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Supporting Information

Concise Synthesis of Linderaspirone A and Bi-linderone

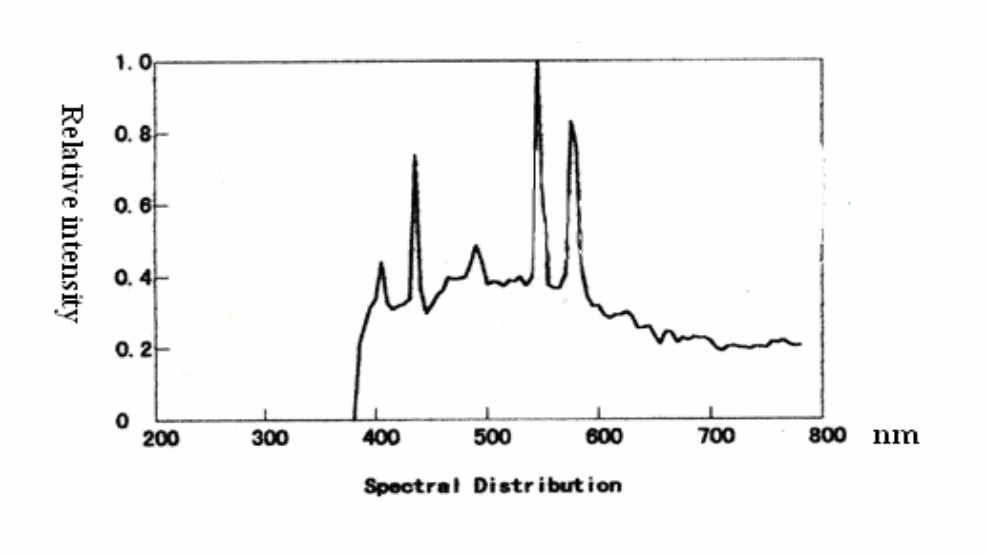
Fenfen Xiao,[a] Wu Liu,[a] Yunxia Wang,[a] Qing Zhang,[a] Xiang Li,[a] and Xiangdong Hu*[a, b]

ajoc_201200184_sm_miscellaneous_information.pdf

Context

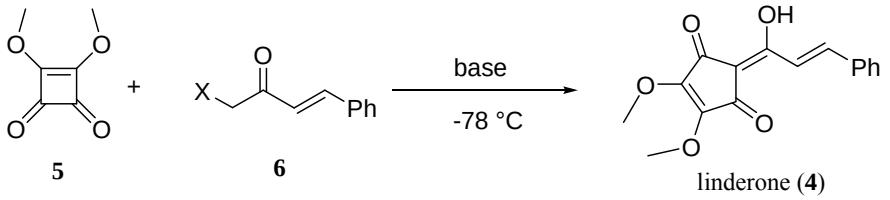
I. Information of the metal halide lamp applied for thedimerization of methyl-linderone

The metal halide lamp (400W) was purchased from Xian Bilon Biological Technology Co., LTD in China. And the relative spectral energy distribution curve obtained from the manufacturer is shown as below:



2. The study on the darzens cyclopentenedione synthesis

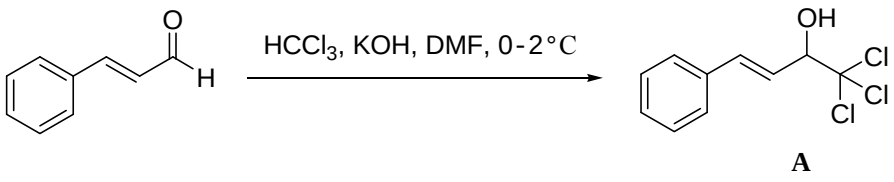
Table S1 the darzens cyclopentenedione synthesis



Entrry	X	Base (eq.)	Yield (**4**)
1	Cl	LiHMDS (2.6 eq.)	20.3%
2	I	LiHMDS (2.6 eq.)	30.4%
3	Br	LiHMDS (2.6 eq.)	48.0%
4	Br	LiHMDS (1.2 eq.)	32.5%

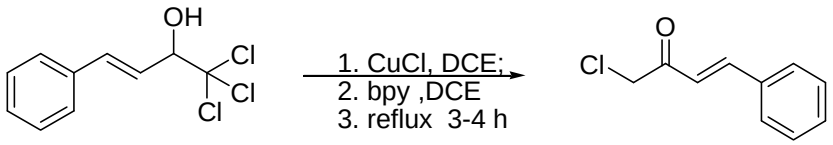
Notes: LiHMDS = lithium hexamethyldislazide; 23% was recovery of **3** in entry 3.

(*E*)-1,1,1-trichloro-4-phenylbut-3-en-2-ol A :[1]



To 0 - 2℃ pre-cooled solution of chloroform (6.45 mL, 0.08 mol) in 25 mL anhydrous DMF was added powdered potassium hydroxide (4.5 g, 0.08 mol). After 30min, cinnamaldehyde (2.52 mL, 0.02 mol) was slowly added to the mixture by syringe. The reaction was monitored by thin layer chromatography (TLC). After the reaction finished, the mixture was poured into 10 mL distilled water and extracted with ethyl acetate. The combined organic extract was washed with water, dried (Na_2SO_4) and evaporated. The crude product was purified by column chromatography using ethyl acetate and petroleum ether (1/30 = v/v) as an eluent to afford **A** (4.91 g, 97.6%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 4.74 - 4.76 (dd, *J* = 1.2 Hz, *J* = 6 Hz, 1 H), δ = 6.33 – 6.39 (dd, *J* = 6 Hz, *J* = 16 Hz, 1 H), δ = 6.88 (d, *J* = 15.6 Hz, 1 H), δ = 7.29 – 7.44 (m, 5 H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 88.3, 102.8, 122.6, 126.9, 128.6, 128.7, 135.6, 136.7 ppm.

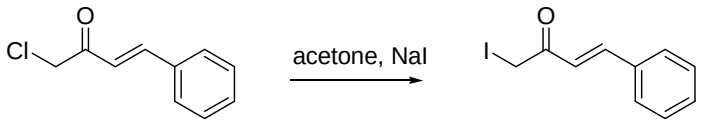
(E)-1-chloro-4-phenylbut-3-en-2-one 6b[1]:



A **6 b**

To a flame dried reaction tube was added **A** (0.005 mol), CuCl (1.00 g, 0.01 mol) and dry 1,2-dichloroethane (DCE) (10 mL). The solution of 2,2–bi-pyridine (bpy) (1.562 g, 0.01 mol) in DCE (10 mL) was injected into the tube through the rubber septum. After the completion of the reaction, the reaction mixture was cooled and filtered and the filtrate was evaporated under reduced pressure. The crude product was purified by flash column chromatography (ether : petroleum ether = 1 : 10) to give pure chloromethyl ketone **6b** (560 mg, 62%). ^{1}H NMR ($CDCl_3$, 400 MHz) : δ = 4.31 (s, 2 H), δ = 6.98 (d, *J* = 16 Hz, 1 H), δ = 7.40-7.43 (m, 3 H), δ = 7.58-7.60 (m, 2 H), δ = 7.72 (d, *J* = 16Hz, 1 H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) : δ = 47.4, 121.5, 128.5, 129.0, 131.1, 133.8, 145.1, 191.1 ppm; HRMS (M + Na^+) : Calcd for $C_{10}H_9ClNaO^+$: 203.0234, found : 203.0245.

(E)-1-iodo-4-phenylbut-3-en-2-one 6c:

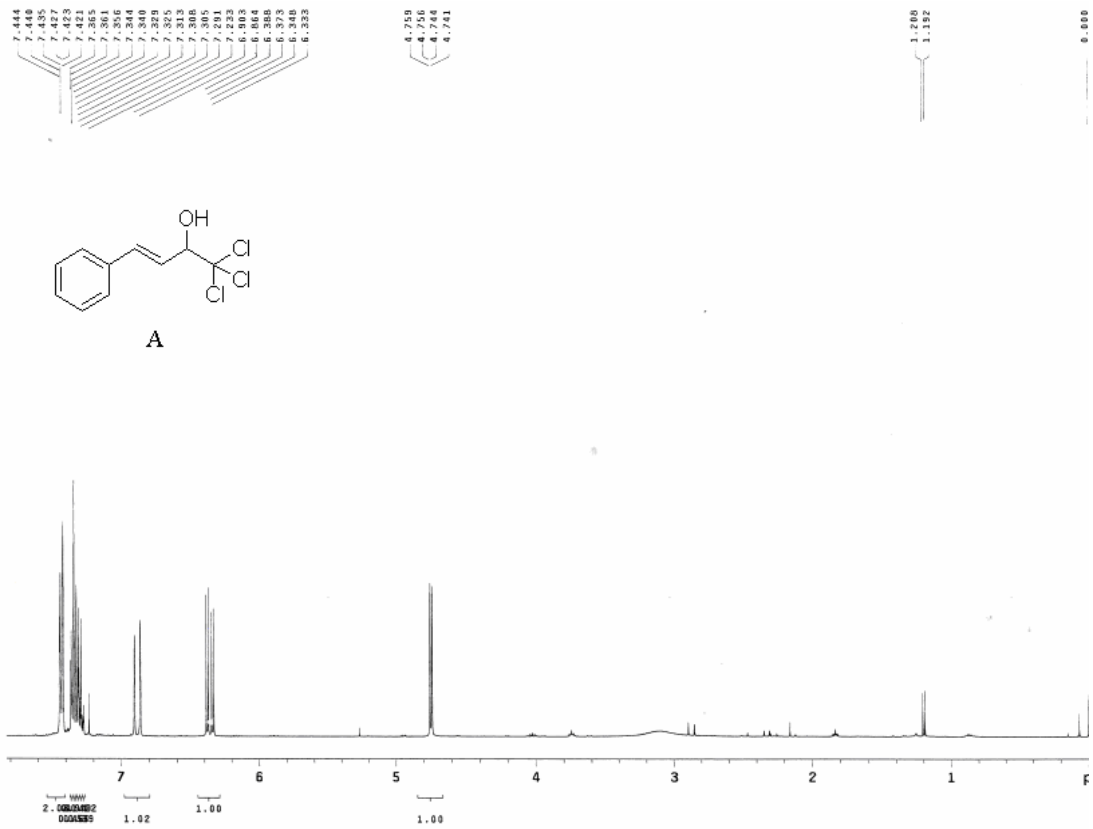


6 b **6 c**

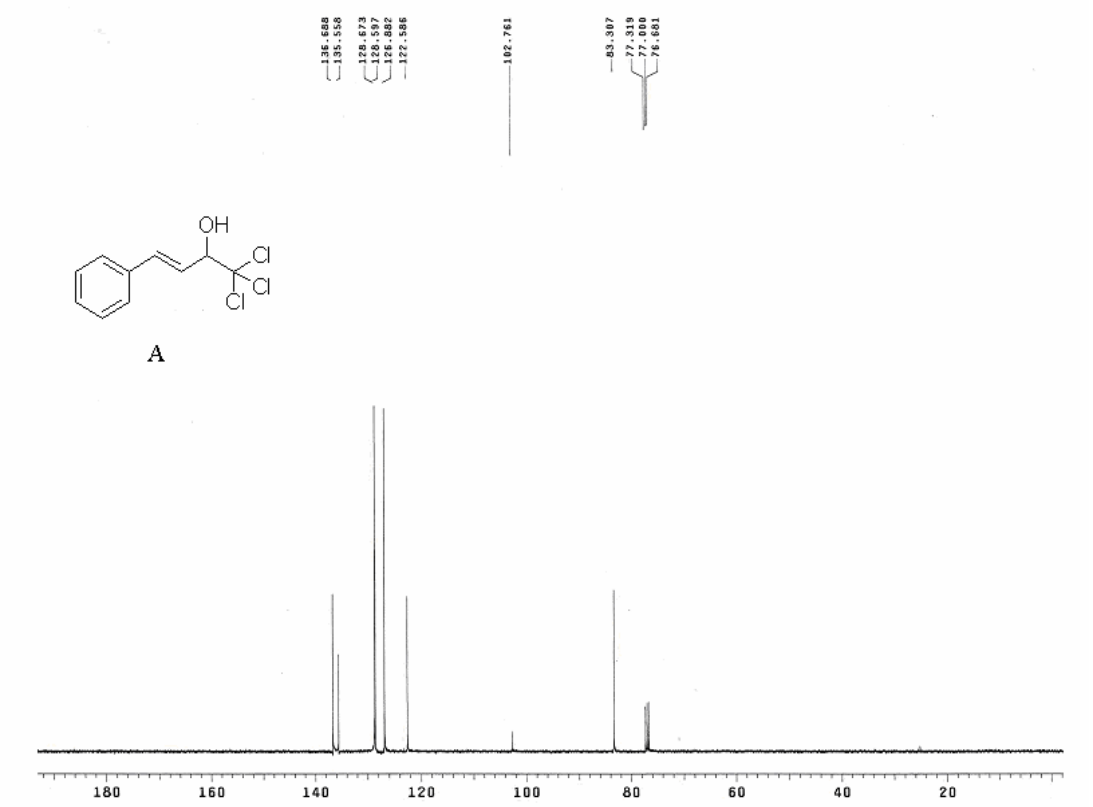
To the 75 mL acetone charged with **6b** (654 mg, 3.62 mmol) was added NaI (1 eq), the reaction mixture under an argon atmosphere was stirred at room temperature about 1 h. TLC showed the presence of a single compound having the same Rf value as the starting material. After the completion of the reaction, the reaction mixture was filtered and concentrated. The crude product was quickly purified by flash column chromatography (ether : petroleum ether = 1 : 5) to give pure 886.6 mg **6c** in 90% yield. ^{1}H NMR ($CDCl_3$, 400 MHz) : δ = 4.02 (s, 1 H), δ = 6.89 (d, *J* = 16 Hz, 1 H), δ = 7.42 - 7.43 (m, 3 H), δ = 7.56 - 7.59 (m, 2 H), δ = 7.69 (d, ***J*** = 16 Hz, 1 H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) : δ = 5.0, 122.1, 128.5, 128.9, 130.9, 133.9, 145.0, 192.1 ppm; HRMS (M + Na^+) : Calcd for $C_{10}H_9INaO^+$: 294.9590, found : 294.9575.

II. Copies of ^{1}H NMR, ^{13}C NMR spectra

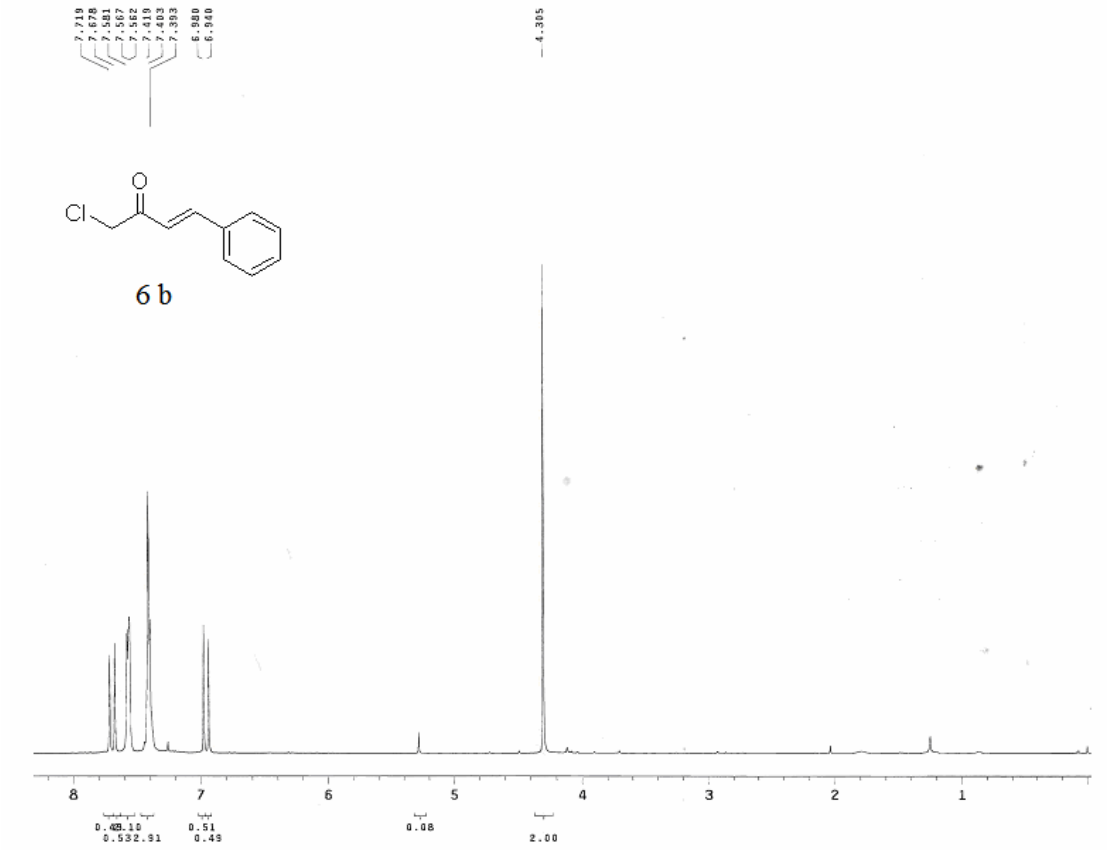
^{1}H NMR spectra of compound A



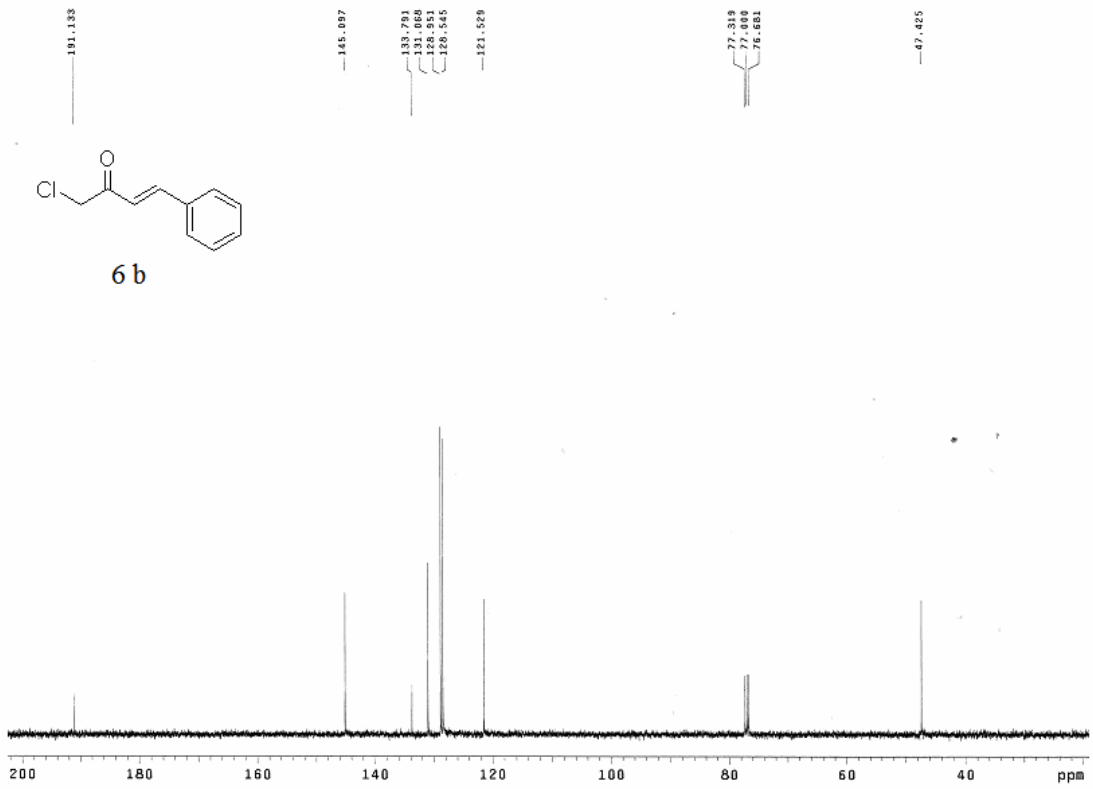
^{13}C NMR spectra of compound A



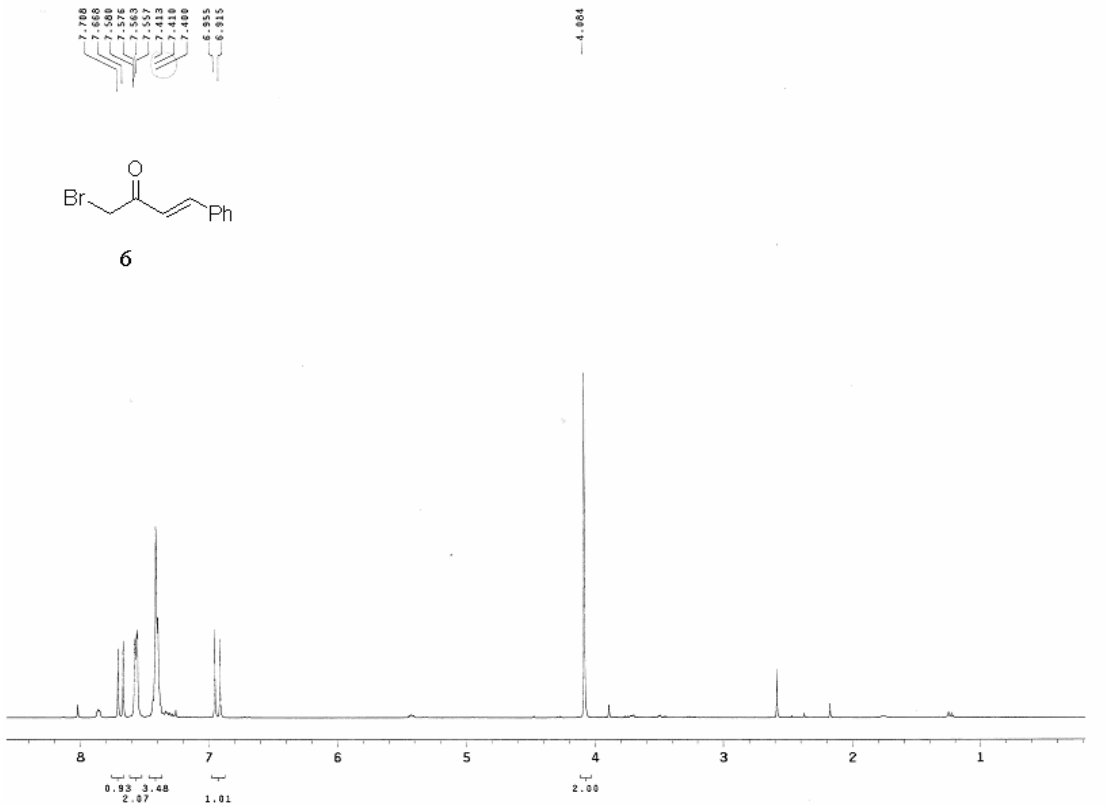
^{1}H NMR spectra of compound 6 b



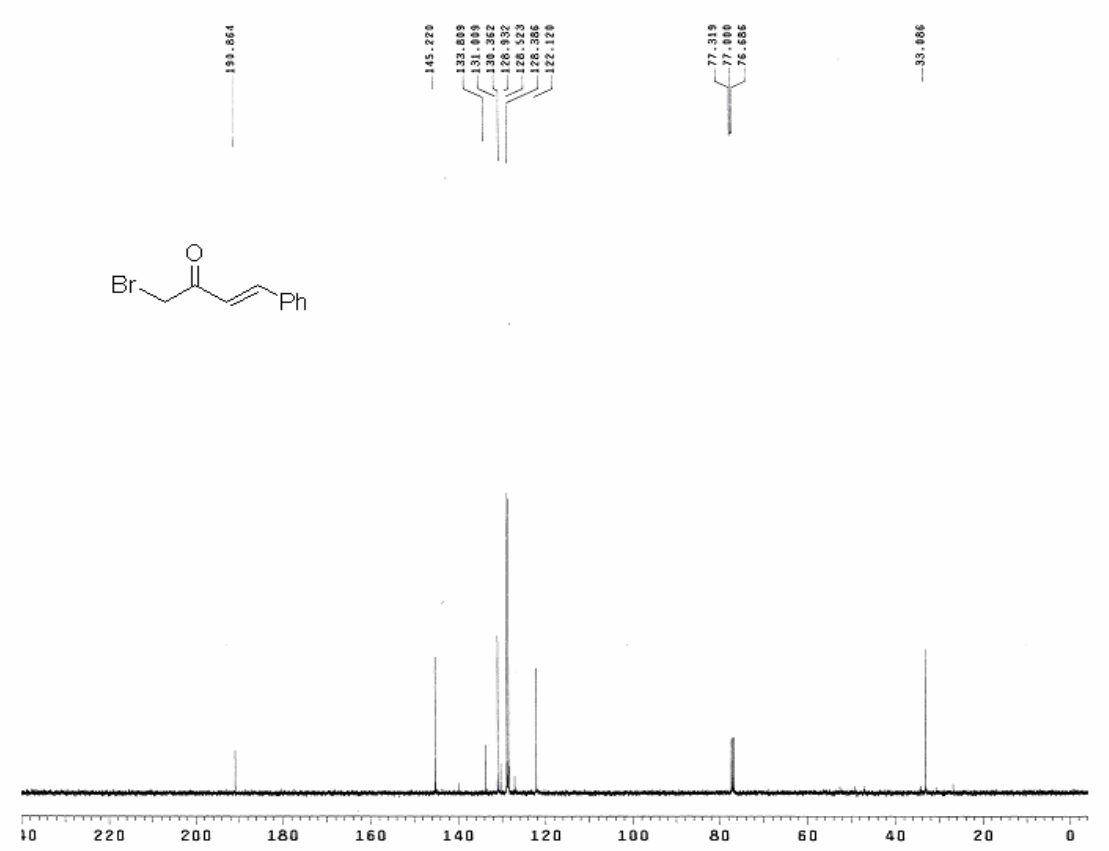
^{13}C NMR spectra of compound 6 b



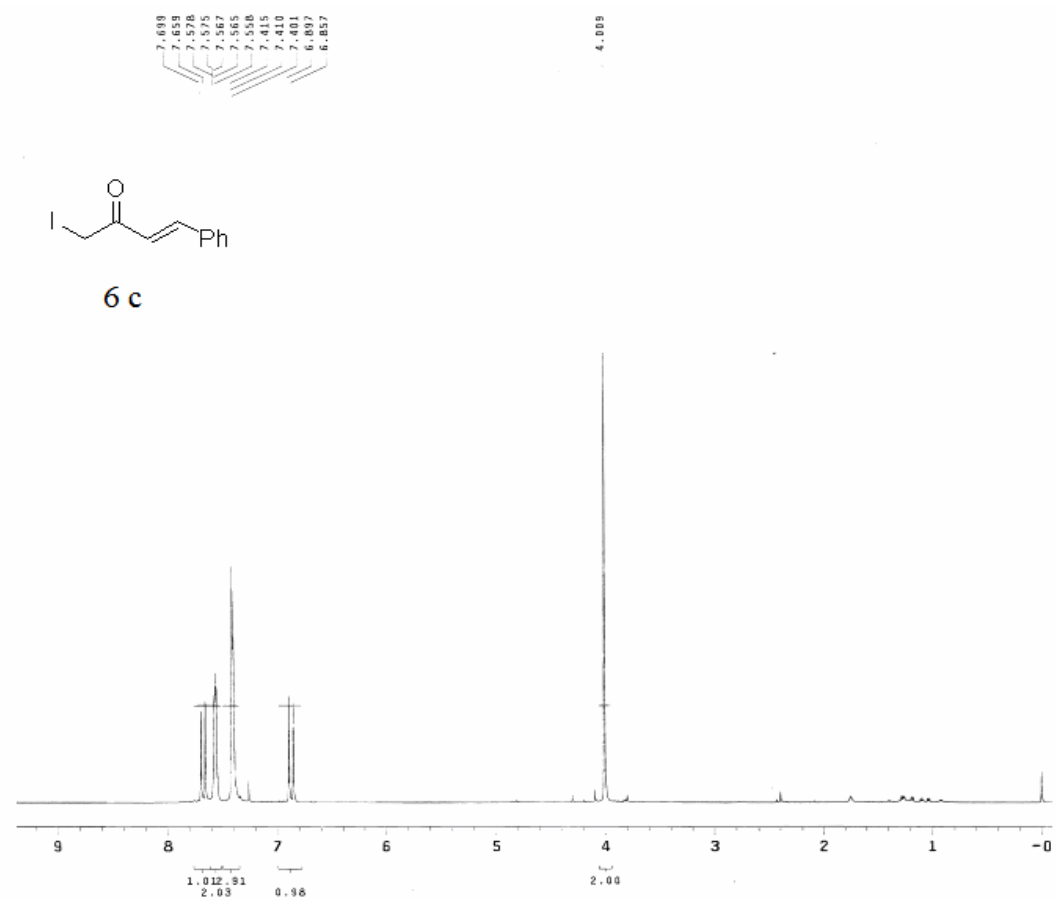
^{1}H NMR spectra of compound 6



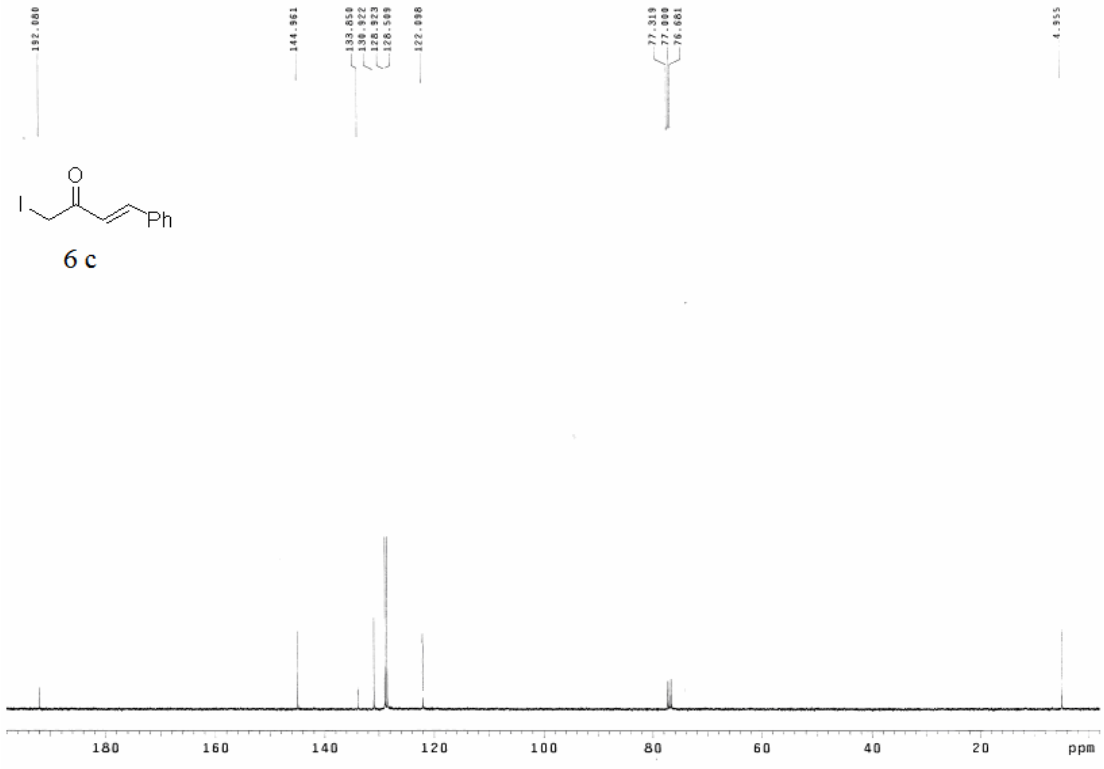
^{13}C NMR spectra of compound 6



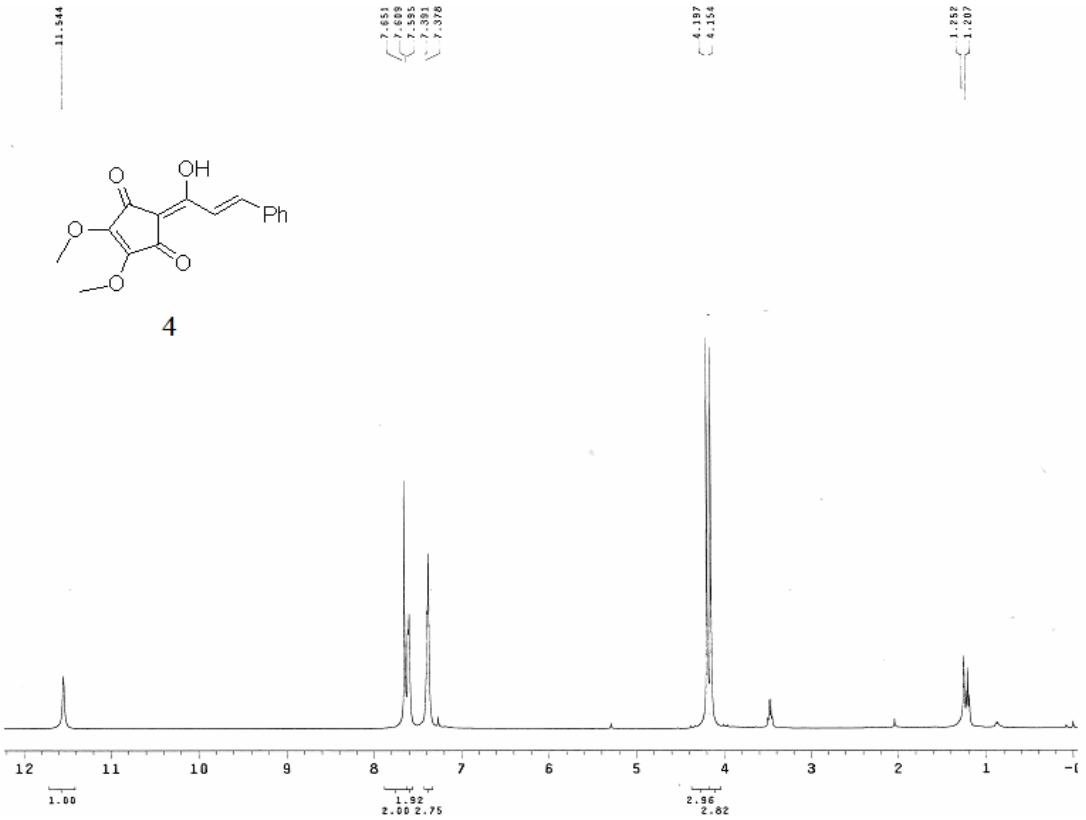
^{1}H NMR spectra of compound 6 c



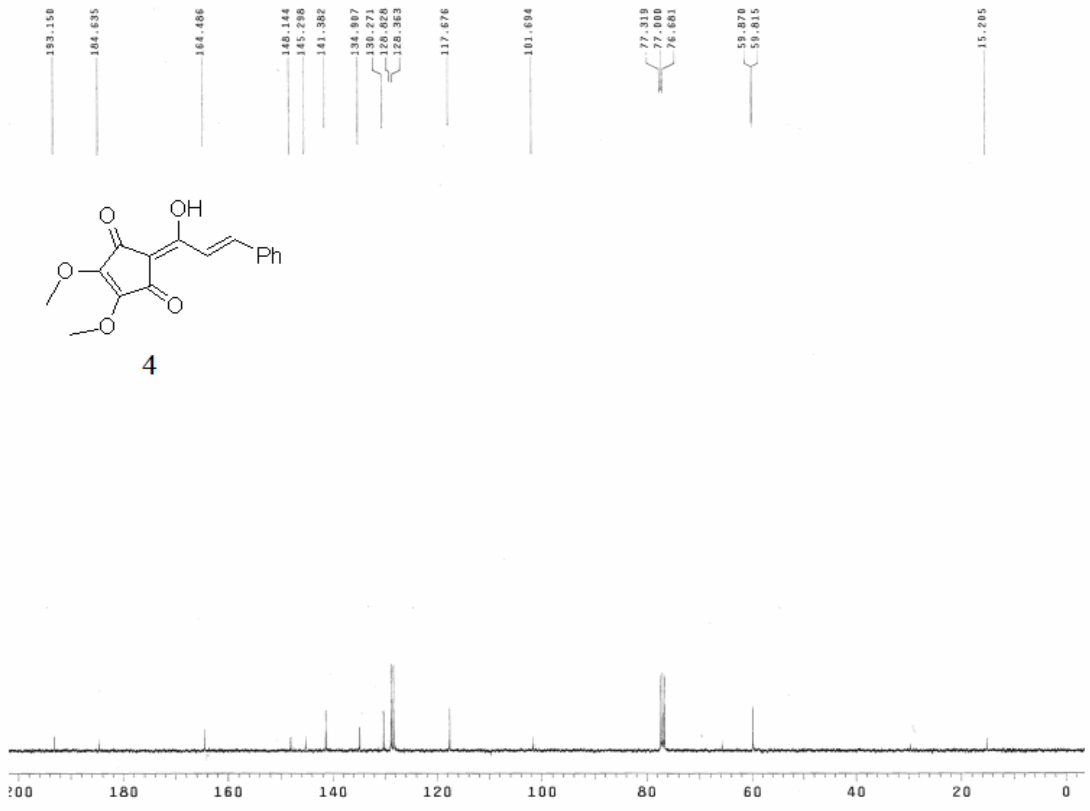
^{13}C NMR spectra of compound 6 c



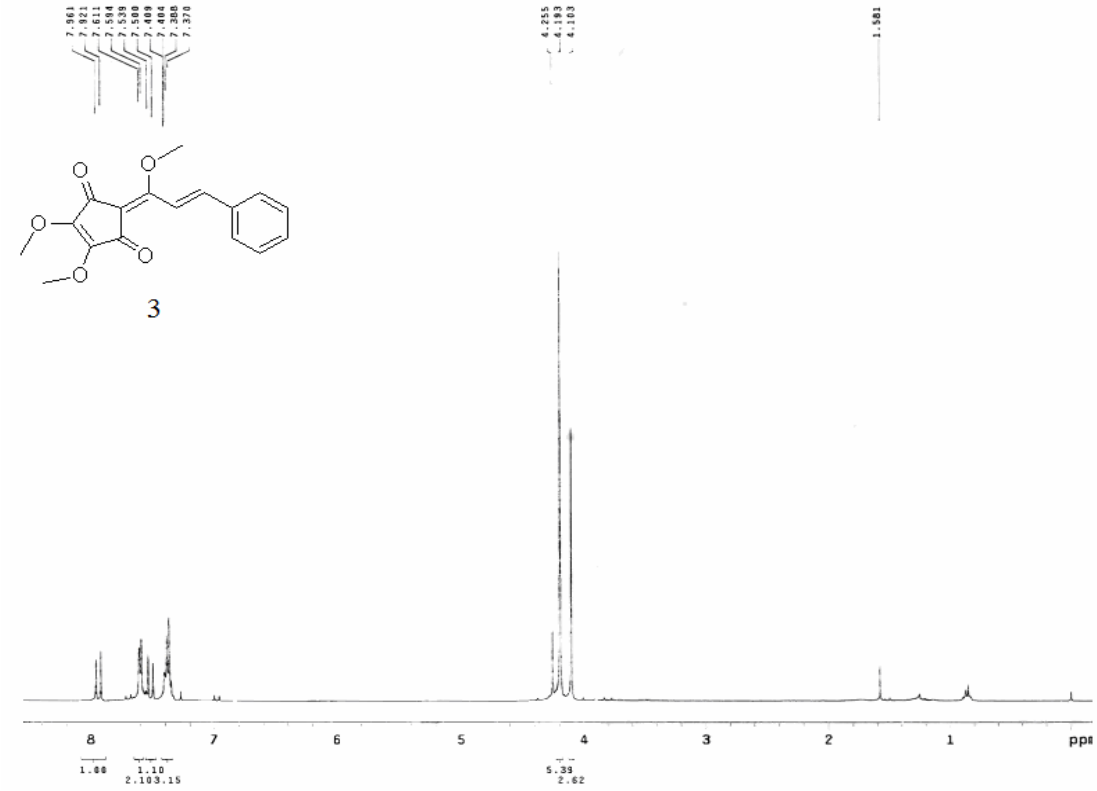
^{1}H NMR spectra of linderone, 4



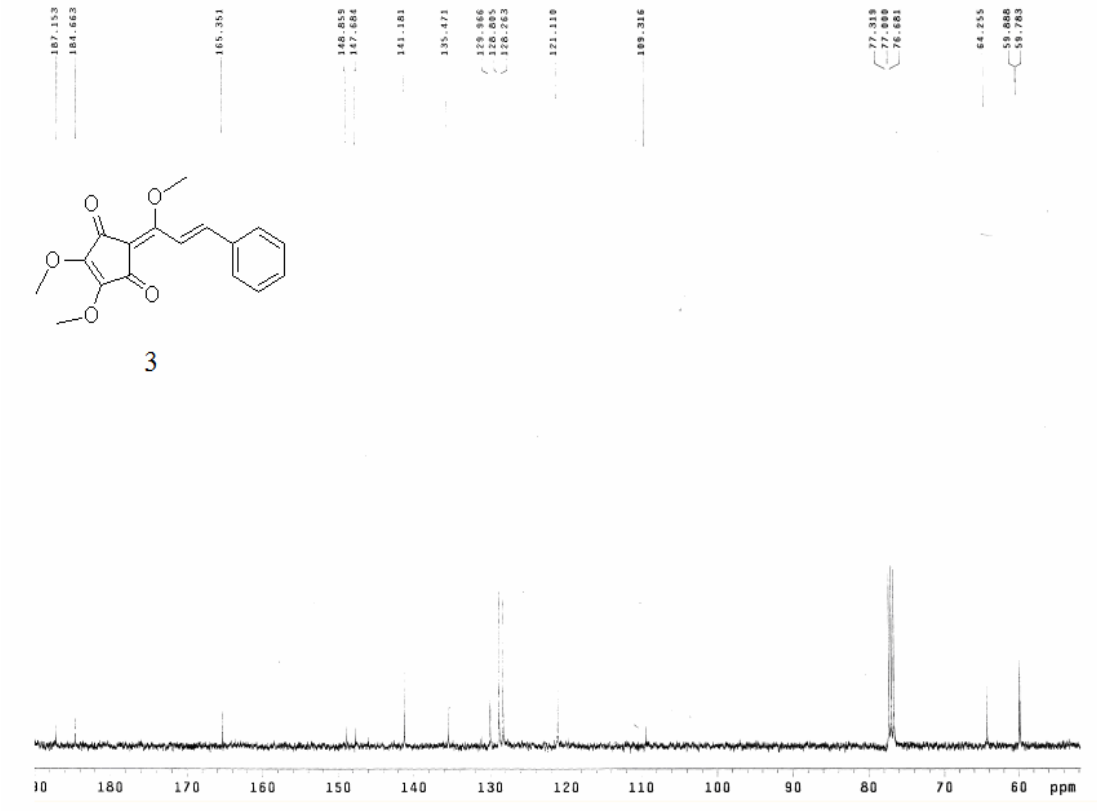
^{13}C NMR spectra of linderone, 4



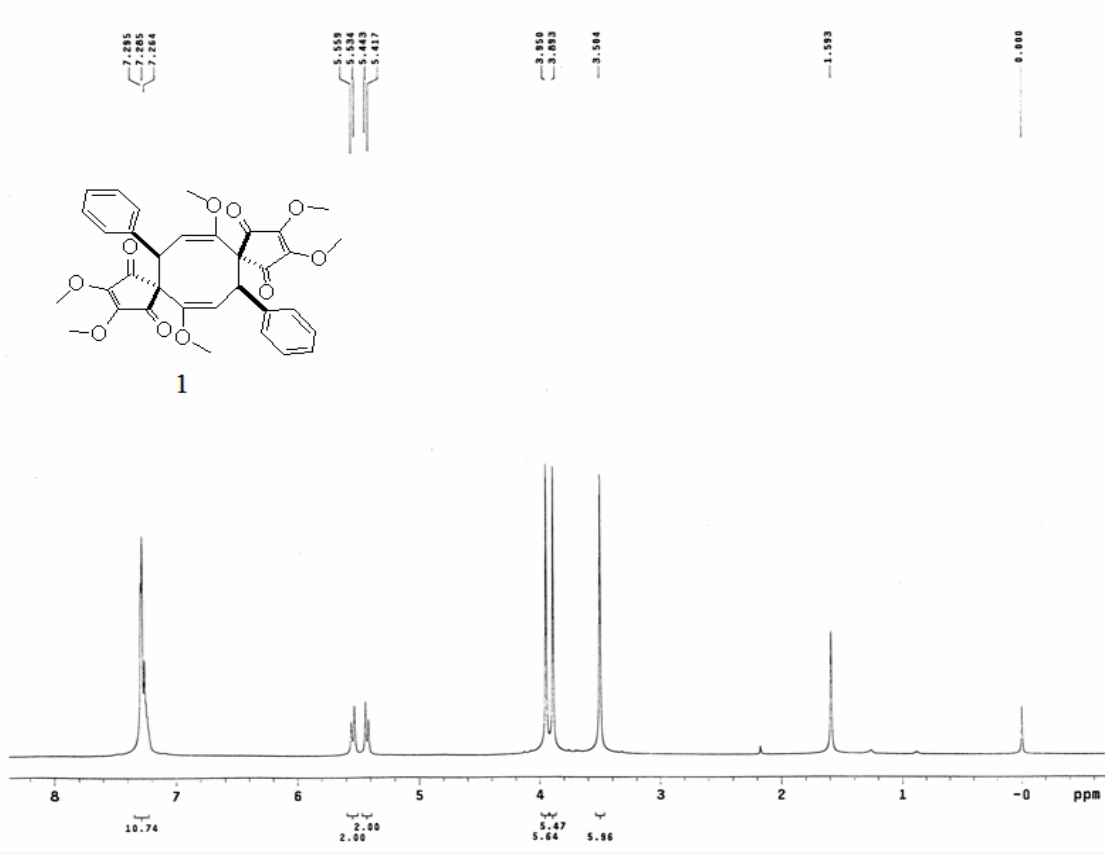
^{1}H NMR spectra of methyl-linderone, 3



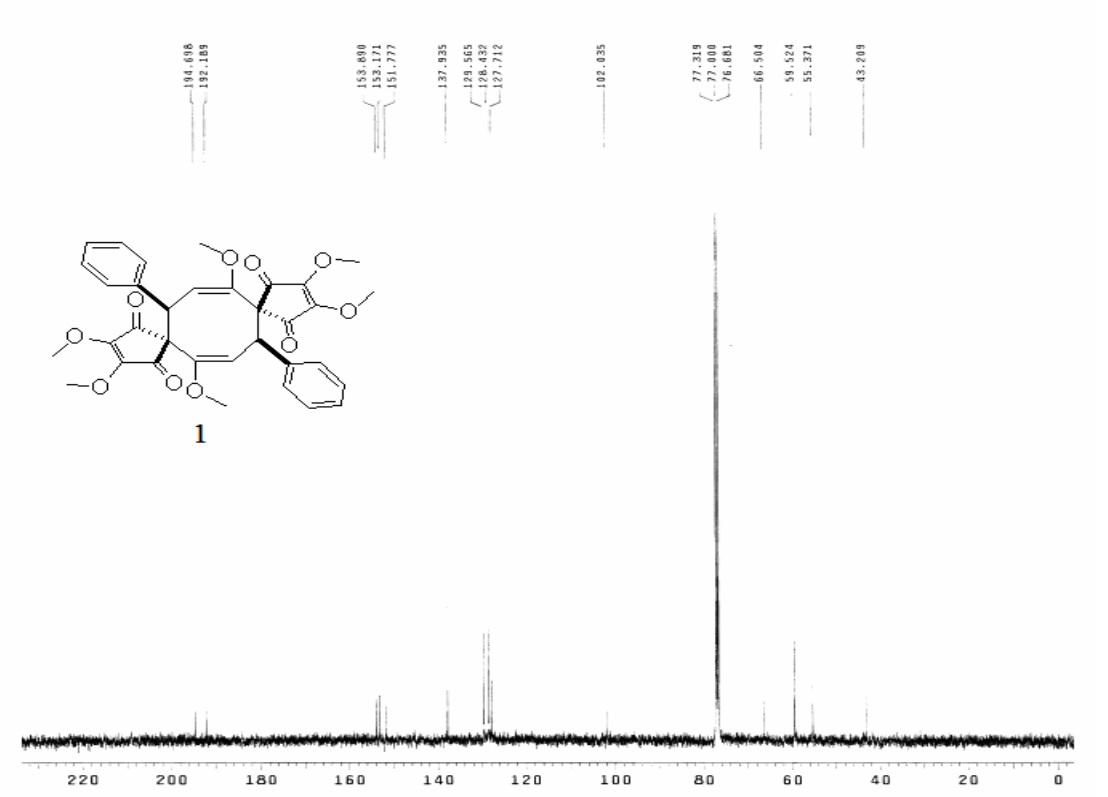
^{13}C NMR spectra of methyl-linderone, 3



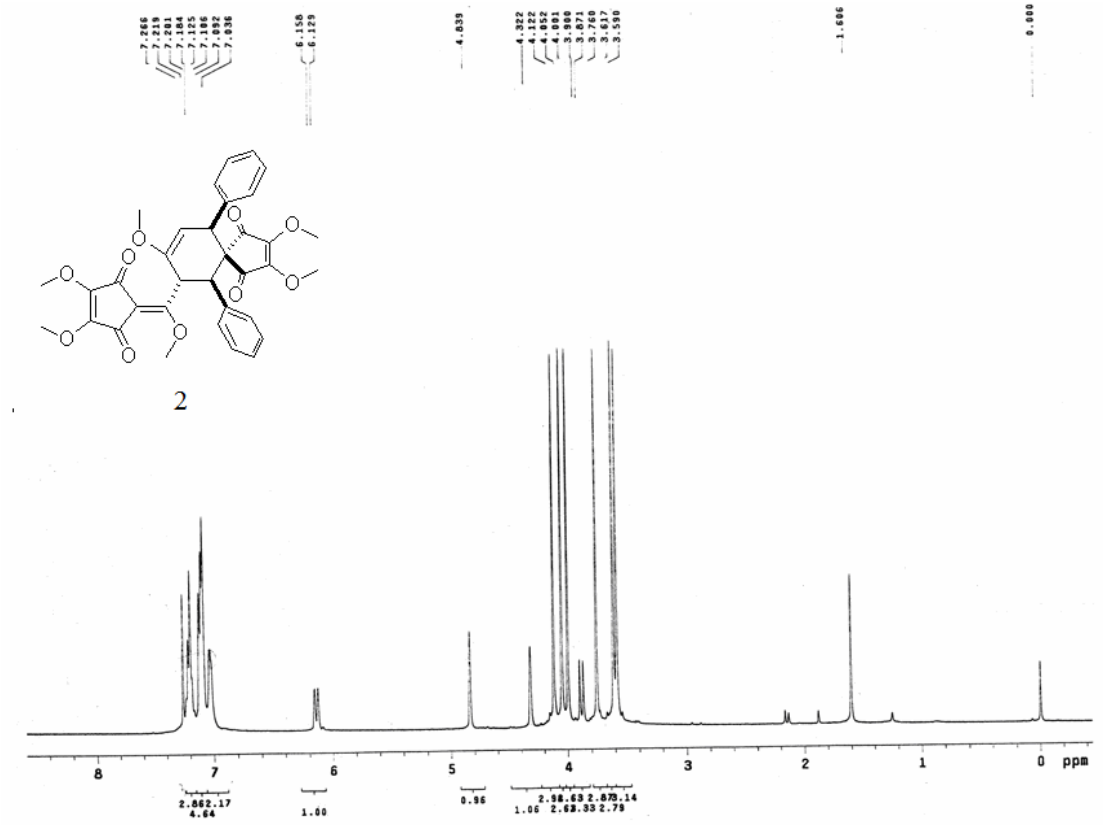
^{1}H NMR spectra of linderaspirone A, **1**



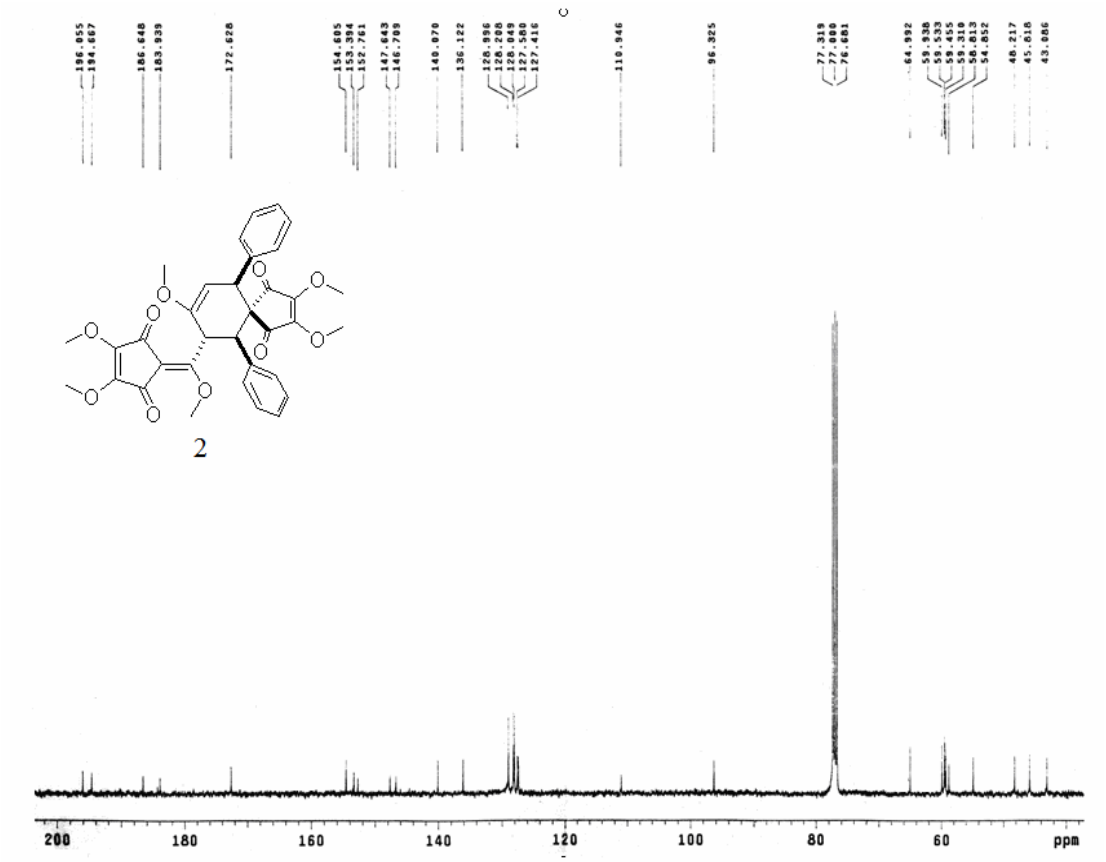
^{13}C NMR spectra of linderaspirone A, **1**



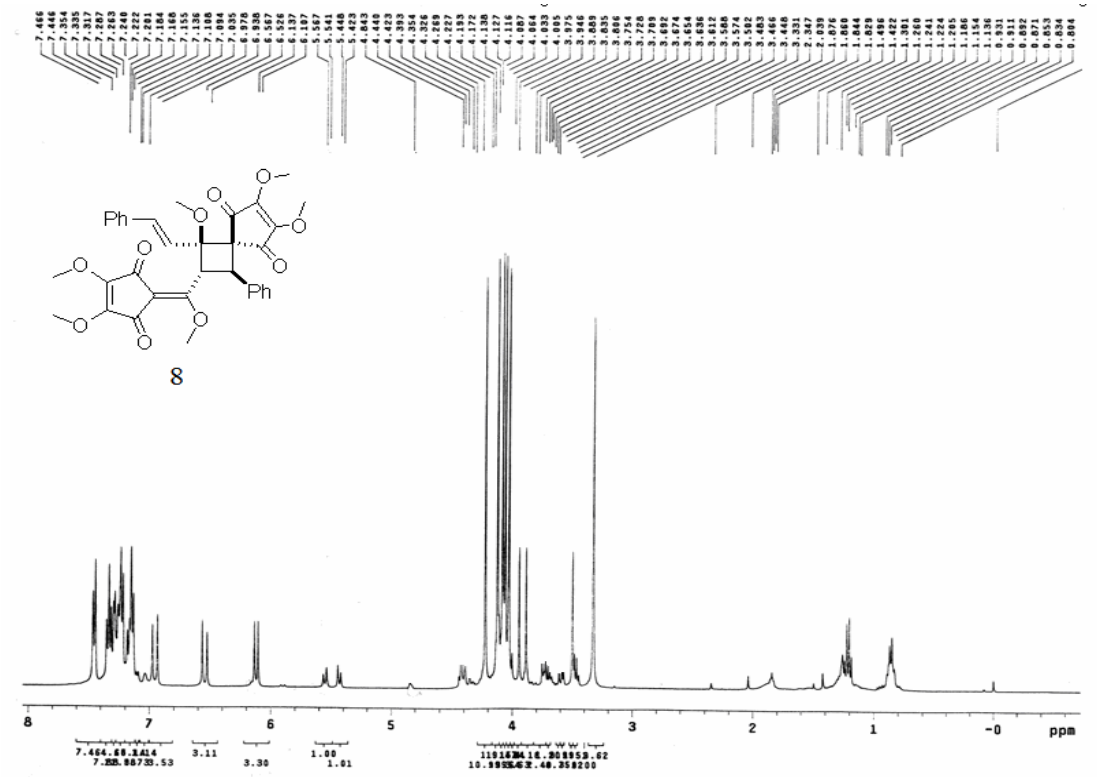
^{1}H NMR spectra of bi-linderone, 2



^{13}C NMR spectra of bi-linderone, 2



^{1}H NMR spectra of compound 8



Containing round 14% of linderaspirone A

III. X-ray Crystal Structure and Data of bi-linderone

X-ray Crystal Structure of bi-linderone

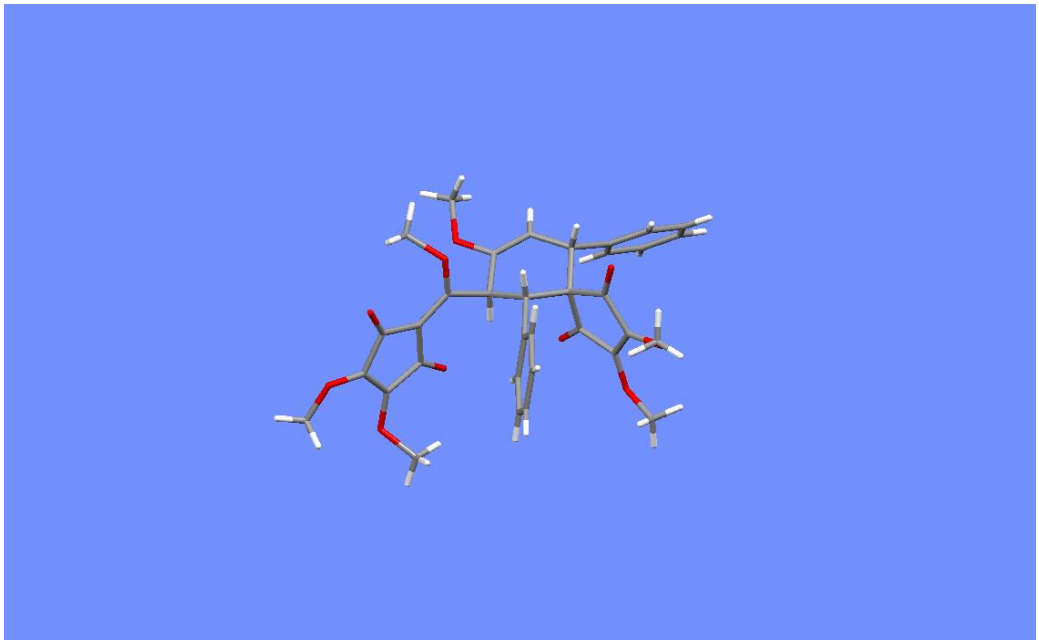


Table 1. Crystal data and structure refinement for bi-linderone.

Empirical formula	$C_{34}\ H_{32}\ O_{10}$
Formula weight	600.60
Temperature	296(2) K
Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group	Pbca
Unit cell dimensions	a = 13.599(5) Å alpha = 90º.
	b = 16.236(6) Å beta = 90º.
	c = 27.279(10) Å gamma = 90º.
Volume	6023(4) $Å^3$
Z	8
Calculated density	1.325 Mg/m^3
Absorption coefficient	0.098 mm^{-1}
F(000)	2528
Crystal size	0.35 x 0.26 x 0.15 mm^3
Theta range for data collection	1.49 to 25.10º
Limiting indices	-16<=h<=16, -9<=k<=19, -30<=l<=32
Reflections collected / unique	28814 / 5342 [R(int) = 0.1514]
Completeness to theta = 25.10º	99.6 %
Absorption correction	None
Max. and min. transmission	0.9851 and 0.9670
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5342 / 0 / 404
Goodness-of-fit on F^2	1.017
Final R indices [I>2sigma(I)]	R1 = 0.0838, wR2 = 0.2003
R indices (all data)	R1 = 0.1787, wR2 = 0.2607
Extinction coefficient	0.0029(7)
Largest diff. peak and hole	0.295 and -0.257 e. $Å^{-3}$

Table 2. Bond lengths [Å] and angles [º] for bi-linderone.

Bond lengths [Å] for bi-linderone

O(1)-C(3)	1.353(6)
O(1)-C(1)	1.434(7)
O(2)-C(4)	1.337(6)
O(2)-C(2)	1.392(8)
O(3)-C(7)	1.216(5)
O(4)-C(5)	1.228(6)
O(5)-C(8)	1.346(5)
O(5)-C(9)	1.445(6)

O(6)-C(11)	1.346(5)
O(6)-C(22)	1.436(6)
O(7)-C(26)	1.206(5)
O(8)-C(23)	1.225(6)
O(9)-C(24)	1.341(6)
O(9)-C(28)	1.419(7)
O(10)-C(25)	1.346(6)
O(10)-C(27)	1.435(7)
C(1)-H(1A)	0.9600
C(1)-H(1B)	0.9600
C(1)-H(1C)	0.9600
C(2)-H(2A)	0.9600
C(2)-H(2B)	0.9600
C(2)-H(2C)	0.9600
C(3)-C(4)	1.342(7)
C(3)-C(7)	1.458(7)
C(4)-C(5)	1.471(8)
C(5)-C(6)	1.465(6)
C(6)-C(8)	1.352(6)
C(6)-C(7)	1.484(7)
C(8)-C(10)	1.496(6)
C(9)-H(9A)	0.9600
C(9)-H(9B)	0.9600
C(9)-H(9C)	0.9600
C(10)-C(11)	1.521(6)
C(10)-C(15)	1.531(7)
C(10)-H(10)	0.9800
C(11)-C(12)	1.313(6)
C(12)-C(13)	1.501(6)
C(12)-H(12)	0.9300
C(13)-C(29)	1.505(6)
C(13)-C(14)	1.559(6)
C(13)-H(13)	0.9800
C(14)-C(23)	1.515(7)
C(14)-C(26)	1.517(7)
C(14)-C(15)	1.548(6)
C(15)-C(16)	1.524(6)
C(15)-H(15)	0.9800
C(16)-C(21)	1.375(7)
C(16)-C(17)	1.397(7)
C(17)-C(18)	1.366(7)
C(17)-H(17)	0.9300
C(18)-C(19)	1.361(9)
C(18)-H(18)	0.9300

C(19)-C(20)	1.354(9)
C(19)-H(19)	0.9300
C(20)-C(21)	1.387(7)
C(20)-H(20)	0.9300
C(21)-H(21)	0.9300
C(22)-H(22A)	0.9600
C(22)-H(22B)	0.9600
C(22)-H(22C)	0.9600
C(23)-C(24)	1.473(7)
C(24)-C(25)	1.348(7)
C(25)-C(26)	1.473(7)
C(27)-H(27A)	0.9600
C(27)-H(27B)	0.9600
C(27)-H(27C)	0.9600
C(28)-H(28A)	0.9600
C(28)-H(28B)	0.9600
C(28)-H(28C)	0.9600
C(29)-C(30)	1.369(7)
C(29)-C(34)	1.398(7)
C(30)-C(31)	1.378(7)
C(30)-H(30)	0.9300
C(31)-C(32)	1.386(8)
C(31)-H(31)	0.9300
C(32)-C(33)	1.343(9)
C(32)-H(32)	0.9300
C(33)-C(34)	1.369(7)
C(33)-H(33)	0.9300
C(34)-H(34)	0.9300

Bond angles [º] for bi-linderone

C(3)-O(1)-C(1)	116.6(4)
C(4)-O(2)-C(2)	118.5(5)
C(8)-O(5)-C(9)	120.5(4)
C(11)-O(6)-C(22)	118.9(4)
C(24)-O(9)-C(28)	118.0(4)
C(25)-O(10)-C(27)	118.7(4)
O(1)-C(1)-H(1A)	109.5
O(1)-C(1)-H(1B)	109.5
H(1A)-C(1)-H(1B)	109.5
O(1)-C(1)-H(1C)	109.5
H(1A)-C(1)-H(1C)	109.5
H(1B)-C(1)-H(1C)	109.5
O(2)-C(2)-H(2A)	109.5

O(2)-C(2)-H(2B)	109.5
H(2A)-C(2)-H(2B)	109.5
O(2)-C(2)-H(2C)	109.5
H(2A)-C(2)-H(2C)	109.5
H(2B)-C(2)-H(2C)	109.5
C(4)-C(3)-O(1)	127.0(5)
C(4)-C(3)-C(7)	110.2(5)
O(1)-C(3)-C(7)	122.7(5)
O(2)-C(4)-C(3)	134.4(5)
O(2)-C(4)-C(5)	115.9(5)
C(3)-C(4)-C(5)	109.7(5)
O(4)-C(5)-C(6)	129.2(5)
O(4)-C(5)-C(4)	123.2(5)
C(6)-C(5)-C(4)	107.4(5)
C(8)-C(6)-C(5)	129.1(5)
C(8)-C(6)-C(7)	125.2(4)
C(5)-C(6)-C(7)	105.3(4)
O(3)-C(7)-C(3)	124.2(5)
O(3)-C(7)-C(6)	128.5(4)
C(3)-C(7)-C(6)	107.1(4)
O(5)-C(8)-C(6)	124.6(4)
O(5)-C(8)-C(10)	110.6(4)
C(6)-C(8)-C(10)	124.7(4)
O(5)-C(9)-H(9A)	109.5
O(5)-C(9)-H(9B)	109.5
H(9A)-C(9)-H(9B)	109.5
O(5)-C(9)-H(9C)	109.5
H(9A)-C(9)-H(9C)	109.5
H(9B)-C(9)-H(9C)	109.5
C(8)-C(10)-C(11)	110.0(4)
C(8)-C(10)-C(15)	109.8(4)
C(11)-C(10)-C(15)	109.6(4)
C(8)-C(10)-H(10)	109.2
C(11)-C(10)-H(10)	109.2
C(15)-C(10)-H(10)	109.2
C(12)-C(11)-O(6)	125.9(4)
C(12)-C(11)-C(10)	123.5(4)
O(6)-C(11)-C(10)	110.6(4)
C(11)-C(12)-C(13)	124.5(4)
C(11)-C(12)-H(12)	117.8
C(13)-C(12)-H(12)	117.8
C(12)-C(13)-C(29)	114.7(4)
C(12)-C(13)-C(14)	113.0(4)
C(29)-C(13)-C(14)	111.3(4)

C(12)-C(13)-H(13)	105.7
C(29)-C(13)-H(13)	105.7
C(14)-C(13)-H(13)	105.7
C(23)-C(14)-C(26)	101.9(4)
C(23)-C(14)-C(15)	108.8(4)
C(26)-C(14)-C(15)	112.1(4)
C(23)-C(14)-C(13)	108.8(4)
C(26)-C(14)-C(13)	114.7(4)
C(15)-C(14)-C(13)	110.0(3)
C(16)-C(15)-C(10)	113.3(4)
C(16)-C(15)-C(14)	112.2(3)
C(10)-C(15)-C(14)	111.2(4)
C(16)-C(15)-H(15)	106.5
C(10)-C(15)-H(15)	106.5
C(14)-C(15)-H(15)	106.5
C(21)-C(16)-C(17)	117.4(5)
C(21)-C(16)-C(15)	120.0(5)
C(17)-C(16)-C(15)	122.5(5)
C(18)-C(17)-C(16)	120.1(6)
C(18)-C(17)-H(17)	120.0
C(16)-C(17)-H(17)	120.0
C(19)-C(18)-C(17)	122.0(6)
C(19)-C(18)-H(18)	119.0
C(17)-C(18)-H(18)	119.0
C(20)-C(19)-C(18)	118.8(6)
C(20)-C(19)-H(19)	120.6
C(18)-C(19)-H(19)	120.6
C(19)-C(20)-C(21)	120.6(6)
C(19)-C(20)-H(20)	119.7
C(21)-C(20)-H(20)	119.7
C(16)-C(21)-C(20)	121.1(6)
C(16)-C(21)-H(21)	119.4
C(20)-C(21)-H(21)	119.4
O(6)-C(22)-H(22A)	109.5
O(6)-C(22)-H(22B)	109.5
H(22A)-C(22)-H(22B)	109.5
O(6)-C(22)-H(22C)	109.5
H(22A)-C(22)-H(22C)	109.5
H(22B)-C(22)-H(22C)	109.5
O(8)-C(23)-C(24)	125.2(5)
O(8)-C(23)-C(14)	125.1(4)
C(24)-C(23)-C(14)	109.7(5)
O(9)-C(24)-C(25)	127.0(5)
O(9)-C(24)-C(23)	124.4(5)

C(25)-C(24)-C(23)	108.2(4)
O(10)-C(25)-C(24)	131.9(5)
O(10)-C(25)-C(26)	116.3(5)
C(24)-C(25)-C(26)	111.8(4)
O(7)-C(26)-C(25)	125.4(5)
O(7)-C(26)-C(14)	126.8(4)
C(25)-C(26)-C(14)	107.7(5)
O(10)-C(27)-H(27A)	109.5
O(10)-C(27)-H(27B)	109.5
H(27A)-C(27)-H(27B)	109.5
O(10)-C(27)-H(27C)	109.5
H(27A)-C(27)-H(27C)	109.5
H(27B)-C(27)-H(27C)	109.5
O(9)-C(28)-H(28A)	109.5
O(9)-C(28)-H(28B)	109.5
H(28A)-C(28)-H(28B)	109.5
O(9)-C(28)-H(28C)	109.5
H(28A)-C(28)-H(28C)	109.5
H(28B)-C(28)-H(28C)	109.5
C(30)-C(29)-C(34)	116.5(5)
C(30)-C(29)-C(13)	122.6(5)
C(34)-C(29)-C(13)	120.9(5)
C(29)-C(30)-C(31)	122.1(6)
C(29)-C(30)-H(30)	119.0
C(31)-C(30)-H(30)	119.0
C(30)-C(31)-C(32)	119.4(6)
C(30)-C(31)-H(31)	120.3
C(32)-C(31)-H(31)	120.3
C(33)-C(32)-C(31)	119.7(6)
C(33)-C(32)-H(32)	120.1
C(31)-C(32)-H(32)	120.1
C(32)-C(33)-C(34)	120.5(6)
C(32)-C(33)-H(33)	119.8
C(34)-C(33)-H(33)	119.8
C(33)-C(34)-C(29)	121.8(6)
C(33)-C(34)-H(34)	119.1
C(29)-C(34)-H(34)	119.1

V. Reference:

1. Ram, R.N., and Manoj, T. P. *J. Org. Chem*. **2008**, *73,* 5633 - 5635