

Supporting Information

Total synthesis of γ -indomycinone and kidamycinone by means of two regioselective Diels-Alder reactions.

Thibaud Mabit^{† 1}, Aymeric Siard^{† 1}, Mathilde Pantin[†], Doumadé Zon[†], Laura Foulgoc[†], Drissa Sissouma[†], André Guingant[†], Monique Mathé-Allainmat[†], Jacques Lebreton[†], François Carreaux[‡], Gilles Dujardin[§] and Sylvain Collet^{†*}

[†]*Université de Nantes, CNRS, Chimie Et Interdisciplinarité: Synthèse, Analyse, Modélisation (CEISAM), UMR CNRS n° 6230, 2, rue de la Houssinière – BP 92208 – 44322 NANTES Cedex 3 (France)*

[‡]*Institut des Sciences Chimiques de Rennes, UMR 6226 CNRS-Université de Rennes 1, 263, avenue du Général Leclerc, Campus de Beaulieu, Bâtiment 10A, 35042 Cedex Rennes, France*

[§]*Université du Maine, Institut des Molécules et Matériaux du Mans, UMR CNRS 6283, Faculté des Sciences, Avenue O. Messiaen, 72085 Le Mans cedex 9, France*

*E-mail : sylvain.collet@univ-nantes.fr

Table of Contents

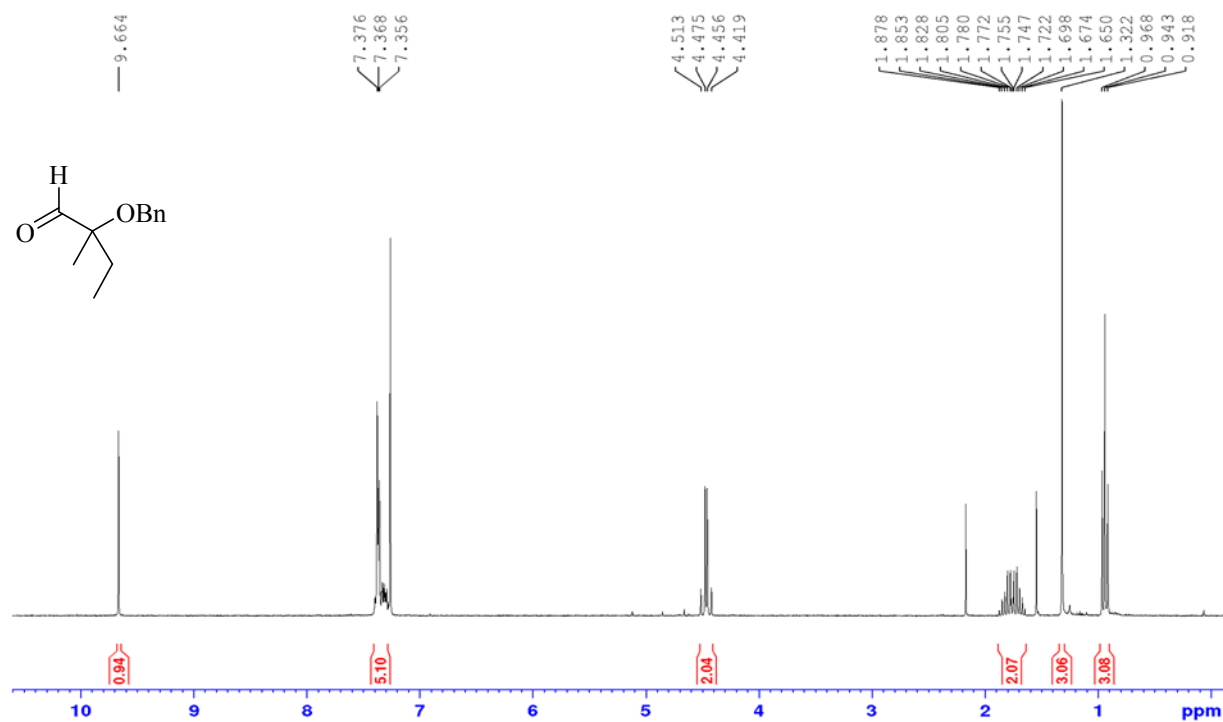
1. ¹ H NMR and ¹³ C NMR Spectra of Compounds	S3
1H NMR and 13C NMR Spectra of Compound 5	S3
1H NMR and 13C NMR Spectra of Compound 6	S4
1H NMR and 13C NMR Spectra of Compound 7	S5
1H NMR and 13C NMR Spectra of Compound 9	S6
1H NMR and 13C NMR Spectra of Compound 14	S7
1H NMR and 13C NMR Spectra of Compound 15	S8
1H NMR and 13C NMR Spectra of Compound 16	S9

¹ *These authors contributed equally to this work*

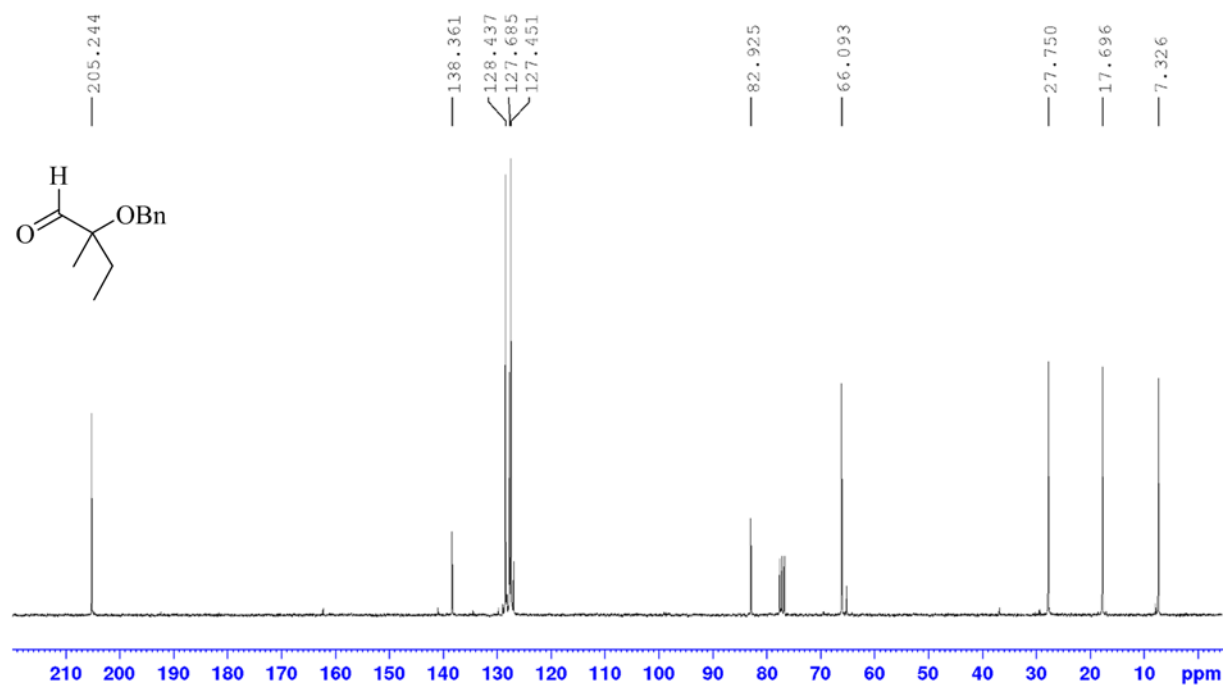
1H NMR and 13C NMR Spectra of Compound 1	S10
1H NMR and 13C NMR Spectra of Compound 11	S11
1H NMR and 13C NMR Spectra of Compound 12	S12
1H NMR and 13C NMR Spectra of Compound 4b	S13
1H NMR and 13C NMR Spectra of Compound 17	S14
1H NMR and 13C NMR Spectra of Compound 19	S15
1H NMR and 13C NMR Spectra of Compound 20	S16
1H NMR and 13C NMR Spectra of Compound 21	S17
1H NMR and 13C NMR Spectra of Compound 2	S18
1H NMR and 13C NMR Spectra of Compound 22	S19
2. X-Ray derived ORTEP of 19	S20
3. Computational details.....	S22
3.1. DFT methods.....	S22
3.2. Coordinates of all stationary points (the best conformers).....	S23

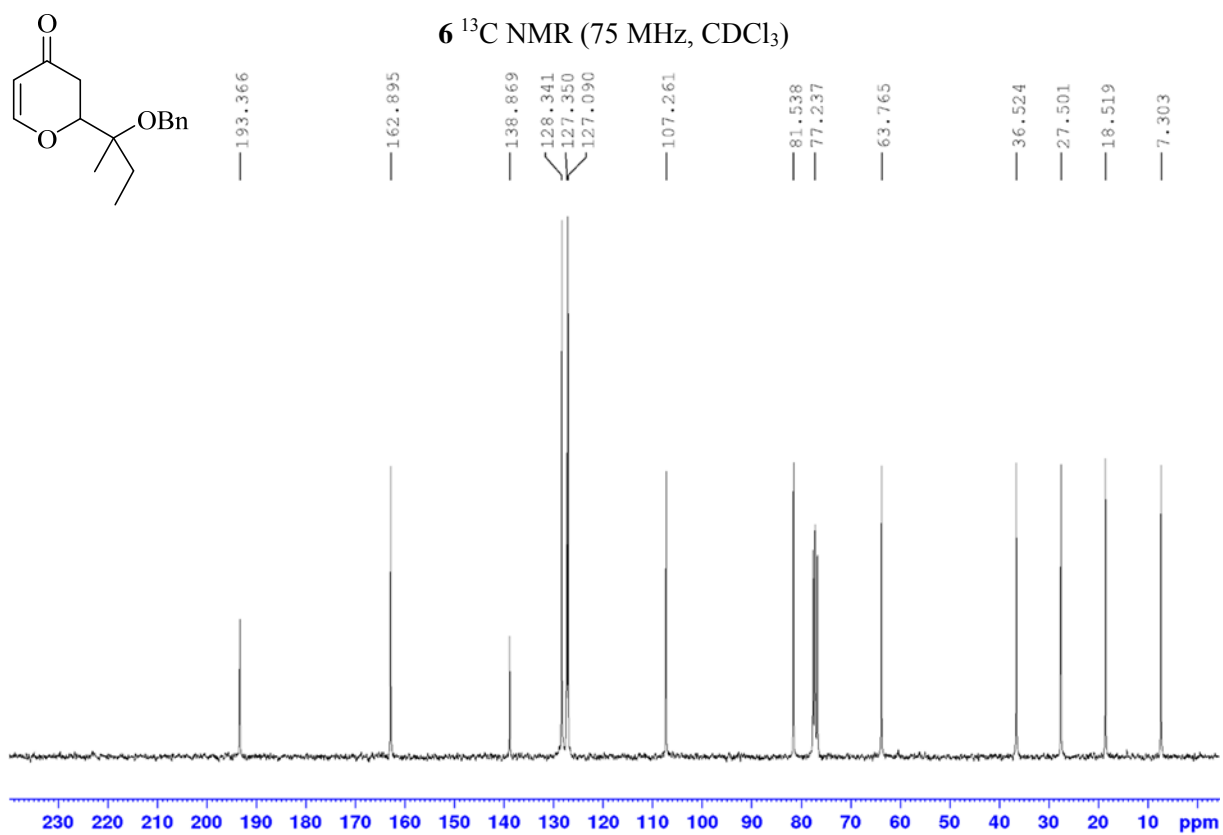
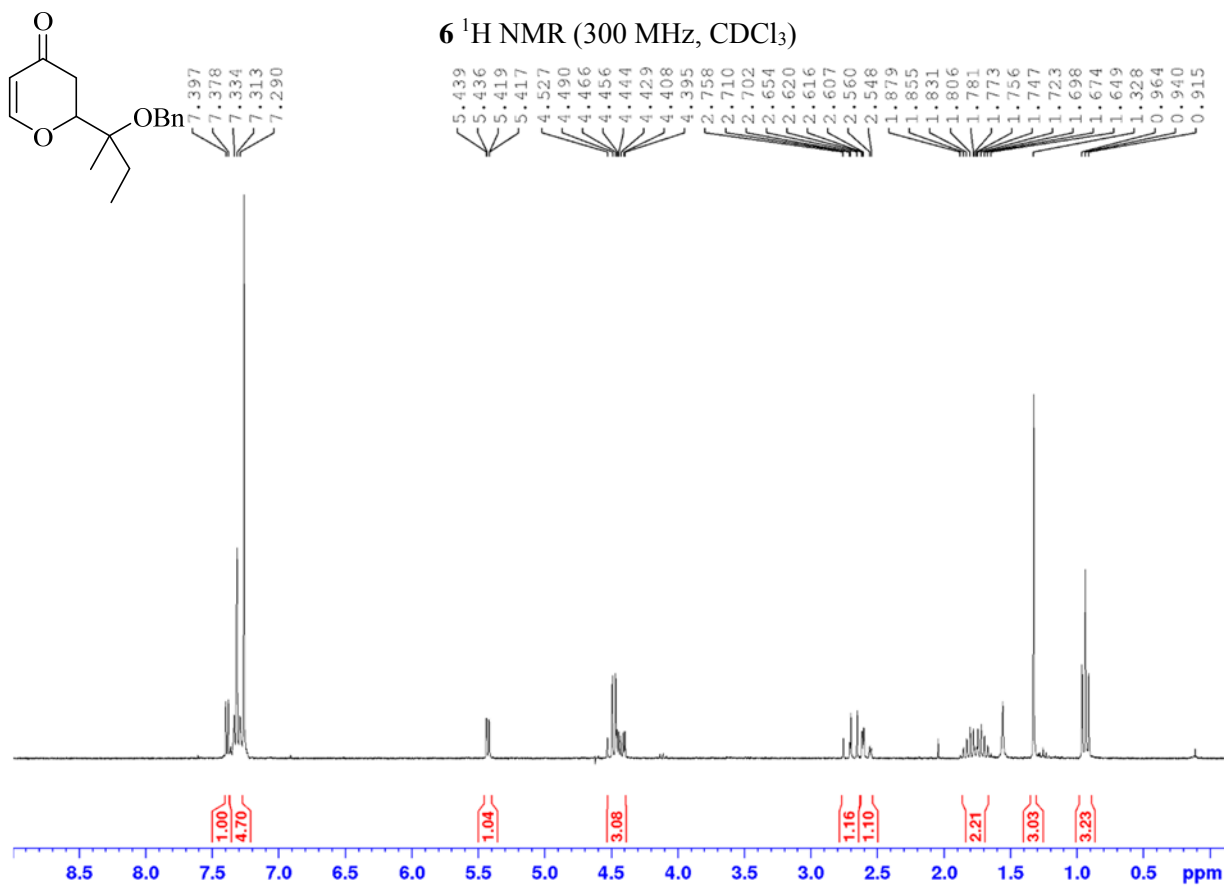
1. ¹H NMR and ¹³C NMR Spectra of Compounds

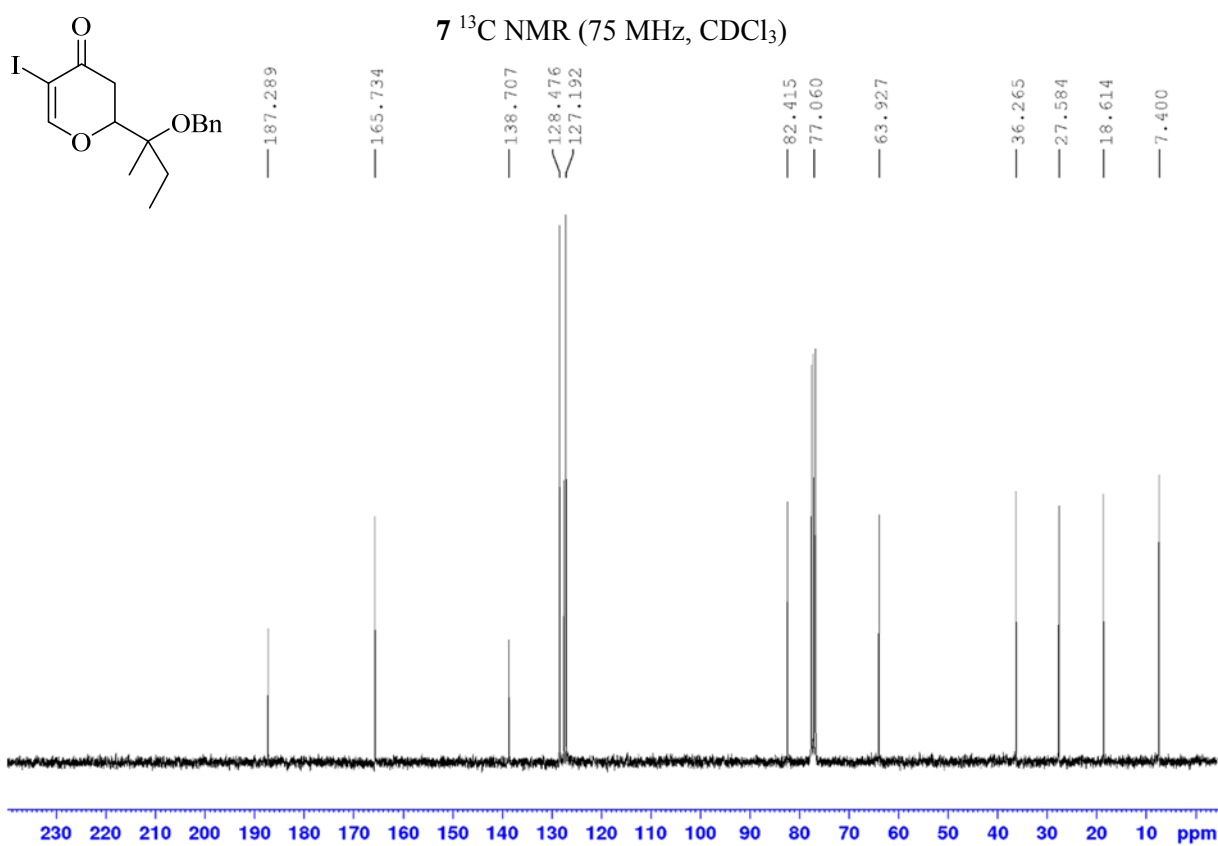
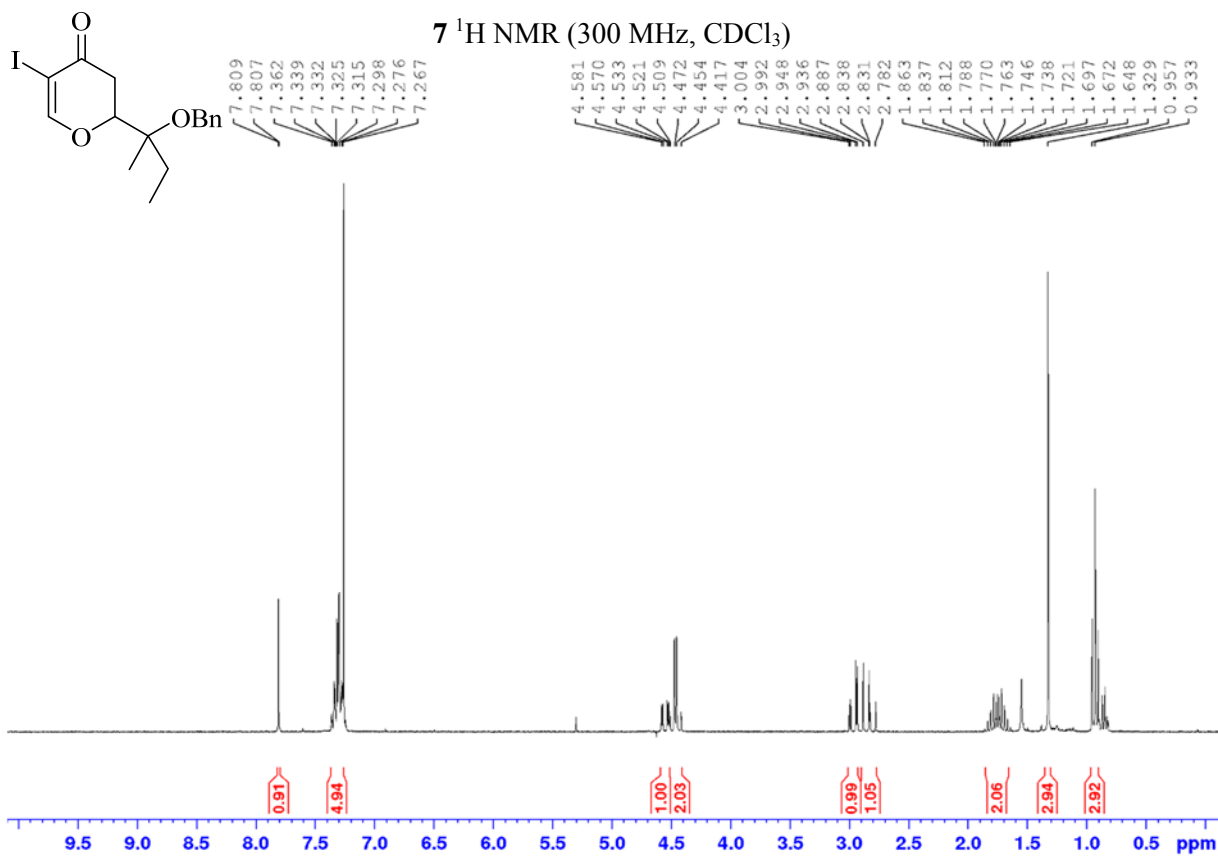
5 ¹H NMR (300 MHz, CDCl₃)



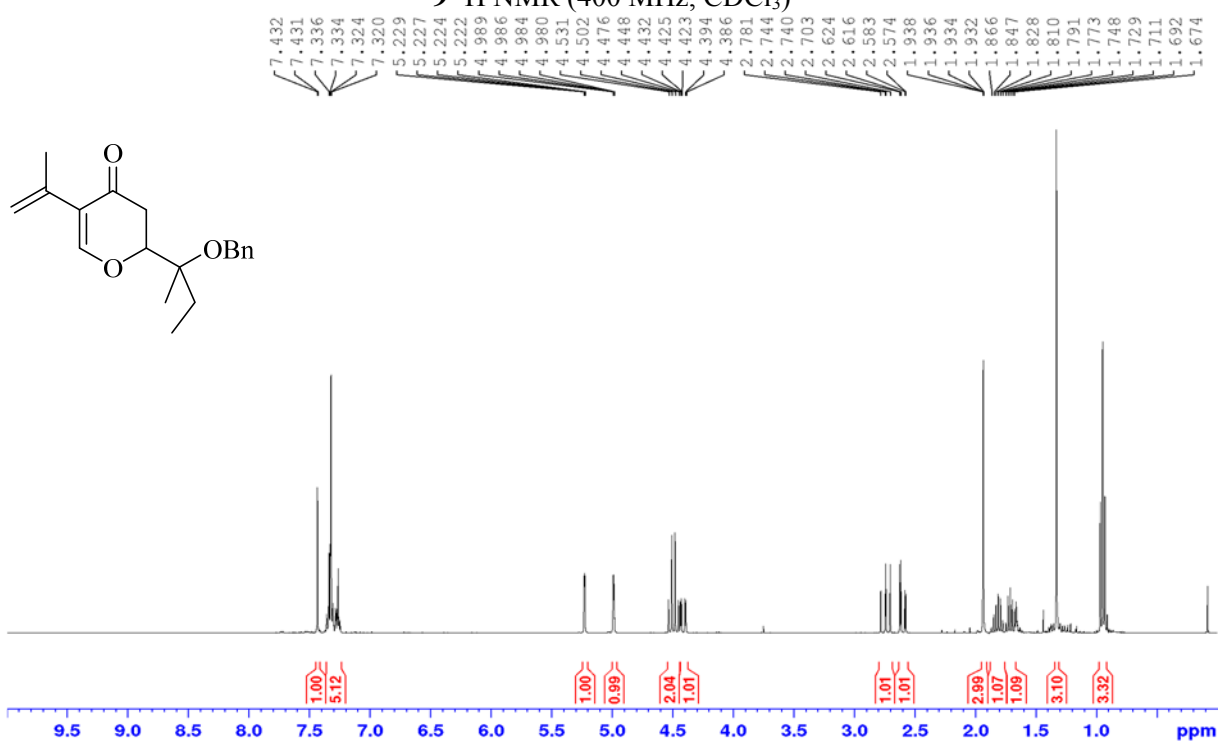
5 ¹³C NMR (75 MHz, CDCl₃)



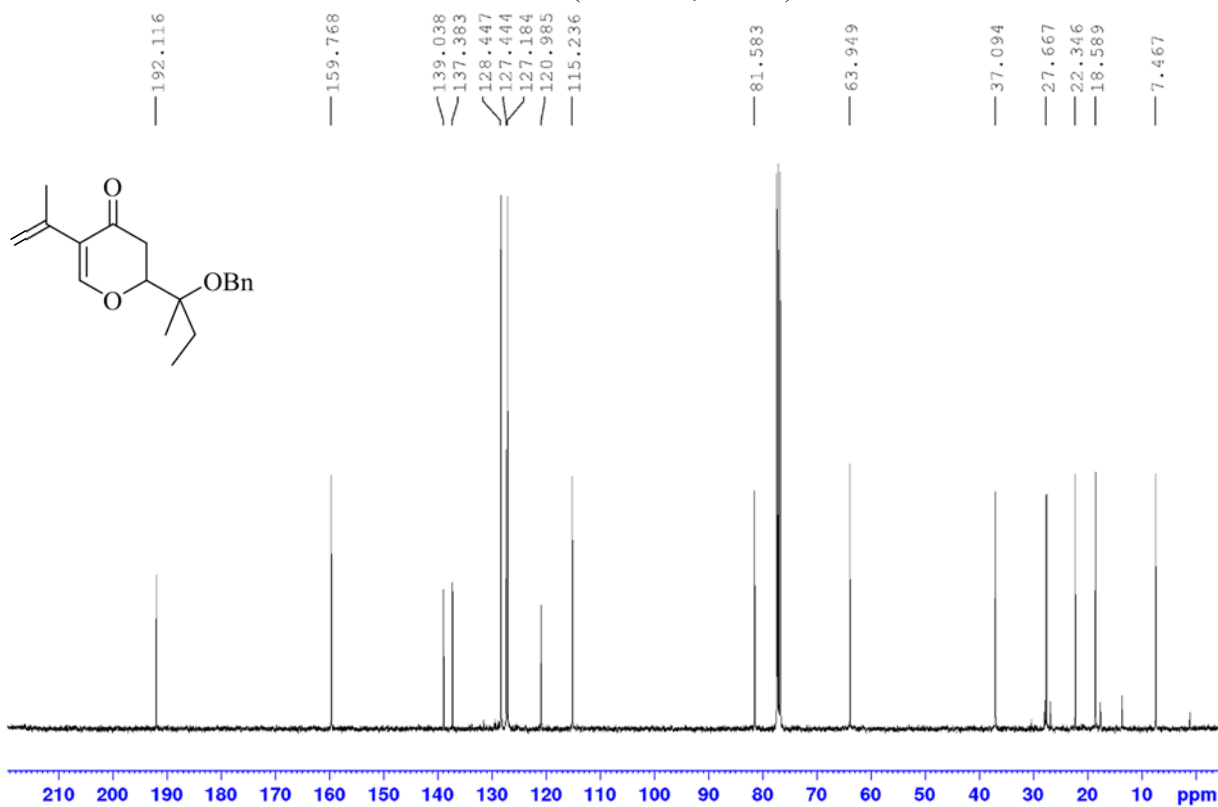




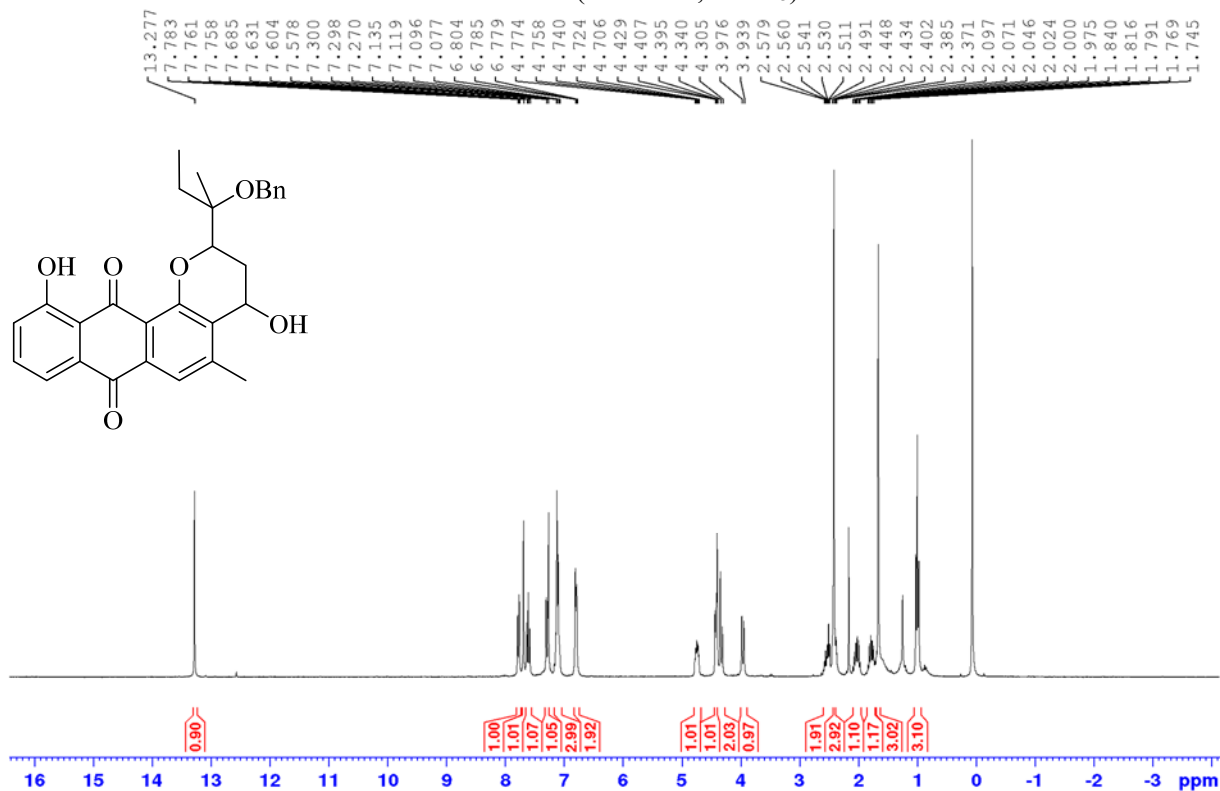
9 ¹H NMR (400 MHz, CDCl₃)



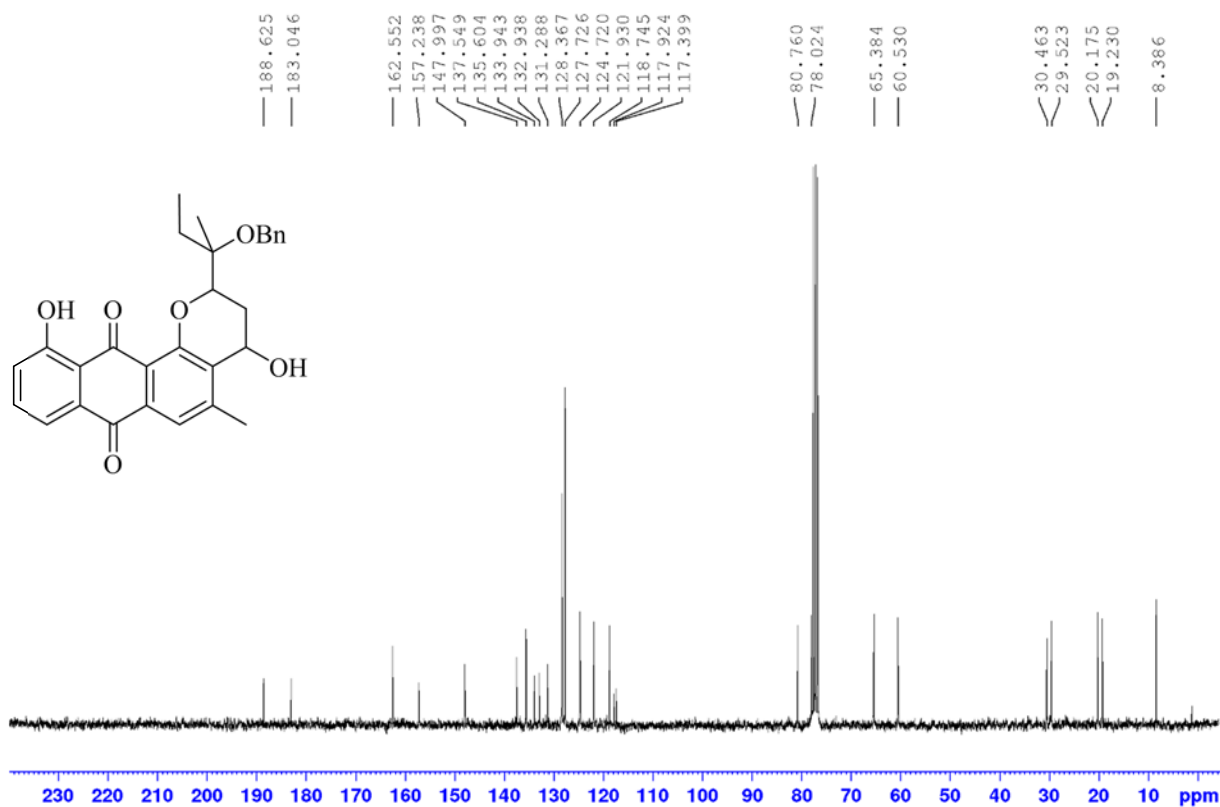
9 ¹³C NMR (100 MHz, CDCl₃)



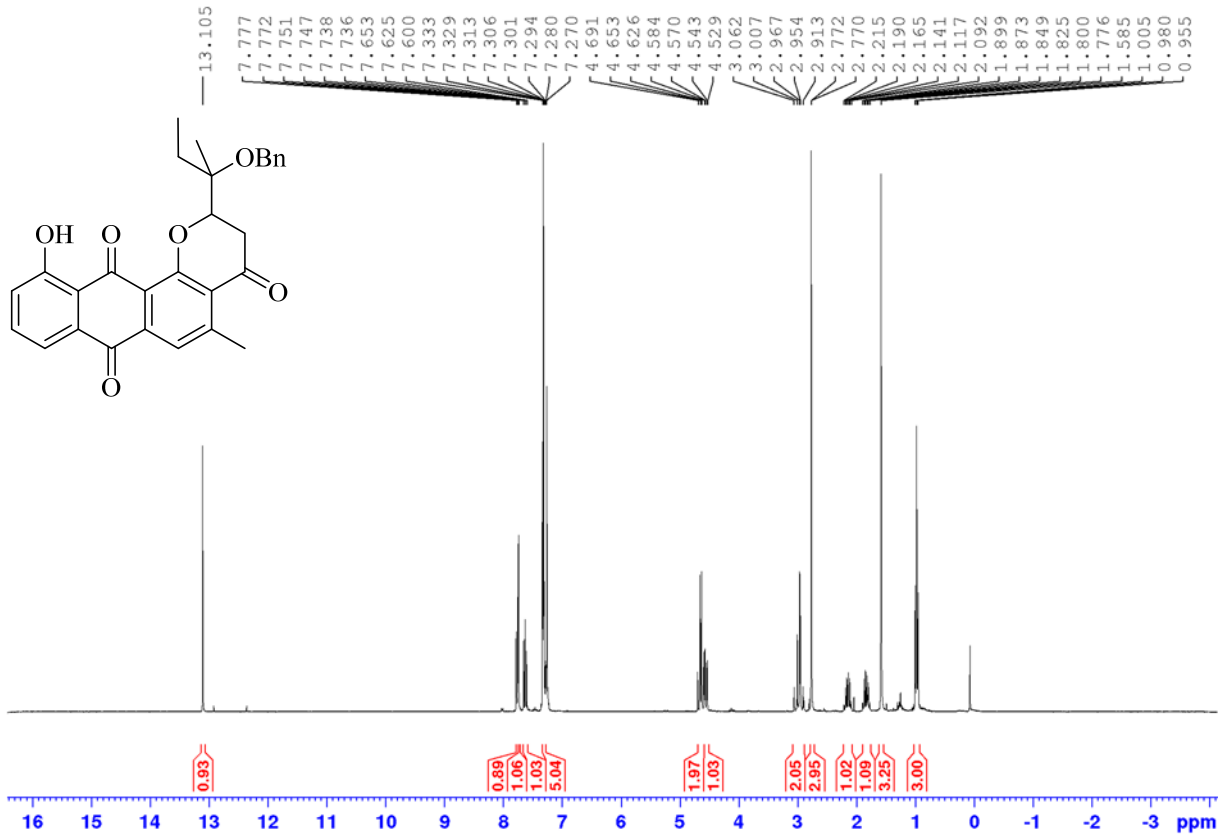
14 ^1H NMR (300 MHz, CDCl_3)



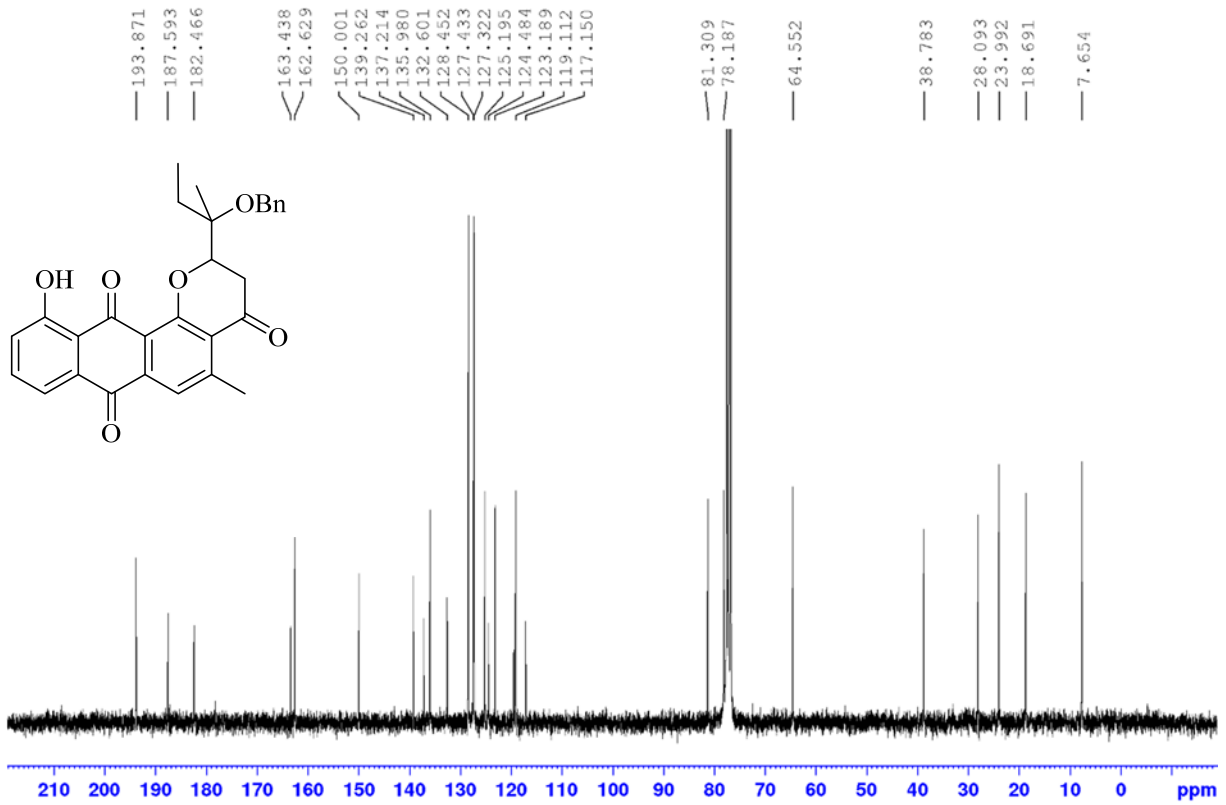
14 ^{13}C NMR (75 MHz, CDCl_3)

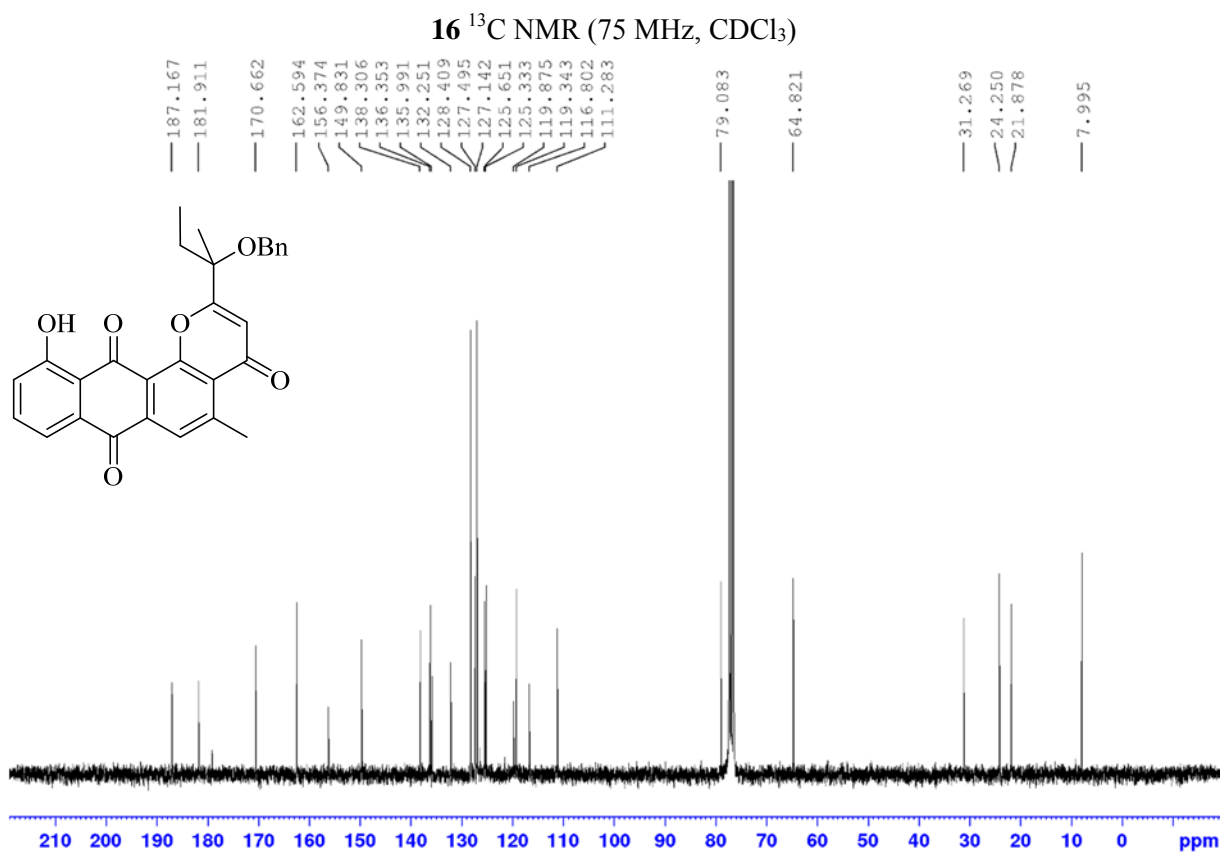
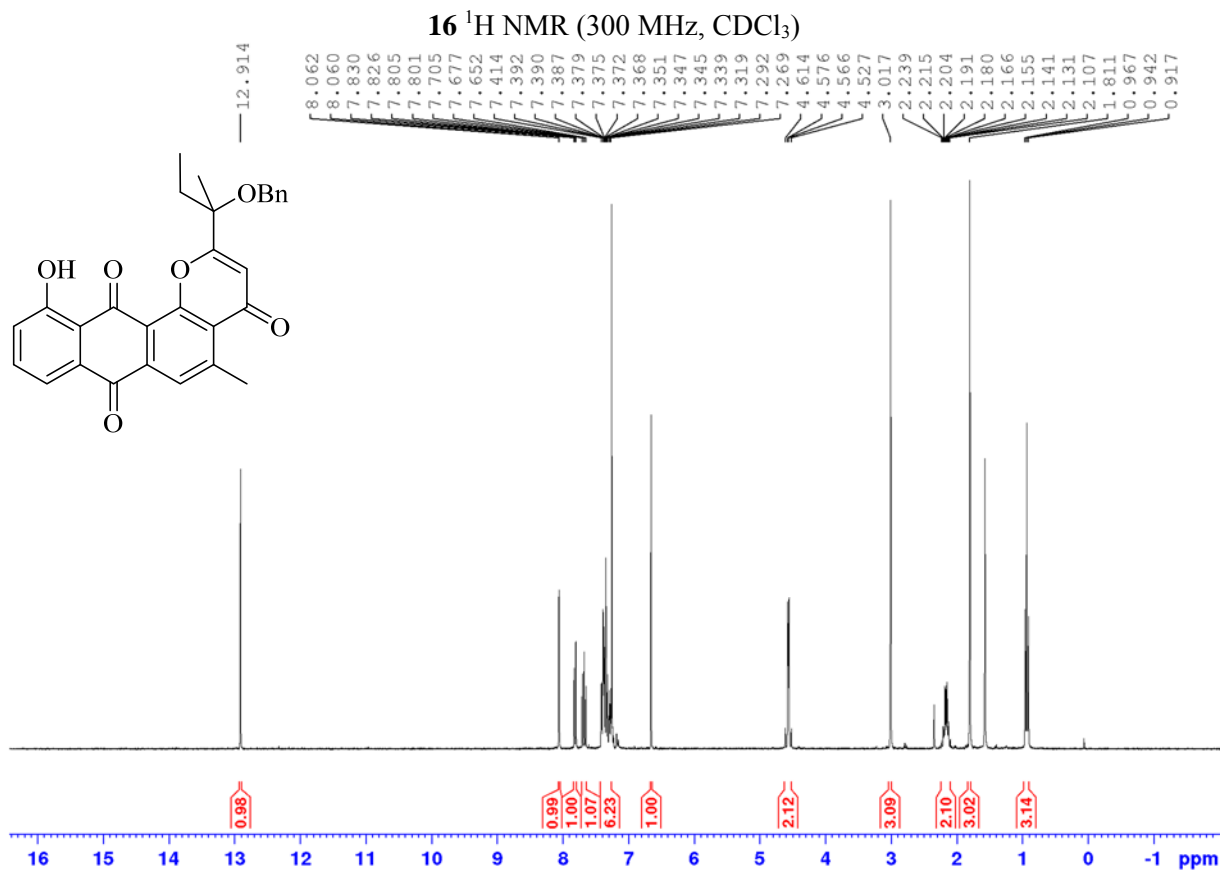


15 ^1H NMR (300 MHz, CDCl_3)

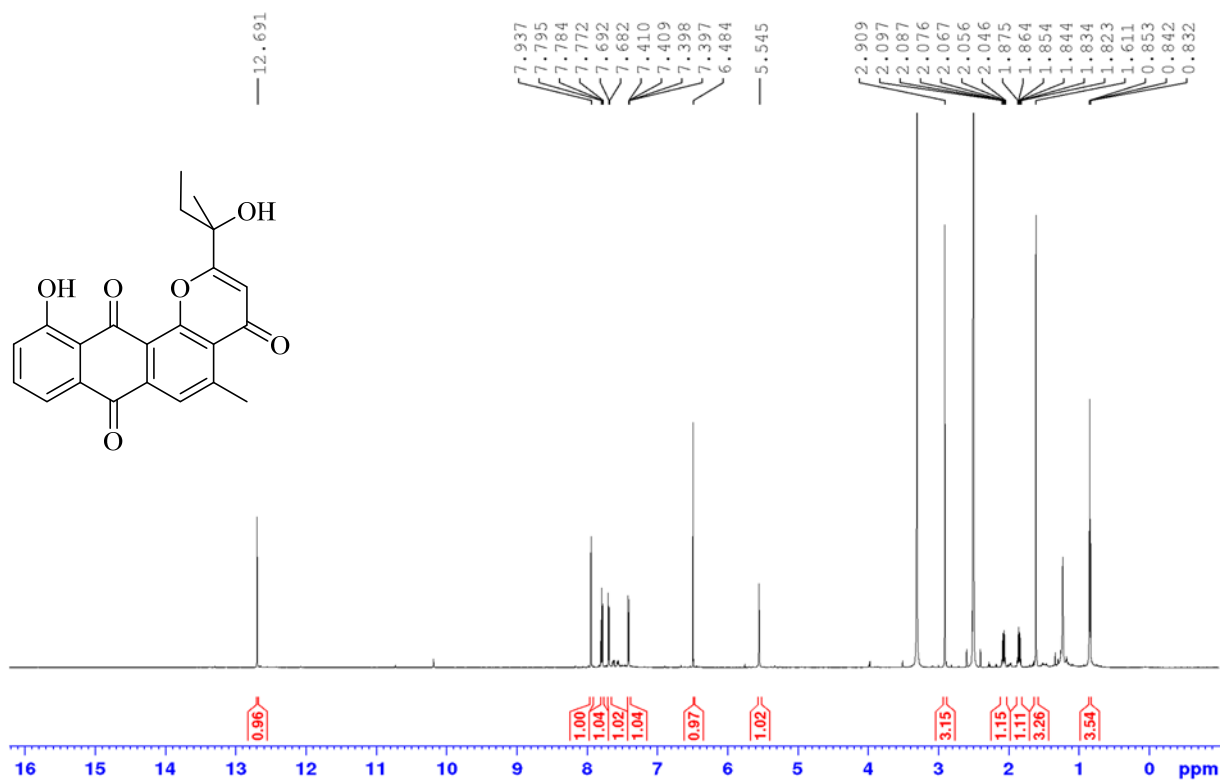


15 ^{13}C NMR (75 MHz, CDCl_3)

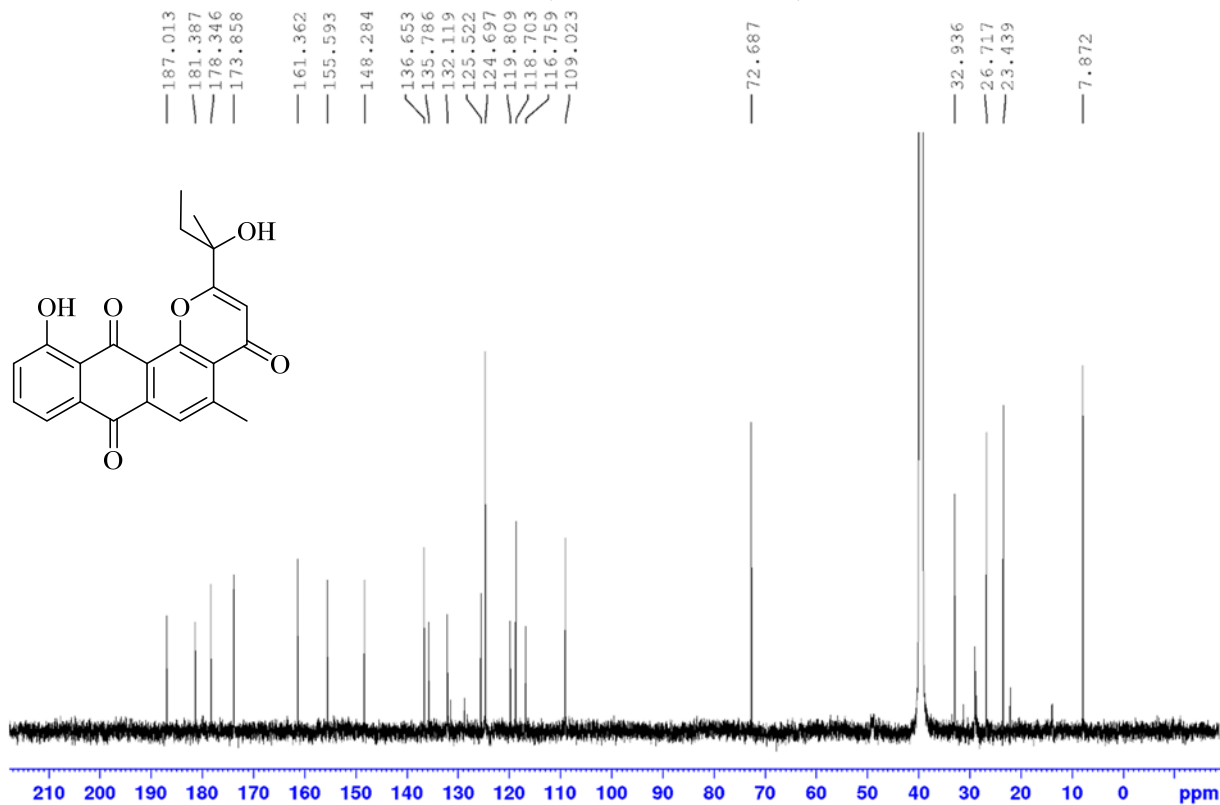




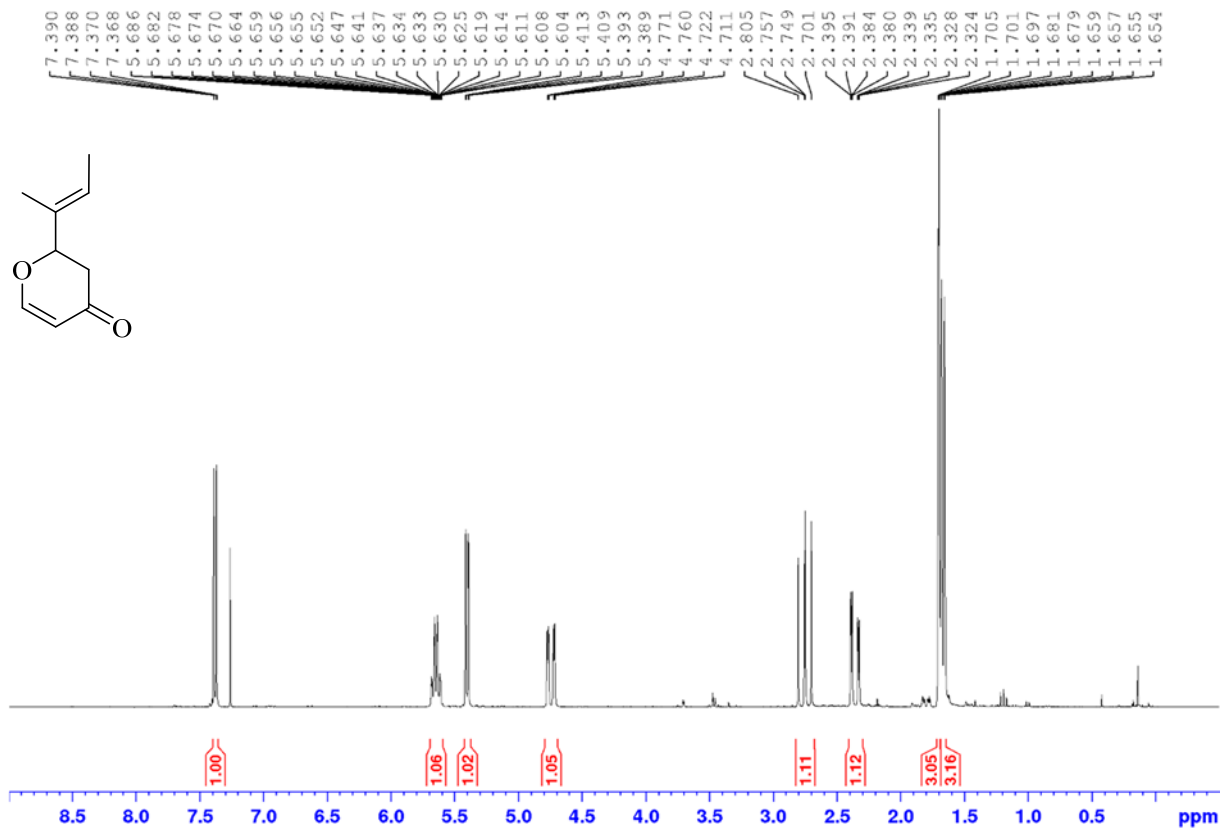
1 ^1H NMR (700 MHz, $\text{DMSO-}d_6$)



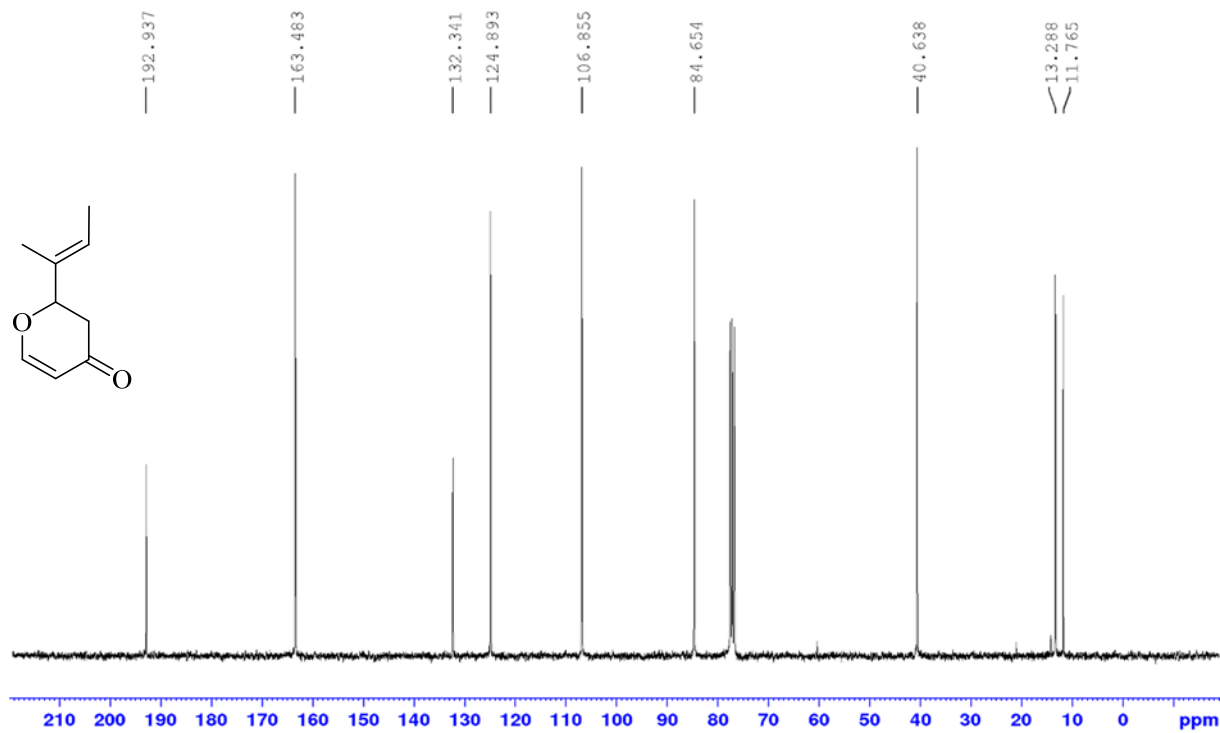
1 ^{13}C NMR (175 MHz, $\text{DMSO-}d_6$)

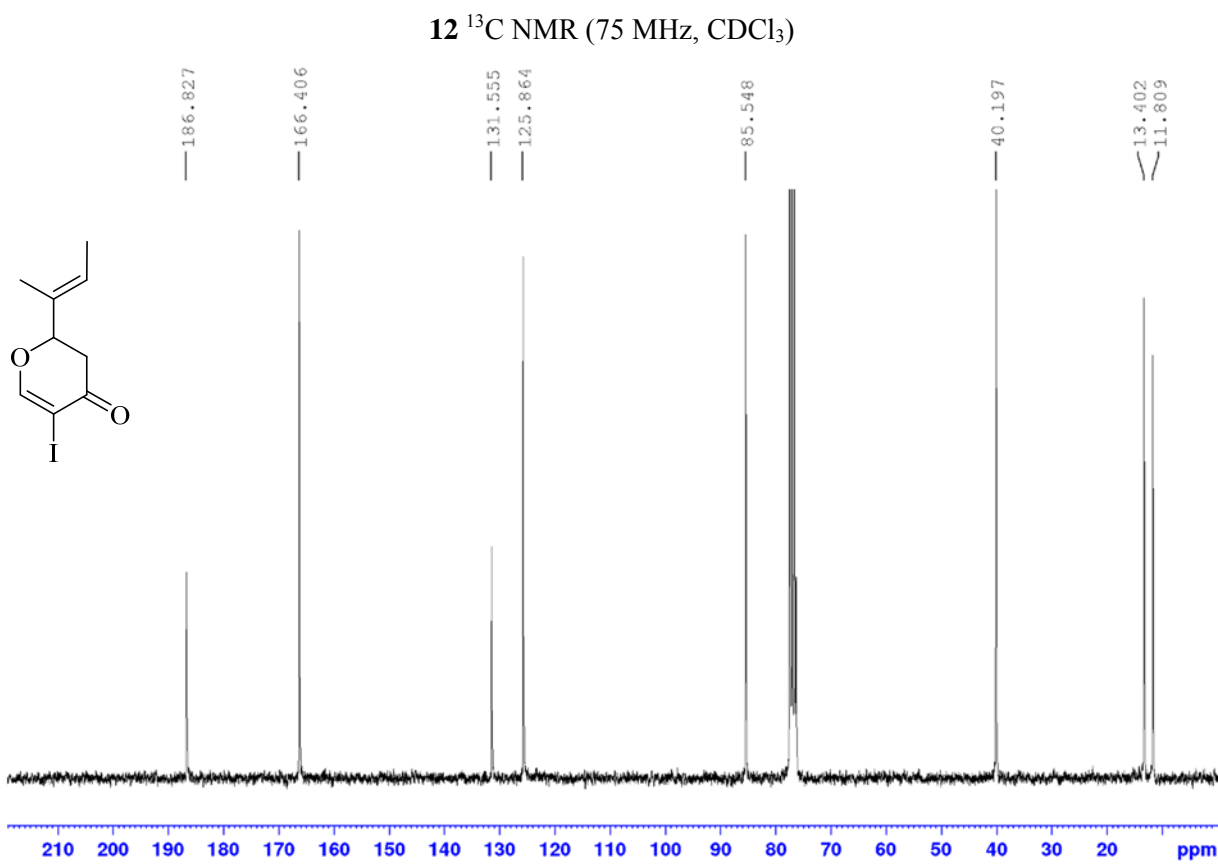
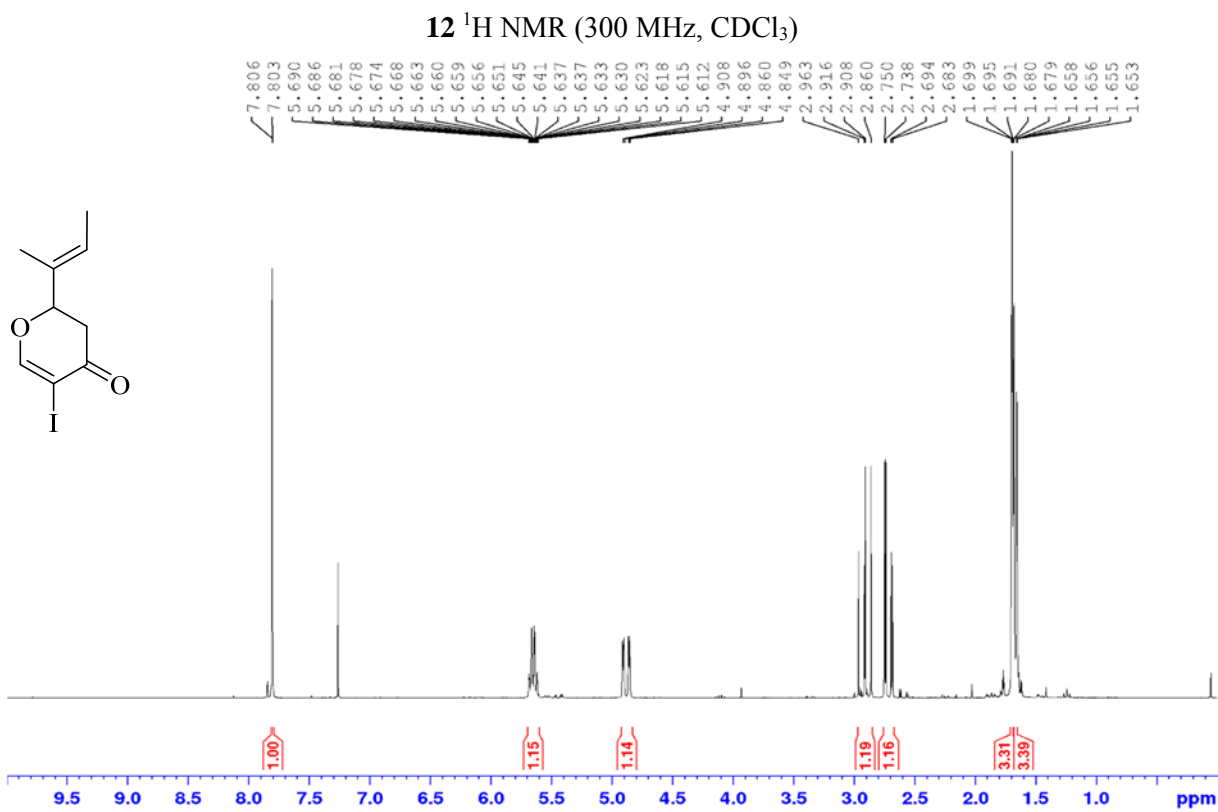


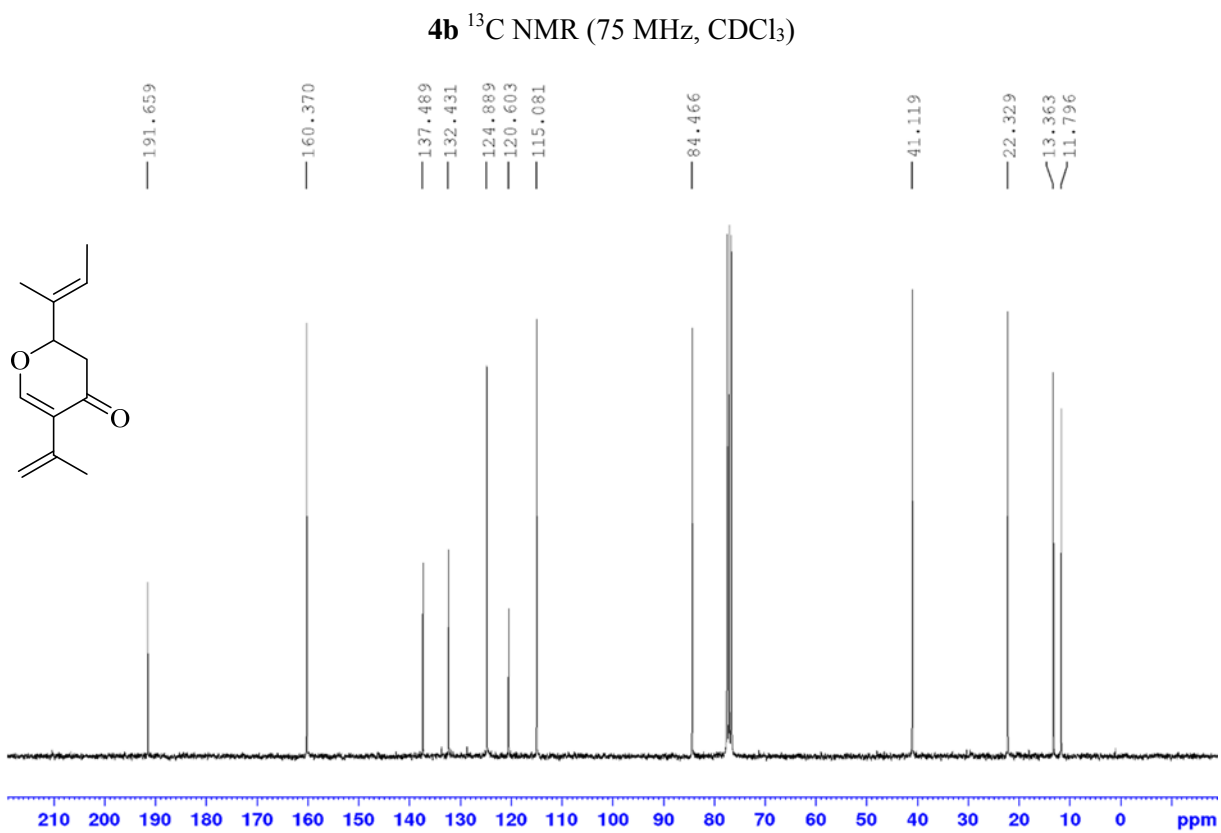
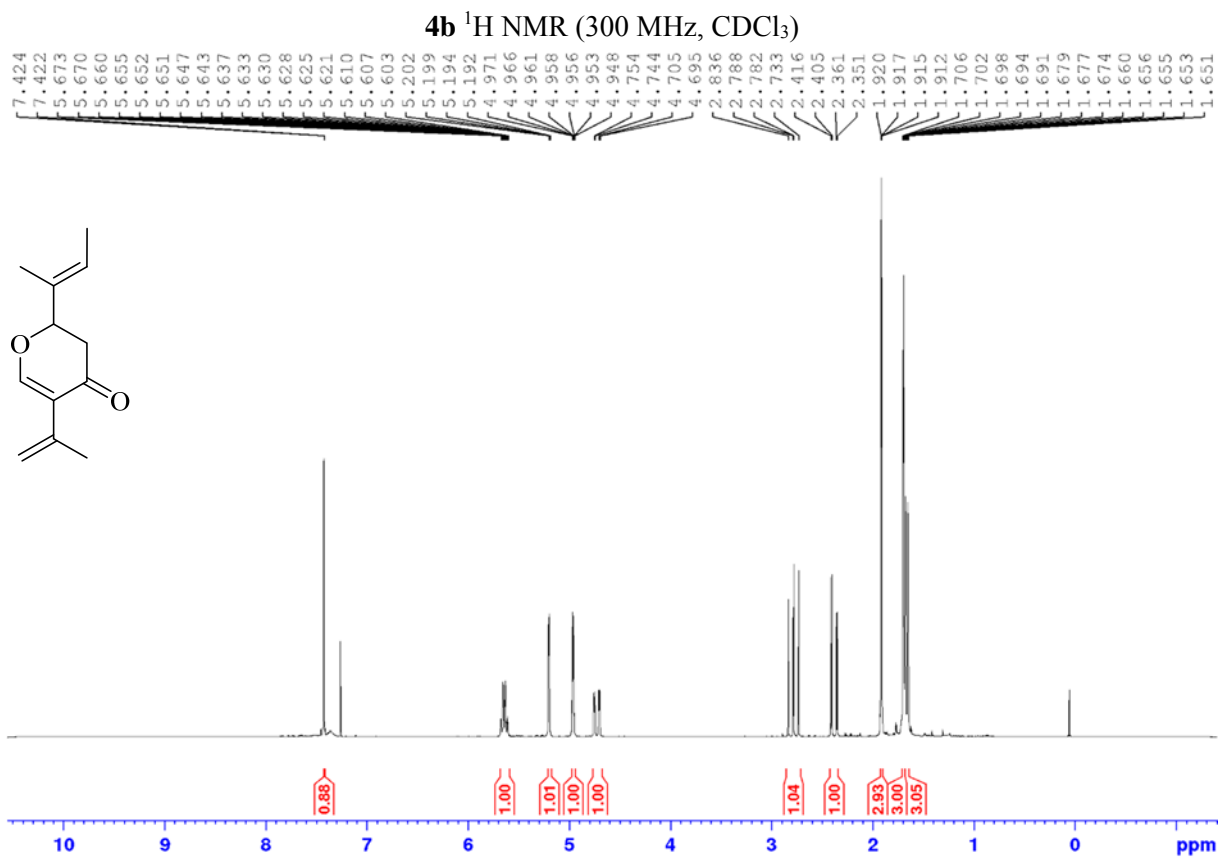
11 ^1H NMR (300 MHz, CDCl_3)



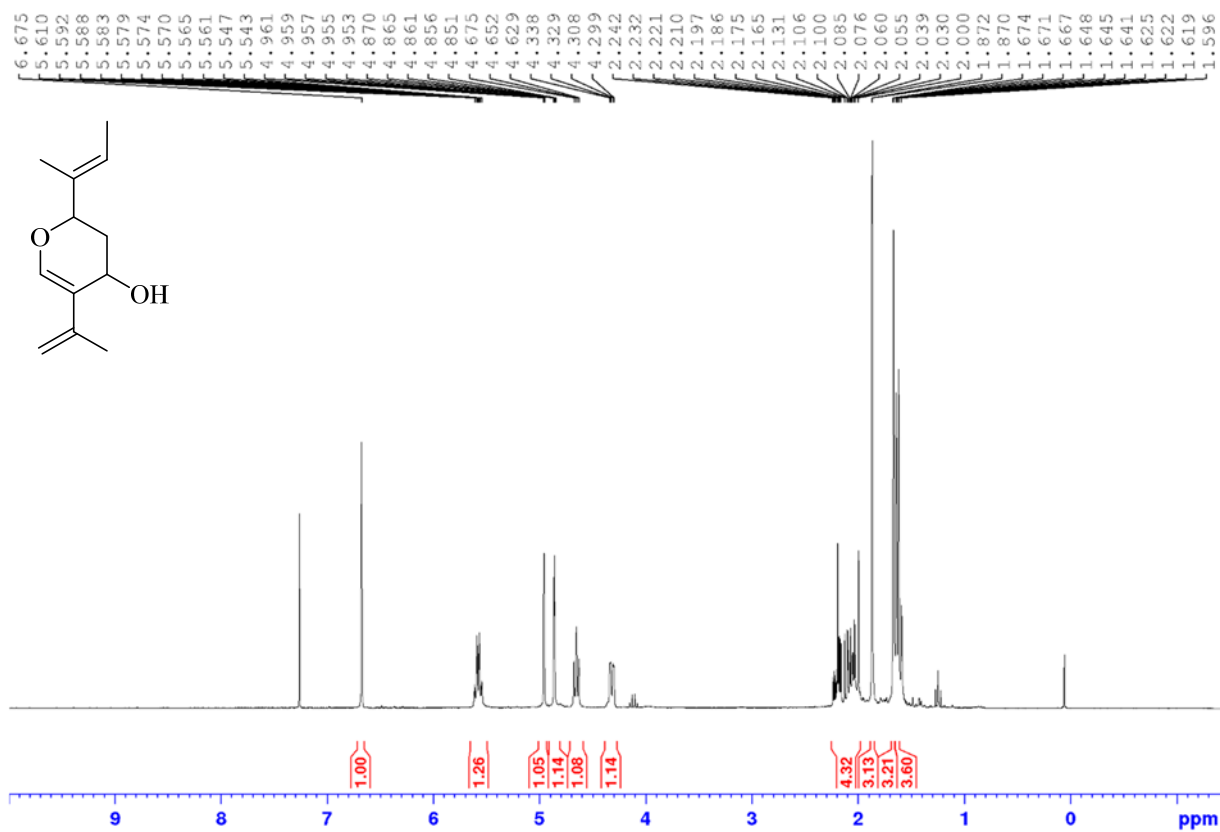
11 ^{13}C NMR (75 MHz, CDCl_3)



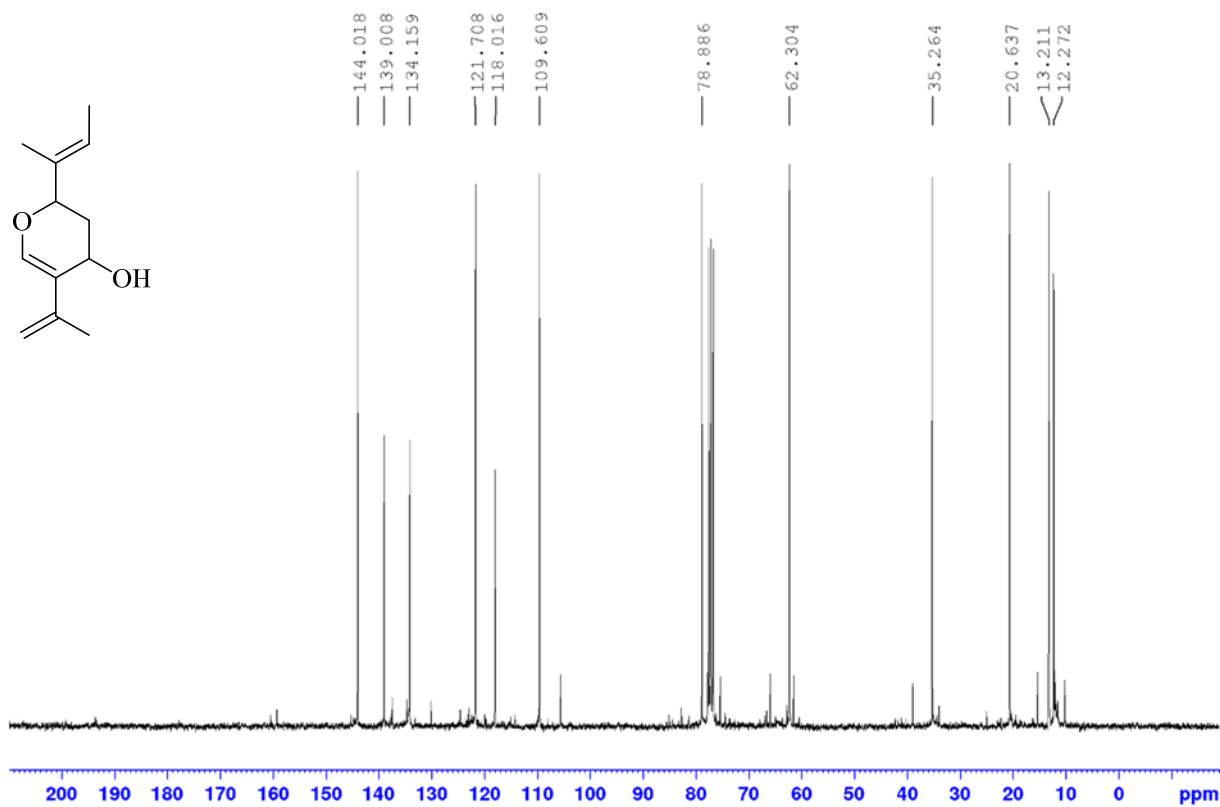




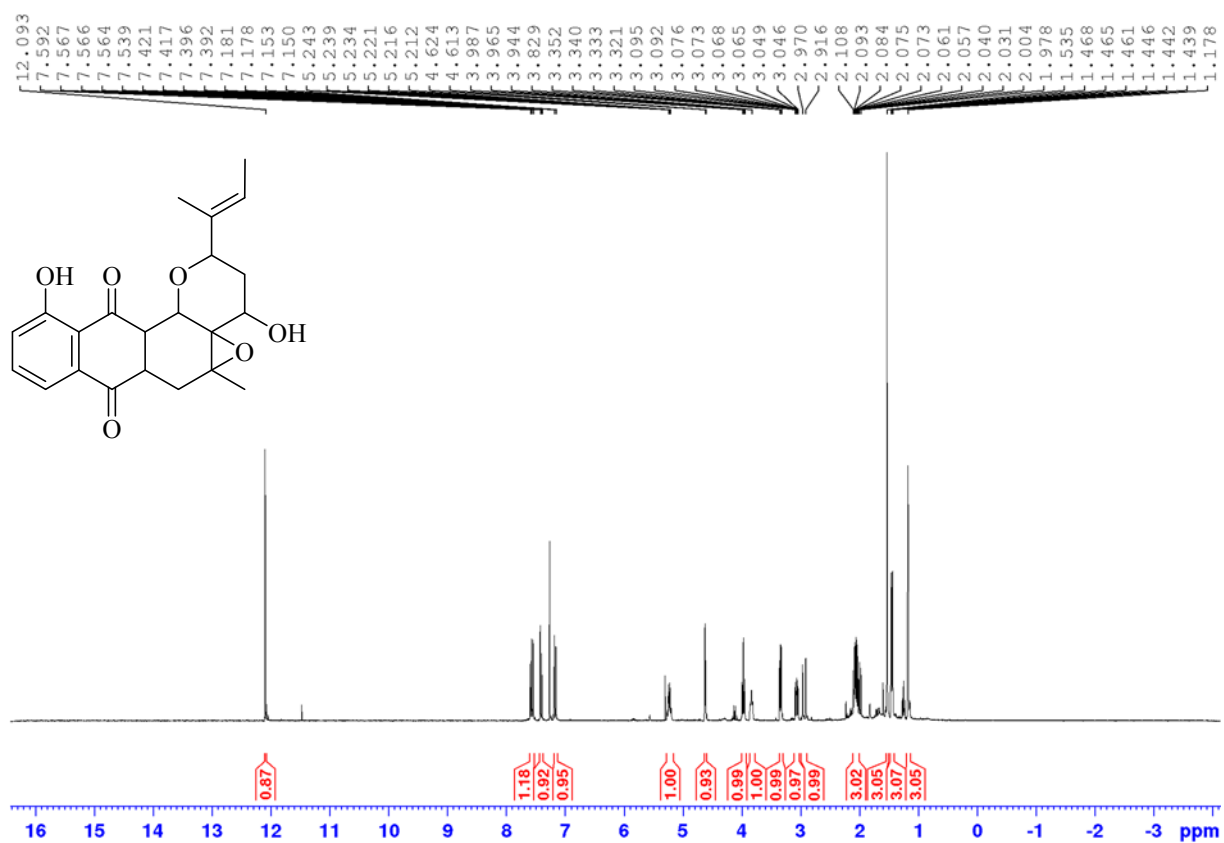
17 ¹H NMR (300 MHz, CDCl₃)



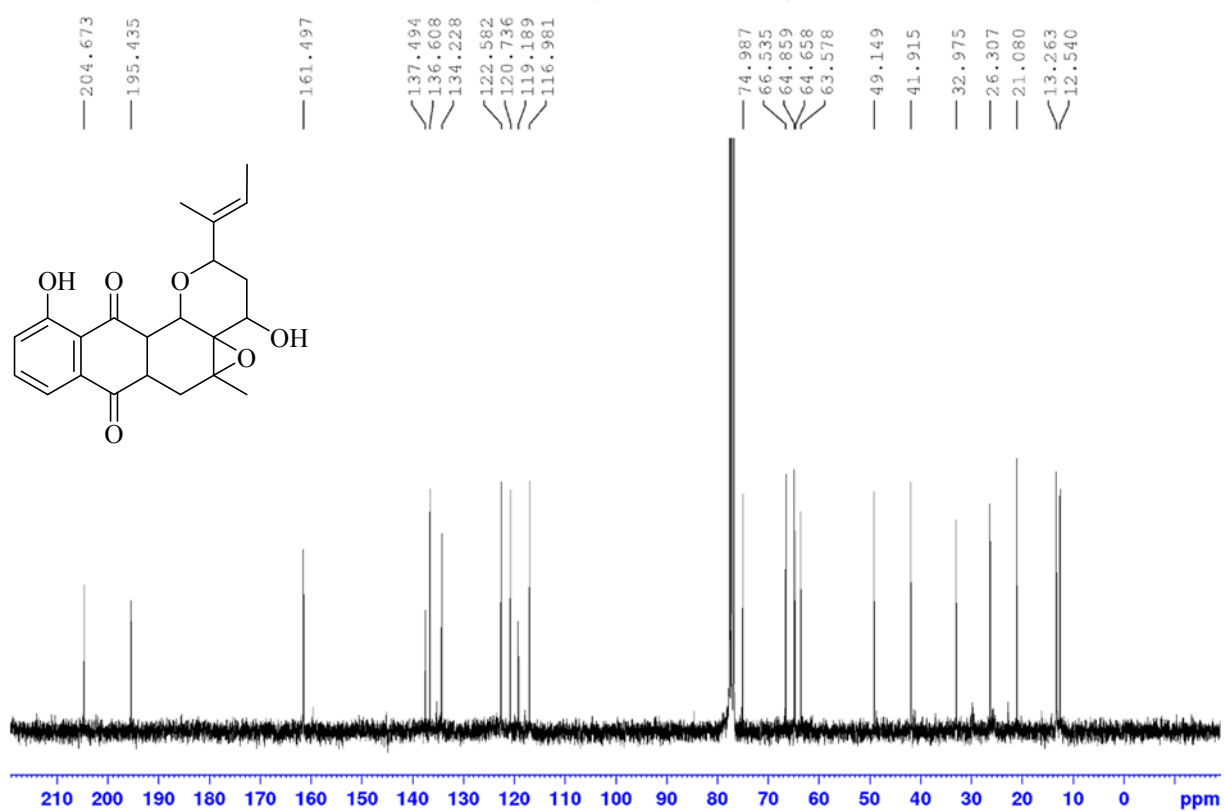
17 ¹³C NMR (75 MHz, CDCl₃)



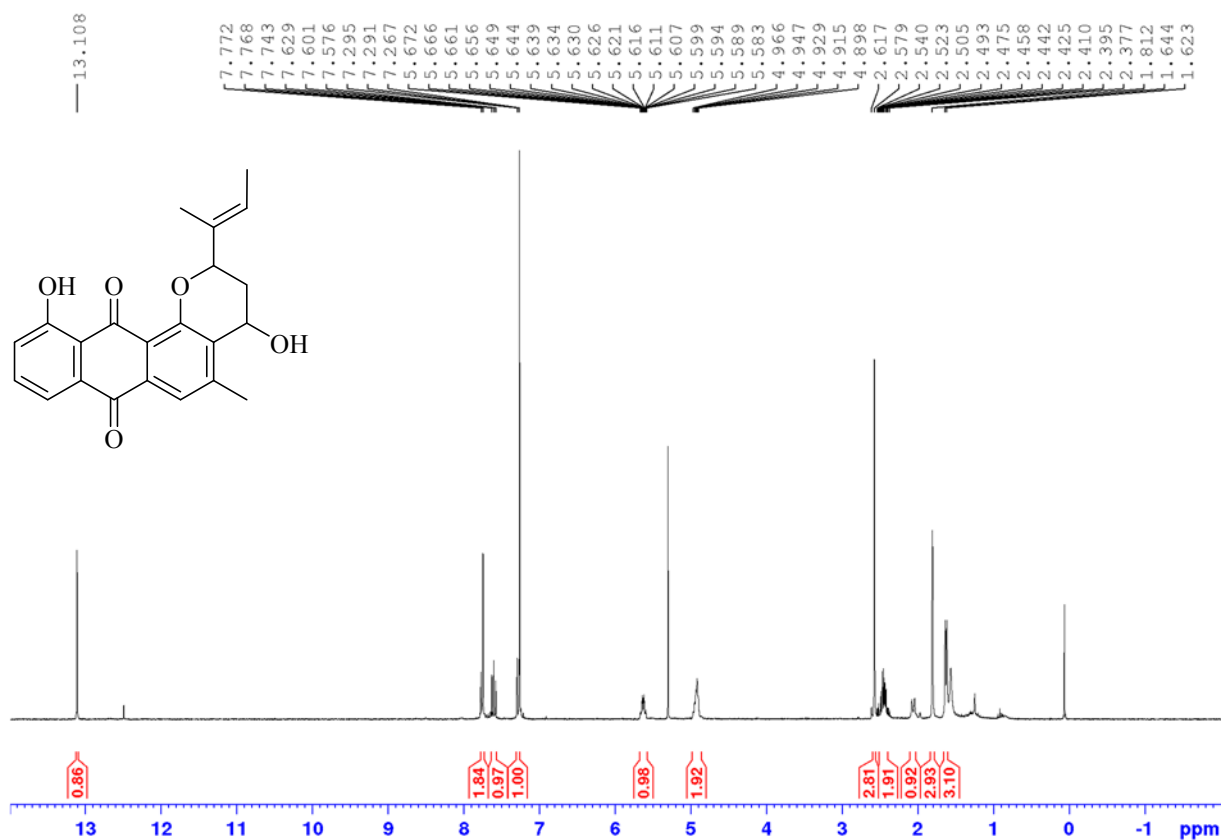
19 ^1H NMR (300 MHz, CDCl_3)



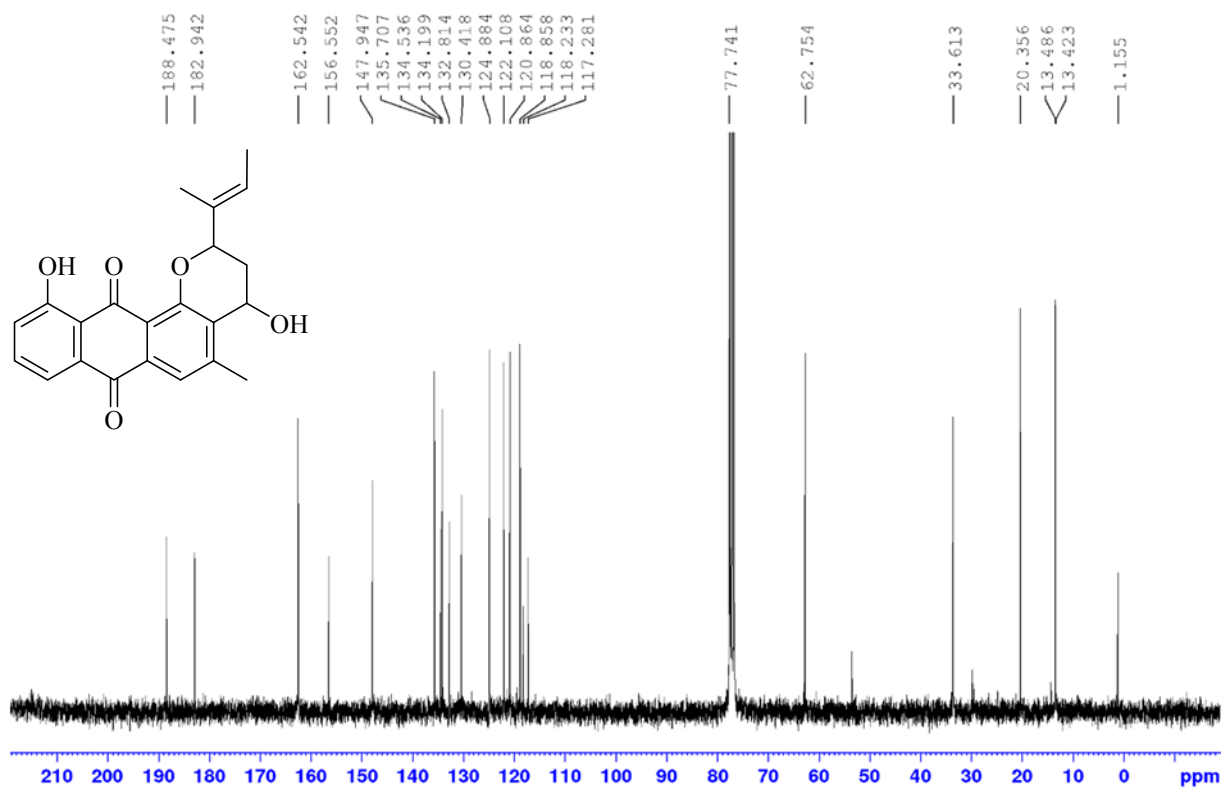
19 ^{13}C NMR (75 MHz, CDCl_3)

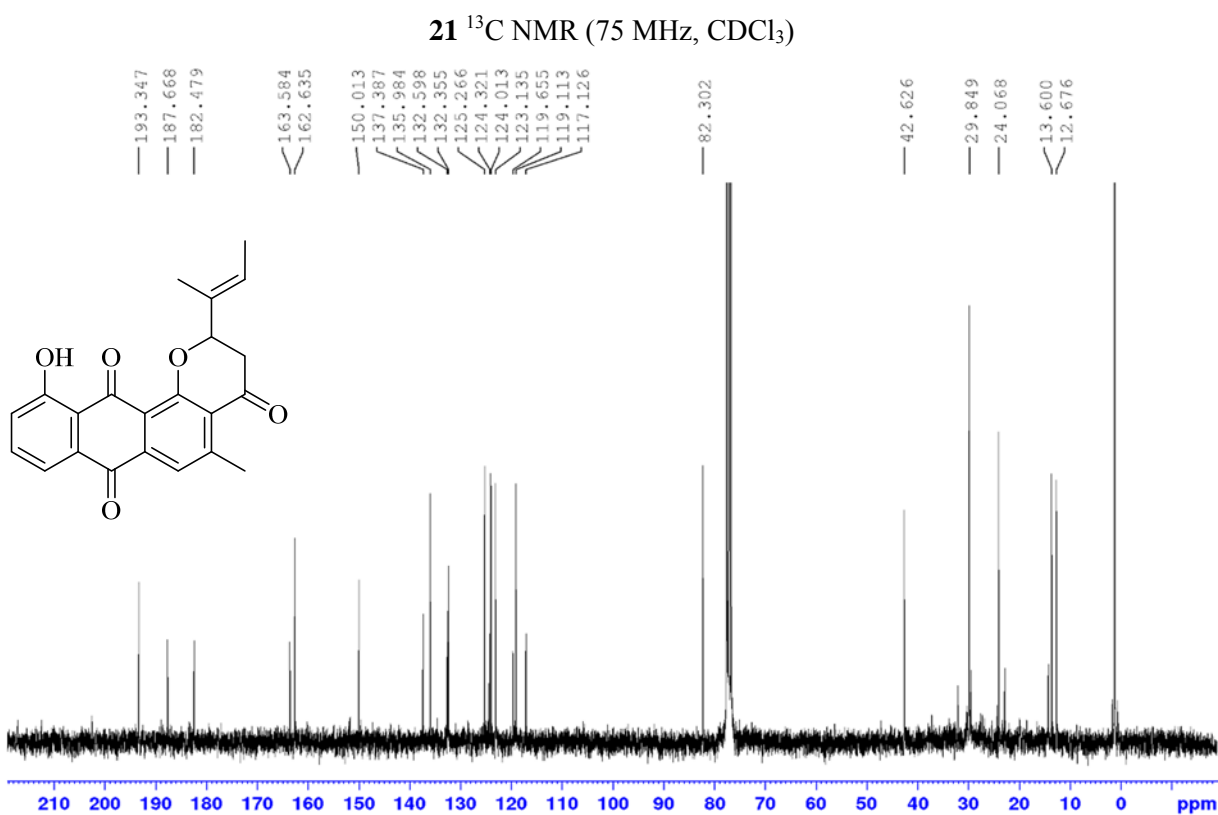
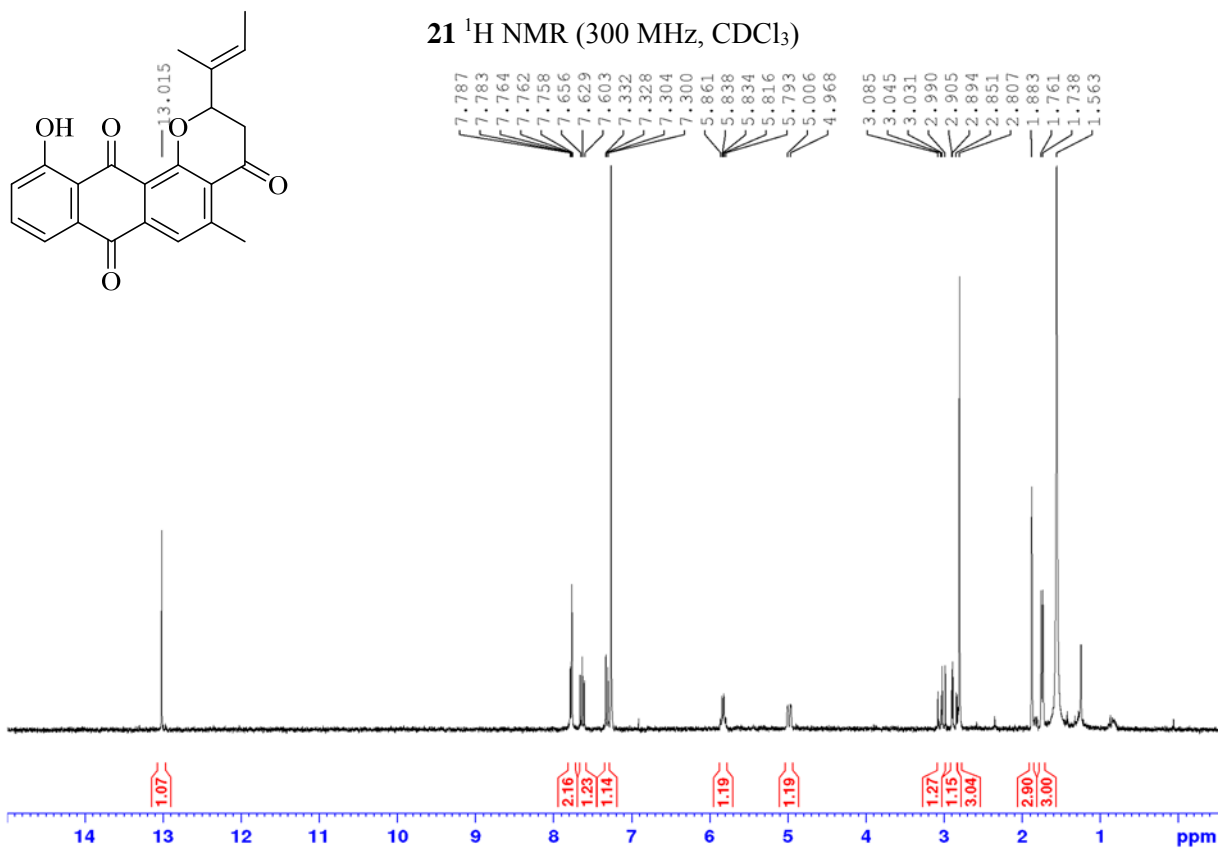


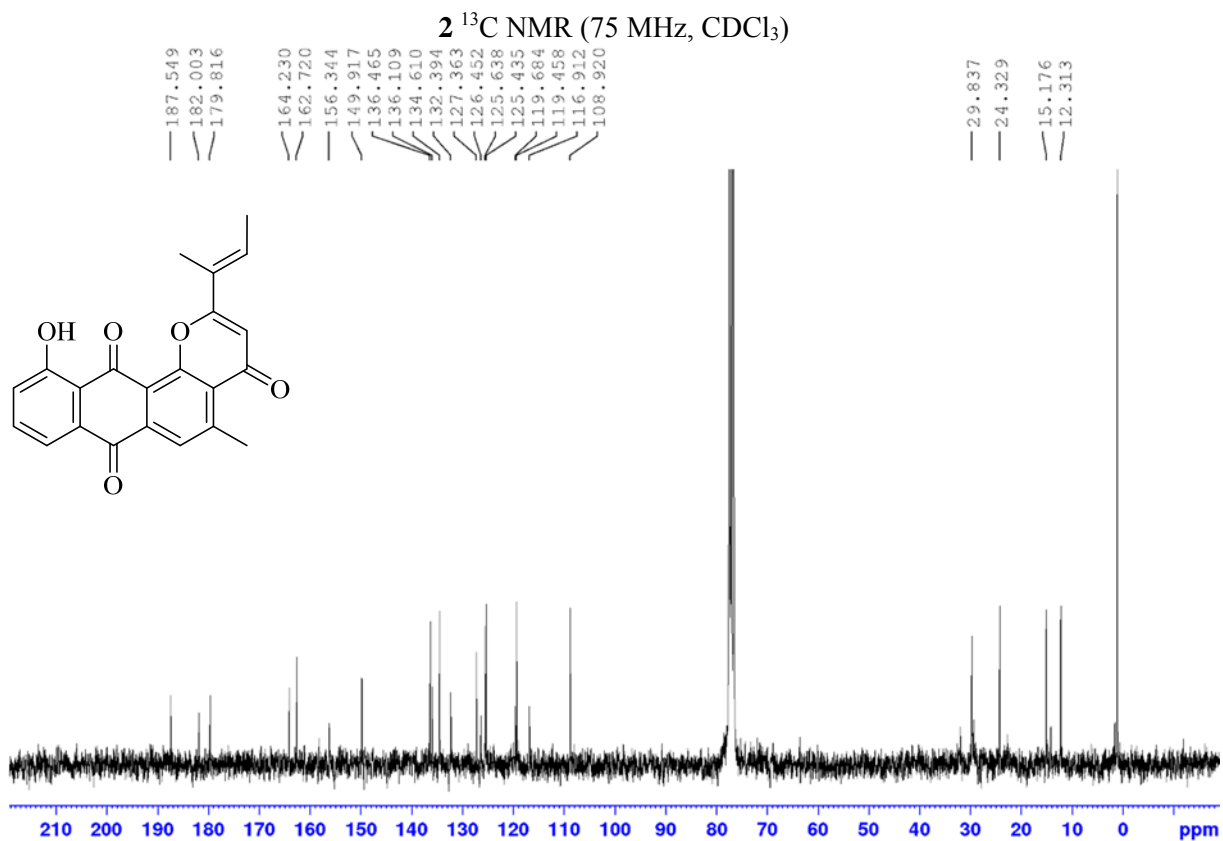
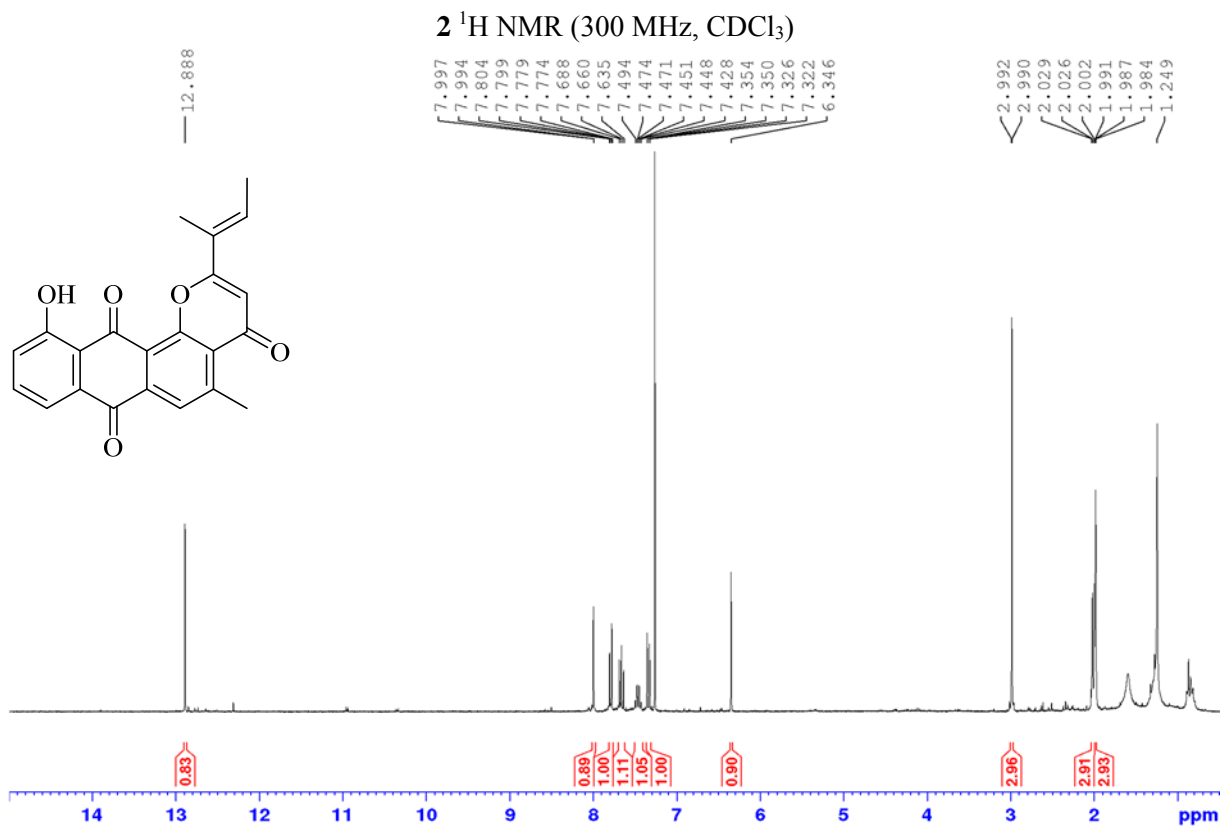
20 ^1H NMR (300 MHz, CDCl_3)

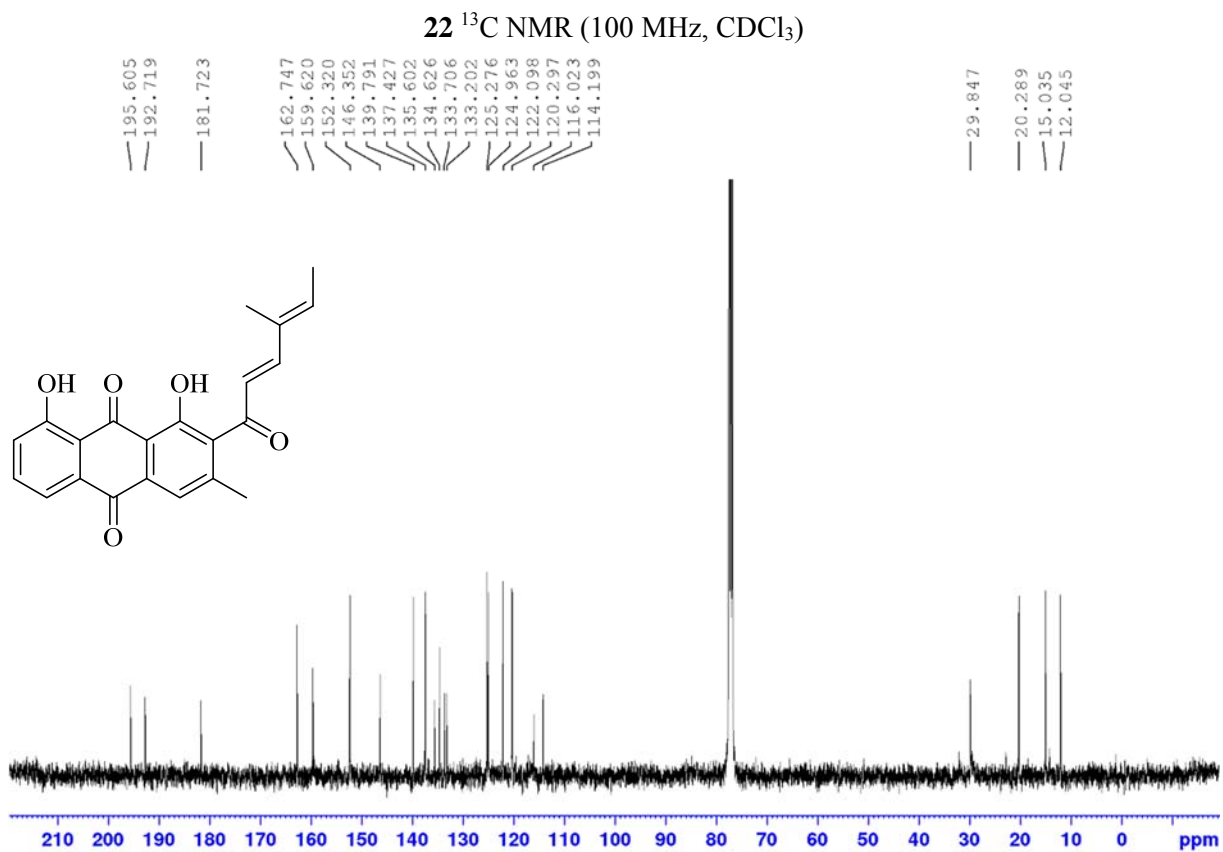
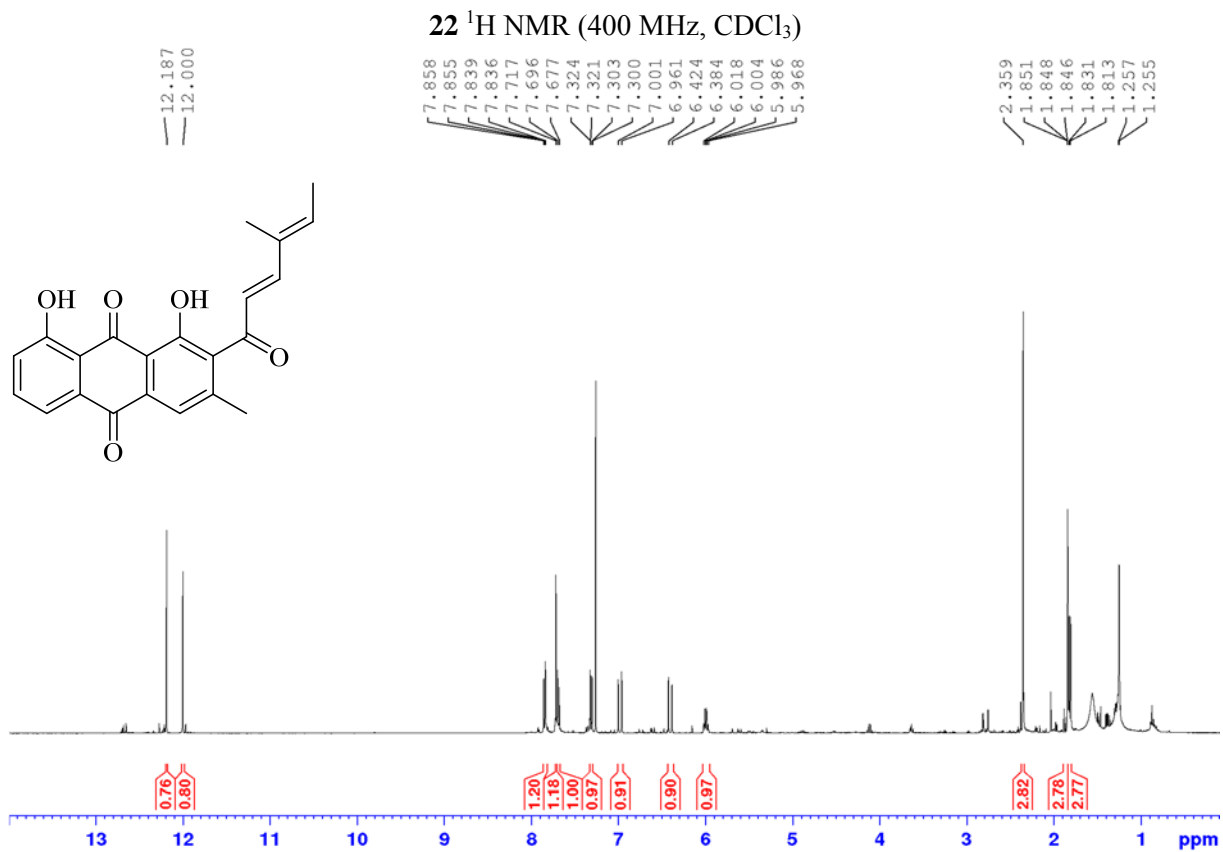


20 ^{13}C NMR (75 MHz, CDCl_3)

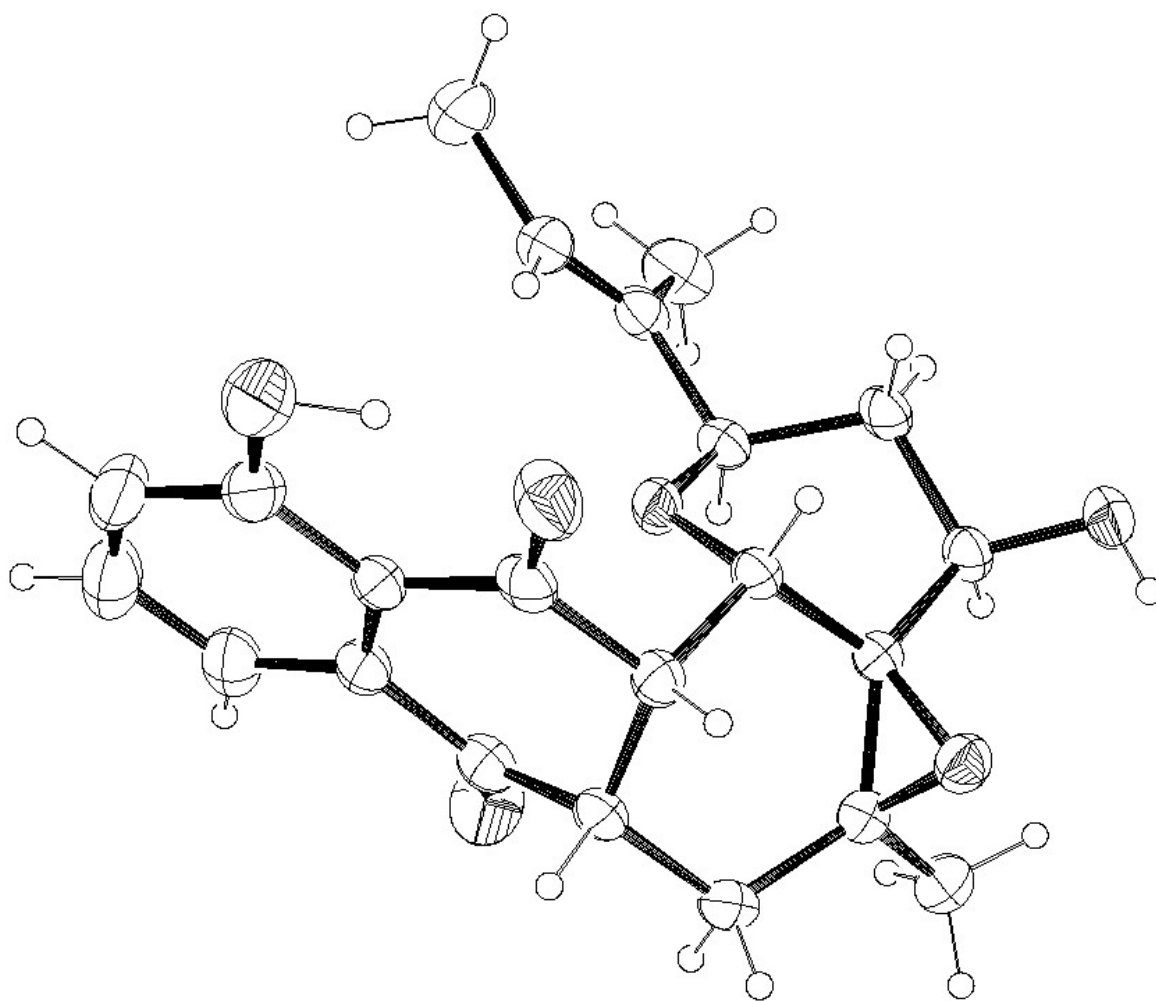








2. X-Ray derived ORTEP of 19



Crystal Structure Data for C₂₂H₂₄O₆ $M_w = 384.4$, colourless prisms, $0.45 \times 0.35 \times 0.1 \text{ mm}^3$, monoclinic, $P2_1/n$, $\alpha = 90^\circ$; $\beta = 117.184^\circ$; $\gamma = 90^\circ$; $a = 15.6246 \text{ \AA}$; $b = 8.2035 \text{ \AA}$; $c = 16.7827 \text{ \AA}$; $V = 1913.5 \text{ \AA}^3$, $Z = 4$. 32830 reflections were measured on a Nonius-Kappa CCD diffractometer, using graphite-monochromatized MoK-L_{2,3} radiation ($\lambda = 0.71073 \text{ \AA}$) up to a resolution of $(\sin \theta/\lambda)_{\text{max}} = 0.66 \text{ \AA}^{-1}$ at 293K. 4470 reflections were unique. The crystal was mounted at the tip of Lindemann capillary by means of a solvent free glue. The structure was solved using the charge flipping algorithm¹ implemented in the Superflip program² and refined with JANA2006 program³ against F^2 for all reflections. Non-hydrogen atoms were refined with anisotropic displacement parameters. All H atoms were introduced in geometrically optimized positions and refined with a riding model. Altogether, 261 parameters were refined. $R_1/wR_2 [I \geq 2\sigma(I)] = 0.0681/0.1317$. Crystallographic data for **19** is available free of charge from the Cambridge Crystallographic Data Centre, (www.ccdc.cam.ac.uk/data_request/cif under deposition number 1527990).

(1) Oszlanyi G., Suto A. *Acta Crystallogr.* **2004**, *A60*, 134-141

(2) Palatinus L., Chapuis G. *Superflip J. Appl. Cryst.* **2007**, *40*, 786-790

(3) Petricek, V., Dusek, M. & Palatinus, L. *Jana2006*. The crystallographic computing system. Institute of Physics, Praha, Czech Republic, **2006**.

3. Computational details

3.1. DFT Methods

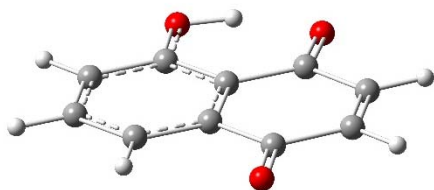
Density functional [B3LYP/6-31G(d)] calculations were used for the geometry optimization using PCM calculations in acetonitrile. Thermochemical free energies (G_{298}) have been calculated at the same level as that used for geometry optimization. A frequency calculation was performed on all compounds and transition state to verify minima and first order saddle points, respectively. Intrinsic reaction coordinate (irc) calculations were used to connect transition state **TS** with the corresponding reactants and product (see attached corresponding IRC.mpg in SI). The calculations were performed with the Gaussian09 package.

Full reference Gaussian .³⁹

Gaussian 09, Revision A.02, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, Ö. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, and D. J. Fox, Gaussian, Inc., Wallingford CT, **2009**.

3.2. Coordinates of all stationary points (the best conformers)

3



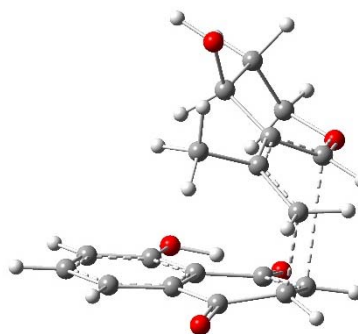
19 atoms

$G_{298} = -610.250599$

C	-1.405839	2.325913	0.000009
C	-0.016319	2.125739	0.000006
C	0.491875	0.832954	0.000001
C	-0.381491	-0.284249	-0.000002
C	-1.780098	-0.067067	-0.000002
C	-2.279868	1.249849	0.000005
H	-1.803255	3.336435	0.000013
H	0.670820	2.964311	0.000007
C	1.968429	0.622694	-0.000003
C	0.153184	-1.647553	-0.000001
H	-3.355481	1.393705	0.000006
C	1.620102	-1.824995	0.000011
C	2.459921	-0.776156	0.000013
H	1.973710	-2.851793	0.000020
H	3.538643	-0.901294	0.000022
O	-2.662330	-1.078515	-0.000008
H	-2.132755	-1.919542	-0.000017
O	-0.586132	-2.651116	-0.000005
O	2.764579	1.559056	-0.000021

H	-3.540250	-0.525458	-0.090244
H	-1.977896	1.183357	-1.035522
O	-1.778607	-1.444787	-0.501292
C	-0.451700	0.985810	0.463635
C	0.281677	-0.260499	-0.007189
C	1.762637	-0.396480	0.083414
C	2.304098	-1.474641	0.677073
H	3.380699	-1.630486	0.693792
H	1.692926	-2.227287	1.167063
H	0.060230	-2.212550	-0.837266
C	2.650519	0.661036	-0.538655
H	2.387840	0.824431	-1.591290
H	2.528240	1.626015	-0.039131
H	3.702719	0.363327	-0.483959
O	0.181426	2.153836	-0.077977
H	-0.229023	2.920790	0.353766
H	-0.395122	1.033717	1.563468

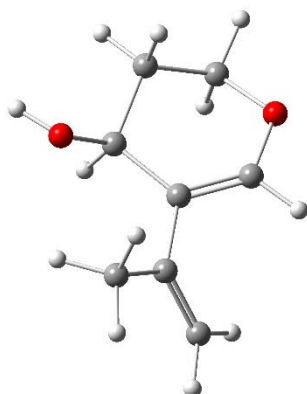
TS



41 atoms

$G_{298} = -1072.520822$

A



22 atoms

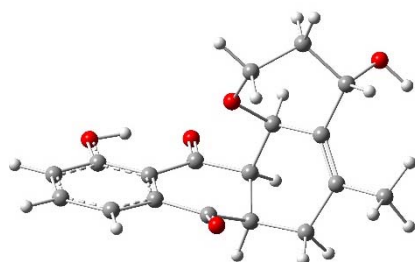
$G_{298} = -462.318119$

C	-1.925159	0.931575	0.030350
C	-2.505563	-0.454689	0.251742
C	-0.424985	-1.319999	-0.453600
H	-2.514882	1.675127	0.579505
H	-2.467174	-0.736044	1.313353

C	3.203836	0.840213	0.940879
C	2.831831	1.551396	-0.343024
C	2.008059	-0.528394	-1.134318
H	3.359421	1.572645	1.740309
H	1.891336	2.104165	-0.258868
H	3.613424	2.228484	-0.689114
H	4.144391	0.295751	0.798316
O	2.675056	0.584625	-1.418921
C	2.118862	-0.169862	1.344266
C	1.622949	-0.951478	0.131877
C	0.724077	-2.044339	0.274018
C	0.195224	-2.718787	-0.848245
H	-0.426741	-3.587370	-0.649064
H	0.794875	-2.818831	-1.747191
H	1.884817	-1.137908	-2.018692
C	0.182076	-2.429450	1.631624
H	0.904827	-3.059501	2.161570
H	-0.007527	-1.564185	2.272975
H	-0.747146	-2.995348	1.521462

O	2.649903	-1.109905	2.283702
H	2.756306	-0.642575	3.128308
H	1.271009	0.367233	1.796591
C	-2.732814	1.198705	2.069753
C	-2.787413	0.006039	1.343637
C	-2.079337	-0.105425	0.145485
C	-1.322810	0.981136	-0.352470
C	-1.301176	2.191187	0.382875
C	-1.996767	2.282476	1.599128
H	-3.273393	1.286931	3.007824
H	-3.367714	-0.840457	1.693787
C	-2.139901	-1.378372	-0.625813
C	-0.597210	0.886506	-1.643489
H	-1.956624	3.217732	2.149192
C	-0.560064	-0.380212	-2.294853
C	-1.167896	-1.529954	-1.753587
H	-0.091323	-0.416864	-3.273666
H	-1.439699	-2.328682	-2.439822
O	-0.613796	3.265978	-0.055927
H	-0.283572	3.003071	-0.972671
O	-0.057463	1.922337	-2.142089
O	-2.933179	-2.274611	-0.345228

B



41 atoms

$G_{298} = -1072.583400$

O	-0.450792	-0.937729	0.965659
O	-4.113017	-1.894369	-0.074280
O	0.198514	2.565033	0.804883
O	1.467190	-1.968278	-1.760208
O	3.861604	-1.945661	-0.771786
C	-1.124699	-0.866094	-0.309843
C	2.234145	-0.200867	-0.380149
C	-0.111191	1.274941	-1.219615
C	1.929416	1.016736	0.284423
C	-0.148125	-0.259586	-1.336463
C	0.610261	1.688197	0.058333
C	-2.654685	-1.625371	1.802447
C	-3.890588	1.920465	-0.530470
C	-1.508885	1.874482	-1.379955
C	2.862167	1.618220	1.120474
C	-2.426676	-0.112026	-0.170306
C	1.228433	-0.886996	-1.195719

C	4.121527	1.027096	1.294439
C	-1.331077	-0.926210	2.101952
C	-3.419107	-0.886115	0.680529
C	-2.608980	1.132255	-0.648117
C	4.448881	-0.158001	0.650038
C	3.511530	-0.787973	-0.186656
H	5.419631	-0.624808	0.782844
H	4.854457	1.502352	1.940010
H	2.605626	2.547199	1.617342
H	0.528140	1.654141	-2.031071
H	-0.518126	-0.536098	-2.329767
H	-1.492917	2.912833	-1.028543
H	-1.760416	1.921656	-2.449341
H	-4.190890	2.293162	-1.518638
H	-4.725961	1.348002	-0.122925
H	-3.739784	2.805144	0.102328
H	-1.346503	-1.893262	-0.634568
H	-4.142862	-0.196632	1.130736
H	-2.455884	-2.650396	1.468667
H	-3.261763	-1.690007	2.711405
H	-1.511199	0.113460	2.412877
H	3.070038	-2.247785	-1.293474
H	-4.586761	-1.440023	-0.790213
H	-0.786910	-1.429829	2.906127