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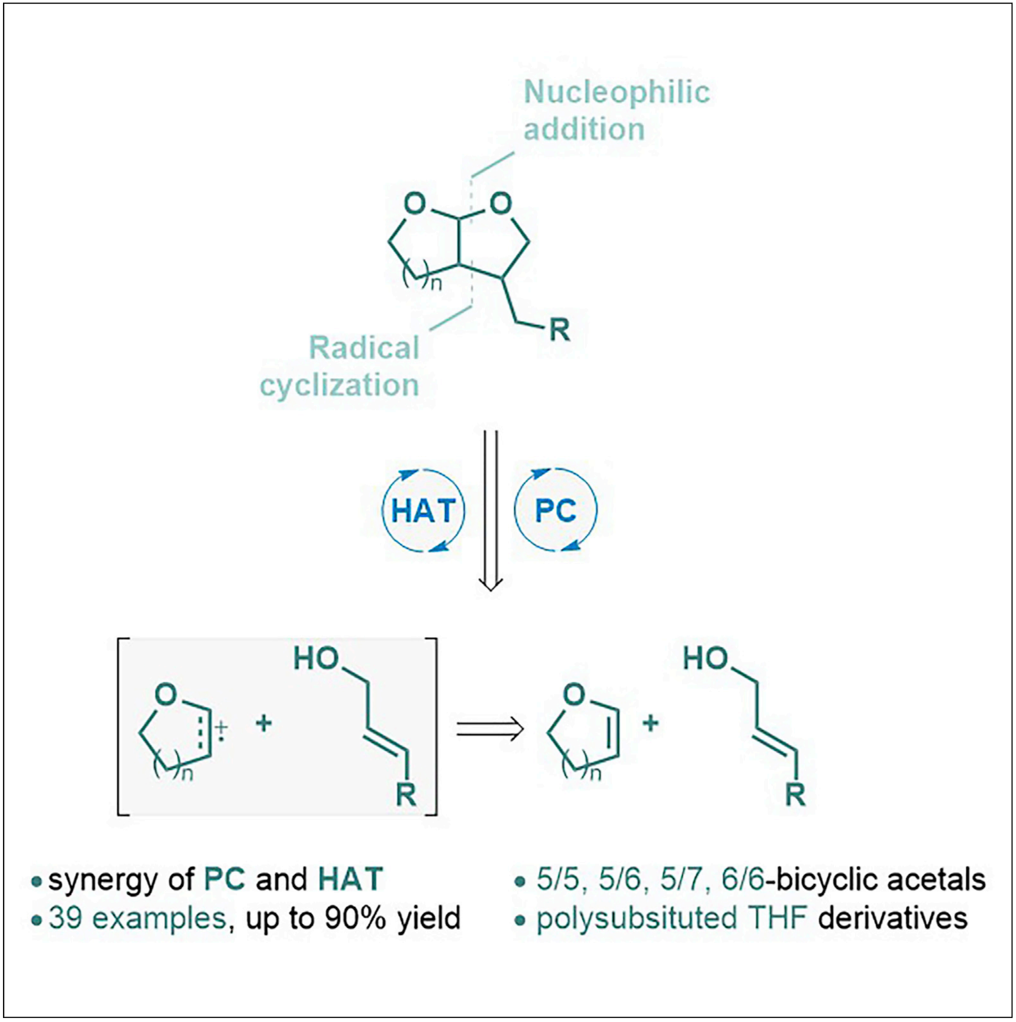

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HIGHLIGHTS

Synergistic catalysis of photocatalyst and HAT reagent

5/5, 5/6, 5/7, 6/6 bicyclic acetals and polysubstituted THF formed in one step

High stability of bicyclic acetal in SIF and SGF

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Direct Synthesis of Bicyclic Acetals via Visible Light Catalysis

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SUMMARY

Polysubstituted bicyclic acetals are a class of privileged pharmacophores with a unique 3D structure and an adjacent pair of hydrogen bond acceptors. The key, fused acetal functionality is often assembled, via intramolecular cyclization, from linear substrates that are not readily available. Herein, we report a formal cycloaddition between cinnamyl alcohols and cyclic enol ethers under ambient photoredox catalysis conditions. Polysubstituted bicyclic acetals can be prepared in one step from readily available building blocks. Employment of sugar-derived enol ethers allows easy access to a library of scaffolds with intriguing conformation and medicinal chemistry potential.

INTRODUCTION

Bicyclic acetals are prevalent structural motifs in natural products, pharmaceuticals, and agrochemicals (Pirrung et al., 1989; Brady et al., 2004; Alonso et al., 2005; Henry and Townsend, 2005; Zhou and Corey, 2005; Baird et al., 2009; Sastraruji et al., 2010; Mori et al., 2015; Ghosh et al., 2017; Karimov et al., 2018; Pan et al., 2018; Lenci et al., 2019; Bera et al., 2018). Compared with other privileged pharmacophores, such as biaryls, bicyclic acetals possess rigorous conformational rigidity, low molecular weight, and a pair of endogenous hydrogen bonding acceptors (King et al., 2004; Surleraux et al., 2005; Ghosh et al., 2009, 2011). They are strong binders to a number of important enzymes and do not carry the liability of instability at low pH environments like their acyclic counterparts (Evans et al., 1981; Coppola, 1984; Tufariello and Winzenberg, 1986; Stern and Swenton, 1989; Roush and Sciotti, 1994). For instance, the bicyclic acetal interacts tightly with two neighboring amino acid residues in HIV-1 protease (Asp-29 and Asp-30), making them excellent candidates for antiviral agents (Figure 1) (King et al., 2004; Surleraux et al., 2005; Ghosh et al., 2009, 2011).

Considerable attention has been drawn to access bicyclic acetals. In general, two synthetic approaches are employed, both of which require linear synthesis of starting materials. The first approach uses gem-disubstituted alkenes bearing two terminal hydroxyl groups that can undergo Wacker-type oxidation, followed by ketalization to furnish the target skeleton (Figure 2A) (Alonso et al., 1998, 2003, 2011; Lorenzo et al., 2000a, 2000b; Roggenbuck et al., 2002; Messerle and Vuong, 2007; Velthuisen et al., 2013). The second option starts from α-halogenated monocyclic acetal. Halide atom abstraction generates an alkyl radical that is captured intramolecularly by a double or triple bond. This Ueno-Stork-type annulation has often been adopted to synthesize the bicyclic acetal core structures (Figure 2B) (Ueno et al., 1982; Stork et al., 1983; Cossy et al., 1994; Yanada et al., 2004; Hayashi et al., 2005; Fukuyama et al., 2016; Hwang et al., 2016; Kyne et al., 2018; Thapa et al., 2017; Venning et al., 2017). Both protocols feature intramolecular cyclization via pre-assembly start materials, which decreases structure versatility, especially when it comes to multisubstituted bicyclic acetals. We envisioned a formal cycloaddition, from readily available olefinic substrates, might present an alternative and modular approach to this type of structures. Herein, we report visible-light-mediated, formal [3 + 2] cycloadditions between commercially available allylic alcohols and cyclic enol ethers (Figure 2C). This transformation delivers the desired bicyclic acetals in a single step and polysubstituted analogs can be accessed.

In recent years, we developed a series of formal cycloaddition reactions involving styrenes catalyzed by strong photooxidants, acridinium salts (Riener and Nicewicz, 2013; Wang et al., 2017; Wu et al., 2018). Based on the work before, we envisioned that, if the styrene substrates bear a free hydroxy group, an

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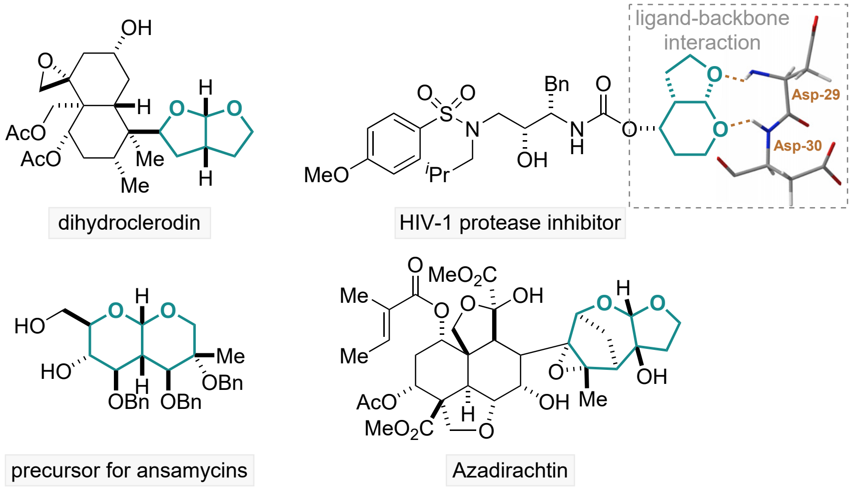


Figure 1. Examples of Bioactive Compounds Containing Bicyclic Acetal

intramolecular event might occur to deliver cyclic acetals. If cyclic enol ethers are employed, the desired bicyclic acetal products might be obtained.

RESULT AND DISCUSSION

Our investigation began using cinnamyl alcohol and dihydropyran (DHP) as substrates. Preliminary trials, using PS-A and PhSSPh as catalysts, afforded the target bicyclic acetal (**1**) in 25% yield (Table 1, entry 1). The [5, 6] fused ring scaffold is in *cis*-configuration and moderate dr was observed for the pendant benzyl group (dr = 1.8:1). Side products of DHP were also observed concomitant with product formation. It appears that the addition of DHP to its radical cation **A** (Figure 2C) might be a competing major side reaction, giving rise to polymeric side products. Increasing the concentration of DHP effectively improves conversion, and high yields were obtained when 4 equiv. of DHP was used (entry 2). Additional acridinium salts were examined, and it was determined that the identity of both the counter ion and N-substituent are important for this reaction (entries 3 and 4). Transition metal-based photosensitizers are incompetent photooxidants, and no desired cycloadduct **1** was detected under these conditions (entries 5 and 6). A survey of additional solvents confirms 1, 2-dicholoethane is the preferred reaction medium (entries 7–9). When either photocatalyst or light is omitted, the cycloadduct is not observed and PhSSPh is also essential to product formation.

The divergent aspect of this transformation was evaluated using various allylic alcohols and cyclic enol ethers (Figure 3). Cinnamyl alcohols show broad tolerance for substitution and electronic perturbation (products **1**–**4**). Fused aryl substituents can be accommodated by the standard reaction conditions (products **5** and **6**). Both α- and γ-alkyl-substituted cinnamyl alcohols undergo smooth cycloaddition to yield bicyclic acetals bearing a vicinal stereogenic center (products **7** and **8**). Heteroaryl analogs react with DHP in good efficiency (products **9**–**12**). Besides DHP, cyclic enol ethers with different ring size show similar efficiency in forming the radical cation intermediate. The one-step protocol affords 5/5-7 fused cyclic acetals in moderate to good yield, some of which are undocumented scaffolds. In addition to cinnamyl alcohol, 2-aryl substituted allylic alcohols undergo formal [4 + 2] cycloaddition with DHP to give cyclic acetals with 6/6 ring juncture (products **15**, **17**). Alkyl allylic alcohols are also applicable to this formal cycloaddition reactions. However, we experienced isolation difficulties for certain substrates. For example, 2-ethylprop-2-en-1-ol reacted smoothly to give the corresponding [6,6] bicyclic acetal **16**. On the other hand, the reaction using 3-methylbut-2-en-1-ol suffered from inseparable side products. NOE experiments confirmed formal *cis*-cycloaddition. Although the diastereoselectivity of the described reaction is moderate, it can be particularly valuable for drug screening, when biologically preferred stereochemistry is unknown. Alkynes can also be intercepted by the radical ring closure. Propargyl alcohols react with DHP to yield bicyclic acetals with an exocyclic double bond (products **18, 19, 20**).

Further substitution of those bicyclic acetals can be accomplished using readily available enol ethers derived from monosaccharides (Figure 4). Natural product-like, polyoxy-substituted bicyclic acetals can

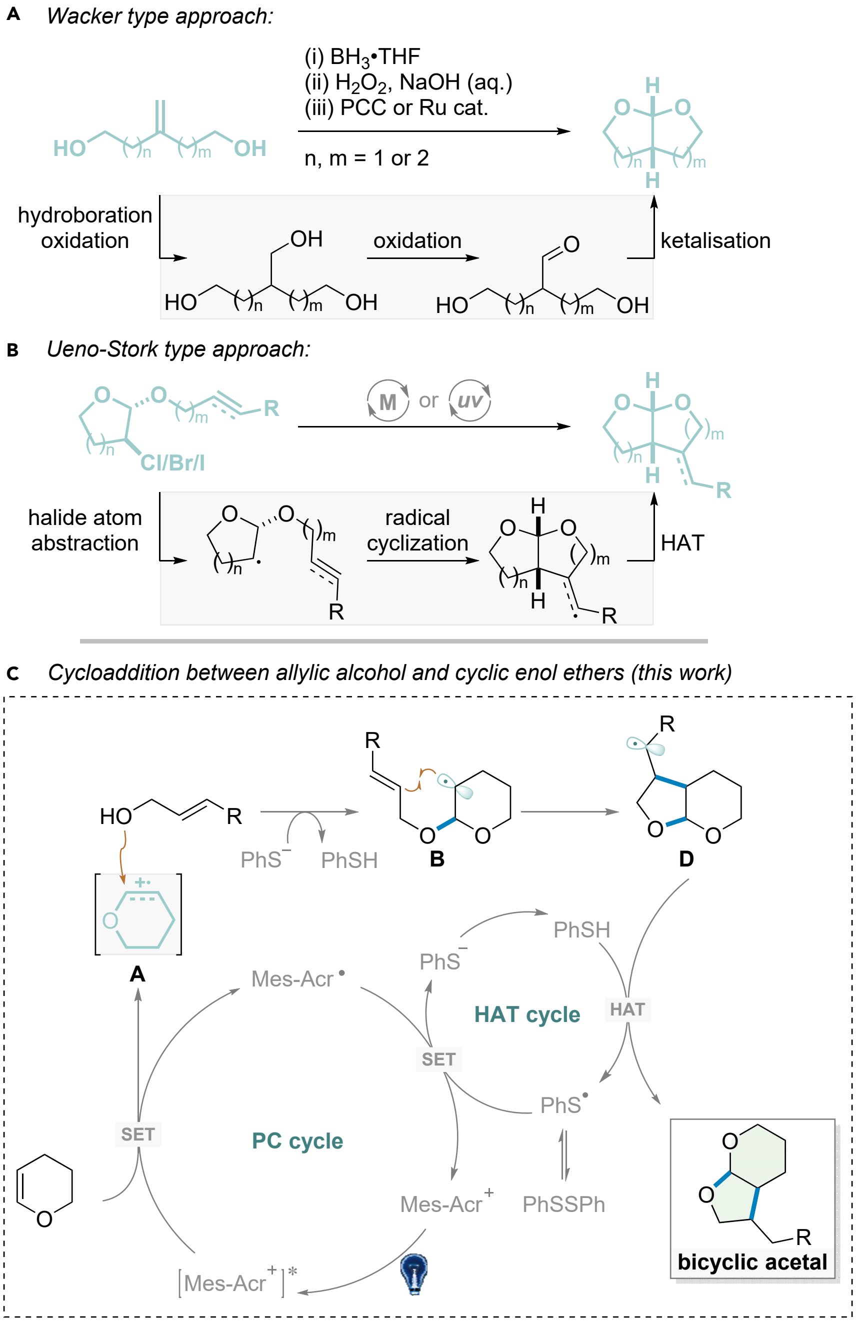


Figure 2. Strategies for Constructing Bicyclic Acetals

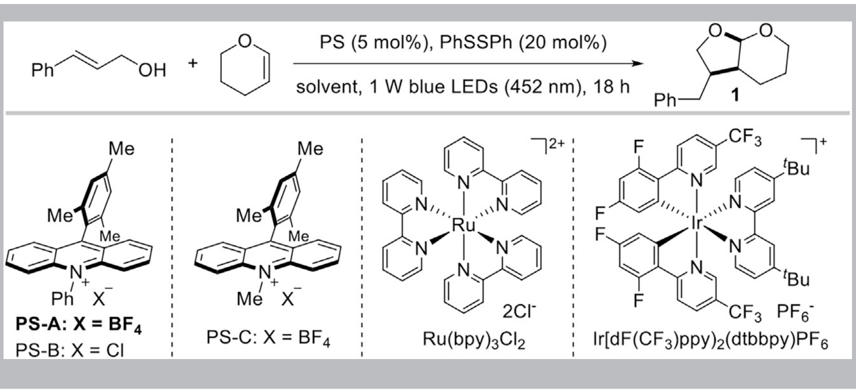
(A) Wacker type approach.

(B) Ueno-Stork type approach.

(C) Cycloaddition of allylic alcohol and cyclic enol ethers.

be prepared in moderate yield (Jiang et al., 2016). The stereochemistry of the substituents is predefined by the type of sugar starting materials used. Biological evaluation of this intriguing compound library is currently underway.

This cycloaddition can also be extended beyond cyclic enol ethers, as substituted vinyl ethers were also investigated against the standard reaction conditions (Figure 5). The reactions maintain comparable



Entry	Photosensitizer (PS)	Solvent	DHP (Eq.)	Yield (%)
1	PS-A	DCE	1	25
2	PS-A	DCE	4	95 (81)
3	PS-B	DCE	4	10
4	PS-C	DCE	4	5
5	$Ru(bpy)_3Cl_2$	DCE	4	0
6	$Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$	DCE	4	0
7	PS-A	MeCN	4	35
8	PS-A	toluene	4	0
9	PS-A	DMF	4	0

Table 1. Condition Survey for [3 + 2] Cycloaddition Leading to Bicyclic Acetals

Unless otherwise specified, reactions were performed using photosensitizer (0.01 mmol, 5 mol%), PhSSPh (0.04 mmol, 20 mol %), cinnamyl alcohol (0.2 mmol), dihydropyran (DHP) in 3 mL of solvent. Yield of **1** was determined by GC using *n*-decane as internal standard. Number in parentheses is isolated yield.

efficiency and selectivity. Polysubstituted tetrahydrofuran (THF) analogs can be accessed in good yield. Ethyl vinyl ether (EVE) reacts smoothly with cinnamyl alcohols to give 2, 4-substitued THFs (products **28** and **29**). β-Substituted EVEs lead to 2,3,4-trisubstituted products (**30–39**). Interestingly, alkyl allylic alcohols are good substrate for β-phenyl EVEs. The relatively high redox potential of the unactivated double bond in these alcohols does not support single electron (SET) oxidation by the excited photosensitizer (Romero and Nicewicz, 2014). The olefin moiety of the enol ether is more prone to SET oxidation (for β-phenyl EVE, $E_{p/2}$ = +1.20 V versus SCE). As a consequence, β, β-disubstituted allylic alcohols can react with β-phenyl EVE to deliver a product bearing a quaternary carbon center (**35**) with complete anti-selectivity. Isolated double bonds in substrates do not interfere with the photoredox process (**37**). A D-galactopyranose-derived allylic alcohol was also applied to the formal cycloaddition to give product with an additional sugar moiety (**39**).

The reaction between cinnamyl alcohol and DHP was monitored closely using GC. We found that acetal **40** was formed immediately upon mixing. It is intriguing that the concentration of **40** remained nearly consistent, at ca. 22%, for the first half of the reaction period, and bicyclic acetal product **1** was gradually formed (Figure 6).

Subjecting **40** alone to the standard reaction conditions failed to yield product **1** (Figure 6A), suggesting intramolecular cyclization is not operative. However, mixing **40** with DHP under the same conditions generates product **1** in 88% yield (GC, Figure 6B). This result indicates **40** might be a resting state, which helps prevent homodimerization of cinnamyl alcohols (Hamilton and Nicewicz, 2012; Grandjean and Nicewicz, 2013; Nicewicz and Nguyen, 2014; Perkowski et al., 2015; Margrey and Nicewicz, 2016). A competition experiment using **40** and substrate **41**, was carried out (Figure 6C). Comparable yield of **1** and **3** was

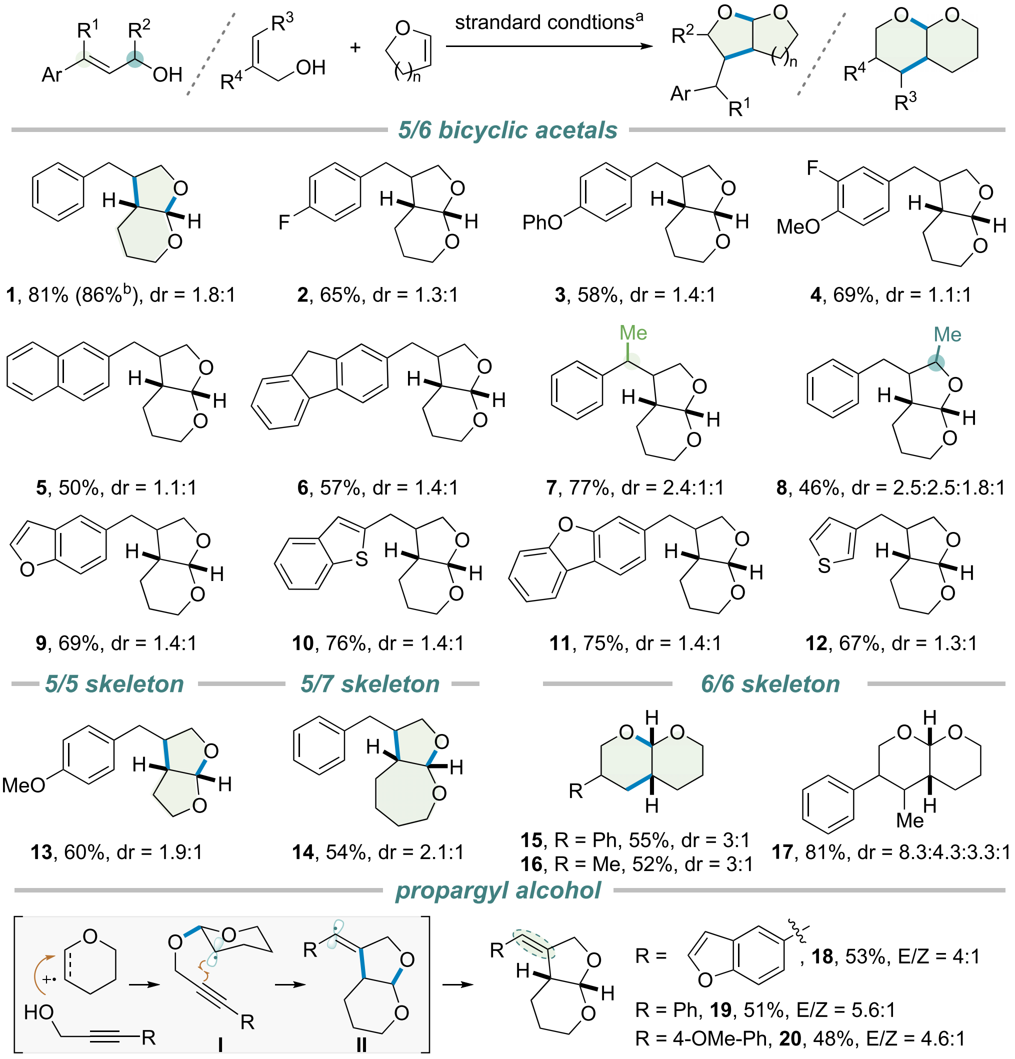
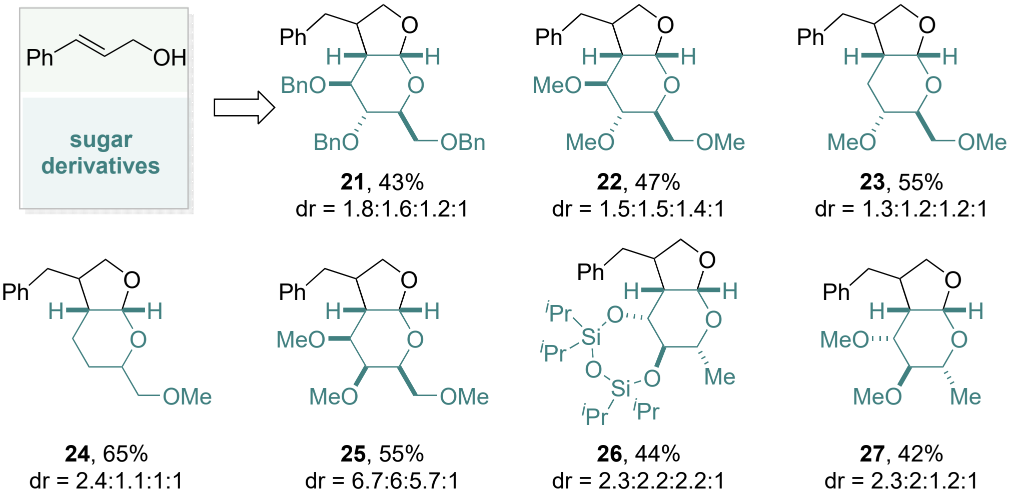


Figure 3. Substrate Scope for Bicyclic Acetals

Reaction conditions: photosensitizer (0.01 mmol, 5 mol%), PhSSPh (0.04 mmol, 20 mol%), allylic alcohol (0.2 mmol), dihydropyran (0.8 mmol) in 3 mL of DCE. Yield in parenthesis was for 1 mmol preparative-scale reaction. [a]Reaction conditions: photosensitizer (0.01 mmol, 5 mol%), PhSSPh (0.04 mmol, 20 mol%), allylic alcohol (0.2 mmol), dihydropyran (0.8 mmol) in 3 mL of DCE. [b]Yield in parenthesis was for 1 mmol preparative-scale reaction.

obtained. These results suggest acetal **40** might also serve as a competitive nucleophile that reacts with DHP radical cation. It is also plausible that the combination of **40**, DHP, and the acridinium salt generates catalytic amounts of acid that cause retro acetal formation to free up cinnamyl alcohol.

Unlike previous cycloaddition reactions involving styrene, DHP ($E_{p/2}$ = +1.51 V vs. SCE) is more prone, than cinnamyl alcohol ($E_{p/2}$ = +1.77 V vs. SCE), to single electron oxidation. Presumably, the acridinium salt is first excited to a highly oxidizing state (Mes-Acr+* $E_{p/2}$ = +2.06 V versus SCE) by blue LED irradiation. In contrast to nucleophilic addition to styrene-derived radical cation, which features exclusive anti-Markovnikov selectivity, the DHP radical cation reacts with the allylic alcohol at its α-carbon, likely due to oxonium stabilization (Schmittel, 1994). DHP is oxidized by Mes-Acr^{+*} to generate a key DHP radical cation (Roth et al., 2016), Subsequently, cinnamyl alcohol, or acetal intermediate **40** formed during the reaction, acts as a nucleophile to trap the DHP radical cation, which is followed by a Ueno-Stork-type annulation (Alonso et al., 2011; Velthuisen et al., 2013; Ueno et al., 1982; Stork et al., 1983; Cossy et al., 1994; Yanada et al., 2004; Hayashi et al., 2005; Fukuyama et al., 2016; Hwang et al., 2016; Kyne et al., 2018). Subsequent HAT process, catalyzed by PhSSPh, closes the catalytic cycle.



21, 43%
dr = 1.8:1.6:1.2:1

22, 47%
dr = 1.5:1.5:1.4:1

23, 55%
dr = 1.3:1.2:1.2:1

24, 65%
dr = 2.4:1.1:1:1

25, 55%
dr = 6.7:6:5.7:1

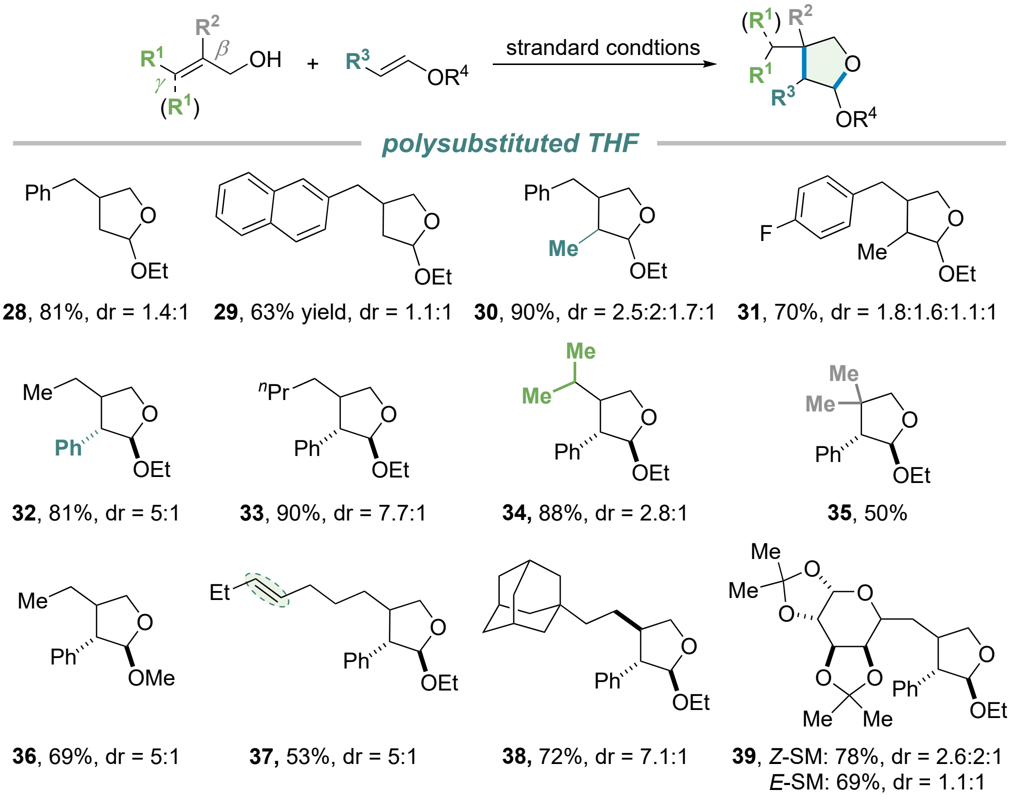
26, 44%
dr = 2.3:2.2:2.2:1

27, 42%
dr = 2.3:2:1.2:1

Figure 4. Structurally Sophisticated Bicyclic Acetals Derived from Saccharides

Reaction conditions: photosensitizer (0.01 mmol, 5 mol%), PhSSPh (0.04 mmol, 20 mol%), allylic alcohol (0.2 mmol), monosaccharides (0.8 mmol) in 3 mL of DCE.

Several cyclic acetals were evaluated for their preliminary metabolic stability. As shown in Table 2 (see also Tables S1–S6), all four products are stable after incubation with simulated intestinal fluid (**SIF**, pH 6.8) for 3 h. Stability after 1-h incubation with simulated gastric fluid (**SGF**, pH 1.2) varies, depending on structure. Bicyclic acetals **15**, **1**, and **27** are more stable than monocyclic product **35**. The 6, 6-bicyclic product **15**



28, 81%, dr = 1.4:1

29, 63% yield, dr = 1.1:1

30, 90%, dr = 2.5:2:1.7:1

31, 70%, dr = 1.8:1.6:1.1:1

32, 81%, dr = 5:1

33, 90%, dr = 7.7:1

34, 88%, dr = 2.8:1

35, 50%

36, 69%, dr = 5:1

37, 53%, dr = 5:1

38, 72%, dr = 7.1:1

39, *Z*-SM: 78%, dr = 2.6:2:1
E-SM: 69%, dr = 1.1:1

Figure 5. Synthesis of Polysubstituted THF Derivatives

Reaction conditions: photosensitizer (0.01 mmol, 5 mol%), PhSSPh (0.04 mmol, 20 mol%), allylic alcohol (0.2 mmol), vinyl ether (0.8 mmol) in 3 mL of DCE.

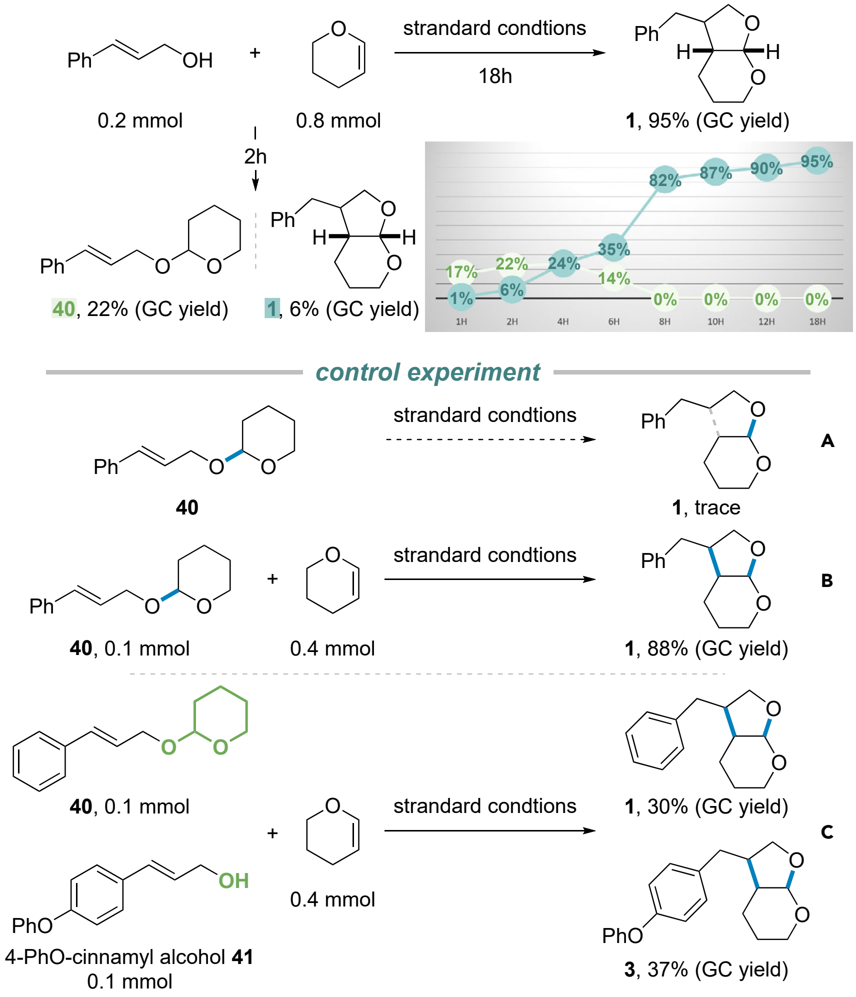


Figure 6. Control Experiments

is more stable than its corresponding 6, 5-bicyclic analog **1**. Substituents on the six-membered ring have impacts on stability as tri-substitution of **1** leads to compound **27**, which is the most stable scaffold tested. This exercise demonstrates that these bicyclic acetals are fairly stable in stimulated intestinal fluids, indicating degradation of these molecules might be very low at major human absorption sites. Furthermore, by modulating ring size and substitution pattern, bicyclic acetals can accomplish good stability in SGF.

	35	15 (Two Isomers)	1	27 (Four Isomers)
SGF, 1 h				
Degradation (%)	99.4	4.4	12.4	1.3
Classification	Unstable	Fairly stable	Unstable	Fairly stable
SIF, 3 h				
Degradation (%)	−2.6	0.1	0.1	0.5
Classification	Fairly stable	Fairly stable	Fairly stable	Fairly stable

Table 2. Stability of Cyclic Acetals in Simulated GI Fluids

Conclusion

In summary, we developed an efficient strategy to prepare libraries of bicyclic acetals from allylic alcohols and cyclic enol ethers. This reaction pathway is distinct from reported [2 + 2], [4 + 2], and linear coupling involving styrenes. Under synergistic catalysis of an acridinium salt and PhSSPh, structurally intriguing scaffolds involving 5/5, 5/6, 5/7, and 6/6 bicyclic acetals are synthesized in one step. This approach can be applied to monosaccharide-derived substrates, gaining access to previously unattainable polysubstituted analogs. Additionally, use of acyclic vinyl ethers offers a straightforward entry to poly-substituted THF derivatives. Preliminary stability studies in simulated gastric fluids demonstrate bicyclic acetals are a promising class of chemical modality for medicinal chemistry.

Limitations of the Study

A transformation in diastereoselective version cannot be realized under the current reaction conditions.

Resource Availability

Lead Contact

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Materials Availability

This study did not generate new unique reagents. All materials used in the work were sourced from public or commercial resources as described under Transparent Methods (see Supplemental Information).

Data and Code Availability

This study did not generate or use any new datasets or machine code.

METHODS

All methods can be found in the accompanying Transparent Methods supplemental file.

SUPPLEMENTAL INFORMATION

Supplemental Information can be found online at https://doi.org/10.1016/j.isci.2020.101395.

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AUTHOR CONTRIBUTIONS

Methodology, F.W., D.A.N., J.C., and Y.H.; Investigation, F.W., L.W., Y.J., and G.Z.; Writing - Original Draft, F.W. and H.S.; Writing - Review & Editing, D.A.N., J.C., and Y.H.; Supervision, D.A.N., J.C., and Y.H.

DECLARATION OF INTERESTS

The authors declare no competing interests.

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Supplemental Information

Direct Synthesis of Bicyclic Acetals via Visible Light Catalysis

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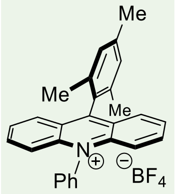
Supporting Information

I. Transparent Methods

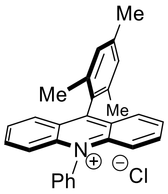
General Information

All solvents were distilled according to general practice prior to use. Solvents for flash column chromatography were technical grade and distilled prior to use. ^{1}H NMR and ^{13}C NMR data were recorded on Bruker 400 MHz (100 MHz for ^{13}C) nuclear resonance spectrometers unless otherwise specified. ^{1}H and ^{13}C NMR chemical shifts are given in ppm relative to $SiMe_4$, with the solvent resonance used as internal reference. Chemical shifts (δ) are given in parts per million and referenced to the residual solvent signal; and all coupling constants are reported in Hz. The following abbreviations were used to explain the multiplicities: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet). Thin-layer chromatography (TLC) was conducted with 0.25 mm Yantai silica gel plates (60F-254) and visualized by exposure to UV light (254 nm) or stained with phosphomolybdic acid in EtOH. Flash column chromatography was performed using Tsingdao silica gel (60, particle size 0.040–0.063 mm). HRMS (ESI) analysis was performed by The Analytical Instrumentation Center at Peking University; Shenzhen Graduate School and (HRMS) data were reported with ion mass/charge (m/z) ratios as values in atomic mass units.

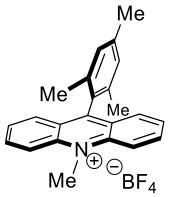
Preparation of acridinium photocatalysts



PS-A



PS-B



PS-C

Photocatalysts (PS-A, PS-B, PS-C) used in this study were synthesized by the method of Fukuzumi et al. (Fukuzumi et al., 2004). Tetrafluoroboric acid (diethyl ether complex) was used for hydrolysis in PS-A and PS-C synthesis. HCl (4.0 M in 1, 4-dioxane) was used for hydrolysis in PS-B synthesis. Spectral data for these compounds matches the reported value in the literature.

9-mesityl-10-phenylacridin-10-ium tetrafluoroborate (PS-A):

Yellow solid. ^{1}H NMR (500 MHz, Chloroform-d) δ 8.14 (s, 2H), 7.89 (dq, J = 14.2, 7.4, 6.8 Hz, 5H), 7.79 (t, J = 7.7 Hz, 2H), 7.75 – 7.69 (m, 2H), 7.60 (d, J = 9.1 Hz, 2H), 7.18 (s, 2H), 2.49 (s, 3H), 1.83 (s, 6H).

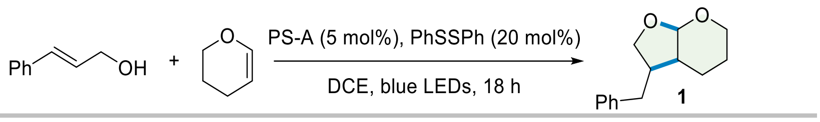
9-mesityl-10-phenylacridin-10-ium chloride (PS-B)：

Yellow solid. ^{1}H NMR (300 MHz, Chloroform-d) δ 8.23 (ddd, J = 8.9, 6.2, 1.8 Hz, 2H), 7.97 – 7.81 (m, 7H), 7.72 (d, J = 7.6 Hz, 2H), 7.59 (d, J = 9.0 Hz, 2H), 7.14 (s, 2H), 2.44 (s, 3H), 1.78 (s, 6H).

9-mesityl-10-methylacridin-10-ium tetrafluoroborate (PS-C):

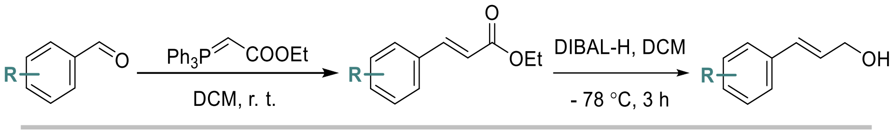
Yellow solid. ^{1}H NMR (300 MHz, Chloroform-d) δ 8.81 (d, J = 9.3 Hz, 2H), 8.41 (ddd, J = 9.3, 6.5, 1.8 Hz, 2H), 8.05 – 7.59 (m, 4H), 7.15 (s, 2H), 5.11 (s, 3H), 2.48 (s, 3H), 1.73 (s, 6H).

General procedure for acetals



PhSSPh (0.04 mmol, 8.7 mg), Mes-Acr-PhBF$_4$ (PS-A) (0.02 mmol, 4.6 mg) and (E)-3-phenylprop-2-en-1-ol (0.2 mmol, 26.8 mg) were weighed in an oven-dried 8 mL vial equipped with a magnetic starring bar. The reaction vial was capped with a rubber septum and anhydrous DCE (3 mL) was added under an argon atmosphere. Then 3, 4-dihydro-2H-pyran (0.8 mmol, 73 μL) was added and the reaction vessel was fixed on a blue LED light reaction equipment (1 W, 452 nm). After TLC indicated a full conversion (usually 18 hours), the reaction was purified by flash silica gel column chromatography directly.

General procedure for substrates

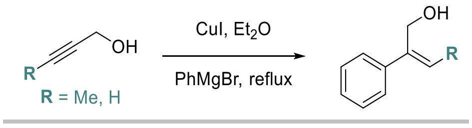


Step 1:

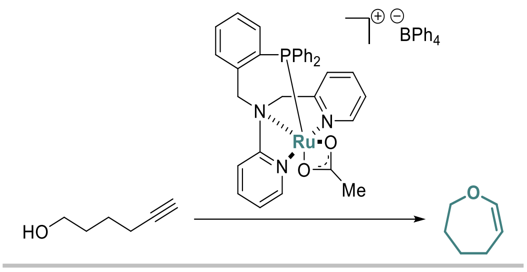
To a stirred solution of aldehyde (10.3 mmol) in DCM (20 mL) at room temperature was added ethyl (triphenylphosphoranylidene)acetate (1.1 eq, 11.3 mmol). The reaction solution was stirred for 15 hours and then concentrated under vacuum condition. The residue was purified by flash silica gel column chromatography directly.

Step 2:

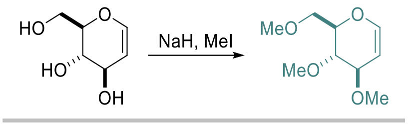
To a solution of corresponding ester (8.84 mmol) in DCM (70 mL) at -78 °C was added a 1.0 M solution of DIBAL-H (in hexane, 2.5 eq, 22 mmol) dropwise. After 3 hours, the reaction mixture was warmed to room temperature and quenched with 1N HCl (40 mL). The aqueous phase was separated and extracted with DCM. The combined organic extracts were washed with $NaHCO_3$, dried over Na_2SO_4. Then the solution was filtered and concentrated under vacuum condition. The residue was further purified by flash silica gel column chromatography.



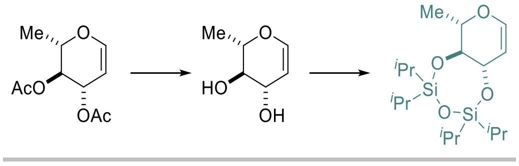
To a solution of PhMgBr (25 mmol) in 30 ml of Et_2O was added CuI (0.29 g, 1.5 mmol). The mixture was stirred at room temperature for 0.5 hours. Then a solution of corresponding propargyl alcohol (10 mmol) in 10 mL Et_2O was added slowly. After the addition was completed, the reaction mixture was refluxed for 24 hours. After cooling to room temperature, an aqueous solution of NH_4Cl was added slowly. The organic layer was separated and aqueous layer was extracted with Et_2O. The combined organic extracts were dried over Na_2SO_4. Then the solution was filtered and concentrated under vacuum condition. The residue was purified by flash silica gel column chromatography (Duan et al., 2009).



Catalyst [Ru(N$_3$P)(OAc)][BPh$_4$] (0.005 mmol) was added to a solution of alkynol (17.6 mmol) in THF (15 mL). The resulting solution was stirred at 80 °C and monitored by TLC. When the maximum conversion was reached, the desired product was isolated by flash column chromatography on silica gel (Liu et al., 2010).

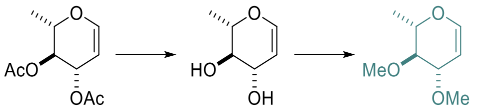


D-Galactal (730 mg, 5 mmol), which had been pre-dried under vacuum in a flame-dried flask for 1 h, was dissolved in anhydrous DMF (30 mL) under a N$_2$ atmosphere. The reaction mixture was cooled to 0 °C, after which NaH (60% wt in mineral oil, 900 mg, 22.5 mmol) was added portionwise. When addition was completed the reaction was allowed to warm to room temperature. After being stirred at room temperature for 30 min, the solution was cooled to 0 °C and iodomethane (140 µL, 22.5 mmol) was added dropwise. The reaction mixture was then allowed to warm to room temperature and stirred for another 3 hours, and quenched with MeOH (0.5 mL). The solution was diluted with EtOAc (40 mL) and washed with water (3x 20 mL) and brine (20 mL), dried over Na$_2$SO$_4$ and concentrated in vacuum. Purification by column chromatography afforded target product as a pale yellow liquid (752 mg, 80%). Proton and carbon NMR were consistent with literature data (Balmond et al., 2014).



3, 4-O-Di-acetyl-L-rhamnal (520 mg, 2.43 mmol) was dissolved in a solution of MeOH (8 mL), H$_2$O (1 mL) and Et$_3$N (1 mL), and stirred for 18 hours. Then the solvent was removed to afford L-rhamnal as a solid. L-Rhamnal and imidazole (332 mg, 4.88 mmol) were dissolved in distilled pyridine (20 mL) under N$_2$ atmosphere and the solution was cooled to 0 °C. 1,3-Dichloro-

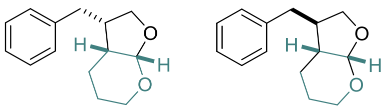
1,1,3,3-tetraisopropyldisiloxane (1.2 mL, 3.75 mmol) was added dropwise and the solution was then allowed to warm to room temperature and stirred for 18 h. The reaction was quenched with H_2O (30 mL), extracted with EtOAc (50 mL). The organic layer was washed with brine (20 mL), dried over $MgSO_4$, filtered and concentrated in vacuum. Following purification by column chromatography afforded the desired product as a white solid (846 mg, 96%).



3, 4-O-Di-acetyl-L-rhamnal (1.0 g, 4.67 mmol) was dissolved in a solution of MeOH (15 mL), H_2O (2 mL) and Et_3N (2 mL) and stirred for 18 hours. Then the solvents were removed and the residue was dissolved in EA, washed with H_2O and brine, and dried over Na_2SO_4. Following purification by column chromatography, L-rhamnal was obtained as a white solid (546 mg, 90% yield). L-rhamnal (546 mg, 4.2 mmol) was dissolved in anhydrous DMF (25 mL) under N_2 atmosphere. The reaction mixture was cooled to 0 °C, after which NaH (60%wt in mineral oil, 504 mg, 12.6 mmol) was added portionwise. When addition was completed the reaction was allowed to warm to room temperature. After being stirred at room temperature for 30 min, the solution was cooled to 0 °C and iodomethane (78 μL, 12.6 mmol) was added dropwise. The reaction mixture was then allowed to warm to room temperature and stirred for another 3 hours, and quenched with MeOH (0.5 mL). The solution was diluted with EtOAc (40 mL) and washed with water (3 x 20 mL) and brine (20 mL), dried over Na_2SO_4 and concentrated in vacuum. Purification by column chromatography afforded the target product as a pale yellow liquid (498 mg, 75%). Proton and carbon NMR were consistent with literature data.

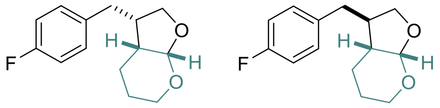
II. Date S1: ^{1}H NMR and ^{13}C NMR spectra data of products (Related to Figure 3-5)

3-benzylhexahydro-4H-furo[2,3-b]pyran (1)



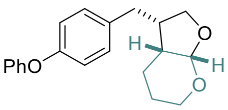
Eluent for purification: hexane: ethyl acetate = 10:1. Colorless oil (35.3 mg, 81% yield, dr = 1.8:1). Proton and carbon NMR were consistent with literature data. **Cis-syn: ^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.32 – 7.26 (m, 2H), 7.24 – 7.19 (m, 1H), 7.19 – 7.14 (m, 2H), 5.29 (d, *J* = 3.7 Hz, 1H), 3.92 – 3.85 (m, 1H), 3.82 – 3.74 (m, 2H), 3.65 (t, *J* = 8.1 Hz, 1H), 2.79 –2.55 (m, 3H), 1.96 (m, 1H), 1.79 – 1.73 (m, 1H), 1.86 – 1.53 (m, 3H). **Cis-anti: ^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.32–7.26 (m, 2H), 7.24–7.19 (m, 1H), 7.19–7.14 (m, 2H), 5.04 (d, *J* = 3.6 Hz, 1H), 4.18 (t, *J* = 8.2 Hz, 1H), 3.92 – 3.85 (m, 1H), 3.65 (t, *J* = 8.1 Hz, 1H), 3.43 (td, *J* = 11.3, 2.4 Hz, 1H), 2.87 (dd, *J* = 13.3, 5.2 Hz, 1H), 2.79–2.55 (m, 2H), 1.86-1.53 (m, 4H), 1.38–1.32 (m, 1H). **^{13}C NMR (trans & cis mixture)** (101 MHz, Chloroform-*d*) δ 140.12, 140.08, 128.51, 128.49, 128.36, 126.22, 126.18, 102.13, 101.96, 73.64, 69.87, 64.37, 60.98, 43.84, 42.52, 39.42, 38.73, 36.58, 33.38, 23.17, 22.45, 20.74, 19.57. **HRMS** calculated for $C_{14}H_{18}O_2$ (M + Na^+): 241.1149, found: 241.1202.

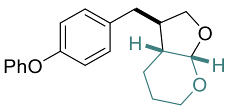
3-(4-fluorobenzyl)hexahydro-4H-furo[2,3-b]pyran (2)



Eluent for purification: hexane: ethyl acetate = 10:1. Colorless oil (30.7 mg, 65% yield, dr = 1.3:1). Proton and carbon NMR were consistent with literature data (Yan et al., 2012). **Cis-syn: ^{1}H NMR** (400 MHz, Chloroform-d) δ 7.11 (m, 2H), 7.00 – 6.93 (m, 2H), 5.27 (d, *J* = 3.7 Hz, 1H), 3.90 – 3.83 (m, 1H), 3.81 – 3.71 (m, 2H), 3.67 – 3.58 (m, 1H), 2.77 – 2.47 (m, 3H), 2.00 – 1.90 (m, 1H), 1.78 – 1.71 (m, 1H), 1.88 – 1.44 (m, 3H). **Cis-anti: ^{1}H NMR** (400 MHz, Chloroform-d) ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.11 (m, 2H), 7.00 – 6.93 (m, 2H), 5.02 (d, *J* = 3.4 Hz, 1H), 4.15 (t, *J* = 8.2 Hz, 1H), 3.90 – 3.83 (m, 1H), 3.67 – 3.58 (m, 1H), 3.46 – 3.37 (m, 1H), 2.82 (dd, *J* = 12.8, 4.6 Hz, 1H), 2.77 – 2.47 (m, 2H), 1.88 – 1.44 (m, 4H), 1.34 (m, *J* = 10.1, 5.4, 3.0 Hz, 1H). **^{13}C NMR (trans & cis mixture)** (101 MHz, Chloroform-*d*) δ 162.66 (d, *J* = 245.3 Hz), 162.60 (d, *J* = 245.0 Hz), 135.72 , 135.69, 129.88 (d, *J* = 8.0 Hz), 129.72 (d, *J* = 7.07 Hz), 115.41 (d, *J* = 21.2 Hz), 115.39 (d, *J* = 21.4 Hz), 102.11, 101.93, 73.52, 69.76, 64.38, 60.99, 43.79, 42.60, 39.53, 37.89, 36.52, 32.62, 23.11, 22.45, 20.69, 19.54. **HRMS** calculated for $C_{14}H_{17}FO_2$ (M + Na^+): 259.1105, found: 259.1105.

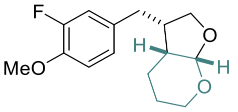
3-(4-phenoxybenzyl)hexahydro-4H-furo[2,3-b]pyran (3)

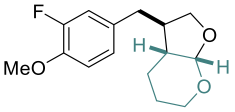




Eluent for purification: hexane: ethyl acetate = 10:1. White solid (36.0 mg, 58% yield, dr = 1.4:1). **Cis-syn: ^{1}H NMR** (400 MHz, Chloroform-d) δ 7.37 – 7.29 (m, 2H), 7.16 – 7.05 (m, 3H), 7.07 – 6.98 (m, 2H), 6.98 – 6.88 (m, 2H), 5.30 (d, J = 3.7 Hz, 1H), 3.90 (t, J = 7.7 Hz, 1H), 3.85 – 3.74 (m, 2H), 3.72 – 3.58 (m, 1H), 2.80 – 2.51 (m, 3H), 1.98 (ddt, J = 12.1, 10.2, 5.0 Hz, 1H), 1.82 – 1.71 (m, 1H), 1.60 – 1.46 (m, 3H). **Cis-trans: ^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.36 – 7.30 (m, 2H), 7.15 – 7.06 (m, 3H), 7.03 – 6.97 (m, 2H), 6.97 – 6.91 (m, 2H), 5.05 (d, *J* = 3.5 Hz, 1H), 4.20 (t, *J* = 8.2 Hz, 1H), 3.89 (ddt, *J* = 11.7, 4.3, 2.4 Hz, 1H), 3.65 (dd, *J* = 8.4, 7.5 Hz, 1H), 3.49 – 3.38 (m, 1H), 2.84 (dd, *J* = 13.0, 4.7 Hz, 1H), 2.69 – 2.50 (m, 2H), 1.91 – 1.76 (m, 2H), 1.76 – 1.62 (m, 3H), 1.41 – 1.29 (m, 1H). **Cis-syn: ^{13}C NMR** (101 MHz, Chloroform-*d*) δ 157.35, 155.59, 134.97, 129.69, 129.54, 123.12, 119.00, 118.70, 101.97, 69.86, 60.99, 42.65, 36.58, 32.67, 23.16, 19.57. **Cis-anti: ^{13}C NMR** (101 MHz, Chloroform-*d*) δ 157.41, 155.52, 135.01, 129.72, 129.69, 123.07, 119.07, 118.60, 102.13, 73.61, 64.38, 43.78, 39.55, 37.95, 22.48, 20.75. **HRMS** calculated for $C_{20}H_{22}O_3$ (M + Na^+): 333.1461, found: 333.1459.

3-(3-fluoro-4-methoxybenzyl)hexahydro-4H-furo[2,3-b]pyran (4)

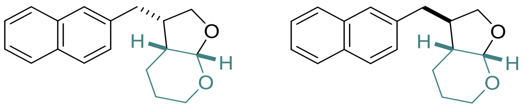




Eluent for purification: hexane: ethyl acetate = 10:1. Colorless oil (36.7 mg, 69% yield, dr = 1.1:1). Isolated as an inseparable mixture of diastereomers. Spectral data for two diastereomers is given herein. **Cis-syn: ^{1}H NMR** (400 MHz, Chloroform-*d*) δ 6.90 – 6.86 (m, 1H), 6.87 – 6.84 (m, 2H), 5.27 (d, *J* = 3.7 Hz, 1H), 3.86 (s, 4H), 3.75 (ddd, *J* = 12.8, 10.2, 7.9 Hz, 2H), 3.67 – 3.55 (m, 1H), 2.70 – 2.45 (m, 3H), 1.94 (dtd, *J* = 10.3, 6.3, 3.9 Hz, 1H), 1.85 – 1.70 (m, 2H), 1.67 – 1.51 (m, 3H). **Cis-trans: ^{1}H NMR** (400 MHz, Chloroform-*d*) δ 6.87 – 6.82 (m, 3H), 5.02 (d, *J* = 3.3 Hz, 1H), 4.16 (t, *J* = 8.2 Hz, 1H), 3.86 (s, 4H), 3.67 – 3.55 (m, 1H), 3.46 – 3.37 (m, 1H), 2.77 (dd, *J* = 13.3, 5.1 Hz, 1H), 2.70

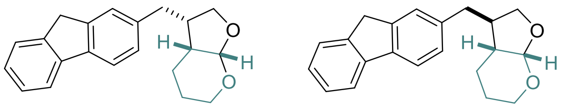
– 2.45 (m, 2H), 1.85 – 1.70 (m, 2H), 1.67 – 1.51 (m, 2H), 1.33 (dq, *J* = 13.1, 2.9, 2.5 Hz, 1H). **^{13}C NMR (trans & cis mixture)** (101 MHz, Chloroform-*d*) δ 153.49 (d, *J* = 246.3 Hz), 153.47 (d, *J* = 246.9 Hz), 145.98 (d, *J* = 5.7 Hz), 145.93 (d, *J* = 5.7 Hz), 133.16, 133.11, 123.99 (d, *J* = 19.6 Hz), 123.96 (d, *J* = 12.6 Hz), 116.22 (d, *J* = 32.4 Hz), 116.08 (d, *J* = 3.5 Hz), 113.51 (d, *J* = 2.0 Hz), 113.49 (d, *J* = 2.0 Hz), 102.09, 101.92, 73.48, 69.73, 64.36, 60.99, 56.31, 56.30, 43.75, 42.45, 39.44, 37.77, 36.51, 32.47, 23.10, 22.46, 20.71, 19.53. **HRMS** calculated for $C_{15}H_{19}FO_3$ (M + Na$^+$): 289.1210, found: 289.1203.

3-(naphthalen-2-ylmethyl)hexahydro-4H-furo[2,3-b]pyran (5)



Eluent for purification: hexane: ethyl acetate = 10:1. Colorless oil (26.8 mg, 50% yield, dr = 1.1:1). **Cis-syn: ^{1}H NMR** (400 MHz, Chloroform-d) δ 7.80 (m, 3H), 7.62 (d, J = 1.7 Hz, 1H), 7.53 – 7.43 (m, 2H), 7.32 (dd, J = 8.4, 1.8 Hz, 1H), 5.31 (d, J = 3.7 Hz, 1H), 3.96 – 3.87 (m, 1H), 3.88 – 3.75 (m, 2H), 3.66 (dtd, J = 11.3, 3.3, 1.7 Hz, 1H), 2.91 (dd, J = 10.8, 5.7 Hz, 1H), 2.87 – 2.75 (m, 2H), 2.05 – 1.95 (m, 1H), 1.82 (dq, J = 9.7, 2.2 Hz, 1H), 1.68 – 1.58 (m, 3H). **Cis-trans: ^{1}H NMR** (400 MHz, Chloroform-d) δ 7.88 – 7.73 (m, 3H), 7.61 (d, J = 1.7 Hz, 1H), 7.52 – 7.38 (m, 2H), 7.31 (dd, J = 8.5, 1.8 Hz, 1H), 5.07 (d, J = 3.7 Hz, 1H), 4.21 (t, J = 8.0 Hz, 1H), 3.89 (dq, J = 11.7, 2.6 Hz, 1H), 3.70 (dd, J = 8.4, 7.3 Hz, 1H), 3.44 (ddd, J = 11.6, 10.6, 2.3 Hz, 1H), 3.15 – 2.96 (m, 1H), 2.85 – 2.66 (m, 2H), 1.93 (dq, J = 9.0, 4.8, 4.0 Hz, 1H), 1.85 – 1.64 (m, 3H), 1.42 – 1.29 (m, 1H). **Cis-syn: ^{13}C NMR** (101 MHz, Chloroform-d) δ 137.60, 133.55, 132.10, 128.18, 127.62, 127.40, 126.94, 126.56, 126.10, 125.40, 101.99, 69.93, 61.02, 42.35, 36.65, 33.60, 23.17, 19.61. **Cis-trans: ^{13}C NMR** (101 MHz, Chloroform-*d*) δ 137.61, 133.53, 132.12, 128.13, 127.62, 127.44, 127.08, 126.69, 126.09, 125.40, 102.15, 73.68, 64.37, 43.93, 39.34, 38.97, 22.55, 20.78. **HRMS** calculated for $C_{18}H_{20}O_2$ (M + Na$^+$): 291.1356, found: 291.1356.

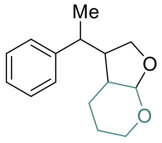
3-((9H-fluoren-2-yl)methyl)hexahydro-4H-furo[2,3-b]pyran (6)



Eluent for purification: hexane: ethyl acetate = 10:1. White solid (34.9 mg, 57% yield, dr = 1.4:1). **Cis-syn: ^{1}H NMR** (400 MHz, Chloroform-

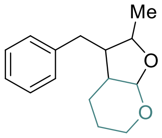
d) δ 7.76 (d, *J* = 7.6 Hz, 1H), 7.70 (d, *J* = 7.7 Hz, 1H), 7.54 (dt, *J* = 7.4, 1.0 Hz, 1H), 7.41 – 7.34 (m, 2H), 7.33 – 7.27 (m, 1H), 7.18 (dd, *J* = 7.7, 1.5 Hz, 1H), 5.31 (d, *J* = 3.7 Hz, 1H), 3.90 (d, *J* = 14.7 Hz, 3H), 3.86 – 3.75 (m, 2H), 3.66 (ddq, *J* = 11.0, 3.1, 1.7 Hz, 1H), 2.92 – 2.58 (m, 3H), 2.00 (dt, *J* = 10.8, 2.9 Hz, 1H), 1.80 (dt, *J* = 9.4, 2.6 Hz, 1H), 1.66 – 1.58 (m, 3H). **Cis-trans: ^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.77 (dt, *J* = 7.5, 0.9 Hz, 1H), 7.70 (d, *J* = 7.8 Hz, 1H), 7.54 (dq, *J* = 7.4, 1.0 Hz, 1H), 7.42 – 7.35 (m, 2H), 7.34 – 7.27 (m, 2H), 7.24 – 7.06 (m, 1H), 5.06 (d, *J* = 3.6 Hz, 1H), 4.22 (t, *J* = 8.1 Hz, 1H), 3.95 – 3.81 (m, 3H), 3.74 – 3.63 (m, 1H), 3.44 (ddd, *J* = 11.6, 10.7, 2.3 Hz, 1H), 2.96 – 2.84 (m, 1H), 2.77 – 2.58 (m, 2H), 1.98 – 1.85 (m, 1H), 1.83 – 1.65 (m, 3H), 1.43 – 1.30 (m, 1H). **Cis-syn: ^{13}C NMR** (101 MHz, Chloroform-*d*) δ 143.69, 143.07, 141.49, 139.94, 138.79, 126.98, 126.73, 126.47, 125.02, 124.98, 119.83, 119.65, 101.99, 69.94, 61.00, 42.73, 36.82, 36.64, 33.55, 23.19, 19.61. **Cis-trans: ^{13}C NMR** (101 MHz, Chloroform-*d*) δ 143.66, 143.10, 141.52, 139.95, 138.79, 127.14, 126.73, 126.47, 125.18, 125.00, 119.82, 119.67, 102.19, 73.71, 64.39, 43.89, 39.68, 38.92, 36.82, 22.52, 20.77. **HRMS** calculated for $C_{21}H_{22}O_2$ (M + Na$^+$): 329.1512, found: 329.1512.

3-(1-phenylethyl)hexahydro-4H-furo[2,3-b]pyran (7)



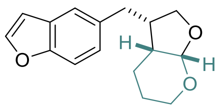
Eluent for purification: hexane: ethyl acetate = 10:1. Colorless oil (35.8 mg, 77% yield, dr = 2.4:1:1). Isolated as an inseparable mixture of diastereomers. Spectral data for the major diastereomer is given herein. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.32 – 7.26 (m, 2H), 7.23 – 7.12 (m, 3H), 5.00 (d, *J* = 3.4 Hz, 1H), 4.01 (t, *J* = 8.6 Hz, 1H), 3.89 (dtd, *J* = 11.7, 3.9, 1.4 Hz, 1H), 3.54 (dd, *J* = 8.8, 6.7 Hz, 1H), 3.44 (ddd, *J* = 11.5, 10.4, 2.6 Hz, 1H), 2.75 (dq, *J* = 8.7, 6.9 Hz, 1H), 2.50 (qd, *J* = 8.1, 6.2 Hz, 1H), 1.97 – 1.37 (m, 4H), 1.25 (m, 1H), 1.31 (d, *J* = 7.0 Hz, 3H). **^{13}C NMR (three isomers)** (101 MHz, Chloroform-*d*) δ 145.69, 145.25, 145.03, 128.56, 128.52, 128.44, 127.49, 127.12, 126.84, 126.50, 126.47, 126.37, 102.65, 102.38, 101.94, 72.69, 71.81, 68.92, 64.39, 64.14, 60.74, 48.01, 44.60, 44.42, 44.17, 43.30, 43.16, 42.25, 38.14, 35.77, 25.45, 24.06, 23.30, 22.57, 21.46, 21.08, 20.73, 20.56, 18.89. **HRMS** calculated for $C_{15}H_{20}O_2$ (M + Na$^+$): 255.1356, found: 255.1354.

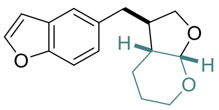
3-benzyl-2-methylhexahydro-4H-furo[2,3-b]pyran (8)



Eluent for purification: hexane: ethyl acetate = 10:1. Colorless oil (21.3 mg, 46% yield, dr = 2.5:2.5:1.8:1). Isolated as an inseparable mixture of diastereomers. Spectral data for the major diastereomer is given herein. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.30 (s, 2H), 7.21 (d, *J* = 3.0 Hz, 3H), 5.04 (d, *J* = 3.6 Hz, 1H), 4.57 (p, *J* = 6.7 Hz, 1H), 3.89 – 3.87 (m, 1H), 3.40 (dt, *J* = 11.3, 2.2 Hz, 1H), 2.89 – 2.82 (m, 1H), 2.70 (dd, *J* = 7.7, 3.2 Hz, 1H), 2.60 (dd, *J* = 13.6, 8.0 Hz, 1H), 1.94 (dd, *J* = 6.5, 3.1 Hz, 1H), 1.74 (s, 1H), 1.56 (dt, *J* = 10.7, 3.7 Hz, 3H), 1.10 (d, *J* = 6.1 Hz, 3H). **^{13}C NMR (four isomers)** (126 MHz, Chloroform-*d*) δ 140.53, 140.37, 139.79, 128.94, 128.51, 128.47, 128.40, 126.27, 126.19, 126.08, 126.05, 101.56, 100.82, 100.51, 100.18, 82.11, 73.86, 64.44, 64.19, 61.06, 60.92, 50.43, 46.33, 45.08, 43.36, 42.58, 38.03, 37.59, 37.04, 34.62, 31.31, 30.98, 25.39, 23.56, 23.31, 22.63, 22.44, 22.19, 21.40, 20.82, 20.79, 20.72, 19.84, 18.85, 17.38. **HRMS** calculated for $C_{15}H_{20}O_2$ (M + Na^+): 255.1356, found: 255.1355.

3-(benzofuran-5-ylmethyl)hexahydro-4H-furo[2,3-b]pyran (9)

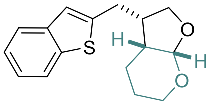


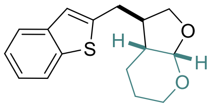


Eluent for purification: hexane: ethyl acetate = 10:1. Colorless oil (35.6 mg, 69% yield, dr = 1.4:1). **Cis-syn: ^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.61 (d, *J* = 2.2 Hz, 1H), 7.49 – 7.33 (m, 2H), 7.10 (dd, *J* = 8.4, 1.8 Hz, 1H), 6.72 (dd, *J* = 2.2, 1.0 Hz, 1H), 5.29 (d, *J* = 3.7 Hz, 1H), 3.89 (t, *J* = 7.8 Hz, 1H), 3.79 (ddd, *J* = 10.1, 8.6, 5.3 Hz, 2H), 3.66 (ddq, *J* = 11.1, 3.1, 1.8 Hz, 1H), 2.83 (dd, *J* = 10.6, 6.0 Hz, 1H), 2.78 – 2.67 (m, 2H), 2.03 – 1.90 (m, 1H), 1.80 (ddd, *J* = 9.9, 6.6, 4.4 Hz, 1H), 1.63 – 1.53 (m, 3H). **Cis-trans: ^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.61 (d, *J* = 2.2 Hz, 1H), 7.45 – 7.34 (m, 2H), 7.09 (dd, *J* = 8.4, 1.8 Hz, 1H), 6.72 (dd, *J* = 2.2, 1.0 Hz, 1H), 5.05 (d, *J* = 3.6 Hz, 1H), 4.25 – 4.11 (m, 1H), 3.92 – 3.82 (m, 1H), 3.74 – 3.62 (m, 1H), 3.43 (ddd, *J* = 11.6, 10.7, 2.3 Hz, 1H), 3.07 – 2.88 (m, 1H), 2.74 – 2.59 (m, 2H), 1.88 (ddt, *J* = 8.9, 5.9, 2.9 Hz, 1H), 1.84 – 1.64 (m, 3H), 1.34 (m, 1H). **Cis-syn: ^{13}C NMR** (101 MHz, Chloroform-*d*) δ 153.67, 145.28, 134.55, 127.64, 124.72, 120.45, 111.25, 106.33, 101.99, 69.91, 60.99, 43.01, 36.60, 33.27, 23.17, 19.58. **Cis-anti: ^{13}C NMR**

(101 MHz, Chloroform-*d*) δ 153.71, 145.26, 134.53, 127.62, 124.89, 120.63, 111.22, 106.36, 102.16, 73.65, 64.36, 43.80, 39.93, 38.64, 22.52, 20.77. **HRMS** calculated for $C_{16}H_{18}O_3$ (M + Na$^+$): 281.1148, found: 281.1148.

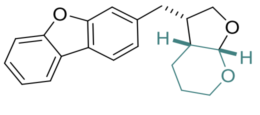
3-(benzo[b]thiophen-2-ylmethyl)hexahydro-4H-furo[2,3-b]pyran (10)

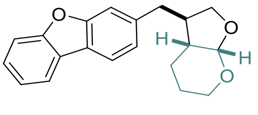




Eluent for purification: hexane: ethyl acetate = 10:1. Colorless oil (41.6 mg, 76% yield, dr = 1.4:1). **Cis-syn: ^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.82 – 7.71 (m, 1H), 7.68 (dd, *J* = 7.4, 1.3 Hz, 1H), 7.35 – 7.25 (m, 2H), 7.08 – 6.97 (m, 1H), 5.31 (d, *J* = 3.7 Hz, 1H), 4.03 (t, *J* = 8.1 Hz, 1H), 3.80 (ddd, *J* = 13.1, 6.7, 3.0 Hz, 2H), 3.72 – 3.60 (m, 1H), 3.05 (ddd, *J* = 14.9, 7.9, 1.0 Hz, 1H), 2.94 (ddd, *J* = 14.9, 7.6, 1.1 Hz, 1H), 2.87 – 2.73 (m, 1H), 2.09 (dq, *J* = 9.3, 2.7 Hz, 1H), 1.81 (ddd, *J* = 11.2, 6.4, 3.3 Hz, 1H), 1.63 – 1.56 (m, 3H). **Cis-trans: ^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.77 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.73 – 7.67 (m, 1H), 7.36 – 7.27 (m, 2H), 7.02 (d, *J* = 1.0 Hz, 1H), 5.07 (d, *J* = 3.6 Hz, 1H), 4.33 (t, *J* = 8.4 Hz, 1H), 3.95 – 3.85 (m, 1H), 3.72 (dd, *J* = 8.6, 7.4 Hz, 1H), 3.49 – 3.37 (m, 1H), 3.13 (ddd, *J* = 14.9, 5.5, 1.1 Hz, 1H), 2.89 (ddd, *J* = 14.9, 9.0, 1.0 Hz, 1H), 2.81 – 2.67 (m, 1H), 1.92 (dq, *J* = 9.1, 2.9 Hz, 1H), 1.89 – 1.65 (m, 3H), 1.42 – 1.31 (m, 1H). **Cis-syn: ^{13}C NMR** (101 MHz, Chloroform-*d*) δ 143.76, 139.93, 139.27, 124.26, 123.75, 122.84, 122.13, 121.19, 101.92, 69.77, 61.11, 42.36, 36.62, 28.80, 23.06, 19.52. **Cis-trans: ^{13}C NMR** (101 MHz, Chloroform-*d*) δ 143.78, 139.94, 139.42, 124.25, 123.76, 122.88, 122.14, 121.39, 102.03, 73.48, 64.32, 43.93, 39.62, 33.94, 22.62, 20.77. **HRMS** calculated for $C_{16}H_{18}O_2S$ (M + Na$^+$): 297.0920, found: 297.0920.

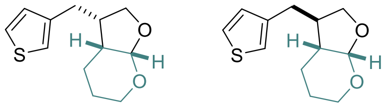
3-((hexahydro-4H-furo[2,3-b]pyran-3-yl)methyl)dibenzo[b,d]furan (11)





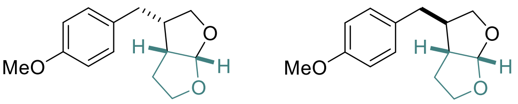
Eluent for purification: hexane: ethyl acetate = 10:1. White solid (46.2 mg, 75% yield, dr = 1.4:1). Isolated as an inseparable mixture of diastereomers. Spectral data for the two diastereomers is given herein. **Cis-syn: ^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.94 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.73 (t, *J* = 2.1 Hz, 1H), 7.56 (d, *J* = 8.2 Hz, 1H), 7.50 – 7.41 (m, 2H), 7.34 (t, *J* = 7.5 Hz, 1H), 7.27 – 7.21 (m, 1H), 5.31 (d, *J* = 3.7 Hz, 1H), 3.93 – 3.84 (m, 1H), 3.84 – 3.77 (m, 2H), 3.73 – 3.63 (m, 1H), 2.94 – 2.85 (m, 1H), 2.82 – 2.66 (m, 2H), 1.99 (q, *J* = 4.8 Hz, 1H), 1.81 – 1.58 (m, 4H). **Cis-trans: ^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.94 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.73 (t, *J* = 2.1 Hz, 1H), 7.56 (d, *J* = 8.2 Hz, 1H), 7.50 – 7.41 (m, 2H), 7.34 (t, *J* = 7.5 Hz, 1H), 7.27 – 7.21 (m, 1H), 5.06 (d, *J* = 3.7 Hz, 1H), 4.21 (t, *J* = 8.0 Hz, 1H), 3.93 – 3.84 (m, 1H), 3.73 – 3.63 (m, 1H), 3.43 (td, *J* = 11.3, 2.4 Hz, 1H), 3.07 – 2.95 (m, 1H), 2.82 – 2.66 (m, 2H), 1.96 – 1.87 (m, 1H), 1.81 – 1.58 (m, 3H), 1.33 (m, 1H). **^{13}C NMR (trans & cis mixture)** (101 MHz, Chloroform-*d*) δ 156.51, 154.91, 154.86, 134.61, 127.64, 127.46, 127.17, 124.42, 124.40, 124.06, 122.66, 120.58, 120.56, 120.17, 120.06, 111.70, 111.54, 111.52, 102.19, 102.00, 73.64, 69.90, 64.37, 61.03, 43.87, 43.00, 39.95, 38.68, 36.66, 33.36, 23.18, 22.55, 20.78, 19.64. **HRMS** calculated for $C_{20}H_{20}O_3$ $(M + Na^+)$: 331.1305, found: 331.1302.

3-(thiophen-3-ylmethyl)hexahydro-4H-furo[2,3-b]pyran (12)



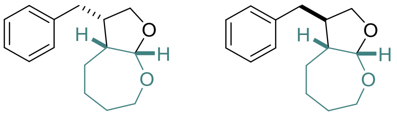
Eluent for purification: hexane: ethyl acetate = 10:1. Colorless oil (30.0 mg, 67% yield, dr = 1.3:1). **Cis-syn: ^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.28 – 7.25 (m, 1H), 6.97 – 6.86 (m, 2H), 5.29 (d, *J* = 3.7 Hz, 1H), 3.94 (t, *J* = 7.8 Hz, 1H), 3.77 (ddd, *J* = 12.8, 10.3, 7.7 Hz, 2H), 3.65 (dtd, *J* = 11.4, 3.3, 1.6 Hz, 1H), 2.83 – 2.57 (m, 3H), 1.99 (ddt, *J* = 12.1, 10.2, 4.9 Hz, 1H), 1.74 (m, 1H), 1.62 – 1.45 (m, 3H). **Cis-trans: ^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.27 (d, *J* = 3.9 Hz, 1H), 6.96 – 6.88 (m, 2H), 5.03 (d, *J* = 3.3 Hz, 1H), 4.25 (t, *J* = 8.1 Hz, 1H), 3.89 (ddt, *J* = 11.7, 4.2, 2.5 Hz, 1H), 3.67 – 3.59 (m, 1H), 3.48 – 3.32 (m, 1H), 2.94 – 2.81 (m, 1H), 2.71 – 2.56 (m, 2H), 1.83 (m, 1H), 1.80 – 1.62 (m, 3H), 1.41 – 1.29 (m, 1H). **Cis-syn: ^{13}C NMR** (101 MHz, Chloroform-*d*) δ 140.36, 127.90, 125.71, 120.59, 101.97, 69.98, 61.05, 41.85, 36.63, 27.98, 23.13, 19.47. **Cis-anti: ^{13}C NMR** (101 MHz, Chloroform-*d*) δ 140.42, 128.03, 125.76, 120.75, 102.11, 73.75, 64.38, 43.89, 38.84, 33.14, 22.45, 20.75. **HRMS** calculated for $C_{12}H_{16}O_2S$ $(M + Na^+)$: 247.0763, found: 247.0763.

3-(4-methoxybenzyl)hexahydrofuro[2,3-b]furan (13)



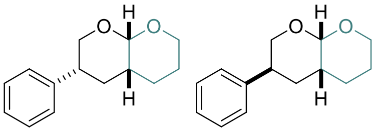
Eluent for purification: hexane: ethyl acetate = 10:1. Colorless oil (28.1 mg, 60% yield, dr = 1.9:1). Isolated as an inseparable mixture of diastereomers. Spectral data for the two diastereomer is given herein. **Cis-syn: ^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.11 – 7.05 (m, 2H), 6.83 (dd, *J* = 8.6, 2.0 Hz, 2H), 5.71 (d, *J* = 4.9 Hz, 1H), 3.97 – 3.92 (m, 1H), 3.88 – 3.83 (m, 2H), 3.79 (s, 3H), 3.54 (dd, *J* = 10.2, 8.4 Hz, 1H), 2.77 (tt, *J* = 10.9, 5.2 Hz, 1H), 2.68 (dd, *J* = 11.0, 4.5 Hz, 1H), 2.62 (dd, *J* = 8.2, 3.3 Hz, 1H), 2.28 – 2.19 (m, 1H), 2.08 – 1.95 (m, 3H). **Cis-trans: ^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.11 – 7.05 (m, 2H), 6.83 (dd, *J* = 8.6, 2.0 Hz, 2H), 5.74 (d, *J* = 5.1 Hz, 1H), 3.97 – 3.92 (m, 1H), 3.88 – 3.83 (m, 2H), 3.79 (s, 3H), 3.61 (dd, *J* = 9.0, 3.9 Hz, 1H), 2.62 (dd, *J* = 8.2, 3.3 Hz, 2H), 2.55 (ddt, *J* = 8.5, 5.5, 3.0 Hz, 1H), 2.28 – 2.19 (m, 1H), 2.08 – 1.95 (m, 1H), 1.89 – 1.83 (m, 1H), 1.66 – 1.57 (m, 1H). **^{13}C NMR (trans & cis mixture)** (101 MHz, Chloroform-*d*) δ 158.05, 158.03, 131.99, 131.96, 129.76, 129.21, 113.96, 113.90, 109.82, 109.17, 72.21, 72.19, 69.13, 67.76, 55.25, 48.36, 47.47, 45.43, 44.00, 38.69, 32.88, 31.91, 25.12. **HRMS** calculated for $C_{14}H_{18}O_3$ (M + Na^{+}): 257.1148, found: 257.1150.

3-benzyloctahydrofuro[2,3-b]oxepine (14)



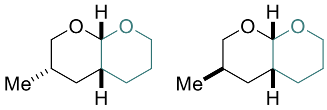
Eluent for purification: hexane: ethyl acetate = 10:1. Colorless oil (25.1 mg, 54% yield, dr = 2.1:1). Isolated as an inseparable mixture of diastereomers. Spectral data for the two diastereomer is given herein. **Cis-syn: ^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.30 – 7.25 (m, 2H), 7.21 – 7.13 (m, 3H), 5.22 (d, *J* = 5.5 Hz, 1H), 4.05 (td, *J* = 4.0, 1.2 Hz, 1H), 4.02 (td, *J* = 4.0, 1.2 Hz, 1H), 3.77 (dd, *J* = 8.5, 6.1 Hz, 1H), 3.69 (dd, *J* = 8.5, 5.9 Hz, 1H), 2.60 (dd, *J* = 13.4, 10.5 Hz, 1H), 2.47 – 2.30 (m, 2H), 1.86 – 1.79 (m, 2H), 1.67 (ddt, *J* = 8.8, 5.8, 3.2 Hz, 2H), 1.44 – 1.33 (m, 3H). **Cis-trans: ^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.30 – 7.25 (m, 2H), 7.21 – 7.13 (m, 3H), 5.16 (d, *J* = 5.6 Hz, 1H), 4.15 – 4.07 (m, 2H), 3.48 (t, *J* = 8.5 Hz, 1H), 3.38 (ddd, *J* = 12.6, 6.0, 2.6 Hz, 1H), 2.83 (dd, *J* = 13.6, 5.3 Hz, 1H), 2.55 – 2.40 (m, 2H), 2.47 – 2.30 (m, 2H), 2.04 – 1.97 (m, 1H), 1.86 – 1.79 (m, 2H), 1.67 (ddt, *J* = 8.8, 5.8, 3.2 Hz, 2H), 1.44 – 1.33 (m, 2H). **^{13}C NMR (trans & cis mixture)** (101 MHz, Chloroform-*d*) δ 140.92, 140.04, 128.65, 128.58, 128.43, 126.17, 125.96, 109.91, 109.53, 73.29, 71.96, 69.28, 68.91, 51.10, 48.49, 45.29, 42.83, 38.21, 34.07, 32.76, 32.33, 28.85, 26.70, 25.29, 24.72. **HRMS** calculated for $C_{15}H_{20}O_2$ (M + Na$^+$): 255.1356, found: 255.1355.

3-phenylhexahydro-2H, 5H-pyrano[2,3-b]pyran (15)



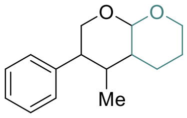
Eluent for purification: hexane: ethyl acetate = 20:1. Colorless oil (24.0mg, 55% yield, dr = 3:1). Isolated as an inseparable mixture of diastereomers. Spectral data for the major diastereomer is given herein. **Cis-syn: ^{1}H NMR** (400 MHz, Chloroform-d) δ 7.35 – 7.29 (m, 2H), 7.26 – 7.21 (m, 3H), 4.88 (d, J = 2.2 Hz, 1H), 4.19 – 4.06 (m, 1H), 3.99 – 3.85 (m, 1H), 3.79 – 3.66 (m, 1H), 3.65 – 3.52 (m, 1H), 3.15 – 3.02 (m, 1H), 1.94-1.92 (m, 1H), 1.92 – 1.75 (m, 2H), 1.75 – 1.70 (m, 2H), 1.70 – 1.59 (m, 1H), 1.59 – 1.51 (m, 1H). **Cis-anti: ^{1}H NMR** (400 MHz, Chloroform-d) δ 7.35 – 7.29 (m, 2H), 7.26 – 7.21 (m, 3H), 4.81 (d, J = 2.6 Hz, 1H), 4.19 – 4.06 (m, 1H), 3.99 – 3.85 (m, 1H), 3.79 – 3.66 (m, 1H), 3.65 – 3.52 (m, 1H), 2.95 (tt, J = 11.9, 4.0 Hz, 1H), 2.22 (q, J = 12.5 Hz, 1H), 2.07 – 1.94 (m, 2H), 1.92 – 1.75 (m, 1H), 1.70 – 1.59 (m, 2H), 1.35 – 1.24 (m, 1H). **^{13}C NMR (trans & cis mixture)** (101 MHz, Chloroform-*d*) δ 142.11, 141.55, 128.52, 127.42, 127.36, 126.71, 97.96, 97.23, 71.91, 67.52, 66.02, 61.68, 42.31, 36.97, 34.99, 34.81, 34.07, 29.40, 28.10, 25.03, 23.21, 20.54. **HRMS** calculated for $C_{14}H_{18}O_2$ (M + Na$^+$): 241.1199, found: 241.1202.

3-methylhexahydro-2H, 5H-pyrano[2,3-b]pyran (16)



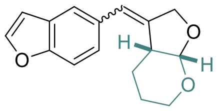
Eluent for purification: hexane: ethyl acetate = 20:1. Colorless oil (16.2 mg, 52% yield, dr = 3:1). Isolated as an inseparable mixture of diastereomers. Spectral data for the two diastereomer is given herein. **Cis-syn: ^{1}H NMR** ^{1}H NMR (400 MHz, Chloroform-*d*) δ 4.69 (d, *J* = 2.6 Hz, 1H), 3.92 (ddd, *J* = 11.4, 4.4, 2.5 Hz, 1H), 3.89 – 3.81 (m, 1H), 3.62 (m, 1H), 3.10 (dd, *J* = 11.4, 10.3 Hz, 1H), 1.83 – 1.70 (m, 3H), 1.62 – 1.50 (m, 3H), 1.48 – 1.43 (m, 1H), 1.34 – 1.25 (m, 1H), 0.78 (d, *J* = 6.7 Hz, 3H). **Cis-anti: ^{1}H NMR** (400 MHz, Chloroform-*d*) δ 4.69 (d, *J* = 2.6 Hz, 1H), 4.07 – 3.98 (m, 1H), 3.58 – 3.46 (m, 2H), 3.41 (t, *J* = 11.1 Hz, 1H), 1.83 – 1.70 (m, 3H), 1.62 – 1.50 (m, 3H), 1.41 – 1.34 (m, 1H), 1.25 – 1.17 (m, 1H), 0.81 (d, *J* = 6.6 Hz, 3H). **^{13}C NMR (trans & cis mixture)** (101 MHz, Chloroform-*d*) δ 97.96, 97.30, 67.42, 67.06, 62.89, 34.59, 30.98, 30.67, 30.41, 28.12, 25.43, 20.48, 19.73, 17.27, 16.65. **HRMS** calculated for $C_9H_{16}O_2$ $(M + H^+)$: 157.1223, found: 157.1223.

4-methyl-3-phenylhexahydro-2H,5H-pyrano[2,3-b]pyran (17)



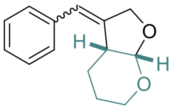
Eluent for purification: hexane: ethyl acetate = 10:1. Colorless oil (37.6 mg, 81% yield, dr = 8.3:4.3:3.3:1). Isolated as an inseparable mixture of diastereomers. Spectral data for the major diastereomer is given herein. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.32 – 7.27 (m, 2H), 7.23 – 7.18 (m, 1H), 7.18 – 7.13 (m, 2H), 5.01 (d, *J* = 3.4 Hz, 1H), 4.01 (t, *J* = 8.6 Hz, 1H), 3.54 (td, *J* = 8.5, 1.9 Hz, 2H), 3.46 (ddd, *J* = 11.6, 10.5, 2.7 Hz, 1H), 2.54 – 2.47 (m, 1H), 1.94 (q, *J* = 3.3 Hz, 2H), 1.80 – 1.69 (m, 1H), 1.57 – 1.51 (m, 1H), 1.43 (m, 1H), 1.32 (m, 1H). **^{13}C NMR (four isomers)** (101 MHz, Chloroform-*d*) δ 145.70, 145.25, 128.52, 128.44, 127.49, 127.12, 126.47, 126.37, 102.65, 102.38, 72.68, 71.81, 64.39, 64.13, 44.61, 44.16, 43.30, 43.16, 42.25, 24.06, 22.57, 21.08, 20.73, 20.55. **HRMS** calculated for $C_{15}H_{20}O_2$ $(M + Na^+)$: 255.1356, found: 255.1355.

3-(benzofuran-5-ylmethylene)hexahydro-4H-furo[2,3-b]pyran (18)



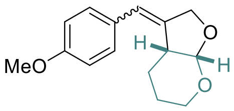
Eluent for purification: hexane: ethyl acetate = 20:1. Colorless oil (30.0 mg, 67% yield, E:Z = 4:1). Isolated as an inseparable mixture of diastereomers. Spectral data for the two isomers is given herein. **E-isomer**: **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.62 (d, J = 2.2 Hz, 1H), 7.51 – 7.44 (m, 2H), 7.22 (dd, J = 8.6, 1.8 Hz, 1H), 6.76 (dd, J = 2.3, 1.0 Hz, 1H), 6.40 (dd, J = 10.3, 2.3 Hz, 1H), 5.26 (d, J = 3.9 Hz, 1H), 4.76 (dt, J = 12.9, 1.9 Hz, 1H), 4.46 (dd, J = 12.8, 1.8 Hz, 1H), 3.95 – 3.86 (m, 1H), 3.68 (dtd, J = 11.1, 4.0, 1.4 Hz, 1H), 3.05 – 2.95 (m, 1H), 1.99 (m, 1H), 1.71 – 1.58 (m, 1H), 1.57 – 1.54 (m, 2H). **Z-isomer**: **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.62 (d, J = 2.2 Hz, 1H), 7.51 – 7.44 (m, 1H), 7.37 (d, J = 1.7 Hz, 1H), 7.12 (dd, J = 8.6, 1.9 Hz, 1H), 6.76 (dd, J = 2.3, 1.0 Hz, 1H), 6.40 (dd, J = 10.3, 2.3 Hz, 1H), 5.21 (d, J = 3.8 Hz, 1H), 4.93 (dt, J = 13.6, 2.5 Hz, 1H), 4.83 (dt, J = 13.6, 2.2 Hz, 1H), 3.95 – 3.86 (m, 1H), 3.51 (td, J = 11.2, 2.5 Hz, 1H), 2.85 (m, 1H), 2.18 (m, 1H), 1.71 – 1.58 (m, 1H), 1.57 – 1.54 (m, 1H), 1.29 (d, J = 3.8 Hz, 1H). **^{13}C NMR (E & Z mixture)** (101 MHz, Chloroform-d) δ 153.95, 153.74, 145.53, 145.50, 140.70, 138.49, 132.14, 131.75, 127.76, 127.65, 124.80, 124.56, 121.64, 120.61, 120.24, 111.33, 111.26, 106.66, 106.62, 101.34, 100.62, 70.02, 70.00, 64.46, 61.56, 43.47, 38.33, 23.26, 23.03, 22.55, 20.62. **HRMS** calculated for $C_{16}H_{16}O_3$ (M + Na^+): 279.0992, found: 279.0988.

3-benzylidenehexahydro-4H-furo[2,3-b]pyran (19)



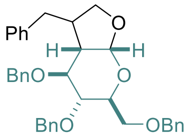
Eluent for purification: hexane: ethyl acetate = 20:1. Colorless oil (22.5 mg, 52% yield, E:Z = 5.6:1). **E-isomer**: **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.38 – 7.32 (m, 2H), 7.28 (d, *J* = 12.3 Hz, 3H), 6.31 (q, *J* = 2.0 Hz, 1H), 5.26 (d, *J* = 3.9 Hz, 1H), 4.75 (dt, *J* = 13.1, 1.9 Hz, 1H), 4.45 (ddd, *J* = 13.1, 2.0, 0.6 Hz, 1H), 3.97 – 3.86 (m, 1H), 3.69 (dtd, *J* = 11.0, 3.8, 1.4 Hz, 1H), 3.02 – 2.95 (m, 1H), 2.05 – 1.94 (m, 1H), 1.72 – 1.63 (m, 1H), 1.61 – 1.54 (m, 2H). **Z-isomer**: **^{1}H NMR**(400 MHz, Chloroform-*d*) δ 7.35 (t, *J* = 7.7 Hz, 2H), 7.25 – 7.19 (m, 1H), 7.19 – 7.11 (m, 2H), 6.29 (q, *J* = 2.6 Hz, 1H), 5.20 (d, *J* = 3.8 Hz, 1H), 4.90 (dt, *J* = 13.8, 2.5 Hz, 1H), 4.80 (dt, *J* = 13.9, 2.2 Hz, 1H), 3.93 – 3.81 (m, 1H), 3.50 (td, *J* = 11.3, 2.4 Hz, 1H), 2.84 (s, 1H), 2.21 – 2.07 (m, 1H), 2.08 – 1.92 (m, 1H), 1.72 – 1.63 (m, 1H), 1.36 (dq, *J* = 13.7, 3.4 Hz, 1H). **E-isomer**: **^{13}C NMR** (101 MHz, Chloroform-d) δ 141.89, 136.74, 128.47, 127.85, 126.90, 121.51, 101.29, 69.85, 61.46, 38.30, 23.23, 22.58. **Z-isomer**: **^{13}C NMR** (101 MHz, Chloroform-d) δ 139.95, 136.99, 128.54, 127.91, 126.65, 120.49, 100.56, 70.01, 64.46, 43.56, 23.01, 20.59. **HRMS** calculated for $C_{14}H_{16}O_2$ (M + H^+): 217.1123, found: 217.1124.

3-(4-methoxybenzylidene)hexahydro-4H-furo[2,3-b]pyran (20)



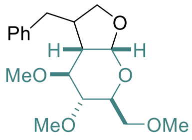
Eluent for purification: hexane: ethyl acetate = 20:1. Colorless oil (30.0 mg, 67% yield, E:Z = 4.6:1). **E-isomer**: **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.26 – 7.18 (m, 2H), 6.91 – 6.84 (m, 2H), 6.24 (q, *J* = 1.9 Hz, 1H), 5.25 (d, *J* = 3.9 Hz, 1H), 4.72 (dt, *J* = 12.8, 1.9 Hz, 1H), 4.42 (dd, *J* = 12.9, 1.8 Hz, 1H), 3.99 – 3.85 (m, 1H), 3.82 (s, 3H), 3.69 (dtd, *J* = 11.0, 3.9, 1.6 Hz, 1H), 3.03 – 2.87 (m, 1H), 2.04 – 1.95 (m, 1H), 1.67 – 1.55 (m, 3H). **Z-isomer**: **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.15 – 7.02 (m, 2H), 6.94 – 6.85 (m, 2H), 6.23 (q, *J* = 2.6 Hz, 1H), 5.19 (d, *J* = 3.8 Hz, 1H), 4.88 (dt, *J* = 13.7, 2.5 Hz, 1H), 4.77 (dt, *J* = 13.7, 2.2 Hz, 1H), 3.88 (ddt, *J* = 9.7, 4.0, 1.6 Hz, 1H), 3.82 (s, 3H), 3.50 (ddd, *J* = 11.6, 10.9, 2.4 Hz, 1H), 2.87 – 2.72 (m, 1H), 2.20 – 2.07 (m, 1H), 1.99 (m, 1H), 1.68 – 1.61 (m, 1H), 1.36 (dt, *J* = 13.7, 3.5 Hz, 1H). **E-isomer**: **^{13}C NMR** (126 MHz, Chloroform-*d*) δ 158.57, 139.84, 129.48, 129.09, 120.96, 113.96, 101.34, 69.91, 61.47, 55.30, 38.21, 23.22, 22.65. **Z-isomer**: **^{13}C NMR** (101 MHz, Chloroform-d) δ 158.29, 137.45, 129.89, 129.14, 119.82, 113.99, 100.59, 70.01, 64.45, 55.28, 43.41, 23.00, 20.60. **HRMS** calculated for $C_{15}H_{18}O_3$ ($M + Na^+$): 269.1148, found: 269.1147.

3-benzyl-4,5-bis(benzyloxy)-6-((benzyloxy)methyl)hexahydro-4H-furo[2,3-b]pyran (21)



Eluent for purification: hexane: ethyl acetate = 6:1. Colorless oil (47.3 mg, 43% yield, dr = 1.8:1.6:1.2:1). Isolated as an inseparable mixture of diastereomers. Spectral data for the major diastereomer is given herein. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.38 – 7.15 (m, 18H), 7.11 – 7.01 (m, 2H), 5.57 (d, *J* = 5.3 Hz, 1H), 4.69 – 4.50 (m, 5H), 4.44 (d, *J* = 11.0 Hz, 1H), 4.08 (dd, *J* = 8.9, 6.7 Hz, 1H), 3.83 (dt, *J* = 9.2, 3.1 Hz, 1H), 3.74 (dd, *J* = 10.6, 3.8 Hz, 1H), 3.70 – 3.62 (m, 2H), 3.58 (dd, *J* = 8.9, 4.3 Hz, 1H), 3.43 (t, *J* = 6.8 Hz, 1H), 2.65 (d, *J* = 7.8 Hz, 2H), 2.51 (dq, *J* = 11.2, 3.6 Hz, 1H), 2.27 – 2.14 (m, 1H). **^{13}C NMR (four isomers)** (101 MHz, Chloroform-*d*) δ 140.10, 139.46, 138.46 , 138.43, 138.41, 138.12, 138.08, 138.01, 129.06, 128.89, 128.63, 128.55, 128.52, 128.49, 128.46, 128.42, 128.40, 128.36, 128.34, 128.32, 128.30, 127.98, 127.92, 127.89, 127.84, 127.78, 127.75, 127.72 , 127.70, 127.58, 127.55, 127.43, 127.38, 126.36, 126.29, 126.17, 102.55, 102.33, 102.24, 101.15, 81.20, 80.88, 79.23, 79.07, 77.54, 77.25, 77.19, 75.69, 75.25, 74.91, 74.85, 74.50, 74.40, 74.12, 73.99, 73.93, 73.70, 73.62, 73.50, 73.46, 73.40, 73.31, 72.90, 72.00, 71.67, 71.55, 71.53, 70.83, 69.32, 69.22, 69.08, 68.47, 49.71, 47.73, 46.68, 46.36, 42.71, 42.54, 40.43, 40.39, 39.60, 38.88, 38.23, 34.87. **HRMS** calculated for $C_{36}H_{38}O_5$ ($M + H^+$): 551.2792, found: 551.2789.

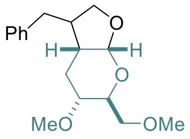
3-benzyl-4,5-dimethoxy-6-(methoxymethyl)hexahydro-4H-furo[2,3-b]pyran (22)



Eluent for purification: hexane: ethyl acetate = 6:1. Colorless oil (31.2 mg, 47%

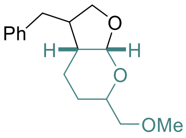
yield, dr = 1.5:1.5:1.4:1). Isolated as an inseparable mixture of diastereomers. Spectral data for the major diastereomer is given herein. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.31 – 7.26 (m, 2H), 7.21 – 7.15 (m, 3H), 5.40 (d, *J* = 4.3 Hz, 1H), 3.81 (t, *J* = 8.0 Hz, 1H), 3.76 – 3.70 (m, 1H), 3.70 – 3.64 (m, 3H), 3.63 (s, 3H), 3.57 (s, 3H), 3.42 (s, 3H), 3.41 – 3.31 (m, 2H), 3.12 (dd, *J* = 13.8, 4.9 Hz, 1H), 2.72 (dddd, *J* = 15.8, 10.6, 7.6, 5.1 Hz, 1H), 2.48 (dd, *J* = 13.8, 10.1 Hz, 1H), 2.21 (ddd, *J* = 9.4, 5.5, 4.2 Hz, 1H). **^{13}C NMR (four isomers)** (101 MHz, Chloroform-*d*) δ 141.44, 140.55, 140.23, 139.44, 129.03, 128.86, 128.61, 128.53, 128.52, 128.41, 128.39, 128.28, 126.40, 126.24, 126.13, 125.97, 102.56, 102.42, 102.25, 101.11, 83.16, 82.66, 80.54, 80.33, 79.07, 78.32, 77.40, 76.83, 74.11, 74.06, 73.88, 73.85, 71.93, 71.72, 71.61, 71.58, 71.13, 71.02, 70.73, 70.60, 60.42, 60.23, 59.91, 59.30, 59.18, 59.06, 58.95, 58.63, 58.59, 58.54, 57.54, 48.94, 47.17, 45.81, 45.65, 42.62, 42.33, 40.31, 40.25, 39.51, 38.81, 37.89, 34.35. **HRMS** calculated for $C_{18}H_{26}O_5$ (M + Na^+): 345.1672, found: 345.1672.

3-benzyl-5-methoxy-6-(methoxymethyl)hexahydro-4H-furo[2,3-b]pyran (23)

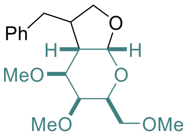


Eluent for purification: hexane: ethyl acetate = 6:1. Colorless oil (32.1 mg, 55% yield, dr = 1.3:1.2:1.2:1). Isolated as an inseparable mixture of diastereomers. Spectral data for the major diastereomer is given herein. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.32 – 7.26 (m, 2H), 7.24 – 7.13 (m, 3H), 5.47 (d, *J* = 5.4 Hz, 1H), 4.23 – 4.16 (m, 1H), 3.91 – 3.73 (m, 1H), 3.71 – 3.62 (m, 1H), 3.62 – 3.52 (m, 2H), 3.39 (s, 3H), 3.35 – 3.29 (m, 1H), 3.25 (s, 3H), 2.81 – 2.47 (m, 3H), 2.19 – 2.09 (m, 1H), 2.08 – 1.98 (m, 1H), 1.93 – 1.77 (m, 1H). **^{13}C NMR (four isomers)** (101 MHz, Chloroform-*d*) δ 140.27, 139.84, 139.80, 139.67, 128.89, 128.79, 128.59, 128.57, 128.53, 128.50, 128.38, 128.26, 126.33, 126.30, 126.26, 126.18, 103.10, 102.56, 101.96, 101.25, 75.06, 74.60, 73.77, 73.57, 73.31, 73.25, 72.36, 72.31, 72.23, 72.09, 71.61, 71.56, 71.52, 71.19, 69.88, 59.31, 59.26, 57.07, 56.59, 56.57, 56.40, 44.75, 44.64, 42.33, 42.09, 41.25, 40.25, 39.38, 38.55, 37.73, 36.85, 34.17, 33.11, 27.62, 27.56, 25.68, 22.13. **HRMS** calculated for $C_{17}H_{24}O_4$ (M + Na^+): 315.1567, found: 315.1566.

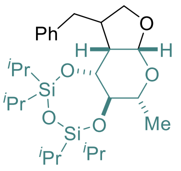
3-benzyl-6-(methoxymethyl)hexahydro-4H-furo[2,3-b]pyran (24)


Eluent for purification: hexane: ethyl acetate = 6:1. Colorless oil (34.1 mg, 65% yield, dr = 2.4:1.1:1:1). Isolated as an inseparable mixture of diastereomers. Spectral data for the major diastereomer is given herein. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.30 – 7.26 (m, 2H), 7.22 – 7.17 (m, 1H), 7.16 – 7.12 (m, 2H), 5.09 (d, *J* = 3.2 Hz, 1H), 4.19 (t, *J* = 8.2 Hz, 1H), 3.64 (t, *J* = 8.3 Hz, 1H), 3.58 – 3.49 (m, 1H), 3.47 – 3.41 (m, 1H), 3.39 (d, *J* = 8.8 Hz, 1H), 3.36 (s, 3H), 2.85 (dd, *J* = 12.9, 4.5 Hz, 1H), 2.67 – 2.52 (m, 2H), 1.84 (ddq, *J* = 10.1, 5.0, 2.3, 1.8 Hz, 2H), 1.76 (tt, *J* = 12.1, 3.2 Hz, 2H), 1.40 (m, 1H). **^{13}C NMR (four isomers)** (101 MHz, Chloroform-*d*) δ 140.85, 140.04, 139.97, 139.93, 128.75, 128.62, 128.52, 128.49, 128.30, 126.23, 126.20, 126.07, 102.99, 102.65, 102.62, 101.18, 75.60, 75.47, 75.39, 75.27, 74.09, 73.55, 72.39, 71.61, 70.53, 69.56, 69.02, 68.56, 59.24, 44.90, 44.02, 42.44, 39.44, 39.09, 38.78, 38.59, 36.15, 36.01, 33.12, 25.25, 24.34, 23.67, 22.68, 21.81, 19.45. **HRMS** calculated for $C_{16}H_{22}O_3$ (M + Na$^+$): 285.1461, found: 285.1465.

3-benzyl-4,5-dimethoxy-6-(methoxymethyl)hexahydro-4H-furo[2,3-b]pyran (25)

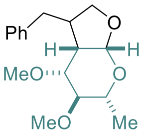

Eluent for purification: hexane: ethyl acetate = 10:1. Colorless oil (35.4 mg, 55% yield, dr = 6.7:6:5.7:1). Isolated as an inseparable mixture of diastereomers. Spectral data for the major diastereomer is given herein. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.30 – 7.27 (m, 2H), 7.24 7.18 (m, 3H), 5.42 (d, *J* = 4.2 Hz, 1H), 3.79 – 3.76 (m, 2H), 3.71 – 3.69 (m, 1H), 3.67 – 3.65 (m, 1H), 3.64 (s, 3H), 3.57 (s, 3H), 3.44 (dd, *J* = 4.6, 1.6 Hz, 2H), 3.41 (s, 3H), 3.35 – 3.32 (m, 1H), 3.11 (dd, *J* = 9.8, 2.5 Hz, 1H), 2.75 (ddd, *J* = 7.5, 5.9, 4.2 Hz, 1H), 2.64 – 2.59 (m, 1H), 2.21 – 2.17 (m, 1H). **^{13}C NMR (four isomers)** (126 MHz, Chloroform-*d*) δ 141.10, 140.50, 139.69, 128.91, 128.67, 128.51, 128.50, 128.37, 128.27, 126.29, 126.21, 125.90, 102.74, 102.31, 101.04, 80.87, 80.83, 80.67, 74.77, 74.20, 72.64, 71.93, 71.51, 71.30, 71.14, 70.97, 70.91, 70.91, 70.39, 69.94, 69.63, 61.05, 60.83, 60.67, 59.19, 59.19, 59.16, 57.09, 57.03, 55.49, 48.16, 44.33, 42.48, 42.41, 40.95, 40.02, 39.80, 39.00, 35.26. **HRMS** calculated for $C_{18}H_{26}O_5$ (M + Na$^+$): 345.1672, found: 345.1672.

10-benzyl-2,2,4,4-tetraisopropyl-6-methylhexahydro-6H-furo[3',2':5,6]pyrano[3,4-f][1,3,5,2,4]trioxadisilepine (26)



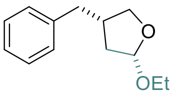
Eluent for purification: hexane: ethyl acetate = 6:1. Colorless oil (44.6 mg, 44% yield, dr = 2.3:2.2:2.2:1). Isolated as an inseparable mixture of diastereomers. Spectral data for the major diastereomer is given herein. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.31 – 7.26 (m, 2H), 7.25 – 7.12 (m, 3H), 5.44 (d, *J* = 4.5 Hz, 1H), 4.19 – 3.99 (m, 1H), 3.82 – 3.67 (m, 2H), 3.40 (t, *J* = 8.9 Hz, 1H), 3.29 – 3.22 (m, 1H), 2.79 – 2.59 (m, 1H), 2.25 (dt, *J* = 9.5, 5.0 Hz, 1H), 1.98 (dd, *J* = 9.0, 4.5 Hz, 1H), 1.37 (d, *J* = 6.2 Hz, 1H), 1.15 – 1.00 (m, 31H). **^{13}C NMR (four isomers)** (101 MHz, Chloroform-*d*) δ 140.77, 140.22, 139.51, 129.18, 128.78, 128.69, 128.56, 128.50, 128.47, 128.43, 128.21, 126.26, 126.09, 102.31, 101.86, 101.00, 77.91, 77.57, 77.21, 76.74, 76.33, 75.89, 74.01, 73.61, 73.52, 71.10, 71.06, 70.59, 70.54, 69.36, 68.63, 52.26, 49.36, 48.29, 43.41, 42.58, 41.05, 39.82, 39.00 , 35.08, 18.14, 17.92, 17.90, 17.81, 17.75, 17.71, 17.67, 17.60, 17.53, 17.49, 17.44, 17.42, 17.38, 17.32, 17.30, 17.30, 17.25, 17.23, 17.21, 16.99, 13.48, 12.98, 12.97, 12.92, 12.87, 12.78, 12.76, 12.73, 12.71, 12.34, 12.24, 12.20, 12.19. **HRMS** calculated for $C_{27}H_{46}O_5Si_2$ (M + Na$^+$): 529.2776, found: 529.2768.

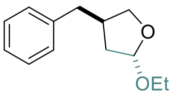
3-benzyl-4,5-dimethoxy-6-methylhexahydro-4H-furo[2,3-b]pyran (27)



Eluent for purification: hexane: ethyl acetate = 10:1. Colorless oil (36.7mg, 77% yield, dr = 2.3:2:1.2:1). Isolated as an inseparable mixture of diastereomers. Spectral data for the major diastereomer is given herein. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.33 – 7.26 (m, 2H), 7.20 (t, *J* = 6.9 Hz, 3H), 5.44 (d, *J* = 5.7 Hz, 1H), 4.18 (dd, *J* = 8.8, 6.6 Hz, 1H), 3.70 – 3.63 (m, 1H), 3.63 (s, 3H), 3.37 (d, *J* = 4.2 Hz, 3H), 3.32 (t, *J* = 9.2 Hz, 1H), 3.05 – 2.95 (m, 2H), 2.83 (dd, *J* = 8.9, 5.4 Hz, 1H), 2.76 – 2.68 (m, 1H), 2.53 – 2.36 (m, 1H), 2.17 (dq, *J* = 20.3, 5.3 Hz, 1H), 1.29 (t, *J* = 6.5 Hz, 3H). **^{13}C NMR (four isomers)** (101 MHz, Chloroform-*d*) δ 141.41, 140.62, 140.28, 139.48, 129.03, 128.85, 128.56, 128.54, 128.51, 128.44, 128.41, 128.29, 126.40, 126.23, 126.13, 126.01, 102.25, 102.13, 101.92, 100.85, 86.91, 84.50, 83.46, 83.03, 82.72, 82.57, 80.11, 78.74, 77.23, 74.06, 73.80, 71.75, 70.69, 70.53, 70.23, 68.00, 67.55, 60.78, 60.60, 60.43 , 59.04, 58.76, 58.51, 58.44, 57.54, 48.97, 47.30, 45.97, 42.70, 42.35, 40.39, 40.21 , 39.54, 38.95, 38.20, 34.32, 18.65, 18.42, 17.94, 17.40. **HRMS** calculated for $C_{17}H_{24}O_4$ (M + Na$^+$): 315.1567, found: 315.1565.

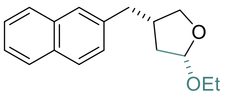
4-benzyl-2-ethoxytetrahydrofuran (28)

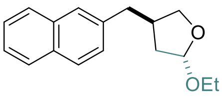




Eluent for purification: hexane: ethyl acetate = 100:1. Colorless oil (33.4 mg, 81% yield, dr = 1.4:1). Isolated as an inseparable mixture of diastereomers. Spectral data for the two diastereomers is given herein. **cis-isomer**: **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.29 (dd, *J* = 8.1, 6.8 Hz, 3H), 7.23 – 7.15 (m, 2H), 5.19 – 5.09 (m, 1H), 3.91 (dd, *J* = 8.4, 7.1 Hz, 1H), 3.74 (ddq, *J* = 27.0, 9.6, 7.1 Hz, 1H), 3.65 – 3.55 (m, 1H), 3.44 (ddq, *J* = 18.4, 9.6, 7.1 Hz, 1H), 2.84 – 2.71 (m, 2H), 2.49 (ddd, *J* = 15.9, 8.7, 7.4 Hz, 1H), 2.21 (ddd, *J* = 13.3, 9.1, 5.6 Hz, 1H), 1.67 – 1.58 (m, 1H), 1.23 (t, *J* = 7.1 Hz, 3H). **trans-isomer**: **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.29 (dd, *J* = 8.1, 6.8 Hz, 3H), 7.23 – 7.15 (m, 2H), 5.19 – 5.09 (m, 1H), 3.99 (dd, *J* = 8.4, 7.0 Hz, 1H), 3.74 (ddq, *J* = 27.0, 9.6, 7.1 Hz, 1H), 3.65 – 3.55 (m, 1H), 3.44 (ddq, *J* = 18.4, 9.6, 7.1 Hz, 1H), 2.74 – 2.64 (m, 3H), 2.00 (ddd, *J* = 13.1, 7.1, 1.3 Hz, 1H), 1.71 (ddd, *J* = 13.2, 7.9, 5.2 Hz, 1H), 1.18 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (trans & cis mixture)** (126 MHz, Chloroform-*d*) δ 140.86, 140.56, 128.69, 128.62, 128.44, 126.13, 126.05, 104.42, 103.95, 71.79, 71.72, 63.09, 62.69, 40.15, 39.93, 39.28, 39.16, 38.83, 15.37, 15.26. **HRMS** calculated for $C_{13}H_{18}O_2$ (M + Na$^+$): 229.1199, found: 229.1197.

2-ethoxy-4-(naphthalen-2-ylmethyl)tetrahydrofuran (29)

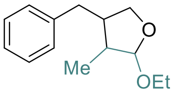




Eluent for purification: hexane: ethyl acetate = 100:1. Colorless oil (32.3 mg, 63% yield, dr = 1.1:1). Isolated as an inseparable mixture of diastereomers. Spectral data for the two diastereomers is given herein. **cis-isomer**: **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.83 – 7.75 (m, 3H), 7.64 – 7.59 (m, 1H), 7.45 (pd, *J* = 6.9, 1.6 Hz, 2H), 7.32 (dt, *J* = 8.4, 2.0 Hz, 1H), 5.20 – 5.13 (m, 1H), 3.94 (dd, *J* = 8.3, 7.2 Hz, 1H), 3.82 –

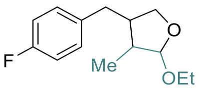
3.61 (m, 2H), 3.46 (ddq, *J* = 16.8, 9.7, 7.0 Hz, 1H), 2.95 (dd, *J* = 7.8, 2.1 Hz, 2H), 2.60 (ddd, *J* = 15.8, 8.6, 7.3 Hz, 1H), 2.23 (ddd, *J* = 13.4, 9.1, 5.6 Hz, 1H), 1.73 – 1.67 (m, 1H), 1.26 (t, *J* = 7.0 Hz, 3H). **trans-isomer**: **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.83 – 7.75 (m, 3H), 7.64 – 7.59 (m, 1H), 7.45 (pd, *J* = 6.9, 1.6 Hz, 2H), 7.32 (dt, *J* = 8.4, 2.0 Hz, 1H), 5.20 – 5.13 (m, 1H), 4.04 – 3.98 (m, 1H), 3.82 – 3.61 (m, 2H), 3.46 (ddq, *J* = 16.8, 9.7, 7.0 Hz, 1H), 2.89 – 2.80 (m, 3H), 2.04 (ddd, *J* = 12.8, 6.2, 1.9 Hz, 1H), 1.77 (ddd, *J* = 12.7, 7.5, 5.2 Hz, 1H), 1.19 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (trans & cis mixture)** (101 MHz, Chloroform-*d*) δ 138.35, 138.06, 133.59, 133.55, 128.04, 128.02, 127.61, 127.46, 127.31, 127.29, 126.85, 126.77, 126.01, 125.98, 125.32, 125.28, 104.41, 103.95, 71.74, 63.10, 62.70, 40.10, 40.04, 39.45, 39.17, 38.82, 38.70, 15.38, 15.25. **HRMS** calculated for $C_{17}H_{20}O_2$ (M + Na^+): 279.1356, found: 279.1355.

4-benzyl-2-ethoxy-3-methyltetrahydrofuran (30)



Eluent for purification: hexane: ethyl acetate = 100:1. Colorless oil (39.6 mg, 90% yield, dr = 2.4:2:1.7:1). Isolated as an inseparable mixture of diastereomers. Spectral data for the major diastereomers is given herein. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.29 (m, 2H), 7.23 – 7.15 (m, 3H), 4.91 (d, *J* = 4.8 Hz, 1H), 4.00 – 3.89 (m, 1H), 3.84 – 3.62 (m, 1H), 3.55 (t, *J* = 8.3 Hz, 1H), 3.44 (m, 1H), 2.96 – 2.75 (m, 2H), 2.59 – 2.45 (m, 1H), 2.39 – 2.28 (m, 1H), 1.24 (td, *J* = 7.1, 0.9 Hz, 3H), 1.03 – 0.99 (m, 3H). **^{13}C NMR (four isomers)** (101 MHz, Chloroform-*d*) δ 141.51, 140.77, 140.56, 140.47, 128.80, 128.59, 128.52, 128.44, 128.42, 128.39, 128.35, 126.06, 126.02, 125.80, 110.88 , 110.04, 105.52, 105.37, 72.47, 72.09, 71.36, 71.22, 63.42, 63.07, 62.79, 62.74, 48.15, 46.06, 44.73, 44.23, 42.03, 41.48, 41.47, 40.49, 38.87, 38.32, 35.53, 33.79, 16.94, 15.45, 15.36, 15.27, 15.24, 11.76, 11.68, 9.14. **HRMS** calculated for $C_{14}H_{20}O_2$ (M + Na^+): 243.1356, found: 243.1354.

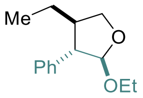
2-ethoxy-4-(4-fluorobenzyl)-3-methyltetrahydrofuran (31)

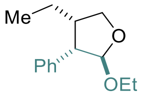


Eluent for purification: hexane: ethyl acetate = 100:1. Colorless oil (33.3mg, 70% yield, dr = 1.8:1.6:1.1:1). Isolated as an inseparable mixture of diastereomers. Spectral data for the major diastereomers is given herein. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.16 –

7.06 (m, 2H), 6.95 (td, *J* = 8.7, 1.8 Hz, 2H), 4.70 (d, *J* = 3.1 Hz, 1H), 3.96 – 3.87 (m, 1H), 3.80 – 3.69 (m, 1H), 3.64 – 3.59 (m, 1H), 3.47 – 3.38 (m, 1H), 2.90 – 2.69 (m, 2H), 2.67 – 2.58 (m, 1H), 2.00 (tq, *J* = 8.7, 7.0 Hz, 1H), 1.23 – 1.20 (m, 3H), 0.98 (dd, *J* = 7.2 Hz, 3H). **^{13}C NMR (four isomers)** (101 MHz, Chloroform-*d*) δ 162.59, 162.58, 160.17, 160.15, 137.09 (d, *J* = 3.2 Hz), 136.19 (d, *J* = 3.2 Hz), 136.09 (d, *J* = 3.2 Hz), 130.08 (d, *J* = 7.7 Hz), 129.95 (d, *J* = 7.7 Hz), 129.93 (d, *J* = 7.9 Hz), 129.76, 115.29 (d, *J* = 21.1 Hz),, 115.27 (d, *J* = 21.2 Hz), 115.24 (d, *J* = 21.3 Hz), 115.18 (d, *J* = 21.1 Hz), 110.81, 110.00, 105.51, 105.32, 72.31, 71.94, 71.24, 71.06, 63.37, 63.07, 62.81, 62.75, 48.20, 45.89, 44.84, 44.17, 41.93, 41.57, 40.48, 38.04, 37.55, 34.74, 32.95, 17.01, 15.42, 15.33, 15.23, 15.20, 11.75, 11.61, 9.11. **HRMS** calculated for $C_{14}H_{19}FO_2$ (M + Na$^+$): 261.1261, found: 261.1260.

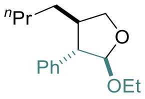
2-ethoxy-4-ethyl-3-phenyltetrahydrofuran (32)

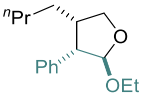




Eluent for purification: hexane: ethyl acetate = 100:1. Colorless oil (35.7 mg, 81% yield, dr = 5:1). Isolated as an inseparable mixture of diastereomers. Spectral data for the two diastereomers is given herein. **trans-trans-isomer**: **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.35 – 7.29 (m, 2H), 7.28 – 7.18 (m, 3H), 5.05 (d, *J* = 3.2 Hz, 1H), 4.23 (dt, *J* = 12.0, 8.1 Hz, 1H), 3.81 – 3.68 (m, 2H), 3.51 – 3.37 (m, 1H), 2.89 (dd, *J* = 8.2, 3.3 Hz, 1H), 2.28 – 2.18 (m, 1H), 1.65 – 1.57 (m, 1H), 1.50 – 1.41 (m, 1H), 1.20 (t, *J* = 7.1 Hz, 3H), 0.86 (t, *J* = 7.5 Hz, 3H). **cis-trans-isomer: ^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.35 – 7.29 (m, 2H), 7.28 – 7.18 (m, 3H), 5.13 (s, 1H), 4.23 (dt, *J* = 12.0, 8.1 Hz, 1H), 3.81 – 3.68 (m, 1H), 3.65 (dd, *J* = 9.5, 8.3 Hz, 1H), 3.51 – 3.37 (m, 1H), 3.31 (d, *J* = 7.5 Hz, 1H), 2.75 (m, 1H), 1.73 – 1.68 (m, 1H), 1.23 (t, *J* = 7.1 Hz, 3H), 1.08 (dt, *J* = 13.8, 7.0 Hz, 1H), 0.82 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (126 MHz, Chloroform-*d*) δ 142.21, 138.60, 128.72, 128.61, 128.33, 127.72, 126.57, 110.89, 108.97, 72.55, 72.18, 63.43, 62.64, 58.96, 54.58, 50.26, 43.25, 24.93, 21.74, 15.32, 15.30, 13.07, 12.81. **HRMS** calculated for $C_{14}H_{20}O_2$ (M +Na$^+$): 243.1356, found: 243.1356.

4-butyl-2-ethoxy-3-phenyltetrahydrofuran (33)

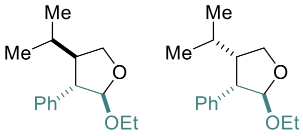




Eluent for purification: hexane: ethyl acetate = 100:1. Colorless oil

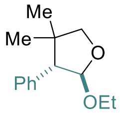
(44.7 mg, 90% yield, dr = 7.7:1). Isolated as an inseparable mixture of diastereomers. Spectral data for the two diastereomers is given herein. **trans-trans-isomer**: **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.35 – 7.28 (m, 2H), 7.27 – 7.16 (m, 3H), 5.03 (d, *J* = 3.3 Hz, 1H), 4.25 – 4.16 (m, 1H), 3.78 – 3.67 (m, 2H), 3.41 (dq, *J* = 9.6, 7.0 Hz, 1H), 2.87 (dd, *J* = 8.4, 3.3 Hz, 1H), 2.27 (dtdd, *J* = 9.9, 8.6, 7.2, 5.5 Hz, 1H), 1.60 – 1.48 (m, 1H), 1.44 – 1.35 (m, 1H), 1.25 – 1.14 (m, 7H), 0.82 (t, *J* = 7.0 Hz, 3H). **cis-trans-isomer: ^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.35 – 7.28 (m, 2H), 7.27 – 7.16 (m, 3H), 5.12 (s, 1H), 4.25 – 4.16 (m, 1H), 3.78 – 3.67 (m, 1H), 3.66 – 3.59 (m, 1H), 3.41 (dq, *J* = 9.6, 7.0 Hz, 1H), 3.28 (d, *J* = 7.5 Hz, 1H), 2.84 – 2.75 (m, 1H), 1.60 – 1.48 (m, 1H), 1.25 – 1.14 (m, 7H), 1.06 – 1.02 (m, 1H), 0.82 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 142.06, 138.57, 128.66, 128.56, 128.28, 127.70, 126.54, 126.51, 110.81, 108.86, 72.74, 72.31, 63.43, 61.85, 59.20, 54.65, 48.60, 41.25, 31.64, 30.59, 28.23, 22.80, 22.69, 15.29, 15.25, 13.91. **HRMS** calculated for $C_{16}H_{24}O_2$ (M + Na$^+$): 271.1669, found: 271.1671.

2-ethoxy-4-isopropyl-3-phenyltetrahydrofuran (34)



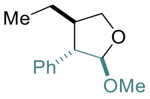
Eluent for purification: hexane: ethyl acetate = 100:1. Colorless oil (43.7 mg, 88% yield, dr = 2.8:1). Isolated as an inseparable mixture of diastereomers. Spectral data for the two diastereomers is given herein. **trans-trans-isomer**: **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.34 – 7.18 (m, 5H), 4.95 (d, *J* = 2.5 Hz, 1H), 4.17 (t, *J* = 8.0 Hz, 1H), 3.82 – 3.64 (m, 2H), 3.49 – 3.34 (m, 1H), 3.01 (dd, *J* = 7.4, 2.5 Hz, 1H), 2.15 – 2.03 (m, 1H), 1.75 (dp, *J* = 8.8, 6.6 Hz, 1H), 1.20 (dt, *J* = 16.8, 7.1 Hz, 3H), 0.87 – 0.82 (m, 6H). **cis-trans-isomer: ^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.34 – 7.18 (m, 5H), 5.01 (s, 1H), 4.22 (t, *J* = 8.5 Hz, 1H), 3.82 – 3.64 (m, 2H), 3.49 – 3.34 (m, 1H), 3.30 (d, *J* = 7.2 Hz, 1H), 2.53 (tdd, *J* = 10.7, 8.6, 7.1 Hz, 1H), 1.20 (dt, *J* = 16.8, 7.1 Hz, 3H), 1.08 (dq, *J* = 10.9, 6.5 Hz, 1H), 0.87 – 0.82 (m, 3H), 0.77 (d, *J* = 6.6 Hz, 3H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 143.65, 138.72, 129.03, 128.53, 128.30, 127.74, 126.58, 126.32, 111.23, 109.49, 71.55, 71.03, 62.99, 62.50, 57.41, 55.58, 54.08, 49.24, 31.48, 27.41, 21.93, 21.85, 21.70, 21.04, 15.27. **HRMS** calculated for $C_{15}H_{22}O_2$ (M + Na$^+$): 257.1512, found: 257.1511.

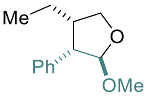
2-ethoxy-4,4-dimethyl-3-phenyltetrahydrofuran (35)



Eluent for purification: hexane: ethyl acetate = 100:1. Colorless oil (22.0 mg, 50% yield). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.29 – 7.22 (m, 2H), 7.22 – 7.17 (m, 1H), 7.14 – 7.08 (m, 2H), 5.34 (d, *J* = 4.8 Hz, 1H), 3.88 – 3.79 (m, 1H), 3.73 (dq, *J* = 9.5, 7.1 Hz, 1H), 3.66 (d, *J* = 8.1 Hz, 1H), 3.39 (dq, *J* = 9.5, 7.1 Hz, 1H), 2.93 (d, *J* = 4.8 Hz, 1H), 1.11 (t, *J* = 7.1 Hz, 3H), 1.03 (s, 3H), 0.69 (s, 3H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 137.38, 128.91, 128.17, 126.74, 109.17, 80.00, 64.00, 62.54, 43.39, 24.75, 22.86, 15.30. **HRMS** calculated for $C_{14}H_{20}O_2$ (M + Na^+): 243.1356, found: 243.1355.

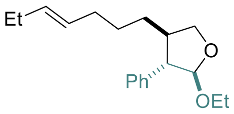
4-ethyl-2-methoxy-3-phenyltetrahydrofuran (36)

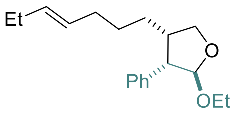




Eluent for purification: hexane: ethyl acetate = 100:1. Colorless oil (28.4 mg, 69% yield, dr = 5:1). Isolated as an inseparable mixture of diastereomers. Spectral data for the two diastereomers is given herein. **trans-trans-isomer**: **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.27 – 7.21 (m, 2H), 7.18 – 7.09 (m, 3H), 4.86 (d, *J* = 3.1 Hz, 1H), 4.20 – 4.11 (m, 1H), 3.59 (ddd, *J* = 12.6, 9.7, 8.4 Hz, 1H), 3.27 (s, 3H), 2.79 (dd, *J* = 8.2, 3.1 Hz, 1H), 2.15 (dtdd, *J* = 9.9, 8.3, 7.3, 5.7 Hz, 1H), 1.51 (dtd, *J* = 15.0, 7.5, 5.7 Hz, 1H), 1.45 – 1.29 (m, 1H), 0.77 (t, *J* = 7.4 Hz, 3H). **cis-trans-isomer: ^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.27 – 7.21 (m, 2H), 7.18 – 7.09 (m, 3H), 4.93 (s, 1H), 4.20 – 4.11 (m, 1H), 3.59 (ddd, *J* = 12.6, 9.7, 8.4 Hz, 1H), 3.31 (s, 3H), 3.22 (d, *J* = 7.5 Hz, 1H), 2.69 – 2.56 (m, 1H), 1.51 (dtd, *J* = 15.0, 7.5, 5.7 Hz, 1H), 1.45 – 1.29 (m, 1H), 0.77 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR (trans & cis mixture)** (126 MHz, Chloroform-*d*) δ 205.16, 204.81, 157.10, 154.80, 128.78, 123.41, 123.38, 122.56, 120.34, 110.83, 110.80, 103.78, 103.73, 57.67, 57.54, 33.58, 33.35, 32.95, 31.89, 19.76, 17.95, 16.83, 16.45, 12.21, 12.09. **HRMS** calculated for $C_{13}H_{18}O_2$ (M + H^+): 207.1380, found: 207.1370.

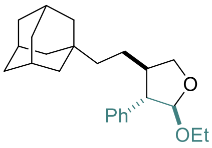
2-ethoxy-4-((E)-hept-4-en-1-yl)-3-phenyltetrahydrofuran (37)

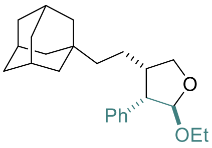




Eluent for purification: hexane: ethyl acetate = 100:1. Colorless oil (30.6 mg, 53% yield, dr = 5:1). Isolated as an inseparable mixture of diastereomers. Spectral data for the two diastereomers is given herein. **trans-trans-isomer**: **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.34 – 7.27 (m, 2H), 7.26 – 7.20 (m, 3H), 5.38 – 5.23 (m, 2H), 5.02 (d, *J* = 3.3 Hz, 1H), 4.24 – 4.16 (m, 1H), 3.80 – 3.65 (m, 2H), 3.49 – 3.35 (m, 1H), 2.87 (dd, *J* = 8.4, 3.3 Hz, 1H), 2.27 (dtdd, *J* = 10.0, 8.6, 7.3, 5.6 Hz, 1H), 1.99 – 1.87 (m, 4H), 1.54 (ddd, *J* = 13.2, 10.7, 6.3 Hz, 1H), 1.40 (dtd, *J* = 13.2, 8.7, 6.5 Hz, 1H), 1.28 – 1.23 (m, 3H), 1.19 (t, *J* = 7.2 Hz, 3H), 0.92 (t, *J* = 7.2 Hz, 3H). **cis-trans-isomer: ^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.34 – 7.27 (m, 2H), 7.26 – 7.20 (m, 2H), 7.19 – 7.15 (m, 1H), 5.38 – 5.23 (m, 2H), 5.11 (s, 1H), 4.24 – 4.16 (m, 1H), 3.80 – 3.65 (m, 1H), 3.62 (dd, *J* = 9.6, 8.2 Hz, 1H), 3.49 – 3.35 (m, 1H), 3.28 (d, *J* = 7.5 Hz, 1H), 2.79 (dt, *J* = 16.6, 8.3 Hz, 1H), 1.99 – 1.87 (m, 4H), 1.54 (ddd, *J* = 13.2, 10.7, 6.3 Hz, 1H), 1.40 (dtd, *J* = 13.2, 8.7, 6.5 Hz, 1H), 1.28 – 1.23 (m, 3H), 1.19 (t, *J* = 7.2 Hz, 3H), 0.92 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (trans & cis mixture)** (101 MHz, Chloroform-*d*) δ 142.05, 141.99, 132.37, 131.93, 128.66, 128.56, 127.69, 126.55, 110.81, 108.86, 72.69, 72.69, 63.44, 63.42, 59.14, 54.59, 48.45, 41.19, 32.56, 32.38, 31.59, 31.35, 28.56, 28.33, 25.52, 20.45, 15.27, 14.30, 13.90. **HRMS** calculated for $C_{19}H_{28}O_2$ (M + Na^+): 311.1982, found: 311.1981.

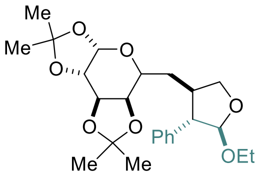
4-(2-((3r,5r,7r)-adamantan-1-yl)ethyl)-2-ethoxy-3-phenyltetrahydrofuran (38)

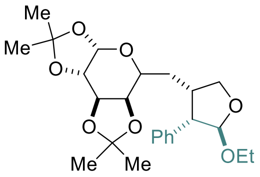




Eluent for purification: hexane: ethyl acetate = 100:1. Colorless oil (51.0 mg, 72% yield, dr = 7.1:1). Isolated as an inseparable mixture of diastereomers. Spectral data for the two diastereomers is given herein. **trans-trans-isomer**: **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.35 – 7.28 (m, 2H), 7.27 – 7.16 (m, 3H), 5.02 (d, *J* = 3.3 Hz, 1H), 4.19 (dd, *J* = 8.2, 7.2 Hz, 1H), 3.81 – 3.57 (m, 2H), 3.43 (ddq, *J* = 16.7, 9.7, 7.0 Hz, 1H), 2.87 (dd, *J* = 8.2, 3.2 Hz, 1H), 2.18 (dddd, *J* = 13.1, 9.8, 8.7, 7.4 Hz, 1H), 1.95 – 1.87 (m, 3H), 1.71 – 1.47 (m, 8H), 1.39 (d, *J* = 2.8 Hz, 6H), 1.18 (t, *J* = 7.1 Hz, 3H), 1.02 – 0.85 (m, 2H). **cis-trans-isomer: ^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.35 – 7.28 (m, 2H), 7.27 – 7.16 (m, 3H), 5.10 (s, 1H), 4.19 (dd, *J* = 8.2, 7.2 Hz, 1H), 3.81 – 3.57 (m, 2H), 3.43 (ddq, *J* = 16.7, 9.7, 7.0 Hz, 1H), 3.28 (d, *J* = 7.5 Hz, 1H), 2.70 (qd, *J* = 9.0, 4.4 Hz, 1H), 1.95 – 1.87 (m, 2H), 1.87 – 1.80 (m, 1H), 1.71 – 1.47 (m, 8H), 1.37 – 1.30 (m, 6H), 1.18 (t, *J* = 7.1 Hz, 3H), 1.02 – 0.85 (m, 3H). **^{13}C NMR (trans & cis mixture)** (101 MHz, Chloroform-*d*) δ 142.20, 138.39, 128.75, 128.56, 128.24, 127.70, 126.53, 126.51, 110.83, 108.97, 72.78, 72.38, 63.38, 62.56, 59.24, 54.37, 49.09, 43.41, 43.06, 42.31, 42.19, 41.99, 37.20, 37.14, 37.10, 32.13, 32.05, 29.69, 28.83, 28.68, 28.63, 24.92, 20.97, 15.29, 15.27. **HRMS** calculated for $C_{24}H_{34}O_2$ $(M + Na^+)$: 377.2451, found: 377.2453.

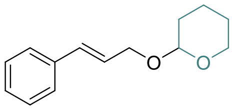
(3aS,5aR,8aR,8bS)-5-((5-ethoxy-4-phenyltetrahydrofuran-3-yl)methyl)-2,2,7,7 tetramethyltetrahydro-5H-bis([1,3]dioxolo)[4,5-b:4',5'-d]pyran (39)





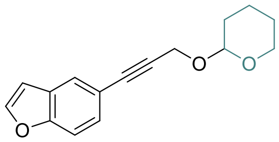
Eluent for purification: hexane: ethyl acetate = 10:1. Colorless oil (Z: 42 mg, 78% yield, dr = 2.6:2:1; E: 42 mg, 69% yield, dr = 1.1:1). Isolated as an inseparable mixture of diastereomers. Spectral data for the major diastereomers is given herein. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.34 – 7.14 (m, 5H), 5.47 (dd, *J* = 5.2, 1.9 Hz, 1H), 5.01 (t, *J* = 3.2 Hz, 1H), 4.51 (m, 1H), 4.34 – 4.21 (m, 2H), 3.95 – 3.93 (m, 1H), 3.80 – 3.69 (m, 2H), 3.64 – 3.56 (m, 1H), 3.39 (m, 1H), 2.90 (dt, *J* = 8.7, 3.1 Hz, 1H), 2.62 – 2.52 (m, 1H), 1.79 – 1.76 (m, 1H), 1.63 – 1.49 (m, 1H), 1.50 (s, 3H), 1.44 – 1.37 (m, 9H), 1.17 (td, *J* = 7.1, 2.5 Hz, 3H). **^{13}C NMR (trans & cis mixture)** (101 MHz, Chloroform-*d*) δ 141.39, 141.35, 138.51, 128.68, 128.57, 128.44, 127.85, 127.77, 126.65, 126.62, 126.59, 110.81, 110.00, 109.07, 109.01, 108.98, 108.75, 108.24, 108.16, 96.52, 96.46, 96.41, 77.24, 73.12, 72.99, 72.85, 72.16, 71.77, 70.91, 70.89, 70.43, 70.38, 70.28, 67.47, 66.21, 65.69, 63.43, 63.34, 62.54, 59.30, 59.00, 47.27, 43.87, 36.95, 32.50, 32.21, 29.68, 29.20, 26.02, 25.98, 25.91, 24.86, 24.82, 24.44, 24.25, 15.29, 15.18. **HRMS** calculated for $C_{24}H_{34}O_7$ $(M + Na^+)$: 457.2197, found: 457.2196

2-(cinnamyloxy)tetrahydro-2H-pyran (40)



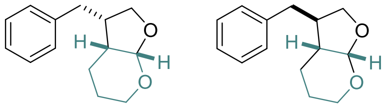
Eluent for purification: hexane: ethyl acetate = 20:1. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.44 – 7.37 (m, 2H), 7.36 – 7.29 (m, 2H), 7.27 – 7.21 (m, 1H), 6.64 (dt, *J* = 15.9, 1.5 Hz, 1H), 6.33 (ddd, *J* = 15.9, 6.6, 5.6 Hz, 1H), 4.72 (dd, *J* = 4.2, 3.0 Hz, 1H), 4.42 (ddd, *J* = 12.9, 5.6, 1.6 Hz, 1H), 4.17 (ddd, *J* = 12.9, 6.6, 1.4 Hz, 1H), 3.93 (ddd, *J* = 11.3, 8.0, 3.4 Hz, 1H), 3.61 – 3.49 (m, 1H), 1.94 – 1.82 (m, 1H), 1.81 – 1.71 (m, 1H), 1.67 – 1.51 (m, 4H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 136.81, 132.30, 128.50, 127.59, 126.48, 126.01, 97.86, 67.63, 62.24, 30.64, 25.48, 19.48. **HRMS** calculated for $C_{14}H_{18}O_2$ (M + Na$^+$): 241.1199, found: 241.1197.

5-(3-((tetrahydro-2H-pyran-2-yl)oxy)prop-1-yn-1-yl)benzofuran



Eluent for purification: hexane: ethyl acetate = 20:1. Colorless oil (6 mg, 23% yield). **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.73 (d, *J* = 1.5 Hz, 1H), 7.64 (d, *J* = 2.2 Hz, 1H), 7.48 – 7.37 (m, 2H), 6.75 (d, *J* = 2.1 Hz, 1H), 4.94 (t, *J* = 3.5 Hz, 1H), 4.61 – 4.43 (m, 2H), 3.92 (ddd, *J* = 11.6, 9.0, 3.0 Hz, 1H), 3.59 (dtd, *J* = 11.0, 4.3, 1.6 Hz, 1H), 1.93 – 1.83 (m, 1H), 1.79 (tt, *J* = 10.2, 3.4 Hz, 1H), 1.72 – 1.57 (m, 4H). **^{13}C NMR** (126 MHz, Chloroform-*d*) δ 154.65, 145.83, 128.28, 127.50, 125.09, 117.30, 111.47, 106.50, 96.89, 86.13, 83.70, 62.08, 54.90, 30.37, 25.45, 19.14. **HRMS** calculated for $C_{16}H_{16}O_3$ (M + Na$^+$): 279.0992, found: 279.0993.

(**1**)



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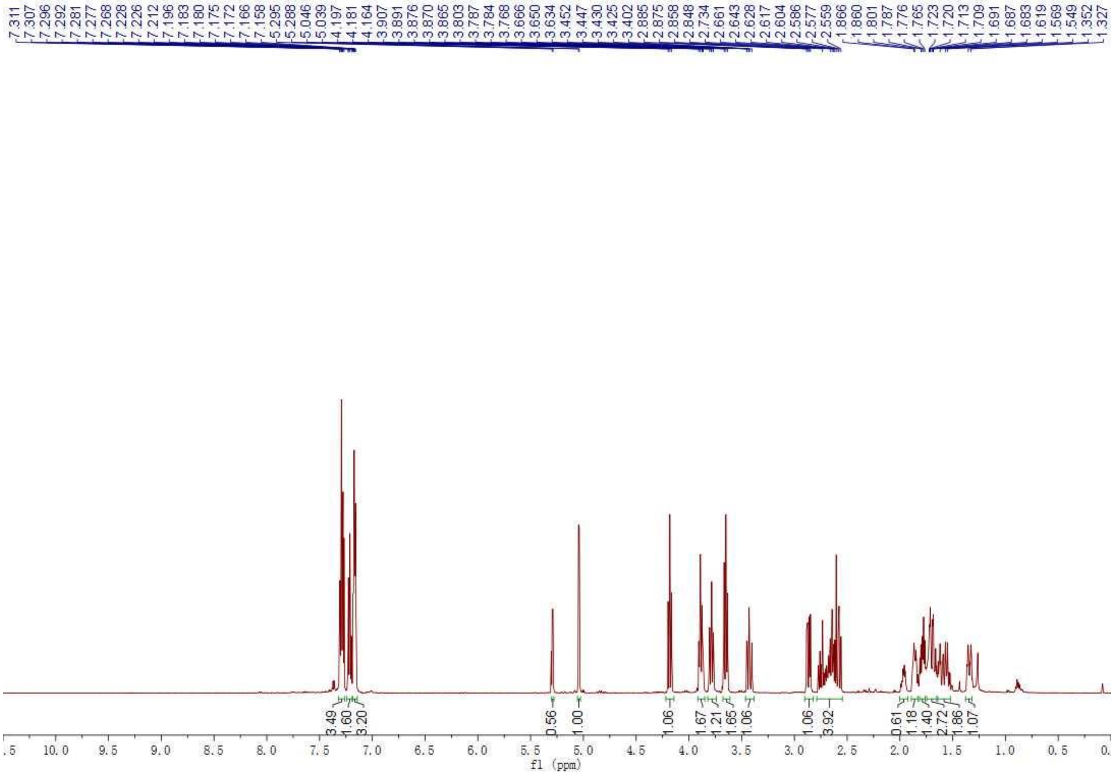

7.311
7.307
7.296
7.292
7.281
7.277
7.268
7.228
7.226
7.212
7.196
7.183
7.180
7.175
7.172
7.166
7.158
5.295
5.288
5.046
5.039
4.197
4.181
4.164
3.907
3.891
3.876
3.870
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3.803
3.787
3.784
3.768
3.666
3.650
3.634
3.452
3.447
3.430
3.425
3.402
2.885
2.875
2.858
2.848
2.734
2.661
2.643
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2.617
2.604
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2.577
2.559
1.866
1.860
1.801
1.787
1.776
1.765
1.723
1.720
1.713
1.709
1.691
1.687
1.683
1.619
1.569
1.549
1.352
1.327
3.49
1.60
3.20
0.56
1.00
1.06
1.67
1.21
1.65
1.06
1.06
3.92
0.61
1.18
1.40
2.72
1.86
1.07
.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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3.5
3.0
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1.5
1.0
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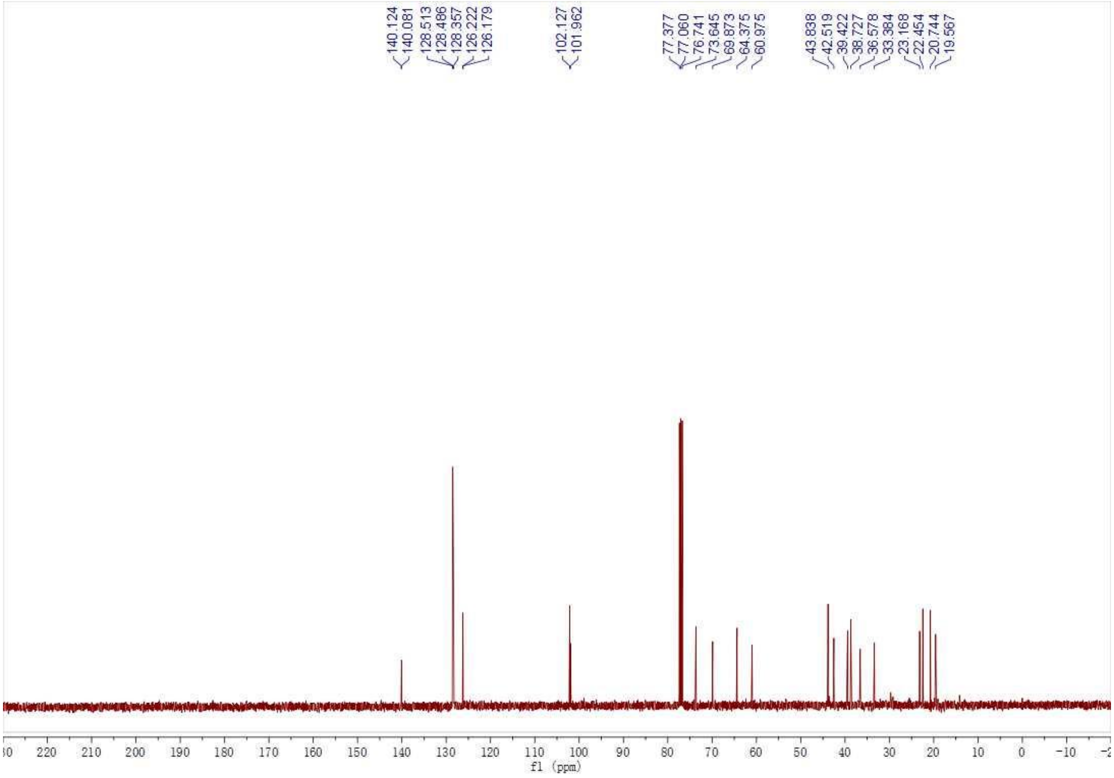
0.
f1 (ppm)



140.124
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128.513
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101.962
77.377
77.060
76.741
73.645
69.873
64.375
60.975
43.838
42.519
39.422
38.727
36.578
33.384
23.168
22.454
20.744
19.567
220
210
200
190
180
170
160
150
140
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120
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100
90
80
70
60
50
40
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20
10
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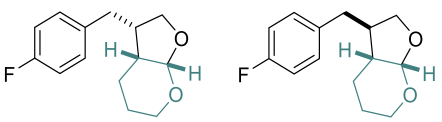
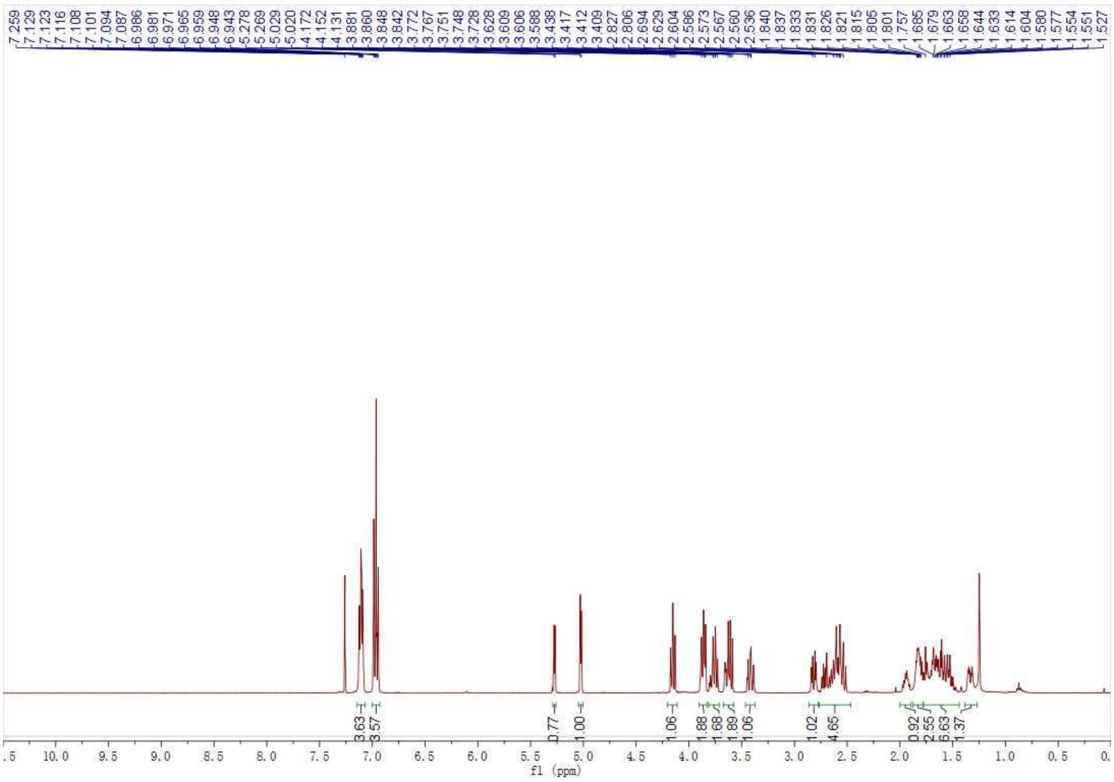
-10
f1 (ppm)

(**2**)



F
H
O
H
O
F
H
O
H
O



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7.116
7.108
7.101
7.094
7.087
6.986
6.981
6.971
6.965
6.959
6.948
6.943
5.278
5.269
5.029
5.020
4.172
4.152
4.131
3.881
3.860
3.848
3.842
3.772
3.767
3.751
3.748
3.728
3.628
3.609
3.606
3.588
3.438
3.417
3.412
3.409
2.827
2.806
2.694
2.629
2.604
2.586
2.573
2.567
2.560
2.536
1.840
1.837
1.833
1.831
1.826
1.821
1.815
1.805
1.801
1.757
1.685
1.679
1.663
1.658
1.644
1.633
1.614
1.604
1.580
1.577
1.554
1.551
1.527
3.63
3.57
0.77
1.00
1.06
1.88
1.68
1.89
1.06
1.02
4.65
0.92
2.55
6.63
1.37
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
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3.0
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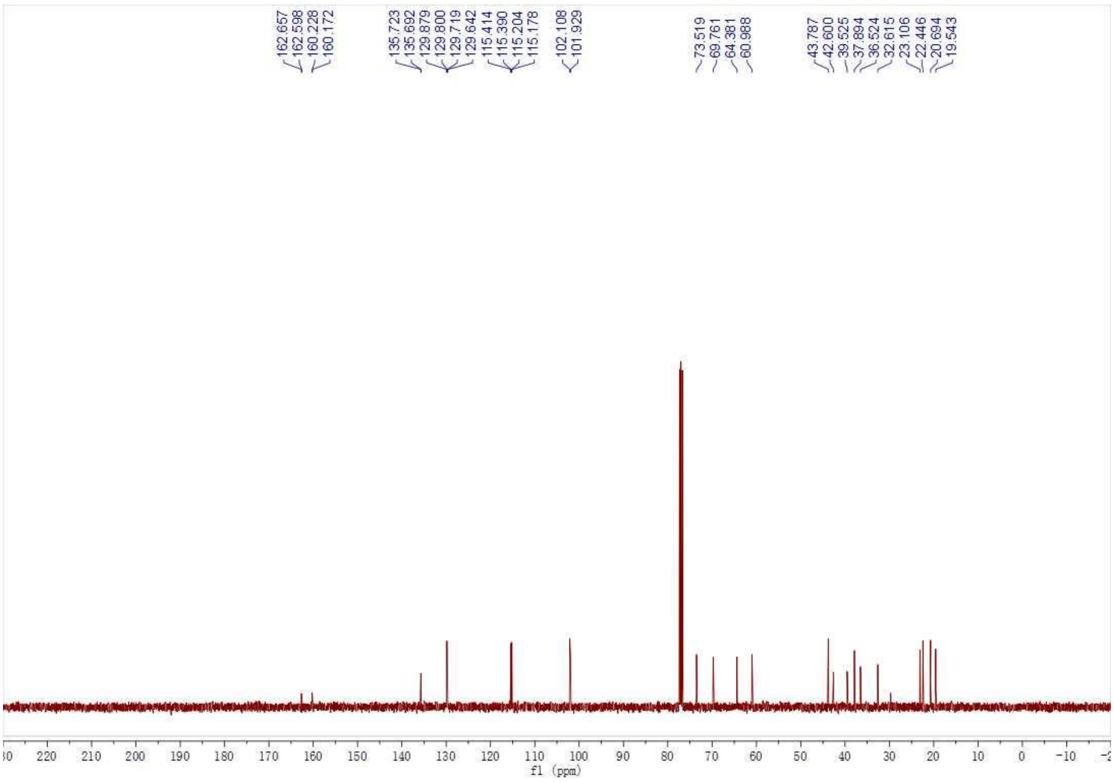
f1 (ppm)



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129.719
129.642
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115.390
115.204
115.178
102.108
101.929
73.519
69.761
64.381
60.988
43.787
42.600
39.525
37.894
36.524
32.615
23.106
22.446
20.694
19.543
220
210
200
190
180
170
160
150
140
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120
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100
90
80
70
60
50
40
30
20
10
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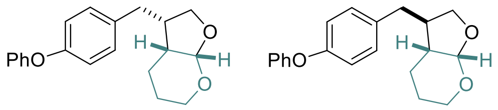
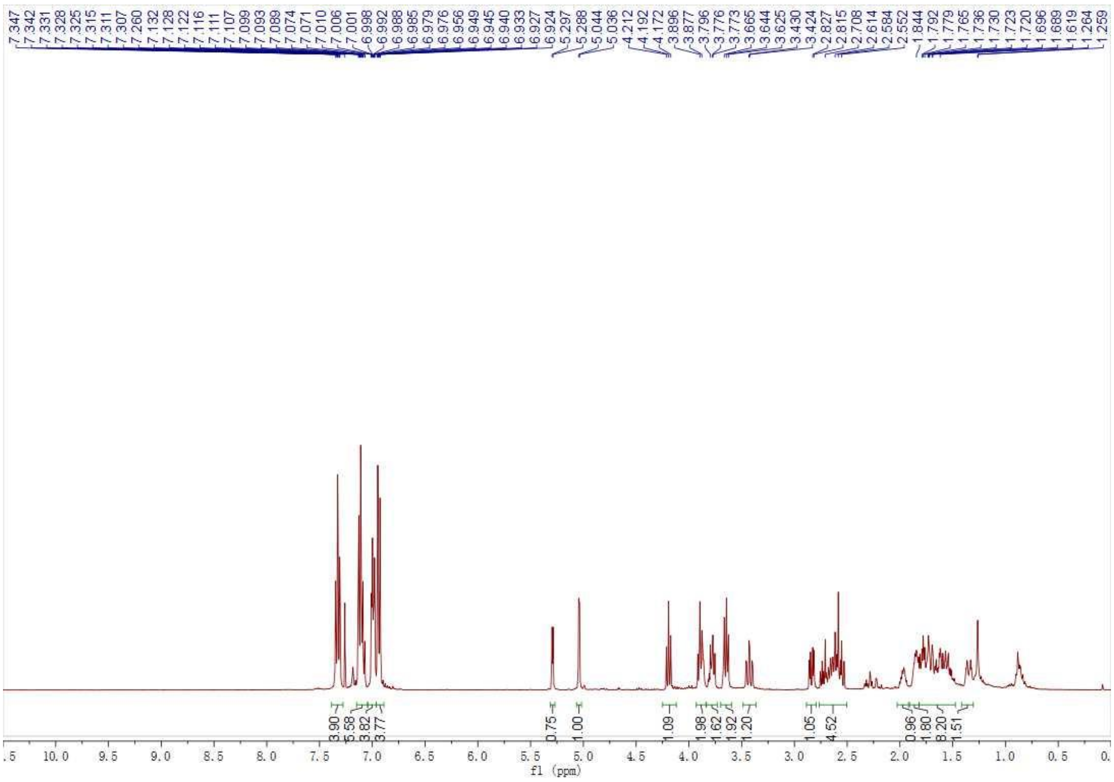
−10
f1 (ppm)

(**3**)



PhO
H
O
H
O
PhO
H
O
H
O



7.347
7.342
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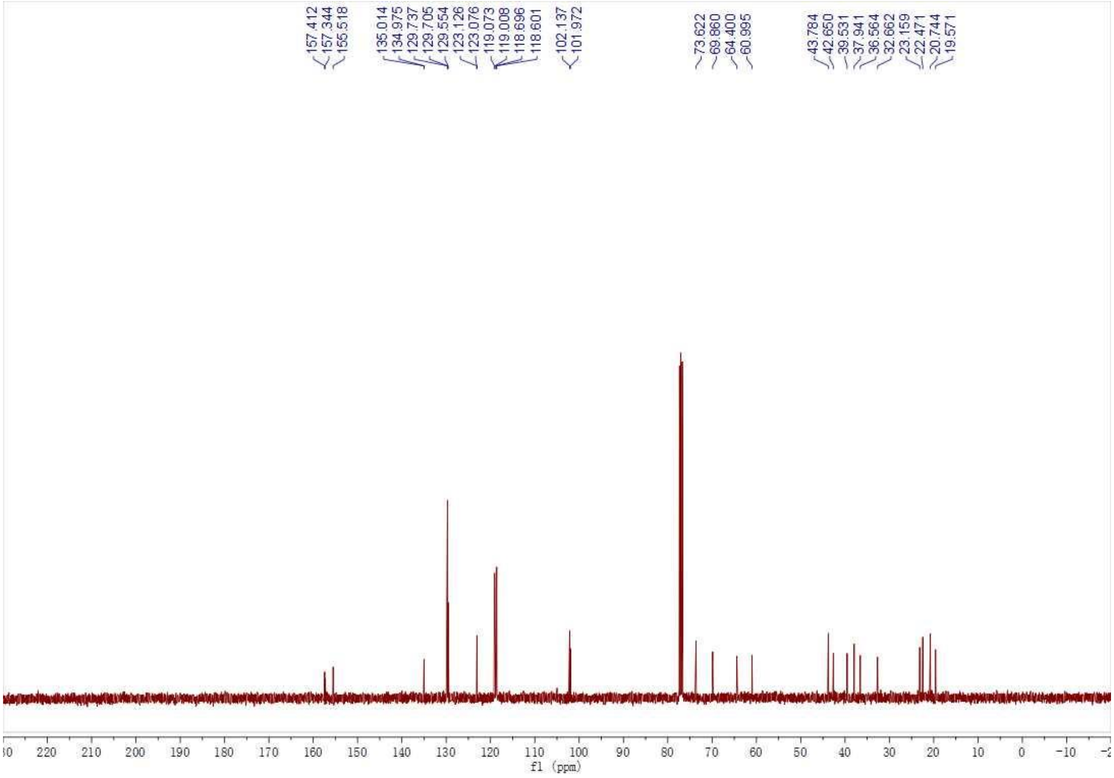
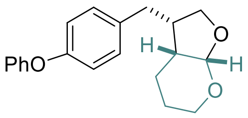
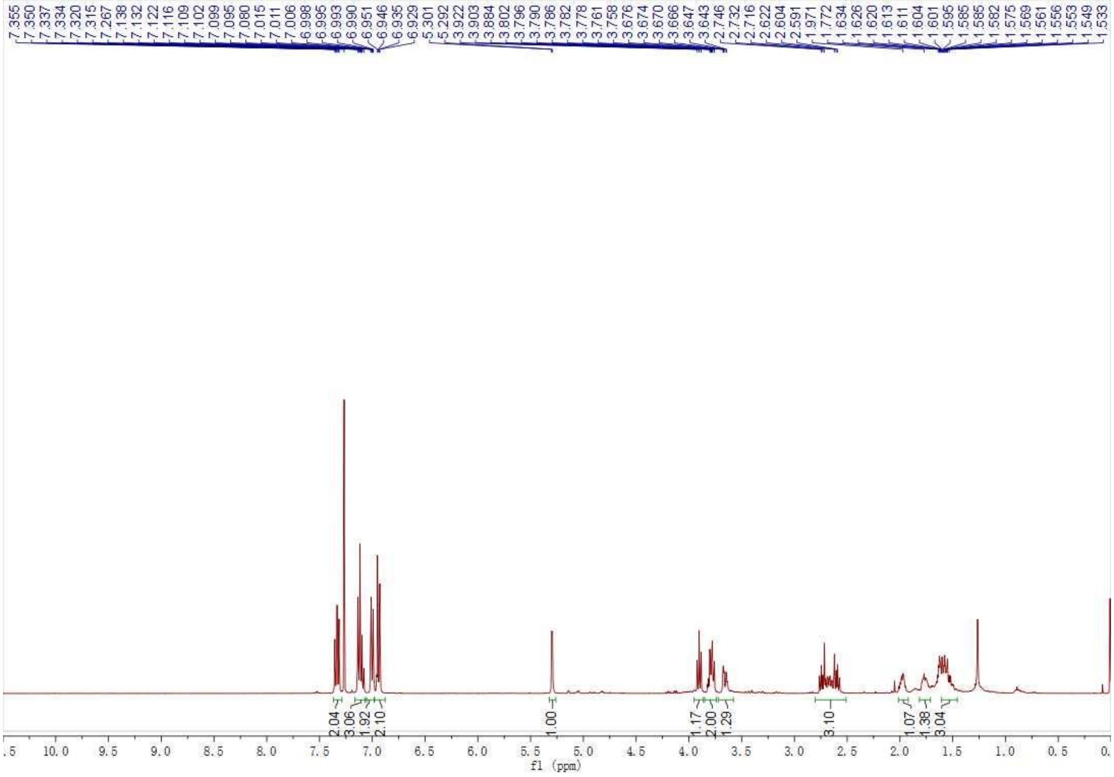
7.328
7.325
7.315
7.311
7.307
7.260
7.132
7.128
7.122
7.116
7.111
7.107
7.099
7.093
7.089
7.074
7.071
7.010
7.006
7.001
6.998
6.992
6.988
6.985
6.979
6.976
6.956
6.949
6.945
6.940
6.933
6.927
6.924
5.297
5.288
5.044
5.036
4.212
4.192
4.172
3.896
3.877
3.796
3.776
3.773
3.665
3.644
3.625
3.430
3.424
2.827
2.815
2.708
2.614
2.584
2.552
1.844
1.792
1.779
1.765
1.736
1.730
1.723
1.720
1.696
1.689
1.619
1.264
1.259
3.90
5.58
3.82
3.77
0.75
1.00
1.09
1.98
1.62
1.92
1.20
1.05
4.52
0.96
1.80
8.20
1.51
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
f1 (ppm)



157.412
157.344
155.518
135.014
134.975
129.737
129.705
129.554
123.126
123.076
119.073
119.008
118.696
118.601
102.137
101.972
73.622
69.860
64.400
60.995
43.784
42.650
39.531
37.941
36.564
32.662
23.159
22.471
20.744
19.571
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


PhO
H
H
O
O

cis-syn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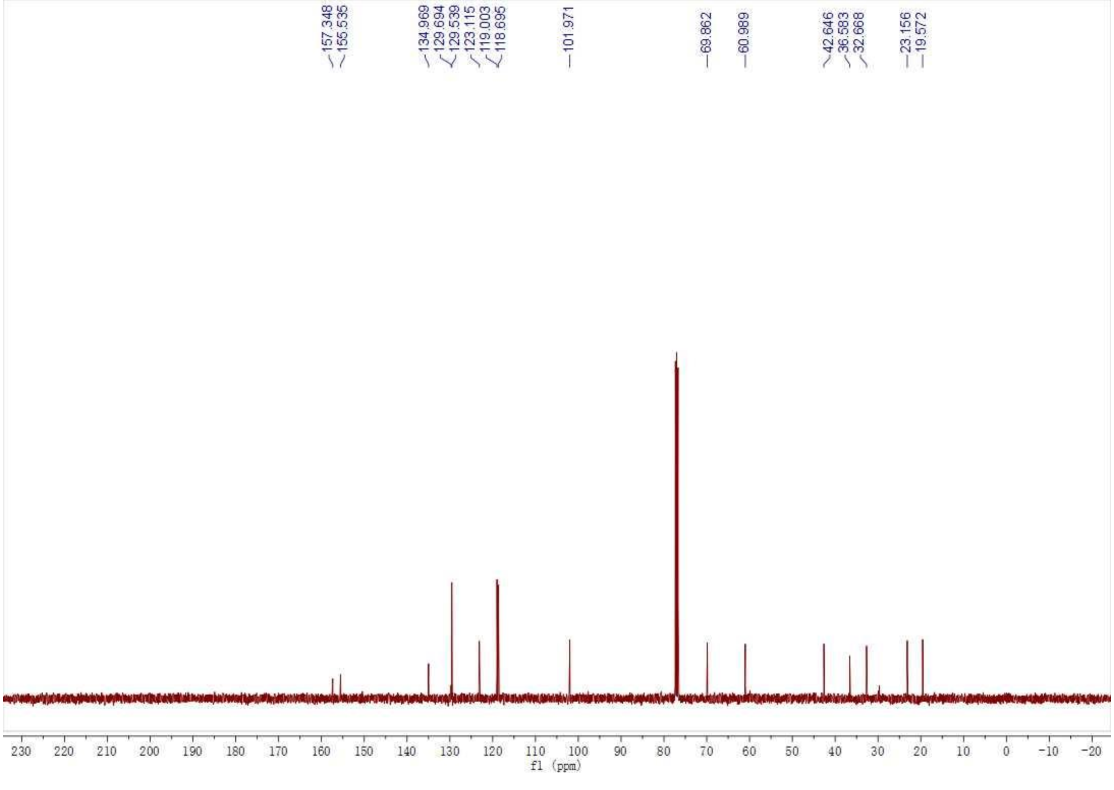
7.315
7.267
7.138
7.132
7.122
7.116
7.109
7.102
7.099
7.095
7.080
7.015
7.011
7.006
6.998
6.995
6.993
6.990
6.951
6.946
6.935
6.929
5.301
5.292
3.922
3.903
3.884
3.802
3.796
3.790
3.786
3.782
3.778
3.761
3.758
3.676
3.674
3.670
3.666
3.647
3.643
2.746
2.732
2.716
2.622
2.604
2.591
1.971
1.772
1.634
1.626
1.620
1.613
1.611
1.604
1.601
1.595
1.585
1.585
1.582
1.575
1.569
1.561
1.556
1.553
1.549
1.533
2.04
3.06
1.92
2.10
1.00
1.17
2.00
1.29
3.10
1.07
1.38
3.04
.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.
f1 (ppm)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123.115
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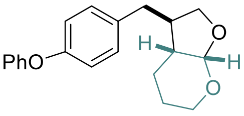
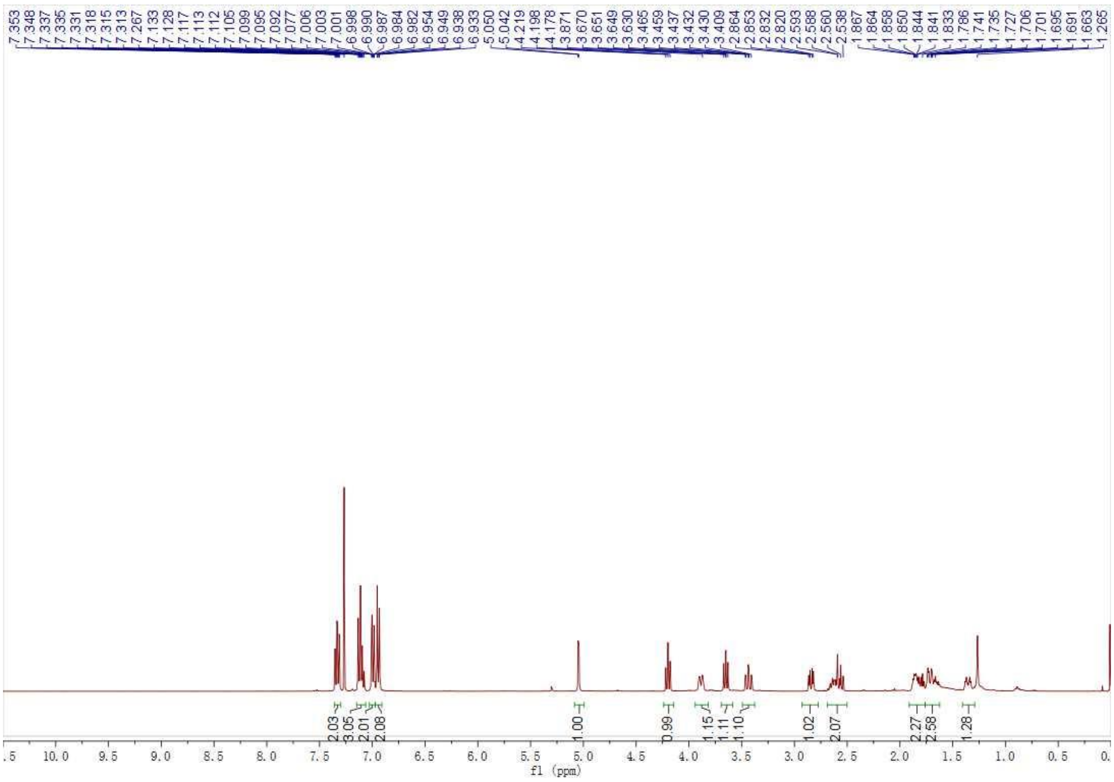
118.695
101.971
69.862
60.989
42.646
36.583
32.668
23.156
19.572
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)


PhO
H
H
O
O

cis-anti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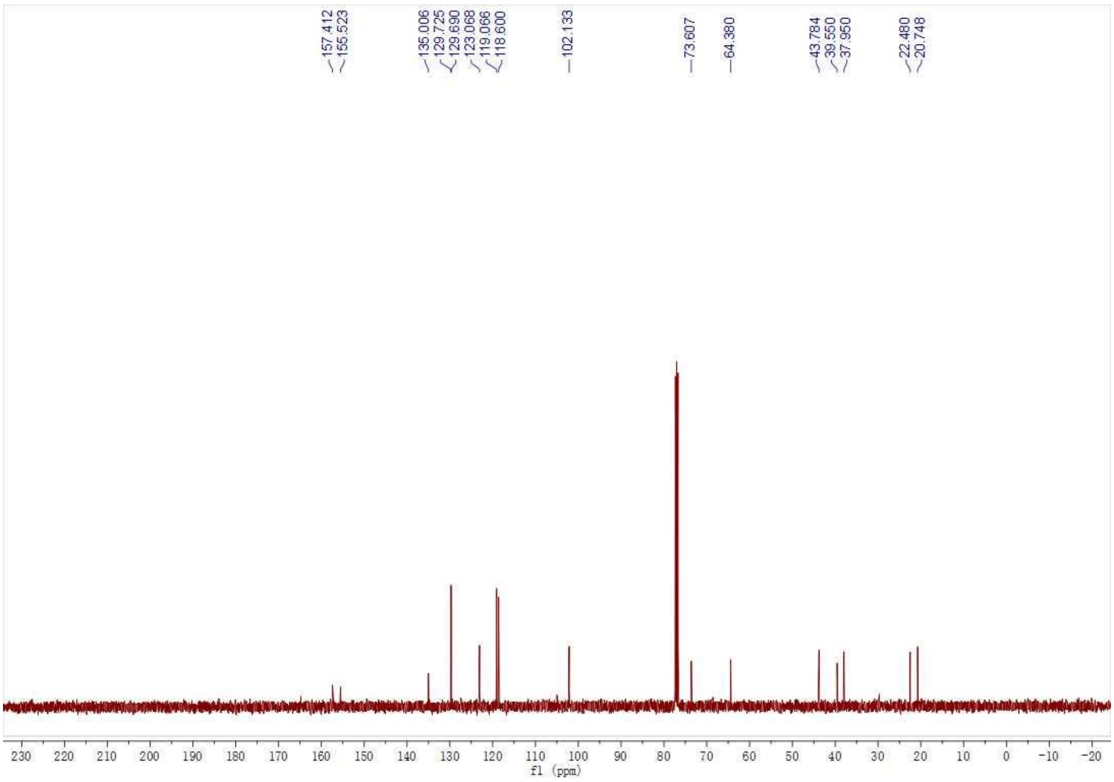
7.315
7.313
7.267
7.133
7.128
7.117
7.113
7.112
7.105
7.099
7.095
7.092
7.077
7.006
7.003
7.001
6.998
6.990
6.987
6.984
6.982
6.954
6.949
6.938
6.933
5.050
5.042
4.219
4.198
4.178
3.871
3.670
3.651
3.649
3.630
3.465
3.459
3.437
3.432
3.430
3.409
2.864
2.853
2.832
2.820
2.593
2.588
2.560
2.538
1.867
1.864
1.858
1.850
1.844
1.841
1.833
1.786
1.741
1.735
1.727
1.706
1.701
1.695
1.691
1.663
1.265
2.03
3.05
2.01
2.08
1.00
0.99
1.15
1.11
1.10
1.02
2.07
2.27
2.58
1.28
.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.
f1 (ppm)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123.068
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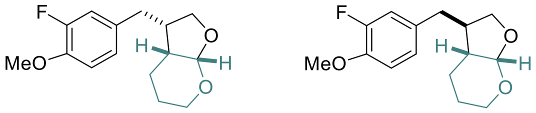
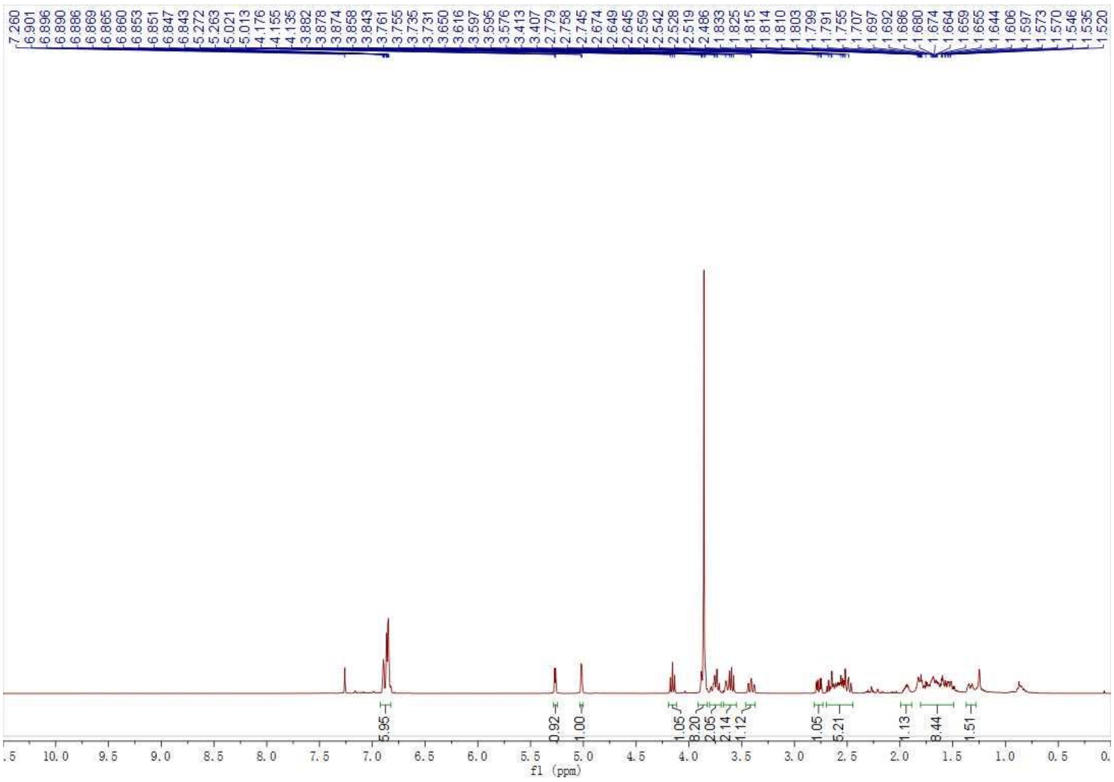
118.600
102.133
73.607
64.380
43.784
39.550
37.950
22.480
20.748
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)

(**4**)



F
MeO
H
O
H
O
F
MeO
H
O
H
O



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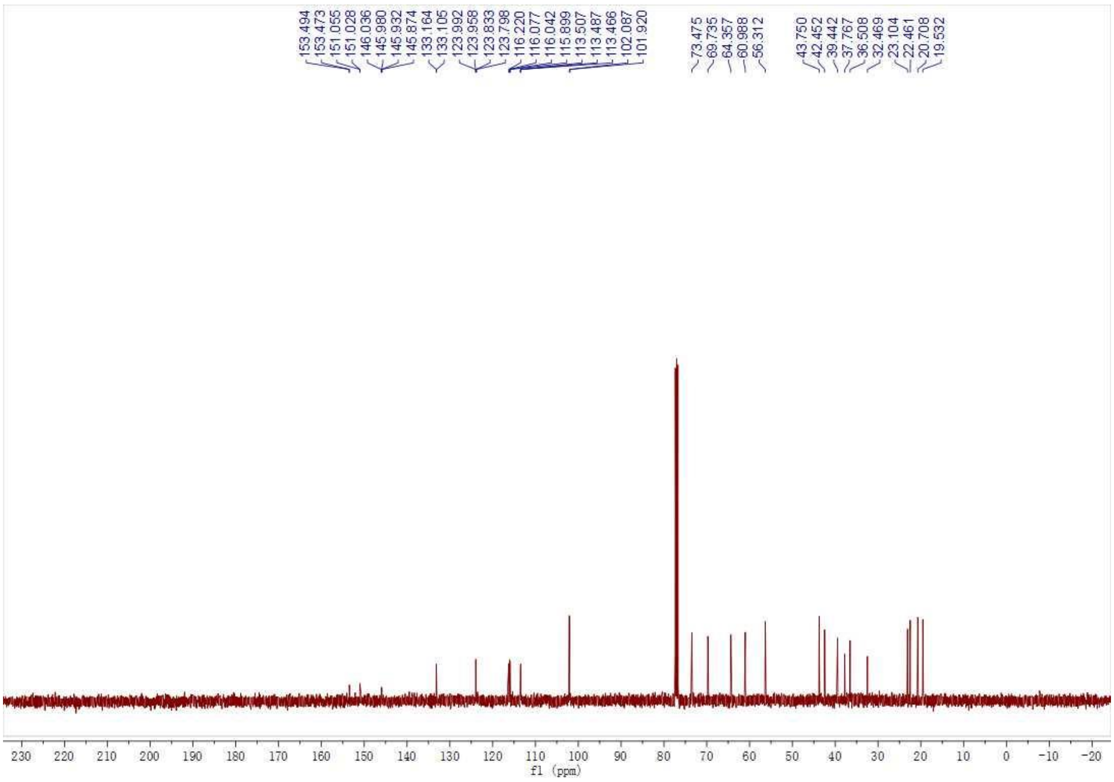
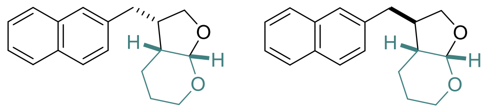
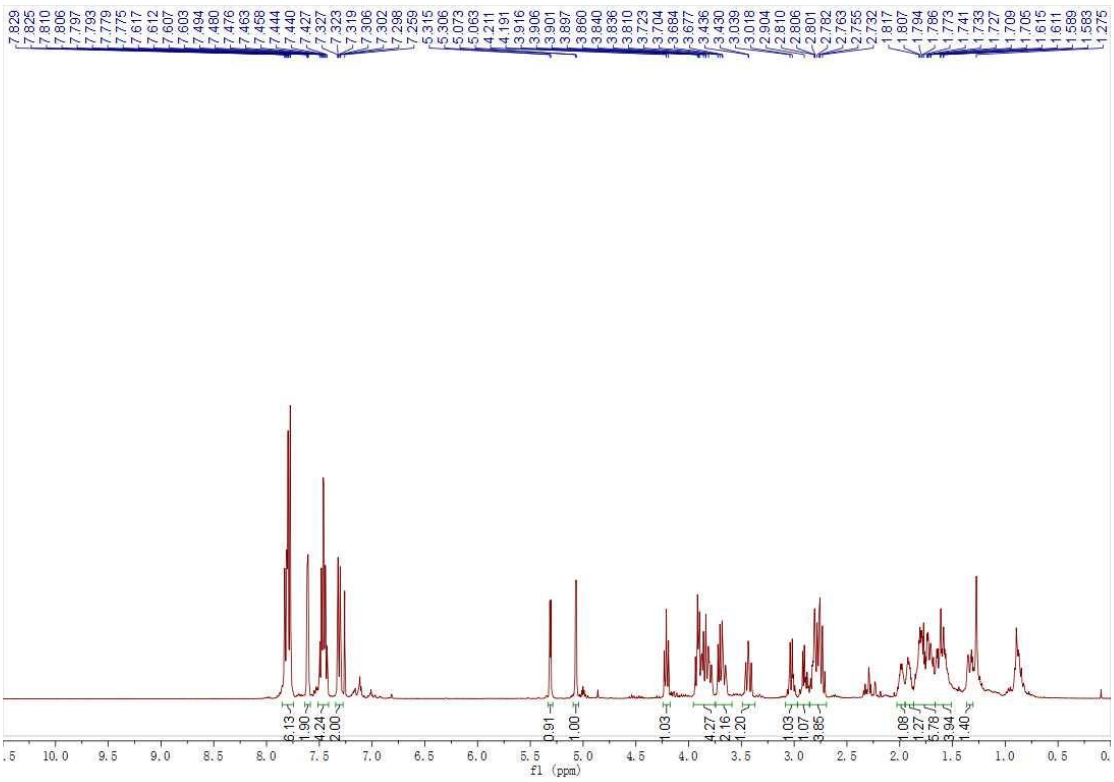
6.860
6.853
6.851
6.847
6.843
5.272
5.263
5.021
5.013
4.176
4.155
4.135
3.882
3.878
3.874
3.858
3.843
3.761
3.755
3.735
3.731
3.650
3.616
3.597
3.595
3.576
3.413
3.407
2.779
2.758
2.745
2.674
2.649
2.645
2.559
2.542
2.528
2.519
2.486
1.833
1.825
1.815
1.814
1.810
1.803
1.799
1.791
1.755
1.707
1.697
1.692
1.686
1.680
1.674
1.664
1.659
1.655
1.644
1.606
1.597
1.573
1.570
1.546
1.535
1.520
5.95
0.92
1.00
1.05
8.20
2.05
2.14
1.12
1.05
5.21
1.13
8.44
1.51
.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.
f1 (ppm)



153.494
153.473
151.055
151.028
146.036
145.980
145.932
145.874
133.164
133.105
123.992
123.958
123.833
123.798
116.220
116.077
116.042
115.899
113.507
113.487
113.466
102.087
101.920
73.475
69.735
64.357
60.988
56.312
43.750
42.452
39.442
37.767
36.508
32.469
23.104
22.461
20.708
19.532
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)

(5)


H
O
H
O
H
O
H
O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7.607
7.603
7.494
7.480
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7.444
7.440
7.427
7.327
7.323
7.319
7.306
7.302
7.298
7.259
5.315
5.306
5.073
5.063
4.211
4.191
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3.906
3.901
3.897
3.860
3.840
3.836
3.810
3.723
3.704
3.684
3.677
3.436
3.430
3.039
3.018
2.904
2.810
2.806
2.801
2.782
2.763
2.755
2.732
1.817
1.807
1.794
1.786
1.773
1.741
1.733
1.727
1.709
1.705
1.615
1.611
1.589
1.583
1.275
6.13
1.90
4.24
2.00
0.91
1.00
1.03
4.27
2.16
1.20
1.03
1.07
3.85
1.08
1.27
5.78
3.94
1.40
.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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4.5
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3.5
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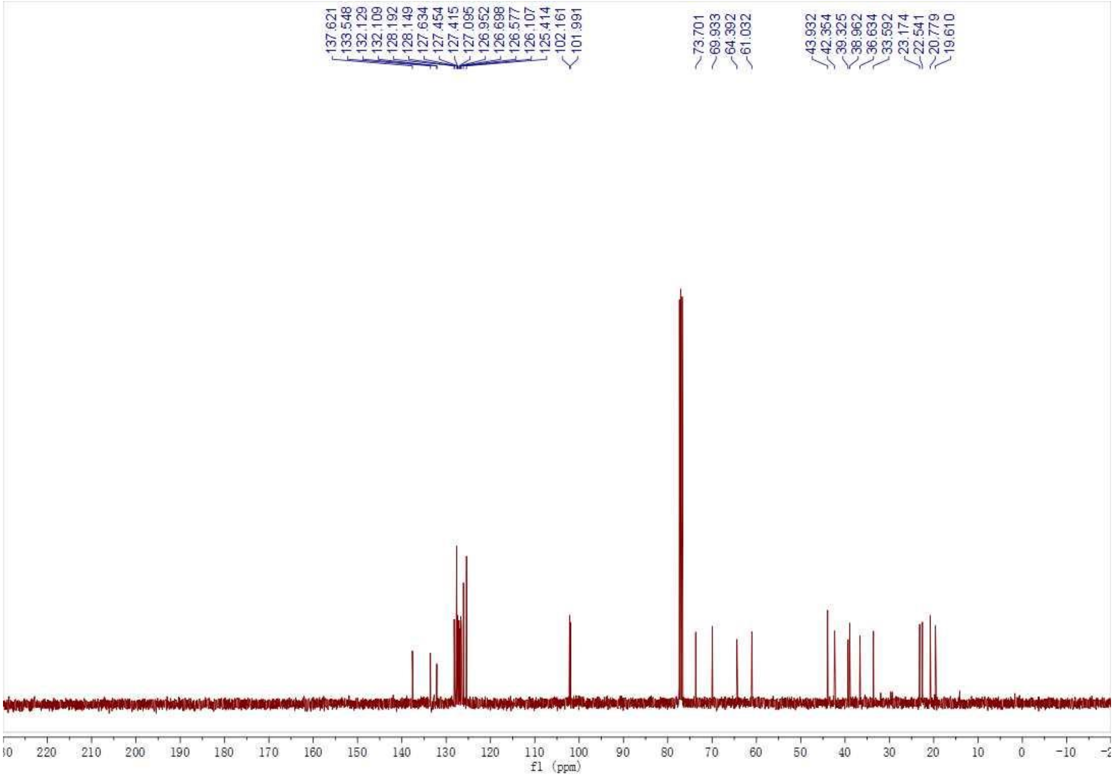
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)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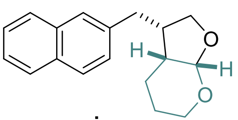
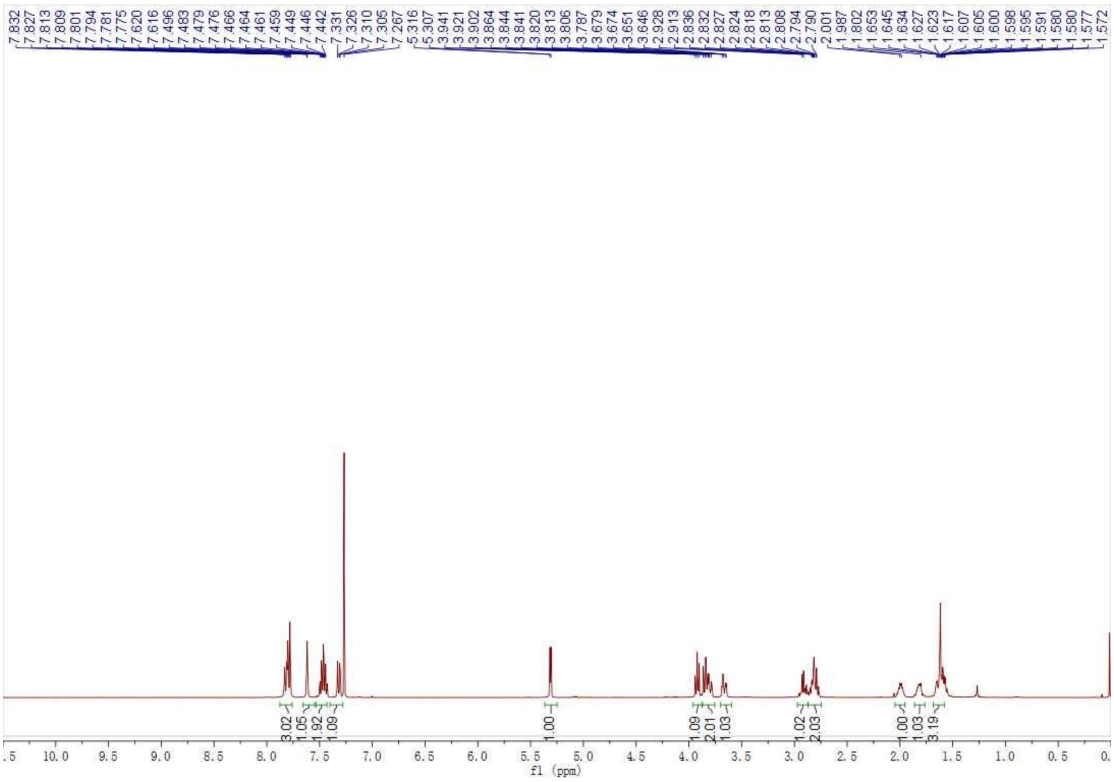
128.149
127.634
127.454
127.415
127.095
126.952
126.698
126.577
126.107
125.414
102.161
101.991
73.701
69.933
64.392
61.032
43.932
42.354
39.325
38.962
36.634
33.592
23.174
22.541
20.779
19.610
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


O
H
H
O

cis-syn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7.479
7.476
7.466
7.464
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7.459
7.449
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7.442
7.331
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7.310
7.305
7.267
5.316
5.307
3.941
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2.808
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1.987
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1.595
1.591
1.580
1.580
1.577
1.572
3.02
1.05
1.92
1.09
1.00
1.09
2.01
1.03
1.02
2.03
1.00
1.03
3.19
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9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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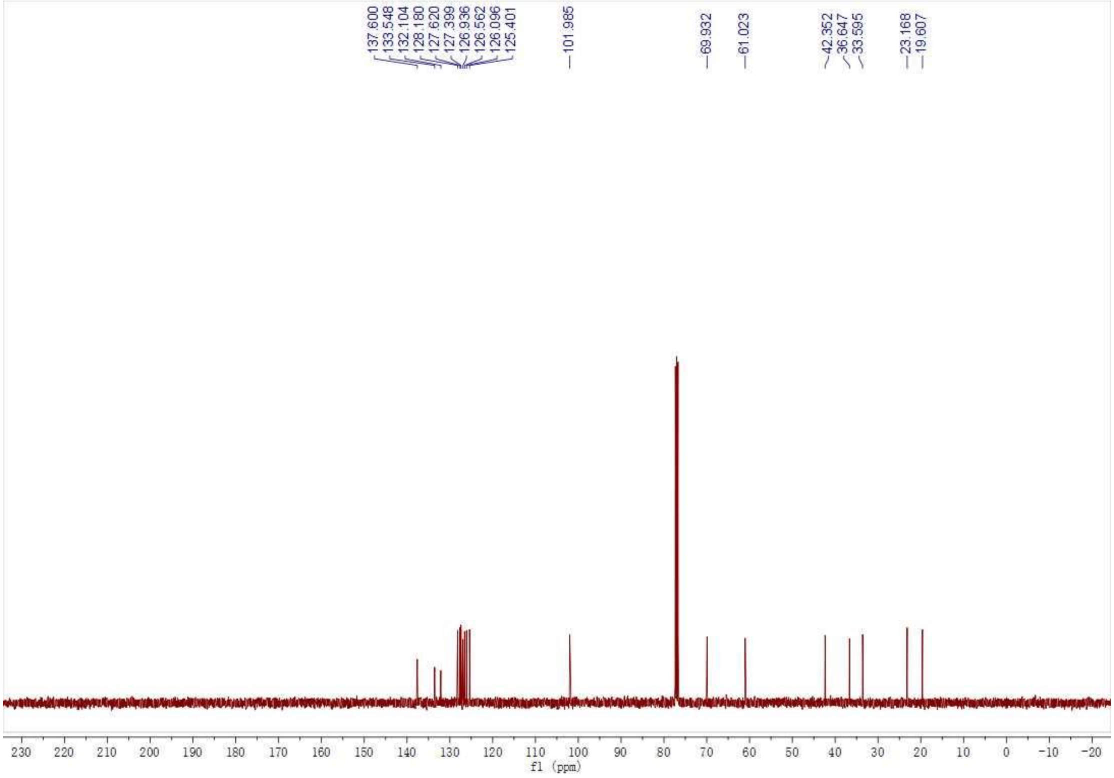
f1 (ppm)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126.936
126.562
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125.401
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69.932
61.023
42.352
36.647
33.595
23.168
19.607
230
220
210
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180
170
160
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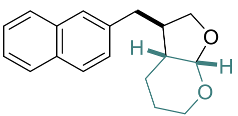
f1 (ppm)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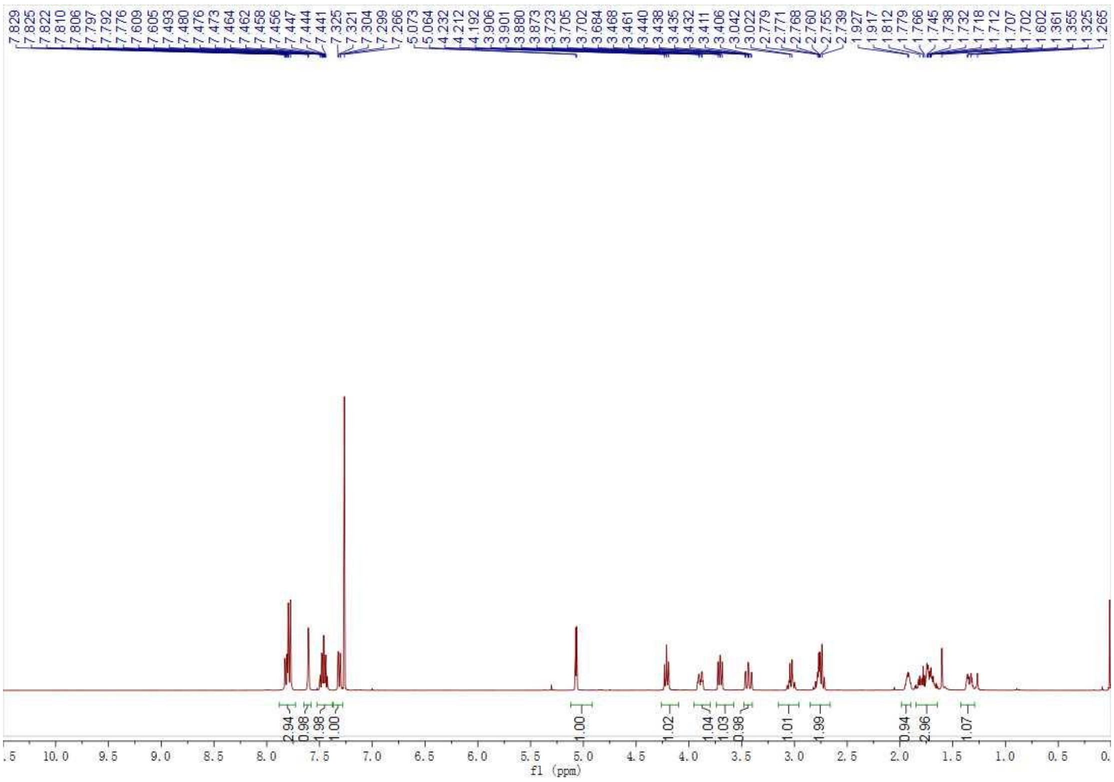
H
O

cis-anti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7.605
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7.462
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7.441
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3.901
3.880
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3.702
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3.461
3.440
3.438
3.435
3.432
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3.406
3.042
3.022
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1.812
1.779
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1.745
1.738
1.732
1.718
1.712
1.707
1.702
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1.361
1.355
1.325
1.265
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1.98
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1.00
1.02
1.04
1.03
0.98
1.01
1.99
0.94
2.96
1.07
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6.5
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5.5
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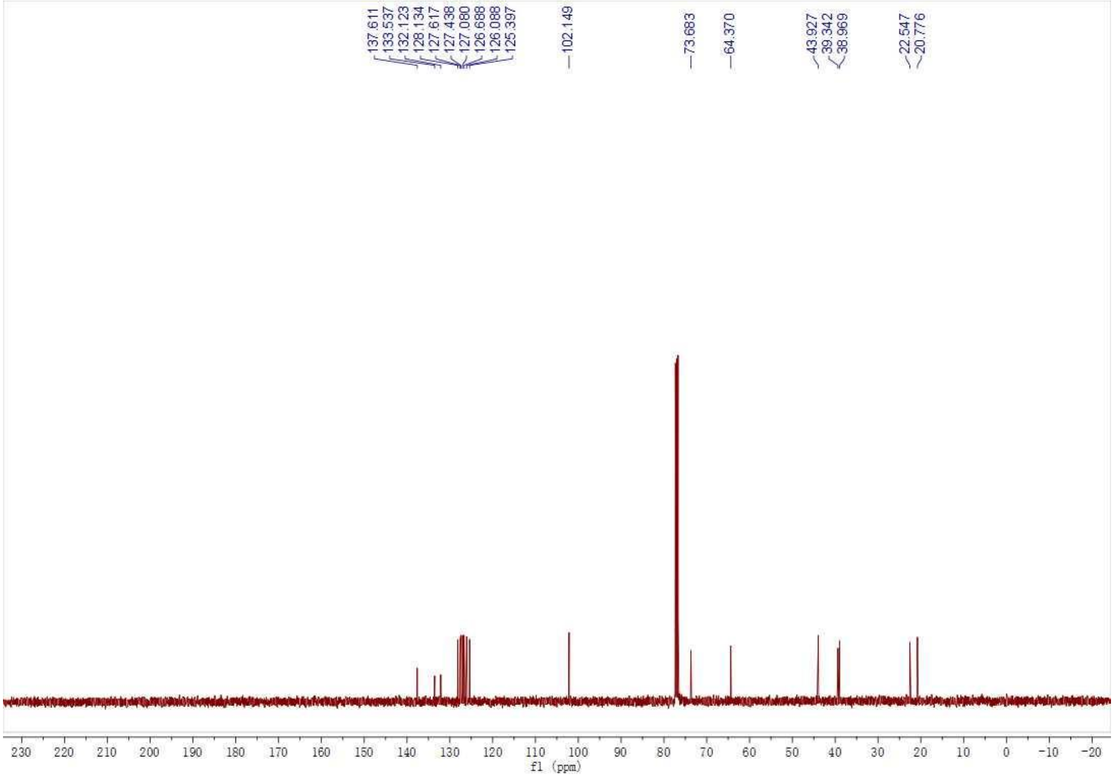
f1 (ppm)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64.370
43.927
39.342
38.969
22.547
20.776
230
220
210
200
190
180
170
160
150
140
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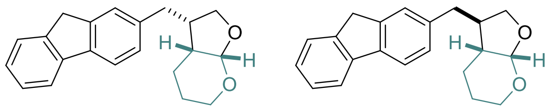
-20
f1 (ppm)

(**6**)



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H
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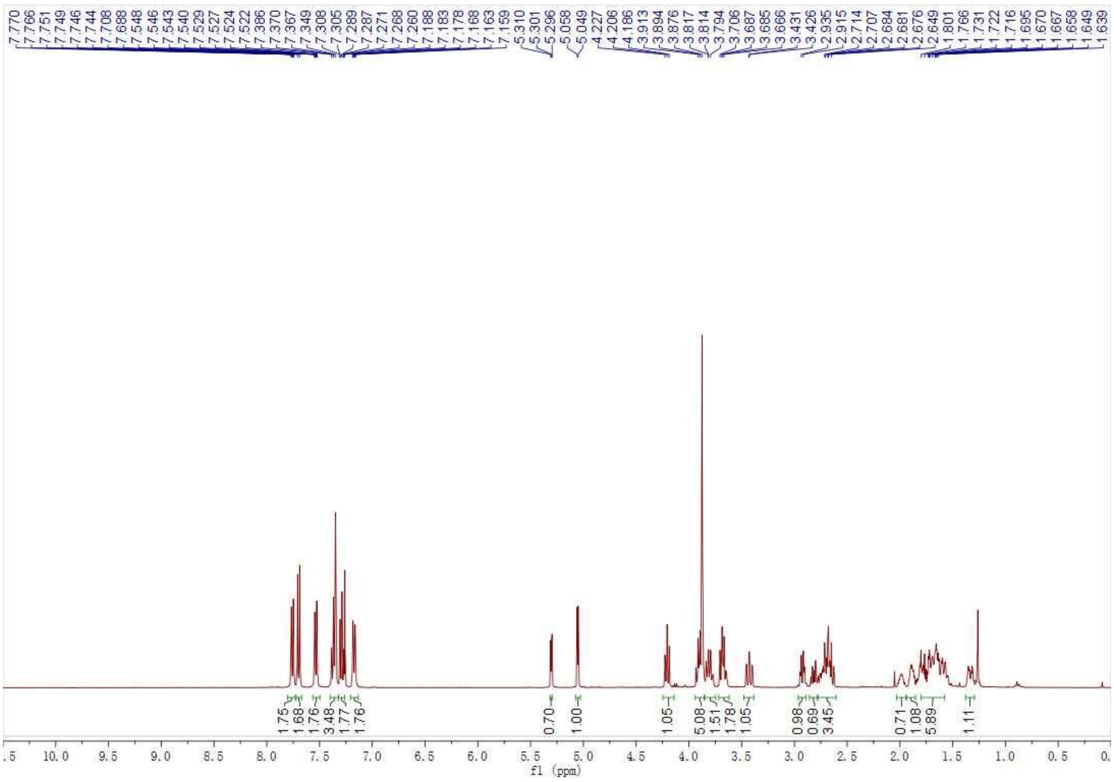
H
O
H
O



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7.766
7.751
7.749
7.746
7.744
7.708
7.688
7.548
7.546
7.543
7.540
7.529
7.527
7.524
7.522
7.386
7.370
7.367
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7.308
7.305
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7.287
7.271
7.268
7.260
7.188
7.183
7.178
7.168
7.163
7.159
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5.301
5.296
5.058
5.049
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4.186
3.913
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3.876
3.817
3.814
3.794
3.706
3.687
3.685
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3.426
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2.915
2.714
2.707
2.684
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2.676
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1.722
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1.695
1.670
1.667
1.658
1.649
1.639
1.75
1.68
1.76
3.48
1.77
1.76
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5.08
1.51
1.78
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0.98
0.69
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0.71
1.08
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6.0
5.5
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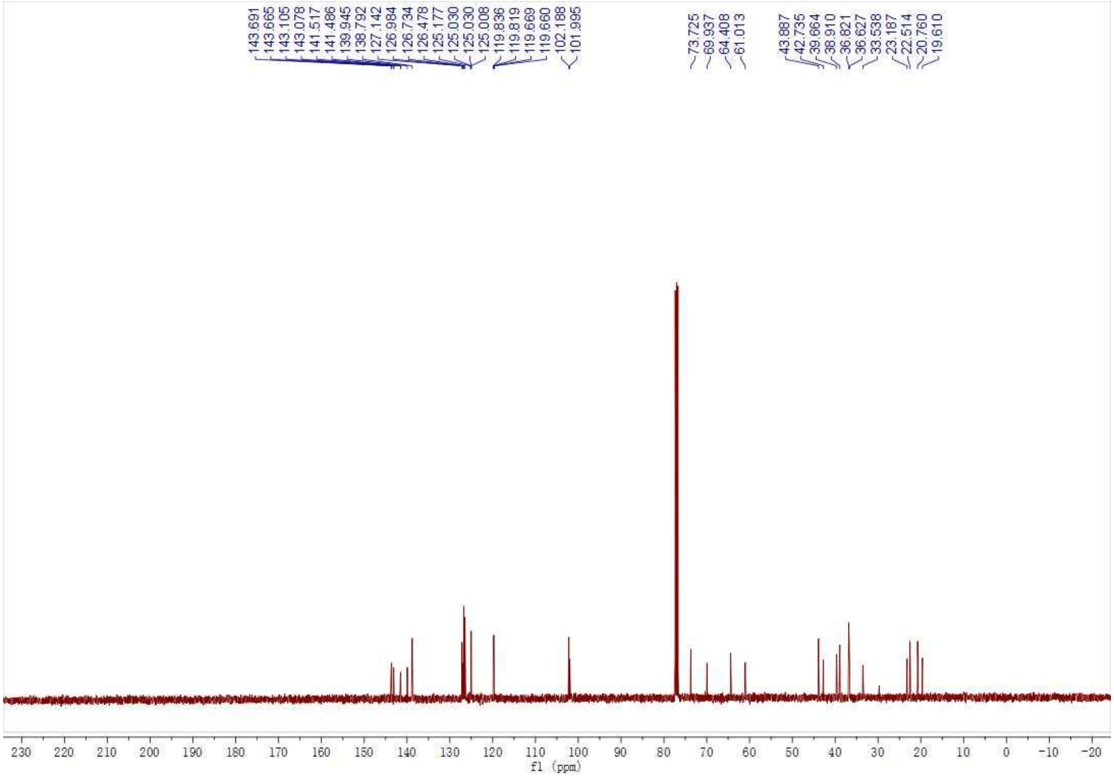
f1 (ppm)



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139.945
138.792
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126.734
126.478
126.177
125.030
125.030
125.008
119.836
119.819
119.669
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101.995
73.725
69.937
64.408
61.013
43.887
42.735
39.664
38.910
36.821
36.627
33.538
23.187
22.514
20.760
19.610
230
220
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200
190
180
170
160
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20
10
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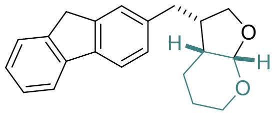
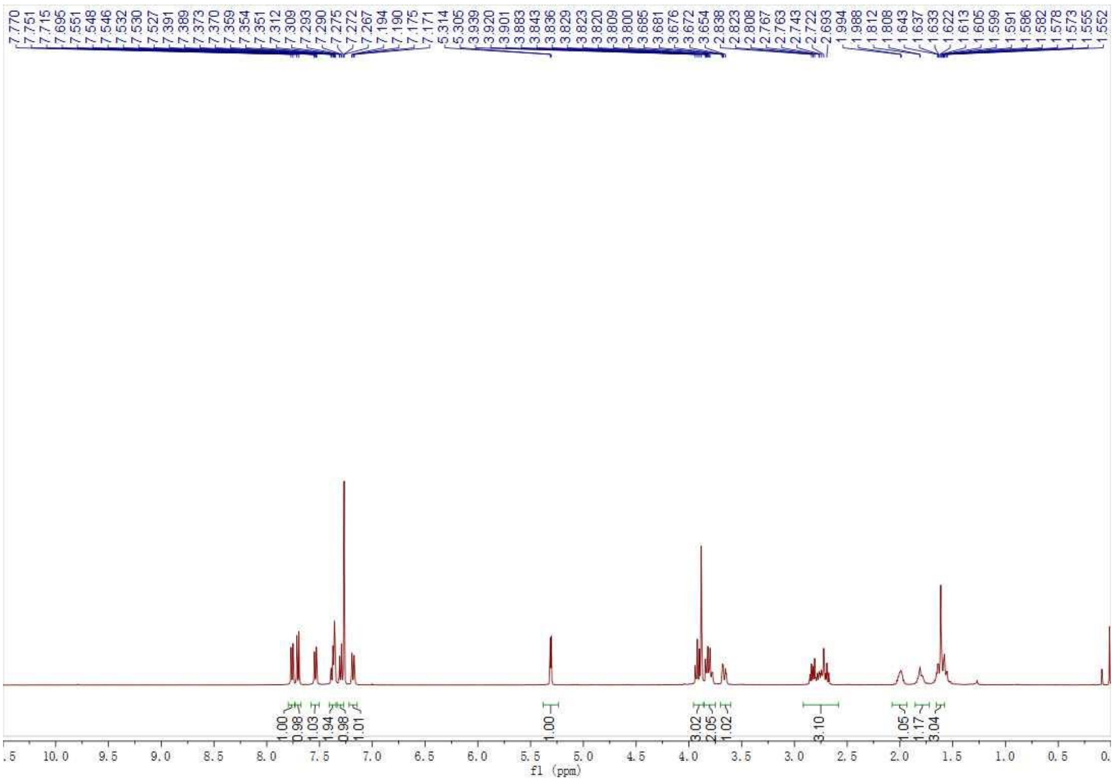
-20
f1 (ppm)


H
H
O
O

cis-syn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7.370
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7.354
7.351
7.312
7.309
7.293
7.290
7.275
7.272
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7.190
7.175
7.171
5.314
5.305
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3.901
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3.829
3.823
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3.800
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3.681
3.676
3.672
3.654
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2.823
2.808
2.767
2.763
2.743
2.722
2.693
1.994
1.988
1.812
1.808
1.643
1.637
1.633
1.622
1.613
1.605
1.599
1.591
1.586
1.582
1.578
1.573
1.555
1.552
1.00
0.98
1.03
1.94
0.98
1.01
1.00
3.02
2.05
1.02
3.10
1.05
1.17
3.04
.5
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9.5
9.0
8.5
8.0
7.5
7.0
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6.0
5.5
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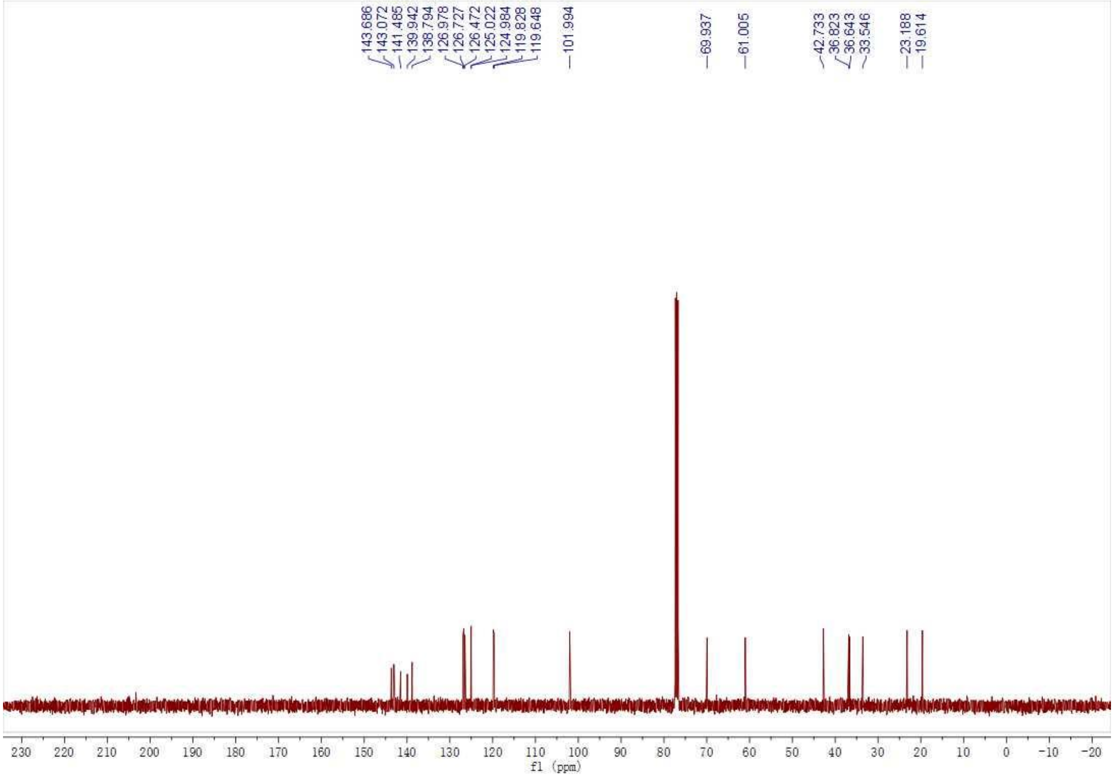
f1 (ppm)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125.022
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101.994
69.937
61.005
42.733
36.823
36.643
33.546
23.188
19.614
230
220
210
200
190
180
170
160
150
140
130
120
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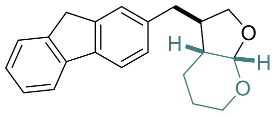
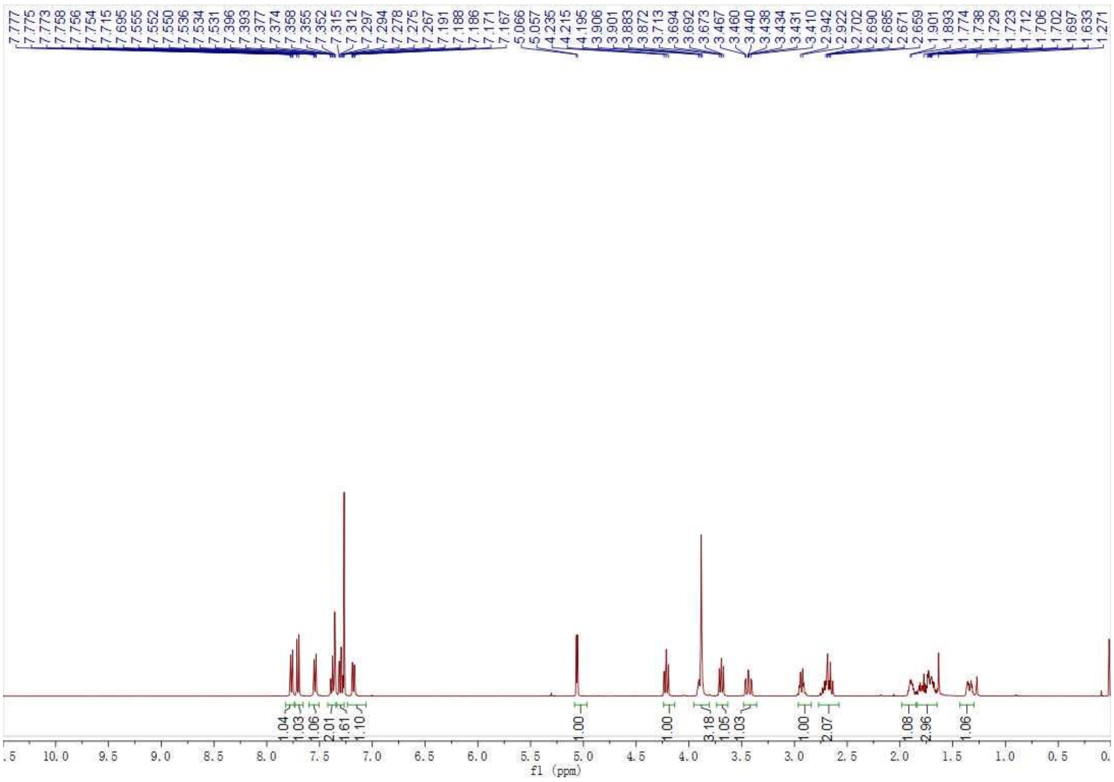
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)


H
O
H
O

cis-anti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7.355
7.352
7.315
7.312
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7.188
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7.171
7.167
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3.901
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3.431
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1.706
1.702
1.697
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1.04
1.03
1.06
2.01
1.61
1.10
1.00
1.00
3.18
1.05
1.03
1.00
2.07
1.08
2.96
1.06
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9.0
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7.5
7.0
6.5
6.0
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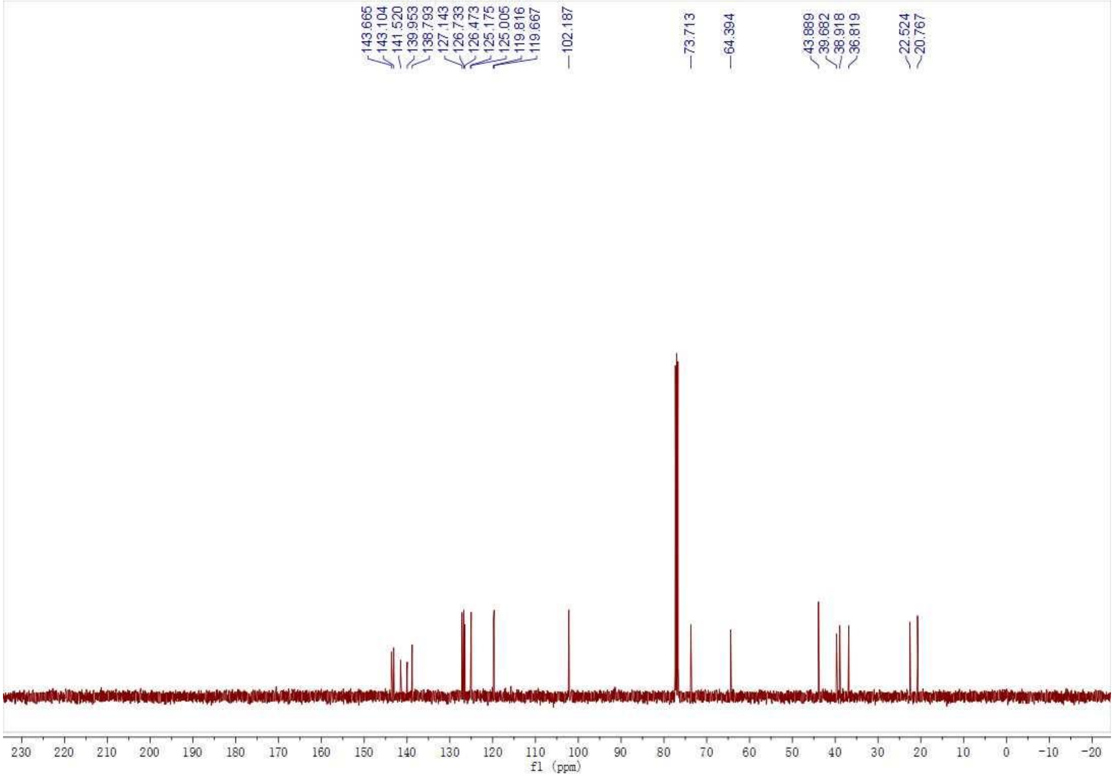
f1 (ppm)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73.713
64.394
43.889
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36.819
22.524
20.767
230
220
210
200
190
180
170
160
150
140
130
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80
70
60
50
40
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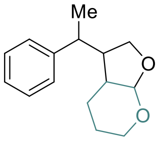
20
10
0
-10
-20
f1 (ppm)

(**7**)


Me
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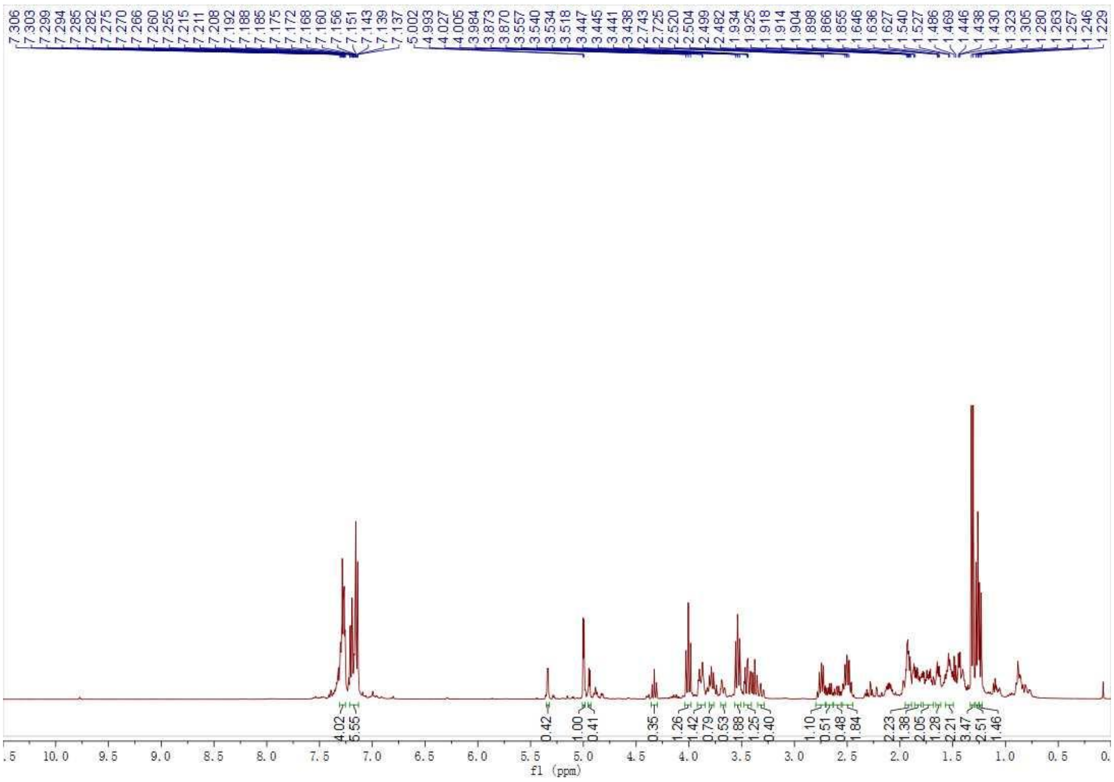
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7.208
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7.188
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7.175
7.172
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7.156
7.151
7.143
7.139
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3.441
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8.0
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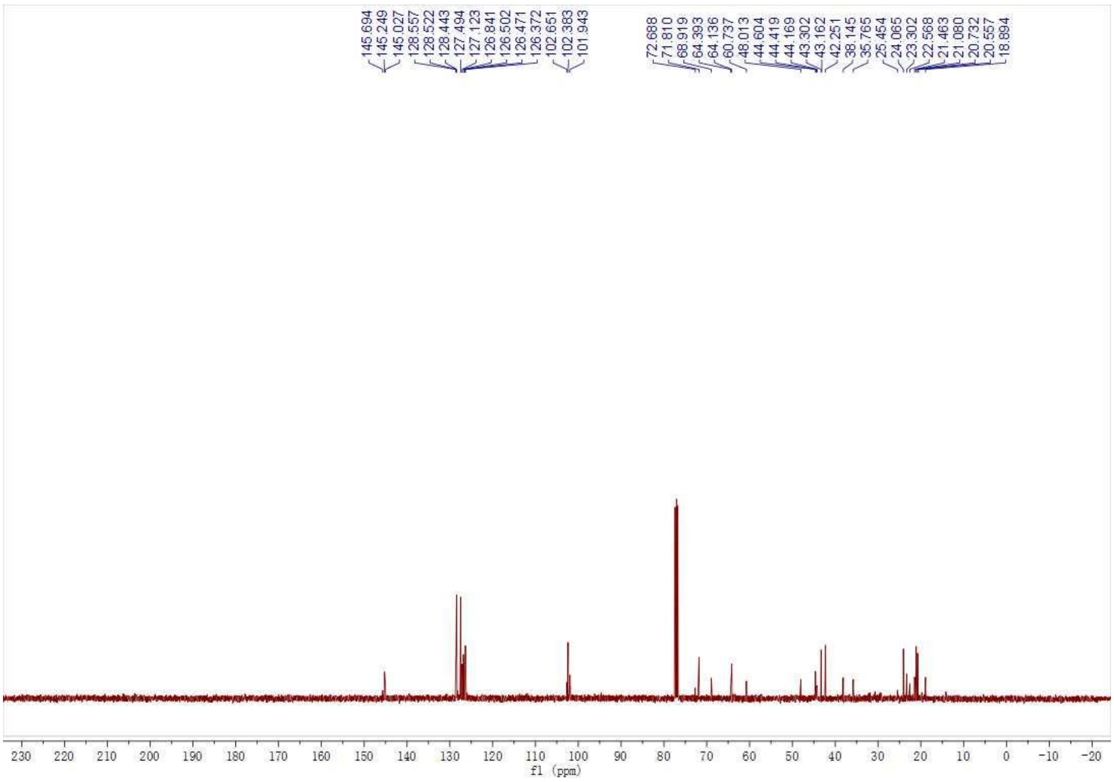
f1 (ppm)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126.372
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102.383
101.943
72.688
71.810
68.919
64.393
64.136
60.737
48.013
44.604
44.419
44.169
43.302
43.162
42.251
38.145
35.765
25.454
24.065
23.302
22.568
21.463
21.080
20.732
20.557
18.894
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170
160
150
140
130
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80
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40
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0
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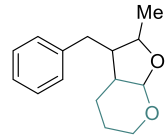
-20
f1 (ppm)

(**8**)


Me
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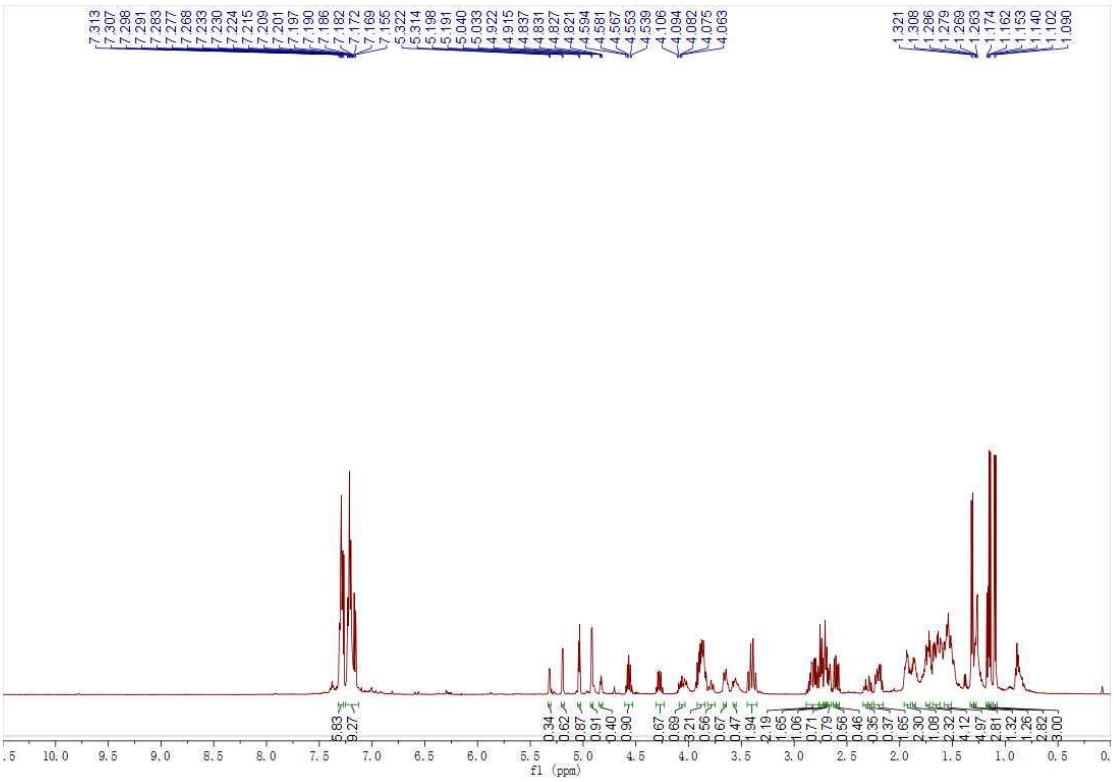
O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7.182
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0.90
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0.56
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0.37
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1.26
2.82
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.5
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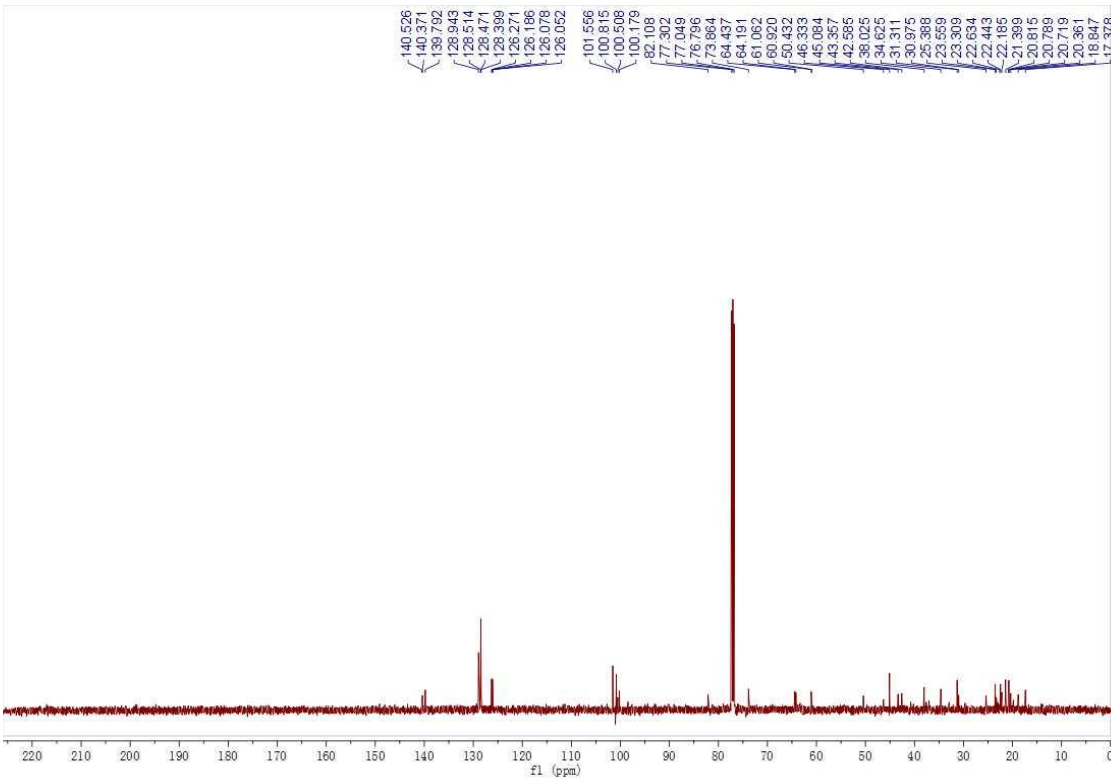
f1 (ppm)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100.508
100.179
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76.796
73.864
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46.333
45.084
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38.025
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20.789
20.719
20.361
18.847
17.378
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200
190
180
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80
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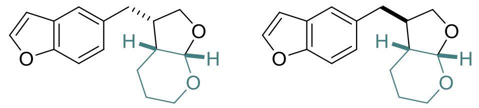
40
30
20
10
f1 (ppm)

(9)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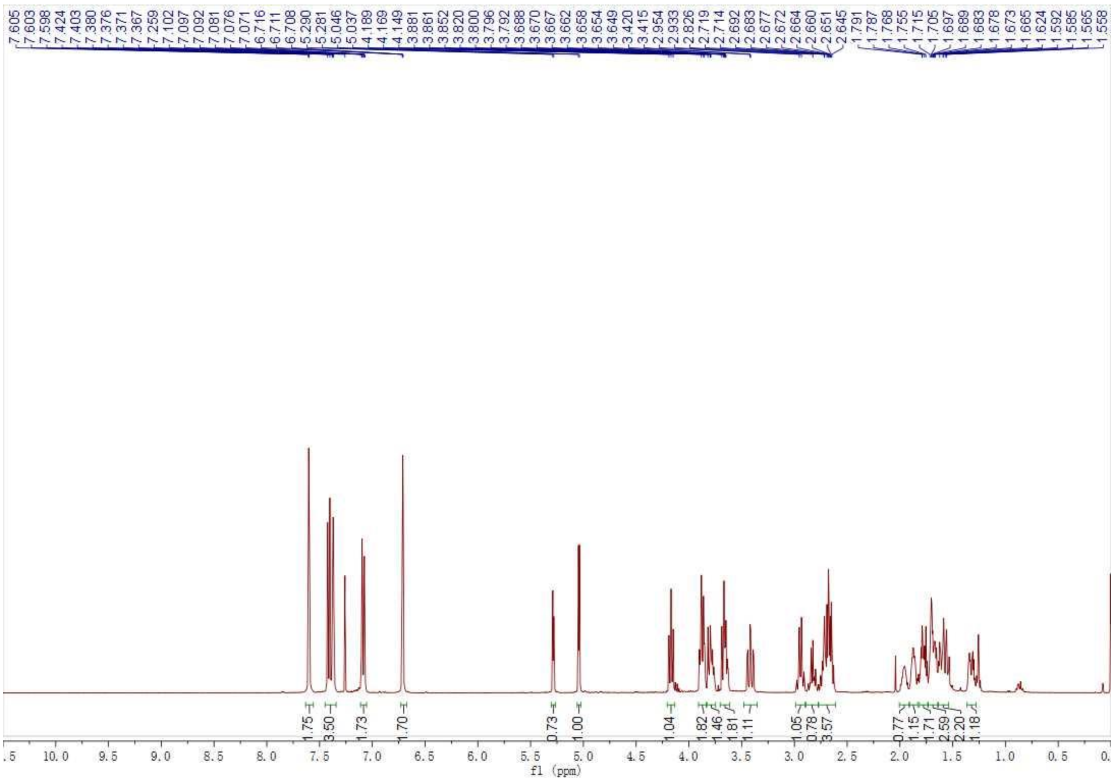
O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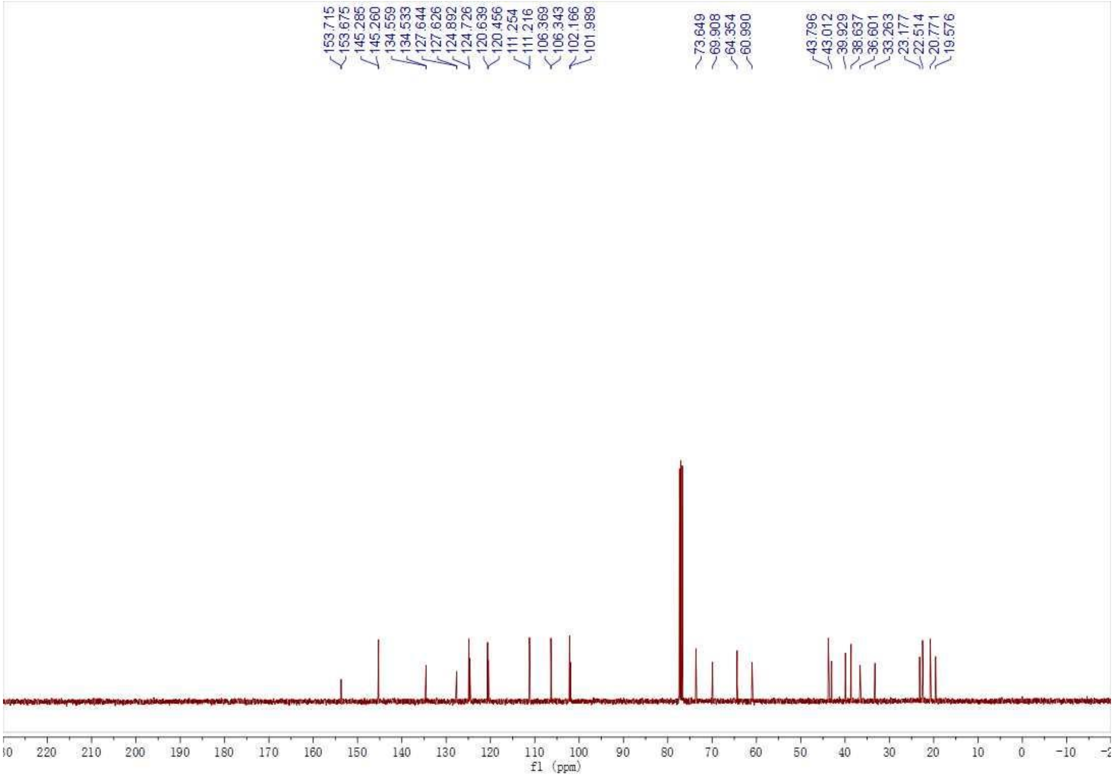
f1 (ppm)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124.892
124.726
120.639
120.456
111.254
111.216
106.369
106.343
102.166
101.989
73.649
69.908
64.354
60.990
43.796
43.012
39.929
38.637
36.601
33.263
23.177
22.514
20.771
19.576
220
210
200
190
180
170
160
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120
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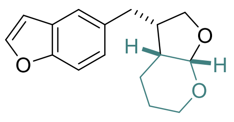
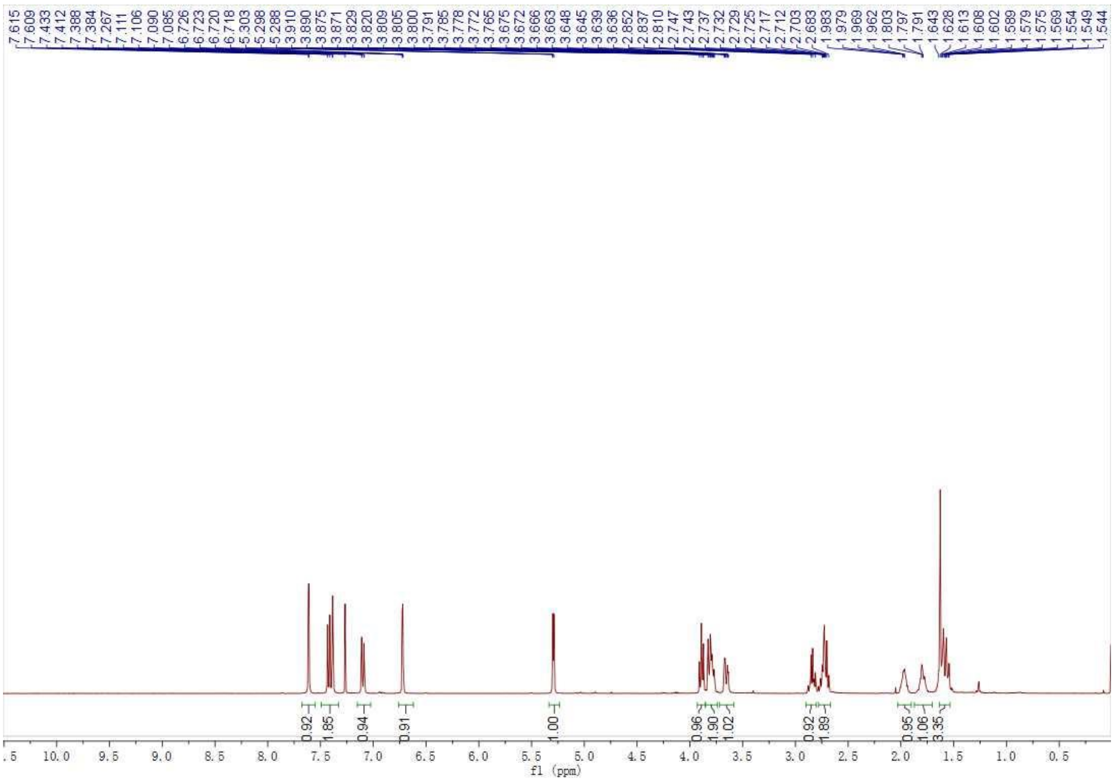
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)



cis-syn



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7.433
7.412
7.388
7.384
7.267
7.111
7.106
7.090
7.085
6.726
6.723
6.720
6.718
5.303
5.298
5.288
3.910
3.890
3.875
3.871
3.829
3.820
3.809
3.805
3.800
3.791
3.785
3.778
3.772
3.765
3.675
3.672
3.666
3.663
3.648
3.645
3.639
3.636
2.852
2.837
2.810
2.747
2.743
2.737
2.732
2.729
2.725
2.717
2.712
2.703
2.683
1.983
1.979
1.969
1.962
1.803
1.797
1.791
1.643
1.628
1.613
1.608
1.602
1.589
1.579
1.575
1.569
1.554
1.549
1.544
0.92
1.85
0.94
0.91
1.00
0.96
1.90
1.02
0.92
1.89
0.95
1.06
3.35
.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
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3.0
2.5
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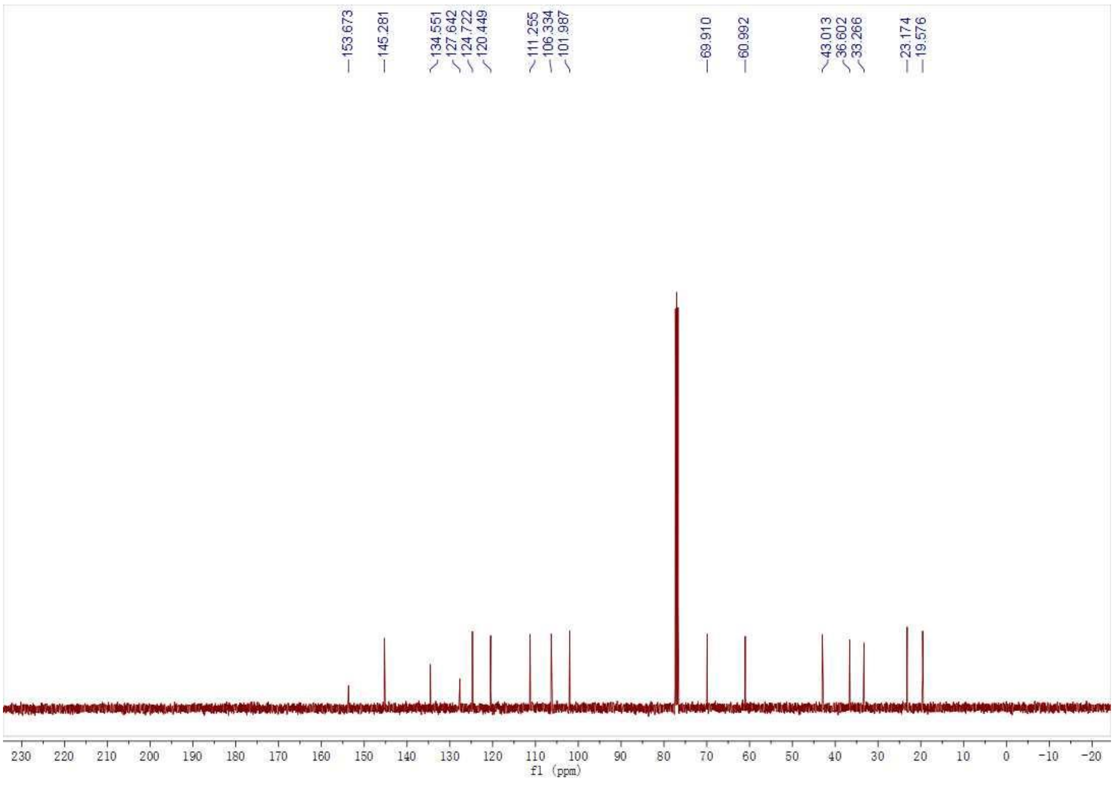
1.5
1.0
0.5
f1 (ppm)



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134.551
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124.722
120.449
111.255
106.334
101.987
69.910
60.992
43.013
36.602
33.266
23.174
19.576
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
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40
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20
10
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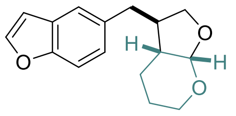
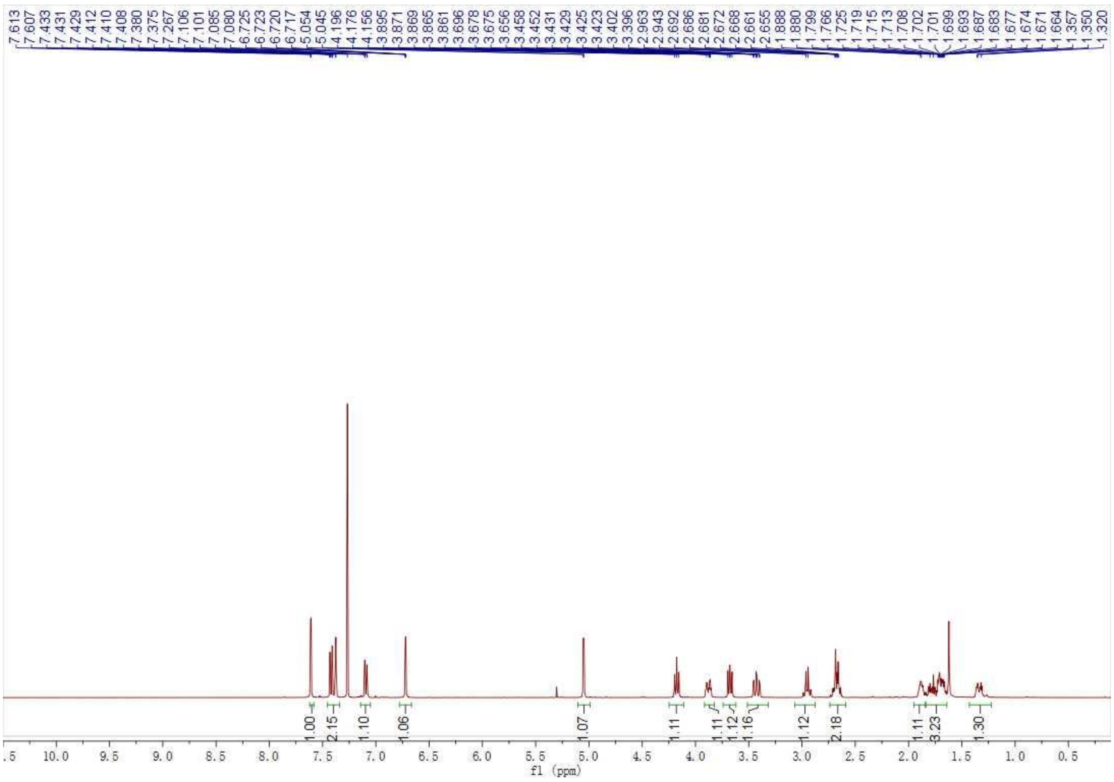
-10
-20
f1 (ppm)


O
H
O
H
O

cis-anti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7.433
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7.429
7.412
7.410
7.408
7.380
7.375
7.267
7.106
7.101
7.085
7.080
6.725
6.723
6.720
6.717
5.054
5.045
4.196
4.176
4.156
3.895
3.871
3.869
3.865
3.861
3.696
3.678
3.675
3.656
3.458
3.452
3.431
3.429
3.425
3.423
3.402
3.396
2.963
2.943
2.692
2.686
2.681
2.672
2.668
2.661
2.655
1.888
1.880
1.799
1.766
1.725
1.719
1.715
1.713
1.708
1.702
1.701
1.699
1.693
1.687
1.683
1.677
1.674
1.671
1.664
1.357
1.350
1.320
1.00
2.15
1.10
1.06
1.07
1.11
1.11
1.12
1.16
1.12
2.18
1.11
3.23
1.30
.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
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4.0
3.5
3.0
2.5
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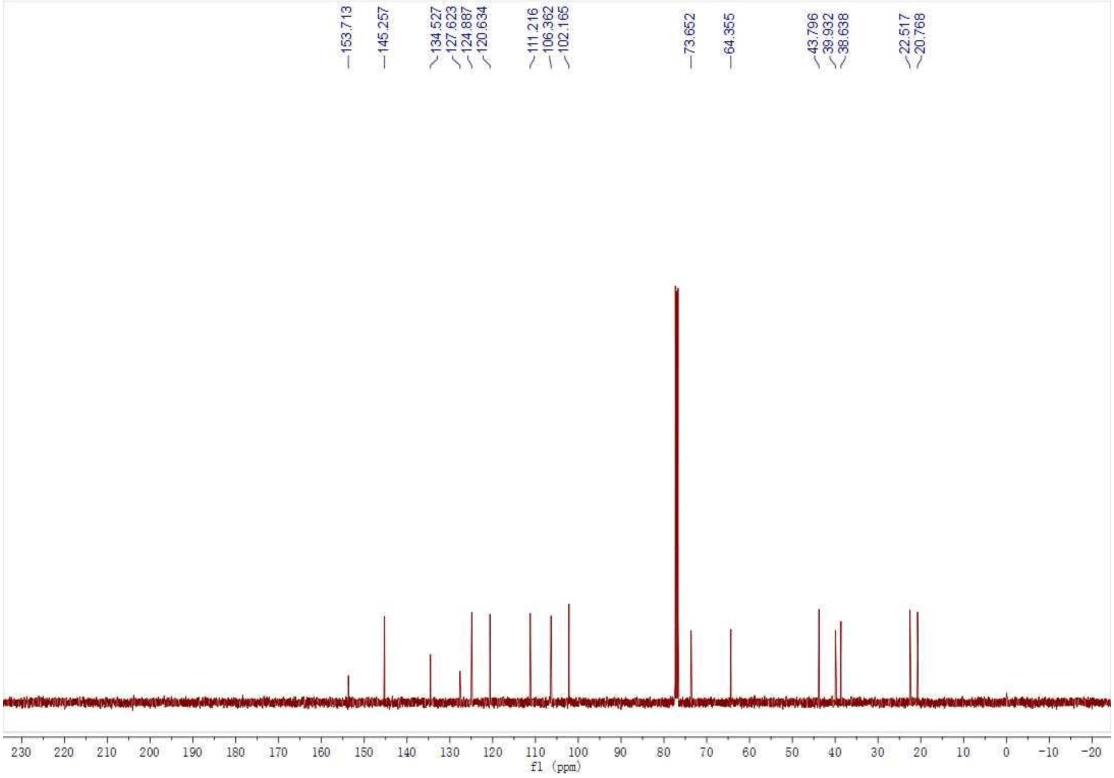
1.5
1.0
0.5
f1 (ppm)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106.362
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64.355
43.796
39.932
38.638
22.517
20.768
230
220
210
200
190
180
170
160
150
140
130
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100
90
80
70
60
50
40
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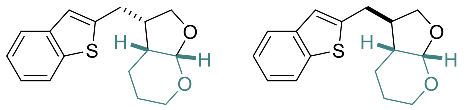
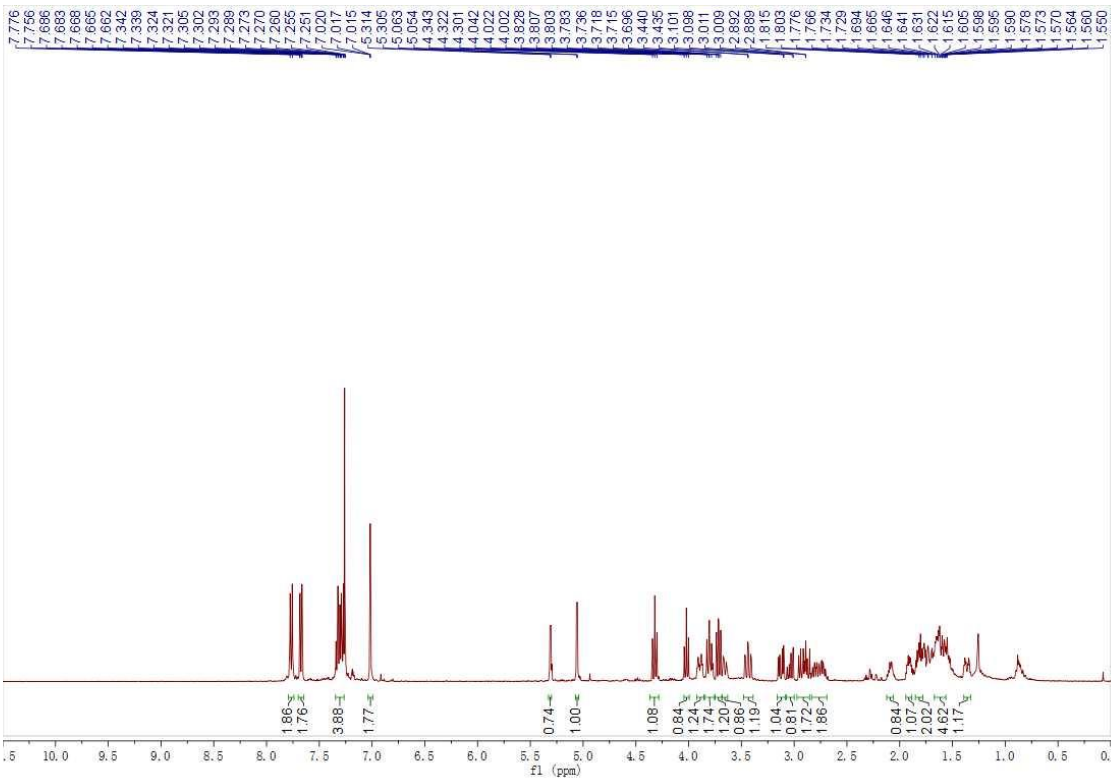
10
0
-10
-20
f1 (ppm)

(**10**)



S
H
O
H
O
S
H
O
H
O



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7.683
7.668
7.665
7.662
7.342
7.339
7.324
7.321
7.305
7.302
7.293
7.289
7.273
7.270
7.260
7.255
7.251
7.020
7.017
7.015
5.314
5.305
5.063
5.054
4.343
4.322
4.301
4.042
4.022
4.002
3.828
3.807
3.803
3.783
3.736
3.718
3.715
3.696
3.440
3.435
3.101
3.098
3.011
3.009
2.892
2.889
1.815
1.803
1.776
1.766
1.734
1.729
1.694
1.665
1.646
1.641
1.631
1.622
1.615
1.605
1.598
1.595
1.590
1.578
1.573
1.570
1.564
1.560
1.550
1.86
1.76
3.88
1.77
0.74
1.00
1.08
0.84
1.24
1.74
1.20
0.86
1.19
1.04
0.81
1.72
1.86
0.84
1.07
2.02
4.62
1.17
.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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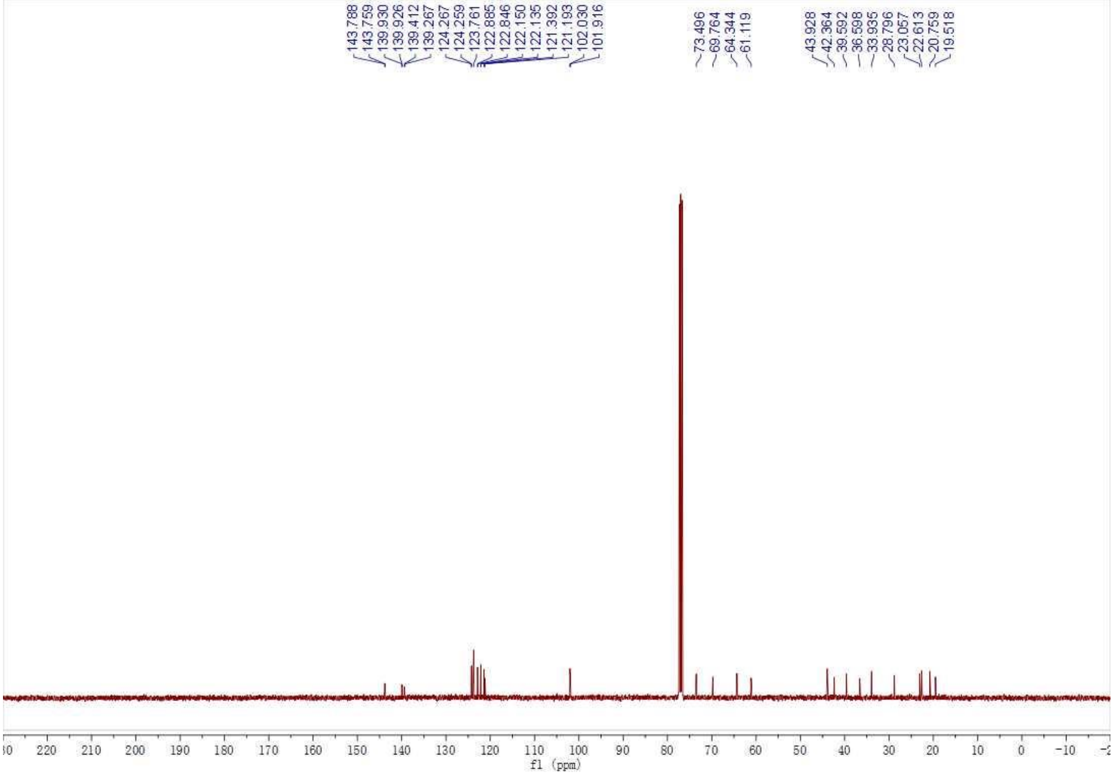
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)



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139.926
139.412
139.267
124.267
124.259
123.761
122.885
122.846
122.150
122.135
121.392
121.193
102.030
101.916
73.496
69.764
64.344
61.119
43.928
42.364
39.592
36.598
33.935
28.796
23.057
22.613
20.759
19.518
0
220
210
200
190
180
170
160
150
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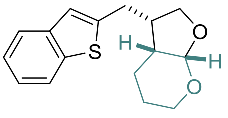
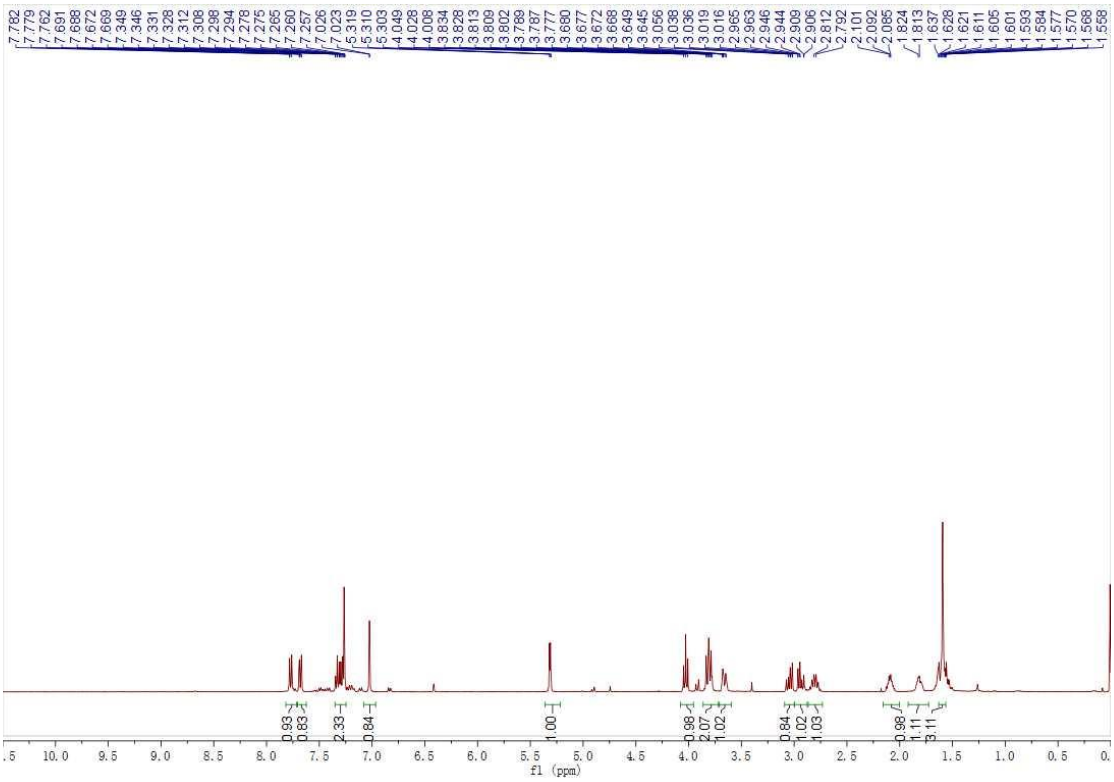
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
−
f1 (ppm)


H
O
H
S
O

cis-syn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7.688
7.672
7.669
7.349
7.346
7.331
7.328
7.312
7.308
7.298
7.294
7.278
7.275
7.265
7.260
7.257
7.026
7.023
5.319
5.310
5.303
4.049
4.028
4.008
3.834
3.828
3.813
3.809
3.802
3.789
3.787
3.777
3.680
3.677
3.672
3.668
3.649
3.645
3.056
3.038
3.036
3.019
3.016
2.965
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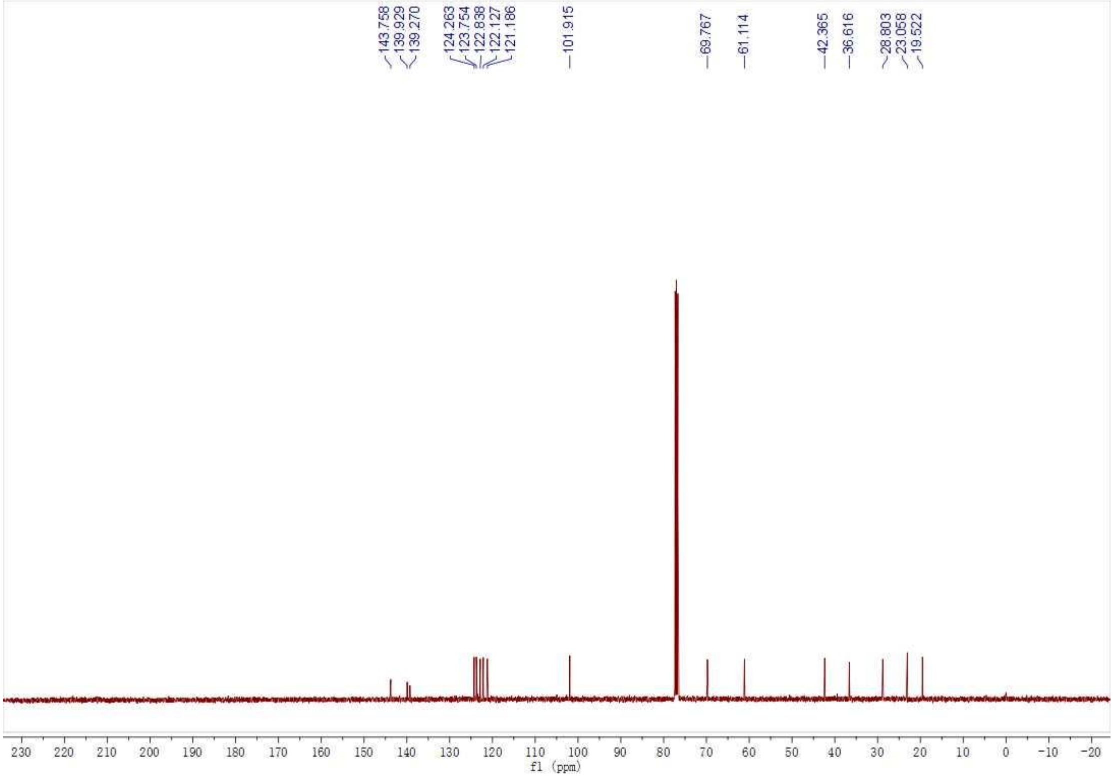
2.946
2.944
2.909
2.906
2.812
2.792
2.101
2.092
2.085
1.824
1.813
1.637
1.628
1.621
1.611
1.605
1.601
1.593
1.584
1.577
1.570
1.568
1.558
0.93
0.83
2.33
0.84
1.00
0.98
2.07
1.02
0.84
1.02
1.03
0.98
1.11
3.11
.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)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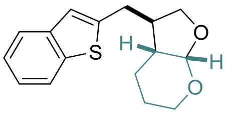
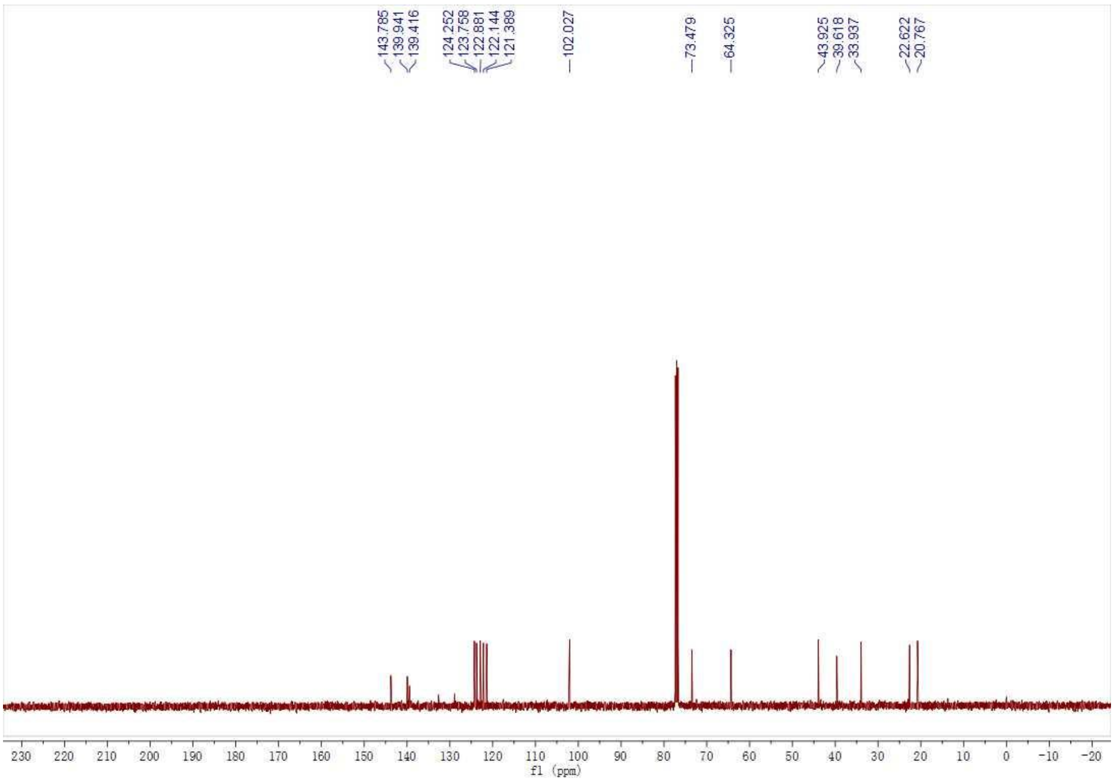
122.838
122.127
121.186
101.915
69.767
61.114
42.365
36.616
28.803
23.058
19.522
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)


S
H
O
H
O

cis-anti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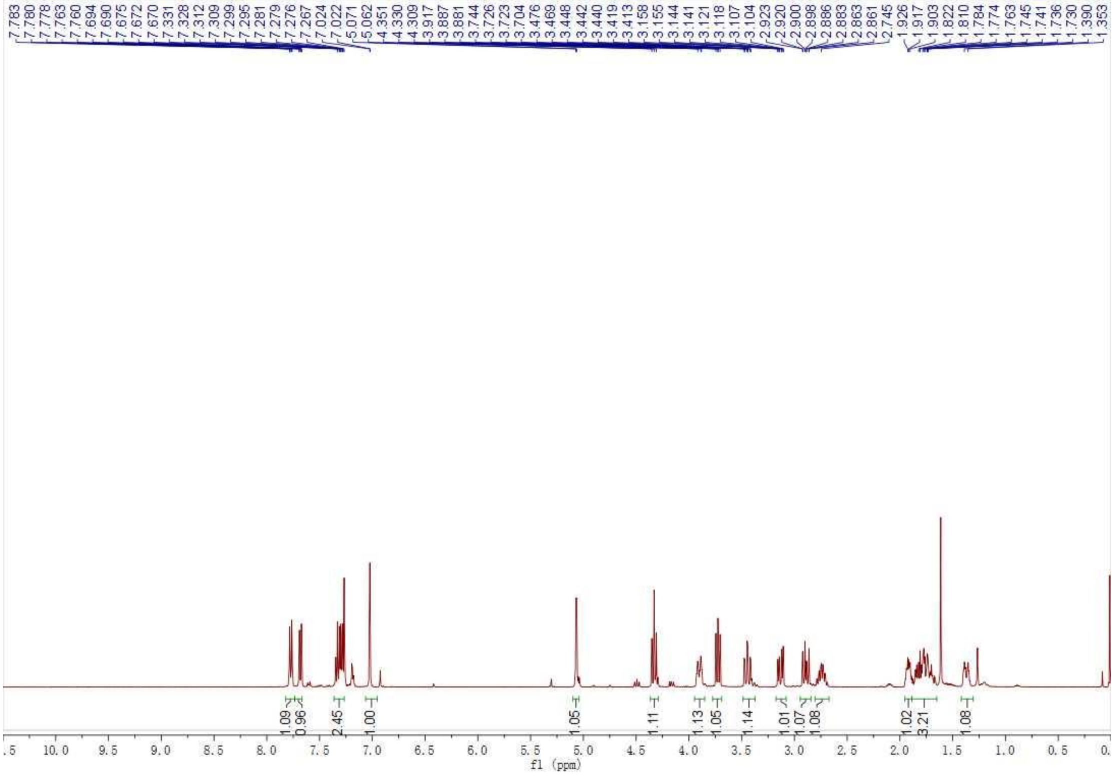
122.144
121.389
102.027
73.479
64.325
43.925
39.618
33.937
22.622
20.767
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)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7.763
7.760
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7.690
7.675
7.672
7.670
7.331
7.328
7.312
7.309
7.299
7.295
7.281
7.279
7.276
7.267
7.024
7.022
5.071
5.062
4.351
4.330
4.309
3.917
3.887
3.881
3.744
3.726
3.723
3.704
3.476
3.469
3.448
3.442
3.440
3.419
3.413
3.158
3.155
3.144
3.141
3.121
3.118
3.107
3.104
2.923
2.920
2.900
2.898
2.886
2.883
2.863
2.861
2.745
1.926
1.917
1.903
1.822
1.810
1.784
1.774
1.763
1.745
1.741
1.736
1.730
1.390
1.353
1.09
0.96
2.45
1.00
1.05
1.11
1.13
1.05
1.14
1.01
1.07
1.08
1.02
3.21
1.08
.5
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9.0
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8.0
7.5
7.0
6.5
6.0
5.5
5.0
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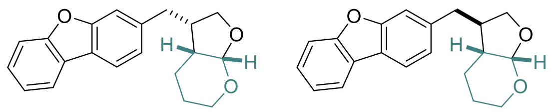
0.5
0.
f1 (ppm)

(**11**)



O
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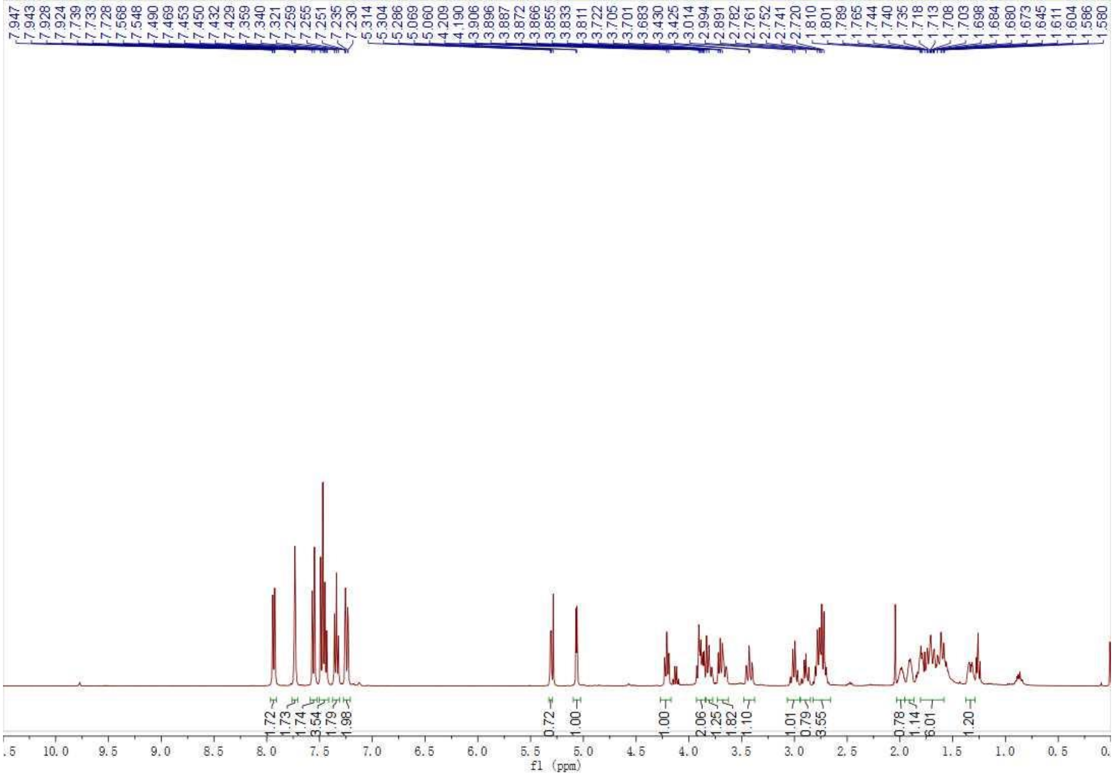
H
O



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7.728
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7.548
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7.453
7.450
7.432
7.429
7.359
7.340
7.321
7.259
7.255
7.251
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7.230
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5.304
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5.069
5.060
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4.190
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3.855
3.833
3.811
3.722
3.705
3.701
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1.703
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1.00
1.00
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1.82
1.10
1.01
0.79
3.55
0.78
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9.0
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8.0
7.5
7.0
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6.0
5.5
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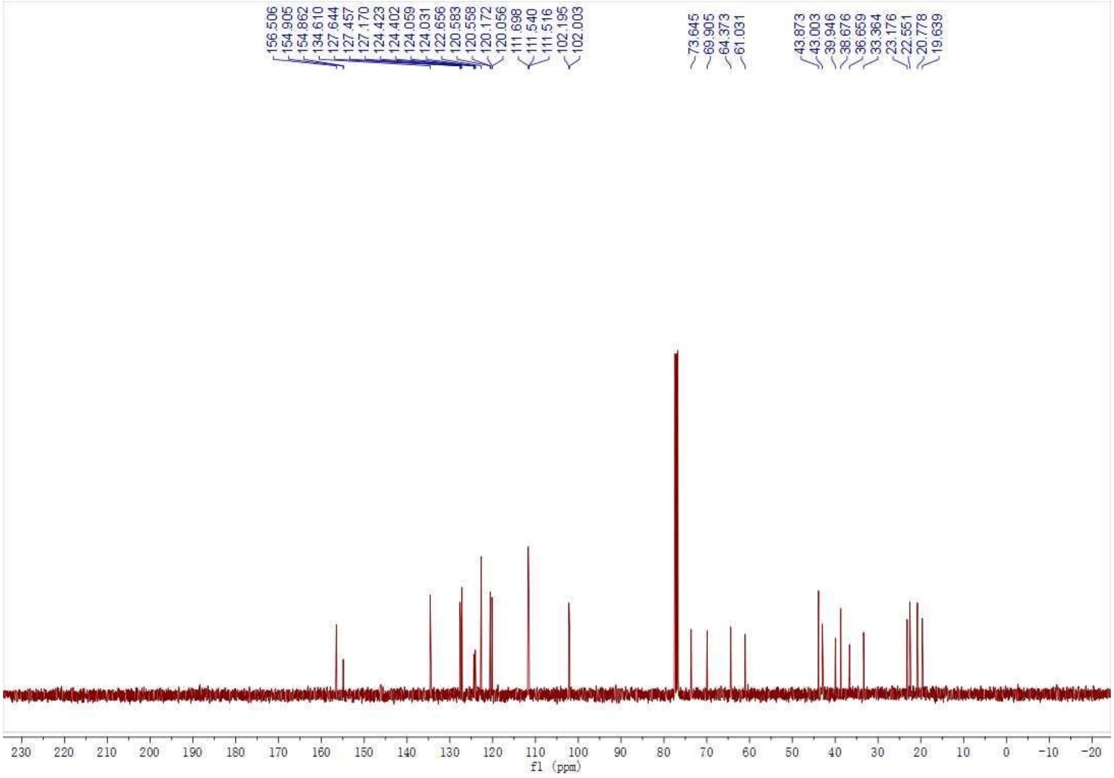
1.0
0.5
0.
f1 (ppm)



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127.644
127.457
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124.423
124.402
124.059
124.031
122.656
120.583
120.558
120.172
120.056
111.698
111.540
111.516
102.195
102.003
73.645
69.905
64.373
61.031
43.873
43.003
39.946
38.676
36.659
33.364
23.176
22.551
20.778
19.639
230
220
210
200
190
180
170
160
150
140
130
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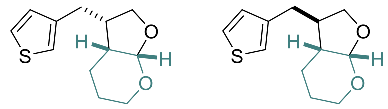
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)

(12)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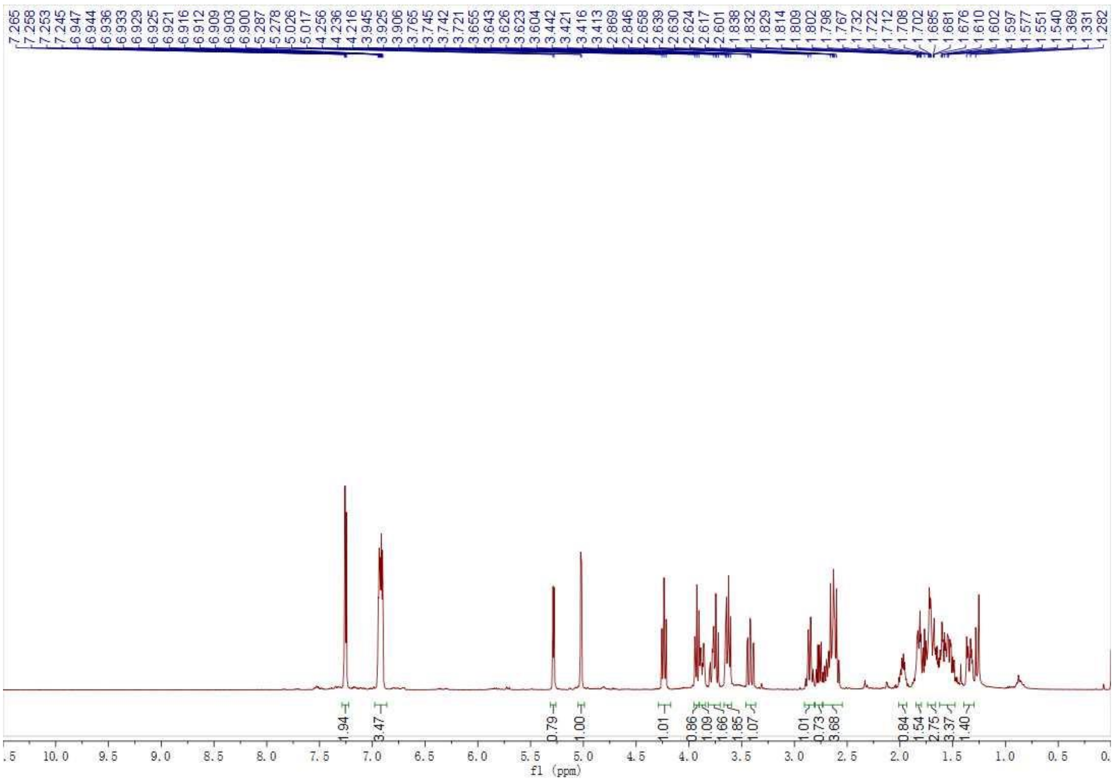
O
H
O
S
H
O
H
O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7.245
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6.916
6.912
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6.903
6.900
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5.278
5.026
5.017
4.256
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2.601
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1.832
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1.809
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1.708
1.702
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1.331
1.282
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0.79
1.00
1.01
0.86
1.09
1.66
1.85
1.07
1.01
0.73
3.68
0.84
1.54
2.75
3.37
1.40
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
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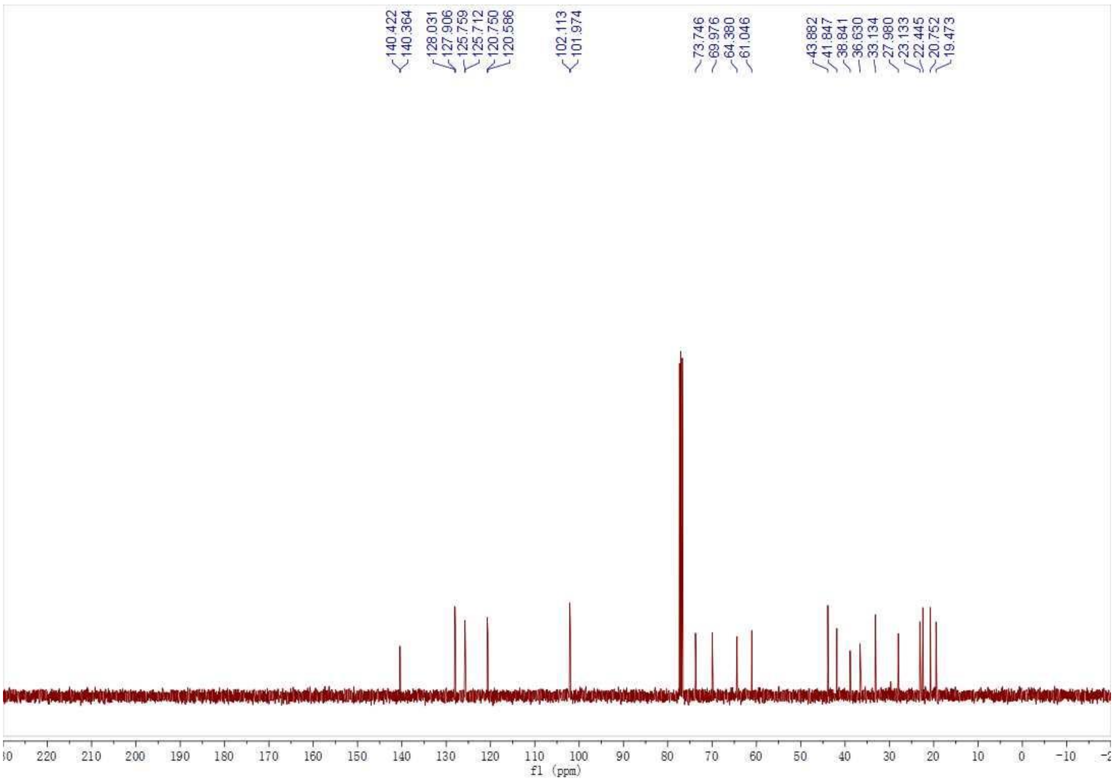
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)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125.712
120.750
120.586
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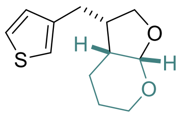
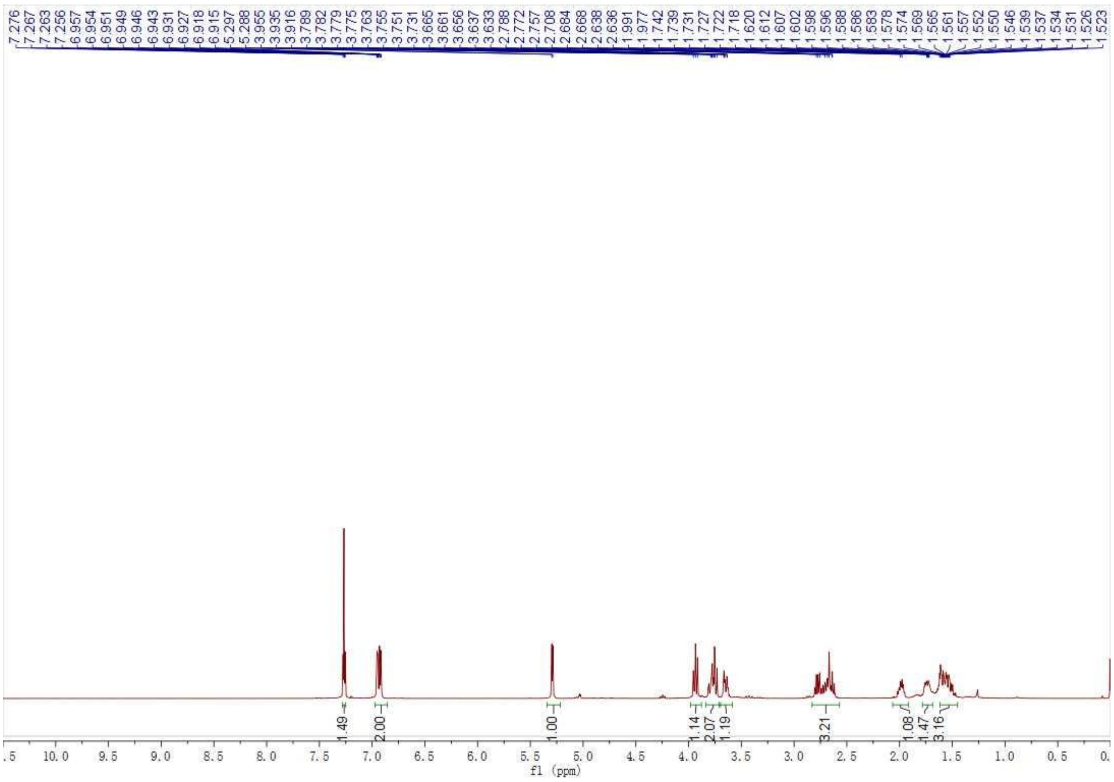
101.974
73.746
69.976
64.380
61.046
43.882
41.847
38.841
36.630
33.134
27.980
23.133
22.445
20.752
19.473
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


S
H
O
H
O

cis-syn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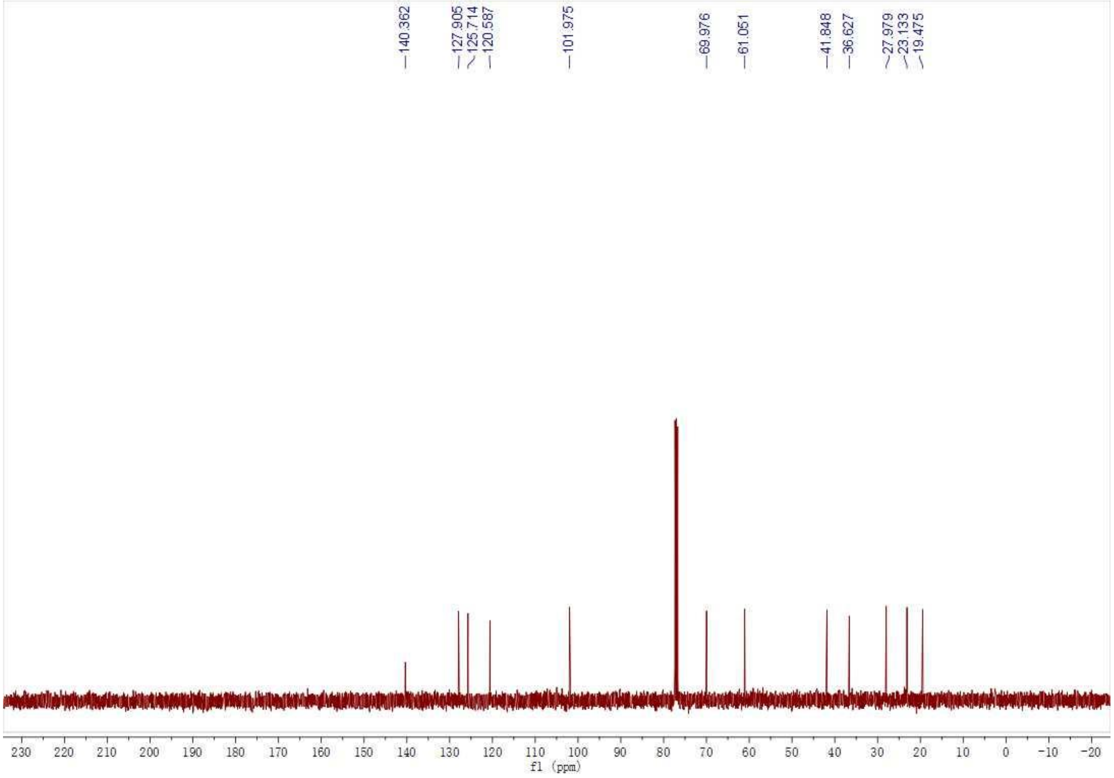
7.267
7.263
7.256
6.957
6.954
6.951
6.949
6.946
6.943
6.931
6.927
6.918
6.915
5.297
5.288
3.955
3.935
3.916
3.789
3.782
3.779
3.775
3.763
3.755
3.751
3.731
3.665
3.661
3.656
3.637
3.633
2.788
2.772
2.757
2.708
2.684
2.668
2.638
2.636
1.991
1.977
1.742
1.739
1.731
1.727
1.722
1.718
1.620
1.612
1.607
1.602
1.598
1.596
1.588
1.586
1.583
1.578
1.574
1.569
1.565
1.561
1.557
1.552
1.550
1.546
1.539
1.537
1.534
1.531
1.526
1.523
1.49
2.00
1.00
1.14
2.07
1.19
3.21
1.08
1.47
3.16
.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.
f1 (ppm)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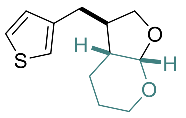
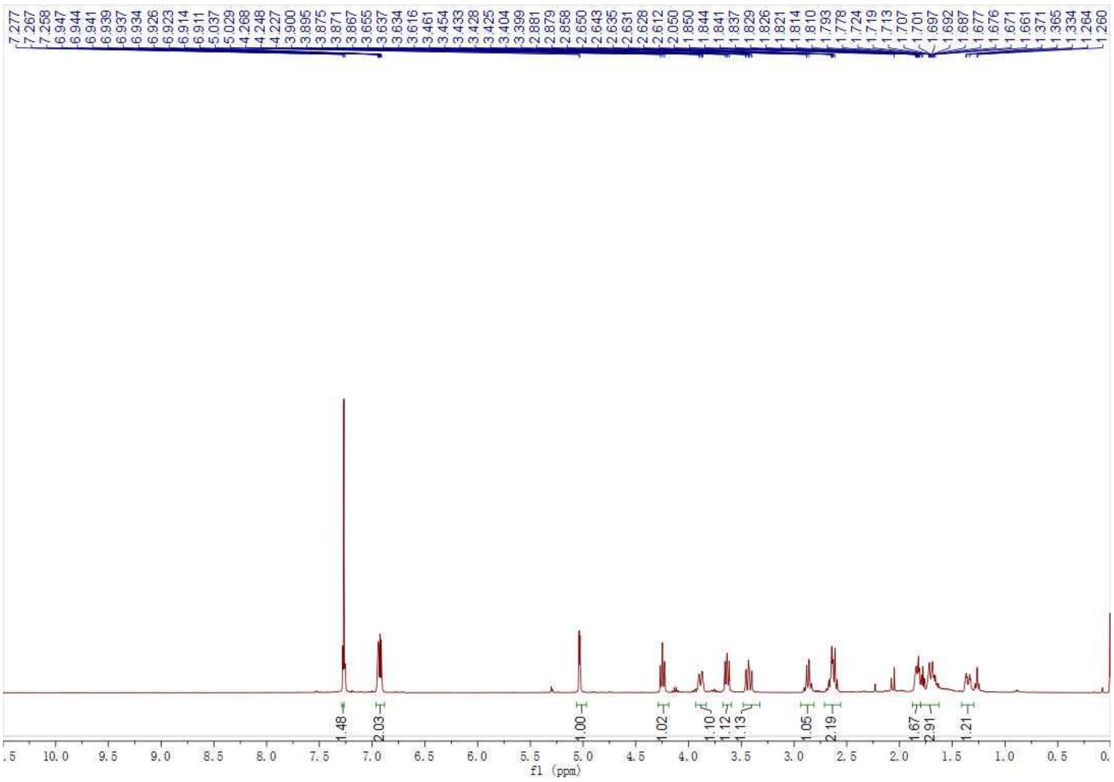
36.627
27.979
23.133
19.475
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)



cis-anti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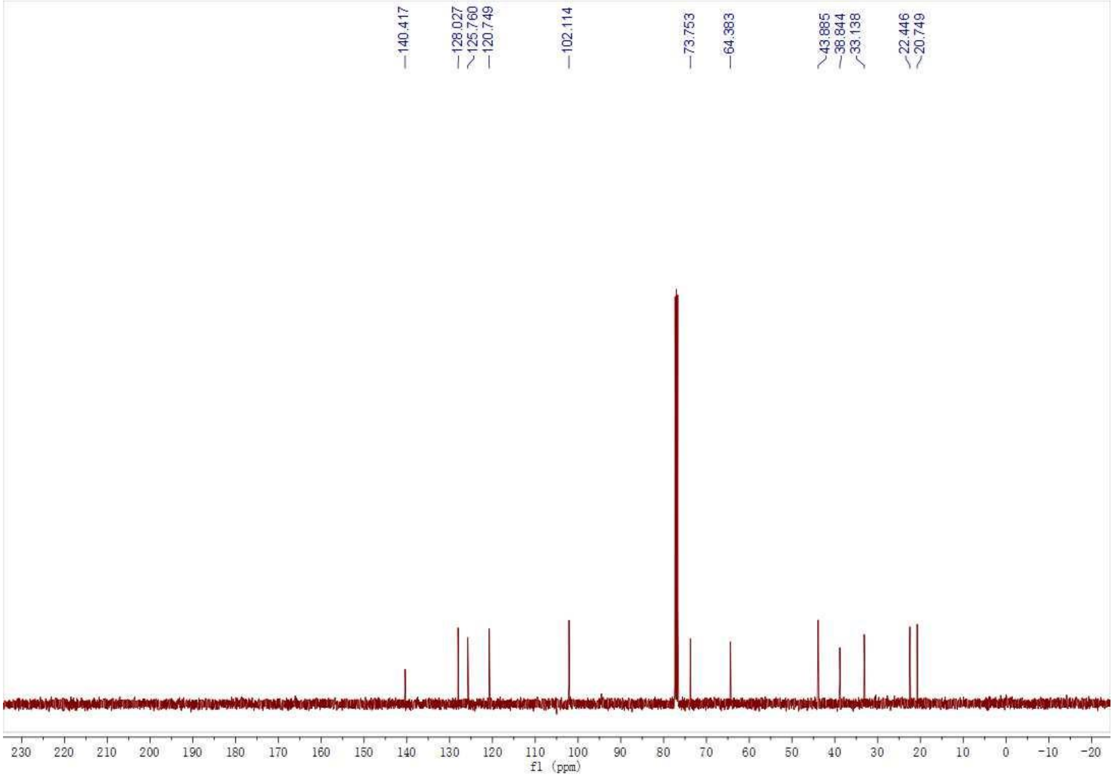
7.267
7.258
6.947
6.944
6.941
6.939
6.937
6.934
6.926
6.923
6.914
6.911
5.037
5.029
4.268
4.248
4.227
3.900
3.895
3.875
3.871
3.867
3.655
3.637
3.634
3.616
3.461
3.454
3.433
3.428
3.425
3.404
3.399
2.881
2.879
2.858
2.650
2.643
2.635
2.631
2.628
2.612
2.050
1.850
1.844
1.841
1.837
1.829
1.826
1.821
1.814
1.810
1.793
1.778
1.724
1.719
1.713
1.707
1.701
1.697
1.692
1.687
1.677
1.676
1.671
1.661
1.371
1.365
1.334
1.264
1.260
1.48
2.03
1.00
1.02
1.10
1.12
1.13
1.05
2.19
1.67
2.91
1.21
.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.
f1 (ppm)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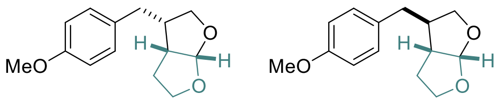
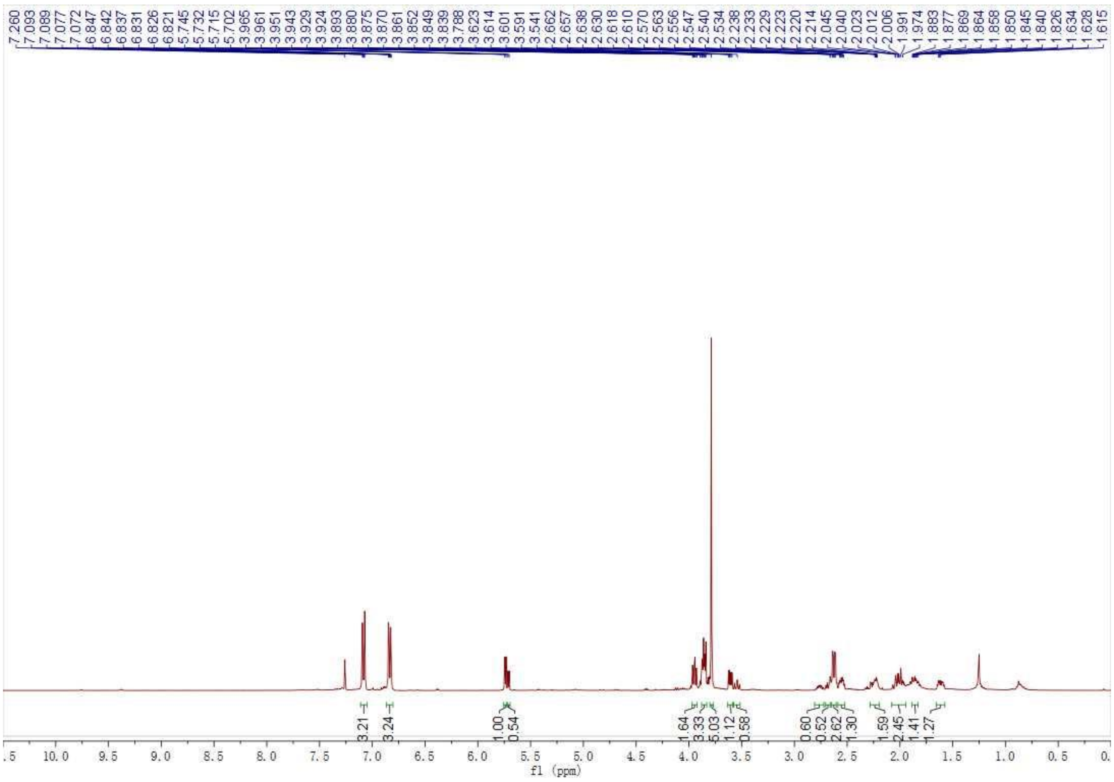
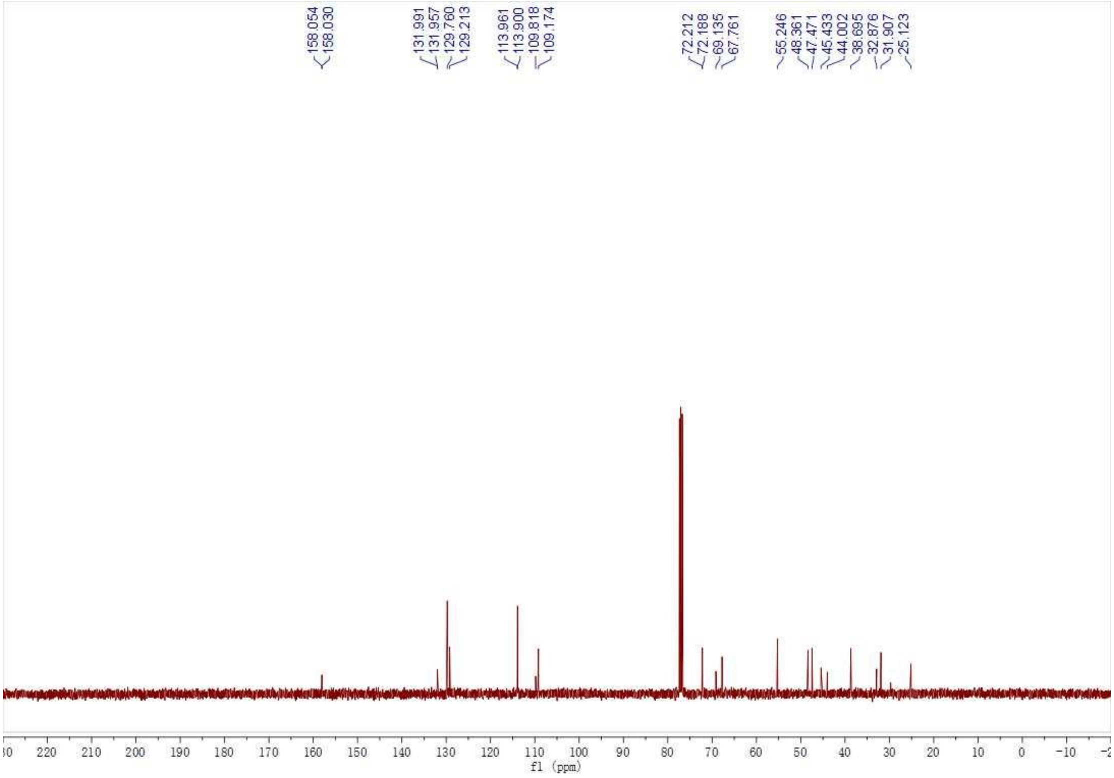
128.027
125.760
120.749
102.114
73.753
64.383
43.885
38.844
33.138
22.446
20.749
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)

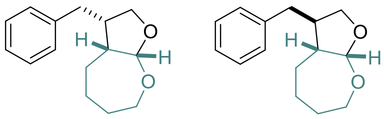
(**13**)

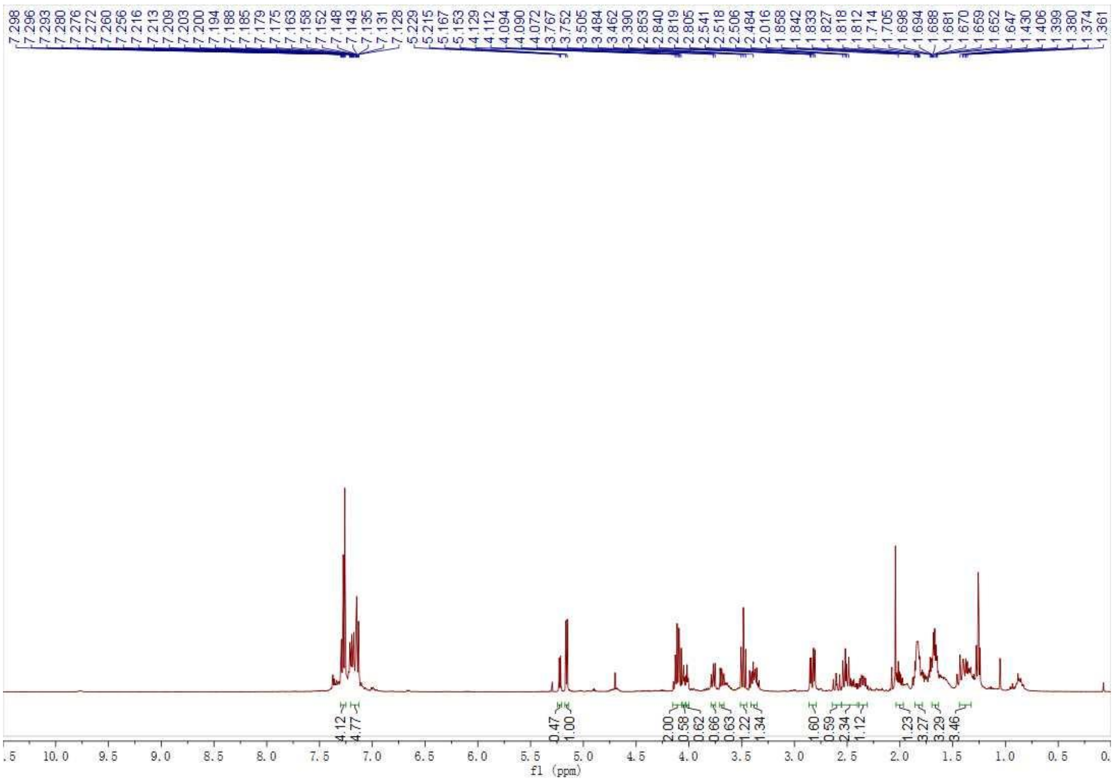

MeO
H
O
H
O
MeO
H
O
H
O


7.260
7.093
7.089
7.077
7.072
6.847
6.842
6.837
6.831
6.826
6.821
5.745
5.732
5.715
5.702
3.965
3.961
3.951
3.943
3.929
3.924
3.893
3.880
3.875
3.870
3.861
3.852
3.849
3.839
3.788
3.623
3.614
3.601
3.591
3.541
2.662
2.657
2.638
2.630
2.618
2.610
2.570
2.563
2.556
2.547
2.540
2.534
2.238
2.233
2.229
2.223
2.220
2.214
2.045
2.040
2.023
2.012
2.006
1.991
1.974
1.883
1.877
1.869
1.864
1.858
1.850
1.845
1.840
1.826
1.634
1.628
1.615
3.21
3.24
1.00
0.54
1.64
3.33
5.03
1.12
0.58
0.60
0.52
2.62
1.30
1.59
2.45
1.41
1.27
.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.
f1 (ppm)


158.054
158.030
131.991
131.957
129.760
129.213
113.961
113.900
109.818
109.174
72.212
72.188
69.135
67.761
55.246
48.361
47.471
45.433
44.002
38.695
32.876
31.907
25.123
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

(**14**)


H
O
H
O
H
O
H
O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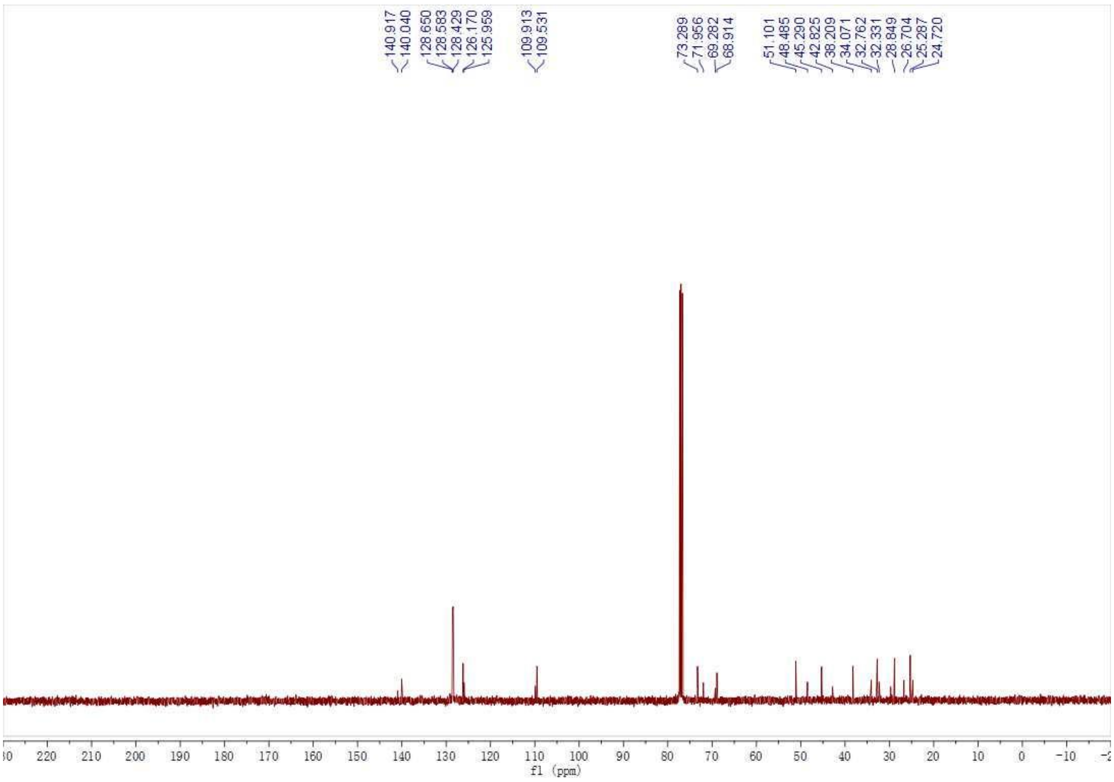
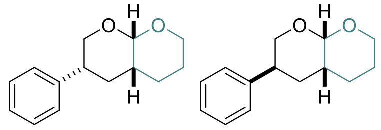
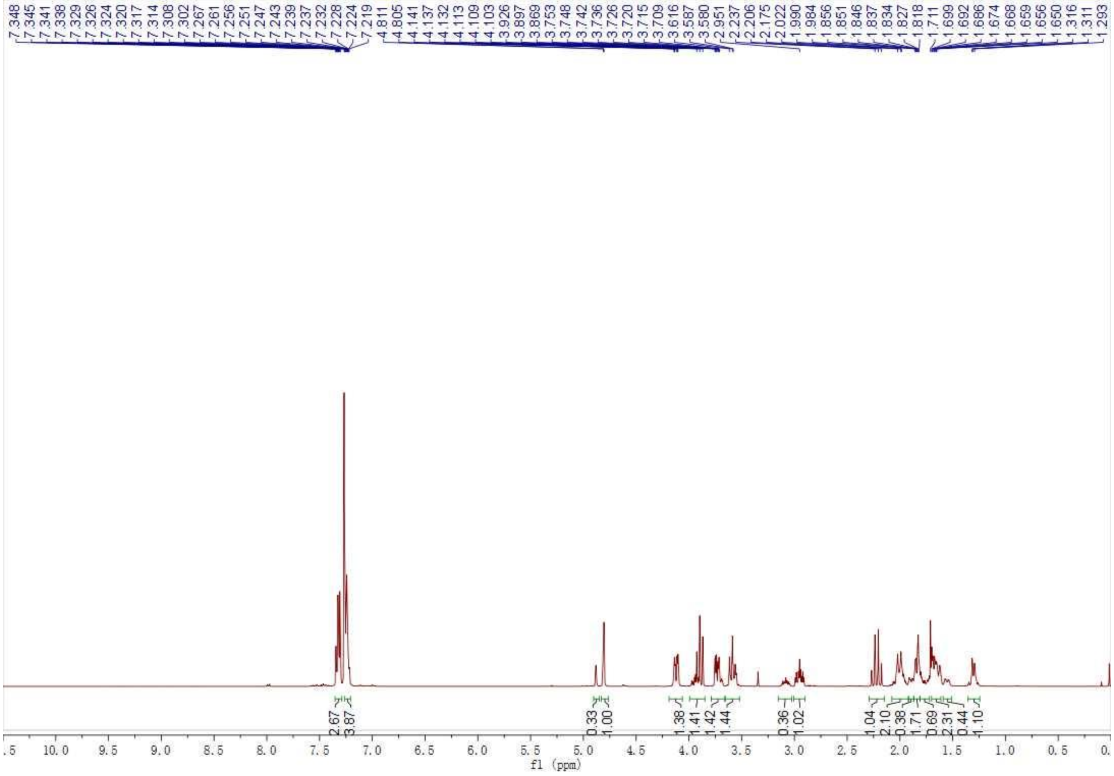
7.296
7.293
7.280
7.276
7.272
7.260
7.256
7.216
7.213
7.209
7.203
7.200
7.194
7.188
7.185
7.179
7.175
7.163
7.158
7.152
7.148
7.143
7.135
7.131
7.128
5.229
5.215
5.167
5.153
4.129
4.112
4.094
4.090
4.072
3.767
3.752
3.505
3.484
3.462
3.390
2.853
2.840
2.819
2.805
2.541
2.518
2.506
2.484
2.016
1.858
1.842
1.833
1.827
1.818
1.812
1.714
1.705
1.698
1.694
1.688
1.681
1.670
1.659
1.652
1.647
1.430
1.406
1.399
1.380
1.374
1.361
4.12
4.77
0.47
1.00
2.00
0.58
0.62
0.66
0.63
1.22
1.34
1.60
0.59
2.34
1.12
1.23
3.27
3.29
3.46
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
f1 (ppm)


140.917
140.040
128.650
128.583
128.429
126.170
125.959
109.913
109.531
73.289
71.956
69.282
68.914
51.101
48.485
45.290
42.825
38.209
34.071
32.762
32.331
28.849
26.704
25.287
24.720
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

(**15**)


O
H
O
H
O
H
O
H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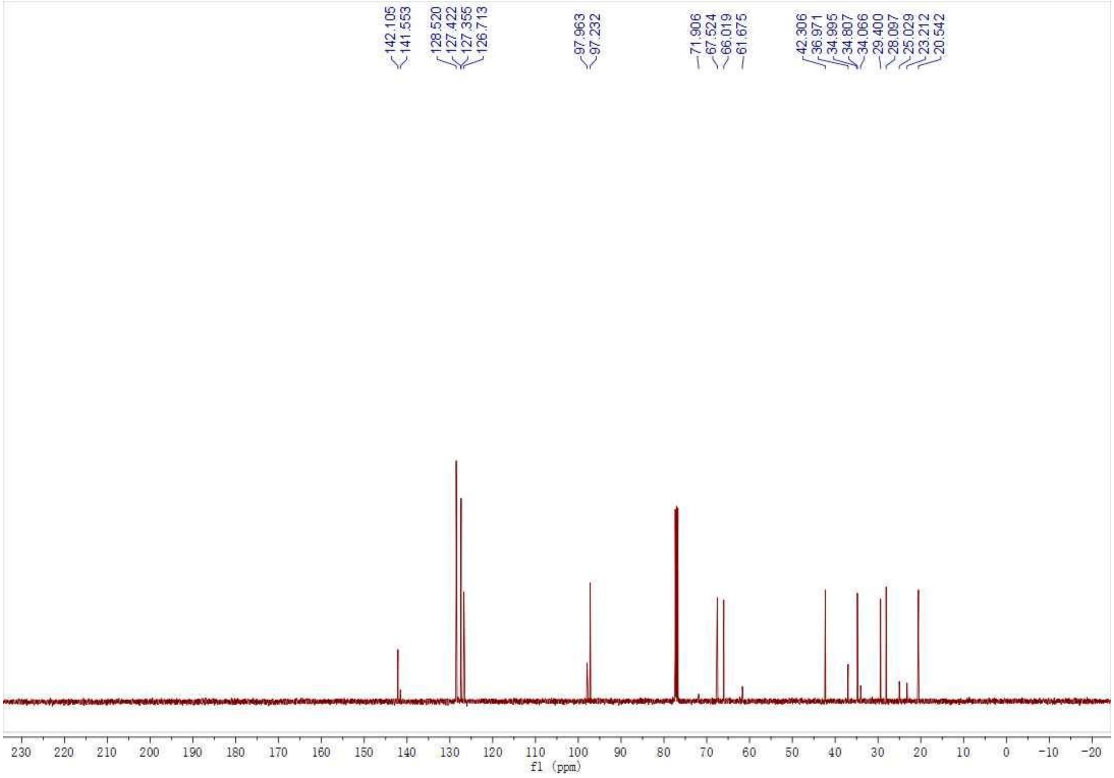
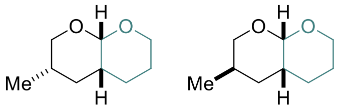
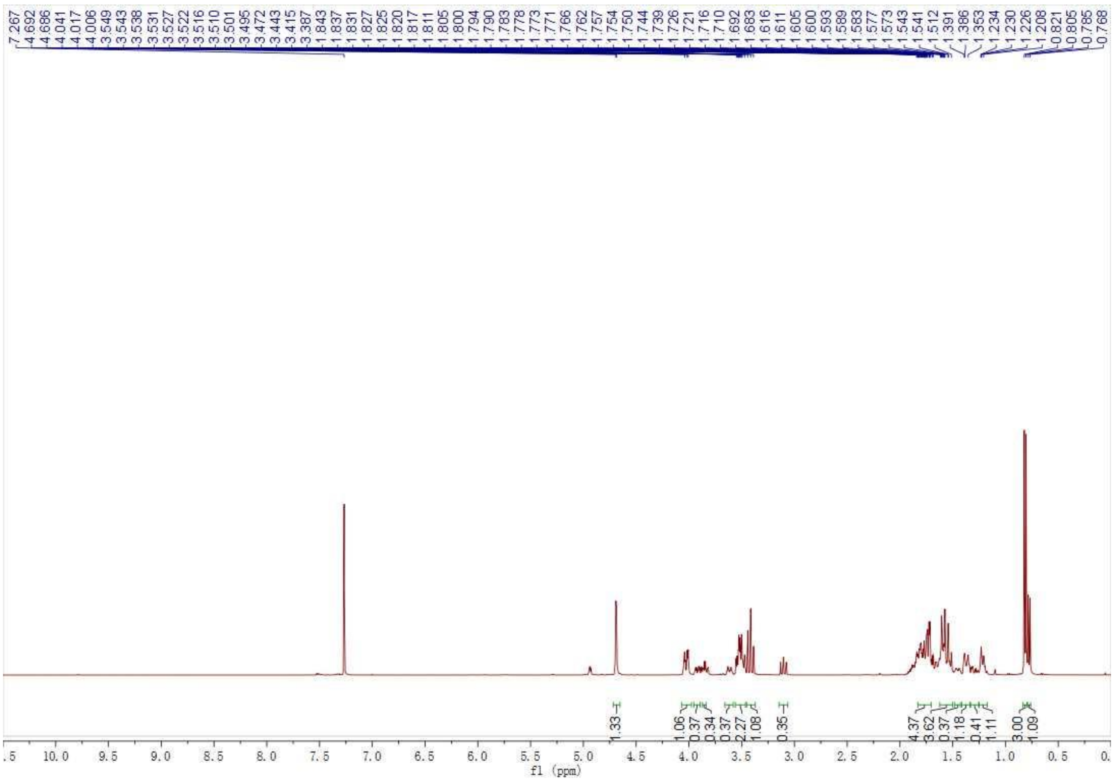
7.329
7.326
7.324
7.320
7.317
7.314
7.308
7.302
7.267
7.261
7.256
7.251
7.247
7.243
7.239
7.237
7.232
7.228
7.224
7.219
4.811
4.805
4.141
4.137
4.132
4.113
4.109
4.103
3.926
3.897
3.869
3.753
3.748
3.742
3.736
3.726
3.720
3.715
3.709
3.616
3.587
3.580
2.951
2.237
2.206
2.175
2.022
1.990
1.984
1.856
1.851
1.846
1.837
1.834
1.827
1.818
1.711
1.699
1.692
1.686
1.674
1.668
1.659
1.656
1.650
1.316
1.311
1.293
2.67
3.87
0.33
1.00
1.38
1.41
1.42
1.44
0.36
1.02
1.04
2.10
0.38
1.71
0.69
2.31
0.44
1.10
.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.
f1 (ppm)


142.105
141.553
128.520
127.422
127.355
126.713
97.963
97.232
71.906
67.524
66.019
61.675
42.306
36.971
34.995
34.807
34.066
29.400
28.097
25.029
23.212
20.542
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)

(**16**)


O
H
O
Me
H
O
H
O
Me
H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4.006
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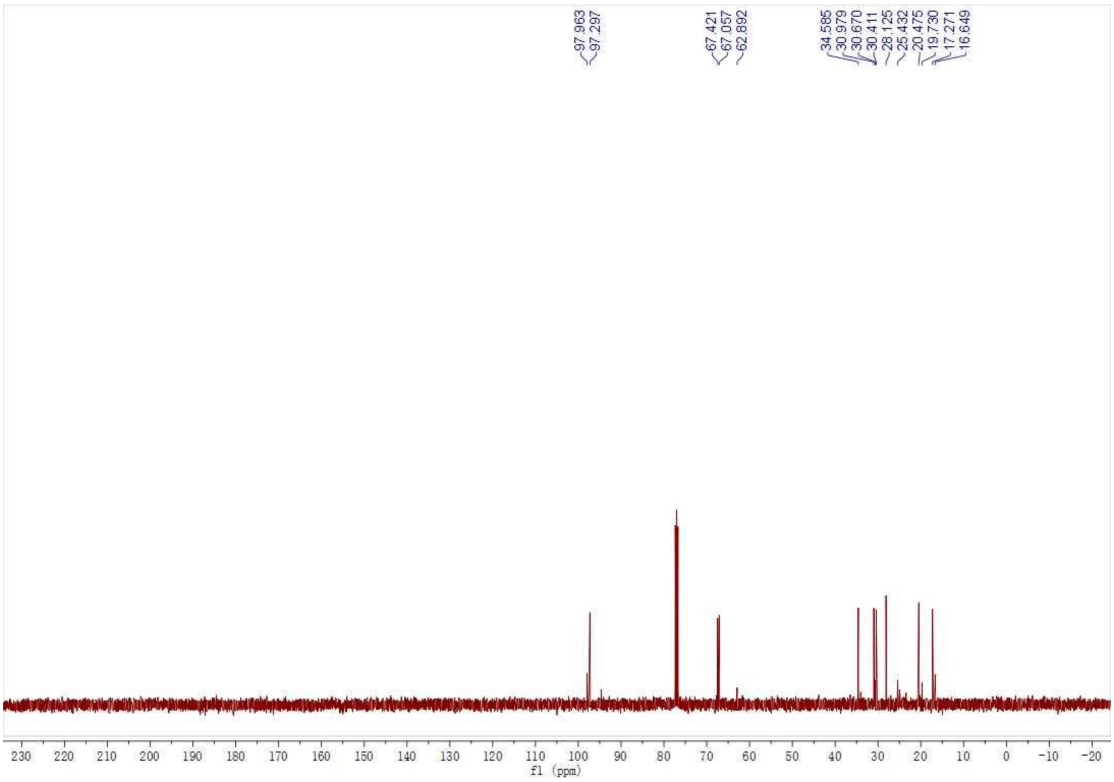
3.543
3.538
3.531
3.527
3.522
3.516
3.510
3.501
3.495
3.472
3.443
3.415
3.387
1.843
1.837
1.831
1.827
1.825
1.820
1.817
1.811
1.805
1.800
1.794
1.790
1.783
1.778
1.773
1.771
1.766
1.762
1.757
1.754
1.750
1.744
1.739
1.726
1.721
1.716
1.710
1.692
1.683
1.616
1.611
1.605
1.600
1.593
1.589
1.583
1.577
1.573
1.543
1.541
1.512
1.391
1.386
1.353
1.234
1.230
1.226
1.208
0.821
0.805
0.785
0.768
1.33
1.06
0.37
0.34
0.37
2.27
1.08
0.35
4.37
3.62
0.37
1.18
0.41
1.11
3.00
1.09
.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.
f1 (ppm)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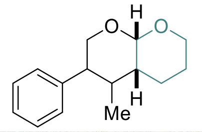
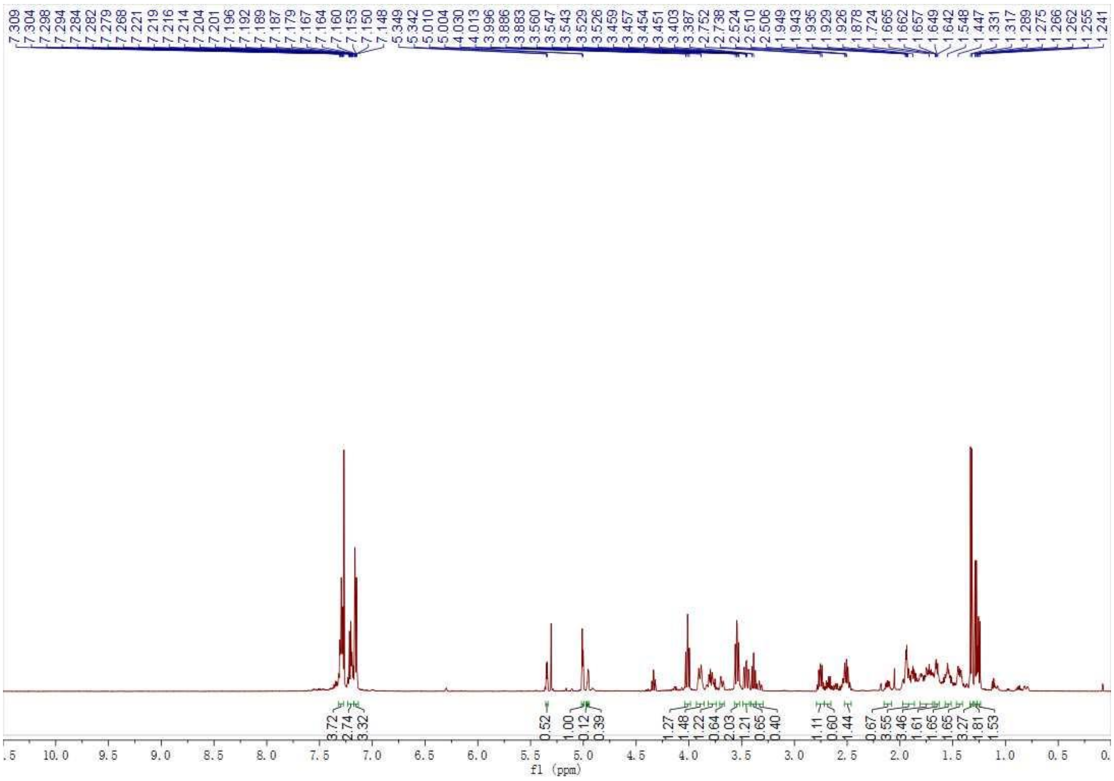
67.057
62.892
34.585
30.979
30.670
30.411
28.125
25.432
20.475
19.730
17.271
16.649
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)

(**17**)


O
H
O
H
Me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7.268
7.221
7.219
7.216
7.214
7.204
7.201
7.196
7.192
7.189
7.187
7.179
7.167
7.164
7.160
7.153
7.150
7.148
5.349
5.342
5.010
5.004
4.030
4.013
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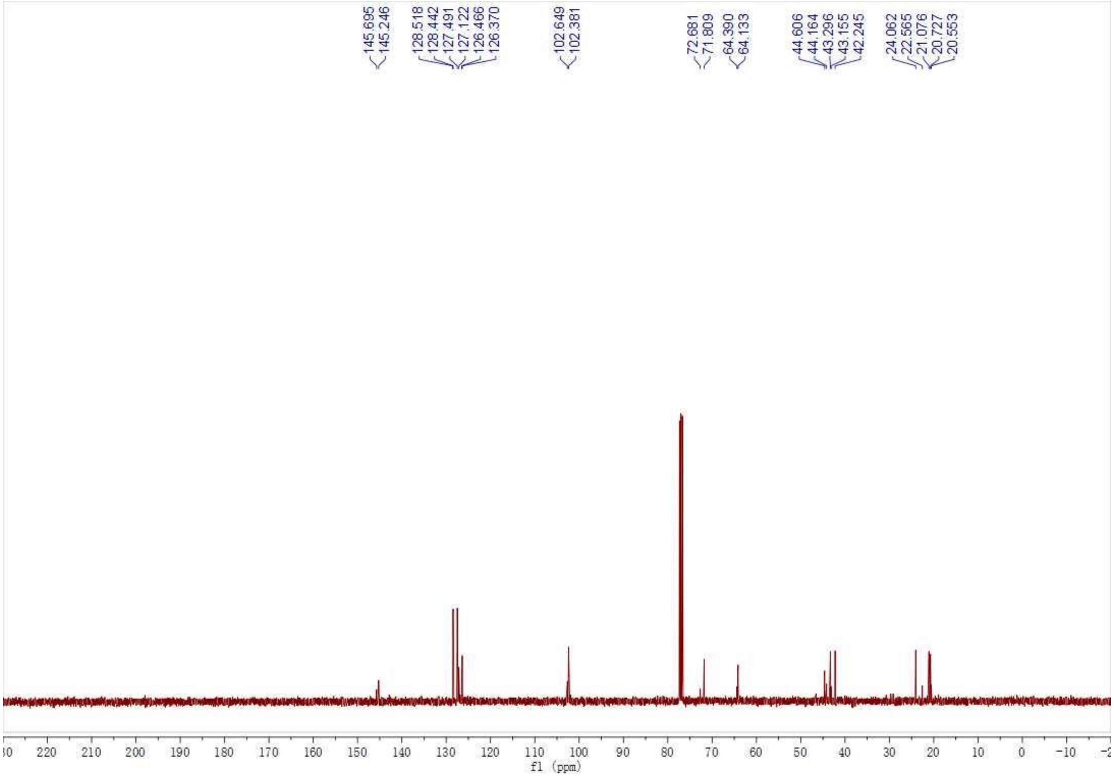
3.886
3.883
3.560
3.547
3.543
3.529
3.526
3.459
3.457
3.454
3.451
3.403
3.387
2.752
2.738
2.524
2.510
2.506
1.949
1.943
1.935
1.929
1.926
1.878
1.724
1.665
1.662
1.657
1.649
1.642
1.548
1.447
1.331
1.317
1.289
1.275
1.266
1.262
1.255
1.241
3.72
2.74
3.32
0.52
1.00
0.12
0.39
1.27
1.48
1.22
0.64
2.03
1.21
0.65
0.40
1.11
0.60
1.44
0.67
3.55
3.46
1.61
1.65
1.65
3.27
1.81
1.53
.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.
f1 (ppm)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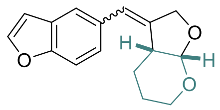
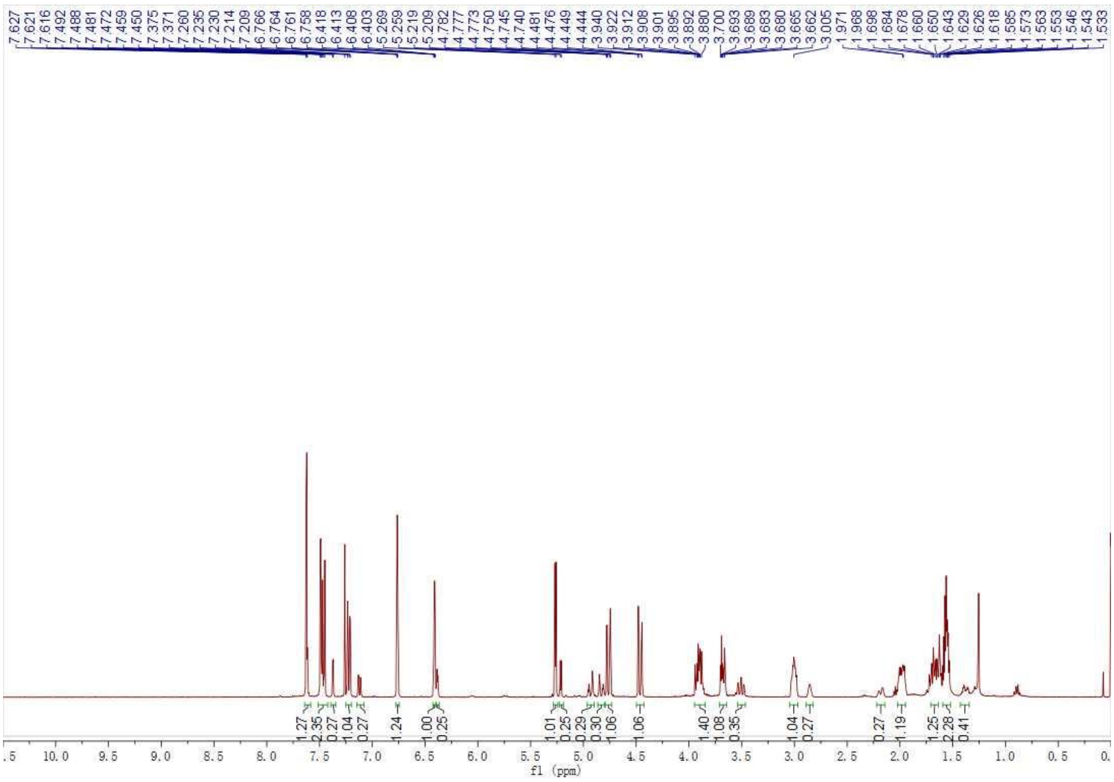
128.442
127.491
127.122
126.466
126.370
102.649
102.381
72.681
71.809
64.390
64.133
44.606
44.164
43.296
43.155
42.245
24.062
22.565
21.076
20.727
20.553
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

(**18**)


O
H
O
H
O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7.481
7.472
7.459
7.450
7.375
7.371
7.260
7.235
7.230
7.214
7.209
6.766
6.764
6.761
6.758
6.418
6.413
6.408
6.403
5.269
5.259
5.219
5.209
4.782
4.777
4.773
4.750
4.745
4.740
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4.444
3.940
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3.912
3.908
3.901
3.895
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3.880
3.700
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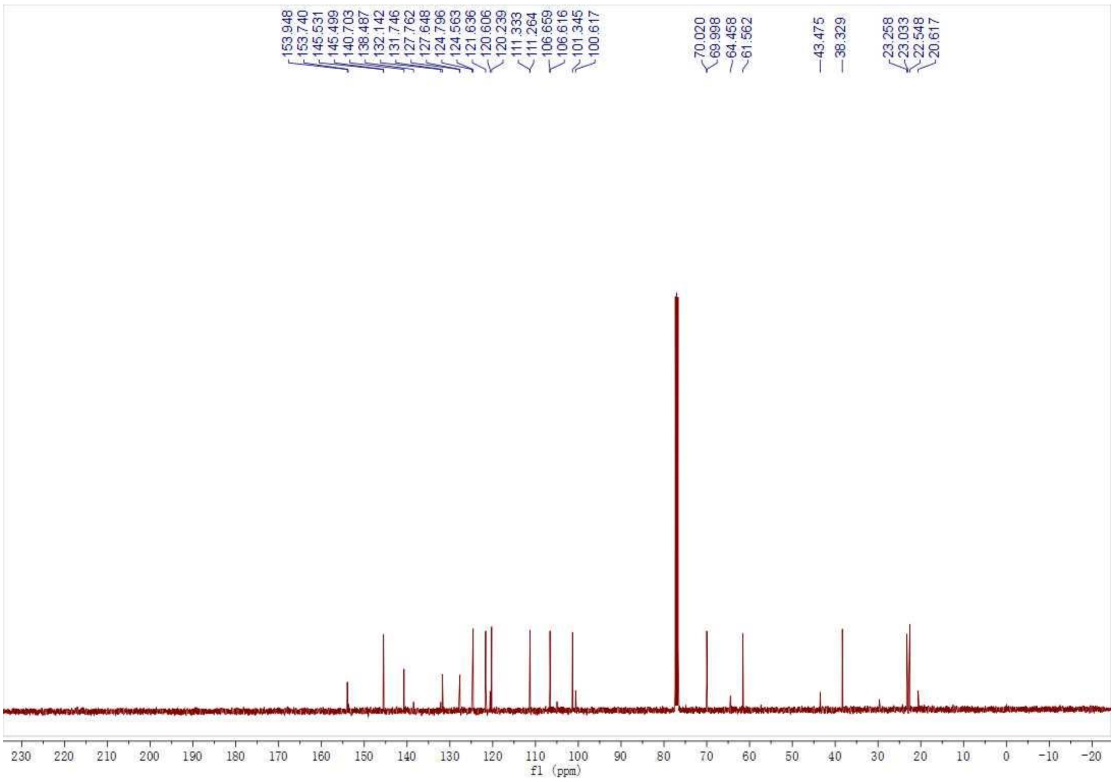
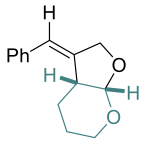
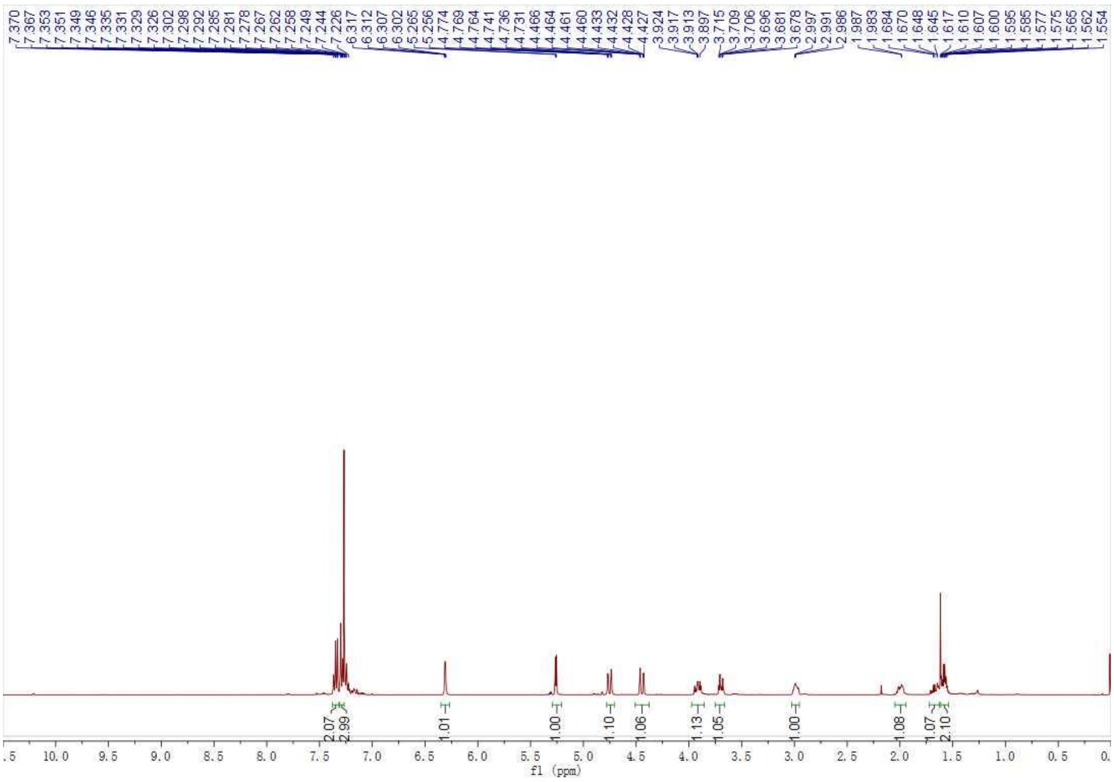
3.689
3.683
3.680
3.665
3.662
3.005
1.971
1.968
1.698
1.684
1.678
1.660
1.650
1.643
1.629
1.626
1.618
1.585
1.573
1.563
1.553
1.546
1.543
1.533
1.27
2.35
0.27
1.04
0.27
1.24
1.00
0.25
1.01
0.25
0.29
0.30
1.06
1.06
1.40
1.08
0.35
1.04
0.27
0.27
1.19
1.25
2.28
0.41
.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)

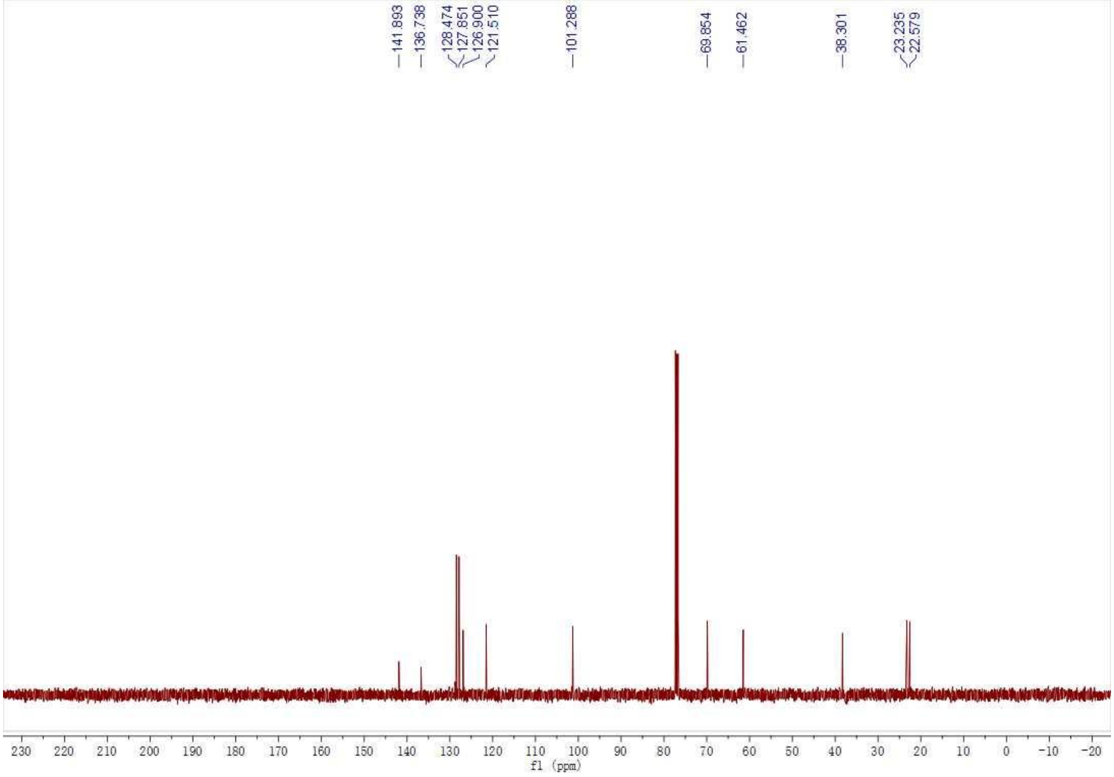

153.948
153.740
145.531
145.499
140.703
138.487
132.142
131.746
127.762
127.648
124.796
124.563
121.636
120.606
120.239
111.333
111.264
106.659
106.616
101.345
100.617
70.020
69.998
64.458
61.562
43.475
38.329
23.258
23.033
22.548
20.617
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)

(**19**)

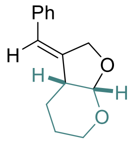

H
Ph
O
H
H
O

E-isomer

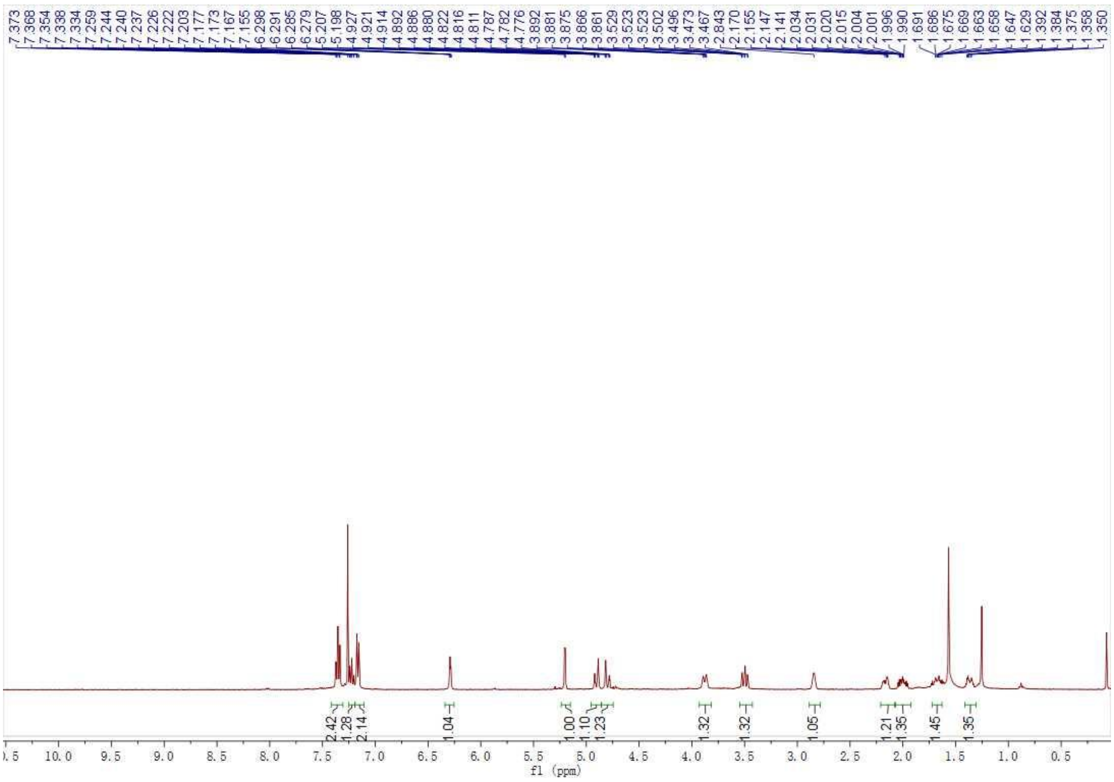

7.370
7.367
7.353
7.351
7.349
7.346
7.335
7.331
7.329
7.326
7.302
7.298
7.292
7.285
7.281
7.278
7.267
7.262
7.258
7.249
7.244
7.226
6.317
6.312
6.307
6.302
5.265
5.256
4.774
4.769
4.764
4.741
4.736
4.731
4.466
4.464
4.461
4.460
4.433
4.432
4.428
4.427
3.924
3.917
3.913
3.897
3.715
3.709
3.706
3.696
3.681
3.678
2.997
2.991
2.986
1.987
1.983
1.684
1.670
1.648
1.645
1.617
1.610
1.607
1.600
1.595
1.585
1.577
1.575
1.565
1.562
1.554
2.07
2.99
1.01
1.00
1.10
1.06
1.13
1.05
1.00
1.08
1.07
2.10
.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.
f1 (ppm)

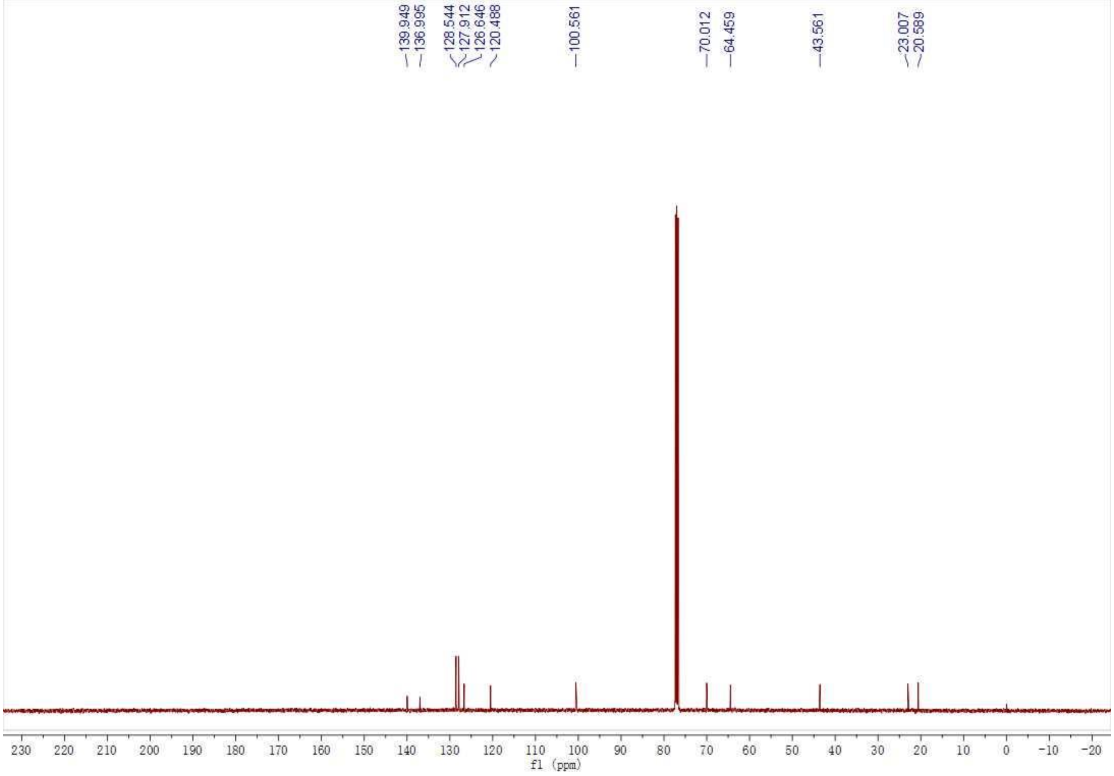

141.893
136.738
128.474
127.851
126.900
121.510
101.288
69.854
61.462
38.301
23.235
22.579
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)

(**19**)

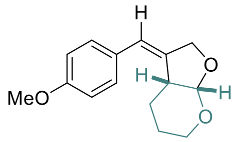

Ph
H
H
O
H
O

Z-isomer

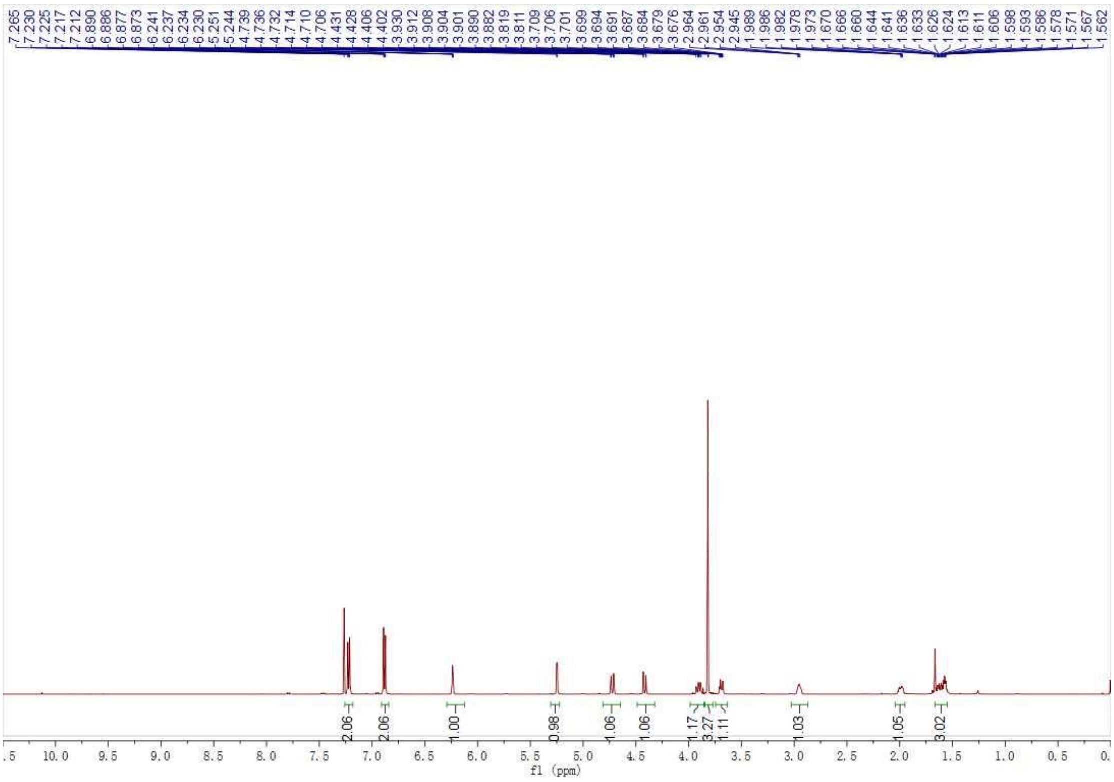

7.373
7.368
7.354
7.338
7.334
7.259
7.244
7.240
7.237
7.226
7.222
7.203
7.177
7.173
7.167
7.155
6.298
6.291
6.285
6.279
5.207
5.198
4.927
4.921
4.914
4.892
4.886
4.880
4.822
4.816
4.811
4.787
4.782
4.776
3.892
3.881
3.875
3.866
3.861
3.529
3.523
3.502
3.496
3.473
3.467
2.843
2.170
2.155
2.147
2.141
2.034
2.031
2.020
2.015
2.004
2.001
1.996
1.990
1.691
1.686
1.675
1.669
1.663
1.658
1.647
1.629
1.392
1.384
1.375
1.358
1.350
2.42
1.28
2.14
1.04
1.00
1.10
1.23
1.32
1.32
1.05
1.21
1.35
1.45
1.35
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
f1 (ppm)

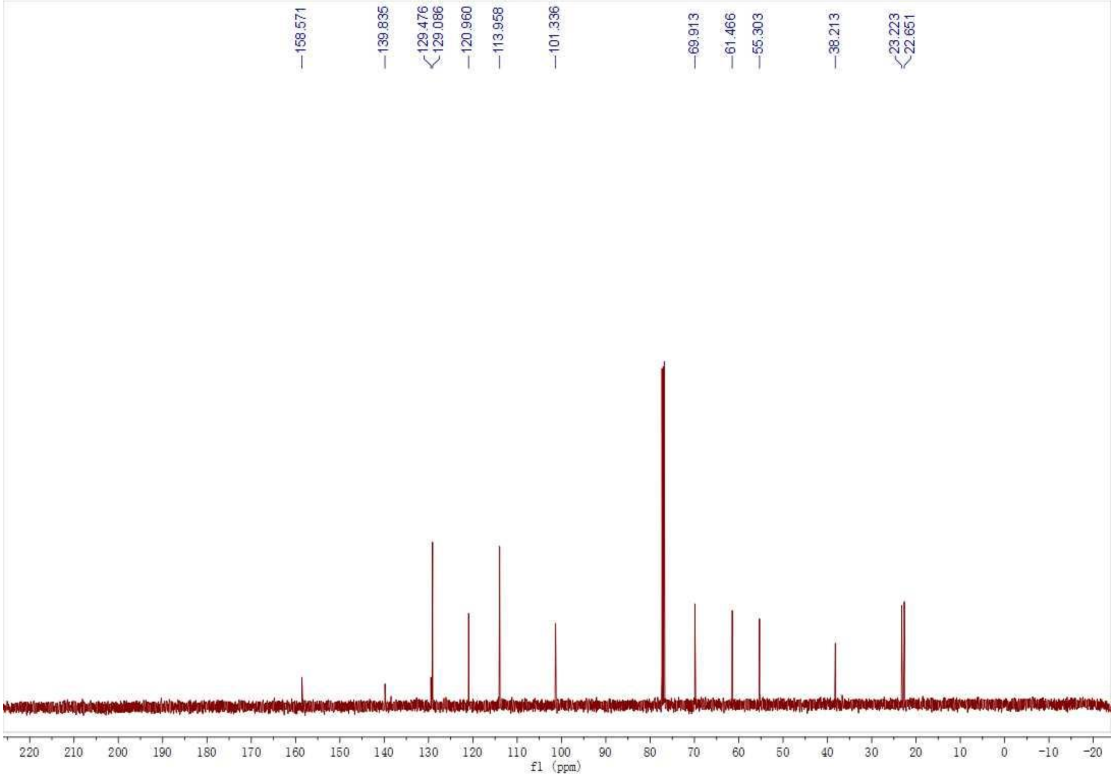

139.949
136.995
128.544
127.912
126.646
120.488
100.561
70.012
64.459
43.561
23.007
20.589
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)

(**20**)

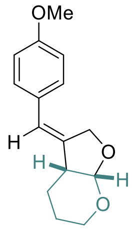

H
O
H
H
O
MeO

E-isomer

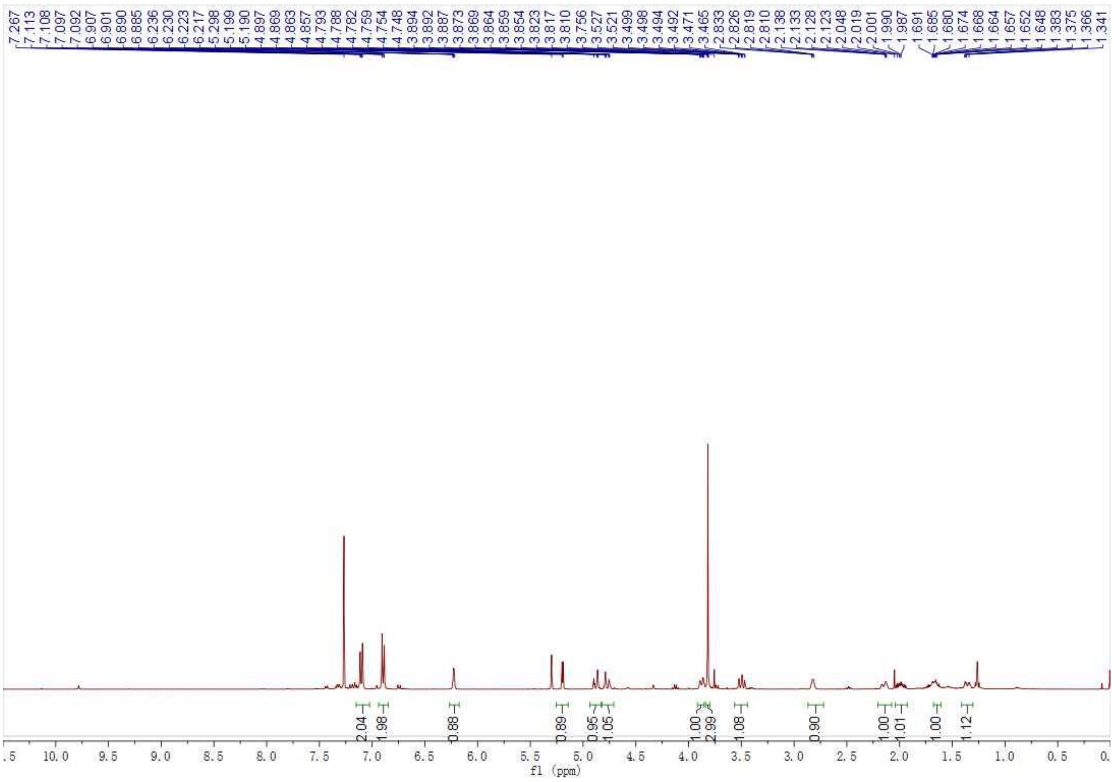

7.265
7.230
7.225
7.217
7.212
6.890
6.886
6.877
6.873
6.241
6.237
6.234
6.230
5.251
5.244
4.739
4.736
4.732
4.714
4.710
4.706
4.431
4.428
4.406
4.402
3.930
3.912
3.908
3.904
3.901
3.890
3.882
3.819
3.811
3.709
3.706
3.701
3.699
3.694
3.691
3.687
3.684
3.679
3.676
2.964
2.961
2.954
2.945
1.989
1.986
1.982
1.978
1.973
1.670
1.666
1.660
1.644
1.641
1.636
1.633
1.626
1.624
1.613
1.611
1.606
1.598
1.593
1.586
1.578
1.571
1.567
1.562
2.06
2.06
1.00
0.98
1.06
1.06
1.17
3.27
1.11
1.03
1.05
3.02
.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.
f1 (ppm)

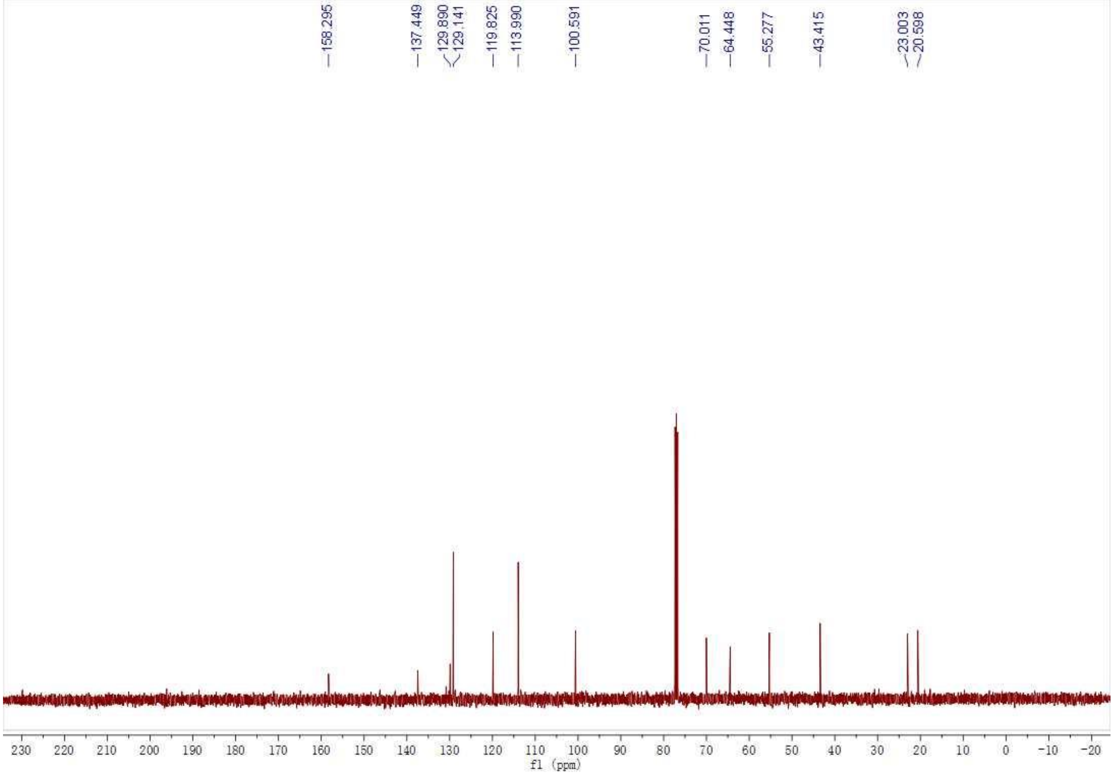

158.571
139.835
129.476
129.086
120.960
113.958
101.336
69.913
61.466
55.303
38.213
23.223
22.651
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)

(**20**)

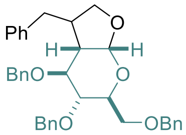

OMe
H
H
O
H
O

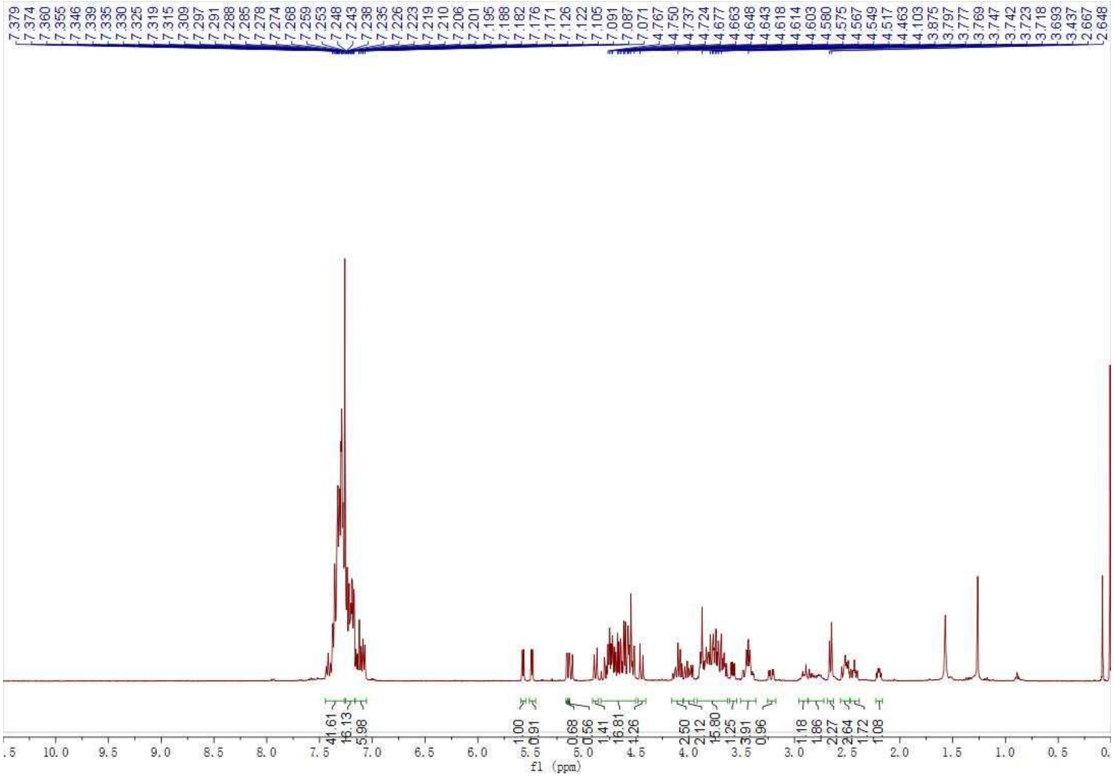
Z-isomer

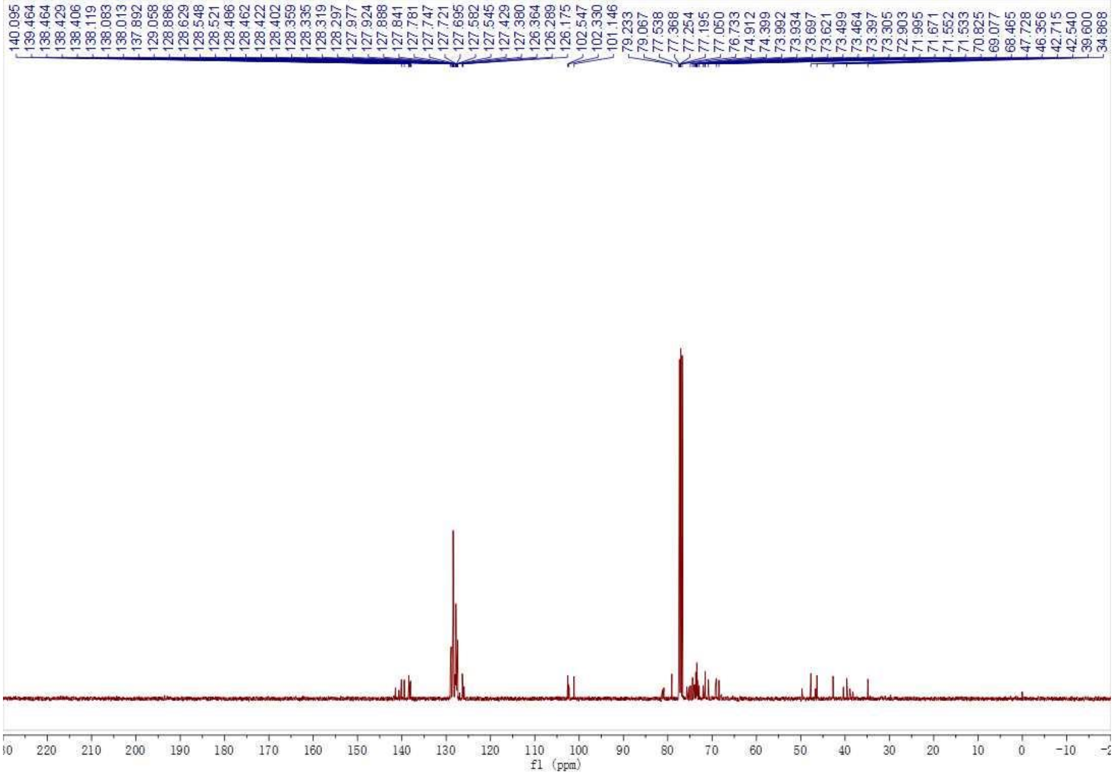

7.267
7.113
7.108
7.097
7.092
6.907
6.901
6.890
6.885
6.236
6.230
6.223
6.217
5.298
5.199
5.190
4.897
4.869
4.863
4.857
4.793
4.788
4.782
4.759
4.754
4.748
3.894
3.892
3.887
3.873
3.869
3.864
3.859
3.854
3.823
3.817
3.810
3.756
3.527
3.521
3.499
3.498
3.494
3.492
3.471
3.465
2.833
2.826
2.819
2.810
2.138
2.133
2.128
2.123
2.048
2.019
2.001
1.990
1.987
1.691
1.685
1.680
1.674
1.668
1.664
1.657
1.652
1.648
1.383
1.375
1.366
1.341
2.04
1.98
0.88
0.89
0.95
1.05
1.00
2.99
1.08
0.90
1.00
1.01
1.00
1.12
.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.
f1 (ppm)


158.295
137.449
129.890
129.141
119.825
113.990
100.591
70.011
64.448
55.277
43.415
23.003
20.598
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)

(21)


Ph
O
H
H
BnO
O
BnO
OBn


7.379
7.374
7.360
7.355
7.346
7.339
7.335
7.330
7.325
7.319
7.315
7.309
7.297
7.291
7.288
7.285
7.278
7.274
7.268
7.259
7.253
7.248
7.243
7.238
7.235
7.226
7.223
7.219
7.210
7.206
7.201
7.195
7.188
7.182
7.176
7.171
7.126
7.122
7.105
7.091
7.087
7.071
4.767
4.750
4.737
4.724
4.677
4.663
4.648
4.643
4.618
4.614
4.603
4.580
4.575
4.567
4.549
4.517
4.463
4.103
3.875
3.797
3.777
3.769
3.747
3.742
3.728
3.723
3.718
3.693
3.437
2.667
2.648
41.61
16.13
5.98
1.00
0.91
0.68
0.56
1.41
16.81
1.26
2.50
2.12
15.80
1.25
3.91
0.96
1.18
1.86
2.27
2.64
1.72
1.08
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
f1 (ppm)


140.095
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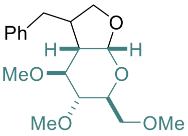
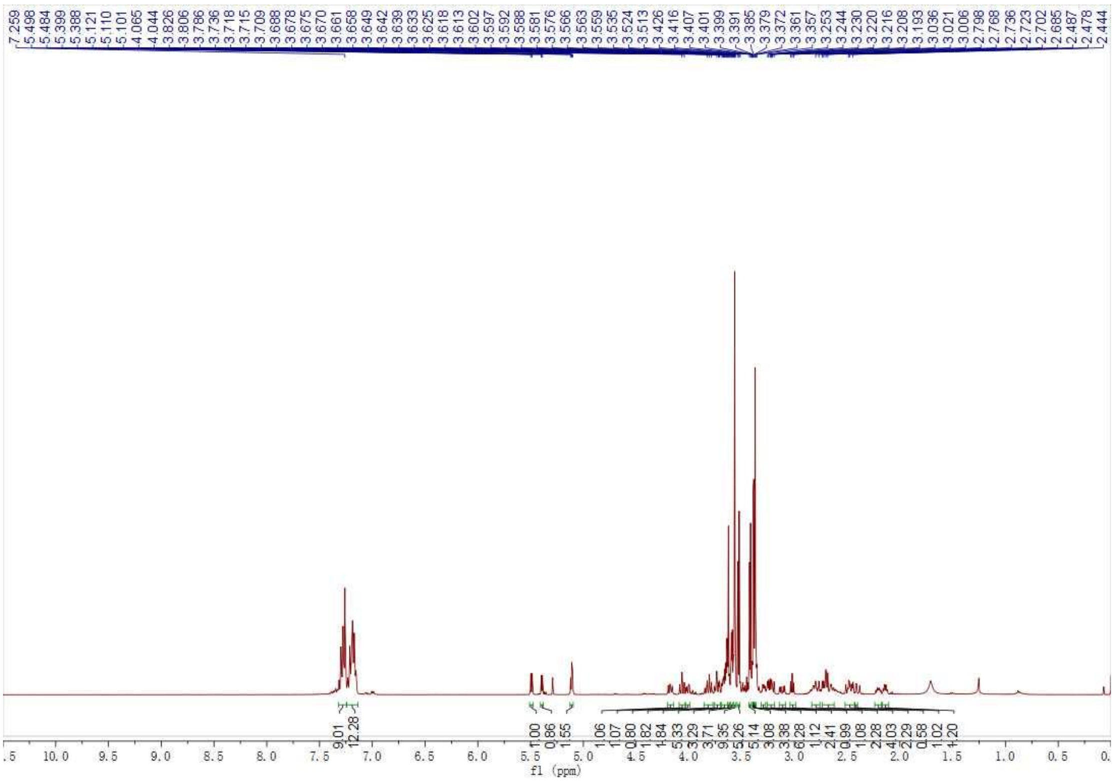
138.464
138.429
138.406
138.119
138.083
138.013
137.892
129.058
128.886
128.629
128.548
128.521
128.486
128.462
128.422
128.402
128.359
128.335
128.319
128.297
127.977
127.924
127.888
127.841
127.781
127.747
127.721
127.695
127.582
127.545
127.429
127.380
126.364
126.289
126.175
102.547
102.330
101.146
79.233
79.067
77.538
77.368
77.254
77.195
77.050
76.733
74.912
74.399
73.992
73.934
73.697
73.621
73.499
73.464
73.397
73.305
72.903
71.995
71.671
71.552
71.533
70.825
69.077
68.465
47.728
46.356
42.715
42.540
39.600
34.868
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

(22)


Ph
O
H
H
MeO
O
MeO
OMe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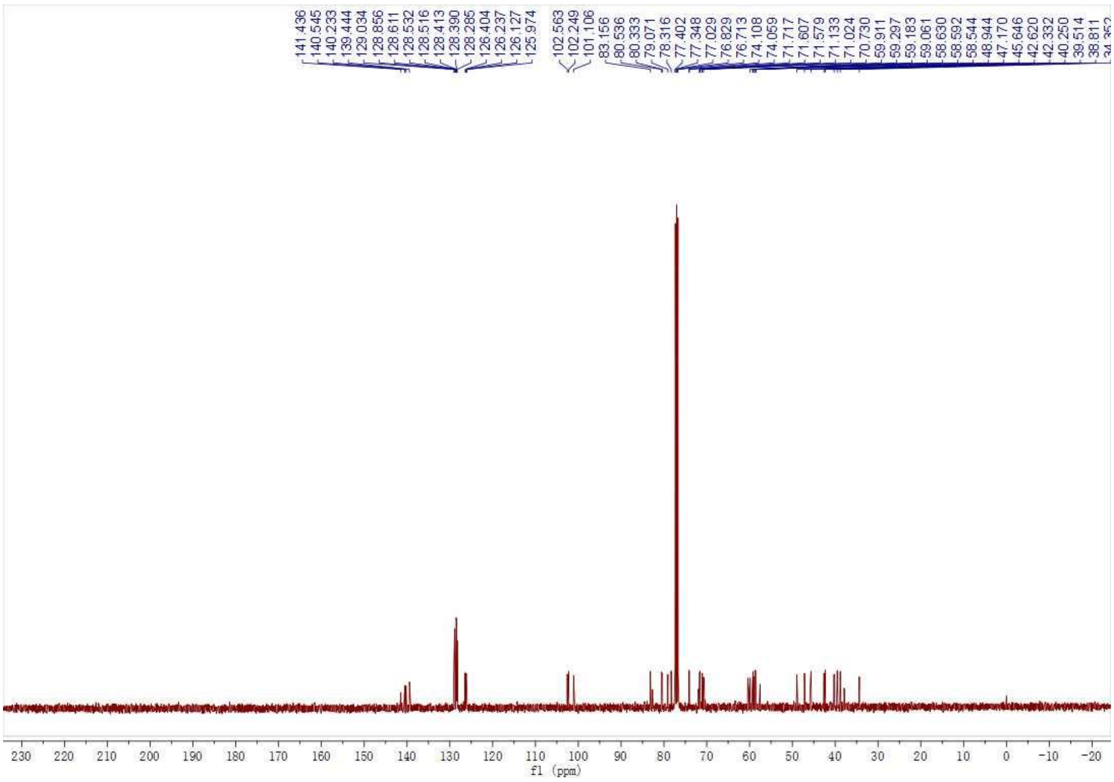
5.101
4.065
4.044
3.826
3.806
3.786
3.736
3.718
3.715
3.709
3.688
3.678
3.675
3.670
3.661
3.658
3.649
3.642
3.639
3.633
3.625
3.618
3.613
3.602
3.597
3.592
3.588
3.581
3.576
3.566
3.563
3.559
3.535
3.524
3.513
3.426
3.416
3.407
3.401
3.399
3.391
3.385
3.379
3.372
3.361
3.357
3.253
3.244
3.230
3.220
3.216
3.208
3.193
3.036
3.021
3.006
2.798
2.768
2.736
2.723
2.702
2.685
2.487
2.478
2.444
9.01
12.28
1.00
0.86
1.55
1.06
1.07
0.80
1.82
1.84
5.33
3.29
3.71
9.35
5.26
5.14
3.08
3.38
6.28
1.12
2.41
0.99
1.08
2.28
4.03
2.29
0.58
1.02
1.20
.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.
f1 (ppm)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140.233
139.444
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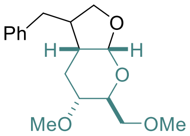
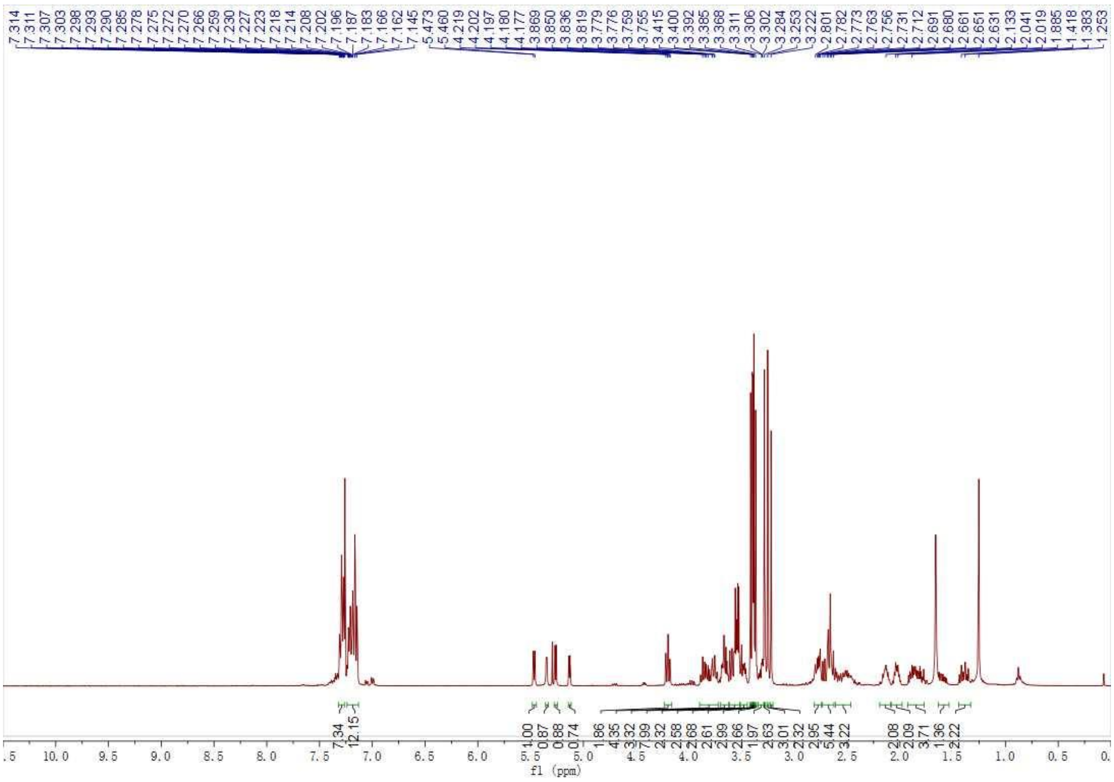
128.856
128.611
128.532
128.516
128.413
128.390
128.285
126.404
126.237
126.127
125.974
102.563
102.249
101.106
83.156
80.536
80.333
79.071
78.316
77.402
77.348
77.029
76.829
76.713
74.108
74.059
71.717
71.607
71.579
71.133
71.024
70.730
59.911
59.297
59.183
59.061
58.630
58.592
58.544
48.944
47.170
45.646
42.620
42.332
40.250
39.514
38.811
34.352
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)

(**23**)



Ph
O
H
H
O
MeO
OMe



7.314
7.311
7.307
7.303
7.298
7.293
7.290
7.285
7.278
7.275
7.272
7.270
7.266
7.259
7.230
7.227
7.223
7.218
7.214
7.208
7.202
7.196
7.187
7.183
7.166
7.162
7.145
5.473
5.460
4.219
4.202
4.197
4.180
4.177
3.869
3.850
3.836
3.819
3.779
3.776
3.759
3.755
3.415
3.400
3.392
3.385
3.368
3.311
3.306
3.302
3.284
3.253
3.222
2.801
2.782
2.773
2.763
2.756
2.731
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2.691
2.680
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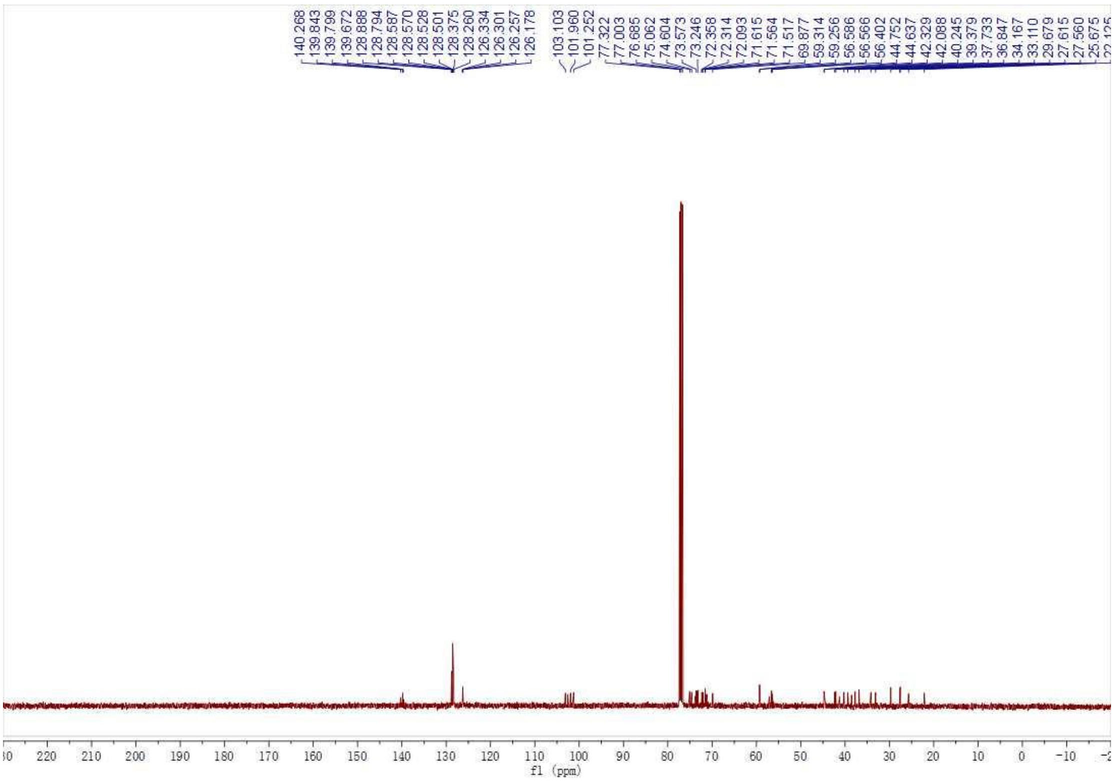
2.651
2.631
2.133
2.041
2.019
1.885
1.418
1.383
1.253
7.34
12.15
1.00
0.87
0.88
0.74
1.86
4.35
3.32
7.99
2.32
2.58
2.68
2.61
2.99
2.66
1.97
2.63
3.01
2.32
2.95
5.44
3.22
2.08
2.09
3.71
1.36
2.22
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)



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139.799
139.672
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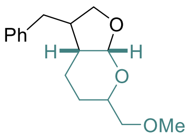
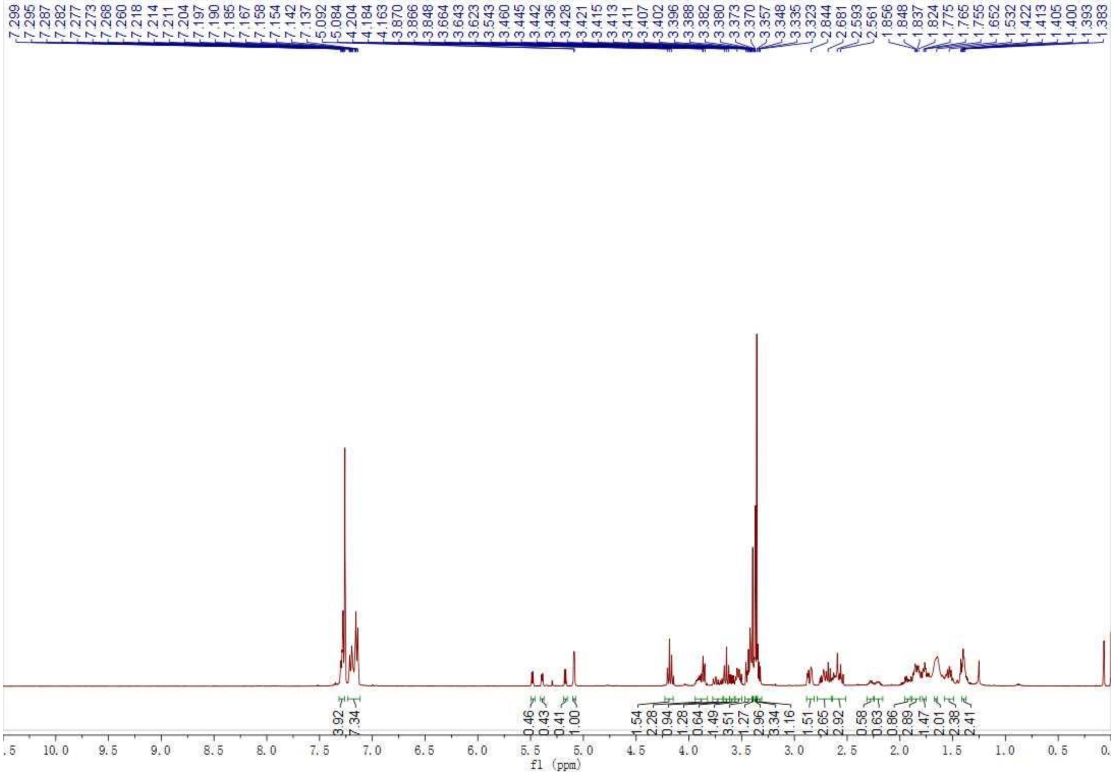
128.794
128.587
128.570
128.528
128.501
128.375
128.260
126.334
126.301
126.257
126.178
103.103
101.960
101.252
77.322
77.003
76.685
75.062
74.604
73.573
73.246
72.358
72.314
72.093
71.615
71.564
71.517
69.877
59.314
59.256
56.586
56.566
56.402
44.752
44.637
42.329
42.088
40.245
39.379
37.733
36.847
34.167
33.110
29.679
27.615
27.560
25.675
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

(**24**)



Ph
O
H
H
O
OMe



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7.295
7.287
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7.273
7.268
7.260
7.218
7.214
7.211
7.204
7.197
7.190
7.185
7.167
7.158
7.154
7.142
7.137
5.092
5.084
4.204
4.184
4.163
3.870
3.866
3.848
3.664
3.643
3.623
3.543
3.460
3.445
3.442
3.436
3.428
3.421
3.415
3.413
3.411
3.407
3.402
3.396
3.388
3.382
3.380
3.373
3.370
3.357
3.348
3.335
3.323
2.844
2.681
2.593
2.561
1.856
1.848
1.837
1.824
1.775
1.765
1.652
1.532
1.422
1.413
1.405
1.400
1.393
1.383
3.92
7.34
0.46
0.43
0.41
1.00
1.54
2.28
0.94
1.28
0.64
1.49
3.51
1.27
2.96
3.34
1.16
1.51
2.65
2.92
0.58
0.63
0.86
2.89
1.47
2.01
2.38
2.41
.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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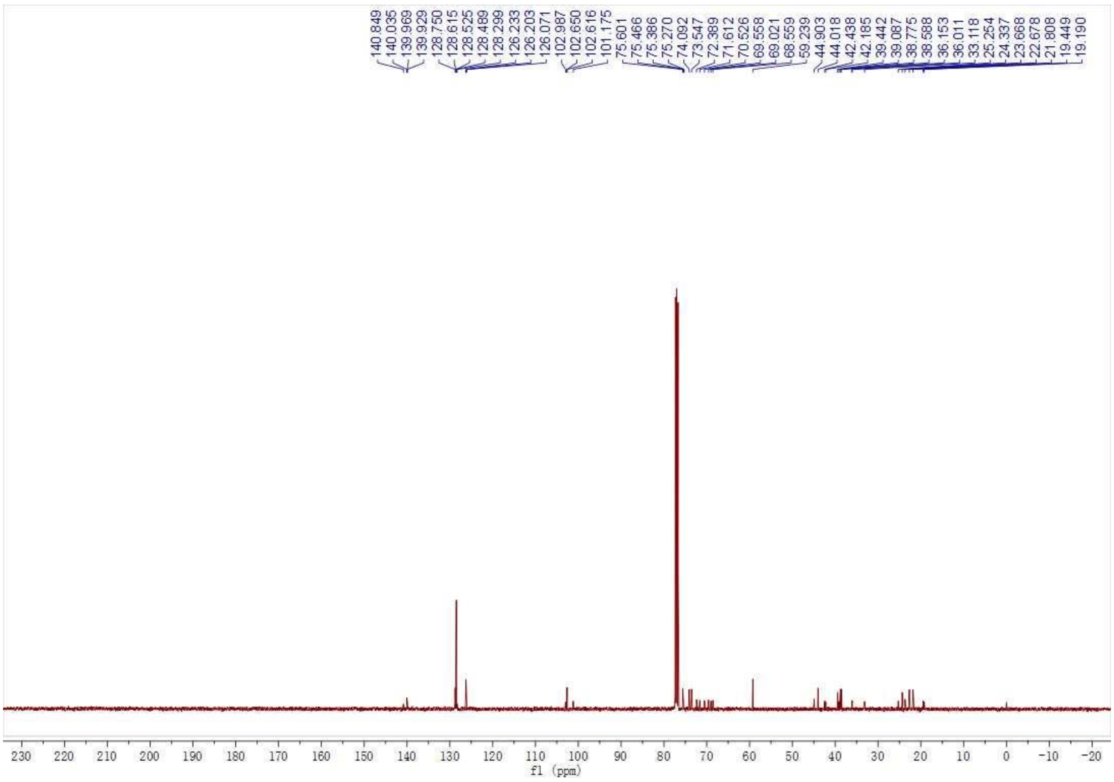
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)



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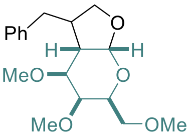
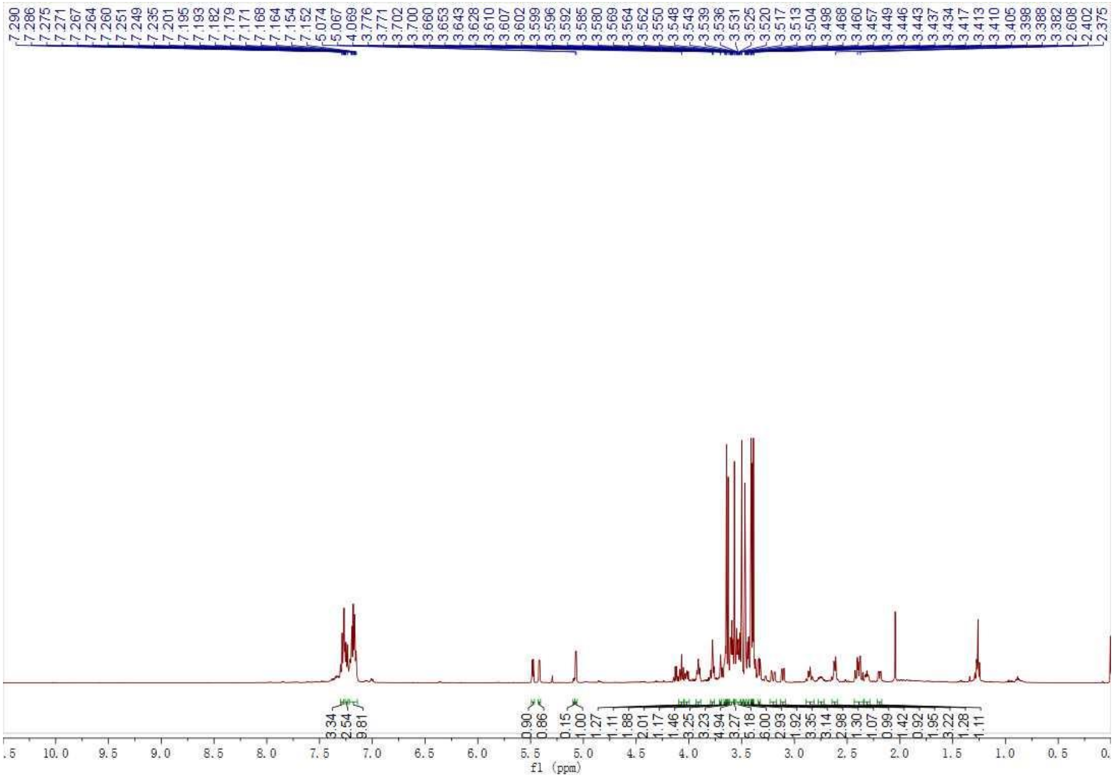
140.035
139.969
139.929
128.750
128.615
128.525
128.489
128.299
126.233
126.203
126.071
102.987
102.650
102.616
101.175
75.601
75.466
75.386
75.270
74.092
73.547
72.389
71.612
70.526
69.558
69.021
68.559
59.239
44.903
44.018
42.438
42.185
39.442
39.087
38.775
38.588
36.153
36.011
33.118
25.254
24.337
23.668
22.678
21.808
19.449
19.190
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
−20
f1 (ppm)

(**25**)


Ph
O
H
H
MeO
O
MeO
OMe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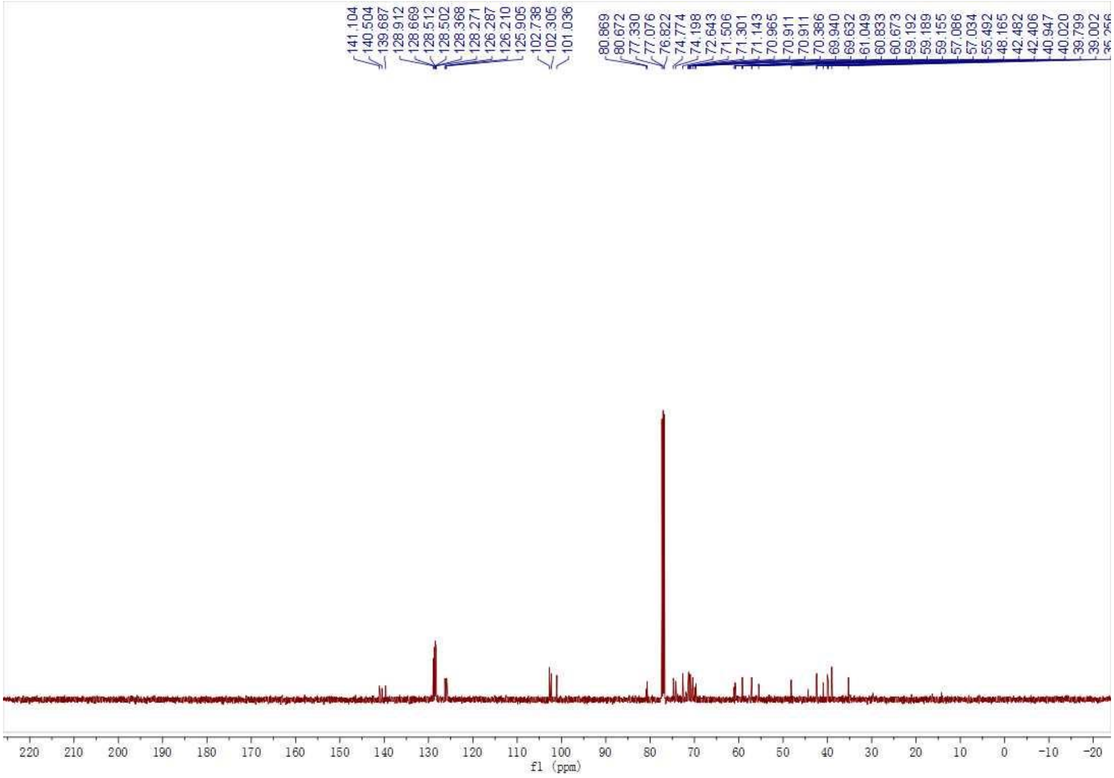
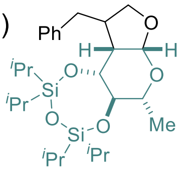
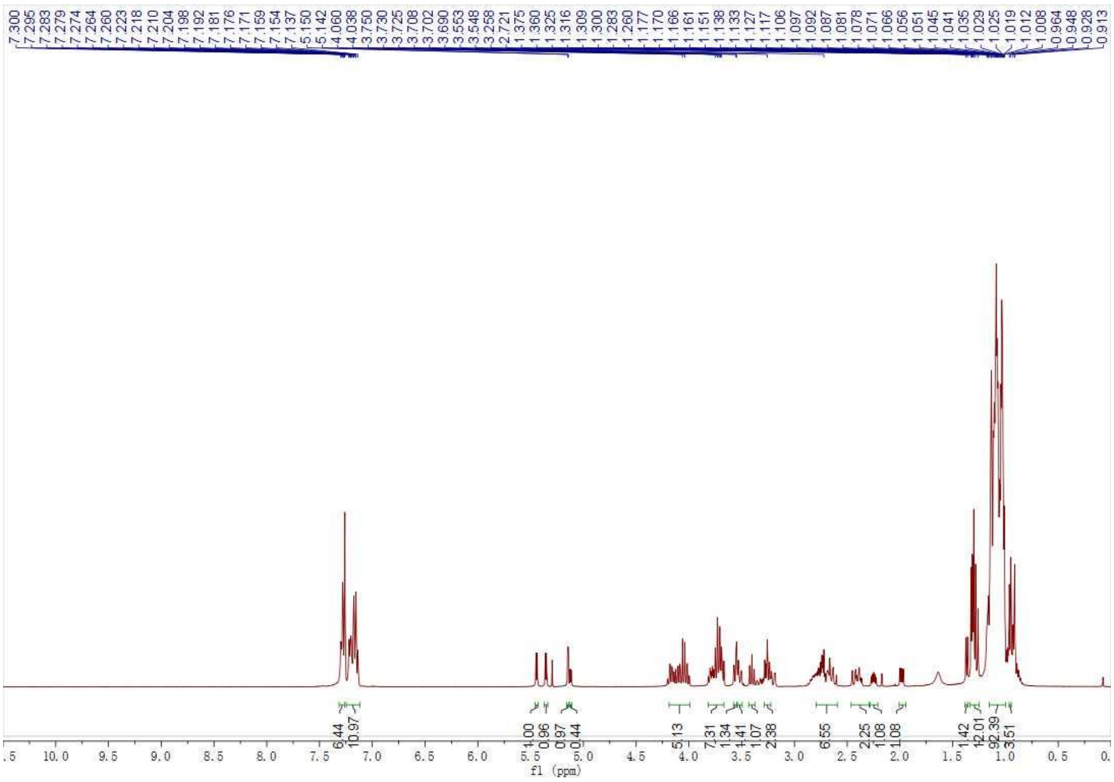
7.286
7.275
7.271
7.267
7.264
7.260
7.251
7.249
7.235
7.201
7.195
7.193
7.182
7.179
7.171
7.168
7.164
7.154
7.152
5.074
5.067
4.069
3.776
3.771
3.702
3.700
3.660
3.653
3.643
3.628
3.610
3.607
3.602
3.599
3.596
3.592
3.585
3.580
3.569
3.564
3.562
3.550
3.548
3.543
3.539
3.536
3.531
3.525
3.520
3.517
3.513
3.504
3.498
3.468
3.460
3.457
3.449
3.446
3.443
3.437
3.434
3.417
3.413
3.410
3.405
3.398
3.388
3.382
2.608
2.402
2.375
3.34
2.54
9.81
0.90
0.86
0.15
1.00
1.27
1.11
1.88
2.01
1.17
1.46
3.25
3.23
4.94
3.27
5.18
6.00
2.93
1.92
3.35
3.14
2.98
1.30
1.07
0.99
1.42
0.92
1.95
3.22
1.28
1.11
.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.
f1 (ppm)


141.104
140.504
139.687
128.912
128.669
128.512
128.502
128.368
128.271
126.287
126.210
125.905
102.738
102.305
101.036
80.869
80.672
77.330
77.076
76.822
74.774
74.198
72.643
71.506
71.301
71.143
70.965
70.911
70.911
70.386
69.940
69.632
61.049
60.833
60.673
59.192
59.189
59.155
57.086
57.034
55.492
48.165
42.482
42.406
40.947
40.020
39.799
39.002
35.25
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)

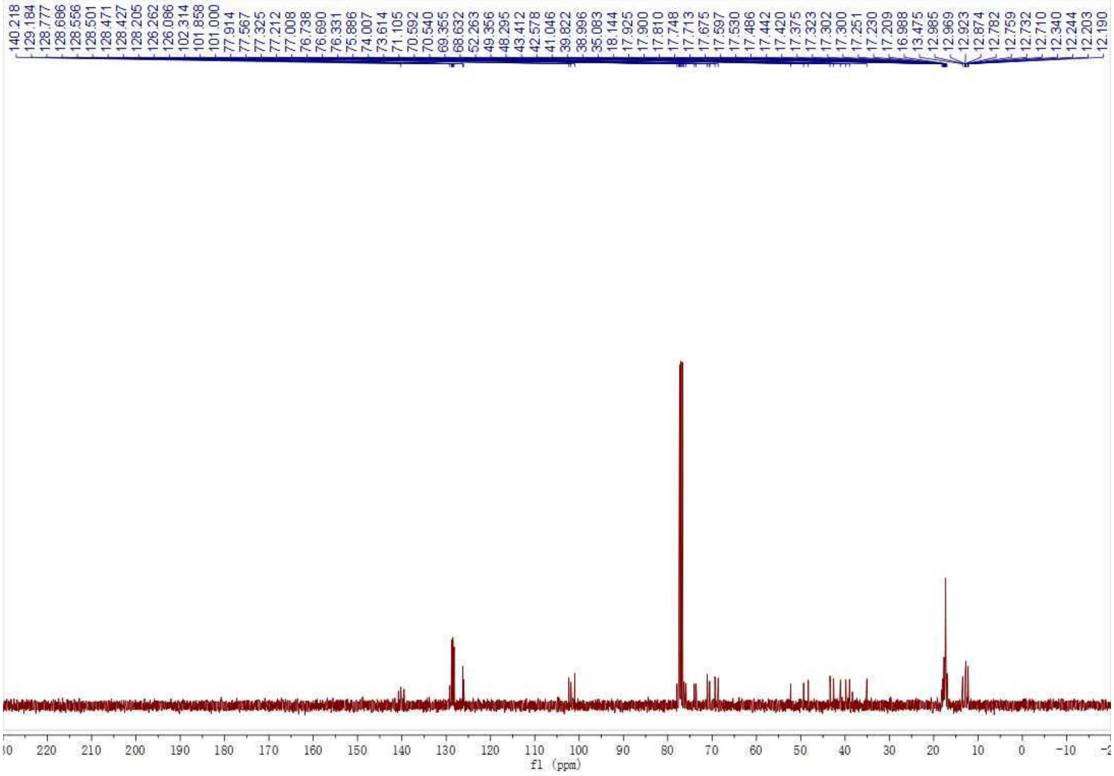
(**26**)



Ph
O
H
H
O
^{i}Pr
O
Si
^{i}Pr
O
Si
O
Me
^{i}Pr
^{i}Pr

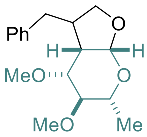


7.300
7.295
7.283
7.279
7.274
7.264
7.260
7.223
7.218
7.210
7.204
7.198
7.192
7.181
7.176
7.171
7.159
7.154
7.137
5.150
5.142
4.060
4.038
3.750
3.730
3.725
3.708
3.702
3.690
3.553
3.548
3.258
2.721
1.375
1.360
1.325
1.316
1.309
1.300
1.283
1.260
1.177
1.170
1.166
1.161
1.151
1.138
1.133
1.127
1.117
1.106
1.097
1.092
1.087
1.081
1.078
1.071
1.066
1.056
1.051
1.045
1.041
1.035
1.029
1.025
1.019
1.012
1.008
0.964
0.948
0.928
0.913
6.44
10.97
1.00
0.96
0.97
0.44
5.13
7.31
1.34
1.41
1.07
2.38
6.55
2.25
1.08
1.08
1.42
12.01
92.39
3.51
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
f1 (ppm)

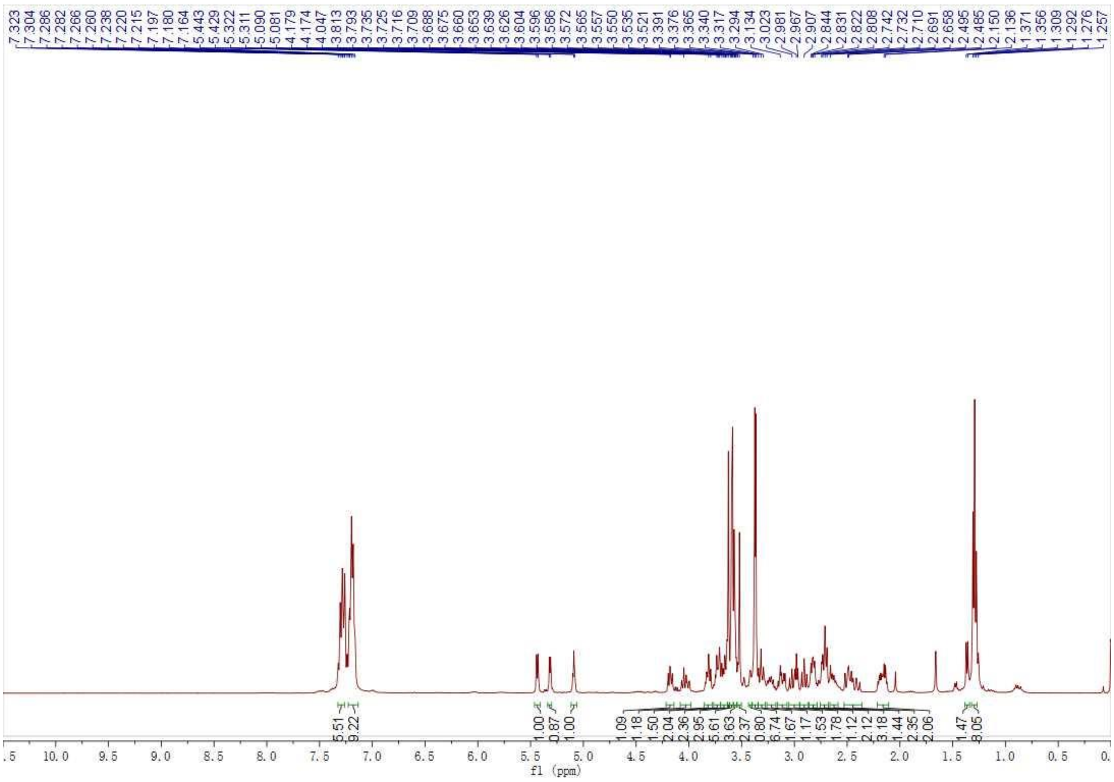


140.218
129.184
128.777
128.686
128.556
128.501
128.471
128.427
128.205
126.262
126.086
102.314
101.858
101.000
77.914
77.567
77.325
77.212
77.008
76.738
76.690
76.331
75.886
74.007
73.614
71.105
70.592
70.540
69.355
68.632
52.263
49.356
48.295
43.412
42.578
41.046
39.822
38.996
35.083
18.144
17.925
17.900
17.810
17.748
17.713
17.675
17.597
17.530
17.486
17.442
17.420
17.375
17.323
17.302
17.300
17.251
17.230
17.209
16.988
13.475
12.985
12.969
12.923
12.874
12.782
12.759
12.732
12.710
12.340
12.244
12.203
12.190
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

(**27**)



Ph
O
H
H
MeO
O
MeO
Me



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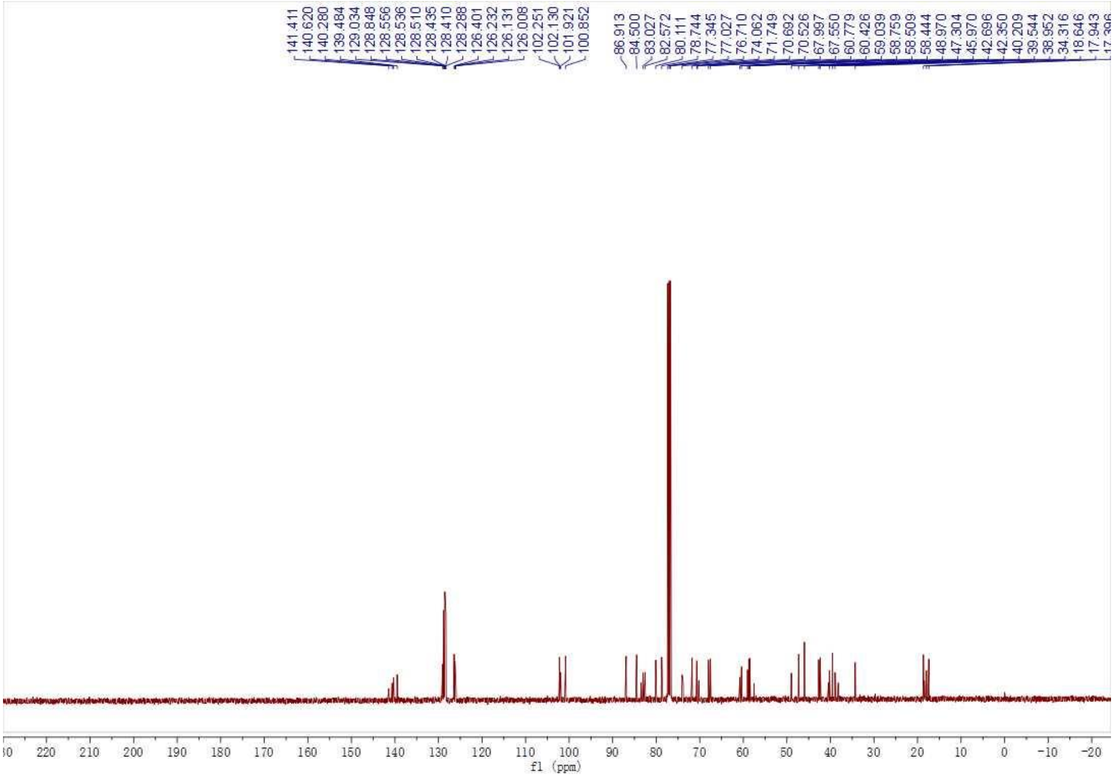
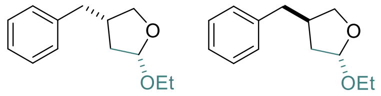
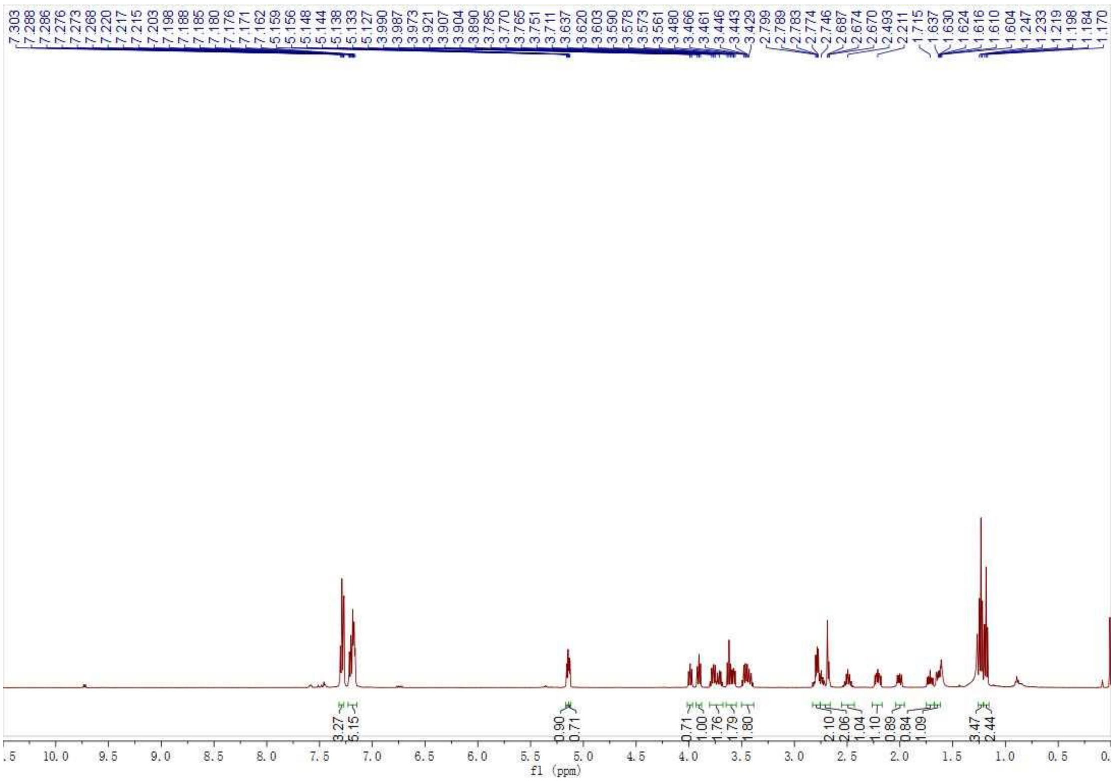
7.260
7.238
7.220
7.215
7.197
7.180
7.164
5.443
5.429
5.322
5.311
5.090
5.081
4.179
4.174
4.047
3.813
3.793
3.735
3.725
3.716
3.709
3.688
3.675
3.660
3.653
3.639
3.626
3.604
3.596
3.586
3.572
3.565
3.557
3.550
3.535
3.521
3.391
3.376
3.365
3.340
3.317
3.294
3.134
3.023
2.981
2.967
2.907
2.844
2.831
2.822
2.808
2.742
2.732
2.710
2.691
2.658
2.495
2.485
2.150
2.136
1.371
1.356
1.309
1.292
1.276
1.257
5.51
9.22
1.00
0.87
1.00
1.09
1.18
1.50
2.04
2.36
2.95
5.61
3.63
2.37
0.80
6.74
1.67
1.17
1.53
1.78
1.12
2.12
3.18
1.44
2.35
2.06
1.47
8.05
.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.
f1 (ppm)



141.411
140.620
140.280
139.484
129.034
128.848
128.556
128.536
128.510
128.435
128.410
128.288
126.401
126.232
126.131
126.008
102.251
102.130
101.921
100.852
86.913
84.500
83.027
82.572
80.111
78.744
77.345
77.027
76.710
74.062
71.749
70.692
70.526
67.997
67.550
60.779
60.426
59.039
58.759
58.509
58.444
48.970
47.304
45.970
42.696
42.350
40.209
39.544
38.952
34.316
18.646
17.943
17.39
0
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)

(28)


O
OEt
O
OEt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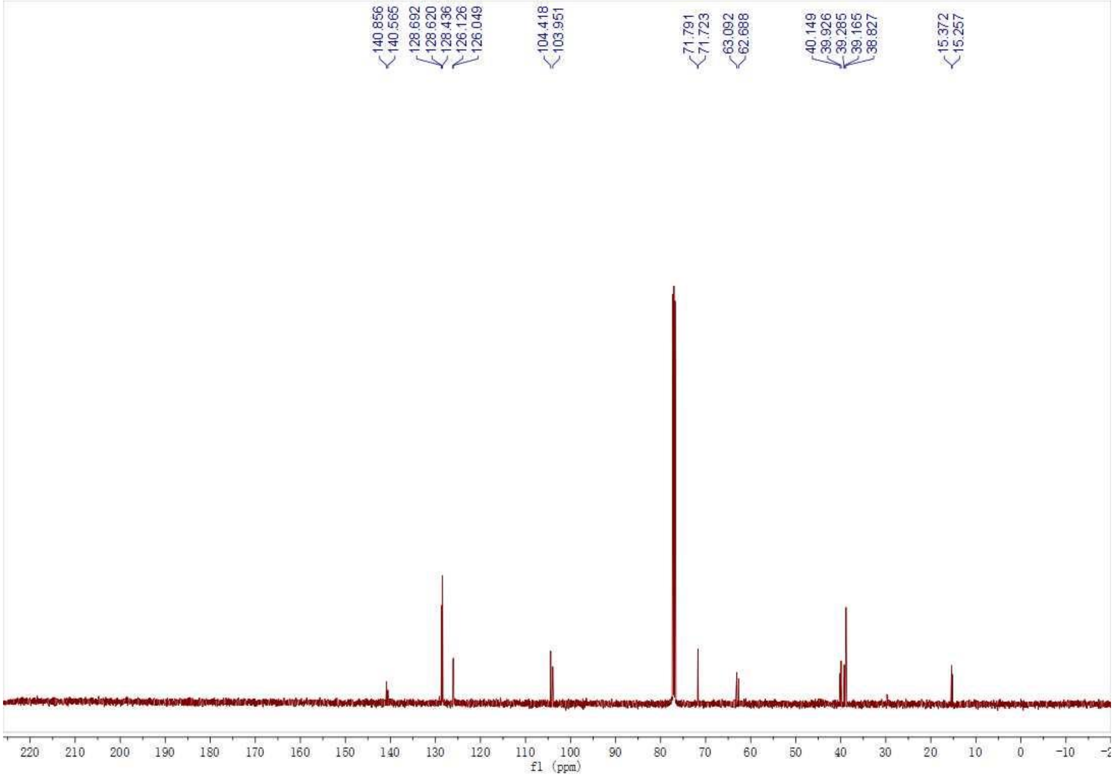
7.217
7.215
7.203
7.198
7.188
7.185
7.180
7.176
7.171
7.162
5.159
5.156
5.148
5.144
5.138
5.133
5.127
3.990
3.987
3.973
3.921
3.907
3.904
3.890
3.785
3.770
3.765
3.751
3.711
3.637
3.620
3.603
3.590
3.578
3.573
3.561
3.480
3.466
3.461
3.446
3.443
3.429
2.799
2.789
2.783
2.774
2.746
2.687
2.674
2.670
2.493
2.211
1.715
1.637
1.630
1.624
1.616
1.610
1.604
1.247
1.233
1.219
1.198
1.184
1.170
3.27
5.15
0.90
0.71
0.71
1.00
1.76
1.79
1.80
2.10
2.06
1.04
1.10
0.89
0.84
1.09
3.47
2.44
.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.
f1 (ppm)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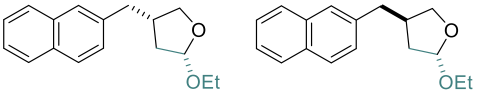
126.049
104.418
103.951
71.791
71.723
63.092
62.688
40.149
39.926
39.285
39.165
38.827
15.372
15.257
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-2
f1 (ppm)

(29)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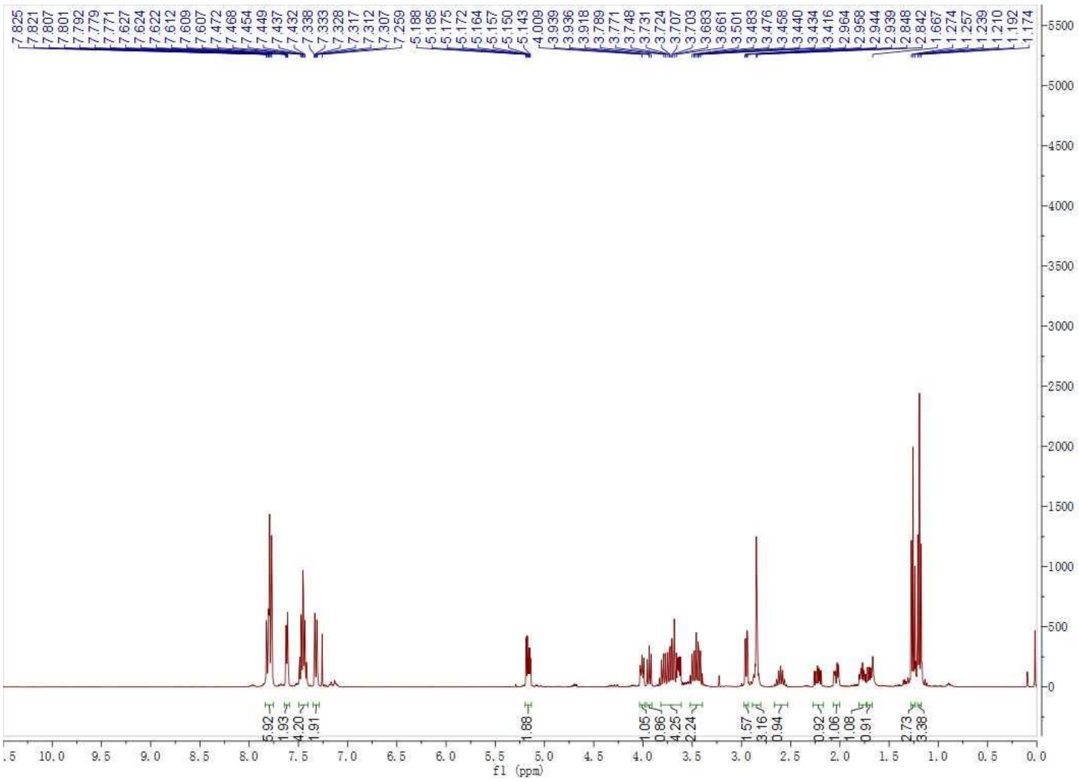
OEt
O
OEt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7.622
7.612
7.609
7.607
7.472
7.468
7.454
7.449
7.437
7.432
7.338
7.333
7.328
7.317
7.312
7.307
7.259
5.188
5.185
5.175
5.172
5.164
5.157
5.150
5.143
4.009
3.939
3.936
3.918
3.789
3.771
3.748
3.731
3.724
3.707
3.703
3.683
3.661
3.501
3.483
3.476
3.458
3.440
3.434
3.416
2.964
2.958
2.944
2.939
2.848
2.842
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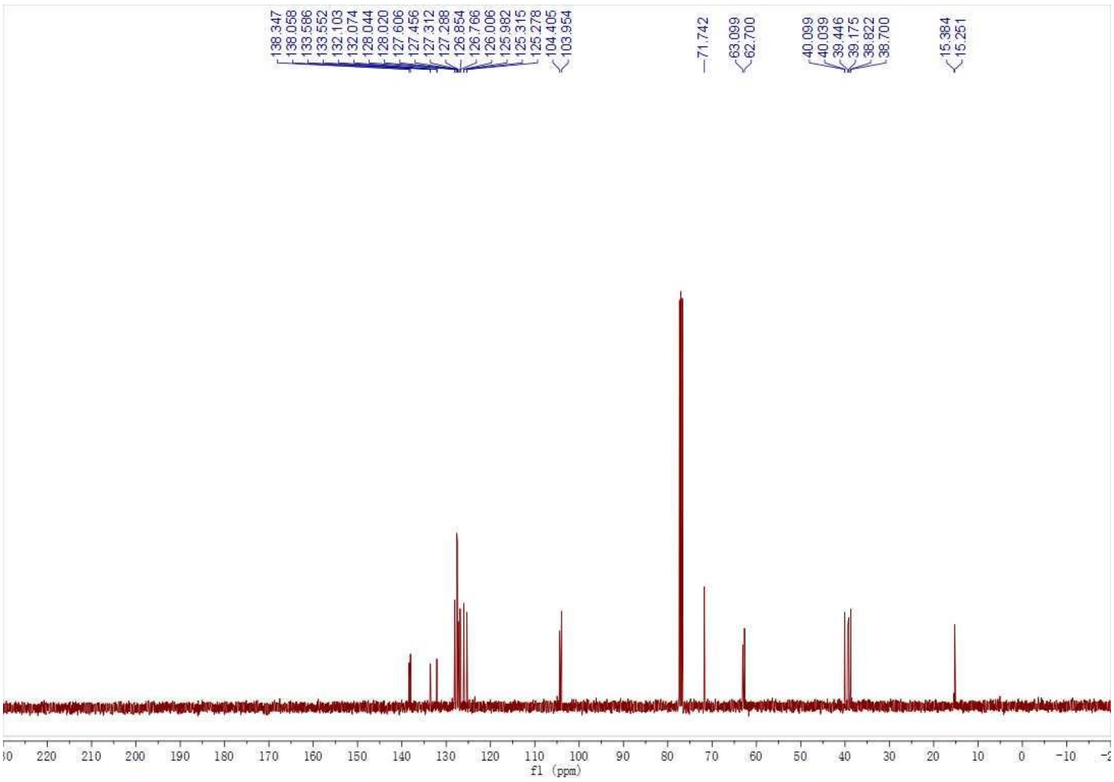
1.257
1.239
1.210
1.192
1.174
5.92
1.93
4.20
1.91
1.88
1.05
0.86
4.25
2.24
1.57
3.16
0.94
0.92
1.06
1.08
0.91
2.73
3.38
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


138.347
138.058
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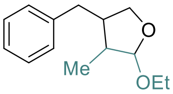
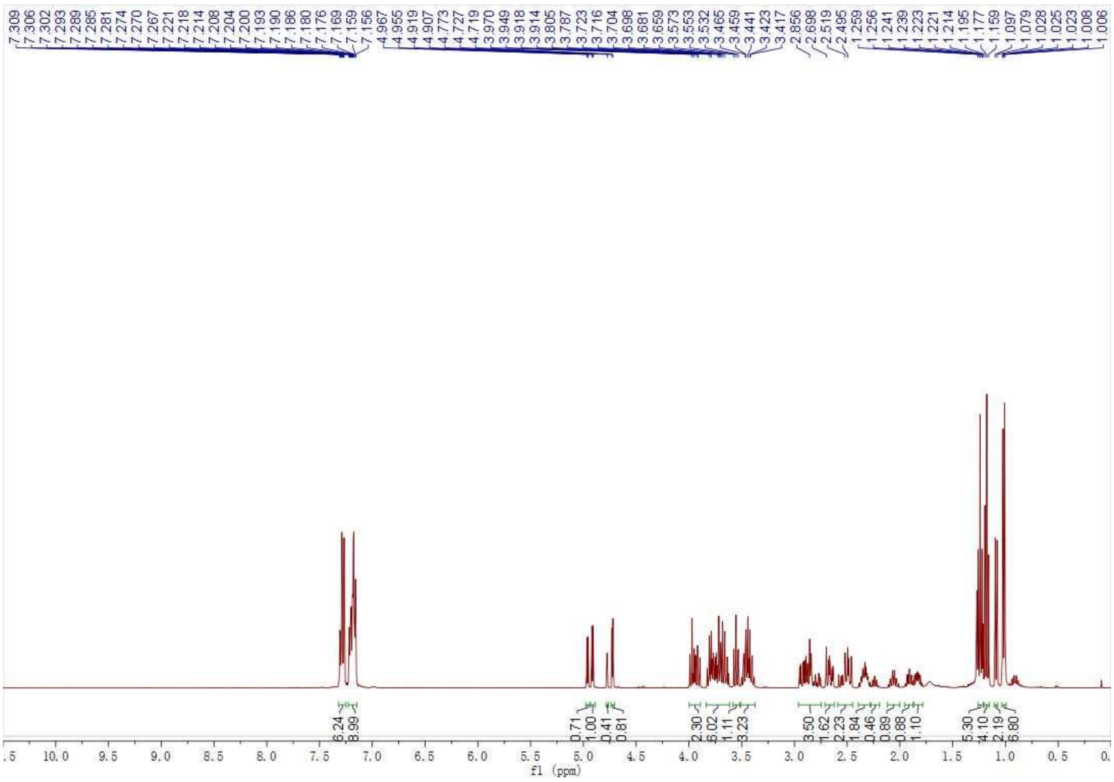
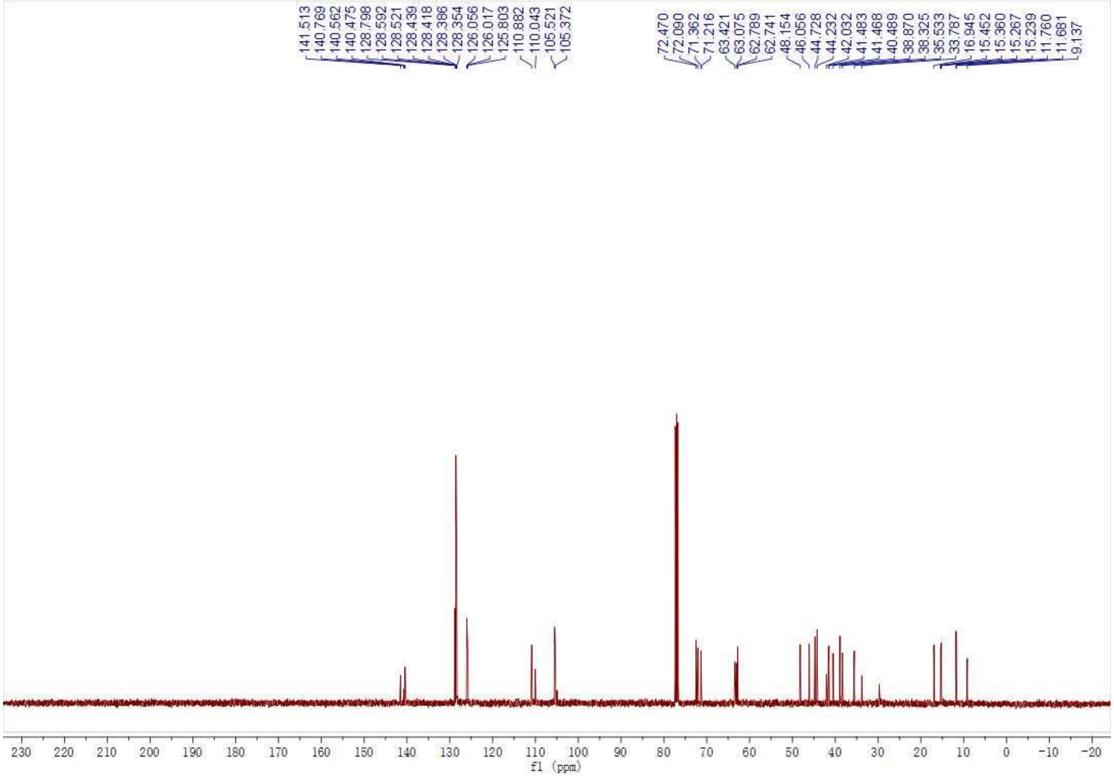
133.552
132.103
132.074
128.044
128.020
127.606
127.456
127.312
127.288
126.854
126.766
126.006
125.982
125.315
125.278
104.405
103.954
71.742
63.099
62.700
40.099
40.039
39.446
39.175
38.822
38.700
15.384
15.251
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

(30)


O
Me
OEt


7.309
7.306
7.302
7.293
7.289
7.285
7.281
7.274
7.270
7.267
7.221
7.218
7.214
7.208
7.204
7.200
7.193
7.190
7.186
7.180
7.176
7.169
7.159
7.156
4.967
4.955
4.919
4.907
4.773
4.727
4.719
3.970
3.949
3.918
3.914
3.805
3.787
3.723
3.716
3.704
3.698
3.681
3.659
3.573
3.553
3.532
3.465
3.459
3.441
3.423
3.417
2.856
2.698
2.519
2.495
1.259
1.256
1.241
1.239
1.223
1.221
1.214
1.195
1.177
1.159
1.097
1.079
1.028
1.025
1.023
1.008
1.006
6.24
8.99
0.71
1.00
0.41
0.81
2.30
6.02
1.11
3.23
3.50
1.62
2.23
1.84
0.46
0.89
0.88
1.10
5.30
4.10
2.19
6.80
.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.
f1 (ppm)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140.562
140.475
128.798
128.592
128.521
128.439
128.418
128.386
128.354
126.056
126.017
125.803
110.882
110.043
105.521
105.372
72.470
72.090
71.362
71.216
63.421
63.075
62.789
62.741
48.154
46.056
44.728
44.232
42.032
41.483
41.468
40.489
38.870
38.325
35.533
33.787
16.945
15.452
15.360
15.267
15.239
11.760
11.681
9.137
230
220
210
200
190
180
170
160
150
140
130
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80
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50
40
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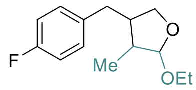
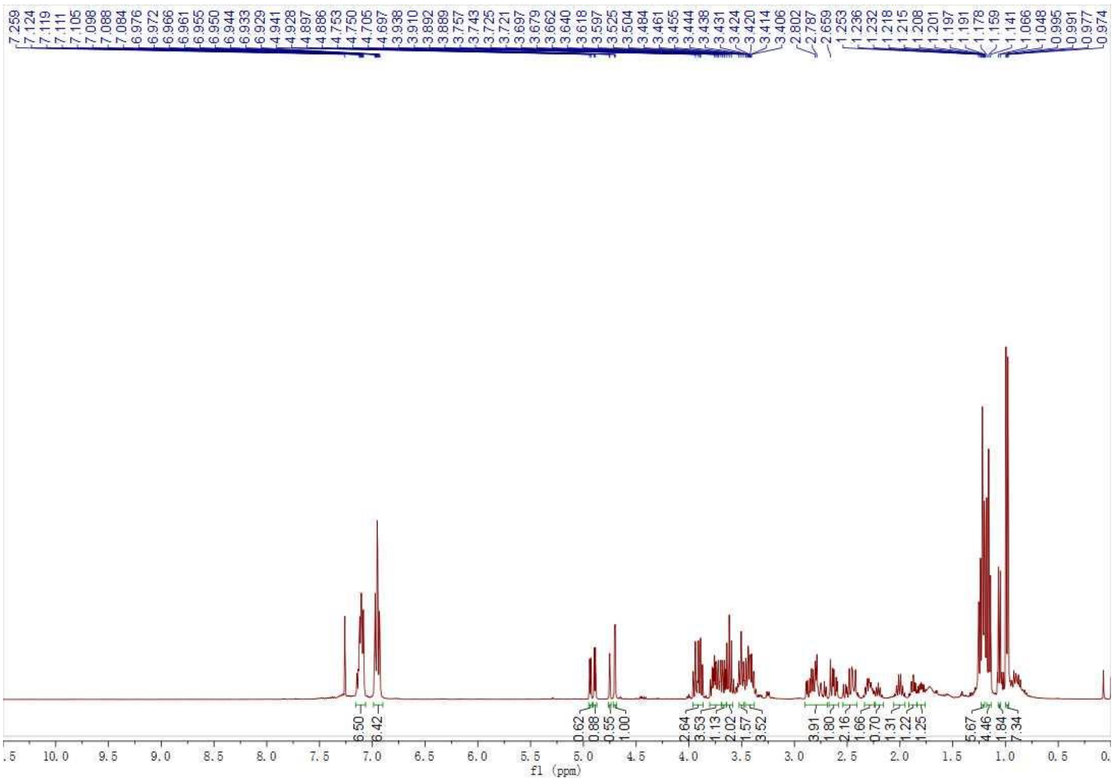
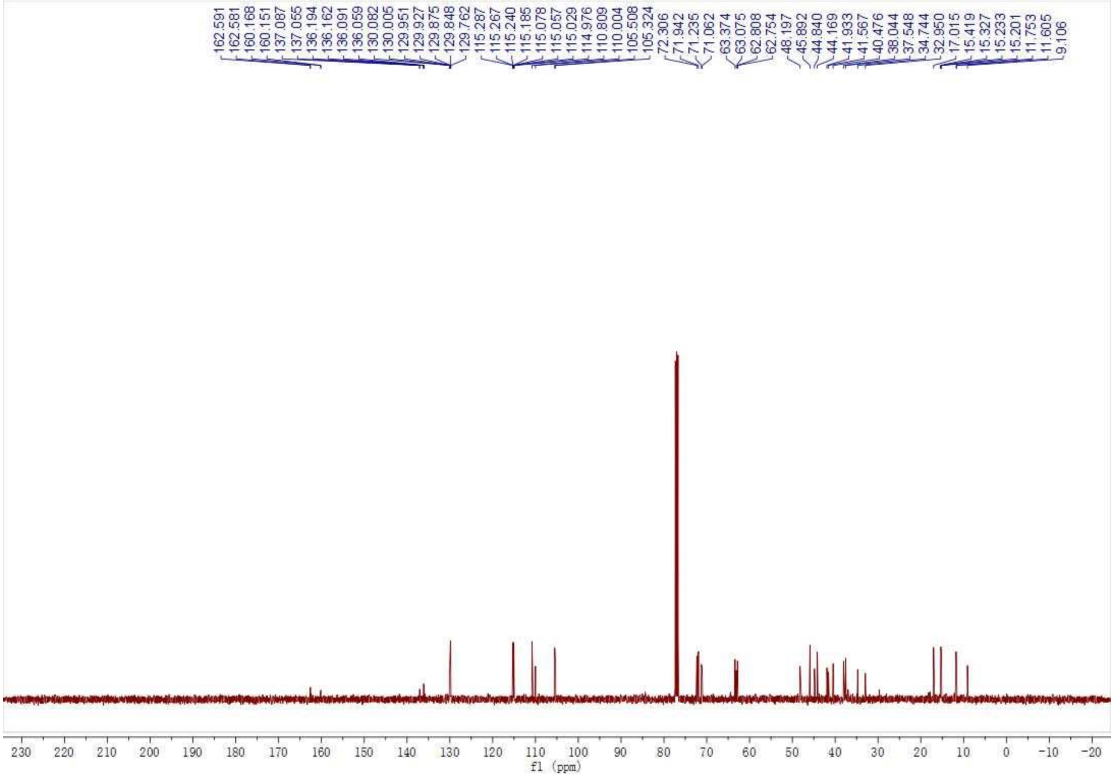
20
10
0
-10
-20
f1 (ppm)

(31)


F
Me
O
OEt


7.259
7.124
7.119
7.111
7.105
7.098
7.088
7.084
6.976
6.972
6.966
6.961
6.955
6.950
6.944
6.933
6.929
4.941
4.928
4.897
4.886
4.753
4.750
4.705
4.697
3.938
3.910
3.892
3.889
3.757
3.743
3.725
3.721
3.697
3.679
3.662
3.640
3.618
3.597
3.525
3.504
3.484
3.461
3.455
3.444
3.438
3.431
3.424
3.420
3.414
3.406
2.802
2.787
2.659
1.253
1.236
1.232
1.218
1.215
1.208
1.201
1.197
1.191
1.178
1.159
1.141
1.066
1.048
0.995
0.991
0.977
0.974
6.50
6.42
0.62
0.88
0.55
1.00
2.64
3.53
1.13
2.02
1.57
3.52
3.91
1.80
2.16
1.66
0.70
1.31
1.22
1.25
5.67
4.46
1.84
7.34
.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.
f1 (ppm)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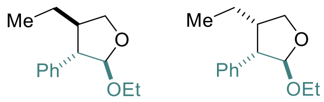
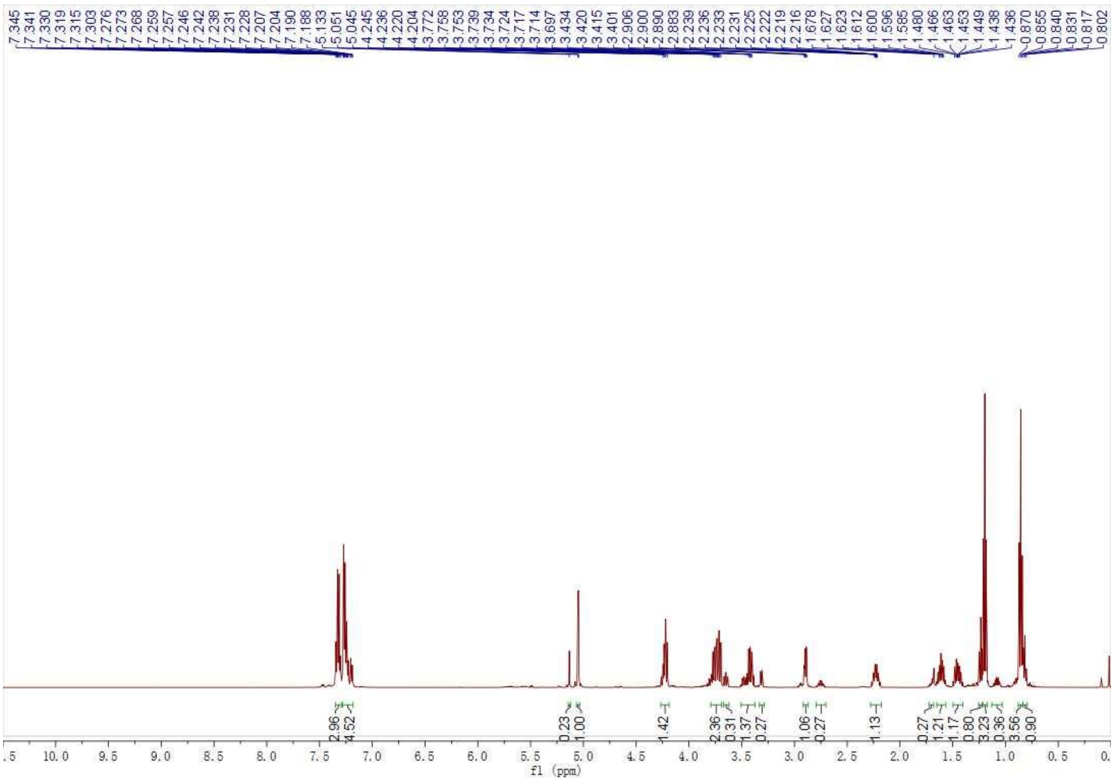
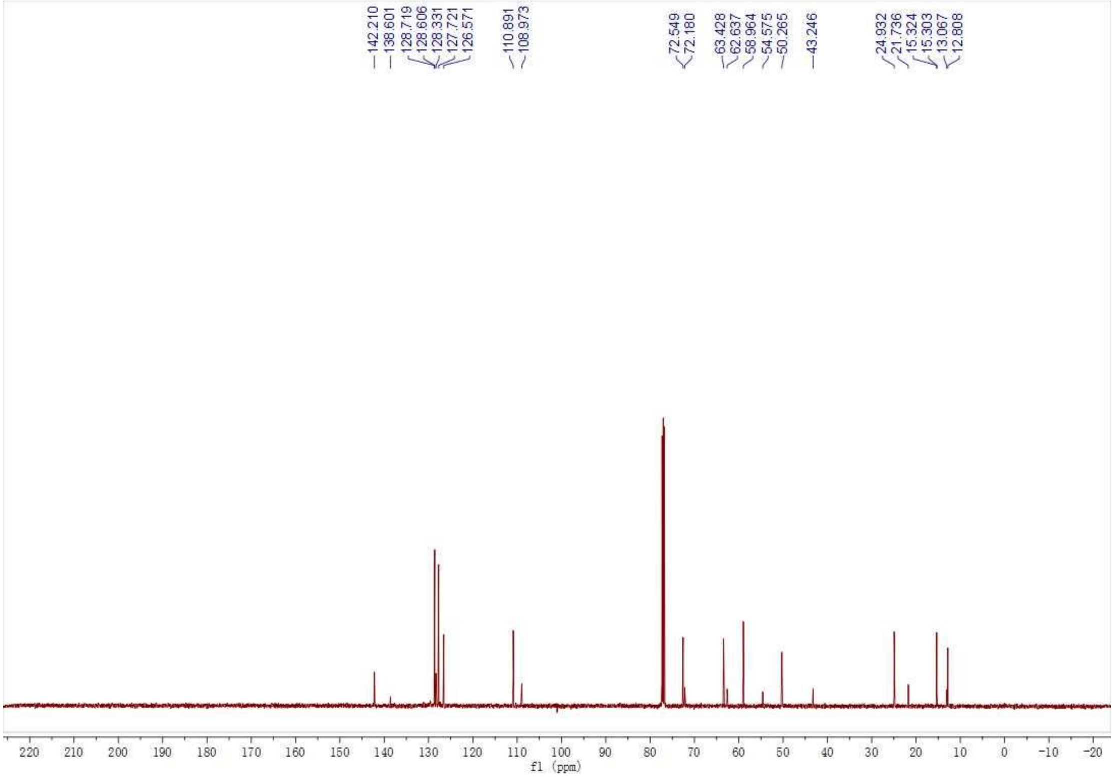
162.581
160.168
160.151
137.087
137.055
136.194
136.162
136.091
136.059
130.082
130.005
129.951
129.927
129.875
129.848
129.762
115.287
115.240
115.185
115.078
115.057
115.029
114.976
110.809
110.004
105.508
105.324
72.306
71.942
71.235
71.062
63.374
63.075
62.808
62.754
48.197
45.892
44.840
44.169
41.933
41.567
40.476
38.044
37.548
34.744
32.950
17.015
15.419
15.327
15.233
15.201
11.753
11.605
9.106
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)

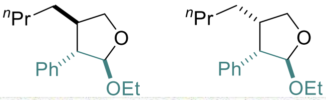
(32)


Me
O
Ph
OEt
Me
O
Ph
OEt

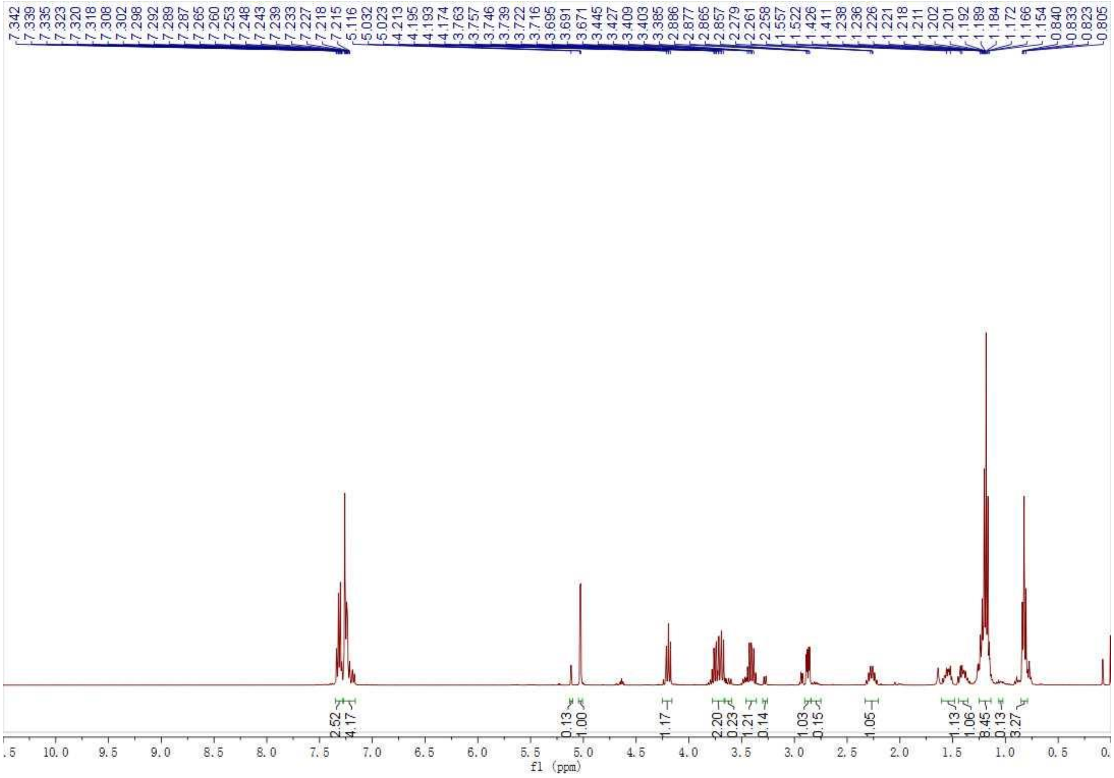

7.345
7.341
7.330
7.319
7.315
7.303
7.276
7.273
7.268
7.259
7.257
7.246
7.242
7.238
7.231
7.228
7.207
7.204
7.190
7.188
5.133
5.051
5.045
4.245
4.236
4.220
4.204
3.772
3.758
3.753
3.739
3.734
3.724
3.717
3.714
3.697
3.434
3.420
3.415
3.401
2.906
2.900
2.890
2.883
2.239
2.236
2.233
2.231
2.225
2.222
2.219
2.216
1.678
1.627
1.623
1.612
1.600
1.596
1.585
1.480
1.466
1.463
1.453
1.449
1.438
1.436
0.870
0.855
0.840
0.831
0.817
0.802
2.96
4.52
0.23
1.00
1.42
2.36
0.31
1.37
0.27
1.06
0.27
1.13
0.27
1.21
1.17
0.80
3.23
0.36
3.56
0.90
.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.
f1 (ppm)


142.210
138.601
128.719
128.606
128.331
127.721
126.571
110.891
108.973
72.549
72.180
63.428
62.637
58.964
54.575
50.265
43.246
24.932
21.736
15.324
15.303
13.067
12.808
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)

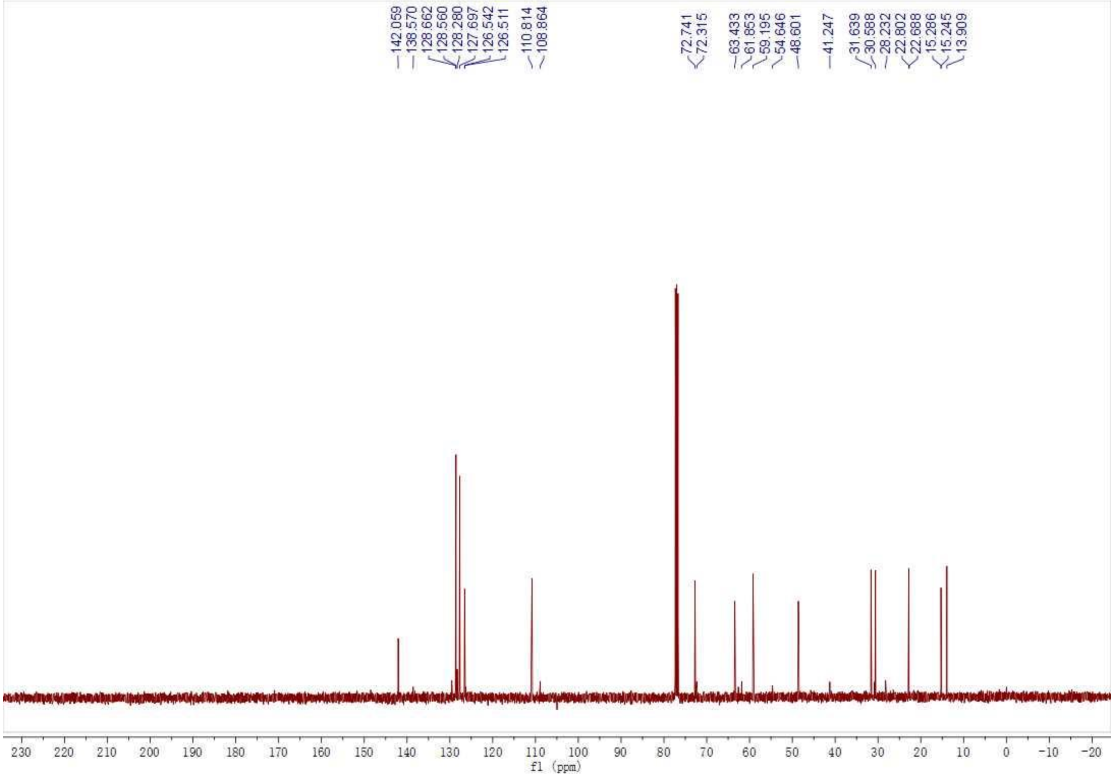
(33)



^{n}Pr
Ph
O
OEt
^{n}Pr
Ph
O
OEt

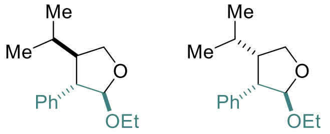


7.342
7.339
7.335
7.323
7.320
7.318
7.308
7.302
7.298
7.292
7.289
7.287
7.265
7.260
7.253
7.248
7.243
7.239
7.233
7.227
7.218
7.215
5.116
5.032
5.023
4.213
4.195
4.193
4.174
3.763
3.757
3.746
3.739
3.722
3.716
3.695
3.691
3.671
3.445
3.427
3.409
3.403
3.385
2.886
2.877
2.865
2.857
2.279
2.261
2.258
1.557
1.522
1.426
1.411
1.238
1.236
1.226
1.221
1.218
1.211
1.202
1.201
1.192
1.189
1.184
1.172
1.166
1.154
0.840
0.833
0.823
0.805
2.52
4.17
0.13
1.00
1.17
2.20
0.23
1.21
0.14
1.03
0.15
1.05
1.13
1.06
8.45
0.13
3.27
.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.
f1 (ppm)

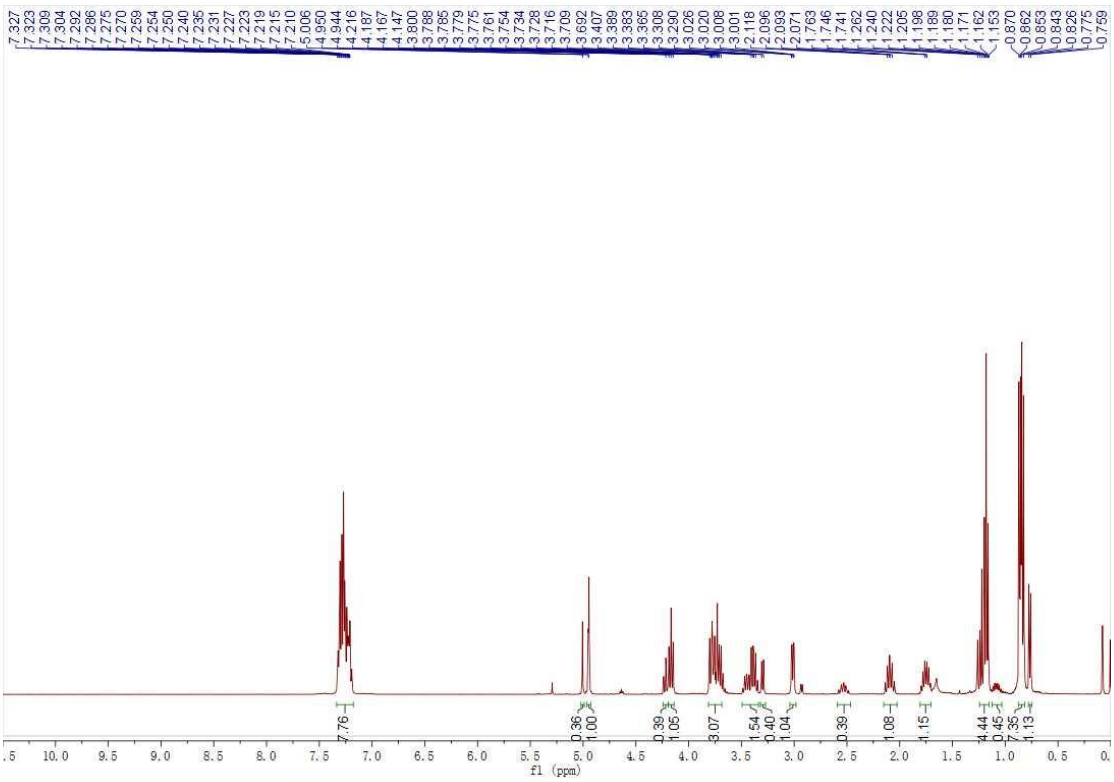


142.059
138.570
128.662
128.560
128.280
127.697
126.542
126.511
110.814
108.864
72.741
72.315
63.433
61.853
59.195
54.646
48.601
41.247
31.639
30.588
28.232
22.802
22.688
15.286
15.245
13.909
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)

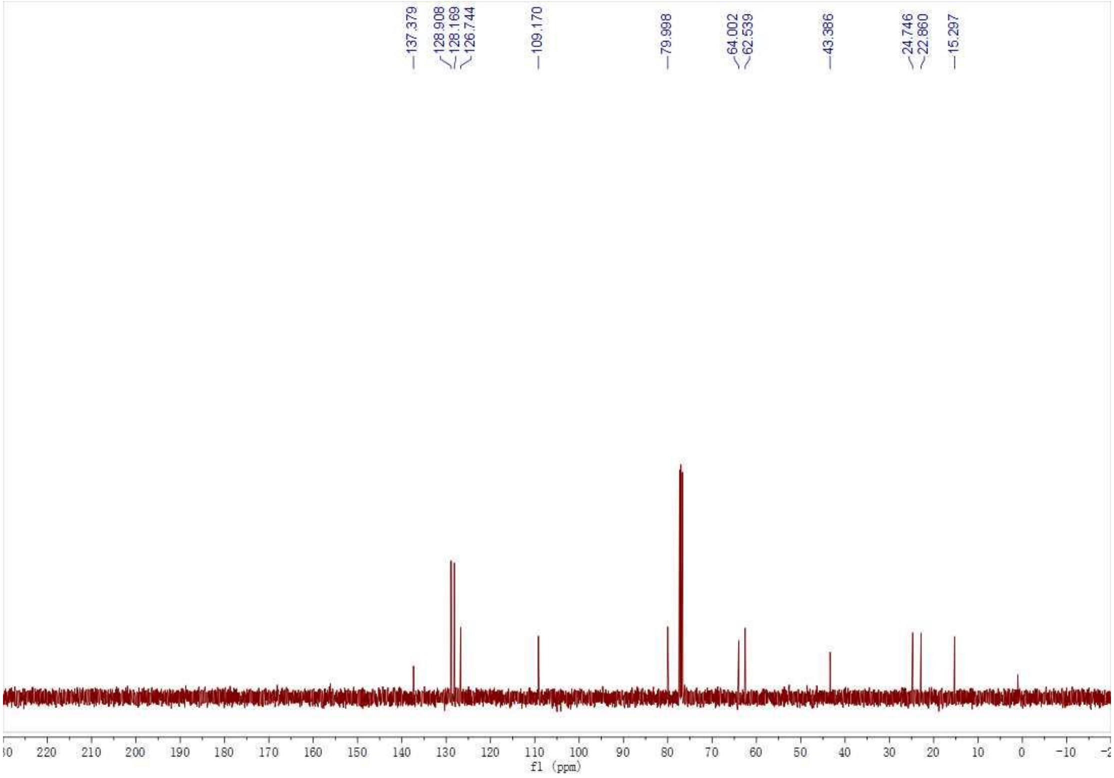
(**34**)



Me
Me
O
Ph
OEt
Me
Me
O
Ph
OEt

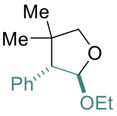


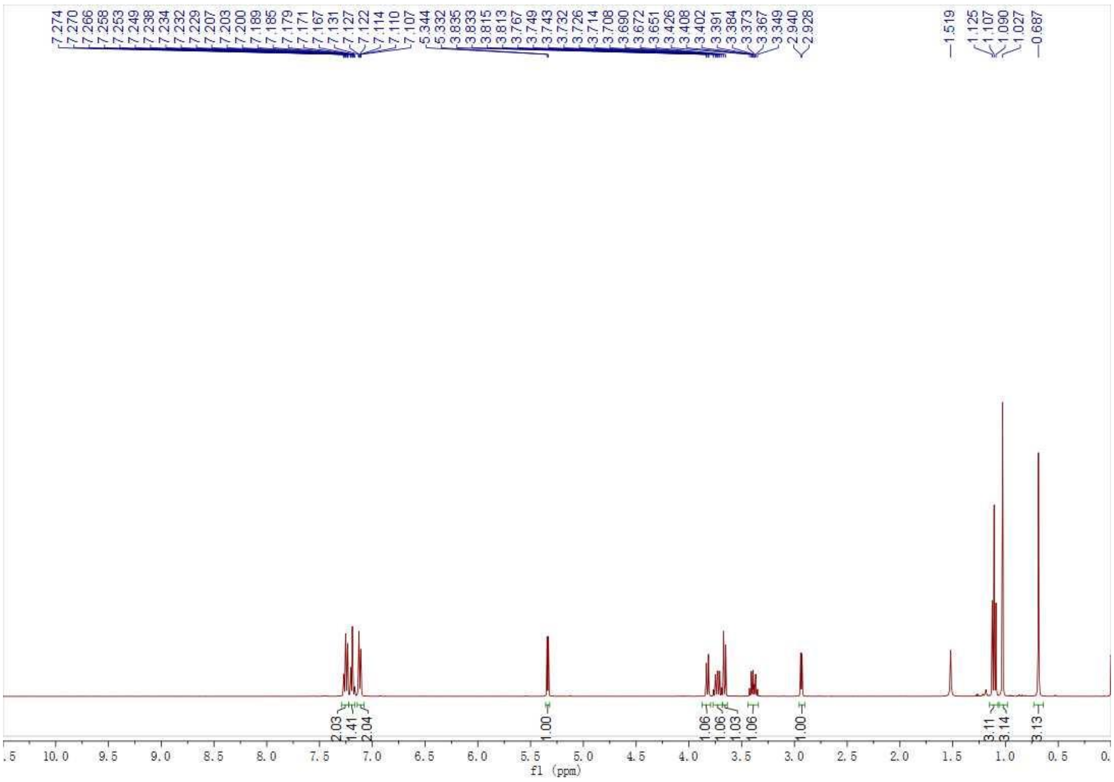
7.327
7.323
7.309
7.304
7.292
7.286
7.275
7.270
7.259
7.254
7.250
7.240
7.235
7.231
7.227
7.223
7.219
7.215
7.210
5.006
4.950
4.944
4.216
4.187
4.167
4.147
3.800
3.788
3.785
3.779
3.775
3.761
3.754
3.734
3.728
3.716
3.709
3.692
3.407
3.389
3.383
3.365
3.308
3.290
3.026
3.020
3.008
3.001
2.118
2.096
2.093
2.071
1.763
1.746
1.741
1.262
1.240
1.222
1.205
1.198
1.189
1.180
1.171
1.162
1.153
0.870
0.862
0.853
0.843
0.826
0.775
0.759
7.76
0.36
1.00
0.39
1.05
3.07
1.54
0.40
1.04
0.39
1.08
1.15
4.44
0.45
7.35
1.13
.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.
f1 (ppm)

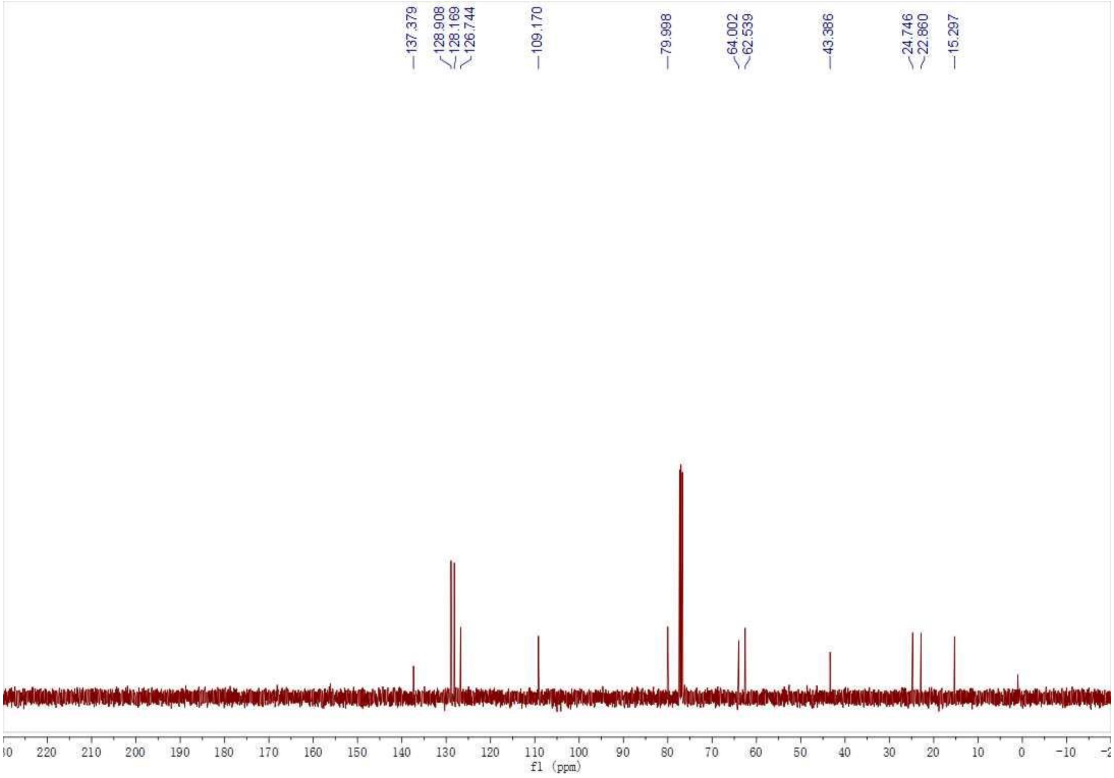


137.379
128.908
128.169
126.744
109.170
79.998
64.002
62.539
43.386
24.746
22.860
15.297
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-2
f1 (ppm)

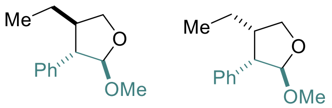
(**35**)

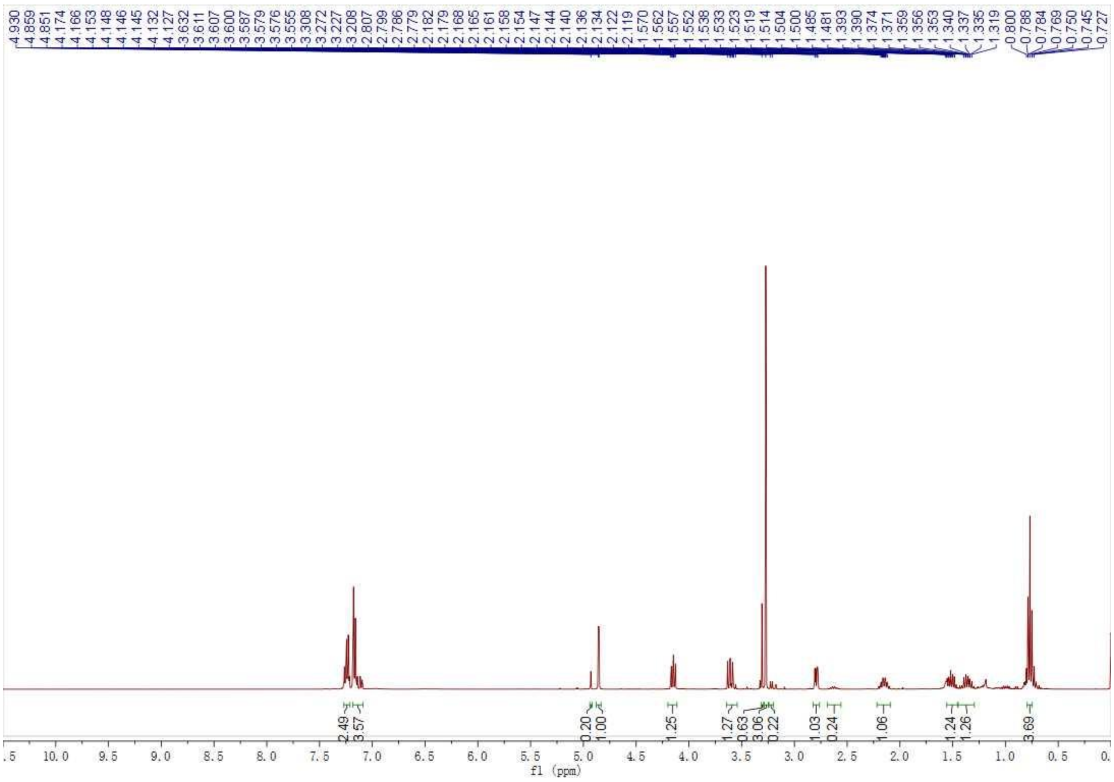

Me
Me
O
Ph
OEt

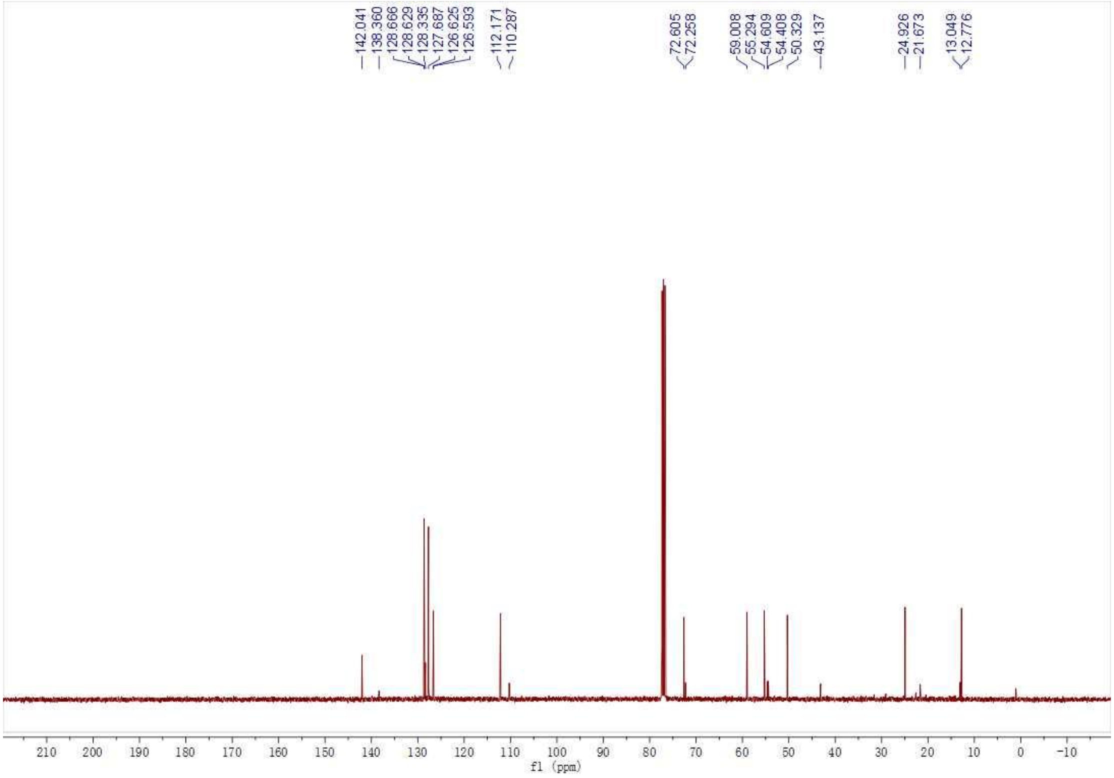

7.274
7.270
7.266
7.258
7.253
7.249
7.238
7.234
7.232
7.229
7.207
7.203
7.200
7.189
7.185
7.179
7.171
7.167
7.131
7.127
7.122
7.114
7.110
7.107
5.344
5.332
3.835
3.833
3.815
3.813
3.767
3.749
3.743
3.732
3.726
3.714
3.708
3.690
3.672
3.651
3.426
3.408
3.402
3.391
3.384
3.373
3.367
3.349
2.940
2.928
1.519
1.125
1.107
1.090
1.027
0.687
2.03
1.41
2.04
1.00
1.06
1.06
1.03
1.06
1.00
3.11
3.14
3.13
.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.
f1 (ppm)


137.379
128.908
128.169
126.744
109.170
79.998
64.002
62.539
43.386
24.746
22.860
15.297
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

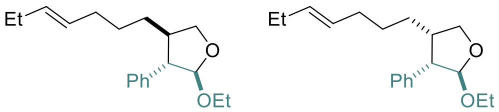
(36)


Me
O
Ph
OMe
Me
O
Ph
OMe


4.930
4.859
4.851
4.174
4.166
4.153
4.148
4.146
4.145
4.132
4.127
3.632
3.611
3.607
3.600
3.587
3.579
3.576
3.555
3.308
3.272
3.227
3.208
2.807
2.799
2.786
2.779
2.182
2.179
2.168
2.165
2.161
2.158
2.154
2.147
2.144
2.140
2.136
2.134
2.122
2.119
1.570
1.562
1.557
1.552
1.538
1.533
1.523
1.519
1.514
1.504
1.500
1.485
1.481
1.393
1.390
1.374
1.371
1.359
1.356
1.353
1.340
1.337
1.335
1.319
0.800
0.788
0.784
0.769
0.750
0.745
0.727
2.49
3.57
0.20
1.00
1.25
1.27
0.63
3.06
0.22
1.03
0.24
1.06
1.24
1.26
3.69
.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.
f1 (ppm)


142.041
138.360
128.666
128.629
128.335
127.687
126.625
126.593
112.171
110.287
72.605
72.258
59.008
55.294
54.609
54.408
50.329
43.137
24.926
21.673
13.049
12.776
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

(37)


Et
Ph
O
OEt
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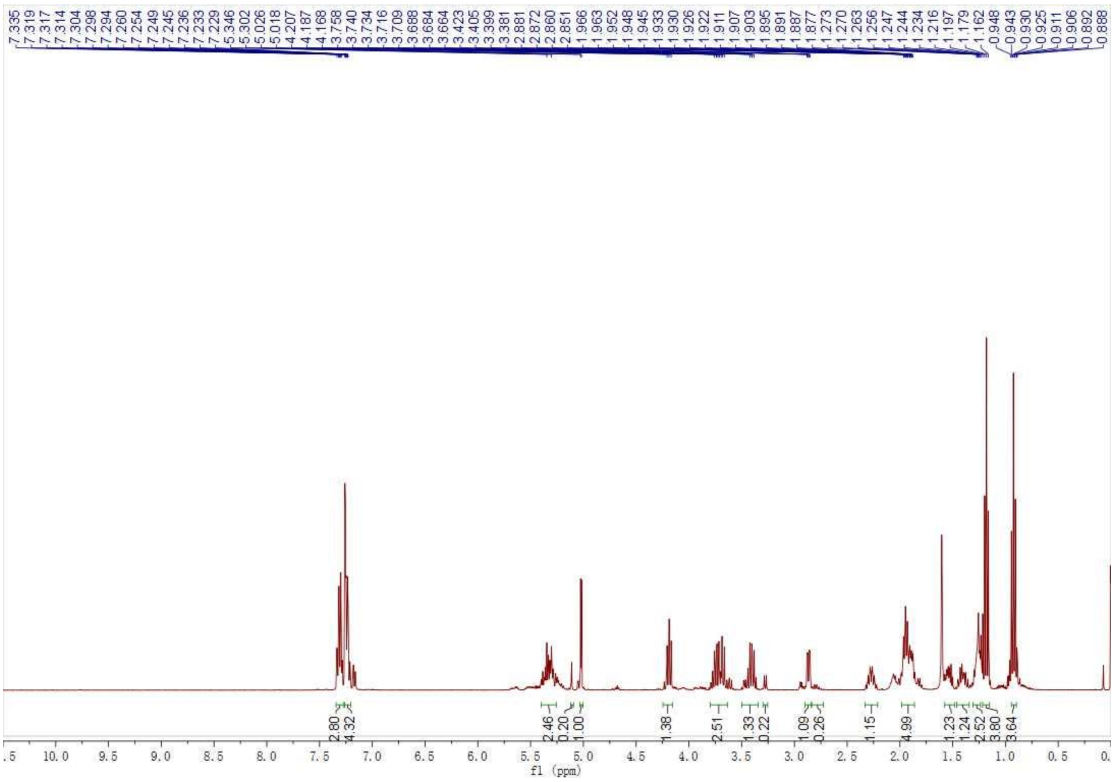
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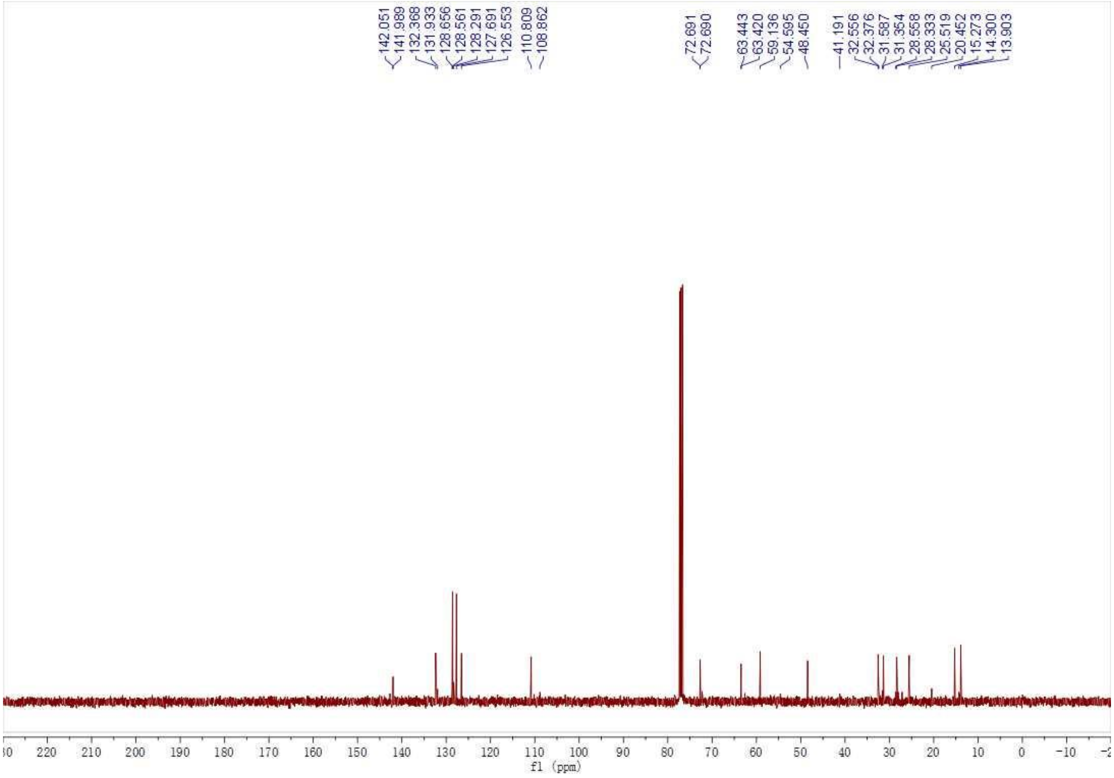
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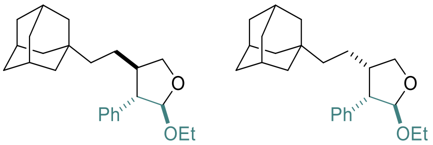
(**38**)



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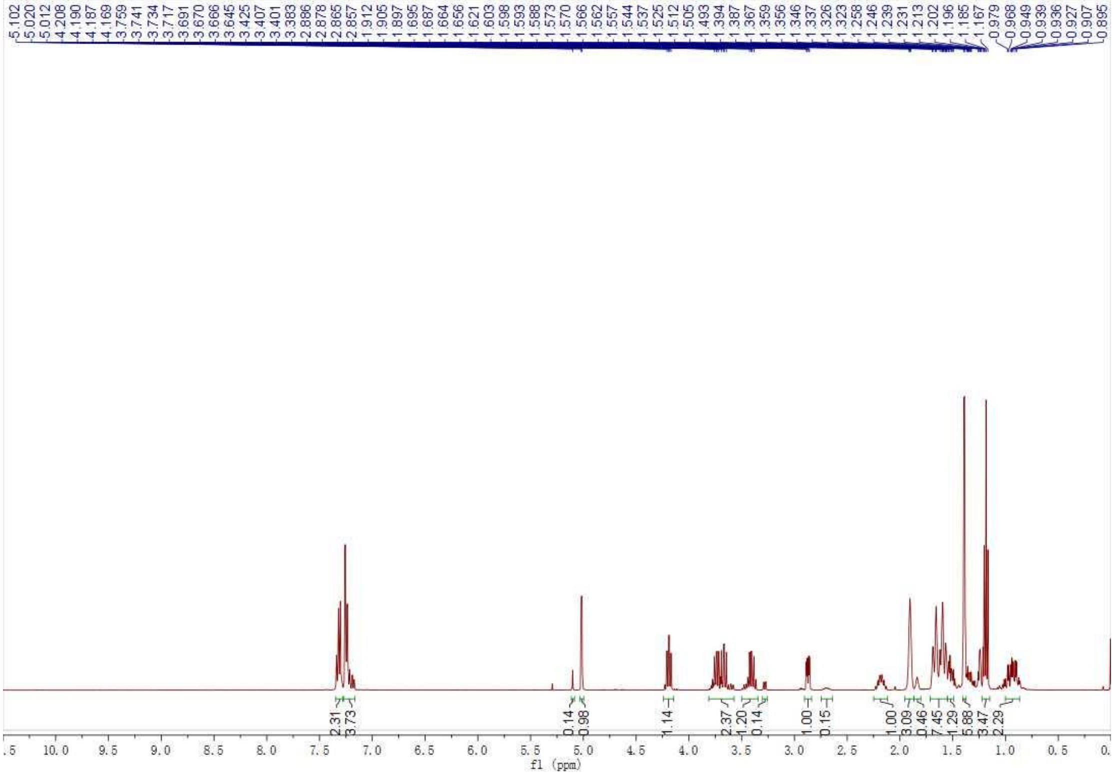

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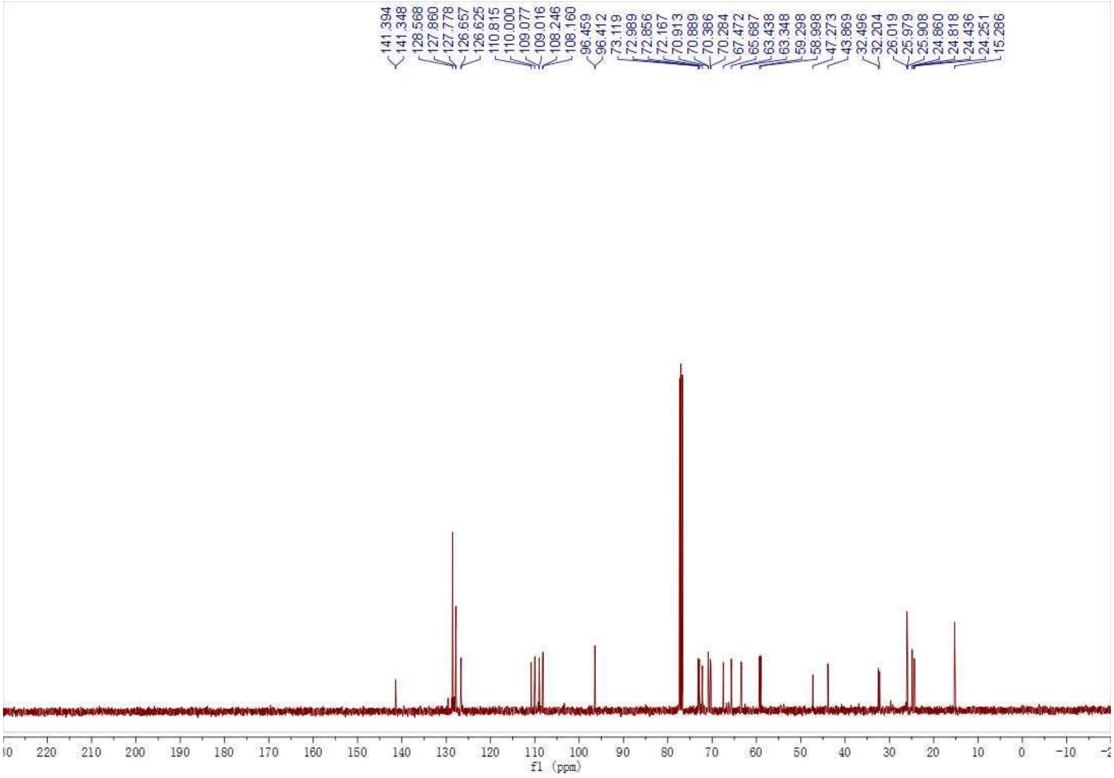

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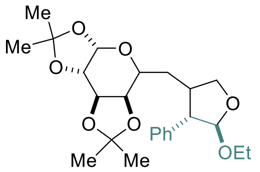
f1 (ppm)

(**39**)



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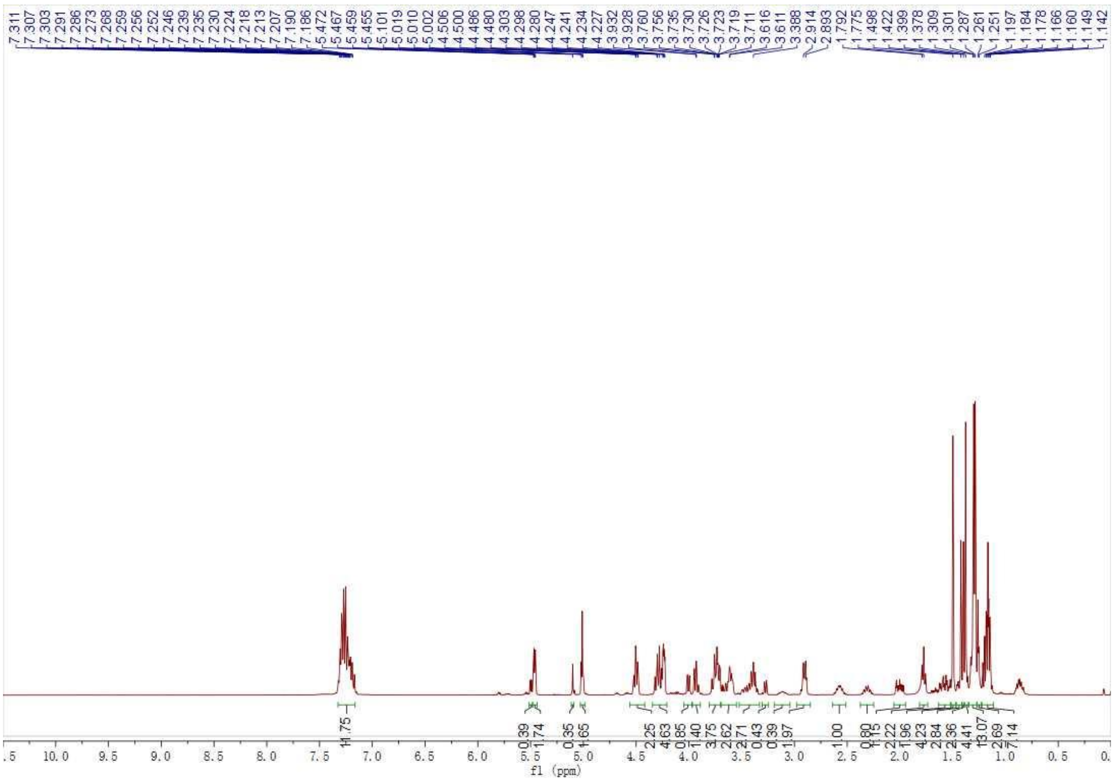

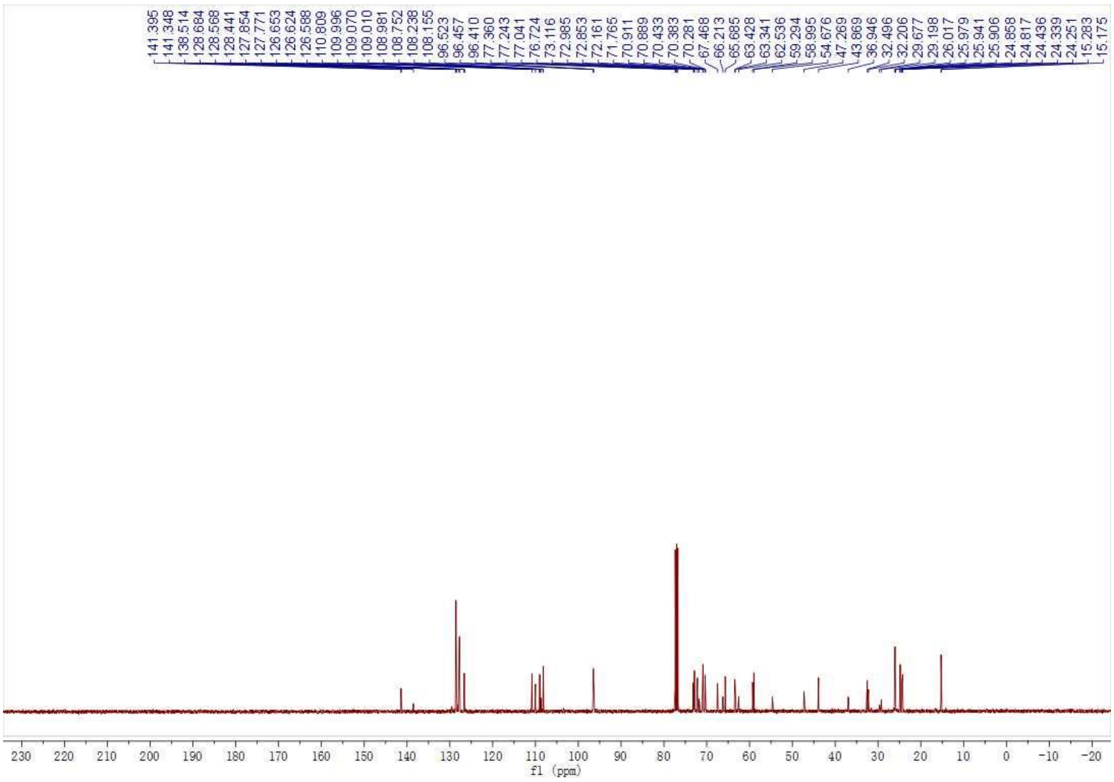

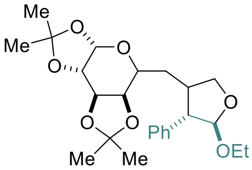

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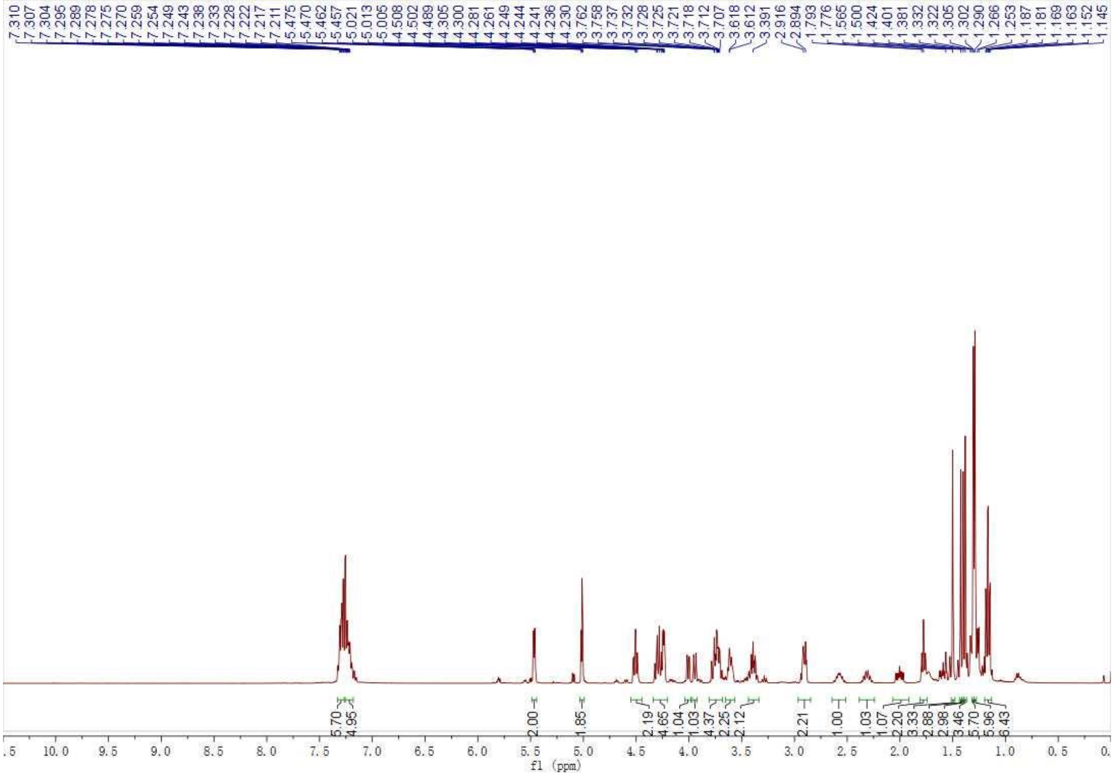

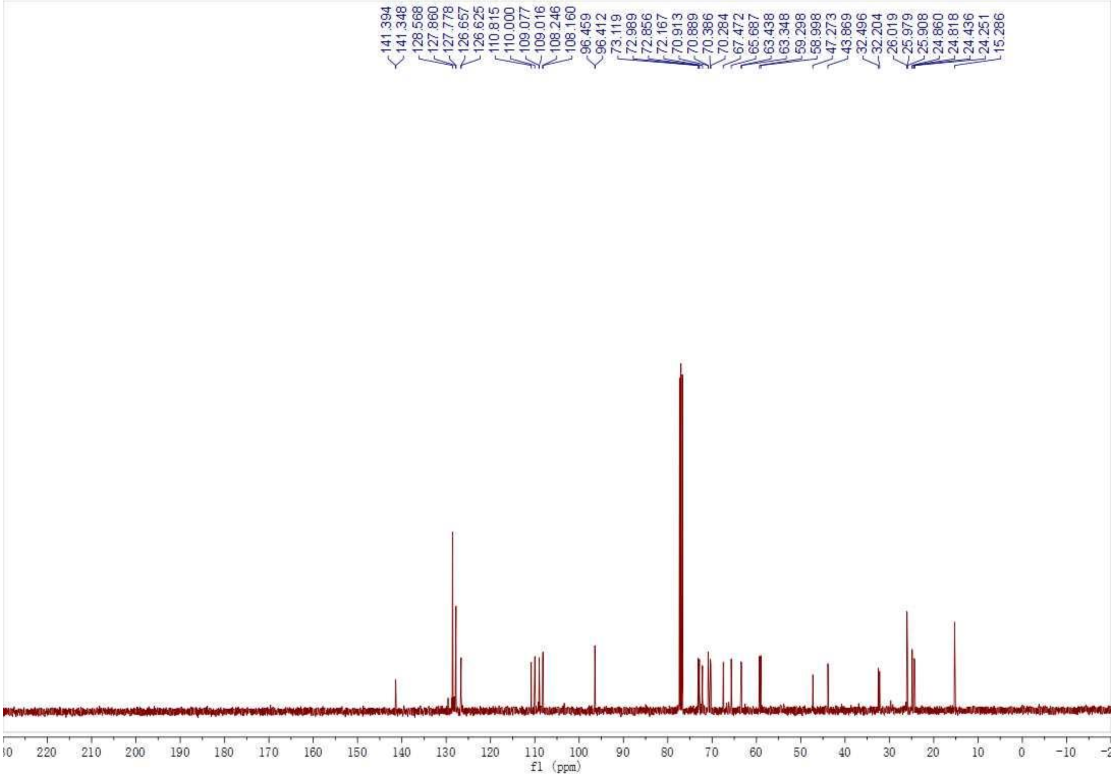

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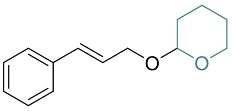
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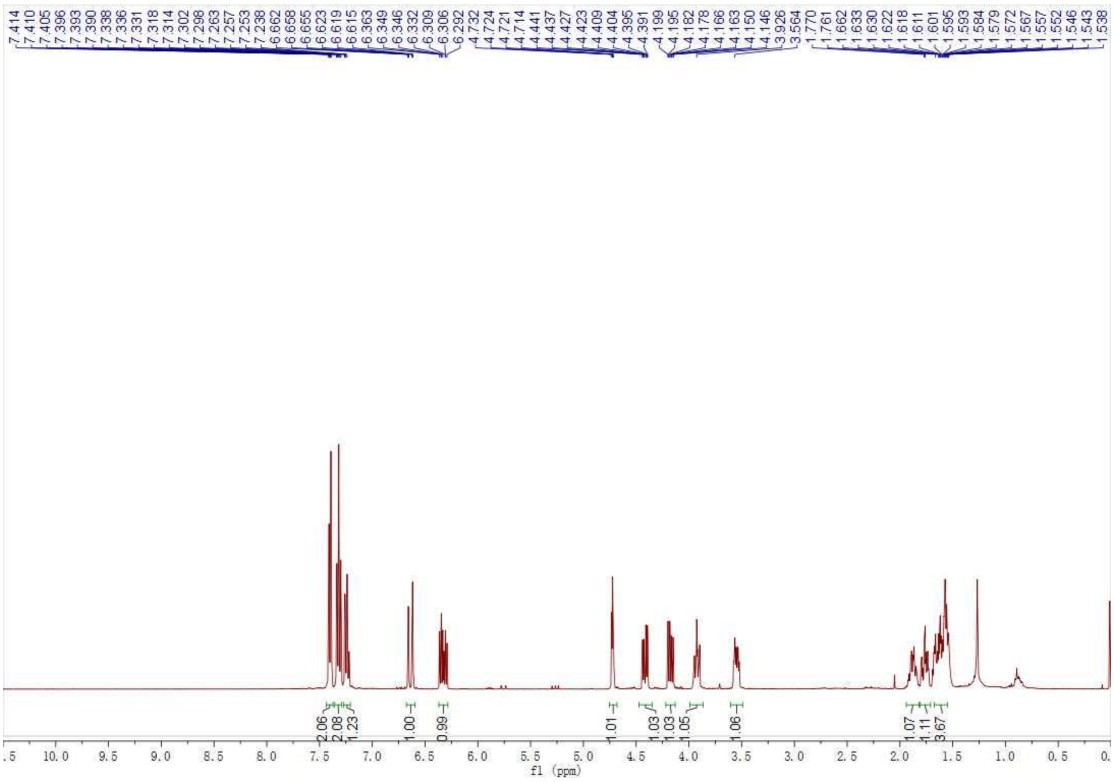
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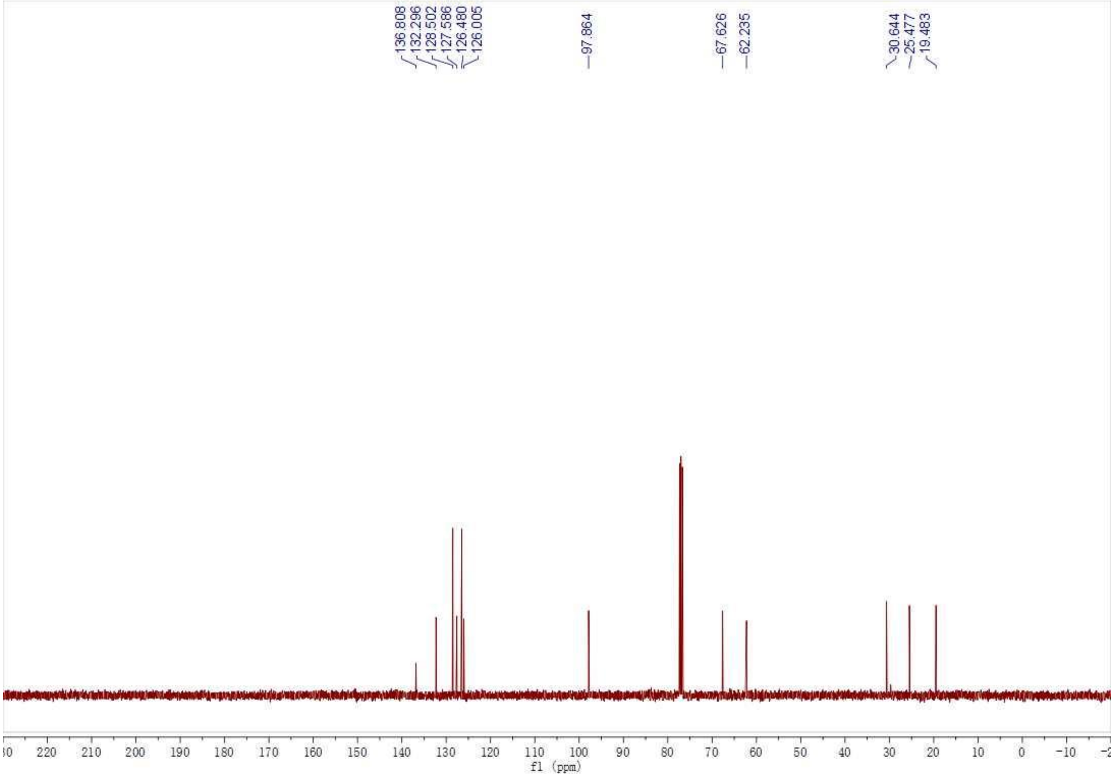
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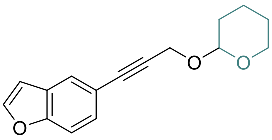

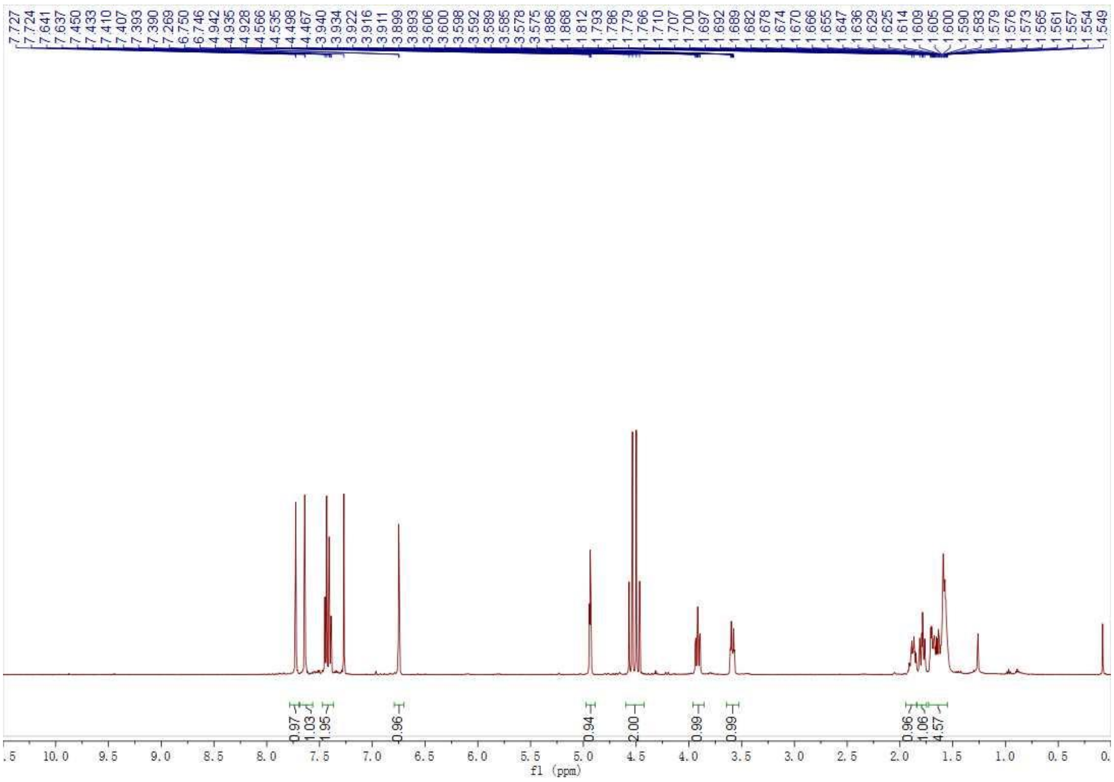
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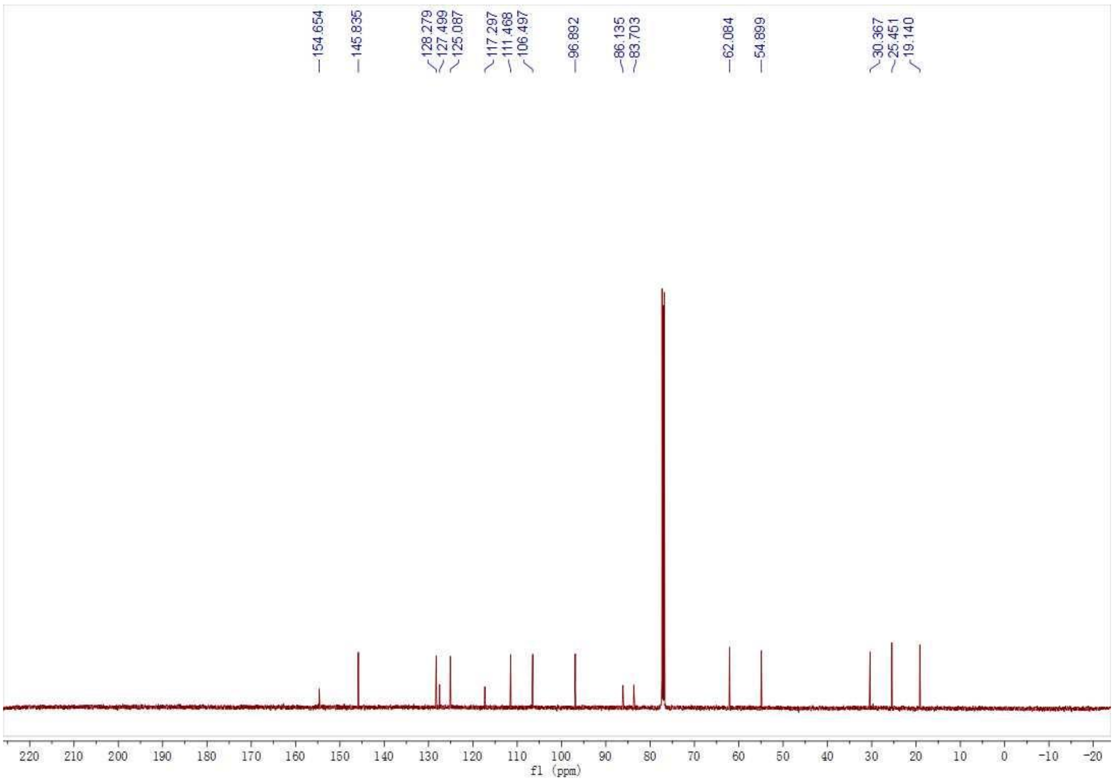
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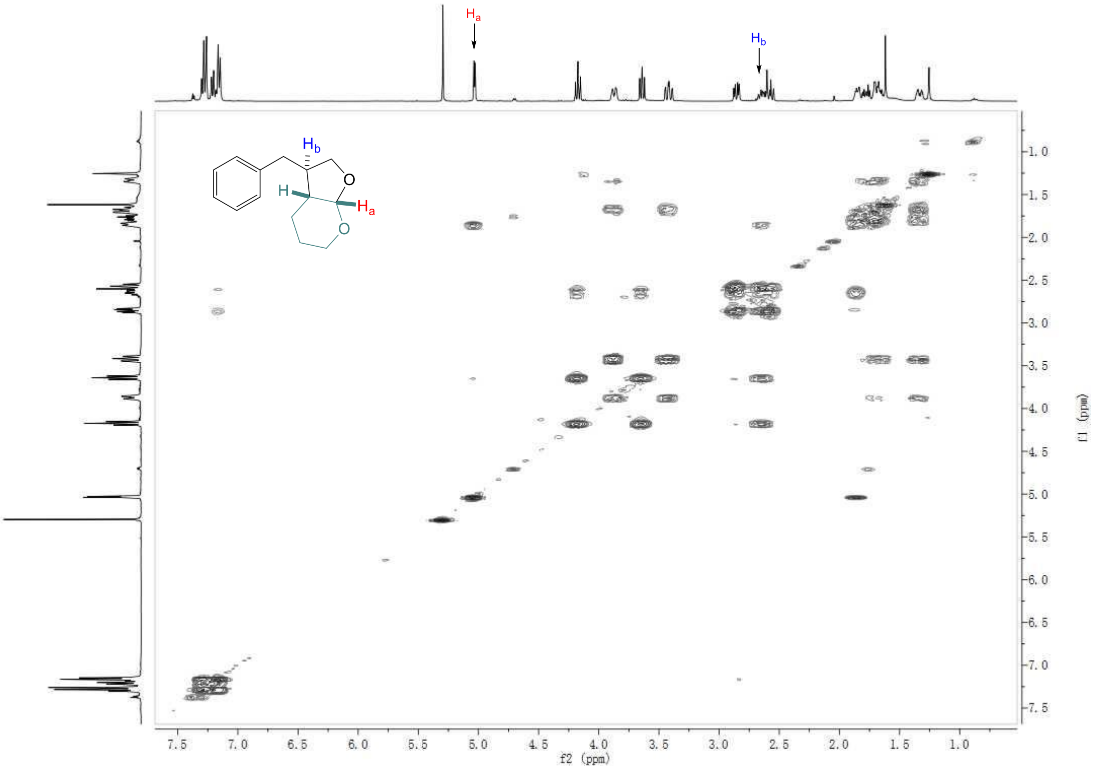
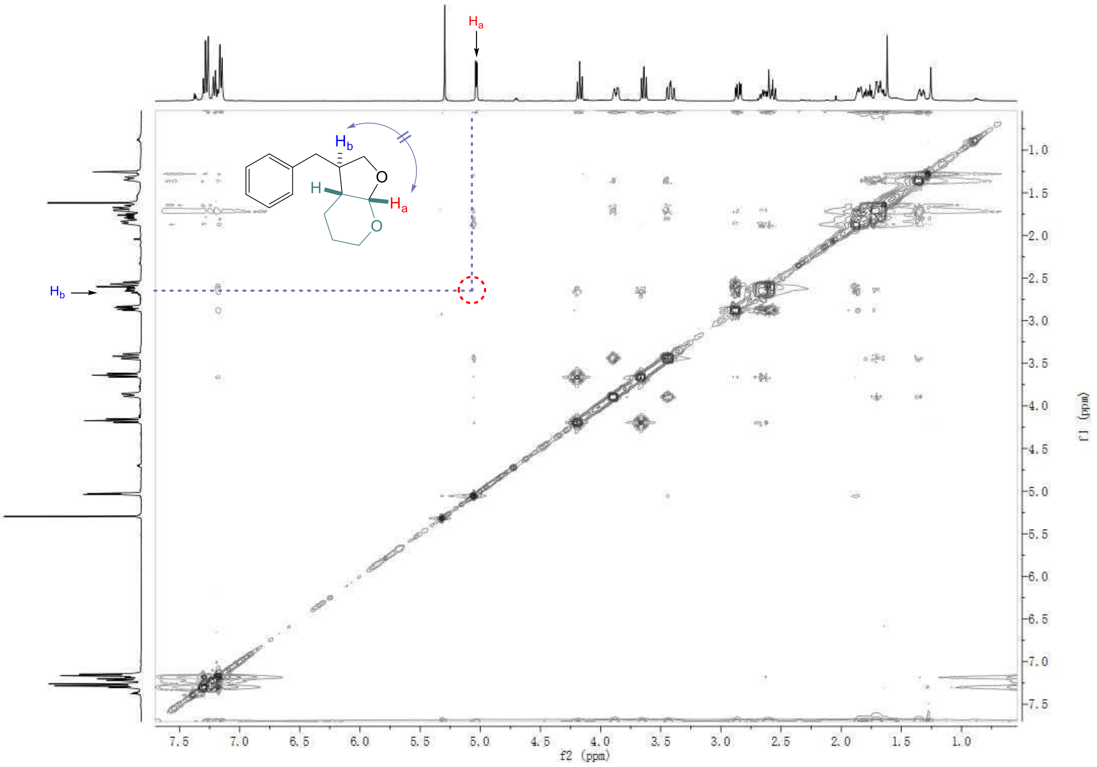
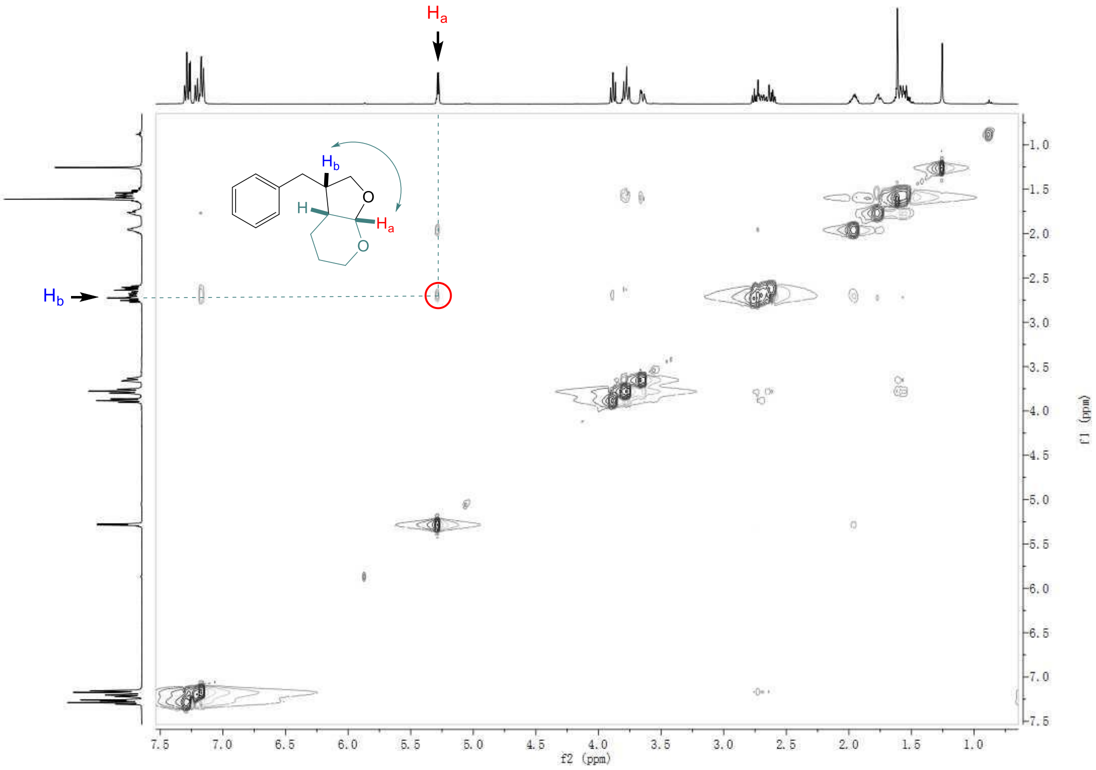
f1 (ppm)

H^1-H^1 COSY and H^1-H^1 2D-NOESY NMR spectrums of product **1**



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4.0
3.5
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1.0
f2 (ppm)
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2.0
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3.0
3.5
4.0
4.5
5.0
5.5
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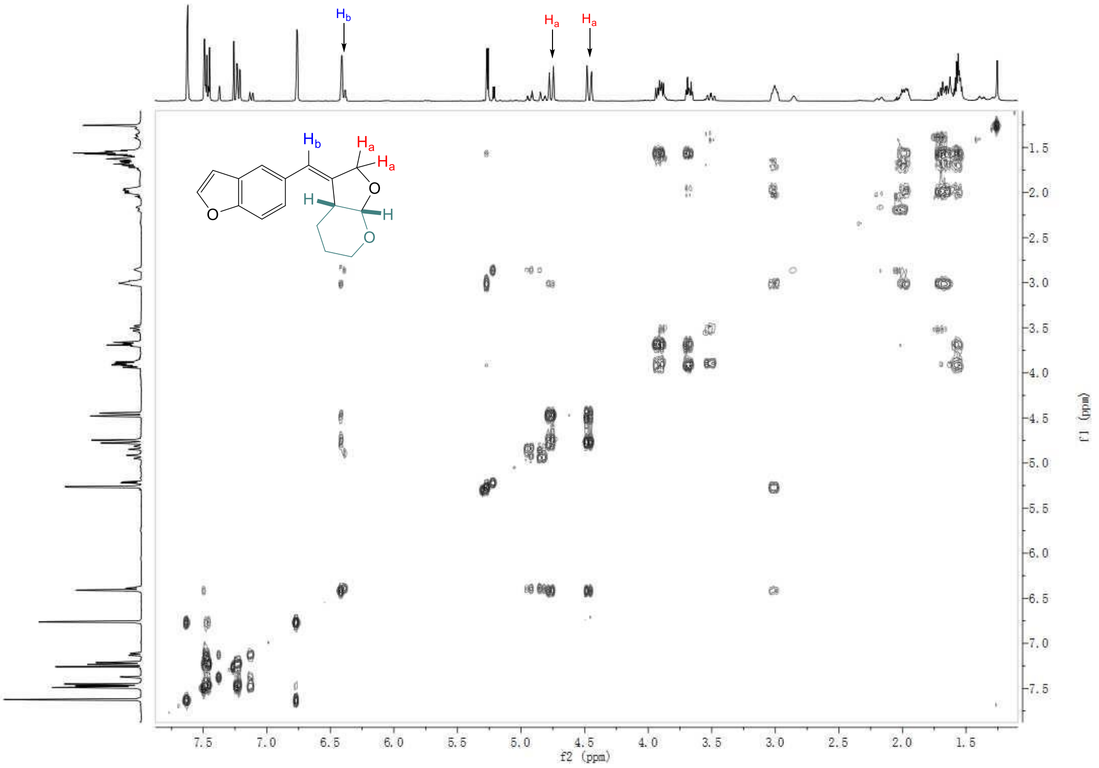
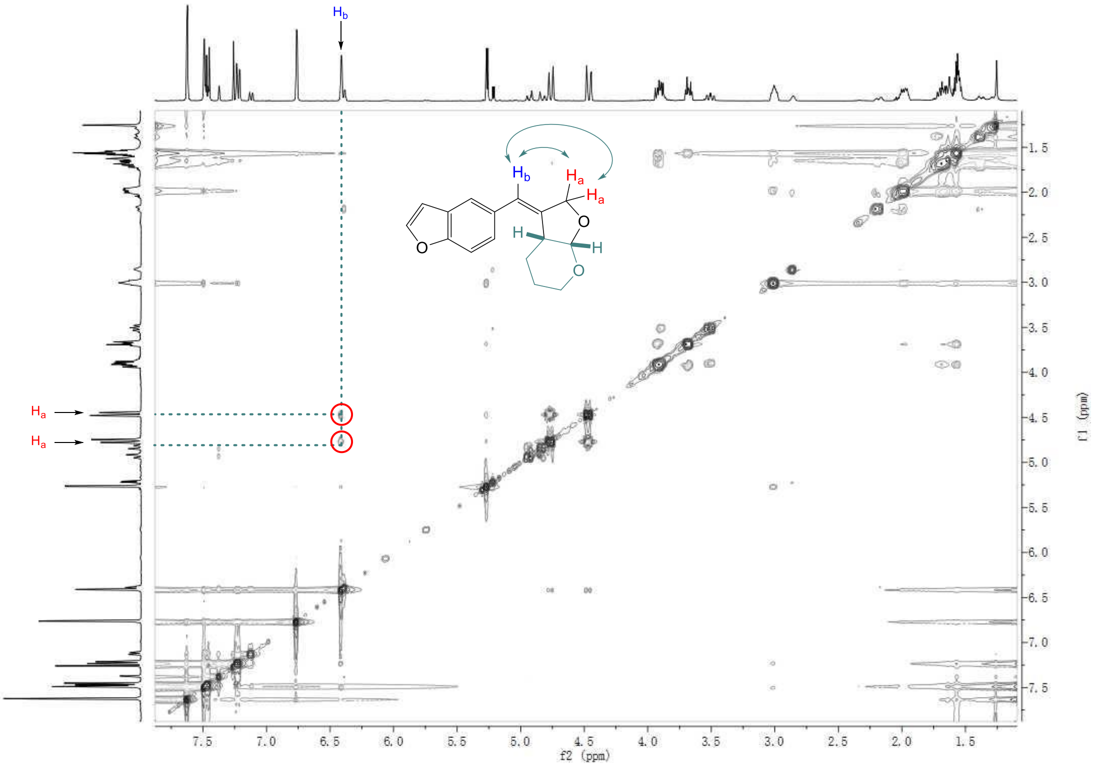
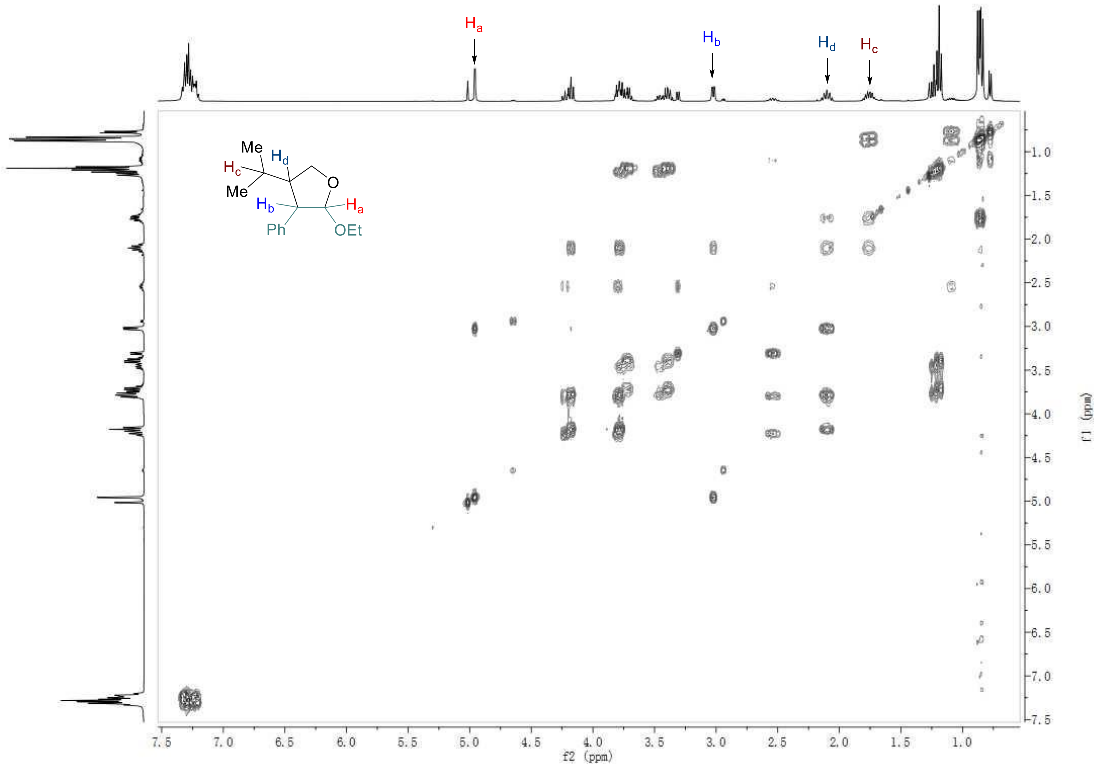
7.0
7.5
f1 (ppm)

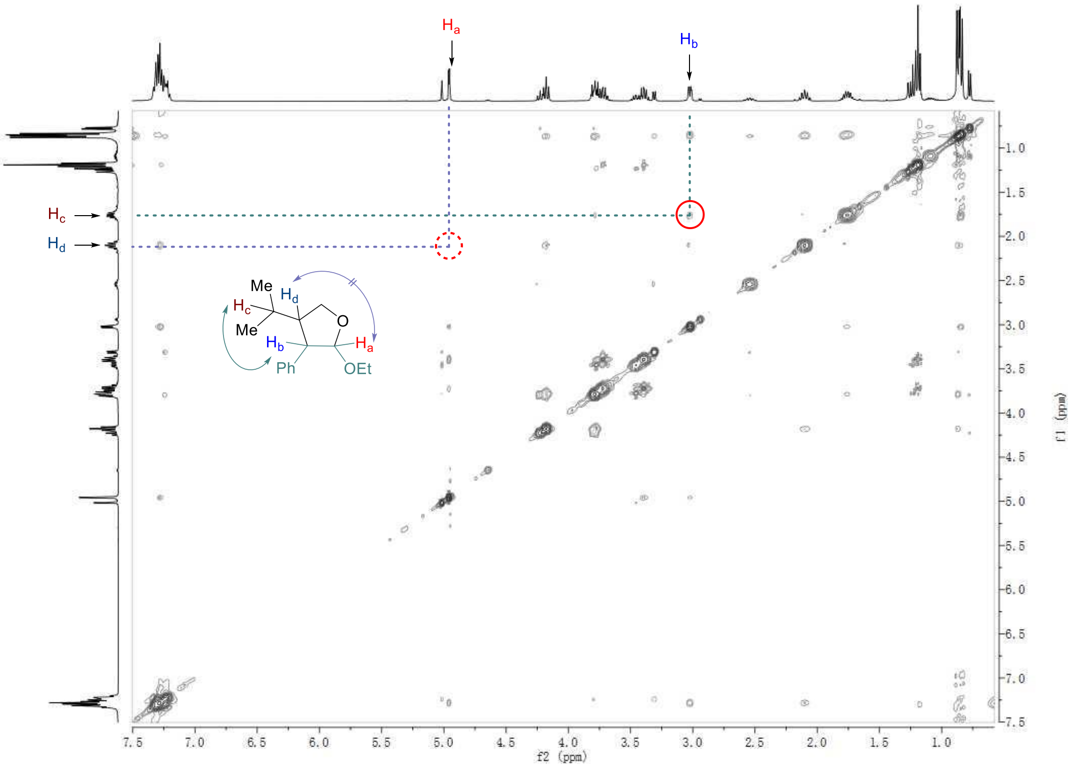
H^1-H^1 COSY and H^1-H^1 2D-NOESY NMR spectrums of compound **18**



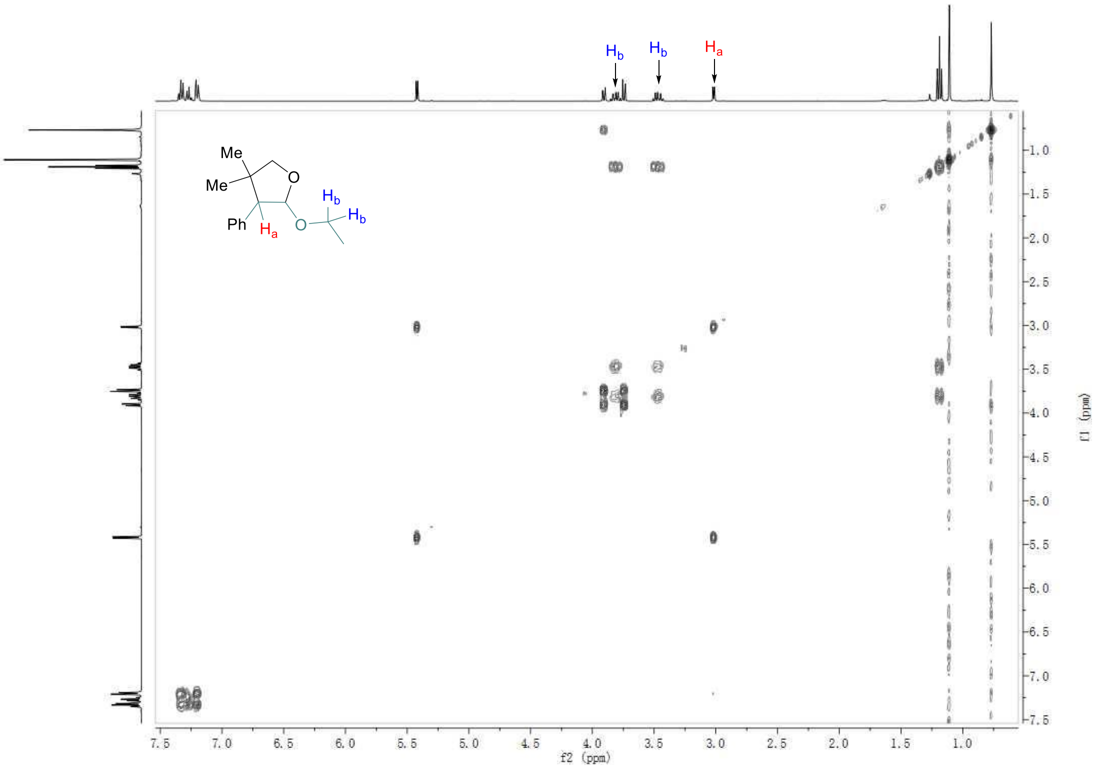


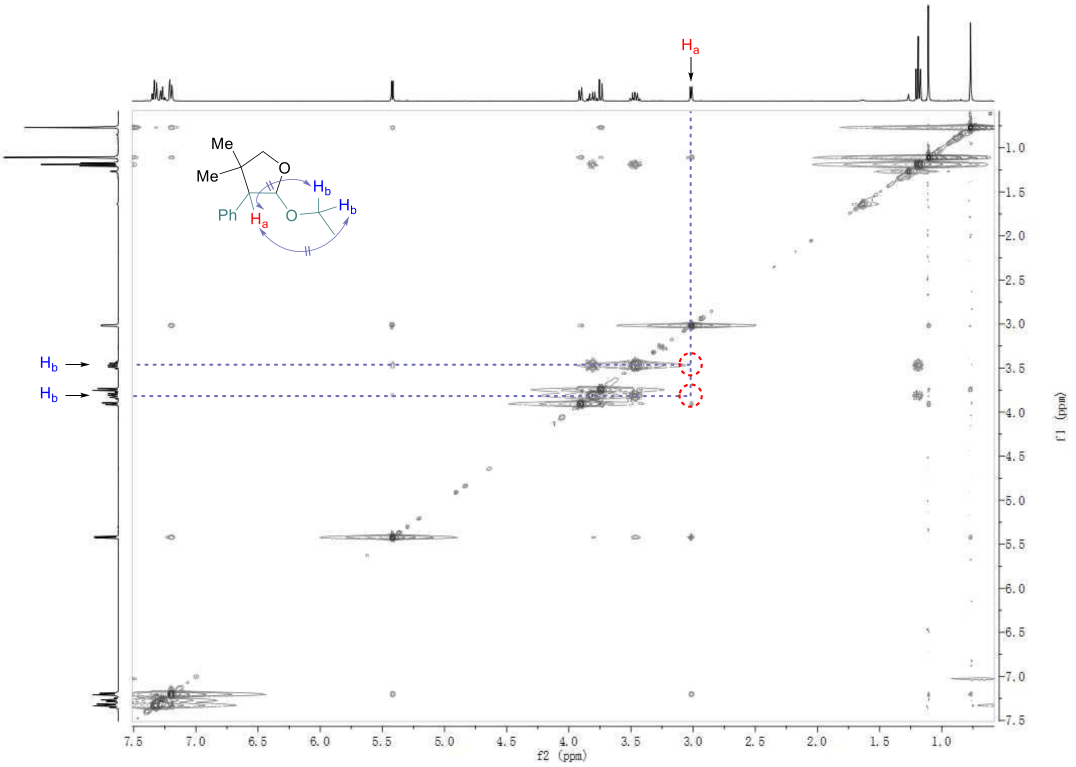
H^1-H^1 COSY and H^1-H^1 2D-NOESY NMR spectrums of compound **34**





H1-H1 COSY and H1-H1 2D-NOESY NMR spectrums of compound **35**





III. Date S2: Stability of cyclic acetals in simulated GI fluids (Related to Table 2)

Instruments and Equipments:
Agilent 1260 HPLC with DAD and 6420 Triple Quad MS
Waters Xbridge C8 (4.6 mm× 150 mm × 3.5 μm) column
Waters CSH C18 (4.6 mm× 150 mm × 3.5 μm) column
Eppendorf ThermoMixer C
Eppendorf Multipette Xstream
Mettler Toledo Seven Excellence pH meter

Reagents and Materials:
Purified water, Milli-Q HPLC grade
Acetonitrile, Sigma-Aldrich HPLC grade
Ammonium Bicarbonate, Sigma-Aldrich
Simulated Gastric Fluid USP without enzymes (SGF, pH 1.2)
Simulated Intestinal Fluid USP without enzymes (SIF, pH 6.8)
Compounds **1**, **15**, **27**, **35**.

Experiment:
HPLC method

Instrument	Agilent 1260 HPLC with DAD and 6420 Triple Quad MS
Column	Waters Xbridge C8 (4.6 mm× 150 mm × 3.5 μm) column for Compound A, B, C, E Waters CSH C18 (4.6 mm× 150 mm × 3.5 μm) column for Compound D
Column temperature	40 °C
Mobile phase	A: 10 mM NH4HCO3 in water B: ACN
Gradient program	Time (min) A% B% 0.00 95 5 15.00 5 95 20.00 5 95 20.10 95 5 25.00 95 5
Flow rate	0.7 mL/min
Detector	UV 214nm for Compound A, B, C, D UV 224nm for Compound E
Injection volume	10 μL

The solution stability of four compounds were evaluated in SGF and SIF at 37 °C. Detailed information is shown in Table S1.

Table S1 Stability testing plan, related to **Table 2**

Conditions	Time point	Test media	Testing items
37 °C	1 hr	SGF	Final pH, % Purity, % Degradation.
	3 hr	SIF	

Testing media:
Simulated Gastric Fluid USP without enzymes (SGF, pH 1.2)
Simulated Intestinal Fluid USP without enzymes (SIF, pH 6.8)

Initial solution:
Compound **35** was dissolved in ACN to make 2.5 mg/mL stock solutions. The solutions were diluted with ACN:water 1:1 to get 0.25 mg/mL initial solutions.
Compound **15** was dissolved in ACN to make a 5 mg/mL stock solution. The solution was diluted with ACN:water 1:1 to get 0.5 mg/mL initial solution.
Compounds **1** and **27** were dissolved in ACN and methanol to make a 2.5 mg/mL stock solution. The solution was diluted with ACN:water 1:1 to get 0.25 mg/mL initial solutions.

Sample solution:
100 μL of each stock solutions were diluted with 900 μL of SGF and 900 μL of SIF.

Testing procedure:
All the sample solutions were placed in Thermomixer according to Table S1 conditions respectively. The final pH values were measured by pH meter. The purities and concentrations were determined by HPLC-MS. Significant degradation (> 5 percent) of a compound in this study could suggest potential instability.

Table S2 Degradation studies in SIF and SGF at 37 °C (According to FDA: Waiver of In Vivo Bioavailability and Bioequivalence Studies), related to **Table 2**

Classification	Degradation (%) after 1 h at 37 °C in SGF	Degradation (%) after 3 h at 37 °C in SIF
Fairly stable	< 5%	< 5%
Unstable	> 5%	> 5%

Results:
The stability results of five intermediates and final pH values are listed in **Table S3** – **S6** with stability classification remarks.

Table S3 Stability results of compound **35** (λ = 214 nm), related to **Table 2**

Condition	Test Media	Time	Purity (%)	Conc. (mg/mL)	Recovery (%)	Degradation (%)	Classification	Final pH
Initial	ACN:water	0	95.74	0.25				

37 °C	SGF	1hr	0.56	0.0015	0.60	99.4151	Unstable	1.06
	SIF	3hrs	98.22	0.2381	95.23	-2.5903	/	6.92

Table S4 Stability results of compound **15** (λ = 214 nm), related to **Table 2**

Condition	Test Media	Time	Purity (%)	Conc. (mg/mL)	Recovery (%)	Degradation (%)	Classification	Final pH
Initial	ACN:water	0	93.70	0.5000				
37 °C	SGF	1hr	89.58	0.4585	91.71	4.3970	Fairly stable	1.08
	SIF	3hrs	93.61	0.4848	96.97	0.0961	Fairly stable	6.89

Table S5 Stability results of compound **1** (λ = 214 nm), related to **Table 2**

Condition	Test Media	Time	Purity (%)	Conc. (mg/mL)	Recovery (%)	Degradation (%)	Classification	Final pH
Initial	ACN:water	0	92.05	0.2500				
37 °C	SGF	1hr	80.65	0.2311	92.44	12.3846	Unstable	1.09
	SIF	3hrs	91.95	0.2618	104.73	0.1086	Fairly stable	6.88

Table S6 Stability results of compound **27** (λ = 224 nm), related to **Table 2**

Condition	Test Media	Time	Purity (%)	Conc. (mg/mL)	Recovery (%)	Degradation (%)	Classification	Final pH
Initial	ACN:water	0	99.78	0.2500				
37 °C	SGF	1hr	98.45	0.2598	103.90	1.3329	Fairly stable	1.07
	SIF	3hrs	99.27	0.2663	106.54	0.5111	Fairly stable	6.87

IV. Reference

Balmond, E. I., Benito-Alifonso, D., Coe, D. M., Alder, R. W., Mcgarrigle, E. M. and Galan, M. C. (2014). A 3,4-trans-fused cyclic protecting group facilitates α-selective catalytic synthesis of 2-deoxyglycosides. Angew. Chem. Int. Ed. *53*, 8190-8194.

Duan, Z. C., Hu, X. P., Zhang, C., Wang, D. Y., Yu, S. B. and Zheng, Z. (2009). Highly enantioselective rh-catalyzed hydrogenation of beta,gamma-unsaturated phosphonates with chiral ferrocene-based monophosphoramidite ligands. J. Org. Chem. *74*, 9191-9194.

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