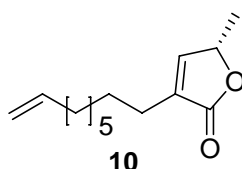
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* jiang_sheng@gibh.ac.cn; or yaoz@nju.edu.cn

1. Chemistry

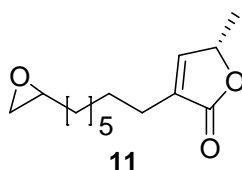
General Experimental Methods: ^1H NMR and ^{13}C NMR spectra were recorded on Bruker Avance ARX- 400 (or Bruker Avance ARX- 500). Mass spectra were performed on Kompact Axima-CFR MALDI mass spectrometers. Optical rotations were recorded on a Perkin Elmer 341 polarimeter. Anhydrous solvents were obtained as follows: THF by distillation from sodium and benzophenone; dichloromethane from CaH_2 . All other solvents were reagent grade. All moisture sensitive reactions were carried out in flame dried flask under argon atmosphere.



(S)-5-methyl-3-(non-8-enyl)furan-2(5H)-one (10)

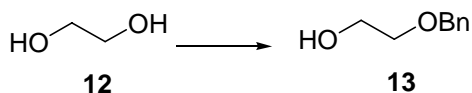
To a solution of diisopropylamine (6.4 mL, 0.046 mol) in anhydrous THF (100 mL) was added $n\text{-BuLi}$ (18.2 mL, 1.6 M in hexane, 0.046 mol) at 0 °C, and the mixture was stirred for 30 min. After the mixture was stirred for an additional 30 min at -78 °C, anhydrous HMPA (10.6 mL, 0.065 mol) was added, and the mixture was stirred for 30 min. A solution of **9** (6.0 g, 0.03 mol) in THF (20 mL) was injected into the above mixture. After 30 min, a solution of O-THP-(S)-lactal (5.8 g, 0.036 mol) in THF (30 mL) was introduced, and the reaction mixture was stirred for 2 h at -78 °C. The mixture was quenched with saturated aqueous NH_4Cl and extracted with ether. The organic layer was washed with brine and dried (Na_2SO_4). Removal of the solvents afforded a crude oil, which was treated with 10% H_2SO_4 (60 mL) in THF (100 mL) for 20 h at rt. The reaction mixture was diluted with ether, washed with saturated aqueous NaHCO_3 and brine, dried (Na_2SO_4), and evaporated to give a crude oil. To the mixture of the above oil and Et_3N (17 mL, 0.12 mol) in CH_2Cl_2 (50 mL) at 0 °C was added $(\text{CF}_3\text{CO})_2\text{O}$ (8 mL, 0.061 mmol). The reaction was stirred at 0 °C for 12 h and at rt for 6 h, quenched with saturated NH_4Cl , and extracted with CH_2Cl_2 .

After being dried (Na_2SO_4), the extracts were filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel to afford pure **10** (4.47 g, 67%). $[\alpha]_{\text{D}}^{25} = +46.28$ (c 0.72, CHCl_3); ^1H NMR (400 MHz, CDCl_3): 6.98 (d, $J = 2.8$ Hz, 1H), 5.80 (ddt, $J = 16.8, 10.2, 6.4$ Hz, 1H), 5.01-4.78 (m, 3H), 2.26 (m, 2H), 2.05 (m, 2H), 1.54 (m, 2H), 1.40 (d, $J = 6.8$ Hz, 3H), 1.31 (brs, 8H) ppm; MS (EI, m/z): 223 $[\text{M}+\text{H}]^+$. Anal. calcd for $\text{C}_{14}\text{H}_{22}\text{O}_2$ (%): C, 75.68; H, 9.91. Found: C, 75.30; H, 9.54.



(5S)-5-methyl-3-(7-(oxiran-2-yl)heptyl)furan-2(5H)-one (11)

To a 100 mL flask were added **10** (2.22 g, 10.0 mmol), dry CH_2Cl_2 (30 mL), and MCPBA (1.73 g, 10.0 mmol) in dry CH_2Cl_2 (20 mL) at 0 °C under a N_2 atmosphere. The reaction mixture was stirred at rt for 12 h. Excess MCPBA was removed by the addition of aqueous sodium thiosulfate. The mixture was transferred to a separating funnel. The organic layer was diluted with CH_2Cl_2 (20 mL), washed successively with saturated NaHCO_3 and saturated brine, and then dried over Na_2SO_4 . The solvent was removed under reduced pressure, and the residue was chromatographed on silica gel to give **11** as a colorless oil (2.05 g, 86%). ^1H NMR (400 MHz, CDCl_3): δ 6.96 (d, $J = 2.8$ Hz, 1H), 4.95 (dq, $J = 6.8, 1.7$ Hz, 1H), 2.85 (m, 1H), 2.71-2.68 (m, 1H), 2.41 (dd, $J = 5.0, 2.7$ Hz, 1H), 2.21 (t, $J = 7.7$ Hz, 2H), 1.51-1.29 (m, 12H), 1.36 (d, $J = 6.8$ Hz, 3H) ppm. ^{13}C NMR (100 MHz, CDCl_3): δ 173.7, 148.9, 134.2, 77.3, 52.2, 46.9, 32.4, 29.2, 29.1, 29.0, 27.3, 25.8, 25.1, 19.1 ppm. MS (ESI, m/z): 239 $[\text{M}+1]^+$.



2-(benzyloxy)ethanol (13). To a mixture of sodium hydride (5.10 g, 0.17 mol, 80%, w/w) in 300 mL dried THF was added dry ethylene glycol (50.2 mL, 0.9 mol) at room temperature over 1 h, stirred another 0.5 h, and a large amount of white precipitate had formed. Then the mixture was refluxed and benzyl bromide (17.8 mL, 0.15 mol) was added over 2 h. The mixture was refluxed for 15 h, cooled to room temperature, quenched with saturated aqueous NH₄Cl (5 mL) solution and evaporated THF through reduced pressure. The residue was extracted with ethyl acetate (30 mL × 3). The combined organic layers were washed with saturated aqueous NH₄Cl solution and brine, dried over anhydrous Na₂SO₄, filtered and concentrated under reduced pressure. The resulting oil was distilled under reduced pressure to afford **13** (18.5 g, 81%) as a colorless oil. ¹H NMR (400 MHz, CDCl₃): δ 7.35-7.29 (m, 5H), 4.57 (s, 2H), 3.78-3.74 (m, 2H), 3.62-3.59 (m, 2H), 2.10 (br, 1H, OH) ppm.

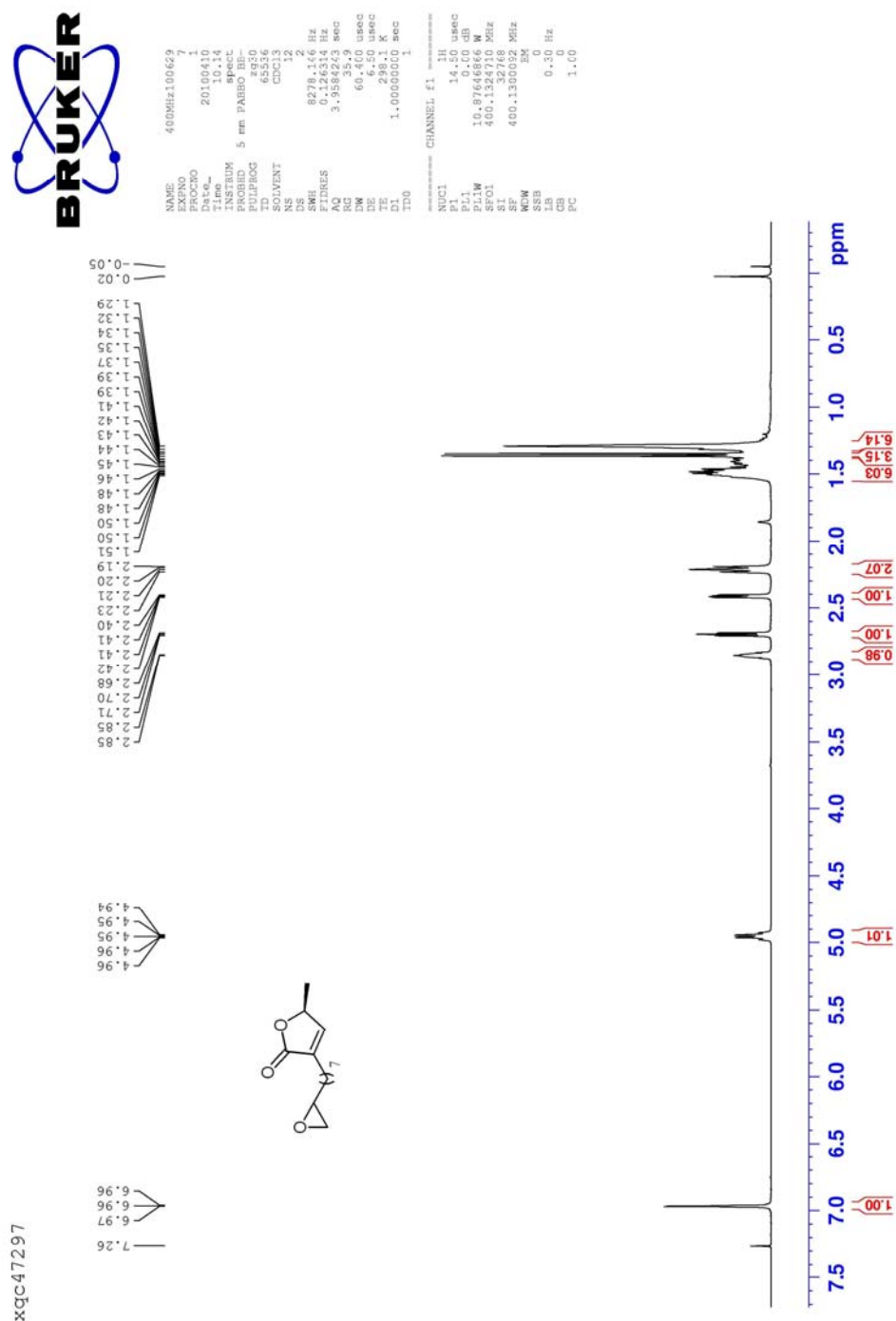
2. RP-HPLC Data of the Compounds 2–8.

Table S1

compounds	t _R	purity	methanol/water	MS calcd	HRMS
2	5.41	99%	88%	515.3942	515.3939
3	8.72	98%	88%	591.4231	591.4234
4	10.59	96%	78%	549.3786	549.3784
5	7.06	97%	78%	587.3786	587.3555
6	8.45	95%	75%	601.3711	601.3712
7	8.36	97%	85%	647.3918	647.3915
8	7.91	99%	78%	651.3876	651.3865

^a Analytical HPLC method: Agilent C18 column (250 × 4.6 mm); solvent system, A, 0.05% TFA in water; B, methanol; B in water over 30 min; flow rate, 1.0 mL/min; wavelength, 215 nm. ^c Purified products were further characterized by mass spectrometers.

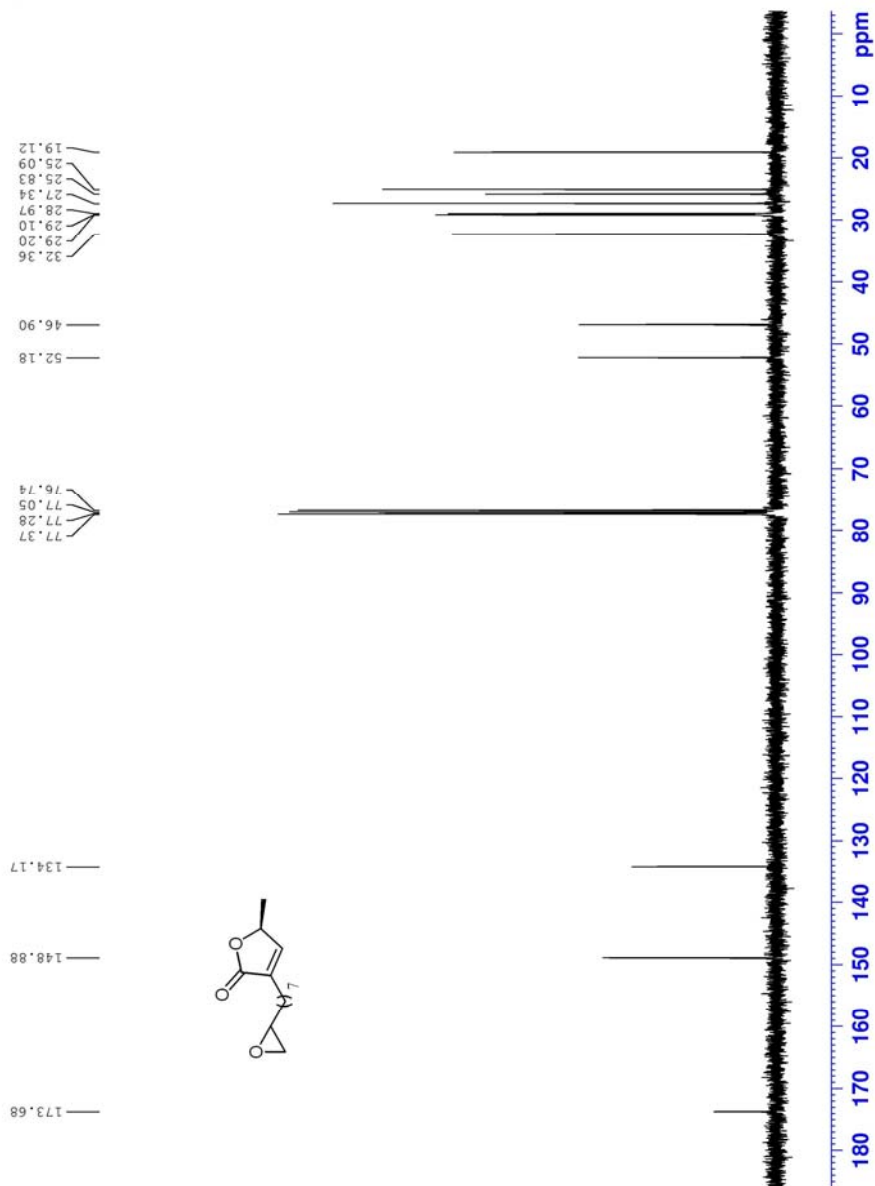
3. copies of ^1H and ^{13}C NMR



^1H NMR Spectra of Compound **11**



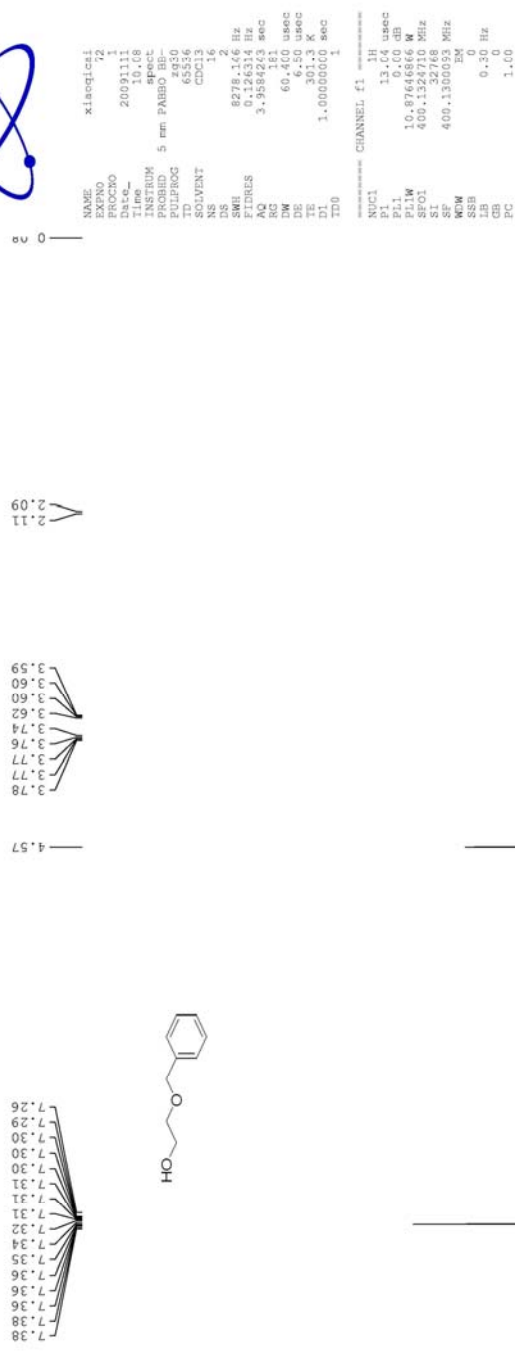
xqc47297



¹³C NMR spectra of compound 11



xiaocicai-145129



¹H NMR spectra of compound **13**

xiaocqicai-145081

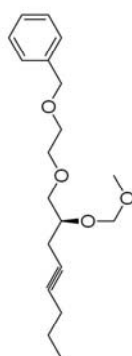


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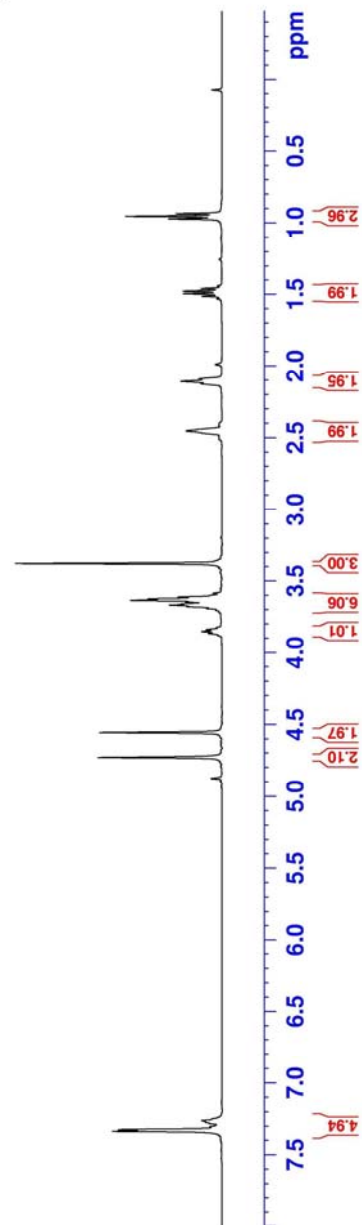
¹H NMR spectra of compound 14



xiaoqicai-145150



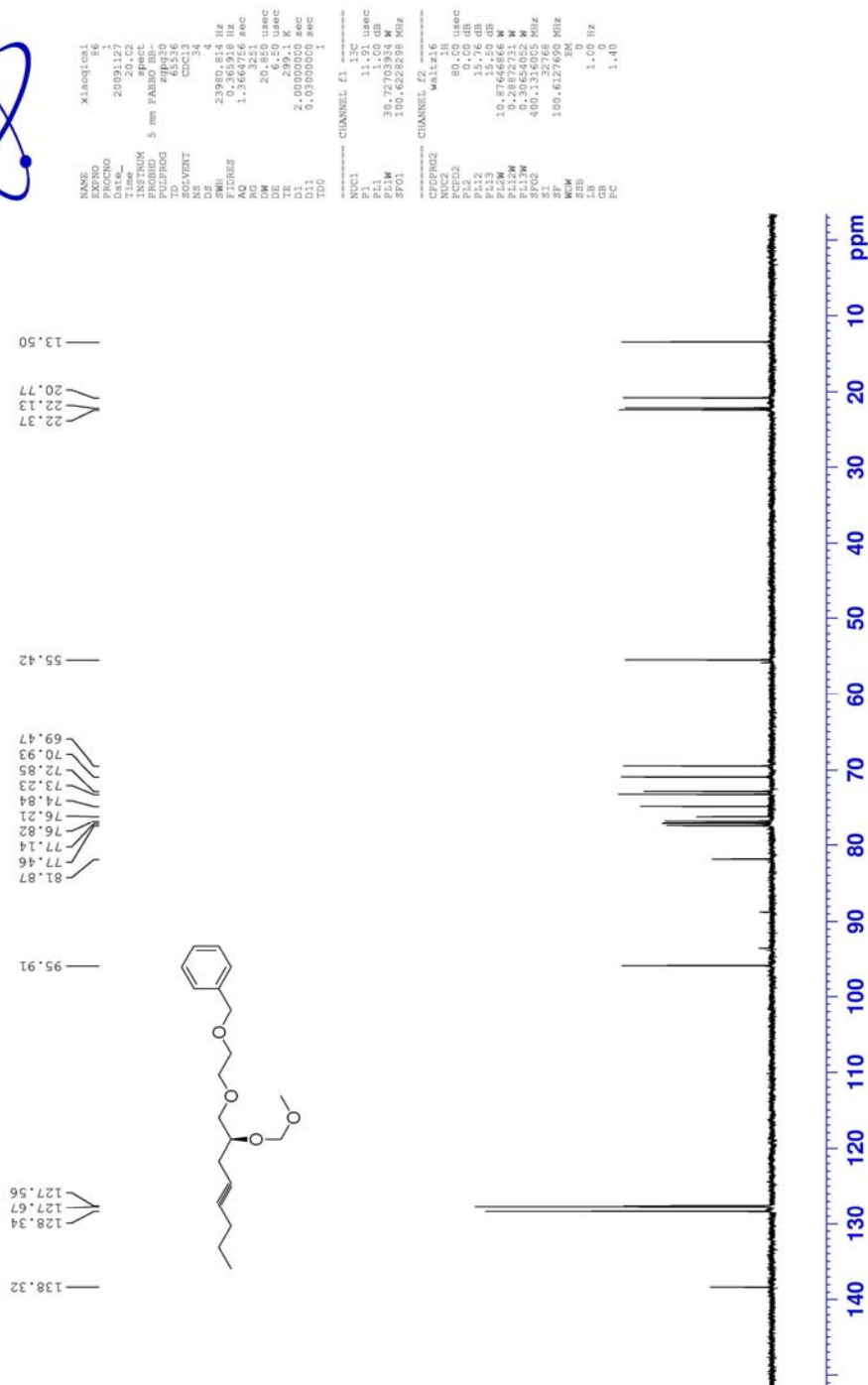
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^1H NMR spectra of compound 22



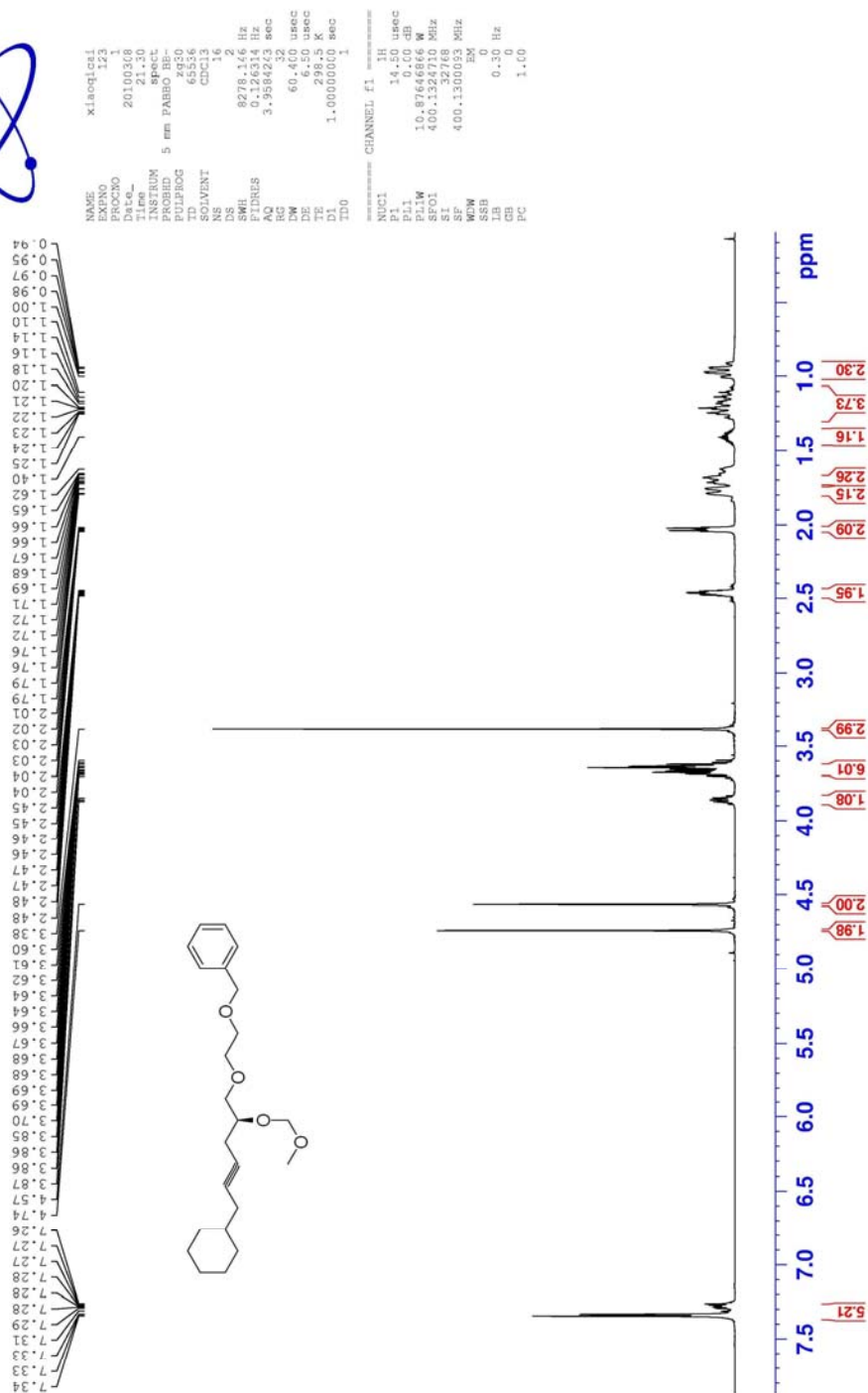
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¹³C NMR spectra of compound 22



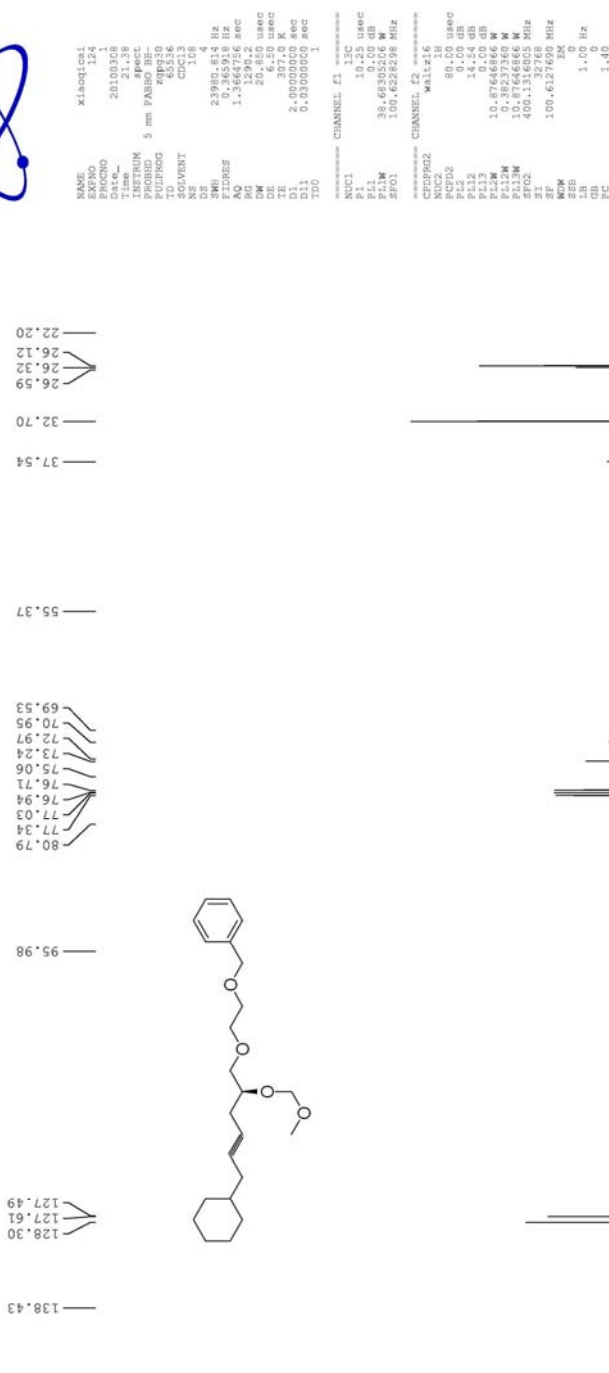
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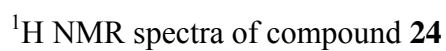
¹H NMR spectra of compound 23



xiaoqicai-47246

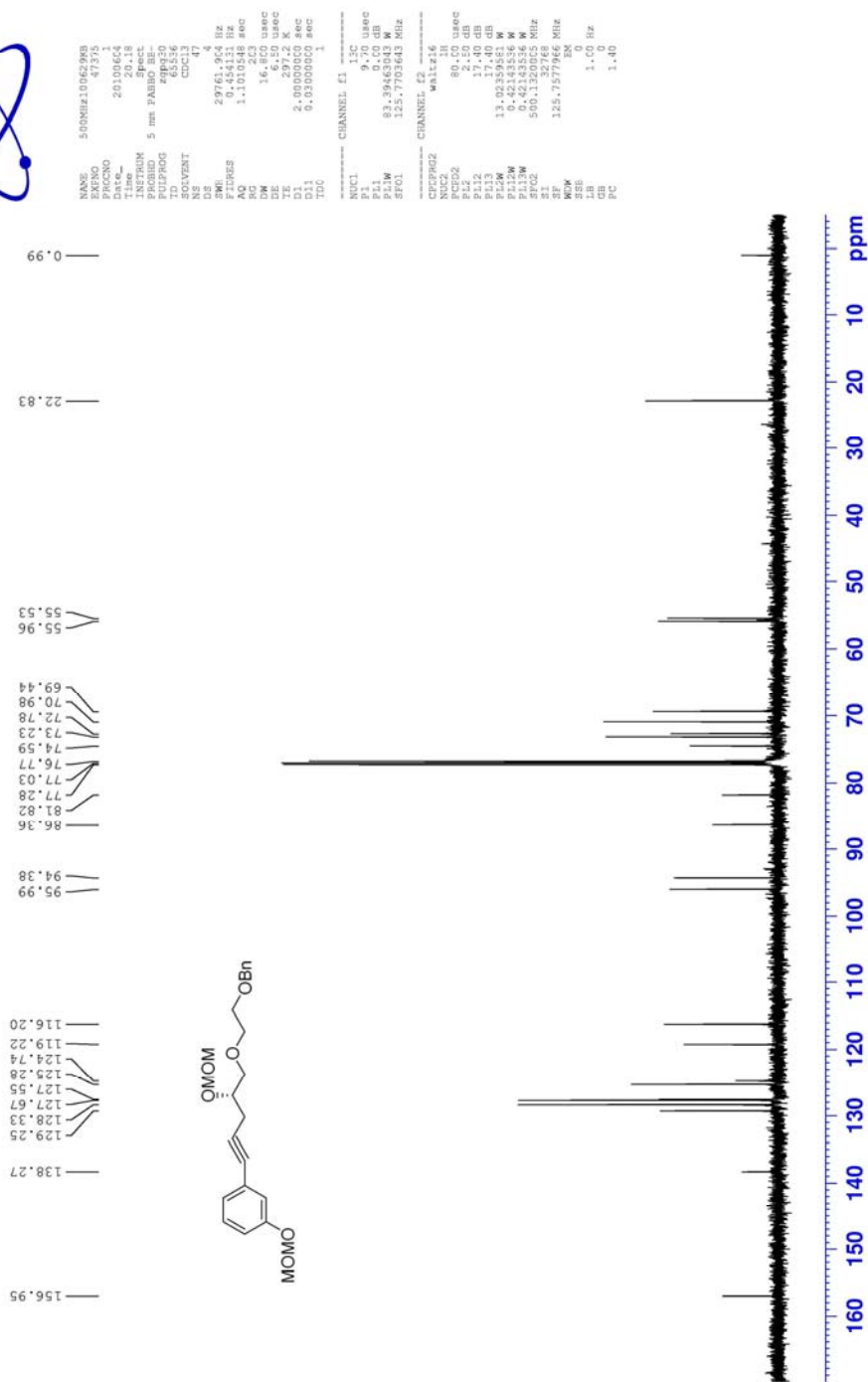


¹³C NMR spectra of compound 23



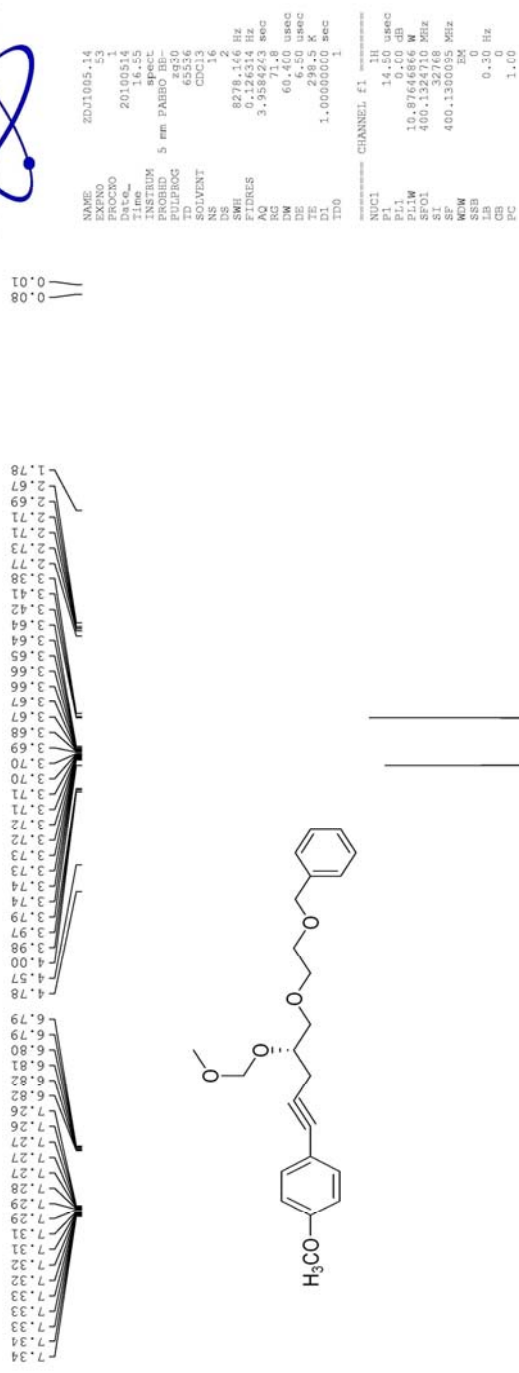


xqc47375



¹³C NMR spectra of compound 25

XQC47338



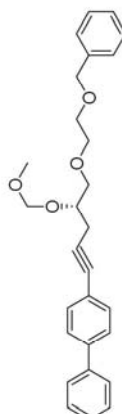
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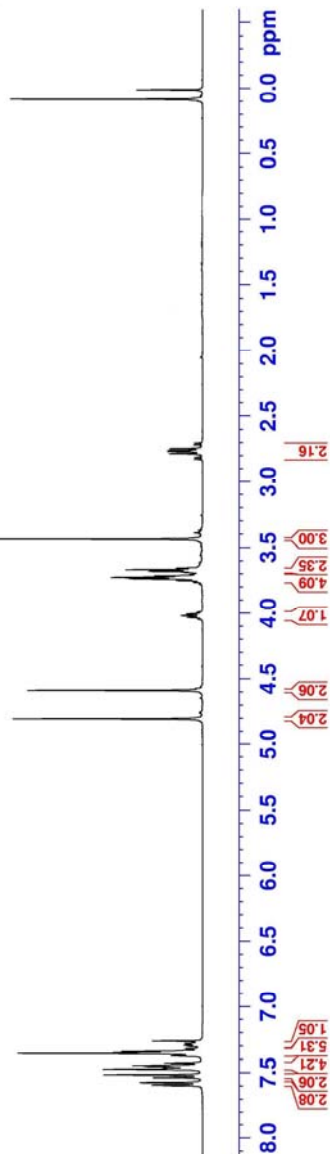
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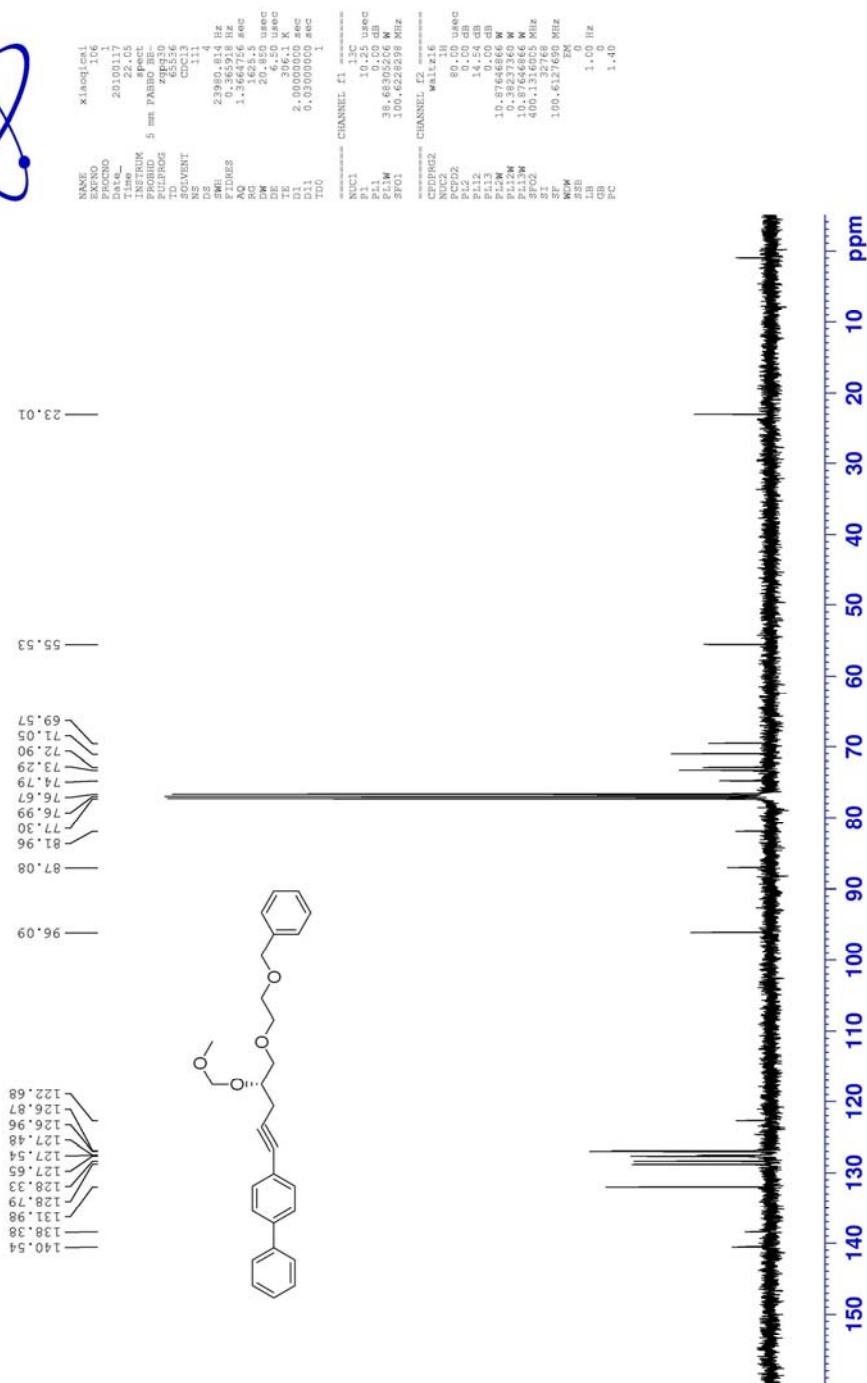
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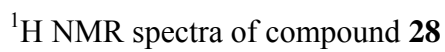
¹H NMR spectra of compound 27



xiaoqicai-145178

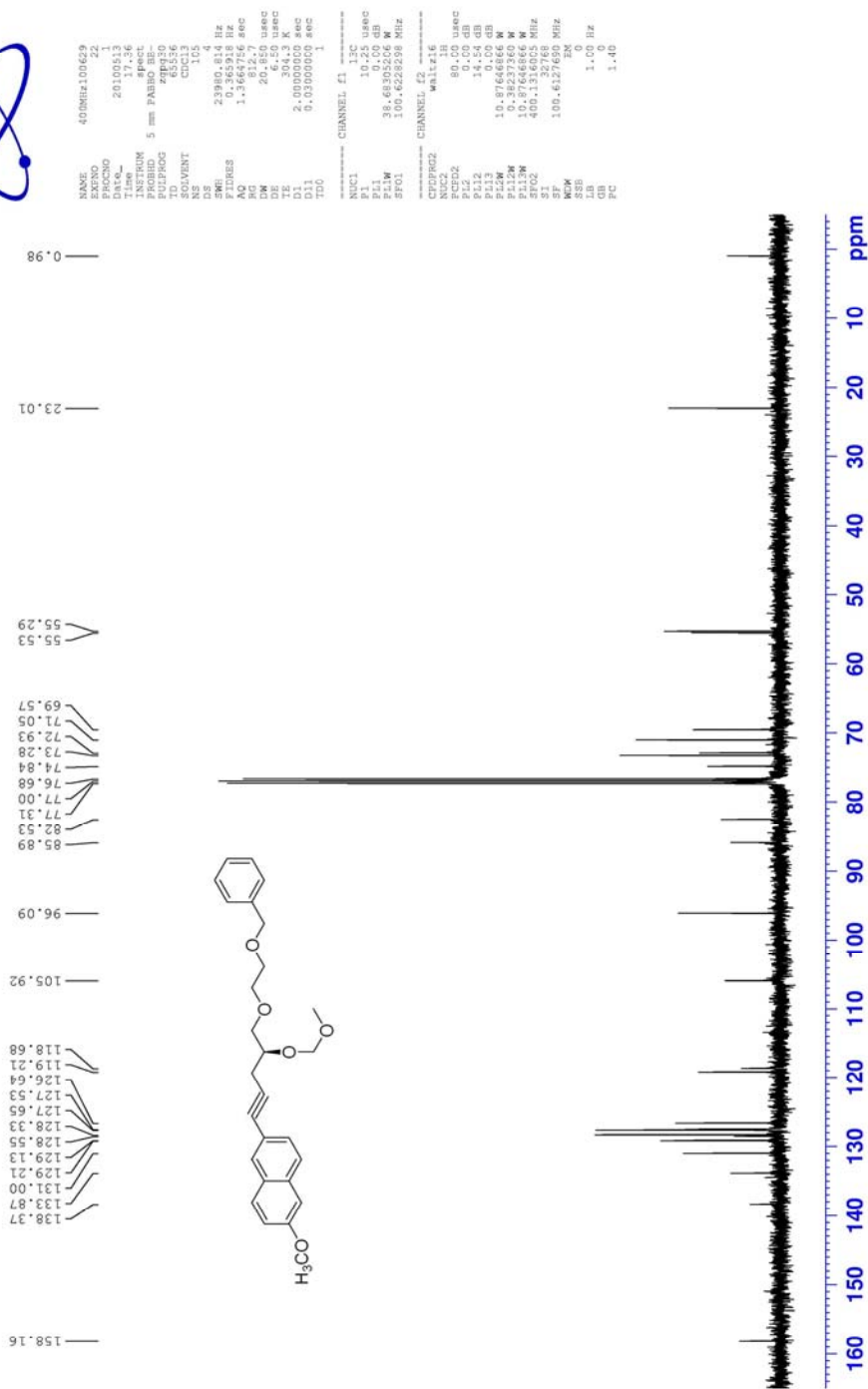


¹³C NMR spectra of compound 27

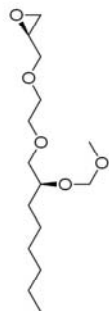




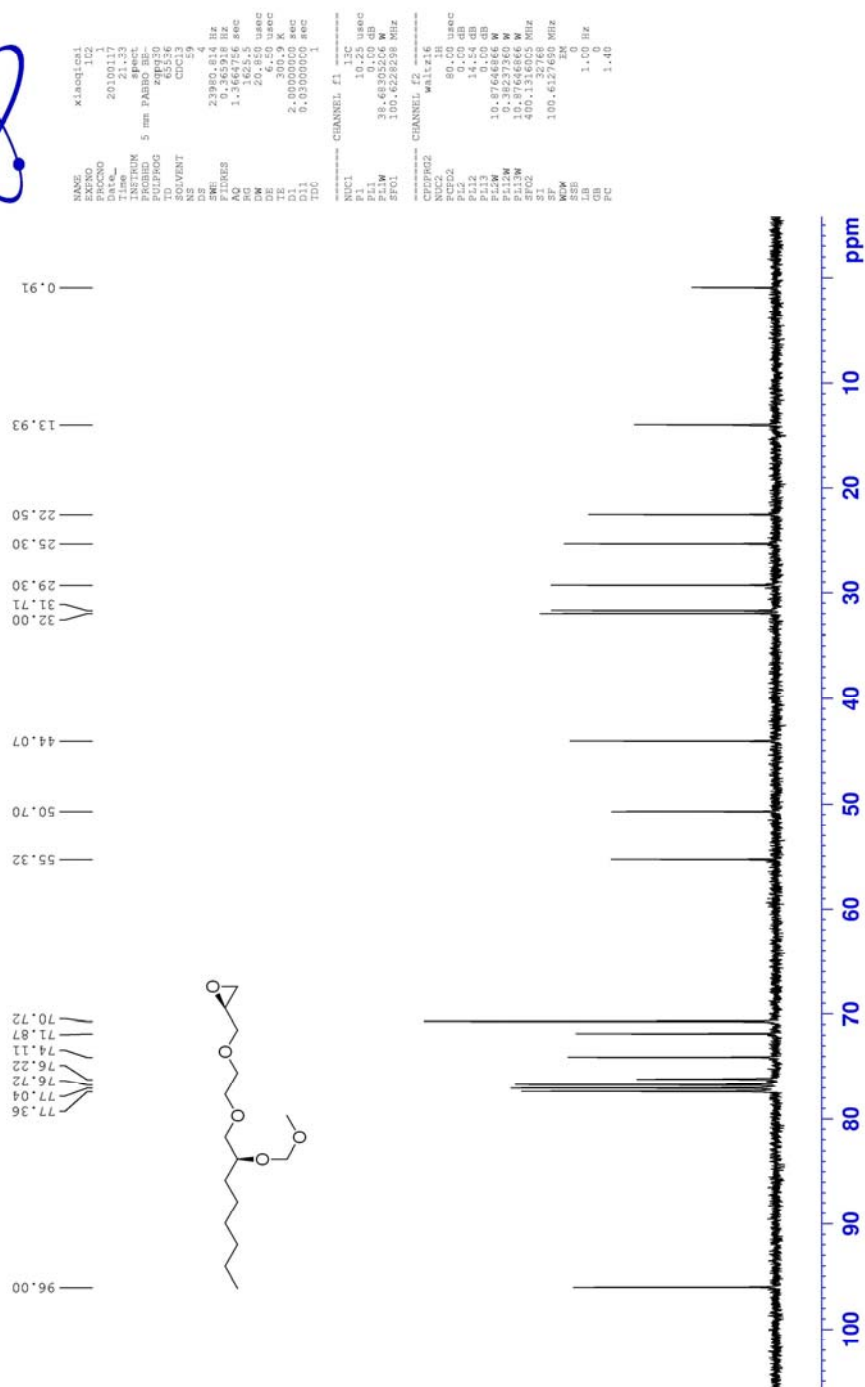
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¹³C NMR spectra of compound 28

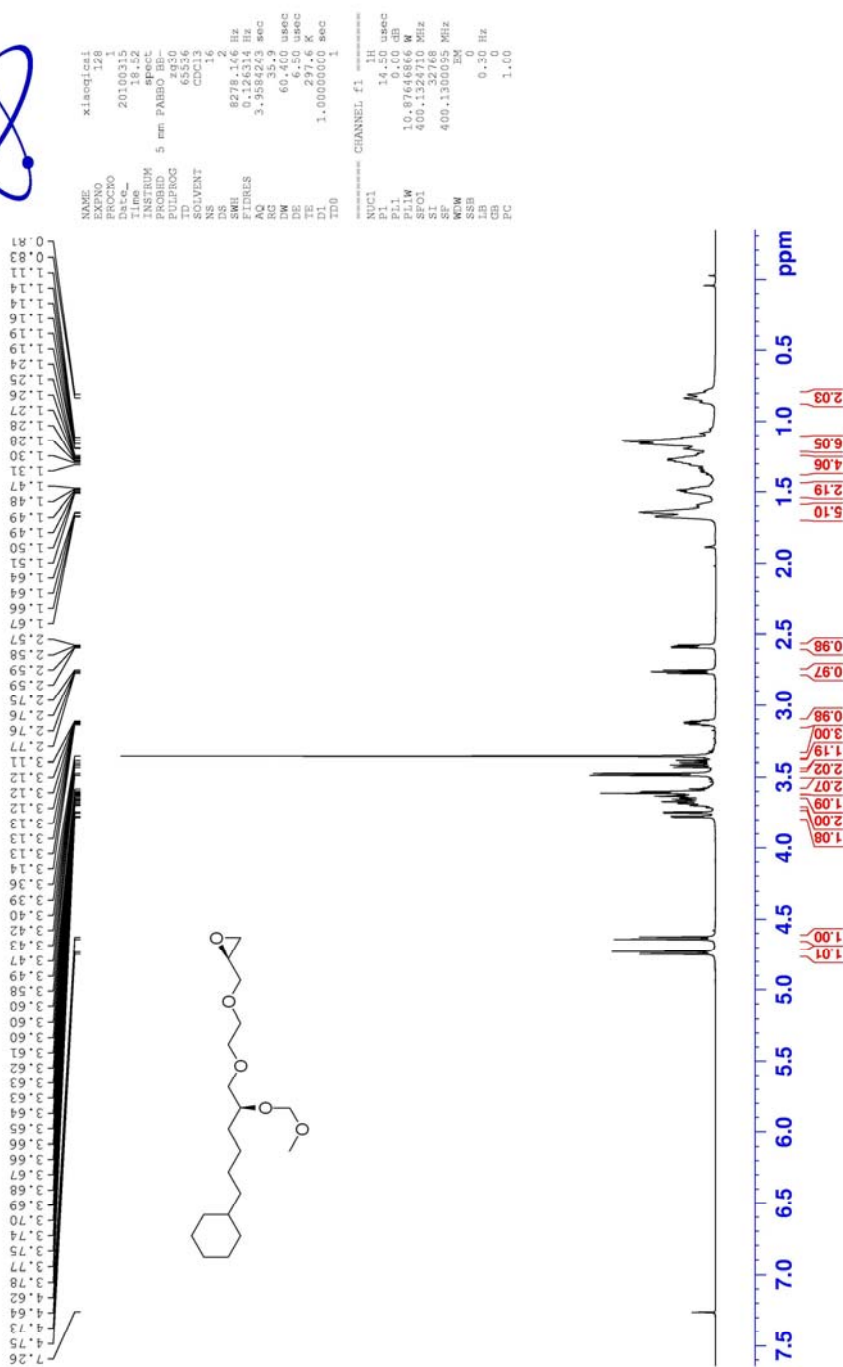


S23

¹³C NMR spectra of compound **29**



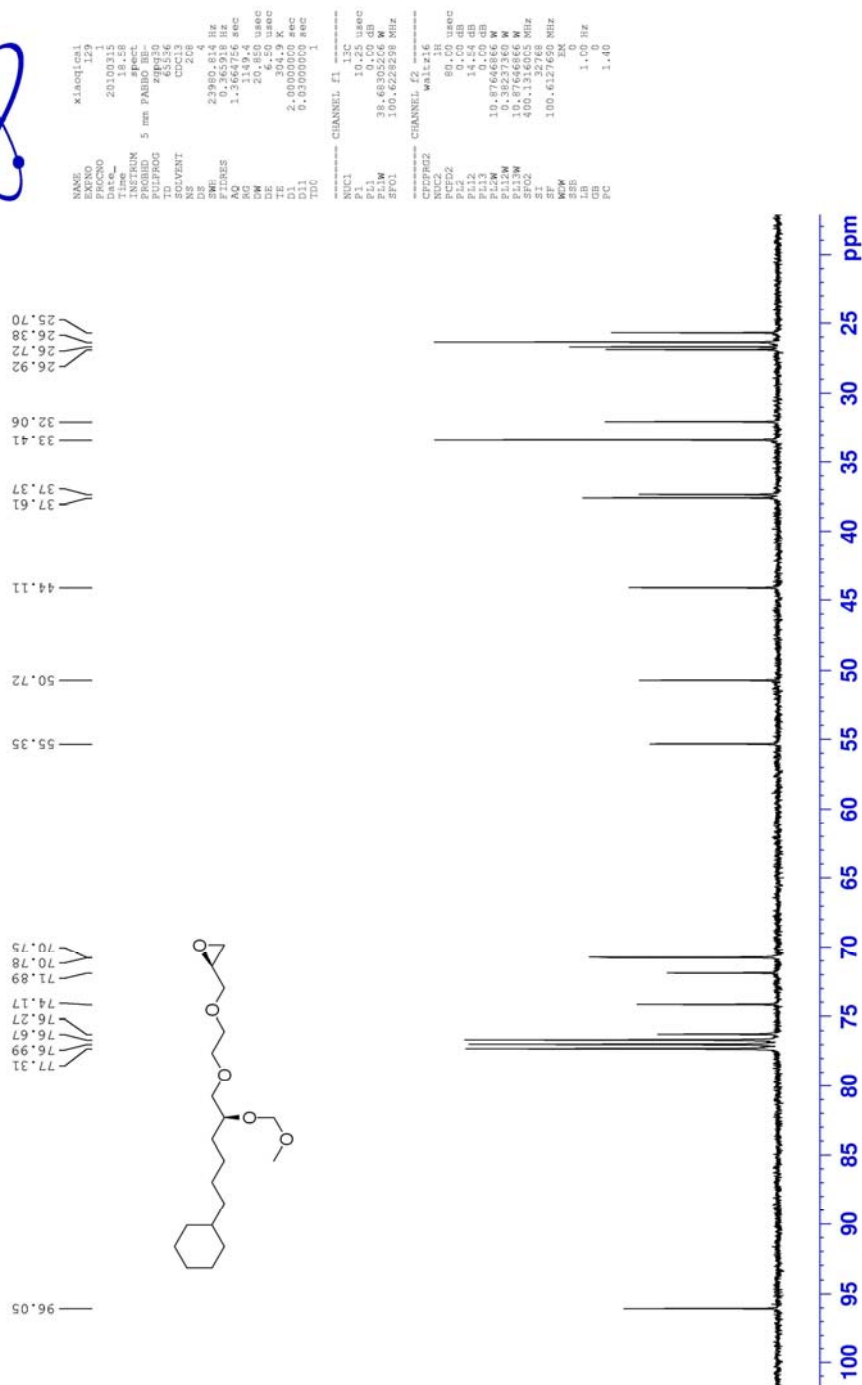
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¹H NMR spectra of compound **30**



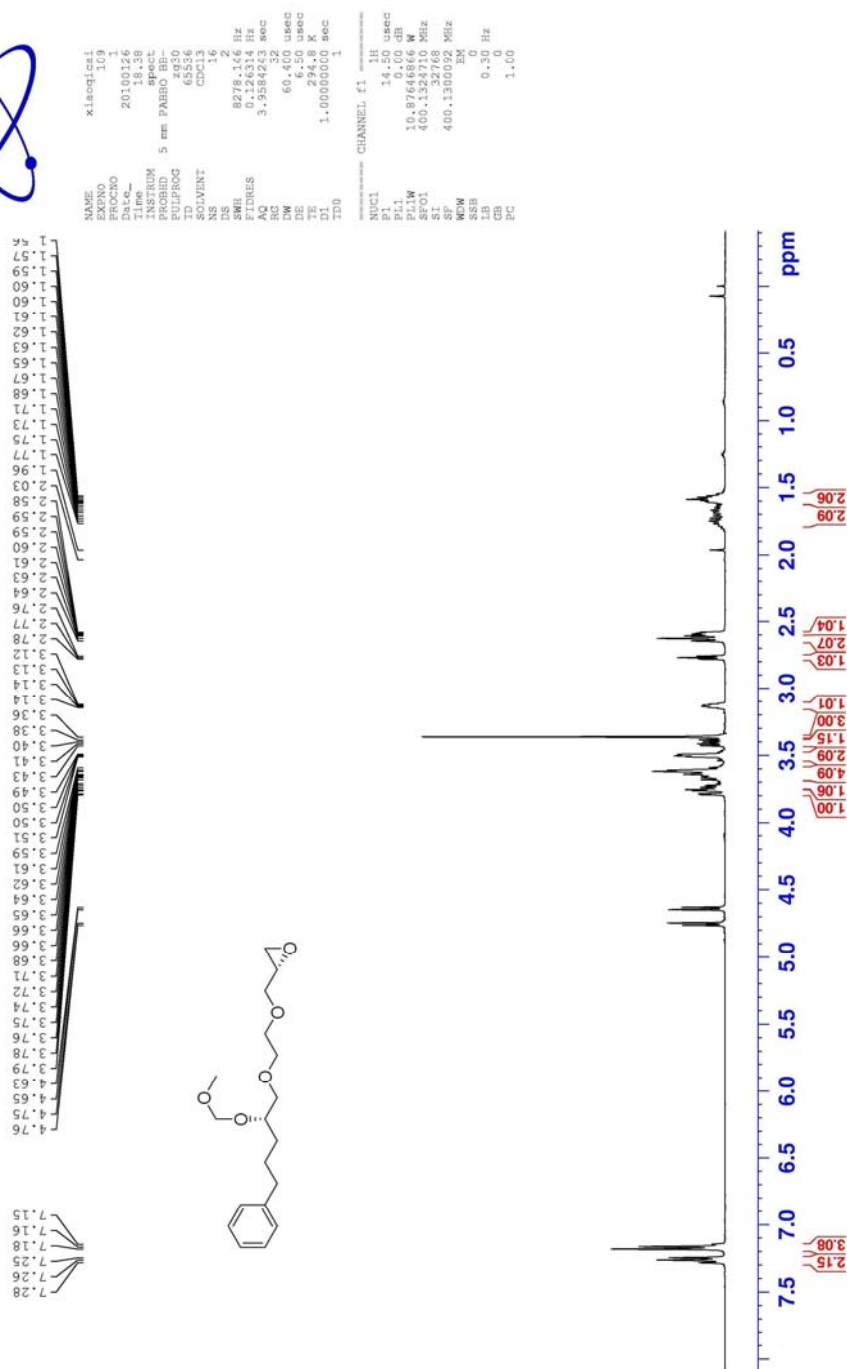
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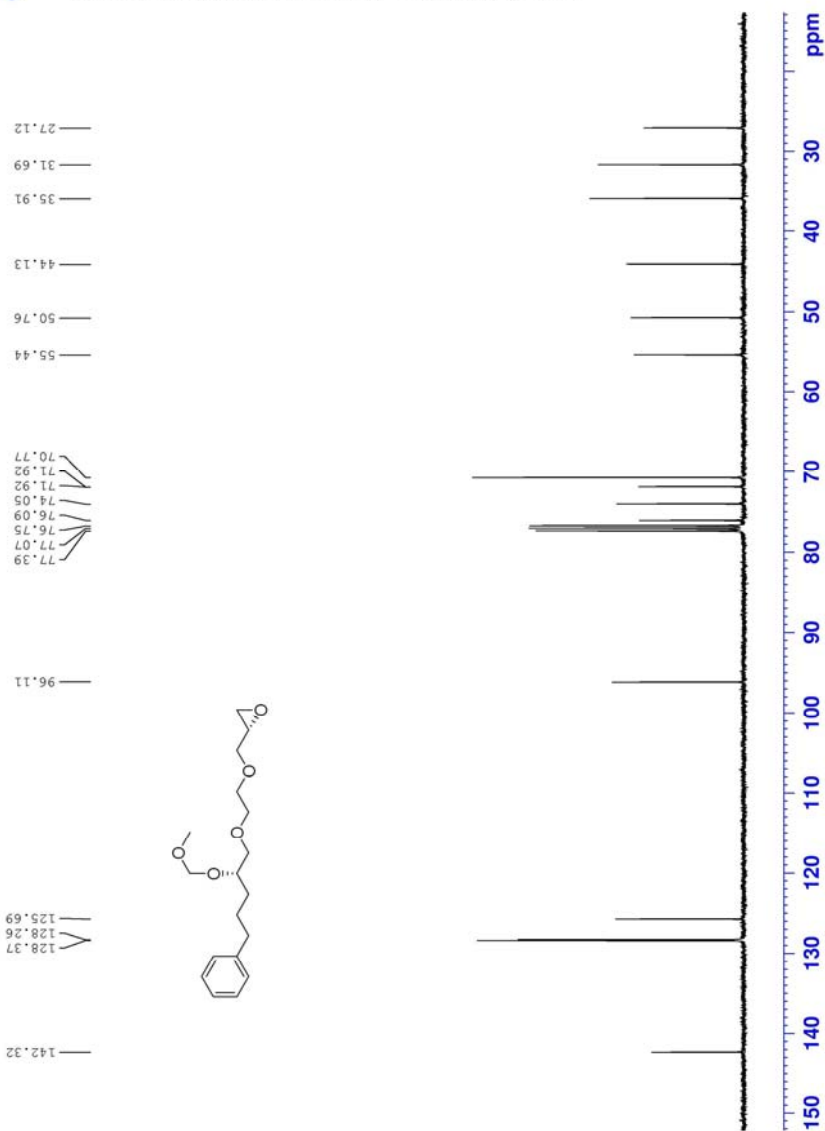
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¹H NMR spectra of compound **31**



xiaoqicai-47214

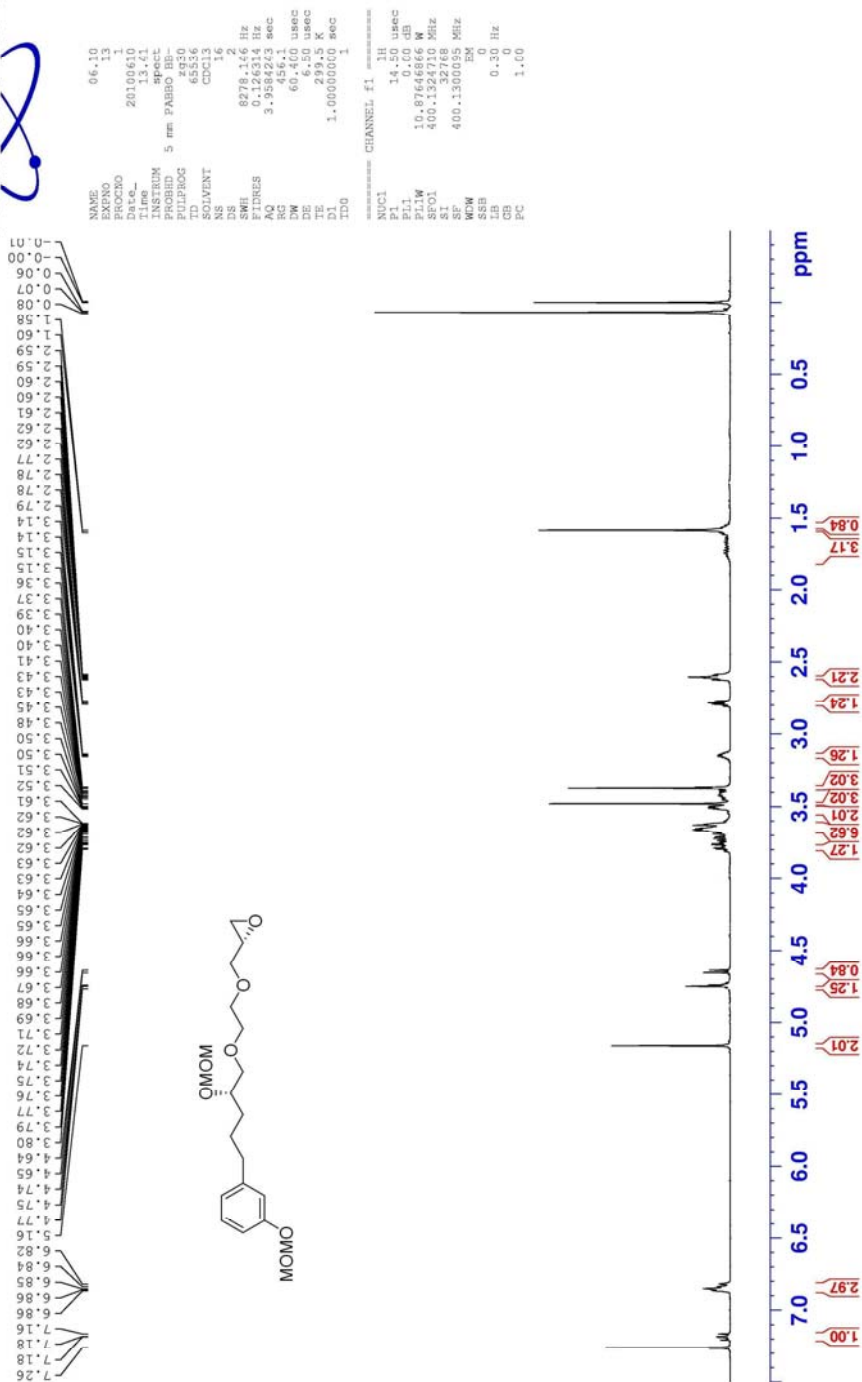


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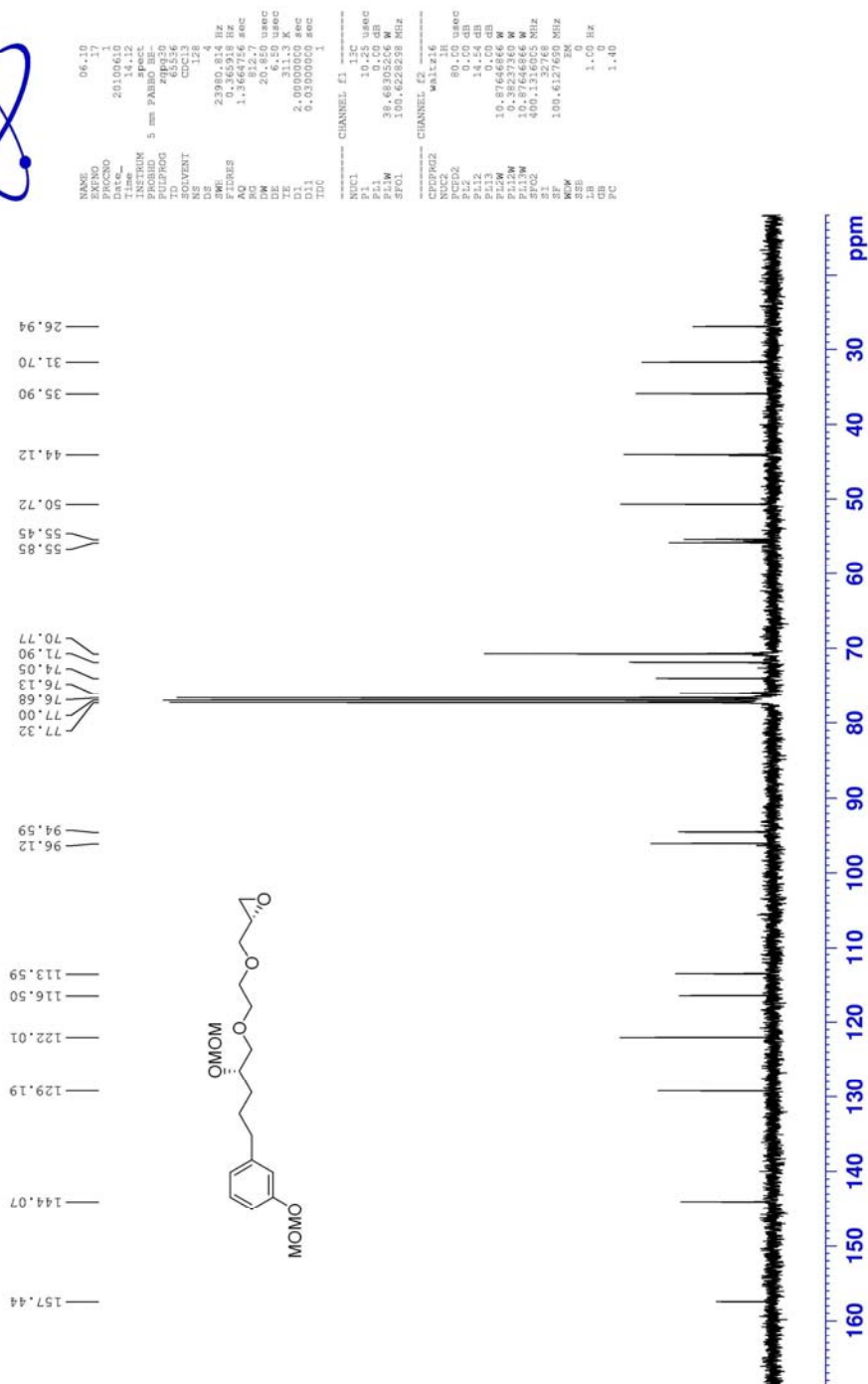
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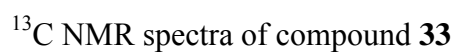
¹H NMR spectra of compound 32



47383

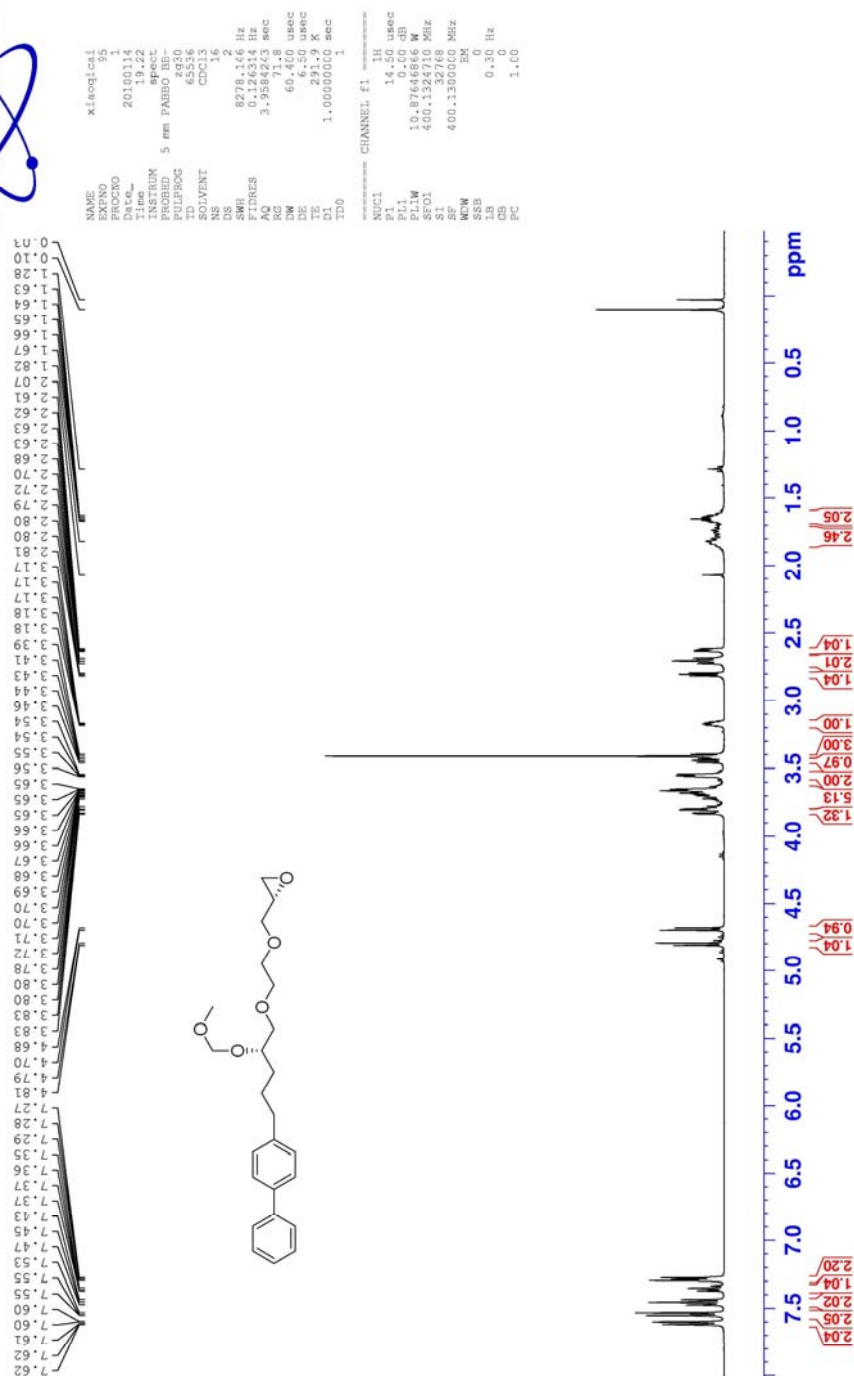


¹³C NMR spectra of compound 32





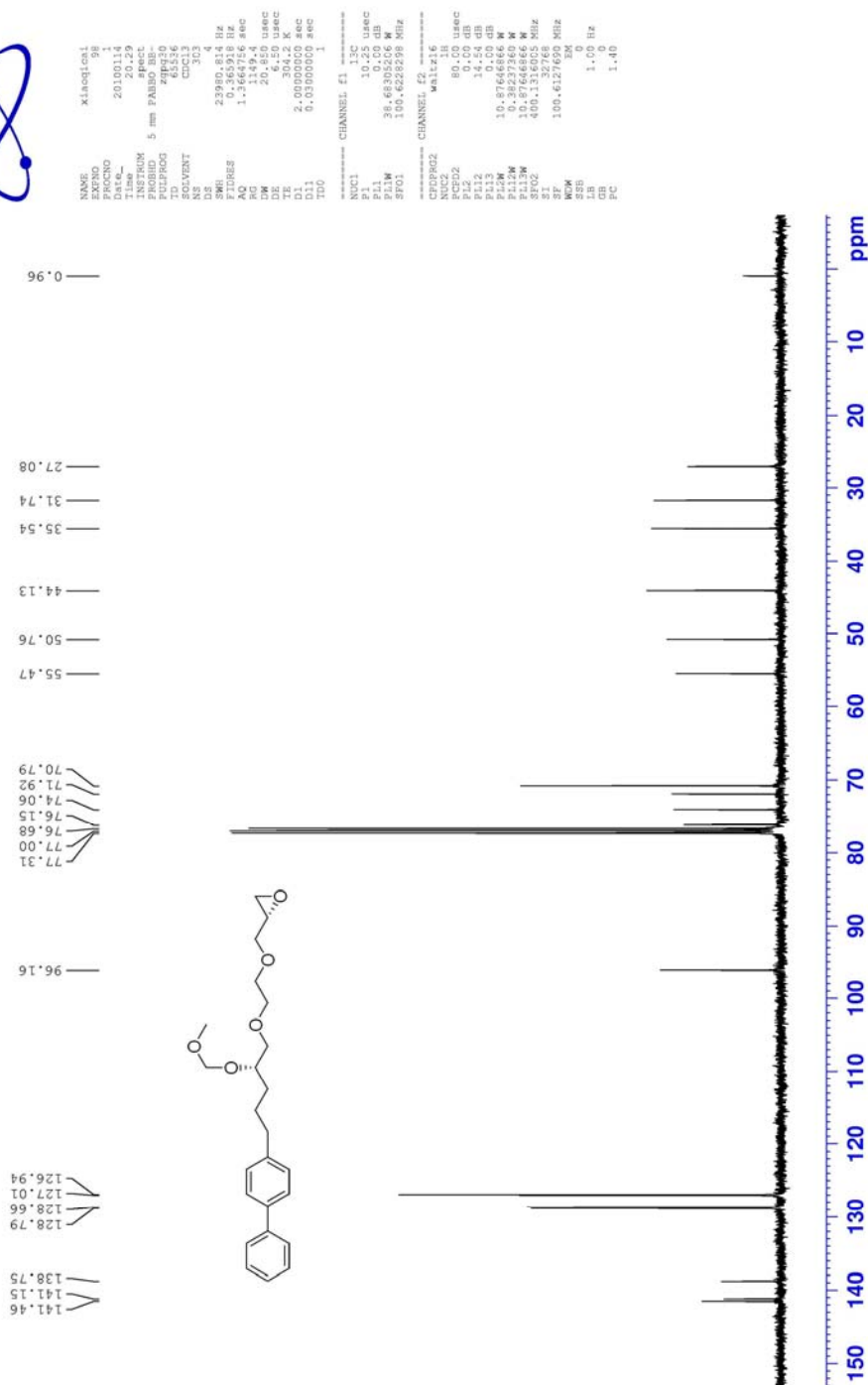
xiaocqicai-145187



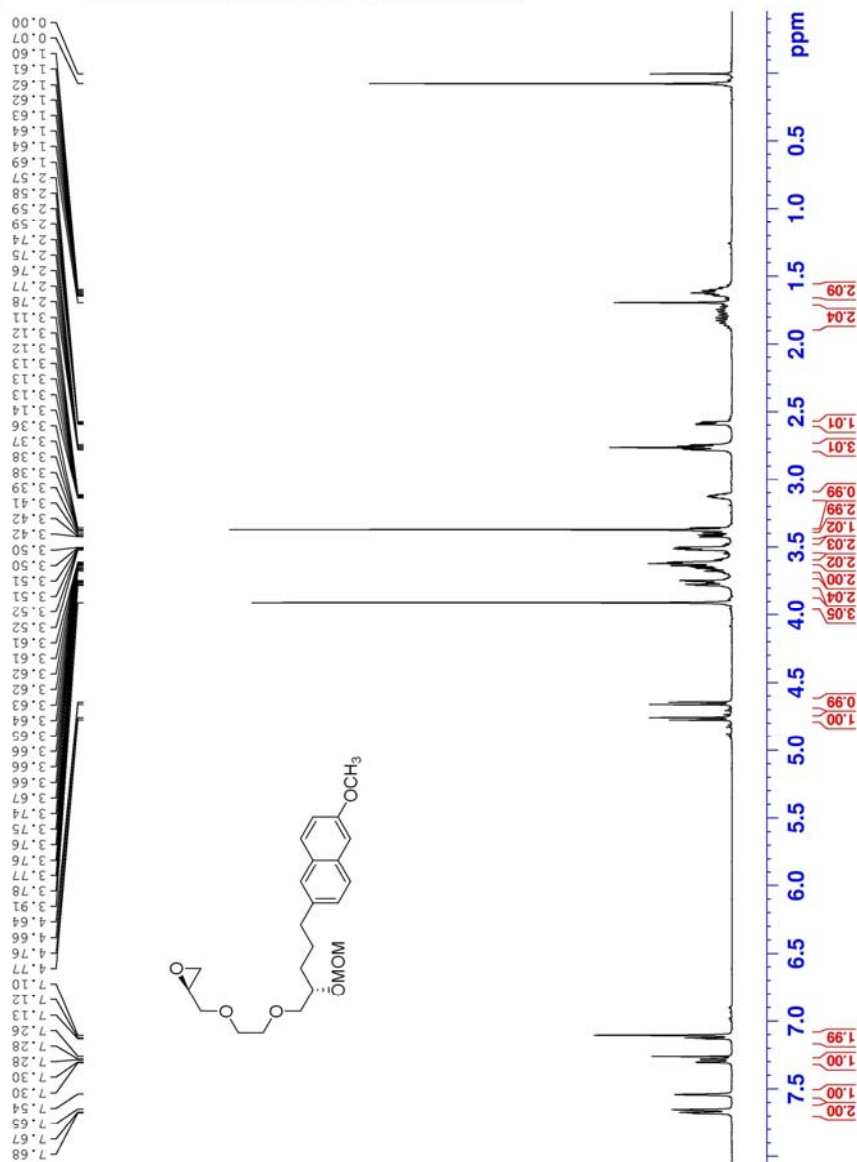
¹H NMR spectra of compound **34**



xiaoqicai-145187



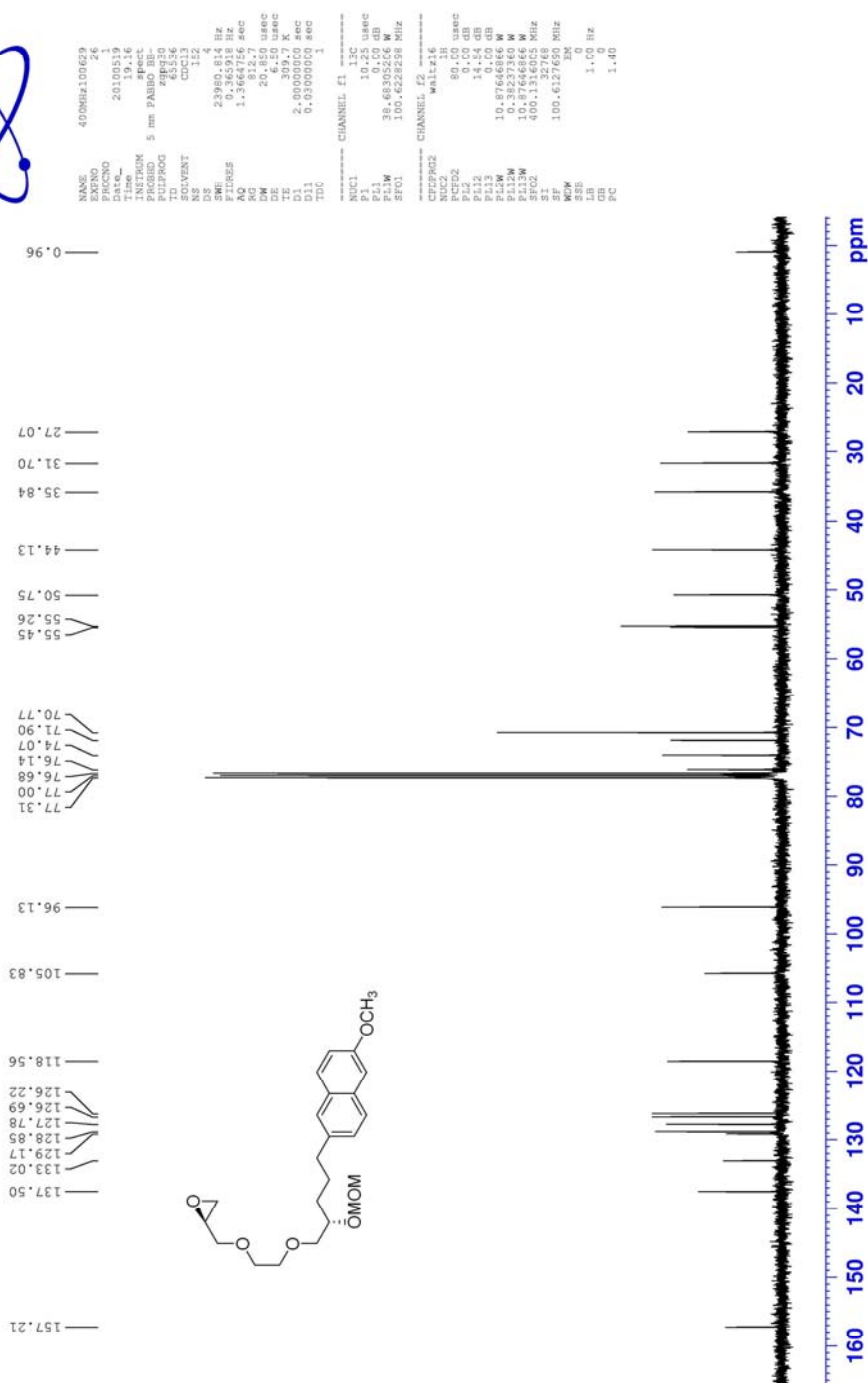
¹³C NMR spectra of compound **34**



¹H NMR spectra of compound **35**



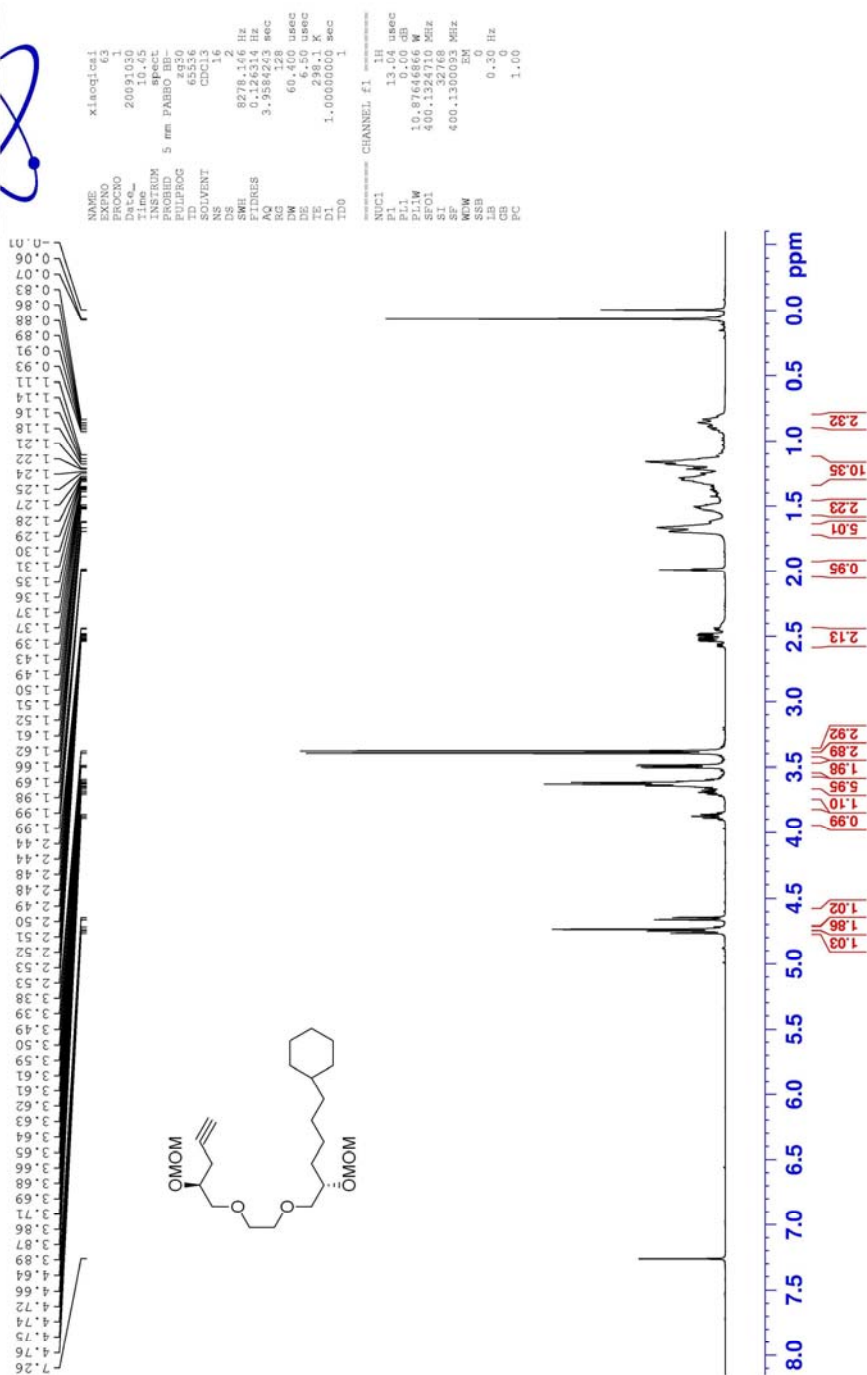
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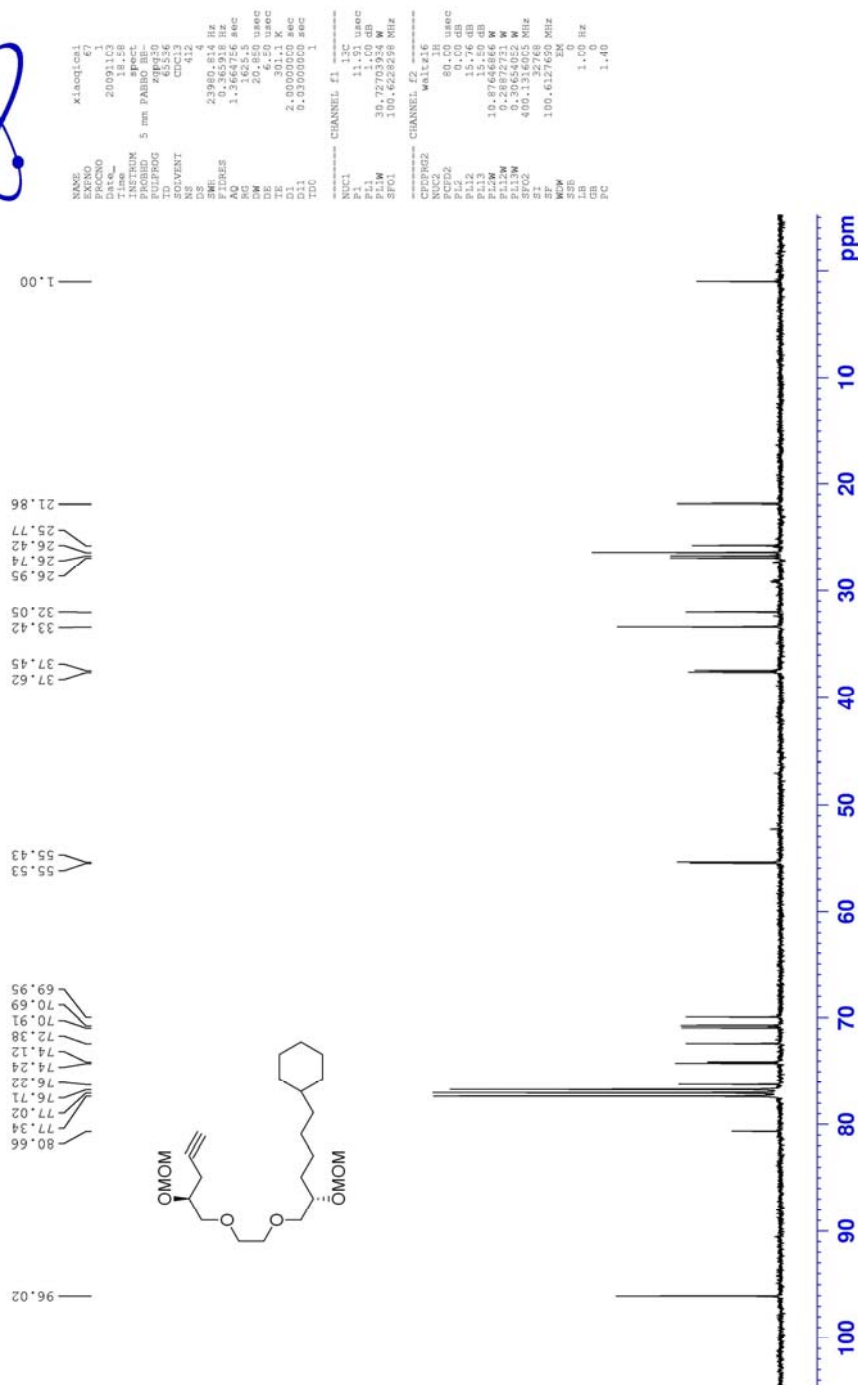
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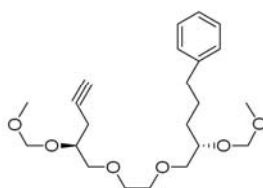


xiaogical-145116



¹H NMR spectra of compound **37**

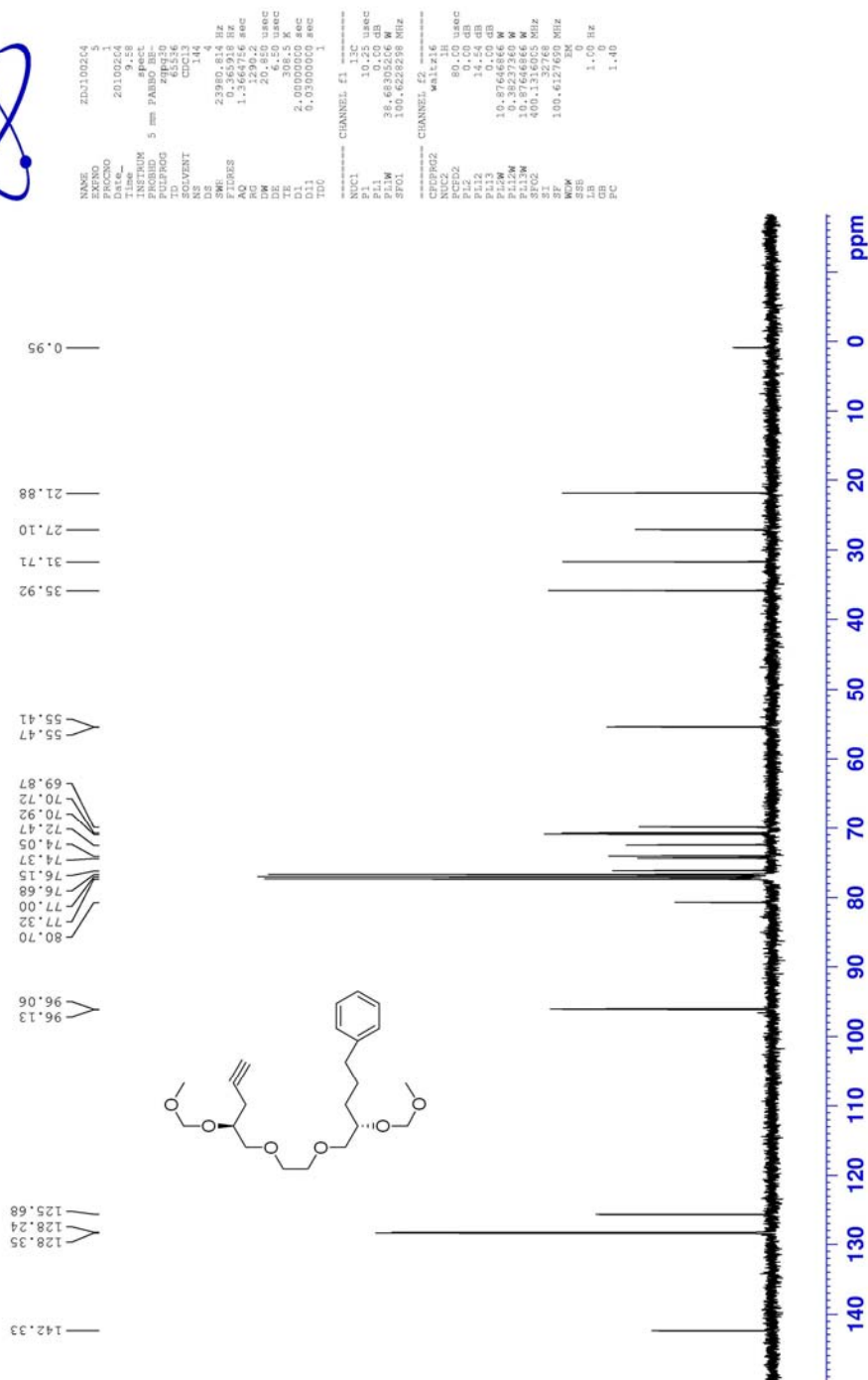




¹H NMR spectra of compound **38**

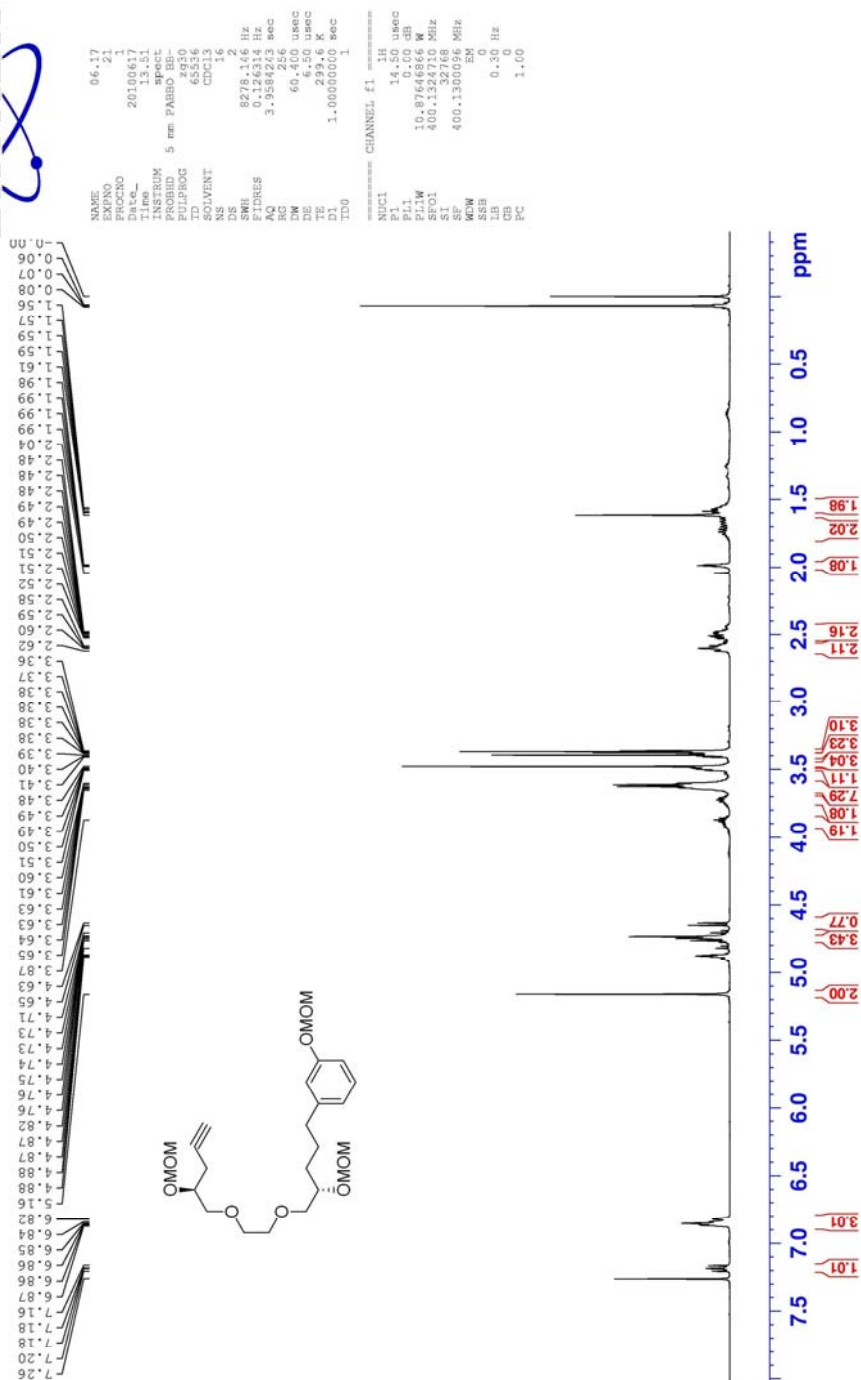


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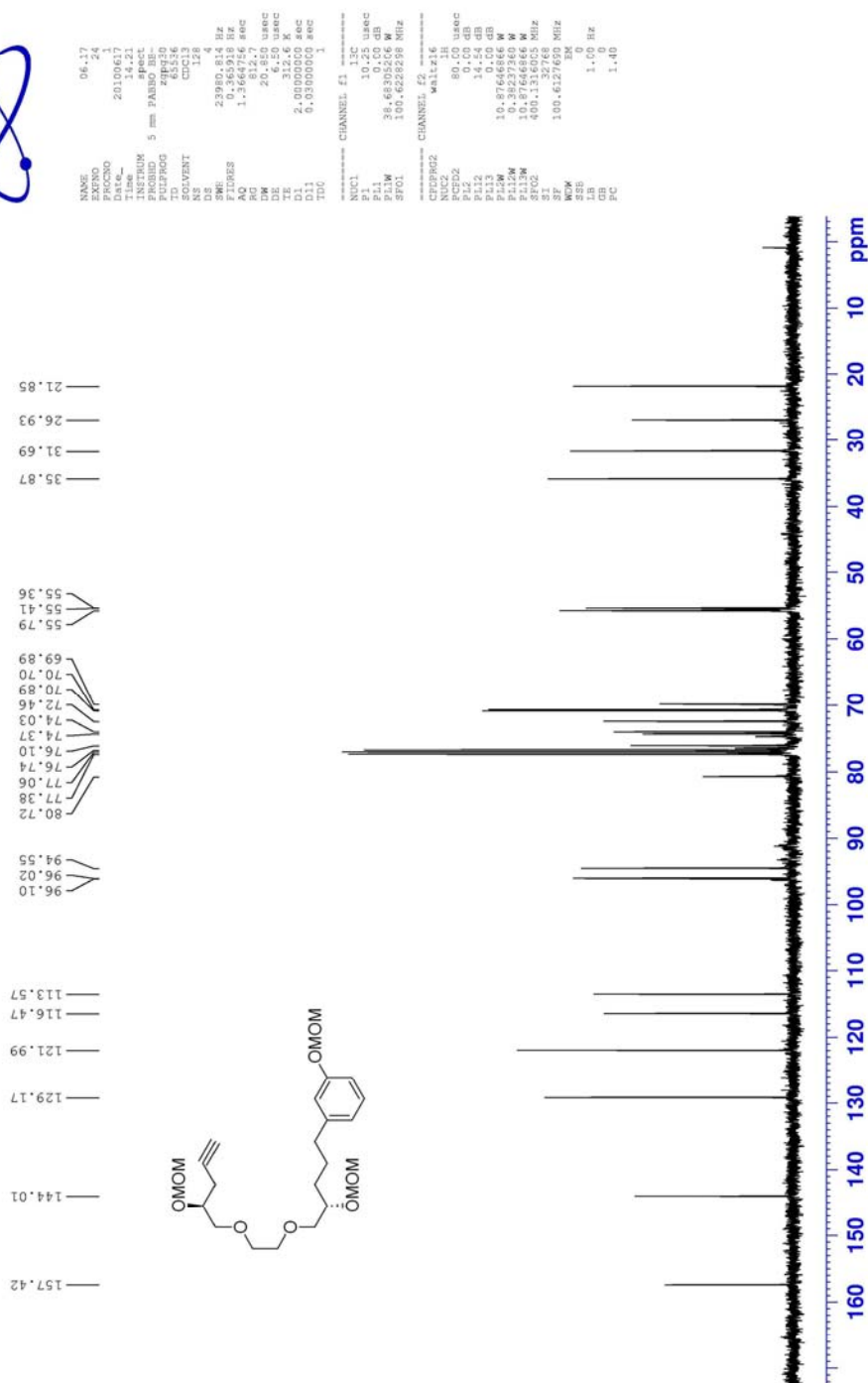




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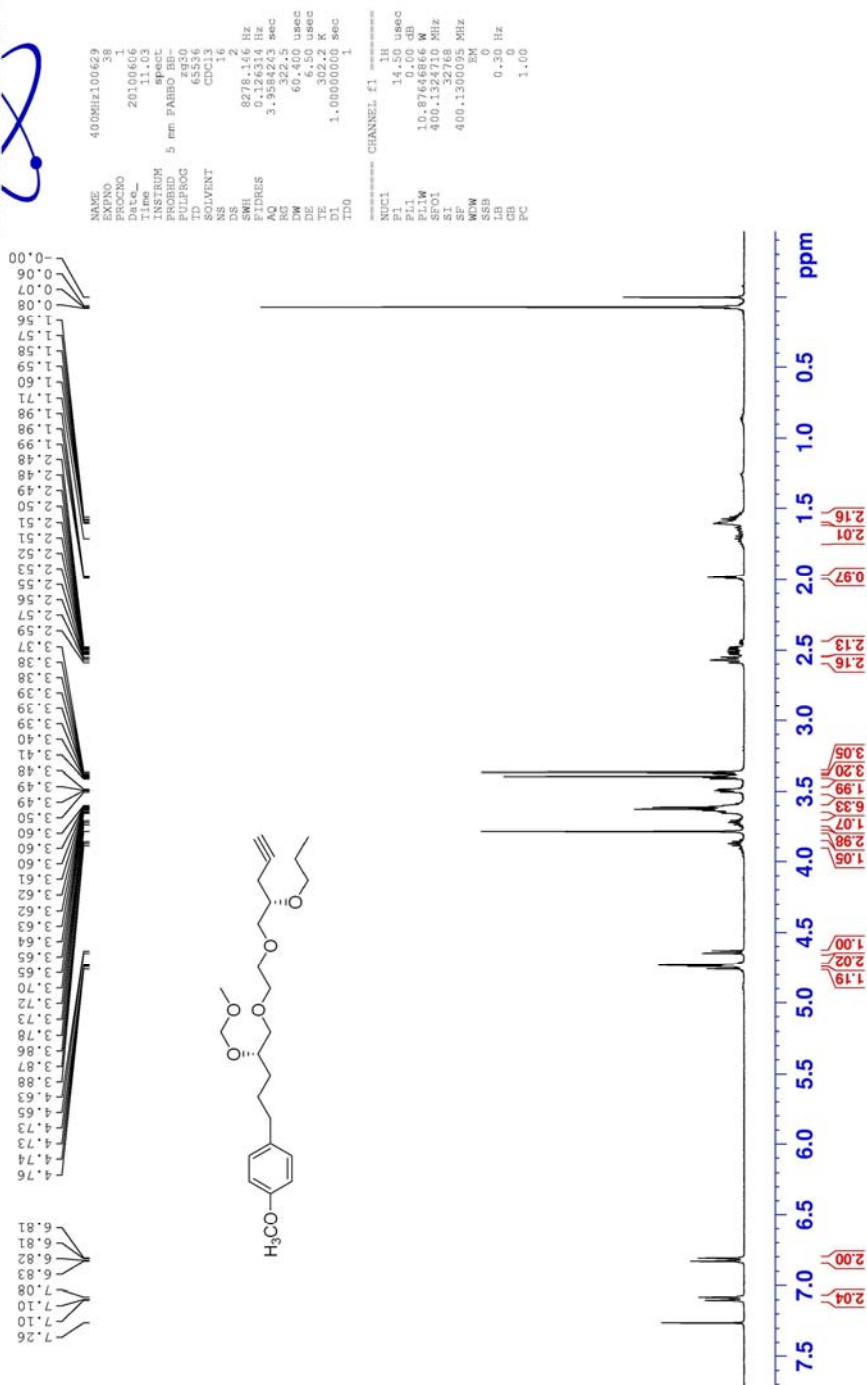


¹H NMR spectra of compound 39

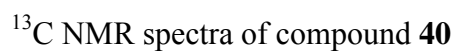
 ^{13}C NMR spectra of compound **39**



xqc47376

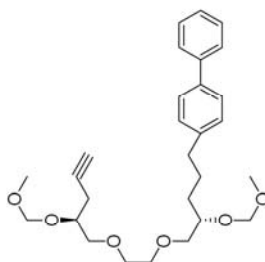


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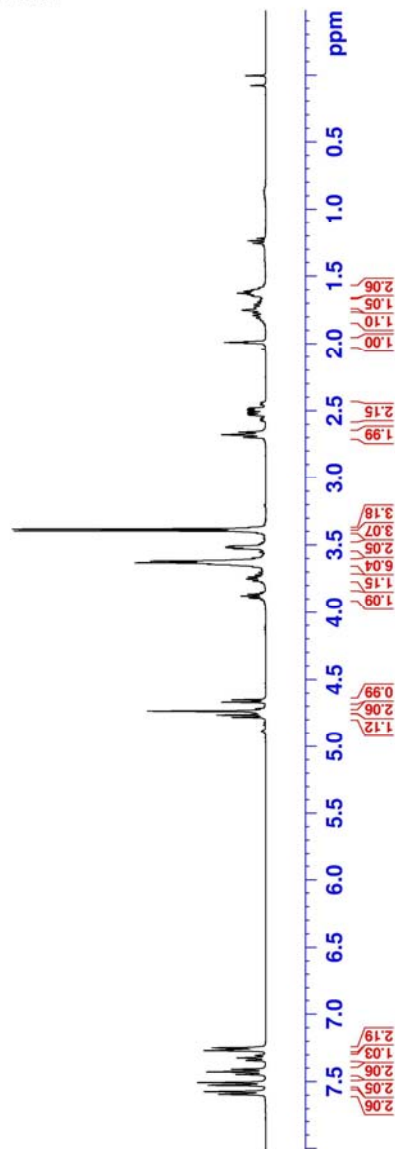




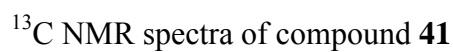
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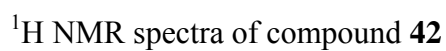


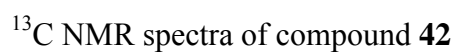
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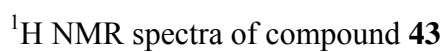


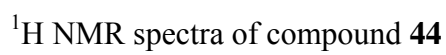
^1H NMR spectra of compound **41**

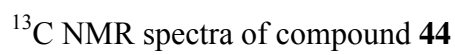


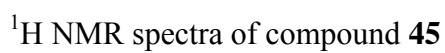






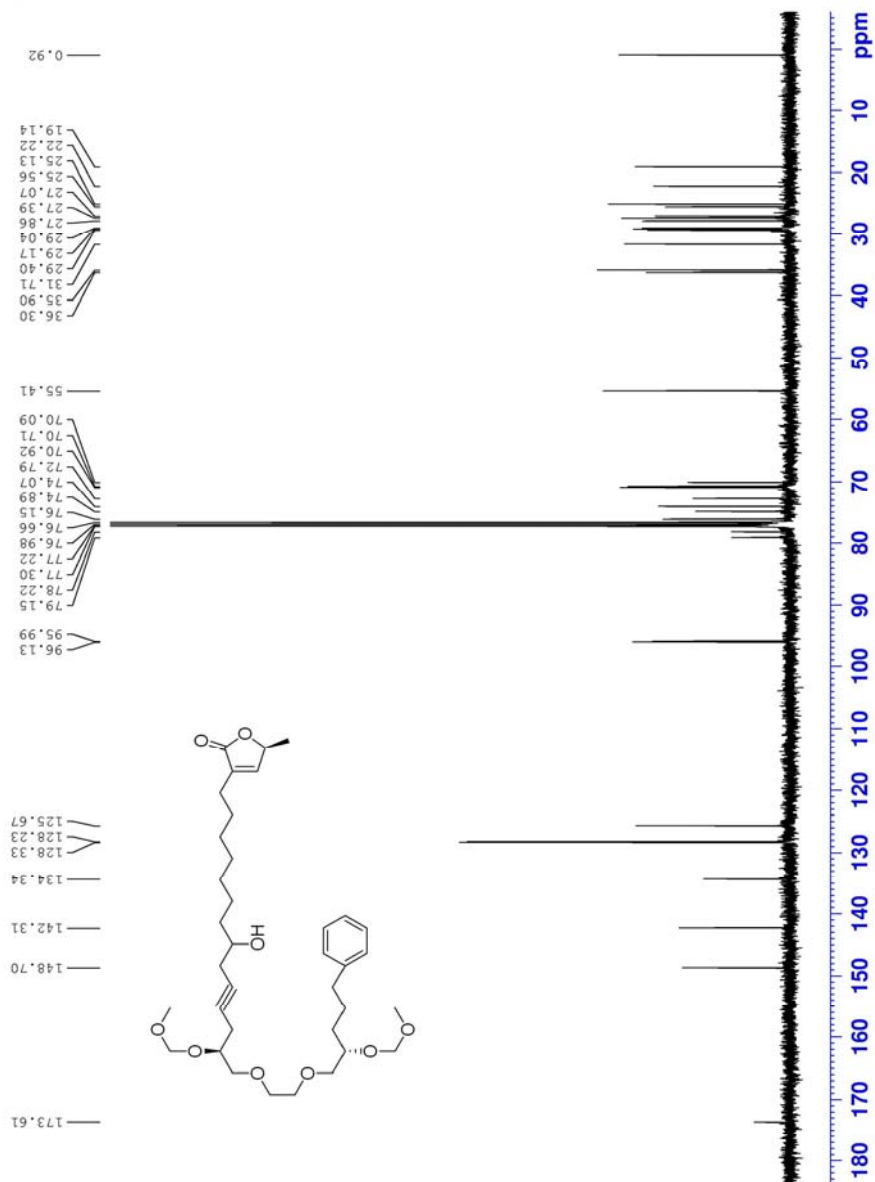








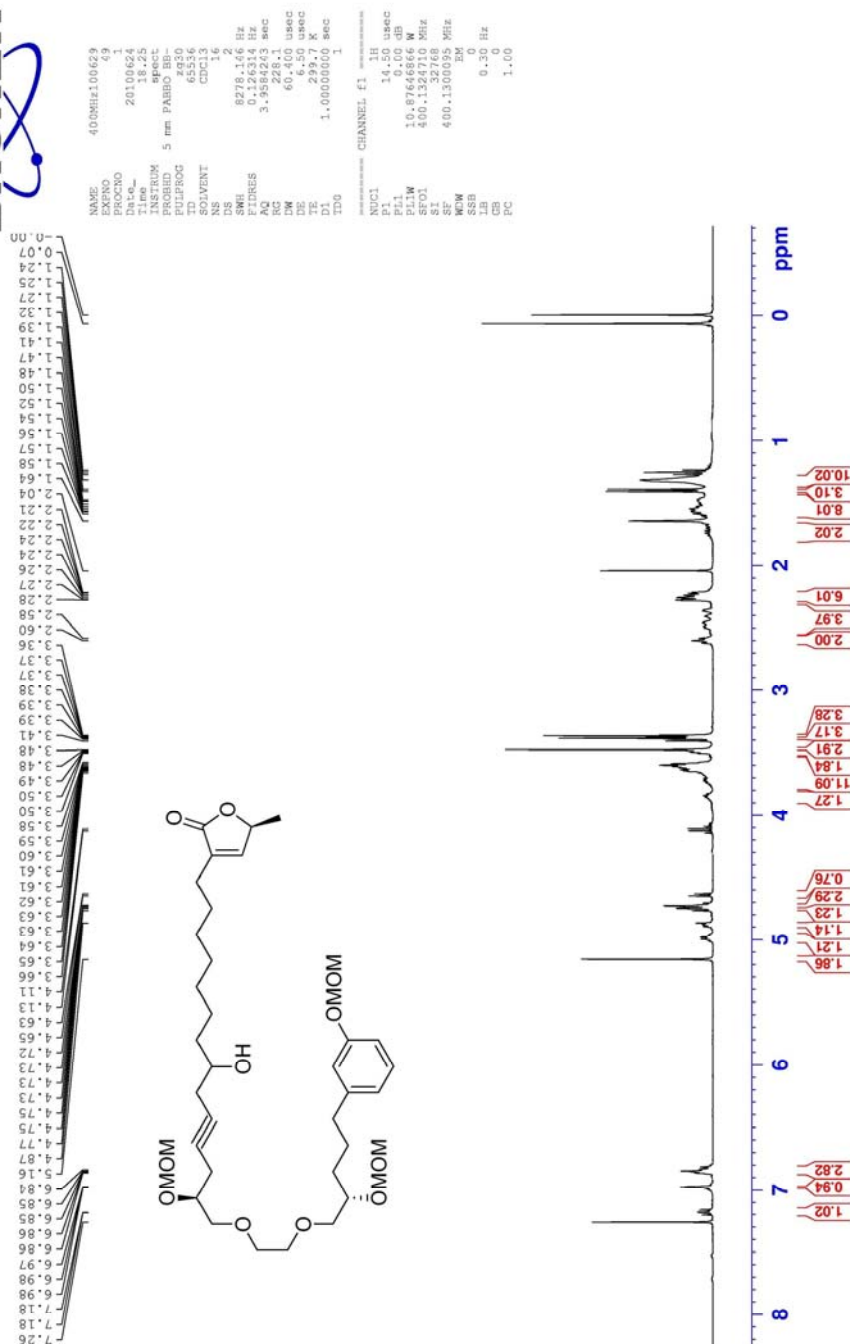
xiaocqicai-47242



¹³C NMR spectra of compound 45



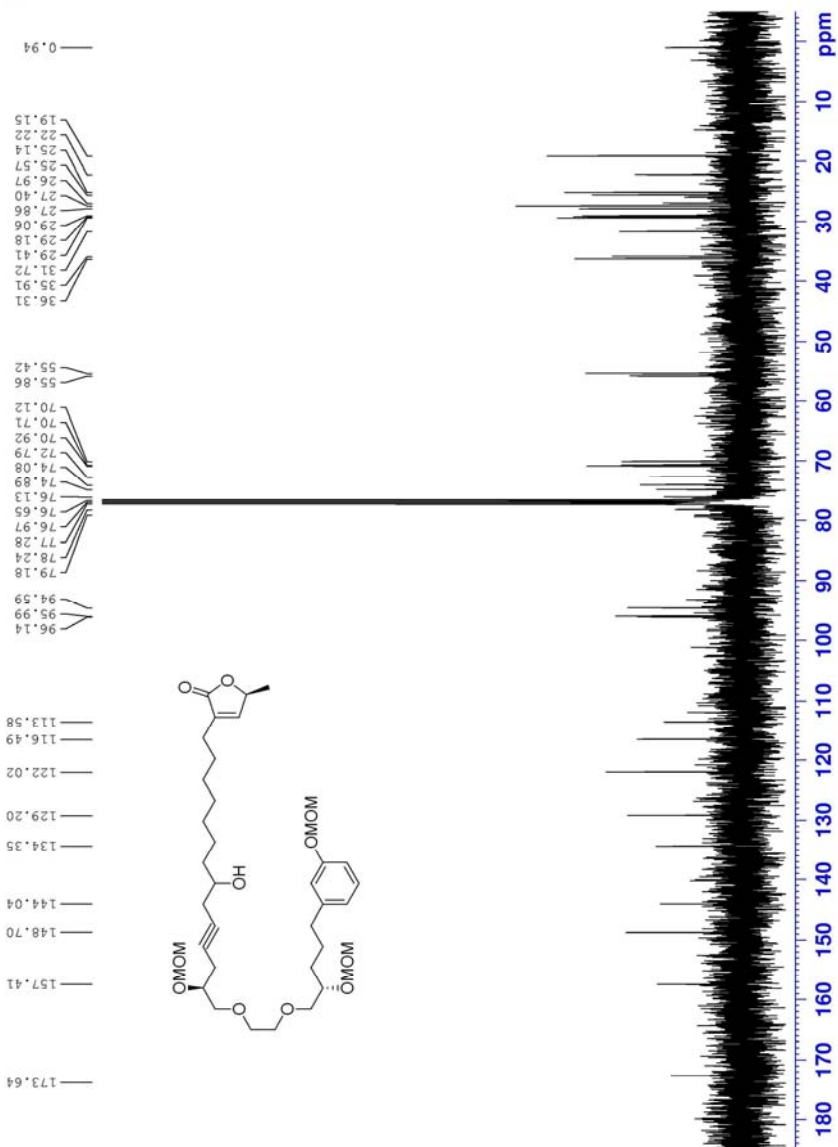
xqc47393



¹H NMR spectra of compound 46



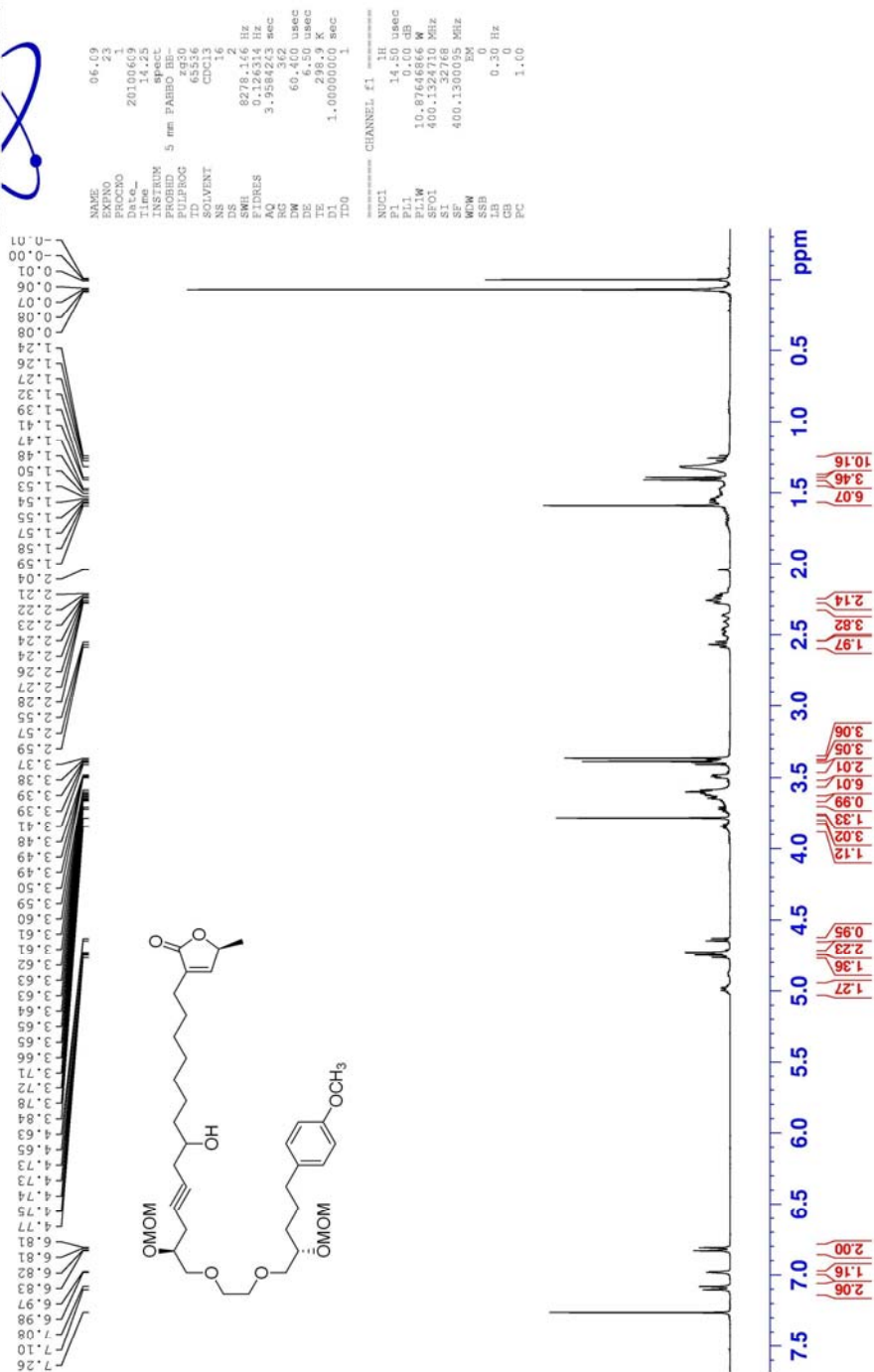
xqc47393



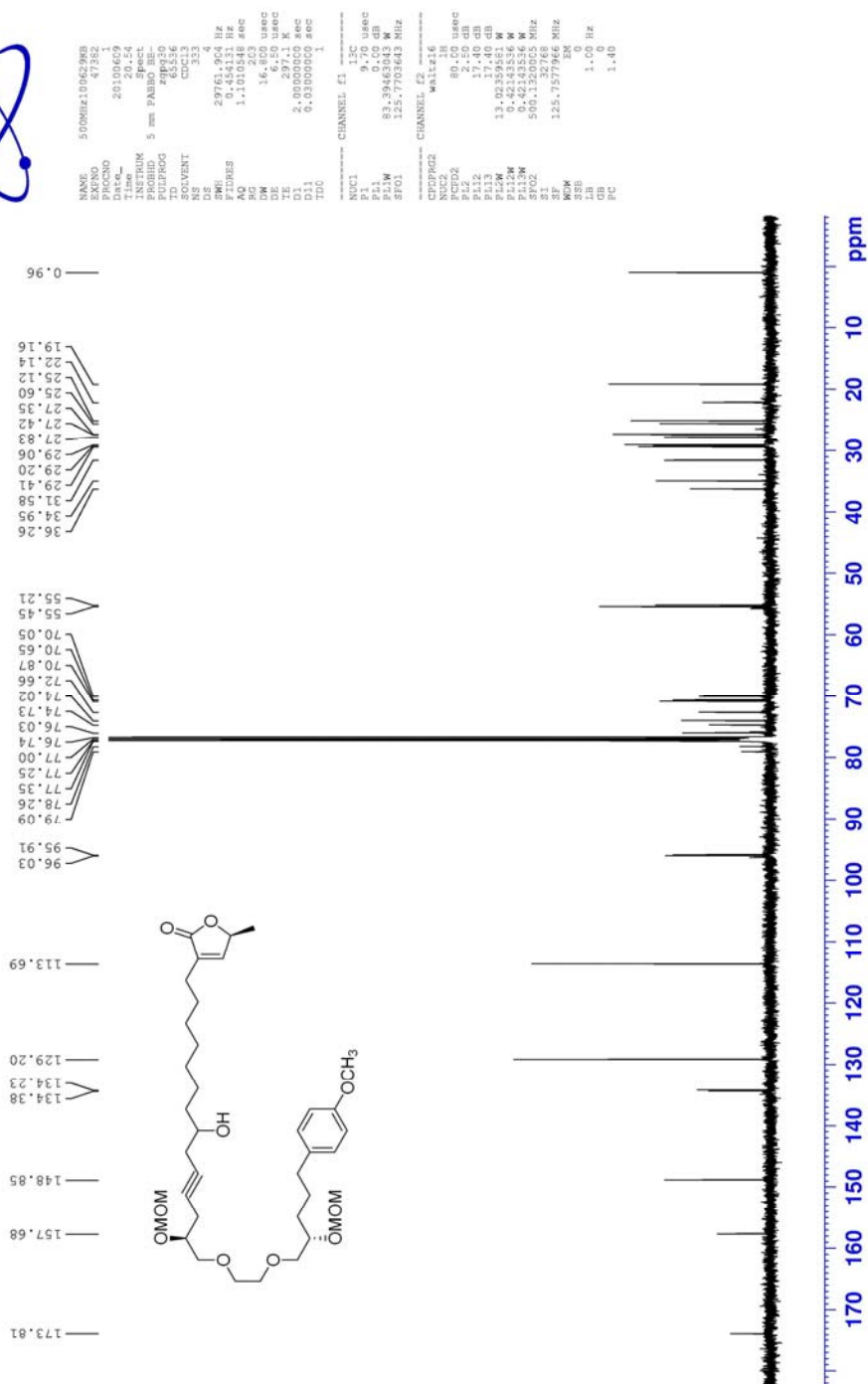
¹³C NMR spectra of compound 46



xqc47382

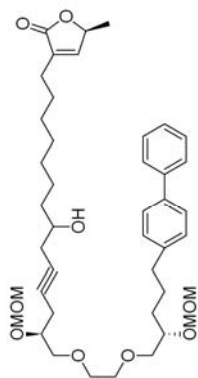
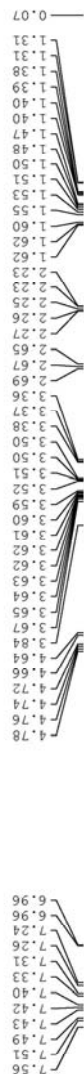


¹H NMR spectra of compound 47

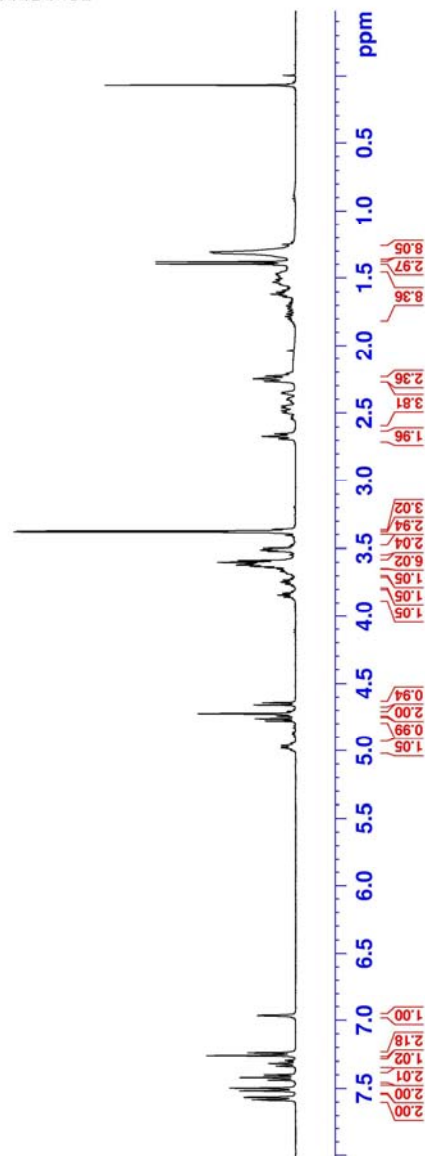




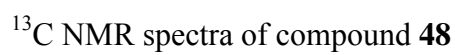
xiaocqicai-47245



NAME xiaocqicai
EXPNO 121
PROCNO 1
Date_ 20180908
Time 14.11
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8278.346 Hz
F2 0.718441 MHz
AQ 3.9558423 sec
RG 71.8
DM 60.400 usec
DE 14.50 usec
TE 29.9
D1 1.00000000 sec
TD0 1
CHANNEL f1
NUC1 1H
P1 14.50 usec
PL1 0.00 dB
PL12 0.00 dB
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SFO 400.132768 MHz
SI 32768
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WDW EM
SSB 0
GB 0
PC 1.00

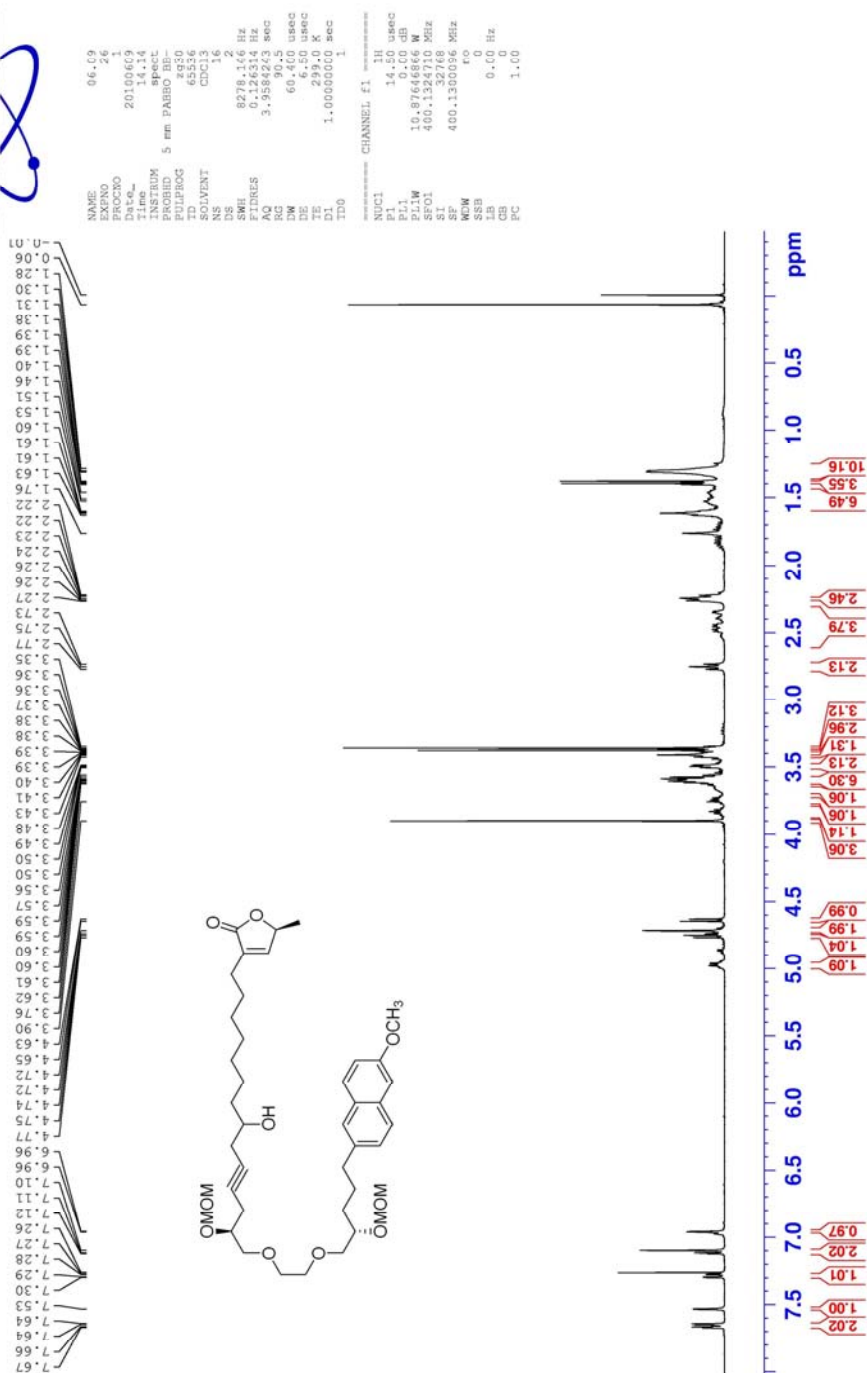


¹H NMR spectra of compound 48

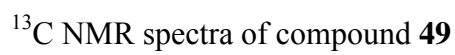




xqc47381

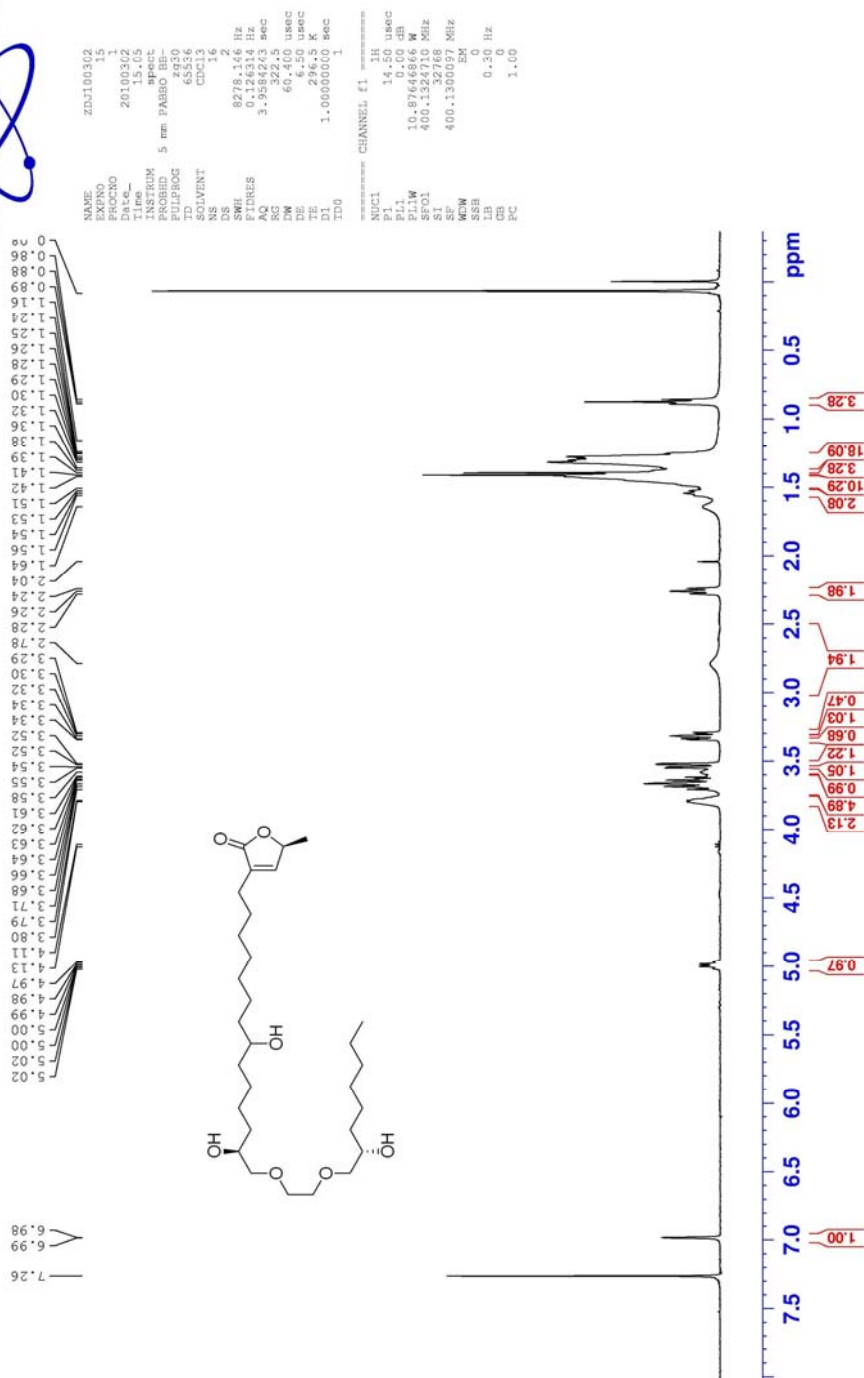


¹H NMR spectra of compound 49





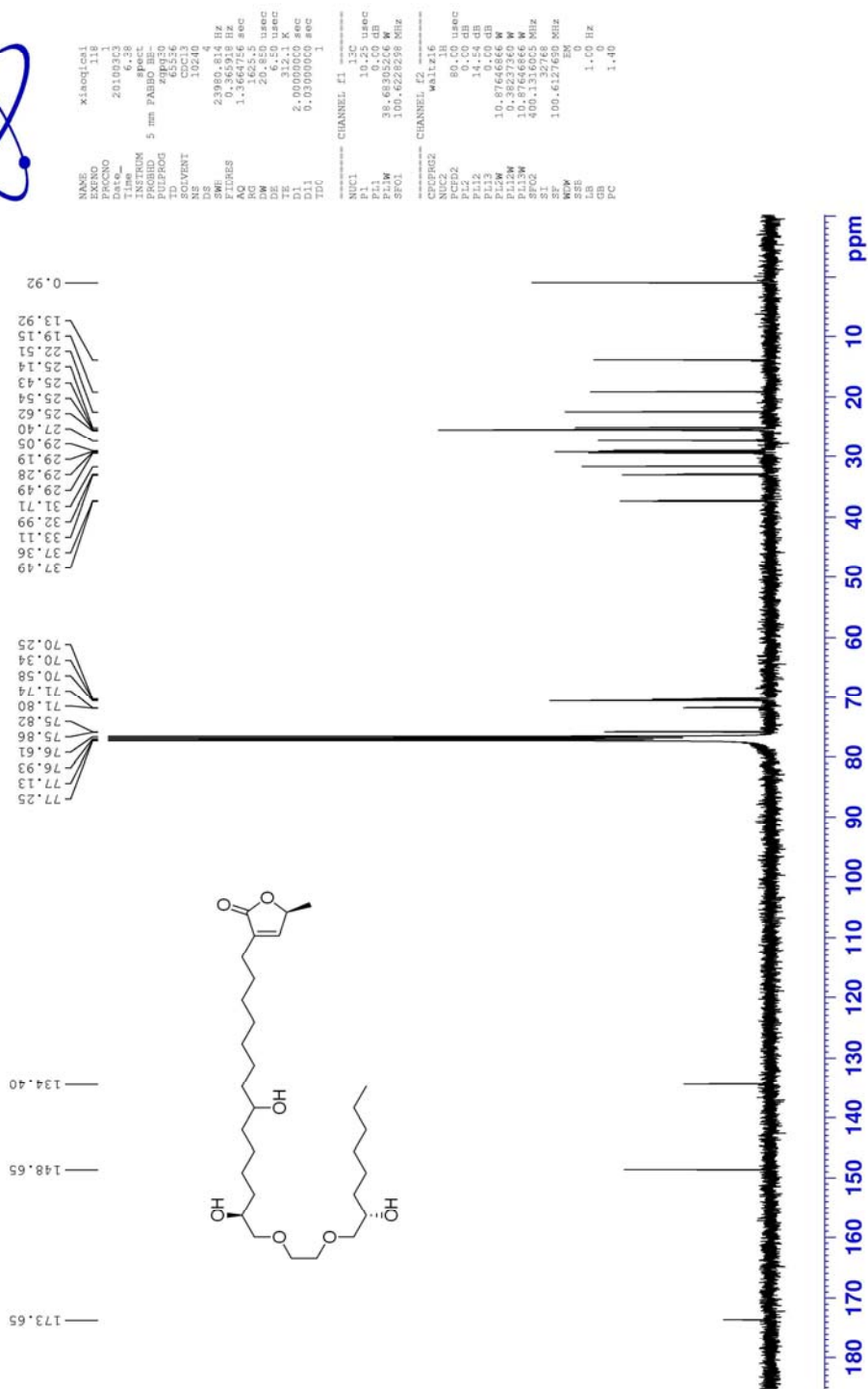
xqc47238



¹H NMR spectra of compound 2

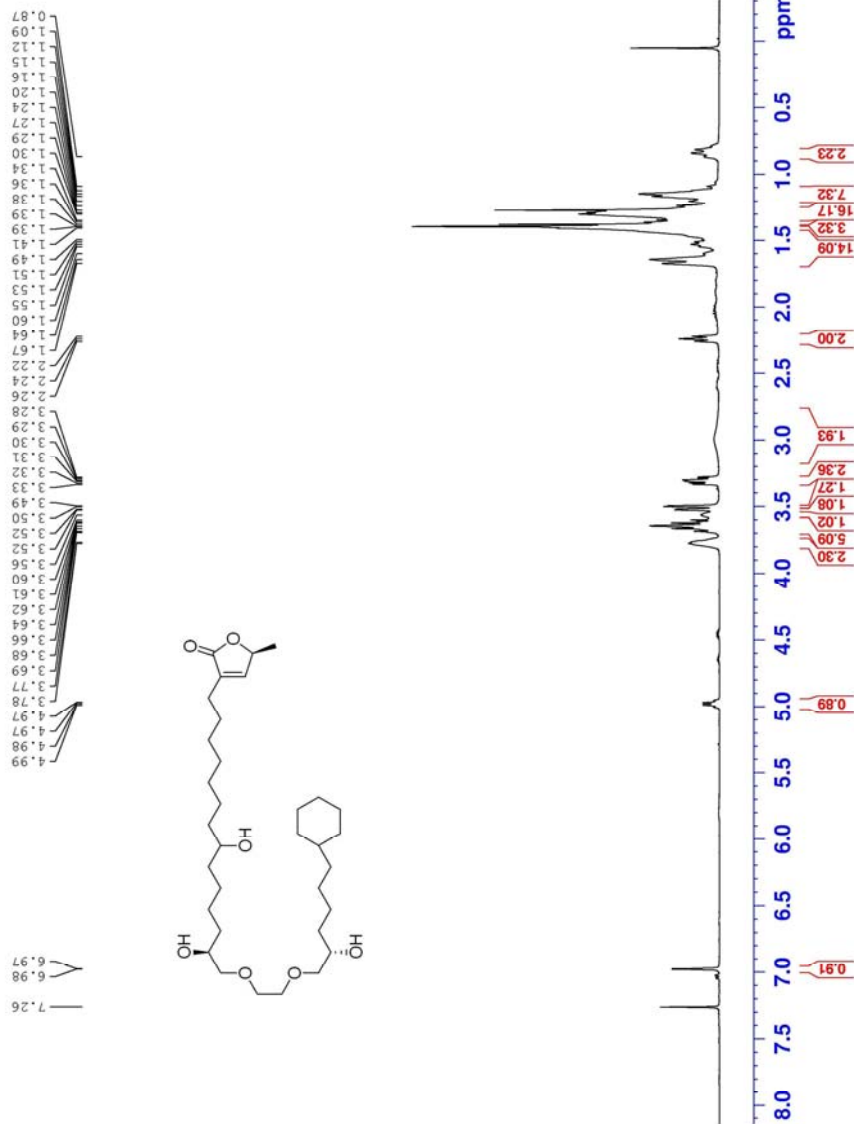


xqc47238



^{13}C NMR spectra of compound 2

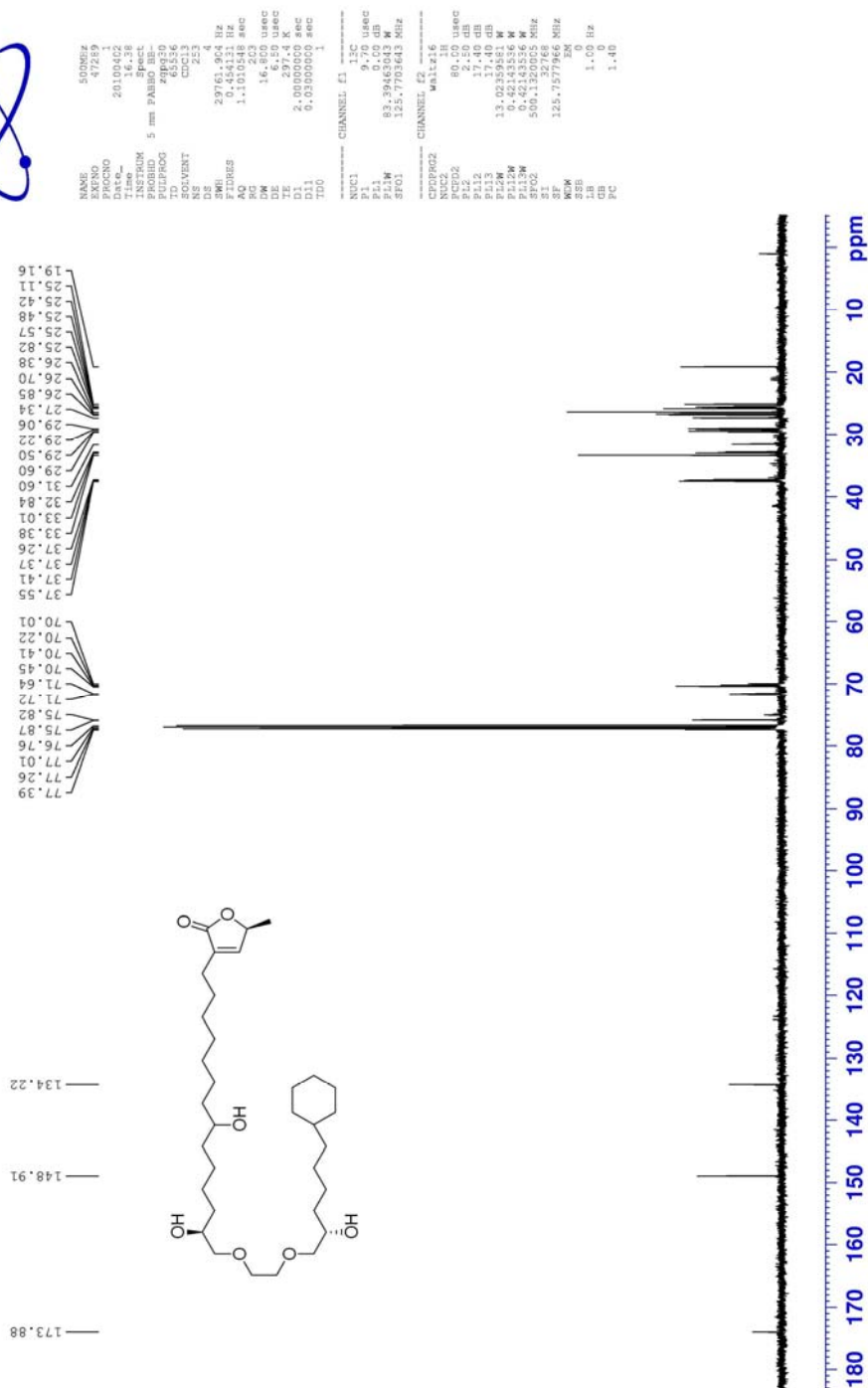
xqc47289

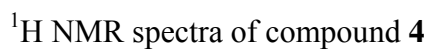


¹H NMR spectra of compound 3



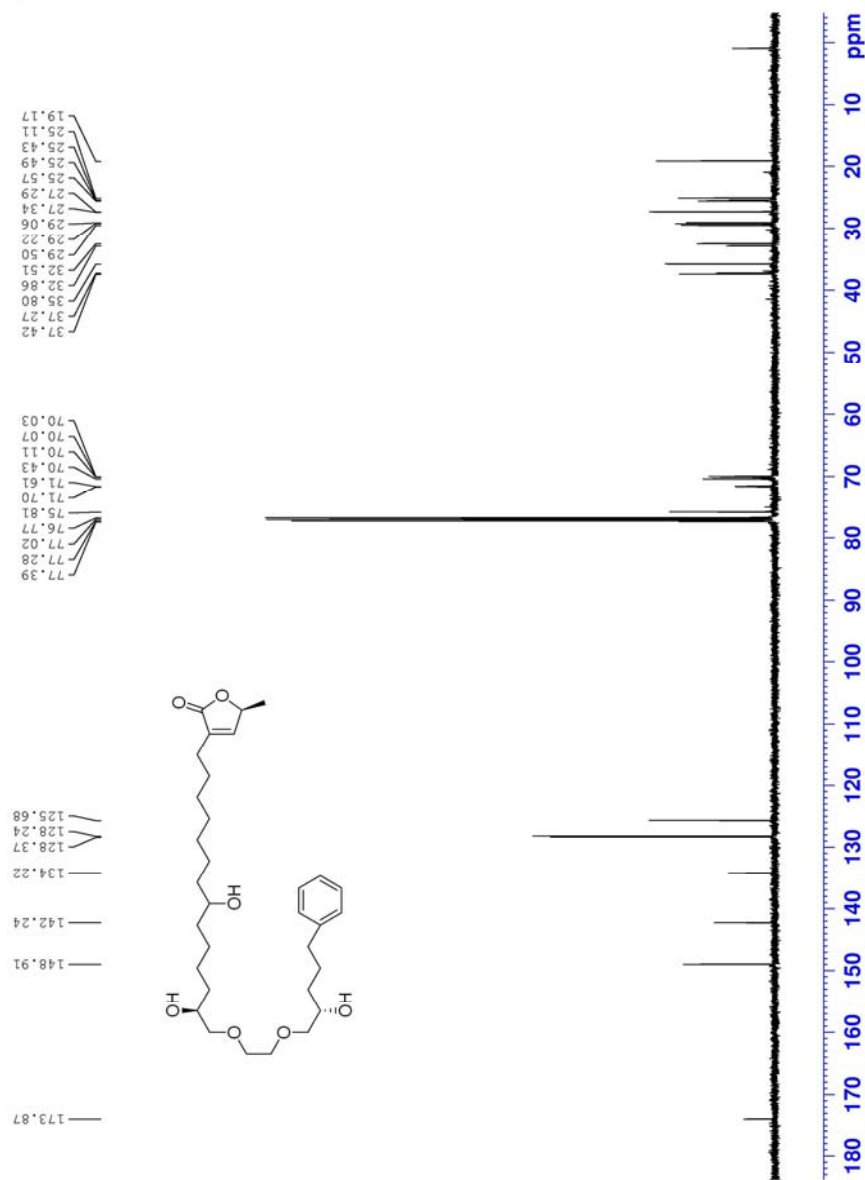
xqc47289



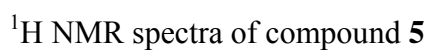




xqc47261

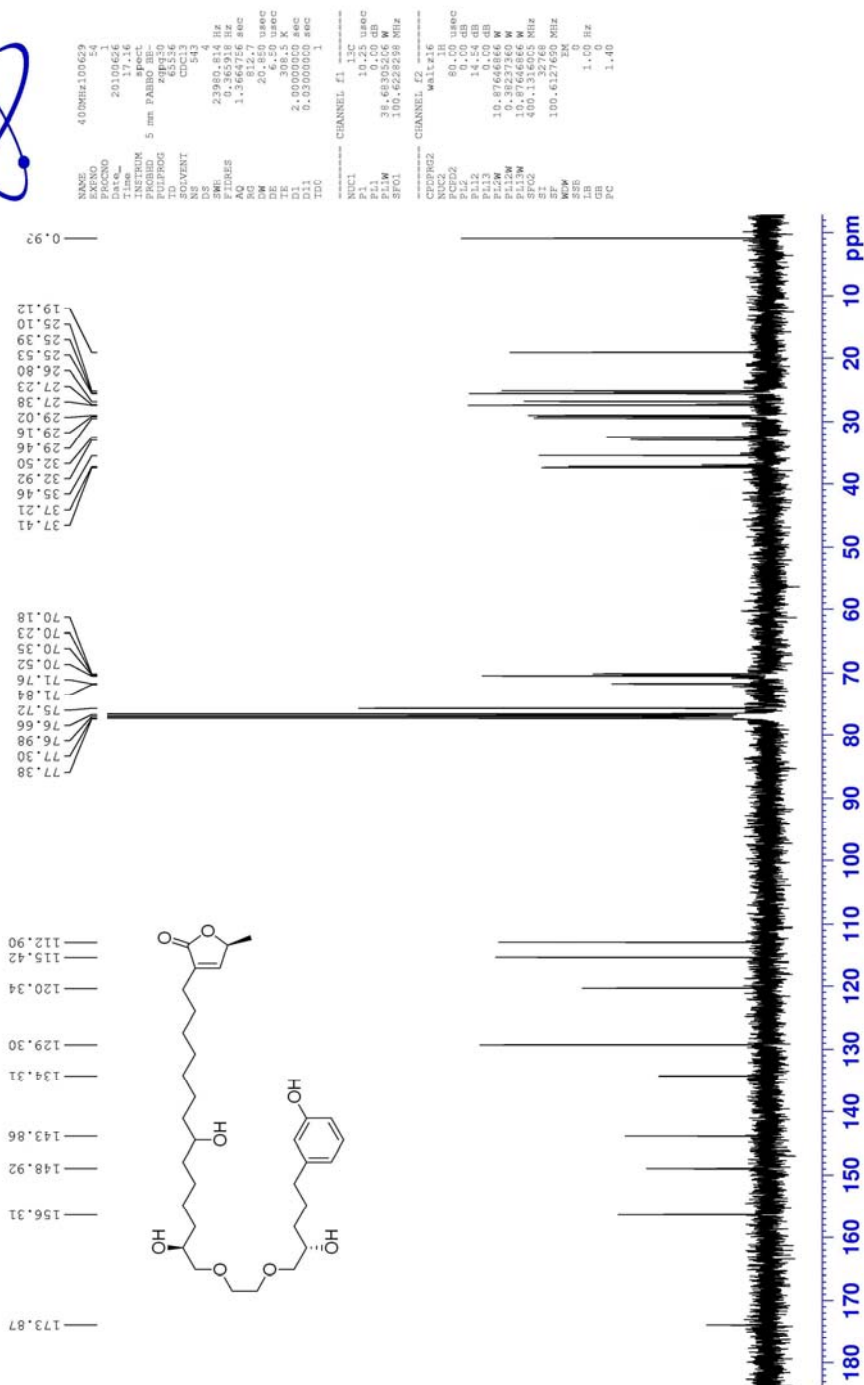


¹³C NMR spectra of compound 4





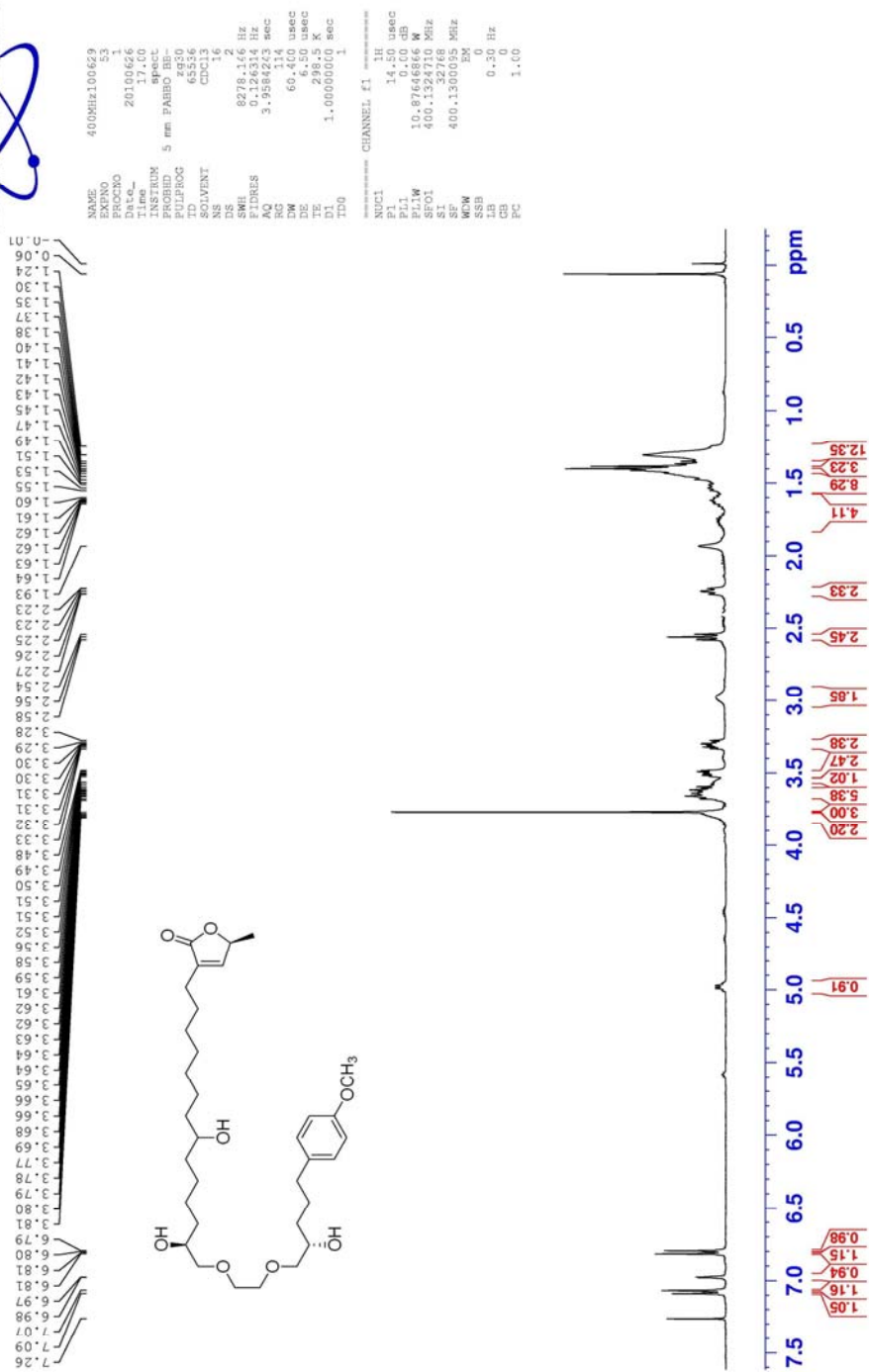
xqc47395



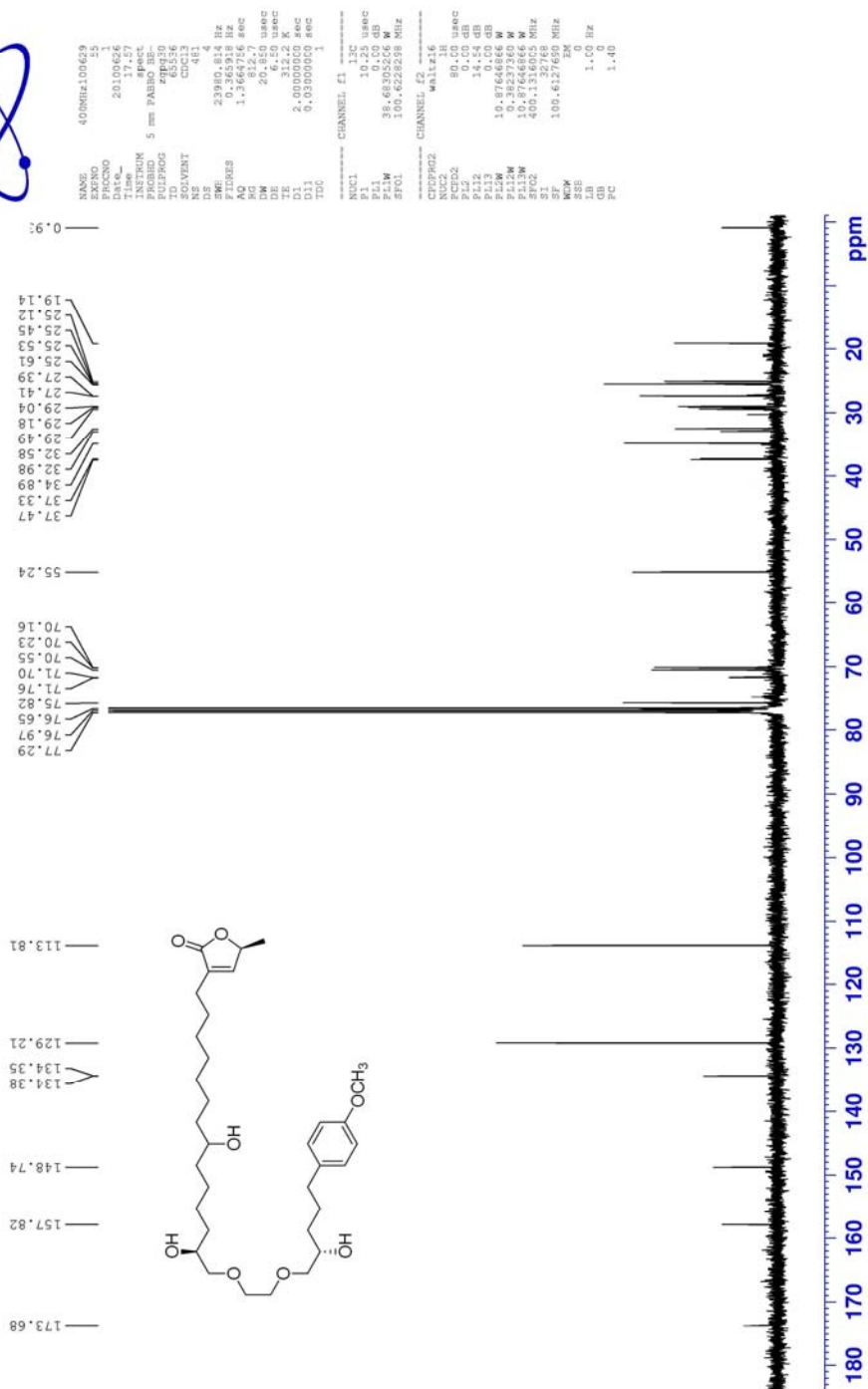
¹³C NMR spectra of compound 5



xqc47396

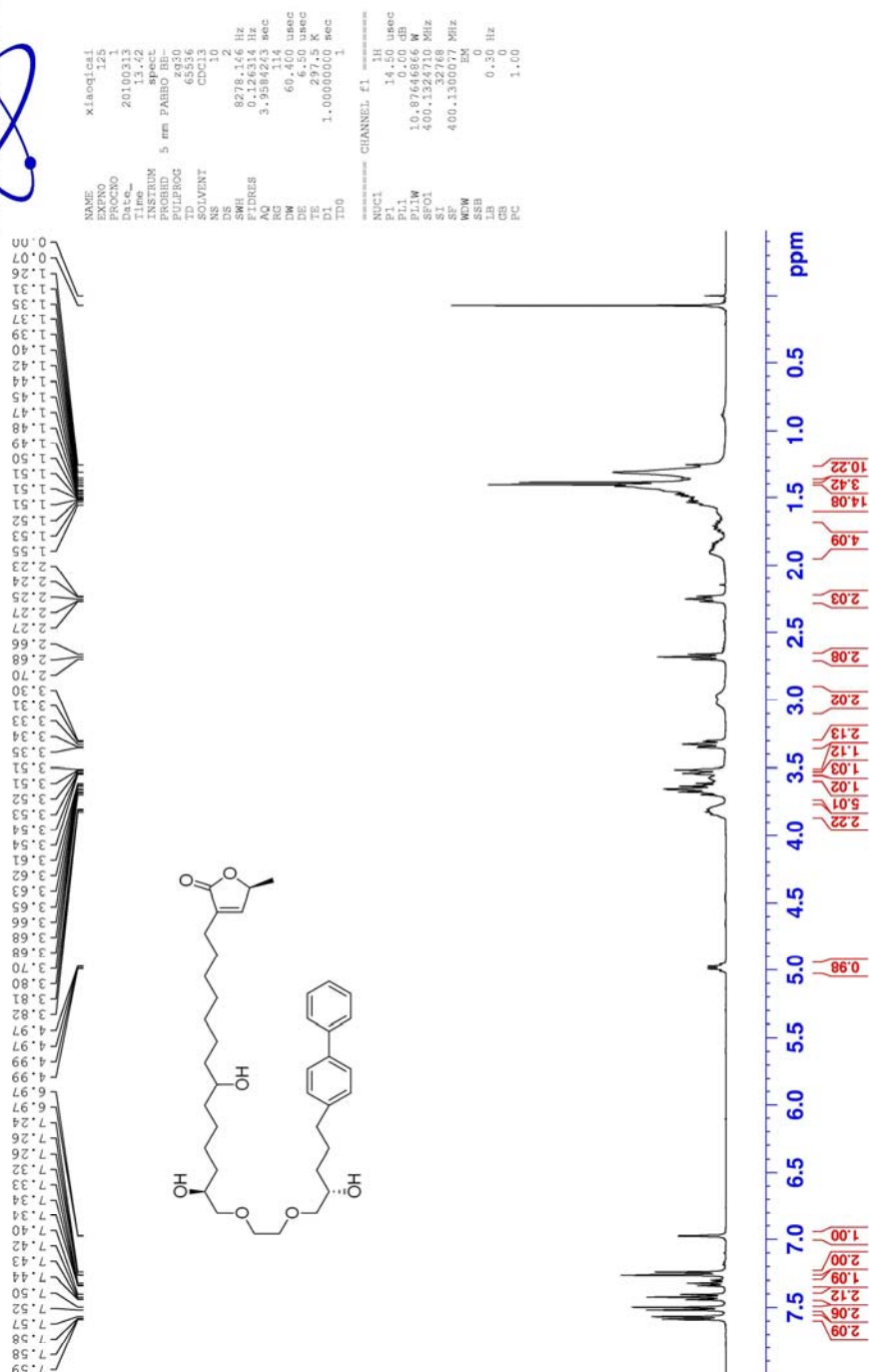


^1H NMR spectra of compound 6

¹³C NMR spectra of compound **6**



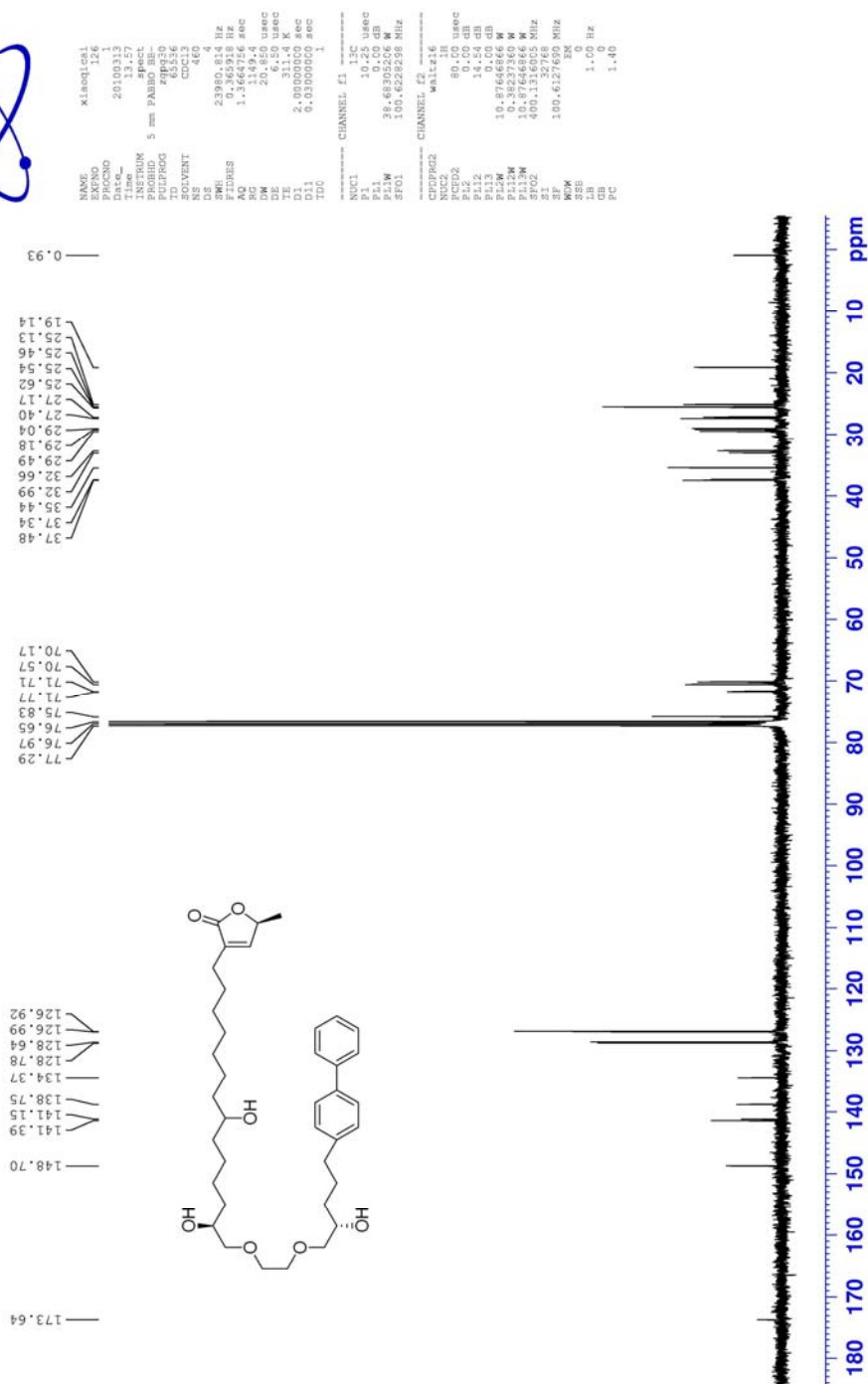
xiaogicai-47257



¹H NMR spectra of compound 7



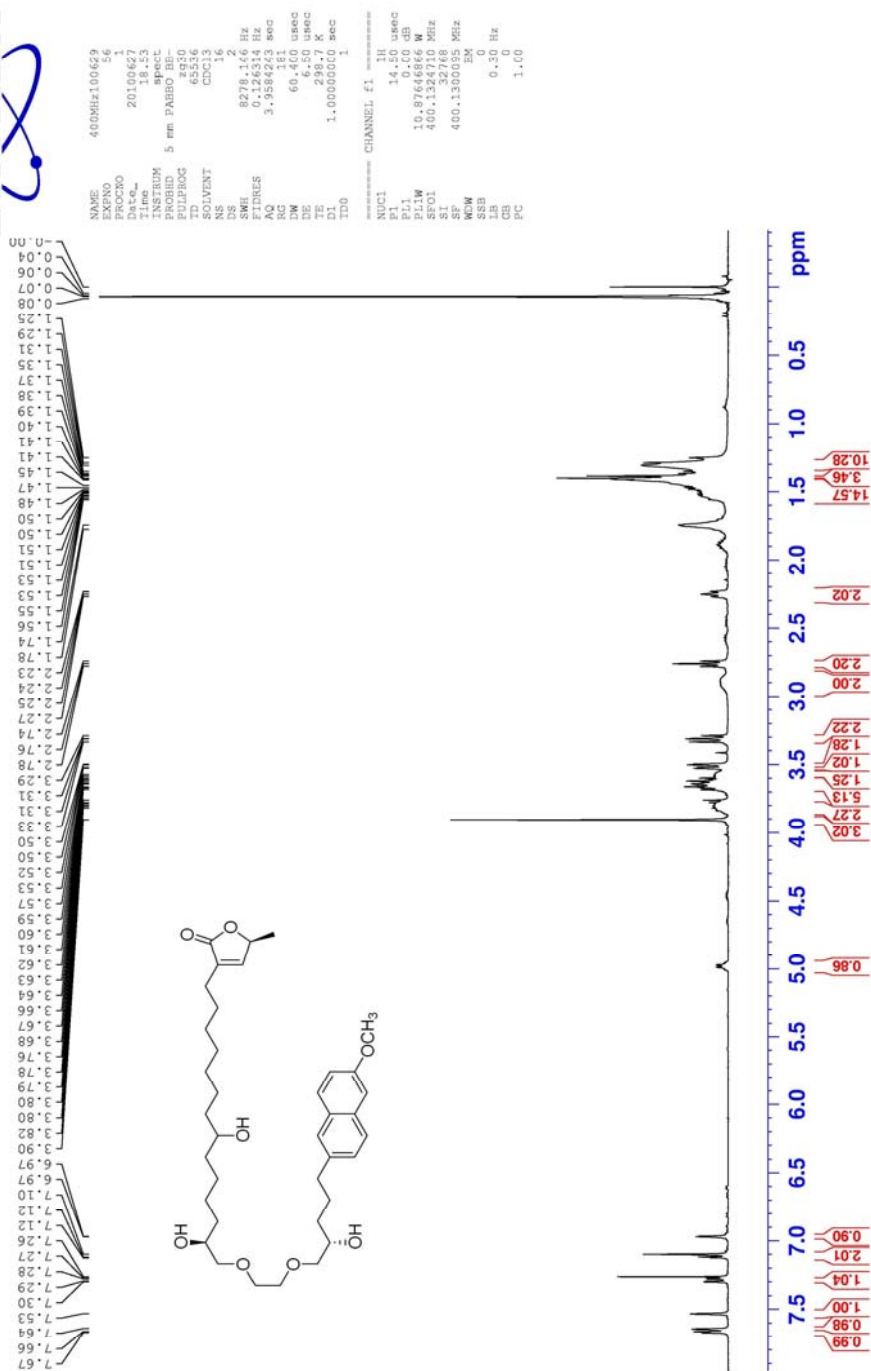
xiaoqicai-47257



¹³C NMR spectra of compound 7

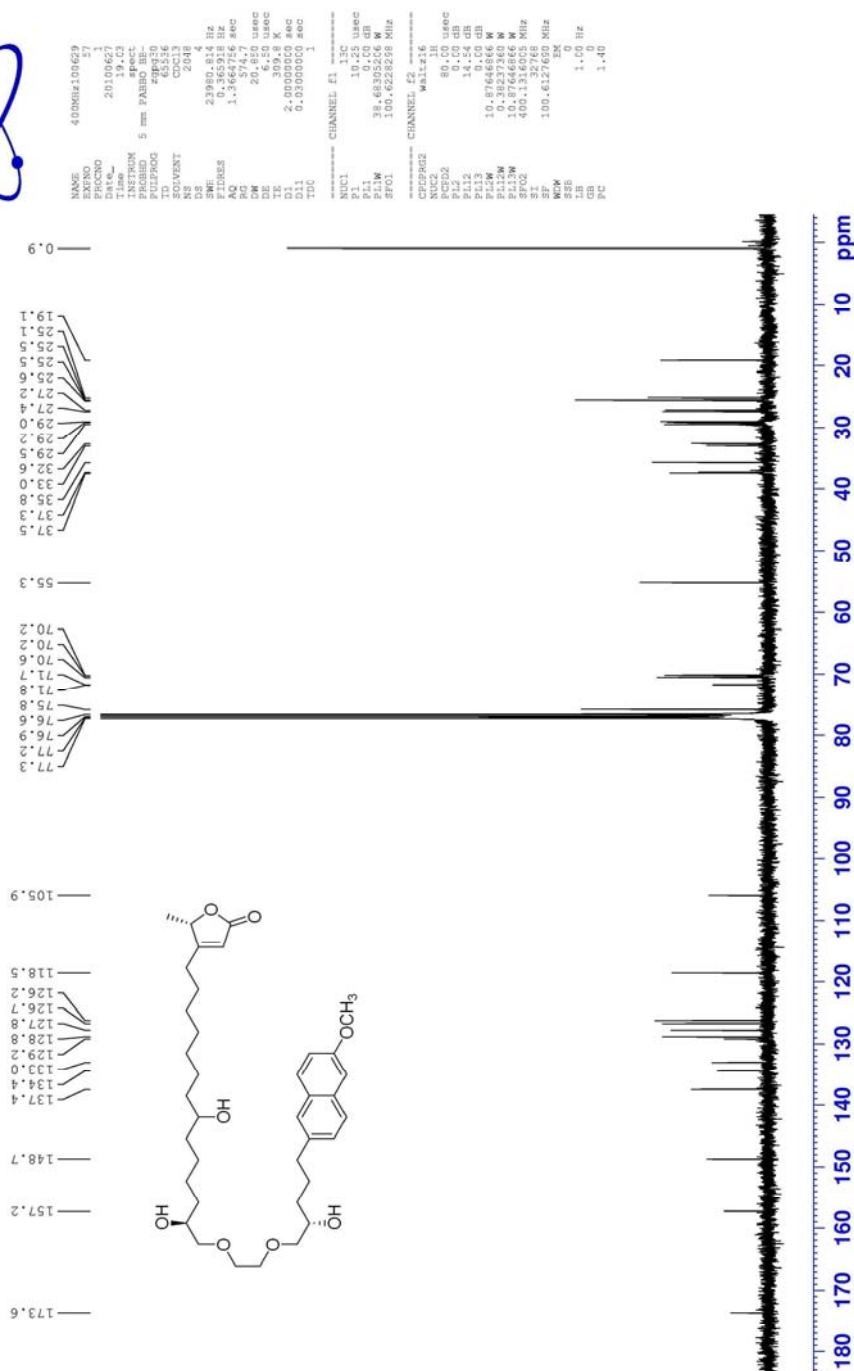


xqc47398



¹H NMR spectra of compound 8

xqc47398



¹³C NMR spectra of compound 8