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Mechanism of cyclopropylidenoid ring opening reactions

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Mechanism

of

cyclopropylidenoid ring opening reactions

by

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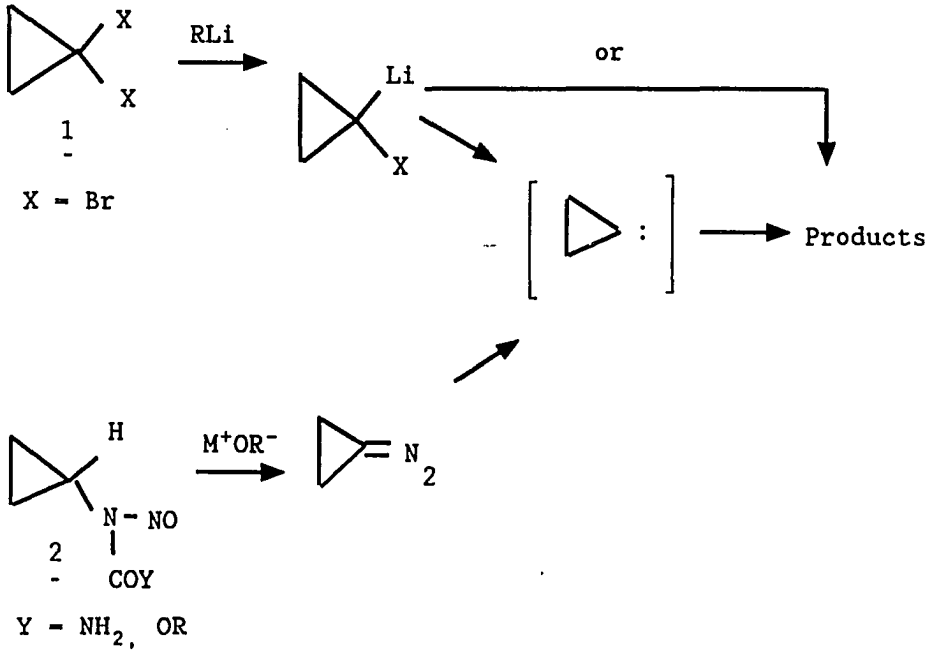
INTRODUCTION

The preparation of allenes by the ring opening of cyclopropylidenoids has been used widely in the synthesis of both cyclic and acyclic[1-51] allenes since the reaction was first reported by Doering[52] in 1958.

Two general methods for generating cyclopropylidenoids are outlined in Scheme 1.

Scheme 1

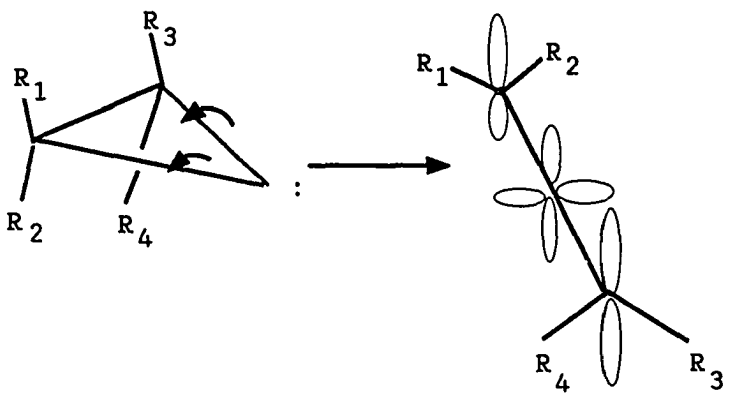


For the dehalogenation of 1, methyllithium in ether at reduced temperatures is most often used, since n-butyllithium may rearrange the product allenes to their acetylenic isomers.[2] The dibromides 1 are normally preferred over the less reactive dichlorides.

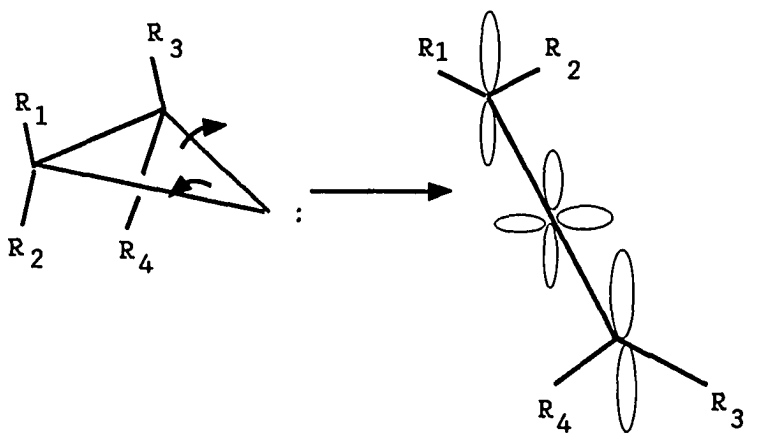
The conversion of 1 into allene starts with a

metal-halogen exchange, the radical character of which has been detected by chemical-induced dynamic nuclear polarization (CIDNP).[44] The α-elimination of LiX is usually considered to give "carbenoids", while loss of nitrogen from a diazoalkane is regarded as giving a "free carbene". If all the transformations take place via a free carbene, this species may undergo opening by at least four pathways.[53]

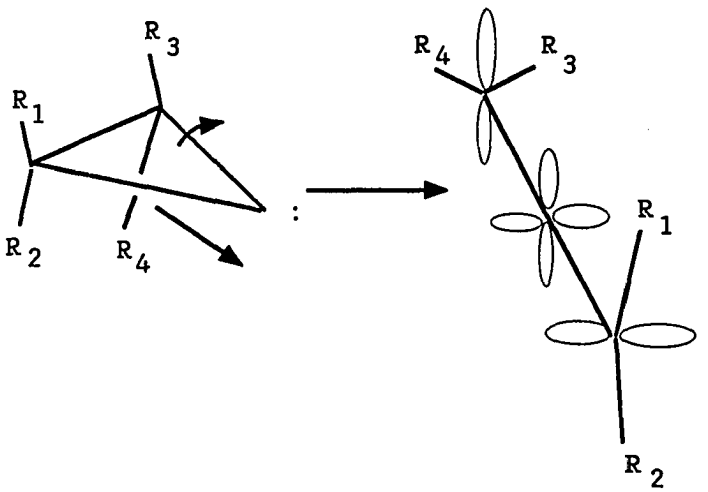
(1) A conrotatory opening leading to a planar allene.



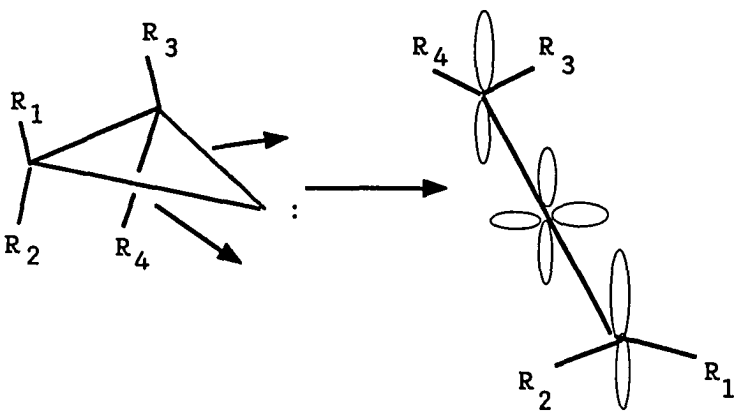
(2) A disrotatory opening to give a planar allene.



(3) A monorotatory opening to give an orthogonal allene.



(4) A nonrotatory opening to give a planar allene.



Potential energy surfaces have been calculated for these four alternatives for both singlet and triplet cyclopropylidene.[53-54] For the singlet case, and using semiempirical MINDO/2, Dewar[53b] concluded that cyclopropylidene opens in a nonrotatory fashion with an activation energy of 13.8 kcal/mol. The rotation of the groups into the allene configuration does not occur until after the nonrotated transition structure has been passed but before the carbon skeleton becomes linear. Dillon and Underwood,[53a] using the INDO method and the SIMPLEX

algorithm, found that the ring opens initially by a disrotatory motion but that motion of one of the methylene groups is reversed until an asymmetrical transition structure with the $C_1C_2C_3$ angle near 96° is achieved. From the transition state, the barrier was calculated to be 7.2 kcal/mol.

In the earliest reported ab initio investigation of the reaction, Pasto[54a] proposed a third but similar mechanism. He found that the reaction proceeds initially in a disrotatory fashion almost to the transition structure near which there occurs a rapid transition from the disrotatory structure to a distorted monorotated structure. The sudden change occurs between the $C_1C_2C_3$ bond angles of 90° and 100°. The reaction finishes by nonrotatory conversion of the 100° structure to allene. The transition structure was found to lie between 90° and 94.5°. Calculation at the 4-31G level on structures optimized at the STO-3G level yielded a barrier of 18 kcal/mol and an exothermicity of about 74 kcal/mol for the reaction.

Ruedenberg et al.[55a] have also mapped this energy surface in great detail. They used the Fully Optimized Reaction Space (FORS) model, which was introduced by Ruedenberg and Sunberg.[55b] MCSCF energies were calculated using a minimal basis set (STO-3G). Ruedenberg et al.[55a] found that at a $C_1C_2C_3$ angle of 80° the first bifurcation was reached. This corresponds to the choice between two degenerate, disrotatory paths that the molecule may take. As the ring continues to open, the transition region was found to lie between 84° and 85°. At 85° a second bifurcation was revealed, which provides a path to each two enantiomeric geometries. A

barrier of approximately 40 kcal/mol was found with these minimal basis calculations. Ruedenberg et al.[55a] describe the "transition region" containing the second bifurcation, as relatively flat. After the energy surface had been calculated in detail using a minimal basis set, they recalculated with an expanded basis set. These new calculations by Ruedenberg at al. serve the purpose of more carefully defining the activation barrier. The changes made include the use of Dunning and Hay[55c] basis plus polarization functions, and even-tempered Gaussian basis[55d] of double-zeta quality. These changes result in a lowering of the ring opening barrier to 13 kcal/mol. A notable change is that the extended basis calculation finds only one transition structure. The second bifurcation comes after the transition state at a valley ridge inflection point; the walls of the valley gradually lower, flatten and invert (the inflection point) as the molecule descends from the transition state. In a further calculation they employed the extended basis set with single and double excitation configuration interactions (SDCI) to yield a value of 7.4 kcal/mol for the ring opening barrier. This value is not corrected for zero point energy differences.

The conversion of triplet cyclopropylidene to triplet allene has also been investigated by Pasto,[54a] as well as by Dillon and Underwood.[53a] Both of them have concluded that the ring opening occurs initially by a nonrotatory rupture of the C_1C_3 bond until the transition structure is approached at a $C_1C_2C_3$ angle of about 105° or 90°. In both studies, disrotatory motion commences near 90° and is essentially complete (in relation to the final planar product) at 105°. In both studies, a plane of symmetry

was preserved throughout the course of the reaction. The reaction was found [54a] to be exoergic by about 37 kcal/mol and to have an activation energy of about 19 kcal/mol.

Rauk et al.[54b] reported a different calculation of the ring opening reaction of cyclopropylidene to allene at levels of theory significantly higher than those used previously. Geometries of equilibrium structures and transition structures have been determined at the Hartree-Fock (HF) level with analytical gradient procedures and the split valence 3-21G basis set. Improved estimates for relative energies were obtained by calculation of the energies using s 6-31G** basis. They found the singlet reaction has an activation energy of 11.5 kcal/mol. The reaction coordinate branches prior to passage over chiral and enantiotopic transition structures which account for the high degree of stereoselectivity on the basis of steric factors observed for the conversion of anti-substituted cyclopropylidenes to allenes, and for the very low degree of stereoselectivity observed in the case of syn-substitution. They also suggested a transition structure which resembles the one depicted in Figure 1. The analogous reaction of triplet cyclopropylidene is hindered by a higher barrier, calculated as 23.6 kcal/mol. Here the transition structure is reached by means of a nonrotatory but unsymmetrical rupture of the bond opposite to the carbene site.

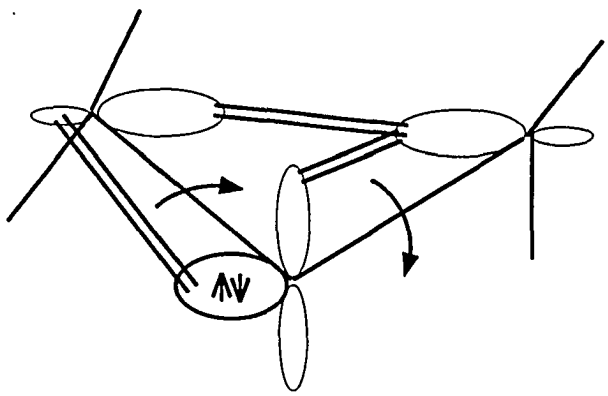
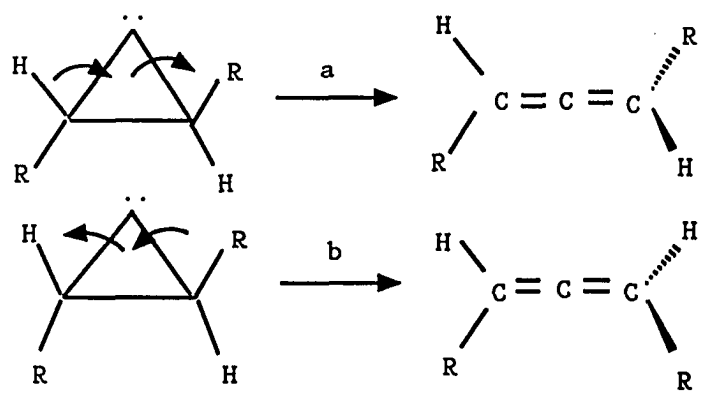


Figure 1. Transition structure of cyclopropylidene Ring-opening

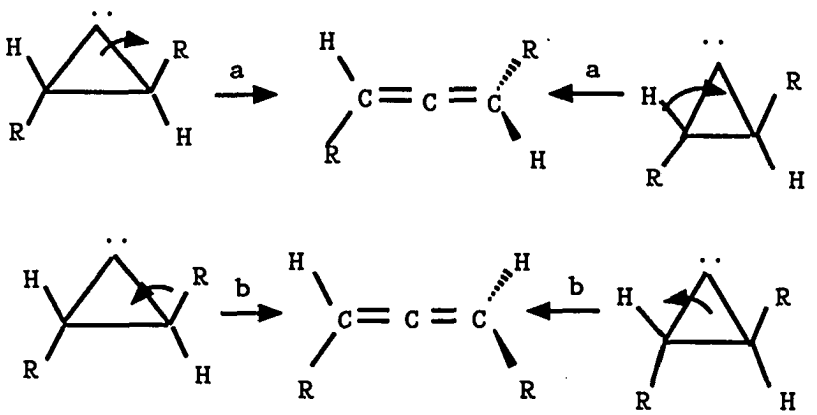
Jones et al.[56-57] and Walbrick et al.[58] have reported that optically active trans-2,3-diphenylcyclopropylidene opens to give optically active 1,3-diphenylallene. Similar results have been obtained for optically active trans-2,3-dimethyl,[57,58] -2,3-dibutyl,[57] and -2,3-diethylcyclopropylidene.[57] Jones and Walbrick[59] interpreted these results in terms of steric control of conrotatory ring opening, as shown in Scheme 2.

Scheme 2. Conrotatory ring-opening pathways for cyclopropylidenes



Path a in Scheme 2 is preferred over path b for steric reasons. The experimental results could equally be rationalized in terms of steric control of monorotatory opening, as shown in Scheme 3.

Scheme 3. Monorotatory ring-opening pathways for cyclopropylidenes

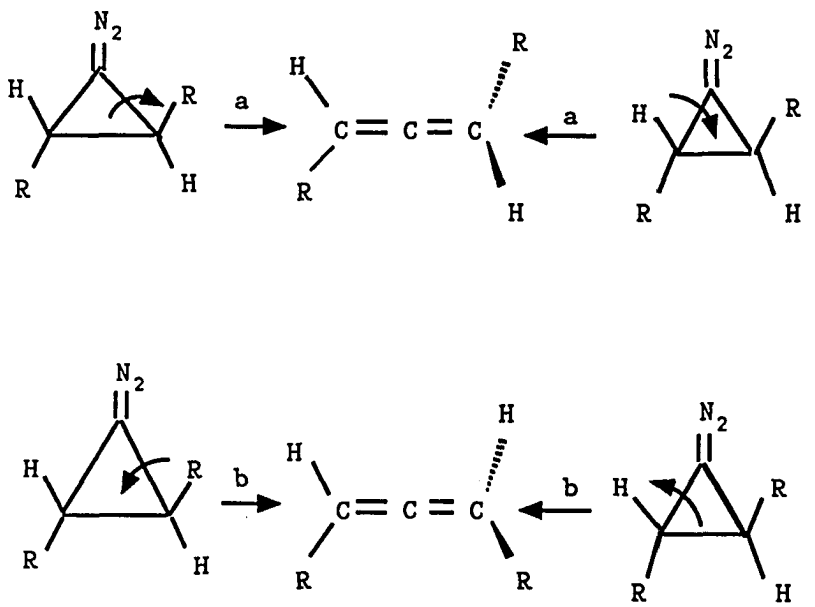


Path a in Scheme 3 is favored relative to path b. Although path a would be expected to be preferred over path b in the opening of free cyclopropylidene, if the opening occurs from a carbenoid or diazoalkane precursor then path b may have less steric interaction between the substituents and the leaving group.

Jones and Walbrick's work[59] can be interpreted as showing that if diazo-trans-2,3-diphenylcyclopropane opens with loss of N_2, rather than by the initial formation of the carbene, the repulsive interactions between the substituents and the leaving group are less than between the phenyl groups and the rest of the molecule as shown in Scheme 4.

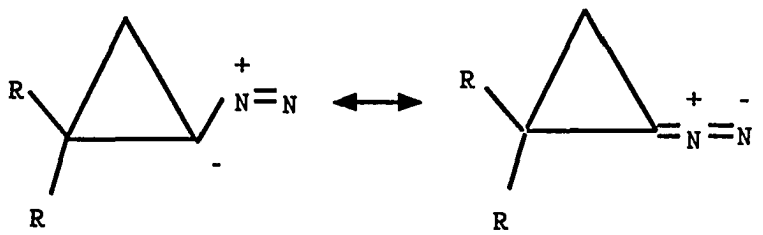
The proposal of steric control of conrotatory or monorotatory openings is consistent with the fact that trisubstituted cyclopropylidenoids open to allenes,

Scheme 4. Diazocyclopropane ring-opening pathway



whereas tetrasubstituted cyclopropylidenoids do not.[60] Jones and Grasley also reported[34] that the loss of nitrogen from the ring to give the "carbene" must be quite rapid to compete with the concerted decomposition to the allene. Possible explanation for this reactivity is that ring strain holds the nitrogen of the diazocyclopropane out of the plane of the ring. This, in turn, decreases the double bond character of the carbon-nitrogen bond by effectively reducing the contribution of form 3 to the diazocyclopropane hybrid. This, of course, would lower the activation energy for loss of the nitrogen shown in Figure 2.

Optically active cis-2,3-disubstituted cyclopropylidenes (unsymmetrical substitution) have been shown to yield optically active allenes,[61] and in the cases investigated the resultant asymmetry did not appear

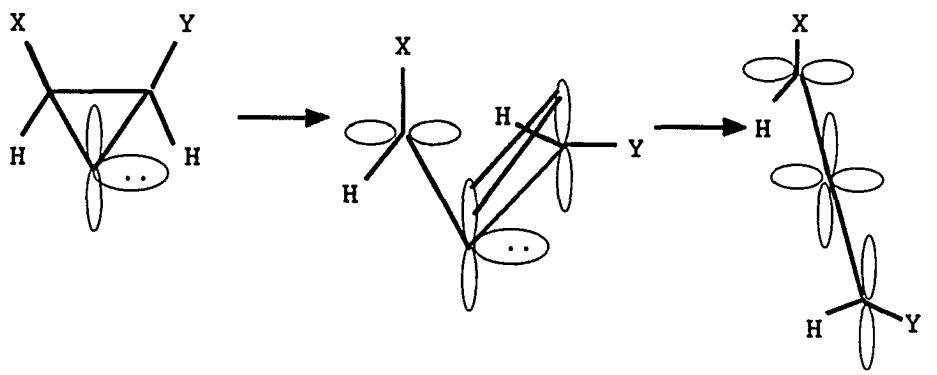


3

Figure 2. Loss of nitrogen in diazocyclopropane

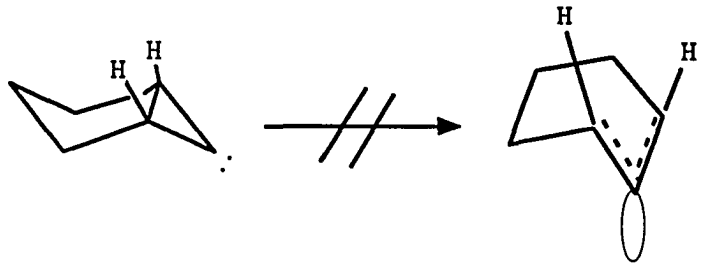
to be derived from steric control. It was therefore suggested that a monorotatory opening occurred in which the rotating group supplied a pair of electrons to the vacant p orbital of the carbene, i.e., electronic factors were proposed to determine which group would rotate as shown in Scheme 5.

Scheme 5. Electronic effect on cyclopropylidene ring-opening



This retention of optical activity precludes the intermediacy of any planar species, thus eliminating disrotatory and nonrotatory ring opening modes. On the other hand, monorotatory opening of 6-carbenabicyclo[3.1.0]hexane would lead to a geometrically impossible, orthogonal 1,2-cyclohexadiene.

Similarly, conrotatory opening (to a planar allene) would give an impossibly strained transoid allene:

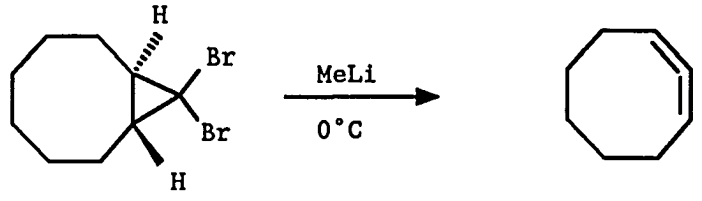


Therefore, in this case at least, it seems that the opening must proceed in a disrotatory or nonrotatory sense.[53a]

Moore and Bach[62] also found that at 0°C, neither method in Scheme 6 is completely stereospecific.

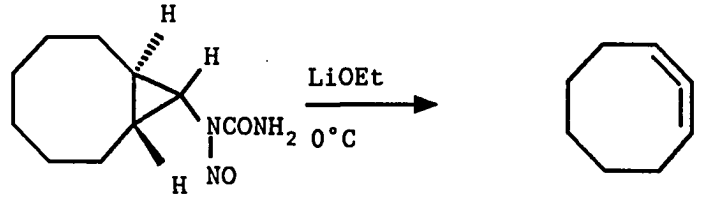
Based on their estimation, the rotation of optically pure allene is $[\alpha]_D$=170-175° (CH_2Cl_2). However, the two methods give very nearly the same stereochemical results, which certainly suggests that in the product forming stage, these reactions are similar. The two types of reaction clearly involve different intermediates in the steps preceding the product forming stage, namely an α-halocyclopropyllithium and a diazocyclopropane. Both types of intermediates clearly have the potential for generating a carbene which might serve as the immediate precursor of the products. But they could not conclude whether or not in either case a carbene actually is formed as an intermediate which enters into the product determining step. In any event, in neither case is a true free carbene likely since the reaction conditions involve a variety of polar species capable of interacting (solvating) with a carbene. In view of this parallel behavior, Moore and Bach[62] suggested that both types of

Scheme 6



(-)-4 $[\alpha]_D$= -150° (CH_2Cl_2)

6



(-)-5 $[\alpha]_D$= -159° (CH_2Cl_2)

6

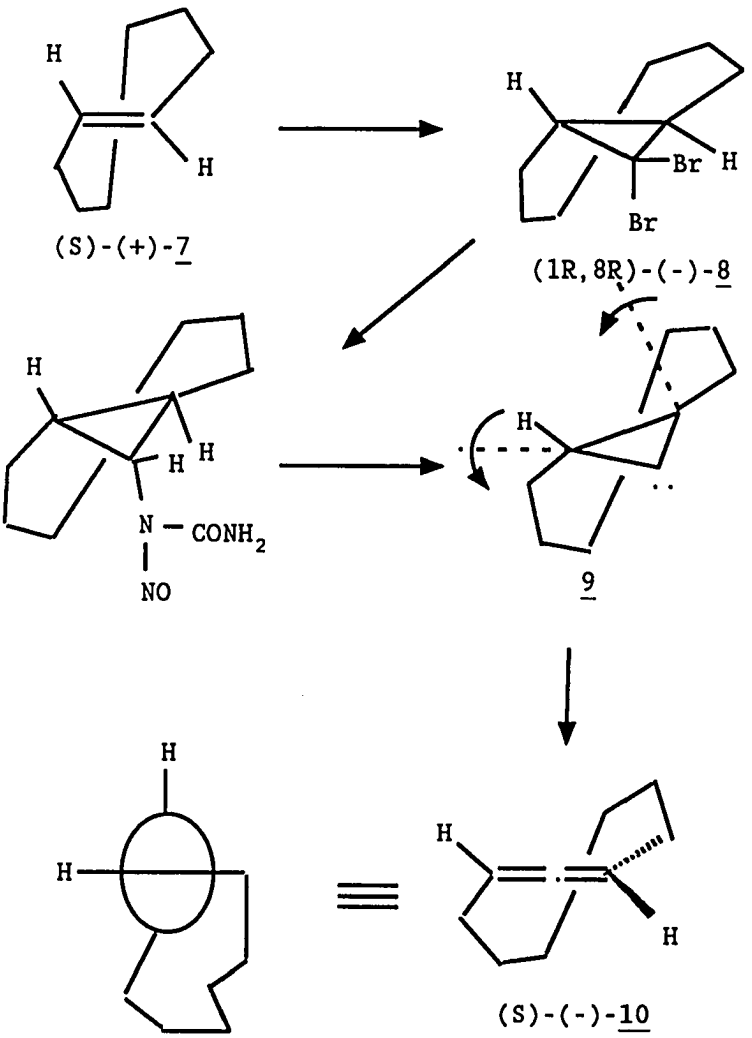
reactions can be interpreted in terms of the generation of short-lived cyclopropylidenes, influenced by the nature of the immediate environment in which they are generated, which give rise to closely related product forming transition states.

Moore and Bach also reported[62] that the stereochemical results of this reaction (Scheme 7) correspond to either conrotatory or monorotatory opening with the methylene groups moving inward. It is important to note that the sense of the reaction is opposite to that observed by Walbrick et al.[58], Jones and Walbrick[59] for trans-2,3-diphenylcyclopropylidene and trans-2,3-dimethylcyclopropylidene. For a preference,

one mode of conrotatory (or monorotatory) opening must have a steric origin. A group which rotates inward, away from the cyclopropylidene carbon atom, must experience nonbonded repulsions. Hence a hydrogen atom, by its small size, will be more readily accommodated than any other group. Steric control of this sort is illustrated in the strikingly different behavior of tri- and tetrasubstituted cyclopropylidenes. The former open to allenes, but the latter, due to retardation of ring opening, survive long enough to undergo virtually complete intramolecular C-H insertion, yielding bicyclobutane derivatives.[60]

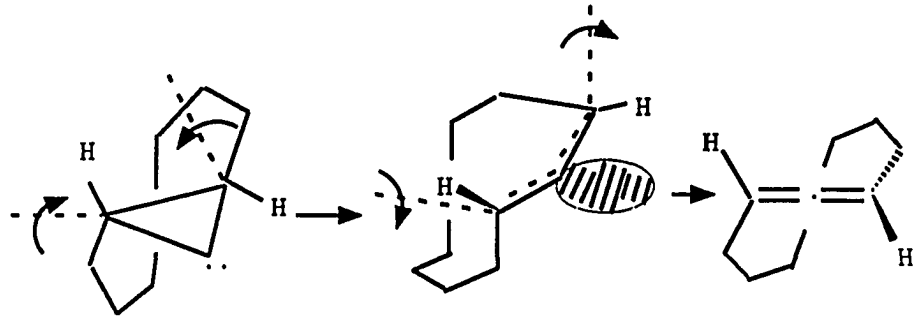
In the case of 9, however, the steric effect clearly must be overwhelmed by the strain which directs the opening in the opposite sense. Thus the methylenes rotate inwardly, and the abnormal monorotatory or conrotatory opening is observed. Rotation of the 1,8-hydrogen atoms inward should tend to increase the torsional strain, whereas rotation in the opposite direction must decrease this strain. Clearly the relief of strain must be more than sufficient to override steric repulsions encountered on rotating the methylene groups inward. The fact that the cyclopropylidene in Scheme 7 undergoes opening to allene rather than intramolecular C-H insertion establishes that the rate of allene formation must be comparable to that of simpler cyclopropylidenoids. Although Moore and Bach[62] described the formation of 6 in terms of a one-step least-motion opening of cyclopropylidene, they cannot preclude two-step mechanisms involving formation of an intermediate planar bent allene, a species which would serve as the precursor for the orthogonal allene. In a

Scheme 7



case where an acyclic allene were to be formed from a chiral cyclopropylidene, such a planar intermediate would be nondissymmetric, and accordingly would lead to a racemic product. In contrast, in this cyclic system, whether such potential planar intermediate would be dissymmetric or not would depend upon the orientation of the methylene chain. Dissymmetric conformations clearly are not only possible but are also probable. Provided the chirality of the methylene chain, i.e., the sense in which it is twisted, were maintained throughout the transformation from cyclopropylidene to planar allene to orthogonal allene, the sequence would amount to a stereospecific pathway. This possibility is illustrated in Scheme 8 for disrotatory opening. It is apparent that this two-step process would lead to opening of the three-membered ring in the stereochemical sense which Moore observed.

Scheme 8



9 11

Since the formation of a transoid system, 11, which must be somewhat strained should tend to inhibit this mode of opening, this process probably is not a main pathway. In acyclic systems, the formation of optically

active allenes can only be accounted for by the opening proposed by Jones. However, if racemic allene is formed, it may not be the result of opening in the reverse (sterically hindered) sense, but may well be due to the intervention of planar intermediates.[62]

It is necessary to more clearly delineate the mechanism of the cyclopropylidenoid ring opening reaction. We herein report the use of nuclear magnetic resonance with chiral shift reagents to measure the enantiomeric ratio of the resulting allene from optically pure dihalocyclopropanes and ethyl(-N-nitroso-N-cyclopropyl)carbamates.

We hope this work sheds some light on this matter.

RESULTS AND DISCUSSION

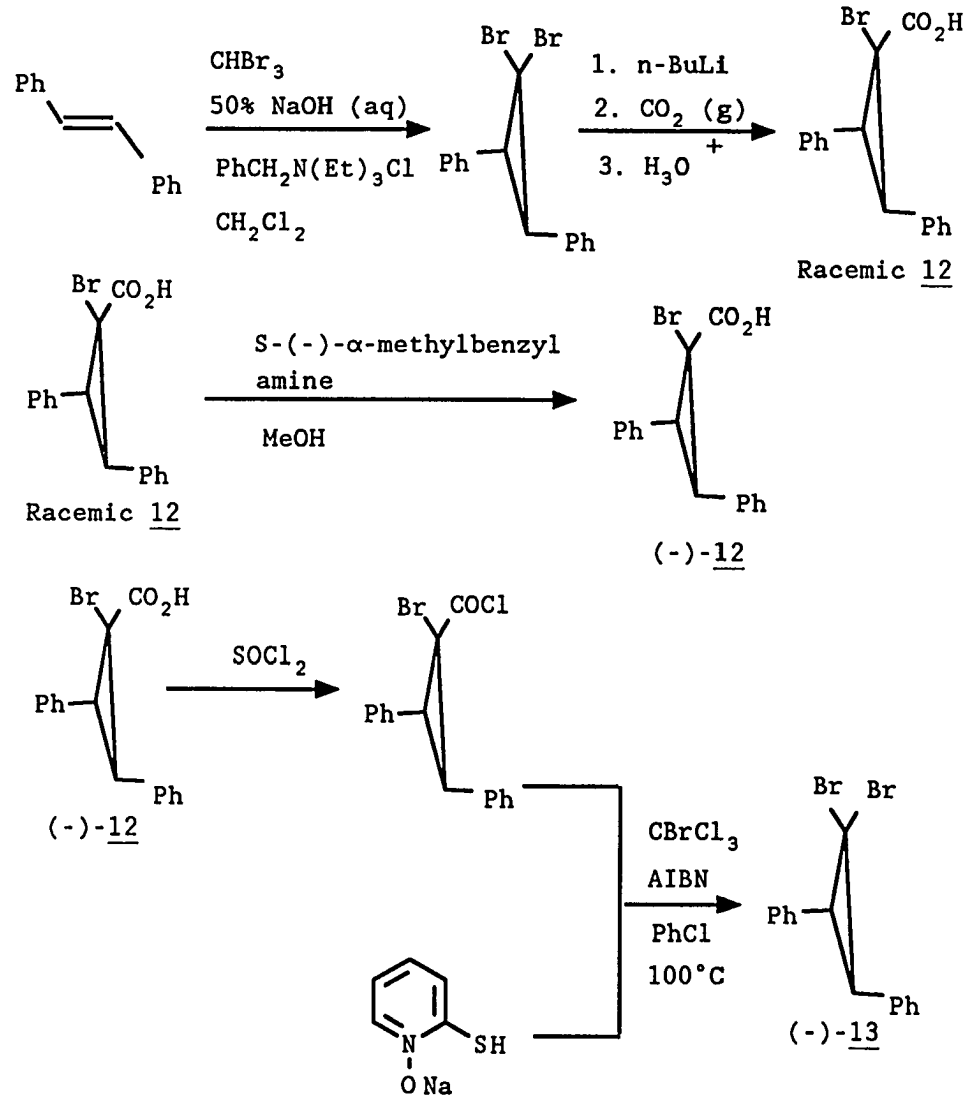
The synthesis of optically active 1,1-dibromo-trans-2,3-diphenylcyclopropane is outlined in Scheme 9.

The dibromocarbene addition in the first step of Scheme 9 was carried out using a phase transfer catalyst in 50% aqueous sodium hydroxide solution and methylene chloride.[63] The resulting dibromide was then converted to the bromoacid 12. By using (-)-α-methylbenzylamine with methanol as solvent, the racemic bromoacids 12 were resolved, and the levorotatory form isolated. The bromoacid was then smoothly converted to resolved dibromocyclopropane in fair yield by the modified Hunsdiecker equivalent reaction with the help of N-hydroxy-pyridine-2-thione.[64] The optical purity of the 1-bromo-trans-2,3-diphenylcyclopropane carboxylic acid was determined via its amide derivative of S-(-)-α-methylbenzylamine.[65] That reaction sequence is shown in Scheme 10.

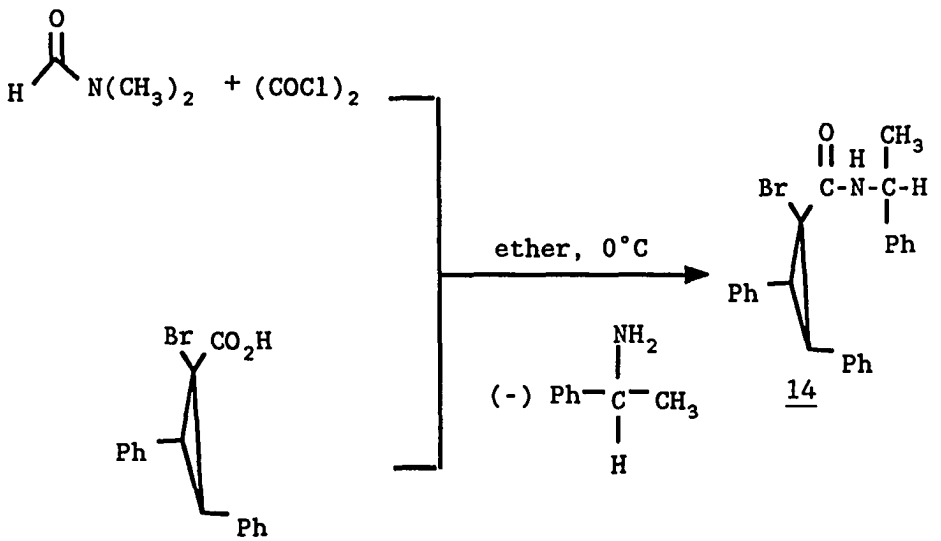
The diastereomeric amides, prepared from the racemic mixture of 12, have two sets of AB quartets at δ=3.8 ppm and 3.3 ppm (cyclopropyl ring protons, 4 peaks respectively) and two sets of doublets at δ=1.4 ppm and 1.2 ppm (methyl protons). All these peaks have equal areas. The amide made from (-)-12 gave only one AB quartet at δ=3.8 ppm and 3.3 ppm and one doublet at δ=1.4 ppm. This clearly told that (-)-12 was optically pure. And we can make an assumption that the dibromide (-)-13 inherited the same optical purity from the bromoacid (-)-12 through the decarboxybromination process.

Jones and Wilson[57] reported the absolute

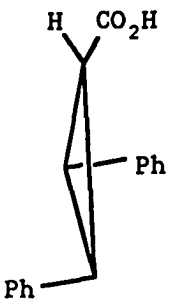
Scheme 9


Ph
Ph
CHBr3
50% NaOH (aq)
PhCH2N(Et)3Cl
CH2Cl2
Br Br
Ph
Ph
1. n-BuLi
2. CO2 (g)
3. H3O+
Br CO2H
Ph
Ph
Racemic 12
Br CO2H
Ph
Ph
Racemic 12
S-(-)-α-methylbenzyl amine
MeOH
Br CO2H
Ph
Ph
(-)-12
Br CO2H
Ph
Ph
(-)-12
SOCl2
Br COCl
Ph
Ph
CBrCl3
AIBN
PhCl
100°C
N
O Na
SH
Br Br
Ph
Ph
(-)-13

Scheme 10



configuration of (-)-trans-2,3-diphenylcyclopropane carboxylic acid to be the structure in Figure 3.

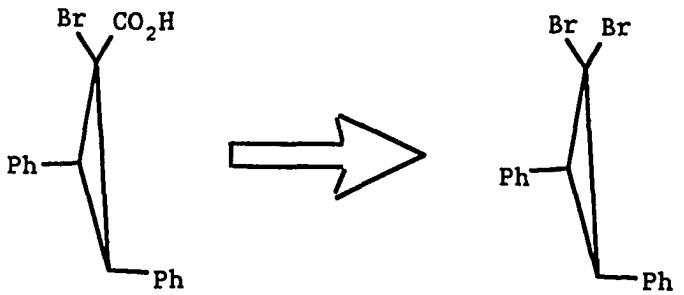


(-)-15

Figure 3. Absolute configuration of (-)-15

The methyl ester of (-)-15, prepared by reaction with diazomethane, had a negative rotation in ethanol ($[\alpha]_D$=-23°). However, when the bromoacid (-)-12 was treated with diazomethane, followed by t-butyl lithium,

and water, there results an ester with positive rotation in ethanol ($[\alpha]_D$=25°). These experiments establish the absolute configuration of bromoacid (-)-12 and dibromide (-)-13 to be as shown in Figure 4.



(-)-12 (-)-13

Figure 4. Absolute configuration of bromoacid (-)-12 and dibromide (-)-13

The optically pure (-)-13 was treated with methyl lithium in ether at various temperatures. The reaction mixture was thin layer chromatographed over silica with hexane. The specific rotation of optically pure 1,3-diphenylallene was reported[58,66] as 1020° based on a theoretical study, and polarimetry measurements. This suggests that determination of the enantiomeric ratio by polarimetry would not be reliable and accurate enough for the small amount of samples in our course of study. We think it is more reliable to use NMR which allows a direct determination of the enantiomeric ratios. The racemic 1,3-diphenylallene was mixed with 1:1 tris[3-heptafluoropropylhydroxymethylene-(+)-camphorato] ytterbium (III) and

6,6,7,7,8,8,8-heptafluoro-2,2-dimethyl-3,5-octanedionato silver in deuterochloroform. The signal for the olefinic protons at δ=6.8 ppm split into two peaks at δ=6.9 ppm and 7.03 ppm with equal integration. Table 1 gives the enantiomeric allene ratios from (-)-13, as analyzed by NMR.

Table 1. Enantiomeric ratios of allene from the reaction of(-)-13 with methyllithium

Temperature (°C)	Enantiomeric Ratio 1	2	3	4
0	74/26	76/24	79/21	
-23	75/25	82/18	82/18	82/18[a]
-63	79/21	86/14	85/15	

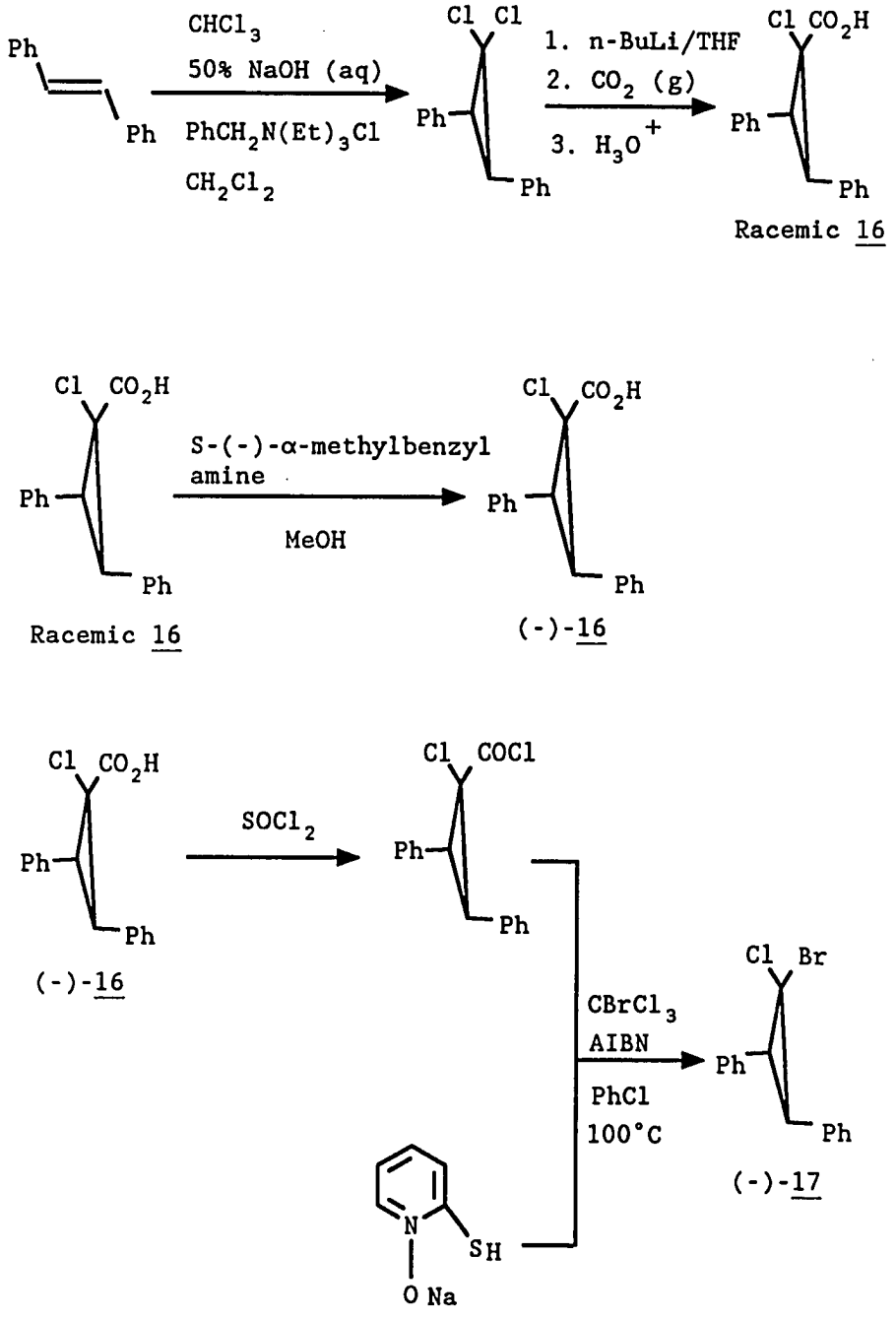
[a]10 eq. of LiBr was added, solvent was THF and ether (1:15).

Column 4 in Table 1 shows the effect of 10 equivalents of lithium bromide salt. This result suggests adding salts will not affect the stereochemistry of allene formatiom.

In order to examine the effect of halogen on the ring-opening reaction, the optically active 1-bromo-1-chloro-trans-2,3-diphenylcyclopropane, (-)-17, was prepared. The preparation of (-)-17 is shown in Scheme 11; it involves using $CHCl_3$ instead of $CHBr_3$ in the first step of Scheme 9.

The optical purity of the (-)-16 produced was 88% ee as determined by the same method as for (-)-12. The

Scheme 11


Ph
Ph
CHCl3
50% NaOH (aq)
PhCH2N(Et)3Cl
CH2Cl2
Cl Cl
Ph
Ph
1. n-BuLi/THF
2. CO2 (g)
3. H3O+
Cl CO2H
Ph
Ph
Racemic 16
Cl CO2H
Ph
Ph
Racemic 16
S-(-)-α-methylbenzyl amine
MeOH
Cl CO2H
Ph
Ph
(-)-16
Cl CO2H
Ph
Ph
(-)-16
SOCl2
Cl COCl
Ph
Ph
CBrCl3
AIBN
PhCl
100°C
Cl Br
Ph
Ph
(-)-17
N
SH
O Na

allene obtained from (-)-17 had an enantiomeric ratio of 79:21 at -23°C, which is about the same ratio as (-)-13 reacted at the same temperature, considering that the (-)-17 used contained 12% racemate.

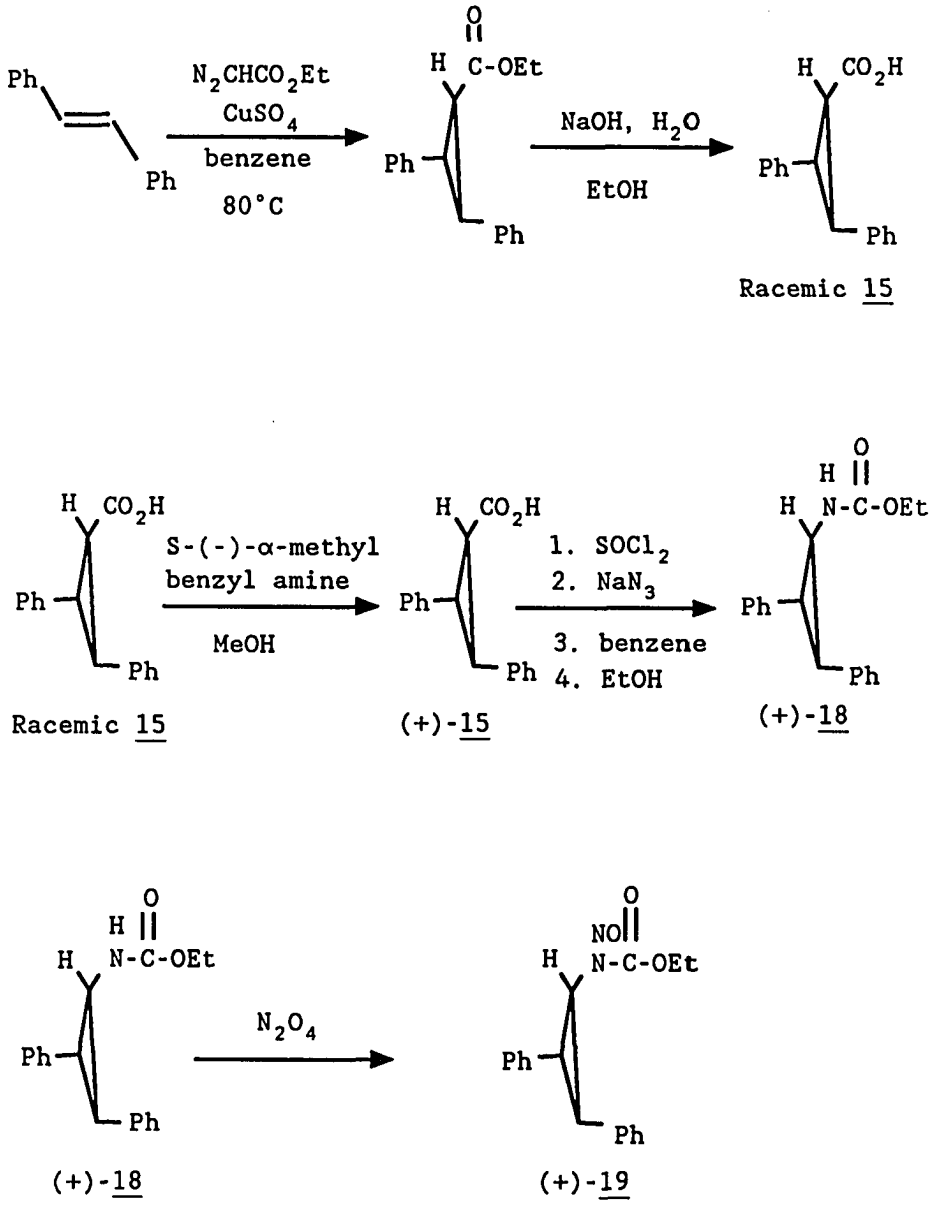
According to Walbrick et al.[58] recrystallization will increase the resulting allene's specific rotation (about 2 fold after one recrystallization). This result is difficult to explain, because one allene sample from dibromide (-)-13 had an enantiomeric ratio of 74:26 before recrystallization, and 69:31 after recrystallization (NMR analysis). The slight decrease in ratio was probably due to racemization during recrystallization. The ratios before and after recrystallization show that recrystallization cannot improve the ee of one of the enantiomers. Also an allene with a 69:31 enantiomeric ratio, heated in hexane for 3 minutes, racemized completely. The only possible explanation for the increase in specific rotation by recrystallization is removal of impurities.

We also reinvestigated Walbrick et al.'s work[58] with some modifications. The preparation of trans-2,3-diphenylcyclopropane-1-carboxylic acid is shown in Scheme 12.

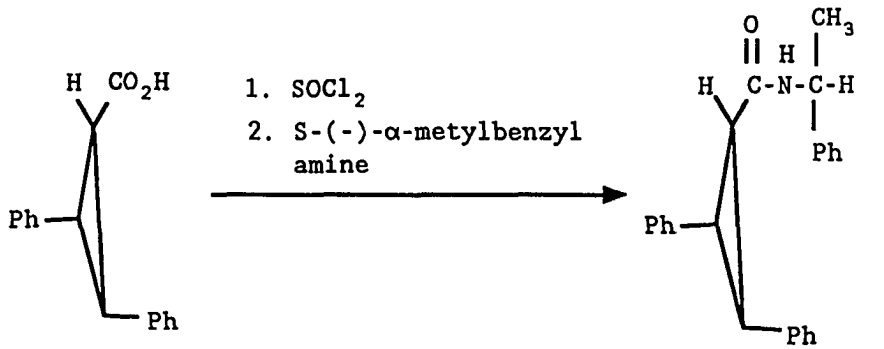
The resolution of 15 was carried out with S-(-)-α-methylbenzylamine, which was different from previous literature.[58,67] The optical purity of (+)-15 was determined after conversion to its amide, using optically active amine as shown in Scheme 13.

The diastereomeric amides made from racemic 15 have two sets of doublets at δ=1.7 ppm and 1.6 ppm with equal integration by NMR analysis. The amide made from (+)-15 has only one set of doublets at δ=1.7 ppm by NMR

Scheme 12


Ph
Ph
N_2CHCO_2Et
$CuSO_4$
benzene
80°C
H C-OEt
O
Ph
Ph
NaOH, H_2O
EtOH
H CO_2H
Ph
Ph
Racemic 15
H CO_2H
Ph
Ph
S-(-)-α-methyl
benzyl amine
MeOH
Racemic 15
H CO_2H
Ph
Ph
(+)-15
1. $SOCl_2$
2. NaN_3
3. benzene
4. EtOH
H N-C-OEt
O
Ph
Ph
(+)-18
H N-C-OEt
O
Ph
Ph
(+)-18
N_2O_4
NO N-C-OEt
O
Ph
Ph
(+)-19

Scheme 13



analysis. The ethyl-N-nitrosocarbamate (+)-19 was treated with excess base in hexane and the NMR results are in Table 2.

Table 2. Enantiomeric ratios of allene from the reaction of (+)-19 with base

Temperature (°C)	Enantiomeric Ratio 1[a]	2[a]	3[b]	4[b]
35	63/37	65/37	71/29	
25	67/33	66/34	70/30	69/31
0	65/35	68/32	73/27	
-23	66/34	72/28	73/27	
-45	67/33	74/26	73/27	

[a]Sodium methoxide was suspended in methanol.

[b]Sodium was dissolved in methanol.

The base used in columns 1 and 2 was a suspension of sodium methoxide in methanol. Columns 3 and 4 are results from experiments with dissolved base in methanol.

If one uses ether instead of hexane at -23°C, the resulting allene has a ratio of 67:33. This implies a small, if any, solvent dependence on the ring-opening reaction. By using N-nitrosourea at -23°C in hexane, the resulting allene has a ratio 72:28. This demonstrates that there is no precusor dependence on enantiomeric allene formation. A ratio of 69:31 was obtained with t-butoxide in t-butanol at -23°C, which suggested no base dependence either.

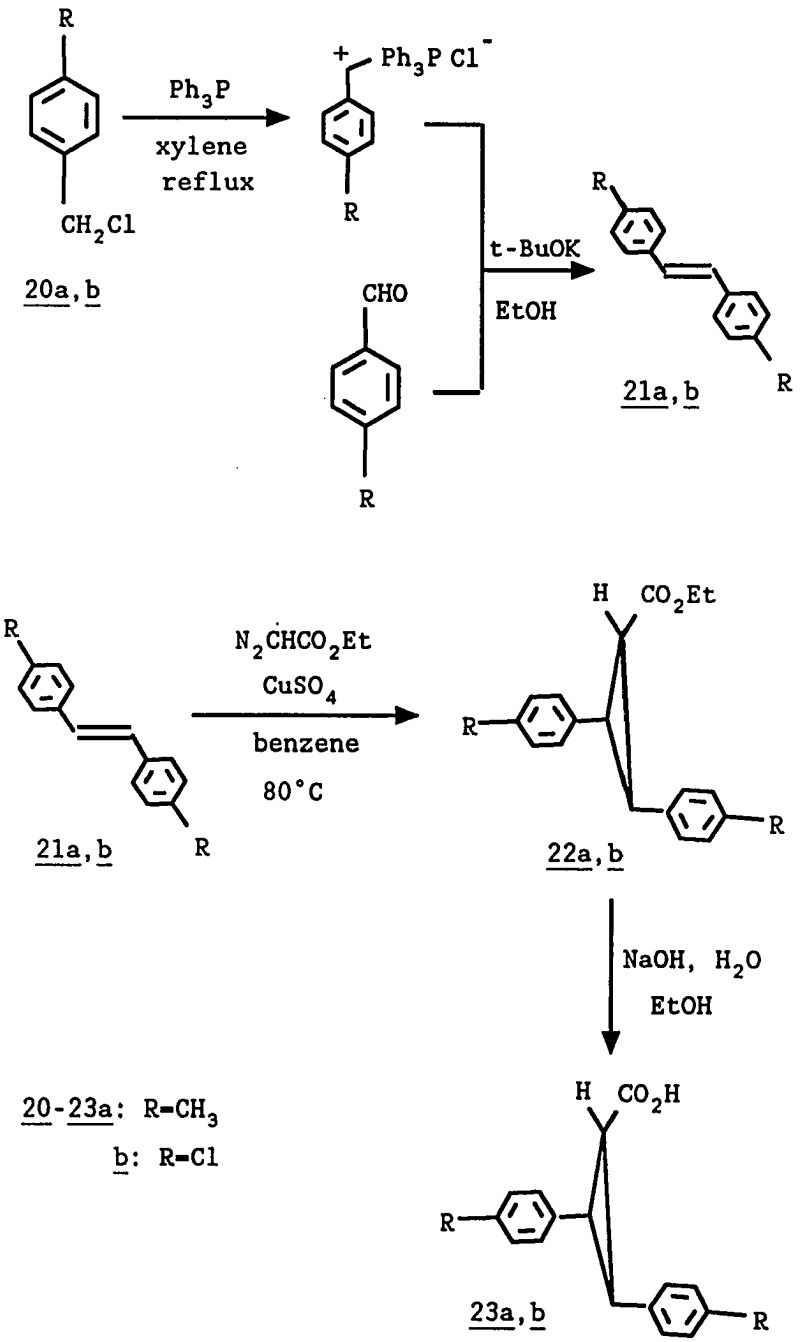
A sample of 1,3-diphenylallene which had been thin layer chromatographed on silica and had a ratio of 70:30 was subjected to a second thin layer chromatography on silica; the resulting ratio was 68:32. This result demonstrates that there is no significant racemization associated with thin layer chromatographic separation.

An attempt was made to study electronic effects on the chirality of the ring opening reaction. To this end, di(4-methylphenyl)- and di(4-chlorophenyl)-stilbene were prepared.[67] They were then converted to the corresponding acids shown in Scheme 14.

The dimethyl substituted acid 23a was resolved using brucine in ethylacetate to give (-)-23a. Dichloro substituted acid 23b was resolved using quinine in ethanol to give (-)-23b. The optical purities of the two acids were determined to be 100% with their S-(-)-α-methylbenzylamine derivatives. The conversion to the ethyl-N-nitroso carbamates was accomplished by the same procedure used in Scheme 12.

The 1,3-di(4-methylphenyl)allene made from the

Scheme 14


R
Ph3P
xylene
reflux
CH2Cl
20a,b
+ Ph3P Cl-
R
CHO
R
t-BuOK
EtOH
R
R
21a,b
R
N2CHCO2Et
CuSO4
benzene
80°C
21a,b
R
H CO2Et
R
R
22a,b
NaOH, H2O
EtOH
H CO2H
R
R
23a,b
20-23a: R=CH3
b: R=Cl

corresponding N-nitroso carbamate at 0°C had an enantiomeric ratio of 75:25. The 1,3-di(4-chlorophenyl)-allene made from the corresponding N-nitroso carbamate had an enantiomeric ratio of 18:82.

From Table 1 and Table 2, we can see that the ring opening of the gem-dihalocyclopropane is more stereospecific than the ring opening of the N-nitroso carbamate (or urea). This may imply more free carbene character at the product forming stage for α-elimination of the carbenoid from the dibromocyclopropane, although loss of nitrogen from a diazoalkane is thought to give a free carbene intermediate. This may also suggest that a one-step least-motion (disrotatory or monorotatory) opening to an orthogonal allene is the main pathway. And the loss of nitrogen from the diazoalkane may not be due to the intervention of a two-step mechanism involving formation an intermediate planar allene. A planar bent allene would be equivalent to an allyl radical without the central hydrogen atom or the corresponding allyl cation without the central proton, and would lead to the formation of a racemic product. However, from the experimental results this pathway is by no means a major one. However, it must be recognized that the departing bromide ion, in a two-step ring-opening/LiBr loss, would contribute to the product chirality so long as it did not achieve coplanarity with the pseudo-planar allyl segment. So the LiBr loss could involve a non-carbene mechanism, and still lead to retained product chirality.

By substituting both para positions on the phenyl rings, we can minimize the steric interactions to examine the donor/acceptor influence on the transition state of the ring-opening reaction. From our previous work[68], the

following conclusions have been drawn:

(i) The cyclopropylidene to allene ring opening rate increases when electron donors are attached to C_2 and/or C_3, and decreases when electron acceptors are similarly attached.

(ii) The transition state is cationic in nature insofar as C_2 and C_3 are concerned, with a fairly large interaction existing between the carbene center and the developing p-orbitals at C_2 and C_3.

(iii) Relative to insertion into methanol, the ring opening of cyclopropylidene is favored entropically, while being disfavored enthalpically.

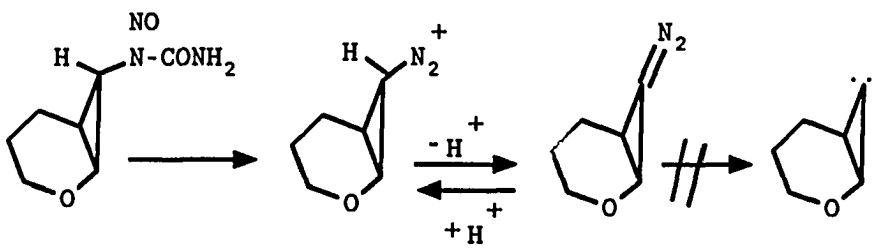
(iv) It was predicted that at least some unsymmetrically disubstituted cyclopropylidenes pass through ring-opening transition states which are unsymmetrical with respect to the developing p-orbitals. It was further predicted that if these compounds were optically active, they would yield allenes of higher optical purity than symmetrically disubstituted cyclopropylidenes.

The results now show that electron withdrawing substituents produce more stereospecific ring-opening than electron donating substituents. However this is just a preliminary conclusion. Because of the high electrophilicity of the trifluoromethyl group, we were so far unable to prepare that di-p-substituted aryl cyclopropylidene precursor.

There are three observations related to the ring-opening of α-halocyclopropyllithiums shown in Scheme 15. Reaction 1[15,60b,69] in Scheme 15 goes with no or little ring-opening, and reaction 2[70-71] goes with ring-opening as the major pathway. Could this be true

for "carbenes" (24-26) generated via nitrosocarbamate precursors?

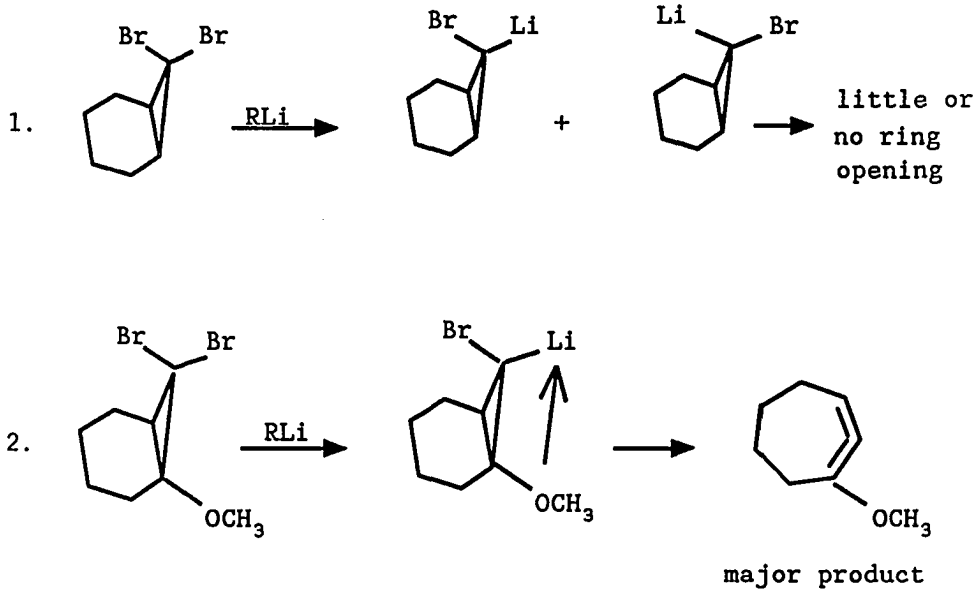
From our previous work we know that 24 does not ring-opening under the reaction conditions used. And Jendralla has reported[72] that when the precursor of 26 was treated with base, exclusively diazonium ion chemistry resulted.

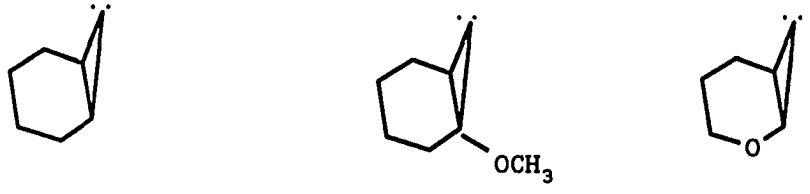


The preparation of the precursor of 25 is shown in Scheme 16. Because of the unexpected difficulty encountered in the preparation of the methoxy analog of acid 28, we used the ethoxy derivative instead.

When 30 was treated with sodium methoxide in methanol, there resulted about 30% insertion products and impurities from the carbamate (GC-MS analysis). The correspoding dibromide, treated with excess methyllithium, gave mainly ring-opening products (91%, uncorrected GC yield). The methoxyl did dramatically alter the reactivity of the carbenoid, since the investigation of other "cyclopropylidenes" in the bicyclo[4.1.0]heptyl series did not display any evidence of allene formation.[72b]

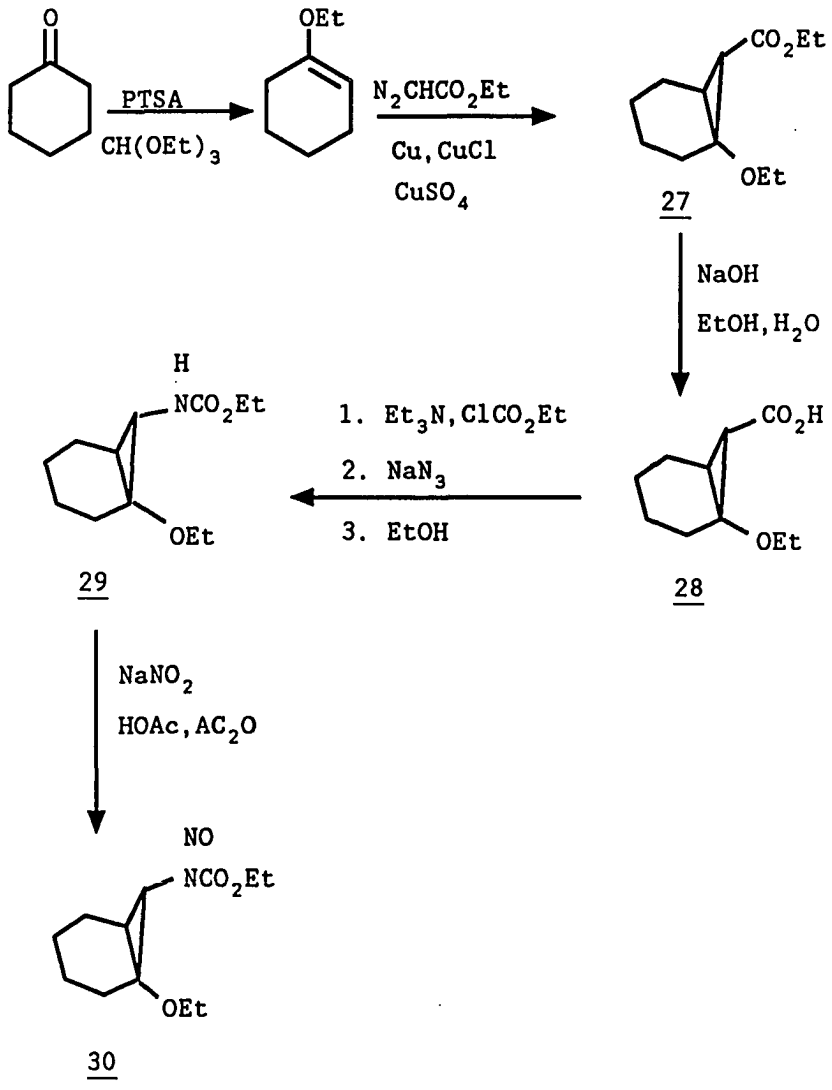
Scheme 15





24 25 26

Scheme 16


O
OEt
PTSA
CH(OEt)3
N2CHCO2Et
Cu, CuCl
CuSO4
CO2Et
OEt
27
NaOH
EtOH, H2O
CO2H
OEt
28
1. Et3N, ClCO2Et
2. NaN3
3. EtOH
H
NCO2Et
OEt
29
NaNO2
HOAc, AC2O
NO
NCO2Et
OEt
30

EXPERIMENTAL

General

Infrared spectra were recorded on an IBM FT-IR 98 spectrophotometer or on a Mattson 4020 GC/FT-IR spectrophotometer which was fitted with a Hewlett-Packard HP-5890 II Gas Chromatograph equipped with a DB-5 capillary column. Direct FT-IR spectra were recorded using potassium bromide pellets for solid samples, or neat for liquid samples. The proton magnetic resonance spectra were obtained on a Varian EM-360 Spectrometer or on a Varian VX-300 FT-NMR Spectrometer or on a Nicolet 300 MHz FT-NMR Spectrometer, using deuterochloroform as solvent and tetramethylsilane as internal standard. Exact mass and GC exact mass spectra were recorded on the high resolution Kratos MS-50 MASS Spectrometer at 70 ev unless otherwise stated. GC analysis was performed on a Hewlett-Packard HP-5890 Gas Chromatograph, which was fitted with a 30 meter DB-1 or DB-5 capillary column and flame ionization detector. GC/MS spectra were obtained on Perkin-Elmer 8420 Gas Chromatograph fitted with a DB-1 capillary column and ion-trap detector. Optical rotations were measured on a Perkin-Elmer 360 Polarimeter with various weights of samples in 5 mL of absolute ethanol. Melting points were taken on a Thomas-Hoover melting point apparatus and were not corrected.

Synthesis and Reaction

1. (±)-1,1-dibromo-trans-2,3-diphenylcyclopropane, 13

A mixture of 18 g of trans-stilbene, 64 g of

bromoform, 40 mL methylene chloride and 40 mL of 50% sodium hydroxide was stirred mechanically at room temperature. To this mixture, 0.68 g of benzyltriethylammonium chloride were added, and the stirring was continued for 24 hours.

The organic layer was separated from the reaction mixture and washed successively with dilute hydrochloric acid, saturated sodium bicarbonate solution and water. The organic layer was then dried over anhydrous magnesium sulfate and rotatory evaporated to a brown oil. The brown oily crude product was then heated under reduced pressure at 40°C to remove excess bromoform. The residue was extracted with 300 mL of skelly A. After removal of skelly A, a yellow solid was obtained. The yellow solid was recrystallized from 95% ethanol to give 28 g (75%) of pale yellow crystals, mp 60°-61°C (Lit.[63] 79-87% yield, mp 60°-62.5°C).

^{1}H-NMR: δ= 7.4(s), 3.3(s). (Fig. 5)

IR: cm^{-1}= 3032(m), 1497(s), 1450(m), 695(s). (Fig. 6)

MASS: calculated for $C_{15}H_{12}Br$ (M^+-Br) m/e 271.01226; measured m/e 271.01257, 271(37), 192(100), 165(28). (Fig. 7)

2. (±)-1-bromo-trans-2,3-diphenylcyclopropane carboxylic acid, 12

In 30 mL of dry THF were dissolved 3.5 g of 2,2-dibromo-trans-2,3-diphenylcyclopropane. The solution was then cooled with a dry ice/acetone bath and 0.011 mole of n-butyllithium in hexane was added dropwise through a dropping funnel over a period of 5-10 minutes under nitrogen with vigorous stirring. After the addition was completed, dry CO_2 gas was bubbled into the

reaction flask for 15 minutes. The reaction mixture was then allowed to warm up to room temperature slowly. The THF solution was washed with 10% hydrochloric acid and was extracted twice with 20 mL of 10% sodium hydroxide solution. The basic extract was washed with 20 mL of ether, and acidified with concentrated hydrochloric acid. The acidic mixture then was extracted twice with 20 mL of ether. The ether layer were combined and washed with water. After removal of ether, the yellow oil was crystallized from carbon tetrachloride to give 1.6 g of white solid, mp 164°-165°C (52% yield).

^{1}H NMR:δ= 7.7(s), 3.7(d), 3.5(d). (Fig. 8)

IR:cm^{-1}= 3055(m), 3028(m), 1684(s), 1497(m), 1448(m), 1306(m), 1292(m), 1231(m), 932(m), 964(s). (Fig. 9)

MASS: calculated for $C_{16}H_{13}O_2Br$ m/e 316.00998; measured m/e 316.0102, 316(1), 237(8), 220(5), 192(100), 165(27), 115(26). (Fig. 10)

3. (-)-1-bromo-trans-2,3-diphenylcyclopropane carboxylic acid, (-)-12

To 2.289 g of racemic bromoacid 12 dissolved in 50 mL of hot methanol, was added 0.875 g of S-(-)-α-methylbenzylamine. The mixture was kept in the freezer for 1 day, after which the solid formed was filtered off from the solution and recrystallized from methanol twice to give 0.6 g of white fluffy crystals (mp 178°-180°C with decomposition).

The amine salt was then suspended in 20 mL of water and 5% sodium hydroxide solution was added until all the solid was dissolved. The aqueous solution was washed with ether and was acidified with concentrated

hydrochloric acid. The acidic solution was extracted with 20 mL of ether twice. The ether layer was then washed with water and the ether was removed in vacuo. The crude product was recrystallized from carbon tetrachloride to give 0.25 g of a white solid, mp 140°-141°C, $[\alpha]_D$= -51.4° (0.016g).
^{1}H NMR, IR and MASS were the same as for (±)-12.

4. N-[(S)-α-methylbenzyl]-1-bromo-trans-2,3-diphenylcyclopropane-1-carboxamide, 14

A solution of 0.8 mL DMF and 0.26 mL of oxalyl chloride in 10 mL of methylene chloride was cooled with an ice-water bath. The mixture was vigorously stirred for 1 hour at 0°C under nitrogen. The volatile fractions were removed under reduced pressure to give a white powder. Dry ether (20 mL) was then added, and the mixture was cooled to -28°C. Then 0.16 g of acid 12 in 5 mL of dry ether was added through a syringe, and the mixture was stirred for another 2 hours at -28°C. Following this, 0.45 mL of S-(-)-α-methylbenzylamine was added into the mixture, and stirring continued for another 10 minutes. The resulting reaction mixture was allowed to warm up to 0°C over 30 minutes, after which water was added. The amides were extracted into ether. The ether layer was washed successively with dilute hydrochloric acid, water, dilute sodium hydroxide and water, and dried over anhydrous sodium sulfate. After removal of the solvent, the crude product was thin layer chromatographed over silica with benzene.
^{1}H NMR: δ= From (±)-12; 7.2-7.4(m), 4.8(m), 3.8(q), 3.3(q), 1.5(d), 1.2(d). (Figs. 11-13)
From (-)-12; 7.2-7.4(m), 4.8(m), 3.8(d), 3.3(d),

1.5(d). (Figs. 14-15)

5. (-)-1,1-dibromo-trans-2,3-diphenylcyclopropane, (-)-13

A mixture of 0.632 g bromoacid (-)-9 and 15 mL of thionyl chloride was heated to reflux for 1 hour. Excess thionyl chloride was then removed under reduced pressure to give a yellow oil. Then 10 mL of chlorobenzene and 0.025 g of AIBN were mixed with the acid chloride and transferred to a dropping funnel. In a round-bottom flask were dissolved 0.09 g of N-hydroxypyridine-2-thione sodium salt in 15 mL of bromotrichloromethane and 10 mL of chlorobenzene. The flask was then heated in an oil bath at 100°C, and the acid chloride solution added dropwise over a period of 30 minutes under nitrogen with vigorous stirring. Heating was continued for another 2 hours. The reaction mixture was then washed successively with dilute hydrochloric acid, dilute sodium hydroxide and water. The solvent was then removed under reduced pressure. The oily residue was column chromatographed over silica (eluted with hexane), and recrystallized from 90% ethanol. There resulted 0.21 g (31%) of white crystals, mp 73°-75°C, $[\alpha]_D$= -31° (0.0127 g). ^{1}H NMR and MASS were the same for the racemic mixture.

6. (-)-methyl trans-2,3-diphenylcyclopropane-1-carboxylate

In 10 mL of ether was dissolved 0.036 g of (-)-15 ($[\alpha]_D$= -19.3°), to which excess diazomethane in ether was added. The reaction mixture was quenched with acetic acid and washed successively with water, 10% sodium bicarbonate and water. The solvent was removed under reduced pressure to give a white solid. The resulting ester had $[\alpha]_D$= -23.7° (0.0135 g).

^{1}H NMR: δ= 7.2-7.4(m), 3.5(s), 3.2(q), 3.0(q), 2.4(q). (Fig. 16)

MASS: 252(12), 221(9), 193(100), 192(86), 178(27), 115(16). (Fig. 17)

7. (+)-methyl trans-2,3-diphenylcyclopropane-1-carboxylate

In 10 mL of ether was dissolved 0.317 g of bromoacid (-)-9, after which excess diazomethane in ether was added. The reaction mixture was quenched with acetic acid and washed successively with water, 10% sodium bicarbonate and water. The solvent was removed under reduced pressure to give the bromoester.

In 10 mL THF was dissolved 0.155 g of the crude ester, and the solution cooled to -78°C. To this was added 2 mL of t-butyllithium in pentane (1.7 M) via a syringe under nitrogen with vigorous stirring. Stirring was continued for 15 minutes and the reaction mixture was quenched with dilute hydrochloric acid. The aqueous layer was separated and was extracted twice with 10 mL of ether. The organic layers were combined and washed successively with 5% sodium bicarbonate and water. The ether was removed under reduced pressure to give a yellow oil. The crude oily product was thin layer chromatgraphed over silica with carbon tetrachloride and hexane (10:1) to give a white solid $[\alpha]_D$= 25.5° (0.0092 g).

^{1}H NMR and MASS were same as from (-)-15.

8. Reaction of (-)-1,1-dibromo-trans-2,3-diphenylcyclopropane (-)-13 with methyllithium

The dibromide (-)-13 (30 mg) was dissolved in 20 mL of dry ether and cooled to the desired temperature. To this solution was added 4 equivalents of methyllithium in ether (complexed with lithium bromide) via a syringe under nitrogen with vigorous stirring. Stirring was continued for 30 minutes, followed by a water quench. The aqueous layer was separated, and extracted with 10 mL of ether. The organic layers were combined and washed successively with dilute hydrochloric acid, 5% sodium bicarbonate and water. The solvent was removed under reduced pressure. The crude product was thin layer chromatographed over silica with hexane. The allene band was washed out with methanol and the methanol was removed under reduced pressure. The resulting allene then was subjected to analysis.

^{1}H NMR: δ= 7.2-7.4(m), 6.6(s). (Fig. 18)
with chiral shift reagents; 7.8(s), 7.1(s), 6.9(s). (Fig. 19)

MASS: 192(100), 191(85), 165(25), 115(26), 95.6(16), 94.5(26), 89(17), 82.4(21), 63(22), 51(16), 39(18). (Fig. 20)

9. trans-2,3-diphenylcyclopropane carboxylic acid, 15

A mixture of 18 g of trans-stilbene, 0.6 g of anhydrous copper sulfate and 30 mL of benzene was heated with an oil bath at 80°C under nitrogen with mechanical stirring. Then 22 g of ethyl diazoacetate in 10 mL of benzene was added dropwise through a dropping funnel over a period of 5 hours. The excess trans-stilbene was

filtered off from the cooled reaction mixture. The solvent was then removed under reduced pressure. The residue was distilled in vacuo. Ethyl trans-2,3-diphenylcyclopropyl carboxylate was collected at 156°C at 0.3 mm Hg. The oil was then dissolved in 150 mL 95% ethanol and 30 mL 10% sodium hydroxide. The mixture was refluxed on a steam bath for 3 hours. The alcohol was distilled off with steam. The aqueous solution was filtered once to remove any solid particles and then acidified with 10% sulfuric acid. The yellow solid formed was collected on a Buchner funnel to give 20 g (84% yield), mp 152°-154°C (Lit.[67] 155°-157°C).

^{1}H NMR: δ= 7.2(m), 3.2(t), 2.8(t), 2.2(t). (Fig. 21)

IR: 3077(s), 1686(s), 1447(s), 1220(s), 698(s). (Fig. 22)

MASS: calculated for $C_{16}H_{14}O_2$ m/e 238.2354; measured m/e 238.05, 238(17), 237(15), 219(37), 192(100), 191(13), 189(30), 178(24), 165(21), 159(23), 115(61), 91(20). (Fig. 23)

10. (+)-trans-2,3-diphenylcyclopropane carboxylic acid, (+)-15

To a solution of 5.6 g of racemic acid 15 in 70 mL of hot methanol was added 2.85 g of S-(-)-α-methylbenzylamine. The mixture was kept in the freezer overnight. The resulting solid was filtered off and recrystallized twice from methanol to give white crystals, mp 189°-191°C.

The solid product was suspended in 50 mL of water and 10% sodium hydroxide was added until all solid dissolved. The solution was then extracted twice with 10 mL of ether and the aqueous layer was acidified with concentrated

hydrochloric acid. The acid was collected on a Buchner funnel, mp 134°-136°C.
^{1}H NMR, IR and MASS were same as for the racemic mixture.

11. N-[(S)-α-methylbenzyl]-trans-2,3-diphenylcyclopropane- 1-carboxamide

Acid 15 was stirred with excess thionyl chloride (15 mL) at room temperature for 1 hour. The excess thionyl chloride was then removed under reduced pressure. Then 10 mL dry benzene was added and the solution was transferred to a dropping funnel which was attached on a flask. The flask was charged with 0.7 mL (-)-α-methylbenzylamine, 2 mL dry pyridine and 15 mL dry benzene. The flask was cooled with an ice bath, and the acid chloride solution was added dropwise with stirring under nitrogen. The stirring was continued for another 3 hours at room temperature. The reaction mixture was then washed successively with dilute hydrochloric acid, dilute sodium hydroxide and water. The solvent was removed under reduced pressure to give crude amide which was recrystallized from ethanol/water. The amide made from racemic acid had mp 131°-148°C, while the amide made from (+)-acid had mp 166°-167°C.

^{1}H NMR: δ= From (±)-15; 7.2(m), 4.9(m), 3.2(m), 2.8(m), 2.2(m), 1.4(d), 1.2(d). (Figs. 24-25)
From (-)-15; 7.2(m), 4.9(m), 3.2(q), 2.8(q), 2.2(q), 1.4(d). (Figs. 26-27)

IR: 3324(s), 1649(s), 1541(s), 1495(m), 1447(m), 1220(m), 785(m), 690(s). (Fig. 28)

MASS: calculated for $C_{24}H_{23}NO$ m/e 341.17797; measured m/e 341.17731, 341(1.6), 194(35), 193(100), 178(19), 116(10), 115(76), 105(42), 91(17),

77(13). (fig. 29)

12. (+)-ethyl nitroso-trans-2,3-diphenylcyclopropane-1-carbamate, (+)-19

To 1.37 g of acid (+)-15 was added 15 mL thionyl chloride, and the resulting mixture stirred at room temperature for 1 hour, after which all traces of thionyl chloride were removed by distillation under reduced pressure. To the residual acid chloride was added 15 mL of dry acetone. The mixture was then stirred and cooled in an ice bath. To the cold solution was rapidly added 0.5 g of sodium azide dissolved in a minimum amount of water. The resulting mixture was stirred with cooling for 1 hour, after which it was poured into water and extracted with benzene. The benzene layer was dried over anhydrous magnesium sulfate. The benzene solution of acid azide was refluxed for 3 hours, after which 50 mL of ethanol was added. The mixture was then refluxed for another 3 hours. Removal of the solvent gave a brown oil. This oil was subjected to nitrosation without further purification, as follows.

A mixture of 0.2 g of the brown oil, 0.5 g of anhydrous sodium acetate, 0.35 g of anhydrous sodium sulfate and 20 mL of dry methylene chloride was cooled to -20°C, and a solution of excess dinitrogen tetroxide in ether (prepared by bubbling the gas into ether at -50°C) was added all at once to the cooled stirring solution. The excess dinitrogen tetroxide and some solvent were removed in vacuo, followed by the addition of 15 mL of cold ether. The reaction mixture was then washed once with cold saturated sodium chloride solution, twice with cold saturated sodium chloride-5% sodium bicarbonate

solution,and once again with saturated sodium chloride solution. The organic layer was dried over sodium sulfate and evaporated at room temperature by use of a rotatory evaporator to yield a yellow oil. This oil was chromatographed over a column of deactivated silica (prepared by slowly packing silica with water-saturated ether and eluting with dry 50% pentane-ether) to give the N-nitroso-carbamate as a yellow oil.

IR: 3050(m), 2154(s), 1755(s), 1720(s), 1526(s), 1499(s), 1377(m), 1225(s), 1186(s), 760(s) 698(s). (Fig. 30)

13. Reaction of N-nitrosocarbamate 19 with base

The general reaction procedure was to take 30 mg of the N-nitrosocarbamate dissolved in 30 mL of hexane (or different solvent), and add the base to this solution at the desired temperature under nitrogen. Stirring was continued for 15 minutes. Dilute hydrochloric acid was then added, and the aqueous layer separated and extracted twice with 10 mL hexane. The organic layers were combined and washed with 5% sodium bicarbonate and water. The solvent was removed under reduced pressure after which the crude product was thin layer chromatographed over silica with hexane. Analysis of the allene band by GC using a DB-1 capillary column gave only one peak (GC conditions involved a 80°-280°C temperature program). The allene-containing band was concentrated in vacuo and subjected to NMR analysis.

14. 1,1-dichloro-trans-2,3-diphenylcyclopropane

A mixture of 13 g of trans-stilbene, 30 mL of chloroform, 30 mL of 50% sodium hydroxide and 0.5 g of

benzyltriethylammonium chloride was stirred mechanically for 24 hours. The crude mixture was filtered and extracted into 300 mL of pentane. The pentane extract was washed successively with dilute hydrochloric acid, 10% sodium bicarbonate and water. The solvent was removed and the crude product distilled at 104°C/0.025 mm Hg (Lit.[73] 130°C/0.2 mm Hg) to give 16 g (85% yield) solid, mp 46°-47°C.

^{1}H NMR: δ= 7.4(s), 3.2(s). (Fig. 31)

IR: 3067(s), 3034(s), 1601(s), 1497(s), 1451(s), 1220(s), 1090(s), 780(s), 695(s). (Fig. 32)

MASS: 264(3), 263(1), 229(25), 228(13), 227(74), 192(32), 191(72), 189(18), 165('15), 151(32), 149(100). (Fig. 33)

15. 1-chloro-trans-2,3-diphenylcyclopropane carboxylic acid, 16

A solution of 4.55 g of 1,1-dichloro-trans-2,3-diphenylcyclopropane in 100mL of dry THF was cooled with a dry ice/acetone bath. Then 6 mL 2.5 M n-butyllithium in hexane was added dropwise through a dropping funnel with stirring under nitrogen. Anhydrous carbon dioxide was bubbled through for 15 minutes after which the mixture was allowed to warm up to room temperature. The reaction mixture was extracted twice with 15 mL of water.

The aqueous layers were combined and washed with ether. The aqueous layer was acidified with concentrated hydrochloric acid. The acidic solution was extracted twice with 15 mL of ether. The ether layers were combined and washed with water. The ether was removed after which the product was crystallized from carbon

tetrachloride and hexane to give 1.63 g of white solid, mp 152°- 155°C.

^{1}H NMR: δ= 7.3(m), 3.8(d), 3.4(d). (Fig. 34)

IR: 3036(w), 1690(m), 1460(m), 950(m), 698(s). (Fig. 35)

MASS: calculated for $C_{16}H_{13}ClO_2$ m/e 272.06041; measured m/e 272.06051, 274(16), 273(9), 272(49), 237(22), 236(46), 219(69), 192(72), 191(100), 189(31), 165(23), 159(50), 131(21), 115(31), 91(19). (Fig. 36)

16. (-)-1-chloro-trans-2,3-diphenylcyclopropane carboxylic acid, (-)-16

To a solution of 1.63 g of racemic acid 16 in 25 mL hot methanol was added 0.7 mL of (-)-α-methylbenzylamine, and the mixture kept in the freezer overnight. The resulting solid was collected on a Buchner funnel and recrystallized twice from methanol, mp 187°-190°C. The salt was suspended in 50 mL of water and 10% sodium hydroxide was added until all solid was completely dissolved. The basic solution was washed with ether and acidified with concentrated hydrochloric acid. The solution was extracted twice with 10 mL ether and the combined ether layers were washed with water. The solvent was removed and the crude product recrystallized from carbon tetrachloride to give a white solid, mp 135°-137°C, $[\alpha]_D$= -29.1° (0.0086 g).

^{1}H NMR, IR and MASS were same as for the racemic mixture.

17. N-[(S)-α-methylbenzyl]-1-chloro-trans-2,3-diphenylcyclopropane-1-carboxamide

Chloro acid 16 (0.21 g) was refluxed with 15 mL of

thionyl chloride for 1 hour, after which excess thionyl chloride was distilled off in vacuo. Then 15 mL of dry benzene was added into the acid chloride residue, and the resulting solution transferred to a dropping funnel, whereupon it was added to a mixture of 0.1 mL (-)-α-methylbenzylamine, 10 mL of dry pyridine and 10 mL dry benzene under nitrogen. The mixture was stirred at room temperature for 2 hours. It was then washed successively with 10% hydrochloric acid, saturated sodium bicarbonate and water. The solvent was removed under reduced pressure and then the residue thin layer chromatographed over silica with benzene.

^{1}H NMR:δ= From (±)-16: 7.2-7.4(m), 4.9(m), 3.9(t), 3.3(q), 1.5(d), 1.3(d). (Figs. 37-39)
From (-)-16: 7.2-7.4(d), 4.9(m), 3.9(d), 3.3(d), 1.5(d). (Figs. 40-41)

MASS: calculated for $C_{24}H_{22}ClON$ m/e 375.19300; measured m/e 375.13919, 377(22), 376(16), 375(66), 235(30), 192(52), 191(41), 105(100), 77(20). (Fig. 42)

18.

(-)-1-bromo-1-chloro-trans-2,3-diphenylcyclopropane

A mixture of 0.22 g of chloroacid (-)-16 and 15 mL of thionyl chloride was refluxed for 1 hour, after which the excess thionyl chloride was distilled off in vacuo. Then 0.05 g of AIBN and 10 mL of dry chlorobenzene was added to the acid chloride, and the resulting solution transferred to a dropping funnel. A mixture of 0.2 g of N-hydroxy-pyridine-2-thione sodium salt, 15 mL of bromotrichloromethane and 10 mL of chlorobenzene was heated under nitrogen with vigorous stirring to 100°C.

The acid chloride solution was then added dropwise over a period of 30 minutes, and the reaction mixture heated for another 2 hours. After the mixture was cooled to room temperature, it was washed successively with 10% hydrochloric acid, 10% sodium carbonate and water. The solvent was removed in vacuo to give a yellow solid, which was recrystallized from ethanol/water to give 0.075 g (30%) white crystals, mp 77°-78°C, $[\alpha]_D$= -37.5° (0.0024 g).

^{1}H NMR:δ= 7.2(s), 3.4(d), 3.2(d). (Fig. 43)

IR: 3032(s), 1601(m), 1497(m), 1459(m), 1080(m), 756(s), 694(s). (Fig. 44)

MASS: calculated for $C_{15}H_{12}Br$ m/e 271.01224; measured m/e 271.01217, calculated for $C_{15}H_{12}Cl$ m/e 227.06276; measured 227.06269, 273(2), 271(2), 229(27), 228(14), 227(81), 192(36), 191(74), 189(21), 151(33), 149(100). (Fig. 45)

19. trans-di(4-methylphenyl)stilbene, 21a

A mixture of 11 g of α-chloro-p-xylene, 22 g of triphenylphosphine and 100 mL of xylene was heated to reflux for 18 hours. After the mixture was cooled to room temperature, the white crystalline precipitate was filtered off. Then 20 g of this solid were mixed with 6 g of p-tolualdehyde, 100 mL of ethanol and 6.3 g of potassium t-butoxide. The resulting reaction mixture was stirred for 1 hour at room temperature, after which 40 mL of water was added and the product was filtered off to give 5.5 g (50%) of olefin as a crystalline white solid, mp 179°-180°C.

^{1}H NMR:δ= 7.4(d), 7.2(d), 7.1(s), 2.4(s). (Fig. 46)

IR: 3021(m), 2915(m), 1514(m), 1450(m), 970(s),

822(s). (Fig. 47)

20. trans-di(4-chlorophenyl)stilbene, 21b

A mixture of 13 g of 4-chlorobenzylchloride, 22 g of triphenylphosphine and 100 mL of xylene was heated to reflux for 18 hours. After the mixture was cooled to room temperature, the white crystalline precipitate was filtered off. Then 20 g of this solid were mixed with 6.6 g of p-chlorobenzaldehyde, 100 mL of ethanol and 5.5 g of potassium t-butoxide. The resulting reaction mixture was stirred for 1 hour at room temperature, after which 40 mL of water was added and the product filtered off to give a white solid. This solid was then 100% isomerized by refluxing in toluene with iodine to afford 6.3 g of white crystals, mp 271°-272°C.

^{1}H NMR: δ= 7.5(d), 7.3(d), 7.1(s). (Fig. 48)

IR: 3050(m), 3017(m), 1591(m), 1493(s), 1400(m), 1090(s), 831(s). (Fig. 49)

21. Reaction of ethyl diazoacetate with trans-di(4-methylphenyl)stilbene and trans-di(4-chlorophenyl)stilbene, 22a,b

A mixture of 5 g of olefin, 0.8 g of anhydrous copper sulfate and 30 mL of benzene was heated to 80°C with mechanical stirring under nitrogen. Then 7 g of ethyl diazoacetate in 15 mL of benzene was added through a dropping funnel over a period of 5 hours. The product mixture was cooled to room temperature, and all solid residues filtered off. The solvent was then removed in vacuo, and 100 mL of 70% ethanol was added. A second filtration to remove the excess unreacted olefins was carried out. The crude esters were heated under reduced

pressure at 65°-70°C (0.03 mm Hg) to remove diethyl fumarate. Then the crude esters were saponified in 5% alcoholic sodium hydroxide solution. After the alcohol was distilled off, the basic solution was washed with ether and acidified with concentrated hydrochloric acid. The acidic mixture was then extracted twice with 25 mL of ether and the ether layers were combined and washed with water. The ether was then removed under reduced pressure. The crude acid was crystallized from ethanol/water to give:

(i) 23a, mp 135°-136°C (19% yield)

(ii) 23b, mp 185°-187°C (30% yield)

^{1}H NMR: δ= 23a: 7.0-7.2(m), 3.1(t), 2.9(t), 2.3(s). (Fig. 50)

23b: 7.1-7.3(m), 3.1(t), 2.9(t), 2.4(q). (fig. 51)

IR: 23a: 3050(s), 1700(s), 1520(m), 1450(m), 1250(s), 930(m), 820(s). (Fig. 52)

23b: 3256(s), 1734(s), 1701(s), 1450(m), 1400(m), 1159(s), 870(s). (Fig. 53)

MASS: 23a: calculated for $C_{18}H_{18}O_2$ m/e 266.13068; measured m/e 266.13021, 266(78), 251(22), 248(20), 221(100), 220(59), 207(25), 205(26), 129(65). (Fig. 54)

23b: calculated for $C_{16}H_{12}O_2Cl_2$ m/e 306.02144; measured m/e 306.02152, 310(8), 309(8), 308(41), 307(11), 306(61), 271(42), 263(63), 262(41), 261(100), 260(40), 228(20), 227(23), 226(50), 225(50), 191(38), 189(25), 149(60), 125(29), 94.5(20). (Fig. 55)

22. (-)-trans-2,3-di(4-methylphenyl)cyclopropane carboxylic acid, (-)-23a

A solution of 0.56 g of racemic acid 23a and 0.84 g of brucine (1 eq.) in 50 mL hot ethylacetate was kept in the freezer overnight. The solid formed was filtered and recrystallized from ethylacetate to give white crystals, mp 186°-189°C. A 0.5 g aliquot of this solid was dissolved in 10% sodium hydroxide solution and extracted three times with 10 mL portions of chloroform. The aqueous layer was then acidified with hydrochloric acid and extracted with ether. The ether extract was washed with water and the ether was removed in vacuo. The final white solid had mp 148°-150°C, $[\alpha]_D$= -26° (0.0098 g). ^{1}H NMR, IR and MASS were the same as the racemic mixture.

23. (-)-trans-2,3-di(4-chlorophenyl)cyclopropane carboxylic acid, (-)-23b

A mixture of 0.63 g of racemic acid 23b and 0.67 g of quinine was dissolved in 30 mL of hot ethanol, and the solution kept in the freezer 1 day. The solids formed were filtered off and recrystallized twice from ethanol to give white crystals, mp 218°-220°C (with decomposition). A 0.5 g aliquot of this solid was dissolved in 10% hydrochloric acid and extracted twice with 20 mL of chloroform. The combined chloroform extracts were washed with water, and the solvent removed in vacuo. The crude acid was then recrystallized from ethanol/water to give a white solid, mp 147°-148°C, $[\alpha]_D$= -42.3° (0.0098 g).
^{1}H NMR, IR and MASS were the same as the racemic mixture.

24. N-[(S)-α-methylbenzyl]-trans-2,3-

di(4-methylphenyl)cyclopropane-1-carboxamide

A 0.2 g sample of acid 23a was refluxed with 15 mL of thionyl chloride for 1 hour, after which the excess thionyl chloride were distilled off in vacuo. Then 10 mL of benzene was added and the acid chloride solution was transferred to a dropping funnel. The acid chloride solution was added dropwise to a mixture of 0.1 g of (-)-α-methylbenzylamine, 2 mL of pyridine and 10 mL of benzene while stirring at 0°C. The stirring was continued for 6 hours. The mixture was then washed successively with 10% hydrochloric acid, 10% sodium carbonate and water. The solvent was removed under reduced pressure. The crude amide was recrystallized from ethanol/water. The yield was about 70%. The melting point for the amide from the racemic acid was 161°-174°C, while (-)-23a gave amide with mp 135°- 137°C.

^{1}H NMR:δ= From (±)-23a: 6.9-7.4(m), 5.6(m), 5.0(m), 3.2(m), 2.7(t), 2.3(s), 2.2(m), 1.4(d), 1.3(d). (Figs. 56-58)

From (-)-23a: 6.9-7.4(m), 5.6(d), 5.0(t), 3.2(t), 2.7(t), 2.3(s), 2.2(q), 1.3(d). (Figs. 59-61)

IR: 3306(s), 2971(m), 1647(s), 1545(s), 1235(m), 702(m). (Fig. 62)

MASS: calculated for $C_{26}H_{27}NO$ m/e 369.20927; measured m/e 369.20974, 369(4), 222(68), 221(100), 129(29), 105(33). (Fig. 63)

25. N-[(S)-α-methylbenzyl]-trans-2,3-di(4-chlorophenyl)cyclopropane-1-carboxamide

A mixture of 0.25 g of acid 23b and 15 mL of thionyl chloride was refluxed for 1 hour, after which the excess

thionyl chloride was distilled off in vacuo. Then 10 mL of benzene was added and the acid chloride solution was transferred to a dropping funnel. The acid chloride solution was then added dropwise to a mixture of 0.1 g of (-)-α-methylbenzylamine, 2 mL of pyridine and 10 mL of benzene, while stirring at room temperature. The stirring was continued for 3 hours. The mixture was washed successively with 10% hydrochloric acid, 10% sodium carbonate and water. The solvent was then removed in vacuo. The crude amide was recrystallized from ethanol/water. The yield was about 80%. The racemic acid gave an amide with mp 158°-170°C, while the (-)-23b gave an amide with mp 130°-132°C.

^{1}H NMR:δ= From (±)-23b: 7.1-7.3(m), 5.7(m), 5.0(t), 3.2(m), 2.7(m), 2.2(m), 1.4(d), 1.3(d). (Figs. 64-66)
From (-)-23b: 7.1-7.3(m), 5.7(d), 5.0(t), 3.2(q), 2.7(q), 2.2(q), 1.3(d). (Fig. 67-69)

IR: 3322(s), 3030(m), 1649(s), 1532(s), 1493(s), 1092(m), 872(m), 704(m). (Fig. 70)

MASS: calculated for $C_{24}H_{21}Cl_2NO$ m/e 409.10003; measured m/e 409.10079, 411(1.4), 410(0.7), 409(2), 265(12), 264(14), 263(67), 262(22), 261(87), 227(18), 105(100). (Fig. 71)

26. ethyl nitroso trans-2,3-di(4-methylphenyl) cyclopropane-1-carbamate

A mixture of 0.266 g of acid (-)-23a, 0.158 g of triethylamine, 100 mL of benzene and 0.289 g of diphenylphosphorylazide was refluxed for 5 hours. Then 50 mL of ethanol was added and refluxing continued for another 3 hours. The mixture was then washed

successively with 5% citric acid solution, saturated sodium bicarbonate and water. The solvent was removed and the product recrystallized from ethanol/water to give 0.234 g (76% yield), mp 63°-65°C, $[\alpha]_D$= -82° (0.0039 g).

^{1}H NMR: δ= 7.0-7.5(m), 4.5(s), 4.1(q), 3.1(m), 2.6(m), 2.5(m), 2.4(s), 2.3(s), 1.2(t). (Fig. 72)

IR: 3347(s), 1694(s), 1516(s), 1250(s). (Fig. 74)

MASS: calculated for $C_{20}H_{23}NO_2$ m/e 309.17288;measured m/e 309.17295, 310(5), 309(27), 294(42), 280(20), 237(16), 236(61), 221(27), 220(100), 219(73), 205(21), 178(20), 118(23), 105(39). (Fig. 76)

A mixture of 0.11 g of carbamate, 15 mL of acetic anhydride, 0.25 g of sodium nitrite and 50 μL of acetic acid was cooled in an ice bath and stirred for 2 hours. The mixture was then poured into 250 mL of ice water. The solution was extracted with 150 mL of hexane and was washed with cold 5% sodium bicarbonate and water. The solvent was removed in vacuo. The product was dried on a vacuum line.

27. ethyl nitroso trans-2,3-di(4-chlorophenyl) cyclopropane-1-carbamate

A mixture of 0.307 g of acid (-)-23b, 0.152 g of triethylamine, 100 mL of benzene and 0.289 g of diphenylphosporyl azide was refluxed for 5 hours. Then 50 mL of ethanol was added and refluxing continued for another 3 hours. The mixture was then washed with 5% citric acid solution, saturated sodium bicarbonate and water. The solvent was removed and the product recrystallized from ethanol/water to give 0.234 g (67% yield), mp 77°-79°C, $[\alpha]_d$= -117.9° (0.0053 g).

^{1}H NMR: δ= 7.3(m), 4.5(s), 4.1(q), 3.1(m), 2.5(m), 1.2(t). (Fig. 73)

IR: 3368(s), 2976(s), 1680(s), 1597(s), 1256(s), 795(s). (Fig. 75)

MASS: calculated for $C_{18}H_{17}Cl_2NO_2$ m/e 349.06364; measured m/e 349.06394, 353(7), 352(10), 351(40), 350(20), 349(66), 322(37), 320(50), 278(67), 277(23), 276(94), 262(35), 261(50), 260(48), 259(70), 248(23), 225(30), 212(20), 179(30), 178(100), 176(26), 149(40), 138(38), 125(48), 81(26), 69(44). (Fig. 77)

A mixture of 0.125 g of carbamate, 15 mL of acetic anhydride, 0.25 g of sodium nitrite and 50 μL of acetic acid was cooled in an ice bath and stirred for 2 hours. The mixture was then poured into 250 mL of ice water. The solution was extracted with 150 mL of hexane and washed with cold 5% sodium bicarbonate and water. The solvent was removed in vacuo. The product was dried on a vacuum line.

(a) 1,3-di(4-methylphenyl)allene

^{1}H NMR: with chiral shift reagents δ= 7.2(t), 7.1(d), 6.6(s), 6.5(s), 2.4(s). (Figs. 78-79)

MASS: 221(16), 220(90), 206(18), 205(100), 203(19), 202(19). (Fig. 82)

(b) 1,3-di(4-chlorophenyl)allene

^{1}H NMR: with chiral shift reagents δ= 7.2(s), 6.7(s), 6.6(s). (Fig. 80-81)

MASS: 262(23), 260(33), 227(40), 225(100), 189(44), 75(26), 63(27), 50(24). (fig. 83)

28. 1-ethoxycyclohexene

Equimolar quantities of cyclohexanone and triethyl orthoformate (1 mole each) were mixed with 5 mmol of p-toluenesulfonic acid. The mixture was stirred at room temperature for 24 hours. The ethanol was removed by fractional distillation, after which the reaction mixture was heated to reflux for another 4 hours. The product was distilled off after reflux, bp 85°-87°C (60 mm Hg).

^{1}H NMR: δ= 3.6(q), 1.3-2.4(m), 1.2(t). (Fig. 84)

IR: 2976(s), 2933(s), 1716(s), 1664(s), 1446(m), 1375(m), 1190(s) (Fig. 85)

MASS: 126(36), 98(44), 97(45), 83(79), 70(68), 55(100). (Fig. 86)

29. 1-ethoxybicyclo[4.1.0]heptane-7-carboxylic acid, 27

A mixture of 20 mL of 1-ethoxycyclohexene, 0.3 g of copper bronze, 0.1 g of cuprous chloride and 0.3 g of anhydrous copper sulfate was heated at 80°C in an oil bath under nitrogen with mechanical stirring. Then 20 mL of ethyl diazoactate and 5 mL of 1-ethoxycyclohexene were added dropwise over a period of 4 hours. The ester (19 g) was collected at 80°-84°C (0.3 mm Hg).

^{1}H NMR: δ= 4.0(m), 3.5(m), 1.4-2.2(m), 1.2(t), 1.1(t). (Fig. 87)

IR: 2978(s), 2934(s), 1730(s), 1448(m), 1369(s), 1182(s), 1153(s). (Fig. 88)

MASS: 212(2), 183(21), 137(100), 124(19), 96(38), 55(41). (Fig. 89)

Next 3 g of sodium hydroxide was dissolved in 15 mL of water, and 100 mL of 95% ethanol was added to the basic solution; then 5 g of the esters was added to the basic solution and the resulting solution stirred

vigorously for 3 hours. The ethanol was removed in vacuo at room temperature, after which 50 mL of water was added. The aqueous layer was washed once with ether and then acidified with concentrated hydrochloric acid. The resulting mixture was extracted with ether and the organic layer was washed with water. After removal of ether, the crude product was dried under vacuum. This crude product could not be distilled under reduced pressure because it decomposed to a compound that has the same molecular weight in MS analysis (Fig. 90), while the IR shows it is more like an ester (Fig. 91, ^{1}H- and ^{13}C-NMR: Figs. 92-93).

This problem also occurred in the hydrolysis of ethyl-1-methoxybicyclo[4.1.0]heptane-7-carboxylate. After acidification the basic aqueous solution, an oil which could not be redissolved in base was obtained. This compound had the same molecular weight as the expected acid in MS analysis (Figs. 94-96). In both cases, we think the acidic proton catalyzed an intramolecular alkoxy transfer to give, after ring-opening, a cycloalkanone carboxylic acid ester, of currently unidentified structure.

^{1}H NMR: δ= 3.6(m), 3.2-3.4(m), 1.3-2.1(m), 1.1(t). (Fig. 97)

IR: 3500(b), 2936(m), 1697(s), 1448(w), 1309(w), 1269(w), 1184(m). (Fig. 98)

30. ethyl-N-nitroso-1-ethoxybicyclo[4.1.0]heptane-7-carbamate, 30

A mixture of 1 g of acid 27, 15 mL of dry acetone and 0.8 g of triethylamine was cooled with an ice-ethanol bath. Then 0.9 g of ethylchloroformate in 15 mL of dry

acetone was added dropwise with vigorous stirring under nitrogen. The stirring was continued for 15 minutes, after which 1 g of sodium azide in 20 mL of water was added to the mixture dropwise. The stirring was continued for another 1 hour. The reaction mixture was then poured over 50 mL of ice-water and extracted with toluene. The organic layer was separated and dried over magnesium sulfate. The toluene solution was then heated to reflux for 1 hour under nitrogen, after which 50 mL of absolute alcohol was added and the solution refluxed overnight. After removal of solvents, the brown oil was separated over silica gel with toluene to give a yellow oil.

^{1}H NMR: δ= 4.0(b,m), 3.2-3.6(m), 1.0-2.0(m). (Fig. 99)

IR: 3437(s), 3325(b), 2976(s), 2935(s), 1707(s), 1527(s), 1253(m), 1060(m). (Fig. 100)

MASS: 226(1000), 196(35), 181(33), 153(20), 138(62), 125(53), 108(21), 81(21), 55(21). (Fig. 101)

A mixture of 0.506 g of the carbamate, 20 mL of acetic anhydride and 1.6 g of sodium nitrite was cooled with an ice bath under nitrogen with vigorous stirring. Then 10 μL of acetic acid was added to the mixture and the stirring was continued for 30 minutes. The reaction mixture was then poured over 100 mL of ice-water and was extracted with hexane. The organic layer was separated and washed succesively with cold 5% sodium bicarbonate solution and water. The solvent was removed in vacuo. The crude product was dried under reduced pressure.

^{1}H NMR: δ= 4.2(m), 3.3-4.0(m), 3.1(q), 1.1-2.0(m), 1.0(t) (Fig. 102)

IR: 3350(m), 2978(s), 2937(s), 2868(s), 2104(s), 1724(s), 1516(s), 1448(m), 1379(m). (Fig. 103)

31. Reaction of 30 with base

To a solution of 150 mg of 30 in 15 mL of hexane at room temperature was added 5 mL of 7.2 M sodium methoxide in methanol all at once under nitrogen with vigorous stirring. The stirring was continued for 30 minutes. The reaction mixture was quenched with water and extracted with more hexane. The organic layer was washed twice with water and was dried over sodium sulfate. The crude product was analyzed by GC, GC-MS and GC-IR.

GC-MS: chromatogram:(Fig. 104)
insertion product (Fig. 105)
methanol insertion product (Fig. 106)
other uncharacteristic products (Figs. 107-109)

32. 1-methoxy-7,7-dibromobicyclo[4.1.0]heptane[70]

A mixture of 11 g of potassium-t-butoxide, 6 g of 1-methoxycyclohexene[74] and 40 mL of pentane was cooled with a dry ice-CCl_4 bath. A solution of 13 g of bromoform in 30 mL of pentane was added dropwise over a 1 hour period with stirring under nitrogen. The stirring was continued for another hour and then water was added. The organic layer was separated and washed with water and then dried over sodium sulfate. The solvent was removed under reduced pressure and the residue was dissolved in pentane and passed over a column of 20 g of alumina. The first 75 mL of eluent was collected and concentrated in vacuo to give a yellow oil. The yellow oil was dissolved in pentane and cooled to -80°C. The supernatant was decanted from the crystals. This was repeated twice to give 8.5 g of a clear, colorless oil.

^{1}H NMR:δ= 3.4(s), 2.2(m), 2.9(d). (Fig. 110)

IR: 2939(s), 1444(m), 1205(m), 1109(m), 761(m). (Fig. 111)

MASS: 204(82), 202(84), 123(100), 108(25), 91(89), 79(50). (Fig. 112)

33. Reaction of 1-methoxy-7,7-dibromobicyclo[4.1.0]heptane with methyllithium

A solution of 0.52 g of the dibromide from experiment 33 in 15 mL of dry ether was cooled to -78°C. Next 10 equivalents of methyllithium were added dropwise with vigorous stirring under nitrogen. The stirring was continued for 15 minutes, and then the solution was warmed to room temperature and stirred for another 30 minutes. After quenching with water, the organic layer was washed twice with water and dried over sodium sulfate. Removal of solvent yielded a yellow oil which is the ring-opening product dimer, as previously described in the literature report.[70]

GC-MS: chromatogram (Fig. 113)

peak 1:155(100), 141(15), 123(10), 85(25), 73(23). (Fig. 114)

peak 2:248(80), 233(50), 125(100), 105(20). (Fig. 115)

SPECTRA

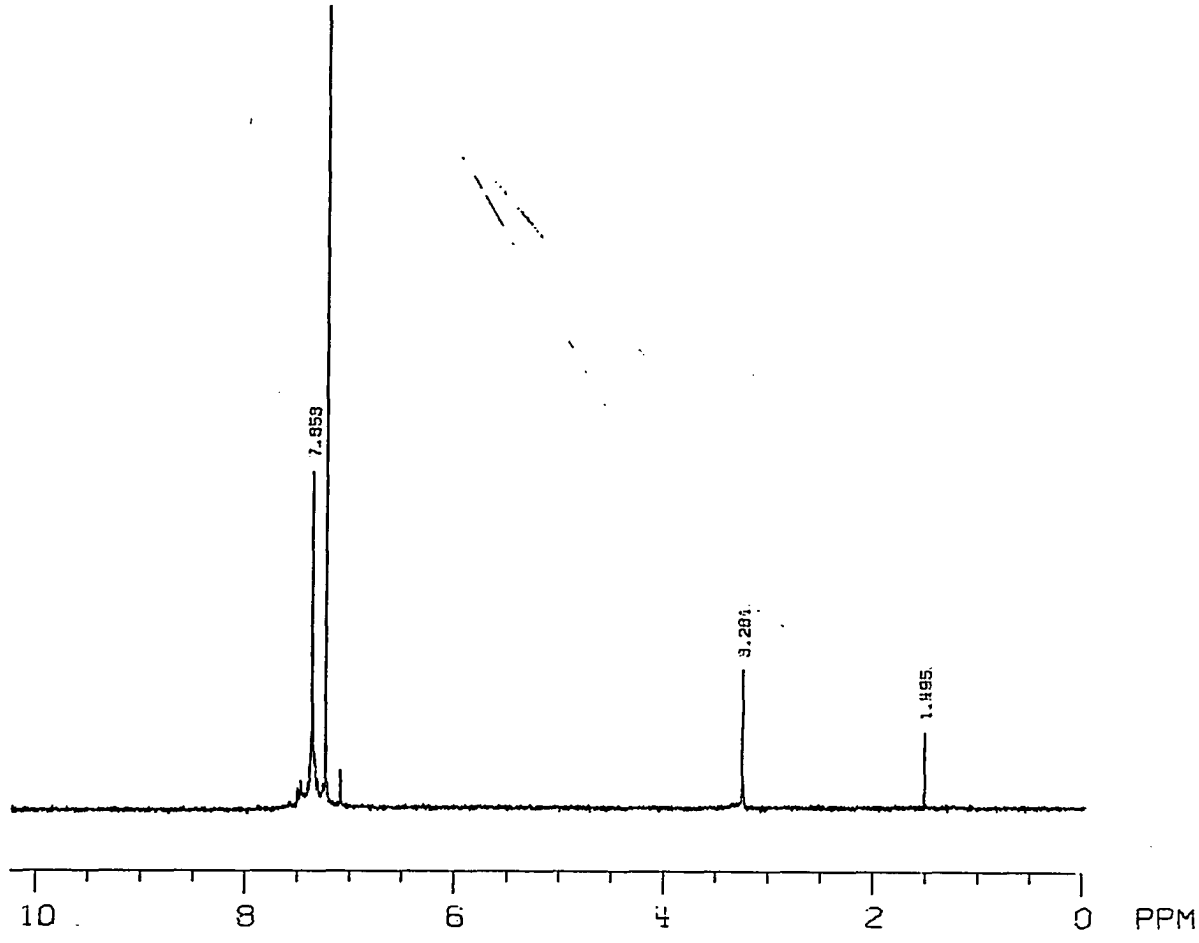


Figure 5. ^{1}H NMR of 1,1-dibromo-trans-2,3-diphenylcyclopropane

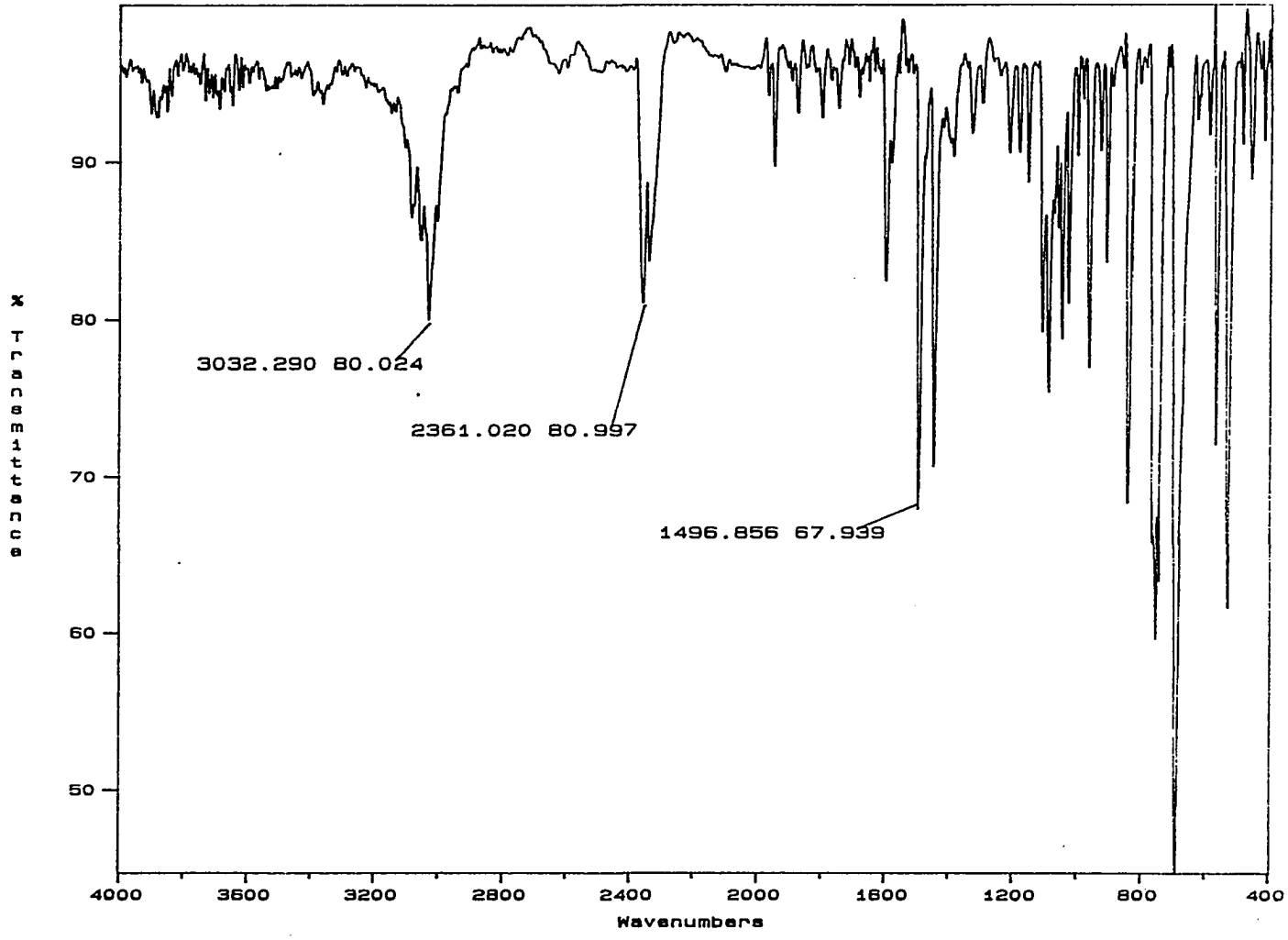


Figure 6. IR of 1,1-dibromo-trans-2,3-diphenylcyclopropane

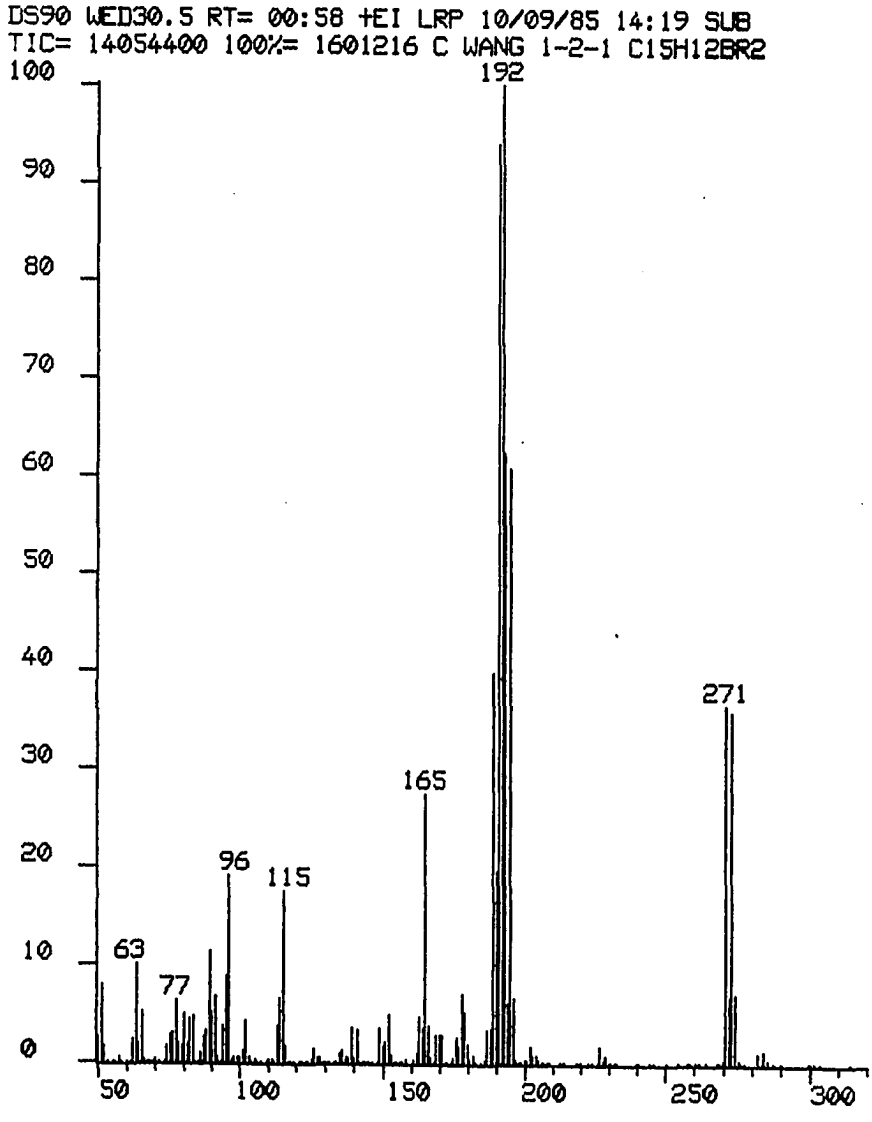


Figure 7. MASS of
1,1-dibromo-trans-2,3-diphenylcyclopropane

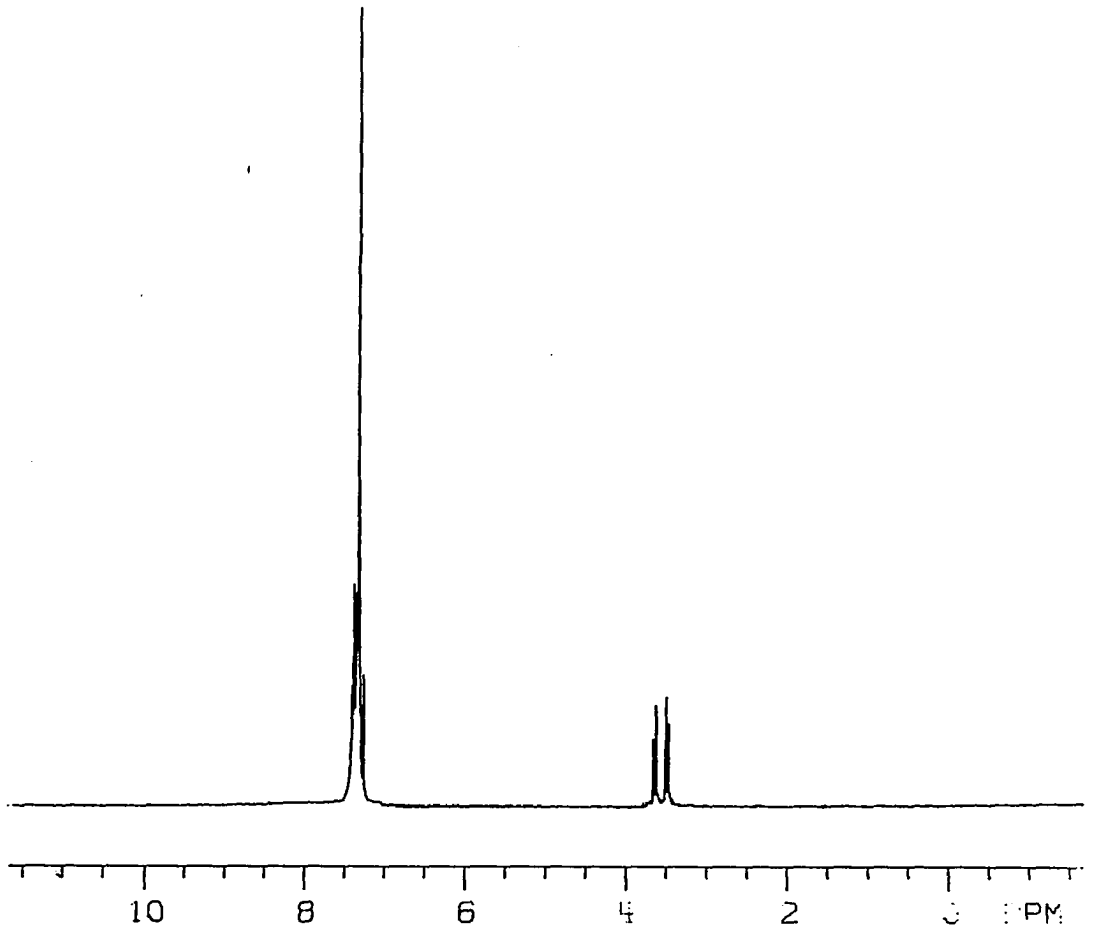


Figure 8. ^{1}H NMR of 1-bromo-trans-2,3-diphenylcyclopropane carboxylic acid

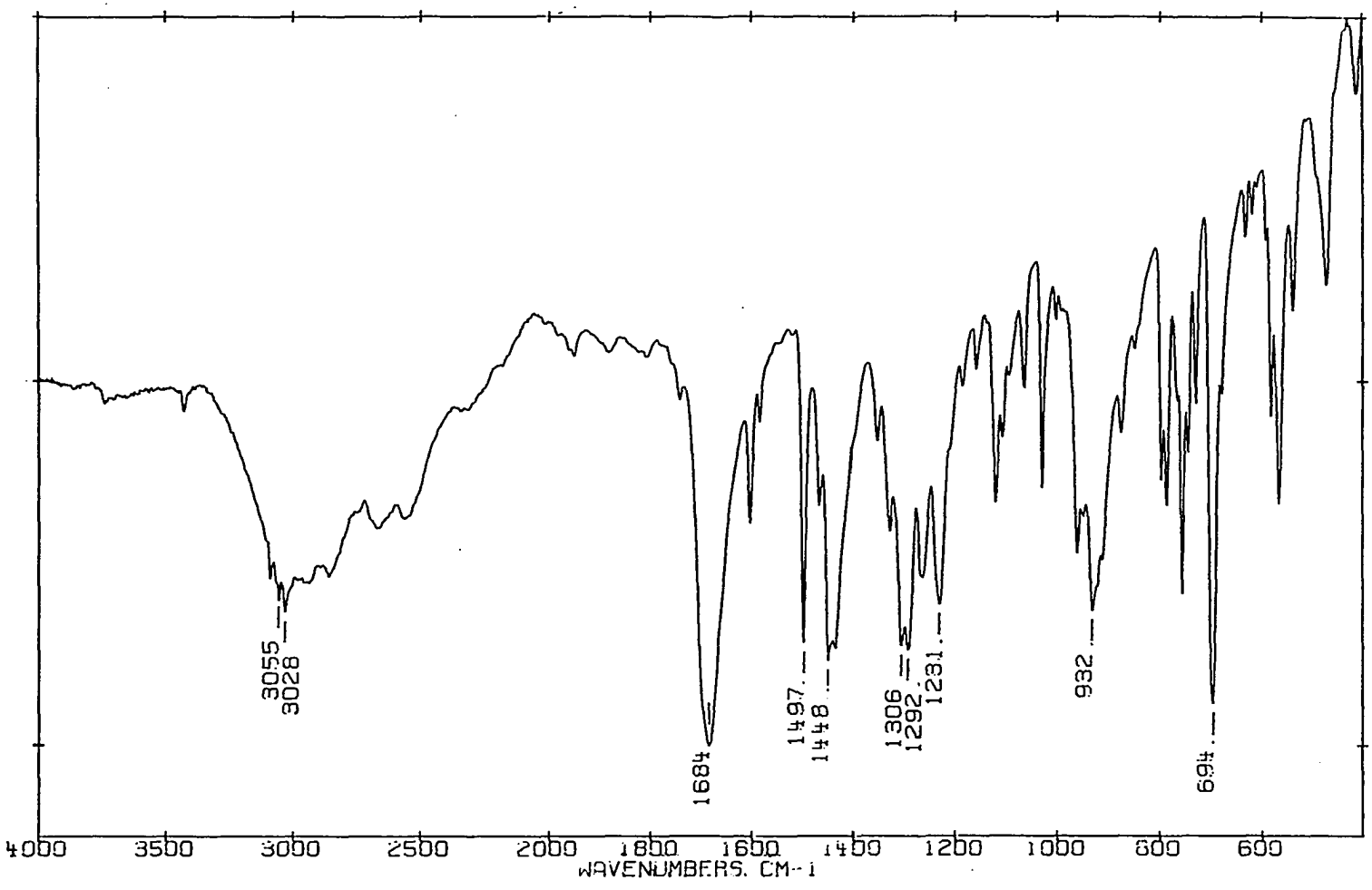


Figure 9. IR of 1-bromo-trans-2,3-diphenylcyclopropane carboxylic acid

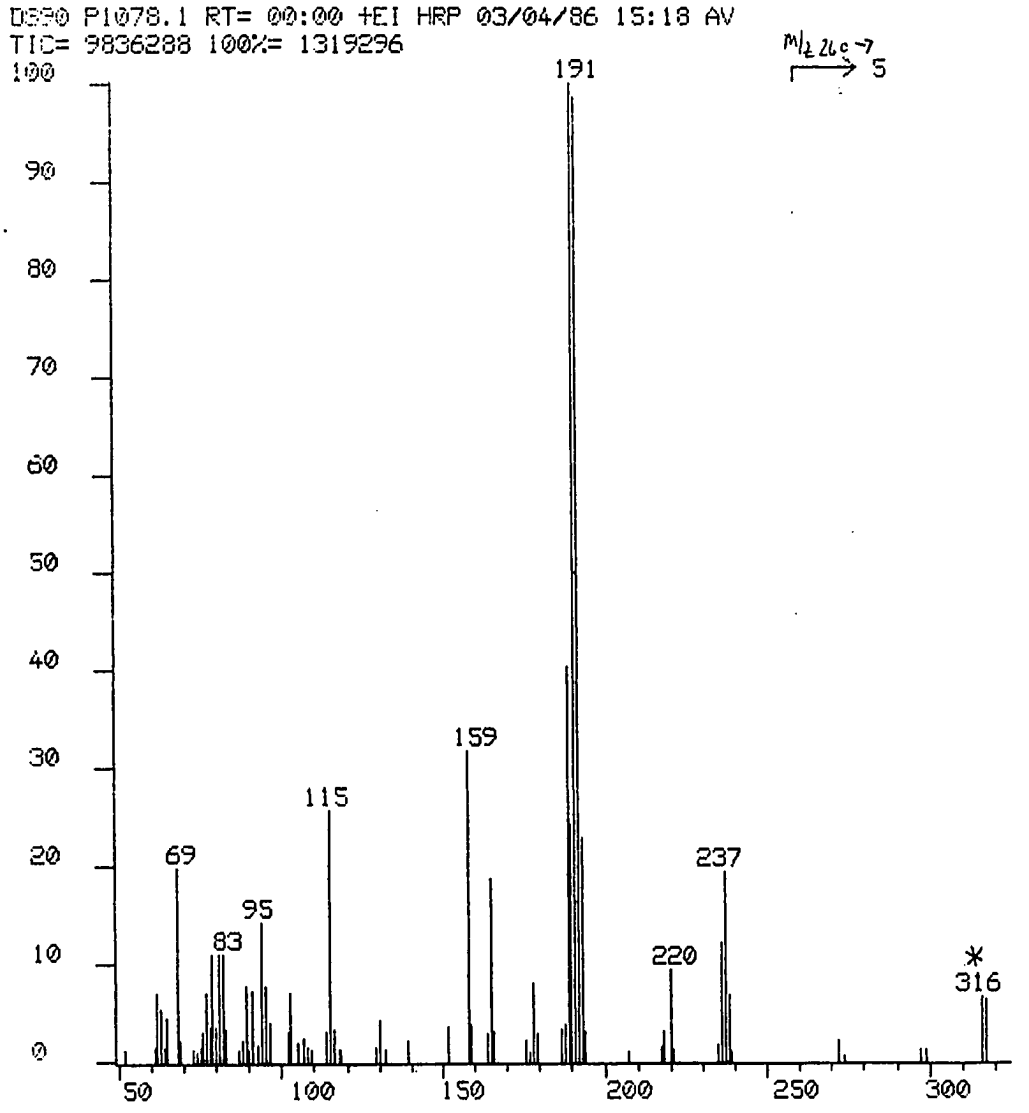


Figure 10. MASS of 1-bromo-trans-2,3-diphenylcyclopropane carboxylic acid

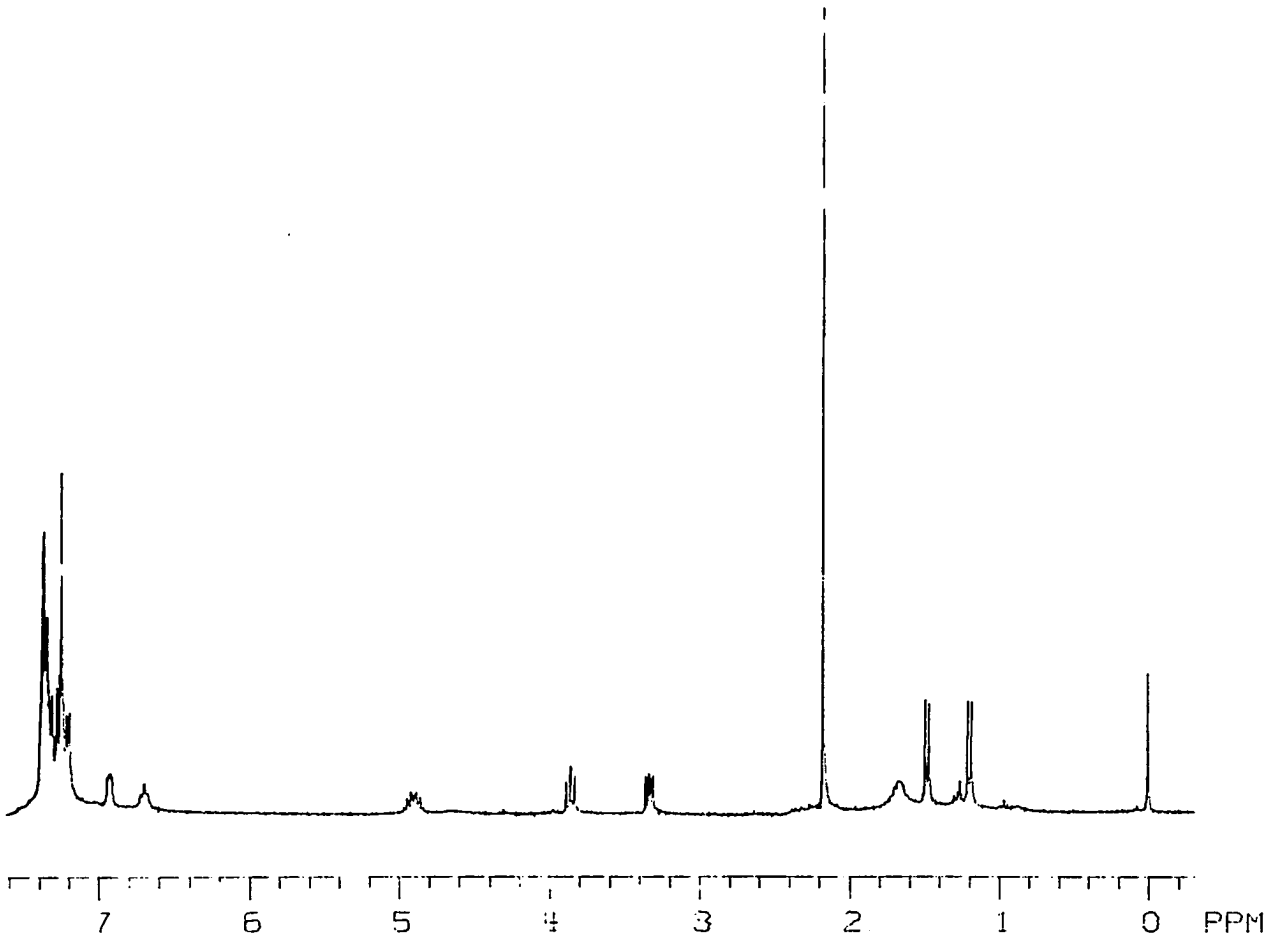


Figure 11. ^{1}H NMR of N-[(S)-α-methylbenzyl]-1-bromo-trans-2,3-diphenylcyclopropane-1-carboxamide from racemic acids

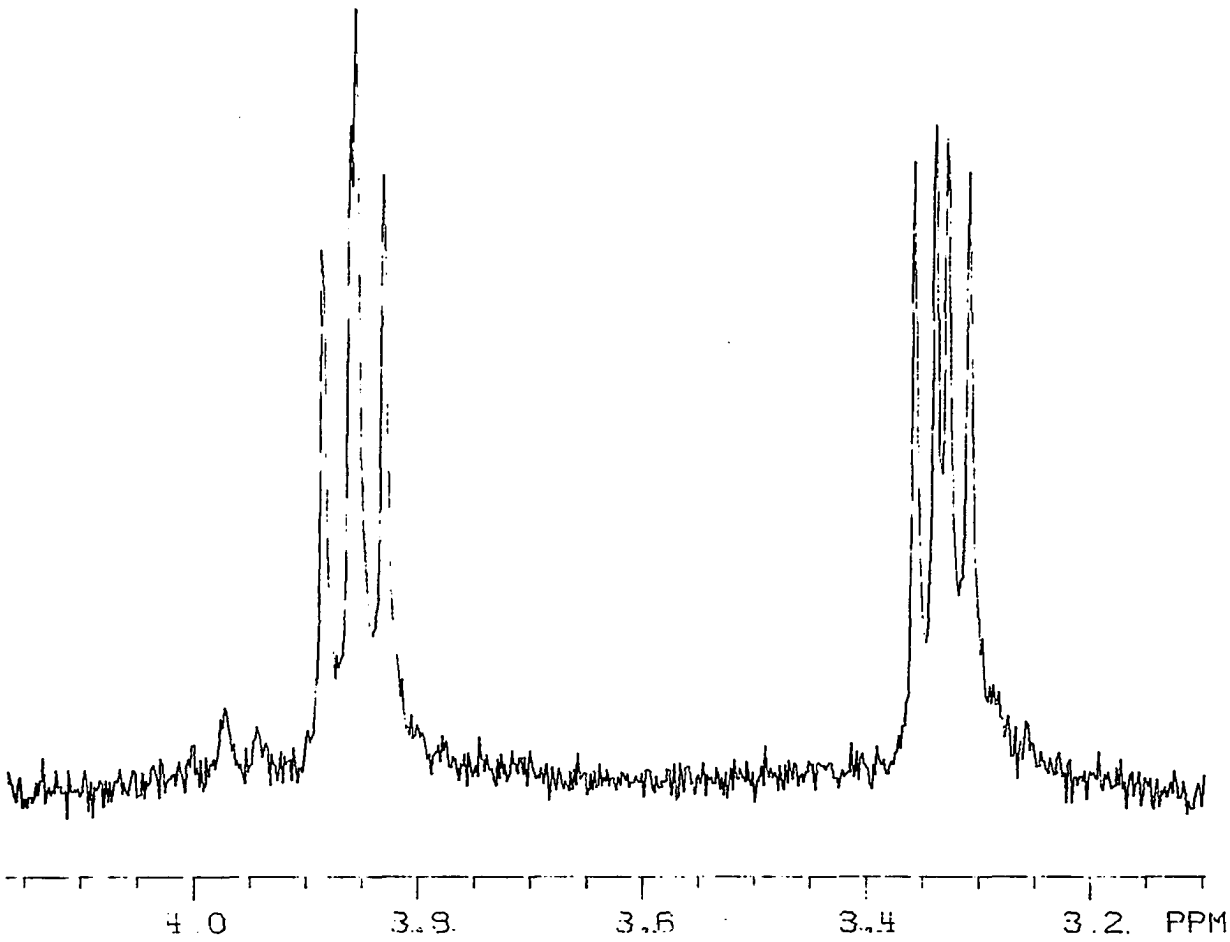


Figure 12. Partial enlargement in Figure 11

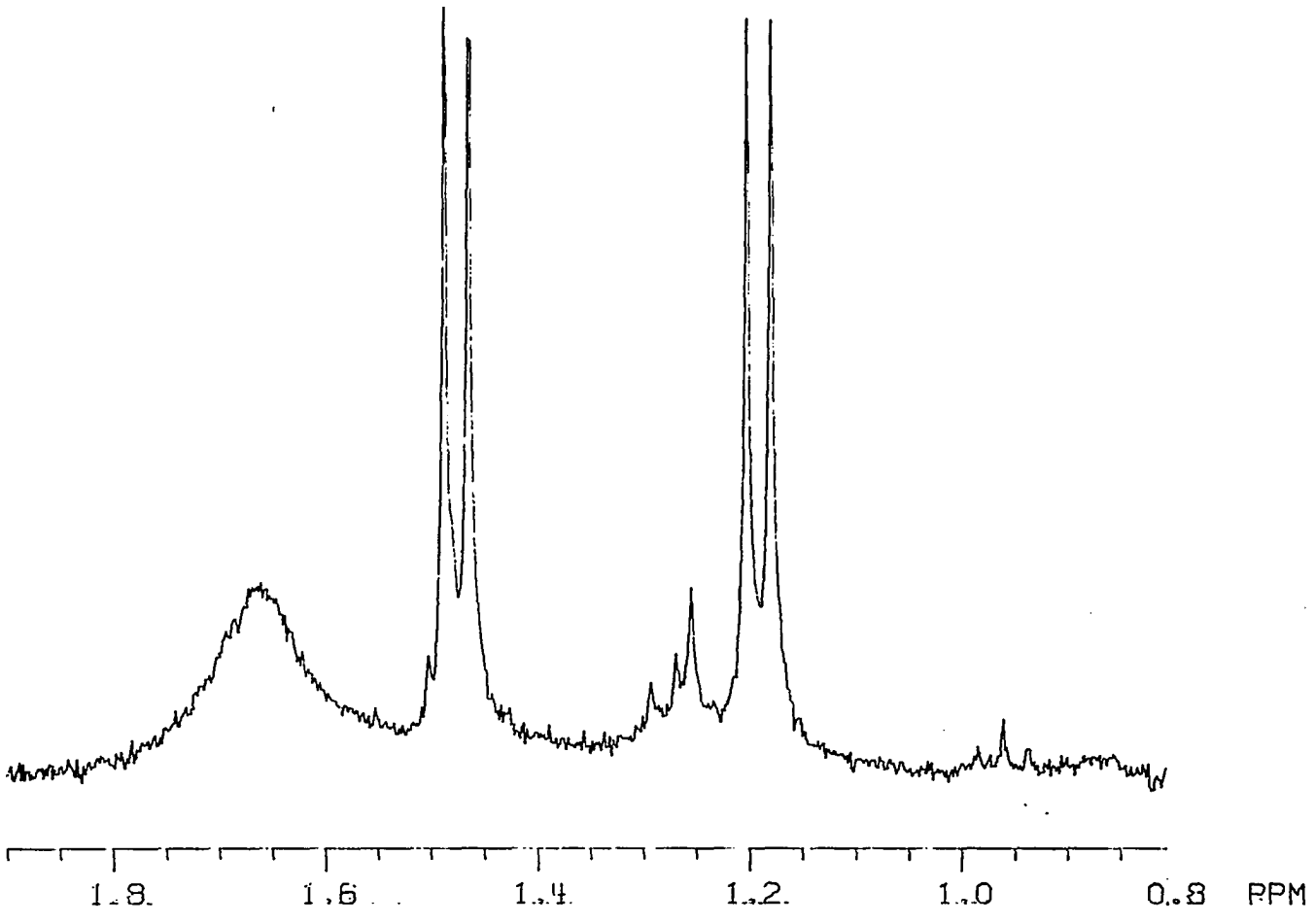


Figure 13. Partial enlargement in Figure 11

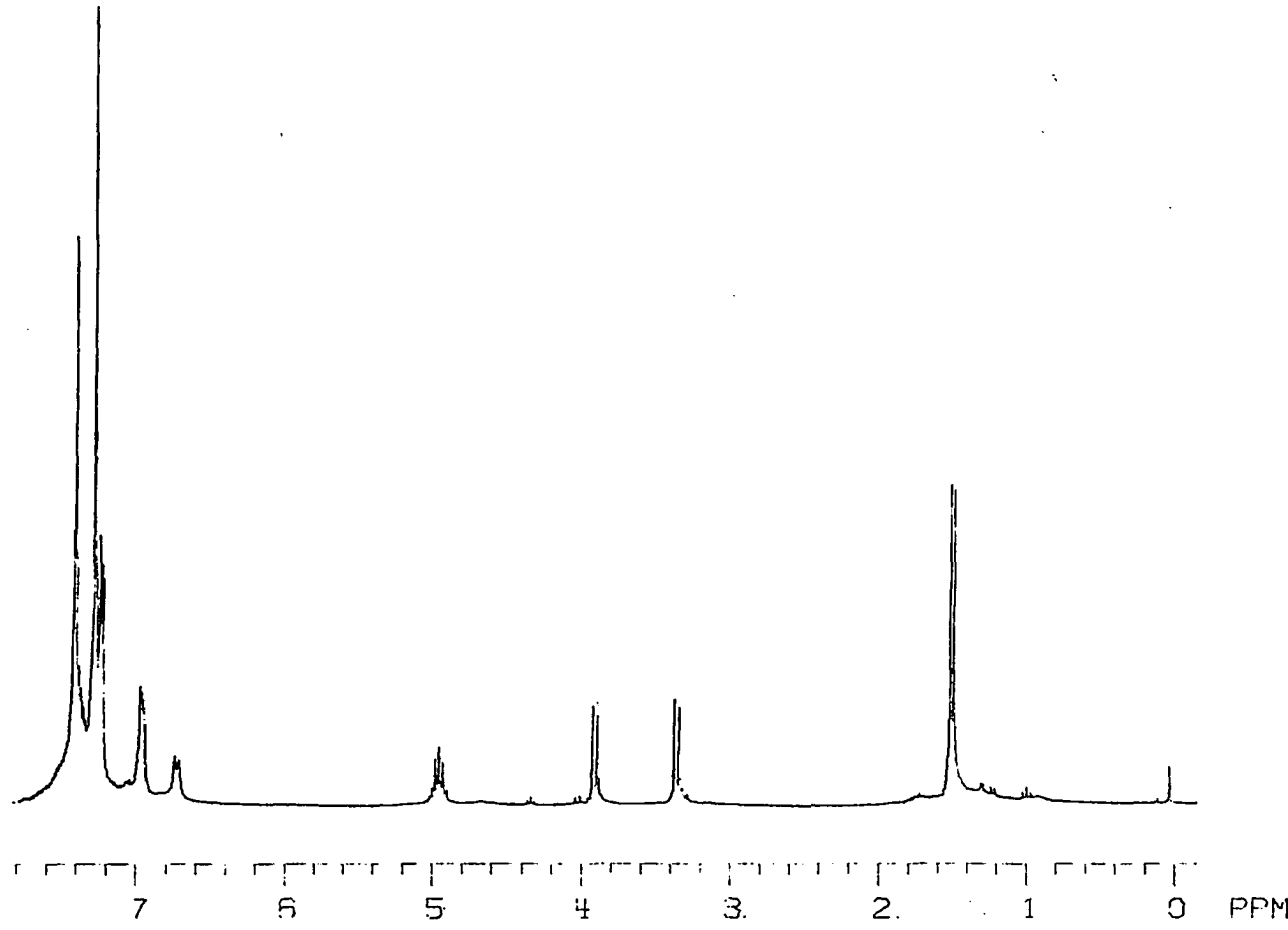


Figure 14. ^{1}H NMR of N-[(S)-α-metylbenzyl]-1-bromo-trans-2,3-diphenylcyclopropane-1-carboxamide from optically active acid

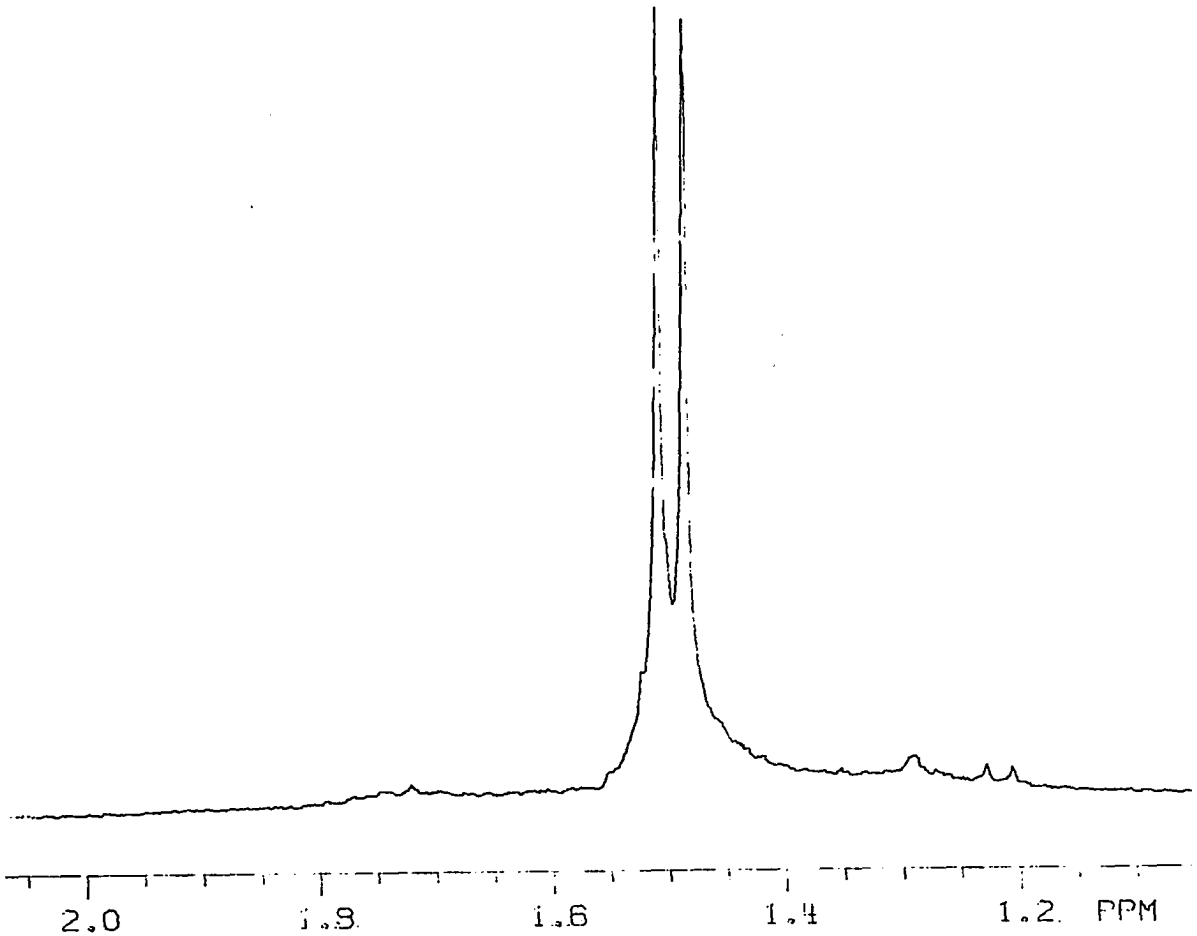


Figure 15. Partial enlargement in Figure 14

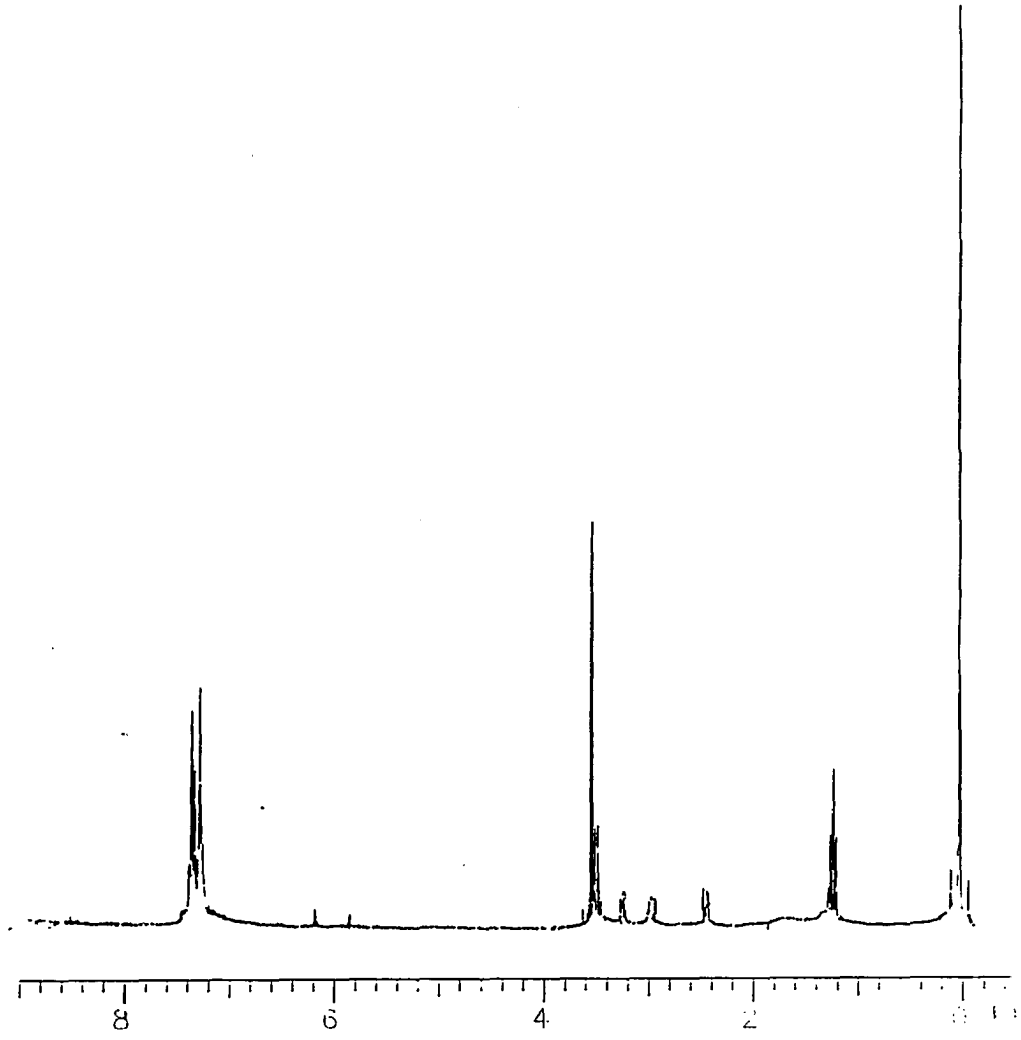


Figure 16. ^{1}H NMR of (-)-methyl trans-2,3-diphenylcyclopropane carboxylate

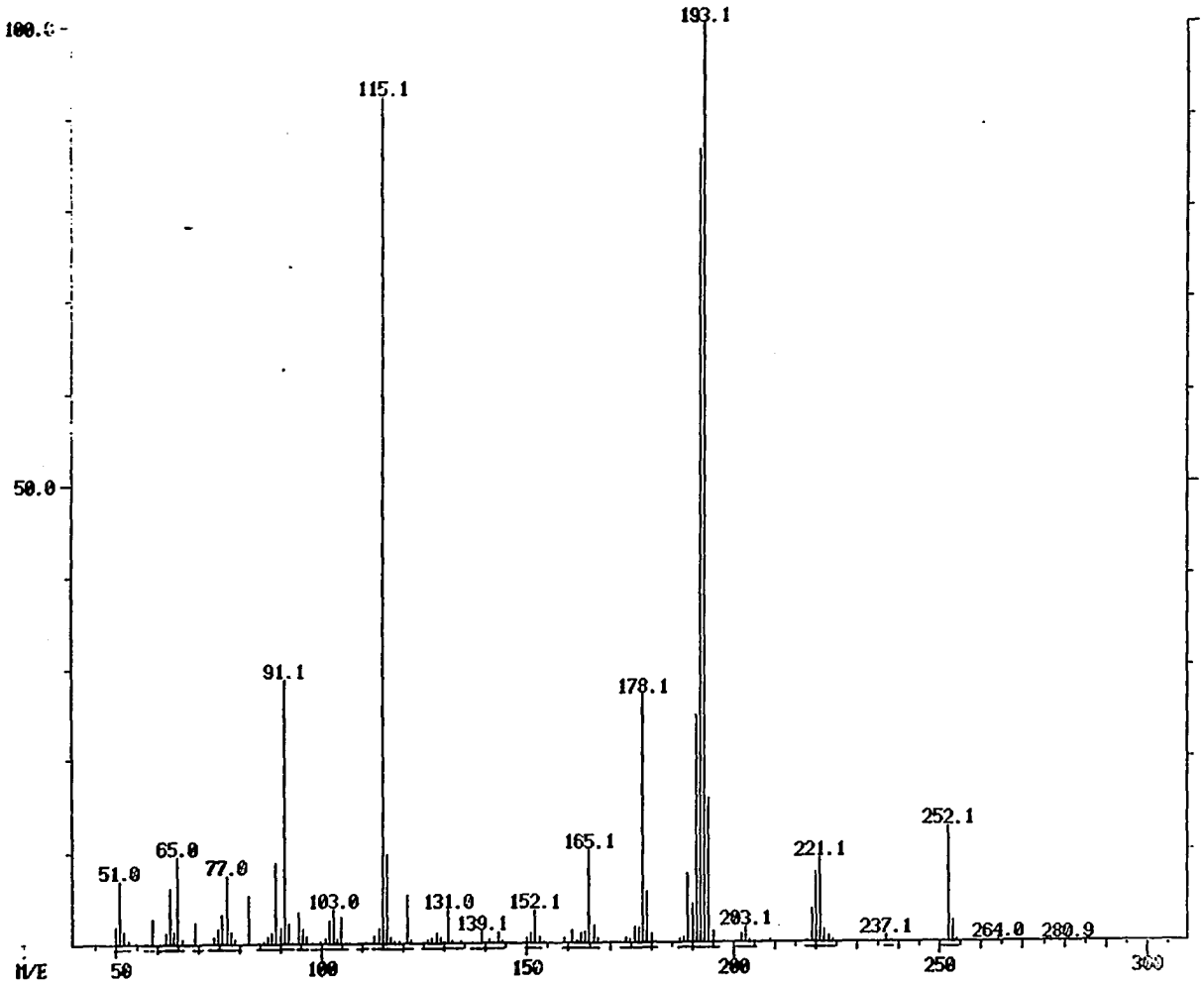


Figure 17. MASS of (-)-methyl trans-2,3-diphenylcyclopropane carboxylate

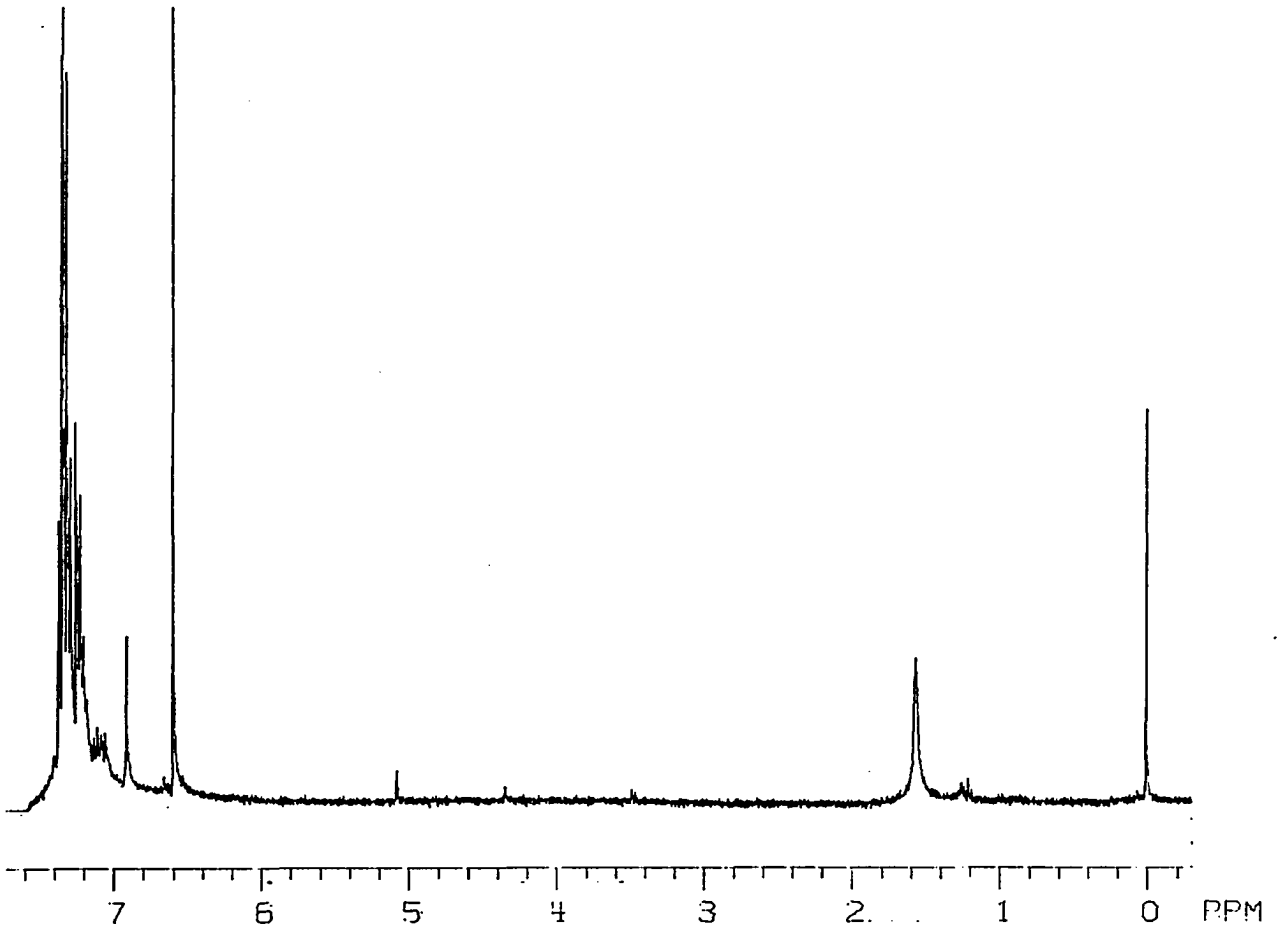


Figure 18. ^{1}H NMR of 1,3-diphenylallene

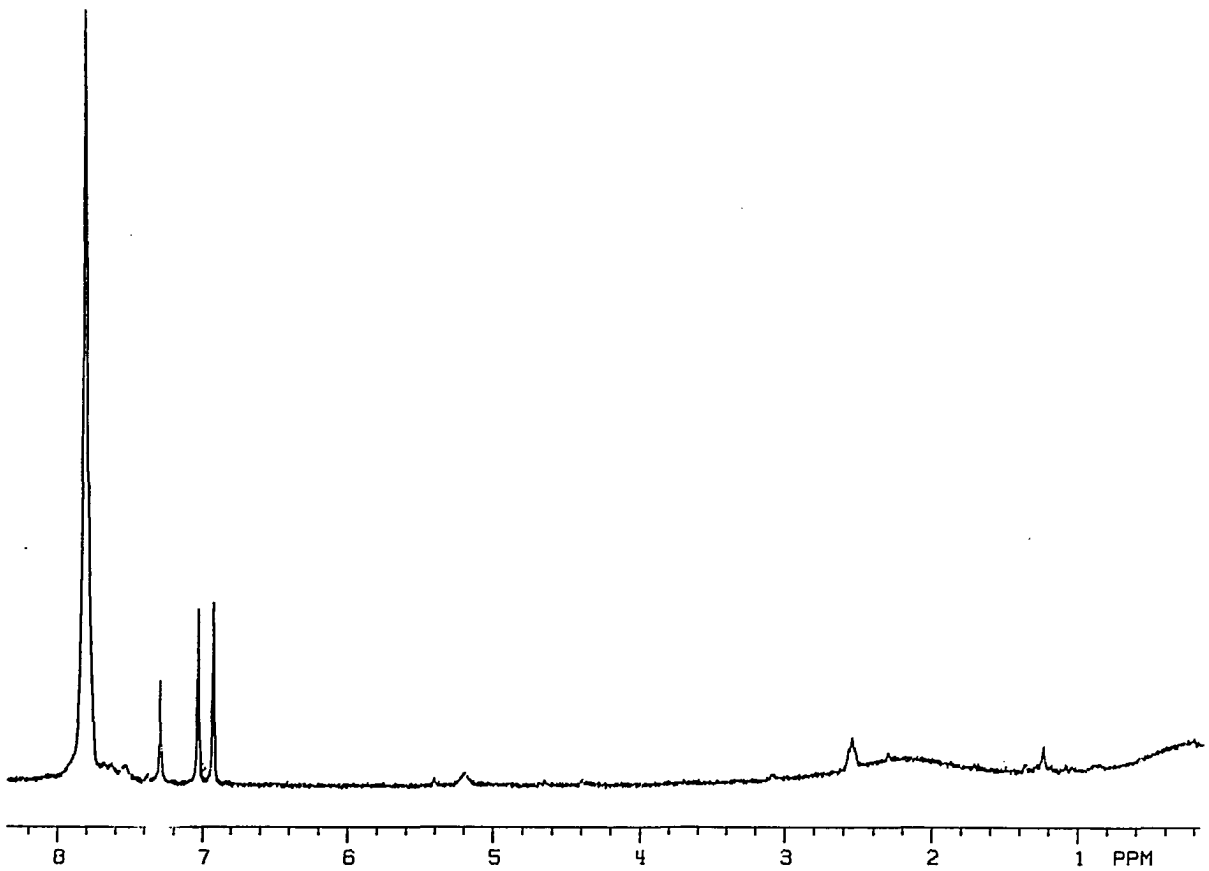


Figure 19. ^{1}H NMR of 1,3-diphenylallene with chiral shift reagents

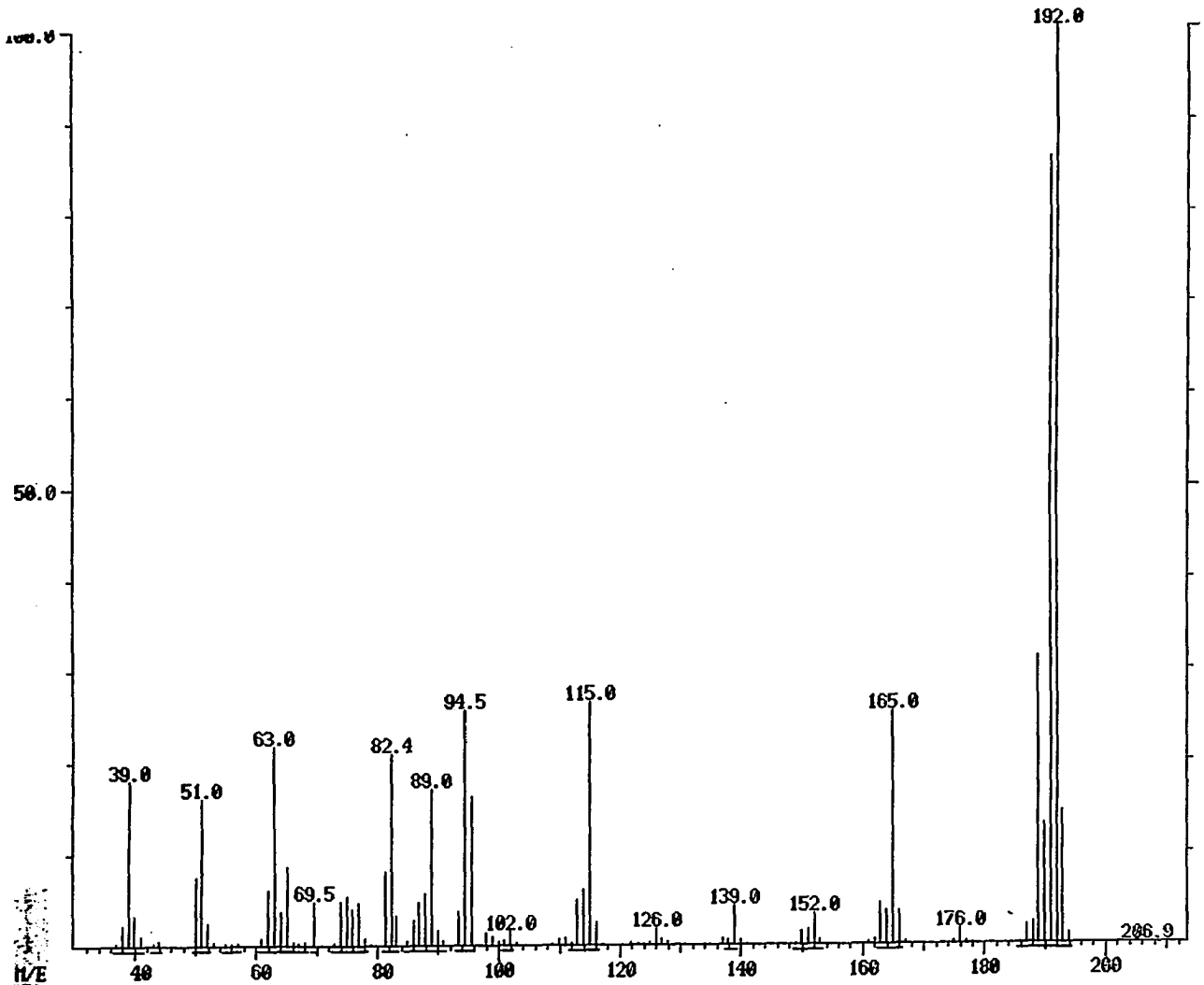


Figure 20. MASS of 1,3-diphenylallene

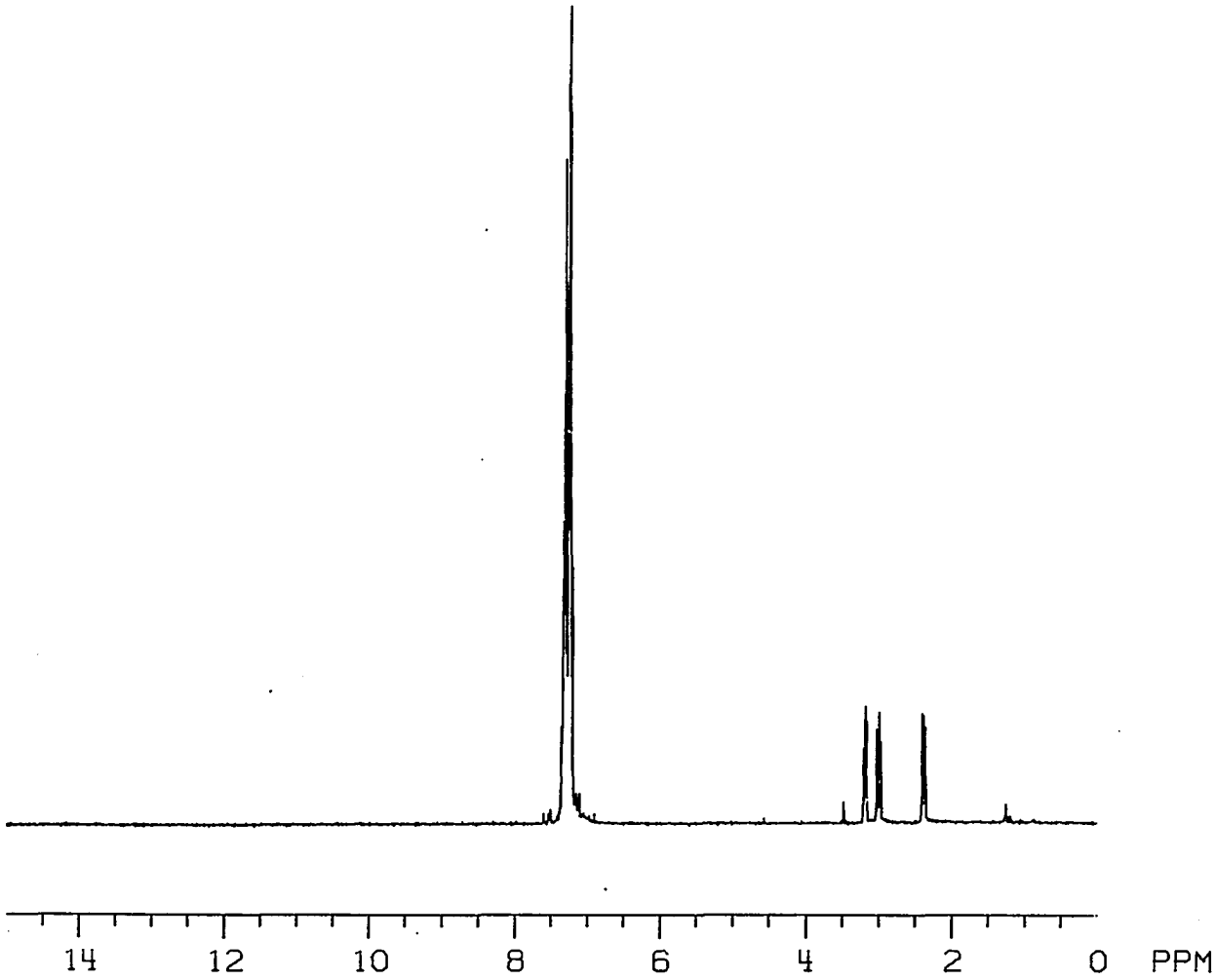


Figure 21. ^{1}H NMR of trans-2,3-diphenylcyclopropane carboxylic acid

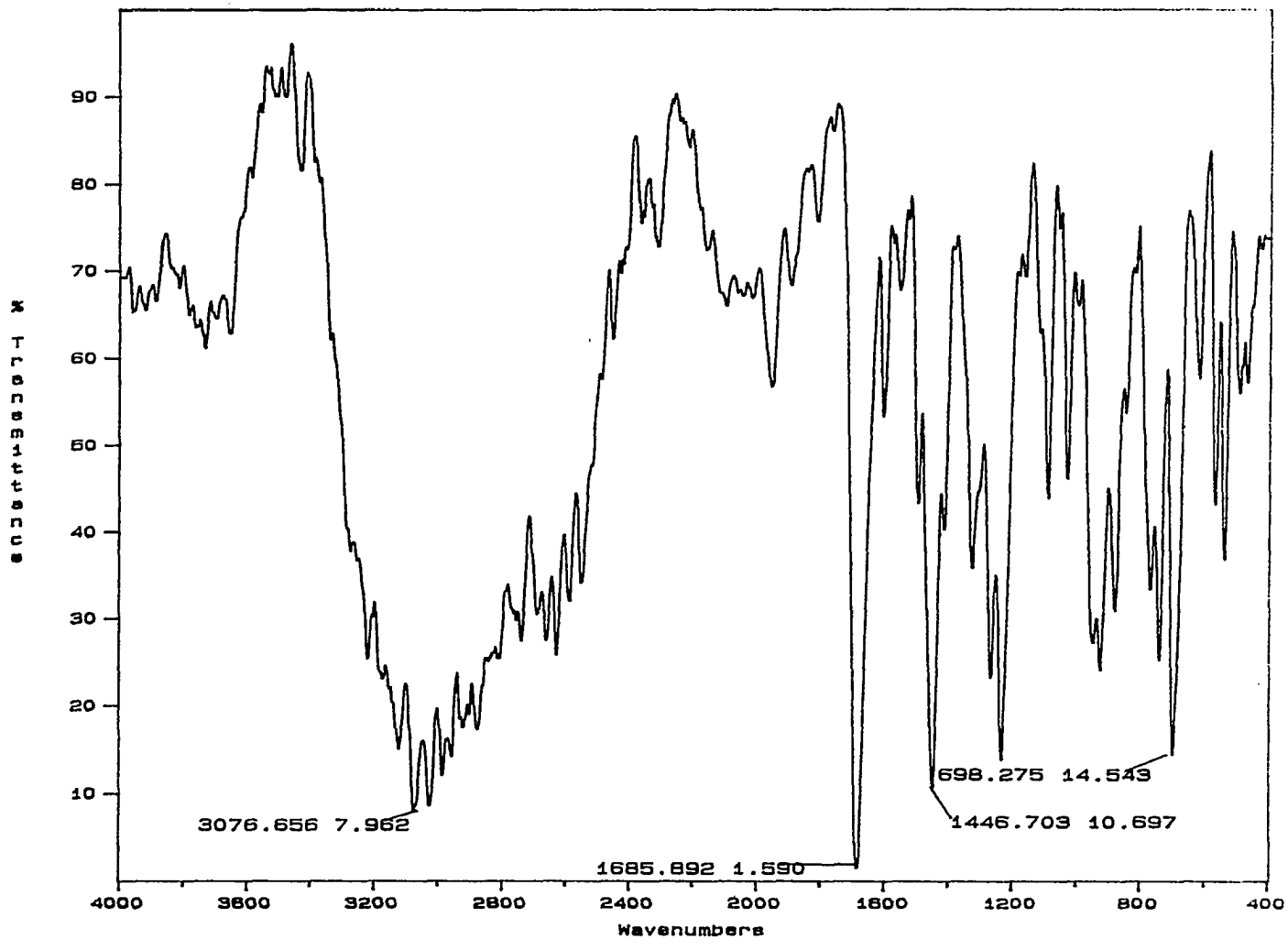


Figure 22. IR of trans-2,3-diphenylcyclopropane carboxylic acid

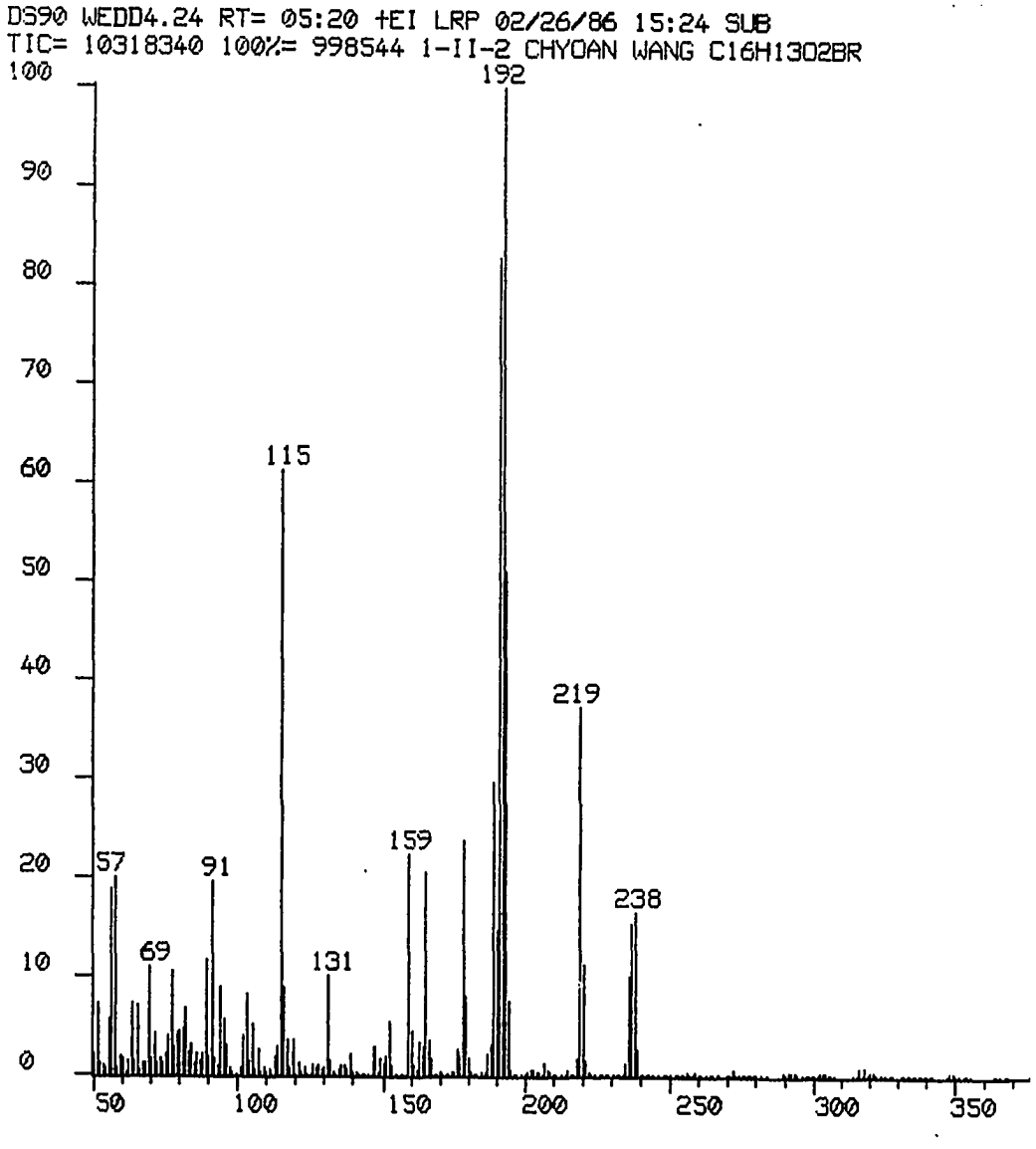


Figure 23. MASS of trans-2,3-diphenylcyclopropane carboxylic acid

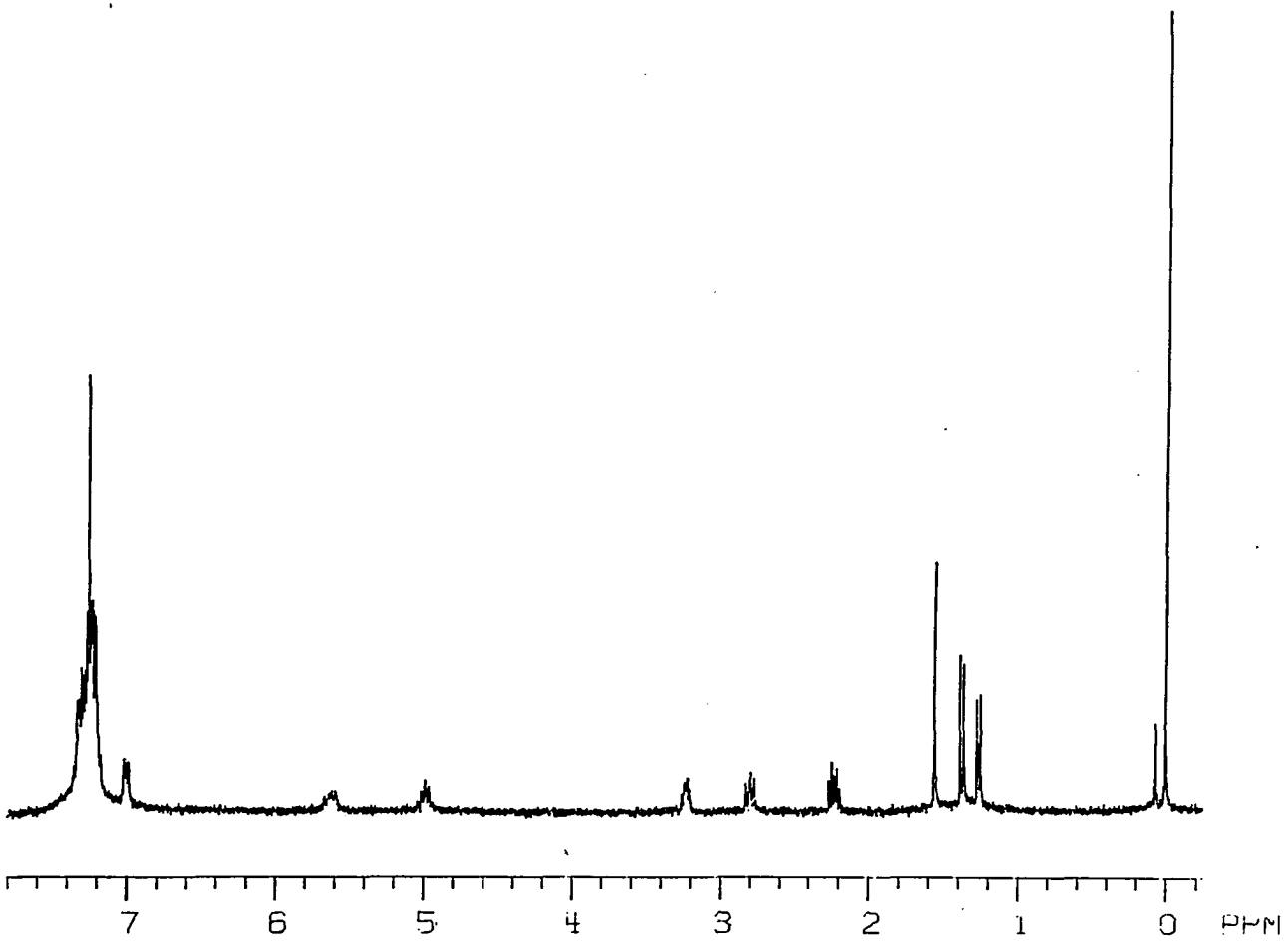


Figure 24. ^{1}H NMR of N-[(S)-α-methylbenzyl]-trans-2,3-diphenylcyclopropane-1-carboxamide from racemic acids

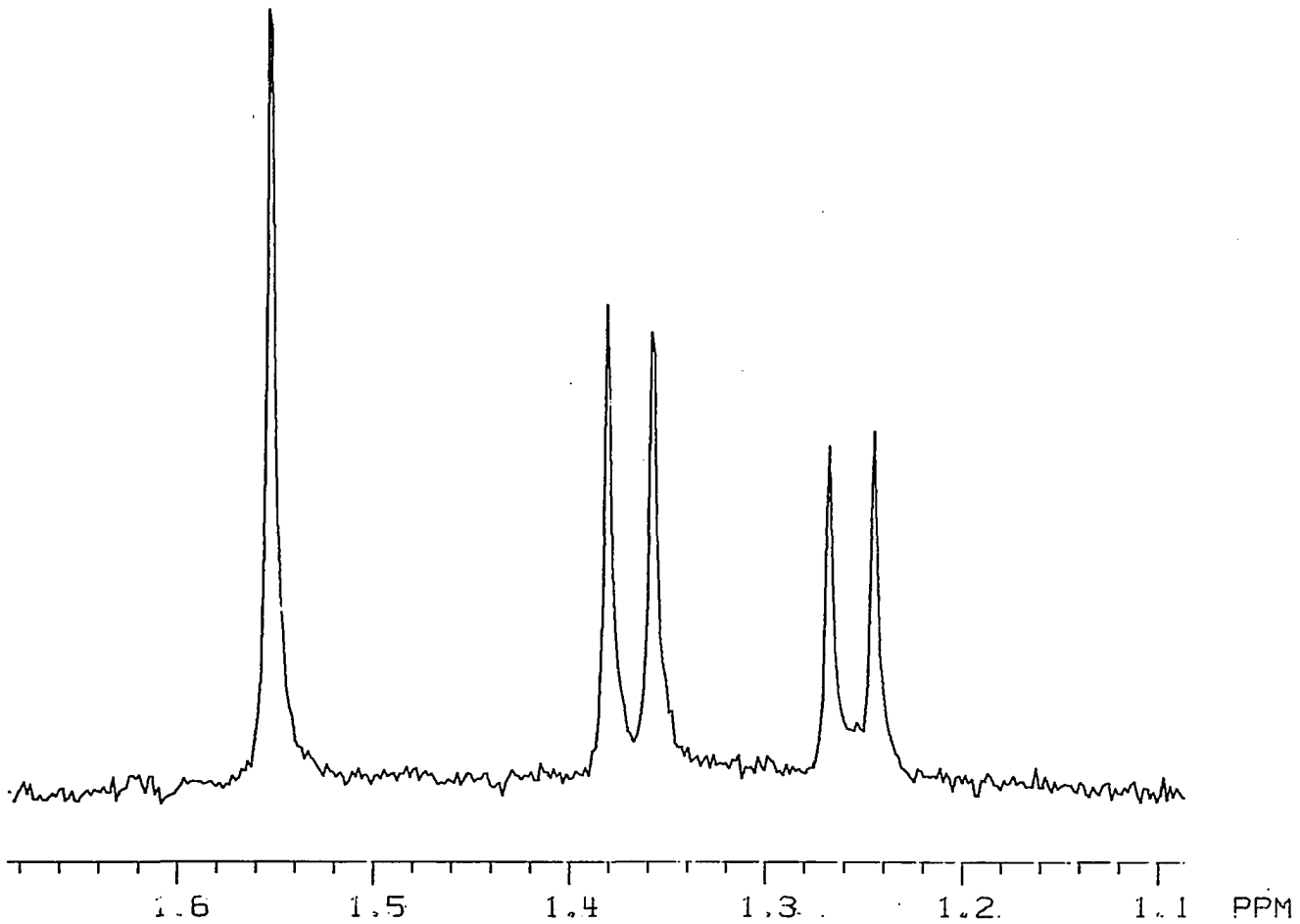


Figure 25. Partil enlargement in Figure 24

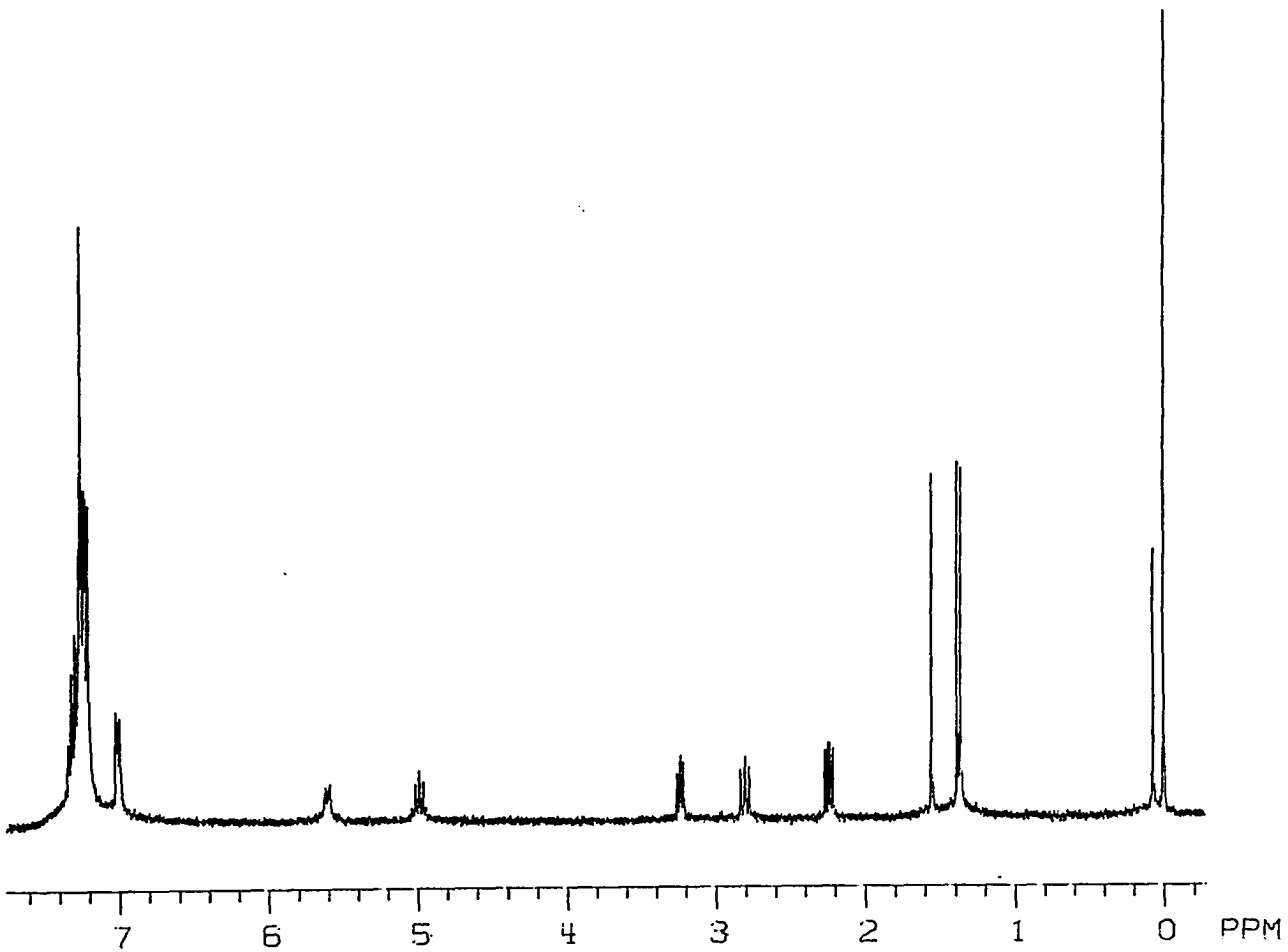


Figure 26. ^{1}H NMR of N-[(S)-α-methylbenzyl]-trans-2,3-diphenylcyclopropane-1-carboxamide from optically active acid

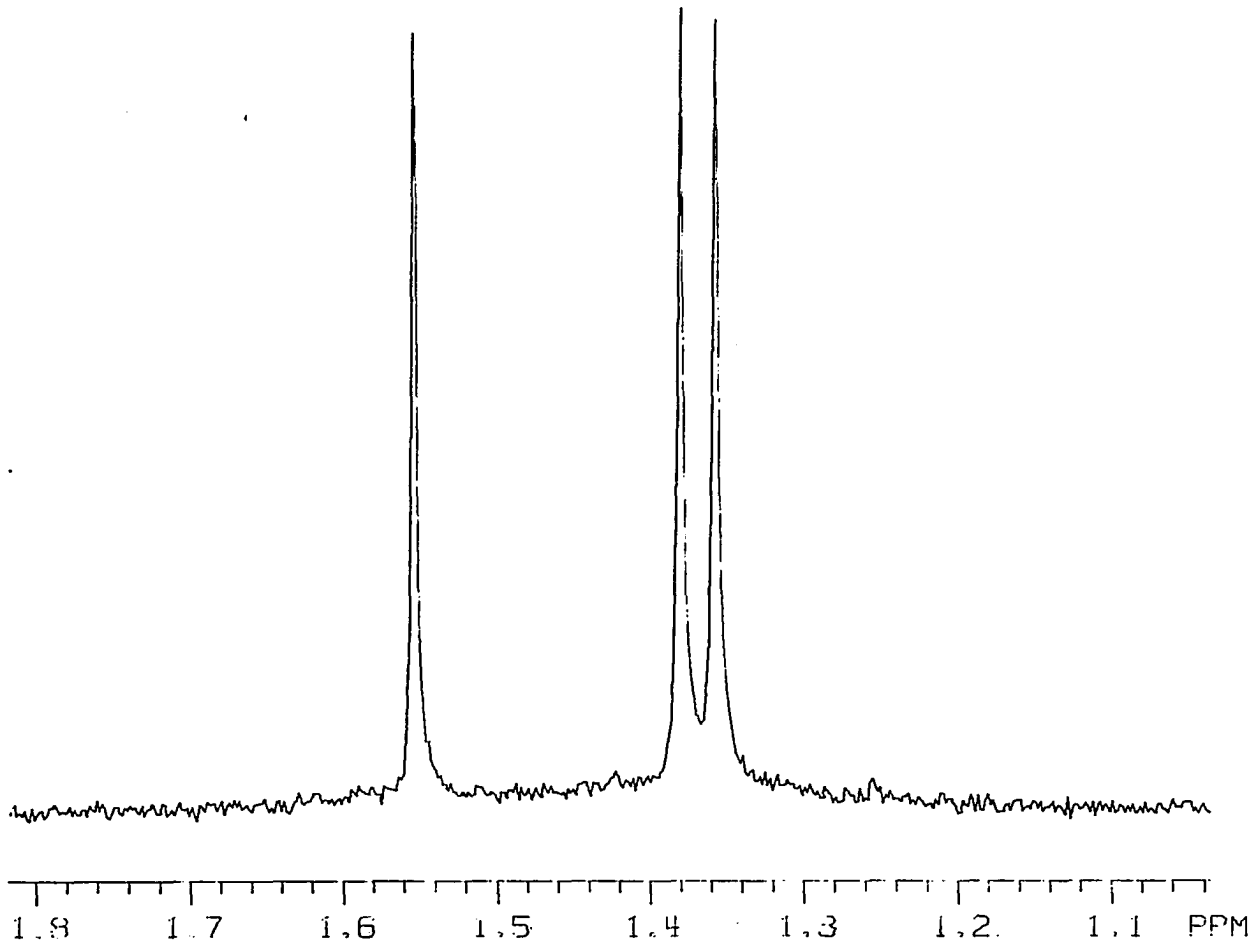


Figure 27. Partial enlargement in Figure 26

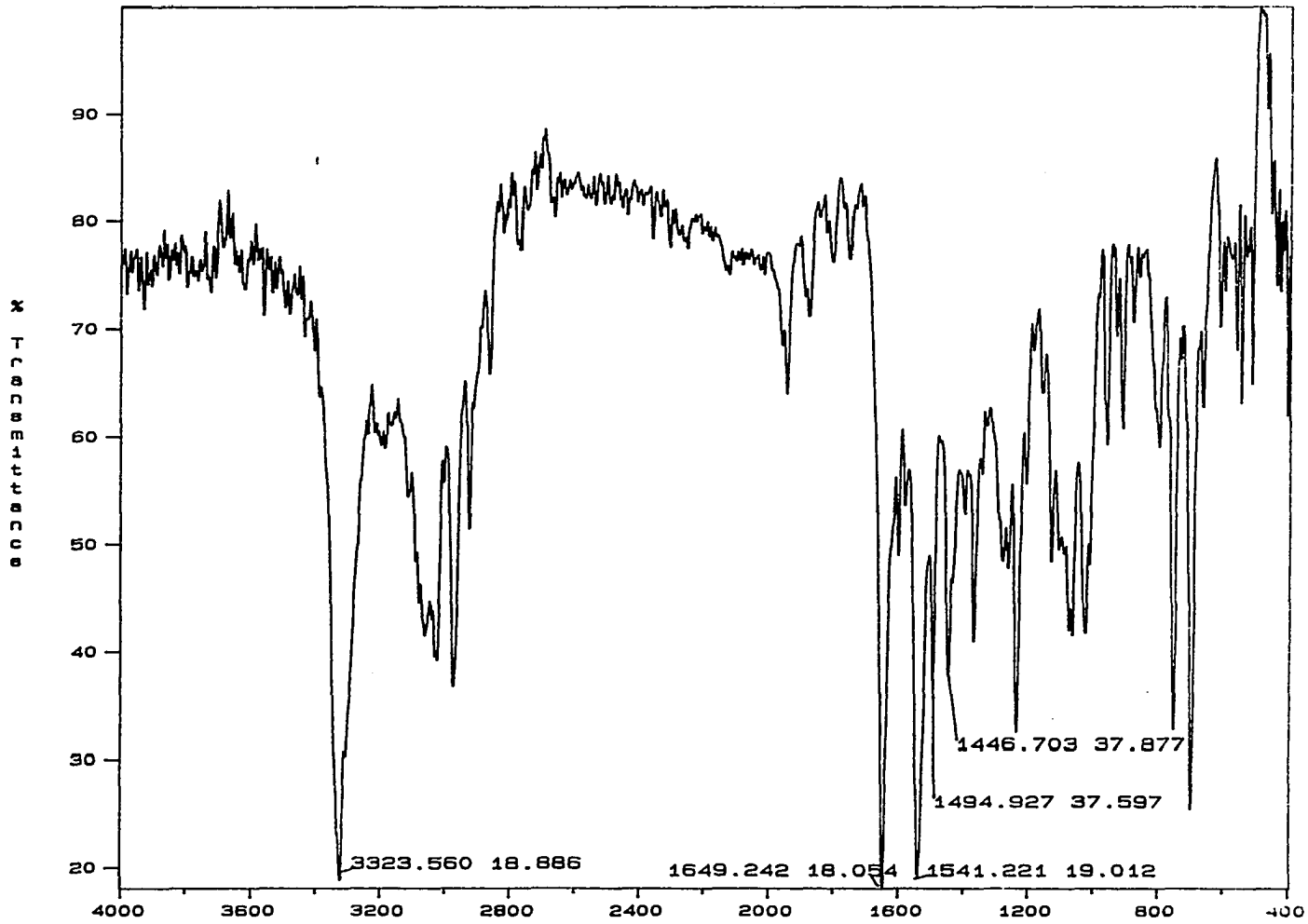


Figure 28. IR of N-[(S)-α-methylbenzyl]-trans-2,3-diphenylcyclopropane-1-carboxamide

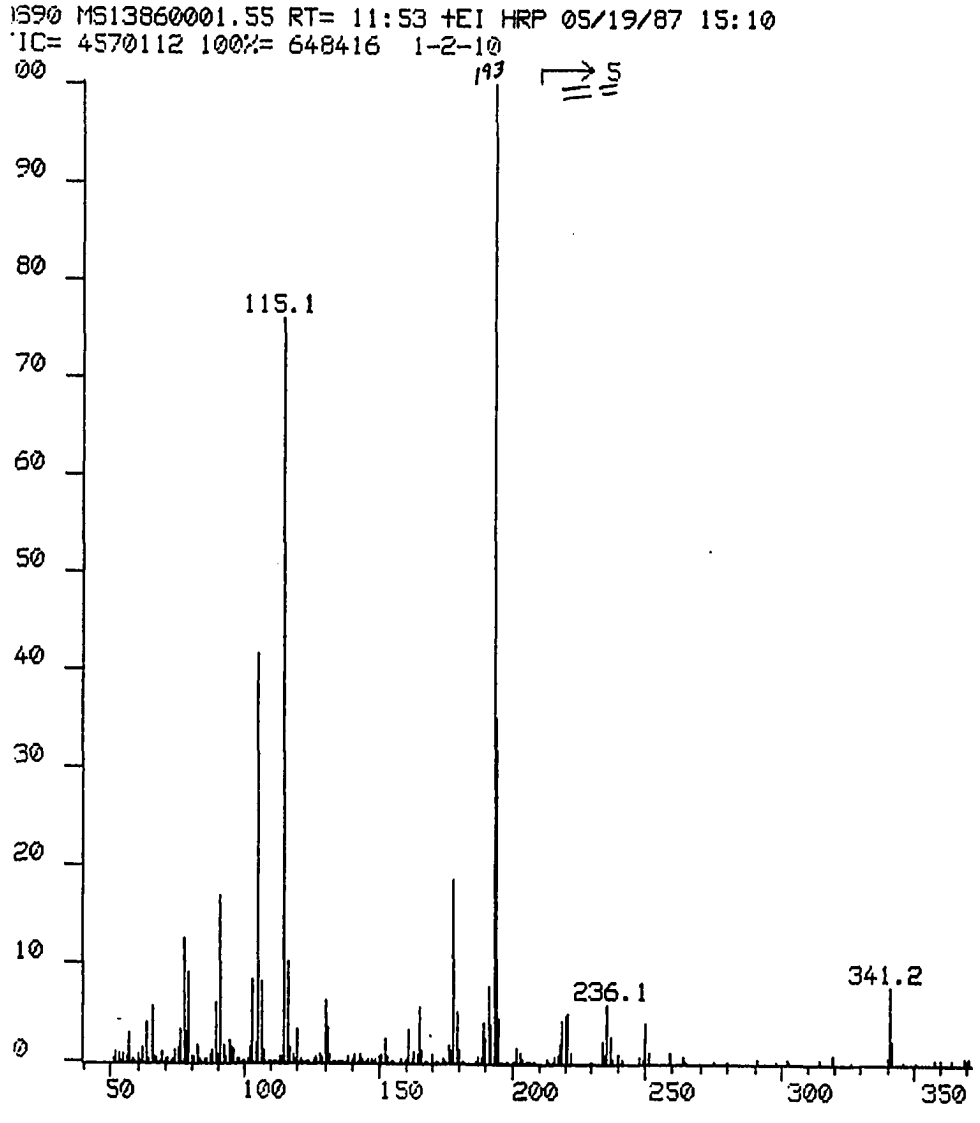


Figure 29. MASS of N-[(S)-α-methylbenzyl]-trans-2,3-diphenylcyclopropane-1-carboxamide

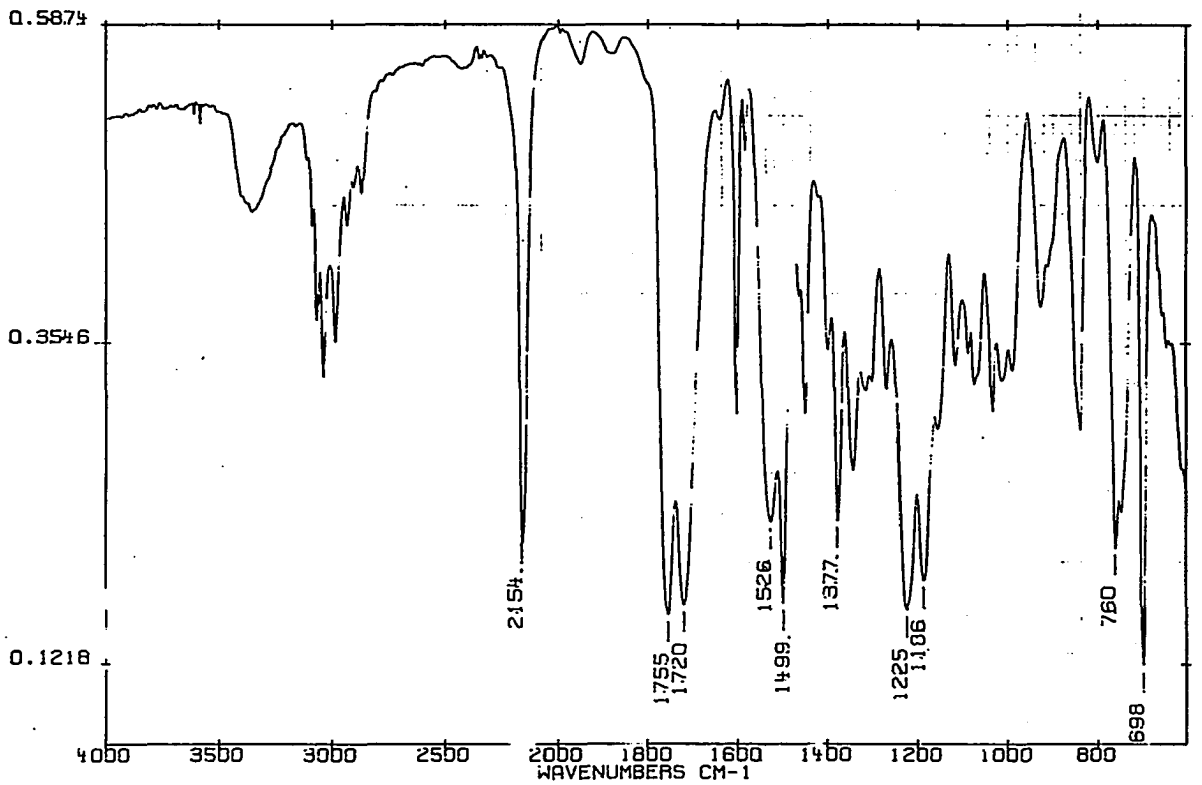


Figure 30. IR of (+)-ethyl nitroso-trans-2,3-diphenylcyclopropane-1-carbamate

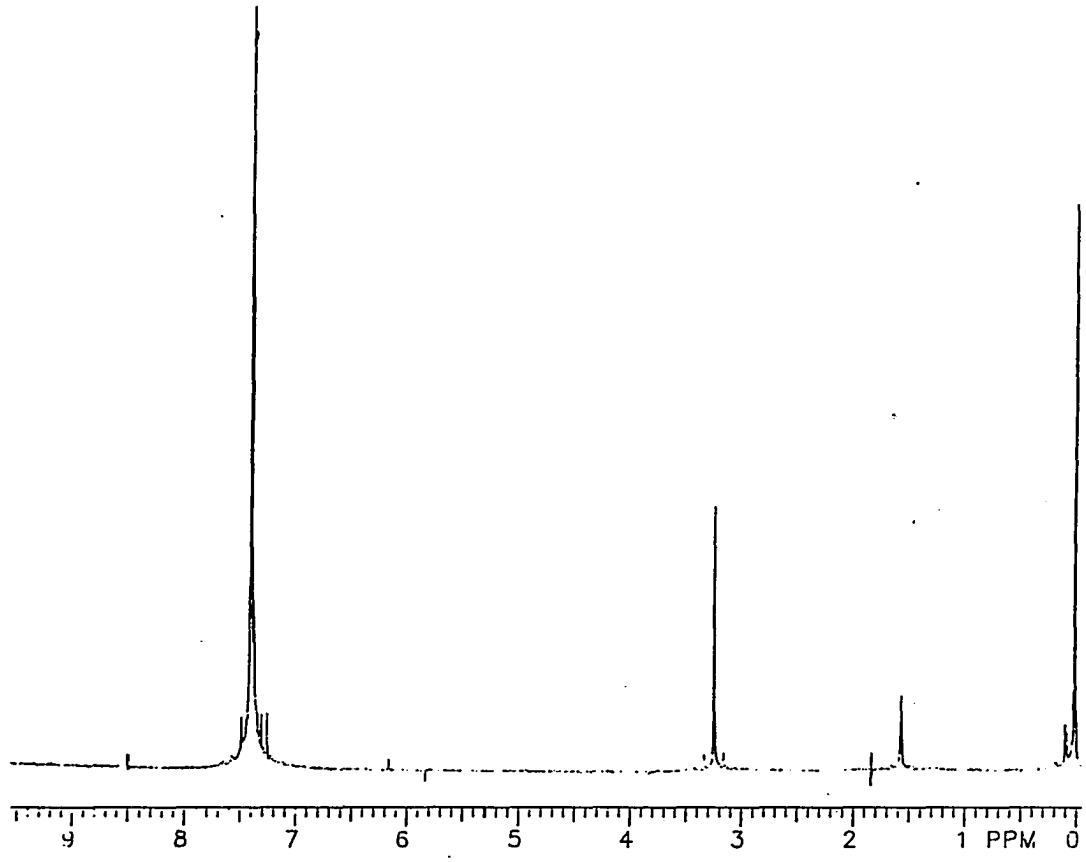


Figure 31. ^{1}H NMR of 1,1-dichloro-trans-2,3diphenylcyclopropane

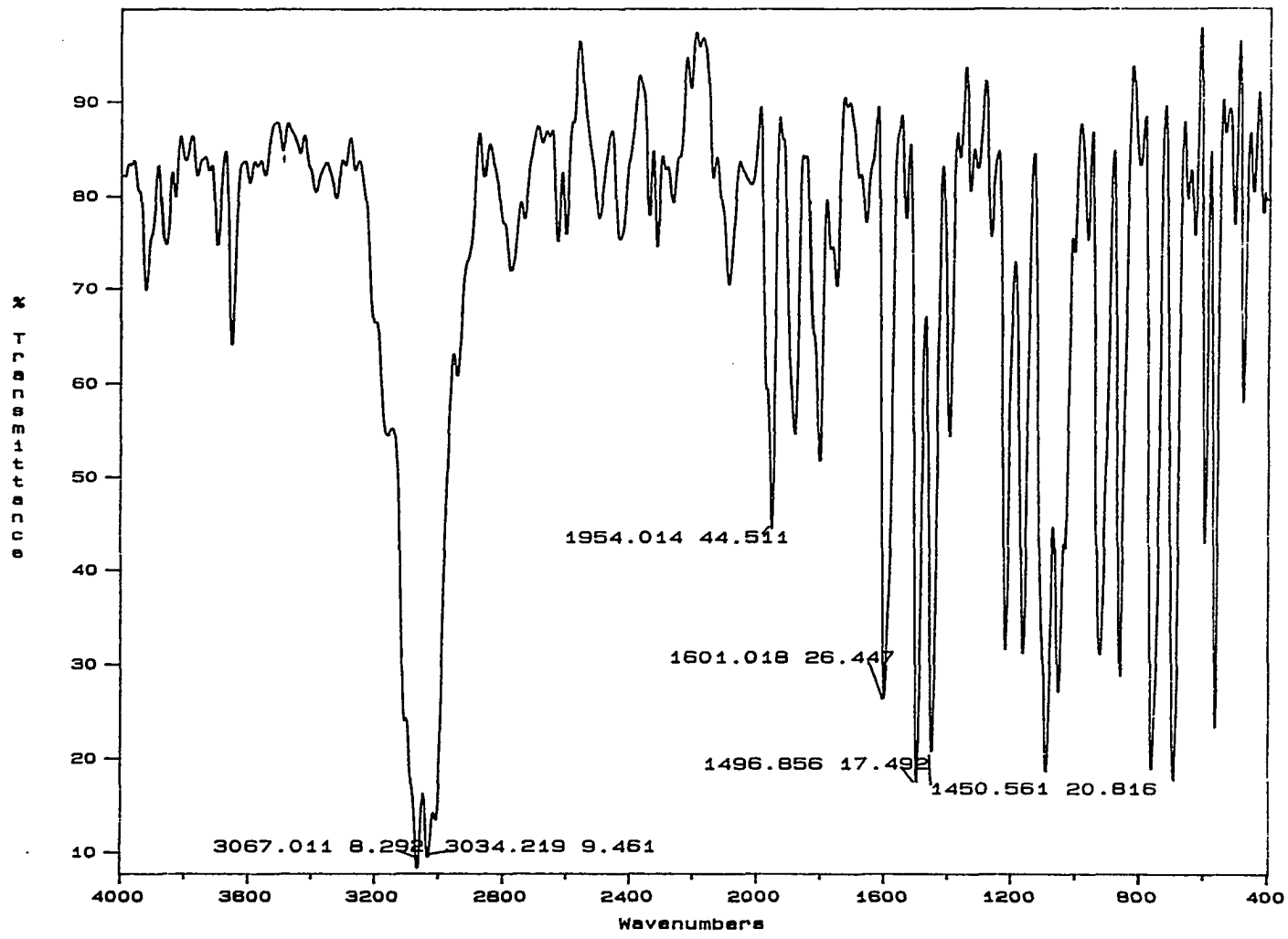


Figure 32. IR of 1,1-dichloro-trans-2,3-diphenylcyclopropane

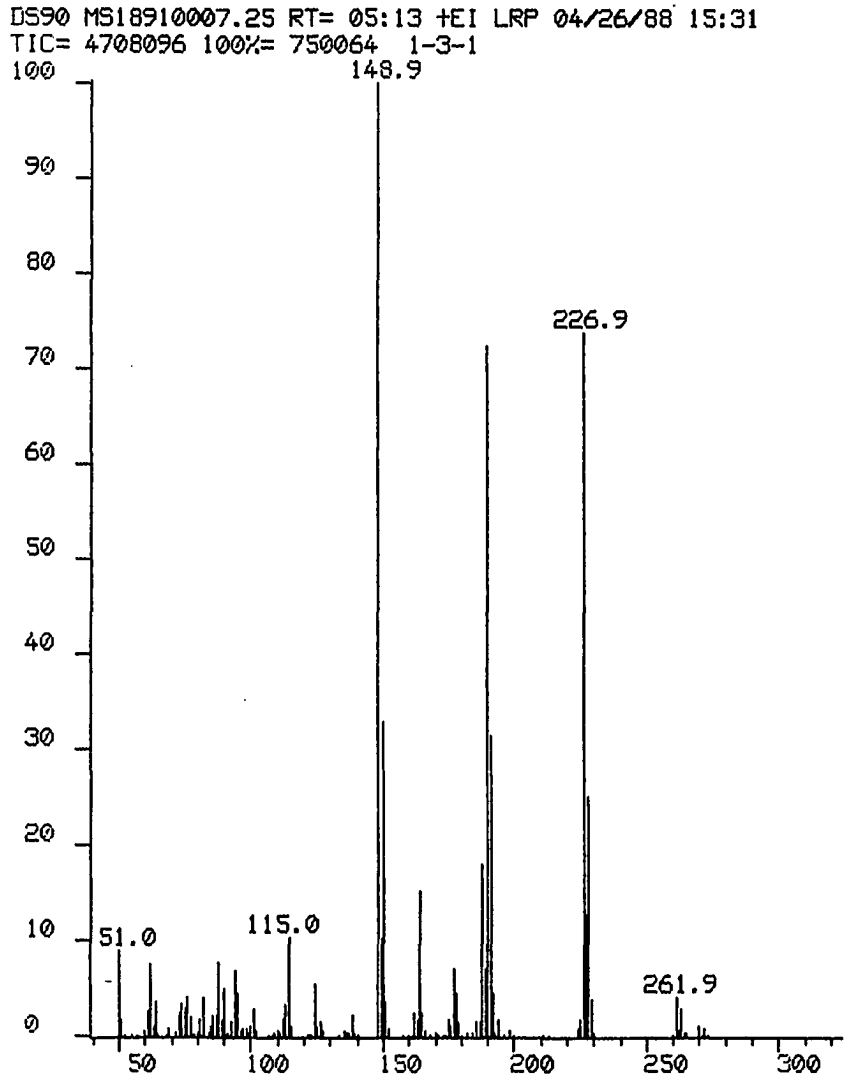


Figure 33. MASS of 1,1-dichloro-trans-2,3-diphenylcyclopropane

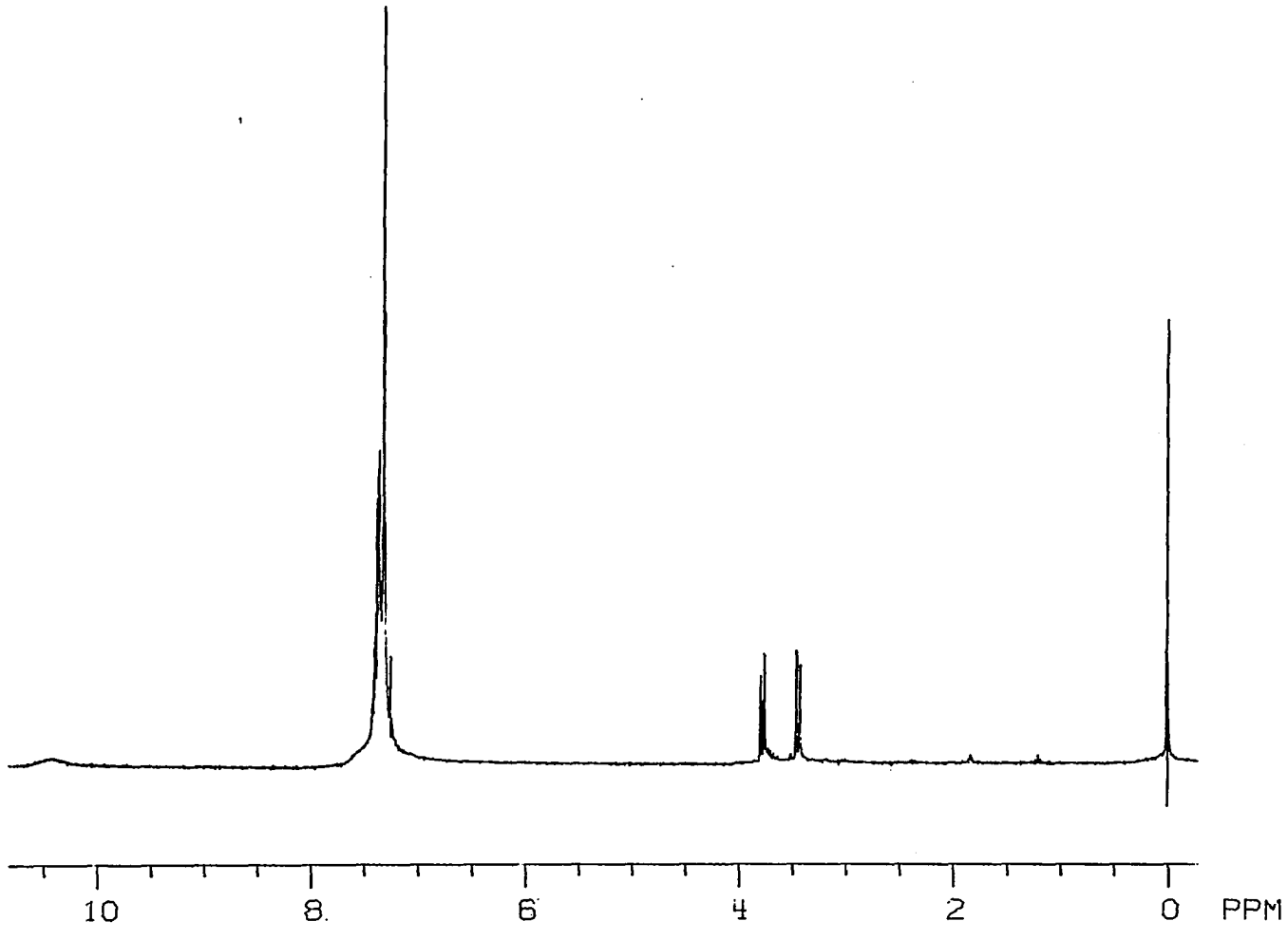


Figure 34. ^{1}H NMR of 1-chloro-2,3-diphenylcyclopropane carboxylic acid

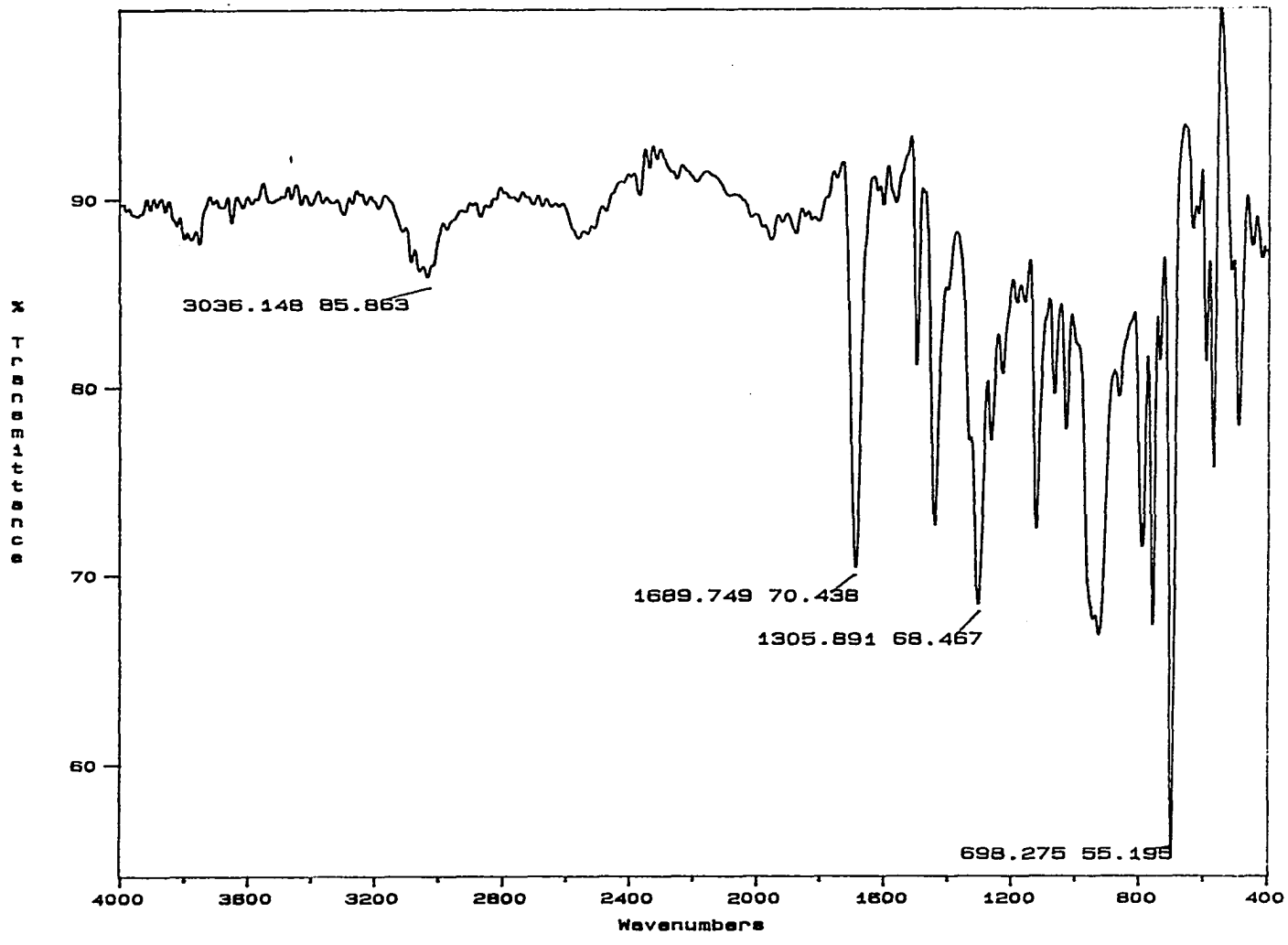


Figure 35. IR of 1-chloro-trans-2,3-diphenylcyclopropane carboxylic acid

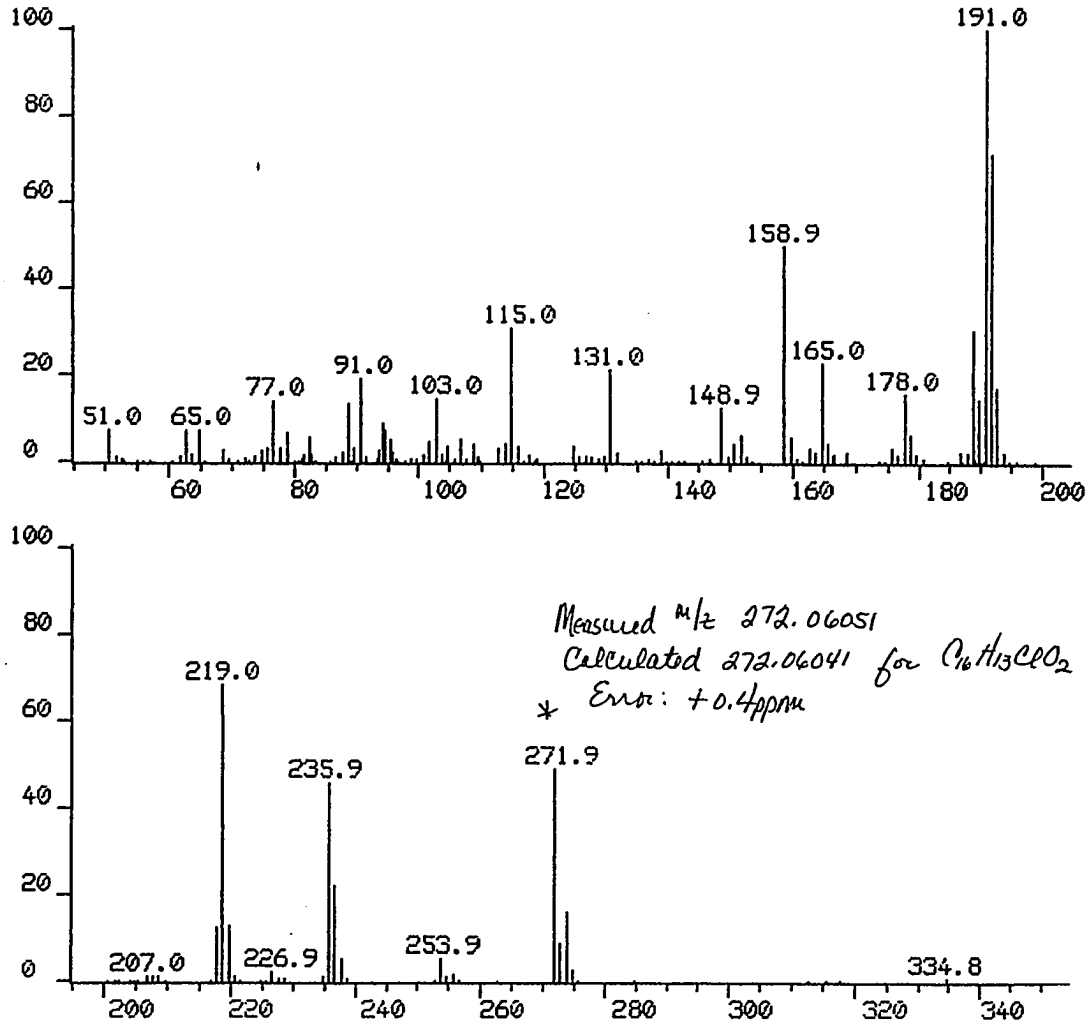


Figure 36. MASS of 1-chloro-trans-2,3-diphenylcyclopropane carboxylic acid

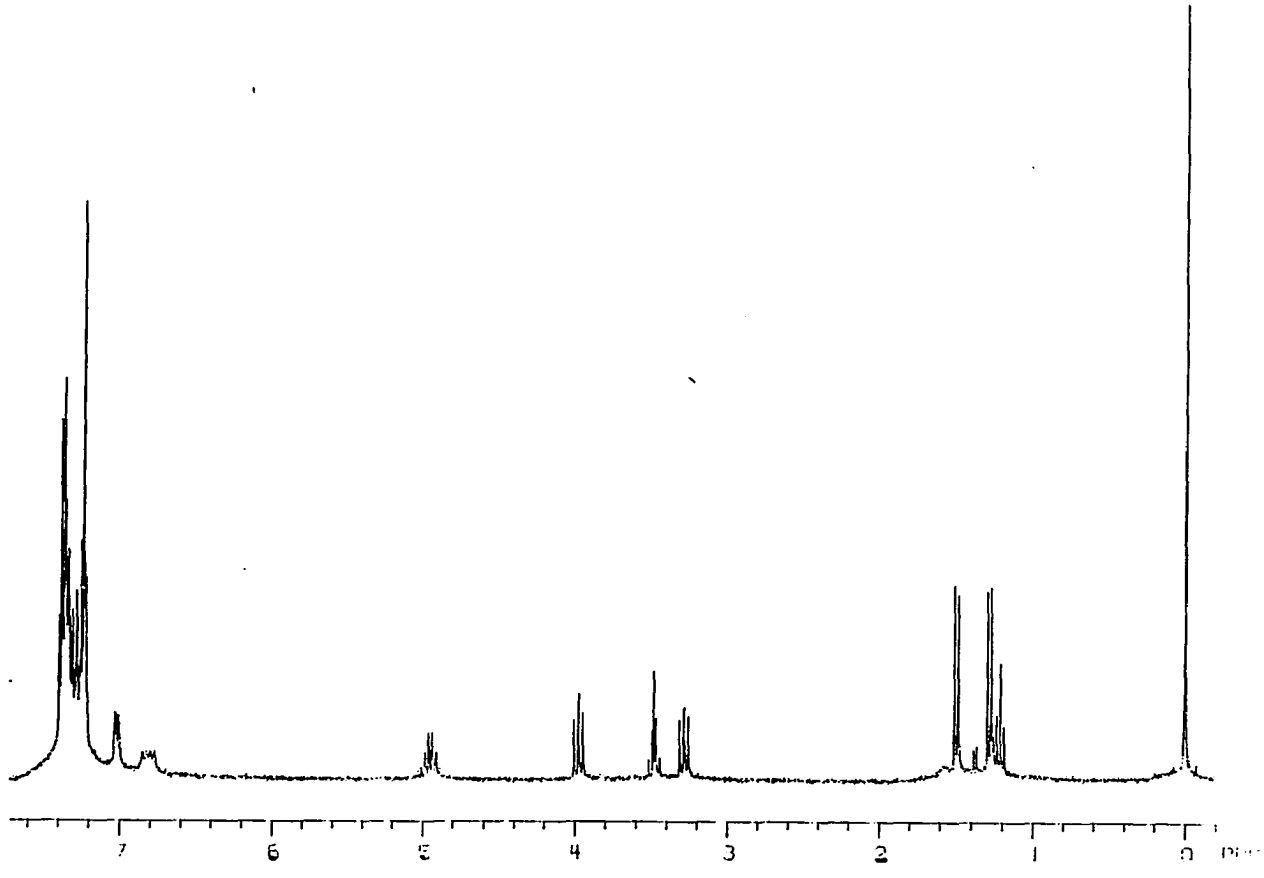


Figure 37. ^{1}H NMR of N-[(S)-α-methylbenzyl]-1-chloro-trans-2,3-diphenylcyclopropane-1-carboxamide from racemic acids

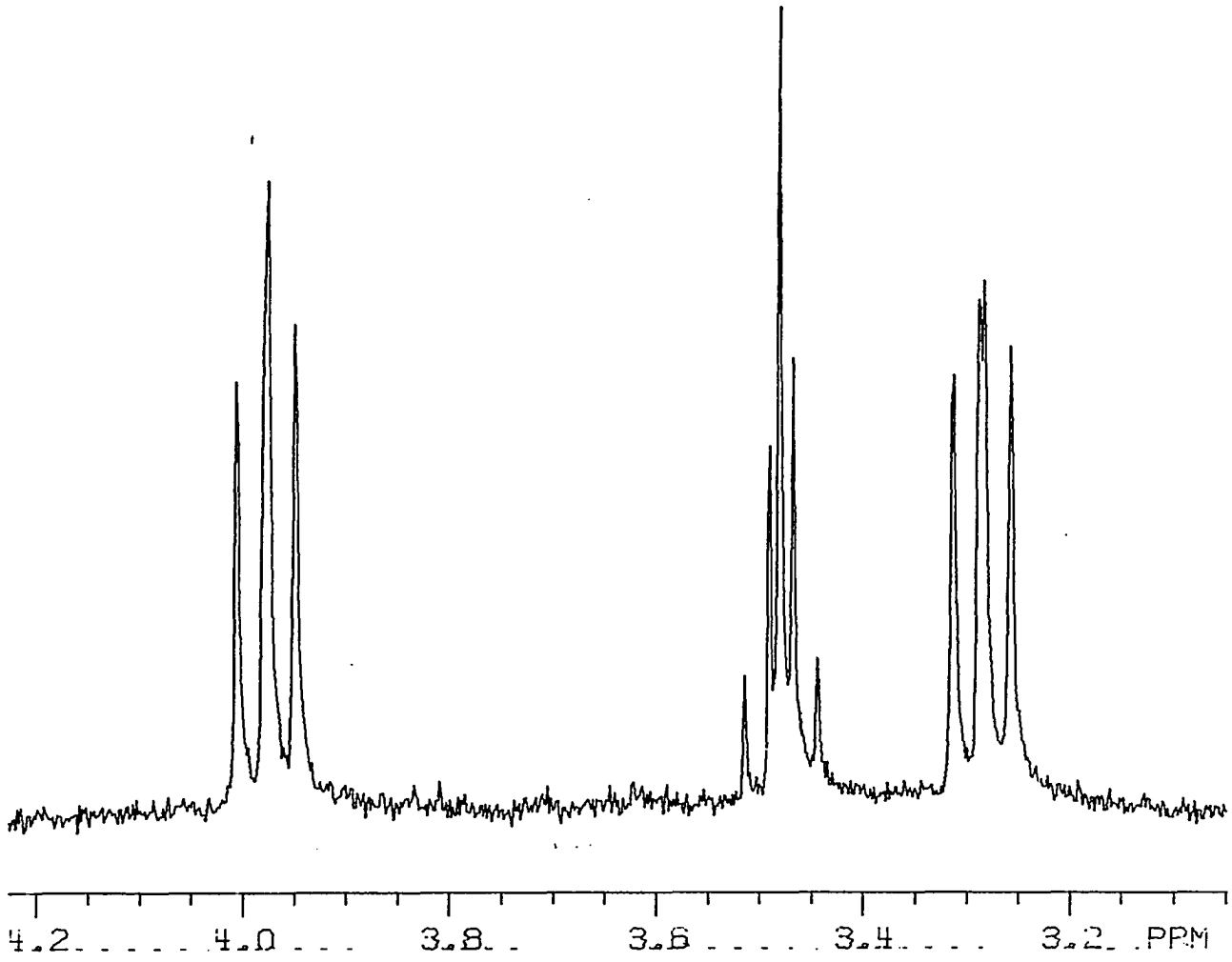


Figure 38. Partial enlargement in Figure 37

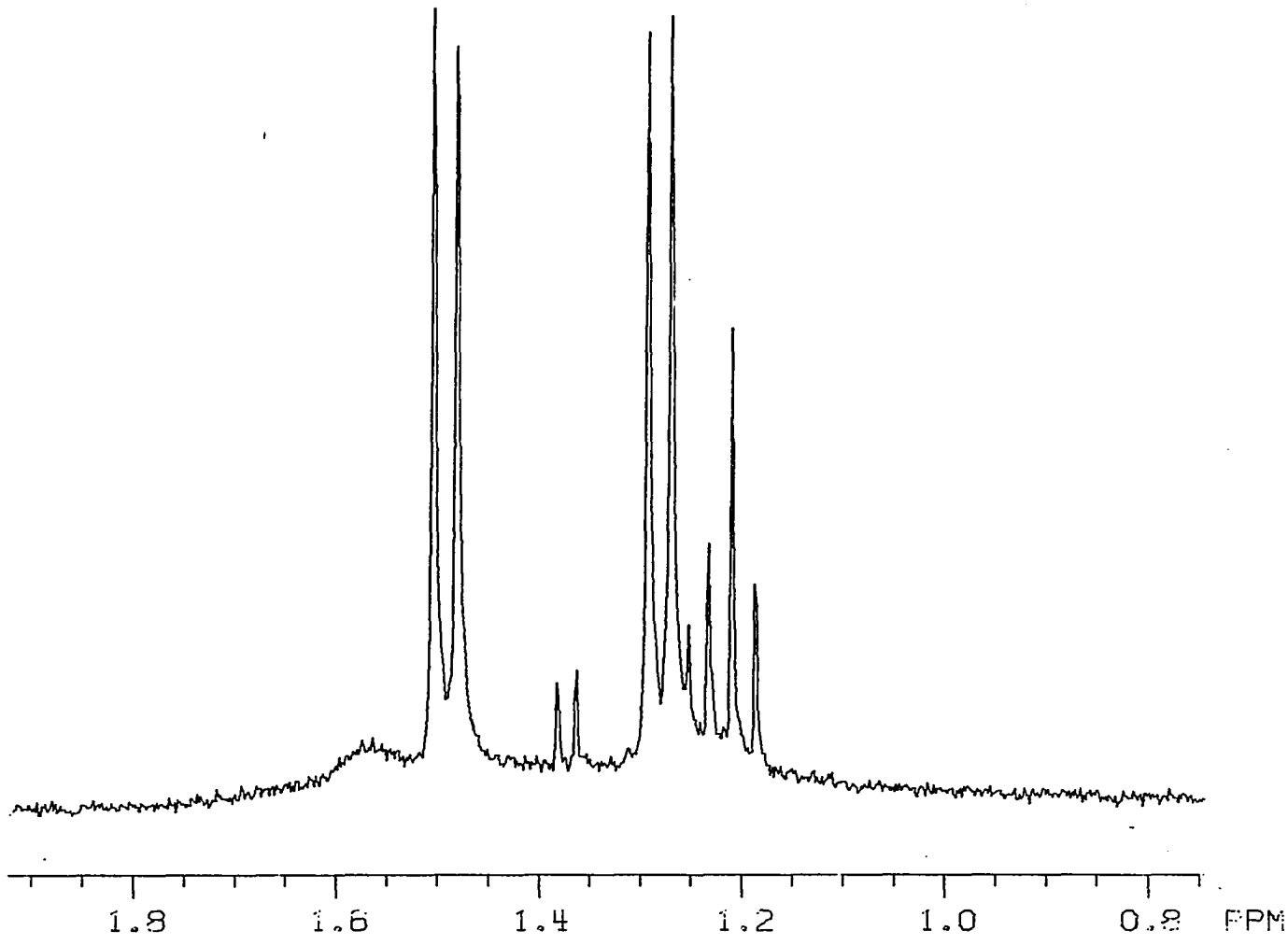


Figure 39. Partial enlargement in Figure 37

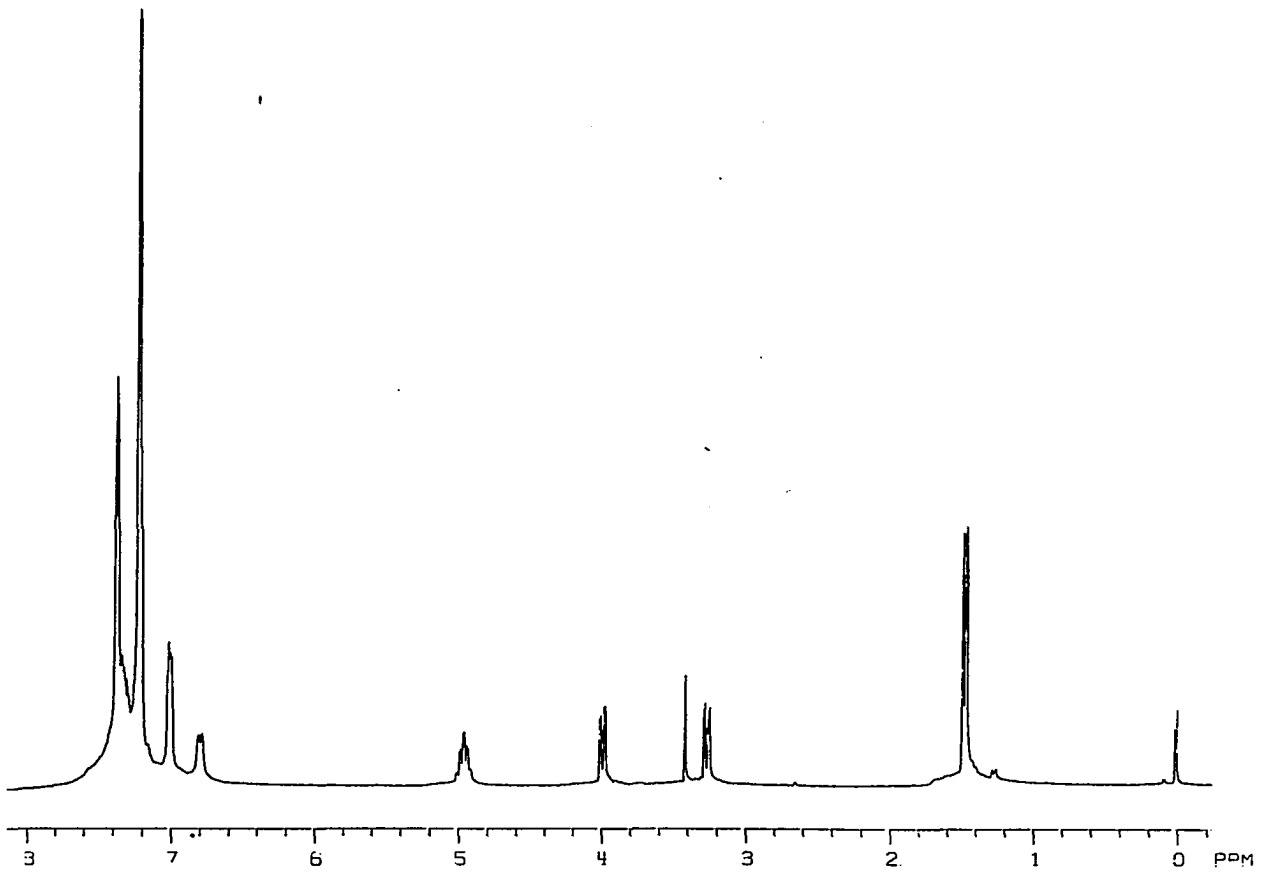


Figure 40. ^{1}H NMR of N-[(S)-α-methylbenzyl]-1-chloro-trans-2,3-diphenylcyclopropane-1-carboxamide from optically active acid

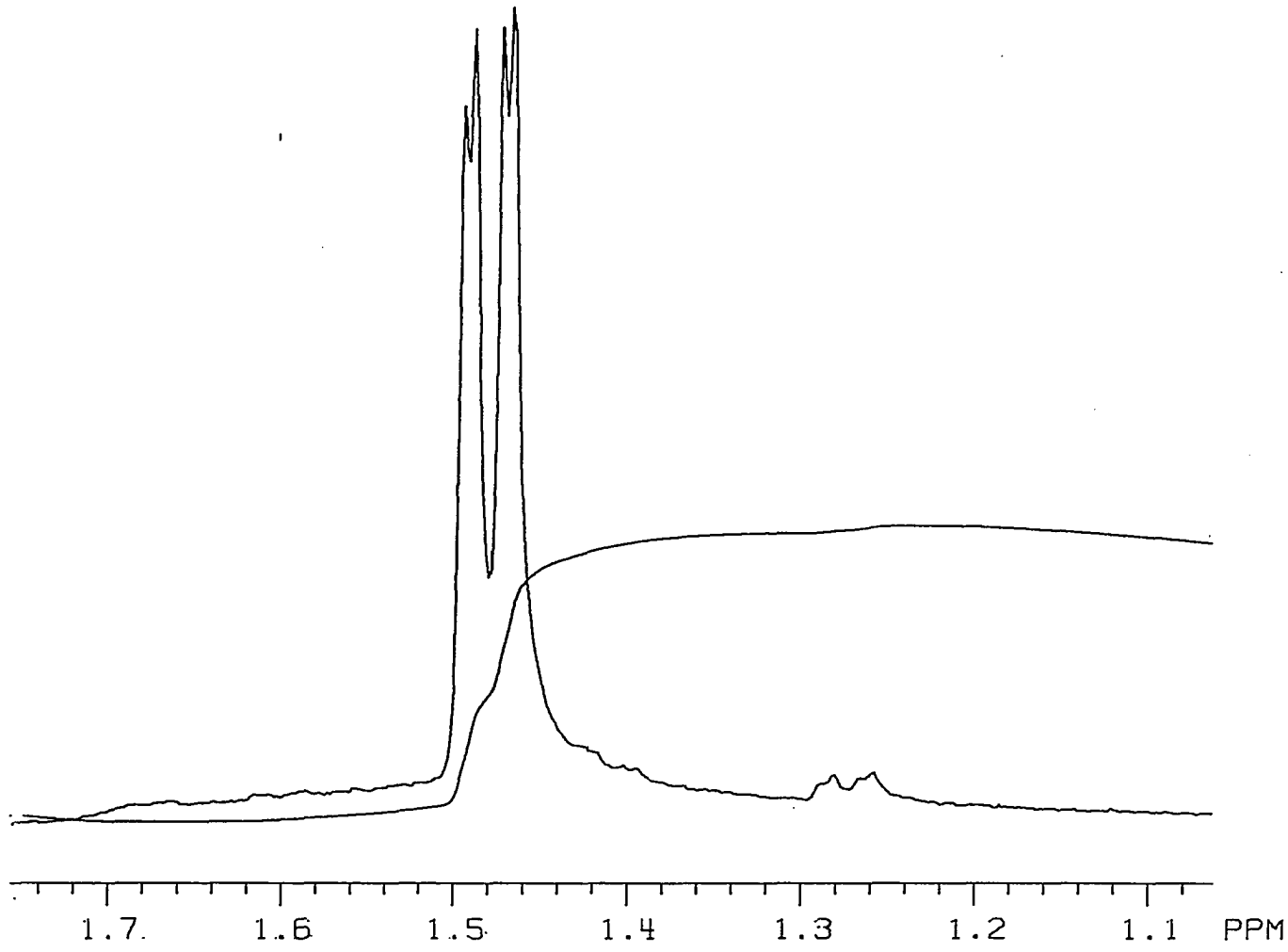


Figure 41. Partial enlargement in Figure 40

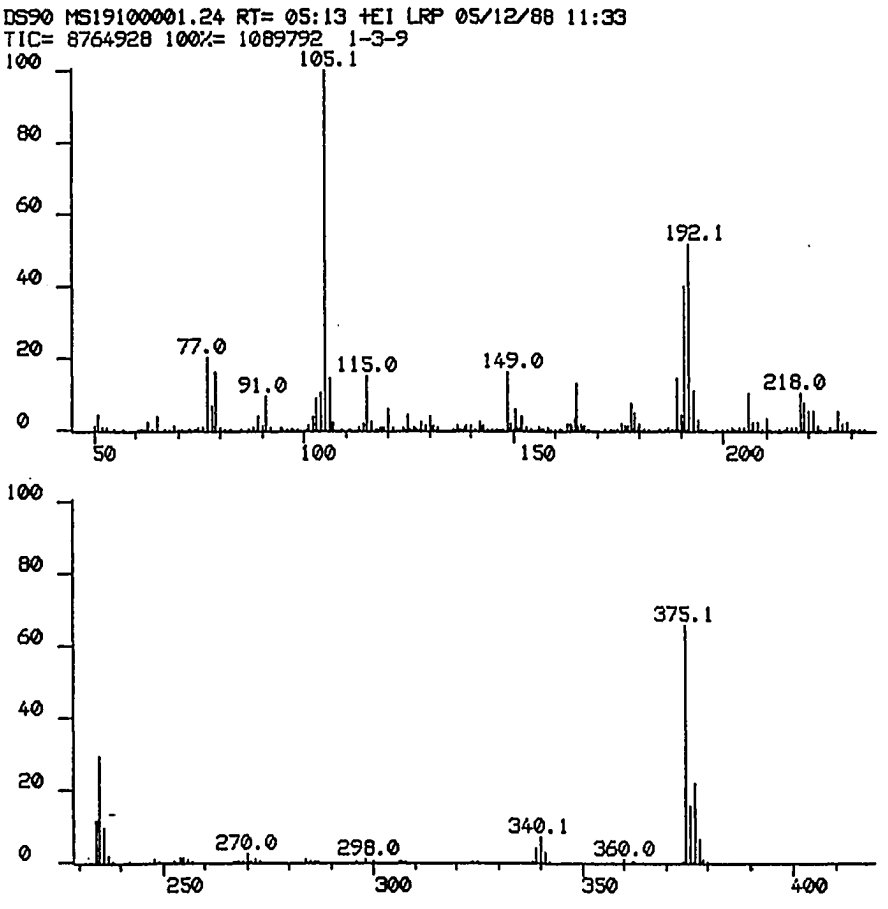


Figure 42. MASS of N-[(S)-α-methylbenzyl]-1-chloro-trans-2,3-diphenylcyclopropane-1-carboxamide

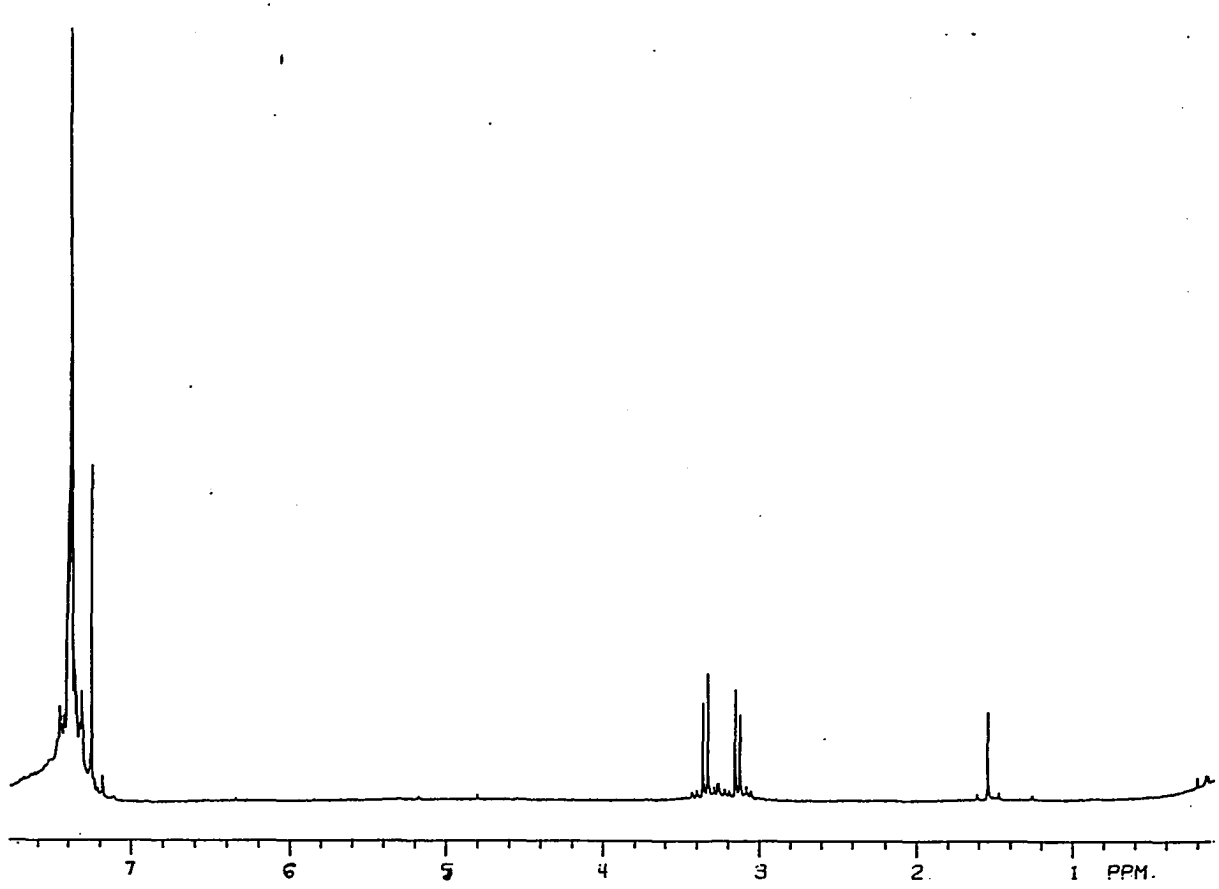


Figure 43. ^{1}H NMR of (-)-1-bromo-1-chloro-trans-2,3-diphenylcyclopropane

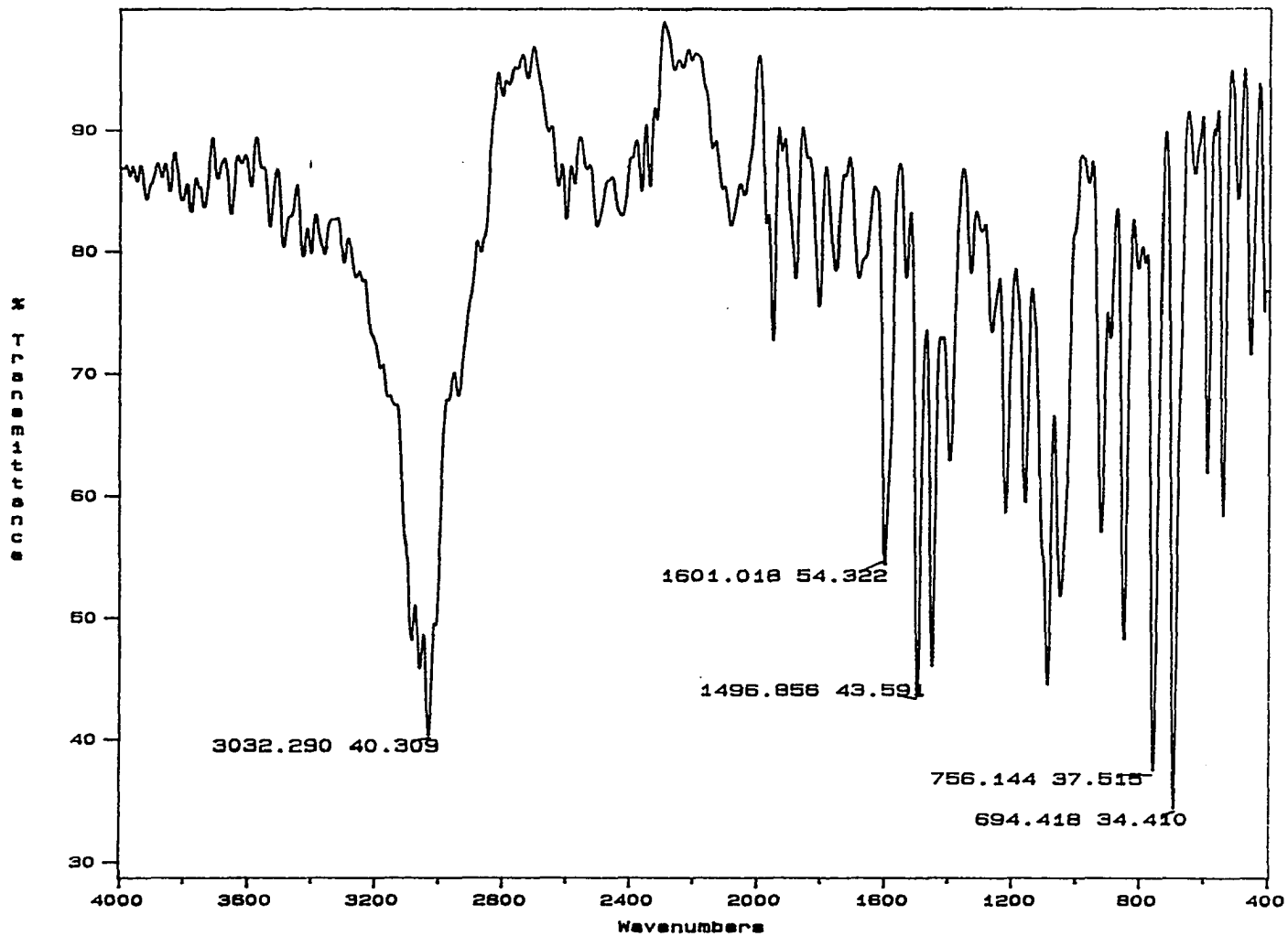


Figure 44. IR of (-)-1-bromo-1-chloro-trans-2,3-diphenylcyclopropane

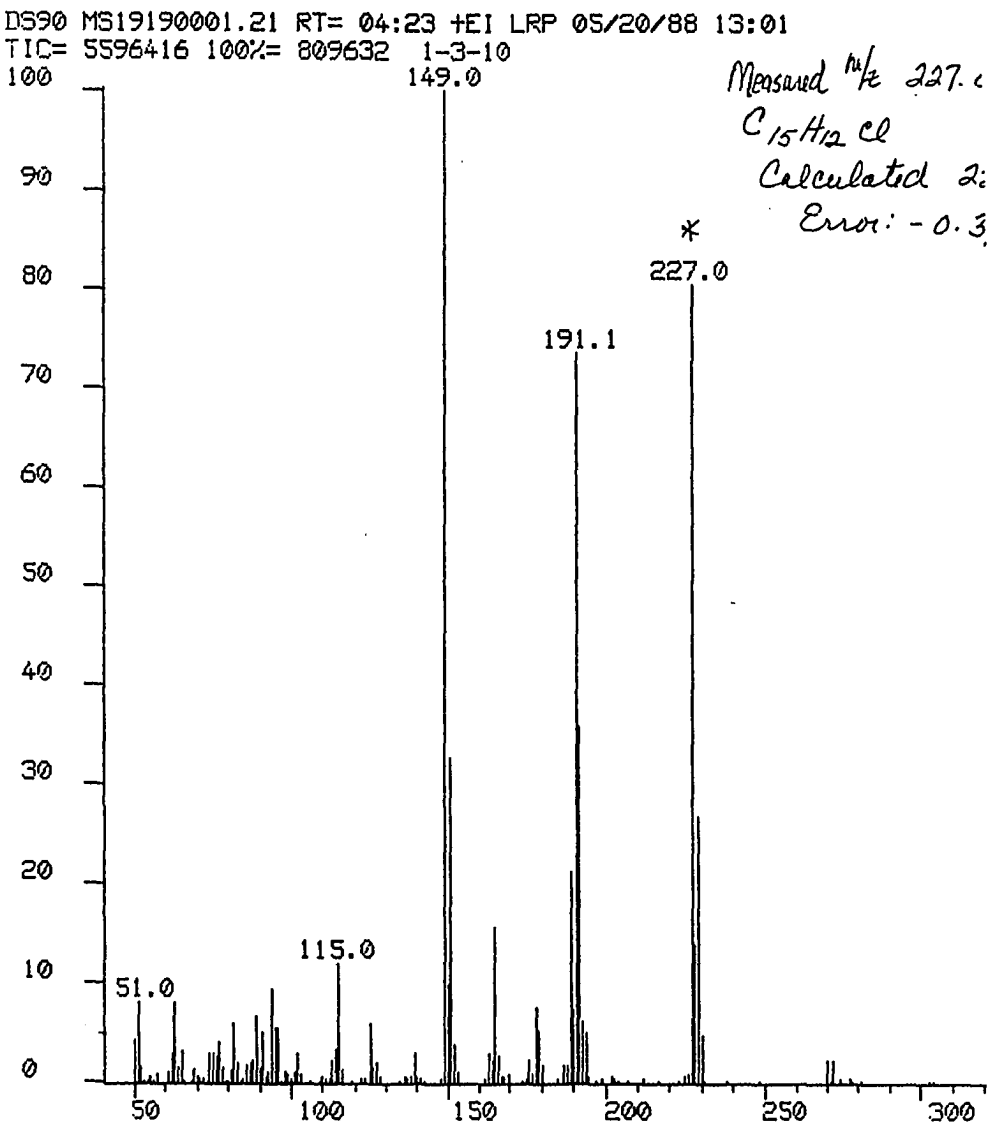


Figure 45. MASS of (-)-1-bromo-1-chloro-trans-2,3-diphenylcyclopropane

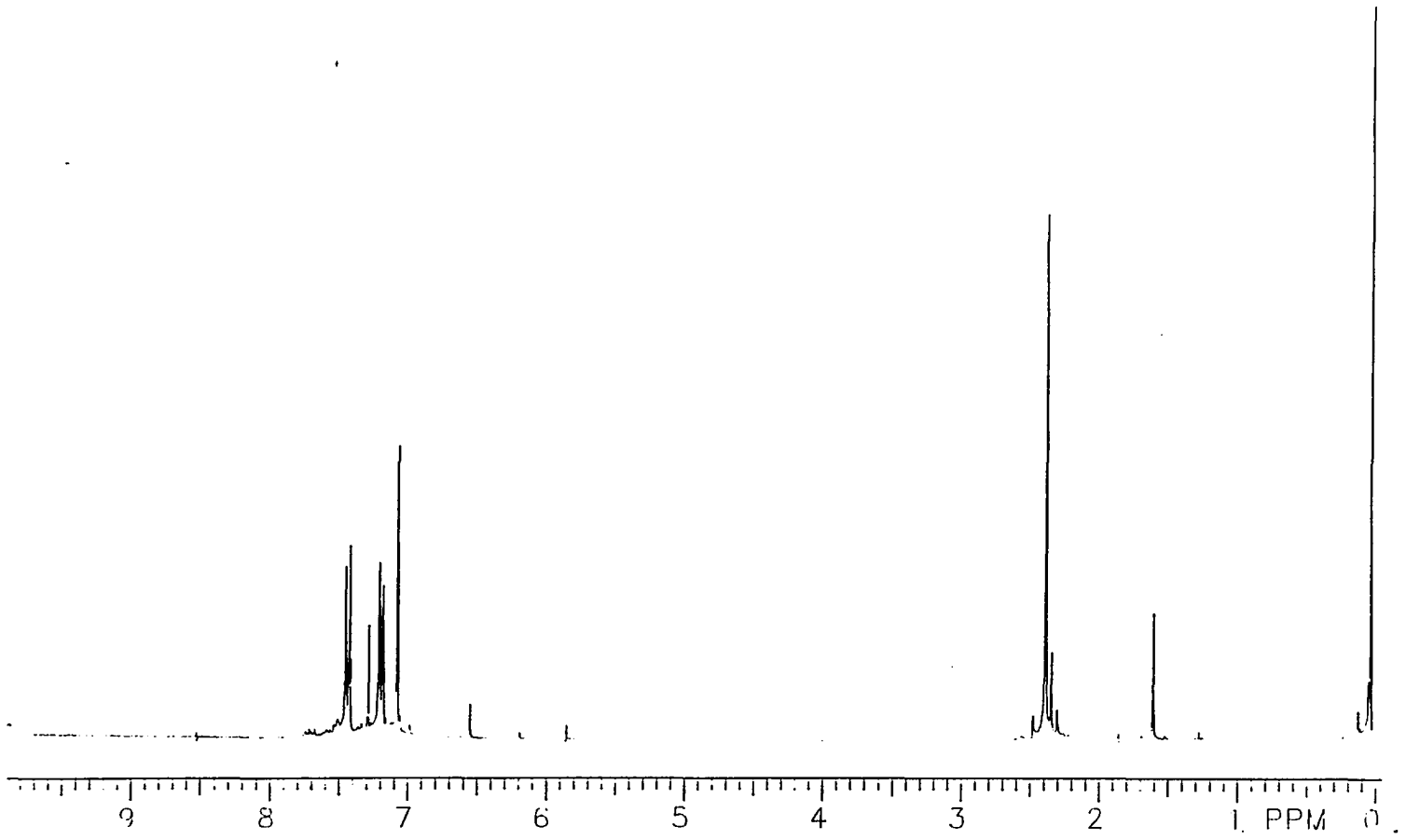


Figure 46. ^{1}H NMR of trans-di(4-methylphenyl)stilbene

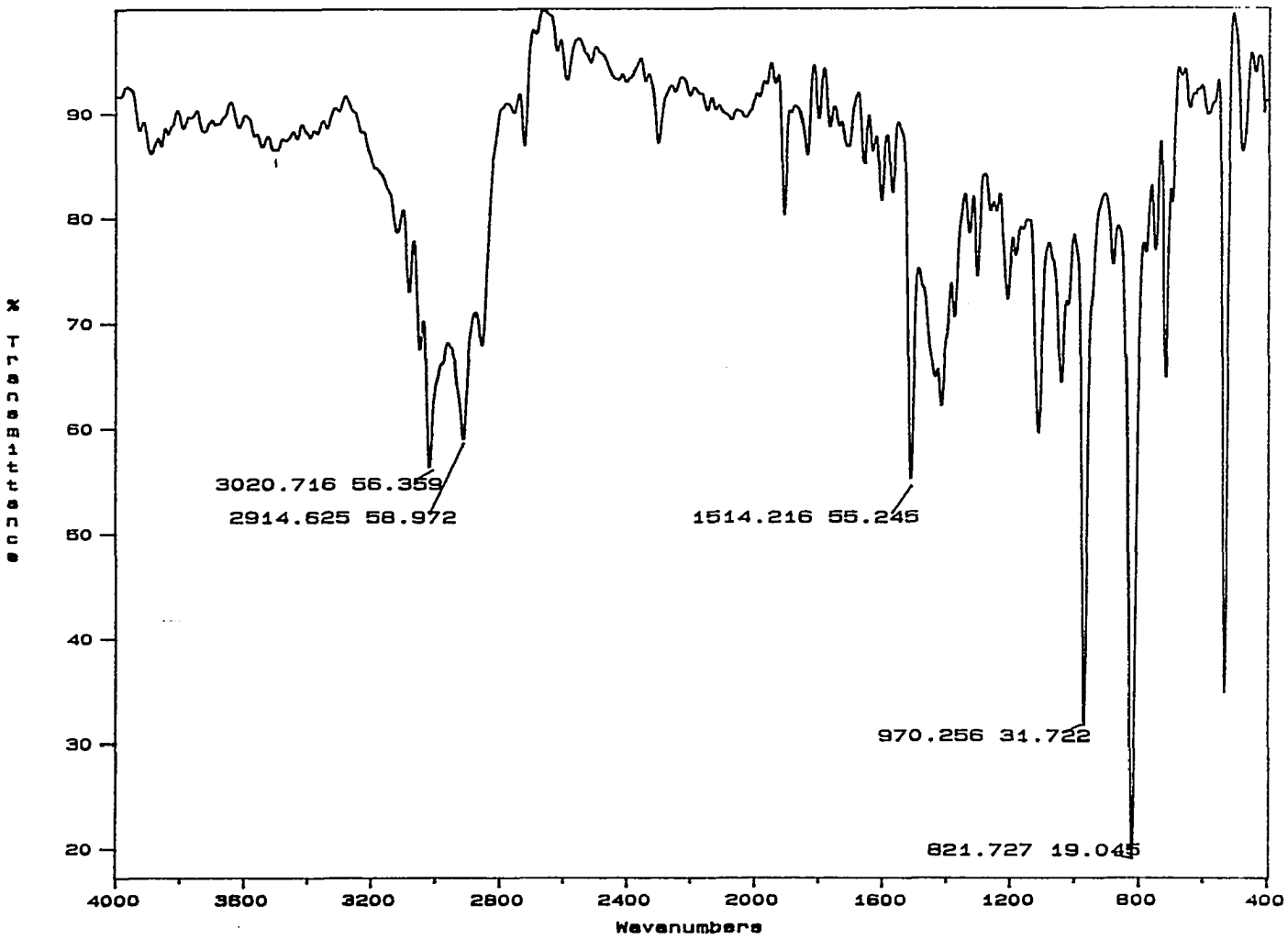


Figure 47. IR of trans-di(4-methylphenyl)stilbene

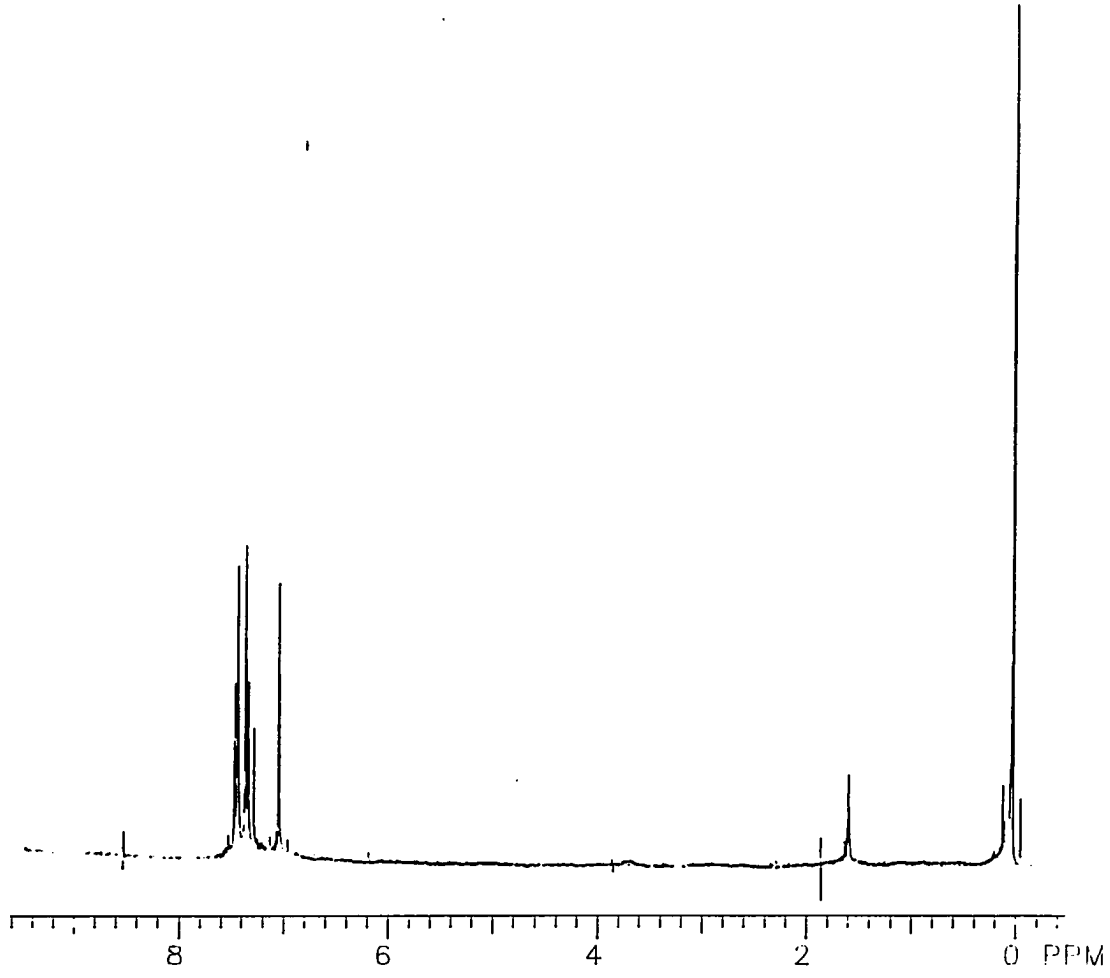


Figure 48. ^{1}H NMR of trans-di(4-chlorophenyl)stilbene

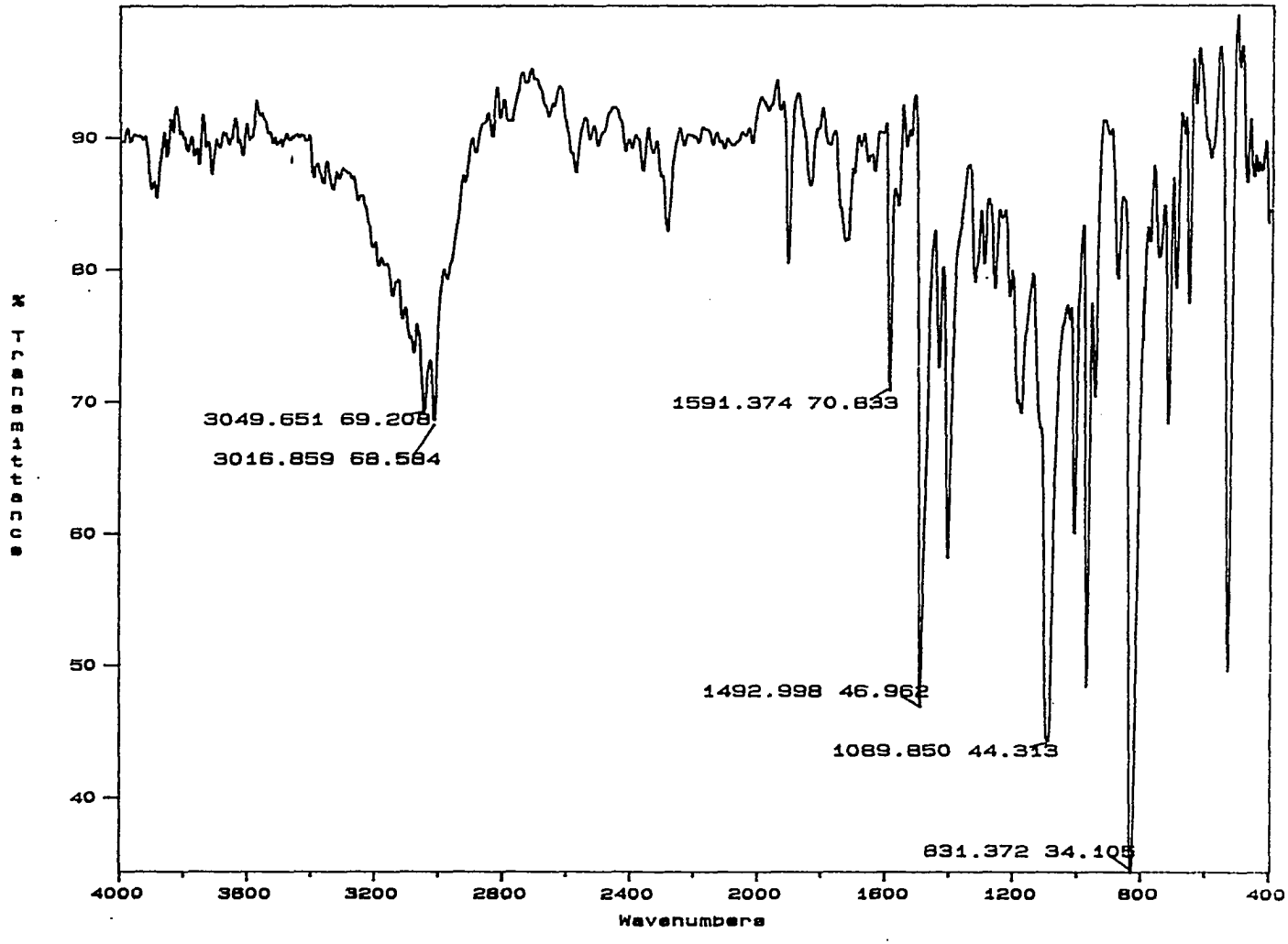


Figure 49. IR of trans-di(4-chlorophenyl)stilbene

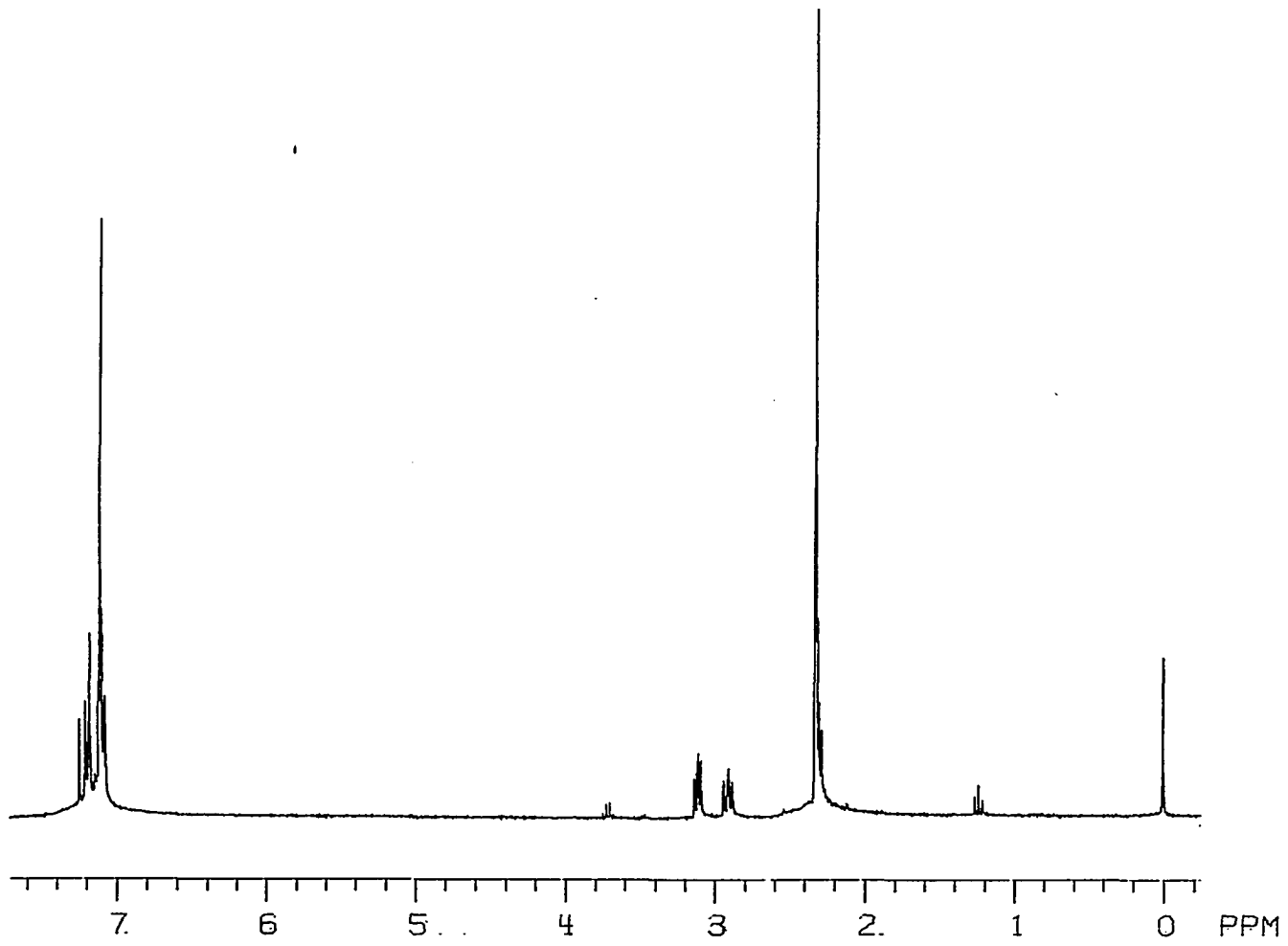


Figure 50. ^{1}H NMR of trans-2,3-di(4-methylphenyl)cyclopropane carboxylic acid

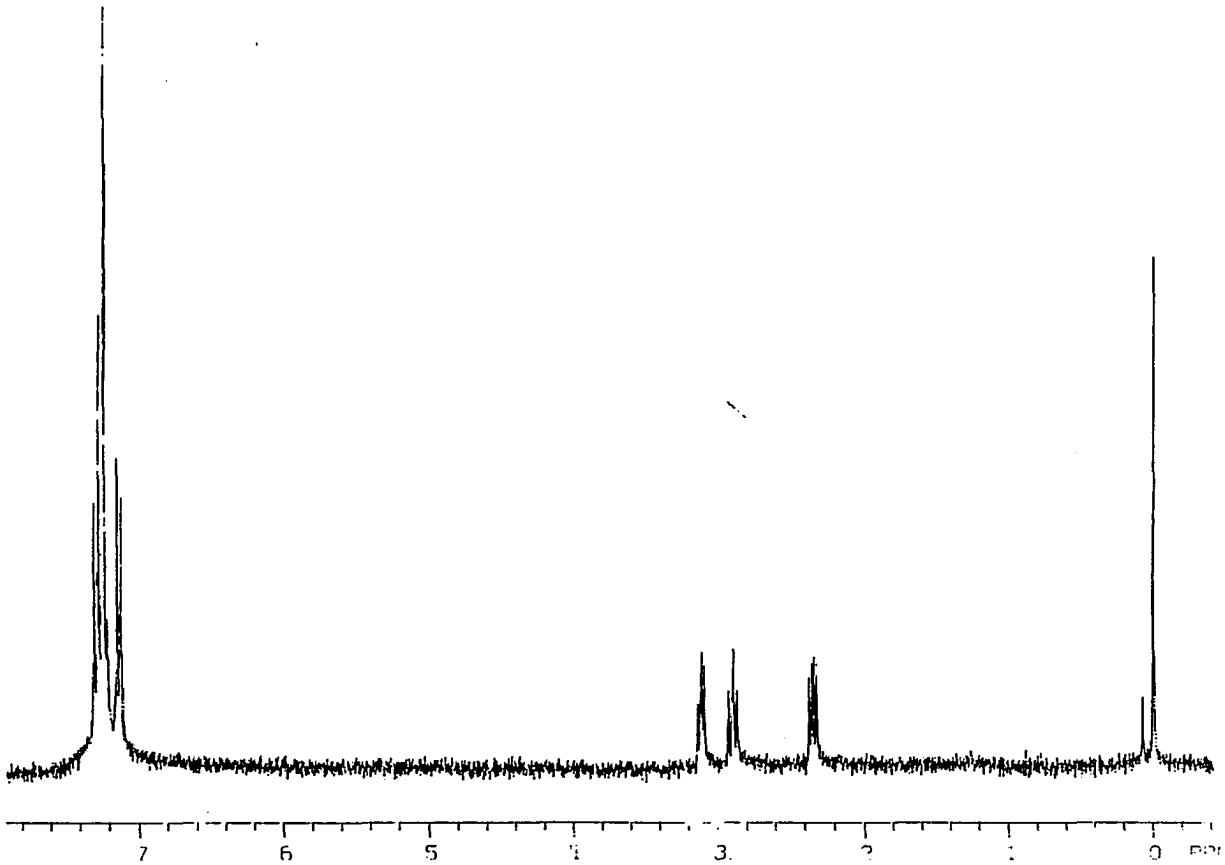


Figure 51. ^{1}H NMR of trans-2,3-di(4-chlorophenyl)cyclopropane carboxylic acid

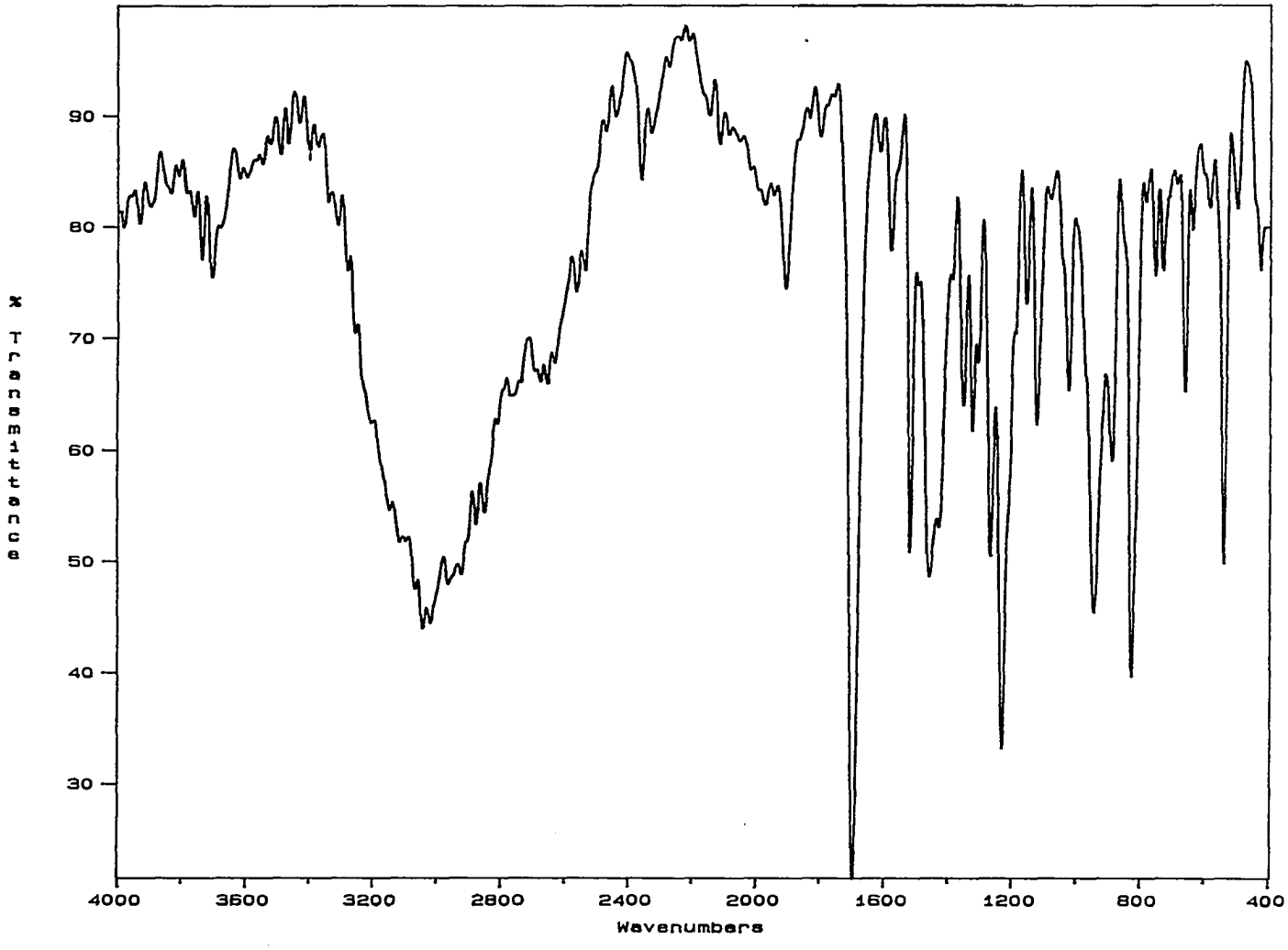


Figure 52. IR of trans-2,3-di(4-methylphenyl)cyclopropane carboxylic acid

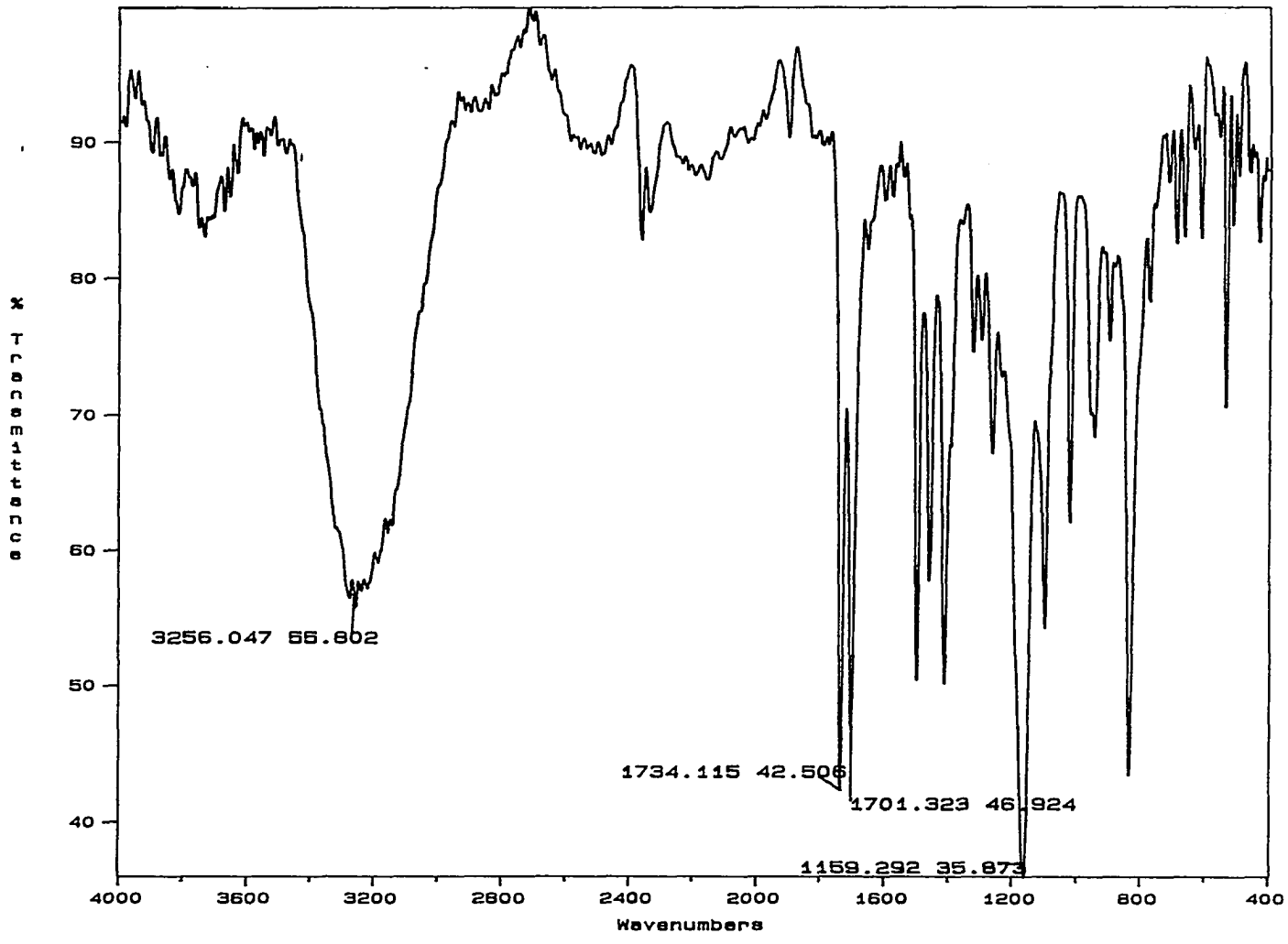


Figure 53. IR of trans-2,3-di(4-chlorophenyl)cyclopropane carboxylic acid

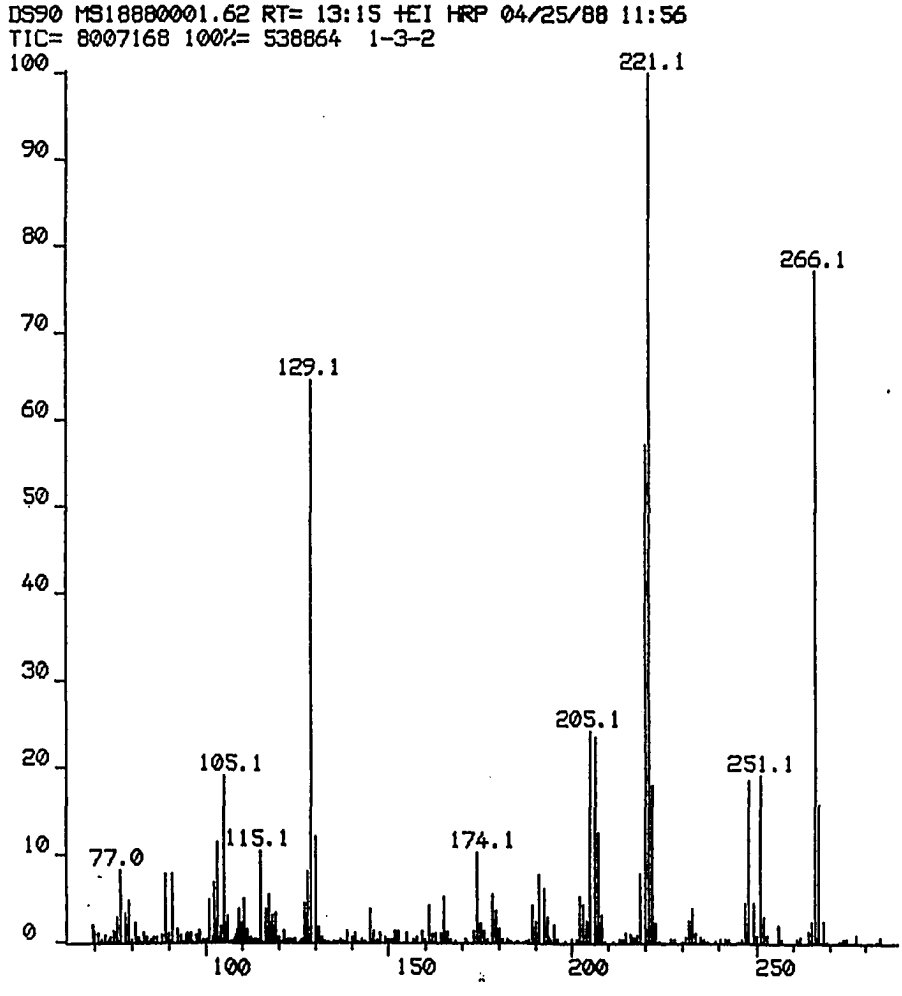


Figure 54. MASS of trans-2,3-di(4-methylphenyl) cyclopropane carboxylic acid

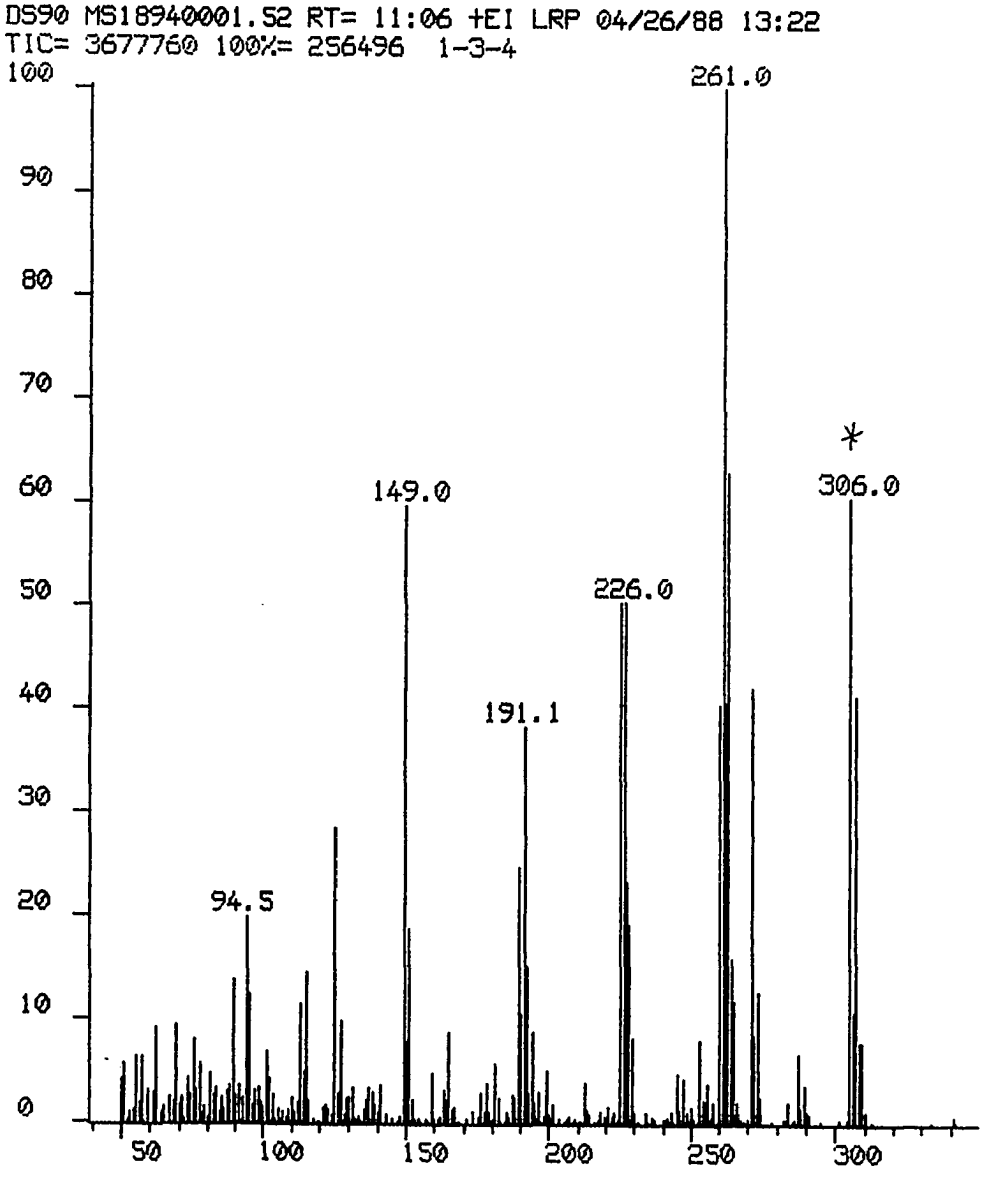


Figure 55. MASS of trans-2,3-di(4-chlorophenyl) cyclopropane carboxylic acid

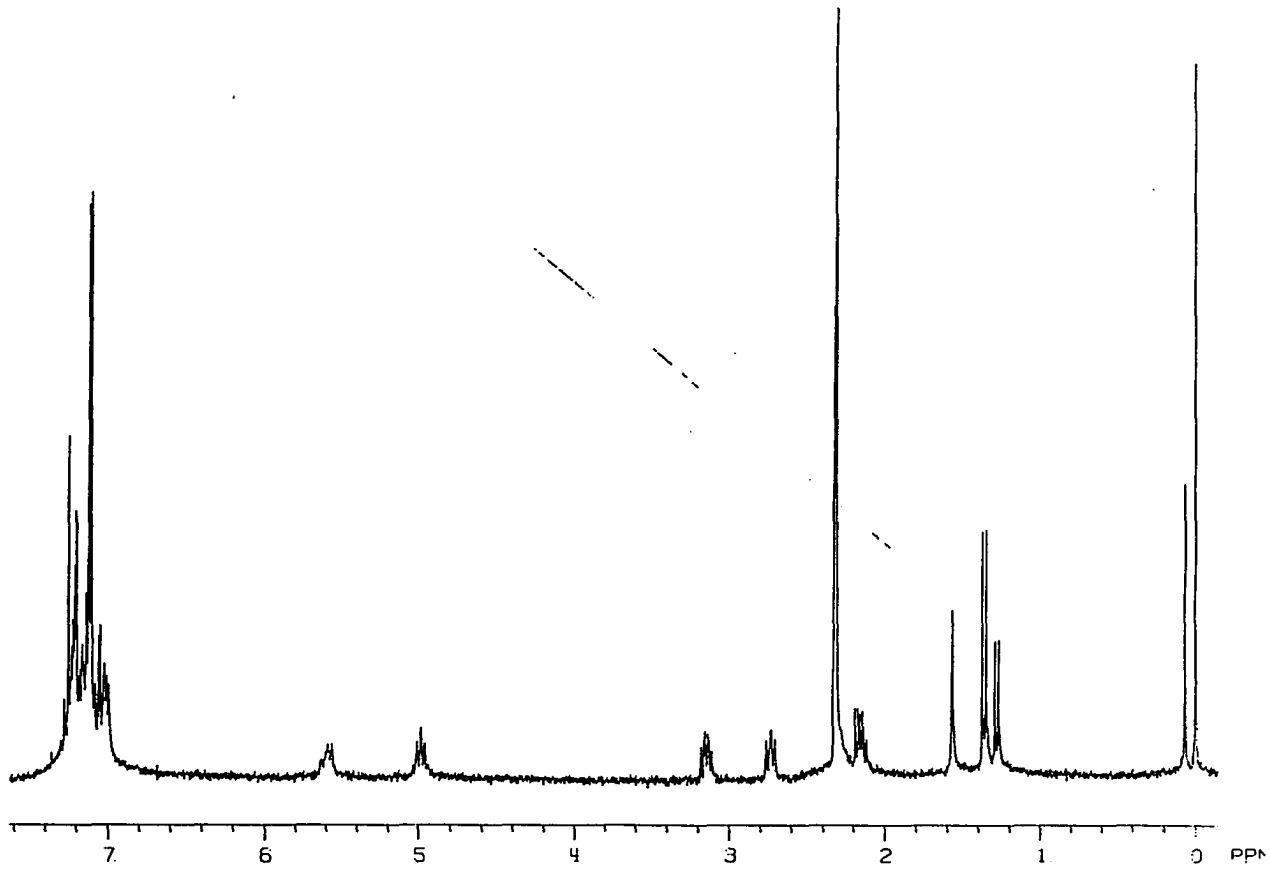


Figure 56. ^{1}H NMR of N-[(S)-α-methylbenzyl]-trans-2,3-di(4-methylphenyl)cyclopropane-1-carboxamide from racemic acid

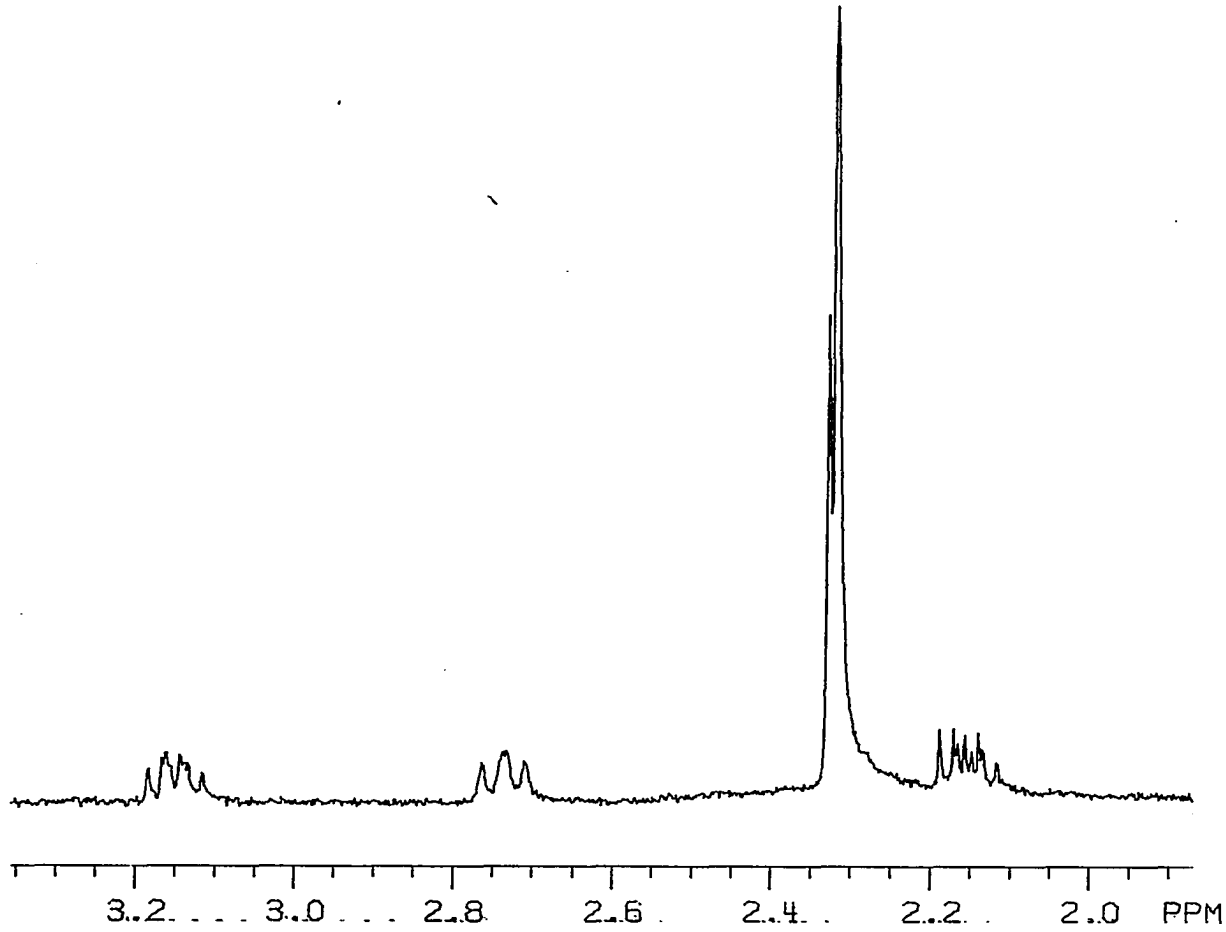


Figure 57. Partial enlargement in Figure 56

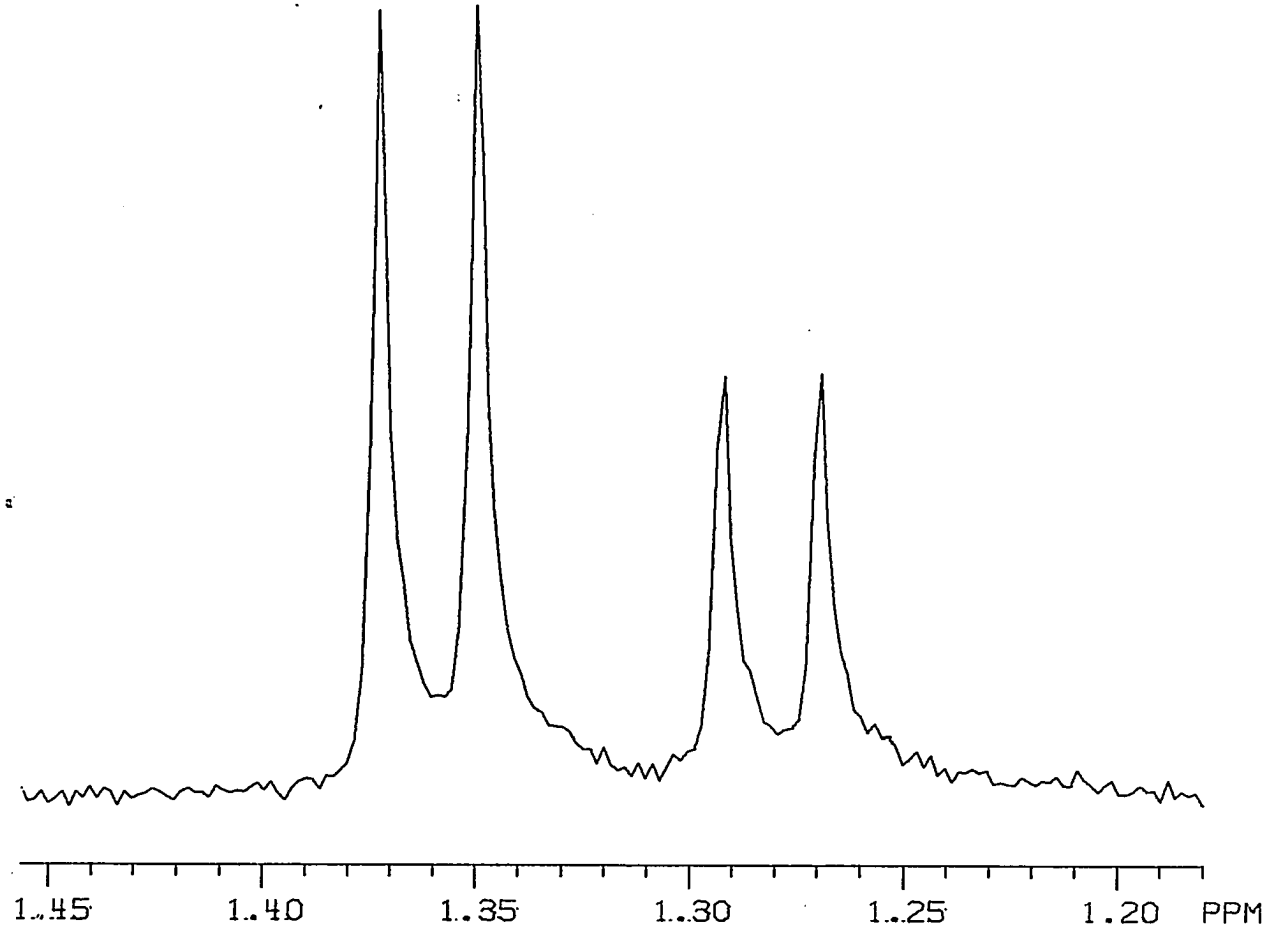


Figure 58. Partial enlargement in Figure 56

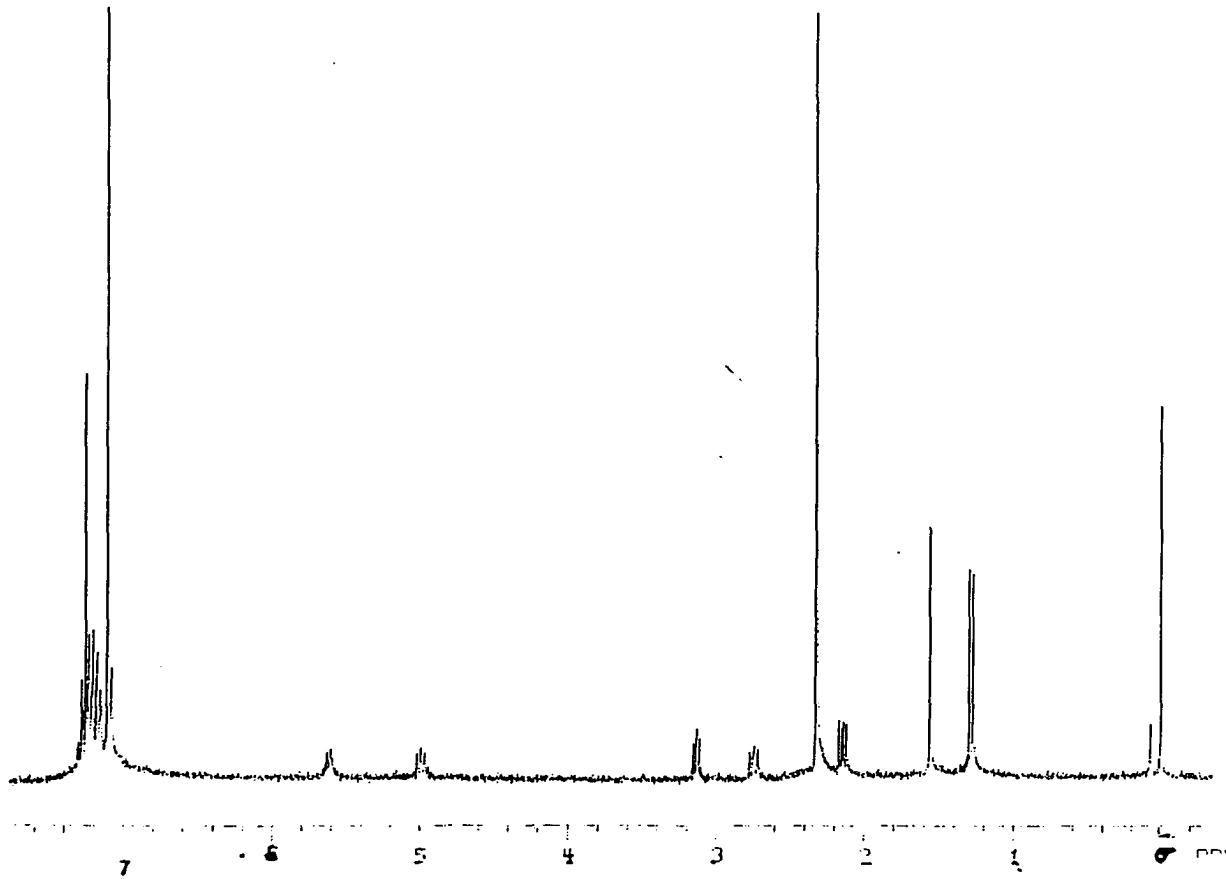


Figure 59. ^{1}H NMR of N-[(S)-α-methylbenzyl]-trans-2,3-di(4-methylphenyl)cyclopropane-1-carboxamide from optically active acid

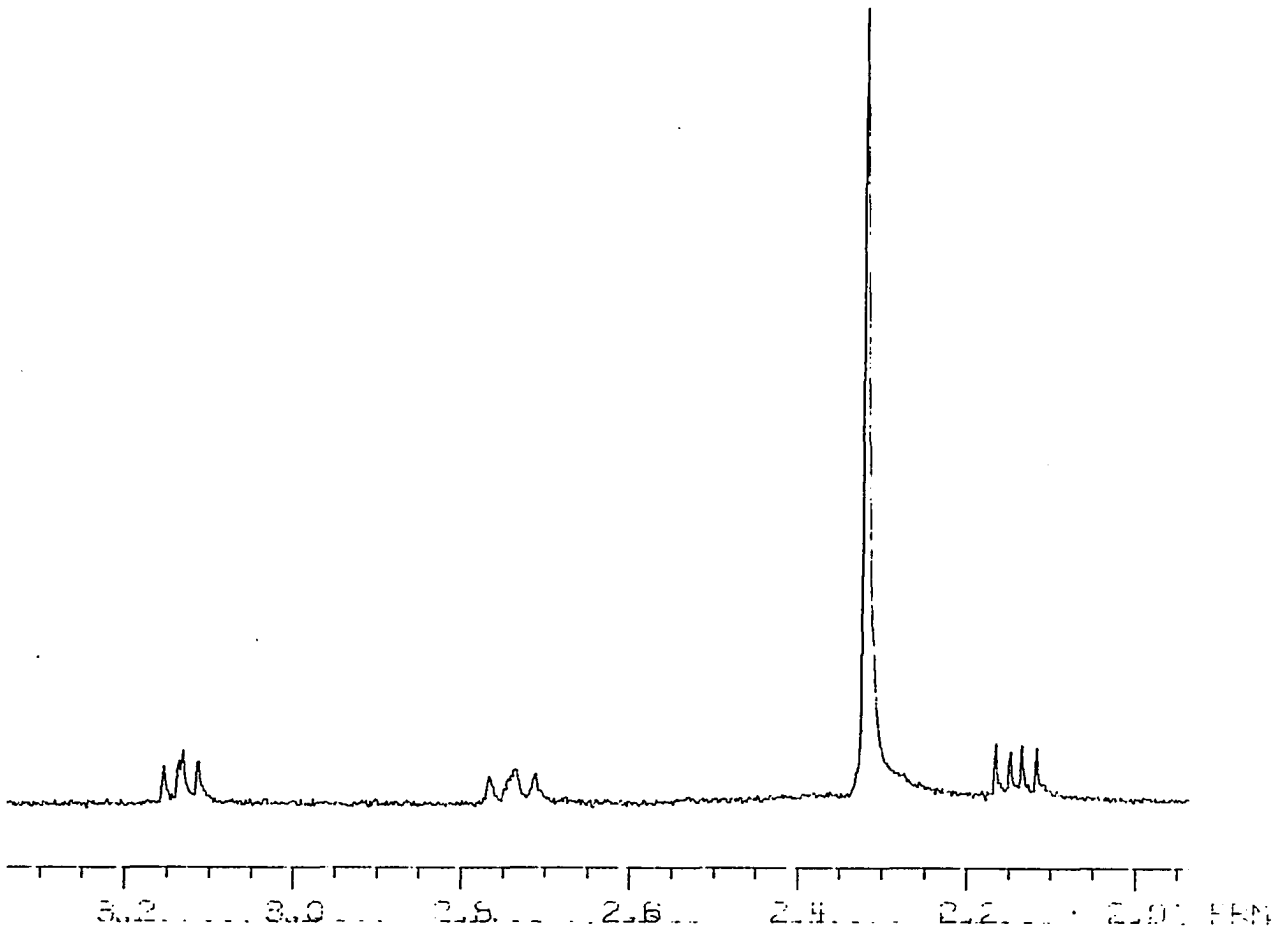


Figure 60. Partial enlargement in Figure 59

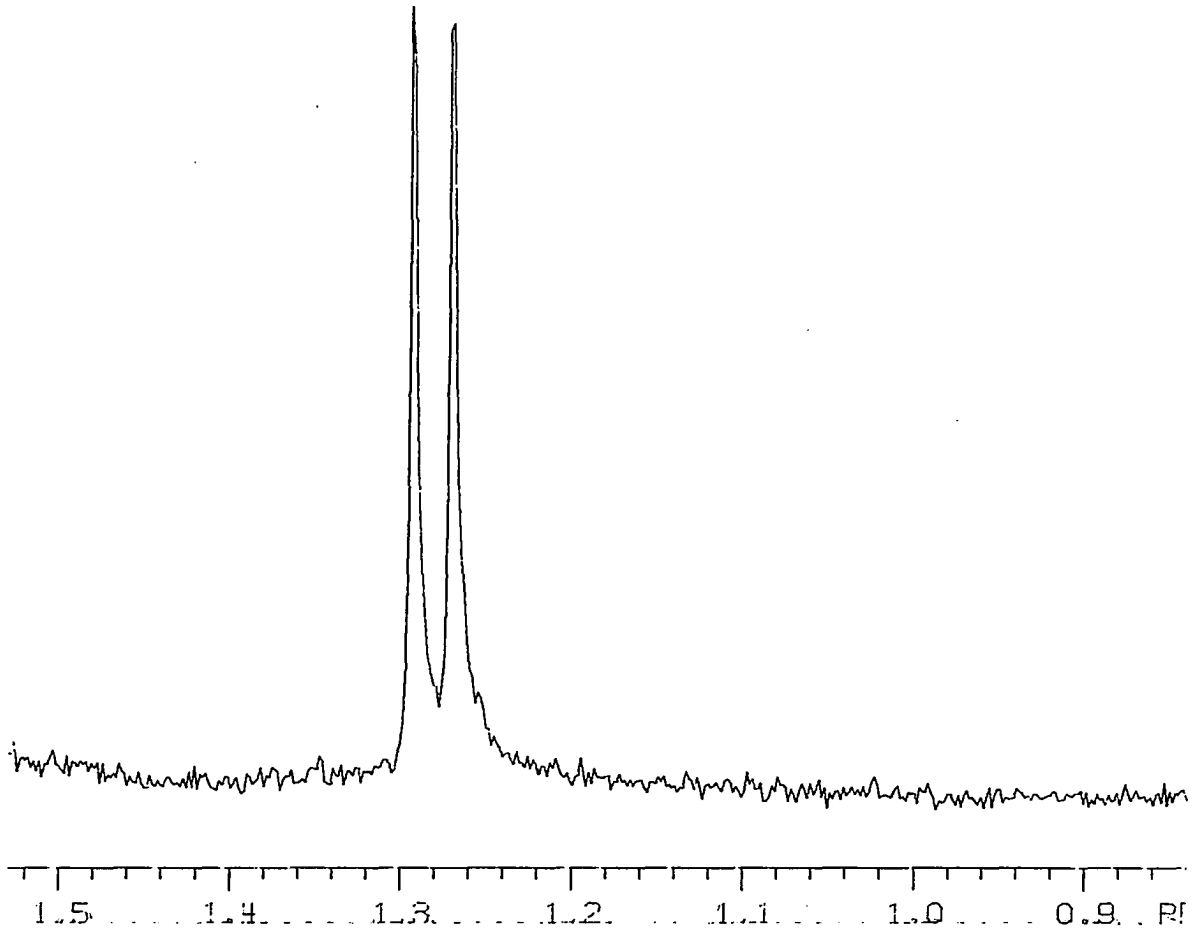


Figure 61. Partial enlargement in Figure 59

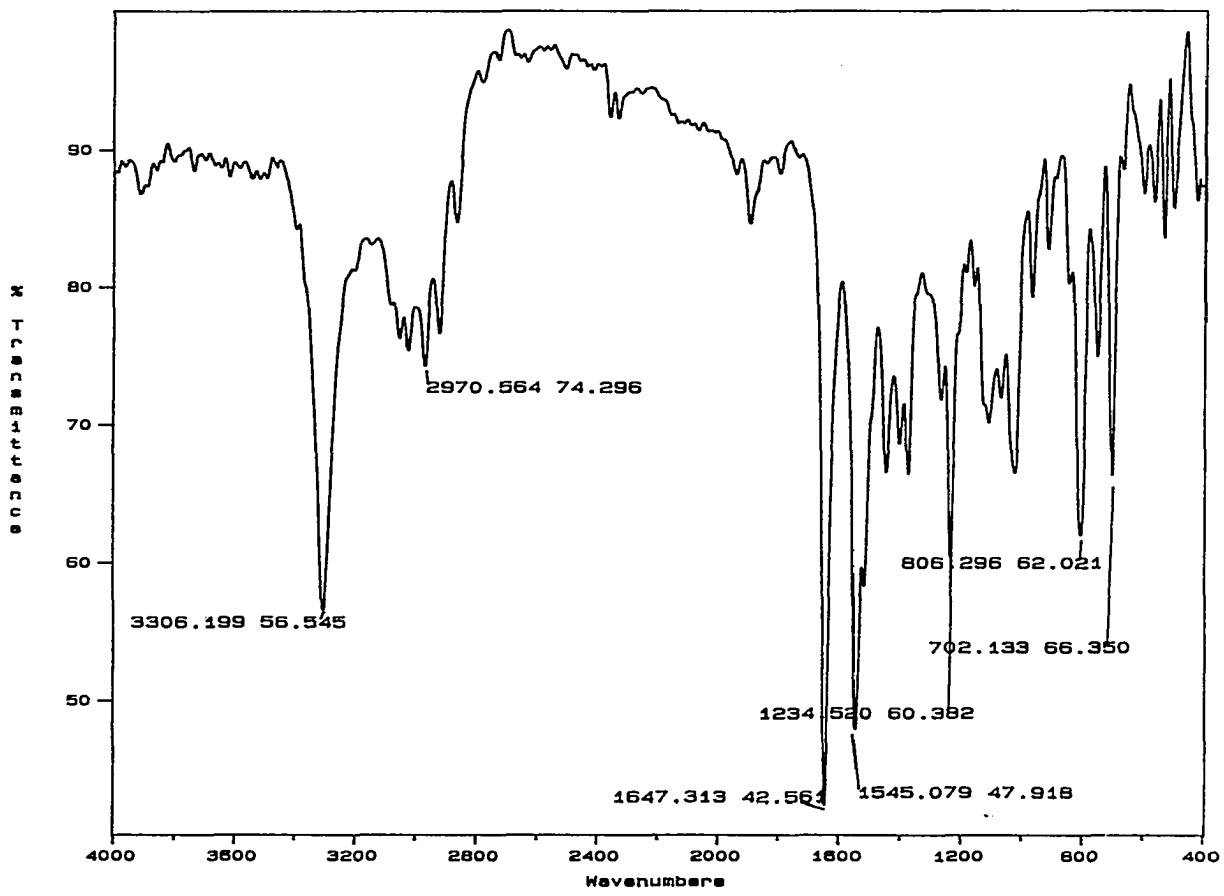


Figure 62. IR of (S)-N-(α-methylbenzyl)-trans-2,3-di(4-methylphenyl)cyclopropane-1-carboxamide

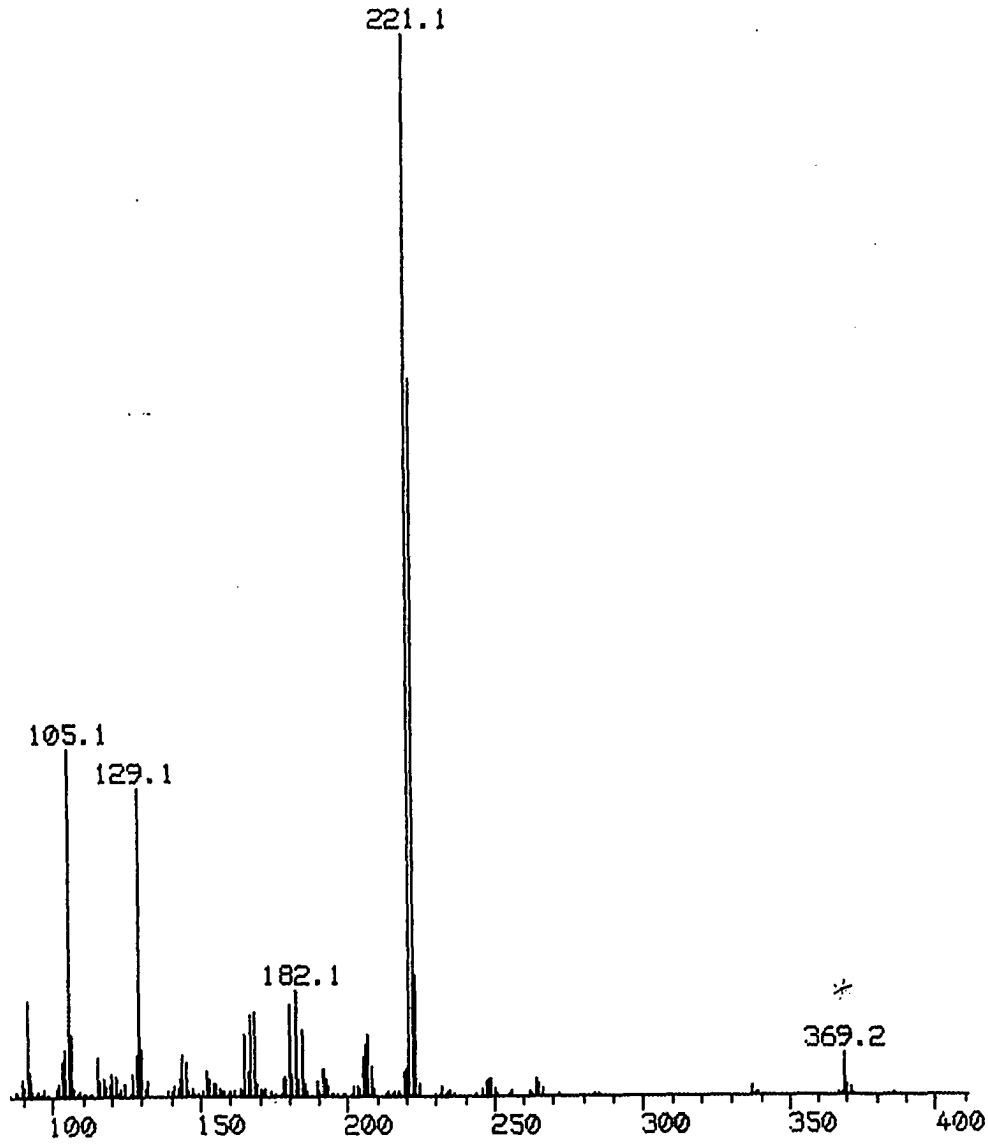


Figure 63. MASS of N-[(S)-α-methylbenzyl]-trans-2,3-di(4-methylphenyl)cyclopropane-1-carboxamide

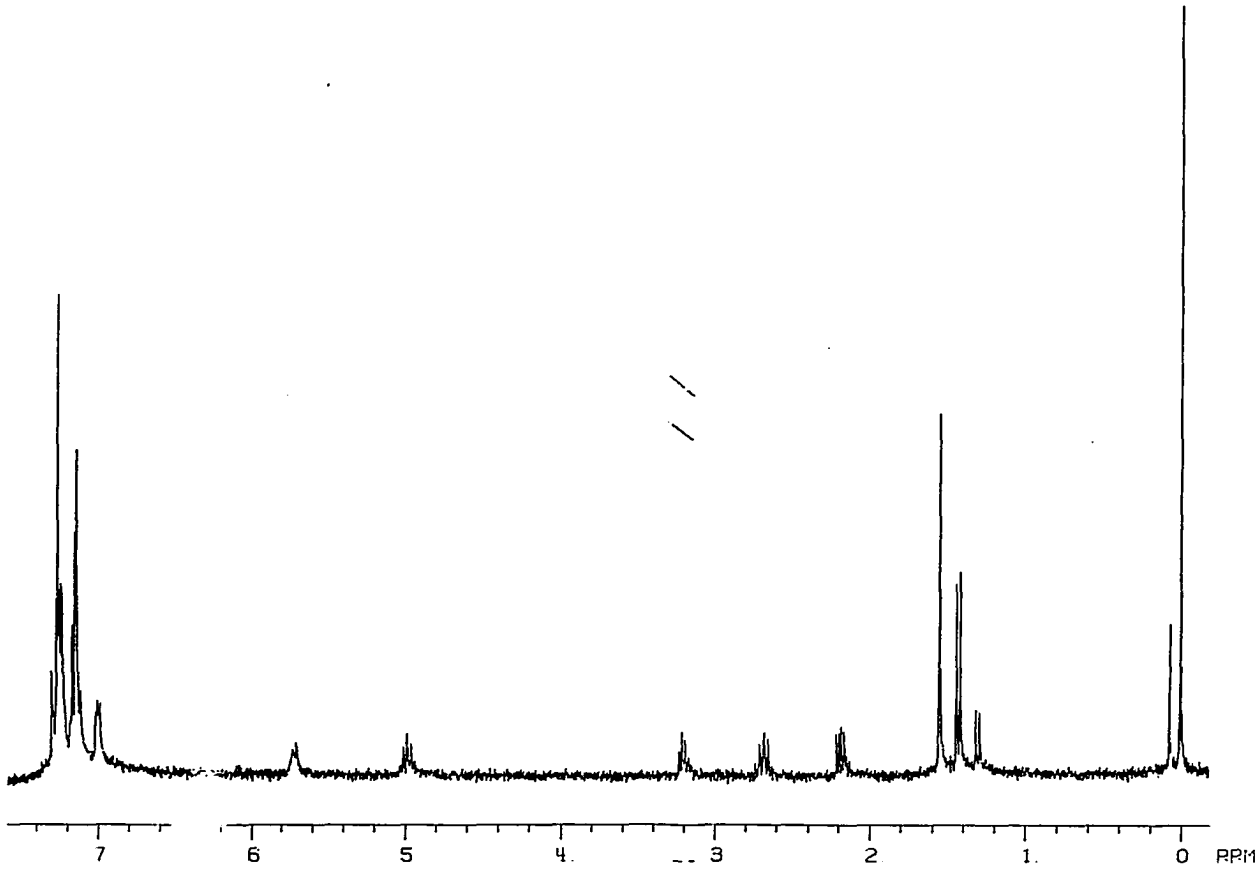


Figure 64. ^{1}H NMR of N-[(S)-α-methylbenzyl]-trans-2,3-di(4-chlorophenyl)cyclopropane-1-carboxamide from racemic acids

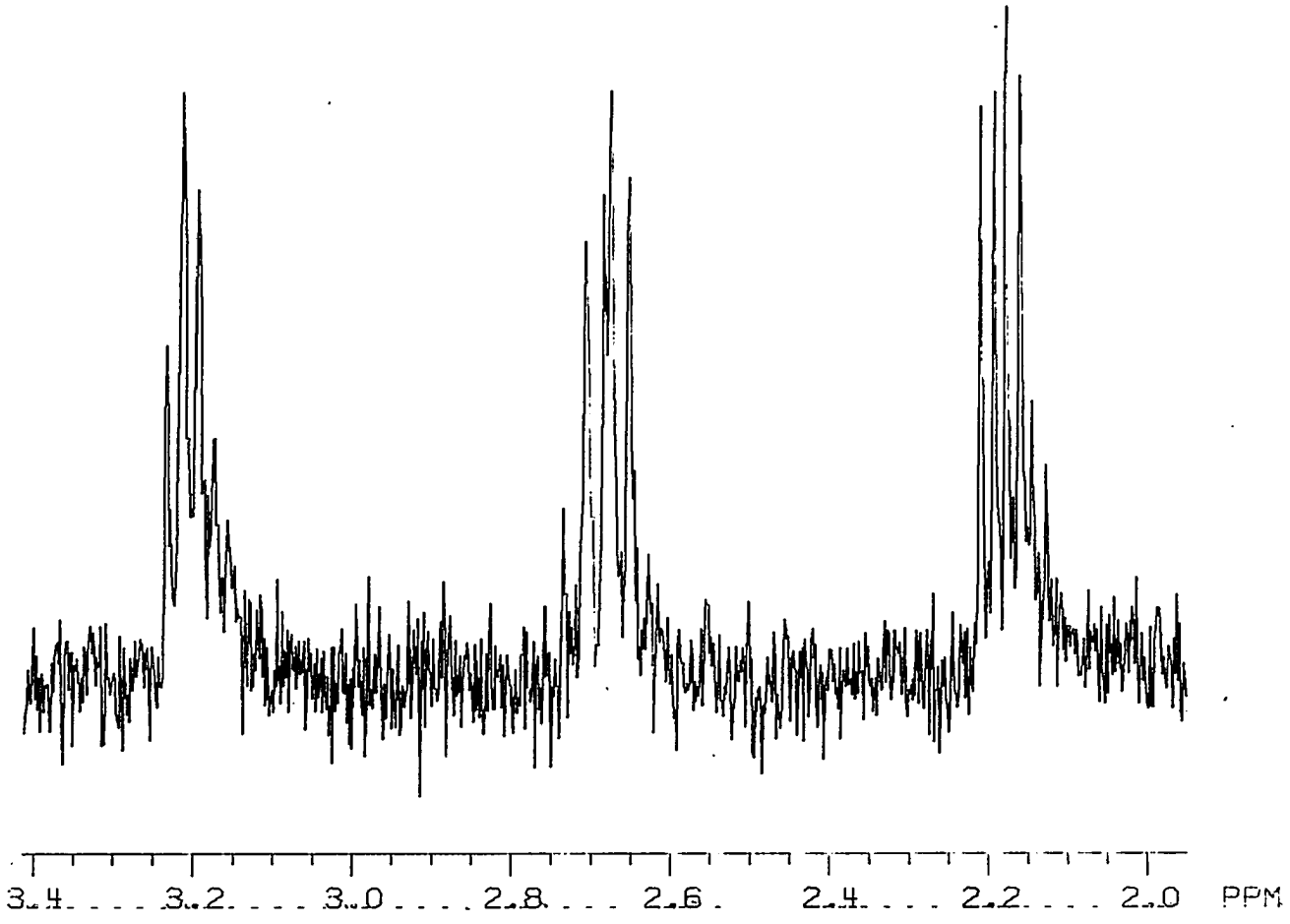


Figure 65. Partial enlargement in Figure 64

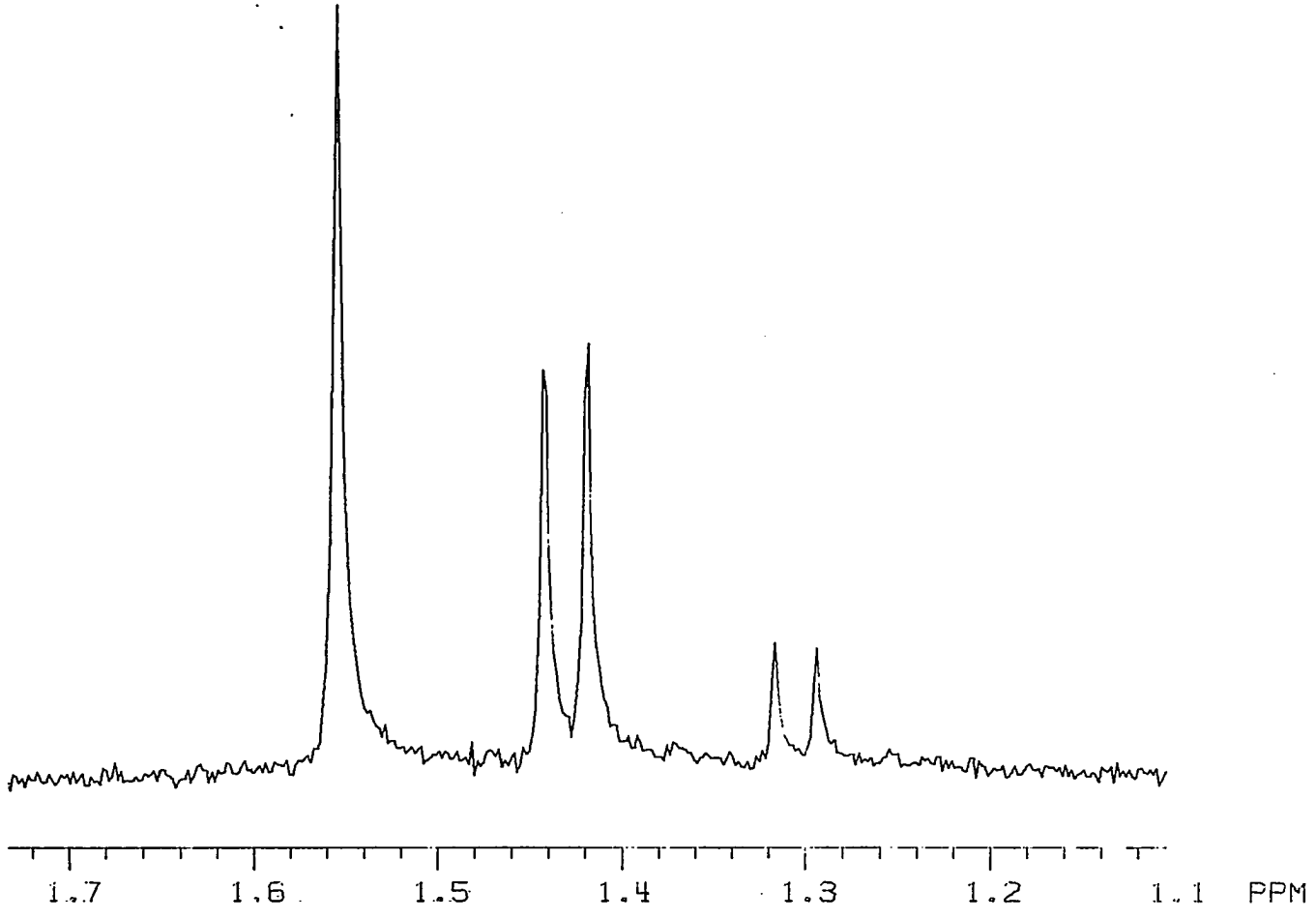


Figure 66. Partial enlargement in Figure 64

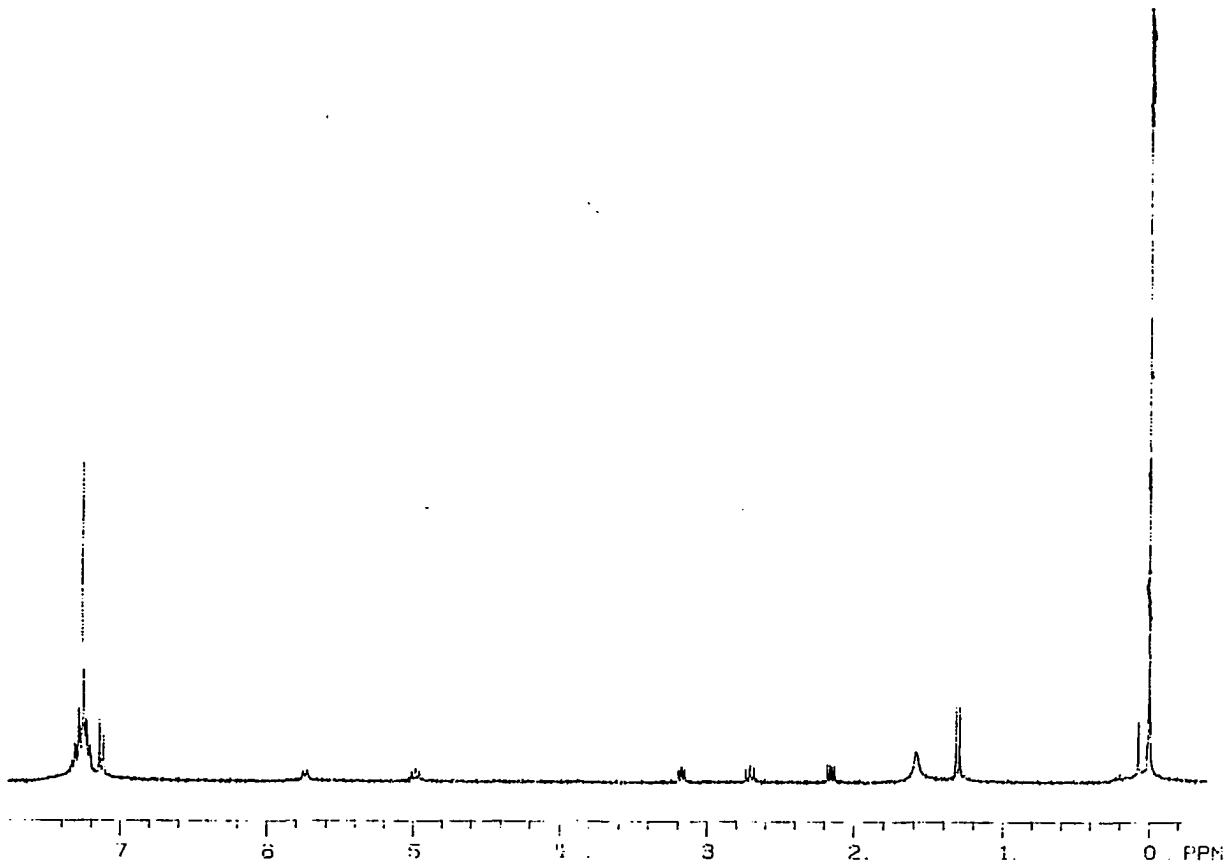


Figure 67. ^{1}H NMR of N-[(S)-α-methylbenzyl]-trans-2,3-di(4-chlorophenyl)cyclopropane-1-carboxamide from optically active acid

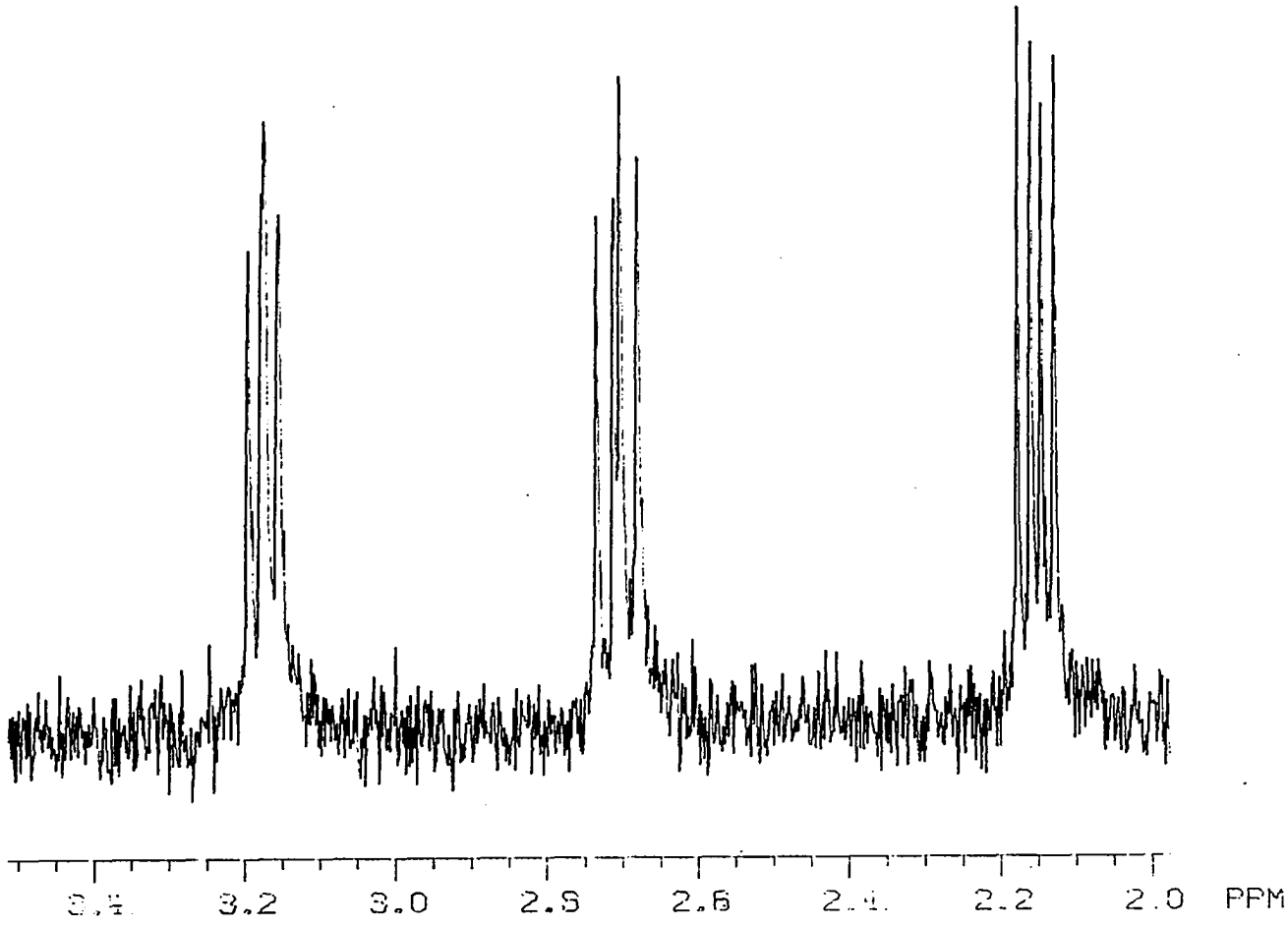


Figure 68. Partial enlargement in Figure 67

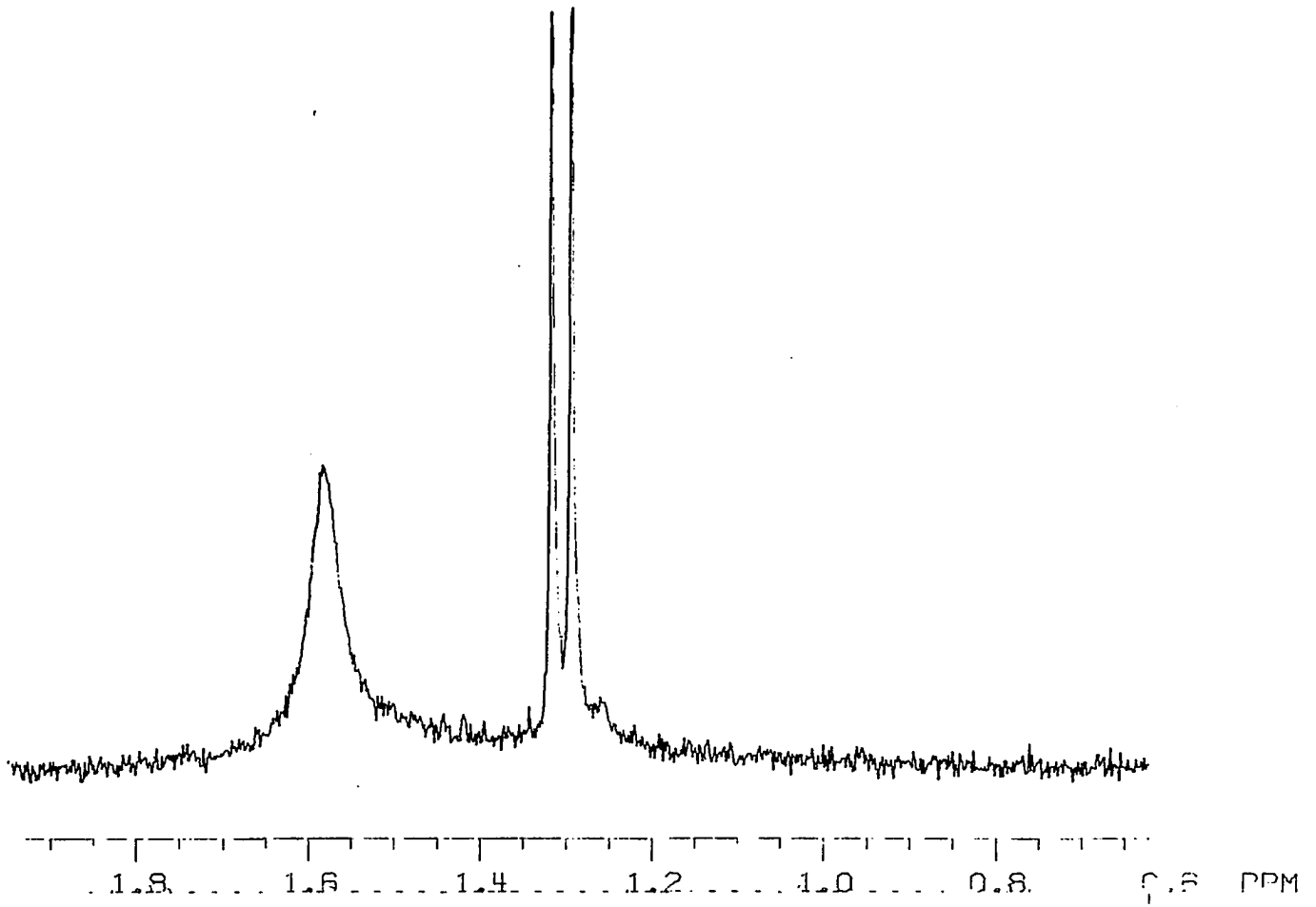


Figure 69. Partial enlargement in Figure 67

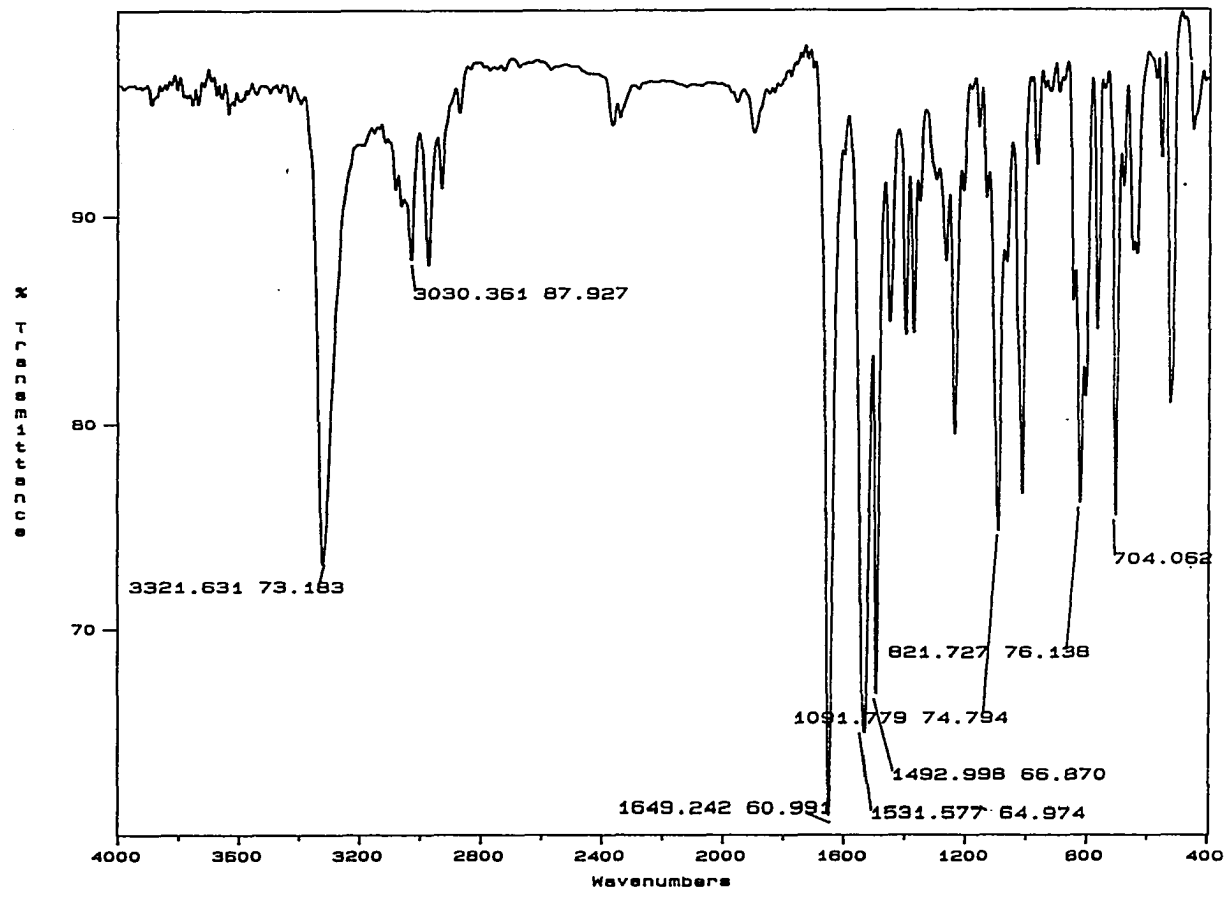


Figure 70. IR of N-[(S)-α-methylbenzyl]-trans-2,3-di(4-chlorophenyl)cyclopropane-1-carboxamide

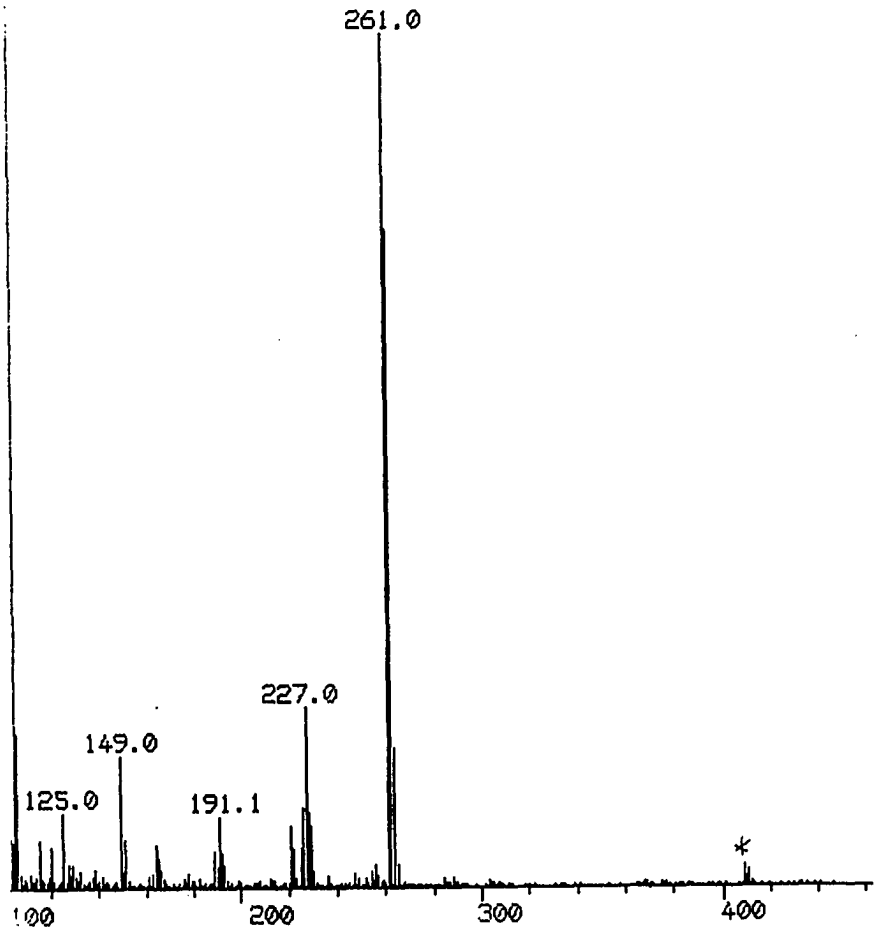


Figure 71. MASS of N-[(S)-α-methylbenzyl]-trans-2,3-di(4-chlorophenyl)cyclopropane-1-carboxamide

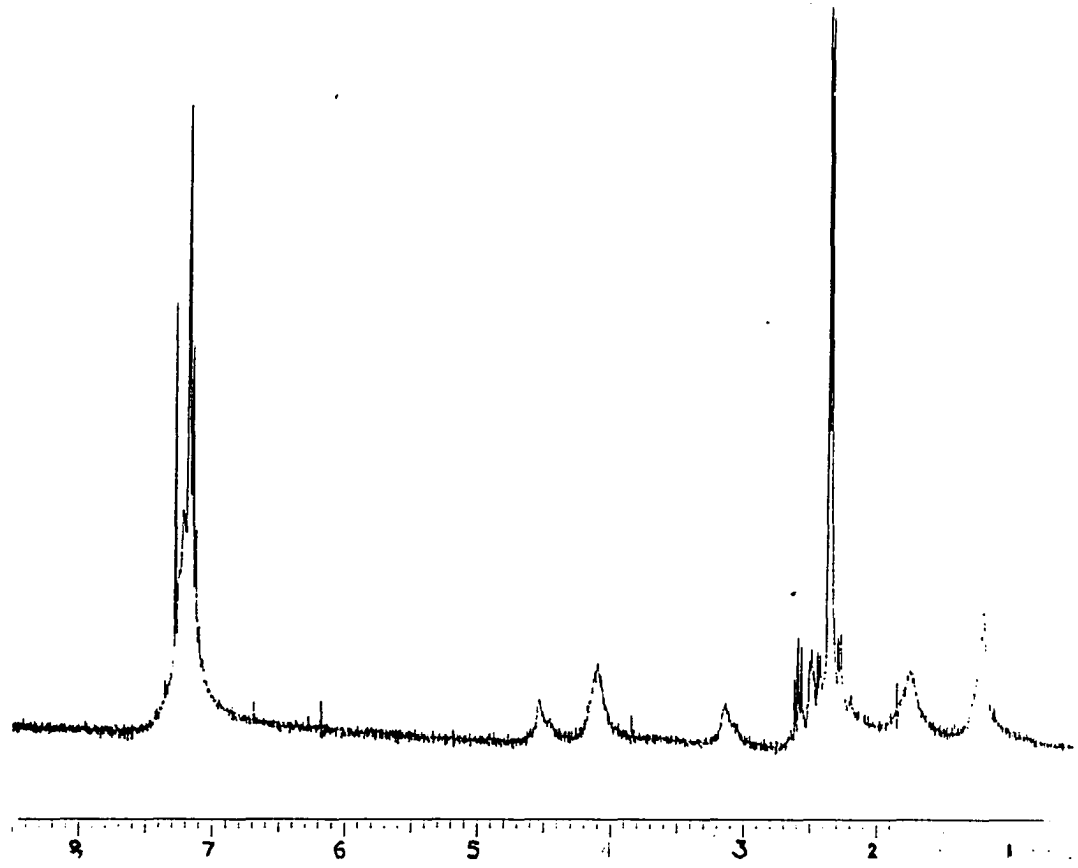


Figure 72. ^{1}H NMR of
(-)-ethyl trans-2,3-di(4-methylphenyl)cyclopropane-1-carbamate

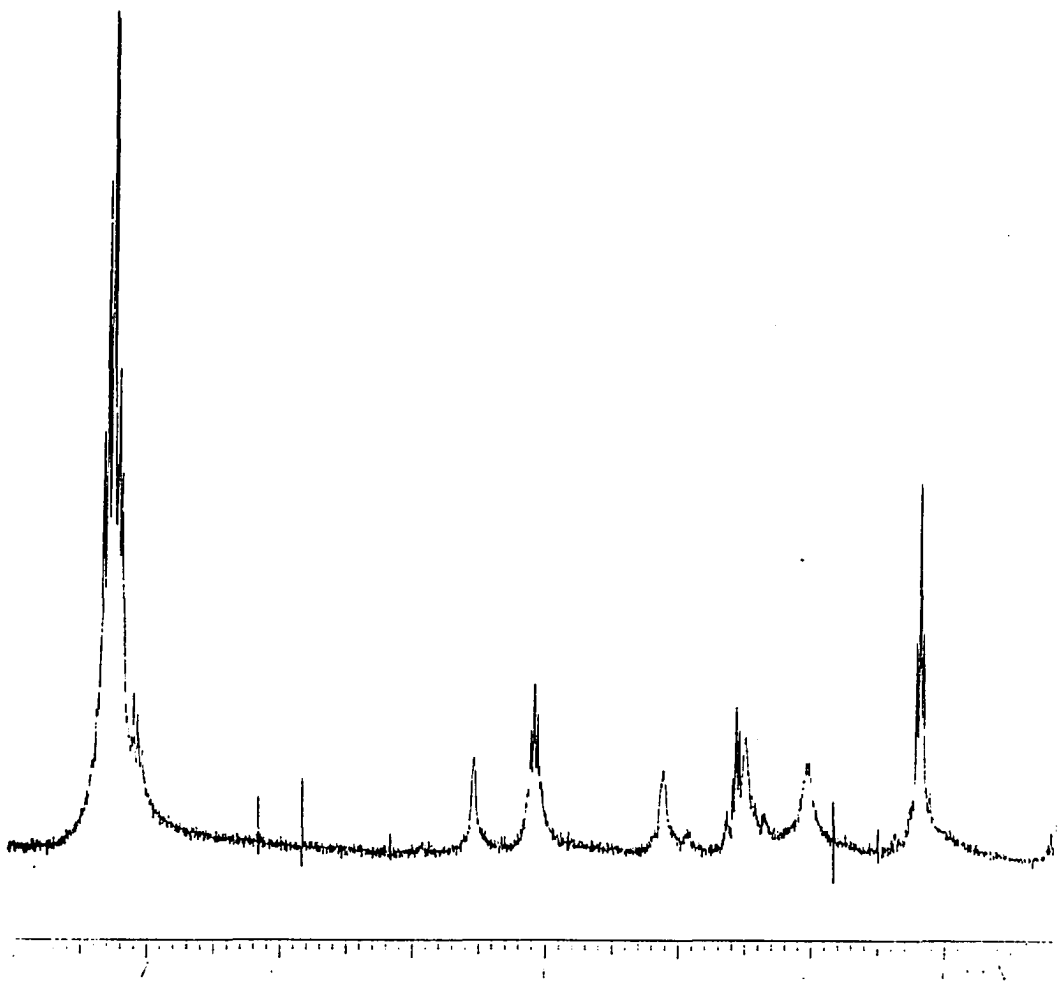


Figure 73. ^{1}H NMR of
(-)-ethyl trans-2,3-di(4-chlorophenyl)cyclopropane-1-carbamate

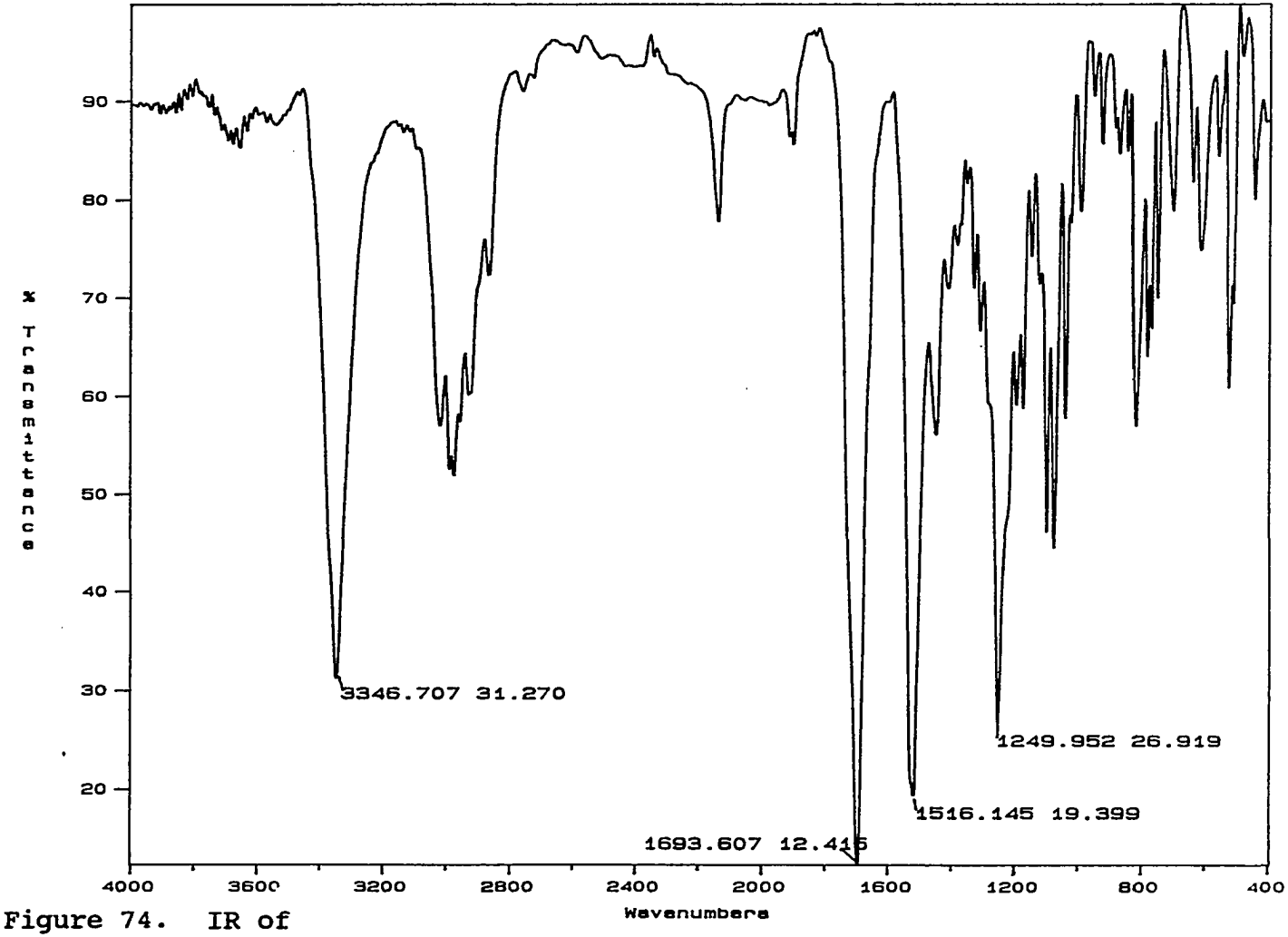


Figure 74. IR of
(-)-ethyl trans-2,3-di(4-methylphenyl)cyclopropane-1-carbamate

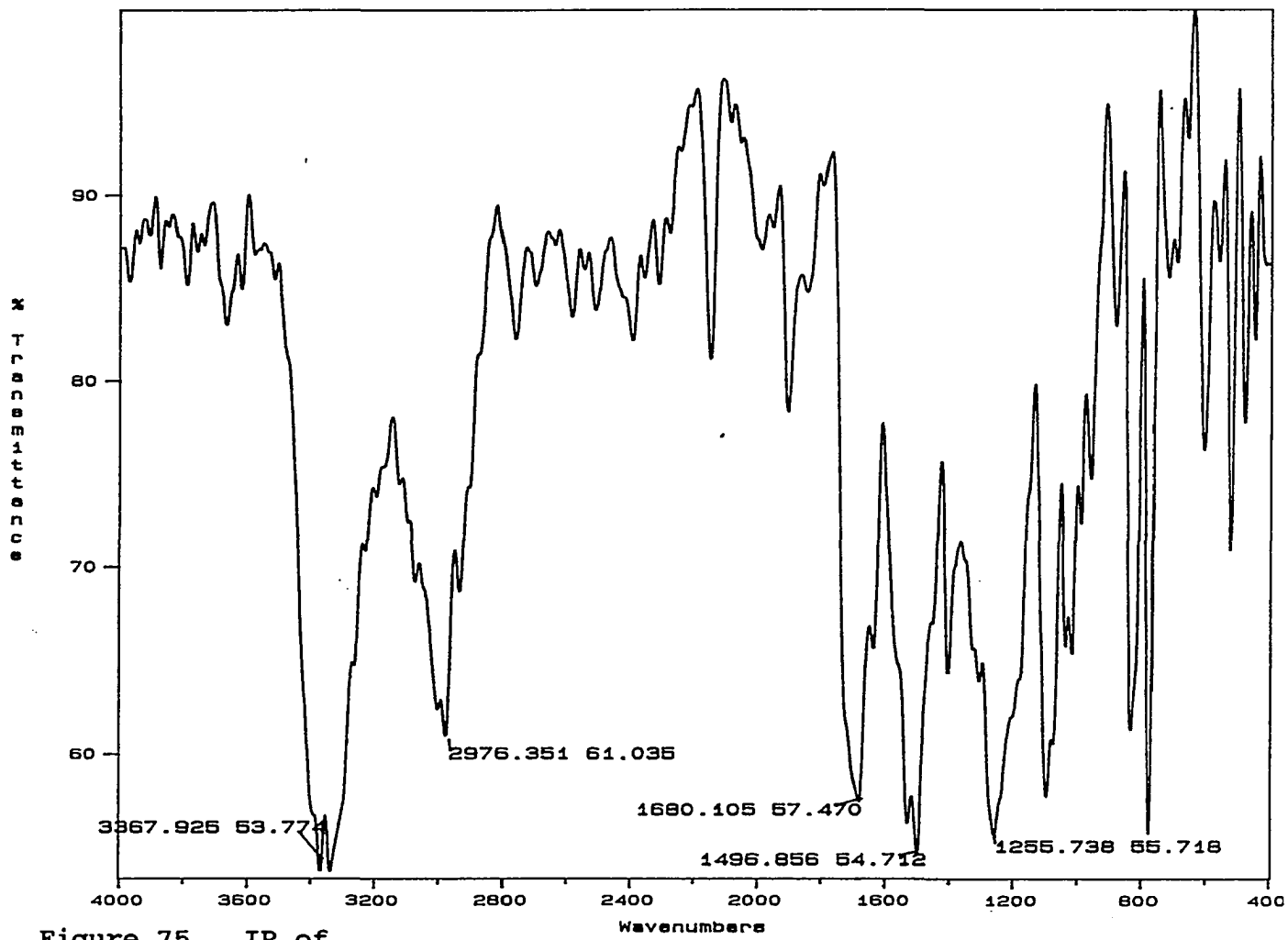
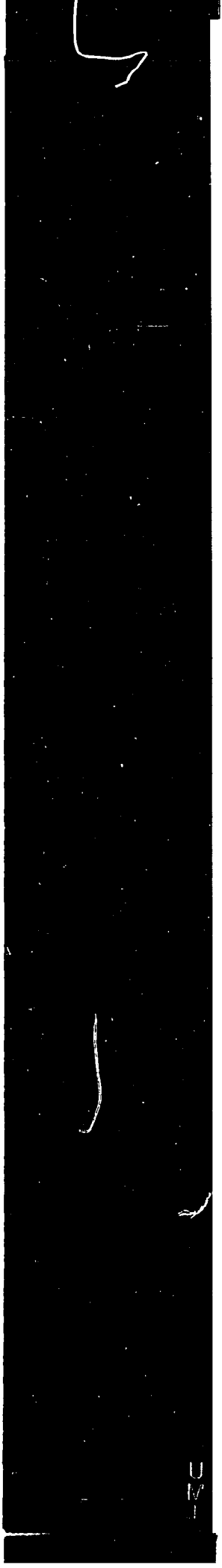


Figure 75. IR of

(-)-ethyl trtans-2,3-di(4-chlorophenyl)cyclopropane-1-carbamate



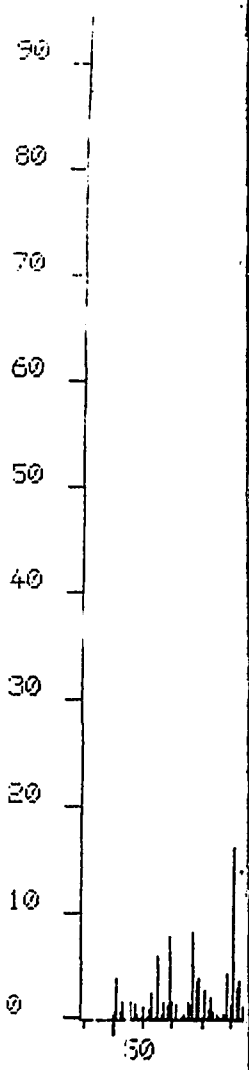


Figure 76. MA
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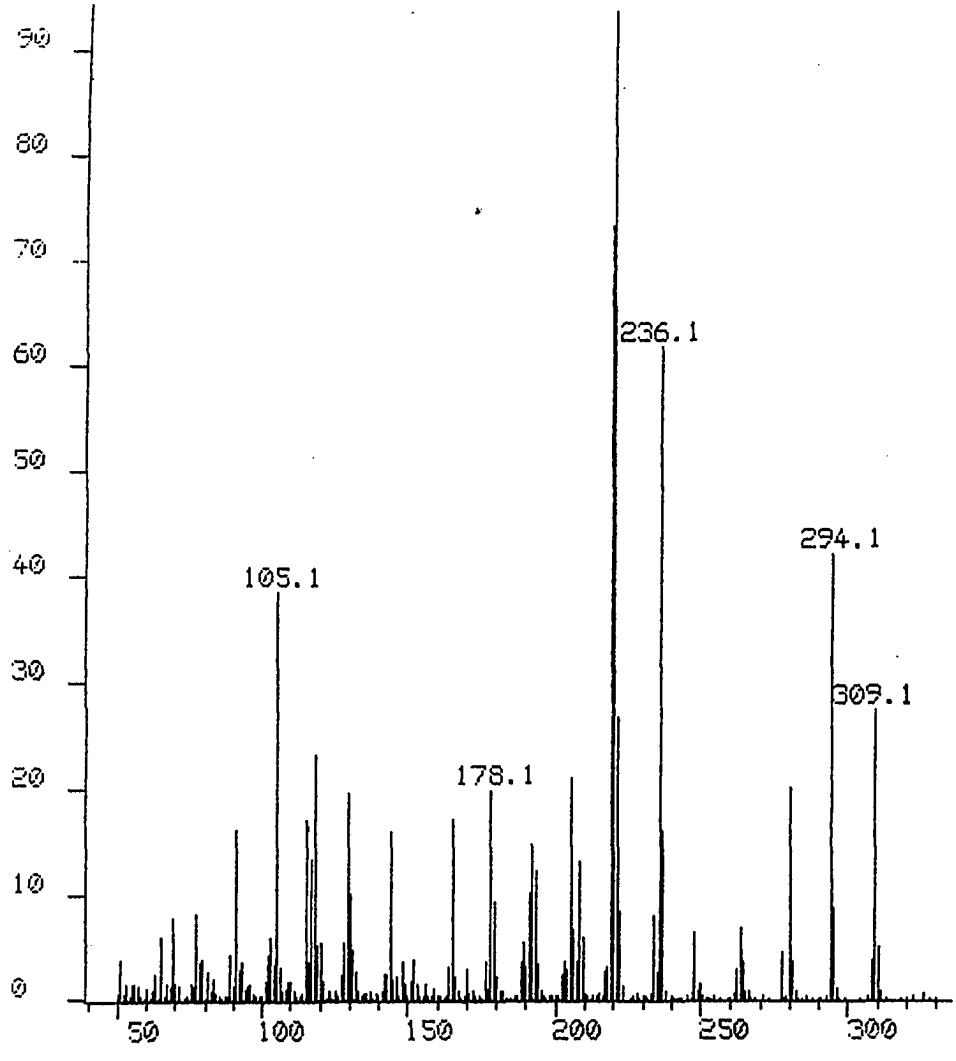

Figure 76. MASS of (-)-ethyl trans-2,3-di(4-methylphenyl)cyclopropane-1-carbamate

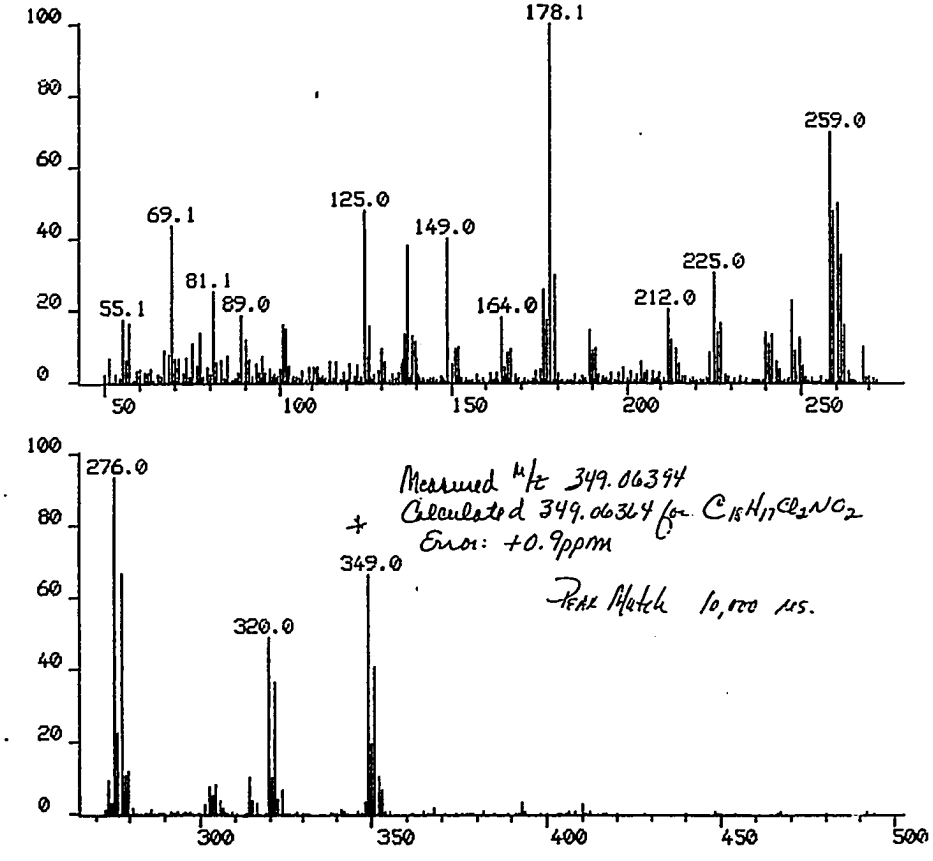

Figure 77. MASS of
(-)-ethyl trans-2,3-di(4-chlorophenyl)cyclopropane-1-carbamate

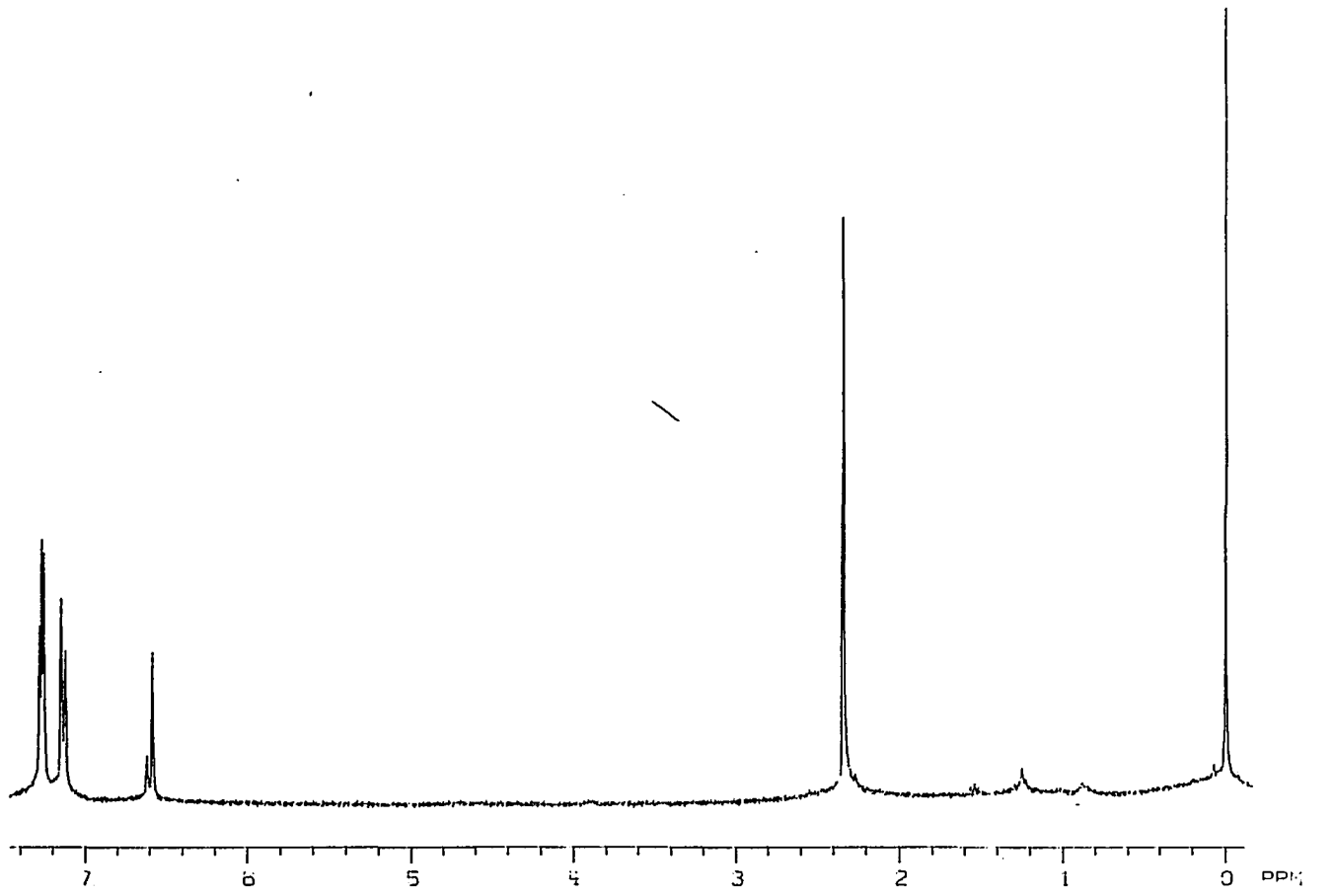

Figure 78. ^{1}H NMR of 1,3-di(4-methylphenyl)allene with chiral shift reagents

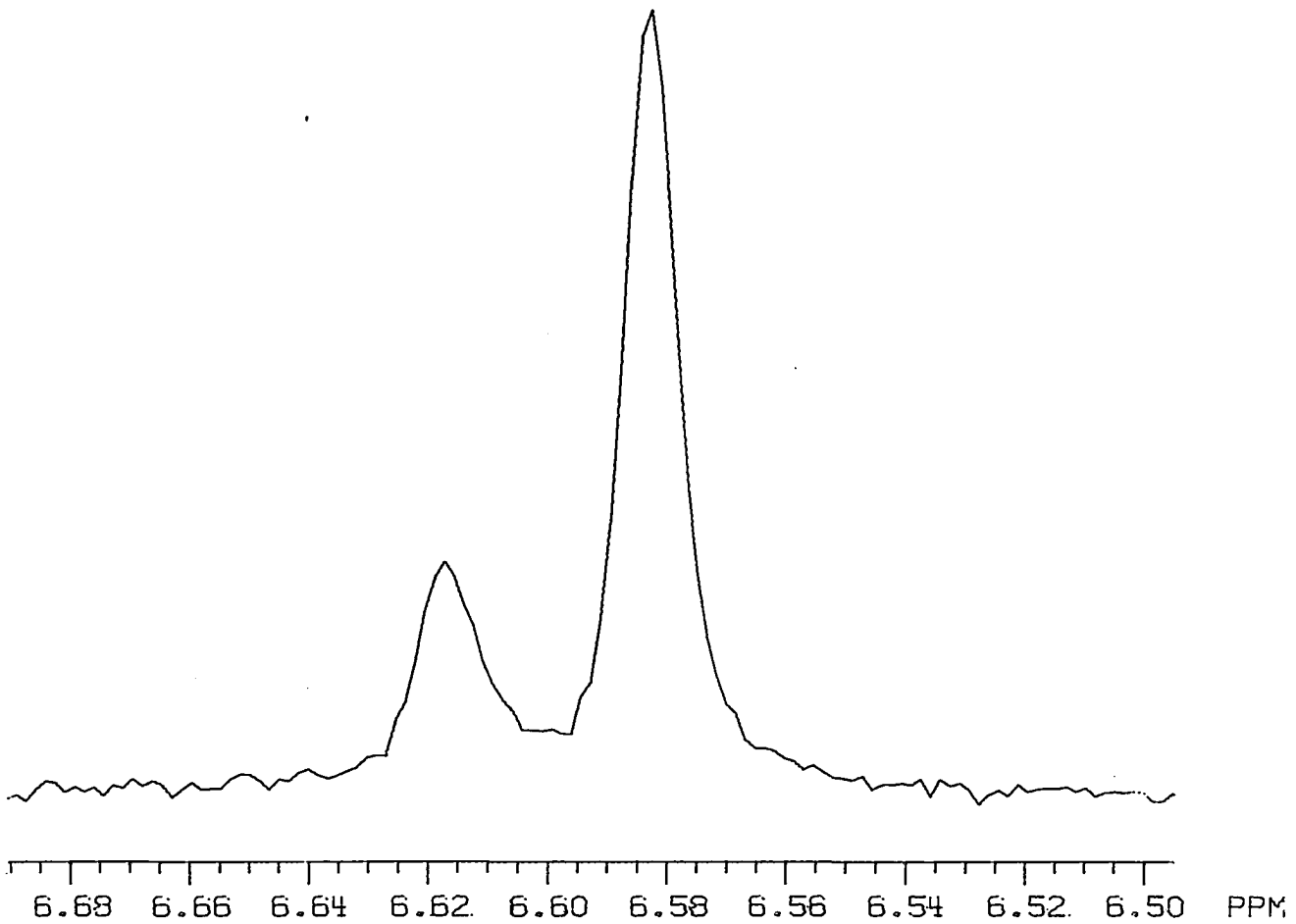

Figure 79. Partial enlargement in Figure 78

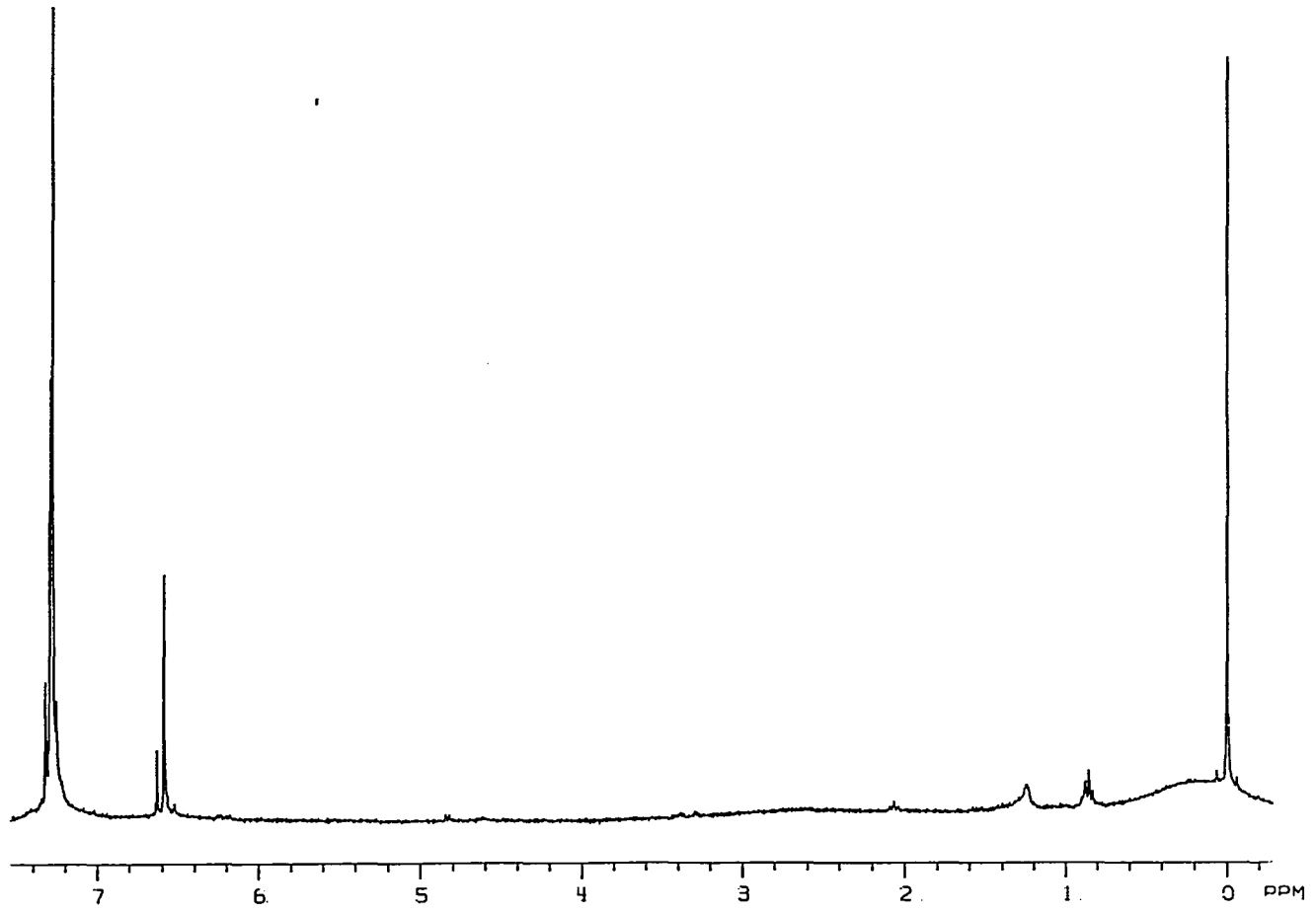

Figure 80. ^{1}H NMR of 1,3-di(4-chlorophenyl)allene with chiral shift reagents

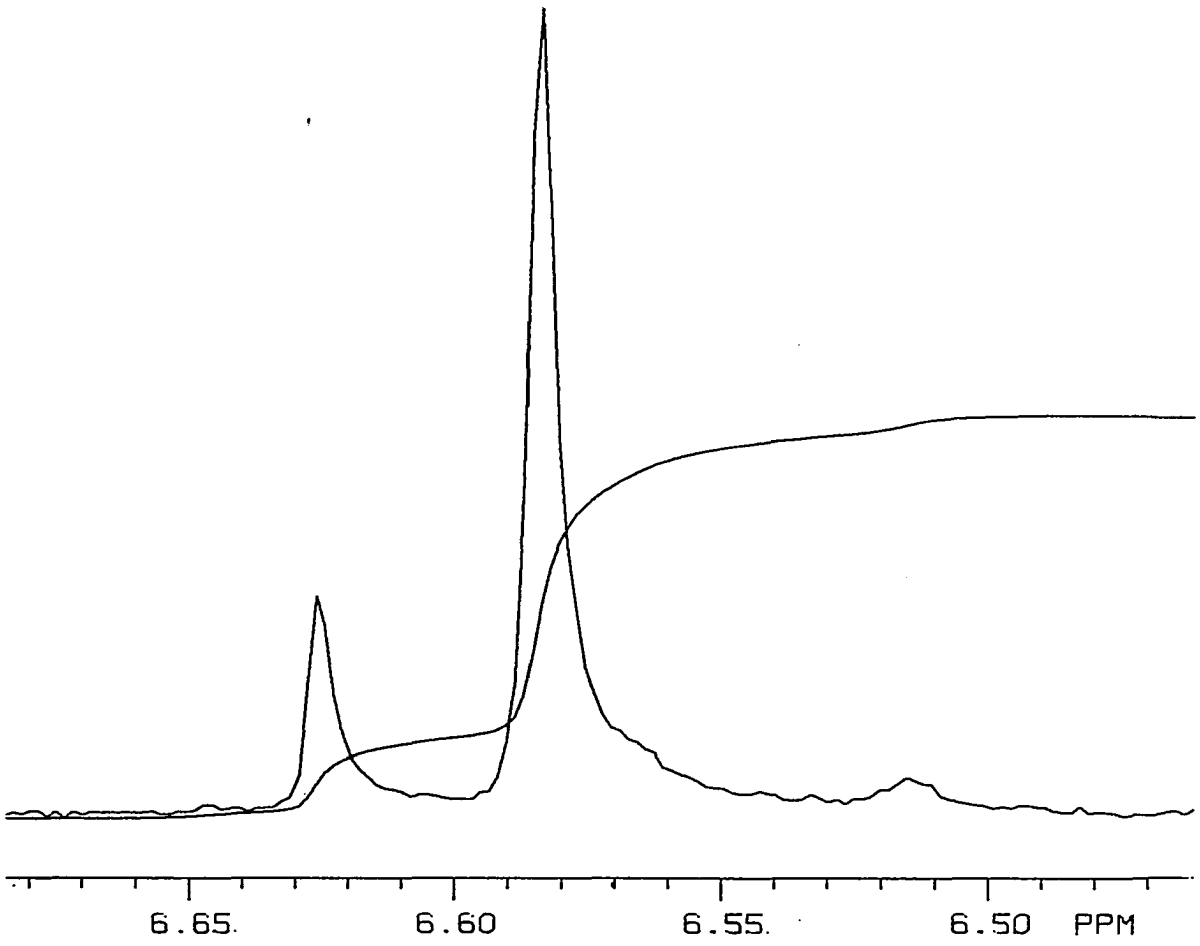

Figure 81. Partial enlargement in Figure 80

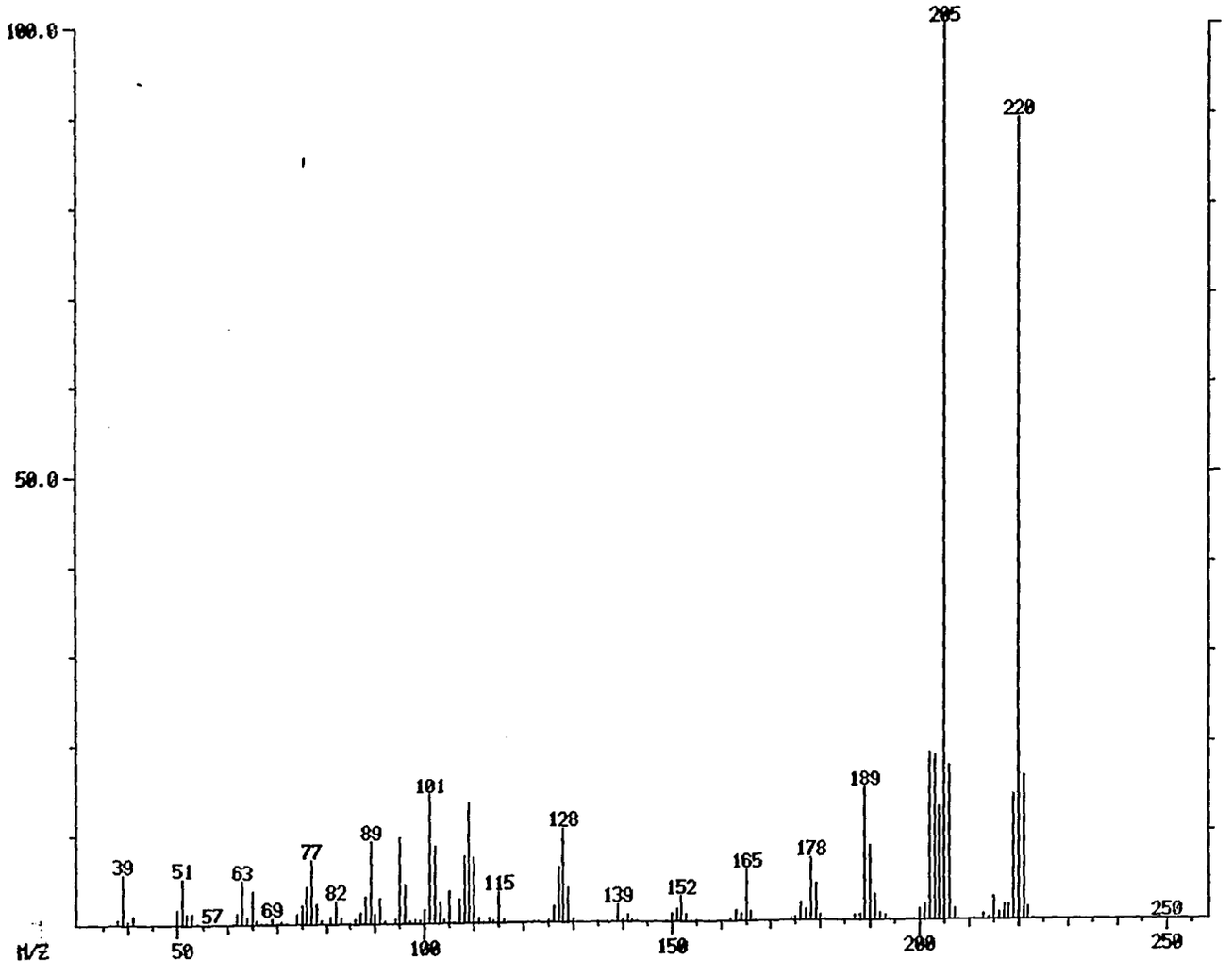

Figure 82. MASS of 1,3-di(4-methylphenyl)allene

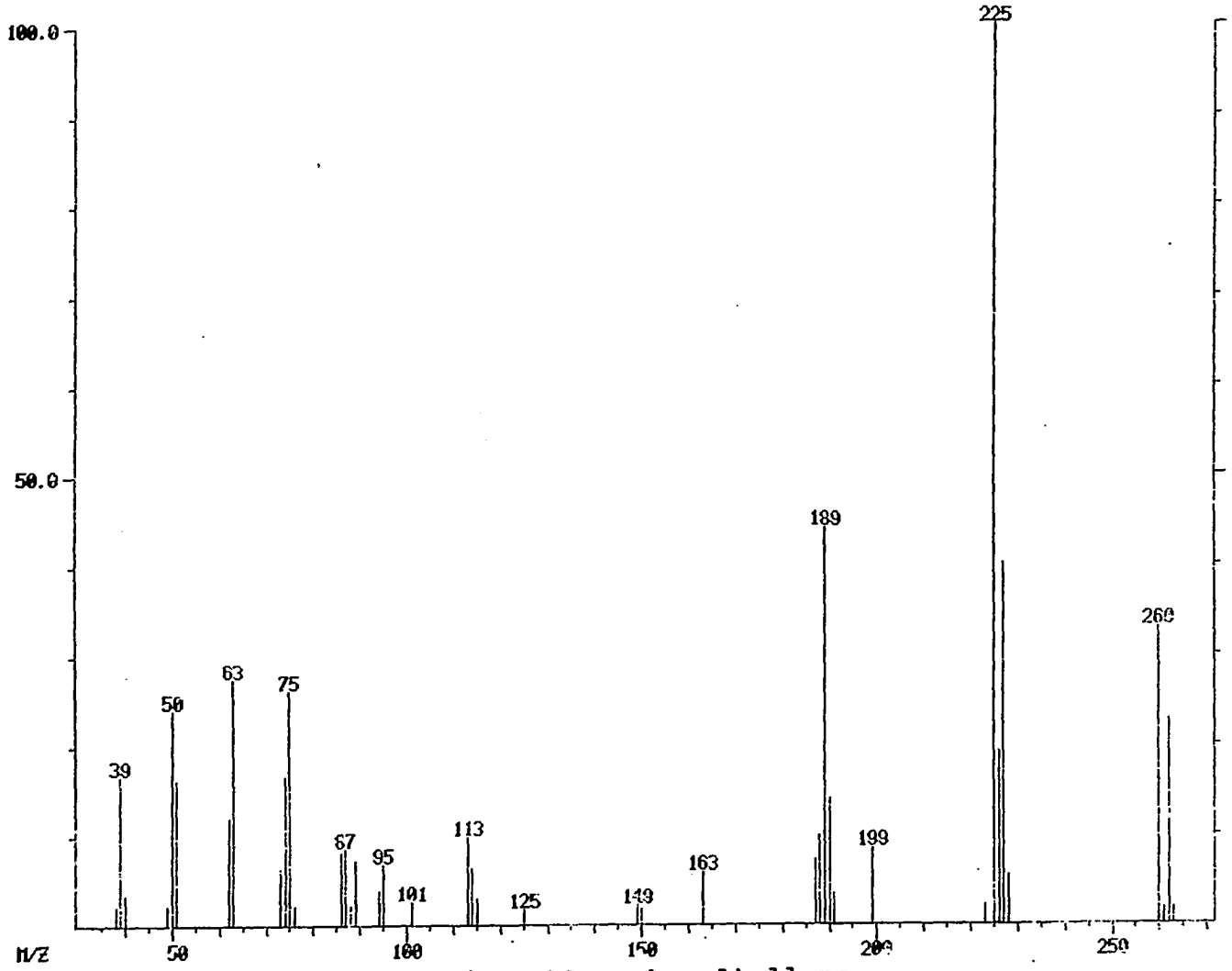

Figure 83. MASS 1,3-di(4-chlorophenyl)allene

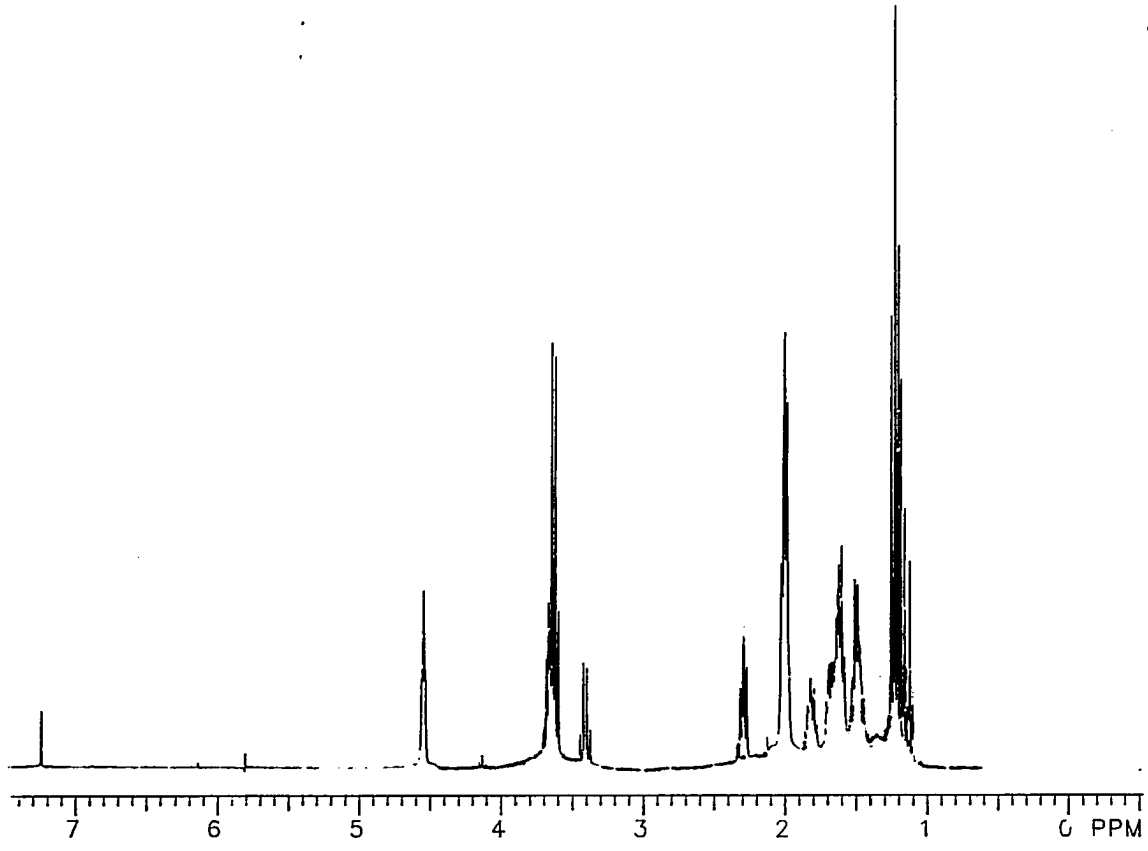

Figure 84. ^{1}H NMR of 1-ethoxycyclohexene

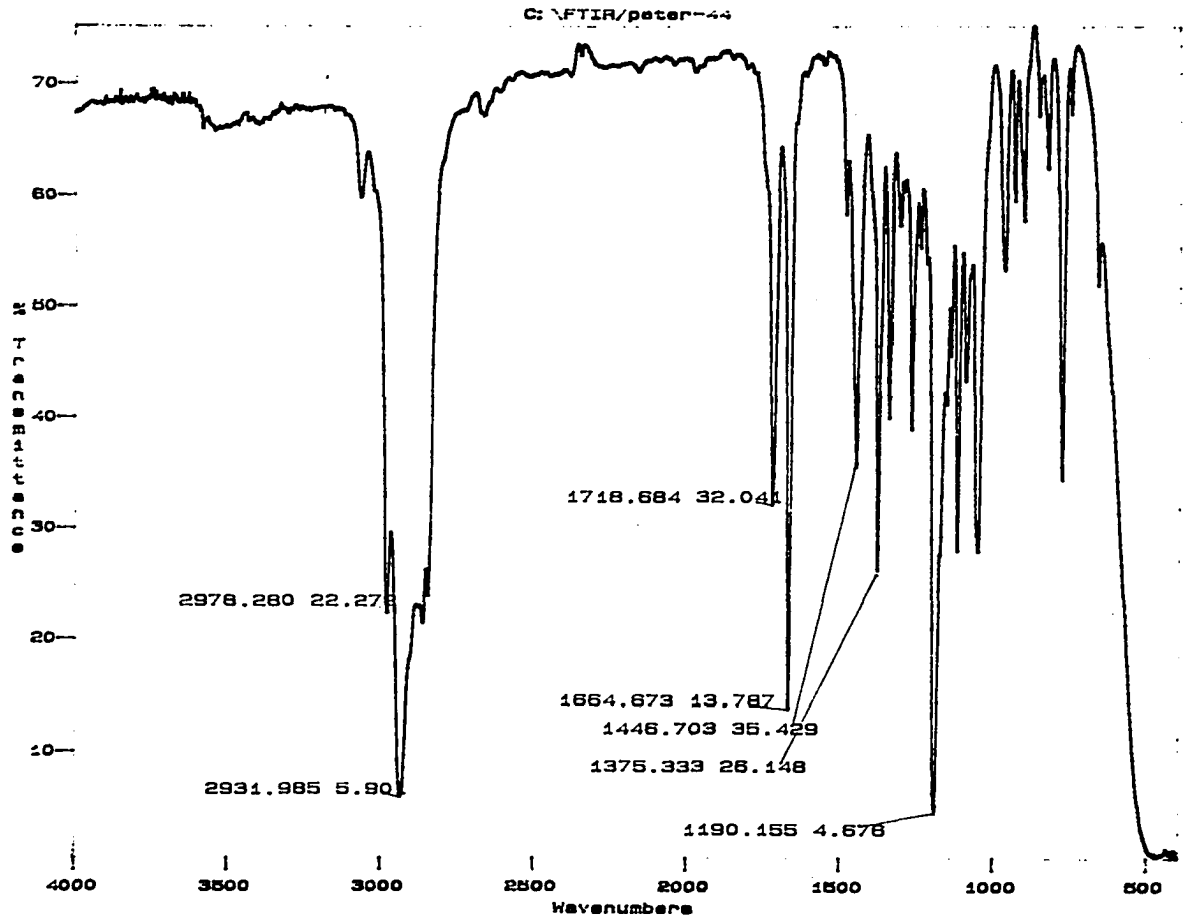

Figure 85. IR of 1-ethoxycyclohexene

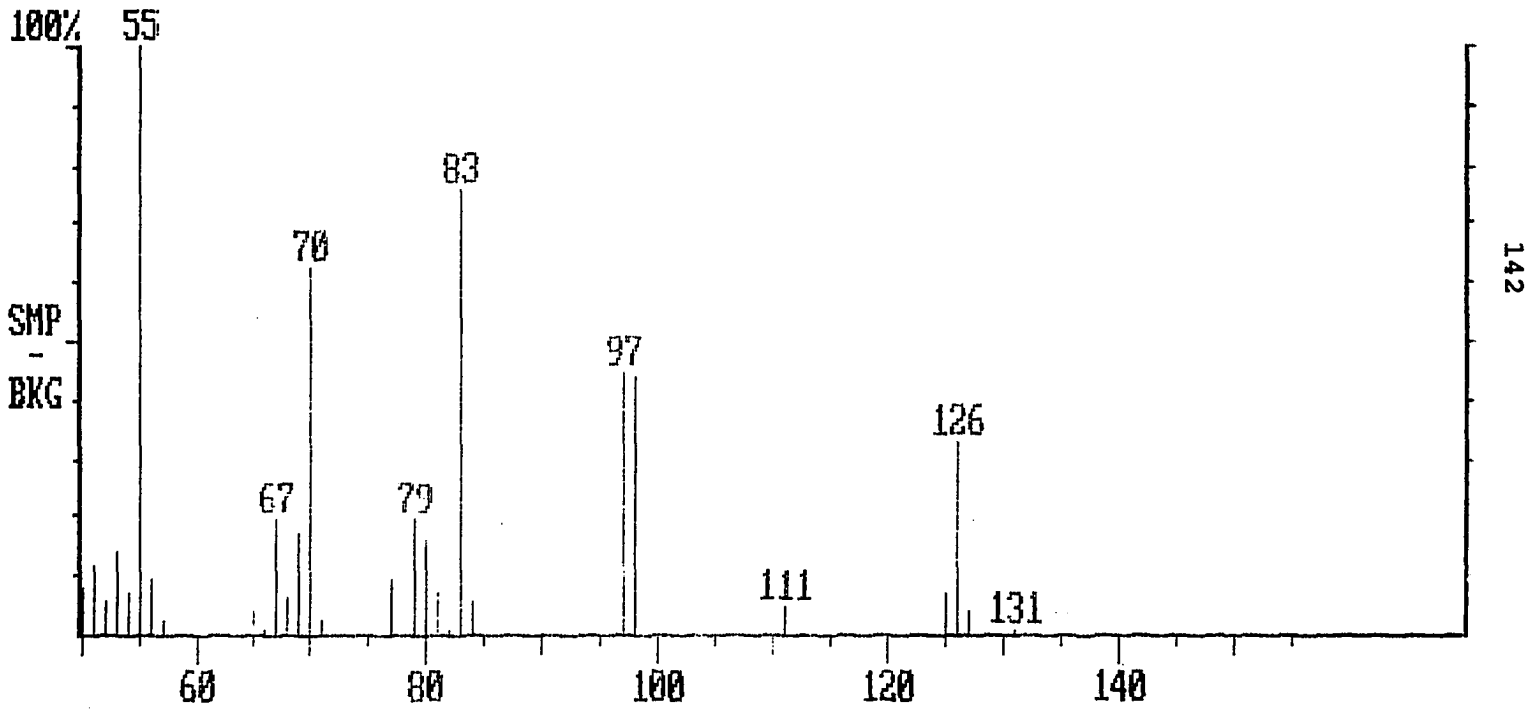

Figure 86. MASS of 1-ethoxycyclohexene

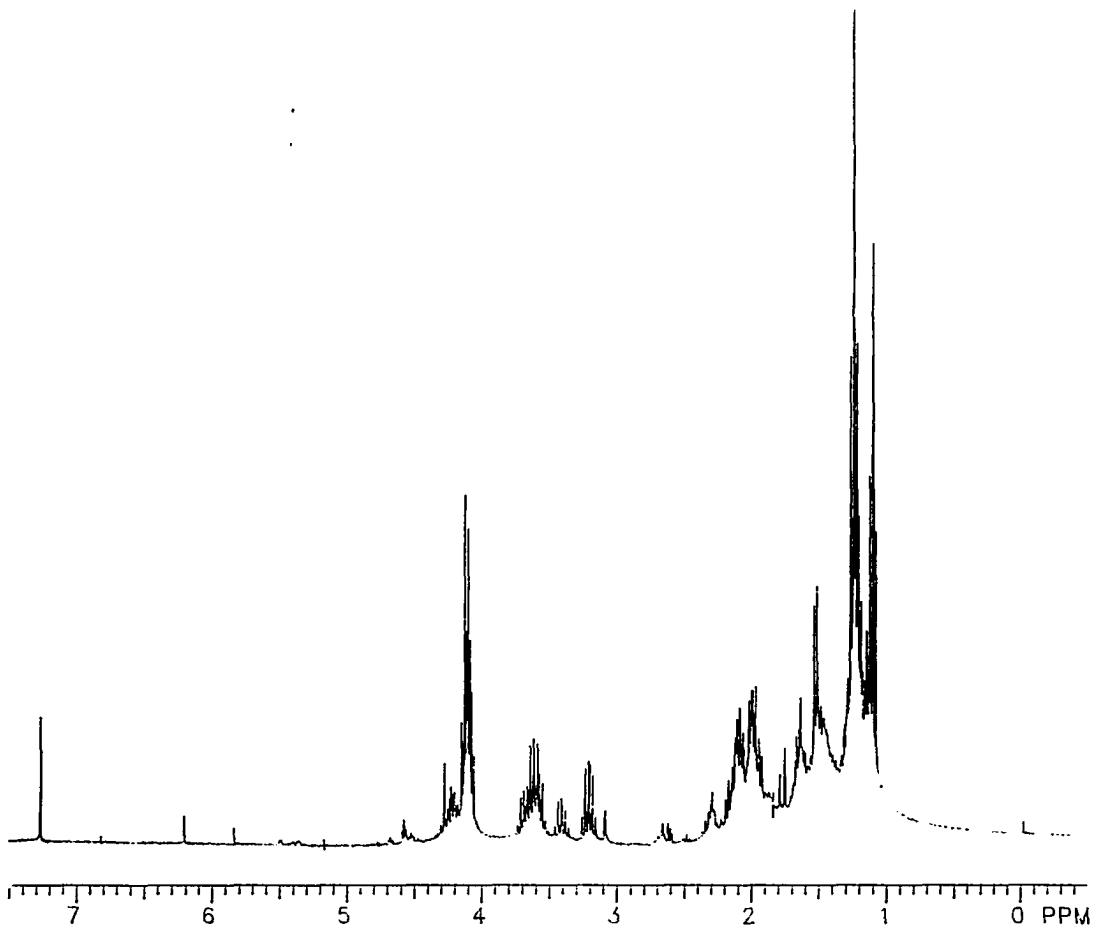

Figure 87. ^{1}H NMR of ethyl 1-ethoxybicyclo[4.1.0]heptane-7-carboxylate

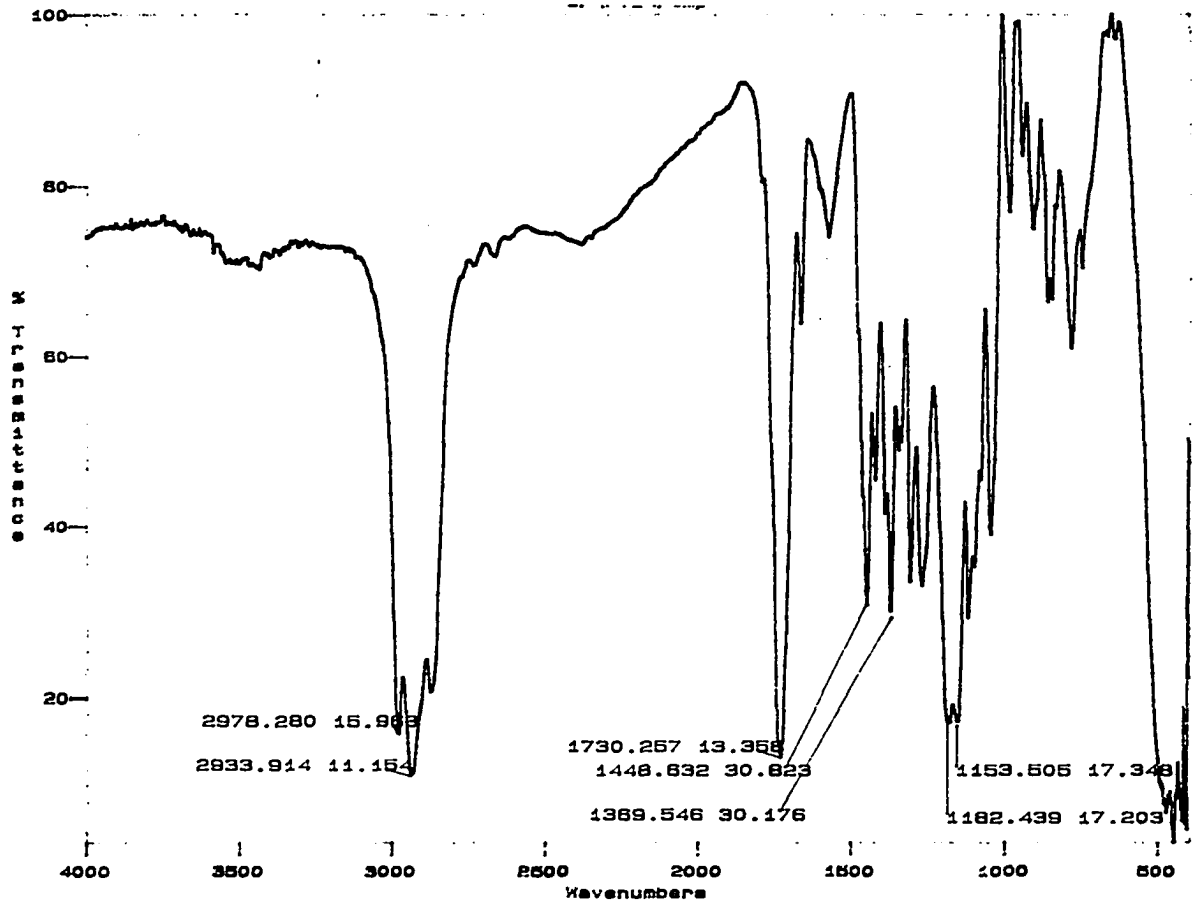

Figure 88. IR of ethyl 1-ethoxybicyclo[4.1.0]heptane-7-carboxylate

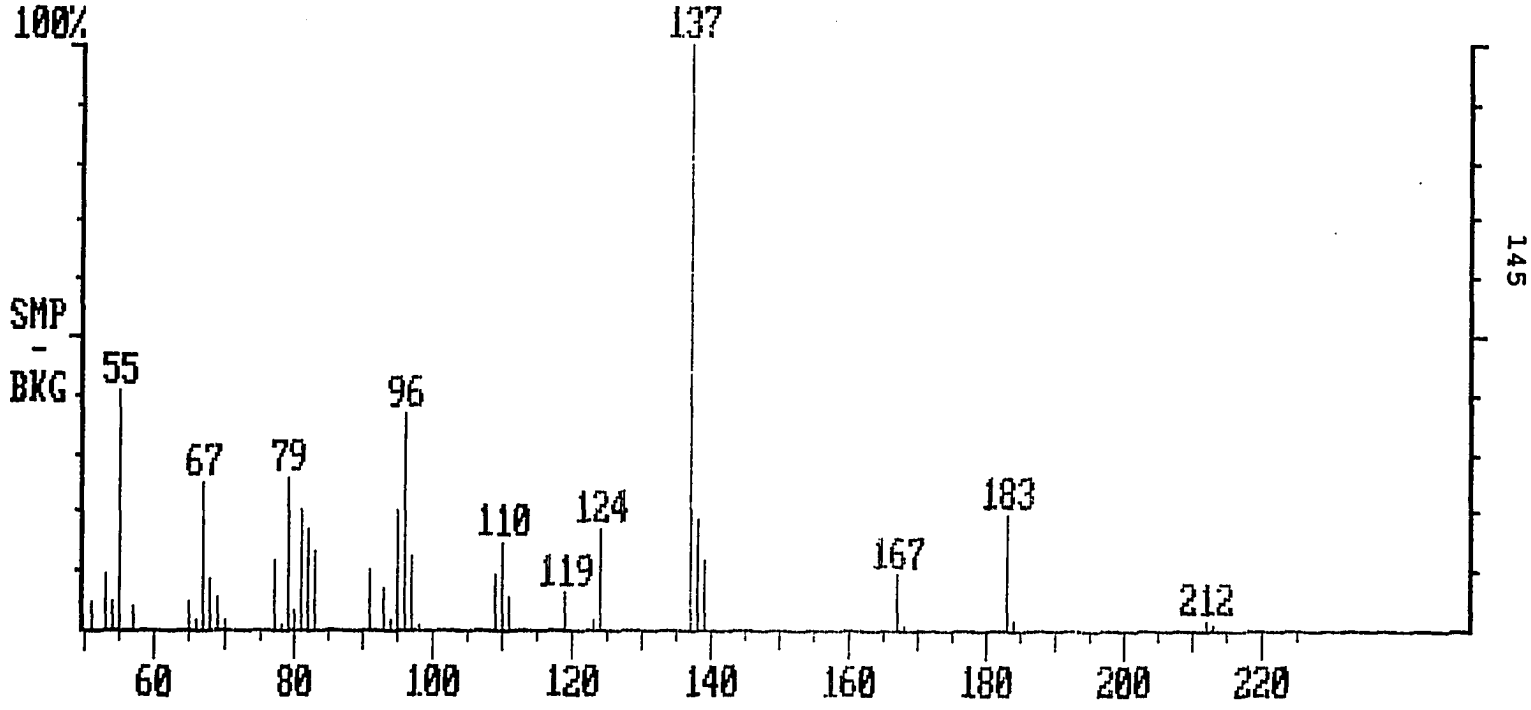

Figure 89. MASS of ethyl 1-ethoxybicyclo[4.1.0]heptane-7-carboxylate

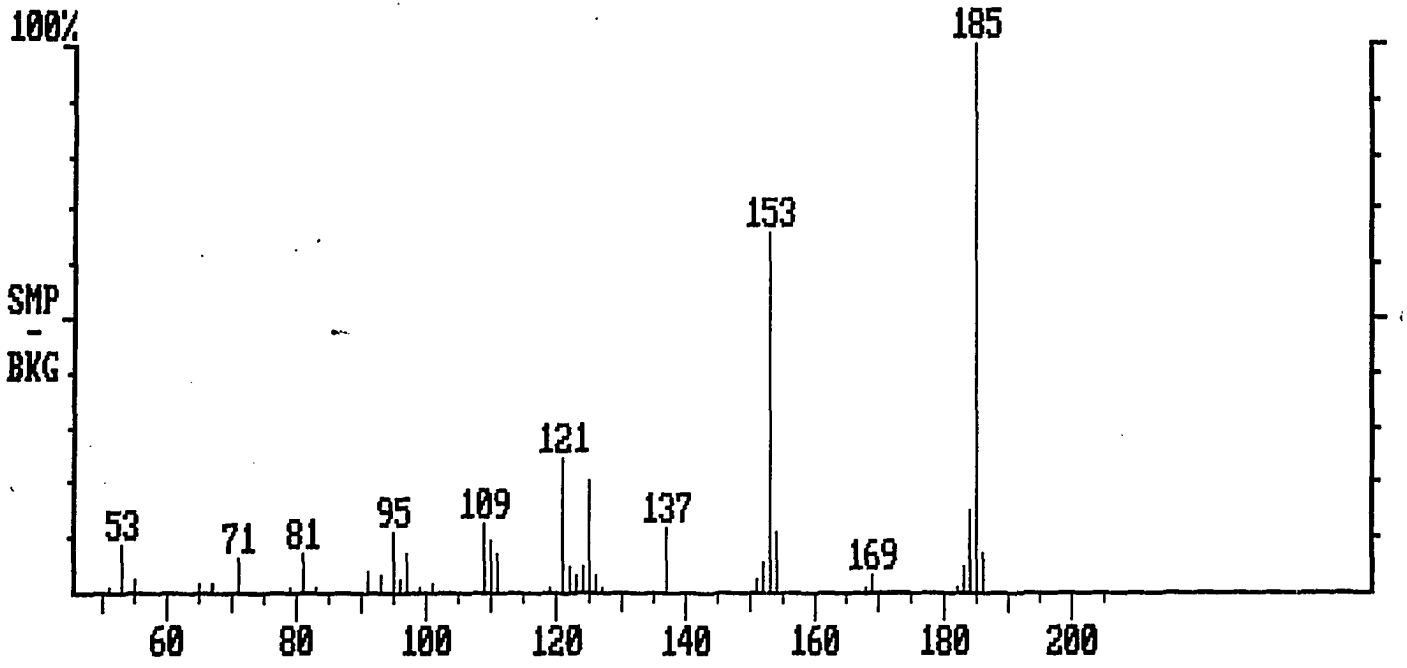

Figure 90. MASS of the decomposed product of ethoxy acid

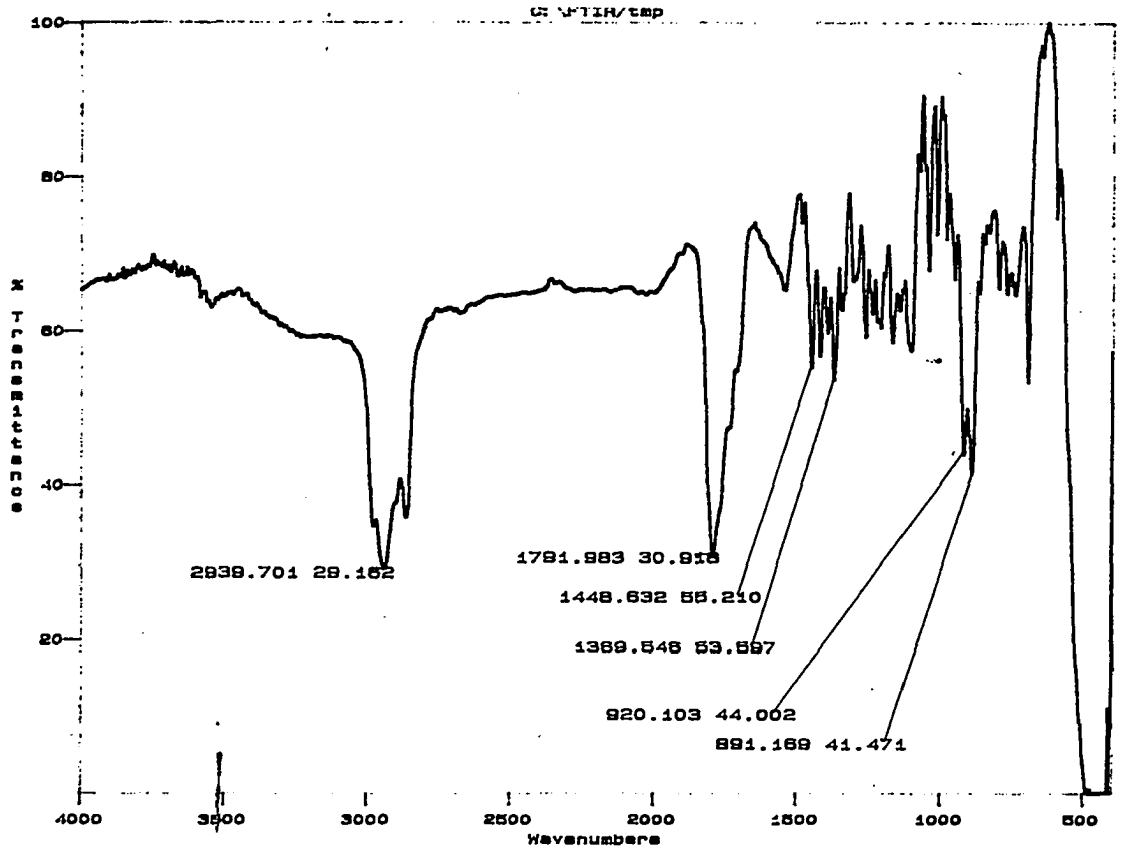

Figure 91. IR of the decomposed product of ethoxy acid

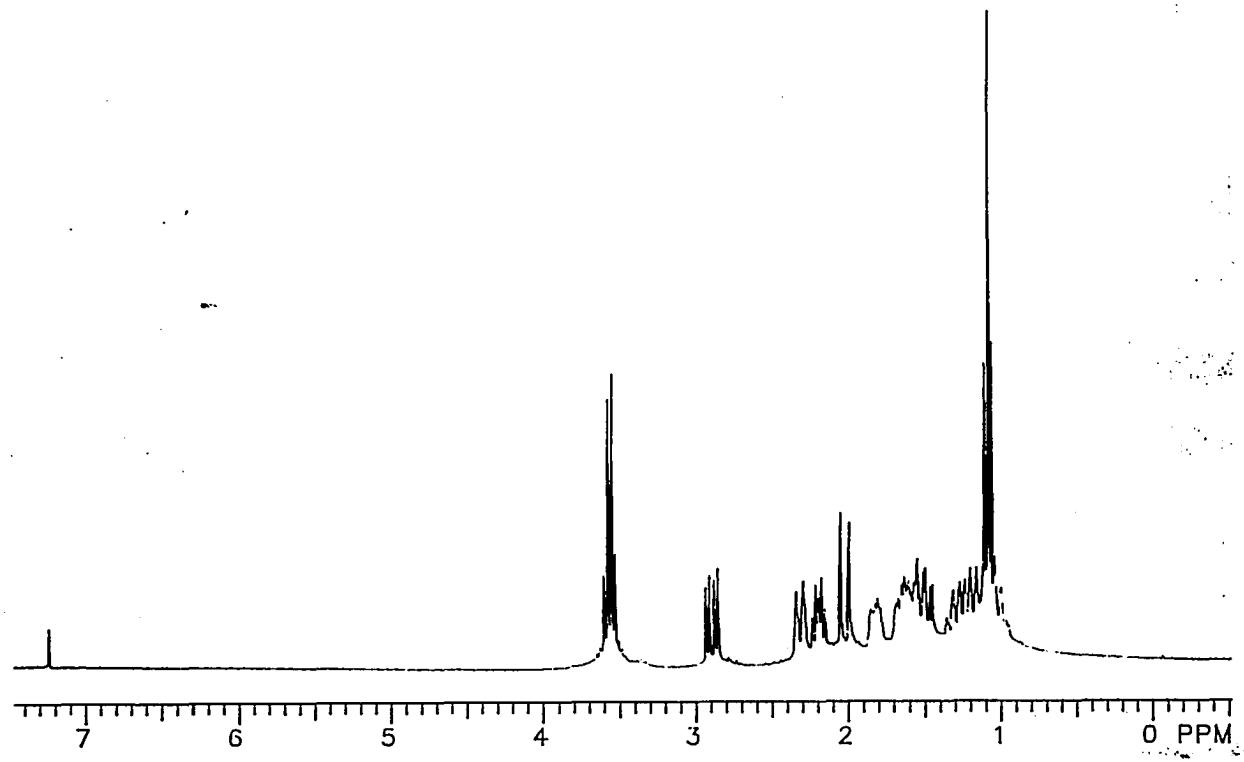

Figure 92. ^{1}H NMR of the decomposed product of ethoxy acid

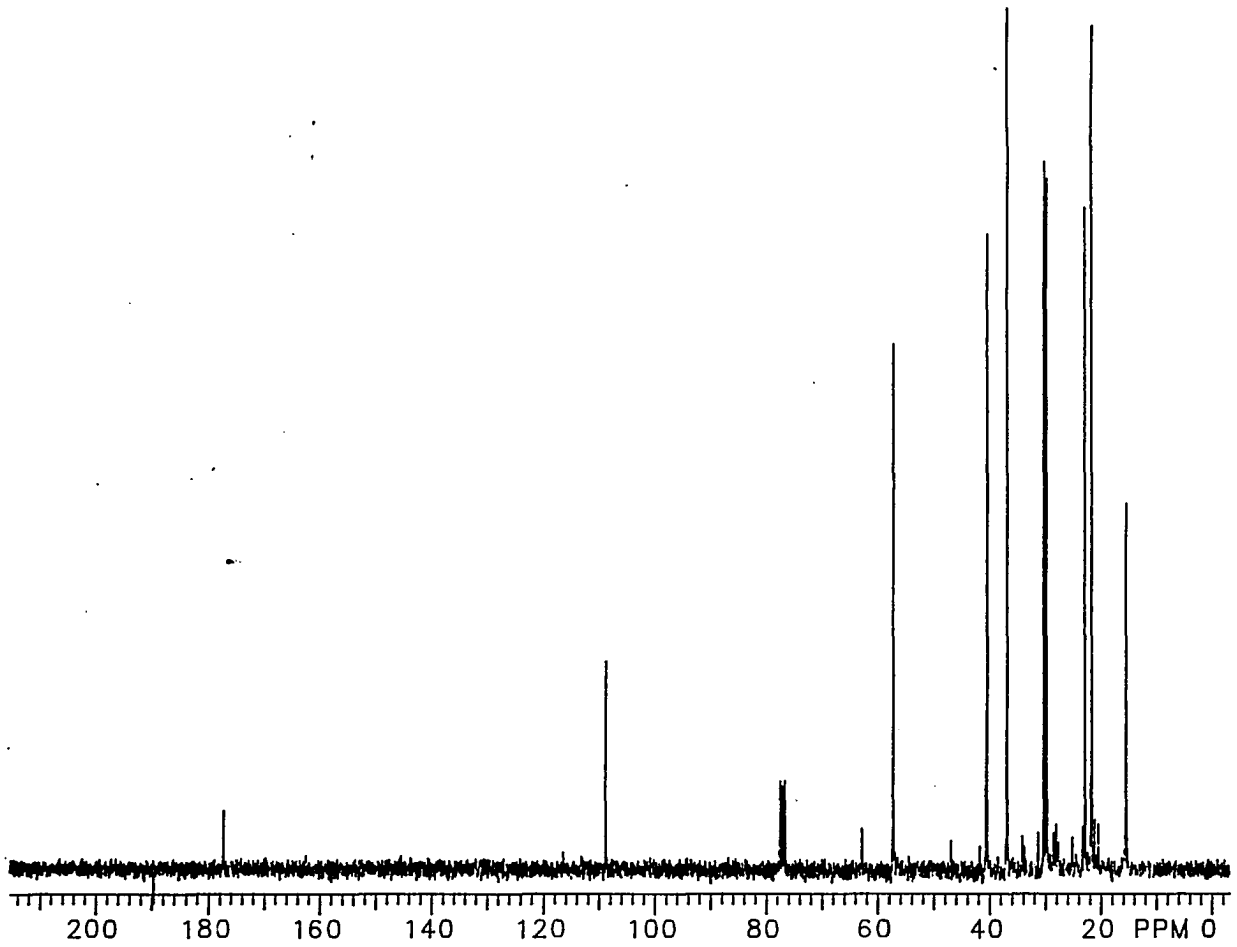

Figure 93. ^{13}C NMR of the decomposed product of ethoxy acid

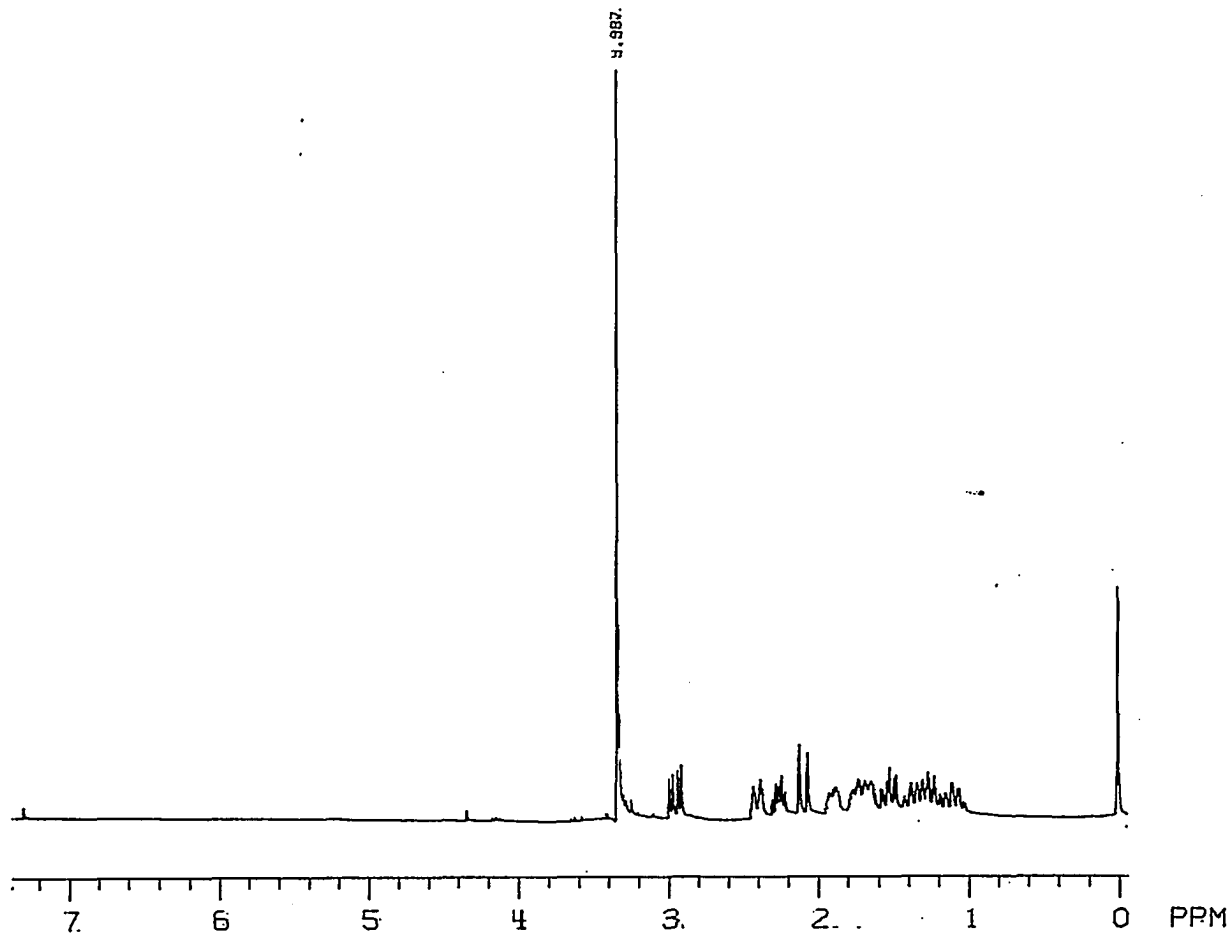

Figure 94. ^{1}H NMR of the decomposed product of the methoxy acid

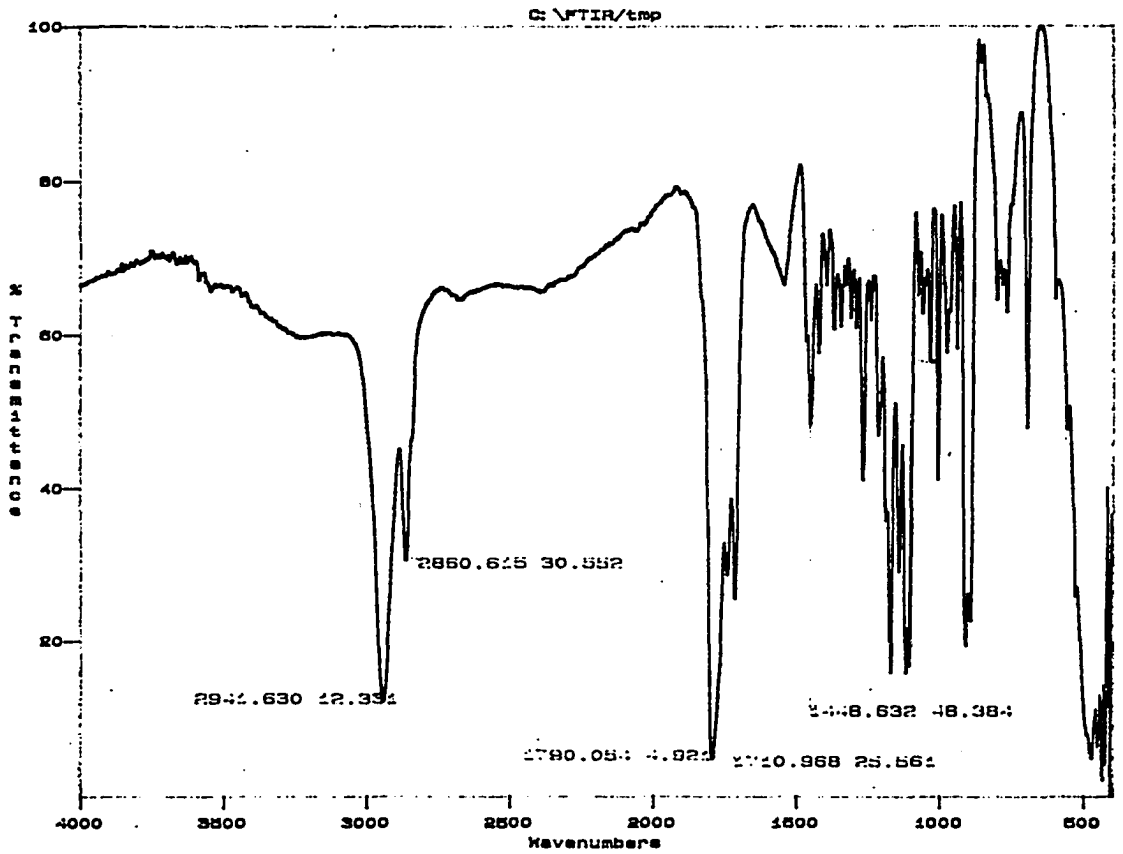

Figure 95. IR of the decomposed product of the methoxy acid

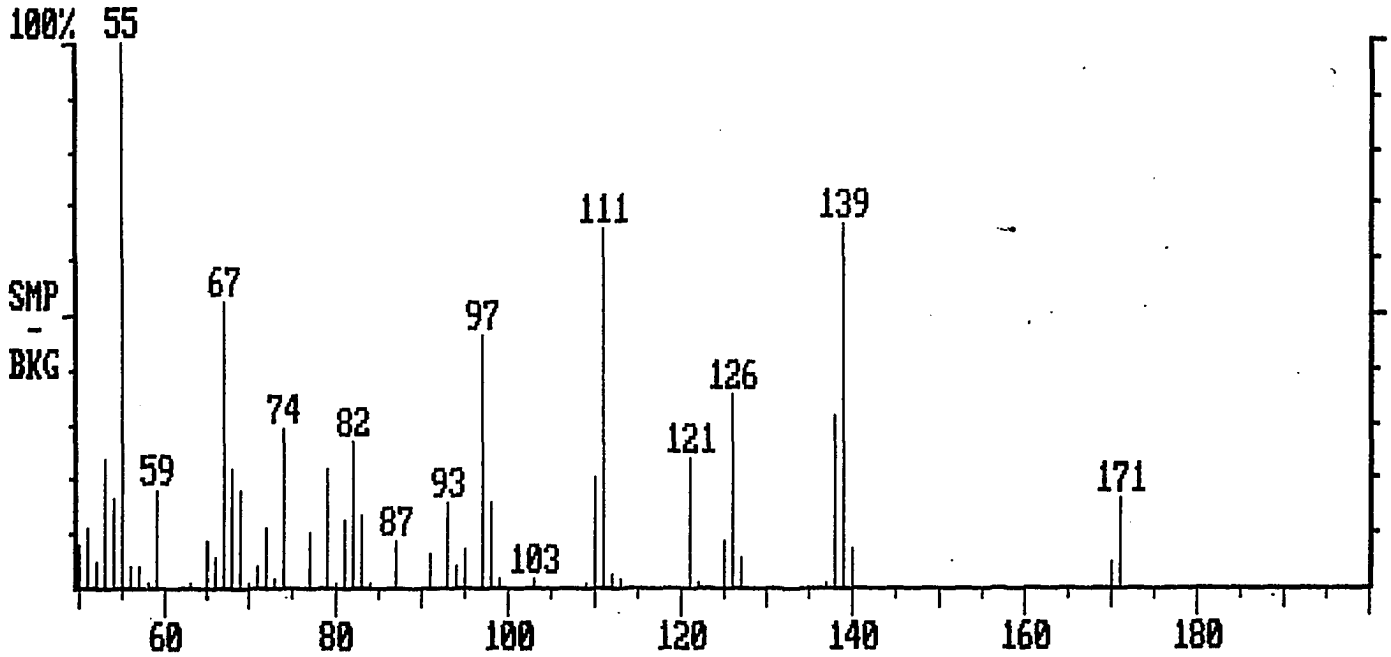

Figure 96. MASS of the decomposed product of the methoxy acid

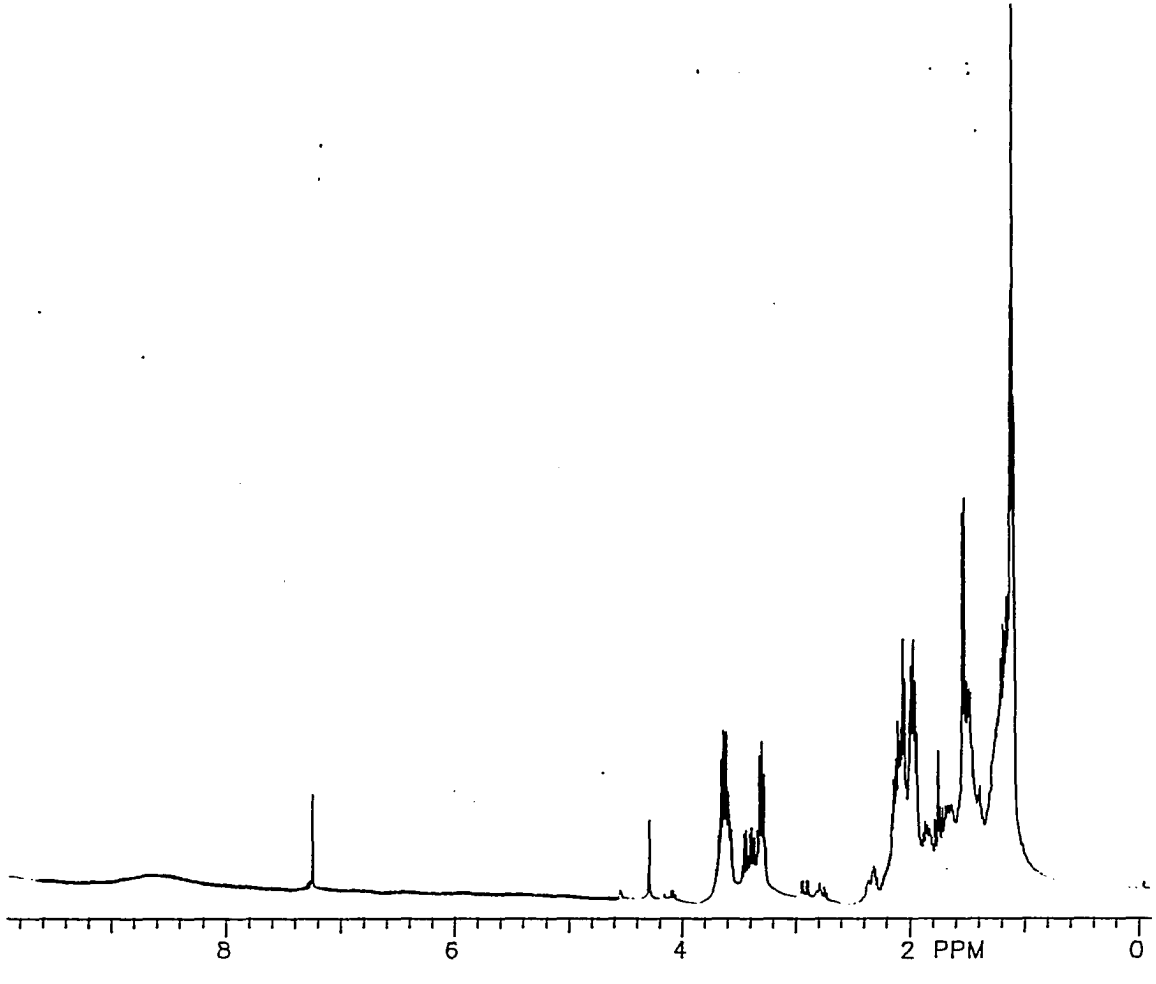

Figure 97. ^{1}H NMR of 1-ethoxybicyclo[4.1.0]heptane-7-carboxylic acid

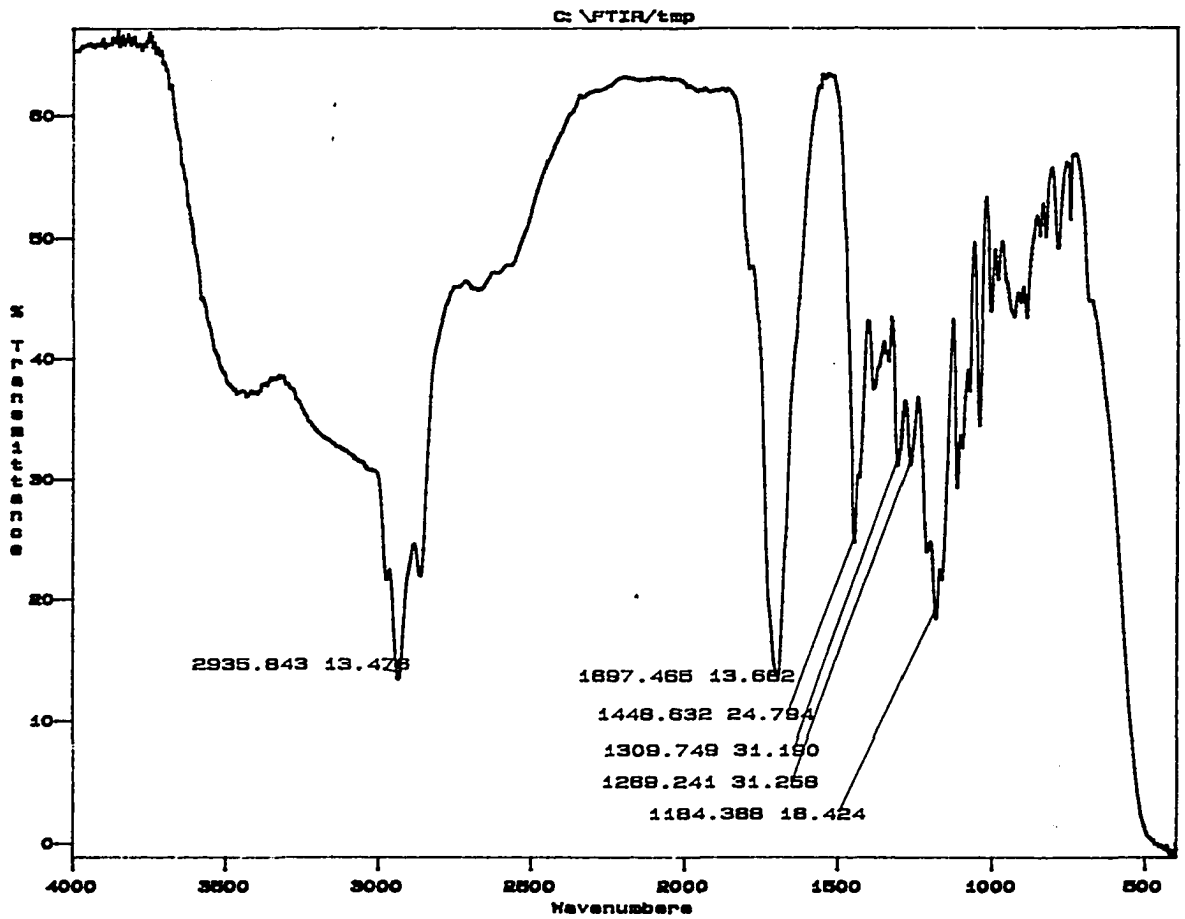

Figure 98. IR of 1-ethoxy[4.1.0]heptane-7-carboxylic acid

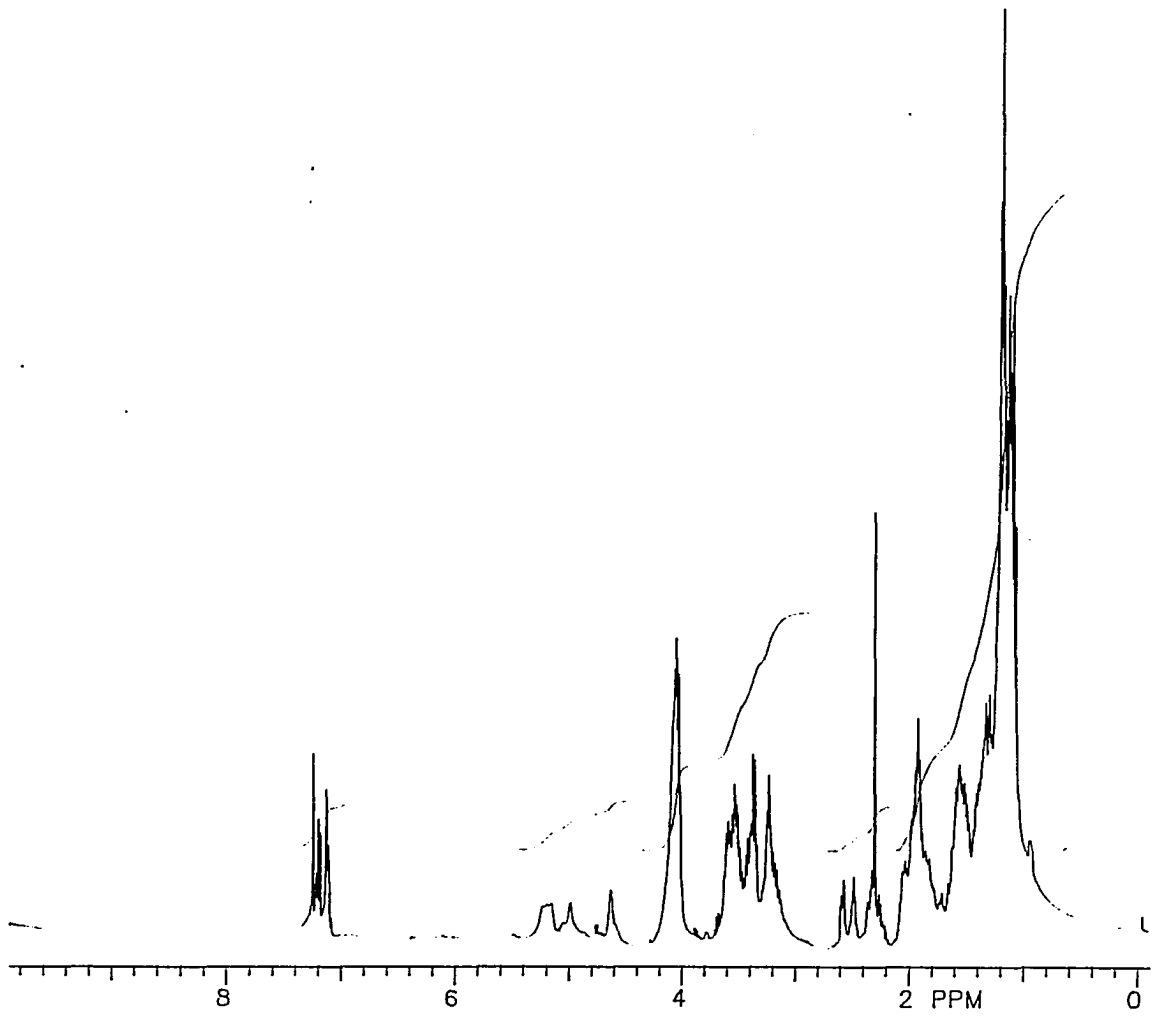

Figure 99. ^{1}H NMR of ethyl 1-ethoxybicyclo[4.1.0]heptane-7-carbamate

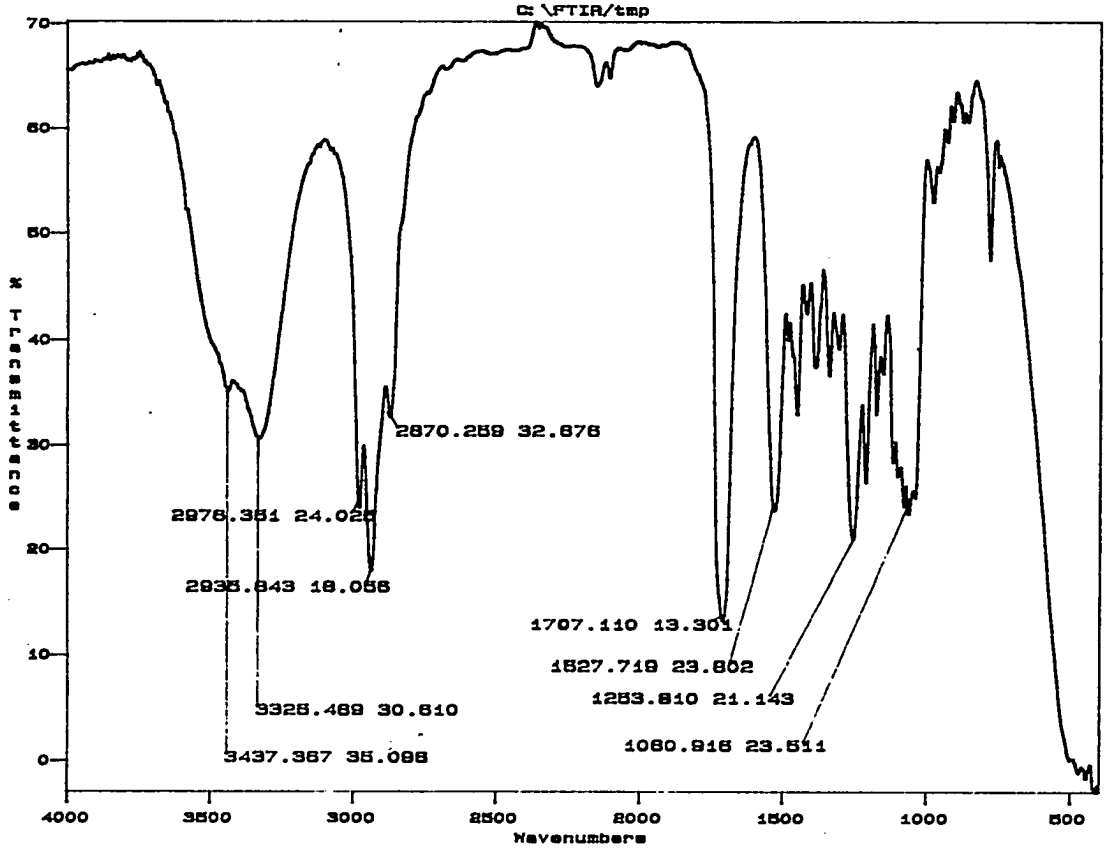

Figure 100. IR of ethyl 1-ethoxybicyclo[4.1.0]heptane-7-carbamate

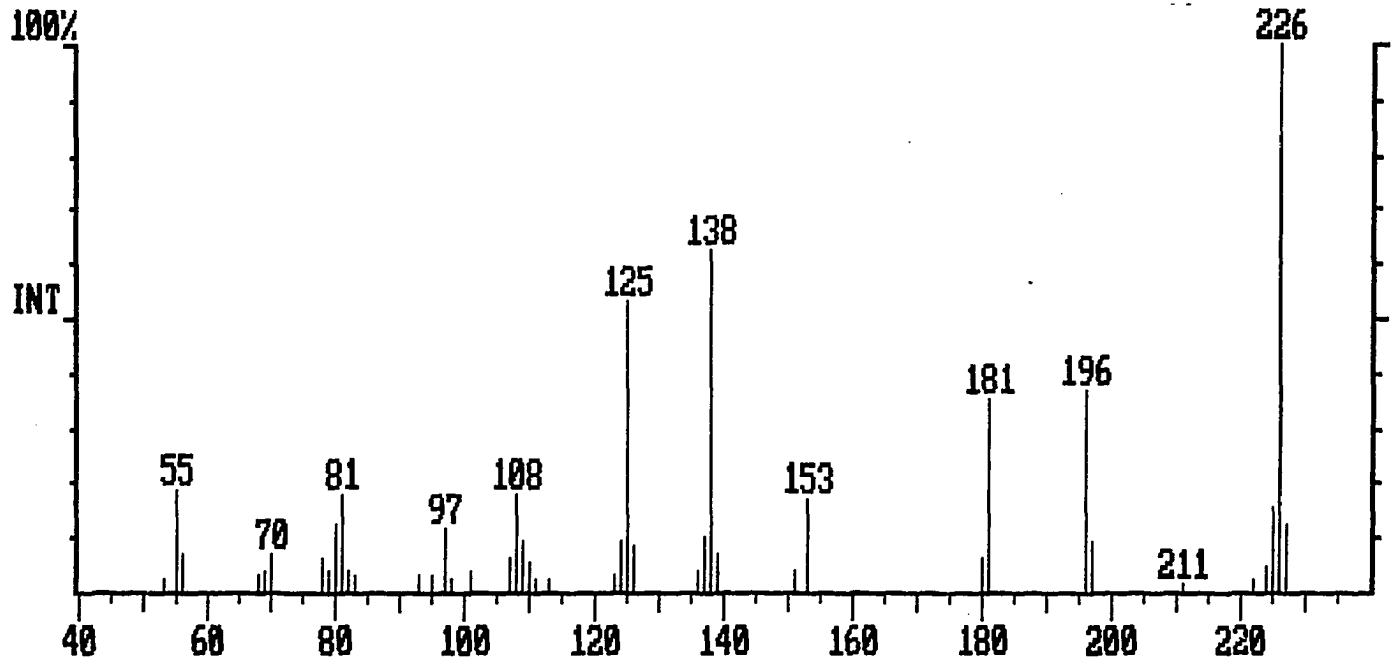

Figure 101. MASS of ethyl 1-ethoxybicyclo[4.1.0]heptane-7-carbamate

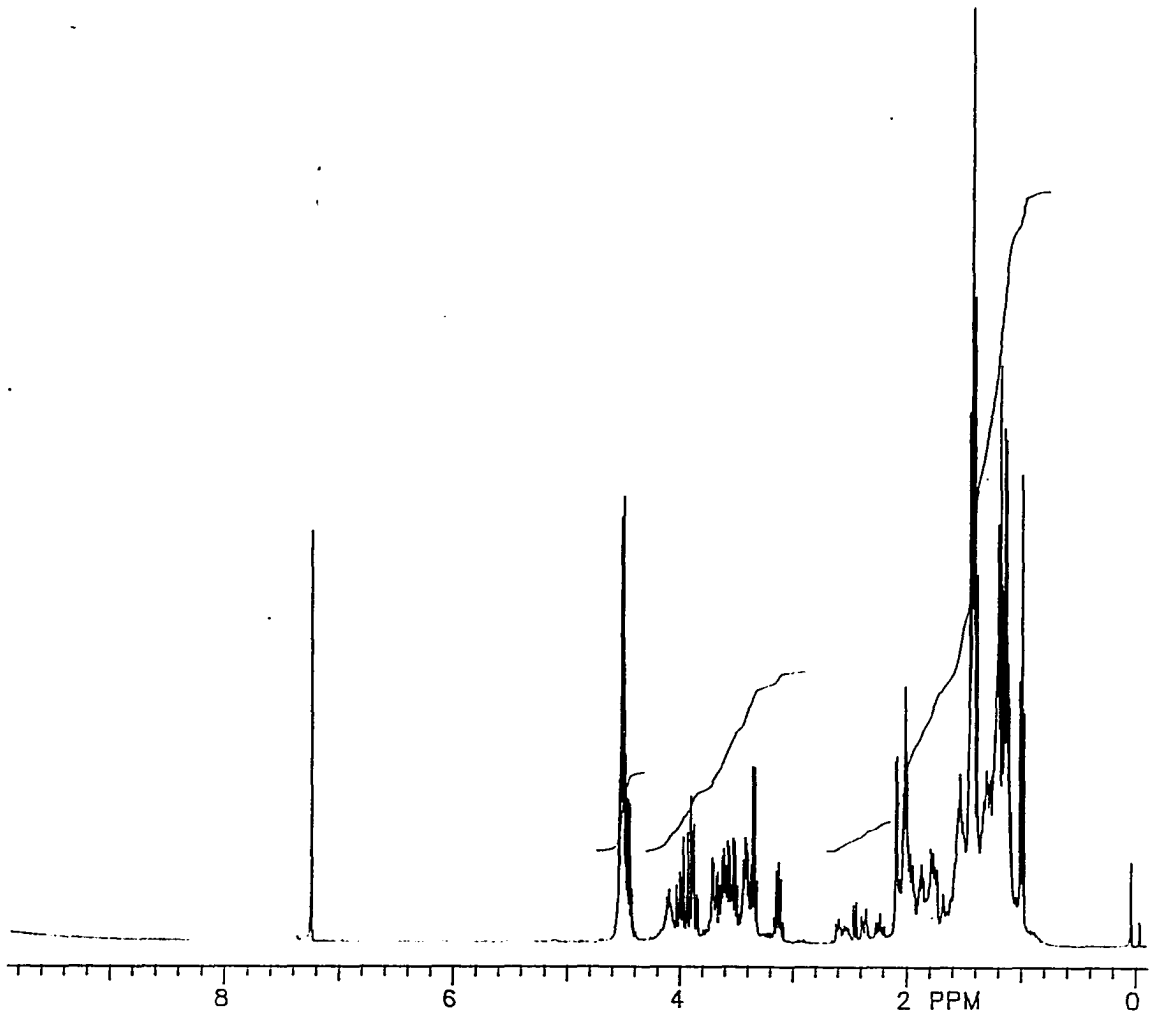

Figure 102. ^{1}H NMR of ethyl nitroso-1-ethoxy[4.1.0]heptane-1-carbamate

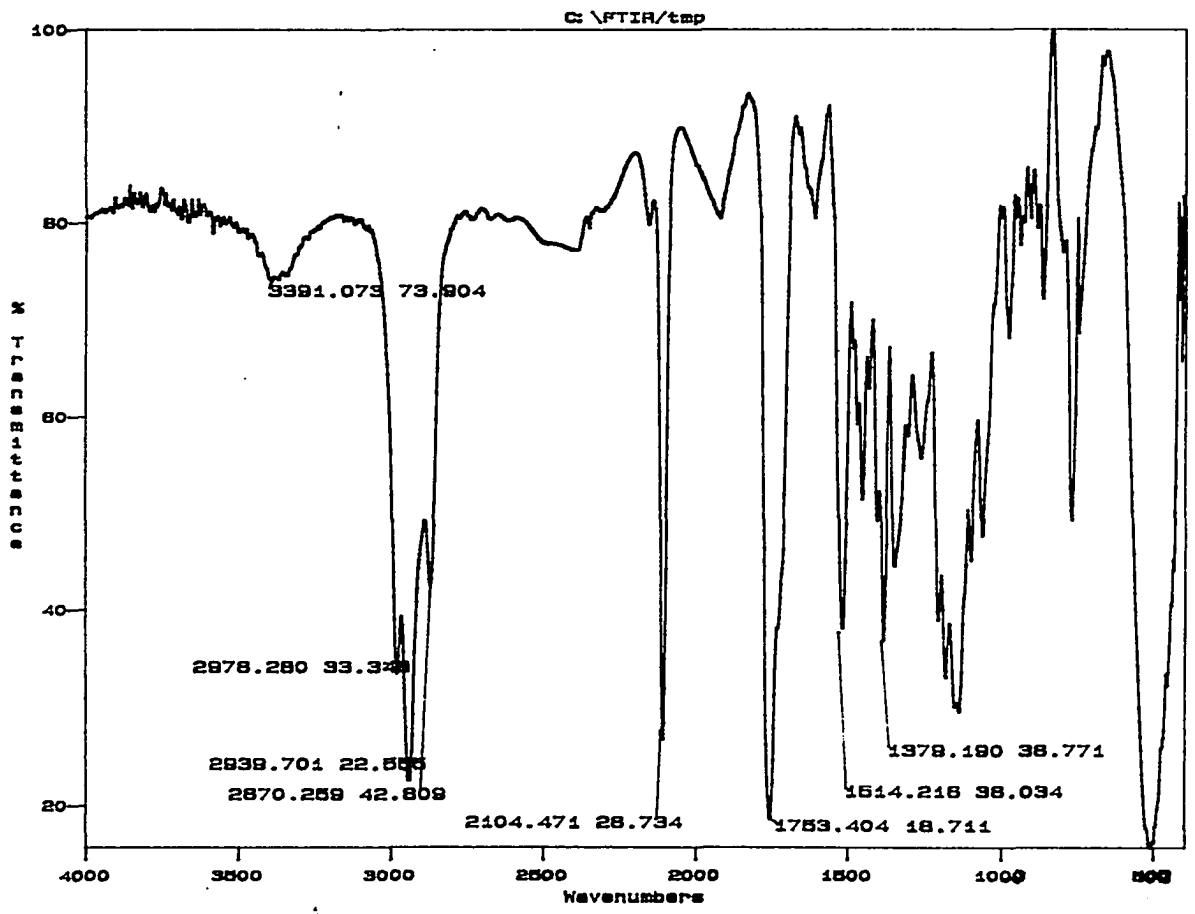

Figure 103. IR of ethyl nitroso-1-ethoxybicyclo[4.1.0]heptane-7-carbamate

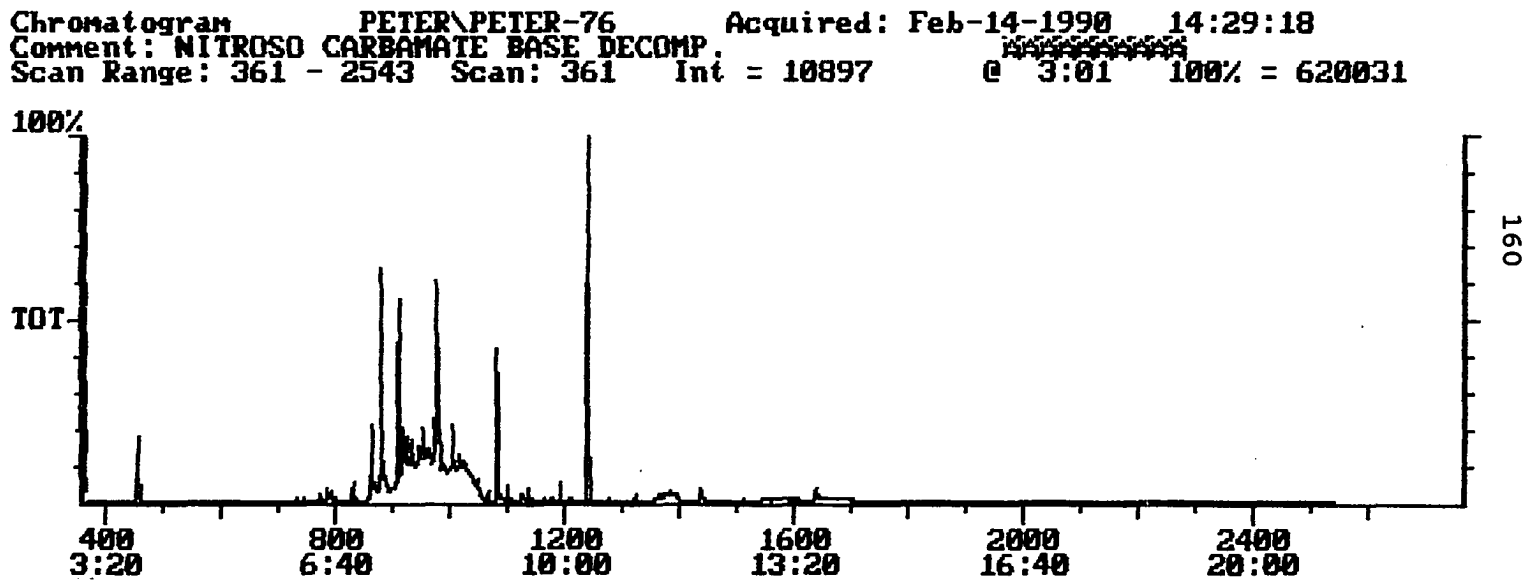

Figure 104. Chromatogram of base decomposition of ethyl nitroso-1-ethoxybicyclo[4.1.0]heptane-7-carbamate

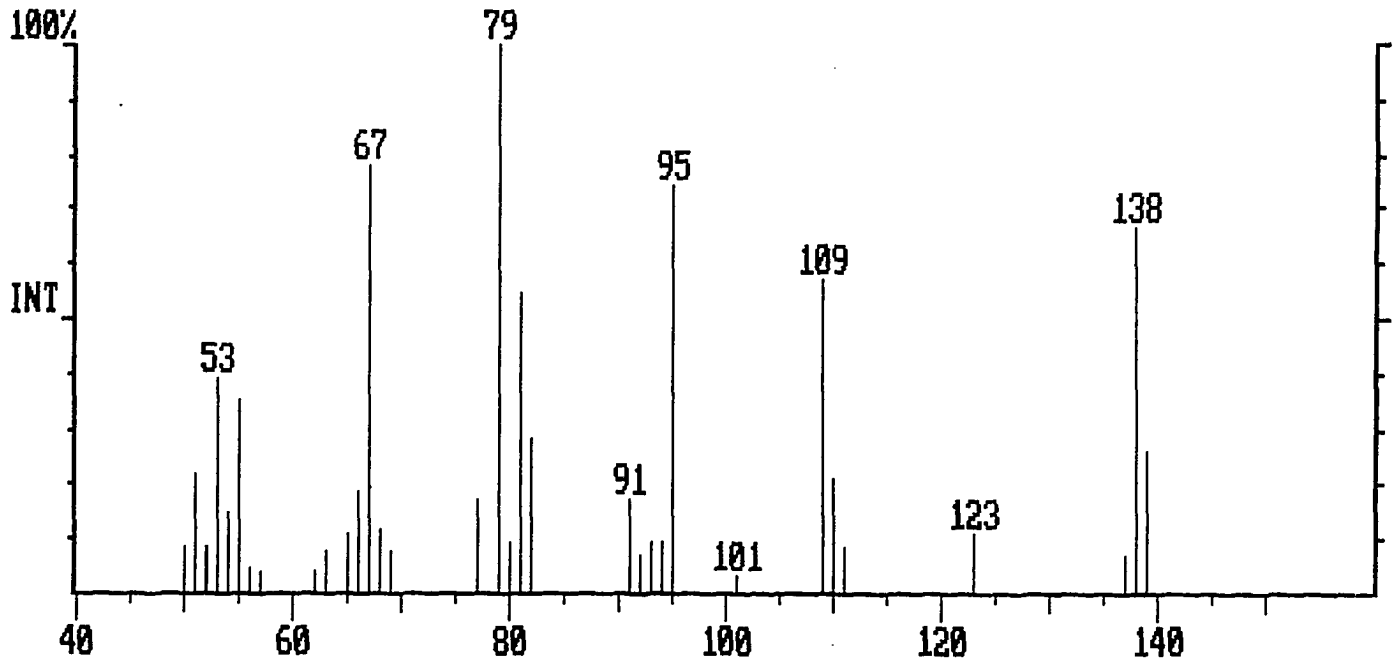

Figure 105. MASS of insertion product

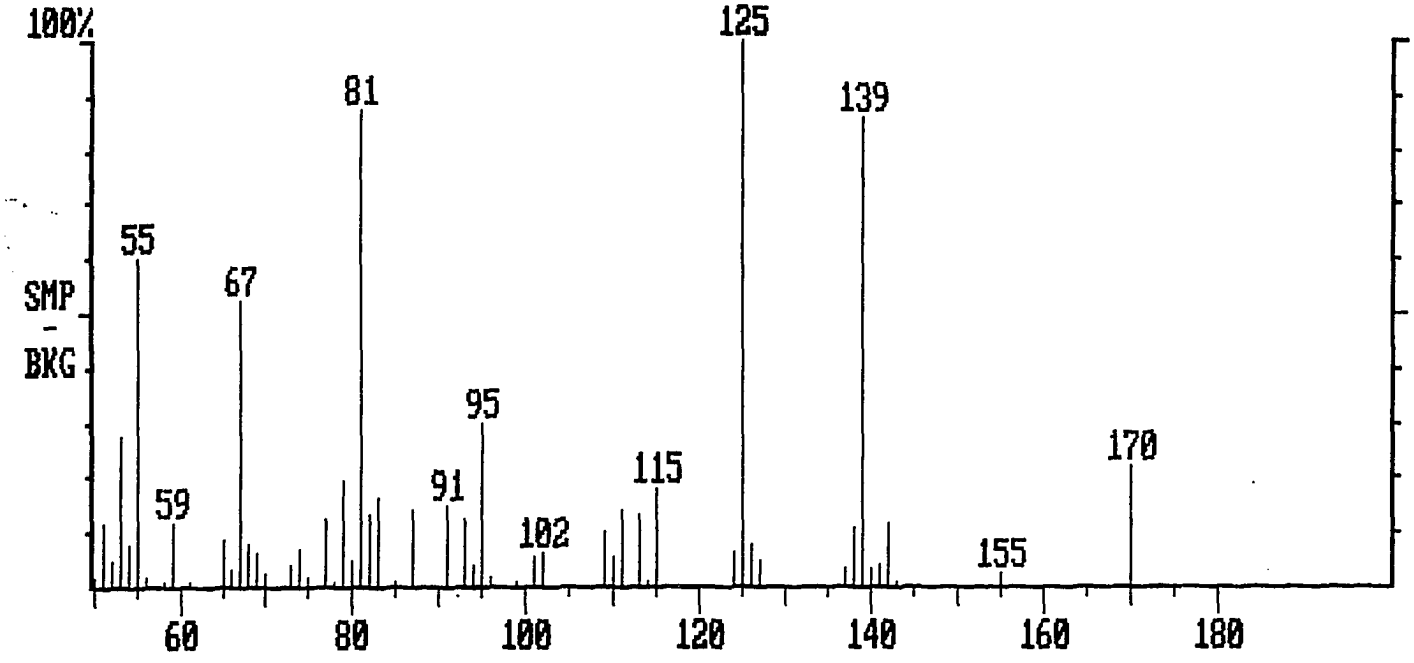

Figure 106. MASS of methanol insertion product

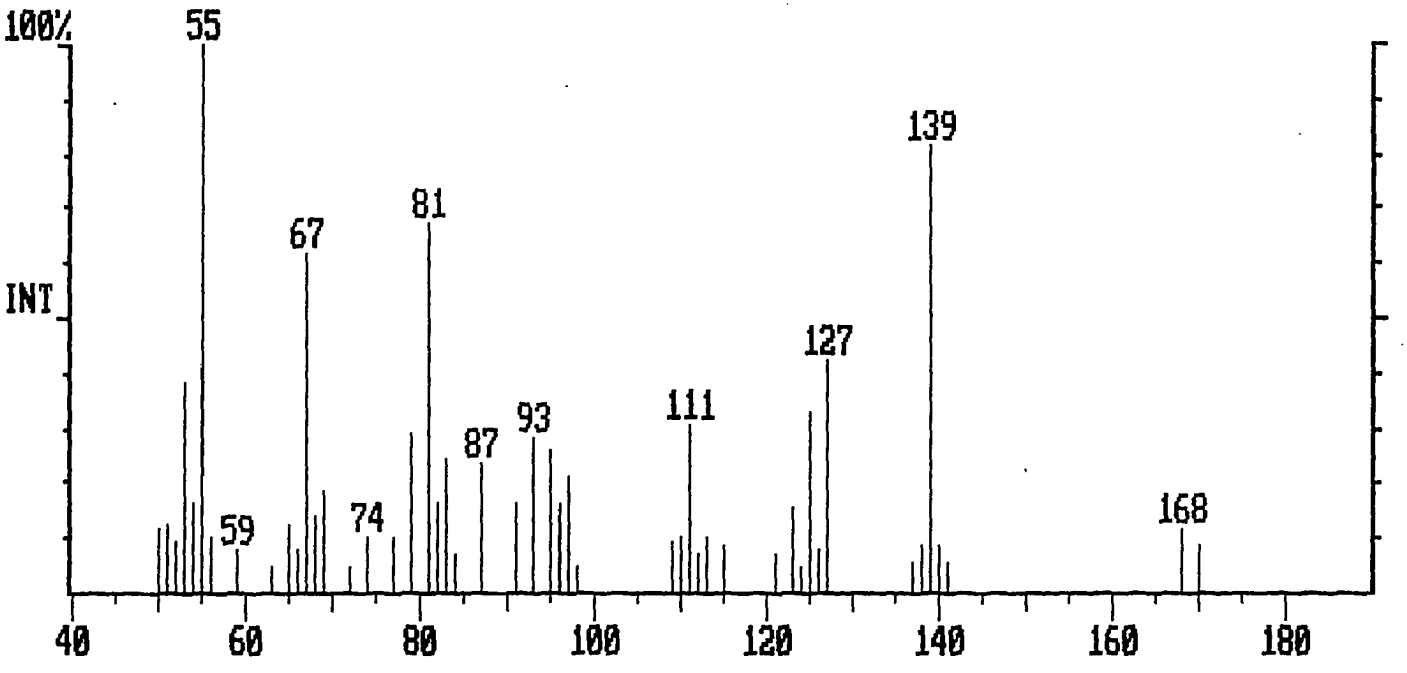

Figure 107. MASS of scan 917 in Fig. 104

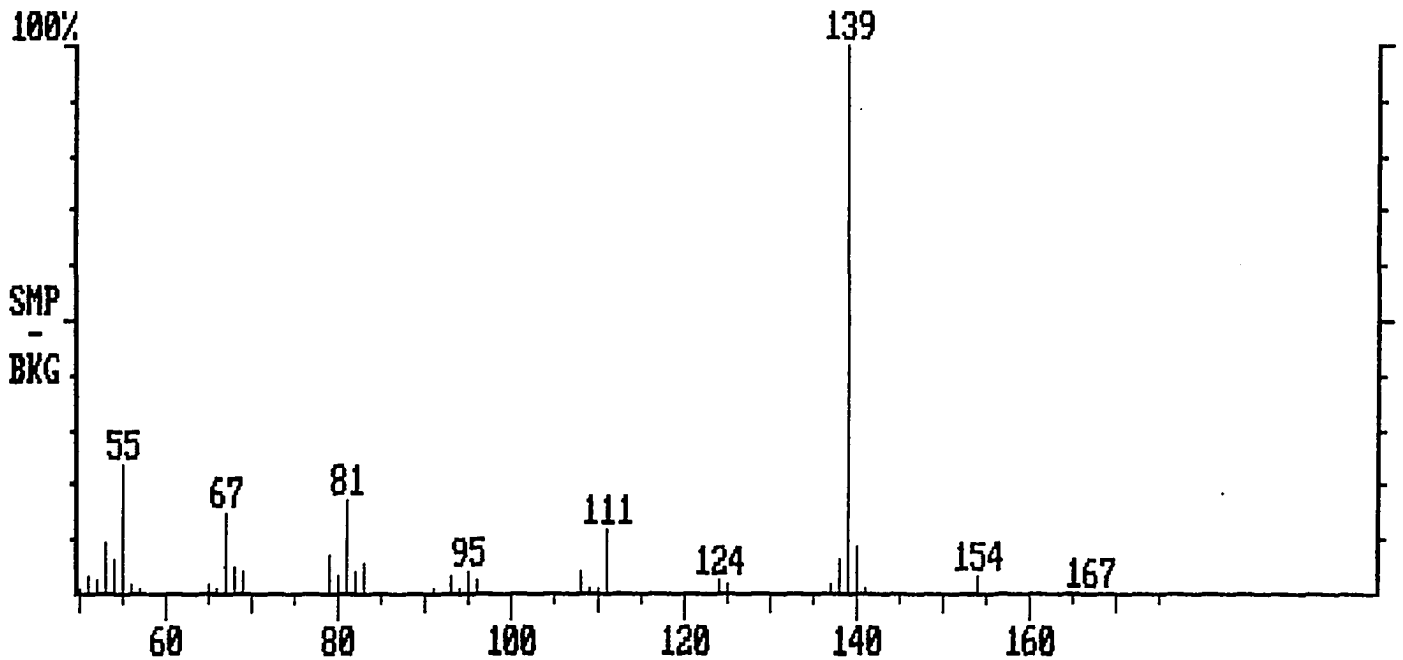

Figure 108. MASS of scan 973 to 977 in Fig. 104

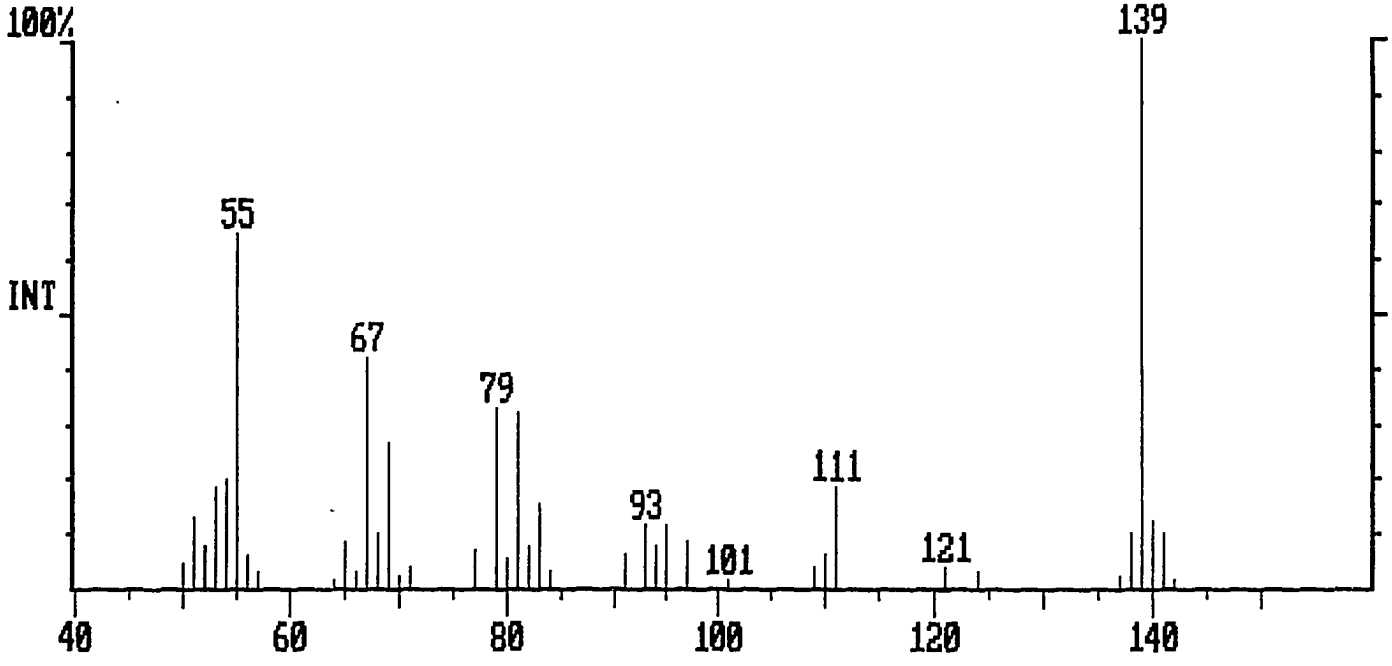

Figure 109. MASS of scan 1004 in Fig. 104

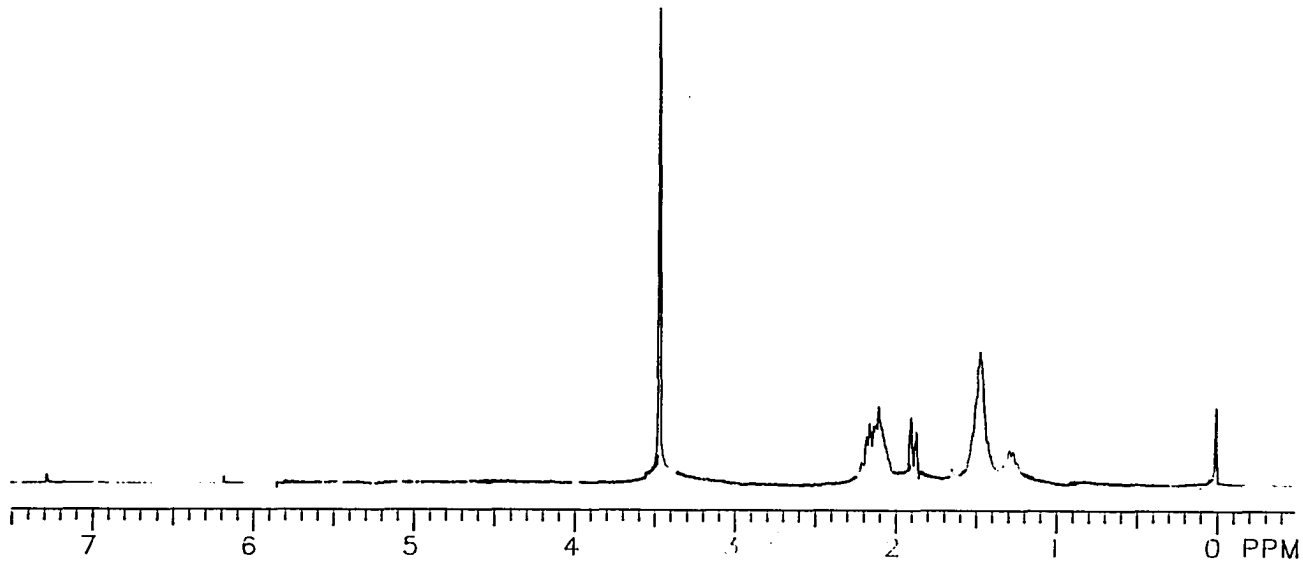

Figure 110. ^{1}H **NMR of 1-methoxy-7,7-dibromobicyclo[4.1.0]heptane**

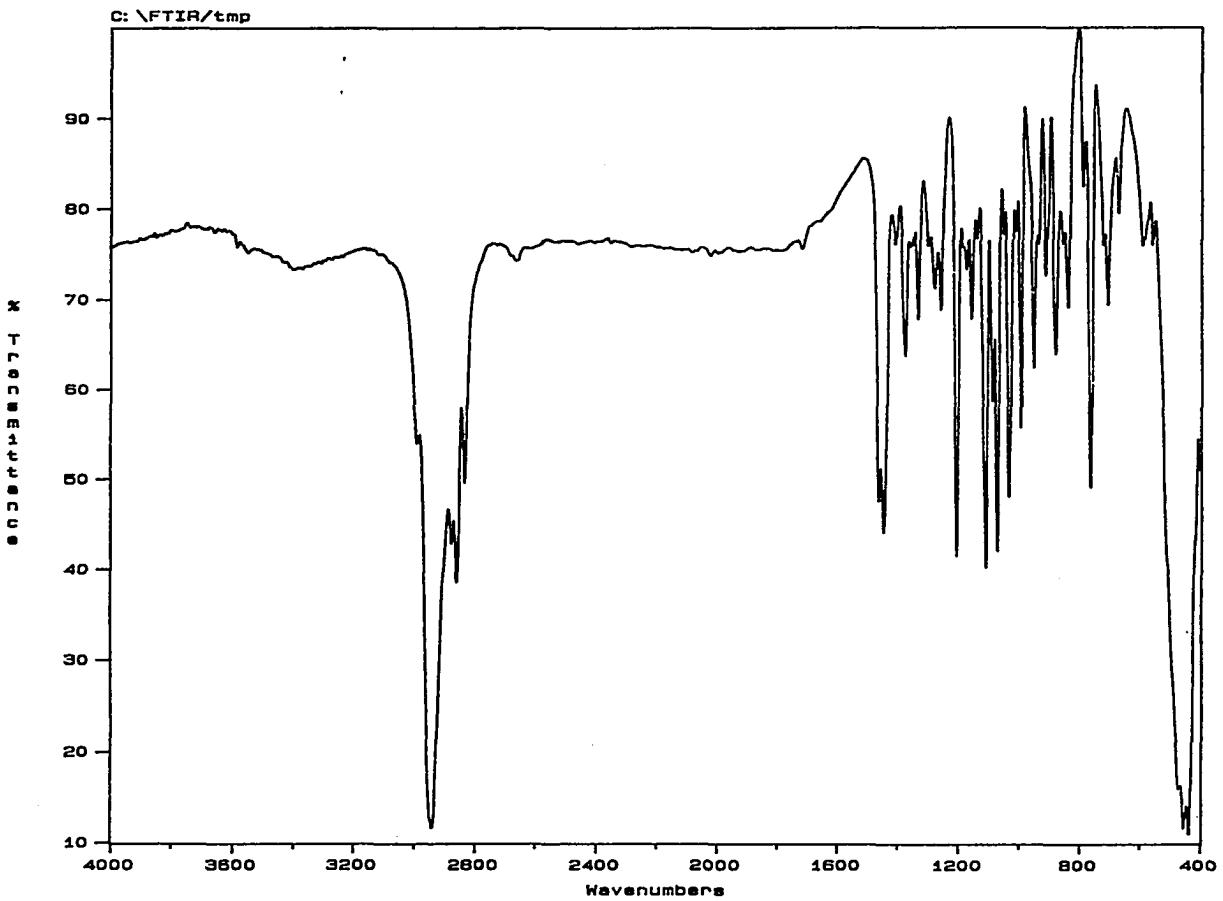

Figure 111. IR of 1-methoxy-7,7-dibromobicyclo[4.1.0]heptane

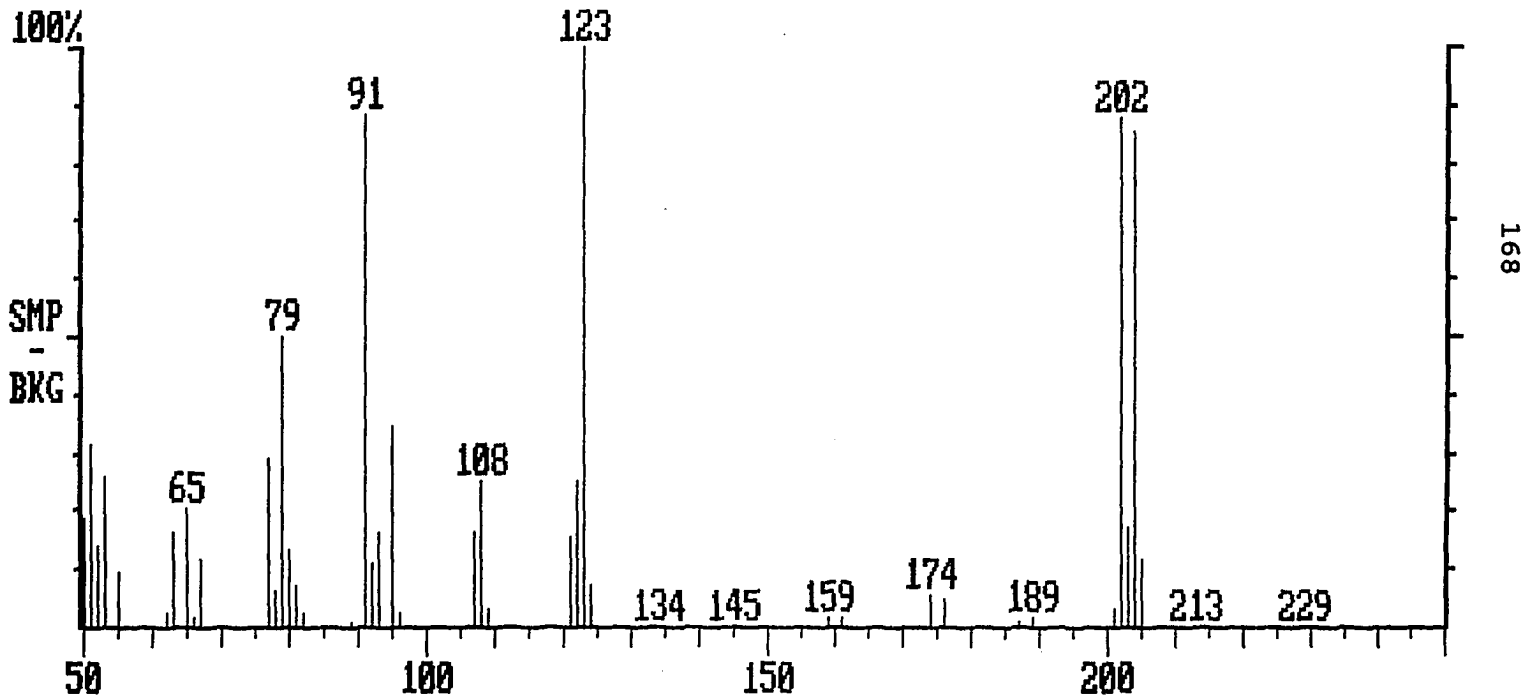

Figure 112. MASS of 1-methoxy-7,7-dibromobicyclo[4.1.0]heptane

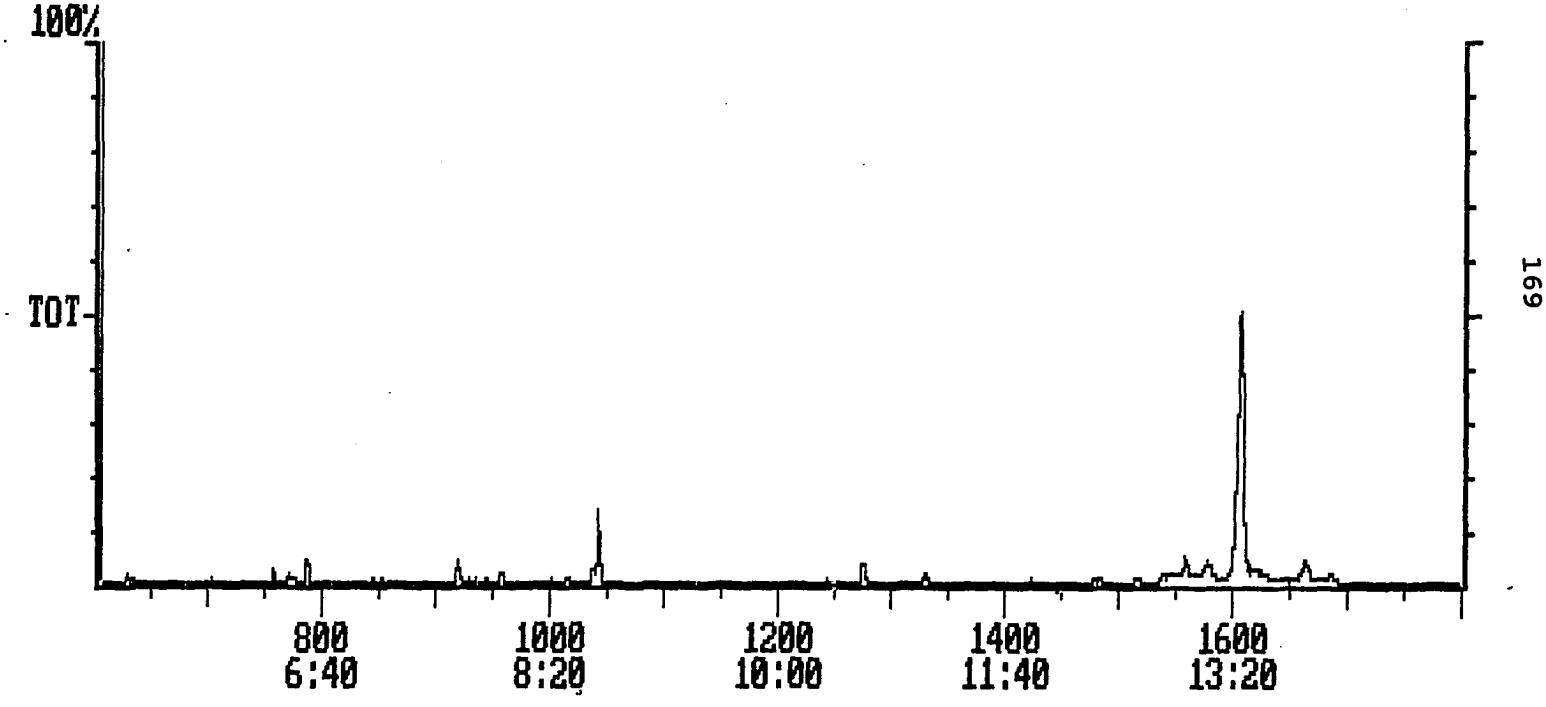

Figure 113. Chromatogram of ring opening reaction mixture of 1-methoxy-7,7-dibromobicyclɔ[4.1.0]heptane

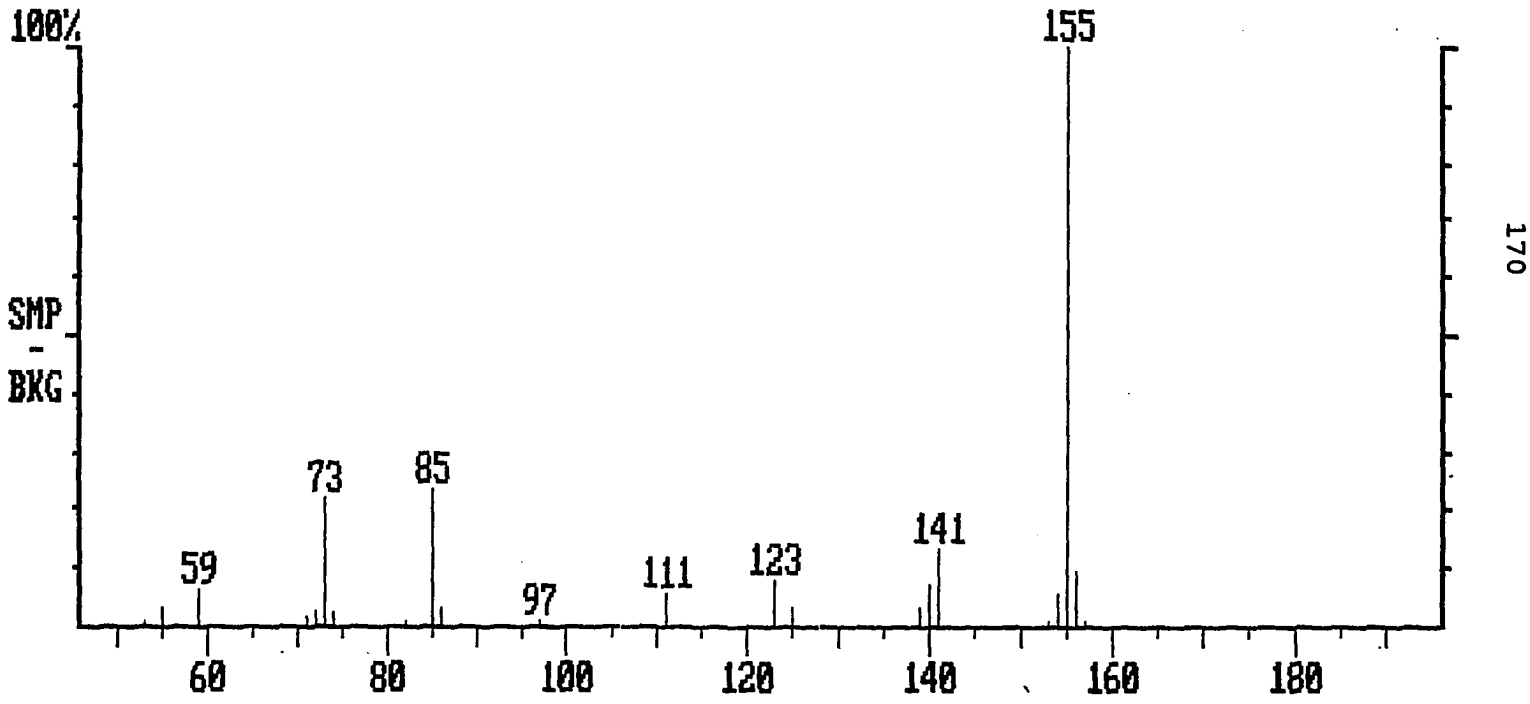

Figure 114. MASS of first peak in Figure 97

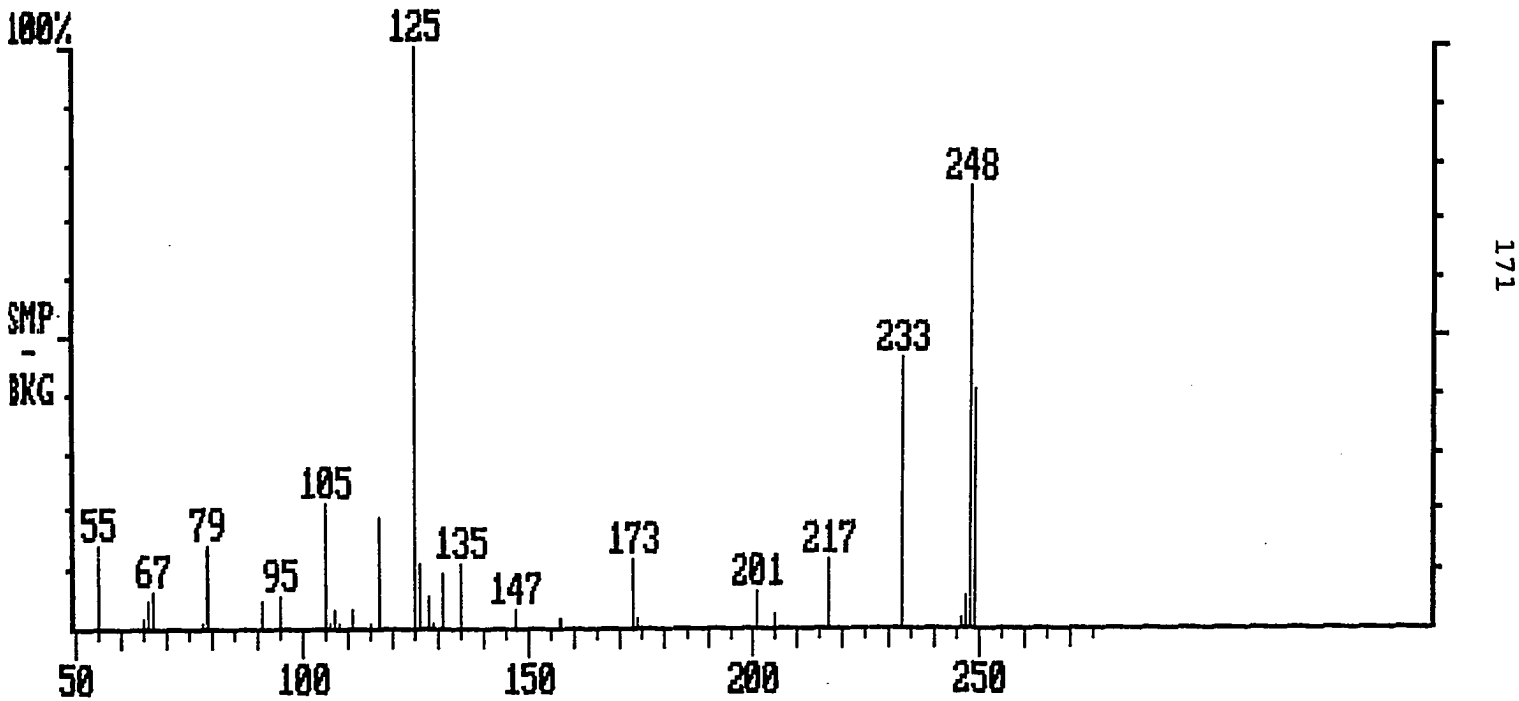

Figure 115. MASS of second peak in Figure 97

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