A Diversity Oriented Synthesis Pathway for Ieodoglucomide Analogues

Thesis Submitted towards the Partial fulfillment of

BS-MS dual degree programme

by

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20081044

Under the guidance of

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CERTIFICATE

This is to certify that this dissertation entitled "**A Diversity Oriented Synthesis Pathway for Ieodoglucomide Analogues**" towards the partial fulfilment of the BS-MS dual degree programme at the Indian Institute of Science Education and Research, Pune represents original research carried out by **Iti Kapoor**, IISER Pune under the supervision of **Dr. Srinivas Hotha**, Associate Professor - Chemistry, IISER Pune during the academic year 2012-2013.

Date :

Place:

Srinivas Hotha, Ph. D.
Associate Professor - Chemistry

DECLARATION

I hereby declare that the matter embodied in the report entitled "**A Diversity Oriented Synthesis Pathway for Ieodoglucomide Analogues**" are the results of the investigations carried out by me at the Department of Chemistry, IISER Pune, under the supervision of Dr. Srinivas Hotha and the same has not been submitted elsewhere for any other degree.

Date:

Iti Kapoor

Place: BS-MS Dual Degree Program, IISER Pune

ACKNOWLEDGEMENTS

It gives me an immense pleasure to thank my mentor, **Dr. Srinivas Hotha** for giving me this wonderful opportunity to work in his group under his guidance. His continuous encouragement and generous support during the every stage of my fifth year project, be it a failure or a success. I do sincerely acknowledge his willingness to share new ideas, enthusiasm to initiate novel projects and determination to drive them to an end that will be helpful for me to shape my research career. I am extremely grateful to him for encouraging the independent and friendly environment in the laboratory. I really feel proud after having spent one whole year working in his group, this brings a lot of confidence and learning experience in me.

I am highly thankful to my senior labmates Ashif Shaikh, Abhijeet Kayastha, Shivaji Thadke, B. V. Rao, Maidul Islam, Bijoyananda Mishra and C. Manish for helping me a lot and developing the interest for the experimental work. I would deeply acknowledge their contribution and devotion, for guiding me throughout the project and for planning, supporting and its implementation. It would not have been possible for me to come to this successful ending of my project without their support.

I owe my gratitude to Dr.Sayam Sen Gupta from NCL, Pune**,** and all the faculty members of Chemistry at IISER Pune for giving me constant valuable suggestions and developing an immense interest for Chemistry in me through their encouraging lectures during last five years.

I wholeheartedly, give my special thanks and sincere regards to all my friends for their unconditional suppor, tcontinuous encouragement, and making my work more interesting by providing generous and friendly environment throughout my stay at IISER Pune.

I am highly obliged by Kishore Vaigyanik Protsahan Yojana providing me stipend for my project. Last but not the least, I would like to thank all the NMR and HRMS operators for providing me my spectra on priority whenever needed.

The successful implementation of this project would not have been possible for me without the great scientific and learning environment provided by IISER Pune.

Above all, I would like to thank my parents, my sister and my younger brother for their emotional support for last five years.

Iti Kapoor

Contents

Abbreviations

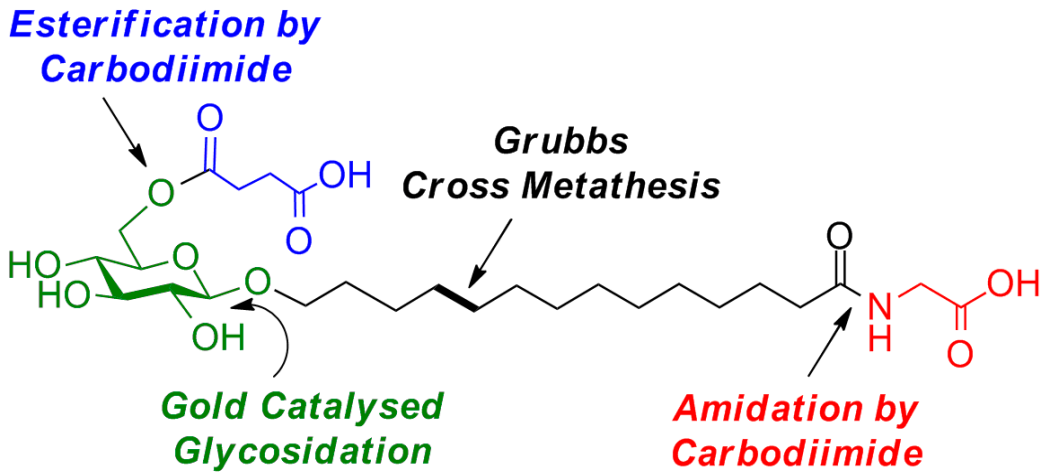
TLC	Thin Layer Chromatography
M. S.	Molecular Sieves
NMR	Nuclear Magnetic Resonance
HRMS	High Resolution Mass Spectrometry
J	Coupling Constant
Hz	Hertz
MHz	MegaHertz
Ac	Acetyl
Bz	Benzoyl
Bn	Benzyl
CSA	Camphorsulphonic Acid
DMAP	N, N'-dimethylamino pyridine
DIC	N, N'-diisopropylcarbodiimide
DMF	N, N-dimethylformamide
mg	Milligram
g	Gram
h	hour
M	Molar
mL	Millilitre
mol	Mole
Me	Methyl
PTSA	para toluene sulphonic acid
TBDPSCl	*Tert*-butyldiisopropylsilyl chloride
TBAI	*Tert*-butylammonium iodide
Tr	Trityl (Triphenylmethyl)
TBAF	*Tert*-butylammonium fluoride
THF	Tetrahydrofuran
pTSA	pera- Toluene Sulphonic Acid

Abstract

A diversity oriented synthesis pathway for the synthesis of biologically active glycolipids Ieodoglucomodes A and B was developed using Gold catalyzed glycosidation, Grubbs cross metathesis reaction and carbodiimide based estification and amidation as key steps. The synthesis is achieved in 9 steps overall and 4 steps from easily accessible building blocks.

Graphical Abstract

A DOS pathway for Ieodoglucomide Analogues



Total Steps: 9 from Glucose, 4 Steps from building blocks

For many years, the chemistry and biology of carbohydrates have been considered as a Cinderella field,[1,2]that involves a lot of work but still stays in the shadow of her cousins, glycomics and proteomics. Carbohydrates were seen only as the source of energy until 1980s when, the field of glycobiology emerged as an integrated field of traditional carbohydrate chemistry and biochemistry with the modern understanding of cell and molecular biology of glycans and their conjugates with lipids and proteins.[2] Carbohydrates are the integral parts of cell surface because of tremendous structural diversity.[7] The complexity of carbohydrates can be attributed to the fact that in cells, oligosaccharides usually form glycoconjugates, which include glycolipids, glycoproteins and glycophosphatidyl inositols (GIP).[15]

Glycolipids, as the word itself says, are composed of the lipids which are attached to a carbohydrate moiety. Glycolipids are found as the membrane receptors of various animals, fungi, bacteria and plants. From the earlier studies on glycolipids, [3] it has been envisioned that different animal species have different compounds as their major glycolipids.[9] Glycolipids are ubiquitously expressed on the outer surface of the cell membranes and mediate diverse pathological and biological processes viz, providing ion permeability, balancing the proportions of bilayer-prone and non-bilayer prone lipids, contributing to the density of surface charge hydration (Figure 1).[5,17]

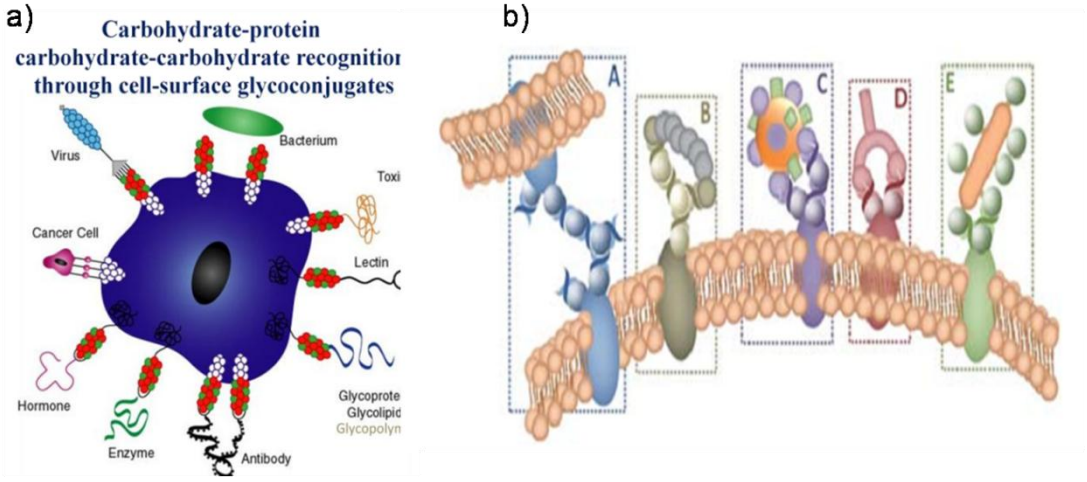


Fig 1: a) Carbohydrate-protein and carbohydrate-carbohydrate interaction through cell-surface glycans b)[2] Participation of cell-surface glycans in recognition with another cell (A) toxins, (B) viruses, (C) antibodies, (D) and (E) bacteria

Glycolipids are amphiphatic compounds, whose structures show both hydrophilic and hydrophobic groups. Glycolipids are the molecules, containing one or more monosaccharides, often glucose and galactose (in their α- or β- configurations),[3] covalently bound via a glycosidic linkage to a hydrophobic group such as sphingolipid or ceramide. Having this amphiphatic character, glycolipids can fulfil the functional requirement of various biological processes such as cell growth, fertility, immunity and viral and microbial invasions.[3,9]

Glycolipids can be broadly classified into three categories, namely, sphingoglycolipids (glycolipids containing amino alcohol sphingosines), glycerophospholipid and glyceroglycolipids.[8] Unlike glycerophospholipids, sphingolipids seem to occupy only a small portion of the plasma membrane. The dual character of sphingoglycolipids, due to the presence of both hydrogen acceptor and hydrogen donors, makes it more potent to form a more rigid and uniquely ordered region next to the surface of the hydrophobic zone of hydrocarbon chains than glycerophospholipids which have only acceptors (Fig. 2). Another property of sphingoglycolipids, with applications in health sciences is their protective effect against certain pathogens.

Crystal structures of membrane proteins reveal that glycolipids are indispensible at very specific sites for protein/lipid interactions.[7] Glycolipids are characterised as functional and dynamic components in eukaryotic cells. As they are part of the

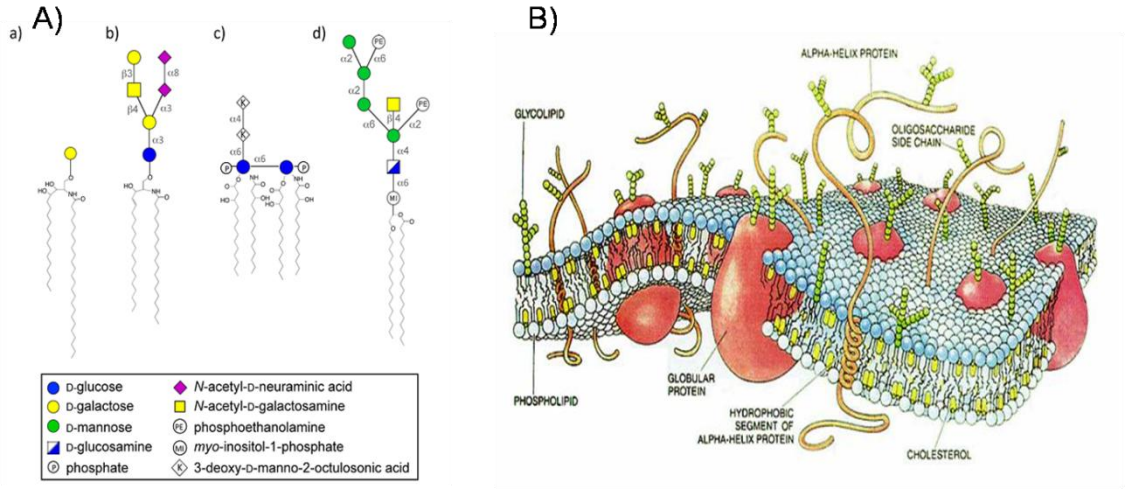


Figure 2: A) Glycolipids make up a diverse molecular class with different sugar moeities B) Role of Glycolipids on cell- surface.

micro-regions in membrane known as “lipid-rafts”,[3] they help in the flow and regulation of the cells. Each cell- surface glycolipid is considered as structural and static component of lipid bi-layer of biological membrane. Involvement of glycolipids in the information- controlling machinery of the cells is attributed to their assymetrical location in the outer half of the surface membrane bilayer.[8]

More than 40 decades ago, the function of glycolipids as annular lipids was investigated.[9] Until then, the glycolipids were only considered as the energy providers. Annular glycolipids are the lipids which surround a functional membrane protein. From the numerous studies, already done on ‘glycolipids as receptors and cell-surface markers’ it is clear that the glycolipids work as markers for the cellular recognition especially in the malignant transformation of the cells, cell division and cell behaviour.[10]

Recent studies have shown that the glycolipids based on microorganisms have great biological potency. Knowledge of structure, functions and biosynthesis of glycolipids lead to the search and production of anti-microbial pharmaceuticals based on natural compounds of microbial origin.[5,12] They have become an objective in the fight against cancer and other degenerative diseases.[5] Several groups have accounted for marine bacteria as potential producers of bioactive compounds with unique structural characteristics. Due to these above mentioned reasons, we chose to work on designing a combinatorial route for the synthesis of the natural compounds, Ieodoglucomides A and B, recently isolated from a marine derived bacteria, *Bacillus licheniformis* (Figure 3).

B. licheniformis is a saprophytic, gram positive and thermophilic bacteria with potential industrial, medical and synthetic applications.[14] It is typically used in the fermentation industries to make amylases, proteases and special chemicals, make

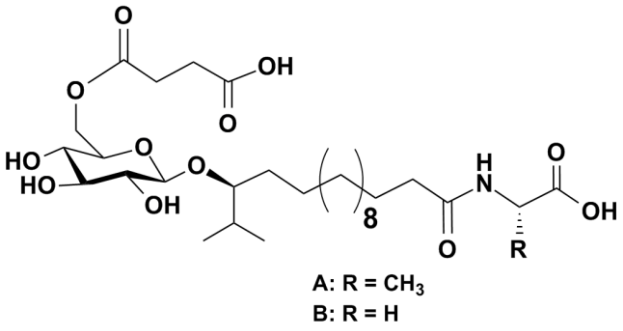


Figure 3: Structure of glycolipopeptides, Ieodoglucomides A and B

more human and environment friendly with low risk of adverse effects. Some groups have already investigated molecules isolated from this strain as biosurfactants, antibiotics and antifungal compounds.[16] The Ieodogluconamides are isolated from B. licheniformis in very small quantities and purified by complicated purification methods and thus the chemical synthesis is the most preferred method.[10,11]

Glycolipopeptides **A** and **B**, have unique structure with four different functionalities, an amino acid, a new fatty acid, a succinic acid and a sugar with absolute stereochemistry. Tareq *et.al* have isolated these compounds recently and characterised them using ^{1}H,^{13}C NMR and HMBC. The stereochemical analysis was performed using Mosher's method.[12,13] Besides, these compounds exhibited cytotoxicity against lung cancer and stomach cancer cell lines.[14]The complexity in achieving the stereo-, regio- selectivity and incorporation of these diverse functionalities into the same molecule coupled with an interesting biological significance, prompted us to develop a route for the synthesis of Ieodoglucomides A and B that should enable synthesis of a combinatorial library.

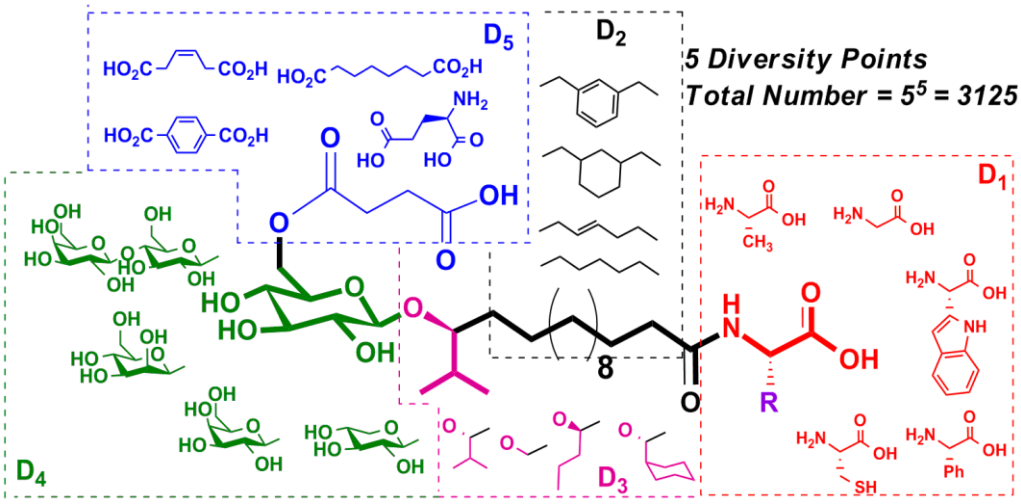


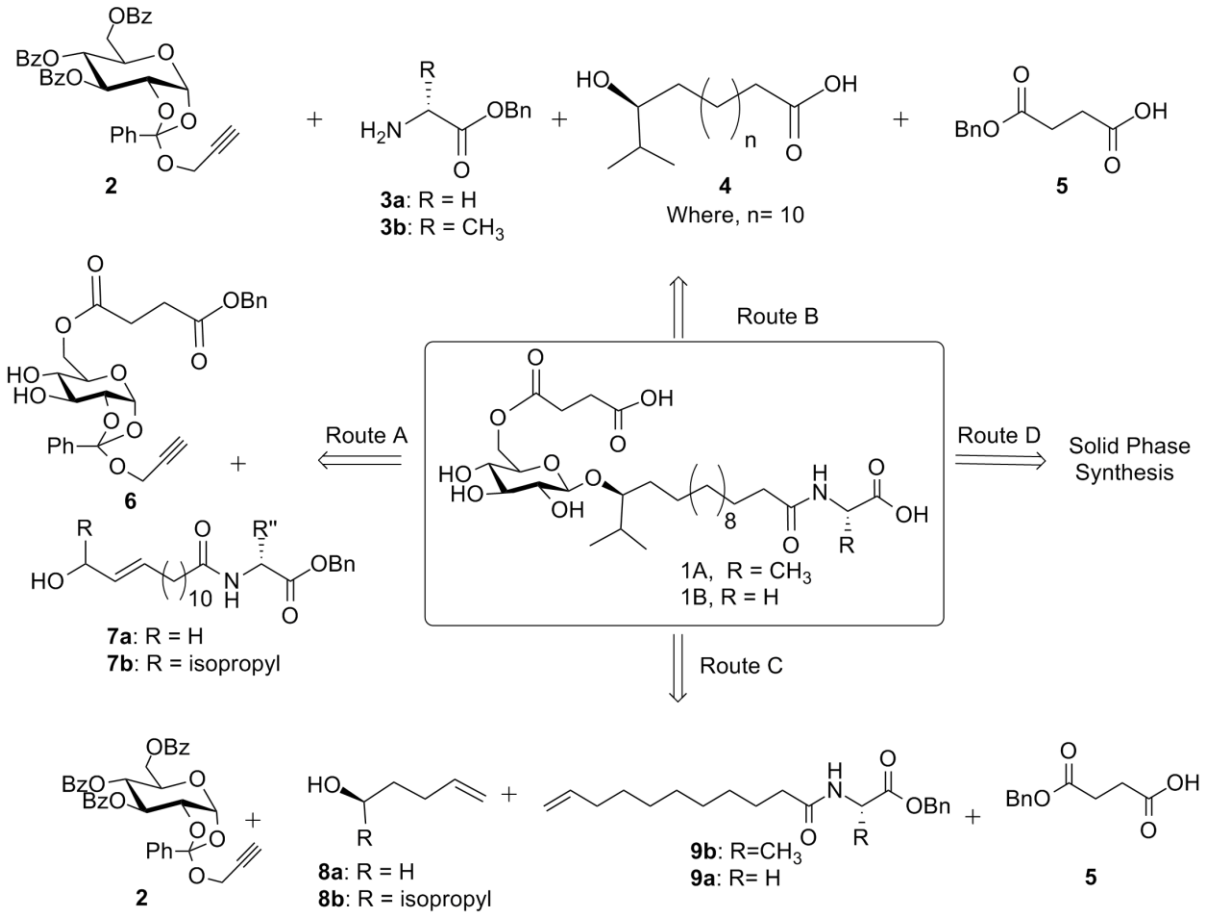
Figure 4. Diversification sites in Ieodoglucomides

Herein, a synthetic methodology that enables preparation of combinatorial library of Ieodoglucomide A and B via four different routes was developed. The library of Ieodoglucomides have five different diversification sites and thus if we consider atleast 5 different building blocks for each diversification site, then, a total of 5^5 = 3125 would be possible (Figure 4). The building blocks were chosen in such a way that there will be two compounds which are already been isolated form B.

licheniformis. The developed library will have regio- and stereo- chemical isomers. In future, all the compounds synthesized in this endeavour are thought to be subjected to anticancer property evaluation in collaboration.

Retrosynthetically, the Ieodoglucomides can be synthesized from five different components (D_1-D_5) viz. a sugar 1,2-orthoester, an alkene, an alkenamide, amino acid and a diacid. Many established protocols are available for esterification and amidation reactions. The installation of 1,2-*trans* or β- glycosides can conveniently be realized by the gold(III) catalyzed activation of the alkynyl 1,2-orthoester protocol developed in our group.[15] The alkene and alkenamide can be ligated by the popular Grubbs' cross metathesis reaction (Scheme 1).

Scheme 1. Retrosynthetic analysis of Ieodoglucomides



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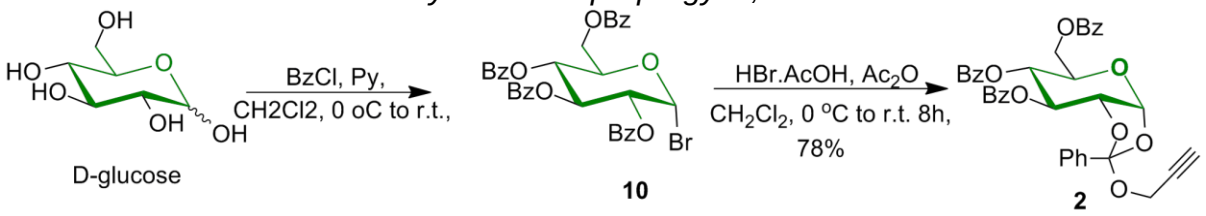
Unique structure of Ieodoglucomides with four diversification sites and interesting biological profile encouraged us to develop a novel route to synthesize these molecules and a combinatorial library. Four different synthesis pathways are envisaged to achieve the target Ieodoglucomides library as shown in the retrosynthetic analysis (Scheme 1).

Among all the four routes stated above, route C seems to be the most suitable one because the gold(III) catalysed glycosidation on propargyl 1,2-orthoesters (**2**)gives an easy access to 1,2-*trans* glycosides. The complete deprotection under the saponification conditions in route C (Scheme 2), shall enable us to get final compounds. Use of benzyl ester as the protecting group shall need a special mention as they would facilitate us to perform solid phase synthesis (route D)eventually using modified Wang resin (which contains *p*-methoxy benzyl group), to realize a combinatorial library. Besides, all the building blocks, (D_1, D_2, D_3, D_4 and D_5) are either commercially available or can be prepared by known procedures unlike in route B, where compounds such as **4**(D_3) are not commercially available and it's not very easy to incorporate both alcohol and acid groups.

In route A, the glycosyl donor **6** contains an ester at the *C*-6 position which was earlier found in our group to actually prevent the glycosidation reaction. All the above delineated observations encouraged to choose the path C to realize the target library of Ieodoglucomides. In a nutshell, route C involves the following key reactions *viz.* gold catalysed glycosidation, Grubbs' cross metathesis, regioselective esterification and hydrogenation.

Scheme 2: Synthesis of propargyl 1,2 orthoester.[4]

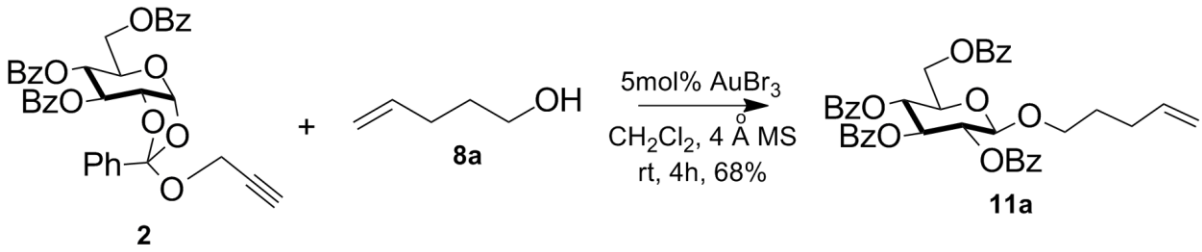


Reagents: a) BzCl, Py, CH_2Cl_2, 0 ^oC to r.t., 12h, b) HBr.AcOH, Ac_2O, CH_2Cl_2, 0 ^oC to r.t., 8h (70% over two steps) c) Propargyl alcohol, 2,6-lutidine, TBAI, reflux, 24h, 65%.

Accordingly, the synthetic endeavour started with the synthesis of propargyl 1,2-orthoesters starting from hexoses. For example, propargyl 1,2-orthoester of glucose was obtained in three convenient steps with an overall yield of 70%. per-*O*-Benzoylation of glucose followed by bromination using HBr.AcOH resulted in bromoglucopyranose (**10**) which was refluxed in propargyl alcohol, 2,6-lutidine and catalytic amount of TBAI for 24h to obtain the 1,2-orthoester **2** (Scheme 2).

Orthoester**2** is stable to bases but in the presence of mild acids it undergoes stereoelectronic rearrangements. Similarly mannosyl and galactosyl 1,2-orthoesters were synthesized. All orthoesters were confirmed by ^{1}H, ^{13}C NMR spectral analysis and also matched with that reported values.[3] For example, characteristic resonances at δ 121.3ppm for the orthoester methine and three carbonyls 166.7 ppm confirmed 1,2- orthoester **2**.

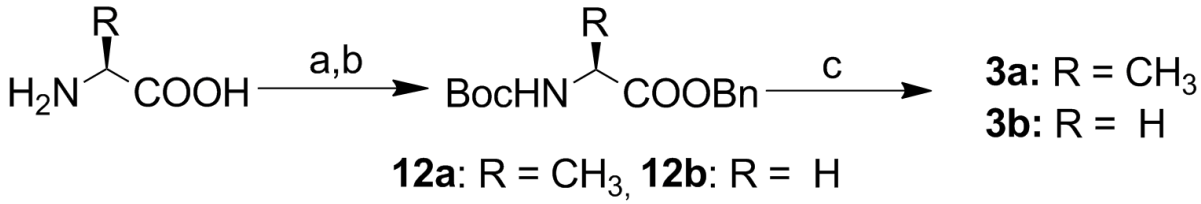
Scheme 3: Gold catalysed glycosidation on propargyl 1,2- orthoester[6]



Earlier in our group, 1,2-orthoesters were found to yield 1,2-*trans* glycosides in the presence of catalytic amount of $AuBr_3$in a stereoselective manner.[15] Thus, 5mol% of $AuBr_3$ was added to a dichloromethane solution of propargyl orthoester (**2**) and 4-pentene-1-ol (**8a**) and stirred under argon atmosphere for 4h to obtain **11a** in 68% yield (Scheme 3). Addition of freshly activated powder of 4Åmolecular sieves is essential for minimization of per-*O*-benzoylated lactol.

Improper activation of molecular sieves might lead to the formation of lactol;use of good quality $AuBr_3$is essential to avoid the formation of transorthoesterification. 1,2-cis glycosides can be synthesized by simply refluxing aglycon and the hexose in the presence of acid for a long period of time which is also called as Fischer glycosidation. Thus glucose and pentene-1-ol (**8a**) were refluxed in the presence of PTSA to give 1,2-*cis* pentenyl glucoside in 75% yield; formation of 1,2-*cis* product can be attributed to the strong anomeric effect. Glycosylation, when tried with the trichloroacetamidate donor gave the same 1,2-*trans*-glycoside **10a** but the very less

Scheme 4: Synthesis of Benzyl protected glycine and alanine

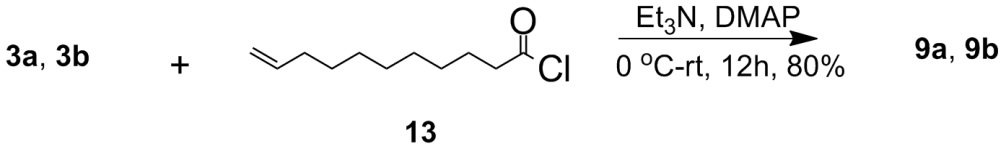


Reagents: a) $(Boc)_2O$,10%Na_2CO_3,THF,r.t.,6h (93%) b) BnOH, DIC, DMAP, CH_2Cl_2,rt, overnight (92 %) c) TFA:CH_2Cl_2(1:1), r.t.,1h (97%)

stability of the donor and its high potency to decompose to a lactol, directed us to follow the $AuBr_3$ glycosylation for further experiments.

The other set of building blocks for the Ieodoglucomide library requires the benzyl ester of amino acid which was obtained conveniently in three steps. Amino group of alanine and glycine were first protected as Boc-carabamate under standard condition and the esterification was carried out with BnOH in the presence of DIC/DMAP at room temperature. Resonances in the aromatic region at δ_H7.32 ppm and strong singlet at 0.99 ppm showed presence of both benzyl and Boc moieties.Amines**3a** and **3b** were obtainedby the deprotection of Boc group with TFA in DCM. Benzyl esters cna be obtained by the use of K_2CO_3,BnBr in DMF in 2.5h with 80% yield; however,it requires excess of BnBr and removal of BnBr is quite cumbersome as it is lachrymator.

Scheme 5: Amide coupling reaction using acid chloride



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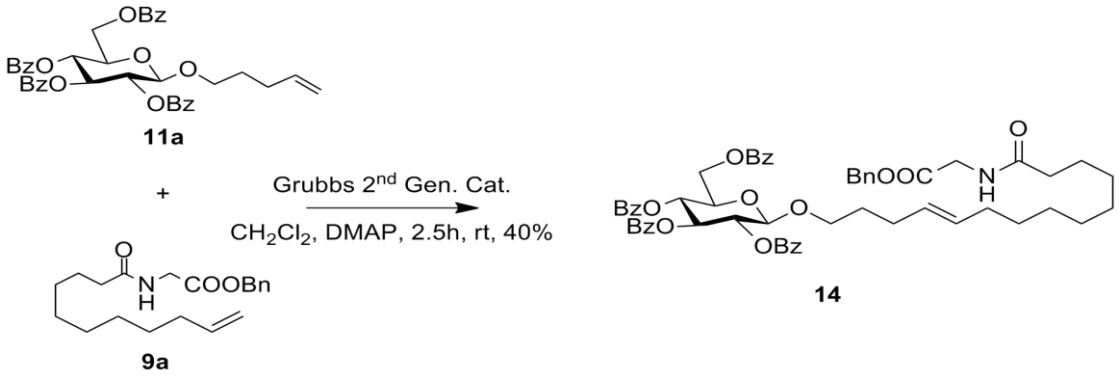
Amidation reaction was easily carried out by the use of acyl chloride. For example, benzyl protected amino ester **3a** or **3b** was treated with undecenoyl chloride **13** in the presence of Et_3N and DMAP at 0^oC-rt for 12h to obtain the required amide **9a,b** in 80%.

Pentenyl glucoside (**11a**) and the alkenyl amide **9a** were ligated by the use of cross metathesis reaction using Grubbs 2^{nd} generation catalyst to obtain the glycolipid **14**. The cross metathesis gave 40% yield as the self metathesis products as by-products which are characterized by TLC-MS. Olefin resonances were noticed around 6.06

ppm in the ^{1}H NMR spectrum and the ^{13}C NMR showed those at around 114 ppm and ~δ139 which confirmed the product in an unambiguous manner.

Scheme 6: Grubb's cross metathesis reaction



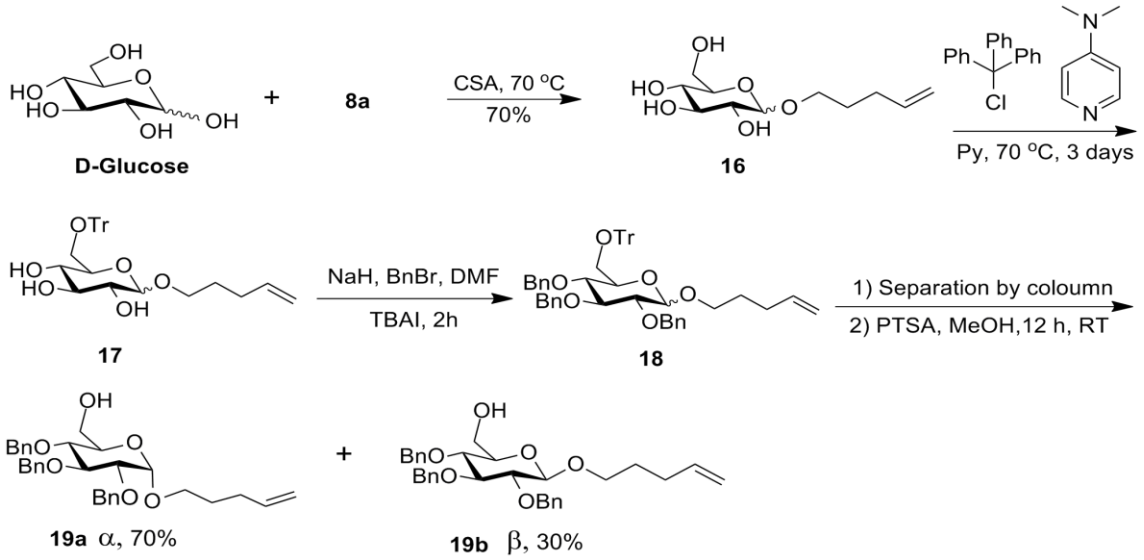
The attempted deprotection of benzoate groups of **14** under Zémplen conditions (NaOMe, MeOH) resulted in the transesterification to give the methyl ester due to the presence of MeOH as the solvent. Efforts to carry out the selective hydrolysis of benzoates in the presence of benzyl esters failed and thus thought of using Bn ethers on the carbohydrate portion as well.

Hence, there were two basic problems which have been encountered in this route: (1) Increase in the number of steps to achieve the target because of the replacement of -OBn group with -OMe, while deprotection of benzoyl groups using NaOMe. (2) Regioselective esterification of might pose a problem. (3) In the meantime, thorough characterization of **11a** showed that it is actually a pentenyl orthoester (**15**) and not the required pentenyl glucosides as we thought (NMR appended).

To overcome these shortcomings, a synthetic methodology needs to be followed through which esterification can be performed selectively on primary alcohol and thus C-6 OH free pentenyl glycosides are required. Pentenyl glucosides**16** were synthesized by aforementioned Fischer glycosidation conditions to obtain α,β-mixture in favour of α- glucoside and the primary hydroxyl group was protected as the trityl ether**17**. The remaining hydroxyl groups were protected as benzyl ethers and the trityl ether was deprotected under acidic conditions to get the required *C*-6 hydroxy free pentenyl glucosides**19a** and**19b** (Scheme 7). Purification of α,β-glucosides was performed by the flash silica gel column chromatography. Exclusive synthesis of β-isomer was carried out by the aforementioned 1,2-orthoester strategy.

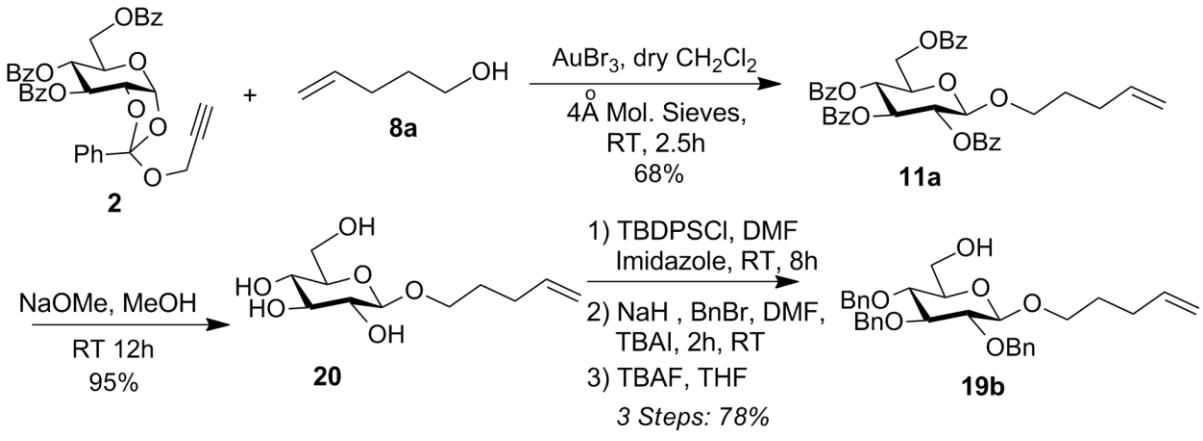
Appearance of δ_c97.6 and 103.2 ppm respectively for α– and β–glucosides confirmed the authenticity of the preparation.

Scheme 7: Synthesisof the analogue of α-analogue of Ieododoglucomides

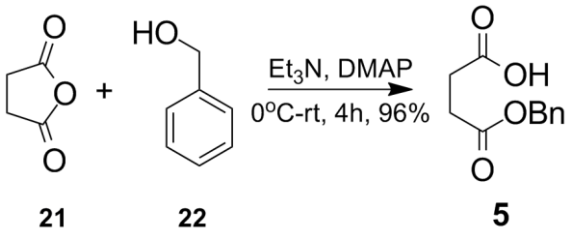


β glucoside **19b** was also prepared by using gold (III) bromide catalyzed glycosidation of propargyl 1,2- *trans*orthoesters followed by the deprotection of all the benzoates[17] resulting **11a** with 95% yield. The scheme was progressed by selective TBDPS protection of primary alcohol and consecutively, benzyl protection of secondary alcohols and selective deprotection of TBDPS using TBAF, THF respectively, resulted into the compound **12a**, (75% yield) with free primary alcohol. (Scheme 8).

Scheme 8: Synthesis ofβ–analogue of Ieodoglucomides

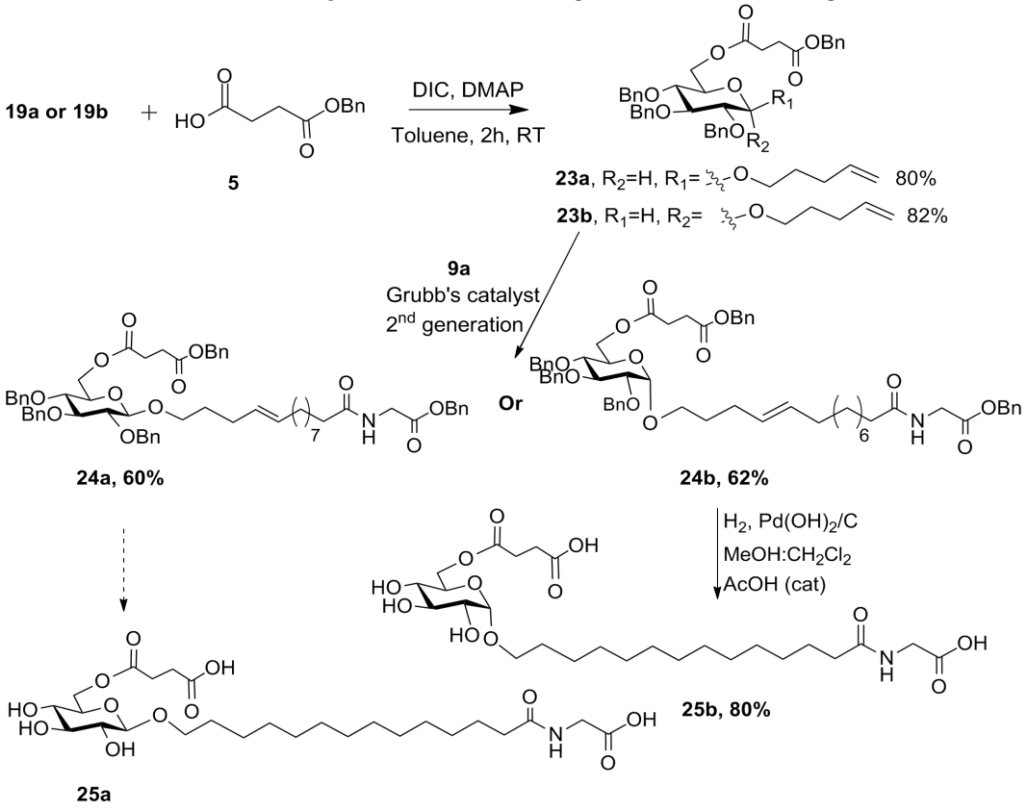


Scheme 9: Synthesis of Monobenzyl ester of succinic anhydride



The third building block that is required for the synthesis of Ieodoglucomides was synthesized by the ring opening of succinic anhydride**21** with benzyl alcohol**22**. Same results were observed by adding only 1eq. Et_3N to a stirred solution of succinic anhydride and benzyl alcohol in dichoromethane which can be inferred that Et_3N is acting like a base here not as a nucleophile hence the reaction does not require more amount of that. Here, some amount of disubstituted succinic acid ester was also formed and hence the compound was purified using silica gel column chromatography (Scheme 9). In the ^1H NMR spectrum of **5**, both the CH_2s showed

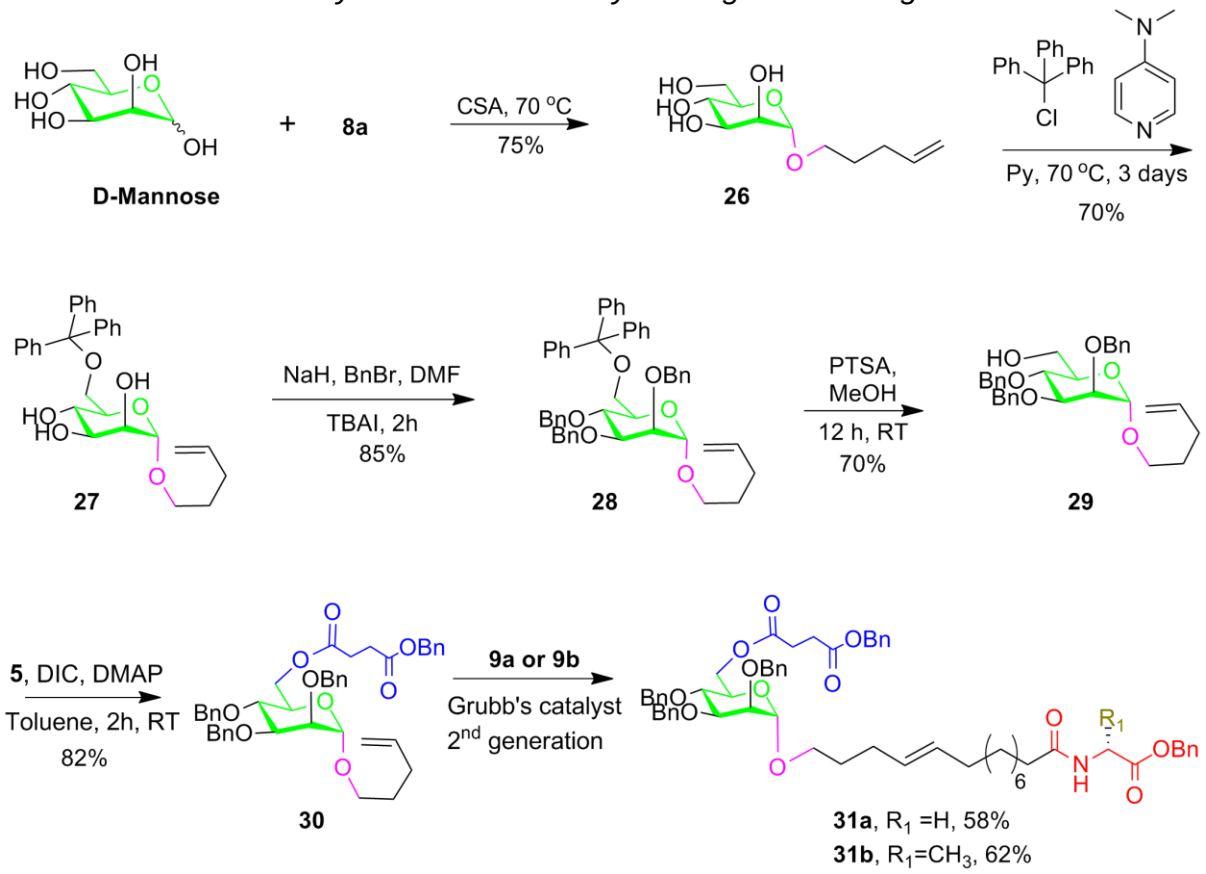
Scheme 11: Synthesis of Ieodoglucomides Analogues



different triplets and in the ^{13}C NMR spectra, two separate peaks for two carbonyl groups, confirm the formation of the mono protected acid product only as dibenzyl ester of succinic acid will give only one signal for all equivalent 4H's.

Having obtained all the required building blocks, the synthesis of Ieodoglucomide analogues was initiated. To begin, pentenyl glucosides**19a**and **19b**, were individually esterified with compound **5**prepared *vide supra* using DIC and DMAP to obtain esters **23a** and **23b** in 80% and 82% yield respectively (Scheme 11). In the ^{1}H NMR spectrum, resonances of $2CH_2$'s were noticed at ~δ2.66 ppm and the carbonyl presence was confirmed by ^{13}C NMR spectroscopy.

Scheme 12: Synthesis of mannosyl analogue of Ieodoglucomides



Both compounds **23a** and **23b**, were treated with Grubbs second generation catalyst to obtain **24a** and **24b** in 60% and 62% yields, respectively.

Finally, upon treatment with H_2, $Pd(OH)_2/C$, all the benzyl groups were deprotected along with the reduction of double bond to get target **25b,** an α-analogue of the final

compound, Ieodoglucomide B in 80% yield. Disappearance of all the peaks from aromatic region (δ_H:7-8 ppm) in ^{1}H NMR and from aromatic region (δ_C:125-135 ppm) confirmed the deprotection of all the benzyl groups and the reduction of double bond.

Similar methodology was applied for the synthesis of compounds, mannosyl analogues **31a** and **31b** (Scheme 12). Theβ–isomer of mannosyl glycoside**21,** is comparatively very difficult because the neighbouring group participation due to the -OBn group at C2 position, favours the attack form top side by the attacking aglycon, yielding α anomer exclusively. An identical strategy can be applied for the synthesis of galactoside and lactoside analogues of Ieodoglucomide.

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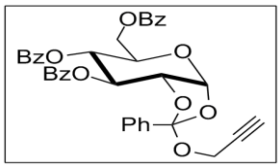
- All the chemicals were purchased from Sigma-Aldrich, RanKem and Spetrochemicals.
- ^{1}HNMR, ^{13}CNMR and DEPT spectra were recorded on Jeol-400 MHz spectrometer using tetramethylsilane (TMS) as an integral standard. Chemical shifts have been expressed in ppm units downfield from TMS.
- ESI HRMS data were recorded on Waters Synapt G2 spectrometer.
- Optical rotations were measured with a JACSO DIP 670 digital polarimeter.
- All reactions were monitored by Thin Layer Chromatography (TLC) carried out on 0.25 mm E-Merck silica gel plates (60F-254) with UV-light, staining with I_2 and anisaldehyde in ethanol, ninhydrine and PMA.
- All reactions were carried out under nitrogen atmosphere with dry solvents purchased from Merck and Finar.
- All evaporations were carried out under reduced pressure on B$\ddot{u}$chi rotatory evaporator below 40 ^{o}C unless otherwise specified.
- Silica gel (100 -200) mesh were used for coloumn chromatography.

Synthesis of 3,4,6 - tri - O - benzoyl - α - D - glucopyranose - 1,2 - (prop -2- ynyl orthobenzoate)(2): To a stirred solution of D- glucose (15g, 83.33 mmol) in 150 mL of pyridine, catalytic amount of N,N'-dimethyl aminopyridine was added. Benzoyl chloride (82g, 583 mmol) was added dropwise to the above stirred solution at 0 ^{o}C. The reaction mixture was let come down to room tem 

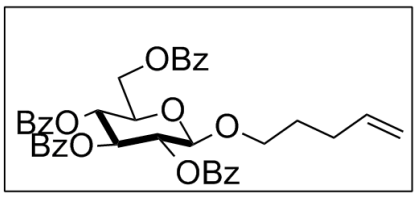
perature. After overnight stirring, ice cooled water was added to the reaction mixture and stirred for another 30 min at room tempertaure and the mixture was extracted with CH_2Cl_2(2x200mL). The collected organic layer was washed with 10%HCl (3x100mL), saturated solution of $NaHCO_3$, brine solution and dried over anhydrous sodium sulphate. The resultant organic layer was concentrated in *vacuo* and used for next step without any further purification.

To this resultant crude in dichloromethane, was added acetic anhydride (60mL) followed by the addition of hydrobromic acid in glacial acetic acid solution at 0 ^{o}C. The reaction mixture was warmed to room temperature and stirred for another 8h at room temperature. The progress of reaction was monitored using TLC and after completion of reaction, the cooled reaction mixture was diluted with dichloromethane and then poured into the ice-water. The organic layer (200 mlx2) was separated from aq. layer and washed with saturated solution of $NaHCO_3$, brine solution and dried over anhydrous sodium sulphate. The collected organic layer was concentrated in rota-vapour and the crude was dried in *vaccuo.*

To a solution of 2,3,4,6-tetra- O- benzoyl-a-D-glucopyranosyl bromide (47g, 71.25 mmol) in anhydrous dichloromethane (150mL) was added propargyl alchohol (6.22mL, 106.88 mmol), 2,6-lutidine (16.5mL) followed by a catalytic amount of tertra-n-butylammonium iodide (2.63g) at room temperature under nitrogen atmosphere. The reaction mixture was then, refluxed at 65 ^{o}C for 24h. After stirring for 24hours, the reaction mixture was diluted with dichloromethane (2 x100mL) and was extracted with water (2x 100mL). The organic layer was washed with aqueous solution of 10 % oxalic acid followed by washing with saturated solution of $NaHCO_3$.

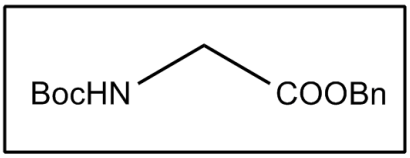
The organic layer was dried over anhydrous sodium sulphate solution after washing it with brine and concentrated in *vaccuo*. The resulting crude was purified by silica gel column chromatography using petroleum ether- ethyl acetate (4:1) as the mobile phase to obtain 3,4,6-tri-O- benzoyl-α-D-glucopyranose-1,2-(prop-2-ynyl orthobenzoate) (25g, 60%) as a yellowish thick gel (**2**): Characterisation data:$[\alpha]^{25}_{D}$ ($CHCl_3$, *c* 1.3)= -2.9°;^{1}H NMR (399.78 MHz, Chloroform-*d*): δ 2.37 (t, *J* = 2.4 Hz, 1H), 3.95 – 3.99 (m, 2H), 4.14 (ddd, *J* = 8.2, 4.6, 3.0 Hz, 1H), 4.38 (dd, *J* = 12.1, 4.8 Hz, 1H), 4.53 (dd, *J* = 12.1, 2.9 Hz, 1H), 4.86 (ddd, *J* = 5.3, 3.1, 1.2 Hz, 1H), 5.51 (d, *J* = 8.7 Hz, 1H), 5.76 (dd, *J* = 2.9, 1.3 Hz, 1H), 6.09 (d, *J* = 5.3 Hz, 1H), 7.19 – 7.30 (m, 2H), 7.43 (p, *J* = 6.9 Hz, 8H), 7.56 – 7.63 (m, 2H), 7.78 (dd, *J* = 7.9, 1.6 Hz, 2H), 7.90 – 7.96 (m, 4H), 8.03 – 8.11 (m, 2H); ^{13}C NMR (100.53 MHz, Chloroform-*d*): δ 52.5, 64.0, 67.6, 68.5, 69.1, 72.1, 74.1, 79.2, 97.9, 121.3, 126.6, 128.3, 128.6, 128.6, 128.7, 129.0, 129.1, 129.8, 130.0, 130.1, 130.2, 133.1, 133.7, 133.8, 134.1, 164.6, 165.3, 166.1; HRMS (Waters Synapt G2): m/z calcd for $[C_{37}H_{30}O_{10}+Na]^+$: 657.1737; Found: 657.1736.

Gold catalysed synthesis of pentenyl glucopyronuside (11a): 4 A°M. S. (500 mg) were added to the stirred solution of **2** (500 mg, 7.88 mmol) in dichloromethane.



After continuous stirring for 10 min, 4-pent-1-ene-ol (0.122 mL, 1.182 mmol) was added along with the catalytic amount of $AuBr_3$. The mixture was stirred for another two hours. The reaction was monitored using TLC and TLC-MS. After the completion of reaction, the reaction mixture was filtered using sintered funnel and celite and the filtrate was concentrated under vacuum. The resultant was then purified using 60-120 mesh size silica gel coloumn chromatography with ethyl acetate –pet ether (1:5) eluting system. The fraction was collected and concentrated under vacuum. Yellowish thick liquid was obtained with 65% yield. The resulting crude was purified by silica gel column chromatography using petroleum ether- ethyl acetate (4:1) as the mobile phase to obtain 2,3,4,6-tetra-O-benzoyl-β-D-glucopyranose-4-pent-1-eneyl) glycoside (320 mg, 65%) as a yellowish thick gel.

Characterisation data: Rotation:$[\alpha]_D^{25}$ ($CHCl_3$, *c* 1.0) = +0.22°;^{1}H NMR (399.78 MHz, Chloroform-*d*): δ 1.52 – 1.72 (m, 2H), 1.87 – 2.08 (m, 2H), 3.54 (dt, *J* = 9.7, 6.7 Hz, 1H), 3.91 (dt, *J* = 9.6, 6.2 Hz, 1H), 4.07 – 4.22 (m, 1H), 4.49 (dd, *J* = 12.1, 5.3 Hz, 1H), 4.58 – 4.64 (m, 1H), 4.76 – 4.84 (m, 1H), 4.83 (s, 1H), 5.51 (dd, *J* = 9.7, 7.8 Hz, 1H), 5.57 – 5.69 (m, 2H), 5.66 (t, *J* = 9.7 Hz, 1H), 5.89 (t, *J* = 9.7 Hz, 1H), 6.99 – 7.63 (m, 12H), 7.70 – 8.15 (m, 8H);^{13}C NMR (101 MHz, Chloroform-*d*): δ 28.6, 29.9, 63.3, 69.5, 69.9, 72.0, 72.2, 73.0, 101.3, 115.0, 128.4, 128.4, 128.4, 128.4, 128.5, 128.5, 128.5, 128.9, 128.9, 129.4, 129.7, 129.8, 129.8, 129.8, 129.8, 129.8, 129.9, 129.9, 129.9, 129.9, 133.2, 133.3, 133.3, 133.5, 137.8, 165.2, 165.3, 165.9, 166.3;
HR-MS (Waters synapt G2) m/z Calcd for $C_{39}H_{36}O_{10}Na$, 687.2206; Found, 687.2200.

Synthesis of benzyl esters of Boc-Gly (12b) :L-glycine (5g, 66.66 mmol) was dissolved in 120 mL solution of 10% Na_2CO_3(11.89 g, 112.24 mmol) and THF (50 mL). The mixture was cooled down to 0 

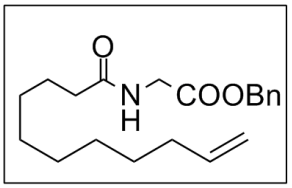
°C and ice-cooled solution of $(Boc)_2O$ (13.5 mL, 66.66 mmol) in 50 mL THF was added dropwise to the above stirred solution at 0°C. After continuous stirring for 6h, THF was evaporated and the mixture was diluted with EtOAc. $Na_2CO_3$was neutralized with 10% HCl (200 mL) and then the aqueous layer was extracted twice with EtOAc. The collected organic layer was dried over anhydrous sodium sulphate and was concentrated in *vacuo.* White solid (12g, 75%) was obtained. The product was directly used for the synthesis of benzyl ester of boc protected glycine (**12b**) after confirming with the HR-MS data (Waters synapt G2) m/z Calculated: 175.1824 Found from HR-MS: 198.1219(M^++ Na).

Boc protected glycine (3g, 17.14 mmol) was dissolved in 20 mL CH_2Cl_2 and 5 mL N, N-dimethyl formamide. The mixture was cooled down to 0°C and N, N'-diisopropylcarbodiimide (2.65 mL, 17.14 mmol) was added to the above stirred solution at 0°C. After addition of Benzyl alcohol (1.7 mL, 17.14 mmol) and N, N'-dimethyl aminopyridine (209.43 mg, 1.714 mmol) the reaction mixture was continued to stir for overnight. The CH_2Cl_2 was evaporated, and the mixture was diluted with 100mL EtOAc. The EtOAc layer was extracted twice with 10% Na_2CO_3 and once with brine.The collected organic layer was dried over anhydrous sodium sulphate

and was concentrated in *vacuo.* A filtration coloumn was performed to obtain pure benzyl ester of boc-glycine (**12b**) with 85% yield. Characterisation data:^{1}H NMR (399.78 MHz, Chloroform-*d*)**:** δ 1.42 (s, 9H), 3.92 (d, *J* = 4.4 Hz, 2H), 5.15 (d, *J* = 1.8 Hz, 2H), 7.32 (s, 5H); ^{13}C NMR (100.53 MHz, Chloroform-*d*): δ 28.2, 28.2, 28.2, 42.4, 67.0, 79.9, 128.3, 128.3, 128.4, 128.5, 128.5, 135.2, 155.6, 170.2.; HRMS (Waters Synapt G2): m/z calculated for $[C_{15}H_{23}NO_4+Na]^+$: 265.3050; Found: 288.1211.

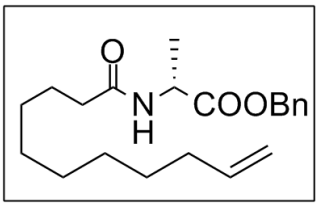
This obtained white solid (5b, 500 mg, 1.88 mmol) was dissolved in CH_2Cl_2: TFA (10mL: 10mL) and the mixture was allowed to stir at room temperature for 1 hour. The progress of reaction was monitored using TLC. After completion of reaction, both TFA and CH_2Cl_2 were evaporated using Rotatory evaporator. Remaining TFA and the salt (TFA.gly-OBn) were neutralized by saturated solution of Na_2CO_3. The reaction mixture was extracted with EtOAc (3x 50mL). Collected organic layer was dried over anhydrous Na_2SO_4 and was concentrated *invacuo.*Obtained yellowish liquid **(12b**) was directly used for the synthesis of **9b**

Similar procedure was followed for the synthesis of benzyl ester of Boc- ala (**12a**).

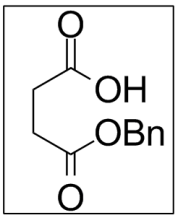
Synthesis of Benzyl N-(dec-9-enecarbonyl)glycinate(9a): To a stirring solution of Benzyl ester of glycine (1.26g, 7.64 mmol) dissolved in 10mL CH_2Cl_2,triethylamine (4.25mL, 30.56 mmol) and catalytic amount of N, N'-dimethylaminopyridine (93.337mg , 0.764 mmol) were added. 

The mixture was cooled down to 0 ^{o}C and a solution of 10- undecenoyl chloride in 2mL CH_2Cl_2 was added dropwise to the above reaction mixture. White precipitate was observed upon slow addition of acid chloride. After continuous stirring for overnight, triethylamine and CH_2Cl_2were evaporated under vacuum. The mixture was washed with washed with water and the aqueous layer was extracted with EtOAc. The above process was repeated 3 times. Collected organic layer was washed once with brine and dried with anhydrous sodium sulphate. After concentrating the collected layer under high vacuum, pale yellowish power was obtained (7b, 1.13g, 91 %yield). Characterisation data:^{1}H NMR (399.78 MHz, Chloroform-*d*): δ 1.24 – 1.41 (m, 11H), 1.63 (quintet, *J* = 7.5 Hz, 2H), 2.03 (q, *J* = 6.9 Hz, 2H), 2.24 (t, *J* = 7.5 Hz, 2H), 4.08 (d, *J* = 5.2 Hz, 2H), 4.83 – 5.07 (m, 2H), 5.18 (s, 2H), 5.80 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1H), 6.07 (s, 1H), 7.20 – 7.54 (m, 4H); ^{13}C NMR (100.53 MHz, Chloroform-*d*) δ 25.6, 29.0, 29.1,

29.3, 29.4, 29.4, 33.9, 36.5, 41.4, 67.3, 114.2, 128.4, 128.5, 128.6, 128.7, 128.7, 135.2, 139.3, 170.1, 173.4; HRMS(Waters synapt G2) m/z Calcd for $C_{20}H_{31}O_3NNa$, 354.2045; Found, 354.2049.

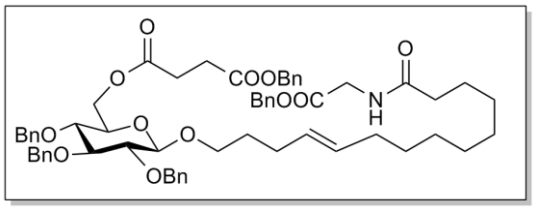
Similar procedure was followed for the synthesis of compound, **Benzyl N-(dec-9-enecarbonyl)alaninate (9b):**$[\alpha]_D^{25}$ ($CHCl_3$, *c* 1.0) = -4.0^o; ^{1}H NMR (399.78 MHz, Chloroform-*d*): δ 1.17 – 1.36 (m, 11H), 1.39 (d, *J* = 7.2 Hz, 3H), 1.59 (q, *J* = 7.2 Hz, 2H), 2.01 (q, *J* = 7.6 Hz, 2H), 2.18 (t 

, *J* = 7.4 Hz, 2H), 4.64 (quintet, *J* = 7.3 Hz, 1H), 4.80 – 5.08 (m, 2H), 5.18 (ABq, *J* = 12.3 Hz, 2H), 5.78 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 6.06 (d, *J* = 7.2 Hz, 1H), 7.07 – 7.80 (m, 4H); ^{13}C NMR (100.53 MHz, Chloroform-*d*): δ 18.5, 25.5, 28.8, 29.0, 29.1, 29.2, 29.2, 33.7, 36.5, 47.9, 67.1, 114.1, 128.1, 128.1, 128.4, 128.6, 128.6, 135.3, 139.1, 172.6, 173.1; HRMS(Waters synapt G2) m/z Calcd for $C_{21}H_{31}O_3NNa$, 368.2202; Found, 368.2209.

4-(benzyloxy)-4-oxobutanoic acid (5): To a stirred solution of succinic anhydride (**21,** 2g, 19.98 mmol) dissolved in CH_2Cl_2: Et_3N (10mL: 10mL), catalytic amount of N, N'-dimethylamino pyridine (244mg, 1. 998 mmol) was add 

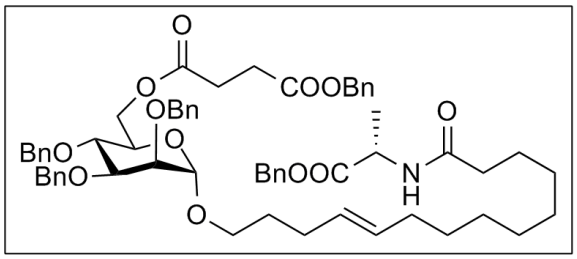
ed at room temperature. Benzyl alcohol (**22**,2.16mL, 19.98 mmol) was added dropwise to the above stirred solution at 0 ^{o}C. After stirring for 24 hours, dichloromethane and triethyl amine were evaporated using rotatory evaporator. The resultant was diluted with CH_2Cl_2 and was extracted with 1N HCl solution. The above mentioned procedure was repeated twice and then the collected organic layer was dried over anhydrous sodium sulphate after washing it with 1N HCl solution, followed by washing with saturated solution of $NaHCO_3$. White solid (8, 3.85g, 92.6%) was obtained with 92.6%yield.**:**^{1}H NMR (399.78 MHz, Chloroform-*d*): δ 2.70 (td, *J* = 4.3, 1.1 Hz, 4H), 5.15 (s, 2H), 7.28 – 7.46 (m, 5H); ^{13}C NMR (100.53 MHz, Chloroform-*d*): δ 28.9, 66.6, 128.2, 128.2, 128.3, 128.6, 128.6, 135.6, 172.0, 177.9;HRMS(Waters synapt G2) m/z Calcd for $C_{11}H_{12}O_4NNa$, 231.0633; Found, 231.0626.

Benzyl-2-(14-(6-*O*-(4-(benzyloxy)-4-oxobutanoyl)-2-3-4-tri-*O*-benzyl-β-D-glucopyranosyloxy)-E-tetradec-10-enamido) acetate (24a):1eqiv. Of both the alkenes 17a and 9a were dried under high vacuum and then a septum with Nitrogen atmosphere was put over it. Dry DCM (10mL) was added to it and then 0.1equiv of



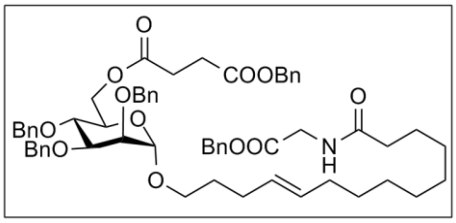
Grubb's 2nd g eneration catalyst was added to the above stirred solution. The recation mixture was allowed to stir for 2.5 hours. The reaction was monitored using TLC. This reaction does not go for completion and gives the self metathesis product as the side product. The reaction mixture was concentrated under vacuum and purified using silica gel coloumn chromatography with 35 % EA/PE as eluting system. $[\alpha]_D^{25}$ ($CHCl_3$, *c* 1.2) = -37.4^o;^{1}H NMR (399.78 MHz, Chloroform-*D*): δ 1.18 – 1.38 (m, 10H), 1.56 – 1.77 (m, 4H), 1.85 – 2.13 (m, 4H), 2.15 – 2.26 (m, 2H), 2.62 – 2.69 (m, 4H), 3.39 – 3.46 (m, 1H), 3.47 – 3.56 (m, 3H), 3.65 (t, *J* = 8.7 Hz, 1H), 3.91 (dt, *J* = 9.8, 6.4 Hz, 1H), 4.08 (d, *J* = 5.0 Hz, 2H), 4.26 (dd, *J* = 11.7, 4.4 Hz, 1H), 4.33 (d, *J* = 1.6 Hz, 1H), 4.37 (d, *J* = 7.7 Hz, 1H), 4.56 (d, *J* = 10.8 Hz, 1H), 4.71 (d, *J* = 10.9 Hz, 1H), 4.79 (d, *J* = 10.8 Hz, 1H), 4.85 (d, *J* = 10.7 Hz, 1H), 4.95 (d, *J* = 11.0 Hz, 2H), 5.11 (s, 2H), 5.18 (s, 2H), 5.35 – 5.41 (m, 2H), 5.94 (s, 1H), 7.02 – 7.76 (m, 25H);^{13}C NMR (100.53 MHz, Chloroform-*D*) δ 25.5, 29.0, 29.0, 29.0, 29.1, 29.1, 29.2, 29.2, 29.3, 29.3, 29.5, 29.6, 32.5, 36.4, 41.3, 63.4, 66.5, 67.2, 69.6, 72.7, 74.8, 75.0, 75.7, 82.0, 82.1, 84.6, 103.6, 127.6, 127.7, 127.8, 127.9, 127.9, 128.1, 128.1, 128.1, 128.2, 128.2, 128.2, 128.3, 128.4, 128.4, 128.4, 128.4, 128.4, 128.5, 128.5, 128.5, 128.5, 128.6, 128.6, 129.1, 131.1, 135.1, 135.7, 137.8, 138.3, 138.4, 170.0, 171.9,s 171.9, 173.2; HRMS(Waters synapt G2) m/z Calcd for $C_{61}H_{73}O_{12}NNa$, 1034.5030; Found, 1034.5106.

Benzyl-2-(R)-Methyl-2-(14-(6-*O*-(4-(benzyloxy)-4-oxobutanoyl)-2-3-4-tri-*O*-benzyl-α-D-mannopyranosyloxy)-E-tetradec-10-enamido)acetate(31b):Similar procedure as 18a was followed here. The two alkenes taken were 17d and 9b. $[\alpha]_D^{25}$



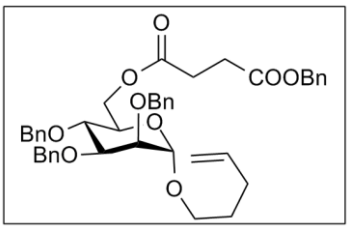
($CHCl_3$, *c* 1.4) = -21.8°;^{1}H NMR (200.13 MHz, Chloroform-*d*): δ 1.27 (s, 10H), 1.40 (d, *J* = 7.2 Hz, 3H), 1.59 (q, *J* = 6.8 Hz, 4H), 1.85 – 2.06 (m, 4H), 2.08 – 2.26 (m, 3H), 2.66 (s, 4H), 3.35 (dt, *J* = 13.5, 7.0 Hz, 1H), 3.61 (dt, *J* = 9.5, 6.7 Hz, 1H), 3.72 – 3.82 (m, 2H), 3.92 (d, *J* = 6.2 Hz, 2H), 4.35 (d, *J* = 3.3 Hz, 2H), 4.52 – 4.69 (m, 4H), 4.71 (d, *J* = 2.4 Hz, 2H), 4.76 – 4.86 (m, 1H), 4.92 (d, *J* = 10.8 Hz, 1H), 5.10 (s, 2H), 5.16 (d, *J* = 1.7 Hz, 2H), 5.30 – 5.46 (m, 1H), 6.05 (d, *J* = 7.4 Hz, 1H), 7.07 – 7.53 (m, 25H); ^{13}C NMR (50 MHz, CHLOROFORM-*d*) δ 18.5, 25.5, 28.9, 29.0, 29.0, 29.1, 29.2, 29.2, 29.2, 29.3, 29.5, 32.5, 36.5, 47.9, 63.7, 66.4, 67.0, 67.1, 70.0, 72.1, 72.6, 74.5, 74.8, 75.1, 80.2, 97.9, 127.5, 127.5, 127.6, 127.6, 127.7, 127.7, 127.7, 128.0, 128.0, 128.0, 128.0, 128.1, 128.1, 128.1, 128.1, 128.1, 128.2, 128.3, 128.3, 128.3, 128.3, 128.5, 128.5, 128.5, 128.6, 129.0, 131.1, 135.3, 135.8, 138.2, 138.3, 138.4, 171.9, 172.0, 172.6, 173.0; HRMS(Waters synapt G2) m/z Calcd for $C_{62}H_{75}O_{12}NNa$, 1048.5187; Found, 1048.5186.

Benzyl-2-(14-(6-*O*-(4-(benzyloxy)-4-oxobutanoyl)-2-3-4-tri-*O*-benzyl-α-D-mannopyranosyloxy)-E-tetradec-10-enamido)acetate (31a):Similar procedure as 18a was followed here. The two alkenes taken were 17d and 9a. $[\alpha]_D^{25}$ ($CHCl_3$, *c* 1.0) = -30.6°; ^{1}H NMR (200.13 MHz, Chloroform-*d*) δ 1.27 (s, 10H), 1.46 – 1.75 (m, 4H), 1.85 – 2.05 (m, 4H), 2.



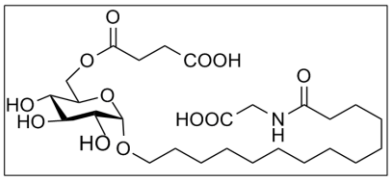
22 (t, *J* = 7.4 Hz, 3H), 2.66 (s, 4H), 3.34 (dt, *J* = 9.9, 6.5 Hz, 1H), 3.61 (dt, *J* = 9.3, 6.5 Hz, 1H), 3.77 (s, 1H), 3.92 (d, *J* = 6.2 Hz, 2H), 4.07 (d, *J* = 5.2 Hz, 2H), 4.35 (d, *J* = 3.3 Hz, 2H), 4.58 (d, *J* = 10.8 Hz, 1H), 4.63 (s, 2H), 4.71 (d, *J* = 2.4 Hz, 2H), 4.76 – 4.85 (m, 1H), 4.92 (d, *J* = 10.8 Hz, 1H), 5.10 (s, 2H), 5.17 (s, 2H), 5.28 – 5.44 (m, 2H), 5.98 (s, 1H), 6.97 – 7.53 (m, 25H); ^{13}C NMR (50.32 MHz, Chloroform-*d*): δ 25.5, 29.0, 29.1, 29.1, 29.1, 29.1, 29.2, 29.2, 29.2, 29.3, 29.5, 36.3, 41.3, 63.8, 66.4, 67.1, 67.1, 70.1, 72.1, 72.6, 74.5, 74.8, 75.1, 80.2, 97.9, 127.5, 127.6, 127.6, 127.6, 127.7, 127.7, 128.1, 128.1,

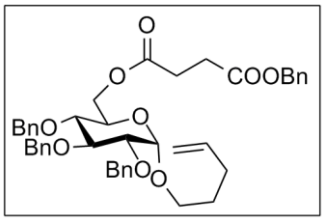
128.1, 128.1, 128.1, 128.1, 128.1, 128.2, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.3, 128.4, 128.5, 128.5, 128.6, 131.1, 135.1, 135.8, 138.2, 138.3, 138.4, 170.0, 171.9, 172.0, 173.2; HRMS(Waters synapt G2) m/z Calcd for $C_{61}H_{73}O_{12}NNa$, 1034.5030; Found, 1034.5039.

Pent-4-enyl)-6-*O*-(4-(benzyloxy)-4-oxobutanoyl)-2-3-4-tri-*O*-benzyl-α-d-Mannopyranoside (30): Compound 12d (1equiv.) was dissolved in 10mL of toluene and the mixture was stirred for two hours. Compound 5 (1 equiv.) was added to the above stirred 

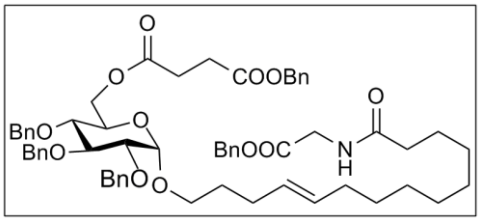
solution. The mixture was cooled down to room temperature and DIC (1equiv.) was added to it at 0 ^{o}C along with a catalytic amount of DMAP. After 2hrs, the solvent was evaporated under reduced pressure and the mixture was extracted with EtOAc. The organic layer was collected and concentrated under under vacuum.$[\alpha]_D^{25}$ ($CHCl_3$, *c* 1.0) = -31.5^{o}; ^{1}H NMR (399.78 MHz, Chloroform-*D*) δ 1.61 (quintet, *J* = 6.8 Hz, 2H), 2.05 (q, *J* = 6.5 Hz, 2H), 2.66 (s, 4H), 3.34 (dt, *J* = 9.7, 6.4 Hz, 1H), 3.63 (dt, *J* = 9.7, 6.6 Hz, 1H), 3.74 – 3.77 (m, 1H), 3.78 (dt, *J* = 4.8, 2.5 Hz, 1H), 3.91 (d, *J* = 6.3 Hz, 1H), 4.35 (dABq, *J* = 11.7, 2.5 Hz, 2H), 4.58 (d, *J* = 10.8 Hz, 1H), 4.64 (s, 2H), 4.71 (ABq, *J* = 12.4 Hz, 2H), 4.80 (d, *J* = 1.6 Hz, 1H), 4.92 (d, *J* = 10.7 Hz, 1H), 4.96 (d, *J* = 1.5 Hz, 1H), 4.97 – 5.04 (m, 1H), 5.11 (d, *J* = 1.8 Hz, 1H), 5.11 (ABq, *J* = 10.5 Hz, 2H), 5.76 (ddt, *J* = 16.9, 10.2, 6.5 Hz, 1H), 7.05 – 7.52 (m, 20H); ^{13}C NMR (100.53 MHz, Chloroform-*D*): δ 28.6, 29.1, 29.2, 30.3, 63.9, 66.6, 67.2, 70.2, 72.2, 72.7, 74.6, 74.7, 75.3, 80.3, 98.0, 115.1, 127.7, 127.7, 127.8, 127.8, 127.9, 127.9, 128.3, 128.3, 128.3, 128.3, 128.3, 128.4, 128.4, 128.4, 128.5, 128.5, 128.5, 128.5, 128.6, 128.6, 135.9, 138.0, 138.3, 138.4, 138.5, 172.1, 172.2; HRMS(Waters synapt G2) m/z Calcd for $C_{43}H_{48}O_9Na$, 731.3196; Found, 731.3190.

2-(14-(6-*O*-(4-hydroxy-4-oxobutanoyl)-α-D-glucopyranosyloxy)-*E*-tetradec-10-enamido)acetic acid (25b):Compound 18b was dissolved in 10mL MeOH and EtOAc. Catalytic amount of $Pd(OH)_2$ on Charcoal was added to it and thereaction

was performed in the parr reactor by applying 18  bar H_2 gas . The mixture was stirred for 48 h. After completion, the mixture was filtered off and the filtrate was concentrated and washed once with toluene and once with chloroform.$[\alpha]_D^{25}$ ($CHCl_3$, *c*0.9) = +33.2^o;^{1}H NMR (399.78 MHz, Chloroform-*d*): δ 1.16 – 1.42 (m, 18H), 1.55 (dq, *J* = 13.4, 6.9 Hz, 4H), 1.92 (s, 1H), 2.18 (t, *J* = 7.5 Hz, 2H), 2.48 – 2.63 (m, 4H), 3.20 (t, *J* = 9.3 Hz, 1H), 3.27 (s, 1H), 3.33 (dd, *J* = 9.7, 3.8 Hz, 1H), 3.38 (dt, *J* = 8.0, 6.4 Hz, 1H), 3.57 (t, *J* = 9.2 Hz, 2H), 3.60 – 3.66 (m, 1H), 3.69 (ddd, *J* = 9.7, 6.0, 1.8 Hz, 1H), 3.81 (s, 2H), 4.14 (dd, *J* = 11.7, 6.1 Hz, 1H), 4.30 (dd, *J* = 11.8, 1.9 Hz, 1H), 4.68 (d, *J* = 3.7 Hz, 1H); ^{13}C NMR (100.53 MHz, Chloroform-*d*) δ 29.5, 30.0, 32.5, 32.7, 32.9, 33.1, 33.2,33.2, 33.2, 33.2, 33.3,33.3, 33.3,33.3, 39.5, 67.8, 72.0, 73.8, 74.5, 76.0, 77.6, 102.7, 176.8, 176.8, 176.8, 179.4; HRMS(Waters syngpt G2) m/z Calcd for $C_{26}H_{45}O_{12}NNa$, 586.2839; Found, 586.2850

(Pent-4-enyl)-6-*O*-(4-(benzyloxy)-4-oxobutanoyl)-2-3-4-tri-*O*-benzyl-α-d-gluco-pyranoside (23b):Compound 17c (1equiv.) was dissolved in 10mL of toluene and the mixture was stirred for two hours. Compound 5 (1 equiv.) was added to the above stirred solution. The mixture was cooled down to room temperature and DIC (1equiv.) was added to it at 0 ^{o}C along with a  catalytic amount of DMAP. After 2hrs, the solvent was evaporated under reduced pressure and the mixture was extracted with EtOAc. The organic layer was collected and concentrated under under vacuum.$[\alpha]_D^{25}$ ($CHCl_3$, *c* 1.6) = +30.6^o; ^{1}H NMR (400 MHz, Chloroform-*D*) δ 1.73 (dtt, *J* = 10.2, 6.8, 3.1 Hz, 2H), 2.13 (hept, *J* = 7.8 Hz, 2H), 2.59 – 2.69 (m, 4H), 3.41 (dt, *J* = 9.8, 6.5 Hz, 1H), 3.48 (t, *J* = 9.7 Hz, 1H), 3.52 (dd, *J* = 9.6, 3.6 Hz, 1H), 3.62 (dt, *J* = 9.8, 6.9 Hz, 1H), 3.84 (ddd, *J* = 10.1, 4.3, 2.2 Hz, 1H), 4.01 (t, *J* = 9.2 Hz, 1H), 4.25 (dd, *J* = 11.9, 2.2 Hz, 1H), 4.31 (dd, *J* = 11.9, 4.4 Hz, 1H), 4.56 (d, *J* = 10.8 Hz, 1H), 4.64 (d, *J* = 12.0 Hz, 1H), 4.70 (d, *J* = 3.6 Hz, 1H), 4.77 (d, *J* = 12.0 Hz, 1H), 4.83 (d, *J* = 10.8 Hz, 1H), 4.87 (d, *J* = 10.7 Hz, 1H), 4.93 – 5.06 (m, 2H), 5.00 (s, 1H), 5.09 (s, 2H), 5.80 (ddt, *J* = 16.9, 10.3, 6.7 Hz, 1H), 7.25 –

7.38 (m, 20H); ^{13}C NMR (100.53 MHz, Chloroform-*D*): δ 28.5, 28.9, 29.0, 30.2, 63.3, 66.5, 67.6, 68.6, 73.2, 75.1, 75.7, 77.5, 80.1, 82.0, 96.8, 115.0, 127.6, 127.9, 127.9, 127.9, 127.9, 128.0, 128.0, 128.2, 128.2, 128.2, 128.2, 128.2, 128.4, 128.4, 128.4, 128.4, 128.4, 128.5, 128.5, 128.5, 135.7, 137.9, 137.9, 138.2, 138.7, 171.9, 171.9; HRMS(Waters synapt G2) m/z Calcd for $C_{43}H_{48}O_9Na$, 731.3196; Found, 731.3185.

Benzyl-2-(14-(6-*O*-(4-(benzyloxy)-4-oxobutanoyl)-2-3-4-tri-*O*-benzyl-α-D-glucopyranosyloxy)-E-tetradec-10-enamido)acetate (24b):Similar procedure as 18d was followed. Grubb's cross metathesis was performed with 9a and 17c$[\alpha]_D^{25}$ (

$CHCl_3$, *c* 1. 0) = +21.7^o; ^{1}H NMR (399.78 MHz, Chloroform-*d*): δ 1.16 – 1.39 (m, 10H), 1.55 – 1.77 (m, 4H), 1.89 – 2.11 (m, 4H), 2.16 – 2.26 (m, 2H), 2.27 – 2.42 (m, 1H), 2.54 – 2.70 (m, 4H), 3.35 – 3.44 (m, 1H), 3.46 (t, *J* = 9.8 Hz, 1H), 3.52 (dd, *J* = 9.7, 3.7 Hz, 1H), 3.54 – 3.66 (m, 1H), 3.75 – 3.89 (m, 1H), 4.01 (t, *J* = 9.2 Hz, 1H), 4.08 (d, *J* = 5.1 Hz, 2H), 4.24 (d, *J* = 11.9 Hz, 1H), 4.29 – 4.36 (m, 1H), 4.56 (d, *J* = 10.8 Hz, 1H), 4.64 (d, *J* = 12.1 Hz, 1H), 4.72 (dd, *J* = 10.4, 3.6 Hz, 1H), 4.76 (d, *J* = 12.0 Hz, 1H), 4.85 (dd, *J* = 19.9, 10.7 Hz, 2H), 4.97 – 5.04 (m, 1H), 5.09 (s, 2H), 5.18 (s, 2H), 5.32 – 5.46 (m, 1H), 5.96 (s, 1H), 7.22 – 7.51 (m, 25H); ^{13}C NMR (100.53 MHz, Chloroform-*d*): δ 25.6, 29.0, 29.0, 29.1, 29.1, 29.1, 29.2, 29.3, 29.4, 29.6, 29.6, 32.7, 32.7, 32.7, 32.8, 36.5, 41.4, 63.4, 66.6, 67.3, 67.9, 68.2, 68.7, 68.7, 73.2, 75.1, 75.2, 75.8, 80.1, 80.2, 82.1, 96.9, 127.7, 128.0, 128.1, 128.1, 128.1, 128.2, 128.3, 128.3, 128.3, 128.5, 128.5, 128.5, 128.5, 128.5, 128.6, 128.6, 128.7, 128.7, 128.7, 135.2, 135.8, 138.0, 138.3, 138.8, 170.1, 172.0, 172.1, 173.4; HRMS(Waters synapt G2) m/z Calcd for $C_{61}H_{73}O_{12}NNa$, 1034.5030; Found, 1034.5039.

Experimental procedures for compounds 19a, 19b and 29 can be found in Ref. 18.

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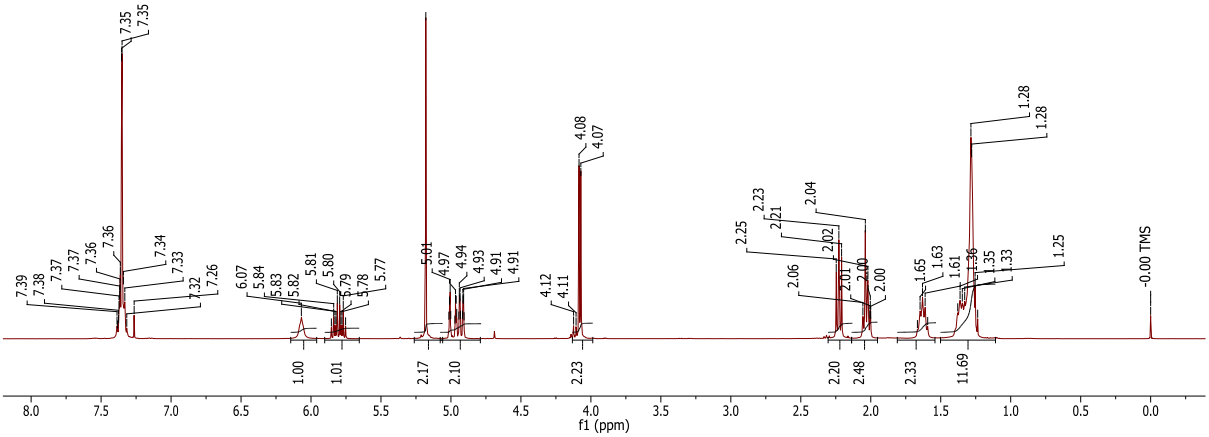
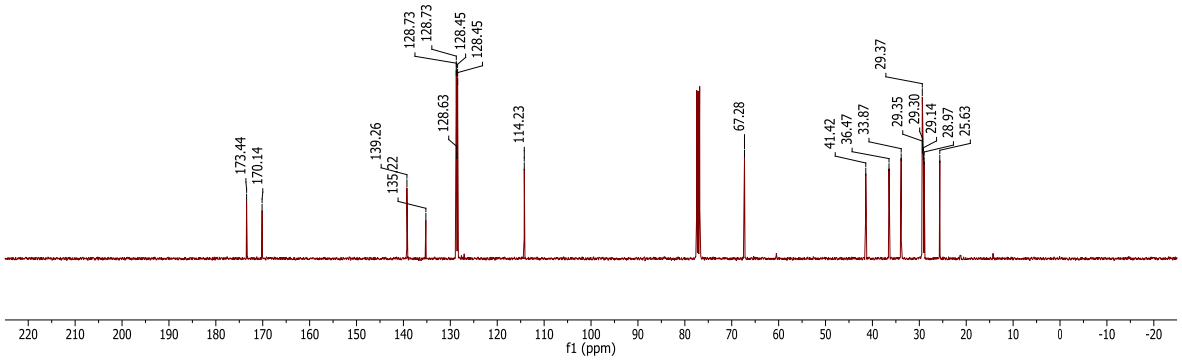
Conclusions

A synthetic approach was developed for the synthesis of biologically active glycolipids Ieodoglucomides A and B. Ieodoglucomides synthesis involved four key reactions viz. glycosidation, cross metathesis reaction, esterification and amidation. The developed route is amenable for the solid phase synthesis of combinatorial library of Ieodoglucomides. Glycosidation reaction was carried out by the gold catalysis, the cross metathesis with the Grubbs 2nd generation catalyst, esterification and amidation were carried out by exploiting carbodiimide chemistry. All the reactions are high yielding and easy to perform. Extrapolation of the identified route to the solid phase combinatorial synthesis of Ieodoglucomides is currently under development.

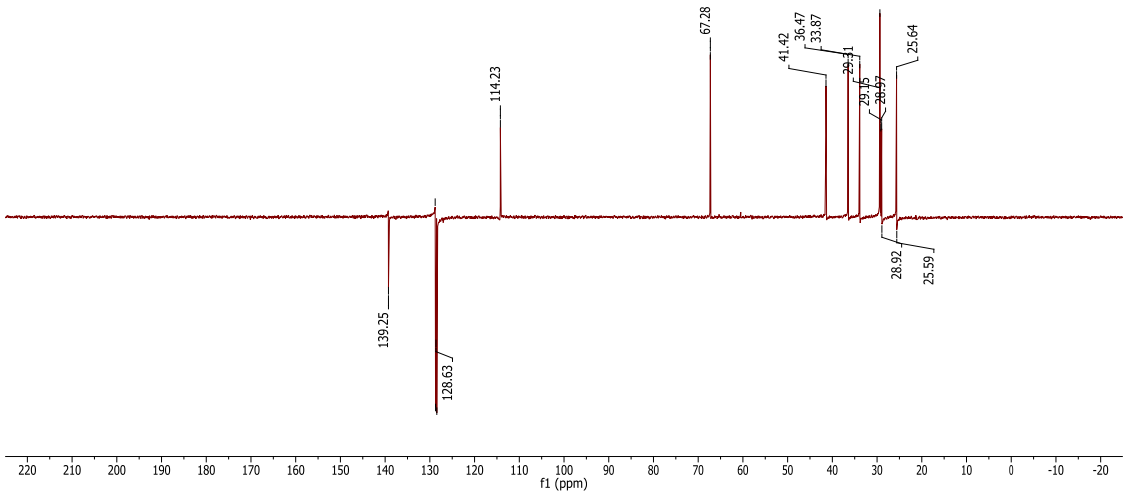
^{1}H NMR Spectrum (399.78MHz, $CDCl_3$) of Compound **9a**



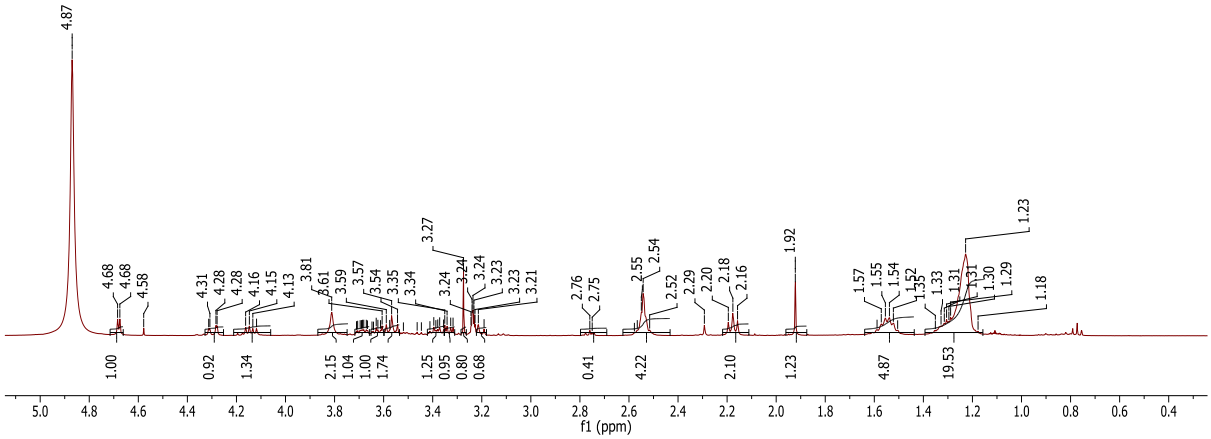
^{13}C NMR Spectrum (100.53MHz, $CDCl_3$) of Compound **9a**



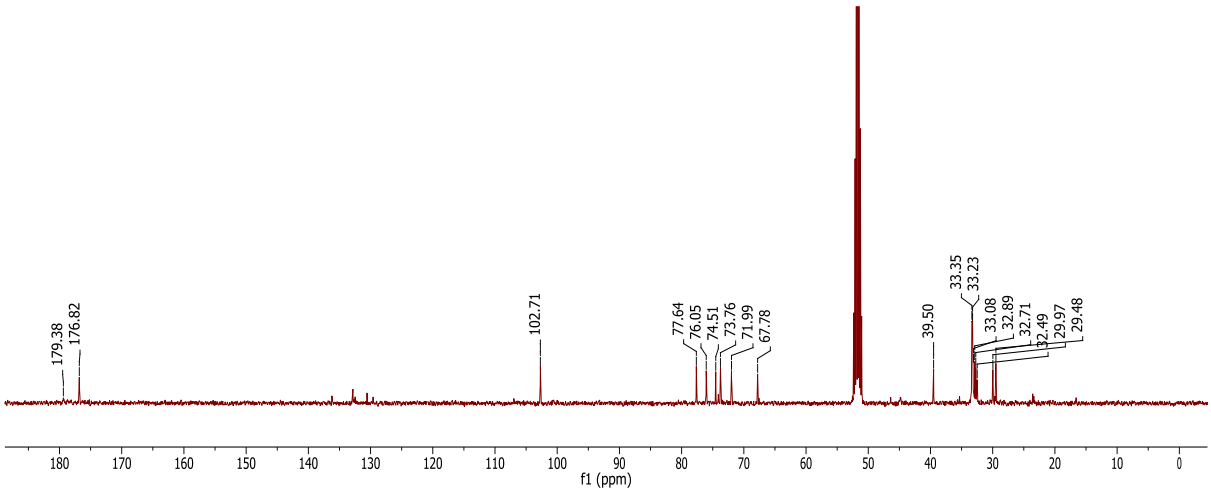
DEPT NMR Spectrum (100.53MHz, $CDCl_3$) of Compound **9a**



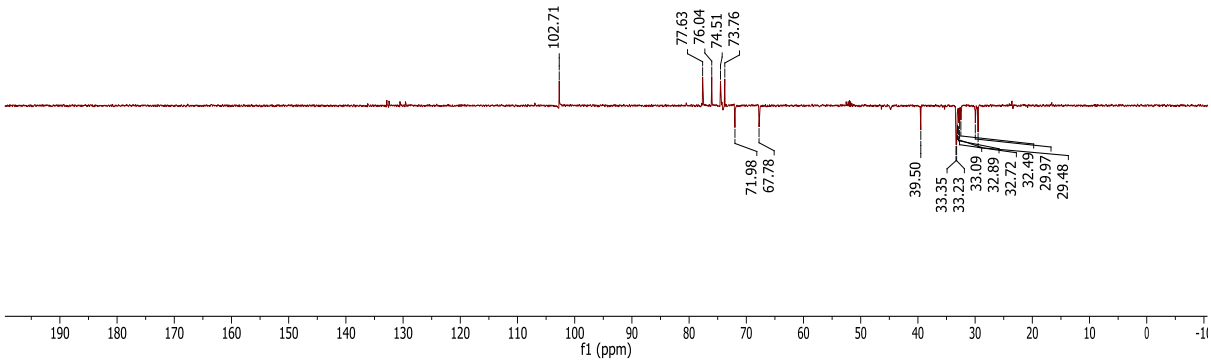
^{1}H NMR Spectrum (399.78MHz, $CDCl_3$) of Compound **25b**



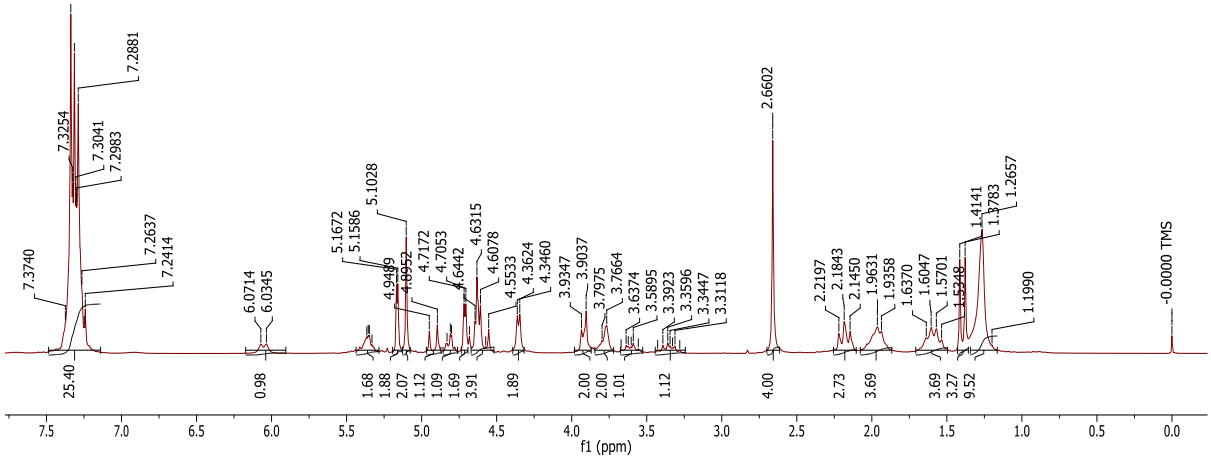
^{13}C NMR Spectrum (100.53MHz, $CDCl_3$) of Compound **25b**



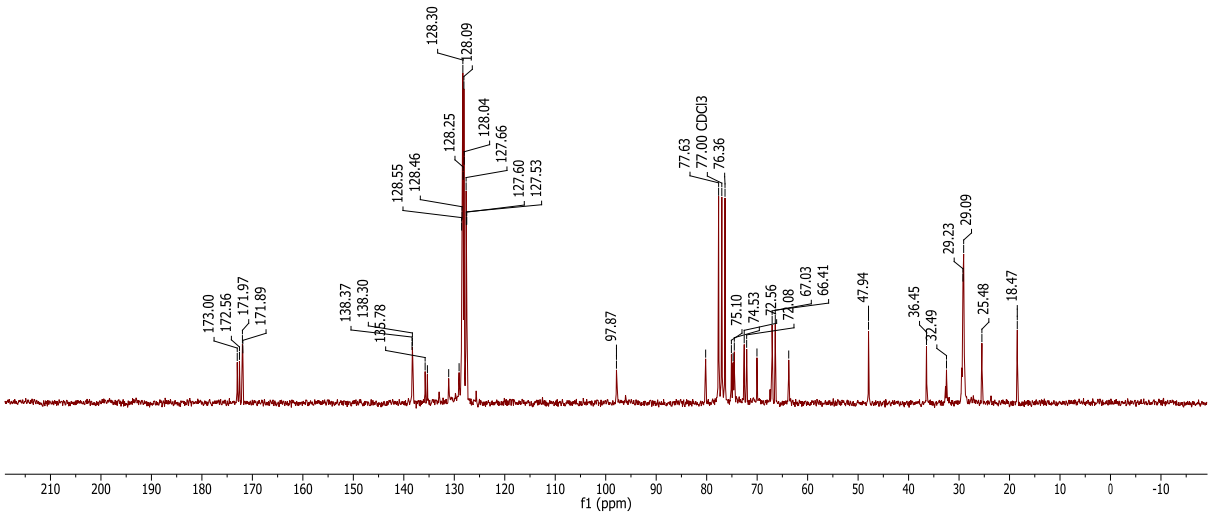
DEPT NMR Spectrum (100.53MHz, $CDCl_3$) of Compound **25b**



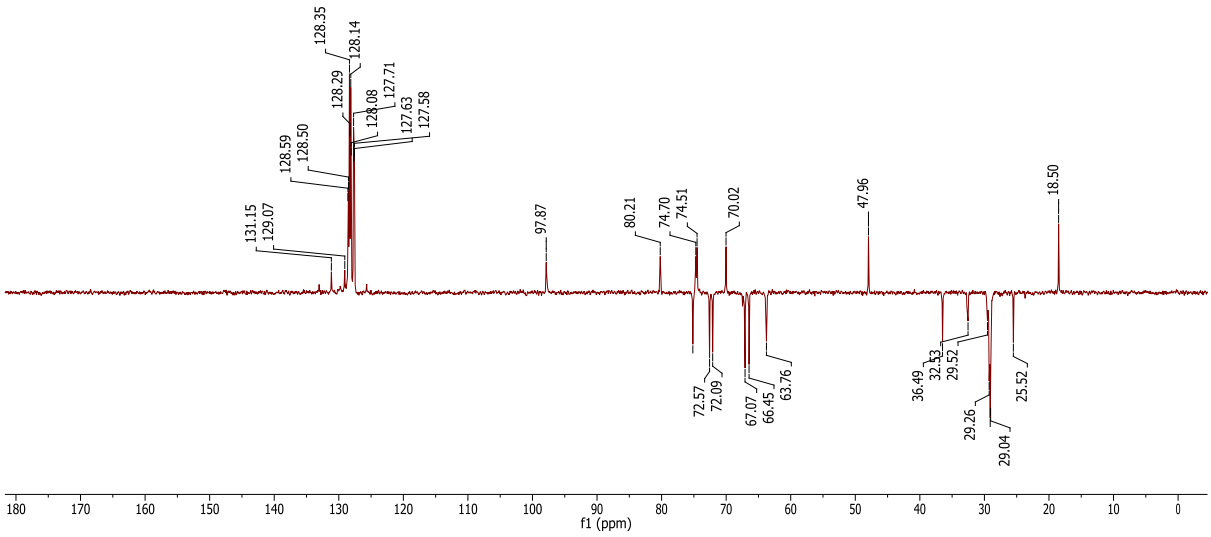
^{1}H NMR Spectrum (399.78MHz, $CDCl_3$) of Compound **31b**



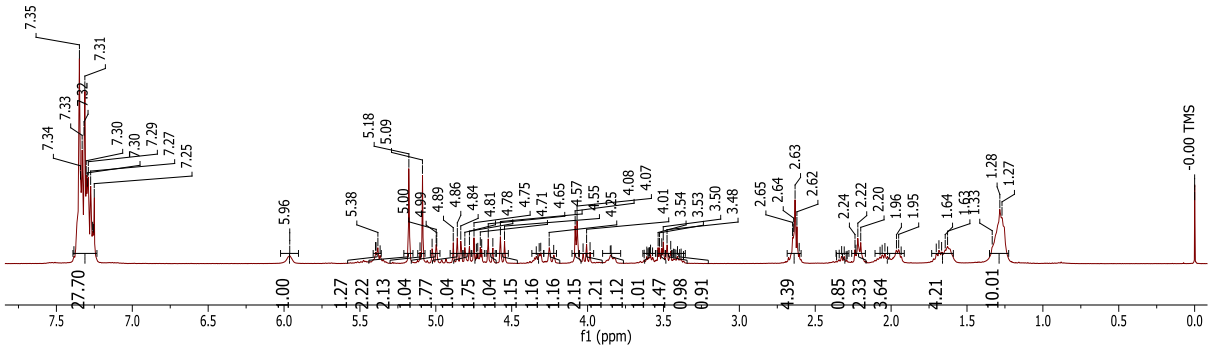
^{13}C NMR Spectrum (100.53MHz, $CDCl_3$) of Compound **31b**



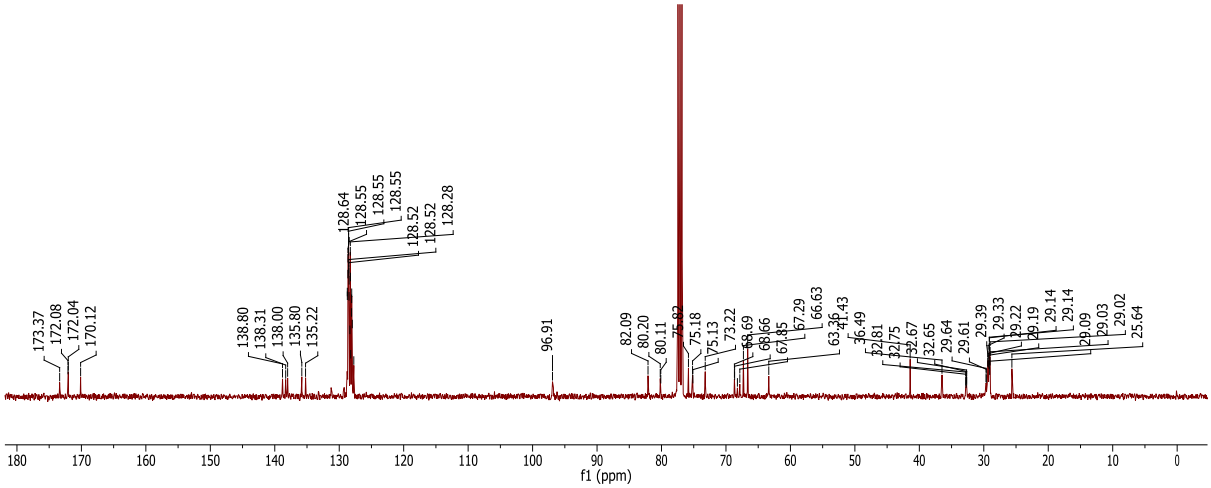
DEPT NMR Spectrum (100.53MHz, $CDCl_3$) of Compound **31b**



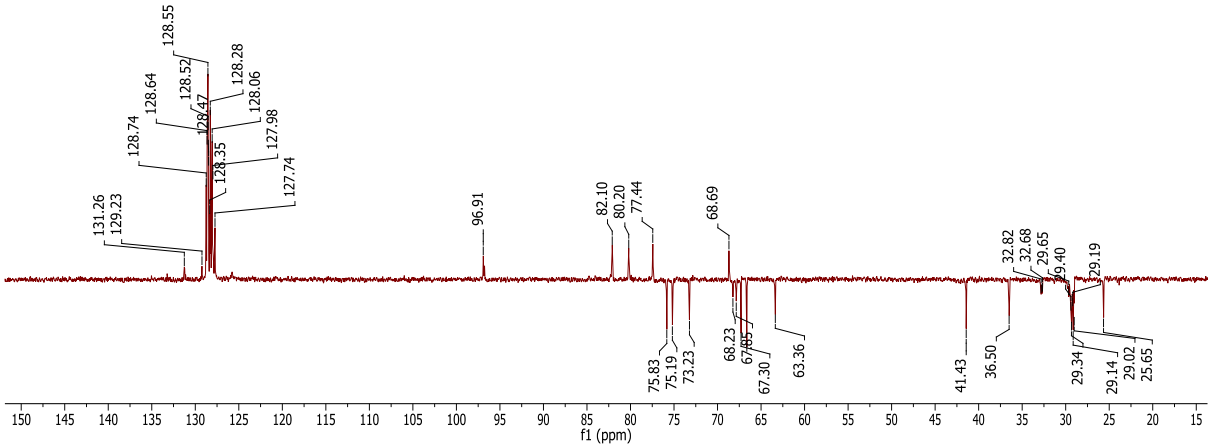
^{1}H NMR Spectrum (399.78MHz, $CDCl_3$) of Compound **24b**



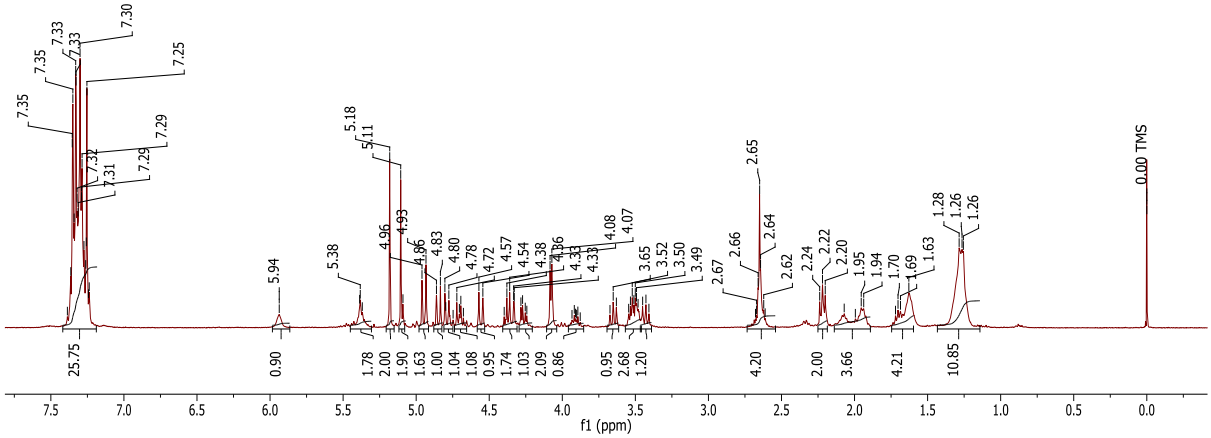
^{13}C NMR Spectrum (100.53MHz, $CDCl_3$) of Compound **24b**



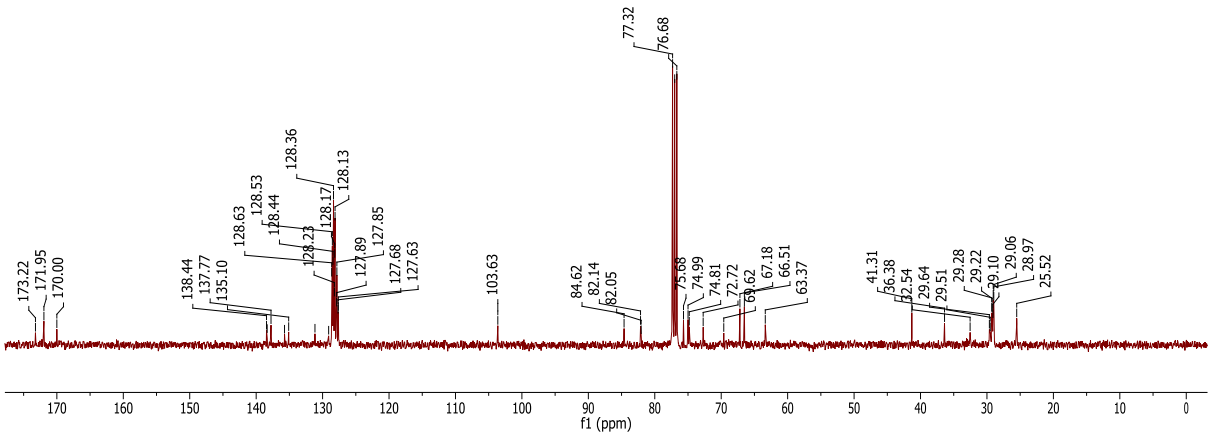
DEPT NMR Spectrum (100.53MHz, $CDCl_3$) of Compound **24b**



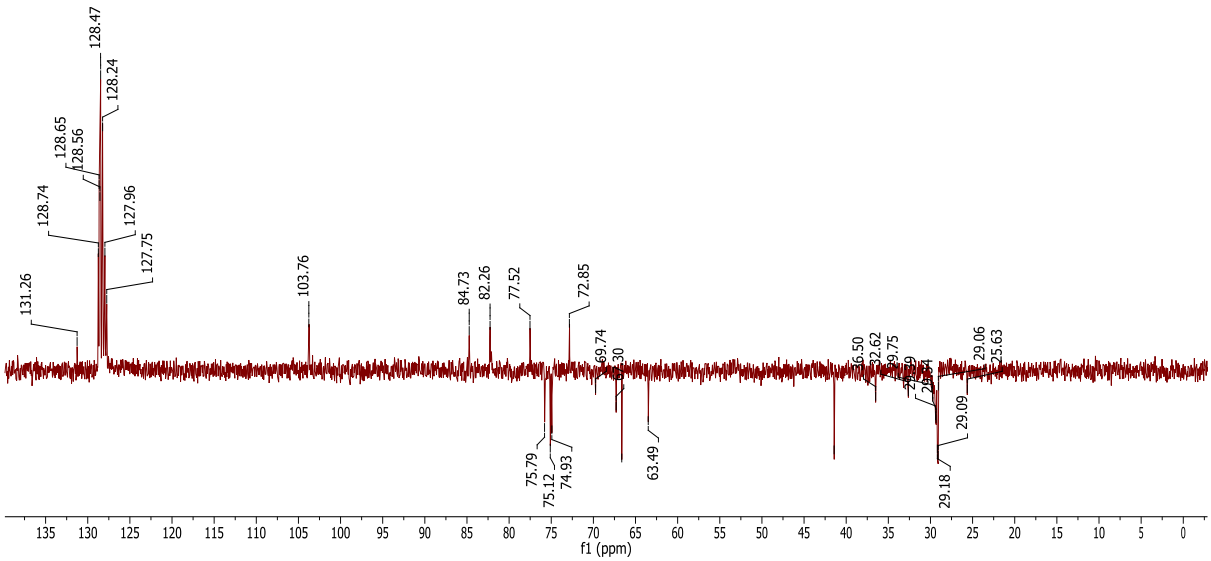
^{1}H NMR Spectrum (399.78MHz, $CDCl_3$) of Compound **24a**



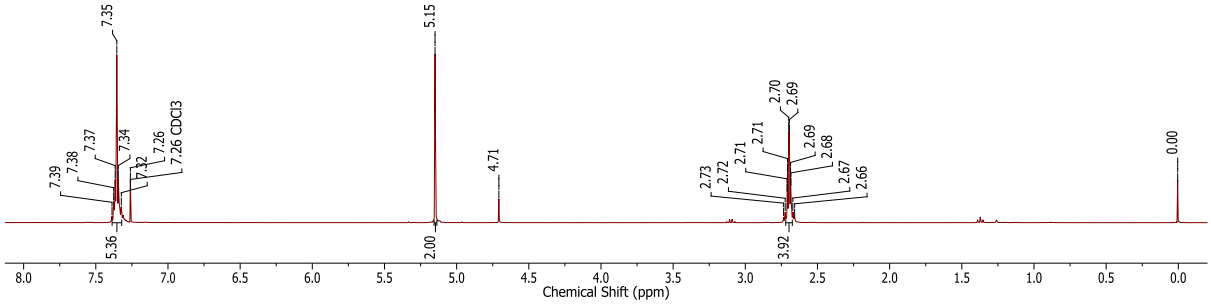
^{13}C NMR Spectrum (100.53MHz, $CDCl_3$) of Compound **24a**



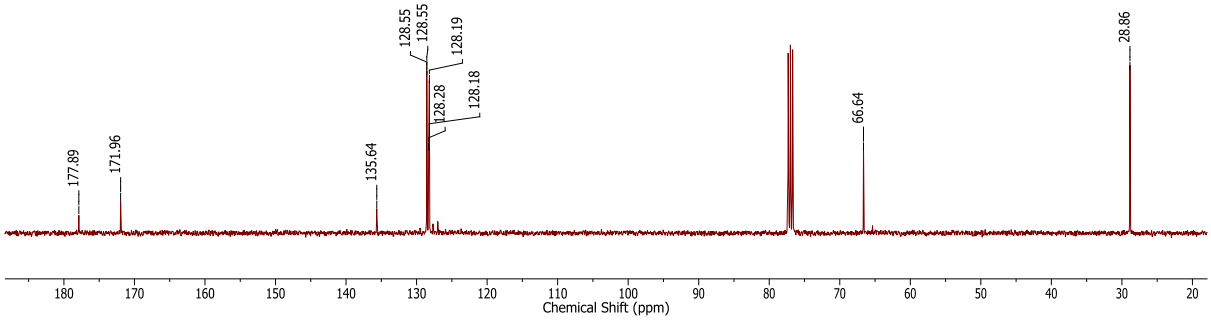
DEPT NMR Spectrum (100.53MHz, $CDCl_3$) of Compound **24a**



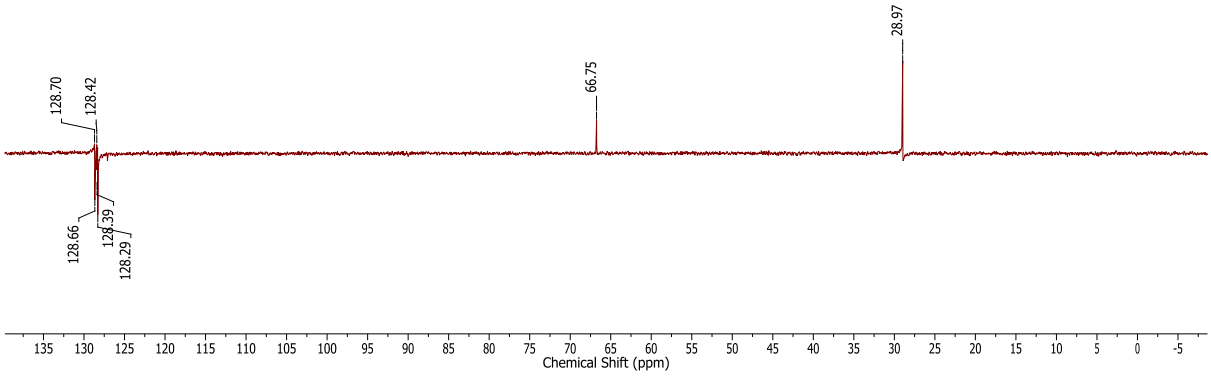
^{1}H NMR Spectrum (399.78MHz, $CDCl_3$) of Compound **5**



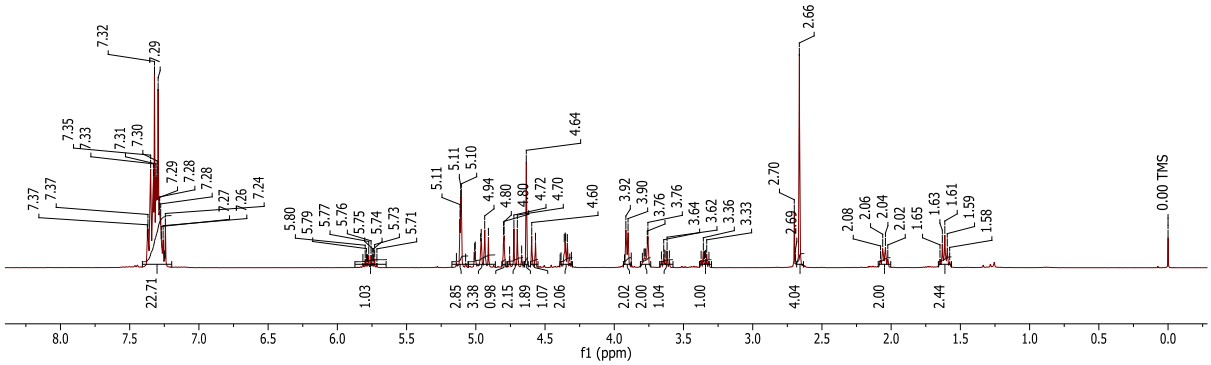
^{13}C NMR Spectrum (100.53MHz, $CDCl_3$) of Compound **5**



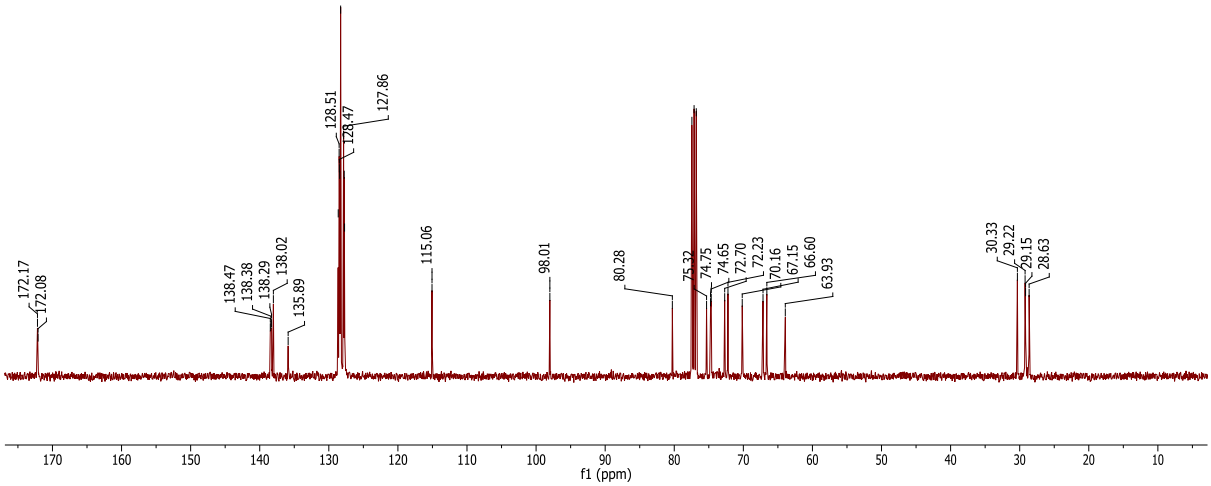
DEPT NMR Spectrum (100.53MHz, $CDCl_3$) of Compound **5**



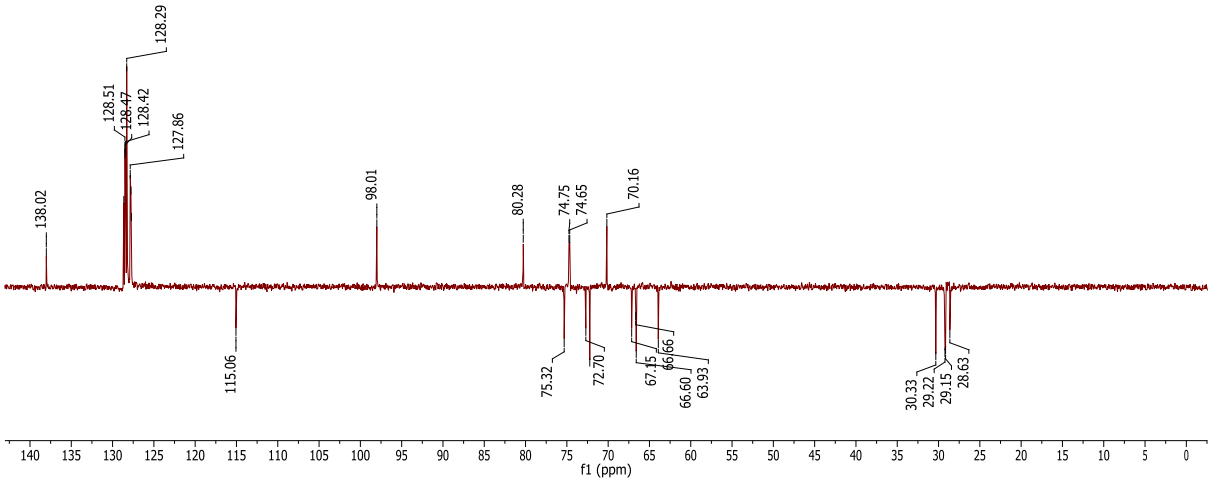
^{1}H NMR Spectrum (399.78MHz, $CDCl_3$) of Compound **23b**



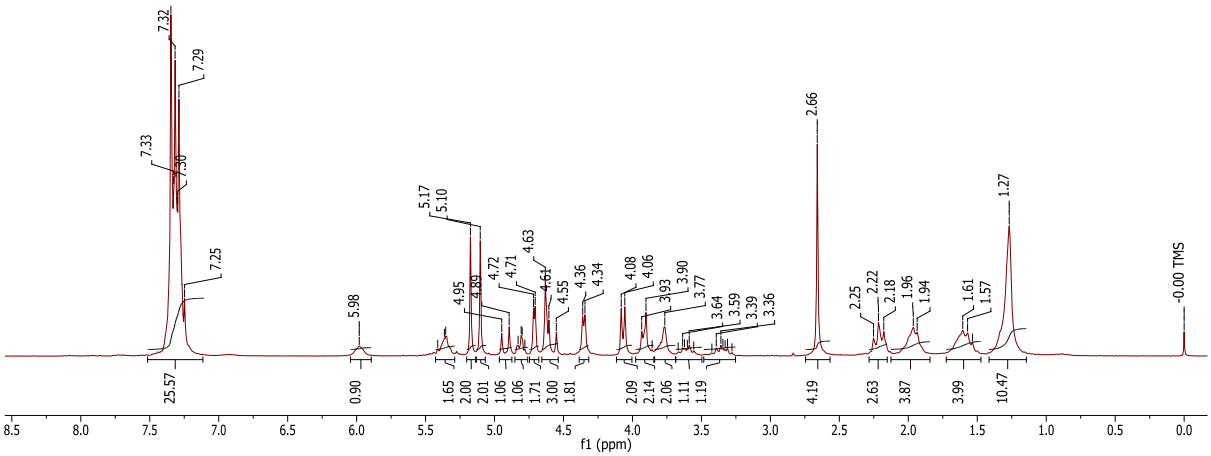
^{13}C NMR Spectrum (100.53MHz, $CDCl_3$) of Compound **23b**



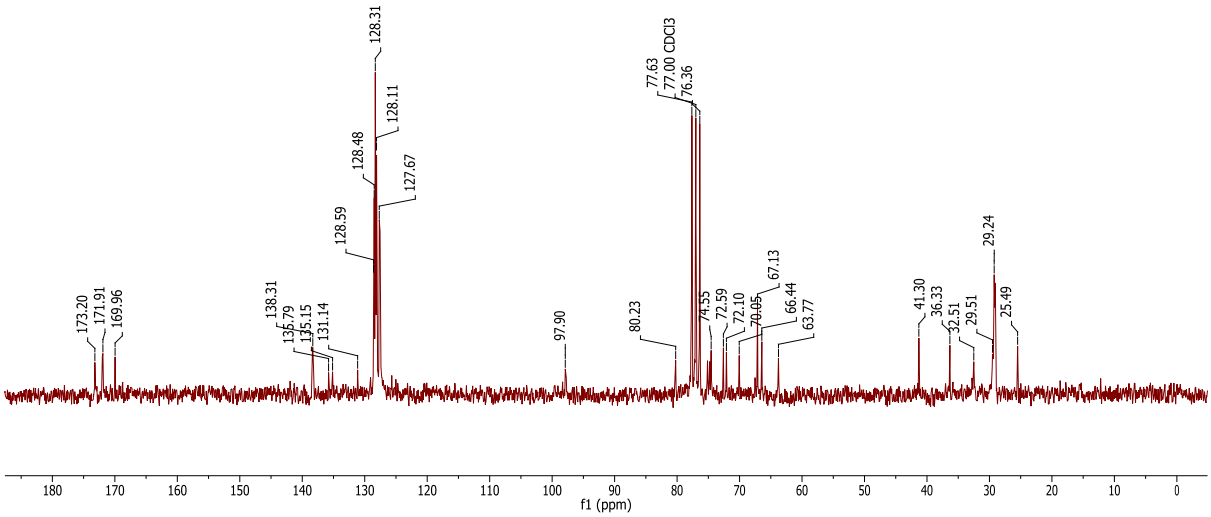
DEPT NMR Spectrum (100.53MHz, $CDCl_3$) of Compound **23b**



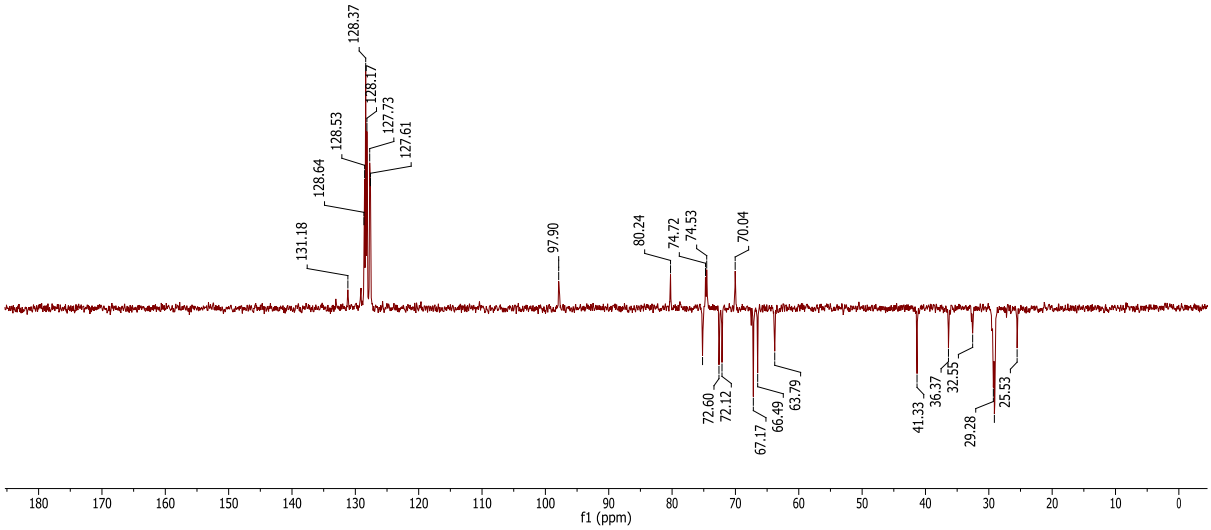
^{1}H NMR Spectrum (399.78MHz, $CDCl_3$) of Compound **31a**



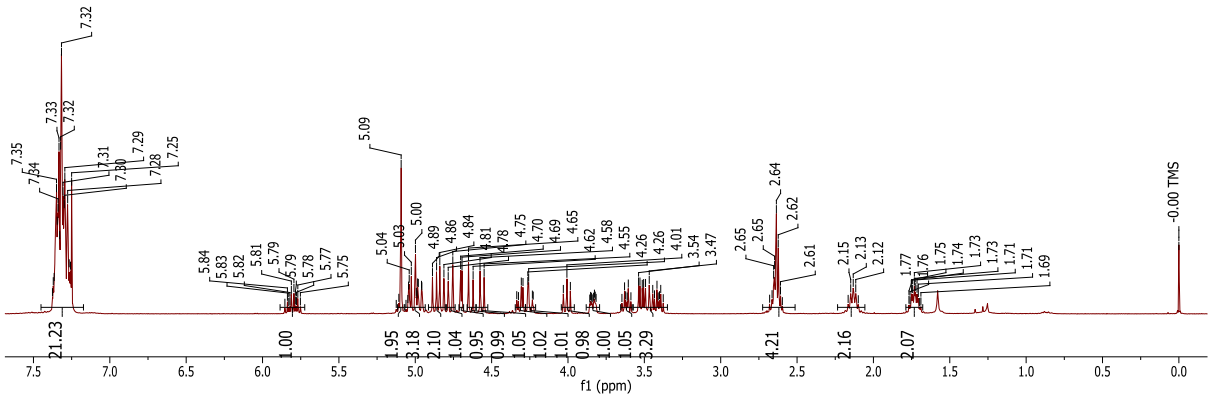
^{13}C NMR Spectrum (100.53MHz, $CDCl_3$) of Compound **31a**



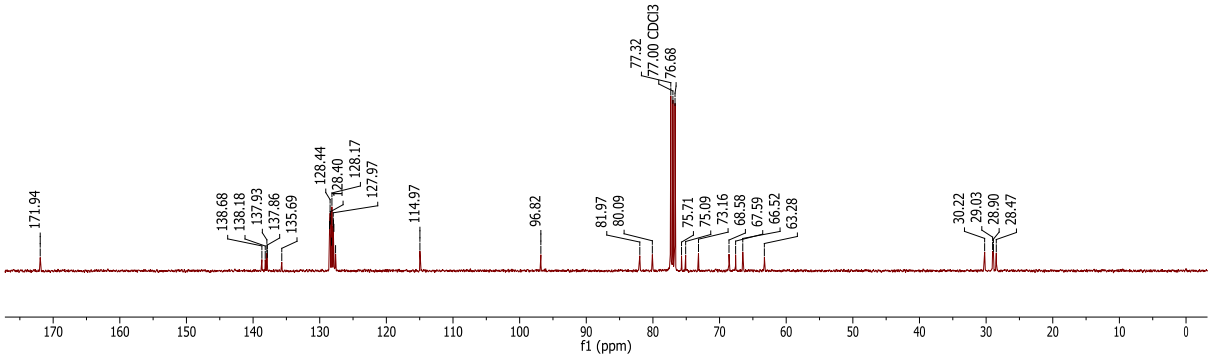
DEPT NMR Spectrum (100.53MHz, $CDCl_3$) of Compound **31a**



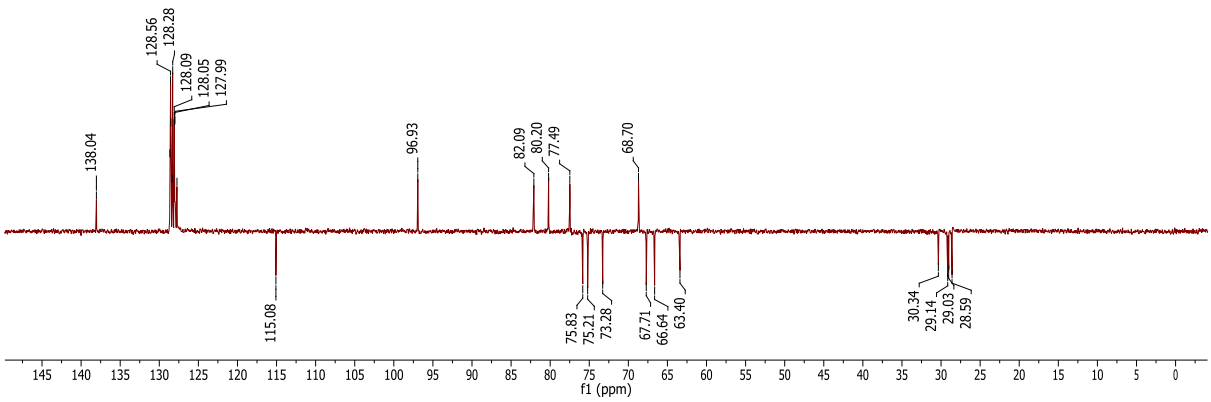
^{1}H NMR Spectrum (399.78MHz, $CDCl_3$) of Compound **23b**



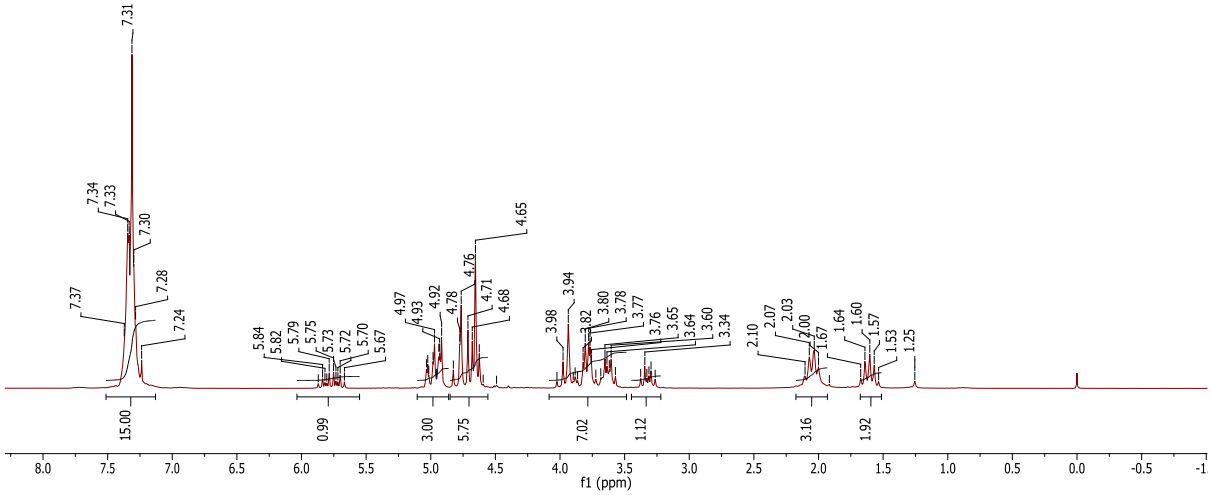
^{13}C NMR Spectrum (100.53MHz, $CDCl_3$) of Compound **23b**



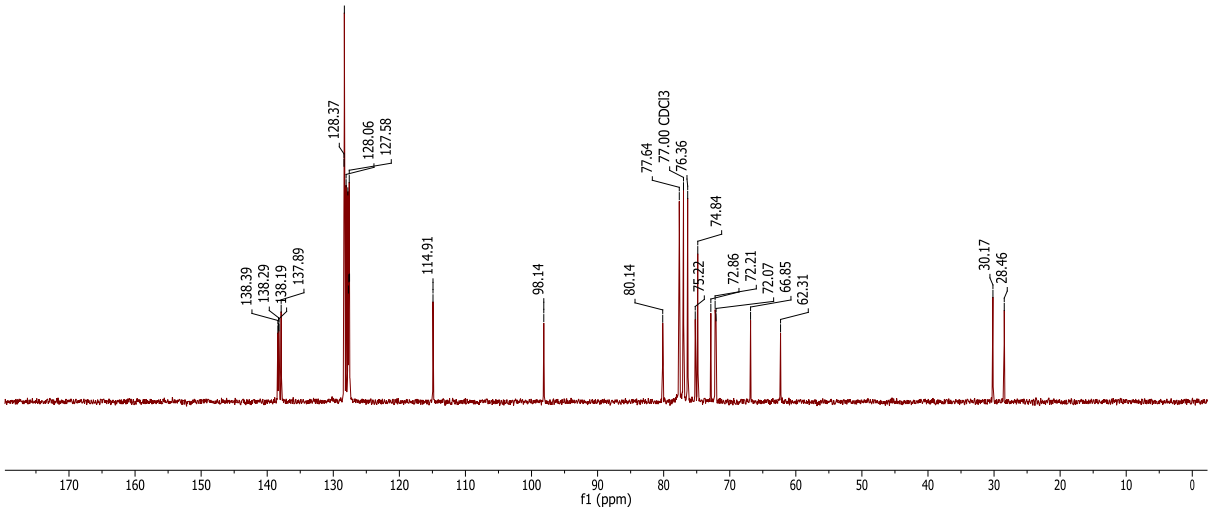
DEPT NMR Spectrum (100.53MHz, $CDCl_3$) of Compound **23b**



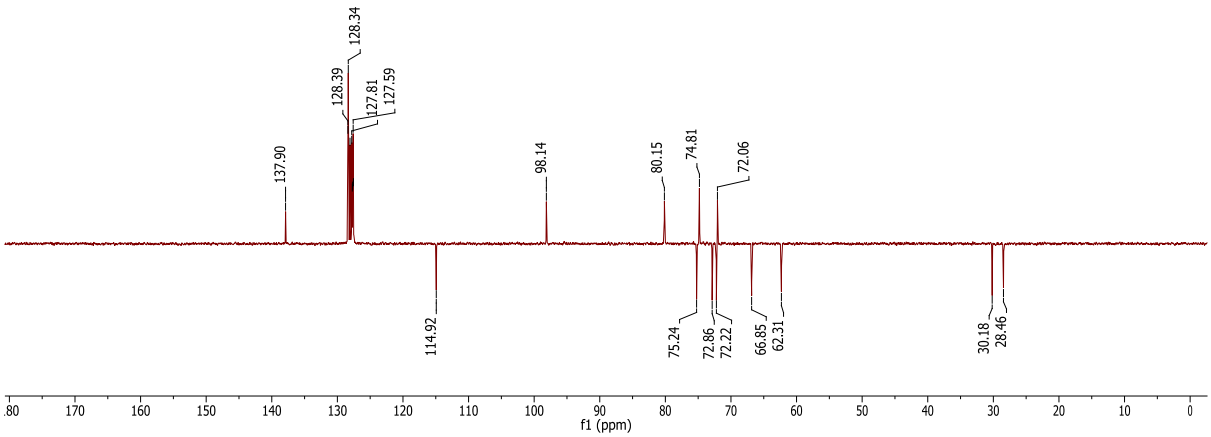
^{1}H NMR Spectrum (399.78MHz, $CDCl_3$) of Compound **29**



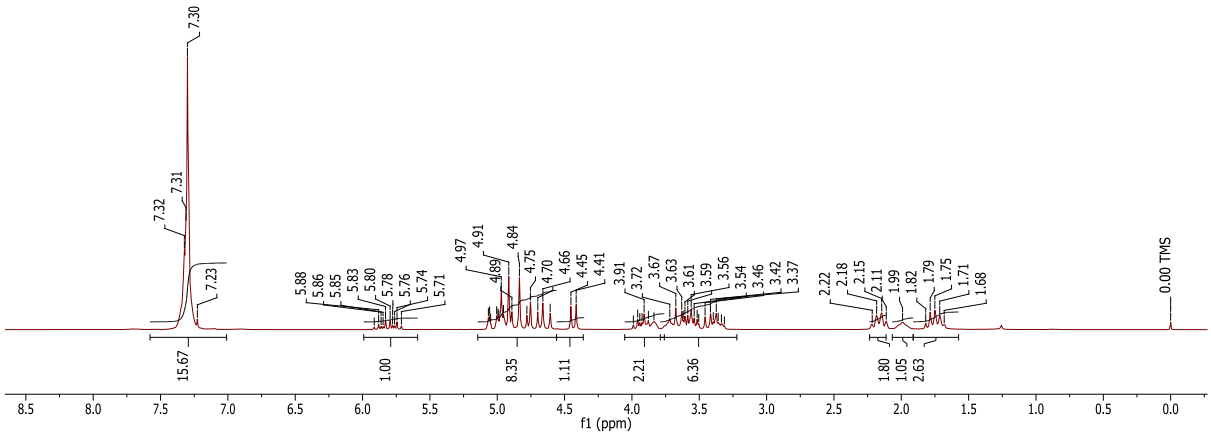
^{13}C NMR Spectrum (100.53MHz, $CDCl_3$) of Compound **29**



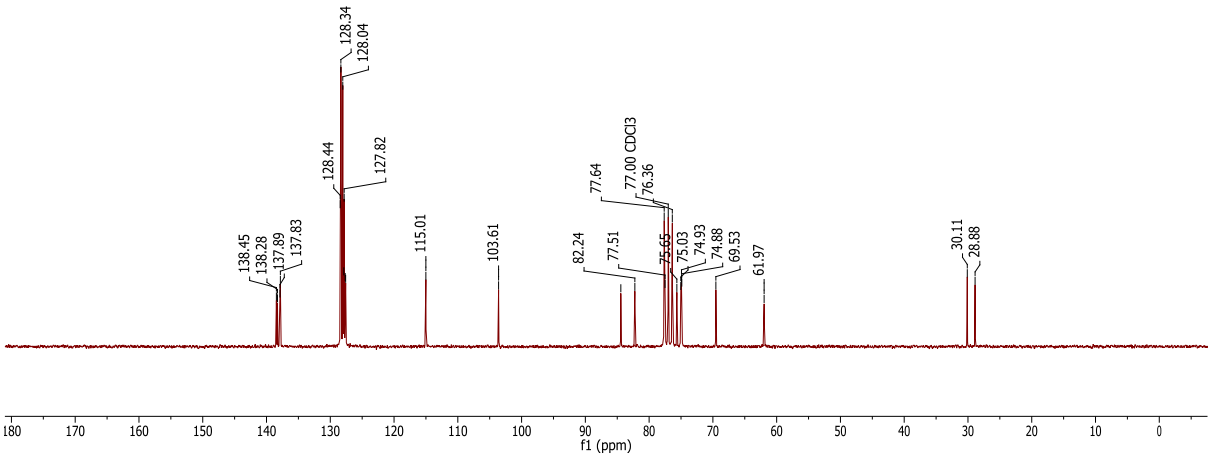
DEPT NMR Spectrum (100.53MHz, $CDCl_3$) of Compound **29**



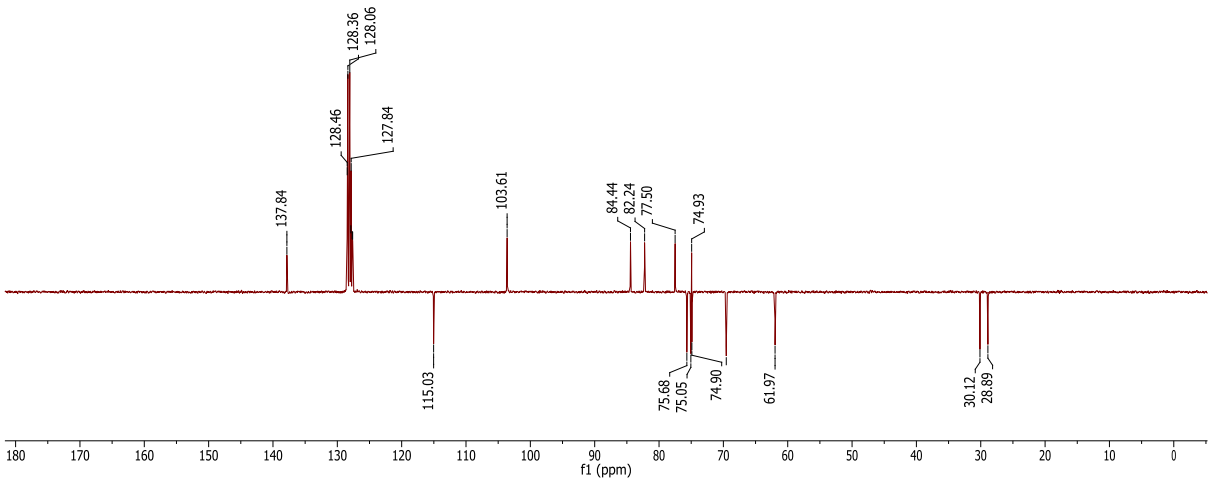
^{1}H NMR Spectrum (399.78MHz, $CDCl_3$) of Compound **19b**



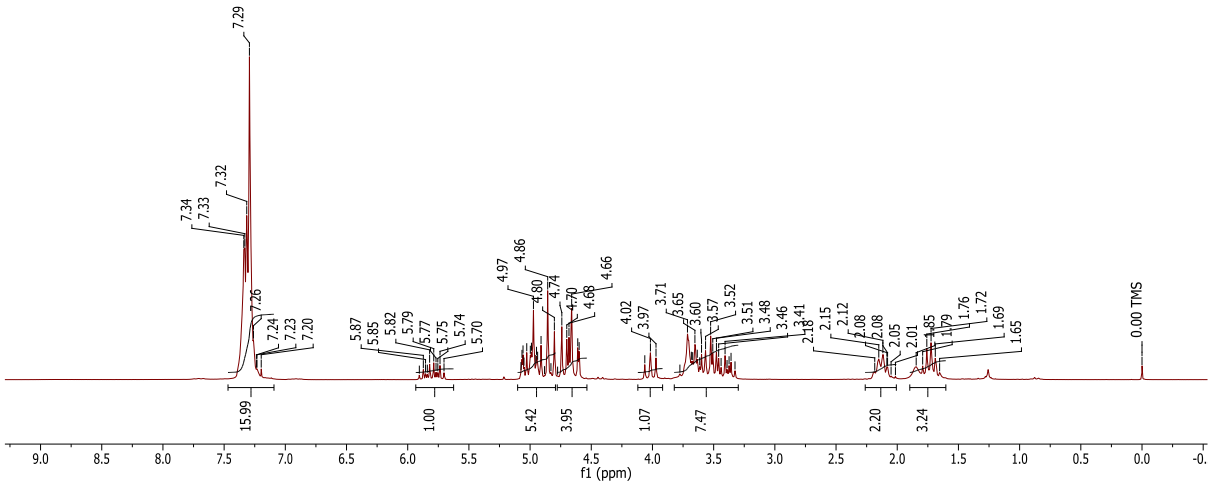
^{13}C NMR Spectrum (100.53MHz, $CDCl_3$) of Compound **19b**



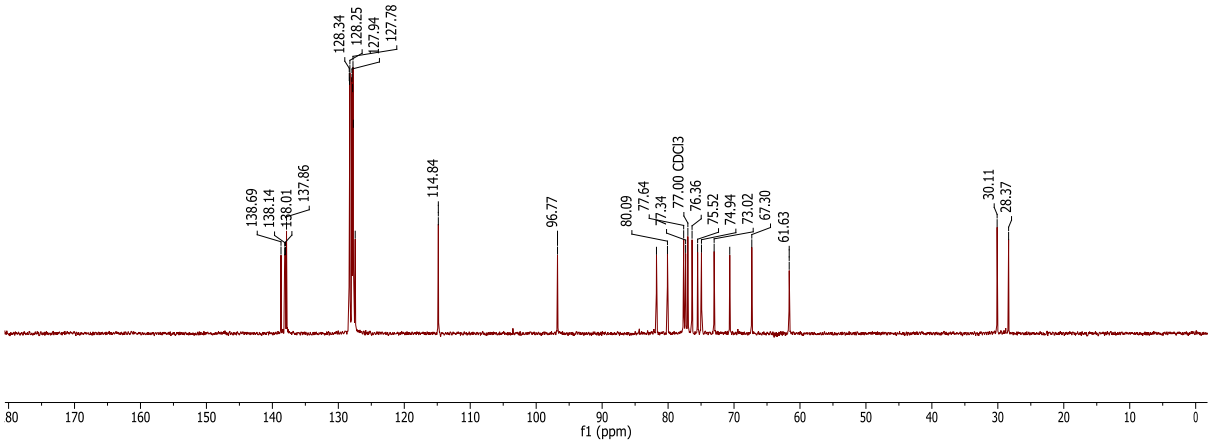
DEPT NMR Spectrum (100.53MHz, $CDCl_3$) of Compound **19b**



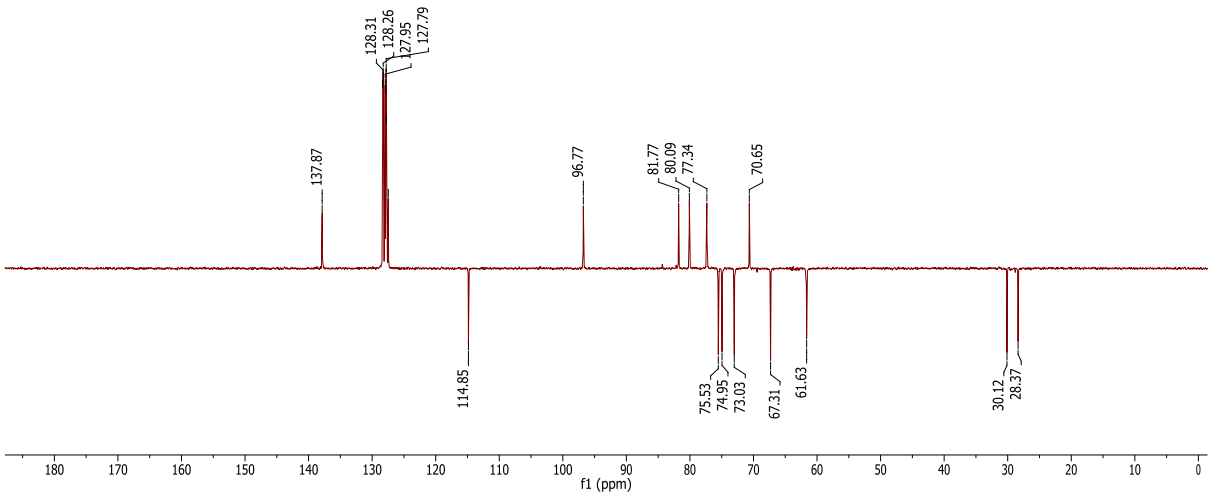
^{1}H NMR Spectrum (399.78MHz, $CDCl_3$) of Compound **19a**



^{13}C NMR Spectrum (100.53MHz, $CDCl_3$) of Compound **19a**



DEPT NMR Spectrum (100.53MHz, $CDCl_3$) of Compound **19a**



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