Supporting Information

Aromatization Mechanism of Ligustilide

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Contents

Computational Details

Geometry optimizations and frequency calculations were performed with the Gaussian 09.[1] The theoretical methodology comprised the gradient-corrected density functional theory (DFT) (U)B3LYP[2] functional with the polarized basis set of 6-311+G (d, p).[3] Frequency analysis was used to characterize each minimum with zero imaginary frequencies and each transition-state (TS) structure with only one imaginary frequency. Intrinsic reaction coordinate (IRC) calculations were performed for selected TSs to identify associated reactants and products. Besides gas phase calculations, all structures were fully optimized in methanol (ε = 32.61) with the SMD Method.[4] Because thermal corrections based on the ideal gas phase model overestimated the entropy contributions to free energies for reactions involving component change, [5] a correction of 4.3 kcal/mol applied to per component change for a reaction at 298.15 K and 1 atm (i.e., a reaction from m- to n-components has an additional correction of (n-m) × 4.3 kcal/mol).

For open-shell singlet diradical $^1\mathbf{O_2}$, $^1\mathbf{A}$, $^1\mathbf{TS2}$ and $^1\mathbf{A'}$, the broken symmetry method (using the keyword guess = mix) combined with UB3LYP functional was used to calculate their structure and energies. [6] Besides, the stability of wave function of $^1\mathbf{A}$ and $^1\mathbf{TS2}$ was tested by using the keyword stable=opt, showing the wavefunctions were stable. The $\langle S^2 \rangle$ values of open shell singlet states are given in Table S1. Nucleus-independent chemical shift (NICS) values are calculated to track the aromaticity of each minimum (Table S2). Because we were unable to locate the symmetry broken state of $^1\mathbf{TS2}$ by using the B3LYP method, the UM06-2X[7] method was used to optimize its structure with the polarized basis set of 6-31G(d) in vacuo. The energies of ^{1}TS2 in vacuo and methanol were obtained by single-point calculations at the UB3LYP/6-311+G (d, p) theoretical level based on the UM06-2X optimized structure. The approximate spin-projection (AP) method[8] pioneered by the Yamaguchi group serves to refine Gibbs free energies of all singlet species that suffer from contamination by their lower-energy triplet state.

$$J_Y = \frac{E_{BS} - E_T}{S_T^2 - S_{BS}^2} \quad \textbf{(1)}$$

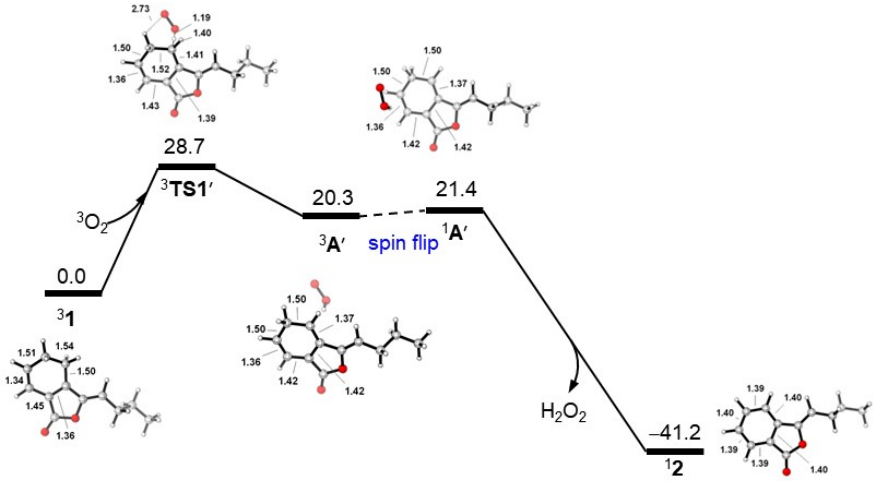


Figure S1 Free energy profiles for the aromatization of **1** by triplet O_2 at the B3LYP (SMD, methanol)/6-311+G (d, p) theoretical level, which first abstracts the hydrogen at C6 of **1** and then at C5. The relative free energies at 298.15 K in methanol are given in kcal/mol. The key distances for each structure are given in Å.

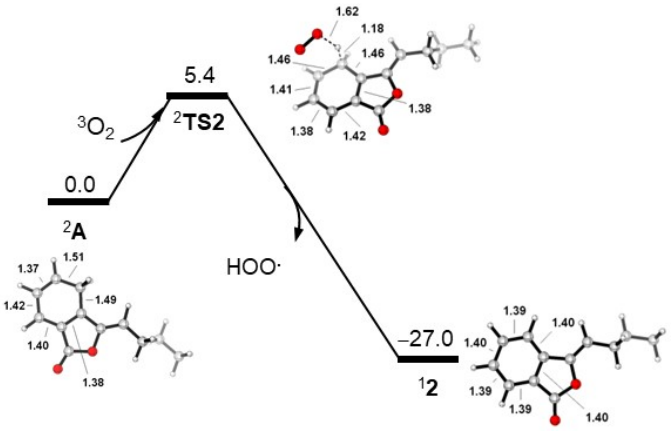


Figure S2. Free energy profiles for the aromatization of **1** by another triplet O_2 at the B3LYP(SMD, methanol)/6-311+G (d, p) theoretical level. The relative free energies at 298.15 K in methanol are given in kcal/mol. The key distances for each structure are given in Å.

Table S1. The spin contaminations $<S^2>$ of ^{1}**A**, ^{1}**TS2** and ^{1}**A′**.

molecule	**$<S^2>$**
^{1}**A**	1.05
^{1}**TS2**	0.76
^{1}**A′**	1.03

Table S2. NICS values (in ppm cm^3 mol^{-1}) of the six-membered ring in ^{1}**1**, ^{3}**A**, ^{1}**A**, ^{3}**2** and ^{1}**2**. (keyword: NMR=GIAO)[9]

state	NICS (0)	NICS (1)
^{1}**1**	2.4	-0.3
^{3}**A**	4.0	0.0
^{1}**A**	19.3	1.8
^{3}**2**	-5.0	-7.7
^{1}**2**	-7.7	-10.0

Reference

1. 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, T.; Keith, 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, O.; Farkas, J. B.; Foresman, J. V.; Ortiz, J.; Cioslowski, D. J. ; Fox, *Gaussian, Inc*., Wallingford CT, 2010. Gaussian09 Rev. B.01, Gaussian, Inc., Wallingford CT, 2010.

2. (a) A. D. Becke, *Phys. Rev. A. Gen. Phys.,* **1988**, *38*, 3098. (b) C. Lee, W. Yang, R. G. Parr, *Phys. Rev. B,* **1988**, *37*, 785.

3. J. A. Jr. Montgomery, J. W. Ochterski, G. A. A. Petersson, *J. Chem. Phys.,* **1994**, *101*, 5900–5909.

4. A. V. Marenich, C. J. Cramer, D. G. Truhlar, *J. Phys. Chem. B.,* **2009,** *113,* 6378–6396.

5. S. L. Qu, H. G. Dai, Y. F. Dang, C. Y. Song, Z. X. Wang, H. R. Guan, H. R. *ACS Catal.,* **2014**, *4*, 4377–4388.

6. (a) L. Noodleman, *J. Chem. Phys.,* **1981**, *74*, 5737–5743. (b) L. Noodleman, E. R. Davidson, *Chem. Phys.,* **1986**, *109*, 131–143.

7. Y. Zhao, D. G. *Acc Chem Res.*, **2008**, *41*, 157–167.

8. (a) T. Saito, S. Nishihara, Y. Kataoka, Y. Nakanishi, T. Matsui, Y. Kitagawa, T. Kawakami, M. Okumura, K. Yamaguchi, *Chem. Phys. Lett.,* **2009,** *483*, 168–171. (b) S. Yamanaka, T. Kawakami, H. Nagao, K. Yamaguchi,

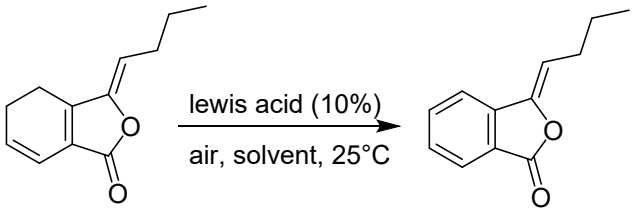
Chem. Phys. Lett., **1994**, *231*, 25–33.

9. R. A. Matute, P. Pérez, E. Chamorro, N. Villegas-Escobar, D. Cortés-Arriagada, B. Herrera, S. Gutiérrez-Oliva, A. Toro-Labbé. *J. Org. Chem*. **2018**, *83*, 5969–5974.

Table S3. The barrier of rate-determining transition state in different solution.

entry	lewis acid	solvent	barrier(kcal/mol)
1	/	/	30.5
2	/	Toluene	31.7
3	/	DCM	28.5
4	/	MeOH	26.9
6	BF_3	DCM	24.9
7	BF_3	MeOH	22.2

Table S4. Parallel experiments considering the effects of lewis acid and solvent[a]



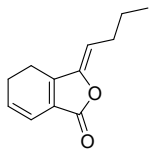
1 **2**

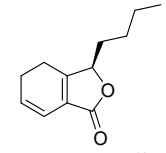
entry	lewis acid	solvent	yield[b] (%)
1	/	/	9
2	/	Toluene	12
3	/	DCM	19
4	/	MeOH	22
5	BF_3	DCM	39
6	BF_3	MeOH	40

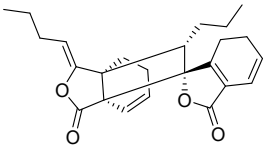
[a]All reactions were carried out on a 0.2 mmol scale in 10.0 mL of solution with 10 mol % catalyst loading at 25 °C for 24 h. [b]The yield was determined by ^1H NMR spectroscopy.

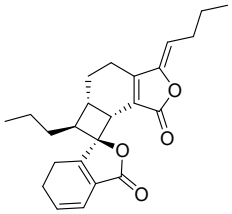
Scheme S1. Phthalide compounds with the cyclohexadiene structural motif that have been reported to have

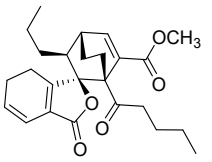
antioxidation activity.


Z-ligustiide[9]

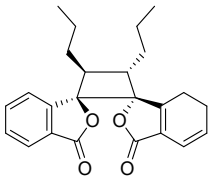

Senkyunolide A[10]


Tokiaerialide[11]


6.8',7.3'-diligustilide[12]



Methyl ester derived from angeolide[12]


Diangeliphalide A[12]

Reference

10. (a) L. Rui, J. R. Du, B. Wang, *Natural Nat. Prod. Res. Delv.*, **2020**, 22. (b) M. D. Zhu, L. X. Zhao, X. T. Wang, Y. J. Gao, Y. J. Z. J. Zhang, *Brain Res Bull*., **2014**, *109*, 54–60.

11. (a) T. Uto, N. H. Tung, R. Taniyama, T. Miyanowaki, O. Morinaga, Y. Shoyama, *Phytother. Res*., **2015**, *29*, 1956–1963. (b) H. B. Sowbhagya, *Crit. Rev. Food Sci. Nutr.*, **2014**, *54*, 389–398.

12. F. Tang, Y. M. Yan, H. L. Yan, L. X. Wang, C. J. Hu, H. L. Wang, H. Ao, C. Peng, Y. Z. Tan, *Bioorg. Chem*. **2021**, *107*, 104523.

13. H. Yan, Y. Zhou, F. Tang, C. Wang, J. Wu, C. Hu, X. Xie, C. Peng, Y. Tan, *Food Funct.,* **2022**, *13*, 1092–1107.

Experimental Details and General Procedures

Ligustilide was isolated from the extract of *Angelica sinensis* in our previous work[13] and its structure was confirmed by NMR and high resolution mass spectra.

Methanol (MeOH) and Dichloromethane (DCM) were purchased from Guangdong Guanghua Sci-Tech Co., Ltd. (Guangdong, China). Toluene was obtained from Guangzhou Chemical Reagent Factory (Guangzhou, China). Boron Trifluoride (BF_3) was purchased from Meryer (Shanghai) Chemical Technology Co., Ltd. 3.

^{1}H-NMR and ^{13}C-NMR spectra were recorded on Bruker AV-400 (Bruker BioSpin Group, Faellanden, Switzerland). Chemical shifts were reported in ppm from tetramethylsilane with solvent resonance as the internal standard ($CDCl_3$, δ_H = 7.26/δ_C = 77.0). Spectra were reported as follows: chemical shift (δ ppm). High resolution mass spectra (HRMS) were performed on Waters Synapt G2 TOF mass spectrometer (Waters Corporation, Milford, USA) and data were reported as (m/z). Column chromatography (CC) was carried out on silicagel (100-200, 200–300 mesh) (Qingdao Haiyang Chemical Group Corporation, Qingdao, China), and TLC was performed on precoated silica gel plate (SGF254, 0.2 mm, Yantai Chemical Industry Research Institute, China)

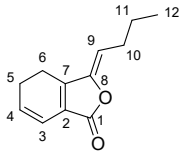
Aromatization reaction of Ligustilide:

To a stirred solution of **1** (38 mg, 0.2 mmol) in reaction solution (10 mL) at room temperature, lewis acid (0.1eq) was added, if needed. The mixture was slowly stirred at 25 °C for 12 h. At the end of the reaction, the reaction mixture was concentrated under reduced pressure and filtered through silica gel. Purification by flash column chromatography (SiO, EtOAc–Petroleum Ether, 1:150 to 1:30) provided butylidenephthalide. The ^{1}H-NMR peak area ratio was used to calculate the yield of **2**. (^{1}H-NMR Spectra of reaction mixture of entry 1-6 are presented in figure S3-8. The yield was calculated by:

$$y\% = \frac{the\ peak\ area\ of\ characteristic\ peak\ of\ 2(5.61, 1H, J = 7.8\ Hz)}{the\ peak\ area\ of\ characteristic\ peak\ of\ 1(5.20,\ 1H,\ J = 8.0\ Hz) + the\ peak\ area\ of\ characte} \times 100\%)$$

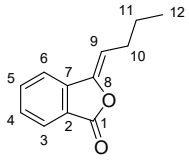
Characterization Data for Final Products

Ligustilide (**1**):



^{1}H-NMR (400 MHz, $CDCl_3$) δ 6.25 (dt, J = 9.7, 2.0 Hz, 1H, H-3), 5.97 (q, J = 9.6, 4.3 Hz, 1H, H-4), 5.20 (t, J = 8.0 Hz, 1H, H-9), 2.57 (m, 2H, H-5), 2.44 (m, 2H, H-6), 2.34 (td, J = 7.6 Hz, 2H, H-10), 1.47 (m, 2H), 0.92 (t, J = 7.4 Hz, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 167.7 (C-1) , 148.7 (C-7) , 147.2 (C-8) , 130.0 (C-4) , 124.1 (C-2) , 117.2 (C-3) , 113.0 (C-9) , 28.2 (C-10) , 22.5 (C-5) , 22.4 (C-6) , 18.6 (C-11), 13.9 (C-12). ESI-HRMS calcd. for $[C_{12}H_{15}O_2]^+$: 191.1072, found in 191.1076. The results were similar to those in Ref. [1514].

Butylidenephthalide (**2**):



^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.82 (br d, J = 7.7 Hz, 1H, H-3), 7.66-7.58 (m, 2H, H-4, 5), 7.45 (m, 1H, H-6), 5.61 (t, J = 7.8 Hz, 1H, H-9), 2.41 (q, J = 7.6 Hz, 2H. H-10), 1.48-1.54 (m, 2H, H-11), 0.94 (t, J = 7.4 Hz, 3H, H-12). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 167.2 (C-1) , 145.8 (C-8) , 139.6 (C-7) , 134.3 (C-5) , 129.4 (C-3) , 125.2 (C-4), 124.5 (C-2), 119.7 (C-6) , 109.5 (C-9), 27.8 (C-10) , 22.5 (C-11) , 13.8 (C-12). ESI-HRMS calcd. for $[C_{12}H_{15}O_2]^+$: 189.0916, found in 189.0923. The results were similar to those in Ref. [15].

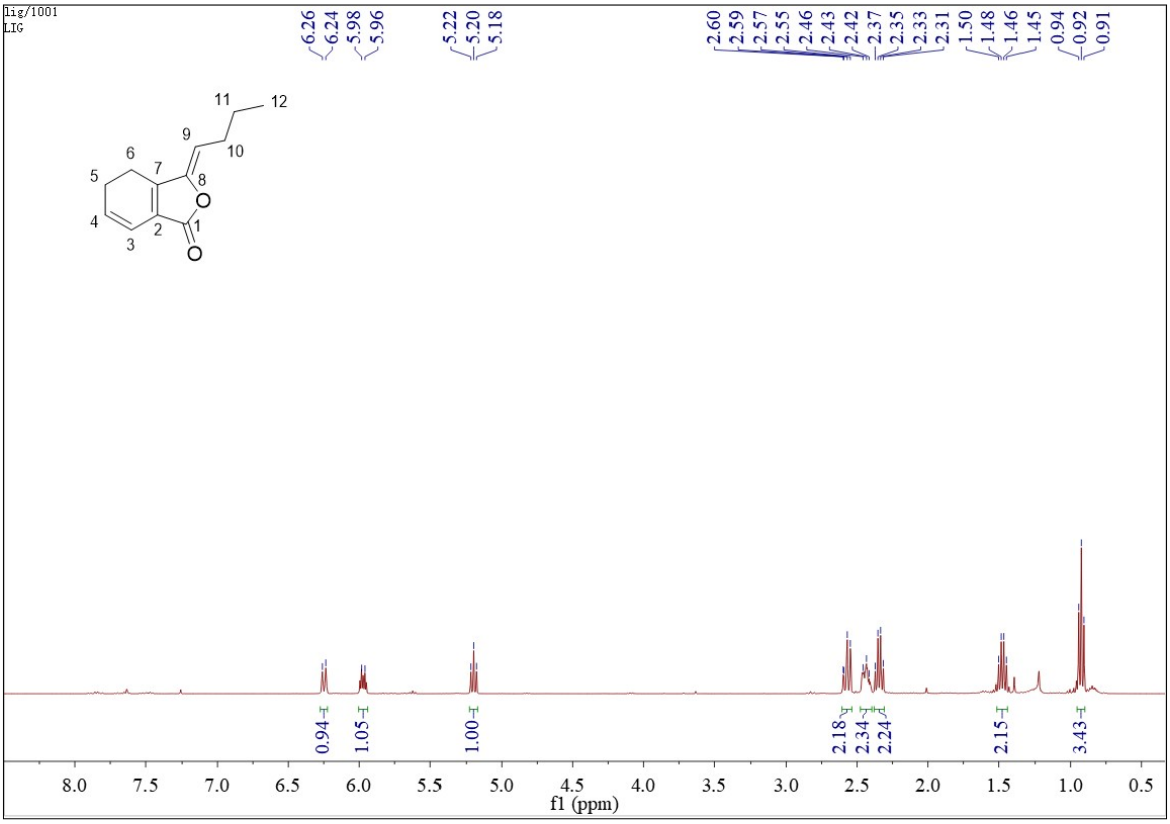
Reference

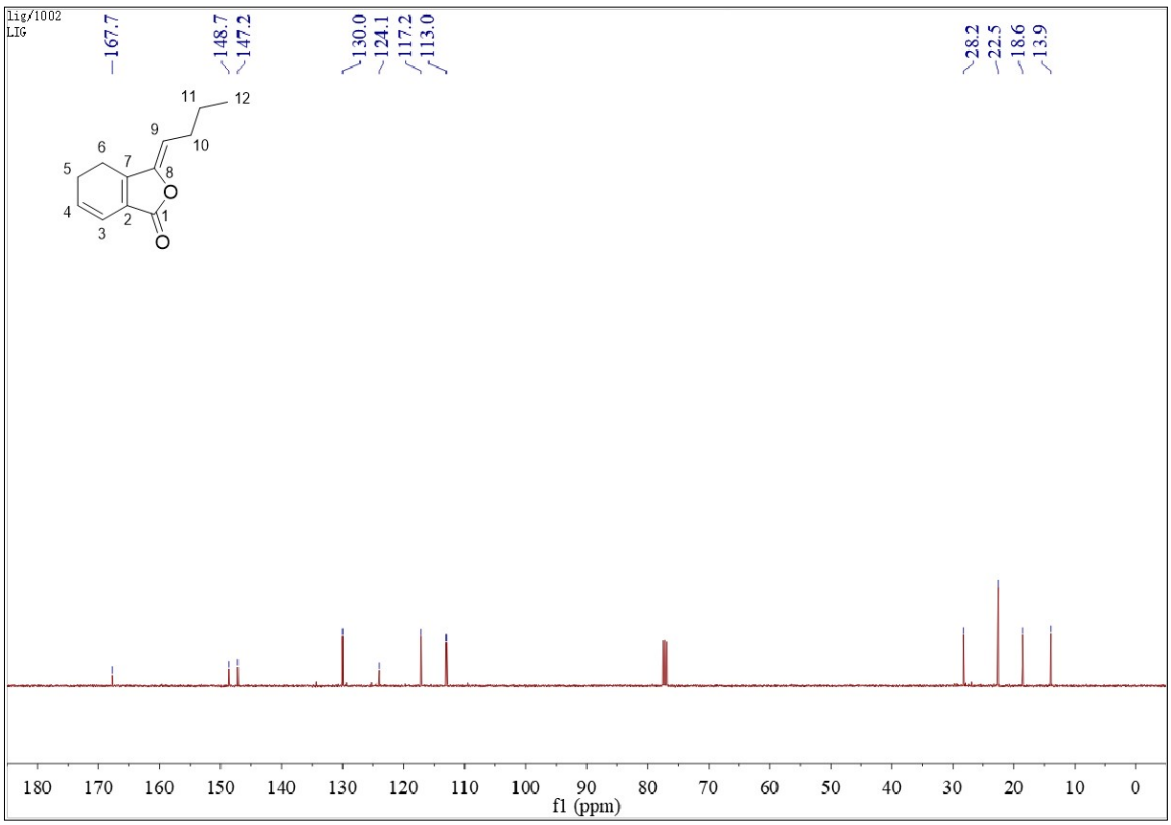
14. J. Zou, G. D. Chen, H. Zhao, X. X. Wang, Z. J. Zhang, Y. B. Qu, R. R. He, K. F. So, X. S. Yao, H. Gao, *Chem. Commun. (Camb)*., **2019**, *55*, 6221–6224.

15. Q. C. Chen, J. Lee, W. Jin, U. Youn, H. Kim, I. S. Lee, X. Zhang, K. Song, Y. Seong, K. Bae, K. *Arch. Pharm. Res*., **2007**, *30*, 565–569.

16. C. Roscini, D. M. Davies, M. Berry, A. J. Orr-Ewing, K. I. Booker-Milburn, *Angew. Chem. Int. Ed. Engl.*, **2008**, *47*, 2283–2286.

^{1}H and ^{13}C-NMR Spectra of Substrates and HRMS report



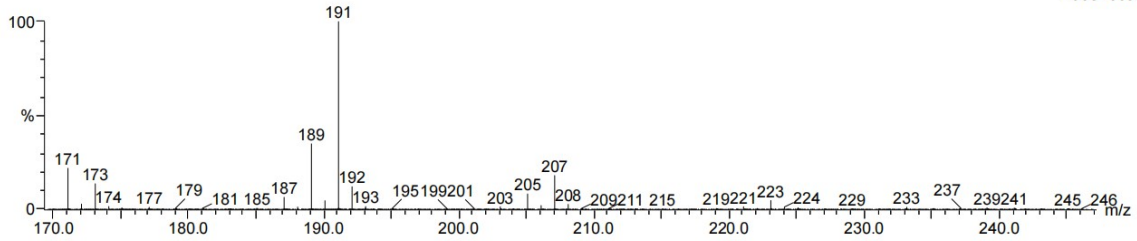


Elemental Composition Report **Page 1**

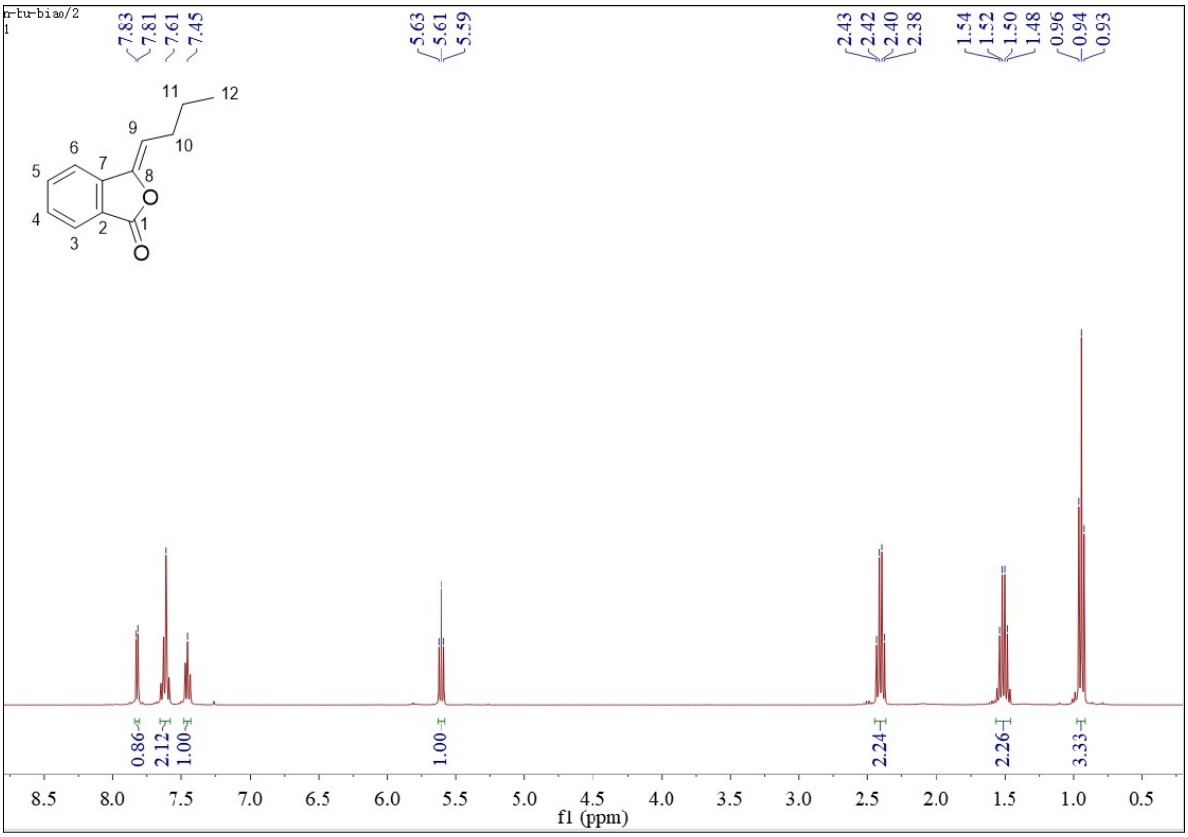
Single Mass Analysis
Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

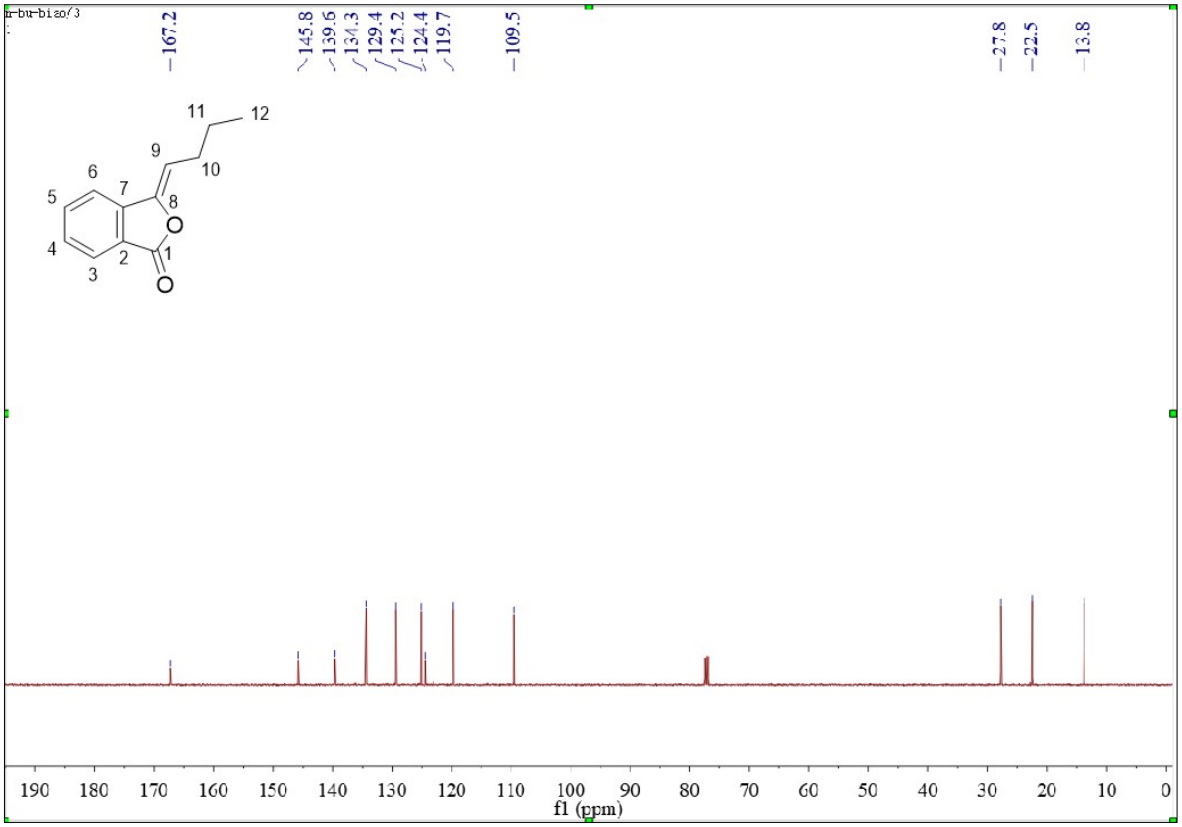
Monoisotopic Mass, Even Electron Ions
15 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-30 H: 0-30 O: 0-5
LZG-190
20220725-13 208 (1.679)

1: TOF MS ES+
1.90e+005



Minimum:				-1.5				
Maximum:		5.0	10.0	50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
191.1076	191.1072	0.4	2.1	5.5	647.0	n/a	n/a	C12 H15 O2



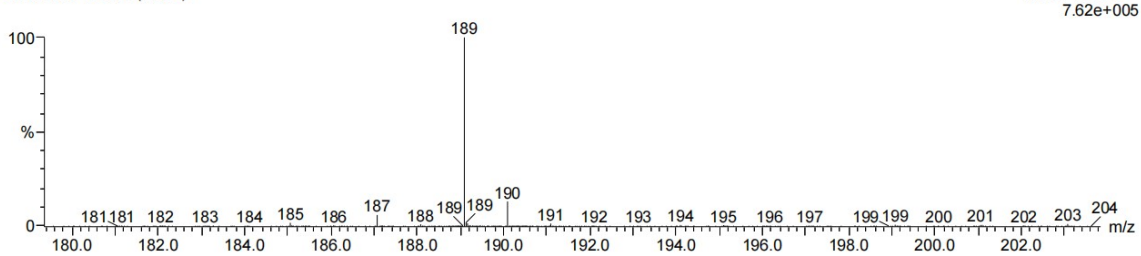


Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
15 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-30 H: 0-30 O: 0-5
BU-188
20220725-16 210 (1.694)

1: TOF MS ES+
7.62e+005



Minimum:				-1.5				
Maximum:		5.0	10.0	50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
189.0923	189.0916	0.7	3.7	6.5	670.0	n/a	n/a	C12 H13 O2

The yield of 2 determined by ^{1}H NMR spectroscopy.

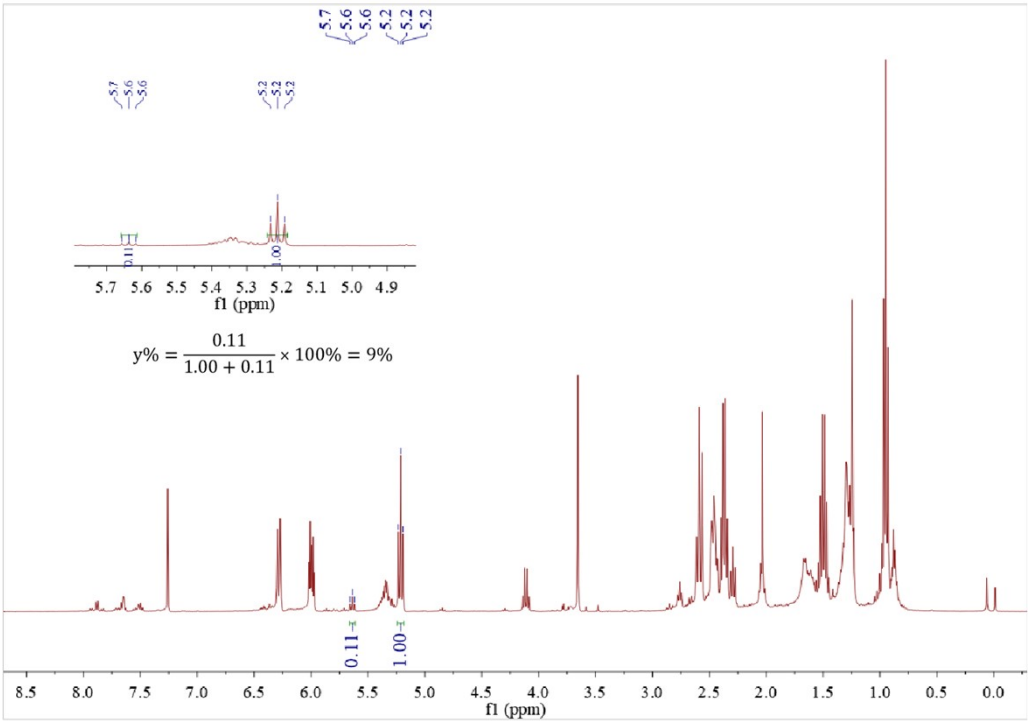


Figure S3. ^{1}H-NMR Spectra of reaction mixture of entry 1 in Table S4: the new triplet (5.61, 1H, J = 7.8 Hz) is the characteristic peak of **2**.

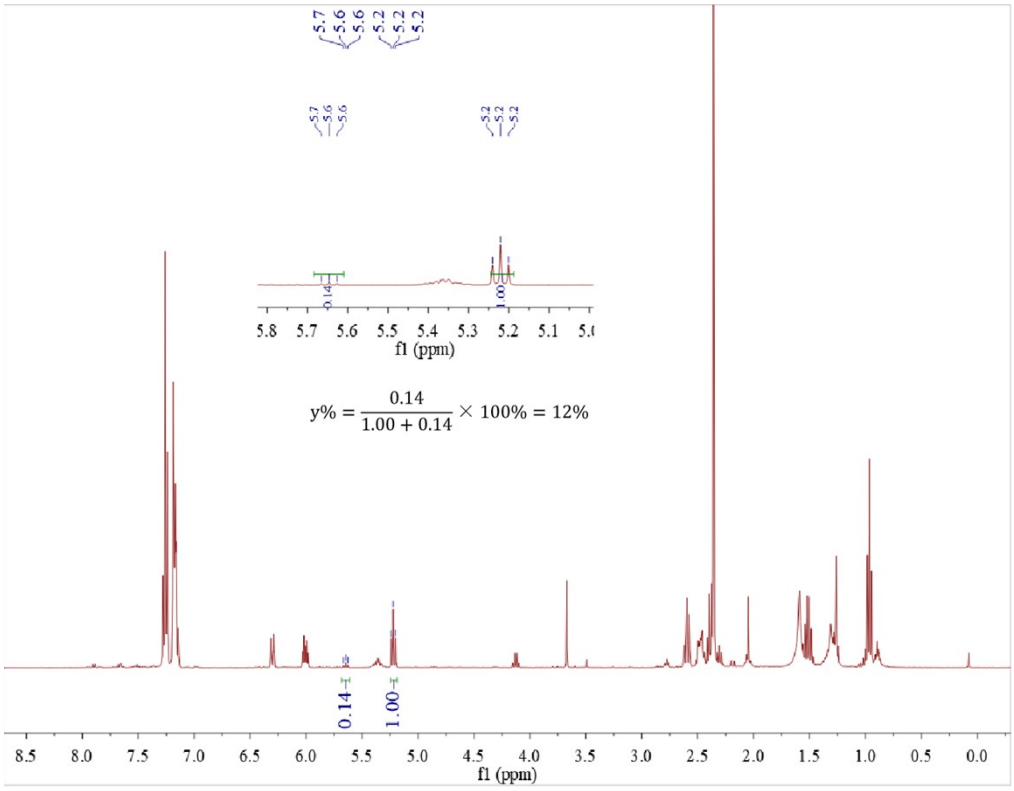


Figure S4. ^{1}H-NMR Spectra of reaction mixture of entry 2 in Table S4.

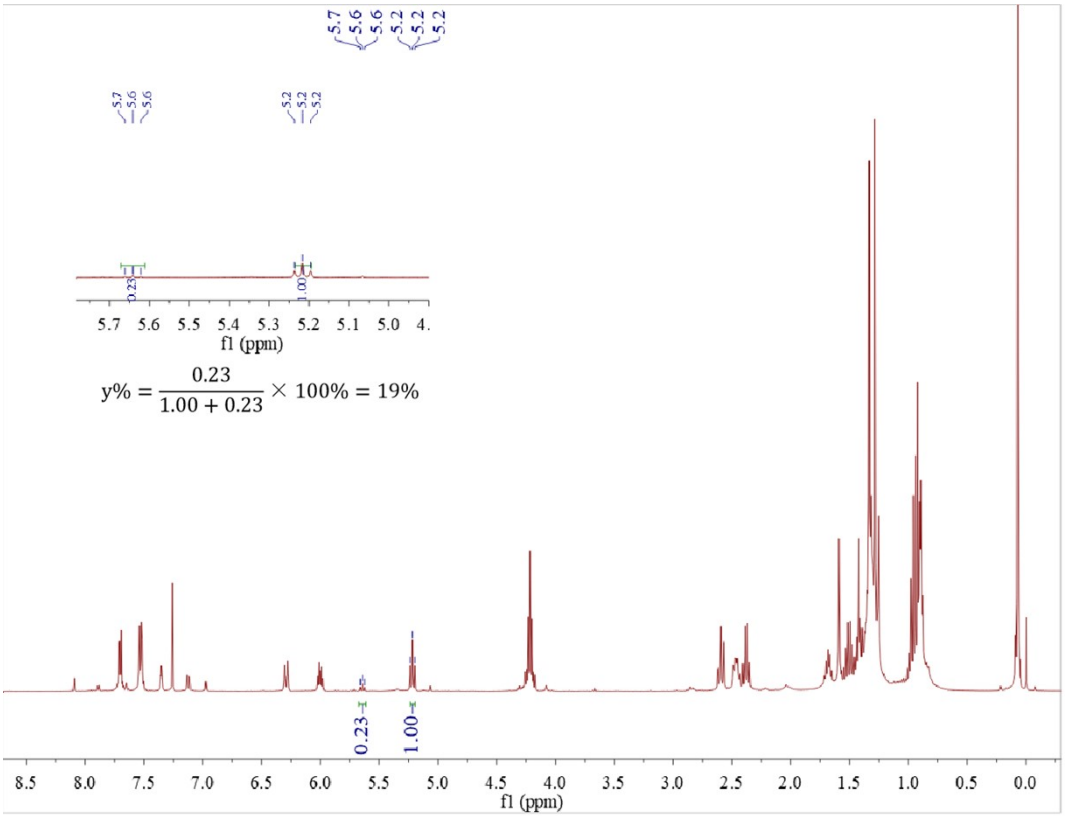


Figure S5. [1]H-NMR Spectra of reaction mixture of entry 3 in Table S4.

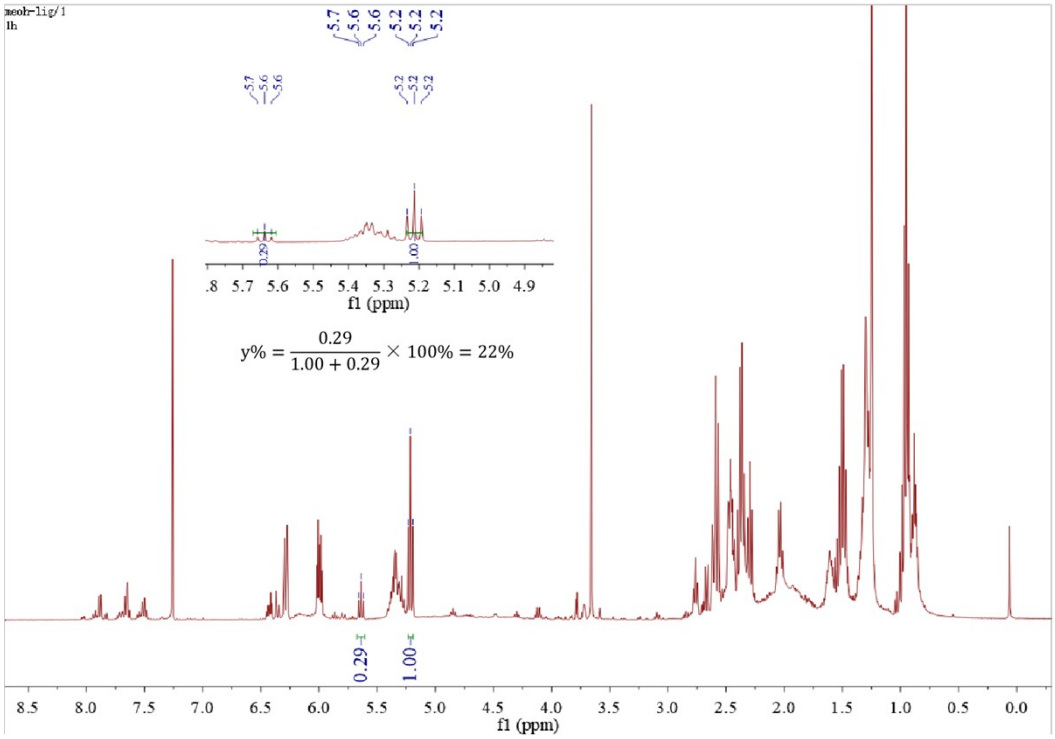


Figure S6. [1]H-NMR Spectra of reaction mixture of entry 4 in Table S4.

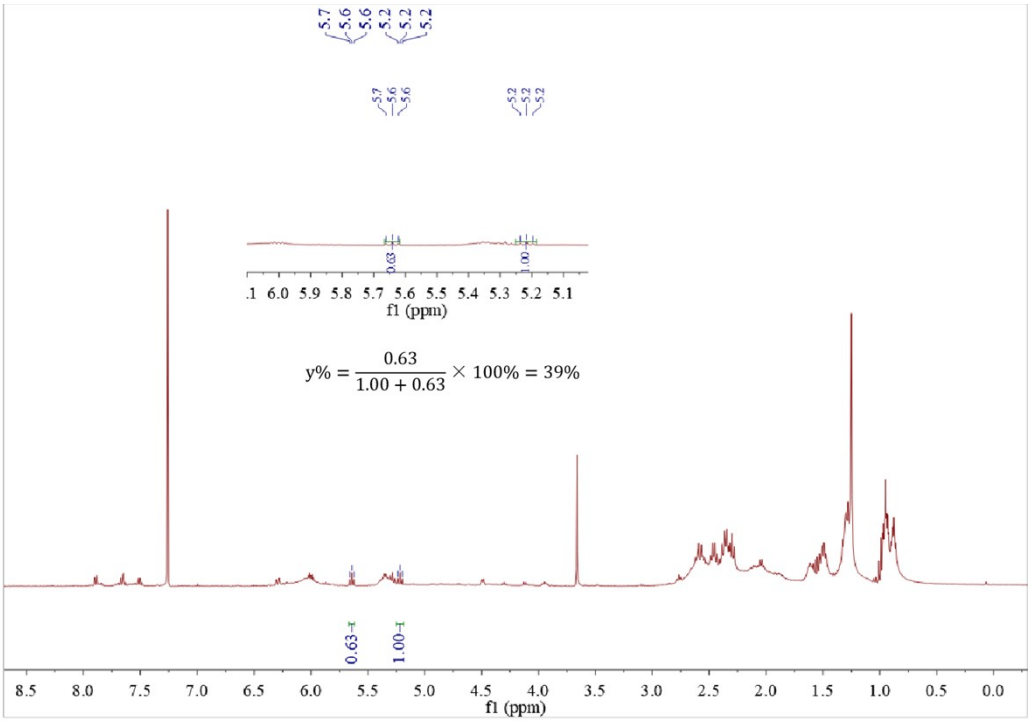


Figure S7. ^{1}H-NMR Spectra of reaction mixture of entry 5 in Table S4.

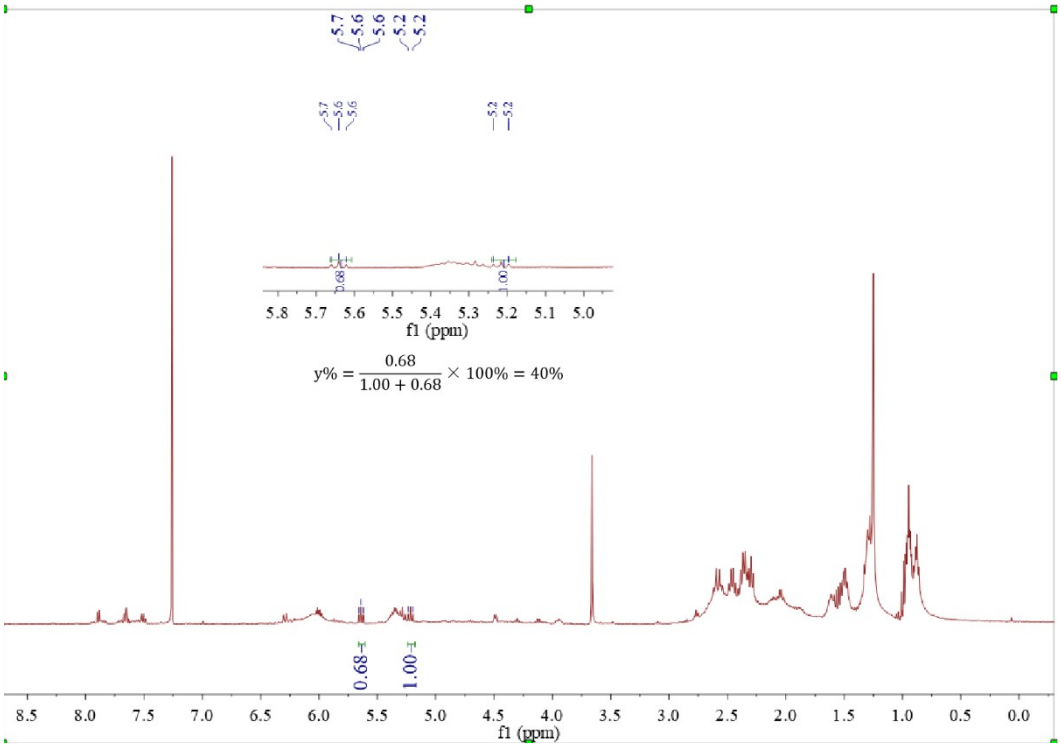


Figure S8. ^{1}H-NMR Spectra of reaction mixture of entry 6 in Table S4.

Cartesian Coordinates of All the Structures

Cartesians Coordinates ((B3LYP/6-311+G (d, p) (solution))

Oxygen

0 3

O	-0.06186200	3.44274800	0.00000000
O	-1.26767700	3.44274800	0.00000000

Energy = -150.3704141

Free Energy = -150.386660

Oxygen (guess = mix)

0 1

O	-0.08396947	3.44274804	0.00000000
O	-1.24556947	3.44274804	0.00000000

Energy (0K) = -150.3540028

Free Energy (298K) = -150.369221

Oxygen

0 1

O	-0.08396947	3.44274804	0.00000000
O	-1.24556947	3.44274804	0.00000000

Energy = -150.3089529

Free Energy= -150.324186

Z-Ligustilide

0 1

C	-0.85487200	3.55263400	0.20081400
C	-1.22875900	2.05794600	0.05145800
C	0.01023000	1.21734000	-0.05467900
C	1.17658300	1.61034000	0.51641100
C	1.33292000	2.87907000	1.20448100
C	0.35449300	3.79408500	1.08360600
C	0.20979200	-0.10341400	-0.62045700
O	1.52663500	-0.48127200	-0.38269500

C	2.16863700	0.53951300	0.32680600
O	3.31982500	0.45041800	0.67103100
C	-0.64589200	-0.90499800	-1.27704200
C	-0.33502600	-2.27266600	-1.80443500
C	-1.21252800	-3.37260300	-1.17072200
C	-0.92520600	-4.75985100	-1.75255300
H	-0.63831300	3.97417900	-0.79463600
H	-1.72103900	4.10795600	0.57760000
H	2.23394700	3.06122400	1.78227000
H	0.44620800	4.76585900	1.56267600
H	-1.65659800	-0.52643900	-1.41843500
H	-0.49831100	-2.28249300	-2.89348600
H	0.72322100	-2.50042200	-1.64042100
H	-1.04504000	-3.38083700	-0.08615300
H	-2.27248500	-3.12202700	-1.31759100
H	-1.55648700	-5.52397600	-1.28545000
H	-1.11434000	-4.78446100	-2.83282200
H	0.12083300	-5.04708800	-1.59225600
H	-1.89319700	1.91951000	-0.80856500
H	-1.79390100	1.72372000	0.93573600

Energy = -616.3282176

Free Energy = - 616.136544

^{3}TS1

0 3

C	-1.26221900	3.62413100	0.19485900
C	-1.63250000	2.14197700	0.17874200
C	-0.41233100	1.28301500	0.07201100
C	0.85288400	1.77964400	0.23046600
C	1.13516300	3.15422500	0.47889500
C	0.07014400	4.03596600	0.49184500

C	-0.30368600	-0.14180600	-0.14676800
O	1.04537400	-0.48915900	-0.11571500
C	1.80529100	0.65532500	0.11665100
O	3.00593700	0.62733200	0.19633900
C	-1.26227500	-1.06169600	-0.36073300
C	-1.03979900	-2.52797000	-0.56678700
C	-1.74061000	-3.39481100	0.50112500
C	-1.55352200	-4.89420300	0.25181700
H	-1.39891200	3.91762300	-1.21325000
H	-2.06250700	4.29487600	0.51286400
H	2.15643200	3.47812100	0.64779000
H	0.25358600	5.09288100	0.66979200
H	-2.28848800	-0.69916500	-0.37270500
H	-1.43195500	-2.81092100	-1.55603300
H	0.03351100	-2.74315900	-0.57697300
H	-1.34720000	-3.12906700	1.49059700
H	-2.81245600	-3.15330200	0.51923100
H	-2.05551900	-5.48876400	1.02307800
H	-1.96685400	-5.18968600	-0.72024600
H	-0.49154600	-5.16704900	0.25805400
H	-2.33136500	1.94249700	-0.64994800
H	-2.19333200	1.88069700	1.09364900
O	-2.55431500	3.12040400	-2.63910000
O	-1.69568200	4.03736800	-2.34376600

Energy = -66.6570247

Free Energy = -766.473690

^{3}A

0 3

C	-0.99050400	2.78578200	0.79245000
C	-1.33974200	1.33166200	0.61057900

C	-0.11601400	0.49947300	0.41450400
C	1.15689800	1.03616400	0.45886100
C	1.41841600	2.40000400	0.66913800
C	0.29397600	3.25801000	0.82740000
C	-0.00061700	-0.90857200	0.17173400
O	1.37344900	-1.21581200	0.07315000
C	2.10416400	-0.06313000	0.24292400
O	3.31608700	-0.08020300	0.20033800
C	-0.93535100	-1.86494600	0.03277300
C	-0.69452800	-3.31684100	-0.22292600
C	-1.31035600	-4.22150700	0.86338000
C	-1.11329100	-5.70831400	0.56407900
H	-0.59631800	3.50371400	-1.47373100
H	-1.81868100	3.47340700	0.92819800
H	2.43058000	2.78215500	0.70080800
H	0.46419000	4.31821800	0.98401900
H	-1.96636200	-1.53391100	0.12333100
H	-1.15251900	-3.57723600	-1.18731200
H	0.37559100	-3.51929700	-0.31260200
H	-0.85933500	-3.97523000	1.83101500
H	-2.38020900	-4.00035800	0.95084900
H	-1.55737900	-6.32905100	1.34826300
H	-1.58076900	-5.98639300	-0.38645600
H	-0.05011700	-5.96278700	0.50020400
H	-2.03743100	1.20901100	-0.23128900
H	-1.91137300	0.97605000	1.48335100
O	-1.94688500	3.21536000	-2.72341900
O	-0.72554100	3.63489500	-2.44353900

Energy = -766.6728584

Free Energy = -766.487767

^{1}A

0 1

C	-2.54500000	-0.61420400	1.54857000
C	-1.13358500	-1.02326000	1.21846500
C	-0.40780400	0.06331600	0.49623900
C	-0.99307200	1.28437500	0.21805800
C	-2.31133600	1.61301000	0.57292000
C	-3.06834000	0.61409000	1.24798500
C	0.93297400	0.08323000	-0.01049400
O	1.14893000	1.34562700	-0.60365300
C	0.00520700	2.09977100	-0.48266600
O	-0.04634700	3.22983900	-0.92023600
C	1.90161000	-0.84909300	0.00479100
C	3.27953200	-0.71437800	-0.55599800
C	4.37589300	-0.93659100	0.50540300
C	5.78416900	-0.86501100	-0.08666900
H	-3.81297600	-0.90437400	-0.56007700
H	-3.15394800	-1.34319400	2.07282900
H	-2.73355500	2.58222700	0.34059600
H	-4.08982100	0.83966400	1.53668900
H	1.64423400	-1.78938900	0.48458300
H	3.40615700	-1.46942900	-1.34433600
H	3.40992400	0.26333300	-1.02636300
H	4.26652000	-0.18422500	1.29432500
H	4.22358900	-1.91261300	0.98014300
H	6.54331500	-1.02173200	0.68575100
H	5.92913600	-1.62959100	-0.85724900
H	5.97282300	0.11123600	-0.54551000
H	-1.13491100	-1.95256500	0.62873600
H	-0.59985600	-1.29593000	2.14319900

O	-3.80465100	-2.60175600	-1.32628500
O	-4.14694600	-1.32682800	-1.38644300

Energy = -766.6728312

Free Energy = -766.487457

^{3}TS2

0 3

C	-0.71852500	3.02897000	1.09280200
C	-1.22053300	1.74496400	0.59413000
C	-0.17847300	0.70475400	0.51745200
C	1.19513300	1.04123400	0.70172000
C	1.62058500	2.28009500	1.05445200
C	0.60210200	3.29386800	1.27305200
C	-0.23068900	-0.62324300	0.15106300
O	1.05318600	-1.16799500	0.11680400
C	1.96534700	-0.18783800	0.44498500
O	3.14684100	-0.41995300	0.48186000
C	-1.30855900	-1.46462200	-0.17207200
C	-1.13724700	-2.89882300	-0.53285000
C	-1.05878200	-3.80142700	0.71643400
C	-0.90764700	-5.27073100	0.33844000
H	-0.66666200	0.41475800	-2.44501500
H	-1.44854200	3.80894100	1.29012900
H	2.67320300	2.50849100	1.18772500
H	0.91458900	4.27732200	1.60897000
H	-2.30045600	-1.04235400	-0.05483000
H	-1.98081000	-3.22222500	-1.15235900
H	-0.22057600	-3.03539800	-1.11933100
H	-0.20947700	-3.47935700	1.33067100
H	-1.96242000	-3.65738000	1.32003300
H	-0.84996800	-5.90356900	1.22959400

H	-1.75915600	-5.61007000	-0.26158700
H	0.00267100	-5.43188100	-0.24938700
H	-1.50540500	1.94979100	-0.69124100
H	-2.20705800	1.44177200	0.95425200
O	-1.59845300	1.95064000	-1.91777300
O	-1.60531900	0.61905000	-2.26798100

Energy = -766.6347049

Free Energy = -766.453708

^{1}TS2

0 1

C	-2.73712900	-0.64339600	1.25596000
C	-1.37176400	-1.05632600	0.84789000
C	-0.57845600	0.08036400	0.34914300
C	-1.13421800	1.31116500	0.11357900
C	-2.46920300	1.62379000	0.41498800
C	-3.24804600	0.61404400	1.01086100
C	0.80971200	0.14319300	-0.05682200
O	1.07253500	1.42808000	-0.51142900
C	-0.07482700	2.18871900	-0.43699000
O	-0.11400800	3.33549900	-0.77574800
C	1.75044000	-0.80854900	-0.04890500
C	3.16809800	-0.62022600	-0.48531100
C	4.16429700	-0.86959800	0.65633600
C	5.61009600	-0.71999000	0.19158000
H	-3.69469500	-1.14356200	-1.28323000
H	-3.35211700	-1.38259100	1.75721100
H	-2.85808800	2.61822900	0.22769400
H	-4.26736700	0.83687700	1.31122400
H	1.45174700	-1.78633100	0.32413000
H	3.38903300	-1.31952400	-1.30374500

H	3.29975600	0.39152500	-0.88128600
H	3.95510000	-0.16624500	1.47022300
H	4.00492000	-1.87596000	1.06352500
H	6.31222300	-0.89410400	1.01147800
H	5.83988000	-1.43368100	-0.60651100
H	5.79118300	0.28650000	-0.19909500
H	-1.50362400	-1.80836600	-0.01001500
H	-0.85730500	-1.65188200	1.61325400
O	-2.43788400	-2.49971600	-1.25802400
O	-3.62622300	-2.03011600	-0.87588900

Energy = -766.6814566

^{1}TS2 (M062X/6-31g(d))

0 1

C	-2.72962700	-0.66292100	1.20468500
C	-1.39818300	-0.99169100	0.83052300
C	-0.59203200	0.08214000	0.36312000
C	-1.14871700	1.32120000	0.11685600
C	-2.48375600	1.61170400	0.40200300
C	-3.26579300	0.60667600	0.95850800
C	0.80814300	0.14892600	-0.03969300
O	1.06194300	1.43834200	-0.48435600
C	-0.08443100	2.20093300	-0.41869000
O	-0.11982700	3.34877500	-0.75077800
C	1.74798300	-0.79798700	-0.03675300
C	3.16410700	-0.60604300	-0.47716400
C	4.16380900	-0.87909800	0.65571700
C	5.60782400	-0.72648000	0.18650900
H	-3.90634200	-1.45768000	-1.40635900
H	-3.34318000	-1.42408400	1.67007300
H	-2.87814700	2.60468500	0.20968500

H	-4.29737900	0.80710700	1.22727700
H	1.45327200	-1.77946800	0.32971900
H	3.37576000	-1.29302700	-1.30805600
H	3.29709100	0.41142700	-0.85745700
H	3.96136500	-0.18957100	1.48305500
H	4.00277900	-1.89200900	1.04547700
H	6.31269500	-0.91800200	1.00003400
H	5.83100400	-1.42678600	-0.62509600
H	5.79108100	0.28613000	-0.18683000
H	-1.66709700	-1.62002100	-0.27308400
H	-0.93017900	-1.87113900	1.27256300
O	-2.29772500	-2.39275800	-1.22463600
O	-3.61172500	-2.15457500	-0.79707000

Thermal correction to Gibbs Free Energy (298K) = 0.193286

$^{3}2$

0 3

C	-0.42168500	2.94148200	2.73069000
C	-0.89288600	1.70810900	2.28097900
C	-0.32071500	1.17020800	1.12579100
C	0.69235600	1.86517000	0.45576400
C	1.16840300	3.09720900	0.89901900
C	0.59704700	3.63251400	2.05165400
C	-0.56401400	-0.07020400	0.38916800
O	0.30970100	-0.08197100	-0.70540700
C	1.10057400	1.06997600	-0.71266300
O	1.92484100	1.25540000	-1.56954200
C	-1.42151000	-1.07354900	0.61318000
C	-1.56585000	-2.31698300	-0.21176800
C	-1.21961100	-3.59936300	0.57434900
C	-1.38590500	-4.86209500	-0.27609500

H	-0.85204600	3.37917700	3.62722100
H	1.95600700	3.61153800	0.35702100
H	0.93824700	4.59080300	2.43180900
H	-2.05493900	-0.97759000	1.49359400
H	-2.60804500	-2.39251200	-0.55903000
H	-0.93403900	-2.25520200	-1.10307000
H	-0.18493200	-3.52732900	0.93277000
H	-1.85412900	-3.66466800	1.46936100
H	-1.12930000	-5.76102500	0.29536600
H	-2.42005400	-4.97262900	-0.62555300
H	-0.73611500	-4.82779200	-1.15830700
H	-1.68075200	1.18852300	2.81827300

Energy = -615.0617844

Free Energy = -614.897516

$^{1}2$

0 1

C	-0.05080000	2.76557100	2.88264400
C	-0.56488800	1.54625200	2.45146800
C	-0.32291700	1.16382700	1.13095600
C	0.41484200	1.99562400	0.28547900
C	0.93259800	3.21637100	0.71046800
C	0.69036000	3.59583000	2.02592100
C	-0.70444900	-0.02175100	0.36600800
O	-0.18434600	0.13739000	-0.92642500
C	0.51262200	1.34491000	-1.02851900
O	1.04603600	1.66874400	-2.05087400
C	-1.40538400	-1.10118200	0.72335200
C	-1.73838600	-2.28833600	-0.12481800
C	-1.10385200	-3.59150800	0.40400400
C	-1.47397900	-4.80542800	-0.45158000

H	-0.22612400	3.08343800	3.90424200
H	1.50192800	3.84031900	0.03205500
H	1.07460600	4.53829000	2.39752000
H	-1.75062800	-1.11530600	1.75390700
H	-2.82974700	-2.41202700	-0.13643700
H	-1.42728400	-2.12697000	-1.15777300
H	-0.01610300	-3.47151700	0.42133100
H	-1.41850700	-3.75548700	1.44184200
H	-1.01670800	-5.71725500	-0.05790600
H	-2.55764000	-4.95942200	-0.47504600
H	-1.12922900	-4.67461500	-1.48073400
H	-1.13424400	0.91945600	3.12727900

Energy = -615.1446284

Free Energy = -614.974320

H_2O_2

0 1

H	1.67877000	-2.44277500	-3.44742200
H	-0.01470000	-0.96118900	-2.62183500
O	-0.04170500	-1.67728300	-3.28007000
O	0.99640600	-2.55629700	-2.77158400

Energy = -151.6187797

Free Energy = -151.614749

BF_3

0 1

B	1.79789200	2.44639100	-0.34428100
F	1.54767300	2.09191800	-1.59108300
F	1.43767300	1.65763600	0.65093300
F	2.41152400	3.58806800	-0.09312600

Energy = -324.6685727

Free Energy = -324.683114

$^{3}TS1_{BF3}$

0 3

C	-1.53469300	3.82770100	0.41286000
C	-1.78196600	2.34740100	0.65971000
C	-0.53592300	1.57967600	0.40536000
C	0.70070500	2.16956200	0.45319100
C	0.89311300	3.55567200	0.64921000
C	-0.24465300	4.36506300	0.64216900
C	-0.34689700	0.20108000	0.04004800
O	1.02350100	-0.03739100	-0.06831200
C	1.70093400	1.12967600	0.14600700
O	2.90237300	1.19288000	0.07650200
C	-1.25579200	-0.73449200	-0.26539700
C	-0.94897200	-2.11310400	-0.74101100
C	-1.58705900	-3.18726100	0.15130400
C	-1.31025700	-4.59050400	-0.37685100
H	-1.38428900	3.83592400	-0.93969100
H	-2.38495100	4.48771900	0.57337200
H	1.88910700	3.97565000	0.73535400
H	-0.12661900	5.44380200	0.69011800
H	-2.30028400	-0.44577900	-0.16047300
H	-1.35007100	-2.21483700	-1.75940400
H	0.13353400	-2.26397800	-0.80021800
H	-1.19616100	-3.08523000	1.17032500
H	-2.66844500	-3.01330400	0.20677100
H	-1.76464600	-5.35122100	0.26538100
H	-1.71561200	-4.71483300	-1.38702300
H	-0.23336600	-4.78650400	-0.42128800
H	-2.62089700	1.97014500	0.06818200
H	-2.06664500	2.20819500	1.71748600

O	-1.38184500	2.23458300	-2.23946000
O	-0.99729700	3.46606400	-2.13436400
B	-0.43187400	1.42601400	-3.22537500
F	-0.34874200	2.14324500	-4.38454200
F	0.76436400	1.33943300	-2.54940500
F	-1.08041100	0.22654400	-3.34739300

Energy = -1091.3472535

Free Energy = -1091.157518

$^{3}A_{BF3}$

0 3

C	-0.87286400	2.85654000	0.55409500
C	-1.16287100	1.44764300	0.89780200
C	-0.01585100	0.75794700	1.51768300
C	1.21644600	1.40169100	1.68181600
C	1.43237500	2.71016300	1.28773500
C	0.35543200	3.43856800	0.71887900
C	0.13028500	-0.56038100	1.97943900
O	1.40473600	-0.77121400	2.41985000
C	2.14523100	0.43163500	2.27700200
O	3.28647600	0.48828000	2.62511500
C	-0.82667600	-1.63679200	2.03900700
C	-0.72610100	-2.85392100	1.17785300
C	-2.06318200	-3.59373500	1.03463000
C	-1.96618200	-4.81317800	0.11783500
H	-1.68709600	3.43386400	0.12998100
H	2.40695900	3.16982600	1.40685600
H	0.51517000	4.46754400	0.42197200
H	-1.68695900	-1.48646100	2.68696800
H	-0.33542800	-2.57187700	0.19165000
H	0.03279700	-3.53206000	1.60385300

H	-2.40797100	-3.90077900	2.02850900
H	-2.81368000	-2.89891500	0.64245600
H	-2.93138300	-5.32304200	0.04339500
H	-1.66290500	-4.52513600	-0.89404400
H	-1.23470700	-5.53666400	0.49302100
H	-1.43227700	0.92518000	-0.04646000
H	-2.08212200	1.37693200	1.49694100
O	-1.25348900	0.25490000	-1.98710700
O	-2.12963300	1.13765400	-2.73685400
B	0.01426000	0.08279600	-2.71422600
F	-0.16598400	-0.61528200	-3.92964700
F	0.62455800	1.33013900	-2.98956600
F	0.82836300	-0.67267200	-1.84259500
H	-1.82825500	2.01885700	-2.46294200

Energy = -1091.3557813

Free Energy = -1091.167290

$^{1}A_{BF3}$

0 1

C	-1.04646700	3.12508300	1.70036800
C	-1.26887500	1.65796300	1.53481700
C	0.01183500	0.90801500	1.63896200
C	1.22199100	1.53859500	1.86629700
C	1.36753100	2.92253700	2.01596000
C	0.18820700	3.69624800	1.92366000
C	0.27514500	-0.48603800	1.54136600
O	1.59281700	-0.74596900	1.70406700
C	2.26079400	0.48851800	1.91394200
O	3.43928700	0.51266200	2.08347800
C	-0.61305600	-1.55943600	1.31350600
C	-0.23156800	-2.97496700	1.23589400

C	-0.61229100	-3.60477300	-0.13689400
C	-0.28033800	-5.09505600	-0.17766300
H	-1.92111700	3.76260400	1.63834900
H	2.33534600	3.37284900	2.19178000
H	0.25841200	4.77252900	2.03235000
H	-1.65399200	-1.28529000	1.17455700
H	0.82950300	-3.12039700	1.44179900
H	-0.80777600	-3.51188300	2.00586500
H	-1.67979600	-3.44781900	-0.31658700
H	-0.07084600	-3.07454900	-0.92538300
H	-0.54337100	-5.51545900	-1.15302600
H	0.78764900	-5.27016700	-0.01490100
H	-0.83444100	-5.64693800	0.58803200
H	-1.76850800	1.46030900	0.57201300
H	-1.99918900	1.30417100	2.28204800
O	-2.58094700	0.23022700	-1.90235700
O	-3.84221800	-0.22115000	-2.47210900
B	-1.59509600	0.36823100	-2.98091500
F	-1.35838500	-0.85650800	-3.64918100
F	-1.99172700	1.33404700	-3.93840800
F	-0.41470100	0.79450000	-2.32924400
H	-4.34633900	0.60535700	-2.53154000

Energy = -1091.4188273

Free Energy = -1091.225851

$^{1}TS2_{BF3}$

0 1

C	1.09244200	0.96884800	-1.99841100
C	0.00241800	0.31601100	-1.35584000
C	-0.78403900	1.09629400	-0.45920300
C	-0.39289800	2.40192500	-0.16322500

C	0.70928400	3.00712000	-0.76375200
C	1.45439000	2.27739500	-1.68948200
C	-1.98727000	0.81791300	0.29410100
O	-2.28564700	1.97955400	1.04210400
C	-1.35568500	2.95522400	0.79819400
O	-1.41682300	4.03938000	1.33107300
C	-2.80457300	-0.23910200	0.38694700
C	-2.65295800	-1.54918300	-0.32661000
C	-3.71007400	-2.57924400	0.09089400
C	-3.55217200	-3.91195700	-0.64049600
H	1.67448600	0.40430400	-2.71760300
H	0.97554700	4.02845600	-0.51582700
H	2.30954300	2.72889700	-2.17602100
H	-3.65917600	-0.12092100	1.04902800
H	-2.71231200	-1.38055400	-1.41038000
H	-1.65001900	-1.95367600	-0.14369700
H	-3.64353800	-2.74164500	1.17264800
H	-4.70703600	-2.16717100	-0.10253400
H	-4.31790400	-4.62666900	-0.32467300
H	-3.64347900	-3.78338800	-1.72435500
H	-2.57417100	-4.36195500	-0.43931100
H	0.92225500	-0.30686200	-0.36285000
H	-0.37427300	-0.61461900	-1.76640200
O	1.64324300	-1.04599700	0.67064500
O	1.04646500	-2.34873100	0.77776400
B	3.16094000	-1.13983600	0.48020100
F	3.71107700	-1.76204000	1.59732600
F	3.42983800	-1.87082700	-0.68226500
F	3.56758900	0.18674100	0.36765800
H	1.20775500	-2.75099000	-0.09488600

Energy = -1091.4059946