THE SYNTHESIS AND STUDY OF A WIDE-BITE ANGLE BIDENTATE PHOSPHINE LIGAND PAIRED WITH A CROWN ETHER SYSTEM

AN HONORS THESIS (HONORS 499)

By

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MUNCIE, INDIANA

SPRING 2003

ACKNOWLEDGEMENT

First and foremost, I would like to express my deepest gratitude to Dr. Bruce Storhoff for giving me the opportunity to take part in his research group. I have had the privilege of working on this project with Dr. Storhoff for the past two years, and his insight into the specific details of this project and his knowledge of laboratory protocol have proved to be both constructive and valuable. I would also like to thank the Ball State University Department of Chemistry for giving me the chance to do research as an undergraduate. There are few chemistry departments across the country that gives their undergraduate students the unique opportunity to do research, and I believe that it has been an invaluable learning experience. I must also say thank you to Carl Jenks, who worked with me in the early stages of this project. Carl's knowledge of organic chemistry, especially in the area of ethanol-related substances, has proved to be very useful. Finally, I would like to thank my parents, Daniel and Jennifer Schroeder for their constant love and support.

THESIS ABSTRACT

THESIS:	Synthesis of a Novel Wide-Bite Angle Bidentate Phosphine Ligand Paired with a Crown Ether
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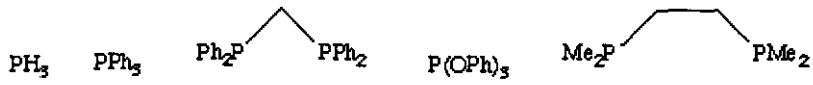
DEGREE:	Bachelor of Science
DEPARTMENT:	Honors College
DATE:	April 2003

The first known example of a novel wide-bite angle phosphorus ligand paired with a crown ether system has been prepared. This thesis examines the relevant history of phosphine ligands and crown ethers, as well as the synthetic steps taken to derive this fascinating molecule. Examination of the molecule by both nuclear magnetic resonance (NMR) and elemental analysis has revealed that the molecule has been isolated, and can be complexed with either a transition metal or an alkaline earth metal. The special structure of this ligand could have a great impact on the stability and reactivity of various transition metal complexes, as the crown ether system imparts "tunability" on the molecule, which is dependant upon the size and shape of the ion that is complexed. In addition, the ability of this molecule to transport transition metals between aqueous and non-aqueous solutions is an exciting topic of future study.

PHOSPHORUS AS A LIGAND

The element phosphorus was first isolated from a urine specimen in 1669 by a German chemist named H. Brandt. Brandt discovered that the element, when isolated in air, glowed in the dark, and thus derived the name "phosphorus" from the Greek terms *phos*, meaning light, and *phorus* meaning bringing.[1] Elemental phosphorus is known to exist as one of three distinct allotropes: white (which usually appears yellow), red, and black—the latter two existing as a fine powder of the appropriate color.[2] This element can also be found in such useful products as steel, fertilizers, matchsticks, detergents, and fine glass and chinaware.[2]

Phosphorus as a ligand, a molecule that is involved in the bonding of positively charged metal ions, has been studied extensively for many years. Examples of well-known phosphorus ligands include the following: phosphine **(1)**, triphenylphosphine **(2)**, diphenylphosphinomethane (DPPM) **(3)**, triphenylphosphite **(4)**, and dimethylphosphinoethane (DMPE) **(5)**. Compounds such as **(2)** have the unique ability

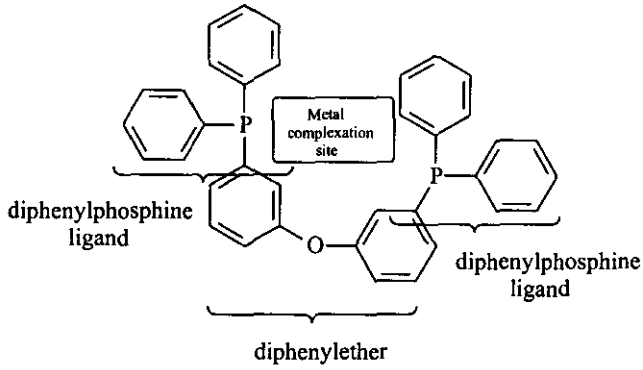


(1) **(2)** **(3)** **(4)** **(5)**

of being both σ-donating ligands, and strong π acceptors.[1] This means that the phosphorus molecule is able to donate electrons from its σ bonding orbitals to metal ions, as well as accept π electrons from other atoms and molecules for use in chemical bonding. Historically, phosphine-ligated metals have been used for a number of applications, such as catalytic or stoichiometric reagents for organic reactions[3] and even as a vital component of the rheumatoid arthritis drug, Aurofin[4].

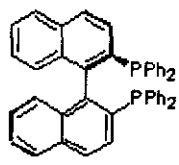
The specific phosphine ligand that we have produced in the laboratory is a wide-

bite angle diphenylphosphine ligand. In our molecule, the two-diphenylphosphine groups are an example of a bidentate ligand because there are actually two phosphine ligands branching off a single diphenylether group **(6)**. When discussing the bite angle of



(6)

phosphine ligands, there must be some mention of the Tolman cone angle of the phosphorus sub-group. For phosphorus atoms, the cone angle is defined as the apex angle of a cylindrical cone, centered 2.28 Å from the center of the P atom, which touches the outermost atoms of the model. It has been reported that a two phosphine-containing ligand, of the type shown in **(7)** and **(8)**, as well as our compound, have the characteristic of being able to widen the P-Metal-P (P = phosphorus) angle during the migration of metal ions in solution, thus accelerating migration reactions.[5] In future studies of our molecule, the bite angle of the phosphine ligands will be of particular interest, as will



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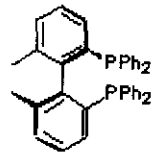


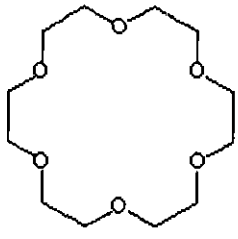
(8)

metal complexation, and the molecular transformations that accompany this alteration. The bite angles can be calculated by manipulation of data obtained through the infrared

spectrum of our compound. The introduction of a metal ion onto a ligand can affect the dipole moment of the ligand in such a way that infrared light, when it is passed through the sample, is absorbed at different frequencies than would normally be observed. Phosphine ligands are best characterized, however, by x-ray analysis, which gives a precise atomic picture of the molecule. This and other spectral properties of phosphorus ligands make them interesting molecules not only to bench chemists, but also to spectroscopists.

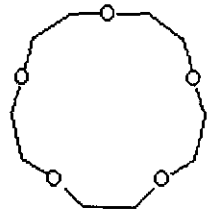
CROWN ETHERS

Crown ether molecules have been at the center of much academic and industrial research since C. J. Pederson first reported their astonishing chemical properties in 1967.[6] A simple organic ether compound is composed of a chain of carbon atoms substituted at various points in the chain with oxygen atoms, each of which have two pairs of nonbonding electrons. The oxygen atoms, being quite a bit more electronegative than the carbon atoms in the chain, possess a slight negative charge, as well as the ability to attract positively charged ions. When these ether hydrocarbon chains are folded back onto themselves, they form a molecule that resembles a "molecular crown" **(9), (10), (11),** such that the electronegative oxygen atoms face the center of the crown, while the



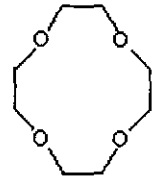
18-crown-6

(9)



15-crown-5

(10)

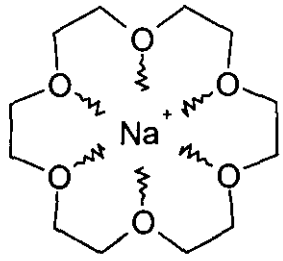


12-crown-4

(11)

carbon atoms point towards the outside of the molecule when complexed with a metal ion.

Of major importance is the fact that many of these cyclic polyethers form complexes with the salts of various elements. Ions of such elements as K, Na, Ca, and even Li form salt-polyether complexes by ion-dipole interaction between the cation and the negatively charged oxygen atoms symmetrically placed in the crown **(12)**. The conditions for the formation of crown ether complexes include: the relative sizes of the ion and the hole in the crown, the number of oxygen atoms in the crown, and the

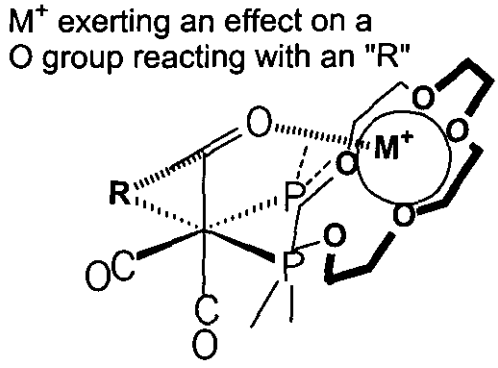


(12)

coplanarity of the oxygen atoms.[6] If these conditions are met, the chemical structure of the molecule is altered by the complexation of molecular ions, and "tunability" is imparted on the outlying molecular branches.

Scientists are constantly attempting to discover reaction pathways that incorporate speed and efficiency, while maintaining high product yields. By developing different catalysts to drive these reactions, they gain a general understanding of the kinetics and selectivity that guide chemical reactions. As an example, it has been found that crown ether-alkali metal molecules can accelerate the migratory-insertion step in carbonylation reactions by anionic (negatively charged) metal complexes.[7] **(13)** What this means is that by adding a crown ether complexed with a group-one metal (Na, K, etc.), certain

carbonylation reactions will take place at a higher rate than normal. This is just one example of many that illustrate the wide variety of useful applications of crown ether system.



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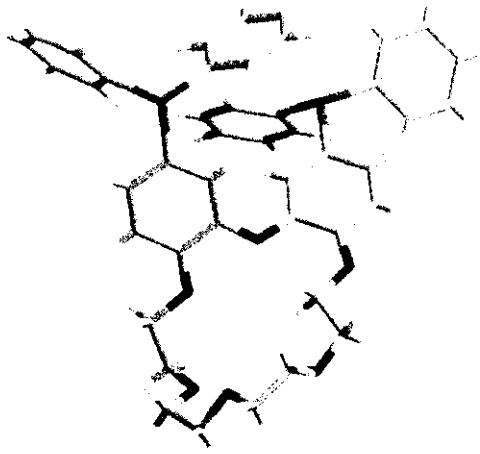
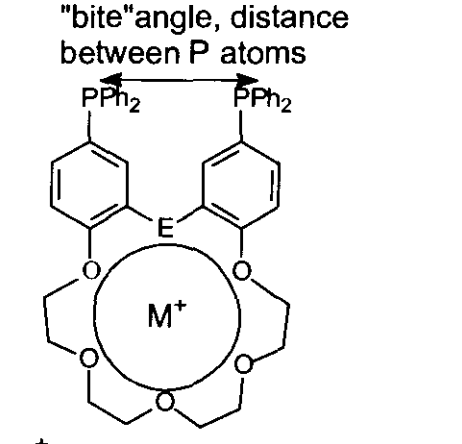
OUR MOLECULE –A NOVEL WIDE-BITE ANGLE BIDENTATE DIPHOSPHINE LIGAND PAIRED WITH A CROWN ETHER

At present, there are no known examples of wide-bite angle bidentate diphosphine ligands functionalized with crown ether systems. As separate entities, both bidentate diphosphine ligands and crown ether systems display remarkable chemical[1,3,5] and biological[4] activity, but together, the applications of this molecule appear to be endless. A three-dimensional structure of our molecule **(14)** was created utilizing BioRad Chem Window 6. Molecular modeling techniques utilized in this calculation include computations of both coulombic and Van der Waal's atomic interactions. Recent research has focused on the overall understanding of the affect of metal complexation by crown ether systems on the molecular geometries, redox potentials, and chemical and spectroscopic properties of these structures.



(14)

One of the most fascinating aspects of this molecule is the "tunability" that could be imparted upon the diphosphine ligand branches. One of the conditions that regulate the coordination of metals by crown ethers is the size of the molecular ion that is being complexed. By inserting both larger and smaller molecular ions into the crown cavity, the phosphine branches should move and rotate, similar to the "rabbit ears" on a television antennae **(15).** This movement should allow different transition metals the

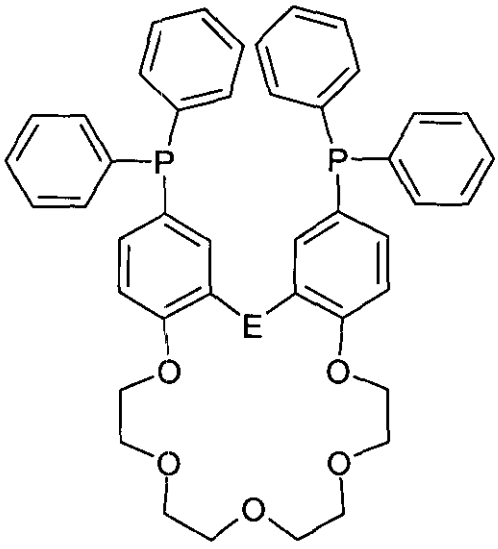


(15)

opportunity to complex at the phosphorus-binding site than would normally be observed. This transfer of information from the crown ether to the phosphorus ligands should lead to insight as to what kind of donor properties the ligand groups comprise. Analysis by FTIR, and x-ray analysis will be especially important in the future, as different molecular conformations, as well as metal complexations should yield absorption at different frequencies.

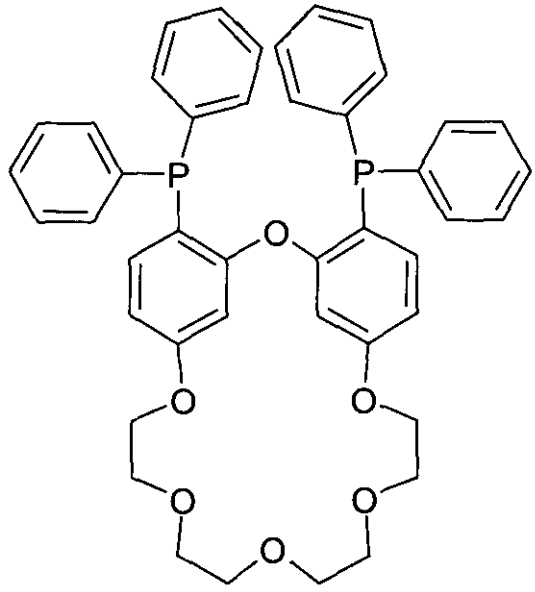
It has been understood for some time that complexed crown ether systems are quite adept at catalyzing reactions involving phase transfer of reagents. The positively charged, complexed crown ether ring is able to form an ion pair with a negatively charged species, such as a cyanide group. Because the outside ring of the complexed crown ether is largely hydrocarbon in nature, it is able to pass from an aqueous environment, which may contain the negatively charged species, to a nonaqueous (organic) environment that contains a chemical needed for reaction with the negatively charged species. The presence of the crown ether molecule facilitates the reaction of the two species.

Future studies of crown molecules associated with diphenylphosphine ligands will include **(16)**, **(17)**, and **(18)**, as each should display different donor abilities with regards to varying the identity of "E". This variance in donor abilities will lead to increased studies of the "tunability" of the diphenylphosphine ligands. Other fascinating uses for our molecule include the possibility of development of a molecular switch, in which the switch is triggered by the presence or absence of either a crown-complexed ion or a charged long-chain hydrocarbon guided through the crown. Finally, another possible



E = O, S, NR

S = **(16)**, NR = **(17)**



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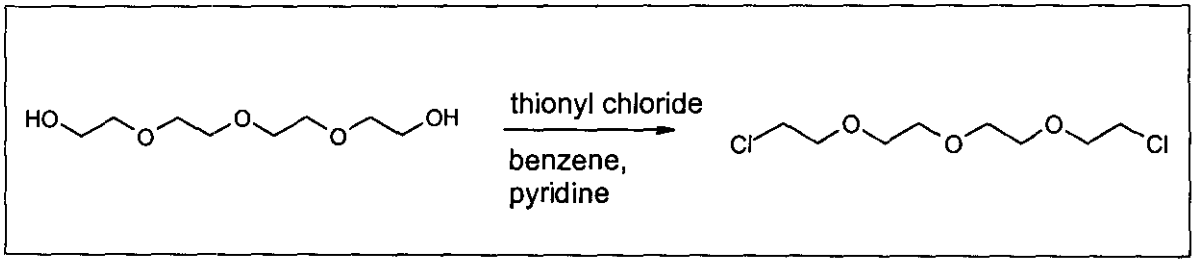
area of interest is the selective interaction of our compound with various substrates owning specific conformations. Ultimately, the sky is the limit as to how far we would be interested in investigating the chemical and biological properties of this compound.

Experimental Section

Reagents and Materials. Triethyleneglycol, thionyl chloride, guiacol, sodium methoxide, ultra-dry THF, *n*-butyllithium, and dry chlorobenzene were obtained from Aldrich Chemical Co., Inc. Molecular bromine was purchased from Fisher Scientific Int.

Methods and Instruments. All reactions and purifications were performed under a blanket of argon. ^{1}H, ^{13}C, and ^{31}P NMR spectra were recorded on a 400MHz JEOL Fourier Transform instrument, and dissolved in chloroform-D. Separation by chromatographic column was carried out using a Biotage Flash 40 apparatus, and a Biotage Si 40S 3191-1 column. Elemental analysis was carried out by Midwest Microlab Ltd., Indianapolis, IN.

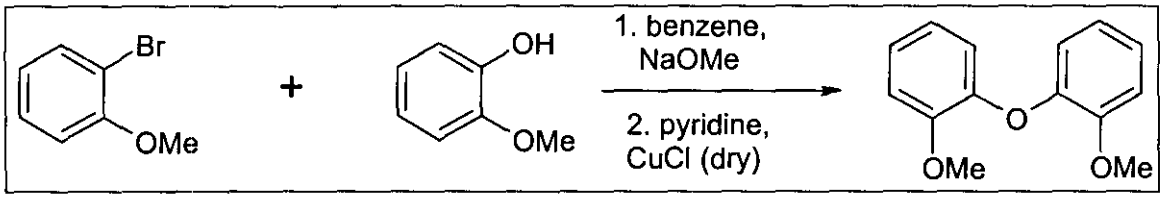
Preparation of Triethylenedichloride from Triethyleneglycol[8]



In a dry, 1500mL three-necked round bottom flask, 465mL benzene and 91.8mL of pyridine were added to 100.0g (88.9mL, 0.515mol) of triethylene glycol. This mixture was heated to ~86°C and allowed to reflux under argon with stirring. 139.9g (82.7mL, 1.176mol) of thionyl chloride ($SOCl_2$) were added dropwise with stirring over three hours. Following the addition of thionyl chloride, the mixture was allowed to reflux at ~78°C for 16 hours to ensure mixing. The mixture was then allowed to cool to room temperature prior to adding 11.7mL of concentrated HCl diluted with 46mL of distilled

H_2O dropwise over 15 minutes. The product, tetraethylenedichloride, was in the benzene layer, which must be separated from the water layer that containes the pyridine salts and other reagents. A separatory funnel is used to isolate the organic layer, which is then rotary evaporated to remove excess solvent. The remainder of the product was isolated by short path distillation under vacuum and collected in an ice-filled receiver. The product distilled at about 115° C under vacuum as a clear, yellowish, dense liquid.

The Ullman Reaction – The preparation of 2,2'-Dimethoxydiphenyl ether[9]

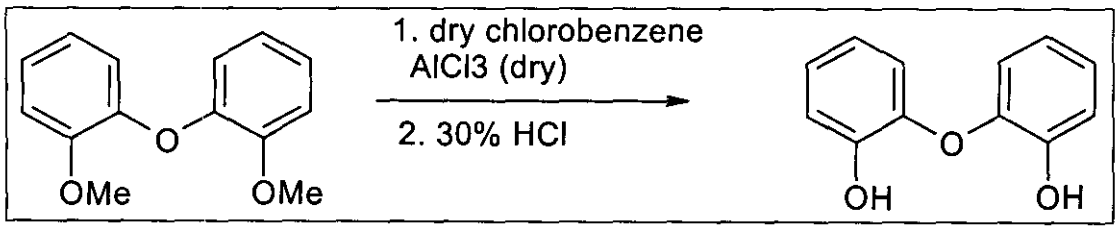


In an extremely dry 2000mL three-necked round bottom flask, 73.6mL (83.2g, 0.670mol) guiacol were added to ~1000mL of benzene with stirring. 43.6g (0.807mol) of sodium methoxide were carefully added to the mixture of benzene and guiacol. Approximately 30 minutes after the sodium methoxide was added, a white solid precipitate formed. The mixture was put on the rotary evaporator in order to evaporate the benzene portion, leaving the guiacol salt. 1000mL pyridine were added in order to dissolve the guiacol salt with stirring under argon. This mixture was allowed to reflux for 30 minutes to ensure mixing. After the mixture cooled to room temperature, 40.0g CuCl, which has been dried in an oven at 125° C, through the condenser were added. The system was allowed to reflux during the addition of 166mL (250g, 1.337mol) of *o*-bromoanisole, which was added dropwise over a period of six hours. *Ortho*-bromoanisole can be diluted with pyridine in order to ensure that the reagent is being added slowly. Following

the addition of the *o*-bromoanisole, the system was left at a gentle reflux under argon for a period of three days.

Following the reflux period, the solution was made acidic by the addition of 2M HCl until a precipitate formed (a color change was also observed). To separate the product from the water layer, hexane was added and a separatory funnel used to divide the layers. The hexane layer was then put on the rotary evaporator and found to contain both the product and excess *o*-bromoanisole. The water layer was rinsed several times with hexane to ensure that the entire product was extracted and added to the organic layer for purification. The solvent (hexane) was then put on the rotary evaporator. The remaining side products, including the o-bromoanisole starting reagent was then vacuum distilled to leave the product. 86.82g (0.377mol) of 2,2'-Dimethoxydiphenyl ether were recovered (56.3%) in the running of this reaction. ^{1}H NMR δ 3.85 (6H, s, -OC**H$_3$**), 6.85 (2H, q, aromatic), 6.98 (2H, d, aromatic), 7.06 (2H, t, aromatic). ^{13}C NMR δ 56.0 (2C, -O**C**H$_3$), 77.0 (1C, $CDCl_3$), 113.1 (2C, aromatic), 119.0 (2C, aromatic), 121.0 (2C, aromatic), 124.0 (2C, aromatic), 146.2 (2C, aromatic –OC), 150.8 (2C, aromatic – **C**OCH$_3$).

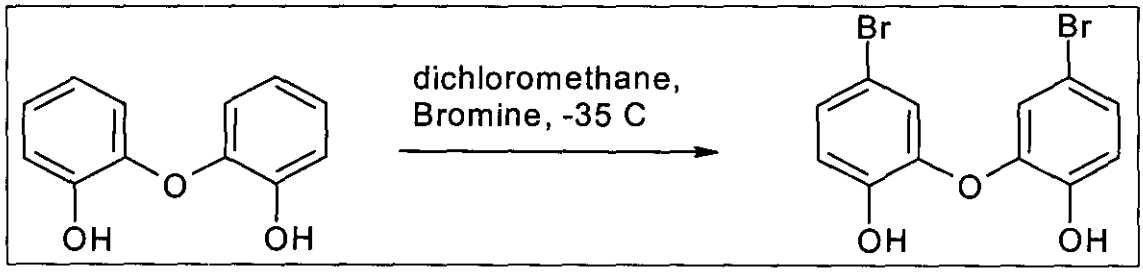
Demethylation / Hydroxylation of 2,2'-Dimtethoxydiphenyl ether[10]



In a 2000mL three-necked round bottom flask, 86.82g (0.377mol) 2,2'-Dimethoxydiphenyl ether were dissolved in 868mL of dry chlorobenzene. Once the

reagent dissolved, 173.6g of dry $AlCl_3$ were added. This mixture was heated to a gentle reflux under argon for a total of two hours. After the mixture cooled to room temperature, enough 30% HCl was added to bring the pH of the solution to about three. By adding acid to the solution, the product precipitated out as a white solid. About 250mL diethyl ether were added to dissolve the product and separate it from the acid layer. The ether layer also contained the excess chlorobenzene, which must be removed via hi-vac. The impure product was recrystallized by ether-hexane. More specifically, just enough ether was added to dissolve the entire impure product. After the ether was added, hexane was added dropwise until the first signs of a precipitate formed. The solution was placed in the freezer so that the whole of the product was able to precipitate out of solution. Excess solvent was poured off and the crystals dried on the hi-vac. 32.79g (0.162mol) of 2,2'-Dihydroxydiphenyl ether was recovered (43.0%) in the running of this reaction. ^{1}H NMR δ 5.85 (2H, s, Ph-O**H**), 6.85 (8H, d, aromatic). ^{13}C NMR δ 77.0 (1C, $CDCl_3$), 117.0 (2C, aromatic), 118.2 (2C, aromatic), 121.4 (2C, aromatic), 125.0 (2C, aromatic), 143.8 (2C, aromatic,-**C**O**C**-), 147.0 (2C, aromatic, **C**OH).

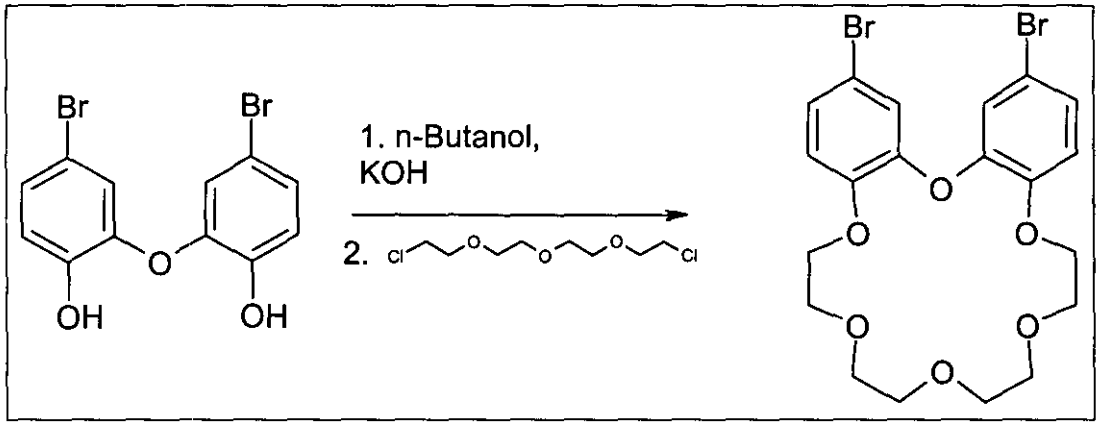
***para*-Bromination of 2,2'-Dihydroxydiphenyl ether[8]**



In a 1000mL three-necked round bottom flask, 15.0g (0.074mol) of 2,2'-Dihydroxydiphenyl ether was added to 450mL of dichloromethane. An ice bath

consisting of a slurry of acetonitrile and liquid nitrogen was used to bring the temperature of the mixture to -35° C. By decreasing the temperature, bromination is sure to occur *para* to the hydroxyl groups on the benzene ring systems. 27.0g (0.169g) of molecular bromine was added over a six-hour period with stirring, under argon at a temperature of -35° C. Following the addition of bromine, the ice bath was warmed to room temperature. The mixture stirred at room temperature for ~12 hours, or until all of the bromine color disappeared. When the red coloring did not disappear, a saturated aqueous solution of sodium thiosulfate was added. The solvent was removed by rotary vacuum evaporation and the solid dissolved in CH_2Cl_2, and washed with 25mL of distilled H_2O five times. The organic portion was dried with solid sodium sulfate to remove any excess water. Sodium sulfate was removed by vacuum filtration and the remainder of the solvent was evaporated by rotary vacuum evaporation. The product was purified and recrystallized by adding enough dichloromethane or chloroform to just dissolve all of the crystals. The mixture was slowly heated to concentrate the product in the solvent. Enough hexane was added so that the first sign of precipitate were seen, and the system was allowed to cool to room temperature. The product was placed in the freezer, and the remainder of the solid was allowed to precipitate out of solution. Excess solvent was poured off, and the crystals were dried under high vacuum. 19.39g (0.054mol) of 5,5'-Dibromo-2,2'-dihydroxydiphenyl ether was prepared (73.0%) in the running of this reaction. ^{1}H NMR δ 5.87 (2H, s, Ph-O**H**), 6.90 (2H, d, HOCC-**H**), 6.96 (2H, s, R-C**H**-CBr), 7.17 (2H, dd, OC-C**H**-CBr). ^{13}C NMR δ 77.0 (1C, $CDCl_3$), 112.2 (2C, R**C**BrR), 118.1 (2C, aromatic), 121.5 (2C, aromatic), 128.7 (2C, aromatic), 143.9 (2C, -**C**OC-), 146.2 (2C, R**C**OHR).

Crowning of 5,5'-Dibromo-2,2'-dihydroxydiphenyl ether[10]

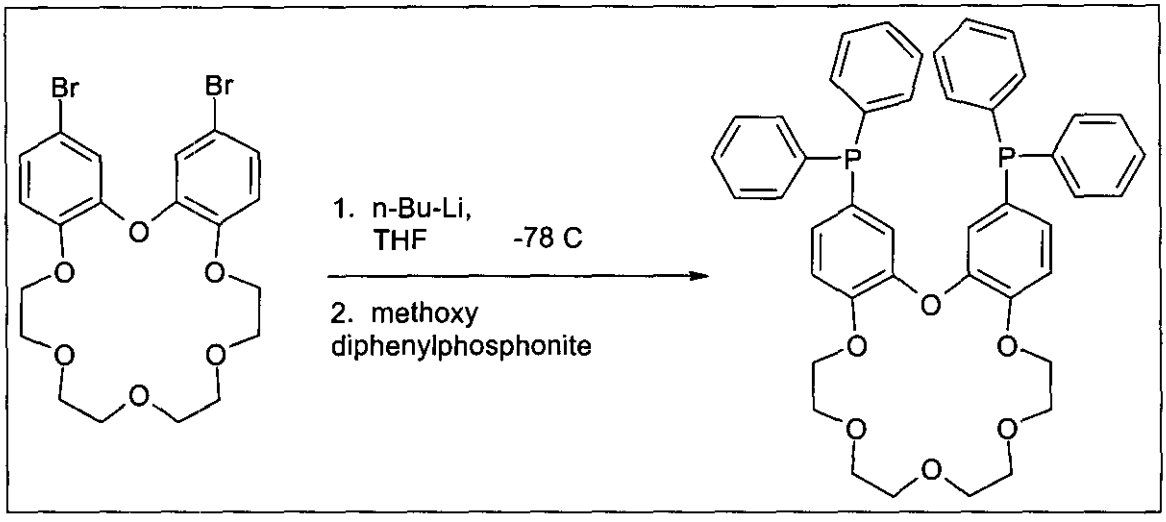


In a 1000mL, three-necked round bottom flask, 250mL n-Butanol were added to 8.00g (0.022mol) dry 5,5'-Dibromo-2,2'-dihydroxydiphenyl ether. The reagent was dissolved in the butanol and allowed to stir for five minutes. In a separate beaker, 20mL of distilled water were added to 2.72g (0.048mol) of potassium hydroxide. The aqueous potassium hydroxide was added straight to the solvent to make the salt of the 5,5'-Dibromo-2,2'-dihydroxydiphenyl ether. The system was then diluted with 100mL n-butanol. The system was placed under argon, and 5.59g (0.024mol) of diluted tetraethylenedichloride were added dropwise over a period of two hours. The system was allowed to reflux under argon with stirring for a minimum of 36 hours. After the reaction had cooled to room temperature, the n-butanol was rotary evaporated, and the system was placed under high-vacuum to remove all excess water. The crude product was dissolved in dichloromethane and the side products were extracted three times with 3M HCl. The crown ether product remained in the organic solvent, which was placed on the rotary evaporator.

The crude crown ether was extracted from any remaining side products, by the addition ~250mL of heptane and boiled for 3 minutes before the supernatant was poured off into a beaker. As the heptane cooled, the purified crown precipitated out of solution.

The hot heptane extraction was repeated until no more precipitation was observed. The crown-heptane mixture was placed in the freezer after it had cooled to room temperature in order to allow maximum precipitation. 10.50g (0.0.020mol) of dibrominated, diphenyl 18-crown-6 were prepared (90.9%) in the running of this reaction. ^{1}H NMR δ 3.60 (8H, t, -OC**H**$_2$C**H**$_2$O), 3.77 (4H, t, PhOCH$_2$C**H**$_2$O), 4.13 (4H, t, PhOC**H**$_2$CH$_2$), 6.85 (2H, d, ROCC-**H**), 6.94 (2H, s, R-C**H**-CBr), 7.14 (2H, dd, OC-C**H**-CBr). ^{13}C NMR δ 69.5 (4C, crown), 71.2 (4C, crown), 77.0 (1C, $CDCl_3$), 112.2 (2C, R**C**BrR), 118.1 (2C, aromatic), 121.5 (2C, aromatic), 128.7 (2C, aromatic), 143.9 (2C, -**C**OC-), 146.2 (2C, R**C**OHR).

Phosphorylation of 5,5'-Dibromodiphenyl-18-crown-6



In an extremely dry 500mL, three-necked round bottom flask equipped with a magnetic stirbar and argon, 300mL dry THF was added through a septum to 6.0g (0.0116 mol) of purified 5,5'-Dibromodiphenyl-18-crown-6. The crown ether was completely dissolved before the addition of any n-Butyllithium. An ice bath was prepared that was composed of a slurry of ethyl acetate and liquid nitrogen that brought the temperature to -78° C. Using a 5mL plastic syringe and metal needle, 9.3mL (7.21g, 0.113mol) of n-

Butyllithium were added in two portions—one-5mL portion and one-4.3mL portion. This reagent was added over two 10-minute periods. When adding n-Butyllithium, the metal needle was cooled with liquid nitrogen periodically so that the reagent was cool upon entering the system. Following the addition of n-Butyllithium, the system was allowed to sit for ~20 minutes at -80° C. Again, using a 5mL plastic syringe and metal needle, 4.64mL (5.002g, 0.023mol) of methoxydiphenyl phosphonite was added over a period of 15 minutes. Following the addition of the phosphonite, the ice bath was allowed to warm to room temperature and the mixture to sit overnight.

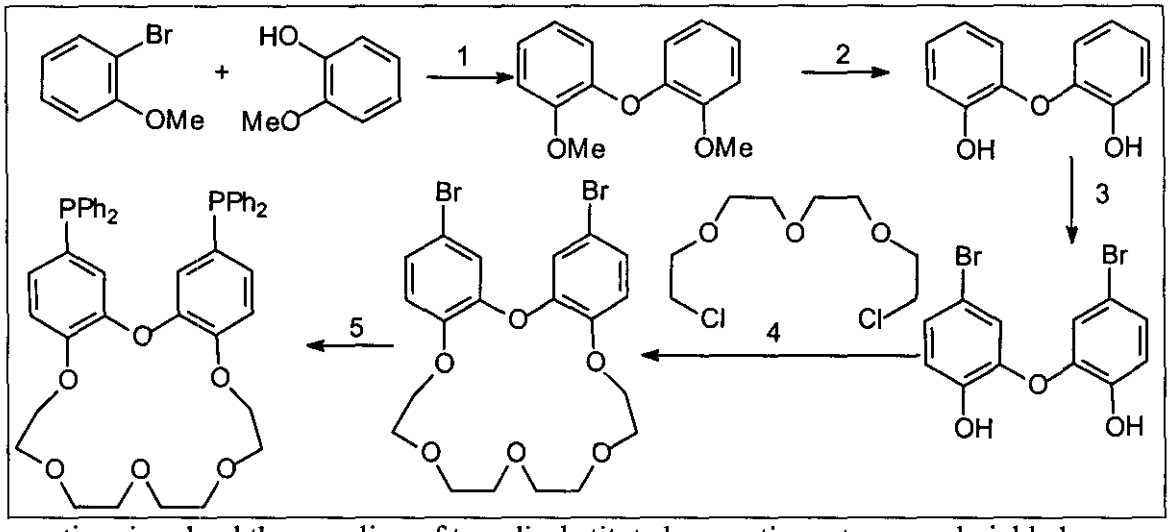
Two milliliters of 10% aqueous ammonium chloride and 2mL triethylamine were added to the system at room temperature. In order to separate the crude phosphine crown, the THF/organic layer was rotary evaporated and placed on the hi-vac. The crude phosphine crown was a very viscous, clear liquid. In a first attempt to recrystallize the diphenylphosphine crown, the compound was boiled in heptane and poured off into a large beaker, allowed to cool and placed in the freezer to induce precipitation. After two days, it appeared that a precipitate had formed and accumulated at the bottom of the beaker. The heptane was poured off to reveal a white layer of what appeared to be solid. As the solvent evaporated, the white solid changed to a clear, sticky agar-like film at the bottom of the beaker. The film was dissolved in 50 mL dichloromethane, collected in a 100 mL round bottom flask, and placed on the rotary hi-vacuum, but failed to solidify.

In an attempt to induce precipitation, the viscous liquid was boiled in absolute ethanol at ~85° C for 30 minutes, allowed to cool to room temperature, and placed in the freezer. The next day, it appeared as though the diphosphine crown had crystallized in the ethanol. When placed on the rotary hi-vac, the solvent evaporated completely to

leave a dense, viscous liquid. When this liquid was placed on the high vacuum, it expanded rather quickly to yield a filmy, bubbly solid. After spectral analysis by NMR, it was discovered that impurities existed in the compound. Using a Biotage Flash 40 column chromatography apparatus equipped with a Biotage column, a separation was performed, isolating 0.20 g of pure diphenylphosphine 18-crown-6. ^{1}H NMR δ 3.60 (8H, s, -OC**H**$_2$C**H**$_2$O), 3.72 (4H, s, PhOCH$_2$C**H**$_2$O), 4.13 (4H, s, PhOC**H**$_2$CH$_2$), 6.71 (2H, s, split, -OCC**H**CBr), 6.87 (2H, s, split, ROCC-**H**), 6.96 (2H, s, split, R-C**H**-CBr), 7.21 (20H, **phenyl**phosphine). ^{31}P NMR δ -5.78 (2P, s, Ph**P**Ph$_2$).

Results and Discussion

Through the five-step organic reaction scheme shown below, 0.20g of pure diphenylphosphine 18-crown-6 was produced. The first step, the classic Ullmann



reaction, involved the coupling of two disubstituted aromatic systems, and yielded 86.82g (0.377mol) of dimethoxydiphenyl ether in 56.3% yield. Step two involved the demethylation/hydroxylation reaction of the dimethoxydiphenyl ether molecule. In this reaction, aluminum trichloride acted as a catalyst that facilitated the removal of the methyl group prior to the protonation of the system, which was done by 30% HCl. Successful hydroxylation of the methoxy groups yielded 32.79g (0.162mol) in a 43.0%

yield. The bromination of dihydroxydiphenyl ether was performed in an ice bath of acetonitrile and liquid nitrogen. These conditions were vital to produce a product that was brominated -para to the hydroxyl group. The successful bromination yielded 19.39g (0.054mol) of dibromodihydroxydiphenyl ether in 73.0% yield.

The crowning of the dibromodihydroxydiphenyl ether compound (reaction 4 in the scheme above) produced 10.50g (0.0.020mol) of 18-crown-6 in an alarming 90.9% yield. In this nucleophilic substitution reaction, potassium hydroxide is ionized, and the potassium was used to form the ring portion of the crown. The positively charged potassium ion binds to the partially negatively charged oxygen atoms in the tetraethylenedichloride molecule, effectively wrapping the crown ether around the potassium ion. In this way, the crown is sure to bond to the dibromodihydroxydiphenyl ether molecule.

Finally, the organic scheme was completed through the phosphorylation of the crown ether molecule. Because of the complex purification process that was involved in the recrystallization of this molecule, only 0.20g of spectroscopically pure product were produced. The product was a very viscous liquid that can be solidified for a time following submission to the high-vacuum for several hours. Recrystallization was attempted by boiling the product in absolute ethanol for 30 minutes at ~85° C. The ethanol solution was allowed to cool to room temperature, and placed in the freezer. The next day, it appeared as though the diphosphine crown had crystallized in the ethanol. When placed on the rotary high vacuum, the solvent evaporated completely to leave the same dense, viscous liquid. When this liquid was placed on the high vacuum, it expanded rather quickly to yield a filmy, bubbly solid. Using a Biotage Flash 40 column

chromatography apparatus equipped with a Biotage column, a separation was performed, isolating 0.20 g of spectroscopically pure diphenylphosphine 18-crown-6. Verification of the purified product was provided by ^{1}H NMR with shifts at δ 3.60 (8H, s, -OC**H**$_2$C**H**$_2$O), 3.72 (4H, s, PhOCH$_2$C**H**$_2$O), 4.13 (4H, s, PhOC**H**$_2$CH$_2$), 6.71 (2H, s, split, -OCC**H**CBr), 6.87 (2H, s, split, ROCC-**H**), 6.96 (2H, s, split, R-C**H**-CBr), 7.21 (20H, **phenyl**phosphine). ^{31}P NMR spectra revealed a shift at δ -5.78 (2P, s, Ph**P**Ph$_2$), which is exactly where it would be expected to be found. Finally, ^{13}C NMR revealed that each of ten spectroscopic carbons were represented. Please refer to the ^{13}C NMR spectrum entitled, "BRS18c._crude_after_chromatography.3" to observe the following peaks, all of which fall in the aromatic region of the ^{13}C NMR spectrum. ^{13}C NMR δ 114.2 (2C, d), 124.1 (2C, d), 128.5 (2C, d), 128.6 (2C, s), 130.0 (2C, d), 132.1 (2C, d), 133.5 (2C, d), 137.7 (2C, d), 146.1 (2C, d), and 152.0 (2C, s), for a total of 20 aromatic carbons. The majority of these carbons are doublets because of the presence of the phosphorus, which cause splitting of carbon spectroscopic peaks.

In conclusion, a five-step series of organic synthesis reactions have been utilized to produce the novel target molecule. Thorough spectroscopic methods, including proton, phosphorus and carbon NMR have been used to identify the target molecule.

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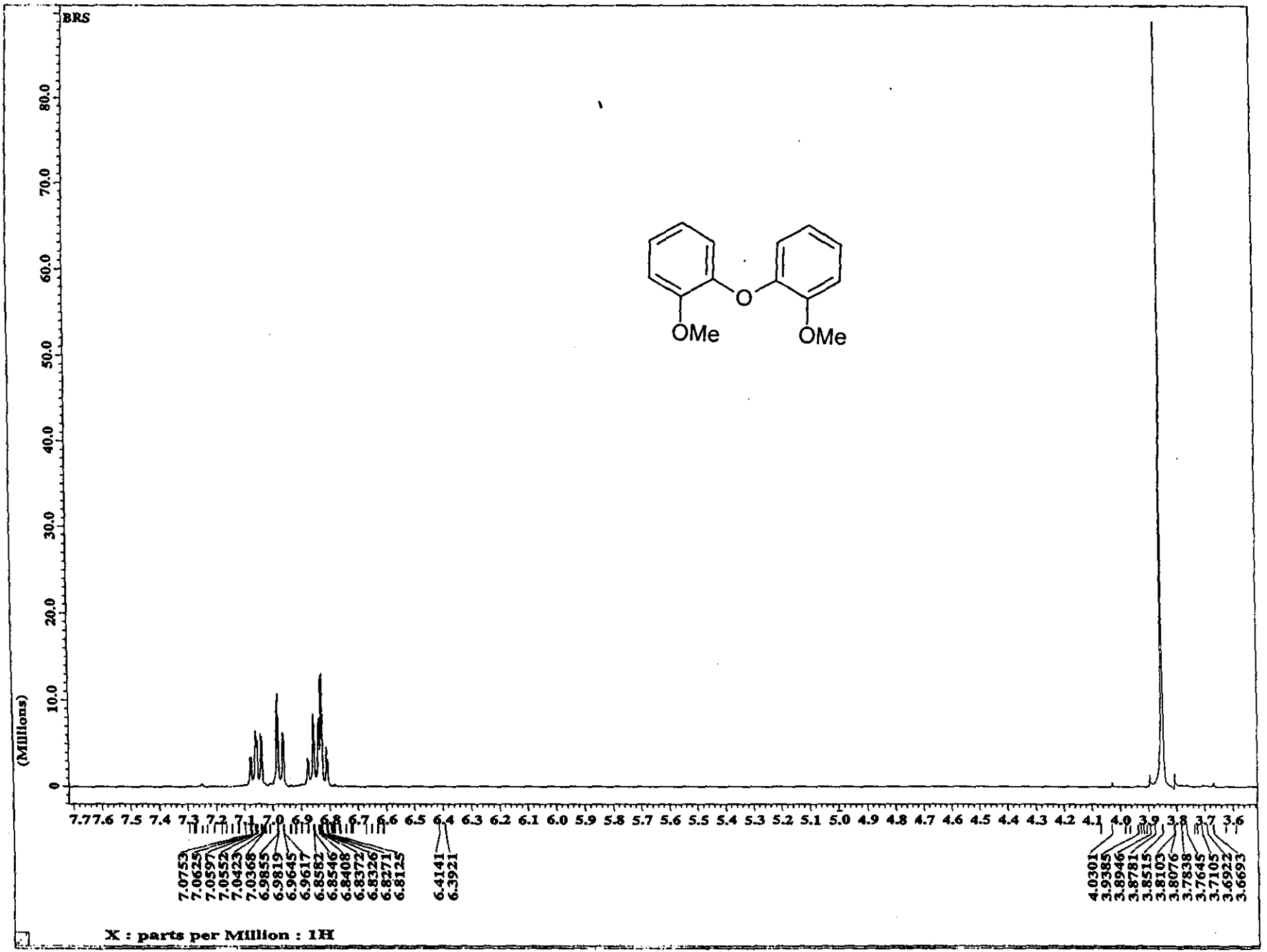
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40.0
30.0
20.0
10.0
0
OMe
O
OMe
7.0753
7.0625
7.0597
7.0552
7.0423
7.0368
6.9855
6.9819
6.9645
6.9617
6.8582
6.8546
6.8408
6.8372
6.8326
6.8271
6.8125
6.4141
6.3921
4.0301
3.9385
3.8946
3.8781
3.8515
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3.8076
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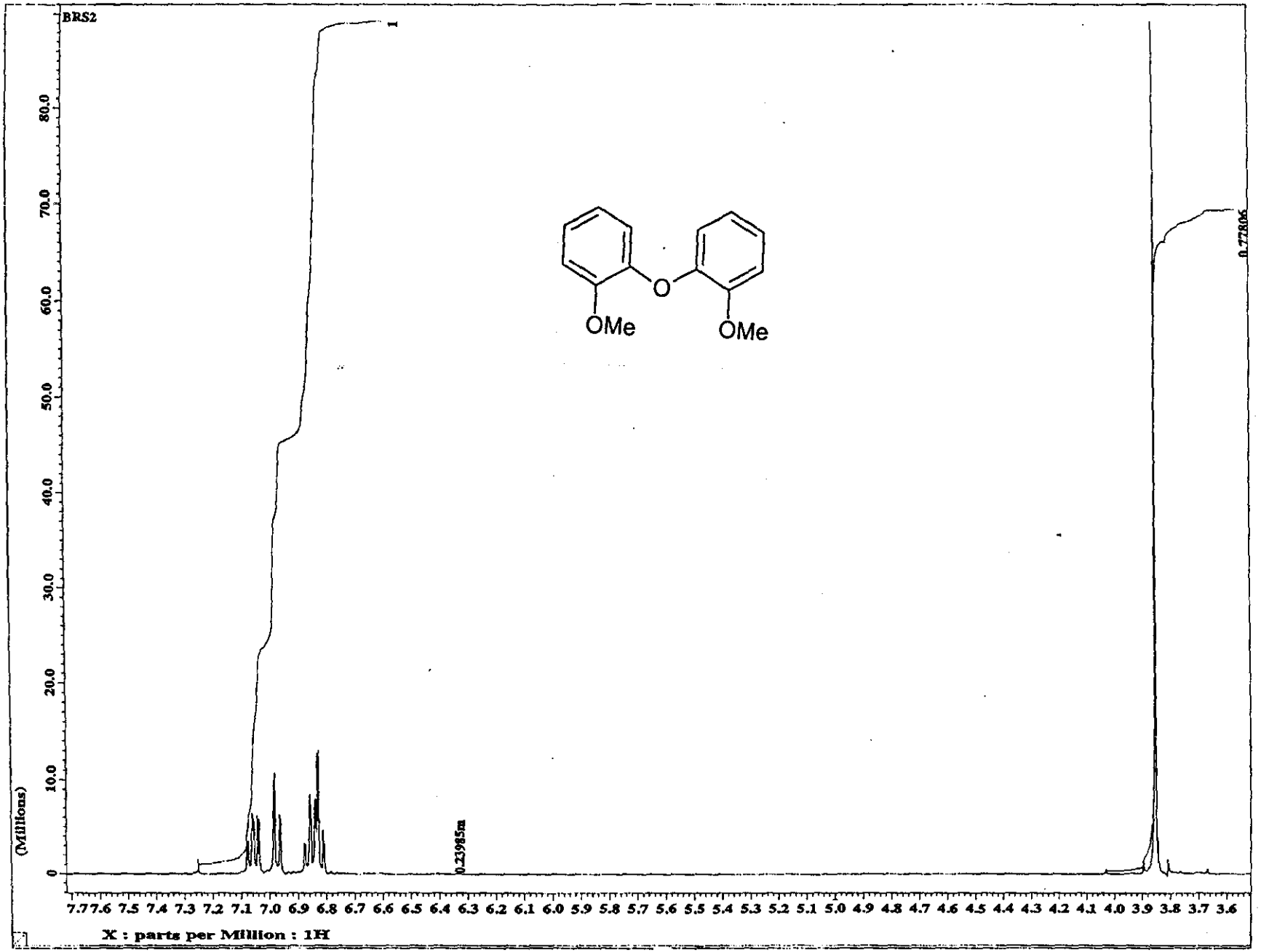
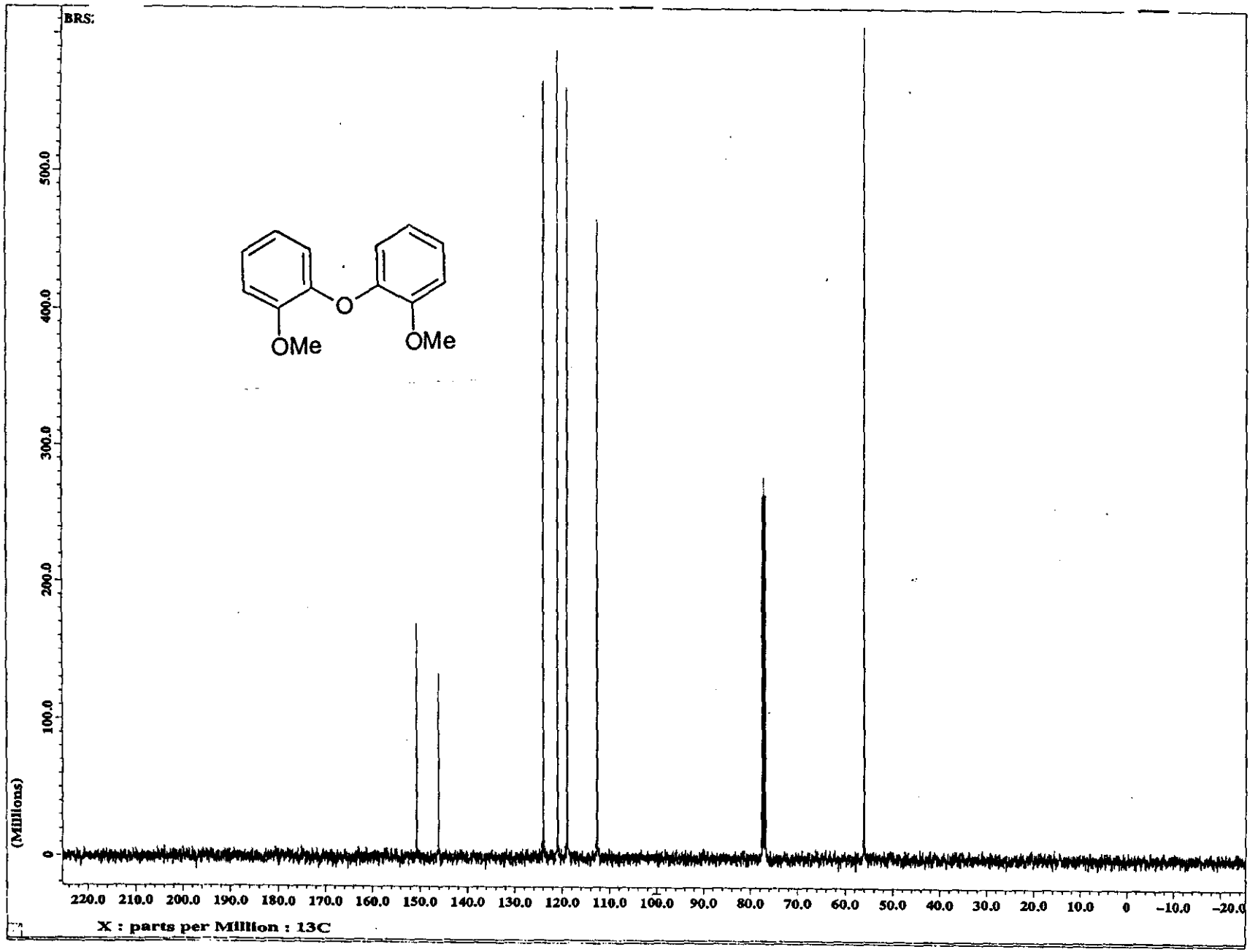
3.7105
3.6922
3.6693
X : parts per Million : 1H


BRS2
OMe
OMe
(Millions)
X : parts per Million : 1H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O
OMe
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200.0
100.0
0
(Millions)
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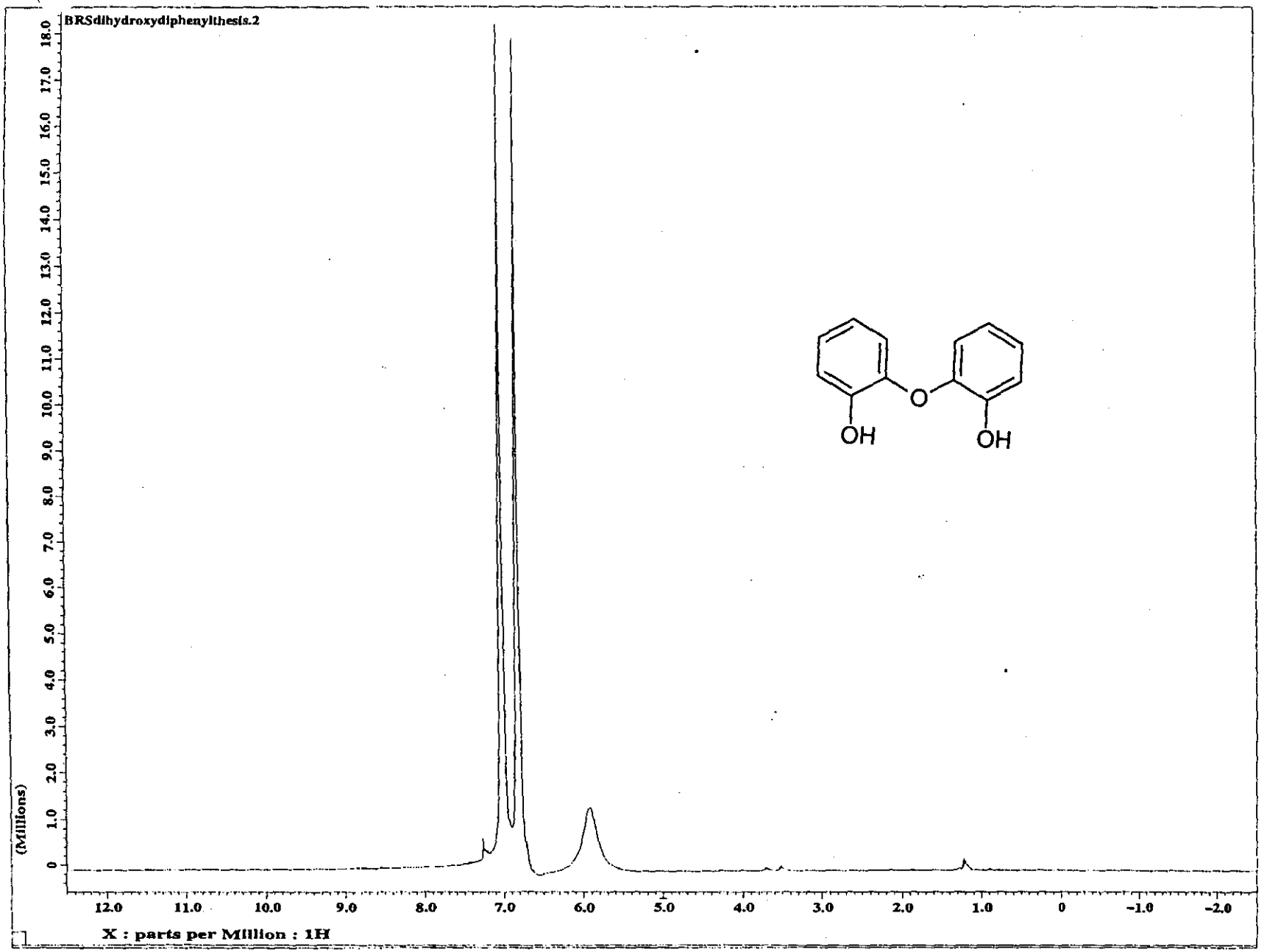
X : parts per Million : 13C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11.0
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3.0
2.0
1.0
0
12.0
11.0
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6.0
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1.0
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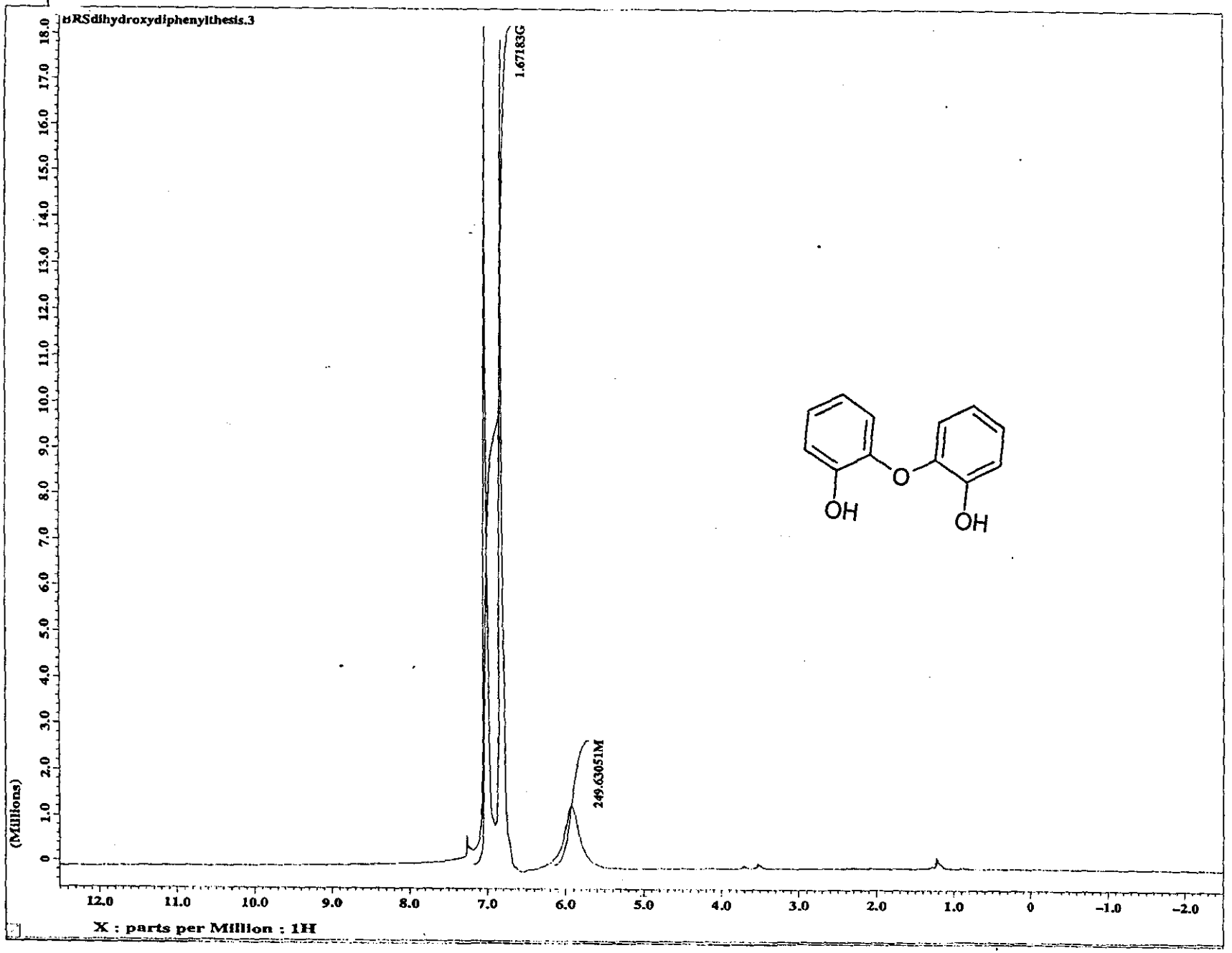
-2.0
X : parts per Million : 1H
OH
O
OH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2.0
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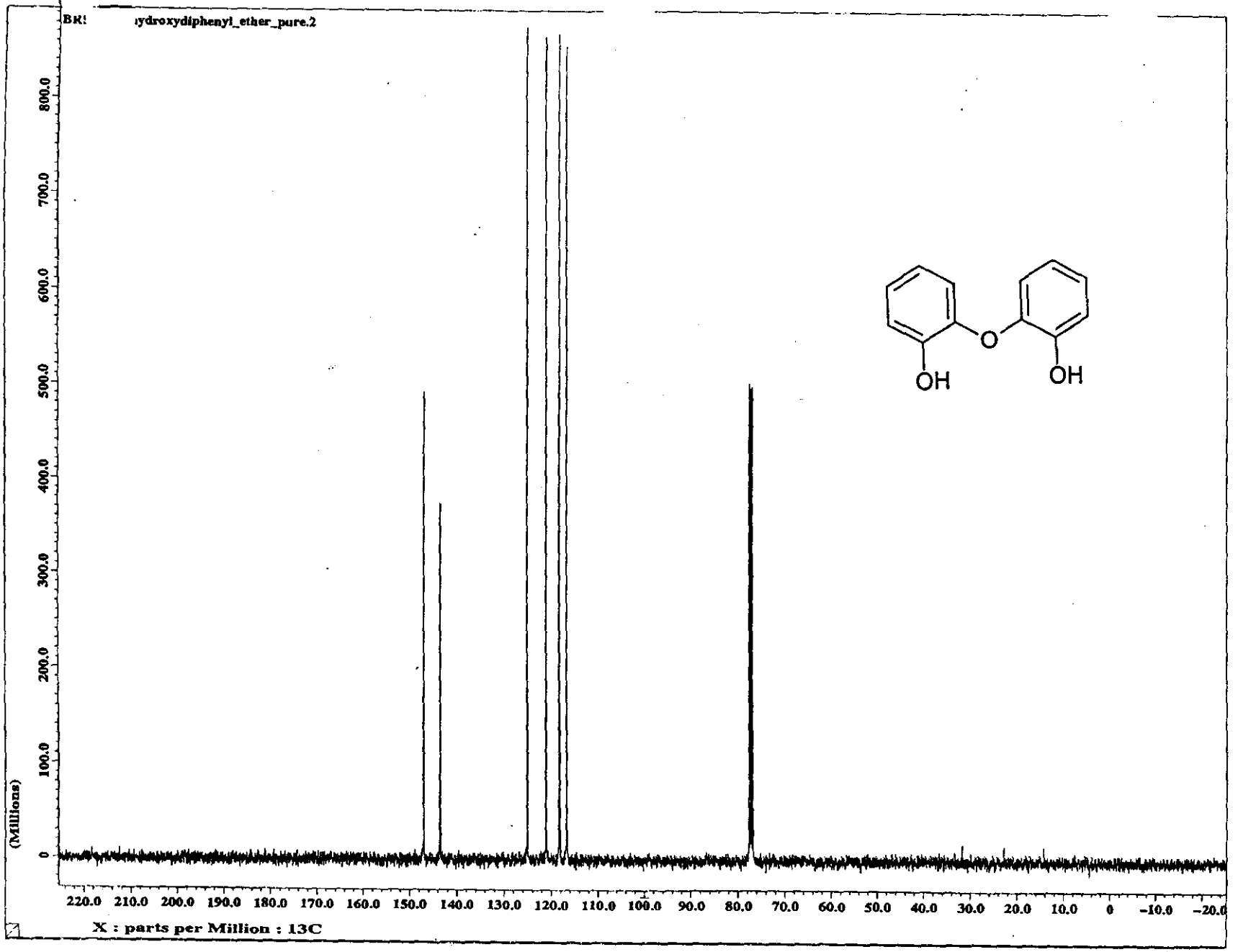
-2.0
X : parts per Million : 1H
O
OH
OH


BR!
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(Millions)
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700.0
600.0
500.0
400.0
300.0
200.0
100.0
0
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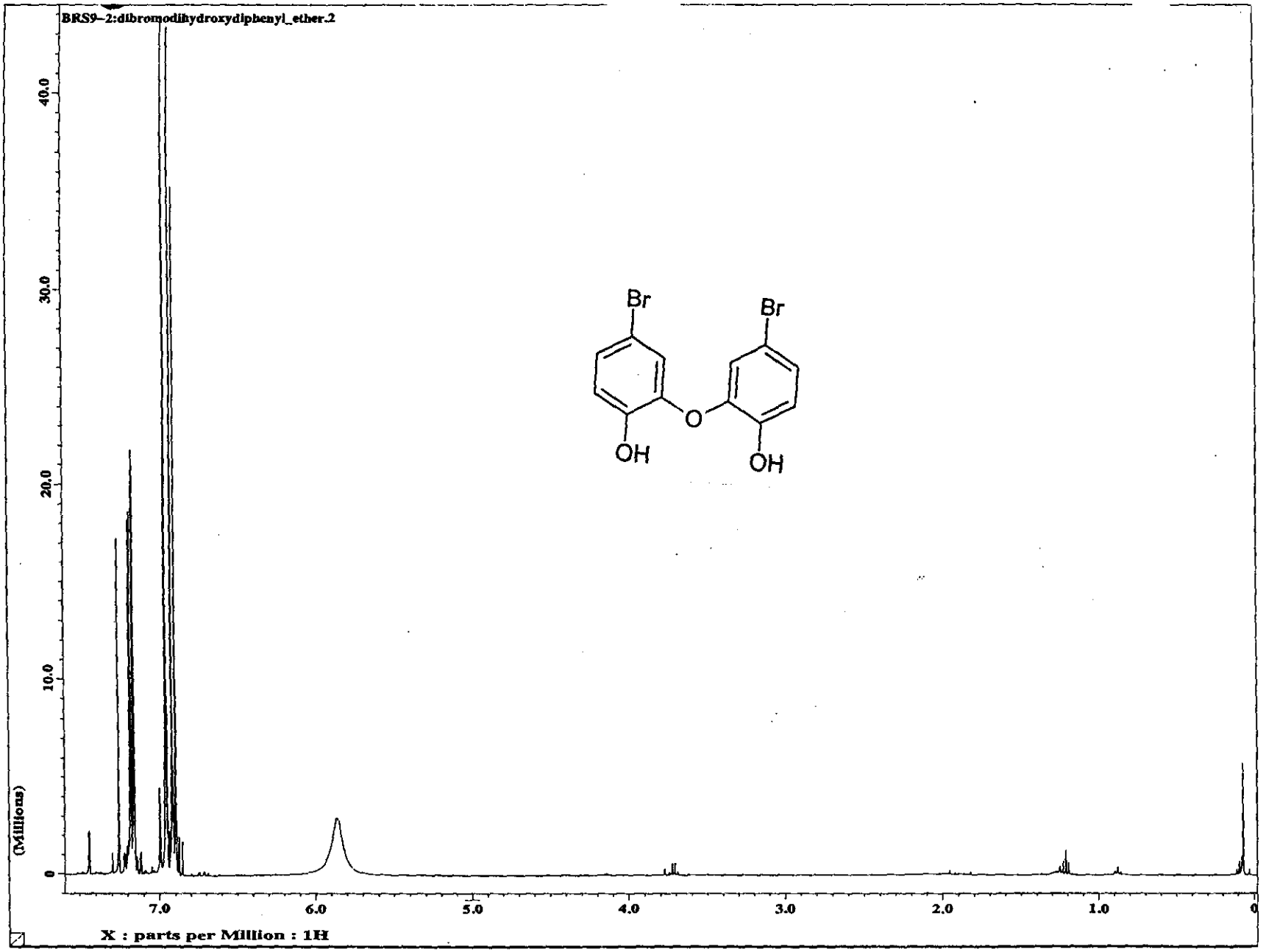
O
OH
OH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O
OH
OH
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(Millions)
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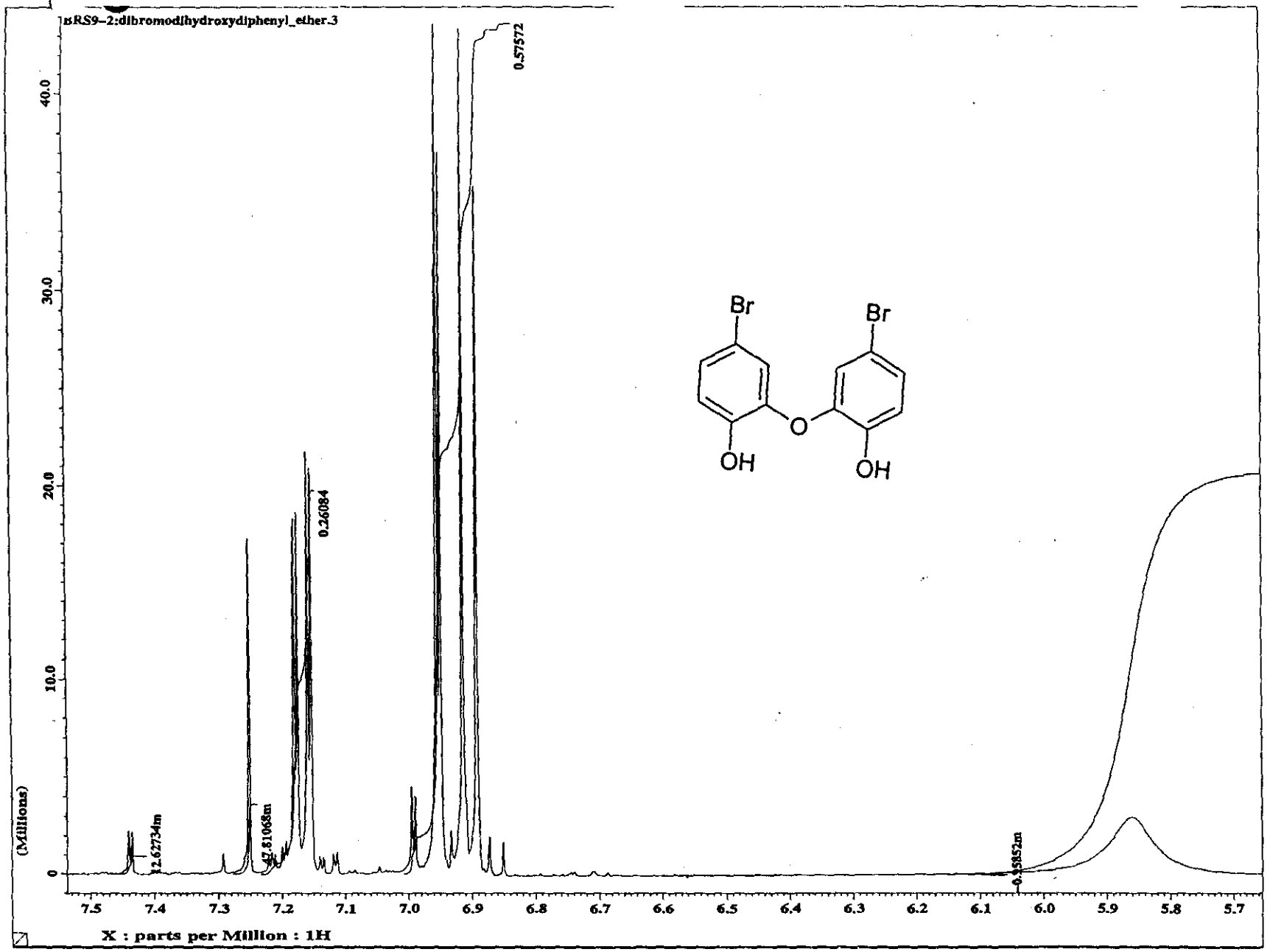
X : parts per Million : 1H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Br
Br
O
OH
OH
(Millions)
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30.0
20.0
10.0
0
7.5
7.4
7.3
7.2
7.1
7.0
6.9
6.8
6.7
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6.5
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6.1
6.0
5.9
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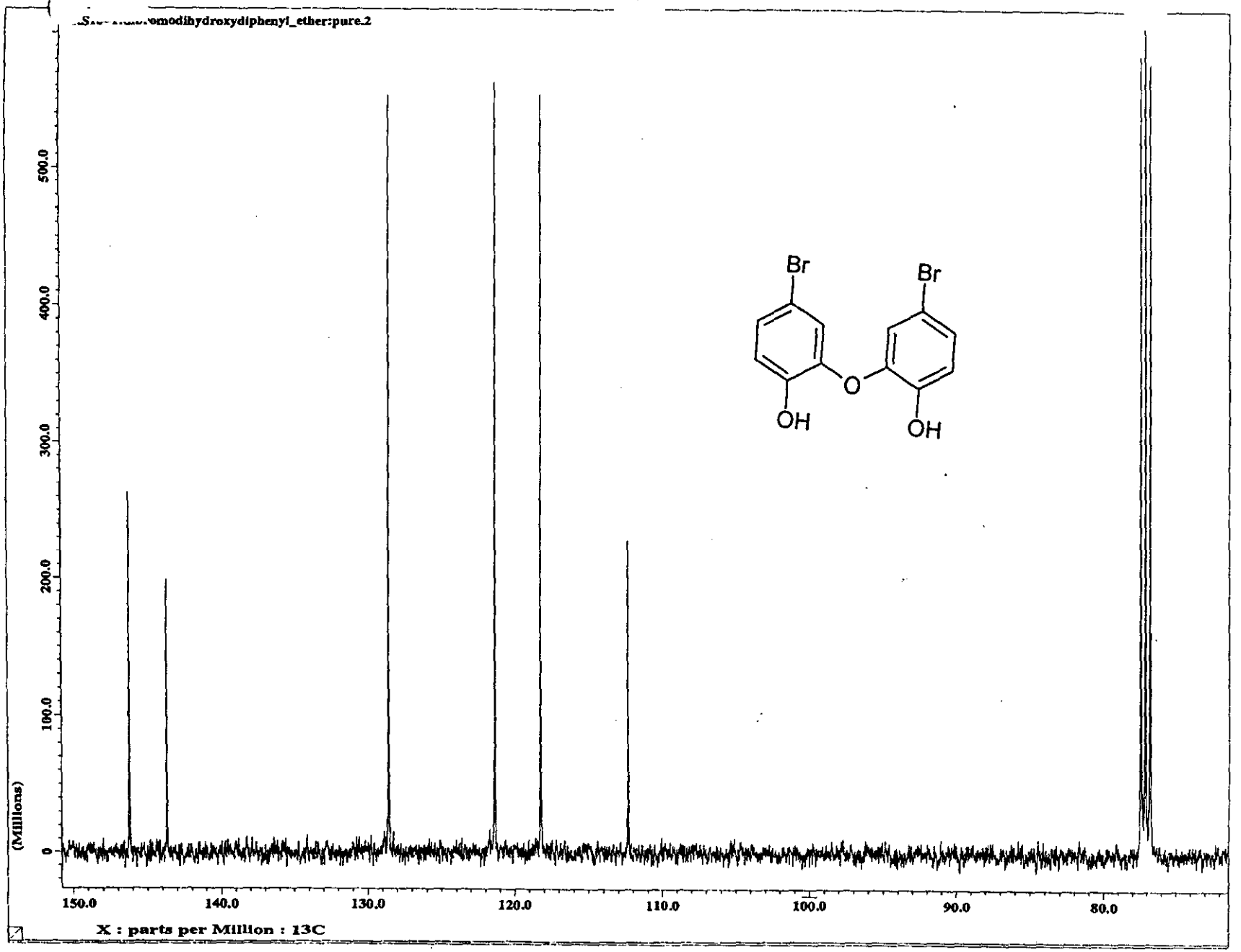
X : parts per Million : 1H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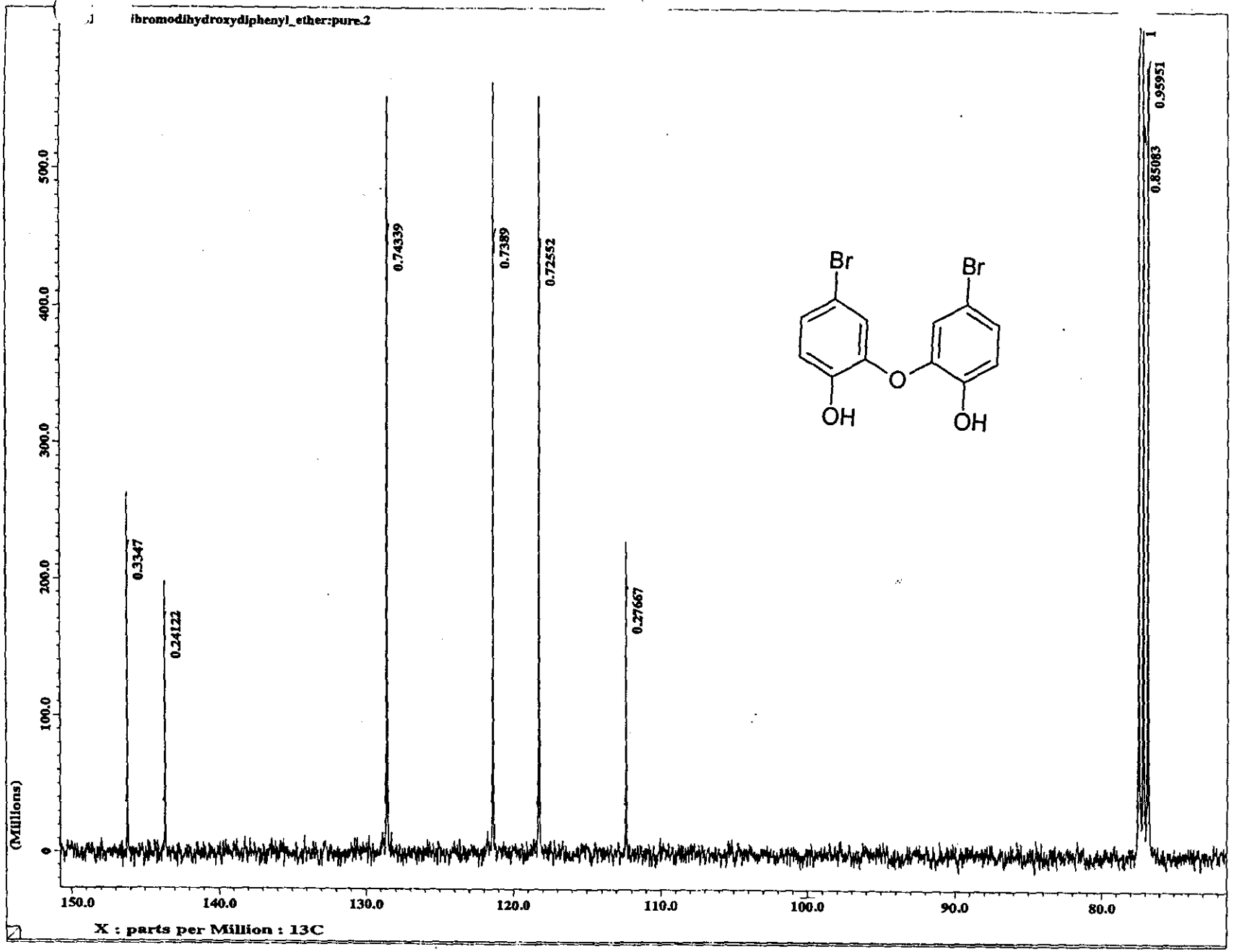
X : parts per Million : 13C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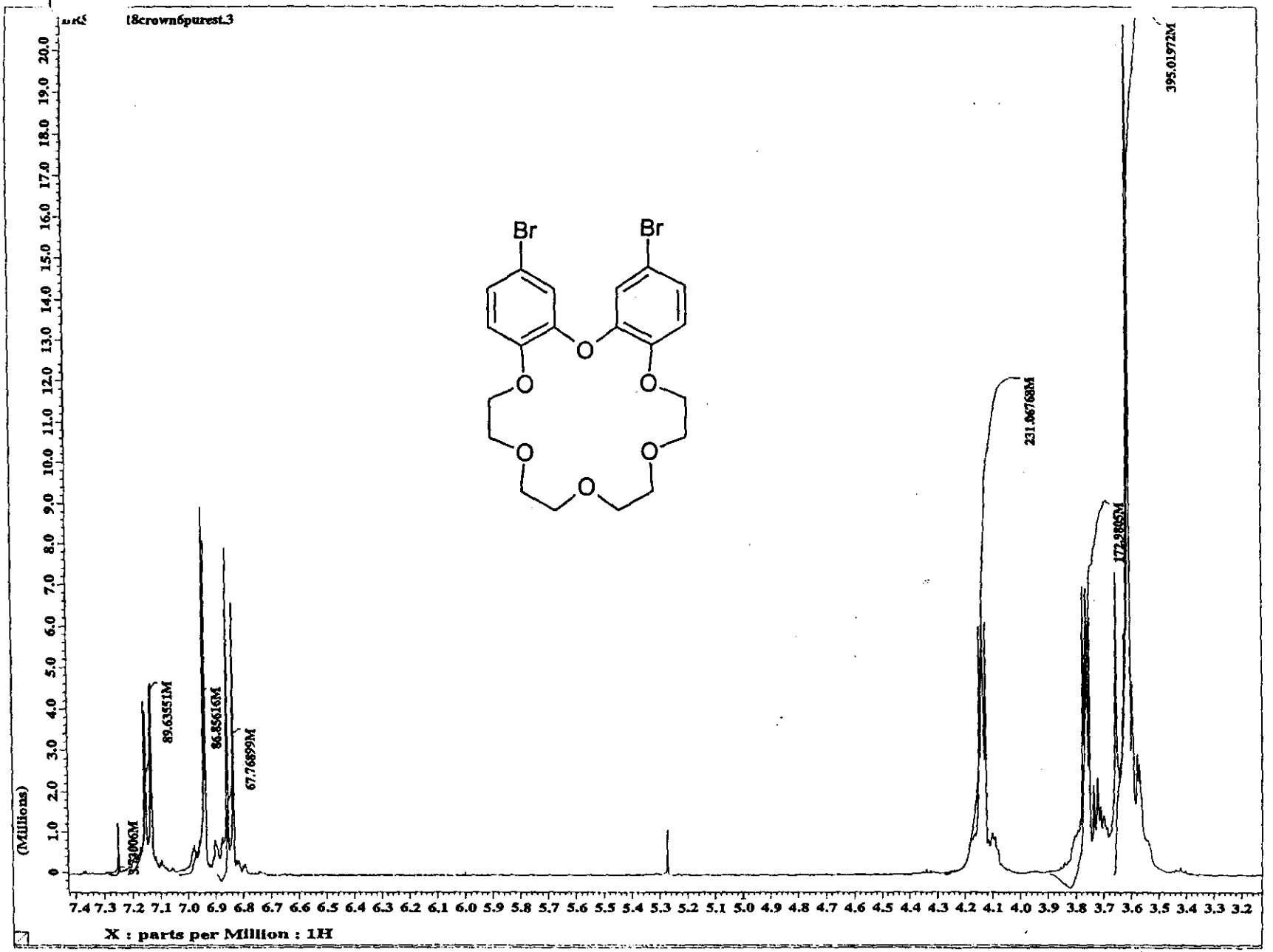
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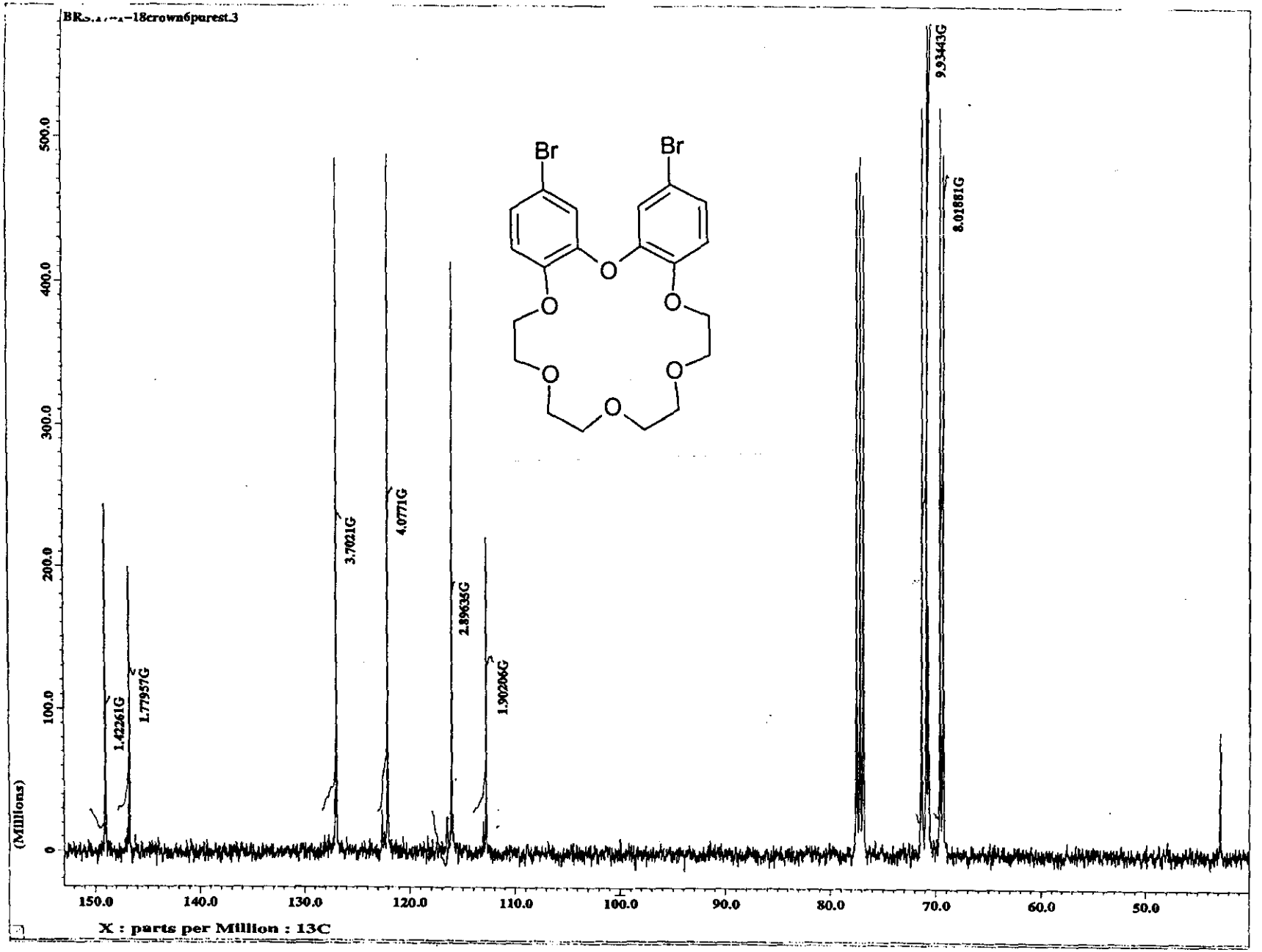
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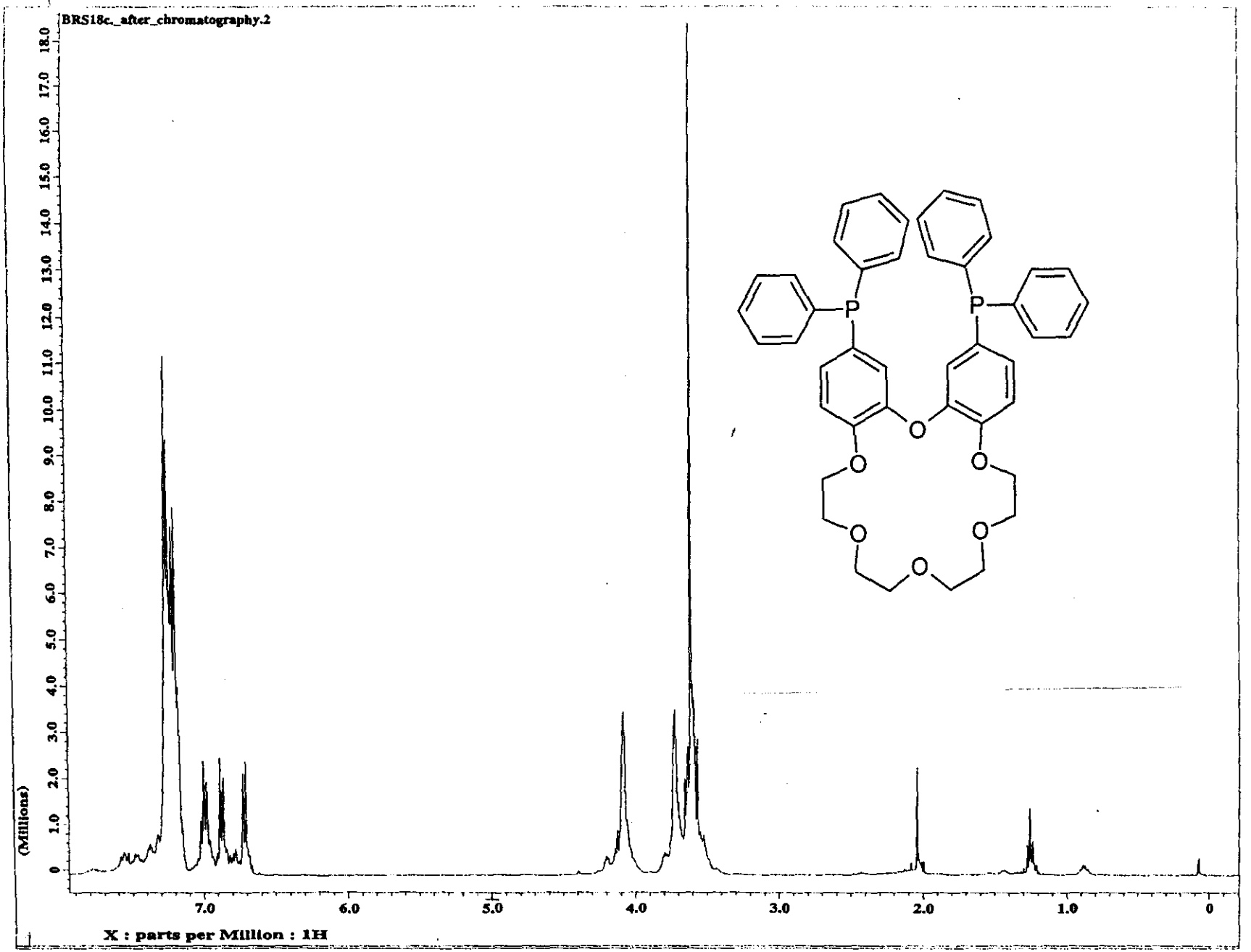
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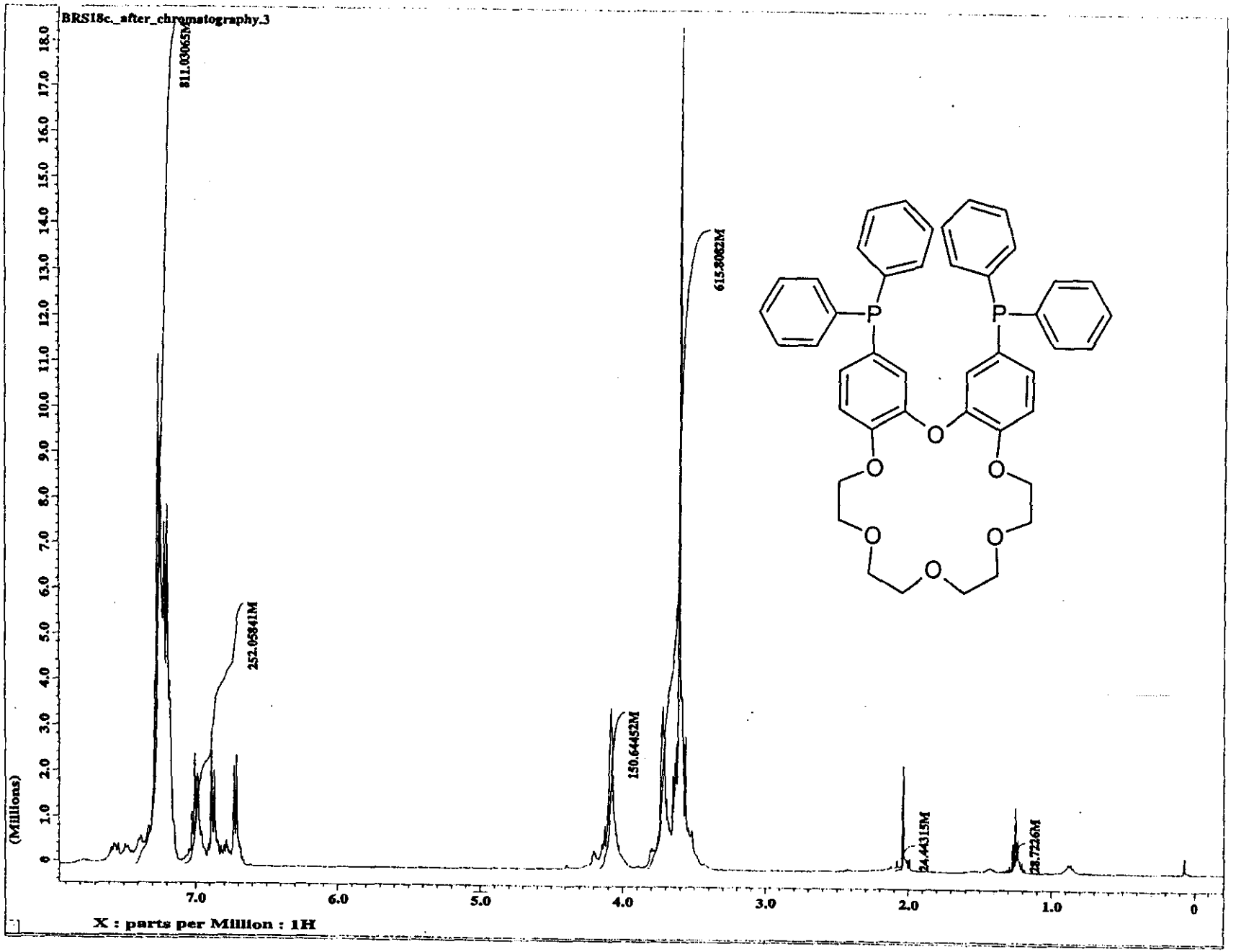
O
O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X : parts per Million : 1H
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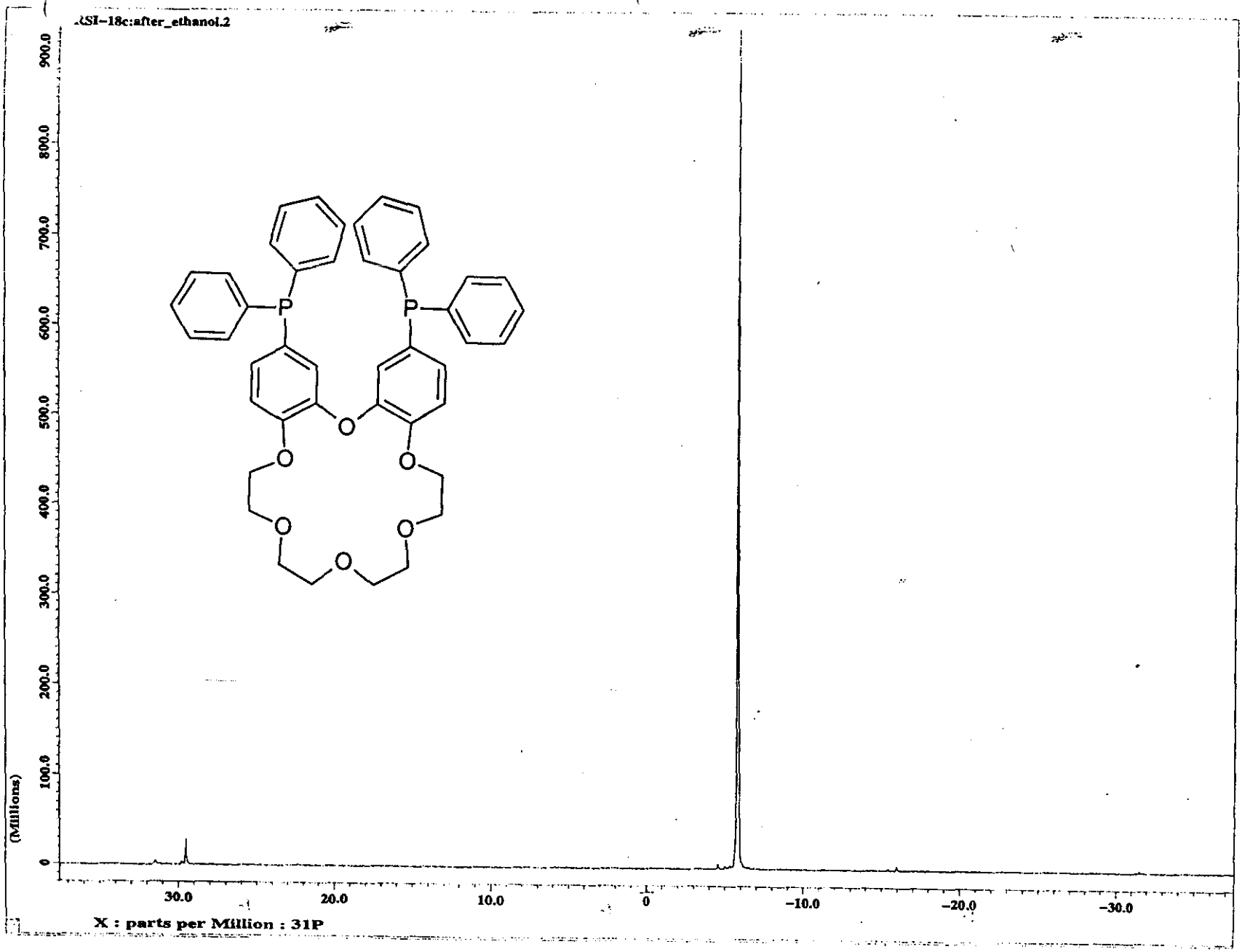
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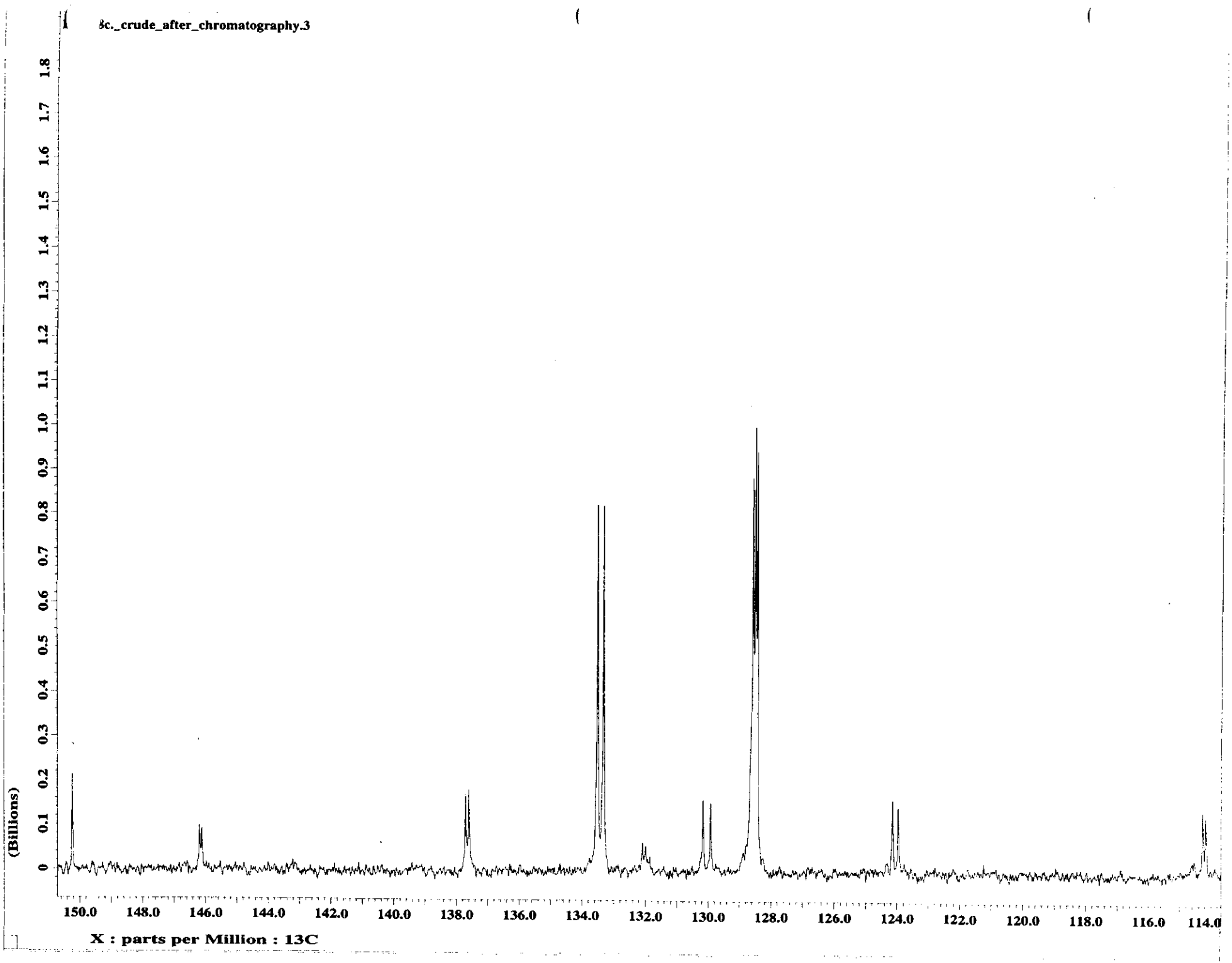
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1.4
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1.6
1.7
1.8
150.0
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116.0
114.0
X : parts per Million : 13C