Electronic Supplementary Material (ESI) for New Journal of Chemistry.

Supporting Information

An Efficient Merging of DBU/Enolate and DBU/Benzyl Bromide Organocycles for the Synthesis of alpha Benzylated 1-Indanone Derivatives

Shikha Singh,[a] Laxmikant Trivedi,[a] Prema G. Vasudev,[a] Daniele Passarella,[b]and Arvind S. Negi*[a]

[a] CSIR-Central Institute of Medicinal and Aromatic Plants, Lucknow-226015,India

[b]Universitrà degli Studi di Milano, Dept of Chemistry, Via Golgi 19, 20133 Milano, Italy.

*E-mail: as.negi@cimap.res.in; arvindcimap@rediffmail.com

Table of Contents

1. General Information:

Melting points (mp) were determined on E-Z Melt automated MP apparatus, Stanford Research System, USA and were uncorrected. Reactions were monitored on Merck precoated TLC plates, visualizing in UV (254 and 365 nm). Column chromatography was carried out on silica gel (100–200 mesh, Thomas Baker, India). FT-NMR spectra were obtained on Bruker–Advance 500 MHz using tetramethylsilane as internal standard, using $CDCl_3$ as solvent and chemical shifts expressed in δ ppm. All the 1 H and 13C NMR are reported. The abbreviations used in 1 H NMR are as; s, singlet; d, doublet; t, triplet; dd, double doublet; bs, broad singlet; bd, broad doublet; bt, broad triplet; m, multiplet. Electrospray ionization mass spectrometry (ESI-MS) was obtained on Shimadzu LC-MS and HRMS was recorded on Agilent 6520 Q-TOF after dissolving compounds in methanol. Diastereomeric ratio (dr) of compounds **6** was determined by 1HNMR.

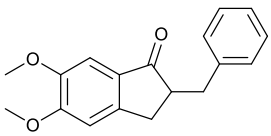
2. Experimental Section:

2.1 Representative Procedure for the synthesis of 2-benzyl-5,6-dimethoxy-2,3-dihydro-1H-inden-1-one (3a):

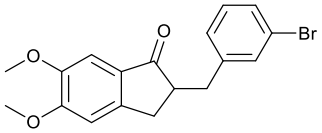
To a solution of 5,6-dimethoxy-1-indanone**1** (0.050 g, 0.26mmoles, 1.0 equiv), benzyl bromide(0.05 mL, 0.31 mmoles, 1.2 equivalent) and DBU (0.08 mL,0.52 mmole, 2 equiv., added slowly over 5- 10 min.) in MeCN (10 mL), then the reaction was stirred for 8 hr 50 °C temperature. After completion of the reaction (monitored by TLC), the reaction was quenched with 1 M aq HCl and was extracted with ethyl acetate, washed with water, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. Desired 2-benzyl-5,6-dimethoxy-2,3-dihydro-1H-inden-1-one (**3a**)product was obtained as white solid after column chromatography (100-200 mesh silica; Hexane/Ethyl Acetate 8:2), (0.053 g, white solid, 94% yield).

Analytical Data:

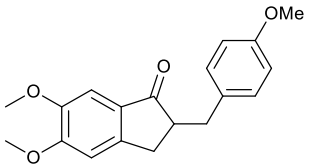
3.2 Characterization of prducts (3):



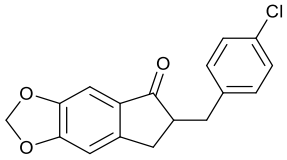
2-benzyl-5,6-dimethoxy-2,3-dihydro-1H-inden-1-one (3a): white solid, mp 126-128 °C 0.054 g, yield 94%,; **^{1}H NMR** (500 MHz, $CDCl_3$) δ_H2.68-2.73 (m, 1H), 2.83 (dd, *J*1=16.8 Hz, *J*2=3.3 Hz, 1H),3.03-3.06 (m, 1H), 3.10-3.15 (m, 1H), 3.44 (dd, *J*1=14 Hz, *J*2=4.20 Hz, 1H), 3.97 (s, 3H), 3.99 (s, 3H), 6.87 (s, 1H), 7.26-7.31(m, 4 H), 7.33-7.37 (m, 2H);**^{13}C NMR** (100 MHz, $CDCl_3$) δ_C31.9, 37.3, 49.1, 56.1, 56.2, 104.5, 107.4, 126.3, 128.5, 128.9, 129.27, 139.8, 148.9, 149.5, 155.6, 206.4 ;**ESI-HRMS** calcd for $C_{18}H_{19}O_3$ $[M+H]^+$: 283.1329; found: 283.1329.



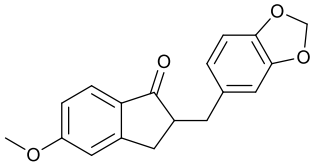
2-(3-bromobenzyl)-5,6-dimethoxy-2,3-dihydro-1H-inden-1-one (3b): Brown solid, mp 123-125 ºC, 0.057 g, yield 78%; **^{1}H NMR** (500 MHz, $CDCl_3$) δ_H 2.69-2.73 (m, 1H), 2.83 (dd, *J*1=16.0 Hz, *J*2=3.2 Hz, 1H),3.02-3.07 (m, 1H), 3.10-3.14 (m, 1H), 3.43 (dd, *J*1=13.95 Hz, *J*2= 4.15 Hz, 1H), 3.97 (s, 3H), 3.99 (s, 3H), 6.87 (s, 1H), 7.27-7.29(m, 3H), 7.34-7.37 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ_C 31.9, 37.3, 49.1, 56.1, 56.2, 104.4, 107.2, 126.3, 128.5, 129.27,130.9, 139.8, 148.9, 149.5, 155.6, 206.5 ;**ESI-HRMS** calcd for$C_{18}H_{17}BrO_3$ $[M+H]^+$: 361.0434; found: 361.0436.



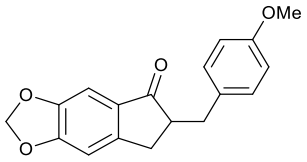
5,6-dimethoxy-2-(4-methoxybenzyl)-2,3-dihydro-1H-inden-1-one (3c): White solid, mp 125-127 ºC, 0.051 g, yield 82%; **^{1}H NMR** (500 MHz, $CDCl_3$) δ_H 2.60-2.65 (m, 1H), 2.76 (dd, *J*1=17.0 Hz, *J*2=3.3 Hz, 1H), 2.01-2.96 (m, 1H), 3.03-3.08 (m, 1H), 3.28 (dd, *J*1=18 Hz, *J*2=4.3 Hz, 1H), 3.78 (s, 3H), 3.90 (s, 3H), 3.93 (s, 3H), 6.81-6.84 (m, 3H), 7.13-7.16 (m. 2 H), 7.12 (s, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ_C 31.8, 36.4, 49.3, 55.2, 56.1, 56.2, 104.5, 107.4, 113.9, 129.3, 129.9, 131.7, 149.0. 149.5, 155.6, 158.1, 206.6;**ESI-HRMS** calcd for $C_{19}H_{21}O_4$ $[M+H]^+$: 313.1434; found: 313.1437.



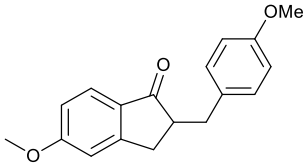
6-(4-chlorobenzyl)-6,7-dihydro-5H-indeno[5,6-d][1,3]dioxol-5-one (3d): yellow oil, 0.055 g, yield 65%; **^{1}H NMR** (500 MHz, $CDCl_3$) δ_H 2.63-2.77 (m, 2H), ,3.00-3.08 (m, 2H), 3.38 (dd, *J*1=14.1 Hz, *J*2=4.1 Hz, 1H), 6.07 (s, 2H), 6.77 (s, 1H), 7.13-7.18(m, 1 H), 7.21-7.33 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ_C 32.1, 37.2, 49.4, 102.2, 102.5, 105.7, 126.3. 128.5, 128.9, 130.3, 131.1, 139.7, 148.3, 151.2, 154.4, 205.7; **ESI-HRMS** calcd for $C_{17}H_{14}ClO_3$ $[M+H]^+$: 301.0626; found: 301.0627.



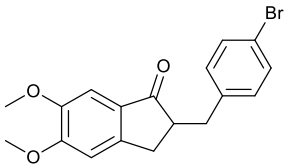
2-(benzo[d][1,3]dioxol-5-ylmethyl)-5-methoxy-2,3-dihydro-1H-inden-1-one (3e): White solid, mp 118-120 ºC, 0.080g, yield 87%; **^{1}H NMR** (500 MHz, $CDCl_3$) δ_H 2.59-2.64 (m, 1H), 2.82 (dd, *J*1=17.2 Hz, *J*2=4.05 Hz, 1H),2.92-2.97 (m, 1H), 3.10-3.15 (m, 1H), 3.29 (dd, *J*1=14 Hz, *J*2=4.4 Hz, 1H), 3.88 (s, 3H), 5.94 (s, 2H), 6.68-6.71 (m, 1 H), 6.74-6.76 (m, 2H), 6.85 (s, 1 H), 6.92 (dd, *J*1=8.6 Hz, *J*2= 2.2 Hz, 1H), 7.72 (d, *J* = 8.5 Hz ,1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ_C32.4, 36.9, 49.2, 55.6, 100.9, 108.2, 109.3, 109.7, 115.4, 121.8, 125.7, 129.8, 133.5, 143.5, 146.0, 147.7, 156.6, 165.4, 205.9;**ESI-HRMS** calcd for $C_{18}H_{17}O_4$ $[M+H]^+$: 297.1121; found: 297.1127.



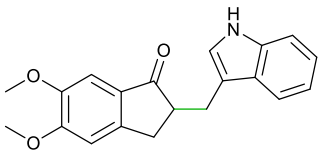
6-(4-methoxybenzyl)-6,7-dihydro-5H-indeno[5,6-d][1,3]dioxol-5-one (3f): Yellow solid, mp 98-101 ºC, 0.059 g, yield 71%; **^{1}H NMR** (500 MHz, $CDCl_3$) δ_H 2.68-2.67 (m, 1H), 2.75 (dd, *J*1=14.3 Hz, *J*2=3.3 Hz, 1H),2.95-2.99 (m, 1H), 3.01-3.07 (m, 1H), 3.29 (dd, *J*1=14 Hz, *J*2=4.3 Hz, 1H), 3.81 (s, 3H), 6.07 (s, 2H), 6.77(s, 1H), 6.86-6.83 (m, 2 H), 7.13-7.17 (m, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ_C 32.0, 36.3, 49.5, 55.3, 102.1, 102.5, 113.9, 129.9, 131.2, 131.6, 148.3, 151.3, 154.3, 158.1, 205.9;**ESI-HRMS** calcd for $C_{18}H_{17}O_4$ $[M+H]^+$: 297.1121; found: 297.1127.



5-methoxy-2-(4-methoxybenzyl)-2,3-dihydro-1H-inden-1-one (3g): Yellow oil, 0.065 g, yield 74%; **^{1}H NMR** (500 MHz, $CDCl_3$) δ_H 2.62-2.67 (m, 1H), 2.83 (dd, *J*1=17.3 Hz, *J*2=3.9 Hz, 1H), 2.96-2.98(m, 1H), 3.09-3.14 (m, 1H), 3.31 (dd, *J*1=14 Hz, *J*2=3.9 Hz, 1H), 3.80 (s, 3H), 3.88 (s, 3H), 6.84-6.87 (m, 3H), 6.90-6.92 (m, 1 H), 7.17(dd, *J*1=6.6 Hz, *J*2=1.95 Hz, 1H), 7.73 (d, *J* =8.55 Hz 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ_C 32.1, 36.3, 49.2, 55.3, 55.6, 109.7, 113.9, 115.4, 125.7, 129.9, 131.7, 156.7, 158.1, 165.4, 206.2;**ESI-HRMS** calcd for $C_{18}H_{19}O_3$ $[M+H]^+$: 283.1329; found: 283.1328.



2-(4-bromobenzyl)-5,6-dimethoxy-2,3-dihydro-1H-inden-1-one (3h): Yellow solid, mp. 126-129 ºC, 0.071 g, yield 73%; **^{1}H NMR** (500 MHz, $CDCl_3$) δ_H 2.60-2.65 (m, 1H), 2.76 (dd, *J*1=17.0 Hz, *J*2=3.4 Hz, 1H), 2.91-2.96 (m, 1H), 3.03-3.08 (m, 1H), 3.28 (dd, *J*1=14 Hz, *J*2=4.1 Hz, 1H), 3.91 (s, 3H), 3.93 (s, 3H), 6.80-6.83 (m, 3H), 7.13-7.15 (m, 2H), 7.19 (s, 1H);**^{13}C NMR** (100 MHz, $CDCl_3$) δ_C32.7, 37.3, 50.2, 56.9, 57.1, 105.3, 108.3, 114.8, 130.2, 130.7, 132.6, 133.9, 149.8, 156.5, 159.0, 207.5 ;**ESI-HRMS** calcd for $C_{18}H_{17}BrO_3$ $[M+H]^+$: 361.0434; found: 361.0435.



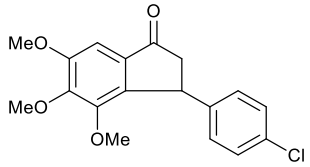
2-((1H-indol-3-yl)methyl)-5,6-dimethoxy-2,3-dihydro-1H-inden-1-one (3i):off-white solid, mp. 197-199 ºC, 0.027 g, yield 32%; **^{1}H NMR** (500 MHz, $CDCl_3$) δ_H 2.81-2.87 (m, 1H), 2.92-2.95 (m, 1H),3.12-3.16 (m, 1H), 3.49 (dd, *J*1=14.8 Hz, *J*2=3.6 Hz, 1H), 3.93 (s, 3H), 3.94 (s, 3H), 6.80 (s, 1H), 7.04 (d, *J* =2.1 Hz, 1 H), 7.14-7.17 (m, 1 H), 7.20-7.24 (m, 2 H), 7.38 (d, *J*= 8.05 Hz, 1 H);**^{13}C NMR** (100 MHz, $CDCl_3$) δ_C 26.6, 32.4, 48.5, 56.1, 56.2,

104.4, 107.5, 111.1, 113.9, 118.9, 119.4, 122.0, 122.1, 127.8, 129.5, 136.2, 149.3, 149.4, 155.5, 207.1;**ESI-HRMS** calcd for $C_{20}H_{20}NO_3$ $[M+H]^+$: 322.1438; found 322.1431.

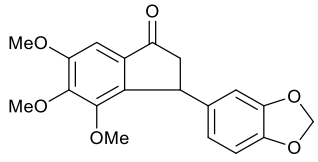
2.2 <u>Representative Procedure for the synthesis of 3-(4-chlorophenyl)-4,5,6-trimethoxy-2,3-dihydro-1H-inden-1-one (5a):</u>

To a solution of **4a** (0.5 g, 1.5 mmol) in DCE (30 mL), was added a solution of SbF_5 (10 mol%) in EtOH (1 equiv.) (0.008 mL of SbF_5 in 0.07 mL EtOH). After completion of the reaction (monitored by TLC), mixture was diluted with ether and filtered through a short silica gel column chromatography. Filtrate was concentration to dryness, and purified by silica gel column chromatography as described in the given literature (*Org. Lett*., **2008**, *10*, 1783), (hexane/AcOEt = 7: 3) afforded **5a** (0.368g, 74% yield) as yellow solid.

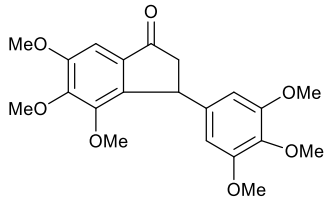
3.2 <u>Characterization of prducts (5)</u>:



3-(4-chlorophenyl)-4,5,6-trimethoxy-2,3-dihydro-1H-inden-1-one (5a):yellow solid, mp 103-107 °C, 0.368g, yield 74%; **^{1}H NMR** (500 MHz, $CDCl_3$) δ_H 2.55 (dd, *J*1=19.3 Hz, *J*2=2.7 Hz, 1H), 2.18 (dd, *J*1=19.3 Hz, *J*2=8.1 Hz, 1H), 3.39 (s, 3H), 3.89 (s, 3H), 3.91 (s, 3H), 4.55 (dd, *J*1=8.0 Hz, *J*2=2.6 Hz, 1H),7.02-7.05 (m, 2H), 7.07 (s, 1H), 7.23-7.25 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ_C 40.9, 47.0, 56.3, 60.1, 60.9, 100.3, 128.62, 128.8, 132.2, 132.3, 142.9, 144.0, 148.7, 150.3, 155.1, 204.9;**ESI-HRMS** calcd for $C_{18}H_{18}ClO_4$ $[M+H]^+$: 333.0888; found: 333.0886.

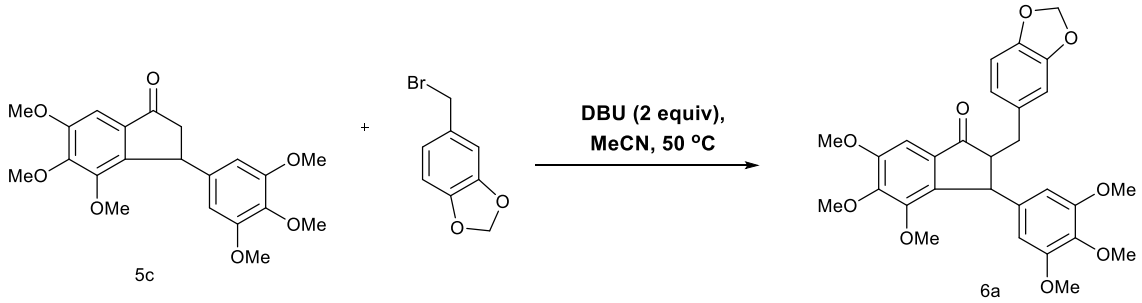


3-(benzo[d][1,3]dioxol-5-yl)-4,5,6-trimethoxy-2,3-dihydro-1H-inden-1-one (5b): Yellow solid, mp 99-103 °C, 0.365g, yield 71%; **^{1}H NMR** (500 MHz, $CDCl_3$) δ_H2.55 (dd, *J*1=19.2 Hz, *J*2= 2.5 Hz, 1H), 3.15 (dd, *J*1=19.3 Hz, *J*2=8.0 Hz, 1H), 3.45 (s, 3H), 3.90 (s, 3H), 3.91 (s, 3H), 4.51 (dd, *J*1=8.0 Hz, *J*2=2.5 Hz, 1H), 5.91 (dd, *J*1=4.9 Hz, *J*2=1.4 Hz, 2H), 6.51 (d, *J* = 1.8Hz, 1H), 6.61 (dd, *J*1=8.0 Hz, *J*2=1.8 Hz, 1H), 6.72 (d, *J* = 7.9 Hz, 1H), 7.07 (s, 1H);**^{13}C NMR** (100 MHz, $CDCl_3$) δ_C41.3, 47.3, 56.3, 60.2, 60.9, 100.3, 100.9, 107.5, 108.3, 120.4, 132.2, 138.3, 144.4, 146.2, 147.9, 148.8, 150.4, 154.9, 205.2;**ESI-HRMS** calcd for $C_{19}H_{19}O_6$ $[M+H]^+$: 343.1176; found: 343.1179.



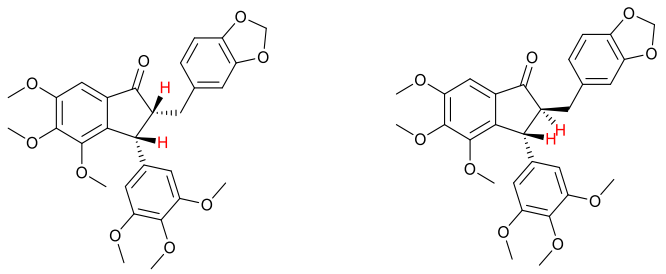
4,5,6-trimethoxy-3-(3,4,5-trimethoxyphenyl)-2,3-dihydro-1H-inden-1-one (5c): Brown solid, mp 102-104 ºC, 0.402g, yield 80%; **^{1}H NMR** (500 MHz, $CDCl_3$) δ_H2.61 (dd, *J*1=19.5 Hz, *J*2=3.0 Hz, 1H), 3.18 (dd, *J*1=19.5 Hz, *J*2=3.0 Hz, 1H), 3.41 (s, 3H), 3.77 (s, 3H), 3.80 (s, 1H), 3.90 (s, 3H), 3.92 (s, 3H), 4.51 (dd, *J*1=8.0 Hz, *J*2=2.5 Hz, 1H), 6.29 (s, 2H), 7.08 (s, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ_C 41.9, 47.1, 56.1, 56.2, 60.2, 60.9, 100.4, 104.3, 132.2, 136.7, 140.1, 144.2, 148.8, 150.4, 153.3, 154.9, 205.4;**ESI-HRMS** calcd for $C_{21}H_{25}O_7$ $[M+H]^+$: 389.1595; found: 389.1598.

2.3 Representative Procedure for the synthesis of 2-(benzo[*d*][1,3]dioxol-5-ylmethyl)-4,5,6-trimethoxy-3-(3,4,5-trimethoxyphenyl)-2,3-dihydro-1*H*-inden-1-one (6a):



To a solution of **5c** (0.050 g, 0.13 mmoles, 1.0 equiv), piperonyl bromide (0.033g, 0.15 mmoles, 1.2 equivalent) and DBU (0.04 mL, 0.26 mmole, 2 equiv.) was added (slowly over a period 5-10 min.) in MeCN (10 mL), then the reaction was stirred for 8 h at 50 ºC temperature. After completion of the reaction (monitored by TLC), the reaction was quenched with 1 M aq HCl, and was extracted with ethyl acetate, washed with water, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. Desired 2-(benzo[d][1,3]dioxol-5-ylmethyl)-4,5,6-trimethoxy-3-(3,4,5-trimethoxyphenyl)-2,3-dihydro-1H-inden-1-one(**6a**) product was obtained as white solid after column chromatography (100-200 mesh silica; Hexane/Ethyl Acetate 6:4), (0.041 g, white solid, 60% yield, dr was determined by 1H NMR; cis:trans = 97:03).

3.3 Characterization of prducts (6)[a]:



Cis-2-(benzo[d][1,3]dioxol-5-ylmethyl)-4,5,6-trimethoxy-3-(3,4,5-trimethoxyphenyl)-2,3-dihydro-1H-inden-1-one (6a): White solid, mp 104-108 ºC, 0.041 g, yield 60%; **Cis**:

Trans [**97**:03 dr]; **^{1}H NMR**(500 MHz, Acetone-d6) δ_H 2.14-2.19 (m, 1H), 3.17 (dd, *J*1=15 Hz, *J*2=3.9 Hz, 1H), 3.3-3.43 (m, 1H), 3.45 (s, 3H), 3.60 (s, 6H), 3.69 (s, 3H), 3.85 (s, 3H), 3.95 (s, 3H), 4.68 (cis, d, *J*=7.7Hz, 1H) 5.93-5.94 (m, 4H), 6.40 (d, *J*=7.9 Hz, 1H), 6.7(d, *J*=1.6 Hz, 1H), 6.68 (d, *J*= 7.9 Hz, 1H), 7.09 (s, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ_C 32.4, 47.3, 55.7, 57.0, 57.3, 61.3, 61.4, 61.8, 101.7, 102.4, 109.2, 110.6, 122.9, 133.0, 135.6, 137.9, 144.1, 147.3, 154.7, 156.8, 206.8;**ESI-HRMS** calcd for $C_{29}H_{31}O_9$ $[M+H]^+$: 523.1963; found: 523.1964.

X-Ray Data Collection and Structure Refinement Details 6a:

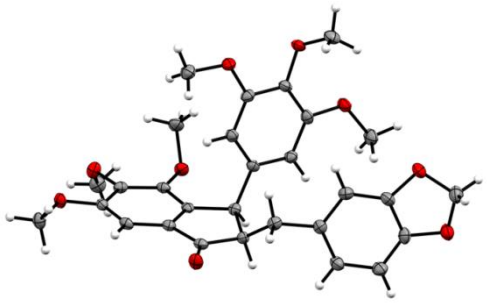


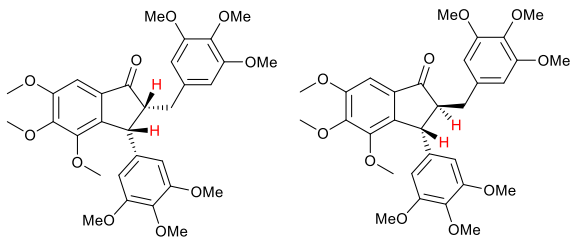
Figure 1 ORTEP diagram drawn with 50% ellipsoid probability for non-H atoms of the molecules in the asymmetric unit of the crystal structure of compound **6a (CCDC 2128756)** determined at 293 K.

Compound 6a: A good quality single crystal of size 0.25 x 0.10 x 0.02 mm, was selected under a polarizing microscope and was mounted on a glass fiber for data collection. Single crystal X-ray data for compound **6a** were collected on the Bruker AXS SMART APEX CCD diffractometer using the monochromated Mo-Kα radiation (λ = 0.71073Å). Data collection was performed using combinations of ϕ and ω scans at room temperature (293 K). Cell determination, data collection and data reduction was performed using the Bruker SMART and SAINT softwares [1]. Structure solution and refinement were performed using SHELXS-97 [2] and SHELXL-14 [3]. Refinement of coordinates and anisotropic thermal parameters of non-hydrogen atoms were carried out by the full-matrix least-squares method. The hydrogen atoms attached to carbon atoms were generated with idealized geometries and isotropically refined using a riding model.

1. Bruker (2012) *SMART, SAINT*. Bruker AXS Inc., Madison, Wisconsin, USA
2. Sheldrick, G. M. Acta Crystallogr., Sect. A 2008, 64, 112–122.
3. Sheldrick, G. M. *Acta Cryst. Sec. C* 2015, 71, 3-8.

Table 1 Crystal data and structure refinement details for Compound **6a**

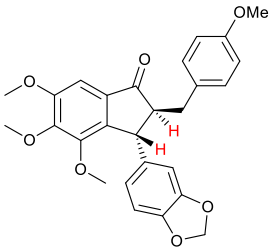
Empirical formula	C_{29} H_{30} O_9
Formula weight	522.5
Crystal System	Triclinic
Space group	P -1
Unit Cell	a (Å) 10.9156 (5), b (Å) 12.4782 (7), c (Å) 19.3575 (9),α (°) = 84.339 (2), β (°) = 81.536 (1), γ (°) =74.961 (1)
V (Å3)	2513.5 (2)
Z	4
D_c (g/cm3)	1.381
F000	1104
μ (mm^{-1})	0.103
Total reflections	28286
Unique reflections	8550
Reflections [I > 2σ (I)]	6359
Parameters	697
R_{int}	0.0468
Goodness-of-fit	0.994
R [I > 2σ (I)]	0.0431
wR	0.1004
CCDC No.	**2128756**



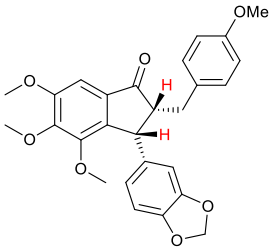
Cis $J_{2,3}$ = 7.2 Hz (70%) Trans $J_{2,3}$ = 2.6 Hz (30%)

Cis-4,5,6-trimethoxy-2-(3,4,5-trimethoxybenzyl)-3-(3,4,5-trimethoxyphenyl)-2,3-dihydro-1H-inden-1-one (6b): Brown solid, mp 109-113 ºC, 0.036 g, yield 49%; **Cis**: Trans (**70**:30 dr); **^{1}H NMR** (500 MHz, $CDCl_3$) δ_H 2.17 (dd, *J*1=14.4 Hz, *J*2=14.2 Hz, 1H), 3.33-3.44 (m, 5 H), 3.62 (s, 6H), 3.75 (s, 6H), 3.78 (s, 3H), 3.80 (s, 3H), 3.89 (s, 3H), 3.93 (s, 3H), 4.57(d, *J*=7.2 Hz, 1H), 5.09 (s, 1H), 6.05 (s, 2H), 6.33-6.40 (m, 1H), 7.14 (s,

1H);**^{13}C NMR** (100 MHz, $CDCl_3$) δ_C 32.4, 45.8, 54.8, 55.9, 56.0, 56.3, 60.3, 60.8, 60.9, 60.96, 100.4, 105.5, 131.0, 135.5, 135.9, 136.1, 136.7, 142.9, 148.8, 150.1, 152.9, 154.9, 205.7;**ESI-HRMS** calcd for $C_{31}H_{36}O_{10}$ $[M+H]^+$: 569.2381; found: 569.2380.

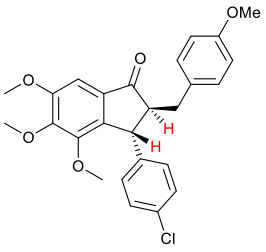


Trans $J_{2,3}$ = 2.7 Hz (78%)

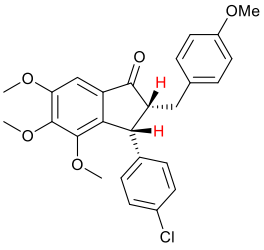


Cis $J_{2,3}$ = 7.3 Hz (22%)

Trans-3-(benzo[d][1,3]dioxol-5-yl)-4,5,6-trimethoxy-2-(4-methoxybenzyl)-2,3-dihydro-1H-inden-1-one (6c): Brown oil, 0.045g, yield 65%; Cis: **Trans** (22:**78** dr); **^{1}H NMR** (500 MHz, $CDCl_3$) δ_H 2.75-2.85 (m, 1H), 3.22 (dd, *J*1=13.4 Hz, *J*2=4.3 Hz, 1H), 3.39 (s, 3H), 3.81 (s, 3H), 3.91 (s, 3H), 3.94 (s, 3H), 4.17 (d, *J*=2.7 Hz, 1H), 5.89-5.89 (m, 2H), 6.22 (d, *J*=15 Hz, 1H),6.26 (dd, *J*1=8 Hz, *J*2=1.8 Hz, 1H), 6.61 (d, *J*=7.9 Hz, 1H), 6.76-6.83 (m, 2H), 7.09 (s, 1H), 7.11-7.14 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ_C36.3, 46.8, 55.3, 56.3, 60.0, 60.1, 60.9, 100.5, 100.9, 107.5, 108.1, 113.8, 120.3, 129.6, 130.3, 130.9, 131.6, 138.1, 143.1,145.9, 147.6, 148.9, 150.4, 154.9, 158.3, 206.6;**ESI-HRMS** calcd for $C_{27}H_{27}O_7$ $[M+H]^+$: 463.1751; found: 463.1754.

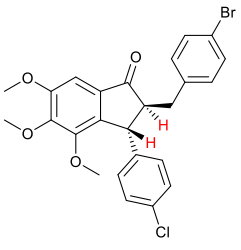


Trans $J_{2,3}$ = 2.9 Hz (89%)

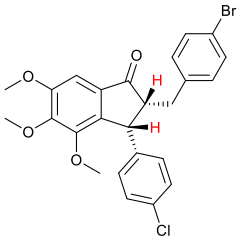


Cis $J_{2,3}$ = 7.1 Hz (11%)

Trans-3-(4-chlorophenyl)-4,5,6-trimethoxy-2-(4-methoxybenzyl)-2,3-dihydro-1H-inden-1-one (6d): Yellow oil, 0.051 g, yield 75%; Cis: **Trans** (11:**89** dr); **^{1}H NMR** (500 MHz, $CDCl_3$) δ_H 2.70-2.82 (m, 2H), 3.19-3.23 (m, 1H), 3.30 (s, 3H), 3.76 (s, 3H), 3.86 (s, 3H), 3.90 (s, 3H), 4.17 (d, *J*=2.9 Hz, 1H), 6.66 (d, *J*2=8.4 Hz, 2H), 6.78 (d,*J*2=8.5 Hz, 2H), 7.06-7.10 (m, 5H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ_C 36.3, 46.6, 55.3, 56.2, 59.9, 60.8, 100.6, 113.9, 128.5, 128.6, 130.2, 130.8, 131.6, 131.9, 142.6, 142.8, 148.9, 150.3, 155.2, 158.4, 206.1;**ESI-HRMS** calcd for $C_{26}H_{26}ClO_5$ $[M+H]^+$: 453.1463; found: 453.1467.



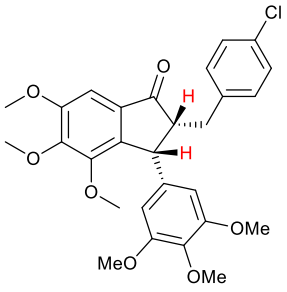
Trans $J_{2,3}$ = 2.9 Hz (92%)



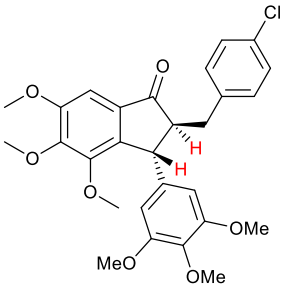
Cis $J_{2,3}$ = 7.4 Hz (8%)

Trans-2-(3-bromobenzyl)-3-(4-chlorophenyl)-4,5,6-trimethoxy-2,3-dihydro-1H-inden-1-one (6e): Transparent oil, 0.049g, yield 65%; Cis: **Trans** (08:**92** dr); **^{1}H NMR** (500 MHz, $CDCl_3$) δ_H2.75-2.79 (m, 1H), 2.85-2.88 (m, 1H), 3.31-3.35 (m, 4H), 3.89 (s, 3H), 3.93 (s,

3H), 4.21 (d, *J*=2.9 Hz, 1H), 6.64 (d, *J*2=8.5 Hz, 2H), 7.08-7.12 (m, 3H), 7.16-7.28 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ_C37.3, 46.6, 56.3, 59.7, 59.9, 60.8, 100.6, 126.6, 128.4, 128.51, 128.52, 129.3, 131.6, 131.9, 138.8, 142.6, 142.8, 149.0, 150.3, 155.2, 205.8;**ESI-HRMS** calcd for $C_{25}H_{23}BrClO_4$ $[M+H]^+$: 501.0463; found: 501.0465.

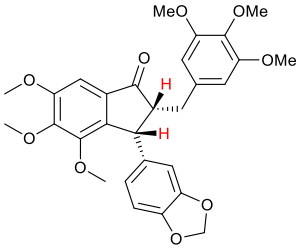


Cis $J_{2,3}$ = 7.2 Hz (89%)



Trans (11%)

Cis-2-(4-chlorobenzyl)-4,5,6-trimethoxy-3-(3,4,5-trimethoxyphenyl)-2,3-dihydro-1H-inden-1-one (6f): White solid, mp 130-133 ºC, 0.049 g, yield 74%; **Cis**: Trans (**89**:11 dr); **^{1}H NMR** (500 MHz, $CDCl_3$) δ_H 2.19-2.24 (m, 1H), 3.35-3.41 (m, 5H), 3.58 (s, 6H), 3.80 (s, 3H), 3.90 (s, 3H), 3.94 (s, 3H), 3.94 (s, 3H), 4.59 (d, *J*=7.2 Hz, 1H), 6.87 (d, *J*=7.0 Hz, 2H), 7.13-7.20 (m, 5H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ_C 32.1, 45.8, 54.4, 55.9, 56.3, 60.3, 60.97, 60.99, 100.4, 125.8, 128.0, 128.6, 131.2, 135.9, 136.7, 139.8, 142.9, 148.7, 150.1, 152.8, 154.9, 205.9;**ESI-HRMS** calcd for $C_{28}H_{30}ClO_7$ $[M+H]^+$: 513.1675; found: 513.1679.

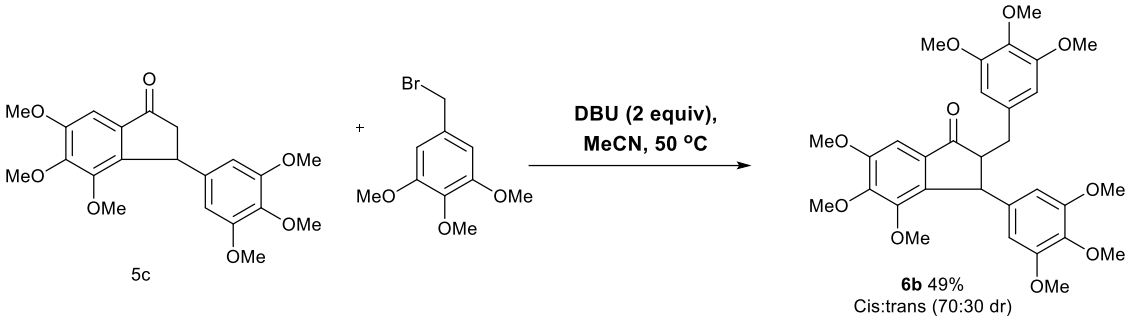


Cis $J_{2,3}$ = 7.3 Hz (100%)

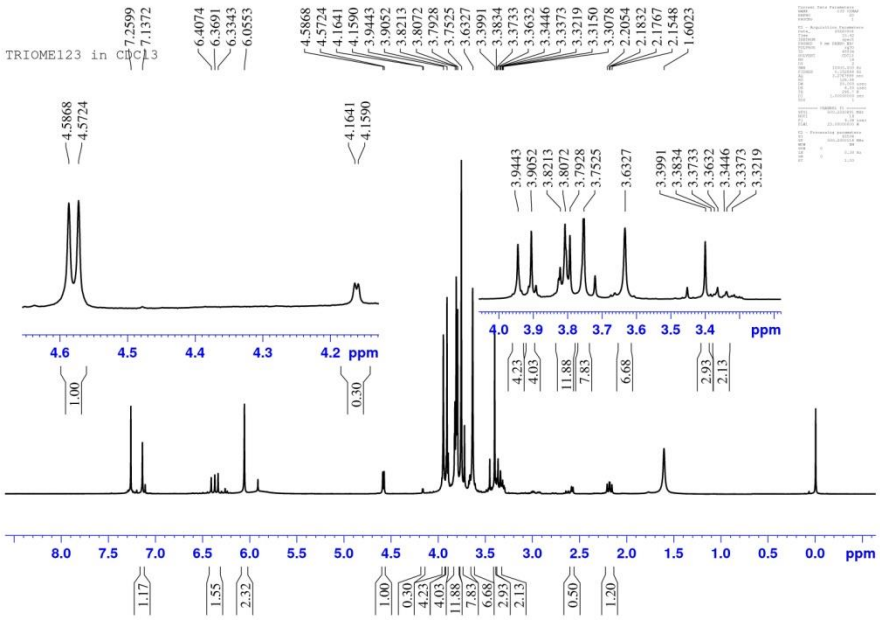
Cis-3-(benzo[d][1,3]dioxol-5-yl)-4,5,6-trimethoxy-2-(3,4,5-trimethoxybenzyl)-2,3-dihydro-1H-inden-1-one (6g): Brown oil, 0.041 g, yield 52%; **Cis**: Trans (**100**:0 dr); **^{1}H NMR** (500 MHz, $CDCl_3$) δ_H 2.14-2.19 (m, 1H), 3.26-3.33 (m, 2H), 3.40 (s, 3H), 3.65 (s, 6H), 3.82 (s, 3H), 3.91 (s, 3H), 3.95 (s, 3H), 4.58 (d, *J*=7.3 Hz, 1H), 5.89-5.90 (m, 2H), 6.30 (d, *J*=7.9 Hz, 1H), 6.38 (d, *J*=1.5 Hz, 1H), 6.64 (d, *J*=7.9 Hz, 1H), 7.13 (s, 1H);**^{13}C NMR** (100 MHz, $CDCl_3$) δ_C 31.8, 45.8, 54.9, 56.0, 56.3, 60.3, 60.9, 61.0, 100.4, 100.7, 107.7, 109.1, 121.4, 131.2, 133.6, 136.0, 136.9, 142.9, 145.6, 147.3, 148.7, 150.1, 152.8, 154.9, 205.7 ;**ESI-HRMS** calcd for $C_{29}H_{31}O_9$ $[M+H]^+$: 523.1963; found: 523.19634.

3.4 Diastereoselectivity of the present method vs Pd/C-Hydrogenetion of chalcone:

1. Synthesis of 6b using present protocol

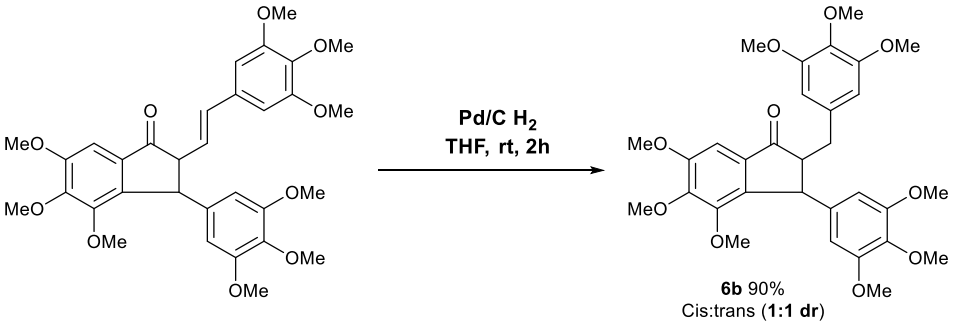


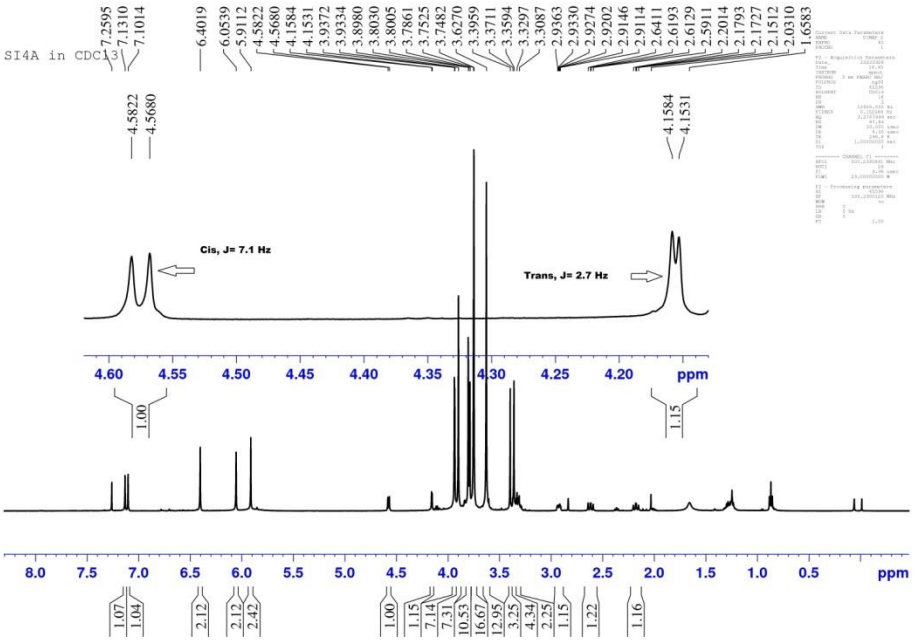
5c



1H NMR (6b): 1:0.3 dr

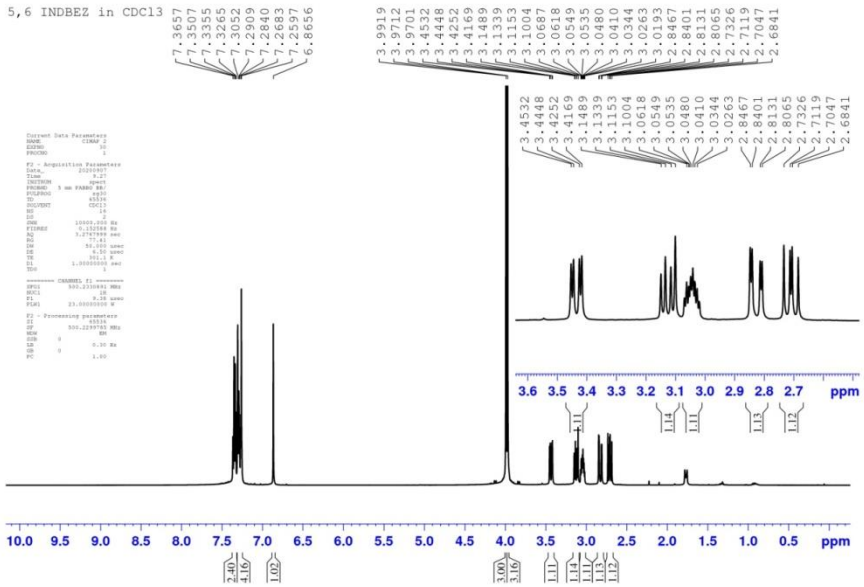
2. Synthesis of 6b by Pd/C hydrogenation:



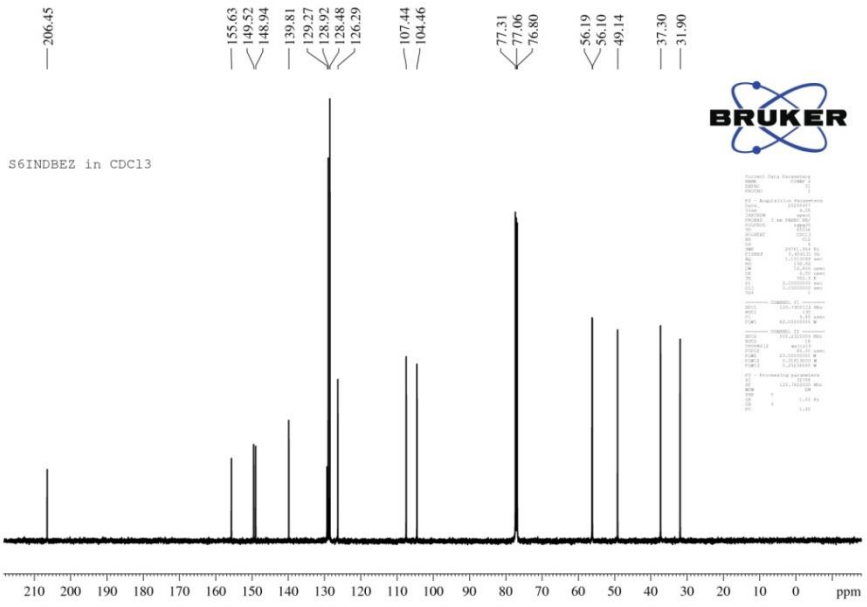


1H NMR **6b** (Pd/C, H_2), (1:1 dr)

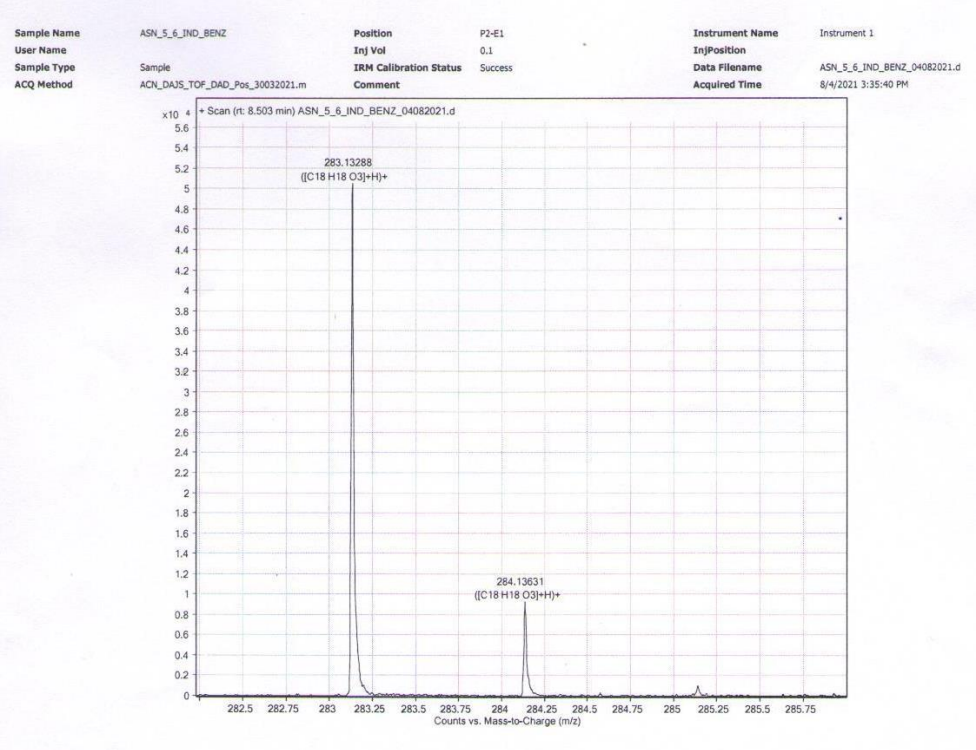
4.1H and 13C NMR Spectra:



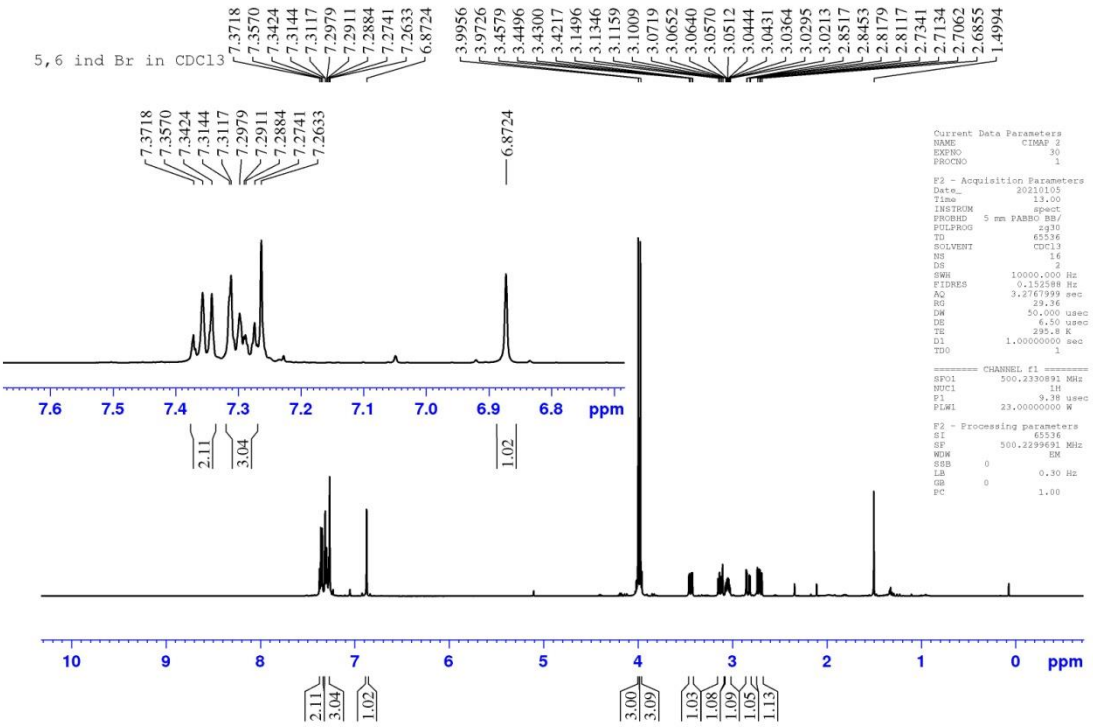
^{1}H NMR Spectra of (**3a)** (500 MHz, $CDCl_3$)



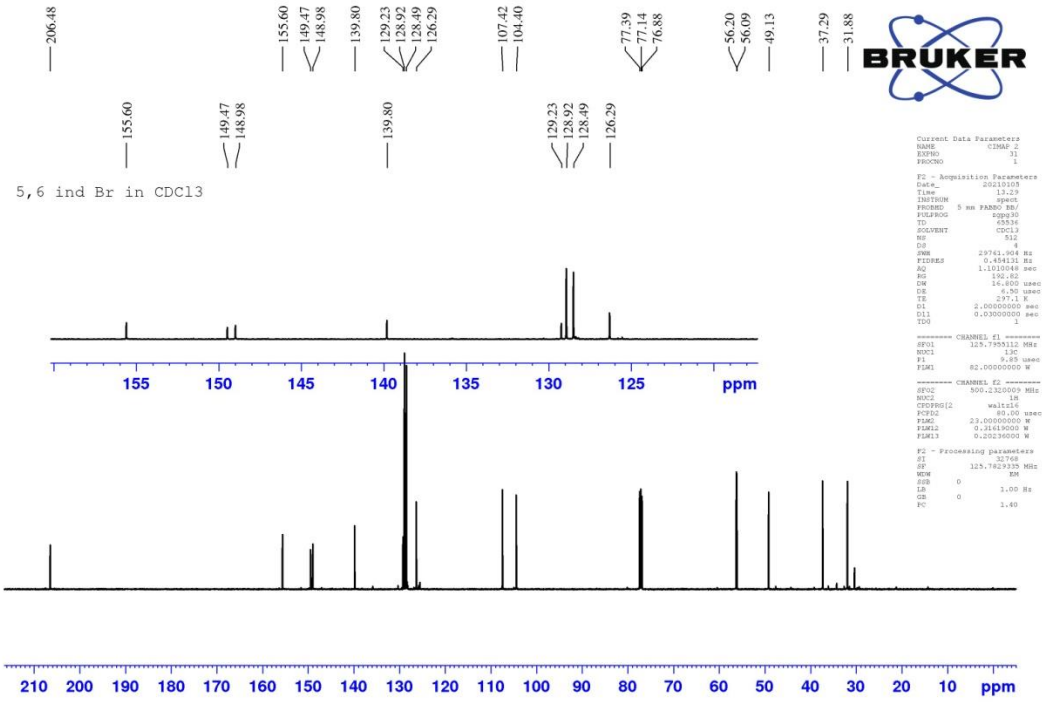
^{13}C NMR Spectra of (**3a)** (100 MHz, $CDCl_3$)



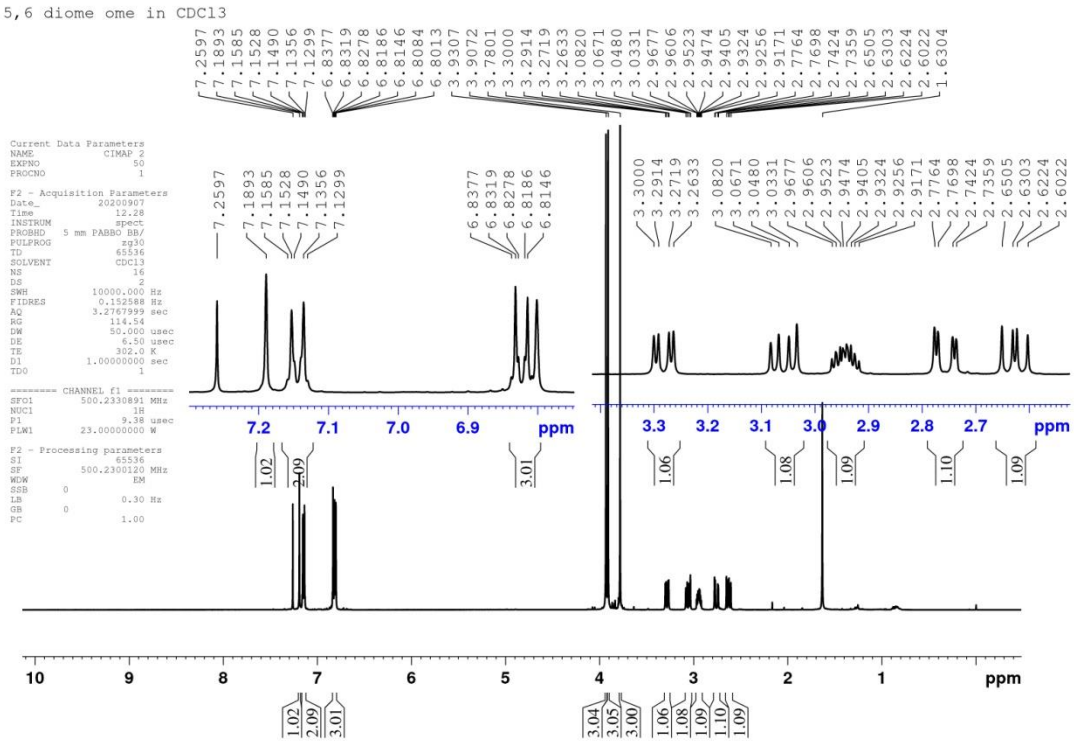
HRMS **3a**



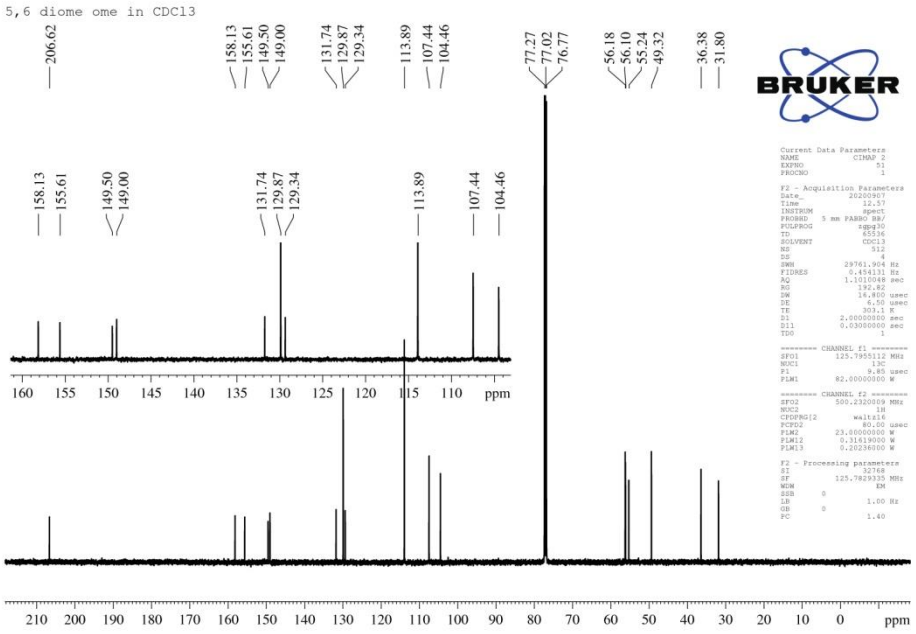
^{1}H NMR Spectra of (**3b)** (500 MHz, $CDCl_3$)



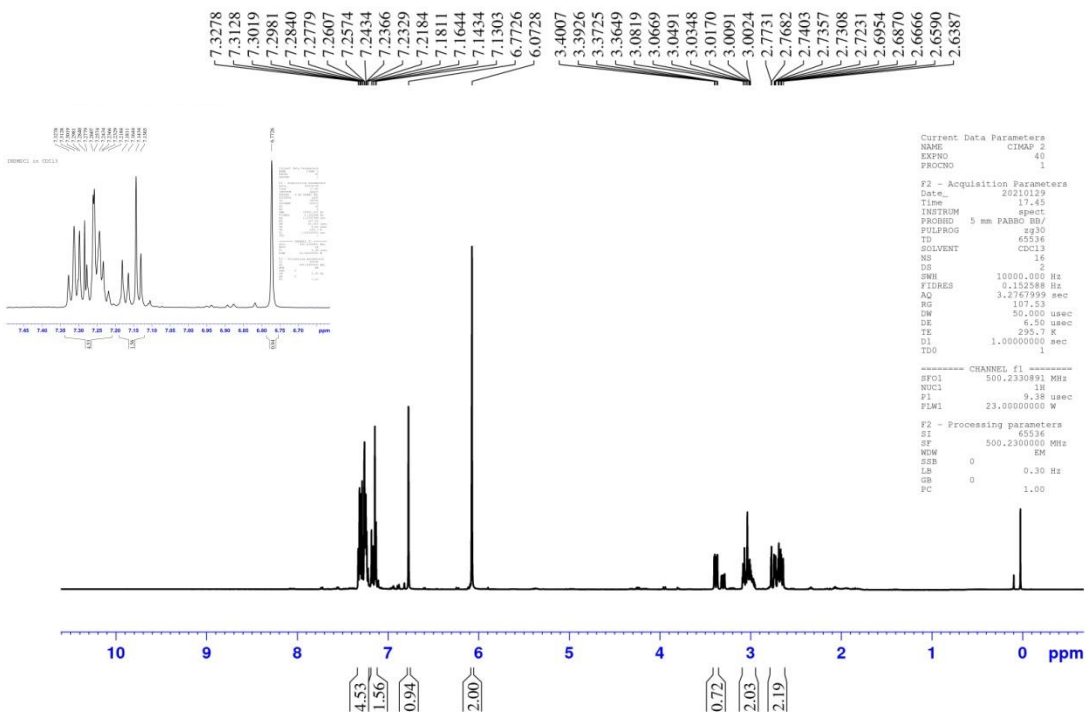
^{13}C NMR Spectra of (**3b)** (100 MHz, $CDCl_3$)



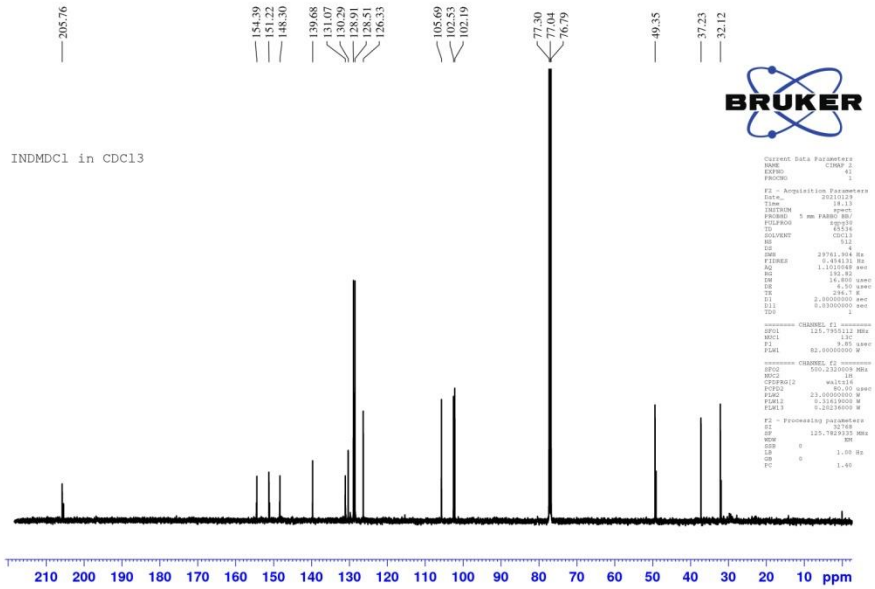
^{1}H NMR Spectra of (**3c)** (500 MHz, $CDCl_3$)



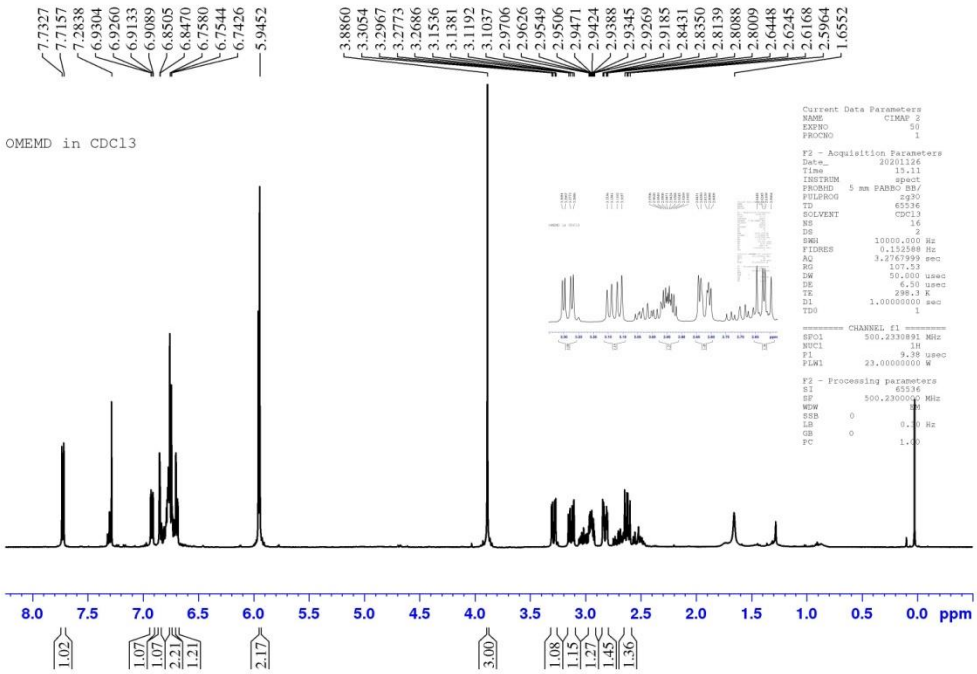
^{13}C NMR Spectra of (**3c)** (100 MHz, $CDCl_3$)



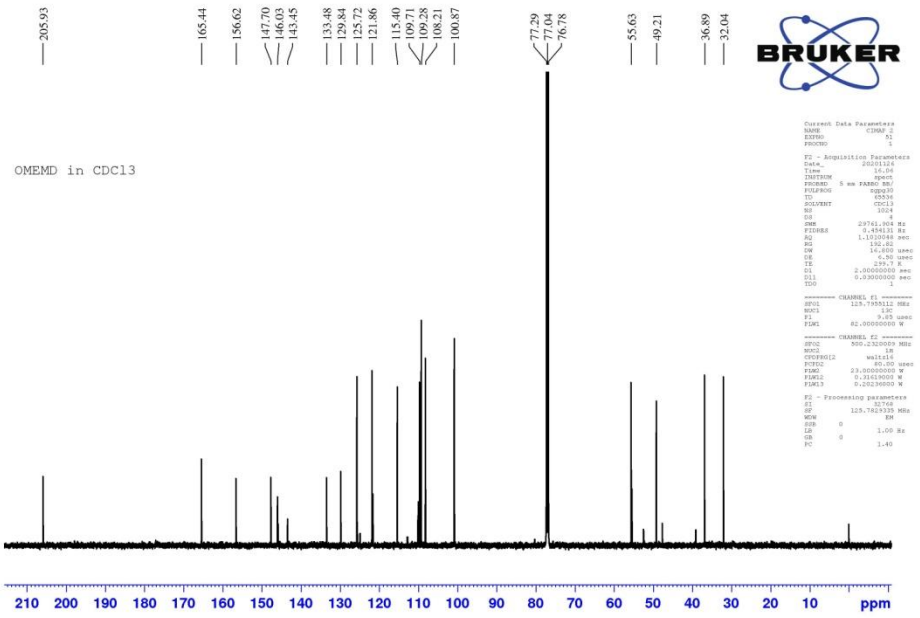
^{1}H NMR Spectra of (**3d)** (500 MHz, $CDCl_3$)



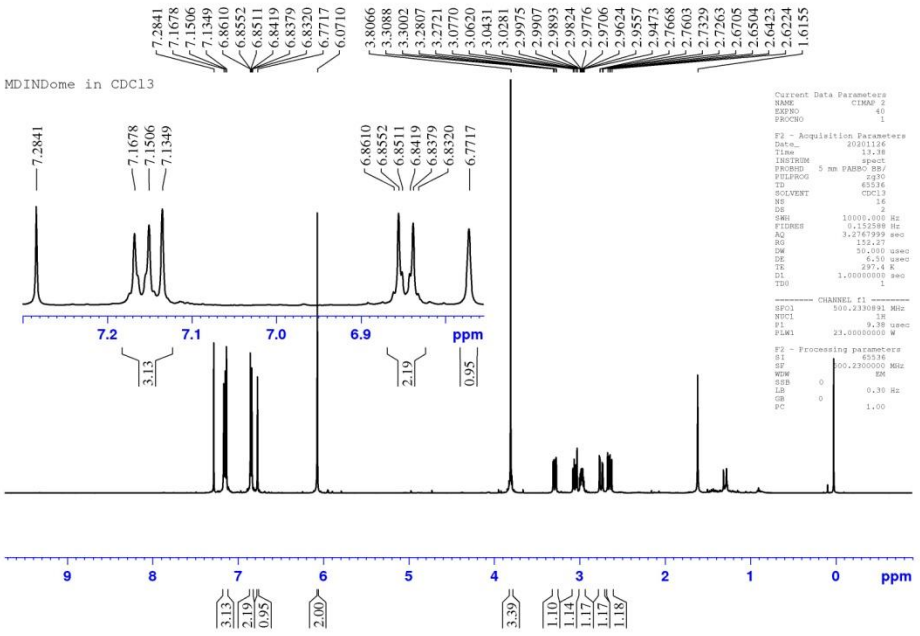
^{13}C NMR Spectra of (**3d)** (100 MHz, $CDCl_3$)



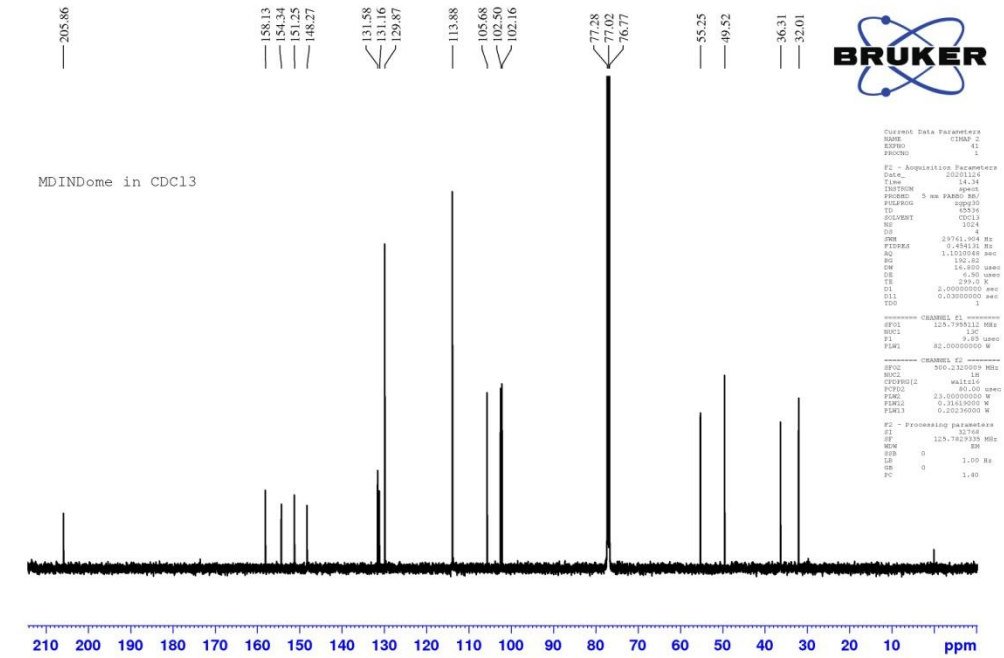
^{1}H NMR Spectra of (**3e)** (500 MHz, $CDCl_3$)



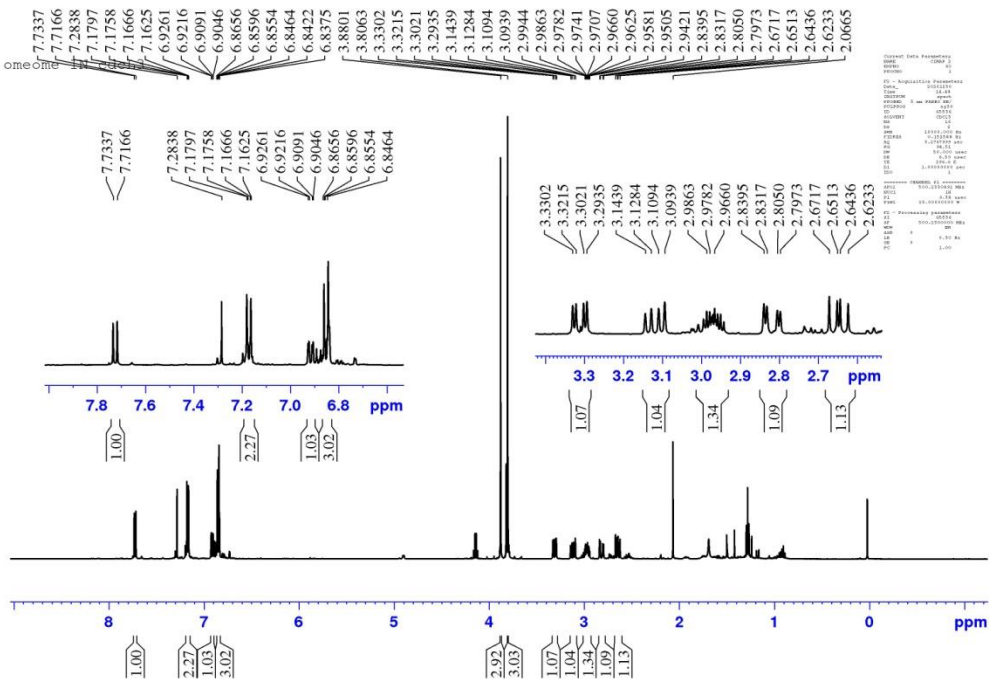
^{13}C NMR Spectra of (**3e)** (100 MHz, $CDCl_3$)



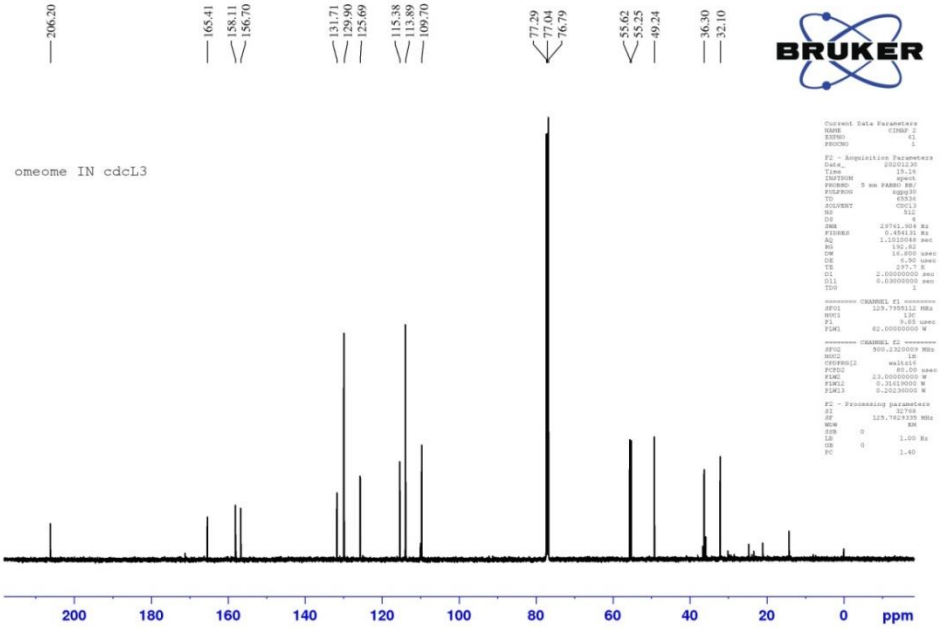
^{1}H NMR Spectra of (**3f)** (500 MHz, $CDCl_3$)



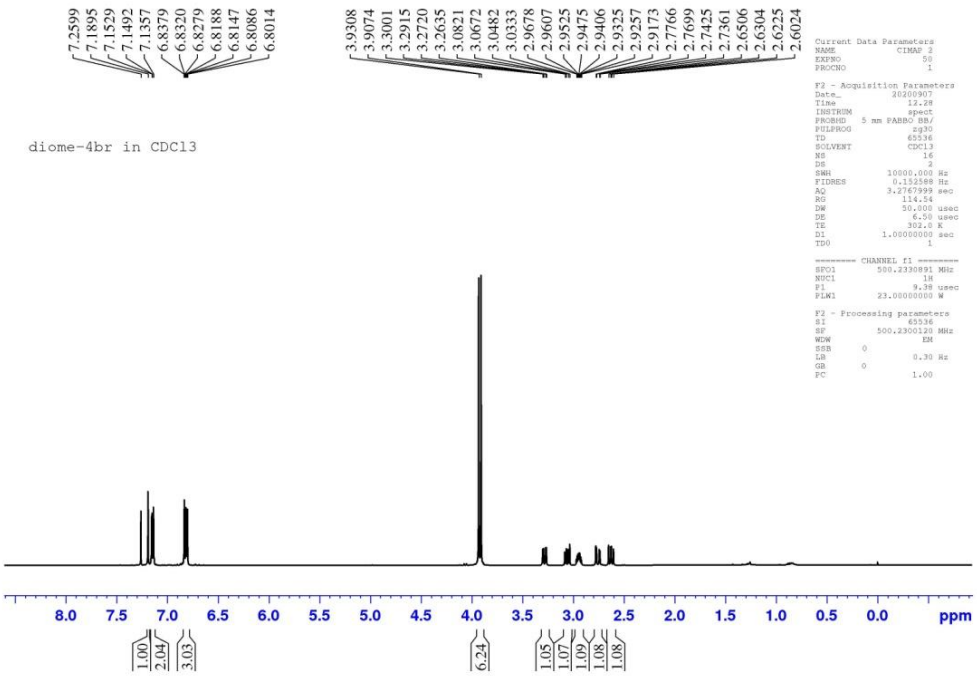
^{13}C NMR Spectra of (**3f)** (100 MHz, $CDCl_3$



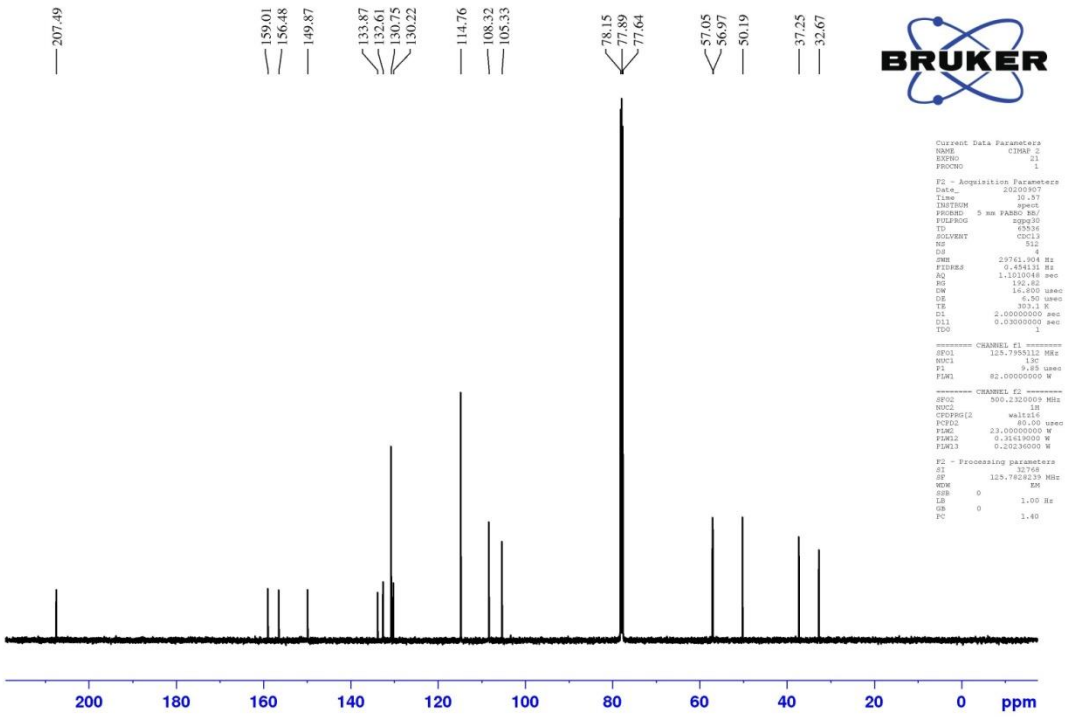
^{1}H NMR Spectra of (**3g)** (500 MHz, $CDCl_3$)



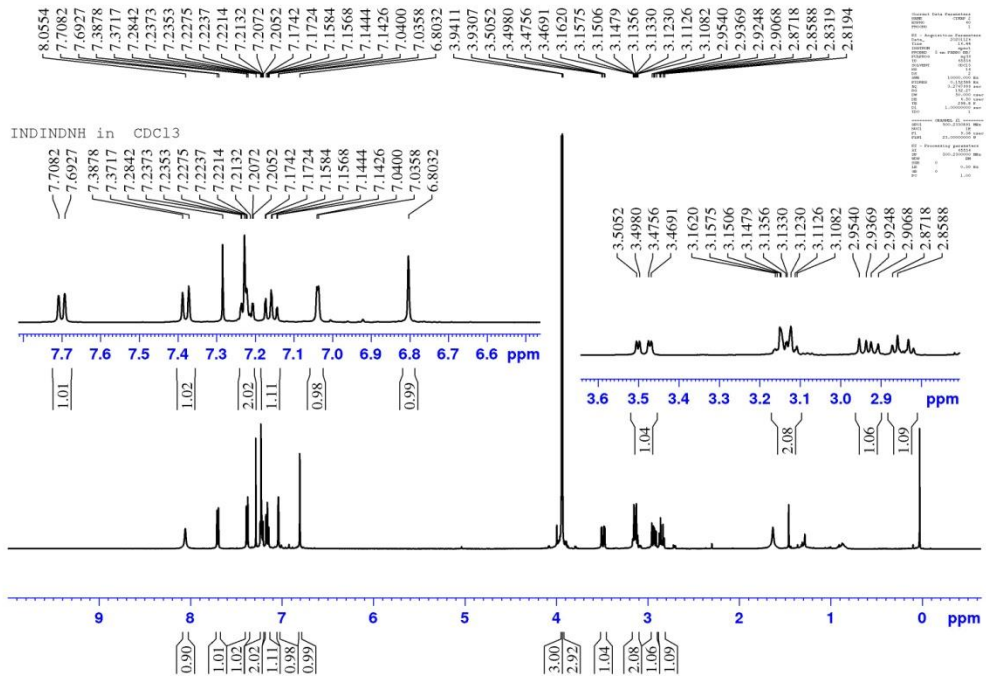
^{13}C NMR Spectra of (**3g)** (100 MHz, $CDCl_3$



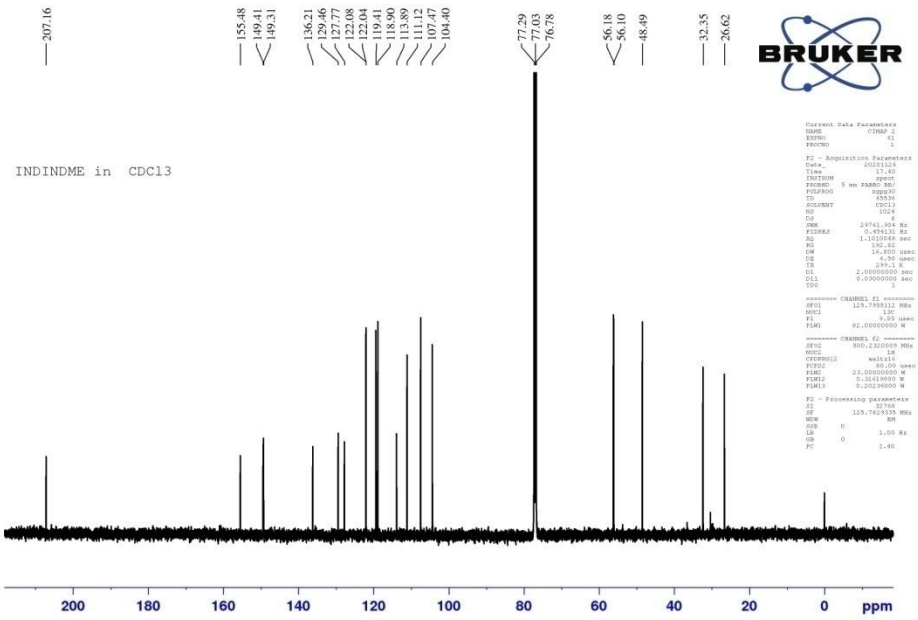
^{1}H NMR Spectra of (**3h)** (500 MHz, $CDCl_3$)



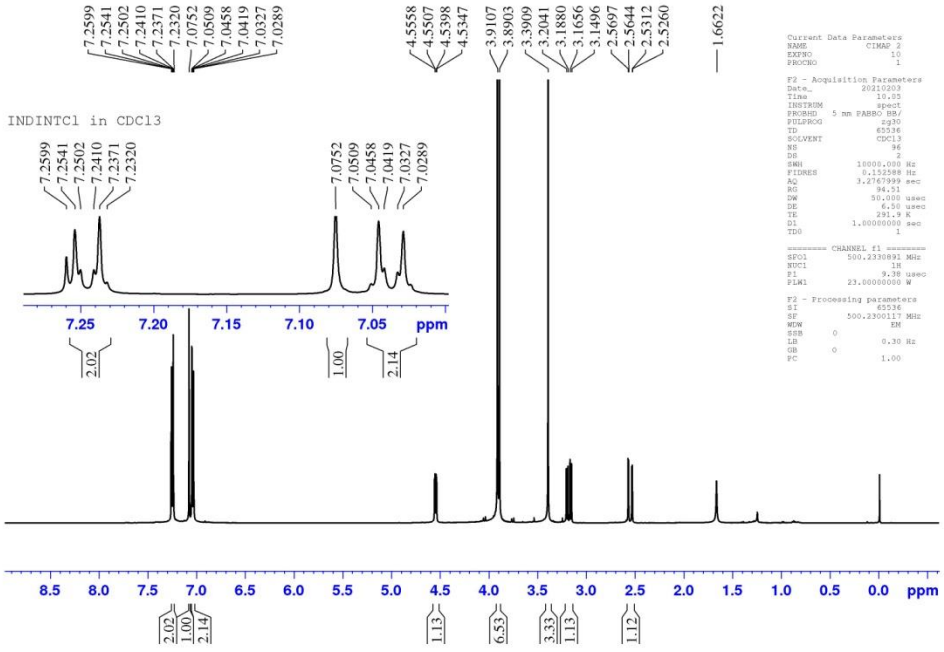
^{13}C NMR Spectra of (**3h)** (100 MHz, $CDCl_3$)



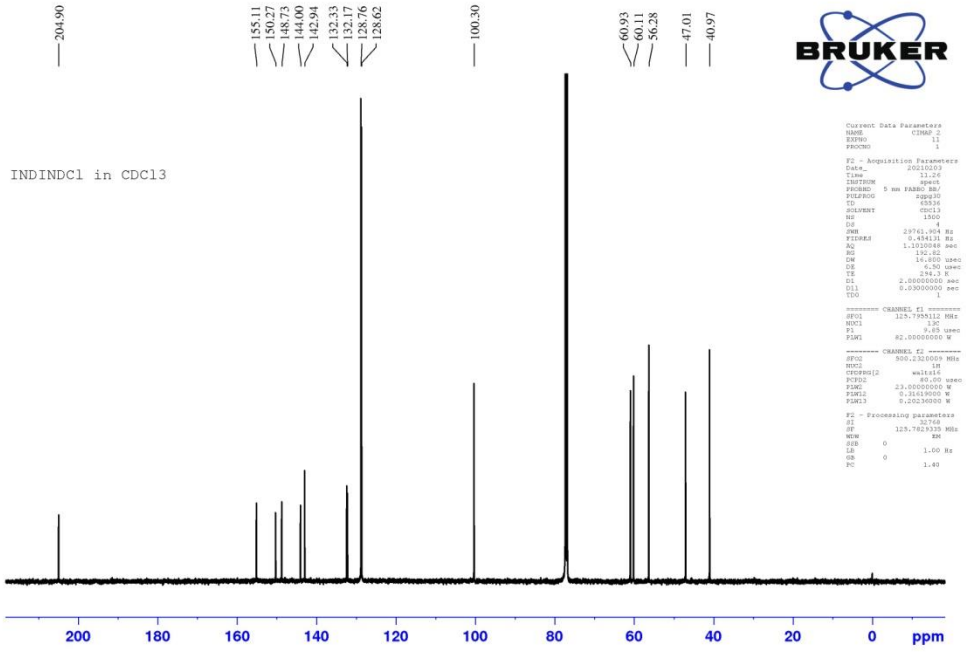
^{1}H NMR Spectra of (**3i)** (500 MHz, $CDCl_3$)



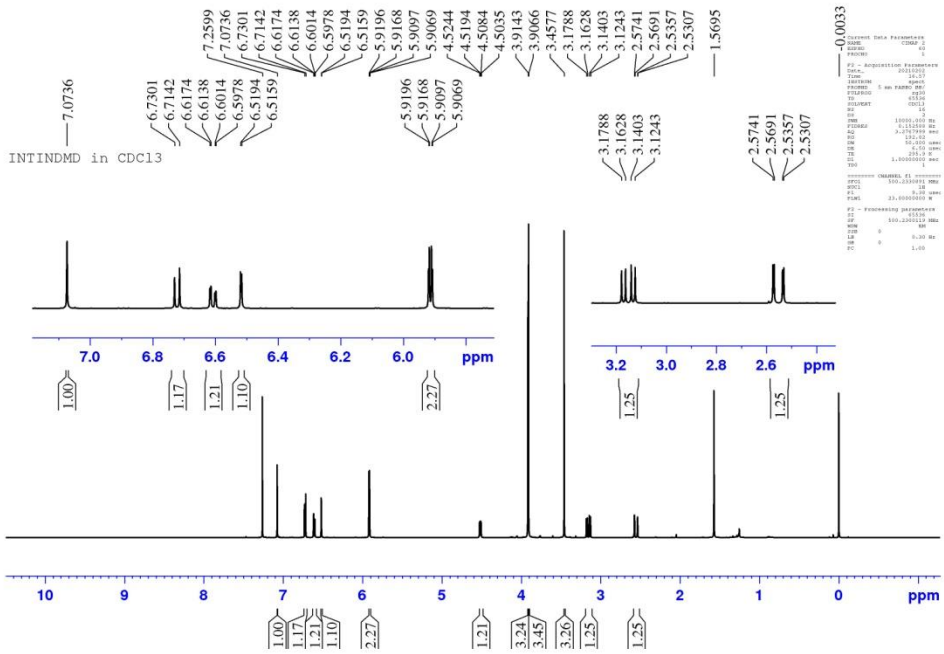
^{13}C NMR Spectra of (**3i)** (100 MHz, $CDCl_3$)



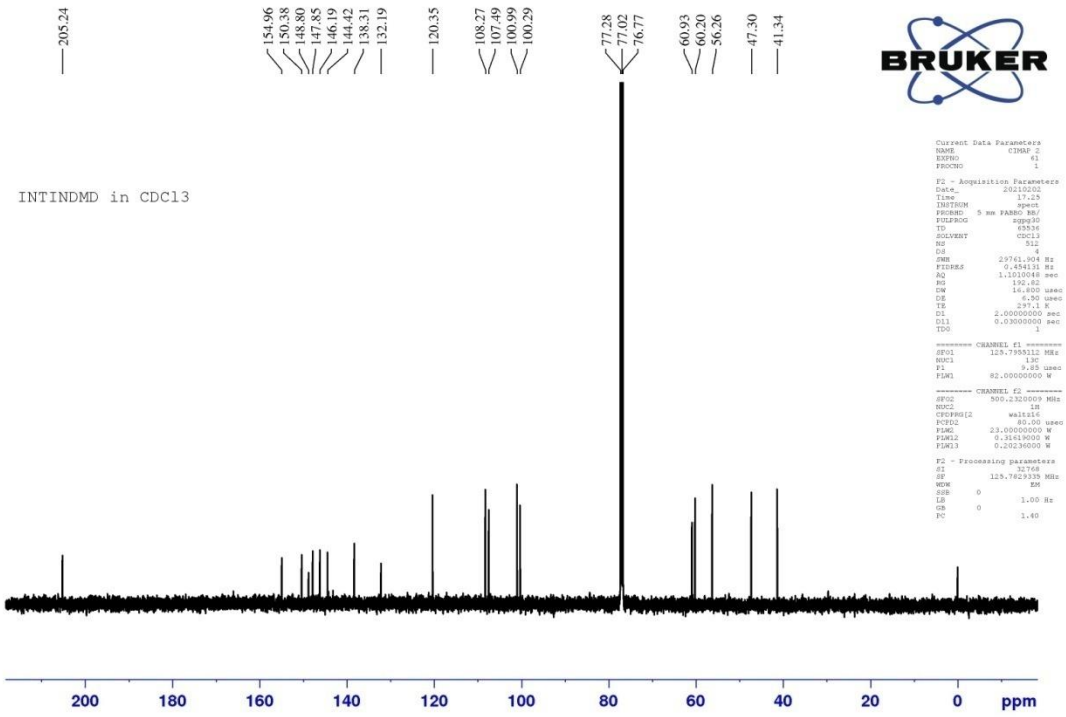
^{1}H NMR Spectra of (**5a)** (500 MHz, $CDCl_3$)



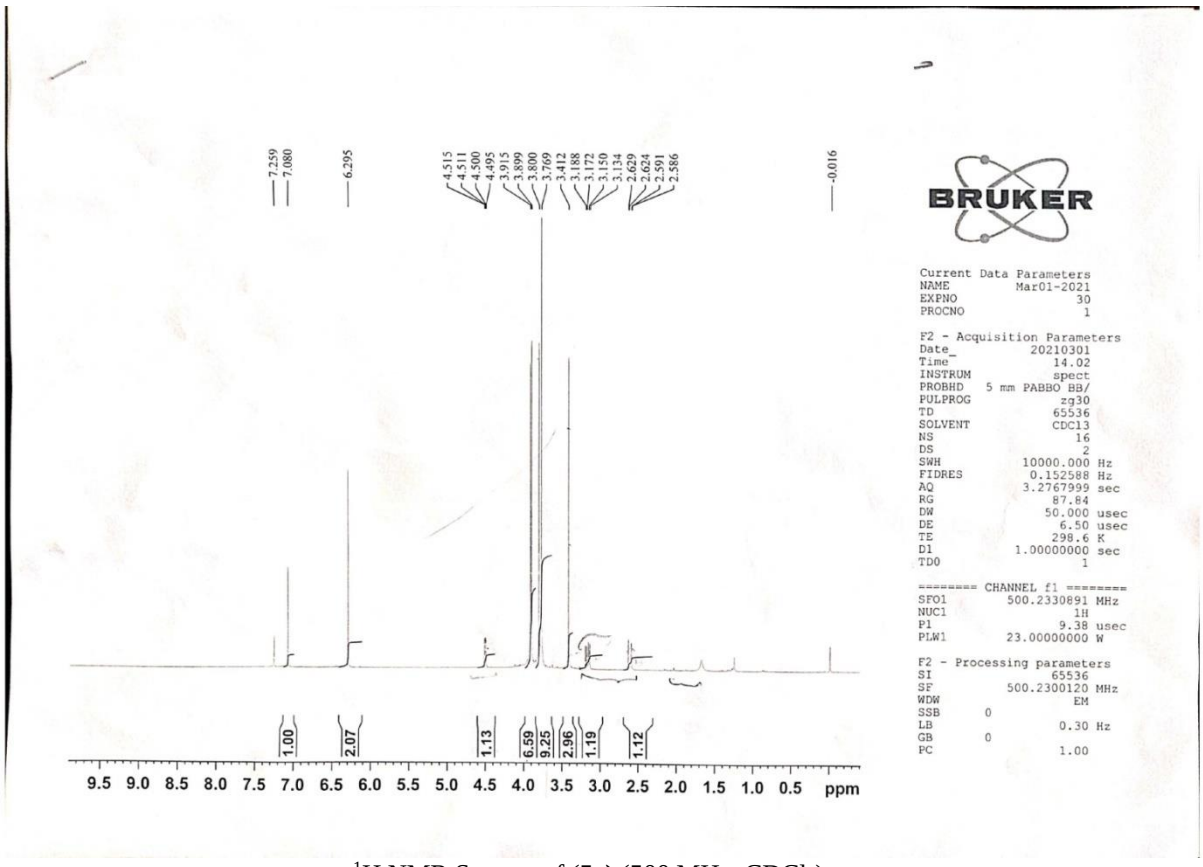
^{13}C NMR Spectra of (**5a)** (100 MHz, $CDCl_3$)



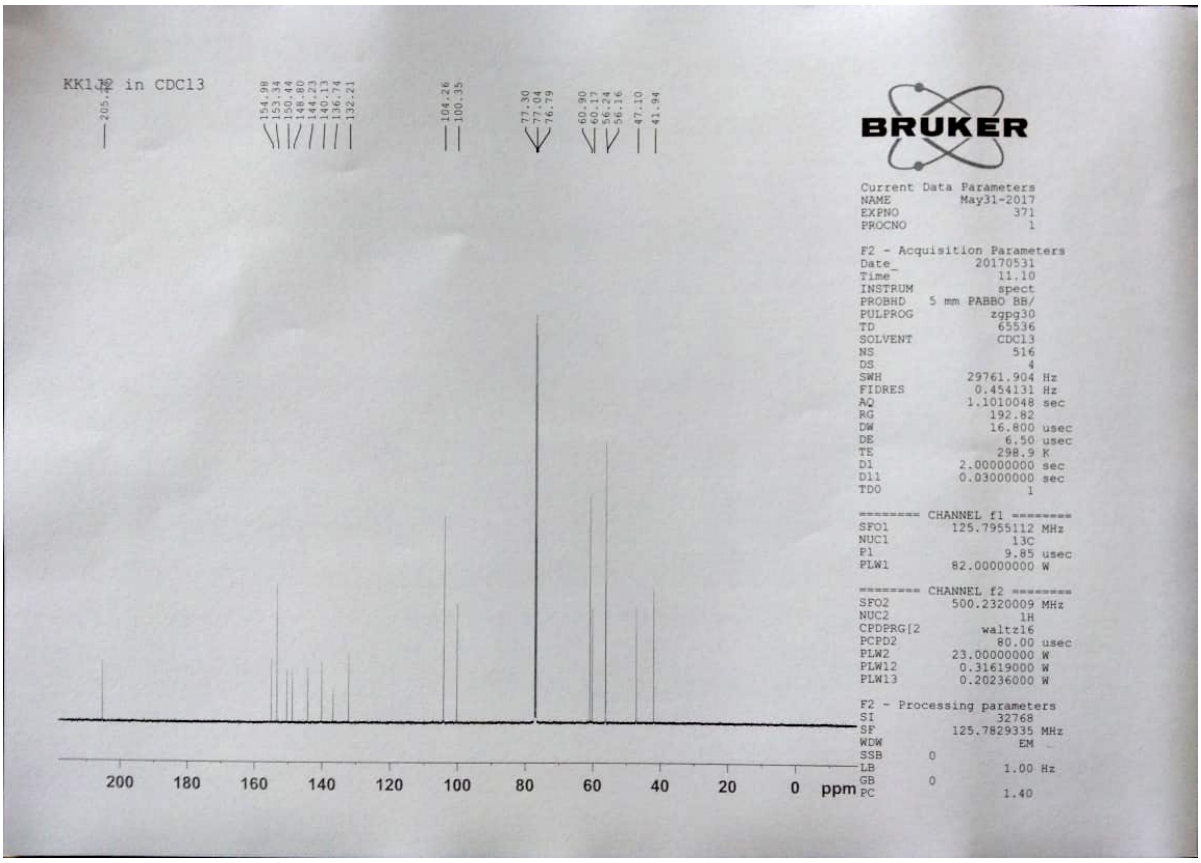
^{1}H NMR Spectra of (**5b)** (500 MHz, $CDCl_3$)



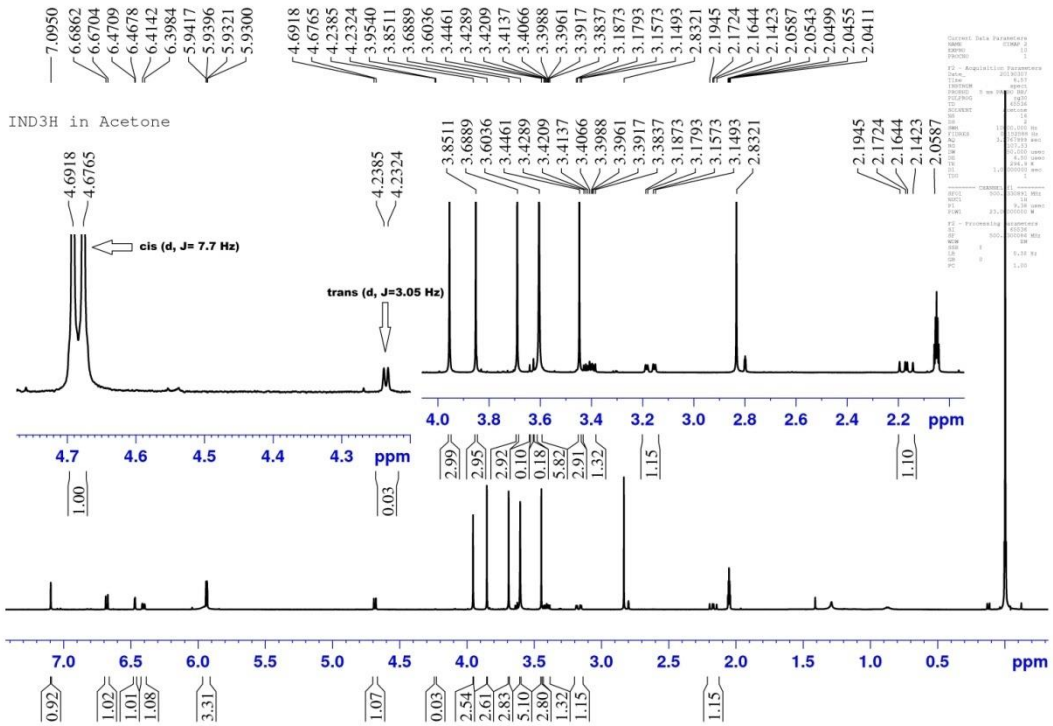
^{13}C NMR Spectra of (**5b)** (100 MHz, $CDCl_3$)



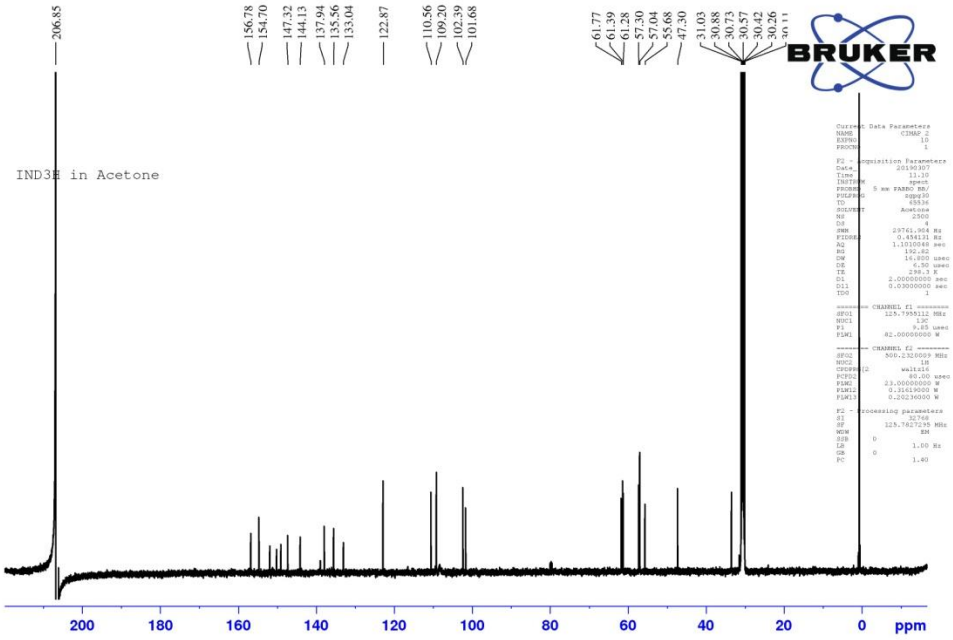
^{1}H NMR Spectra of (**5c)** (500 MHz, $CDCl_3$)



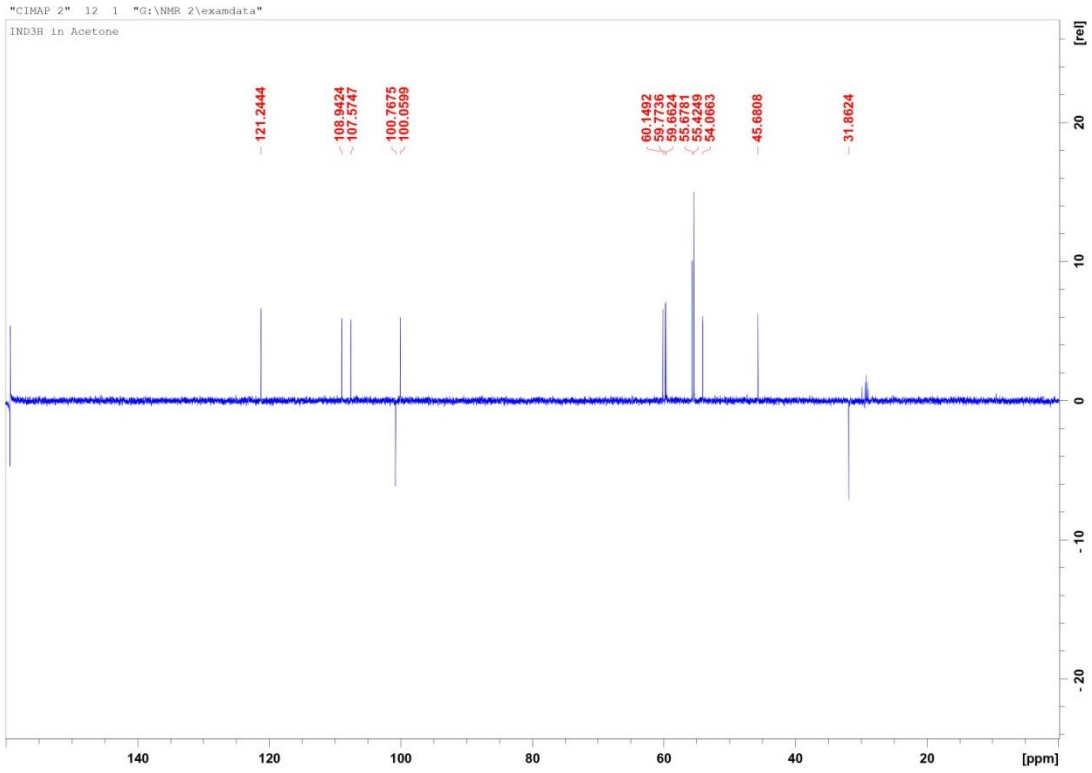
^{13}C NMR Spectra of (**5c)** (100 MHz, $CDCl_3$)



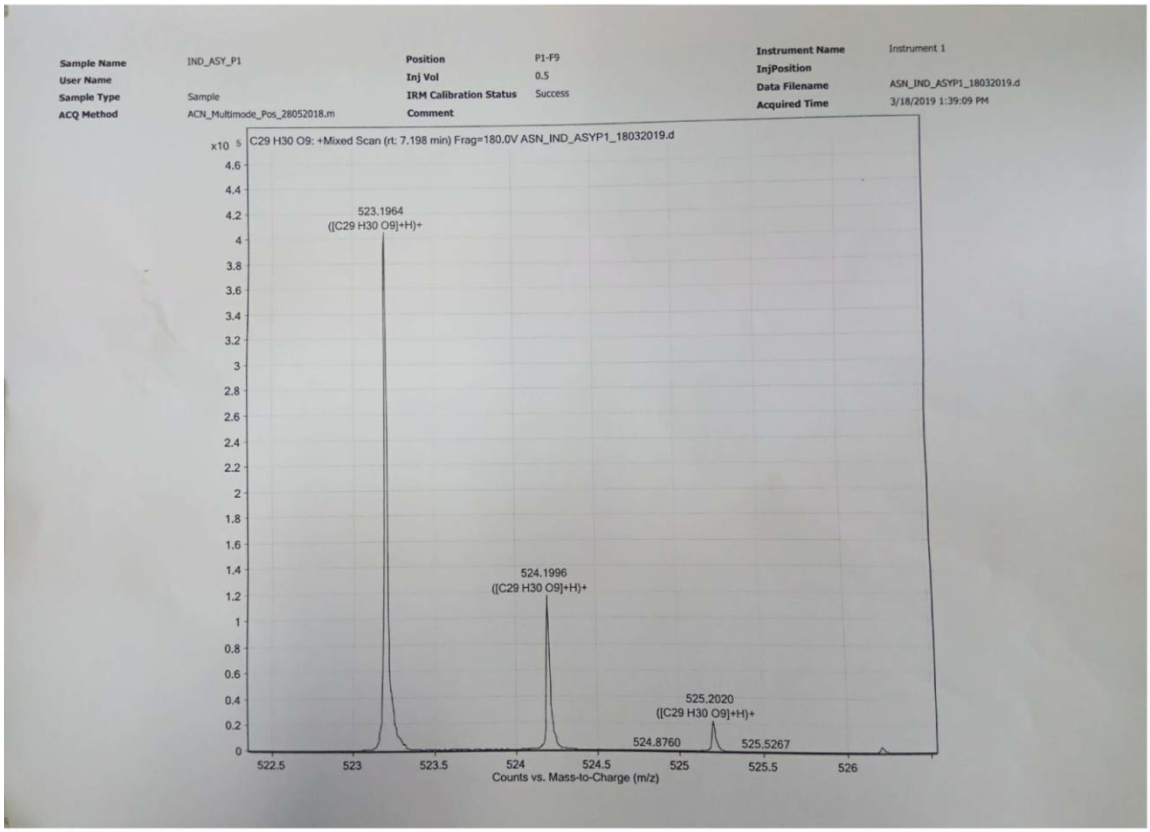
^{1}H NMR Spectra of (**6a)** (500 MHz, Acetone-d6



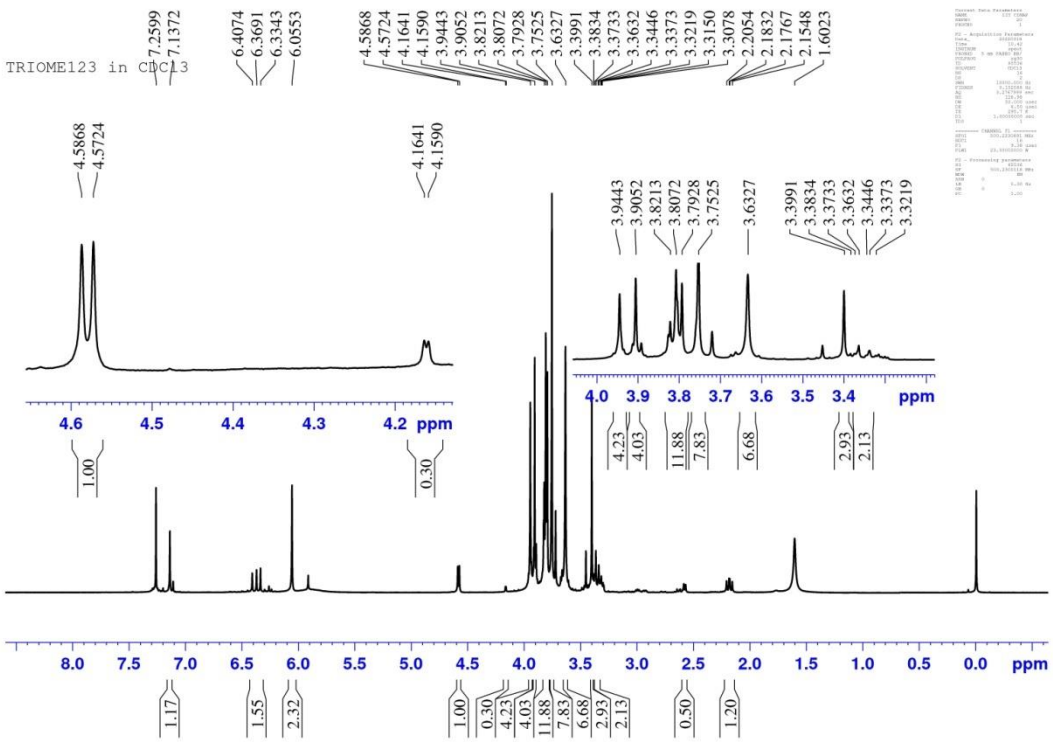
^{13}C NMR Spectra of **(6a)** (100 MHz, Acetone-d6)



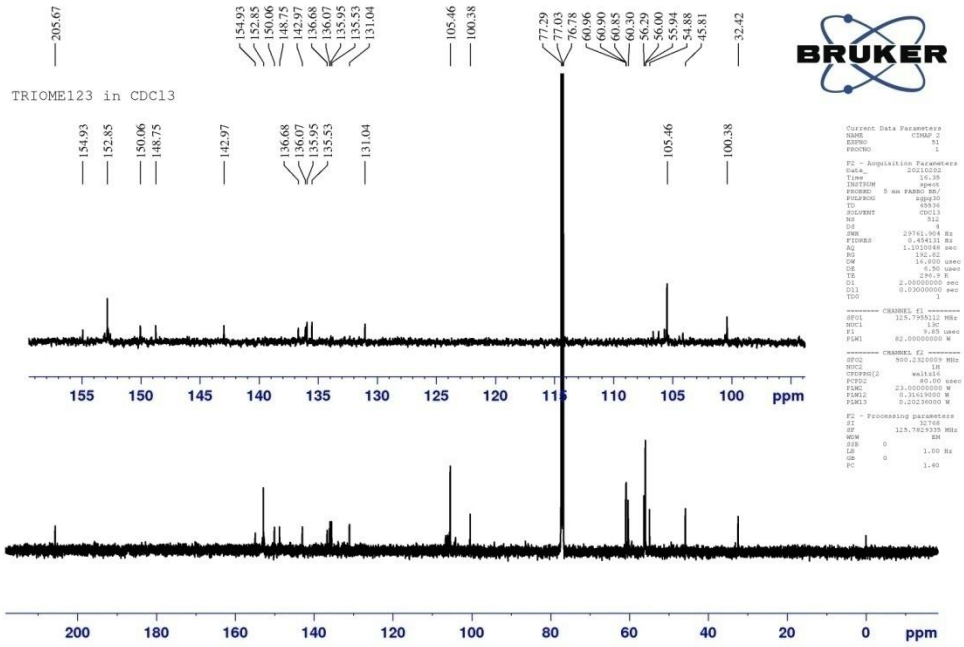
DEPT-135 (**6a**)



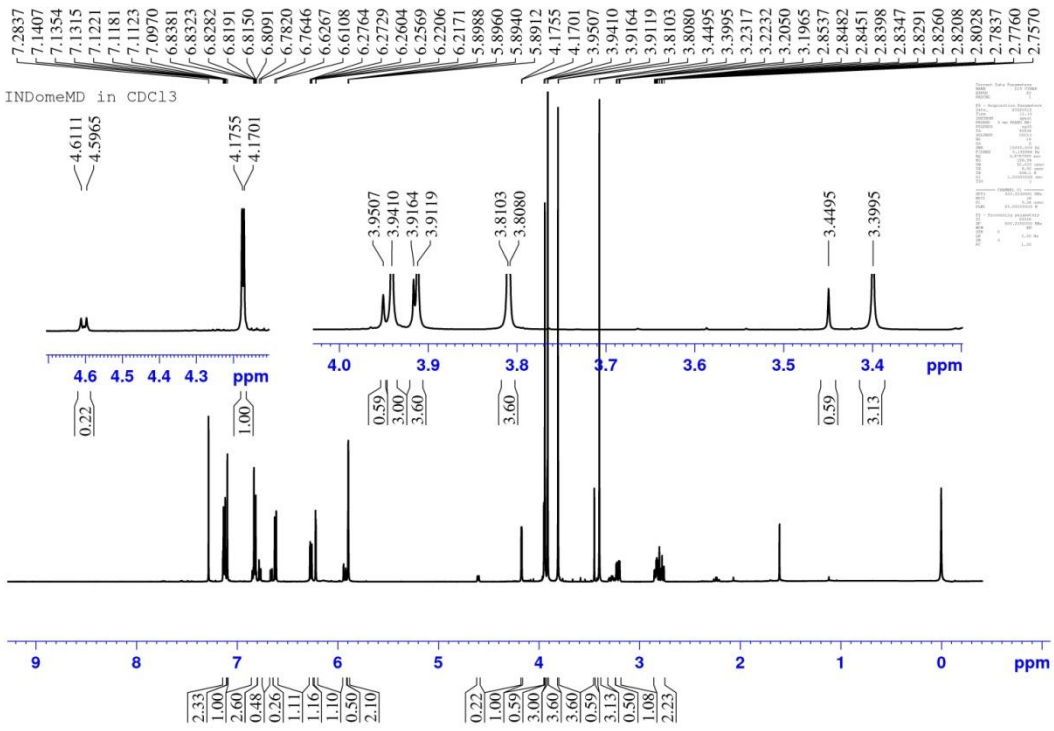
HRMS **6a**



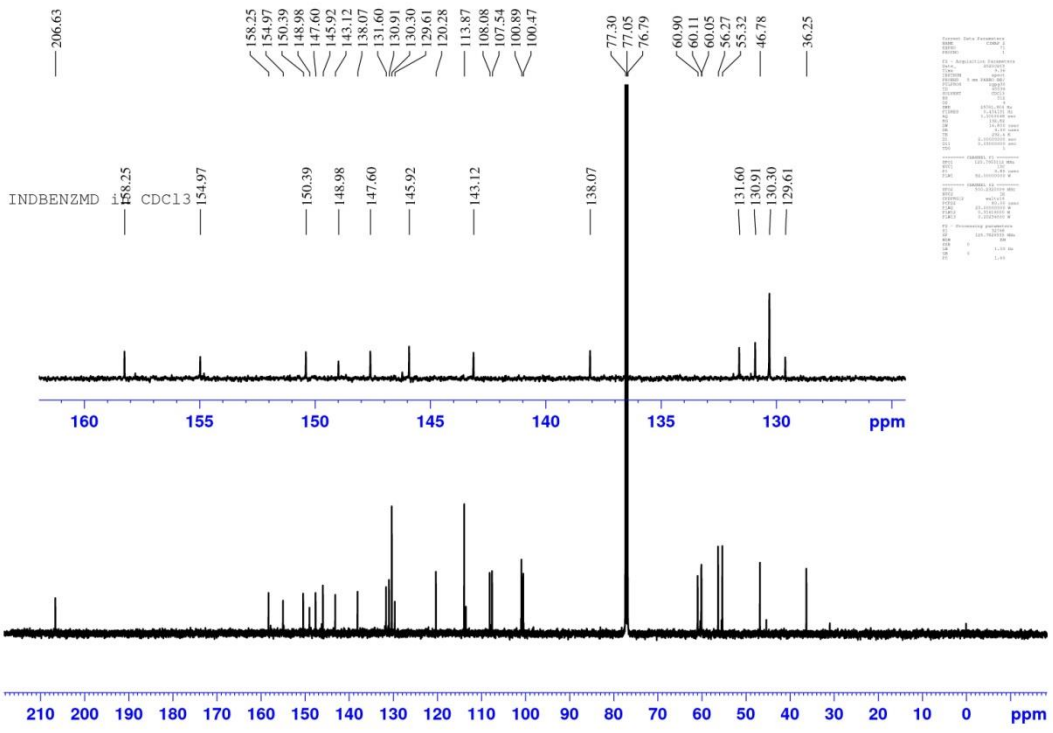
^{1}H NMR Spectra of (**6b)** (500 MHz, $CDCl_3$)



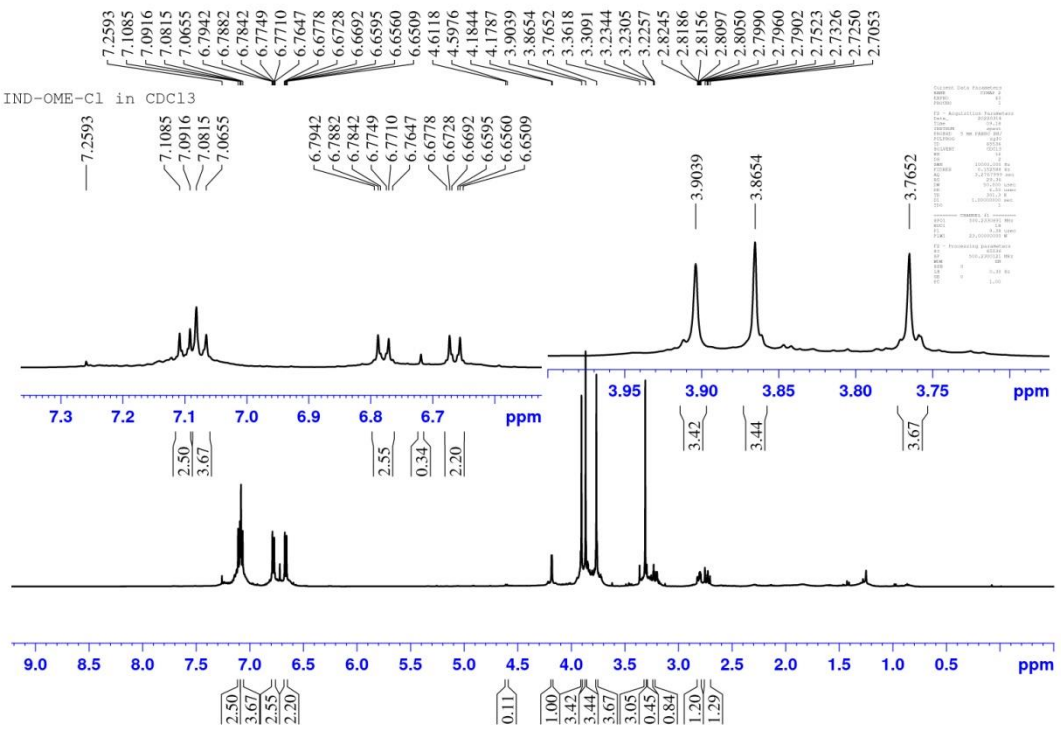
^{13}C NMR Spectra of **(6b)** (100 MHz, $CDCl_3$)



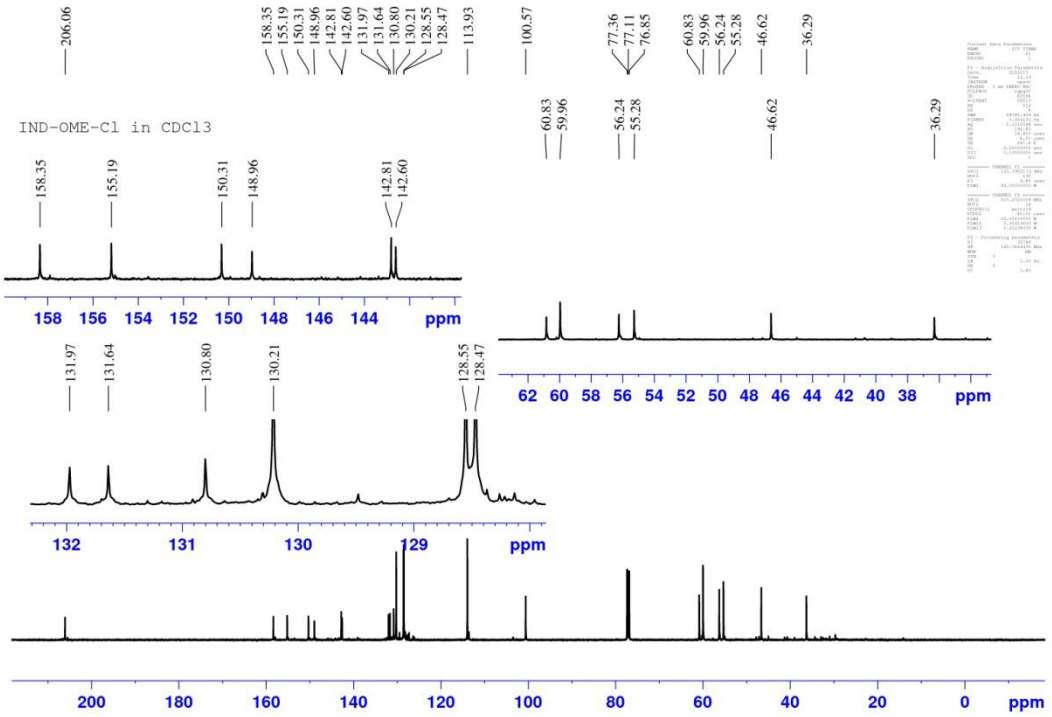
^{1}H NMR Spectra of **(6c)** (500 MHz, $CDCl_3$)



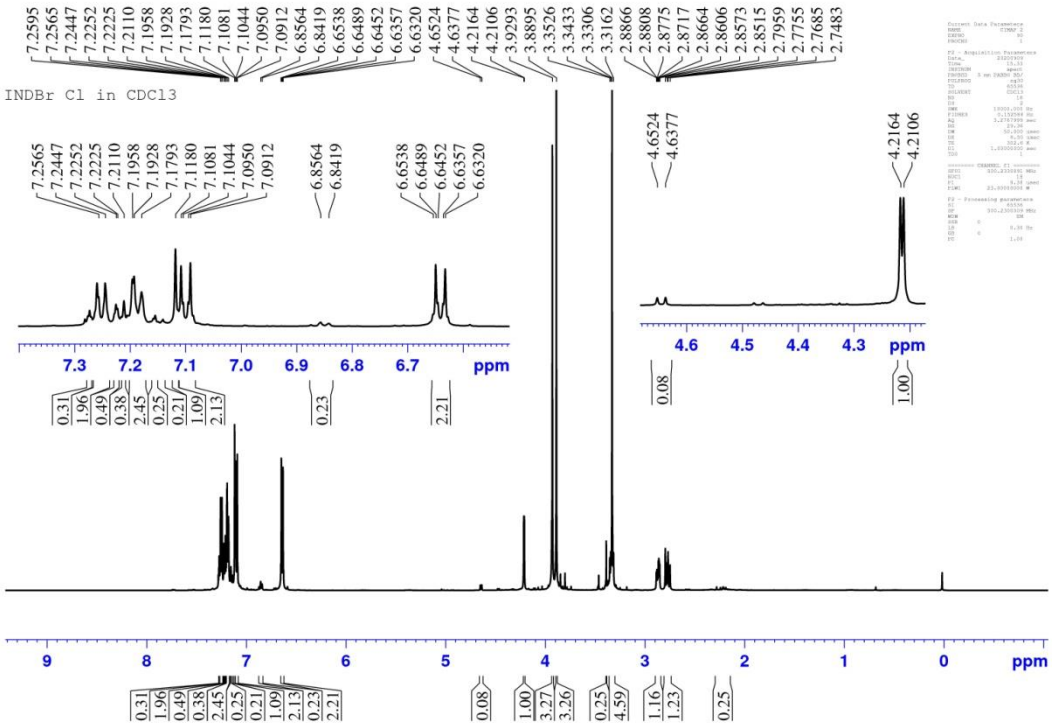
^{13}C NMR Spectra of (**6c)** (100 MHz, $CDCl_3$)



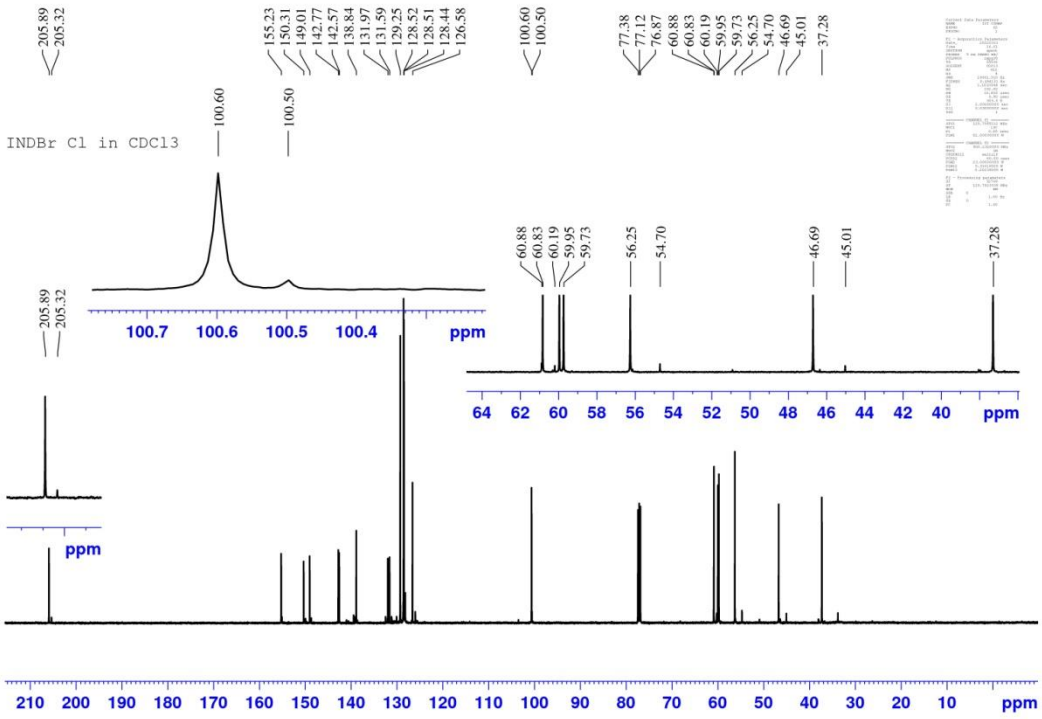
^{1}H NMR Spectra of (**6d)** (500 MHz, $CDCl_3$)



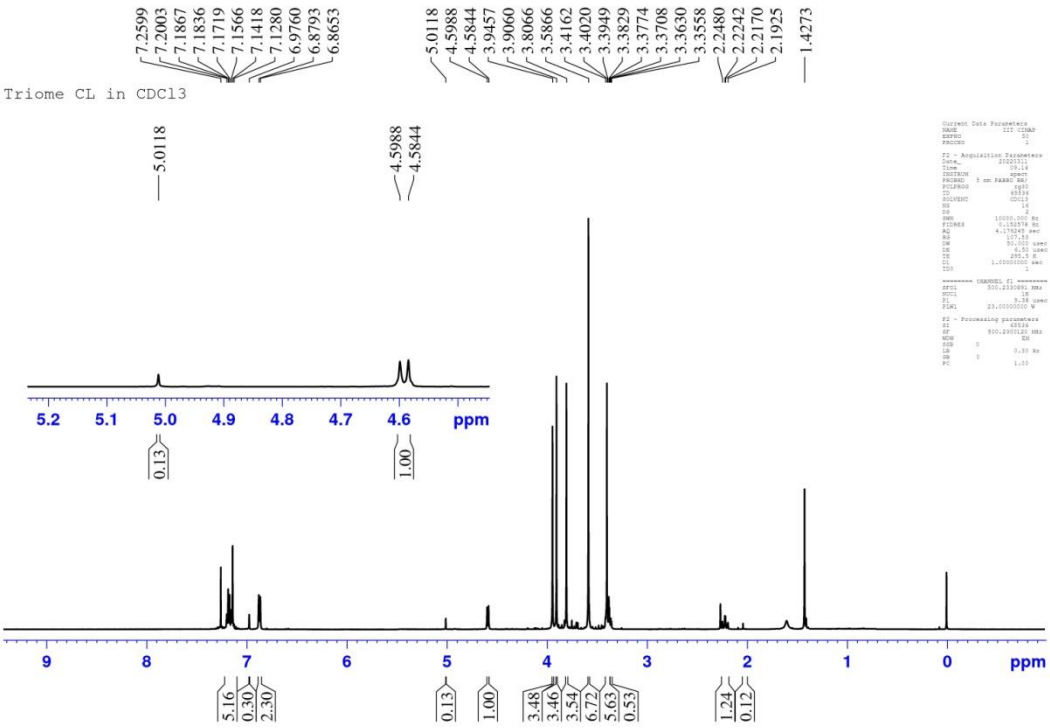
^{13}C NMR Spectra of (**6d)** (100 MHz, $CDCl_3$)



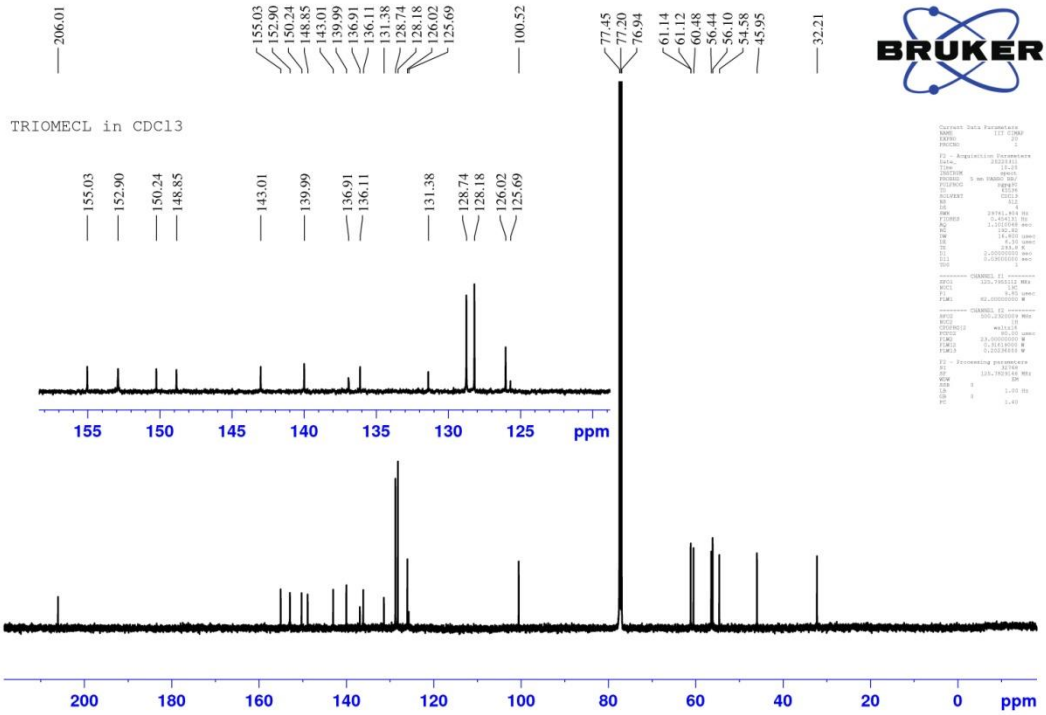
^{1}H NMR Spectra of (**6e)** (500 MHz, $CDCl_3$)



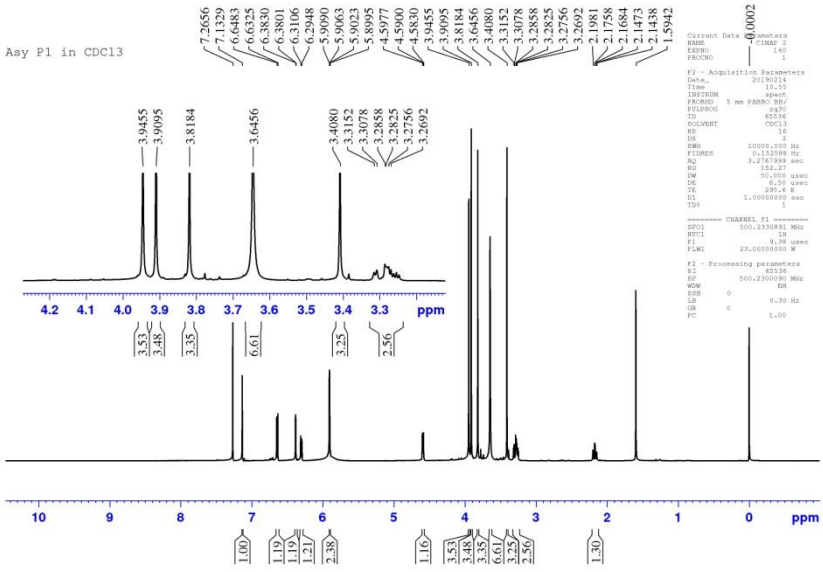
^{13}C NMR Spectra of (**6e)** (100 MHz, $CDCl_3$)



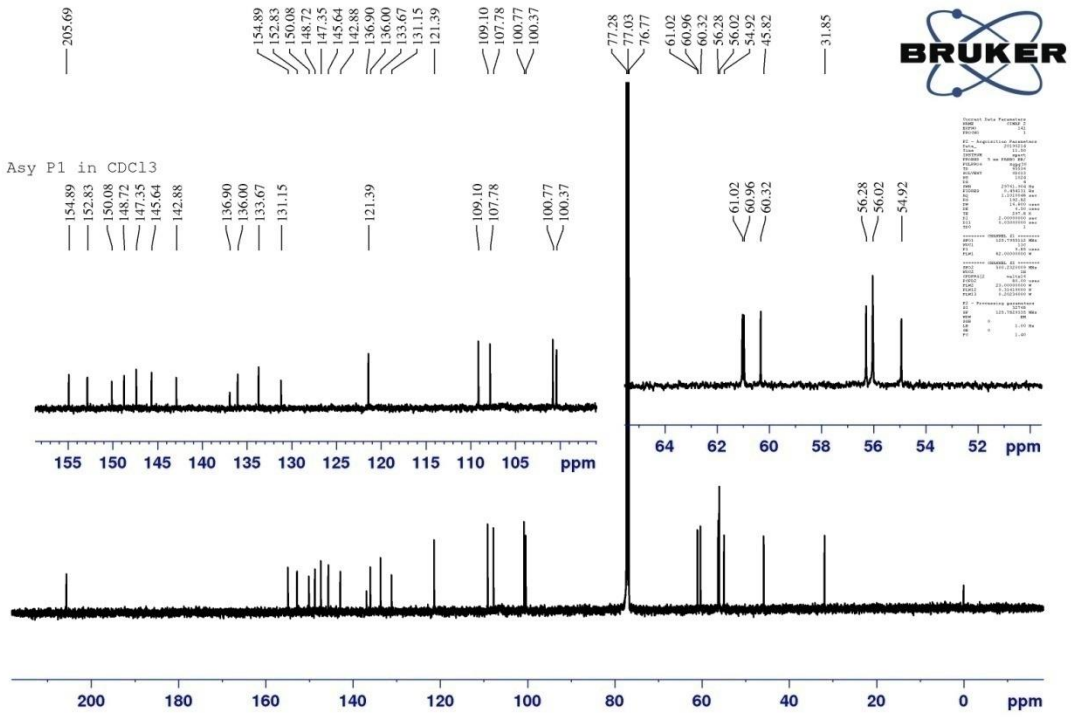
^{1}H NMR Spectra of **(6f)** (500 MHz, $CDCl_3$)



^{13}C NMR Spectra of (**6f)** (100 MHz, $CDCl_3$)



^{1}H NMR Spectra of (**6g)** (500 MHz, $CDCl_3$)



^{13}C NMR Spectra of **(6g)** (100 MHz, $CDCl_3$)

[a]References:

1. **https://organicchemistrydata.org/hansreich/resources/nmr/?page=05-hmr-05-3j/**
2. A. Minatti, X. Zheng and S. L. Buchwald *J. Org. Chem.* 2007, 72, 24, 9253–9258