The Synthesis Of Stannylated C1 Nucleophilic Monosaccharides For Use In The Stille Coupling Reaction

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Abstract

The investigation sought to determine whether a transition metal coupling reaction with aryl halides could be utilized to form glycoconjugates, carbohydrate-containing molecules, specifically C-Aryl Glycosides. Our successful novel application in glycochemistry employs the Stille coupling reaction and improves the viability of accessing a range of glycogonjugates for biological and therapeutic screening.(1) The reaction maintains exceptional retention of configuration from the carbohydrate-metal bond in the completed sp^3 carbon – sp^2 carbon bond of the produced glycoside. A synthesized library of C-aryl Glycosides was established utilizing this methodology; from which a selective schema was submitted for publication. This technology provides a route to discrete carbohydrate building blocks that can be assembled with minimal reagents and moderate synthetic knowledge. These building blocks can then be stereo-specifically attached to molecules of interest under a set of general catalytic conditions; expediting the investigation of carbohydrate's role in biochemical processes that was limited by substrate dependent laborious processes of glycoconjugate formation.

Introduction

Developing a synthetic library of carbohydrate molecules is necessary for advancement in glycoinformatics as there is no template like in DNA, RNA, and proteins, and requires chemical synthesis.[2] Developing the glycomic library has implications for a range of diseases and healthy biology and is a priority to emphasize the importance in the development of new glycomic technology.[3] With the expansion of the glycomic library, including more C-aryl glycoside discoveries, new drug targets can utilize this specific glycoside as they are carbohydrate analogues stable to enzymatic and acid hydrolysis.[4]

Research was founded on the hypothesis that transition metal coupling reactions have potential applications that can revolutionize glycochemistry, with the capability to modify the current approach to the chemistry of glycoconjugate formation. Our methodology demonstrates carbohydrates can be coupled in transition metal coupling reactions with observable complete retention of configuration, that is the configuration of a carbon-metal bond can be absolutely retained in a palladium catalyzed coupling reaction with an electrophile.[5] The objective was to develop a viable route to perform stereospecific coupling reactions of carbohydrates with a multitude of aryl-halide containing molecules. The addition of carbohydrate groups to organic compounds is important as it improves pharmacokinetic properties such as solubility and stability.[6] Moreover, carbohydrates are responsible for mediating numerous cell signaling events such as nutrient sensing, protein degradation, and gene expression.[7]

Traditional methods of carbohydrate synthesis are limited because of arduous synthetic schemes needed to prepare the compounds of interest. Currently the preparation of novel carbohydrate molecules is laborious and primarily restricted to specialized synthetic laboratories

utilizing anomeric halides and nucleophilic carbon sources.[8] Furthermore, the application of Friedel-Crafts electrophilic substitution of the aromatic ring by variable glycans in the presence of a Lewis-Acid has been employed, exhibiting limited substrate dependent diastereoselectivity.[8a]

The chemistry performed in this project enables the synthesis of complex carbohydrate entities in much shorter and efficient ways, and provides a viable route for carbon-carbon bond formation in the presence of fully deprotected sugars. This novel ground work has the capability to enable efficient synthesis of complex carbohydrate-bound targets and provides opportunity for further investigation into selectively applying and refining methodologies of stereoretentive carbon-carbon bond formation. This technology could create a range of new therapeutics and diagnostic applications by providing academic researchers and industry an efficient general protocol that eases the synthetic production of previously complicated carbohydrate reactions that were inherently hard to isolate, purify, and characterize due to glycoconjugates of variable epimeric purity.

Background

Possible therapeutic applications within glycochemistry will be imperative in research, industry, and healthcare. Furthermore, as glycans are involved in pathophysiology of human disease, glycochemical research will have the potential to accelerate the addition of glycans into already significantly characterized biological libraries, leading to novel therapeutics.[9] As surface-bound carbohydrate entities, glycans enable recognition and intercellular communication; it has been known for almost three decades that the carbohydrates residing on the cell surface and their complementary sugar-specific receptors, lectins, play a key role in intercellular signaling and recognition.[10]

This cell signaling and communication on the surface of pathogens and mammalian cells can be exploited in antibiotics and as biomarkers in biological processes. Thus the addition of the associated epitopes or glycotopes can be attached to immunologically active peptides to investigate minimally explored therapeutics in cancer.(11) The abundance of bonding configurations that carbohydrates exhibit from their branched structures lends to a unique ability for great variability in signaling potential.(12) However, this potential for multiple branching configurations exacerbates the difficulty of synthetic glycochemistry. Efficient investigation of carbohydrates and their associated biologically significant coupling partners across broad signaling pathways will require the continued development of novel synthetic methodology. This will enable viable production of synthesizable industrial or public libraries of glycoconjugates with complex carbohydrates bound to coupling partners beyond aryl halides, including the addition of C-O, and C-N bond formation methodologies.

The development of methods that produce building blocks that can be reproducibly assembled will allow glycochemistry to meet a "sorely needed" niche in the biosciences.(13) Few methods have provided this reproducibility with the potential to provide carbohydrate building blocks in discrete packages that can be assembled under a simple set of reagents and conditions. Utilizing Stille transition metal coupling reactions, we have shown through the formation of glycosylated aromatic structures that developing carbohydrate building blocks and subjecting them to a set of catalytic conditions can expand the availability of structures for investigation, applications in industry, and discovery of potential therapeutic approaches.

Exploration of Suzuki-Miyaura coupling

The project began utilizing Suzuki-Miyaura coupling and attempted to develop a methodology that would provide a novel route to C-Aryl Glycosides. The model system was a C1

carbon that was synthesized by ortho-lithiation of 3,4-di-hydro-2H-pyran. This lithium reagent performed a nucleophilic attack on trimethyl borate and after addition of pinacol, the pinacalto boronic ester **MR1** was formed. The double bond was saturated to form a racemic molecule with a coupling nucleophile attached to an sp^3 C1 for the Suzuki-Miyaura reaction; this screens for any combination of catalytic conditions for sp^3 carbon – sp^2 carbon bond formation. The racemic boronic ester removes factors of selectivity for C1 configuration in catalytic conditions and delays consideration of retention until the carbon bond formation was established.

Scheme 1: Synthetic pathway to the saturated pinocalato boronic ester **MR2** that was subjected to a series of unsuccessful coupling conditions with 3-iodotoluene

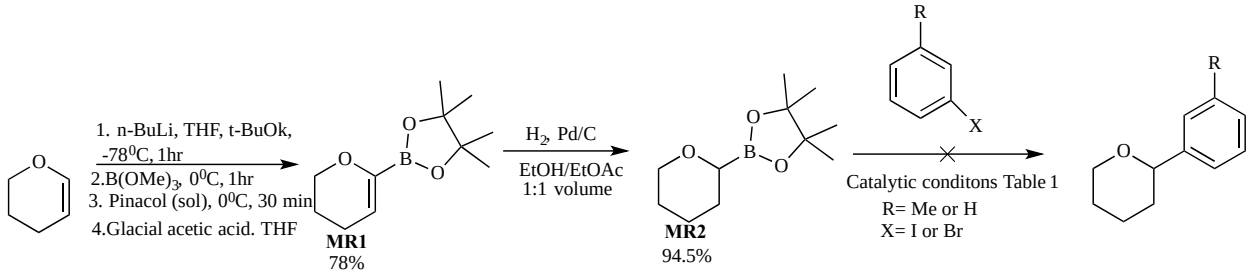


Table 1: A depiction of conditions experimentally determined to be unsuccessful for the pinocalato boronic ester and two simple aryl halides.

Catalyst	**Reagent**	**Conditions**	**Electrophile**	**Results**
$Pd(PPh_3)_4$, (10 mol%)	Na_3PO_4 (5 eq.), Dioxane 2ml	Freeze, pump cycle, rt. 25 min	Bromobenzene (1 eq.)	No Product
$Pd(PPh_3)_4$, (10 mol%)	Na_3PO_4 (5 eq.), Dioxane 2ml	Freeze, pump cycle, rt. 25 min	3-iodotoluene (1 eq.)	No Product
$Pd(PPh_3)_4$, (10 mol%)	Cs_2CO_3 (2 eq.), Dioxane:H_2O (1:1) 40ml (1M)	Freeze, pump cycle, rt. 25 min	3-iodotoluene (1 eq.)	No Product
$Pd(PPh_3)_4$, (10 mol%) Unsaturated boronic ester	Cs_2CO_3 (2 eq.), Dioxane:H_2O (1:1) 50ml (0.8M)	Freeze, pump cycle, rt. 25 min	3-iodotoluene (1 eq.)	No Product
$Pd(dppf)Cl_2$, (10 mol%)	Cs_2CO_3(2 eq.), CuI (1 eq.), Dioxane 1.5ml (0.16M)	Glove box prep, 100⁰C O/N	3-iodotoluene (1 eq.)	No Product
NiBr2 (10 mol%),	n-Hexanol (2 eq.), t-BuOK (1.4 eq.),	In glove box: **A**. L (12%),	3-iodotoluene (1 eq.)	No Product

Ligand: CAS 29841-69-8 (12 mol %) Performed x2 variance of boronic ester equivalence with respect to electrophile 1. 1 eq. 2. 2 eq.	Dioxane 1.5 ml (0.16M)	C(10%),dioxane. 30 min rt. **B.** MR2, *t*-BuOK, *n*-hexanol.30min rt. **C**.Combined, removed,40hr 100^0C.		
$Pd(PPh_3)_4$ (5 mol%)	Cs_2CO_3(2eq.), Dioxane:H_20 (1:1)	Freeze, pump, thaw. Stir 100^0C	3-iodotoluene (1 eq.)	No Product

Suzuki-Miyaura coupling was a target because of proven research that states pharmaceuticals currently utilizing this method are safe for manufacturing and non-toxic. Furthermore, boron containing compounds and boronic acids were concluded safe and possibly efficacious justifying investigation into their therapeutic value as an active constituent of the final molecule or drug [13].

The unsuccessful coupling of the pinacolato borane **MR2** lead to the consideration of a tri-fluoroborate, as the coupling of the BF_3^- nucleophile with aryl-halides has demonstrated has been by Molander et al.[14]

Scheme 2: Synthetic pathway from the saturated pinocalato boronic ester **MR3** to the tri-fluoroborate that was subjected to a series of unsuccessful coupling conditions with 3-iodotoluene

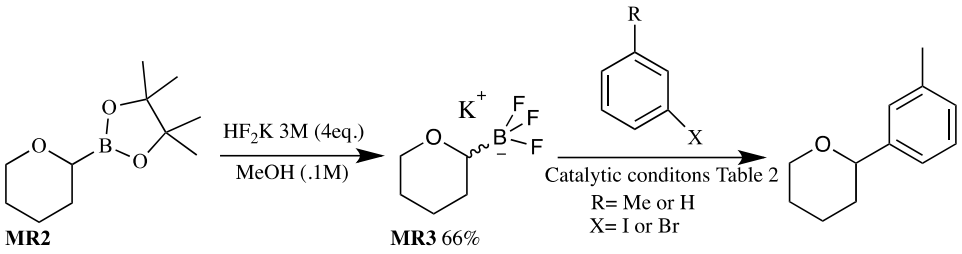


Table 2: Coupling conditions C1-trifluoroborates, proved to be unsuccessful. Note: Dioxane degassed.

Catalyst	**Reagent**	**Conditions**	**Electrophile**	**Results**
$Pd(PPh_3)_4$ 10%	Cs_2CO_3 (2eq.), Dioxane 1.5 ml (0.14 M)	Glove box prep, 100^0 C for 72 hr.	3-iodotoluene	No Product
$NiBr_2$(diglyme) (10 mol%), Ligand*:CAS2984169-8 (12%)	*n*-hexanol (2 eq.), t-BuOK (1.2eq), Dioxane 1.5 ml (0.14M)	In glove box: **A**. L(12%), C(10%), dioaxane. 30 min rt. **B.**MR3, *t*-BuOK, *n*-hexanol. 30 min rt. **C**.Combined, removed, stir 100^0C 40hr.	3-iodotoluene	No Product

The C1-trifluoroborate did not successfully form the desired product under the two catalytic conditions, leading to the reconsideration of the pinacolato boronic ester. In attempt to prepare a carbohydrate model for the application of appropriate catalytic conditions, a tetra-*O*-acetyl-1-bromo-glucose electrophile was subjected to catalytic conditions with bis(pinacolato)diboron.

Scheme 3: Synthetic route to tetra-*O*-acetyl-1-bromo-D-glucopyranose **MR5** from glucose. **MR5** was subjected to coupling conditions as an electrophile with no desired product.

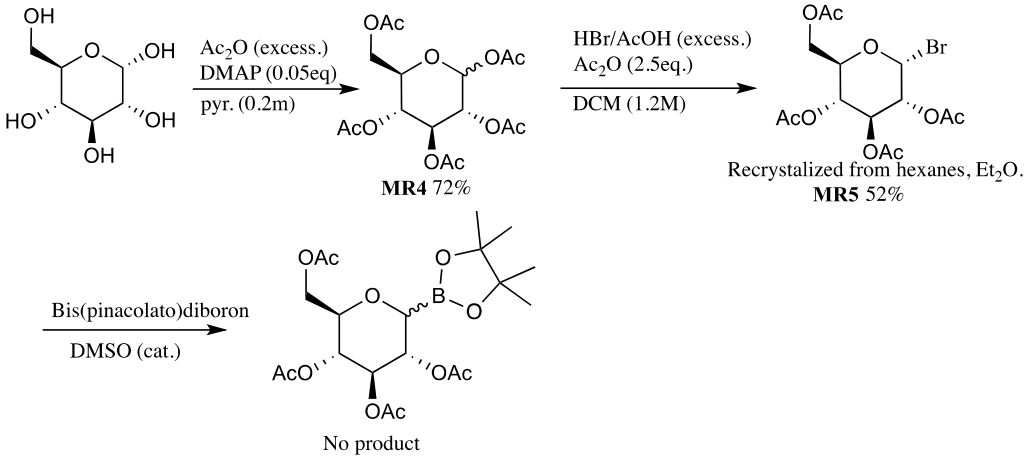


Table 3: A depiction of conditions experimentally determined to be unsuccessful for tetra-*O*-acetyl-1-Bromo-glucose in a 3-neck anh. flask w/ condenser under an N_2 atmosphere.

Catalyst	**Reagent**	**Conditions**	**Electrophile**	**Results**
$Pd(PPh_3)_4$, (15 mol%)	KOAc (10eq.), DMSO 2.5 ml (0.24 M)	Glove box prep, 80^0C, 5 min	Bis(pinacaloto)diboron (1eq.)	No Product
$Pd(PPh_3)_4$, (20 mol%)	KOAc (10eq.), DMSO 2.5 ml (0.24 M)	Glove box prep 80^0C, 30 min.	Bis(pinacaloto)diboron (1eq.)	No Product
$Pd(PPh_3)_4$, (20 mol%)	KOAc (10eq.), DMSO 2.5 ml (0.24 M)	Glove box prep, 80^0C, 7 hr.	Bis(pinacaloto)diboron (1eq.)	No Product
$Pd(PPh_3)_4$, (20 mol%)	Na_3PO_4 (10eq.), DMSO 2.5 ml (0.24 M)	Glove box prep, 80^0C, 7 hr.	Bis(pinacaloto)diboron (1eq.)	No Product
$Pd(dppf)Cl_2$, (20%)	Cs_2CO_3 (10eq.), DMSO1.5 ml (0.24 M)	Glove box prep, 80^0C, 7 hr.	Bis(pinacaloto)diboron (1eq.)	No Product
$Pd(dppf)Cl_2$, (20%)	Na_3PO_4 (10eq.), DMSO1.5 ml (0.24 M)	Glove box prep, 80^0C, 7 hr.	Bis(pinacaloto)diboron (1eq.)	No Product

Exploration of the Stille coupling recation

Approaches to stereo-retentive bond formation utilizing other coupling methods were investigated as we were not able to produce successful reactions with a C1 nucleophilic boronic ester, in consideration with the failed attempts at successfully forming the sp^3 carbon – sp^2 carbon bond via Suzuki coupling. In response, a glycosylstannane utilizing trimethyltin was subjected to catalytic conditions favoring the Stille coupling method. However, the reaction proved to be unsucessful but remains a defining time in the application of coupling reactions to C-glycoside formation.

Scheme 4: Depiction of the trimethyl(tetra-*O*-benzyl-D-glucopyransosyl)stannane **MAW** and desired coupling product

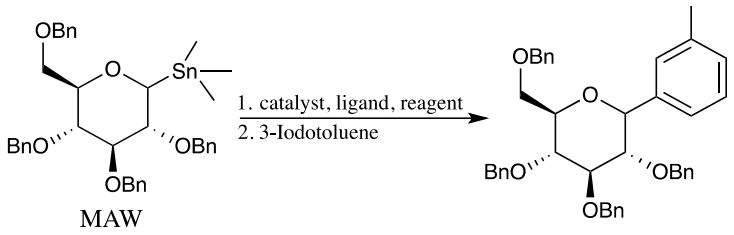
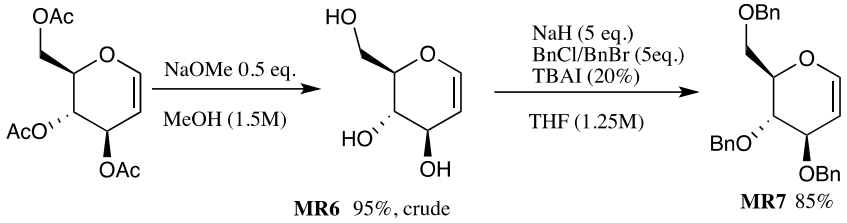


Table 4: A depiction of conditions experimentally determined to be unsuccessful for the Stille coupling reaction of tri-methyl(tri-*O*-benzyl-D-glucopyranosyl)stannane with 3-iodotoluene.

Catalyst	**Reagent**	**Conditions**	**Electrophile**	**Results**
$Pd(PPh_3)_4$ 5%	CuI (0.1eq.), CsF (2eq.), DMF 2ml (0.1M)	Reflux under N_2, 100^0 C, O/N	3-iodotoluene	No Product
$Pd(PPh_3)_4$ 10%	CuI (1eq.), CsF (excess), DMF 2ml (0.1M)	Reflux under N_2, 100^0 C, O/N	3-iodotoluene	No Product
CuCN (8%)	THF	Pressure tube anh., O/N	3-iodotoluene	No Product

Scheme 5: The synthesis of tri-*O*-benzyl-D-glucal from commercial sources of tri-*O*-acetyl-D-glucal



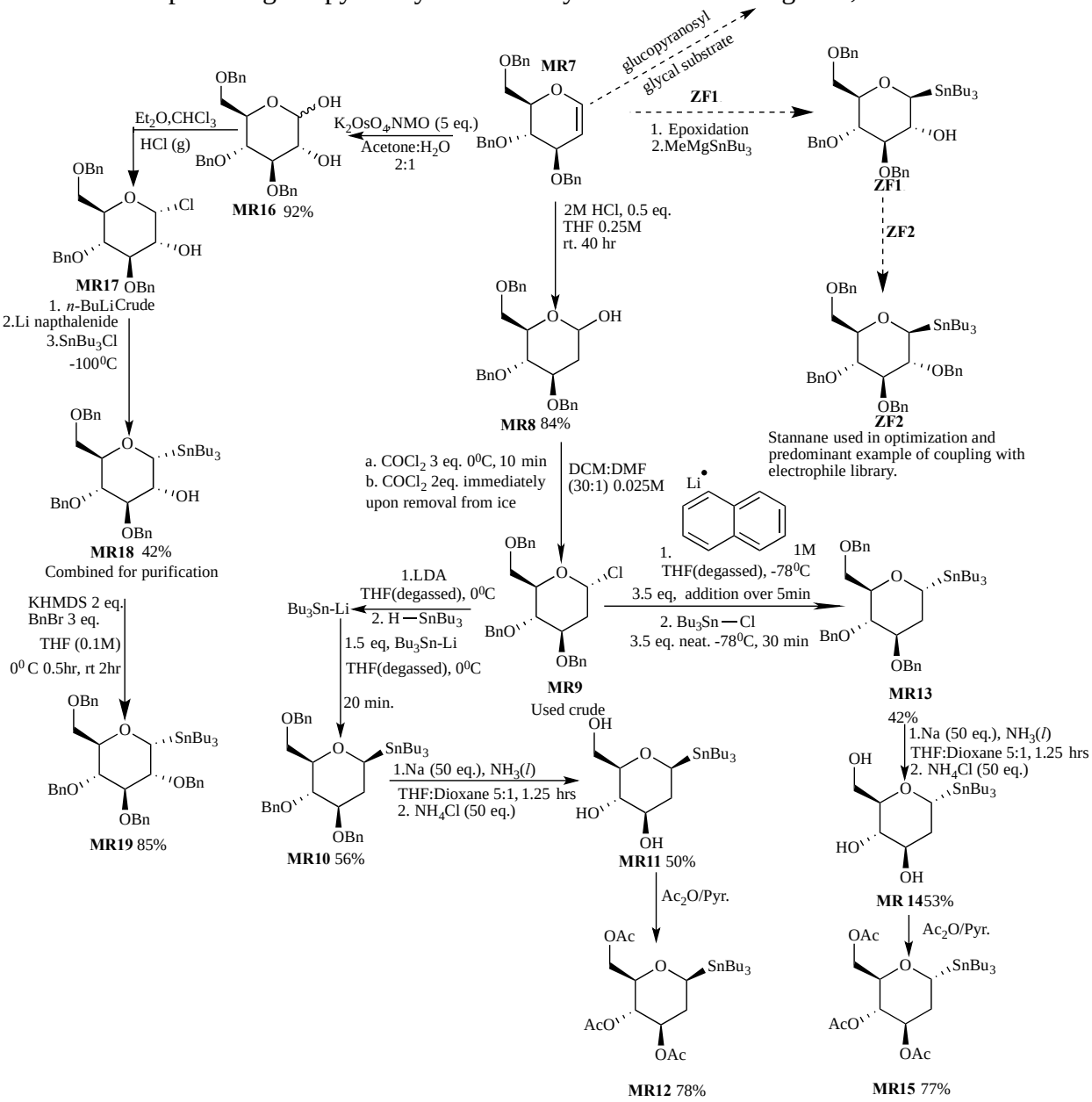
The pursuit of D-glucopyranosyl stanannes began with the glycal building block **MR7.** Scale up of de-acetylation followed by benzylation of D-glucal proved to be seamless as the same number of equivalents of each reactant was utilized on scales reaching 100 g of **MR7**. On a small scale, the reaction was purified at the second step of D-glucal and decreased the final product yield by 7%, and thus determined to be inefficient and was not applied to large scale synthesis. The

reaction proceeds at room temperature and is sensitive to temperatures above 60 ^{0}C, a discovery made by returning to a reaction flask over a hot plate that was unknowingly turned on.

The epoxidation of tri-*O*-benzyl-glucal **MR7** and subsequent opening via $LiSnBu_3$ established a synthetic route to tri-*n*-butyl(3,4,6-tri-*O*-benzyl-β-D-glucopyranosyl)stannane **ZF1** that produced an unsatisfactory yield of 8%. Dr. Zhu optimized the final step in the synthesis by using an alternative $MeMgSnBu_3$, which is a sensitive reagent that requires precise execution of anhydrous/degassed techniques in preparation and utilization. Thus, the yields for other group members using this reagent were miniscule. This led Dr. Zhu to perform the last step of epoxide opening via $MeMgSnBu_3$ across a broad range of carbohydrates. Utilizing **ZF1** modifications at C2 allowed for screening of coupling reaction conditions that allowed the reactions to proceed with retention of configuration.

ZF1 and **ZF2** were utilized in the optimization of the reaction and required the production of large amounts of tri-*O*-benzyl-D-glucal **MR7**, over 1 Kg. The financially viable product that is available commercially is tri-*O*-acetyl-D-glucal. This was de-acetylated followed by benzylation. The scale up of this reaction coincided with the pace of the project as this molecule was the substrate material for the glucopyranosyl C1 nucleophiles exhibited in the project.[(15)]

Scheme 6: Scope of D-glucopyranosylstannanes synthesized from D-glucal, **MR7.** (5)

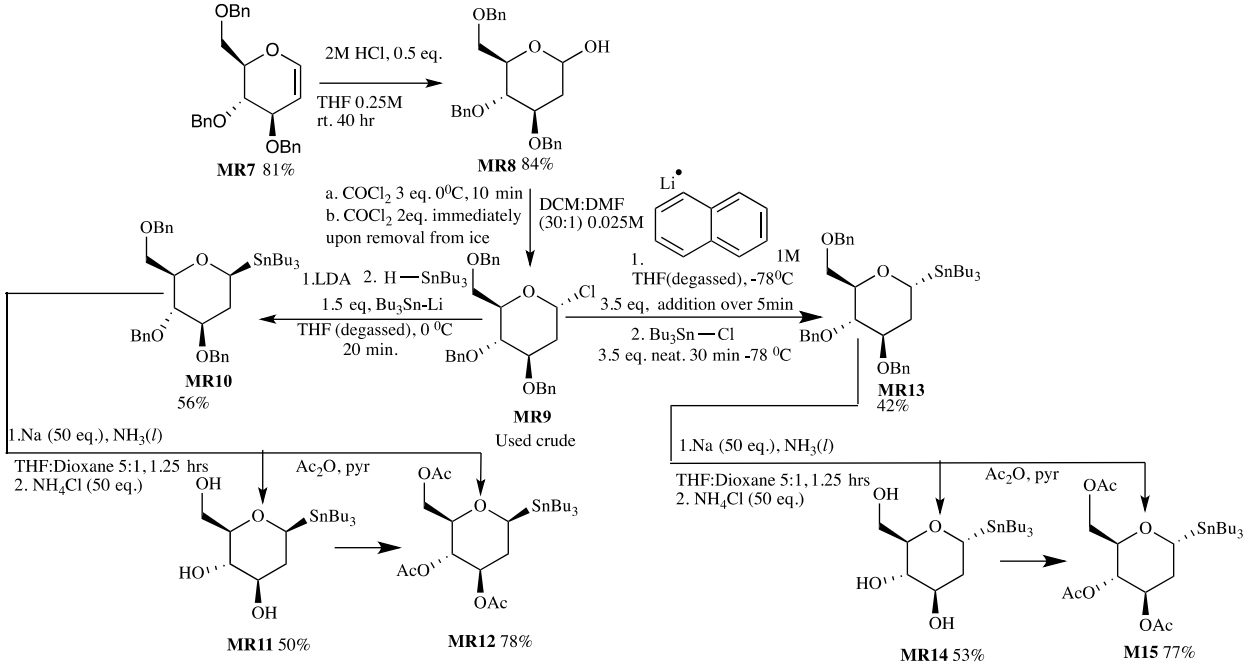


Synthesis of Tri-*n*-butyl-(2-deoxy-D-glucopyranosyl)stannanes

Tri-*O*-benzyl-D-Glucal **MR7** afforded a synthetic route to several glycosylstannanes that were modified to provide 8 examples of nucleophilic stannylated carbohydrates for the coupling

reaction. The first course of action was executing the synthesis of 3,4,6-tri-*O*-benzyl-2-deoxy-α-D-glucopyranosyl chloride.[16] This crude anomeric chloride was utilized to form the α or β 2-deoxy stannanes using the published protocol of Lesimple et al. [17] This article introduced our group to another approach of forming stannane nucleophiles,"tributylstanannyllithium in oxolane", (oxolane is tetrahydrofuran). This was made by subjecting tributyltin hydride to LDA, producing a nucleophilic tin reagent that directly displace the chloride, inverting the configuration to produce **MR10** tri-*n*-butyl-(3,4,6-tri-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)stannane.[18] Reactions in pursuit of the β-stannane were run using tributyltin hydride with *n*-BuLi with no desired product. The α-glucopyranosyl performs a halide lithium exchange, retaining its anion axially due to configuration stability at reduced temperatures, forming an organolithium reagent, that then produces a nucleophile to displace the chloride from tributyltin chloride, forming **MR13** tri-*n*-butyl-(3,4,6-tri-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)stannane. [19]

Scheme 7: Synthetic scheme from the anomeric chloride **MR9** to products: tri-*n*-butyl-(3,4,6-tri-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)stannane **MR10** and its anomer tri-*n*-butyl-(3,4,6-tri-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)stannane **MR13**, followed by the subsequent de-benzylation to produce **MR11/MR14**, and acylation to produce **MR12/MR15.**



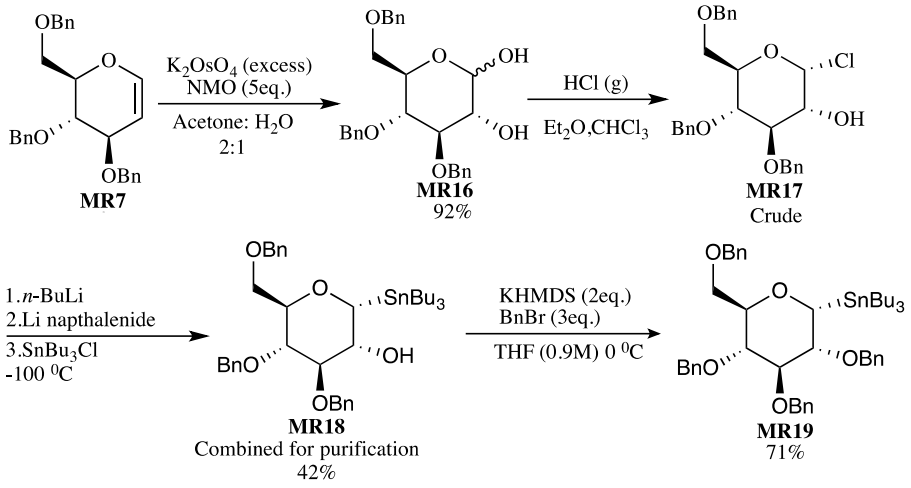
These molecules were then reduced via Birch reduction to remove the three benzyl groups to provide trihydroxyl sugars: tri-*n*-butyl-(2-deoxy-β-D-glucopyranosyl)stannane **MR11** and its anomer tri-*n*-butyl-(2-deoxy-α-D-glucopyranosyl)stannane **MR14**. After characterization, the molecules underwent an acylation procedure to produce tri-*n*-butyl-(3,4,6-tri-*O*-acetyl-2-deoxy-β-D-arabino-hexopyranosyl)stannane **MR12** and tributyl-(3,4,6-tri-*O*-acetyl-2-deoxy-α-D-arabino-hexopyronsyl)stannane **MR15.**

Synthesis of tri-*n*-butyl(tetra/tri-*O*-benzyl-α-D-glucopyranosyl)stannanes

The majority of coupling reactions were run based on a tri-*n*-butyl(tri-*O*-benzyl-β-D-glucopyranosyl)stannane model and the synthesis of the corresponding α-D-glucopyranosyl was important as the contrasting anomer of our model system, supporting the complete retention of configuration for both anomers. Modification of the tri-*O*-benzyl-D-glucal **MR7** was converted

via K_2OsO_4 to produce the diol **MR16.** This was dissolved in $Et_2O/CHCl_3$ followed by the bubbling of HCl at 0 ^{0}C, then sealed in a reaction flask with activated molecular sieves, and allowed to proceed in a cold room. It is important to note that ethanol is a stabilizer for chloroform that diminishes with several washes with water; the washed $CHCl_3$ was exposed to a drying agent, preventing side reactions with $EtOH/H_2O$. This mechanism may proceed by the formation of complimentary Lewis acid/base pair reagents; at C1, a resonance stabilized carbocation forms after the protonated hydroxyl leaves as water and is removed by the sieves. The reaction proceeds by a chlorine anion attacking the C1 carbocation forming the bond observed in **MR17.**

Scheme 8: The synthetic route to tri-*n*-butyl(tri-*O*-benzyl-α-D-glucopyranosyl)stannane **MR18,** and tri-*n*-butyl(tetra-*O*-benzyl-α-D-glucopyranosyl)stannane **MR19.**

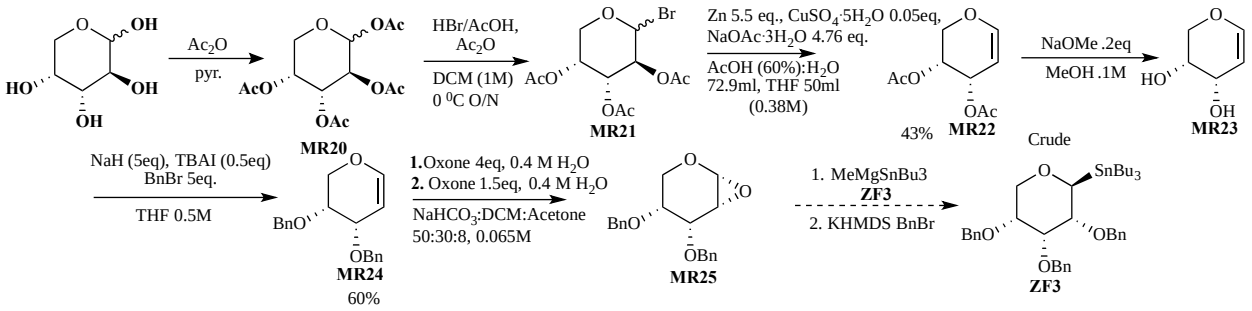


The formation of the α-stannane from the chloride is a temperamental reaction run at -100 ^{0}C, proceeding by a halide lithium exchange and requires *n*-BuLi to remove the proton from the C2-hydroxyl. This reaction was required to run on a relatively small scale (0.5 mmol); thus the reactions were run in parallel and combined for work up prior to benzylation of the C2 hydroxyl to form **MR19**.

Tri-*n*-butyl(2,3,4-Tri-*O*-benzyl-D-arabino-hexapyranosyl)stannane synthesis (MR25/ZF3)

The glycosylstannane of arabinose expands our nucleophilic monosaccharide library. This saccharide upon coupling, could allow for the characterization of synthetic products that provide comparative examples for naturally occurring flavonoid glycosides collected in the laboratory, as investigators report difficulties in the differentiation of xylose and arabinose by UV-vis spectra.[20] The bromonation of synthesized tetra-*O*-acetyl-D-arabinal formed **MR21,** and was subjected to a Zn/$CuSO_4$ reduction, forming di-*O*-acetyl-D-arabinal **MR22**. The production of a glycal, a C1-C2 double bond formation, is a recurring theme through the methodology, offering several routes to variable glycosylstannes and consequentially synthesis of C-aryl glycosides. After de-acylation the product **MR23** was subjected to benzylation arriving at di-*O*-benzyl-arabinal **MR24.** This was epoxidized and opened by Dr Zhu's ring opening procedure.[5,21]

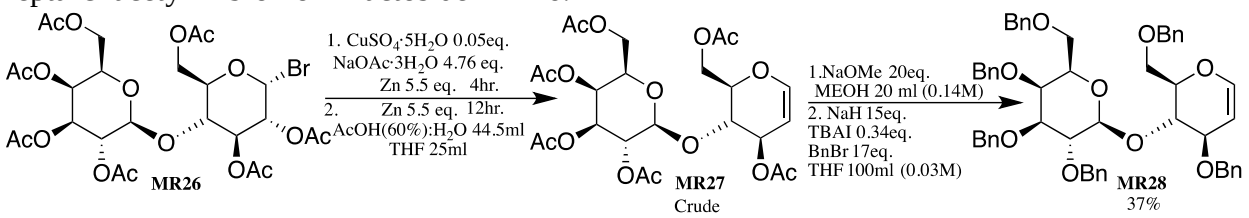
Scheme 9: A synthetic pathway to 3,4-di-*O*-benzyl-D-arabinal **MR24** from the commercially available D-arabinal. This glycal was epoxidized to form **MR25** and opened to form **ZF3.**



Synthesis of hexa-*O*-benzyl-lactal (MR28)

The lactal disacharide example is highlighting the synthetic routes to establish modification of carbohydrates via alkenes adjacent to heterocyclic atoms, glycals, allowing for the selective formation of C1 nucleophilic glycosylstannanes of exceptional anomeric purity.

Scheme 10: The synthetic route to hexa-*O*-benzyl-lactal **MR28** from the commercially available hepta-*O*-acetyl-1-bromo-D-lactoside **MR26**.



Discussion

There are many different configurations of monosaccharides, single carbohydrate subunits. The methodology successfully synthesized a catalog of monosaccharides utilizing an anomeric tributyltin in the Stille coupling reaction. These tin-containing monosaccharides (organostannane) have been proven to be viable nucleophiles for the stille coupling reaction, and were later coupled with an aryl halide compound, in the presence of palladium and a specific ligand. The nucleophiles proceeded in a reaction in which the carbon-carbon bond formation proceeded with retention (>99:1) configuration. The scope of the project includes the variation of two components of our reaction, the organostannane and the aromatic group to which the carbohydrate group will be bound following the successful completion of the reaction. The nucleophilic stannylated carbohydrates utilized in this coupling were the monosaccharides D-glucose, D-galactose, *N*-acetyl-D-glucosamine, and C2-deoxy glucopyranosyls; 2 anomers of each saccharide. The D-arbinose and D-lactose were applied as only **β**-Anomers**.** In this methodology, the coupling partners were aromatic groups that all contained a halide (iodine, bromine or chlorine). The employed aryl-halides included: simple aromatic compounds, heteroaromatics, amino acids/peptides, and other systems of interest. The coupling pairs upon subjection to our catalytic conditions provided a novel route to the formation of sp^3 carbon – sp^2 carbon bonds in the synthesis of *C*-Aryl glycosides. These coupling conditions were optimized for the tributyl(tetra-*O*-benzyl-β-glucopyranosyl)stannane model and were extended to other carbohydrate nucleophiles and

continues to provide a collection of unique glycoconjugates. The products of these reactions have been analyzed using Nuclear Magnetic Resonance spectroscopy (NMR) and mass spectrometry. Upon the analysis of each successful reaction, conditions were optimized for yield and the products fully characterized using ^{1}H NMR, ^{13}C NMR, 2D-NMR, and high resolution mass spectrometry.

Further Investigation

The catalytic method developed through this project provides a viable route to synthesize a broad scope of C-Aryl glycosides that upon characterization can accelerate the integration of glycochemistry into proteomics and genomic libraries, as proteins are currently characterized without determination of their corresponding glycan. Utilizing this methodology requires thorough consideration and investigation into the concentration of alkyl tin in the final products as it could be problematic for human therapeutics. This may require specific removal processes for application in the pharmaceutical industry but offers novel opportunities in biochemistry research, specifically glycan-proteomic characterization as comparative structures can be applied in computational methods to determine glycan arrangement probability. This will open opportunities to comprehensively assess glycan roles in proteomics as we gain understanding of the location of glycans in respect to how a protein interacts with other entities and furthermore how gene expression effects glycan structure, placement, and density. Moving to organo-tin reagents presents toxicity concerns in the application of this technology to life sciences. [(24)]

The stannylated sugars remain configurationally stable while stored at room temperature; this advancement has implications for synthetic approaches to the acquisition of unexplored/synthetically unobtainable natural products. Investigators working with a 3D electrochemical structure of lectins or other structures that selects for, or interacts with, carbohydrates of interest may soon be able to uniquely modify mono, di, tri or oligosaccharides

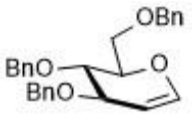
through simple, widely applicable catalytic methodologies. These types of reactions will allow for an extremely large number of coupling pairs, creating molecular libraries that will provide an assessment of a molecule's value to science, society, and prosperity.

With a growing interest in glycochemistry, the near future may allow investigators, biotech industries, and pharmaceutical companies to utilize carbohydrate chains/webs or monosaccharides that only require a proprietary catalyst, ligands, electrophile or nucleophile, solvent kit, and glovebox for assembly. The goal through these advancements is offering a technology with an ability to access the C-N, C-O and C-C bonds utilizing nontoxic reagents.

Supporting Information

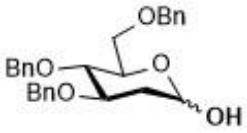
Materials

All chemicals were purchased as reagent grade and used without further purification, unless otherwise noted. Solvents were filtered through a column of activated alumina prior to use. All reactions were carried out under dry N_2 in oven-dried glassware. *m*-Xylene was distilled under nitrogen over sodium and degassed prior to use. Anhydrous 1,4-dioxane, $Pd_2(dba)_3$, **L1-6** and CuCl were purchased from Sigma-Aldrich. Anhydrous KF was purchased from Strem Chemicals, Inc. Aromatic substrates were purchased from Sigma-Aldrich, TCI, Acros Organic, Oakwood Products Inc., AK Scientific, CHEM-IMPEX INT'L INC. CD_3OH, CD_3CN, $CDCl_3$ was purchased from Cambridge Isotope Laboratories and used as received. TLC analyses were performed on Merck TLC plates and visualizations were performed with UV light and/or Hanessian stain and/or sulfuric acid stain (5% H_2SO_4 in MeOH). Column chromatography was performed on silica gel (230-400 mesh). ^1H and ^{13}C NMR spectra were recorded on Bruker/Varian 300/400/500 MHz instruments and are reported as follows: chemical shift (δ), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants (Hz), and integration. The residual solvent reference peaks were used from published literature. 2D-NMR experiments were performed using standard parameters (*200 and More NMR Experiments*, S. Berger, S. Braun, Wiley-VCH, **2004**). IR measurements were performed on Agilent Cary 630 FT/IR instrument and optical rotations were measured on JASCO P- 1030 and are reported as the average of five data points.[5]



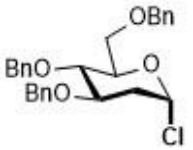
MR7

3,4,6-tri-*O*-benzyl-D-glucal (MR7) [15]. To a solution of tri-*O*-acetyl-D-glucal (25.0 g, 91.7 mmol) in MeOH (175 mL), sodium methoxide (4.30 g, 79.6 mmol) was added and the reaction mixture was stirred 12 h at rt under a nitrogen atmosphere. The reaction mixture was passed through a plaque of silica and concentrated to give a crude oil (15.5 g). Under a nitrogen atmosphere, the crude material was dissolved in anh. THF (150 mL). Tetra-*n*-butylammonium iodide (7.53 g, 20.4 mmol) and NaH (20.0 g, 500 mmol, 60% dispersion in mineral oil) were added and the reaction mixture was allowed to stir at rt for 30 min. The reaction mixture was cooled to 0°C, benzyl bromide (52.3 g, 306 mmol) was added, and the mixture was stirred at rt for 18 h. The reaction mixture was then quenched with MeOH, concentrated, and purified by chromatography on SiO_2 (Hexanes/EtOAc, 1:0 then 10:1) to afford tri-*O*-benzyl-D-glucal **MR7** (33.0 g, 86%) as a white solid. A cautionary consideration as the scale up of this reaction proceeds is the excess NaH increases and can become highly exothermic upon quenching with MeOH. 1H NMR (400 MHz, CDCl3) δ 7.25 – 7.16 (m, 15H), 6.35 (dd, J = 6.1, 1.1 Hz, 1H), 4.80 (dd, J = 6.2, 2.7 Hz, 1H), 4.76 (d, J = 11.3 Hz, 1H), 4.56 (d, J = 11.3 Hz, 1H), 4.55 (d, J = 11.8 Hz, 1H), 4.54 – 4.45 (m, 3H), 4.16 – 4.12 (m, 1H), 3.99 (ddd, J = 8.2, 5.0, 2.9 Hz, 1H), 3.79 (dd, J = 8.7, 6.2 Hz, 1H), 3.74 (dd, J = 10.7, 5.0 Hz, 1H), 3.69 (dd, J = 10.7, 2.9 Hz, 1H).



MR8

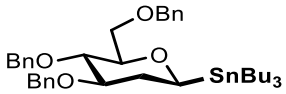
3,4,6-tri-*O*-benzyl-2-deoxy-D-glucopyranose (MR8). To a solution of tri-*O*-benzyl-D-glucal **MR7** (5.00 g, 12.0 mmol) in THF (50 mL), a solution of HCl (3.0 mL, 2.0 M in water) was added and stirred at rt for 40 h. The reaction mixture was quenched with Et_3N (0.85 mL, 6 mmol) followed by toluene (20 mL). The volatiles were removed *in vacuo* and the residue was purified by chromatography on SiO_2 (Hexanes/EtOAc, 5:1) to afford **MR8** (4.40 g, 84%) as a white powder. δ_H(400 MHz, $CDCl_3$) 1.95–2.03 (1H, m), 2.05–2.12 (1H, m,), 2.17–2.19 (1H, m), 2.73–2.80 (1H, m,), 3.32 (2H, s), 3.43–3.59 (5H, m), 3.67–3.74 (3H, m), 3.97–4.01 (1H, m), 4.12 (1H, d, *J*=3.4 Hz), 4.41 and 4.91 (2H, 2d, *J*=11.2 Hz), 4.58 and 4.86 (2H, 2d), 4.58 and 4.86 (2H, 2d, *J*=12.6 Hz), 4.76–4.81 (9H, m), 5.43 (1H,s), 7.22–7.41 (30H, m) [(25)].



MR9

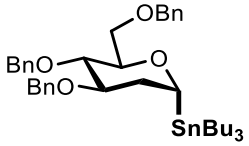
3,4,6-tri-*O*-benzyl-2-deoxy-α-D-arabino-hexopyronsyl chloride (MR9) [16]. To a solution of **MR8** (565 mg, 1.3 mmol) in DCM (22.6 ML), DMF (1 mL) was added followed by stirring at 0° C. To the vented flask, oxalyl chloride (495 mg, 3.9 mmol) was added dropwise and the reaction

mixture was stirred at 0°C for 20 min. Immediately following removal from the ice bath, oxalyl chloride (0.334 mL, 2.6 mmol) was added, the reaction mixture was then allowed to stir at rt for 20 min producing a white precipitate. To the reaction mixture toluene (10 mL) was added and the white precipitate filtered off. The volatiles were concentrated, followed by two co-evaporations with toluene, *in vacuo* at 30°C. The contents placed on high vacuum for 45 min and the resulting yellow oil used directly in the synthesis of **MR10**. 1H NMR (500 MHz, CDCl3): δ 7.24-7.13 (m, 15H), 6.21 (d, J = 3.1 Hz, 1H), 4.79 (d, J = 10.9 Hz, 1H), 4.54 (dd, J = 11.6, 3.3 Hz, 2H), 4.49 (d, J = 11.0 Hz, 1H), 4.43 (d, J = 11.9 Hz, 1H), 4.37 (d, J = 11.9 Hz, 1H), 4.02 (ddd, J = 11.0, 9.1, 4.6 Hz, 1H), 3.94 (dd, BnO O BnO OBn OH Ph Ph Cl Cl BnO O BnO OBn Cl TTBP, CD2Cl 2 S-8 J = 8.2, 1.8 Hz, 1H), 3.96 (dd, J = 7.1, 3.9 Hz, 1H), 3.58-3.54 (m, 2H), 2.43 (dd, J = 8.9, 4.8 Hz), 1.96-1.91 (m, 1H).



MR10

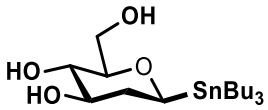
Tributyl-(3,4,6-tri-*O*-benzyl-2-deoxy-β-D-arabino-hexopyranosyl)stannane (MR10) [17]. To a dry flask under a nitrogen atmosphere, anh./degassed THF (10 mL) and distilled $(i\text{-}Pr)_2NH$ (0.800 mL, 5.7 mmol) was added, cooled to 0°C, followed by the dropwise addition of *n*-BuLi (3.125mL, 5 mmol), the reaction mixture were allowed to stir at 0°C for 5 min. Then tributyltin hydride (1.32mL, 1.45g, 5 mmol) was added and the raction was left to stir at 0°C for 20 min producing a tributyltin lithium reagent. To a dry flask under a nitrogen atmosphere, containing a stirring solution of the crude chloride **MR9** (2.6 mmol) in anh./degassed THF (10 mL), the stannane reagent (11.89 mL, 3.9 mmol) was added at 0°C over 20 min. The reaction was left to stir at 0° for 1.5 hr, followed by quenching with Et_2O/H_2O (50 mL, 3:2) then extracted three times with Et_2O, organic layers dried over $MgSO_4$ and the volatiles concentrated *in vacou*. The resultant residue was purified by chromatography on SiO_2 (Hexanes/EtOAc, 1:0, 10:1) to afford the **MR4** (1.04 g, 56%) as a clear oil. $[\alpha]_D^{26}$ = -9.08 (c = 1.00, $CHCl_3$); IR (ATR) ν = 2851, 1746, 1452, 1358, 1095, 875, 730, 694, 595 cm^{-1}; ^1H NMR (400 MHz, CD_3Cl) δ 7.39 - 7.29 (m, 15H), 4.90 (d, *J* = 10.8 Hz, 1H), 4.67 (d, *J* = 12.0 Hz, 2H), 4.62 (d, *J* = 11.2 Hz, 2H), 4.54 (d, *J* = 12.3 Hz, 1H), 3.71 - 3.67 (m, 2H), 3.62 (dd, *J* = 13.3, 1.8 Hz, 1H), 3.58 – 3.50 (m, 1H), 3.47 (t, *J* = 9.0 Hz, 1H), 3.26 - 3.16 (m, 1H), 2.12 (ddd, *J* = 13.1, 5.0, 2.0 Hz, 1H), 1.89 - 1.75 (m, 1H), 1.58 - 1.39 (m, 6H), 1.37 - 1.05 (m, 6H), 1.02 - 0.71 (m, 15H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.0 (2), 138.89, 128.5 (2), 128.4, 128.2, 127.8, 127.7, 127.7, 127.6, 127.4, 83.2, 83.0, 79.3, 75.3, 73.5, 71.7, 70.8, 70.1, 37.1, 29.2, 27.6, 13.9, 8.7; FT-HRMS (ESI) calcd for $C_{39}H_{56}O_4SnNa$ $[M + Na]^+$: 731.3093, found 731.3102



MR13

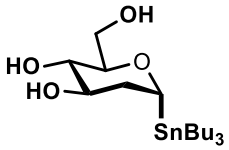
Tributyl-(3,4,6-tri-*O*-benzyl-2-deoxy-α-D-arabino-hexopyronsyl)stannane (MR13) [17].To a flask containing the crude chloride **MR9** (1.30 mmol), anh./degassed THF (11mL) was added

under a nitrogen atmosphere followed by stirring at -78°C. Then, freshly prepared 1M lithium naphthalenide (4.55mL, 4.55 mmol) was added dropwise over 5 min, followed immediately by tributyltin chloride (1.23 mL, 4.55 mmol), and the reaction mixture was allowed to stir at -78°C for 30 min. The reaction mixture was then quenched with Et_2O/H_2O (25 mL, 3:2), extracted three times with Et_2O, organic layers dried over $MgSO_4$ and the volatiles concentrated *in vacuo*. The residue was purified by chromatography on SiO_2 (Hexanes/EtOAc, 1:0 then 5:1) to afford **MR13** (370 mg, 42%) as a colorless oil: $[\alpha]_D^{25} = +77.83$ (c = 0.083, $CHCl_3$); IR (ATR) ν = 3029, 2920, 2858, 2359, 1453, 1359, 1201, 1086, 1016, 907, 731, 694, 594 cm^{-1};^{1}H NMR (400 MHz, CD_3Cl) δ 7.43 - 7.24 (m, 15H), 4.97 (d, *J* = 11.1 Hz, 1H), 4.75 (d, *J* = 11.9 Hz, 1H),4.68(d, J=11.89 Hz, 1H , 4.66 (d, *J* = 12.3 Hz, 2H), 4.60 (d, *J* = 11.1 Hz, 1H), 4.57 (t, *J* = 4.16 Hz, 1H), 4.54 (d, *J* = 12.2 Hz, 1H), 3.78 (dd, *J* = 10.4, 4.2 Hz, 1H), 3.71 (dd, *J* = 10.3, 2.2 Hz, 1H), 3.66 - 3.57 (m, 1H), 3.58 (t, *J* = 8.5 Hz, 1H) 3.22 (dt, *J* = 6.9, 2.1 Hz, 1H), 2.24 (dd, *J* = 7.0, 3.8 Hz, 2H), 1.57 - 1.45 (m, 6H), 1.39 - 1.29 (m, 9H), 0.99 - 0.87 (m, 12H); ^{13}C NMR (101 MHz, CD_3Cl) δ 138.9, 138.7, 138.4, 80.9, 79.3, 78.8, 74.9, 73.6, 72.0, 71.4, 69.5, 36.3, 29.3, 27.6, 13.8, 10.1; FT-HRMS (ESI) calcd for $C_{39}H_{56}O_4SnNa$ $[M + Na]^+$: 731.3093, found 731.3109.



MR11

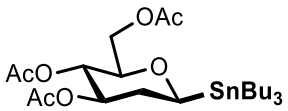
Tri-*n*-butyl-(2-deoxy-β-D-glucopyranosyl)stannane (**MR11**). Freshly cut sodium (0.547 g, 23.8 mmol) was added to liquid NH3 (ca. 40 mL) at -78 oC followed by a solution of **MR10** (0.209 g, 0.295 mmol) in anhydrous dioxane (2 mL). This dark blue reaction mixture was stirred under reflux (-34 oC) for 2 h, was cooled to -78 °C and solid NH4Cl was added portionwise until the blue color disappeared. The resulting suspension was allowed to warm up to rt, the residue was washed with EtOAc (3x), filtered, and concentrated. Purification by column chromatography on SiO2 (CH2Cl2 then CH2Cl2:EtOAc, 1:1) afforded **MR11** (64.0 mg, 50%) as a colorless oil:$[\alpha]_D^{24}$ = -9.2 (c = 0.65, $CHCl_3$); IR (ATR): 3354, 2920, 2867, 1459, 1375, 1251, 1200, 1048, 870, 658, 593 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.00 (br, 1H), 3.76 (m, 3H), 3.56 (m, 1H), 3.51 (br, 1H), 3.38 (t, *J* = 9.0 Hz, 1H), 3.08 (dt, *J* = 9.3, 3.9 Hz, 1H), 2.42 (br, 1H), 2.01 (ddd, *J* = 13.1, 5.0, 2.0 Hz, 1H), 1.81 (td, *J* = 13.3, 10.8 Hz, 1H), 1.49 (m, 6H), 1.37 – 1.23 (m, 6H), 0.89 (m, 15H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 82.2, 74.6, 73.4, 71.2, 63.0, 38.9, 29.2, 38.9, 63.0, 71.2, 73.4, 74.6, 82.2; HRMS (ESI) calculated for $C_{18}H_{38}O_4Sn$ $[M + Na]^+$ 461.16834 found 461.1681.



MR14

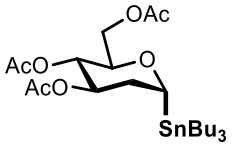
Tri-*n*-butyl-(2-deoxy-α-D-glucopyranosyl)stannane (MR14). Freshly cut sodium (0.580 g, 25.2 mmol) was added to liquid NH3 (ca. 40 mL) at -78 oC followed by a solution of **MR13** (0.203 g, 0.287 mmol) in anhydrous dioxane (2 mL). This dark blue reaction mixture was stirred under reflux (-34 oC) for 2 h, was cooled to -78 °C and solid NH4Cl was added portionwise until the blue color disappeared. The resulting suspension was allowed to warm up to rt, the residue was

washed with EtOAc (3x), filtered, and concentrated. Purification by column chromatography on SiO2 (CH2Cl2 then CH2Cl2:EtOAc, 1:1) afforded **MR14** (66.0 mg,
53%) as a colorless oil:$[\alpha]_D^{25}$ = +36.6 (c = 0.50, $CHCl_3$); IR (ATR): 3354, 2920, 2857, 1459, 1375, 1251, 1200, 1048, 870, 658, 593, 503 cm^{-1}; ^1H NMR (500 MHz, CD_3CN) δ 4.47 (dd, *J* = 4.4, 3.4 Hz, 1H), 3.68 (ddd, *J* = 11.6, 6.2, 3.1 Hz, 1H), 3.56 (dt, *J* = 11.5, 5.7 Hz, 1H), 3.40 (qd, *J* = 8.4, 3.8 Hz, 1H), 3.30 (d, *J* = 4.4 Hz, 1H), 3.17 (d, *J* = 4.3 Hz, 1H), 3.08 (td, *J* = 8.9, 4.0 Hz, 1H), 2.90 (ddd, *J* = 9.0, 5.5, 3.1 Hz, 1H), 2.65 (t, *J* = 6.2 Hz, 1H), 2.01 - 1.96 (m, 2H), 1.59 - 1.44 (m, 6H), 1.39 - 1.25 (m, 7H), 0.99 - 0.91 (m, 6H), 0.89 (t, *J* = 7.3 Hz, 9H); ^{13}C NMR (101 MHz, CD_3CN) δ 81.5, 74.2, 73.7, 73.1, 63.4, 39.5, 29.8, 28.2, 13.9, 10.7; HRMS (ESI) calculated for $C_{18}H_{38}O_4Sn$ $[M + Na]^+$ 461.1684, found 461.1686.



MR12

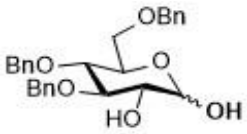
Tributyl-(3,4,6-tri-*O*-acetyl-2-deoxy-β-D-arabino-hexopyranosyl)stannane (MR12)[17]. To a flask containing **(MR11)** (100 mg), pyridine (5.00 mL) was added followed by Ac_2O (1.00 mL) and DMAP (10.0 mg, 0.08 mmol). The reaction mixture was placed under a nitrogen atmosphere and allowed to stir at rt for 12 hr. The reaction mixture was combined with H_2O (50 mL) in a separatory funnel and extracted three times with EtOAc. The organic layer was washed with sat. $CuSO_4$, DI H_2O, then sat. NaCl. The volatiles concentrated *in vacuo* and chromatography on SiO_2 (Hexanes:EtOAC, 10:1 then 5:1) to afford **MR12** (99.0 mg, 77%). Light yellow oil. $[\alpha]_D^{24} = -24.56°$ (c = 1.00, $CHCl_3$); IR (ATR) ν = 2923, 2851, 1743, 1455, 1364, 1225, 1043, 908, 695, 599 cm^{-1}; ^1H NMR (400 MHz, CD_3Cl) δ 4.98 - 4.82 (m, 1H), 4.12 (dd, *J* = 12.0, 5.3 Hz, 1H), 4.04 (d, *J* = 2.4 Hz, 0H), 4.01 (d, *J* = 2.4 Hz, 1H), 3.71 (dd, *J* = 13.3, 1.9 Hz, 1H), 3.38 (ddd, *J* = 9.2, 5.2, 2.3 Hz, 1H), 2.12 (ddd, J = 12.8, 4.9, 2.0 Hz, 1 Hz), 2.02 (d, *J* = 6.2 Hz, 6H), 1.91 (td, *J* = 13.3, 10.2 Hz, 1H), 1.55 - 1.37 (m, 6H), 1.28 (dq, *J* = 14.7, 7.4 Hz, 9H), 1.00 - 0.81 (m, 15H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.0, 170.8, 170.1, 79.2, 74.0, 70.5, 70.1, 63.4, 36.3, 29.1, 27.4, 21.2, 20.9 (2), 13.8, 8.8; FT-HRMS (ESI) calcd for $C_{24}H_{44}O_7SnNa$ $[M + Na]^+$: 587.2001, found 587.2018.



MR15

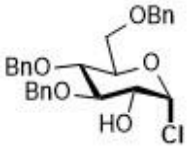
Tributyl-(3,4,6-tri-*O*-acetyl-2-deoxy-α-D-arabino-hexopyronsyl)stannane (MR10) [17].To a flask containing **MR14** (51.0 mg), pyridine (5.00 mL) was added followed by Ac_2O (1.00 mL) and DMAP (10.0 mg, 0.08 mmol). The reaction mixture was placed under a nitrogen atmosphere and allowed to stir at rt for 12 hr. The reaction mixture was combined with H_2O (50 mL) in a separatory funnel and extracted three times with EtOAc. The organic layer was washed with sat. $CuSO_4$, DI H_2O, then sat. NaCl. The volatiles concentrated *in vacuo* and chromatography on SiO_2 (Hexanes:EtOAC, 10:1 then 5:1) to afford **MR15** (50.0 mg, 78%).Light yellow oil: $[\alpha]_D^{25}$ = +39.12 (c = 0.38, $CHCl_3$); IR (ATR) ν =3029, 2922, 2859, 2359, 1744, 1453, 1364, 12225, 1053, 909, 732, 695, 598 cm^{-1}; ^1H NMR (300 MHz, CD_3Cl) δ 4.94 - 4.84 (m, 2H), 4.51 (t, *J* = 4.3 Hz, 1H), 4.26 (dd, *J* = 12.1, 5.7 Hz, 1H), 4.03 (dd, *J* = 12.1, 2.4 Hz, 1H), 3.37 (ddd, *J* = 8.8, 5.7, 2.3 Hz,

1H), 2.23 - 2.14 (m, 2H), 2.06 (s, 3H), 2.04 (s, 3H), 2.01 (s, 3H), 1.66 - 1.42 (m, 6H), 1.39 - 1.22 (m, 6H), 1.03 - 0.75 (m, 15H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.9, 170.4, 170.0, 76.3, 72.2, 70.9, 69.6, 62.9, 35.5, 29.2, 27.5, 21.2, 20.9, 20.9, 13.8, 9.9; FT-HRMS (ESI) calcd for $C_{24}H_{44}O_7SnNa$ $[M + Na]^+$: 587.2001, found 587.2003.



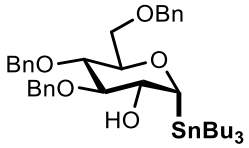
MR16

To a solution of **(MR7)** (6.00 g, 14.4 mmol) in Acetone/H_2O (300 mL, 2:1), K_2OsO_4 (106 mg, 0.144mmol) and 4-methylmorpholine 4-oxide (8.43 g, 72 mmol) was added. The reaction mixture was allowed to stir for 12 hr at rt, then the volatiles were removed *in vacuo.* The residual mixture was extracted three times with EtOAc, the organic layer washed with brine and volatiles removed *in vacuo*, the residue purified with chromatography on SiO_2 (Hexanes:EtOAc, 5:1 the 0:1) to afford (**MR16)** (5.86 g, 90%).1 H NMR (CDCl3, 300 MHz) δ =7.34–7.06 (m), 5.18 (d, J = 4.7 Hz,), 4.85-4.71 (m), 4.55-4.38 (m), 4.03-3.94 (m), 3.74 (t, J = 9.1 Hz), 3.67–3.53 (m), 3.53–3.39 (m,); 13C NMR (CDCl3, 90 MHz): δ =138.6, 138.5, 138.1, 137.9, 137.7, 137,6, 128.4, 128.3, 128.0, 127.9, 127.8, 127.7, 96.7, 92.3, 84.4, 82.5, 77.6, 75.6, 75.3, 75.1, 74.9, 74.8, 73.5, 72.8, 70.4, 68.8.



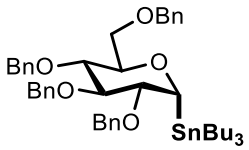
MR17

3,4,6-tri-O-benzyl-2-deoxy-α-D-arabino-hexopyronsyl chloride (MR17) . To a dry flask under a nitrogen atmosphere containing a solution of **(MR16)** in anh. Et_2O/Chloroform (165 mL, 10:1), HCl was bubbled at 0°C for 15 min. The flask was fitted with a glass stopper and the reaction mixture was allowed to stir at 0°C for 48 hr. The reaction mixture was placed under light vacuum to remove HCl via aspiration, before volatiles removed *in vacuo* to afford crude (**MR17)** (2.402 g) as a yellow solid.



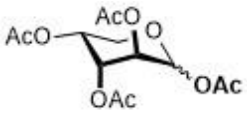
MR18

(3,4,6-Tri-O-benzyl-α-D-glucopyranosyl)tri-n-butylstannane (MR18). A dry flask under a nitrogen atmosphere containing a solution of **(MR17)** (422 mg, 0.900 mmol) in anh./degassed THF (9 mL), was cooled to -100°C by a MeOH/N_2 bath. To the reaction mixture, n-BuLi (0.771 mL, 1.08 mmol) was added drop-wise followed by the immediate drop-wise addition of a 1M lithium naphthalenide solution (1.98 mL, 1.98 mmol) in anh./degassed THF, the dark red reaction mixture was stirred at -100°C for 15 min. Tri-n-butyltin chloride was added and the resulting light yellow reaction mixture was stirred at -100°C for 1 hr. The reaction mixture was then allowed to reach room temperature over 1 hr before quenching with H_2O (10 mL). The resulting mixture was extracted three times with DCM, the organic layer dried over $NaSO_4$, and the volatiles removed *in vacuo*. The resultant residue purified by chromatography on SiO_2 (Hexanes/EtOAc, 1:0 then 10:1, then 5:1) to afford **MR18** (313 mg, 48%): $[\alpha]_D^{26}$ = +59.84 (c = 1.00, $CHCl_3$); IR (ATR) ν = 3301, 3029, 2919, 2857, 1453, 1357, 1206, 1070, 864, 731, 694, 596 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.37 - 7.19 (m, 15H), 4.85 (d, *J* = 11.6 Hz, 1H), 4.75 (d, *J* = 11.1 Hz, 1H), 4.67 (d, *J* = 11.7 Hz, 1H), 4.61 (d, *J* = 12.0 Hz, 1H),4.57 (*J* = 8.31, 2.4 Hz, 1H), 4.51 (d, *J* = 12.1 Hz, 1H), 3.95 (ddd, *J* = 7.3, 6.0, 4.5 Hz, 1H), 3.78 (dd, *J* = 10.4, 4.5 Hz, 1H), 3.68 (dd, *J* = 10.4, 2.9 Hz, 1H), 3.62 (t, *J* = 7.7 Hz, 1H), 3.43 (t, *J* = 7.7 Hz, 1H), 3.37 (ddd, *J* = 7.6, 4.4, 2.9 Hz, 1H), 2.47 (d, *J* = 4.5 Hz, 1H), 1.57-1.42 (m, 6H), 1.31 (h, *J* = 7.1 Hz, 6H), 0.90 (q, *J* = 7.6, 7.1 Hz, 25H);^{13}C NMR (75 MHz, $CDCl_3$) δ 138.7, 138.3, 128.8, 128.5 (2), 128.0, 128.0, 127.9, 127.9, 127.9, 127.7, 83.9, 78.3, 77.4, 75.7, 74.6, 74.1, 73.7, 68.8, 29.3, 27.6, 13.9, 10.4; FT-HRMS (ESI) calcd for $C_{39}H_{56}O_5SnNa$ $[M + Na]^+$: 747.3042, found 747.3048.



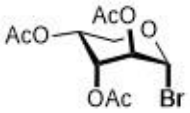
MR19

(2,3,4,6-Tetra-O-benzyl-α-D-glucopyranosyl)tri-n-butylstannane (MR19). A solution of **MR18** (313 mg, 0.432 mmol) in anhydrous THF (5 mL) was cooled to 0 °C, and a 0.5 M solution of KHMDS (1.72 mL, 0.864 mmol) was added. The solution stirred for 0.25 hr at 0 °C before the addition of benzyl bromide (0.154 mL, 1.30 mmol). The resulting solution stirred at 0 °C for 0.5 hr then for 2 hr at rt. After, the reaction is concentrated and directly purified by flash column chromatography (Hexanes/EtOAc, 1:0 then 20:1) to yield **MR19** (299 mg, 85%) as a light yellow oil: $[\alpha]_D^{26}$ = +29.79 (c = 0.43, $CHCl_3$); IR (ATR) ν = 3029, 2920, 2359, 1452, 1357, 1069, 864, 731, 695, 596 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) ^1H NMR δ 7.33-7.21 (m, 18H), 7.13 (dd, *J* = 7.4, 2.2 Hz, 2H), 4.90 (d, *J* = 10.9 Hz, 1H), 4.80 (d, *J* = 9.8 Hz, 2H), 4.69 (d, *J* = 11.7 Hz, 1H), 4.65 (d, *J* = 6.9 Hz, 2H), 4.57 (d, *J* = 12.1 Hz, 1H), 4.50-4.42 (m, 2H), 3.99-3.93 (m, 1H), 3.64 (qd, *J* = 10.4, 2.9 Hz, 2H), 3.58-3.49 (m, 2H), 3.18-3.07 (m, 1H), 1.54-1.37 (m, 6H), 1.31-1.20 (m, 6H), 1.00-0.85 (m, 5H), 0.83 (t, *J* = 7.3 Hz, 10H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.8, 138.6, 138.5, 138.2, 128.5, 128.4, 128.4, 128.4, 128.1, 128.0, 127.9, 127.7, 127.7, 127.7, 86.5, 81.4, 79.3, 78.1, 76.3, 75.6, 75.4, 73.7, 73.6, 69.2, 29.3, 27.7, 13.9, 10.6; FT-HRMS (ESI) calcd for $C_{46}H_{62}O_5SnNa$ $[M + Na]^+$: 837.3511, found 837.3521.



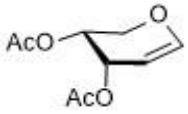
MR20

1,2,3,4-Tetra-*O*-acetyl-D-arabinose (MR20)[13]. To a flask containing a solution of D-arabinose (7.00g, 46.6 mmol) in pyridine (50 mL), Ac_2O (20 mL, 212 mmol) and 4-Dimethylaminopyridine (500 mg, 4.09 mmol) was added. The reaction mixture was allowed to stir for 12 hr at rt before dilution with H_2O (250 mL). The reaction mixture was then extracted three times with EtOAc and the organic layers washed with sat $CuSO_4$, DI H_2O, then brine. The organic layer was dried over $NaSO_4$ and volatiles removed *in vacuo* to afford crude **MR20** (18.2 g).



MR21

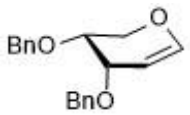
2,3,4-Tri-*O*-acetyl-β-D-arabinopyranosyl bromide (MR21). To a dry flask containing a solution of crude **MR20** (18.2 g, assumed 46.6 mmol from previous reaction) in anh. DCM (46.5 mL), Ac_2O (4.65 mL, 49.2 mmol) and 33% HBr/AcOH (37.3 mL) was added at 0°C. The reaction mixture was then allowed to stir at 0°C for 18 hr. The reaction mixture was then diluted with DCM, H_2O then sat. $NaCO_3H$ at 0°C. The reaction mixture was then extracted three times with EtOAc, the organic layers washed with sat. $NaCO_3H$, sat. NaCl, dried over $NaSO_4$ and the volatiles removed *in vacuo* to afford crude **MR21**; ^{1}H NMR (400 MHz, $CDCl_3$) 1 H NMR δ: 2.03(s, 3H,), 2.11(s, 3H,), 2.15(s, 3H,), 3.94(d, 1H, H-5, J=13.4 Hz), 4.21(d, 1H, H-5′, J=13.4 Hz), 5.09(dd, 1H, H-2, J=10.0, 3.8 Hz), 5.40—5.42(m, 2H, H-3, H-4), 6.70(d, 1H, H-1, J=3.8 Hz)[(26)].



MR22

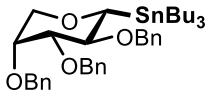
3,4-di-*O*-acetyl-D-arabinal (MR22). To a flask, $CuSO_4$•$5H_2O$ (582 mg, 2.33 mmol), activated Zn (16.8 g, 257 mmol), and NaOAc•$3H_2O$ (30.2 g, 222 mmol) was added. To the mixture, a 60% AcOH:H_2O solution (72.9 mL) was added, and the heterogeneous reaction mixture was stirred at rt for 10 min. Then a solution of crude **MR21** (15.8 g, 46.6 mmol) in THF (50 mL) was added, and the reaction mixture was allowed to stir for 18hr. The reaction mixture was then filtered through celite, and the celite pad washed with EtOAc. To the resultant mixture, H_2O (50 mL) was added, followed by extraction three times with EtOAc. The organic layer was washed with sat. $NaHCO_3$, Di H_2O, sat. NaCl, dried over $NaSO_4$, and the volatiles removed *in vacuo*. The resultant oil was purified by chromatography on SiO_2 (Hexanes/EtOAc, 5:1) to afford D-arabinal **MR22** (4.00g, 43% over 3 steps) as a clear oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.52 (d, 1H, J = 6.0 Hz),

5.46 (t, 1H, *J* = 4.3 Hz), 5.23–5.17 (m, 1H), 4.89–4.84 (m, 1H), 4.07–3.97 (m, 2H), 2.09 (s, 3H), 2.08 (s, 3H). **(26)**



MR23

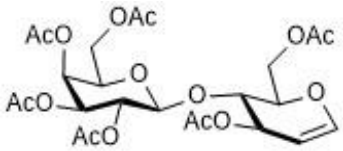
3,4-di-O-benzyl-D-arabinal (MR23) [13]. To a flask containing a solution of **MR22** (2.00 g, 10 mmol) in MeOH (100 mL), NaOMe (108 mg, 2 mmol) was added. The reaction mixture was allowed to stir for 12 hours before the volatiles were removed *in vacuo*. The resultant residue was placed on high vacuum for one hour then placed under a nitrogen atmosphere. To the flask tetra-*n*-butylammonium iodide (1.61 g, 5.00 mmol) and NaH (2.4 g, 50 mmol, 50% dispersion in mineral oil) were added and the reaction mixture was allowed to stir at rt for 30 min. The reaction mixture was cooled to 0°C, benzyl bromide (8.52 g, 5.00 mmol) was added, and the mixture was stirred at rt for 18 h. The reaction mixture was then quenched with MeOH, concentrated, and purified by chromatography on SiO_2 (Hexanes/EtOAc, 1:0 then 10:1) to afford 3,4-di-O-benzyl-D-arabinal **MR23** (1.8 g, 61%) as a clear oil: $[\alpha]_D^{25} = +114.2$ (c = 1.00, $CHCl_3$); IR (ATR) ν = 3029, 2924, 2870, 2360, 1882, 1723, 1640, 1495, 1452, 1355, 1059, 914, 736, 697 cm^{-1}; ^1H NMR (300 MHz,$CDCl_3$) δ 7.51 - 7.22 (m, 10H), 6.42 (d, *J* = 6.0 Hz, 1H), 4.90 (dd, *J* = 6.0, 5.2 Hz, 1H), 4.67 (q, *J* = 12.1 Hz, 4H), 4.12 - 4.00 (m, 3H), 3.77 (dt, *J* = 10.3, 3.9 Hz, 1H); ^{13}C NMR (75 MHz, CDCl3) δ 146.6, 138.8, 138.0, 128.5, 128.4, 127.8, 127.8, 127.7, 127.6, 98.8, 73.2, 71.1, 70.8, 66.7, 63.3.



MR25/ZF3

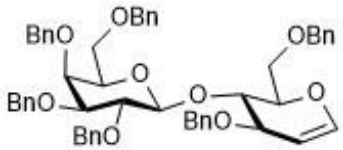
To a solution of 3,4-di-O-benzyl-D-arabinal (500 mg, 1.69 mmol) in a cooled (0 °C), vigorously stirring biphasic solution of DCM (10 mL), satd. aq. $NaHCO_3$ (18 mL), and acetone (1 mL), a solution of Oxone® (4.16 g, 6.76 mmol) in H_2O (18 mL) is added dropwise over 15 min. After the addition, the mixture stirs for 0.5 hr at 0 °C then for 2 hr at rt. The organic phase is then separated, and the aq phase is extracted with DCM (2x 10 mL). The combined organic phases are dried over Na_2SO_3 and concentrated to afford the epoxide as a white solid. The crude epoxide is then dissolved in anhydrous, degassed THF (15 mL) under N_2 and cooled to -20 °C (ice salt bath) for the addition of $MeMgSnBu_3$ (837 mg, 2.53 mmol). The solutions stirs at -20 °C for 2 hr and is then quenched with H_2O (18 mL). The mixture is filtered twice through Celite® and the organic phase is separated. The aqueous phase is extracted with DCM (3x 15 mL), and the combined organic layers are dried over sodium sulfate and concentrated. The crude material was taken directly to the benzylation step and dissolved in anhydrous THF (5 mL) was cooled to 0 °C, and a 0.5 M solution of KHMDS (5.06 mL, 2.53 mmol) was added. The solution stirred for 0.25 hr at 0 °C before the addition of benzyl bromide (0.602 mL, 5.07 mmol). The resulting solution stirred at 0 °C for 0.5 hr then for 2 hr at rt. After, the reaction is concentrated and directly purified by flash column chromatography (Hexanes/EtOAc, 1:0 then 20:1) to yield **ZF3** (340 mg, 29%) as a light yellow oil: $[\alpha]_D^{26}$ = -9.92 (c = 1.00, $CHCl_3$); IR (ATR) ν = 3029, 2921, 2919, 2850, 2359, 1452, 1356, 1088, 864, 731, 694, 594 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.59 - 7.12 (m, 15H), 5.14 (d, *J* =

11.3 Hz, 1H), 4.80 (d, *J* = 12.5 Hz, 1H), 4.75 - 4.63 (m, 3H), 4.58 (d, *J* = 11.7 Hz, 1H), 4.18 - 4.02 (m, 2H), 3.87 (td, *J* = 3.3, 1.6 Hz, 1H), 3.63 (dd, *J* = 8.1, 3.1 Hz, 1H), 3.57 (d, *J* = 9.5 Hz, 1H), 3.24 (dd, *J* = 12.3, 1.6 Hz, 1H), 1.66 - 1.40 (m, 6H), 1.40 - 1.21 (m, 6H), 1.00 - 0.73 (m, 15H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.9, 138.6, 138.3, 128.4, 128.3, 128.2, 128.0, 127.8, 127.6 (2), 127.5, 127.3, 83.7, 78.0, 75.2, 74.1, 73.0, 71.4, 70.8, 69.2, 29.3, 29.1, 29.0, 27.5, 13.7, 9.4; FT-HRMS (ESI) calcd for $C_{38}H_{54}O_4SnNa$ $[M + Na]^+$: 717.2936, found 717.2945.



MR27

Hexa-O-acetyl lactal (MR27)[22]. To a flask, $CuSO_45H_2O$ (35.7 mg, 0.143 mmol), activated Zn (1.03 g, 15.7 mmol), and $NaOAc•3H_2O$ (1.85g, 13.6 mmol) was added. To the mixture, a 60% AcOH:H_2O solution (4.45 mL) was added, and the heterogeneous reaction mixture was stirred at rt for 10 min. Then a solution of bromo-hepta-acetyl-D-lactoside (2.00g, 2.86 mmol) in THF (25 mL) was added. The reaction mixture was allowed to stir and monitored by TLC for 4 hr at rt. Then, a second addition of activated Zn (1.03 g, 15.7 mmol) was added and the reaction mixture was left to stir at rt for 12 hr. The reaction mixture was then filtered through celite, and the celite pad washed with EtOAc. To the resultant mixture, H_2O (30 mL) was added, followed by extraction three times with EtOAc. The organic layer was washed with sat. $NaHCO_3$, Di H_2O, sat. NaCl, dried over $NaSO_4$, and the volatiles removed *in vacuo* to afford crude hexa-O-acetyl lactal **MR27** (1.58 g), as a clear oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.39 (d, 1H, *J* = 6.1 Hz), 5.41–5.36 (m, 1H), 5.34 (d, 1H, *J* = 3.2 Hz), 5.17 (dd, 1H, *J* = 10.4, 8.0 Hz), 4.98 (dd, 1H, *J* = 10.5, 3.4 Hz), 4.82 (dd, 1H, *J* = 6.0, 3.4 Hz), 4.64 (d, 1H, *J* = 8.0 Hz), 4.41 (dd, 1H, *J* = 11.7, 2.4 Hz), 4.20–4.03 (m, 4H), 3.98 (dd, 1H, *J* = 7.3, 5.5 Hz), 3.89 (t, 1H, *J* = 6.8 Hz), 2.13 (s, 3H), 2.09 (s, 3H), 2.06 (s, 3H), 2.04 (s, 3H), 2.03 (s, 3H). [26]

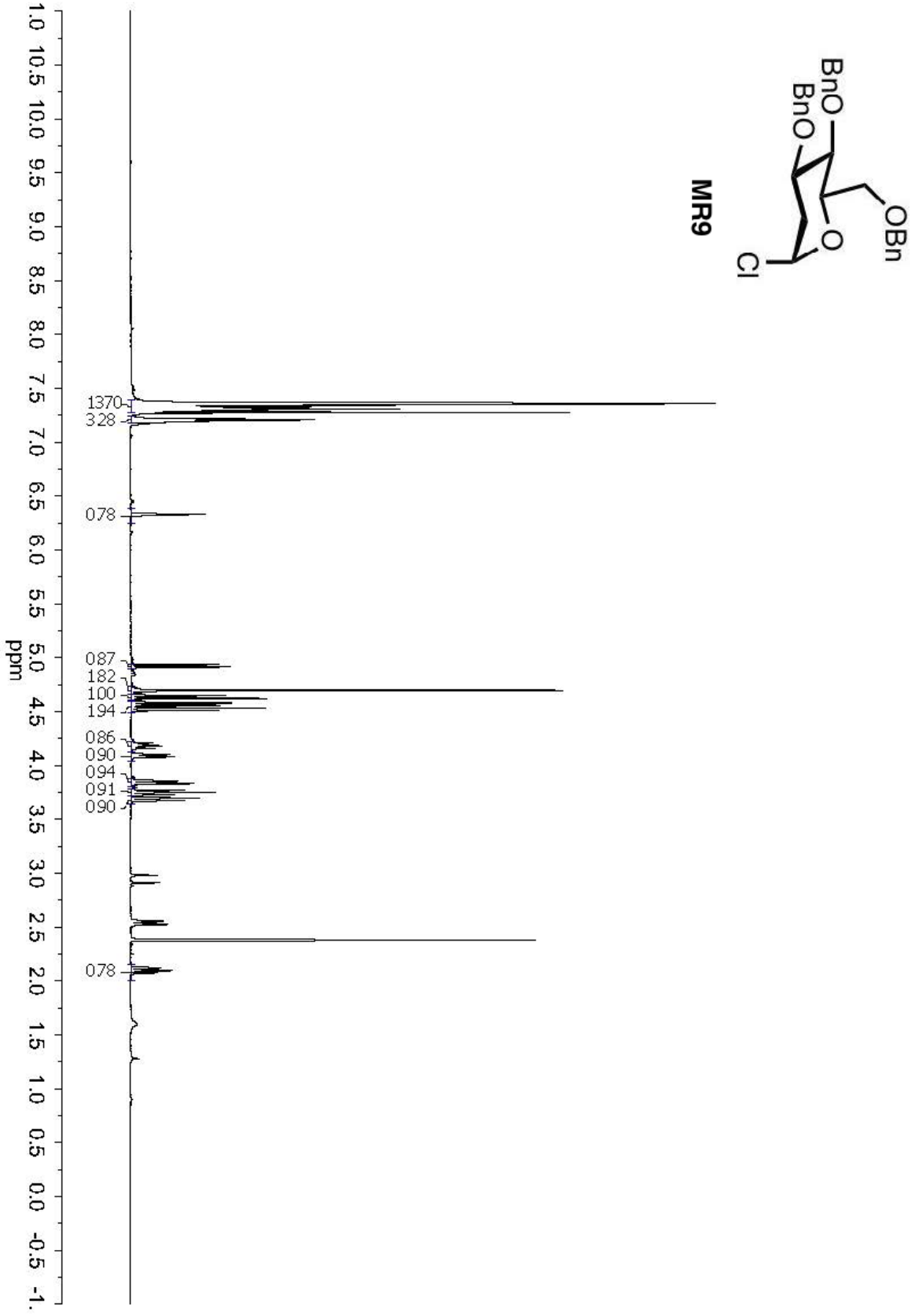


MR28

Hexa-O-Benzyl-lactal (MR28)[22]. The crude oil **MR19** was dissolved in MeOH (20 mL) and NaOMe (152 mg, 2.82 mmol) was added. The reaction mixture was placed under a nitrogen atmosphere and allowed to stir at rt for 18 hours. The volatiles were then removed *in vacuo*, and the resulting opaque solid placed on high vacuum for 1 hr. The flask containing the solid was placed under a nitrogen atmosphere, followed by the addition of anh. THF (100 mL). Then tetra-

n-butylammonium iodide (277 mg, 0.855 mmol) and NaH (1.48 g, 37.1 mmol, 60% dispersion in mineral oil) was added and the contents allowed to stir at rt for 30 min. The contents were then cooled to 0°C, BnBr (5.07 mL, 42.8 mmol) was added and the reaction mixture was stirred at rt for 48 hr. The reaction was quenched with MeOH and the volatiles removed *in vacuo*. The resulting semisolid material was purified with chromatography on SiO_2 (Hexanes/EtOAc, 1:0 then 15:2) to afford **MR28*** (902 mg, 37%) as a clear oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.39–7.27 (m, 30H, Ph), 6.43 (dd, *J*=6.2, 1.1 Hz, 1H, H-1), 4.92 (d, *J*=10.8 Hz, 1H), 4.86 (dd, *J*=6.3, 3.6 Hz, 1H, H-2), 4.82 (d, *J*=11.7 Hz, 1H), 4.71 (d, *J*=9.6 Hz, 1H), 4.70 (brs, 2H), 4.55 (m, 7H), 4.35 (dd, *J*=4.2, 1.0 Hz, 2H), 4.29 (m, 1H), 4.14 (m, 2H), 3.86 (s, 1H), 3.83–3.74 (m, 2H), 3.65 (m, 1H), 3.54–3.41 (m, 5H).[(22)]

*Delivered to Dr. Feng Zhu for epoxide and opening.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BnO
OBn
O
Cl
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078
087
182
100
194
086
090
094
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ppm
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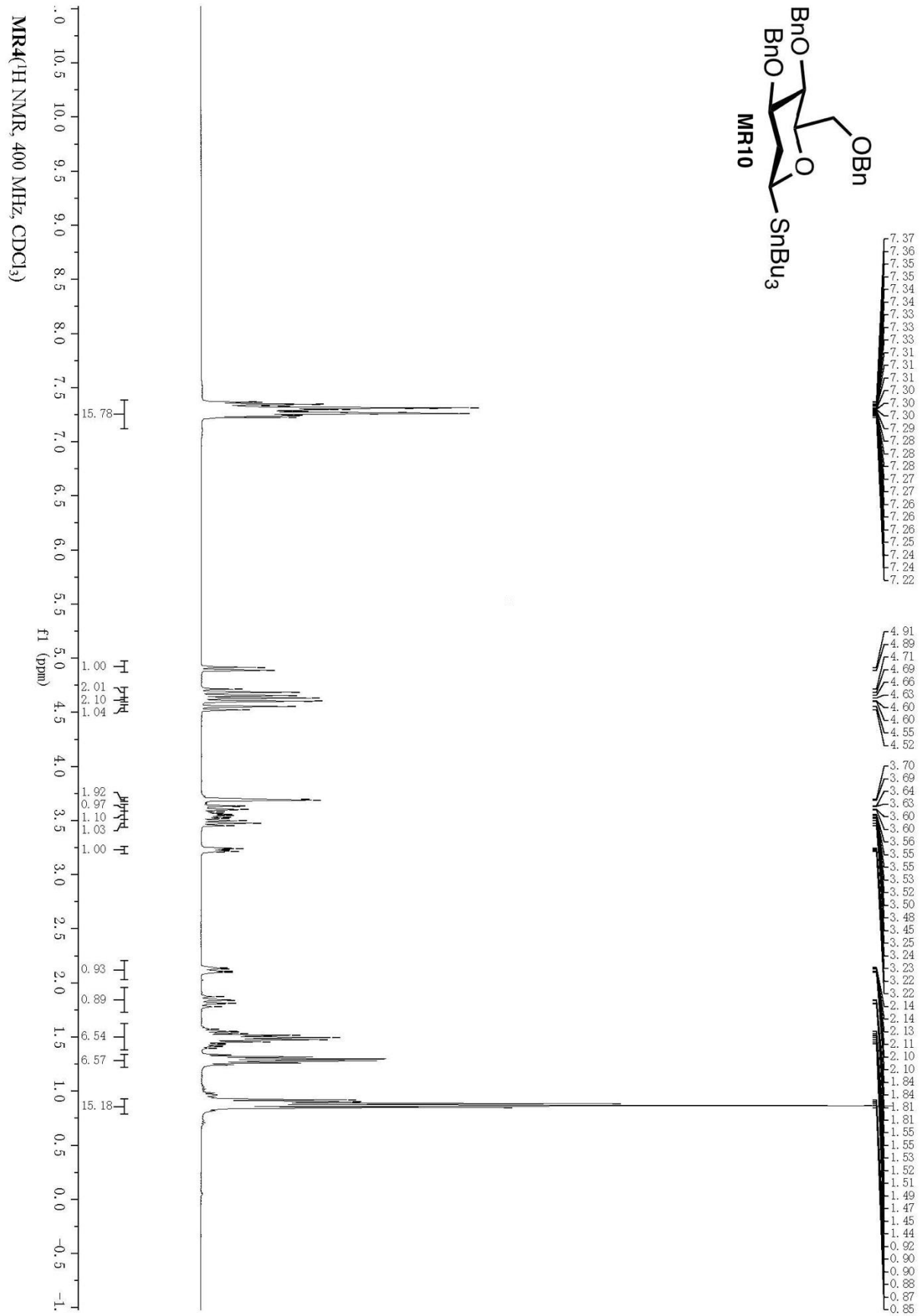
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O
OBn
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2.01
2.10
1.04
1.92
0.97
1.10
1.03
1.00
0.93
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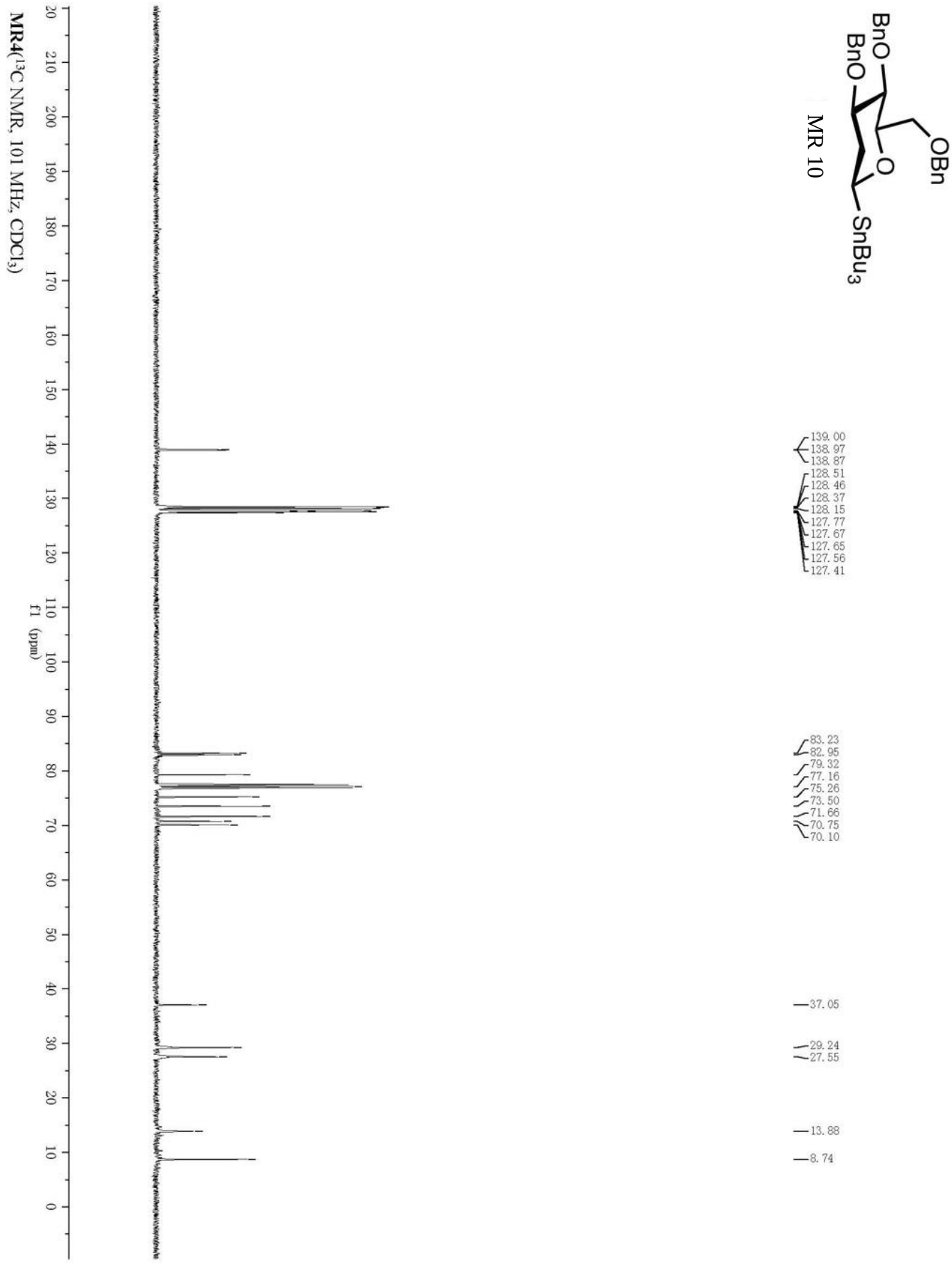
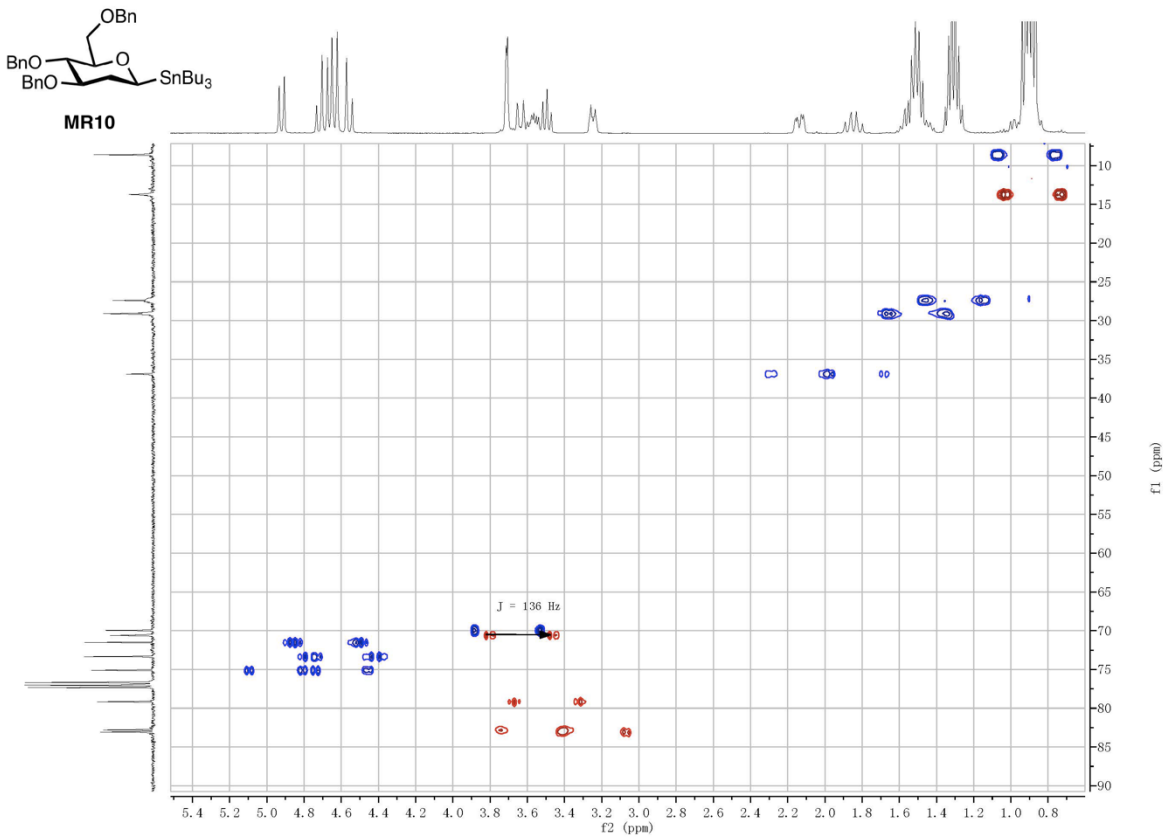
6.57
15.18



MR4(^{13}C NMR, 101 MHz, $CDCl_3$)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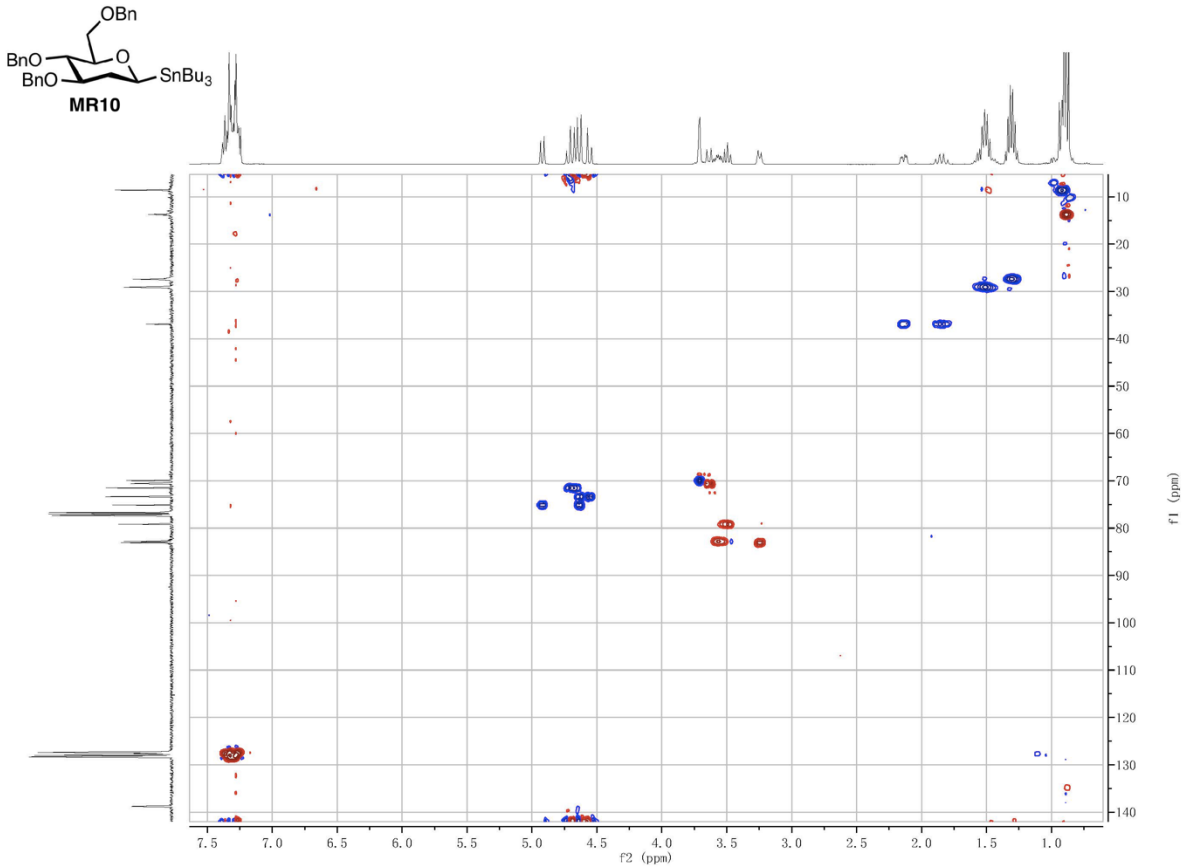
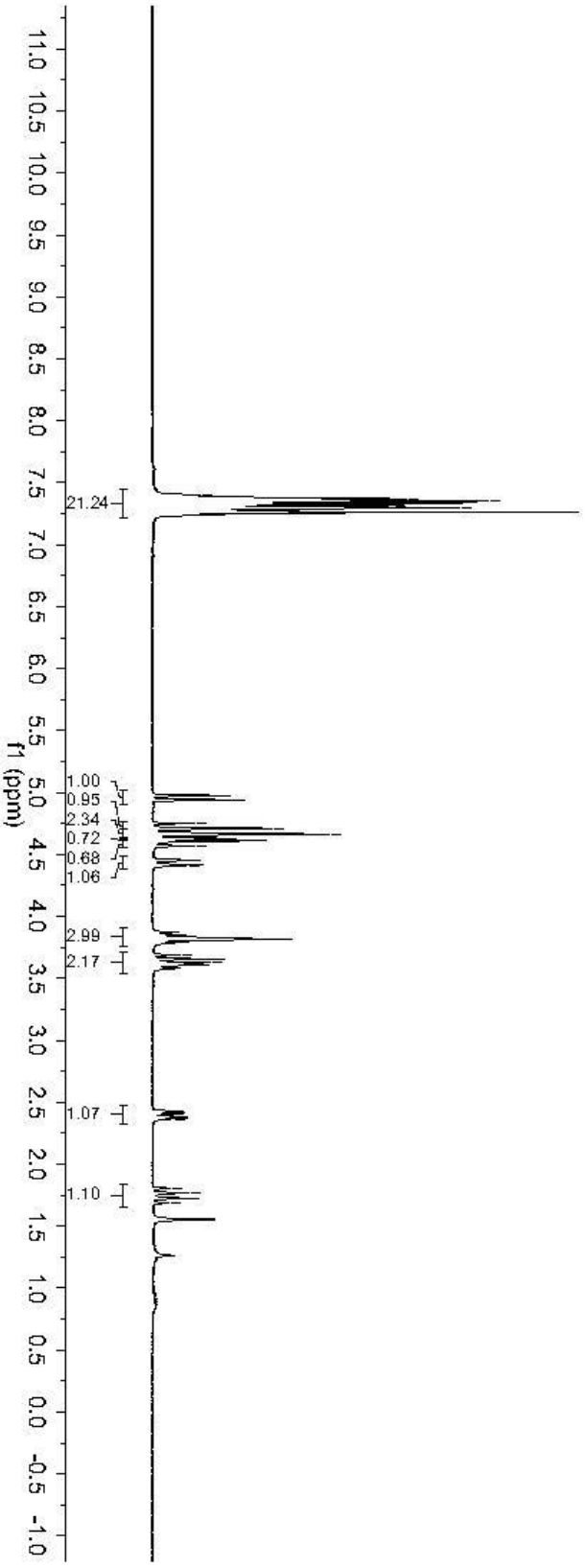
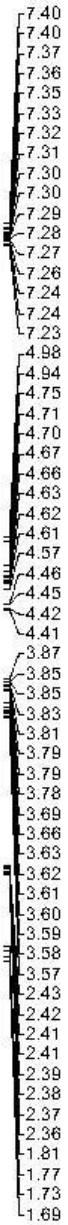
BnO
BnO
O
SnBu3
MR10
J = 136 Hz
f2 (ppm)
f1 (ppm)

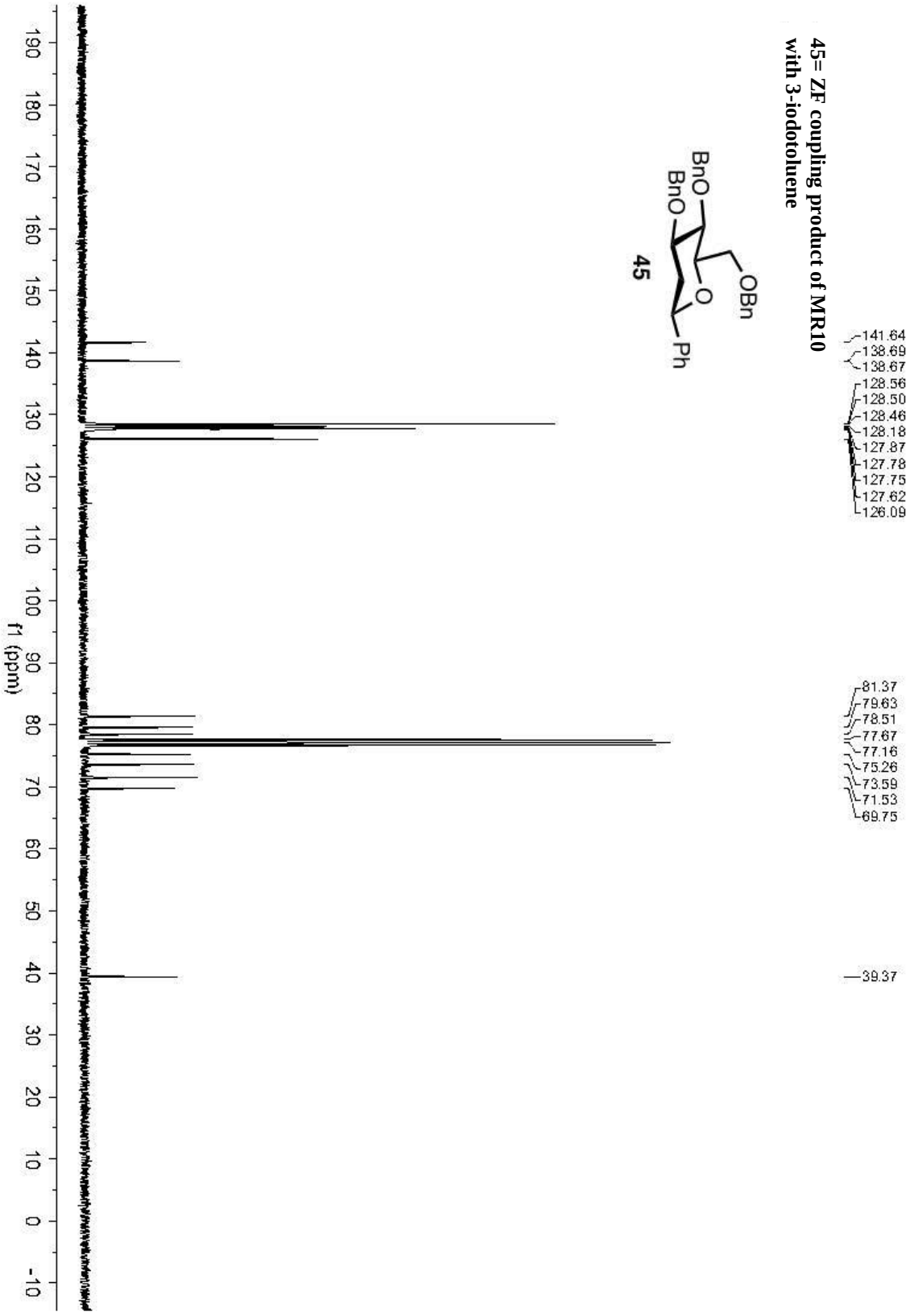

OBn
BnO
BnO
O
SnBu3
MR10
f2 (ppm)
f1 (ppm)



45= ZF coupling product of MR10 with 3-iodotoluene

45




45= ZF coupling product of MR10
with 3-iodotoluene
BnO
BnO
O
OBn
Ph
45
141.64
138.69
138.67
128.56
128.50
128.46
128.18
127.87
127.78
127.75
127.62
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190
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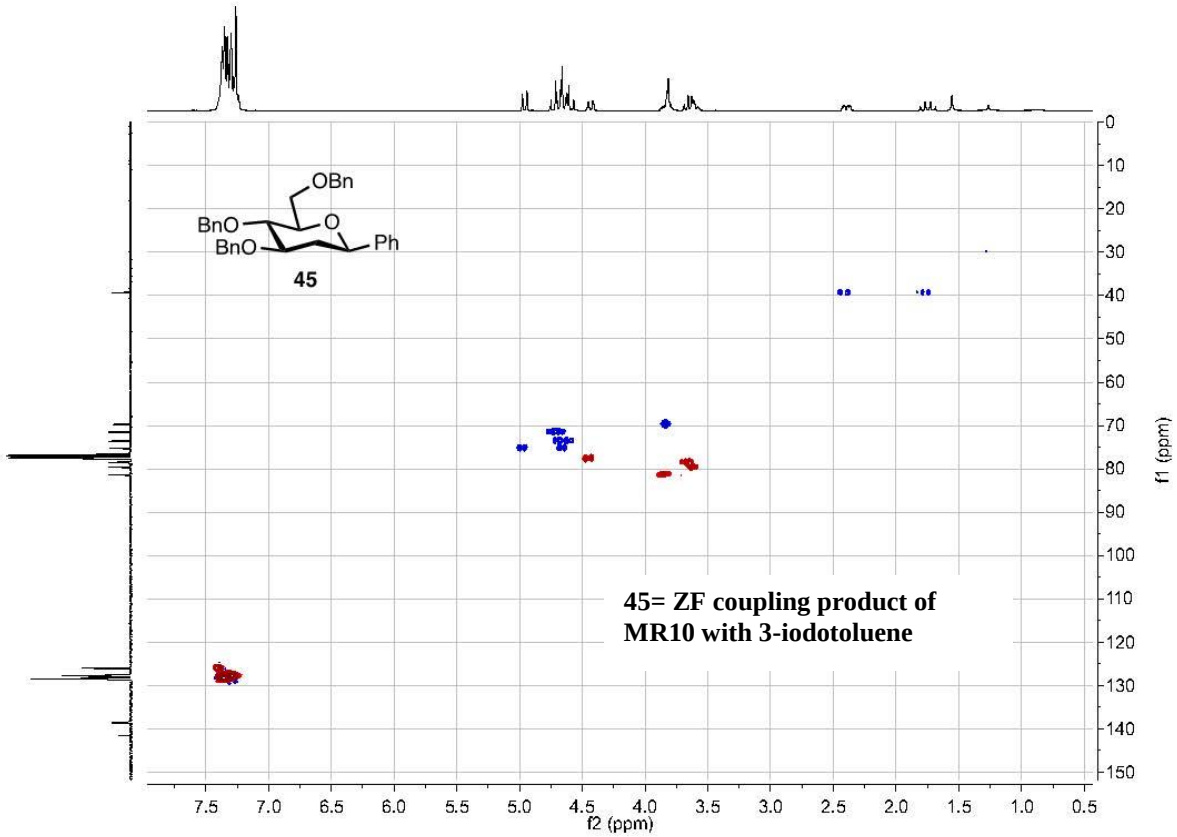
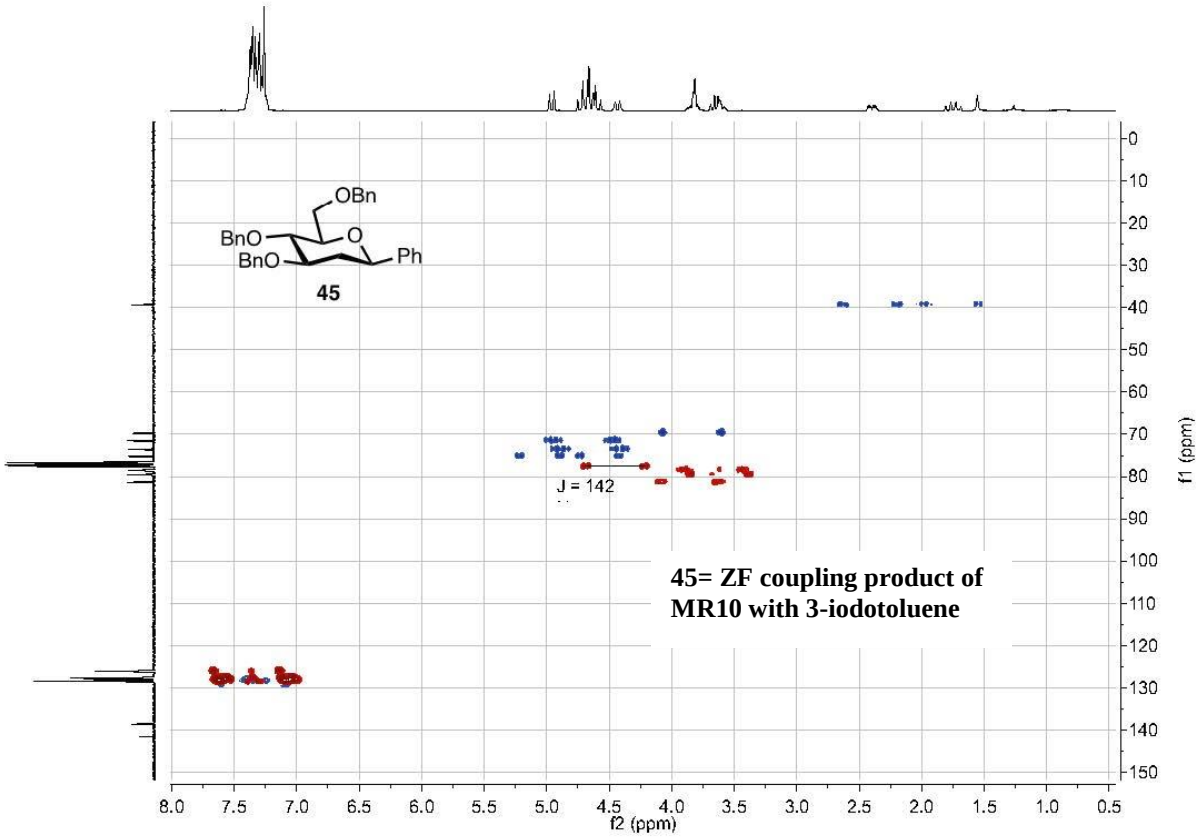
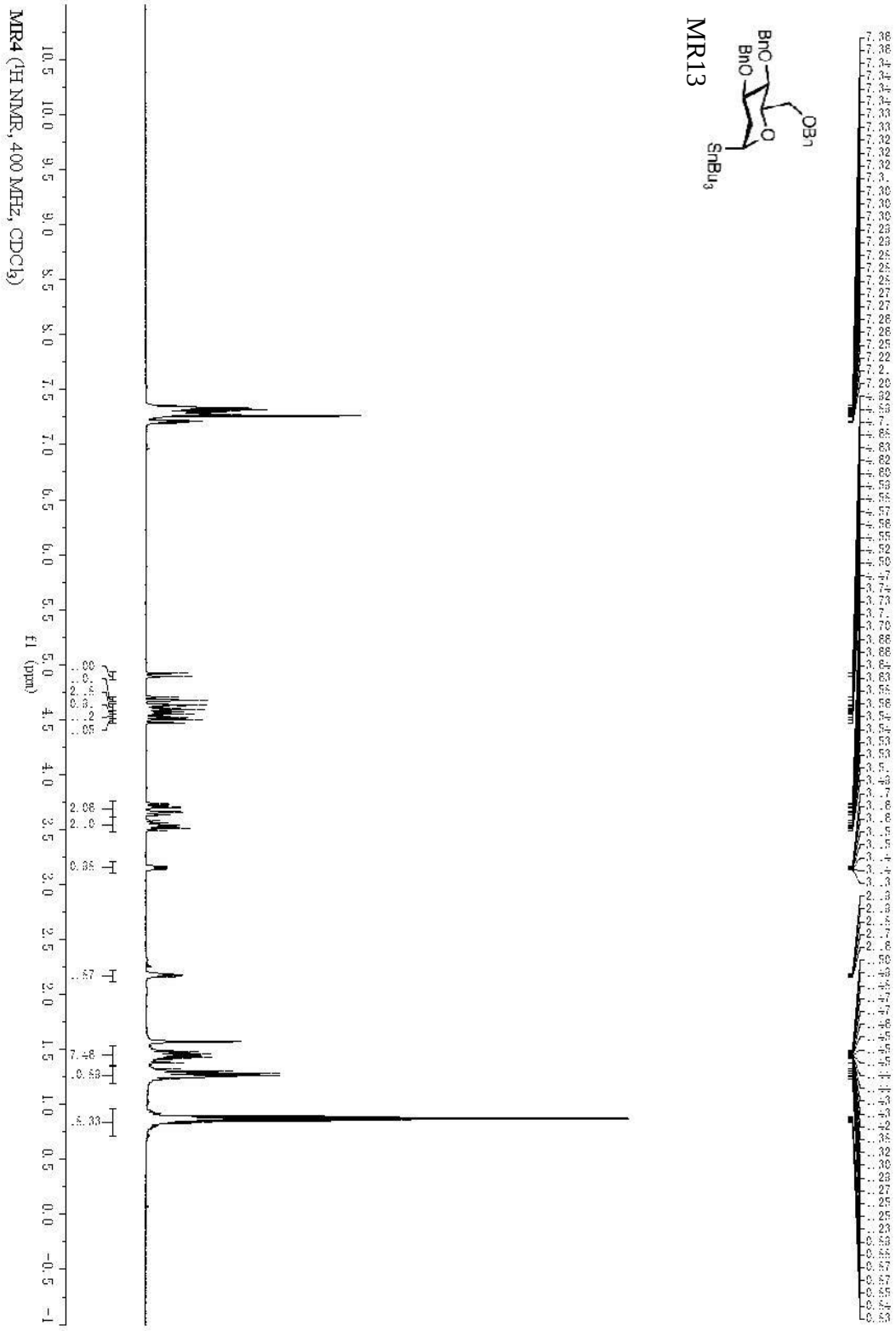
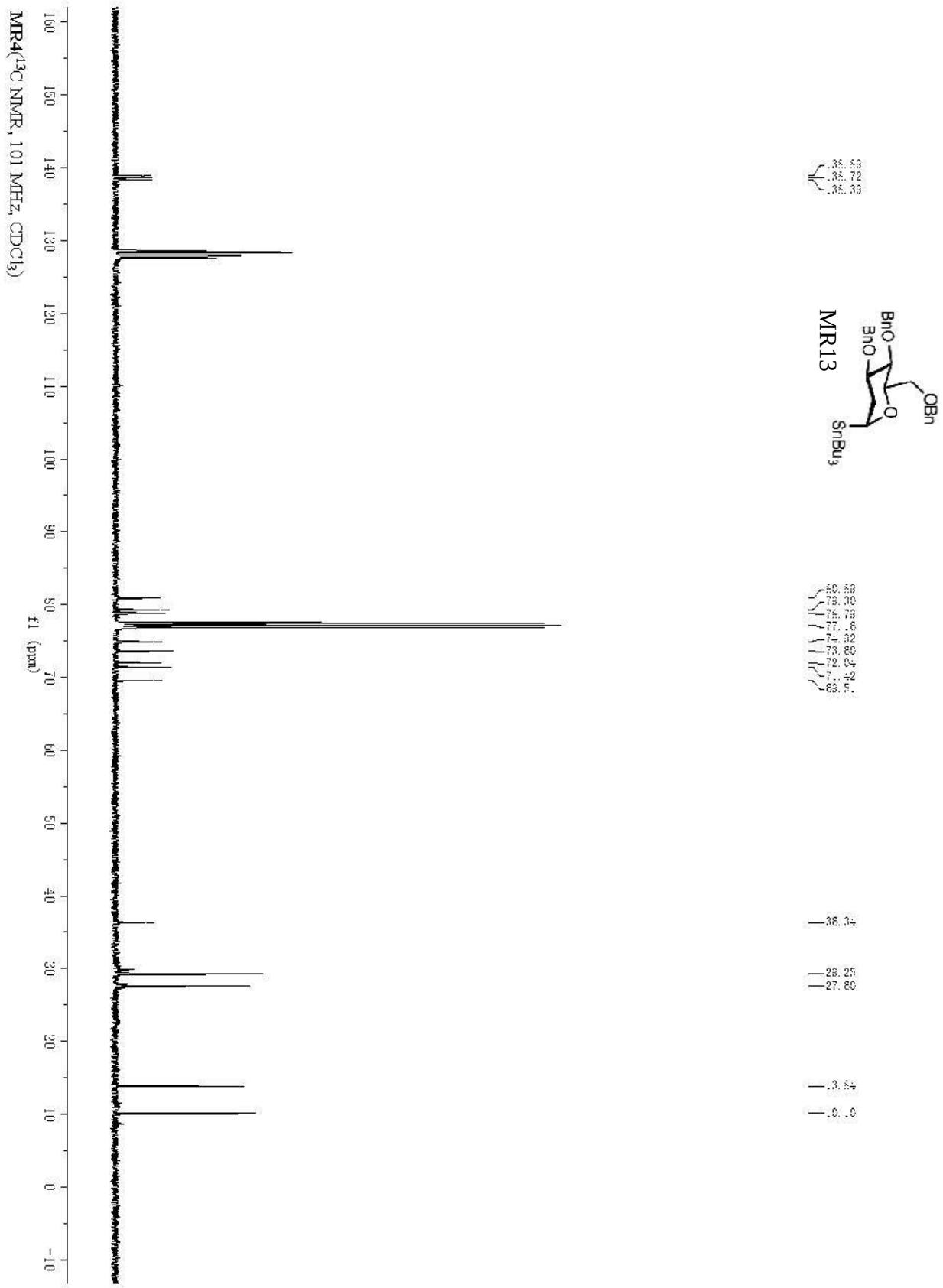
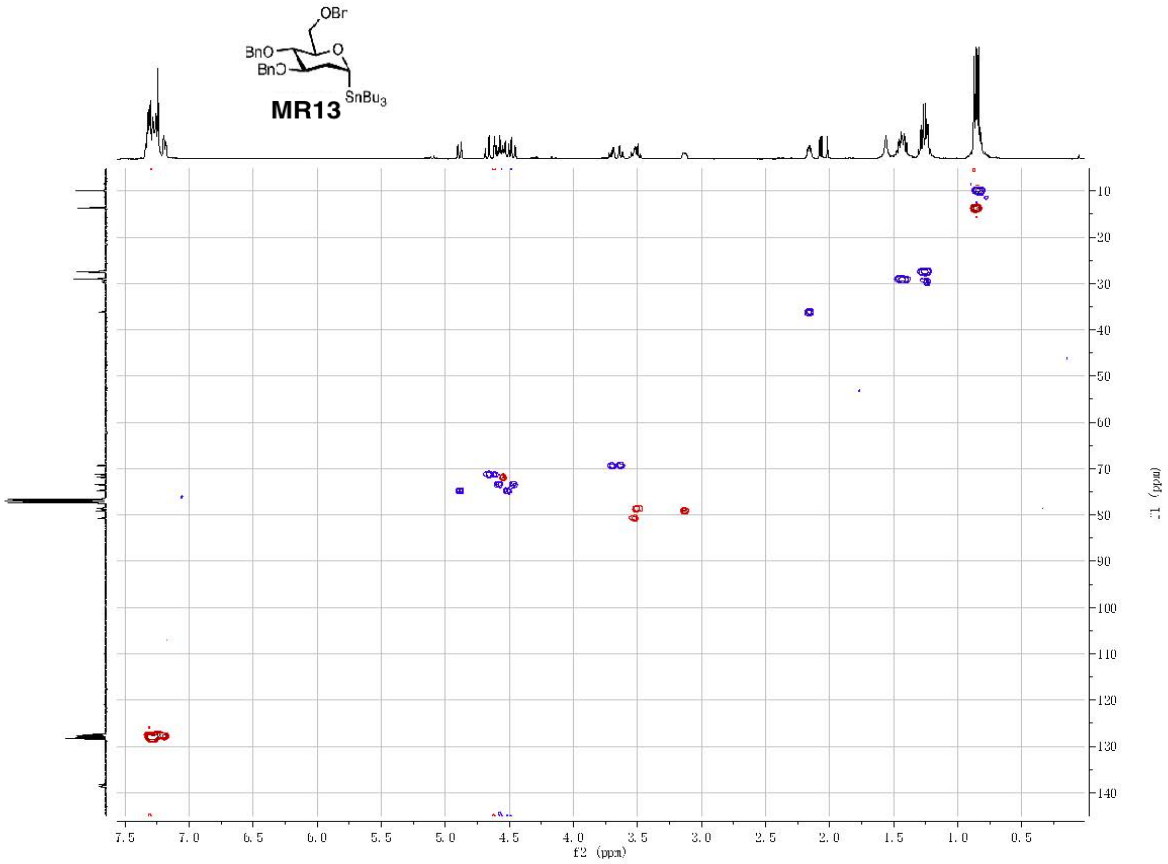
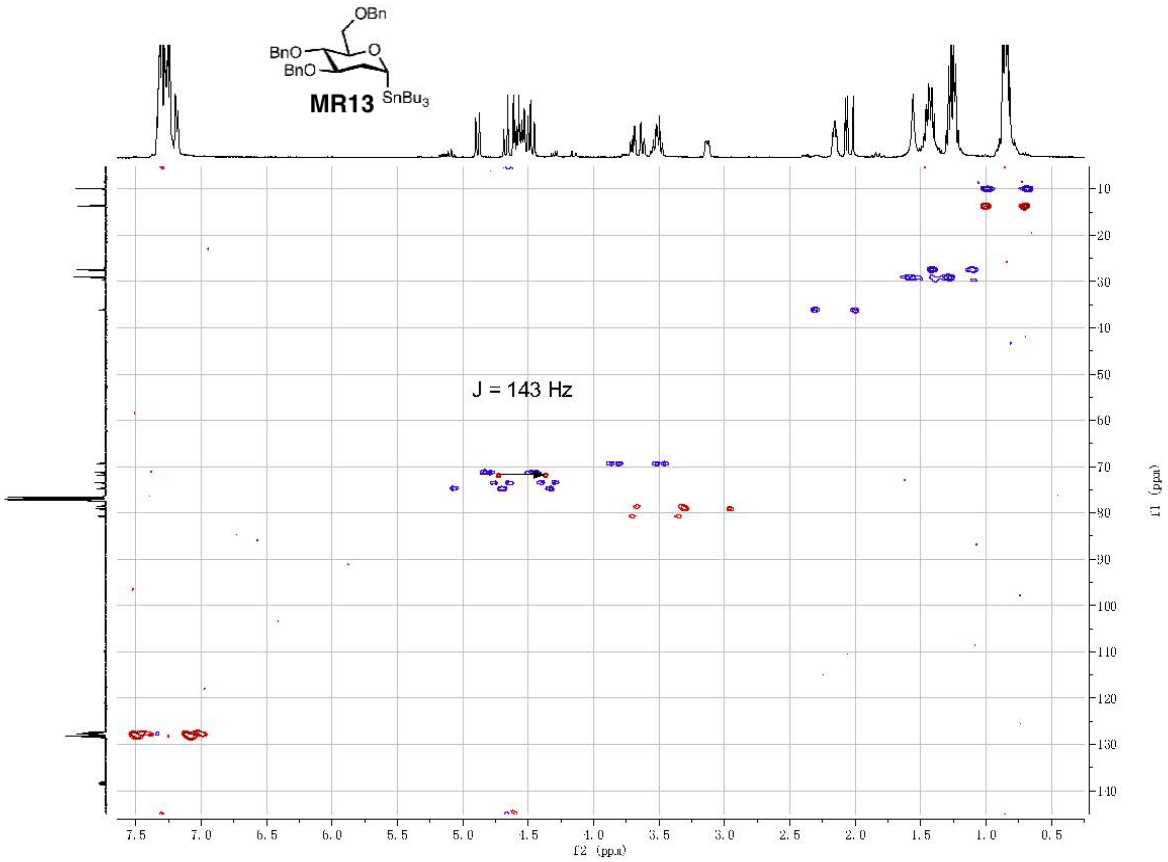

OBn
BnO
BnO
O
Ph
45
45= ZF coupling product of
MR10 with 3-iodotoluene
f2 (ppm)
f1 (ppm)

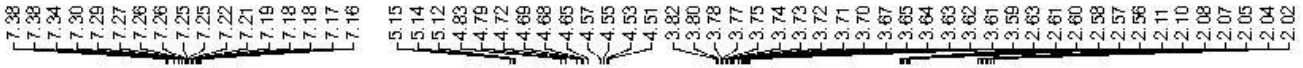

OBn
BnO
O
BnO
Ph
45
J = 142
45= ZF coupling product of
MR10 with 3-iodotoluene
f2 (ppm)
f1 (ppm)

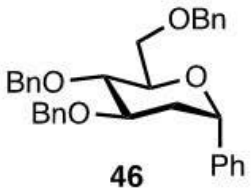

MR4 (1H NMR, 400 MHz, CDCl3)
f1 (ppm)
MR13
BnO
BnO
OBn
O
SnBu3


MR4(13C NMR, 101 MHz, CDCl3)
f1 (ppm)
MR13
BnO
BnO
O
OBn
SnBu3
36.34
28.25
27.69


OBr
BnO
BnO
O
SnBu3
MR13
f2 (ppm)
f1 (ppm)

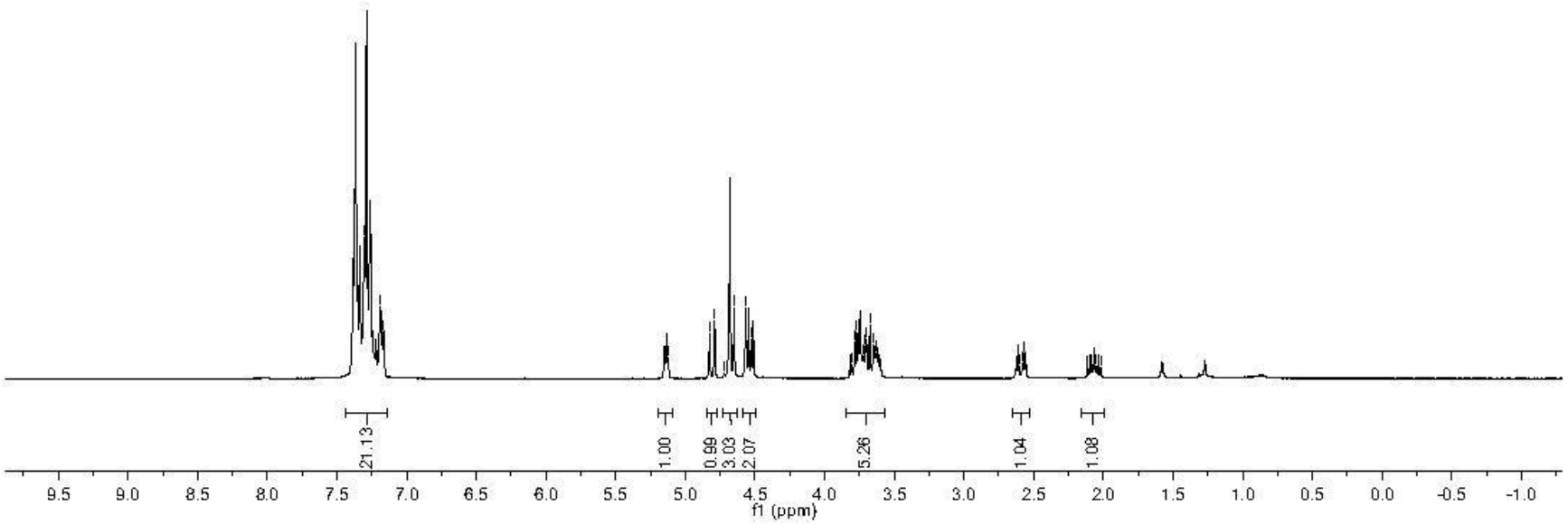

OBn
BnO
BnO
O
MR13
SnBu3
J = 143 Hz
F2 (ppm)
F1 (ppm)



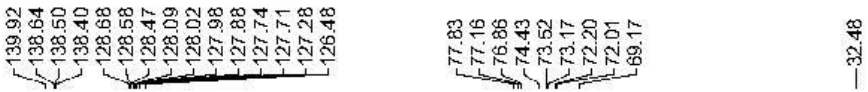


46

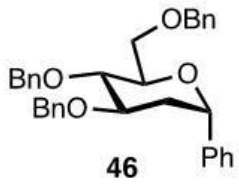
46= ZF coupling product of MR13 with 3-iodotoluene



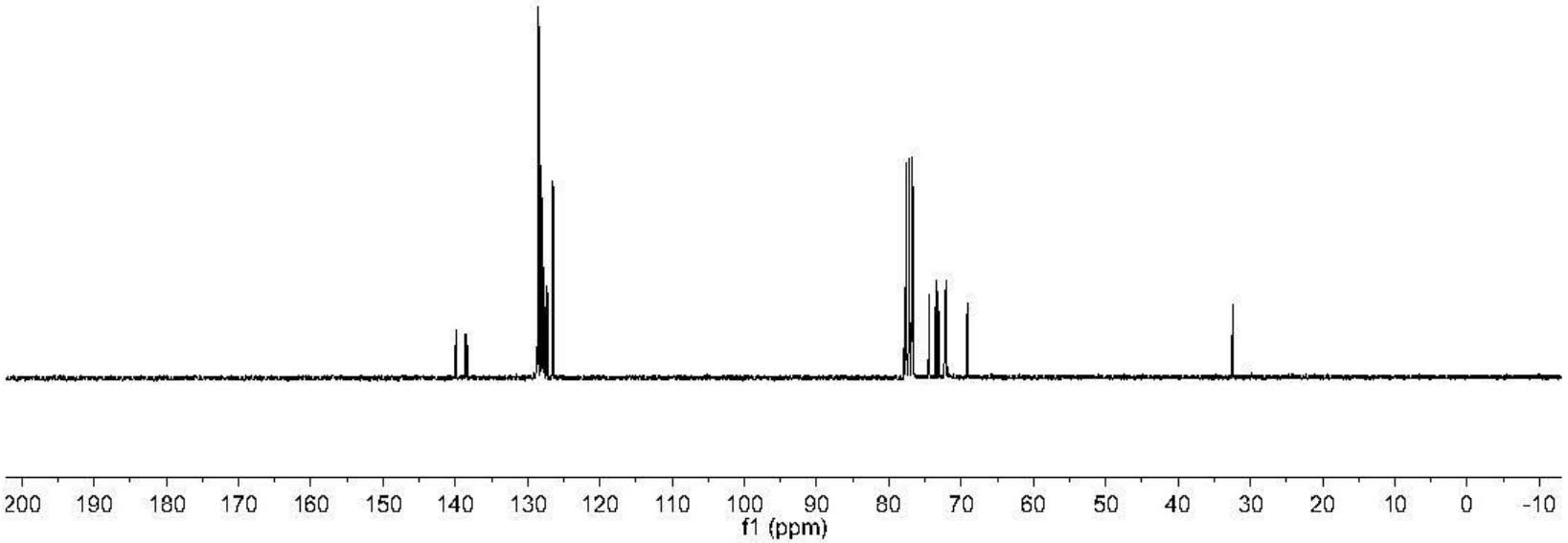
Rourke 46



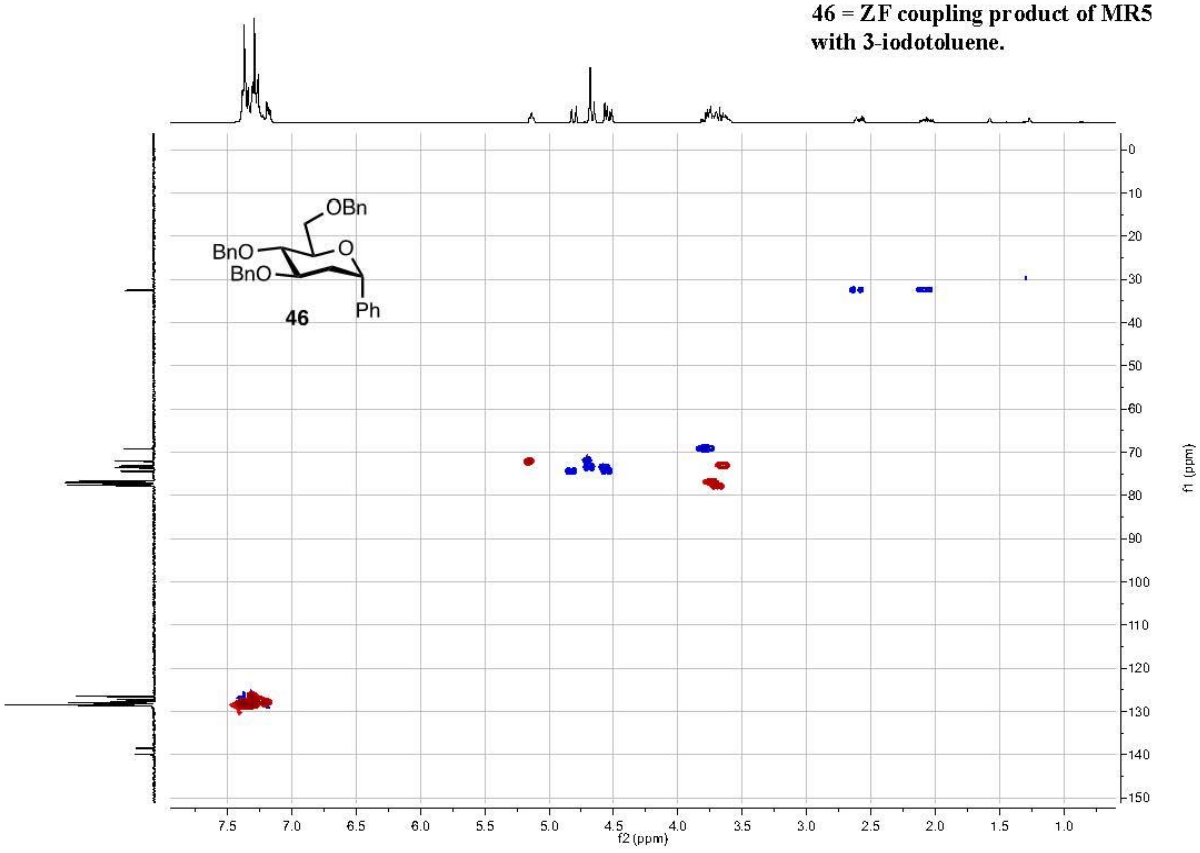
46= ZF coupling product of MR13 with 3-iodotoluene



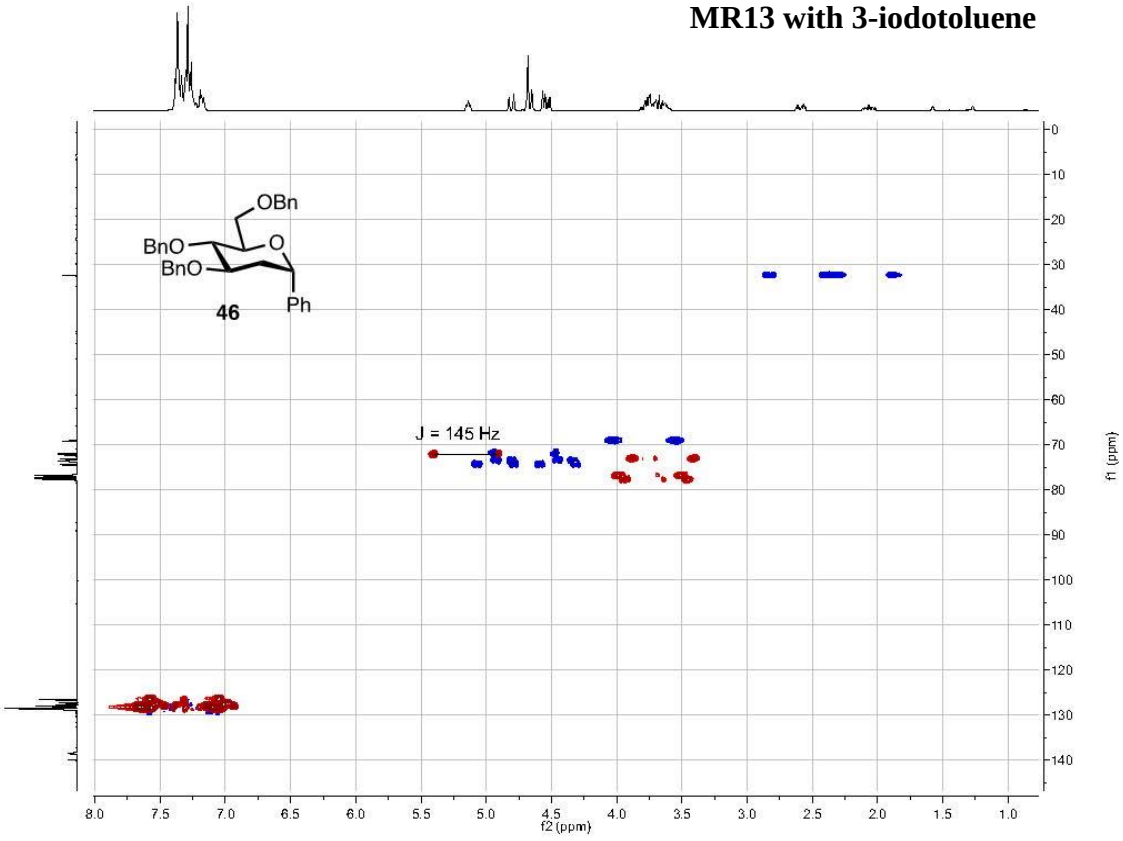
46

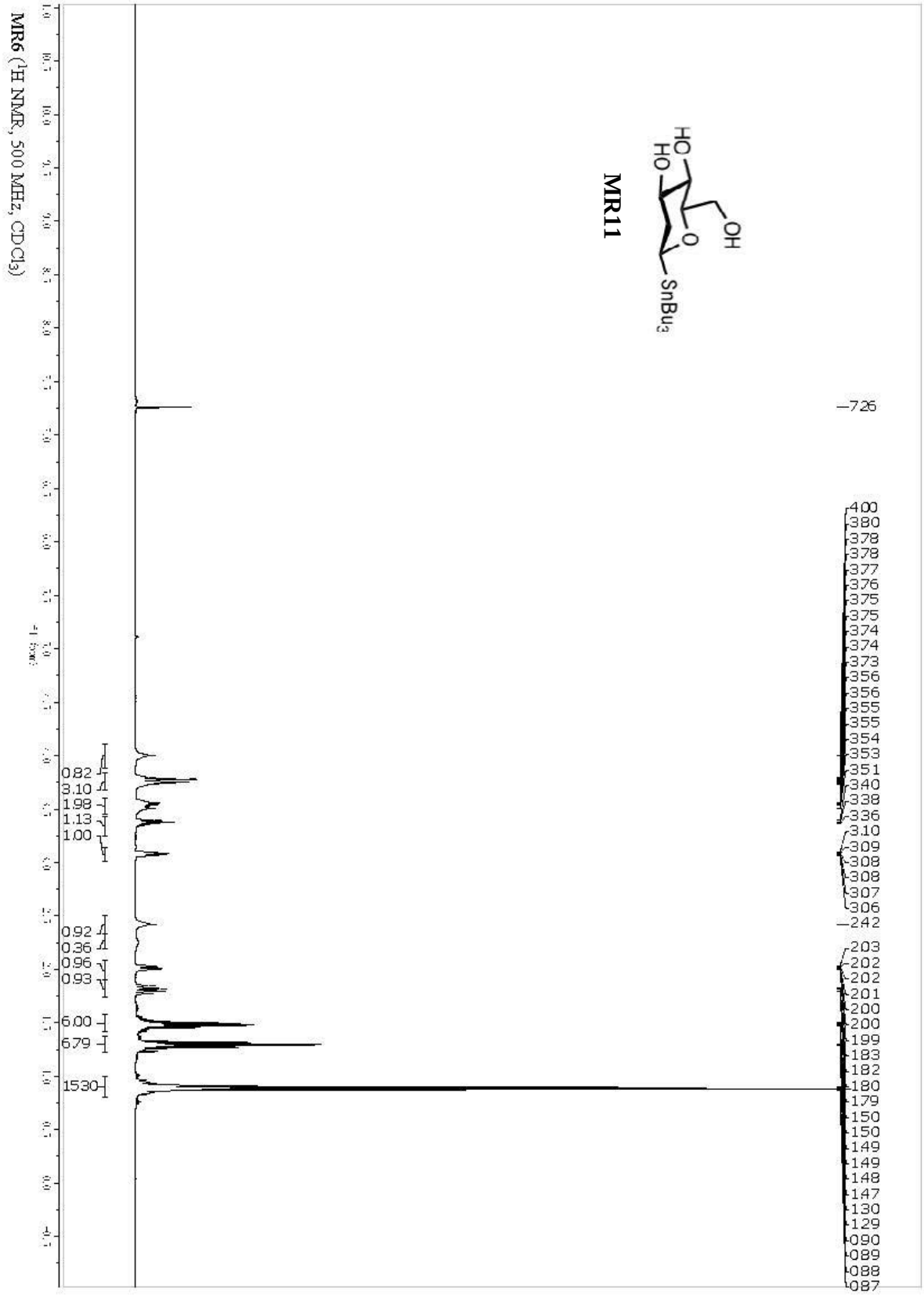


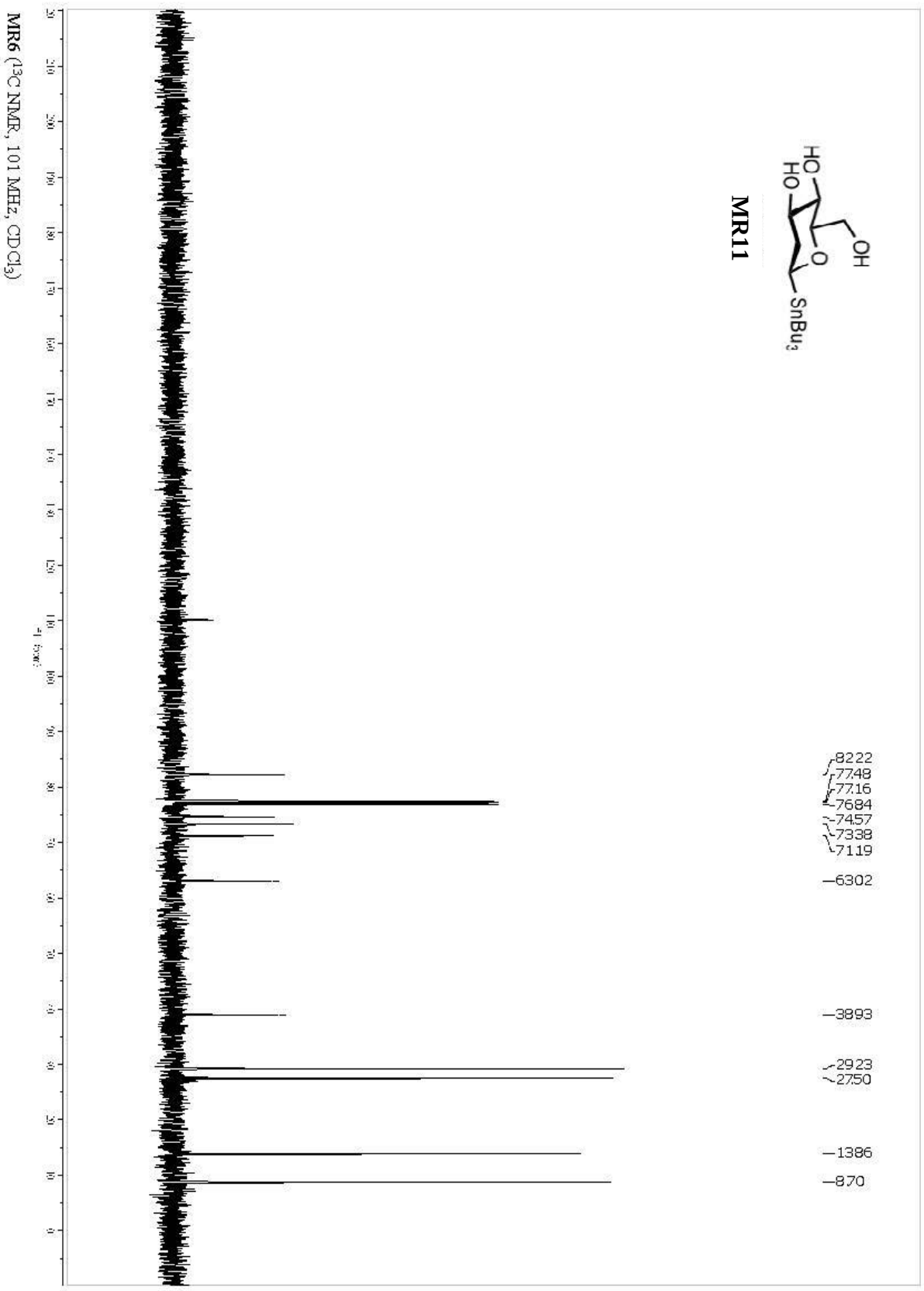
46 = ZF coupling product of MR5 with 3-iodotoluene.

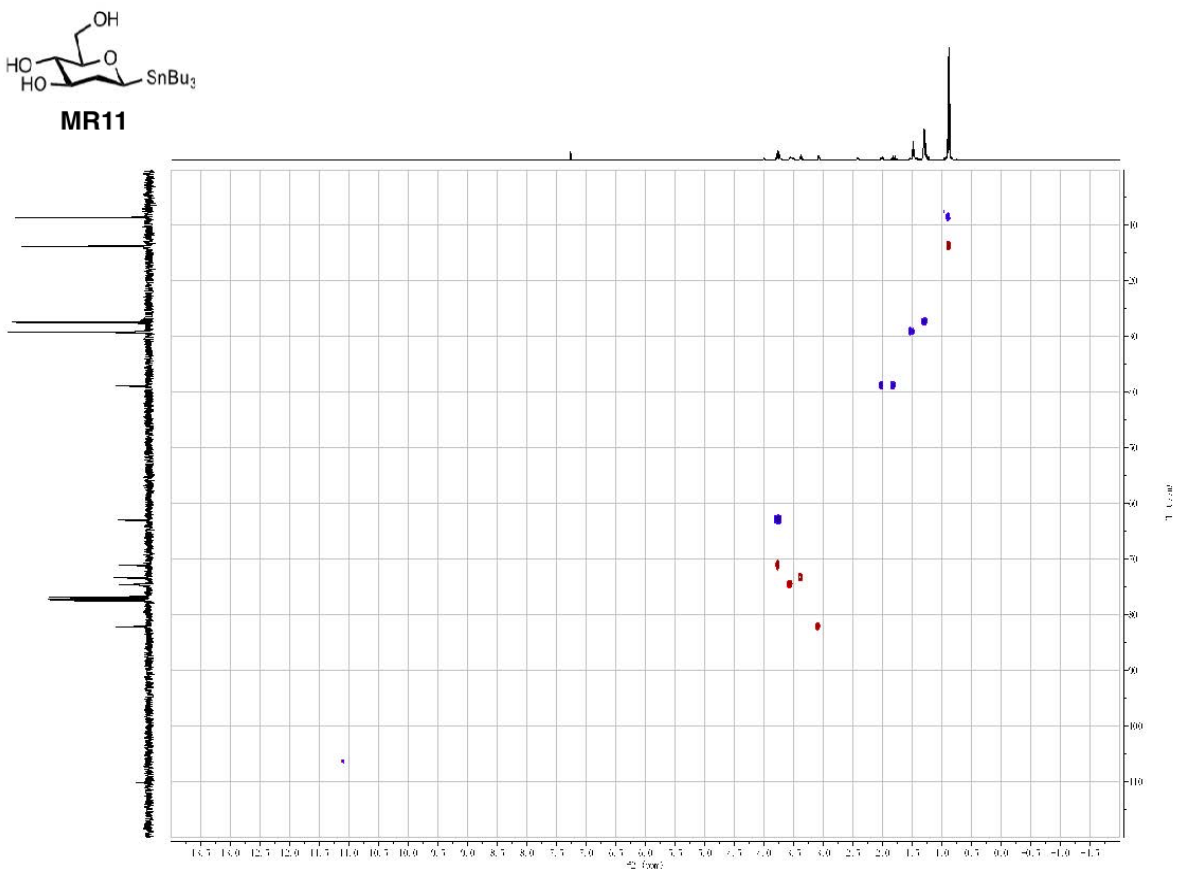


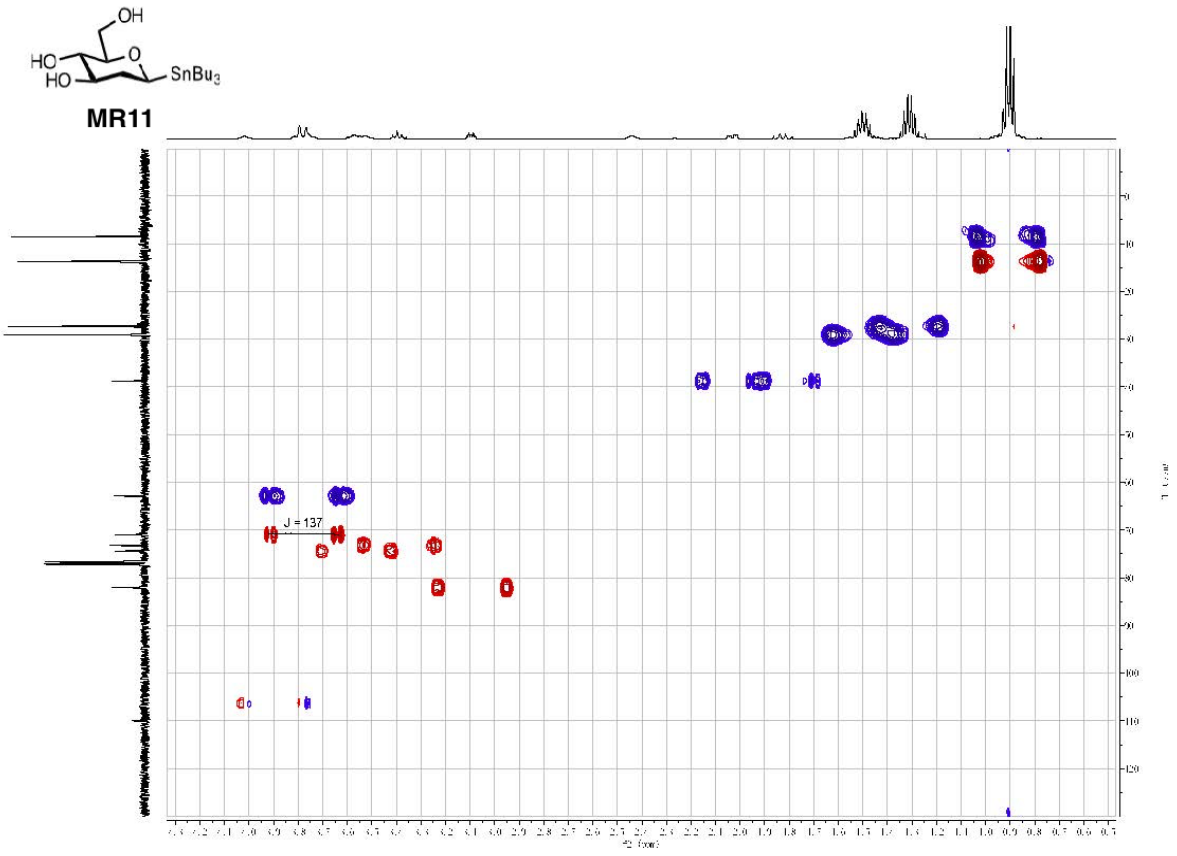
46= ZF coupling product of MR13 with 3-iodotoluene



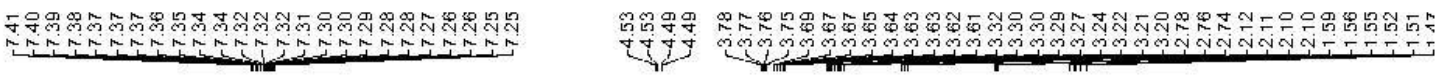

MR6 (1H NMR, 500 MHz, CDCl3)
MR11
HO
HO
O
OH
SnBu3
0.82
3.10
1.98
1.13
1.00
0.92
0.36
0.96
0.93
6.00
6.79
15.30
7.26

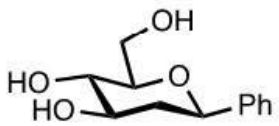

MR6 (13C NMR, 101 MHz, CDCl3)
MR11
HO
HO
O
OH
SnBu3
82.22
77.48
77.16
76.84
74.57
73.38
71.19
63.02
38.93
29.23
27.50
13.86
8.70


OH
HO
HO
O
SnBu3
MR11


OH
HO
HO
O
SnBu3
MR11
J = 137

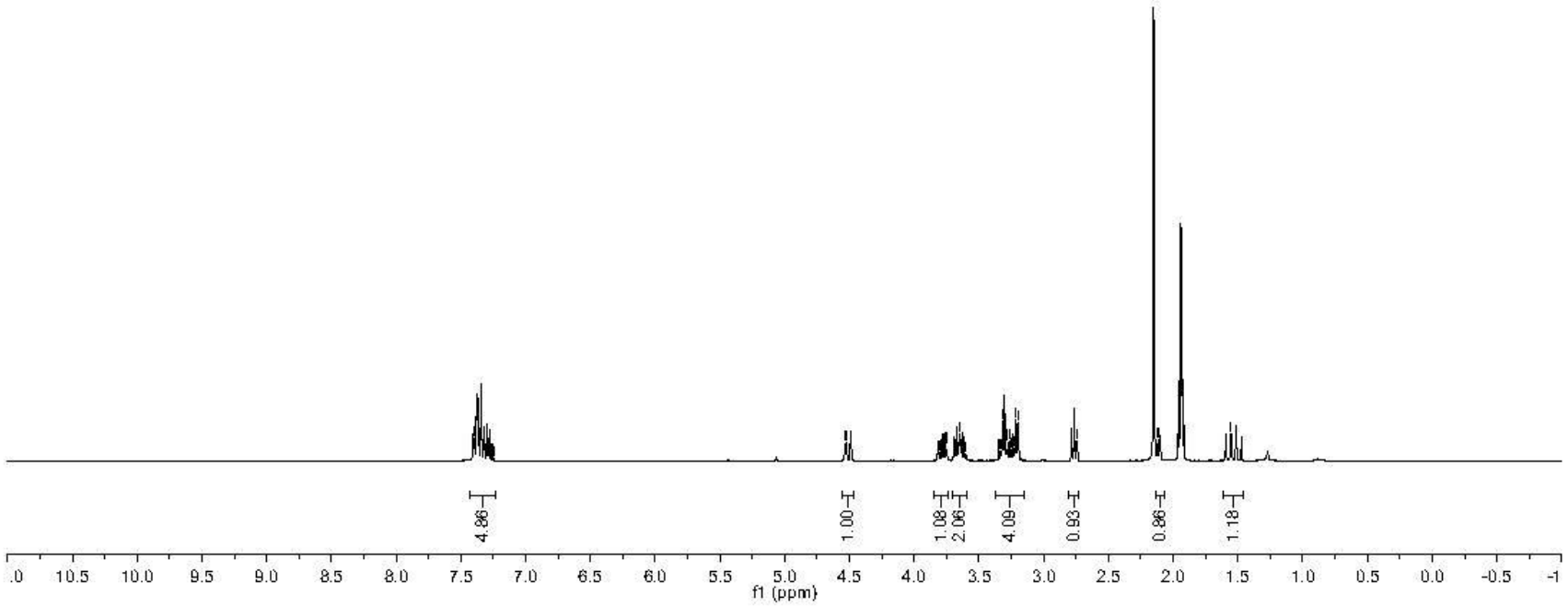
Rourke 53

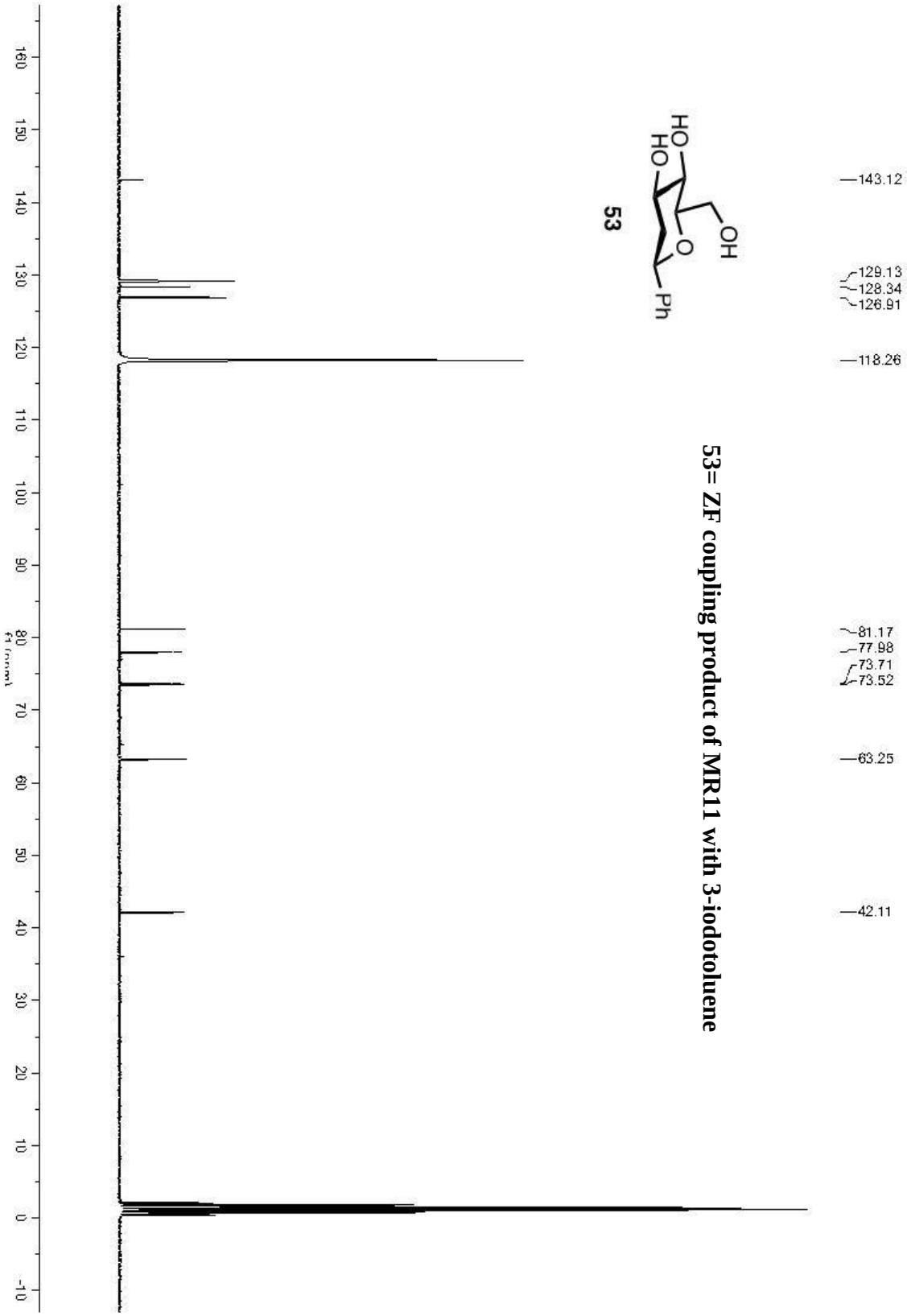




53

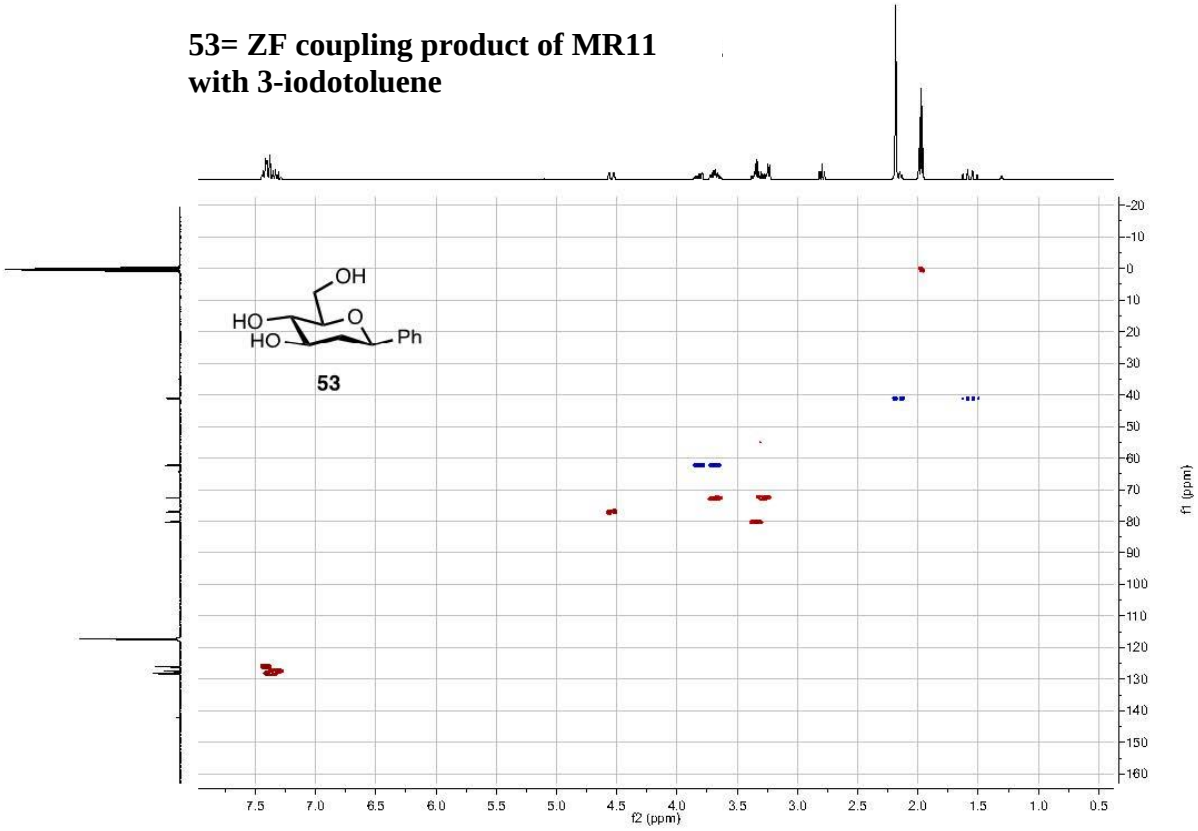
53= ZF coupling product of MR11 with 3-iodotoluene



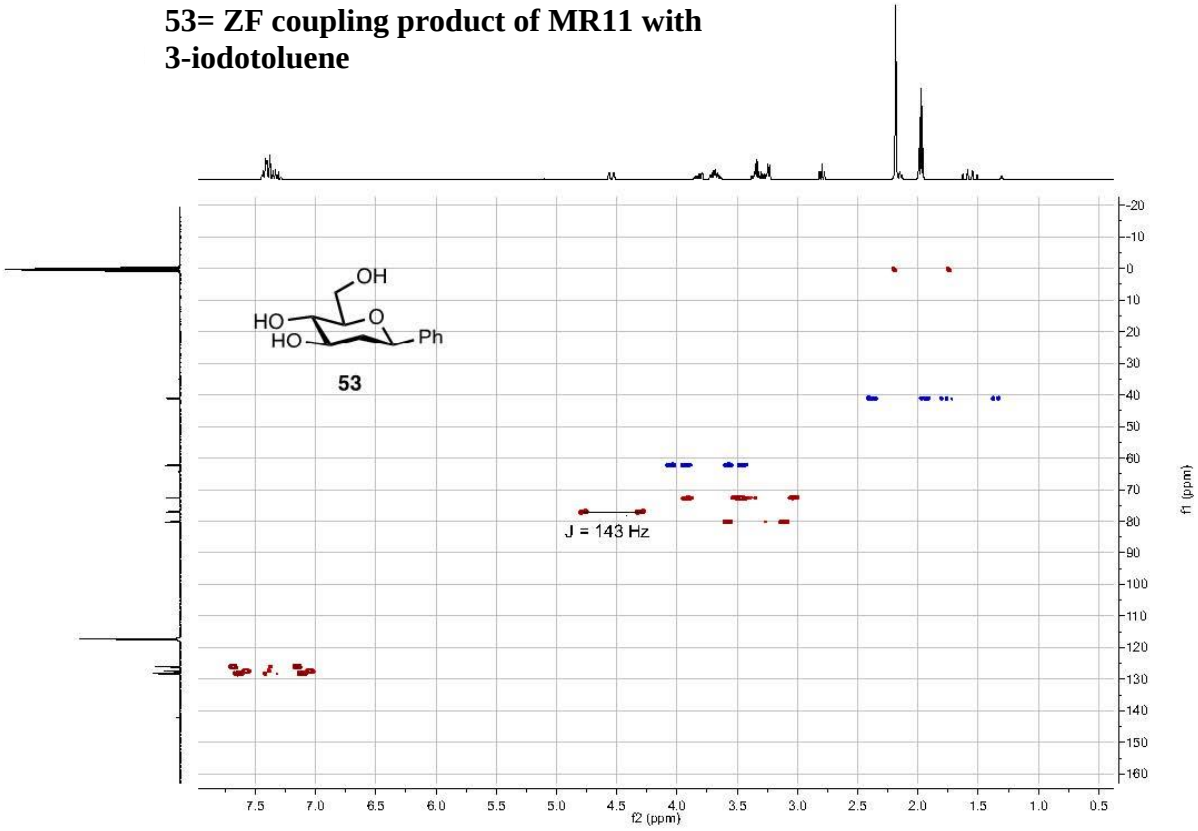


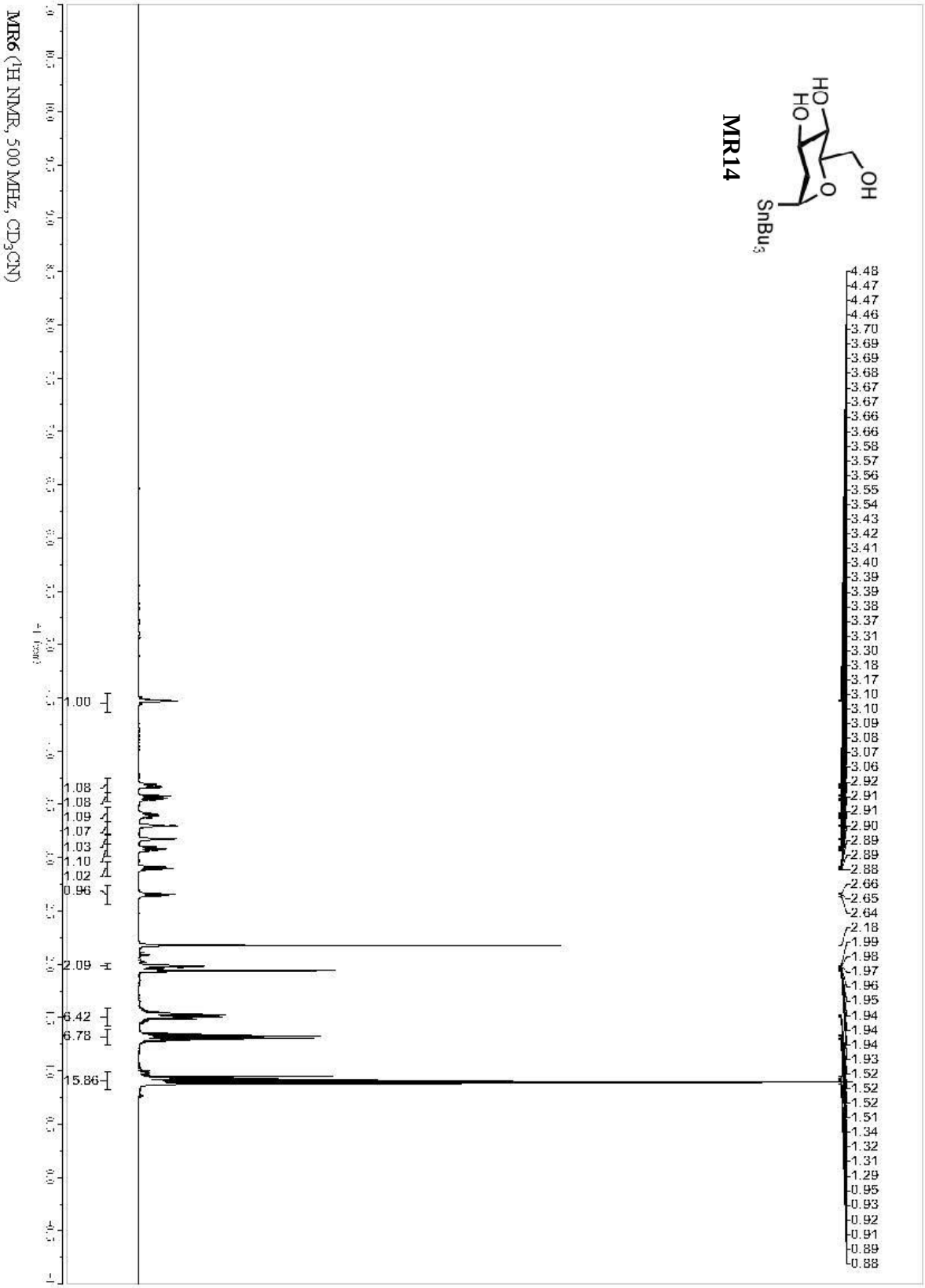
53= ZF coupling product of MR11 with 3-iodotoluene

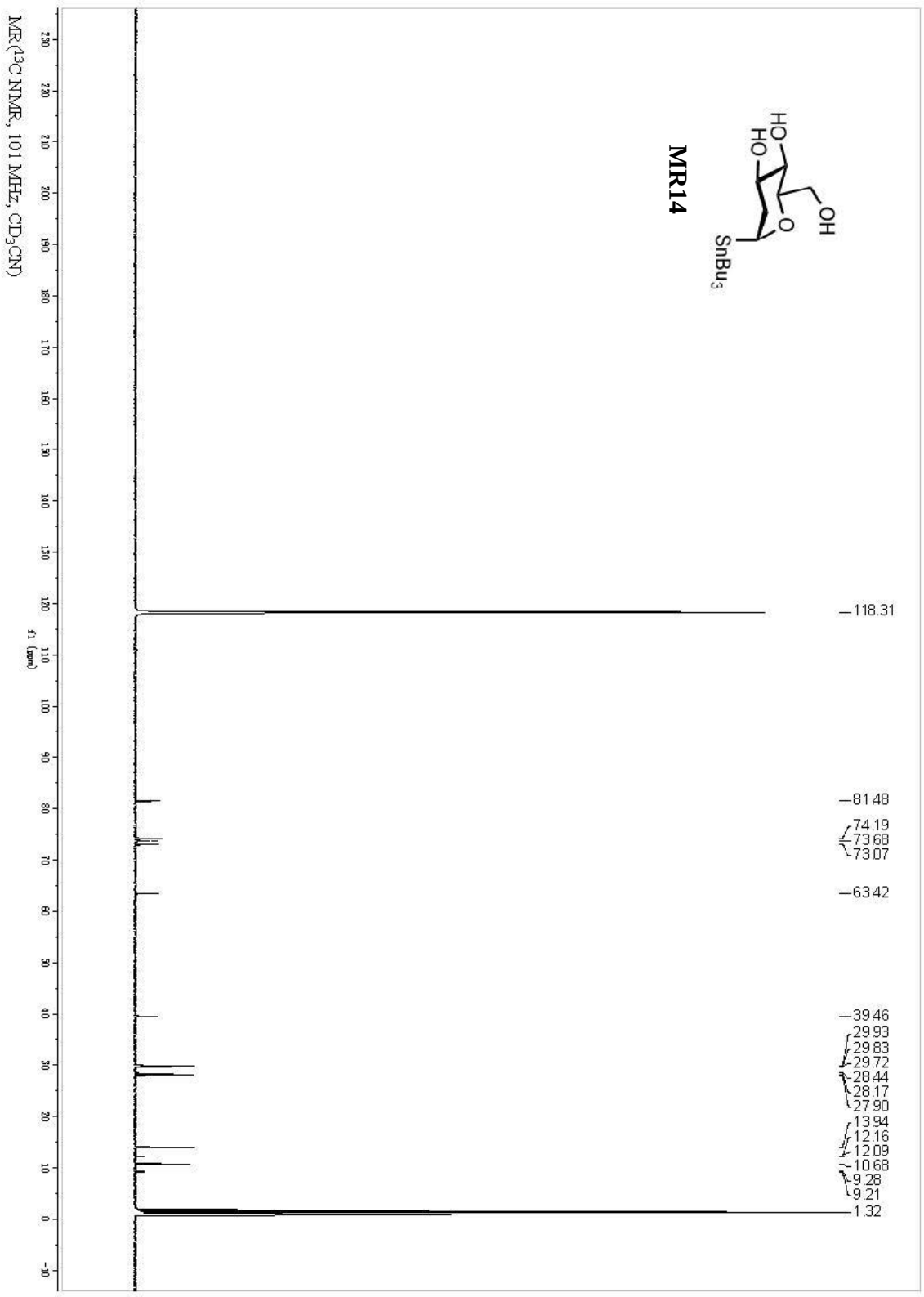
53= ZF coupling product of MR11 with 3-iodotoluene

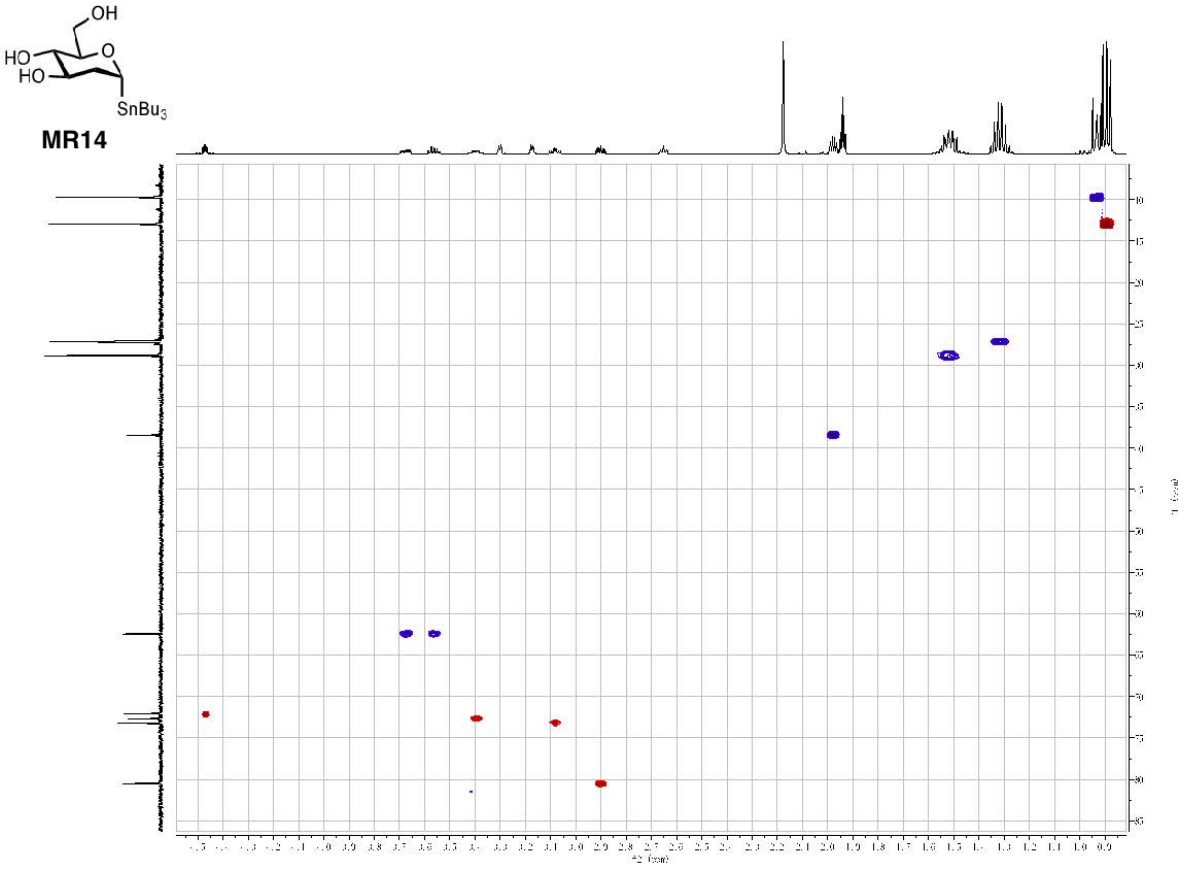


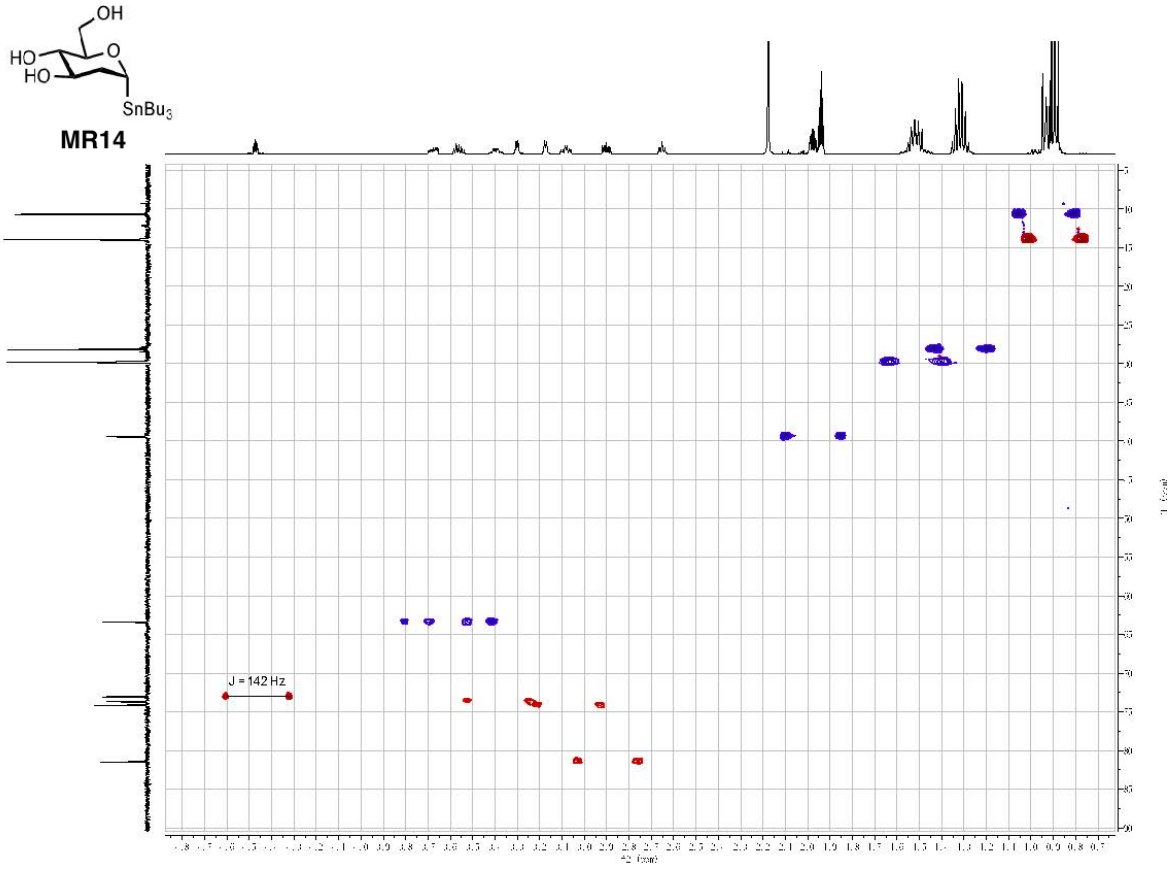
53= ZF coupling product of MR11 with 3-iodotoluene



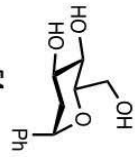

MR6 (1H NMR, 500 MHz, CD3CN)
MR14
SnBu3
OH
HO
HO
O
1.00
1.08
1.08
1.09
1.07
1.03
1.10
1.02
0.96
2.09
6.42
6.78
15.86
4.48
4.47
4.47
4.46
3.70
3.69
3.69
3.68
3.67
3.67
3.66
3.66
3.58
3.57
3.56
3.55
3.54
3.43
3.42
3.41
3.40
3.39
3.39
3.38
3.37
3.31
3.30
3.18
3.17
3.10
3.10
3.09
3.08
3.07
3.06
2.92
2.91
2.91
2.90
2.89
2.89
2.88
2.66
2.65
2.64
2.18
1.99
1.98
1.97
1.96
1.95
1.94
1.94
1.94
1.93
1.52
1.52
1.52
1.51
1.34
1.32
1.31
1.29
0.95
0.93
0.92
0.91
0.89
0.88


MR(13C NMR, 101 MHz, CD3CN)
f1 (ppm)
MR14
SnBu3
OH
HO
HO
O
118.31
81.48
74.19
73.68
73.07
63.42
39.46
29.93
29.83
29.72
28.44
28.17
27.90
13.94
12.16
12.09
10.68
9.28
9.21
1.32

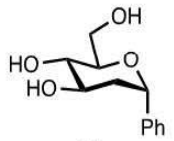

OH
HO
HO
O
SnBu3
MR14


OH
HO
HO
O
SnBu3
MR14
J = 142 Hz

54= ZF coupling product of MR14 with 3-iodotoluene



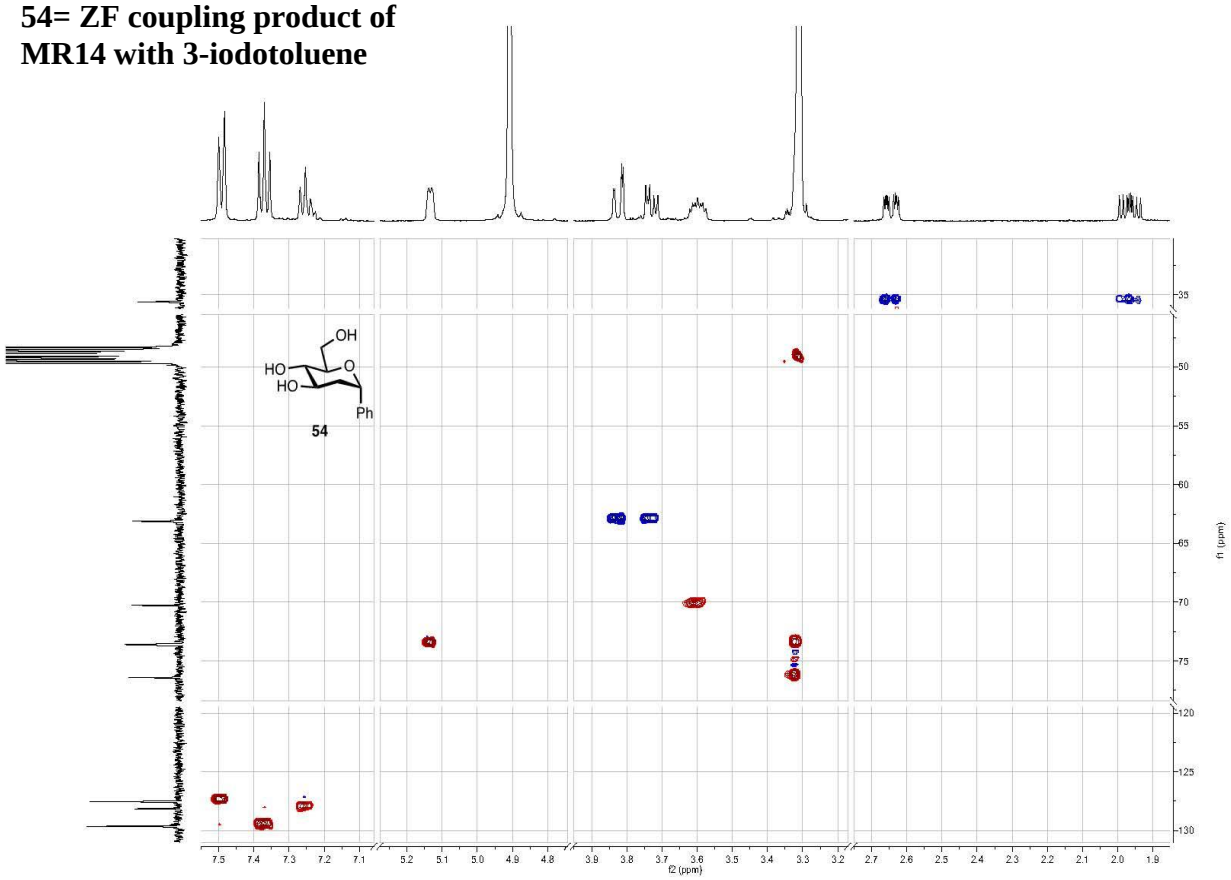
54



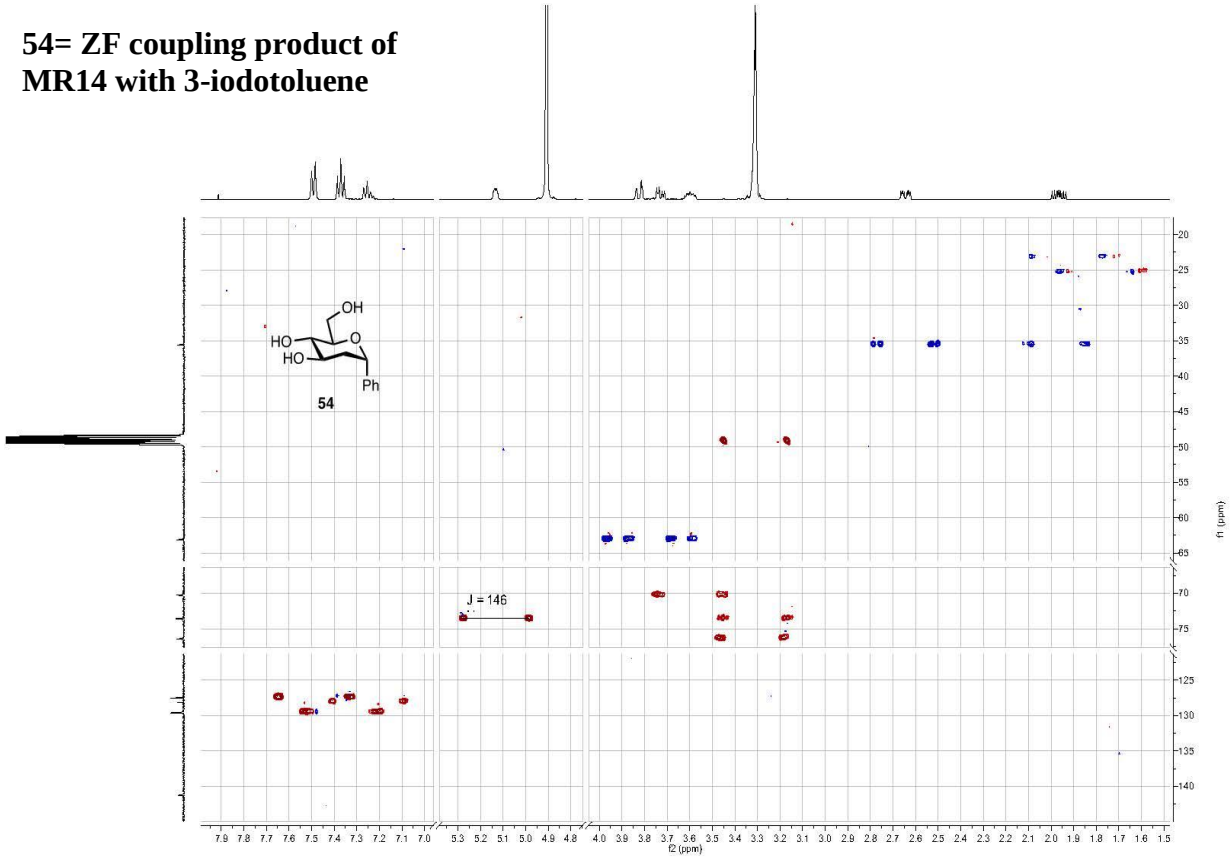
54

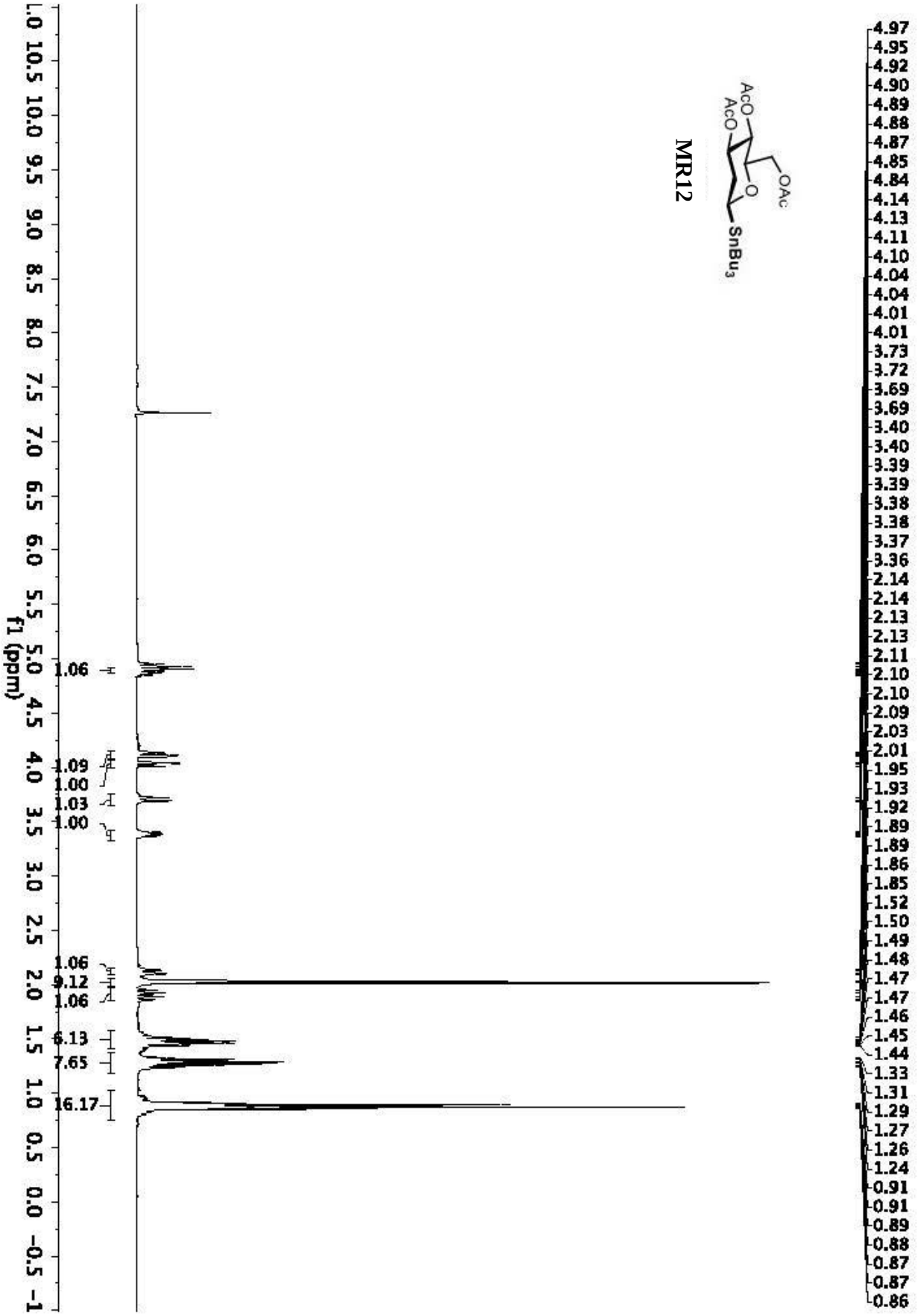
54= ZF coupling product of MR14 with 3-iodotoluene

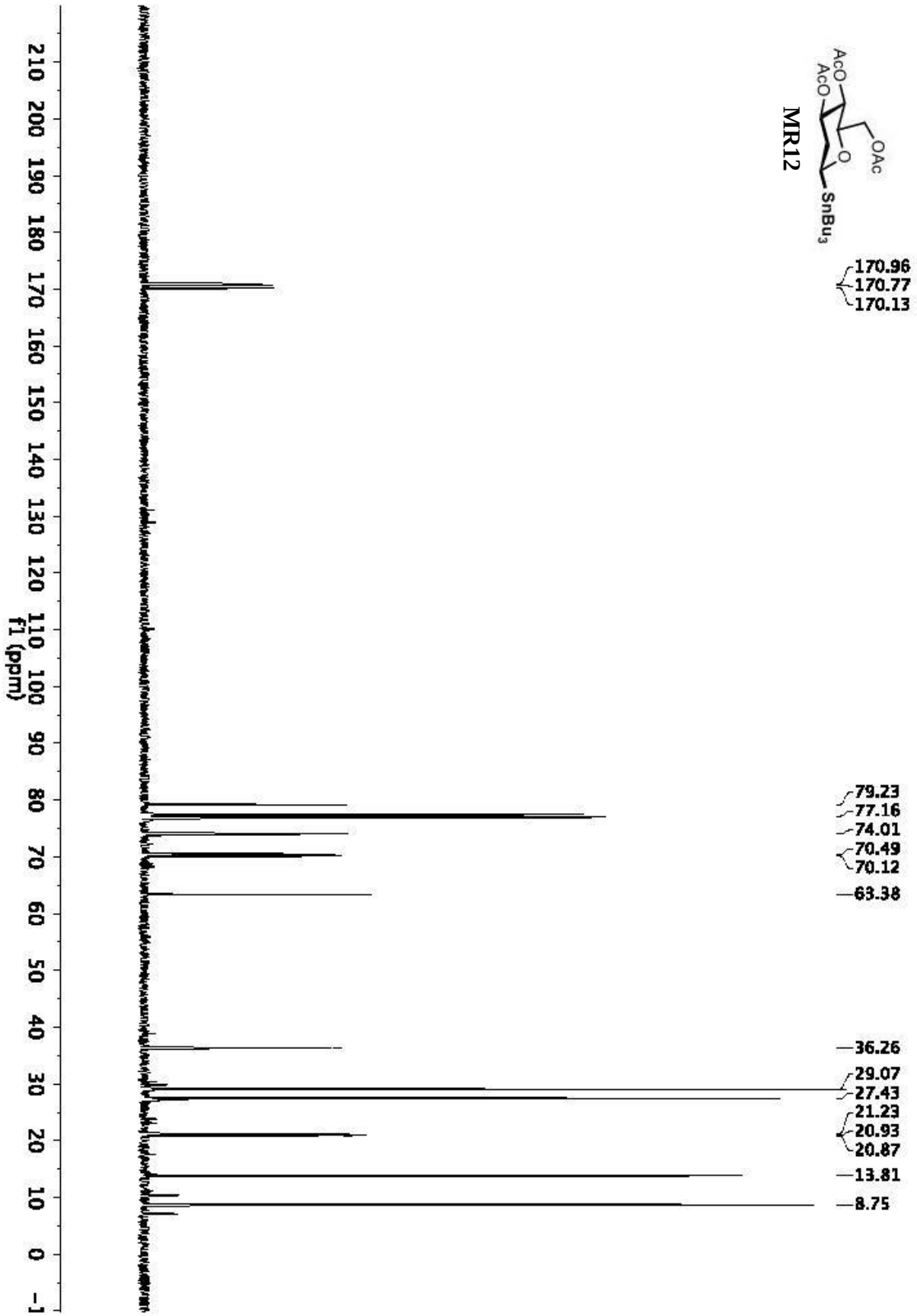
54= ZF coupling product of MR14 with 3-iodotoluene

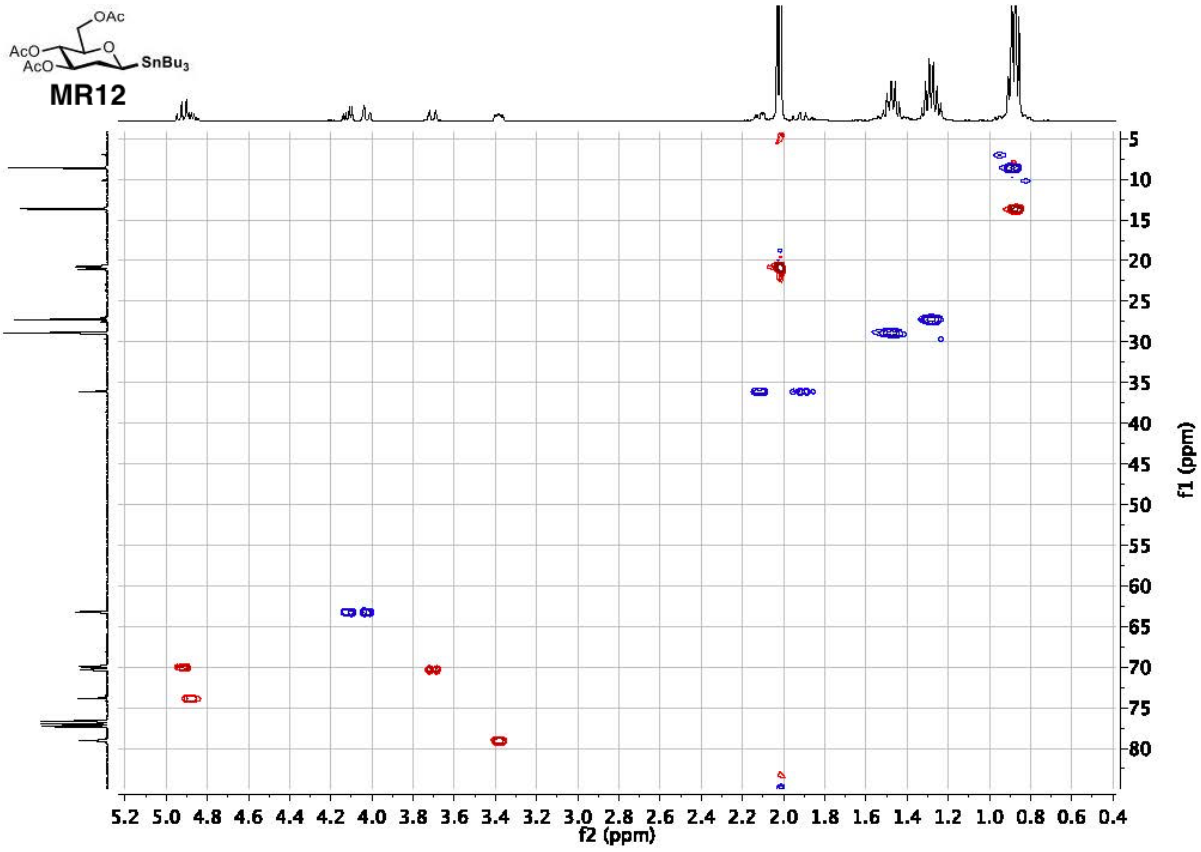


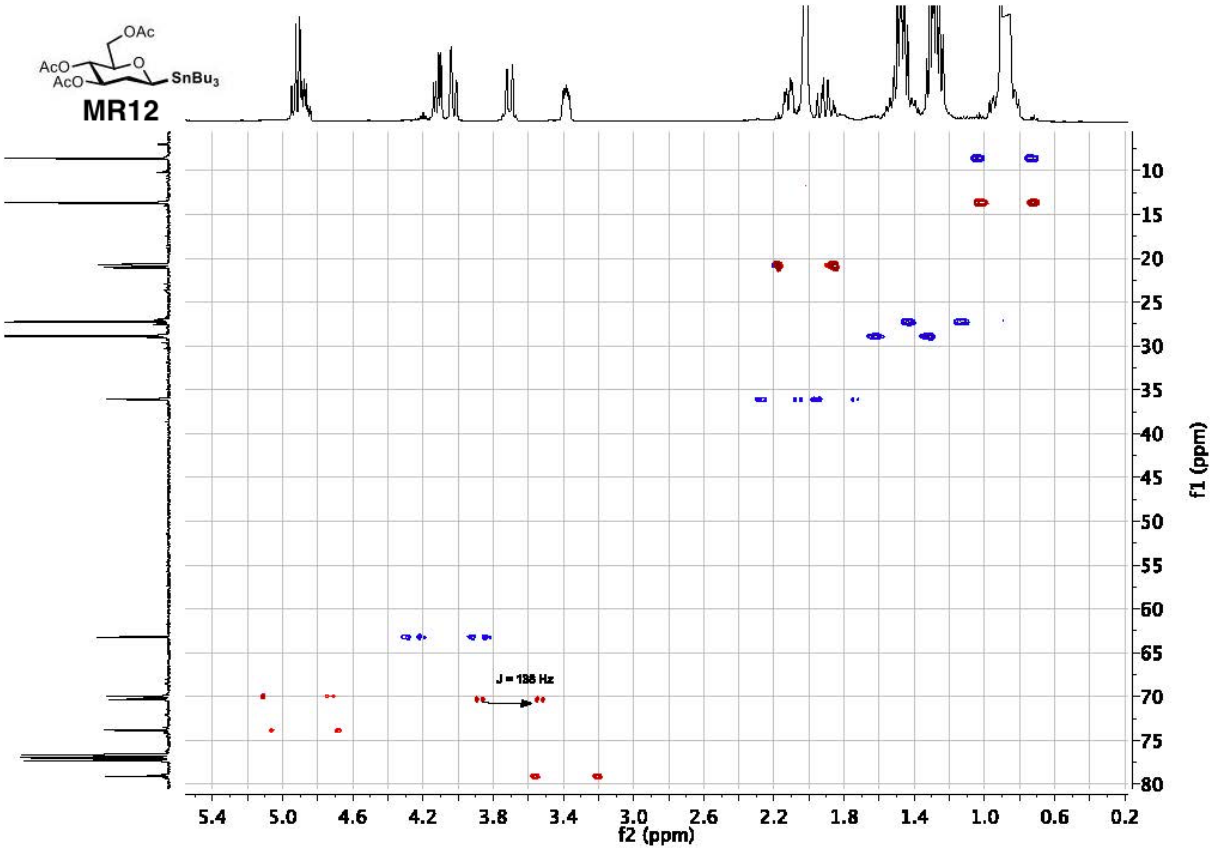
54= ZF coupling product of MR14 with 3-iodotoluene

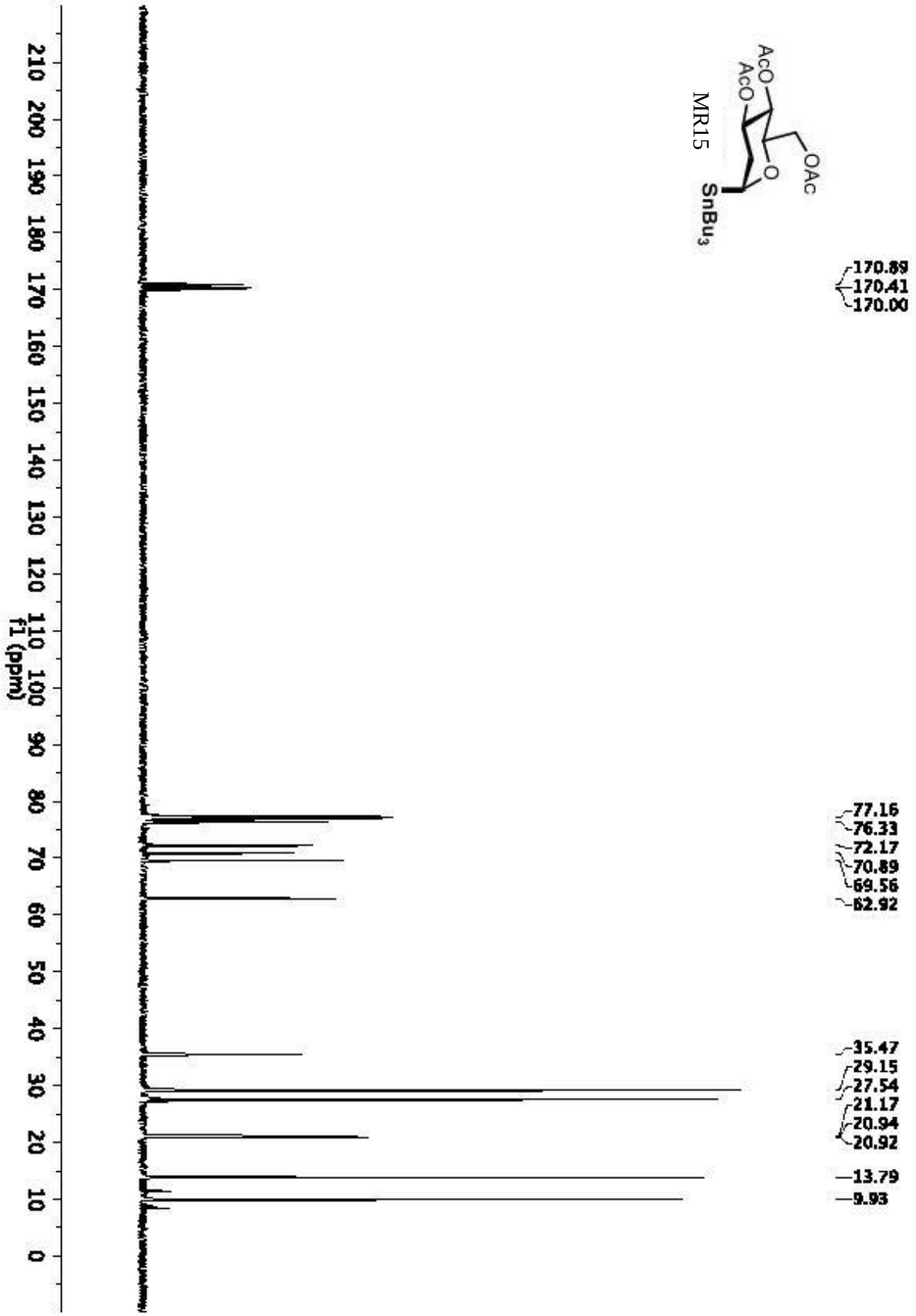


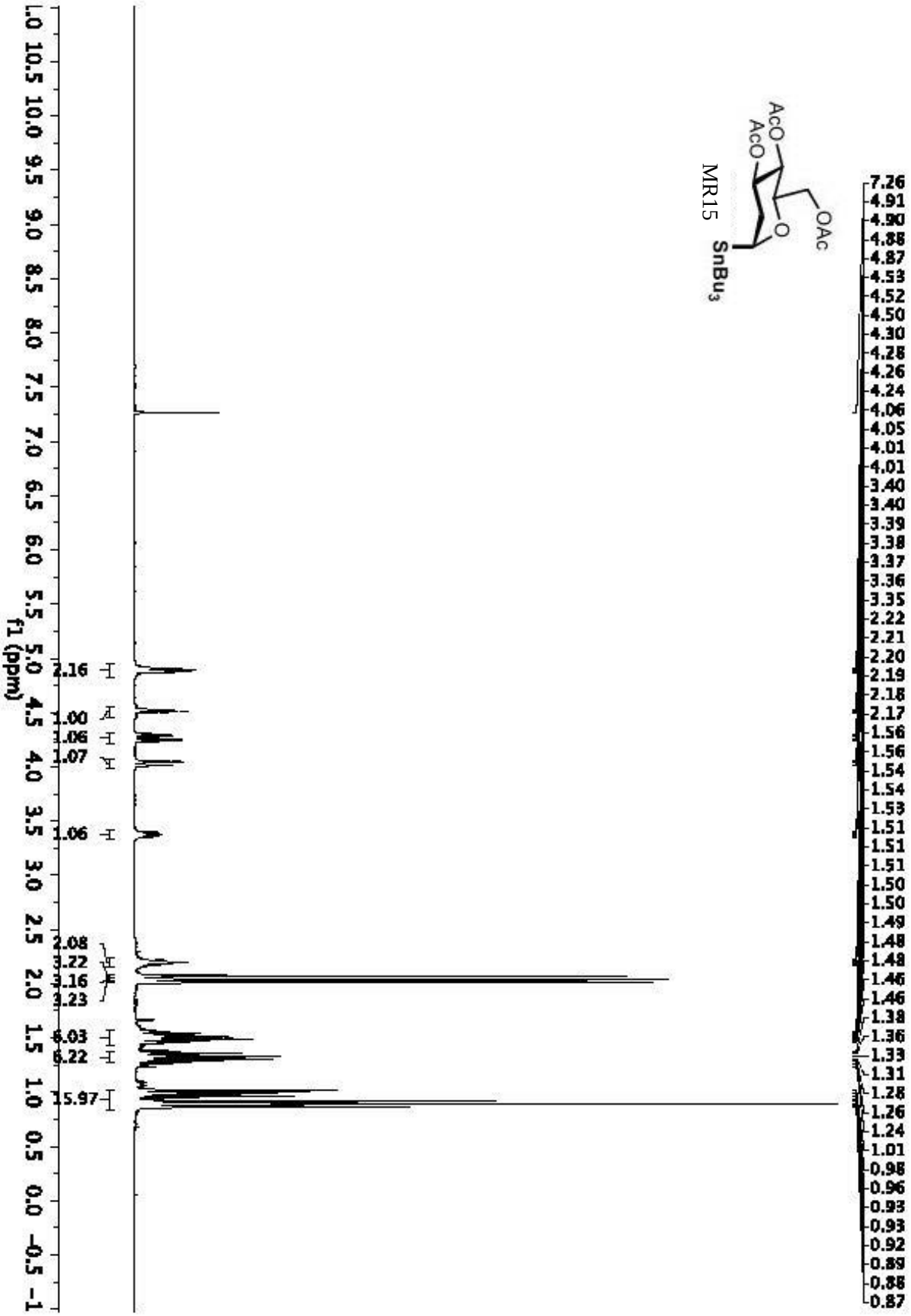

MR12
AcO
AcO
OAc
O
SnBu3
f1 (ppm)
1.06
1.09
1.00
1.03
1.00
1.06
9.12
1.06
6.13
7.65
16.17

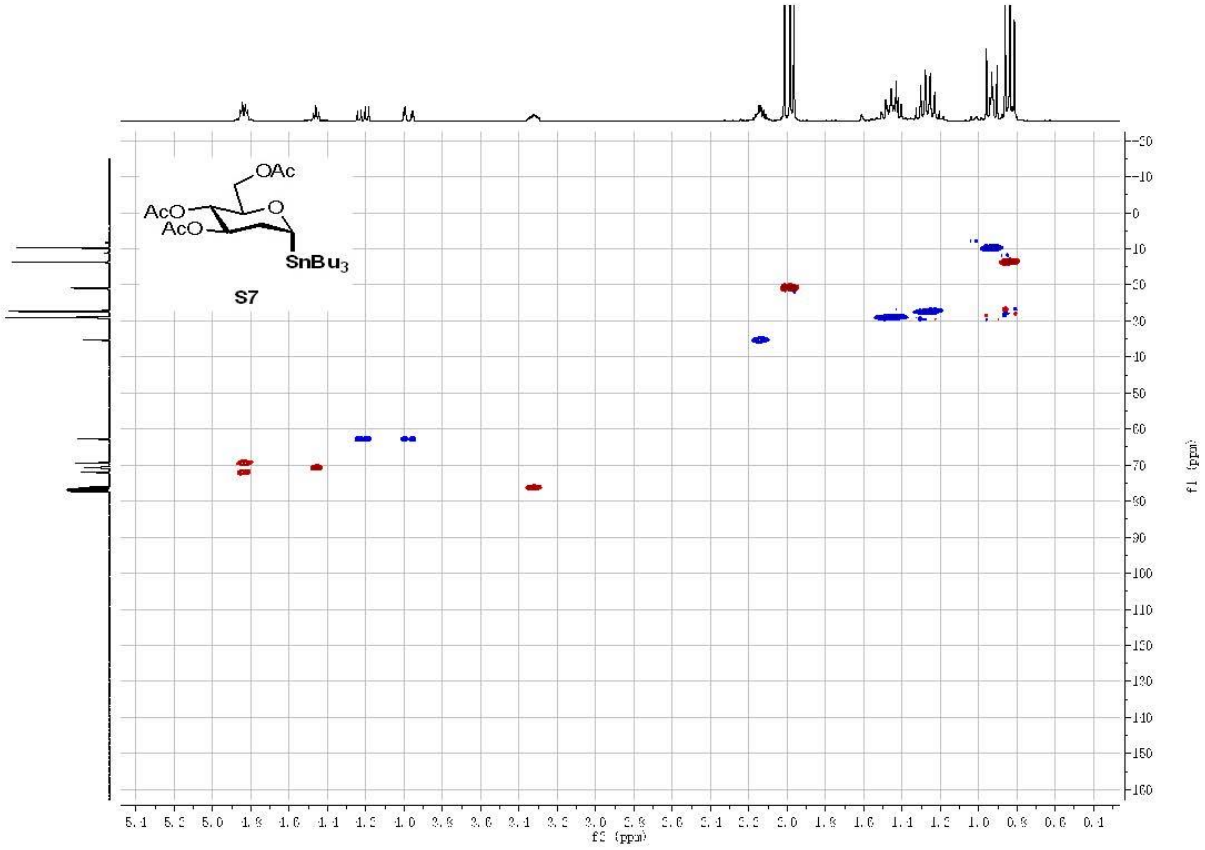

MR12
AcO
AcO
OAc
O
SnBu3
170.96
170.77
170.13
79.23
77.16
74.01
70.49
70.12
63.38
36.26
29.07
27.43
21.23
20.93
20.87
13.81
8.75
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1

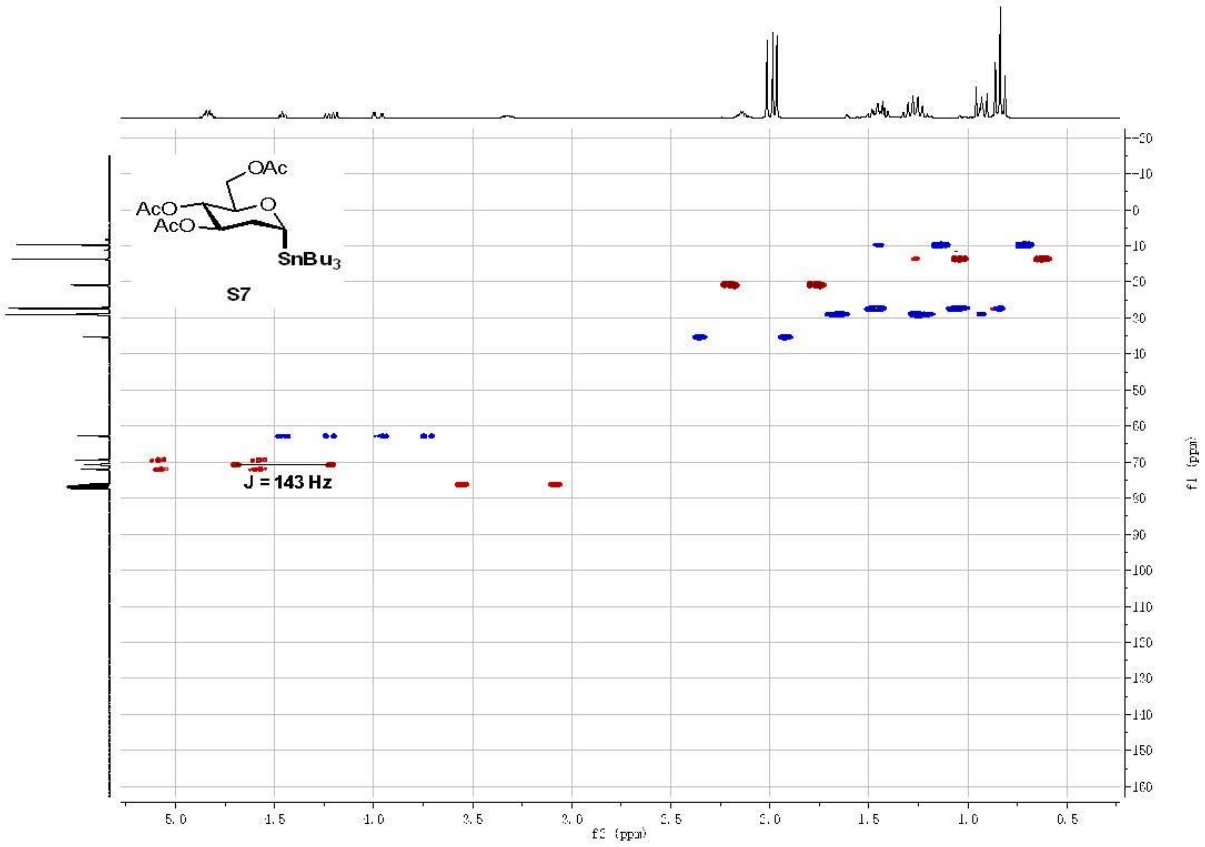

OAc
AcO
AcO
O
SnBu3
MR12
f1 (ppm)
f2 (ppm)

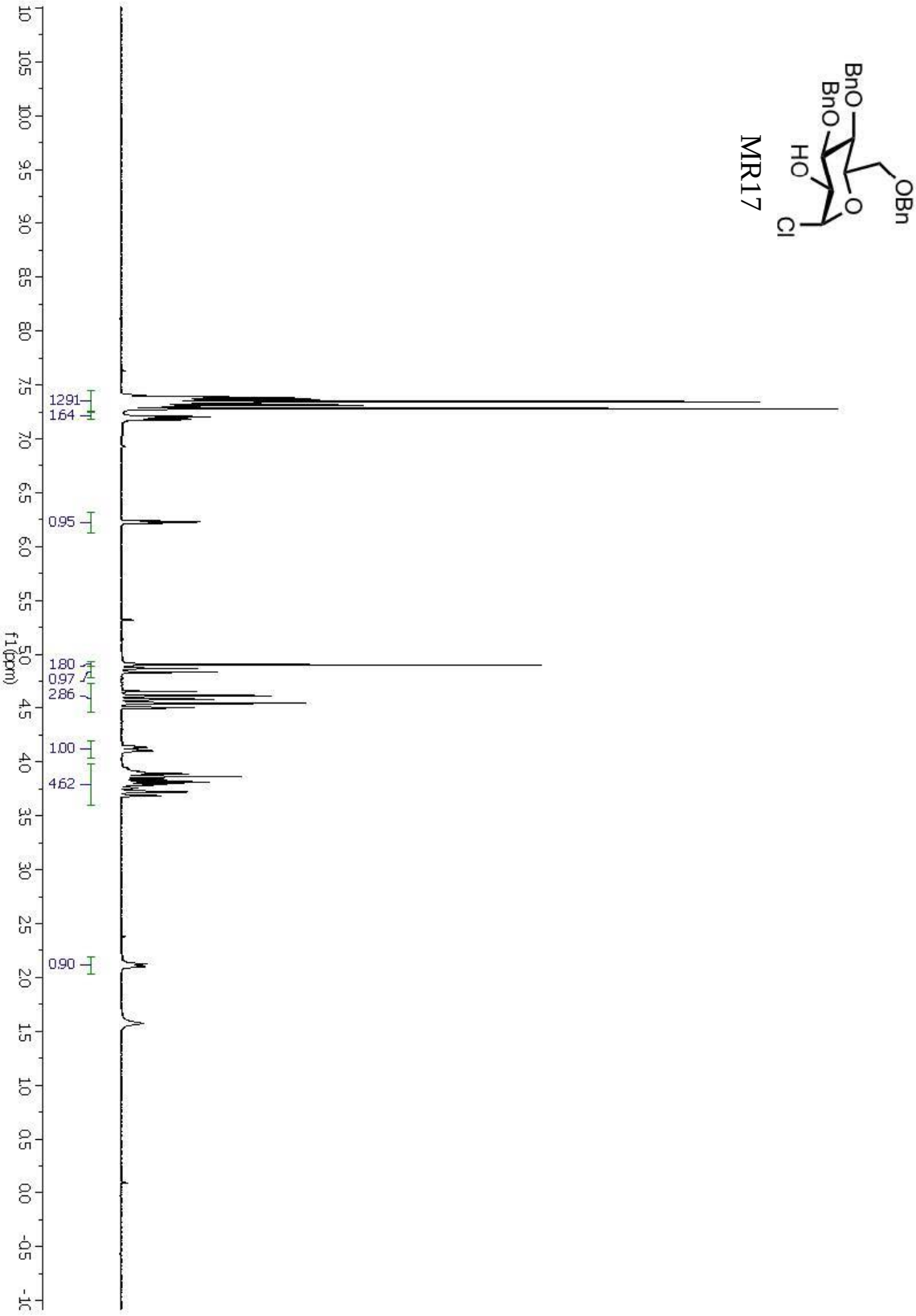

OAc
AcO
AcO
O
SnBu3
MR12
J = 188 Hz
f2 (ppm)
f1 (ppm)
5.4
5.0
4.6
4.2
3.8
3.4
3.0
2.6
2.2
1.8
1.4
1.0
0.6
0.2
10
15
20
25
30
35
40
45
50
55
60
65
70
75
80

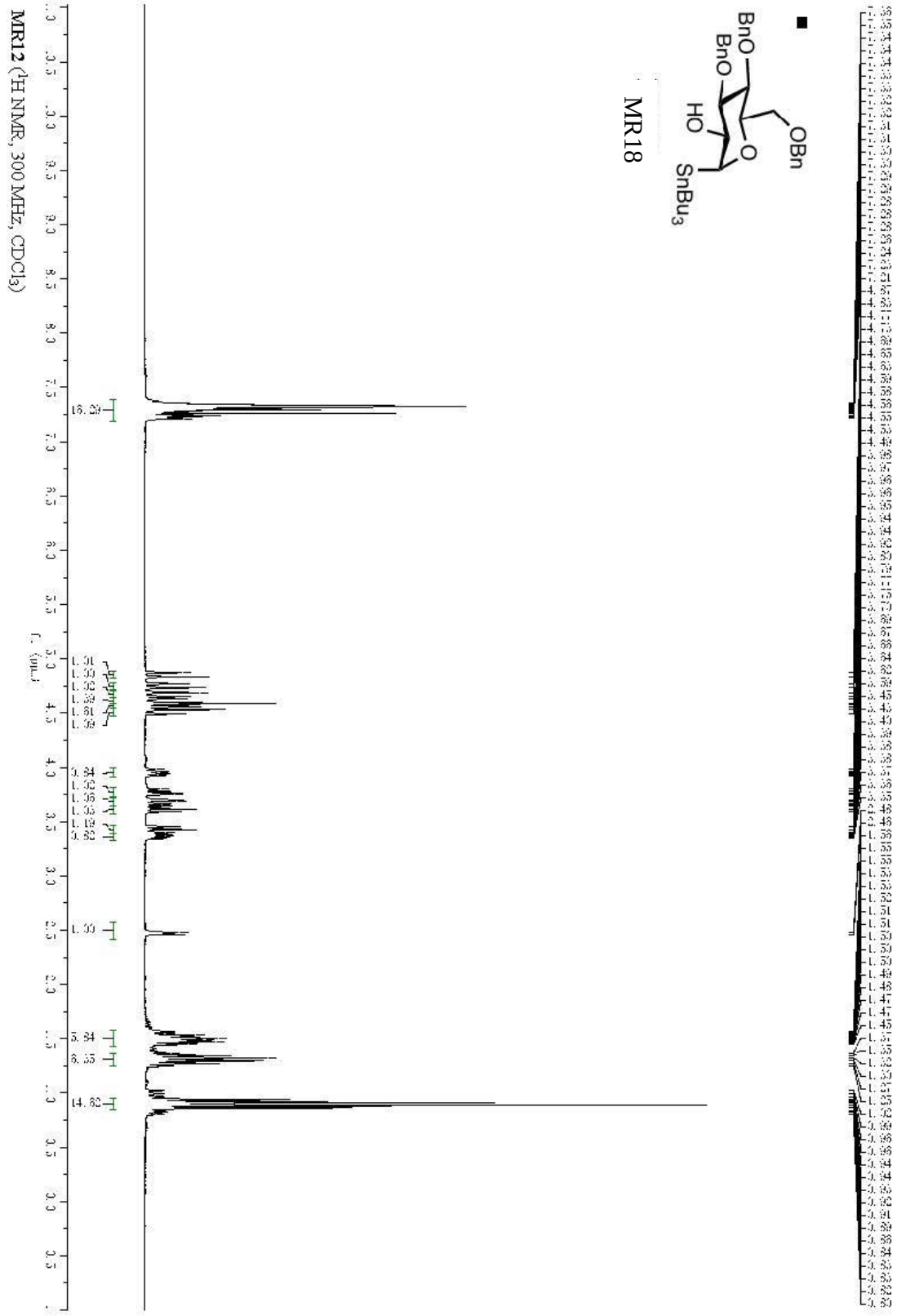

MR15
AcO
AcO
OAc
O
SnBu3
170.89
170.41
170.00
77.16
76.33
72.17
70.89
69.56
62.92
35.47
29.15
27.54
21.17
20.94
20.92
13.79
9.93
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

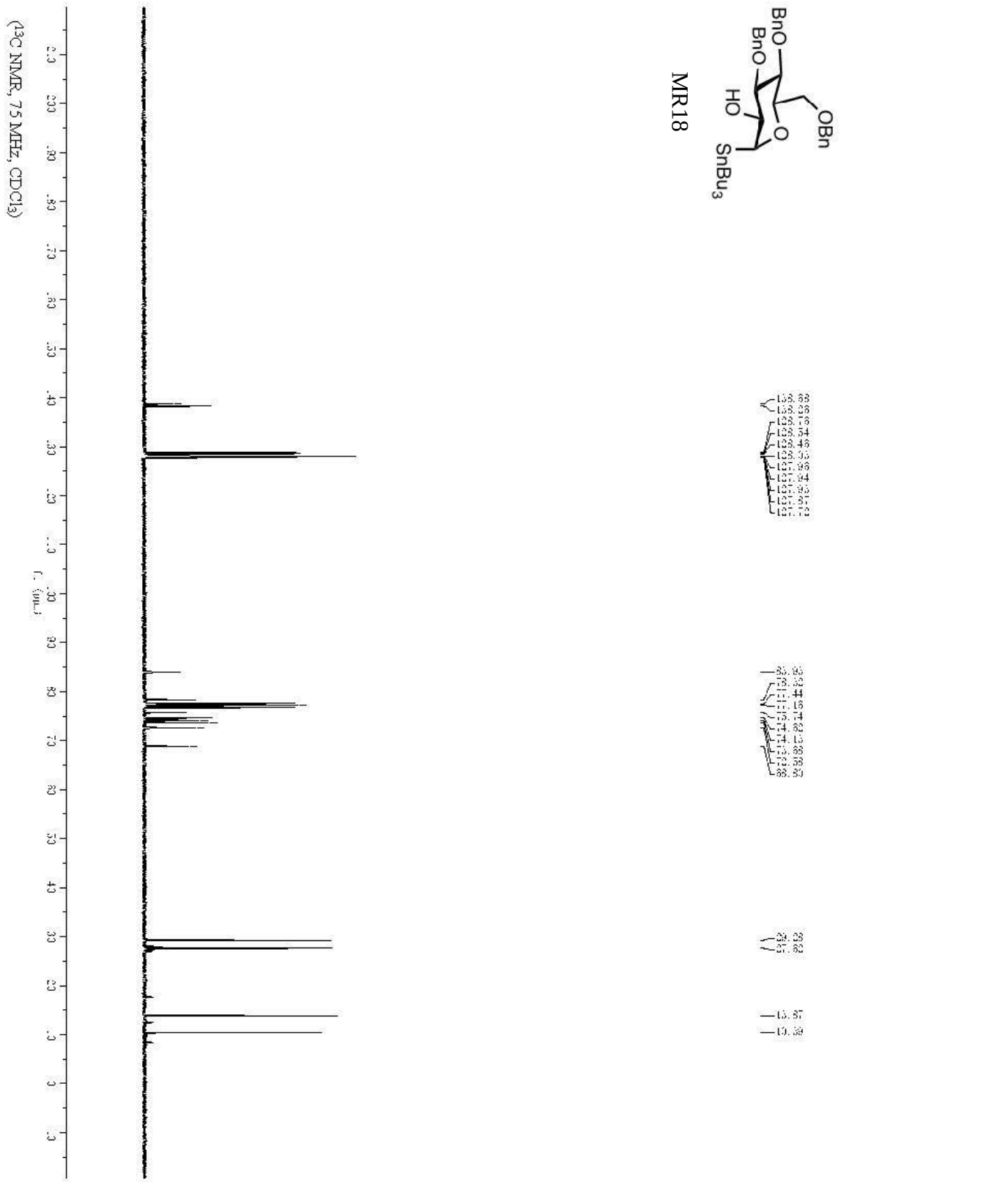

MR15
SnBu3
AcO
AcO
O
OAc
f1 (ppm)
2.16
1.00
1.06
1.07
1.06
2.08
3.22
3.16
3.23
6.03
6.22
15.97

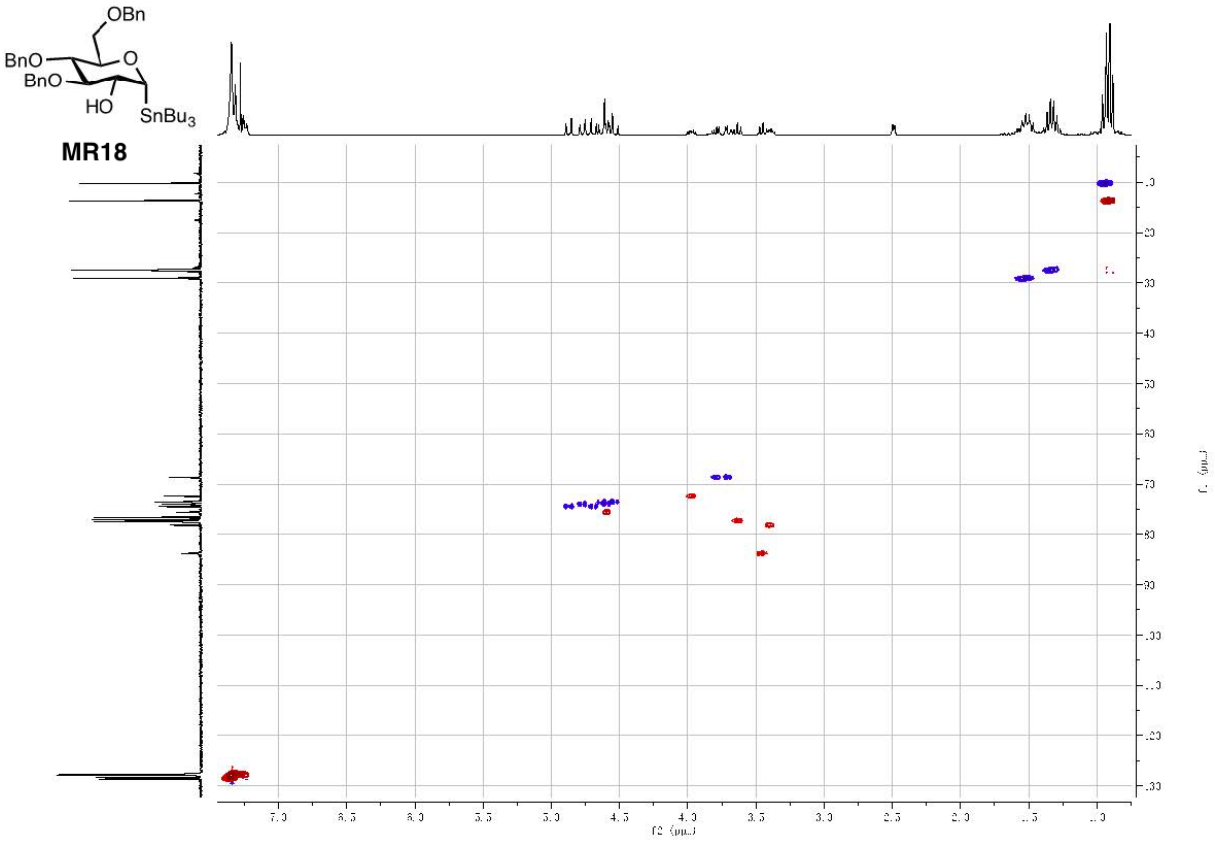

OAc
AcO
AcO
O
SnBu3
S7
f2 (ppm)
f1 (ppm)

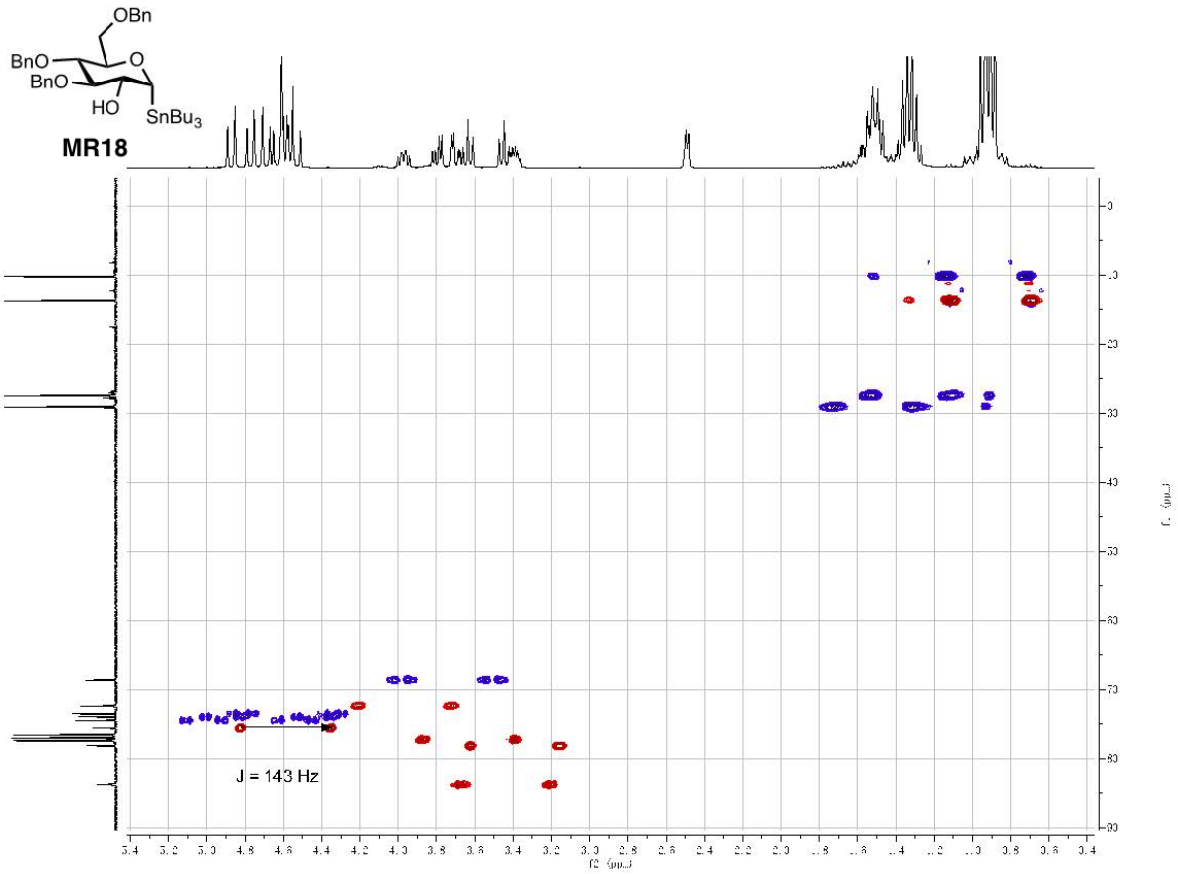

OAc
AcO
AcO
O
SnBu3
S7
J = 143 Hz
f2 (ppm)
f1 (ppm)


MR17
BnO
BnO
HO
O
OBn
Cl
f1(ppm)
12.91
1.64
0.95
1.80
0.97
2.86
1.00
4.62
0.90

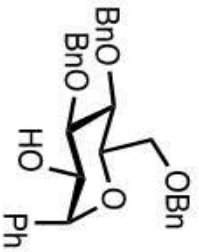

MR18
OBn
BnO
BnO
HO
O
SnBu3
MR12 (1H NMR, 300 MHz, CDCl3)
16.29
1.00
5.84
6.55
14.82

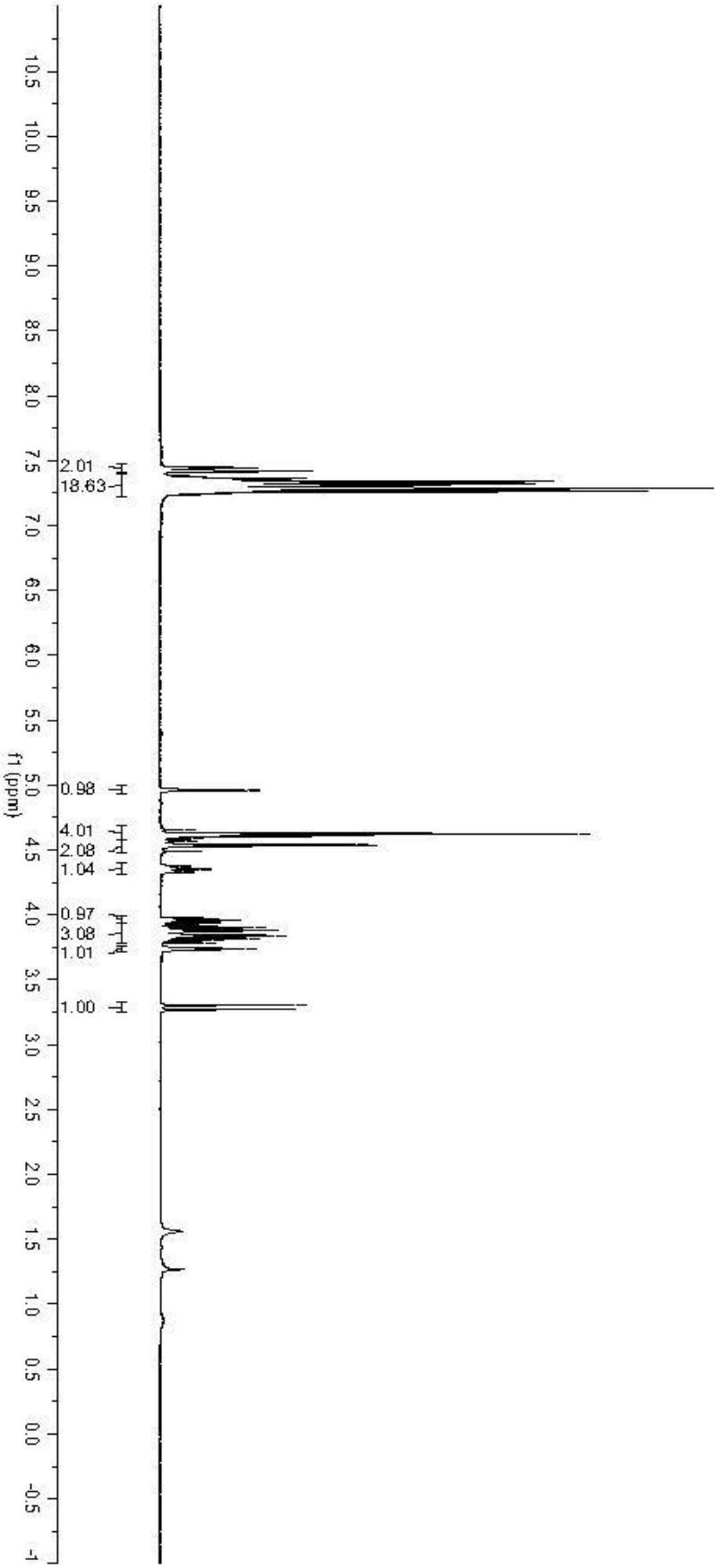

BnO
BnO
HO
O
OBn
SnBu3
MR18
(13C NMR, 75 MHz, CDCl3)

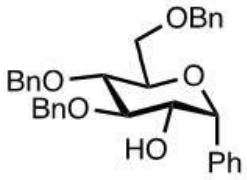

OBn
BnO
BnO
O
HO
SnBu3
MR18


OBn
BnO
BnO
O
HO
SnBu3
MR18
J = 143 Hz

48= ZF coupling product of MR18 with 3-iodotoluene

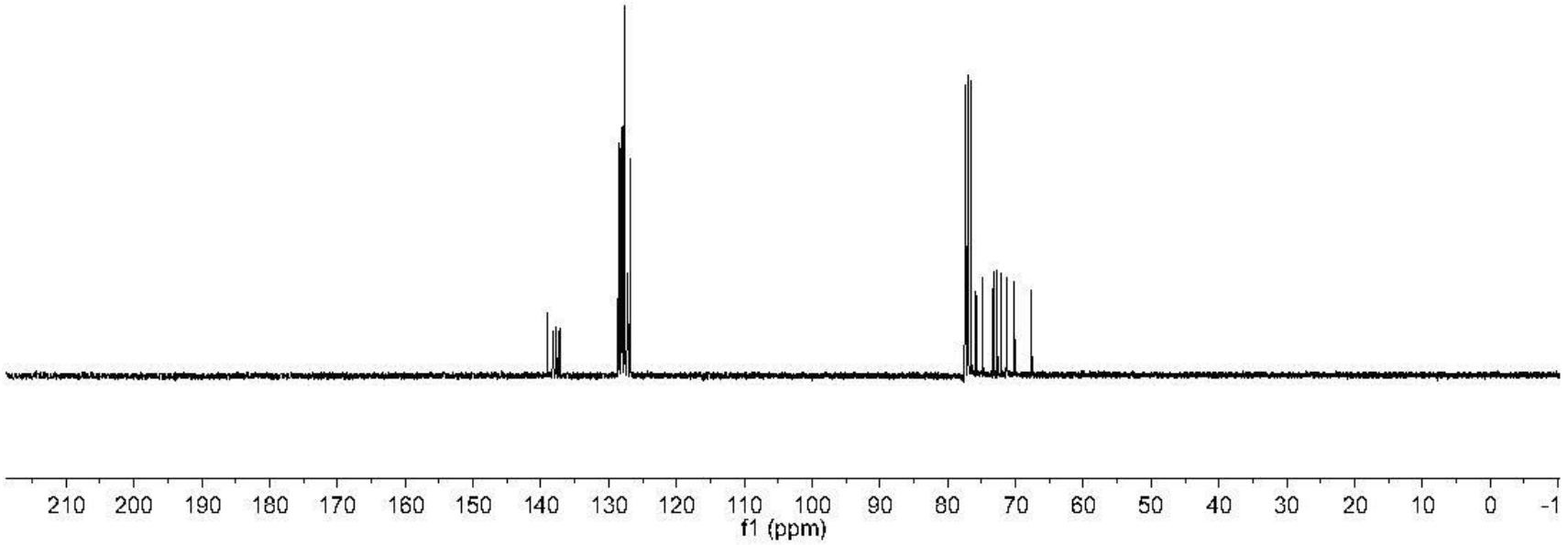




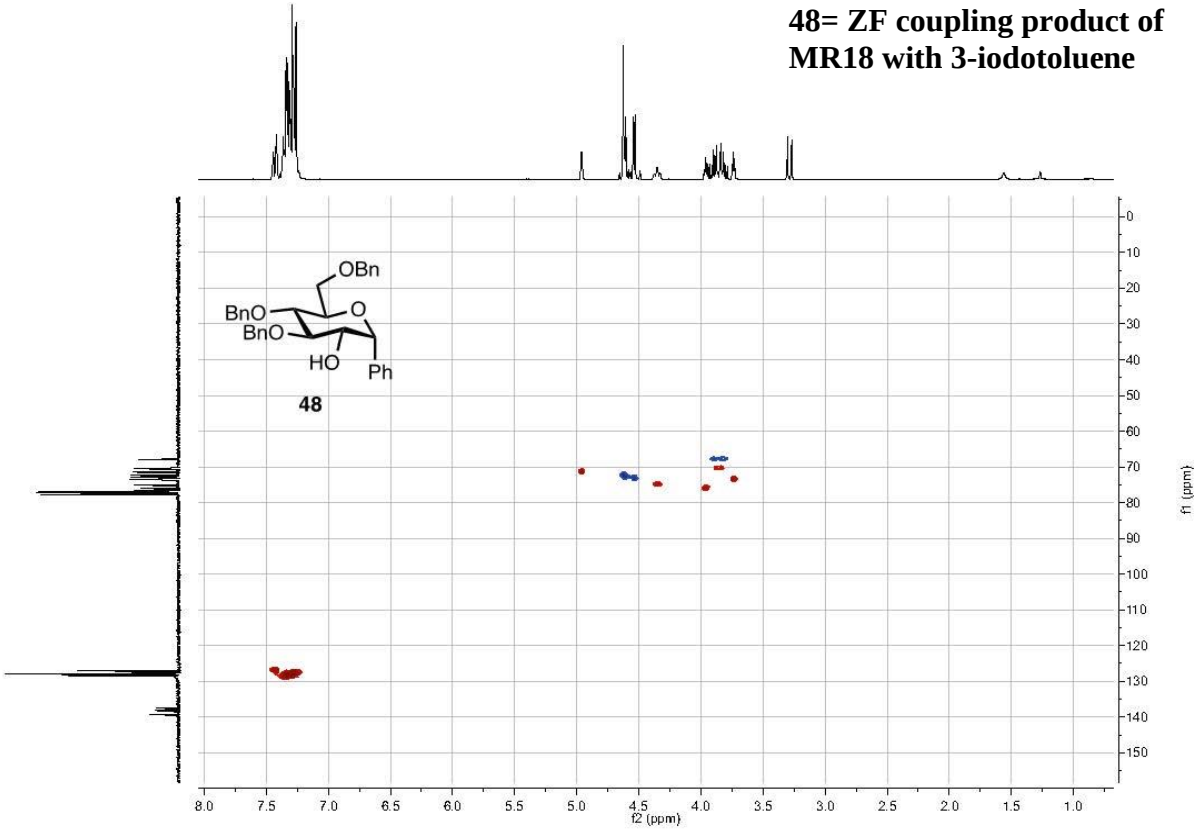


48

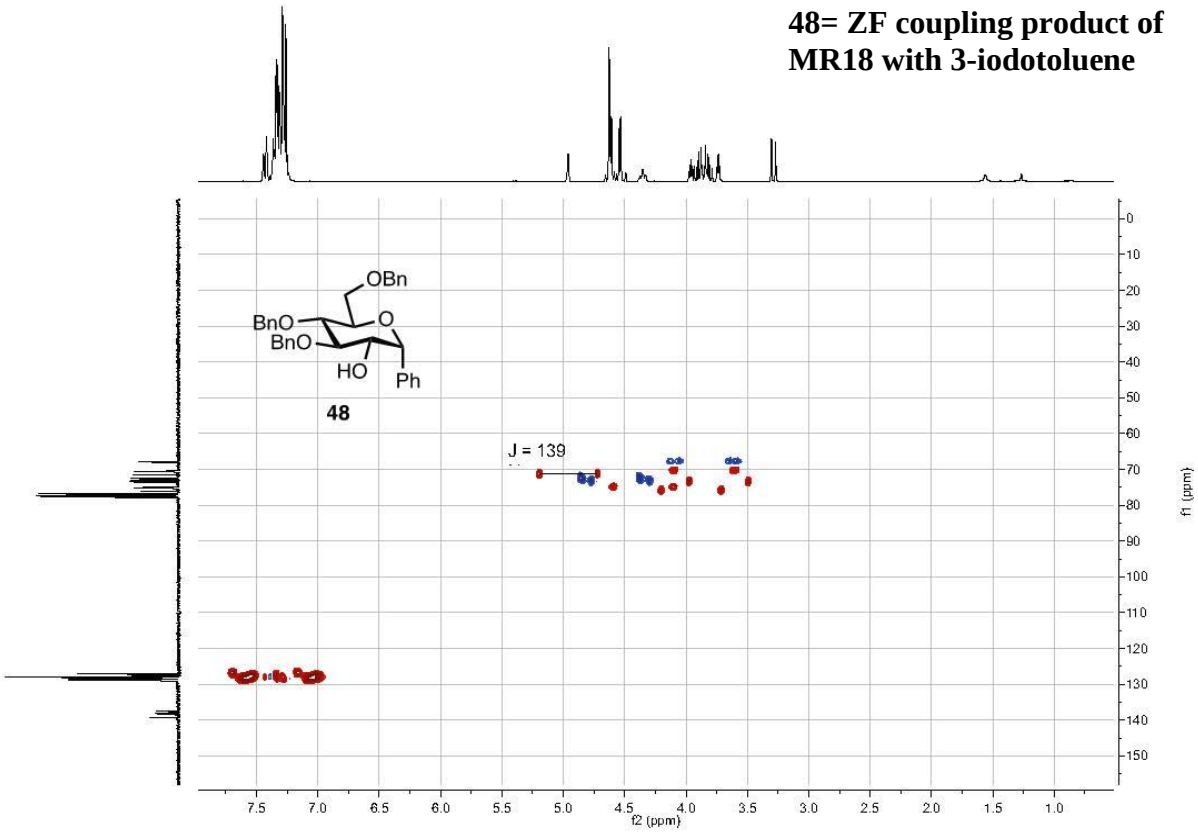
48= ZF coupling product of MR18 with 3-iodotoluene

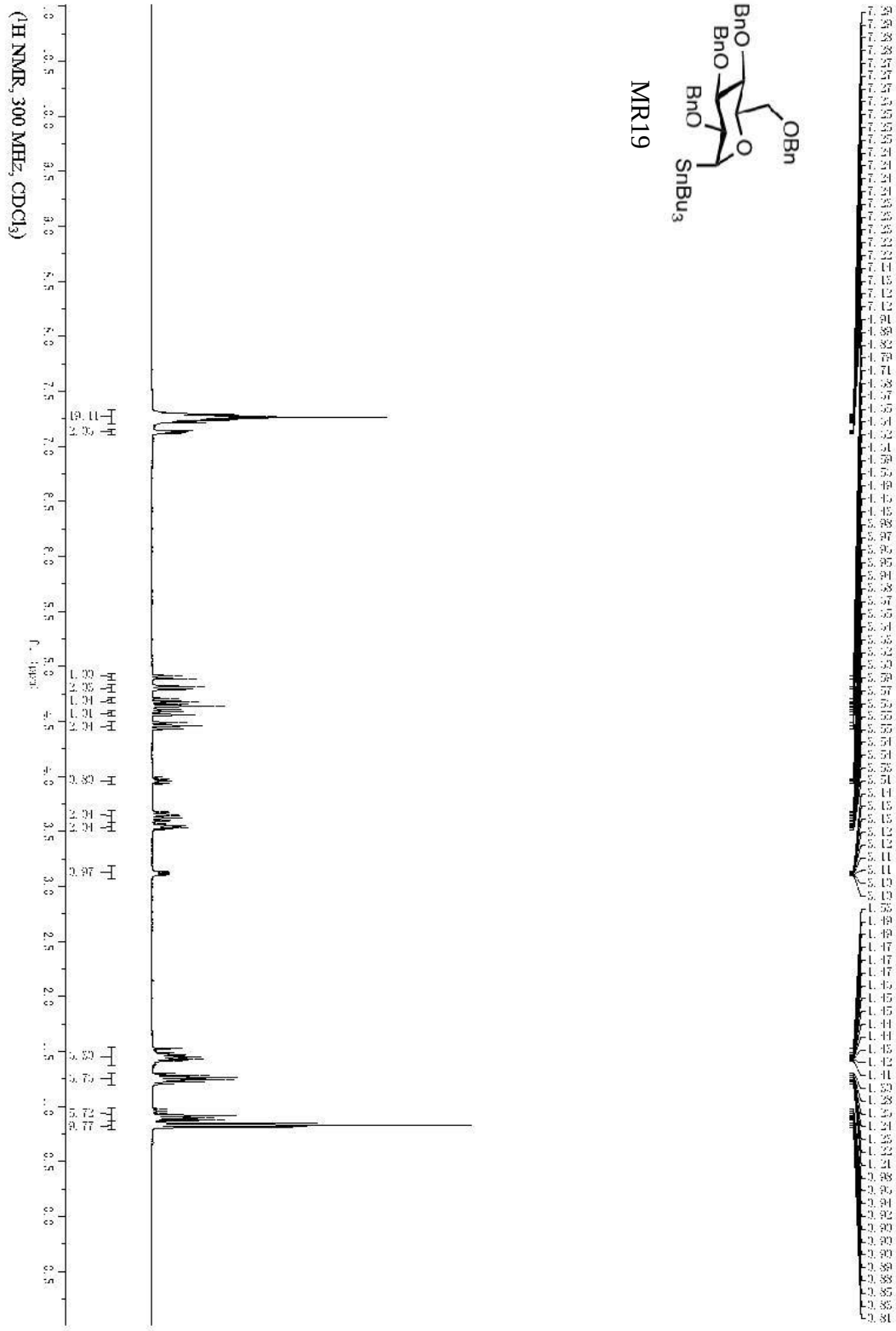


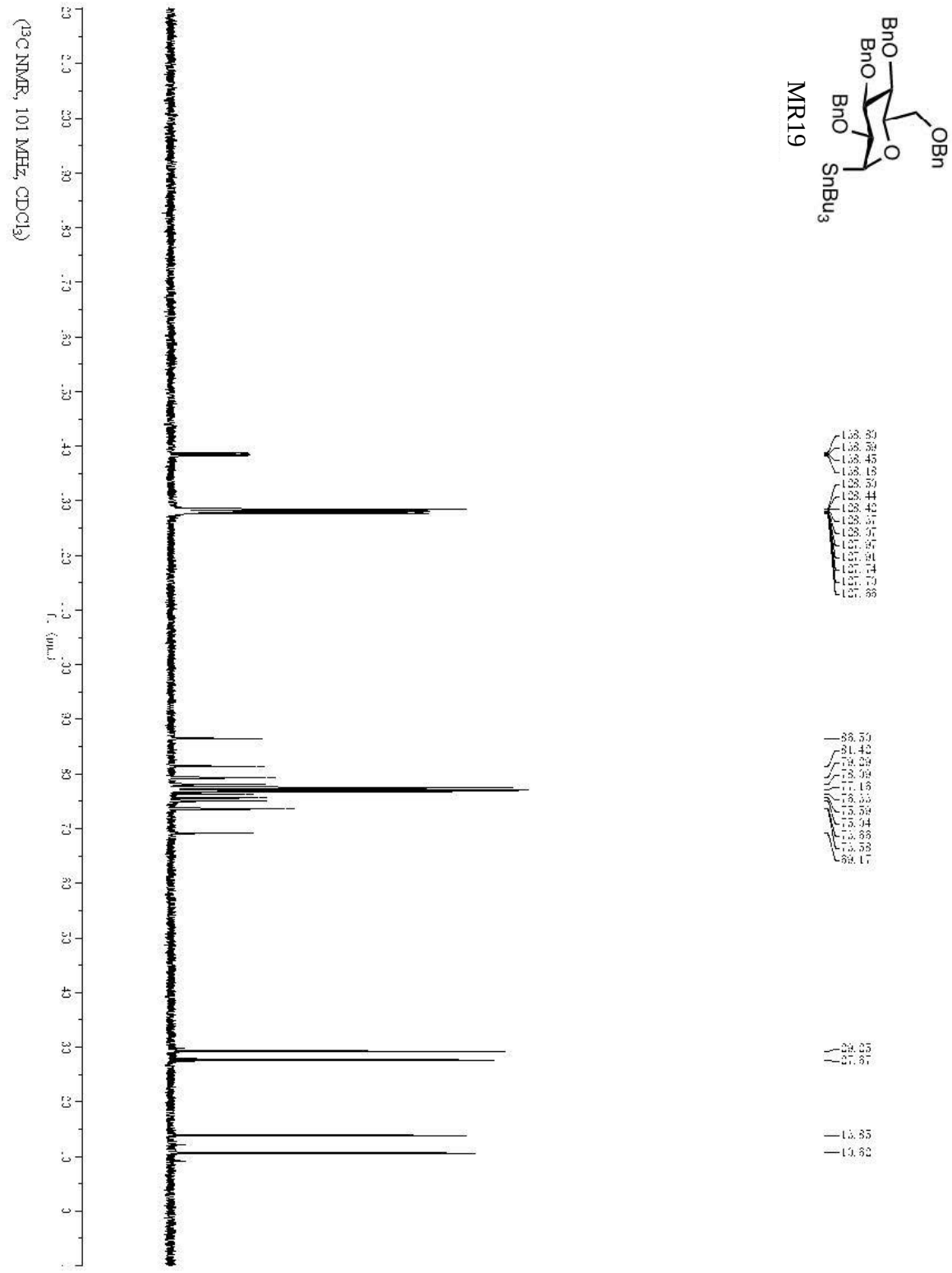
48= ZF coupling product of MR18 with 3-iodotoluene

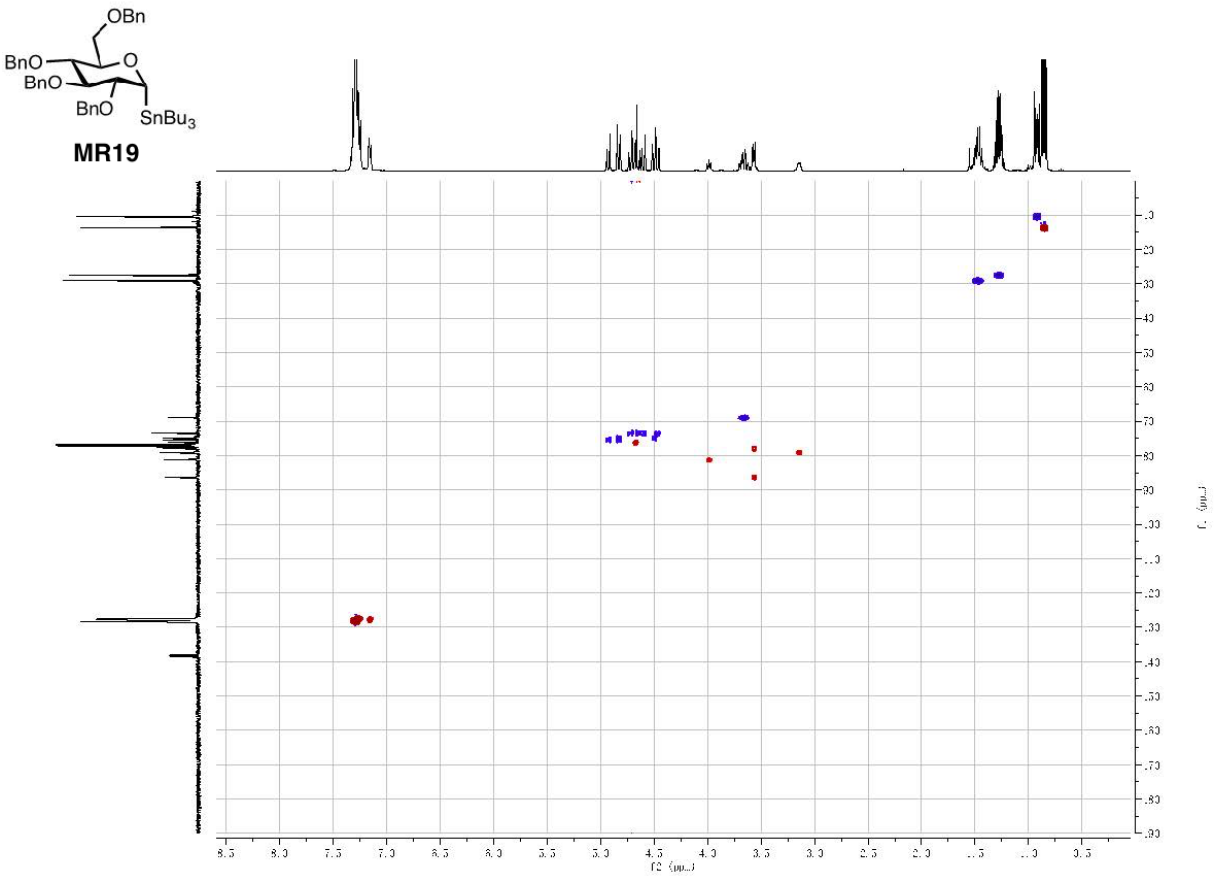


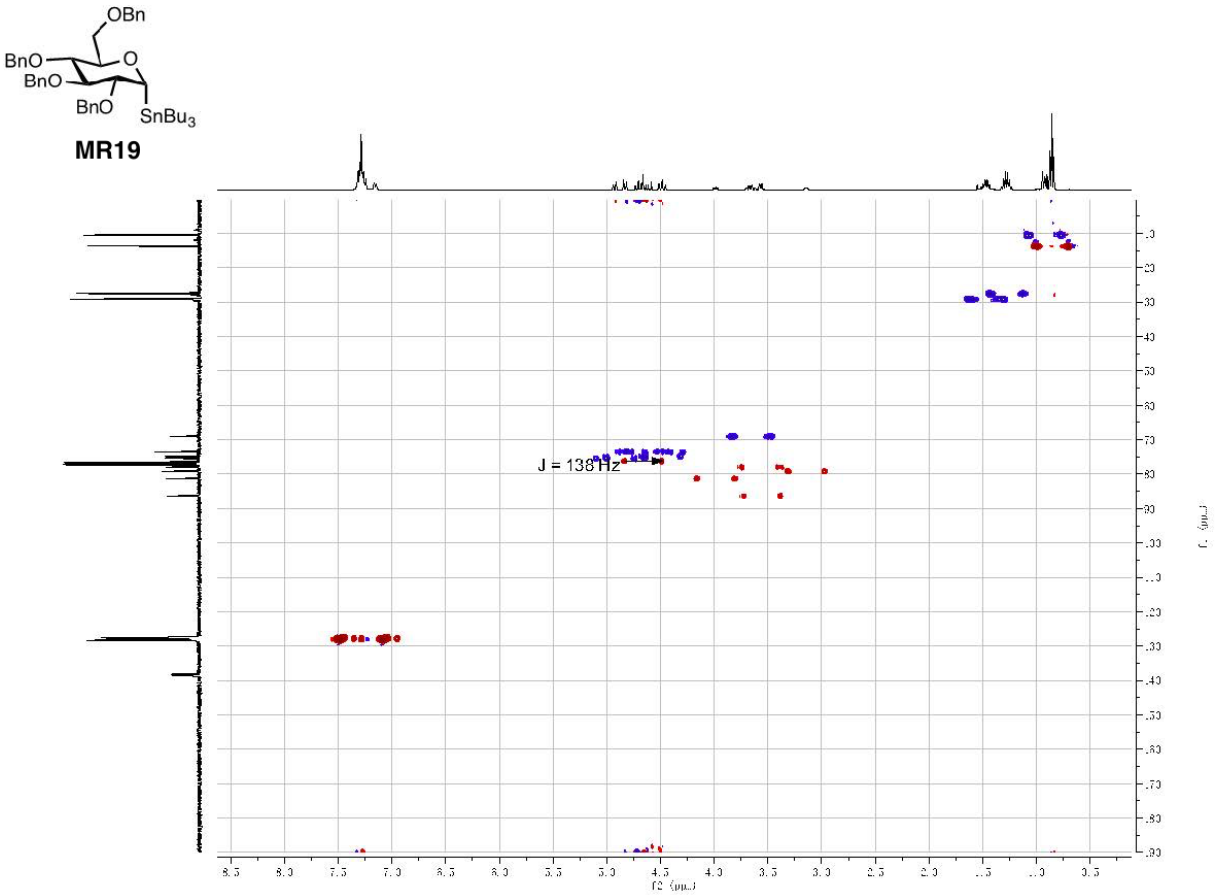
48= ZF coupling product of MR18 with 3-iodotoluene



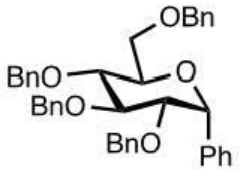

BnO
BnO
BnO
O
OBn
SnBu3
MR19
(^{1}H NMR, 300 MHz, CDCl$_3$)


MR19
BnO
BnO
BnO
OBn
O
SnBu3
(^{13}C NMR, 101 MHz, CDCl$_3$)

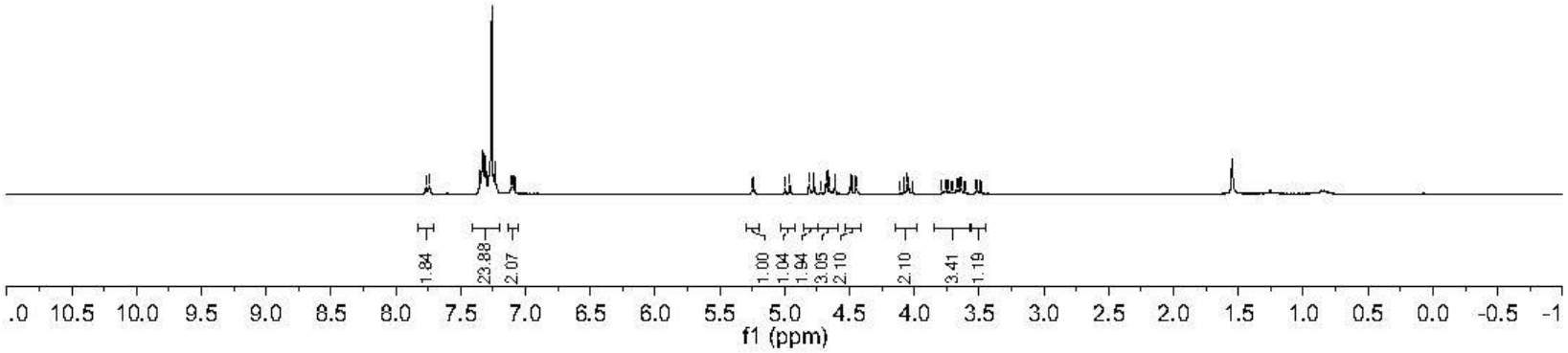

OBn
BnO
BnO
BnO
O
SnBu3
MR19

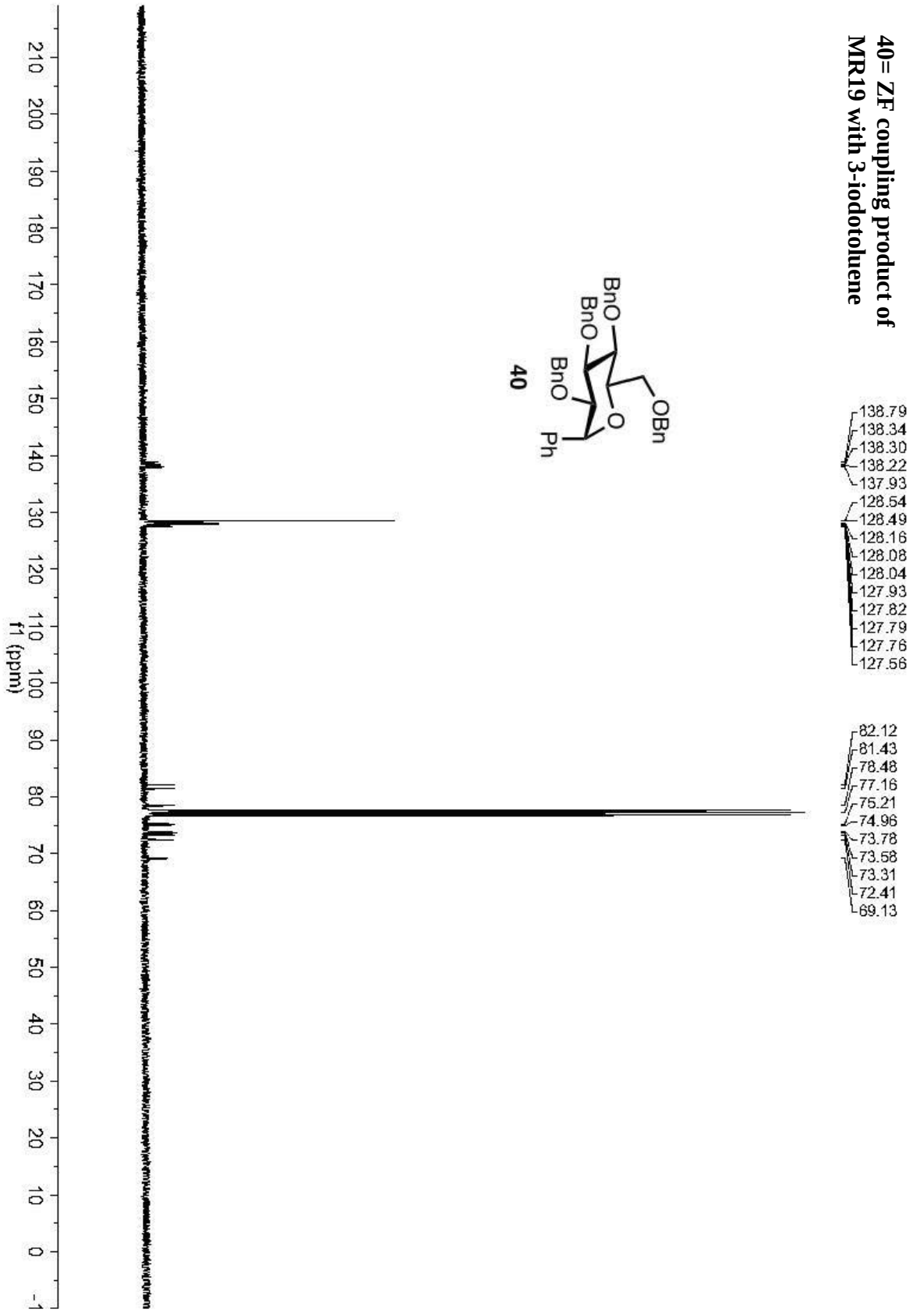

OBn
BnO
BnO
BnO
O
SnBu3
MR19
J = 138 Hz

40= ZF coupling product of MR19 with 3-iodotoluene

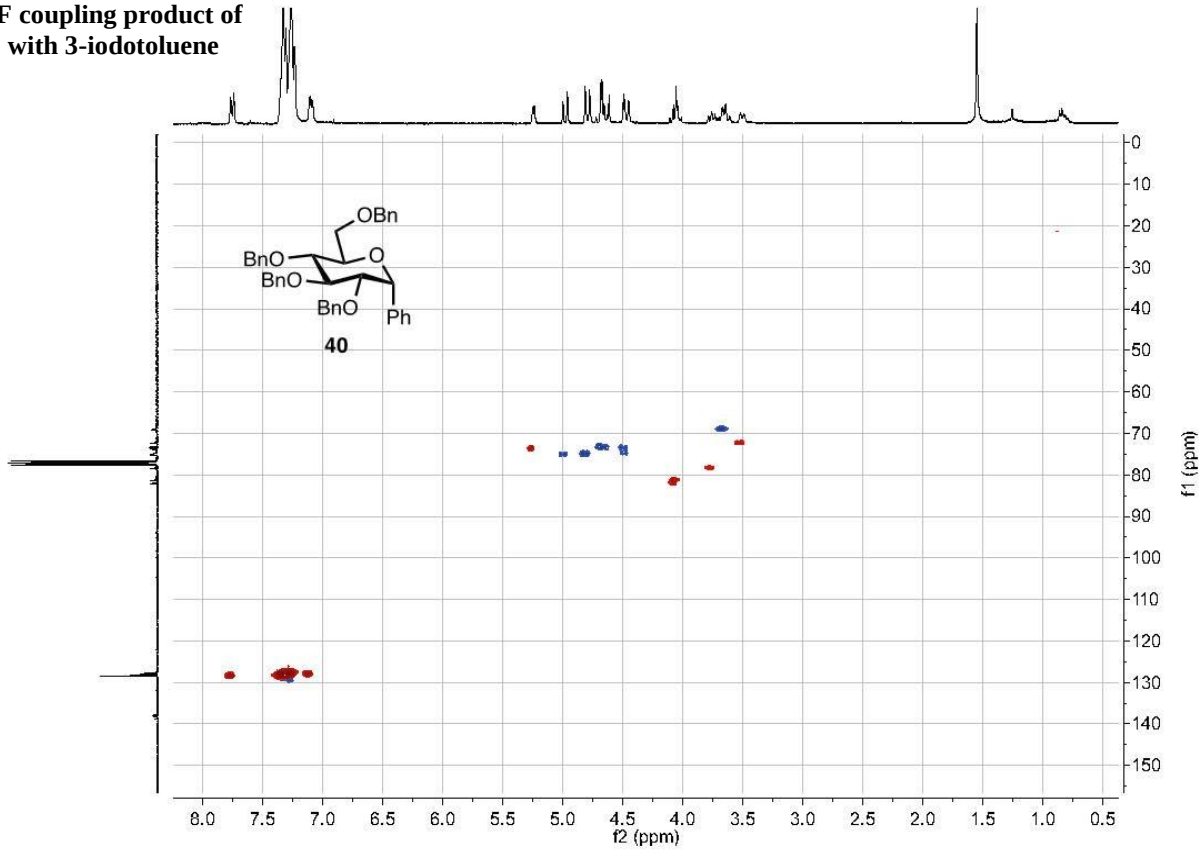


40

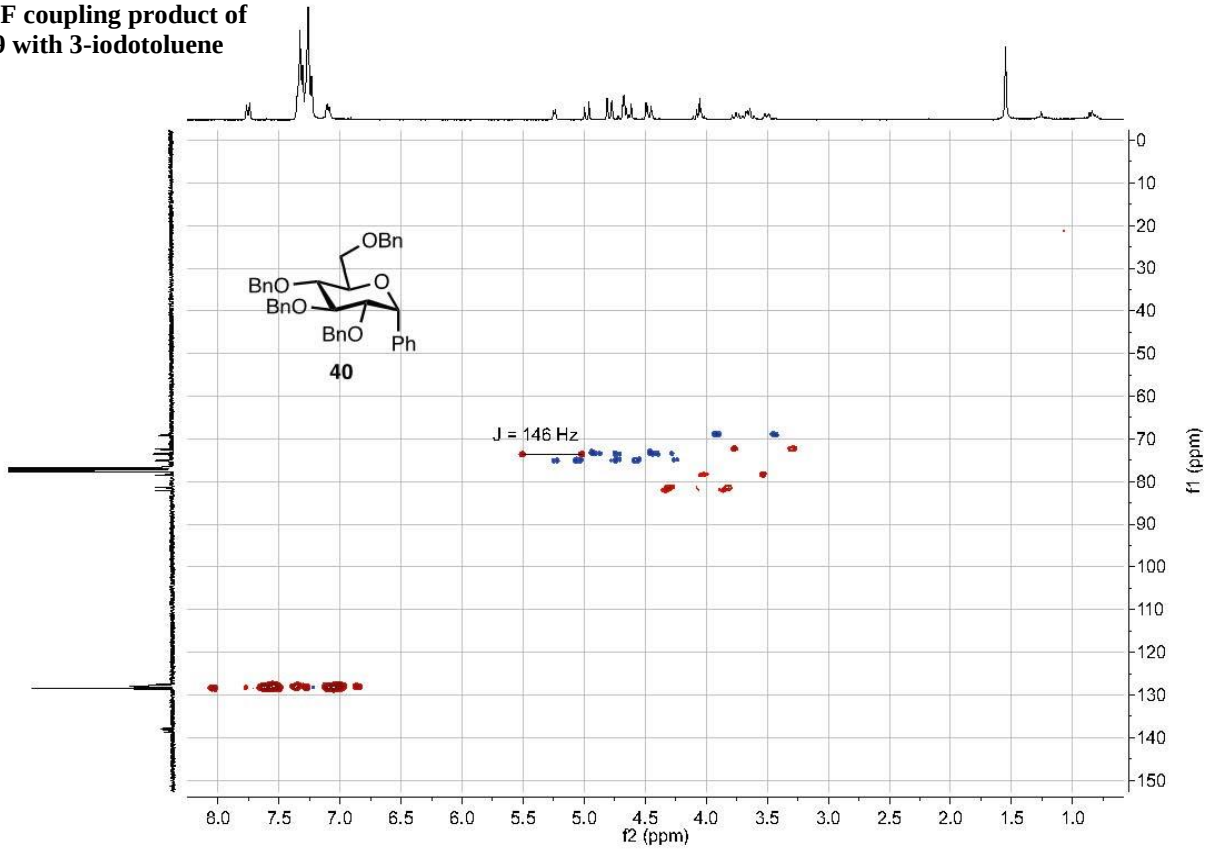


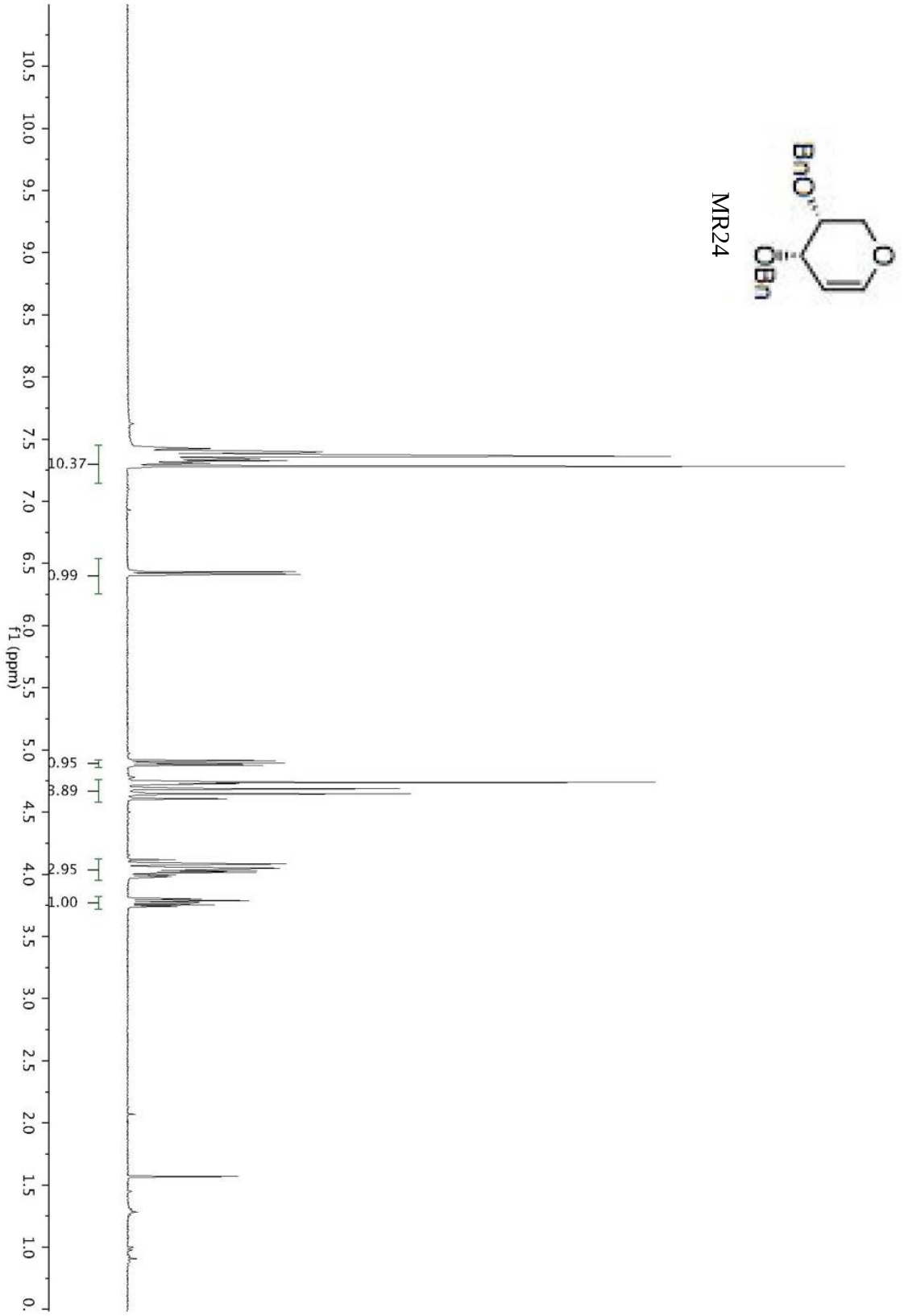

40= ZF coupling product of MR19 with 3-iodotoluene
BnO
BnO
BnO
O
OBn
Ph
40
138.79
138.34
138.30
138.22
137.93
128.54
128.49
128.16
128.08
128.04
127.93
127.82
127.79
127.76
127.56
82.12
81.43
78.48
77.16
75.21
74.96
73.78
73.58
73.31
72.41
69.13
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1

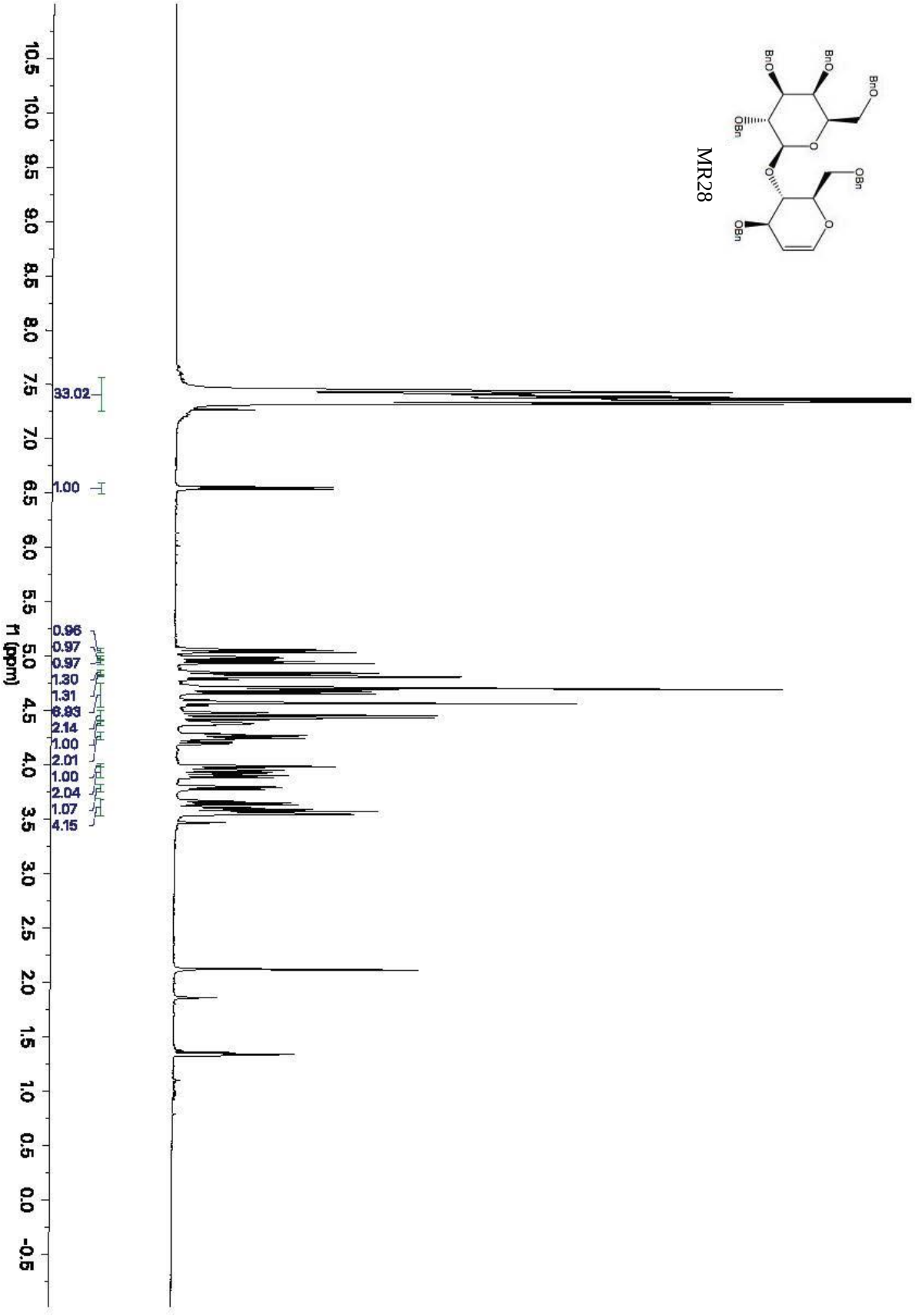
40= ZF coupling product of MR19 with 3-iodotoluene



40= ZF coupling product of MR19 with 3-iodotoluene




BnO
OBn
O
MR24
10.37
0.99
0.95
3.89
2.95
1.00
f1 (ppm)


MR28
BnO
BnO
BnO
OBn
OBn
OBn
O
O
O
33.02
1.00
0.96
0.97
0.97
1.30
1.31
6.93
2.14
1.00
2.01
1.00
2.04
1.07
4.15
f1 (ppm)
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5

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