

Supporting Information

FeCl₃-Catalyzed Oxidative Decarboxylation of Aryl/Heteroaryl Acetic Acids: Preparation of Selected API Impurities

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1. Crystal data information of compound 2

Bond precision	C-C = 0.0017 Å	Wavelength=0.71073
Cell	a=10.1140(5)	b=10.3178(5)
		c=10.5034(5)
Temperature:	105 K	

	Calculated	Reported
Volume	1071.76(9)	071.76(9)
Space group	P 21/c	P 21/c
Hall group	-P 2ybc	-P 2ybc
Moiety formula	C ₁₄ H ₁₁ NO ₂	C ₁₄ H ₁₁ NO ₂
Sum formula	C ₁₄ H ₁₁ NO ₂	C ₁₄ H ₁₁ NO ₂
Mr	225.24	225.24
Dx,g cm ⁻³	1.396	1.396
Z	4	4
Mu (mm ⁻¹)	0.094	0.094
F000	472.0	472.0
F000'	472.22	
h,k,lmax	12,12,12	12,12,12
Nref	1891	1891
Tmin,Tmax	0.962,0.972	0.962,0.972
Tmin'	0.960	

Correction method = # Reported T Limits: T_{min} = 0.962 T_{max} = 0.972

AbsCorr = MULTI-SCAN

Data completeness = 1.000 Theta(max) = 24.990

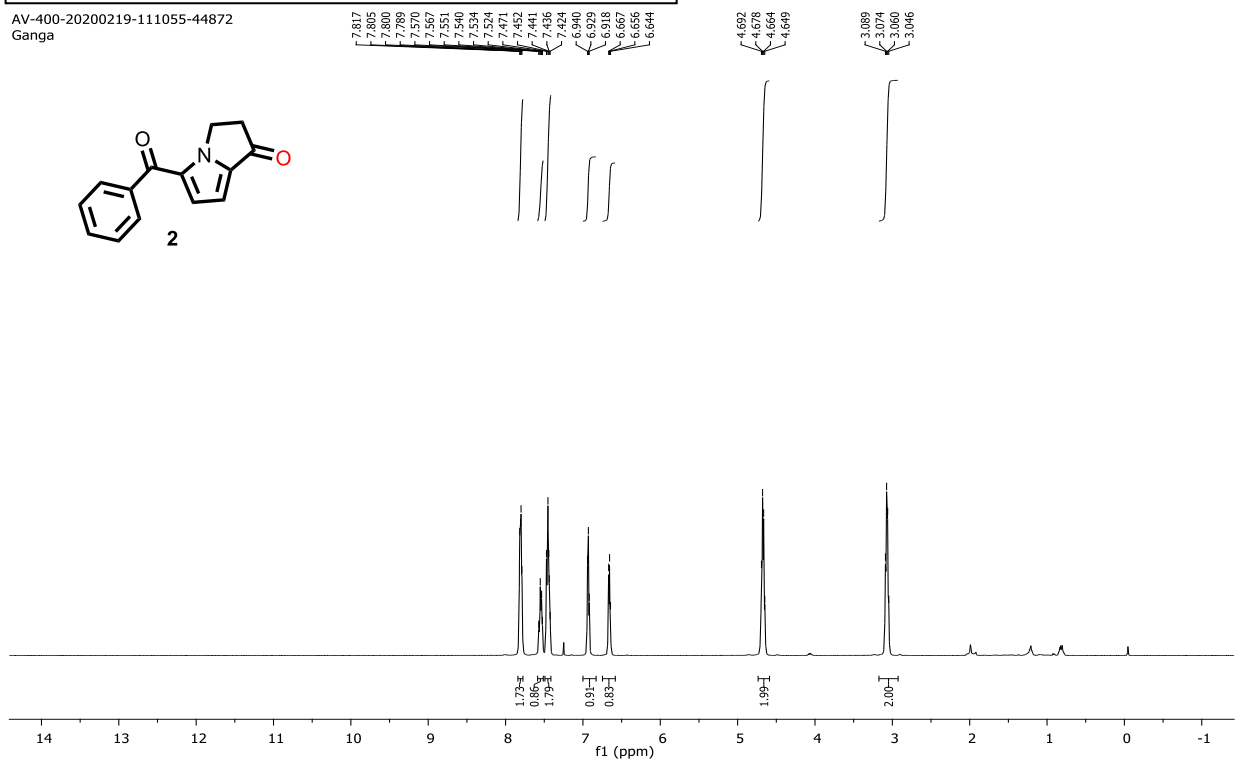
R(reflections) = 0.0309(1781) wR₂ (reflections) = 0.0765(1891)

S = 1.013 Npar = 155

2. Copies of ^1H and ^{13}C spectrum of compounds 2-27

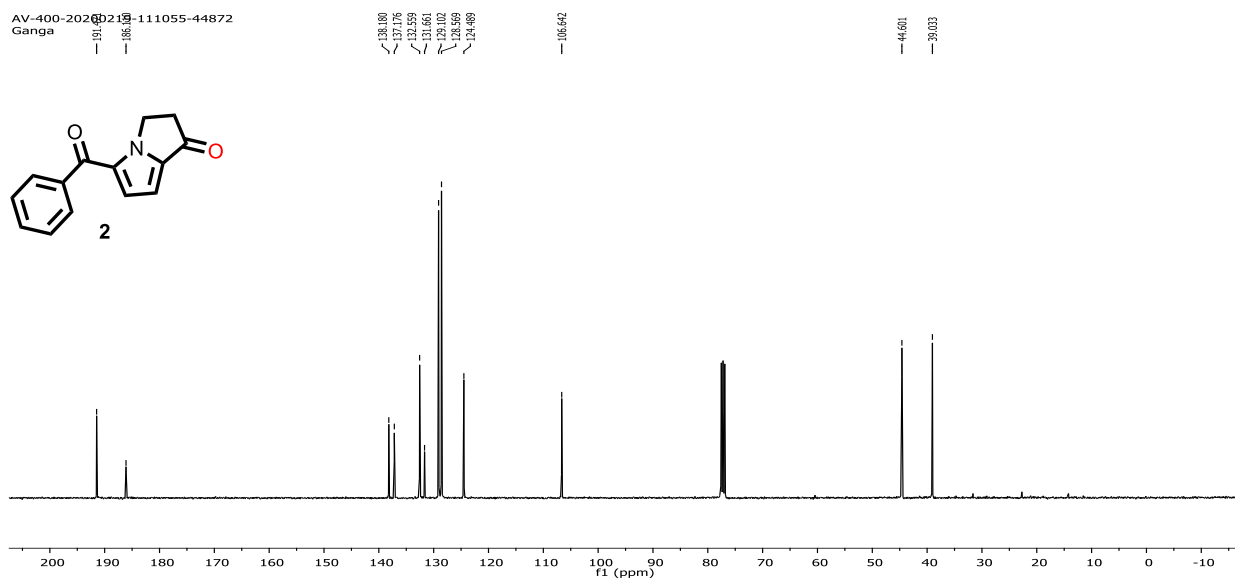
^1H NMR spectrum of compound **2** (CDCl_3 , 400 MHz)

AV-400-20200219-111055-44872
Ganga

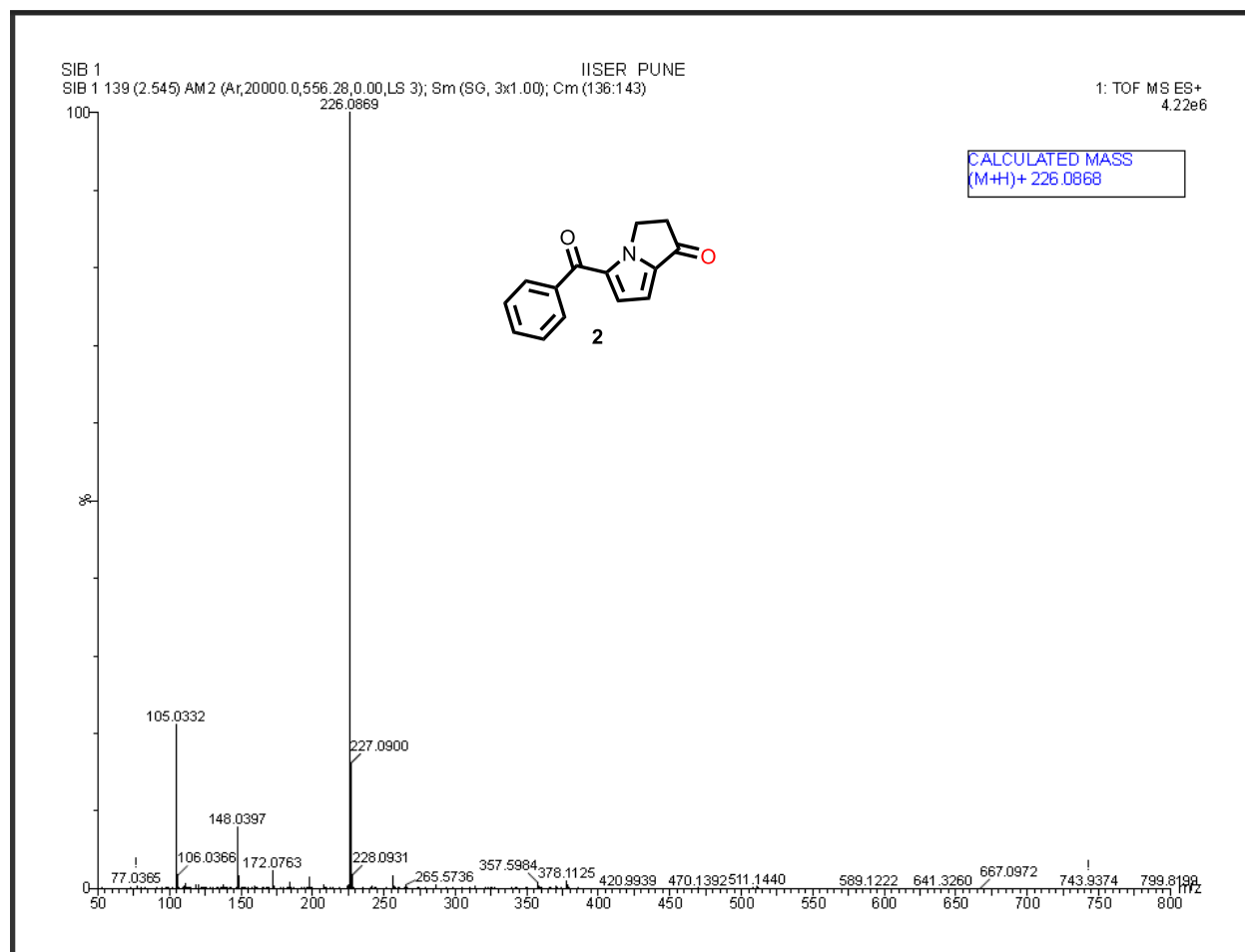


^{13}C NMR spectrum of compound **2** (CDCl_3 , 100 MHz)

AV-400-20200219-111055-44872
Ganga



HRMS spectrum of compound 2



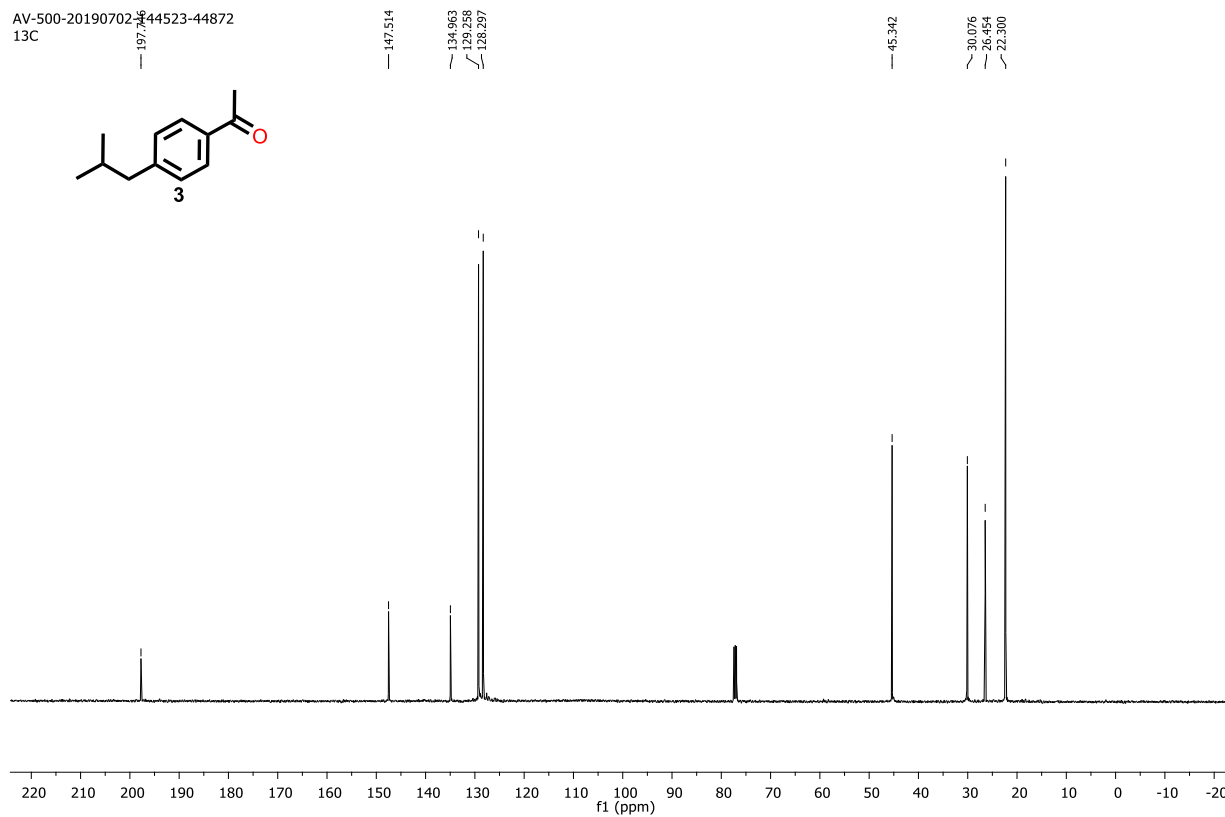
¹H NMR spectrum of compound **3 (CDCl₃, 500 MHz)**

AV-500-20190702-144523-44872
Gangadurai
1H



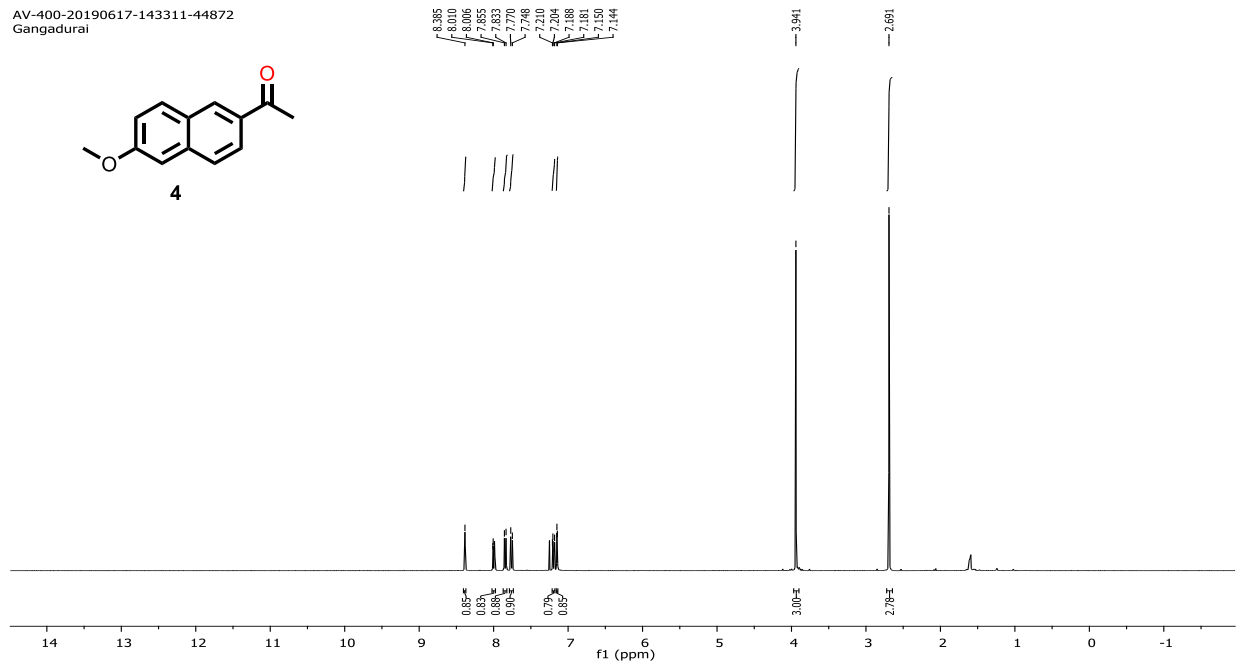
¹³C NMR spectrum of compound **3 (CDCl₃, 125 MHz)**

AV-500-20190702-144523-44872
13C



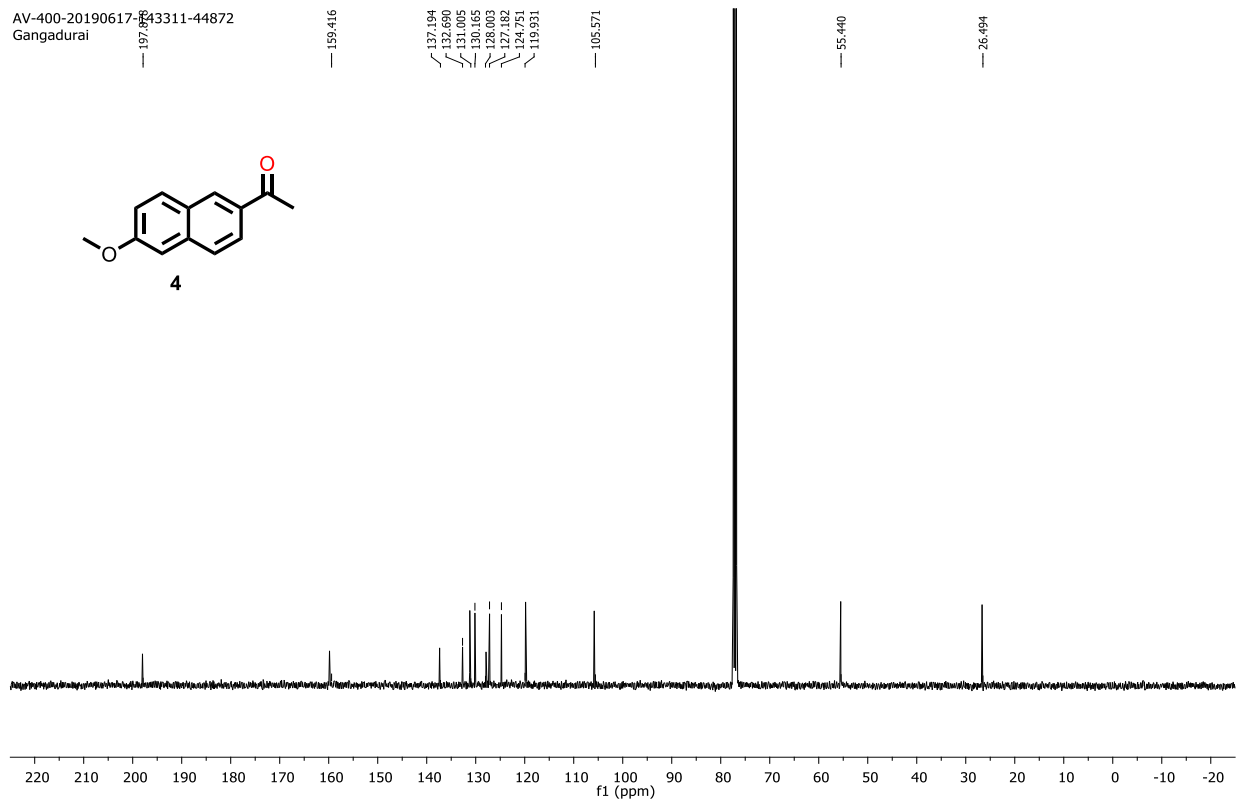
¹H NMR spectrum of compound **4 (CDCl₃, 400 MHz)**

AV-400-20190617-143311-44872
Gangadurai



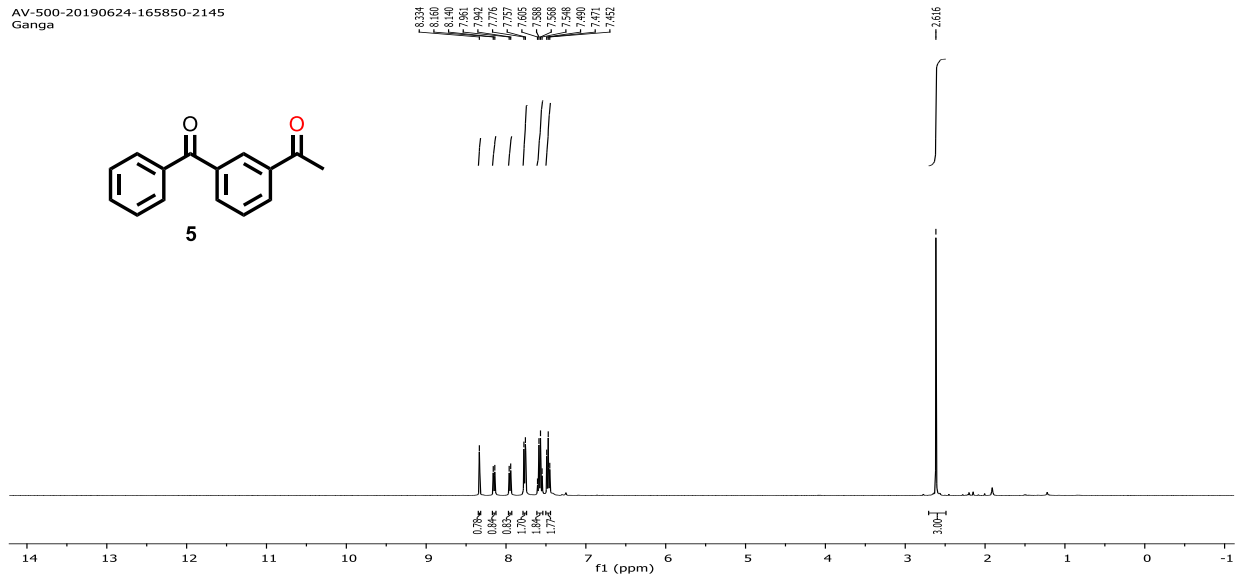
¹³C NMR spectrum of compound **4 (CDCl₃, 100 MHz)**

AV-400-20190617-143311-44872
Gangadurai



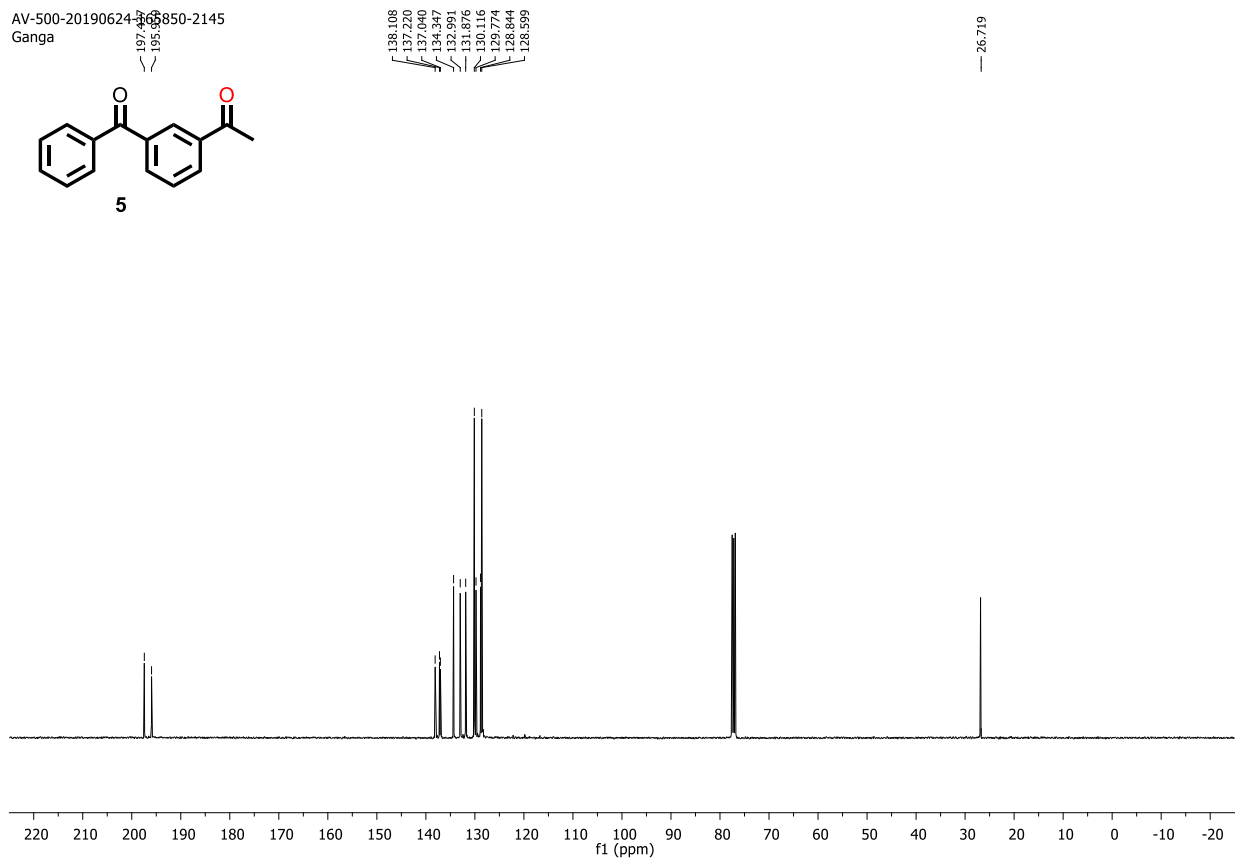
¹H NMR spectrum of compound 5 (CDCl₃, 400 MHz)

AV-500-20190624-165850-2145
Ganga



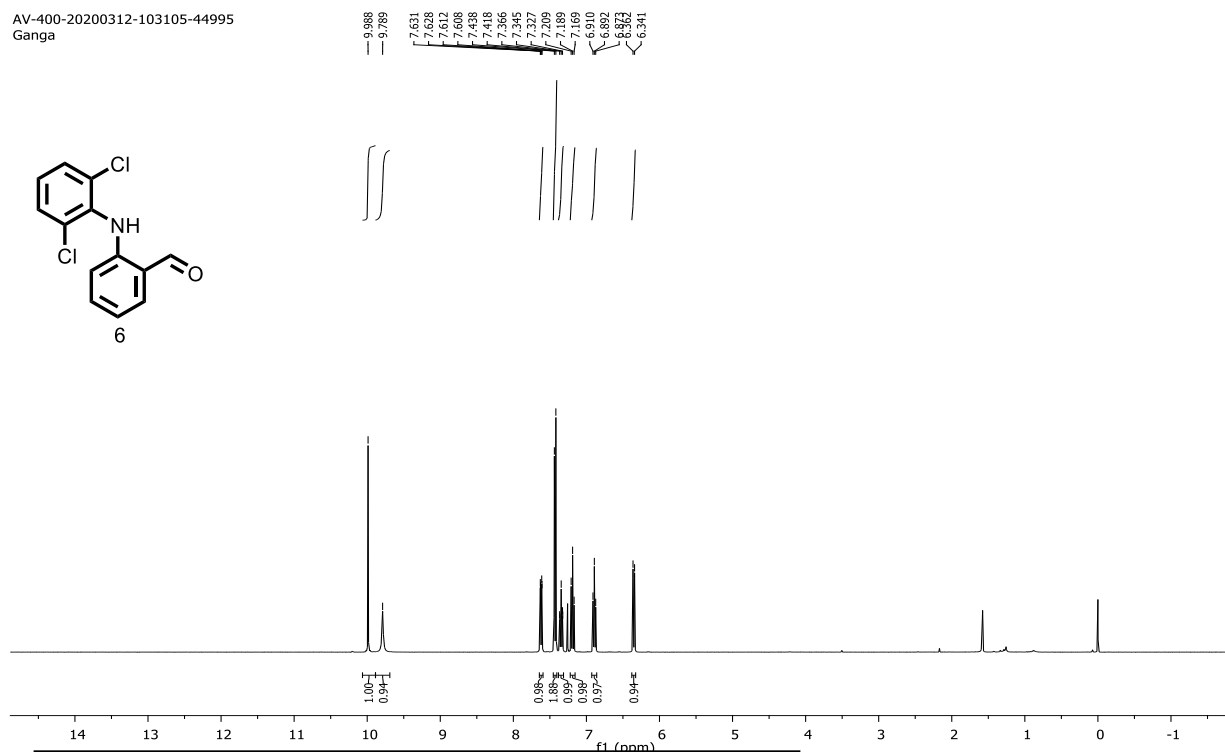
¹³C NMR spectrum of compound 5 (CDCl₃, 100 MHz)

AV-500-20190624-165850-2145
Ganga



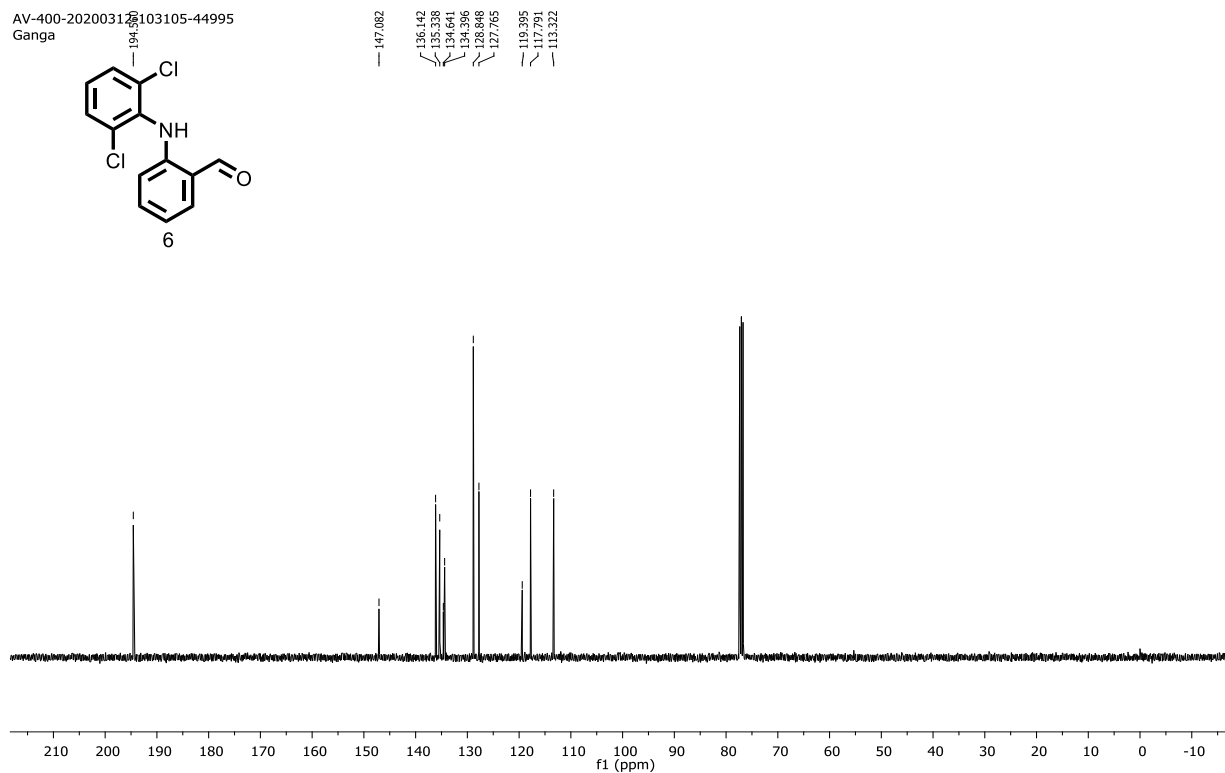
¹H NMR spectrum of compound **6 (CDCl₃, 400 MHz)**

AV-400-20200312-103105-44995
Ganga



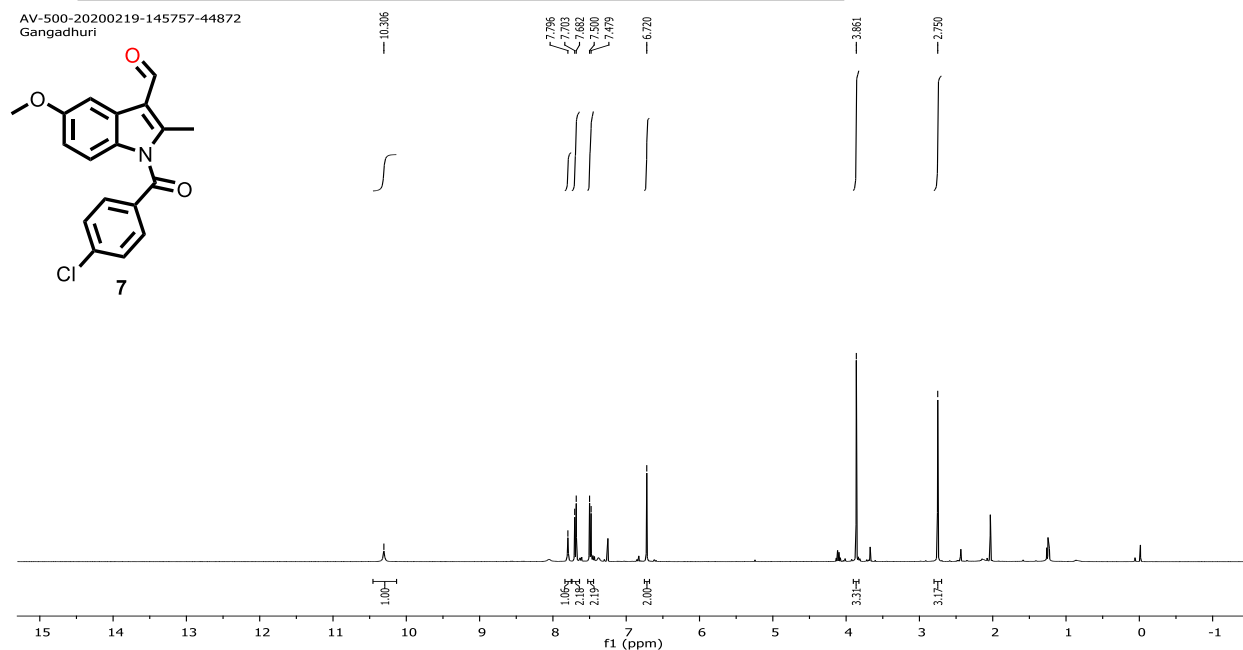
¹³C NMR spectrum of compound **6 (CDCl₃, 100 MHz)**

AV-400-20200312-103105-44995
Ganga



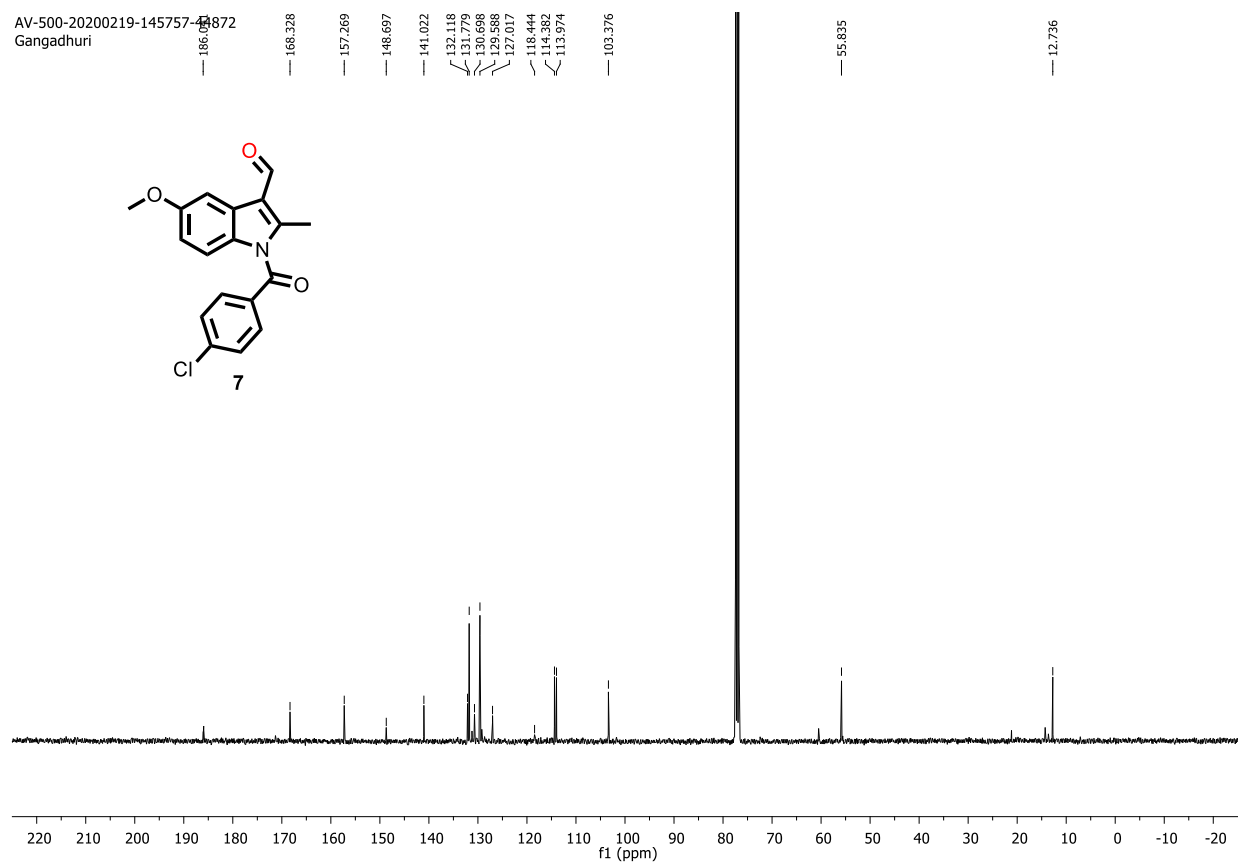
¹H NMR spectrum of compound 7 (CDCl₃, 400 MHz)

AV-500-20200219-145757-44872
Gangadhuri



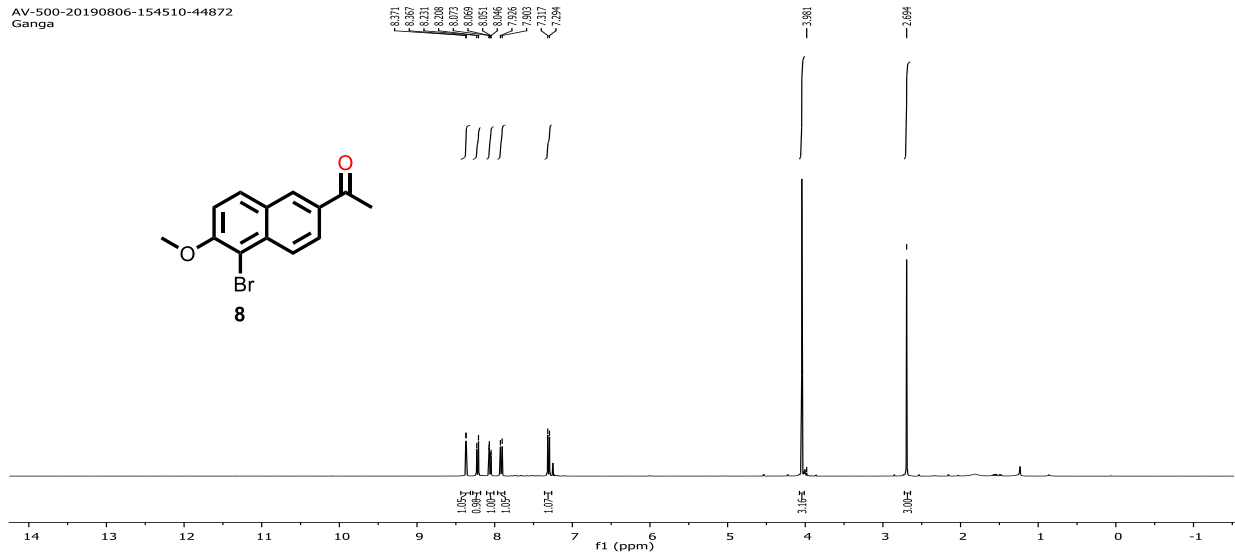
¹³C NMR spectrum of compound 7 (CDCl₃, 100 MHz)

AV-500-20200219-145757-44872
Gangadhuri



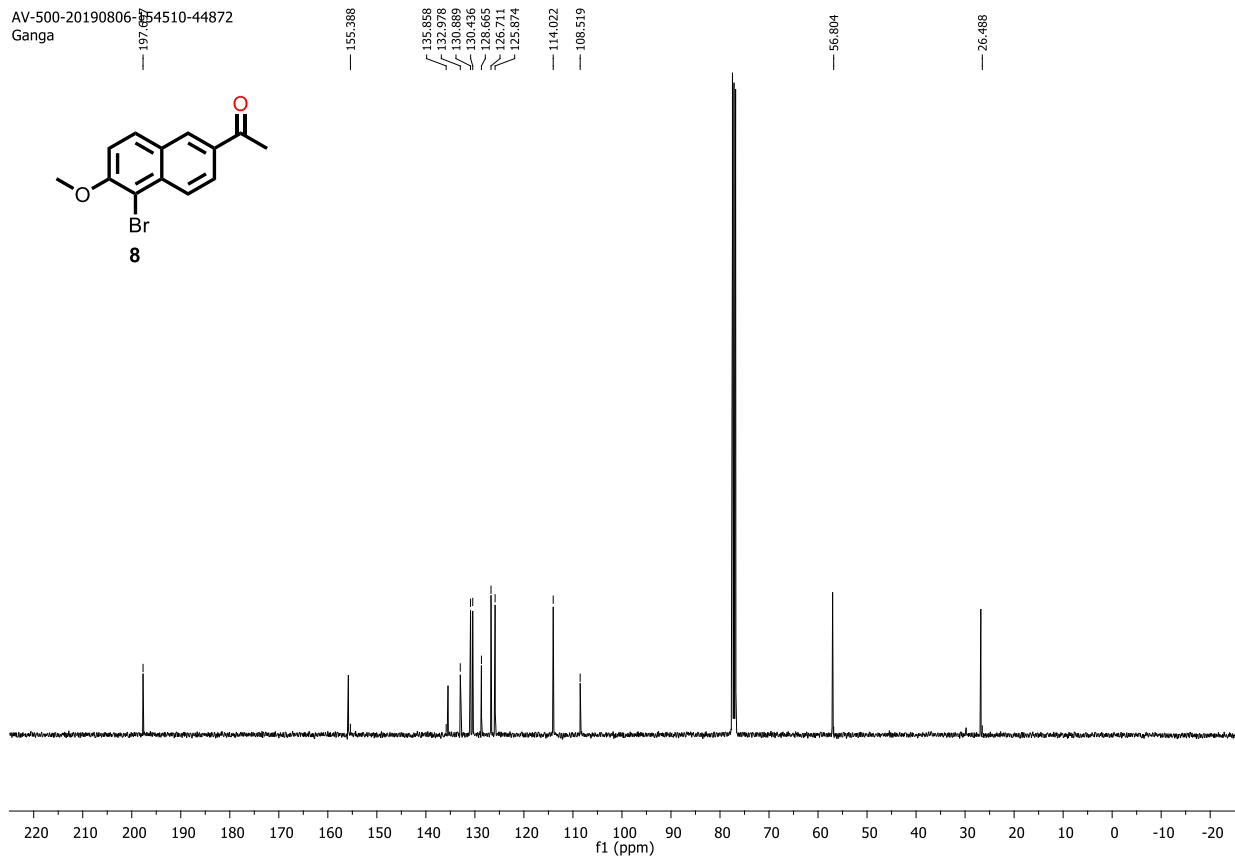
^1H NMR spectrum of compound **8 (CDCl_3 , 500 MHz)**

AV-500-20190806-154510-44872
Ganga



^{13}C NMR spectrum of compound **8 (CDCl_3 , 125 MHz)**

AV-500-20190806-154510-44872
Ganga



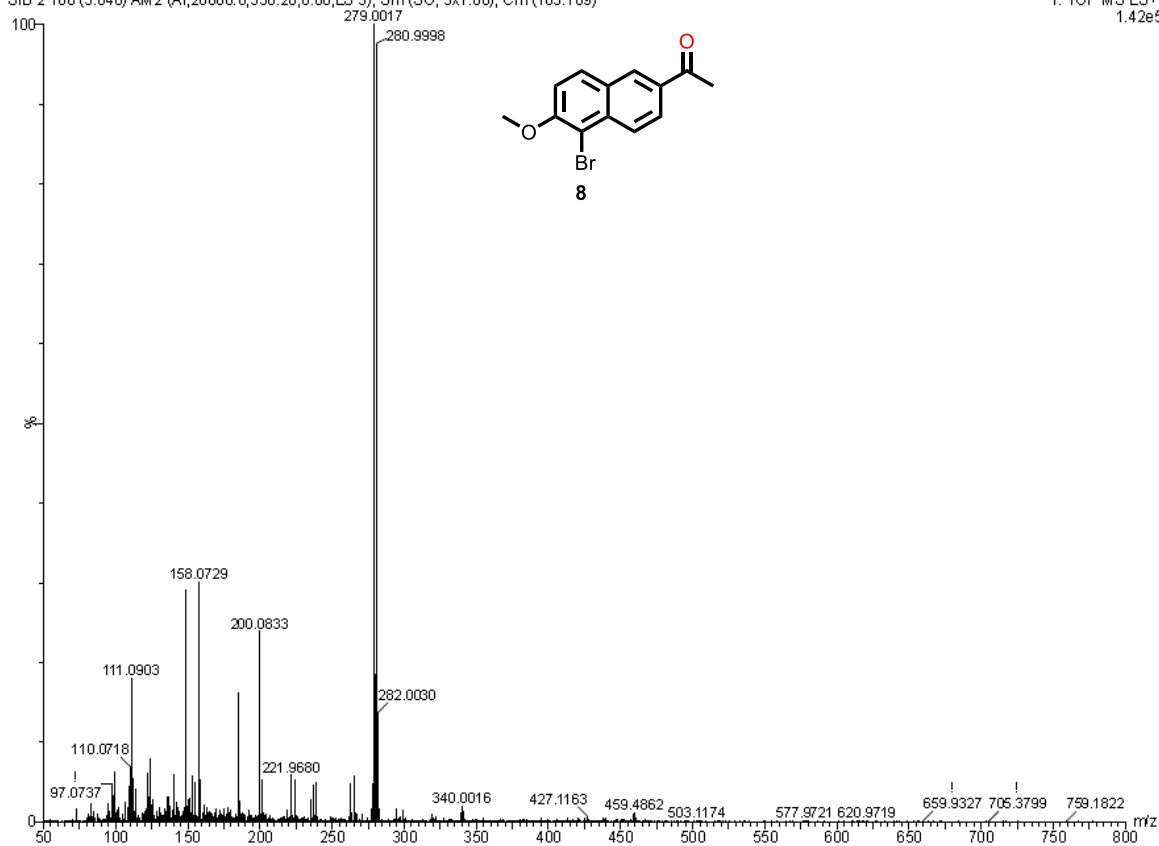
HRMS spectrum of compound 8

SIB 2

SIB 2 166 (3.046) AM 2 (Ar,20000.0,556.28,0.00,LS 3); Sm (SG, 3x1.00); Cm (163:169)

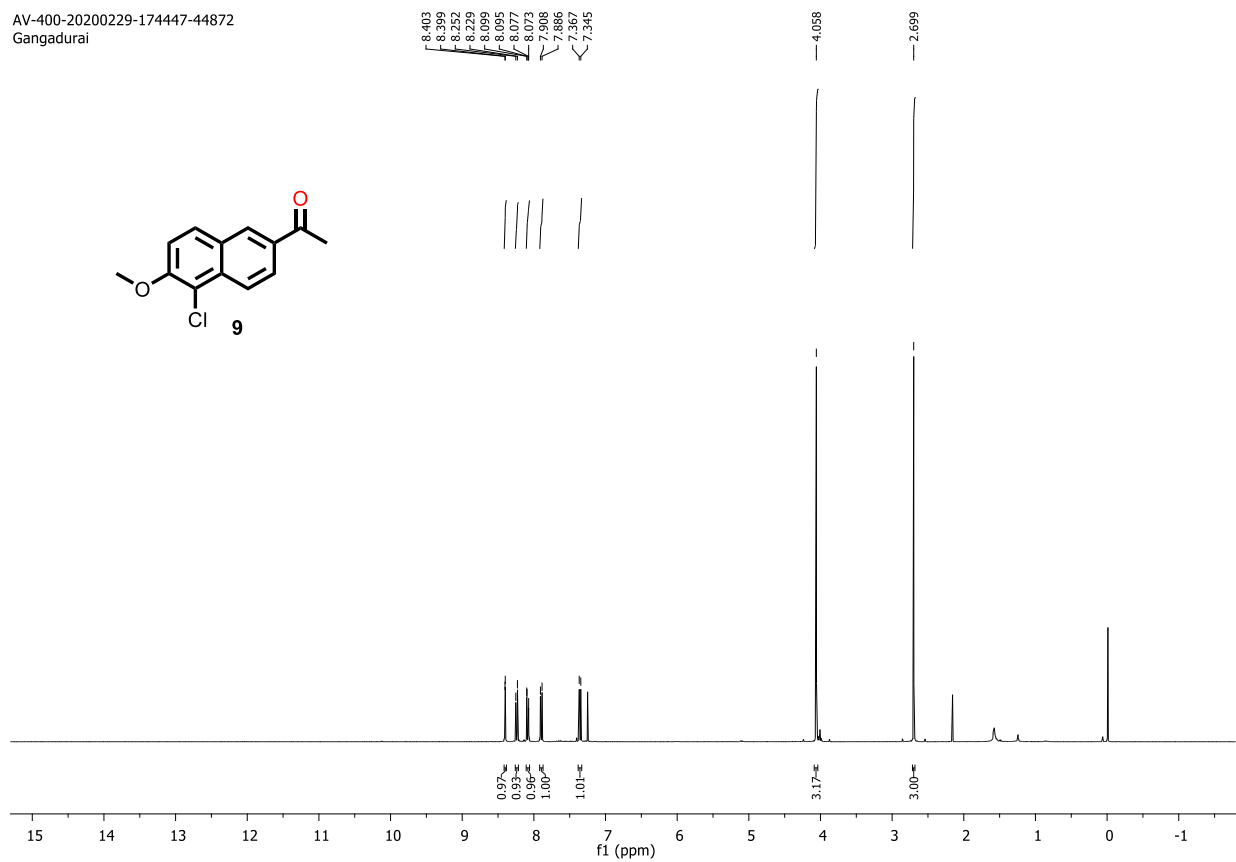
IISER PUNE

1: TOF MS ES+
1.42e5



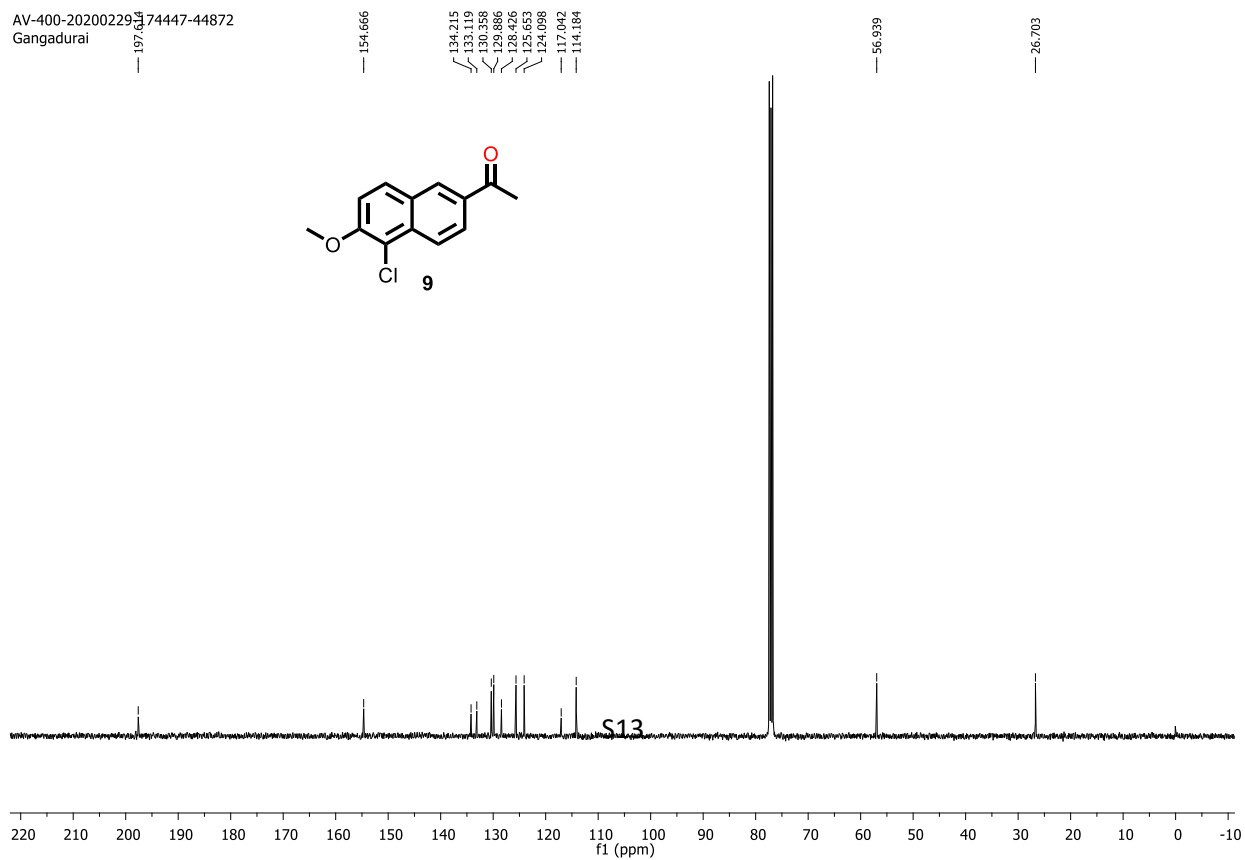
¹H NMR spectrum of compound 9 (CDCl₃, 400 MHz)

AV-400-20200229-174447-44872
Gangadurai



¹³C NMR spectrum of compound 9 (CDCl₃, 100 MHz)

AV-400-20200229-174447-44872
Gangadurai



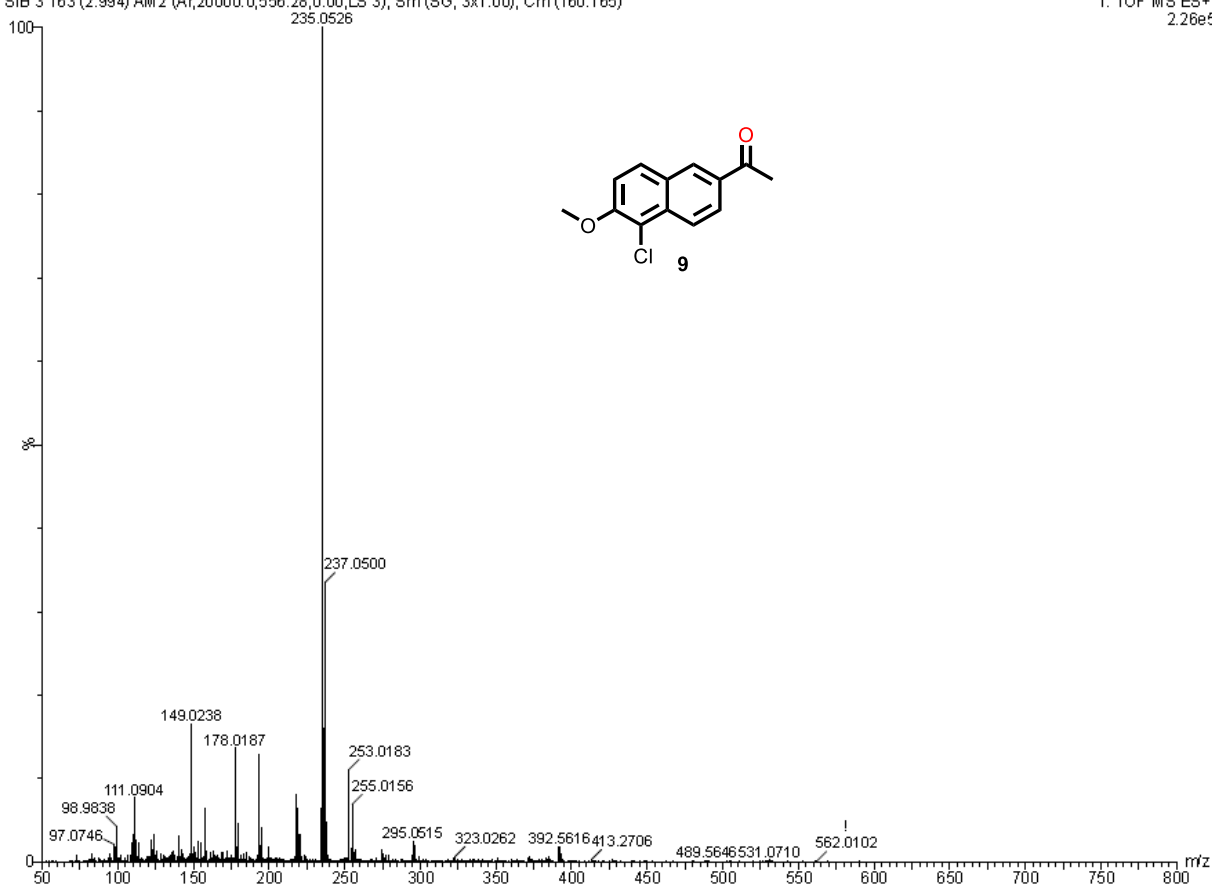
HRMS spectrum of compound 9

SIB 3

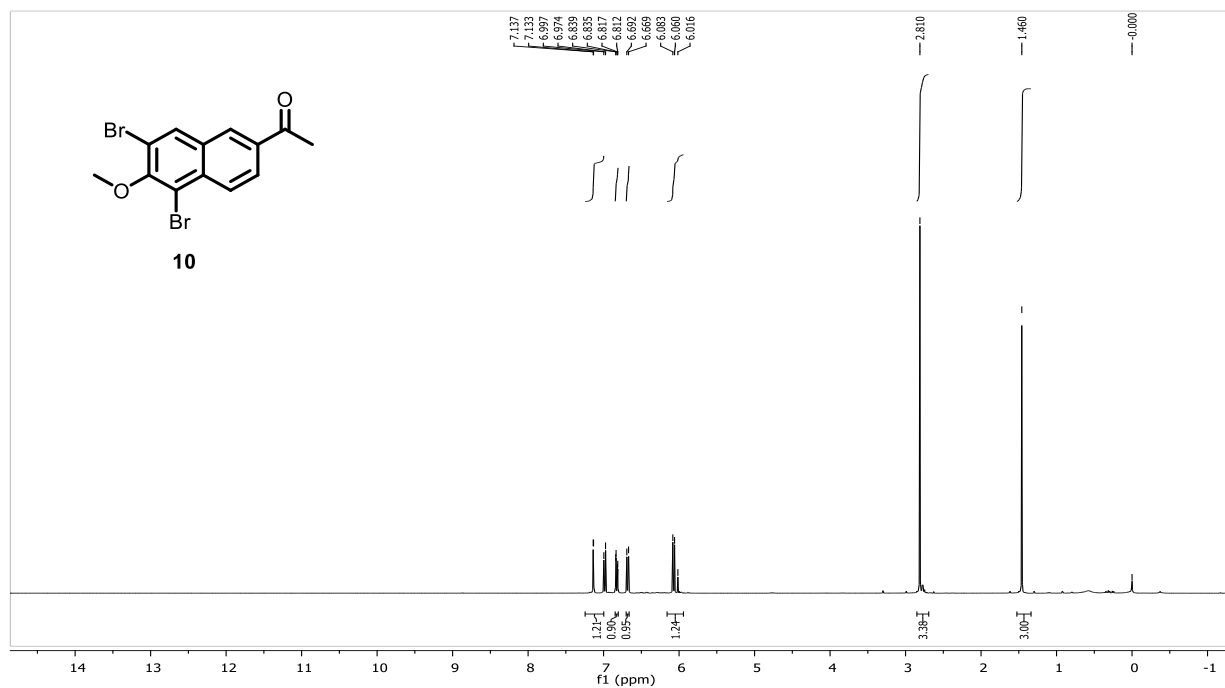
IISER PUNE

SIB 3 163 (2.994) AM 2 (Ar, 20000.0, 556.28, 0.00, LS 3); Sm (SG, 3x1.00); Cm (160:165)

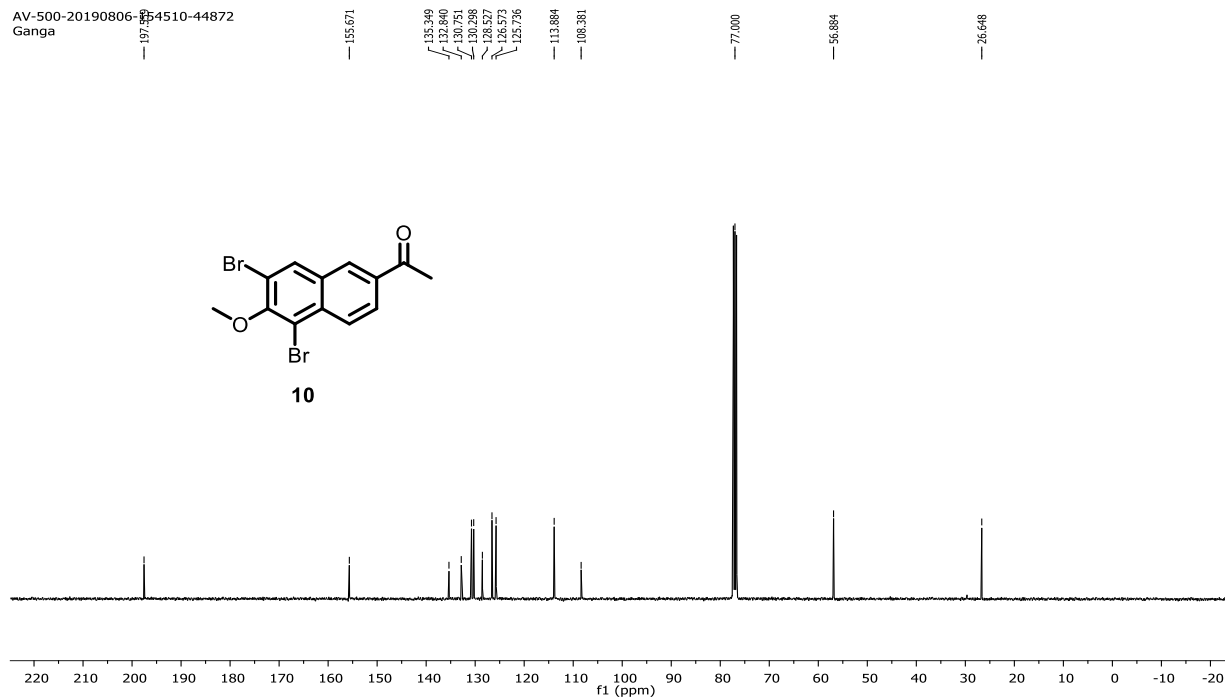
1: TOF MS ES+
2.26e5



¹H NMR spectrum of compound 10 (CDCl₃, 500 MHz)

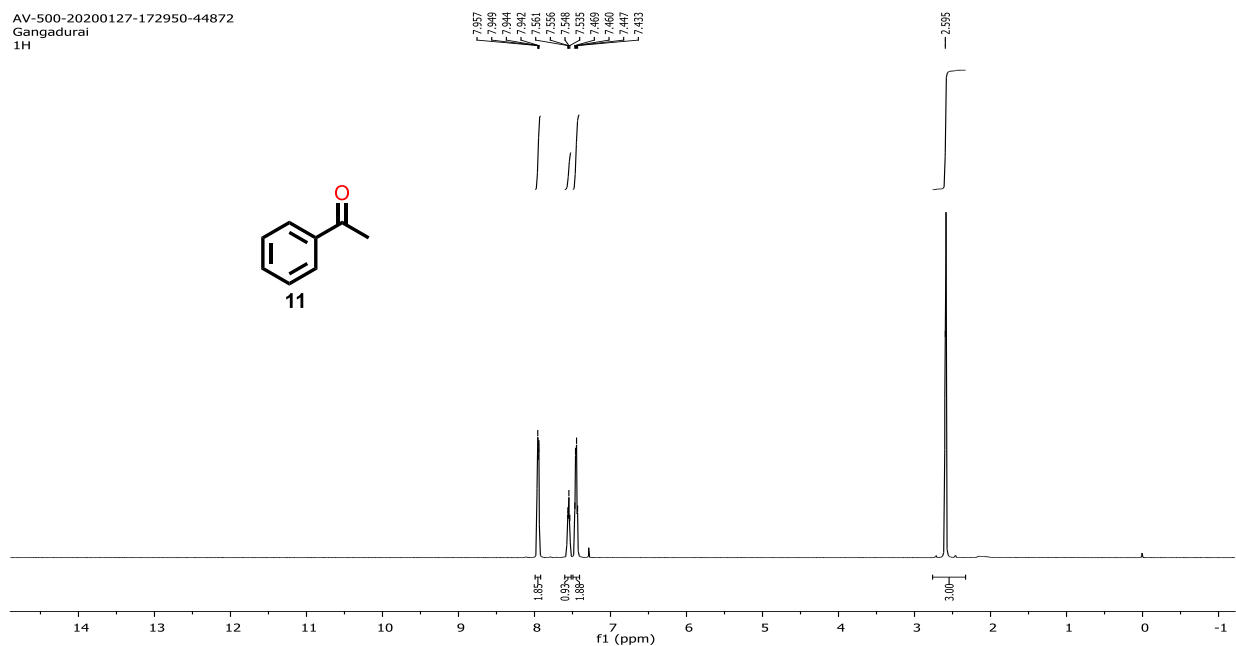


¹³C NMR spectrum of compound 10 (CDCl₃, 125 MHz)



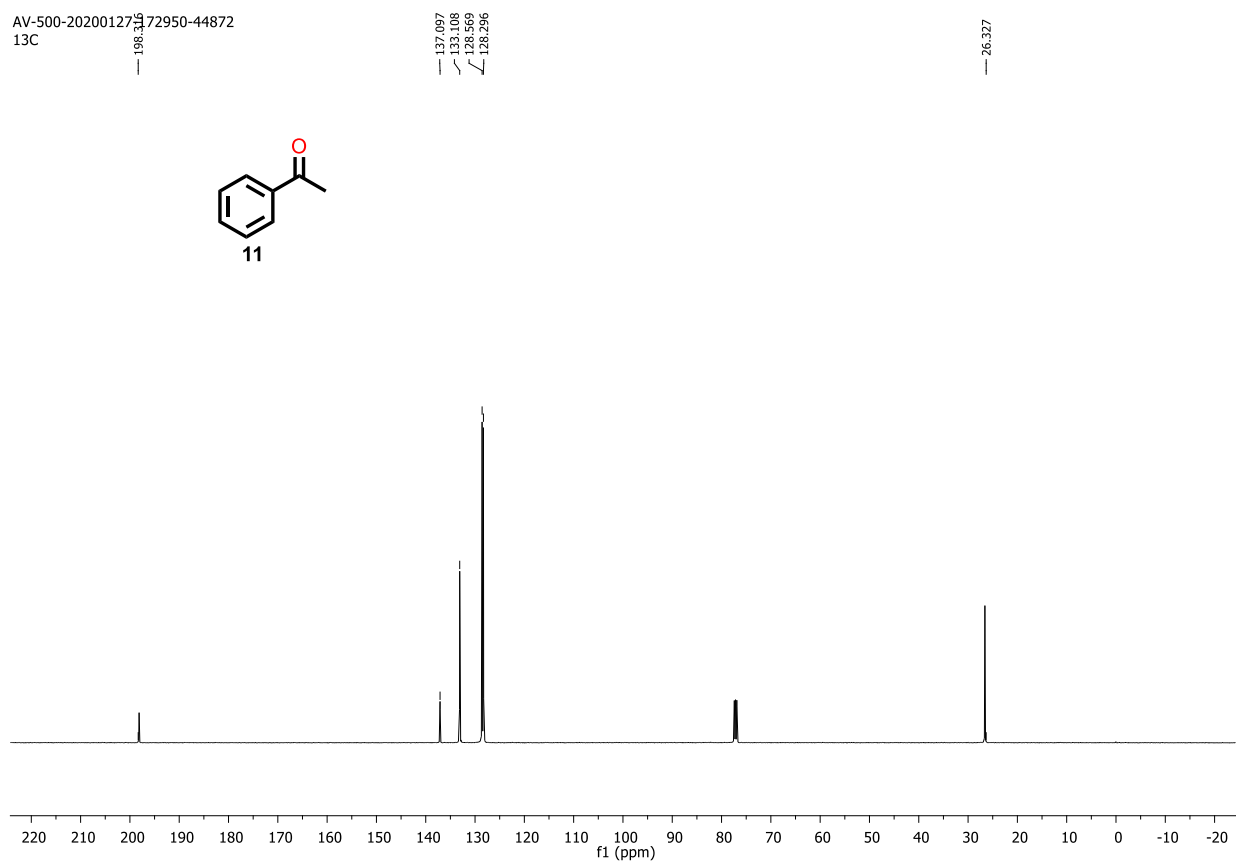
^1H NMR spectrum of compound **11 (CDCl_3 , 500 MHz)**

AV-500-20200127-172950-44872
Gangadurai
 ^1H



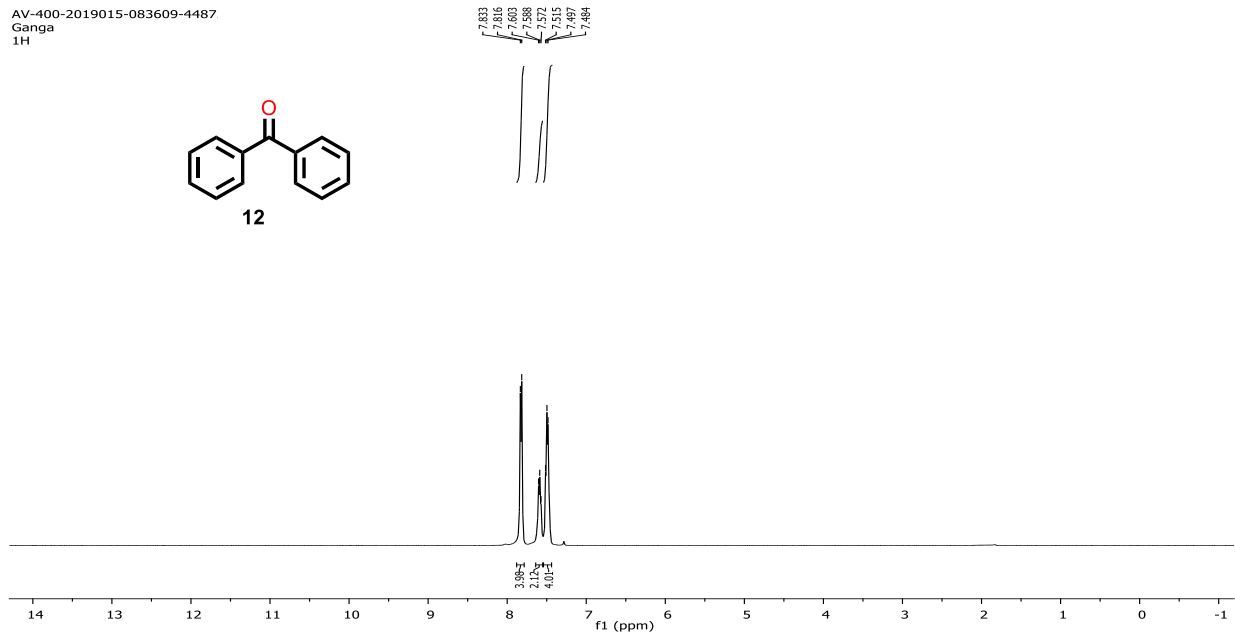
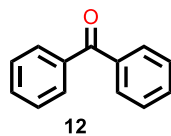
^{13}C NMR spectrum of compound **11 (CDCl_3 , 125 MHz)**

AV-500-20200127-172950-44872
13C



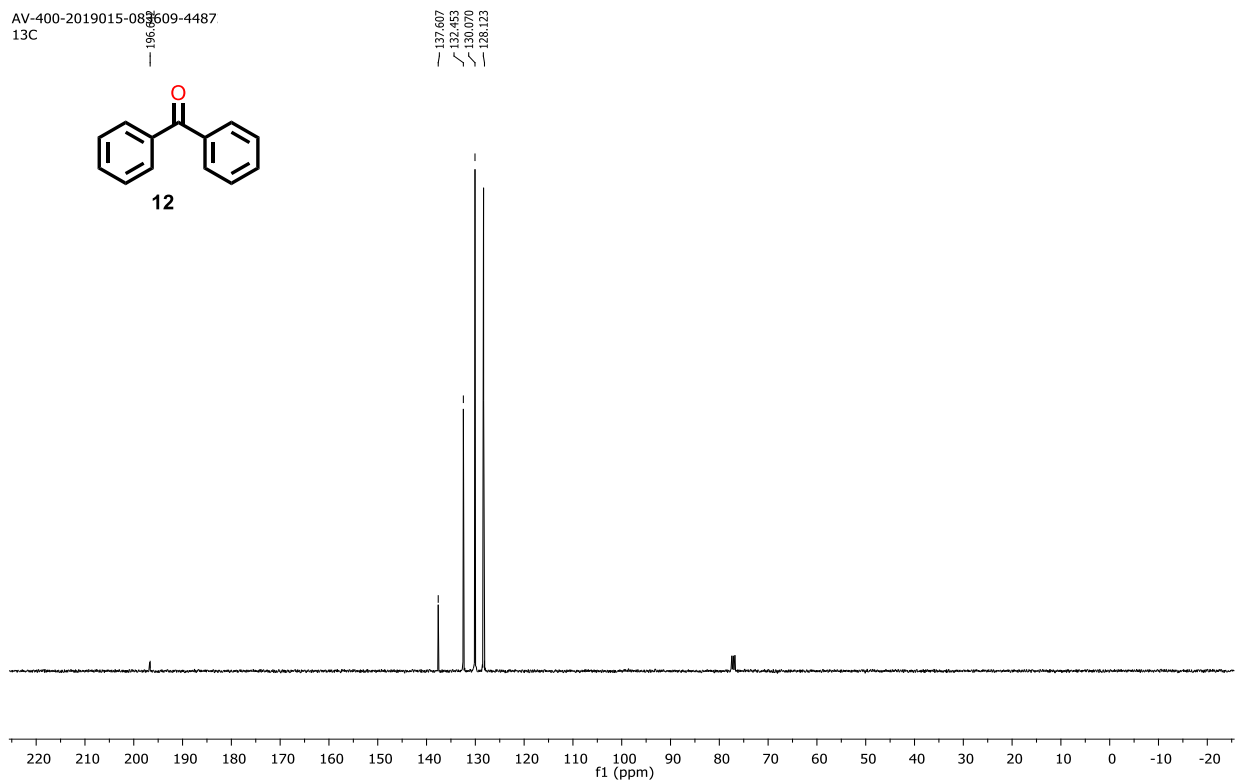
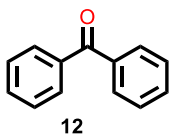
¹H NMR spectrum of compound **12 (CDCl₃, 400 MHz)**

AV-400-2019015-083609-4487
Ganga
1H



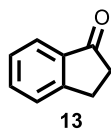
¹³C NMR spectrum of compound **12 (CDCl₃, 100 MHz)**

AV-400-2019015-083609-4487
13C

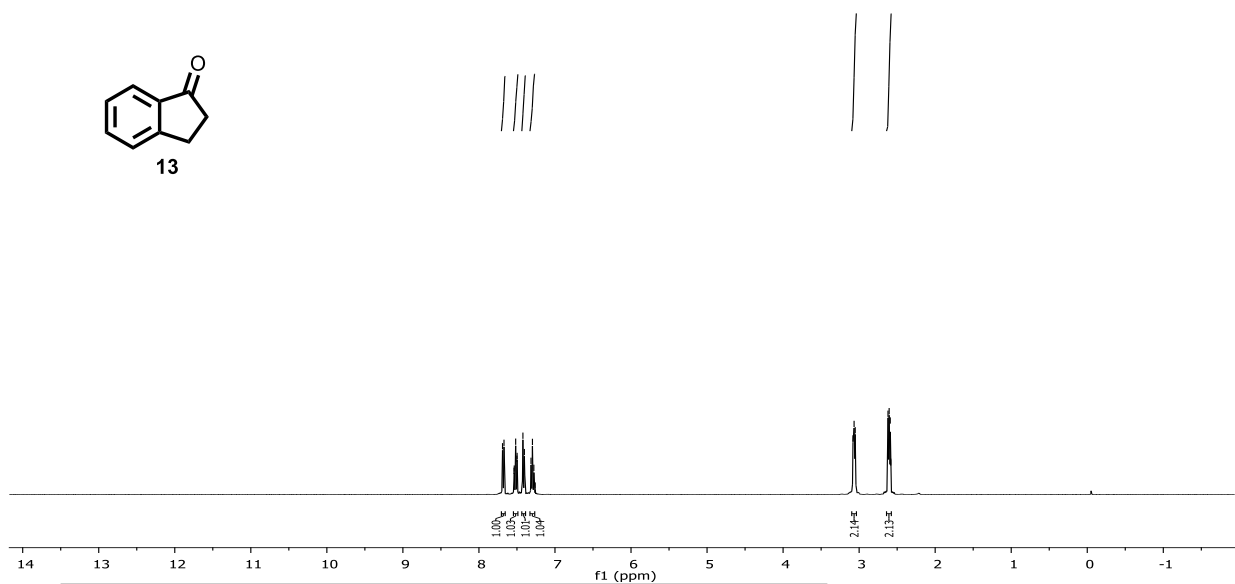


^1H NMR spectrum of compound **13 (CDCl_3 , 400 MHz)**

INPROTICS-AV NEO 400-20200309-162610-2447
Dr D S Reddy



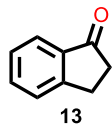
7.690, 7.690, 7.690, 7.598, 7.535, 7.517, 7.501, 7.498, 7.422, 7.402, 7.315, 7.296, 7.278, 7.260, 3.081, 3.066, 3.052, 2.860, 2.844, 2.810, 2.695, 2.601, 2.601, 2.591, 2.586, 2.585



^{13}C NMR spectrum of compound **13 (CDCl_3 , 100 MHz)**

INPROTICS-AV NEO 400-20200309-162610-2447
Dr D S Reddy

206.927



155.103

136.986

134.524

127.184

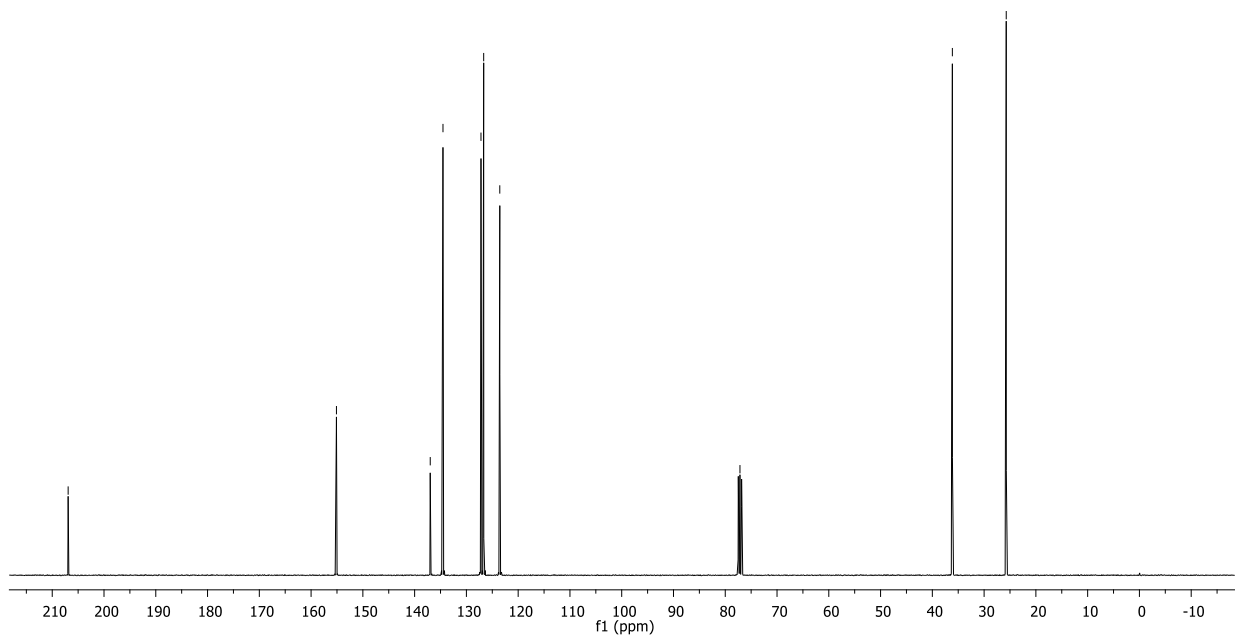
126.662

123.551

77.160 Chloroform-d

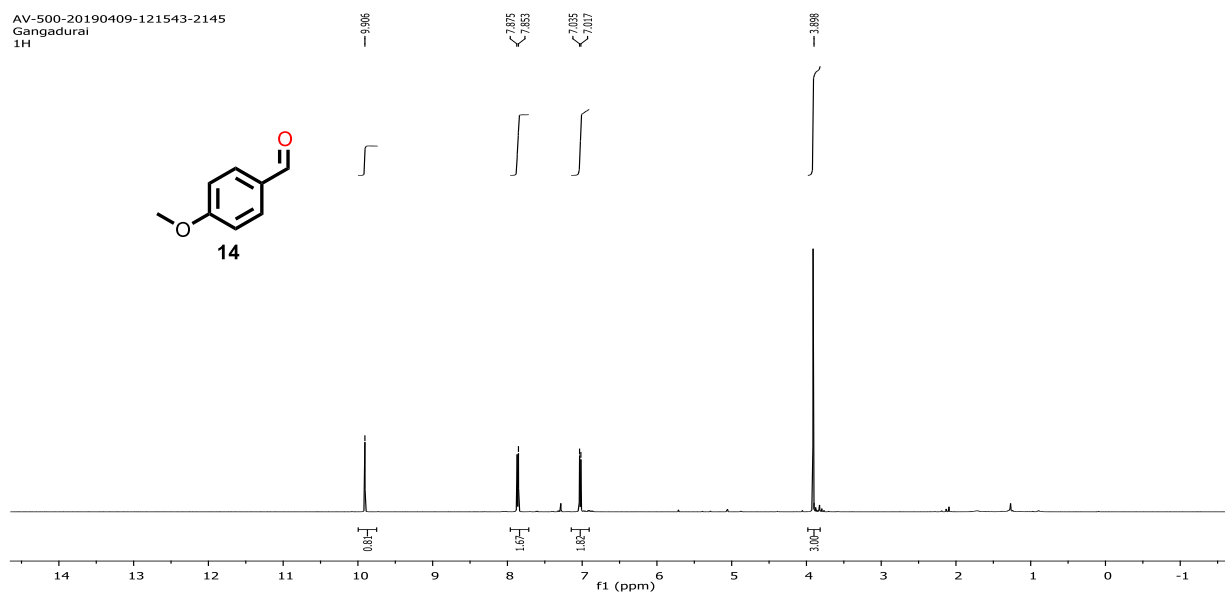
36.132

25.726



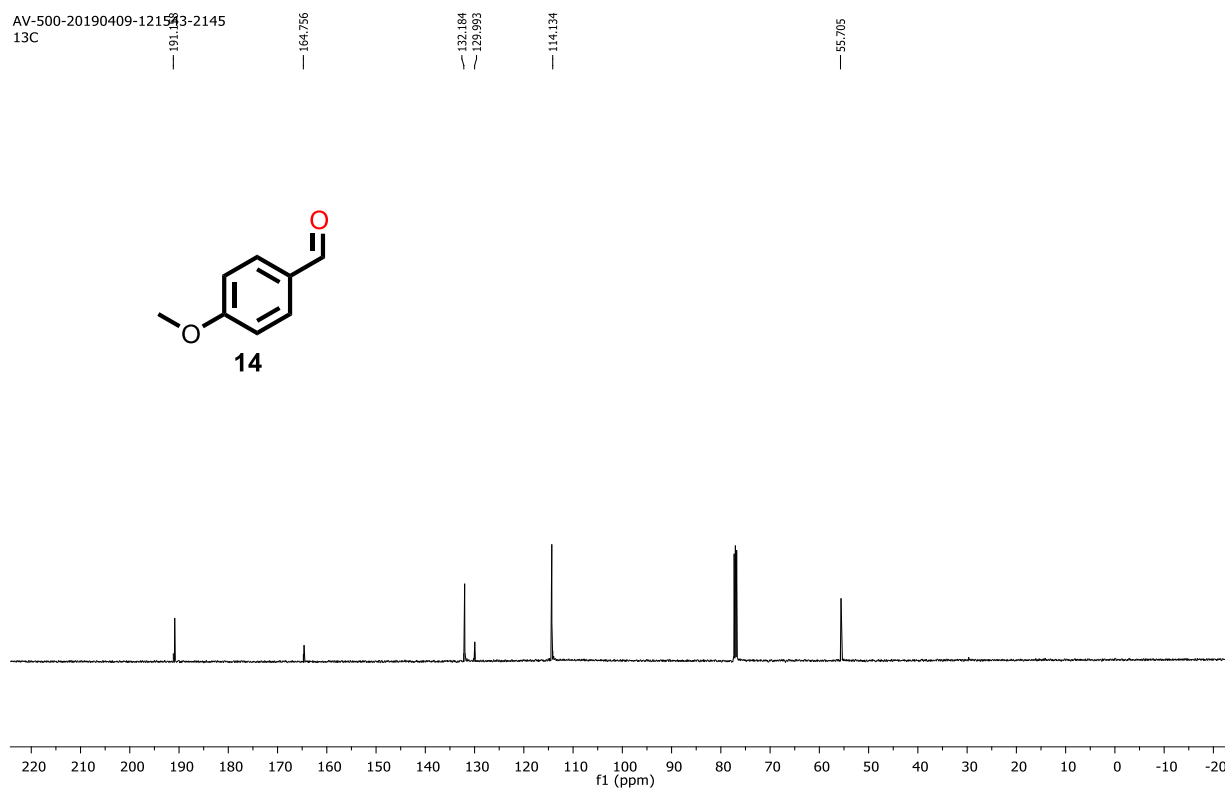
¹H NMR spectrum of compound 14 (CDCl₃, 500 MHz)

AV-500-20190409-121543-2145
Gangadurai
1H



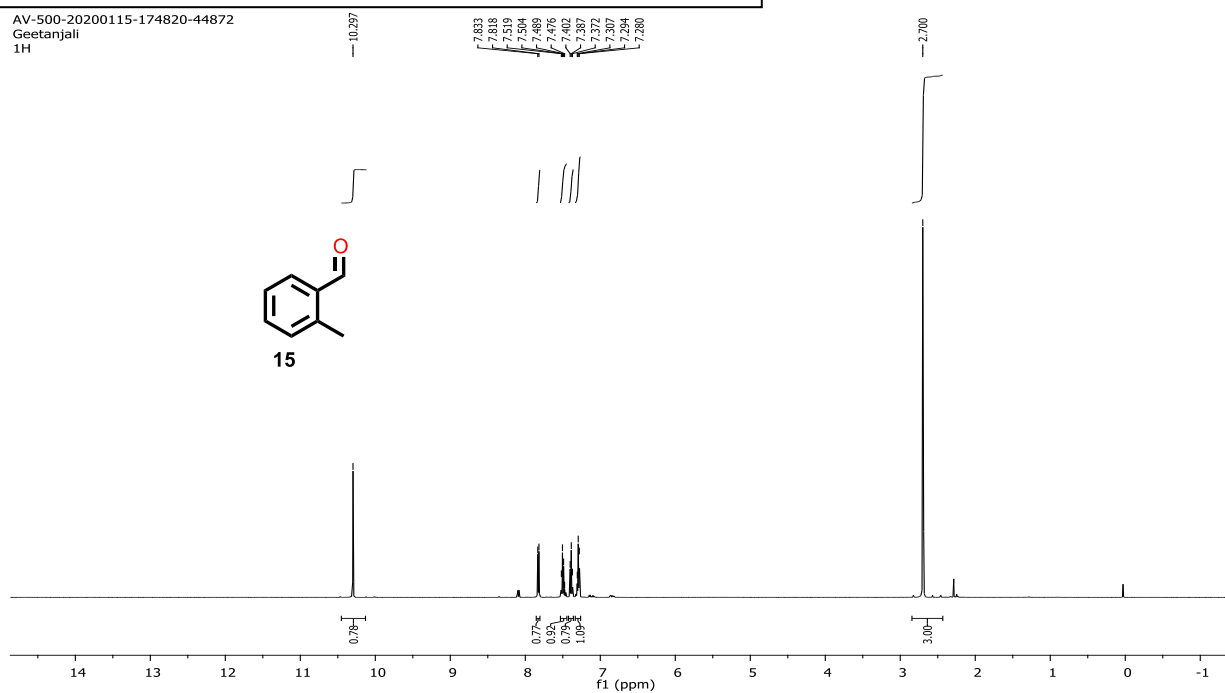
¹³C NMR spectrum of compound 14 (CDCl₃, 125 MHz)

AV-500-20190409-121543-2145
13C



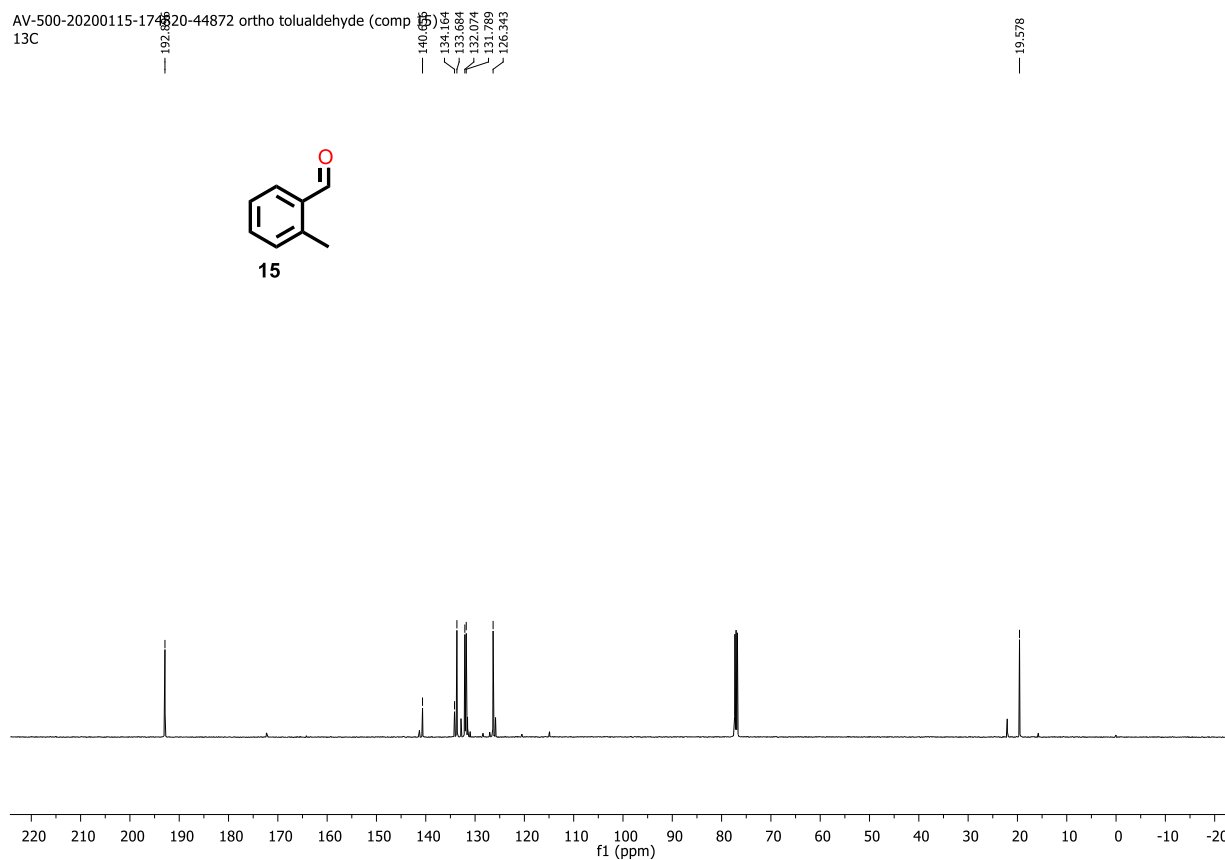
^1H NMR spectrum of compound 15 (CDCl_3 , 500 MHz)

AV-500-20200115-174820-44872
Geetanjali
 ^1H



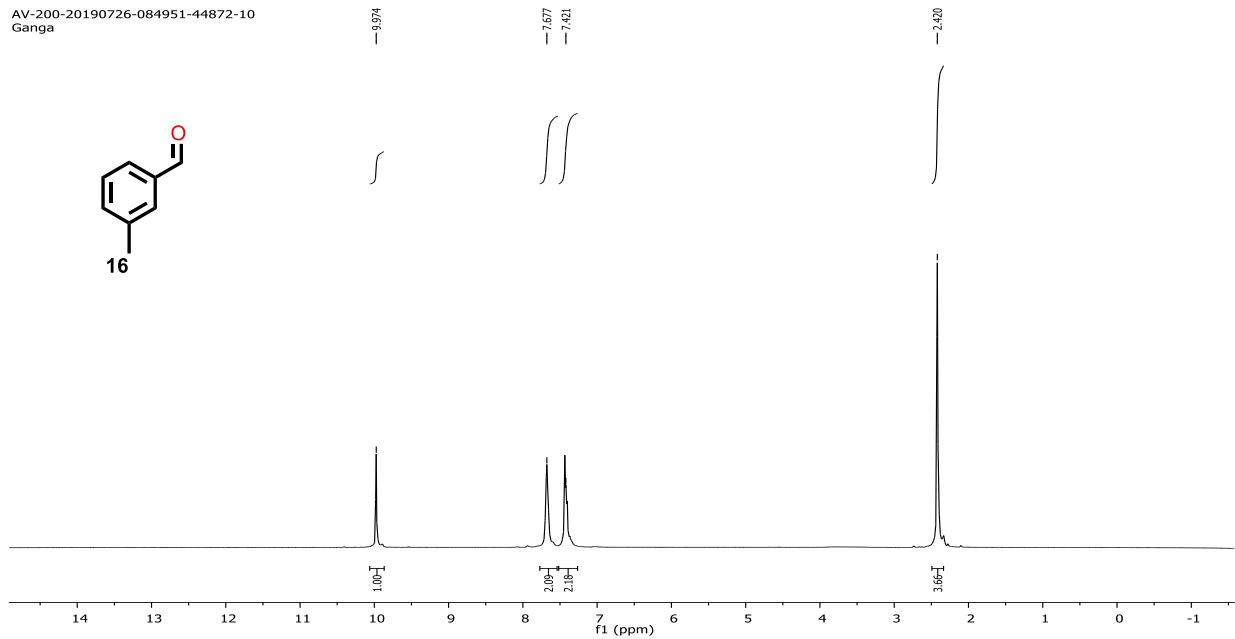
^{13}C NMR spectrum of compound 15 (CDCl_3 , 125 MHz)

AV-500-20200115-174820-44872 ortho-tolaldehyde (comp
 ^{13}C



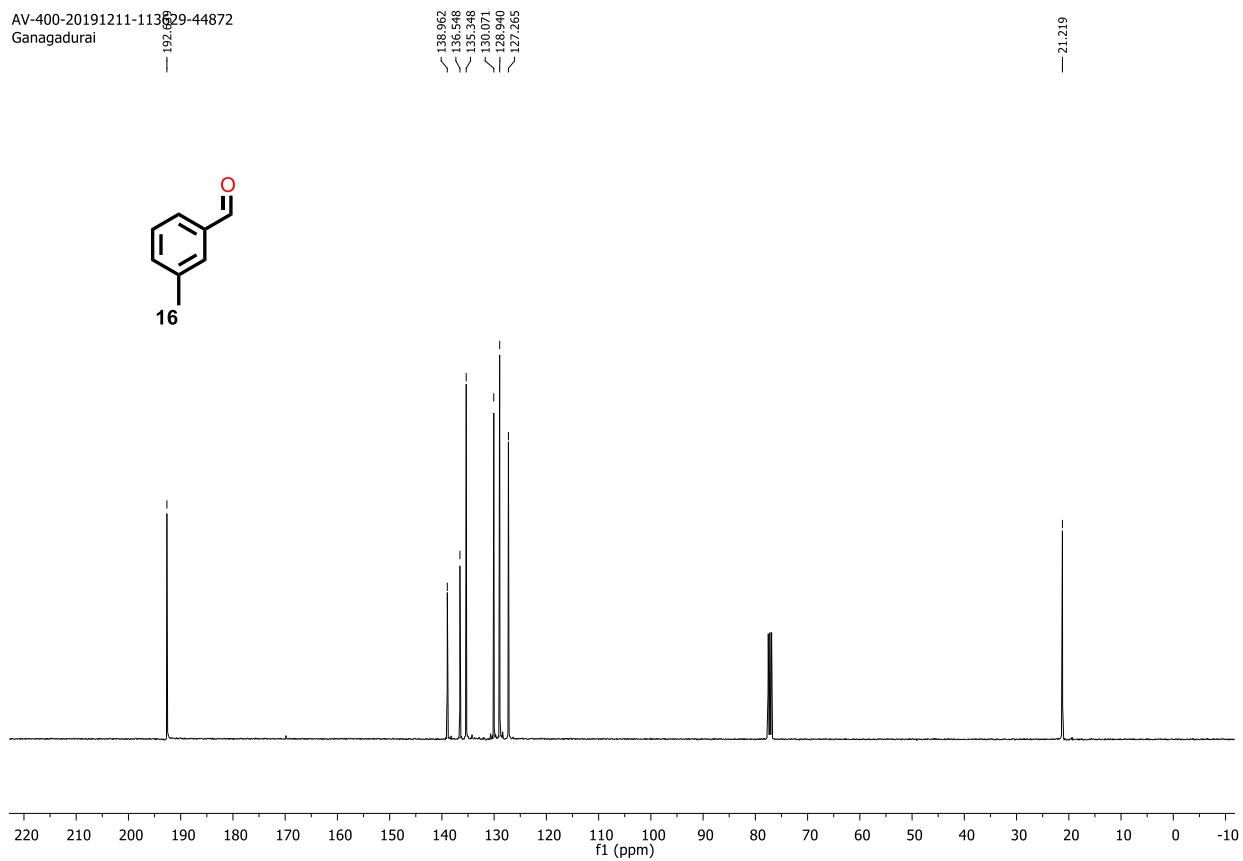
^1H NMR spectrum of compound 16 (CDCl_3 , 200 MHz)

AV-200-20190726-084951-44872-10
Ganga



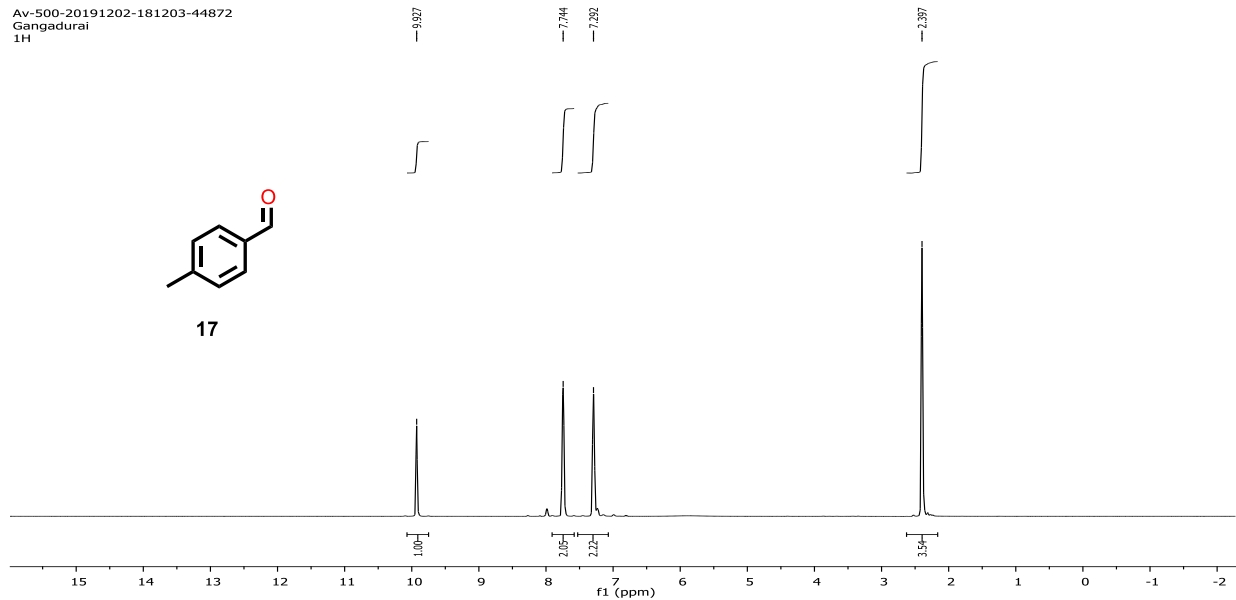
^{13}C NMR spectrum of compound 16 (CDCl_3 , 100 MHz)

AV-400-20191211-113629-44872
Ganagadurai



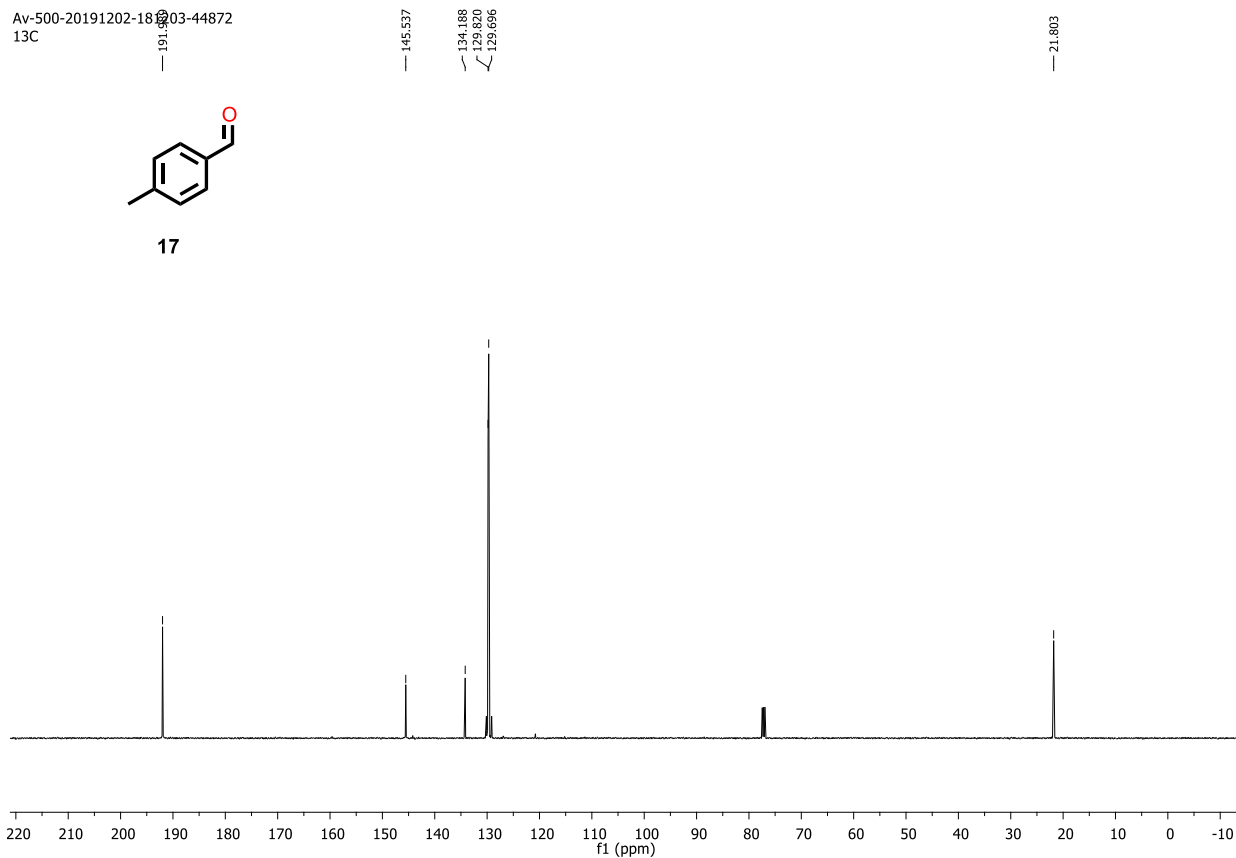
^1H NMR spectrum of compound 17 (CDCl_3 , 500 MHz)

Av-500-20191202-181203-44872
Gangadurai
 ^1H



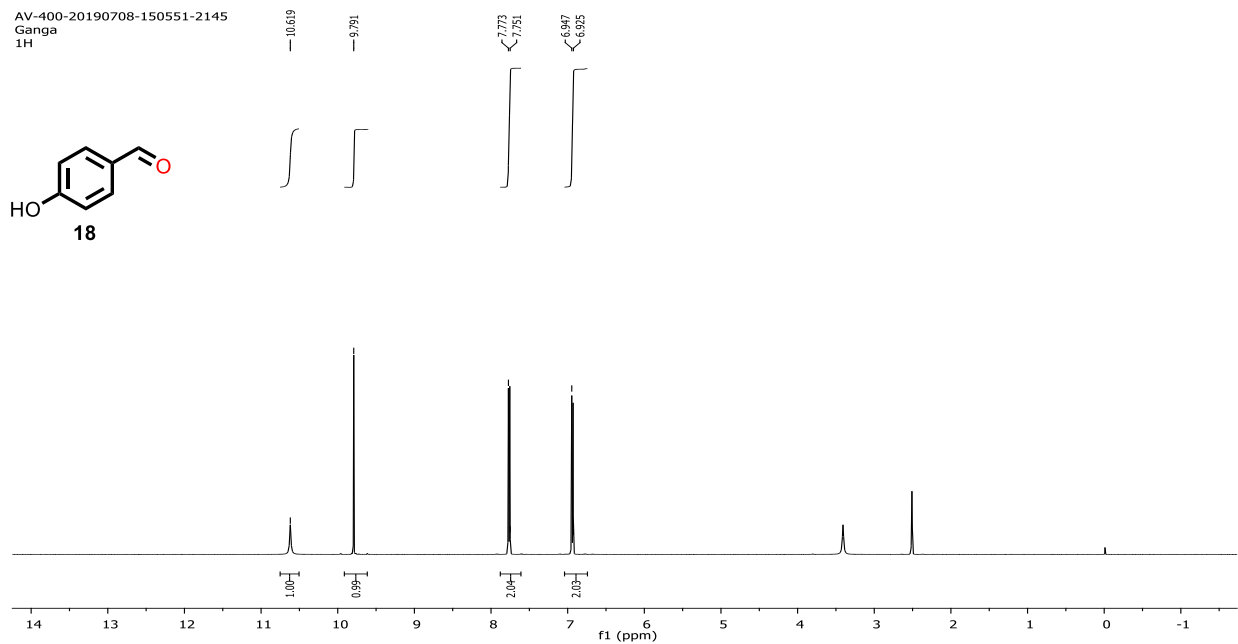
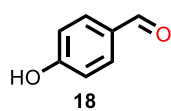
^{13}C NMR spectrum of compound 17 (CDCl_3 , 125 MHz)

Av-500-20191202-181203-44872
13C



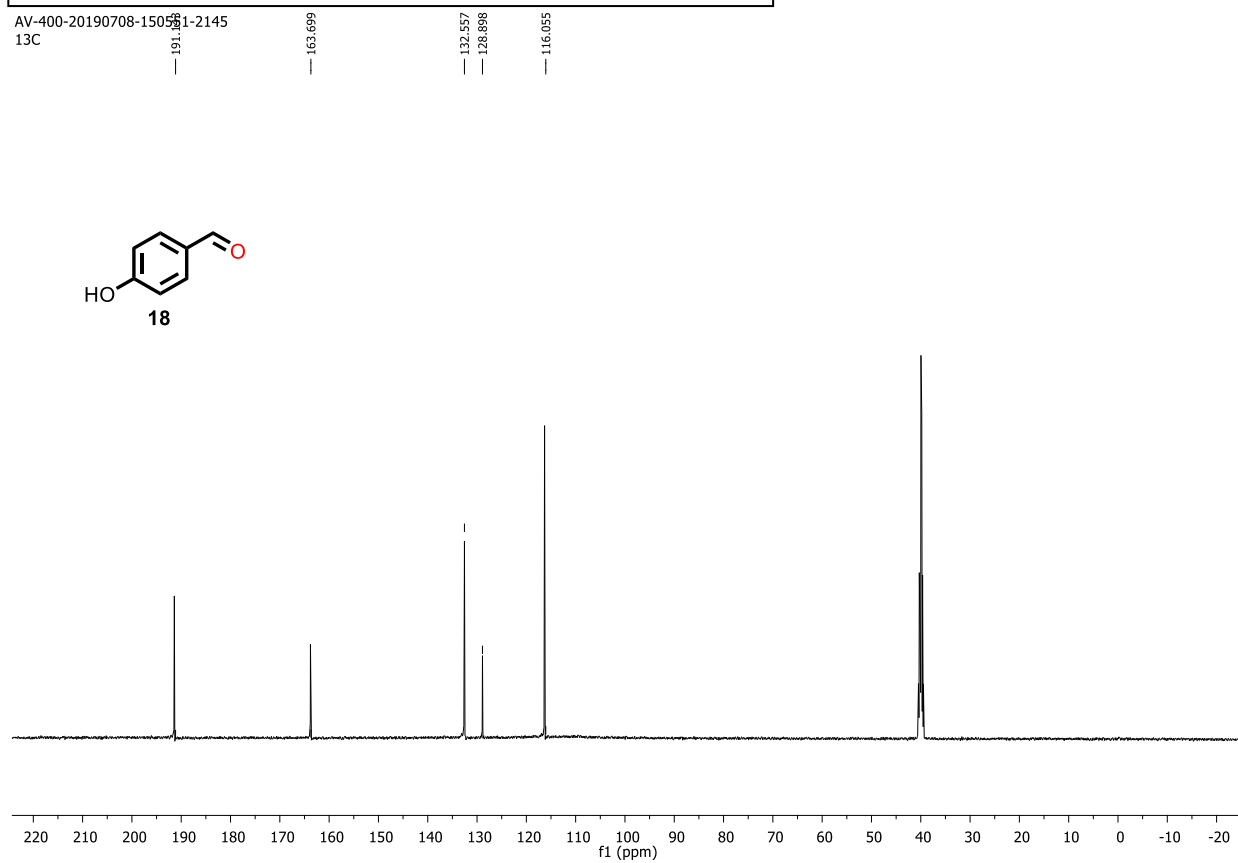
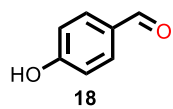
¹H NMR spectrum of compound 18 (CDCl₃, 400 MHz)

AV-400-20190708-150551-2145
Ganga
1H



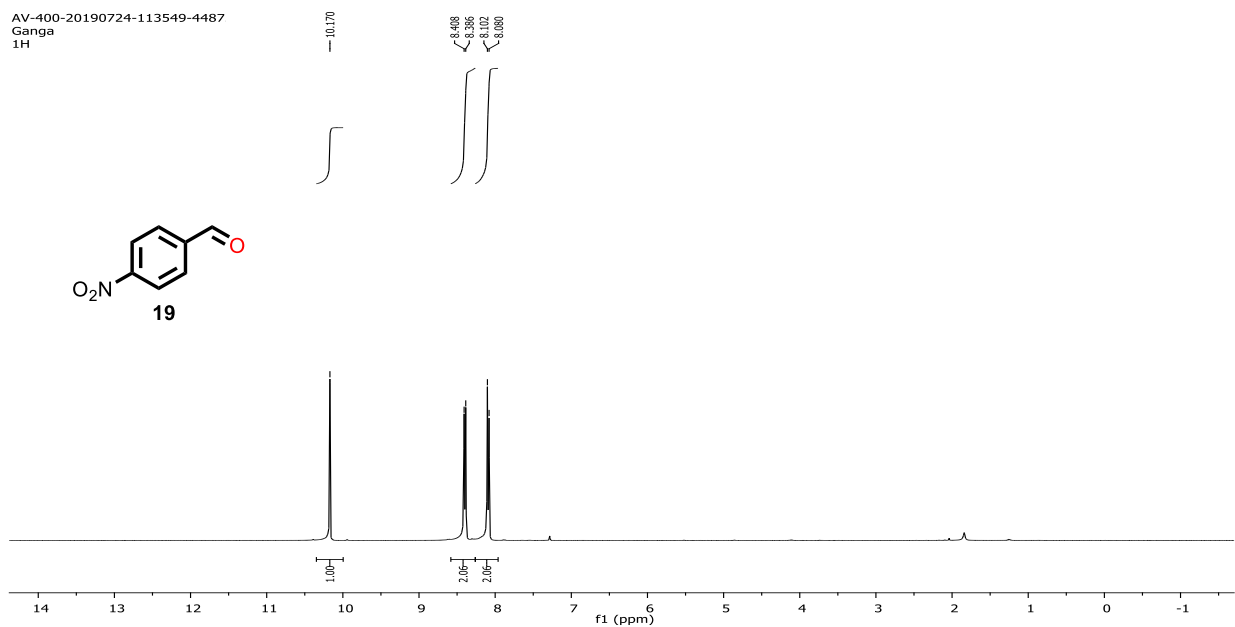
¹³C NMR spectrum of compound 18 (CDCl₃, 100 MHz)

AV-400-20190708-150551-2145
13C



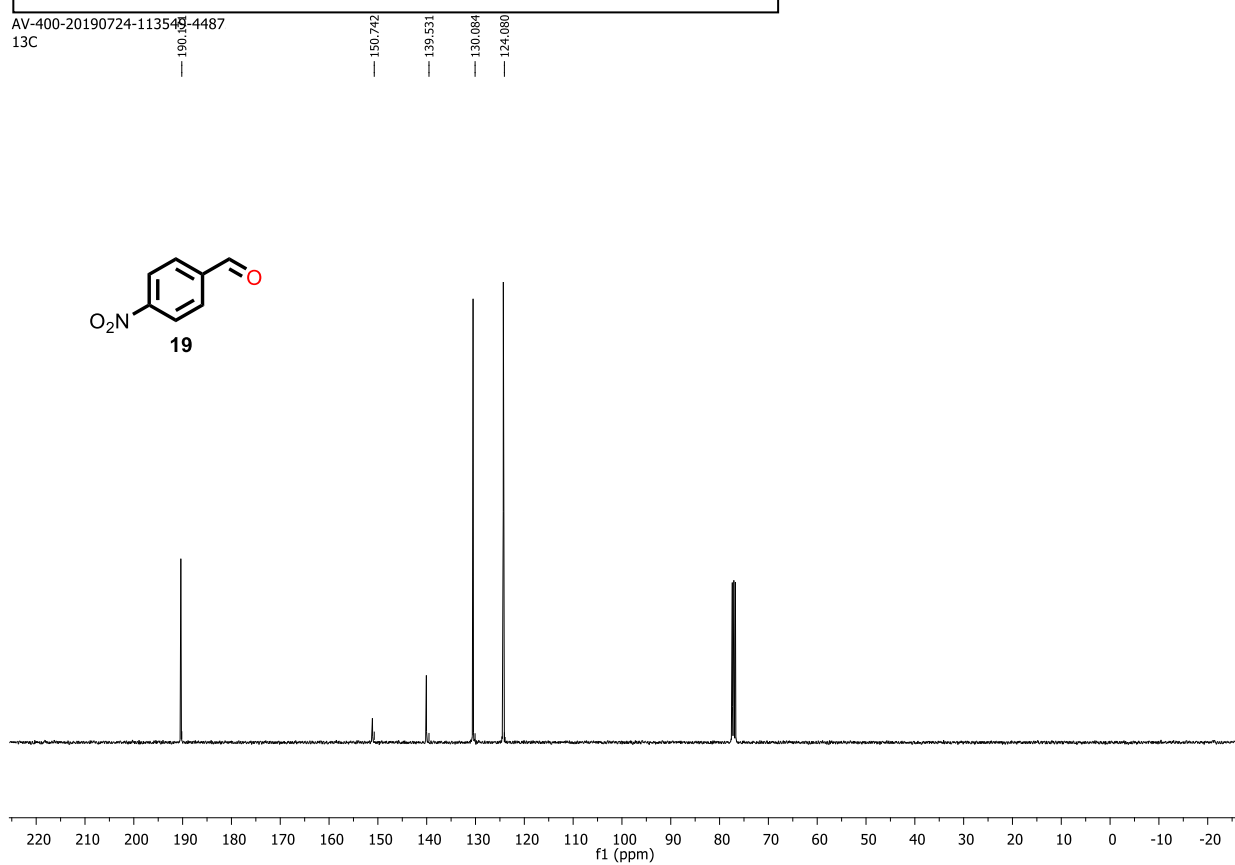
¹H NMR spectrum of compound 19 (CDCl₃, 400 MHz)

AV-400-20190724-113549-4487
Ganga
1H



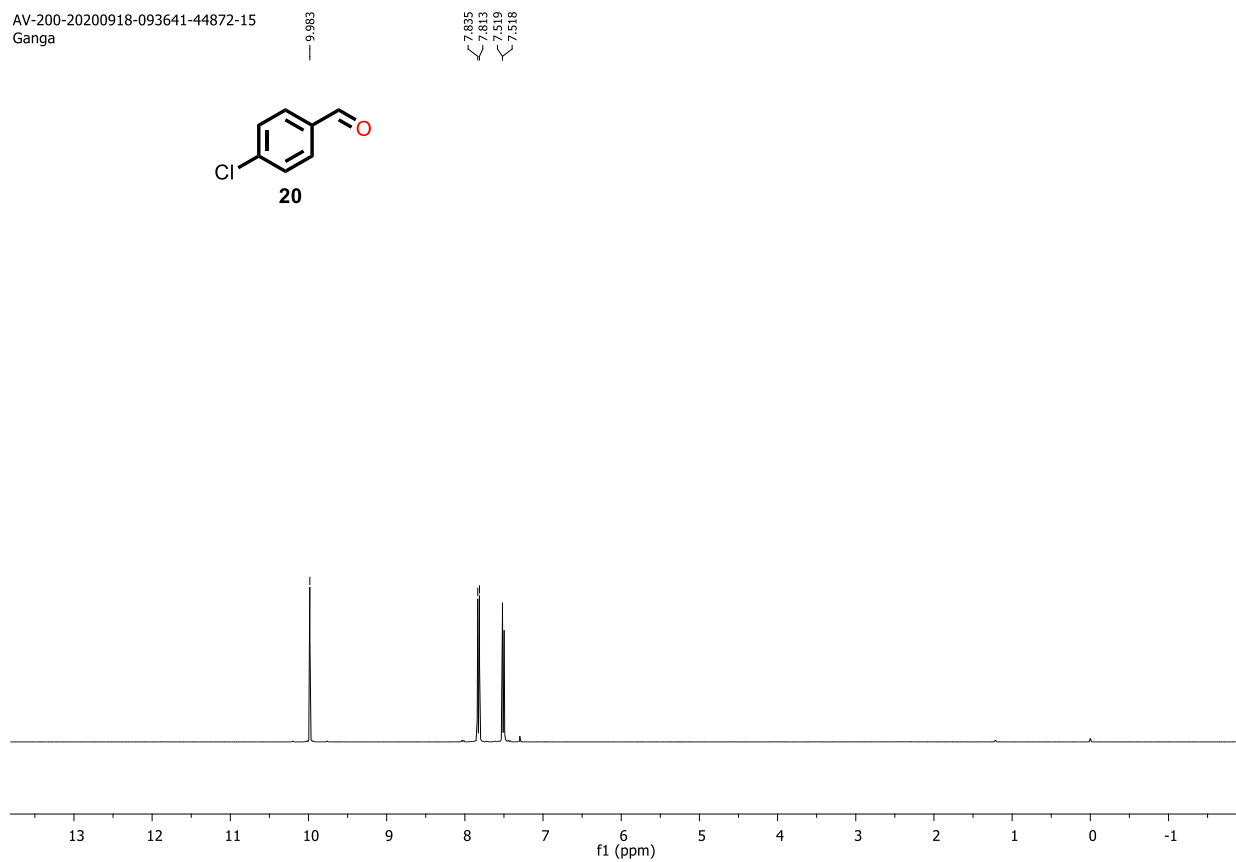
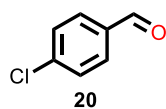
¹³C NMR spectrum of compound 19 (CDCl₃, 100 MHz)

AV-400-20190724-113549-4487
13C

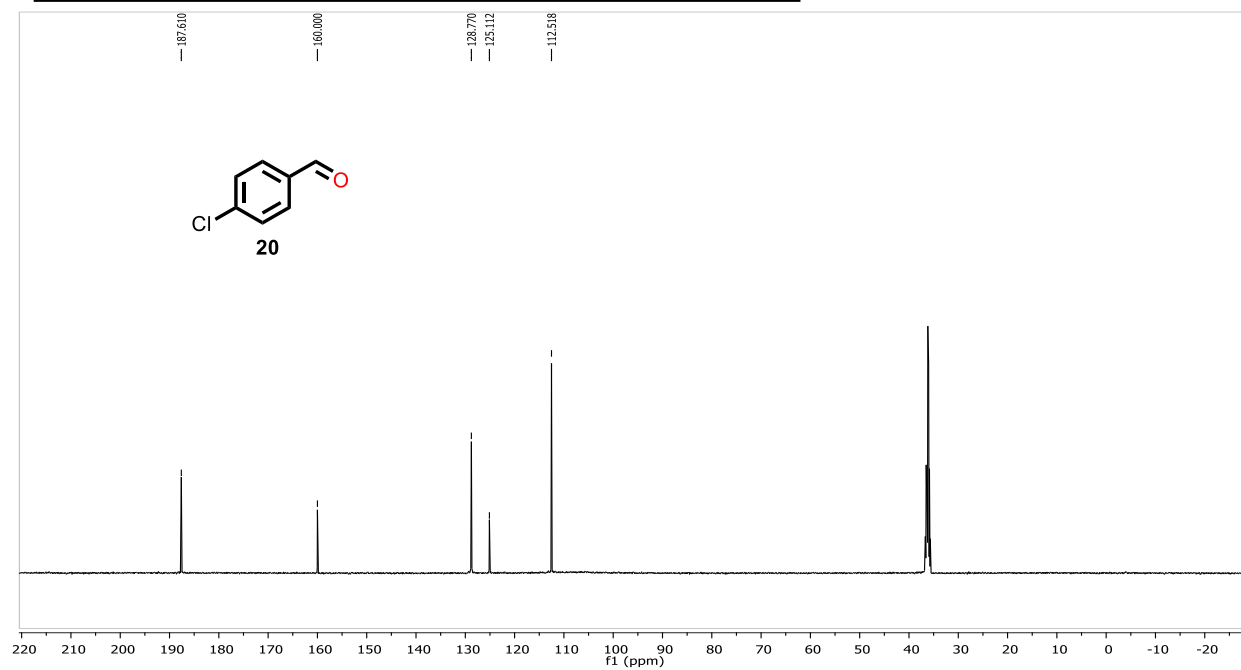
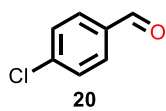


¹H NMR spectrum of compound 20 (CDCl₃, 200 MHz)

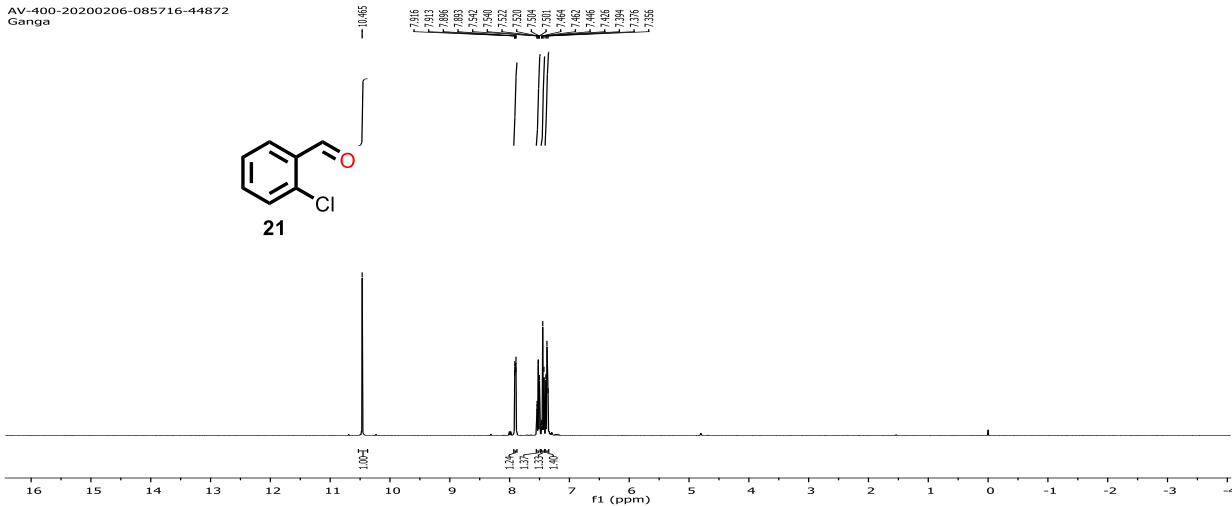
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Ganga



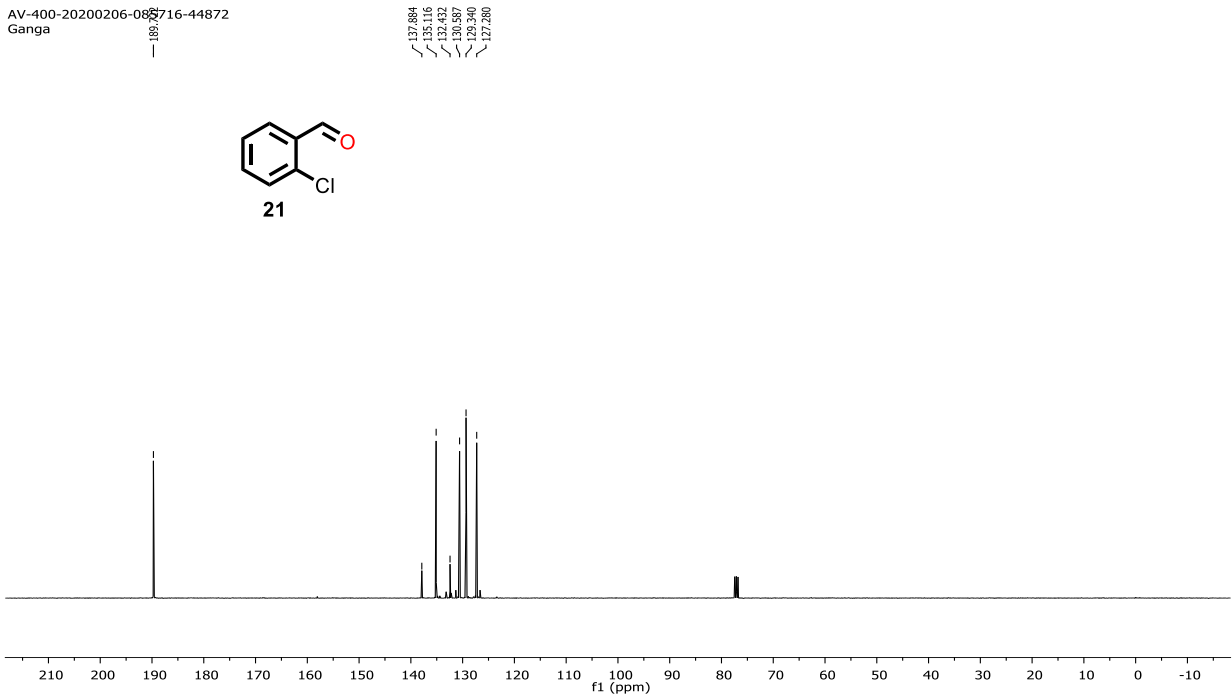
¹³C NMR spectrum of compound 20 (DMSO-d₆, 500 MHz)



¹H NMR spectrum of compound 21 (CDCl₃, 400 MHz)

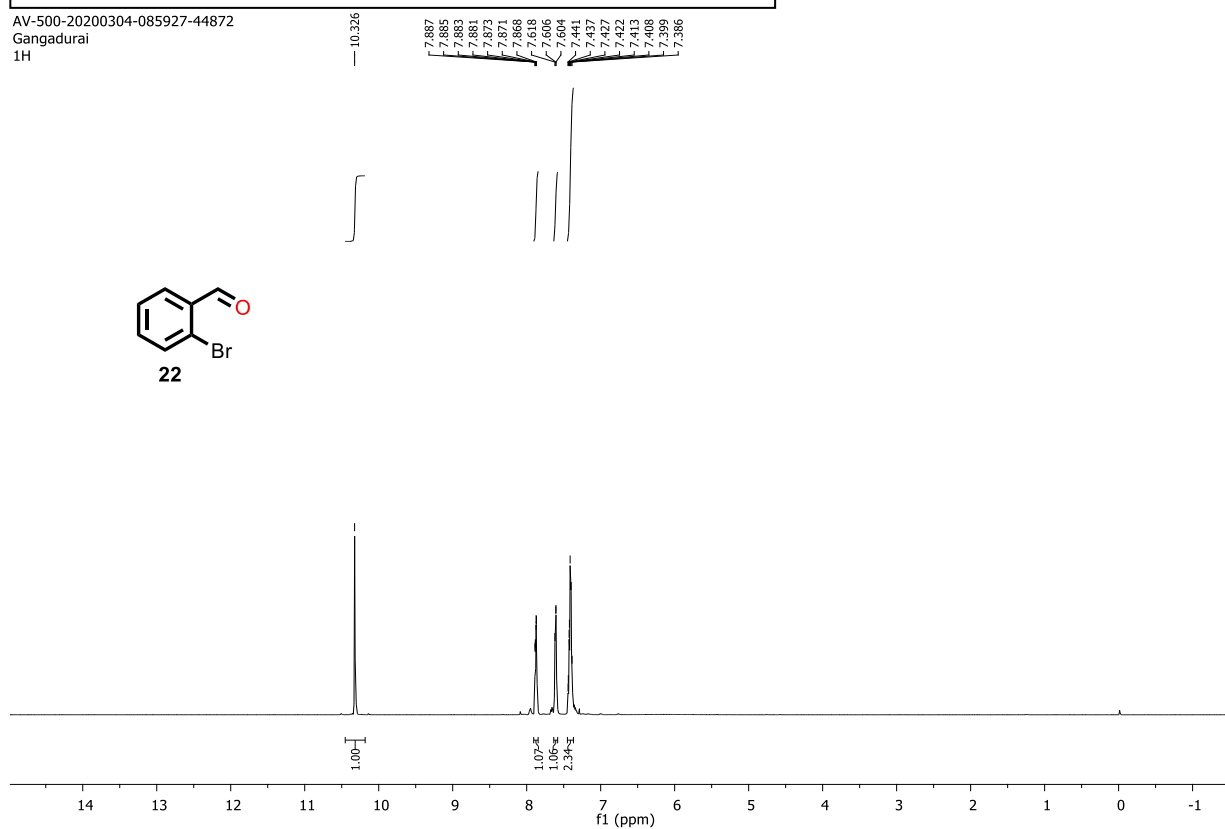


¹³C NMR spectrum of compound 21 (CDCl₃, 400 MHz)



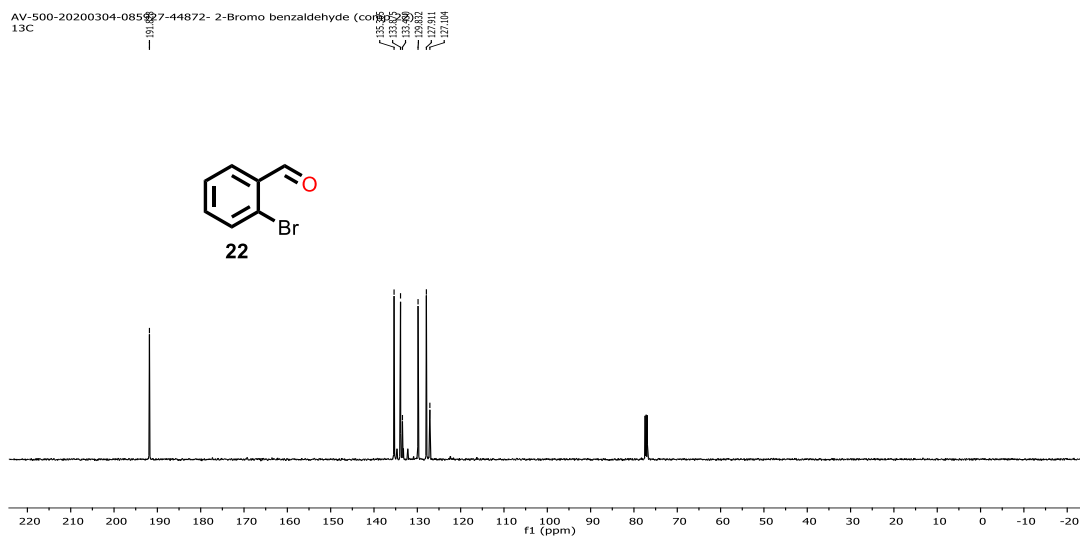
¹H NMR spectrum of compound 22 (CDCl₃, 500 MHz)

AV-500-20200304-085927-44872
Gangadurai
1H



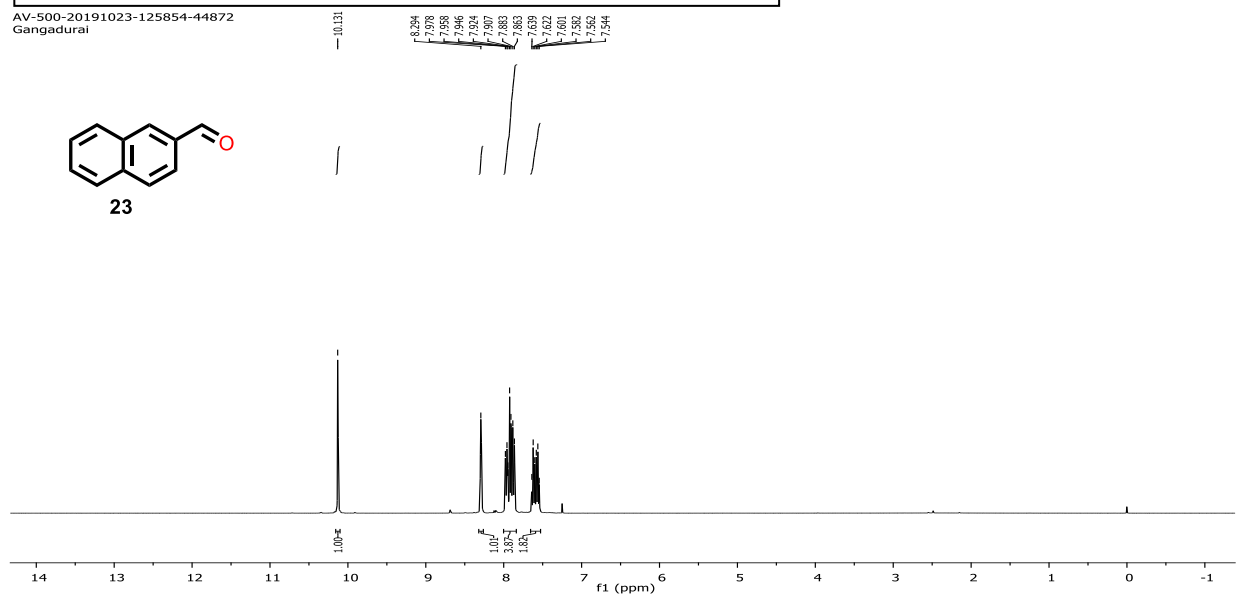
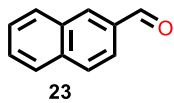
¹³C NMR spectrum of compound 22 (CDCl₃, 125 MHz)

AV-500-20200304-085927-44872- 2-Bromo benzaldehyde (compound 22)
13C



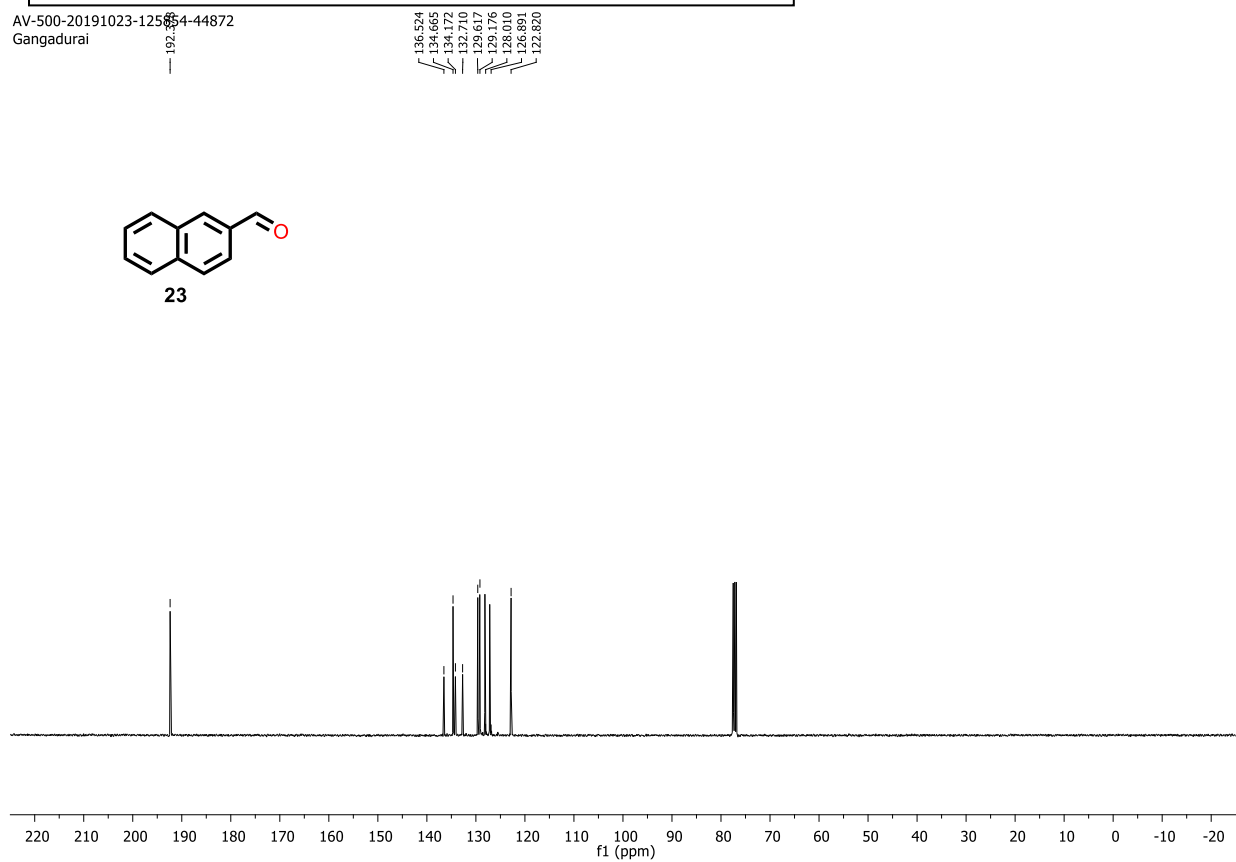
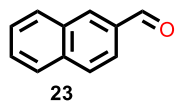
¹H NMR spectrum of compound 23 (CDCl₃, 500 MHz)

AV-500-20191023-125854-44872
Gangadurai



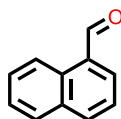
¹³C NMR spectrum of compound 23 (CDCl₃, 125MHz)

AV-500-20191023-125854-44872
Gangadurai

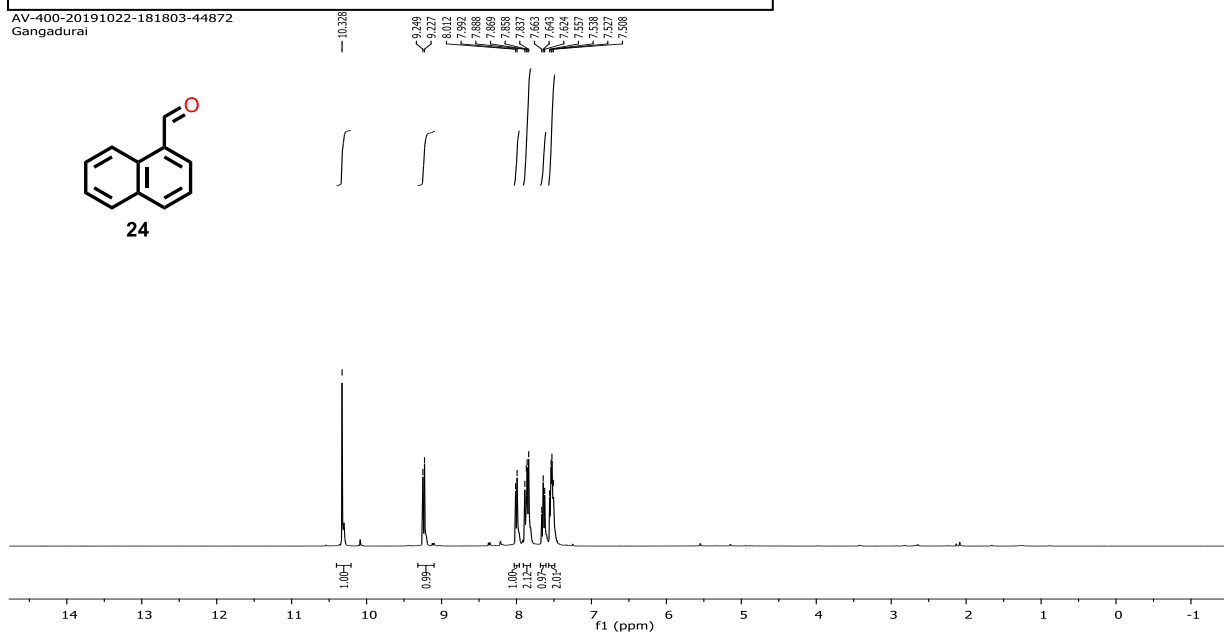


¹H NMR spectrum of compound 24 (CDCl₃, 400 MHz)

AV-400-20191022-181803-44872
Gangadurai

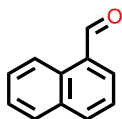


24

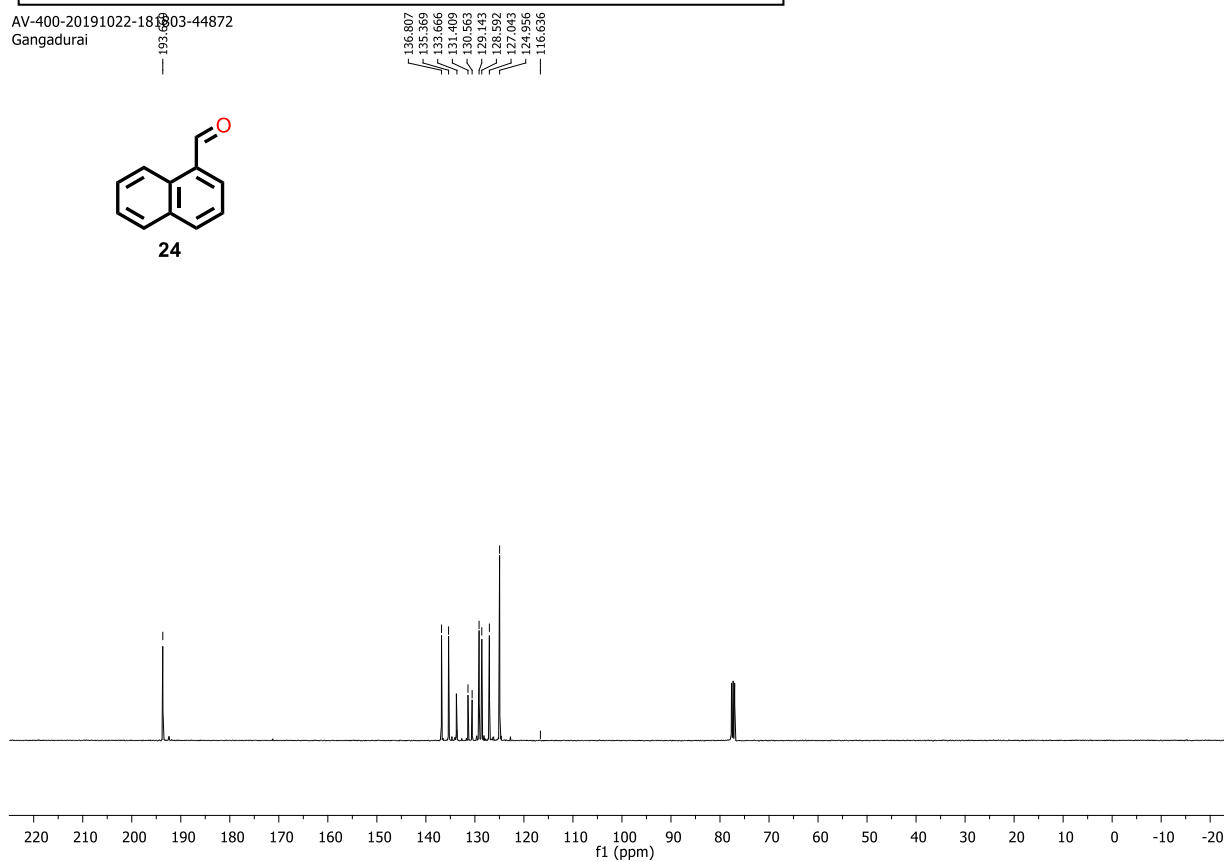


¹³C NMR spectrum of compound 24 (CDCl₃, 100 MHz)

AV-400-20191022-181803-44872
Gangadurai

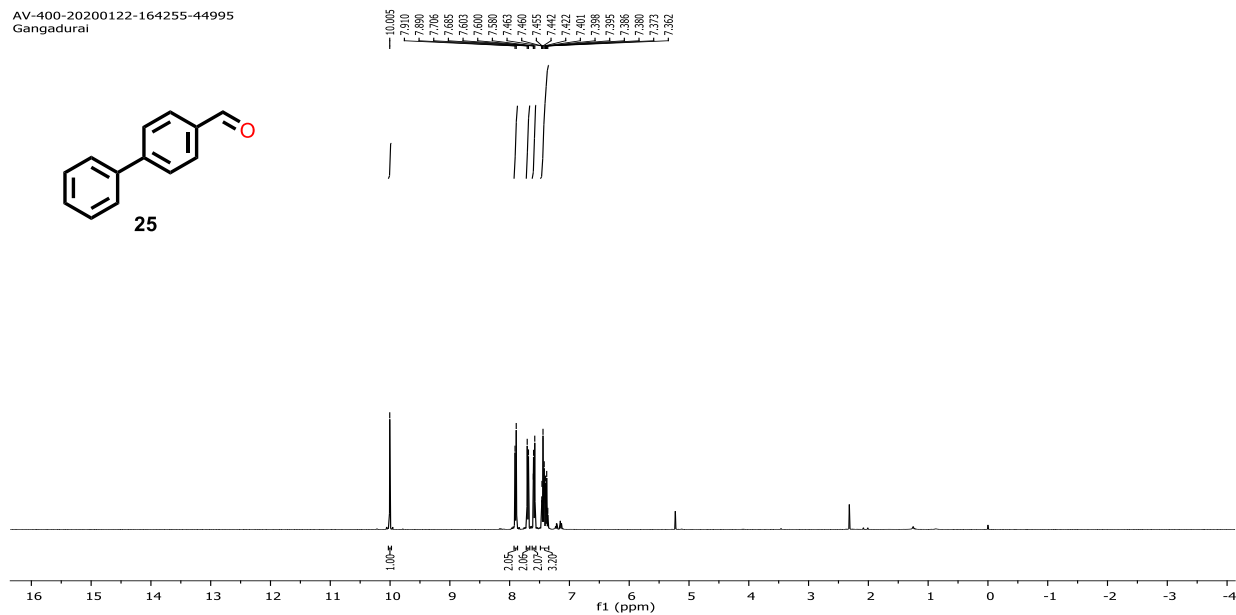
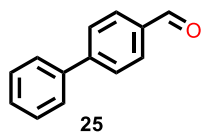


24



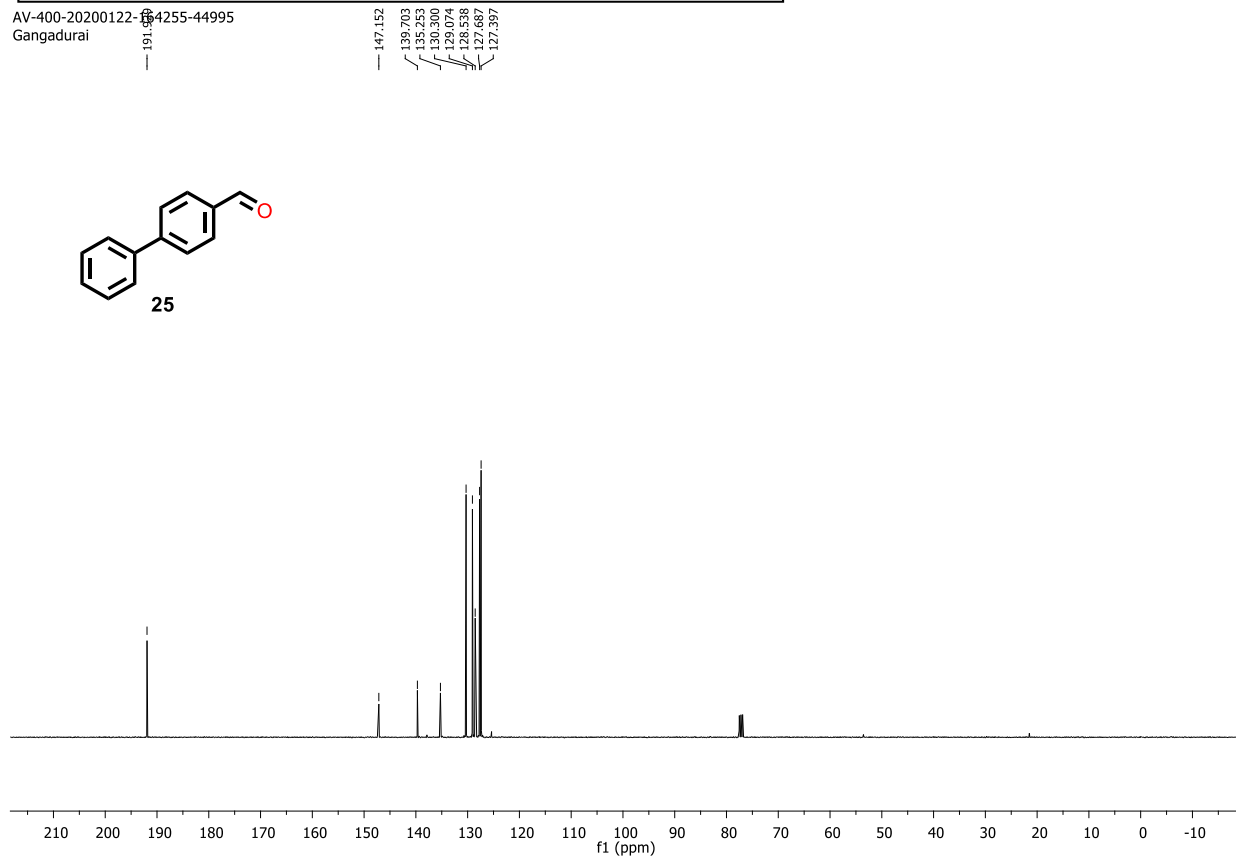
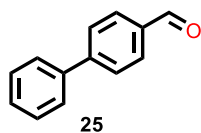
^1H NMR spectrum of compound 25 (CDCl_3 , 400 MHz)

AV-400-20200122-164255-44995
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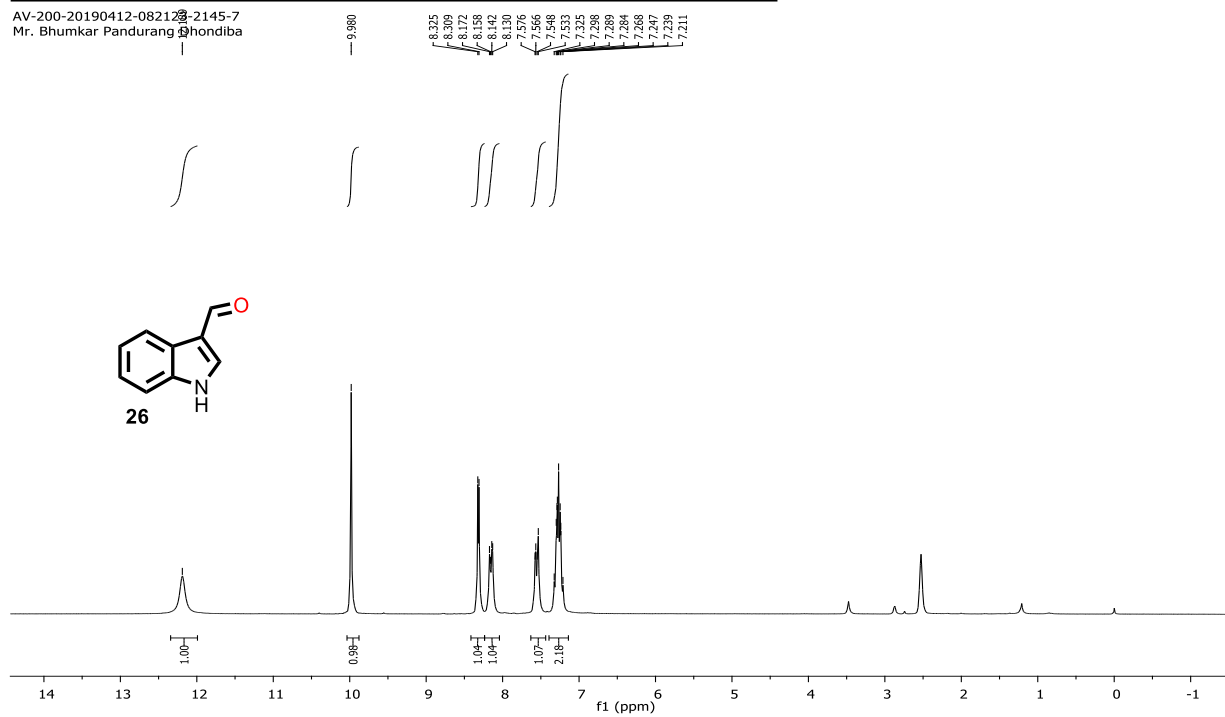
^{13}C NMR spectrum of compound 25 (CDCl_3 , 100 MHz)

AV-400-20200122-164255-44995
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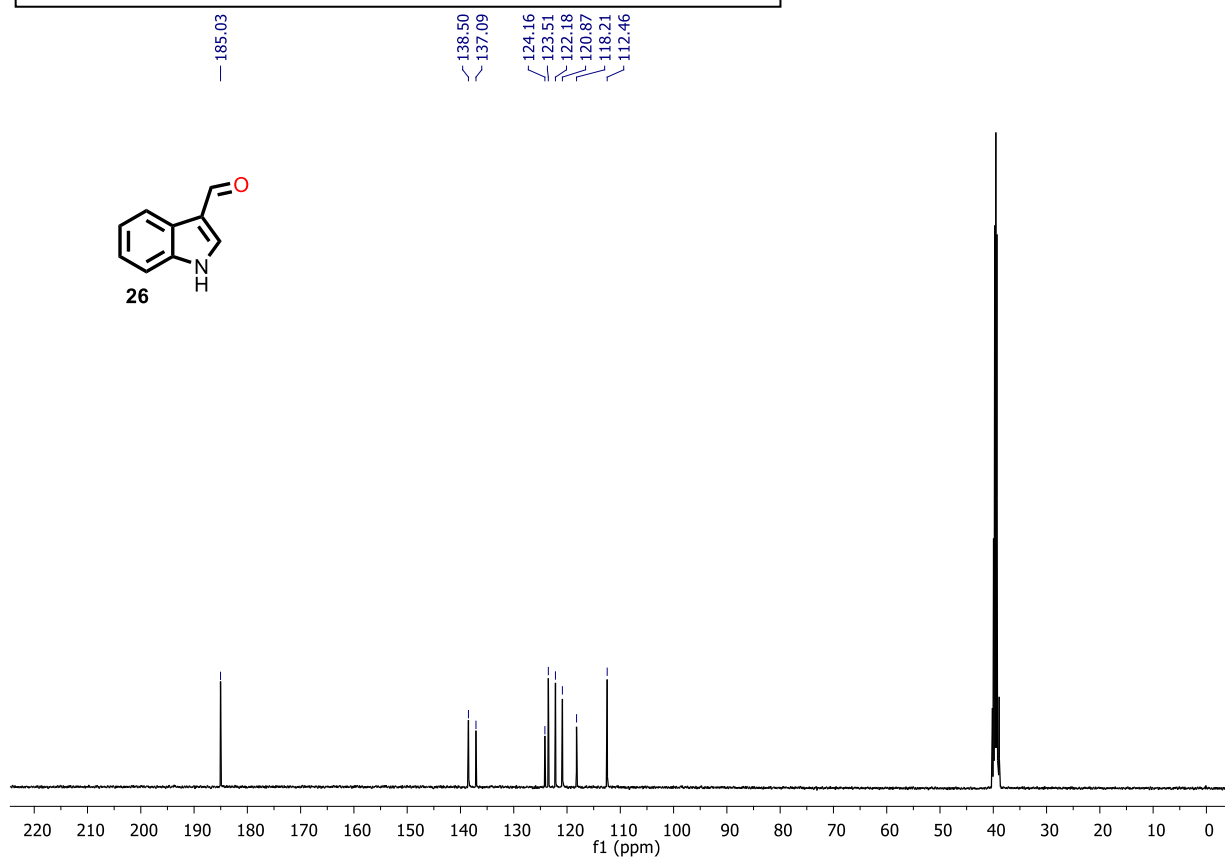


^1H NMR spectrum of compound 26 (CDCl_3 , 200 MHz)

AV-200-20190412-082123-2145-7
Mr. Bhumkar Pandurang Phondiba

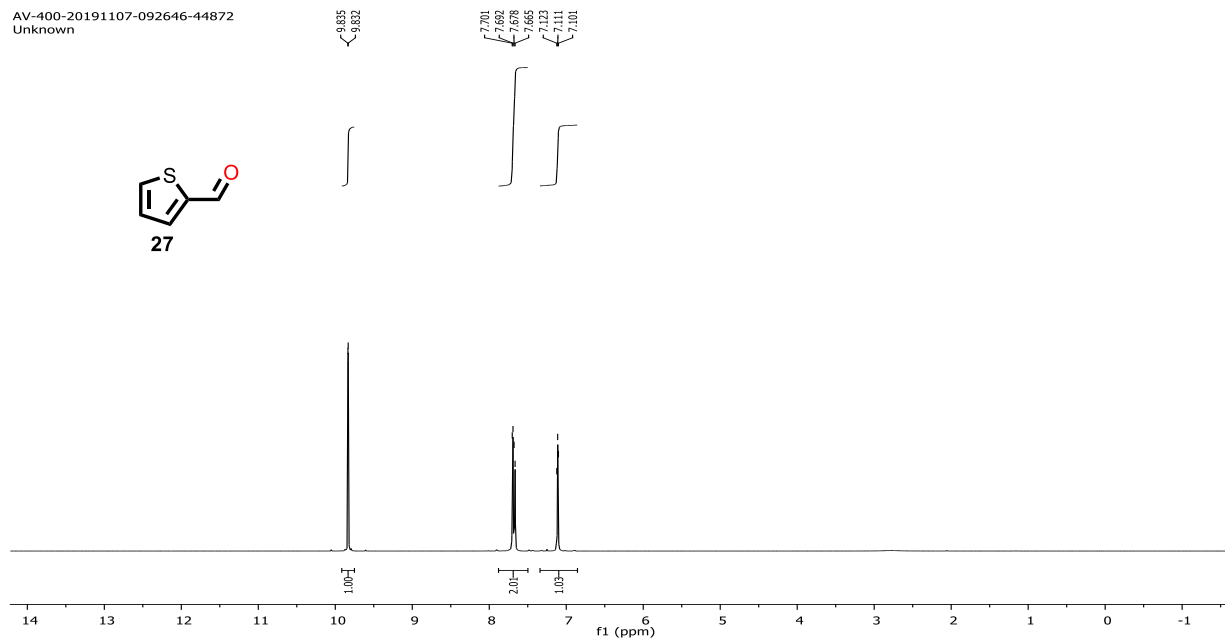


^{13}C NMR spectrum of compound 26 (DMSO-d_6 , 125 MHz)



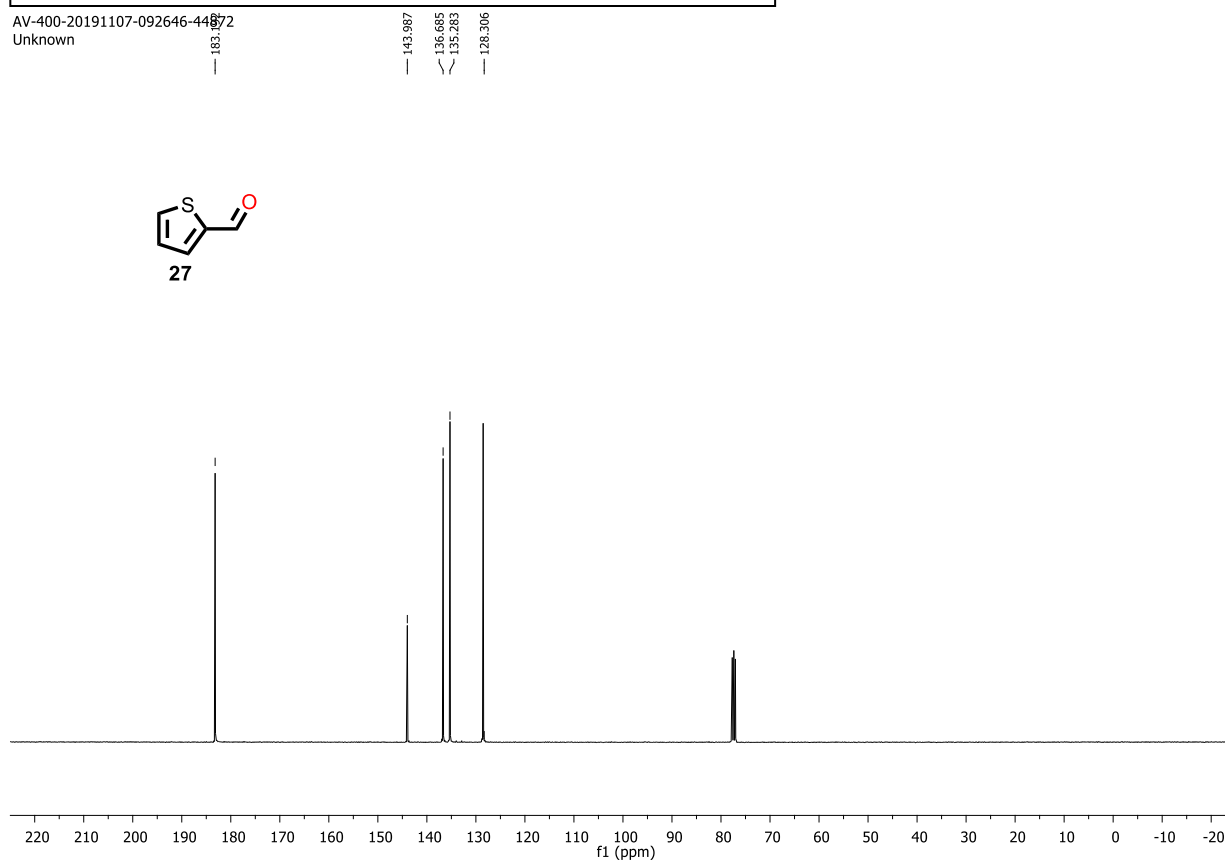
¹H NMR spectrum of compound 27 (CDCl₃, 400 MHz)

AV-400-20191107-092646-44872
Unknown

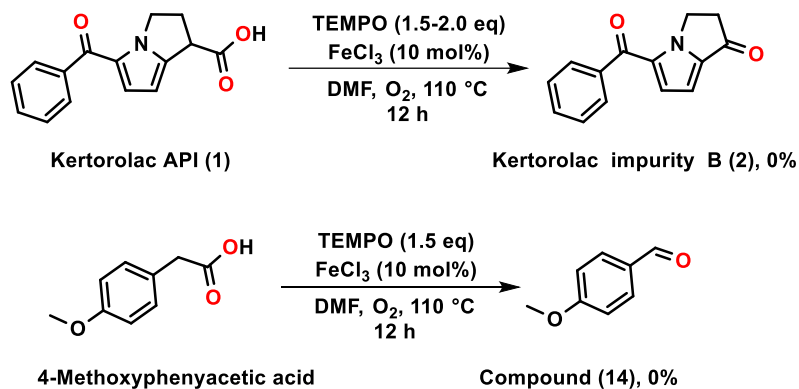


¹³C NMR spectrum of compound 27 (CDCl₃, 100 MHz)

AV-400-20191107-092646-44872
Unknown

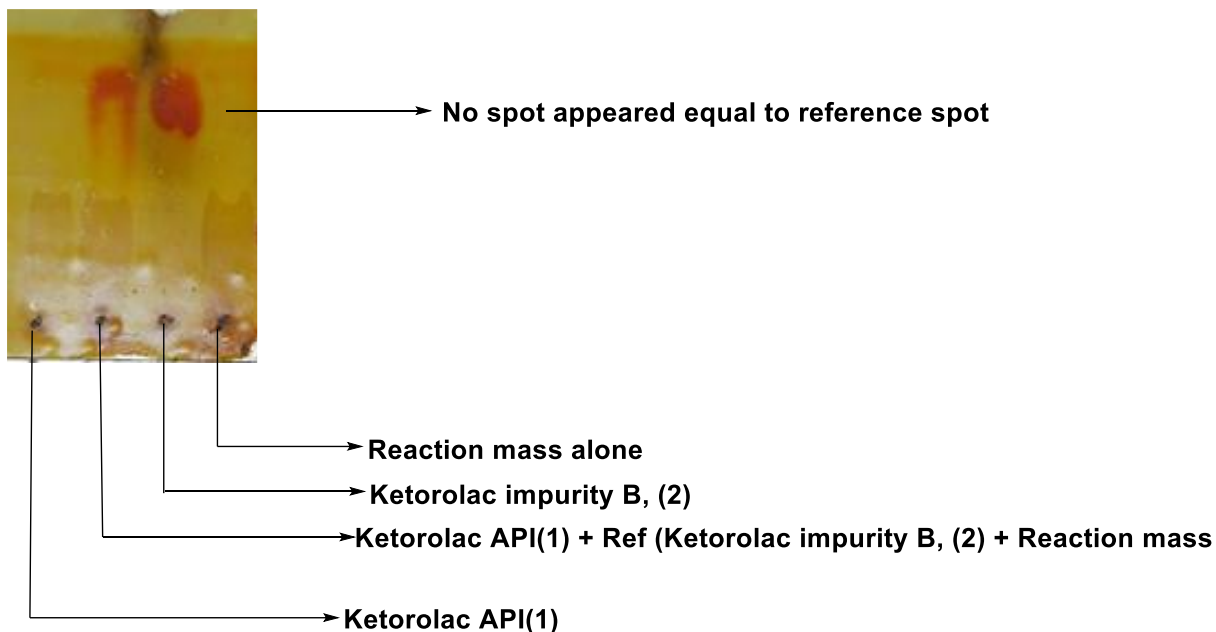


Few control experiments were carried out to elucidate the reaction mechanism. Since the oxygen employing as an oxidant, radical trapping experiments were conducted by using 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) with ketorolac API (1), and 4-methoxy phenylacetic acid under optimized reaction conditions and the reaction was monitored by TLC, even after 24 h no expected spot was identified with reference to the earlier synthesized compound 2. These results showed that the reactions were inhibited by TEMPO and the formed radicals were suppressed (Scheme 1). For the reference TLC profile is shown below (Fig. 1)



Scheme 1. Control experiments

TLC profile; Stain; 2,4-dinitrophenyl hydrazine (DNP) (PMA)



TLC profile; Stain; Phosphomolybdic acid (PMA)

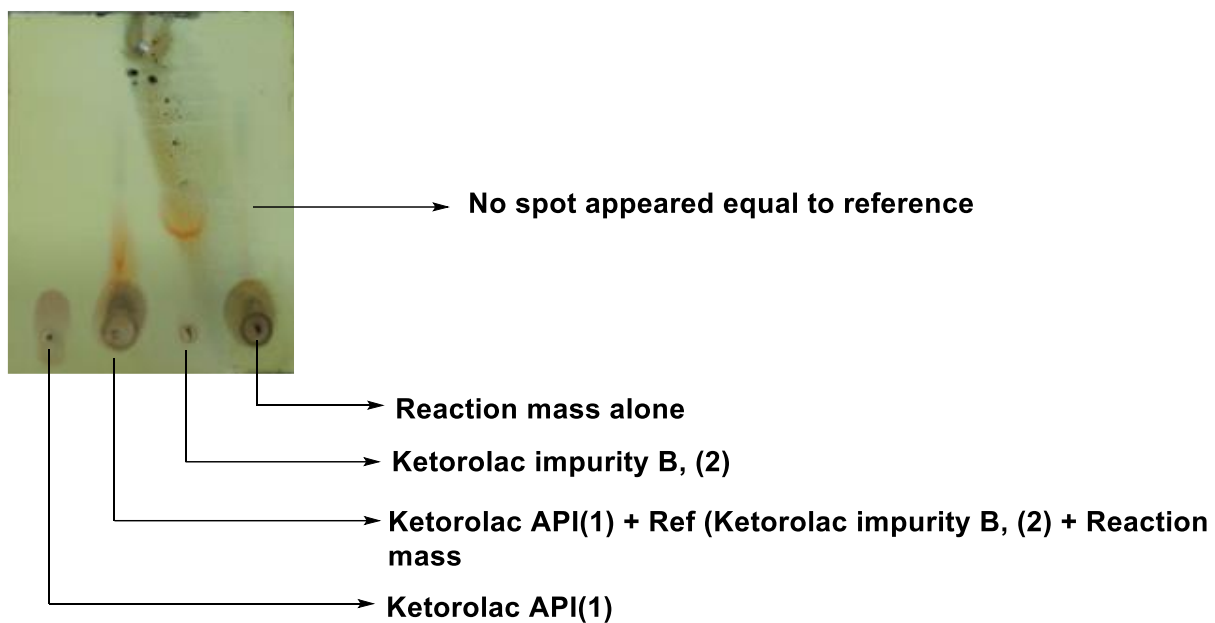


Fig. 1. TLC profile of control experiments

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