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DESIGN AND SYNTHETIC STUDIES TOWARDS THE SYNTHESIS OF TESTUFURAN-A: AS AN ADIPOGENIC AGENT

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Abstract : **Diabetes mellitus is most common chronic disease in India and here it has achieved undesired title 'centre for diabetes in world' with millions of populations and many more rising (Kaveeshwar & Cornwall, 2014). According to International Diabetes Federation (IDF, 2013) only in India 10 lacks 65 thousand people die with age 20-79 and about 30 lacks all around world in year 2013. and Atherosclerosis is the most common metabolic disorder nowadays; many other health issues are also related to this. Adiponectin secretion from mature Adipocytes places a benefitable role in these disorders there by diminishing the risk of metabolic syndrome. From the marine sponge *"Xestospongiatestudineria"* a new brominated acetylenic fatty acids were extracted in which the first compound TESTUFURAN-A shown better results, like when treated with in small amounts it released 4 times of Adiponectin compared to other Anti-diabetic Drugs. When it stimulated differentiation of pre-adipocytes to adipocytes, these cells secreted adiponectin, which exhibits preferable effects towards the suit of conditions in CV-disorders. As the Synthetic procedure is not so complex and the availability of raw materials is easier. So, it is a new scope for prevention of these chronic disorders.**

***IndexTerms* – Diabetes mellitus, fatty acids, chronic disorders, bioactive molecules.**

INTRODUCTION:Drugs from Marine Sources Suitable natural sources for the discovery of new potentially bioactive molecules are numerous, but marine environment, harboring a vast variety of organisms differing in their physiology an adaptation capacity, is becoming a top spot for the identification of new drug leads [2]. From the over 33 animal phyla described to date, 32 are represented in the aquatic environment, with 15 being exclusively marine [2]. Due to technical limitations, exploitation of marine organisms started with the collection of large creatures such as red algae, sponges and soft corals, which were shown to produce a large variety of compounds with quite unique chemical structures [2]. Invertebrates alone comprise approximately 60% of all marine animals and were described as the source of more than 11,000 new NP since 1990 [2]. An additional fact that helped to put MNP back on the agenda of drug discovery programs was the recent development of techniques that allow access to a vast community of microbial sources unattainable until recently [2]. Culture broths of new microorganisms are now very easy to obtain, through small scale, high-throughput cultivation methods that use nutrient deficient media, specific nutrients and long cultivation times[2].

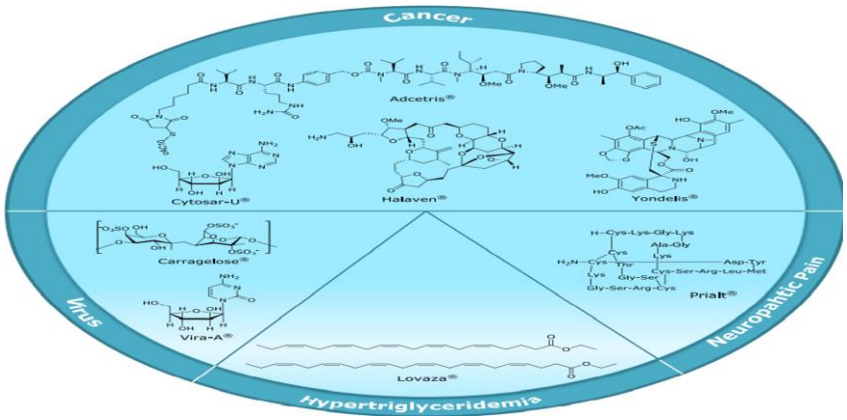


Figure 1: Chemical structures of marine drugs on the market divided by therapeutic area

Screening of extracts from the marine sponge *Xestospongia testudinaria* revealed significant differentiation-inducing activity [6]. From the sponge we isolated active constituents *torospongin-B* and C together with five new brominated acetylenic fatty acids including Testufuran-A, together with 11 known acetylenic acids [6]. *Torospongin-B* and C exhibited antibacterial activity against Cryptococcus neoformans [6]. The molecular formula of Testufuran-A was \text{C}_{18} \text{H}_ {25} \text {BrO}_3. It has two trans carbons; one octane chain attached with bromine on one side with unsaturation and ethyl carboxylic acid chain on either side [6]. Testufuran-A enhances adiponectin secretion from pre adipocytes into mature adipocytes [6]. Terminally differentiated

adipocytes are capable of secreting the beneficial adiponectin protein, which improves chronic syndrome like diabetes mellitus and atherosclerosis [6].

DIABETES MELLITUS

Diabetes mellitus is a chronic metabolic disorder characterized by elevated blood glucose levels (hyperglycemia).[1]. This condition develops either because the pancreas produces insufficient insulin, or because the body cells fail to respond effectively to the insulin produced [1]. The Indian Council of Medical Research (ICMR, 2005) defines diabetes as a complex metabolic and vascular syndrome of multiple etiologies, characterized by distinct disturbances in carbohydrate, protein, and fat metabolism resulting from defects in insulin secretion, insulin action, or both (Nayak et al., 2008) [1]. Diabetes has become one of the most prevalent chronic diseases in India, earning the undesirable title of the "diabetes capital of the world," with millions of affected individuals and a rapidly rising incidence rate (Kaveeshwar & Cornwall, 2014) [1]. According to the International Diabetes Federation (IDF, 2013), approximately 1.06 million people aged 20–79 die annually from diabetes-related complications in India alone, alongside roughly 3 million deaths globally [1].

Patients with diabetes typically present with classic clinical symptoms, including frequent urination (polyuria), excessive thirst (polydipsia), and increased appetite (polyphagia) [1]. If left untreated, chronic hyperglycemia can cause severe, long-term complications, including permanent ocular damage, neuropathy, nephropathy, and cardiovascular disease, imposing a massive socioeconomic burden on the population (MNT Knowledge Center, 2013) [4]. Clinical presentations and demographic prevalence vary considerably across different countries and ethnic populations [4]. For instance, the IDF estimated that by 2013, diabetes affected 24.4 million people in America and 10.9 million in Russia, contributing to a global total of 382 million cases—a figure projected to escalate to 592 million by 2035 [5].

Management of Diabetes and Atherosclerosis:

Whatever the type of diabetes mellitus is, proper diabetes management is required to keep blood sugar in control [1]. Diabetes can cause several metabolic disorders if it remains untreated [1]. The management of T1DM is achieved by regular replacement of insulin, healthy diet, and exercise [5]. For the people having T1DM, it is a balancing act, and they need to stick to their schedules of insulin injections, food intake, and regular check-ups. Even small laps in schedule may lead to rise or fall in blood glucose level (Wherrett et al., 2013) [7].

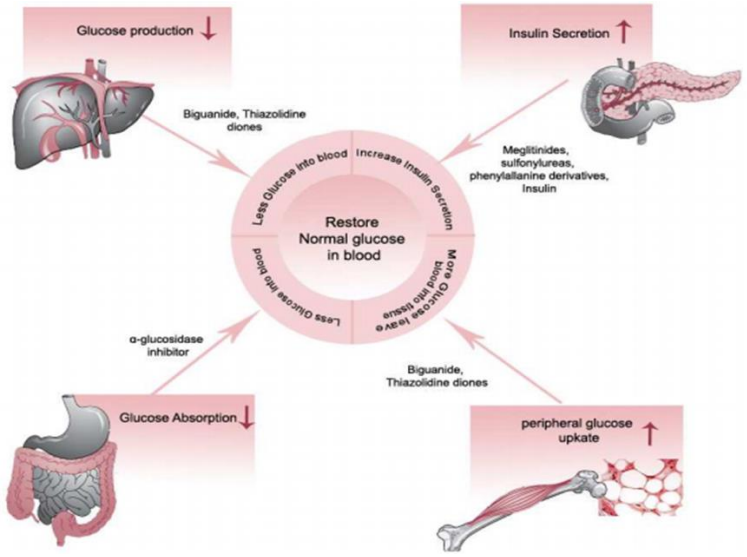


Figure 10: Primary action in Diabetes therapy

The treatment and management of Type 2 Diabetes Mellitus (T2DM) focus on regulation of blood glucose levels too, but here the cause of the same is different than T1DM [4].

One can control this situation in prediabetes stage and avoid developing into diabetes mellitus by controlled diet and physical exercise [1].In case patients fail to control Prediabetes and develop diabetes, it can be controlled with the use of oral anti diabetic agents along with diet control and exercise [1]. These agents act on a particular pathway to regulate blood glucose. Some of these classes of agents with their primary action [5].

IMPORTANCE-OF-ADIPONECTIN

Adiponectin, a hormone present mainly in adipose tissue, is encoded by the APM1 gene (chromosome 3q27) [3].

humans, adiponectin plasma levels range from 3 to 30 µg/mL, which is among the highest plasma concentrations of a circulating protein [3].

The adiponectin molecule is a 247-amino acid polypeptide and is secreted into circulation in three oligomeric isoforms: low molecular weight trimer, an intermediate-molecular weight hexamer, and a high-molecular-weight complex [10]. The lower levels of this form are associated with DM and coronary artery disease [10].

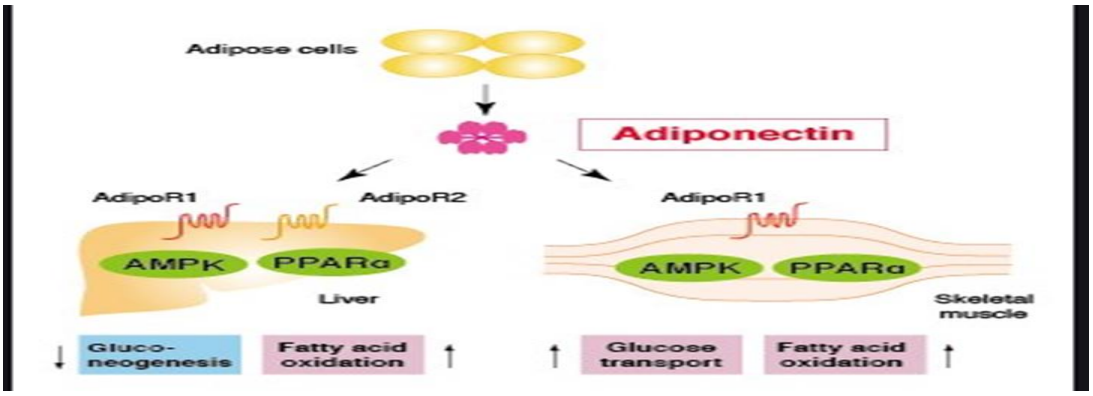


Figure: Role of Adiponectin I DM and Atherosclerosis

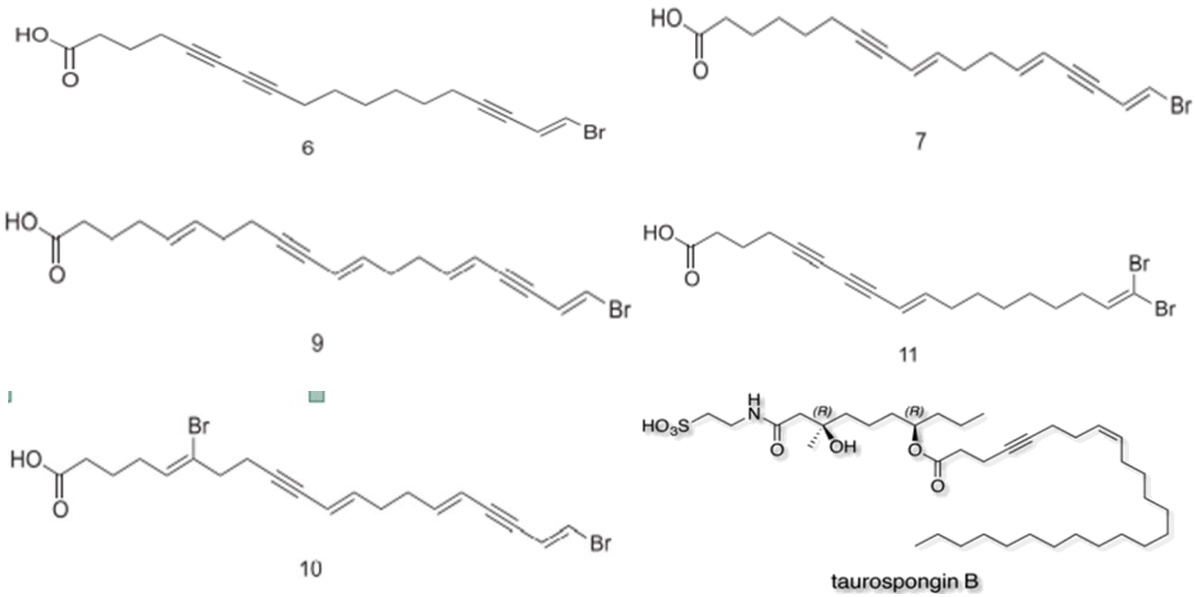
Adiponectin acts through two receptors, AdipoR1 and AdipoR2; the former is expressed at higher levels in muscle tissue, and the latter, in liver tissue [3].

Studies have demonstrated that the AdipoR1 receptor is also present in endothelial cells, cardiomyocytes, and pancreatic beta cells, while AdipoR2 is present in endothelial cells, and both receptors are present in the hypothalamus disease [10]. Resistance to the action of insulin resulting from obesity causes downregulation of adiponectin receptors in muscle and live [3]. Furthermore, adiponectin expression blunts increases in insulin, TNF-α, endothelin-1, and glucocorticoids, factors implicated in the pathogenesis of insulin resistance, subclinical inflammation, endothelial dysfunction, and regulation of energy metabolism, and closely related to the development of MS, DM2, and cardiovascular disease [10]. Accordingly, studies have shown that adiponectin levels are reduced in obesity, DM2, and coronary artery disease [3].

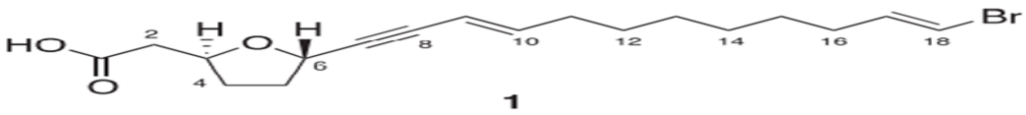
Experimental studies have indicated that adiponectin has potential anti-atherogenic and anti-inflammatory properties [10]. When the vascular endothelium is injured, adiponectin accumulates in the subintimal space of the arterial wall through its interaction with collagens in the vascular intima [3]. Adiponectin dose-dependently inhibited TNF-α–induced monocyte adhesion and expression of endothelial-leukocyte adhesion molecule -1 (E-selectin), vascular cell adhesion molecule -1 (VCAM-1), and intracellular adhesion molecule -1 (ICAM -1) on the endothelium [3].

TESTUFURAN-A

It is a secondary metabolite extracted from the Marine sponge “Xestospongia testudinaria” contains Acetylenic fatty acid residue and is responsible for release of Adiponectin (mainly used in regulation of blood glucose levels and breakdown of fats) [6]. Marine sponges continue to be one of the most prolific sources of new biologically active secondary metabolites [2]. To explore their biomedical potential, we use cell-based assays to isolate biologically active constituents, because these assays are generally inexpensive and afford compounds with membrane permeability, which is desirable for further development [2]. This paper deals with the discovery of enhancers of adiponectin secretion through differentiation of ST-13 preadipocytes to adipocytes [6]. The terminally differentiated adipocytes can secrete the beneficial adipocyte-specific protein, adiponectin, thus contributing to improving the symptoms of metabolic syndromes [6]. We screened the extracts of marine organisms for the differentiation-inducing activity and found that the marine sponge Xestospongia testudinaria exhibited significant activity [2]. From the sponge we isolated active constituents and studied their structures and biological activities. Some of them are like Cytotoxic, Adipogenic, Anti-microbial, Anti-fungal, etc.,[6].



In 2016, Takakai Kubota and Haruna Suzuki have isolated new Acetylenic fatty acid derivatives called Torospongins-B and which are Anti-bacterial (against cryptococcus neoformans) [6].Adiponectin secretion from the mature adipocytes plays beneficial roles in diabetes mellitus and atherosclerosis, thereby diminishing the risk of metabolic syndrome [3] [7]. From the marine sponge Xestospongia testudinaria, we isolated five new brominated acetylenic fatty acids, including Testufuran A,together with 11 known acetylenic acids [8].



1

Molecular Formula: C18H25BrO3

NEED OF THE STUDY

Diabetes mellitus is most common chronic disease in India and here it has achieved undesired title 'centre for diabetes in world' with millions of populations and many more rising [1]. and Atherosclerosis is the most common metabolic disorder nowadays; many other health issues are also related to this [7]. Adiponectin secretion from mature Adipocytes places a benefitable role in these disorders there by diminishing the risk of metabolic syndrome [3].

From the marine sponge "Xestospongia testudinaria" a new brominated acetylenic fatty acids were extracted in which the first compound TESTUFURAN-A shown better results, like when treated with in small amounts it released 4 times of Adiponectin compared to other Anti-diabetic Drugs [6]. When it stimulated differentiation of pre-adipocytes to adipocytes, these cells secreted adiponectin, which exhibits preferable effects towards the suit of conditions in CV-disorders [10].

As the Synthetic procedure is not so complex and the availability of raw materials is easier. So, it is a new scope for prevention of these chronic disorders by developing a laboratory chemical synthesis pathway [3] [10].

OBJECTIVES

The major aim of this Project is to synthesize this metabolite synthetically in the laboratory [6].

As growth of Marine sponges and the extraction process of different metabolites and their separation is a difficult process [2]. So, there is a need to synthesize this particular Metabolite in Laboratory [6].

Due to different climatic conditions, the availability of these sponges and their metabolite production naturally is difficult and obtained in small amounts [2].

Therefore, on a laboratory scale, we can synthesize the compound in bulk amounts [6].

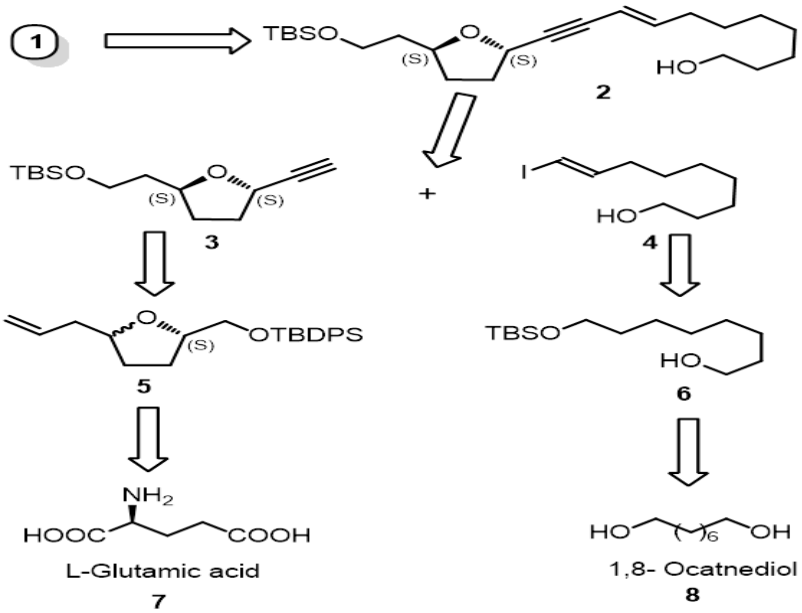
As it was not chemically synthesized in the Laboratory yet [6].

As our Laboratory is mainly involved in Exploring bio actives from Marine sources and their synthesis, so I have opted for this work [2].

Due to the limited availability of natural sources and challenges in isolation, synthetic methods provide a reliable and reproducible approach for obtaining metabolites [2] [6].

RESEARCH AND METHODOLOGY

This is the basis of work which is through retro synthesis analysis of TESTUFURAN-A [6].



SCHEME -1

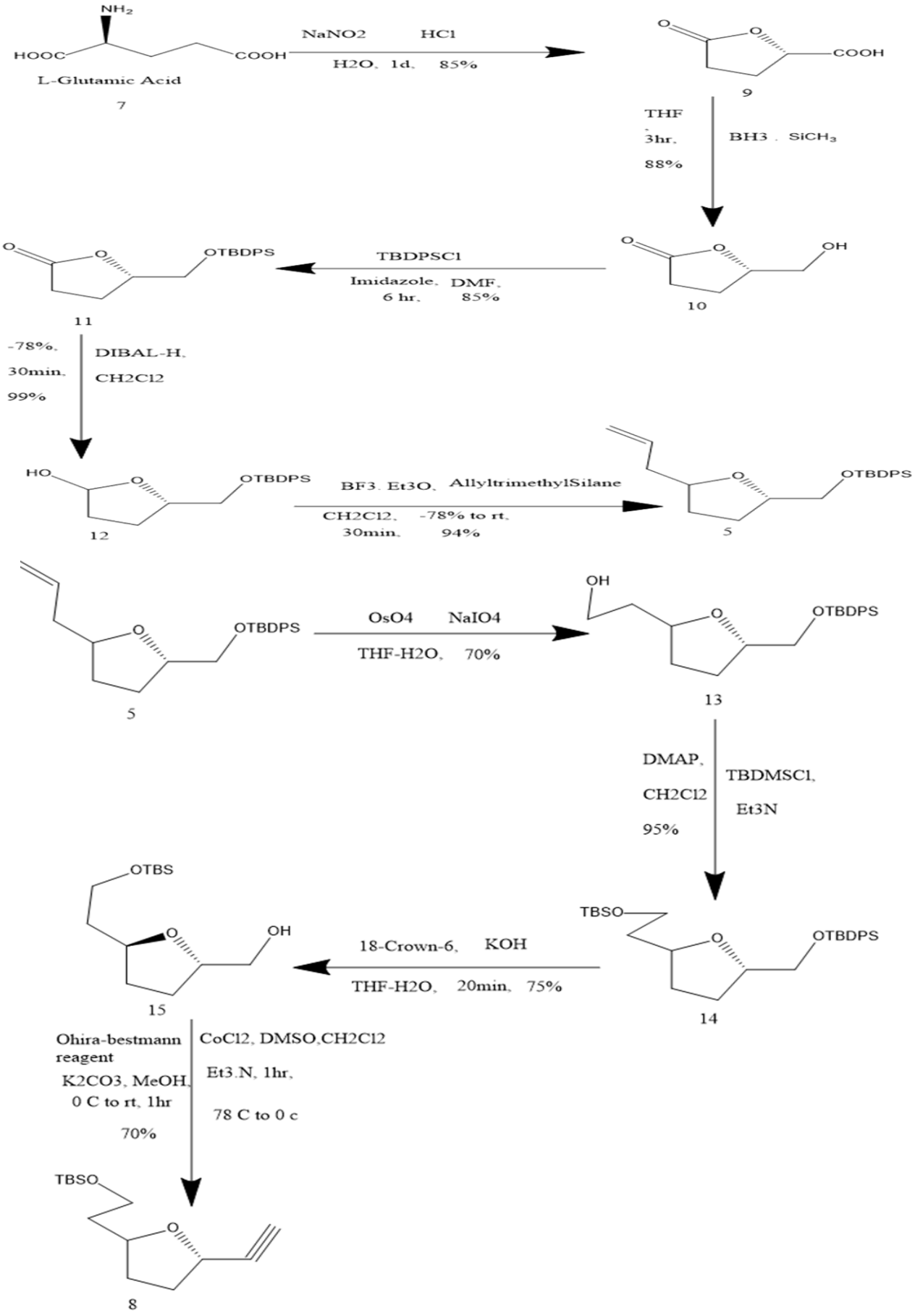
synthesis of fragments –3 [6].

SCHEME –2

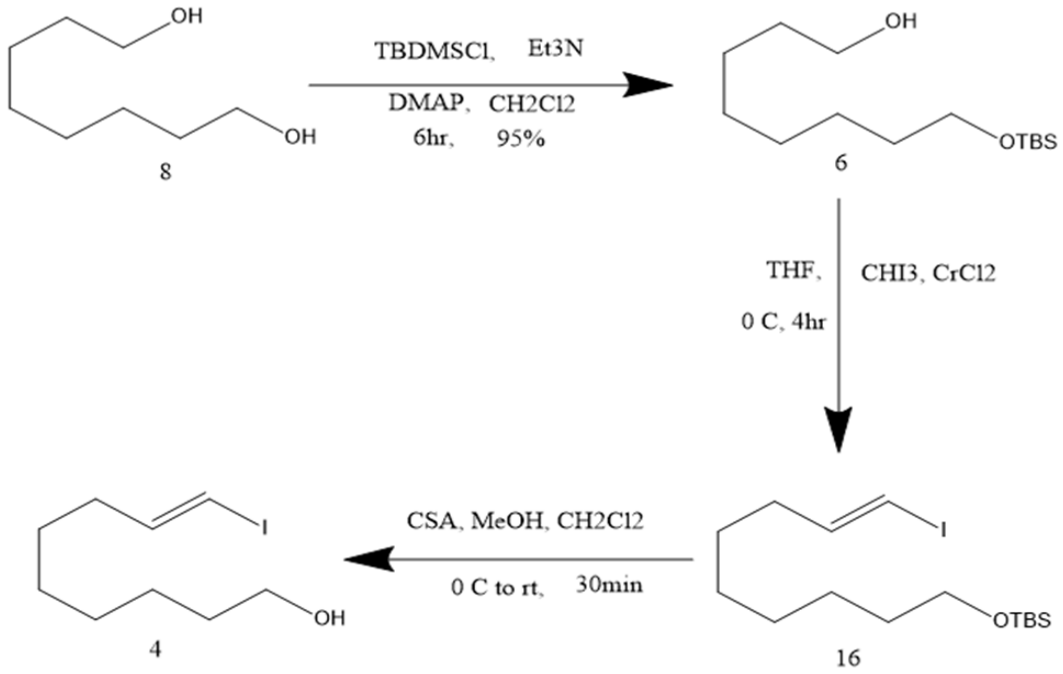
synthesis of vinyl-iodide fragments. [6].

SCHEME-3 sonogashira-coupling of fragments 3&4 [11].

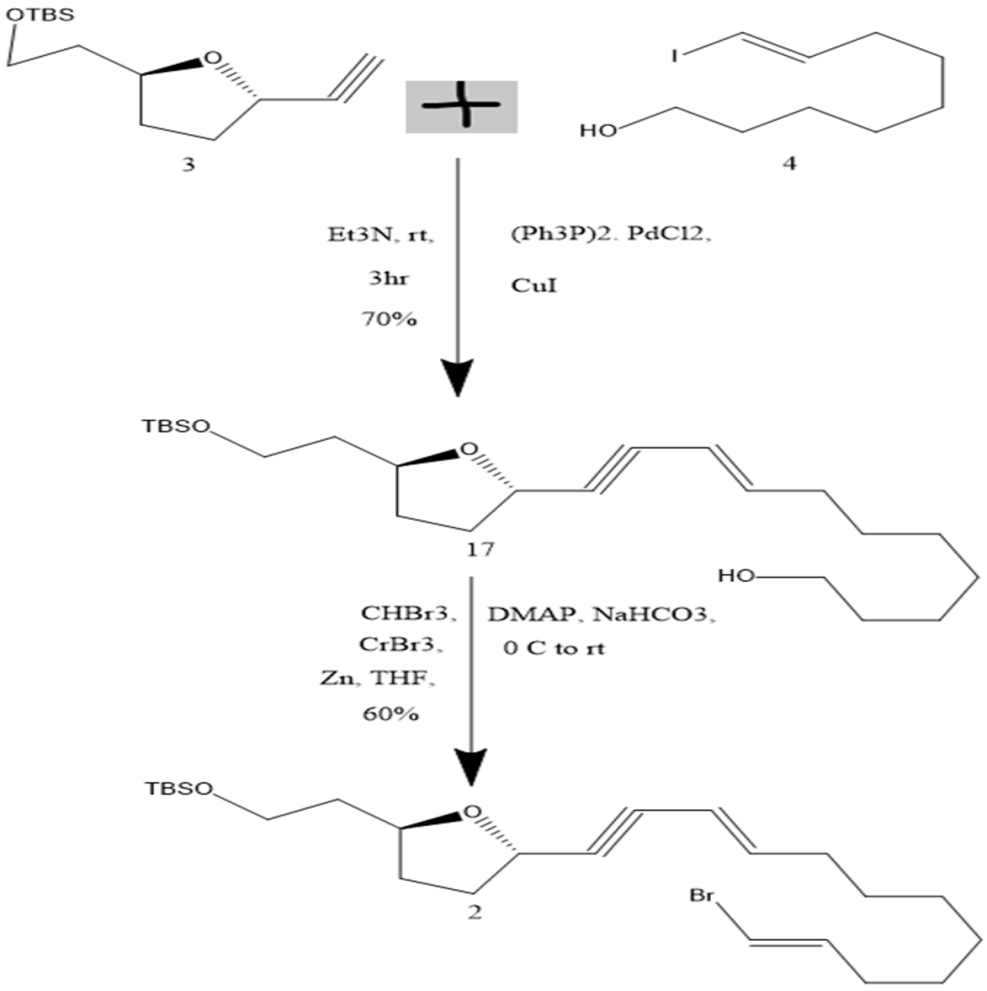
SCHEME-1 [6].

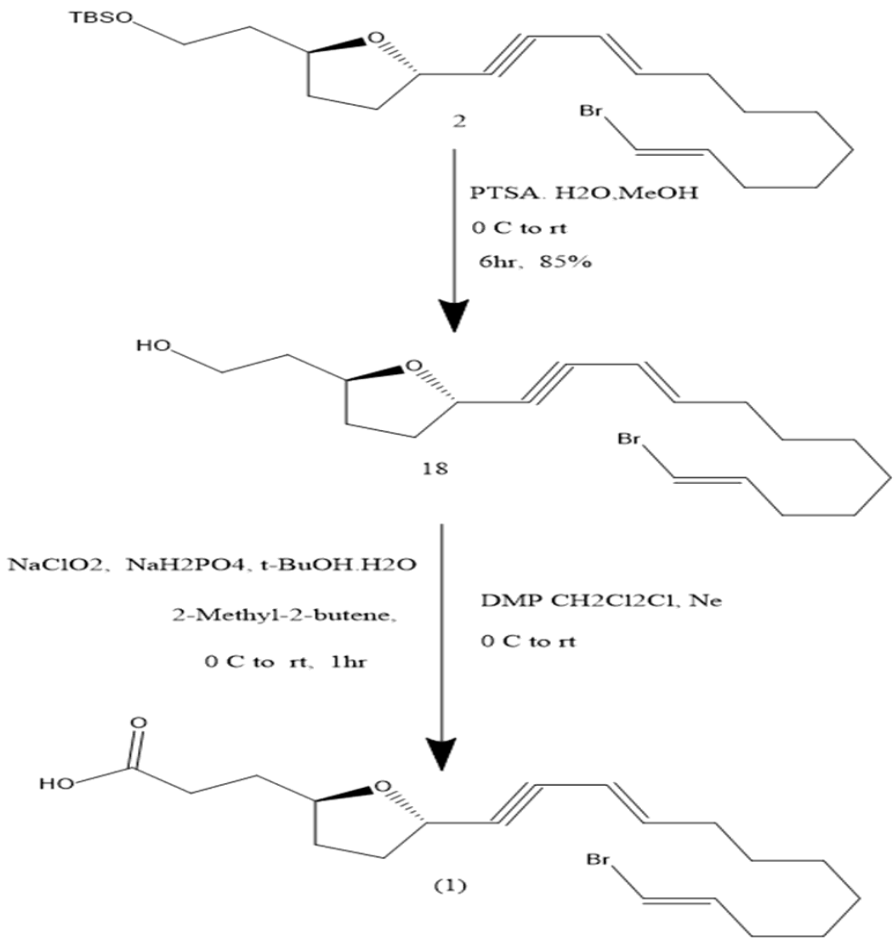


SCHEME-2 [6].



SCHEME-3 [11].



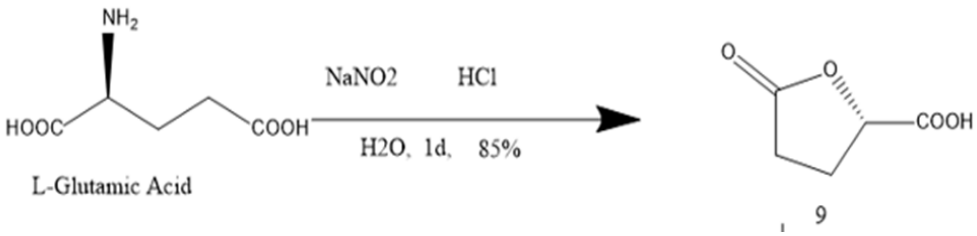


Sonogashira –coupling fragments 3$4 [11].

EXPERIMENTAL METHODOLOGY:

SCHEME-1: Synthesis of Terminal Alkyne (Fragment-3) [6].

Step-1:



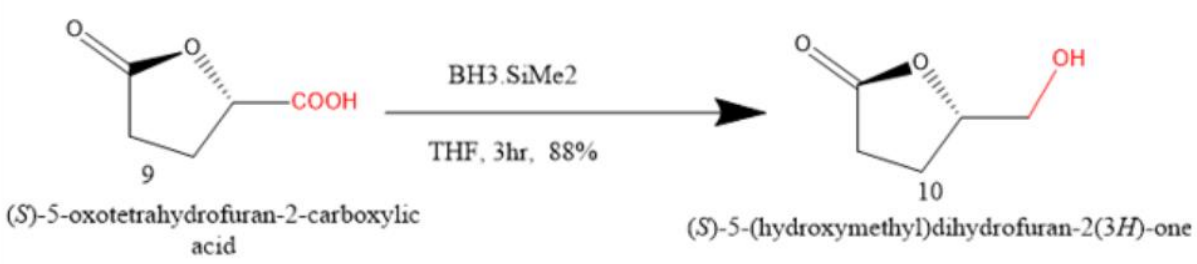
Reaction: (table 1)

S.no	Chemical name	Molecular. Weight g/mol	Quantity	Milli. Moles	Equivalence
1.	L-Glutamic-Acid	147	5g	34	1.0
2.	NaNO2	69	3.5	51	1.2

Indication: Yellow Colour in the TLC after 18 hours [6].

Work-Up: Reaction Mixture was evaporated in vacuum below 50 degrees Celsius to give yellow oil, which was dissolved in Ethyl acetate. The filtrate and washing solution were combined and dried over NaSO4 [6].

Step-2:

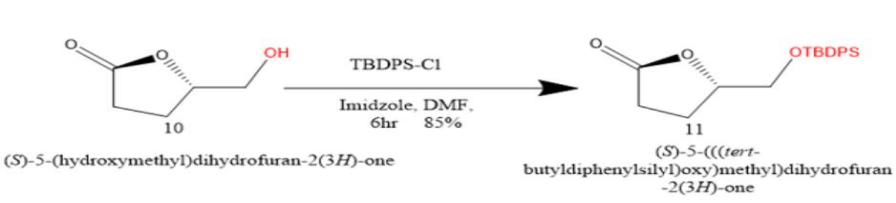


Indication: Green coloured dense spot had appeared in Thin Layer Chromatography and eluted at 40% ethyl acetate/hexane for prolonged time [6].

Work-Up: Methanol to Azeotropes and removed the methanol by rota-vapour. (table-2) [6].
Reaction table *II:*

S.no	Chemical Name	Molecular weight g/mol	Quantity	Milli moles	Equivalence
1	compound 9	130	1g	7.7	1
2	BH3.SiMe2	75.97	0.87ml	9.23	1.2

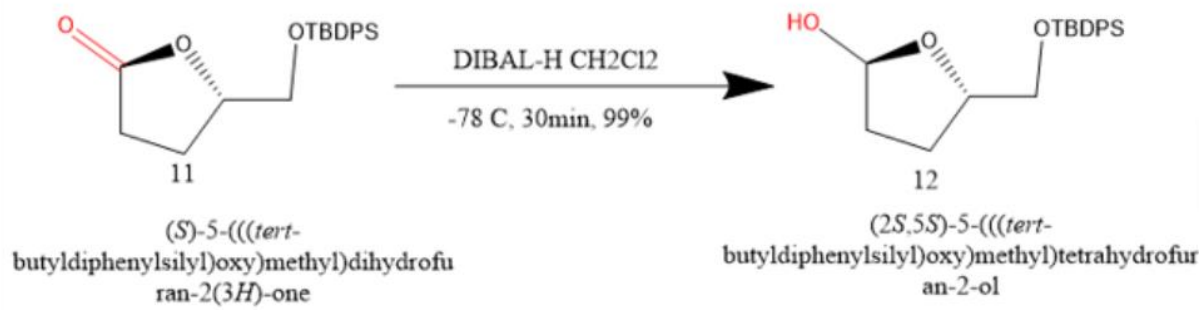
Step-3:



Procedure: Triethyl-amine nd TBDPS-Cl were added subsequently to a solution of compond-10 in dry-DCM at 0 degrees celsius. After being stirred for 15minutes at same temperature. DMAP was added and stirred continuously for 2hours, with slow warming to RT(Keep the reaction overnight) [6].
Indication: Brown coloured spot appeared in Thin Layer Chromatography by taking 20% ethyl acetate/hexane as solvent [6].
Work-up: Add saturated solution of NH4Cl/ethyl acetate/Brine wash and dried over NaSO4 [6].
Reaction table *III:*

S. no	Chemical name	Molecular weight g/mol	Quantity	Milli moles	Equivalence
1	compound-10	116.15	150mg	1.29	1.0
2	TBDPS-Cl	274.86	0.4ml	1.55	1.2

Step-4:
Reaction:



Procedure: A dimethyl dichloride solution of compound-11 was cooled to -78 degrees Celsius and treated with DIBAL and stirred for 1 hour. The reaction mixture was quenched by addition of ethyl acetate and warmed to room temperature [6].

Indication: separated by flash chromatography and loading with 10% Ethyl acetate/hexane [6].

Work-up: Saturated solution of sodium-potassium tartrate was added, and mixture was stirred for 2 hours. The layer was separated, and aqueous layer was extracted with DCM [6].

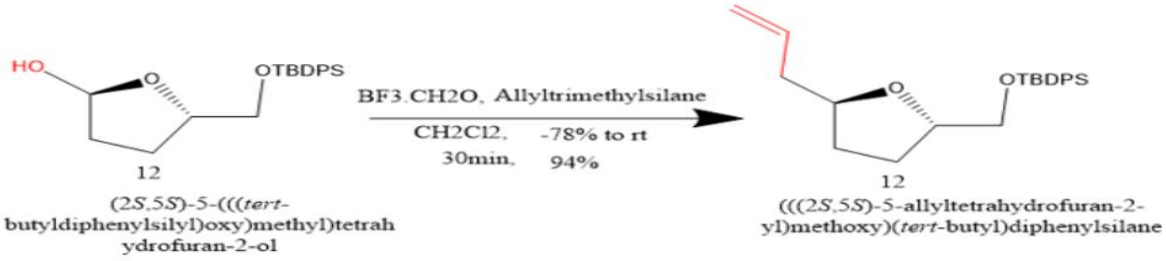
Step-5:

Reaction:

Procedure: To a dimethyl-dichloride, solution of lacteal was added, at 78 degrees Celsius Lewis-acid followed by allyl silane are added. The racemic mixture was stirred for 3 hours [6].

Indication: Black coloured spot appeared in 2% solvent of ethyl acetate and hexane, later through chromatography 2 compounds were separated. By this it was confirmed that the product is racemic mixture [6].

Work-up: Reaction mixture was washed with ammonium chloride, ethyl acetate, brine, water, sodium acetate and dried [6].



12
(2*S*,5*S*)-5-(((*tert*-butyldiphenylsilyl)oxy)methyl)tetrahydrofuran-2-ol

12
(((2*S*,5*S*)-5-allyltetrahydrofuran-2-yl)methoxy)(*tert*-butyl)diphenylsilane

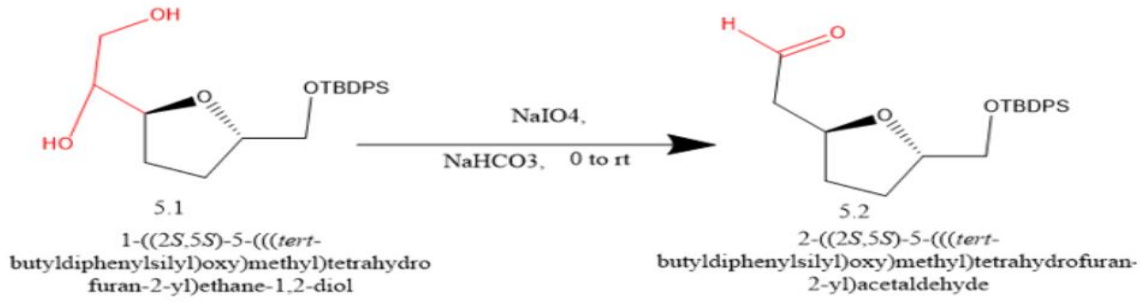
Step-6: It is a two-step process in which Racemic mixture first reacts with OsO4 to form a diol [6].

This again reacts with NaIO4 to form aldehyde(intermediate), this further reduces into secondary alcohol with NaBH4 [6].

Step-6.1:

Reaction:

Indication: dark spot was appeared in 50% ethyl acetate and hexane as solvent



5.1
1-((2*S*,5*S*)-5-(((*tert*-butyldiphenylsilyl)oxy)methyl)tetrahydrofuran-2-yl)ethane-1,2-diol

5.2
2-((2*S*,5*S*)-5-(((*tert*-butyldiphenylsilyl)oxy)methyl)tetrahydrofuran-2-yl)acetaldehyde

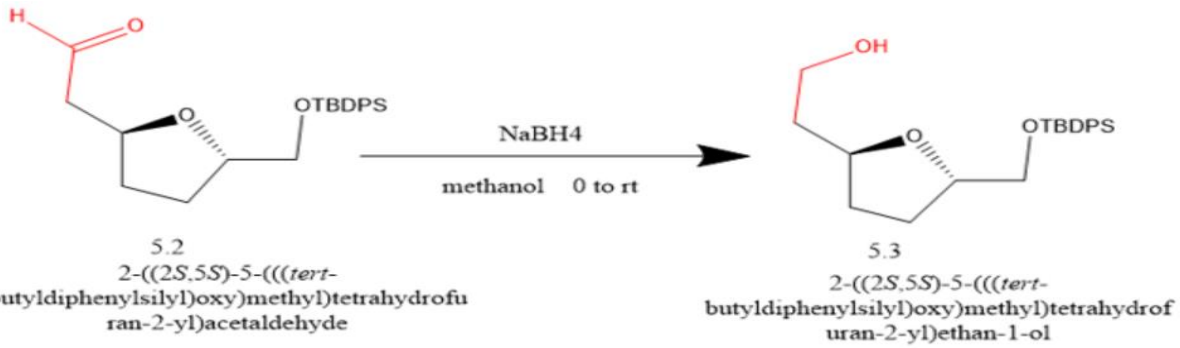
Step-6.2

Reaction:

Procedure: Compound 5.1 was dissolved in DCM/Acetone (100 ml) solution. Cool it to 0 degrees Celsius and then add saturated NaHCO3(0.4gms), followed by NaIO4 and stir at room temperature for 1 hour [6].

Indication: dark spot had appeared in 50% ethyl acetate and hexane as solvent [6].

Work-up: Add sodium sulphate to the reaction mixture and filter through elite [6].

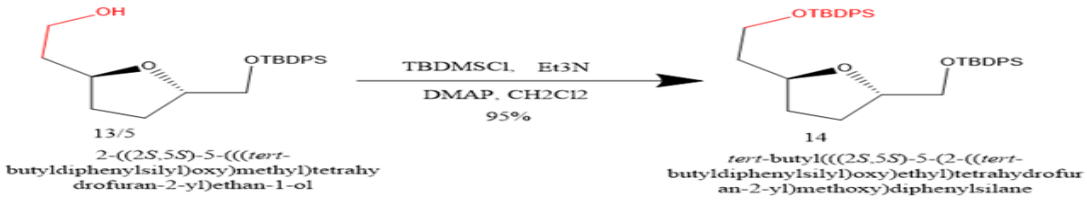


5.2
2-((2*S*,5*S*)-5-(((*tert*-butyldiphenylsilyl)oxy)methyl)tetrahydrofuran-2-yl)acetaldehyde

5.3
2-((2*S*,5*S*)-5-(((*tert*-butyldiphenylsilyl)oxy)methyl)tetrahydrofuran-2-yl)ethan-1-ol

Step-7

Reaction:



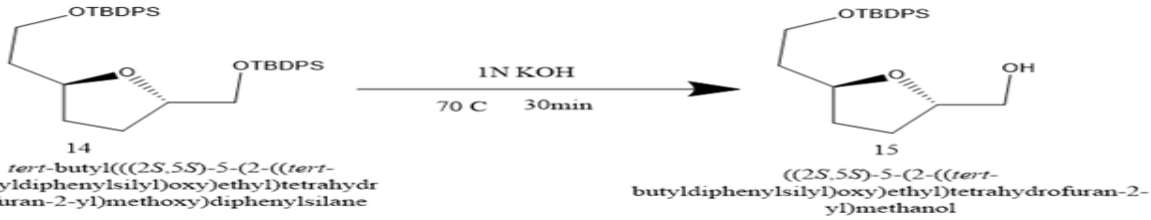
13/5

2-((2*S*,5*S*)-5-(((*tert*-butyldiphenylsilyl)oxy)methyl)tetrahydrofuran-2-yl)ethan-1-ol

14

tert-butyl(((2*S*,5*S*)-5-(2-((*tert*-butyldiphenylsilyl)oxy)ethyl)tetrahydrofuran-2-yl)methoxy)diphenylsilane

Step-8
Reaction:



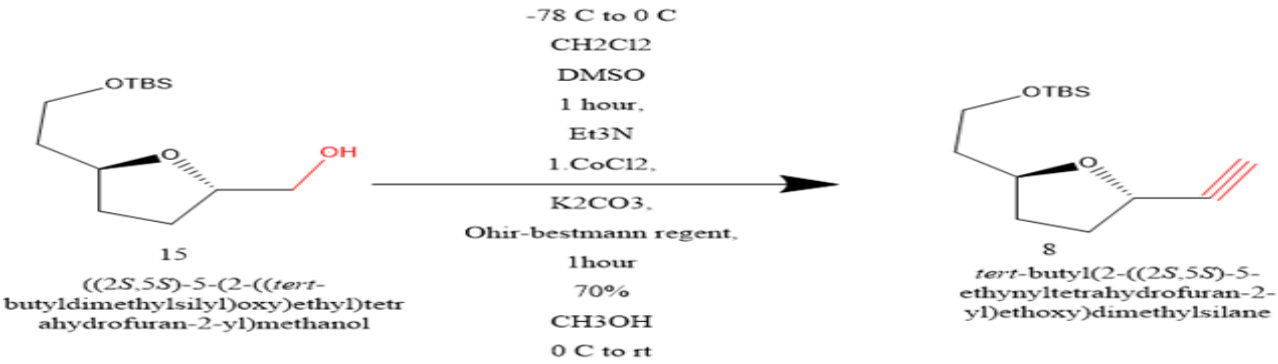
14

tert-butyl(((2*S*,5*S*)-5-(2-((*tert*-butyldiphenylsilyl)oxy)ethyl)tetrahydrofuran-2-yl)methoxy)diphenylsilane

15

((2*S*,5*S*)-5-(2-((*tert*-butyldiphenylsilyl)oxy)ethyl)tetrahydrofuran-2-yl)methanol

Step-9:
It is a two-step process in which alcohol is first converted into aldehyde (an intermediate) and then this aldehyde undergone Ohira-bestmann reaction to convert into alkyn [6]..
Reaction:



15

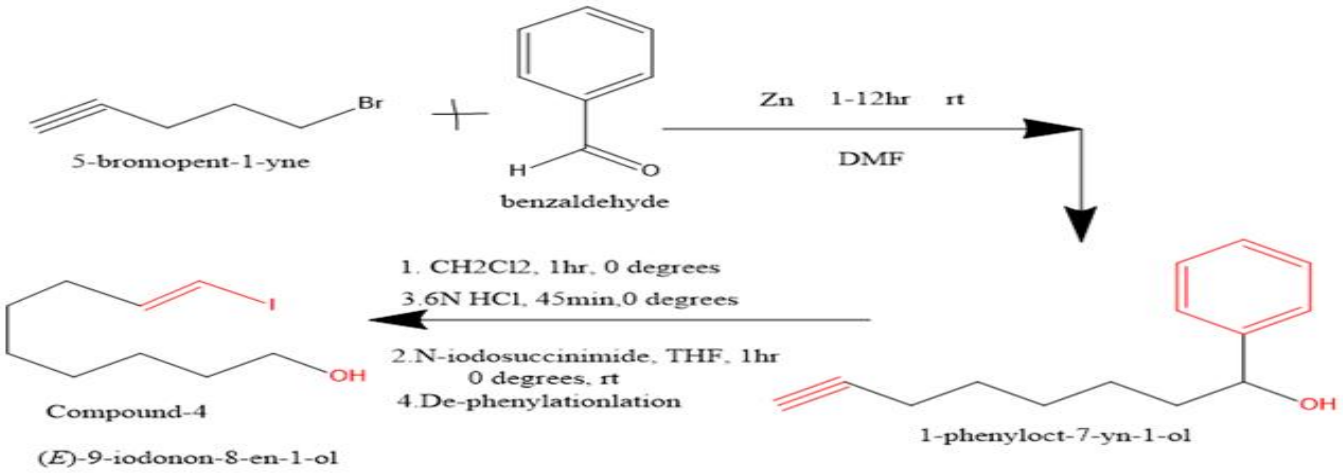
((2*S*,5*S*)-5-(2-((*tert*-butyldimethylsilyl)oxy)ethyl)tetrahydrofuran-2-yl)methanol

8

tert-butyl(2-((2*S*,5*S*)-5-ethynyltetrahydrofuran-2-yl)ethoxy)dimethylsilane

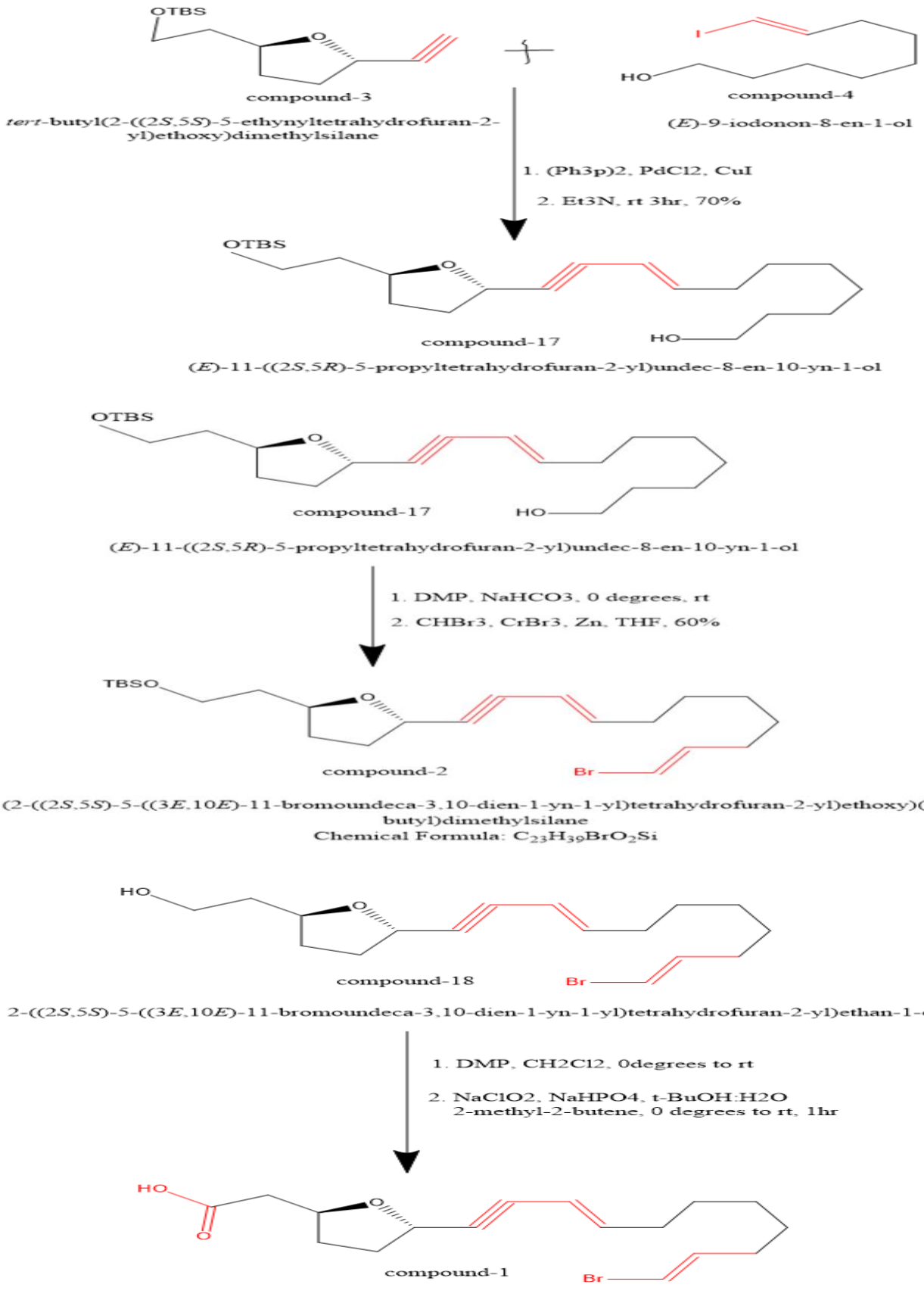
SCHEME-2: Synthesis of Vinyl-iodide containing Alcohol(fragment-4) [6].

Reaction:



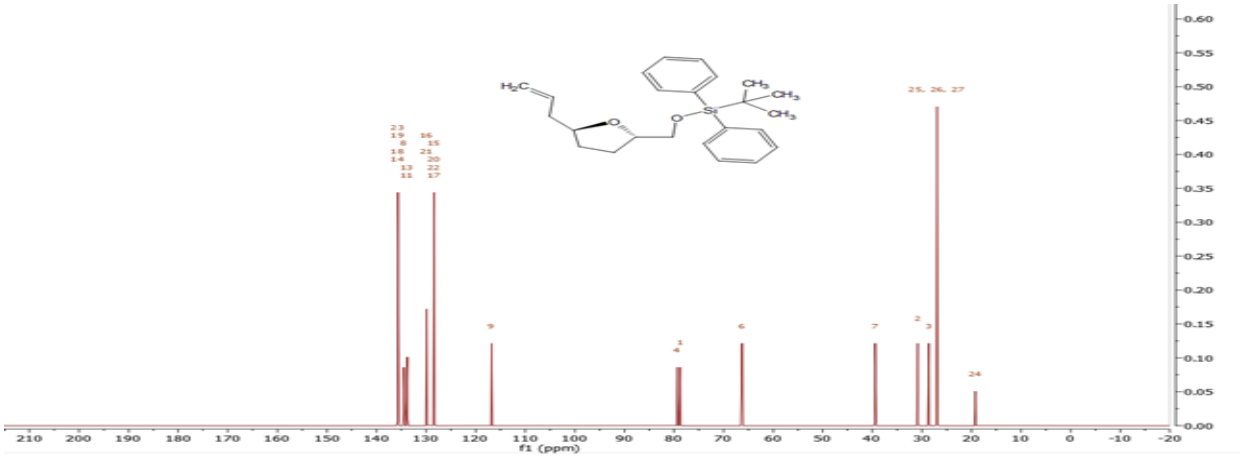
(*E*)-9-iodonon-8-en-1-ol

SCHEME-3: Coupling of Alkyne with Vinyl-iodide fragment through Sonogashira coupling [11].
Sonogashira coupling: It is a Cross-coupling reaction of aryl/vinyl halides with terminal alkynes to generate conjugated enzymes and arylalkynes. The reaction typically proceeds in the presence of a palladium catalyst and an imine base [11].
Reaction 3.1
Reaction 3.2
Reaction 3.3
Indication: Purified pale-yellow liquid when stored in refrigerator, clear oil at room temperature [11].

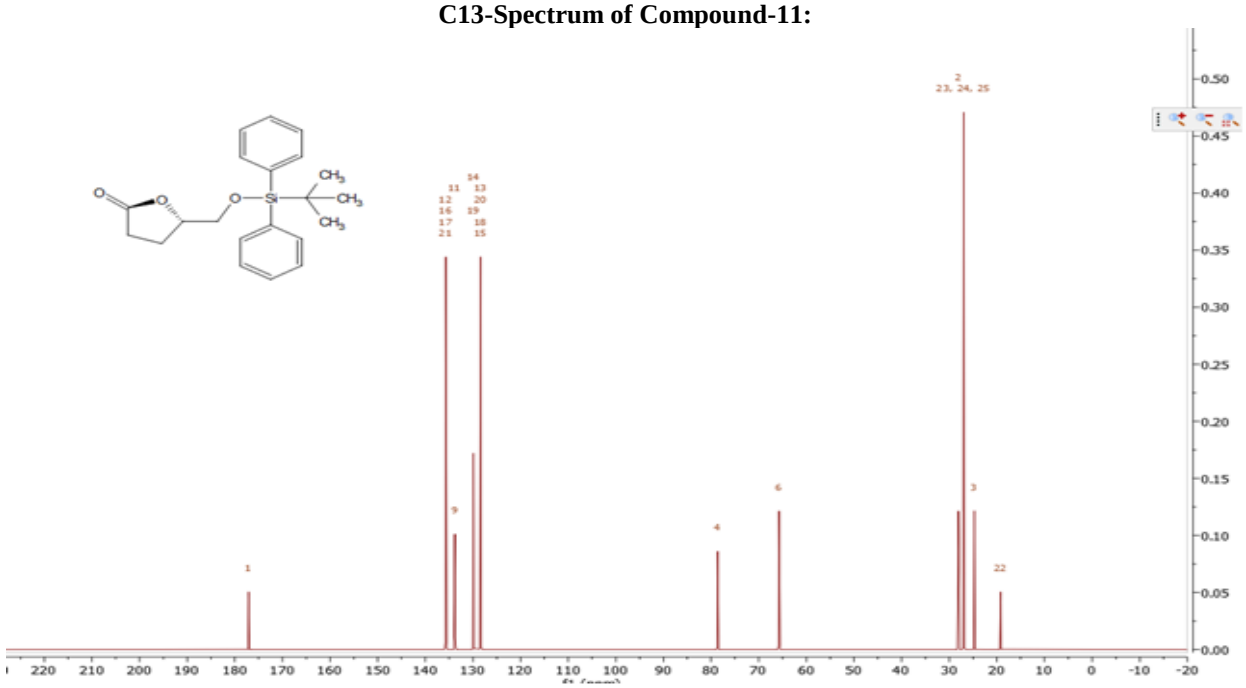


TESTUFURAN-A

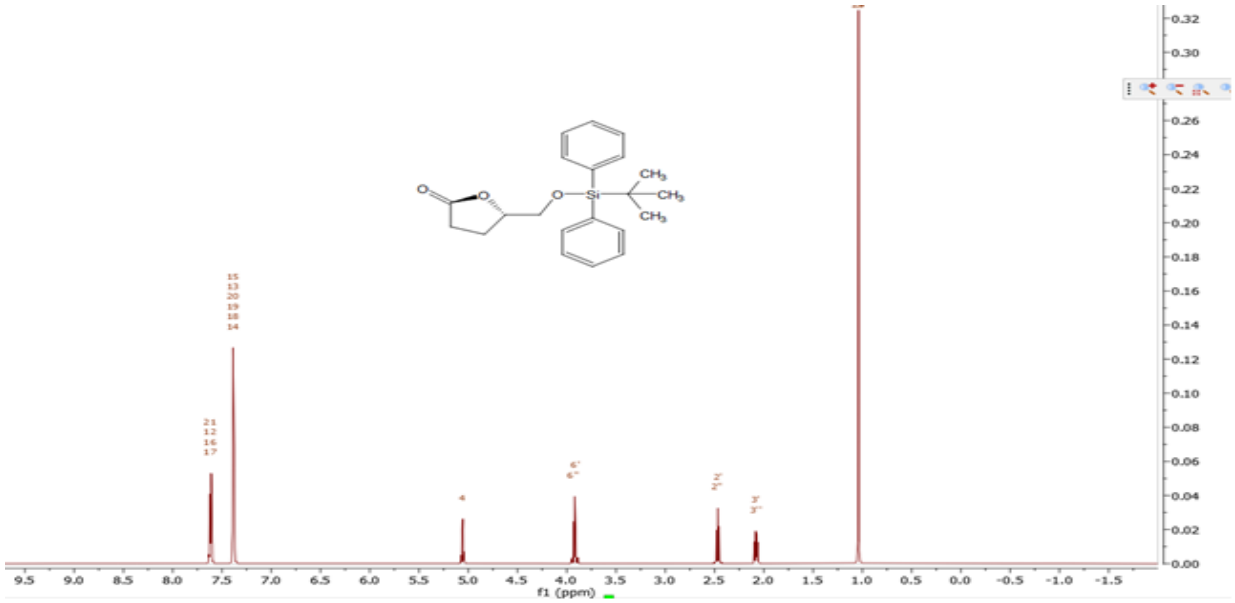
RESULTS AND DISCUSSIONS



C13-Spectrum of Compound-11:

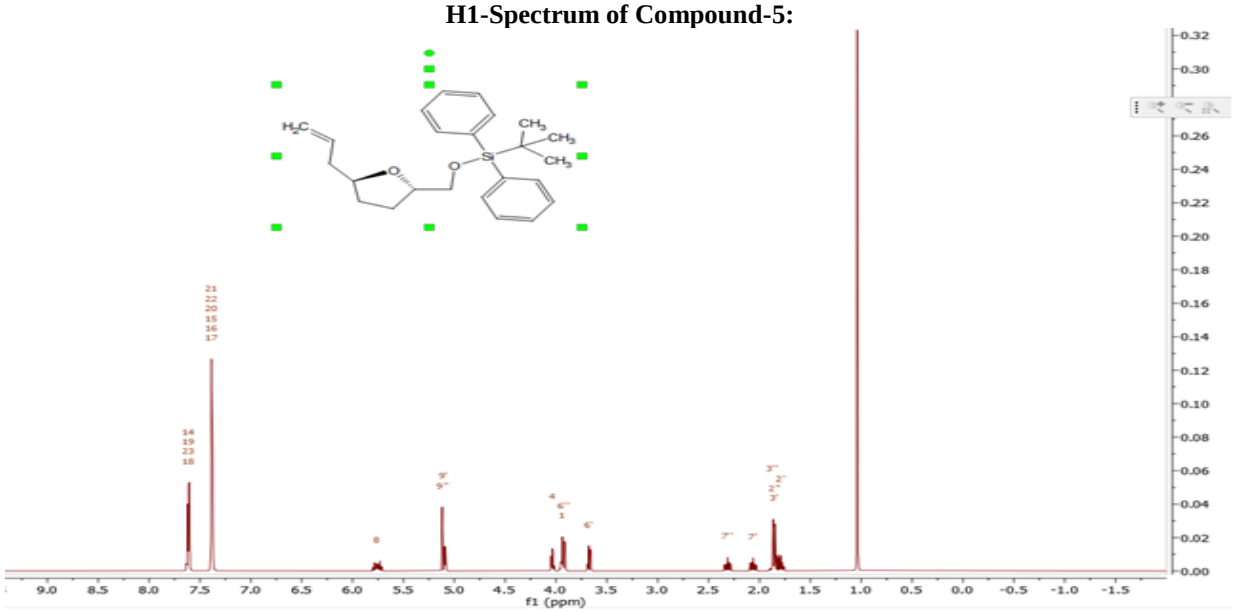


H1-Spectrum of Compound-11:

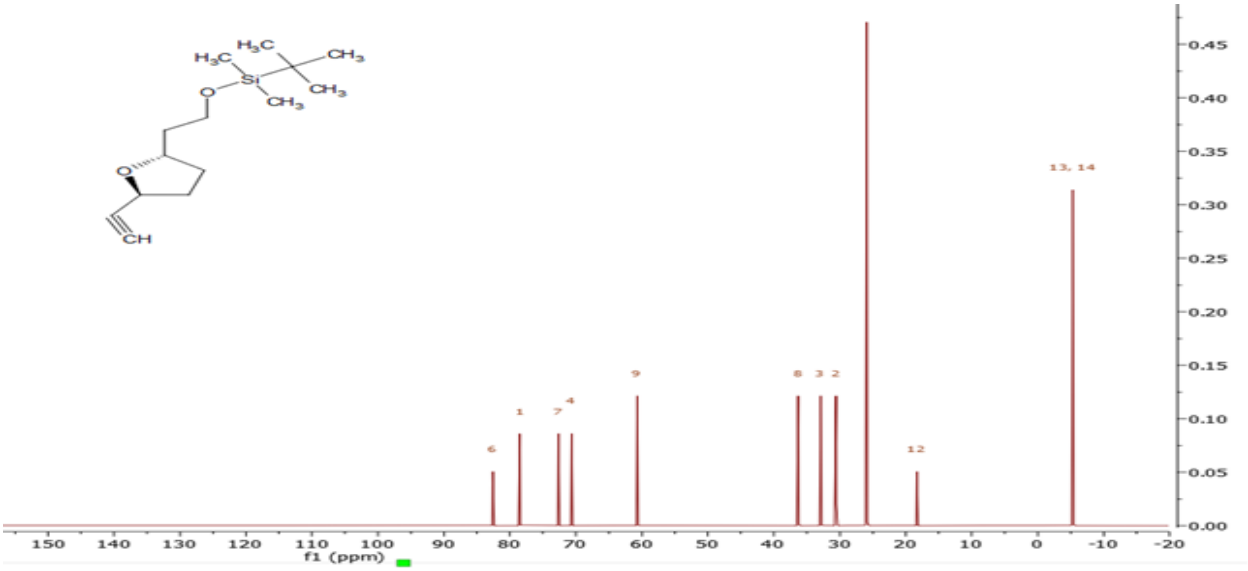


C13-Spectrum of Compound-5:

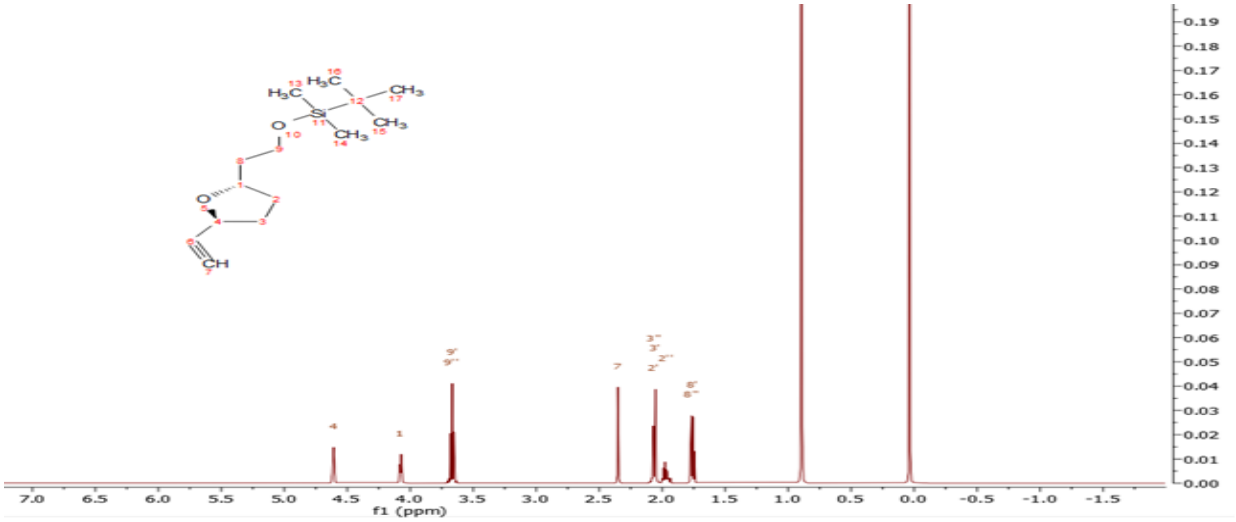
H1-Spectrum of Compound-5:



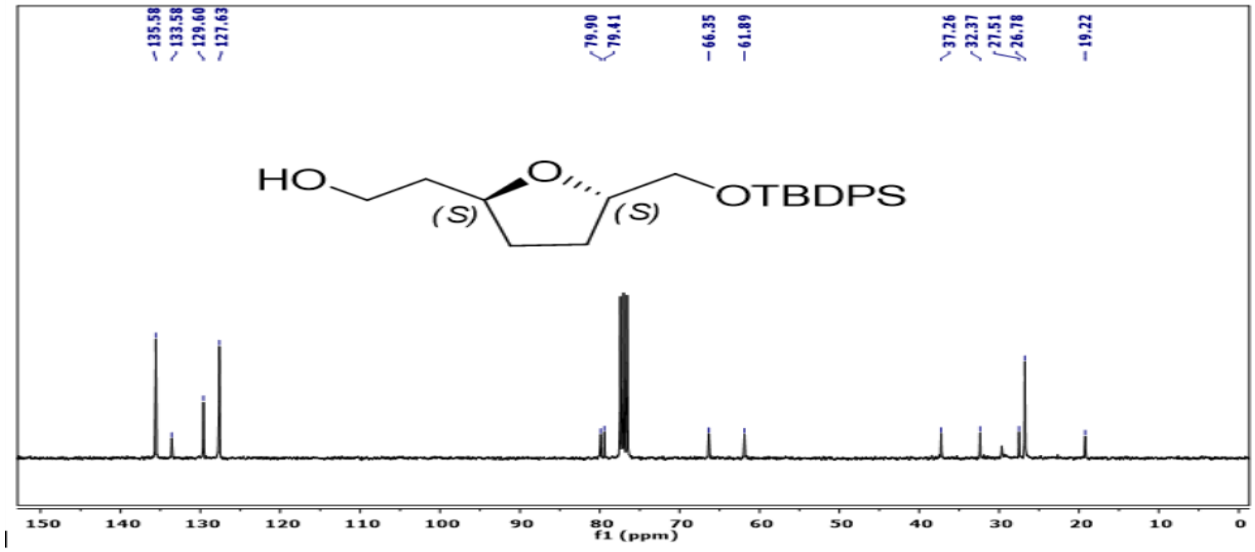
C13-Spectrum of Compound 8



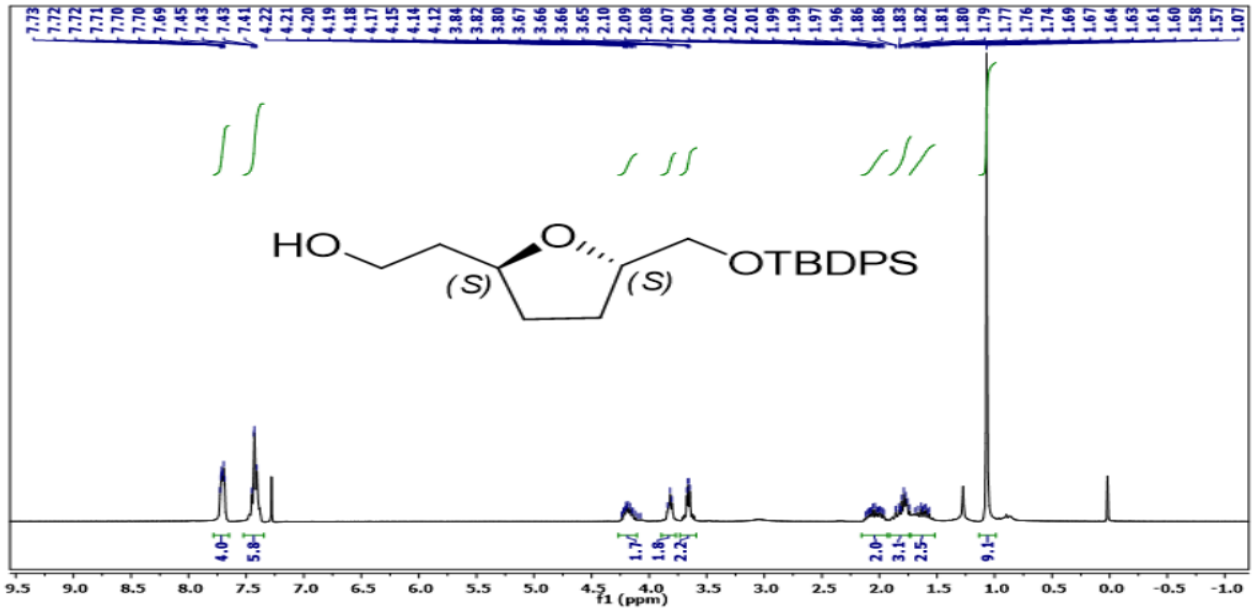
H1-Spectrum of Compound-8:



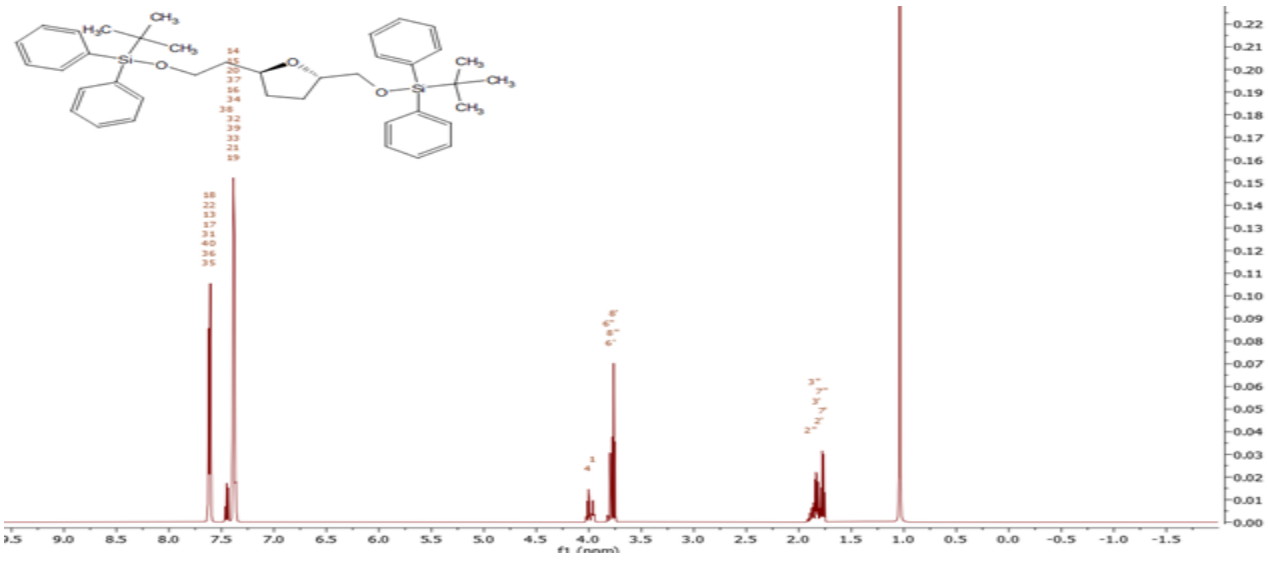
C13-Spectrum of Compound-13:



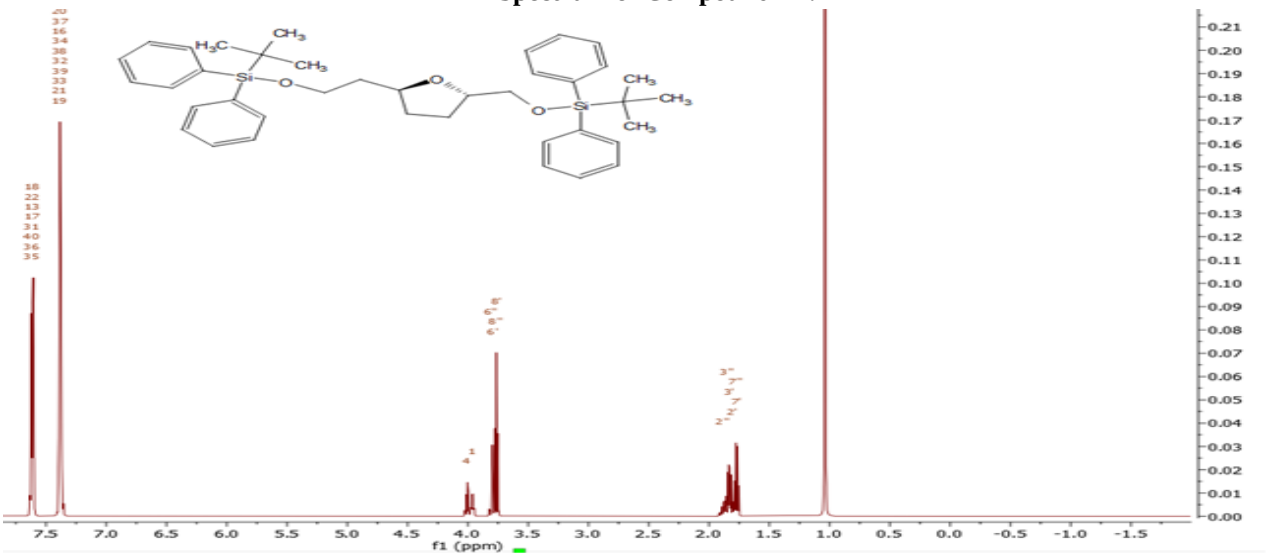
H1-Spectrum of Compound-13:



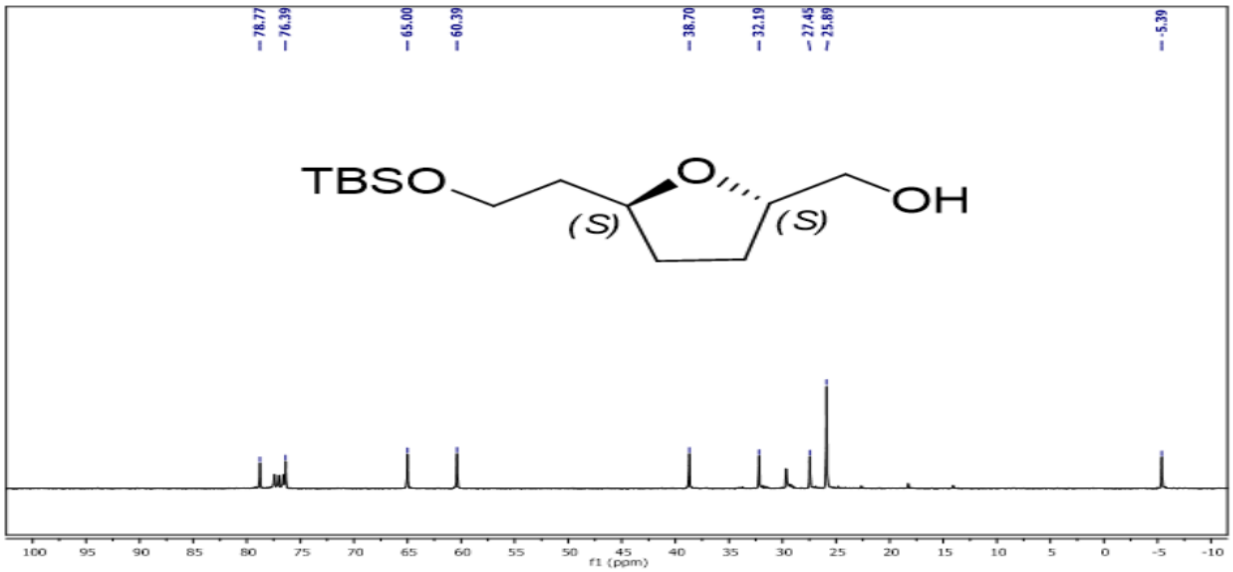
C13 –Spectrum of compound –14:



H1-Spectrum of Compound-14:



C13-Spectrum of Compound-15:



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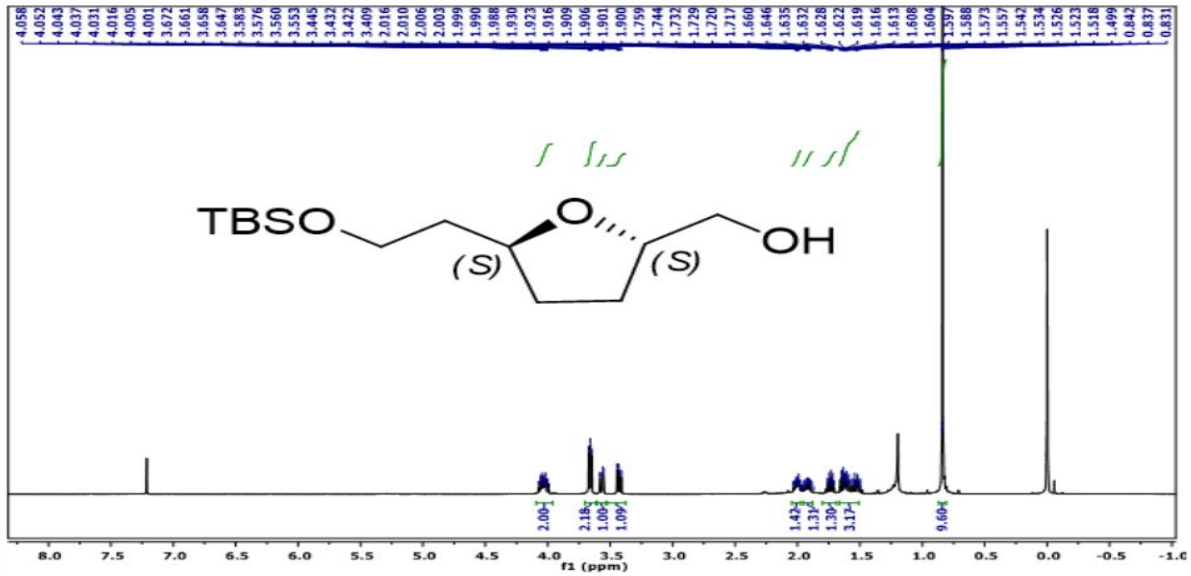

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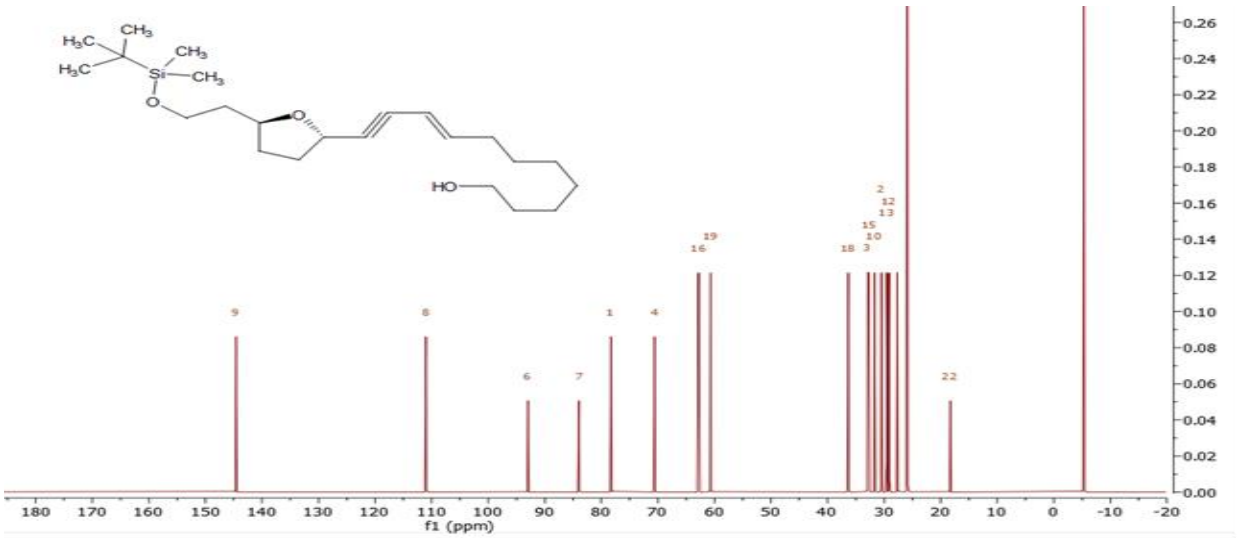

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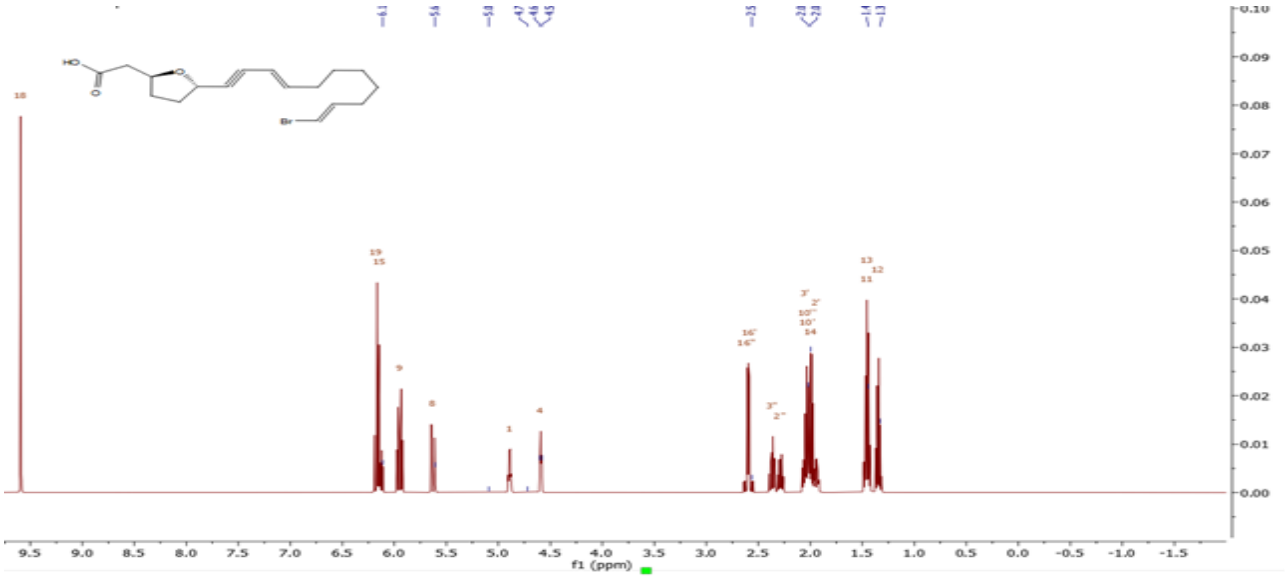
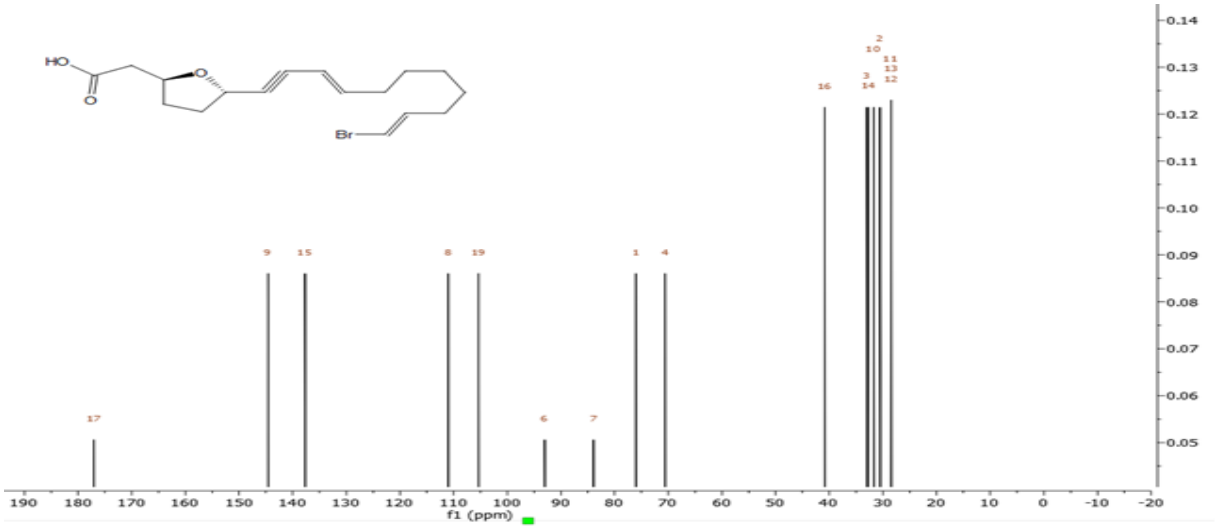
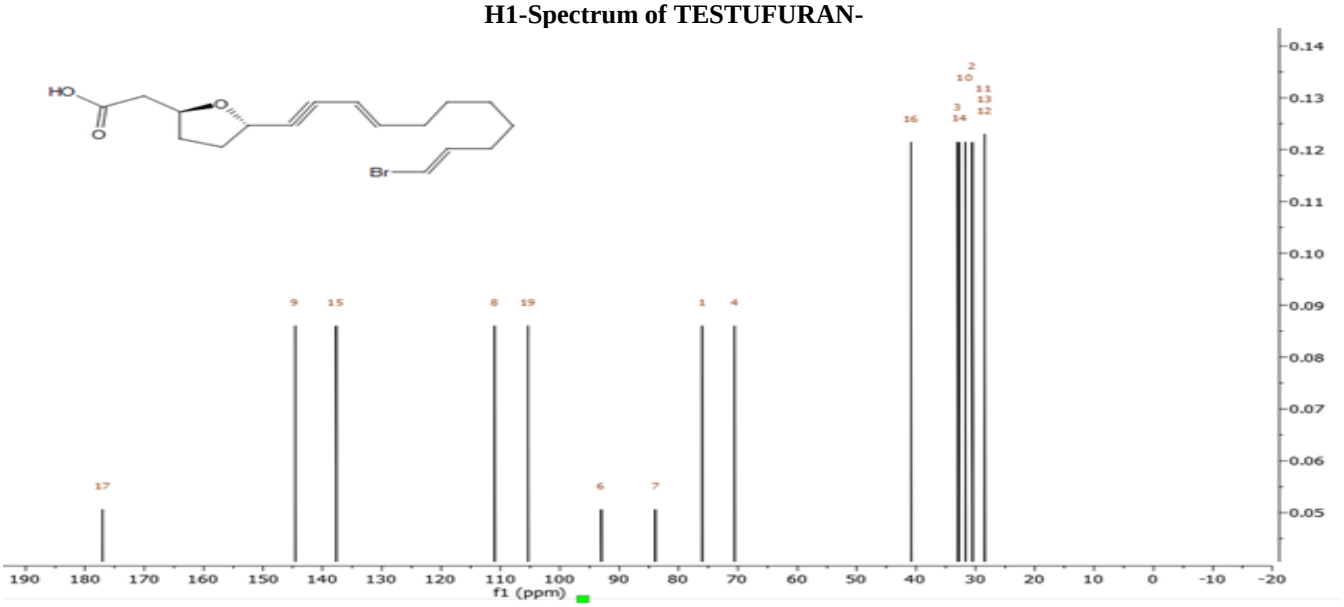


C13-Spectrum of TESTUFURAN-A:



H1-Spectrum of TESTUFURAN-



ADIPONECTIC ACTIVITY

The synthesized compound, Testufuran-A, was evaluated for its effect on adiponectin secretion. Adiponectin is an important biomarker associated with anti-atherosclerotic and anti-diabetic activity [3]. The study revealed that the compound exhibited a significant increase in adiponectin levels when compared to the control [10].
The enhanced adiponectin secretion indicates the potential of the synthesized compound in improving metabolic functions and reducing the risk of atherosclerosis [3].This suggests that Testufuran-A may act as a promising candidate for further pharmacological evaluation [10]
The observed activity supports the relevance of marine-derived metabolites and their synthetic analogs in the development of therapeutic agents [8].

CONCLUSION

- The Synthesis of newly designed TESTUFURAN-A was achieved and characterized by using spectroscopic techniques like H1-NMR, C13-NMR, FT-IR, and LCMS [6].
- Design for the derivatives is done, and its synthesis is under progress. [6].
- It was concluded that the synthesized molecule showed increased release of Adiponectin compared to another Anti-Diabetic drug [3].
- The pure compound of TESTUFURAN-A is obtained, and the yield is about 80%. [6]
- Using Sonogashira Coupling Vinyl iodide fragment is coupled with Alkyl fragment to obtain TESTUFURAN-A [11].

The structure of the synthesized compounds was confirmed by spectral analysis (^{1}H NMR, IR, and Mass spectroscopy).

REFERENCES

[1]. American Diabetes Association. (2013). Diagnosis and classification of diabetes mellitus. *Diabetes Care, 36*(Suppl 1), S67–S74.

[2]. Blunt, J. W., Copp, B. R., Munro, M. H. G., Northcote, P. T., & Prinsep, M. R. (2011). Marine natural products. *Natural Product Reports, 28*(2), 196–268.

[3]. Hotta, K., Funahashi, T., Arita, Y., et al. (2000). Plasma concentrations of adiponectin in type 2 diabetic patients. *Arteriosclerosis, Thrombosis, and Vascular Biology, 20*(6), 1595–1599.

[4]. International Diabetes Federation. (2013). *IDF Diabetes Atlas* (6th ed.). Brussels, Belgium: IDF.

[5]. Kaveeshwar, S. A., & Cornwall, J. (2014). The current state of diabetes mellitus in India. *Australasian Medical Journal, 7*(1), 45–48.

[6] Kubota, T., Suzuki, H., et al. (2016). Brominated acetylenic fatty acids from marine sponge *Xestospongia testudinaria*. *Journal of Natural Products, 79*(6), 1606–1611.

[7]. Libby, P. (2002). Inflammation in atherosclerosis. *Nature, 420*(6917), 868–874.

[8] Mayer, A. M. S., Rodríguez, A. D., Berlinck, R. G. S., & Fusetani, N. (2013). Marine pharmacology from 2009–2011. *Marine Drugs*, *11*(7), 2510–2573.

[9]. Newman, D. J., & Cragg, G. M. (2014). Marine-sourced anticancer agents. *Marine Drugs*, *12*(1), 255–278.

[10] Ouchi, N., Kihara, S., Funahashi, T., Matsuzawa, Y., & Walsh, K. (2003). Obesity, adiponectin, and vascular inflammatory disease. *Current Opinion in Lipidology*, *14*(6), 561–566.

[11] Sonogashira, K., Tohda, Y., & Hagihara, N. (1975). A convenient synthesis of acetylenes: Catalytic substitutions of acetylenic hydrogen with bromoalkenes, iodoarenes and bromopyridines. Tetrahedron Letters, 16(50), 4467–4470. https://doi.org/10.1016/S0040-4039(00)91094-3