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The Selective Oxidation of Dihydrosilanes

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By

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Abstract

Gansle, Paul B., Jr. The Selective Oxidation of Dihydrosilanes. Department of Chemistry, June 1993.

The selective monooxidation of dihexylsilane by a number of oxidants was studied. The list of oxidants included monoperoxyphthalic acid, trioctylphosphine oxide, MCPBA, PCC, Jones Reagent, oxalyl chloride in DMSO, DMDO, $Hg(OAc)_2$, Iodine, Bromine, HBr, N-chlorosuccinimide, and N-bromosuccinimide. Of these, NBS was found to be the most selective oxidant. Further study showed that NBS bromination of R-(+)-naphthylphenylmethylsilane proceeded with retention of stereochemistry. Therefore, this reagent showed the most promise for development into a chiral reagent capable of chiral induction onto a prochiral dihydrosilane. As such, N-bromo-(2S,3S)-2,3-di-p-toluoylsuccinimide was synthesized from (2S,3S)-2,3-di-p-toluoyltartaric acid. This chiral oxidant will hopefully be used in the future to synthesize chiral halosilanes for use in the synthesis of drugs and natural products.

Dedication

I would like to dedicate this thesis to Professor Karl De Jesus, his wife Sena, and their new child, Kirsten Jean. It has been a great pleasure getting to know Prof. De Jesus as an instructor and as a friend. He has given me a great appreciation for both teaching and research. He has also been an example of a teacher that I may someday become. Not only does he teach his students, but he takes an interest in their personal lives and gets to know them on an individual basis. I would like to personally thank him for all that he has done for me since I met him my sophomore year, especially this past year as my research advisor.

It has also been a great pleasure getting to know Sena (and now little Kirsten Jean). I want her to know that I enjoyed all of our chats we held during her visits to the department. Sena is a very special person that I'm glad to have been able to meet. I wish them all the very best in the future. I hope to see you all on my vacations from Colorado.

Acknowledgments

We would like to thank the Council on Undergraduate Research and SmithKline Beecham Pharmaceuticals for their financial support in the form of an Academic - Industrial Undergraduate Research Partnership (AIURP) Fellowship. We would also like to thank Professor Hull and Lalbachan Budhai of the Union College Chemistry Department for a sample of dimethyldioxirane and help in the analysis of the sample. Lastly, I would like to thank each member of the Chemistry Department for any suggestions, help, and advice which they have given me during the terms of my research and also throughout my stay at Union.

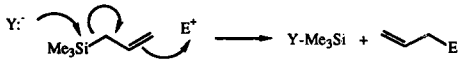
Introduction

Uses of Silanes

The synthesis of drugs and natural products in enantiomerically pure form is a growing area of research. Our laboratory is currently working on synthetic methodologies that would facilitate the production of compounds in such a form. The approach we are taking is to use chiral silanes as templates for the stereochemical control of organic reactions. In order to do this, however, we must first synthesize these silanes enantiomerically pure. This project focuses on the synthesis of chiral silanes by selective oxidation of prochiral dihydrosilanes to yield directly, or by further transformations, halohydrosilanes. These halohydrosilanes can in turn, be used as precursors in the chiral synthesis of a variety of chiral silanes by the nucleophilic displacement of halide in S_N2 fashion.

The choice of silanes as asymmetric templates in a synthetic pathway is due to their usefulness and versatility. Because silanes are easily introduced and removed, they are often used as protecting groups and also as activators for the addition of nucleophiles to electrophilic reagents. A prominent protecting group for alcohols is t-butyldimethylsilane[1], a group we have utilized in the protection of tartrate hydroxy groups. These protecting groups are easily removed by the addition of fluoride ion.

Of greater importance in asymmetric synthesis is the ability of silicon to activate nucleophiles towards electrophilic addition. As an example, a silane group in an allylic position activates this species in its addition to carbonyls and acetals as shown by Sommer et al. in Reaction 1[2]. Silanes are also useful in activating enol ethers towards addition to carbonyls, acetals, and alkyl

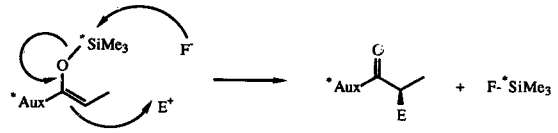


Reaction 1

halides.[3] The first two additions follow a mechanism similar to that given in Reaction 1. The addition to alkyl halides is an S_N2 reaction usually promoted by fluoride ion. Another useful reaction of silanes is the silyl hydride addition to ketones and unsaturated hydrocarbons.[4] In these reactions, Si and H add across a double or triple bond to produce alkoxy or alkylsilanes.

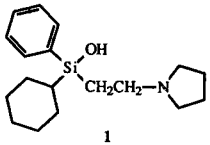
The common feature of all these silane reactions is that they are capable of producing new chiral centers. Should these reactions be able to proceed with absolute control of stereochemistry, they would be an important addition to the already existing enantioselective routes to chiral drugs and natural products. Existing routes, such as the alkylation of enolates developed by Evans and coworkers[5], incorporate chiral auxiliaries onto the carbon framework of the nucleophiles. These chiral auxiliaries require multistep procedures for the introduction and removal of the auxiliary. The latter step can be especially problematic when trying to avoid epimerization. By contrast, silanes are introduced very easily, and many times, removed under the reaction conditions. In addition, silanes, being activators in all these reactions, are intimately involved in the bond making process and, by consequence of being close to the reaction center, should exert a greater influence on the stereochemical outcome. In the case of enolate additions, it may be possible to increase the selectivity of existing chiral auxiliaries. By placing a chiral silane on the oxygen, as shown in Reaction 2, one might be able to achieve some double

diastereodifferentiation if the silane and auxiliary are complementary.



Reaction 2

In all of the above reactions, silanes are used as temporary protecting groups or activators. They are not the primary backbone of the molecule. However, there are a group of compounds, known as sila-drugs, which incorporate silicon as the chiral center of the molecule. Sila-procyclidine, **1**, for example, was found to be two orders of magnitude more potent than its carbon analog.[6] It would be beneficial to add to the arsenal of methods cabable of synthesizing these compounds enantiomerically pure.



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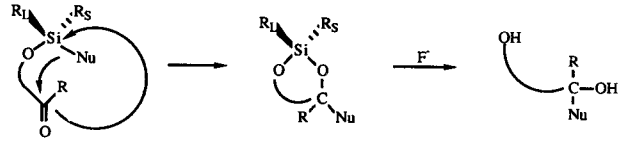
Purpose

The main goal of our laboratory is to develop chiral silanes which will control the absolute stereochemistry of the above reactions. In order to accomplish this, model systems need to be developed which are able to control the stereochemistry. One possibility is to use the conformation and electronic constraints of intramolecular additions to control the stereoselectivity. This model would be applicable to the addition of nucleophiles such as hydrides, enol ethers, and allyl silanes to ketones and aldehydes, as shown in Scheme **1**.

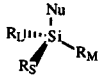
The alkoxysilane resulting from these reactions can be converted to a diol, as



Scheme 1

shown by the addition of fluoride ion. In this model, the large and small alkyl groups, R_L and R_S, will provide a way of selectively choosing which side of the carbonyl the nucleophile will attack. We hope that the resulting diol will be optically active due to chiral induction of the silicon at the carbinol center.

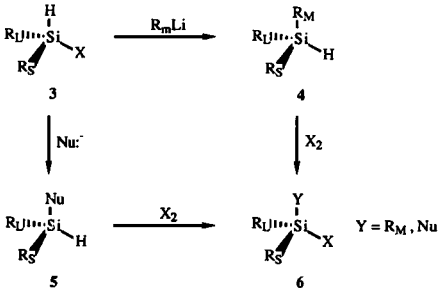
Another route would be to develop highly directing chiral auxiliaries with a general structure such as **2**. The directing effects of the large, medium and small alkyl groups will, hopefully, direct the incoming nucleophile according to Cram's Rule[7].



2

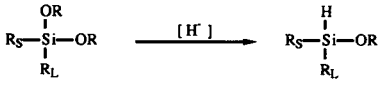
Before these model systems can be studied, however, the model compounds have to be available in optically pure form. Both of these systems can be derived from silane **3** which is a key intermediate, not only for our model systems, but also in the general synthesis of chiral silanes. As such, it can also be used in the synthesis of chiral sila-drugs where control of the absolute stereochemistry at silicon is necessary. The importance of this silane lies in its versatility since it incorporates two possible sites of activation: the silyl hydride and leaving group X. Leaving group X can be used to introduce alkyl, aryl or

activating groups such as R_M by addition of Grignard or alkyl lithium reagents. This would allow us to synthesize **4**. At the same time, substitution of **3** by other nucleophiles such as enolates or cyanide, would yield compounds such as **5**. Both **4** and **5** can be activated by addition of a halogen to yield compounds such as **6**, as shown in Scheme **2.** Compounds such as **6** can be converted to the necessary synthetic intermediates for the intramolecular or highly directing models.



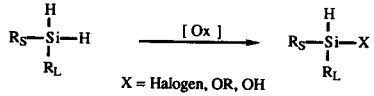
Scheme 2

Therefore, the main goal of my research is the synthesis of compounds such as **3** in high enantiomeric excess. Two strategies have been explored in our group to try to develop a method capable of synthesizing compounds such as **3**. The first strategy used the hydride reduction of dialkoxysilanes to hopefully yield alkoxyhydrosilanes such as **7**, as shown in Reaction **3**.



Reaction 3

The second strategy, the focus of my research, was complementary in nature and involved the selective monooxidation of prochiral dihydrosilanes, as shown in Reaction **4**.



Reaction 4

The reduction strategy had been previously studied in our laboratory and found unsuccessful. After trying several different hydrides, the only products isolated were the starting material and products of double reduction, the dihydrosilanes.

After this setback, attention was turned to the oxidation strategy, which is the main focus of this work. In successfully completing this work, two goals had to be accomplished. The first was to find an oxidizing agent which would give monooxidation as the sole product. Once found, the second goal was to develop a chiral derivative of this reagent, in enantiomerically pure form, and use it to achieve asymmetric induction in the oxidation of dihydrosilanes.

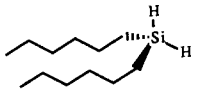
Results and Discussion

The monooxidation of dihydrosilanes could potentially yield several types of compounds, all synthetically useful.[8] Subsequent reactions for these oxidation products can be done without touching the remaining silicon hydride. This allows one to utilize the remaining hydrogen functionality for further transformations at a later time. While there are several types of oxidation products possible, the most versatile compounds are formed from the addition of a halogen to the prochiral dihydrosilanes. These halohydrosilanes are the most reactive, and least stable of all oxidation products. Consequently, they can be substituted by most nucleophiles in an S_N2 displacement reaction. A second group of oxidation products are the pseudohalogens. One such example are the silyl carboxylates. These can be displaced by most nucleophiles just like the halogens, but they are not as reactive as the halosilanes. Both of these oxidation reactions are very easy to carry out and are extremely versatile due to the number of nucleophiles that will react with the products.

Another class of useful oxidative products are the alkoxysilanes. These are more stable than the above two and can easily be formed from them by addition of an alcohol such as methanol. Because they are not as labile as silyl halides and carboxylates, they only react with strong nucleophiles such as organolithium and Grignard reagents. An even less versatile type of oxidation product are silanols. Silanols comprise the last group of oxidation products to be studied. These are also useful synthetic intermediates, although the strength of the Si-O bond does not allow for easy displacement by most nucleophiles. Silanols can, however, undergo most reactions that ordinary alcohols do. In

some cases, these allow a more chemoselective synthesis than would be possible if a halohydrosilane was the synthetic intermediate.

In this study, a series of oxidants were reacted with dihexylsilane, **8**, in hopes of finding a reagent that would give monooxidation exclusively. Dihexylsilane was chosen as a model system due to its nonvolatility, as well as its ease of handling, isolation, and analysis. A successful reaction would yield one of the types of compounds discussed above. Once a suitable monooxidation reagent was found, it would have to be modified for use in an asymmetric synthesis. In order to do this, it was necessary that the reagent be synthesized in a chiral, enantiomerically pure form. Once synthesized, it would be targeted for use in the future as a potential enantioselective oxidant. Eventually, this should yield products such as **4** and **5** in high enantiomeric yield and allow them to be incorporated into the synthesis of drugs and natural products.



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Part I : Survey of Oxidative Reagents

Thirteen oxidants were reacted with dihexylsilane. The results of these reactions are given in Table **1**. Entries **1** to **7** show the unsuccessful attempts to form dihexylsilanol. Oxidants used for this transformation were

Table 1

Entry	Oxidant	Conditions	Intermediate (% by GC)	Workup (% by NMR)
1	MPPA	EtOH, 0° 1h->RT	NR	NR
2	TOPO	neat, 0° 1h->RT	NR	NR
3	MCPBA	CH_2Cl_2, reflux	NR	NR
4	PCC	CH_2Cl_2, reflux	NR	NR
5	Jones rgnt.	acetone, RT	NR	NR
6	Oxalyl chloride	DMSO, reflux	NR	NR
7	DMDO	acetone, CH_2Cl_2, reflux	NR	NR
8	$Hg(OAc)_2$	THF, HOAc, RT	S.M. (>90)	S.M.(64)
			10	**11** (36)
			$Hex_2Si(H)OAc$	
9	$Hg(OAc)_2$	THF, RT	$Hex_2Si(OAc)_2$ (100)	$Hex_2Si(OMe)_2$ (72)
				$Hex_2Si(OAc)(OMe)$ (28)
10	$Hg(OAc)_2$	THF, MeOH, py, RT	S.M. (36)	S.M. (33)
			9 (26)	**9** (21)
			$Hex_2(OMe)_2$ (12)	$Hex_2Si(OMe)_2$ (35)
			$Hex_2(OAc)(OMe)$ (26)	$Hex_2Si(OAc)(OMe)$ (11)
11	I_2	CCl_4, 0° 1h->RT		S.M. (70)
				11 (30)
12	Br_2	CCl_4, 0°C	$Hex_2Si(H)Br$ (92)	**9** (33)
			Hex_2SiBr_2 (8)	$Hex_2(OMe)_2$ (16)
				11 (51)
13	HBr	CCl_4, 0° 1h->RT	NR	NR
14	NCS	CCl_4	S.M. (77)	S.M.(69)
		0° -> RT -> reflux	$Hex_2Si(H)Cl$ (23)	**9** (7)
				$Hex_2(OMe)_2$ (4)
				11 (20)
15	NBS	CCl_4, 0° 1h->RT	S.M.	S.M.(17)
			$Hex_2Si(H)Br$ (92)	**9** (17)
			$Hex_2Si(H)Cl$	$Hex_2(OMe)_2$ (1)
				11 (64)

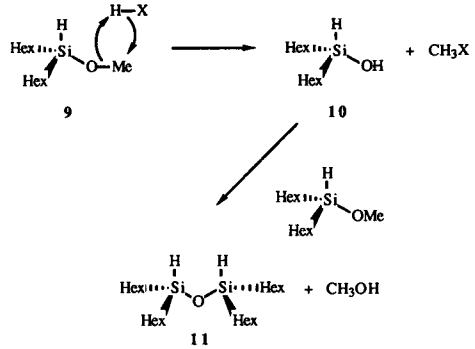
monoperoxyphthalic acid (MPPA), trioctylphospine oxide (TOPO), MCPBA, PCC, Jones reagent, oxalyl chloride in DMSO, and dimethyldioxirane

(DMDO)[9]. None of these reagents reacted with dihexylsilane to any appreciable extent. In retrospect, this is very fortunate since this allows these reagents to be used on a substrate which contains a hydrosilane of similar reactivity without affecting the hydrosilane.

Mercuric acetate was also used as an oxidant to form a silyl carboxylate. This was attempted using three different reaction conditions. The first condition consisted of adding dihexylsilane to acetic acid.[10] The dihydrosilane did not dissolve under these conditions, therefore, THF was added as a cosolvent, followed by the adddition of $Hg(OAc)_2$, as shown in Entry **8**. This reaction went to less than ten percent completion. Since the dihexylsilane was insoluble in acetic acid to begin with, the reaction was repeated using only THF as the solvent. Entry **9** shows that, after addition of two equivalents of $Hg(OAc)_2$ and reaction for 72 hours, the reaction went to completion, forming all diacetate product. Since this reaction appeared to have an equilibrium initially, it seemed probable that the selectivity could be improved by trapping the initial monooxidation products whith methanol and pyridine. Therefore, this reaction was performed, as shown in Entry **10**, and a mixture of products, including starting material, were isolated. Although these reactions did not appear to be very selective, future study on this reaction may be conducted to attempt to optimize the conditions and achieve monooxidation exclusively.

The last group of oxidants studied were the addition of halogens to dihexylsilane.[11] Whenever possible, these reactions were done at 0°C in order to enhance their selectivity. All of the final products were isolated as methoxysilanes by addition of methanol and pyridine to the reaction. The reaction and products were indentified by both GC/MS and

^{1}H NMR. The addition of iodine to dihexylsilane in CCl_4 was not very successful. This reaction went to only 30% completion. As shown in Entry **11**, this was due to a dimer whose GC/MS and ^{1}H NMR were consistent with that of compound **11**. It was not clear at that time how this compound came about. Analysis by GC/MS showed **11** being formed in anhydrous media with its proportion increasing after extractive workup. More than likely, it was formed by halogen attack on methoxysilane **9** to yield silanol **10**, followed by dimerization of these two, as seen in Scheme **3**. Although a source of confusion during the analysis, the dimerization still gave us useful information. As can be seen by the compound's structure, it was the result of monooxidation and could be used to determine the ratio of monooxidation to dioxidation.



Scheme 3

The addition of Br_2 to dihexylsilane was studied next. Again, the expected product was one of monooxidation. When the reaction was performed at room temperature, GC/MS analysis showed that there was a 4:1 ratio of

monobromination to dibromination. However, as shown in Entry **1 2**, when this reaction was repeated at 0°C, the selectivity increased to 92% monobromination and 8% dibromination. After workup with methanol, the product mixture was analyzed by ^1H NMR where it was found that the dioxidation product doubled from 8% to 16%. Since a side product of the reaction of Br_2 and dihexylsilane was HBr, it was thought that reaction of the initial monooxidation products with this could be the cause for the increase in dibromination between analysis of the initial reaction and the workup with methanol and pyridine. A separate reaction of dihexylsilane with gaseous HBr, Entry **1 3**, showed this was not the case since, even at room temperature, HBr did not react with dihexylsilane. The conclusion is that dibromination is part of the equilibrium of the reaction. Since the purpose of this study was to find a reagent that gave exclusively monooxidation, Br_2 would not be a synthetically useful reagent.

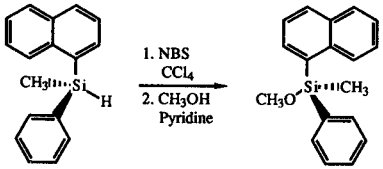
The reaction of N-chlorosuccinimide, NCS, with dihexylsilane was studied next. The expected product in this reaction was chlorodihexylsilane. The reaction was run at 0°C in CCl_4, as shown in Entry **1 4**. Since this reaction did not proceed to any appreciable extent at 0°C, the temperature was raised to room temperature, and finally, the reaction was heated to reflux. Analysis by GC/MS showed that after refluxing for four hours, only 23% reaction had taken place. Nevertheless, as shown by GC/MS, the only product was one of monooxidation. This was very promising from the standpoint of selectivity, although the reactivity was low. Since N-bromosuccinimide is known to be more reactive, it was used as the next oxidant. As suspected, N-bromosuccinimide, NBS, was more reactive. Analysis by GC/MS showed the reaction

going to 50% completion after 3.5 hours at 0°C. This eventually went almost to completion when warmed to room temperature. As shown in entry **1 5**, this gave a product mixture of 92% monobromination. The remaining percents were chlorodihexylsilane and starting material. Extractive workup after addition of methanol and pyridine gave products which were the result of monooxidation on the order of 99%. Once again, dimer **11** was found to be a major component of the methanolysis products. This is really not a major concern, however, because any use of this reaction would include reacting a nucleophile with the bromo product, and not the product of methoxylation where the dimerization occurs.

At this point, NBS was found to show the most promise as a synthetic reagent for monoxidation of dihydrosilanes. If a derivative could be synthesized in a chiral form, it would have the potential to be used in an asymmetric synthesis. Before proceeding with the project, however, it was necessary to check if chiral silanes would racemize under the reaction conditions. It is well established that NBS reacts as a free radical bromine in such reactions as allylic bromination[12, 13, 14]. If this was true in this case, racemization of a chiral silane should occur. Conversely, if NBS reacted in a polar or concerted mechanism, chiral integrity would be preserved. To test this, the oxidation of an enantiomerically pure silane developed by Sommer and coworkers was performed.[15]

R-(+)-naphthylphenylmethylsilane was reacted with NBS. Using optical rotations reported by Sommer, we were able to show that NBS brominated the silane with retention of stereochemistry. The same procedure was followed as in the reaction of NBS with dihexylsilane. NBS was allowed to react with the

chiral silane for three hours at room temperature, followed by the addition of methanol and pyridine. The optical rotation of the product was then taken and found to be +8.0. When compared with that of optically active naphthylphenylmethylmethoxysilane, it was determined that the reaction proceeded with at least 48% retention. This lower value was mostly due to mechanical losses of the product because of a faulty polarimeter cell. The optical rotation obtained indicated that the overall reaction proceeded with inversion of stereochemistry. Since the methoxylation reaction is known to proceed with inversion of the configuration, the silyl bromide must have formed by retention of configuration. This is shown in Reaction **5**. Since this reaction did go with stereochemical control, this means that the NBS reaction must not proceed via a radical mechanism, but a polar or concerted one. This also means that a chiral NBS derivative has the potential to transfer its chirality onto a prochiral dihydrosilane, and in such fashion, induce asymmetry at silicon.



Reaction 5

Part II : Synthesis of a Chiral N-bromosuccinimide Derivative

For the synthesis of the chiral NBS derivative, we chose to use a tartaric acid derived system. These compounds have a C-2 axis of symmetry. As such, reaction from either face of the molecule yields identical products or transition states. Attack of the chiral derivative on a dihydrosilane, as shown in Figure **1**, can best take place via only one of two transition state conformations due to the C-2 axis of symmetry. If the symmetry was removed, four conformations would be possible. With only two possible conformations, it is an easier task to control the stereochemistry of the reaction. This is accomplished by the use of bulky alkoxy protecting groups. Thus, the most favored conformation is the one that minimizes steric interactions between the succinimide alkoxy groups and the large substituent, R_L, of the silane.

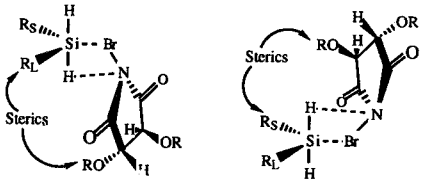
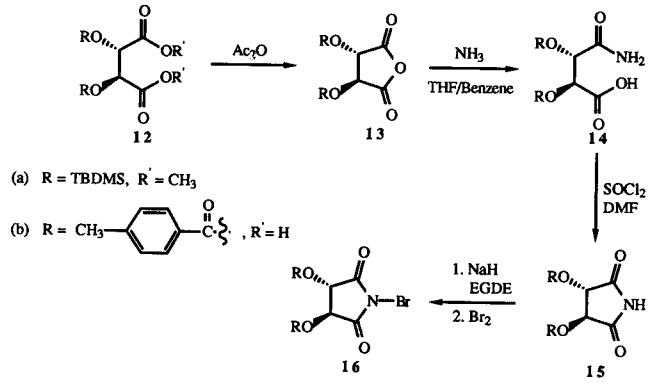


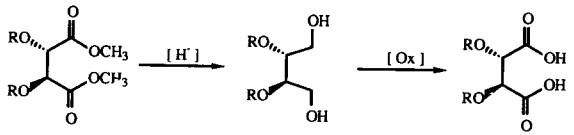
Figure 1

A general synthesis was devised which closely resembled that developed by Polonski for the synthesis of substituted succinic anhydrides and imides.[16] The general synthetic approach is summarized in Scheme **4**. It involved closure of the tartaric acid (**1 2**) to the anhydride (**1 3**), followed by the



Scheme 4

opening by ammonia and closure of the resulting acid-amide (**14**) to a succinimide (**15**). Subsequent bromination yielded the chiral NBS derivative (**16**)[17, 18]. This scheme was applied to two systems, (+)-dimethyl-L-tartrate and (+)-2,3-di-p-toluoyl-D-tartaric acid. Unfortunately, the tartrate system was unsuccessful. In this synthesis, the starting material's hydroxy groups were first protected by TBDMS groups. Problems arose in the hydrolysis of the ester groups, prior to the ring closure and anhydride formation. To circumvent this problem, work is now currently being conducted using a reduction approach to the tartrate system as shown in Scheme **5**.



Scheme 5

As a result of the problems encountered with the synthesis of the TBDMS

tartrate, attention was shifted towards the synthesis of N-bromo-(2S,3S)-2,3-di-p-toluoylsuccinimide, **16b**. A succesful synthesis was completed for this system by following the sequence in Scheme **5**. The first reaction involved the dissolution of toluoyltartaric acid **12b** in acetic anhydride and reaction at room temperature for 24 hours. Filtration at 0°C yielded a white solid with a crude yield of 87%. This was eventually purified by recrystallization from hot toluene (d 196 °C), but was normally used directly without further purification. Evidence for formation of anhydride **13b** was obtained directly from ^{1}H NMR analysis by the disappearance of the hydroxy proton peak at 4.9 ppm. In addition, the FTIR spectrum yielded a peak at 1807 cm^{-1}, which is consistent with an anhydride carbonyl stretch.

The opening with ammonia was carried out by dissolving crude anhydride **13b** in a benzene/THF solution. Gaseous ammonia was bubbled into the solution for about 30 minutes, during which, a white solid precipitated. This solid was filtered at 0°C, giving a crude yield of approximately 100% (d 163 °C). Evidence for the formation of **14b** was seen in the proton NMR. Normally, the protons at C-2 and C-3 are equivalent for the tartaric acid and anhydride due to a C-2 axis of symmetry. The acid-amide, however, lacks this symmetry and, as a consequence, the protons at C-2 and C-3 are no longer identical. This was seen in the proton NMR as protons C-2 and C-3 were found at 5.70 and 5.56 ppm, respectively. In addition, two broad peaks were found at 7.72 and 7.29 ppm, which are indicative of the acid and amide protons. Further evidence for the formation of the acid-amide can be found in the IR with a broad acid peak at 3242 cm^{-1}. In addition there are two carbonyl stretches at 1713

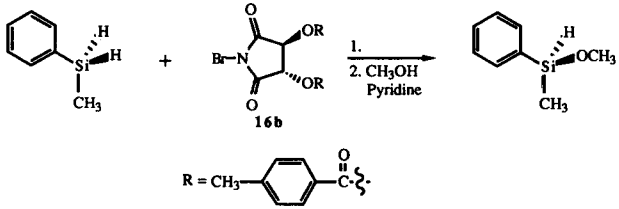
and 1703 cm^{-1} and an amide carbonyl stretch at 1686 cm^{-1}.

The conversion to succinimide **15b** was performed by dissolving the crude acid-amide above in DMF. Thionyl chloride was added to the reaction and allowed to react at room temperature for five hours, after which, a yellow oil was isolated using a Kugelrohr distillation. Recrystallization from hot toluene gave a white solid (d 118 °C) in a 70.8% yield. Evidence for the formation of **15b** was obtained by ^1H NMR analysis. The two doublets seen in the ^1H NMR of the previous product coalesced to form a singlet at 5.88 ppm due to the equivalence of the protons at C-2 and C-3. Also, a broad singlet at 8.6 ppm was a result of the newly formed succinimide hydrogen on the nitrogen. The infrared data was also consistent with succinimide formation as evidenced by the carbonyl stretching bands at 1757 and 1730 cm^{-1}.

The final N-bromsucinimide derivative **16b** was obtained from the addition of Br_2 to a solution of the previous succinimide's anion in ethylene glycol dimethyl ether (EGDE). The anion was formed by the addition of NaH. The N-bromosuccinimide was isolated as a yellow oil with solvent still present. The ^1H NMR evidence for the formation of the derived N-bromo compound was seen in the loss of the N-H peak at 8.56 ppm and a small shift in the C-2/C-3 hydrogen's peak from 5.88 ppm to 5.94 ppm. A redox reaction with NaI gave further evidence for the formation of the N-bromo compound.

The synthesis of N-bromo-(2S,3S)-2,3-di-p-toluoylsuccinimide marked the successful completion of this project. Since this reagent was only recently synthesized, the conditions of the final step in the synthesis have not yet been optimized. Once multigram quantities of the reagent are available, we hope that

this material will be used by future students to study the asymmetric bromination of prochiral dihydrosilanes. One such example is the reaction of **16b** with the prochiral dihydrosilane, phenylmethylsilane, as shown in Reaction **6**.



16b

Reaction 6

Conclusion

This study found that the selective monooxidation of dihydrosilanes is possible. N-bromosuccinimide was found to be the best reagent for this transformation. Further study also showed that NBS reacts with retention of stereochemistry. As such, this had the potential to be developed into a chiral oxidizing agent. The reagent chosen for this purpose was N-bromo-(2S,3S)-2,3-di-p-toluoylsuccinimide, **16b**, whose synthesis was successfully completed. Our next goal is to scale up this synthesis so that multigram quantities of this chiral reagent will become available.

As future asymmetric oxidations are performed with **16b**, there are two problems which may arise. One of these is the rate of bromination. Oxidation with NBS is already slow, taking place at room temperature, and oxidations with the more hindered **16b** should be slower. Another potential problem is that **16b** contains benzylic sites cabable of reacting intra or intermolecularly with an N-bromo group. This problem could be avoided if the toluoyl group is removed and a more stable protecting group such as t-butyldimethylsilane is added. To date, removal of the toluoyl group by hydrolysis with NaOH and methanol has been unsuccessful. These problems will be addressed in the future.

Once the above problems are addressed, future studies will look at the enantiomeric oxidation of prochiral dihydrosilanes with the newly synthesized chiral NBS derivative. Should the selectivity in this reaction be high, this method will be incorporated into the synthesis of a variety of chiral silyl reagents useful in natural product synthesis. This method would also hold great potential in facilitating the production of chiral sila-drugs.

Experimental

General. All ^{1}H NMR and ^{13}C NMR were obtained on a Varian Gemini 200 MHz spectrophotometer. GC chromatograms were obtained on a Hewlett Packard 5890 Series II Gas Chromatograph and all mass spectra were obtained on a Hewlett Packard 5971A Mass Selective Detector. All IR spectra were taken from a Mattson Instruments 6020 Galaxy Series FTIR spectrophotometer. Optical rotations were obtained on an Autopol II Automatic Polarimeter with a sodium D line. All silane reactions were run under nitrogen atmosphere. Anhydrous dichloromethane, THF, methanol, DMF, and ethylene glycol dimethyl ether were purchased from Aldrich Chemical Company. Glacial acetic acid, ethanol, acetone, DMSO, pyridine, CCl_4, and acetic anhydride were reagent grade chemicals. Benzene was an HPLC grade solvent. The anhydrous solvents were transferred by syringe under positive nitrogen pressure.

Part I : Reactions with Dihexylsilane

Dihexylsilane. A solution of dichlorodihexylsilane (5.072 g, 18.8 mmol) in 100 mL of THF was added to a dry 250 mL flask. After cooling to 0°C, $LiAlH_4$ (1.440 g, 37.9 mmol) was added and the reaction was warmed to room temperature and allowed to stir for 24 hours. A saturated solution of potassium tartrate was added, dropwise, at 0°C, to quench the reaction. The reaction mixture was transferred into a separatory funnel using hexane, and washed twice with water and once with brine. The extract was dried over $MgSO_4$, filtered, and the solvent removed under reduced pressure. The product was purified by Kugelrohr distillation with a boiling range of 134-7 °C at 6 mmHg.

This gave 3.861 g of product, which is essentially a 100% yield. This was not purified further and was used, as is, in the subsequent reactions. ^{1}H NMR ($CDCl_3$) δ 3.60 (2H, quin, 3.6Hz, SiH_2), 1.5-1.1 (16H, m, CH_2), 0.88 (6H, bt, 5Hz, CH_3), 0.75-0.55 (4H, m, SiCH_2); ^{13}C NMR ($CDCl_3$) δ 32.8, 31.8, 25.6, 22.8, 14.3, 9.3; IR (liquid film) 2957, 2913, 2848 (C-H), 2123 (Si-H) cm^{-1}; mass spectrum *m/e* 200 (P^+), 199 (P^+-1), 198 (P^+-2), 170, 143, 115 (P^+-hexyl), 87, 73, 59.

Reaction of Dihexylsilane with Monoperoxyphthalic Acid. A solution of dihexylsilane (205 mg, 1.02 mmol) in 2 mL of ethanol was cooled to 0°C and MPPA (633 mg, 1.02 mmol) was added with stirring. After one hour at 0°C and 24 hours at room temperature, GC/MS analysis showed that no reaction had taken place. The reaction mixture was transferred to a separatory funnel using hexane, washed with dilute $NaHCO_3$, water, and brine. The extract was dried over $MgSO_4$, filtered, and the solvent removed under reduced pressure. GC/MS analysis still showed only starting material.

Reaction of Dihexylsilane with Trioctylphosphine Oxide. Dihexylsilane (202 mg, 1.01 mmol) was cooled to 0°C and TOPO (392 mg, 1.01 mmol) was added neat. After stirring at room temperature for 24 hours, the TOPO had not gone into solution, nor reacted, as determined by GC/MS analysis. The reaction was heated at 100°C for three hours. The TOPO dissolved, but no reaction occurred.

Reaction of Dihexylsilane with MCPBA. A similar procedure to that given in Fieser and Fieser was followed[19]. A solution of MCPBA (225 mg, 1.30 mmol) in 2.5 mL of CH_2Cl_2 was added to a solution of dihexylsilane (206

mg, 1.03 mmol) in 1.5 mL of CH_2Cl_2 at room temperature; gas evolution was observed during the addition. GC/MS analysis showed that no reaction had occurred. After 30 minutes the MCPBA reprecipitated. After stirring at room temperature for 24 hours without reacting, the reaction mixture was refluxed in benzene for 6 hours. GC/MS analysis showed that, still, no reaction had occurred. The MCPBA was destroyed with $Na_2S_2O_3$.

Reaction of Dihexylsilane with PCC. A procedure similar to that reported by E.J Corey was followed[20]. PCC (336 mg, 1.04 mmol) was added to a solution of dihexylsilane (209 mg, 1.04 mmol) in 2 mL of CH_2Cl_2. After stirring at room temperature for 24 hours and refluxing for five hours, GC/MS analysis showed that no reaction had occurred.

Reaction of Dihexylsilane with Jones Reagent. A similar procedure to that given in Fieser and Fieser was followed[21]. Jones reagent (300 μL, 2.67 M) was added to a solution of dihexylsilane (207 mg, 1.03 mmol) in 2 mL of acetone at room temperature. A greenish precipitate appeared almost immediately, but analysis by GC/MS showed that no reaction had taken place. After stirring at room temperature for 24 hours, no reaction had occurred.

Reaction of Dihexylsilane with Oxalyl Chloride in DMSO. In a 2 mL conical flask, dihexylsilane (201 mg, 1.00 mmol) was added to 2 mL of DMSO and 2 mL of CH_2Cl_2. The dihexylsilane did not dissolve. Oxalyl chloride (110 μL, 1.25 mmol) was added and the reaction was stirred at room temperature for 24 hours. GC/MS analysis showed almost all starting material, but traces of dihexylsilanol **10** were observed. Upon reflux of the reaction mixture, there was decomposition of the starting material and intractable products.

Dihexylsilanol (10). Mass spectrum *m/e* 131 (P^+-hexyl), 129, 113 (P^+-hexyl-H_2O), 101, 89, 85, 75, 61.

Reaction of Dihexylsilane with Dimethyldioxirane. A solution of DMDO (1.3 mL, ~0.75 M) in 1.3 mL of acetone[22] was added to a solution of dihexylsilane (146 mg, 0.728 mmol) in 2 mL of CH_2Cl_2 at 0°C using a plastic syringe, since it is possible that a metal syringe could decompose the DMDO. After an hour, the reaction was warmed to room temperature and stirred for four hours. The reaction flask was stored at 5°C for 18 hours, followed by refluxing for 4 hours. GC/MS analysis showed that no reaction had occurred. Using a Hewlett Packard 8452A Diode Array Spectrophotometer, a maximum at 335-42 nm showed that DMDO was still present. The reaction mixture was transferred to a separatory funnel using hexane, washed with $Na_2S_2O_3$, water, and brine. The extract was dried over $MgSO_4$, filtered, and the solvent removed under reduced pressure. ^1H NMR analysis showed almost all starting material and traces of dimer **11**.

(Dihexylsiloxy)dihexylsilane (11). ^1H NMR ($CDCl_3$) δ 4.50 (2H, quin, 2.3Hz, Si*H*), 1.5-1.1 (32H, m, CH_2), 0.88 (12H, bt, 5Hz, CH_3), 0.70-0.50 (8H, m, SiCH_2); mass spectrum, *m/e* 329 (P^+-hexyl), 245 (P^+-2 hexyls), 161 (P^+-3 hexyls), 131, 117, 91, 77.

Reaction of Dihexylsilane with $Hg(OAc)_2$ in THF and Acetic Acid. Mercuric acetate (323 mg, 1.01 mmol) was added to a solution of dihexylsilane (202 mg, 1.01 mmol) in 1 mL of glacial acetic acid and 1 mL of THF. The resulting solution was stirred at room temperature for 24 hours. The

reaction mixture was transferred to a separatory funnel using hexane and washed with $NaHCO_3$, water, and brine. The extract was dried over $MgSO_4$, filtered, and the solvent removed under reduced pressure. This yielded 179 mg of product for which a proton NMR showed a 3:2 ratio of starting material to dimer **11**.

Reaction of Dihexylsilane with $Hg(OAc)_2$ in THF. Mercuric acetate (323 mg, 1.01 mmol) was added to a solution of dihexylsilane (202 mg, 1.01 mmol) in 2 mL of THF at room temperature. After 2 hours, GC/MS analysis showed a mixture of mono and dioxidation products. Another 324 mg of $Hg(OAc)_2$ was added and the reaction was stirred for an additional 72 hours. Analysis by GC/MS showed the reaction to be complete, diacetoxydihexylsilane being the sole product. After workup with methanol and pyridine and washing with $NaHCO_3$, water, and brine, the organic extract was dried over $MgSO_4$ and the solvent removed under reduced pressure. This yielded dihexyldimethoxysilane and acetoxydihexylmethoxysilane.

Diacetoxydihexylsilane. Mass spectrum *m/e* 257 (P^+-OAc), 231 (P^+-hexyl), 189, 171, 147, 129, 63.

Dihexyldimethoxysilane. ^1H NMR ($CDCl_3$) δ 3.50 (6H, s, OCH_3), 1.4-1.1 (16H, m, CH_2), 0.88 (6H, bt, 5Hz, CH_3), 0.60 (4H, bt, 7Hz, $SiCH_2$); mass spectrum *m/e* 175 (P^+-hexyl), 143, 91, 61.

Acetoxydihexylmethoxysilane. Mass Spectrum *m/e* 203 (P^+-hexyl), 171, 161, 143, 129, 77.

Reaction of Dihexylsilane with $Hg(OAc)_2$ in THF in the Presence of Methanol and Pyridine. Mercuric acetate (332 mg, 1.04

mmol) was added to a solution of dihexylsilane (208 mg, 1.04 mmol), methanol (100 μL, 2.47 mmol), and pyridine (200 μL, 2.47 mmol) in 2 mL of THF at room temperature. After 5 hours, GC/MS analysis showed a mixture of products; starting material, dihexylmethoxy and dihexyldimethoxysilane, as well as acetoxydihexylmethoxysilane. The reaction mixture was transferred to a separatory funnel using hexane and washed with $NaHCO_3$, water, and brine. The extract was dried over $MgSO_4$, filtered, and the solvent removed under reduced pressure, yielding 214 mg of product of the same composition previous to workup.

Dihexylmethoxysilane (9). ^{1}H NMR ($CDCl_3$) δ 4.41 (1H, quin, 2.4Hz, Si*H*) 3.46 (3H, s, OCH_3), 1.5-1.1 (16H, m, CH_2), 0.88 (6H, bt, 5Hz, CH_3), 0.70-0.50 (4H, m, SiCH_2); mass spectrum *m/e* 230 (P^+), 229 (P^+-H), 228, 145 (P^+-hexyl), 113, 103, 89, 75, 61.

Reaction of Dihexylsilane with Iodine. Iodine (142 mg, 1.12 mmol) was added to a solution of dihexylsilane (218 mg, 1.09 mmol) in 2 mL of CCl_4 at 0°C. The resulting solution was warmed to room temperature and stirred for 24 hours. ^{1}H NMR analysis gave a 70:30 ratio of starting material to dimer **11**.

Reaction of Dihexylsilane with Bromine. Bromine (55 μL, 1.07 mmol) was added to a solution of dihexylsilane (214 mg, 1.07 mmol) in 2 mL of CCl_4 at 0°C. After 30 minutes, 38 μL (1.1eq) of methanol and 93 μL (1.1eq) of pyridine were added and allowed to react for one hour. The reaction mixture was transferred to a separatory funnel using 30 mL of hexane and washed with 1 M $NaHSO_4$, water, and brine. The extract was dried over $MgSO_4$, filtered, and the solvent removed under reduced pressure. GC/MS analysis gave

evidence for the formation of methoxysilane **9**, dimethoxydihexylsilane, and dimer **11**.

Bromodihexylsilane. Mass spectrum *m/e* 280 (P^++2), 278 (P^+), 195 (P^++2-hexyl), 193 (P^+-hexyl), 153, 151, 139, 137, 125, 123, 111, 109, 85, 83.

Dibromodihexylsilane. Mass spectrum *m/e* 275 (P^++4-hexyl), 273 (P^++2-hexyl), 271 (P^+-hexyl), 233, 231, 229, 219, 217, 215, 205, 203, 201, 191, 189, 187.

Reaction of Dihexylsilane with HBr. Gaseous HBr was bubbled into a solution of dihexylsilane (207 mg, 1.03 mmol) in 5 mL of CCl_4 for one hour at 0°C. After stirring for 18 hours, GC/MS analysis detected no reaction. Consequently, HBr was bubbled into the solution for another hour at room temperature, and again, GC/MS analysis showed that no reaction had occured.

Reaction of Dihexylsilane with NCS. N-chlorosuccinimide (140 mg, 1.05 mmol) was added to a solution of dihexylsilane (208 mg, 1.04 mmol) in 2 mL of CCl_4 at 0°C. Analysis by GC/MS showed that after 24 hours at room temperature and four hours at reflux, only 23% conversion had occured. After workup with methanol and pyridine, a mixture of starting material, methoxysilane **9**, dimethoxydihexylsilane, and dimer **11** was isolated.

Chlorodihexysilane. Mass Spectrum *m/e* 234 (P^+), 151 (P^++2-hexyl), 149 (P^+-hexyl), 109, 107, 95, 93, 81, 79.

Reaction of Dihexylsilane with NBS. N-bromosuccinimide (184 mg, 1.03 mmol) was added to a solution of dihexylsilane (206 mg, 1.03 mmol) in 2 mL of CCl_4 at 0°C. The resulting solution was stirred at 0°C for three hours and then at room temperature for one hour. A yellow precipitate was observed

after one hour of reaction. Analysis by GC/MS showed over 92% mono-bromination with the remaining 8% being starting material and chloro-dihexylsilane. The reaction was quenched with excess methanol and pyridine. The reaction mixture was transferred to a separatory funnel using hexane, washed with 1M $NaHSO_4$, water, and brine, and then dried over $MgSO_4$. After filtration, the solvent was removed from the products under reduced pressure. This gave 215 mg of crude product, which by ^1H NMR analysis, was a mixture of starting material, methoxysilane **9**, dihexyldimethoxysilane, and dimer **11**.

Reaction of R-(+)-Naphthylphenylmethylsilane with NBS. A procedure was followed similar to that given in a previous paper by Sommer[15]. R-(+)-naphthylphenylmethylsilane was found to have a rotation of +33.6° (1.0 g in pentane) which is comparable to a value of +33.8° given by Sommer. N-bromosuccinimide (182 mg, 1.02 mmol) was added to a solution of the chiral silane (253 mg, 1.02 mmol) in 2.5 mL of CCl_4 at room temperature. After one hour a precipitate was observed. After three hours, GC/MS analysis showed an 85% conversion to the desired brominated product, and the remaining 15% being intractable products. Excess methanol and pyridine were added and allowed to react for one hour. The reaction mixture was transferred to a separatory funnel using hexane and washed with 1 M $NaHSO_4$, water, and brine. The extract was dried over $MgSO_4$, filtered, and the solvent removed under reduced pressure. The product, naphthylphenylmethylmethoxysilane, weighed 247 mg, an 87% yield. An optical rotation of the product was determined to be +8.0° (1.0 g in pentane), compared to +16.8° given by Sommer. This lower value was in part due to mechanical losses and perhaps some racemization. It should be noticed however, that the reaction proceeded

with at least 48% retention.

Naphthylphenylmethylbromosilane. Mass spectrum *m/e* 328 (P^++2), 326 (P^+), 313 (P^++2-CH_3), 311 (P^+-CH_3), 247, 231, 204, 202, 169, 167, 123, 109, 91.

Naphthylphenylmethylmethoxysilane. $[\alpha]_D$ +8.0° (1.0 g in pentane); ^{1}H NMR ($CDCl_3$) δ 8.2-7.3 (12H, m, aromatic), 3.57 (3H, s, OCH_3), 0.77 (3H, s, $SiCH_3$); mass spectrum *m/e* 278 (P^+), 263 (P^+-CH_3), 233, 202, 155, 141, 121, 105, 59.

Part II : Synthesis of N-bromo-(2S,3S)-2,3-di-p-toluoylsuccinimide.

Reaction of (2S,3S)-2,3-Di-p-toluoyltartaric Acid (12b) with Acetic Anhydride. A solution of the tartaric acid (10.0 g, 25.9 mmol) in 100 mL of acetic anhydride was stirred at room temperature for 24 hours. A white precipitate began forming after one hour. The reaction was cooled to 0°C and the white precipitate was isolated by vacuum filtration. The solvent was removed under reduced pressure yielding 8.337 g of crude (2S,3S)-2,3-di-p-toluoylsuccinic anhydride (**13b**), an 87% yield. The product was further purified by recrystallization from hot toluene. An analytical sample was obtained by Kugelrohr distillation at 100 °C with a P_2O_5 trap. The crude anhydride was used in the next reaction. Data for **13b** : d 196 °C; ^{1}H NMR ($CDCl_3$) δ 7.97 (4H, d, 8.1Hz, *H*Ar), 7.29 (4H, d, 8.1Hz, *H*Ar), 5.94 (2H, s), 2.44 (6H, s, CH_3); ^{13}C NMR ($CDCl_3$) δ 165.6 (*C*=O), 163.2 (*C*=O), 145.8 (*C*Ar), 130.4 (*C*Ar), 129.6 (*C*Ar), 124.5 (*C*Ar), 72.9 (*C*-O), 21.9 (CH_3); IR ($CHCl_3$) 1883 (w), 1807, 1724,

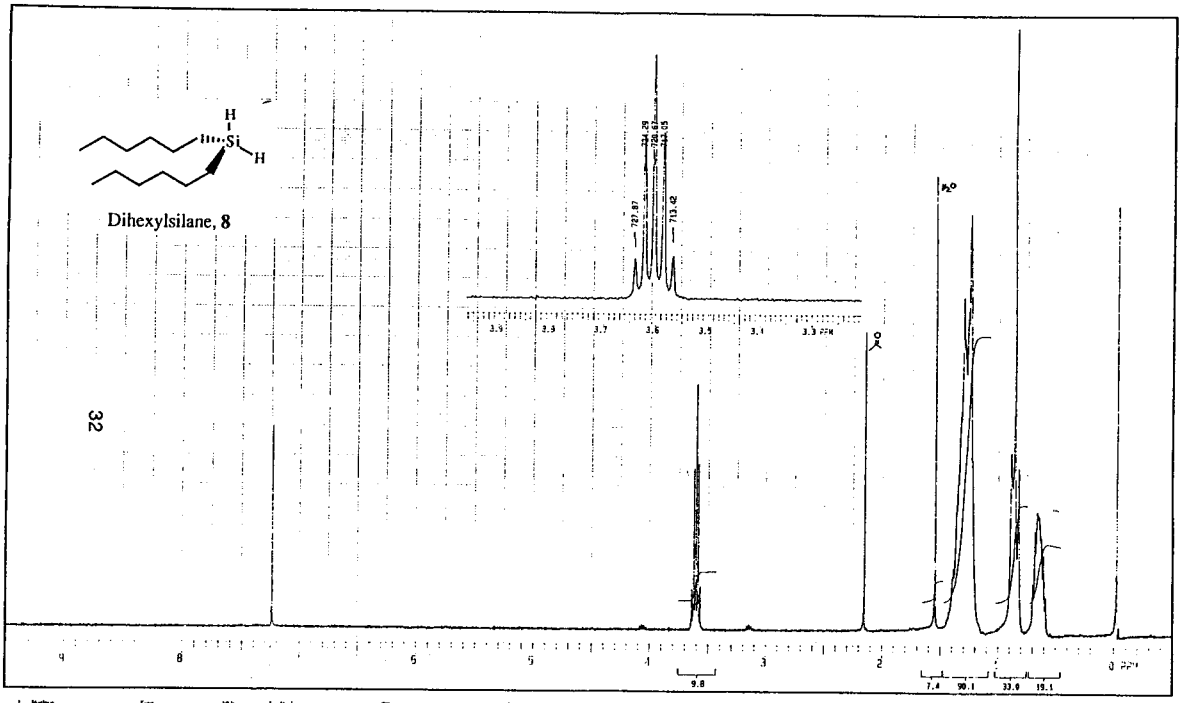
1612, 1269 cm^{-1}.

Reaction of (2S,3S)-2,3-Di-p-toluoylsuccinic Anhydride (13b) with Ammonia. A solution of the crude succinic anhydride (7.00 g, 19.0 mmol) was dissolved in 70 mL each of THF and benzene with the aid of heat. Gaseous ammonia was bubbled into the solution for 35 minutes at room temperature; a white precipitate formed after 15 minutes. After addition of NH_3, the flask was cooled to 0 °C and the precipitate was isolated by vacuum filtration. The excess solvent was removed under reduced pressure giving 8.107 g of crude 3-carbamoyl-(2S,3S)-2,3-di-p-toluoylpropanoic acid (**14b**), essentially a 100% yield. The crude product was used in the following reaction. This product was further purified by recrystallization from hot n-butanol. An analytical sample was obtained by Kugelrohr distillation at 50 °C with a P_2O_5 trap. Data for **14b** : d 163 °C; ^1H NMR (DMSO-d_6) δ 7.92 (4H, d, 8.0Hz, *H*Ar), 7.75 (1H, bs), 7.36 (4H, d, 6.2Hz, *H*Ar), 7.32 (2H, bs), 5.68 (1H, d, 2.4Hz), 5.60 (1H, d, 2.4Hz), 2.40 (6H, s, C*H*$_3$); ^{13}C NMR (DMSO-d_6) δ 168.4 (*C*=O), 167.6 (*C*=O), 165.3 (*C*=O)*, 165.0 (*C*=O), 143.8 (*C*Ar), 143.6 (*C*Ar), 129.7 (*C*Ar), 129.5 (*C*Ar), 129.2 (*C*Ar), 126.8 (*C*Ar), 122.5 (*C*Ar), 73.8 (*C*-O), 73.5 (*C*-O), 21.3 (*C*H_3); IR (KBr) 3242 (broad), 1713, 1703, 1686 cm^{-1}. *Tentative assignment.

Reaction of 3-Carbamoyl-(2S,3S)-2,3-di-p-toluylpropanoic Acid (14b) with $SOCl_2$. Crude acid-amide (7.00 g, 18.2 mmol) was dissolved in 70 mL of DMF with the addition of heat. The solution was cooled to 0°C, $SOCl_2$ (2 mL, 27.3 mmol) was added, and the solution was warmed to room temperature. After five hours, a white precipitate, not the product, was removed by filtration. The reaction mixture was distilled using a Kugelrohr

apparatus at 60-65°C. The resulting yellow oil was recrystallized twice from hot toluene to yield 4.724 g of (2S,3S)-2,3-di-p-toluoylsuccinimide (**15b**), a 70.8% yield. This was further purified with multiple recrystallizations from hot toluene and filtration with decolorizing charcoal. An analytical sample was obtained by Kugelrohr distillation at 50 °C with a P_2O_5 trap. Data for **15b** : d 118 °C; ^1H NMR ($CDCl_3$) δ 8.56 (1H, bs, *H*N), 7.97 (4H, d, 8.1Hz, *H*Ar), 7.27 (4H, d, 8.0Hz, *H*Ar), 5.88 (2H, s), 2.43 (6H, s, C*H*$_3$); IR ($CDCl_3$) 1757, 1730, 1610, 1269 cm^{-1}.

Reaction of (2S,3S)-2,3-Di-p-toluoylsuccinimde (15b) with NaH and Br_2. A suspension of succinimide (202 mg, 0.550 mmol) and NaH (27 mg, 0.675 mmol) in 2 mL of ethylene glycol dimethyl ether was stirred for ten minutes at room temperature; gas evolution (H_2) was observed. After cooling to 0°C, Br_2 (28.3 μL, 0.549 mmol) was added in the dark and allowed to stir for one hour. After the hour, the reaction mixture was transferred with 15 mL of H_2O and then extracted with three aliquots of 10 mL of CH_2Cl_2. The organic extract was concentrated to yield a yellow oil, weighing 237 mg, which was a mixture of N-bromo-(2S,3S)-2,3-di-p-toluoylsucinimide and ethylene glycol dimethyl ether. Data for **16b** : ^1H NMR ($CDCl_3$) δ 7.98 (4H, d, 9Hz, *H*Ar), 7.37 (4H, d, 9Hz, *H*Ar), 5.94 (2H,s), 2.42 (6H, s, C*H*$_3$); IR ($CDCl_3$) 1748, 1733 cm^{-1}.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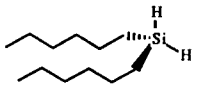
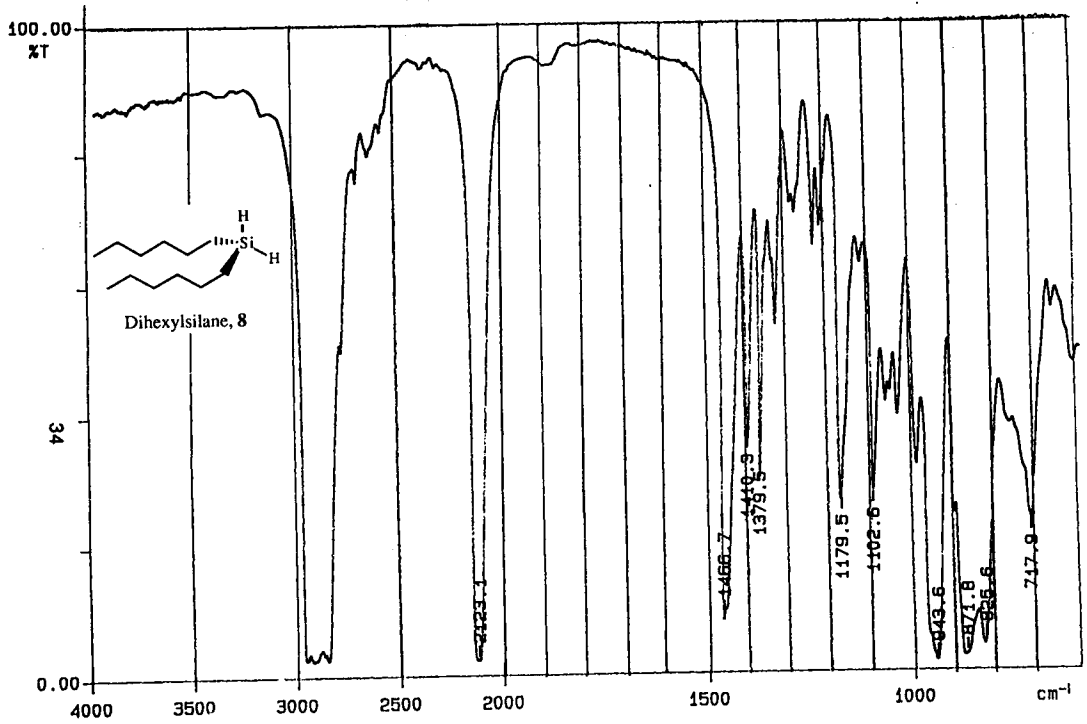


Dihexylsilane, **8**

33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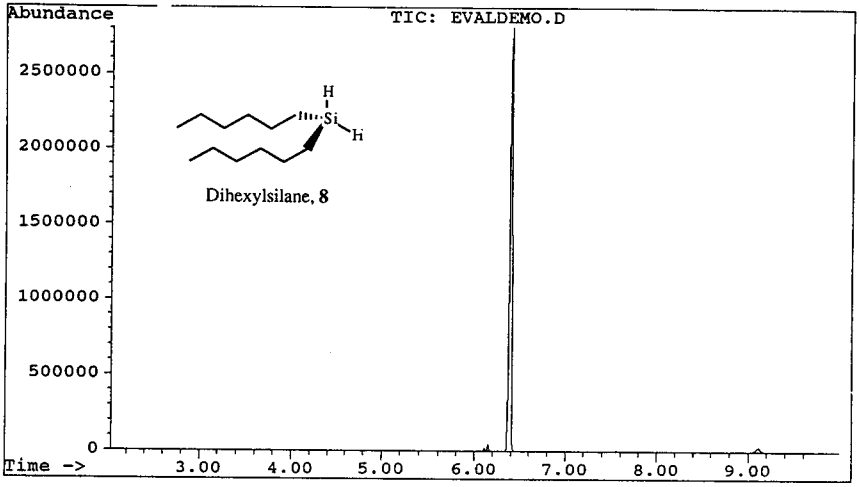
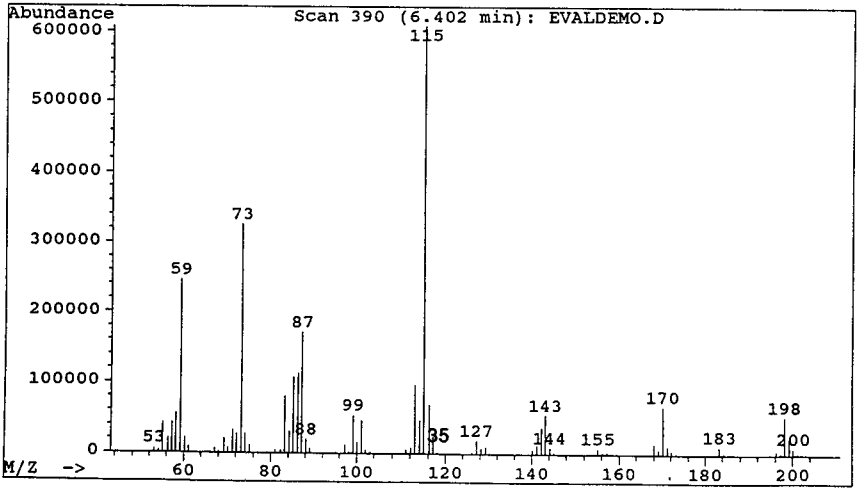
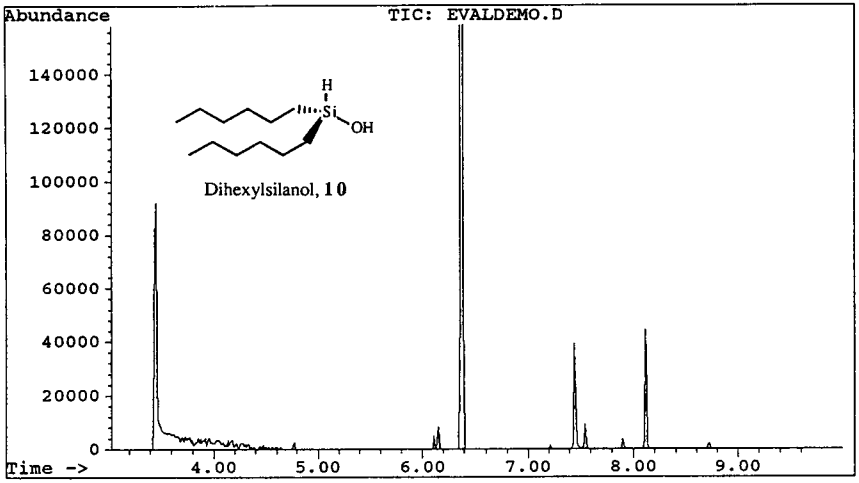
825.6
717.9

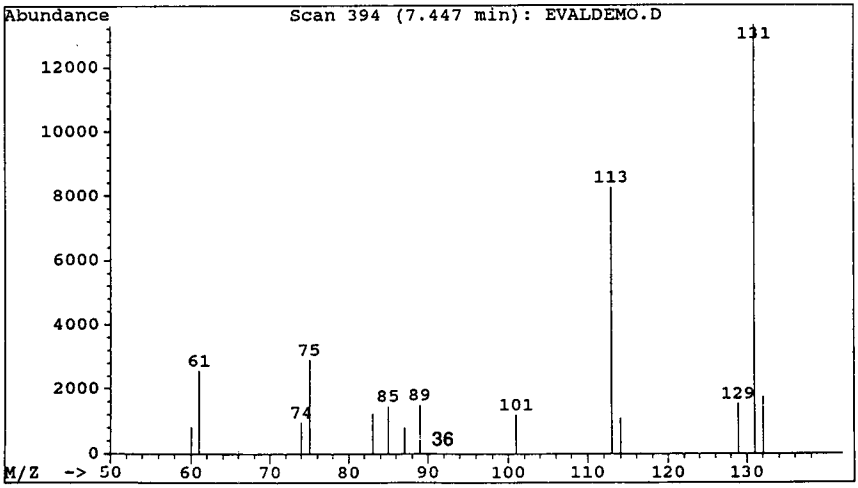


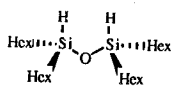
Dihexylsilane, **8**





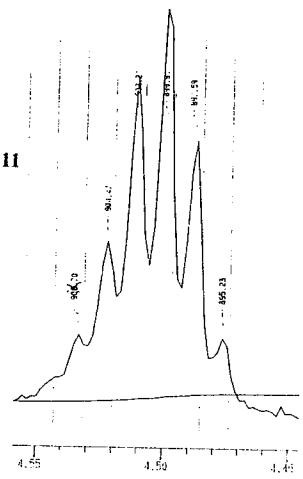
Dihexylsilanol, **10**

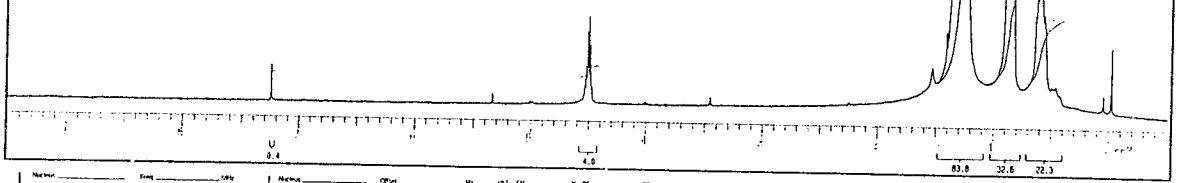


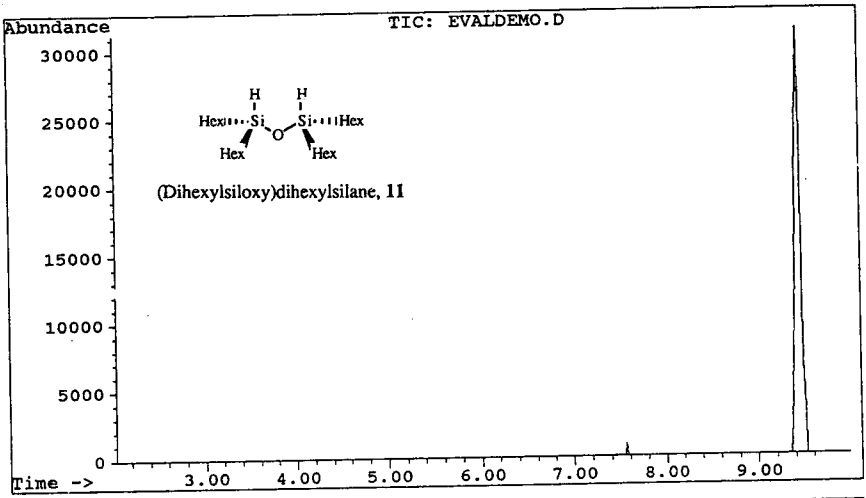


(D exylsiloxy)dihexylsilane, **11**

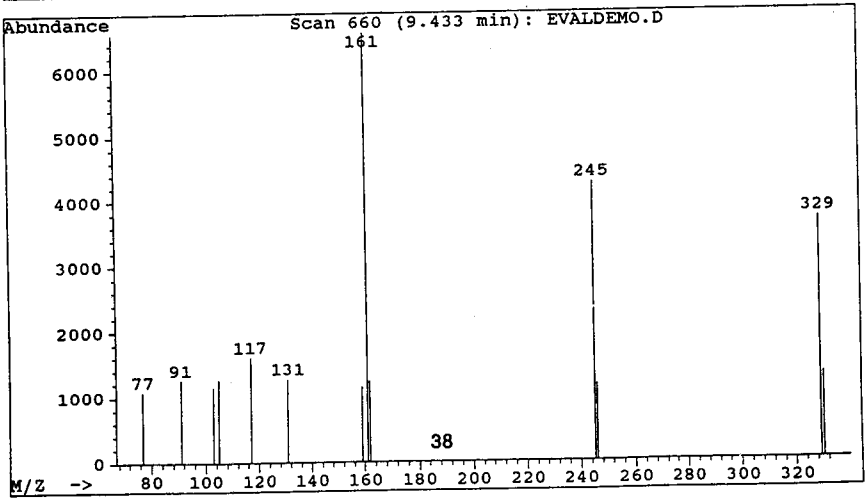
37

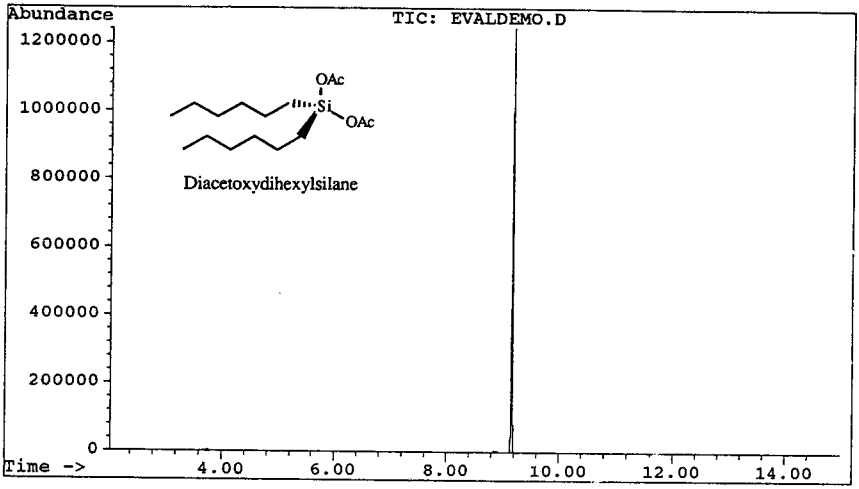


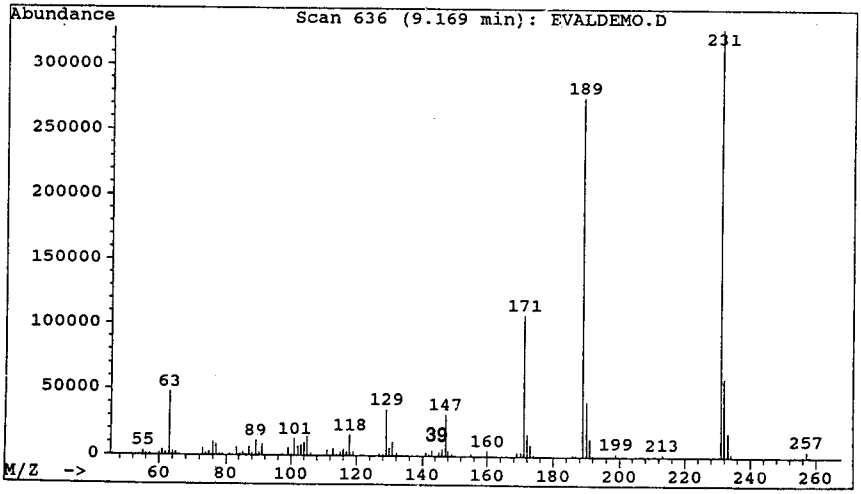




(Dihexylsiloxy)dihexylsilane, **11**

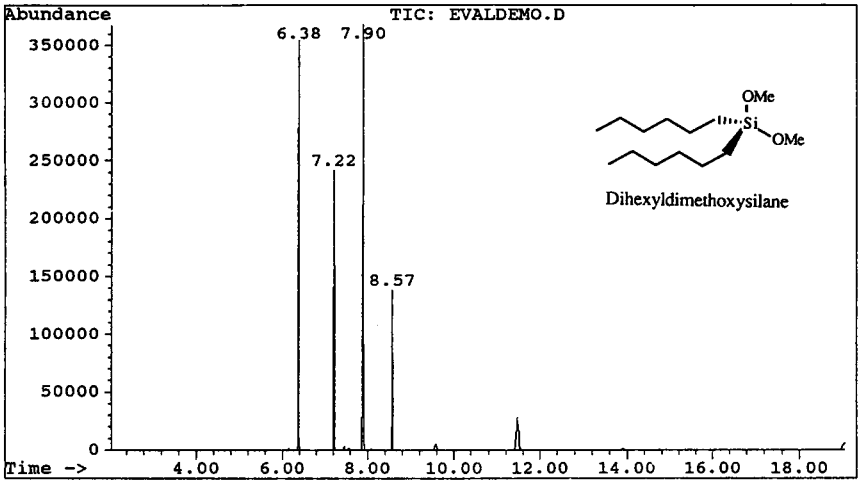


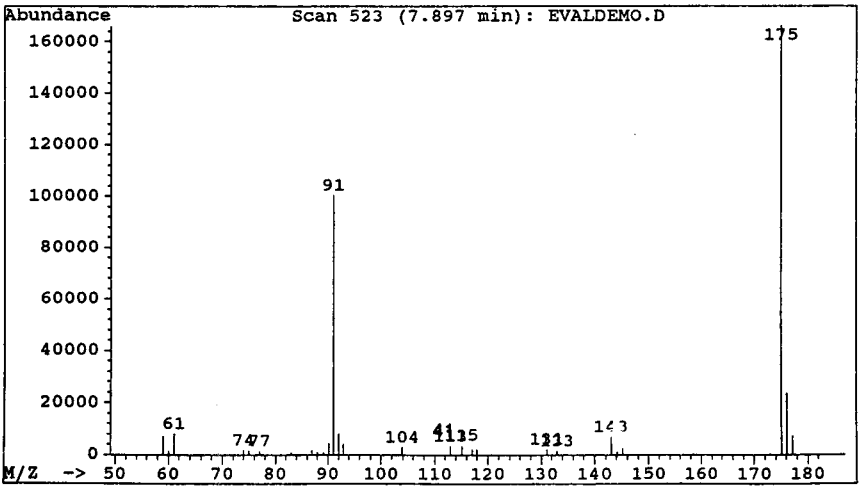

Abundance
TIC: EVALDEMO.D
1200000
1000000
800000
600000
400000
200000
0
OAc
Si
OAc
Diacetoxydihexylsilane
Time ->
4.00
6.00
8.00
10.00
12.00
14.00

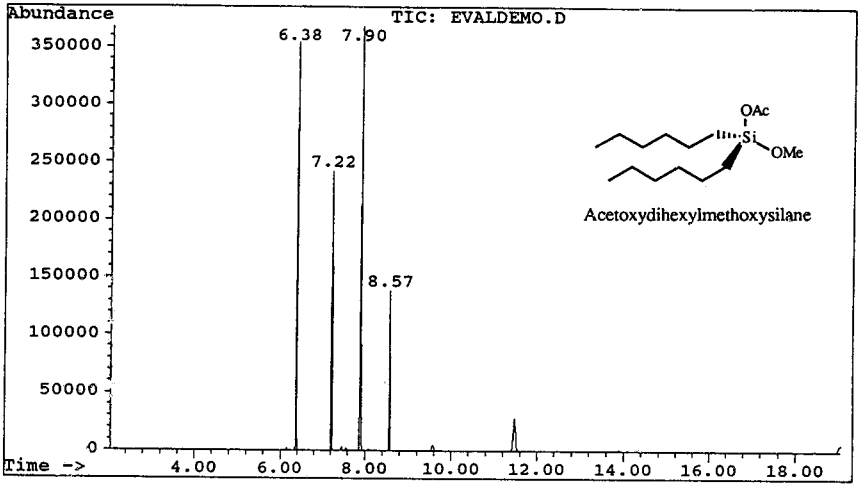

Abundance
Scan 636 (9.169 min): EVALDEMO.D
300000
250000
200000
150000
100000
50000
0
211
189
171
63
129
147
39
55
89
101
118
160
199
213
257
M/Z ->
60
80
100
120
140
160
180
200
220
240
260

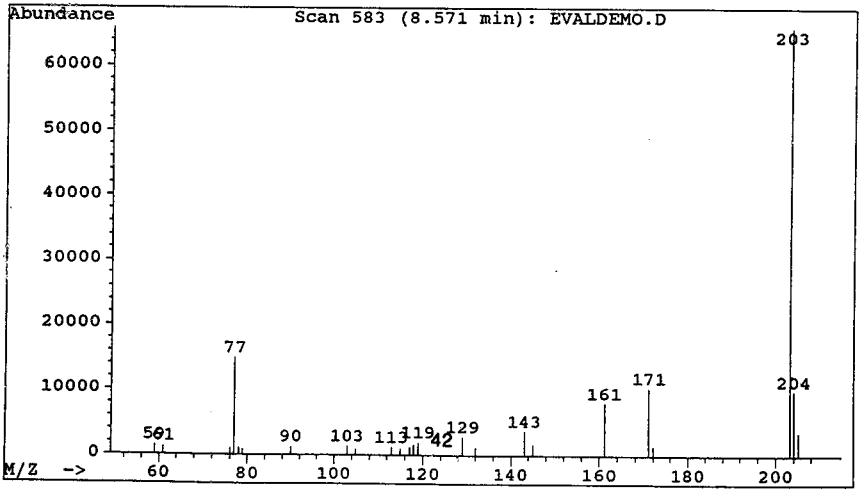
Dihexyldimethoxysilane

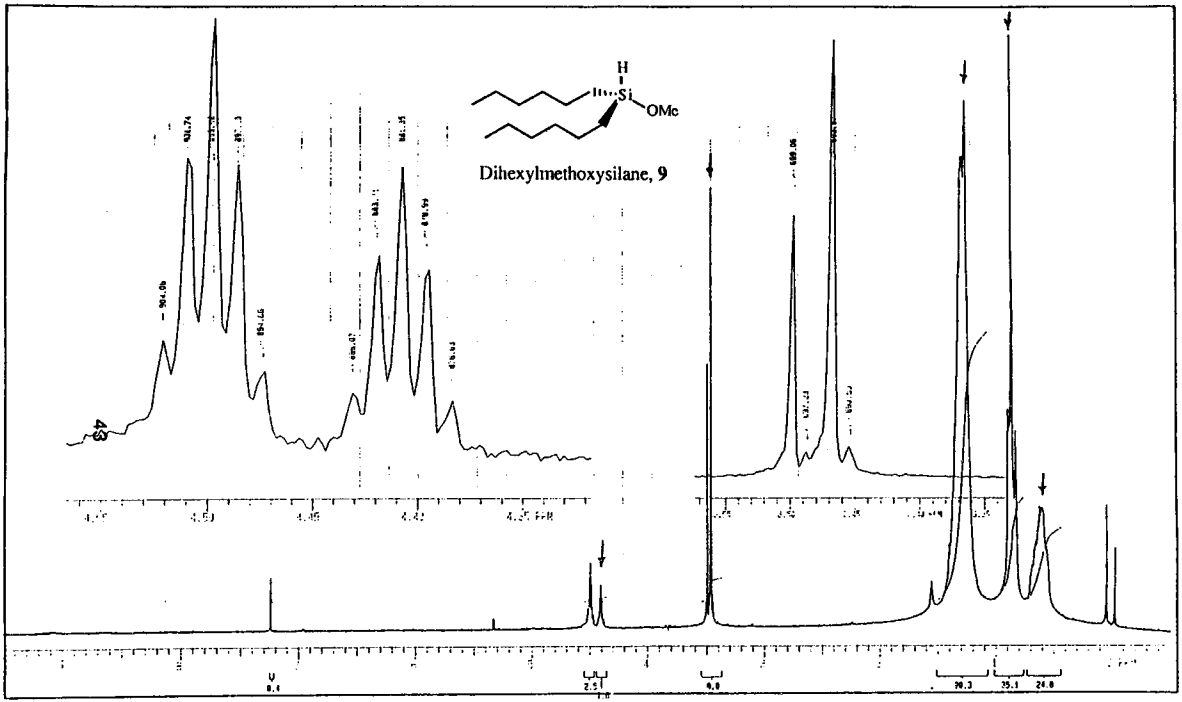
40


Abundance
TIC: EVALDEMO.D
6.38
7.90
7.22
8.57
OMe
Si
OMe
Dihexyldimethoxysilane
Time ->
4.00
6.00
8.00
10.00
12.00
14.00
16.00
18.00


Abundance
Scan 523 (7.897 min): EVALDEMO.D
175
91
61
M/Z ->
50
60
70
80
90
100
110
120
130
140
150
160
170
180


Abundance
TIC: EVALDEMO.D
6.38
7.90
7.22
8.57
OAc
Si
OMe
Acetoxydihexylmethoxysilane
Time ->
4.00
6.00
8.00
10.00
12.00
14.00
16.00
18.00

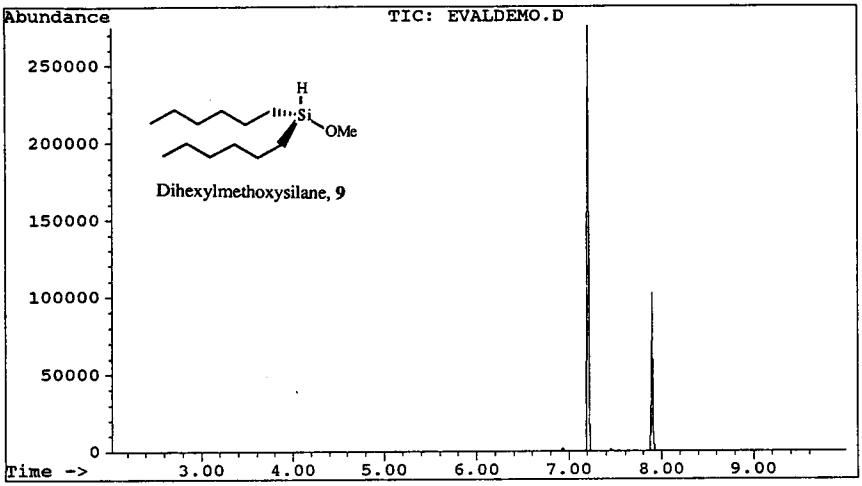

Abundance
Scan 583 (8.571 min): EVALDEMO.D
203
77
171
161
204
143
129
M/Z ->
60
80
100
120
140
160
180
200

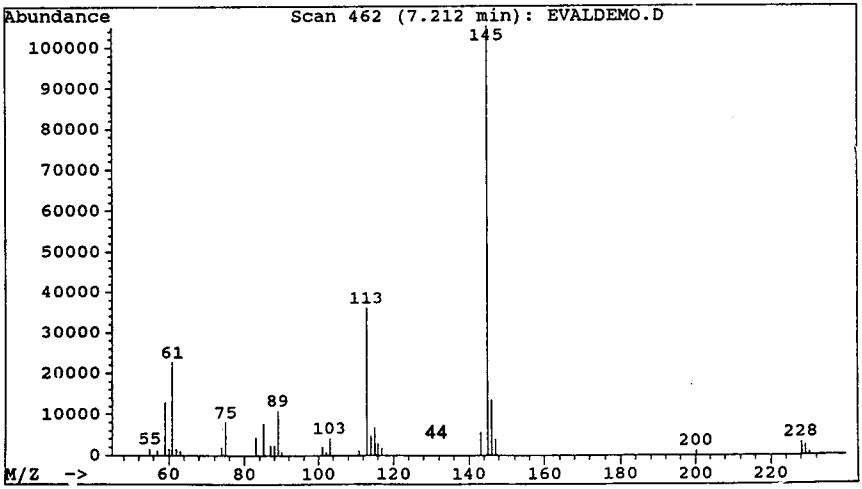


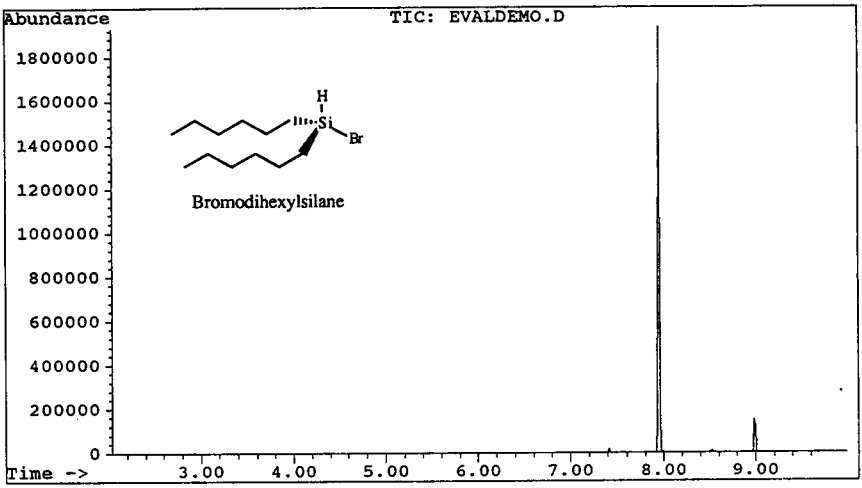
Dihexylmethoxysilane, 9

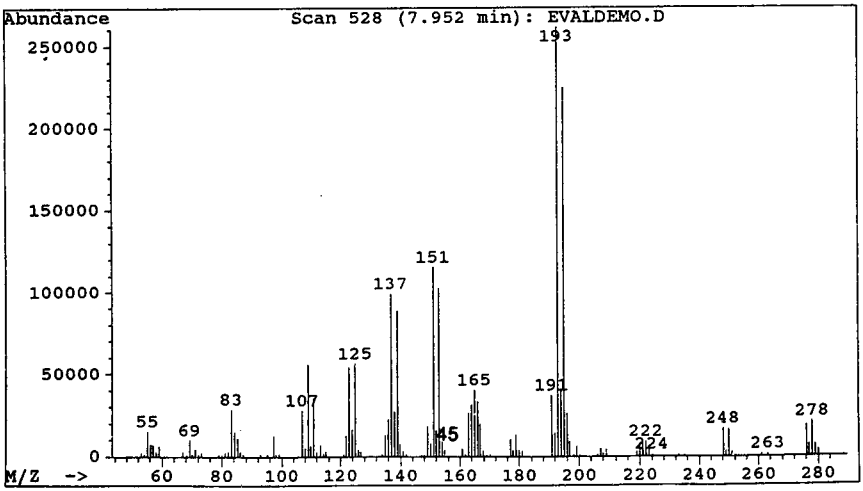
SAMPLE

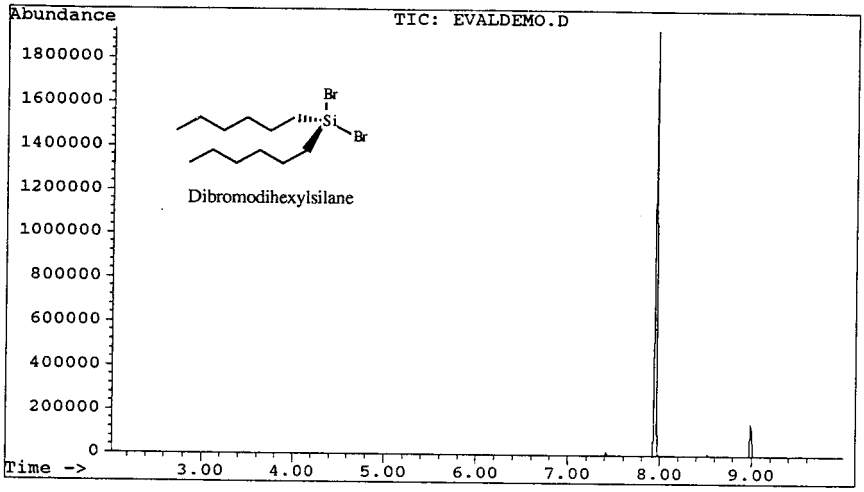
Mixture of methoxysilane, 9 diethoxysilane, and dimer 11


Abundance
TIC: EVALDEMO.D
250000
200000
150000
100000
50000
0
H
Si
OMe
Dihexylmethoxysilane, 9
Time ->
3.00
4.00
5.00
6.00
7.00
8.00
9.00

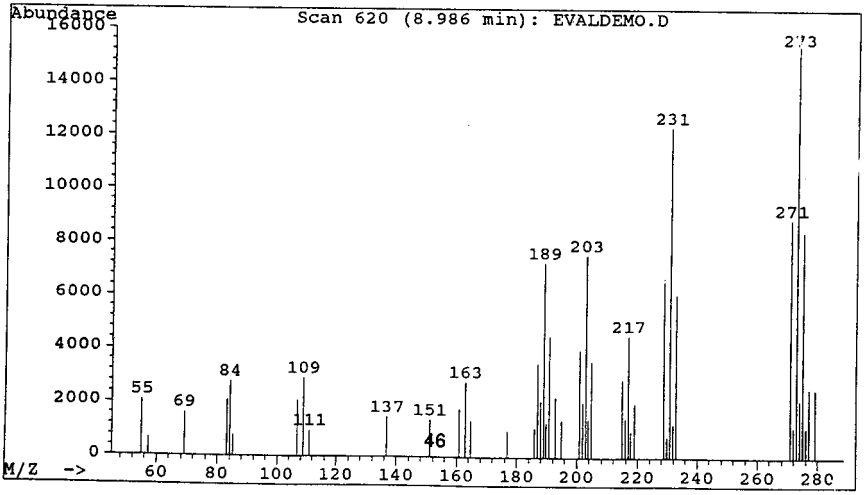

Abundance
Scan 462 (7.212 min): EVALDEMO.D
145
100000
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
113
61
89
75
103
55
44
200
228
M/Z ->
60
80
100
120
140
160
180
200
220

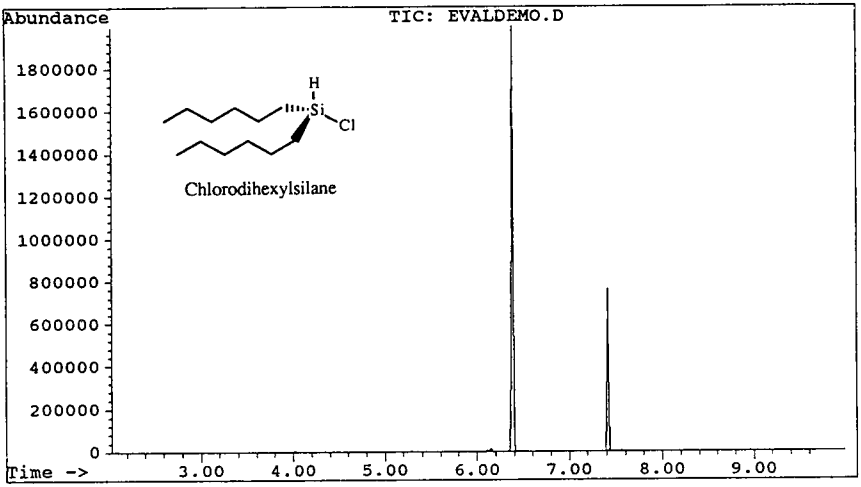

Abundance
TIC: EVALDEMO.D
1800000
1600000
1400000
1200000
1000000
800000
600000
400000
200000
0
Time ->
3.00
4.00
5.00
6.00
7.00
8.00
9.00
H
Si
Br
Bromodihexylsilane

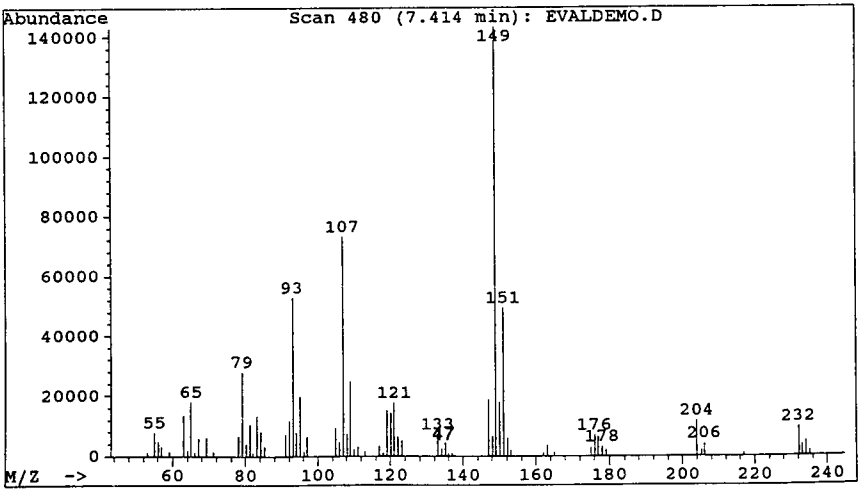

Abundance
Scan 528 (7.952 min): EVALDEMO.D
250000
200000
150000
100000
50000
0
M/Z ->
60
80
100
120
140
160
180
200
220
240
260
280
193
151
137
125
165
191
83
107
55
69
145
222
224
248
263
278

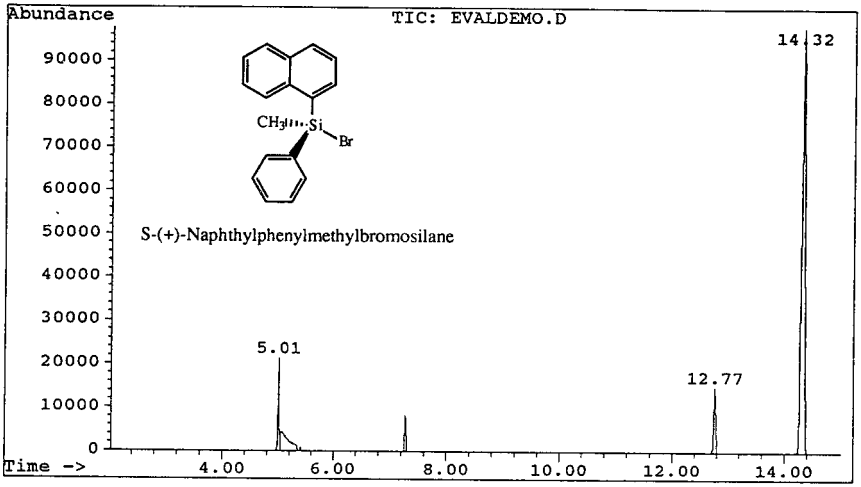


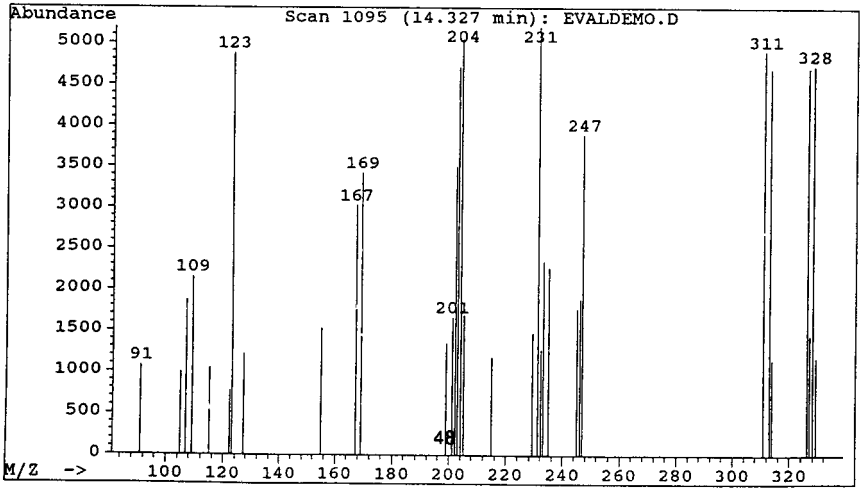
Dibromodihexylsilane

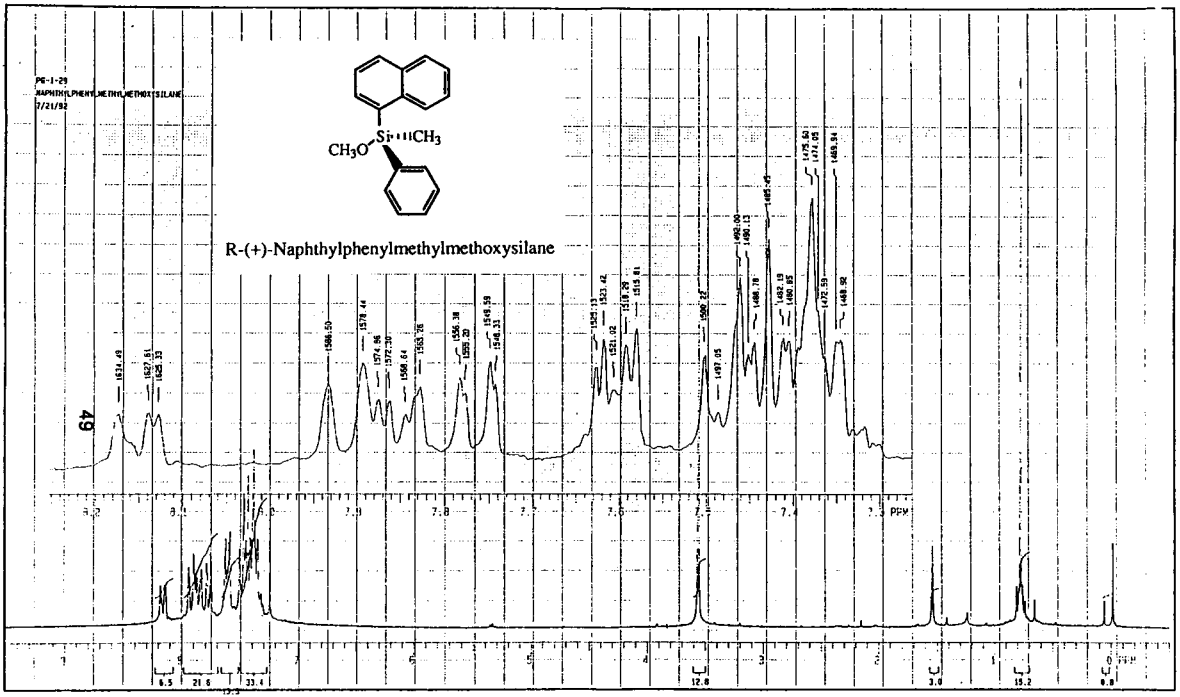


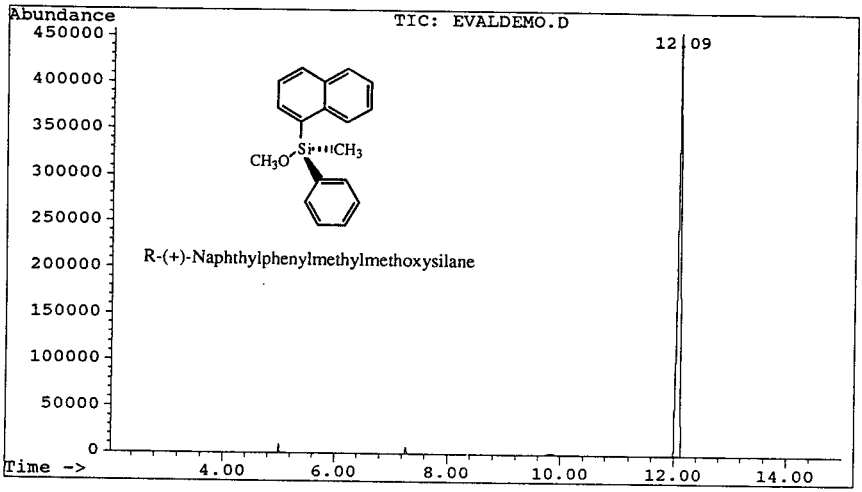

Abundance
TIC: EVALDEMO.D
1800000
1600000
1400000
1200000
1000000
800000
600000
400000
200000
0
H
Si
Cl
Chlorodihexylsilane
Time ->
3.00
4.00
5.00
6.00
7.00
8.00
9.00

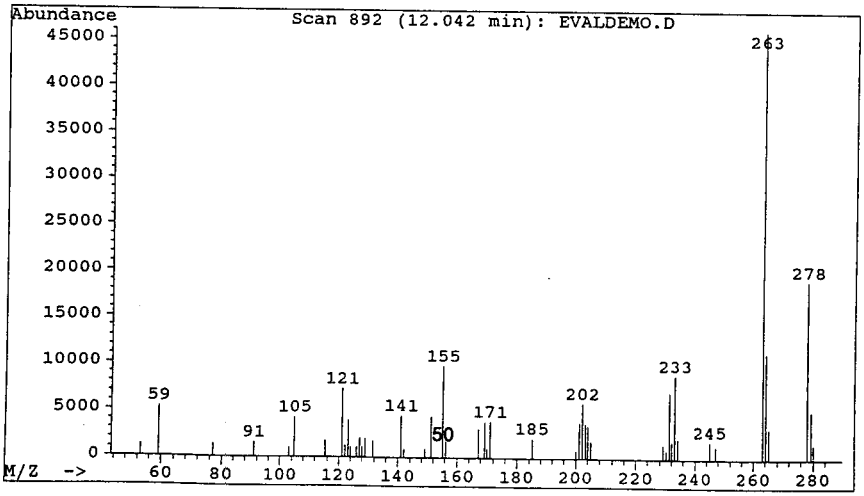

Abundance
Scan 480 (7.414 min): EVALDEMO.D
140000
120000
100000
80000
60000
40000
20000
0
149
107
93
151
79
65
121
55
133
47
176
178
204
206
232
M/Z ->
60
80
100
120
140
160
180
200
220
240

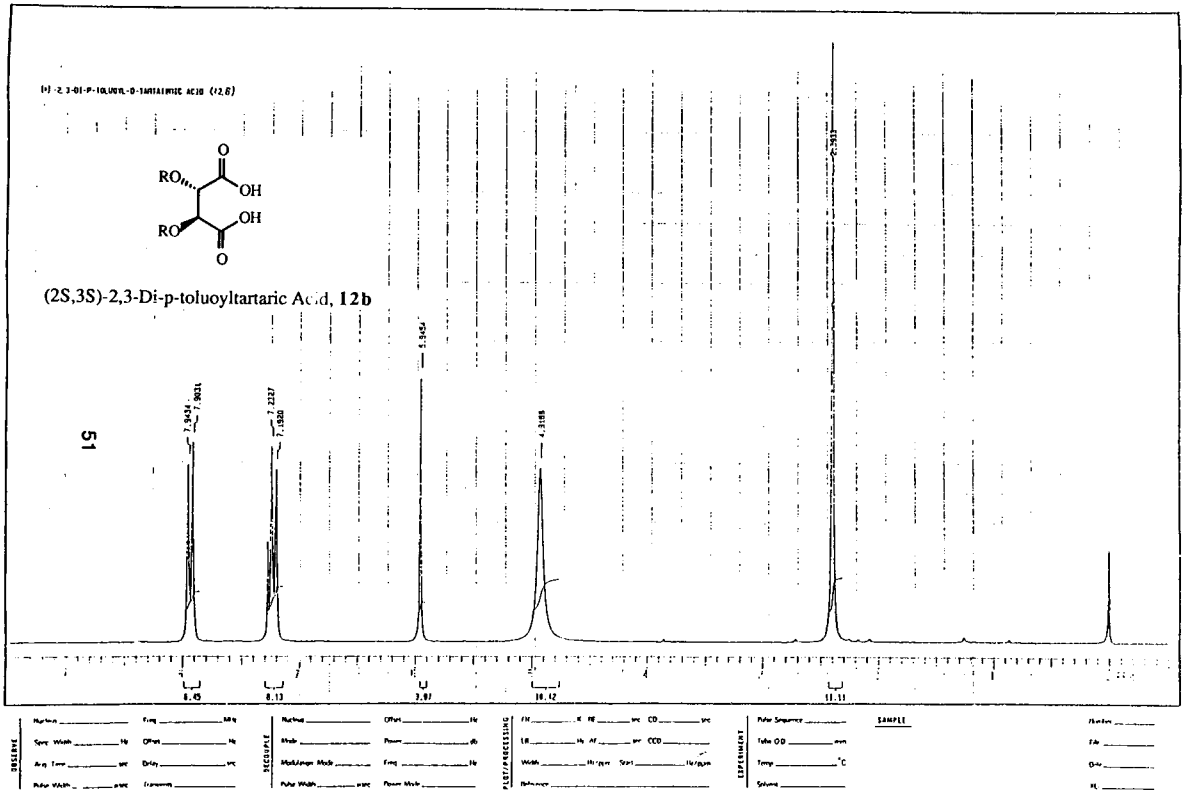

Abundance
TIC: EVALDEMO.D
14.32
5.01
12.77
Time ->
S-(+)-Naphthylphenylmethylbromosilane


Abundance
Scan 1095 (14.327 min): EVALDEMO.D
123
204
231
311
328
247
169
167
109
201
91
M/Z ->
48

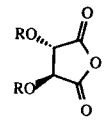

PE-I-29
NAPHTHYLPHENYLMETHYLMETHOXYSILANE
7/21/92
R-(+)-Naphthylphenylmethylmethoxysilane
PPM


Abundance
TIC: EVALDEMO.D
12.09
450000
400000
350000
300000
250000
200000
150000
100000
50000
0
Time ->
4.00
6.00
8.00
10.00
12.00
14.00
CH3O
Si
CH3
R-(+)-Naphthylphenylmethylmethoxysilane


Abundance
Scan 892 (12.042 min): EVALDEMO.D
263
278
155
233
121
59
105
141
202
171
185
91
245
50
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
M/Z ->
60
80
100
120
140
160
180
200
220
240
260
280

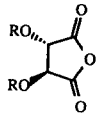

(+) -2,3-DI-P-TOLUOYL-D-TARTARIC ACID (12.6)
RO
O
OH
OH
RO
O
(2S,3S)-2,3-Di-p-toluoyltartaric Acid, 12b
51
7.9434
7.9031
7.2327
7.1920
5.5454
4.3186
2.7511
8.45
8.13
3.87
10.42
11.11
DECOUPLE
FLOAT/PROCESSING
EXPERIMENT
SAMPLE

PS-1-94
(2S, 3S) -2, 3-DI-P-TOLUOYLSUCCINIC ANHYDRIDE (13b)



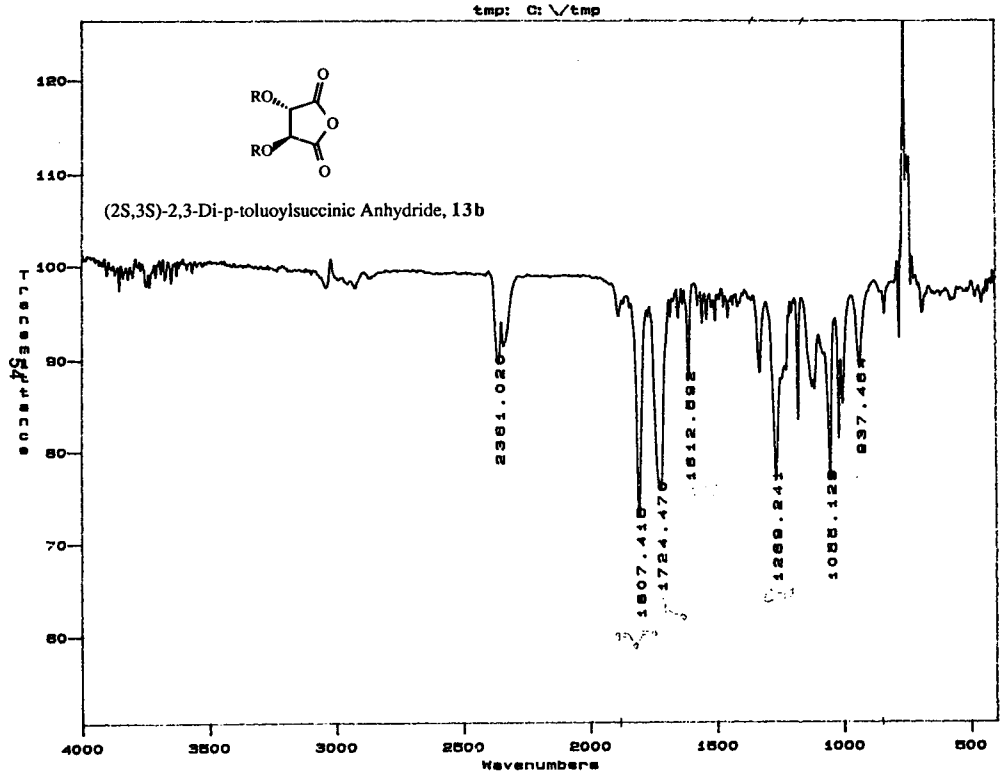
(2S,3S)-2,3-Di-p-toluoylsuccinic Anhydride, **13b**

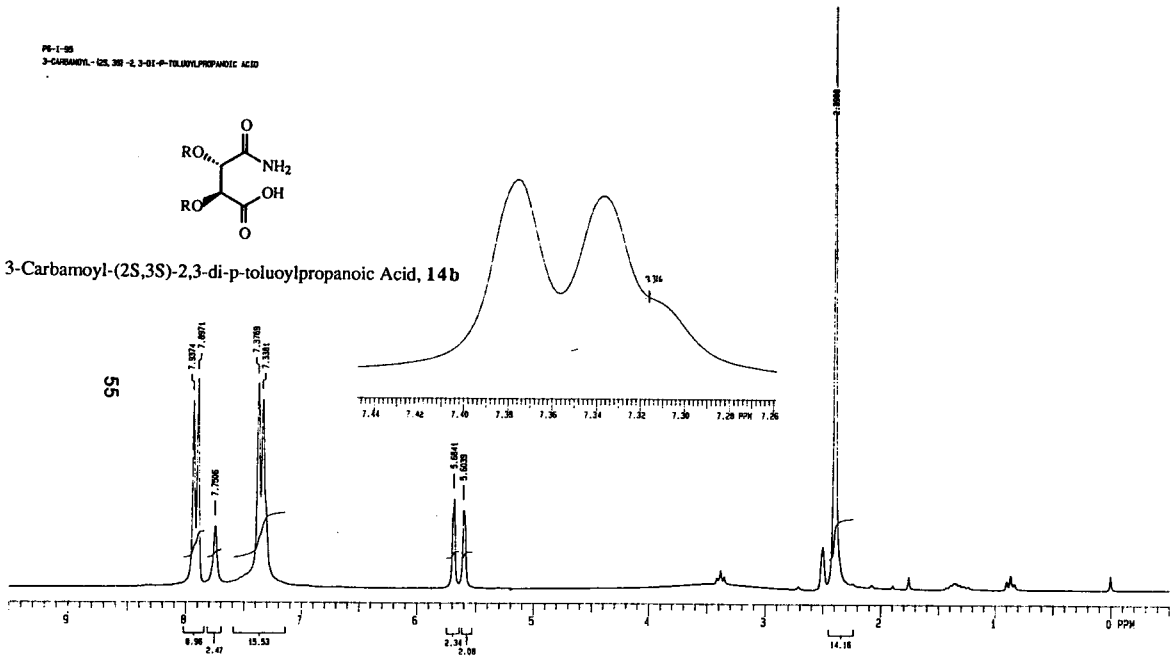
PG-I-84
(2S, 3S)-2, 3-DI-P-TOLUOYLSUCCINIC ANHYDRIDE (13B)

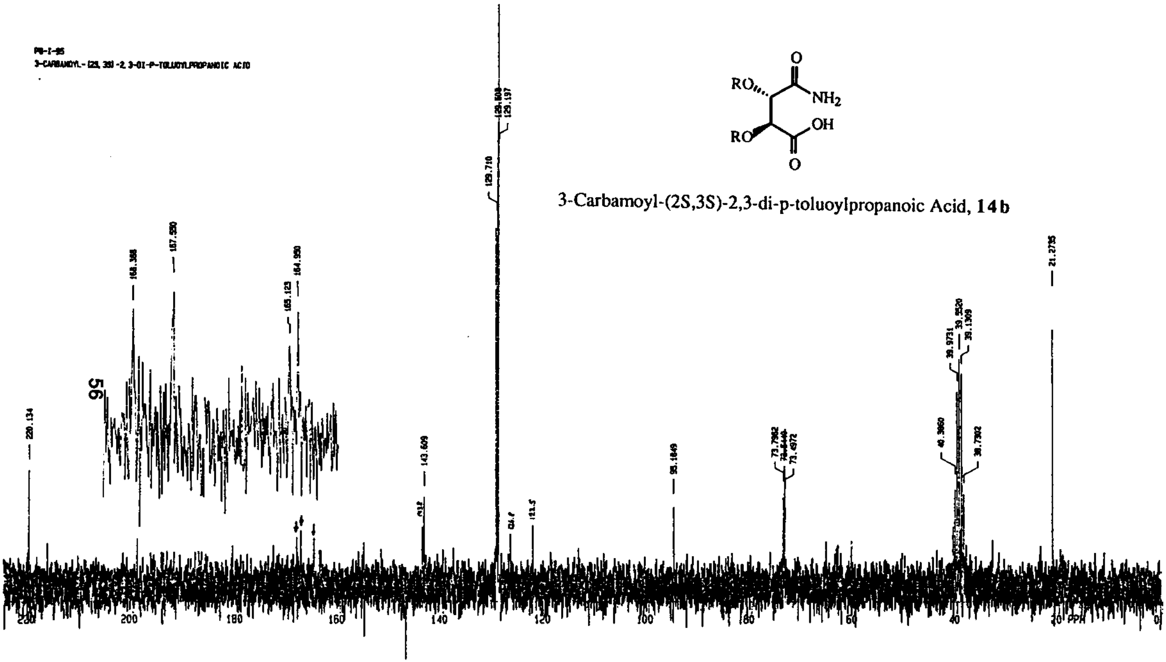


(2S,3S)-2,3-Di-p-toluoylsuccinic Anhydride, **13b**

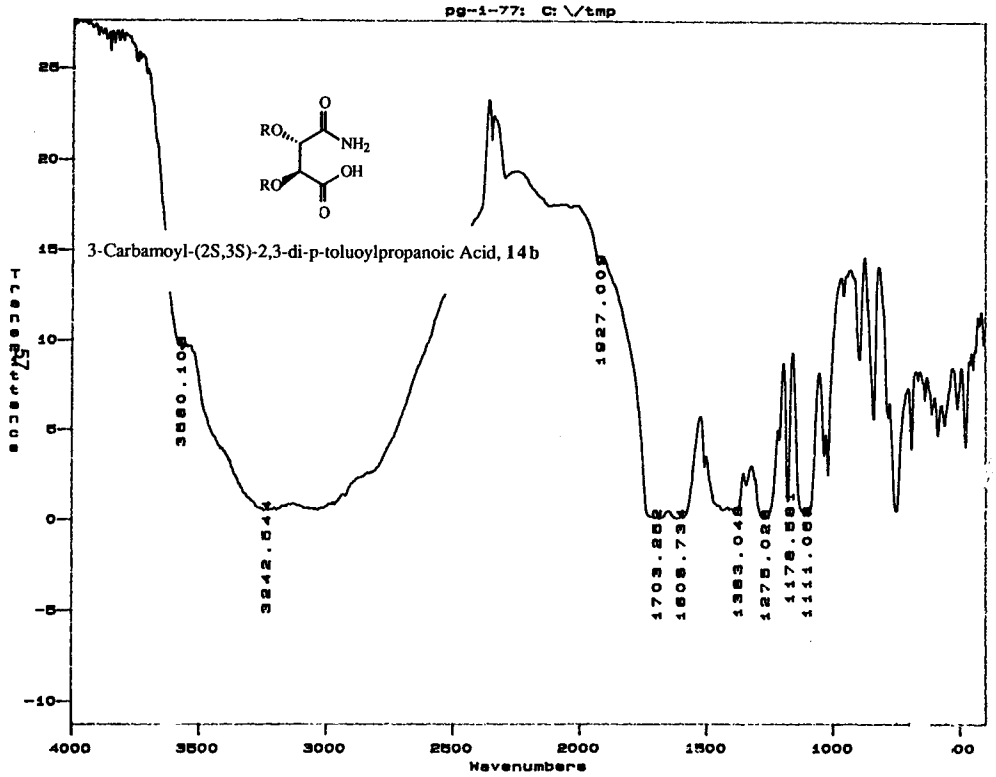
53

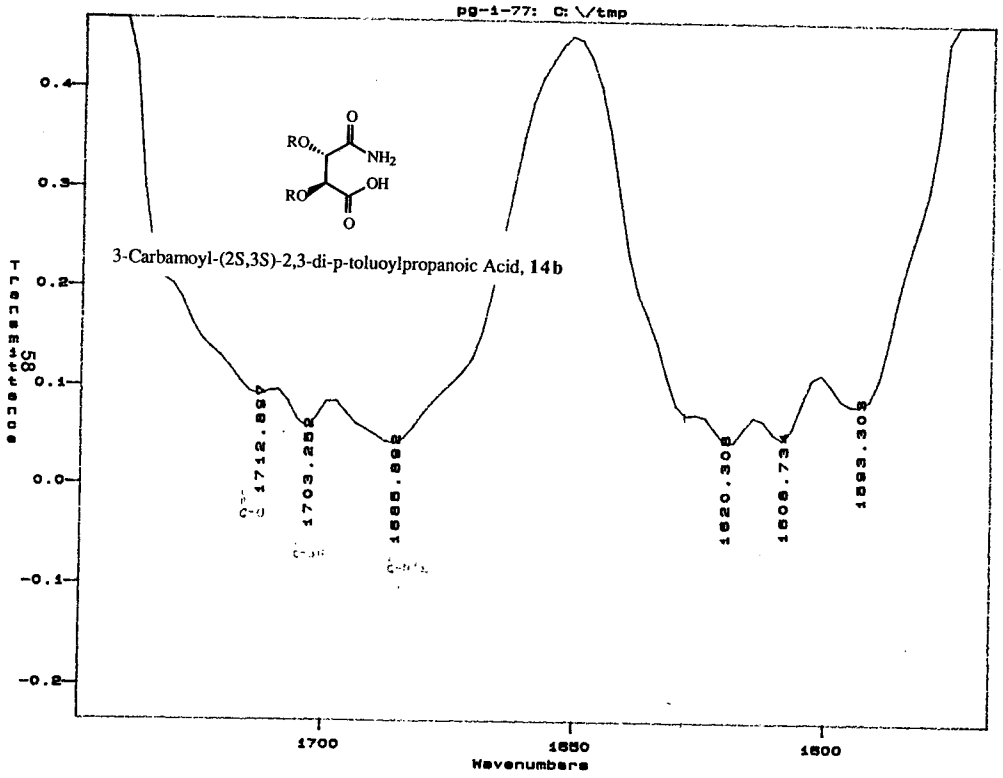

tmp: C:\tmp
RO
RO
O
O
O
O
(2S,3S)-2,3-Di-p-toluoylsuccinic Anhydride, 13b
2361.026
1807.410
1724.476
1612.882
1269.241
1055.128
837.464
Transmittance
120
110
100
90
80
70
60
4000
3500
3000
2500
2000
1500
1000
500
Wavenumbers

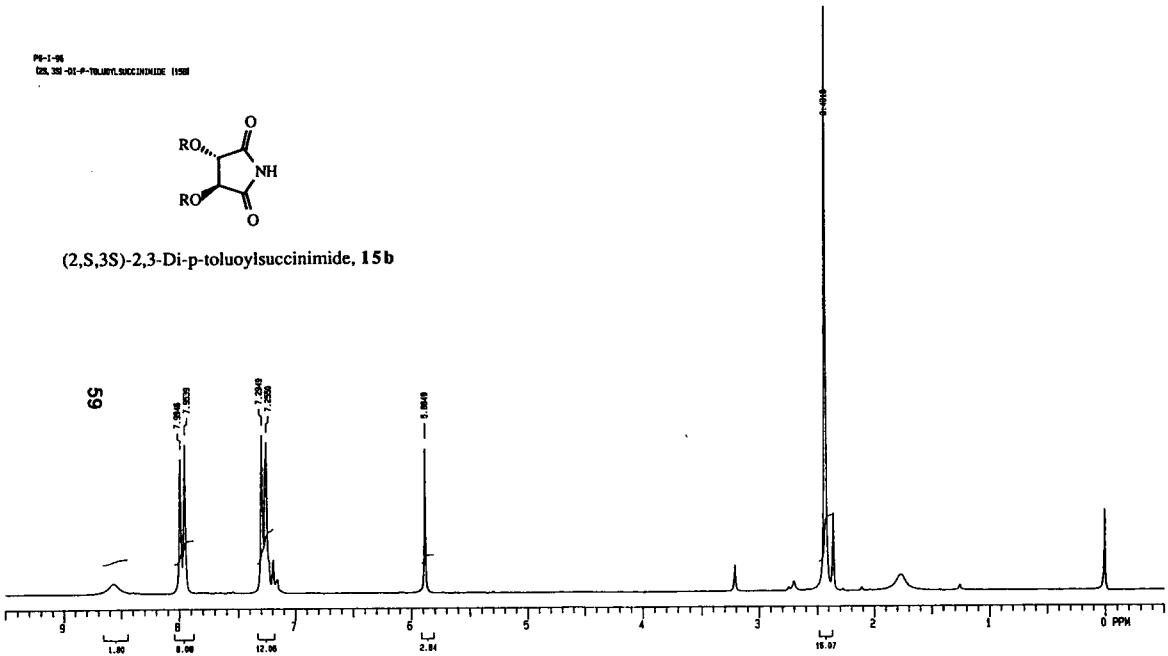

PS-I-55
3-CARBAMOYL-(2S, 3S) -2, 3-DI-P-TOLUOYLPROPANOIC ACID
RO
O
NH2
OH
RO
O
3-Carbamoyl-(2S,3S)-2,3-di-p-toluoylpropanoic Acid, 14b
55
7.8374
7.8971
7.7906
7.3769
7.3381
5.6841
5.6039
2.8888
7.334
7.44 7.42 7.40 7.38 7.36 7.34 7.32 7.30 7.28 PPM 7.26
9 8 7 6 5 4 3 2 1 0 PPM
0.98
2.47
15.53
2.34
2.08
14.18



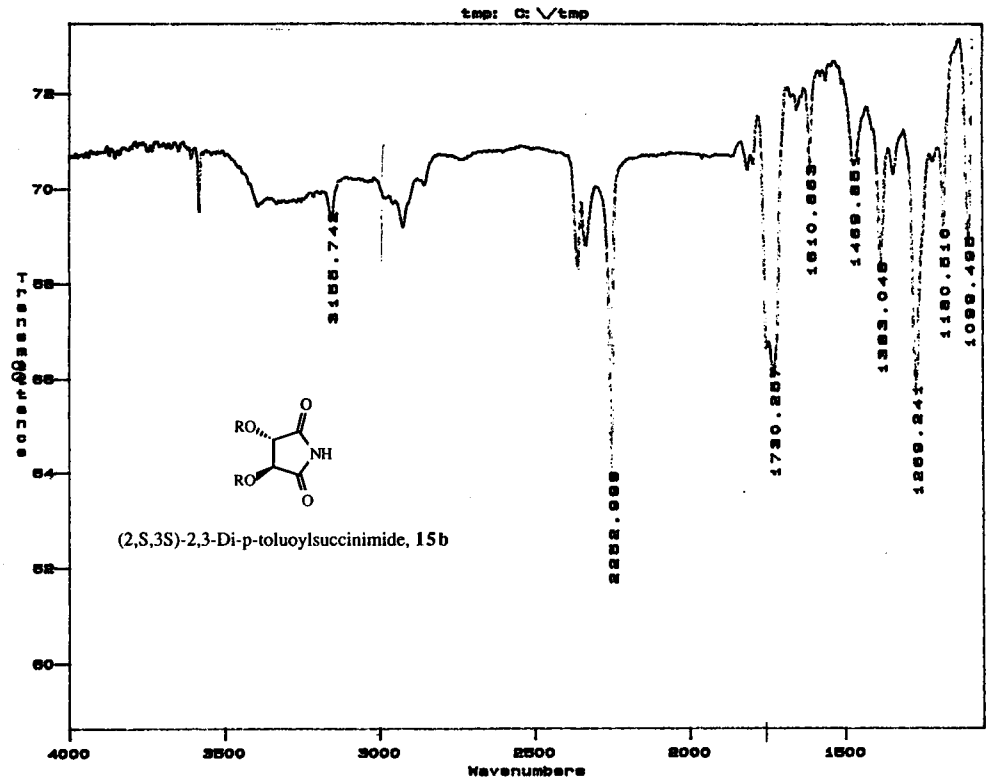
3-Carbamoyl-(2S,3S)-2,3-di-p-toluoylpropanoic Acid, **14b**


pg-1-77: C:\tmp
3-Carbamoyl-(2S,3S)-2,3-di-p-toluoylpropanoic Acid, 14b
RO
NH2
OH
O
3580.10
3242.54
1927.00
1703.25
1608.73
1383.04
1275.02
1178.58
1111.06
Wavenumbers
4000
3500
3000
2500
2000
1500
1000
25
20
15
10
5
0
-5
-10

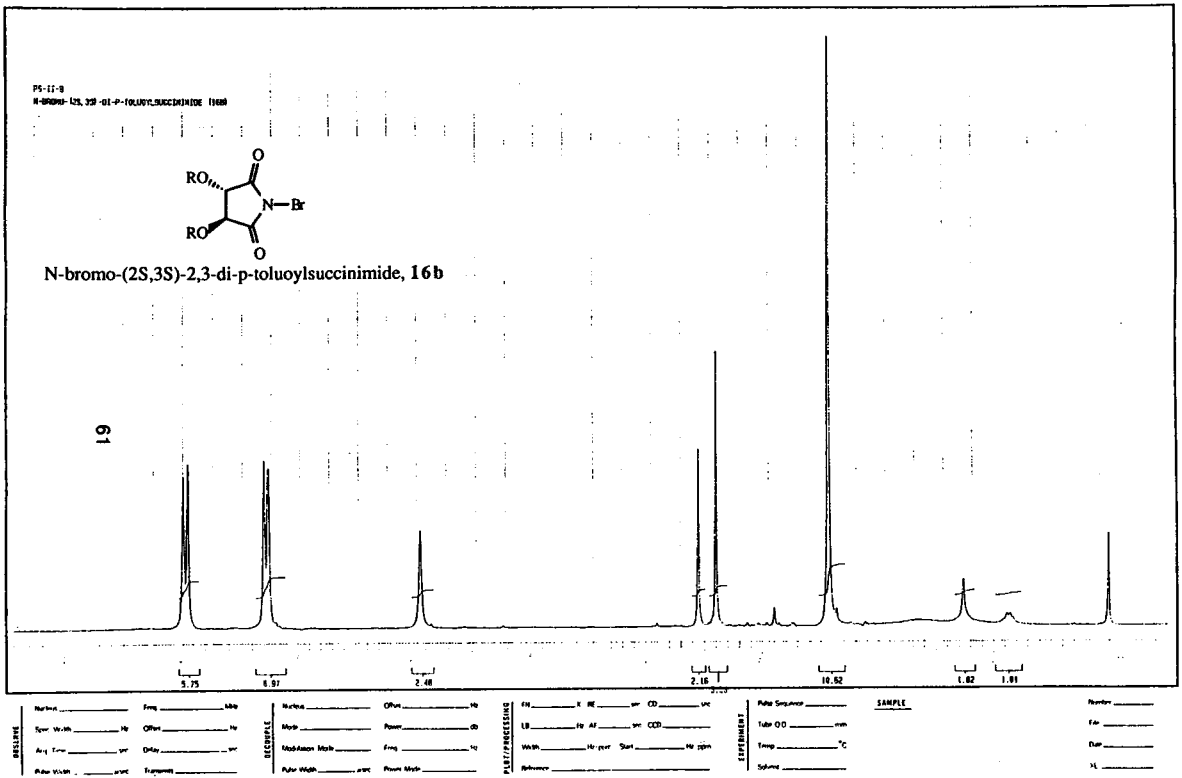

pg-1-77: C:\/tmp
0.4
0.3
0.2
0.1
0.0
-0.1
-0.2
Transmittance
58
1712.85
1703.25
1685.88
1620.30
1606.73
1563.30
1700
1650
1600
Wavenumbers
RO
O
NH2
RO
OH
O
3-Carbamoyl-(2S,3S)-2,3-di-p-toluoylpropanoic Acid, 14b

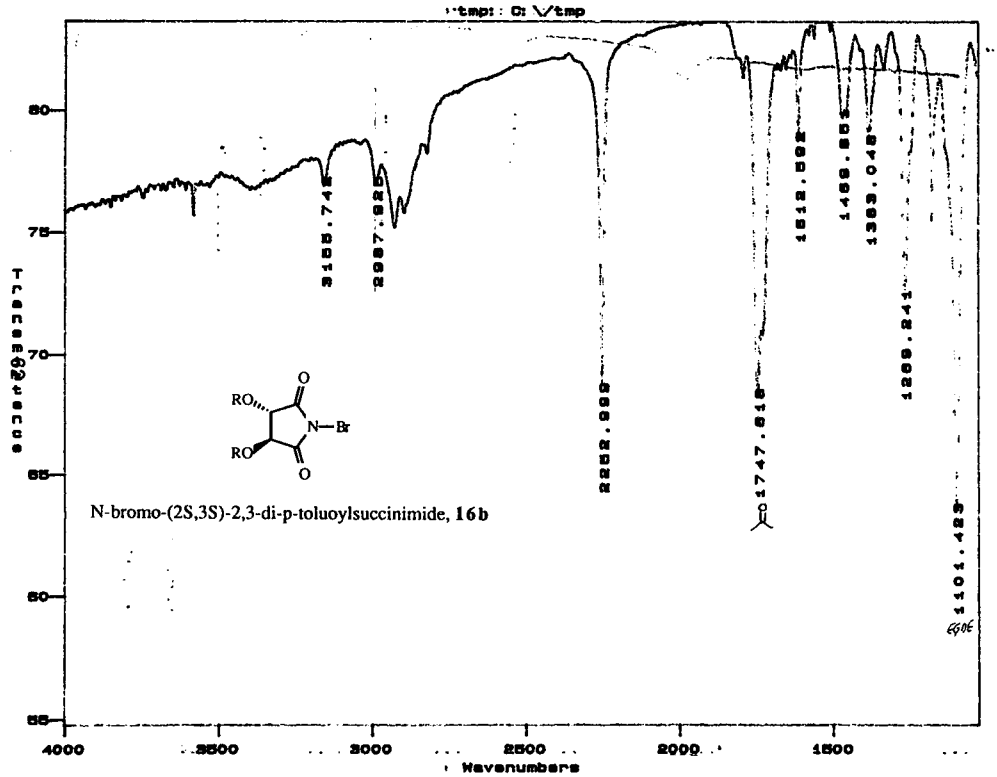


(2,S,3S)-2,3-Di-p-toluoylsuccinimide, **15b**



(2,S,3S)-2,3-Di-p-toluoylsuccinimide, **15b**


PS-II-8
N-BROMO-(2S,3S)-2,3-DI-P-TOLUOYLSUCCINIMIDE (16b)
RO
RO
O
O
N—Br
O
N-bromo-(2S,3S)-2,3-di-p-toluoylsuccinimide, 16b
61
5.75
6.97
2.48
2.16
10.52
1.82
1.91
RESERVE
DECOUPLE
PLOT/PROCESSING
EXPERIMENT
SAMPLE



N-bromo-(2S,3S)-2,3-di-p-toluoylsuccinimide, **16b**

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BOY, I LOVE SUMMER VACATION.
I CAN FEEL MY BRAIN BEGINNING TO ATROPHY ALREADY.
SHHH..