Accepted Manuscript

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PII: S0040-4020(15)00875-3

DOI: 10.1016/j.tet.2015.06.020

Reference: TET 26855

To appear in: *Tetrahedron*

Received Date: 5 May 2015

Revised Date: 1 June 2015

Accepted Date: 3 June 2015

Please cite this article as: Li M, Xiong J, Huang Y, Wang L-J, Tang Y, Yang G-X, Liu X-H, Wei B-G, Fan H, Zhao Y, Zhai W-Z, Hu J-F, Xylapyrrosides A and B, Two Rare Sugar-Morpholine Spiroketal Pyrrole-Derived Alkaloids from Xylaria nigripes: Isolation, Complete Structure Elucidation, and Total Syntheses, Tetrahedron (2015), doi: 10.1016/j.tet.2015.06.020.

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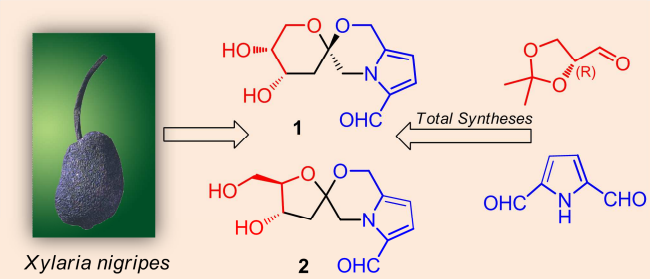

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ARTICLE INFO

Article history:
Received
Received in revised form
Accepted
Available online

Keywords:
Xylaria nigripes
Xylapyrrosides A and B
Spiro-alkaloids
Asymmetric synthesis
Antioxidant

ABSTRACT

Two new [named xylapyrrosides A (**1**) and B (**2**)] along with two known [pollenopyrrosides A (**3**) and B (= acortatarin A, **4**)] naturally occurring spirocyclic pyrrole alkaloids were isolated and identified as minor components from the EtOH extract of the dried mycelia of the edible medicinal fungus *Xylaria nigripes*. Their structures were established by a combination of interpretation of spectroscopic data and single-crystal X-ray diffraction analyses. The isolates possess a unique tricyclic skeleton comprising a common bicyclic 2-formyl-pyrrole-fused morpholine, with a variable ketohexoside ring. This class of alkaloids is quite rare from natural sources. In this study, the total syntheses of compounds **1**, **2** and **4** were successfully achieved by two alternative strategies, and three new analogues [named xylapyrrosides A1 (**1a**), A2 (**1b**) and B1 (**2a**)] were also produced. Notably, the total synthesis of such spiroketal alkaloids with a pyranose ring (e.g.,**1**) was accomplished for the first time. The absolute configurations of the new isolates can be thereafter unequivocally secured by the total syntheses. The above isolated and synthesized spiro-alkaloids were found to show moderate antioxidant effects by preventing the oxidative stress-induced cytotoxicity of A7r5 rat vascular smooth muscle cells (VSMCs).

1. Introduction[1]

As described previously, pyrrole-containing alkaloids, such as discorhabdins[1] and lamellarins[2] with complex structures and interesting biological activities, have greatly stimulated interdisciplinary studies by chemists and biologists worldwide. During the past decade, the number of new pyrrole-related alkaloids isolated, identified, and synthesized for their medicinal potential has increased. This includes a very small class of sugar-morpholine spiroketal pyrrole-derived alkaloids that emerged only in recent years. Capparisines A and B from the fruits of *Capparis spinosa*,[3] pollenopyrrosides A and B from the bee-collected *Brassica campestris* pollen,[4] and acortatarins A and B from the rhizomes of *Acorus tatarinowii*,[5] were independently reported by three Chinese research groups in 2010. About two years later, acortatarins A and C were isolated from the crust of whole wheat bread by Peterson, et al.[6] In general, this group of alkaloids (Figures 1 and 2) contains an unprecedented tricyclic pyrrole–morpholine–ketohexoside fused framework. Among the above spiro-alkaloids, capparisines A and B were previously reported to have no inhibitory effect on human hepatocyte cell HL-7702 apoptosis.[3] But acortatarin A was found to have antioxidant activity by inhibiting reactive oxygen species (ROS) production in high glucose-induced mesangial cells.[5,7]

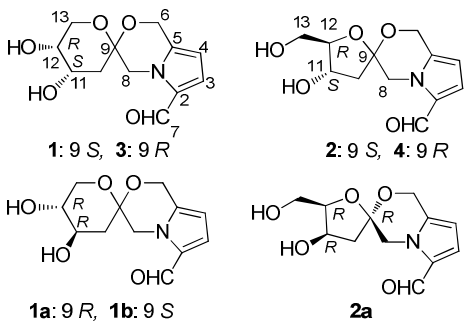

Figure 1. Structures of naturally-occurring (**1**–**4**) spiroketal pyrrole-derived alkaloids from *Xylaria nigripes* and their synthesized analogues (**1a**, **1b**, **2a**).

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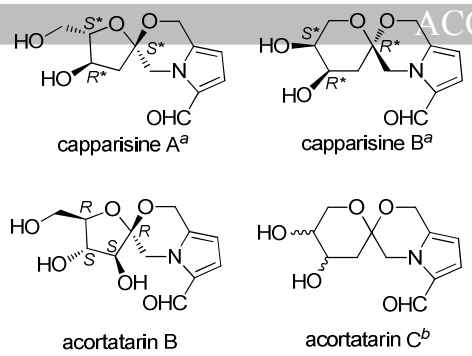


Figure 2. Other previously reported naturally-occurring spiroketal pyrrole-derived alkaloids. [a]The stereochemistries of capparisines A and B reported by Wang et al. were determined by Mo*Kα* (not Cu*Kα*) X-ray crystallographic analysis.[3] [b]The relative and absolute configuration of acortatarin C remains undetermined,[6] and the configurations at C-11 and C-12 were most likely to be *S** and *R**, respectively, based on related biogenetic considerations.[6]

Due to the intriguing structures, this class of alkaloids attracted considerable interest for organic synthesis soon after their isolation. So far, several groups have accomplished the total syntheses of acortatarins A[8-12] and B.[8,9] Inexplicably, the absolute configurations of the naturally occurring acortatarins were initially assigned by both single-crystal X-ray (Mo*Kα*) diffraction analysis and the modified Mosher's method,[5] but they were eventually revised after stereoselective total syntheses.[8] Meanwhile, acortatarin A was found to be identical with pollenopyrroside B.[9,10]

As a part of our continuing interest in novel bioactive alkaloids from nature,[1,2,13] four sugar-morpholine spiroketal pyrrole-derived alkaloids (**1**−**4**, Figure 1) were isolated from the EtOH extract of the dried mycelia of *Xylaria nigripes* (Koltz.) Sacc. (family Xylariaceae), also known by the folklore name of Wuling Shen in Chinese. *X. nigripes* is considered to be a precious medicinal fungus, which is edible and delicious when it is young. Differing from our previously studied wood-rotting fungus *Fomes fomentarius*,[14] the wild *X. nigripes* has a very special ecological niche in that it usually grows in the abandoned nests of the subterranean (*ca* -2 m) termite *Odontotermes formosanus*.[15,16] Although the wild fungus is quite rare in nature, the mycelia of *X. nigripes* nowadays can be largely manufactured through fermentation, and the dried culture filtrate is usually called Wuling Powder in China. As a popular traditional Chinese medicine (TCM) used as a nerve tonic, the commercially available Wuling Capsule (a single herbal formula made from Wuling Powder) has been used clinically for the treatment of insomnia, anxiety disorders and depression in China since 1999.[15,16a,17] Nevertheless, studies on the secondary metabolites and their biological properties of this fungus remain limited.[16b,17f,18] In the present investigation, the pyrrole-fused spiroketal architectures are reported from *X. nigripes* for the first time. We herein describe their isolation, structural elucidation, total syntheses, and their anti-oxidant effects. Regarding to the total syntheses, the reactions proceeded with considerable diastereoselectivity to give the target compounds in good yields.

2. Results and discussion

2.1 Isolation and structural elucidation

The commercially fermented mycelium (20 kg) of *X. nigripes* was extracted with 75% EtOH (20 L) at room temperature three times to afford a brown residue (1.3 kg, semi-dry), which was suspended in H_2O (2.0 L) and then successfully extracted with petroleum ether (3×1.5 L), EtOAc (3×1.5 L), and *n*-BuOH (3×1.5 L). The EtOAc extract (281.6 g) was separated by repeated column chromatography (CC) over silica gel, Sephadex LH-20, and semi-preparative HPLC to furnish compounds **1** (4.0 mg), **2** (21.3 mg), **3** (1.2 mg), and **4** (20.1 mg). By comparing their spectroscopic data and physicochemical properties with those reported in the literature, the structures with absolute configurations of **3** (= pollenopyrroside A[4]), and **4** (= pollenopyrroside B[4] or acortatarin A[5,8-12]) were undoubtedly established as shown in Figure 1. Compound **2** is reported herein as a natural product for the first time, which is identical in all respects with the synthesized 9-*epi*-acortatarin A.[9-13]

Xylapyrroside A (**1**) was obtained as a colorless crystal from acetone. Its molecular formula was determined to be $C_{12}H_{15}NO_5$ based on a molecular ion peak at *m/z* 253.0952 $[M]^+$ in its HR-EIMS, implying six degrees of unsaturation. The UV absorption at 296 nm of **1** indicated the presence of a pyrrole-2-aldehyde moiety.[5] In accordance with the above observation, a typical proton signal at δ 9.39 (1H, s, H-7) for an aldehyde group and two mutually-coupling olefinic protons at δ 7.04 (1H, d, J = 4.0, H-3) and 6.09 (1H, d, J = 4.0 Hz, H-4) were present in the ^{1}H NMR spectrum (Table 1) of **1**.

Table 1.^{1}H (400 MHz) and ^{13}C (100 MHz) NMR data of compound **1**.[a]

No	δ_H (J values in Hz)				δ_C
	1[b]	**1**[c]	**1**[d]	Capparisine B[4,d]	**1**[b]
2					132.4
3	7.04 (d, 4.0)	6.97 (d, 4.0)	6.90 (d, 4.0)	6.92 (d, 3.8)	125.8
4	6.09 (d, 4.0)	6.05(d, 4.0)	5.99 (d, 4.0)	6.01 (d, 3.5)	106.1
5					137.1
6	4.86 (d, 16.0)	4.86 (d, 15.6)	4.80 (d, 15.6)	4.82 (d, 15.2)	58.6
	4.77 (d, 16.0)	4.74 (d, 15.6)	4.71 (d, 15.6)	4.74 (d, 15.7)	
7	9.39 (s)	9.46 (s)	9.42 (s)	9.45 (s)	180.2
8	4.62 (d, 14.0),	4.55 (d, 14.0)	4.68 (d, 13.9)	4.70 (d, 14.4)	53.5
	4.00 (d, 14.0)	3.95 (d, 14.0)	3.99 (d, 13.9)	4.02 (d, 13.8)	
9					96.9
10	2.02 (dd, 12.8, 11.6)	1.98 (dd, 12.8, 11.6)	1.90 (dd, 12.8, 11.6)	1.91 (dd, 12.6, 11.8)	36.1
	1.92 (dd, 12.8, 5.2)	1.90 (dd, 12.8, 5.6)	2.02 (dd, 12.8, 5.6)	2.04 (dd, 12.8, 5.3)	
11	4.10 (ddd, 11.6, 5.2, 2.8)	4.06 (m)	4.14 (ddd, 11.6, 5.6, 2.8)	4.14 m	68.7
12	3.81 (m)	3.85 (m)	3.87 (m, overlapped)	3.88 m	66.0
13	3.83 (br d, 12.0)	3.77 (dd, overlapped)	3.87 (dd, overlapped)	3.89 (d, 12.1)	66.3
	3.78 (br d, 12.0)	3.75 (dd, overlapped)	3.78 (dd, 12.8, 1.2)	3.81 (d, 12.1)	

[a] Assignments were made by a combination of 1D and 2D NMR experiments; [b] in methanol-d_4; [c] in acetone-d_6; [d] in $CDCl_3$.

Additionally, two unequivalent aliphatic methylene protons [δ 2.02 (1H, dd, J = 12.8, 11.6 Hz) and 1.92 (1H, dd, J = 12.8, 5.2 Hz), H_2-10], three heteroatom-bearing methylenes [δ 4.86 and 4.77 (each 1H, d, J = 16.0 Hz, H_2-6); 4.62 and 4.00 (each 1H, d, J = 14.0 Hz, H_2-8); 3.83 and 3.78 (each 1H, br d, J = 12.0 Hz, H_2-13)], and two oxymethines [δ 4.10 (1H, ddd, J = 11.6, 5.2, 2.8 Hz, H-11); 3.81 (1H, m, H-12)] also appeared in the ^{1}H NMR spectrum (Table 1). The ^{13}C NMR spectrum of **1** exhibited twelve well-resolved signals (Table 1) classified by DEPT and HSQC NMR experiments: four methylenes [δ 36.1 (C-10), 53.5 (C-8), 58.6 (C-6) and 66.0 (C-13)], five methines [two oxygenated at δ 66.3 (C-12), 68.7 (C-11), two olefinic at δ 106.1 (C-4) and 125.8 (C-3), and one formyl carbon at δ 180.2 (C-7)], and three quaternary carbons [one ketal at δ 96.9 (C-9), and two olefinic at δ 132.4 (C-2) and 137.1 (C-5)].

The above spectroscopic data (in CD_3OD) closely resembled those of capparisine B (Figure 2), a sugar-morpholine spiroketal pyrrole-derived alkaloid previously isolated from the mature fruits of *Capparis spinosa*.[3] The ^{1}H NMR data of compound **1**

and capparisine B[3] are found to be identical when using the same NMR solvent ($CDCl_3$) (Table 1), indicating both should have the same planar structure with the same relative configuration. The framework of **1** was further confirmed by detailed analyses of 2D NMR spectra (COSY, HSQC, HMBC and NOESY) (Figure 3). However, the optical rotation value ($[\alpha]_D^{25}$ −189 (MeOH)) of compound **1** was found to be quite different from that of capparisine B ($[\alpha]_D^{25}$ +38 (MeOH)) with a (9*R**,11*R**,12*S**) configuration[3](Figure 2), suggesting that the two compounds are enantiomers of each other. The absolute configuration (9*S*,11*S*,12*R*) of **1** was finally confirmed by single-crystal X-ray (Cu*Kα*) diffraction analysis (Figure 4 and Supplementary data).

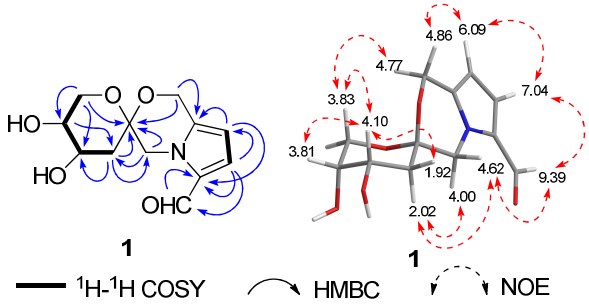


Figure 3. Key COSY, HMBC and NOE correlations of **1**.

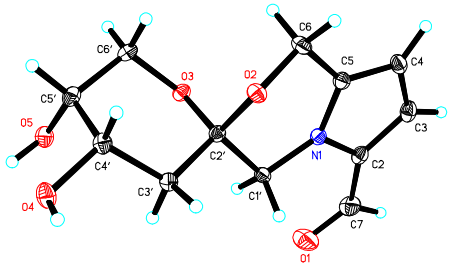
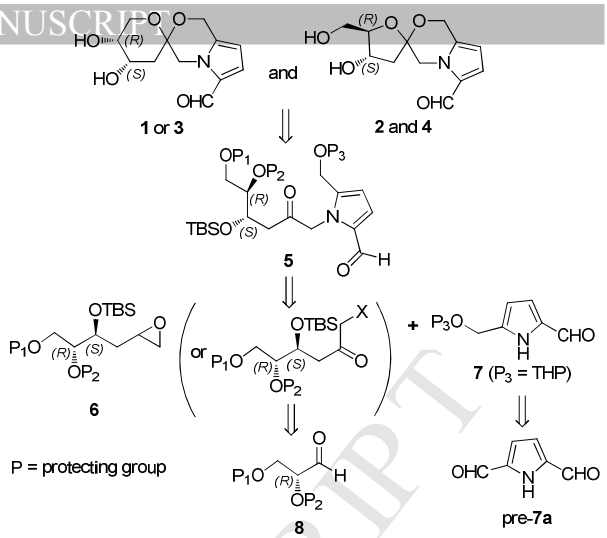


Figure 4. X-ray crystal structure of **1**.

2.2 Total synthesis

Since 2011, total syntheses of such sugar-morpholine[6,5]-spiroketal pyrrole-derived alkaloids with a furanose ring, e.g., acortatarin B, pollenopyrroside B/ acortatarin A and its 9-epimer (**2**, 9-*epi*-acortatarin A), have been carried out by several research groups.[9-13] However, the total synthesis of such structures with a pyranose ring (e.g., **1**) has so far not been achieved. Only in a total synthetic work towards the synthesis of acortatarin A, a presumed [6,6]-spiro compound was mentioned as a minor impure byproduct.[13] Therefore, we sought a process to synthesize such spiro-alkaloids with a pyranose ring to provide enough material for further *in vivo* bioactivity assays such as anti-depression evaluation.

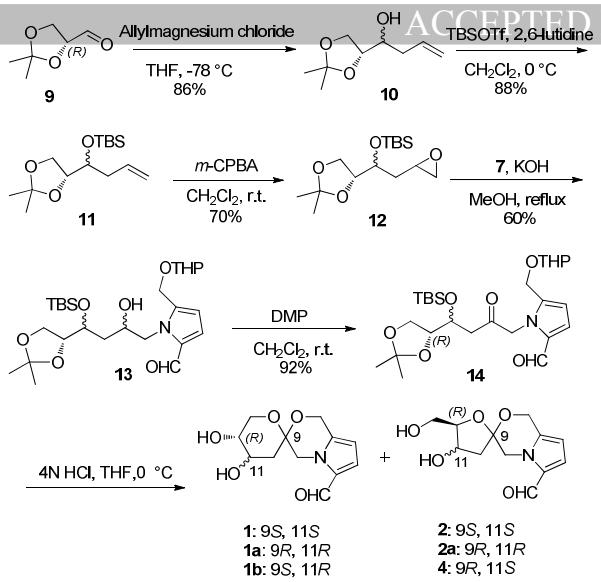
From a retrosynthetic perspective, the [6,6]- (e.g., **1**) and [6,5]- (e.g., **2**) spiroketals could be anticipated and synthesized using the same strategy (Scheme 1), because they would all rely on the spiroketalization of the intermediate **5**. This precursor was envisioned to be available from a protected 2-formyl-5-hydroxymethyl-pyrrole (**7**) by *N*-alkylation with the epoxide **6**,[8,19] which in turn could be generated from the commercially available aldehyde **8**.



Scheme 1. Retrosynthetic analysis for the spiro-alkaloids.

In our first synthetic route, the synthesis of **10** commenced with the commercially available (*R*)-2,2-dimethyl-1,3-dioxolane-4-carbaldehyde (**9**) which was converted to allylic alcohol **10** as an inseparable diastereomeric mixture (*dr* = 5:3, 86% yield) by reaction with allylmagnesium chloride (a Grignard reagent).[20] After the alcohol **10** was protected as its *tert*-butyldimethylsilyl (TBS) ether (**11**) in 88% yield, epoxidation of **11** with *m*-chloroperoxybenzoic acid (*m*-CPBA) gave **12** (70% yield). Subsequent *N*-alkylation[21] of the substituted pyrrole **7** via opening of the epoxide in **12** with KOH/MeOH afforded **13** in a satisfactory yield (60%). Oxidation[22] of the alcohol **13** with Dess-Martin periodinane (DMP) furnished the ketone **14** in 92% yield. The precursor **14** underwent an intramolecular spiroketalization[10,23] in the presence of moderate acidic conditions to deliver a mixture of compounds **1**, **2** and **4**, together with another three new diastereoisomers (**1a**, **1b** and **2a**) (Figure 1 and Scheme 2). Separation of the above six diastereoisomeric spiro-alkaloids was successfully achieved by repeated chromatography on silica gel and followed by semi-preparative HPLC (Figure 5).

Xylapyrrosides A_1 (**1a**) and A_2 (**1b**) were both found by HREIMS to have the same molecular formula ($C_{12}H_{15}NO_5$) as **1**. They also exhibited quite similar ^{1}H and ^{13}C NMR data to those of **1**, and only slight differences around the deoxyketohexose moieties (from C-10 to C-13) could be observed. Further detailed comparison of their COSY and HMBC spectroscopic data (See Supplementary data) with those of **1** revealed that these three compounds possess the same planar structure (Scheme 2) but different relative configurations that can be easily deduced by the observed coupling constants and the NOE correlations. For compound **1a**, the large coupling constants ($J_{H\text{-}10,11}$ = 11.6 Hz; $J_{H\text{-}12,13}$ = 10.7 Hz) indicated both H-11 (δ 3.89) and H-12 (δ 3.50) took axial orientations (i.e., the hydroxyl groups were in opposite orientations and both took equatorial positions). Clear NOE correlations of H-10_{ax} (δ 1.67)/H_2-8 (δ 4.50, 4.04), H-10_{ax}/H-12_{ax} (δ 3.50), H-10_{eq} (δ 2.23)/H-11_{ax} (δ 3.89), and H-11_{ax}/ H-13_{ax} (δ 3.42) were then observed. In a similar way, the relative configuration of compound **1b** was determined as depicted in Scheme 2. The absolute configuration of **1a** was finally unambiguously established as (9*R*,11*R*,12*R*) by Cu*Kα* X-ray crystallographic analysis (Figure 6 and Supplementary data).



Scheme 2. Route1: Synthesis of **1**, **2**, **4**, and related spiro-alkaloids (**1a**, **1b**, **2a**).

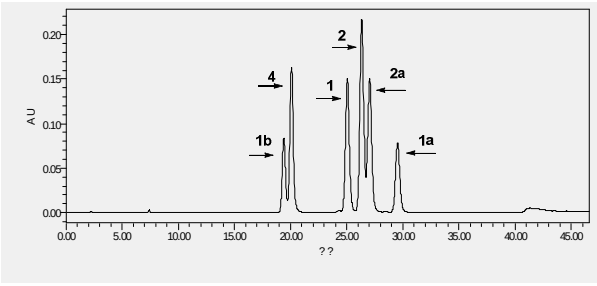


Figure 5. HPLC-PDA profiles of the six synthesized spiro-alkaloids separated on a Fluophase PFP column (7.7 × 250 mm, 5 μm, Thermo): **1** (t_R = 25.1 min), **1a** (t_R = 29.5 min), **1b** (t_R = 19.4 min), **2** (t_R = 26.3 min), **2a** (t_R = 27.0 min), and **4** (t_R = 20.1 min). The PDA detector measured absorbance at 299 nm. The elution program consisted of a linear gradient of methanol in water from 25% to 35% in 35 min, then followed by an isocratic elution with 100% methanol for 15 min (flow rate: 2.0 mL/min).

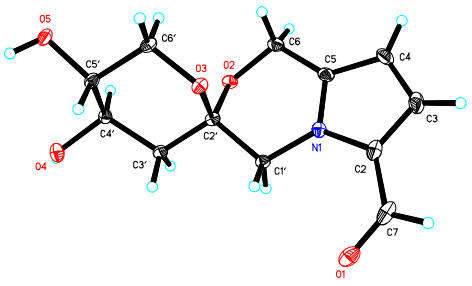
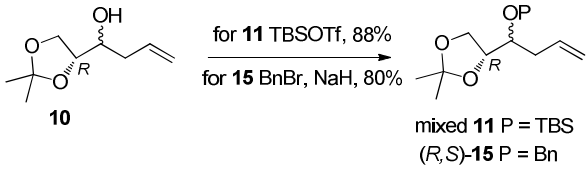


Figure 6. X-ray crystal structure of **1a**.

Xylapyrroside B_1 (**2a**) was also assigned a molecular formula of $C_{12}H_{15}NO_5$ as determined by HR-EIMS, identical with those of compounds **1**−**4**. The ^{1}H and ^{13}C NMR spectra of **2a** resembled those of **2** and **4**,[8-12] in which the deoxyhexose moiety existed as a furanose ring instead of a pyranose ring in **1**. This was supported by the observation of a key HMBC correlation between H-12 (δ 4.14) and C-9 (δ 103.6), as well as the lack of correlation from H_2-13 (δ 3.83 and 3.78) to C-9 (See Supplementary data). Detailed comparison of the NMR data of **2a** with those of **4** suggested that the only difference was the orientation of the hydroxy group at C-11; thus **2a** was assumed to be the 11-epimer of **4**.

Considering that the chiral center at C-12 of the above six synthesized spiro-alkaloids was introduced by the initial chemical (*R*)-**9**, it is reasonable that the absolute configuration at C-12 should be definitively assigned as *R* (Scheme 2). Therefore, the absolute configuration at C-11 of both **1b** and **2a** could be easily determined to be *R* based on the above analysis of their relative configurations. However, due to the shortage of single-crystal data, determination of the absolute configuration at C-9 in **1b** and **2a** seems to be challenging. Interestingly, after careful analysis of the optical rotations of compounds **1**, **1a**, **2**−**4**, and their diastereoisomers reported in the literature,[3-5] we reasoned that the absolute configuration at the spiro-center (C-9) would be the key factor to influence the sign (positive or minus) of the $[\alpha]_D$ values. In general, such sugar-morpholine spiroketal pyrrole-derived alkaloids with a 9*R* configuration all exhibit positive $[\alpha]_D$ values (**1a**: +132; **3**: +65; **4**: +255; capparisine B[3]: +38), while minus values were observed only for those compounds with a 9*S* configuration (**1**: $[\alpha]_D$ −189; **2**: $[\alpha]_D$−187). Accordingly, the absolute configuration at C-9 in **1b** ($[\alpha]_D$ −241) and **2a** ($[\alpha]_D$ +225) could be assigned as 9*S* and 9*R* (Figure 1), respectively.

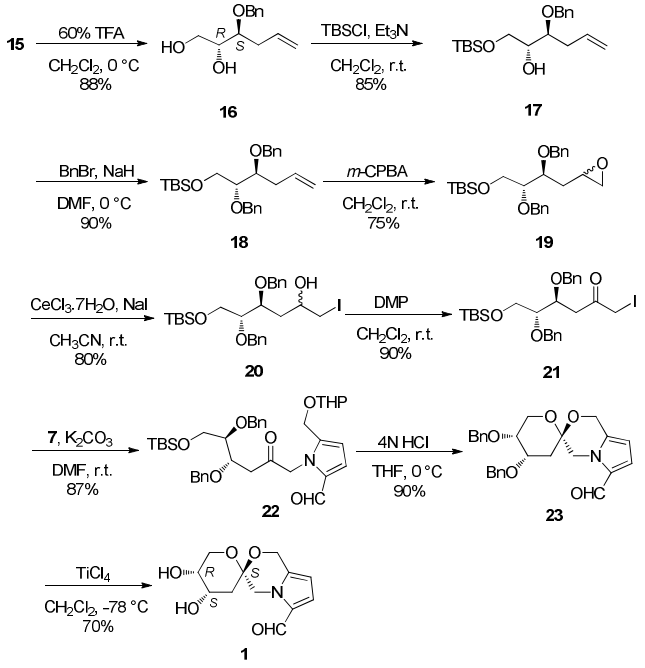
The above synthetic route could efficiently afford the target compounds (only six steps from the commercially available **9**), along with three new analogues (**1a**, **1b**, **2a**) for potential structure-activity relationship (SAR) studies. In Scheme 2, TBS was employed to protect the secondary hydroxyl group in **10**, yielding an inseparable epimeric mixture of **11** (Schemes 2 and 3). Interestingly, when a more rigid protective group (e.g., benzyl) was used instead of TBS, an optical pure product **15** could be obtained as the major product that can be easily separated from its epimer by silica gel CC (Scheme 3). Thus, we explored a second synthetic strategy, which successfully furnished the [6,6]-spiroketal **1** (Scheme 4) or [6,5]-spiroketals **2** and **4** (Scheme 5) with much higher steroselectivity.



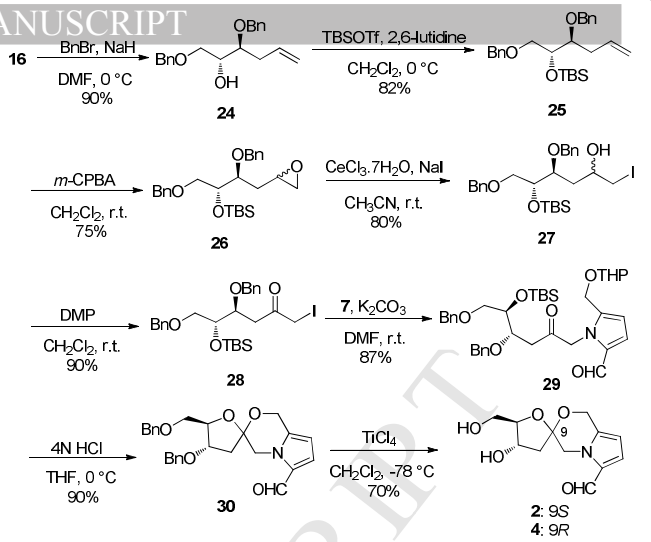
Scheme 3. Different protected groups on the secondary hydroxyl of **10**.

After cleavage of the acetonide by 60% (v/v) TFA, the diol **16** was furnished in 88% yield, and different protective groups were then employed to construct [6,6]- and [6,5]-spiroketals. As shown in Scheme 4, the primary hydroxyl group in **16** was protected with TBS (**17**, 85% yield) and the secondary hydroxyl group was subsequently converted to the benzyl ether **18** (90% yield), which underwent a few steps to proceed the target [6,6]-spiroketal (Scheme 4). In contrast, the [6,5]-spiroketals were constructed by protecting the primary hydroxyl in **16** with benzyl ether (**24**, 75% yield) and the secondary hydroxyl with TBS ether (**25**, 82% yield) followed by a series of reactions (Scheme 5). Actually, subsequent epoxidation of terminal olefins provided **19** and **26** each in 75% yield. Ring opening of the epoxides in the presence of cerous chloride heptahydrate and sodium iodide gave **20** and **27** each in 80% yield,[24] and then the oxidation of both with DMP furnished ketones **21** and **28** each in 90% yield. Treatment of α-iodo ketones and pyrrolederivative **7** with K_2CO_3 in DMF afforded **22** and **29** each in 87% yield.[25] Compound **22** experienced an intramolecular spiroketalization under acidic condition (4N HCl) together with the cleavage of THP and TBS groups, giving **23** as the sole product in a 90% yield, which was then treated with $TiCl_4$ in CH_2Cl_2 to afford **1** (70%) (Scheme 4). Interestingly, the same treatment on compound **29** resulted in a pair of C-9 epimers (**30**, *dr* = 2:1) that finally afforded **2** (37%)

and **4** (32%) (Scheme 5). In our opinion, the large steric hindrance, which may be explained by considering the two possible transition states during the acid catalyzed spiroketalisation of **29**,[26,27] was unfavorable for the production of 9*R*-epimer of **23** by spirocyclization and hence compound **3** could not be obtained. This phenomenon coincided in both synthetic strategies (Schemes 2 and 4), which was also consistent with the previous synthetic work by Teranishi et al.[12]



Scheme 4. Route 2: Stereoselective synthesis of **1**.



Scheme 5. Route 2: Stereoselective synthesis of **2** and **4**.

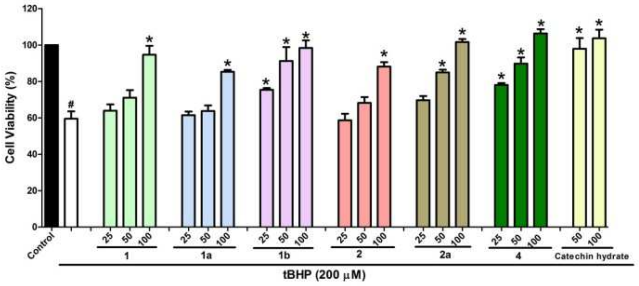


Figure 7. Effects of tested compounds on cell viability of tBHP-stimulated A7r5 cells. Data were generated from at least three independent experiments, and eachperformed in triplicate. $^{\#}p< 0.05$ vs unstimulated cells, $^{*}p< 0.05$ vs tBHP-stimulated cells.

2.3 Antioxidant evaluation

Considering that acortatarin A (**4**) was previously reported to have antioxidant activity,[5,7] the obtained spiro-alkaloids (except the mass-limited **3**) were also evaluated for their antioxidant effects on preventing the oxidative stress-induced cytotoxicity of A7r5 rat vascular smooth muscle cells (VSMCs). Indeed, oxidative stress, generated by excessive reactive oxygen species (ROS), is an important trigger of VSMC apoptosis and has been implicated in the pathogenesis of cardiovascular disorders.[28] As shown in Figure 7, *tert*-butyl hydroperoxide (tBHP), a lipid-soluble source of peroxide radicals employed in this study,[29] caused 40.4% cell death of VSMCs at a concentration of 200 μM. Interestingly, this oxidative stress-induced cytotoxicity was found to be remarkably attenuated by pretreating VSMCs with the spiro-alkaloids and an antioxidant flavonoid (+)-catechin hydrate[30] (positive control). Compared with the tBHP-group, all the tested compounds at 100 μM exhibited significant preventive effects against the tBHP-induced cytotoxicity in VSMCs with viability in the range of 85.3−103.8%. Among them, compounds **4** and **1b** were found to show the most potent anti-oxidative stress activities, i.e., they both could significantly suppress the tBHP-induced apoptosis in VSMCs at all concentrations tested (25, 50, and 100 μM). Moreover, the antioxidant effects of all the spiro-alkaloids were dose-dependent and reached the maximum at 100 μM.

3. Conclusions

In this study, four diastereoisomeric alkaloids (**1**−**4**) with a unique pyrrole-fused morpholine spiroketal architecture, were isolated and identified from the commercially fermented product (Wuling Powder) of *X. nigripes* for the first time. The concise and efficient total syntheses of **1**, **2**, **4** and their analogues were achieved by two alternative strategies. Compared with the known procedures,[8-12] our synthetic procedures possess the following advantages: lower-cost starting material, simple preparation process and higher total yield. Particularly, the total synthesis towards the spiro-alkaloids with a pyranose ring (in the case of **1**, **1a** and **1b**) was reported herein for the first time. The successful total syntheses could not only unambiguously confirm the absolute configurations of the new isolates, but also afford enough samples for future biological screenings. In fact, in order to support the traditional application of Wuling Powder in treating anxiety disorders and depression,[15,16a,17] the well-established mouse behavioral despair tests (i.e., the tail suspension test[31] and the forced swim test[32]) will be used for evaluating the anti-depressant activity of the enriched spiro-alkaloids **1**, **2** and **4**. In the present study, the spiro-alkaloids **4** and **1b** could significantly inhibit the tBHP-induced apoptosis in VSMCs, which would provide new insights into deeper exploration of the unique spiro-alkaloids in drug discovery of cardiovascular diseases, and future studies on the mode of the antioxidant action are needed.

4. Experimental Section

4.1 General information

Optical rotations were measured on a JASCO P-1020 polarimeter. UV and IR spectra were recorded on a Shimadzu UV-2550 and an Avatar 360 ESP FTIR spectrometer, respectively. NMR spectra were recorded on a Varian Mercury Plus 400 MHz and Bruker Avance III 400 or 600 MHz spectrometers. Chemical shifts are expressed in δ (ppm) and referenced to the residual solvent signals. ESI-MS were measured on Waters UPLC H ClassSQD and Agilent 1100 series mass spectrometers; EI-MS was obtained from an Agilent 5975c mass spectrometer. HR-ESI-MS and HR-EI-MS were measured on Bruker Daltonics micrOTOF-QII or Waters Gct Premier mass spectrometers. Semi-preparative HPLC was performed on a Waters e2695 system coupled with a 2998 Photodiode Array Detector (PDA) and a 2424 Evaporating Light Scattering Detector (ELSD), and a Fluophase PFP column (7.7 × 250 nm, 5 μm, Thermo). Column chromatography (CC) was performed using silica gel (200-300 mesh, Kang-Bi-Nuo Silysia Chemical Ltd., Yantai, China) and Sephadex LH-20 (GE Healthcare Bio-Sciences AB, Uppsala, Sweden). Silica gel-precoated plates (GF254, 0.25 mm, Kang-Bi-Nuo Silysia Chemical Ltd., Yantai, China) were used for TLC detection. Spots were visualized using UV light (254 nm) and 15% H_2SO_4-EtOH. All reactions were carried out under an atmosphere of nitrogen or argon unless otherwise specified. All solvents used for column chromatography were of analytical grade (Shanghai Titan Chem Co. Ltd, Shanghai, PR China), and solvents used for HPLC were of HPLC grade (Jiangsu Hanbon Sci. & Tech. Co. Ltd., PR China). All commercially available reagents including the substrates were used as received.

4.2 Isolation of compounds 1−4

The commercially fermented mycelia of *X. nigripes*, also called Wuling Powder, were produced by Zhejiang Jolly Pharmaceutical Company (Deqing County in Zhejiang Province, PR China). In September 2008, the crude samples were dried on site and then shipped to the laboratory, where they were lyophilized upon arrival. A 20 kg aliquot was extracted with 75% EtOH (3 × 20 L) at room temperature to afford a brown residue (1.3 kg), which was suspended in H_2O (2.0 L) and then successively extracted with petroleum ether (PE, 3×1.5 L), EtOAc (3×1.5 L) and *n*-BuOH (3×1.5 L). The EtOAc-soluble fraction (281.6 g) was subjected to silica gel CC (PE/EtOAc, from 20/1 to 2/1, v/v; CH_2Cl_2/MeOH, from 20/1 to 2/1, v/v) to give fifteen fractions (Fr. 1-15). Fr. 11 (3.95 g) was separated by a silica gel column (CH_2Cl_2/MeOH, from 50/1 to 30/1, v/v) to give six sub-fractions (Fr.11A-11F). Fr. 11B (200 mg) was repeatedly chromatographed on silica gel (CH_2Cl_2/MeOH 50:1, v/v) followed by gel permeation chromatography (GPC) on Sephadex LH-20 (MeOH) to furnish compound **4** (20.1 mg). Fr. 11C (140 mg) was first subjected to CC over silica gel (CH_2Cl_2/MeOH 50:1, v/v) and was finally refined by GPC on Sephadex LH-20 (MeOH) to afford compound **1** (4.0 mg). Compounds **2** (21.3 mg) and **3** (1.2 mg) were isolated and purified from Fr. 11D (550 mg) by semi-preparative HPLC on a Fluophase PFP column (MeOH/H_2O, from 25:75 to 35:65 in 40 min, v/v; flow rate: 1.5 mL/min; **2**: t_R = 34.6 min, **3**: t_R = 33.0 min).

Xylapyrroside A (= *ent*-capparisine B, 1): colorless crystal (acetone); $[\alpha]^{22}_D$ −189 (*c* 0.1, MeOH); UV (MeOH) λ_{max} (log ε) 254 (0.62), 296 (2.11) nm; IR (film) ν_{max}: 3408, 1660, 1474, 1036 cm^{-1}; ^{1}H and ^{13}C NMR data see Table 1; (+) ESIMS *m/z* 254 [M + H]$^+$; HREIMS *m/z* 253.0952 [M]$^+$ (calcd for $C_{12}H_{15}NO_5$, 253.0950, Δ = 0.8 ppm).

Xylapyrroside B (= 9-*epi*-acotatarin A,[8-12] 2): colorless gum; $[\alpha]^{22}_D$ −187 (*c* 0.1, MeOH) [lit.[8]: $[\alpha]^{27}_D$ −58 (*c* 0.04, MeOH); lit.[9]: $[\alpha]^{19}_D$ −111 (*c* 1.0, MeOH); lit.[10]: $[\alpha]^{20}_D$ −85 (*c* 0.2, MeOH); lit.[11]: $[\alpha]^{23}_D$ −73 (*c* 0.05, MeOH)]; UV (MeOH) λ_{max} (log ε) 254 (0.36), 296 (1.36) nm; IR (film) ν_{max}: 3336, 1644, 1452, 1046 cm^{-1}; ^{1}H and ^{13}C NMR data (in CD_3OD) see lit.[8]; (+) ESIMS *m/z* 254 [M + H]$^+$; HREIMS *m/z* 253.0951 [M]$^+$ (calcd for $C_{12}H_{15}NO_5$, 253.0950, Δ = 0.4 ppm).

Pollenopyrroside A[4] (3): colorless gum; $[\alpha]^{22}_D$ +65 (*c* 0.01, MeOH) [lit.[4]: $[\alpha]^{20}_D$ +126 (*c* 0.08, MeOH)]; ^{1}H and ^{13}C NMR data (in CD_3OD) are identical with those of literature;[5] (+) ESIMS *m/z* 254 [M+H]$^+$.

Pollenopyrroside B[5] (= acortatarin A,[5,8-12] 4): white powder; $[\alpha]^{22}_D$ +255 (*c* 0.1, MeOH) [lit.[5]: $[\alpha]^{27}_D$ +178 (*c* 0.4, MeOH); lit.[8]: $[\alpha]^{27}_D$ +191 (*c* 0.27, MeOH); lit.[9]: $[\alpha]^{19}_D$ +200 (*c* 0.4, MeOH); lit.[10]: $[\alpha]^{27}_D$ +195 (*c* 0.15, MeOH); lit.[11]: $[\alpha]^{23}_D$ +185 (*c* 0.15, MeOH); lit.[12]: $[\alpha]^{24}_D$ +190 (*c* 0.28, MeOH)]; UV (MeOH) λ_{max} (log ε) 254 (0.58), 296 (2.01) nm; IR (film) ν_{max}: 3326, 1644, 1452, 1035 cm^{-1}; ^{1}H and ^{13}C NMR (in CD_3OD) data see lit.[5,8]; (+) ESIMS *m/z* 254 [M + H]$^+$; HREIMS *m/z* 253.0949 [M]$^+$ (calcd for $C_{12}H_{15}NO_5$, 253.0950, Δ = −0.4 ppm).

4.3 Synthesis

1-((*R*)-2,2-Dimethyl-1,3-dioxolan-4-yl)but-3-en-1-ol (10): To a cooled (-78^{o}C) solution of commercial (*R*)-2,2-dimethyl-1,3-dioxolane-4-carbaldehyde **9** (5.0 g, 38.5 mmol) in anhydrous THF (100 mL), compound **17** (351 mg, 1.0 mmol) was treated with a solution of allylmagnesium chloride in THF (30 mL, 51 mmol, 1.7 M). After being stirred for 3h, the mixture was quenched with a saturated NH_4Cl aqueous solution and warmed to room temperature. Then the mixture was extracted with EtOAc (3 × 50 mL) and the combined organic layers were washed with brine. Dried, filtrated and concentrated, the residue was purified by flash chromatography on silica gel (PE/EtOAc = 10/1) to give an inseparable epimer mixture of **10a** and **10b** (5.68 g, 86%; *dr* = 5:3) as a pale yellow oil. $[\alpha]^{22}_D$ = –25.2 (*c* 0.029, $CHCl_3$); IR (film) ν_{max}: 3402, 2909, 2345, 2328, 1397, 1052, 663 cm^{-1};^{1}H NMR (400 MHz, $CDCl_3$) data of **10a** (major product): δ 5.85 (m), 5.18 (m), 5.13 (m), 4.03 (m), 3.94 (m), 3.78 (m), 2.34 (m), 2.23 (m), 1.44 (s), 1.37 (s) ppm; **10b** (minor product): δ5.85 (m), 5.15 (m), 4.03 (m), 3.76 (m), 3.60 (m), 2.23 (m), 2.18 (m), 1.45 (s), 1.38 (s) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) data of **10a**: δ 134.0, 118.3, 109.1, 78.0, 70.3, 65.2, 37.6, 26.5, 25.2 ppm; **10b**: δ 134.0, 117.9, 109.4, 78.5, 71.6, 66.0, 38.2, 26.6, 25.3 ppm; HREIMS *m/z* 172.1097 [M]$^+$ (calcd for $C_9H_{16}O_3$, 172.1099, Δ = −1.2 ppm).

***Tert*-Butyl((1-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)but-3-en-1-yl)oxy)dimethylsilane (11):** 2,6-Lutidine (5.3 ml, 45.3 mmol) was dropped to a stirred solution of alcohol **10** (3.9 g, 22.7 mmol) in dry CH_2Cl_2 (50 mL) at 0 °C, then TBSOTf (7.8 mL, 34.1 mmol) was dropped and the reaction was stirred 2 h. The mixture was quenched with water and separated. The aqueous layer was extracted with EtOAc (3 × 50 mL) and the combined organic layers were washed with brine. Dried, filtrated and concentrated, the residue was purified by flash chromatography on silica gel (PE/EtOAc = 40/1) to give an inseparable epimer mixture of **11a** and **11b** (*dr* = 5:4). Colorless oil; $[\alpha]^{22}_D$ = +24.7 (*c* 0.049, $CHCl_3$); IR (film) ν_{max}: 2942, 2368, 2334, 1441, 1265, 1090, 821,646 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) data of **11a**: δ 5.84 (m), 5.09 (m), 5.05 (m), 3.96 (m), 3.81 (m), 2.29 (m), 1.39 (s), 1.33 (s), 0.88 (s), 0.07 (s), 0.06 (s); **11b**: δ 5.83 (m), 5.04 (m), 4.05 (dd, *J* = 13.1, 6.6 Hz), 3.96 (m), 3.74 (m), 2.27 (m), 2.10 (ddd, *J* = 14.0, 7.5. 7.0 Hz), 1.41 (s), 1.34 (s), 0.88 (s), 0.07 (s), 0.05 (s) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) data of **11a**: δ 134.1, 117.5, 108.8, 77.8, 72.1, 66.1, 39.2, 26.7, 25.9×3, 25.5, 18.1, -4.2, -4.5; **11b**: δ 135.1, 117.1, 109.1, 78.4, 73.1, 65.4, 37.5,

25.8×3, 26.5, 25.3, 18.2, –4.4, –4.6 ppm; (+) HRESIMS *m/z* 309.1859 $[M+Na]^+$ (calcd for $C_{15}H_{30}O_3SiNa$, 309.1862, Δ = −0.9 ppm).

***Tert*-Butyl(1-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)-2-(oxiran-2-yl)ethoxy)dimethylsilane (12):** To a cooled solution (0 °C) of the ether **11** (3.0 g, 10.5 mmol) in dry CH_2Cl_2 (30 mL) was added *m*-CPBA (2.17 g, 12.6 mmol) in one portion. After stirring for overnight at r.t, the reaction was quenched with a solution of saturated $NaHSO_3$ aqueous solution and stirred for 10 min. Then the mixture was separated and the aqueous layer was extracted with CH_2Cl_2 (3× 50 mL). The combined organic layers were washed with saturated aqueous $NaHCO_3$ solution and brine. Dried, filtrated and concentrated, the residue was purified by flash chromatography on silica gel (PE/EtOAc = 20/1) to give **12** (2.2 g, 70%; containing four inseparable diastereomers) as colorless oil. $[\alpha]^{22}_D$ = +60 (*c* 0.015, $CHCl_3$); IR (film) ν_{max}: 2920, 2854, 2372, 1386, 1265, 1073, 838 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): *δ* 4.14-3.69 (m, 4H), 3.15-3.04 (m, 1H), 2.83-2.76 (m, 1H), 2.55-2.46 (m, 1H), 1.84-1.54 (m, 2H), 1.41-1.40 (Me, 3H), 1.35-1.34 (Me, 3H), 0.90 [Si-C-$(CH_3)_3$, 9H], 0.12-0.07 [$Si(CH_3)_2$, 6H] ppm; ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 109.2, 109.1, 109.0, 108.9; 78.3, 78.3, 78.3, 78.2; 71.5, 70.9, 70.7, 70.7; 66.5, 66.3, 65.4, 65.1; 49.5, 49.3, 48.8, 48.6; 47.9, 47.5, 46.7, 46.6; 38.0, 37.6, 36.3, 35.5; 26.7, 26.5, 26.4, 26.3; 25.7×6, 25.6×6; 25.3, 25.1, 25.0, 24.3; 18.0, 18.0, 17.9, 17.9; –4.4, –4.5, –4.7, –5.0 ppm; HREIMS *m/z* 302.1911 $[M]^+$ (calcd for $C_{15}H_{30}O_4Si$, 302.1913, Δ = −0.7 ppm).

1-(4-((*tert*-Butyldimethylsilyl)oxy)-4-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)-2-hydroxybutyl)-5-(((tetrahydro-2*H*-pyran-2-yl)oxy)methyl)-1*H*-pyrrole-2-carbaldehyde (13): To a suspension of KOH (37 mg, 0.66 mmol) in dry MeOH (5 mL) was added pyrrole **7** (0.55 g, 2.63 mmol; for preparation procedurs, see Supplementary data) under N_2 atmosphere at r.t. Then a solution of epoxide **12** (1.0 g, 3.3 mmol) in MeOH was dropped and the reaction was refluxed for 48h. After cooling, the mixture was quenched with water and extracted with EtOAc (4× 50 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated. The crude was purified by chromatography on silica gel (PE/EtOAc = 8/1) to give **13** (0.93 g, 55%; containing eight inseparable diastereomers) as a pale yellow oil. $[\alpha]^{22}_D$ = +10.5 (*c* 0.1, $CHCl_3$); IR (film) ν_{max}: 3254, 2904, 2849, 1654, 1189, 1008, 767 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): *δ* 9.50–9.49 (CHO, 1H), 6.92 (d, *J* = 3.9 Hz, 1H), 6.29 (d, *J* = 3.8 Hz, 1H), 4.91-4.51 (m, 4H), 4.29-3.68 (m, 6H), 3.62-3.06 (m, 2H), 1.88-1.53 (m, 8H), 1.41-1.33 (2×CH_3, 6H), 0.87 ($C(CH_3)_3$, 9H), 0.14-0.05 ($Si(CH_3)_2$, 6H) ppm; HREIMS *m/z* 511.2968 $[M]^+$ (calcd for $C_{26}H_{45}NO_7Si$, 511.2965, Δ = 0.6 ppm).

1-(4-((*tert*-Butyldimethylsilyl)oxy)-4-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)-2-oxobutyl)-5-(((tetrahydro-2*H*-pyran-2-yl)oxy)methyl)-1H-pyrrole-2-carbaldehyde (14): To a cooled solution (0 °C) of alcohol **13** (2.4 g, 4.7 mmol) in dry CH_2Cl_2 (30 mL) was added DMP (3.98 g, 9.4 mmol) in one portion and stirred for 3h. Then the reaction was carefully quenched with a solution of mixture (V/V = 50: 50) saturated aqueous $NaHCO_3$ and $Na_2S_2O_3$ solution until the mixture turned a clear solution. Then the resulting mixture was separated and the the aqueous layer was extracted with CH_2Cl_2 (2× 50 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtrated and concentrated. The residue was purified by flash chromatography on silica gel (PE/EtOAc = 8/1) to obtain the ketone **14** (2.2 g, 92%; containing four inseparable diastereomers) as a colorless oil. $[\alpha]^{22}_D$ = +13.3 (*c* 0.07, $CHCl_3$); IR (film) ν_{max}: 3354, 2920, 2843, 2357, 1654, 1068, 663 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): *δ* 9.46 (s, 1H), 6.91 (d, *J* = 3.9 Hz, 1H), 6.30 (d, *J* = 3.9 Hz, 1H), 5.28 (d, *J* = 11.2 Hz, 1H, CH_aN), 4.60 (d, *J* = 11.2 Hz, 1H, CH_bN), 4.60-4.32 (m, 3H), 4.24-4.10 (m, 1H), 4.00 (m, 2H), 3.80 (m, 2H), 3.50 (m, 1H), 2.88-2.82 (m, 1H), 2.75-2.60 (m, 1H), 1.83-1.48 (m, 6H), 1.36-1.32 (2×CH_3, 6H), 0.85 (s, 9H; $C(CH_3)_3$), 0.10-0.09 ($Si(CH_3)$, 3H), 0.06-0.04 ($Si(CH_3)_2$, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 202.1, 202.0, 201.7, 201.6, 179.8 (3C) 178.3, 138.9, 138.8 (2C), 138.7, 132.5 (3C), 131.1, 123.7 (2C), 123.6, 122.3, 111.8, 111.7 (2C), 111.6, 109.2 (3C), 107.9, 97.2, 97.1, 97.0, 95.9, 78.6, 78.5, 77.3, 77.2, 76.0, 75.9, 75.6, 75.3, 68.9, 68.7, 67.8, 67.7, 66.6, 65.2, 65.0, 64.9, 62.5 (2C), 62.4, 62.3, 59.3 (2C), 59.2 (2C); 55.2 (2C), 55.1, 53.8, 45.3, 45.2, 43.0, 42.8, 30.1 (3C), 28.9, 26.3 (2C), 26.2, 25.7 (7C), 25.1 (3C), 24.9, 24.8, 24.3, 19.4, 19.3, 19.2, 19.1, 17.9 (2C), 17.3 (2C), –4.5 (2C), –4.9 (2C), –5.0 (4C) ppm; HREIMS *m/z* 509.2811 $[M]^+$ (calcd for $C_{26}H_{43}NO_7Si$, 509.2809, Δ = 0.4 ppm).

Xylapyrrosides A (1), B (2) and their analogues (Method 1): To compound **14** (3.9 g, 7.7 mmol) in THF (50 mL) was dropped a solution of 4N HCl (7.8 mL, 30.8mmol) at 0 °C. After stirring for 4h, the mixture was carefully neutralized with a saturated aqueous $NaHCO_3$ solution and extracted with EtOAc (4 × 50 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$, filtrated and concentrated. Analysis of the product by HPLC with a Fluophase PFP column (a linear gradient of MeOH in water from 25% to 35% over 35 min, then followed by isocratic elution with 100% methanol; flow rate: 2.0 mL/min) clearly revealed the presence of six compounds (Figure 6, detection by PDA at 299 nm), which were isolated by repeated chromatography on silica gel and semi-preparative HPLC with the Fluophase PFP column. The synthesized xylappyrosides A (**1**) and B (**2**), and pollenopyrroside B (**4**) showed physical and spectroscopic characteristics equivalent to the natural products.

Xylapyrroside A_1 (1a): colorless crystal (acetone); $[\alpha]^{22}_D$ +132 (*c* 0.1, MeOH); UV (MeOH) λ_{max} (log ε) 254 (0.59), 295 (2.15) nm; IR (film) ν_{max}: 3375, 1633, 1402, 1024 cm^{-1}; ^1H NMR (400 MHz, CD_3OD): *δ* 9.38 (s, H-7), 7.04 (d, *J* = 4.0 Hz, H-3), 6.09 (d, *J* = 4.0 Hz, H-4), 4.86 (d, *J* = 15.8 Hz, H-6_a), 4.78 (d, *J* = 15.8 Hz, H-6_b), 4.50 (d, *J* = 14.0 Hz, H-8_a), 4.04 (d, *J* = 14.0 Hz, H-8_b), 3.89 (ddd, *J* = 11.2, 8.8, 5.2 Hz, H-11), 3.73 (dd, *J* = 10.4, 5.2 Hz, H-13_a), 3.50 (ddd, *J* = 10.4, 8.8, 5.2 Hz, H-12), 3.42 (dd, *J* = 10.4, 10.4 Hz, H-13_b), 2.23 (dd, *J* = 13.2, 5.2 Hz, H-10_a), 1.67 (dd, *J* = 13.2, 11.2 Hz, H-10_b); ^{13}C NMR (100 MHz, CD_3OD): *δ* 132.4 (C-2), 126.0 (C-3), 106.2 (C-4), 136.9 (C-5), 58.2 (C-6), 180.2 (C-7), 53.1 (C-8), 96.7 (C-9), 41.2 (C-10), 72.3 (C-11), 70.0 (C-12), 65.2 (C-13); ^1H NMR (400 MHz, Acetone-d_6): *δ* 9.46 (s, H-7), 6.97 (d, *J* = 4.0 Hz, H-3), 6.06 (d, *J* = 4.0 Hz, H-4), 4.86 (d, *J* = 15.6 Hz, H-6_a), 4.76 (d, *J* = 15.6 Hz, H-6_b), 4.49 (d, *J* = 14.0 Hz, H-8_a), 4.01 (d, *J* = 14.0 Hz, H-8_b), 3.87 (ddd, *J* = 11.6, 8.8, 5.6 Hz, H-11), 3.68 (dd, *J* = 10.8, 5.2 Hz, H-13_a), 3.51 (ddd, *J* = 10.4, 8.8, 5.2 Hz, H-12), 3.38 (dd, *J* = 10.8, 10.4 Hz, H-13_b), 2.20 (dd, *J* = 13.2, 5.6 Hz, H-10_a), 1.68 (dd, *J* = 13.2, 11.6 Hz, H-10_b); ^1H NMR (400 MHz, $CDCl_3$): *δ* 9.43 (s, H-7), 6.90 (d, *J* = 4.0 Hz, H-3), 5.99 (d, *J* = 4.0 Hz, H-4), 4.79 (d, *J* = 15.6 Hz, H-6_a), 4.74 (d, *J* = 15.6 Hz, H-6_b), 4.59 (d, *J* = 14.4 Hz, H-8_a), 4.03 (d, *J* = 14.0 Hz, H-8_b), 4.00 (ddd, overlapped, H-11), 3.80 (dd, *J* = 10.8, 5.2 Hz, H-13_a), 3.62 (ddd, *J* = 10.4, 8.8, 5.2 Hz, H-12), 3.43 (t-like, *J* = 10.4 Hz, H-13_b), 2.24 (dd, *J* = 12.8, 5.2 Hz, H-10_a), 1.70 (dd, *J* = 12.8, 11.2 Hz, H-10_b); (+) ESIMS *m/z* 254 $[M+H]^+$; HREIMS *m/z* 253.0949 $[M]^+$ (calcd for $C_{12}H_{15}NO_5$, 253.0950, Δ = −0.4 ppm).

Xylapyrroside A_2 (1b): white powder; $[\alpha]^{22}_D$ −241 (*c* 0.1, MeOH); UV (MeOH) λ_{max} (log ε) 254 (0.50), 296 (1.86) nm; IR (film) ν_{max}: 3419, 1633, 1447, 1025 cm^{-1}; ^1H NMR (400 MHz, CD_3OD): *δ* 9.38 (s, H-7), 7.03 (d, *J* = 4.4 Hz, H-3), 6.08 (d, *J* =

4.4 Hz, H-4), 4.89 (d, *J* = 16.0 Hz, H-6_a), 4.82 (d, *J* = 16.0 Hz, H-6_b), 4.60 (d, *J* = 14.0 Hz, H-8_a), 4.16 (dd, *J* = 12.2, 1.6 Hz, H-13_a), 3.95 (d, *J* = 14.0 Hz, H-8_b), 3.91 (m, H-11), 3.61 (br d, *J* = 12.2 Hz, H-13_b), 3.57 (m, H-12),2.20 (dd, *J* = 14.6, 4.4 Hz, H-10_a), 1.92 (dd, *J* = 14.6, 2.8 Hz, H-10_b); ^{13}C NMR (100 MHz, CD_3OD): *δ* 132.4 (C-2), 125.8 (C-3), 106.1 (C-4), 136.9 (C-5), 58.6 (C-6), 180.2 (C-7), 53.2 (C-8), 95.3 (C-9), 34.6 (C-10), 68.6 (C-11), 68.0 (C-12), 62.4 (C-13); ^{1}H NMR (400 MHz, Acetone-d_6): *δ* 9.46 (s, H-7), 6.97 (d, *J* = 4.0 Hz, H-3), 6.06 (d, *J* = 4.0 Hz, H-4), 4.92 (d, *J* = 16.0 Hz, H-6_a), 4.84 (d, *J* = 16.0 Hz, H-6_b), 4.57 (d, *J* = 14.0 Hz, H-8_a), 4.15 (dd, *J* = 12.0, 1.2 Hz, H-13_a), 3.93 (d, *J* = 14.0 Hz, H-8_b), 3.85 (m, H-11), 3.60 (br d, *J* = 12.0 Hz, H-13_b), 3.56 (m, H-12), 2.27 (dd, *J* = 14.4, 4.0 Hz, H-10_a), 1.90 (dd, *J* = 14.4, 3.0 Hz, H-10_b); ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 9.41 (s, H-7), 6.90 (d, *J* = 4.0 Hz, H-3), 6.00 (d, *J* = 4.0 Hz, H-4), 4.87 (d, *J* = 15.6 Hz, H-6_a), 4.82 (d, *J* = 15.6 Hz, H-6_b), 4.66 (d, *J* = 14.0 Hz, H-8_a), 4.14 (br d, *J* = 11.6 Hz, H-13_a), 3.99 (d, *J* = 14.0 Hz, H-8_b), 3.95 (m, H-11), 3.70 (br d, *J* = 11.6 Hz, H-13_b), 3.72 (m, H-12), 2.27 (dd, *J* = 14.8, 4.0 Hz, H-10_a), 1.94 (dd, *J* = 14.8, 2.4 Hz, H-10_b); (+) ESIMS *m*/*z* 254 $[M+H]^+$; HREIMS *m*/*z* 253.0952 $[M]^+$ (calcd for $C_{12}H_{15}NO_5$, 253.0950, Δ = 0.8 ppm).

Xylapyrroside B_1 (2a): colorless gum; $[\alpha]^{22}_D$ +225 (*c* 0.1, MeOH); UV (MeOH) λ_{max} (log ε) 255 (0.85), 296 (2.54) nm; IR (film) ν_{max}: 3364, 1644, 1468, 1035 cm^{-1}; ^{1}H NMR (600 MHz, CD_3OD): *δ* 9.39 (s, H-7), 7.04 (d, *J* = 4.1 Hz, H-3), 6.08 (d, *J* = 4.1 Hz, H-4), 5.00 (d, *J* = 15.6 Hz, H-6_a), 4.83 (d, *J* = 15.6 Hz, H-6_b), 4.75 (d, *J* = 14.0 Hz, H-8_a), 4.53 (ddd, *J* = 6.9, 4.2, 2.9 Hz, H-11), 4.27 (d, *J* = 14.0 Hz, H-8_b), 4.14 (ddd, *J* = 6.8, 4.4, 4.2 Hz, H-12), 3.83 (dd, *J* = 12.0, 4.4 Hz, H-13_a), 3.78 (dd, *J* = 12.0, 6.8 Hz, H-13_b), 2.56 (dd, *J* = 14.5, 6.8 Hz, H-10_a), 2.08 (dd, *J* = 14.5, 2.9 Hz, H-10_b); ^{13}C NMR (150 MHz, CD_3OD): *δ* 132.4 (C-2), 126.1 (C-3), 106.1 (C-4), 137.5 (C-5), 59.2 (C-6), 180.2 (C-7), 52.7 (C-8), 103.6 (C-9), 47.5 (C-10), 72.1 (C-11), 84.6 (C-12), 61.8 (C-13); (+) ESIMS *m*/*z* 254 $[M+H]^+$; HREIMS *m*/*z* 253.0951 $[M]^+$ (calcd for $C_{12}H_{15}NO_5$, 253.0950, Δ = 0.4 ppm).

(*R*)-4-((*S*)-1-(Benzyloxy)but-3-en-1-yl)-2,2-dimethyl-1,3-dioxolane (15): To a stirred solution of alcohol **10** (5.0 g, 29.1 mmol) in anhydrous DMF (50 mL) at 0 °C was added sodium hydride (2.55 g, 64.0 mmol) in two portions and stirred for 30 min, then benzyl bromide (5.2 mL, 43.6 mmol) was added dropwise at the same temperature. After being stirred for 1h at 0-5 °C, the mixture was poured into crushed ice and stirred until the ice disappear. The resulting mixture was extracted with EtOAc (3 × 100 mL) and the combined organic layers were washed with brine, dried over $MgSO_4$, filtrated and concentrated. The residue was purified by flash chromatography on silica gel (PE/EtOAc = 40/1) to give **15** (6.1 g, 80%) and *epi*-**15** (0.7 g, 9.2%). **15** (major product): $[\alpha]^{22}_D$ = +14.6 (*c* 0.1, $CHCl_3$); IR (film) ν_{max}: 2975, 1463, 1254, 1210, 909, 734, 684 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.45–7.29 (m, 5H), 5.97 (ddt, *J* = 17.2, 10.1, 7.1 Hz, 1H), 5.22 (dq, *J* = 17.2, 1.5 Hz, 1H), 5.17 (br d, *J* = 10.2 Hz, 1H), 4.72 (d, *J* = 11.4 Hz, 1H), 4.65 (d, *J* = 11.4 Hz, 1H), 4.17 (ddd, *J* = 6.4, 6.3, 5.9 Hz, 1H), 4.10 (dd, *J* = 8.1, 6.3 Hz, 1H), 3.96 (dd, *J* = 8.1, 6.4 Hz, 1H), 3.64 (dd, *J* = 10.8, 5.9 Hz, 1H), 2.50 (m, 1H), 2.41 (m, 1H), 1.49 (s, 3H), 1.42 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 138.4, 134.2, 128.3 (2C), 127.8, 127.6 (2C), 117.5, 109.0, 78.9, 77.2, 72.5, 66.4, 35.6, 26.7, 25.4 ppm; (+) HRESIMS *m*/*z* 285.1456 $[M+Na]^+$ (calcd for $C_{16}H_{22}O_3Na$, 285.1461, Δ = −1.7 ppm).

(2*R*,3*S*)-3-(Benzyloxy)hex-5-ene-1,2-diol (16): To a solution of **15** (1.0 g, 3.8 mmol) in CH_2Cl_2 (10 mL) was dropped 60% trifluoroacetic acid (5 mL) at 0 °C and stirred for 2h. Then the reaction was carefully quenched with saturated aqueous $NaHCO_3$ solution and the solvent was removed in vacuo. The aqueous layer was extracted with EtOAc (4 × 30 mL) and the combined organic layers were washed with brine, dried over $MgSO_4$, filtrated and concentrated. The residue was purified by flash chromatography on silica gel (PE/EtOAc = 2/1) to produce diol **16** (0.75 g, 88%) as a colorless oil. $[\alpha]^{22}_D$ = –5.6 (*c* 0.1, $CHCl_3$); IR (film) ν_{max}: 3324, 2888, 1651, 1467, 1359, 1113, 842 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.41–7.29 (m, 5H), 5.92 (ddt, *J* = 17.2, 10.2, 7.1 Hz, 1H), 5.19 (dq, *J* = 17.2, 1.5 Hz, 1H), 5.14 (br d, *J* = 10.2 Hz, 1H), 4.65 (d, *J* = 11.4 Hz, 1H), 4.55 (d, *J* = 11.4 Hz, 1H), 3.88–3.65 (m, 5H), 3.56 (m, 1H), 2.45 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 138.1, 134.4, 128.4 (2C), 127.9, 127.8 (2C), 117.6, 79.9, 72.7, 72.3, 63.5, 34.9 ppm; (+) HRESIMS *m*/*z* 245.1157 $[M+Na]^+$ (calcd for $C_{13}H_{18}O_3Na$, 245.1154, Δ = 1.2 ppm).

(2*R*,3*S*)-3-(Benzyloxy)-1-((*tert*-butyldimethylsilyl)oxy)hex-5-en-2-ol (17): To a stirred solution of diol **16** (6.0 g, 27 mmol) and dimethylaminopyridine (0.82 g, 6.75 mmol) in dry CH_2Cl_2 (100 mL) was continuously added triethylamine (7.5 mL, 81 mmol) and *tert*-butyldimethylsilyl chloride (4.95 g, 32.4 mmol) at 0 °C. After stirring for overnight at r.t., the reaction was quenched with water and separated. The aqueous layer was extracted with CH_2Cl_2 (3× 100 mL) and the combined organic layers were washed with a solution of 1M $KHSO_4$ and brine. Dried, filtrated and concentrated, the residual oil was purified by column chromatography on silica gel (PE/EtOAc = 8/1) to generate **17** (7.7 g, 85%) as a colorless oil. $[\alpha]^{22}_D$ = –12.3 (*c* 0.05, $CHCl_3$); IR (film) ν_{max}: 3301, 2915, 2849, 2367, 1249, 1079, 832 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): *δ*7.37–7.29 (m, 5H), 5.94 (ddt, *J* = 17.2, 10.2, 7.1 Hz, 1H), 5.17 (br d, *J* = 17.2 Hz, 1H), 5.10 (br d, *J* = 10.2 Hz, 1H), 4.65 (d, *J* = 11.6 Hz, 1H), 4.53 (d, *J* = 11.6 Hz, 1H), 3.77 (m, 1H), 3.70 (m, 2H), 3.53 (m, 1H), 2.47 (m, 2H), 0.91 (s, 9H), 0.08 (s, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 138.3, 134.8, 128.4 (2C), 127.9 (2C), 127.7, 117.3, 80.5, 73.8, 72.8, 64.0, 35.6, 25.8 (3C), 18.0, –4.4, –4.6 ppm; (+) HRESIMS *m*/*z* 359.2019 $[M+Na]^+$ (calcd for $C_{19}H_{32}O_3SiNa$, 359.2018, Δ = 0.3 ppm).

(((2*R*,3*S*)-2,3-Bis(benzyloxy)hex-5-en-1-yl)oxy)(*tert*-butyl) dimethylsilane (18): To a stirred solution of alcohol **17** (7.5 g, 22.3 mmol) in anhydrous DMF (80 mL) was added sodium hydride (1.82 g, 44.6 mmol) in three portions at 0 °C and stirred for 30 min. Then benzyl bromide (4.13 mL, 26.8 mmol) was added dropwise and the reaction was stirred for 1h at 0-5 °C. The resulting mixture was poured into ice water. The aqueous layer was extracted with EtOAc (3× 150 mL) and the combined organic layers were washed with water, brine, dried over $MgSO_4$, filtrated and concentrated. The residual oil was purified by column chromatography on silica gel (PE/EtOAc = 40/1) to afford **18** (8.5 g, 90%) as a colorless oil. $[\alpha]^{22}_D$ = –29.1 (*c* 0.06, $CHCl_3$); IR (film) ν_{max}: 2931, 2854, 2359, 2334, 1095, 832, 695 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.37–7.28 (m, 10H), 5.90 (ddt, *J* = 17.2, 10.1, 7.1 Hz, 1H), 5.12 (br d, *J* = 17.2 Hz, 1H), 5.06 (br d, *J* = 10.1 Hz, 1H), 4.76 (d, *J* = 11.8 Hz, 1H), 4.65 (d, *J* = 11.8 Hz, 1H),4.60 (s, 2H), 3.86 (dd, *J* = 10.9, 4.2 Hz, 1H), 3.79 (dd, *J* = 10.9, 5.3 Hz, 1H), 3.68 (m, 1H), 3.60 (ddd, *J* = 5.6, 5.3, 4.2 Hz, 1H), 2.45 (m, 2H), 0.92 (s, 9H), 0.07 (s, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): *δ*138.8, 138.6, 135.4, 128.3 (4C), 127.9 (2C), 127.8 (2C), 127.5, 127.4, 116.9, 80.9, 78.5, 72.7, 72.2, 62.8, 35.0, 25.9×3, 18.3, –5.3, –5.4 ppm; (+) HRESIMS *m*/*z* 449.2487 $[M+Na]^+$ (calcd for $C_{26}H_{38}O_3SiNa$, 449.2488, Δ = −0.2 ppm).

((2*R*,3*S*)-2,3-Bis(benzyloxy)-4-(oxiran-2-yl)butoxy)(*tert*-butyl)dimethylsilane (19): To a stirred solution of the TBS protected compound **18** (4.6 g,10.7 mmol) in dry CH_2Cl_2 (50mL) was added *m*-CPBA (3.2 g, 12.8 mmol) in one portion at 0 °C.

After being stirred for overnight at r.t., the reaction was quenched with saturated aqueous $NaHSO_3$ solution and stirred for another 10min. The resulting mixture was separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were washed with saturated aqueous $NaHCO_3$ solution and brine. Dried over $MgSO_4$, filtrated and concentrated, the residue was purified by flash chromatography on silica gel (PE/EtOAc = 20/1) to give the corresponding epoxide as an inseparable epimeric mixture of **19a** and **19b** (3.6 g, 75%; *dr* = 2:1). Colorless oil; $[\alpha]^{22}_D$ = +10.9 (*c* 0.05, $CHCl_3$); IR (film) ν_{max}: 2926, 2854, 1380, 1256, 1210, 1106, 778 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) data assignable to **19a**: δ 7.37-7.29 (m), 4.73 (d, *J* = 11.4 Hz), 4.57 (d, *J* = 11.4 Hz), 4.58-4.48 (m), 4.00 (m), 3.79 (ddd, *J* = 9.6, 3.1, 3.0 Hz), 3.50 (d, *J* = 5.2 Hz), 3.07 (m), 2.79 (dd, *J* = 4.7, 4.2 Hz), 2.51 (dd, *J* = 5.2, 2.7 Hz), 1.89 (ddd, *J* = 14.3, 9.6, 4.4 Hz), 1.57 (ddd, *J* = 14.3, 7.3, 3.0 Hz), 0.89 (s), 0.07 (s), 0.06 (s) ppm; **19b**: δ 7.37–7.29 (m), 4.66 (d, *J* = 11.6 Hz), 4.58–4.48 (m), 4.50 (d, *J* = 12.4 Hz), 4.00 (m), 3.70 (m), 3.53 (d, *J* = 5.2 Hz), 3.07 (m), 2.79 (dd, *J* = 4.6, 4.4 Hz), 2.42 (dd, *J* = 5.0, 2.7 Hz), 1.99 (ddd, *J* = 14.3, 7.6, 5.1 Hz), 1.65 (ddd, *J* = 14.3, 6.1, 3.9 Hz), 0.90 (s), 0.08 (s), 0.07 (s) ppm;^{13}C NMR (100 MHz, $CDCl_3$): δ138.6, 138.5, 138.2, 128.3 (2C) 127.9, 127.8, 127.7 (2C), 127.6, 78.6, 78.4, 73.3, 73.2, 73.1, 72.8, 72.2, 71.8, 71.7, 50.3, 50.2, 47.9, 47.0, 34.1, 33.6, 25.9, 18.2, –4.5, –4.8 ppm;(+) HRESIMS *m/z* 465.2428 $[M+Na]^+$ (calcd for $C_{26}H_{38}O_4SiNa$, 465.2437, Δ = −1.9 ppm).

(4*S*,5*R*)-4,5-Bis(benzyloxy)-6-((*tert*-butyldimethylsilyl)oxy)-1-iodohexan-2-ol (20): To a solution of epoxide **19** (2.0 g, 4.5 mmol) and cerium chloride heptahydrate (2 g, 5.4 mmol) in CH_3CN (20 mL) was added sodium iodide (0.81 g, 5.4 mmol). After stirring for 5 h, the mixture was concentrated in *vacuo* to give crude product, which was purified by flash chromatography on silica gel (PE/EtOAc = 15/1) to give **20** (2.1 g, 80%; *dr* = 2:1) as colorless oil. $[\alpha]^{22}_D$ = +12.5 (*c* 0.075, $CHCl_3$); IR (film) ν_{max}: 3331, 2926, 2849, 1463, 1260, 1057, 827 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ7.46-7.30 (m, 10H), 4.81-4.68 (m, 2H), 4.61-4.52 (m, 2H), 4.13 (ddd, *J* = 6.0, 5.8, 2.4 Hz, 0.34H), 4.09 (ddd, *J* = 5.2, 5.0, 3.2 Hz, 0.66H), 4.00-3.87 (m, 1H), 3.86-3.72 (m, 2H), 3.57-3.52 (m, 1H), 3.31-3.16 (m, 2H), 2.03-1.73 (m, 2H), 0.96-0.94 (9H), 0.14-0.10 (6H) ppm; ^{13}C NMR (100 MHz, CD_3OD): δ 140.1, 139.7, 129.4, 129.3, 129.0, 128.9, 128.8, 128.7, 128.6, 79.4, 74.8, 74.4, 74.0, 73.2, 68.9, 38.9, 38.5, 26.4, 19.1, 14.9, –4.3, –4.4, –5.1 ppm; (+) HRESIMS *m/z* 593.1562 $[M+Na]^+$ (calcd for $C_{26}H_{39}IO_4SiNa$, 593.1565, Δ = −0.5 ppm).

(4*S*,5*R*)-4,5-Bis(benzyloxy)-6-((*tert*-butyldimethylsilyl)oxy)-1-iodohexan-2-one (21): Alcohol **20** (2.0 g, 3.5 mmol) was dissolved in dry CH_2Cl_2 (20 mL) at 0 °C then, DMP (2.98 g, 7.0 mmol) was added in one portion and the mixture was stirred for 3h. A mixture of saturated aqueous $NaHCO_3$ and $Na_2S_2O_3$ solution (V/V = 50:50) was carefully dropped and the resulting mixture was stirred until turned to clear. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 100 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtrated and concentrated to give crude aldehyde, which was purified by flash chromatography on silica gel (PE/EtOAc = 8/1) to produce ketone **21** (1.8 g, 90%) as a colorless oil. $[\alpha]^{22}_D$ = +9.9 (*c* 0.139, $CHCl_3$); IR (film) ν_{max}: 3441, 2942, 2843, 1720, 1375, 1095, 843 cm^{-1}; ^1H NMR (400 MHz, CD_3OD): δ 7.40-7.28 (m, 10H), 4.72 (d, *J* = 11.8 Hz, 1H), 4.63 (d, *J* = 11.8 Hz, 1H), 4.59 (s, 2H), 4.19 (m, 1H), 4.09 (m, 1H), 3.91 (s, 2H), 3.79 (dd, *J* = 10.6, 5.2 Hz, 1H), 3.65 (dd, *J* = 10.6, 6.1Hz, 1H), 3.09 (dd, *J* = 16.6, 8.2 Hz, 1H), 2.99 (dd, *J* = 16.6, 3.7 Hz, 1H), 0.93 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H) ppm; ^{13}C NMR (100 MHz, CD_3OD): δ 203.7, 139.9, 139.6, 129.4, 129.3, 129.1, 129.0, 128.8, 128.7, 81.9, 77.2, 73.7, 73.6, 63.3, 41.7, 26.4, 19.1, 7.8, –5.3, –5.3 ppm; (+) HRESIMS *m/z* 591.1408 $[M+Na]^+$ (calcd for $C_{26}H_{37}IO_4SiNa$, 591.1404, Δ = 0.7 ppm).

1-((4*S*,5*R*)-4,5-Bis(benzyloxy)-6-((*tert*-butyldimethylsilyl)oxy)-2-oxohexyl)-5-(((tetrahydro-2*H*-pyran-2-yl)oxy)methyl)-1*H*-pyrrole-2-carbaldehyde (22): To a solution of potassium carbonate (0.48 g. 3.5 mmol) and compound **7** (0.73 g, 3.5 mmol) in DMF (20 mL) was treated with a solution of ketone **21** (2 g, 3.5 mmol) in DMF (5 mL). After stirring for 6 h, the resulting mixture was poured into water and extracted with EtOAc (3 × 50 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtrated and concentrated. The residual oil was purified by column chromatography on silica gel (PE/EtOAc = 10/1) to give **22** (1.9 g, 87%, *dr* = 2:1) as a colorless oil. $[\alpha]^{22}_D$ = +27.6 (*c* 0.033, $CHCl_3$); IR (film) ν_{max}: 3339, 2936, 2849, 1654, 1386, 1024, 832 cm^{-1}; ^1H NMR (400 MHz, MHz, CD_3OD): 9.44 (s, 0.5H), 9.43 (s, 0.5H), 7.37-7.25 (m, 10H), 7.03 (d, *J* = 4.0 Hz, 1H), 6.33 (dd, *J* = 4.0 Hz, 0.5H), 6.32 (dd, *J* = 4.0 Hz, 0.5H), 5.31 (d, *J* = 16.4, Hz, 1H), 5.27 (d, *J* = 16.4 Hz, 1H), 4.65-4.40 (m, 7H), 4.12 (m, 1H), 4.06 (m, 1H), 3.79 (m, 1H), 3.54-3.43 (m, 3H), 2.91-2.73 (m, 2H), 1.69-1.33 (m, 6H), 0.91 (s, 9H), 0.09–0.06 ($Si(CH_3)_2$, 6H) ppm; ^{13}C NMR (100 MHz, CD_3OD): δ205.3, 205.3, 181.5, 140.9, 139.9, 139.6, 134.3, 129.4, 129.2, 128.9, 128.7, 128.5, 125.4, 112.9, 112.8, 98.9, 98.8, 78.1, 78.0, 74.4, 74.0, 73.9, 73.7, 73.7, 72. 8, 63.6, 63.5, 60.6, 56.4, 41.9, 31.4, 26.4, 20.5, 20.4, 19.0, –4.4, –4.4 ppm; (+) HRESIMS *m/z* 672.3348 $[M+Na]^+$ (calcd for $C_{37}H_{51}NO_7SiNa$, 672.3333, Δ = 2.2 ppm).

(2*S*,4*S*,5*R*)-4,5-Bis(benzyloxy)-1',3,4,4',5,6-hexahydrospiro[pyran-2,3'-pyrrolo[2,1-*c*][1,4]oxazine]-6'-carbaldehyde (23): To ketone **22** (0.8 g, 1.2 mmol) in THF (10 mL) was treated with 4N HCl (1.3 mL, 4.9 mmol) at 0 °C. After being stirred for 4 h, the reaction was carefully neutralized with a saturated aqueous $NaHCO_3$ solution and the resulting mixture was extracted with EtOAc (4 × 50 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$, filtrated and concentrated. The residue was purified by flash chromatography on silica gel (PE/EtOAc = 8:1) to obtain **23** (0.53 g, 86%) as a colorless oil. $[\alpha]^{22}_D$ = +48.8 (*c* 0.025, $CHCl_3$); IR (film) ν_{max}: 3408, 2915, 2843, 1652, 1095, 1051, 684cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.45 (s, 1H), 7.45-7.30 (m, 10H), 6.91 (d, *J* = 4.1 Hz, 1H), 5.98 (d, *J* = 4.1 Hz, 1H), 4.77 (d, *J* = 16.0 Hz, 1H), 4.78-4.68 (m, 4H), 4.56 (d, *J* = 12.1 Hz, 1H), 4.55 (d, *J* = 12.1 Hz, 1H), 4.02 (d, *J* = 14.0 Hz, 1H), 3.98 (ddd, *J* = 12.4, 4.8, 2.8 Hz, 1H), 3.95 (dd, *J* = 12.4, 2.4 Hz, 1H), 3.74 (br s, 1H), 3.56 (dd, *J* = 12.4, 0.8 Hz, 1H), 2.29 (dd, *J* = 12.4, 12.2 Hz, 1H), 2.07 (dd, *J* = 12.4, 4.8 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.7, 138.4, 138.3, 134.2, 131.1, 128.4, 128.4, 127.8, 127.7, 127.6, 127.4, 123.8, 104.6, 95.7, 72.8, 71.3, 71.0, 70.2, 62.5, 57.7, 52.4, 33.6 ppm; (+) HRESIMS *m/z* 456.1762 $[M+Na]^+$ (calcd for $C_{26}H_{27}NO_5Na$, 456.1781, Δ = -4.2 ppm).

Xylapyrroside A (1) (Method 2): According to a known procedure,[8] a solution of compound **23** (0.25 g, 0.6 mmol) in CH_2Cl_2 (30 mL) was carefully treated with $TiCl_4$ at -78 °C for 40 h. Then the reaction was quenched with saturated aqueous $NaHCO_3$ solution and allowed to warm to room temperature. After removing solvent, the resulting mixture was extracted with EtOAc (4 × 20 mL) and the combined organic layers were washed with brine. Dried, filtrated and concentrated, the residue was purified by flash chromatography on silica gel (CH_2Cl_2/MeOH = 40/1) to give xylapyrroside A (**1**, 0.1 g, 70%) as an off-white solid. The spectral data of the synthetic **1** were identical to the reported data of natural product.

(2*R*,3*S*)-1,3-Bis(benzyloxy)hex-5-en-2-ol (24): Compound **16** (7 g, 3.1 mmol) in THF (20 mL) was treated with NaH (1.89 g, 4.7

mmol) at 0 °C for 30 min, then benzyl bromide (3.77 mL, 3.1 mmol) was added dropwise at the same temperature and the reaction was stirred for 3h. The mixture was poured into ice water, and extracted with EtOAc (3 × 200 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtrated and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (PE/EtOAc = 5/1) to give **24** (7.0 g, 75%) as a colorless oil. $[\alpha]^{22}_D$ = +21.2 (*c* 0.07, $CHCl_3$); IR (film) ν_{max}: 3435, 2936, 2849, 1452, 1079, 1030, 750 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.41-7.29 (m, 10H), 5.96 (ddt, *J* = 17.2, 10.1, 7.1 Hz, 1H), 5.18 (dq-like, *J* = 17.2, 2.0 Hz, 1H), 5.13 (dq-like, *J* = 10.1, 2.0 Hz, 1H), 4.65 (d, *J* = 11.4 Hz, 1H), 4.57 (s, 2H), 4.54 (d, *J* = 11.4 Hz, 1H), 3.92 (ddd, *J* = 6.5, 6.4, 3.5 Hz, 1H), 3.69 (dd, *J* = 9.6, 3.5 Hz, 1H), 3.63 (dd, *J* = 9.6, 6.5 Hz, 1H), 3.60 (m, 1H), 2.47 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.3, 137.9, 134.6, 128.4 (2C), 128.3 (2C), 127.8 (4C), 127.7, 127.6, 117.3, 79.1, 73.4, 72.2, 71.5, 71.0, 34.7 ppm; (+) HR-ESIMS *m/z* 335.1614 $[M+Na]^+$ (calcd for $C_{20}H_{24}O_3Na$, 335.1623, Δ = -2.7 ppm).

(((2*R*,3*S*)-1,3-Bis(benzyloxy)hex-5-en-2-yl)oxy)(*tert*-butyl)dimethylsilane (25): The title compound was synthesized from alcohol **24** (3.7 g,11.8 mmol) through the above procedure. Product **25** (4.1 g, 82%) was obtained as colorless oil. $[\alpha]^{22}_D$ = +51.2 (*c* 0.025, $CHCl_3$); IR (film) ν_{max}: 3065, 2923, 2849, 1463, 1254, 816, 728 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ7.37-7.28 (m, 10H), 5.90 (ddt, *J* = 17.2, 10.1, 7.1 Hz, 1H), 5.12 (br d, *J* = 17.2 Hz, 1H), 5.06 (br d, *J* = 10.1 Hz, 1H), 4.63 (d, *J* = 11.6 Hz, 1H), 4.57 (d, *J* = 11.6 Hz, 1H), 4.55 (d, *J* = 12.1 Hz, 1H), 4.51 (d, *J* = 12.1 Hz, 1H), 3.94 (dd, *J* = 9.6, 4.6 Hz, 1H), 3.61 (dd, *J* = 9.7, 4.1 Hz, 1H), 3.60 (m, 1H), 3.56 (dd, *J* = 9.7, 5.5 Hz, 1H), 2.38 (m, 2H), 0.91 (s, 9H), 0.09 (s, 3H), 0.08 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.8, 138.4, 135.6, 128.3 (2C), 128.2 (2C), 127.8 (2C), 127.7 (2C), 127.5, 127.4, 116.8, 80.4, 73.5, 73.4, 72.6, 72.0, 35.3, 25.9 (3C), 18.2, –4.4, –4.7 ppm; (+) HRESIMS *m/z* 449.2489 $[M+Na]^+$ (calcd for $C_{26}H_{38}O_3SiNa$, 449.2488, Δ = 0.2 ppm).

(((2*R*,3*S*)-1,3-Bis(benzyloxy)-4-(oxiran-2-yl)butan-2-yl)oxy)(*tert*-butyl)dimethylsilane (26): The title compound was prepared from compound **25** (3.9 g,9.2 mmol) according to the above procedure. Product **26** (3.0 g, 75%) was obtained as an inseparable mixture of epimers **26a** and **26b** (*dr* = 5:2). Colorless oil; $[\alpha]^{22}_D$ = −18.9 (*c* 0.037, $CHCl_3$); IR (film) ν_{max}: 2947, 2854, 1382, 1249, 1073, 1041, 800 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) data of **26a**: δ 7.36-7.28 (m), 4.74 (d, *J* = 12.0 Hz), 4.67 (d, *J* = 9.6 Hz), 4.64 (d, *J* = 9.6 Hz), 4.59 (d, *J* = 12.0 Hz), 3.81 (m), 3.71 (m), 3.58 (m), 2.99 (m), 2.76 (dd, *J* = 4.8, 4.0 Hz), 2.49 (dd, *J* = 4.8, 2.4 Hz), 1.80 (m), 1.65 (ddd, *J* = 14.3, 7.2, 3.6 Hz), 0.90 (s), 0.06 (s), 0.05 (s) ppm; **26b**: δ 7.36-7.28 (m), 4.78 (d, *J* = 12.0 Hz), 4.60 (d, *J* = 12.0 Hz), 4.58 (d, *J* = 9.6 Hz), 4.56 (d, *J* = 9.6 Hz), 3.81 (m), 3.71 (m), 3.63 (m), 2.89 (m), 2.64 (dd, *J* = 4.8, 4.4 Hz), 2.39 (dd, *J* = 5.0, 2.8 Hz), 1.83 (m), 1.65 (ddd, *J* = 14.3, 7.2, 3.6 Hz), 0.90 (s), 0.06 (s), 0.05 (s) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.6, 138.4, 138.2, 128.3, 128.3, 127.8, 127.8, 127.7, 127.6, 127.6, 127.5, 78.6, 78.4, 73.3, 73.2, 73.1, 72.7, 72.2, 71.8, 71.7, 50.2, 50.1, 47.8, 47.0, 34.1, 33.6, 25.9, 18.1, −4.5, −4.8 ppm; (+) HRESIMS *m/z* 465.2448 $[M+Na]^+$ (calcd for $C_{26}H_{38}O_4SiNa$, 465.2437, Δ = 2.4 ppm).

(4*S*,5*R*)-4,6-Bis(benzyloxy)-5-((*tert*-butyldimethylsilyl)oxy)-1-iodohexan-2-ol (27): The title compound was prepared from epoxide **26** (1.6 g, 3.6 mmol) according to the above procedure. Product **27** (1.7 g, 80%; *dr* = 3:1) was obtained as an inseparable mixture of epimers **27a** and **27b**. Colorless oil; $[\alpha]^{22}_D$ = +25.3 (*c* 0.03, $CHCl_3$); IR (film) ν_{max}: 3413, 2936, 2854, 2361, 1380, 1030, 673 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) data of **27a**: δ7.38-7.25 (m), 4.71 (d, *J* = 12.0 Hz), 4.68 (d, *J* = 12.0 Hz), 4.65 (d, *J* = 11.2 Hz), 4.56 (d, *J* = 11.2 Hz), 3.94 (ddd, *J* = 10.1, 2.8, 2.6 Hz), 3.76 (m), 3.64 (m), 3.51 (m), 3.30 (dd, *J* = 10.1, 5.6 Hz), 3.24 (dd, *J* = 10.1, 5.6 Hz), 1.92 (ddd, *J* = 14.0, 10.4, 2.8 Hz), 1.64 (ddd, *J* = 14.4, 9.7, 2.3 Hz), 0.92 (s), 0.08 (s), 0.07 (s) ppm; **27b**: δ 7.38-7.25 (m), 4.65 (d, *J* = 11.6 Hz), 4.52 (s), 4.47 (d, *J* = 11.6 Hz), 4.12 (ddd, *J* = 6.1, 5.9, 2.8 Hz), 3.76 (m), 3.74 (m), 3.61 (m), 3.18 (dd, *J* = 10.4, 4.0 Hz), 2.98 (dd, *J* = 10.4, 5.2 Hz), 1.84 (ddd, *J* = 14.4, 8.5, 6.0 Hz), 1.74 (ddd, *J* = 14.4, 6.8, 4.0 Hz), 0.93 (s), 0.11 (s), 0.09 (s) ppm;^{13}C NMR (100 MHz, CD_3OD) data of **27a**: δ 140.1, 140.0, 129.4, 129.3, 129.0, 128.7, 128.6, 82.6, 77.8, 73.9, 73.7, 68.9, 63.8, 39.2, 26.4, 19.1, 15.0, −5.2 ppm; **27b**: δ 139.7, 139.6, 129.4, 129.3, 129.0, 128.8, 128.7, 78.7, 74.4, 72.9, 72.6, 68.9, 63.8, 38.1, 26.4, 19.1, 14.9, −4.4 ppm.(+) HRESIMS *m/z* 593.1542 $[M+Na]^+$ (calcd for $C_{26}H_{39}IO_4SiNa$, 593.1560, Δ = -3.0 ppm).

(4*S*,5*R*)-4,6-Bis(benzyloxy)-5-((*tert*-butyldimethylsilyl)oxy)-1-iodohexan-2-one (28): The title compound was furnished from alcohol **27** (1.4 g, 2.5 mmol) according to the above procedure. Product **28** (1.28 g, 90%) was obtained as a colorless oil. $[\alpha]^{22}_D$ = +46.0 (*c* 0.03, $CHCl_3$); IR (film) ν_{max}: 3397, 2926, 2367, 1384, 1090, 805, 657 cm^{-1}; ^1H NMR (400 MHz, CD_3OD): δ7.36-7.27 (m, 10H), 4.62 (d, *J* = 11.2 Hz, 1H), 4.52 (s, 2H), 4.52 (d, *J* = 11.2 Hz, 1H), 4.12-4.04 (m, 2H), 3.90 (s, 2H), 3.51 (dd, *J* = 10.1, 5.6 Hz, 1H), 3.48 (dd, *J* = 10.1, 5.2 Hz, 1H), 3.05 (dd, *J* = 16.6, 8.2 Hz, 1H), 2.93 (dd, *J* = 16.6, 3.7 Hz, 1H), 0.92 (s, 9H), 0.10 (s, 3H), 0.08 (s, 3H) ppm; ^{13}C NMR (100 MHz, CD_3OD): δ 203.9, 139.7, 139.5, 129.4 (2C), 129.3 (2C), 129.1 (2C), 129.0 (2C), 128.7, 128.6, 78.6, 74.3, 73.9, 73.7, 72.7, 41.1, 26.4 (3C), 19.0, 7.7, −4.4 (2C) ppm; (+) HRESIMS *m/z* 591.1415 $[M+Na]^+$ (calcd for $C_{26}H_{37}O_4SiNa$, 591.1398, Δ = 2.9 ppm).

1-((4*S*,5*R*)-4,6-Bis(benzyloxy)-5-((*tert*-butyldimethylsilyl)oxy)-2-oxohexyl)-5-(((tetrahydro-2*H*-pyran-2-yl)oxy)methyl)-1*H*-pyrrole-2-carbaldehyde (29): The title compound was synthesized from ketone **28** (1.1 g, 1.9 mmol) using the above procedure. Product **29** (1.1 g, 87%; *dr* = 1:1) was obtained as a colorless oil. $[\alpha]^{22}_D$ = +3.6 (*c* 0.05, $CHCl_3$); IR (film) ν_{max}: 3408, 2926, 2843, 1665, 1446, 1386, 1024 cm^{-1}; ^1H NMR (400 MHz, CD_3OD): δ 9.44 (s, 0.5H), 9.43 (s, 0.5H), 7.37-7.25 (m, 10H), 7.03 (d, *J* = 4.0 Hz, 1H), 6.33 (dd, *J* = 4.0 Hz, 0.5H), 6.32 (dd, *J* = 4.0 Hz, 0.5H), 5.37-5.18 (m, 2H), 4.72-4.40 (m, 7H), 4.26-3.61 (m, 3H), 3.53-3.44 (m, 3H), 2.97-2.73 (m, 2H), 1.75-1.37 (m, 6H), 0.91 ($SiC(CH_3)_3$, 9H), 0.09-0.06 ($Si(CH_3)_2$, 6H) ppm; ^{13}C NMR (100 MHz, CD_3OD): δ 205.3, 205.1, 181.5, 141.0, 139.9, 139.6, 134.3, 134.2, 129.4, 129.3, 129.2, 129.0, 128.9, 128.9, 128.7, 128.5, 125.4, 112.9, 112.8, 98.9, 98.7, 78.5, 78.0, 74.4, 74.1, 74.0, 73.7, 73.6, 72.8, 60.6, 56.4, 42.0, 31.4, 26.4, 20.6, 20.5, 19.0, –4.3, –4.4, –5.2 ppm; (+) HRESIMS *m/z* 672.3323 $[M+Na]^+$ (calcd for $C_{37}H_{51}NO_7SiNa$, 672.3332, Δ = -1.5 ppm).

(4*S*,5*R*)-4-(Benzyloxy)-5-((benzyloxy)methyl)-1',4,4',5-tetrahydro-3*H*-spiro[furan-2,3'-pyrrolo[2,1-c][1,4]oxazine]-6'-carbaldehyde (30): The title compound was prepared from ketone **29** (0.9 g, 1.6 mmol) according to the above procedure. Product **30** (0.53 g, 86%) was obtained as a pair of epimers (**30a** and **30b,** *dr* = 2:1). Colorless oil; $[\alpha]^{22}_D$ = +33.6 (*c* 0.05, $CHCl_3$); IR (film) ν_{max}: 3463, 2920, 2849, 2361, 1656, 1035, 684 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) data of **30a**: δ9.46 (s), 7.38-7.28 (m), 6.92 (d, *J* = 4.0 Hz), 6.01 (d, *J* = 4.0 Hz), 5.03 (d, *J* = 15.6 Hz), 4.86 (d, *J* = 15.6 Hz), 4.68-4.38 (m), 4.37 (dd, *J* = 8.4, 4.4 Hz), 4.27 (d, *J* = 14.0 Hz), 4.10 (ddd, *J* = 7.9, 3.9, 2.0 Hz), 3.53 (dd, *J* = 10.8, 4.4 Hz), 3.49 (dd, *J* = 10.8, 4.4 Hz), 2.31 (dd, *J* = 14.2, 1.9 Hz), 2.20 (dd, *J* = 14.2, 8.0 Hz) ppm; **30b**: δ 9.44 (s), 7.38–7.28 (m), 6.91 (d, *J* = 4.0 Hz), 6.00 (d, *J* = 4.0 Hz), 5.01 (d, *J* = 15.6 Hz), 4.78 (d, *J* = 15.6 Hz), 4.68-4.38 (m), 4.22 (d, *J* = 14.0

Hz), 3.82 (dd, *J* = 10.4, 4.8 Hz), 3.77 (dd, *J* = 10.4, 7.6 Hz), 2.47 (dd, *J* = 14.0, 1.8 Hz), 2.16 (dd, *J* = 14.0, 6.8 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) data of **30a**: δ 178.7, 137.8, 135.2, 131.1, 128.5, 127.9, 127.7, 127.6, 124.2, 104.8, 103.3, 84.8, 78.7, 73.5, 71.7, 70.0, 57.9, 51.0, 42.4 ppm; **30b**: δ 178.7, 138.0, 135.2, 131.0, 128.4, 127.9, 127.7, 127.6, 124.1, 104.7, 102.8, 83.0, 78.7, 73.4, 71.8, 69.4, 58.4, 51.6, 42.1ppm; (+) HRESIMS *m*/*z* 456.1787 $[M+Na]^+$ (calcd for $C_{26}H_{27}NO_5Na$, 456.1781, Δ = 1.3 ppm).

Xylapyrroside B (2) and acortatarin A (4) (Method 2): According to a known procedure,[19] a solution of compound **30** (0.52 g, 1.2 mmol) in CH_2Cl_2 (50 mL) was carefully treated with $TiCl_4$ at -78 °C for 40 h. Then the reaction was quenched with aqueous saturated $NaHCO_3$ solution and extracted with EtOAc (4 × 30 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$, filtrated and evaporated. The residue was purified by flash chromatography on silica gel (CH_2Cl_2/MeOH = 40/1) to afford compounds **2** (0.1 g, 32%) and **4** (0.11 g, 37%) as an off-white solid and exhibited physical and spectroscopic characteristics agreed to the natural products.

X-ray Crystal Data. Colorless crystals of **1** and **1a** were both obtained in acetone. Crystal data were obtained on a Bruker APEX Duo CCD detector employing graphite monochromated Copper-Kα radiation (λ = 1.54178 Å) at 140(2) K and operating in the φ/ω scan mode. The crystal structure was solved by direct method using the program SHELXS-97 and subsequent Fourier difference techniques, and was finally refined anisotropically by full-matrix least-squares on F2 using SHELXL-97. All non-hydrogen atoms were refined anisotropically. The hydrogen atom positions were geometrically idealized and allowed to ride on their parent atoms. Crystallographic data of **1** and **1a** have been deposited at the Cambridge Crystallographic Data Centre (**1**: deposition No. CCDC-1029230; **1a**: deposition No. CCDC-1029231). Copies of these data can be obtained free of charge *via* www.ccdc.cam.ac.uk/conts/retrieving.html or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB21EZ, UK. [fax: (+44) 1223-336-033; or email: deposit@ccdc.cam.ac.uk].

Xylapyrroside A (1): $C_{12}H_{15}NO_5$, M = 253.25, orthorhombic, *a* = 7.03200(10), *b* = 8.45490(10), *c* = 19.6634(4) Å, α = 90.00, β = 90.00, γ = 90.00 deg., V = 1169.08(3) Å^3, T = 140(2) K, space group $P2_12_12_1$, Z = 4, 4329 reflections measured, 1986 independent reflections (R_{int} = 0.0274). The final R1 values were 0.0312 (I >2σ (I)). The final R1 values were 0.0318 (all data). The final wR_2 values were 0.0807 (all data). The goodness fit on *F2* was 1.041. Flack parameter = 0.19(18). Crystallographic data of **1** have been deposited at the Cambridge Crystallographic Data Centre (deposition No. CCDC-1029230).

Xylapyrroside A$_1$ (1a): $C_{12}H_{15}NO_5$, M = 253.25, orthorhombic, *a* = 7.10980(10), *b* = 8.64620(10), *c* = 18.8598(4) Å, α = 90.00, β = 90.00, γ = 90.00 deg., V = 1159.36(3) Å^3, T = 140(2) K, space group $P2_12_12_1$, Z = 4, 7512 reflections measured, 2153 independent reflections (R_{int} = 0.0463). The final R1 values were 0.0288 (I >2σ(I)). The final R1 values were 0.0290 (all data). The final wR_2 values were 0.0745 (all data). The goodness fit on *F2* was 1.050. Flack parameter = –0.07(15). Crystallographic data of **1a** have been deposited at the Cambridge Crystallographic Data Centre (deposition No. CCDC-1029231).

4.4 Anti-oxidative stress assay

The inhibitory effects of the spiroalkaloids on oxidative stress-induced cellular damage were evaluated in A7r5 rat vascular smooth muscle cells (VSMC). The A7r5 cells, obtained from the American Type Culture Collection (Rockville, MD), were cultured in DMEM containing 10% FBS, 100 U/mL penicillin, and 100 µg/mL streptomycin in 5% CO_2 at 37°C. Cell viability was determined by conventional MTT assay.[29] Catechin hydrate (purity ≥ 98%, Beyotime Biotechology, China) was used as a positive control.[30a] In brief, A7r5 cells in 96-well plates were incubated with different concentrations of compounds (25, 50 and 100 µM) or catechin hydrate (50 and 100 µM) for 4 h, then stimulated with 200 µM of *tert*-Butyl hydroperoxide (tBHP, purity ≥ 99%, Sigma-Aldrich) for 12 h. Cells were then incubated with MTT solution (0.5 mg/mL) in culture medium. After incubation at 37°C for 4 h, the culture medium containing MTT was removed. DMSO was then added into each well, and the absorbance at 570 nm was measured using a microplate reader (M1000, TECAN, Austria GmbH, Austria). Values were expressed as percentage of cell survival. Absorbance from tBHP-untreated cells was set at 100% (control group).

Acknowledgments

This work was supported by NSFC grants (No. 81273401, 81202420, 21472021), grants from the Ph.D. Programs Foundation of Ministry of Education (MOE) of China (No. 20120071110049, 20120071120049), and the National Basic Research Program of China (973 Program, Grant No. 2013CB530700). We also thank Zhejiang Jolly Pharmaceutical Company (ZJPC, Deqing County, China) for providing Wuling Powder and Ms. Jian Chen from ZJPC for the sample identification.

Supplementary data

Copies of NMR spectra, and X-ray crystal structure data are available as Supplementary data.

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Supplementary Material for

Xylapyrrosides A and B, Two Rare Sugar-Morpholine Spiroketal Pyrrole-Derived Alkaloids from *Xylaria nigripes*: Isolation, Complete Structure Elucidation, and Total Syntheses

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Table of Contents

1. X-ray crystallographic data for compounds 1, 1a and 4.

Table S1. X-ray Crystallographic Data for **1** and **1a**.

	Xylapyrroside A (1)	**Xylapyrroside A_1 (1a)**
Empirical formula	$C_{12}H_{15}NO_5$	$C_{12}H_{15}NO_5$
Formula weight	253.25	253.25
Temperature	140(2) K	140(2) K
Wavelength	1.54178 Å	1.54178 Å
Crystal system	Orthorhombic	Orthorhombic
space group	P2(1)2(1)2(1)	P2(1)2(1)2(1)
Unit cell dimensions		
a (alpha)	7.03200(10) Å (90 deg)	7.10980 (10) Å (90 deg)
b (beta)	8.45490(10) Å (90 deg)	8.64620(10) Å (90 deg)
c (gamma)	19.6634(4) Å (90 deg)	18.8598(4) Å (90 deg)
Volume	1169.08(3) $Å^3$	1159.36(3) $Å^3$
Z, Calculated density	4, 1.439 mg/m^3	4, 1.451 mg/m^3
Absorption coefficient	0.952 mm^{-1}	0.960 mm^{-1}
F(000)	536	536
Crystal size	0.10 x 0.05 x 0.04 mm	0.35 x 0.16 x 0.05 mm
Theta range for data collection	4.50 to 69.94 deg.	4.69 to 69.63 deg.
Limiting indices	-8<=h<=8, -10<=k<=8, -23<=l<=18	-8<=h<=8, -7<=k<=10, -22<=l<=22
Reflections collected / unique	4329 / 1986 [R(int) = 0.0274]	7512 / 2153 [R(int) = 0.0463]
Completeness to theta = 69.94	96.6 %	99.1 %
Absorption correction	Semi-empirical from equivalents	Semi-empirical from equivalents
Max. and min. transmission	0.9629 and 0.9108	0.9536 and 0.7300
Refinement method	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2
Data / restraints / parameters	1986 / 0 / 165	2153 / 0 / 166
Goodness-of-fit on F^2	1.041	1.050
Final R indices [I > 2sigma(I)]	R_1 = 0.0312, wR_2 = 0.0798	R_1 = 0.0288, wR_2 = 0.0741
R indices (all data)	R_1 = 0.0318, wR_2 = 0.0807	R_1 = 0.0290, wR_2 = 0.0745
Absolute structure parameter	0.19(18)	-0.07(15)
Largest diff. peak and hole	0.141 and -0.214 e. $Å^{-3}$	0.263 and -0.198 e. $Å^{-3}$

Colorless crystals of **1** and **1a** were both obtained in acetone. Crystal data were obtained on a Bruker APEX Duo CCD detector employing graphite monochromated Copper-Kα radiation (λ=1.54178 Å) at 140(2) K and operating in the φ/ω scan mode. The crystal structure was solved by direct method using the program SHELXS-97 and subsequent Fourier difference techniques, and was finally refined anisotropically by full-matrix least-squares on F2 using SHELXL-97. All non-hydrogen atoms were refined anisotropically. The hydrogen atom positions were geometrically idealized and allowed to ride on their parent atoms. Crystallographic data of **1** and **1a** have been deposited at the Cambridge Crystallographic Data Centre (**1**: deposition No. CCDC-1029230; **1a**: deposition No. CCDC-1029231). Copies of these data can be obtained free of charge *via* www.ccdc.cam.ac.uk/conts/retrieving.html or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB21EZ, UK. [fax: (+44) 1223-336-033; or email: deposit@ccdc.cam.ac.uk].

Table S2. X-ray Crystallographic Data for **4**.

	Acortatarin A (4)
Empirical formula	$C_{12}H_{15}NO_5$
Formula weight	253.25
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Orthorhombic
space group	P2(1)2(1)2(1)
Unit cell dimensions	
a (alpha)	7.1019(3) Å (90 deg)
b (beta)	8.6521(3) Å (90 deg)
c (gamma)	18.8596(7) Å (90 deg)
Volume	1158.85(8) $Å^3$
Z, Calculated density	4, 1.452 mg/m^3
F(000)	536
Reflections collected / unique	2046 / 1214
Data Completeness (theta = 25.01)	1.68/1.00
Max. and min. transmission	0.960 and 0.945
Parameters	163
Goodness-of-fit on F^2	1.076
R (reflections)	R_1 = 0.0252, wR_2 = 0.0636

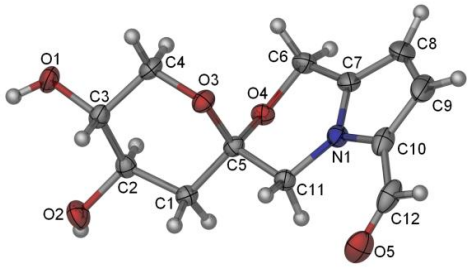
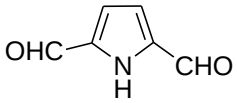


Figure S1. X-ray crystal structure of acortatarin A (**4**).

Colorless crystals of **4** were obtained in MeOH. Crystal data were obtained on a Bruker-AXS SMART APEX II CCD detector employing graphite monochromated Mo-Kα radiation (λ=0.71073 Å) at 173(2) K and operating in the φ/ω scan mode. The crystal structure was solved by direct method using the program SHELXS-97 and subsequent Fourier difference techniques, and was finally refined anisotropically by full-matrix least-squares on F2 using SHELXL-97. All non-hydrogen atoms were refined anisotropically. The hydrogen atom positions were geometrically idealized and allowed to ride on their parent atoms. Crystallographic data for **4** have been deposited at the Cambridge Crystallographic Data Centre (deposition No. CCDC-1029232). Copies of these data can be obtained free of charge *via* www.ccdc.cam.ac.uk/conts/retrieving.html or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB21EZ, UK. [fax: (+44) 1223-336-033; or email: deposit@ccdc.cam.ac.uk].

2. Synthetic procedures towards compound 7

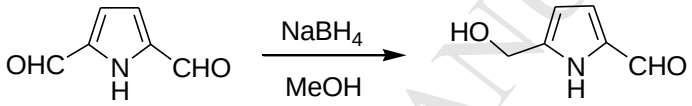
1*H*-Pyrrole-2,5-dicarbaldehyde pre-7a



pre-7a

The 1*H*-pyrrole-2,5-dicarbaldehyde **(pre-7a)** was prepared by known method [Knizhnikov, et al. *Russian J. Org. Chem*. **2007**, *43*, 855–860]. IR (film): ν_{max} 3424, 2909, 2849, 1682, 1660, 1424, 1276, 1167, 794 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 10.33 (br s, 1H), 9.80 (s, 2H), 7.03 (d, J = 1.2 Hz, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 181.2, 135.5, 119.5 ppm; HR-EIMS m/z 123.0321 $[M]^+$ (calcd for $C_6H_5NO_2$, 123.0320, Δ = 0.8 ppm).

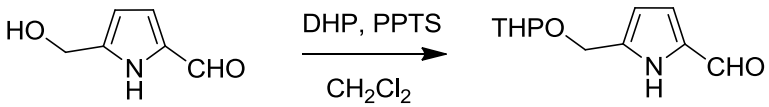
5-(Hydroxymethyl)-1*H*-pyrrole-2-carbaldehyde pre-7b



pre-7a **pre-7b**

To a solution of dialdehyde **pre-7a** (6.0 g, 48.8 mmol) in dry methanol (100 mL) at 0 °C was added sodium borohydride (0.46 g, 12.2 mmol) in one portion. After being stirred for 30 min, the reaction was quenched with ice water and concentrated in vacuum. The resulting aqueous was extracted with EtOAc (3 × 100 mL) and the combined organic layers were washed with brine, dried, filtrated and concentrated. The residue was purified by flash chromatography on silica gel (PE/EtOAc = 4/1) to give mono-aldehyde **pre-7b** (5.92 g, 98%) as a white amorphous powder. IR (film): ν_{max} 3304, 2915, 2849, 1495, 1364, 1200, 1063, 756 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 10.61 (br s, 1H, D_2O-exchangeable), 9.38 (s, 1H), 6.96 (dd, J = 3.7, 2.6 Hz, 1H), 6.22 (dd, J = 3.7, 2.2 Hz, 1H), 4.81 (d, J = 4.2 Hz, 2H), 3.46 (t, J = 4.2 Hz, 1H, D_2O-exchangeable) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 179.2, 141.8, 132.2, 123.4, 109.0, 57.9 ppm; HR-EIMS m/z 125.0478 $[M]^+$ (calcd for $C_6H_7NO_2$, 125.0477, Δ = 0.8 ppm).

5-(((Tetrahydro-2*H*-pyran-2-yl)oxy)methyl)-1*H*-pyrrole-2-carbaldehyde 7



pre-7b **7**

To a solution of **pre-7b** (1.5 g, 12.1 mmol) and PPTS (54 mg, 0.24 mmol) in CH_2Cl_2 (40 mL) was treated with DHP (1.08 g, 13.1 mmol). After stirring for overnight, the reaction was diluted with saturated aqueous $NaHCO_3$ solution. The mixture was separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL). The combined

organic layers were washed with brine. Dried, filtrated and concentrated, the residue was purified by flash chromatography on silica gel (PE/EtOAc = 5/1) to give **7** (2.45 g, 94%, *dr* = 1:1) as a colorless oil. IR (film): ν_{max} 3254, 2942, 1614, 1391, 1178, 1068, 805 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) : δ 9.71 (br s), 9.47 (s), 6.91 (d, J = 3.5 Hz), 6.90 (d, J = 3.5 Hz), 6.22 (d, J = 3.5 Hz), 6.21 (d, J = 3.5 Hz), 4.76 (d, J = 13.5 Hz), 4.69 (m), 4.62 (d, J = 13.5 Hz), 3.91 (m), 3.57 (m), 1.87-1.59 (m, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 180.3, 178.9, 139.3, 137.9, 134.1, 132.6, 123.1, 121.6, 111.2, 109.8, 100.3, 98.8, 64.1, 63.6, 62.7, 62.1, 31.8, 30.4, 26.6, 25.2, 20.9, 19.4 ppm; (+) HR-ESIMS *m*/*z* 232.0944 $[M+Na]^+$ (calcd for $C_{11}H_{15}NO_3Na$, 232.0948, $\Delta = -1.3$ ppm).

Figure S1. ^{1}H NMR spectrum of **1** in CD_3OD

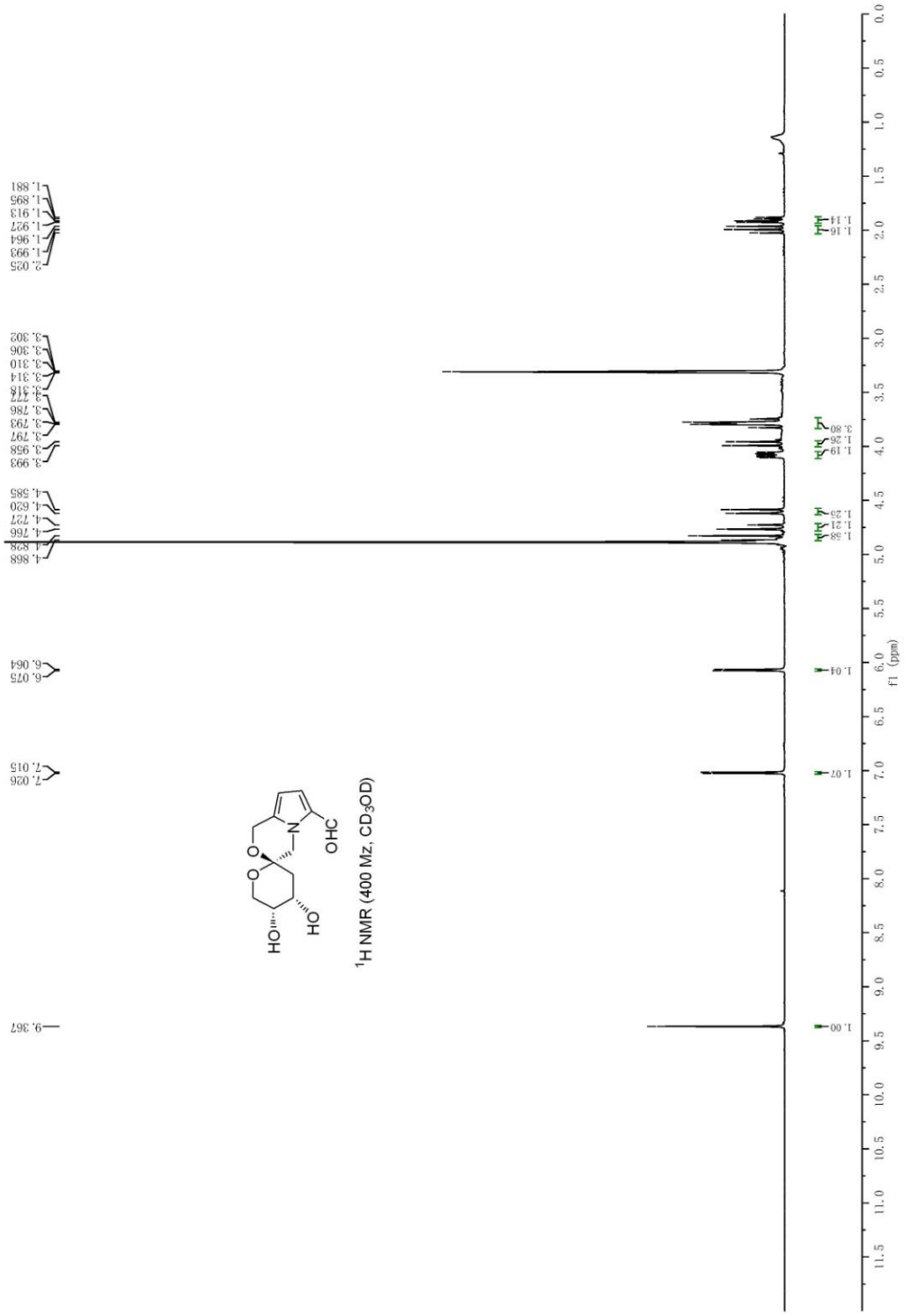


Figure S2. ^{1}H NMR spectrum of **1** in CD_3COCD3

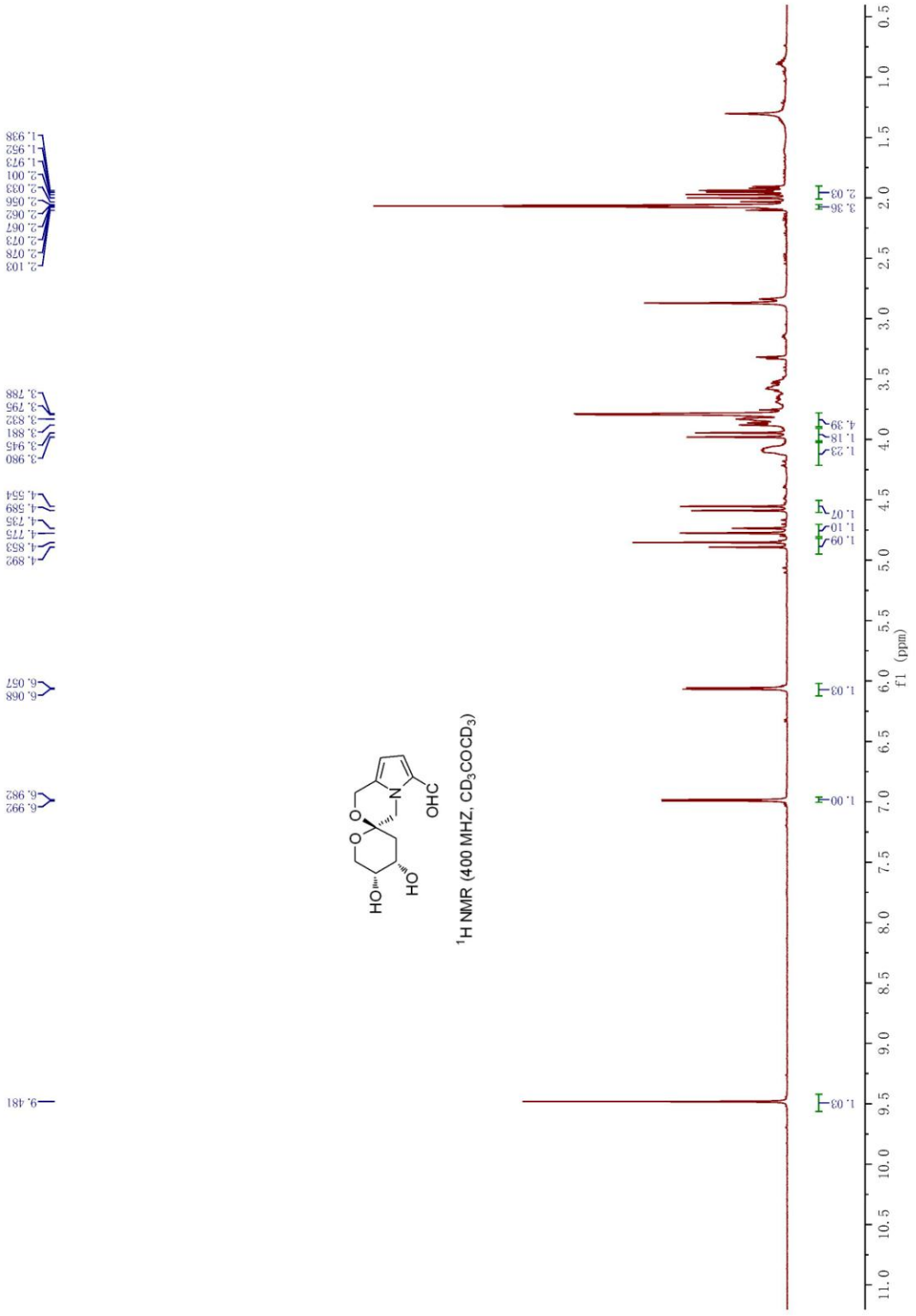


Figure S3. ^{1}H NMR spectrum of **1** in $CDCl_3$

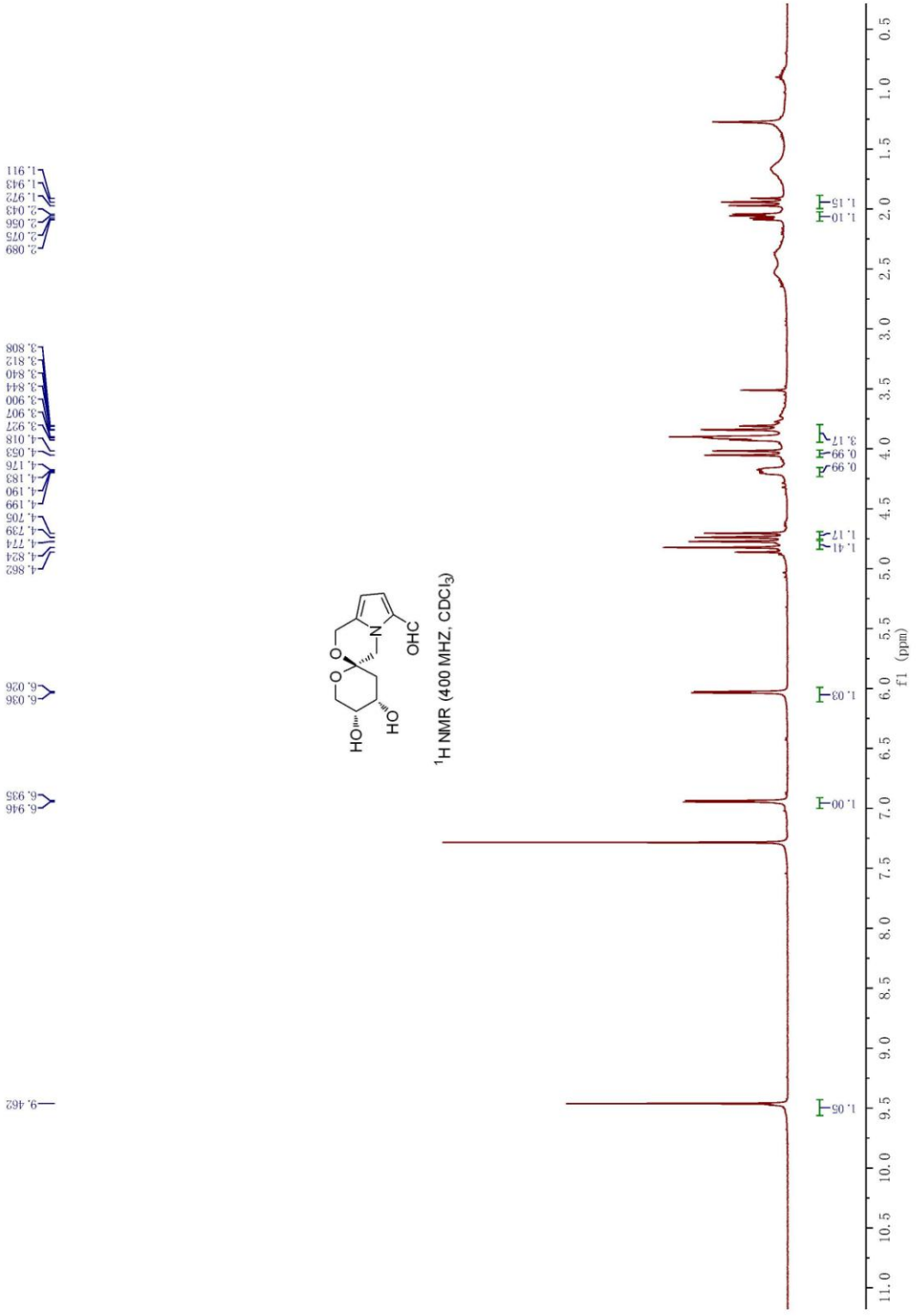


Figure S4. ^{13}C NMR spectrum of **1** in CD_3OD

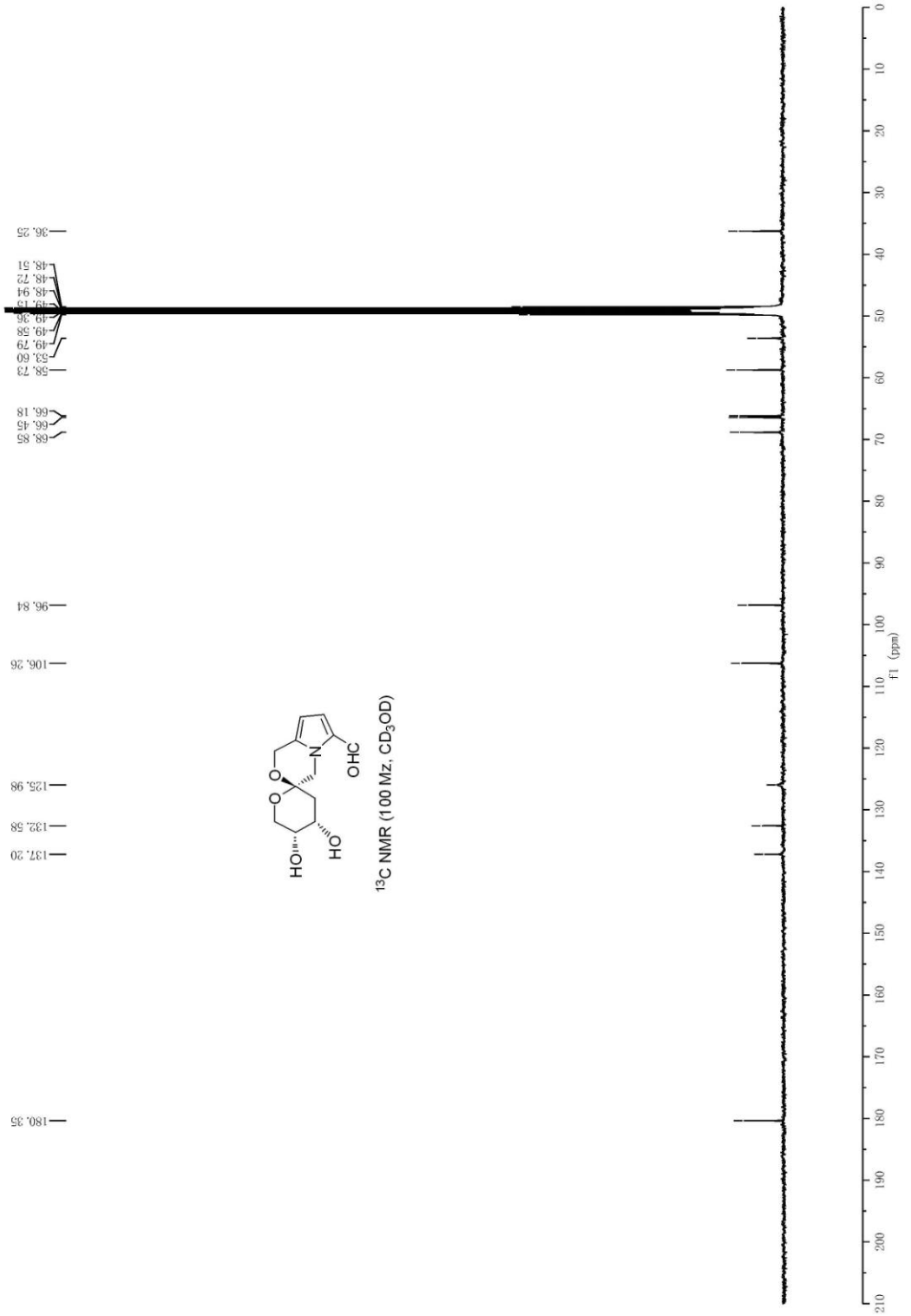


Figure S5. DEPT-135 spectrum of **1** in CD_3OD

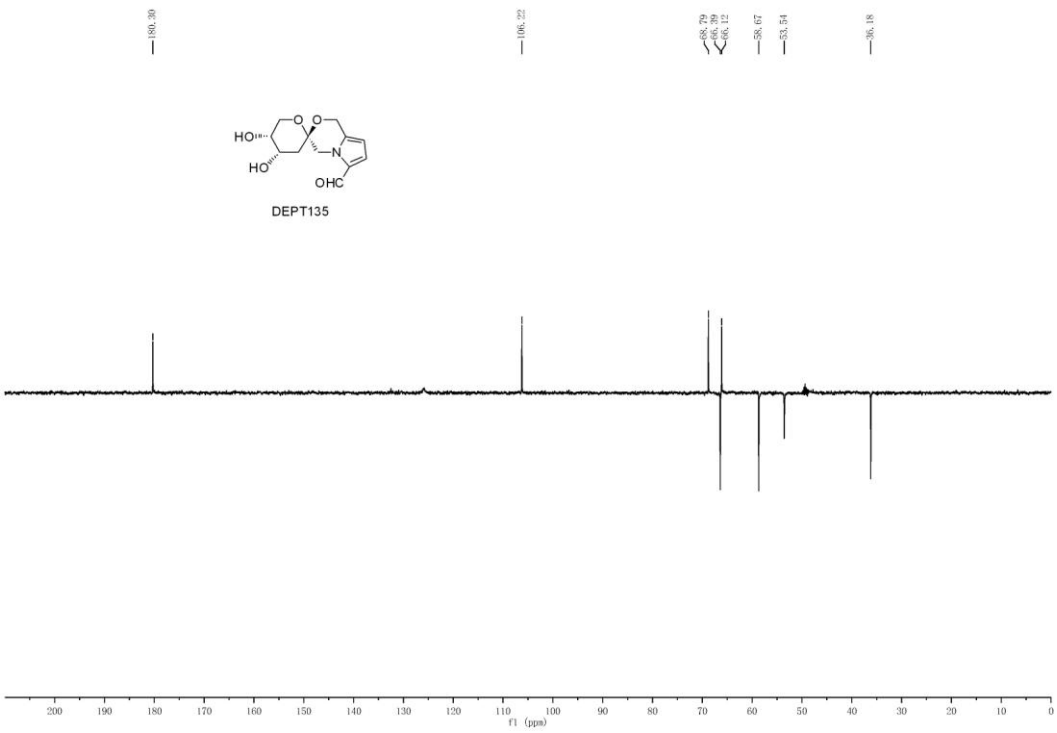


Figure S6. ^{1}H-^{1}H COSY spectrum of **1** in CD_3OD

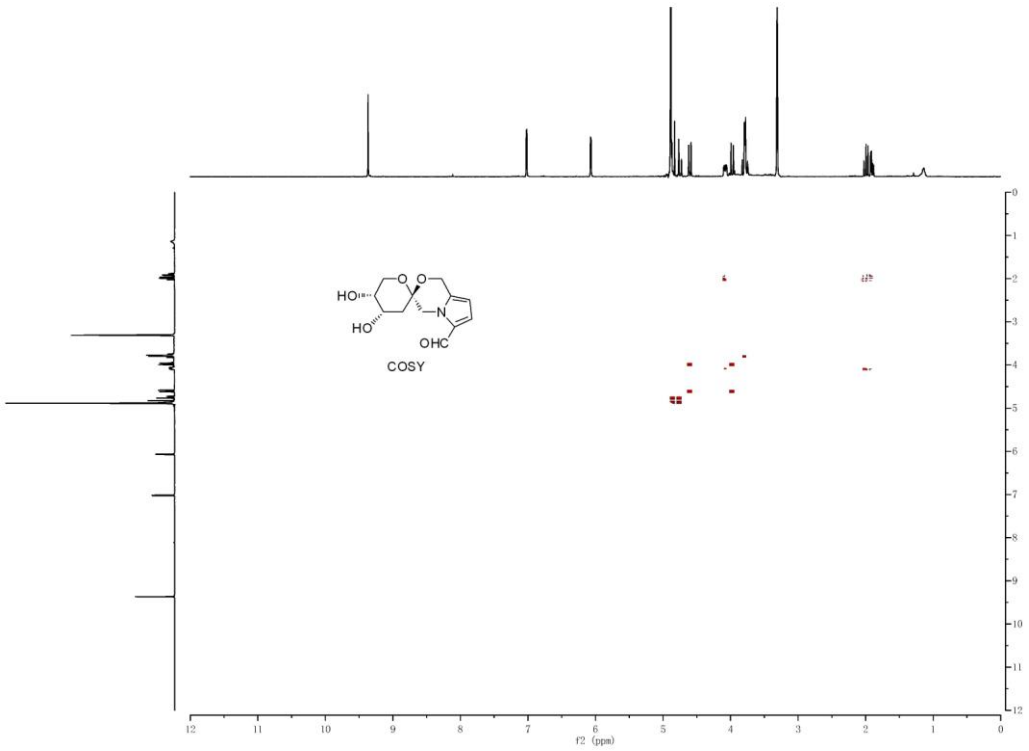


Figure S7. HSQC spectrum of **1** in CD_3OD

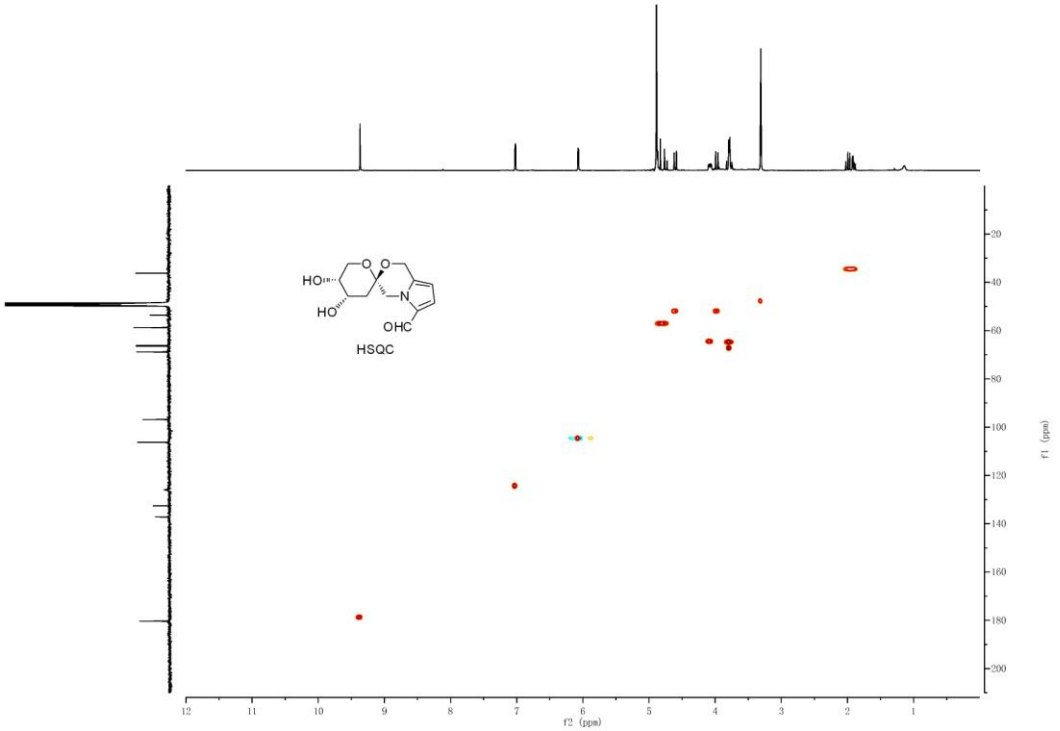


Figure S8. HMBC spectrum of **1** in CD_3OD

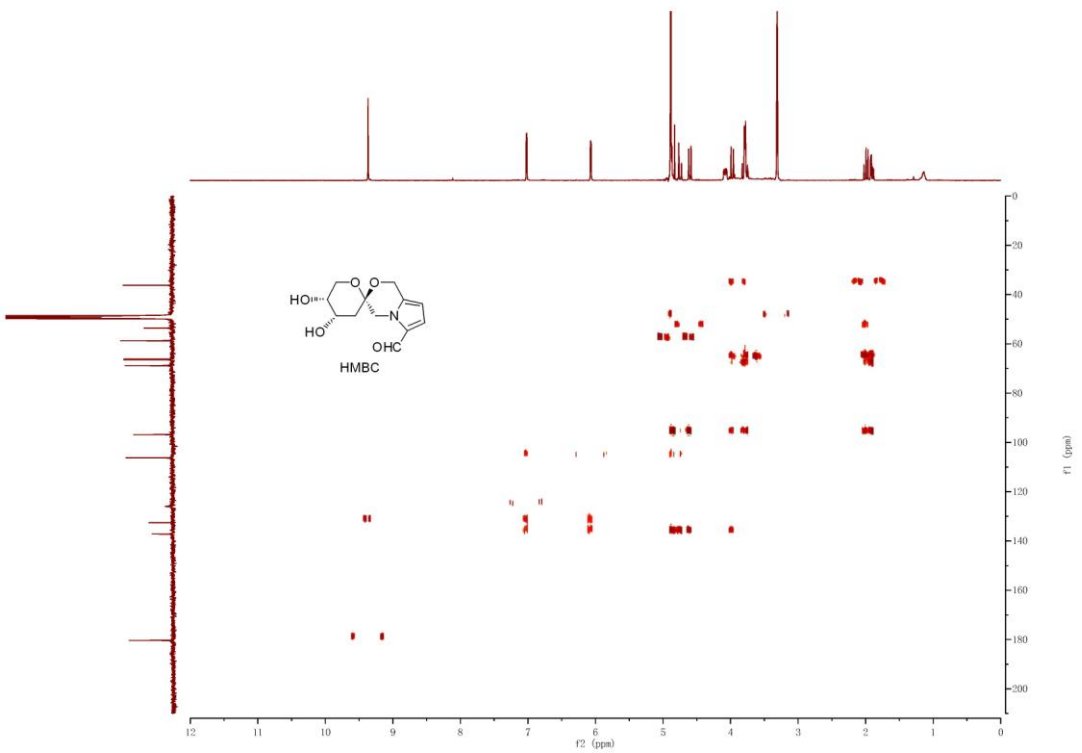


Figure S9. HMBC spectrum of **1** in CD_3OD-expansion

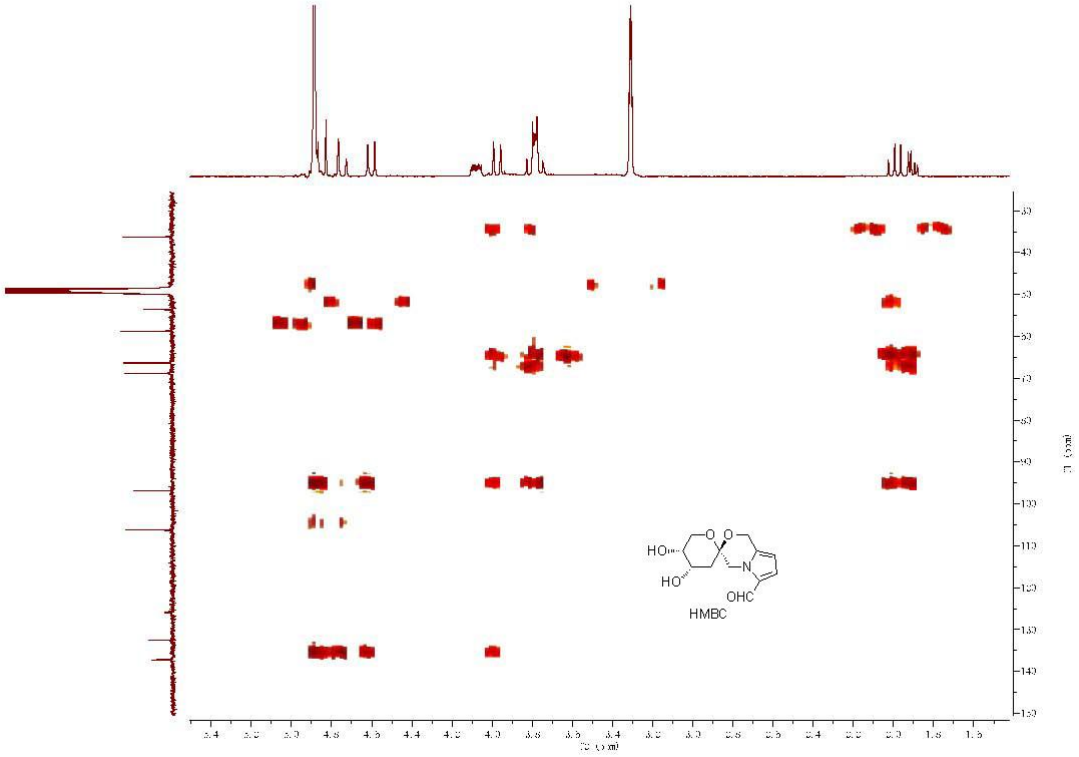


Figure S10. NOESY spectrum of **1** in CD_3OD

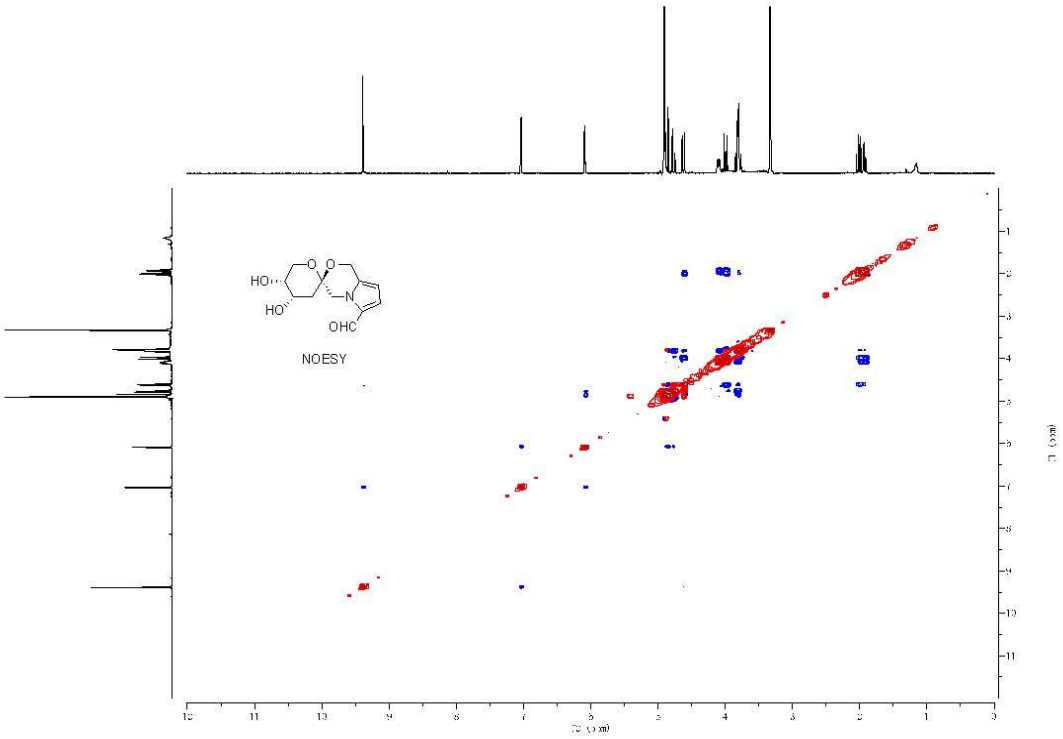


Figure S11. HR-EIMS of **1**

Elemental Composition Report

File Number: 20130412004
Sample Number:LM-4-3

Single Mass Analysis
Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off

Monoisotopic Mass, Odd and Even Electron Ions
11 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-15 H: 0-20 N: 0-1 O: 0-5

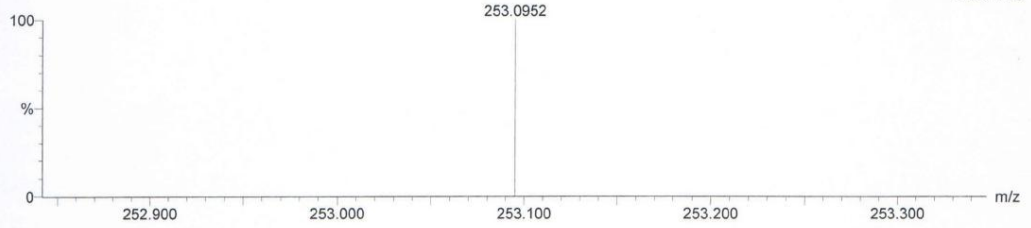
Minimum:				-1.5		
Maximum:		5.0	10.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
253.0952	253.0950	0.2	0.8	6.0	5546077.0	C12 H15 N O5

Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off

Monoisotopic Mass, Odd and Even Electron Ions
11 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-15 H: 0-20 N: 0-1 O: 0-5
LM-4-3
20130412004 334 (5.567)

TOF MS EI+
1.52e+002



Minimum:				-1.5		
Maximum:		5.0	10.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
253.0952	253.0950	0.2	0.8	6.0	5546077.0	C12 H15 N O5

Figure S12. ^{1}H NMR spectrum of **2** in CD_3OD

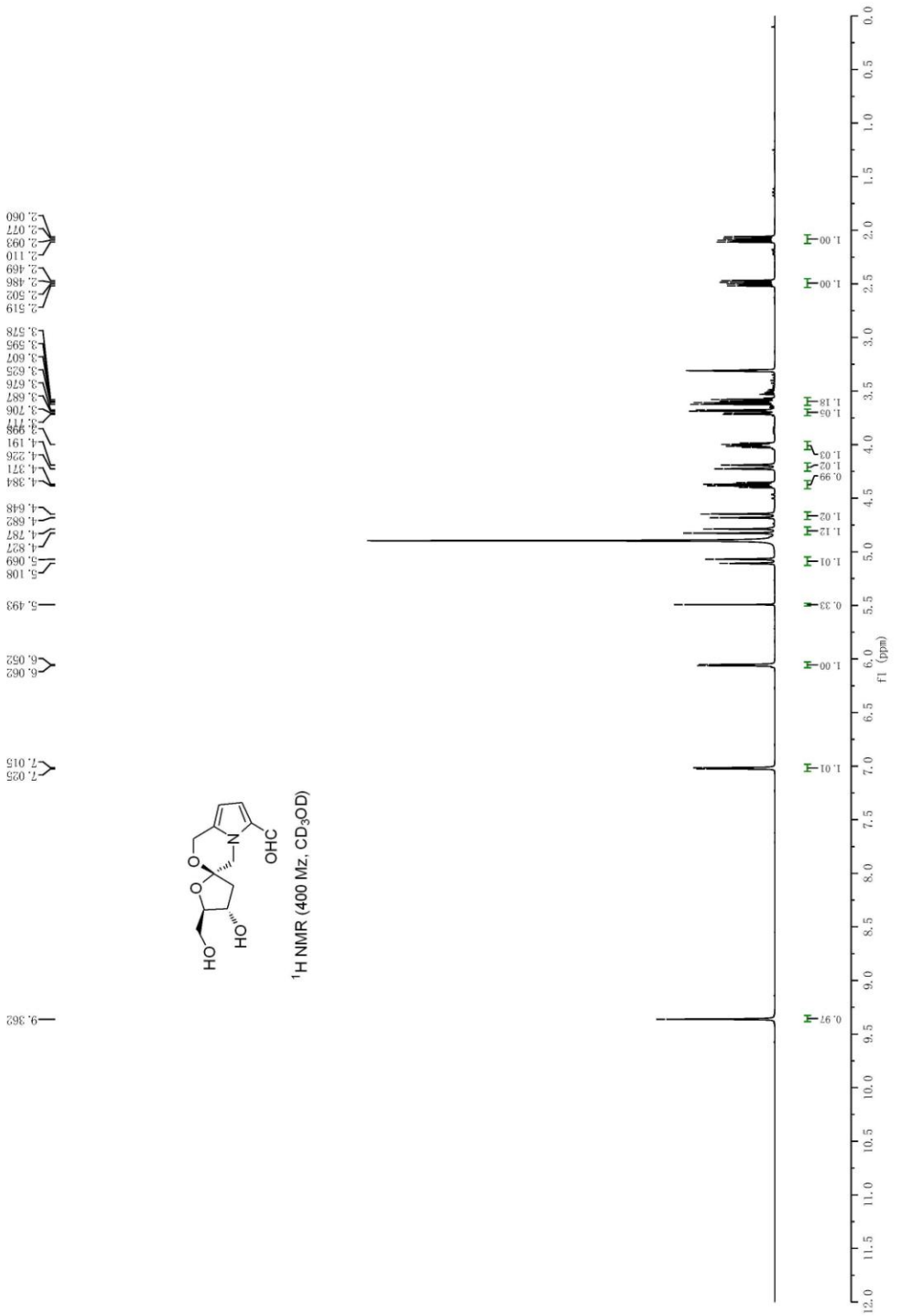


Figure S13. ^{13}C NMR spectrum of **2** in CD_3OD

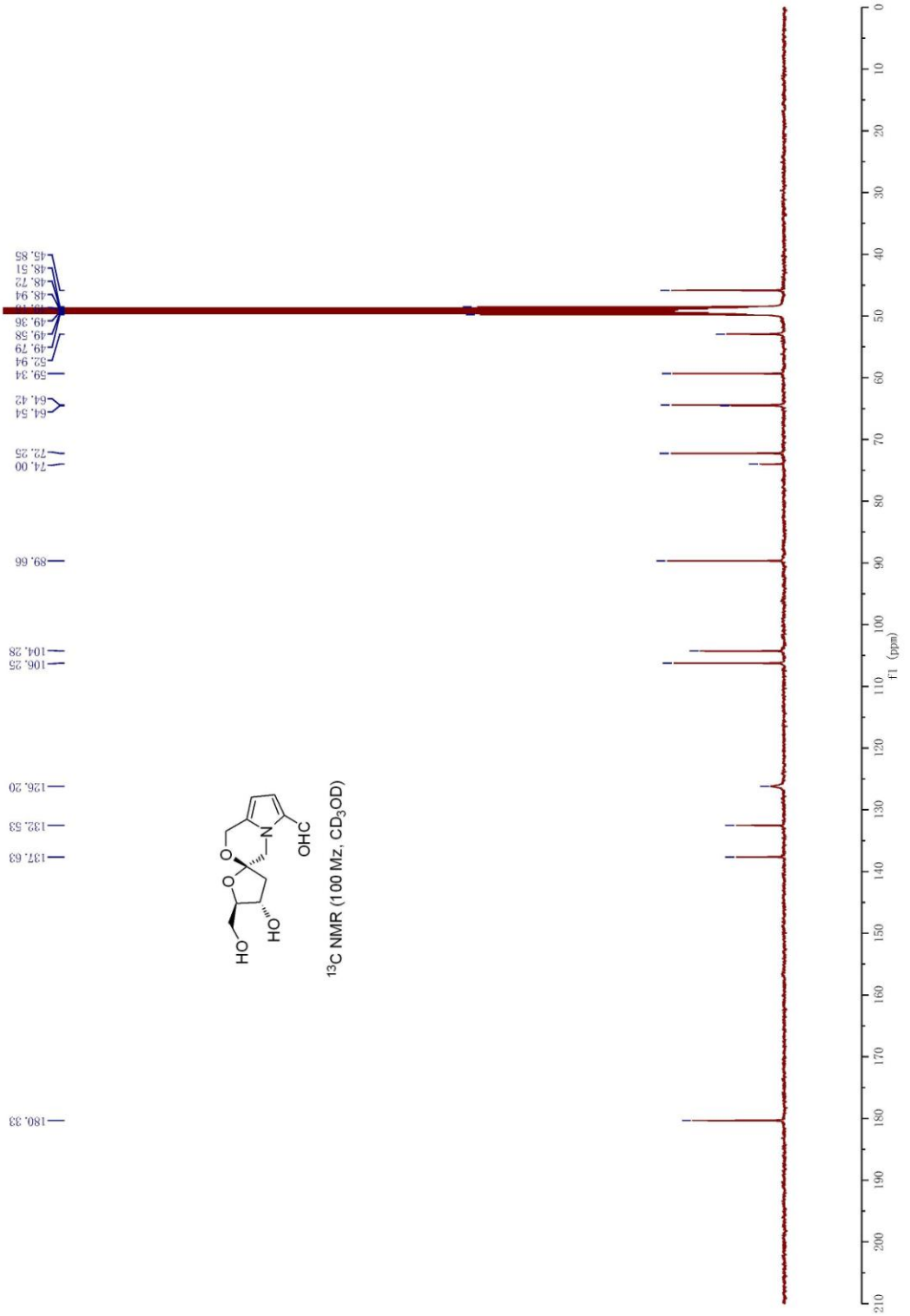


Figure S14. DEPT-135 spectrum of **2** in CD_3OD

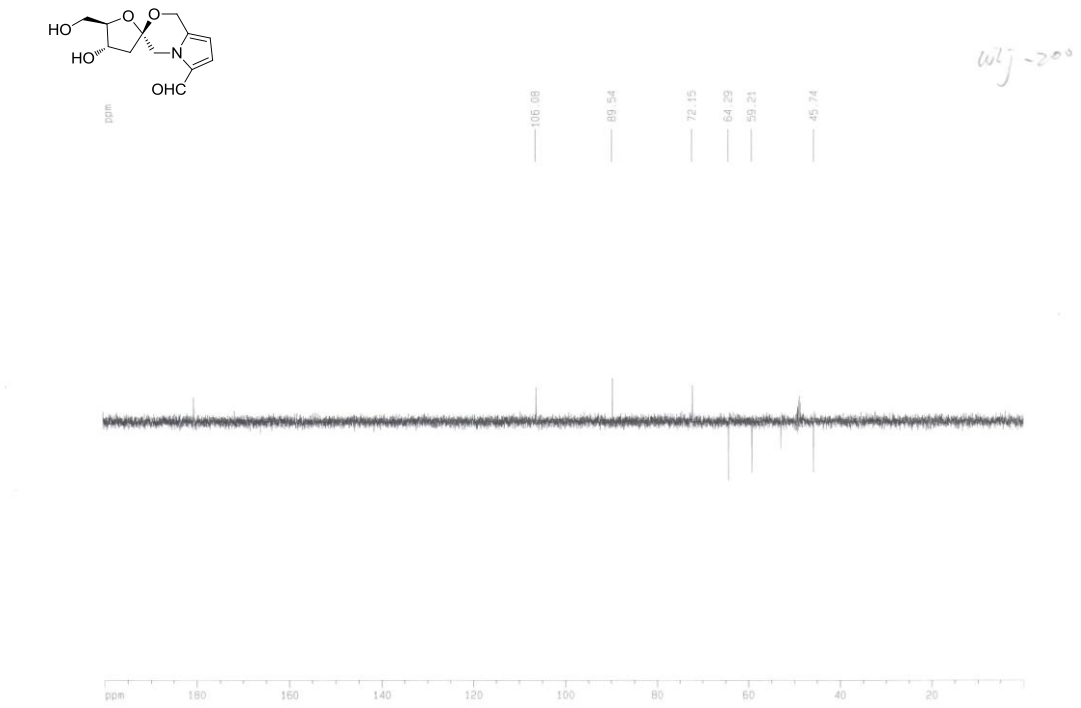


Figure S15. ^1H-^1H COSY spectrum of **2** in CD_3OD

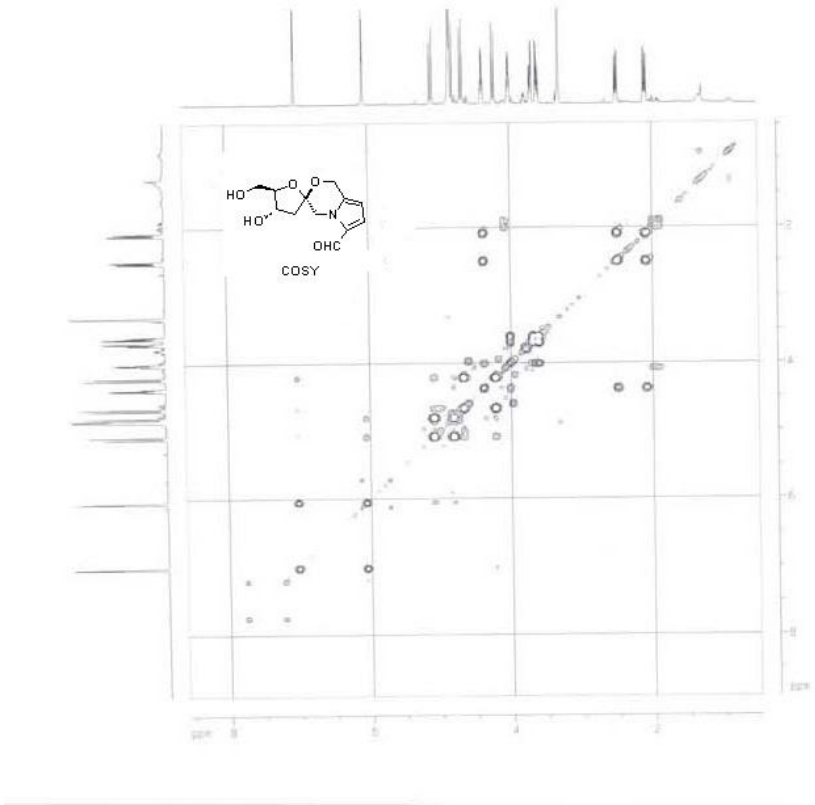


Figure S16. NOESY spectrum of **2** in CD_3OD

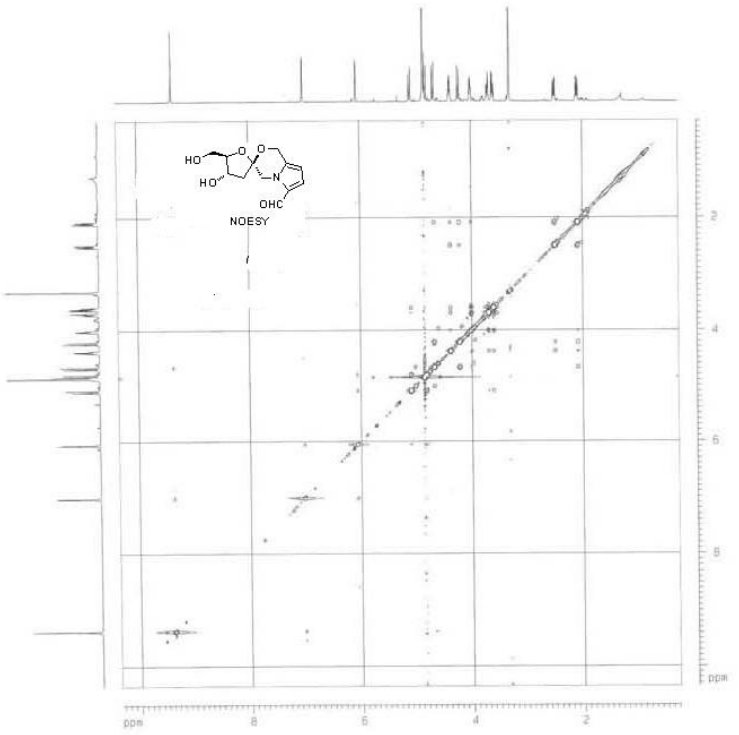


Figure S17. NOESY spectrum of **2** in CD_3OD-expansion

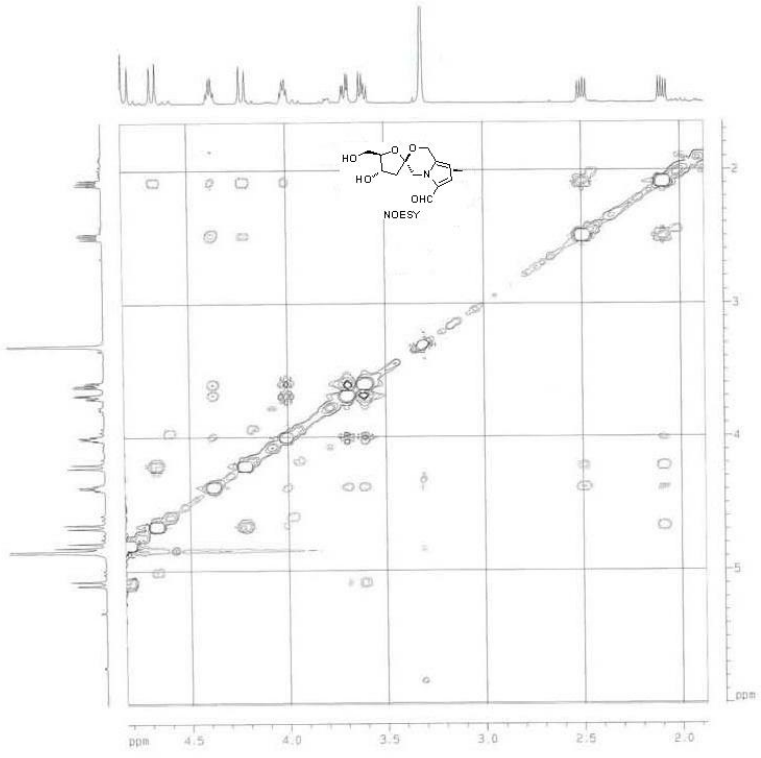


Figure S18. HR-EIMS of **2**

Elemental Composition Report

File Number: 20130412002
Sample Number:LM-4-1

Single Mass Analysis
Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off

Monoisotopic Mass, Odd and Even Electron Ions
11 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-15 H: 0-20 N: 0-1 O: 0-5

Minimum:				-1.5		
Maximum:		5.0	10.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
253.0951	253.0950	0.1	0.4	6.0	5546040.5	C12 H15 N O5

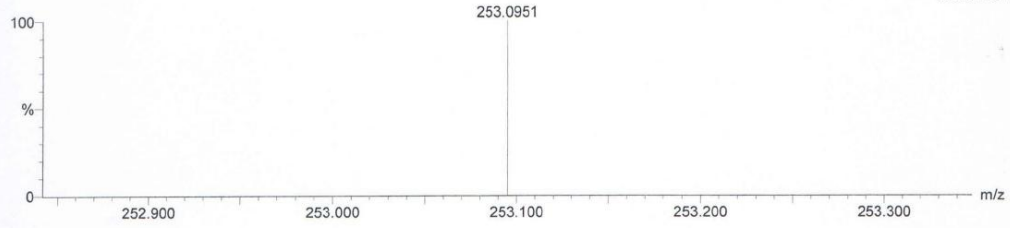
Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off

Monoisotopic Mass, Odd and Even Electron Ions
11 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-15 H: 0-20 N: 0-1 O: 0-5

LM-4-1
20130412002 70 (1.167)

TOF MS EI+
6.68e+001



Minimum:				-1.5		
Maximum:		5.0	10.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
253.0951	253.0950	0.1	0.4	6.0	5546040.5	C12 H15 N O5

Figure S19. ^{1}H NMR spectrum of **3** in CD_3OD

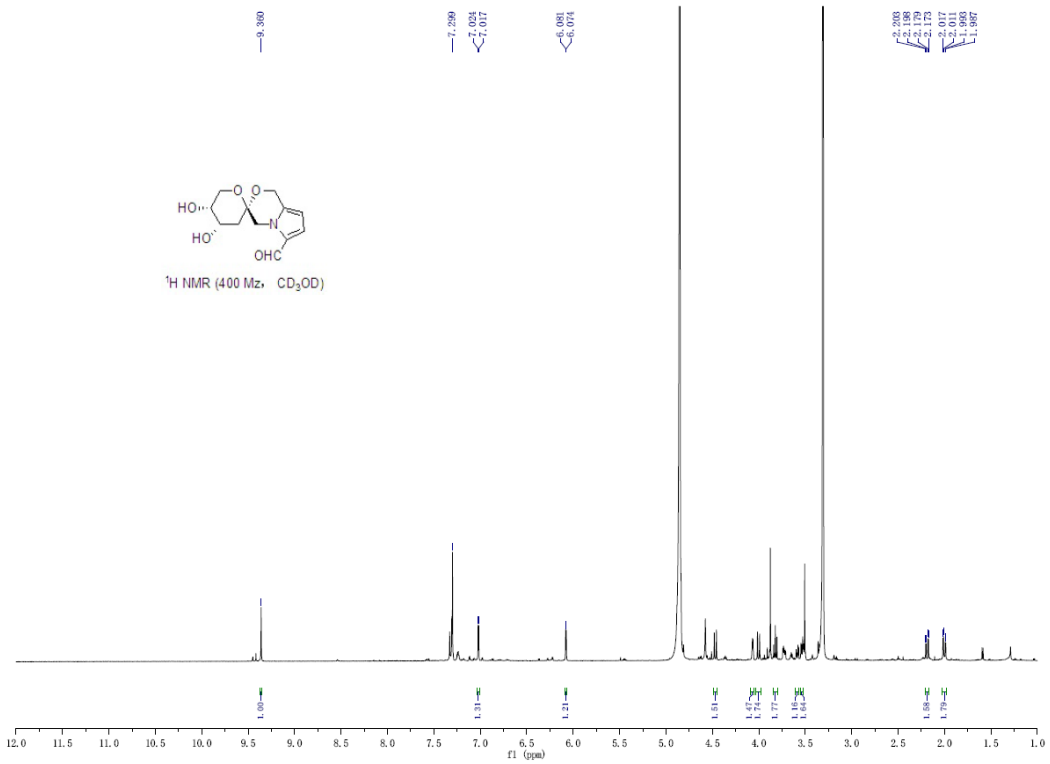


Figure S20. ^{13}C NMR spectrum of **3** in CD_3OD

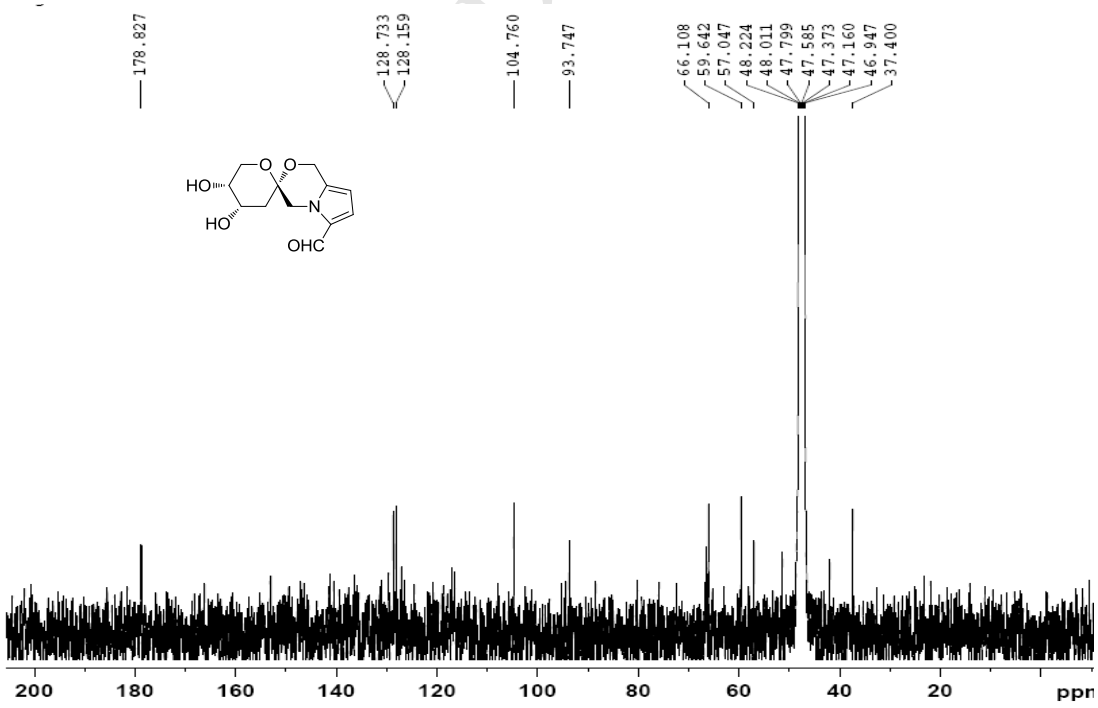


Figure S21. ^{1}H-^{1}H COSY spectrum of **3** in CD_3OD

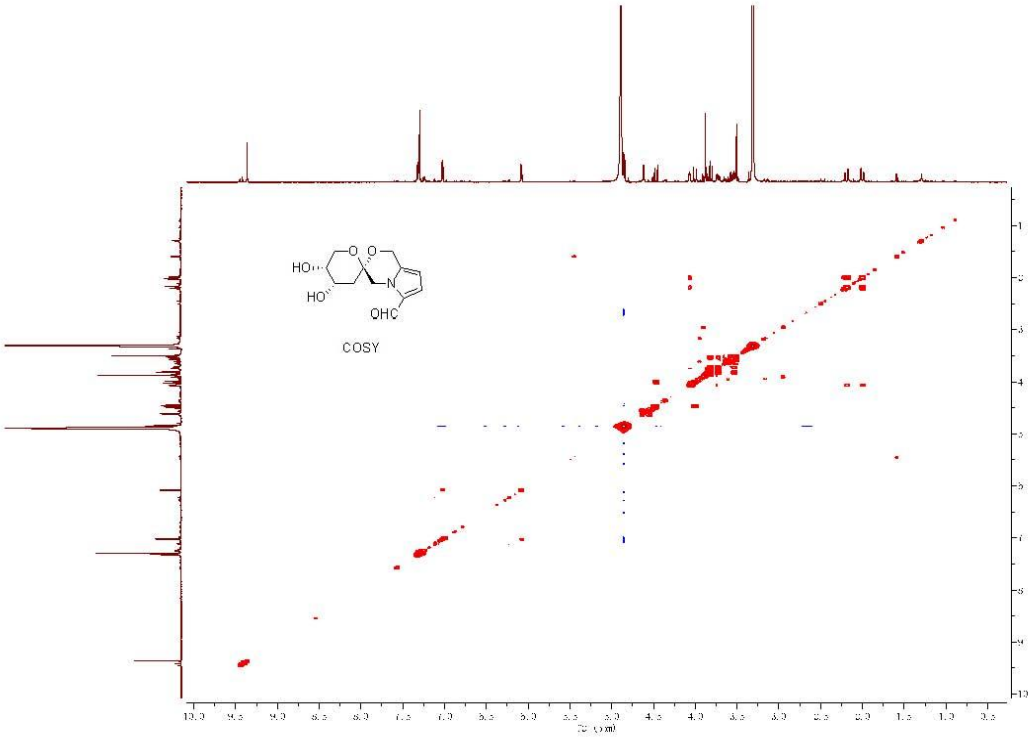


Figure S22. ^{1}H-^{1}H COSY spectrum of **3** in CD_3OD-expansion

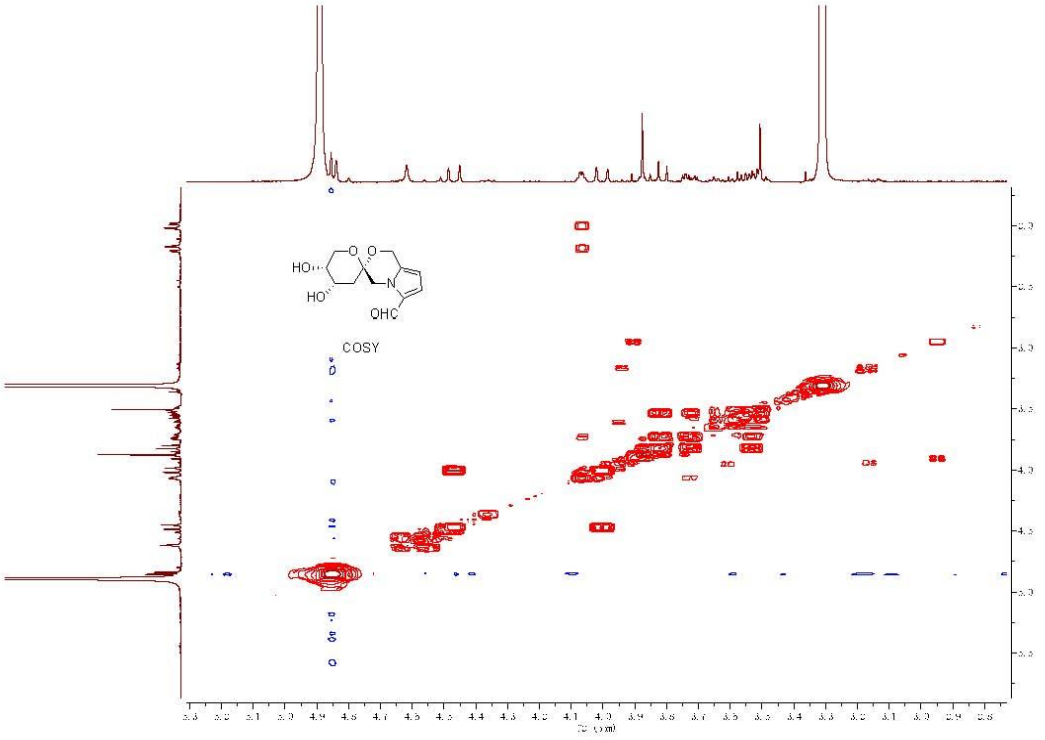


Figure S23. (+) ESI-MS of **3**

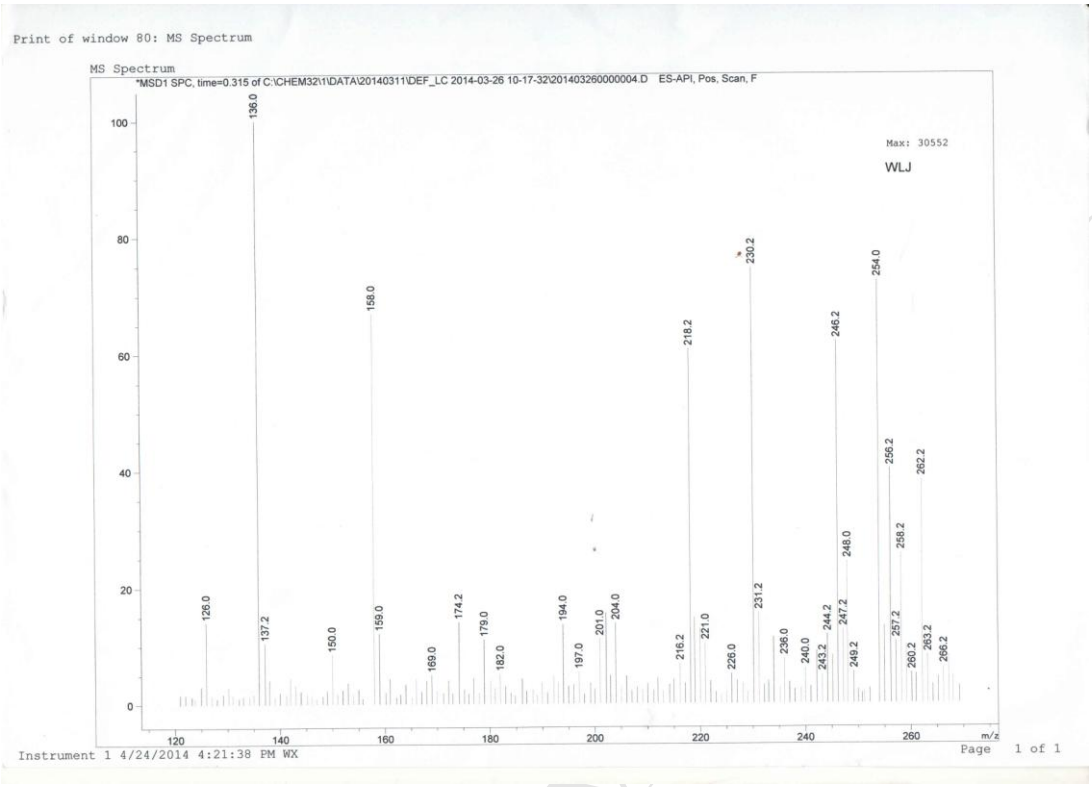


Figure S24. ^{1}H NMR spectrum of **4** in CD_3OD

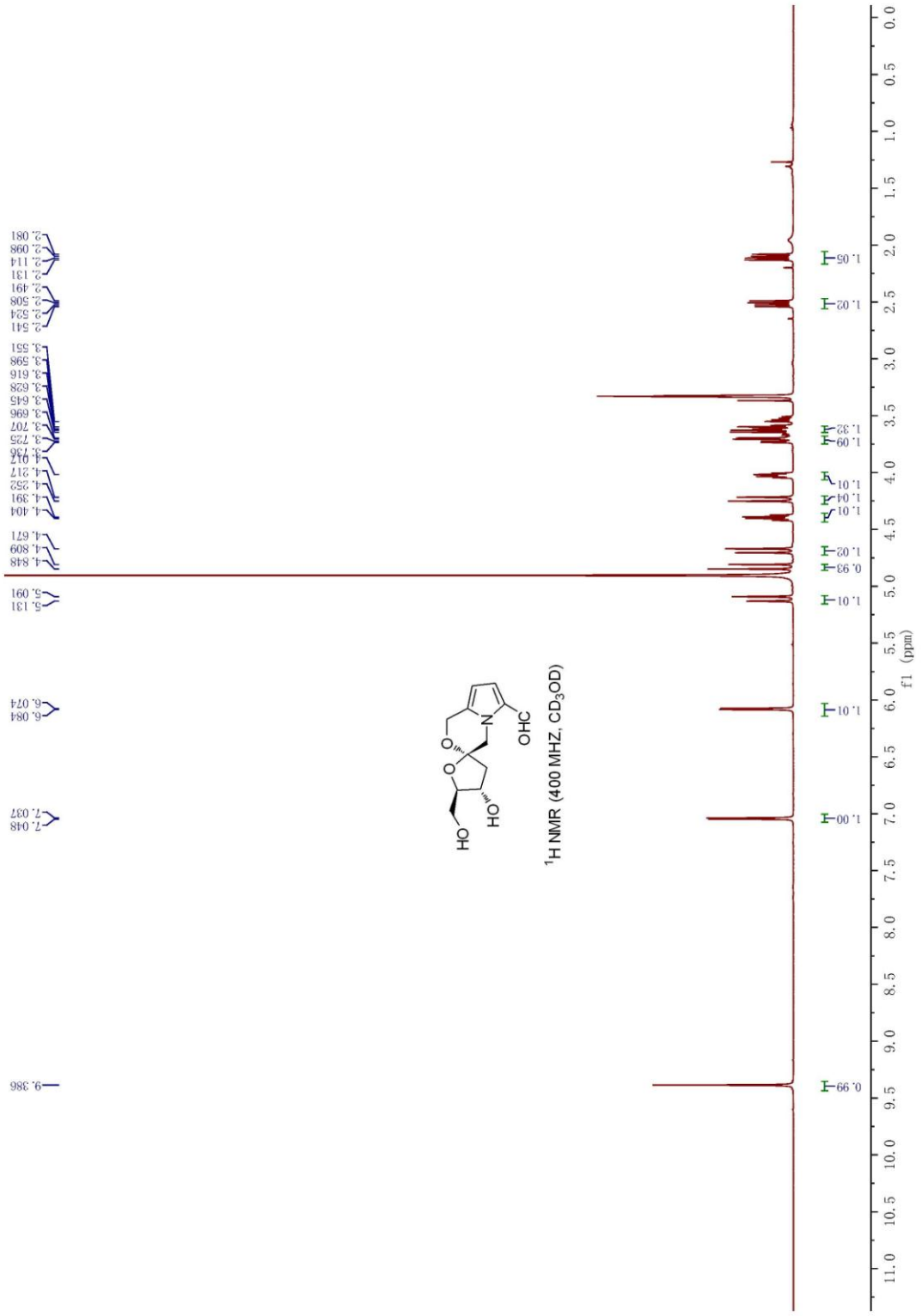


Figure S25. ^{13}C NMR spectrum of **4** in CD_3OD

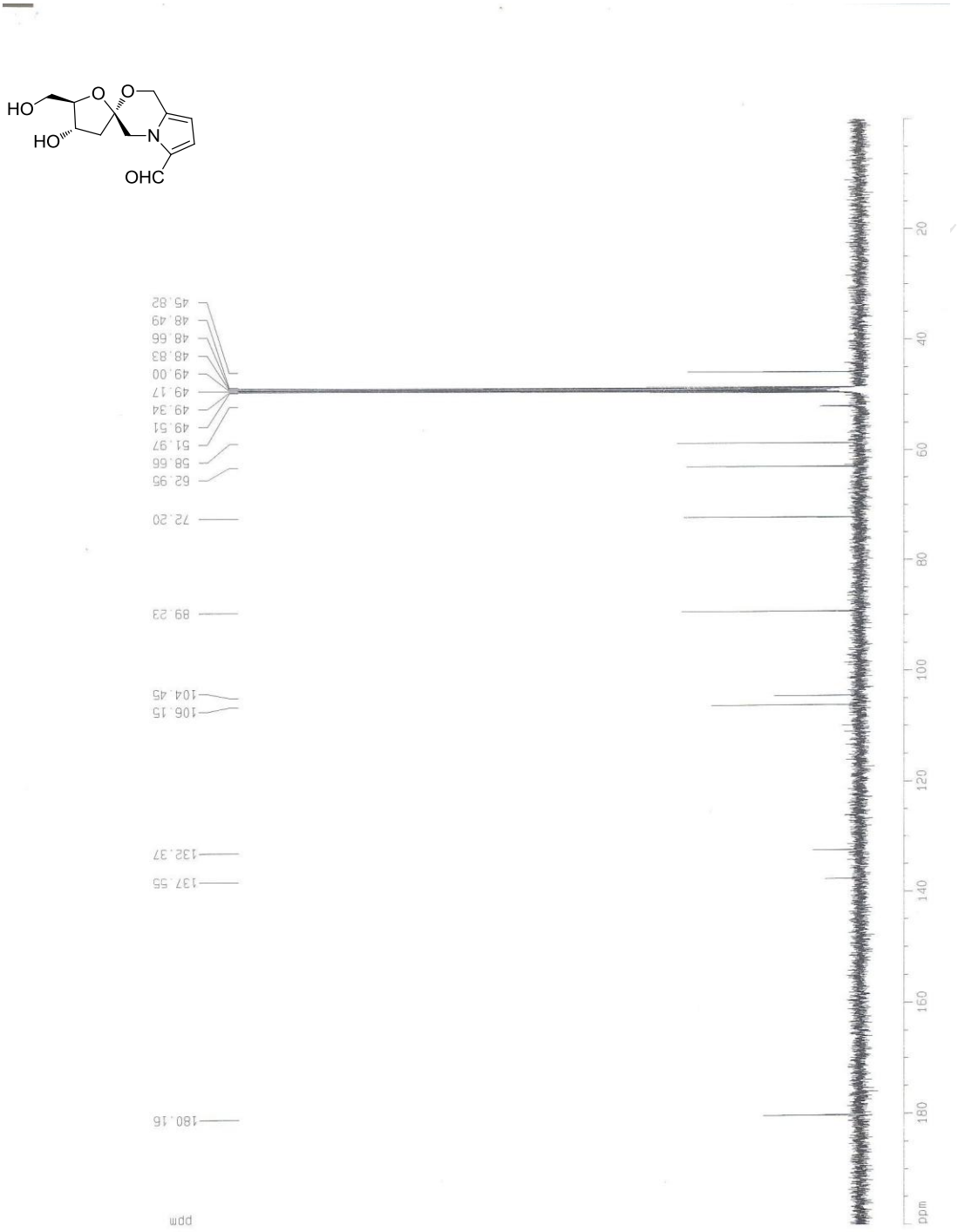


Figure S26. DEPT-135 spectrum of **4** in CD_3OD

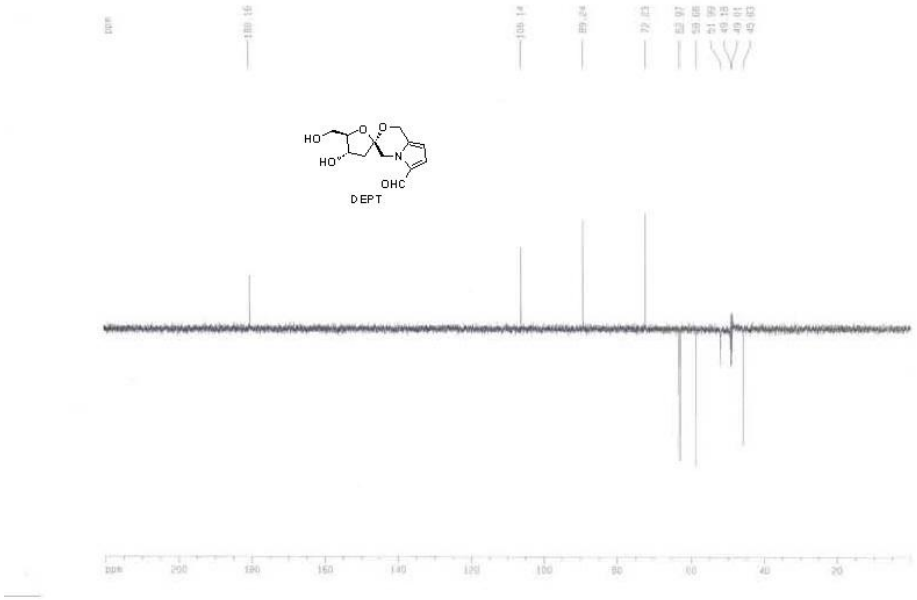


Figure S27. ^{1}H-^{1}H COSY spectrum of **4** in CD_3OD

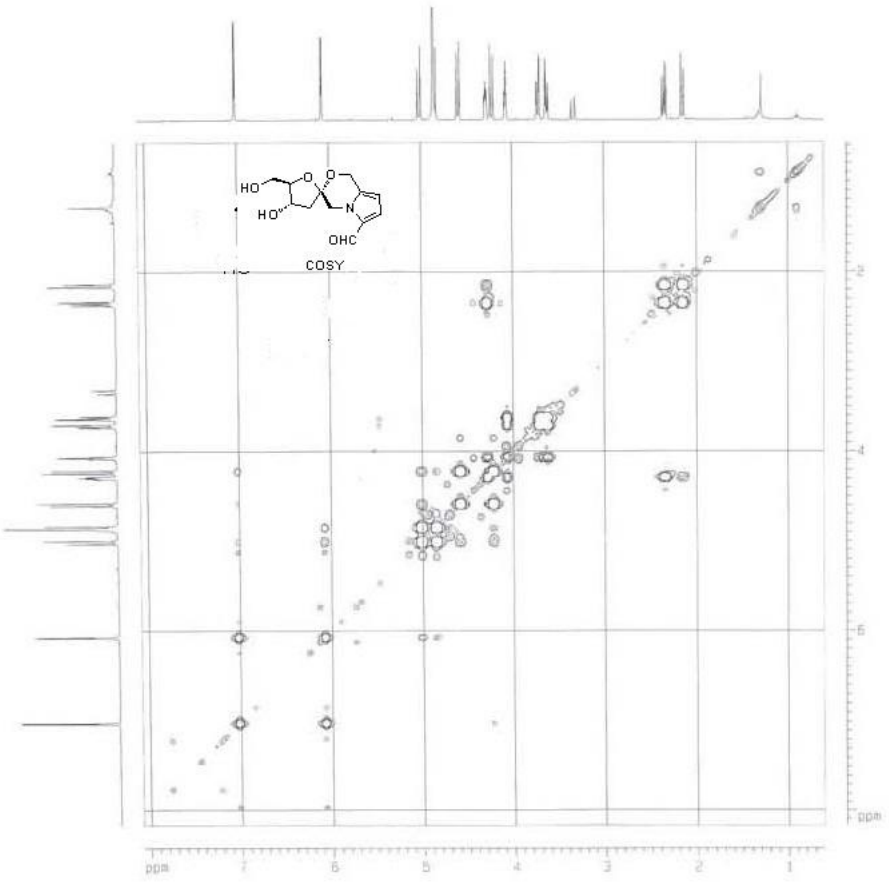


Figure S28. HSQC spectrum of **4** in CD_3OD

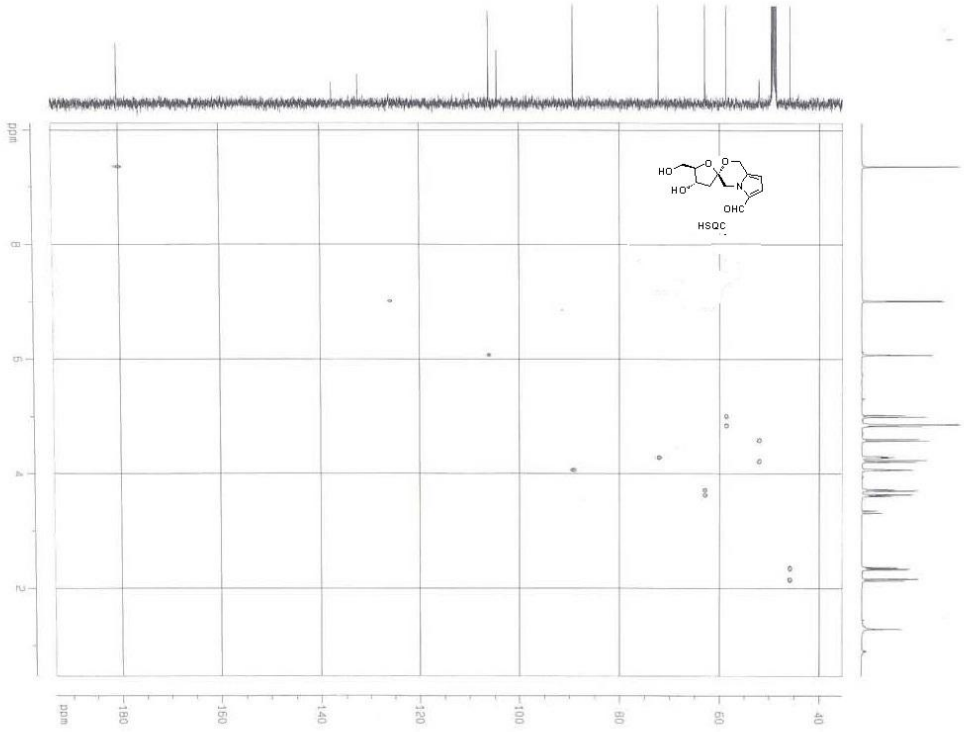


Figure S29. HMBC spectrum of **4** in CD_3OD

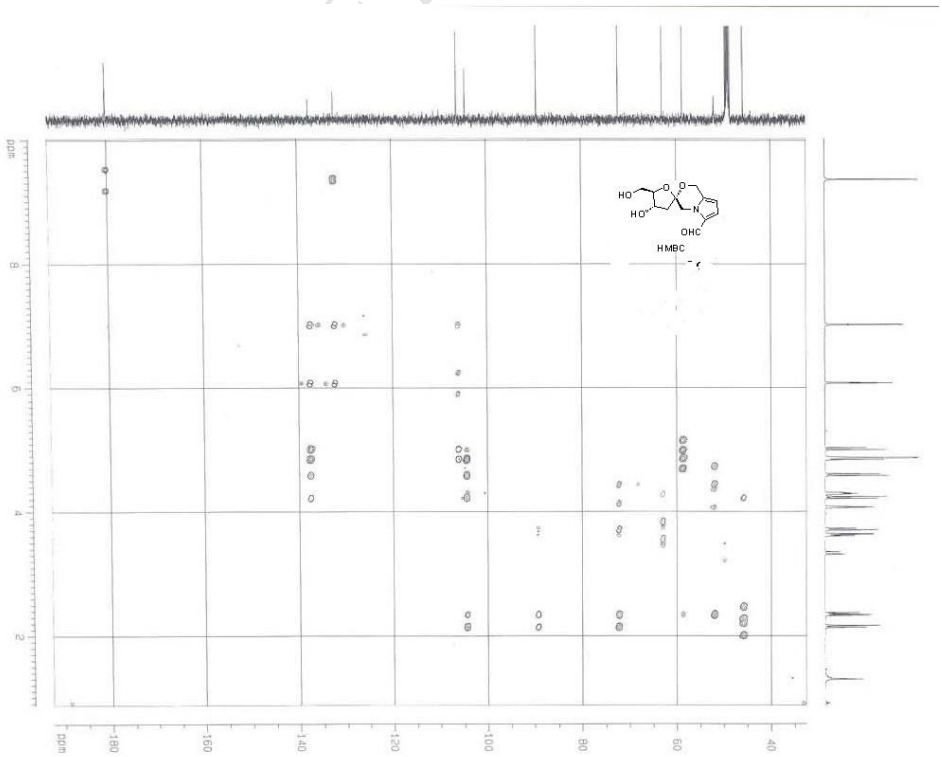


Figure S30. HMBC spectrum of **4** in CD_3OD-expansion

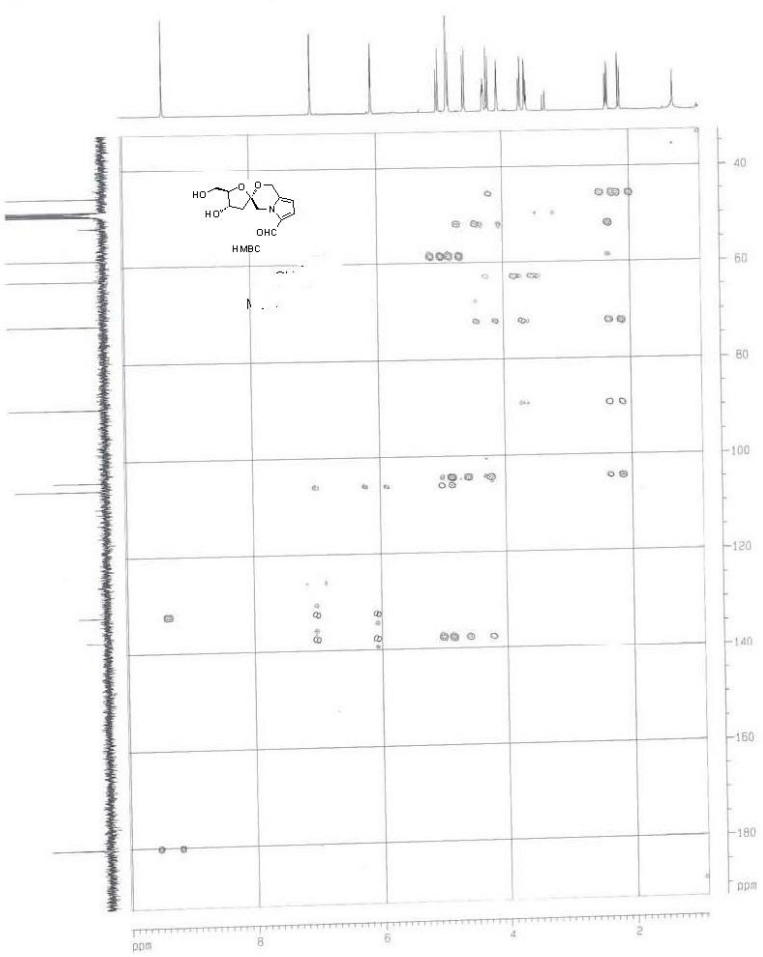


Figure S31. NOESY spectrum of **4** in CD_3OD

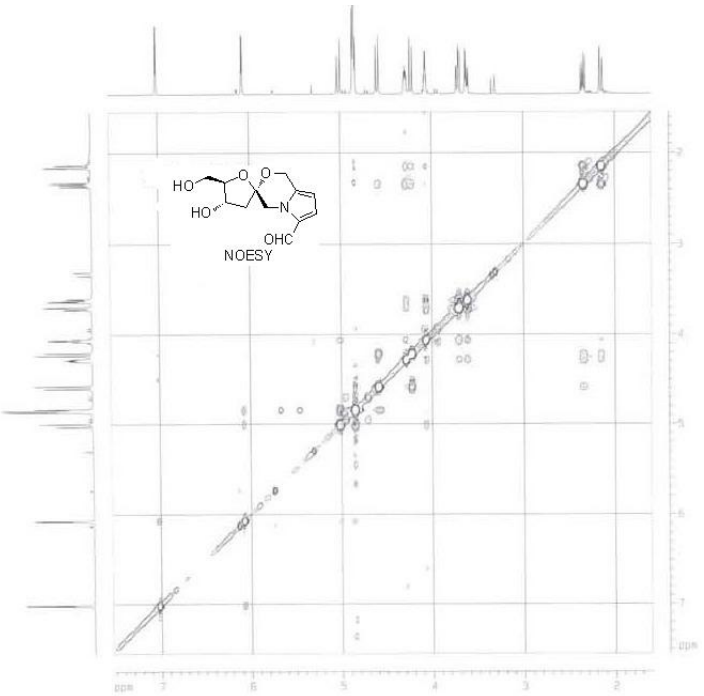


Figure S32. NOESY spectrum of **4** in CD_3OD-expansion

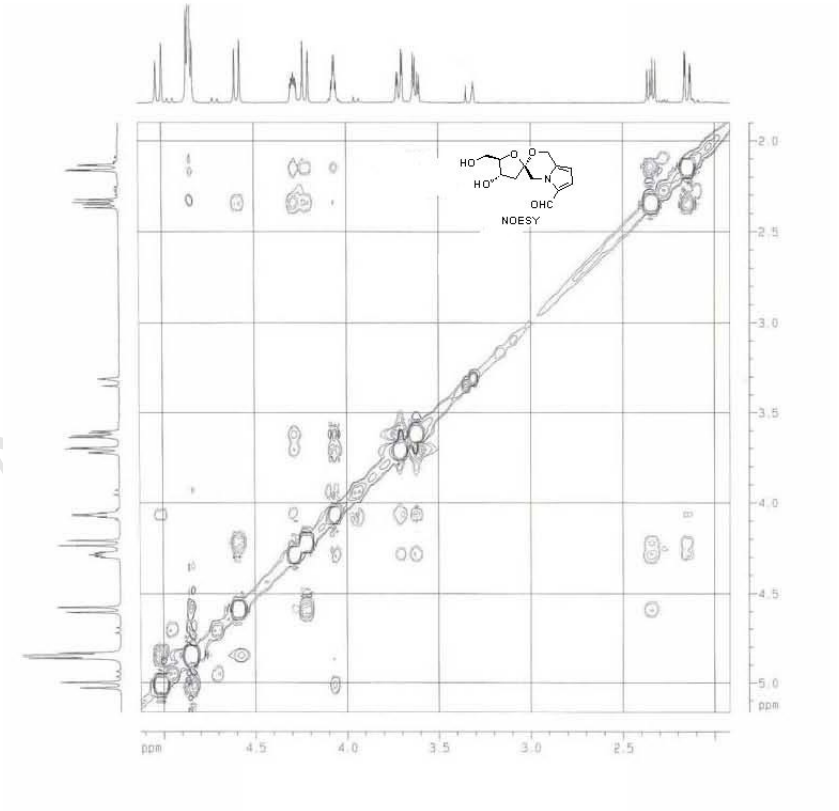


Figure S33. HR-EIMS of **4**

Elemental Composition Report

File Number: 20130412006
Sample Number:LM-4-6

Single Mass Analysis
Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off

Monoisotopic Mass, Odd and Even Electron Ions
11 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-15 H: 0-20 N: 0-1 O: 0-5

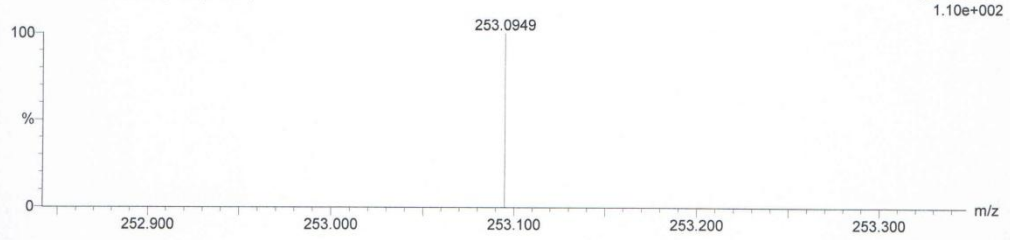
Minimum:				-1.5		
Maximum:		5.0	10.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
253.0949	253.0950	-0.1	-0.4	6.0	5546058.5	C12 H15 N O5

Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off

Monoisotopic Mass, Odd and Even Electron Ions
11 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-15 H: 0-20 N: 0-1 O: 0-5
LM-4-6
20130412006 98 (1.634) Cm (98:112)

TOF MS EI+
1.10e+002



Minimum:				-1.5		
Maximum:		5.0	10.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
253.0949	253.0950	-0.1	-0.4	6.0	5546058.5	C12 H15 N O5

Figure S34. ^{1}H NMR spectrum of **1a** in CD_3OD

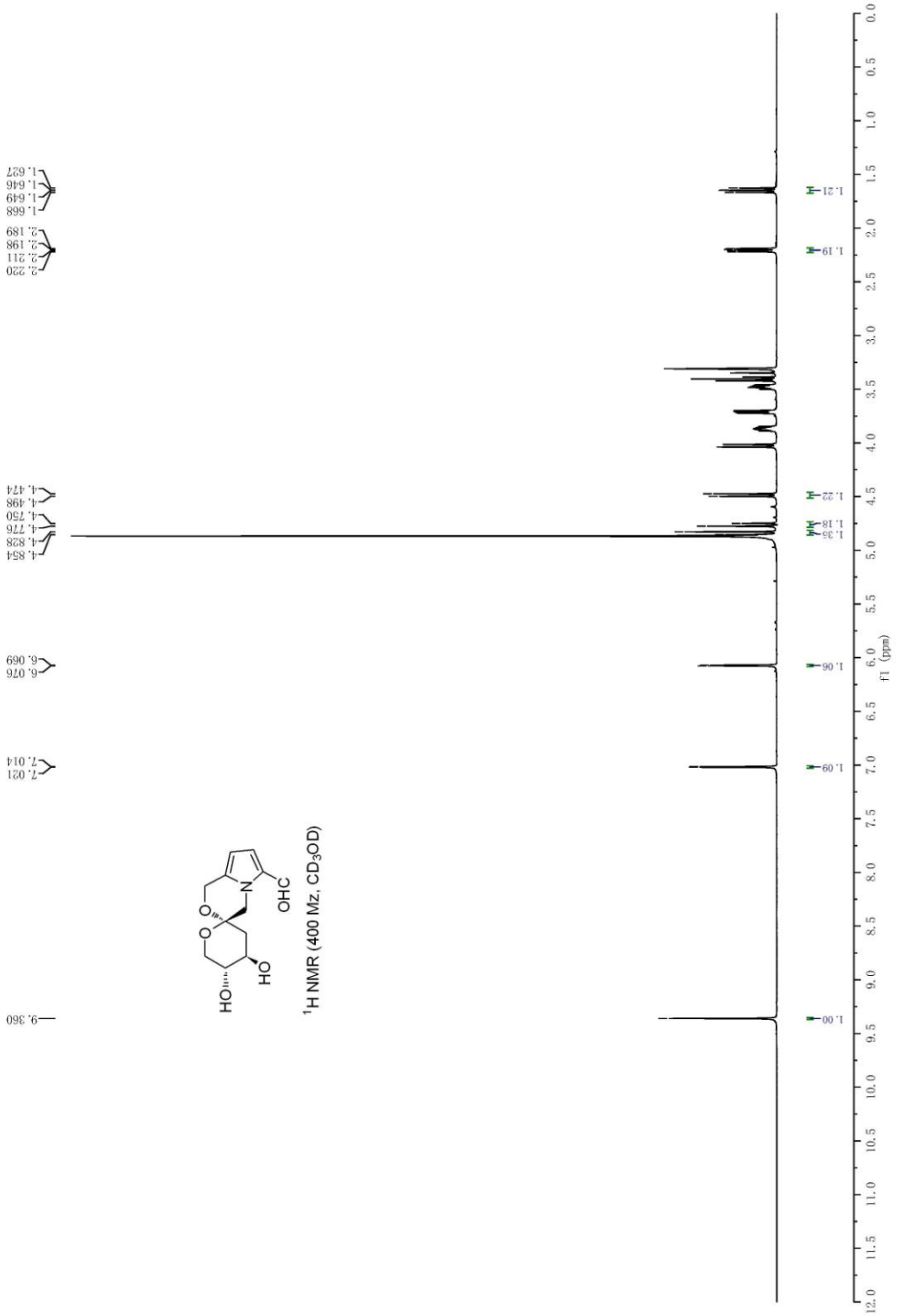


Figure S35. ^{1}H NMR spectrum of **1a** in CD_3COCD_3

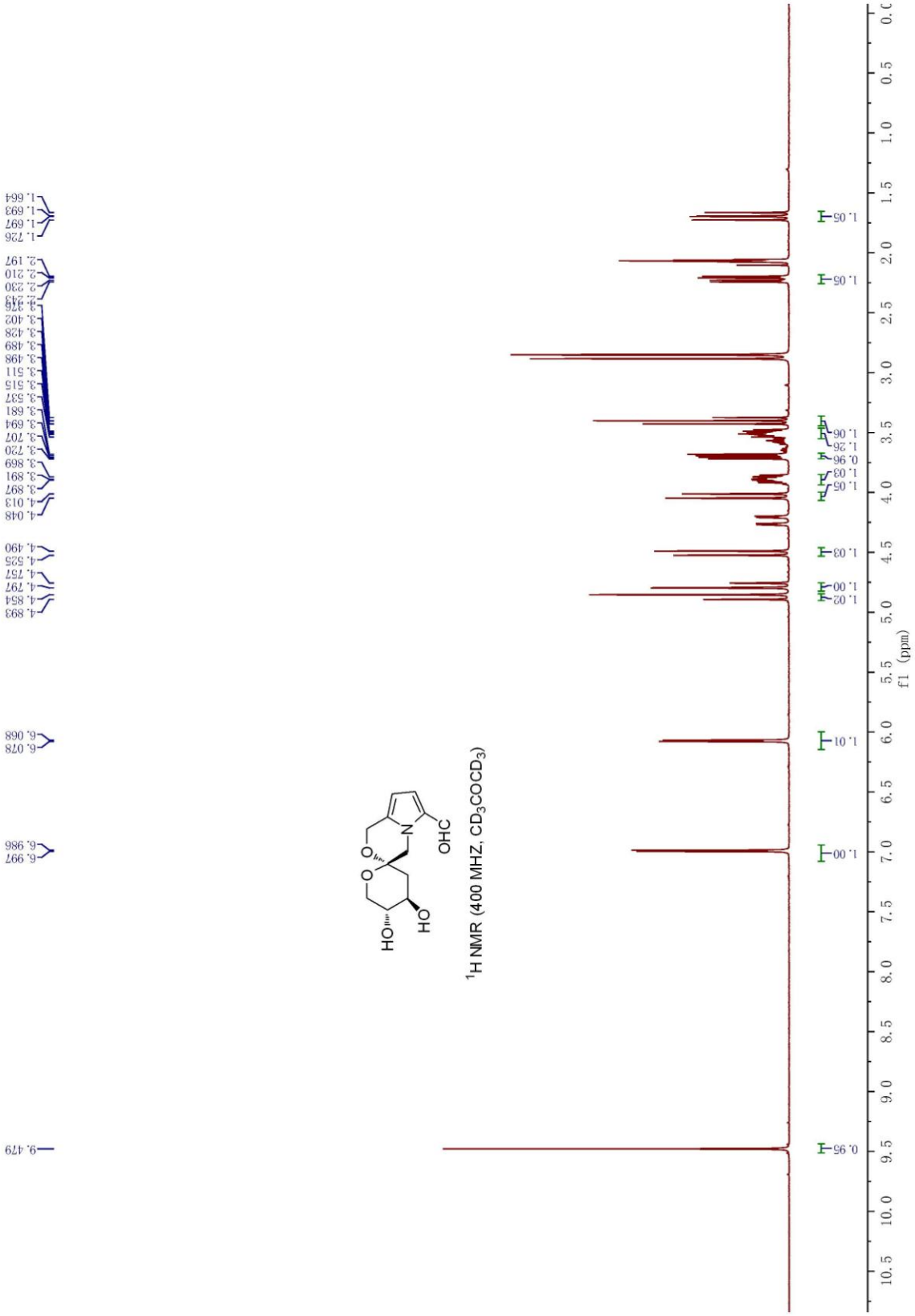


Figure S36. ^{1}H NMR spectrum of **1a** in $CDCl_3$

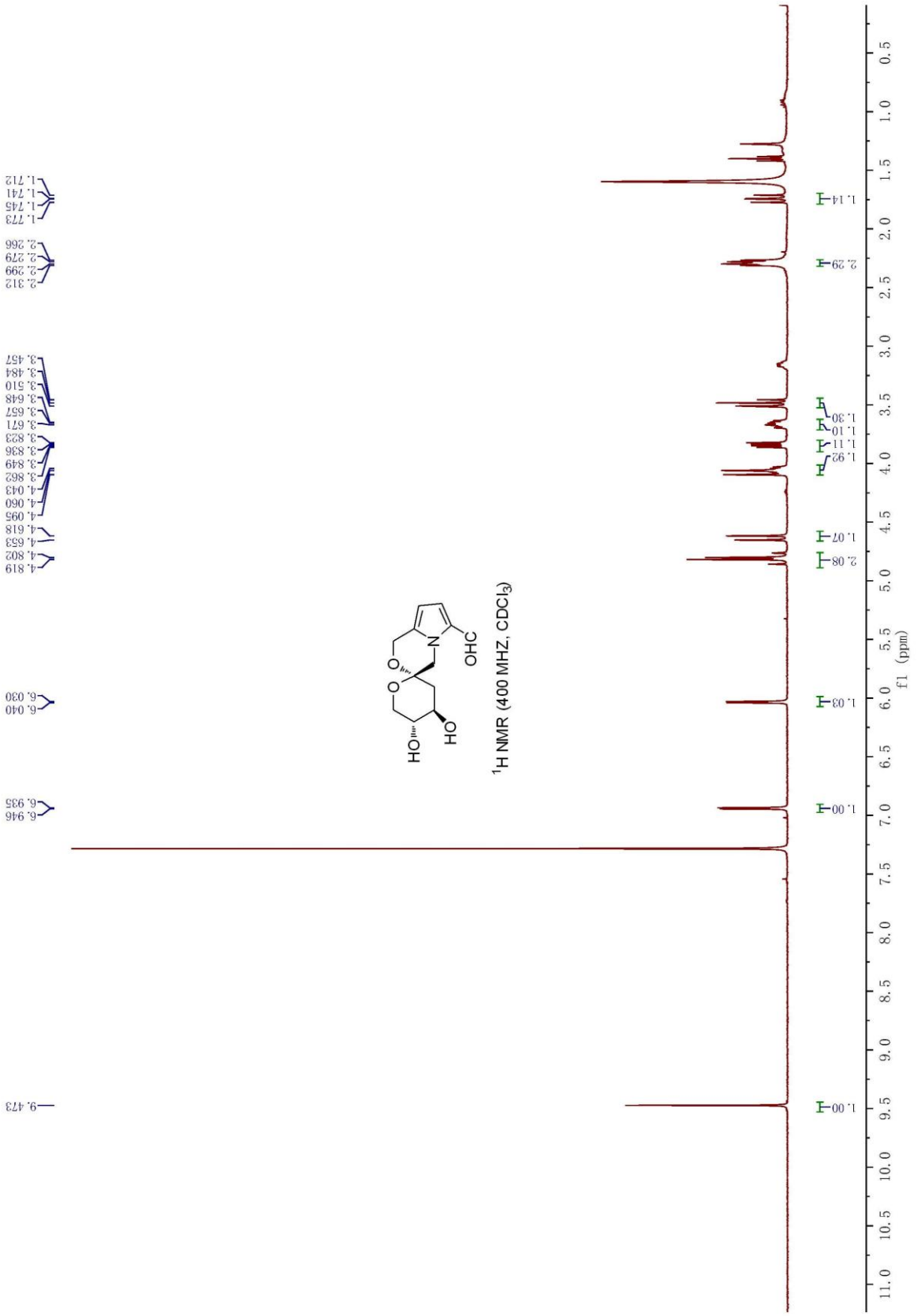


Figure S37. ^{13}C NMR spectrum of **1a** in CD_3OD

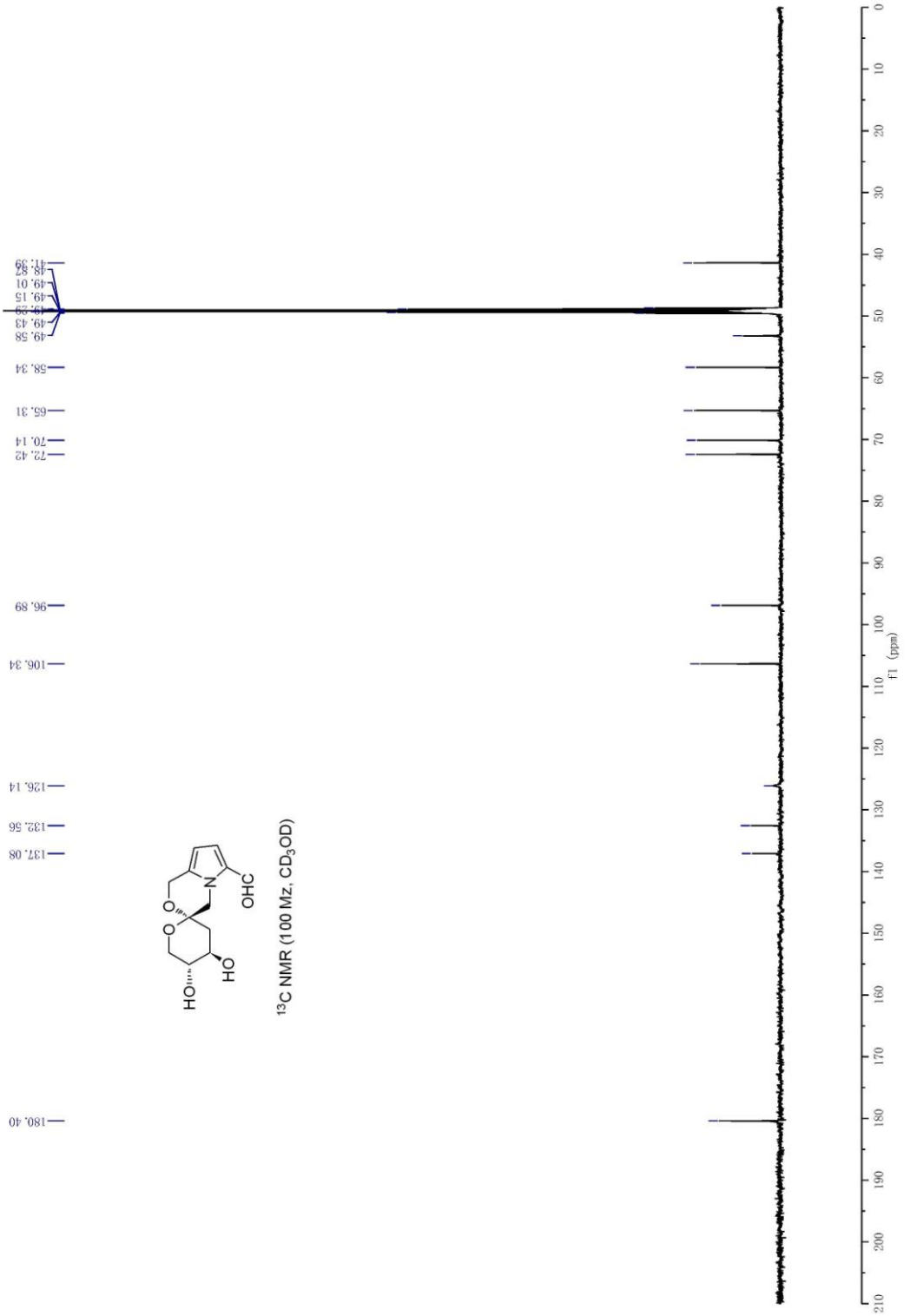


Figure S38. ^{1}H-^{1}H COSY spectrum of **1a** in CD_3OD

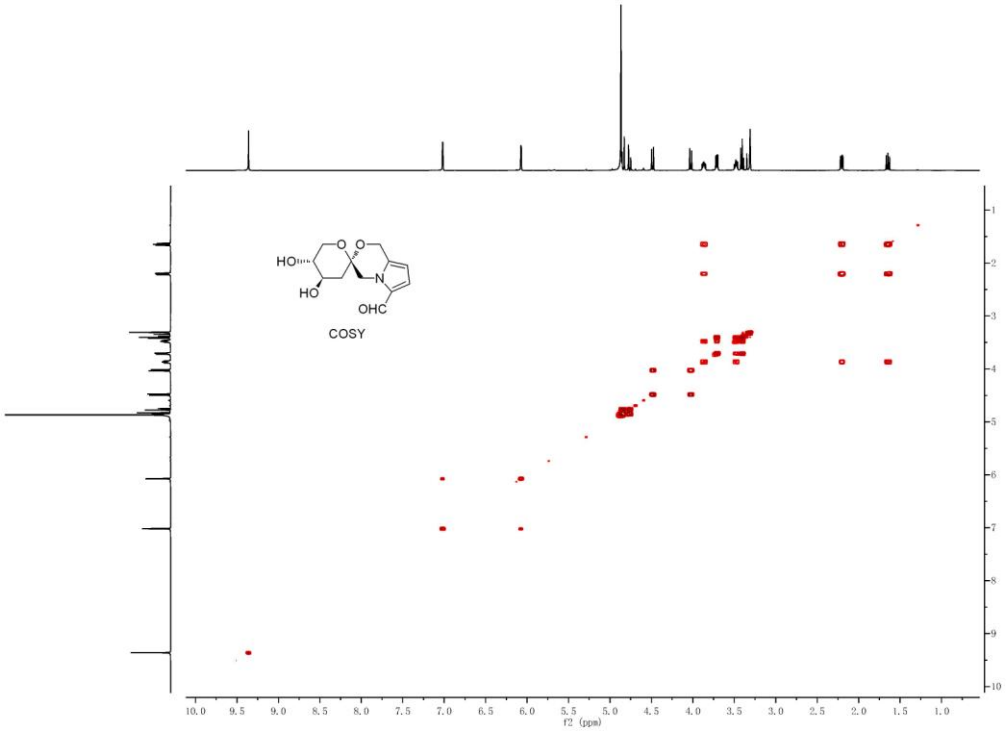


Figure S39. HSQC spectrum of **1a** in CD_3OD

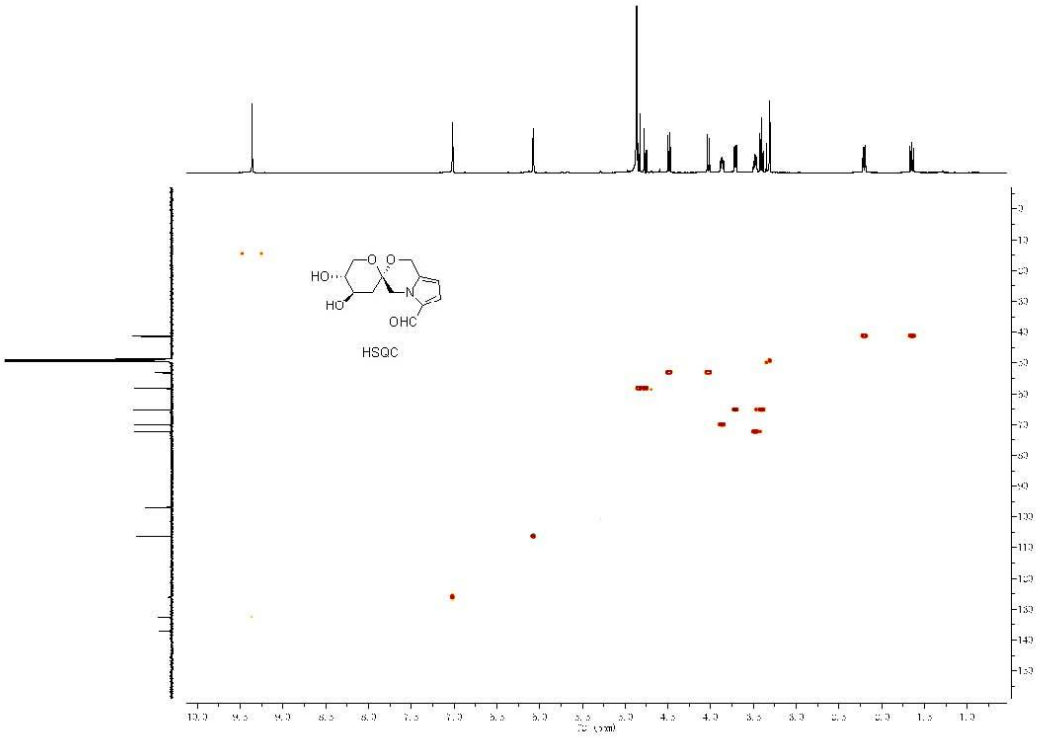


Figure S40. HMBC spectrum of **1a** in CD_3OD

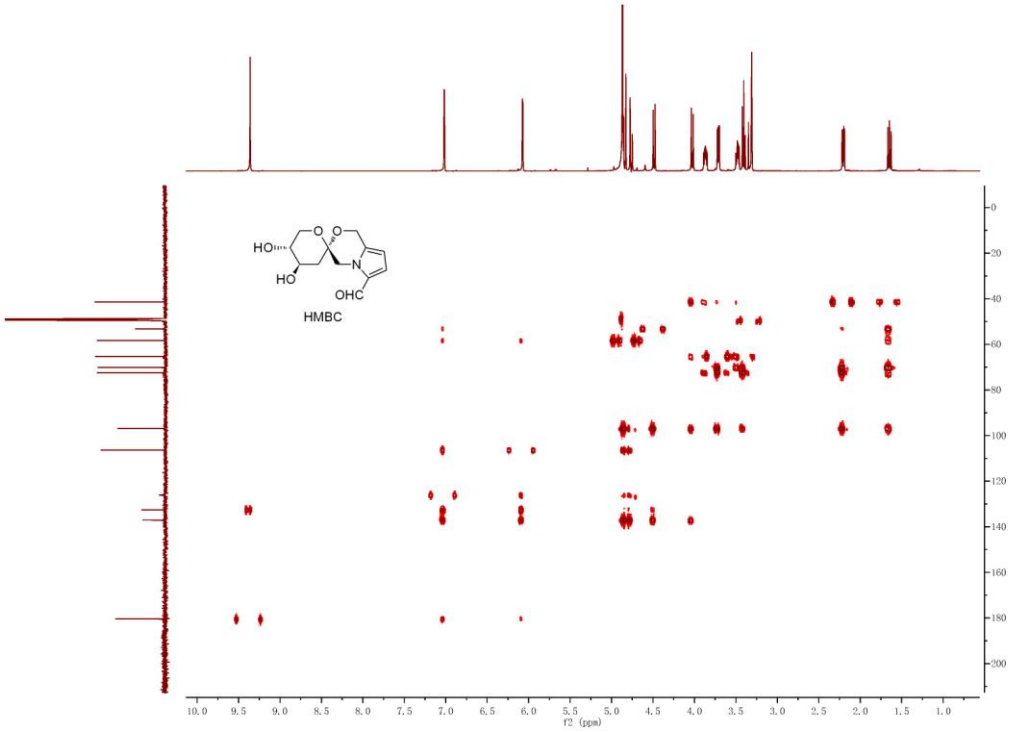


Figure S41. NOESY spectrum of **1a** in CD_3OD

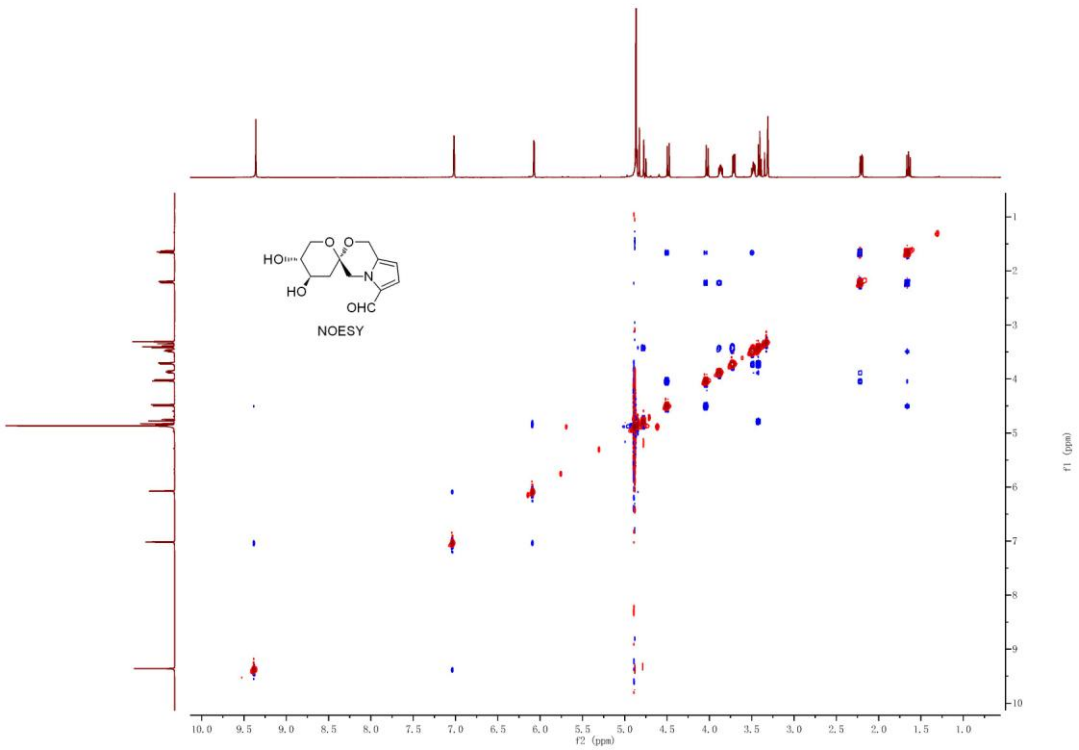
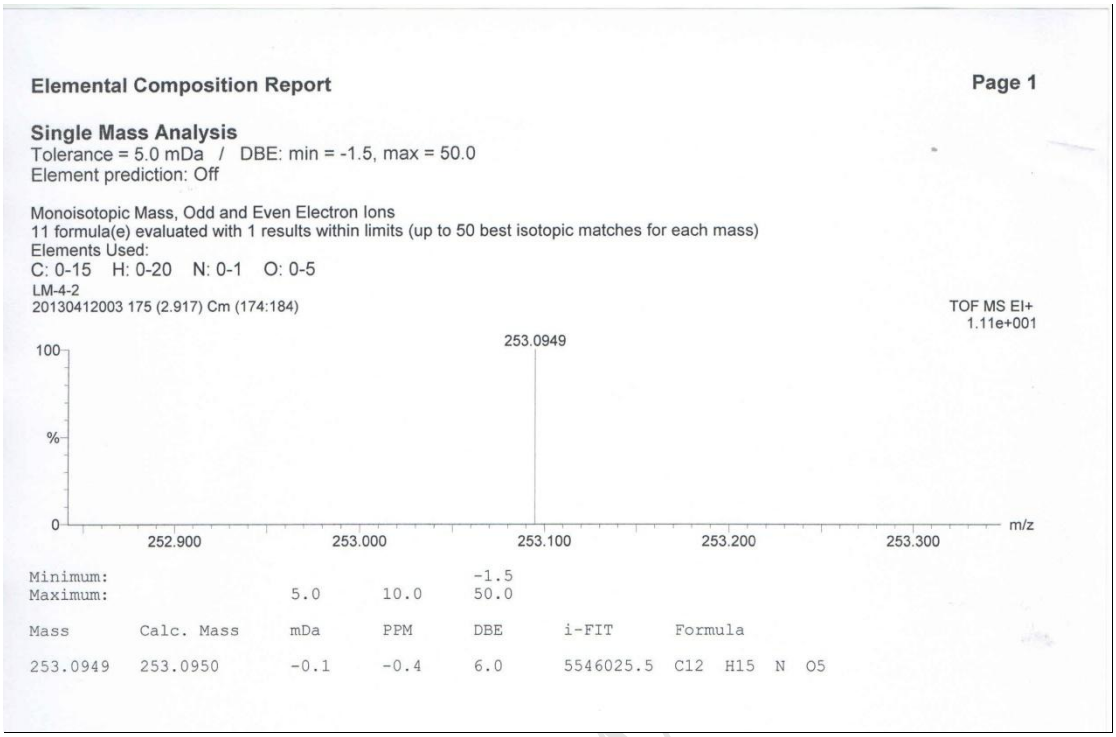


Figure S42. HR-EIMS of **1a**



Elemental Composition Report Page 1

Single Mass Analysis
Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off

Monoisotopic Mass, Odd and Even Electron Ions
11 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-15 H: 0-20 N: 0-1 O: 0-5
LM-4-2
20130412003 175 (2.917) Cm (174:184)

TOF MS EI+
1.11e+001

Minimum:				-1.5		
Maximum:		5.0	10.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
253.0949	253.0950	-0.1	-0.4	6.0	5546025.5	C12 H15 N O5

Figure S43. ^{1}H NMR spectrum of **1b** in CD_3OD

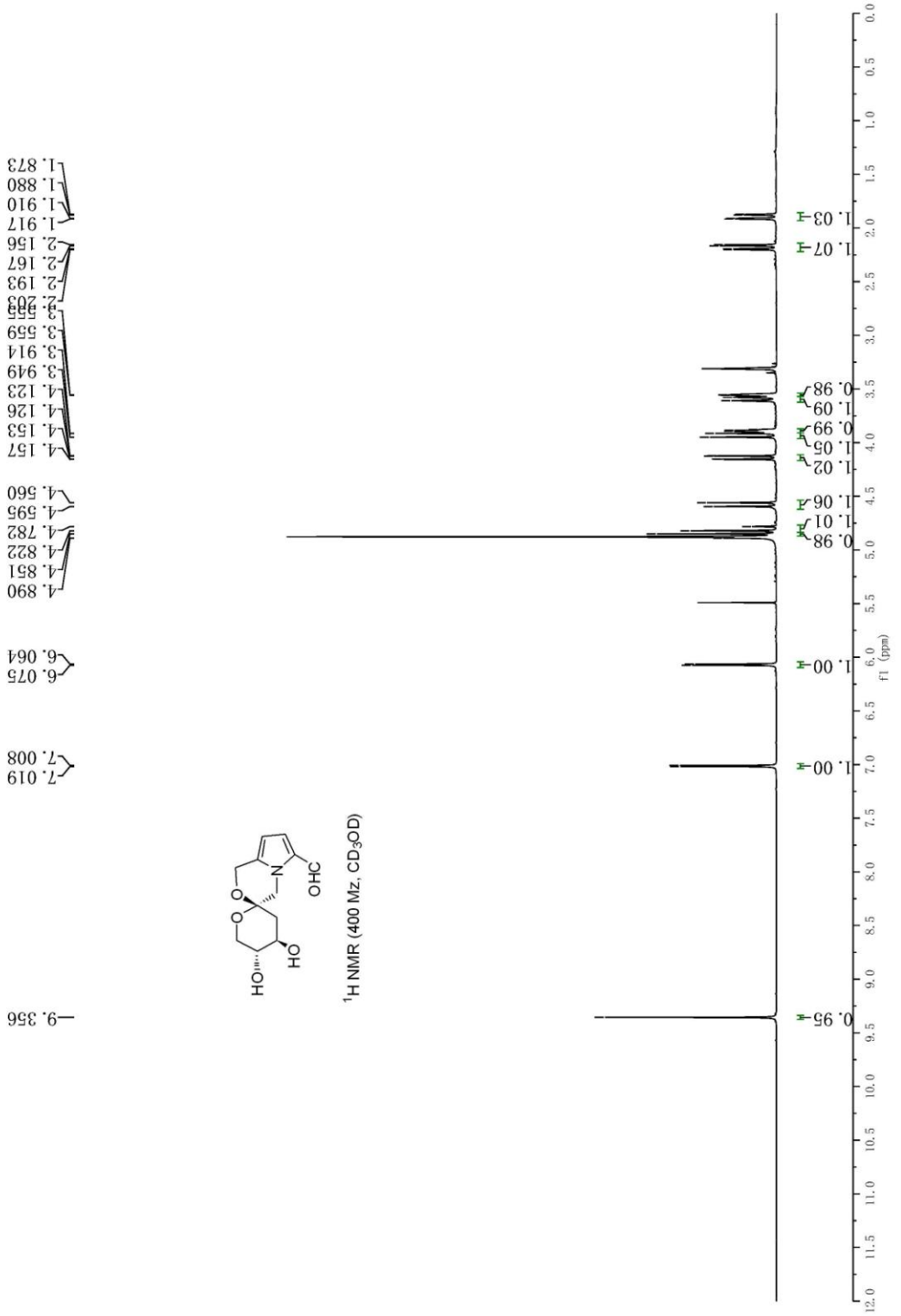


Figure S44. ^{1}H NMR spectrum of **1b** in CD_3COCD_3

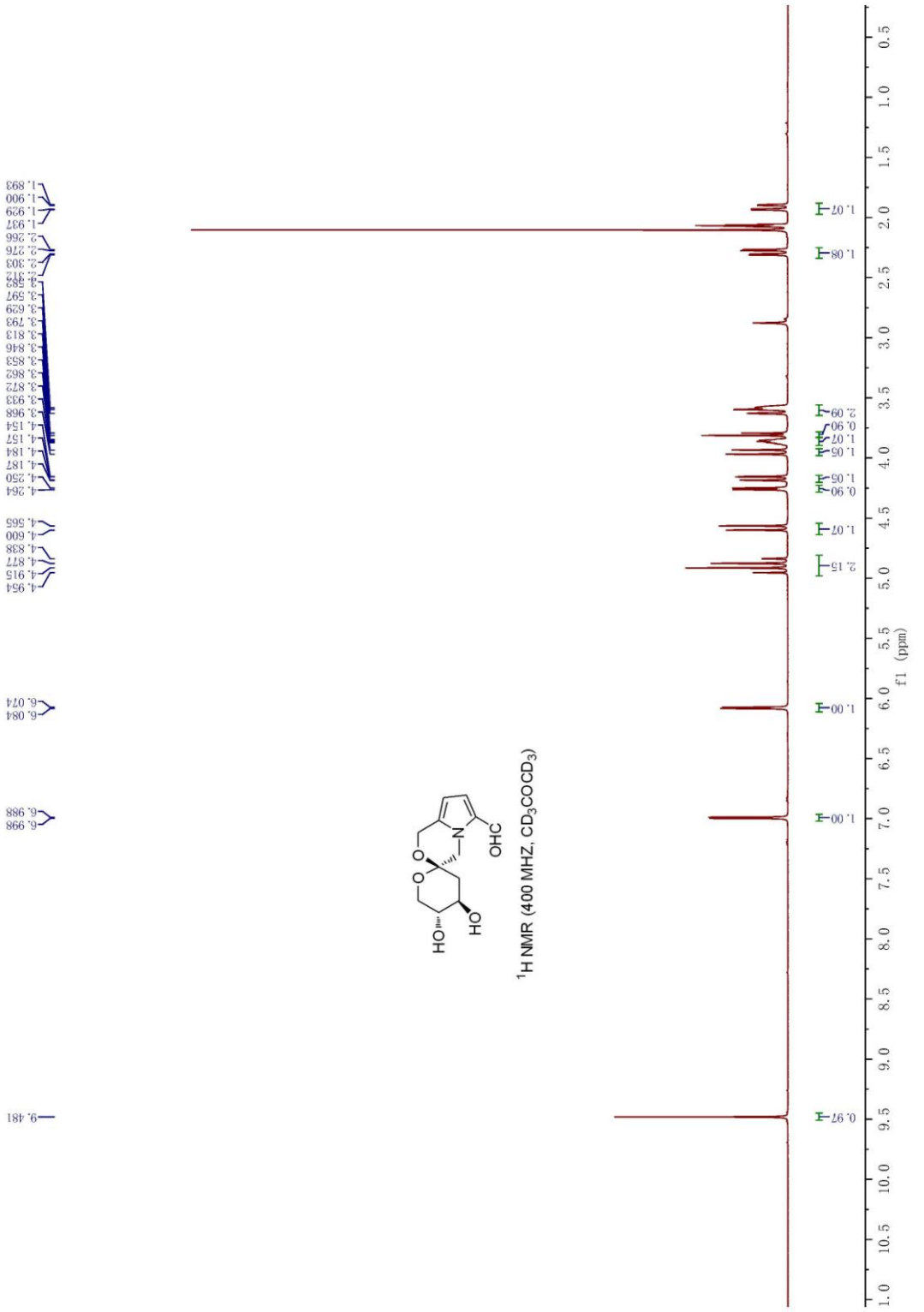


Figure S45. ^{1}H NMR spectrum of **1b** in $CDCl_3$

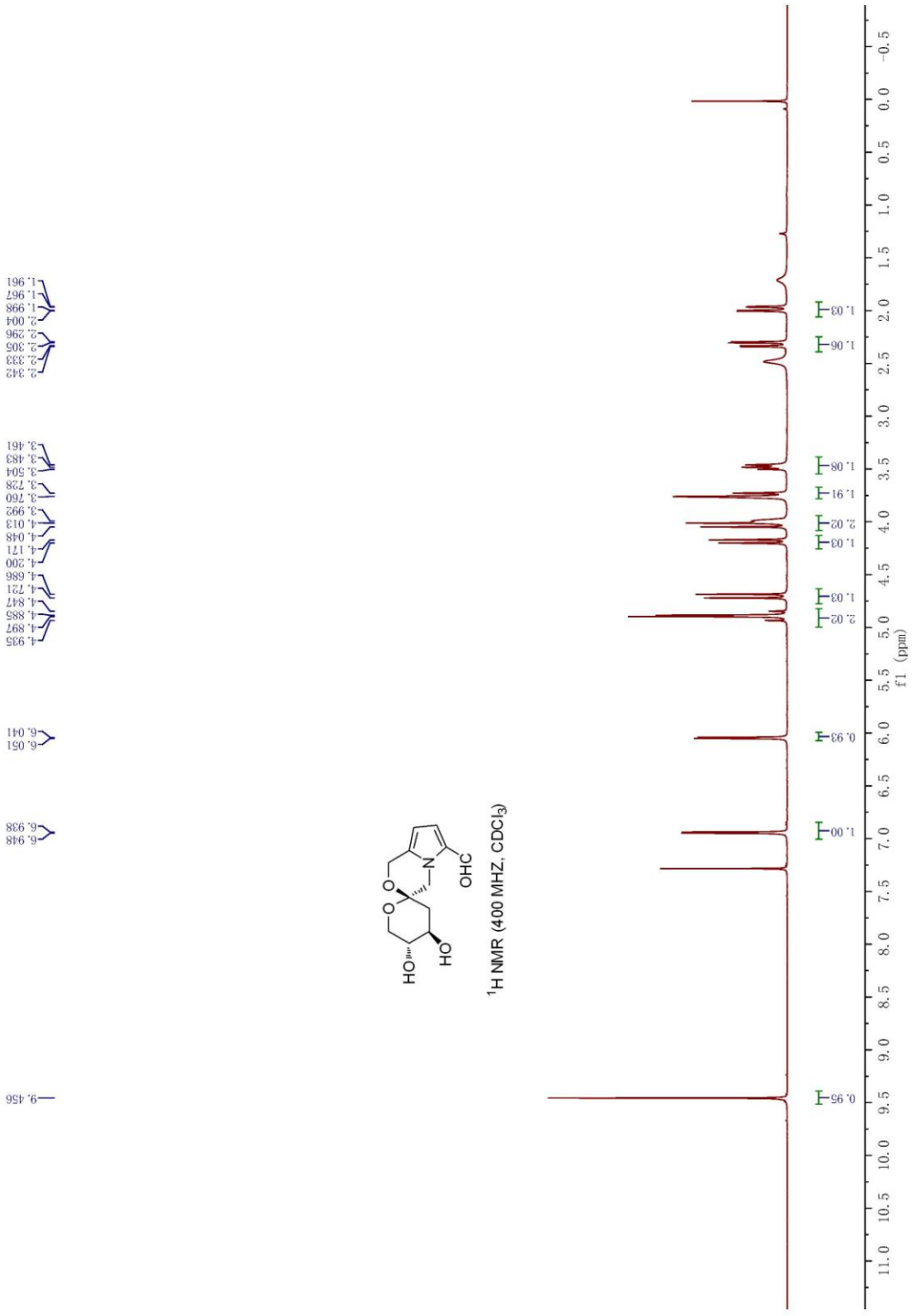


Figure S46. ^{13}C NMR spectrum of **1b** in CD_3OD

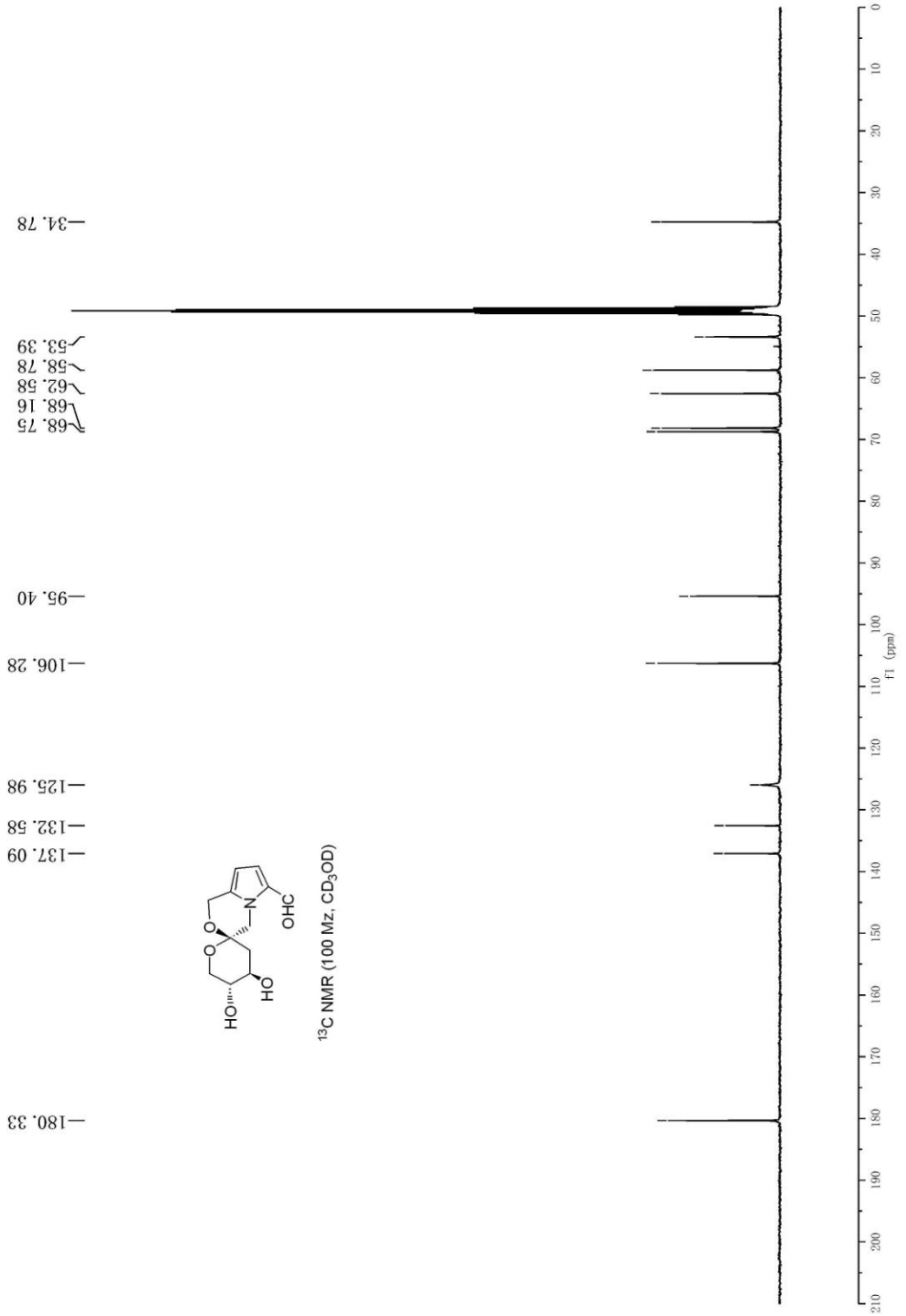


Figure S47. DEPT-135 spectrum of **1b** in CD_3OD

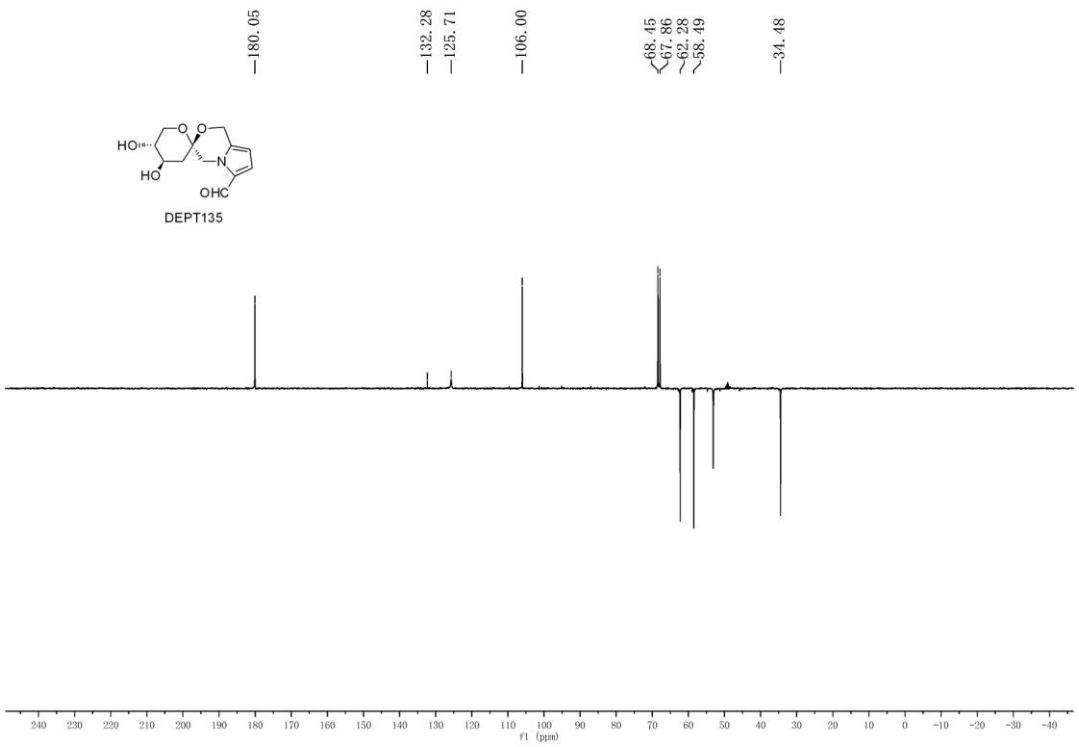


Figure S48. ^{1}H-^{1}H COSY spectrum of **1b** in CD_3OD

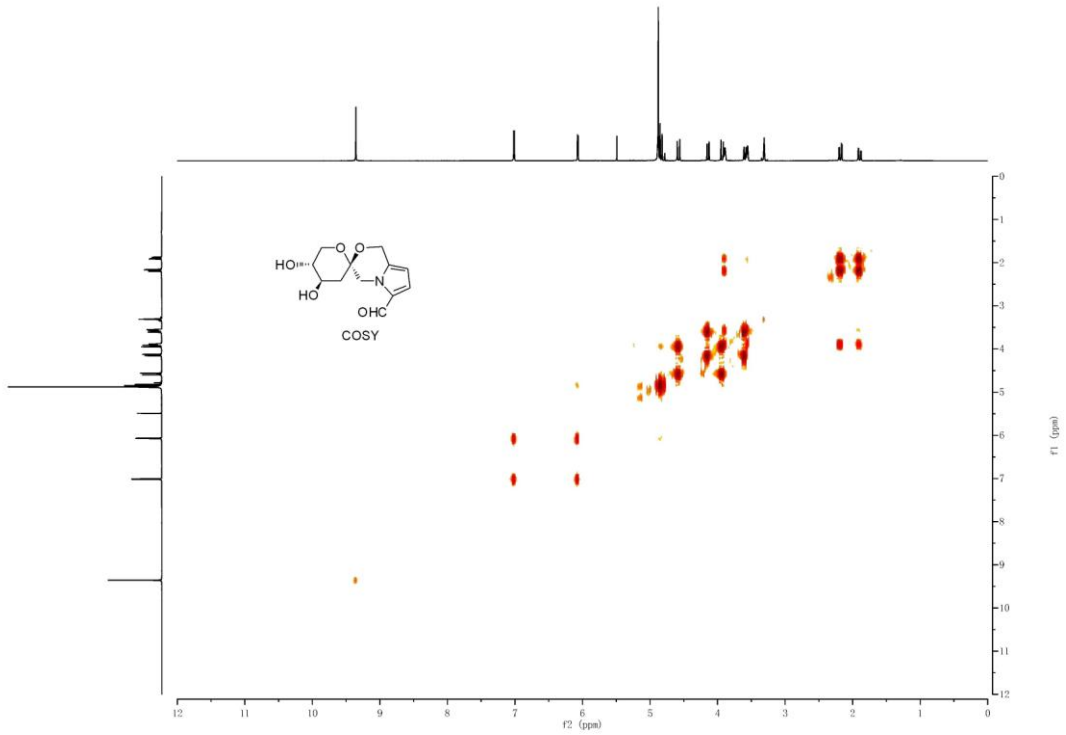


Figure S49. HSQC spectrum of **1b** in CD_3OD

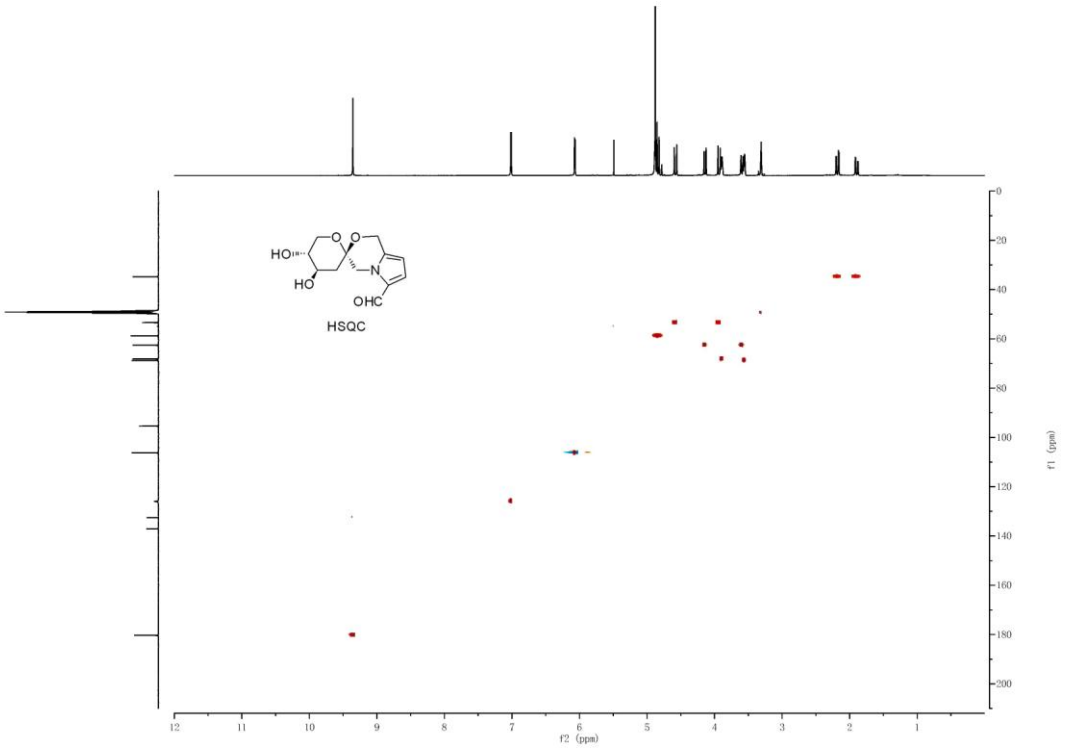


Figure S50. HMBC spectrum of **1b** in CD_3OD

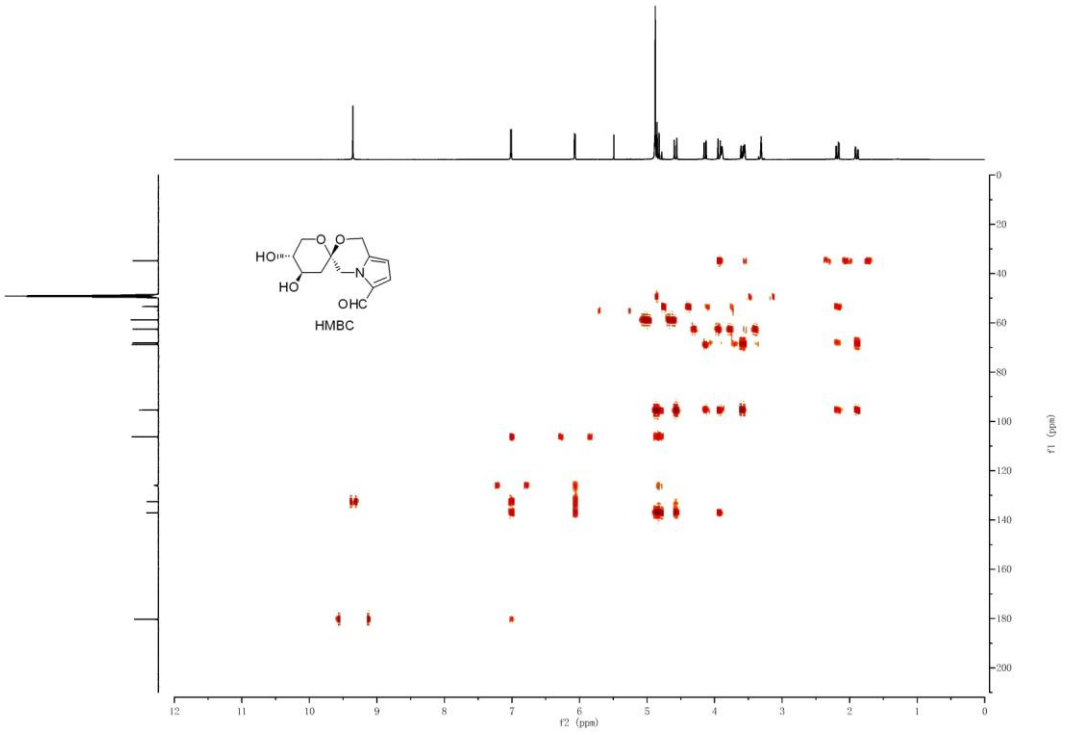


Figure S51. NOESY spectrum of **1b** in CD_3OD

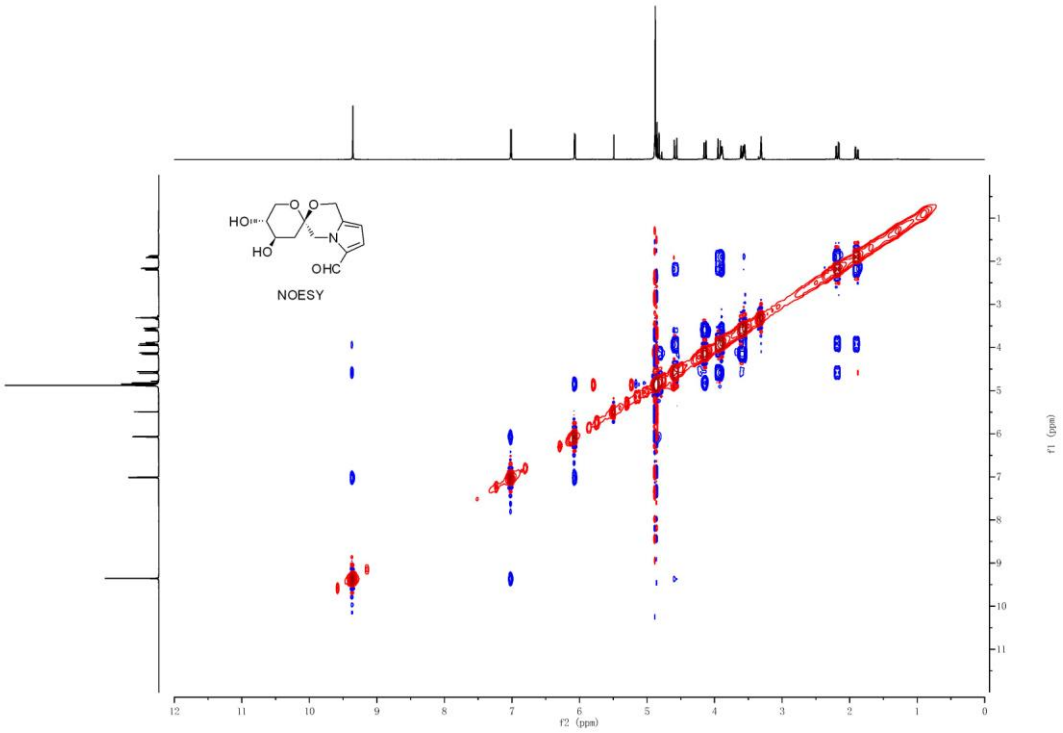


Figure S52. HR-EIMS of **1b**

Elemental Composition Report

File Number: 20130412007
Sample Number:LM-4-6'

Single Mass Analysis
Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off

Monoisotopic Mass, Odd and Even Electron Ions
11 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-15 H: 0-20 N: 0-1 O: 0-5

Minimum:				-1.5		
Maximum:		5.0	10.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
253.0952	253.0950	0.2	0.8	6.0	5546038.5	C12 H15 N O5

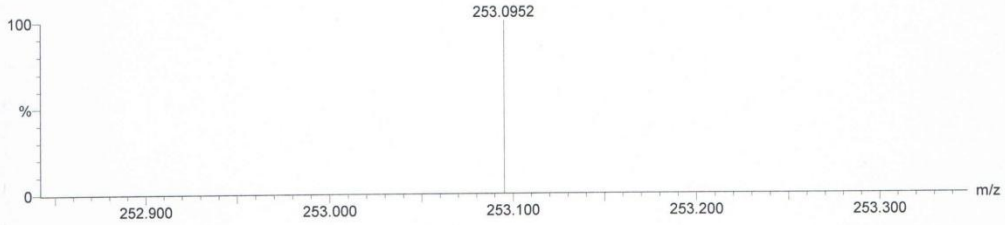
Elemental Composition Report

Single Mass Analysis
Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off

Monoisotopic Mass, Odd and Even Electron Ions
11 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-15 H: 0-20 N: 0-1 O: 0-5

LM-4-6'
20130412007 262 (4.367) Cm (251:264)

TOF MS EI+
6.18e+001



Minimum:				-1.5		
Maximum:		5.0	10.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
253.0952	253.0950	0.2	0.8	6.0	5546038.5	C12 H15 N O5

Figure S53. ^{1}H NMR spectrum of **2a** in CD_3OD

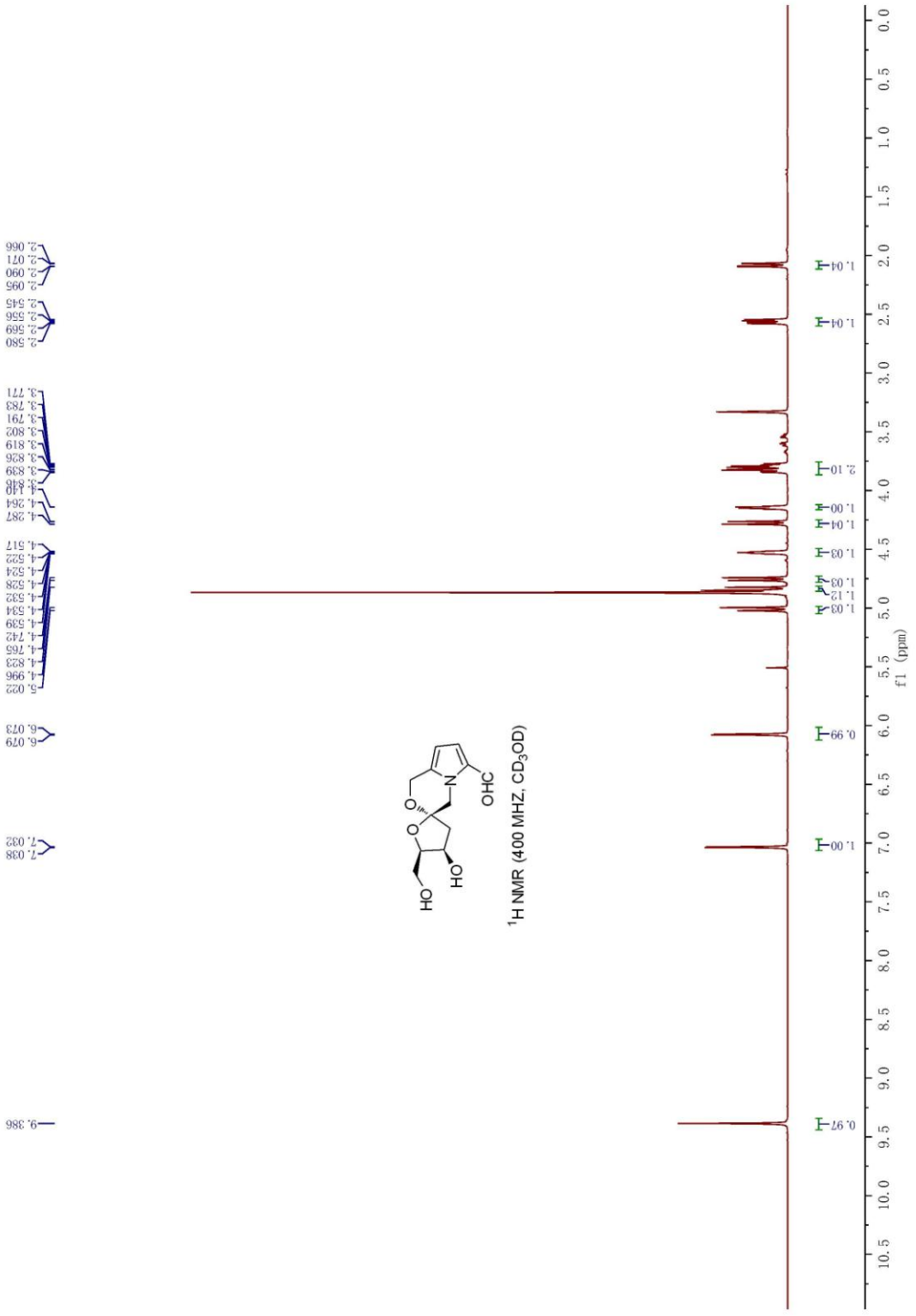


Figure S54. ^{13}C NMR spectrum of **2a** in CD_3OD

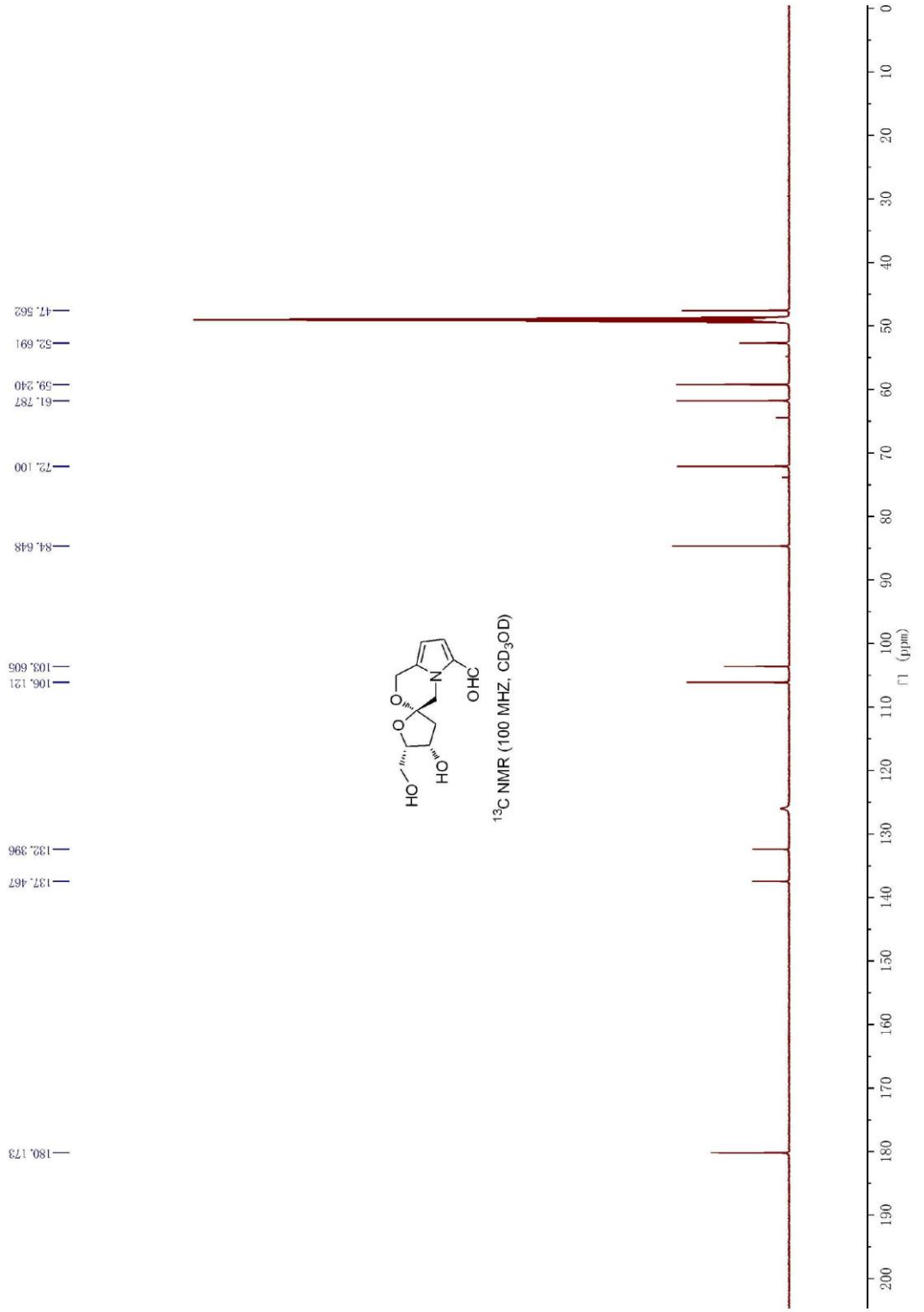


Figure S55. DEPT -135 spectrum of **2a** in CD_3OD

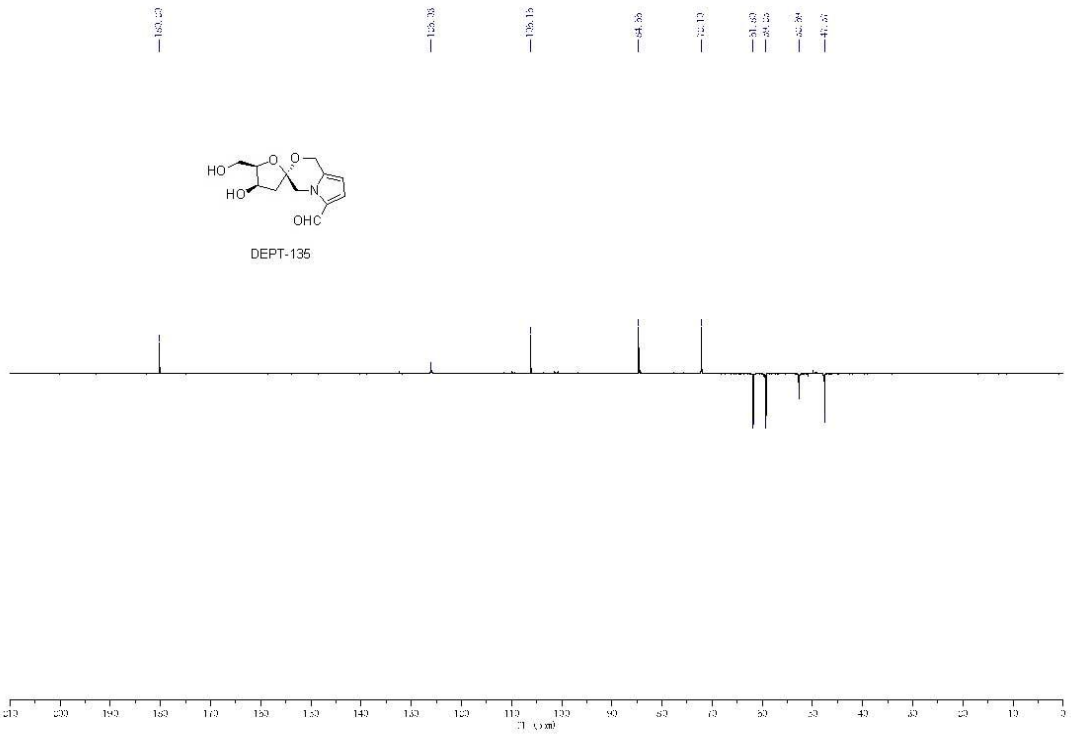


Figure S56. ^1H-^1H COSY spectrum of **2a** in CD_3OD

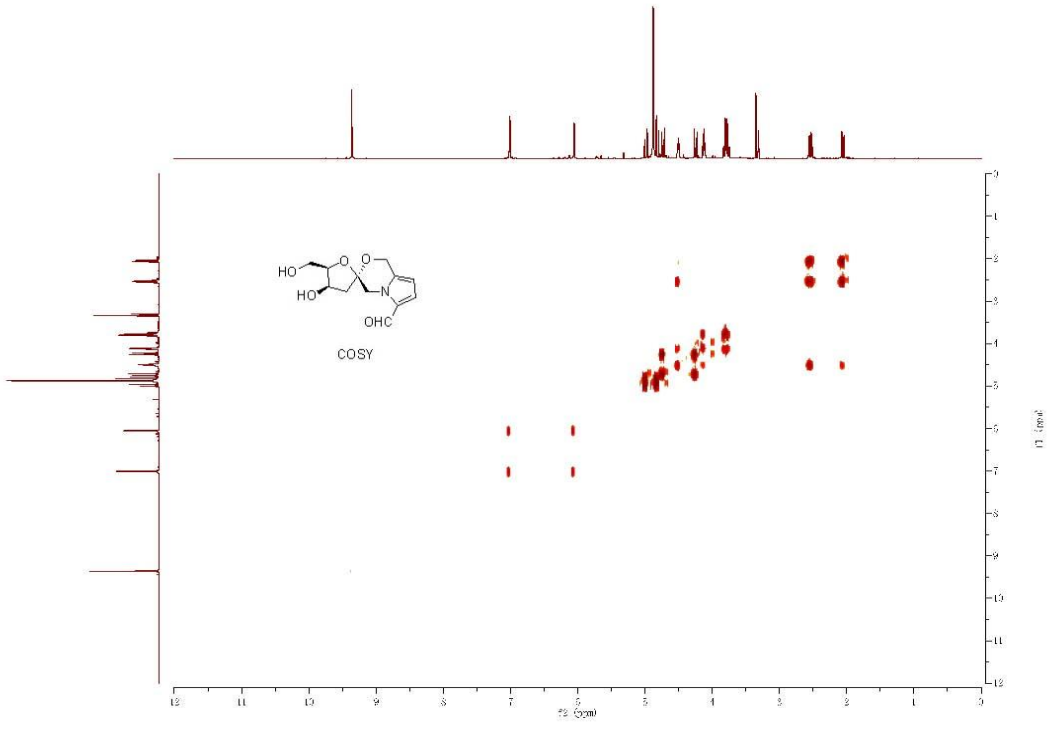


Figure S57. HSQC spectrum of **2a** in CD_3OD

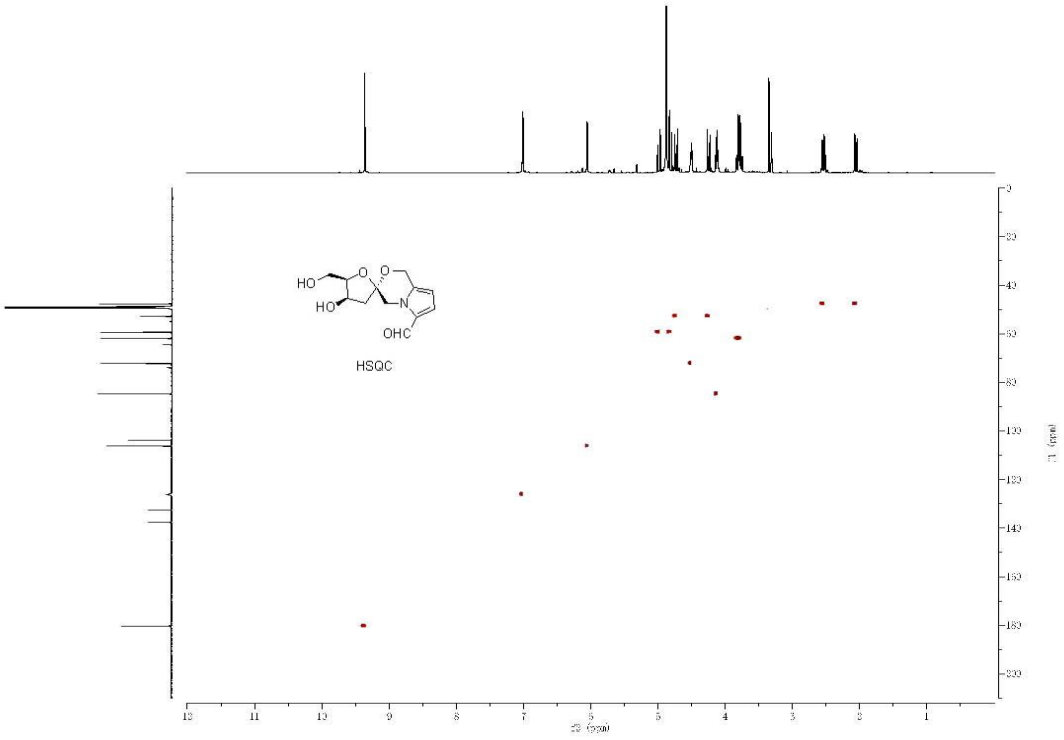


Figure S58. HMBC spectrum of **2a** in CD_3OD

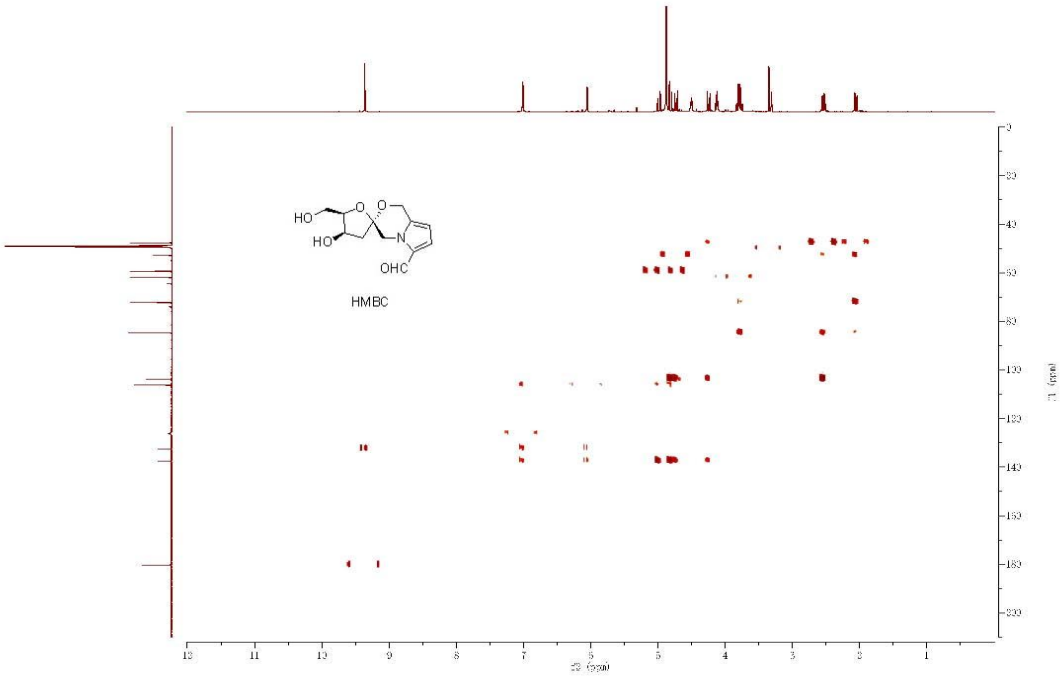


Figure S59. NOESY spectrum of **2a** in CD_3OD

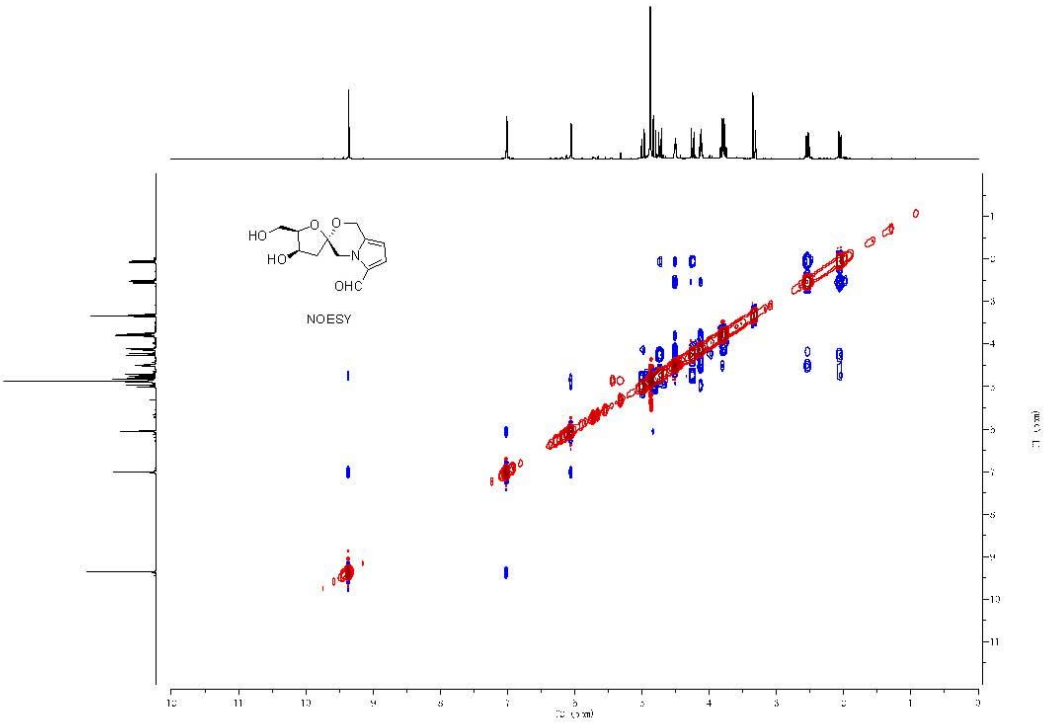


Figure S60. HR-EIMS of **2a**

Elemental Composition Report

File Number: 20130412005
Sample Number:LM-4-5

Single Mass Analysis
Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off

Monoisotopic Mass, Odd and Even Electron Ions
11 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-15 H: 0-20 N: 0-1 O: 0-5

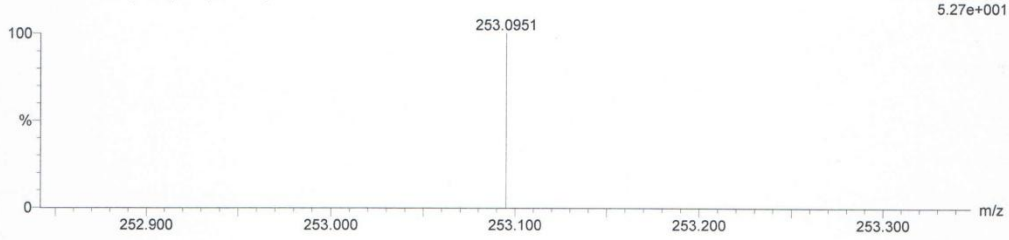
Minimum:				-1.5		
Maximum:		5.0	10.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
253.0951	253.0950	0.1	0.4	6.0	5546035.0	C12 H15 N O5

Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off

Monoisotopic Mass, Odd and Even Electron Ions
11 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-15 H: 0-20 N: 0-1 O: 0-5
LM-4-5
20130412005 240 (4.000) Cm (237:247)

TOF MS EI+
5.27e+001



Minimum:				-1.5		
Maximum:		5.0	10.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
253.0951	253.0950	0.1	0.4	6.0	5546035.0	C12 H15 N O5

Figure S61. ^{1}H NMR spectrum of **pre-7a** in $CDCl_3$

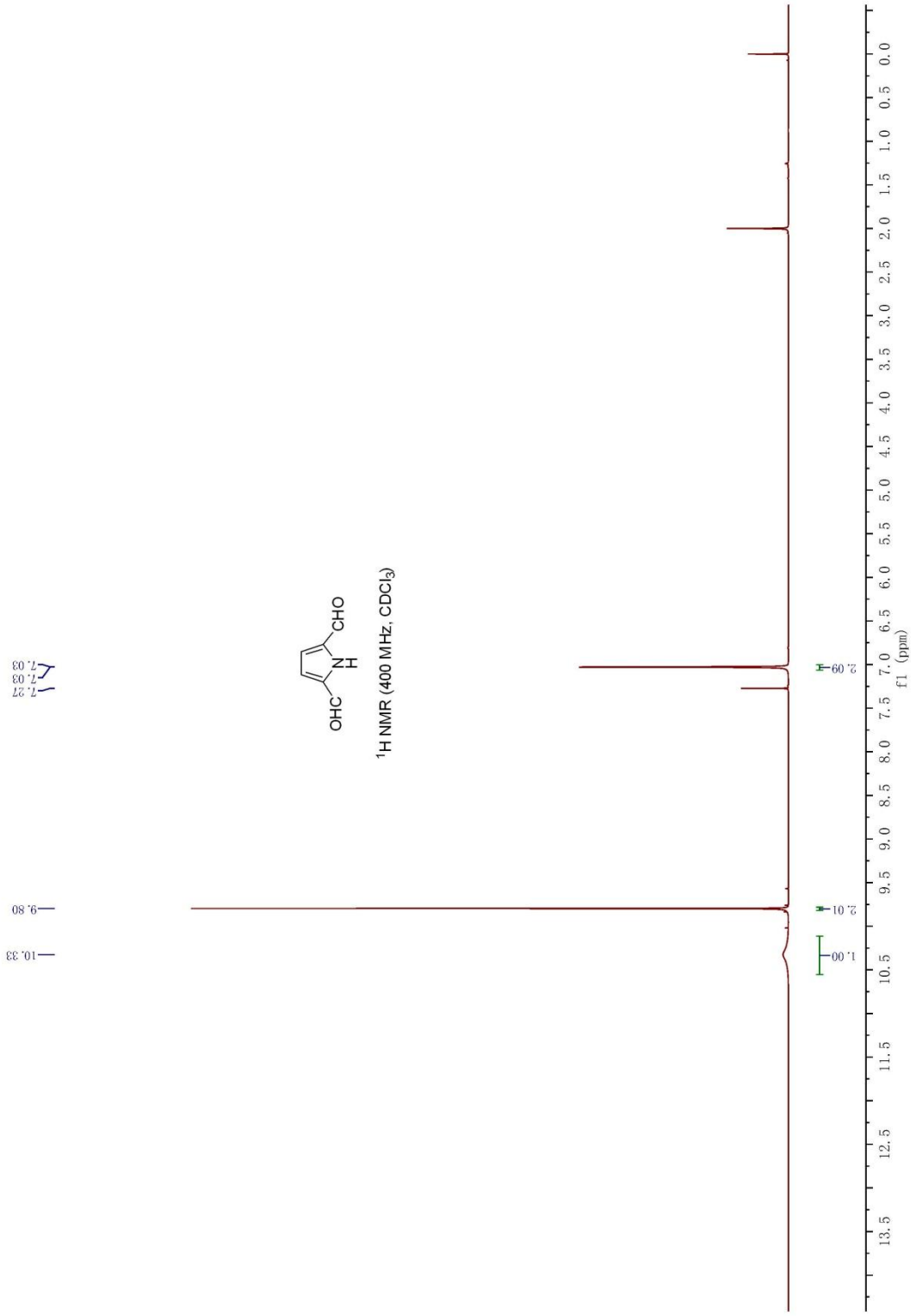


Figure S62. ^{13}C NMR spectrum of **pre-7a** in $CDCl_3$

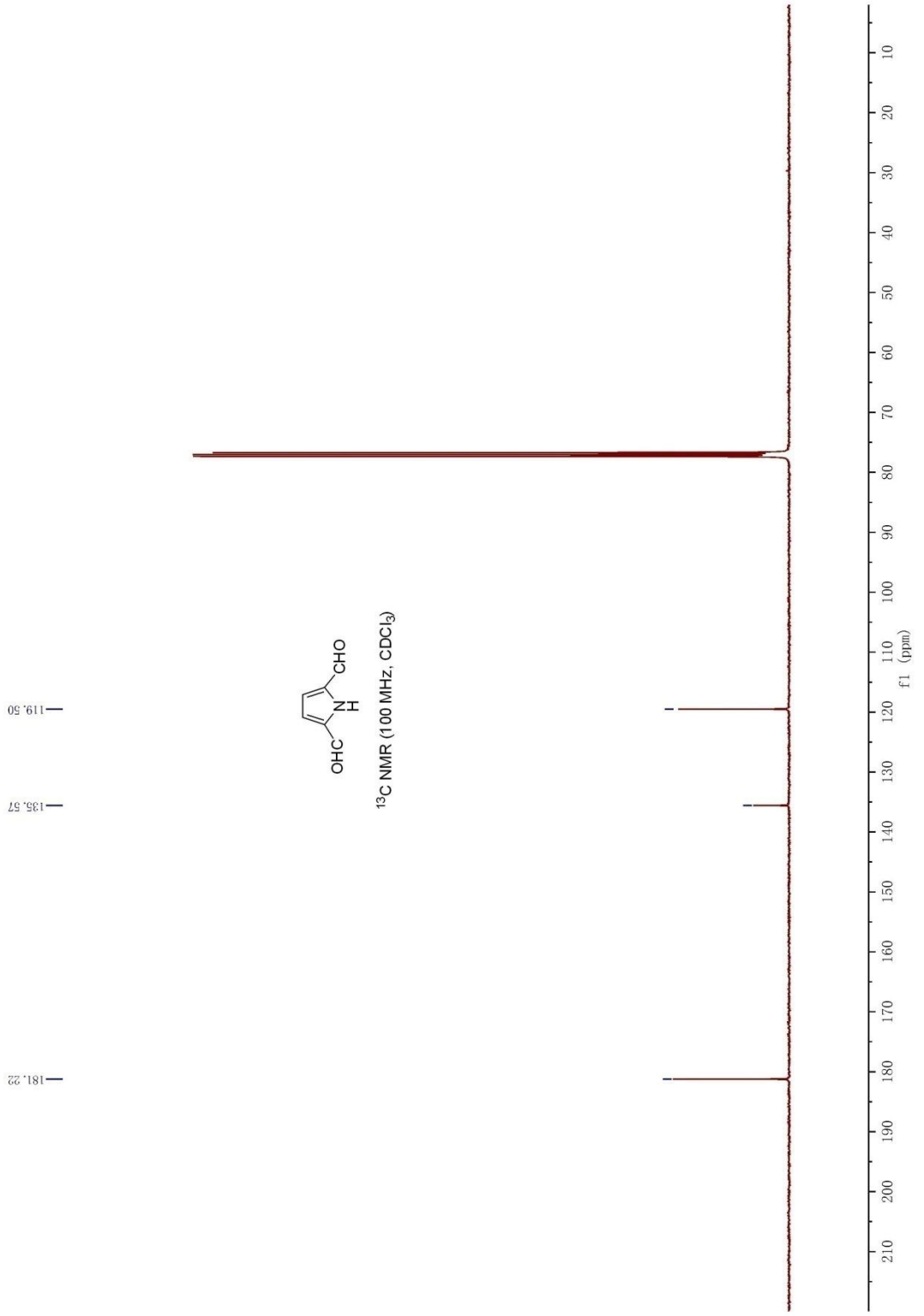


Figure S63. HR-EIMS of **pre-7a**

Elemental Composition Report

File Number: 20130412008
Sample Number:pyr-1

Single Mass Analysis
Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off

Monoisotopic Mass, Odd and Even Electron Ions
11 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-15 H: 0-20 N: 0-1 O: 0-2

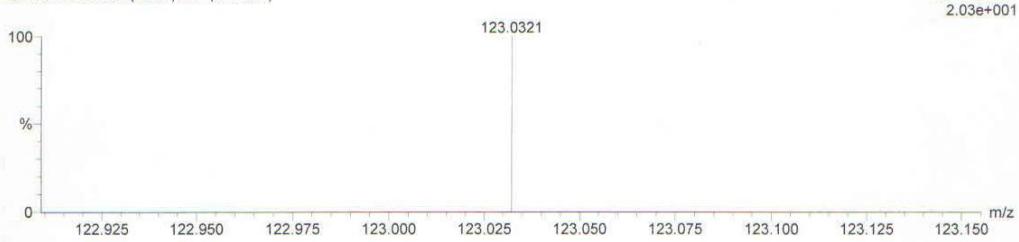
Minimum:				-1.5		
Maximum:		5.0	10.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
123.0321	123.0320	0.1	0.8	5.0	5546025.5	C6 H5 N O2

Elemental Composition Report Page 1

Single Mass Analysis
Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off

Monoisotopic Mass, Odd and Even Electron Ions
11 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-15 H: 0-20 N: 0-1 O: 0-2
pyr-1 (6)
20130412008 333 (5.551) Cm (311:334)

TOF MS EI+
2.03e+001



Minimum:				-1.5		
Maximum:		5.0	10.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
123.0321	123.0320	0.1	0.8	5.0	5546025.5	C6 H5 N O2

Figure S64. ^{1}H NMR spectrum of **pre-7b** in $CDCl_3$

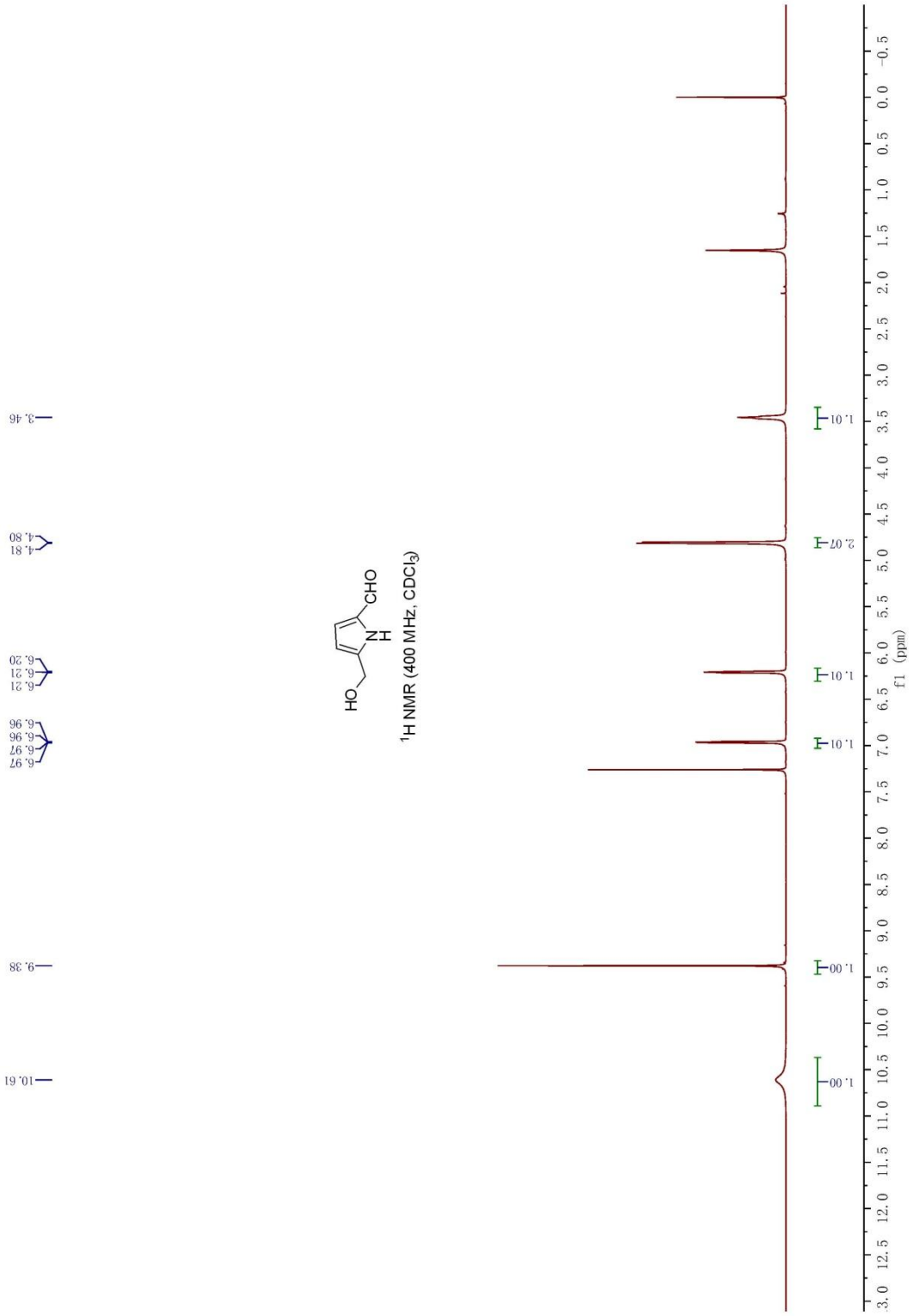


Figure S65. ^{13}C NMR spectrum of **pre-7b** in $CDCl_3$

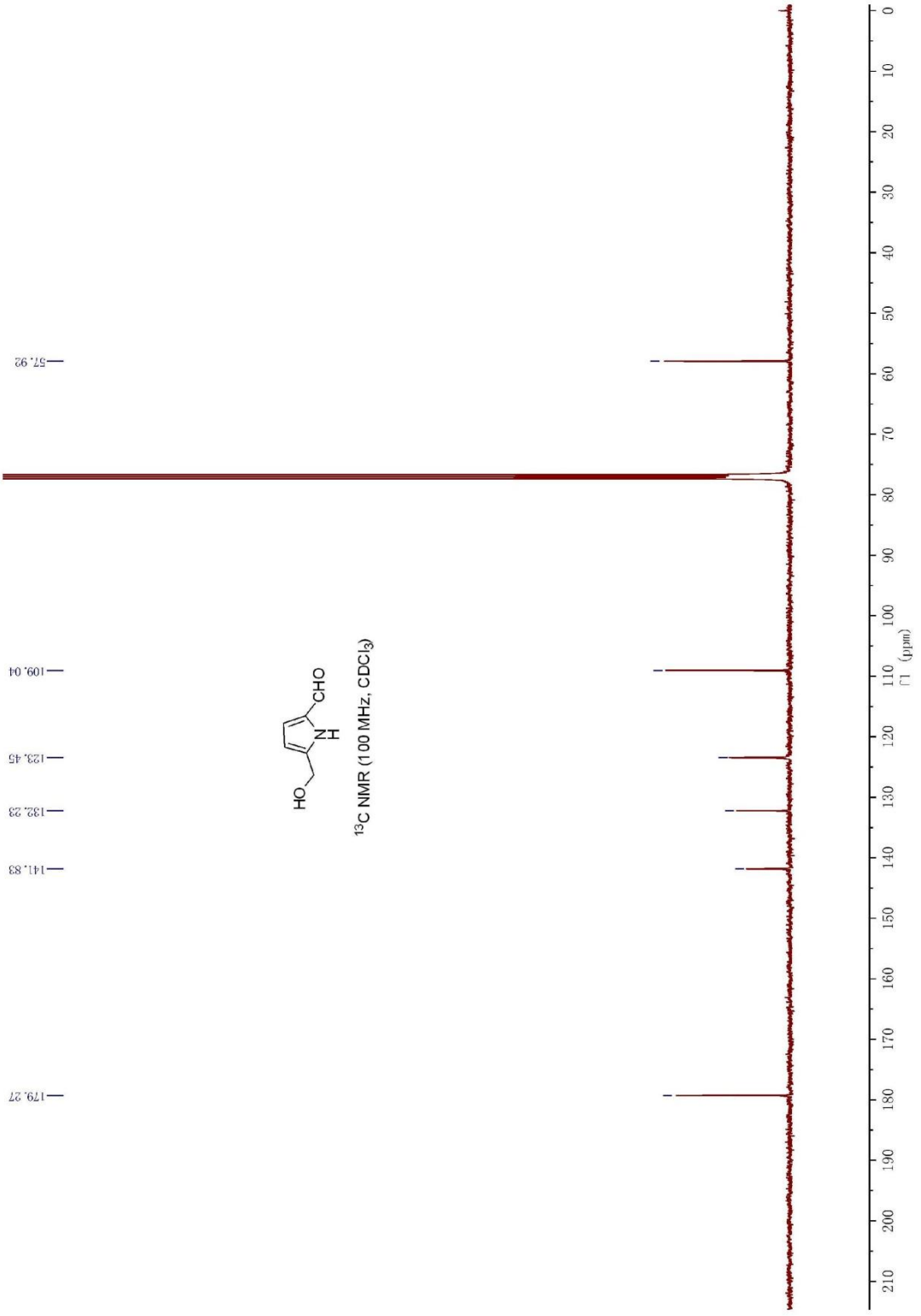
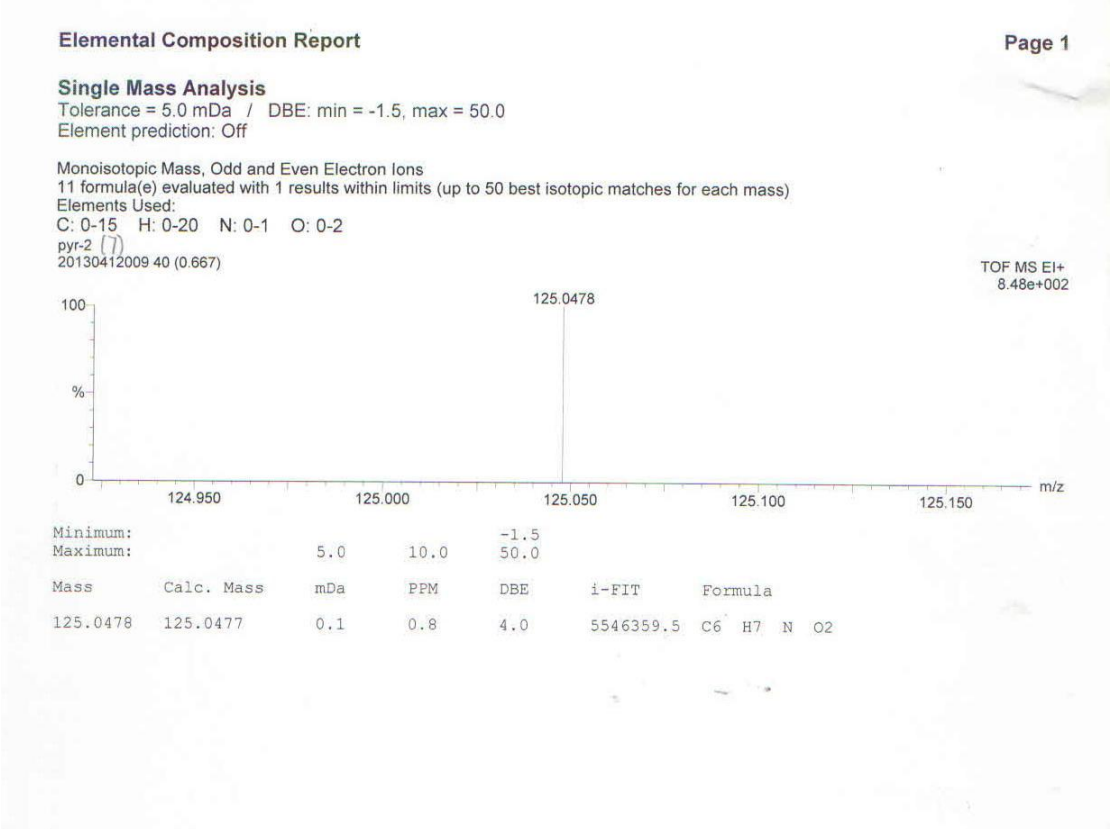


Figure S66. HR-EIMS of **pre-7b**



Elemental Composition Report Page 1

Single Mass Analysis
Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off

Monoisotopic Mass, Odd and Even Electron Ions
11 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-15 H: 0-20 N: 0-1 O: 0-2
pyr-2 (7)
20130412009 40 (0.667)

TOF MS EI+
8.48e+002

Minimum:		5.0	10.0	-1.5		
Maximum:				50.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
125.0478	125.0477	0.1	0.8	4.0	5546359.5	C6 H7 N O2

Figure S67. ^{1}H NMR spectrum of **7** in $CDCl_3$

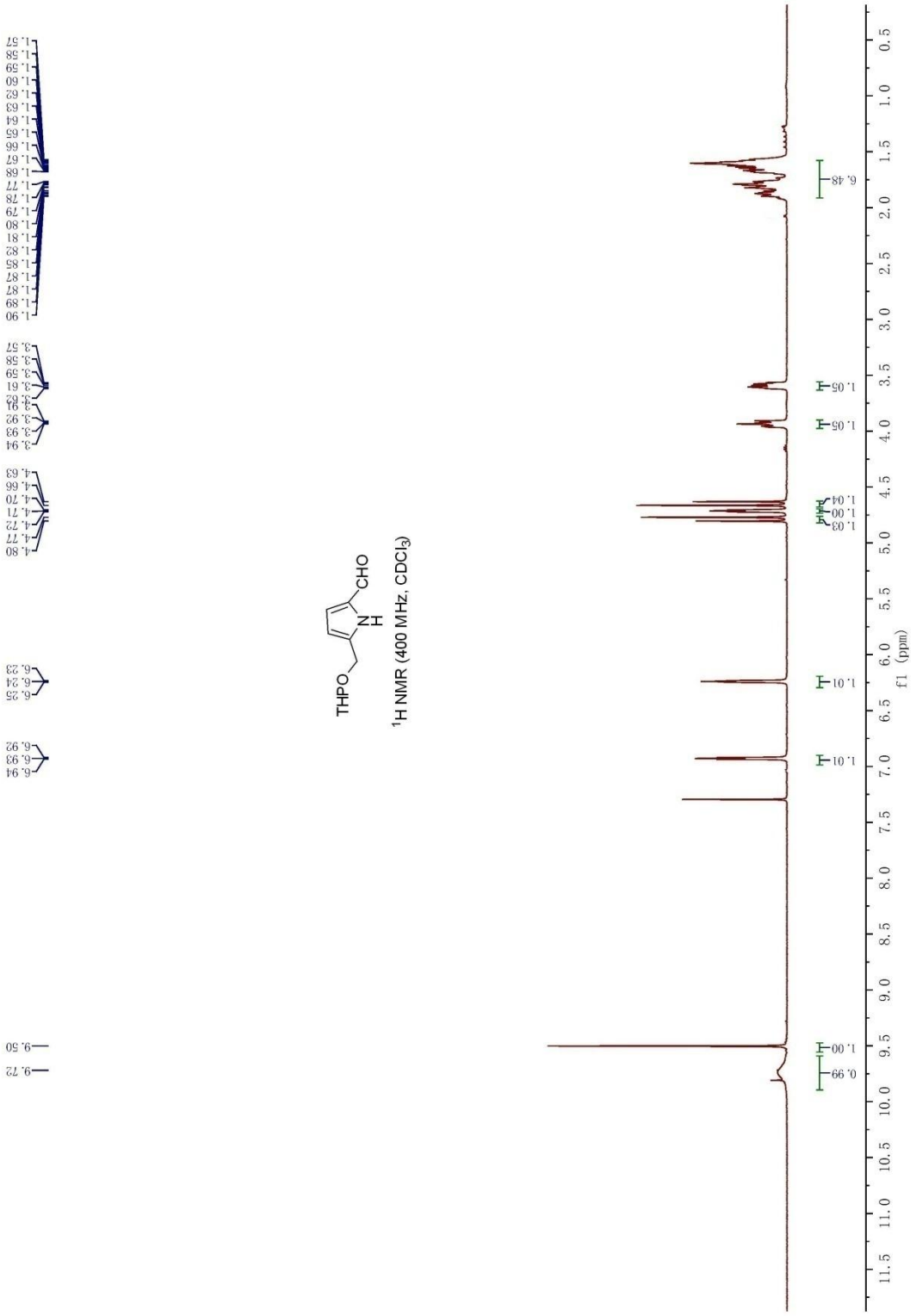


Figure S68. ^{13}C NMR spectrum of **7** in $CDCl_3$

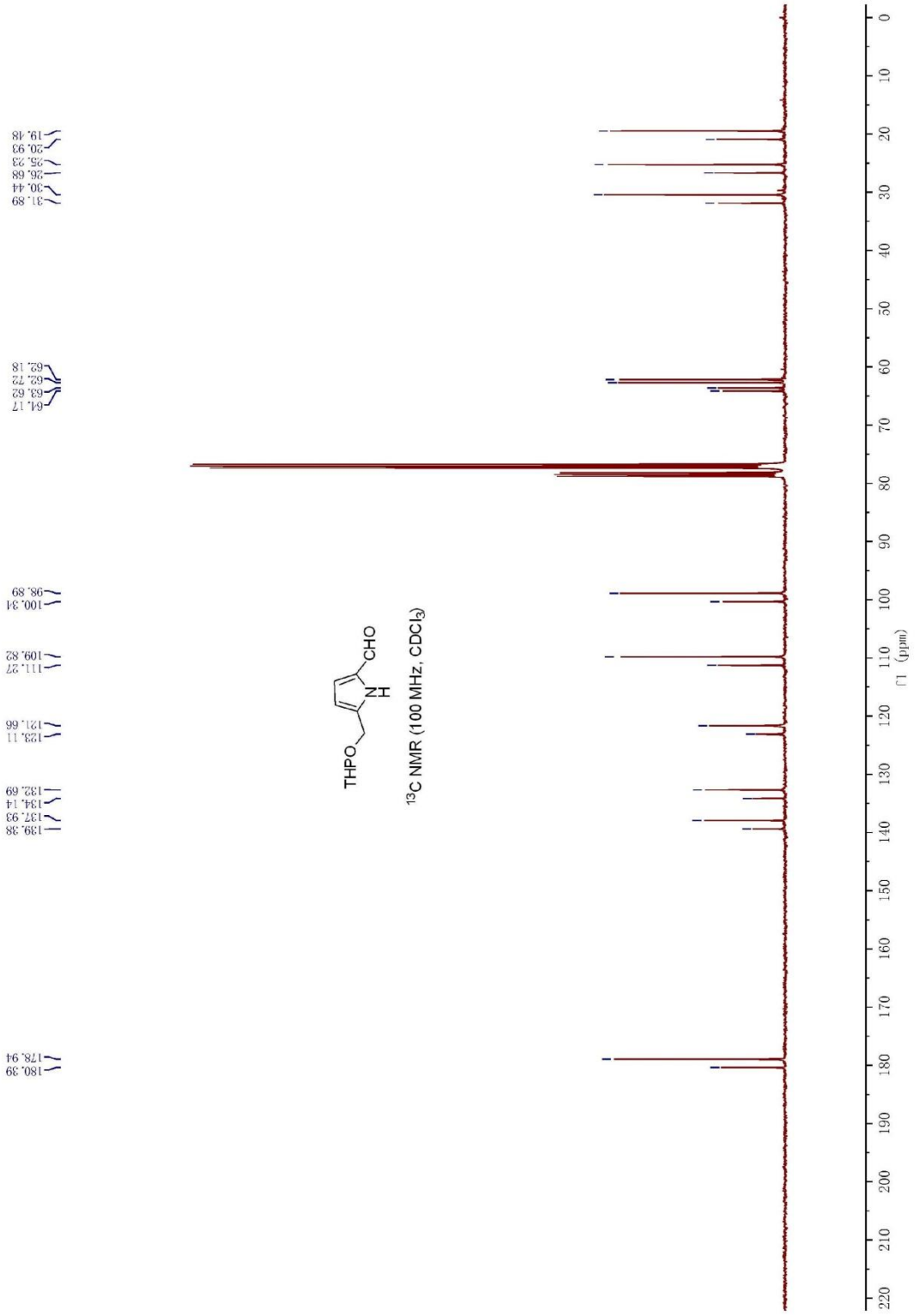
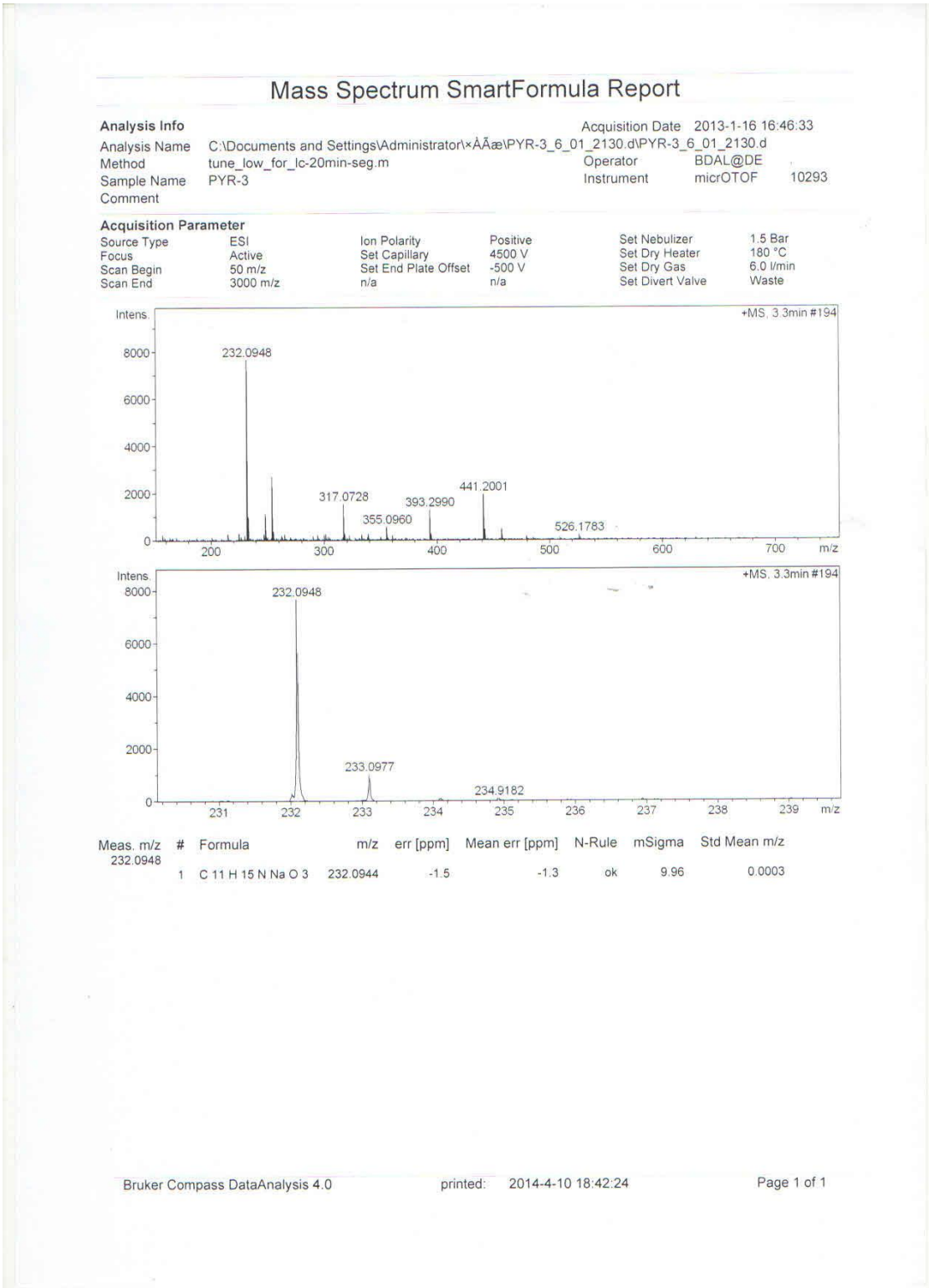


Figure S69. (+) HR-ESIMS of **7**



Mass Spectrum SmartFormula Report

Analysis Info

Analysis Name	C:\Documents and Settings\Administrator\×ÅÃæ\PYR-3_6_01_2130.d\PYR-3_6_01_2130.d	Acquisition Date	2013-1-16 16:46:33
Method	tune_low_for_lc-20min-seg.m	Operator	BDAL@DE
Sample Name	PYR-3	Instrument	micrOTOF 10293
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.5 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	6.0 l/min
Scan End	3000 m/z	n/a	n/a	Set Divert Valve	Waste

Meas. m/z	#	Formula	m/z	err [ppm]	Mean err [ppm]	N-Rule	mSigma	Std Mean m/z
232.0948								
	1	C 11 H 15 N Na O 3	232.0944	-1.5	-1.3	ok	9.96	0.0003

Bruker Compass DataAnalysis 4.0 printed: 2014-4-10 18:42:24 Page 1 of 1

Figure S70. ^{1}H NMR spectrum of **10** in $CDCl_3$

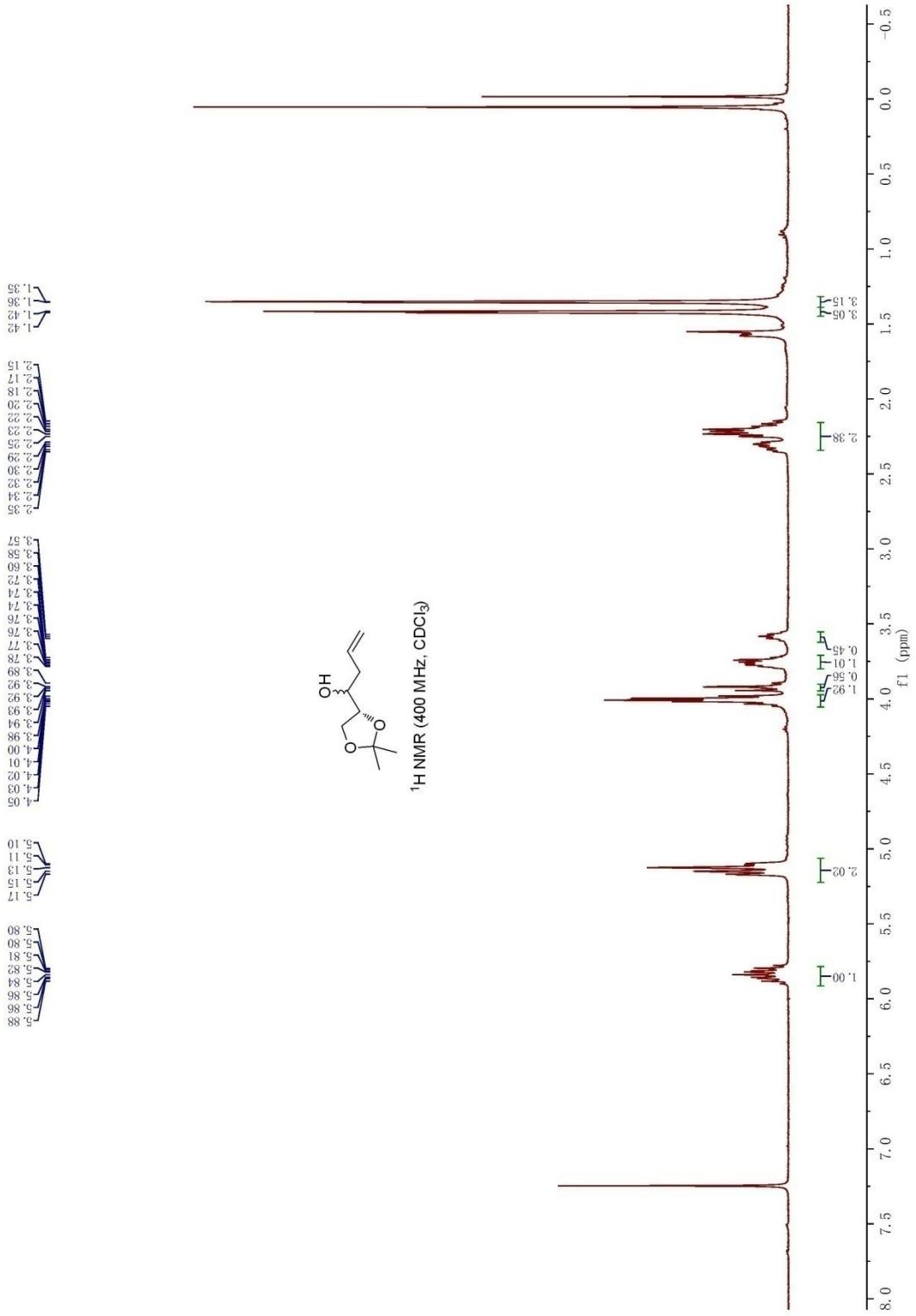


Figure S71. ^{13}C NMR spectrum of **10** in $CDCl_3$

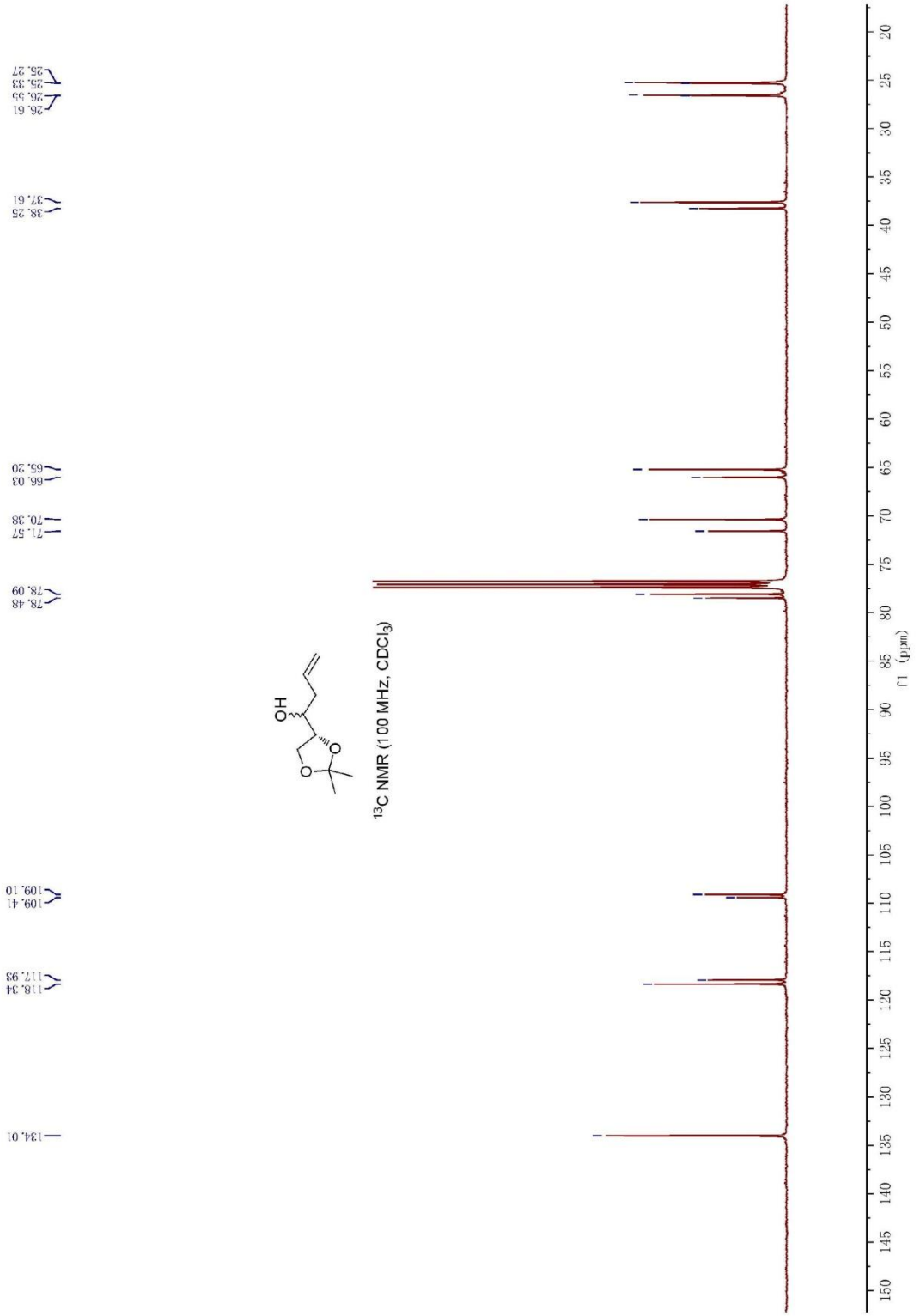


Figure S72. HR-EIMS of **10**

Elemental Composition Report

File Number: 20130415011
Sample Number:WL-2

Single Mass Analysis
Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off

Monoisotopic Mass, Odd and Even Electron Ions
9 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-20 H: 0-25 O: 0-3

Minimum:				-1.5		
Maximum:		5.0	10.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
172.1097	172.1099	-0.2	-1.2	2.0	5546025.5	C9 H16 O3

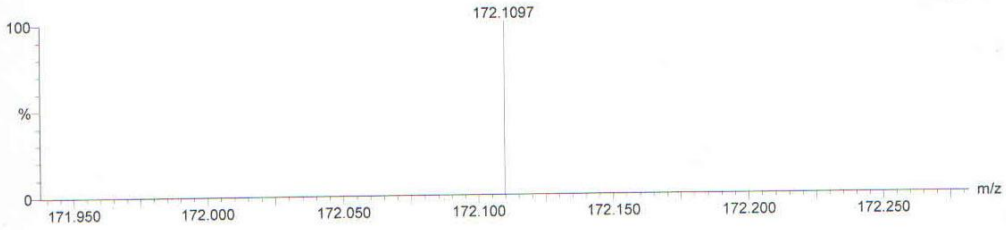
Elemental Composition Report

Single Mass Analysis
Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off

Monoisotopic Mass, Odd and Even Electron Ions
9 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-20 H: 0-25 O: 0-3

WL-2
20130415011 75 (1.250) Cm (75:77)

TOF MS EI+
1.80e+001



Minimum:				-1.5		
Maximum:		5.0	10.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
172.1097	172.1099	-0.2	-1.2	2.0	5546025.5	C9 H16 O3

Figure S73. **^{1}H NMR spectrum of** 11 **in $CDCl_3$**

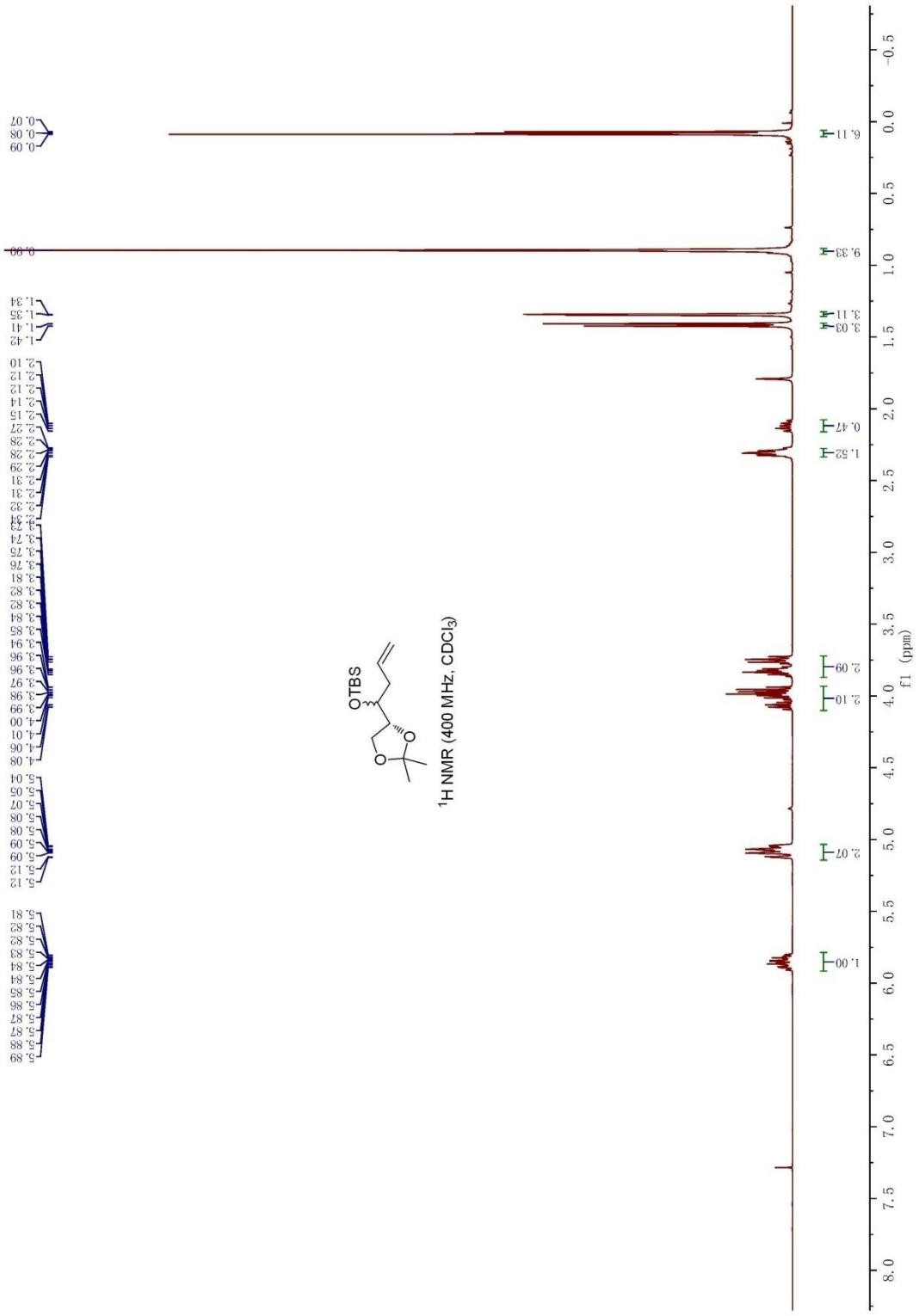


Figure S74. ^{13}C NMR spectrum of **11** in $CDCl_3$

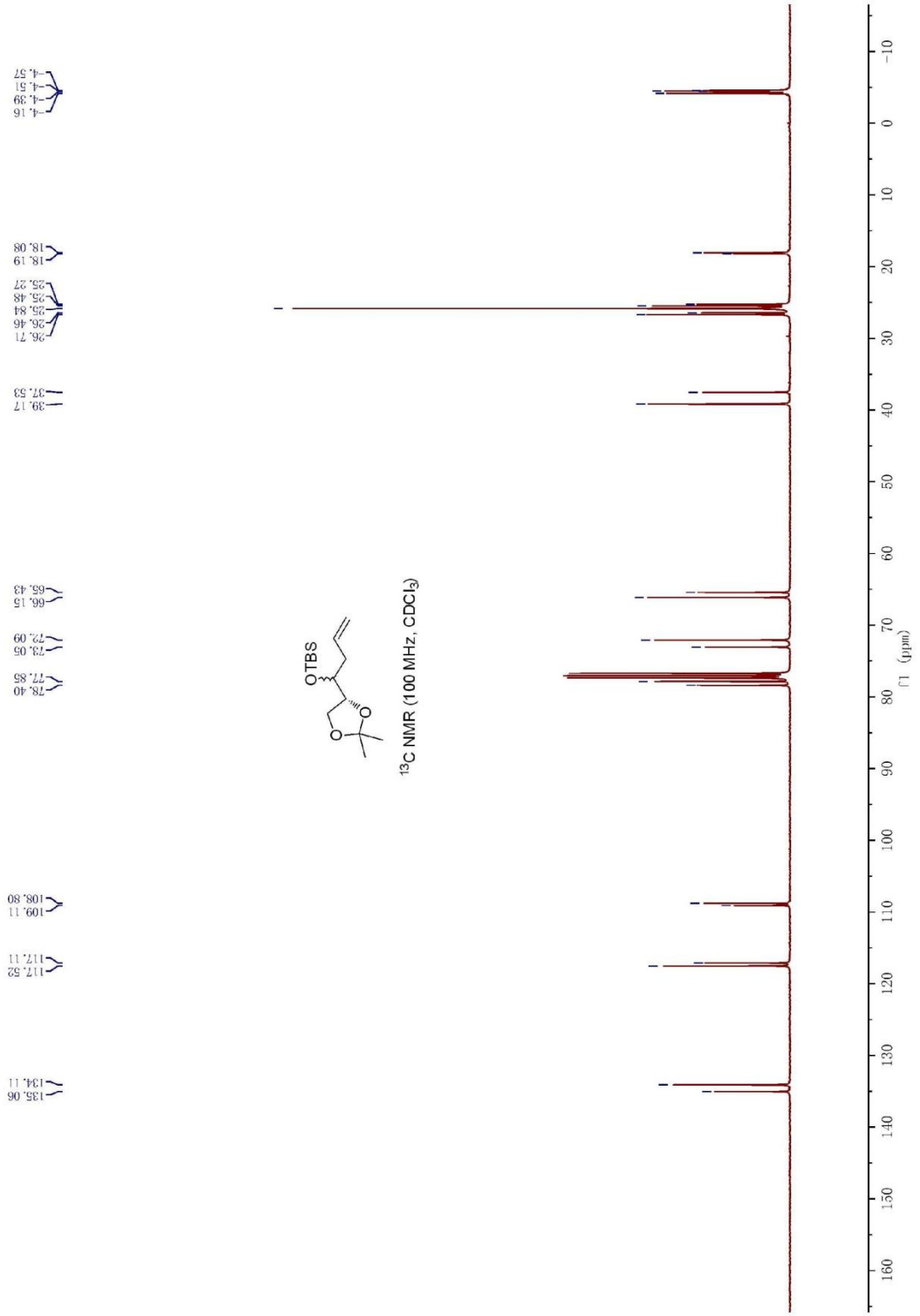


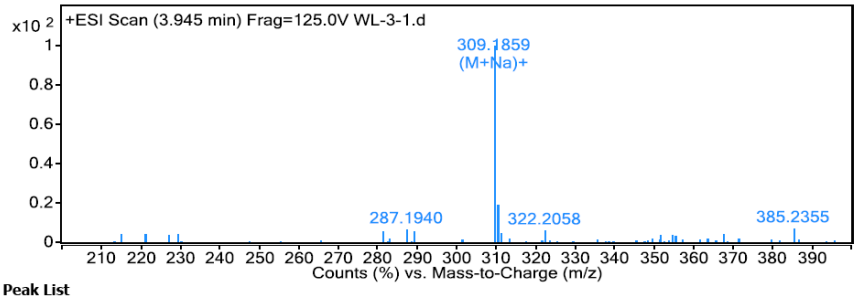
Figure S75. (+) HR-ESIMS of **11**

Qualitative Analysis Report

Data Filename	WL-3-1.d	**Sample Name**	WL-3-1
Sample Type	Sample	**Position**	P1-A5
Instrument Name	Instrument 1	**User Name**	
Acq Method		**Acquired Time**	1/3/2014 5:44:09 PM
IRM Calibration Status	Some Ions Missed	**DA Method**	Screening-Default.m
Comment	containing 0.05% FA		

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
125	0	Esi



Peak List

m/z	z	Abund	Formula	Ion
309.1859	1	739124	C15 H30 Na O3 Si	(M+Na)+

Figure S76. **^{1}H NMR spectrum of** 12 **in $CDCl_3$**

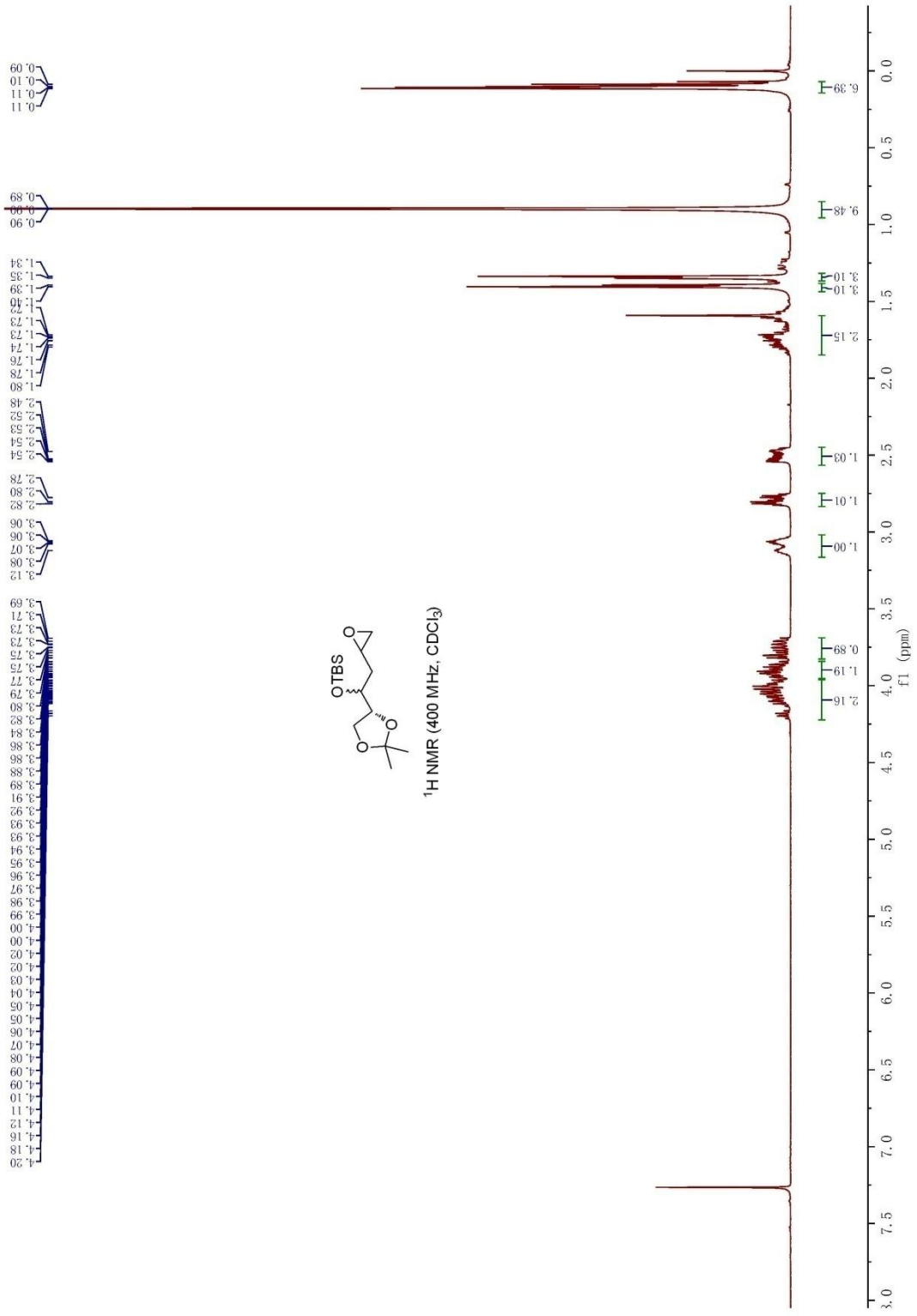


Figure S77. ^{13}C NMR spectrum of **12** in $CDCl_3$

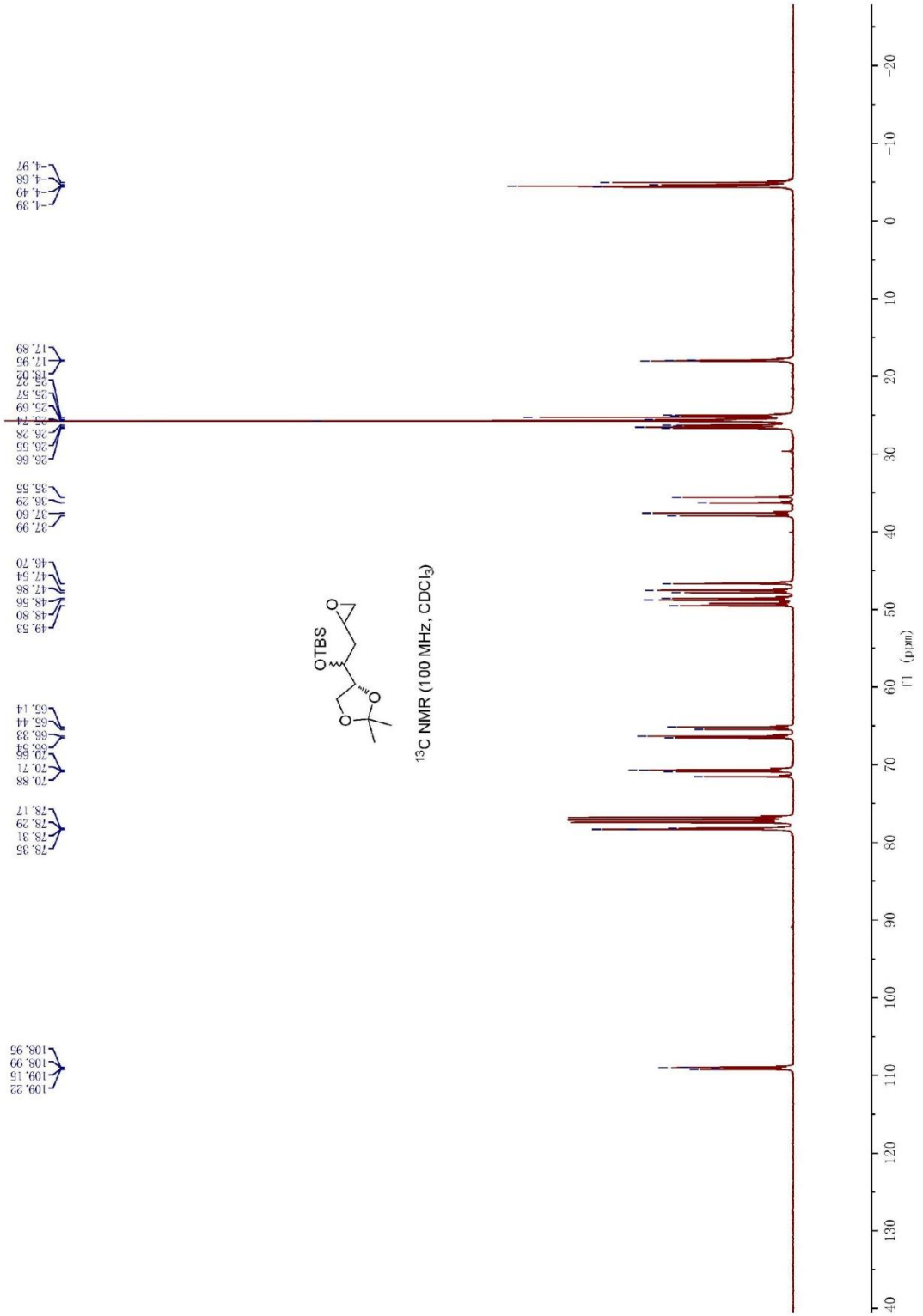


Figure S78. (+) HR-EIMS of **12**

Elemental Composition Report

File Number: 20130329014
Sample Number: WL-I

Single Mass Analysis
Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off

Monoisotopic Mass, Odd and Even Electron Ions
10 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-15 H: 0-30 O: 0-4 Si: 0-1

Minimum:				-1.5		
Maximum:		5.0	10.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
302.1911	302.1913	-0.2	-0.7	2.0	5546192.5	C15 H30 O4 Si

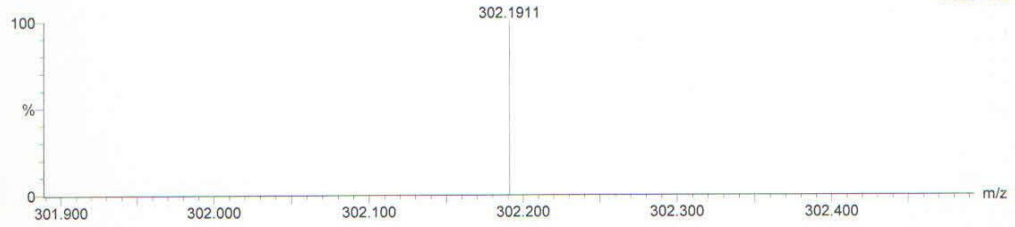
Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off

Monoisotopic Mass, Odd and Even Electron Ions
10 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-15 H: 0-30 O: 0-4 Si: 0-1

WL-I
20130329014 146 (2.434) Cm (146:179)

TOF MS EI+
3.62e+002



Minimum:				-1.5		
Maximum:		5.0	10.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
302.1911	302.1913	-0.2	-0.7	2.0	5546192.5	C15 H30 O4 Si

Figure S79. **^{1}H NMR spectrum of** 13 **in $CDCl_3$**

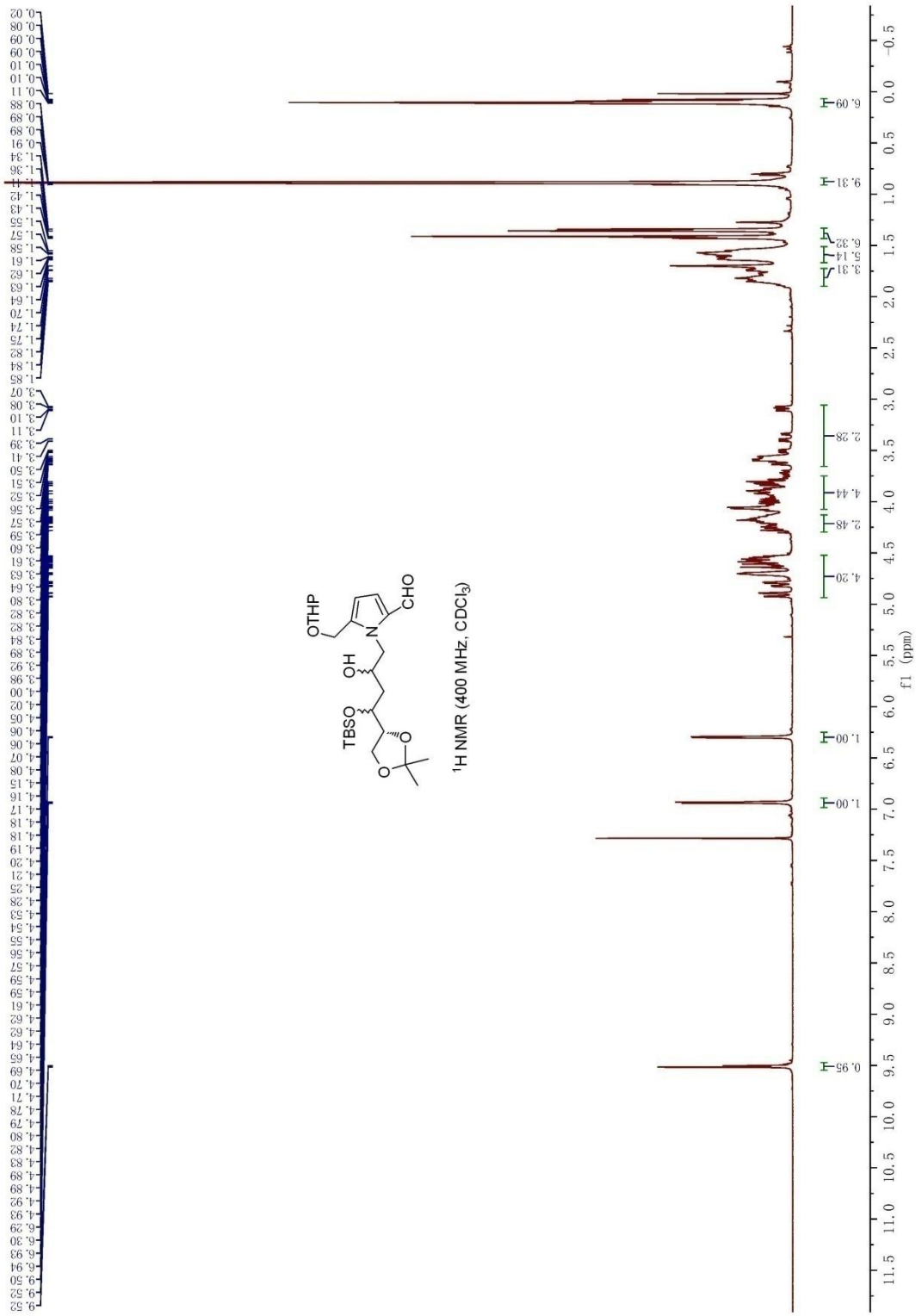


Figure S80. ^{13}C NMR spectrum of **13** in $CDCl_3$

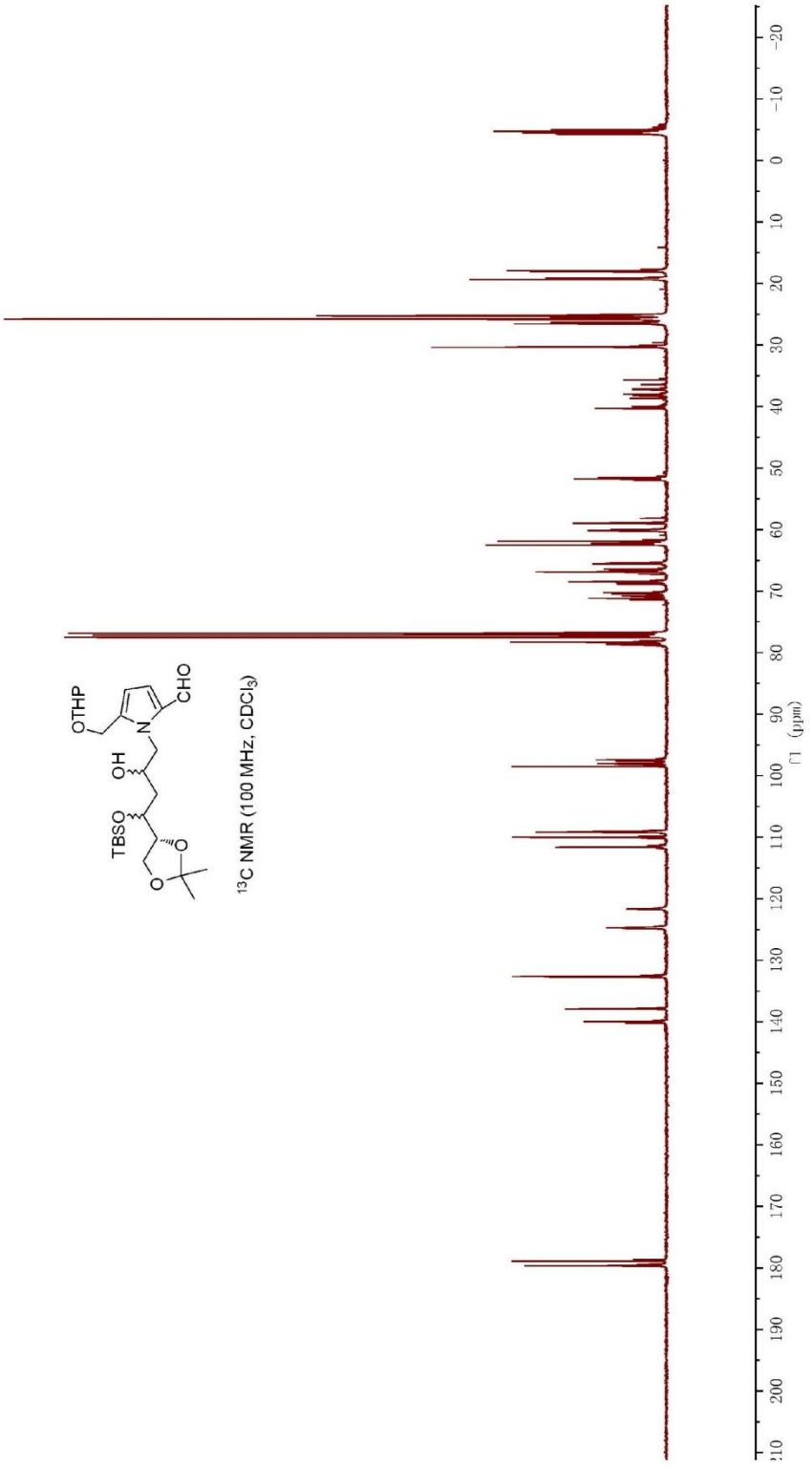


Figure S81. HR-EIMS of **13**

Elemental Composition Report

File Number: 20130329013
Sample Number: WL-II

Single Mass Analysis
Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off

Monoisotopic Mass, Odd and Even Electron Ions
30 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-26 H: 0-45 N: 0-1 O: 0-7 Si: 0-1

Minimum:				-1.5		
Maximum:		5.0	10.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
511.2968	511.2965	0.3	0.6	6.0	5546073.0	C26 H45 N O7 Si

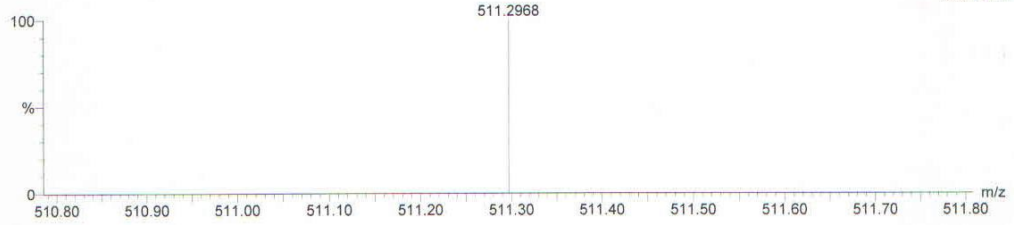
Elemental Composition Report

Single Mass Analysis
Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off

Monoisotopic Mass, Odd and Even Electron Ions
30 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-26 H: 0-45 N: 0-1 O: 0-7 Si: 0-1

WL-II
20130329013 215 (3.584)

TOF MS EI+
1.08e+002



Minimum:				-1.5		
Maximum:		5.0	10.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
511.2968	511.2965	0.3	0.6	6.0	5546073.0	C26 H45 N O7 Si

Figure S82. ^{1}H NMR spectrum of **14** in $CDCl_3$

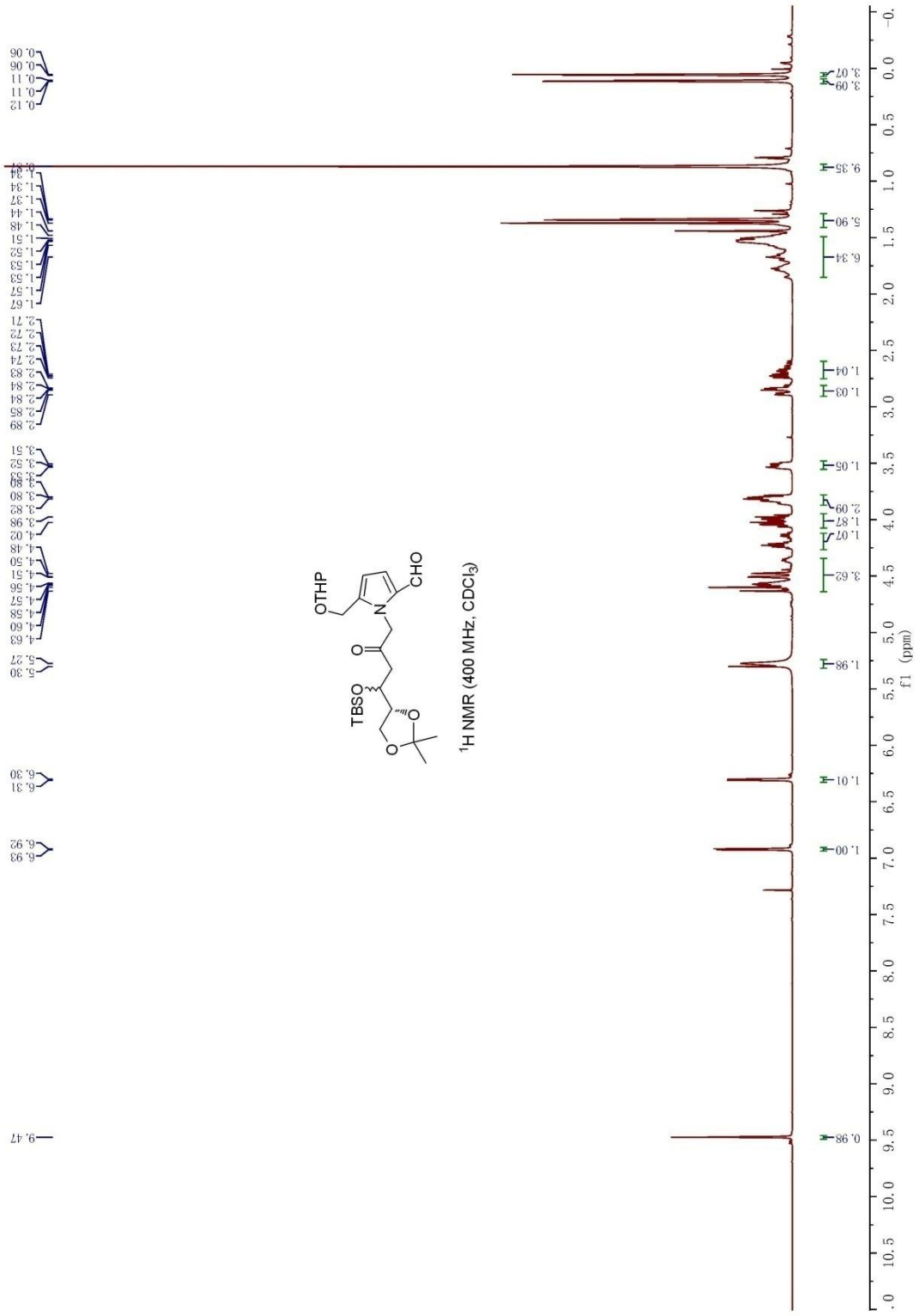


Figure S83. ^{13}C NMR spectrum of **14** in $CDCl_3$

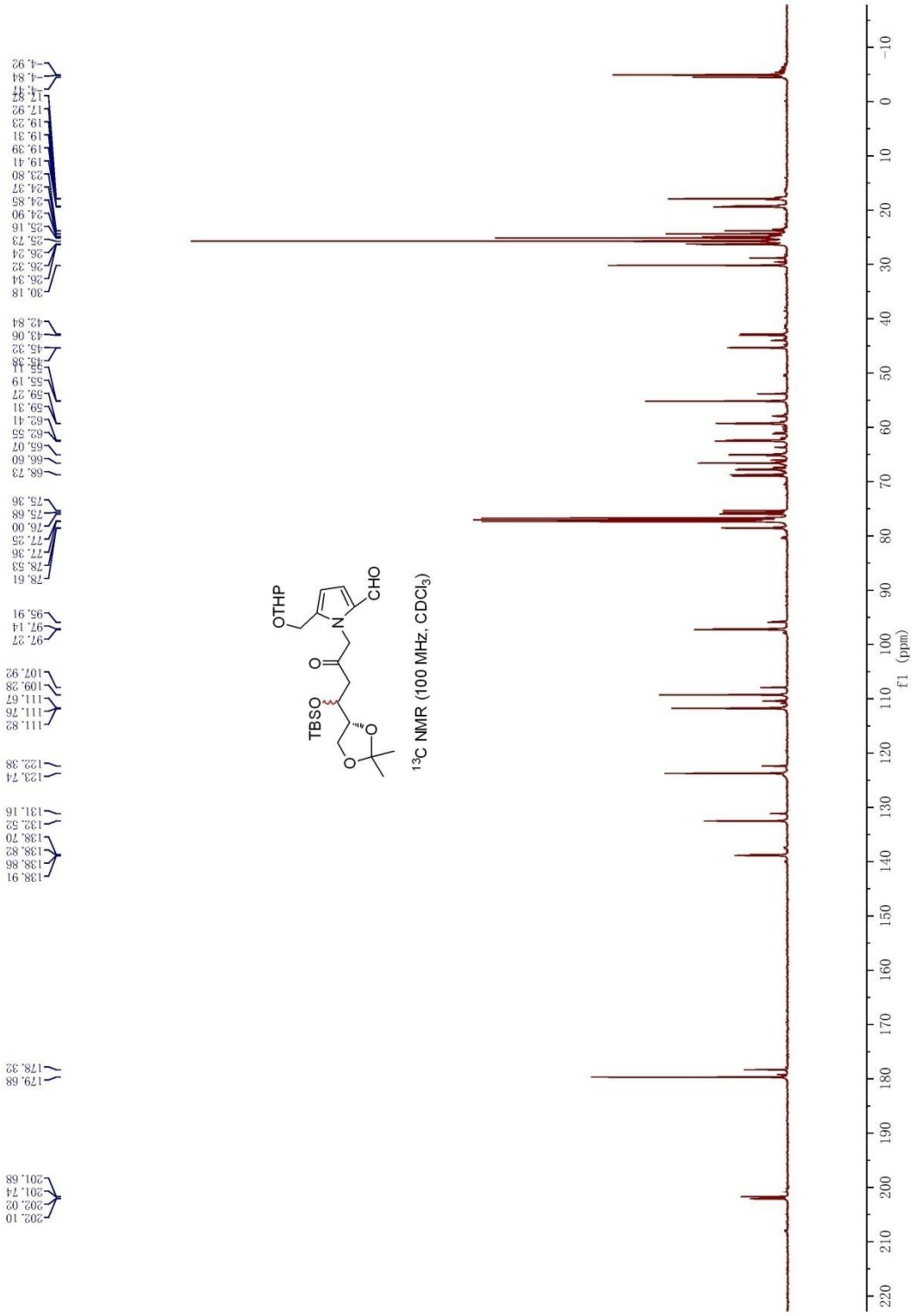


Figure S84. HR-EIMS of **14**

Elemental Composition Report

File Number: 20130329015
Sample Number: WL-III

Single Mass Analysis
Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off

Monoisotopic Mass, Odd and Even Electron Ions
30 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-26 H: 0-45 N: 0-1 O: 0-7 Si: 0-1

Minimum:				-1.5		
Maximum:		5.0	10.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
509.2811	509.2809	0.2	0.4	7.0	5546066.5	C26 H43 N O7 Si

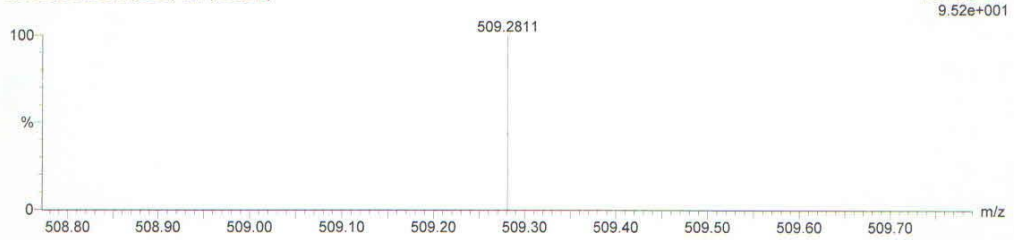
Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off

Monoisotopic Mass, Odd and Even Electron Ions
30 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-26 H: 0-45 N: 0-1 O: 0-7 Si: 0-1

WL-III
20130329015 216 (3.600) Cm (199:216)

TOF MS EI+
9.52e+001



Minimum:				-1.5		
Maximum:		5.0	10.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
509.2811	509.2809	0.2	0.4	7.0	5546066.5	C26 H43 N O7 Si

Figure S85. **^{1}H NMR spectrum of** 15 **in $CDCl_3$**

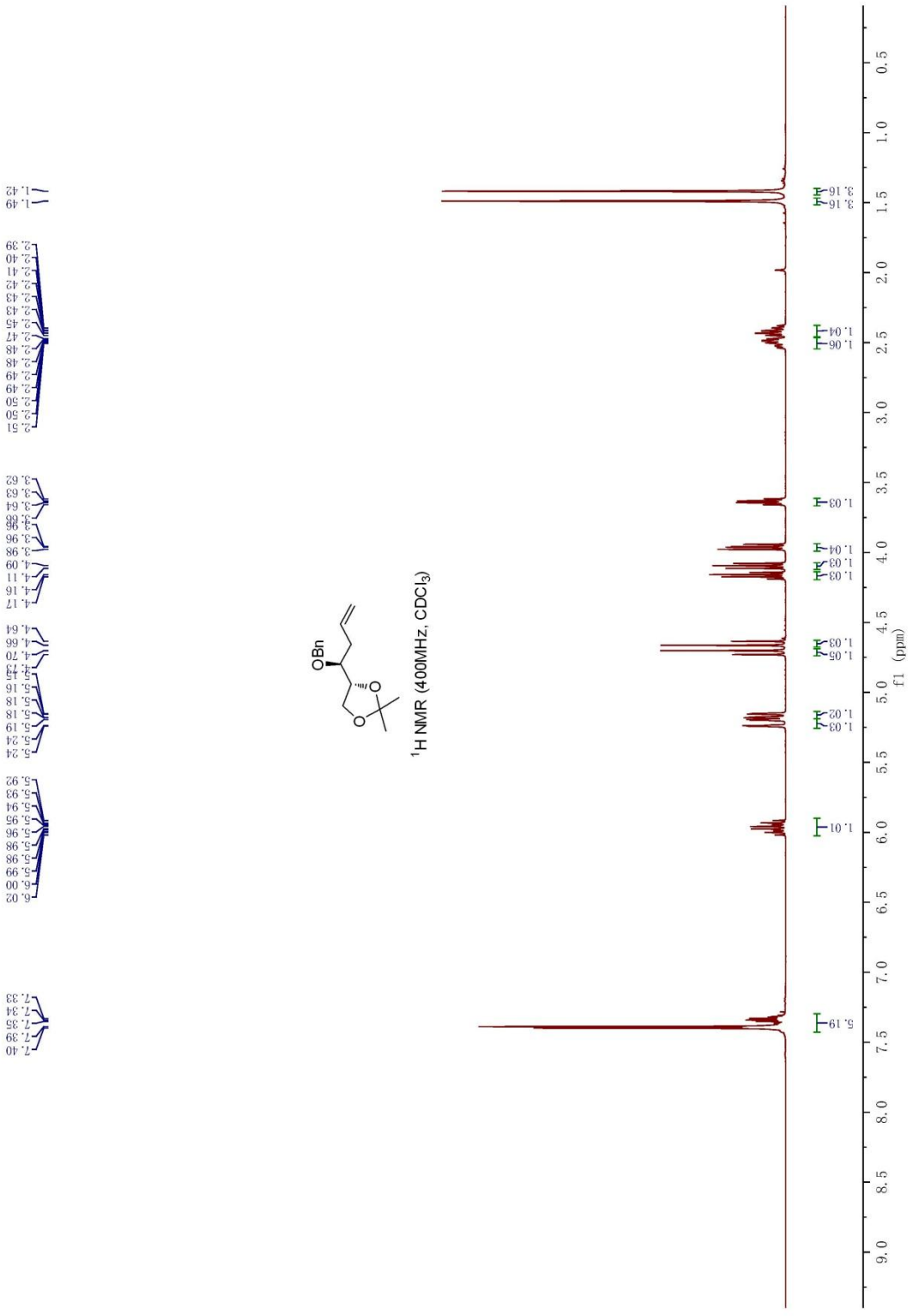


Figure S86. ^{13}C NMR spectrum of **15** in $CDCl_3$

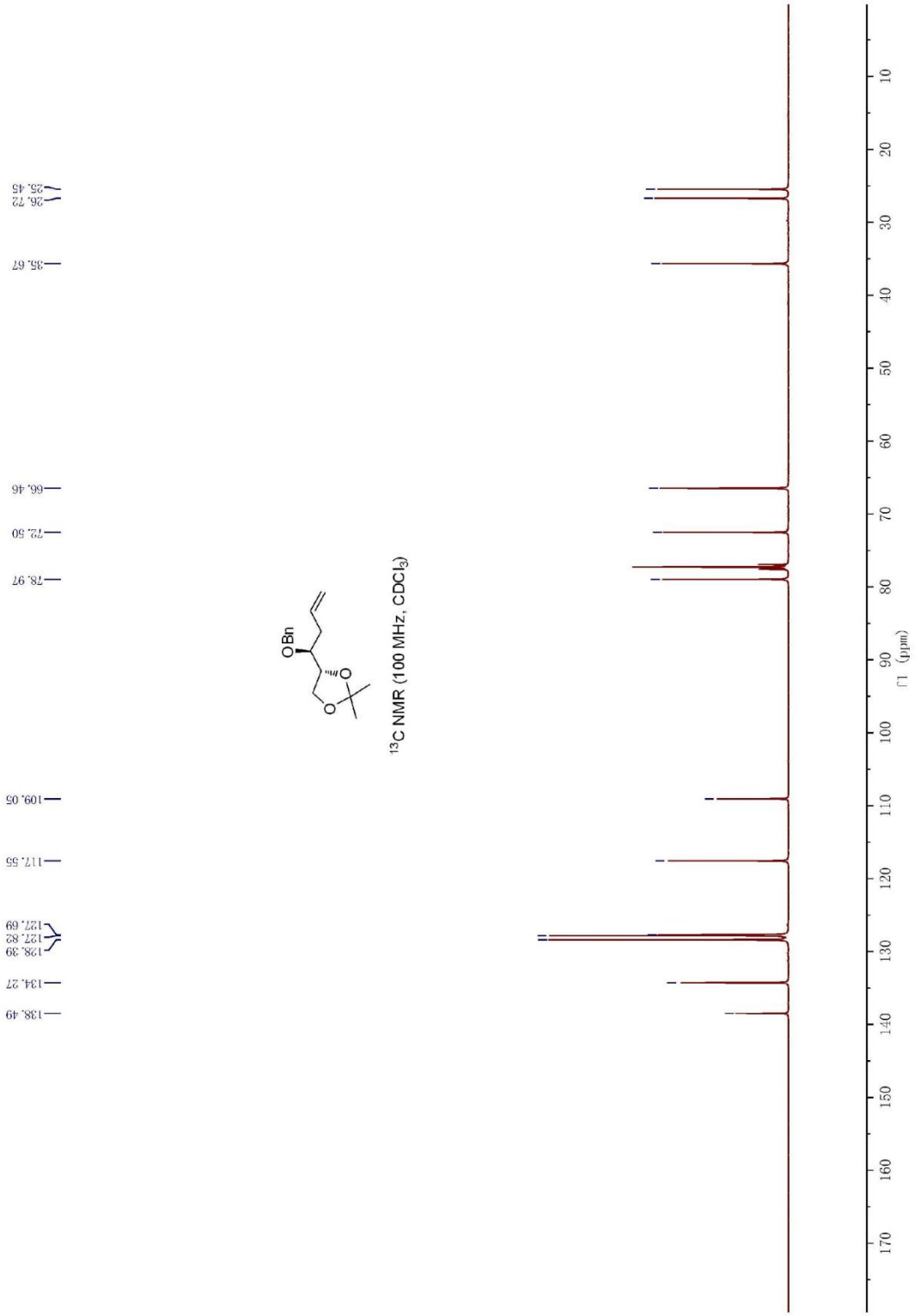


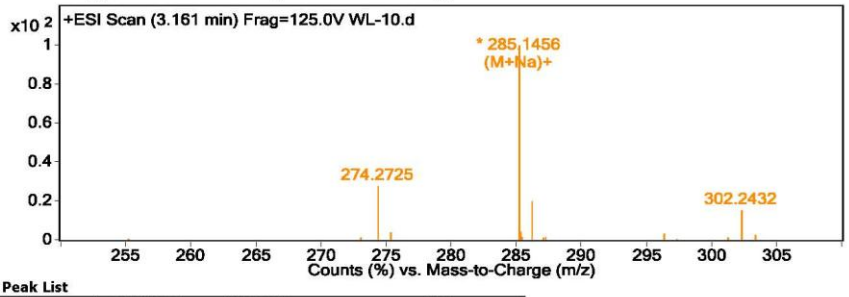
Figure S87. (+) HR-ESIMS of **15**

Qualitative Analysis Report

Data Filename	WL-10.d	**Sample Name**	WL-10
Sample Type	Sample	**Position**	P1-C1
Instrument Name	Instrument 1	**User Name**	
Acq Method	general test 2.m	**Acquired Time**	12/23/2013 1:39:10 PM
IRM Calibration Status	All Ions Missed	**DA Method**	Screening-Default.m
Comment			

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
125	0	Esi



Peak List

m/z	z	Abund	Formula	Ion
285.1456	1	2347843	C16 H22 Na O3	(M+Na)+

Formula Calculator Element Limits

Element	Min	Max
C	3	100
H	0	300
O	0	100
N	0	0
S	0	0
Cl	0	0
Br	0	0
Si	0	0

Formula Calculator Results

Formula	Best	Mass	Tgt Mass	Diff (ppm)	Ion Species	Score
C16 H22 O3	TRUE	262.1564	262.1569	2.04	C16 H22 Na O3	94.14

--- End Of Report ---

Figure S88. ^{1}H NMR spectrum of **16** in $CDCl_3$

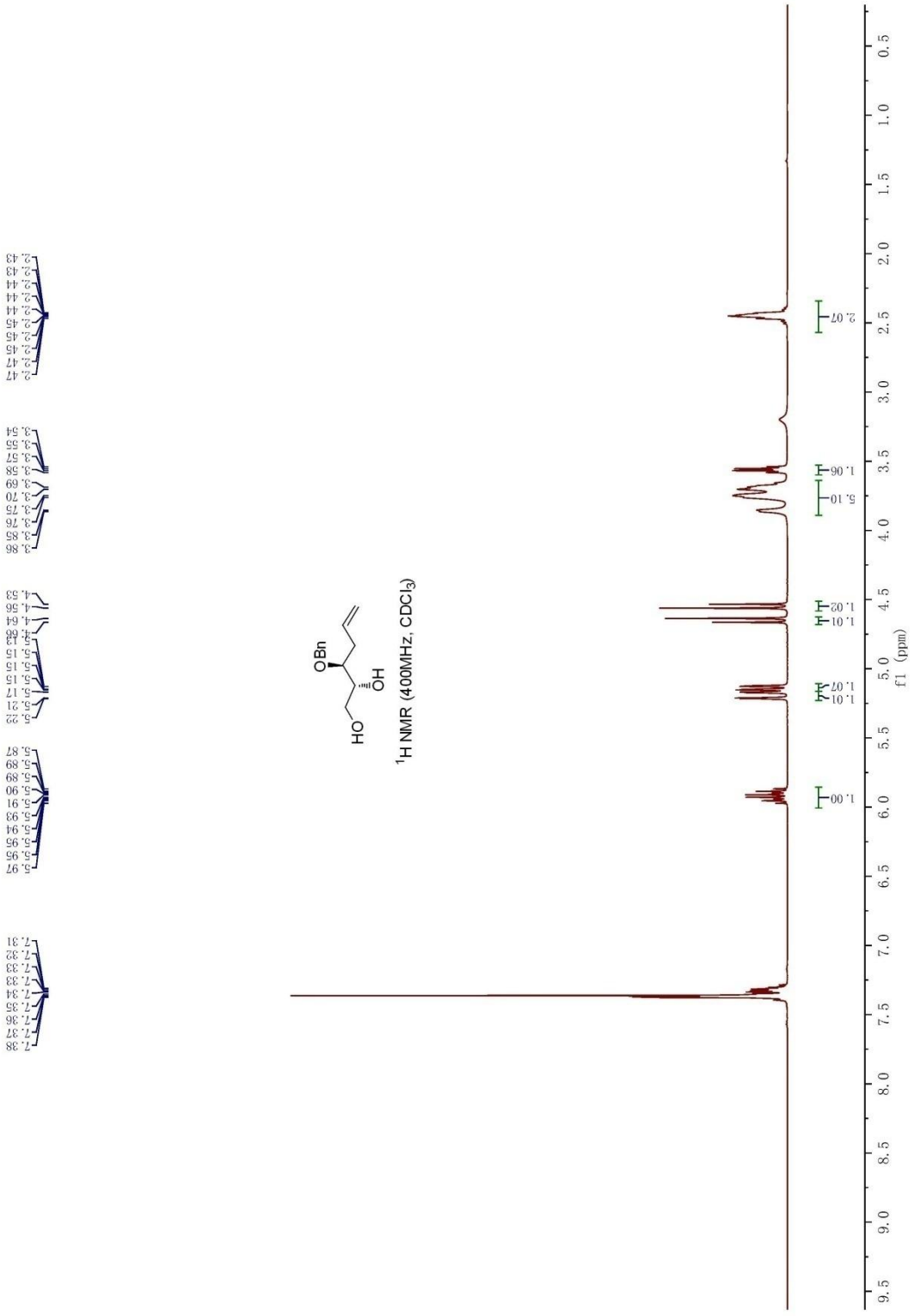


Figure S89. ^{13}C NMR spectrum of **16** in $CDCl_3$

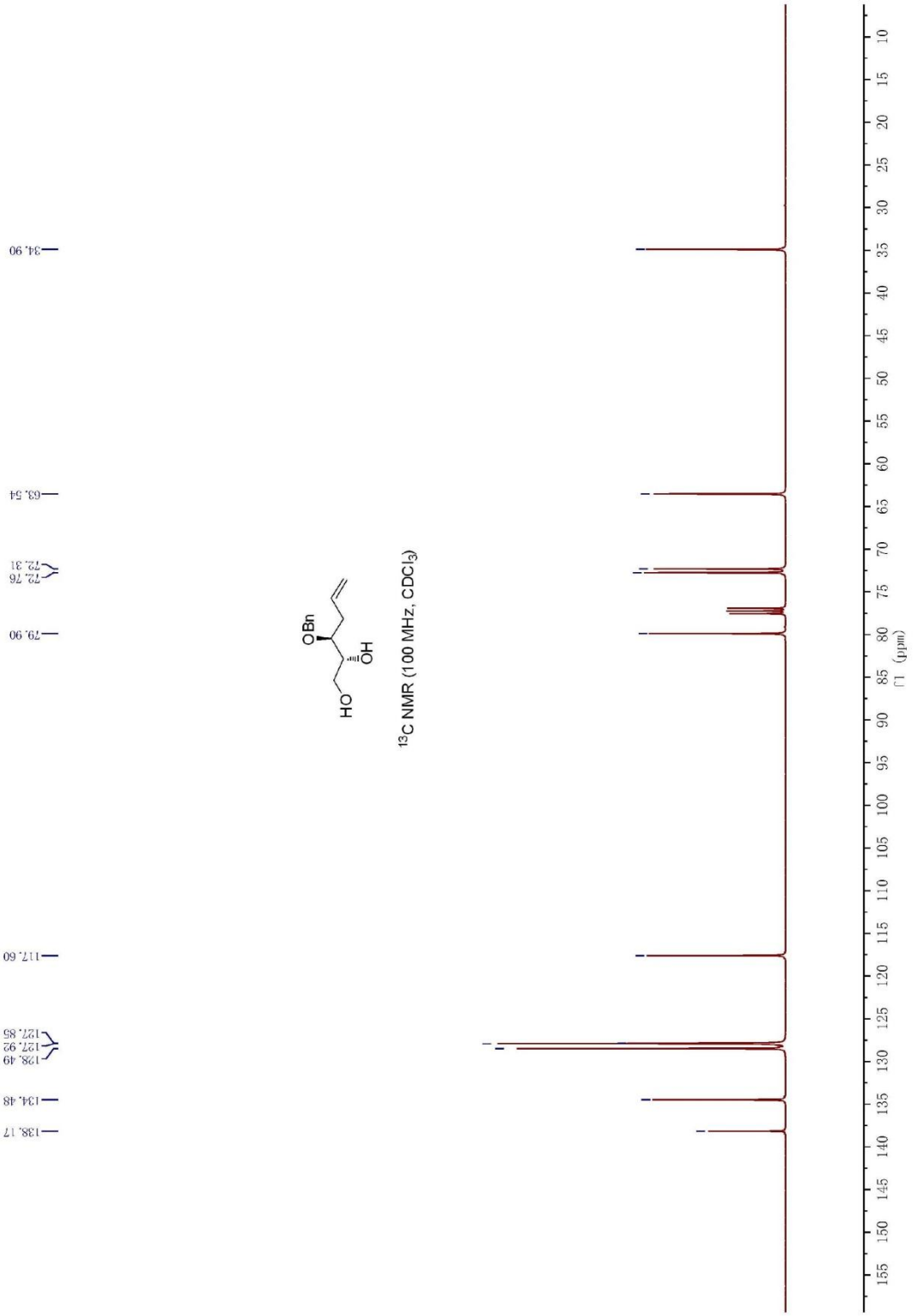
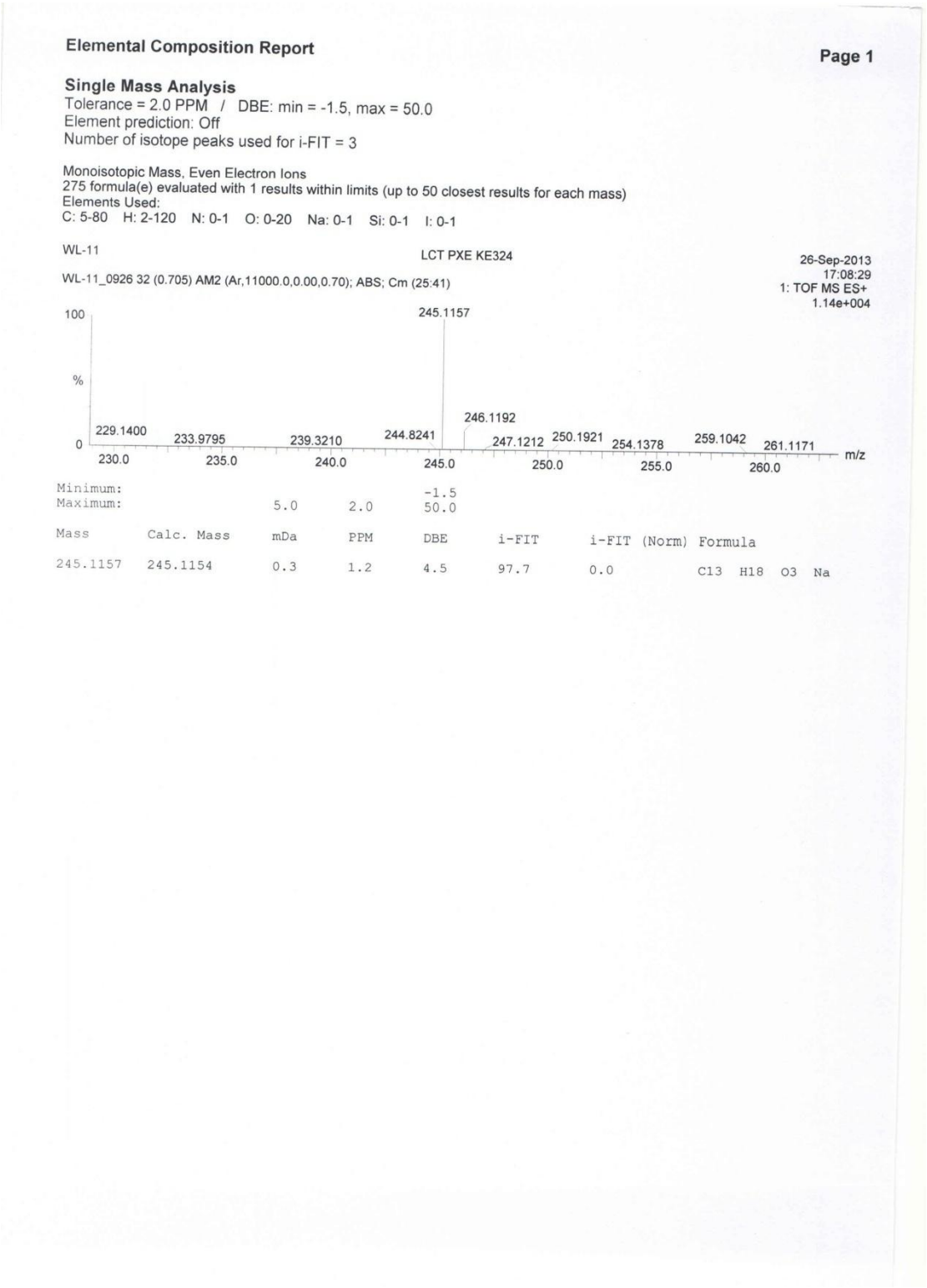


Figure S90. (+) HR-ESIMS of **16**



Elemental Composition Report Page 1

Single Mass Analysis
Tolerance = 2.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
275 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 5-80 H: 2-120 N: 0-1 O: 0-20 Na: 0-1 Si: 0-1 I: 0-1

WL-11 LCT PXE KE324 26-Sep-2013 17:08:29
WL-11_0926 32 (0.705) AM2 (Ar,11000.0,0.00,0.70); ABS; Cm (25:41) 1: TOF MS ES+ 1.14e+004

Minimum:				-1.5			
Maximum:		5.0	2.0	50.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
245.1157	245.1154	0.3	1.2	4.5	97.7	0.0	C13 H18 O3 Na

Figure S91. ^{1}H NMR spectrum of **17** in $CDCl_3$

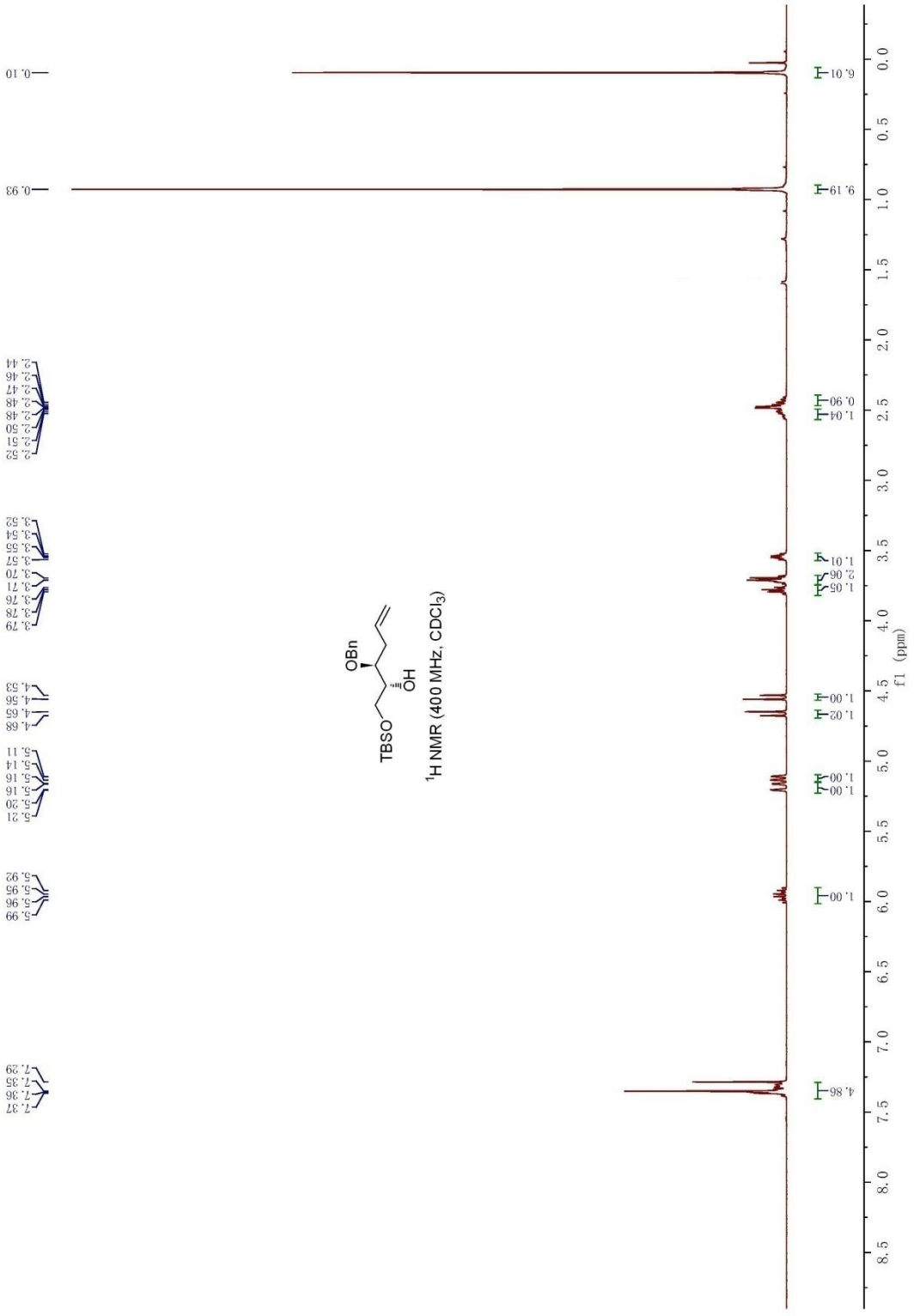


Figure S92. ^{13}C NMR spectrum of **17** in $CDCl_3$

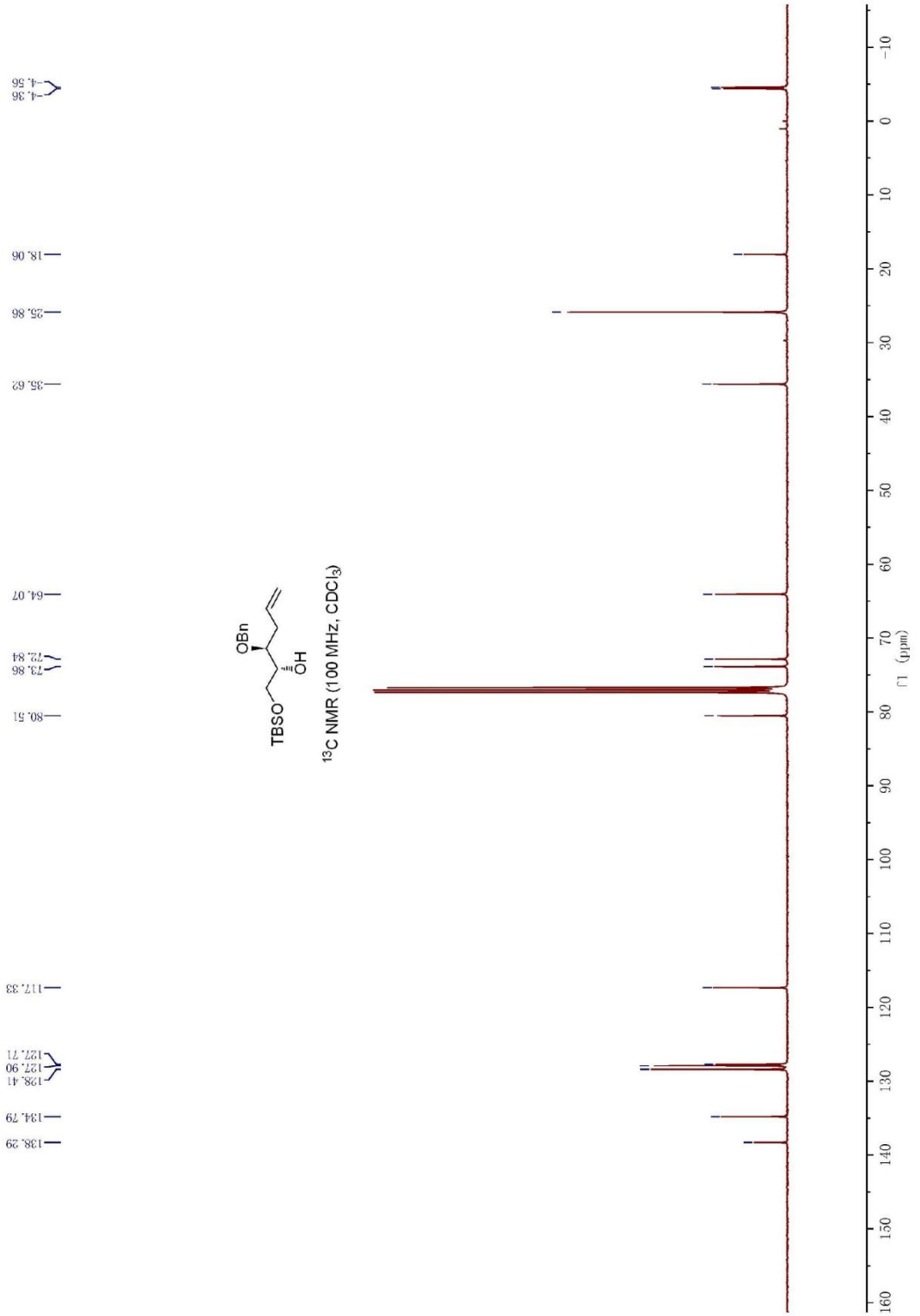
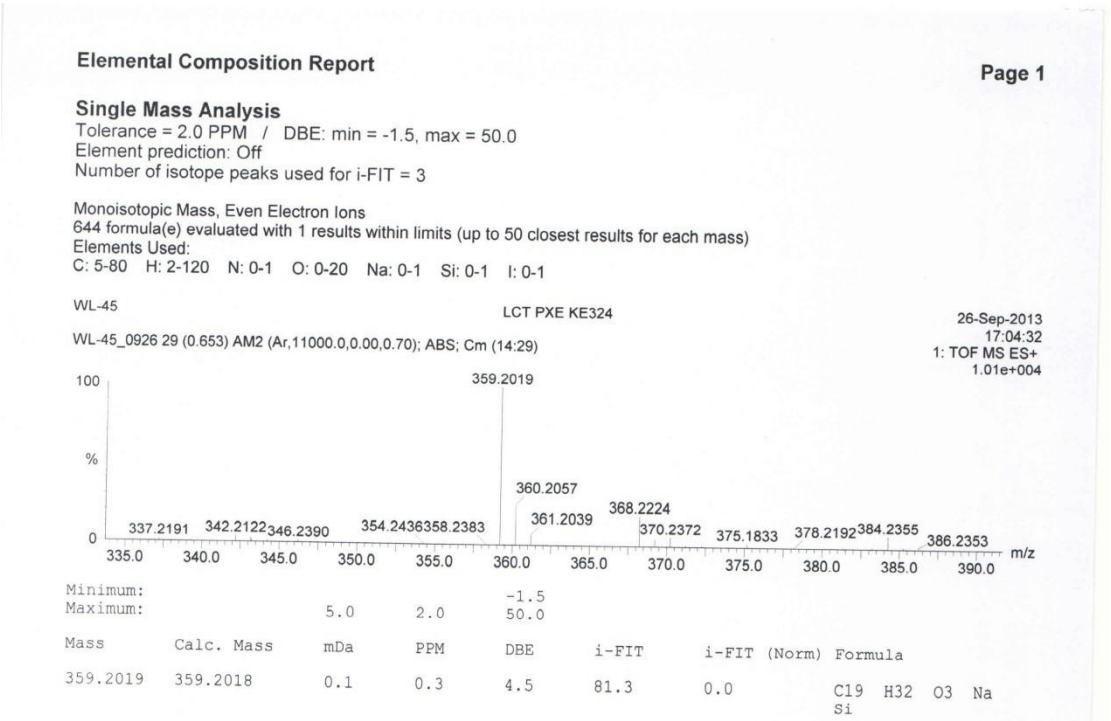


Figure S93. (+) HR-ESIMS of **17**



Elemental Composition Report Page 1

Single Mass Analysis
Tolerance = 2.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
644 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 5-80 H: 2-120 N: 0-1 O: 0-20 Na: 0-1 Si: 0-1 I: 0-1

WL-45
LCT PXE KE324
26-Sep-2013
17:04:32
WL-45_0926 29 (0.653) AM2 (Ar,11000.0,0.00,0.70); ABS; Cm (14:29)
1: TOF MS ES+
1.01e+004

Minimum:				-1.5			
Maximum:		5.0	2.0	50.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
359.2019	359.2018	0.1	0.3	4.5	81.3	0.0	C19 H32 O3 Na Si

Figure S94. ^{1}H NMR spectrum of **18** in $CDCl_3$

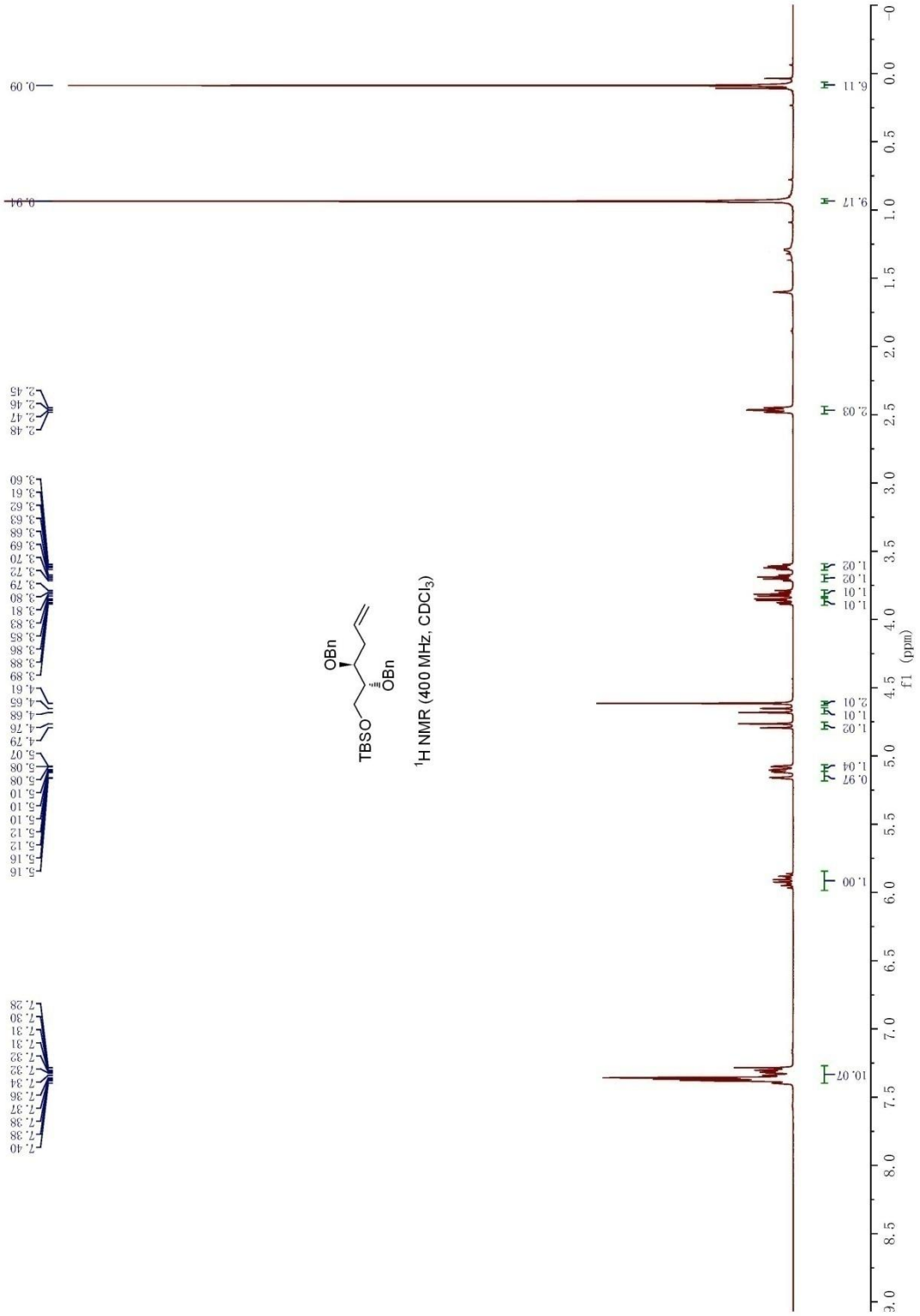


Figure S95. ^{13}C NMR spectrum of **18** in $CDCl_3$

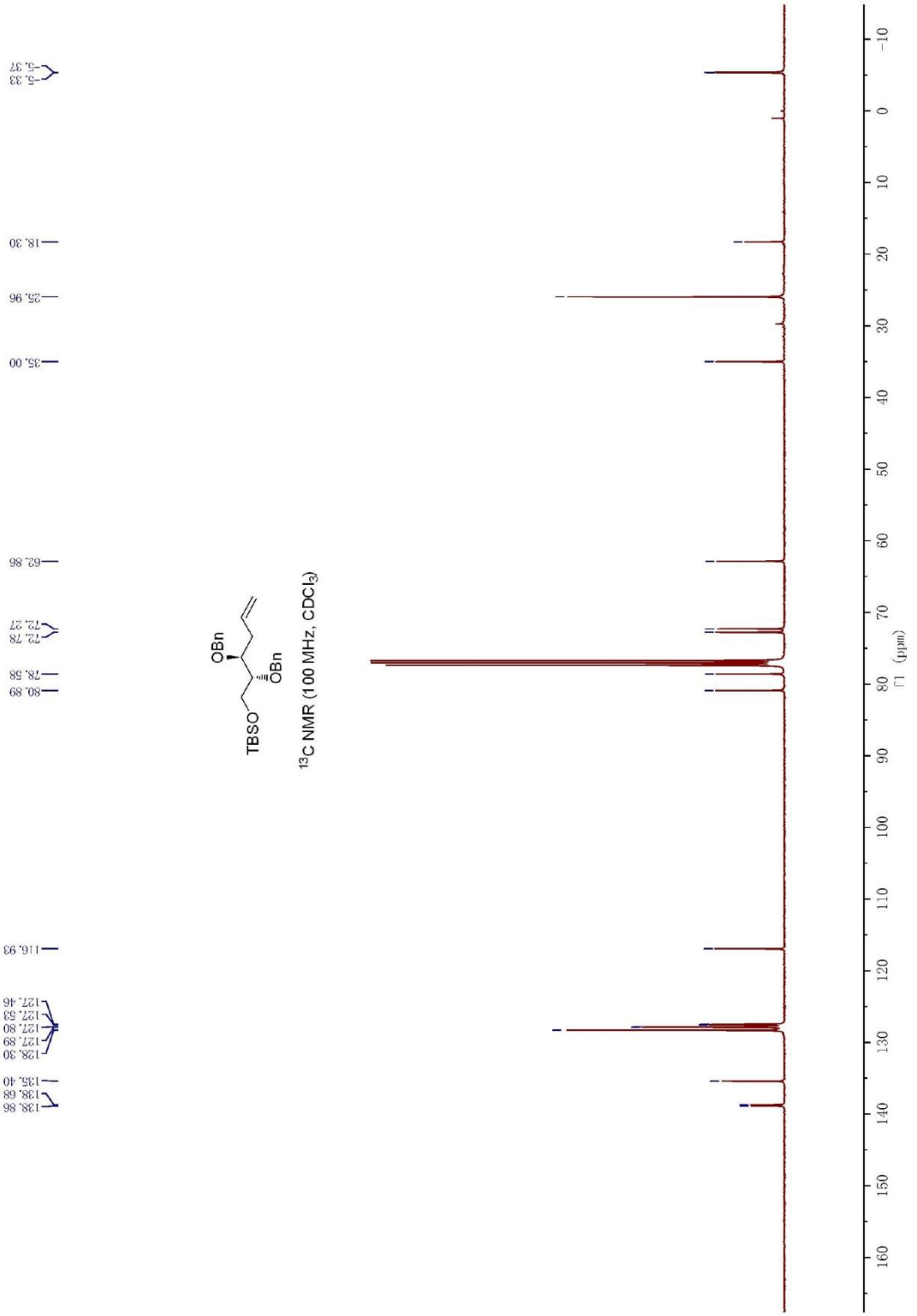
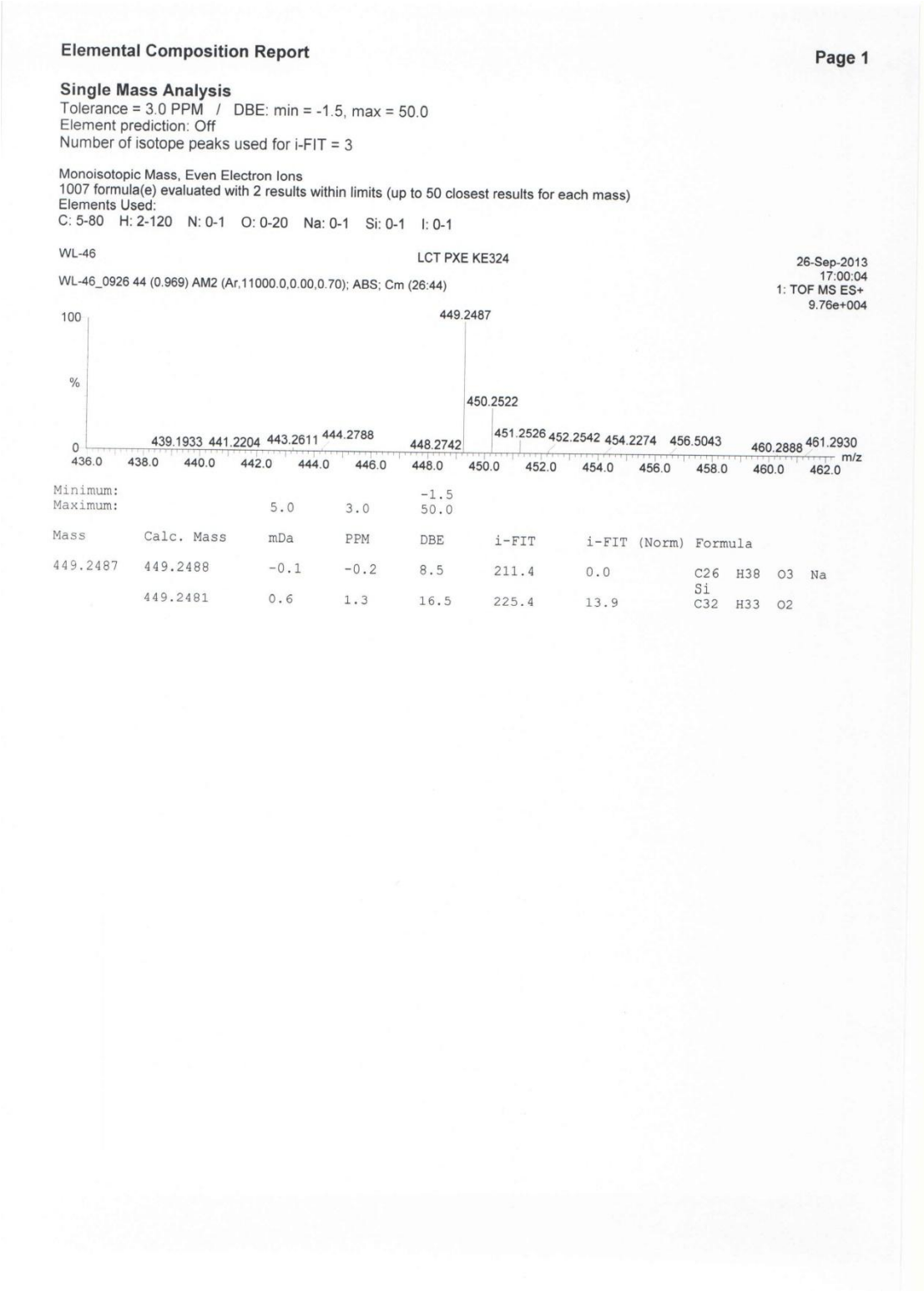


Figure S96. (+) HR-ESIMS of **18**



Elemental Composition Report Page 1

Single Mass Analysis
Tolerance = 3.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
1007 formula(e) evaluated with 2 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 5-80 H: 2-120 N: 0-1 O: 0-20 Na: 0-1 Si: 0-1 I: 0-1

WL-46 LCT PXE KE324 26-Sep-2013 17:00:04
WL-46_0926 44 (0.969) AM2 (Ar,11000.0,0.00,0.70); ABS; Cm (26:44) 1: TOF MS ES+ 9.76e+004

Minimum:				-1.5			
Maximum:		5.0	3.0	50.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
449.2487	449.2488	-0.1	-0.2	8.5	211.4	0.0	C26 H38 O3 Na Si
	449.2481	0.6	1.3	16.5	225.4	13.9	C32 H33 O2

Figure S97. ^{1}H NMR spectrum of **19** in $CDCl_3$

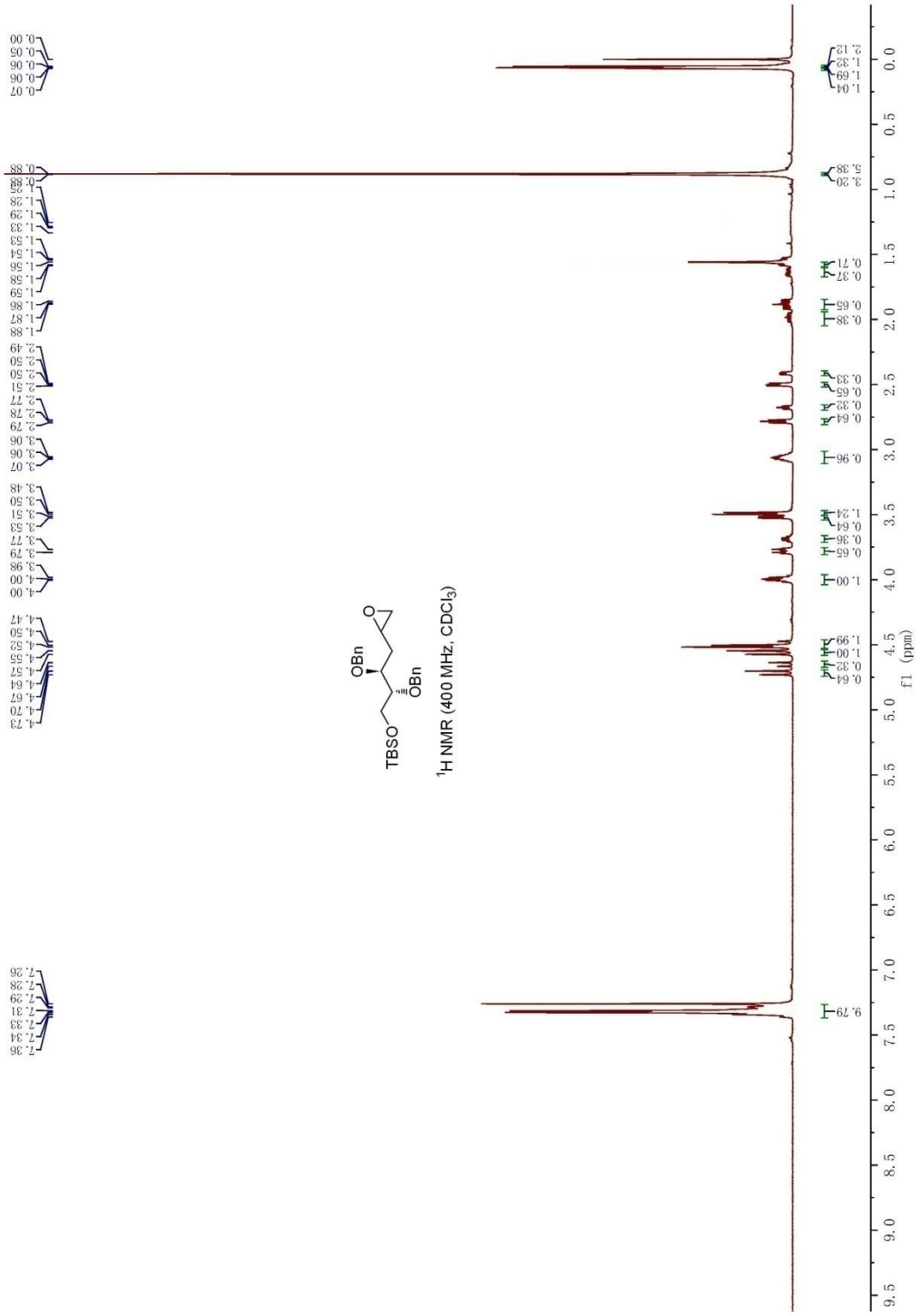


Figure S98. ^{13}C NMR spectrum of **19** in $CDCl_3$

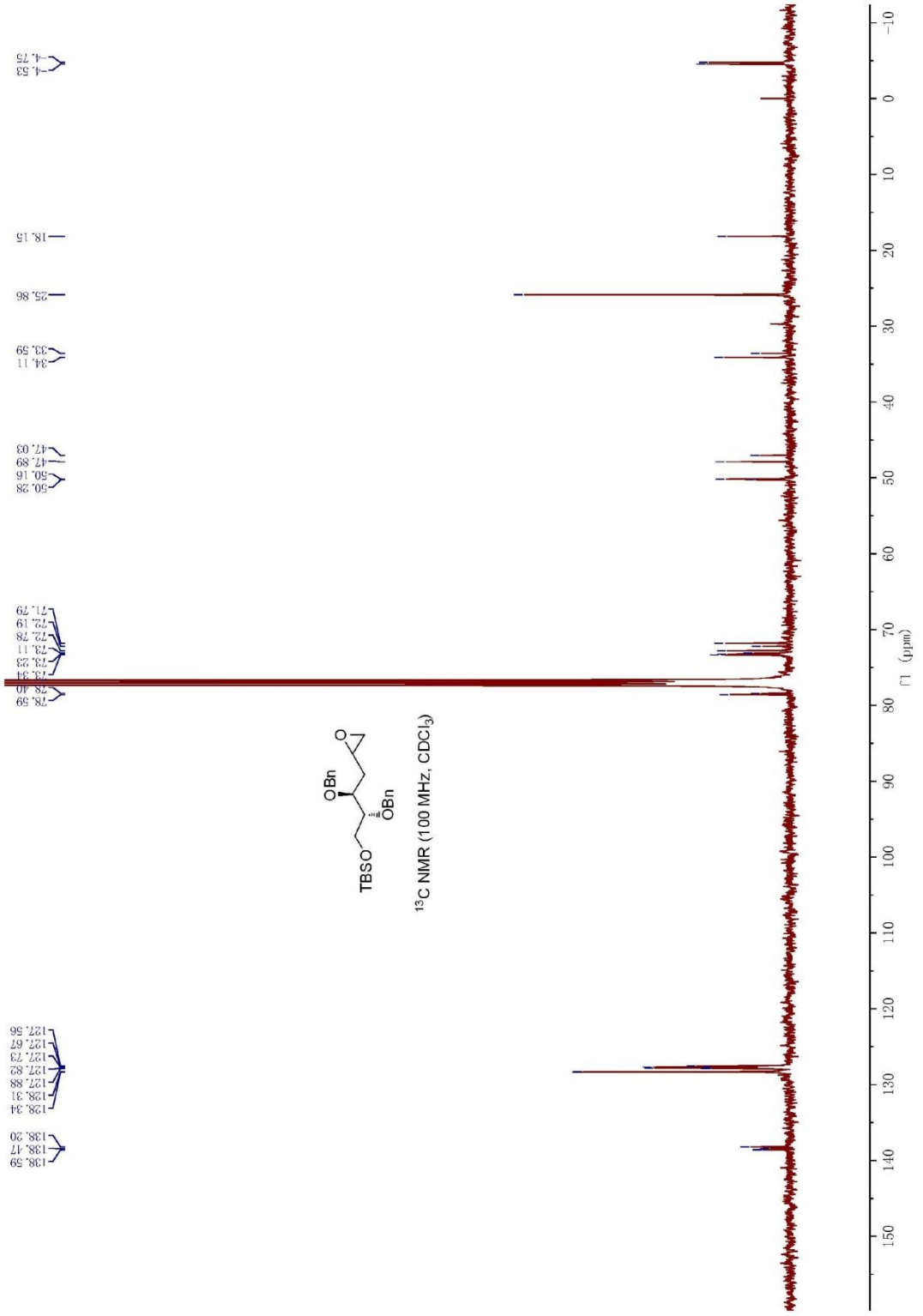
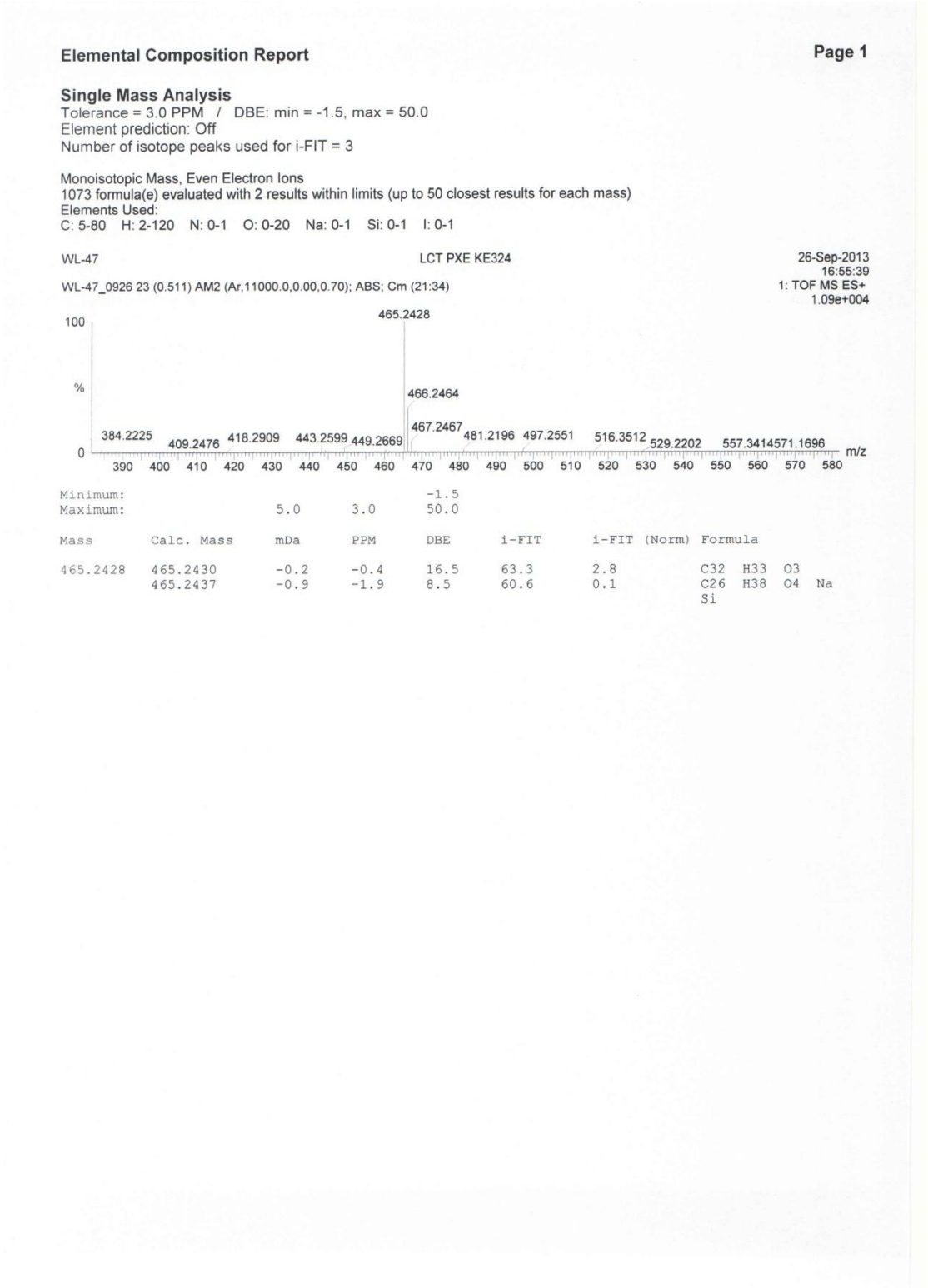


Figure S99. (+) HR-ESIMS of **19**



Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 3.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
1073 formula(e) evaluated with 2 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 5-80 H: 2-120 N: 0-1 O: 0-20 Na: 0-1 Si: 0-1 I: 0-1

WL-47 LCT PXE KE324 26-Sep-2013 16:55:39
WL-47_0926 23 (0.511) AM2 (Ar,11000.0,0.00,0.70); ABS; Cm (21:34) 1: TOF MS ES+ 1.09e+004

Minimum:				-1.5			
Maximum:		5.0	3.0	50.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
465.2428	465.2430	-0.2	-0.4	16.5	63.3	2.8	C32 H33 O3
	465.2437	-0.9	-1.9	8.5	60.6	0.1	C26 H38 O4 Na Si

Figure S100. ^{1}H NMR spectrum of **20** in $CDCl_3$

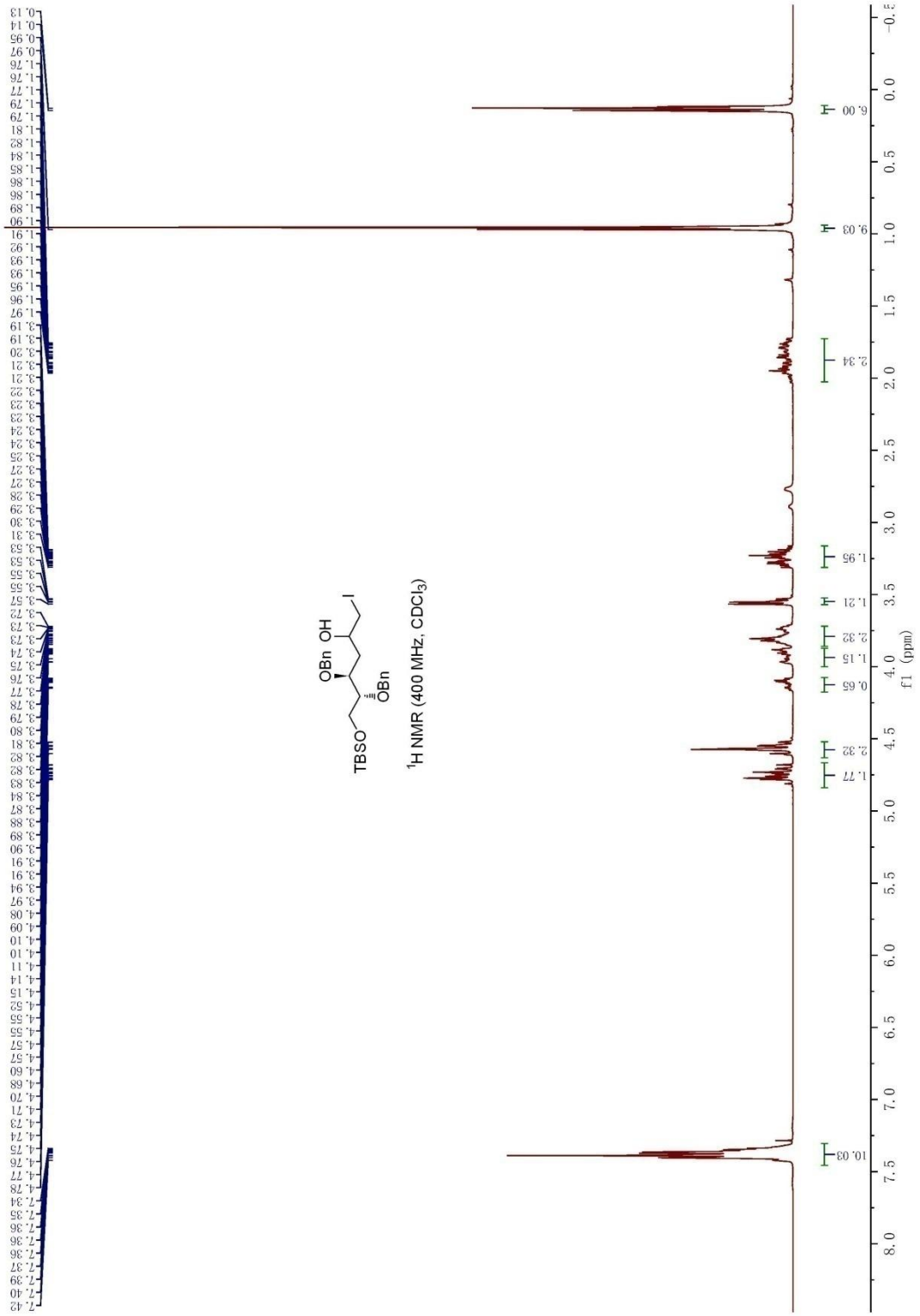


Figure S101. ^{13}C NMR spectrum of **20** in CD_3OD

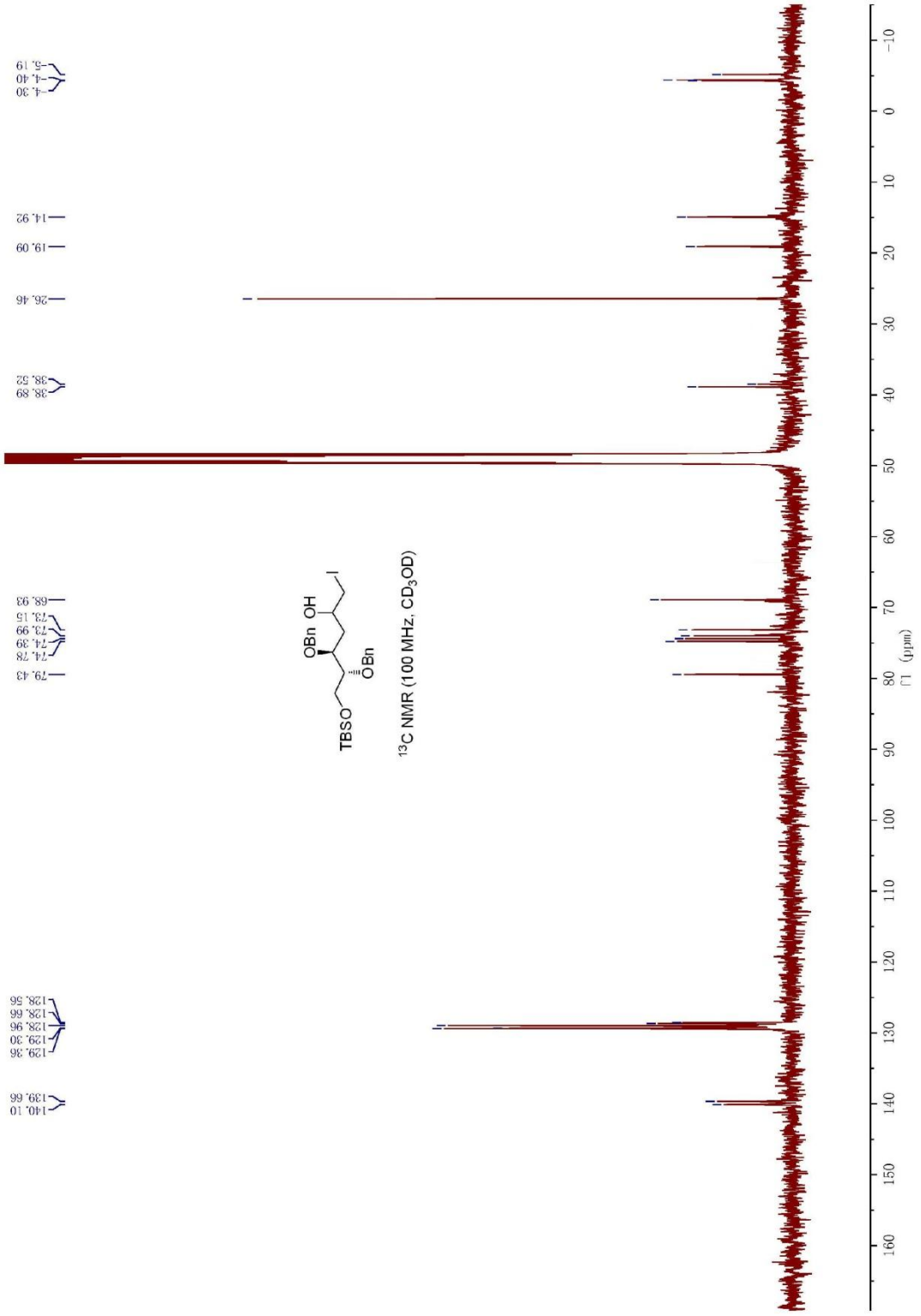
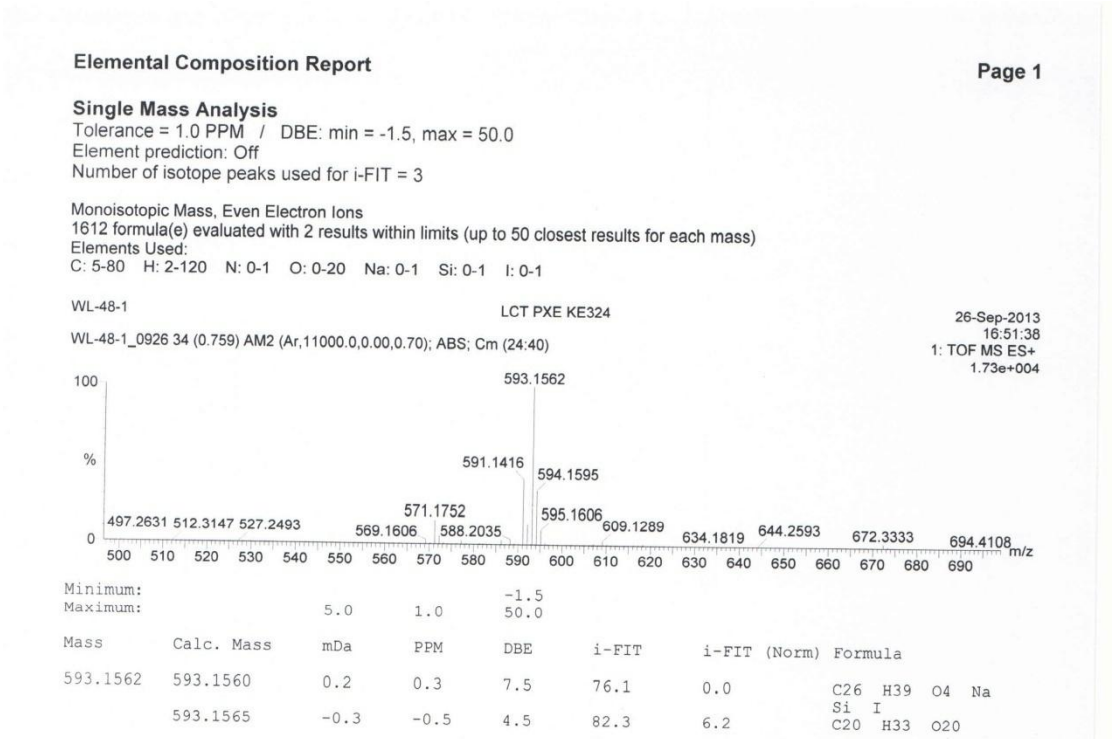


Figure S102. (+) HR-ESIMS of **20**



Elemental Composition Report Page 1

Single Mass Analysis
Tolerance = 1.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
1612 formula(e) evaluated with 2 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 5-80 H: 2-120 N: 0-1 O: 0-20 Na: 0-1 Si: 0-1 I: 0-1

WL-48-1 LCT PXE KE324 26-Sep-2013 16:51:38
WL-48-1_0926 34 (0.759) AM2 (Ar,11000.0,0.00,0.70); ABS; Cm (24:40) 1: TOF MS ES+ 1.73e+004

Minimum:				-1.5			
Maximum:		5.0	1.0	50.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
593.1562	593.1560	0.2	0.3	7.5	76.1	0.0	C26 H39 O4 Na Si I
	593.1565	-0.3	-0.5	4.5	82.3	6.2	C20 H33 O20

Figure S103. ^{1}H NMR spectrum of **21** in CD_3OD

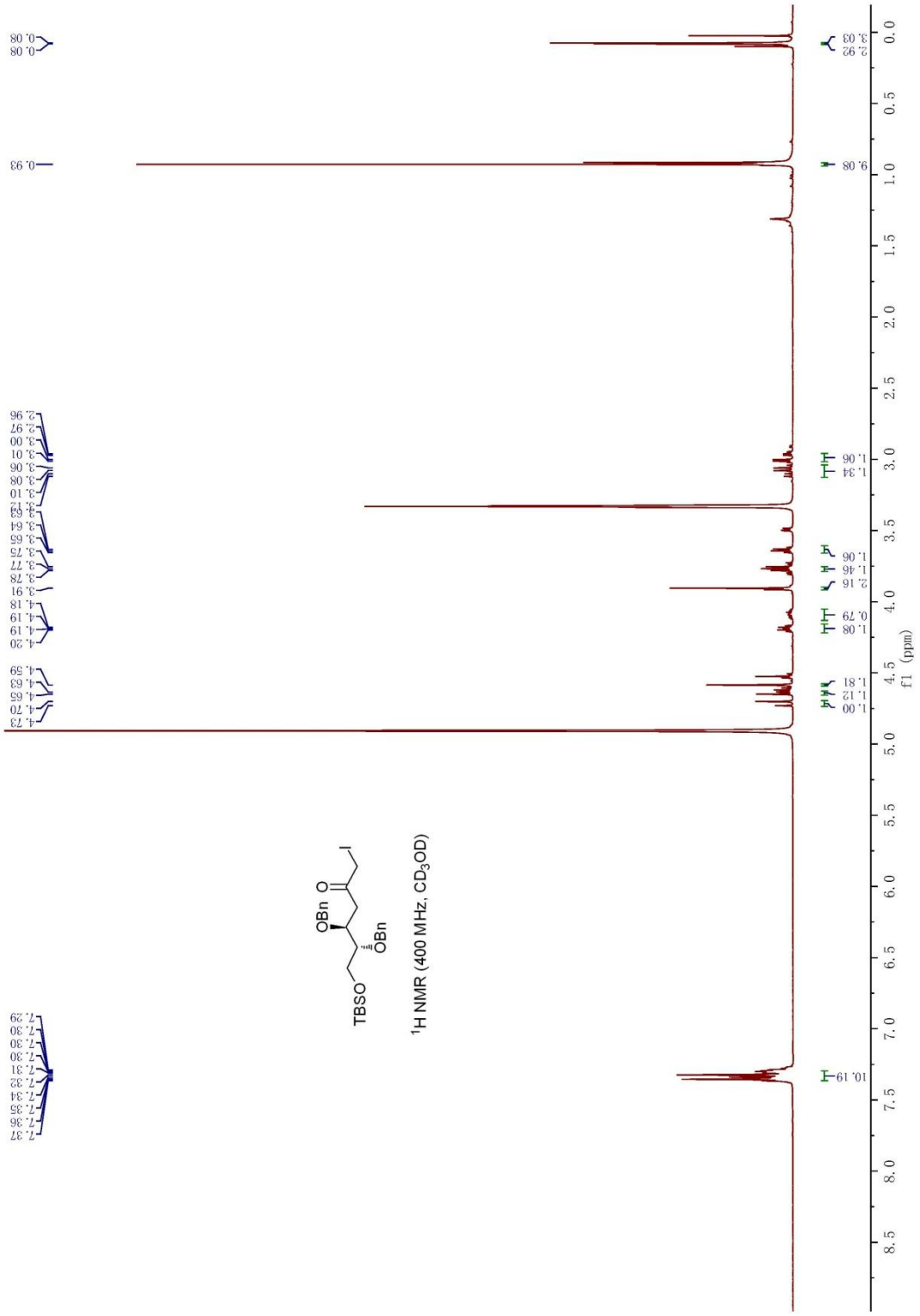


Figure S104. ^{13}C NMR spectrum of **21** in CD_3OD

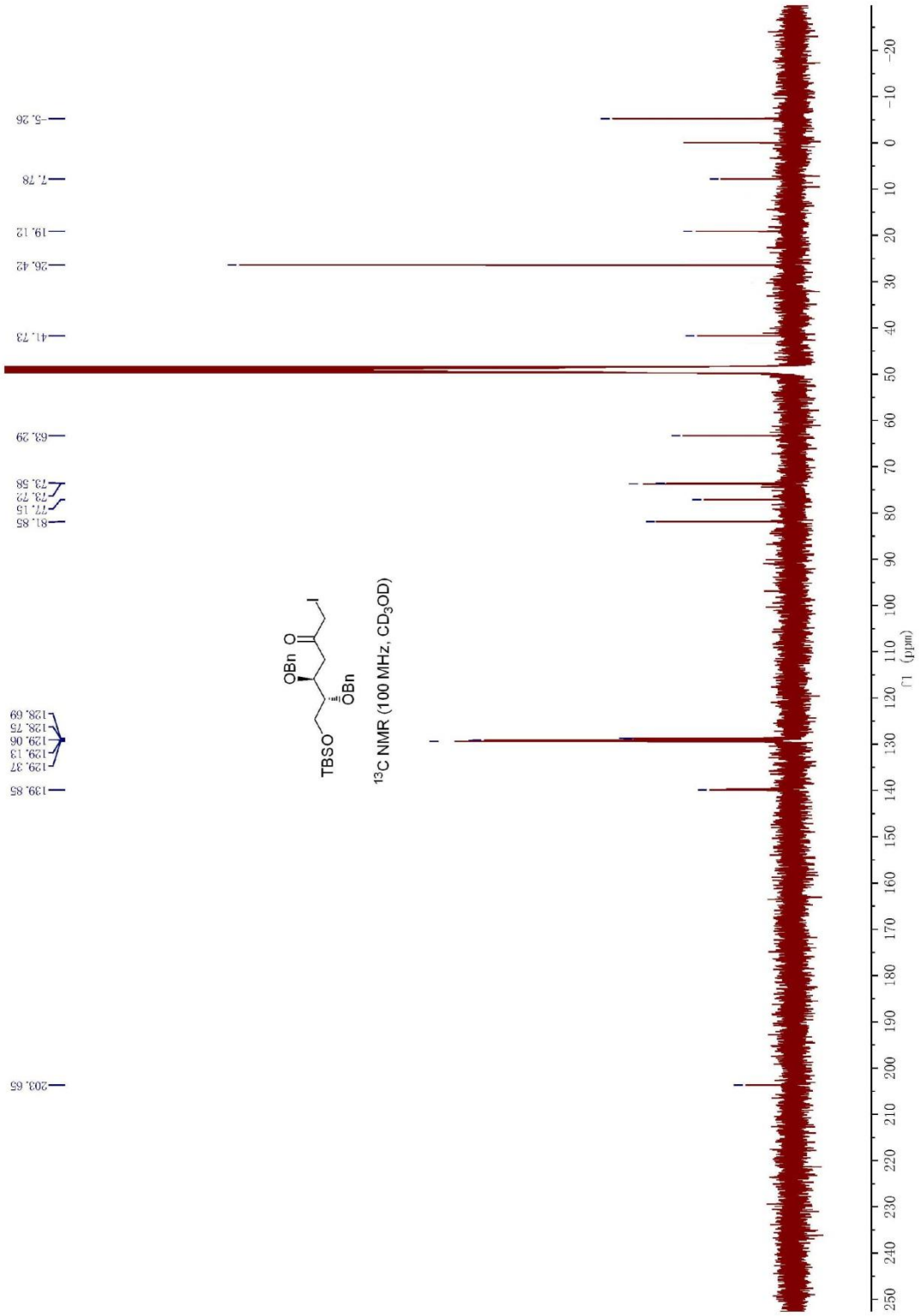
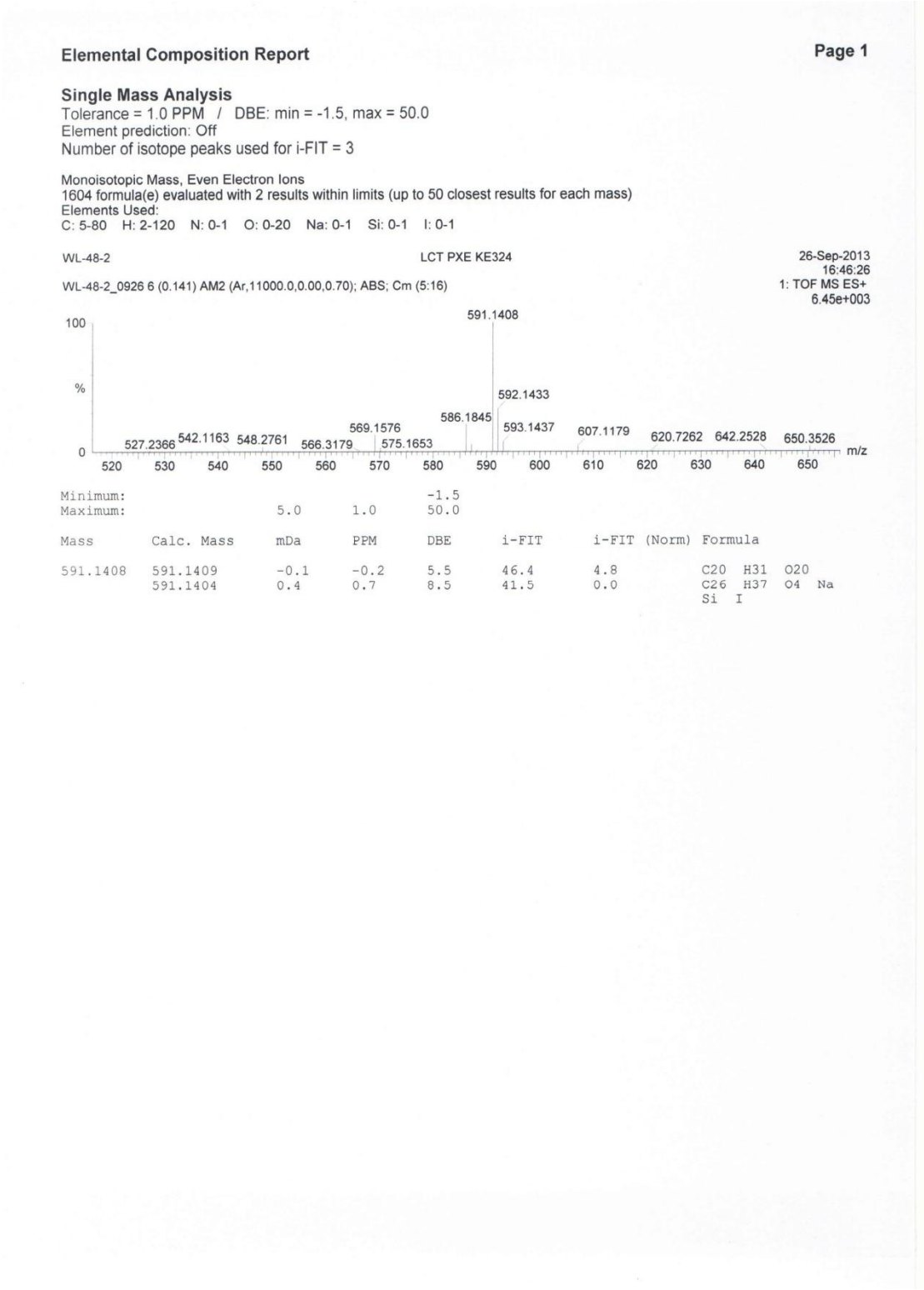


Figure S105. (+) HR-ESIMS of **21**



Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 1.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
1604 formula(e) evaluated with 2 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 5-80 H: 2-120 N: 0-1 O: 0-20 Na: 0-1 Si: 0-1 I: 0-1

WL-48-2 LCT PXE KE324 26-Sep-2013 16:46:26
WL-48-2_0926 6 (0.141) AM2 (Ar,11000.0,0.00,0.70); ABS; Cm (5:16) 1: TOF MS ES+ 6.45e+003

Minimum:				-1.5			
Maximum:		5.0	1.0	50.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
591.1408	591.1409	-0.1	-0.2	5.5	46.4	4.8	C20 H31 O20
	591.1404	0.4	0.7	8.5	41.5	0.0	C26 H37 O4 Na Si I

Figure S106. ^{1}H NMR spectrum of **22** in CD_3OD

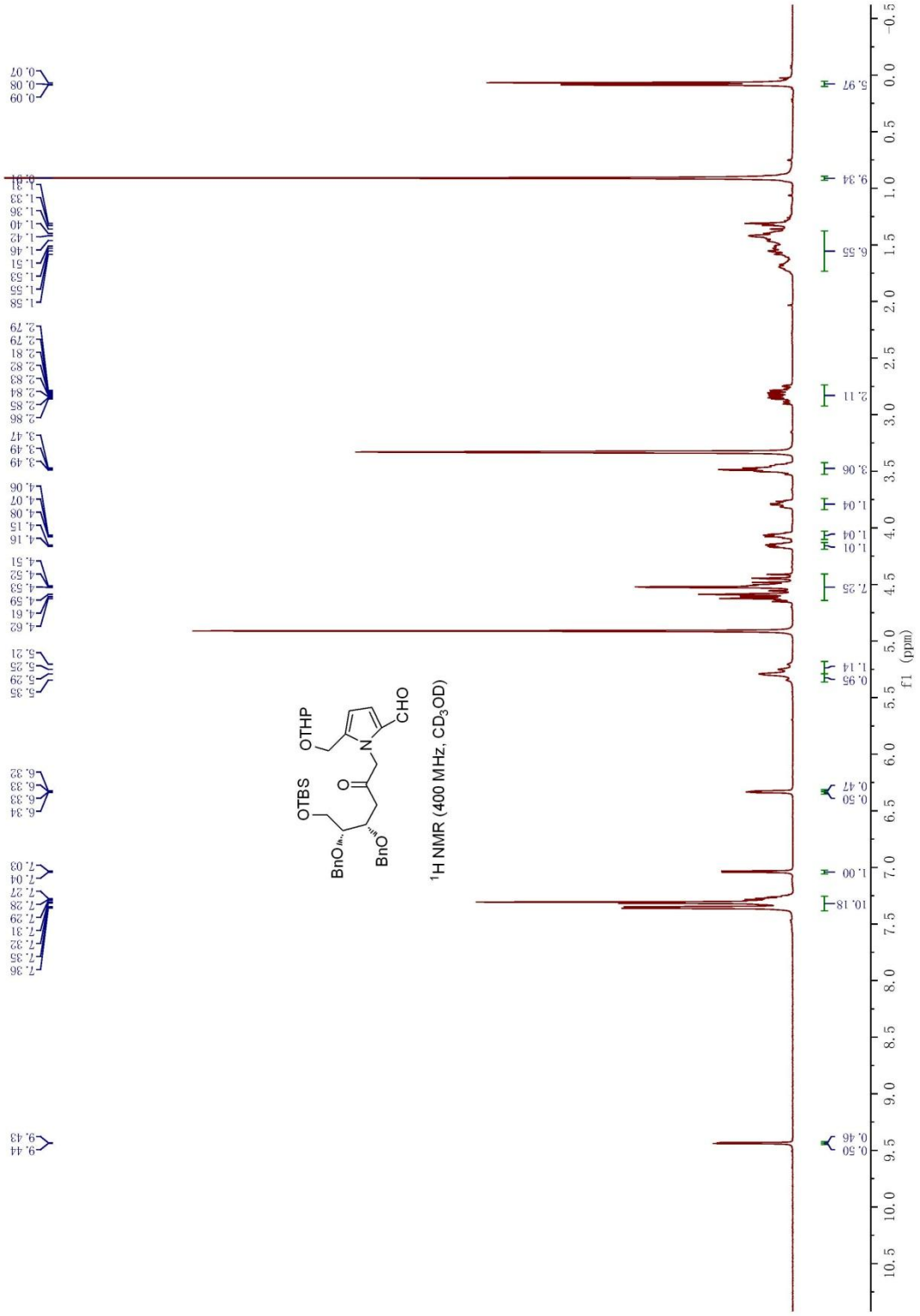


Figure S107. ^{13}C NMR spectrum of **22** in CD_3OD

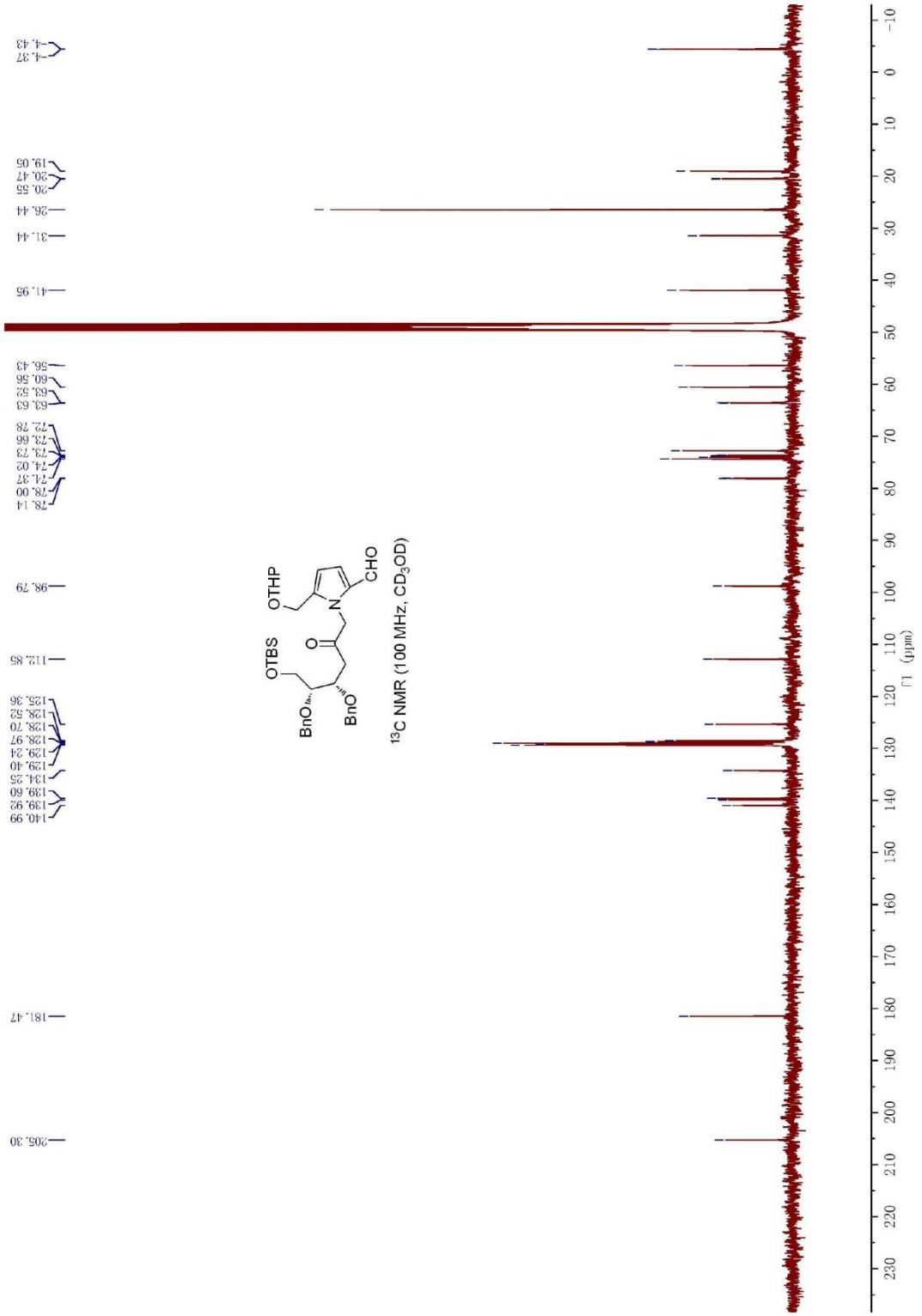


Figure S108. (+) HR-ESIMS of **22**

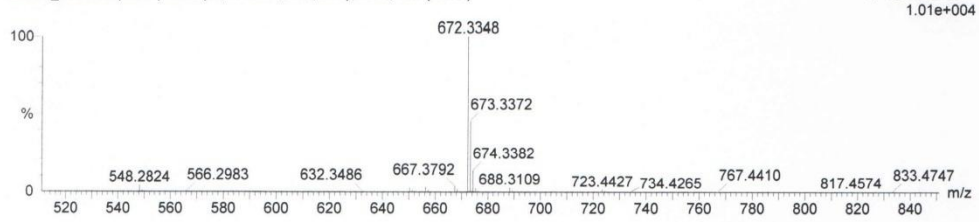
Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 3.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
1098 formula(e) evaluated with 3 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 5-80 H: 2-120 N: 0-1 O: 0-20 Na: 0-1 Si: 0-1

WL-50 LCT PXE KE324 26-Sep-2013 16:38:22

WL-50_0926 32 (0.671) AM2 (Ar,11000.0,0.00,0.70); ABS; Cm (22:39) 1: TOF MS ES+ 1.01e+004



Minimum:				-1.5			
Maximum:		5.0	3.0	50.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
672.3348	672.3357	-0.9	-1.3	16.5	55.8	1.7	C39 H50 N O7 Si
	672.3360	-1.2	-1.8	9.5	59.5	5.3	C34 H51 N O11 Na
	672.3333	1.5	2.2	13.5	54.4	0.2	C37 H51 N O7 Na Si

Figure S109. ^{1}H NMR spectrum of **23** in $CDCl_3$

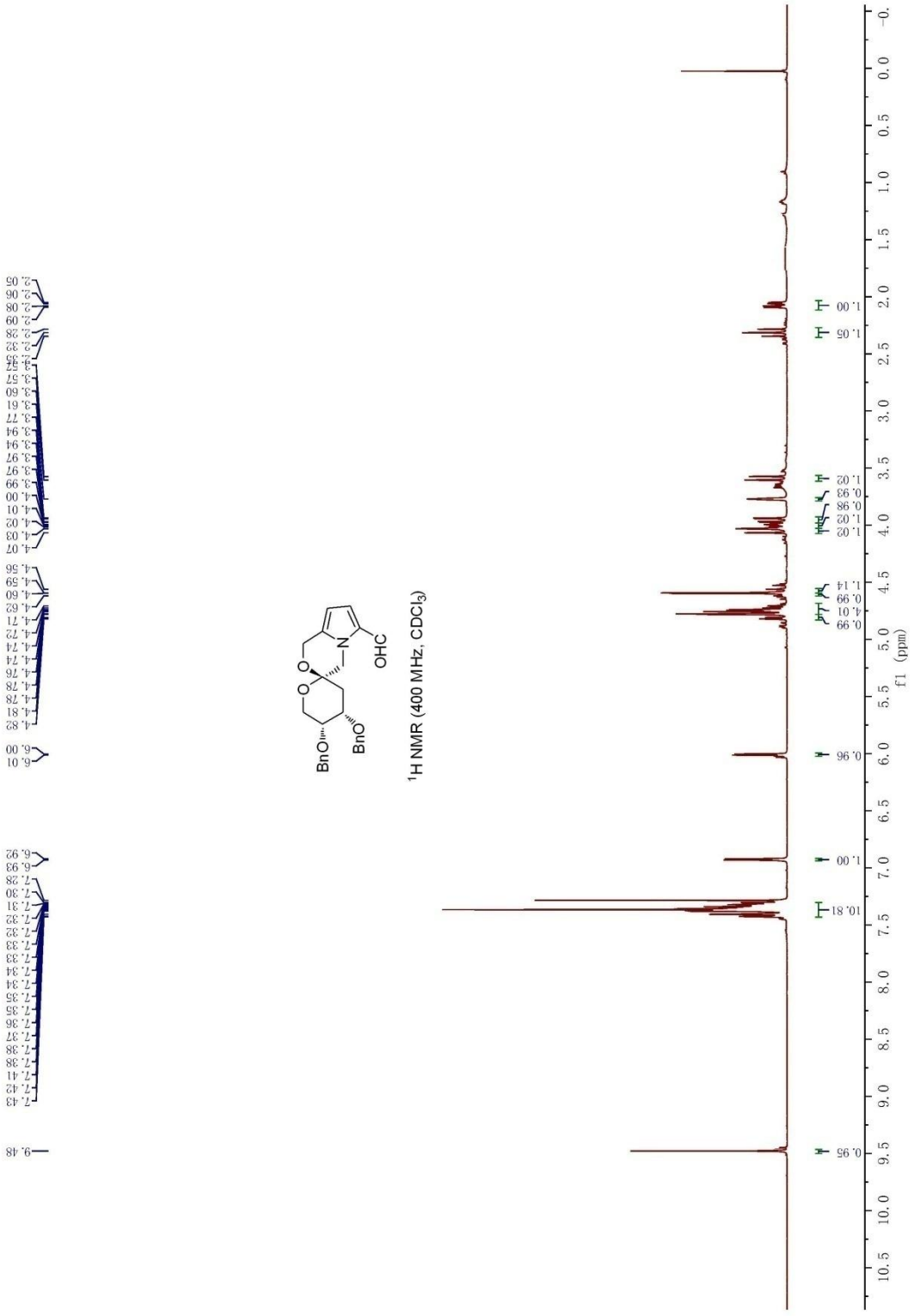


Figure S110. ^{13}C NMR spectrum of **23** in $CDCl_3$

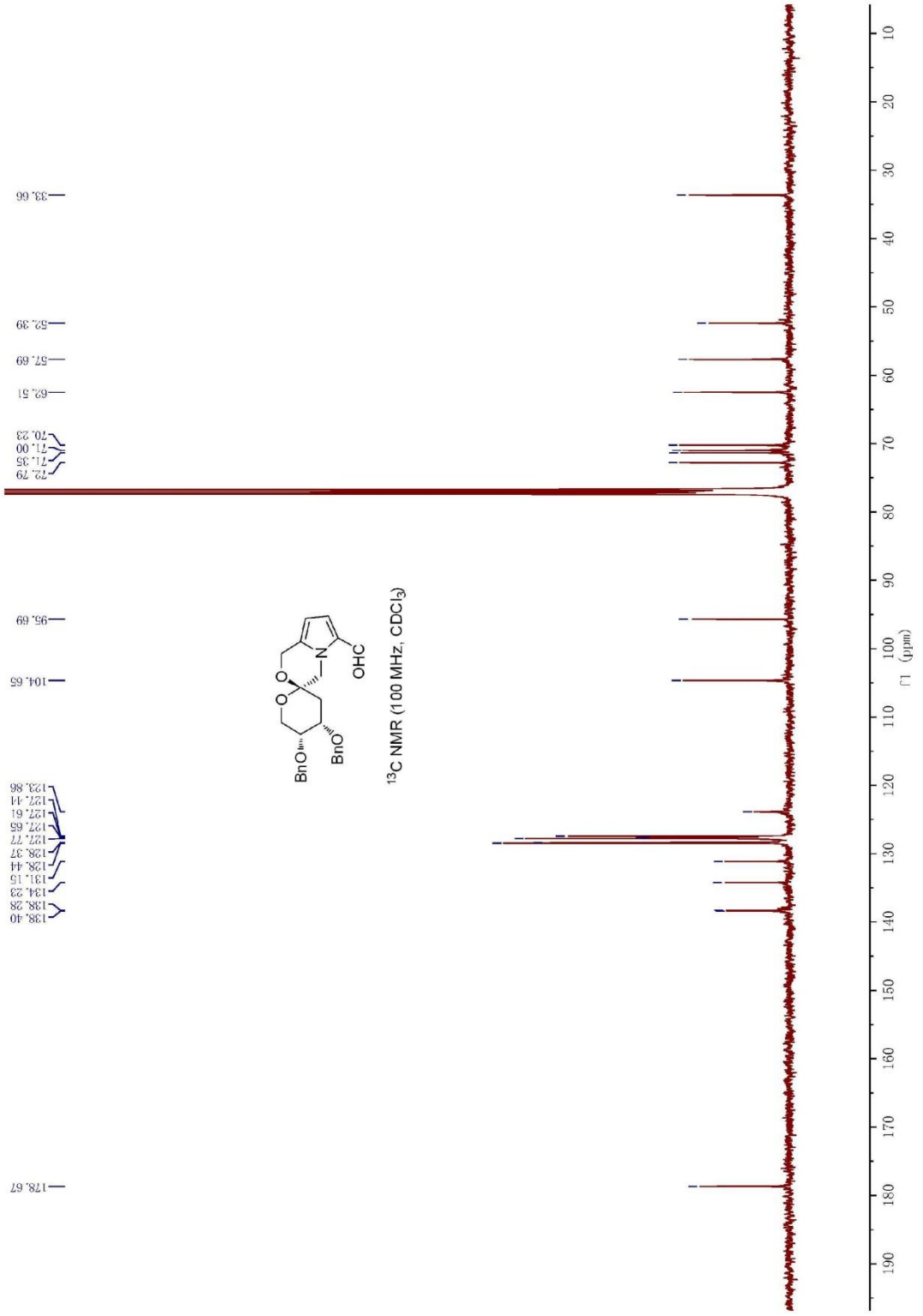


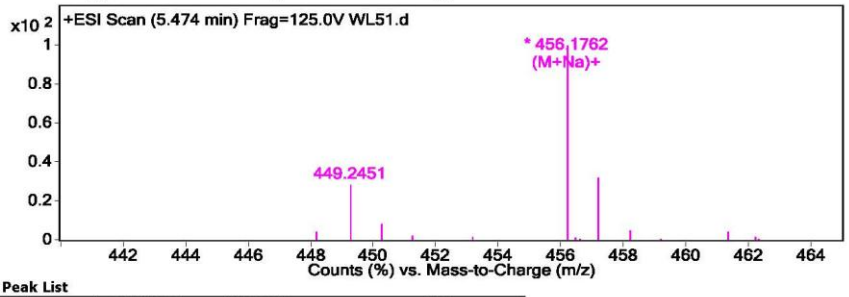
Figure S111. (+) HR-ESIMS of **23**

Qualitative Analysis Report

Data Filename	WL51.d	**Sample Name**	WL51
Sample Type	Sample	**Position**	P1-C7
Instrument Name	Instrument 1	**User Name**	
Acq Method	general test 2.m	**Acquired Time**	12/19/2013 4:17:12 PM
IRM Calibration Status	Some Ions Missed	**DA Method**	Screening-Default.m
Comment			

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
125	0	Esi



Peak List

m/z	z	Abund	Formula	Ion
456.1762	1	1127283	C26 H27 N Na O5	(M+Na)+

Formula Calculator Element Limits

Element	Min	Max
C	3	60
H	0	120
O	0	30
N	0	1
S	0	0
Cl	0	0
Br	0	0
Si	0	0

Formula Calculator Results

Formula	Best	Mass	Tgt Mass	Diff (ppm)	Ion Species	Score
C26 H27 N O5	TRUE	433.187	433.1889	4.55	C26 H27 N Na O5	89.53
C33 H23 N		433.187	433.183	-9.01	C33 H23 N Na	72.57

--- End Of Report ---

Figure S112. ^{1}H NMR spectrum of **24** in $CDCl_3$

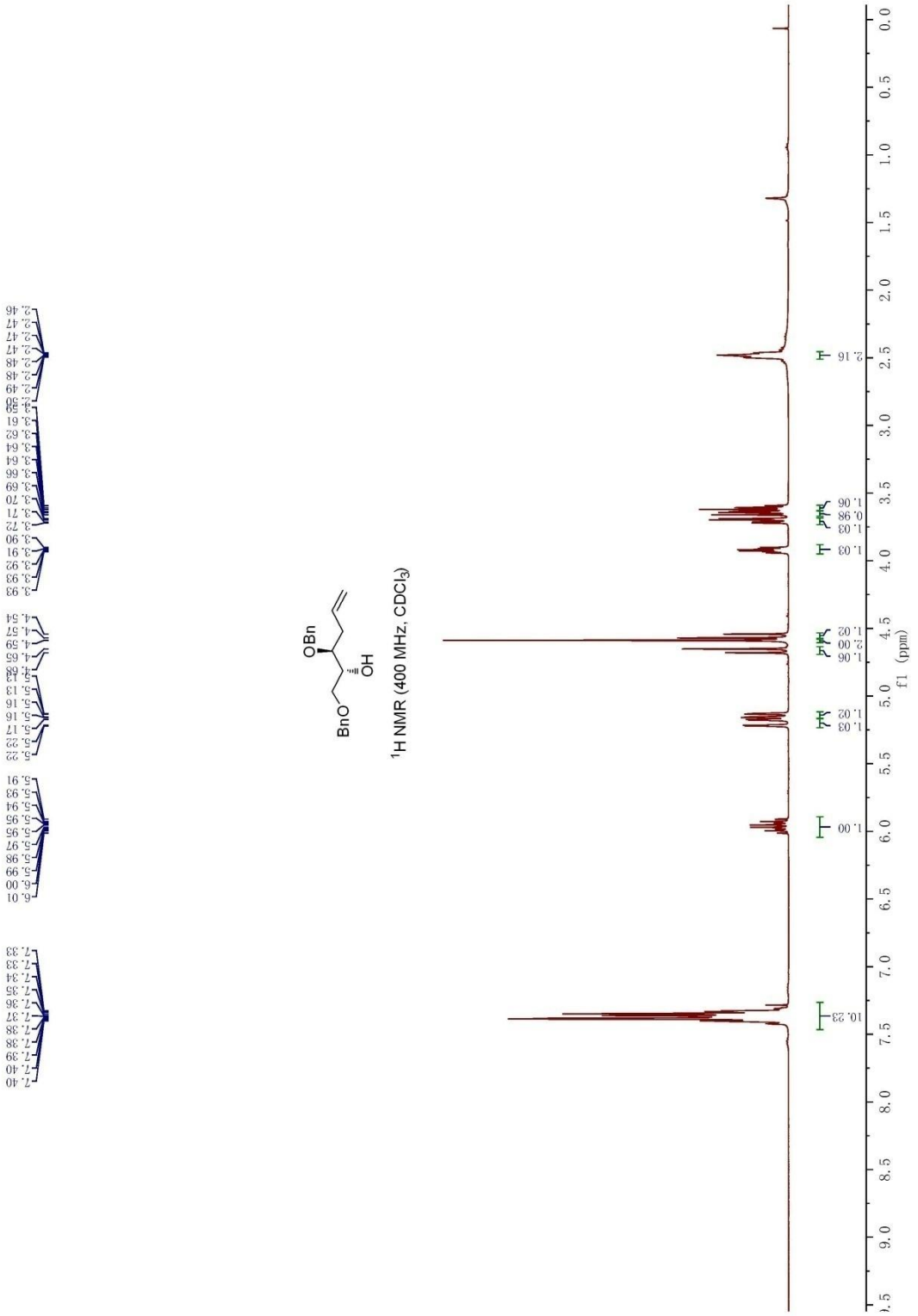


Figure S113. ^{13}C NMR spectrum of **24** in $CDCl_3$

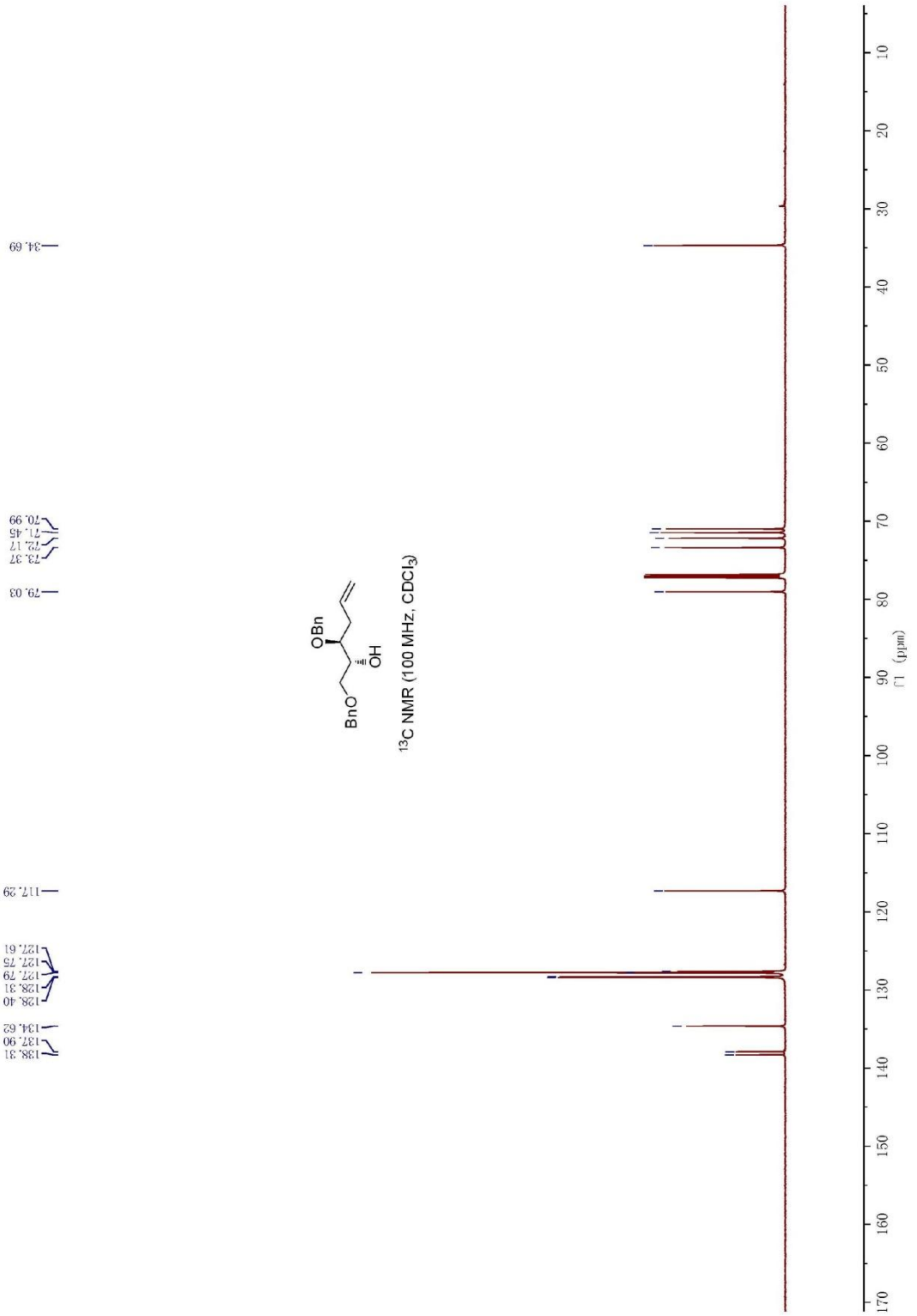


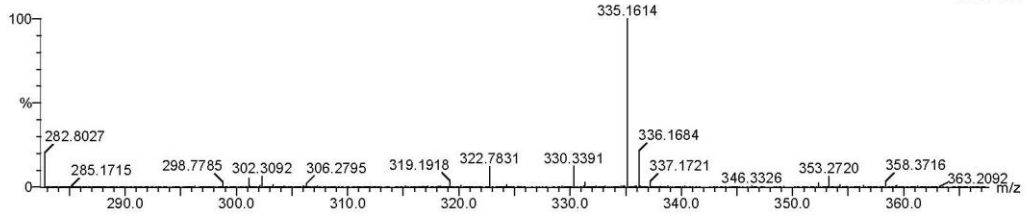
Figure S114. (+) HR-ESIMS of **24**

Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 500.0 mDa / DBE: min = -1.5, max = 500.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 9

Monoisotopic Mass, Even Electron Ions
1 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 10-20 H: 15-25 O: 1-3 Na: 1-1
10:43:30
WL-66A 136 (5.978)

1: TOF MS ES+
1.82e+004



Minimum:				-1.5			
Maximum:		500.0	1000.0	500.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
335.1614	335.1623	-0.9	-2.7	8.5	305.1	0.0	C20 H24 O3 Na

Figure S115. ^{1}H NMR spectrum of **25** in $CDCl_3$

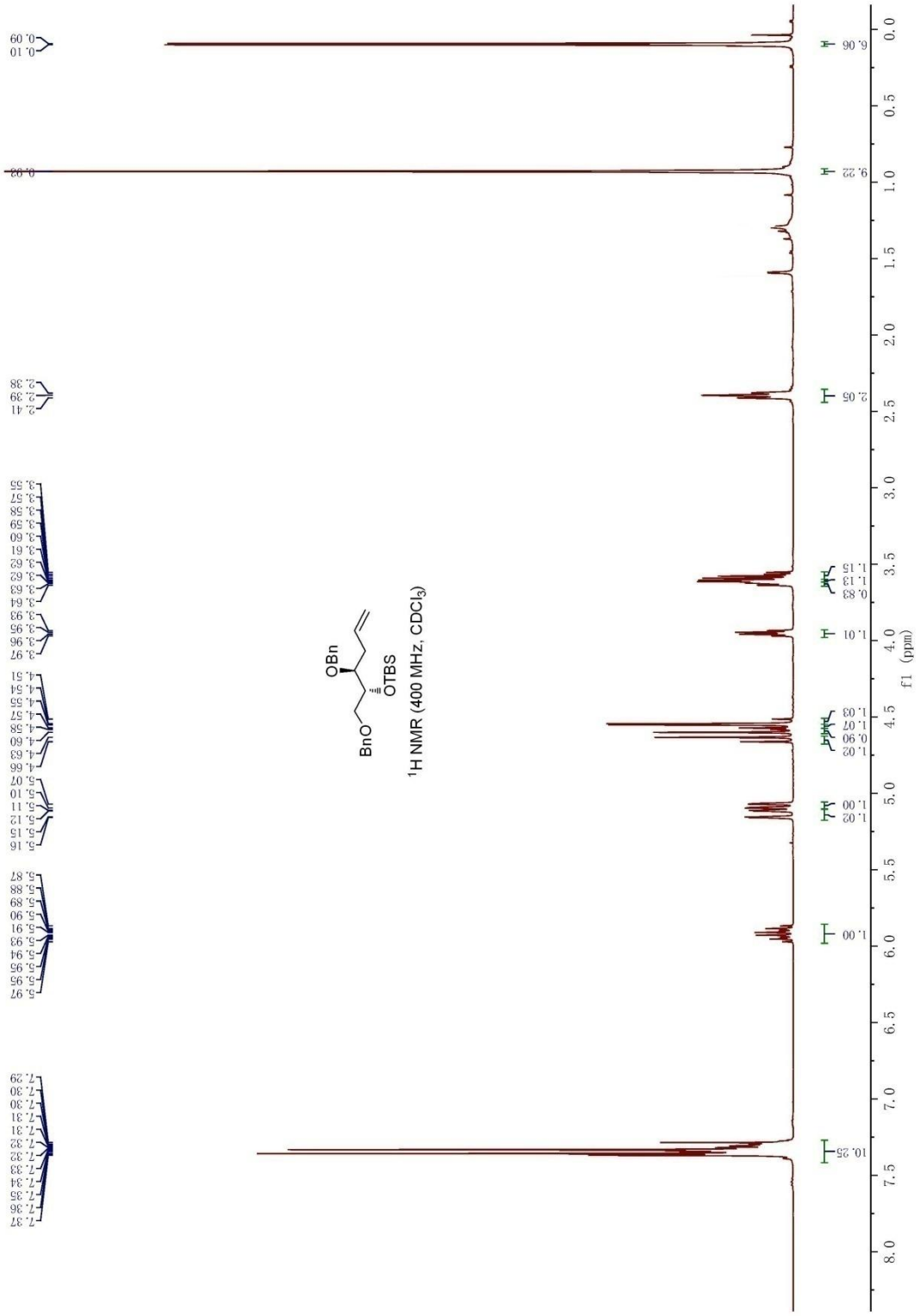


Figure S116. ^{13}C NMR spectrum of **25** in $CDCl_3$

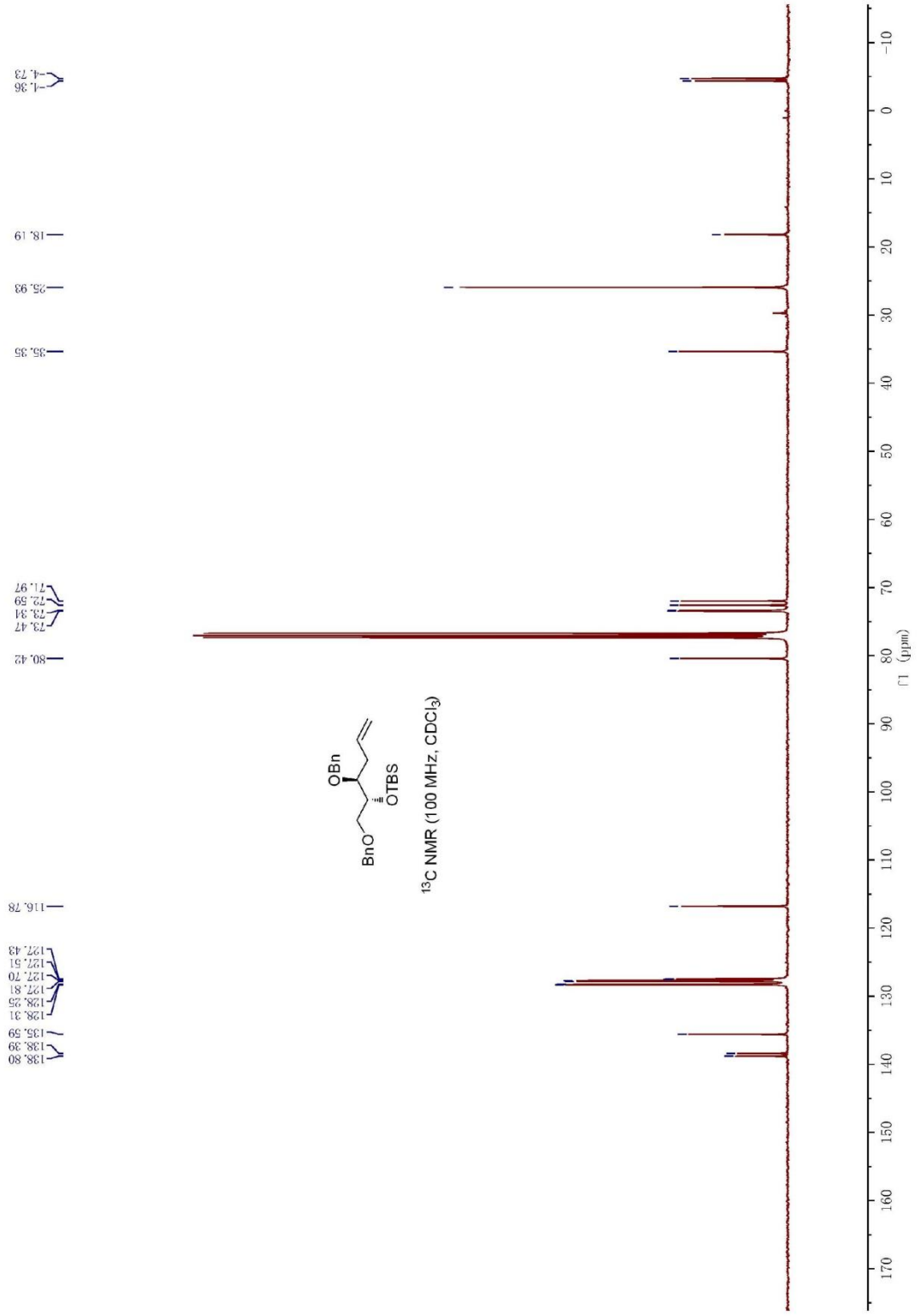


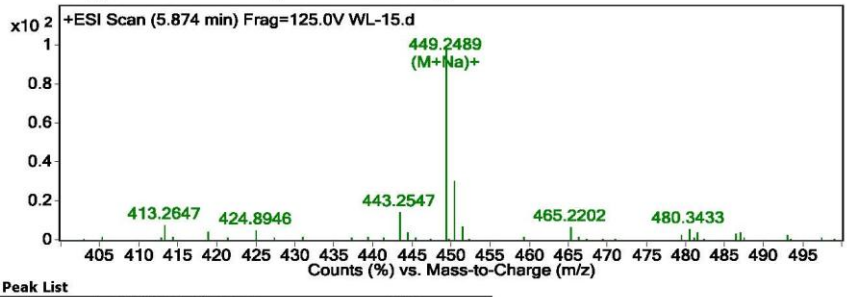
Figure S117. (+) HR-ESIMS of **25**

Qualitative Analysis Report

Data Filename	WL-15.d	**Sample Name**	WL-15
Sample Type	Sample	**Position**	P1-A6
Instrument Name	Instrument 1	**User Name**	
Acq Method	general test 2.m	**Acquired Time**	12/27/2013 2:04:17 PM
IRM Calibration Status	Some Ions Missed	**DA Method**	Screening-Default.m
Comment			

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
125	0	Esi



Peak List

m/z	z	Abund	Formula	Ion
449.2489	1	614749	C26 H38 Na O3 Si	(M+Na)+

Formula Calculator Element Limits

Element	Min	Max
C	3	100
H	0	300
O	0	5
N	0	0
S	0	0
Cl	0	0
Br	0	0
Si	0	1
I	0	1

Formula Calculator Results

Formula	Best	Mass	Tgt Mass	Diff (ppm)	Ion Species	Score
C26 H38 O3 Si	TRUE	426.2596	426.259	-1.43	C26 H38 Na O3 Si	95.75
C30 H34 O2		426.2596	426.2559	-8.76	C30 H34 Na O2	65.6

--- End Of Report ---

Agilent Technologies Page 1 of 1 Printed at: 4:15 PM on: 12/27/2013

Figure S118. ^{1}H NMR spectrum of **26** in $CDCl_3$

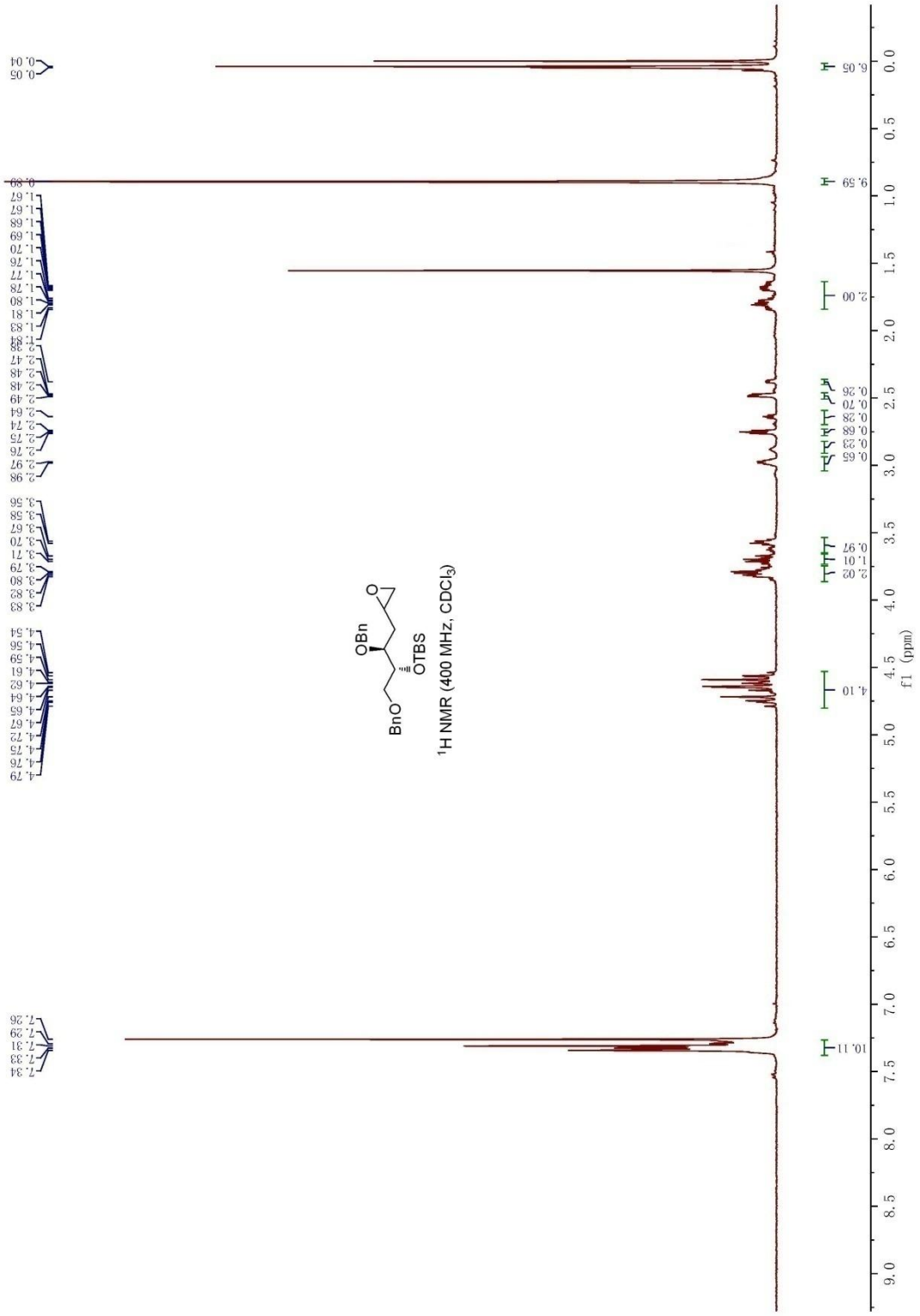


Figure S119. ^{13}C NMR spectrum of **26** in $CDCl_3$

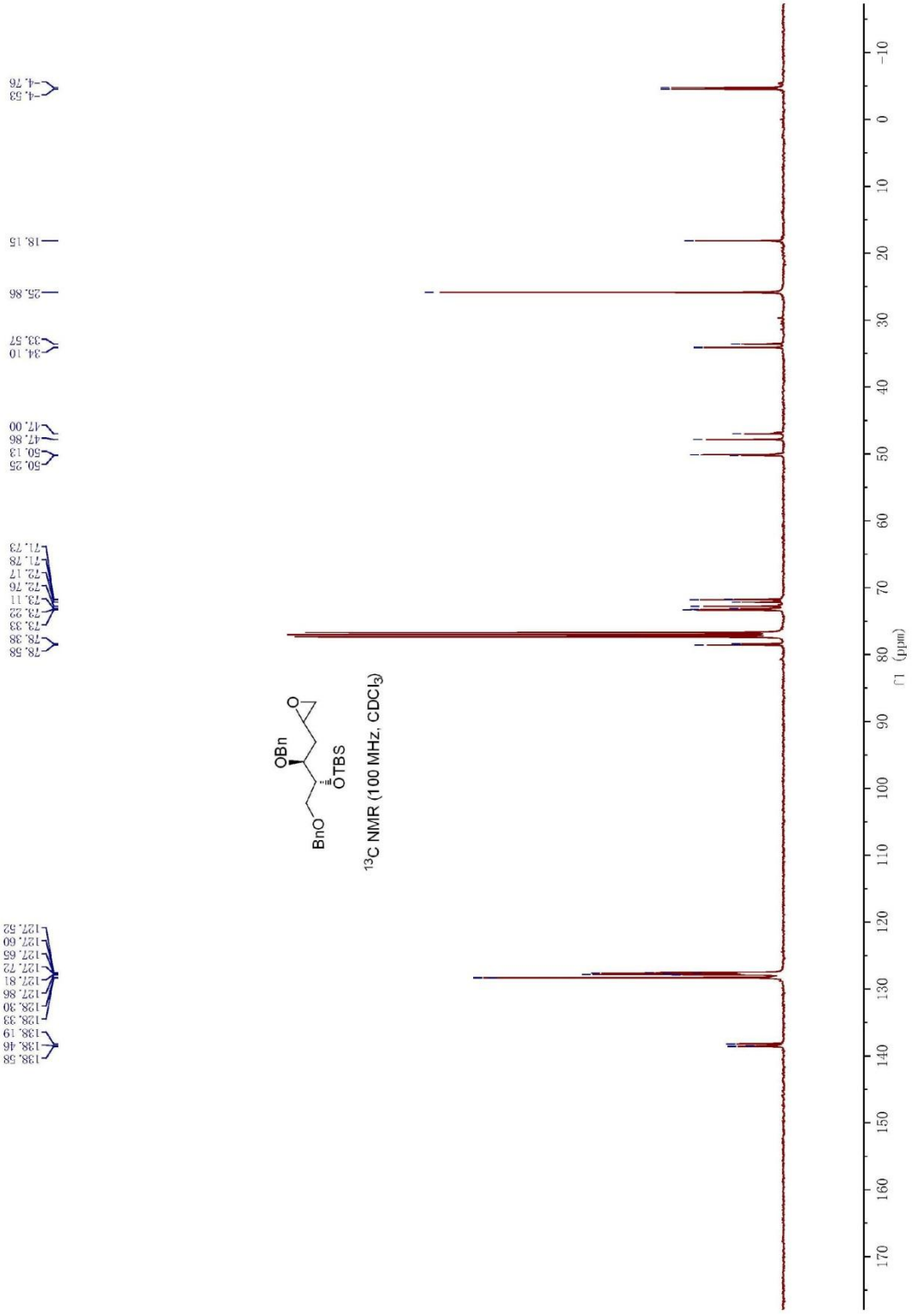


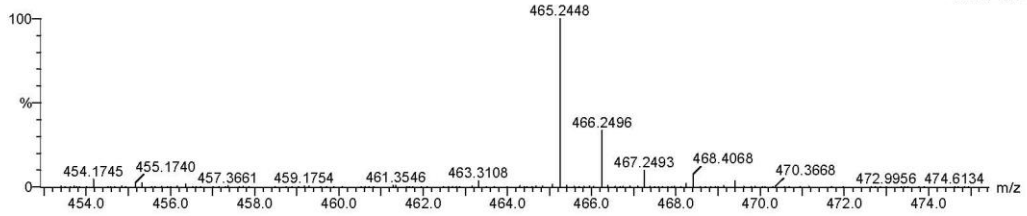
Figure S120. (+) HR-ESIMS of **26**

Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 1000.0 PPM / DBE: min = -1.5, max = 500.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 9

Monoisotopic Mass, Even Electron Ions
1 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 26-26 H: 35-40 O: 4-4 Na: 1-1 Si: 1-1
10:02:46
WL-16A 18 (0.806)

1: TOF MS ES+
3.49e+003



Minimum:				-1.5			
Maximum:		500.0	1000.0	500.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
465.2448	465.2437	1.1	2.4	8.5	218.3	0.0	C26 H38 O4 Na Si

Figure S121. ^{1}H NMR spectrum of **27** in CD_3OD

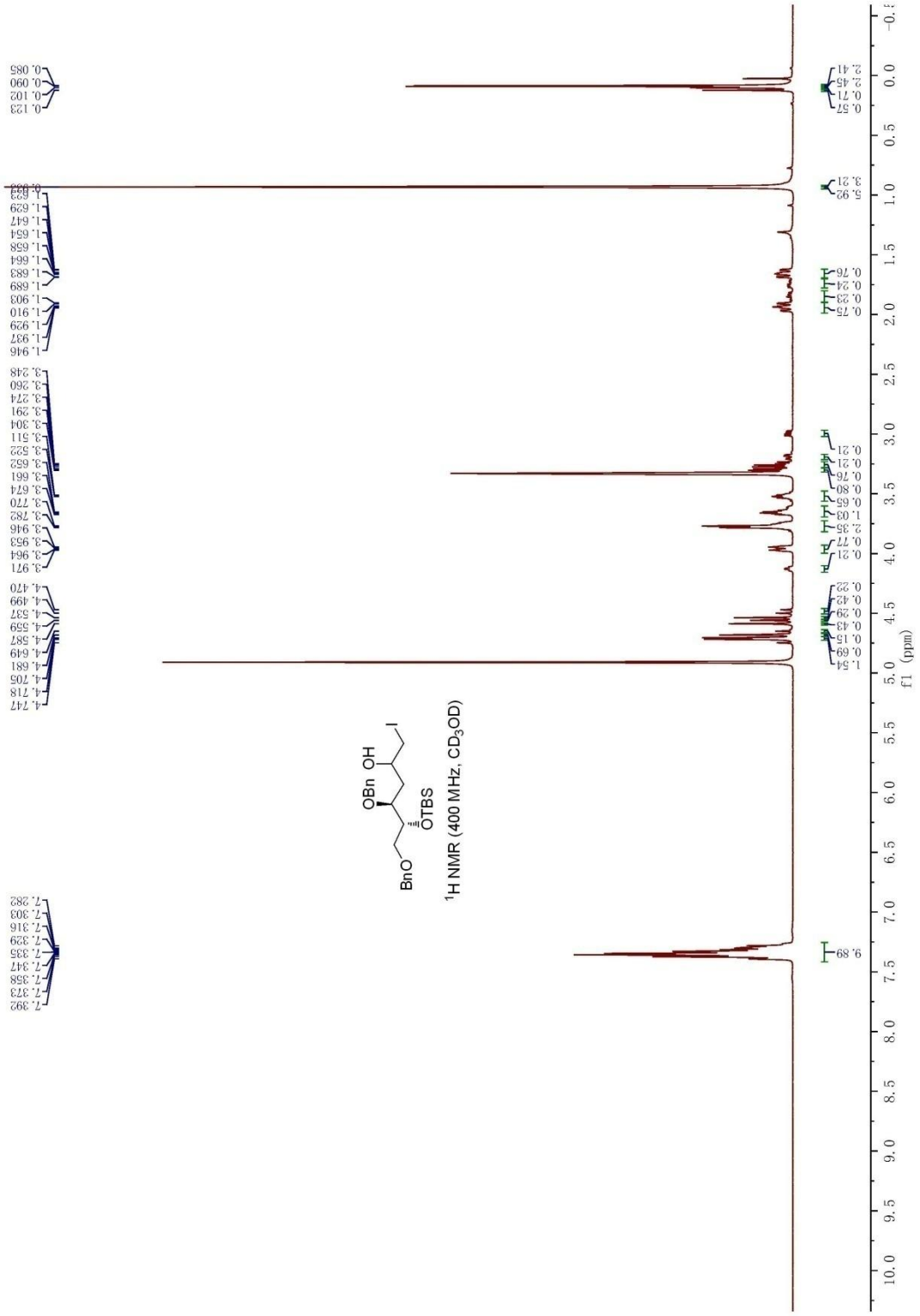


Figure S122. ^{13}C NMR spectrum of **27** in CD_3OD

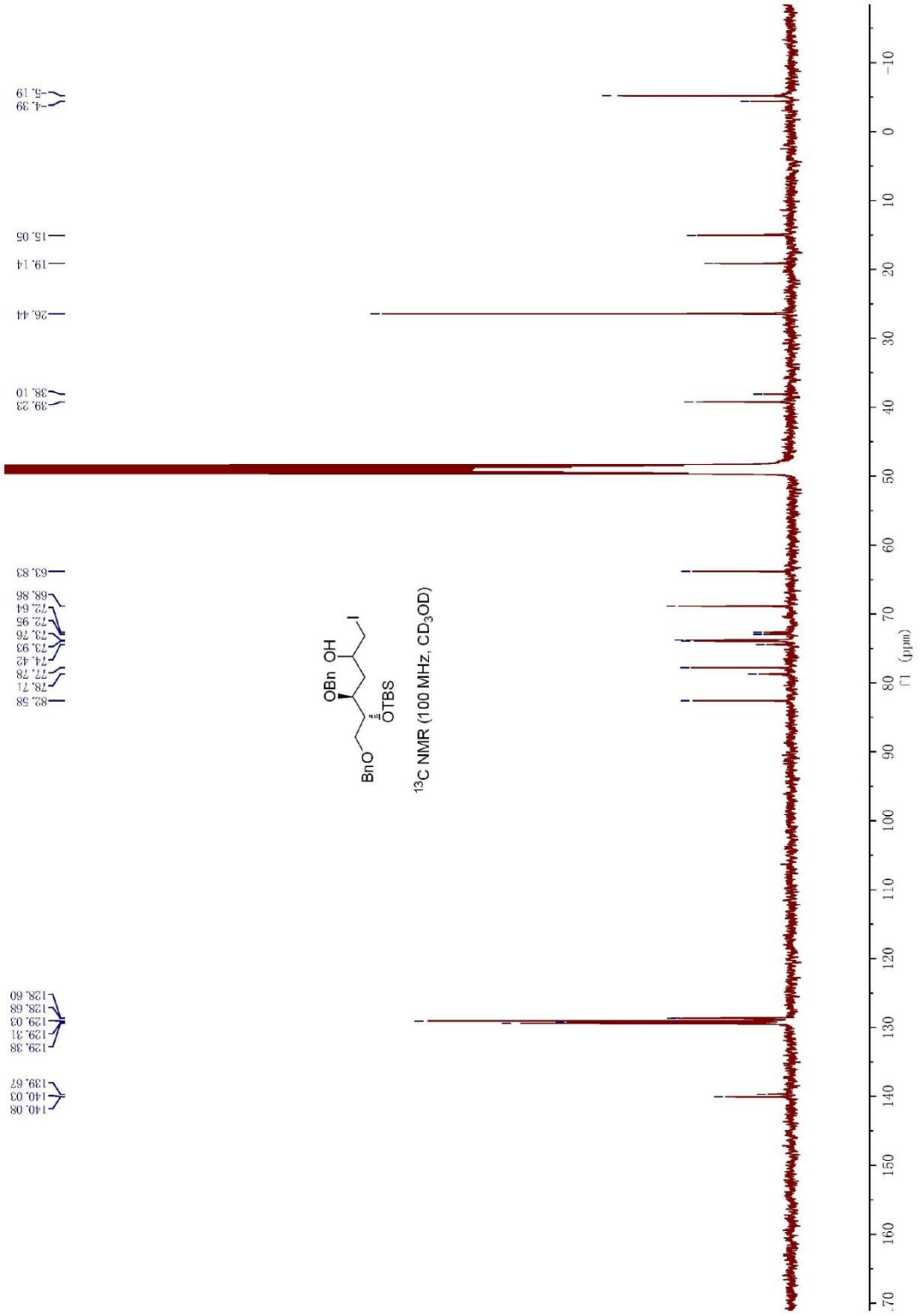


Figure S123. (+) HR-ESIMS of **27**

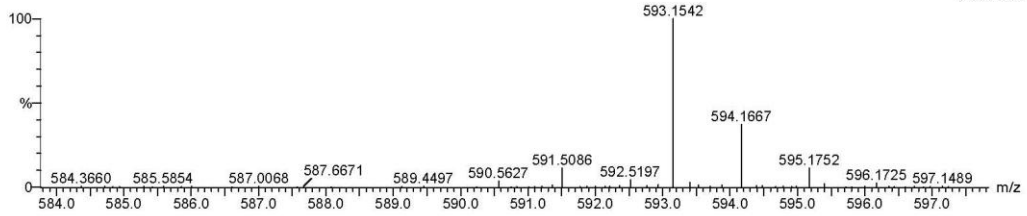
Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 1000.0 PPM / DBE: min = -1.5, max = 500.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 9

Monoisotopic Mass, Even Electron Ions
2 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 26-26 H: 35-40 O: 4-4 Na: 1-1 Si: 1-1 I: 0-1

15:28:17
WL-29A 144 (6.329)

1: TOF MS ES+
4.04e+003



Minimum:				-1.5			
Maximum:		500.0	1000.0	500.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
593.1542	593.1560	-1.8	-3.0	7.5	127.9	0.0	C26 H39 O4 Na Si I

Figure S124. ^{1}H NMR spectrum of **28** in CD_3OD

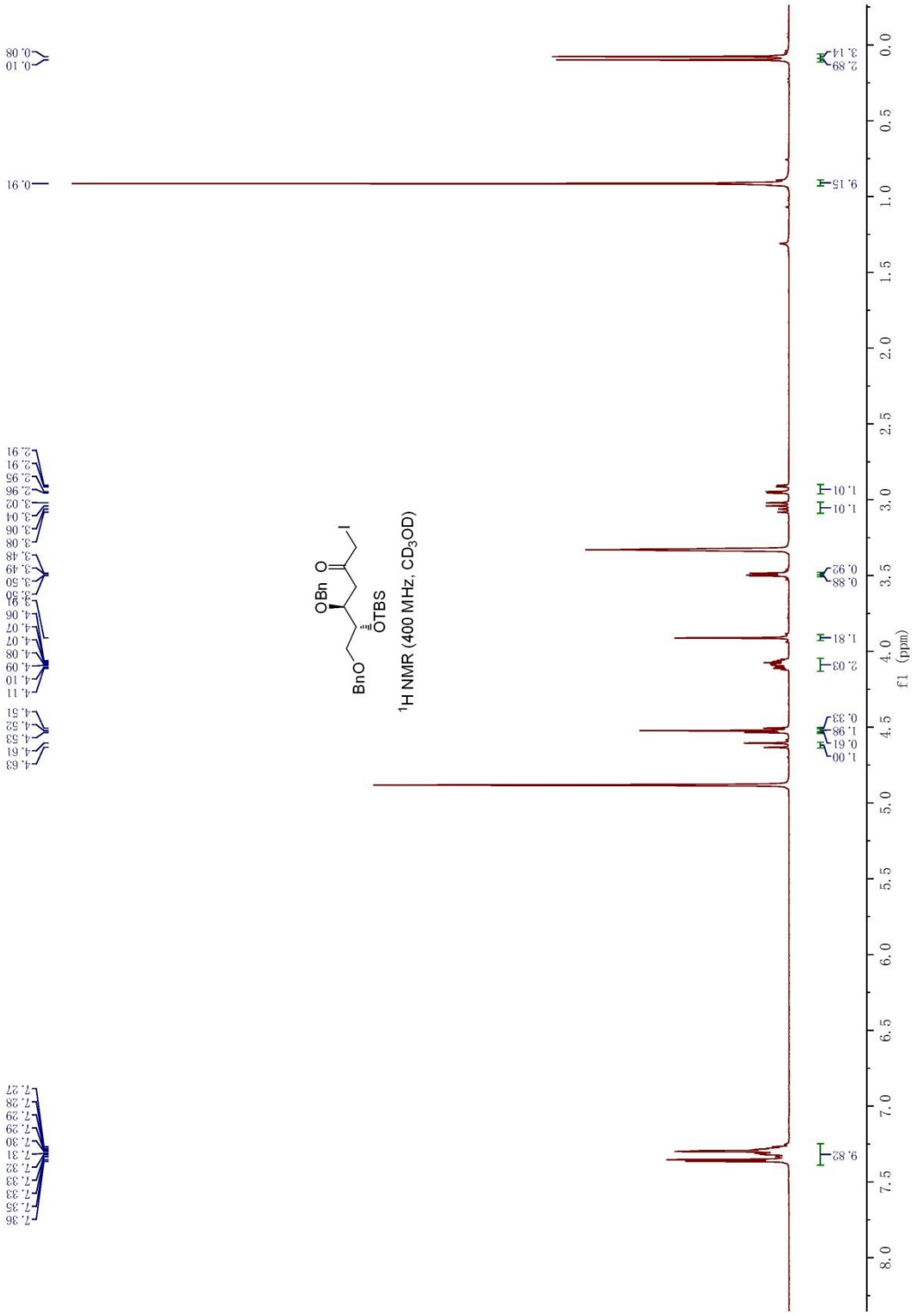


Figure S125. ^{13}C NMR spectrum of **28** in CD_3OD

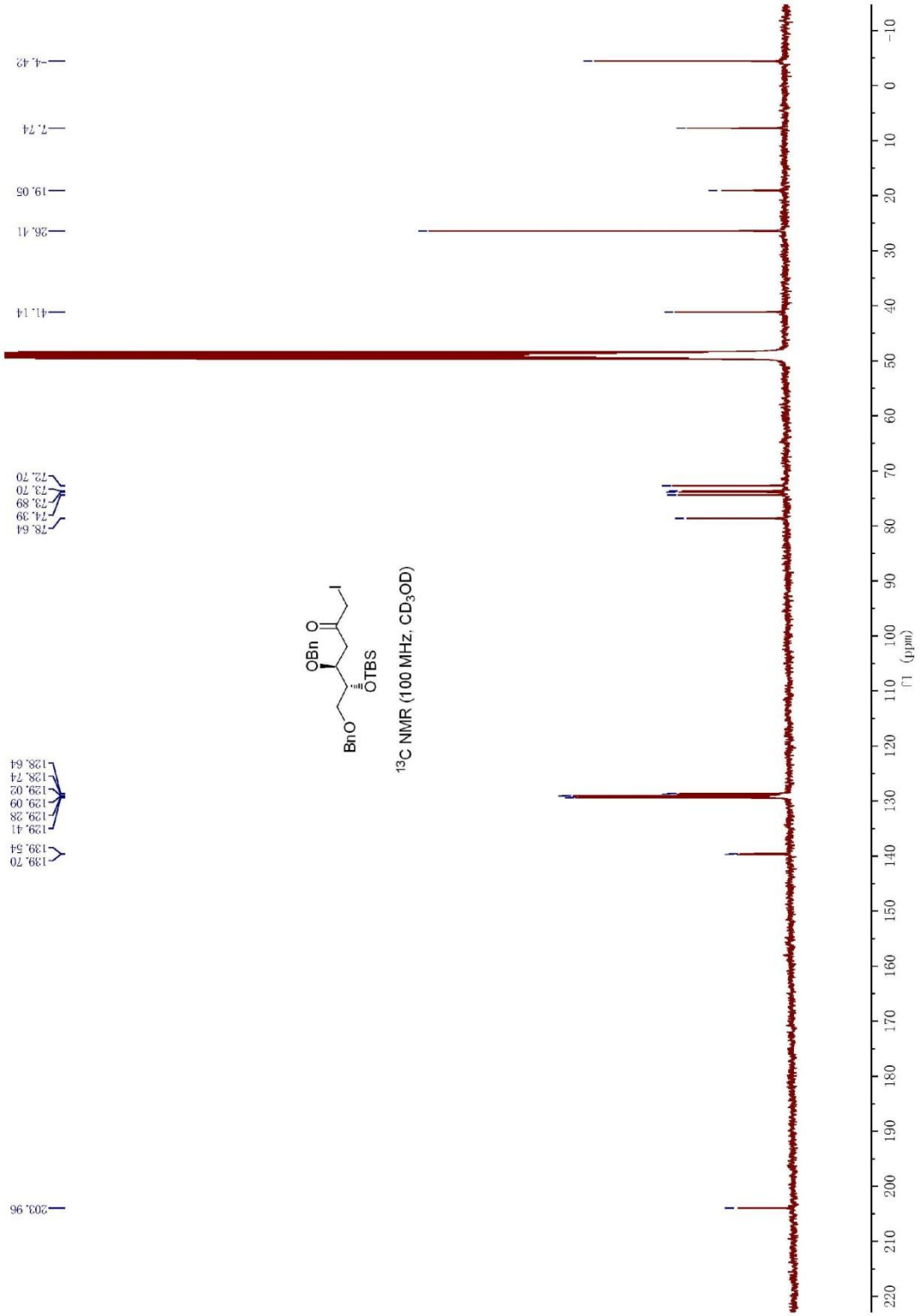


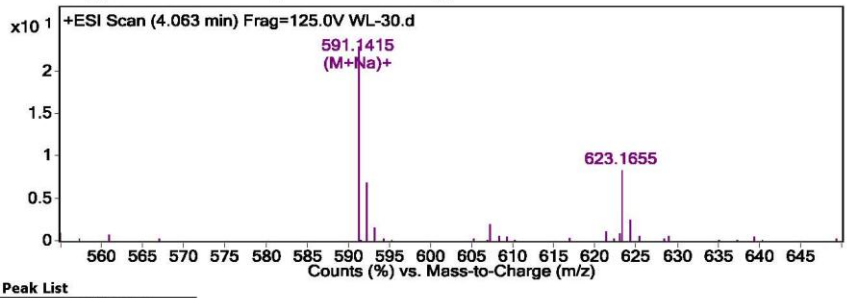
Figure S126. (+) HR-ESIMS of **28**

Qualitative Analysis Report

Data Filename	WL-30.d	**Sample Name**	WL-30
Sample Type	Sample	**Position**	P1-A7
Instrument Name	Instrument 1	**User Name**	
Acq Method	general test 2.m	**Acquired Time**	12/27/2013 2:14:05 PM
IRM Calibration Status	Some Ions Missed	**DA Method**	Screening-Default.m
Comment			

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
125	0	Esi



Peak List

m/z	z	Abund
465.245	1	1732240

Formula Calculator Element Limits

Element	Min	Max
C	3	100
H	0	300
O	0	5
N	0	0
S	0	0
Cl	0	0
Br	0	0
Si	0	1
I	0	1

Formula Calculator Results

Formula	Best	Mass	Tgt Mass	Diff (ppm)	Ion Species	Score
C26 H37 I O4 Si	TRUE	568.1523	568.1506	-2.99	C26 H37 I Na O4 Si	91.32
C39 H24 O3 Si		568.1523	568.1495	-4.93	C39 H24 Na O3 Si	65.62
C30 H33 I O3		568.1523	568.1474	-8.49	C30 H33 I Na O3	62.82

--- End Of Report ---

Figure S127. ^{1}H NMR spectrum of **29** in CD_3OD

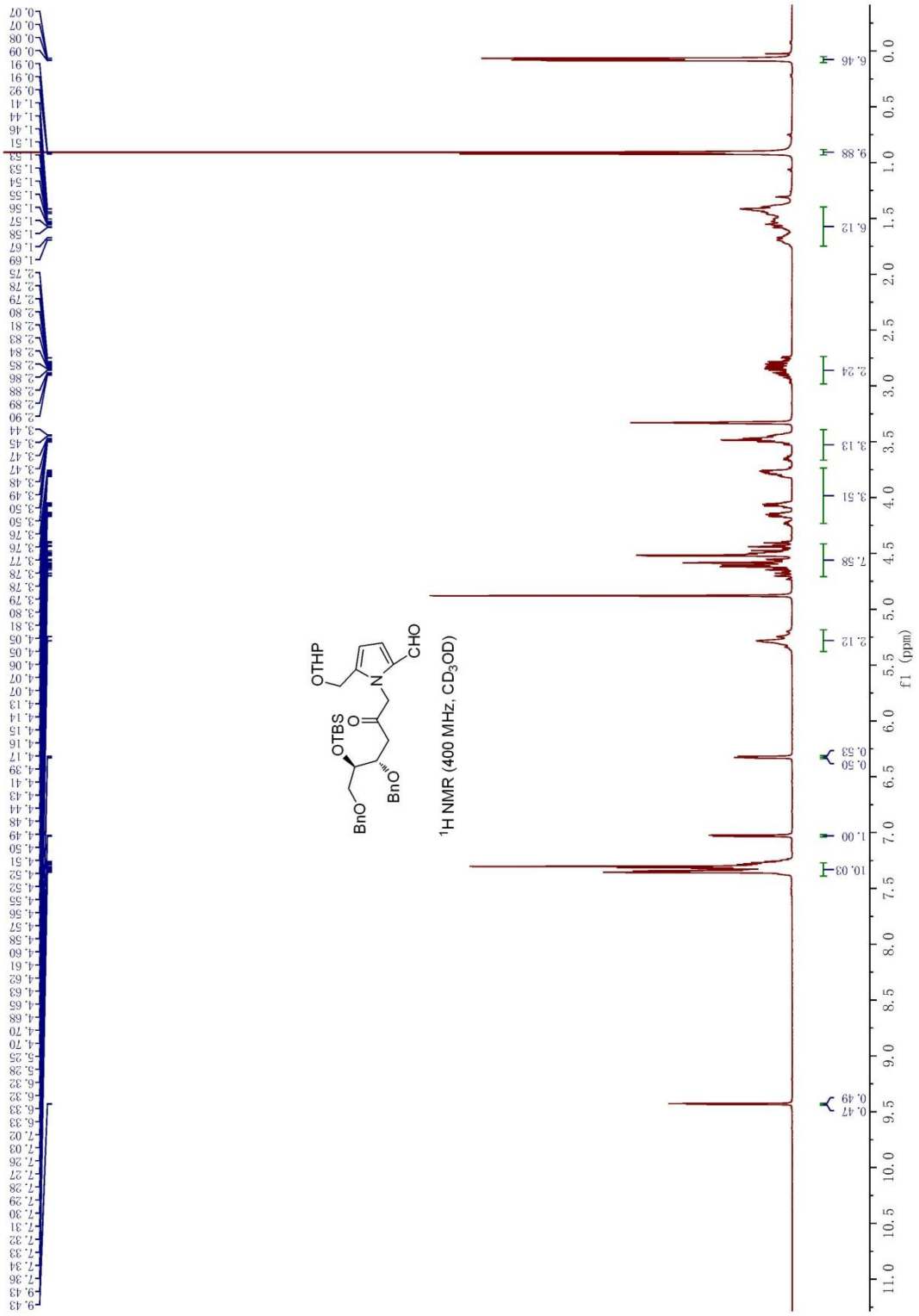


Figure S128. ^{13}C NMR spectrum of **29** in CD_3OD

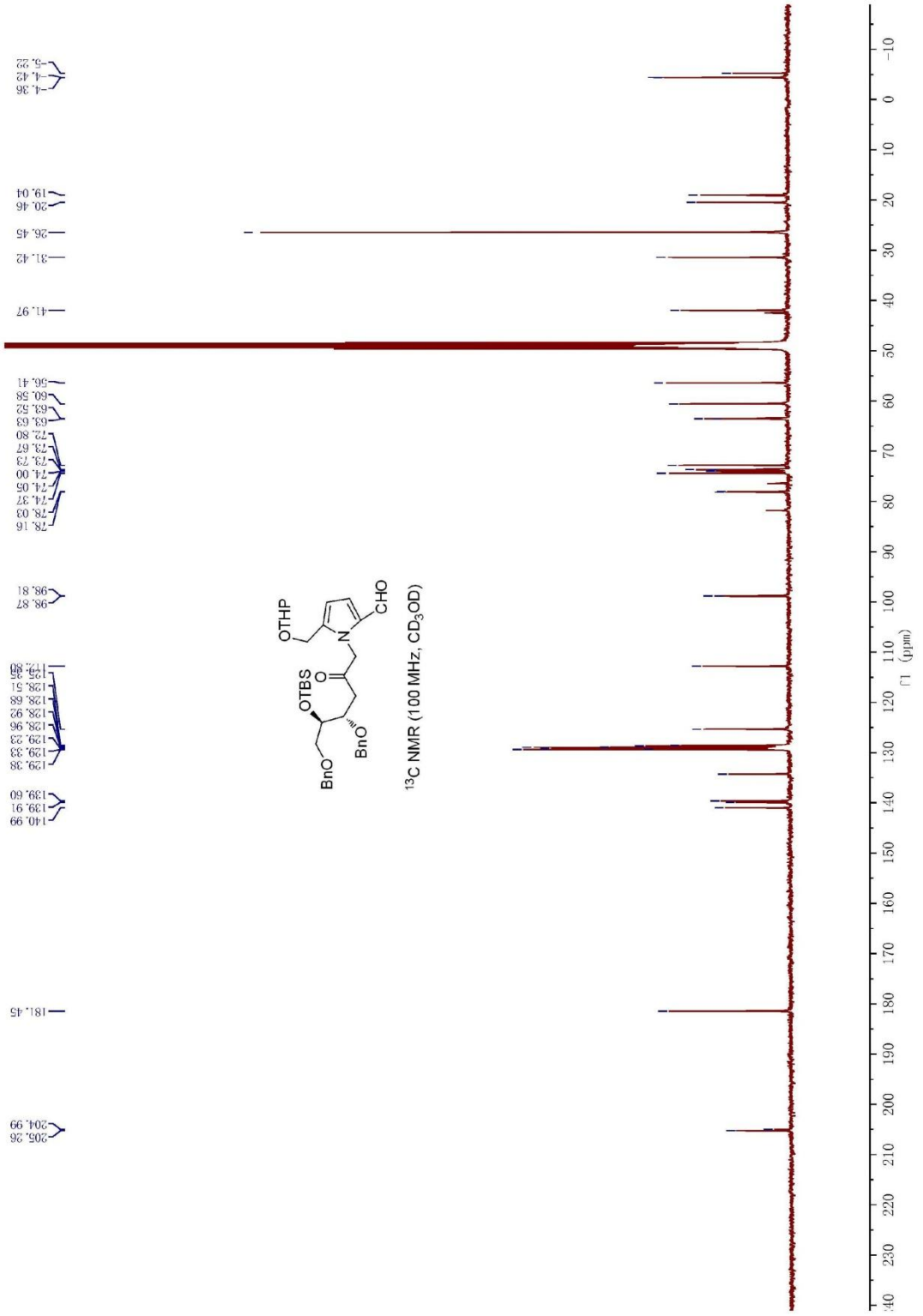


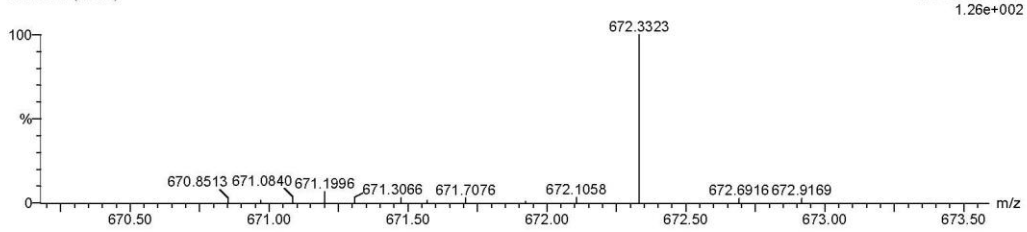
Figure S129. (+) HR-ESIMS of **29**

Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 1000.0 PPM / DBE: min = -1.5, max = 500.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 9

Monoisotopic Mass, Even Electron Ions
1 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 26-37 H: 35-52 N: 1-1 O: 4-7 Na: 1-1 Si: 1-1
09:50:53
WL-20 97 (4.278)

1: TOF MS ES+
1.26e+002



Minimum:				-1.5			
Maximum:		500.0	1000.0	500.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
672.3323	672.3333	-1.0	-1.5	13.5	35.9	0.0	C37 H51 N O7 Na Si

Figure S130. ^{1}H NMR spectrum of **30** in $CDCl_3$

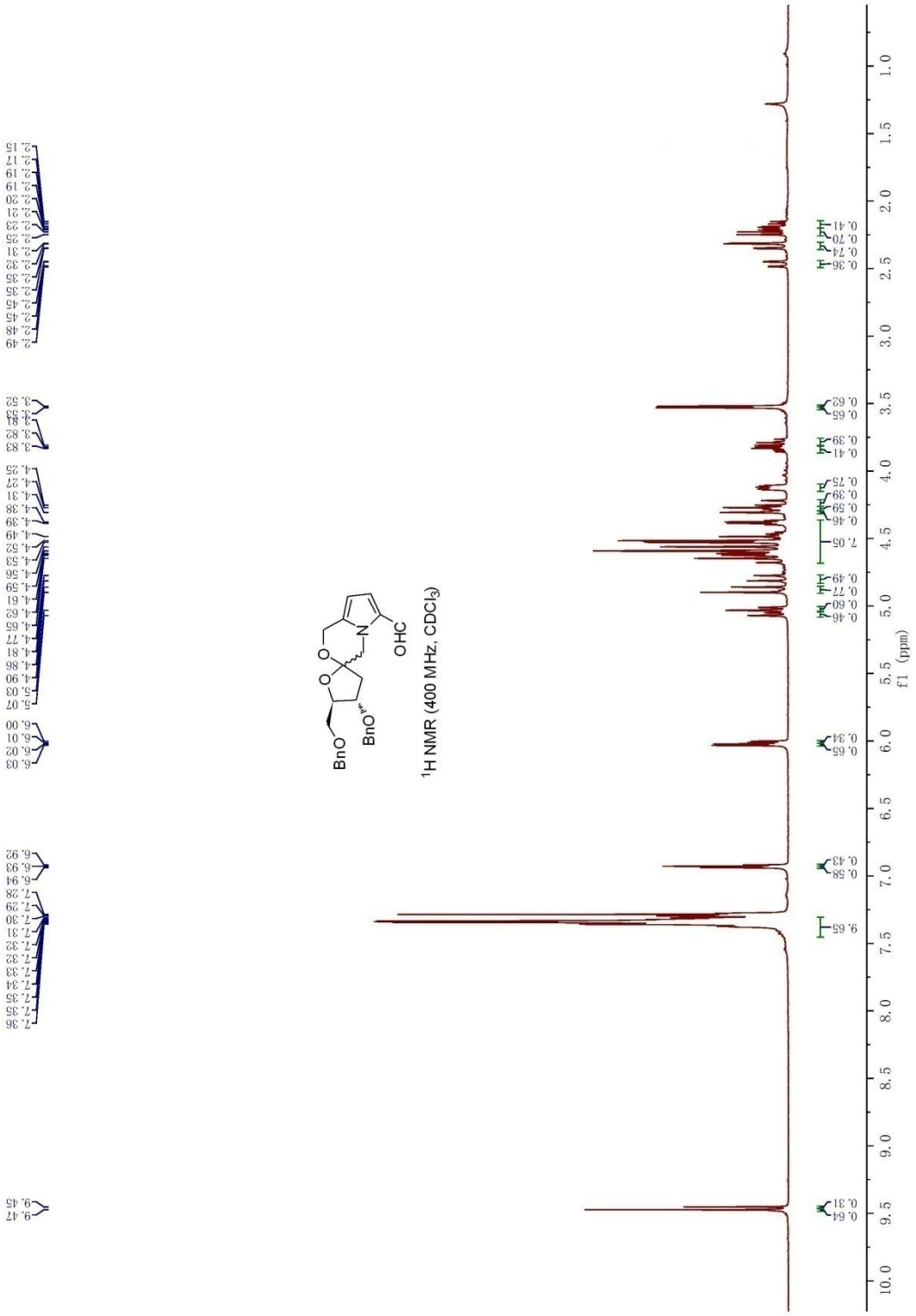


Figure S131. ^{13}C NMR spectrum of **30** in $CDCl_3$

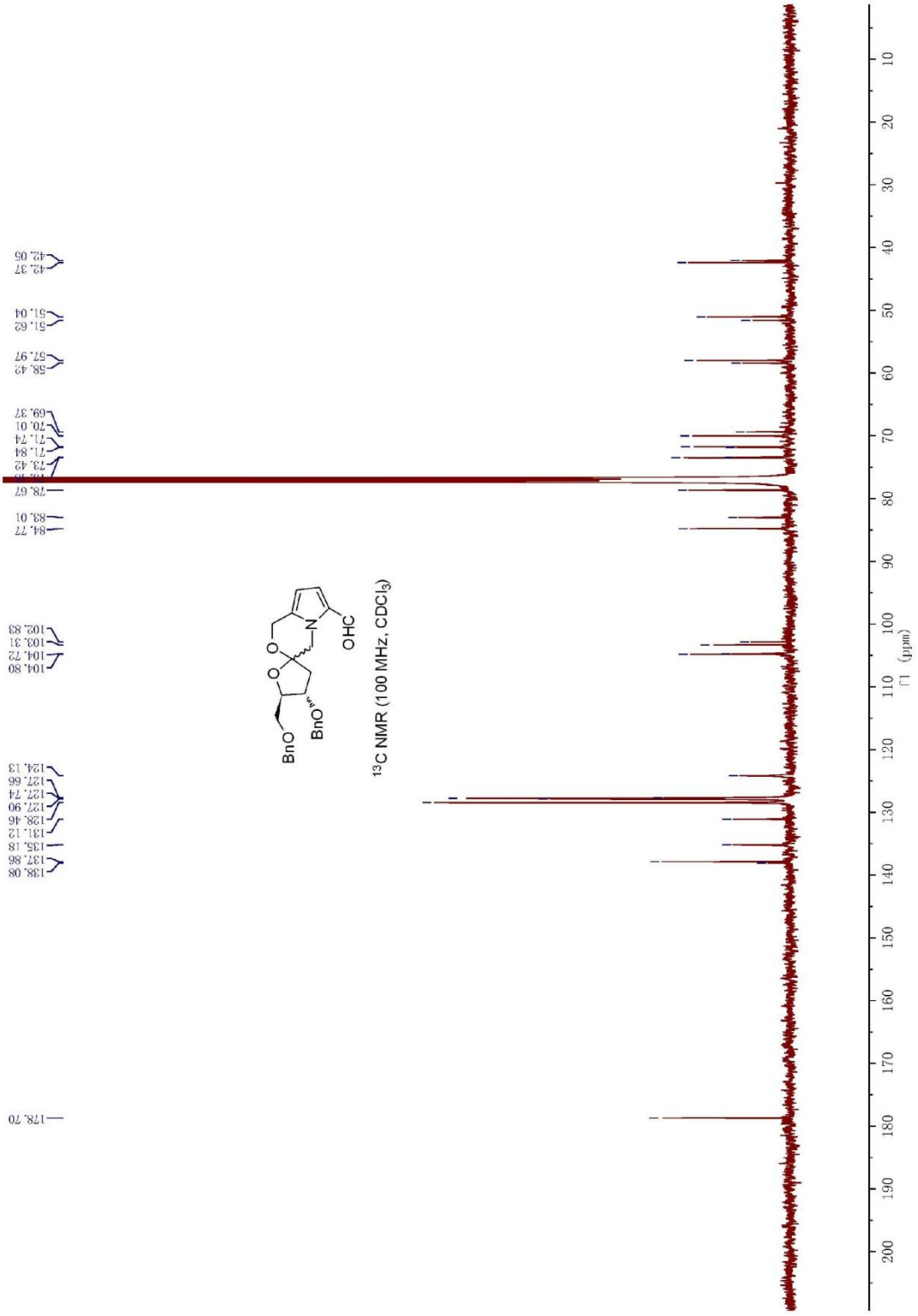


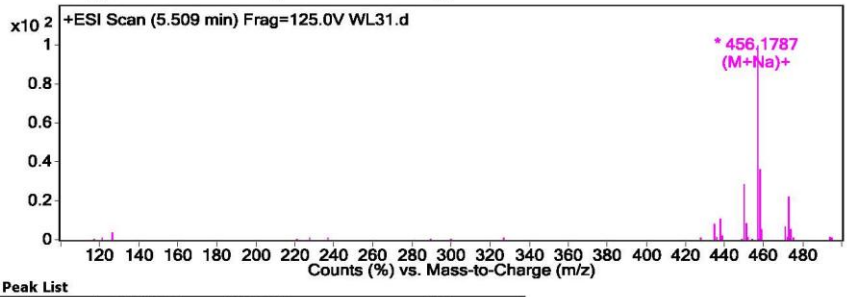
Figure S132. (+) HR-ESIMS of **30**

Qualitative Analysis Report

Data Filename	WL31.d	**Sample Name**	WL31
Sample Type	Sample	**Position**	P1-C5
Instrument Name	Instrument 1	**User Name**	
Acq Method	general test 2.m	**Acquired Time**	12/19/2013 4:01:33 PM
IRM Calibration Status	Some Ions Missed	**DA Method**	Screening-Default.m
Comment			

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
125	0	Esi



Peak List

m/z	z	Abund	Formula	Ion
456.1787	1	2304362	C26 H27 N Na O5	(M+Na)+

Formula Calculator Element Limits

Element	Min	Max
C	3	60
H	0	120
O	0	30
N	0	1
S	0	0
Cl	0	0
Br	0	0
Si	0	0

Formula Calculator Results

Formula	Best	Mass	Tgt Mass	Diff (ppm)	Ion Species	Score
C26 H27 N O5	TRUE	433.1894	433.1889	-1.2	C26 H27 N Na O5	89.29

--- End Of Report ---