Accepted Manuscript

Chiral 1-(1,3-Dithian-2-yl) prop-2-en-1-ols: New Scaffolds for Enantiopure α-Hydroxyaldehydes

Masaru Akehi, Mariko Kawamoto, Tadakatsu Mandai

PII: S0040-4020(15)00697-3

DOI: 10.1016/j.tet.2015.05.039

Reference: TET 26757

To appear in: *Tetrahedron*

Received Date: 20 April 2015

Revised Date: 8 May 2015

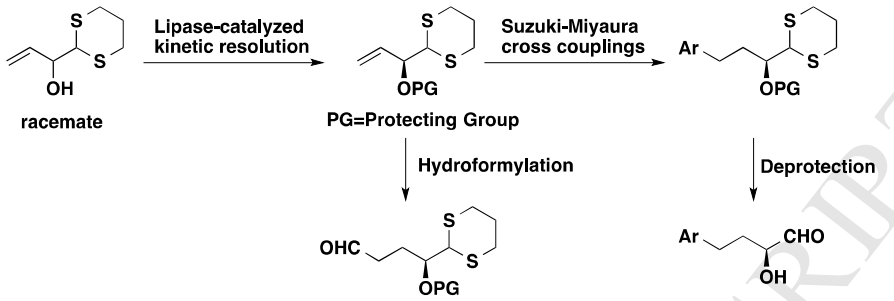
Accepted Date: 11 May 2015

Please cite this article as: Akehi M, Kawamoto M, Mandai T, Chiral 1-(1,3-Dithian-2-yl) prop-2-en-1-ols: New Scaffolds for Enantiopure α-Hydroxyaldehydes, *Tetrahedron* (2015), doi: 10.1016/j.tet.2015.05.039.

Abstract

We have demonstrated that chiral 1-(1,3-dithian-2-yl)prop-2-en-1-ols as new scaffolds, obtained by enzyme-catalyzed kinetic resolution, undergo Suzuki-Miyaura cross-couplings and hydroformylation smoothly. Also, we have found that a 1,3-dithianyl group of the products can be removed without any erosion of the enantiopurity under mild conditions. A new access to a variety of enantiopure α-hydroxyaldehydes with ensured absolute configuration is described.

Graphical abstract



Chiral 1-(1,3-Dithian-2-yl) prop-2-en-1-ols: New Scaffolds for Enantiopure α-Hydroxyaldehydes

Masaru Akehi, Mariko Kawamoto, Tadakatsu Mandai*

Department of Life Science, Kurashiki University of Science & the Arts

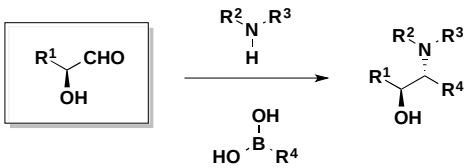
2640 Nishinoura, Tsurajima, Kurashiki 712-8505, Japan

Tel: +81(86)4401080; Fax: +81(86)4401062; E-mail: ted@chem.kusa.ac.jp

Keywords: Scaffold; α-Hydroxyaldehyde; Suzuki-Miyaura cross-coupling; Hydroformylation; 1,3-Dipolar cycloaddition.

1. Introduction

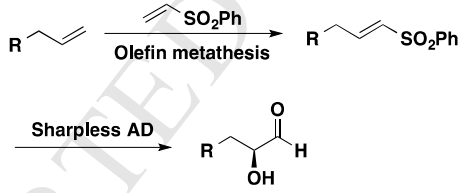
Much attention has been paid to the Petasis protocol,[1] which affords an array of β-amino alcohols in a single step involving a three component coupling reaction of α-hydroxyaldehydes, amines, and organoboronic acids (Scheme 1). The reaction proceeds in a highly diastereoselective manner to exclusively furnish *anti* β-amino alcohols, and hence generally provides single enantiomers (>98% ee) when enantiopure α-hydroxyaldehydes are engaged.



Scheme 1. Petasis protocol.

Regardless of its high potential utility in organic synthesis, the Petasis protocol has found somewhat limited use because enantiopure α-hydroxyaldehydes are not easily available. Several approaches to these valuable intermediates reported to date are based on the derivatization of natural sources. For example, chiral 2,3-dihydroxy-4-butenals were prepared from D-xylose and D-ribose,[2a] and α-hydroxyesters derived from the corresponding natural α-amino acids were converted to α-hydroxyaldehydes via protection of the hydroxyl group followed by ester reduction using DIBAL-H.[2b] The stereogenic centers of products obtained by these approaches are derived directly from the starting materials. Furthermore, chiral 2-hydroxyaldehydes have been obtained via enzyme-mediated kinetic resolution of the 2-hydroxyaldehyde racemate. [2c] In addition, asymmetric synthesis[3] using chiral templates is a powerful and flexible approach for obtaining higher homologs bearing a longer carbon chains, although strict temperature control may be required to obtain a high degree of enantiomeric purity.

Asymmetric dihydroxylation (AD) of 2-alkenyl acetals generating 2,3-dihydroxyaldehydes[4] is of special interest as it provides a more direct approach to α-hydroxyaldehydes through AD of 2-alkenylsulfones (Scheme 2).[5]



Scheme 2. Synthesis of α-hydroxyaldehydes via asymmetric dihydroxylation (AD).

Although these AD methods require great care in the preparation of the starting materials, they hold promise as reliable strategies because the absolute configuration of the products can easily be predicted.

Broadening the synthetic utility of α-hydroxyaldehydes requires the development of a new synthetic method ensuring both high enantiopurity and absolute configuration. We thus devised 1-(1,3-dithian-2-yl) prop-2-en-1-ol (±)-**1** as a scaffold for this purpose, and designed a new strategy leading to a variety of α-hydroxyaldehydes mentioned above. This strategy involves the combination of an enzyme-catalyzed reaction of racemic (±)-**1**[6] and transition metal-catalyzed reactions such as Suzuki-Miyaura cross-coupling[7] or hydroformylation (Figure 1).[8] We were

confident that these metal-catalyzed reactions would proceed well with (±)-**1** on the basis of encouraging reports using substrates containing the 1,3-dithianyl group[9] suggesting that the coordinative 1,3-dithianyl group did not interrupt catalytic cycles mediated by a zero-valent metal species.

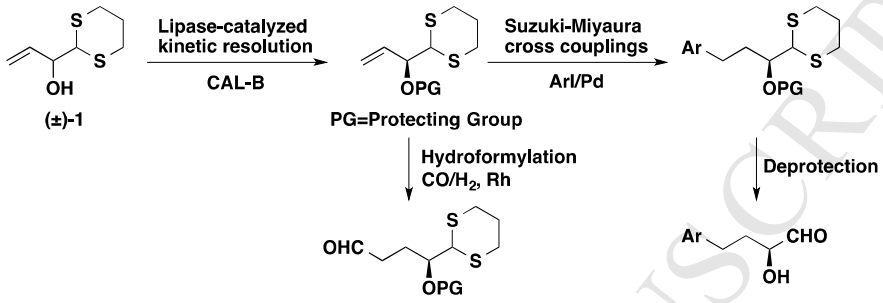
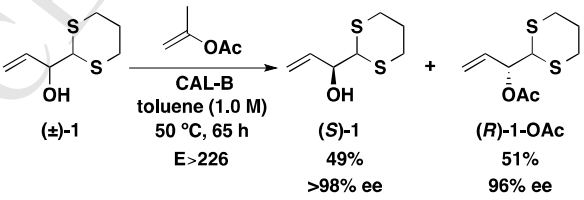


Figure 1. Synthetic design of α-hydroxyaldehydes and its precursors.

2. Results and discussion

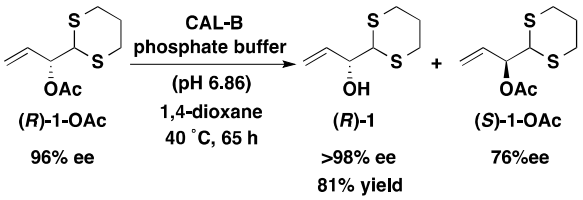
We first investigated into lipase-catalyzed kinetic resolution[10] of (±)-**1** in an organic solvent (Scheme 3). By simply stirring a solution of (±)-**1** and 2-propenyl acetate (2 equiv.) in toluene in the presence of dried CAL-B [11] [20 mg per 1 mmol of (±)-**1**] at 50 °C for 65 h, one enantiomer was predominantly acetylated with excellent enantioselectivity (E>226). Separation by column chromatography gave unreacted alcohol (*S*)-**1**[12] in 49% yield (>98% ee) and the acetate of the enantiomer (*R*)-**1**-OAc[12] in 51% yield (96% ee). The absolute configuration of (*S*)-**1** was tentatively assigned on an empirical basis.[10]



Scheme 3. Lipase-catalyzed kinetic resolution of (±)-**1**.

To improve the enantiopurity of (*R*)-**1**, (*R*)-**1**-OAc was subjected to lipase-catalyzed hydrolysis (Scheme 4). Stirring a solution of (*R*)-**1**-OAc in dioxane/phosphate buffer (pH 6.86) with CAL-B [20 mg per 1 mmol of (*R*)-**1**-OAc] at 40 °C for 65 h provided (*R*)-**1** in 81% yield

(>98% ee)[13] after silica gel column chromatography.



Scheme 4. Lipase-catalyzed hydrolysis of (*R*)-**1**-OAc.

Enantiopure (*S*)-**1** (>98% ee) and (*R*)-**1** (>98% ee) thus obtained were smoothly converted to their *O*-protected derivatives, (*S*)-**2** and (*R*)-**2**, respectively, in good yield (Figure 2). For example, benzyl ether (*S*)-**2a** was prepared in 88% yield by treatment of (*S*)-**1** with NaH and benzyl chloride in dry THF/DMF at room temperature for 2 h. In addition, silyl ethers (*S*)-**2b** and (*S*)-**2c** were prepared in high yields by treatment of (*S*)-**1** with the corresponding silyl chlorides (2 equiv.) and imidazole (4 equiv.) as a base in DMF. Acetals (1*S*)-**2d** and its diastereomer (1*R*)-**2d** were easily obtained in high yields by treatment with ethyl vinyl ether in the presence of a catalytic amount of pyridinium *p*-toluenesulfonate (PPTS) in CH_2Cl_2.

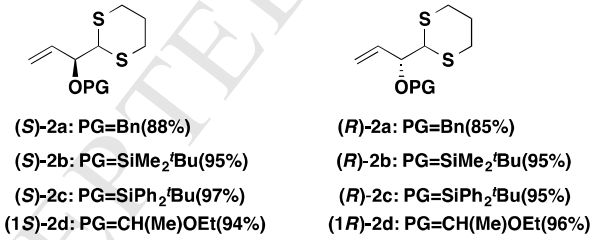
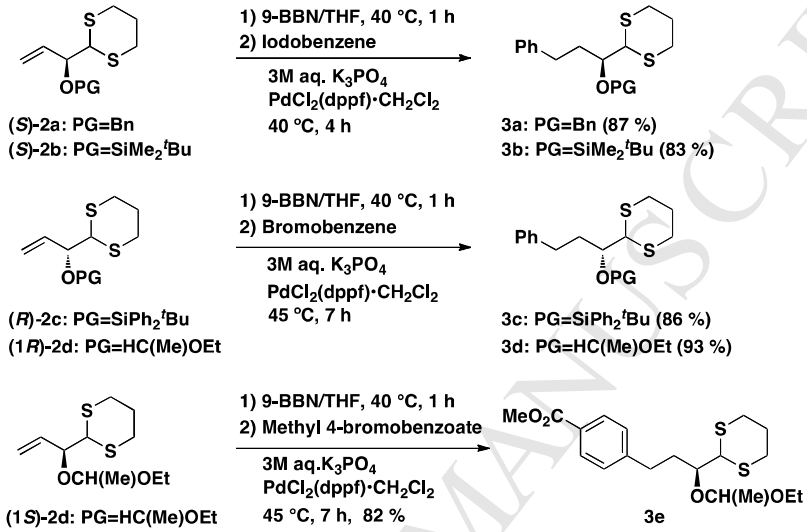


Figure 2. Protected **2**.

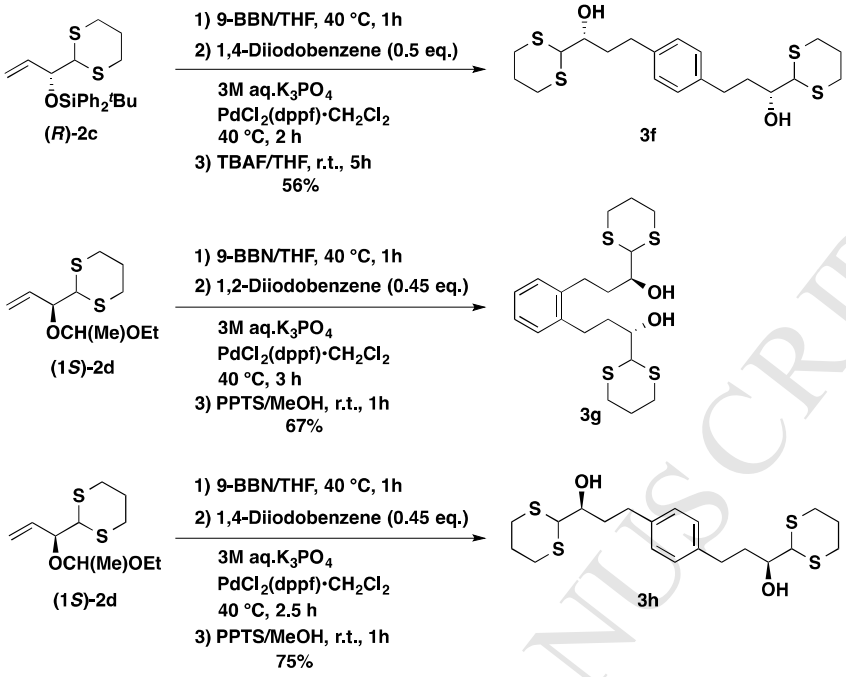
With a variety of *O*-protected derivatives **2** in hand, alkenyl-alkyl cross-coupling reaction was smoothly effected using the Suzuki-Miyaura protocol (Scheme 5).[7] For example, benzyl ether (*S*)-**2a** was reacted with freshly prepared crystalline 9-borabicyclo[3.3.1]nonane dimer (9-BBN)[14] (2 equiv.) in THF at 40 °C for 1 h. To the resulting alkylborane, iodobenzene (2 equiv.), 3 M aq. K_3PO_4 (3 equiv.) and then $PdCl_2(dppf)\cdot CH_2Cl_2$[15] (5 mol%) were added and the reaction mixture was stirred at 40 °C for 4 h, producing **3a** in 87% yield. Also, the cross-coupling of sily ether (*S*)-**2b** with iodobenzene proceeded under the same conditions,

affording **3b** in 83% yield. Subsequently, (*R*)-**2c** and (1*R*)-**2d** were subjected to the cross-coupling reaction with bromobenzene instead of iodobenzene, providing **3c** and **3d** in 86 and 93% yield, respectively. Similarly, the reaction of acetal (1*S*)-**2d** with methyl 4-bromobenzoate uneventfully furnished **3e** bearing an ester functionality in 82% yield.



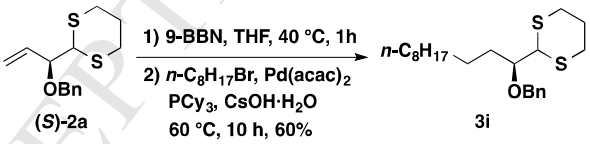
Scheme 5. Suzuki-Miyaura cross-coupling reaction of **2** with ArX.

Additionally, the cross-coupling reaction of **2** with 1,2- and 1,4-diiodobenzenes proceeded effectively, producing several synthetically valuable compounds with bi-functional groups. (Scheme 6). For example, (*R*)-**2c** was treated with 9-BBN (2 eq.) at 40 °C for 1h, then 1,4-diiodobenzene (0.5 equiv.), 3M aq. K_3PO_4 (3 equiv.) and $PdCl_2(dppf)\cdot CH_2Cl_2$ (5 mol %) were added and the reaction proceeded at 40 °C for 2 h. The crude coupling product was treated with tetrabutylammonium fluoride (TBAF) in THF at room temperature for 5 h, providing diol **3f** in 56% isolated yield over two steps. The cross-coupling reaction of (1*S*)-**2d** with 1,2-diiodobenzene or 1,4-diiodobenzene was performed under the same reaction conditions to give diols **3g** and **3h** in 67% and 75% yields, respectively.



Scheme 6. Suzuki-Miyaura cross-coupling reaction of **2** with diiodobenzenes.

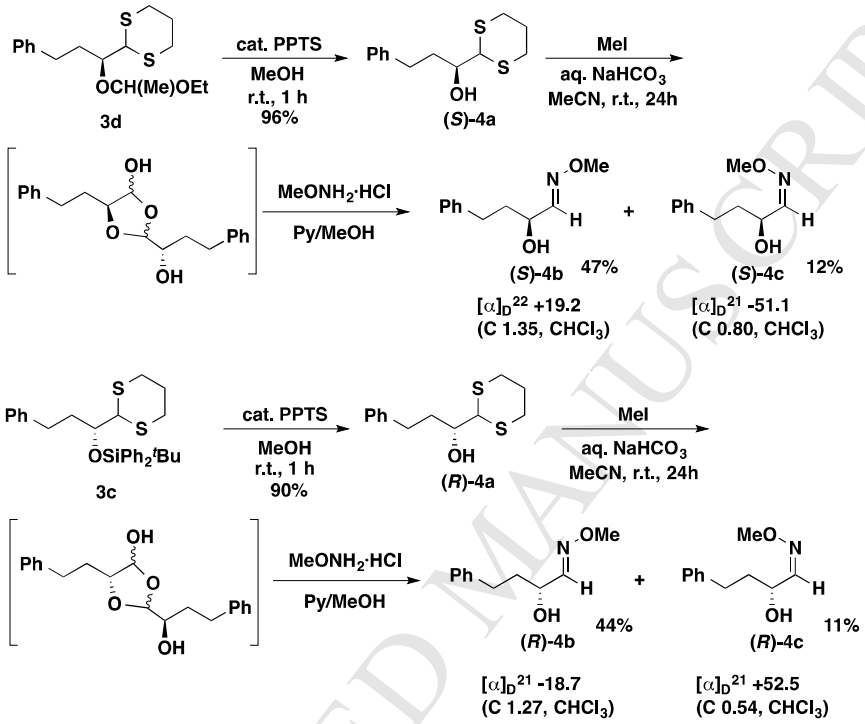
Furthermore, a challenging alkyl-alkyl cross-coupling reaction of (*S*)-**2a** with 1-bromooctane was executed according to a slightly modified protocol developed by Fu,[16] furnishing the coupling product **3i** in 60% yield (Scheme 7).



Scheme 7. Cross-coupling of (*S*)-**2a** with 1-bromooctane.

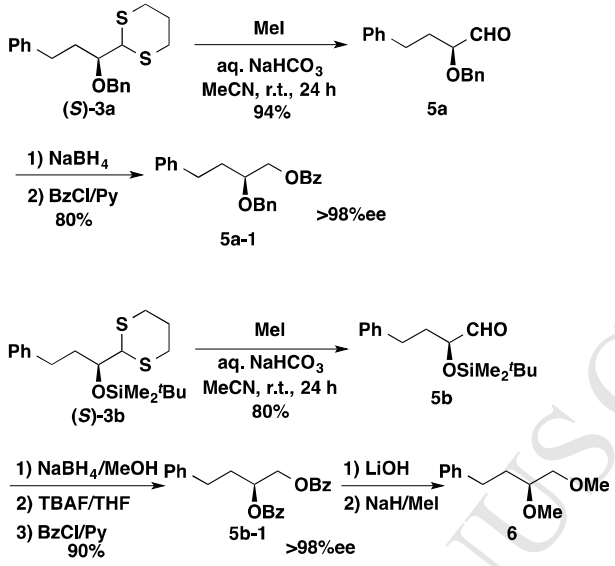
With an array of the cross-coupling products **3** in hand, we then verified that the 1,3-dithianyl group in (1*S*)-**3d** and **3c** could be removed without adversely affecting the enantiomeric excess (Scheme 8). First, (1*S*)-**3d** was treated with PPTS (5 mol%) in MeOH to give alcohol (*S*)-**4a**, which was exposed to an excess of iodomethane (10 equiv.)[17] in a mixture of MeCN and aq. $NaHCO_3$ at room temperature for 24 h, affording an assumed hemiacetal dimer[5a] that provided a complicated ^1H NMR spectrum. Thus, the crude product was treated with $MeONH_2 \cdot HCl$ (2 equiv.) in MeOH in the presence of pyridine (5 equiv.) to afford a separable 4:1 mixture of

oximes (*S*)-**4b** and (*S*)-**4c**. Second, **3c** was also converted to (*R*)-**4b** and (*R*)-**4c** by way of (*R*)-**4a** under the same conditions. We found no discrepancy in the predicted and obtained optical rotation values and confirmed that the chiral centers of (*S*)-**4a** and (*R*)-**4a** were not compromised throughout these transformations.



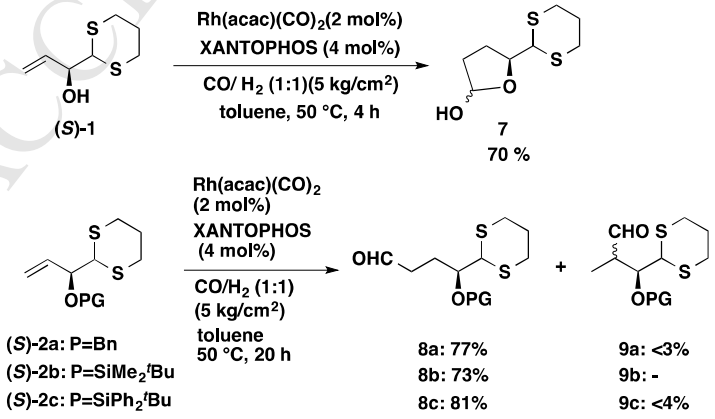
Scheme 8. Oxime formation from (1*S*)-**3d** and **3c**.

O-Protected α-hydroxyaldehydes as well as α-hydroxyaldehydes are synthetically valuable intermediates. We next checked the enantiopurity of *O*-protected aldehydes formed via deprotection of the 1,3-dithianyl group (Scheme 9). For example, (*S*)-**3a** was treated with an excess of MeI (10 eq.) to uneventfully afford aldehyde **5a** in 94% yield. The enantiomeric excess was confirmed by converting **5a** to benzoate **5a-1** via $NaBH_4$ reduction and subsequent benzoylation. HPLC analysis of **5a-1**[18] revealed that no epimerization occurred throughout the process. Additionally, deprotection of (*S*)-**3b** was effected under the same conditions to give aldehyde **5b**, which was converted to dibenzoate **5b-1** in three steps. HPLC analysis of **5b-1**[19] showed that the deprotection step did not adversely affect the enantiopurity. Furthermore, the absolute configuration of (*S*)-**3b** was confirmed to be *S* by converting to the known dimethoxy derivative **6**.[20]



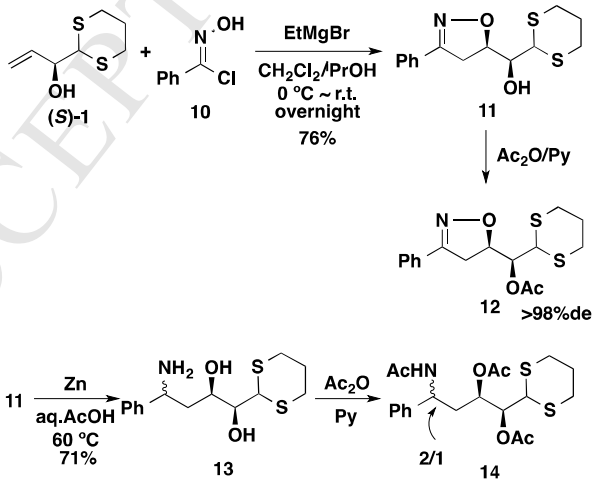
Scheme 9. Formation of *O*-protected α-hydroxyaldehydes.

In addition to Suzuki-Miyaura cross-coupling, the synthetic utility of the terminal olefin in (*S*)-**1** and **(*S*)-2** was exemplified by hydroformylation, which allows incorporation of a formyl group in a highly regioselective fashion (Scheme 10). Initially, we found that hydroformylation of (*S*)-**1** by the catalytic system $Rh(acac)(CO)_2$/XANTPHOS[21] produced hemiacetal **7** in 70% yield together with a trace of complex mixture (<1%). Furthermore, (*S*)-**2a**, (*S*)-**2b** and (*S*)-**2c** gave satisfactory ratios of linear aldehyde **8**/branched aldehyde **9**.



Scheme 10. Hydroformylation of (*S*)-**1** and (*S*)-**2**.

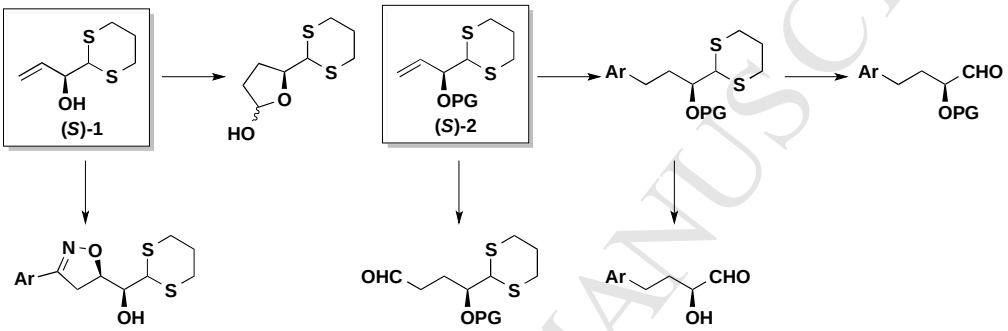
In an effort to expand the synthetic utility of (*S*)-**1** and (*R*)-**1**, we examined the hydroxyl-directed 1,3-dipolar cycloaddition of nitrile oxides (Scheme 11).[22] Initially, the reaction of (*S*)-**1** with benzohydroximinoyl chloride (**10**) using triethylamine as a base furnished **11** with poor diastereoselectivity.[23] Fortunately both the *syn*-selectivity and the yield of alcohol **11** were dramatically improved using the Kanemasa protocol.[24] The *syn/anti* ratio of **11** (>98% dr) was determined by ^{1}H NMR (500 MHz) after converting to the corresponding acetate **12**.[25] Next, the oxazoline ring of **11** was cleaved by treatment with Zn[26] to furnish diol **13**, which was then acetylated by treatment with Ac_2O/pyridine to afford diacetate **14** as a 2:1 separable mixture.[27] From a synthetic point of view, these results are very significant because scaffold (*S*)-**1** permits construction of a densely functionalized α-hydroxyaldehyde in several short steps.



Scheme 11. Hydroxyl-directed 1,3-dipolar cycloaddition of (*S*)-**1**

3. Conclusion

Scaffold (*S*)-**1** and *O*-protected derivatives (*S*)-**2** are amenable to palladium-catalyzed Suzuki-Miyaura cross-coupling and rhodium-catalyzed hydroformylation. Also, (*S*)-**1** undergoes hydroxyl-directed 1,3-dipolar cycloaddition in a highly stereoselective manner, providing a variety of synthetically valuable intermediates (Scheme 12). Most importantly, α-hydroxyaldehyde can be generated without any erosion of enantiopurity, definitively demonstrating the high synthetic value of (*S*)-**2**.



Scheme 12. A variety of transformations of (*S*)-**1** and (*S*)-**2**.

4. Experimental section

4.1 General Procedure

All air- and moisture-sensitive reactions were performed in flame-dried glassware fitted with rubber septa under a positive pressure of argon, unless otherwise noted. THF and DME were distilled from sodium benzophenone ketyl. Dichloromethane was washed with water and brine successively, and dried over 4Å molecular sieves. CAL-B was dried under reduced pressure (<0.5 mmHg) at room temperature for 8 h. Isopropenyl acetate was freshly distilled before use. Other commercially available reagents were used as received, unless otherwise noted. TLC analysis was performed on precoated plates (0.25 mm, silica gel, Merck Kieselgel 60F_{254}). Compounds were visualized by dipping the plates in aq. PMA, ethanolic PMA, or *p*-anisaldehyde, followed by heating. Flash column chromatography was performed with silica gel 60 N (spherical, neutral, 40-50 μm, Kanto Chemical Co., Inc.). IR spectra were recorded on a varian FTIR 7000 e. High performance liquid chromatography (HPLC) analyses were performed with Hitachi High-Technologies Co. using Chiralpak IA or Chiralpak IB column

(0.46 cm x 25 cm). Melting points were recorded with a Büchi 510 apparatus and are not corrected. Optical rotations were measured on a JASCO DIP-1000. Mass spectra were recorded on a JEOL JMS-DX 303. ^{1}H-NMR (500 MHz) and ^{13}C-NMR (125 MHz) spectra were recorded on a JEOL JNM-LA 500. ^{1}H-NMR (400 MHz) and ^{13}C-NMR (100 MHz) spectra were recorded on a JEOL JNM-ECS 400. The chemical shifts are given in δ units relative to internal tetramethylsilane (0 ppm for ^{1}H and ^{13}C), chloroform (7.26 ppm for ^{1}H, 77.0 ppm for ^{13}C), or methanol (3.30 ppm for ^{1}H, 49.0 ppm for ^{13}C). Elemental analysis was done using a Perkin-Elmer 2400 CHN analyzer.

*4.1.1. Racemic 1-(1,3-dithian-2-yl)prop-2-en-1-ols [(±)-**1**].*

A solution of 1,3-dithiane (6.01 g, 50 mmol) in THF (100 mL) was cooled to -70 °C and a solution of *n*-BuLi (1.56 M in hexane, 33.7 mL, 52.6 mmol) was added dropwise over a period of 5 min. The reaction mixture was allowed to warm to -30 °C over the next 1.5 h, and then cooled back down to -70 °C. Acrolein (3.67 mL, 55 mmol) was added dropwise over 2 min. After stirring at this temperature for 10 min, the reaction was terminated by slow addition of 1M HCl (60 mL). The aqueous mixture was diluted with brine (100 mL), and extracted into a mixture of toluene (50 mL) and EtOAc (50 mL). The organic layer was washed with brine (100 mL x 2) and dried over anhydrous $MgSO_4$. Filtration and evaporation of the solvent *in vacuo* followed by short-path distillation provided (±)-**1** (7.93 g, 90% yield) as a colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.00 (ddd, *J* = 16.8, 10.7, 5.8 Hz, 1H), 5.44 (dd, *J* = 17.1, 1.2 Hz, 1H), 5.23 (dd, *J* = 10.4, 1.2 Hz, 1H), 4.40-4.37 (m, 1H), 3.96 (d, *J* = 6.4 Hz, 1H), 2.98-2.92 (m, 2H), 2.80-2.74 (m, 2H), 2.51 (d, *J* = 4.0 Hz, 1H), 2.13-2.06 (m, 1H), 2.01-1.94 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.6, 117.5, 73.3, 51.7, 28.3, 28.0, 25.4; Anal. Calcd. for $C_7H_{12}OS_2$: C, 47.69; H, 6.86. Found: C, 47.29; H, 6.89; HRMS (FAB^+, $[M+H]^+$) *m/z* calcd for $[C_7H_{13}OS_2]^+$: 177.0408 found: 177.0407.

*4.1.2. Lipase-catalyzed kinetic resolution of (±)-**1**.*

*(R)-1-(1,3-Dithian-2-yl)allyl acetate[(R)-**1**-OAc] and (S)-1-(1,3-Dithian-2-yl)prop-2-en-1-ol [(S)-**1**]*

A mixture of (±)-**1** (6.63 g, 37.6 mmol), 2-propenyl acetate (4.14 mL, 37.6 mmol) and CAL-B (752 mg, 20 mg/mmol of (±)-**1**) in toluene (37.6 mL) was stirred at 50 °C for 65 h. The enzyme was removed by filtration through Celite 545, and washed with toluene (5 mL x 2). The filtrate was concentrated *in vacuo* to give a crude oil (7.82 g), which was purified by column chromatography

(silica gel, toluene/EtOAc=20/1~5/1) to afford (*R*)-**1**-OAc (4.30 g) as a pale yellow oil and (*S*)-**1** (3.26 g) as a pale yellow oil, respectively. Short-pass distillation gave (*R*)-**1**-OAc (4.15 g, 50.6%) as a colorless oil and (*S*)-**1** (3.23 g, 48.7%) as a colorless oil, respectively.

(*R*)-**1**-OAc: $[\alpha]_D^{23}$ +20.3 (*c* 1.16, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.96 (ddd, *J* = 17.1, 10.4, 6.7 Hz, 1H), 5.57 (dd, *J* = 6.7, 6.7 Hz, 1H), 5.40 (d, *J* = 17.1 Hz, 1H), 5 33 (d, *J* = 10.4 Hz, 1H), 4.10 (d, *J* = 6.7 Hz, 1H), 2.96-2.90 (m, 2H), 2.81-2.75 (m, 2H), 2.13 (s, 3H), 2.13-2.08 (m, 1H), 1.98-1.92 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.3, 132.9, 118.9, 48.8, 28.4, 28.1, 25.2, 20.7; HRMS (FAB$^+$, $[M+Na]^+$) *m/z* calcd for $[C_9H_{14}O_2S_2Na]^+$: 241.0333 found: 241.0332.

(*S*)-**1**: $[\alpha]_D^{24}$-20.1 (*c* 1.11, $CHCl_3$).

(*R*)-**1**-OAc was converted to (*R*)-**1** by treatment with K_2CO_3 (5 mol%) in MeOH at room temperature for 2 h. HLC analysis: Chiralpak IA, *n*-hexane/2-propanol=9/1, 1.0 mL/min, 254 nm. (*S*)-**1**: t_R 10.8 min (>98% ee), (*R*)-**1**: t_R 12.0 min (96% ee).

*4.1.3. Lipase-catalyzed hydrolysis of (R)-**1**-OAc.*

*(R)-1-(1,3-Dithian-2-yl)prop-2-en-1-ol [(R)-**1**]*

A mixture of (*R*)-**1**-OAc (4.07 g, 18.6 mmol, 96% ee) and CAL-B (372 mg, 20 mg/mmol of (*R*)-**1**-OAc) in a mixed solution of phosphate buffer (pH 6.86, 1.9 mL) and 1,4-dioxane (18.6 mL) was stirred at 40 ºC for 65 h. The reaction mixture was passed through Celite 545 and rinsed with toluene (5 mL x 2). The filtrate was concentrated *in vacuo* and the residue was distributed between EtOAc (30 mL) and brine (20 mL). The separated organic layer was washed with brine (30 mL), dried over anhydrous $MgSO_4$. Filtration and evaporation of the solvent *in vacuo* followed by column chromatography (silica gel, toluene/EtOAc=1/0~15/1~3/1) provided (*S*)-**1**-OAc (645 mg, 2.95 mmol) and (*R*)-**1** (2.67 g, 81% yield) as a colorless oil after short-path distillation.

(*R*)-**1**: $[\alpha]_D^{22}$+21.7 (*c* 1.15, $CHCl_3$).

(*S*)-**1**-OAc was converted to (*S*)-**1** by treatment with K_2CO_3 (5 mol%) in MeOH at room temperature for 2h. HPLC analysis: Chiralpak IA (*n*-hexane/2-propanol=9/1, 1.0 mL/min, 254 nm, (*S*)-**1**: t_R 10.9 min (76% ee), (*R*)-**1**: t_R 12.2 min (>98% ee).

*4.1.4. General procedure for benzylation of (S)-**1** and (R)-**1**.*

*(S)-2-(1-(Benzyloxy)allyl)-1,3-dithiane [(S)-**2a**]*

*(R)-2-(1-(Benzyloxy)allyl)-1,3-dithiane [(R)-**2a**]*

BnCl (0.92 mL, 8.0mmol) was added to a suspension of NaH (55% in mineral oil, 350 mg, 8

mmol) in DMF (8 mL) at 5 °C, and then a solution of (*S*)-**1** (705 mg, 4.0 mmol) in THF (5 mL) was added dropwise over a period of 2 min. The reaction mixture was stirred at room temperature for 2 h, poured into cold water, and extracted with toluene (20 mL x 2). The combined extracts were washed successively with water (20 mL) and brine (20 mL). The organic layer was dried over anhydrous $MgSO_4$, filtrated and concentrated *in vacuo*. Purification of the crude oil by short-path distillation and subsequent column chromatography (silica gel, *n*-hexane/EtOAc=20/1~10/1) gave (*S*)-**2a** (936 mg, 88 % yield) as a colorless oil; $[\alpha]_D^{21}$ +21.1 (*c* 1.13, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38-7.32 (m, 4H), 7.29-7.26 (m, 1H), 5.88 (ddd, *J* = 17.7, 10.4, 8.3 Hz, 1H), 5.40 (d, *J* = 10.5 Hz, 1H), 5.33 (d, *J* = 17.5 Hz, 1H), 4.67 (d, *J* = 12.0 Hz, 1H), 4.44 (d, *J* = 12.5 Hz, 1H), 4.24 (d, *J* = 5.5 Hz, 1H), 3.96 (dd, *J* = 7.7, 6.4 Hz, 1H), 2.90-2.81 (m, 4H), 2.12-2.07 (m, 1H), 1.94-1.86 (m, 1H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 137.2, 134.5, 127.7, 127.2, 126.9, 119.4, 81.5, 69.8, ,50.8, 29.3, 29.4; HRMS (EI^+, $[M]^+$) *m/z* calcd for $[C_{14}H_{18}OS_2]^+$: 266.0799 found: 266.0796.

(*R*)-**2a** was obtained from (*R*)-**1** in 85% yield: $[\alpha]_D^{24}$ -19.1 (*c* 1.09, $CHCl_3$).

*4.1.5. General procedure for silylation of (S)-**1** and (R)-**1** with TBDMSCl.*
*(S)-((1-(1,3-Dithian-2-yl)allyl)oxy)(tert-butyl)dimethylsilane[(S)-**2b**]*
*(R)-((1-(1,3-Dithian-2-yl)allyl)oxy)(tert-butyl)dimethylsilane [(R)-**2b**]*

TBDMSCl (610 mg, 4.05 mmol) was added to a solution of (*S*)-**1** (353 g, 2.0 mmol) and imidazole (681 mg, 10.0 mmol) in DMF (5 mL) at room temperature. After stirring for 4 h, glycerine (2 mL) was added to the reaction mixture, and stirring was continued for an additional 1 h. The reaction mixture was distributed between toluene (30 mL) and water (30 mL). The organic layer was successively washed with sat. aq. $NaHCO_3$ (20 mL) and brine (30 mL), dried over anhydrous $MgSO_4$. Filtration and evaporation of the solvent *in vacuo* followed by column chromatography (silica gel, *n*-hexane/EtOAc=15/1) gave (*S*)-**2b** (564 mg, 95% yield); $[\alpha]_D^{22}$ -13.5 (*c* 0.98, $CHCl_3$); ^{1}H NMR(500 MHz, $CDCl_3$) δ 5.92 (dd, *J* = 17.0, 10.5, 6.5 Hz, 1H), 5.28 (d, *J* = 17.0 Hz, 1H), 5.22 (d, *J* = 10.0 Hz, 1H), 4.23 (dd, *J* = 6.5, 6.0 Hz, 1H), 4.12 (d, *J* = 6.0 Hz, 1H), 2.88-2.82 (m, 4H), 2.10-2.08 (m, 1H), 1.90-1.85 (m, 1H), 0.92 (s, 9H), 0.12 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.9, 116.6, 76.4, 53.6, 29.7, 28.9, 25.6, 18.0, -4.5, -5.0; HRMS (FAB^+, $[M+H]^+$) *m/z* calcd for $[C_{13}H_{27}OS_2Si]^+$: 291.1273 found: 291.1267.

(*R*)-**2b** was obtained from (*R*)-**1** in 95% yield; $[\alpha]_D^{22}$ +14.5 (*c* 1.00, $CHCl_3$).

*4.1.6. General procedure for silylation of (S)-**1** and (R)-**1** with TBDPSCl.*

*(S)-((1-(1,3-Dithian-2-yl)allyl)oxy)(tert-butyl)diphenylsilane[(S)-**2c**]*

*(R)-((1-(1,3-Dithian-2-yl)allyl)oxy)(tert-butyl)diphenylsilane [(R)-**2c**]*

A solution of TBDPSCl (1.10 g, 4.0 mmol) in DMF (5 mL) was added to a solution of (*S*)-**1** (353 mg, 2.0 mmol) and imidazole (681 mg, 10.0 mmol) in DMF (5 mL). The reaction mixture was stirred at room temperature for 12 h. The reaction was quenched by addition of glycerine (2 ml), and stirring was continued for 1 h. The mixture was distributed between toluene (30 mL) and water (50 mL). The organic layer was washed with sat. aq. $NaHCO_3$ (20 mL), dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. The residual viscous oil (1.68 g) was purified by column chromatography (silica gel, *n*-hexane/EtOAc=15/1) to afford (*S*)-**2c** (800 mg, 97% yield) as a white semi-solid; $[\alpha]_D^{22}$ -59.4 (*c* 1.01, $CHCl_3$); FTIR (KBr): 2932, 2857, 1588, 1473, 1428, 1113, 931, 875, 708 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.5 Hz, 2H), 7.66 (d, *J* = 7.0 Hz, 2H), 7.46-7.27 (m, 6H), 5.92 (ddd, *J* = 17.0, 10.5, 6.5 Hz, 1H), 5.11-5.06 (m, 2H), 4.35 (dd, *J* = 5.5, 5.5 Hz, 1H), 3.40 (d, *J* = 5.0 Hz, 1H), 2.82-2.61 (m, 4H), 2.04-2.01 (m, 1H), 1.85-1.77 (m, 1H), 1.09 (s, 9H) ; ^{13}C NMR(125 MHz, $CDCl_3$) δ 136.5, 135.9, 135.9, 133.7, 133.4, 129.7, 129.6, 127.4, 127.4, 117.4, 76.6, 54.4, 30.4, 30.0, 26.9, 26.2, 19.4; HRMS (FAB^+, $[M+H]^+$) *m/z* calcd for $[C_{23}H_{31}OS_2Si]^+$: 415.1586 found: 415.1565.

(*R*)-**2c** was obtained from (*R*)-**1** in 95% yield; $[\alpha]_D^{23}$ +60.3 (*c* 0.90, $CHCl_3$).

*4.1.7. 2-((1S)-1-(1-Ethoxyethoxy)allyl)-1,3-dithiane [(1S)-**2d**].*

To a solution of (*S*)-**1** (1.06 g, 6.0 mmol) and ethyl vinyl ether (1.15 mL, 12.0 mmol) in CH_2Cl_2 (20 mL) was added pyridinium *p*-toluenesulfonate (PPTS) (75 mg, 0.3 mmol) at room temperature. After stirring for 2 h, the reaction was terminated by addition of sat. aq. $NaHCO_3$ solution (20 mL). The organic layer separated was dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. The residue (1.50 g) was purified by column chromatography (silica gel, *n*-hexane/EtOAc/Et_3N=100/5/1) to afford (1S)-**2d** (1.40 g, 94% yield) as a colorless oil; $[\alpha]_D^{23}$ +17.9 (*c* 1.44, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 6.00-5.78 (m, 1H), 5.40-5.28 (m, 2H), 4.82-4.75 (m, 1H), 4.30-4.12 (m, 2H), 3.75-3.40 (m, 2H), 2.95-2.80 (m, 4H), 2.15-2.06 (m, 1H), 1.95-1.85 (m, 1H), 1.40-1.30 (m, 3H), 1.24-1.14 (m, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.5, 134.6, 118.6, 117.1, 98.7, 96.1, 78.7, 78.3, 59.9, 58.1, 51.1, 50.7, 29.2, 25.2, 19.4, 19.2, 14.6, 14.6, 14.3; HRMS (FAB^+, $[M+H]^+$) *m/z* calcd for $[C_{23}H_{31}OS_2Si]^+$: 415.1586 found: 415.1565.

*4.1.8. 2-((1R)-1-(1-Ethoxyethoxy)allyl)-1,3-dithiane [(1R)-**2d**].*

To a solution of (*R*)-**1** (1.76 g, 10.0 mmol) and ethyl vinyl ether (1.92 mL, 20 mmol) in

CH_2Cl_2 (20 mL) was added pyridinium *p*-toluenesulfonate (PPTS) (63 mg, 0.25 mmol) at room temperature. After stirring for 3 h, the reaction was terminated by addition of sat. aq. $NaHCO_3$ solution (20 mL). The organic layer separated was dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. The residue (2.46 g) was purified by column chromatography (silica gel, *n*-hexane/EtOAc/Et_3N=100/5/1) to afford (1*R*)-**2d** (2.39 g, 96% yield) as a colorless oil; $[\alpha]_D^{21}$-17.1 (*c* 1.50, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.00-5.77 (m, 1H), 5.38-5.28 (m, 2H), 4.84-4.75 (m, 1H), 4.28-4.12 (m, 2H), 3.75-3.40 (m, 2H), 2.94-2.80 (m, 4H), 2.15-2.05 (m, 1H), 1.97-1.85 (m, 1H), 1.37-1.32 (m, 3H), 1.23-1.14 (m, 3H).; ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.8, 134.9, 119.2, 117.8, 99.2, 96.6, 79.1, 78.9, 60.5, 58.6, 51.6, 51.3, 29.7, 25.6, 19.8, 19.6, 15.0, 14.7.

*4.1.9. General protocol for Suzuki-Miyaura cross-coupling reaction of (S)-**2** and (R)-**2** with bromobenzene and aryl iodides.*

*4.1.9-1. (S)-2-(1-(Benzyloxy)-3-phenylpropyl)-1,3-dithiane [**3a**].*

To a solution of (*S*)-**2a** (490 mg, 1.84 mmol) in THF (5 mL) was added 9-BBN (449 mg, 3.68 mmol) in one portion and the mixture was stirred at 40 °C for 1 h under argon atmosphere. Then, iodobenzene (0.41 ml, 3.68 mmol), aq. 3M K_3PO_4 (2 mL, 5.52 mmol) and $PdCl_2(dppf)\cdot CH_2Cl_2$ (75 mg, 0.092 mmol) were added and the mixture was purged with argon twice. The dark brown mixture was heated at 40 °C for 4 h. After cooling to room temperature, ethanolamine (0.44 mL, 7.36 mmol) was added to the reaction mixture and stirred for 1 h. The mixture was distributed between hexane (30 mL) and water (20 mL). The organic layer was washed with brine (20 mL x 2), dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. Purification of the residue by column chromatography (silica gel, *n*-hexane/EtOAc=20/1) gave **3a** (554 mg, 87% yield) as coloress oil; $[\alpha]_D^{22}$-37.1 (*c* 1.13, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47-7.14 (m, 10H), 4.76 (d, *J* = 11.5 Hz, 1H), 4.55 (d, *J* = 11.5 Hz, 1H), 4.38 (d, *J* = 5.0 Hz, 1H), 3.64-3.61 (m, 1H), 2.90-2.78 (m, 5H), 2.64-2.59 (m, 1H), 2.13-2.03 (m, 3H), 1.92-1.85 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.5, 137.9, 128.3, 128.2, 127.9, 127.5, 125.6, 80.0, 72.1, 52.0, 33.6, 31.5, 30.4, 26.1; HRMS (FAB$^+$, $[M+H]^+$) *m/z* calcd for $[C_{20}H_{25}OS_2]^+$: 345.1347 found: 345.1353.

*4.1.9-2. (S)-(1-(1,3-Dithian-2-yl)-3-phenylpropoxy)(tert-butyl)dimethylsilane [**3b**].*

Compound **3b** was obtained from (*S*)-**2b** in 83% yield, $[\alpha]_D^{19}$-4.92 (*c* 1.42, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29-7.16 (m, 5H), 4.22 (d, *J* = 5.2 Hz, 1H), 3.93-3.89 (m, 1H), 2.87-2.83 (m, 4H), 2.78-2.72 (m, 1H), 2.26-2.61 (m, 1H), 2.12-2.08 (m, 2H), 2.05-1.97 (m, 1H),

0.95 (s, 9H), 0.15 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.9, 128.3, 128.3, 125.7, 74.1, 54.2, 36.2, 31.1, 30.5, 30.4, 26.3, 25.9, 18.2, -4.4; HRMS (FAB^+, $[M+H]^+$) *m/z* calcd for $[C_{19}H_{33}OS_2Si]^+$: 369.1742 found: 369.1734.

*4.1.9-3. (R)-(1-(1,3-Dithian-2-yl)-3-phenylpropoxy)(tert-butyl)diphenylsilane [**3c**].*

To a solution of (*R*)-**2c** (207 mg, 0.5 mmol) in THF (5 mL) was added 9-BBN (122 mg, 1.0 mmol) and the mixture was stirred at 40 °C for 1 h under argon atmosphere. Then, bromobenzene (0.11 mL, 1.0 mmol), aq. 3M K_3PO_4 (1 mL, 3 mmol) and $PdCl_2(dppf)\cdot CH_2Cl_2$ (41 mg, 0.05 mmol) were added and the mixture was purged with argon twice. The dark brown mixture was heated at 45 °C for 7 h. After cooling to room temperature, ethanolamine (0.18 mL, 3.0 mmol) was added to the reaction mixture and stirred for 1 h. The mixture was distributed between hexane (30 mL) and water (20 mL). The organic layer was washed with brine (20 mL x 2), dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. Purification of the residue by column chromatography (silica gel, *n*-hexane/EtOAc=30/1) gave **3c** (212 mg, 86% yield) as coloress oil; $[\alpha]_D^{22}$ +13.8 (*c* 1.63, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (d, *J* = 7.0 Hz, 2H), 7.72 (d, *J* = 6.7 Hz, 2H), 7.45-7.10 (m, 9H), 6.99 (d, *J* = 7.3 Hz, 2H), 4.06 (d, *J* = 4.0 Hz, 1H), 4.05-3.97 (m, 1H), 2.82-2.58 (m, 5H), 2.48-2.41 (m, 1H), 2.05-1.75 (m, 4H), 1.11 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.6, 136.1, 136.0, 133.9, 133.7, 129.7, 128.2, 128.1, 127.6, 127.5, 125.6, 75.0, 55.1, 36.0, 31.9, 30.8, 30.4, 27.0, 26.4, 19.5; HRMS (FAB^+, $[M+H]^+$) *m/z* calcd for $[C_{29}H_{37}OS_2Si]^+$: 493.2055 found: 493.2039.

*4.1.9-4. 2-((1R)-1-(1-Ethoxyethoxy)-3-phenylpropyl)-1,3-dithiane [**3d**].*

Compound **3d** was obtained from (1*R*)-**2d** in 93% yield; $[\alpha]_D^{22}$ +24.0 (*c* 1.31, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30-7.12 (m, 5H), 4.91 (d, *J* = 5.2 Hz, 0.5H), 4.78 (d, *J* = 5.2 Hz, 0.5H), 4.41 (d, *J* = 4.8 Hz, 0.5H), 4.32 (d, *J* = 4.4 Hz, 0.5H), 3.88-3.47 (m, 3H), 2.92-2.57 (m, 6H), 2.14-1.80 (m, 4H), 1.38 (d, *J* = 5.2 Hz, 1.5H), 1.35 (d, *J* = 5.2 Hz, 1.5 H), 1.20 (t, *J* = 6.8 Hz, 1.5 H), 1.18 (d, *J* = 6.8 Hz, 1.5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.9, 141.5, 128.4, 128.3, 125.9, 125.7, 99.9, 99.7, 78.1, 60.3, 52.8, 52.7, 34.5, 33.2, 31.7, 31.5, 30.9, 30.6, 26.3, 20.2, 20.1, 15.3; HRMS (FAB^+, $[M+H]^+$) *m/z* calcd for $[C_{17}H_{27}O_2S_2]^+$: 327.1452 found: 327.1473.

*4.1.9-5. Methyl 4-((3S)-3-(1,3-dithian-2-yl)-3-(1-ethoxyethoxy)propyl)benzoate [**3e**].*

To a solution of (1*S*)-**2d** (514 mg, 2.07 mmol) in THF (10 mL) was added 9-BBN (505 mg, 4.14 mmol) and the mixture was stirred at 40 °C for 1 h under argon atmosphere. Then, a

solution of methyl 4-bromobenzoate (890 mg, 4.14 mmol) in THF (5mL), aq. 3M K_3PO_4 (3 mL, 9 mmol) and $PdCl_2(dppf)\cdot CH_2Cl_2$ (82 mg, 0.10 mmol) were added and the mixture was purged with argon twice. The dark brown mixture was heated at 45 °C for 7 h. After cooling to room temperature, ethanolamine (0.48 mL, 8.0 mmol) was added to the reaction mixture and stirred for 1 h. The mixture was distributed between hexane (30 mL) and water (20 mL). The organic layer was washed with brine (20 mL x 2), dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. Purification of the residue by column chromatography (silica gel, toluene/EtOAc=20/1~10/1) gave **3e** (650 mg, 82%) as coloress oil; $[\alpha]_D^{23}$ -22.7 (*c* 1.45, $CHCl_3$); FTIR (KBr): 3321, 2894, 1718, 1609, 1431, 1280, 1102, 704, 649 cm-1; ^{1}H NMR (500 MHZ, $CDCl_3$) δ 7.95 (d, *J* = 5.8 Hz, 2H), 7.25-7.30 (m, 2H), 4.92 (q, *J* = 5.5 Hz, 0.5H), 4.79 (q, *J* = 5.5 Hz, 0.5H), 4.44 (d, *J* = 4.6 Hz, 0.5H), 4.34 (d, *J* = 4.9 Hz, 0.5H), 3.90 (s, 3H), 3.90-3.51 (m, 3H), 2.95-2.80 (m, 5H), 2.76-2.65 (m, 1H), 2.16-2.03 (m, 3H), 1.95-1.82 (m, 1H), 1.39 (d, *J* = 5.5 Hz, 1.5H), 1.36 (d, *J* = 5.2 Hz, 1.5H), 1.22 (t, *J* = 7.1Hz, 1.5H), 1.19 (t, *J* = 7.0 Hz, 1.5H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.2, 147.6, 147.2, 130.2, 130.0, 129.9, 129.7, 128.5, 127.9, 127.8, 127.3, 126.7, 100.0, 99.8, 78.0, 70.9, 60.5, 60.4, 52.8, 52.5, 52.0, 42.0, 34.2, 33.0, 32.1, 31.8, 31.6, 30.9, 30.6, 27.4, 27.2, 26.2, 22.7, 22.0, 20.2, 20.1, 15.4; HRMS (FAB^+, $[M+Na]^+$) *m/z* calcd for $[C_{19}H_{28}O_4S_2Na]^+$: 407.1327 found: 407.1312.

*4.1.10. General protocol for Suzuki-Miyaura cross-coupling reaction of (R)-**2** and (1S)-**2d** with diiodobenzenes.*

*4.1.10-1. (1R,1'R)-3,3'-(1,4-Phenylene)bis(1-(1,3-dithian-2-yl)propan-1-ol) [**3f**].*

To a solution of (*R*)-**2c** (829 mg, 2.0 mmol) in THF (8 mL) was added 9-BBN (488 mg, 4.0 mmol) in one portion and the mixture was stirred at 40 °C for 1 h under argon atmosphere. Then, 1,4-diiodobenzene (330 mg, 1.0 mmol, 0.5 equiv.), 3M. aq. K_3PO_4 (3 mL, 9.0 mmol), $PdCl_2(dppf)\cdot CH_2Cl_2$ (82 mg, 0.10 mmol) and THF (10 mL) were added to the mixture in this order. The whole mixture was purged with argon twice. The dark green mixture was heated at 40 °C for 2 h. After cooling to room temperature, ethanolamine (0.48 mL, 8.0 mmol) and toluene (20 mL) were added and the mixture was stirred for 1 h. Hexane (30 mL) and water (30 mL) were added and the organic layer separated was washed with brine (30 mL), dried over anhydrous $MgSO_4$. Filtration and concentration *in vacuo* provided a crude oil, a THF solution (4 mL) of which was treated with Bu_4NF (1 M THF solution, 4 mL) for 5 h. The reaction mixture was distributed between toluene (30 mL) and water (20 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was washed with hot

hexane twice, and purified by column chromatography (silica gel, toluene/ EtOAc = 3/1) to give **3f** (241 mg, 56%) as a white amorphous solid; $[\alpha]_D^{22}$ +64.6 (*c* 1.55, $CHCl_3$); FTIR (KBr): 3427, 3229, 2949, 2928, 2899, 2358, 1419, 1278, 1083, 905, 551 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.15 (s, 4H), 3.91-3.85 (m, 4H), 2.95-2.83 (m, 6H), 2.76-2.66 (m, 6H), 2.45 (d, *J* = 2.5 Hz, 2H), 2.20-1.80 (m, 8H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.1, 128.5, 71.2, 52.1, 35.7, 31.5, 28.2, 27.7, 25.6; HRMS (FAB^+, $[M+H]^+$) *m/z* calcd for $[C_{20}\ H_{31}O_2S_4\ ]^+$: 431.1207 found: 431.1182.

*4.1.10-2. (1S,1'S)-3,3'-(1,2-Phenylene)bis(1-(1,3-dithian-2-yl)propan-1-ol) [**3g**]*

To a solution of (1*S*)-**2d** (497 mg, 2.0 mmol) in THF (8 mL) was added 9-BBN (488 mg, 4.0 mmol) in one portion and the mixture was stirred at 40 °C for 1 h under argon atmosphere. To the reaction mixture, 1,2-diiodobenzene (297 mg, 0.9 mmol, 0.45 equiv.), 3 M aq. K_3PO_4 (3 mL, 9.0 mmol), $PdCl_2(dppf)\cdot CH_2Cl_2$ (82 mg, 0.1 mmol) and THF (8 mL) were added. The resulting dark mixture was heated at 40 °C for 3 h. After cooling to room temperature, ethanolamine (0.48 mL, 8.0 mmol) was added and stirred for 1 h. The mixture was diluted with toluene (30 mL) and brine (20 mL) and the organic layer separated was washed with brine (30 mL), dried over $MgSO_4$, fiiltered and evaporation of the solvent *in vacuo*. The crude oil was purified by short-path column chromatography (silica gel, *n*-hexane/EtOAc =10/1~5/1) to afford a pale yellow oil, which was treated with a catalytic amount of PPTS in MeOH (5 mL) for 1 h. The reaction mixture was distributed between EtOAc (30 mL) and sat. aq. $NaHCO_3$ (20 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated in *vacuo*. Purification of the crude oil by column chromatography (silica gel, toluene/EtOAc=3/1) gave **3g** (260 mg, 67%) as a pale yellow oil; $[\alpha]_D^{23}$ -50.0 (*c* 1.05, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.24-7.15 (m, 4H), 3.95-3.89 (m, 4H), 2.95-2.85 (m, 6H), 2.82-2.68 (m, 8H), 2.20-1.81 (m, 8H), 2.20-1.80 (m, 8H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.5, 129.2, 126.2, 71.5, 52.1, 35.6, 28.3, 27.8, 25.5; HRMS (FAB^+, $[M+Na]^+$) *m/z* calcd for $[C_{20}H_{30}NaO_2S_4\ ]^+$: 453.1026 found: 453.1010.

*4.1.10-3. (1S,1'S)-3,3'-(1,4-phenylene)bis(1-(1,3-dithian-2-yl)propan-1-ol) [**3h**].*

To a solution of (1*S*)-**2d** (497 mg, 2.0 mmol) in THF (8 mL) was added 9-BBN (488 mg, 4.0 mmol) in one portion and the mixture was stirred at 40 °C for 1 h under argon atmosphere. 1,4-Diiodobenzene (297 mg, 0.9 mmol, 0.45 equiv.), 3 M aq. K_3PO_4 (3 ml, 9.0 mmol), $PdCl_2(dppf)\cdot CH_2Cl_2$ (82 mg, 0.1 mmol) and THF (10 mL) were added to the reaction mixture.

The resulting dark mixture was heated at 40 °C for 2.5 h. After cooling to room temperature, ethanolamine (0.48 mL, 8.0 mmol) and toluene (20 mL) were added and the mixture was stirred for 1 h. Hexane (30 mL) and water (30 mL) were added to the mixture and the organic layer separated was washed with brine (30 mL), dried over $MgSO_4$. Filtration and concentration *in vacuo* provided a crude oil, which was treated with a catalytic amount of PPTS in MeOH (5 mL) for 1 h. The reaction mixture was distributed between EtOAc (30 mL) and sat. aq. $NaHCO_3$ (20 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. The residue was washed with hot hexane twice, and purified by column chromatography (silica gel, toluene/EtOAc = 3/1) to give **3h** (291 mg, 75%) as a white amorphous solid; $[\alpha]_D^{22}$ -65.9 (*c* 1.05, $CHCl_3$).

*4.1.11. (S)-2-(1-(Benzyloxy)undecyl)-1,3-dithiane [**3i**].*

A solution of (*S*)-**2a** (133 mg, 0.50 mmol) and 9-BBN (122 mg, 1.0 mmol) in THF (2.0 mL) was stirred at room temperature for 2 h. $Pd(acac)_2$ (8mg, 0.025 mmol), PCy_3 (28 mg, 0.1 mmol), $CsOH{\bullet}H_2O$ (252 mg, 1.5 mmol) and 1-bromooctane (0.26 mL, 1.5 mmol) were added to the mixture, and purged with argon twice. The mixture was heated at 60 °C for 10 h and cooled to room temperature. The mixture was diluted with *n*-hexane (20 mL), washed with brine (20 mL x 2), dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. Purification of the residual oil by column chromatography (silica gel, *n*-hexane/EtOAc = 25/1) provided **3i** (114 mg, 60% yield) as a pale yellow oil; $[\alpha]_D^{21}$ -27.4 (*c* 1.02, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47-7.26 (m, 5H), 4.74 (d, *J* = 11.6 Hz, 1H), 4.56 (d, *J* = 11.6 Hz, 1H), 4.35 (d, *J* = 4.9 Hz, 1H), 3.61-3.57 (m, 1H), 2.92-2.80 (m, 4H), 2.14-2.10 (m, 1H), 1.94-1.85 (m, 1H), 1.72-1.69 (m, 2H), 1.50-1.45 (m, 1H), 1.30-1.24 (m, 15H), 0.88 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.2, 128.3, 128.0, 127.6, 81.0, 72.3, 52.4, 32.1, 31.9, 30.6, 30.59, 29.6, 29.5, 29.3, 26.3, 25.5, 22.7, 14.1; HRMS (FAB$^+$, $[M+H]^+$) *m/z* calcd for $[C_{22}H_{37}OS_2]^+$: 381.2286 found: 381.2296.

*4.1.12. General procedure for oxime formation from **3d** and **3c**.*

*4.1.12-1. (S)-1-(1,3-Dithian-2-yl)-3-phenylpropan-1-ol [(S)-**4a**]. and (R)-1-(1,3-Dithian-2-yl)-3-phenylpropan-1-ol [(R)-**4a**]*

Compound **3d** (784 mg, 2.4 mmol) was treated with PPTS (31.4 mg, 0.125 mmol) in MeOH (5 ml) at room temperature for 1 h. The reaction mixture was distributed between toluene (20 ml) and sat. aq. $NaHCO_3$(10 ml). The organic layer was dried over anhydrous $MgSO_4$.Filtration and evaporation of the solvent *in vacuo* afforded an oil (610 mg), which was

purified by column chromatography (silica gel, *n*-hexane/EtOAc=5/1~4/1) to afford (*S*)-**4a** (586 mg, 96% yield) as a colorless oil; $[\alpha]_D^{21}$-50.7 (c 1.33, $CHCl_3$); FTIR (KBr): 3308, 3246, 3024, 2907, 2364, 1653, 1597, 1496, 1453, 1278, 1070, 750, 698 cm-1; ^{1}H NMR(500 MHz, $CDCl_3$) δ 7.35-7.15 (m, 5H), 3.92-3.85(m, 2H), 2.95-2.84 (m, 3H), 2.76-2.68 (m, 3H), 2.48 (d, *J* = 2.2 Hz, 1H), 2.20-1.84 (m, 4H); ^{13}C NMR(125 MHz, $CDCl_3$) δ 141.6, 128.4, 125.7, 71.1, 52.1, 35.6, 31.8, 28.1, 27.7, 25.5; HRMS (FAB^+, $[M+H]^+$) *m/z* calcd for $[C_{13}H_{19}OS_2]^+$: 255.0877 found: 255.0849.

(*R*)-**4a** was obtained from **3c** in 90% by treatment with TBAF in THF followed by column chromatography (silica gel, *n*-hexane/EtOAc=5/1~4/1); $[\alpha]_D^{24}$+50.8 (c 1.38, $CHCl_3$).

*4.1.12-2. (S, E)-2-Hydroxy-4-phenylbutanal O-methyl oxime [(S)-**4b**], (S, Z)-2-Hydroxy-4-phenylbutanal O-methyl oxime [(S)-**4c**], (R, E)-2-Hydroxy-4-phenylbutanal O-methyl oxime [(R)-**4b**], and (R, Z)-2-Hydroxy-4-phenylbutanal O-methyl oxime [(R)-**4c**].*

The alcohol (*S*)-**4a** (592 mg, 2.33 mmol) was treated with MeI (1.50 mL, 24 mmol) and $NaHCO_3$ (3.02 g, 36 mmol) in MeCN/H_2O (12 mL/3 mL) at room temperature for 24 h. The solvent was evaporated and sat. aq. Na_2SO_3 (10 mL) was added to the residue. The aqueous phase was extracted with $CHCl_3$ (20 mL x 2) and the combined extracts were washed with brine (20 mL), dried over anhydrous $MgSO_4$. Filtration and concentration *in vacuo* provided an oil (428 mg), to which pyridine (1 mL), MeOH (5 mL) and $MeONH_2 \cdot HCl$ (418 mg, 5 mmol) were added. The reaction mixture was stirred at room temperature for 12 h, and distributed with $CHCl_3$ (30 mL) and water (20 mL). The organic layer was washed with brine (20 mL), dried over anhydrous $MgSO_4$. Filtration and evaporation of the solvent gave a mixture of oxime alcohols (380 mg) as an oil, which were purified by column chromatography (silica gel, toluene/EtOAc = 5/1~4/1) to give (*S*)-**4b** (211 mg, 47%) and (*S*)-**4c** (54 mg, 12%), respectively.

(*S*)-4b: R_f = 0.37 (toluene/EtOAc = 5/1), $[\alpha]_D^{22}$ +19.2 (C 1.35, $CHCl_3$), ^{1}H NMR(400 MHz, $CDCl_3$) δ 7.39 (d, *J* = 4.8 Hz, 1H), 4.31-4.26 (m, 1H), 3.86 (s, 3H), 2.36 (d, *J* = 4.0 Hz, 1H), 2.00-1.85 (m, 2H).; ^{13}C NMR(100 MHz, $CDCl_3$) δ 151.3, 141.2, 128.4, 125.9, 68.4, 61.6, 36.7, 31.0; HRMS (FAB^+, $[M+H]^+$) *m/z* calcd for $[C_{11}H_{16}NO_2]^+$: 194.1181 found: 194.1177.

(*S*)-4c: R_f=0.27(toluene/EtOAc = 5/1), $[\alpha]_D^{21}$ -51.1 (C 0.80, $CHCl_3$), ^{1}H NMR(400 MHz, $CDCl_3$) δ 7.39 (d, *J* = 4.8 Hz, 1H), 4.31-4.26 (m, 1H), 3.86 (s, 3H), 2.36 (d, *J* = 4.0 Hz, 1H), 2.00-1.85 (m, 2H); ^{13}C NMR(100 MHz, $CDCl_3$) δ 151.3, 141.2, 128.4, 125.9, 68.4, 61.6, 36.7, 31.0.

(*R*)-**4b** was obtained from (*R*)-**4a** in 44% yield; $[\alpha]_D^{21}$ -18.7 (c 1.27, $CHCl_3$).

(*R*)-**4c** was obtained from (*R*)-**4a** in 11% yield; $[\alpha]_D^{21}$ +52.5 (c 0.54, $CHCl_3$).

*4.1.13. (S)-2-(Benzyloxy)-4-phenylbutanal [**5a**]*.

MeI (0.75 mL, 12.0 mmol) was added to a mixture of (*S*)-**3a** (414 mg, 1.20 mmol) and $NaHCO_3$ (1.26 g, 15.0 mmol) in an aqueous MeCN/water (10 mL/2 mL) at room temperature and the resulting mixture was stirred for 24 h. The reaction mixture was diluted with EtOAc (30 mL), washed with sat. aq. $Na_2S_2O_3$ (15 mL) and brine (20 mL x 2). Drying over $MgSO_4$ and concentration *in vacuo* provided **5a** (288 mg, 94% yield) as an colorless oil; $[\alpha]_D^{22}$ -80.1 (c 1.50, $CHCl_3$): ^{1}H NMR(500 MHz, $CDCl_3$) δ 9.65 (bs, 1H), 7.45-7.15 (m, 10H), 4.68 (d, *J* = 11.6 Hz, 1H), 4.54 (d, *J* = 11.6 Hz, 1H), 3.76 (t, *J* = 5.8 Hz, 1H), 2.85-2.68 (m, 2H), 2.10-1.95 (m, 2H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.4, 140.8, 137.2, 128.5, 128.4, 128.0, 126.1, 82.5, 72.5, 31.6, 30.8; HRMS (FAB^+, $[M+Na]^+$) *m/z* calcd for $[C_{17}H_{18}NaO_2]^+$: 277.1204 found: 277.1215.

*4.1.14. (S)-2-(Benzyloxy)-4-phenylbutyl benzoate [**5a-1**]*.

Aldehyde **5a** (288 mg) was reduced with $NaBH_4$ (43 mg, 1.13 mmol) in MeOH (3 mL) at room temperature for 10 min. The reaction mixture was extracted with toluene (20 mL) and water (10 mL). Drying over anhydrous $MgSO_4$, filtration, and evaporation of the solvent gave alcohol, which was treated with benzoyl chloride (0.35 mL, 422 mg, 3.0 mmol) /pyridine (1 mL) at room temperature for 2 h. The reaction mixture was distributed between toluene (20 mL) and sat. aq. $NaHCO_3$ (20 mL). The organic layer was washed with brine (10 mL x 2), dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*, affording a crude benzoate, which was purified by column chromatography (silica gel, *n*-hexane/EtOAc=12/1) to provide **5a-1** (345 mg, 80% yield) as a colorless oil. $[\alpha]_D^{21}$ -11.7 (*c* 1.04, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, *J* = 7.6 Hz, 2H), 7.60-7.16 (m, 8H), 4.74 (d, *J* = 11.6 Hz, 1H), 4.60 (d, *J* = 11.6 Hz, 1H), 4.49 (dd, *J* = 11.6, 4.0 Hz, 1H), 4.37 (dd, *J* = 11.6, 5.8 Hz, 1H), 3.79-3.74 (m, 1H), 2.87-2.81 (m, 1H), 2.74-2.68 (m, 1H), 2.05-1.92 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.3, 141.6, 138.2, 132.9, 129.9, 129.5, 128.3, 127.8, 127.6, 125.8, 76.0, 66.2, 33.6, 31.4; HRMS (FAB^+, $[M+H]^+$) *m/z* calcd for $[C_{24}H_{25}O_3]^+$: 361.1804 found: 361.1802.

Chiral HPLC: Chiralpak IB, (254 nm, *n*-hexane/2-propanol=100/1, 0.6 ml/min, 254 nm, racemate; t_R 14.2 min and t_R 15.4 min). **5a-1**: t_R 14.2 min, >98% ee

*4.1.15. (S)-2-((tert-Butyldimethylsilyl)oxy)-4-phenylbutanal [**5b**]*.

MeI (0.62 mL, 10.0 mmol) was added to a mixture of (*S*)-**3b** (369 mg, 1.0 mmol) and

$NaHCO_3$ (1.26 g, 15.0 mmol) in an aqueous MeCN/water (10 mL/2 mL) at room temperature and the resulting mixture was stirred for 24 h. The reaction mixture was diluted with EtOAc (30 mL), washed with sat. aq. $Na_2S_2O_3$ (15 mL) and brine (20 mL x 2). Drying over $MgSO_4$ and concentration *in vacuo* provided a crude aldehyde, which was purified by short-path column chromatography (silica gel, toluene) to afford **5b** (223 mg, 80%); $[\alpha]_D^{23}$-15.0 (*c* 1.37, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.60 (bs, 1H), 7.35-7.20 (m, 5H), 4.03-4.00 (m, 1H), 2.75-2.65 (m, 2H), 2.05-1.90 (m, 2H), 0.95(s, 9H), 0.11 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.8, 141.1, 128.3, 126.0, 77.0, 34.4, 30.7, 25.8, 18.1, -4.70, -5.0; HRMS (FAB^+, $[M+H]^+$) *m/z* calcd for $[C_{16}H_{27}O_2Si]^+$: 279.1780 found: 279.1761.

*4.1.16. (S)-4-Phenylbutane-1,2-diyl dibenzoate [**5b-1**].*

The aldehyde **5b** (220 mg, 0.79 mmol) was then reduced with $NaBH_4$ (38 mg, 1.0 mmol) in EtOH (5.0 mL) at room temperature for 10 min. The reaction mixture was distributed between toluene (15 mL) and water (30 mL). The organic layer was washed with brine (30 mL) and dried over anhydrous $MgSO_4$. Filtration and evaporation of the solvent *in vacuo* gave a mixture of alcohols (primary and secondary alcohols), which was treated with TBAF (1.0 M in THF, 2.0 mL, 2.0 mmol) at room temperature for 30 min. The mixture was distributed between EtOAc (15 mL) and brine (20 mL). The organic layer was washed with brine (20 mL), dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo* furnished 1,2-diol (118 mg, 0.71 mmol), which was treated with BzCl (0.56 mL, 4.84 mmol) in pyridine (3.0 mL) at 5 ºC. The mixture was stirred at room temperature for 0.5 h, distributed between EtOAC (20 mL) and water (30 mL). The extract was sequentially washed with 1 M HCl (15 mL x 2), sat. aq. $NaHCO_3$ (15 mL) and brine (15 mL), dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The residue was purified by short-path distillation (150 ºC/1 mmHg) to afford 1,2-dibenzoate **5b-1**(239 mg, 90% yield) as a colorless oil: $[\alpha]_D^{21}$-12.4º (*c* 1.58, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (d, *J* = 7.9 Hz, 2H), 8.00 (d, *J* = 7.6 Hz, 2H), 7.59-7.53 (m, 2H), 7.46-7.40 (m, 4H), 7.30-7.27 (m, 2H), 7.26-7.17 (m, 3H), 5.55-5.51 (m, 1H), 4.60-4.56 (m, 1H), 4.52-4.48 (m, 1H), 2.86-2.74 (m, 2H), 2.26-2.18 (m, 1H), 2.15-2.09 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.1, 166.0, 140.8, 133.0, 130.0, 129.6, 128.4, 128.3, 126.1, 71.6, 65.5, 32.6, 31.5; HRMS (FAB^+, $[M+H]^+$) *m/z* calcd for $[C_{24}H_{23}O_4]^+$: 375.1596 found: 375.1589.

Chiral HPLC: Chiralpak IA, (254 nm, *n*-hexane/2-propanol=50/1, 1.0 ml/min, racemate; t_R 9.1 min and t_R 11.4 min). **5b-1**: t_R 9.09 min, >98% ee

*4.1.17. (S)-(3,4-Dimethoxybutyl)benzene [**6**].*

Dibenzoate **5b-1** was converted to dimethyl ether **6** via alkaline hydrolysis followed by etherification with MeI/NaH/DMF in good yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35-7.25 (m, 5H), 3.43 (d, *J*=5.5 Hz, 1H), 3.42 (s, 3H), 3.37 (s, 3H), 3.35-3.32 (m, 1H), 2.77-2.63 (m, 2H), 1.86-1.81 (m, 2H); $[\alpha]_D^{20}$ + 5.62 (*c* 0.83, $CHCl_3$); [(*R*)-**6**: lit $[\alpha]_D^{25}$ -4.73 (*c* 1.14, $CHCl_3$) (*Ref:* Vikhe, Y. S.; Hande, S. M.; Kawai, N.; Uenishi, J. *J. Org. Chem.* **2009**, *74*, 5174–5180.)

*4.1.18. (5S)-5-(1,3-Dithian-2-yl)tetrahydrofuran-2-ol [**7**].*

In an autoclave, a mixture of (*S*)-**1** (942 mg, 5.34 mmol), $Rh(acac)(CO)_2$ (28 mg, 0.11 mmol) and XANTPHOS (124 mg, 0.214 mmol) in toluene (10 mL) was heated at 50 °C for 4 h under a pressure of H_2/CO (1:1)(5 kg/cm^2). After cooling to room temperature, the yellow-green mixture was passed through florisil pad. The filtrate was concentrated *in vacuo* to afford a brown oil (976 mg), which was purified by short column chromatography (silica gel, *n*-hexane/EtOAc=2/1~1/1 containing 1% Et_3N) provided hemiacetal **7** (767 mg, 70% yield) accompanied by a small amount of complex mixtures (<0.3%): $[\alpha]_D^{24}$ +28.5 (*c* 1.09, $CHCl_3$); FTIR (KBr): 3417, 2901, 2820, 1774, 1463, 1076, 1054, 981, 781, 648 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.64 (bs, 0.6H), 5.53 (bs, 0.4H), 4.50-4.45 (m, 0.6H), 4.29-4.22 (m, 0.4H), 4.17 (d, *J* = 7.3 Hz, 0.4H), 4.11 (d, *J* = 5.8 Hz, 0.6H), 2.93-2.82 (m, 4H), 2.75 (bs, 0.4H), 2.54 (bs, 0.6H), 2.27-1.89 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 98.8, 98.4, 81.0, 79.4, 77.8, 52.0, 51.3, 33.5, 32.7, 29.4, 29.3, 28.8, 28.7, 27.7, 27.2, 25.8, 25.7; HRMS (FAB$^+$, $[M\text{-}OH]^+$) *m/z* calcd for $[C_8H_{13}OS_2]^+$: 189.0408 found: 189.0415.

*4.1.19. General protocol for hydroformylation of (S)-**2**.*

*4.1.19-1. (S)-4-(Benzyloxy)-4-(1,3-dithian-2-yl)butanal [**8a**].*

In an autoclave, a mixture of (*S*)-**2a** (1.0 mmol), $Rh(acac)(CO)_2$ (5 mg, 0.02 mmol) and XANTPHOS (23 mg, 0.04 mmol) in toluene (5 mL) was heated at 50 °C for 20 h under a pressure of H_2/CO (1:1)(5 kg/cm^2). Upon cooling to room temperature, evaporation of the solvent gave a dark oil, which was purified by column chromatography (silica gel, *n*-hexane/EtOAc = 5/1) to furnish linear aldehyde **8a** (228 mg, 77% yield) as a pale yellow oil: $[\alpha]_D^{22}$ -45.0 (*c* 1.46, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.69 (bs, 1H), 7.38-7.25 (m, 5H), 4.75 (d, *J* = 11.5 Hz, 1H), 4.50 (d, *J* = 11.0 Hz, 1H), 4.37 (d, *J* = 5.0 Hz, 1H) 3.67-3.49 (m, 1H), 2.92-2.83 (m, 4H), 2.57-2.44 (m, 2H), 2.15-2.02 (m, 3H), 1.94-1.87 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.6, 137.5, 128.2, 128.0, 126.7, 79.4, 72.2, 51.6, 39.7, 30.3, 26.0, 24.7;

HRMS (FAB$^+$, [M+H]$^+$) *m/z* calcd for [$C_{15}H_{21}O_2S_2$]$^+$: 297.0983 found: 297.0983.
Branched aldehyde **9a** (<3%) was observed as a diastereomeric mixture by NMR analysis, which was contaminated with inseparable unidentified compounds.

*4.1.19-2. (S)-4-((tert-Butyldimethylsilyl)oxy)-4-(1,3-dithian-2-yl)butanal [**8b**].*

Synthesis of **8b** was carried out starting from (*S*)-**2b** (145 mg, 0.50 mmol) as described for **8a**: Purified by column chromatography (silica gel, *n*-hexane/EtOAc=10/1-7/1) to give **8b** (116 mg, 73% yield) as a colorless oil; $[\alpha]_D^{25}$ -18.1 (*c* 1.28, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.78 (bs, 1H), 4.15 (d, *J* = 5.5 Hz, 1H), 3.94-3.91 (m, 1H), 2.89-2.79 (m, 4H), 2.60-2.50 (m, 2H), 2.12-2.01 (m, 3H), 1.90-1.84 (m, 1H), 0.91 (s, 9H), 0.15 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.9, 73.2, 53.9, 39.3, 30.5, 30.3, 26.7, 26.2, 25.8, 18.1, -4.5; HRMS (FAB$^+$, [M+H]$^+$) *m/z* calcd for [$C_{14}H_{29}O_2S_2Si$]$^+$: 321.1378 found: 321.1384

*4.1.19-3. (S)-4-((tert-Butyldiphenylsilyl)oxy)-4-(1,3-dithian-2-yl)butanal [**8c**].*

Synthesis of **8c** was carried out starting from (*S*)-**2c** (414 mg, 1.0 mmol) as described for **8a**: Purification by column chromatography (silica gel, *n*-hexane/EtOAc=10/1-7/1) gave **8c** (361 mg, 81% yield) as a pale yellow viscous oil; $[\alpha]_D^{22}$ -40.2 (*c* 1.27, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.56 (bs, 1H), 7.77 (d, *J* = 7.0 Hz, 2H), 7.68 (d, *J* = 6.8 Hz, 2H), 7.47-7.38 (m, 6H), 4.00-3.97 (m, 2H), 2.81 (d, *J* = 14.1 Hz, 1H), 2.70 (d, *J* = 14.0 Hz, 1H), 2.63-2.48 (m, 3H), 2.40-2.34 (m, 1H), 1.98-1.94 (m, 3H), 1.84-1.76 (m, 1H), 1.09 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.0, 135.8, 135.6, 133.3, 133.0, 129.6, 127.4, 127.3, 73.9, 54.5, 39.5, 30.5, 30.0, 26.8, 26.3, 26.0, 19.2; HRMS (FAB$^+$, [M+H]$^+$) *m/z* calcd for [$C_{24}H_{33}O_2S_2Si$]$^+$: 445.1691 found: 445.1713.
Branched aldehyde **9c** (<4%) was observed as a diastereomeric mixture by NMR analysis, which was contaminated with inseparable unidentified compounds.

*4.1.20. (S)-(1,3-Dithian-2-yl)((R)-3-phenyl-4,5-dihydroisoxazol-5-yl)methanol [**11**].*

A solution of EtMgBr (3.0 M in Et_2O, 8.6 ml, 25.8 mmol) was added to a solution of (*S*)-**1** (1.516 g, 8.6 mmol) and isopropanol (2.17 mL, 28.4 mmol) in CH_2Cl_2 (50 mL) at 5 ºC. After stirring for 10 min, a solution of benzohydroximinoyl chloride (**10**) (2.0 g, 12.9 mmol) in CH_2Cl_2 (30 mL) was added to the reaction mixture at 5 °C over a period of 0.5 h, and then allowed to warm to room temperature over the next 22 h. The reaction was terminated by addition of sat. aq. NH_4Cl (100 mL). The organic layer was washed with brine (30 mL x 2),

dried over $MgSO_4$, filtered and concentrated *in vacuo* to give a crude solid, which was washed with toluene to give **11** (1.94g, 76%) as a white solid. mp 189.7-189.9 ºC, $[\alpha]_D^{20}$ -151.6 (*c* 1.10, $CHCl_3$); FTIR (KBr): 3520, 2953, 2907, 1598, 1420, 1092, 912, 764, 543 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.69-7.67 (m, 2H), 7.41-7.39 (m, 3H), 5.24-5.20 (m, 1H), 4.21 (d, *J* = 8.6 Hz, 1H), 3.89-3.86 (m, 1H), 3.53-3.86 (m, 2H), 2.99-2.92 (m, 2H), 2.81-2.73 (m, 2H), 2.68 (d, *J* = 6.1 Hz, 1H), 2.12-2.09 (m, 1H), 2.05-2.01 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.0, 130.2, 129.2, 128.7, 126.8, 79.5, 73.2, 47.8, 37.7, 28.0, 27.5, 25.4; Anal. Calcd. for $C_{14}H_{17}NO_2S_2$: C, 56.92; H, 5.80; N, 4.74; Found: C, 56.67; H, 5.65; N, 4.45; HRMS (FAB^+, $[M+H]^+$) *m/z* calcd for $[C_{14}H_{18}NO_2S_2]^+$: 296.0779 found: 296.0789.

*4.1.21. (S)-(1,3-Dithian-2-yl)((R)-3-phenyl-4,5-dihydroisoxazol-5-yl)methyl acetate [**12**].*

The alcohol **11** (98.6 mg, 0.334 mmol) was treated with pyridine/Ac_2O (0.5 mL each) at room temperature for 1 h, and the reaction was quenched by addition of sat. aq. $NaHCO_3$ (20 mL). After stirring for 30 min, the mixture was distributed between toluene (30 mL) and sat. aq. $NaHCO_3$ (20 ml). The organic layer was sequentially washed with 1 N HCl (20 mL), sat. aq. $NaHCO_3$ (20 mL) and brine (20 mL). Drying over anyhydrous $MgSO_4$ and evaporation of the solvent *in vacuo* afforded **12** (113 mg, 97%) as a white solid. mp 110.2-110.8 ºC, $[\alpha]_D^{22}$ -93.3 (*c* 1.56, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.66-7.65 (m, 2H), 7.42-7.40 (m, 3H), 5.51-5.47 (m, 1H), 5.43 (d, *J* = 11.5 Hz, 1H), 4.12 (d, *J* = 10.1 Hz, 1H), 3.52 (dd, *J* = 16.8, 11.3 Hz, 1H), 3.09 (dd, *J* = 16.8, 6.8 Hz, 1H), 3.02-2.96 (m, 2H), 2.73-2.69 (m, 1H), 2.62-2.58 (m, 1H), 2.07-2.02 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.8, 156.2, 130.1, 129.0, 128.6, 126.5, 78.2, 72.7, 43.4, 37.3, 26.5, 26.3, 25.0, 20.6; HRMS (FAB^+, $[M+H]^+$) *m/z* calcd for $[C_{16}H_{20}NO_3S_2]^+$: 338.0885 found: 338.0875.

*4.1.22. (1S,2R)-4-Amino-1-(1,3-dithian-2-yl)-4-phenylbutane-1,2-diol [**13**].*

A mixture of **11** (1.94 g, 6.57 mmol) and zinc powder (10.6 g, 162 mmol) in a 50% aqueous acetic acid (20 mL) was heated at 60 ºC for 3h. The mixture was filtered through Celite 545 and the filtrate was concentrated *in vacuo*. The residue was distributed between CH_2Cl_2 (50 mL) and 1 M NaOH (30 mL). The organic layer was washed with brine (50 mL), dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*, providing **13** (1.39 g, 71%) as a mixture of two diastereomers. $[\alpha]_D^{23}$ +6.84 (*c* 1.13, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.38-7.35 (m, 3H), 7.28-7.26 (m, 2H), 4.44-4.42 (m, 0.3H), 4.36 (d, *J* = 9.5 Hz, 0.6H), 4.25 (d, *J* = 8.2 Hz, 0.6H), 4.18-4.08 (m, 1.3H), 3.65 (d, *J* = 7.6 Hz, 0.3H), 3.60 (d, *J* = 7.9 Hz, 0.6H), 2.93-2.70 (m, 4H),

2.12-1.80 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.3, 145.2, 128.8, 128.5, 127.2, 127.1, 125.9, 125.4, 74.6, 74.3, 70.5, 67.9, 55.6, 53.0, 49.2, 49.0, 41.6, 40.9, 28.7, 28.4, 28.3, 28.0, 25.7, 25.6; HRMS (FAB^+, $[M+H]^+$) *m/z* calcd for $[C_{14}H_{22}NO_2S_2]^+$: 300.1092 found: 300.1094.

*4.1.23. (1S,2R)-4-Acetamido-1-(1,3-dithian-2-yl)-4-phenylbutane-1,2-diyl diacetate [**14**]*.

Compound **13** (448 mg, 1.50 mmol) was treated with Ac_2O/pyridine (2 mL each) in the presence of DMAP (10 mg) at room temperature for 2 h. The reaction mixture was concentrated *in vacuo* and the residue was distributed between toluene (30 mL) and sat. aq. $NaHCO_3$ (20 mL). The organic layer was sequentially washed with 1 N HCl (10 mL x 2), sat. aq. $NaHCO_3$ (20 mL) and brine (20 mL). Drying over anhydrous $MgSO_4$ followed by concentration *in vacuo* gave **14** (553 mg) as a brown oil, which was purified by column chromatography (silica gel, toluene/EtOAc=1/2~1/4) to give less polar fraction (369 mg, 58%) as white foam and polar fraction (191 mg, 30 %) as a colorless oil.

Less polar fraction: R_f=0.47 (toluene/EtOAc=1/2), $[\alpha]_D^{22}$ -26.7 (*c* 1.12, $CHCl_3$); FTIR (KBr): 3297, 2938, 1741, 1653, 1540, 1373, 1224, 1027, 702 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47-7.20 (m, 5H), 6.07 (d, *J* = 8.6 Hz, 1H), 5.84 (d, *J* = 9.8 Hz, 1H), 5.53-5.50 (m, 1H), 5.28-5.20 (m, 1H), 3.67 (d, *J* = 9.8 Hz, 1H), 3.20-3.00 (m, 2H), 2.60-2.49 (m, 2H), 2.16 (s, 3H), 2.11-1.90 (m, 4H), 2.04 (s, 3H), 2.02 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.6, 170.3, 169.5, 141.5, 128.6, 127.4, 126.1, 70.5, 70.2, 49.2, 42.4, 37.9, 25.5, 24.8, 23.2, 20.9, 20.7; HRMS (FAB^+, $[M+H]^+$) *m/z* calcd for $[C_{20}H_{27}NO_5S_2]^+$: 426.1409 found: 426.1414.

Polar fraction: R_f = 0.30 (toluene/EtOAc=1/2); $[\alpha]_D^{24}$ +59.9 (*c* 1.15, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40–7.26 (m, 5H), 6.21 (d, *J* = 7.7 Hz, 1H), 5.43-5.41 (m, 1H), 5.31 (d, *J* = 9.5 Hz, 1H), 5.14-5.09 (m, 1H), 3.64 (d, *J* = 9.5 Hz, 1H), 2.88-2.83 (m, 1H), 2.53-2.41 (m, 3H), 2.25-2.20 (m, 1H), 2.25 (s, 3H), 2.14-2.08 (m, 1H), 2.03 (s, 3H), 2.01 (s, 3H), 1.95-1.91 (m, 2H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.8, 170.3, 169.3, 140.5, 128.8, 127.6, 126.6, 71.6, 69.9, 50.2, 43.2, 36.6, 26.2, 25.6, 24.9, 23.2, 20.8.

Acknowledgements

This work was assisted financially by a research grant from Nippon Chemiphar Inc.

Supplementary data

Supplementary data related to this article can be found at

References and notes

1. Petasis, N. A.; Zavialov, I. A. *J. Am. Chem. Soc.* **1998**, *120*, 11798–11799. (b) Candeias, N. R.; Montalbano, F.; Cal, P. M. S. D.; Gois, P. M. P. *Chem. Rev.* **2010**, *110*, 6169–6193. (c) Muncipinto, G.; Moquist, P. N.; Schreiber, S. L.; Schaus, S. E. *Angew. Chem. Int. Ed.* **2011**, *50*, 8172-8175. (d) Norsikian, S.; Soulé, J.-F.; Cannillo, A.; Guillot, R.; Tran Huu Dau, M.-E.; Beau, J.-M. *Org. Lett.* **2012**, *14*, 544–547. (e) Cannillo, A.; Norsikian, S.; Retailleau, P.; Tran Huu Dau, M.-E..; Iorga, B. I.; Beau, J.-M. *Chem. Eur. J.* **2013**, *19*, 9127–9131.

2. (a) Kobori, Y.; Myles, D. C.; Whitesides, G. M. *J. Org. Chem.* **1992,** 57, 5899–5907. (b) Humphrey, A. J.; Turner, N. J.; McCague, R.; Taylor, S. J. C. *J. Chem. Soc., Chem. Commun.* **1995**, 2475–2476. (c) Effenberger, F.; Null, V.; Ziegler, T. *Tetrahedron Lett.* **1992**, *33*, 5157–5160, and references cited therein.

3. (a) Corey, E. J.; Jones, G. B. *Tetrahedron Lett.* **1991**, *32*, 5713–5716. (b) Alexakis, A.; Tranchier, J.-P.; Lensen, N.; Mangeney, P. *J. Am. Chem. Soc.* **1995**, *117*, 10767–10768. (c) Colombo, L.; Giacomo, M. D. *Tetrahedron Lett.* **1999**, *40*, 1977–1980. (d) Enders, D.; Reinhold, U. *Liebigs Annalen* **1996**, 11-26. (e) Vettel, S.; Lutz, C.; Diefenbach, A.; Haderlein, G.; Hammerschmidt, S.; Kühling, K.; Mofid, M.-R.; Zimmermann, T.; Knochel, P. *Tetrahedron: Asymmetry* **1997**, *8*, 779–800. (f) Kobayashi, S.; Ueno, M.; Suzuki, R.; Ishitani, H. *Tetrahedron Lett.* **1999**, *40*, 2175–2178. (g) Davies, S. G.; Hunter, I. A.; Nicholson, R. L.; Roberts, P. M.; Savory, E. D.; Smith, A. D. *Tetrahedron* **2004**, *60*, 7553–7577.

4. (a) Oi, R.; Sharpless, K. B. *Tetrahedron Lett.* **1992**, *33*, 2095–2098. (b) Henderson, I.; Sharpless, K. B.; Wong, C.-H. *J. Am. Chem. Soc.* **1994**, *116*, 558–561.

5. (a) Evans, P.; Leffray, M. *Tetrahedron* **2003**, *59*, 7973–7981. (b) Au, C. W. G.; Pyne, S. G. *J. Org. Chem.* **2006**, *71*, 7097–7099.

6. (a) Annunziata, R.; Cinquini, M.; Cozzi, F.; Raimondi, L. *Tetrahedron* **1988**, *44*, 4645–4652. (b) Annunziata, R.; Cinquini, M.; Cozzi, F.; Giaroni, P.; Raimondi, L. *Tetrahedron Lett.* **1991**, *32*, 1659–1662. (c) Zhang, W.; Sato, K.; Kato, A.; Jia, Y.-M.; Hu, X.-G.; Wilson, F. X.; van Well. R.; Horne, G.; Fleet, G. W. J.; Nash, R. J.; Yu, C.-Y. *Organic Lett.* **2011**, *13*, 4414–4417.

7. (a) Miyaura, N.; Ishiyama, T.; Sasaki, H.; Ishikawa, M.; Satoh, M.; Suzuki, A. *J. Am. Chem. Soc.* **1989**, *111*, 314–321. (b) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457–2483.

8. (a) Breit, B.; Seiche, W. *Synthesis* **2001**,1–36. (b) Breit, B. *Acc. Chem. Res.* **2003**, *36*, 264–275.

9. (a) Uemura, M.; Nishimura, H.; Hayashi, Y. *Tetrahedron Lett*. **1990**, *31*, 2319-2322. (b) Uemura, M.; Nishimura, H.; Minami, T.; Hayashi, Y. *J. Am. Chem Soc.* **1991**, *113*, 5402-5410. (c) Grigg, R.; Kennewell, P; Savic, V. Tetrahedron **1994,** *50*, 5489-5494. (d) Cuny, G. D.; Buchwald, S. L. *J. Am. Chem. Soc*. **1993**, *115*, 2066-2068.

10. (a) Mandai, T.; Oshitari, T.; Susowake, M. *Synlett* **2002**, 1665–1668. (b) Oshitari, T.; Mandai, T. *Synlett* **2003**, 2374–2376, and references cited therein.

11. For reproducible results, CAL-B was dried in vacuo (<0.5 mmHg) at room temperature for 8 h. Although lipase-catalyzed acylation can be conducted in a non-aqueous environment, a minimum amount of water is necessary and preferably should be optimized. Please see the following reference; Orrenius, C.; Norin, T.; Hult, K.; Carrea, G. *Tetrahedron: Asymmetry* **1995**, *6*, 3023-3030.

12. The compound (*R*)-**1**-OAc was transesterified (cat. K_2CO_3/MeOH) to the corresponding alcohol (*R*)-**1**. HPLC analysis: Chiralpak IA (*n*-hexane/2-propanol=9/1, 1.0 mL/min, 254 nm), (*S*)-**1**: t_R 10.8 min (>98% ee) and (*R*)-**1**: t_R 12.0 min (96% ee).

13. HPLC analysis: Chiralpak IA (*n*-hexane/2-propanol=9/1, 1.0 mL/min, 254 nm), (*S*)-**1**: t_R 10.9 min (76% ee) and (*R*)-**1**: t_R 12.2 min (>98% ee).

14. J. A. Soderquist, A. Negron, *Org. Synth. Coll. Vol. IX*, **1998**, 95–99.

15. Hayashi, T.; Konishi, M.; Kumada, M. *Tetrahedron Lett*. **1979,** 1871–1874.

16. Netherton, M. R.; Dai, C.; Neuschütz, K.; Fu, G. C. *J. Am. Chem. Soc.* **2001**, *123*, 10099–10100.

17. Fetizon, M.; Jurion, M. *J.C.S. Chem. Comm.* **1972**, 382–383.

18. HPLC analysis: Chiralpak IB (*n*-hexane/2-propanol=100/1, 0.6 ml/min, 254 nm), racemate; t_R 14.2 min and t_R 15.4 min, **5a-1**: t_R 14.2 min (>98% ee).

19. HPLC analysis: Chiralpak IA (*n*-hexane/2-propanol=50/1, 1.0 mL/min, 254 nm), racemate: t_R 9.10 min and t_R 11.4 min, **5b-1**: t_R 9.10 min (>98% ee).

20. Vikhe, Y. S.; Hande, S. M.; Kawai, N.; Uenishi, J. *J. Org. Chem.* **2009**, *74*, 5174–5180.

21. (a) Kranenburg, M.; van der Burgt, Y. E. M.; Kamer, P. C. J.; van Leeuwen, P. W. N. M.; Goubitz, K.; Fraanje, J. *Organometallics* **1995**, *14*, 3081–3089. (b) Kamer, C. J. P.; van Leeuwen, P. W. N. M.; Reek, J. N. H. *Acc. Chem. Res.* **2001**, *34*, 895–904. Use of BIPHEPHOS as the ligand resulted in poor linear/branched ratio (2/1~3/1). As for BIPHEPHOS, see: Cuny, G. D.; Buchwald, S. L. *J. Am. Chem. Soc.* **1993**, *115*,

2066–2068.

22. (a) Gothelf, K. V.; Jørgensen, K. A. *Chem. Rev.* **1998**, *98*, 863–909. (b) Litvinovskaya, R. P.; A. Khripach, V. *Russian Chem. Rev.* **2001**, *70*, 405–424.

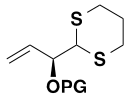
23. Lee, G. A. *Synthesis* **1982**, 508–509. The 1,3-adduct was obtained in 88% in 6:4 syn/anti ratio.

24. (a) Kanemasa, S.; Nishiuchi, M.; Kamimura, A.; Hori, K. *J. Am. Chem. Soc.* **1994**, *116*, 2324-2339. (b) Kanemasa, S. *Synlett* **2002**, 1371–1387. (d) Becker, N.; Carreira, E. M. *Org. Lett.* **2007**, *9*, 3857–3858.

25. In contrast, high *anti*-selectivity (82% dr) was reported for the 1,3-dipolar cycloaddition with *O*-TBDMS protected (±)-**1**. See: Ref. 6(a).

26. Wuts, P. G. M.; Jung, Y. W. *J. Org. Chem.* **1988**, *53*, 5989-5994.

27. The absolute configuration of the NHAc group was not determined.

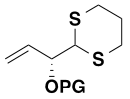


(*S*)-2a: PG=Bn(88%)

(*S*)-2b: PG=$SiMe_2{}^tBu$(95%)

(*S*)-2c: PG=$SiPh_2{}^tBu$(97%)

(1*S*)-2d: PG=CH(Me)OEt(94%)



(*R*)-2a: PG=Bn(85%)

(*R*)-2b: PG=$SiMe_2{}^tBu$(95%)

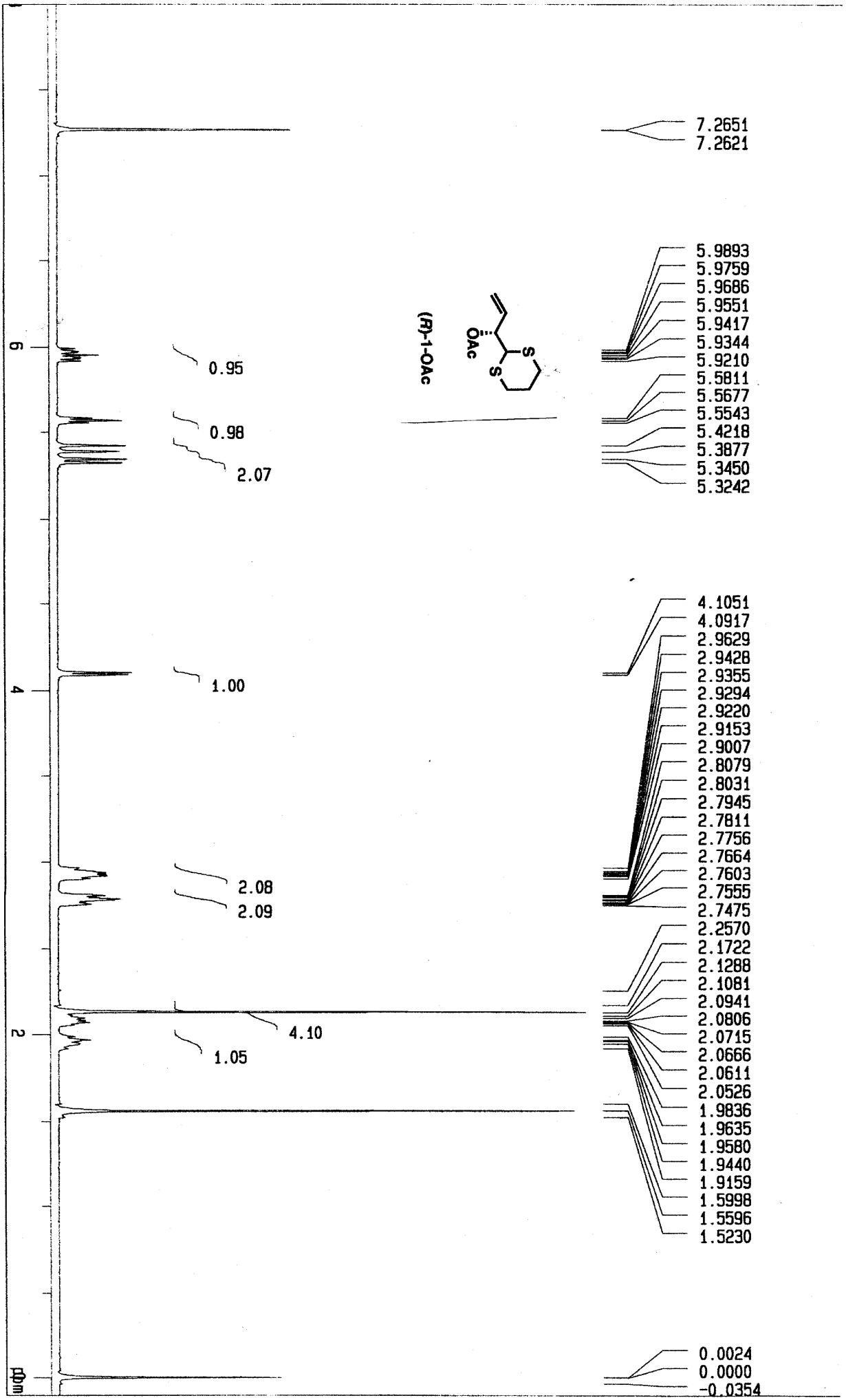
(*R*)-2c: PG=$SiPh_2{}^tBu$(95%)

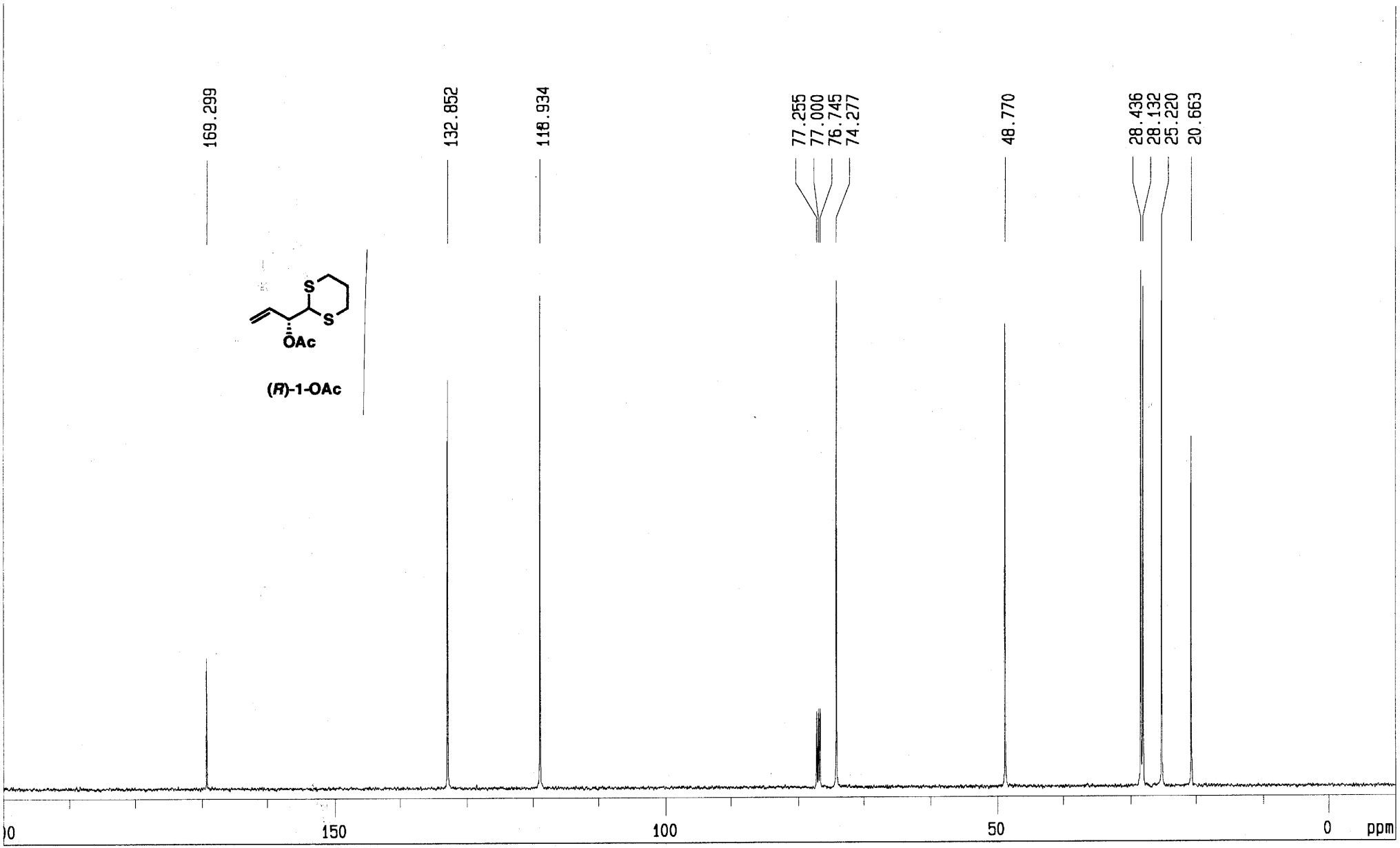
(1*R*)-2d: PG=CH(Me)OEt(96%)

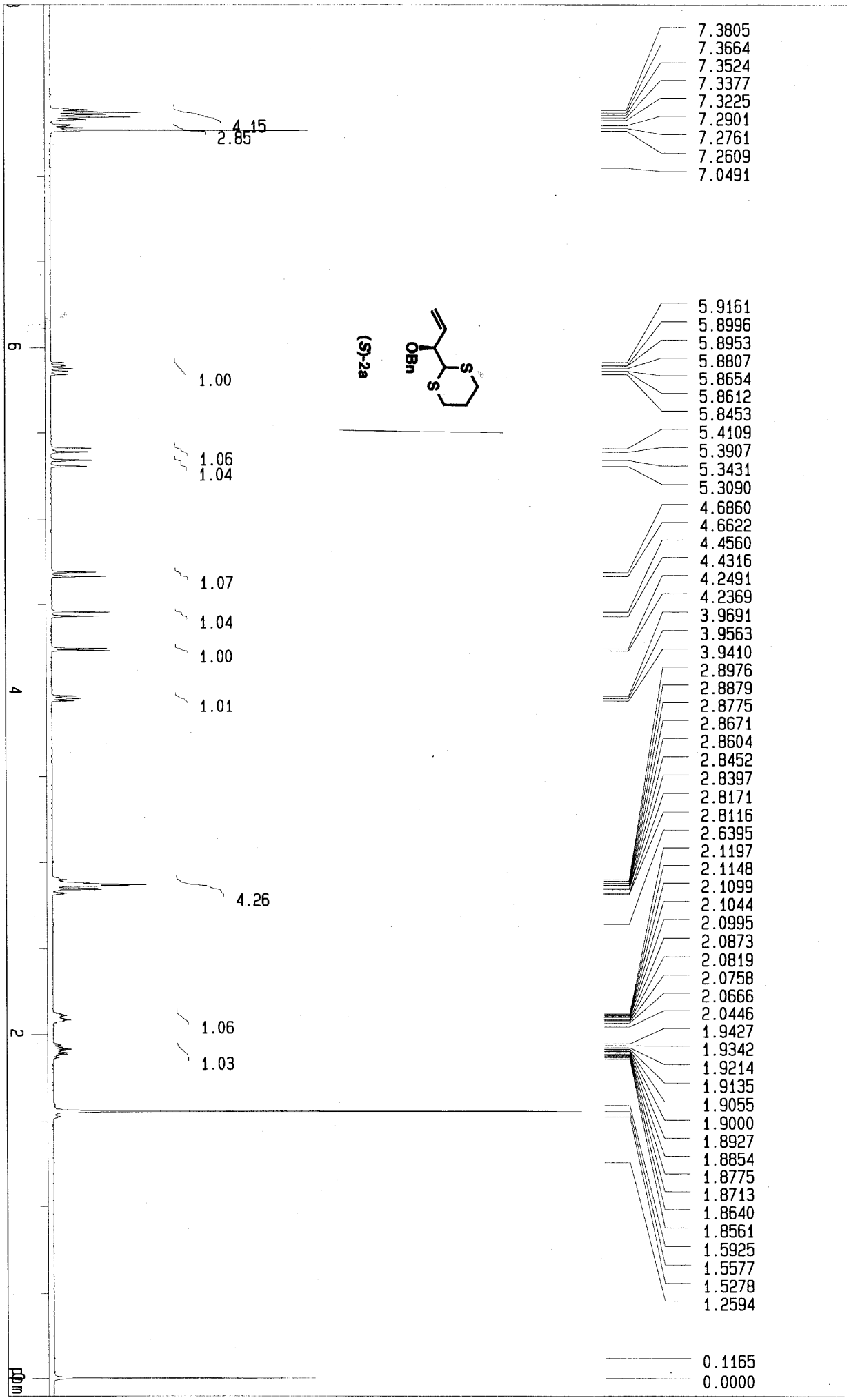
Figure 2. Protected **2.**

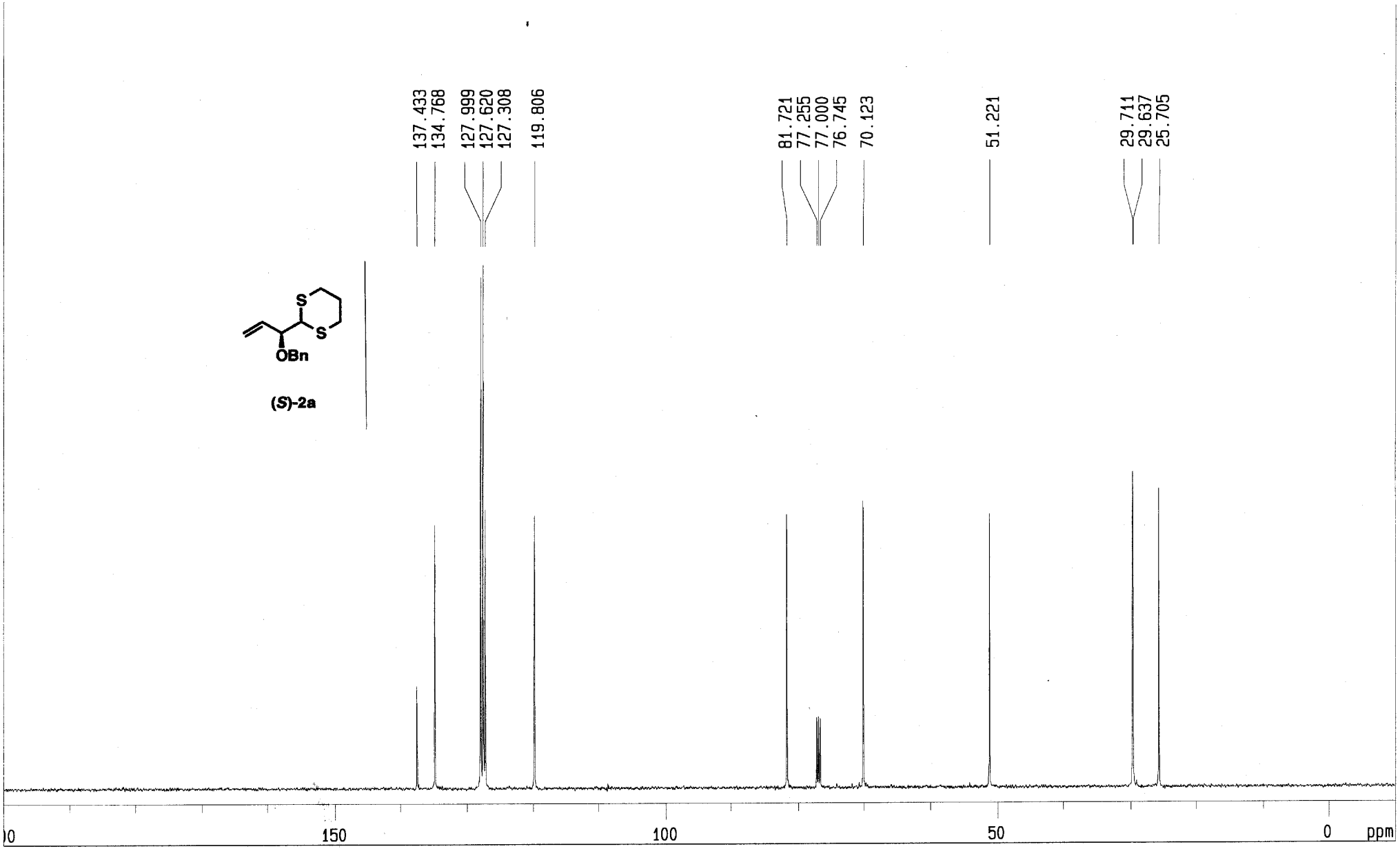
(S)-1
OH
S
S
1.06
1.06
0.94
2.07
2.06
0.96
1.00
1.01
1.03
1.06
ppm
2
4
6
0.0000
1.5834
1.9568
1.9629
1.9659
1.9690
1.9720
1.9781
1.9818
1.9848
1.9909
1.9970
2.0099
2.0690
2.0745
2.0776
2.0831
2.0892
2.0916
2.0977
2.1032
2.1056
2.1118
2.1172
2.1258
2.5224
2.5309
2.7445
2.7524
2.7585
2.7634
2.7726
2.7787
2.7866
2.7921
2.7982
2.7994
2.8055
2.9196
2.9263
2.9336
2.9403
2.9477
2.9544
2.9611
2.9690
2.9751
3.9532
3.9660
4.3669
4.3791
4.3889
4.3980
4.4004
5.2949
5.2974
5.2998
5.3157
5.3181
5.3206
5.4212
5.4237
5.4261
5.4554
5.4578
5.4609
5.9673
5.9795
5.9881
6.0003
6.0015
6.0137
6.0222
6.0344
7.2615
7.2639

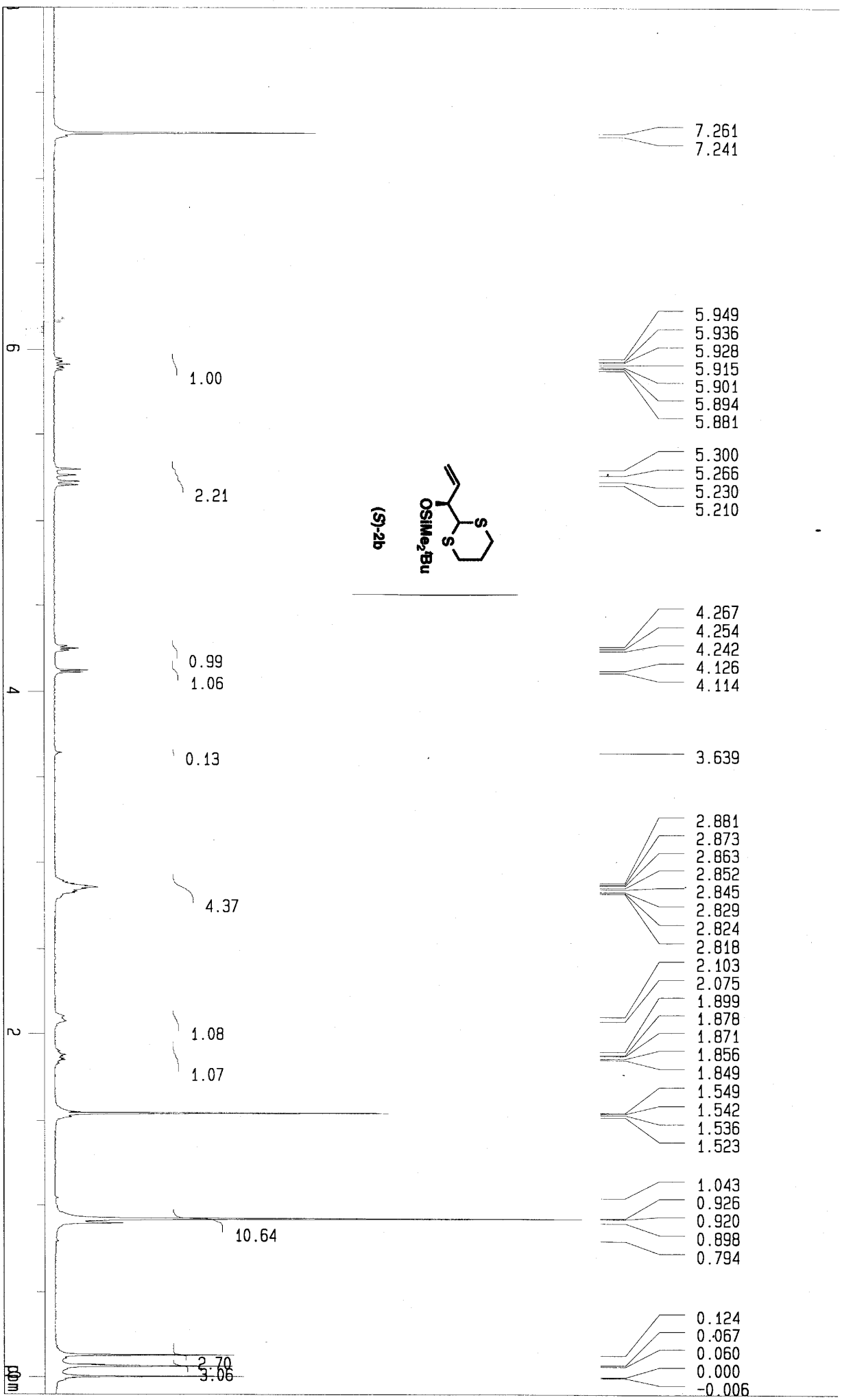
136.833
117.412
77.765
77.510
77.247
73.570
51.994
28.584
28.387
25.607
(S)-1
OH
S
S
ppm
125
100
75
50
25

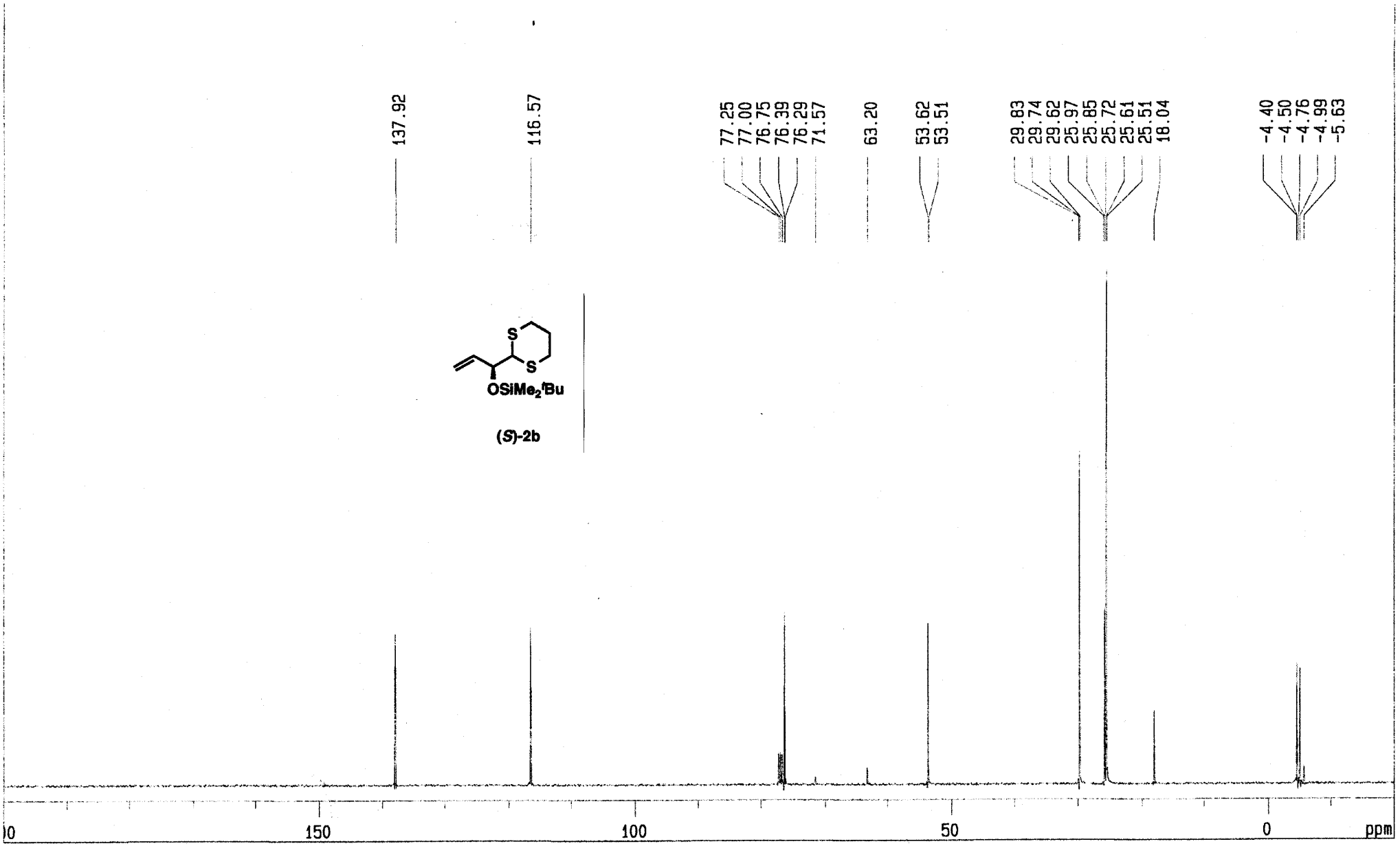

(R)-1-OAc
OAc
S
S
0.95
0.98
2.07
1.00
2.08
2.09
4.10
1.05
7.2651
7.2621
5.9893
5.9759
5.9686
5.9551
5.9417
5.9344
5.9210
5.5811
5.5677
5.5543
5.4218
5.3877
5.3450
5.3242
4.1051
4.0917
2.9629
2.9428
2.9355
2.9294
2.9220
2.9153
2.9007
2.8079
2.8031
2.7945
2.7811
2.7756
2.7664
2.7603
2.7555
2.7475
2.2570
2.1722
2.1288
2.1081
2.0941
2.0806
2.0715
2.0666
2.0611
2.0526
1.9836
1.9635
1.9580
1.9440
1.9159
1.5998
1.5596
1.5230
0.0024
0.0000
-0.0354
6
4
2
0
ppm

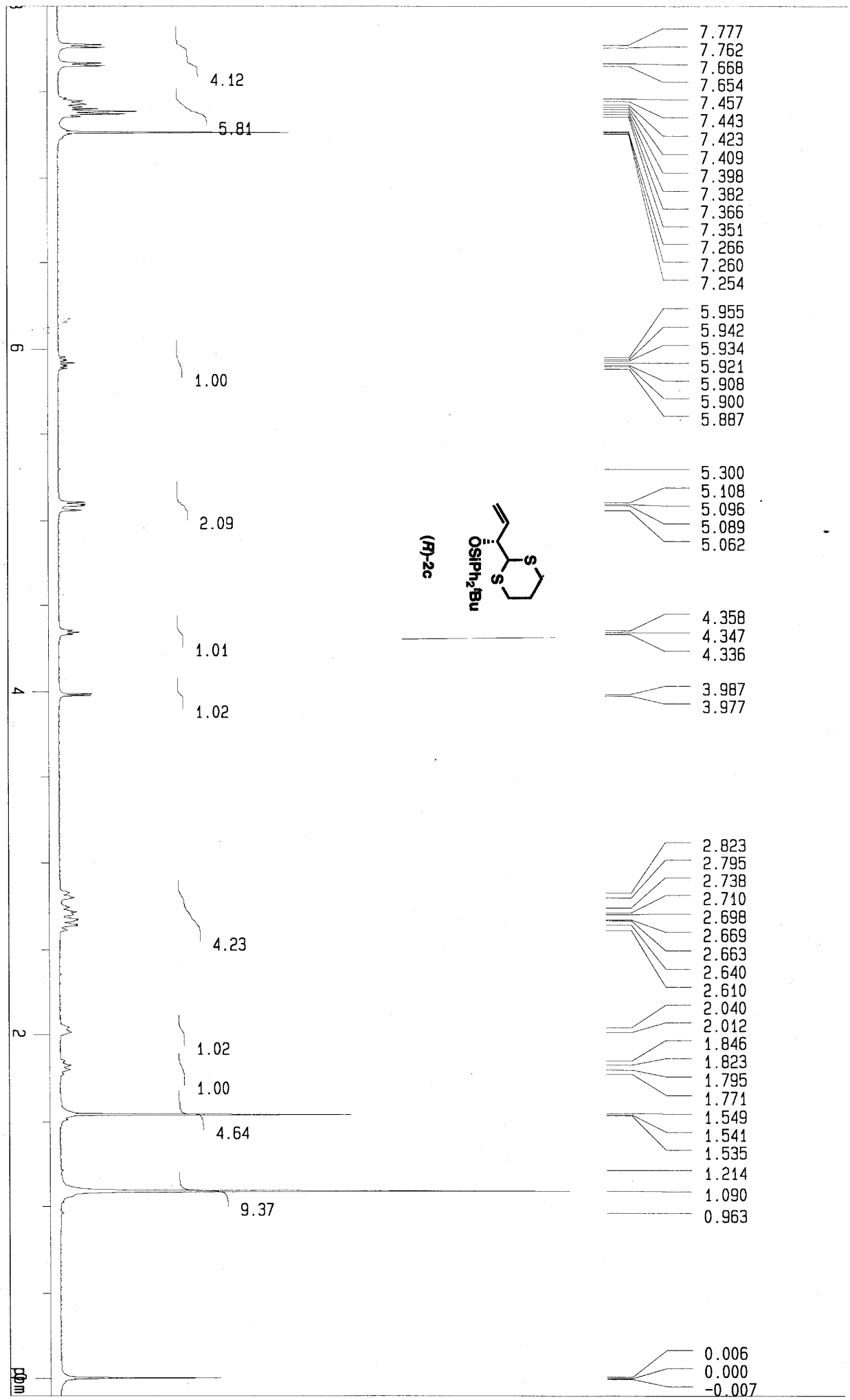

169.299
132.852
118.934
77.255
77.000
76.745
74.277
48.770
28.436
28.132
25.220
20.663
S
S
OAc
(R)-1-OAc
150
100
50
0
ppm

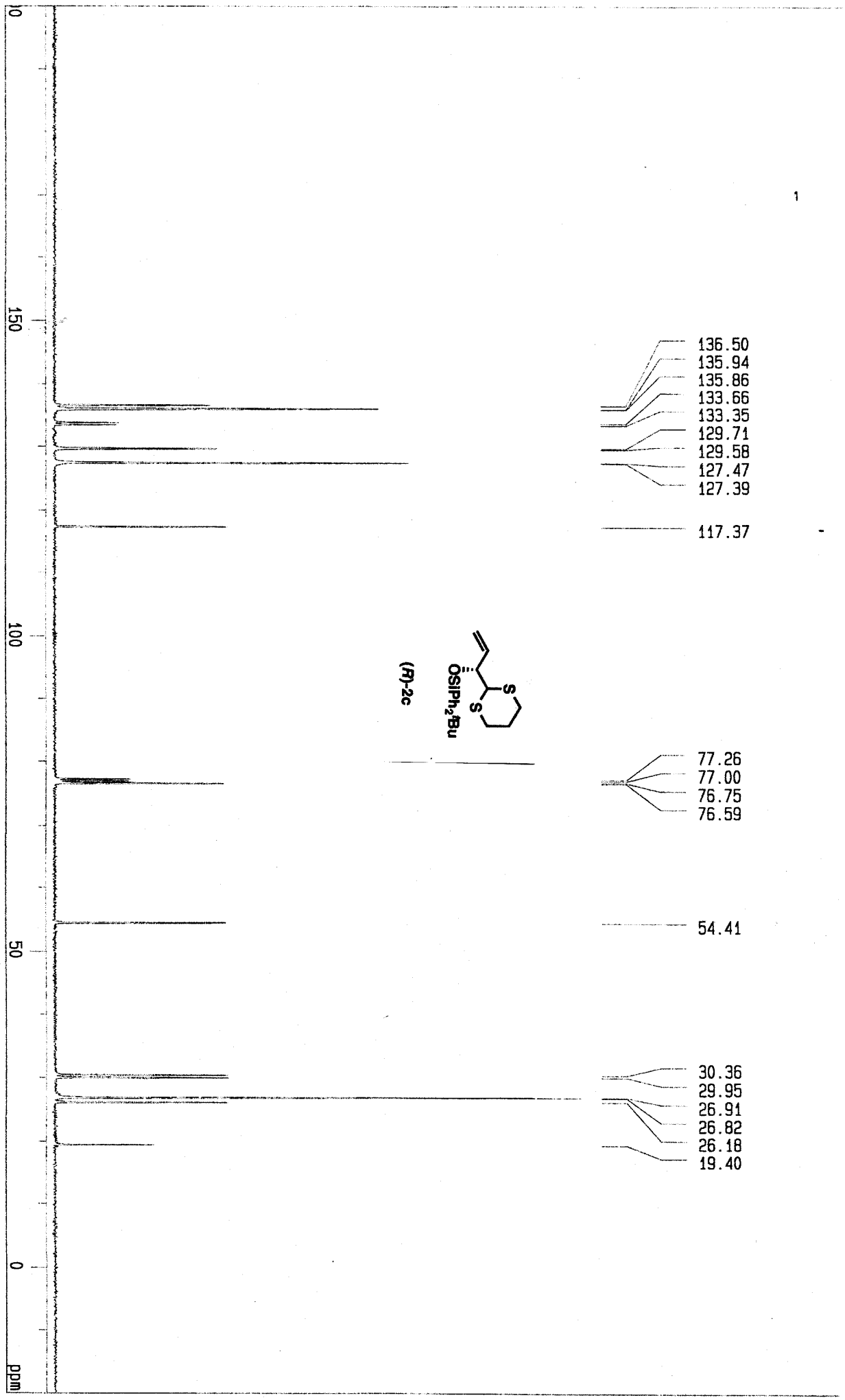

7.3805
7.3664
7.3524
7.3377
7.3225
7.2901
7.2761
7.2609
7.0491
4.15
2.85
(S)-2a
OBn
S
S
5.9161
5.8996
5.8953
5.8807
5.8654
5.8612
5.8453
5.4109
5.3907
5.3431
5.3090
4.6860
4.6622
4.4560
4.4316
4.2491
4.2369
3.9691
3.9563
3.9410
2.8976
2.8879
2.8775
2.8671
2.8604
2.8452
2.8397
2.8171
2.8116
2.6395
2.1197
2.1148
2.1099
2.1044
2.0995
2.0873
2.0819
2.0758
2.0666
2.0446
1.9427
1.9342
1.9214
1.9135
1.9055
1.9000
1.8927
1.8854
1.8775
1.8713
1.8640
1.8561
1.5925
1.5577
1.5278
1.2594
1.00
1.06
1.04
1.07
1.04
1.00
1.01
4.26
1.06
1.03
0.1165
0.0000
6
4
2
0
ppm

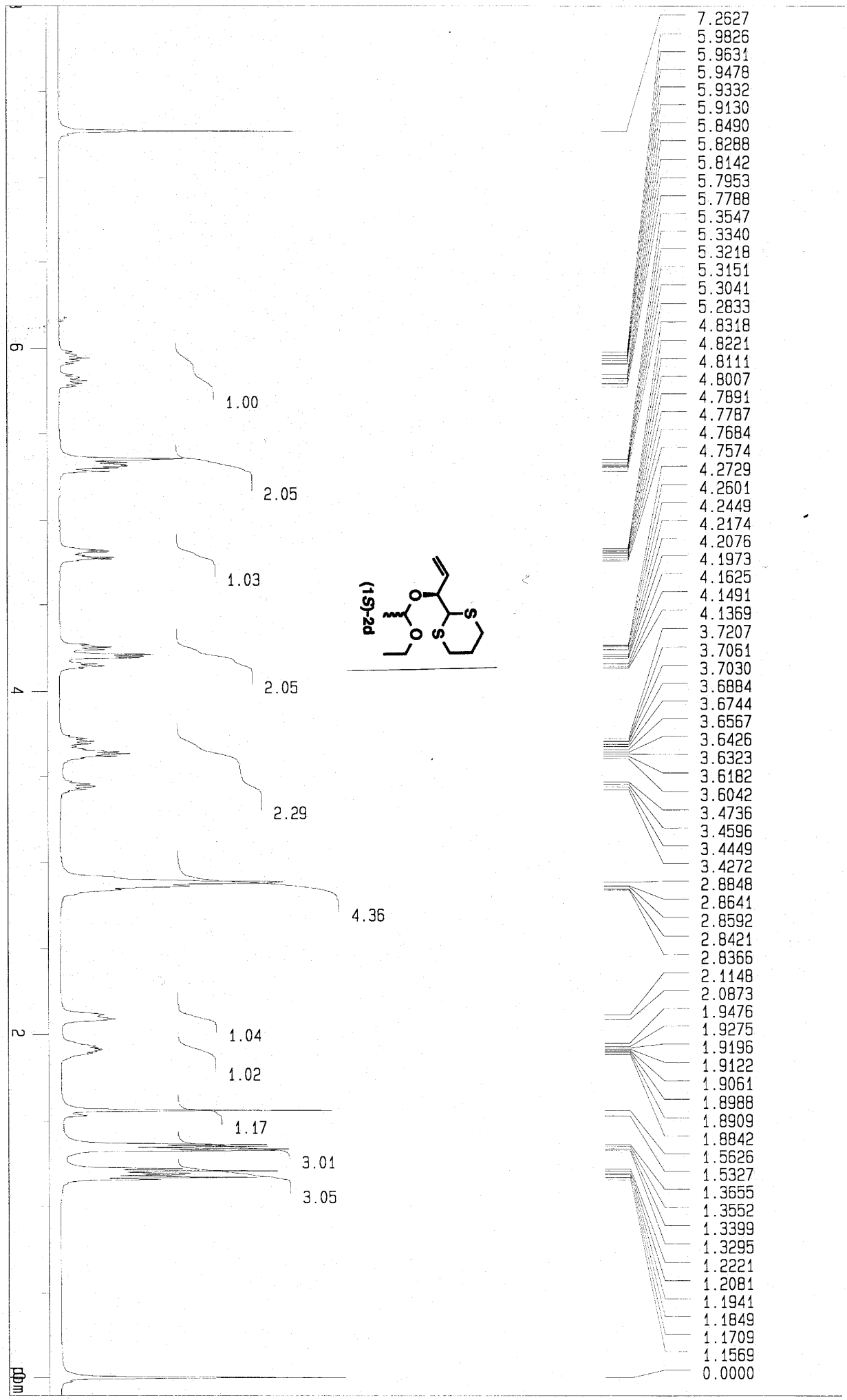

137.433
134.768
127.999
127.620
127.308
119.806
81.721
77.255
77.000
76.745
70.123
51.221
29.711
29.637
25.705
S
S
OBn
(S)-2a
150
100
50
0
ppm

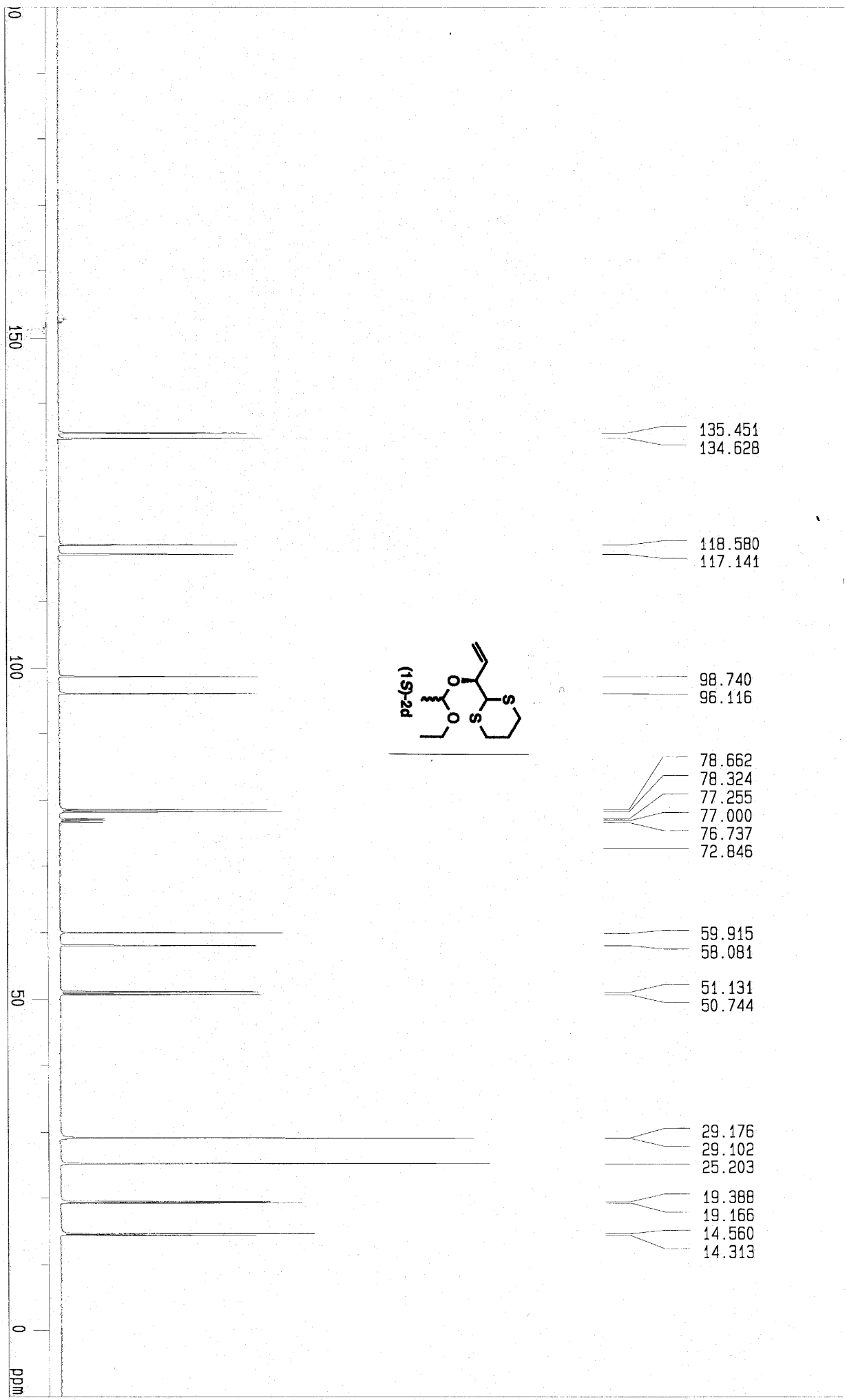

7.261
7.241
5.949
5.936
5.928
5.915
5.901
5.894
5.881
5.300
5.266
5.230
5.210
4.267
4.254
4.242
4.126
4.114
3.639
2.881
2.873
2.863
2.852
2.845
2.829
2.824
2.818
2.103
2.075
1.899
1.878
1.871
1.856
1.849
1.549
1.542
1.536
1.523
1.043
0.926
0.920
0.898
0.794
0.124
0.067
0.060
0.000
-0.006
1.00
2.21
0.99
1.06
0.13
4.37
1.08
1.07
10.64
2.70
3.06
(S)-2b
OSiMe2tBu
S
S
6
4
2
0
ppm

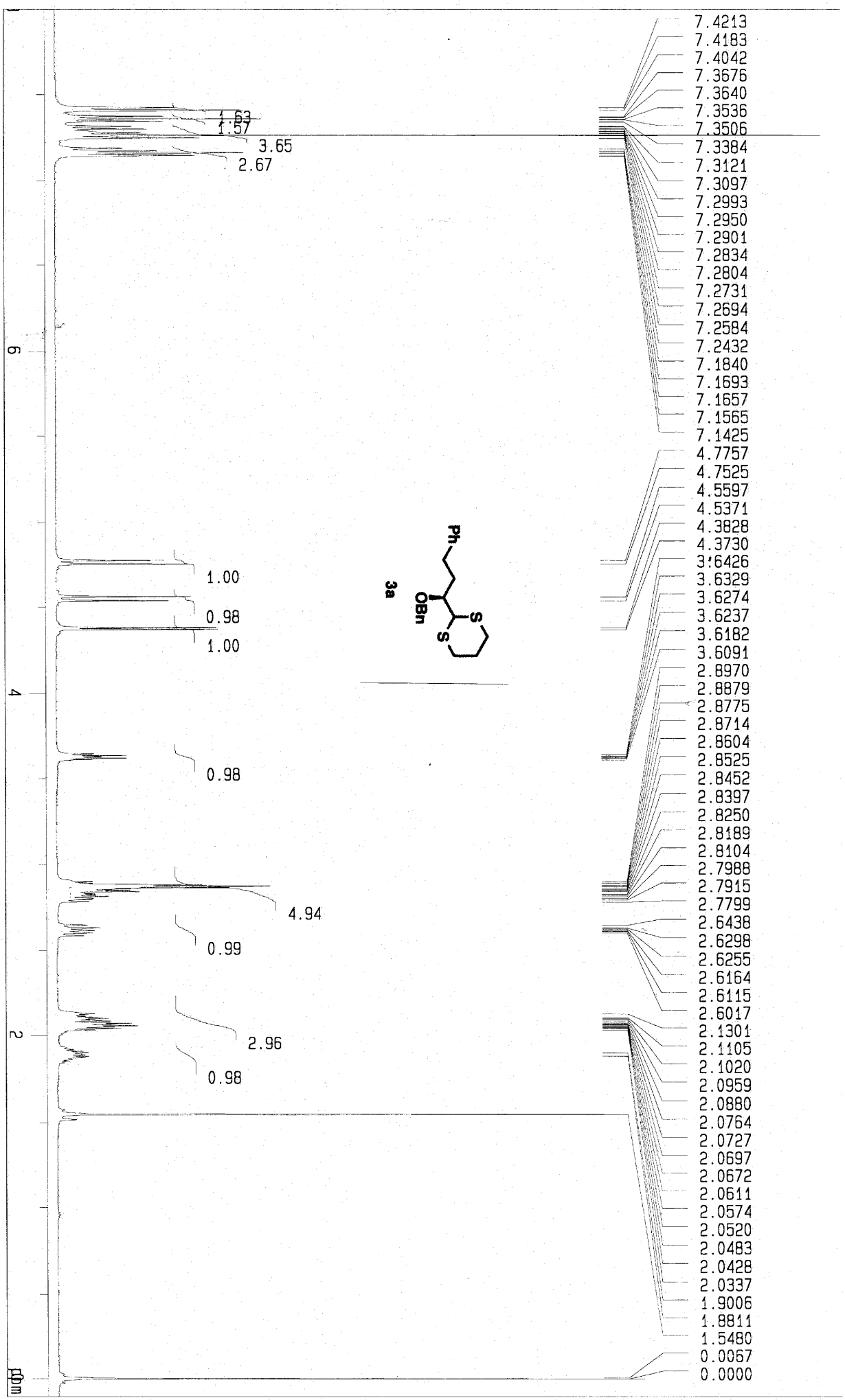

137.92
116.57
77.25
77.00
76.75
76.39
76.29
71.57
63.20
53.62
53.51
29.83
29.74
29.62
25.97
25.85
25.72
25.61
25.51
18.04
-4.40
-4.50
-4.76
-4.99
-5.63
S
S
OSiMe2tBu
(S)-2b
150
100
50
0
ppm

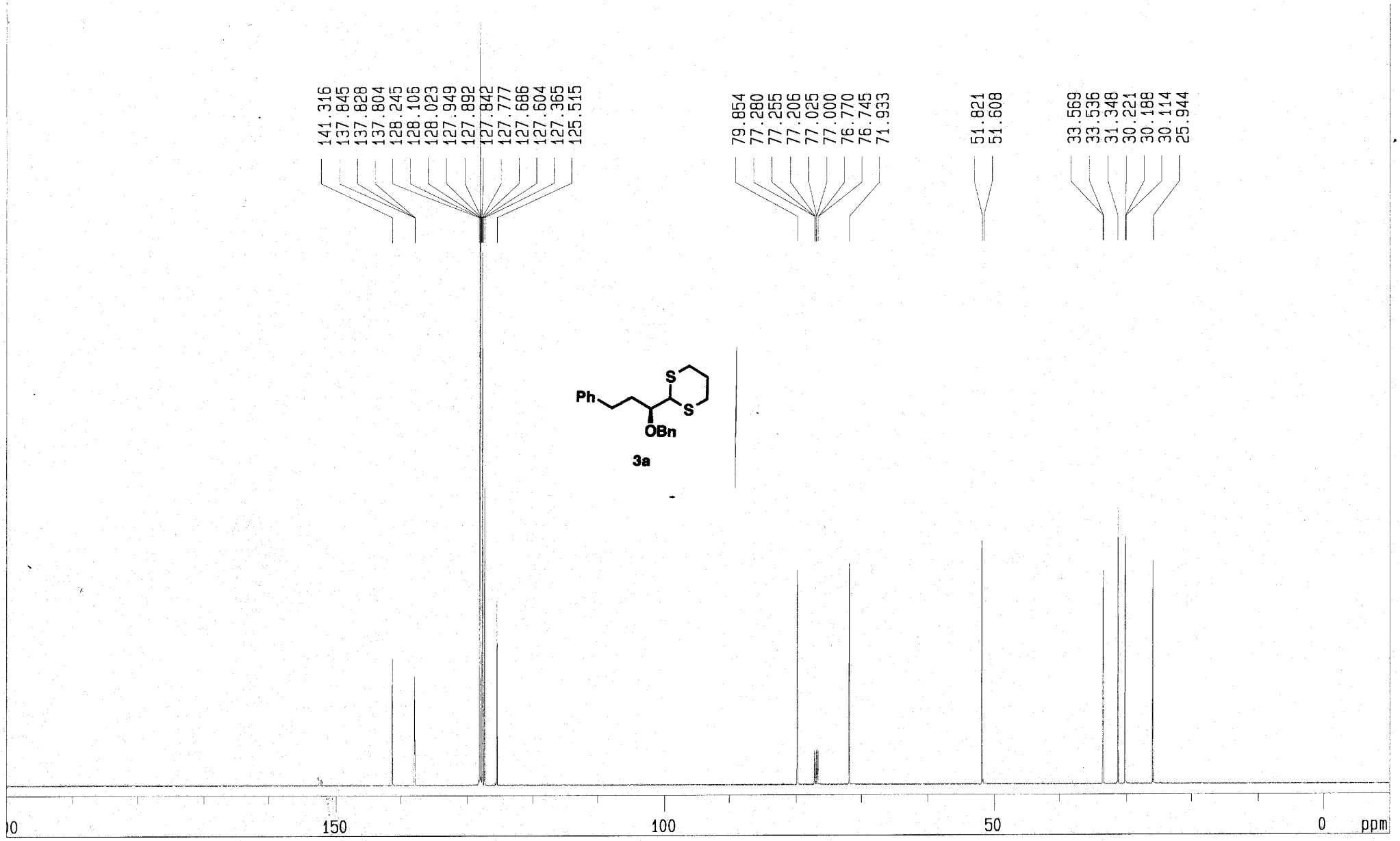

7.777
7.762
7.668
7.654
7.457
7.443
7.423
7.409
7.398
7.382
7.366
7.351
7.266
7.260
7.254
5.955
5.942
5.934
5.921
5.908
5.900
5.887
5.300
5.108
5.096
5.089
5.062
4.358
4.347
4.336
3.987
3.977
2.823
2.795
2.738
2.710
2.698
2.669
2.663
2.640
2.610
2.040
2.012
1.846
1.823
1.795
1.771
1.549
1.541
1.535
1.214
1.090
0.963
0.006
0.000
-0.007
4.12
5.81
1.00
2.09
1.01
1.02
4.23
1.02
1.00
4.64
9.37
OSiPh2tBu
(R)-2c
S
S
6
4
2
0
ppm

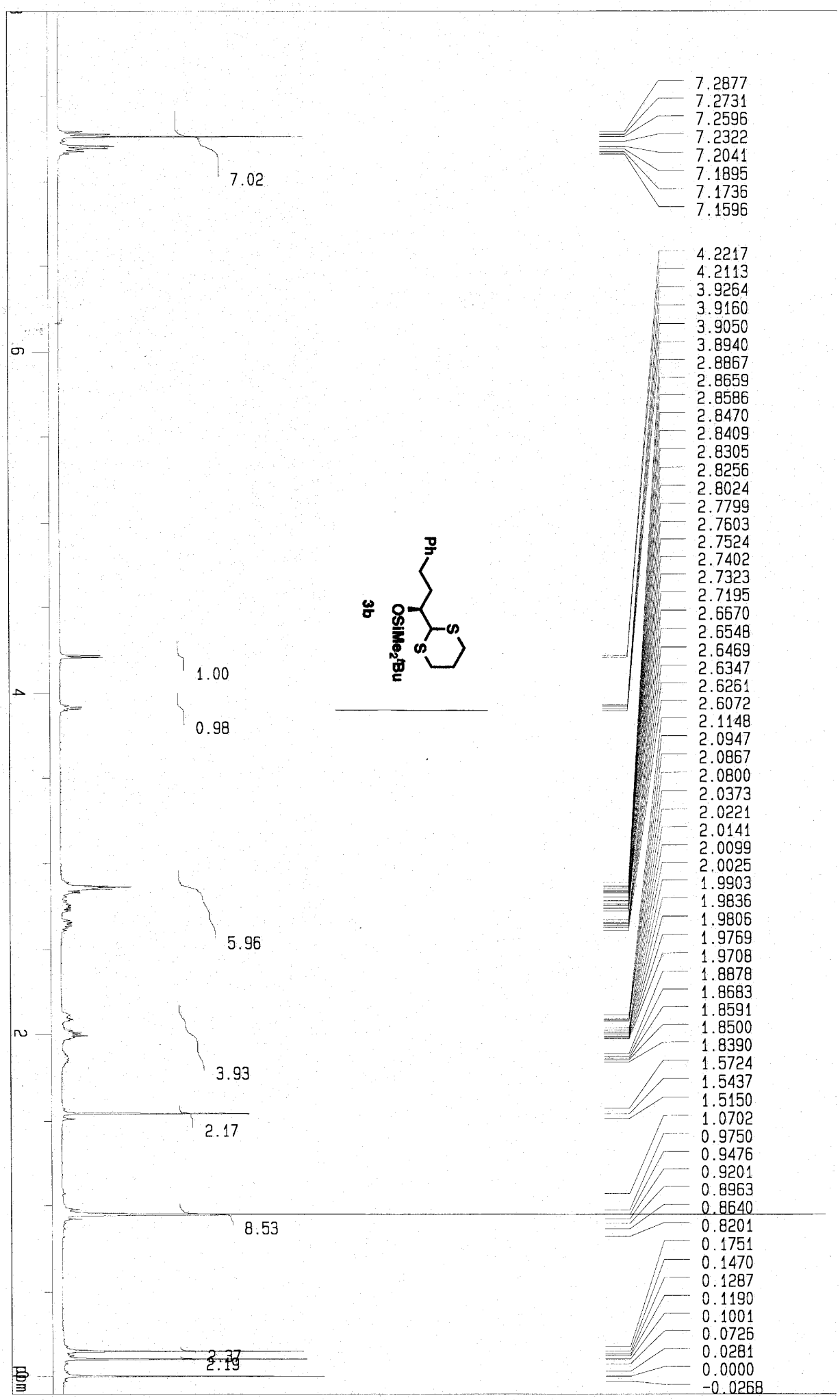

136.50
135.94
135.86
133.66
133.35
129.71
129.58
127.47
127.39
117.37
77.26
77.00
76.75
76.59
54.41
30.36
29.95
26.91
26.82
26.18
19.40
(R)-2c
OSiPh2tBu
S
S
150
100
50
0
ppm

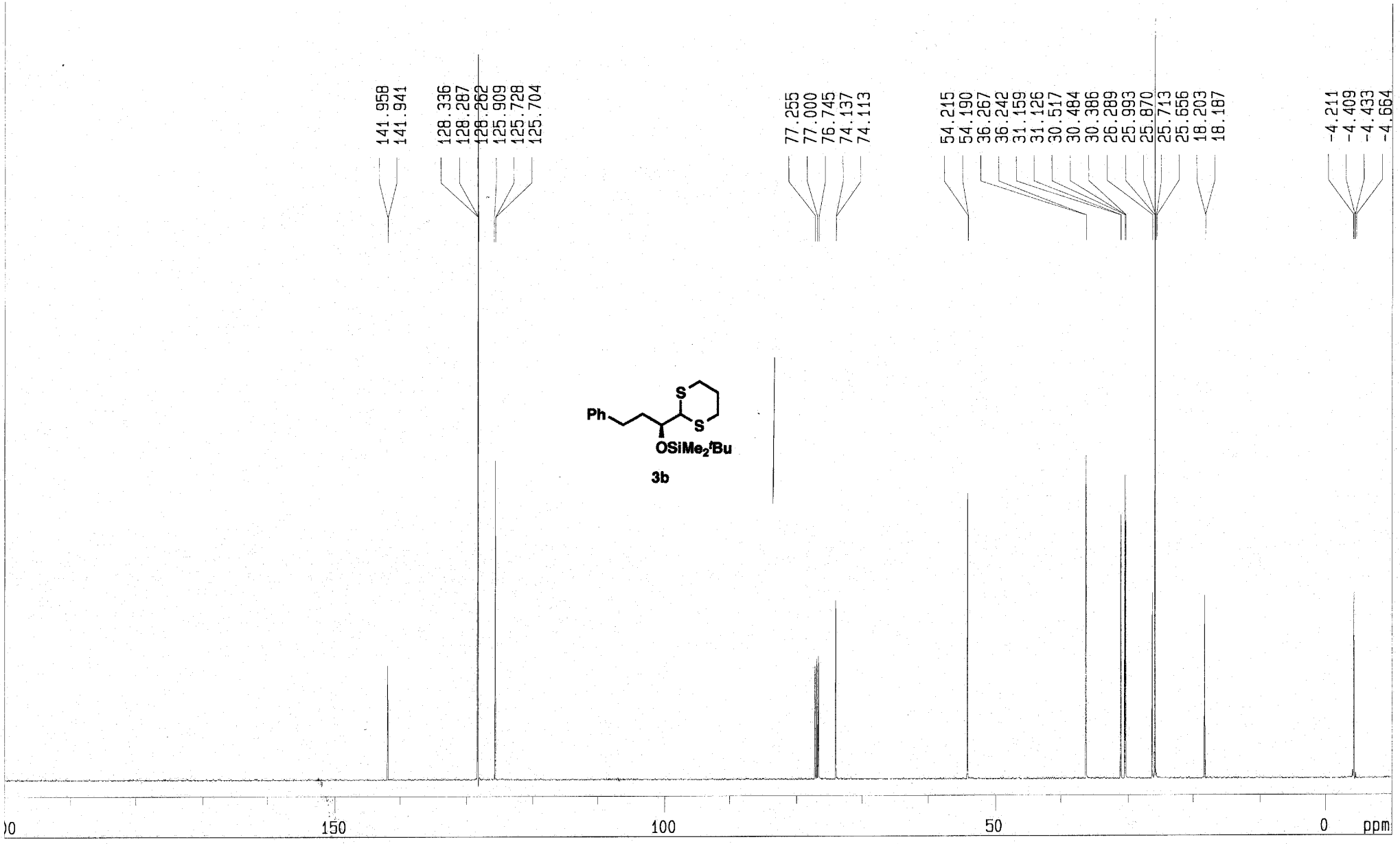

7.2627
5.9826
5.9631
5.9478
5.9332
5.9130
5.8490
5.8288
5.8142
5.7953
5.7788
5.3547
5.3340
5.3218
5.3151
5.3041
5.2833
4.8318
4.8221
4.8111
4.8007
4.7891
4.7787
4.7684
4.7574
4.2729
4.2601
4.2449
4.2174
4.2076
4.1973
4.1625
4.1491
4.1369
3.7207
3.7061
3.7030
3.6884
3.6744
3.6567
3.6426
3.6323
3.6182
3.6042
3.4736
3.4596
3.4449
3.4272
2.8848
2.8641
2.8592
2.8421
2.8366
2.1148
2.0873
1.9476
1.9275
1.9196
1.9122
1.9061
1.8988
1.8909
1.8842
1.5626
1.5327
1.3655
1.3552
1.3399
1.3295
1.2221
1.2081
1.1941
1.1849
1.1709
1.1569
0.0000
1.00
2.05
1.03
2.05
2.29
4.36
1.04
1.02
1.17
3.01
3.05
(1S)-2d
6
4
2
0
ppm

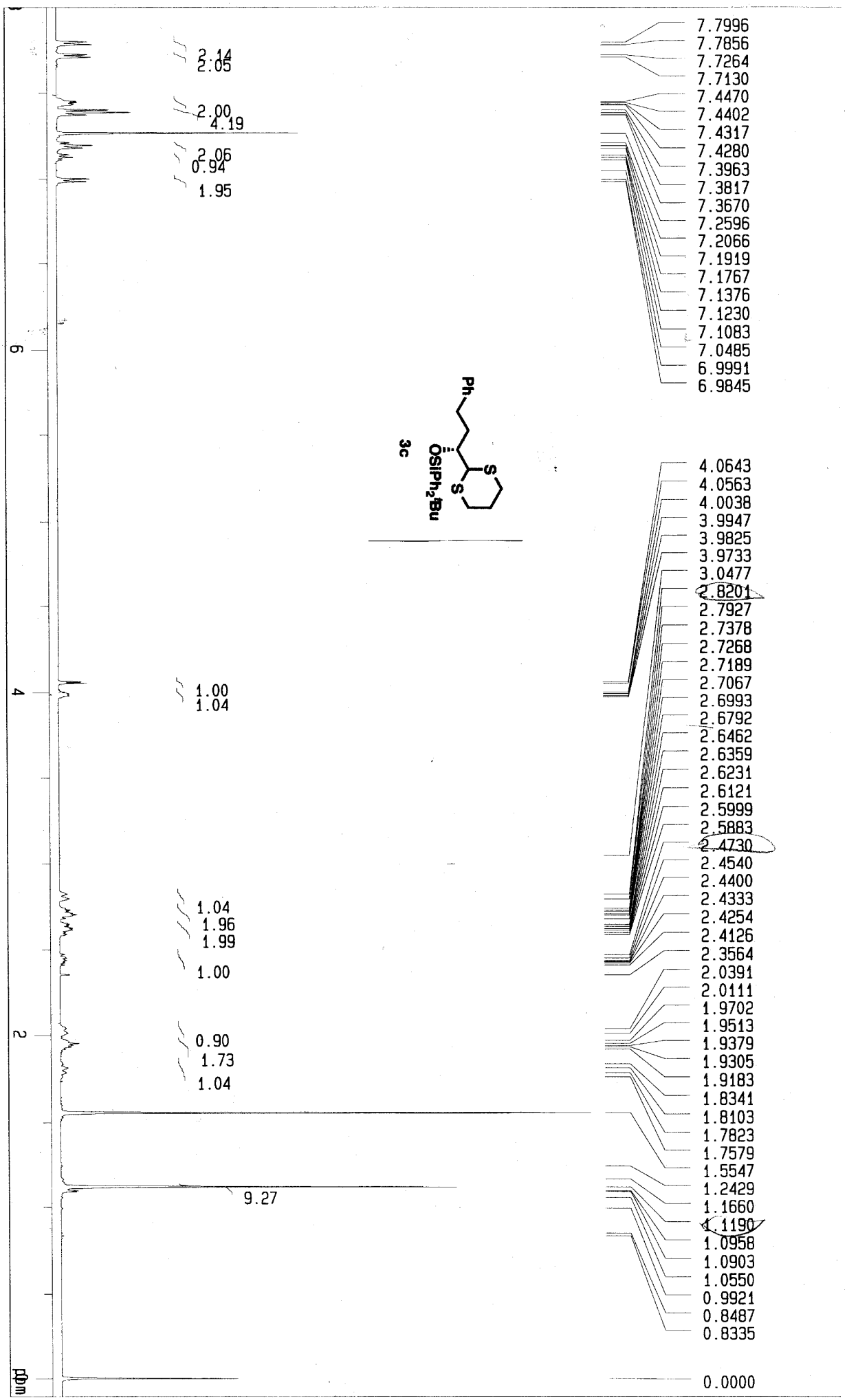

135.451
134.628
118.580
117.141
98.740
96.116
78.662
78.324
77.255
77.000
76.737
72.846
59.915
58.081
51.131
50.744
29.176
29.102
25.203
19.388
19.166
14.560
14.313
pz-(S)-1
O
O
S
S
150
100
50
0
ppm

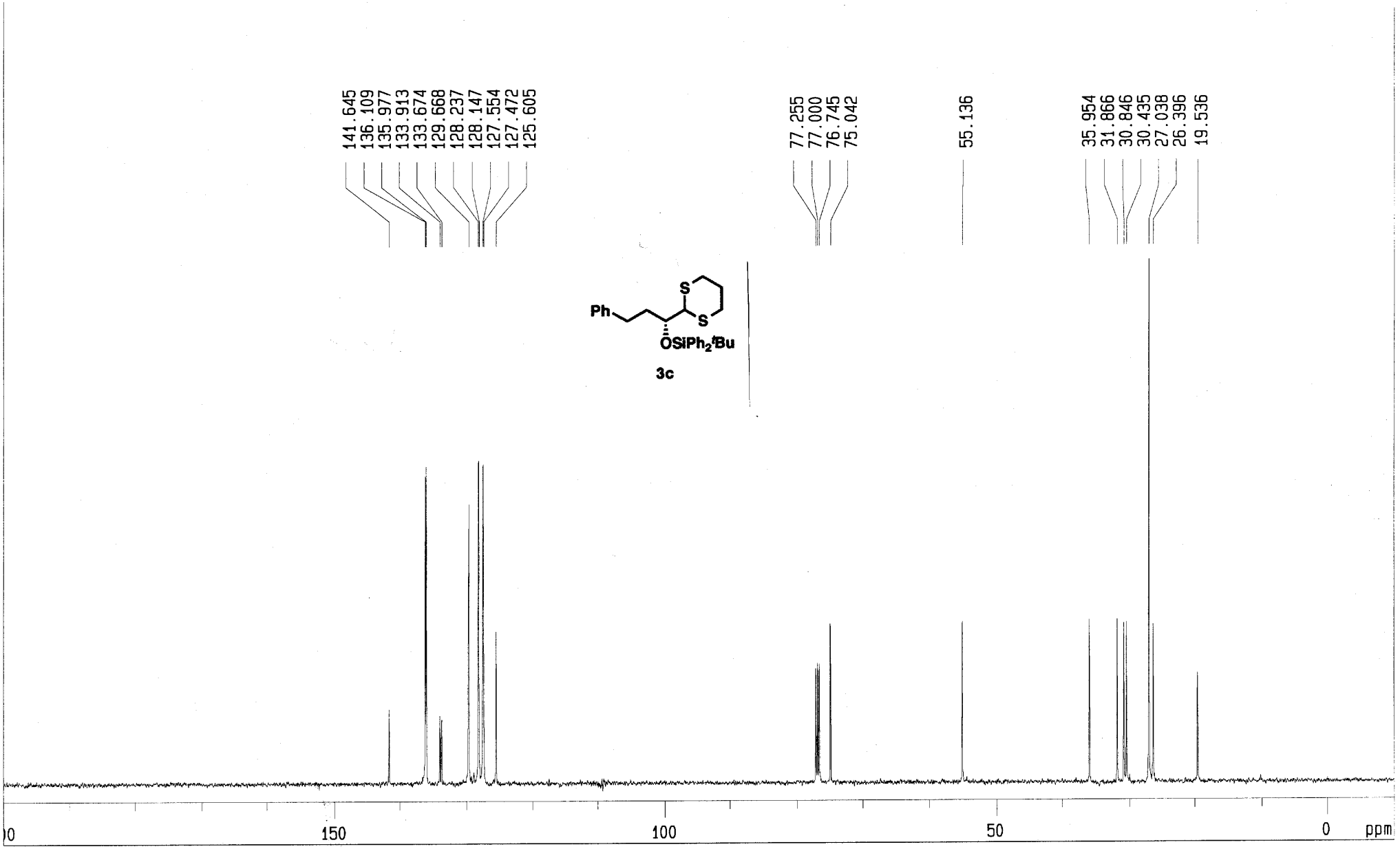

7.4213
7.4183
7.4042
7.3676
7.3640
7.3536
7.3506
7.3384
7.3121
7.3097
7.2993
7.2950
7.2901
7.2834
7.2804
7.2731
7.2694
7.2584
7.2432
7.1840
7.1693
7.1657
7.1565
7.1425
4.7757
4.7525
4.5597
4.5371
4.3828
4.3730
3.6426
3.6329
3.6274
3.6237
3.6182
3.6091
2.8970
2.8879
2.8775
2.8714
2.8604
2.8525
2.8452
2.8397
2.8250
2.8189
2.8104
2.7988
2.7915
2.7799
2.6438
2.6298
2.6255
2.6164
2.6115
2.6017
2.1301
2.1105
2.1020
2.0959
2.0880
2.0764
2.0727
2.0697
2.0672
2.0611
2.0574
2.0520
2.0483
2.0428
2.0337
1.9006
1.8811
1.5480
0.0067
0.0000
1.63
1.57
3.65
2.67
1.00
0.98
1.00
0.98
4.94
0.99
2.96
0.98
Ph
OBn
S
S
3a
6
4
2
ppm


141.316
137.845
137.828
137.804
128.245
128.106
128.023
127.949
127.892
127.842
127.777
127.686
127.604
127.365
125.515
79.854
77.280
77.255
77.206
77.025
77.000
76.770
76.745
71.933
51.821
51.608
33.569
33.536
31.348
30.221
30.188
30.114
25.944
Ph
S
S
OBn
3a
150
100
50
0
ppm

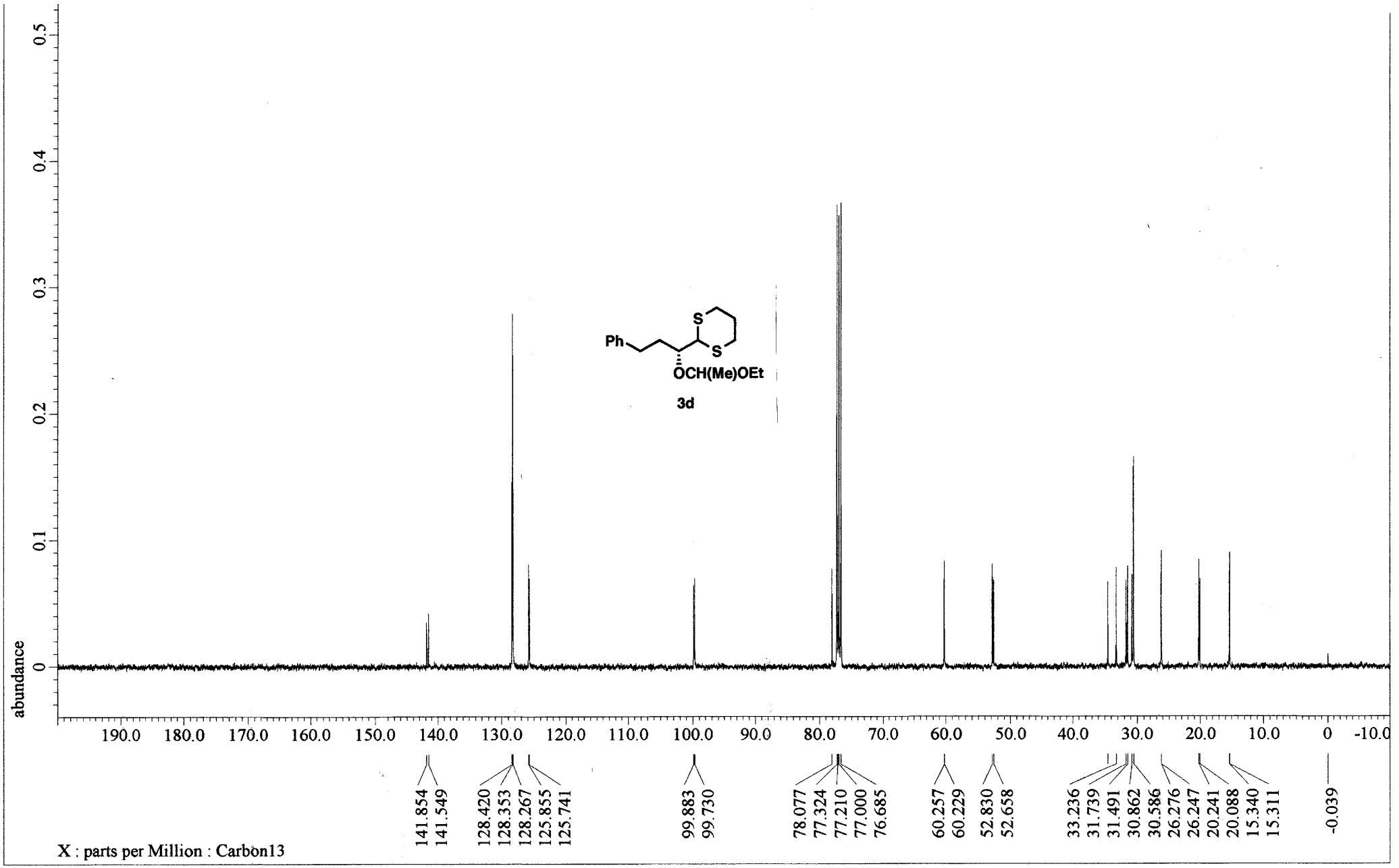

7.2877
7.2731
7.2596
7.2322
7.2041
7.1895
7.1736
7.1596
7.02
4.2217
4.2113
3.9264
3.9160
3.9050
3.8940
2.8867
2.8659
2.8586
2.8470
2.8409
2.8305
2.8256
2.8024
2.7799
2.7603
2.7524
2.7402
2.7323
2.7195
2.6670
2.6548
2.6469
2.6347
2.6261
2.6072
2.1148
2.0947
2.0867
2.0800
2.0373
2.0221
2.0141
2.0099
2.0025
1.9903
1.9836
1.9806
1.9769
1.9708
1.8878
1.8683
1.8591
1.8500
1.8390
1.5724
1.5437
1.5150
1.0702
0.9750
0.9476
0.9201
0.8963
0.8640
0.8201
0.1751
0.1470
0.1287
0.1190
0.1001
0.0726
0.0281
0.0000
-0.0268
Ph
OSiMe2tBu
S
S
3b
1.00
0.98
5.96
3.93
2.17
8.53
2.37
2.19
6
4
2
0
ppm

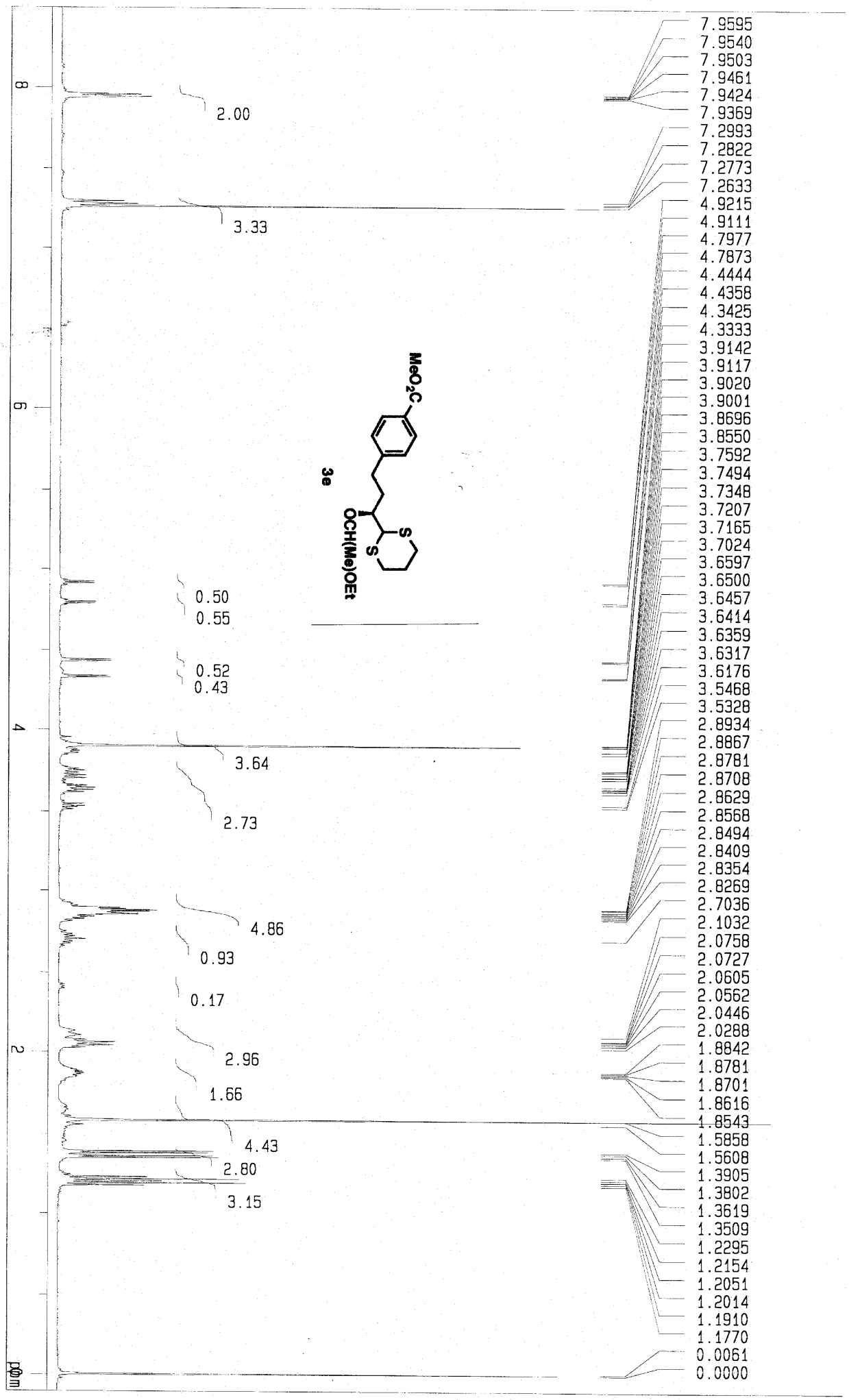

141.958
141.941
128.336
128.287
128.262
125.909
125.728
125.704
77.255
77.000
76.745
74.137
74.113
54.215
54.190
36.267
36.242
31.159
31.126
30.517
30.484
30.386
26.289
25.993
25.870
25.713
25.656
18.203
18.187
-4.211
-4.409
-4.433
-4.664
Ph
S
S
OSiMe2tBu
3b
150
100
50
0
ppm

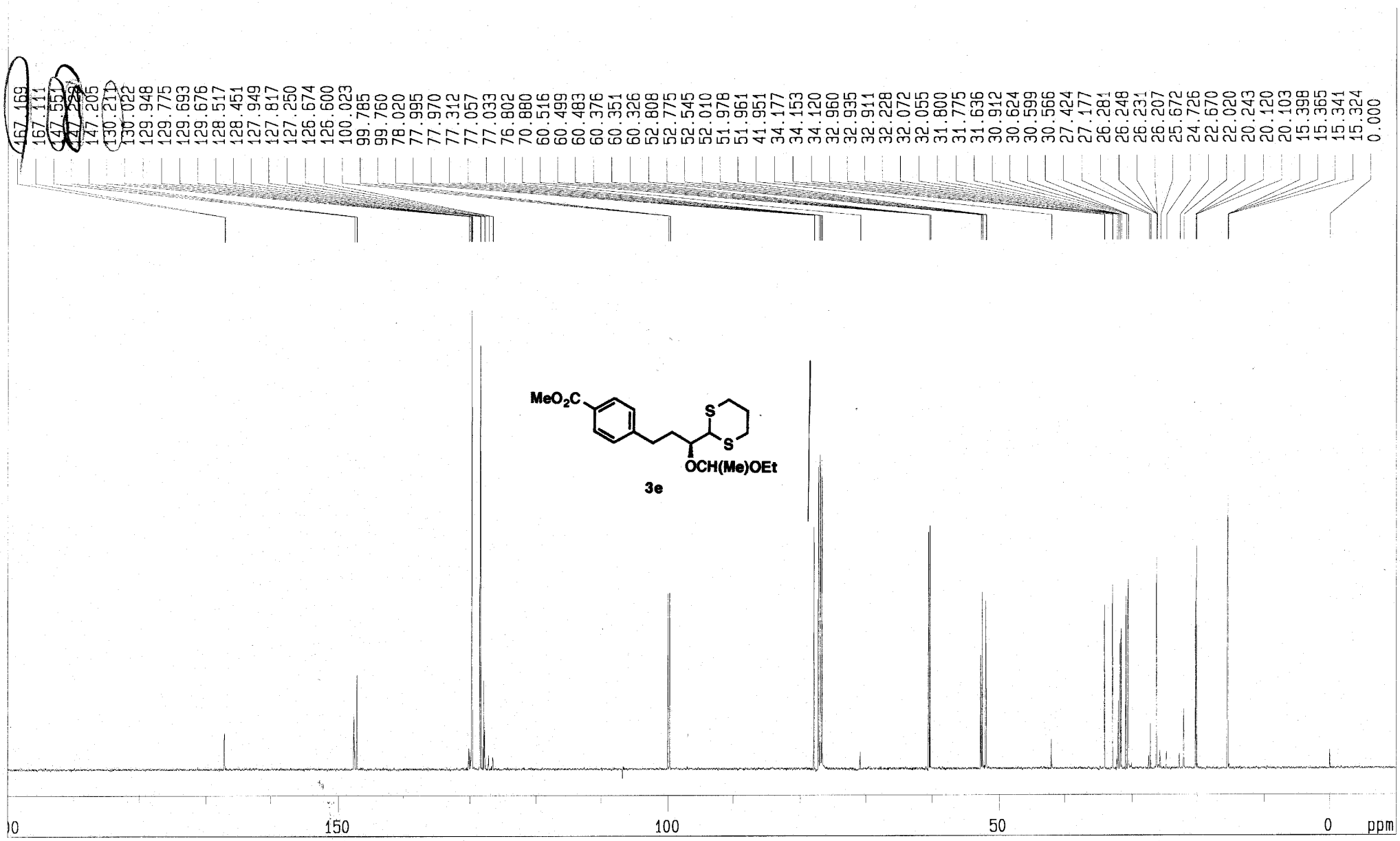

7.7996
7.7856
7.7264
7.7130
7.4470
7.4402
7.4317
7.4280
7.3963
7.3817
7.3670
7.2596
7.2066
7.1919
7.1767
7.1376
7.1230
7.1083
7.0485
6.9991
6.9845
Ph
OSiPh2tBu
3c
S
S
4.0643
4.0563
4.0038
3.9947
3.9825
3.9733
3.0477
2.8201
2.7927
2.7378
2.7268
2.7189
2.7067
2.6993
2.6792
2.6462
2.6359
2.6231
2.6121
2.5999
2.5883
2.4730
2.4540
2.4400
2.4333
2.4254
2.4126
2.3564
2.0391
2.0111
1.9702
1.9513
1.9379
1.9305
1.9183
1.8341
1.8103
1.7823
1.7579
1.5547
1.2429
1.1660
1.1190
1.0958
1.0903
1.0550
0.9921
0.8487
0.8335
0.0000
2.14
2.05
2.00
4.19
2.06
0.94
1.95
1.00
1.04
1.04
1.96
1.99
1.00
0.90
1.73
1.04
9.27
6
4
2
0
ppm

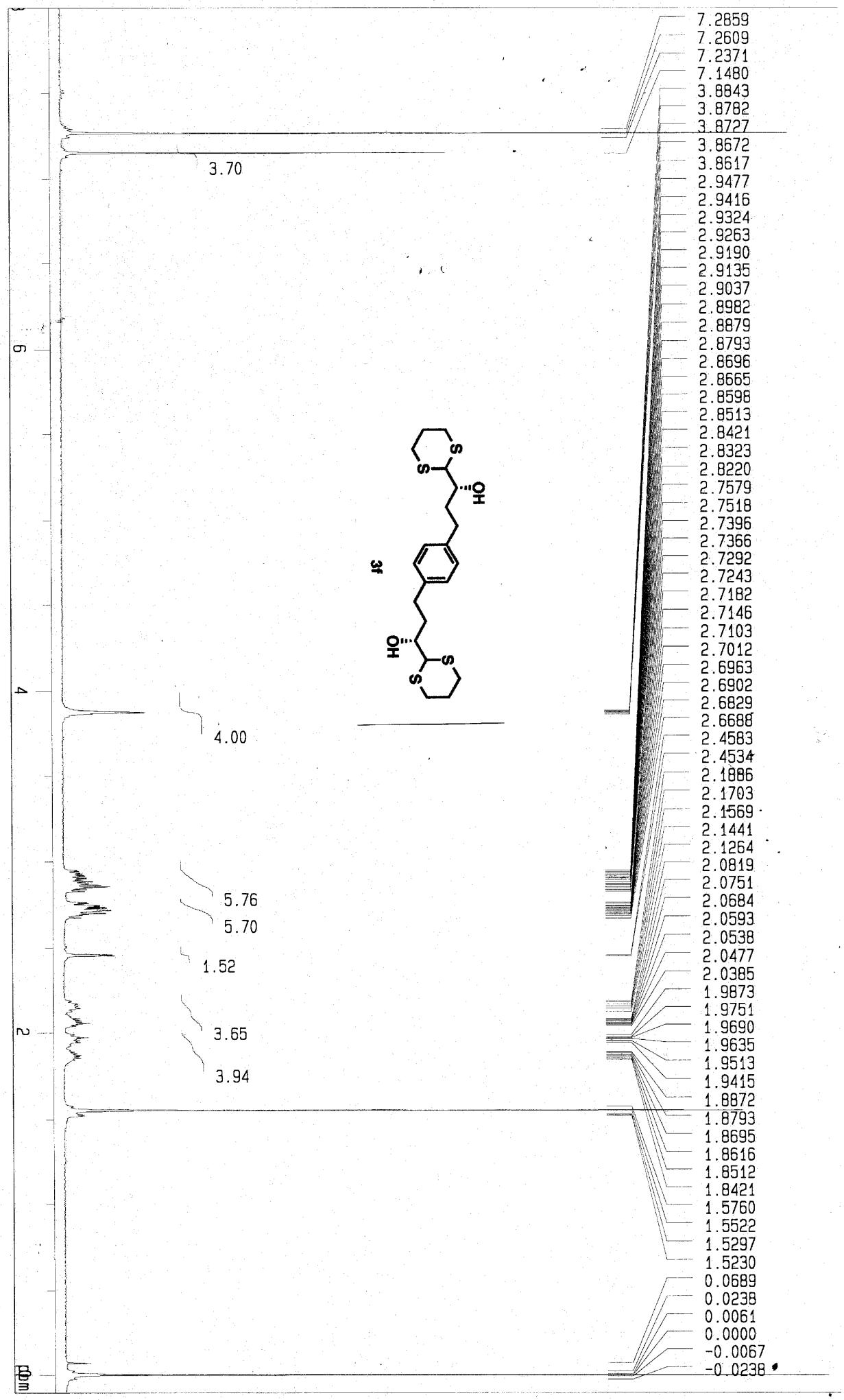

141.645
136.109
135.977
133.913
133.674
129.668
128.237
128.147
127.554
127.472
125.605
77.255
77.000
76.745
75.042
55.136
35.954
31.866
30.846
30.435
27.038
26.396
19.536
Ph
S
S
OSiPh2tBu
3c
150
100
50
0
ppm

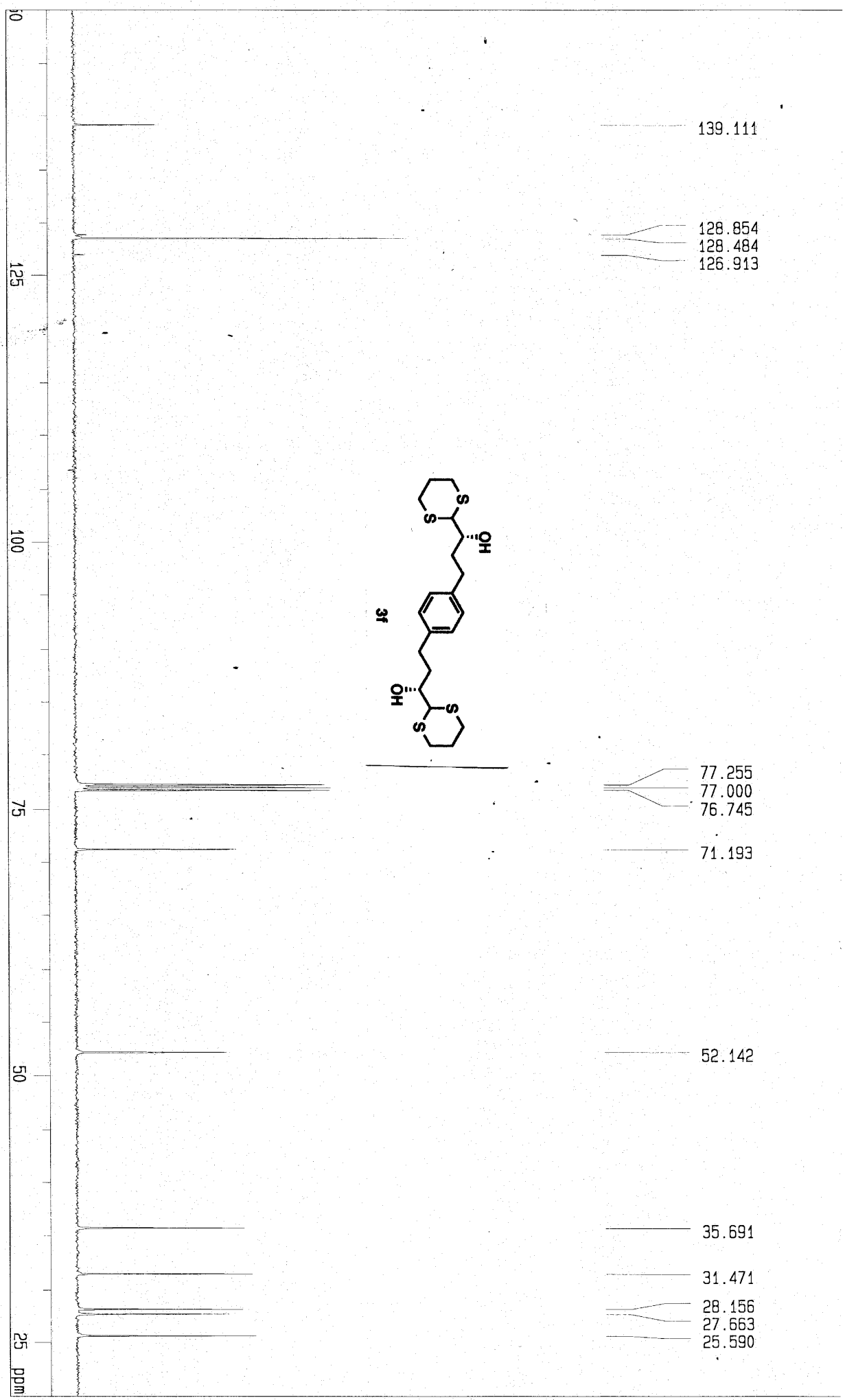
abundance
X : parts per Million : Proton
6.55
1.00
0.98
3.06
5.90
3.67
2.94
2.91
3d
OCH(Me)OEt
Ph
S
S
7.505
7.246
7.194
6.982
4.927
4.914
4.900
4.887
4.786
4.773
4.404
4.324
4.313
3.862
3.845
3.702
3.685
3.648
3.631
3.614
2.867
2.864
2.859
2.854
2.848
2.842
2.240
2.038
1.874
1.854
1.534
1.500
1.352
1.200
0.969
0.949
0.930
0.895
0.133
-0.014

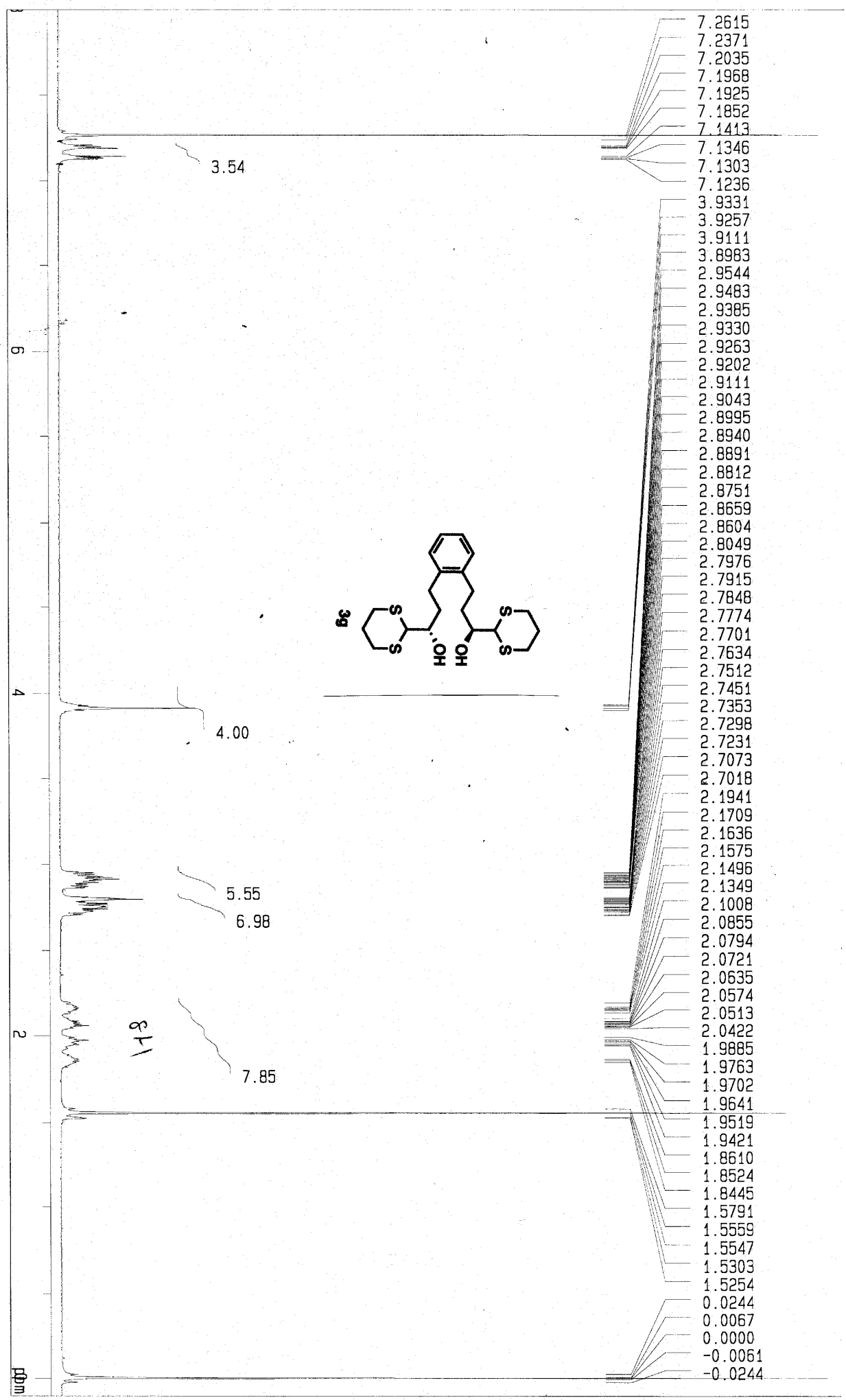

abundance
0.5
0.4
0.3
0.2
0.1
0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
-10.0
Ph
S
S
OCH(Me)OEt
3d
141.854
141.549
128.420
128.353
128.267
125.855
125.741
99.883
99.730
78.077
77.324
77.210
77.000
76.685
60.257
60.229
52.830
52.658
33.236
31.739
31.491
30.862
30.586
26.276
26.247
20.241
20.088
15.340
15.311
-0.039
X : parts per Million : Carbon13

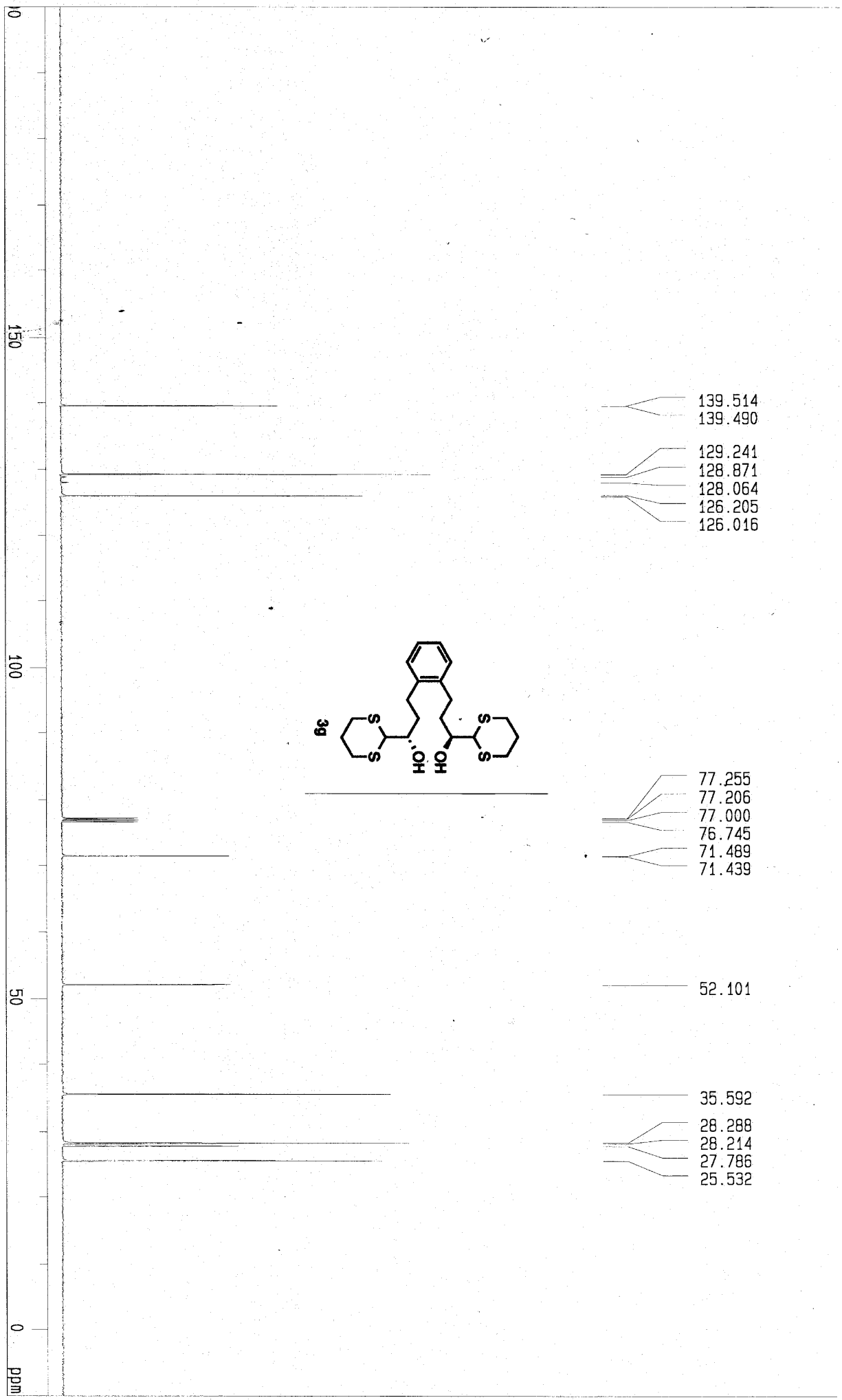

7.9595
7.9540
7.9503
7.9461
7.9424
7.9369
7.2993
7.2822
7.2773
7.2633
4.9215
4.9111
4.7977
4.7873
4.4444
4.4358
4.3425
4.3333
3.9142
3.9117
3.9020
3.9001
3.8696
3.8550
3.7592
3.7494
3.7348
3.7207
3.7165
3.7024
3.6597
3.6500
3.6457
3.6414
3.6359
3.6317
3.6176
3.5468
3.5328
2.8934
2.8867
2.8781
2.8708
2.8629
2.8568
2.8494
2.8409
2.8354
2.8269
2.7036
2.1032
2.0758
2.0727
2.0605
2.0562
2.0446
2.0288
1.8842
1.8781
1.8701
1.8616
1.8543
1.5858
1.5608
1.3905
1.3802
1.3619
1.3509
1.2295
1.2154
1.2051
1.2014
1.1910
1.1770
0.0061
0.0000
2.00
3.33
0.50
0.55
0.52
0.43
3.64
2.73
4.86
0.93
0.17
2.96
1.66
4.43
2.80
3.15
MeO2C
OCH(Me)OEt
S
S
3e
8
6
4
2
ppm

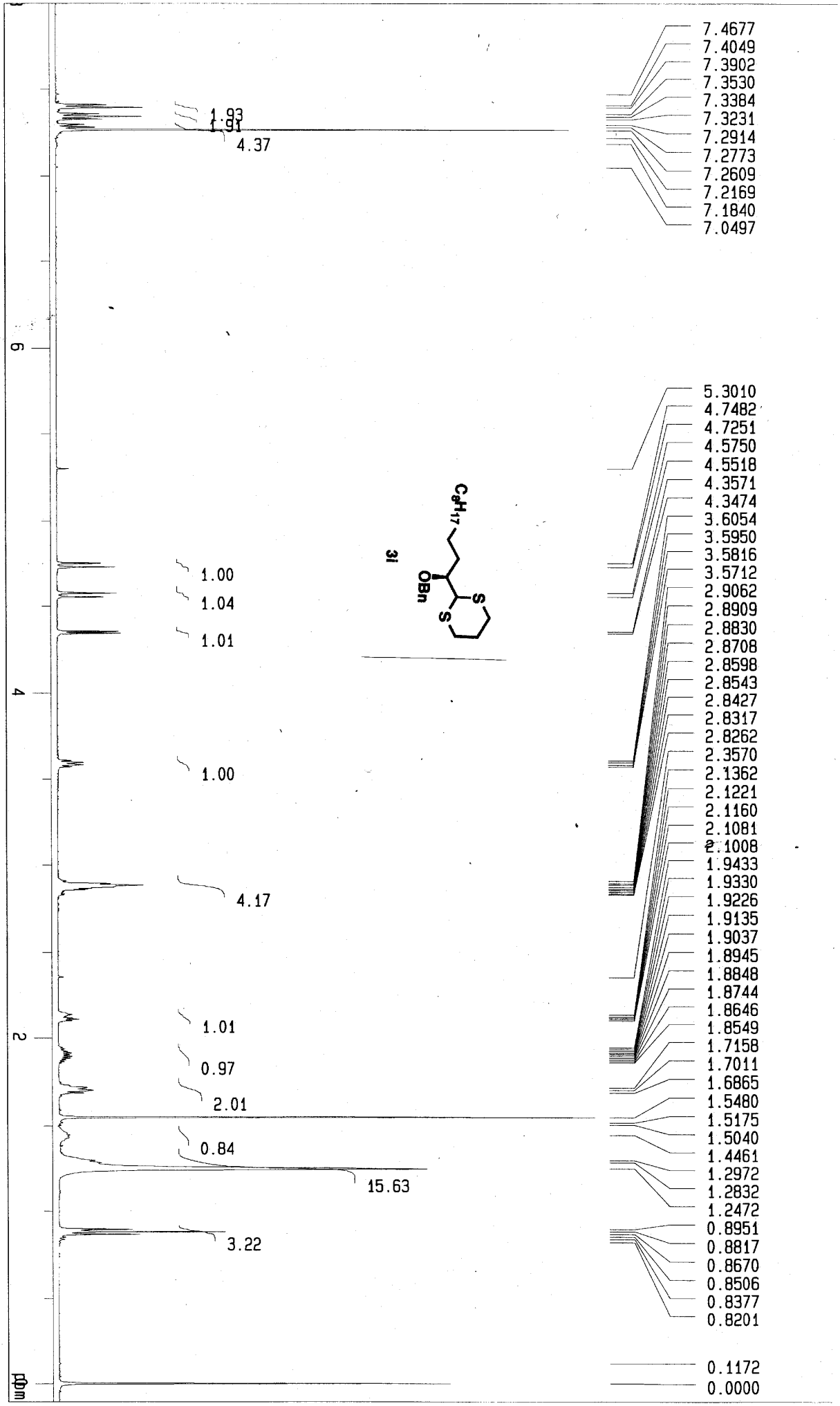

167.169
167.111
147.551
147.229
147.205
130.211
130.022
129.948
129.775
129.693
129.676
128.517
128.451
127.949
127.817
127.250
126.674
126.600
100.023
99.785
99.760
78.020
77.995
77.970
77.312
77.057
77.033
76.802
70.880
60.516
60.499
60.483
60.376
60.351
60.326
52.808
52.775
52.545
52.010
51.978
51.961
41.951
34.177
34.153
34.120
32.960
32.935
32.911
32.228
32.072
32.055
31.800
31.775
31.636
30.912
30.624
30.599
30.566
27.424
27.177
26.281
26.248
26.231
26.207
25.672
24.726
22.670
22.020
20.243
20.120
20.103
15.398
15.365
15.341
15.324
0.000
MeO2C
S
S
OCH(Me)OEt
3e
150
100
50
0
ppm

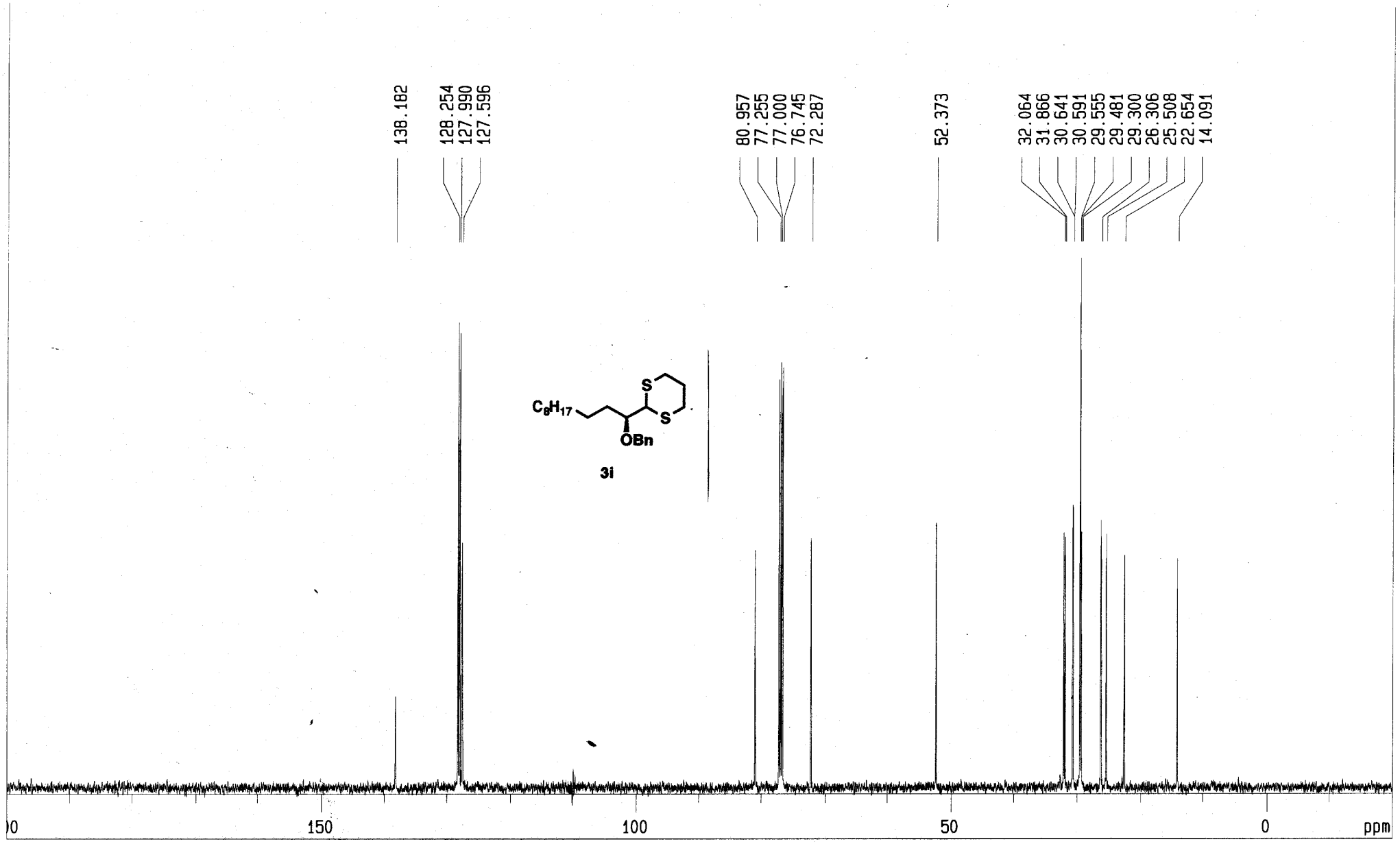

7.2859
7.2609
7.2371
7.1480
3.8843
3.8782
3.8727
3.8672
3.8617
2.9477
2.9416
2.9324
2.9263
2.9190
2.9135
2.9037
2.8982
2.8879
2.8793
2.8696
2.8665
2.8598
2.8513
2.8421
2.8323
2.8220
2.7579
2.7518
2.7396
2.7366
2.7292
2.7243
2.7182
2.7146
2.7103
2.7012
2.6963
2.6902
2.6829
2.6688
2.4583
2.4534
2.1886
2.1703
2.1569
2.1441
2.1264
2.0819
2.0751
2.0684
2.0593
2.0538
2.0477
2.0385
1.9873
1.9751
1.9690
1.9635
1.9513
1.9415
1.8872
1.8793
1.8695
1.8616
1.8512
1.8421
1.5760
1.5522
1.5297
1.5230
0.0689
0.0238
0.0061
0.0000
-0.0067
-0.0238
3.70
4.00
5.76
5.70
1.52
3.65
3.94
OH
OH
S
S
S
S
3f
6
4
2
0
ppm

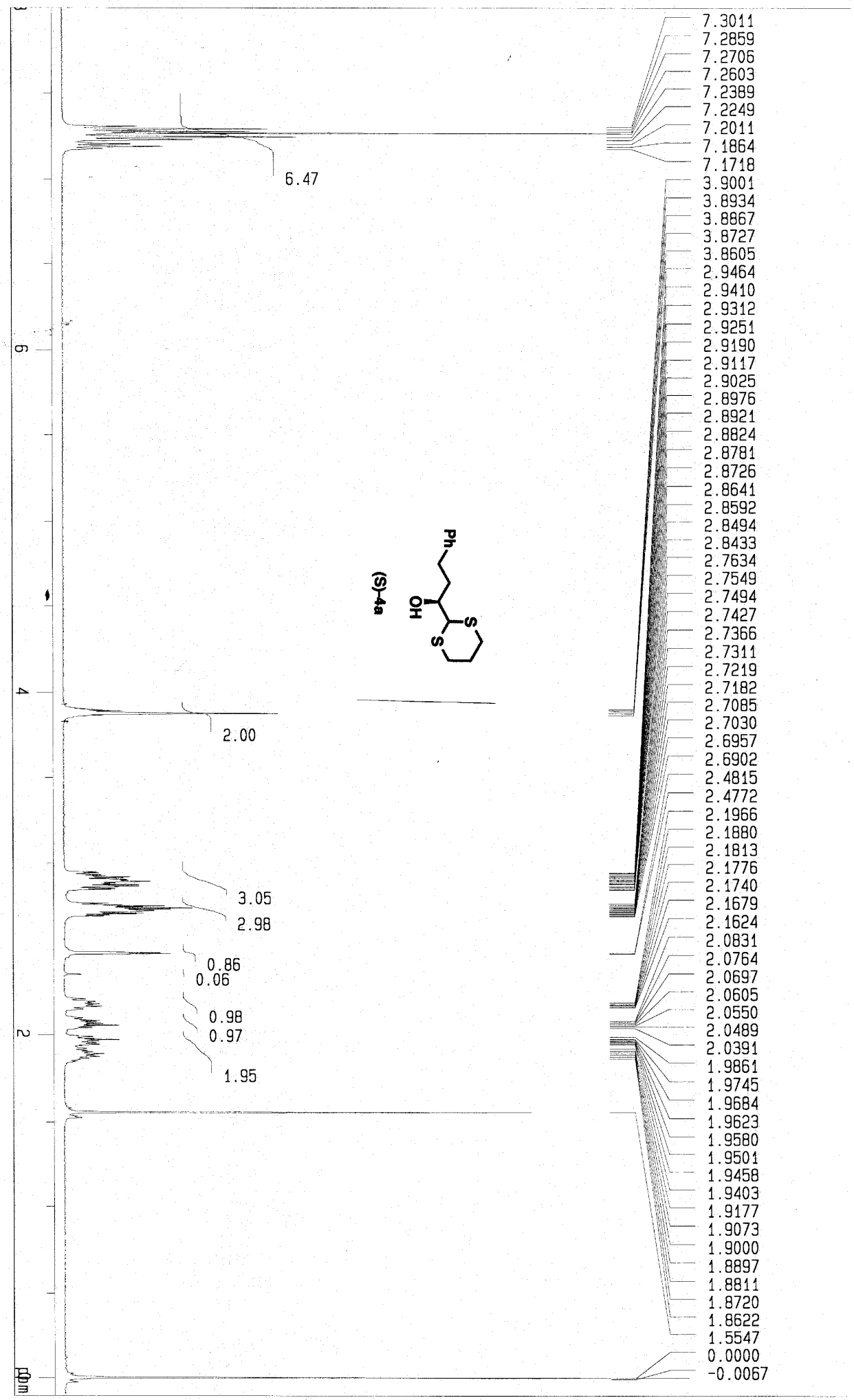

139.111
128.854
128.484
126.913
77.255
77.000
76.745
71.193
52.142
35.691
31.471
28.156
27.663
25.590
OH
OH
S
S
S
S
3f
125
100
75
50
25
ppm

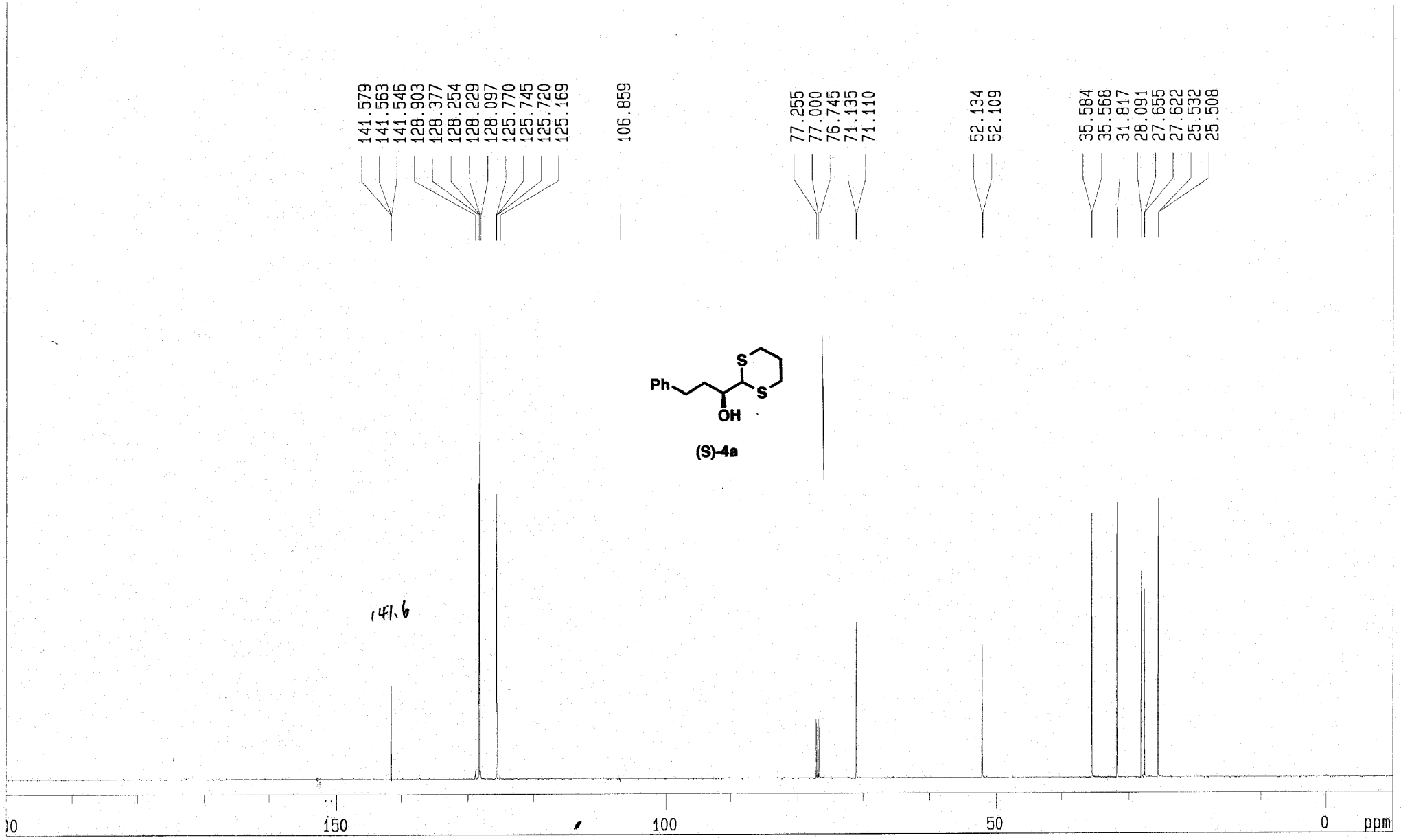

7.2615
7.2371
7.2035
7.1968
7.1925
7.1852
7.1413
7.1346
7.1303
7.1236
3.9331
3.9257
3.9111
3.8983
2.9544
2.9483
2.9385
2.9330
2.9263
2.9202
2.9111
2.9043
2.8995
2.8940
2.8891
2.8812
2.8751
2.8659
2.8604
2.8049
2.7976
2.7915
2.7848
2.7774
2.7701
2.7634
2.7512
2.7451
2.7353
2.7298
2.7231
2.7073
2.7018
2.1941
2.1709
2.1636
2.1575
2.1496
2.1349
2.1008
2.0855
2.0794
2.0721
2.0635
2.0574
2.0513
2.0422
1.9885
1.9763
1.9702
1.9641
1.9519
1.9421
1.8610
1.8524
1.8445
1.5791
1.5559
1.5547
1.5303
1.5254
0.0244
0.0067
0.0000
-0.0061
-0.0244
3.54
4.00
5.55
6.98
7.85
3g
HO
HO
S
S
S
S
6
4
2
ppm


0
50
100
150
ppm
139.514
139.490
129.241
128.871
128.064
126.205
126.016
77.255
77.206
77.000
76.745
71.489
71.439
52.101
35.592
28.288
28.214
27.786
25.532
3g
OH
OH
S
S
S
S

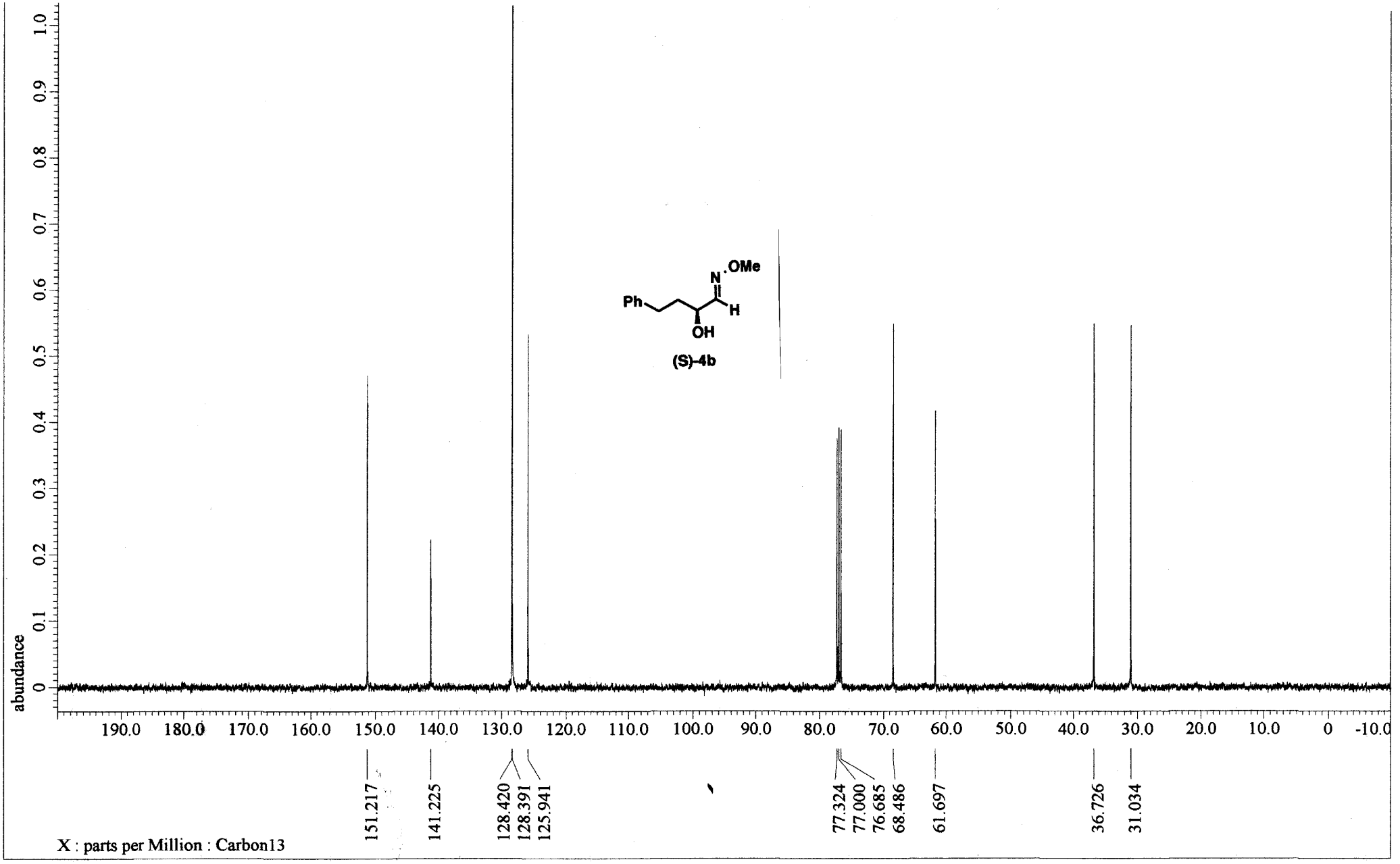

7.4677
7.4049
7.3902
7.3530
7.3384
7.3231
7.2914
7.2773
7.2609
7.2169
7.1840
7.0497
1.93
1.91
4.37
5.3010
4.7482
4.7251
4.5750
4.5518
4.3571
4.3474
3.6054
3.5950
3.5816
3.5712
2.9062
2.8909
2.8830
2.8708
2.8598
2.8543
2.8427
2.8317
2.8262
2.3570
2.1362
2.1221
2.1160
2.1081
2.1008
1.9433
1.9330
1.9226
1.9135
1.9037
1.8945
1.8848
1.8744
1.8646
1.8549
1.7158
1.7011
1.6865
1.5480
1.5175
1.5040
1.4461
1.2972
1.2832
1.2472
0.8951
0.8817
0.8670
0.8506
0.8377
0.8201
0.1172
0.0000
3i
C8H17
OBn
S
S
1.00
1.04
1.01
1.00
4.17
1.01
0.97
2.01
0.84
15.63
3.22
6
4
2
ppm

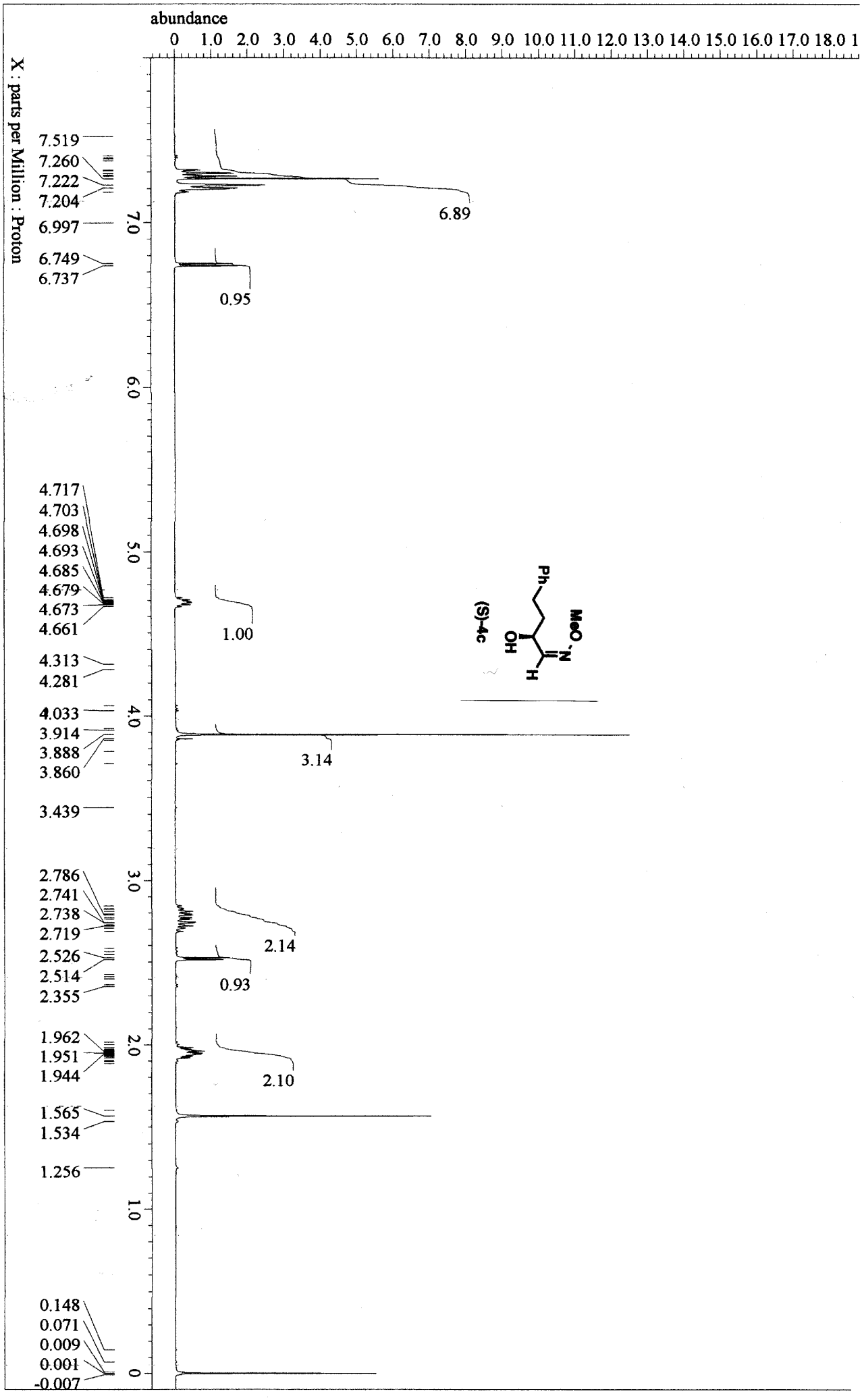

138.182
128.254
127.990
127.596
80.957
77.255
77.000
76.745
72.287
52.373
32.064
31.866
30.641
30.591
29.555
29.481
29.300
26.306
25.508
22.654
14.091
S
S
C8H17
OBn
3i
150
100
50
0
ppm

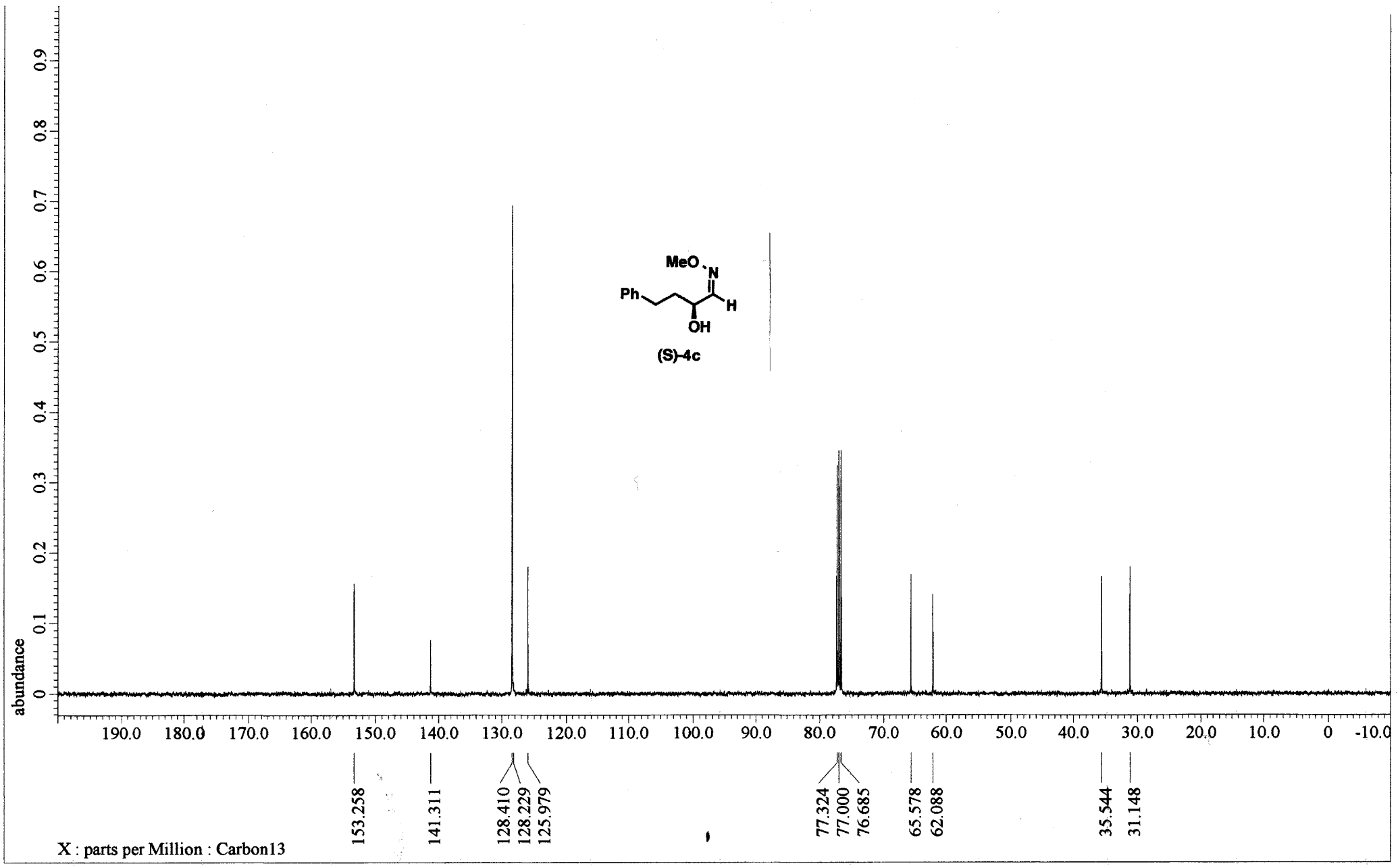

7.3011
7.2859
7.2706
7.2603
7.2389
7.2249
7.2011
7.1864
7.1718
3.9001
3.8934
3.8867
3.8727
3.8605
2.9464
2.9410
2.9312
2.9251
2.9190
2.9117
2.9025
2.8976
2.8921
2.8824
2.8781
2.8726
2.8641
2.8592
2.8494
2.8433
2.7634
2.7549
2.7494
2.7427
2.7366
2.7311
2.7219
2.7182
2.7085
2.7030
2.6957
2.6902
2.4815
2.4772
2.1966
2.1880
2.1813
2.1776
2.1740
2.1679
2.1624
2.0831
2.0764
2.0697
2.0605
2.0550
2.0489
2.0391
1.9861
1.9745
1.9684
1.9623
1.9580
1.9501
1.9458
1.9403
1.9177
1.9073
1.9000
1.8897
1.8811
1.8720
1.8622
1.5547
0.0000
-0.0067
6.47
2.00
3.05
2.98
0.86
0.06
0.98
0.97
1.95
(S)-4a
Ph
OH
S
S
6
4
2
0
ppm

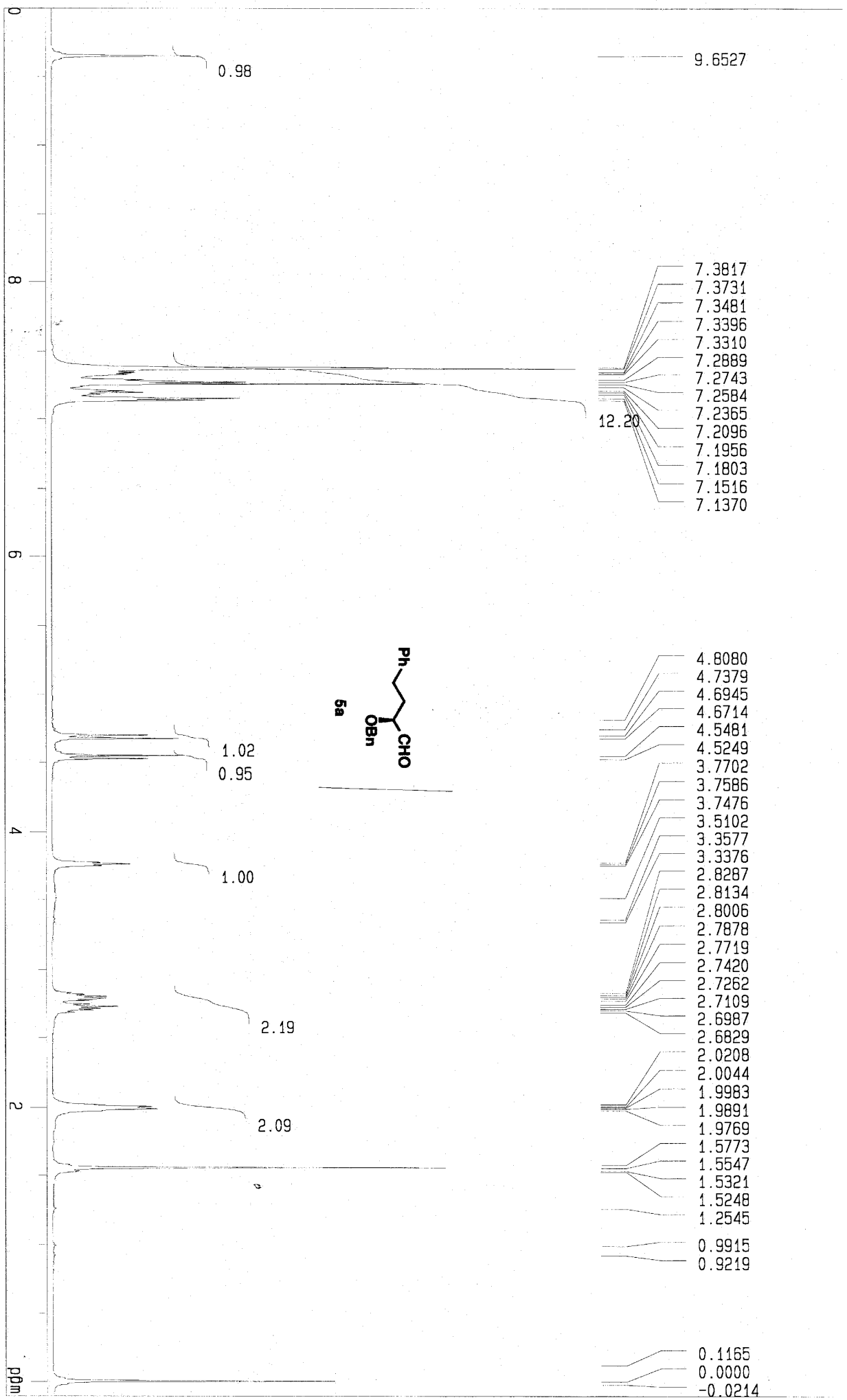

141.579
141.563
141.546
128.903
128.377
128.254
128.229
128.097
125.770
125.745
125.720
125.169
106.859
77.255
77.000
76.745
71.135
71.110
52.134
52.109
35.584
35.568
31.817
28.091
27.655
27.622
25.532
25.508
Ph
S
S
OH
(S)-4a
141.6
150
100
50
0
ppm

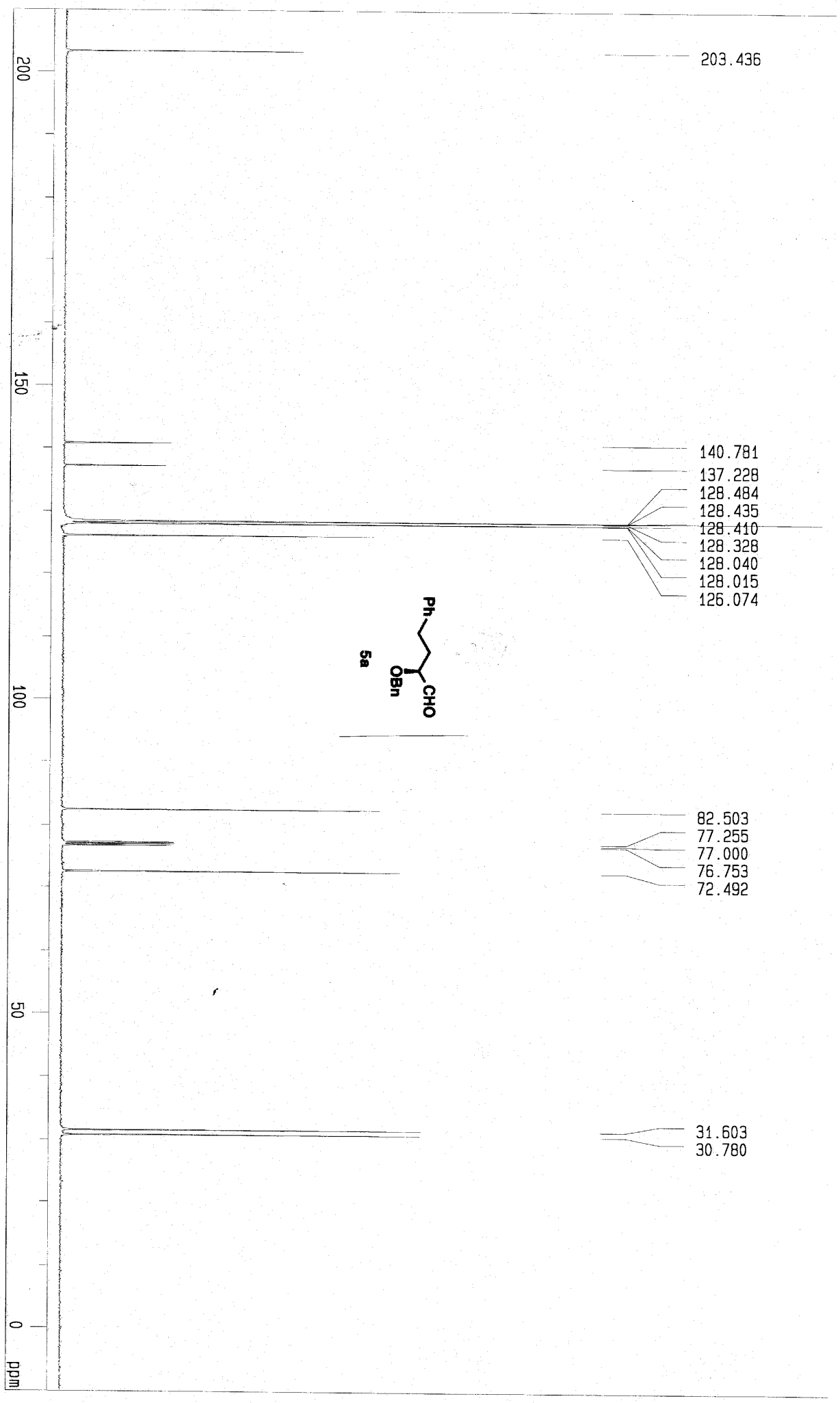
abundance
X : parts per Million : Proton
7.519
7.260
7.216
7.197
6.997
4.313
4.306
4.299
4.294
4.287
4.281
4.269
4.037
3.888
3.860
3.754
3.437
3.328
2.786
2.781
2.764
2.758
2.365
2.355
1.943
1.939
1.922
1.563
1.533
1.278
1.260
1.243
0.148
0.001
3.14
0.94
3.02
3.05
1.00
2.07
0.94
2.08
OMe
N
H
OH
Ph
(S)-4b


abundance
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
-10.0
151.217
141.225
128.420
128.391
125.941
77.324
77.000
76.685
68.486
61.697
36.726
31.034
Ph
N
OMe
H
OH
(S)-4b
X : parts per Million : Carbon13

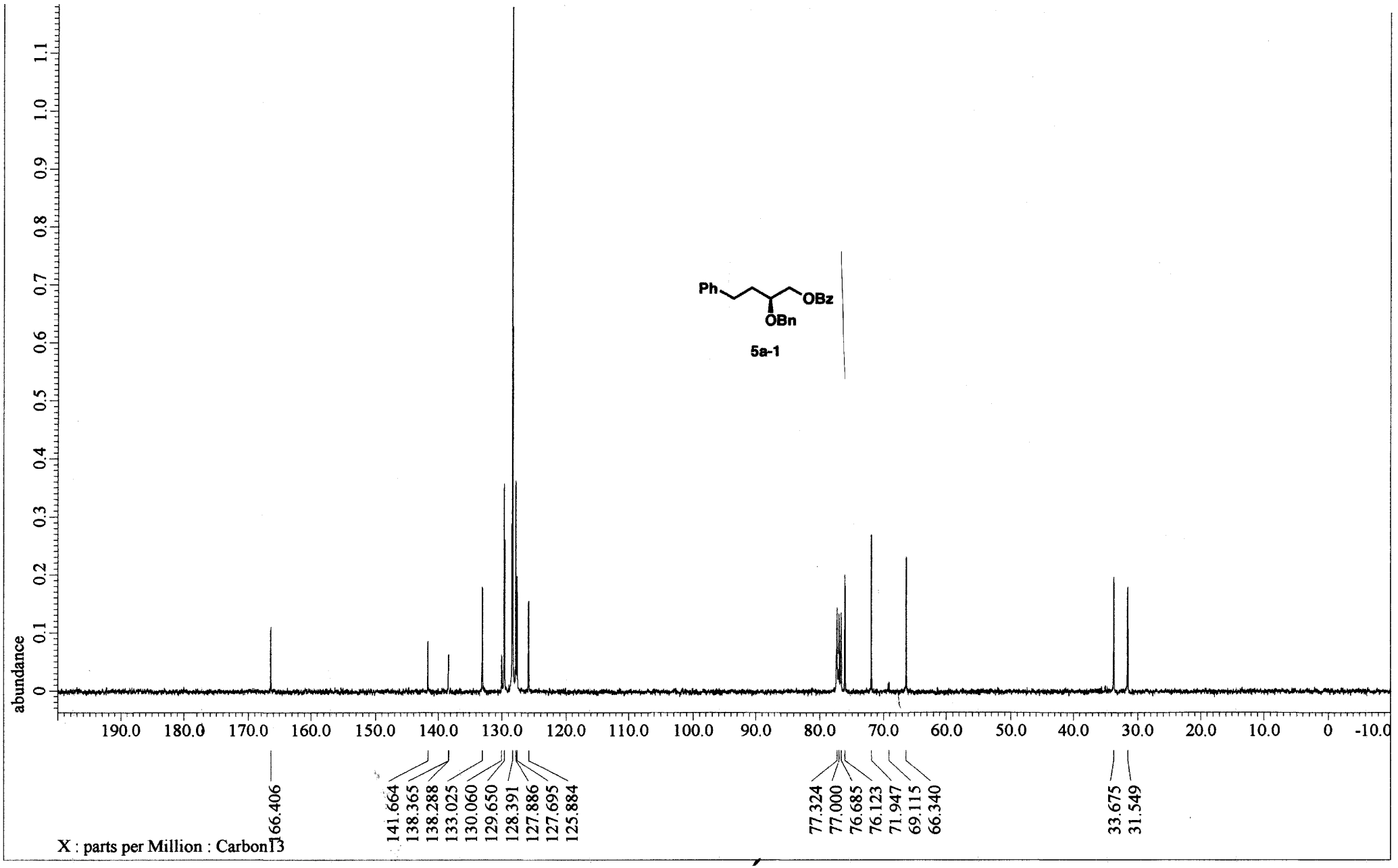

abundance
0 1.0 2.0 3.0 4.0 5.0 6.0 7.0 8.0 9.0 10.0 11.0 12.0 13.0 14.0 15.0 16.0 17.0 18.0 1
X : parts per Million : Proton
7.519
7.260
7.222
7.204
6.997
6.749
6.737
4.717
4.703
4.698
4.693
4.685
4.679
4.673
4.661
4.313
4.281
4.033
3.914
3.888
3.860
3.439
2.786
2.741
2.738
2.719
2.526
2.514
2.355
1.962
1.951
1.944
1.565
1.534
1.256
0.148
0.071
0.009
0.001
-0.007
6.89
0.95
1.00
3.14
2.14
0.93
2.10
(S)-4c
Ph
OH
MeO
N
H

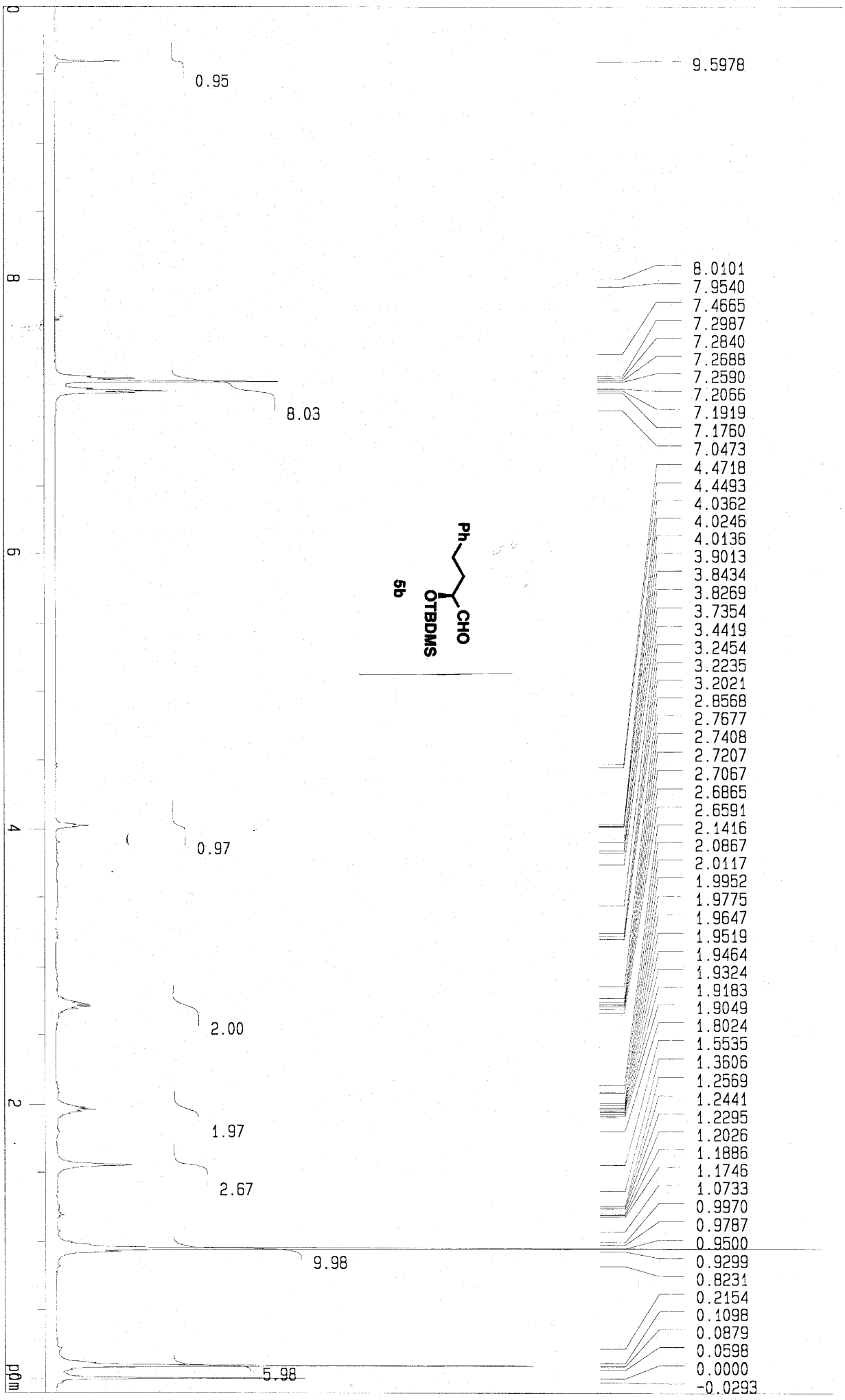

MeO
N
Ph
H
OH
(S)-4c
abundance
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
-10.0
153.258
141.311
128.410
128.229
125.979
77.324
77.000
76.685
65.578
62.088
35.544
31.148
X : parts per Million : Carbon13

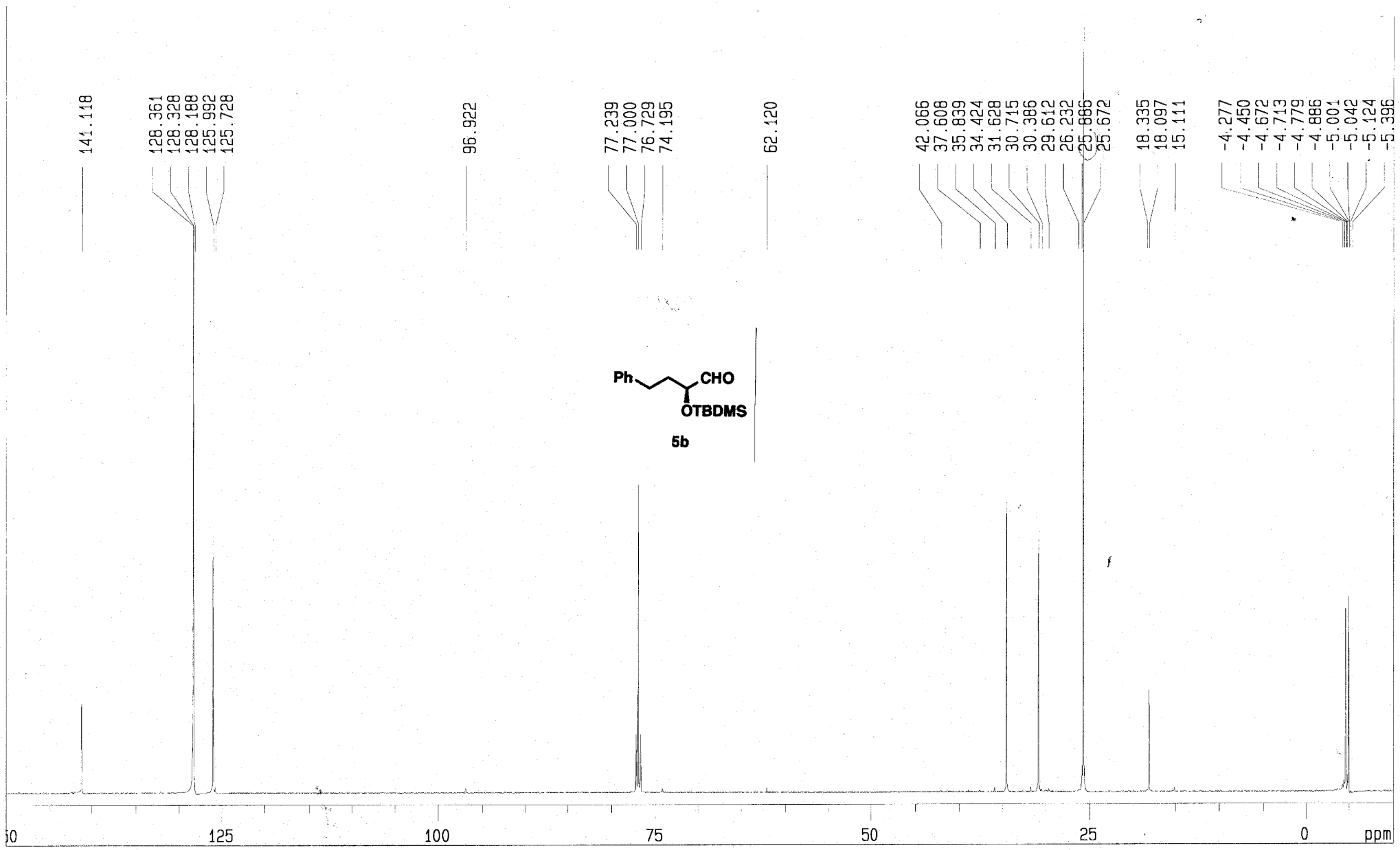

9.6527
0.98
7.3817
7.3731
7.3481
7.3396
7.3310
7.2889
7.2743
7.2584
7.2365
12.20
7.2096
7.1956
7.1803
7.1516
7.1370
Ph
CHO
OBn
5a
4.8080
4.7379
4.6945
4.6714
4.5481
4.5249
1.02
0.95
3.7702
3.7586
3.7476
3.5102
3.3577
3.3376
1.00
2.8287
2.8134
2.8006
2.7878
2.7719
2.7420
2.7262
2.7109
2.6987
2.6829
2.19
2.0208
2.0044
1.9983
1.9891
1.9769
2.09
1.5773
1.5547
1.5321
1.5248
1.2545
0.9915
0.9219
0.1165
0.0000
-0.0214
0
2
4
6
8
ppm


203.436
140.781
137.228
128.484
128.435
128.410
128.328
128.040
128.015
126.074
Ph
OBn
CHO
5a
82.503
77.255
77.000
76.753
72.492
31.603
30.780
200
150
100
50
0
ppm

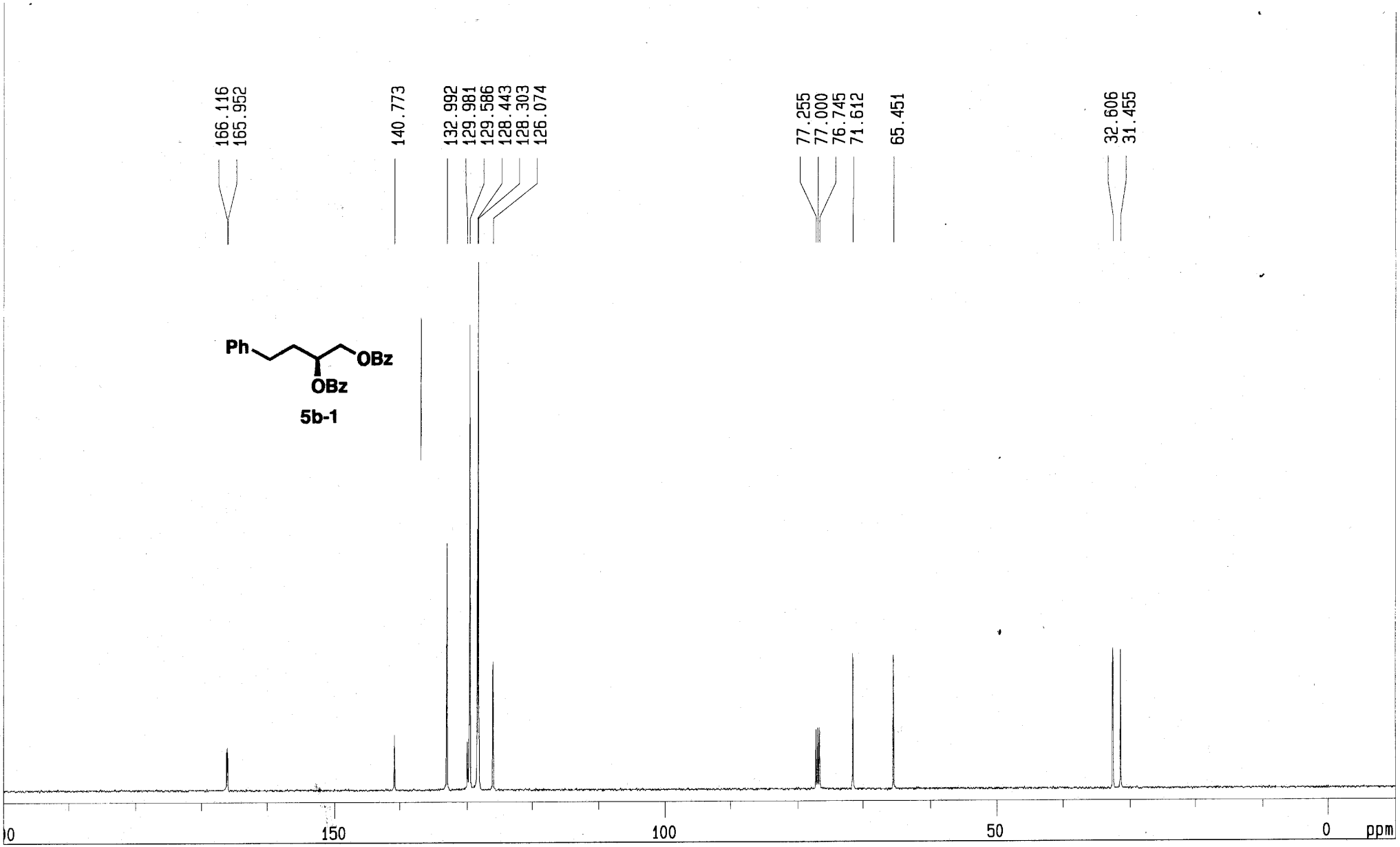
abundance
X : parts per Million : Proton
OBz
OBn
Ph
5a-1
11.59
2.05
1.99
1.97
1.00
0.99
0.98
0.89
8.048
8.030
8.026
7.885
7.444
7.331
7.281
7.260
7.186
6.995
4.751
4.723
4.483
4.473
4.397
4.383
3.795
3.783
3.770
3.765
3.750
2.843
2.829
2.819
2.805
2.733
2.726
2.709
2.041
2.017
1.959
1.952
1.935
1.547
1.544
1.515
1.014
0.149
0.002

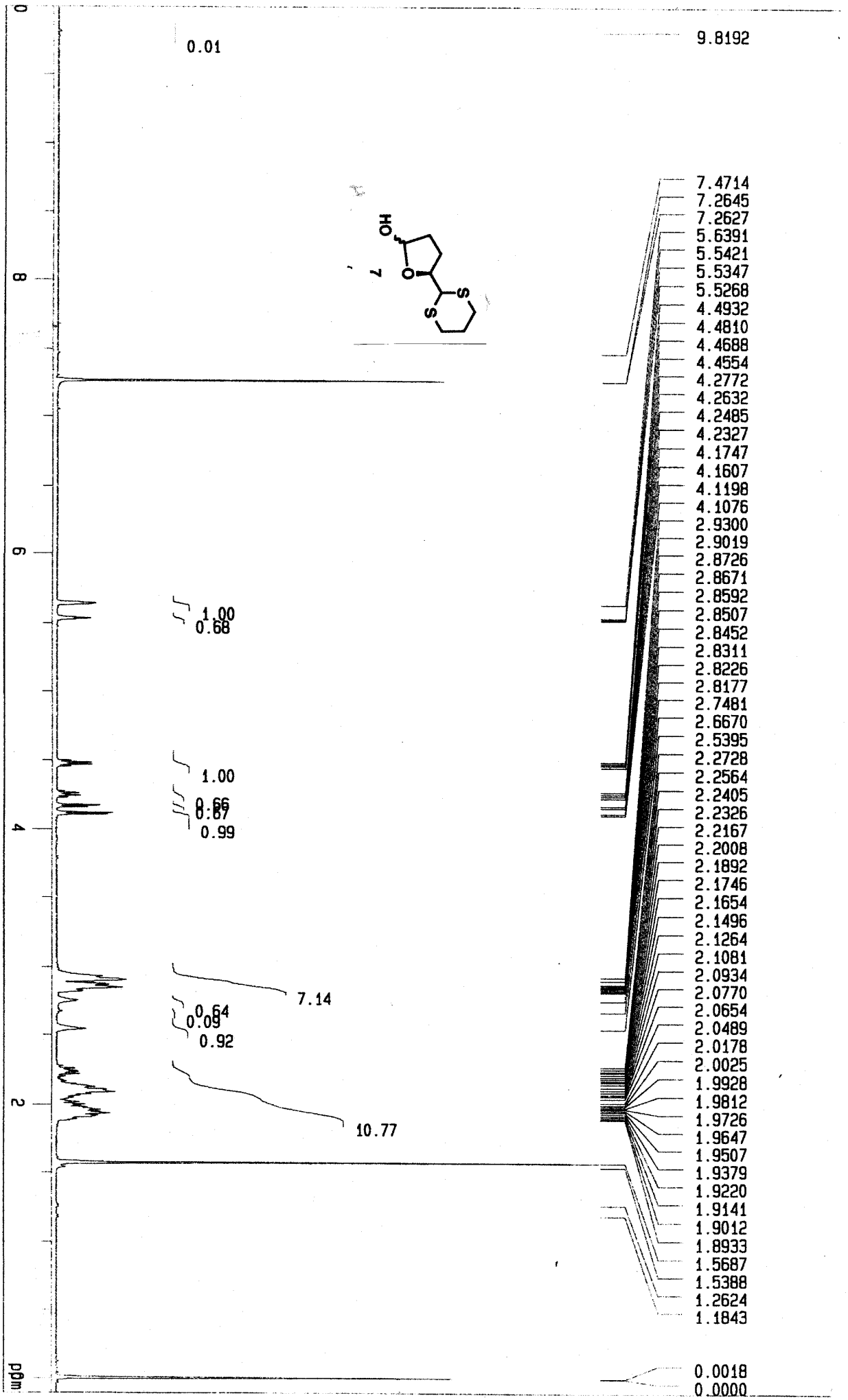

Ph
OBz
OBn
5a-1
abundance
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1.0
1.1
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
-10.0
166.406
141.664
138.365
138.288
133.025
130.060
129.650
128.391
127.886
127.695
125.884
77.324
77.000
76.685
76.123
71.947
69.115
66.340
33.675
31.549
X : parts per Million : Carbon13

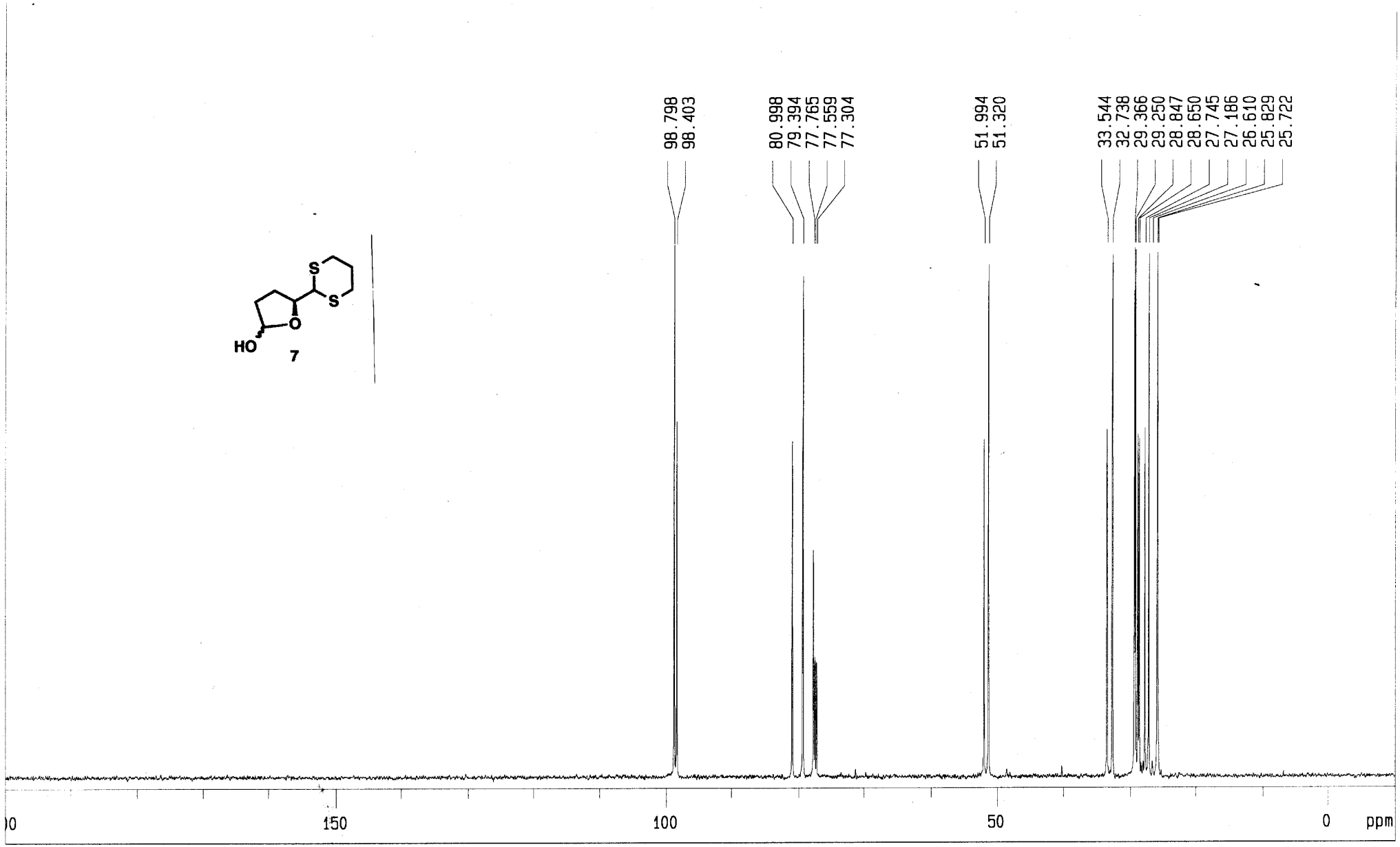

0.95
8.03
0.97
2.00
1.97
2.67
9.98
5.98
9.5978
8.0101
7.9540
7.4665
7.2987
7.2840
7.2688
7.2590
7.2066
7.1919
7.1760
7.0473
4.4718
4.4493
4.0362
4.0246
4.0136
3.9013
3.8434
3.8269
3.7354
3.4419
3.2454
3.2235
3.2021
2.8568
2.7677
2.7408
2.7207
2.7067
2.6865
2.6591
2.1416
2.0867
2.0117
1.9952
1.9775
1.9647
1.9519
1.9464
1.9324
1.9183
1.9049
1.8024
1.5535
1.3606
1.2569
1.2441
1.2295
1.2026
1.1886
1.1746
1.0733
0.9970
0.9787
0.9500
0.9299
0.8231
0.2154
0.1098
0.0879
0.0598
0.0000
-0.0293
Ph
CHO
OTBDMS
5b
0
2
4
6
8
ppm

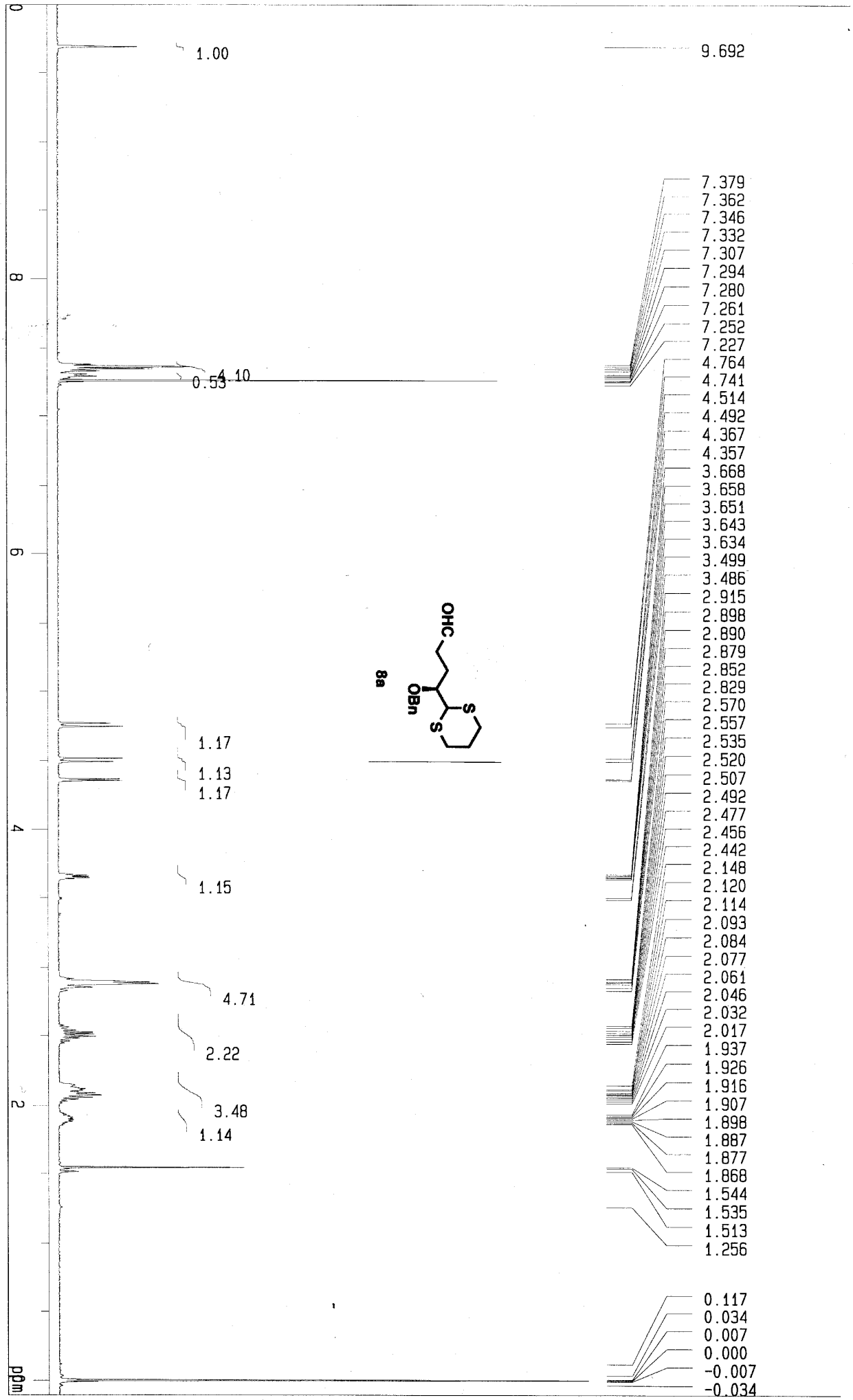

141.118
128.361
128.328
128.188
125.992
125.728
96.922
77.239
77.000
76.729
74.195
62.120
42.066
37.608
35.839
34.424
31.628
30.715
30.386
29.612
26.232
25.866
25.672
18.335
18.097
15.111
-4.277
-4.450
-4.672
-4.713
-4.779
-4.886
-5.001
-5.042
-5.124
-5.396
Ph
CHO
OTBDMS
5b
125
100
75
50
25
0
ppm

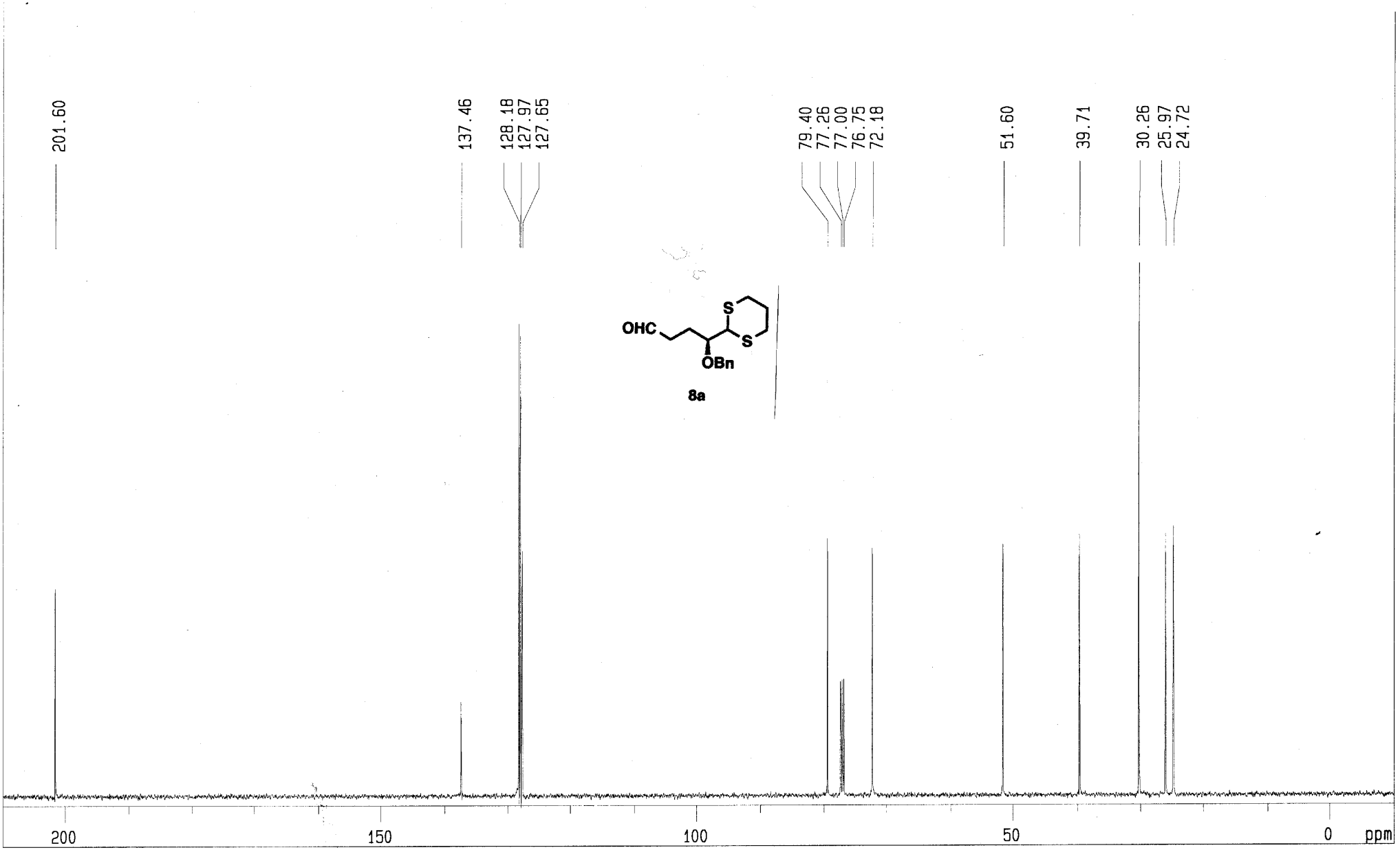
0.0000
0.1165
1.5211
1.5522
1.5901
2.0855
2.0989
2.1142
2.1276
2.1337
2.1435
2.1563
2.1807
2.1990
2.2100
2.2277
2.2387
2.2564
2.3564
2.7420
2.7549
2.7701
2.7829
2.7884
2.7970
2.8018
2.8092
2.8165
2.8281
2.8366
2.8445
2.8561
4.4804
4.4932
4.5042
4.5170
4.5646
4.5719
4.5884
4.5957
5.5085
5.5256
5.5317
5.5378
5.5543
7.0485
7.1742
7.1937
7.2090
7.2603
7.2670
7.2822
7.2975
7.3988
7.4146
7.4305
7.4476
7.4628
7.5306
7.5458
7.5574
7.5708
7.5855
7.9949
8.0101
8.0480
8.0638
OBz
OBz
Ph
5b-1
0.99
0.99
2.09
1.00
1.03
1.06
2.00
1.99
2.01
4.12
5.82
3.00
ppm
2
4
6
8

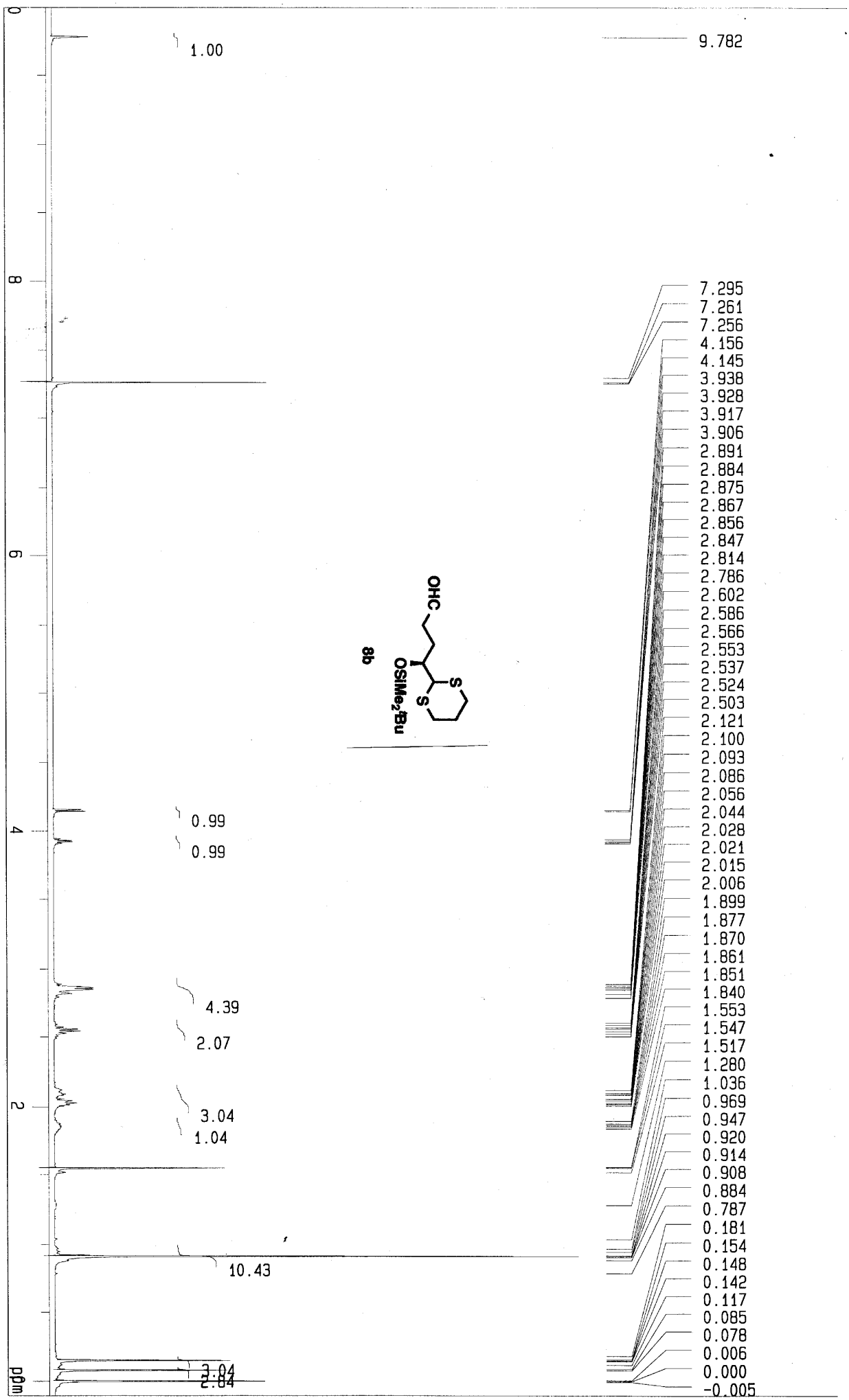

166.116
165.952
140.773
132.992
129.981
129.586
128.443
128.303
126.074
77.255
77.000
76.745
71.612
65.451
32.606
31.455
Ph
OBz
OBz
5b-1
150
100
50
0
ppm

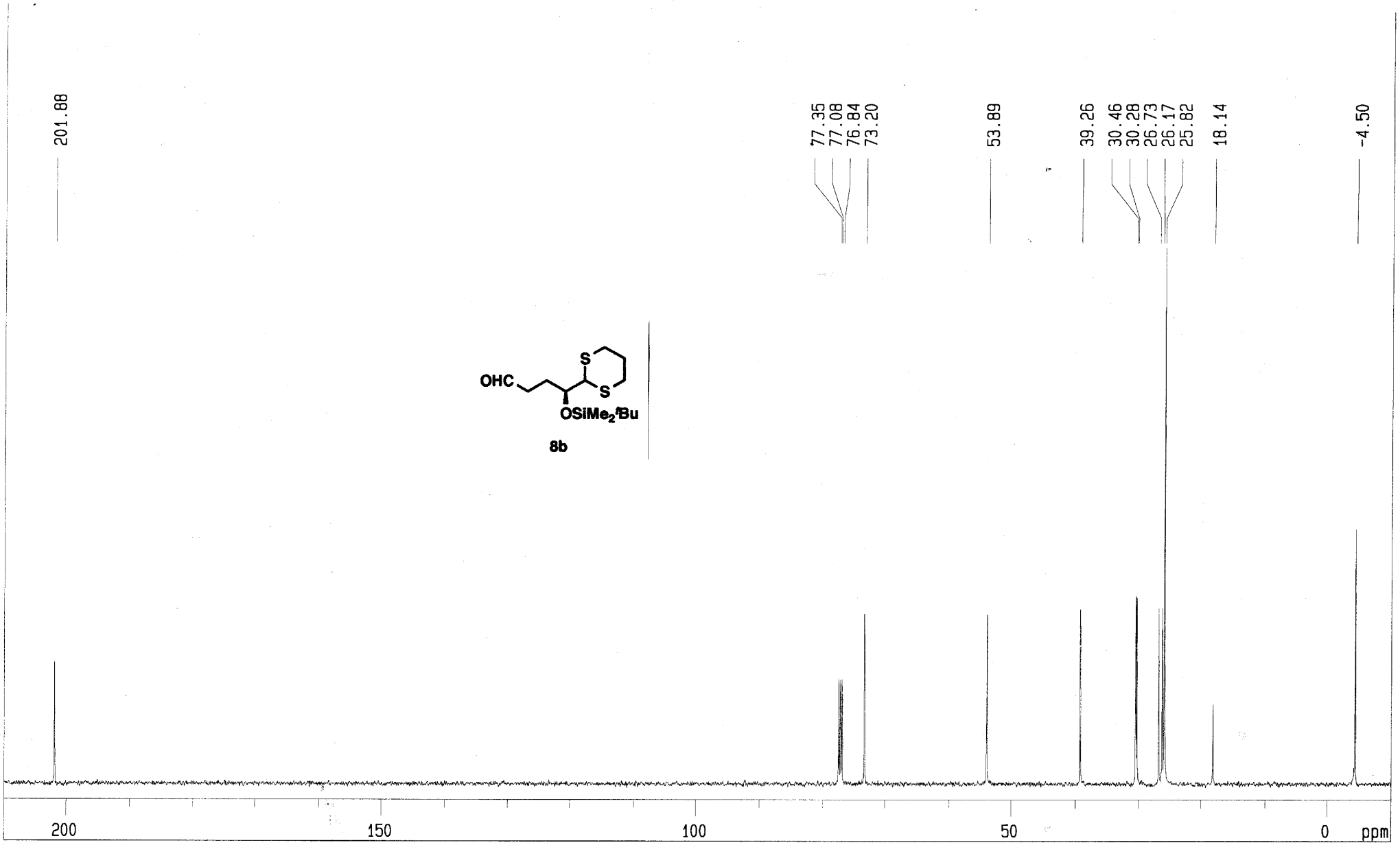

0.01
9.8192
7.4714
7.2645
7.2627
5.6391
5.5421
5.5347
5.5268
4.4932
4.4810
4.4688
4.4554
4.2772
4.2632
4.2485
4.2327
4.1747
4.1607
4.1198
4.1076
2.9300
2.9019
2.8726
2.8671
2.8592
2.8507
2.8452
2.8311
2.8226
2.8177
2.7481
2.6670
2.5395
2.2728
2.2564
2.2405
2.2326
2.2167
2.2008
2.1892
2.1746
2.1654
2.1496
2.1264
2.1081
2.0934
2.0770
2.0654
2.0489
2.0178
2.0025
1.9928
1.9812
1.9726
1.9647
1.9507
1.9379
1.9220
1.9141
1.9012
1.8933
1.5687
1.5388
1.2624
1.1843
0.0018
0.0000
1.00
0.68
1.00
0.66
0.87
0.99
7.14
0.64
0.09
0.92
10.77
HO
O
S
S
7
8
6
4
2
0
ppm

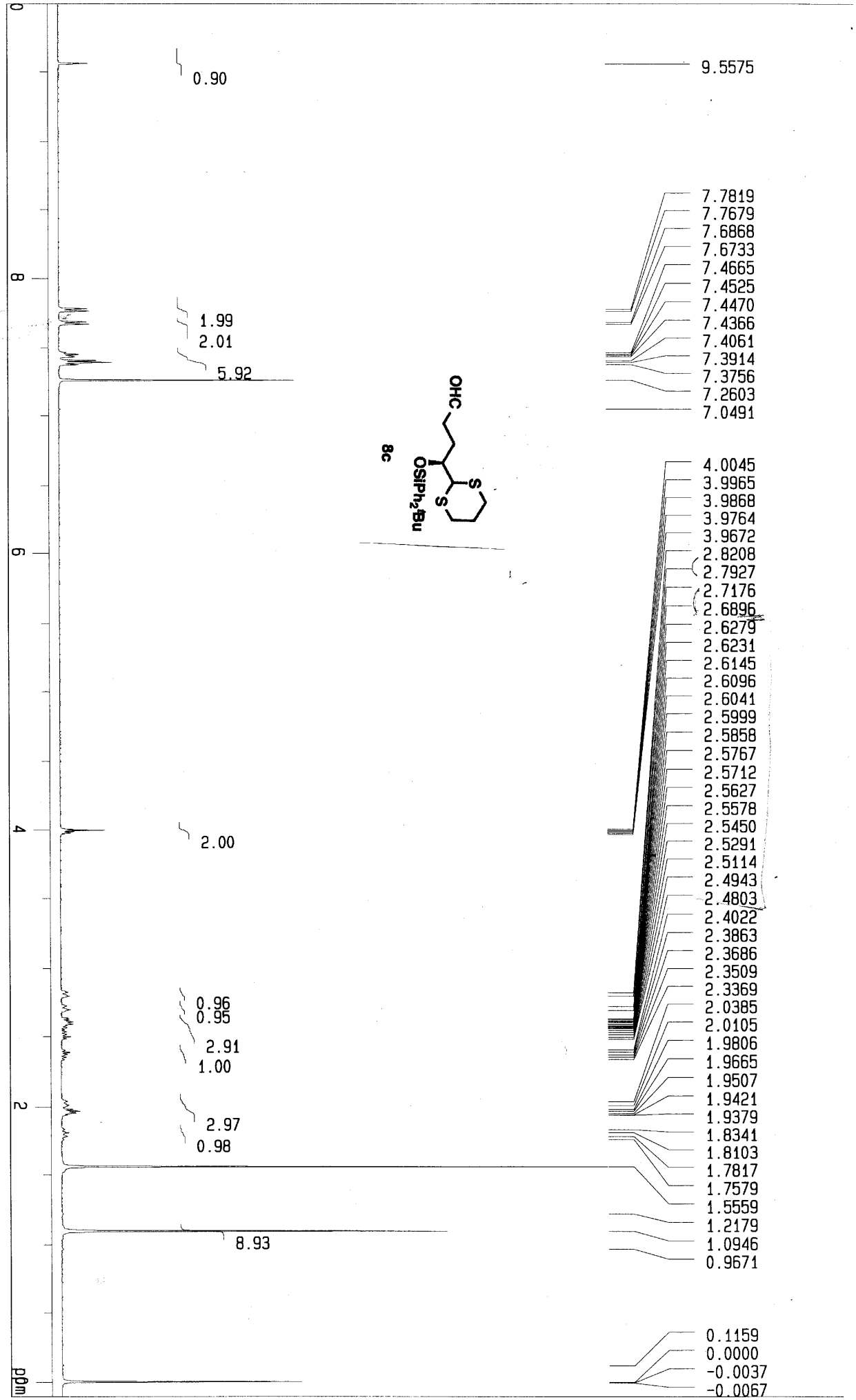

98.798
98.403
80.998
79.394
77.765
77.559
77.304
51.994
51.320
33.544
32.738
29.366
29.250
28.847
28.650
27.745
27.186
26.610
25.829
25.722
S
S
O
HO
7
150
100
50
0
ppm

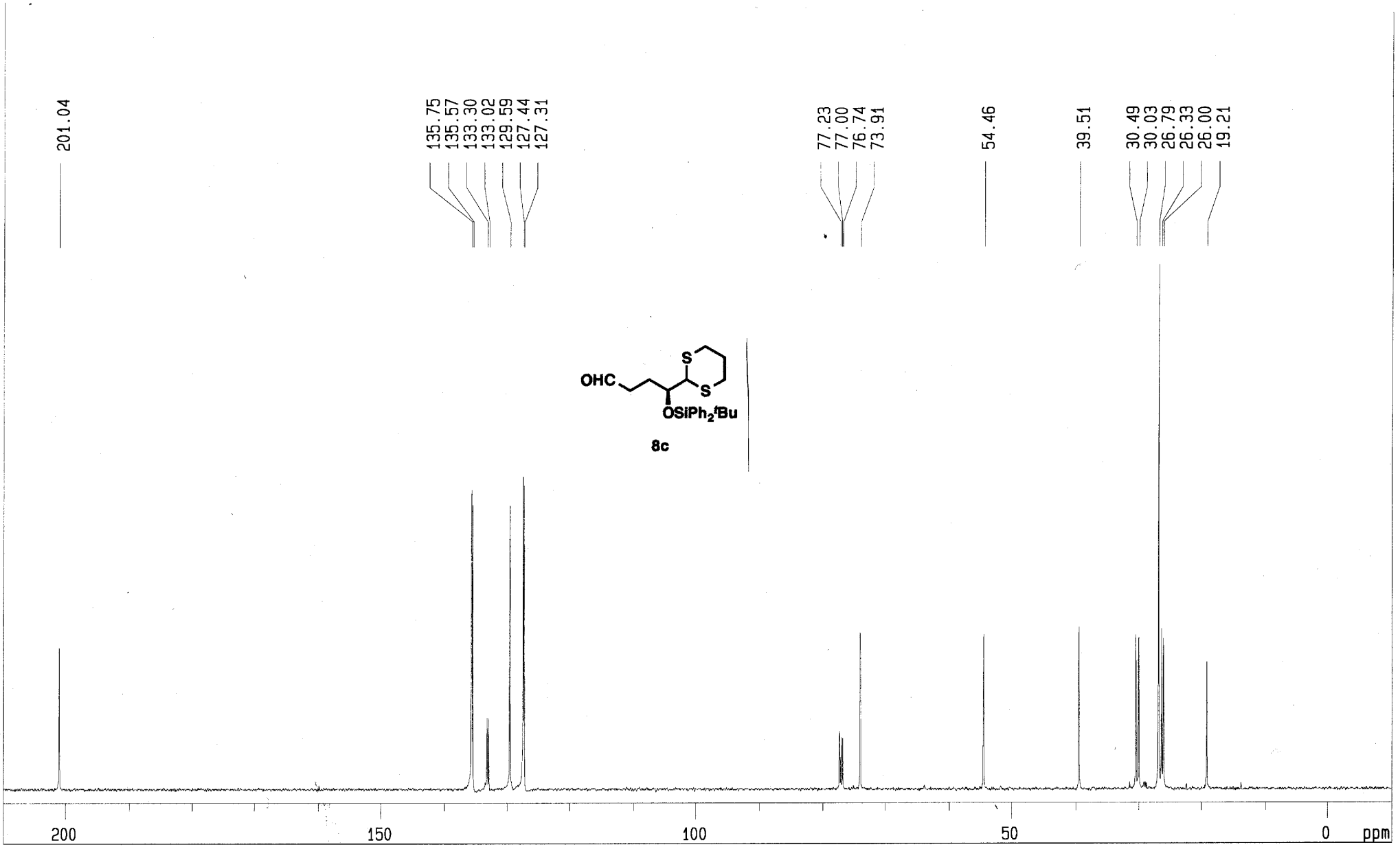

1.00
0.53
4.10
1.17
1.13
1.17
1.15
4.71
2.22
3.48
1.14
9.692
7.379
7.362
7.346
7.332
7.307
7.294
7.280
7.261
7.252
7.227
4.764
4.741
4.514
4.492
4.367
4.357
3.668
3.658
3.651
3.643
3.634
3.499
3.486
2.915
2.898
2.890
2.879
2.852
2.829
2.570
2.557
2.535
2.520
2.507
2.492
2.477
2.456
2.442
2.148
2.120
2.114
2.093
2.084
2.077
2.061
2.046
2.032
2.017
1.937
1.926
1.916
1.907
1.898
1.887
1.877
1.868
1.544
1.535
1.513
1.256
0.117
0.034
0.007
0.000
-0.007
-0.034
OHC
OBn
S
S
8a
0
8
6
4
2
ppm

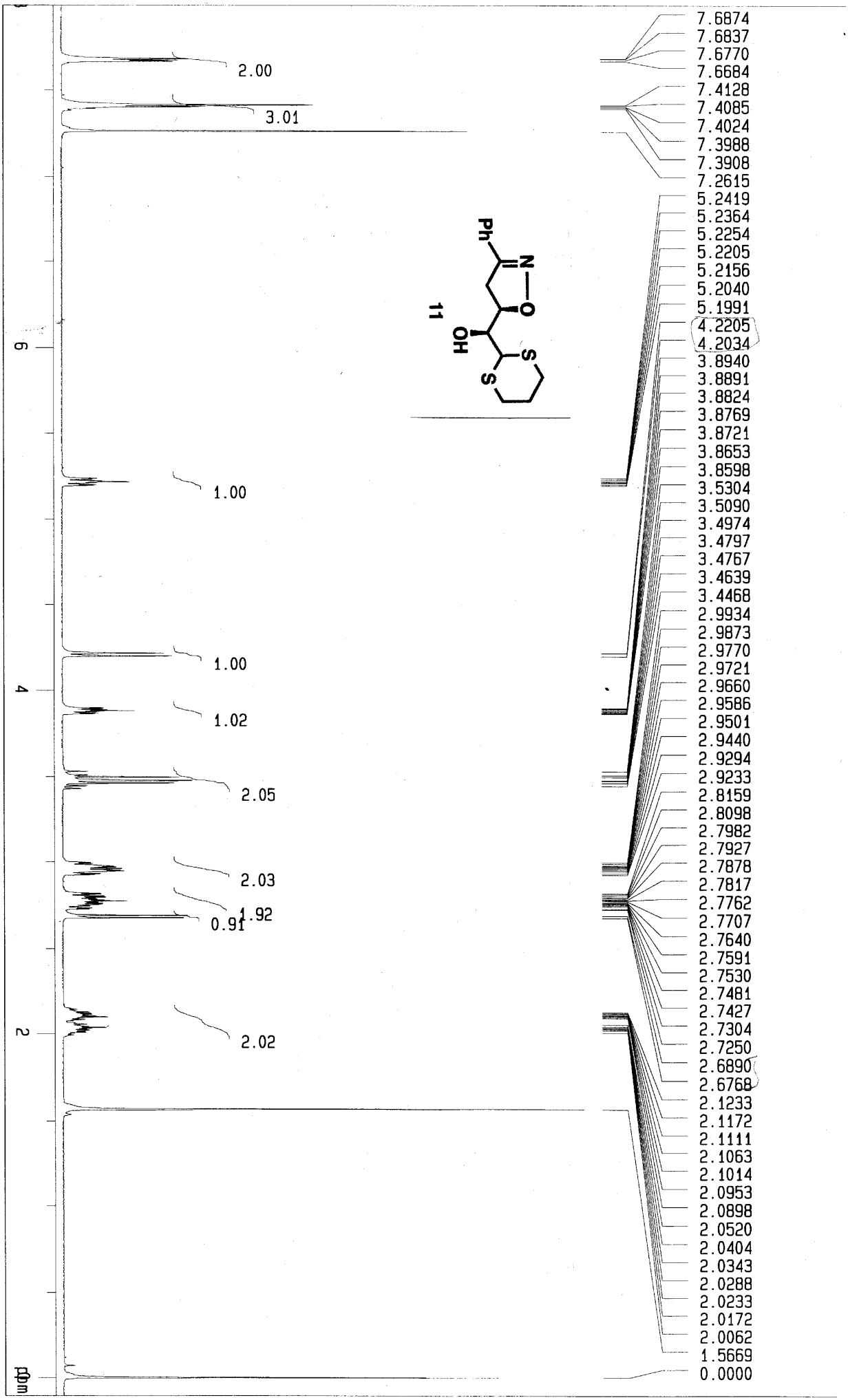

201.60
137.46
128.18
127.97
127.65
79.40
77.26
77.00
76.75
72.18
51.60
39.71
30.26
25.97
24.72
OHC
S
S
OBn
8a
200
150
100
50
0
ppm

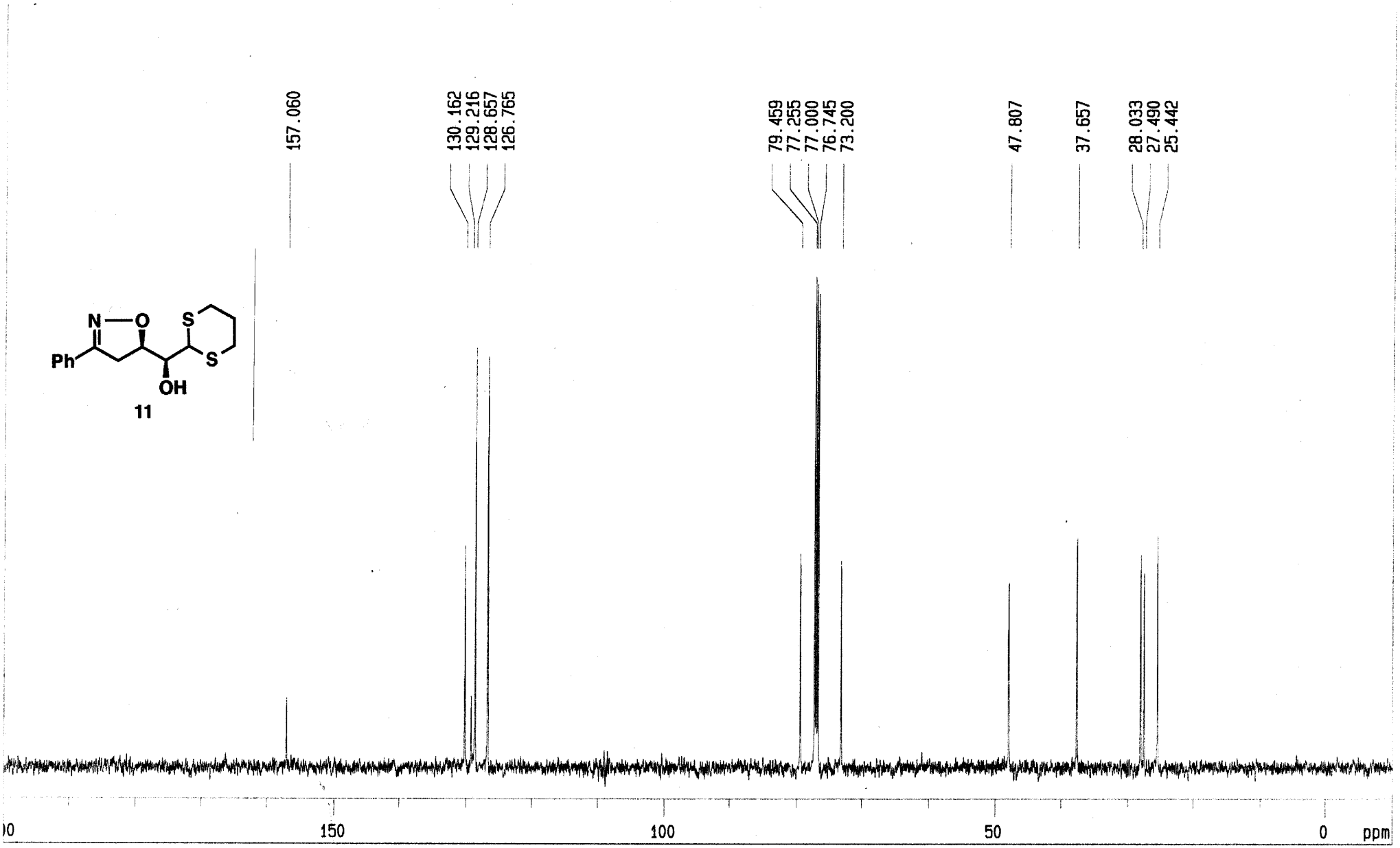

1.00
0.99
0.99
4.39
2.07
3.04
1.04
10.43
3.04
2.84
9.782
7.295
7.261
7.256
4.156
4.145
3.938
3.928
3.917
3.906
2.891
2.884
2.875
2.867
2.856
2.847
2.814
2.786
2.602
2.586
2.566
2.553
2.537
2.524
2.503
2.121
2.100
2.093
2.086
2.056
2.044
2.028
2.021
2.015
2.006
1.899
1.877
1.870
1.861
1.851
1.840
1.553
1.547
1.517
1.280
1.036
0.969
0.947
0.920
0.914
0.908
0.884
0.787
0.181
0.154
0.148
0.142
0.117
0.085
0.078
0.006
0.000
-0.005
OHC
OSiMe2tBu
S
S
8b
0
2
4
6
8
ppm

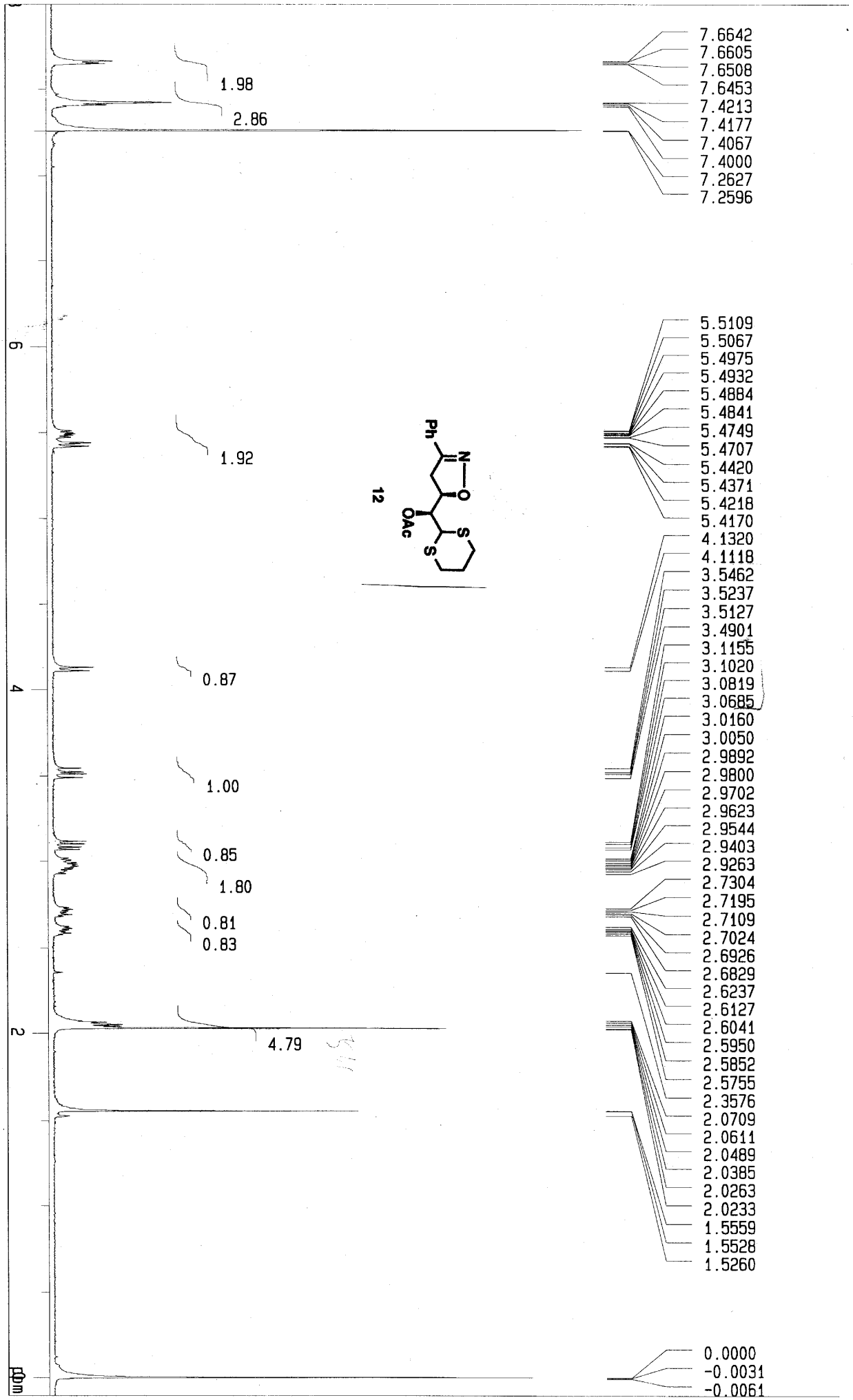

201.88
77.35
77.08
76.84
73.20
53.89
39.26
30.46
30.28
26.73
26.17
25.82
18.14
-4.50
OHC
S
S
OSiMe2tBu
8b
200
150
100
50
0
ppm

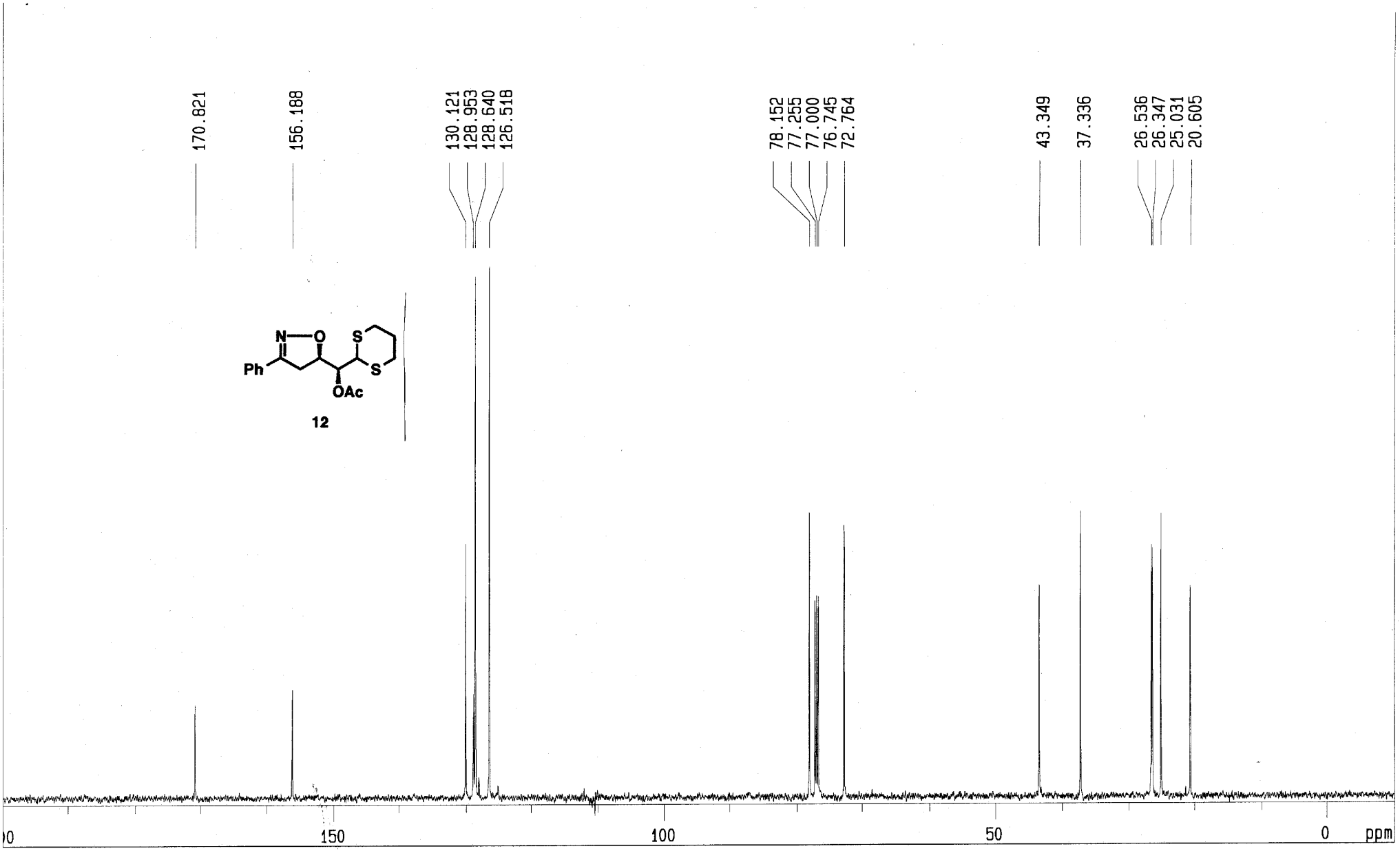

0.90
1.99
2.01
5.92
2.00
0.96
0.95
2.91
1.00
2.97
0.98
8.93
9.5575
7.7819
7.7679
7.6868
7.6733
7.4665
7.4525
7.4470
7.4366
7.4061
7.3914
7.3756
7.2603
7.0491
4.0045
3.9965
3.9868
3.9764
3.9672
2.8208
2.7927
2.7176
2.6896
2.6279
2.6231
2.6145
2.6096
2.6041
2.5999
2.5858
2.5767
2.5712
2.5627
2.5578
2.5450
2.5291
2.5114
2.4943
2.4803
2.4022
2.3863
2.3686
2.3509
2.3369
2.0385
2.0105
1.9806
1.9665
1.9507
1.9421
1.9379
1.8341
1.8103
1.7817
1.7579
1.5559
1.2179
1.0946
0.9671
0.1159
0.0000
-0.0037
-0.0067
OHC
OSiPh2tBu
S
S
8c
0
8
6
4
2
ppm

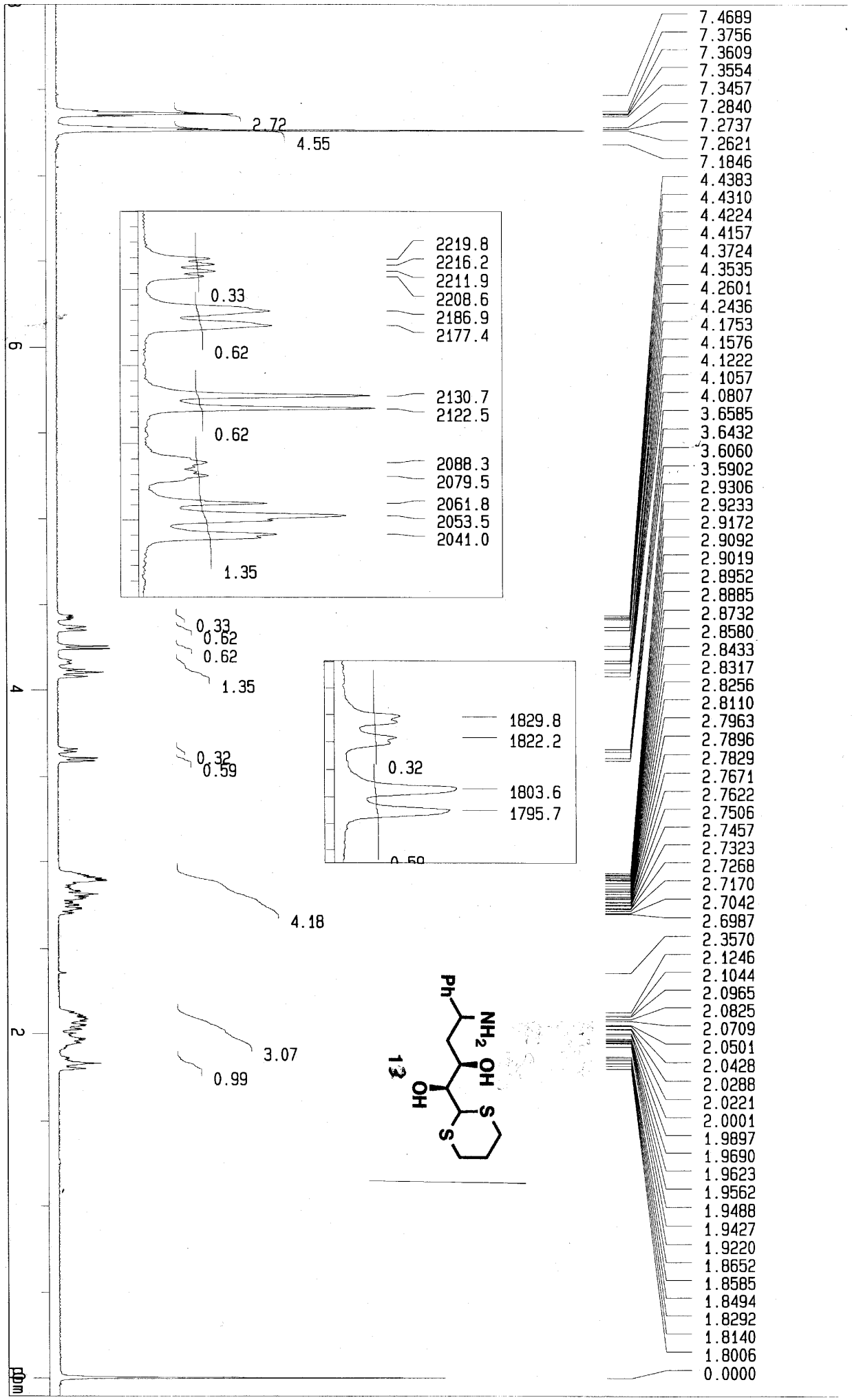

201.04
135.75
135.57
133.30
133.02
129.59
127.44
127.31
77.23
77.00
76.74
73.91
54.46
39.51
30.49
30.03
26.79
26.33
26.00
19.21
OHC
S
S
OSiPh2tBu
8c
200
150
100
50
0
ppm

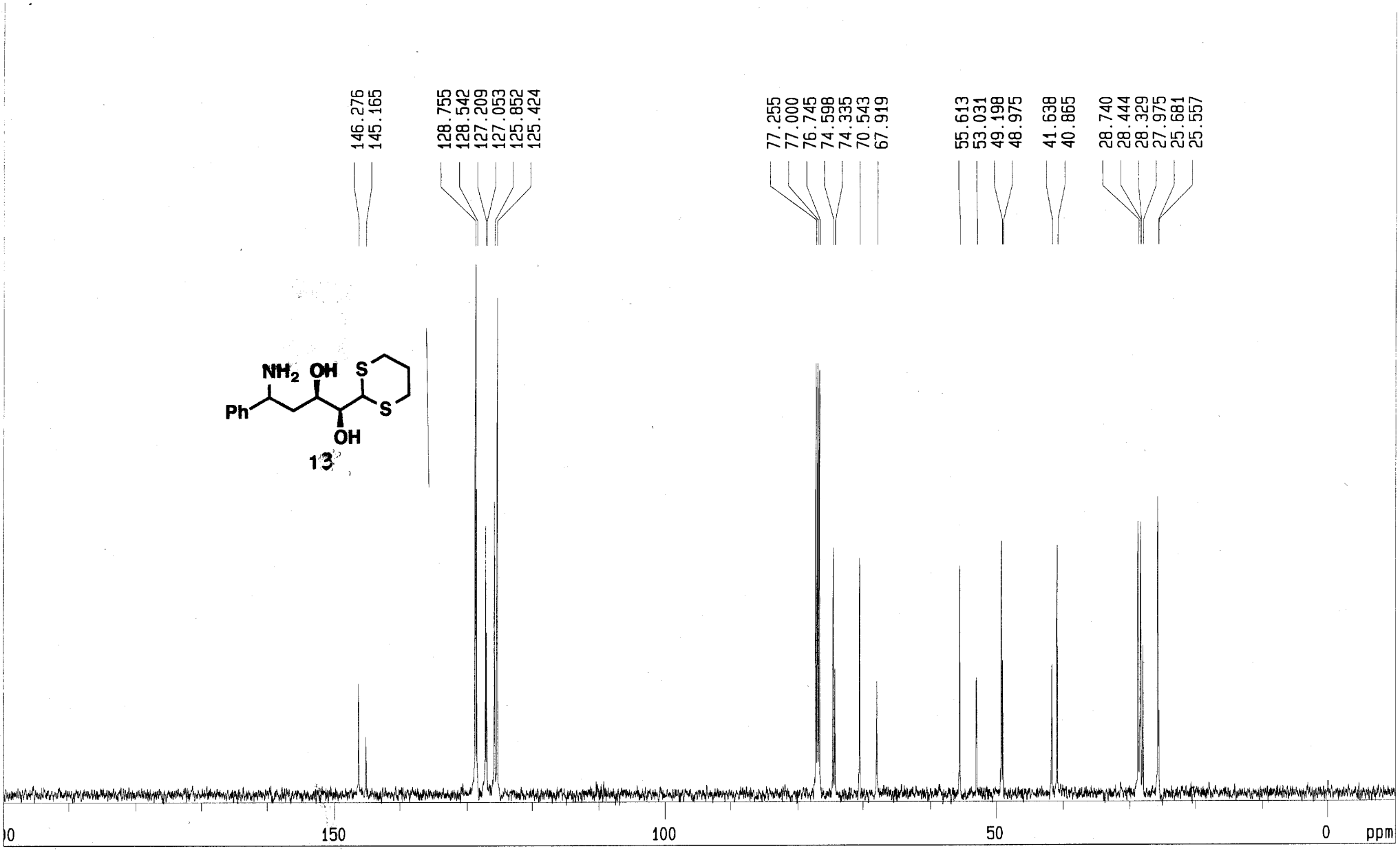

2.00
3.01
1.00
1.00
1.02
2.05
2.03
1.92
0.91
2.02
Ph
N
O
OH
S
S
11
6
4
2
ppm
7.6874
7.6837
7.6770
7.6684
7.4128
7.4085
7.4024
7.3988
7.3908
7.2615
5.2419
5.2364
5.2254
5.2205
5.2156
5.2040
5.1991
4.2205
4.2034
3.8940
3.8891
3.8824
3.8769
3.8721
3.8653
3.8598
3.5304
3.5090
3.4974
3.4797
3.4767
3.4639
3.4468
2.9934
2.9873
2.9770
2.9721
2.9660
2.9586
2.9501
2.9440
2.9294
2.9233
2.8159
2.8098
2.7982
2.7927
2.7878
2.7817
2.7762
2.7707
2.7640
2.7591
2.7530
2.7481
2.7427
2.7304
2.7250
2.6890
2.6768
2.1233
2.1172
2.1111
2.1063
2.1014
2.0953
2.0898
2.0520
2.0404
2.0343
2.0288
2.0233
2.0172
2.0062
1.5669
0.0000

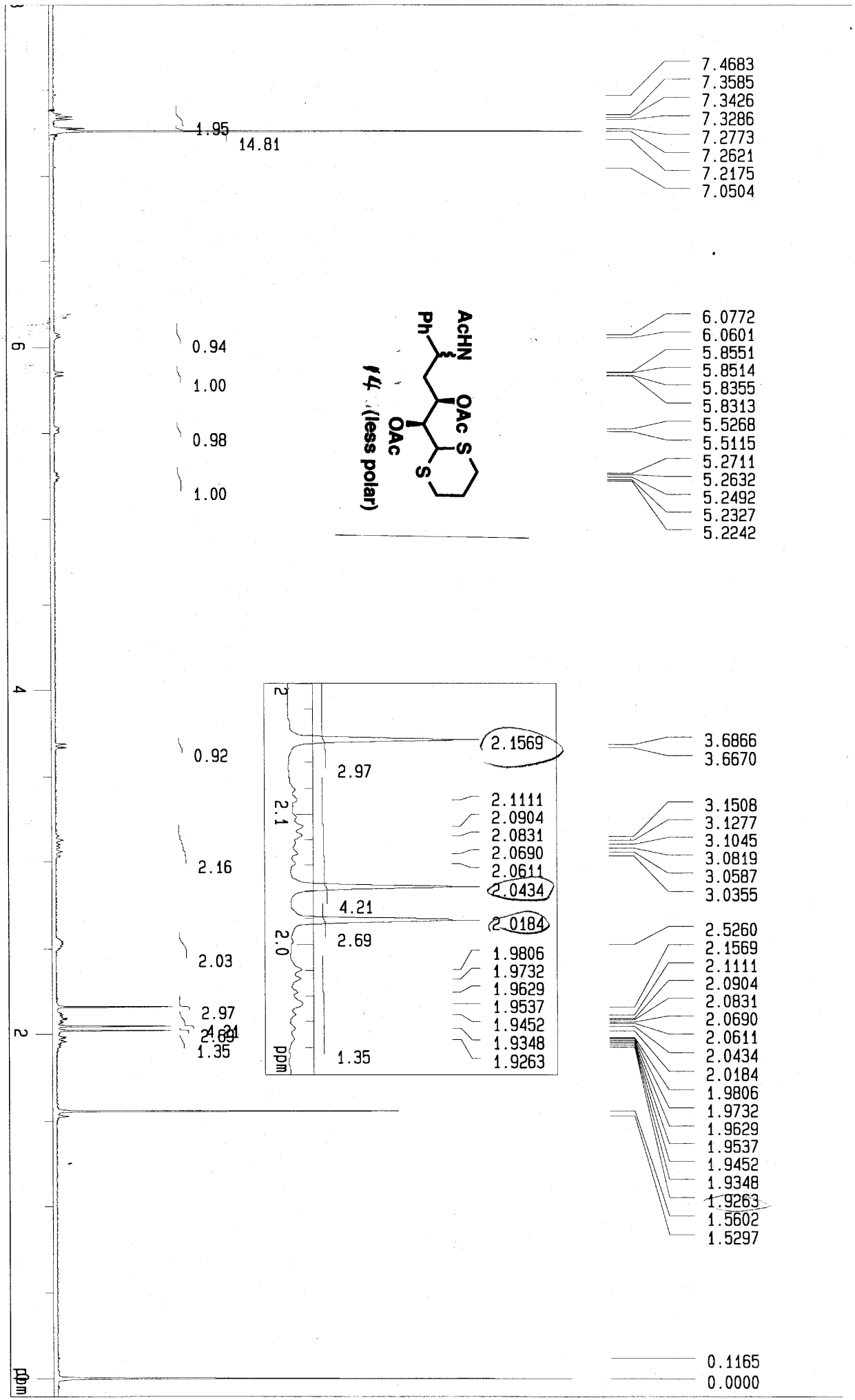

157.060
130.162
129.216
128.657
126.765
79.459
77.255
77.000
76.745
73.200
47.807
37.657
28.033
27.490
25.442
N
O
S
S
Ph
OH
11
150
100
50
0
ppm

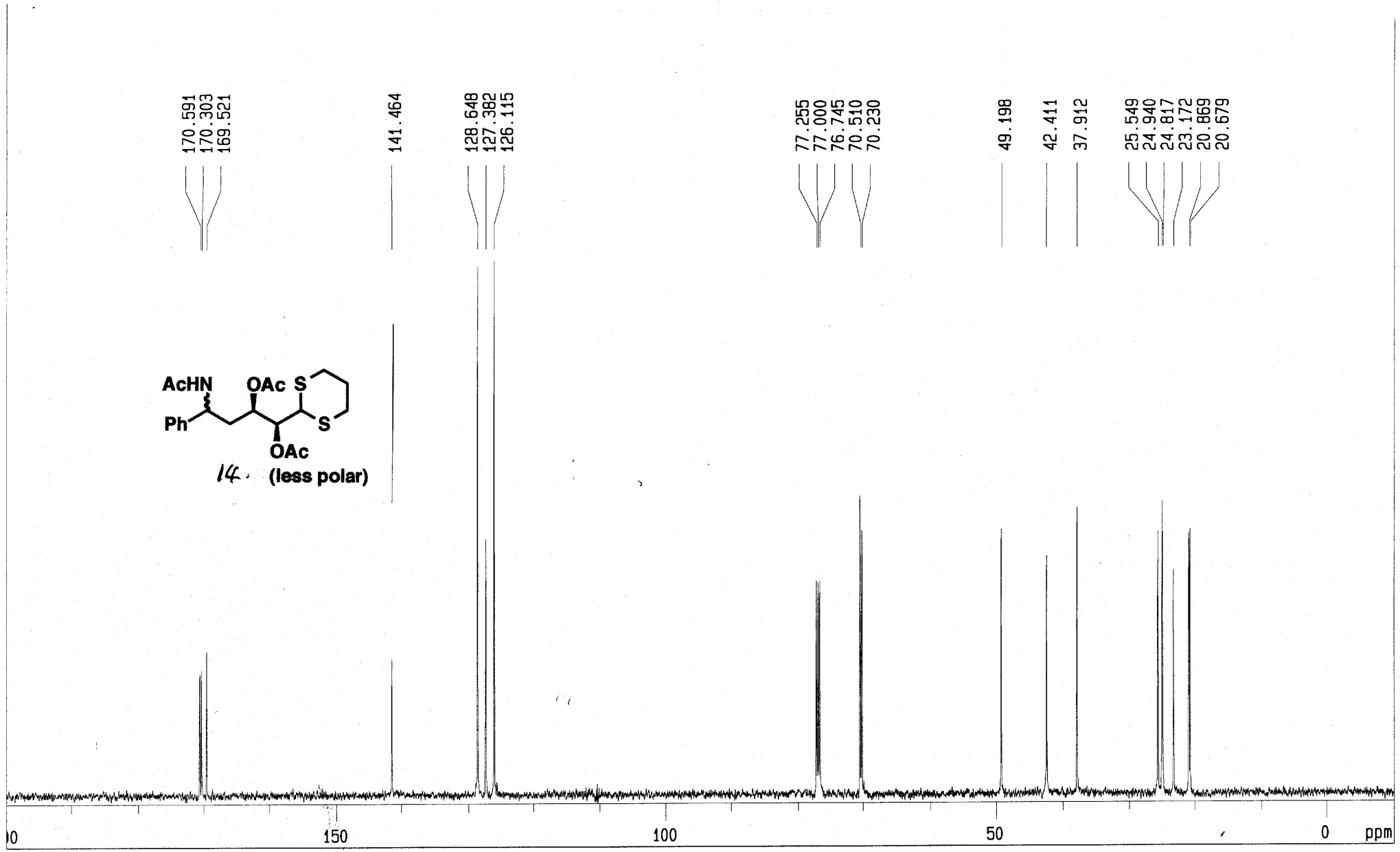

7.6642
7.6605
7.6508
7.6453
7.4213
7.4177
7.4067
7.4000
7.2627
7.2596
5.5109
5.5067
5.4975
5.4932
5.4884
5.4841
5.4749
5.4707
5.4420
5.4371
5.4218
5.4170
4.1320
4.1118
3.5462
3.5237
3.5127
3.4901
3.1155
3.1020
3.0819
3.0685
3.0160
3.0050
2.9892
2.9800
2.9702
2.9623
2.9544
2.9403
2.9263
2.7304
2.7195
2.7109
2.7024
2.6926
2.6829
2.6237
2.6127
2.6041
2.5950
2.5852
2.5755
2.3576
2.0709
2.0611
2.0489
2.0385
2.0263
2.0233
1.5559
1.5528
1.5260
0.0000
-0.0031
-0.0061
1.98
2.86
1.92
0.87
1.00
0.85
1.80
0.81
0.83
4.79
Ph
N
O
S
S
OAc
12
6
4
2
0
ppm

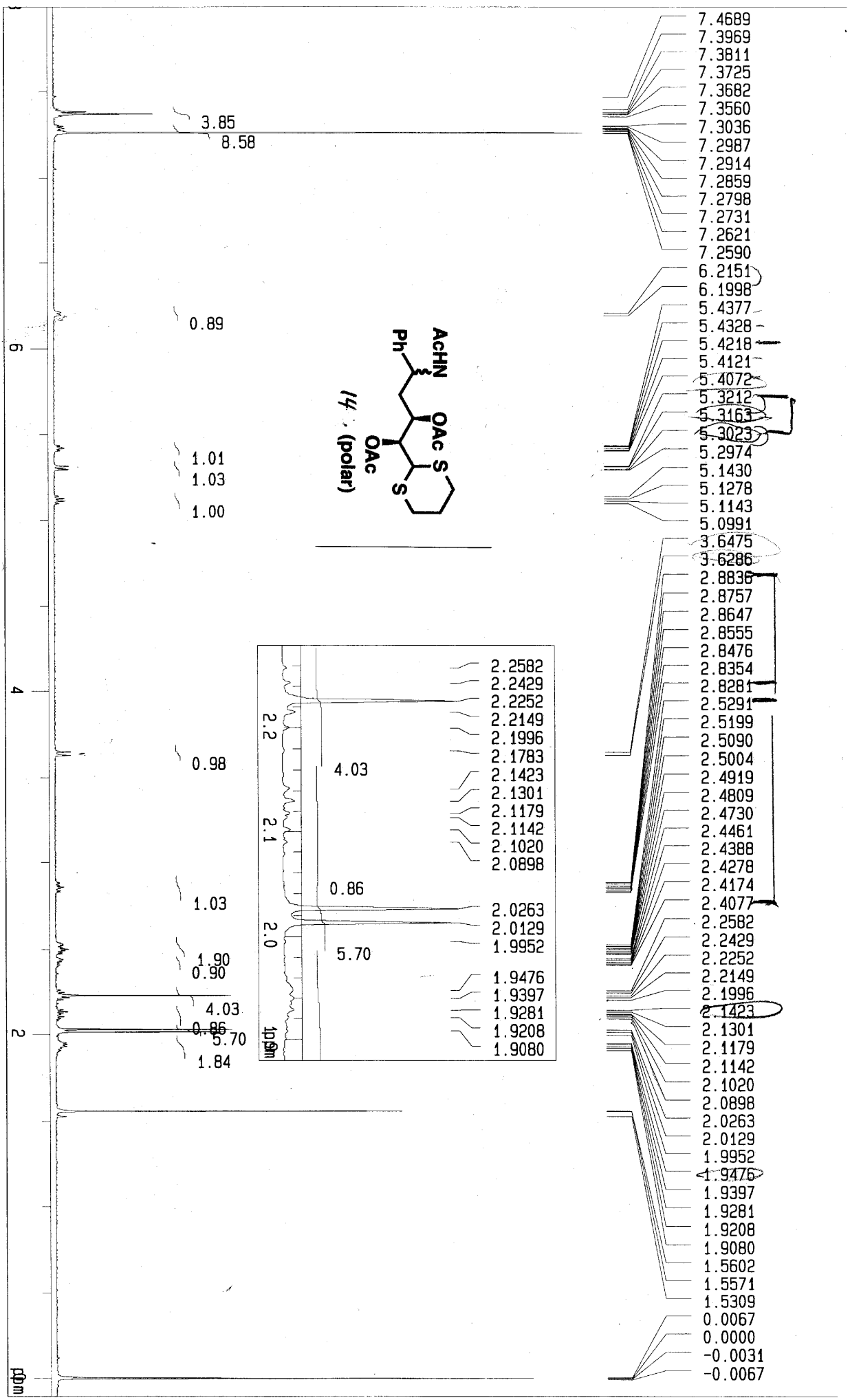

170.821
156.188
130.121
128.953
128.640
126.518
78.152
77.255
77.000
76.745
72.764
43.349
37.336
26.536
26.347
25.031
20.605
N
O
S
S
Ph
OAc
12
150
100
50
0
ppm

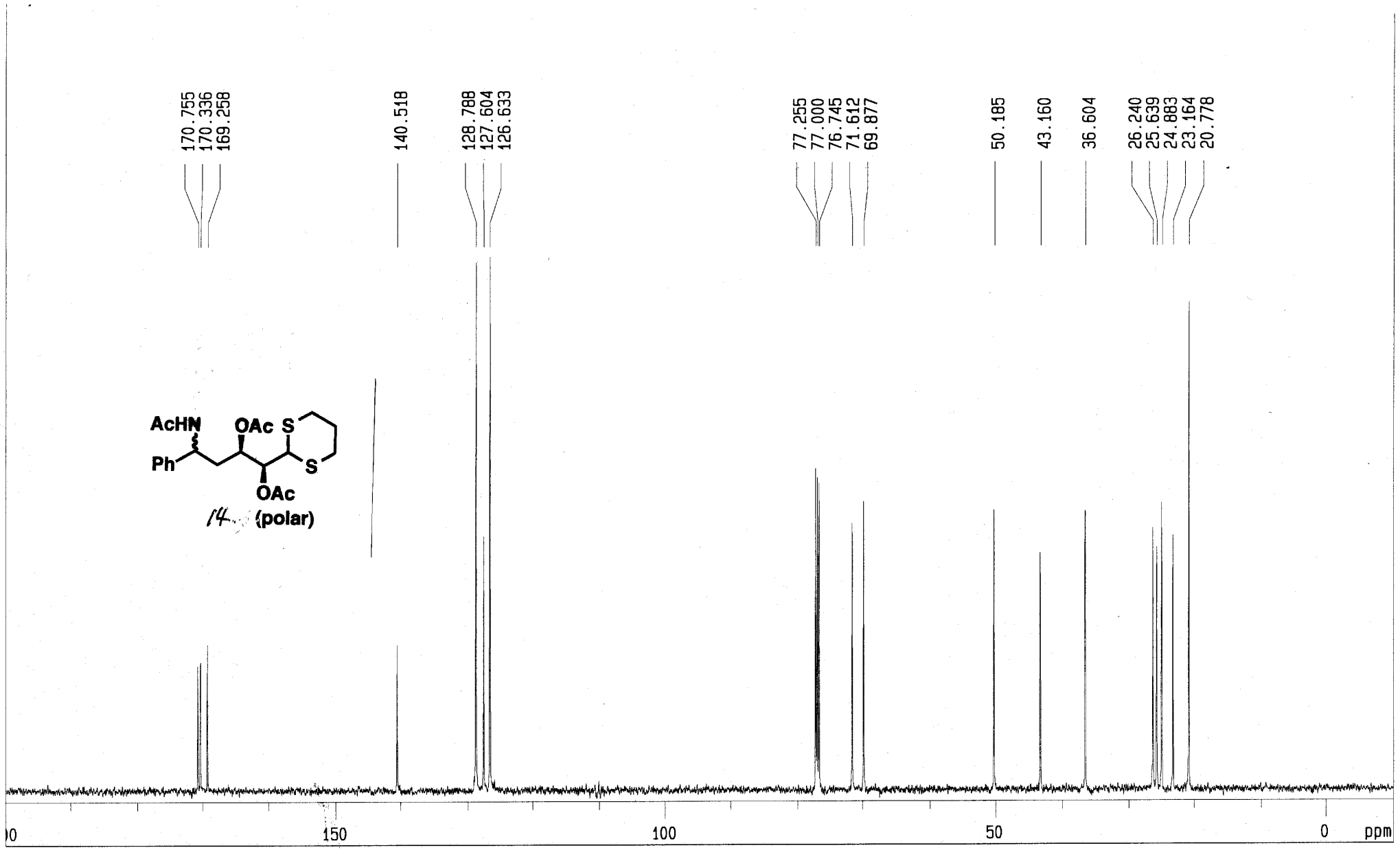

7.4689
7.3756
7.3609
7.3554
7.3457
7.2840
7.2737
7.2621
7.1846
4.4383
4.4310
4.4224
4.4157
4.3724
4.3535
4.2601
4.2436
4.1753
4.1576
4.1222
4.1057
4.0807
3.6585
3.6432
3.6060
3.5902
2.9306
2.9233
2.9172
2.9092
2.9019
2.8952
2.8885
2.8732
2.8580
2.8433
2.8317
2.8256
2.8110
2.7963
2.7896
2.7829
2.7671
2.7622
2.7506
2.7457
2.7323
2.7268
2.7170
2.7042
2.6987
2.3570
2.1246
2.1044
2.0965
2.0825
2.0709
2.0501
2.0428
2.0288
2.0221
2.0001
1.9897
1.9690
1.9623
1.9562
1.9488
1.9427
1.9220
1.8652
1.8585
1.8494
1.8292
1.8140
1.8006
0.0000
2.72
4.55
2219.8
2216.2
2211.9
2208.6
2186.9
2177.4
0.33
0.62
2130.7
2122.5
0.62
2088.3
2079.5
2061.8
2053.5
2041.0
1.35
0.33
0.62
0.62
1.35
1829.8
1822.2
0.32
1803.6
1795.7
0.32
0.59
4.18
3.07
0.99
Ph
NH2
OH
OH
S
S
13
6
4
2
ppm


146.276
145.165
128.755
128.542
127.209
127.053
125.852
125.424
77.255
77.000
76.745
74.598
74.335
70.543
67.919
55.613
53.031
49.198
48.975
41.638
40.865
28.740
28.444
28.329
27.975
25.681
25.557
NH2
OH
S
Ph
S
OH
13
150
100
50
0
ppm


7.4683
7.3585
7.3426
7.3286
7.2773
7.2621
7.2175
7.0504
1.95
14.81
0.94
1.00
0.98
1.00
AcHN
Ph
OAc
OAc
S
S
14 (less polar)
6.0772
6.0601
5.8551
5.8514
5.8355
5.8313
5.5268
5.5115
5.2711
5.2632
5.2492
5.2327
5.2242
0.92
2.16
2.03
2.97
4.21
2.69
1.35
2.1569
2.97
2.1111
2.0904
2.0831
2.0690
2.0611
2.0434
4.21
2.0184
2.69
1.9806
1.9732
1.9629
1.9537
1.9452
1.9348
1.9263
1.35
3.6866
3.6670
3.1508
3.1277
3.1045
3.0819
3.0587
3.0355
2.5260
2.1569
2.1111
2.0904
2.0831
2.0690
2.0611
2.0434
2.0184
1.9806
1.9732
1.9629
1.9537
1.9452
1.9348
1.9263
1.5602
1.5297
0.1165
0.0000
ppm


170.591
170.303
169.521
141.464
128.648
127.382
126.115
77.255
77.000
76.745
70.510
70.230
49.198
42.411
37.912
25.549
24.940
24.817
23.172
20.869
20.679
AcHN
OAc
S
Ph
S
OAc
14. (less polar)
150
100
50
0
ppm


7.4689
7.3969
7.3811
7.3725
7.3682
7.3560
7.3036
7.2987
7.2914
7.2859
7.2798
7.2731
7.2621
7.2590
6.2151
6.1998
5.4377
5.4328
5.4218
5.4121
5.4072
5.3212
5.3163
5.3023
5.2974
5.1430
5.1278
5.1143
5.0991
3.6475
3.6286
2.8836
2.8757
2.8647
2.8555
2.8476
2.8354
2.8281
2.5291
2.5199
2.5090
2.5004
2.4919
2.4809
2.4730
2.4461
2.4388
2.4278
2.4174
2.4077
2.2582
2.2429
2.2252
2.2149
2.1996
2.1783
2.1423
2.1301
2.1179
2.1142
2.1020
2.0898
2.0263
2.0129
1.9952
1.9476
1.9397
1.9281
1.9208
1.9080
1.5602
1.5571
1.5309
0.0067
0.0000
-0.0031
-0.0067
3.85
8.58
0.89
1.01
1.03
1.00
0.98
4.03
0.86
5.70
1.03
1.90
0.90
4.03
0.86
5.70
1.84
AcHN
Ph
OAc
OAc
S
S
14 (polar)
2.2
2.1
2.0
1.9
ppm
6
4
2
ppm


170.755
170.336
169.258
140.518
128.788
127.604
126.633
77.255
77.000
76.745
71.612
69.877
50.185
43.160
36.604
26.240
25.639
24.883
23.164
20.778
AcHN
OAc
S
Ph
S
OAc
14 (polar)
150
100
50
0
ppm