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Divinylcyclobutane Cope
Rearrangements of Aromatic Substrates

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Kenneth Rehder

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William Reusch
Major professor

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DIVINYLCYCLOBUTANE COPE REARRANGEMENTS OF AROMATIC SUBSTRATES

By

Ken Steven Rehder

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ABSTRACT

DIVINYLCYCLOBUTANE COPE REARRANGEMENTS OF AROMATIC SUBSTRATES

By

Ken Steven Rehder

The use of the divinylcyclobutane Cope rearrangement is a powerful method for the stereocontrolled construction of cyclooctanoid natural products and other structurally novel compounds. However, there have been relatively few examples of this method being used where one or more of the vinyl groups are incorporated into an aromatic substrate. The synthesis of a number of aromatic divinylcyclobutane Cope rearrangement precursors will be described, and their behavior under a wide variety of Cope rearrangement conditions will be discussed. In the cases studied, an alternative mechanistic pathway to the Cope rearrangement appears to be operative, involving the potential intermediacy of a 1,4 diradical resulting from homolytic scission of the cyclobutane bond. Attempts to prove the intermediacy of this diradical will also be examined.

To my high school chemistry teacher, Roger Palmer, who showed me that science must be taught and learned with a sense of humor.

ACKNOWLEDGEMENTS

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INTRODUCTION

Cyclobutanes are known to possess a considerable inherent ring strain energy (approximately 26 kcal/mole),[1] which serves to introduce or enhance reactivity in suitably constructed organic substrates, permitting entry into systems which otherwise might be inaccessible. An interesting and synthetically useful application of cyclobutanes in organic chemistry occurs as a central component in [3,3] sigmatropic shifts such as the Cope rearrangement (see Figure 1).[2]

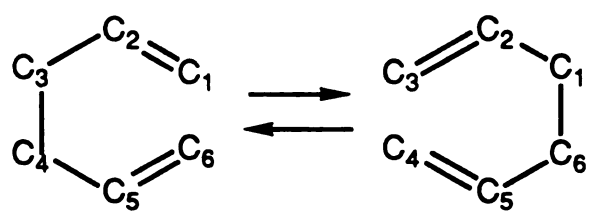


Figure 1. The Cope Rearrangement.

The concerted nature of the Cope rearrangement, with a well ordered and predictable transition state, gives products in excellent stereoselectivity and yield, even in highly functionalized systems. Unfortunately, the Cope rearrangement of a 1,5 hexadiene requires temperatures in excess of 200 °C, is reversible, and generally favors the more substituted diene system. In order to alleviate some of these difficulties, a number of modifications have been developed.

One of the most widely used modifications of the Cope rearrangement is the oxy-Cope rearrangement (see Figure 2).[3] In this variant, a hydroxyl group has been introduced at the C3 position of the rearranging framework. The initial rearrangement generates an enol, which can then tautomerize to the more stable ketone. Since ketones are in general around 15 kcal/mole lower in energy than the corresponding enol, this modification effectively eliminates the reverse rearrangement and allows for isolation of the desired rearranged product.

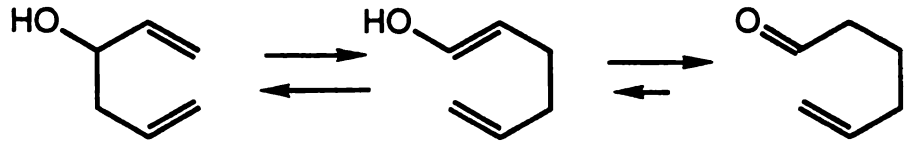


Figure 2. The Oxy-Cope Rearrangement.

Another variant is the anionic oxy-Cope rearrangement (see Figure 3).[4] This rearrangement has essentially the same structural framework as the oxy-Cope, but has an oxygen anion at the 3 position rather than a hydroxyl group. There is a dramatic rate enhancement of 10^{10} to 10^{17} over the simple oxy-Cope rearrangement when the counterion present is potassium, which allows for considerably lower reaction temperatures and shorter reaction times. In addition, the initial rearrangement product is an enolate rather than an enol, and can be subsequently manipulated using standard enolate chemistry. These two advantages have led to the widespread use of the anionic oxy-Cope rearrangement in natural product syntheses.

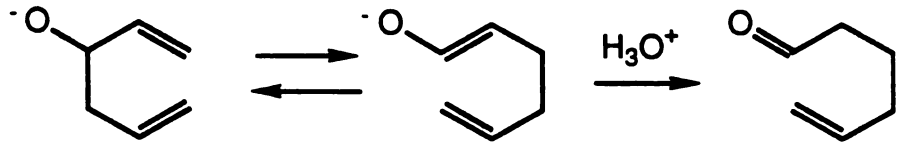


Figure 3. The Anionic Oxy-Cope Rearrangement.

Another modification is the palladium-catalyzed Cope rearrangement (see Figure 4).[5] This modification has a different mechanism than the previously discussed Cope rearrangements, and has been termed a "cyclization-induced rearrangement catalysis" mechanism. Like the anionic oxy-Cope, dramatically reduced reaction temperatures and times can be used. The main drawback is the apparent necessity for the rearranging 1,5 hexadiene framework to be substituted at C5 and unsubstituted at C2, thereby limiting the scope of this reaction. These limitations are thought to be due to the need for both a sterically undemanding palladium coordination site at C2 and a cation-stabilizing center at C5.

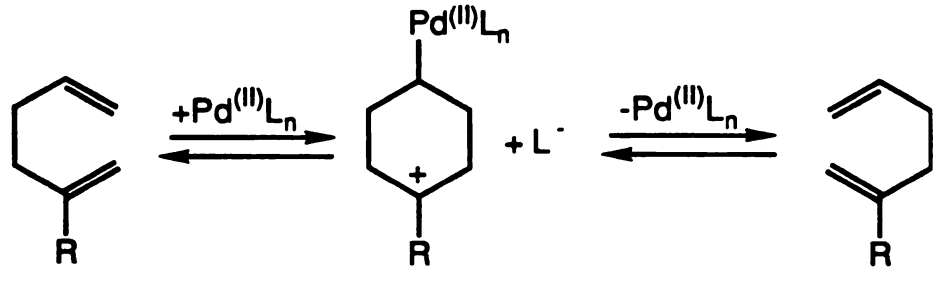


Figure 4. The Palladium Catalyzed Cope Rearrangement.

Finally, a powerful but specialized modification is found in the divinylcyclobutane Cope rearrangement (see Figure 5).[6] By

incorporating a strained cyclobutane ring into the rearranging framework, the reaction can be driven in the forward direction by the release of ring strain energy of approximately 26 kcal/mole, forming a less strained cyclooctadiene as the product.

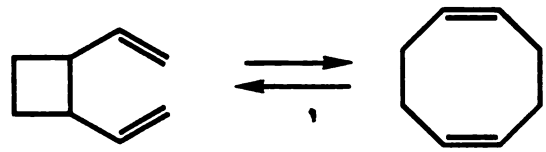
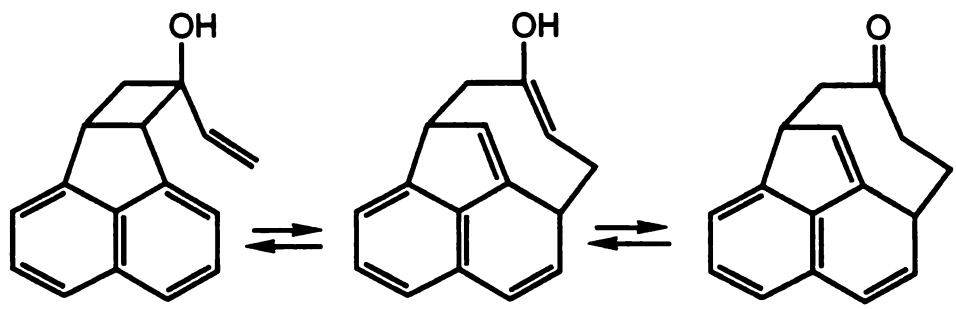


Figure 5. The Divinylcyclobutane Cope Rearrangement.

The Cope rearrangement and the modified Cope rearrangements have been utilized to good advantage in a wide variety of synthetic applications. One area where these reactions have not been extensively used, however, is in the rearrangement of aromatic substrates.[7] Despite the obvious synthetic utility of this type of rearrangement, the high energy cost of disrupting an aromatic ring incorporated in the rearranging framework has made this route unattractive. This is in contrast to the analogous but successfully used aromatic Claisen rearrangement.[8] Procedures which could circumvent this limitation would be a valuable addition to Cope rearrangement synthetic methodology.

In this dissertation the proposal that the Cope rearrangement of an aromatic substrate can be achieved if the rearranging framework is suitably constructed will be examined. In particular, the concept of using the release of ring strain energy of a cyclobutane ring to help overcome the loss of resonance energy due to disruption of an aromatic ring system during a Cope rearrangement will be explored. In order to probe this idea, the aromatic divinylcyclobutanol **5** was proposed as an initial synthetic target and Cope rearrangement precursor (see Figure 6). This compound contains many of the

features necessary to test the above proposal, including the presence of a hydroxyl group in the C3 position of the 1,5-hexadiene framework to form an oxy-Cope system, a divinylcyclobutane Cope system, and an aromatic ring in the form of a substituted naphthalene. Cope rearrangement of this compound must necessarily proceed via a boat transition state, with cleavage of one of the cyclobutane bonds and disruption of resonance in the naphthalene ring system. This will form a cyclooctadienol, which can then tautomerize to a cyclooctenone. Use of the oxy-anionic or palladium-catalyzed Cope rearrangement modifications is also possible for this appropriately substituted divinylcyclobutanol system.



5

Figure 6. Proposed Cope Rearrangement of Aromatic Substrate **5**.

By analyzing the bond energy differences between the starting divinylcyclobutanol and the product cyclooctenone, the validity of the above proposal from a thermodynamic standpoint can be probed. Of particular interest is knowing whether the product of the Cope rearrangement is substantially lower in energy than the starting material. The key terms to consider are the cyclobutane bond cleavage energy, the naphthalene bond resonance energy, the strain in the cyclooctadiene structure. Two methods can be used for this

analysis. Simple use of bond energy tables can give a rough estimate of the difference in energy between the product and the precursor. Molecular mechanics can also be used to give a more accurate analysis of the reaction energetics. Note, however, that these analyses will yield no information regarding the activation energy of this transformation.

Simple use of bond dissociation energy tables[9] shows that the product is substantially lower in energy than the precursor. Cyclobutane ring strain energy has been estimated at 26 kcal/mole. The cost of energy for disrupting the aromatic naphthalene ring can be estimated by subtracting the resonance energy of benzene from the resonance energy of naphthalene, giving 61 kcal/mole minus 36 kcal/mole, or 25 kcal/mole. The difference in energy between a ketone and the enol form has been estimated at 15 kcal/mole, favoring of the ketone. Thus the total amount of energy in favor of the product is approximately 16 kcal/mole. This simple analysis may not be fully accounting for a number of other potentially important energy terms, including the strain of the intermediate cyclooctadiene, the presence of a trans double bond in the product, and the inevitable transannular interactions, but the magnitude of the difference seems to favor the desired product.

Use of molecular mechanics can help to eliminate some the uncertainty which is inevitable in simple bond energy calculations. Molecular mechanics[10] calculations predict a total energy of 63 kcal/mole for the starting material while in a conformation suitable for rearrangement, a total energy of 71 kcal/mole for the initial enol product, and a total energy for the final ketone product of 49 kcal/mole. Thus the energy difference is 14 kcal/mole in favor of the final product. Note that the energy difference between the starting material and product corresponds nicely with those found during the simple bond energy calculations. Another interesting feature of this rearrangement was found during molecular mechanics calculations. They show that the final ketone product can exist in two different conformations, one with the ketone carbonyl moiety "up", or pointing away from the naphthalene rings, and another with the carbonyl "down", or pointing towards the naphthalene rings.

These two conformations differ in energy by about 3 kcal/mole in favor of the "down" conformer. This difference in energy should permit the isolation of these isomers if the desired Cope rearrangement product is formed.

Examination of the product of this Cope rearrangement is interesting for other reasons. The substituted trans-cyclooctenone may possess unusual or enhanced reactivity due to torsional strain, transannular interactions, and the densely packed variety of functional groups present. This might permit further useful elaboration or isomerization. In addition, there is a growing theoretical, medicinal, and synthetic interest in eight-membered carbocyclic ring compounds such as ophiobolin A,[11] dactylol,[12] pleuromutilin,[13] and stegnanacin[14] (see Figure 7). The Cope rearrangement of aromatic divinylcyclobutanes offers a general entry to such eight-membered ring structures. Information obtained during this study may prove useful for synthetic efforts directed toward these and other natural products.

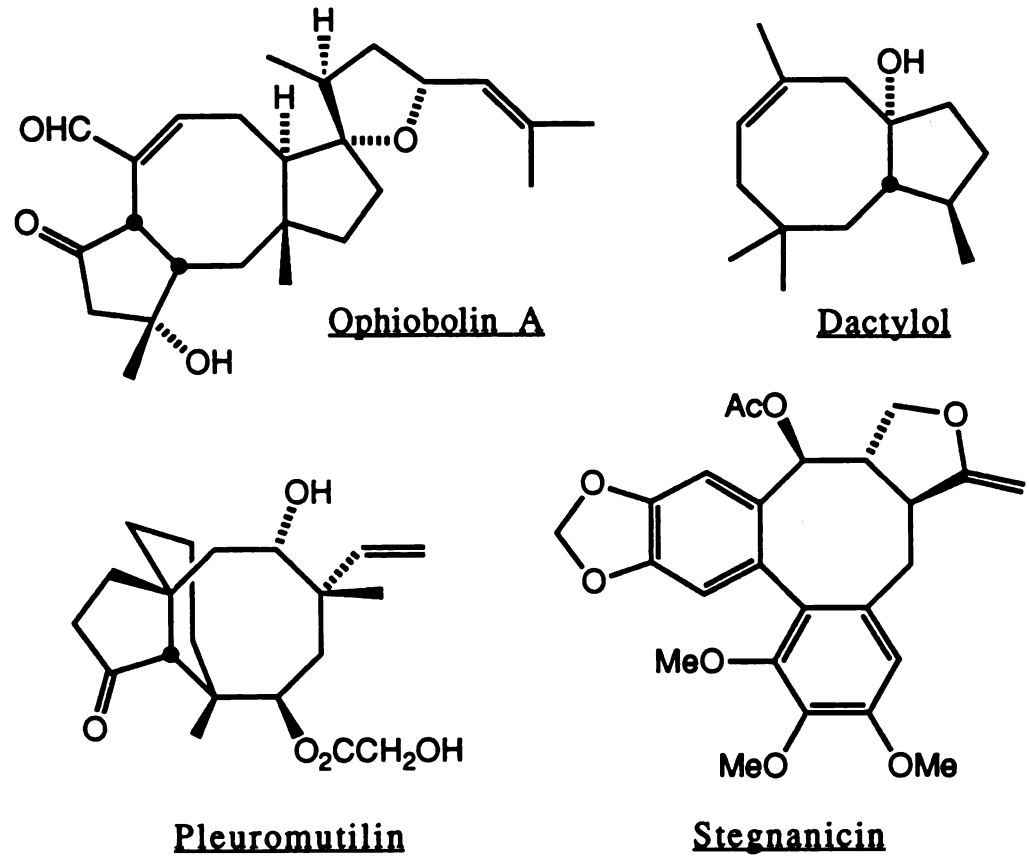


Figure 7. Eight-membered Carbocyclic Ring Natural Products.

SYNTHESIS

Base Catalyzed Isomerization

The initial attempt to synthesize the necessary endo vinylcyclobutanol Cope rearrangement precursor was essentially a modification of a procedure initially outlined these laboratories[15] (see Figure 8). Cycloaddition of dichloroketene[16] to a cyclic olefin generated a cis-bicyclo[n.2.0]dichloroketone, and subsequent reductive removal of the chlorines provided the requisite fused ring cyclobutanone.[17] Reaction with the appropriate Wittig reagent gave the ethylidene derivative. There is an inherent steric bias in this system, which favors the approach of reagents from the less hindered exo face (cis to the bridgehead hydrogens). Thus epoxidation from the exo face, followed by base catalyzed isomerization,[18] was expected to give the desired endo vinylcyclobutanol.

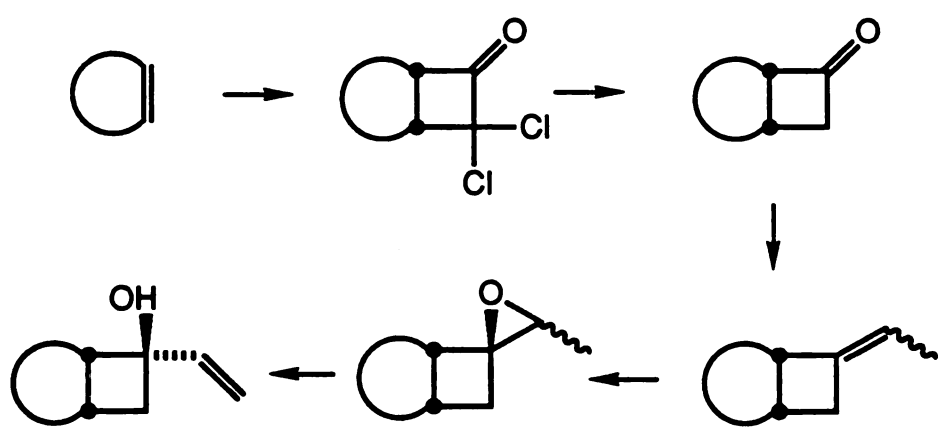


Figure 8. Cycloalkene to Endo Vinylcyclobutanol Synthesis.

In the event, ultrasound promoted [2 + 2] cycloaddition of acenaphthylene with in situ-generated dichloroketene, followed by dechlorination of the crude dichlorocyclobutanone **1** gave the known cyclobutanone **2** in 85% yield.overall (see Figure 9). Wittig reaction gave the ethylidene cyclobutanes **3** as a 1 : 1 mixture (^{1}H NMR) of inseparable stereoisomers in 37% unoptimized yield. Epoxidation of this mixture gave the spiro ethylidene oxides **4** as a 10 : 1 mixture of stereoisomers about the epoxide center in 99% yield. Subjecting the major epoxide isomers (presumably exo due to the folded nature of the substrate and the relative inaccessibility of the endo face) to base catalyzed rearrangement conditions did not give the expected endo vinylcyclobutanol **5**, but rather the substituted acenaphthylene derivative **6** in 83% yield. Modifications of the reaction conditions and changes in the base used gave similar results. Base catalyzed opening of the epoxide ring in **4** by initial removal of the endocyclic benzylic proton rather than the desired primary one, and subsequent electrocyclic opening of the resultant cyclobutene explain this result. Structural elucidation of the diene was effected by Diels-Alder reaction with dimethylacetylene dicarboxylate to give an adduct in 70% yield, whose properties were consistent with the expected **7**.

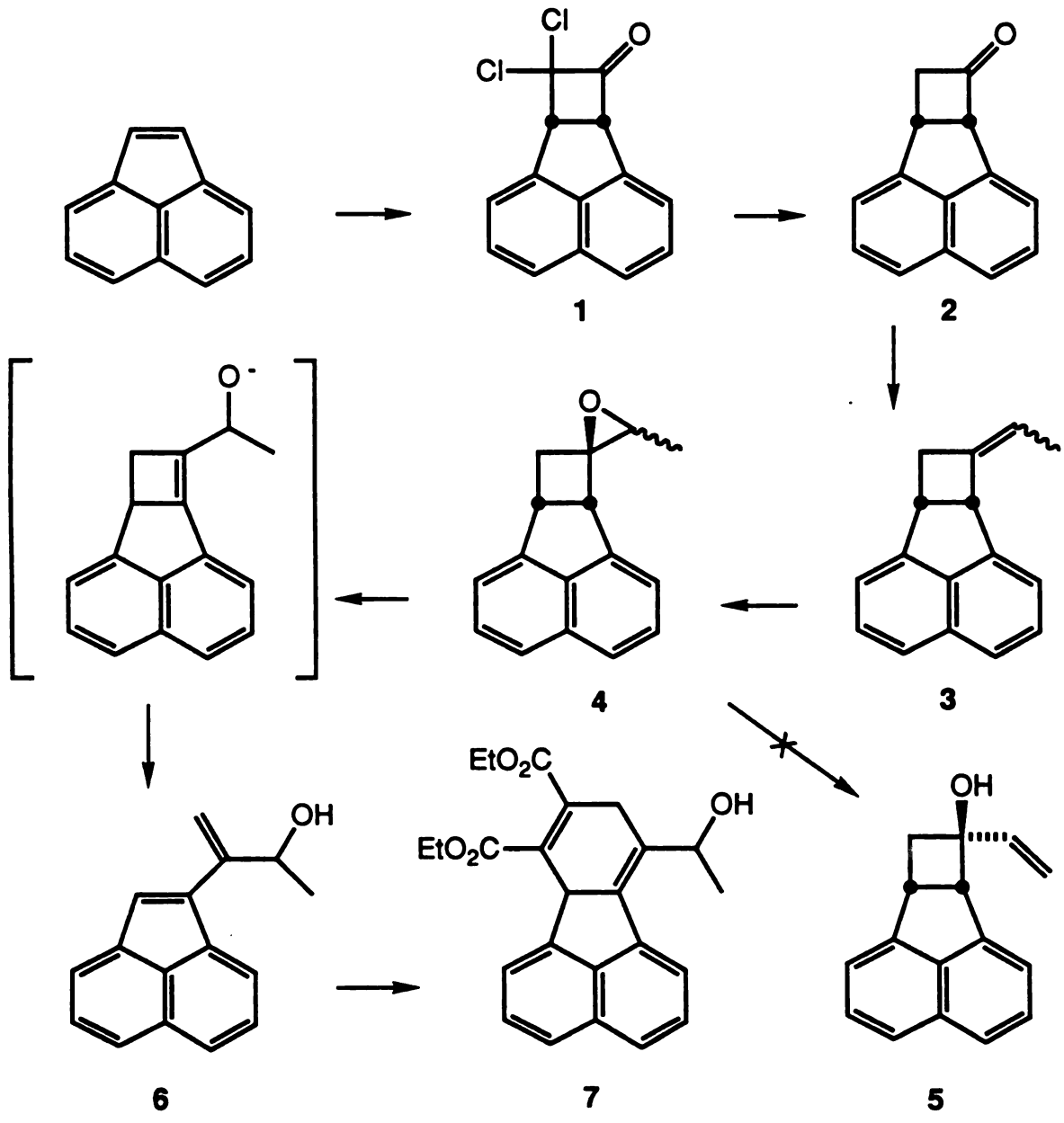


Figure 9. Base Catalyzed Isomerization

Earlier workers[19] had shown that in the base catalyzed isomerization of certain spiro alkylidene oxide systems similar to this one, endocyclic proton removal can be the preferred pathway, especially if there is an available low energy syn coplanar transition state.[20] Examination of models shows that the epoxide oxygen and the benzylic hydrogen in **4** are suitably aligned for such a transformation. The enhanced acidity of the benzylic proton, a factor not present in the previous work,[15] may also be an important reason for this divergence in behavior.

Payne Rearrangement

A revised approach to the Cope precursor (see Figure 10) included Horner-Emmons olefination[21] of the cyclobutanone **2**, reduction of the α,β-unsaturated ester **8**, epoxidation of the resulting allylic alcohol **9** from the less hindered exo face, and Payne rearrangement[22] of the spiro epoxy alcohol **10** to the epoxy cyclobutanol **11**. Conversion of this epoxide to the corresponding alkene would generate the desired endo vinylcyclobutanol **5**. Although this Payne rearrangement (**10** to **11**) proceeds contrary to previously observed substituent effects, the angle strain of the spiro epoxide might override these tendencies, thus favoring, in this case, the less substituted epoxide. This expectation was supported by molecular mechanics calculations, which showed the spiro epoxide **10** to be approximately 10 kcal higher in energy than the monosubstituted epoxide **11**.

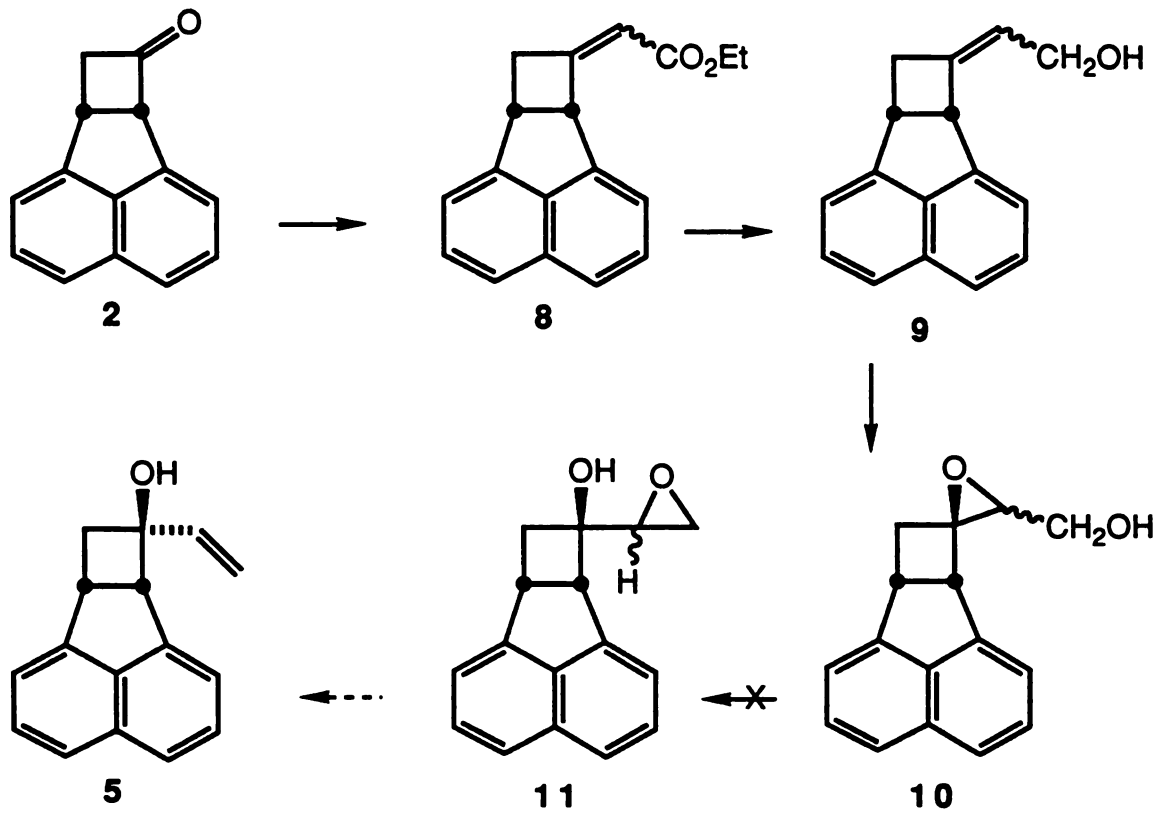
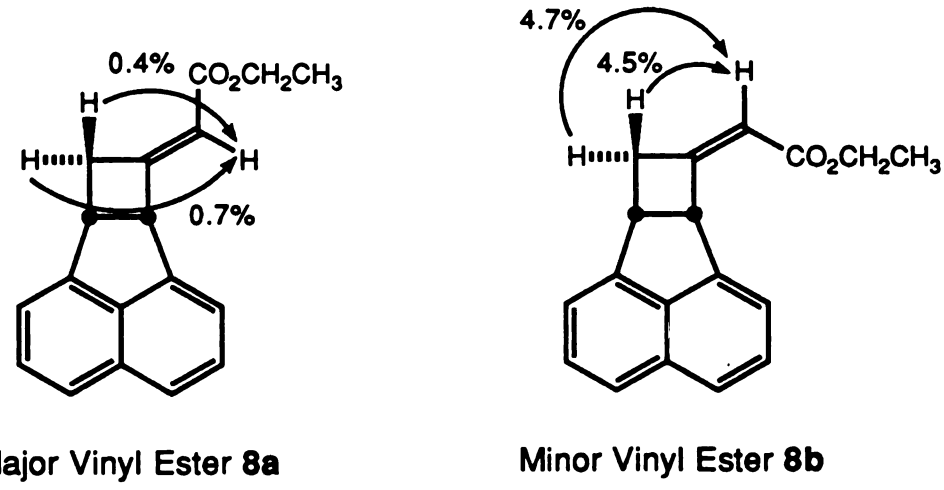


Figure 10. Payne Rearrangement.

In the event, reaction of cyclobutanone **2** with the anion of triethylphosphonoacetate gave the α, β-unsaturated ester **8** as a 10 : 1 mixture of stereoisomers (^{1}H NMR) in 72% yield. The stereochemistry of the major isomer **8a** and the minor isomer **8b** were assigned through use of NOE experiments (see Figure 11). Reduction of the major isomer **8a** gave the allylic alcohol **9a** in 61% yield, and epoxidation yielded the spiro epoxy alcohol **10** as a 2 : 1 mixture of stereoisomers (^{1}H NMR) in 99% yield. The major isomer **10a**, again presumably exo, was subjected to Payne rearrangement conditions, but failed to give any rearranged product; only starting material was recovered. Application of more forcing conditions gave

identical results. Attempted rearrangement of the minor isomer **10b** also gave only recovered starting material.



Major Vinyl Ester **8a** Minor Vinyl Ester **8b**

Figure 11. NOE's of Vinyl Esters **8a** and **8b**.

There are two main questions concerning the course of this reaction which must be addressed. Is true Payne rearrangement equilibrium between the two different epoxy alcohols actually being achieved? If so, why does the equilibrium favor the calculated higher energy isomer? In order to fully answer these questions, synthesis of all eight of the possible spiro epoxy alcohol and epoxy cyclobutanol isomers and examination of the rearrangement capabilities of each might be necessary. The relationship between these various isomers is shown in Figure 12. As stated earlier, reduction of the major α,β-unsaturated ester isomer **8a** gave **9a**, and epoxidation furnished **10a** and **10b**. Similar treatment of the minor isomer of **8b** to yield **10c** and **10d** was not attempted. Obtaining the Payne rearrangement equilibrium isomers from the opposite direction should be possible by epoxidation of endo vinylcyclobutanol **5** to yield **11a** and **11b**, and epoxidation of exo vinylcyclobutanol **19** should yield **20a** and **20b**. However, efforts to

obtain **11a**, **11b**, **20a**, and **20b** through either standard or modified epoxidation procedures gave only poor yields of recovered starting materials. This surprising and frustrating result has not been explained, and further attempts to synthesize these compounds were abandoned.

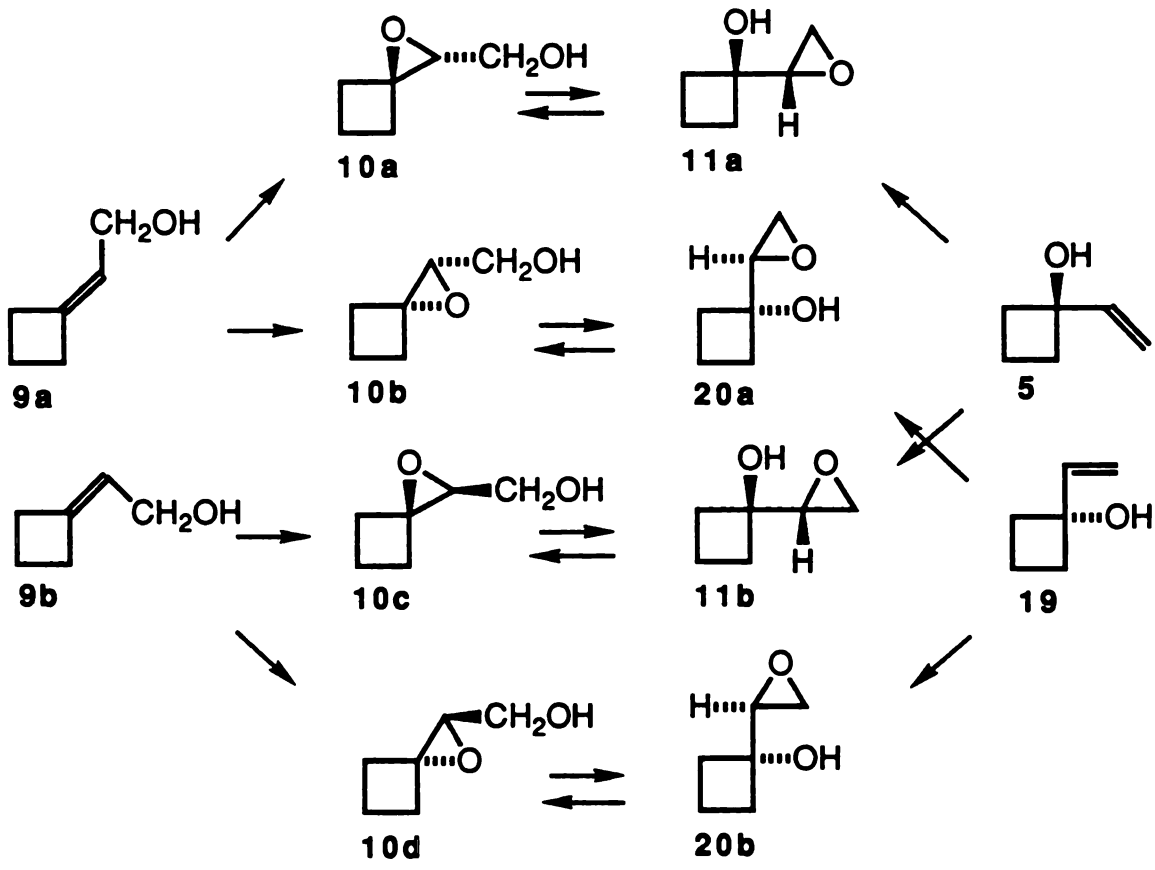


Figure 12. Cyclobutyl Epoxy Alcohol-Epoxy Cyclobutanol Manifold.

Reductive Elimination

Failure of the Payne rearrangement prompted modification of the synthetic approach to the Cope rearrangement precursor **5**. Already having the allylic alcohol **9** (and the epoxy alcohol **10**) in hand, utilization of a known procedure for allylic alcohol transposition was next attempted (see Figure 13).[23] This procedure involves epoxidation of the double bond and conversion of the hydroxyl moiety to a methane sulfonate ester (mesylate). Treatment of this mesylate with a suitable reducing agent effects concomitant mesylate removal and epoxide opening to afford the transposed allylic alcohol.

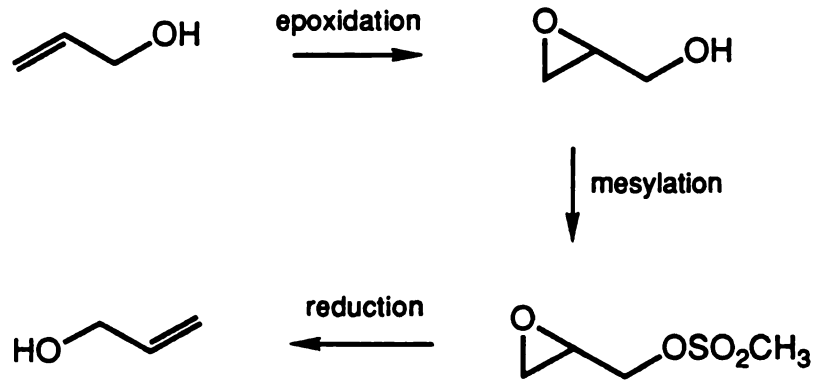


Figure 13. Allylic Alcohol Transposition.

In the event, mesylation of the spiro epoxy alcohol **10** mixture gave the spiro epoxy mesylate **12**, as a 2 : 1 mixture (^{1}H NMR) in 98% yield (see Figure 14). Treatment of the major isomer **12a** with sodium naphthalide[24] gave, in 42% yield, not the expected endo vinylcyclobutanol **5**, but rather a compound whose spectral properties, especially the high field ^{1}H NMR signals, indicated a single spiro cyclopropanol **13** with unspecified stereochemistry at both the

carbinol and the quaternary cyclobutane carbon. Partial structural elucidation of **13** included decoupling experiments and conversion to a geminal methyl aldehyde **14**.

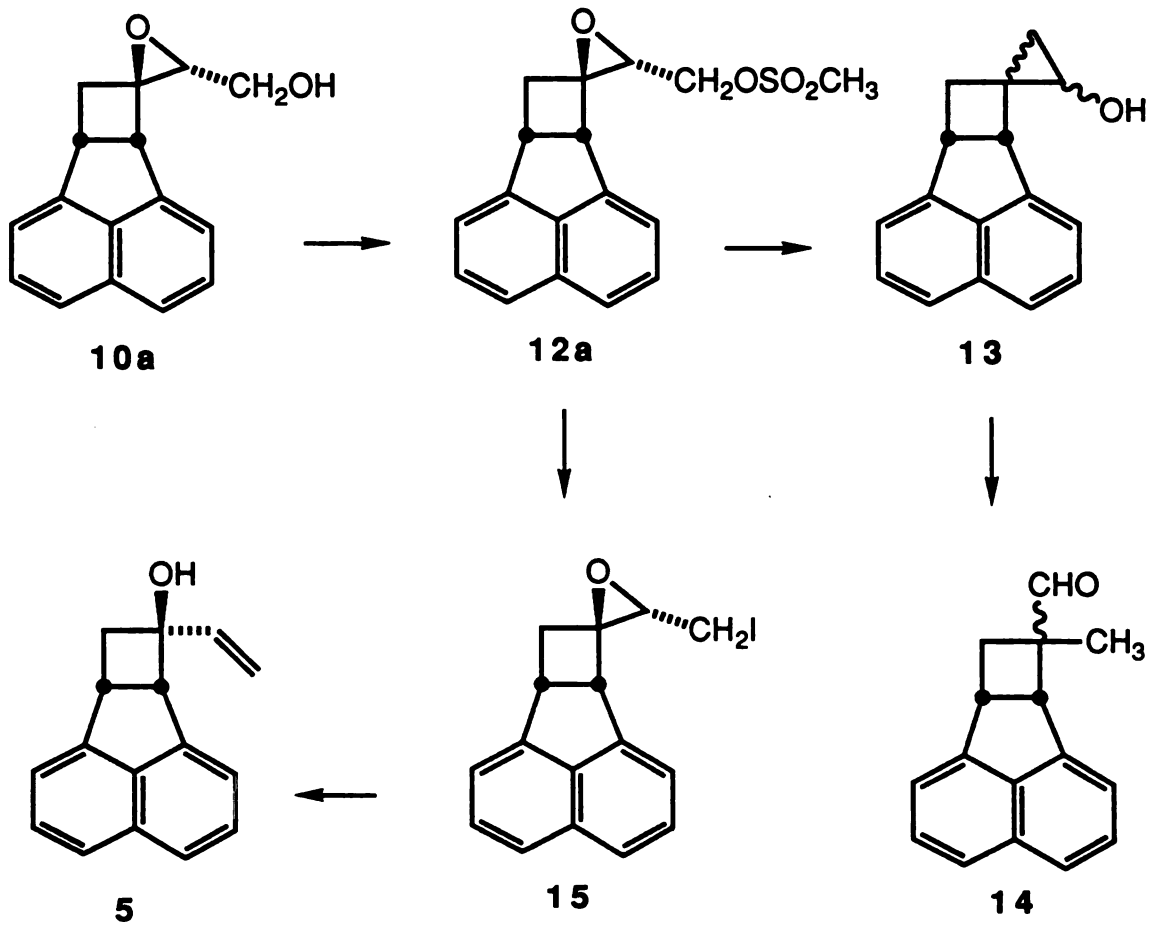


Figure 14. Reductive Elimination

Further structural proof was planned by an independent synthesis of **14** (see Figure 15). Wittig reaction of cyclobutanone **2** with the ylide derived from methoxymethyl triphenylphosphonium bromide should give the cyclobutyl enol ether **16**. Hydrolysis would yield the aldehyde **17**, and enolate formation followed by capture with methyl iodide should yield the exomethylcyclobutyl aldehyde **18**, assuming approach of the alkylating agent from the less hindered exo face. This compound should either be identical with **14**, or differ in configuration about the quaternary center (i.e. the endomethylcyclobutyl aldehyde). Unfortunately, attempts to synthesize **16** were unsuccessful, so the the stereochemistry of **14** remains unspecified.

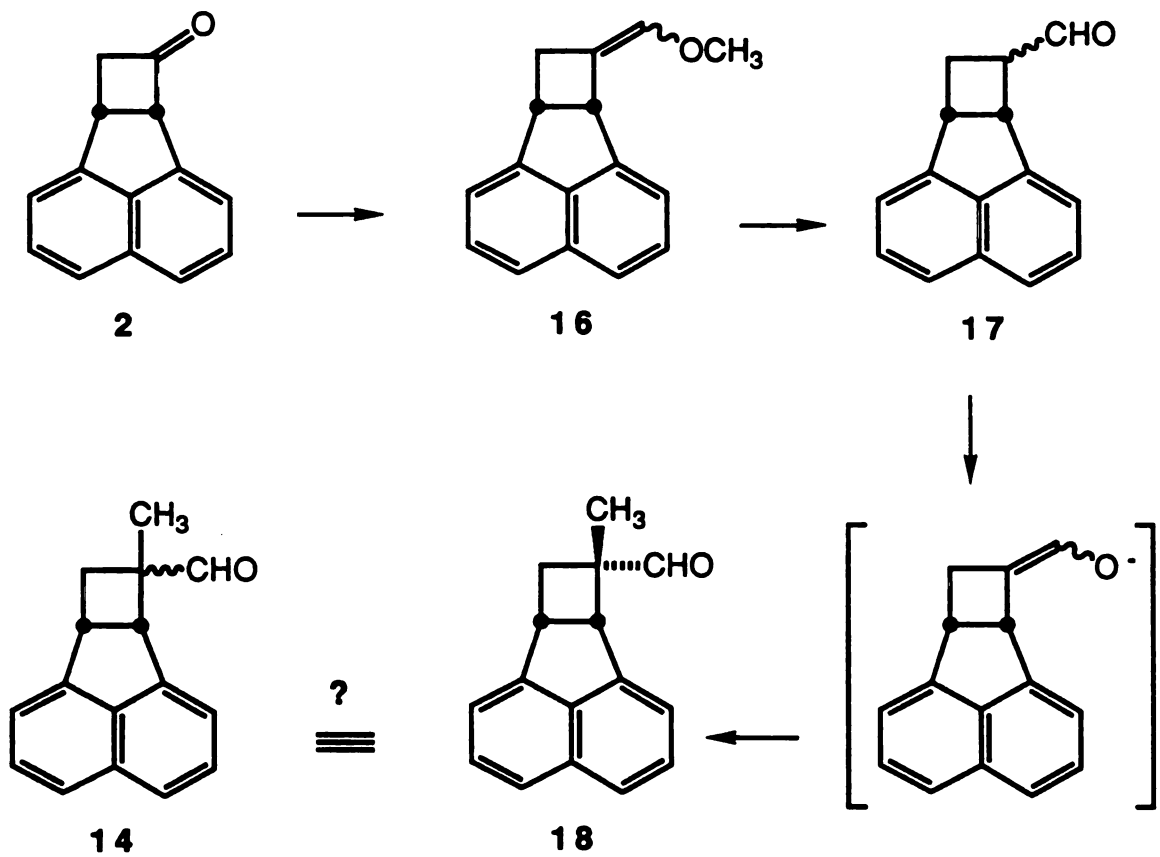


Figure 15. Structural Proof of Geminal Methyl Aldehyde.

The presumed mechanism[24] of reductive elimination in the 1,3 allylic alcohol transposition outlined in Figure 13 involves electron transfer by the reducing agent to the mesylate group followed by cleavage of what was the carbinol carbon to oxygen bond. The alkyl radical is then reduced further to the carbanion, then opens the epoxide to yield the allylic alkoxide. However, due to the naphthalene ring system present in **12**, a different reaction pathway could be envisioned (see Figure 16). The standard oxidation potentials[25] (in DME vs. SCE) of sodium naphthalene (NaNp, 2.60 V) and sodium acenaphthylene (NaAc, 1.65V), which can be used as a rough model for **12**, are substantially different, with NaAc being more easily reduced. Thus treatment of **12** with NaNp might first involve electron transfer from NaNp to generate the radical anion of **12**. This then might intramolecularly attack the epoxide either as the anion or the radical to give a strained cyclopropane, which could be reduced further, either at the naphthalene ring or at the cyclopropane ring. This reduction would cause cyclopropane bond cleavage followed by mesylate expulsion to yield the cyclopropanol **13**. Use of the minor mesylate isomer (derived from **8b**) should yield a cyclopropanol which differs in configuration only about the hydroxyl center. The course of the reaction of the minor epoxy mesylate isomer **12b** (and its isomer derived from **8b**) with reducing agents was not determined.

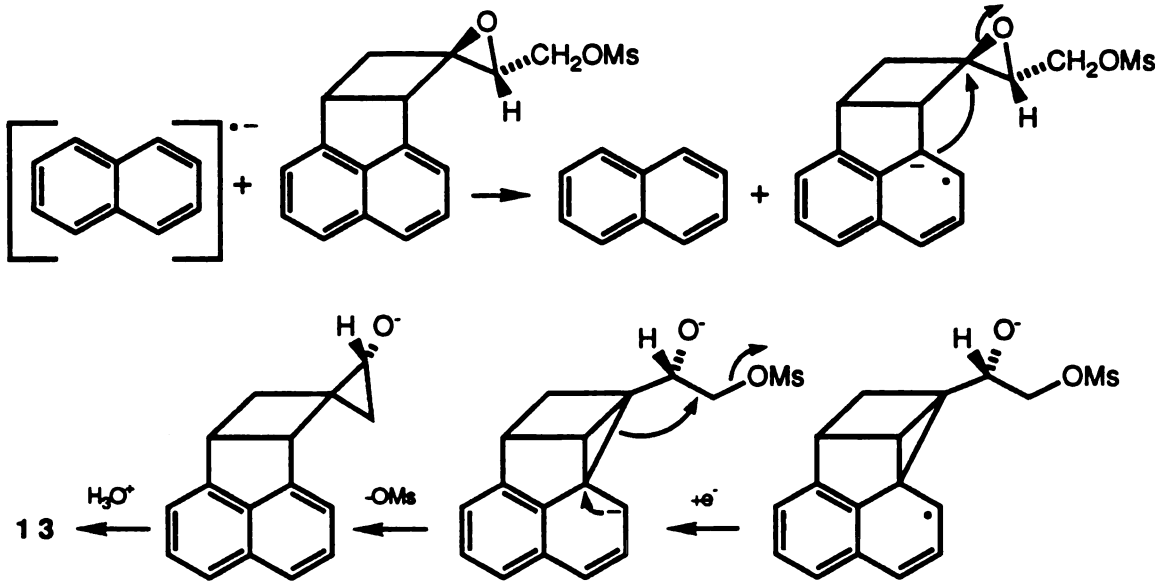


Figure 16. Possible Mechanism of Formation of **13**.

In a modification of the reductive elimination protocol, the major spiro epoxy mesylate isomer **12a** was treated with sodium iodide to generate the intermediate spiro epoxy iodide **15**, which was converted <u>in situ</u> to the desired endo vinylcyclobutanol **5** (see Figure 14) in 41% yield. This result supports the earlier assumption that the major spiro epoxy alcohol **10a** had the assigned configuration, as only this isomer should eventually give rise to the endo vinylcyclobutanol **5**. Further support for this assumption comes from the conversion of the minor (endo) spiro epoxy mesylate **12b** to the exo vinylcyclobutanol **19**, which was obtainable by an independent route, namely addition of vinyl magnesium bromide to cyclobutanone **2** to give **19** in 67% yield (see Figure 17).

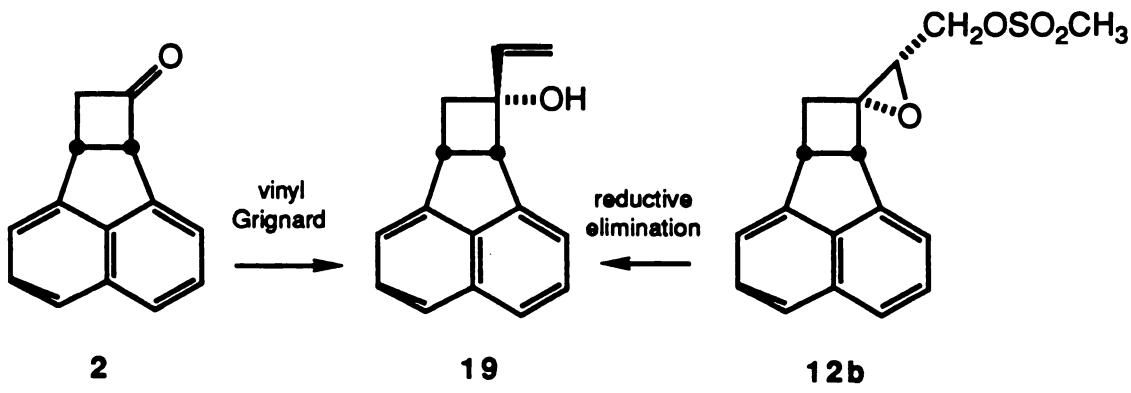


Figure 17. Synthesis of Exo Vinylcyclobutanol **19**.

COPE REARRANGEMENTS

With both the "correct", stereoproximal endo vinylcyclobutanol **5** necessary for the [3,3] sigmatropic Cope rearrangement, and the "incorrect", stereodistal exo vinylcyclobutanol **19** in hand, the rearrangement properties of these two divinylcyclobutane systems could be studied. Molecular mechanics calculations had shown that the stereoproximal isomer was able to align itself in a low energy conformation to allow both termini of the [3,3] system to approach each other at distance amenable to rearrangement. Further calculations showed that the ultimate product, a trans-cyclooctenone, after passing through a high energy intermediate enol, was substantially lower in energy than the starting material, primarily through relief of strain in the cyclobutane bond cleavage. In addition, the possibility that the stereodistal isomer might rearrange also existed, as other studies[26] of divinylcyclobutane systems have shown that some stereodistal isomers can, under certain reaction conditions, isomerize to the stereoproximal isomer, followed by Cope rearrangement.

Anionic Oxy-Cope Rearrangement

The initial attempt at rearrangement made use of the rate accelerated anionic oxy-Cope rearrangement protocol.[4] Treatment of endo vinylcyclobutanol **5** by the recommended basic conditions gave a single compound in 59% yield. The spectral properties of this compound suggested a cyclohexanone such as **21** or **22** (see Figure 18). Differentiation between these two fragmentation-recombination possibilities (path a to **21**, or path b to **22**) was achieved by exhaustive deuteration of the carbons α to the carbonyl to give either **23a** (from **21**) or **23b** (from **22**) in 86% yield. Thus cyclohexanone

21, with four α-hydrogens, will incorporate four deuteriums, while cyclohexanone **22** will only incorporate three. Analysis of **23**, especially by the ^1H NMR integration values and mass spectrum, indicated the tetradeuterated derivative **23a**, thus implying that the rearrangement product was **21**, not **22**.

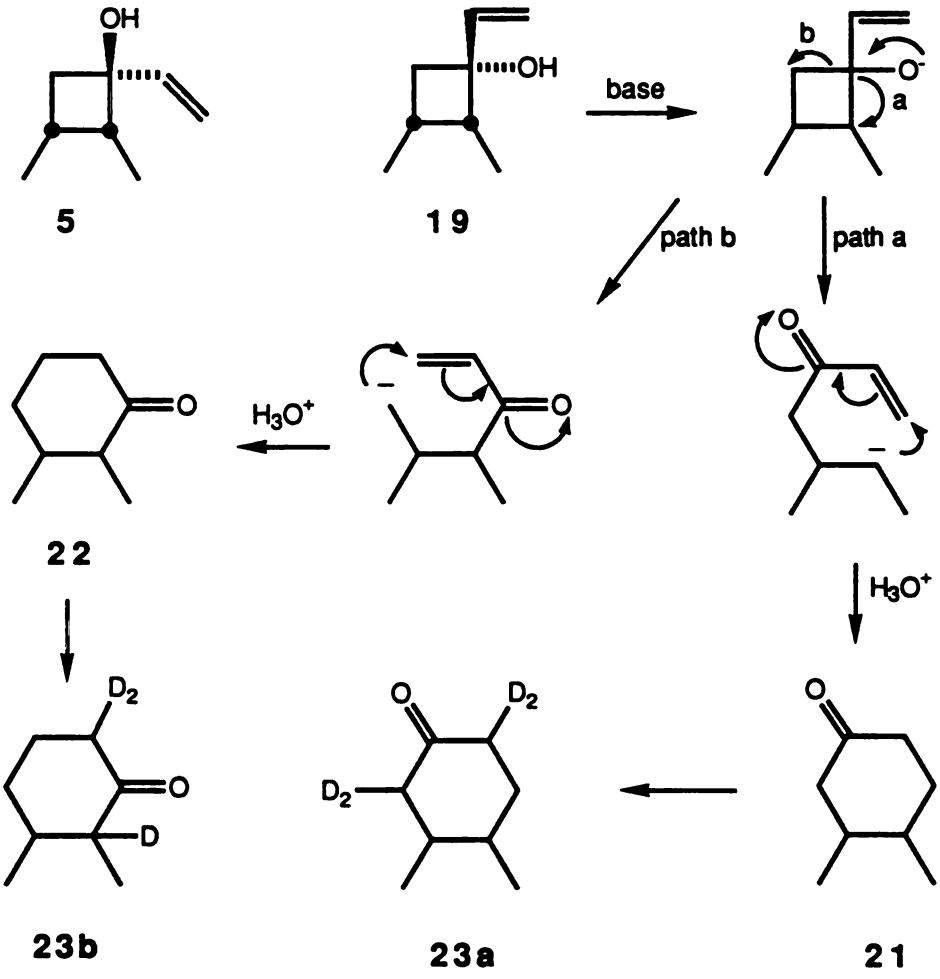


Figure 18. Anionic Oxy-Cope Rearrangement.

The stereochemistry of the ring fusion in **21** was assigned through decoupling experiments and conformational analyses of **21**, **23a**, and the ethylene dithioketal derivative of **21**(**24**). Molecular mechanics calculations showed that the lowest energy conformers of cis-**21** were the exo-boat form **21a** and the endo-boat form **21b**, present in roughly equivalent amounts (See Figure 19). The cis-**21** exo- and endo-chair forms were calculated to be almost 3 kcal higher in energy; as such they should be present in less than 1%, and thus were ignored for the purpose of this analysis. Selected dihedral angles and calculated coupling constants for the two cis boat conformers **21a** and **21b** and for trans-fused **21c** are shown in Table 1, along with some of the observed coupling constants for **21**, **23a**, and **24**. The NMR spectrum of **21** showed H_x and H_y as clearly resolved doublets of doublets (J_{ax} = 6.4 Hz, J_{ay} = 7.0 Hz, J_{xy} = 15.6 Hz), and the spectrum of **23a** also displayed H_m and H_n, as doublets of doublets (J_{bm} = 5.6 Hz, J_{bn} = 7.0 Hz, J_{mn} = 14.1 Hz).

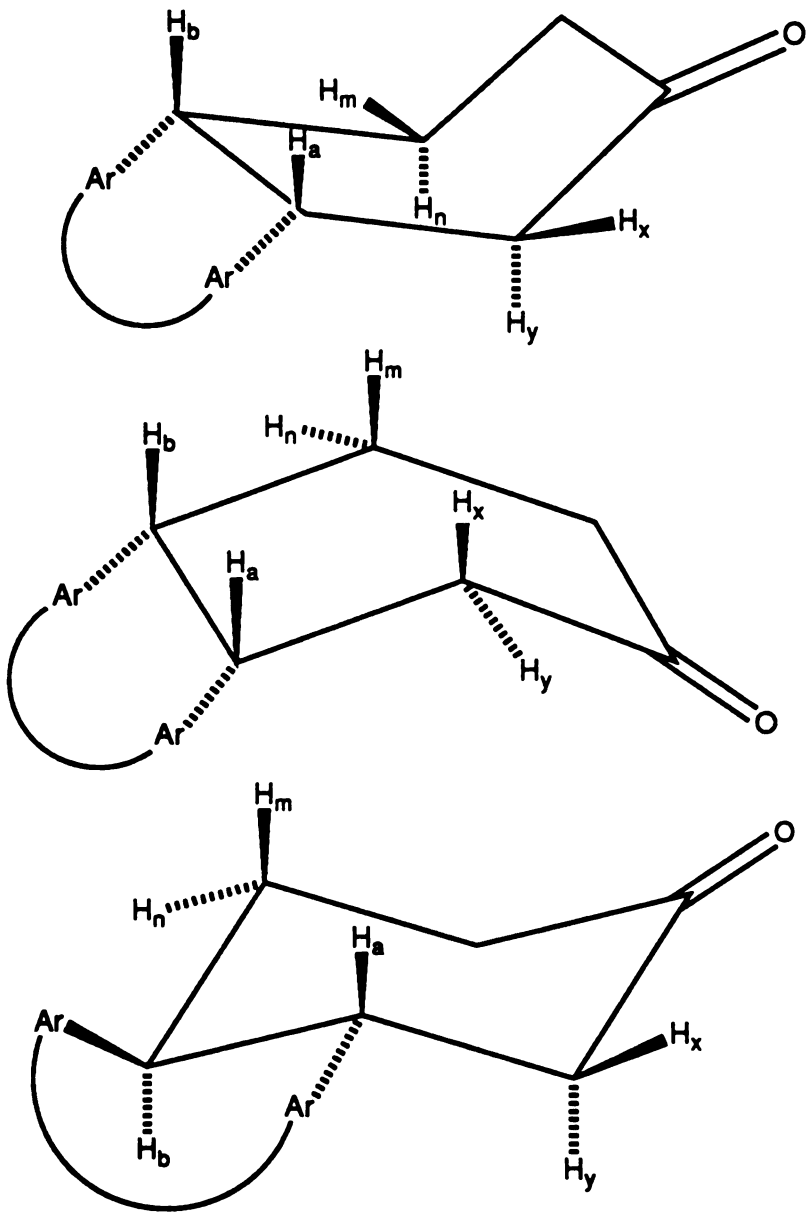


Figure 19. Conformations of Cyclohexanone 21 with calculated Molecular Mechanics Energies.

Although the observed coupling constants match the calculated cis-boat values better than the trans values, the decisive factor in choosing the cis stereochemistry for **21** proved to be couplings observed in the thioketal derivative **24**. If **21** were trans, there would be little change in the observed couplings, as the unavoidable conformational rigidity of both the ketone and the thioketal would result in similar dihedral angles for H_a, H_x, and H_y. If **21** were cis, however, there should be an increased population of the exo conformer, as the endo conformer has a serious 1,3 diaxial interaction between a sulfur atom of the thioketal moiety and the naphthalene ring system. This equilibrium shift should result in slightly increased J_{ax} values and more dramatically increased J_{ay} values. This is in fact observed: J_{ax} changes very little (actually drops from 6.4 to 6.0 Hz), and J_{ay} shows a more substantial change (increases from 7.0 to 10.6 Hz). On the basis of these accumulated observations, the cis stereochemistry for the cyclohexanone **21** was decided upon.

Table 1. Selected Coupling Constants (and dihedral angles) of **21** and Derivatives. The first four entries represent MM2 derived values, while the last three entries represent actual observed values.

Structure	J_{ax}(Hz)	J_{ay}(Hz)	J_{bm}(Hz)	J_{bn}(Hz)
cis endo boat **21b**	3.9 (54°)	2.3 (63°)	4.4 (52°)	2.2 (64°)
cis exo boat **21a**	4.6 (49°)	11.8 (108°)	4.4 (50°)	11.8 (167°)
trans chair **21c**	2.7 (60°)	12.4 (179°)	2.4 (62°)	12.4 (178°)
averaged cis boat	4.3	7.4	4.4	7.3
cyclohexanone **21**	6.4	7.0		
d_4-cyclohexanone **23a**			5.6	7.0
thioketal **24**	6.0	10.6		

The formation of **21** from **5** was not entirely unexpected, as earlier work[27] had shown that the oxy-anionic rearrangement of a 1-vinylcyclobutanol system with an anionic stabilizing thiophenyl group in the 2 position gave cyclohexanones of this type, although in that case a mixture of cis and trans isomers was formed. The mechanism of this transformation was presumed to occur by conversion of the oxy-anionic vinylcyclobutane to a ring-opened vinyl ketone-stabilized anion, followed by intramolecular Michael reaction. Under similar conditions the isomeric exo vinylcyclobutanol **19** also gave cyclohexanone **21** in 56% yield In neither case was the isomeric vinylcyclobutanol or the trans cyclohexanone observed among the products.

Palladium Catalyzed Cope Rearrangement

Having unsuccessfully attempted the anionic oxy-Cope rearrangement, we next turned to transition metal catalysts, specifically palladium(II). Palladium dichloride has been used successfully as a catalyst for various types of [3,3] sigmatropic shifts,[5] including the oxy-Cope variant, and we hoped that the mild reaction conditions used would help to minimize undesirable byproducts. One possible mechanistic pathway for this transformation is what has been called a "cyclization induced rearrangement catalysis" (see Figure 20). The most pronounced trend favoring this mechanism is the generally observed requirement for a hydrogen substituent at C2 of the 1,5-hexadiene unit, and a non-hydrogen substituent at C5. C2 must be relatively unencumbered to allow the bulky palladium electrophile (E^+) to attach itself at that site, and stabilization of the intermediate cyclohexenyl carbocation at C5 will be facilitated by suitable electron donating substituents in that position. Both **5** and **19** appear to meet both of these requirements, being unsubstituted at C2 and able

to achieve benzylic carbocation resonance stabilization at C5. Note, however, that the mechanistic picture of the palladium(II) catalyzed Cope rearrangement of cis 1,2-divinylcyclobutanes is somewhat unclear.[28] Products are sometimes obtained other than those of the analogous thermal Cope reaction, thus this type of transformation for this class of compounds must be considered a special case. This is probably due to the strain of the four membered ring and the necessarily constricted boat conformation of intermediates or transition states whose appearance may involve various degrees of concertedness in the bond cleavage and formation.

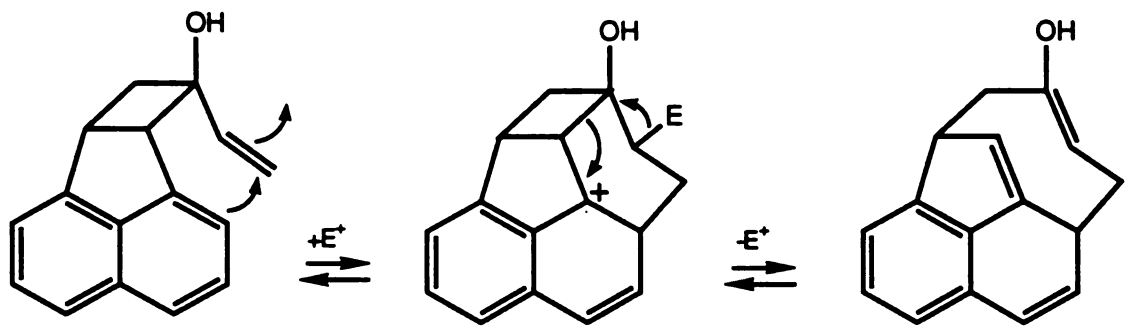


Figure 20. Cyclization Induced Rearrangement Mechanism.

In the event, treatment of endo vinylcyclobutanol **5** with bis (acetonitrile) palladium dichloride yielded a mixture of cyclopentanones in 61% yield (**25**:**26**:**27**:**28**=1:1:14:4), but no desired Cope product (see Figure 21). Treatment of exo vinylcyclobutanol **19** with the same catalyst gave a similar mixture of cyclopentanones in 68% yield (**25**:**26**:**27**:**28**=1:7:22:3). These results can be explained by initial coordination of the palladium species to the vinyl group, followed by electrophilic addition to the double bond. Migration of a cyclobutane bond to the electron deficient center followed by β-hydride elimination yields the α-methylene cyclopentanone **25**. Readdition of the expelled metal hydride species then forms an α-

palladocyclopentanone. This can then β-hydride eliminate the same hydrogen to give back **25** or, if the palladium added from the less hindered exo face, it can eliminate the syn coplanar benzylic hydrogen to yield the α,β-unsaturated cyclopentenone **26**. If the palladium species remains attached to the cyclopentanone rather than eliminates, then reductive removal during workup will afford the α-methyl cyclopentanones **27** and **28**. The stereochemistry of the methyl group is dependent on the direction of the initial attack of metal hydride on the α-methylene cyclopentanone **25**, assuming there was no epimerization of this center. Products of this type have been observed previously.[29] However, in those cases there was a marked preference for the the endocyclic α,β-unsaturated ketone. The considerable strain of the analogous product in our case, compound **26**, may explain this divergence.

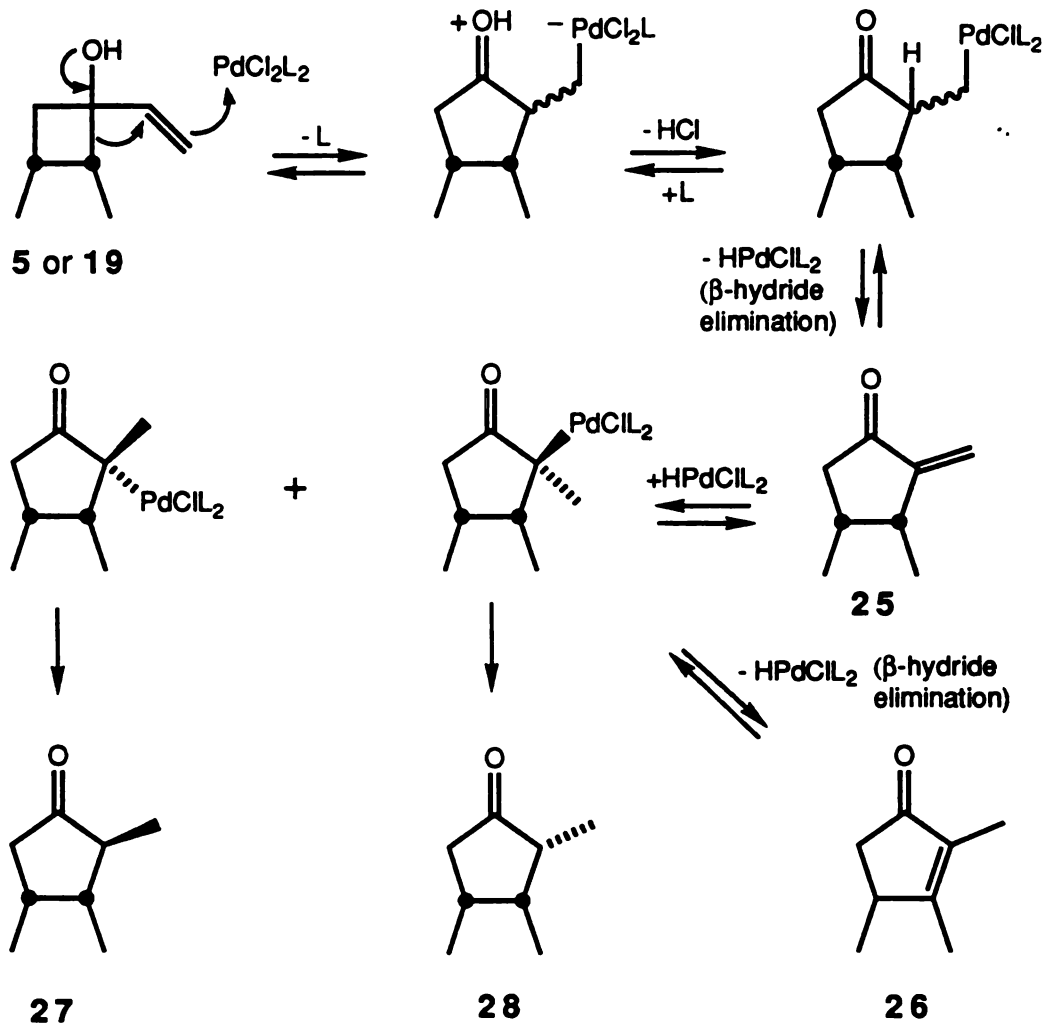


Figure 21. Palladium Catalyzed Cope Rearrangement

Solution Thermolysis

Thermal rearrangement of the vinylcyclobutanols in hydrocarbon solvents was next attempted. No reaction was observed for either isomer in refluxing benzene or toluene; however, a solution of endo vinylcyclobutanol **5** in refluxing o-xylene yielded, after 48 hours, a 2 : 1 mixture of cyclohexanone **21** and the previously unobserved vinyl ketone **29** (see Figure 22). Interestingly, subjecting exo vinylcyclobutanol **19** to the same conditions gave identical results: a 2 : 1 mixture of **21** and **29**. In neither case was the isomeric vinylcyclobutanol or desired Cope product observed. Previous work in this area[30] has shown that cis 1,2-divinyl cyclobutane systems, such as **5**, generally undergo a [3,3] sigmatropic shift to cyclooctenes, while the trans isomers, such as **19**, rearrange predominantly through a [1,3] sigmatropic shift to form 4-vinyl cyclohexenes. An alternative pathway, the retro-ene ring opening,[31] is available when a hydroxyl substituent is present. Also known as a β-hydroxy olefin cleavage, this reaction is essentially a [1,5] hydrogen shift yielding a γ,δ-unsaturated vinyl ketone. Any or all of these processes, as well as various radical intermediates, might be involved in these examples . Obviously, either isomer could undergo the [1,3] shift to eventually form **21** after passing through the enol. Although **5** and **19** are geometrically constrained to pass through, respectively, the [3,3] and [1,5] rearrangement manifolds, the possibility of an initial isomerization exists; therefore, all of these pathways must be considered viable alternatives for both isomers. Additionally, one final mode of rearrangement might be possible. Assuming the Cope rearrangement and ketonization of the cyclooctadienol to have taken place via either **5** or **19**, a 1,5 hydrogen shift of the α-hydrogen of the transcyclooctene product could occur (intramolecular ene reaction),[32] yielding the vinyl ketone **29**, or a [1,3] alkyl shift giving cyclohexanone **21**.

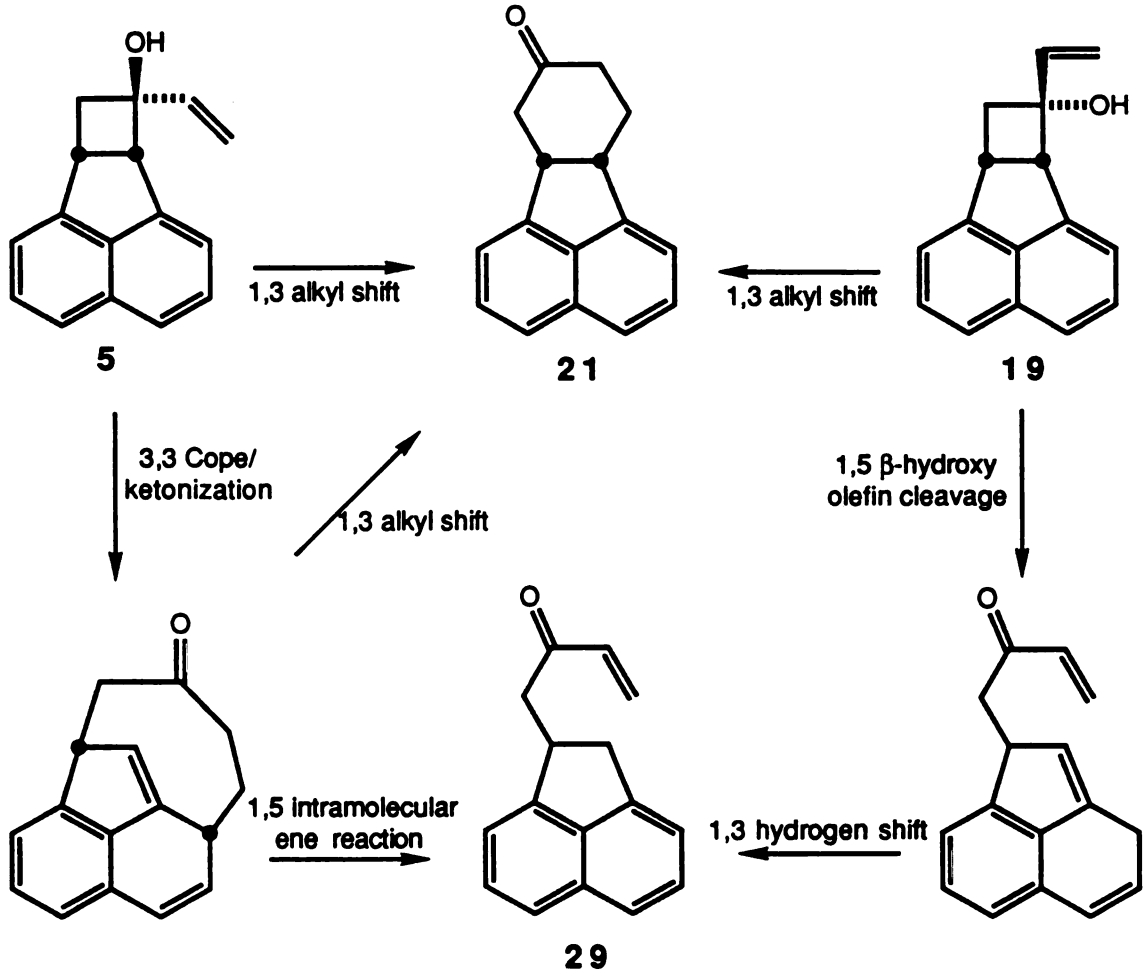


Figure 22. Thermal Solvated Rearrangements of Vinylcyclobutanols.

Flash Thermolysis

One possible explanation for the absence of the expected [3,3] Cope product or [1,5] retro-ene β-hydroxy olefin cleavage product in the previous studies is the severity and/or duration of the reaction conditions. Extended heating in refluxing o-xylene (bp 165 °C) might allow the undoubtedly thermally labile [1,5] product to rearomatize to form **29**, the trans cyclooctene [3,3] product to rearrange to the less strained **21**, or allow the intramolecular ene reaction to take place. To circumvent these possibilities, the use a flash thermolysis system was explored. Minimization of the total contact time of the substrates with heated surfaces was desired, thereby improving chances of isolating one or more of these unstable intermediates. A detailed description of this system can be found in the Experimental Section. Basically this system consisted of a glass column filled with Pyrex glass beads and heated with a ceramic jacket. A solution of the sample was introduced by an addition funnel, carried through the column in an Argon stream, collected in a dry-ice cooled vessel, and the condensate analyzed. Note that this was not a Flash Vacuum Pyrolysis (FVP) system. The results of these experiments are presented in Table 2.

Table 2. Thermolysis Experiments. The product column indicates the amount of acenaphthalene, vinyl ketone **29**, and cyclohexanone **21** obtained.

Entry	Compound	Addition time(hrs)	Temp. (°C)	Starting material(mgs)	Product (mgs)
1	**5**	2.0	300	10.3	3/3/4
2	**5**	1.5	300	14.1	2/3/5
3	**19**	3.0	300	100.0	15/12/18
4	**19**	1.0	300	100.0	4/6/11
5	**19**	2.2	300	100.0	13/13/20
6	**19**	2.2	245	100.0	0/12/15
7	**21**	2.5	300	17.6	0/0/12
8	**29**	2.0	300	13.7	0/7/0

The first two entries show the results of the thermolysis of the endo vinylcyclobutanol **5**. Heating this compound at 300 °C yielded essentially a equal mixture of acenaphthylene, vinyl ketone **29**, and cyclohexanone **21**. Entries 3-5 show that the same reaction for exo vinylcyclobutanol **19** gave virtually the same results. Note that the mass balance in these and other thermolyses is disappointingly low. This is probably due to the deposition of intractable polymeric material at the top of the thermolysis column, this being clearly visible after the reaction was completed and the apparatus cooled and dismantled. The manner in which this material is produced is not known. Entry 6 shows the result of lowering the reaction temperature. Only **21** and **29** were formed, paralleling the previously observed result of refluxing o-xylene thermolysis, indicating that perhaps the pathway for formation of acenaphthylene may involve a higher energy intermediate or transition state than that for formation of **21** or **29**. Entries 7 and 8 show that **21** and **29** are probably not interconverting to other products during the course

of the reaction (although the low mass balances preclude any definitive conclusions regarding this result).

The similar results obtained for the thermolysis of **5** and **19** in all our thermolysis studies seem to indicate the existence of some common intermediate during these transformations. The formation of acenaphthylene at higher temperatures also needs to be accounted for. Both of these experimental results can be rationalized by invoking the intermediacy of a diradical (See Scheme 23).[33] Scission of the cyclobutane bond not only relieves considerable strain, but also forms a highly stabilized benzyl-allyl diradical. This diradical could recombine to form an enol which would then ketonize to yield **21**. Abstraction of the hydroxyl proton would form the vinyl ketone **29**. Finally, a Norrish type II cleavage reaction[34] could account for the formation of acenaphthylene; obviously methyl vinyl ketone would be a by-product of this process.

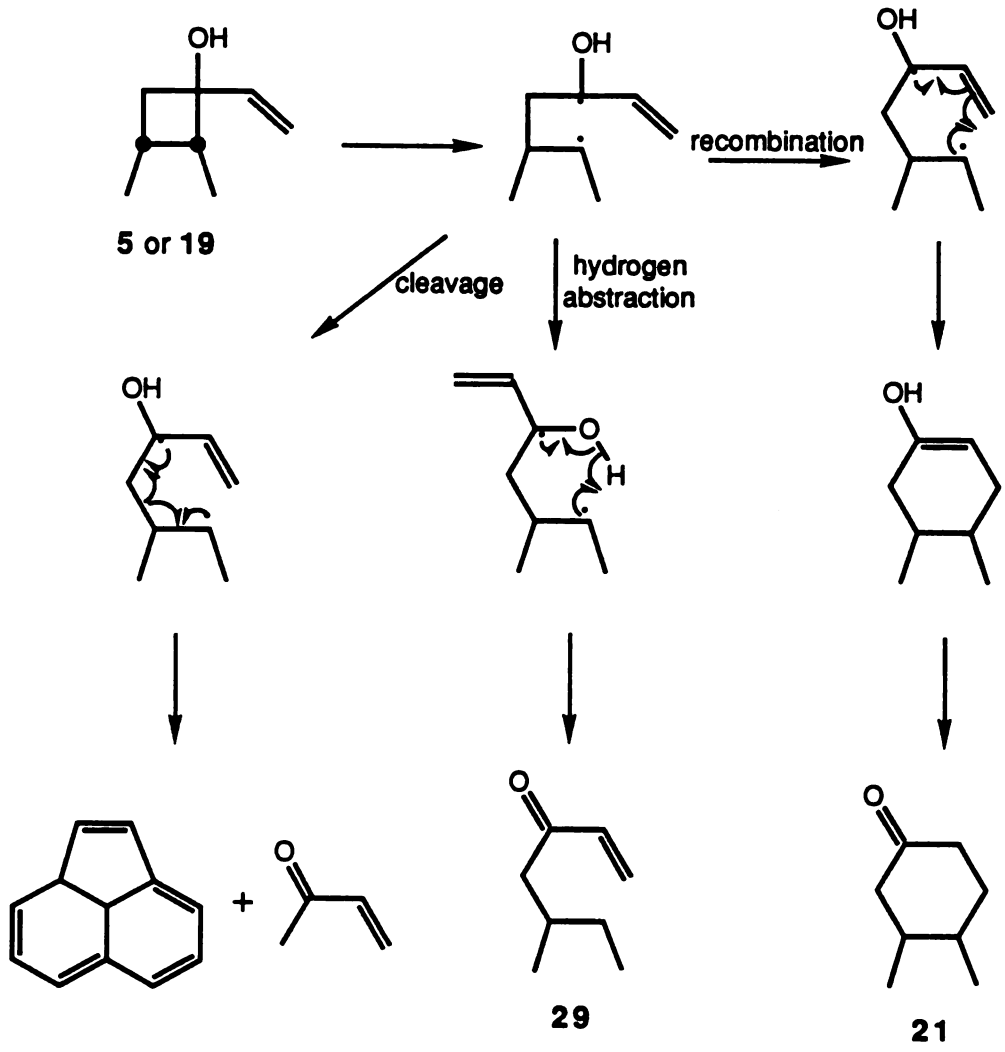


Figure 23. Diradical Intermediates.

MECHANISTIC INVESTIGATION

Rationalization of the thermoyses results by postulation of a diradical intermediate is tempting. Although proving the existence of such intermediates in these flash thermolyses will be difficult, this may be possible in the solution thermolyses. Addition of known radical trapping agents to reaction mixture (such as tributyltin hydride) may may lead to new products indicative of radical intermediates. Alternatively, a structural subunit known to give a characteristic transformation when in proximity to a radical site might be incorporated into the substrate undergoing pyrolysis. An example of this approach would be the conversion of the vinyl group in **5** or **19** to a cyclopropyl group. If a 1,4 diradical species was formed from these substrates, a cyclopropylmethyl radical would then be present. This would create a cyclobutyl-cyclopropylmethyl-homoallyl radical manifold, which might give rise to rearranged products indicative of radical intermediates.

Derivative Synthesis and Thermolysis

The initial strategy in synthesizing derivatives of the parent cyclobutane system was to attempt selective suppression of the various rearrangement pathways available to the intermediate 1,4-diradical. The first implementation of this idea was to convert both the exo vinylcyclobutanol **19** and the endo vinylcyclobutanol **5** into their corresponding acetates, the exo vinylcyclobutyl acetate **30** and the endo vinylcyclobutyl acetate **31** (see Figure 24). With non-abstractable groups present on the oxygen, we anticipated that upon thermolysis these derivatives would undergo only the recombination mode of rearrangement to give the cyclohexyl enol acetate **32**. Accordingly, **30** and **31** were synthesized in 89% and 87% yield by

acetylation of **19** and **5**, respectively. Unfortunately, solution thermolysis under the standard conditions of refluxing o-xylene for 48 hours of both **30** and **31** gave only recovered starting material, with no observed **32** or epimerization to the isomeric acetate. Interestingly, **32** was produced in 41% yield by use of our flash thermolysis system with **30** at 250 °C. The structure of **32** was confirmed by examination of the ^1H NMR spectrum and by acidic hydrolysis to the previously observed cyclohexanone **21**.

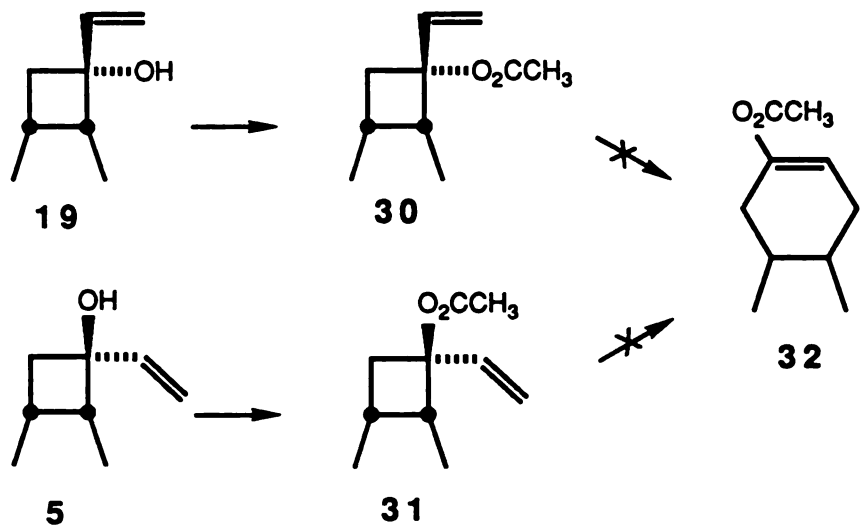


Figure 24. Synthesis and Thermolysis of Exo and Endo Vinylclobutyl Acetates **30** and **31**.

The exo methylcyclobutanol **33** was next synthesized in 81% yield by direct addition of methyllithium to the cyclobutanone **2** (see Figure 25). With the vinyl group absent, the only mode of rearrangement for the diradical is the hydrogen abstraction pathway. Once again, however, thermolysis gave only recovered starting material and no observed methyl ketone **34**.

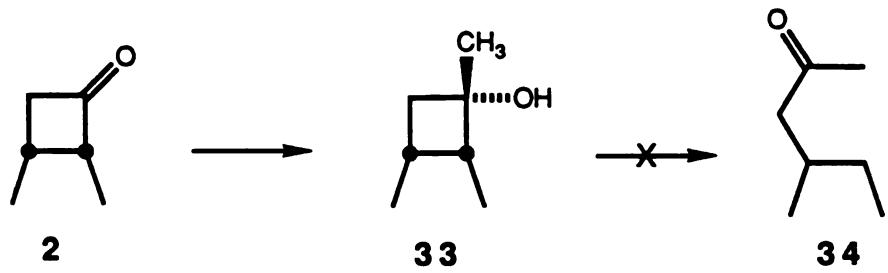


Figure 25. Synthesis and Thermolysis of Exo Methylcyclobutanol **34**.

The next synthetic target was the endo vinylcyclobutane **35** (see Figure 26). The proposed approach to this compound involved reduction of the allylic alcohol **9** by catalytic hydrogenation from the less hindered exo face to give primary alcohol **36**, followed by dehydration to give **35**. Thermolysis of **35**, with only the recombination mode of rearrangement available, should give the cyclohexene **37**.

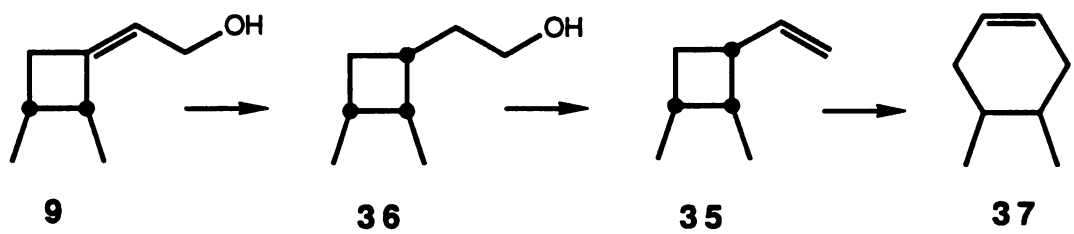


Figure 26. Synthetic Approach to Endo Vinylcyclobutane **35**.

In the event, catalytic hydrogenation of **9** gave alcohol **36** in essentially quantitative yield (see Figure 27). Mesylation of **36** proceeded in 90% to give **38**. Treatment with DBU surprisingly gave no reaction, even under forcing conditions. Changing the base to potassium t-butoxide gave roughly equal amounts of the t-butoxy

ether **39** and the previously observed ethylidene derivative **3** as a 1:1 mixture (^{1}H NMR) of stereoisomers in 78% yield. In a modification of this elimination strategy, the xanthate ester **40** was synthesized in 89% yield by sequential treatment of alcohol **36** with sodium hydride, carbon disulfide, and methyl iodide. Flash thermolysis of **40** at 250 °C or in refluxing o-dichlorobenzene resulted in complete destruction of the starting material with no observable products. No further attempts to synthesize **35** have been made.

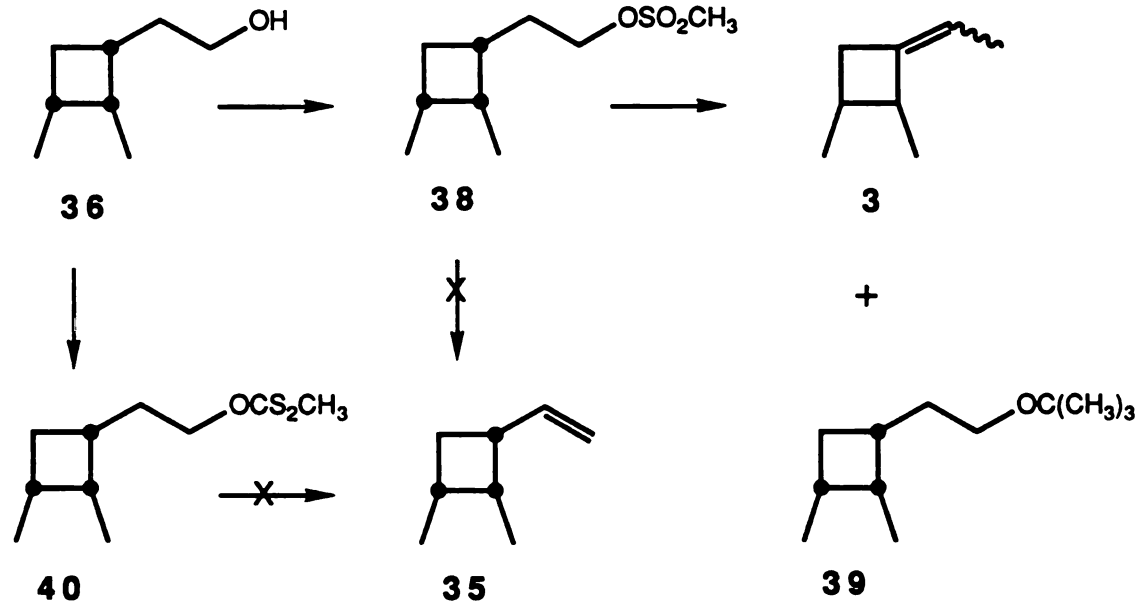


Figure 27. Attempted Synthesis of Endo Vinylcyclobutane **35**.

The lack of observed rearrangement products in the solution thermolyses of the vinylcyclobutyl acetates **30**, **31**, and the exo methylcyclobutanol **33** may be due to a destabilizing influence of the substituents present in these compounds on the formation of the 1,4-diradical, relative to the vinylcyclobutanols **19** and **5**. The acetoxy groups are less effective at stabilizing radicals than the hydroxyl and

vinyl groups. For instance, an allylic radical is generally estimated to be around 10 kcal/mole[9] more stable than the analogous alkyl radical. The important structural dependence of this rearrangement forced consideration of only synthetic targets whose radical stabilizing characteristics upon thermolysis would closely resemble that of **19** and **5**.

The next synthetic targets were the exo vinyl t-butyldimethylsilyl ether **41** and the exo phenylcyclobutanol **44** (see Figure 28). The siloxy group in **41** should have similar radical stabilizing properties as the hydroxyl group, but will allow only the recombination mode of rearrangement to the silyl enol ether **43**. Likewise, the phenyl group should approximate the vinyl group in radical stabilizing ability, but only the hydrogen abstraction mode of rearrangement should be available, leading to phenyl ketone **44**. Synthesis of both targets was straightforward. Silylation of exo vinylcyclobutanol **19** with t-butyldimethylsilyl chloride gave the silyl ether **41** in 92% yield. Addition of phenyllithium to cyclobutanone **2** gave the exo phenylcyclobutanol **42** in 78% yield. With these two compounds in hand, examination of their thermolysis behavior was now possible.

Standard thermolysis of **41** gave a 3:1 mixture of cyclohexanone **21** and recovered starting material. Although the expected silyl enol ether **43** was not observed, it is not unreasonable to assume that **43** was formed, but under the reaction conditions was converted to **21**. These results indicate that selective suppression of the hydrogen abstraction process is possible, while allowing the recombination process to occur unimpeded. The recovered starting material, however, emphasizes the critical structural dependence of this rearrangement, as both **19** or **5** are completely consumed under these reaction conditions. Thermolysis of **42** was unfortunately not as informative, as only recovered starting material was found, with no evidence of phenyl ketone **44**. This result is somewhat surprising, considering the known radical stabilizing properties of the phenyl group. One possible explanation for this lack of reactivity is that the phenyl group is unable to attain a low energy conformation where the p orbitals present in the aromatic ring can effectively overlap with the incipient radical orbital.

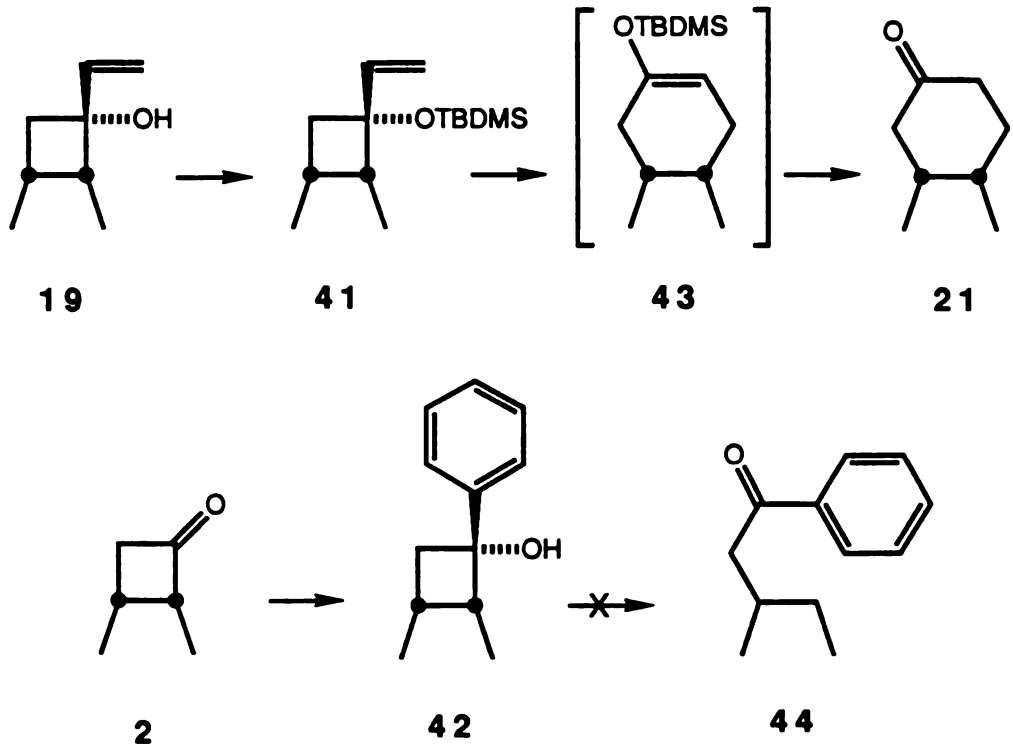


Figure 28. Synthesis and Thermolysis of Exo Vinyl Silyl Ether **41** and Exo Phenylcyclobutanol **42**.

The final structural modification was introduction of a cyclopropyl group into the latent 1,4-diradical system (see Figure 29). Addition of cyclopropyl magnesium bromide to cyclobutanone **2** gave the cyclopropylcyclobutanol **45** in 41% yield, along with recovered starting material. If thermolysis of this compound forms an intermediate diradical, products derived from cleavage and rearrangement of the cyclopropylcarbinyl radical may be observed. The possibility of formation of the cycloheptanone **46** was of particular interest. This could arise by rearrangement of the methylcyclopropyl radical to the homoallyl radical, followed by capture of the benzylic radical. In addition, formation of cyclopropyl ketone **47** via the hydrogen abstraction process may also occur. In the event, thermolysis of **45** primarily recovered starting material

and a small amount (<10%) of unidentified side products. No further attempts to demonstrate the existence of an intermediate diradical by internal diversion through structural modification have been conducted.

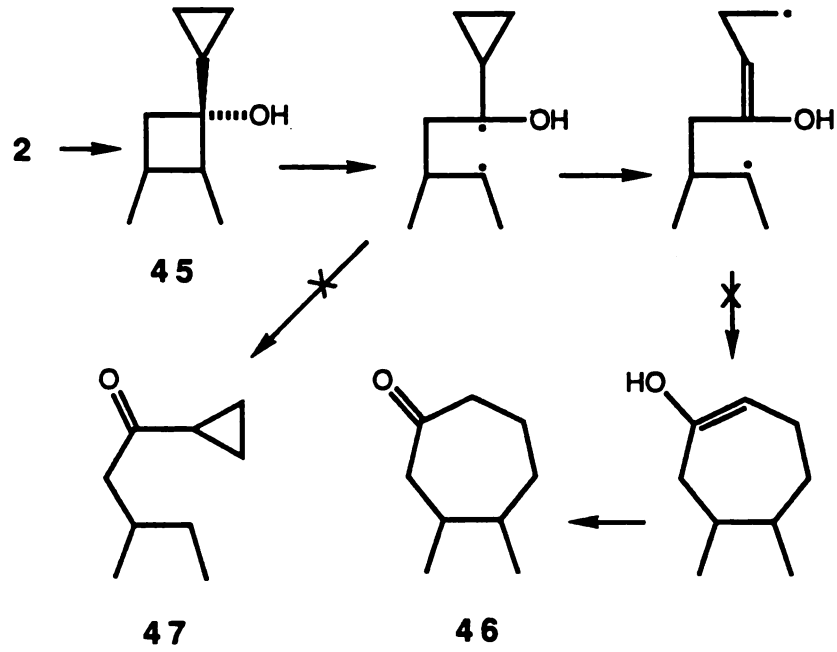


Figure 29. Synthesis and Thermolysis of Cyclopropylcyclobutanol **45**.

Trapping Studies

Failure of structural modifications to yield conclusive evidence regarding the existence of the proposed 1,4-diradical prompted the development of an alternative approach to capture this elusive intermediate. Specifically, a hydrogen atom donor, known to react rapidly with radical species, might intercept the diradical intermediate and yield products characteristic of that species. Towards this goal, a number of solution thermolyses were performed

under standard reaction conditions with addition of tributyltin hydride as a hydrogen atom donor. The results of these experiments summarized in Table 3.

Table 3. Thermolysis of Cyclobutane Derivatives with added Tributyltin hydride. Products include cyclohexanone **21** (CH), acenaphthylene (ACE), starting material (SM), and vinyl ketone **29** (VK). NR indicates no reaction.

Entry	Compound	Equiv. nBu_3SnH	Time (hrs)	Yield (%)	Products
1	**19**	2.5	20.5	63	CH/ACE (5:1)
2	**19**	4.6	16.0	64	CH/ACE (6:1)
3	**41**	5.0	16.0	81	CH/ACE (2:1)
4	**30**	4.7	28.5	NR	-
5	**45**	5.0	28.5	NR	-
6	**19**	5.2	1.0	79	CH/ACE/SM (20:6:1)
7	**41**	6.2	1.0	72	CH/ACE/SM (5:1:1)
8	**19**	0.0	1.0	57	CH/VK/SM (4:1:30)
9	**42**	2.3	1.0	NR	-

Entries 1 and 2 show that the thermolysis of exo vinylcyclobutanol **19** with added tributyltin hydride gives different product ratios than those obtained without the hydrogen atom donor. Vinyl ketone **29** is no longer formed, and instead only cyclohexanone **21** and acenaphthylene are observed. This is also the case with the exo vinyl silyl ether **41** (entry 3). These are the first cases where acenaphthylene has been observed during the lower temperature solution thermolyses of our cyclobutane derivatives. Thermolysis of exo vinyl acetate **30** or cyclopropylcyclobutanol **45** (entries 6 and 7) under these conditions gave no reaction, identical to their failure to react in the absence tributyltin hydride. Further experiments with **19** and **41** (entries 6 and 7) show that this alternative reaction

pathway occurs at dramatically reduced reaction times. The control experiment using **19** with no added tributyltin hydride (entry 8) confirms that these rearrangements are occurring at an accelerated rate and are giving different product ratios than those previously observed. Entry 9 shows that the exo phenylcyclobutanol **42** does not react under these modified rearrangement conditions, paralleling its' behavior in the absence of tributyltin hydride.

The results of these tributyltin hydride radical trapping experiments are difficult to interpret. The tributyltin hydride appears to be accelerating the reaction of **19** and **41** in a manner slightly different from the previously observed rearrangements, but a rationalization for this acceleration is not apparent. One aspect of these results is irrefutable: no products corresponding to a hydrogen atom trapped intermediate 1,4-diradical has been observed in any of these reactions. Thus, the goal of proving the intermediacy of the diradical has not been achieved.

CONCLUSION

This dissertation describes the synthesis of exo- and endo vinylcyclobutanols **19** and **5**, and efforts to effect a divinylcyclobutane oxy-Cope rearrangement of the latter to generate a unusually bridged acenaphthylene system. Central to this proposal was the idea that the strain energy inherent in the four-membered ring would help to overcome the energy cost of disrupting aromatic resonance as this reaction proceeded to rearranged products.

Calculations and models supported the expectation that **5** could achieve the correct geometry for reaction, and that the rearranged product was thermodynamically more stable. Successful application of this proposal would be useful both as a addition to existing Cope rearrangement synthetic methodology and as an entry to the study of novel bridged naphthalenes.

Despite these expectations, no Cope rearrangement products were isolated or observed under the wide variety of reaction conditions applied. The key tetrasubstituted cyclobutane bond, with certain substitution patterns, appears to be susceptible to a number of alternative transformations, whose activation energies may be lower than that of the desired Cope rearrangement pathway. The anionic oxy-Cope gave cyclohexanone **21** by a formal [1,3] shift, which may proceed by heterolytic fragmentation of the cyclobutane bond to the benzylic anion followed by Michael reaction. The palladium catalyzed Cope gave cyclopentanones **25-28** by migration of the cyclobutane bond to an electrophilic center. The thermal Cope gave cyclohexanone **21**, vinyl ketone **29**, and acenaphthylene, presumably by homolytic cleavage of the cyclobutane bond to a diradical, followed by recombination (to give **21**), hydrogen abstraction (to give **29**), and Norrish type II cleavage (to give acenaphthylene).

The structural restrictions on homolysis to this presumed diradical were studied extensively, and appear to be quite severe. Products characteristic of the diradical appear to be formed only when the substituents on the key cyclobutane bond are good radical

stabilizers, although this was not invariably the case. There may also be a steric and/or stereoelectronic effect on the formation of this reactive intermediate.

Attempts to prove the existence of the diradical by structural modification or addition of radical traps were unsuccessful. This was perhaps not unexpected, considering the undoubtedly short lifetime of this intermediate. During the course of these investigations a mechanistically unusual transformation was uncovered involving tributyltin hydride; future investigation into this reaction may shed light on the critical structural dependency on formation of the diradical during the thermolysis experiments.

Despite the failure to induce the desired Cope rearrangement, the results of this dissertation should be useful to future investigators in this field. The divinylcyclobutane Cope rearrangement has been shown to have limitations under certain substitution patterns, with diradical formation via homolytic cyclobutane bond scission appearing to be the primary alternative pathway in the cases studied. In addition, if the diradical could be efficiently and reliably formed, it could be used as a reactive intermediate to effect further synthetic transformations.

EXPERIMENTAL

General. All reaction sensitive to oxygen or moisture were performed using oven dried glassware under an argon atmosphere. ^1H spectra were obtained on a Varian VXR 300 (300 MHz), Varian VXR (500 MHz), or Bruker 250 (250 MHz) spectrometer. Chemical shifts for proton resonances are reported in parts per million (δ) downfield from tetramethylsilane (δ = 0 ppm) or residual chloroform (δ = 7.24 ppm) as an internal standard. Signal patterns are indicated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br s, broad singlet; overlapping m, overlapping multiplet. Coupling constants (J) are given in hertz. ^{13}C NMR spectra were obtained on a Varian VXR 300 (75 MHz) or Bruker 250 (69.8 MHz). Chemical shifts for carbon resonances are reported in parts per million (δ) downfield from the deuterated solvent signal (δ = 77.0 ppm). Infrared (IR) spectra were obtained on a Nicolet PC/IR Fourier transform spectrometer system equipped with a Nicolet IR/42 optical bench. Mass spectra (MS) were obtained on a Finnegan 4000 mass spectrometer equipped with a Incos 4021 data system. Melting points were measured in glass capillary tubes on a Hoover-Thomas melting point apparatus and are uncorrected. Thin layer chromatography (TLC) analyses were performed using Merck aluminum-backed F_{254} silica gel plates, using ultraviolet light and either 30% aqueous sulfuric acid or ammonium molybdate in 10% aqueous sulfuric acid as a visualization reagent. Flash chromatography was performed using Merck Silica Gel 60 (230-400 mesh, ASTM, column diameter 10-40 mm) according to the method of Still.[35] Elemental analyses were conducted by Spang Microanalytical Laboratory, Eagle Harbor, MI. All reagents were obtained from commercial suppliers and used without purification, unless otherwise indicated. Diethyl ether and tetrahydrofuran were freshly distilled under nitrogen from sodium/benzophenone ketyl.

Toluene, o-xylene, benzene, hexane, methylene chloride, hexamethylphosphoramide, dimethylformamide, triethylamine, diisopropylamine, and dimethylsulfoxide were freshly distilled under argon or nitrogen from calcium hydride. Sodium iodide was dried by heating in a round bottomed flask (ca. 150 °C, 0.1 Torr) for 4-6 h.

Dichlorocyclobutanone (1). Method A: To a 500 mL 3-neck round bottomed flask equipped with a reflux condenser, addition funnel, Argon inlet, and rubber septa was charged acenaphthylene (7.00 g, 46.0 mmol), zinc dust (10.10 g, 154.5 mmol), and ether (200 mL). The entire apparatus was suspended approximately 1 cm from the bottom of a laboratory ultrasonic cleaner (Branson 2200) and immersed in 0 °C water. Sonication was initiated, and to the agitated solution was added over 1 hr. a solution of trichloroacetylchloride (17.0 mL, 152.3 mmol) in ether (100 mL). The solution was sonicated an additional 3 hrs., filtered through a Celite pad, then washed with 1N HCl, water, sat'd $NaHCO_3$, and brine to give a crude dark brown oil, which was used directly without further purification in the next step.

Method B: A 500 mL 3-neck round bottomed flask was equipped with a reflux condenser, addition funnel, Argon inlet, and an ultrasonic processor (S & M, Inc. VC500, 500W, 20 kHz; 40% continuous output) fitted with a 1/2" extended horn was charged and the reaction run and worked up as above. Again, the crude product was used directly for the next step, but a small amount was chromatographed (2:1 hexanes to ether) to give dichlorocyclobutanone 1, which was crystallized from hexanes to give off white crystals, mp115 °C: ^1H NMR (250 MHz, $CDCl_3$) δ 7.8-7.2 (m, 6 H), 5.51 (d, J = 7.3 Hz, 1 H), 4.91 (d, J = 7.3 Hz, 1 H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 191.5, 139.3, 138.5, 136.2, 131.8, 128.4, 128.1, 125.3, 124.8, 124.3, 121.1, 87.0, 67.1, 57.9; IR(CH_2Cl_2) 1807 cm^{-1}; MS (EI) m/z (rel. int.) 262 (3), 199 (100), 163 (31), 152 (29).

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Cyclobutanone (2). To a 0 °C solution of crude dichlorocyclobutanone **1** (11.4 g 43.4 mmol) in ammonium chloride saturated methanol (200 mL) was added zinc powder (11.0 g, 168.3 mmol). The solution was stirred 30 min. at 0 °C, 30 min. at 25 °C, and refluxed 8 hrs. The solution was filtered through a Celite pad, the solvent removed in vacuo, and the brownish residue taken up in ether. The organic phase was washed with 1N HCl, water, sat'd $NaHCO_3$, and brine, then dried over sodium sulfate. The solvent was removed in vacuo, and the crude material chromatographed (silica gel, 2:1 hexanes to ether) to yield cyclobutanone **2** (6.69 g, 84% from acenaphthylene), which was crystallized from hexanes to give off-white needles, mp 78 °C: ^1H NMR (250 MHz, $CDCl_3$) δ 7.8-7.2 (m, 6 H), 5.18 (m, 1 H), 4.25 (m, 1 H), 3.61 (ddd, J = 18.3, 9.5, 3.7 Hz, 1 H), 2.83 (ddd, J = 18.3, 4.4, 3.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.31, 146.23, 139.13, 137.91, 131.91, 128.53, 128.25, 124.09, 123.80, 120.60, 120.15, 71.94, 52.61, 34.63; IR (CH_2Cl_2) 1780 cm^{-1}; MS (EI) m/z (rel. int.) 194 (7), 165 (28), 154 (100).

Ethylidene Cyclobutane (3). To a 25 °C solution of ethyltriphenylphosphonium bromide (6.40 g, 17.2 mmol) in toluene (10.0 mL) was added 0.91 M potassium t-amyloxide in toluene (19.0 mL, 17.3 mmol). The solution was refluxed 45 min., then a solution of cyclobutanone **2** (0.50 g, 2.57 mmol) in toluene (15.0 mL) was added in one portion. The solution was refluxed 1 hr., then cooled over 15 min. to 25 °C. The solution was washed with water, sat'd $NaHCO_3$, and brine. The organic phase was dried over sodium sulfate, then removed in vacuo to give a crude product, which was chromatographed (silica gel, hexanes) to yield ethylidene cyclobutane **3** as a yellow oil (0.20 g, 37%) in a 1:1 mixture (^1H NMR) of inseparable stereoisomers: ^1H NMR (250 MHz, $CDCl_3$) δ 7.8-7.2 (m, 12 H), 5.42 (m, 1 H), 5.20 (m, 1 H), 4.88 (m, 1 H), 4.74 (m, 1 H), 4.19 (m, 2 H), 3.26 (m, 2 H), 2.45 (m, 2 H), 1.76 (m, 3 H), 1.41 (m, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.78, 147.12, 146.10, 141.06, 139.93, 139.91, 132.17, 132.08, 128.15, 128.00, 127.95, 123.39, 122.83, 122.79, 122.72, 122.68, 122.63, 119.97, 119.11, 119.04, 119.00,

118.73, 118.69, 118.52, 53.48, 52.34, 40.32, 40.20, 36.95, 34.95, 13.94, 13.28; MS (EI) m/z (rel. int.) 206(6), 191(5), 152(6), 40 (100).

Spiro Ethylidene Oxide (4). To a 25 °C solution of alkenes 3 (124.3 mg, 0.60 mmol) in methylene chloride (2.00 mL) was added over 1 hr. a 25 °C solution of metachloroperbenzoic acid (129.0 mg, 0.75 mmol) in methylene chloride (5.00 mL). After addition was complete, the solution was washed with sat'd sodium bisulfite, sat'd $NaHCO_3$, and brine. The organic phase was dried over magnesium sulfate and the solvent removed in vacuo to yield spiro ethylidene oxides **4** as a yellow oil (133.6 mg, 99%) in a 10:10:1:1 mixture (^1H NMR) of stereoisomers : ^1H NMR (250 MHz, $CDCl_3$) δ 7.8-7.2 Hz (m, 6 H), 4.55 (d, J = 6.5 Hz, 1 H), 4.40 (d, J = 6.5 Hz, 1 H), 4.1 (overlapping m, 1 H), 2.8 (overlapping m, 2 H), 2.2 (overlapping m, 1 H), 1.38 (d, J = 5.5 Hz, 3 H), 1.21 (d, J = 5.5, 3 H), 1.15 (d, J = 5.5 Hz, 3 H), 0.77 (d, J = 5.5 Hz, 3 H); MS (EI) m/z (rel. int.) 222 (8), 207 (2), 193 (1), 178 (17), 165 (100), 152 (64).

Endo Vinylcyclobutanol (5). To a 25 °C solution of the major spiro epoxy mesylate isomer **12a** (36.0 mg, 0.99 mmol) in acetone (25.0 mL) was added sodium iodide (2.00 g, 13.34 mmol). The solution was refluxed 72 hrs., then the solvent removed in vacuo. The solid residue was taken up in ether, washed with water, and dried over sodium sulfate. The solvent was removed in vacuo to yield a crude product which was chromatographed (silica gel, 2:1 hexanes to ether) to yield spiro epoxy iodide **15** (45.0 mg, 13%), starting spiro epoxy mesylate **12a** (38.0 mg, 11%), and endo vinylcyclobutanol **5** (89.2 mg, 41%) as an off white solid, mp 87 °C: ^1H NMR (250 MHz, $CDCl_3$) δ 7.8-7.2 (m, 6 H), 5.43 (dd, J = 17.4, 10.7 Hz, 1 H), 4.92 (dd, J = 17.4, 1.2 Hz, 1 H), 4.72 (dd, J = 10.7, 1.2 Hz, 1 H), 4.20 (m, 2 H), 2.63 (ddd, J = 12.7, 9.2, 2.7 Hz, 1 H), 2.42 (br s, 1 H), 2.09 (dd, J = 12.7, 5.2 Hz, 1 H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 148.7, 143.0, 141.5, 140.2, 131.9, 127.9, 127.8, 123.2, 122.8, 121.4, 118.9, 112.3, 78.3, 58.6, 41.7, 37.1; IR (CH_2Cl_2) 3685, 3056, 1605, 1179 cm^-

^{1}; MS (EI) m/z (rel. int.) 222 (3), 205 (1), 193 (17), 178 (7), 165 (36), 152 (53), 55 (100). Thermolysis: A solution of endo vinylcyclobutanol **5** (44.2 mg, 0.20 mmol) in o-xylene (15.0 mL) was refluxed 48 hrs., the solvent removed, and the residue chromatographed (silica gel, 2:1 hexanes to ether) to yield cyclohexanone **21** (18.9 mg, 43%) and vinyl ketone **29** (12.0 mg, 27%).

Diene (6). To a 0 °C 1 M solution (5:1 hexanes to ether) of lithium diisopropylamide (0.30 mL, 0.30 mmol) was added in one portion a solution of the major isomers of epoxide **4** (50.2 mg, 0.23 mmol) in ether (3.00 mL). The solution was stirred 30 min., then washed with 1N HCl, water, sat'd $NaHCO_3$, and brine. The organic phase was dried over magnesium sulfate, and the solvent removed in vacuo to give a crude product which was chromatographed (silica gel, methylene chloride) to yield diene **6** as a pale yellow oil (41.7 mg, 83%): ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.8-7.3 (m , 6 H), 7.08 (s, 1 H), 5.69 (s, 1 H), 5.61 (s, 1 H), 4.92 (q, J = 8.3 Hz, 1 H), 1.85 (br s, 1 H), 1.49 (d, J = 8.3 Hz, 3 H), ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 147.8, 140.8, 139.0, 129.0, 128.2, 127.8, 127.5, 127.0, 125.3, 124.4, 123.8, 112.7, 77.5, 77.0, 76.5, 69.7, 23.0; MS (EI) m/z (rel. int.) 222 (4), 178 (9), 152 (72), 43 (100).

Diels-Alder Cycloadduct (7). A solution of diene **6** (15.0 mg, 0.07 mmol) and dimethylacetylene dicarboxylate (0.02 mL, 0.16 mmol) was refluxed 44 hrs. The crude product was chromatographed (silica gel, 4:1 hexanes to ether) to yield Diels-Alder cycloadduct **7** (17.3 mg, 70%): ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.8-7.3 (m, 6 H), 5.48 (q, J = 8.3 Hz, 1 H), 4.08 (dd, J = 7.9, 5.0 Hz, 1 H), 3.92 (s, 3 H), 3.63 (s, 3 H), 3.32 (dd, J = 17.5, 7.9 Hz, 1 H), 2.30 (br s, 1 H), 1.44 (d, J = 8.3 Hz, 3 H); MS (EI) m/z (rel. int.) 364 (3), 332 (8), 315 (6), 304 (26), 287 (12), 273 (23), 261 (30), 229 (93), 217 (41), 202 (100).

Vinyl Ester (8). To a 25 °C solution of sodium hydride (1.20 g, 48.5 mmol) in benzene (50.0 mL) was added over 25 min. a solution of triethylphosphonoacetate (10.0 mL, 50.4 mmol) in benzene (25.0 mL). The solution was stirred 20 min., then a 25 °C solution of cyclobutanone **2** (7.30 g, 37.6 mmol) in benzene (50.0 mL) was added over 1 hr. The solution was stirred an additional 45 min., then quenched with 1N HCl. The organic layer was washed with water, sat'd $NaHCO_3$, and brine, then dried over sodium sulfate. The solvent was removed in vacuo, and the crude product chromatographed (silica gel, 2:1 hexanes to ether) to yield vinyl esters **8** as a pale yellow oil (7.17 g, 72%) in a 10:1 mixture (^1H NMR) of stereoisomers. Rechromatography (silica gel, 4:1 hexanes to ether) allowed for isolation of each isomer, both a pale yellow oils: Major isomer (**8a**): ^1H NMR (250 MHz, $CDCl_3$) δ 7.8-7.2 (m, 6 H), 5.83 (dd, J = 4.6, 2.8 Hz, 1 H), 4.74 (br s, 1 H), 4.16 (m, 1 H), 4.00 (q, J = 7.0 Hz, 2 H), 3.65 (dddd, J = 18.9, 9.2, 2.8, 1.2 Hz, 1 H), 2.91 (ddd, J = 18.9, 4.6, 4.0 Hz, 1 H), 1.12 (t, J = 7.0 Hz, 3 H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 166.3, 166.2, 147.4, 144.1, 139.7, 132.0, 128.2, 123.6, 123.1, 119.4, 119.3, 115.1, 59.7, 54.3, 41.6, 39.7, 14.2; IR (CH_2Cl_2) 1709, 1265 cm^{-1}; MS (EI) m/z (rel. int.) 264 (39), 249 (2), 235 (16), 218 (24), 205 (6), 189 (57), 179 (24), 165 (19), 152 (100). Minor isomer (**8b**): ^1H NMR (250 MHz, $CDCl_3$) δ 7.8-7.2 (m, 6 H), 5.62 (dd, J = 4.3, 2.1 Hz, 1 H), 5.39 (br s, 1 H), 4.27 (q, overlapping m, 3 H), 3.36 (ddt, J = 9.0, 8.0, 2.1 Hz, 1 H), 2.64 (dm, J = 18.0 Hz, 1 H), 1.34 (t, J = 7.0 Hz, 3 H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 166.0, 165.0, 148.7, 144.5, 139.6, 132.0, 128.4, 127.8, 123.5, 123.1, 121.9, 118.8, 114.1, 59.8, 55.4, 41.2, 38.8, 14.4; IR (CH_2Cl_2) 1711, 1201, 1097, 787 cm^{-1}; MS (EI) m/z (rel. int.) 264 (30), 249 (1), 235 (10), 218 (16), 205 (4), 189 (34), 179 (12), 165 (27), 152 (100).

Allylic Alcohol (9). To a 0 °C 1N solution of diisobutyl aluminum hydride in hexane (15.0 mL, 15.0 mmol) was added over 30 min. a 25 °C solution of major vinyl ester isomer **8a** (3.00 g, 11.4 mmol) in ether (25.0 mL). The solution was stirred 30 min. at 0 °C, then 20 hrs at 25 °C. The reaction was quenched with 1N HCl, and

the organic phase washed with water, sat'd $NaHCO_3$, and brine, then dried over sodium sulfate. The solvent was removed in vacuo, and the crude product chromatographed (silica gel, 2:1 hexanes to ether) to yield unreacted vinyl ester **8a** (0.97 g, 32%) and allylic alcohol **9** (1.54 g, 61%), which was crystallized from hexanes to give off-white needles, mp 75-76 °C: ^1H NMR (250 MHz, $CDCl_3$) δ 7.8-7.2 (m, 6 H), 5.41 (m, 1 H), 4.62 (br s, 1 H), 4.05 (m, 1 H), 3.67 (t, J = 5.5 Hz, 2 H), 3.17 (ddt, J = 16.5, 9.5, 1.4 Hz, 1 H), 2.37 (ddt, J = 16.5, 5.8, 3.1 Hz, 1 H), 1.82 (br s, 1 H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 148.1, 144.9, 139.7, 131.9, 128.1, 128.0, 123.0, 122.9, 122.5, 119.5, 119.1, 118.9, 59.2, 53.4, 40.5, 35.2; IR (CH_2Cl_2) 3605, 3055, 2927, 2876, 1603 cm^{-1}; MS (EI) m/z (rel. int.) 222 (18), 203 (50), 191 (26), 178 (33), 165 (20), 152 (100).

Spiro Epoxy Alcohol (10). To a 25 °C solution of allylic alcohol **9** (876 mg, 3.94 mmol) in methylene chloride (10.0 mL) was added over 30 min. a 25 °C solution of metachloroperbenzoic acid (880 mg, 5.11 mmol) in methylene chloride (15.0 mL). The solution was stirred 5 min., then washed with sat'd sodium bisulfite and brine, and the organic phase dried over sodium sulfate. The solvent was removed in vacuo to yield spiro epoxy alcohol **10** (940 mg, 99%) as a 2:1 mixture (^1H NMR) of stereoisomers. Chromatography (silica gel, 2:1 ether to hexanes) yielded both isomers as off white pastes: Major isomer (10a): ^1H NMR (250 MHz, $CDCl_3$) δ 7.8-7.2 (m, 6 H), 4.47 (br d, J = 7.0 Hz, 1 H), 4.21 (m, 1 H), 3.40 (br d, J = 12.8 Hz, 1 H), 3.10 (m, 1 H), 2.95 (m, 2 H), 2.24 (ddd, J = 14.0, 4.0, 1.5 Hz, 1 H), 2.10 (br s, 1 H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 147.1, 143.2, 143.1, 131.8, 128.1, 128.0, 123.5, 123.3, 119.7, 119.6, 67.7, 61.2, 58.6, 54.1, 37.7, 34.3; IR (CH_2Cl_2) 3601, 3055, 2938, 1605, 1493 cm^{-1}; MS (EI) m/z (rel. int.) 238(10), 219(3), 207(8), 191(5), 178(27), 165(85), 152(100); Minor isomer (10b): ^1H NMR (250 MHz, $CDCl_3$) δ 7.8-7.2 (m, 6 H), 4.50 (d, J = 5.8 Hz, 1 H), 3.98 (dt, J = 8.8, 5.8 Hz, 1 H), 3.75 (dd, J = 12.2, 3.5 Hz, 1 H), 3.49 (dd, J = 12.2, 5.2 Hz, 1 H), 3.25 (dd, J = 5.2, 3.5 Hz, 1 H), 2.97 (ddd, J = 14.0, 9.0, 1.5 Hz, 1 H), 2.13 (dd, J = 14.0, 4.9 Hz, 1 H), 2.37 (br s, 1 H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 148.3, 141.7, 140.0,

132.1, 128.0, 127.9, 123.4, 123.1, 121.4, 118.6, 64.1, 61.6, 61.2, 53.1, 37.7, 35.5; IR (CH_2Cl_2) 3698, 3601, 3057, 2940, 1604 cm^{-1}; MS (EI) m/z (rel. int.) 238(23), 219(7), 207(27), 178(33), 165(93), 152(100).

Spiro Epoxy Mesylate (12). To a 0 °C solution of a 2:1 mixture of epoxy alcohols **10a/10b** (529 mg, 2.21 mmol) in methylene chloride (10.0 mL) was added triethylamine (0.45 mL, 3.23 mmol) and methanesulfonyl chloride (0.20 mL, 2.58 mmol). The solution was stirred 30 min., then quenched with 1N HCl. The organic phase was washed with water, sat'd $NaHCO_3$, and brine, then dried over sodium sulfate. The solvent was removed in vacuo to yield spiro epoxy mesylates **12** (689 mg, 98%) as a 2:1 mixture (^1H NMR) of stereoisomers. Chromatography (silica gel, 2:1 ether to hexanes) yielded both isomers as unstable pale yellow oils which were used immediately in subsequent steps: Major isomer (12a): ^1H NMR (250 MHz, $CDCl_3$) δ 7.8-7.2 (m, 6 H), 4.46 (d, J = 7.0 Hz, 1 H), 4.19 (m, 1 H), 3.89 (dd, J = 11.9, 3.7 Hz, 1 H), 3.68 (dd, J = 11.9, 7.0 Hz, 1 H), 3.01 (m, 2 H), 2.60 (s, 3 H), 2.22 (ddd, J = 13.9, 3.7, 1.5 Hz, 1 H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 146.6, 142.6, 139.4, 131.9, 128.1, 123.8, 123.5, 120.0, 119.6, 68.9, 68.1, 67.7, 54.8, 53.9, 37.6, 33.9; IR (CH_2Cl_2) 3059, 1604, 1361, 1178, 956 cm^{-1}; MS (EI) m/z (rel. int.) 316 (6), 219 (3), 207 (3), 191 (9), 178 (35), 165 (100), 152 (88). Minor isomer (12b): ^1H NMR (250 MHz, $CDCl_3$) δ 7.8-7.2 (m, 6 H), 4.60 (br d, J = 5.8 Hz, 1 H), 4.39 (dd, J = 11.9, 4.0 Hz, 1 H), 4.06 (m, 2 H), 3.45 (dd, J = 6.4, 4.3 Hz, 1 H), 3.04 (m, 1 H), 3.02 (overlapping s, 3 H), 2.19 (ddd, J = 14.0, 5.2, 1.2 Hz, 1 H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 147.8, 141.2, 139.8, 132.0, 128.0, 123.6, 123.2, 121.5, 118.7, 69.0, 57.5, 52.9, 37.6, 37.5, 34.9.

Spiro Cyclopropanol (13). Sodium Naphthalide: To a 25 °C solution of naphthalene (2.05 g, 16.0 mmol) in tetrahydrofuran (50.0 mL) was added sodium metal (0.34 g, 14.8 mmol). The solution turned dark green after 20 min., and was stirred a total of 2 hrs. before use in the next step.

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Reduction: To the 25 °C 0.30 M solution of sodium naphthalide (1.10 mL, 0.33 mmol) prepared above was added over 5 min. a 25 °C solution of major spiro epoxy mesylate isomer **12a** (16.6 mg, 0.05 mmol) in tetrahydrofuran (5.00 mL). The solution was stirred 2 min., then quenched with sat'd aqueous ammonium chloride solution. The organic phase was separated, and the aqueous phase extracted with ether. The combined organic phases were dried over sodium sulfate, the solvent removed in vacuo, and the crude product chromatographed (silica gel, 2:1 hexanes to ether) to yield spiro cyclopropanol **13** (4.9 mg, 42%): ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.8-7.2 (m, 6 H), 4.30 (m, 1 H), 4.02 (d, J = 5.8 Hz, 1 H), 3.53 (dd, J = 6.9, 3.4 Hz, 1 H), 2.97 (dd, J = 12.2, 9.6 Hz, 1 H), 1.87 (dd, J = 12.2, 4.4 Hz, 1 H), 0.76 (t, 6.9 Hz, 1 H), 0.09 (dd, J = 6.9, 3.4 Hz, 1 H); MS (EI) m/z (rel. int.) 222 (8), 203 (3), 193 (11), 178 (20), 165 (26), 152 (100).

Geminal Methyl Aldehyde (14). To a 25 °C 0.93 M solution (1:1 methanol to water) of potassium hydroxide (2.00 mL, 1.86 mmol) was added cyclopropanol **13** (17.6 mg, 0.079 mmol). After 2 hrs., no reaction was observable by TLC, so an additional 2.0 mLs of methanol was added to help increase solubility. After 6 hrs., there was still no observable reaction, and 2.0 mLs of tetrahydrofuran was added. The reaction was stirred an additional 14 hrs., then refluxed 8 hrs. The solution was cooled and poured into ether, then washed with 1N HCl, water, sat'd $NaHCO_3$, and brine. The solvent was dried over sodium sulfate, then removed in vacuo to give a crude product which was chromatographed (silica gel, 2:1 ether to hexanes) to yield geminal methyl aldehyde **14** (6.4 mg, 36%): ^{1}H NMR (250 MHz, $CDCl_3$) δ 9.40 (s, 1 H), 7.8-7.2 (m, 6 H), 4.47 (d, J = 7.9 Hz, 1 H), 4.08 (m, 1 H), 3.05 (ddd, J = 13.3, 10.8, 0.8 Hz, 1 H), 1.66 (dd, J = 13.3, 10.8 Hz, 1 H), 0.88 (s, 3 H); MS (EI) m/z (rel. int.) 222(5), 193(4), 178(9), 165(38), 152(100).

Exo Vinylcyclobutanol (19). To a 25 °C solution of magnesium turnings (1.70 g, 70.0 mmol) in tetrahydrofuran (5.0 mL) was added

over 1 hr. a 25 °C solution of vinyl bromide (5.00 mL, 70.9 mmol) in tetrahydrofuran (45.0 mL). The solution was stirred an additional 1 hr., then 5.00 mL (1.42 M, 7.09 mmol) was transferred by syringe into a separate reaction vessel. The solution was cooled to 0 °C, and a 25 °C solution of cyclobutanone **2** (840 mg, 4.32 mmol) in tetrahydrofuran (20.0 mL) was added over 50 min. The solution was stirred an additional 20 min., then quenched with 1N HCl. The organic phase was washed with water, sat'd $NaHCO_3$, and brine, then dried over sodium sulfate. The solvent was removed in vacuo, and the crude product chromatographed (silica gel, methylene chloride) to yield exo vinylcyclobutanol **15** (629 mg, 67 %), which was crystallized from hexanes to give off-white needles, mp= 82-83 °C: ^1H NMR (250 MHz, $CDCl_3$) δ 7.8-7.2 (m, 6 H), 6.37 (d, J = 17.7, 10.4 Hz, 1 H), 5.47 (d, J =17.7 Hz, 1 H), 5.23 (d, 10.4 Hz, 1 H), 4.41 (br d, J = 6.1 Hz, 1 H), 3.84 (dt, J = 8.5, 6.1 Hz, 1 H), 2.97 (ddd, J = 12.8, 8.5, 2.4 Hz, 1 H), 1.96 (br s, 1 H), 1.88 (dd, 12.8, 6.1 Hz, 1 H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 149.6, 143.0, 141.4, 140.6, 132.1, 127.9, 127.7, 123.7, 122.5, 122.2, 118.4, 111.3, 73.2, 57.4, 43.5, 34.9; IR (CH_2Cl_2) 3572, 3053, 1604, 1363, 1221, 1009 cm^{-1}; MS (EI) m/z (rel. int.) 222 (6), 167 (15) 152 (100). Thermolysis: A solution of exo vinylcyclobutanol **19** (0.296 g, 1.33 mmol) in o-xylene (20.0 mL) was refluxed 48 hrs., the solvent removed, and the residue chromatographed (silica gel, 2:1 hexanes to ether) to yield cyclohexanone **21** (0.135 g, 46%) and vinyl ketone **29** (0.075 g, 25%).

Cyclohexanone (21). To a -15 °C solution of potassium hydride (1.67 g, 40.00 mmol) in tetrahydrofuran (10.0 mL) was added hexamethylphosphoramide (8.00 mL, 46.00 mmol) and exo vinylcyclobutanol **19** (197 mg, 0.89 mmol). The solution was stirred 1 hr. at -15 °C, 1 hr. at 0 °C, and 30 min at 25 °C, then poured into a 0 °C solution of a 1:1 mixture of aqueous acetic acid and pentane. The aqueous layer was extracted with pentane, and the combined organic layers washed with water, sat'd $NaHCO_3$, and brine. The organic phase was dried over sodium sulfate, then the solvent removed in vacuo to yield a crude product which was chromatographed (silica

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gel, methylene chloride) to yield cyclohexanone **21** (111 mg, 56%), which was crystallized from hexanes to give clear colorless needles, mp 113 °C: ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.8-7.2 (m, 6 H), 4.04 (m, 1 H), 3.91 (m, 1 H), 2.91 (dd, J = 15.6, 6.4 Hz, 1 H), 2.66 (dd, J = 15.6, 7.0 Hz, 1 H), 2.5-2.3 (m, 1 H), 2.3-2.1 (m, 1 H), 2.1-1.9 (m, 2 H); ^{13}C NMR (62.5 MHZ, $CDCl_3$) δ 212.1, 131.3, 128.2, 123.2, 123.1, 119.1, 119.0, 43.0, 41.8, 40.9, 36.9, 26.5; IR (CH_2Cl_2) 3055, 1715, 1605, cm^{-1}; MS (EI) m/z (rel. int.) 222 (40), 193 (3), 179 (18), 165 (100), 152 (20).

Tetradeuteriocyclohexane (23a). To a solution of cyclohexanone **21** (12.6 mg, 0.06 mmol) in dimethylformamide (1.00 mL) was added triethylamine (0.05 mL, 0.36 mmol) and deuterium oxide (0.10 mL, 5.53 mmol). The solution was refluxed 24 hrs., then washed with 1 N HCl, water, sat'd $NaHCO_3$, and brine. The organic phase was dried over sodium sulfate, and the solvent removed in vacuo and the crude product chromatographed (silica gel, 2:1 hexanes to ether) to yield tetradeuteriocyclohexanone **23a** (11.0 mg, 86%): ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.8-7.2 (m, 6 H), 4.07 (m, 1 H), 3.96 (m, 1 H), 2.42 (dd, J = 14.1, 5.6 Hz, 1 H), 2.03 (dd, J = 14.1, 7.0 Hz, 1 H); MS (EI) m/z (rel. int.) 226(92), 181(31), 165(100), 152(32).

Thioketal (24). To a 25 °C solution of cyclohexanone **21** (1.30 g, 4.50 mmol) in methylene chloride (20.0 mL) was added dithioethane (1.50 mL, 17.2 mmol) and boron trifluoride etherate (0.50 mL, 4.07 mmol). The solution was stirred 20 min., then quenched with water. The organic layer was separated and dried over sodium sulfate, then the solvent was removed in vacuo to give a crude product. Chromatography (silica gel, 1:1 hexanes to ether) yielded thioketal **24** (1.26 g, 94%) as a yellow oil: ^{2}H NMR (250 MHz, $CDCl_3$) δ 7.8-7.2 (m, 6 H), 3.68 (m, 1 H), 3.53 (m, 1 H), 3.15 (m, 4 H), 2.39 (ddd, J = 13.6, 6.0, 0.9 Hz, 1 H), 2.15 (m, 2 H), 1.95 (m, 2 H), 1.71 (dd, J = 13.6, 10.7 Hz, 1 H); MS (EI) m/z (rel. int.) 298 (25), 281 (3), 269 (5), 237 (7), 205 (100), 165 (77), 152 (56).

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Cyclopentanes (25-28). To a 25 °C solution of endo vinylcyclobutanol **5** (20.3 mg, 0.09 mmol) in tetrahydrofuran (3.00 mL) was added bis(acetonitrile) palladium dichloride (2.6 mg, 0.01 mmol). The reaction was stirred for 24 hrs., filtered through a Celite pad, and the residue chromatographed (silica gel, 1:1 hexanes to ether) to give a mixture of cyclopentanes **25-28** (12.3 mg, 61%) as a 1:1:14:4 mixture (^{1}H NMR). Similar treatment of exo vinylcyclobutanol 19 gave a similar mixture (1:7:22:3). Repeated chromatography allowed for isolation of the exomethylcyclopentanone **27** and for partial spectral assignment of **26-28**. Exo methylenecyclopentanone (25): ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.8-7.2 (m, 6 H), 6.16 (d, J = 1 Hz, 1 H), 5.78 (d, J = 1 Hz, 1 H), 4.88 (m, 1 H), 4.30 (m, 1 H), 3.13 (dd, J = 19.2, 9.6 Hz, 1 H), 2.67 (dd, J = 19.2, 4.4 Hz, 1 H); Methylcyclopentenone (26): ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.8-7.2 (m, 6 H), 4.71 (m, 1 H), 3.21 (dd, J = 18.0, 7.6 Hz, 1 H), 2.71 (dd, J = 18.0, 5.8 Hz, 1 H), 2.08 (d, J = 2.4 Hz, 3 H); Exo methylcyclopentanone (27): ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.8-7.2 (m, 6 H), 4.17 (m, 1 H), 3.68 (t, J = 8.4 Hz, 1 H), 2.86 (dd, J = 18.8, 10.5 Hz, 1 H), 2.56 (ddd, J = 18.8, 5.5, 1.8 Hz, 1 H), 2.06 (m, 1 H), 1.25 (d, J = 7.3 Hz, 3 H). ^{13}C NMR (75 MHz, CDCl3) δ 219.39, 147.69, 147.64, 137.53, 131.80, 128.34, 128.19, 123.41, 123.35, 119.64, 118.92, 52.85, 50.03, 42.36, 42.08, 14.26; Endo methylcyclopentanone (28): 1 H NMR (250 MHz, CDCl3) d 7.8-7.2 (m, 6 H), 4.6 (m, 1 H), 1.10 (d, J = 7.3 Hz, 3 H).

Vinyl Ketone (29). A solution of endo vinylcyclobutanol **5** (44.2 mg, 0.20 mmol) in o-xylene (15.0 mL) was refluxed 48 hrs, the solvent removed, and the residue chromatographed (silica gel, 2:1 ether to hexanes) to yield cyclohexanone **21** (18.9 mg, 43%) and vinyl ketone **29** (12.0 mg, 27%) as a colorless oil: ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.8-7.2 (m, 6 H), 6.37 (dd, J = 17.7, 10.2 Hz, 1 H), 6.17 (d, J = 17.7 Hz, 1 H), 5.80 (d, J =10.2 Hz, 1 H), 4.15 (m, 1 H), 3.69 (dd, J = 17.4, 8.1 Hz, 1 H), 3.13 (dd, J= 17.4, 5.2 Hz, 1 H), 2.89 (m, 2 H); ^{13}C NMR (250 MHz, $CDCl_3$) δ 199.6, 144.0, 138.4, 136.8, 128.5, 128.0, 127.8, 123.1, 122.4, 119.4, 118.9, 114.7, 46.7, 38.4, 38.3.

Exo Vinylcyclobutyl Acetate (30). To a 25 °C solution of exo vinylcyclobutanol **19** (84.0 mg, 11.3 mmol) in benzene (2.00 mL) was added triethylamine (0.15 mL, 1.08 mmol), acetic anhydride (7.00 mL, 74.0 mmol), and a few crystals of dimethylaminopyridine. The solution was stirred 3 hrs., then washed with 10% HCl, water, sat'd $NaHCO_3$, and brine. The organic phase was dried over sodium sulfate, then removed in vacuo to give a crude product, which was chromatographed (silica gel, 2:1 ether to hexanes) to yield exo vinylcyclobutyl acetate **30** (89.3 mg, 89%) as a yellow oil: ^1H NMR (250 MHz, $CDCl_3$) δ 7.8-7.2 (m, 6 H), 6.40 (dd, J = 17.4, 10.7 Hz, 1 H), 5.38 (d, J = 17.4 Hz, 1 H), 5.25 (d, J = 10.7 Hz, 1 H), 4.53 (dd, J = 5.5, 2.4 Hz, 1 H), 3.77 (m, 1 H), 2.89 (ddd, J = 12.8, 8.4, 3.1 Hz, 1 H), 2.04 (dd, J = 12.8, 7.3 Hz, 1 H), 1.74 (s, 3 H); ^{13}C NMR (250 MHz, $CDCl_3$) δ 169.9, 148.8, 142.2, 140.8, 132.3, 127.9, 127.7, 123.7, 122.9, 122.8, 118.2, 113.6, 79.5, 55.8, 41.7, 37.3, 21.2; IR (CH_2Cl_2) 1738, 1368, 1252, 1223, 824, 789 cm^{-1}; MS (EI) m/z (rel. int.) 264 (2), 222 (4), 193 (3), 178 (1), 165 (18), 152 (100). Thermolysis: A solution of exo vinylcyclobutyl acetate **30** (0.023 g, 0.09 mmol) in o-xylene (15.0 mL) was refluxed 48 hrs. and the solvent removed. The residue was chromatographed (silica gel, 2:1 hexanes to ether) to yield only recovered starting material.

Endo Vinylcyclobutyl Acetate (31). To a 25 °C solution of endo vinylcyclobutanol **5** (11.8 mg, 0.05 mmol) in benzene (2.00 mL) was added triethylamine (0.02 mL, 0.14 mmol), acetic anhydride (1.00 mL, 10.6 mmol), and a few crystals of dimethylaminopyridine. The solution was stirred 2.5 hrs., then washed with 5% HCl, water, sat'd $NaHCO_3$, and brine. The solvent was dried over sodium sulfate, then removed in vacuo to yield a crude product which was chromatographed (silica gel, 2:1 ether to hexanes) to yield endo vinylcyclobutyl acetate **31** (12.0 mg, 87%): ^1H NMR (250 MHz, $CDCl_3$) δ 7.8-7.2 (m, 6 H), 5.52 (dd, J = 17.4, 11.0 Hz, 1 H), 4.64 (d, J = 11.0 Hz, 1 H), 4.57 (d, J = 17.4 Hz, 1 H), 4.49 (d, J = 7.0, 1 H), 4.11 (m, 1 H),

2.96 (ddd, J = 13.7, 10.1, 1.8 Hz, 1 H), 2.29 (ddd, J = 13.7, 4.6, 1.2 Hz, 1 H), 2.10 (s, 3 H). Thermolysis: A solution of endo vinylcyclobutyl acetate **31** (0.012 g, 0.05 mmol) in o-xylene (15.0 mL) was refluxed 48 hrs. and the solvent removed. The residue was chromatographed (silica gel, 2:1 hexanes to ether) to yield only recovered starting material.

Cyclohexyl Enol Acetate (32). Flash Thermolysis: The results of the flash thermolysis experiments are tabulated in Table 2, Thermolysis Experiments. A representative experimental procedure will be outlined for the thermolysis of exo vinylcylobutyl acetate **31**: The flash thermolysis system used consisted of a 125 mL pressure equalizing addition funnel, which was placed above a glass column filled with glass beads. The column was heated to the appropriate temperature by use of an external ceramic jacket, and the temperature monitored by a thermocouple placed between the jacket and the column. The bottom of the column was attached to a 250 mL round bottomed flask, which was partially filled with tetrahydrofuran cooled to -78 °C in order to trap the effluent. An argon stream was used to carry the solution through the system. A solution of the sample to be thermolyzed in 50.0 mL of tetrahydrofuran was added over a period of 1-3 hrs. The solvent was then removed in vacuo and the condensate analyzed. Cyclohexyl Enol Acetate (32): A solution of exo vinylcyclobutyl acetate **30** (77.0 mg, 0.292 mmol) in tetrahydrofuran (50.0 mL) was thermolyzed using the flash thermolysis system outlined above. Addition time was 1 hr., and the column temperature was 250 °C. Removal of the solvent and chromatography (silica gel, 2:1 hexanes to ether) of the residue yielded recovered starting material (10.0 mg, 13%) and cyclohexyl enol acetate **32** (31.2 mg, 41%): ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.8-7.2 (m, 6 H), 6.45 (t, J = 6.6 Hz, 1 H), 4.01 (q, J = 7.2 Hz, 1 H), 3.83 (q, J = 5.9, 1 H), 2.78 (m, 2 H), 2.30 (m, 2 H), 2.01 (s, 3 H); MS(EI) m/z (rel.int.) 264(8), 222(7), 193(2), 178(2), 164(14), 152(100).

Exo Methylcyclobutanol (33). To a 25 °C solution of 1.50 M methyllithium (2.00 mL, 3.00 mmol) in hexanes was added over 8.5 min. a solution of cyclobutanone **2** (0.130 g, 0.67 mmol) in ether (10.0 mL). The solution was stirred 10 additional minutes, then quenched with water. The organic phase was washed with water, the aqueous phase back-extracted with ether, and the combined organic phases combined and dried over sodium sulfate. The solvent was removed in vacuo and the crude product chromatographed (silica gel, methylene chloride) to yield exo methylcyclobutanol **33** (0.115 g, 81%), which was crystallized from hexanes to give white needles, mp 115 °C: ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.8-7.2 (m, 6 H), 4.12 (m, 1 H), 3.63 (m, 1 H), 2.60 (m, 1 H), 1.80 (br s, 1 H), 1.55 (m, overlapping s, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.01, 142.06, 140.55, 132.32, 128.04, 127.82, 123.78, 122.58, 122.25, 118.44, 71.40, 58.95, 45.70, 34.75, 28.92; IR(CH_2Cl_2) 3574, 3053, 2974, 2932, 1604 cm^{-1}; MS(EI) m/z (rel.int.) 210(17), 167(27), 152(100). Thermolysis: A solution of exo methylcyclobutanol **33** in o-xylene (20.0 mL) was refluxed 48 hrs. and the solvent removed. The residue was chromatographed (silica gel, 2:1 hexanes to ether) to yield only recovered starting material.

Primary Alcohol (36). To a 25 °C solution of allylic alcohol **9** (0.100 g, 0.45 mmol) in 95% ethanol (20.0 mL) was added 10% palladium on charcoal (0.02 g). The solution was stirred under a hydrogen atmosphere for four hours, then filtered and the solvent removed to yield primary alcohol **36** (0.109 g, 100%) as a pale yellow oil: ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.8-7.2 (m, 6 H), 4.22 (m, 1 H), 3.97 (m, 1 H), 3.31 (t, 2 H), 2.91 (m, 1 H), 2.70 (m, 1 H), 2.42 (br s, 1 H), 1.53 (m, 1 H), 1.40 (m, 1 H), 1.01 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.60, 144.97, 140.97, 132.05, 127.80, 127.54, 122.71, 122.32, 121.10, 117.89, 60.63, 47.55, 40.83, 35.85, 34.08, 32.57; IR(CH_2Cl_2) 3617, 3055, 2968, 2934, 1603, 1366, 1046 cm^{-1}; MS(EI) m/z (rel.int.) 224(5), 208 (1), 189(2), 178(5), 165(10), 152(100).

Primary Mesylate (38). To a 25 °C solution of primary alcohol **36** (0.745 g, 3.33 mmol) in methylene chloride (25.0 mL) was added triethylamine (0.70 mL, 5.02 mmol) and methanesulfonyl chloride (0.30 mL, 3.58 mmol). The solution was stirred 48 hrs., then washed with 10% HCl, water, sat'd $NaHCO_3$, and brine. The solvent was dried over sodium sulfate, then removed in vacuo to yield primary mesylate **38** (0.901 g, 90%) as a yellow oil: ^1H NMR (250 MHz, $CDCl_3$) δ 7.8-7.2 (m, 6 H), 4.30 (m, 1 H), 4.02 (m, 1 H), 3.00 (m, 3 H), 2.83 (m, overlapping s, 4 H), 1.74 (m, 1 H), 1.41 (m, 1 H), 1.19 (m,1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.06, 144.15, 140.67, 131.90, 127.77, 127.44, 122.81, 122.28, 120.96, 117.96, 68.13, 47.01, 40.50, 36.78, 33.59, 31.97; IR(CH_2Cl_2) 3055, 1358, 1337, 1177, 972, 943 cm^{-1}; MS(EI) m/z (rel.int.) 302(1), 205(1), 191(2), 178(5), 165(11), 152(100).

(Cyclobutyl)ethyl t-butyl Ether (39). To a 25 °C solution of primary mesylate **38** (37.0 mg, 0.12 mmol) in DMSO (10.0 mL) was added potassium t-butoxide (20.0 mg, 0.19 mmol). The solution was refluxed for 48 hrs., quenched with water, then extracted with ether. The organic phase was dried over sodium sulfate, then removed in vacuo to give crude product. This was chromatographed (silica gel, 2:1 hexanes to ether) to yield ethylidene cyclobutanes **3** (9.2 mg, 37%) as a 1:1 mixture of stereoisomers (^1H NMR) and (cyclobutyl)ethyl t-butyl ether **39** (14.1 mg, 41%): ^1H NMR (250 MHz, $CDCl_3$) δ 7.8-7.2 (m, 6 H), 4.27 (m, J = 1 H), 4.02 (m, 1 H), 3.11 (t, J = 7.3, 2 H), 2.99 (m, 1 H), 2.69 (m, 1 H), 2.00 (br s, 1 H), 1.72 (m, 1 H), 1.36 (m, 1 H), 1.0 (m, overlapping s, 10 H).

Xanthate Ester (40). To a 25 °C solution of sodium hydride (14.5 mg, 0.61 mmol) in ether (10.0 mL) was added a solution of primary alcohol **36** (83.0 mg, 0.37 mmol) in ether (8.00 mL) in one portion. The solution was refluxed 8.5 hrs., then a solution of carbon disulfide (2.00 mL, 3.33 mmol) in ether (10.0 mL) was added in one portion. The solution was stirred 2.5 hrs., then a 0.32 M solution of

methyl iodide (1.00 mL, 0.32 mmol) in ether was added in one portion. The solution was refluxed 11 hrs., then quenched with water and extracted with ether. The organic phase was dried over sodium sulfate, the removed in vacuo to yield xanthate ester **40** (116.6 mg, 96%): ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.8-7.2 (m, 6 H), 4.42 (t, 2 H), 4.29 (m,1 H), 4.05 (m, 1 H), 2.98 (m, 1 H), 2.76 (m, 1 H), 2.45 (s, 3 H), 1.80 (m, 1 H), 1.3 (m, 2 H); MS(EI) m/z (rel.int.) 314(2), 267(2), 207(4), 191(3), 178(6), 165(16), 152(100).

Exovinyl t-butyldimethylsilyl Ether (41). To a 25 °C solution of exo vinylcyclobutanol **19** (0.254 g, 1.142 mmol) in dimethylformamide (50.0 mL) was added imidizole (0.700 g, 10.28 mmol) and t-butyldimethylsilyl chloride (1.700 g, 11.28 mmol). The reaction was stirred 96 hrs., then quenched with sat'd NH_4Cl. The organic phase was separated and washed with 1N HCl, water, sat'd $NaHCO_3$, and brine, then dried over sodium sulfate. The solvent was removed in vacuo, and the crude product chromatographed (silica gel, 2:1 hexanes to ether) to yield exovinyl t-butyldimethylsilyl ether **41** (0.197 g, 51%) as a pale yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.8-7.2 (m, 6 H), 6.36 (dd, J = 17.4, 10.8 Hz, 1 H), 5.45 (d, J = 17.4 Hz, 1 H), 5.20 (d, J = 10.8 Hz, 1 H), 4.28 (d, J = 2.7 Hz, 1 H), 3.77 (dt, J = 8.4, 6.0 Hz, 1 H), 2.96 (ddd, J = 12.3, 8.4, 2.7 Hz, 1 H), 2.00 (dd, J = 12.3, 6.0 Hz, 1 H), 0.64 (s, 9 H), -0.12 (s, 3 H), -0.57 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.85, 145.38, 143.19, 140.90, 132.10, 127.67, 127.41, 123.24, 122.90, 122.61, 117.76, 110.70, 58.34, 42.44, 35.83, 25.56, 17.90, -2.93, -3.69; IR(CH_2Cl_2) 2957, 2930, 1256, 1250, 1127 cm^{-1}. Thermolysis: A solution of exovinyl t-butyldimethylsilyl ether **41** (62.9 mg, 0.187 mmol) in o-xylene (10.0 mL) was refluxed for 48 hrs., the solvent removed, and the residue chromatographed (silica gel, 2:1 hexanes to ether) to yield cyclohexanone **21** (18.9 mg, 45%) and recovered starting material (9.7 mg, 15%).

Exo Phenylcyclobutanol (42). To a -78 °C solution of cyclobutanone **2** (80.1 mg, 0.41 mmol) in tetrahydrofuran (50.0 mL)

was added in one portion a solution of 1.8M phenyllithium (0.50 mL, 0.90 mmol) in 7:3 hexanes to ether. The dry ice bath was removed, and the reaction was allowed to warm to room temperature over 1 hour. The reaction was quenched with ice cold sat'd NH_4Cl, and the organic phase was separated and washed with 1N HCl, water, sat'd $NaHCO_3$, and brine. The solution was dried over sodium sulfate, then the solvent was removed in vacuo to yield crude product. The residue was chromatographed (silica gel, 3:1 hexanes to ether) to give exo phenylcyclobutanol **42** (85.1 mg, 76%) as a white solid, mp 97 °C: ^1H NMR (300 MHz, $CDCl_3$) δ 7.8-7.2 (m, 11 H), 4.63 (d, J = 6.6 Hz, 1 H), 4.00 (dt, J = 9.3, 6.0 Hz, 1 H), 3.27 (ddd, J = 13.2, 9.3, 1.8 Hz, 1 H), 2.14 (s, 1 H), 2.13 (dd, J = 13.2, 6.0 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.75, 146.93, 141.50, 140.85, 132.39, 128.50, 128.30, 127.98, 127.06, 124.63, 124.14, 122.90, 122.35, 118.89, 74.95, 59.57, 45.49, 36.00; IR(CH_2Cl_2) 3568, 3052, 2974, 2932, 1603 1495, 1449 cm^{-1}. Thermolysis: A solution of exo phenylcyclobutanol **42** (29.2 mg, 0.107 mmol) in o-xylene (10.0 mL) was refluxed for 48 hrs., and the solvent removed. The residue was chromatographed (silica gel, 2:1 hexanes to ether) to yield recovered starting material.

Cyclopropylcyclobutanol (45). To a -78 °C solution of cyclobutanone **2** (50.0 mg, 0.25 mmol) in tetrahydrofuran (50.0 mL) was added a 1 M solution of cyclopropyl magnesium bromide (0.50 mL, 0.50 mmol). The solution was allowed to warm to room temperature over 1 hr., then quenched with sat'd NH_4Cl. The organic phase was washed with 1N HCl, water, sat'd $NaHCO_3$, and brine, then dried over sodium sulfate. The solvent was removed in vacuo, and the residue chromatographed (silica gel, 2:1 hexanes to ether) to yield cyclopropylcyclobutanol **45** (48.0 mg, 79%) as a yellowish solid, mp 74 °C: ^1H NMR (300 MHz, $CDCl_3$) δ 7.8-7.2 (m, 6 H), 4.23 (dd, J = 6.6, 0.9 Hz, 1 H), 3.69 (dt, J = 9.0, 6.0 Hz, 1 H), 2,62 (ddd, J = 12.6, 5.7, 2.1 Hz, 1 H), 1.72 (s, 1 H), 1.66 (dd, J = 12.6, 6.0 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.11, 142.00, 140.73, 132.33, 128.10, 127.89, 123.77, 122.67, 122.02, 118.55, 73.74, 56.49, 41.82. 35.70, 20.11, 1.06, 0.74; IR(CH_2Cl_2) 3574, 3053, 2978, 1605, 1221, 1107, 1020 cm^{-1}; MS(EI)

m/z (rel. int.) 236(24), 167(23), 152(100). Thermolysis: A solution of cyclopropylcyclobutanol **45** (111.1 mg, 0.470 mmol) in o-xylene (20.0 mL) was refluxed for 48 hrs., and the solvent removed. The residue was chromatographed (silica gel, 2:1 hexanes to ether) to yield recovered starting material (97.6 mg, 88%) and a small amount of unidentified side product (10.2 mg).

Tributyltin hydride trapping experiments. The results of these experiments are tabulated in Table 3, Thermolysis of Cyclobutane Derivatives with added Tributyltin hydride. A representative experimental procedure will be outlined for the thermolysis of exovinyl t-butyldimethylsilyl ether **41**, entry 7: A solution of exovinyl t-butyldimethylsilyl ether 41 (20.3 mg, 0.060 mmol) and tributyltin hydride (0.10 mL, 0.371 mmol) in o-xylene (10.0 mL) was refluxed for 1 hr., and the solvent removed. The residue was chromatographed (silica gel, 2:1 hexanes to ether) to yield acenaphthylene (1.1 mg, 12%), recovered starting material (2.0 mg, 10%) and cyclohexanone (6.7 mg, 50%).

APPENDIX

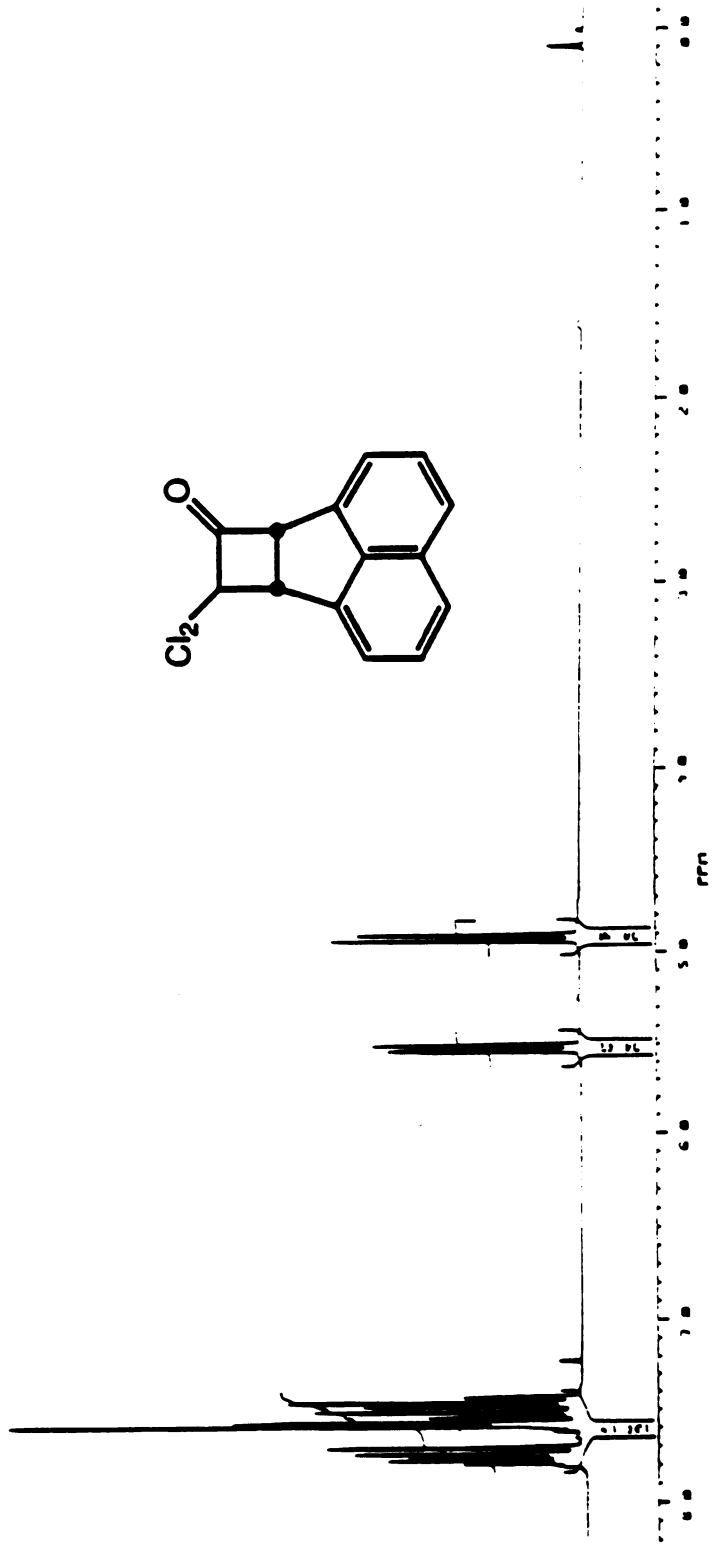

Figure 30. ^1H NMR Spectrum of **1**.

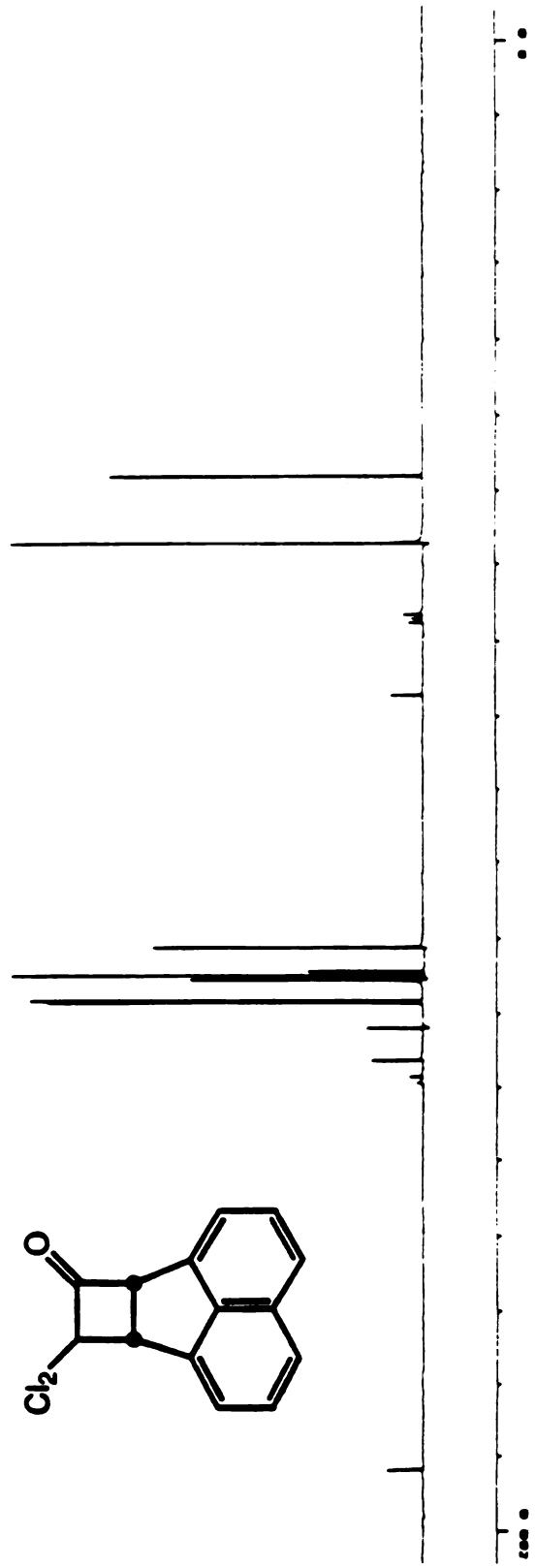

Figure 31. ^{13}C NMR Spectrum of 1.

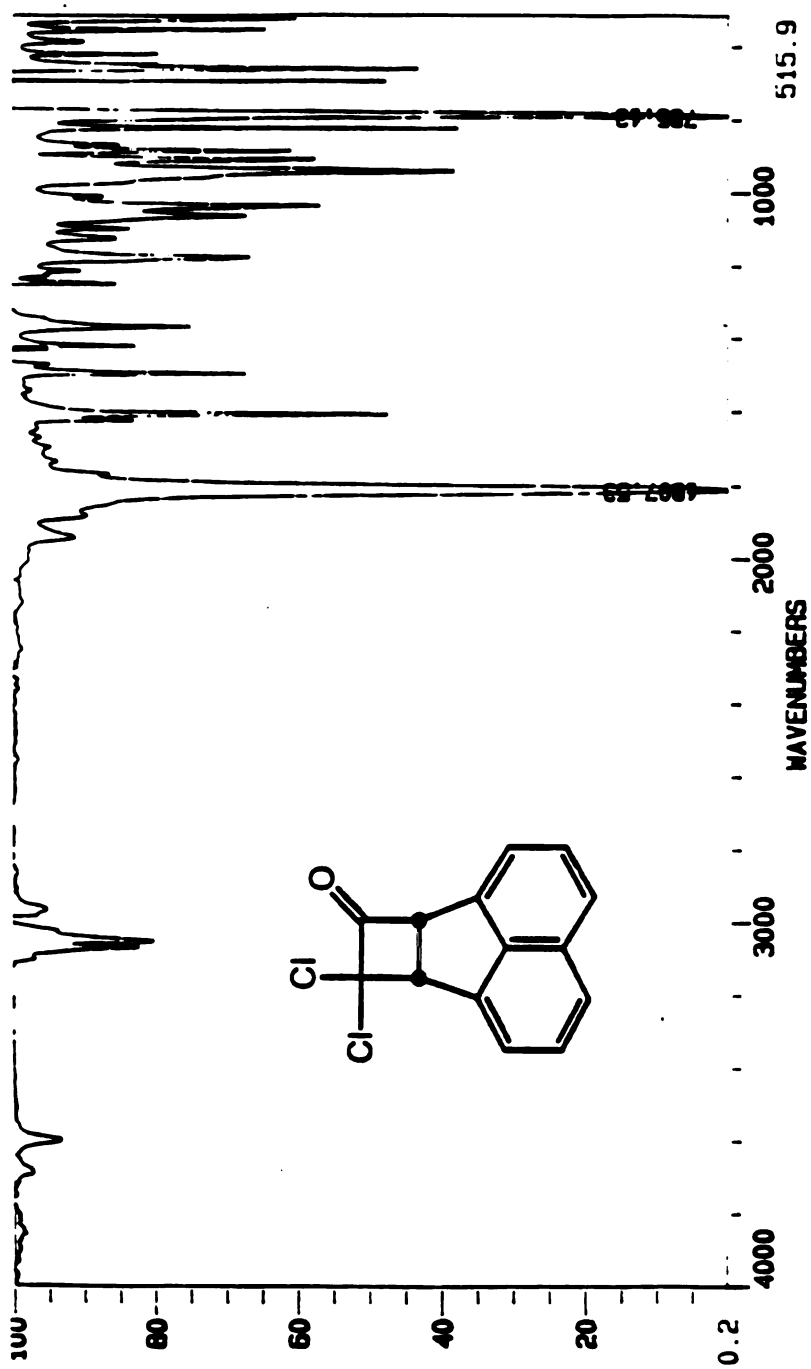

Figure 32. Infrared Spectrum of 1.

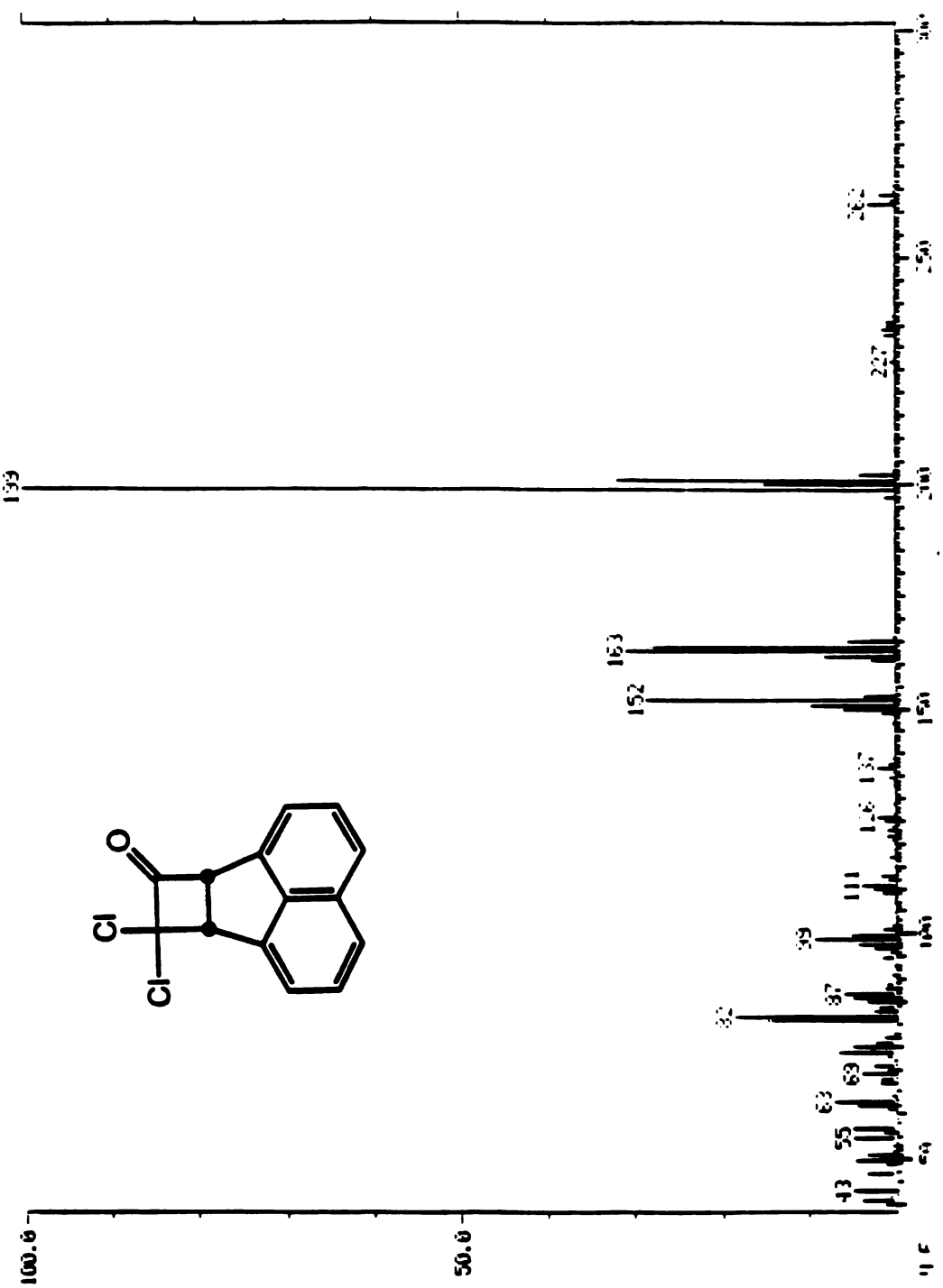

Figure 33. Mass Spectrum of 1.

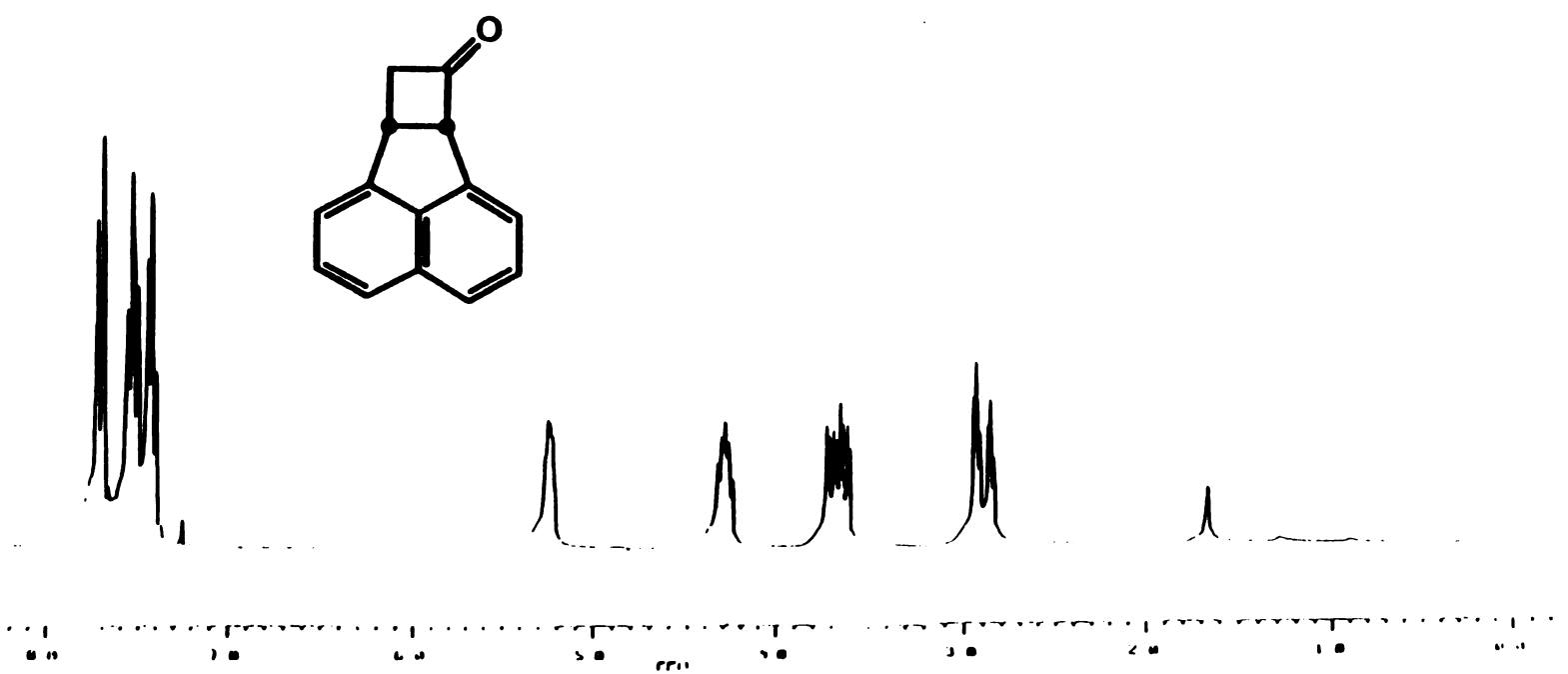

Figure 34. ^{1}H NMR Spectrum of 2.

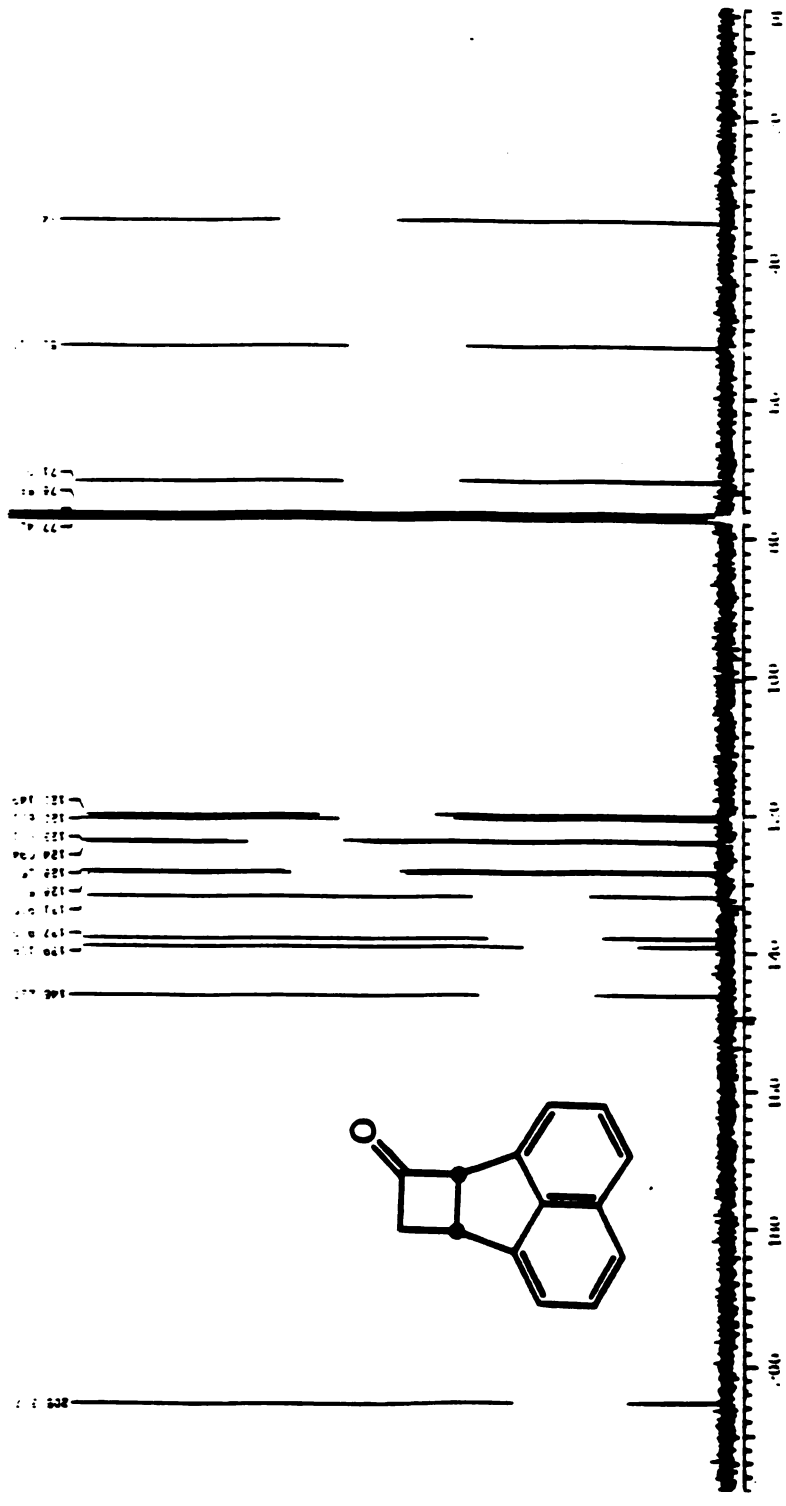

Figure 35. ^{13}C NMR Spectrum of 2.

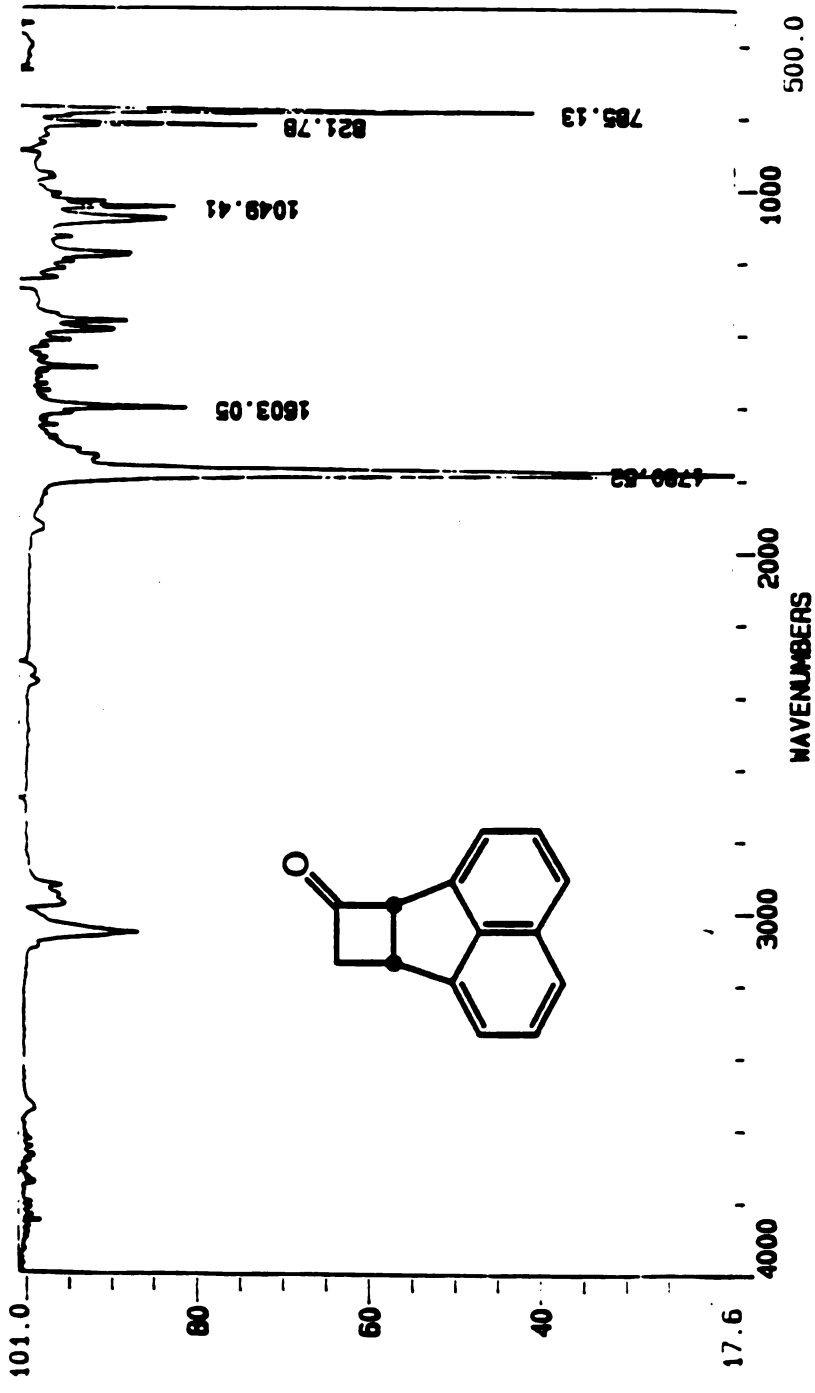

Figure 36. Infrared Spectrum of 2.

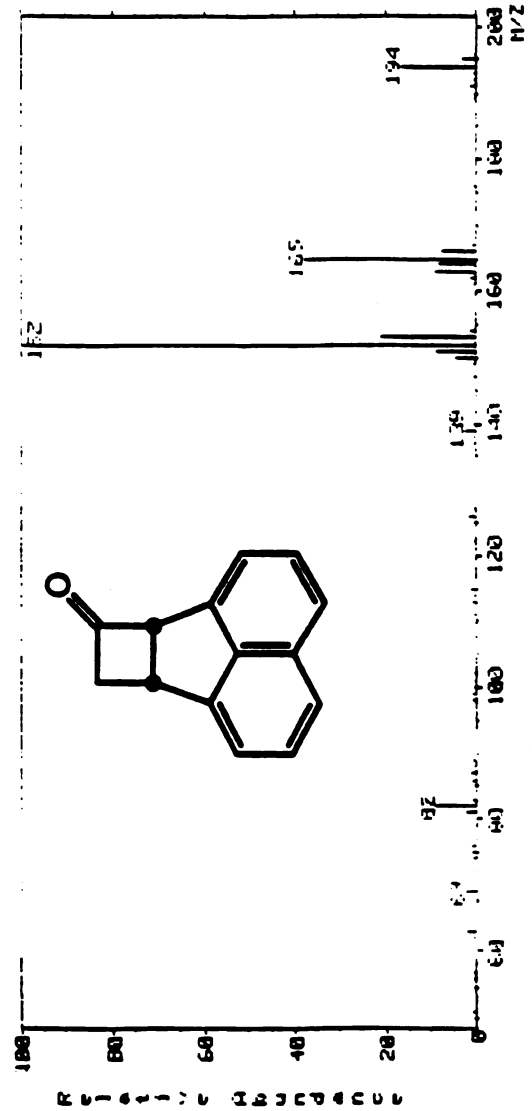

Figure 37. Mass Spectrum of 2.

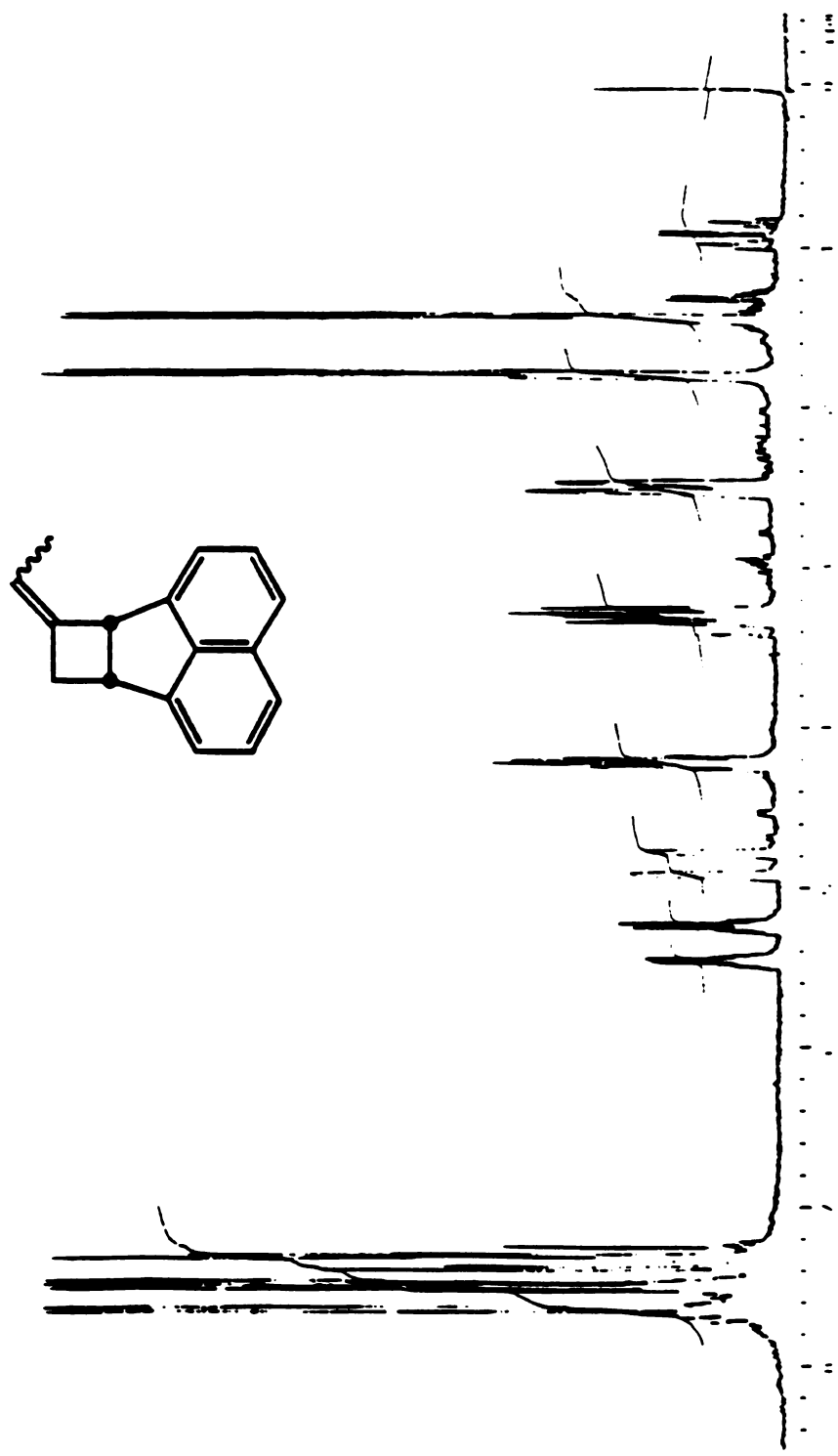

Figure 38. ^1H NMR Spectrum of 3.

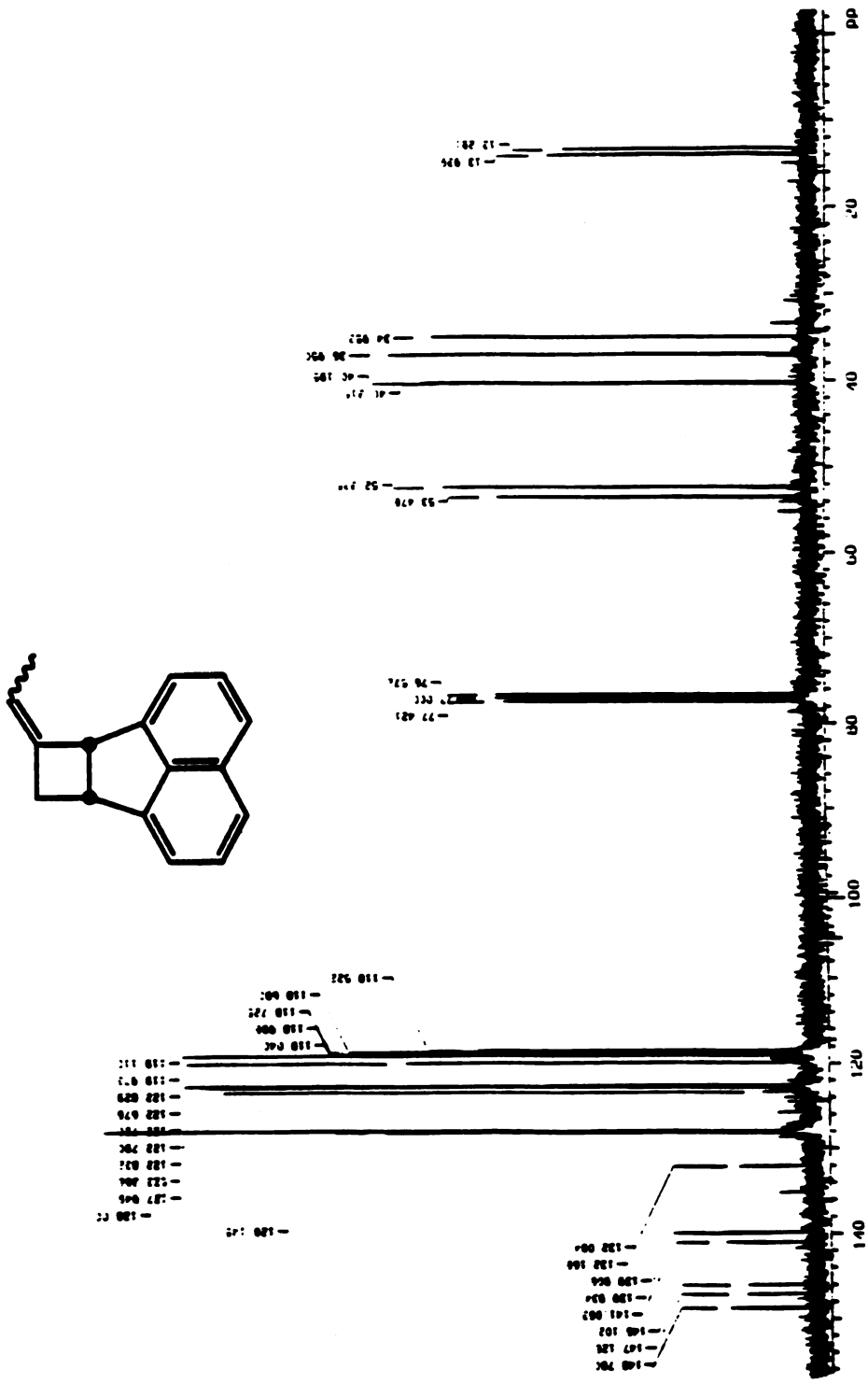

Figure 39. ^{13}C NMR Spectrum of 3.

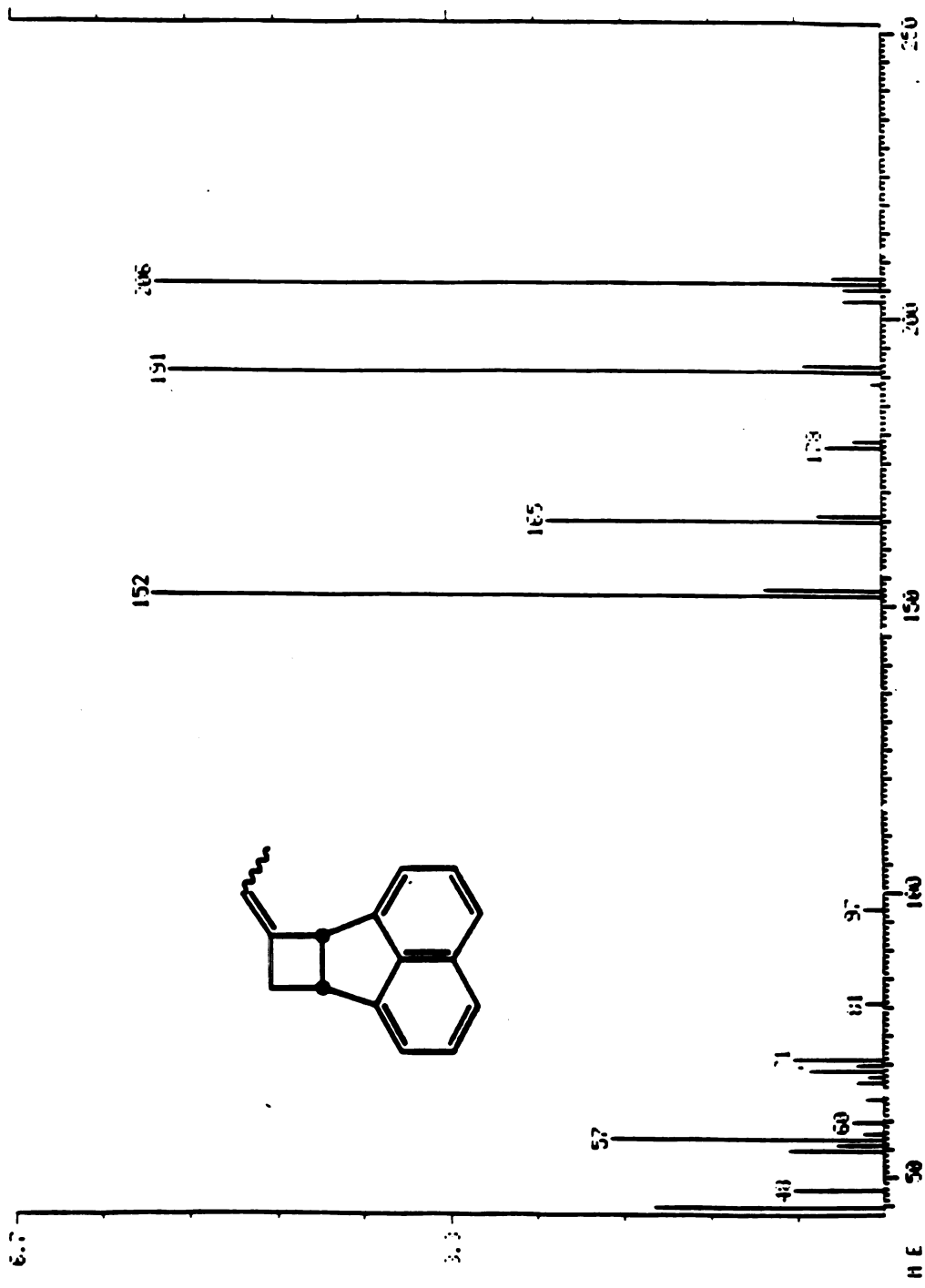

Figure 40. Mass Spectrum of 3.

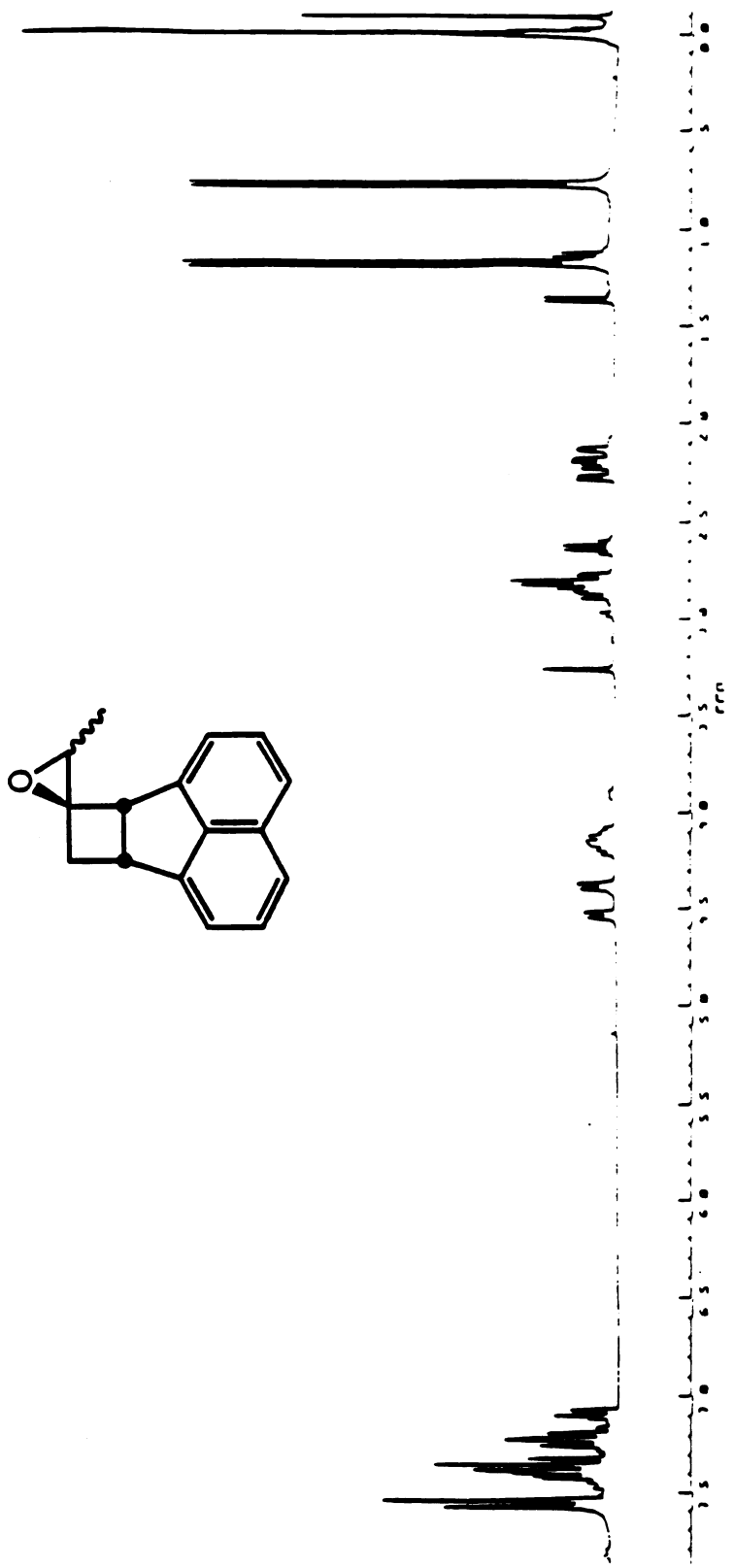

Figure 41. ^{1}H NMR Spectrum of 4.

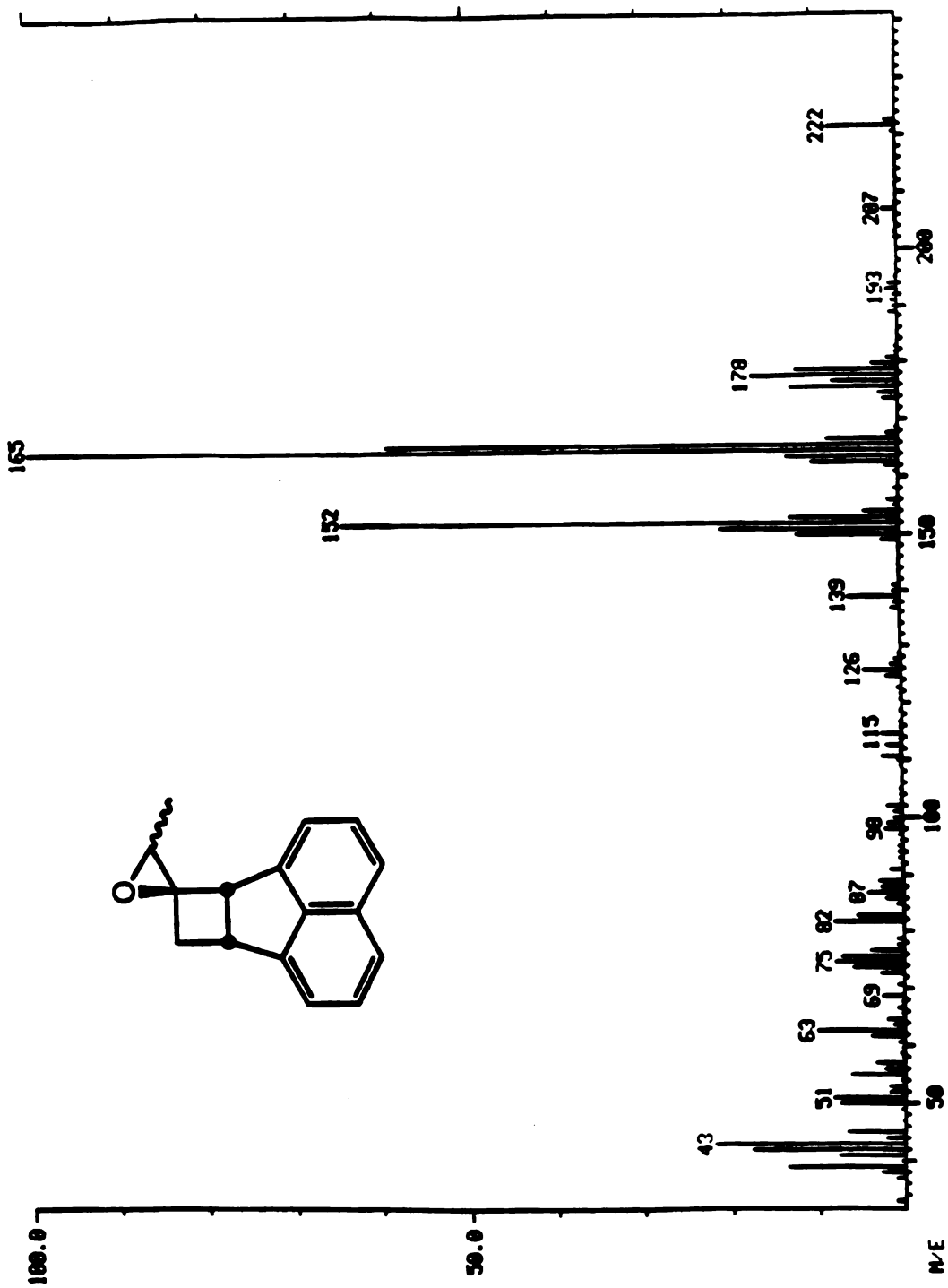

Figure 42. Mass Spectrum of 4.

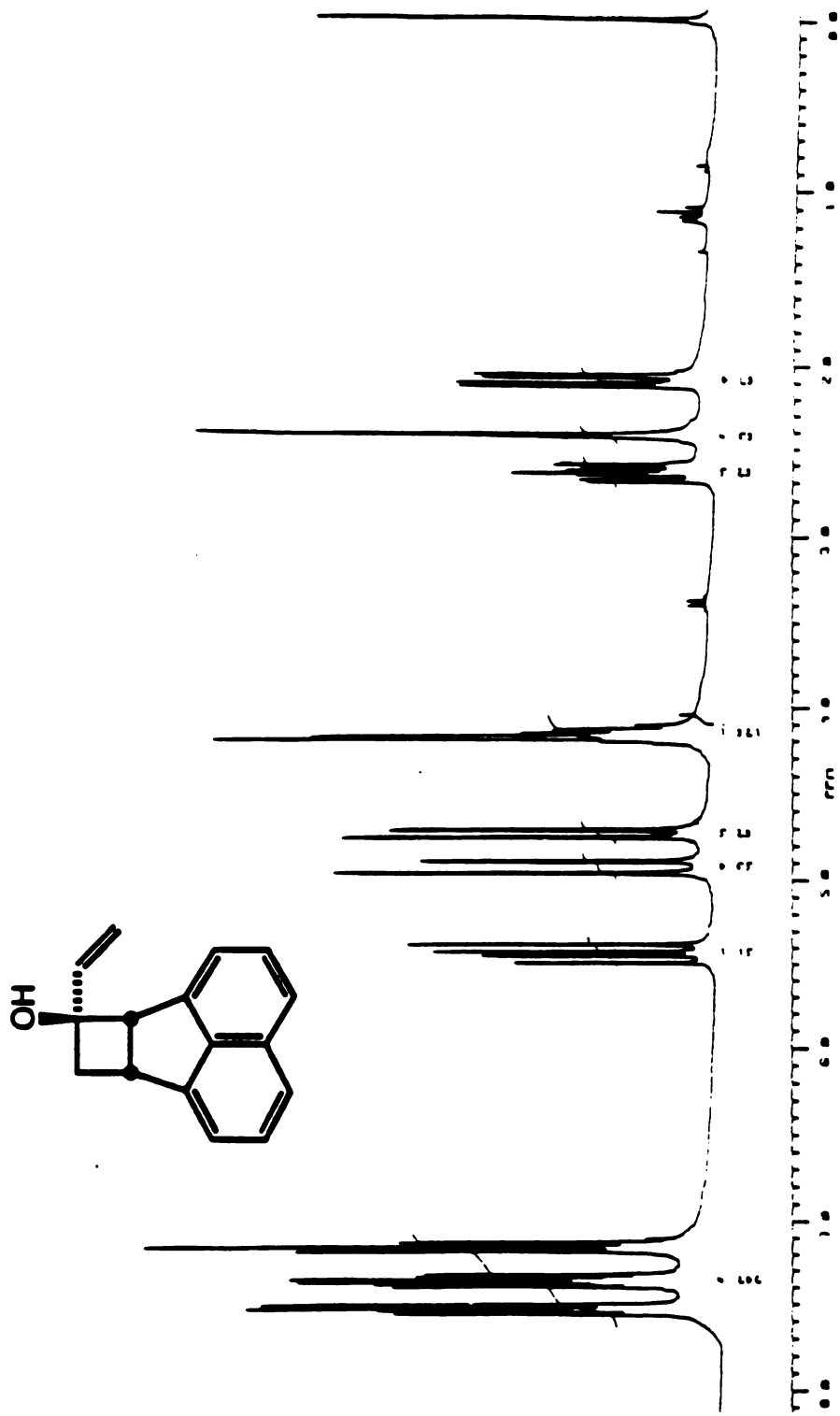

Figure 43. ^1H NMR Spectrum of 5.

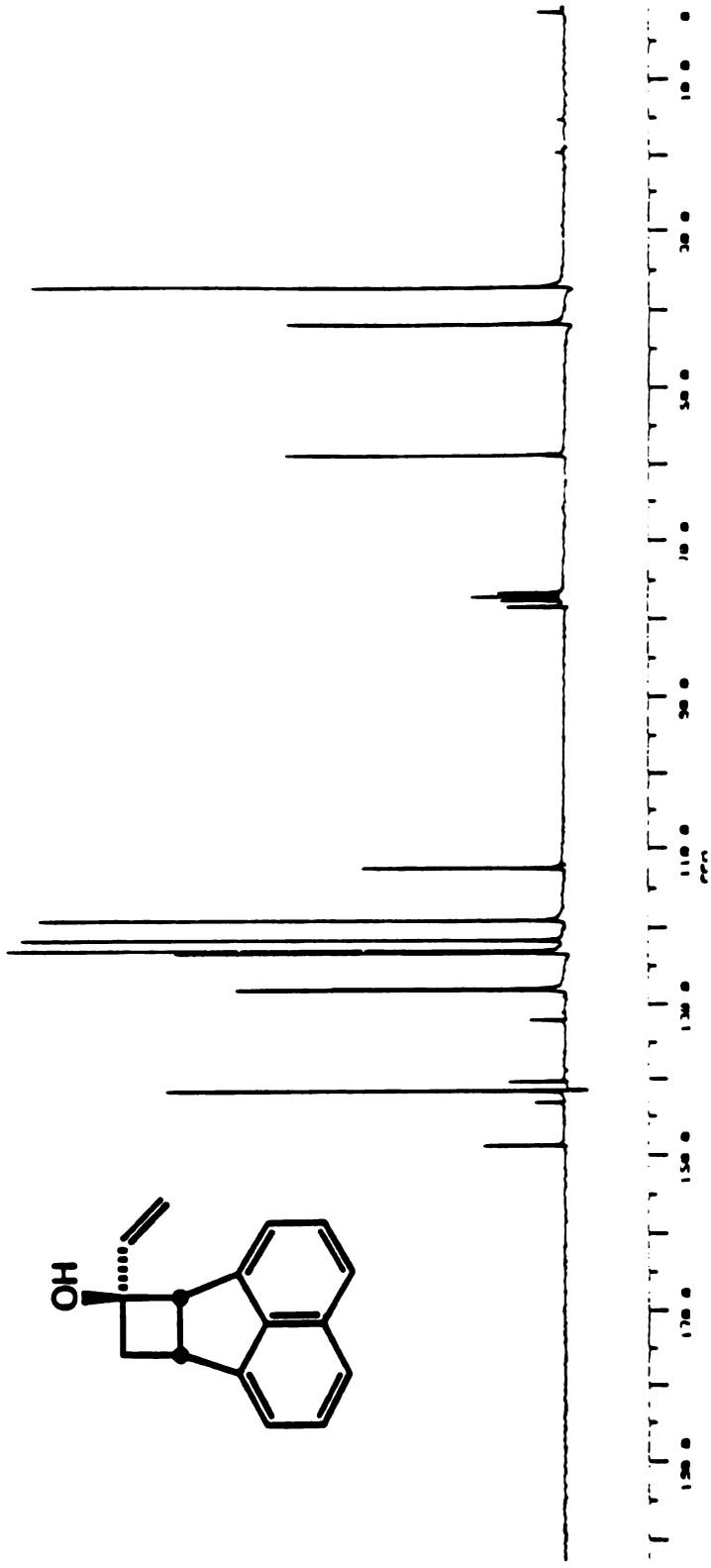

Figure 44. ^{13}C NMR Spectrum of 5.

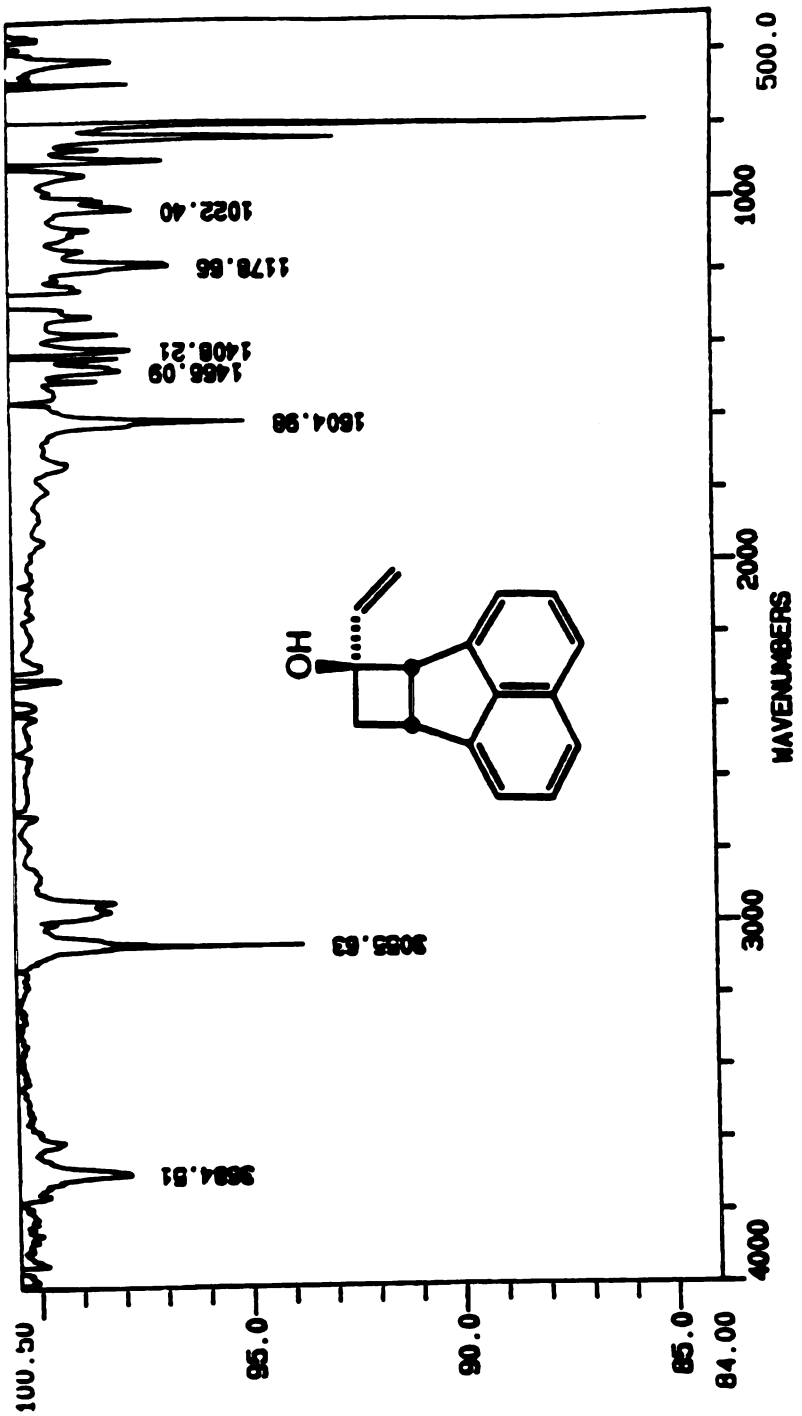

Figure 45. Infrared Spectrum of 5.

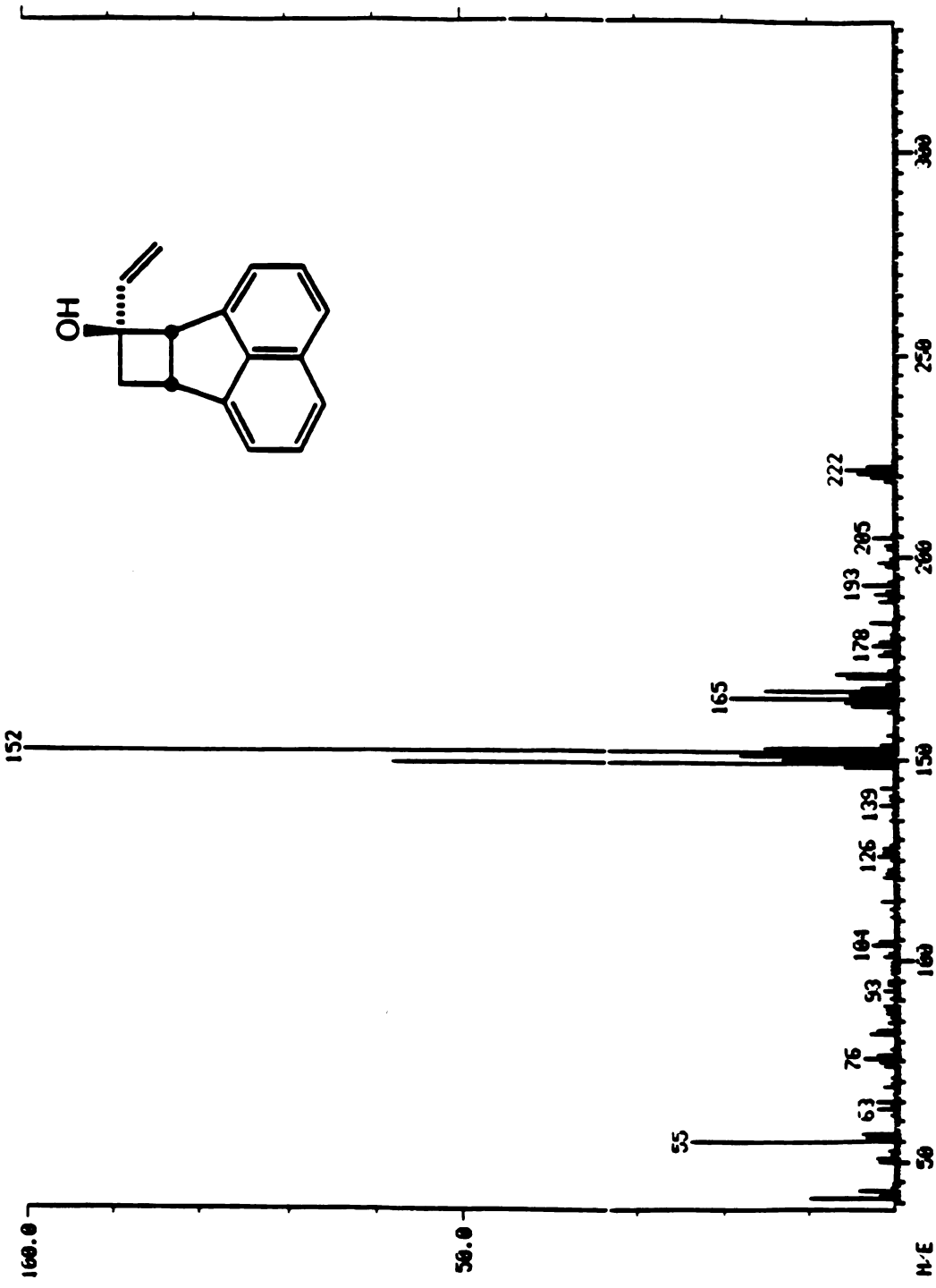

Figure 46. Mass Spectrum of Endo 5.

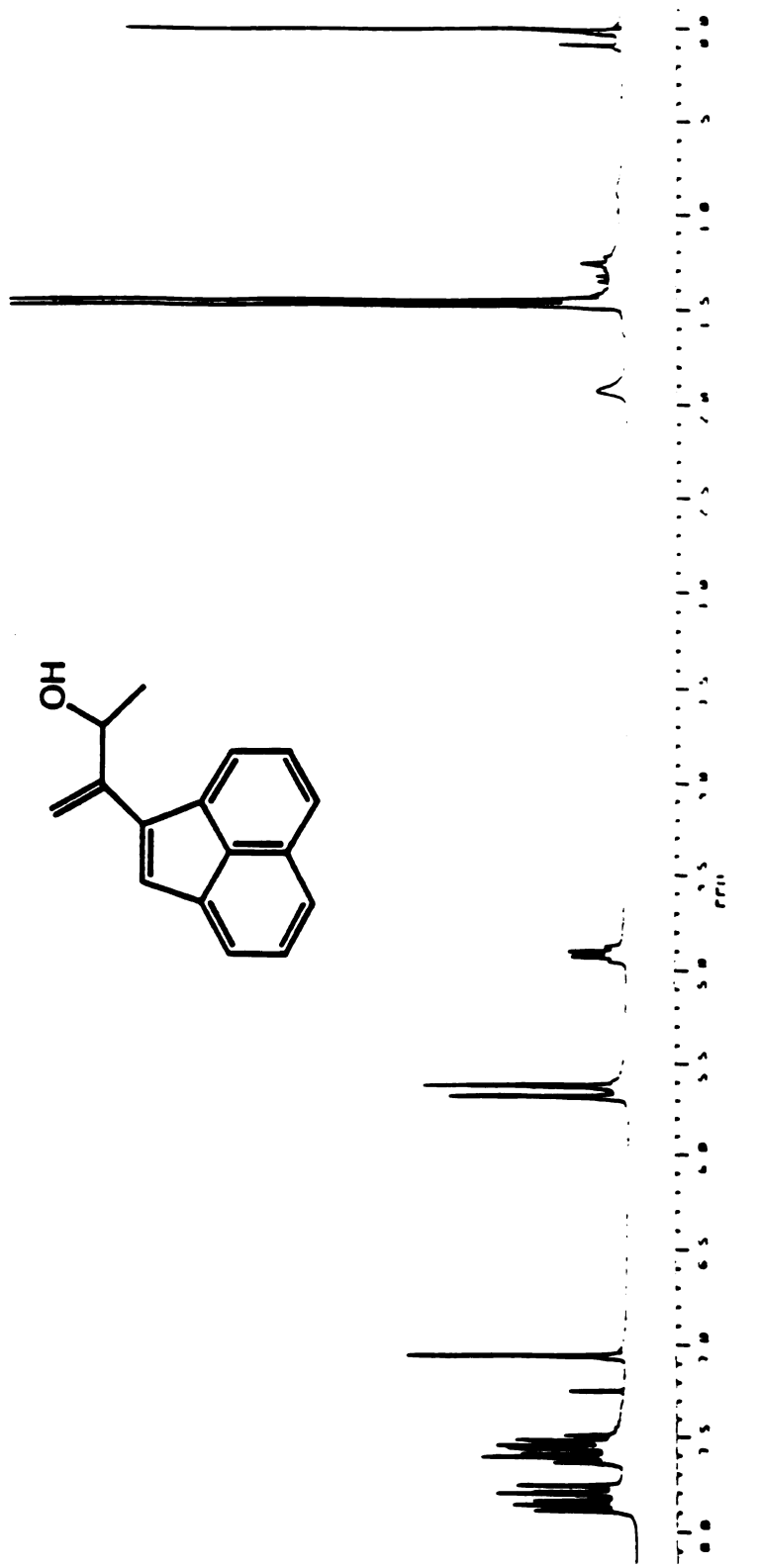

Figure 47. ^{1}H NMR Spectrum of **6**.

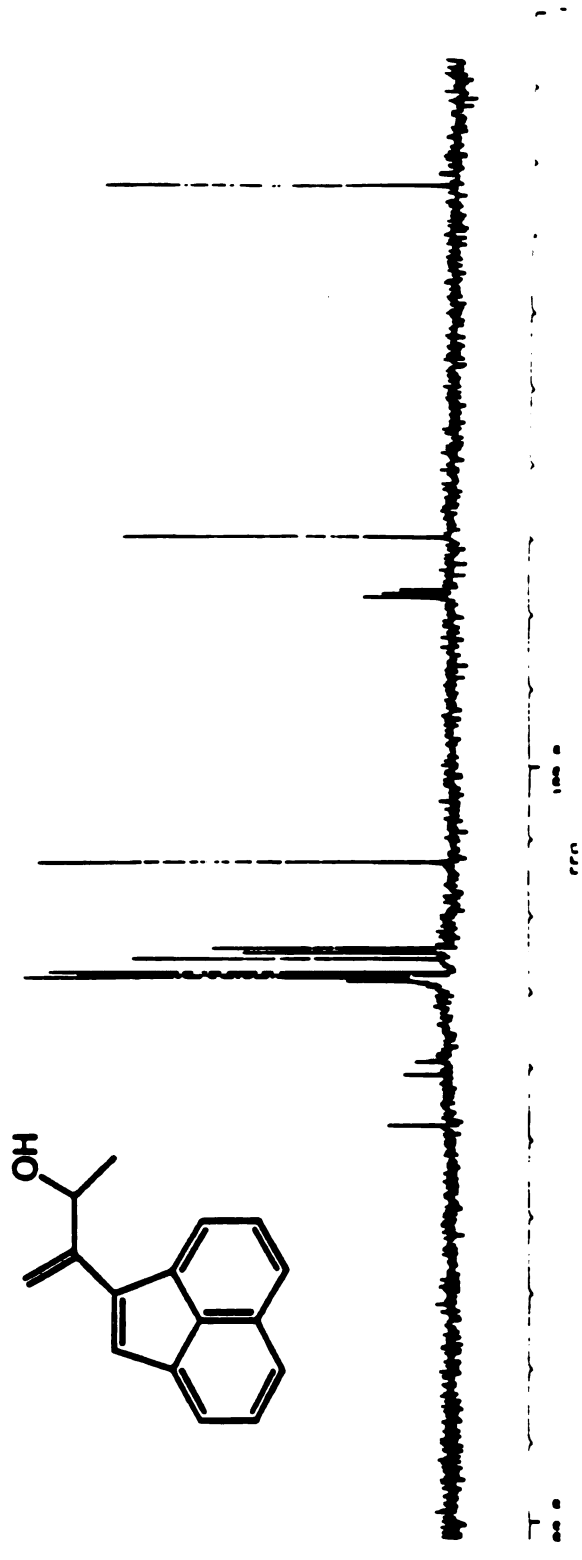

Figure 48. ^{13}C NMR Spectrum of 6.

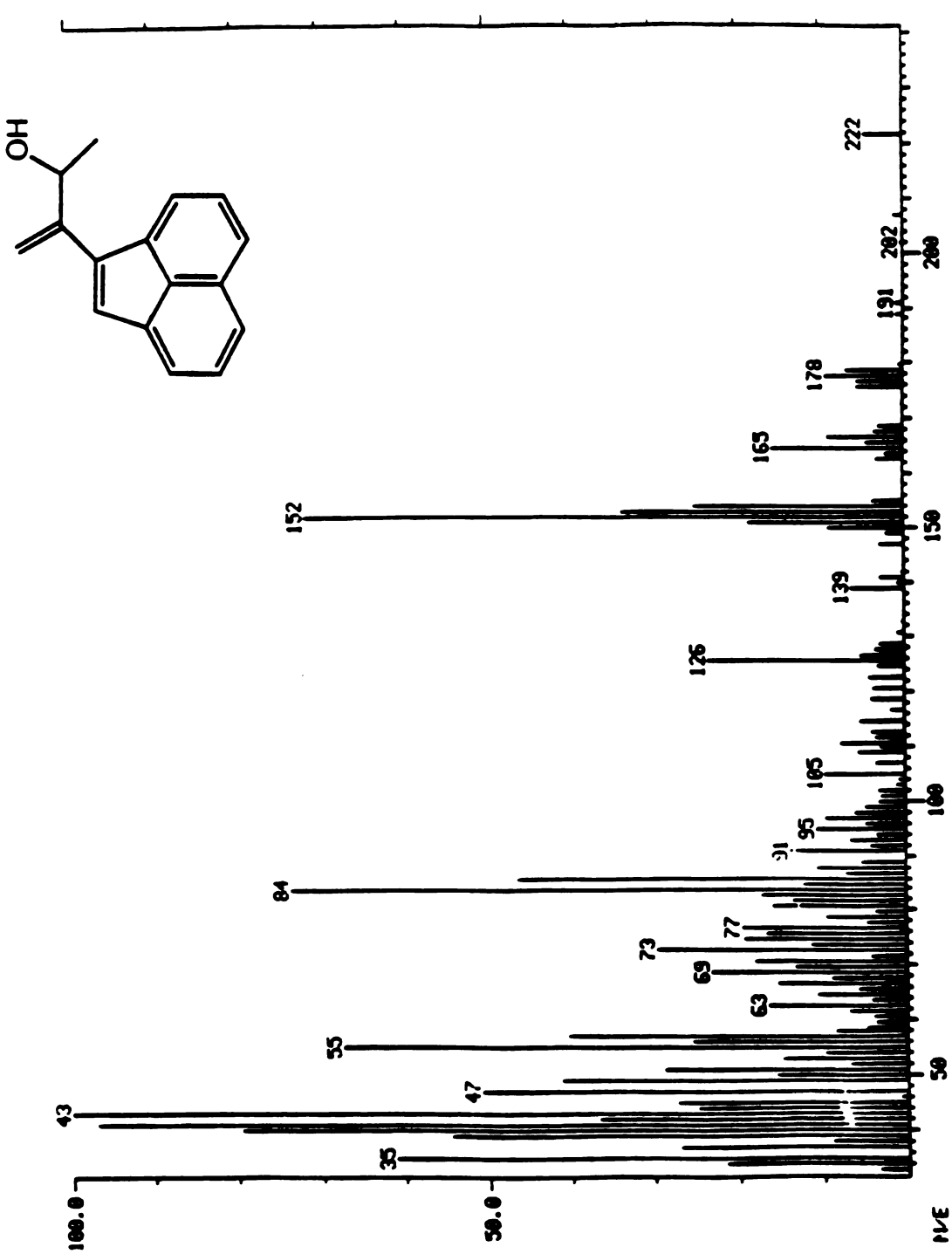

Figure 49. Mass Spectrum of 6.

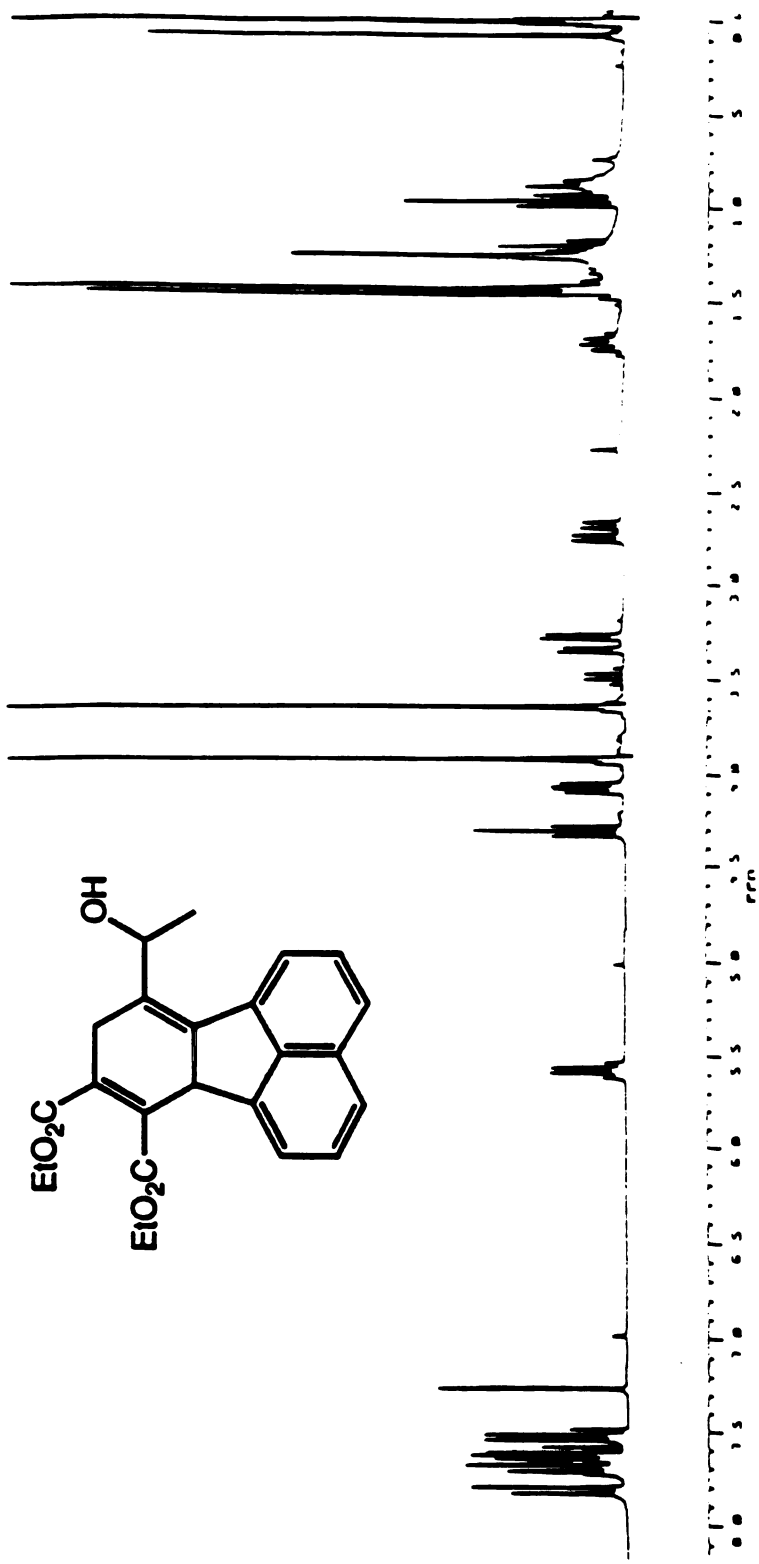

Figure 50. ^{1}H NMR Spectrum of 7.

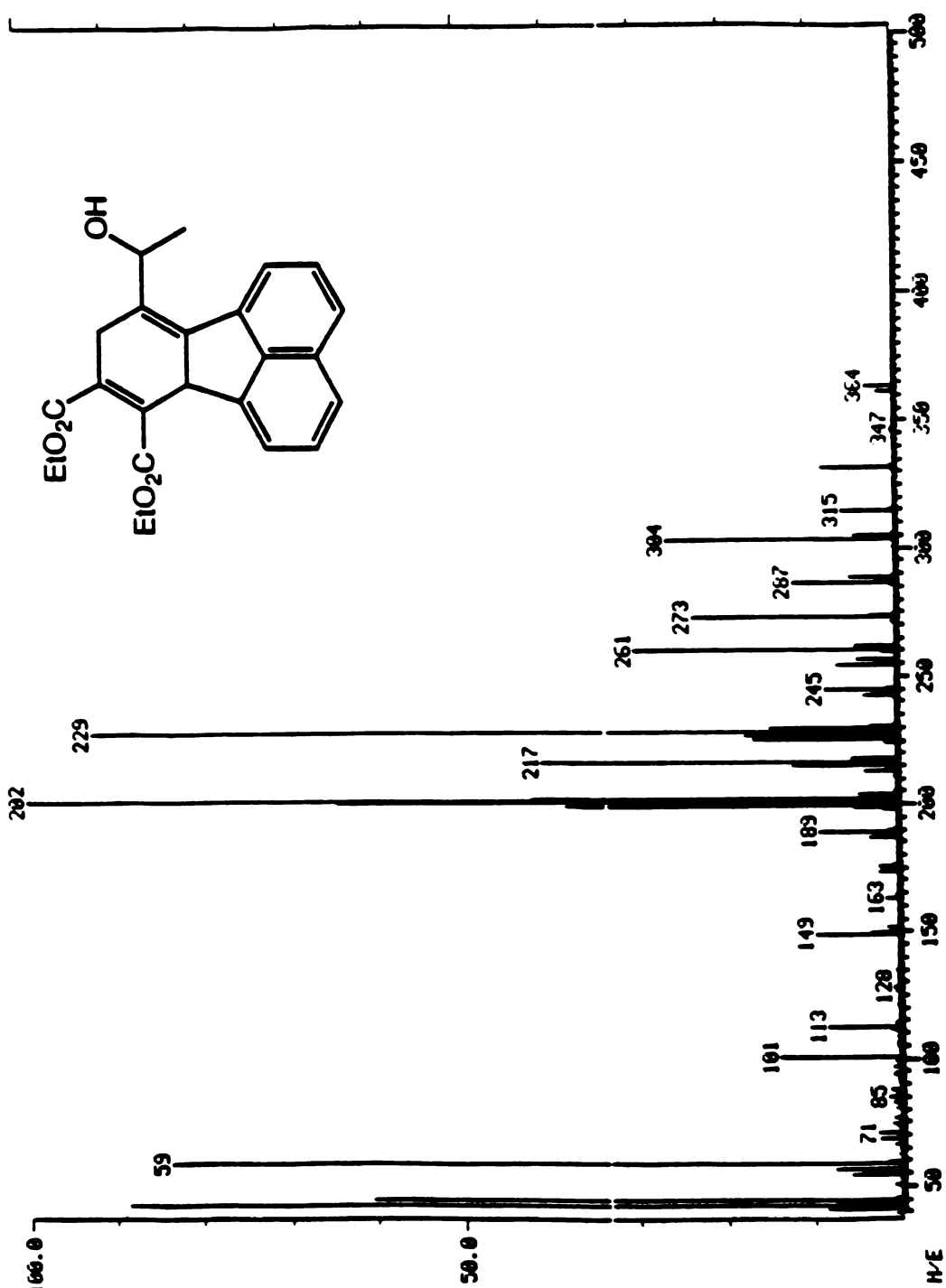

Figure 51. Mass Spectrum of 7.

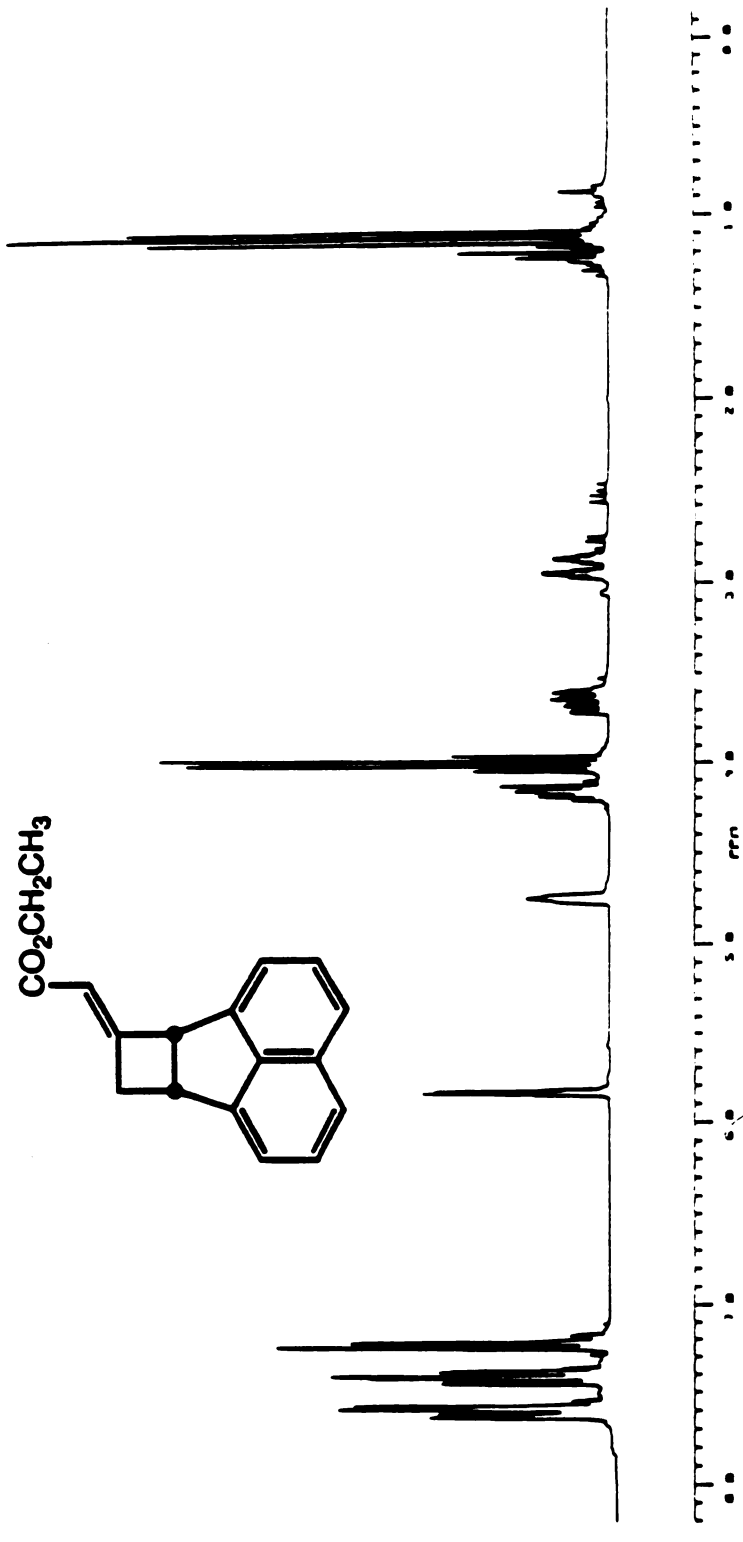

Figure 52. ^{1}H NMR Spectrum of **8a**.

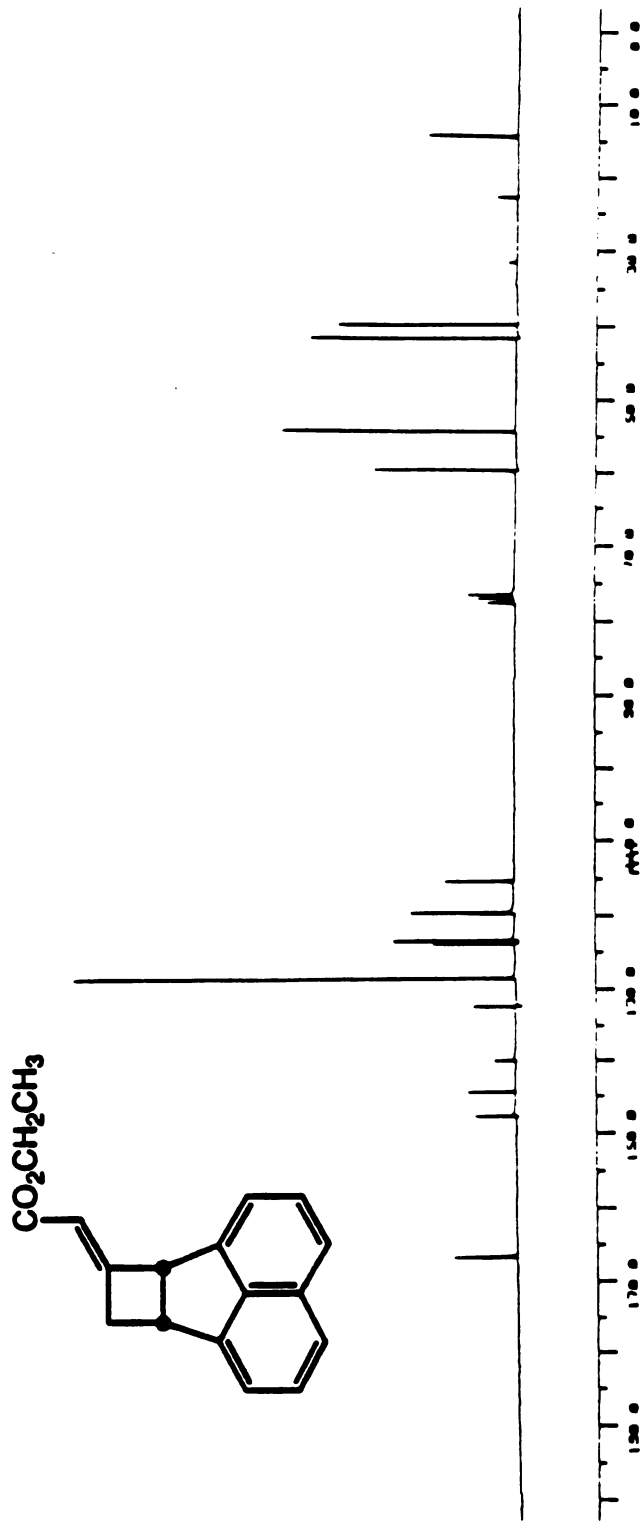

Figure 53. ^{13}C NMR Spectrum of **8a**.

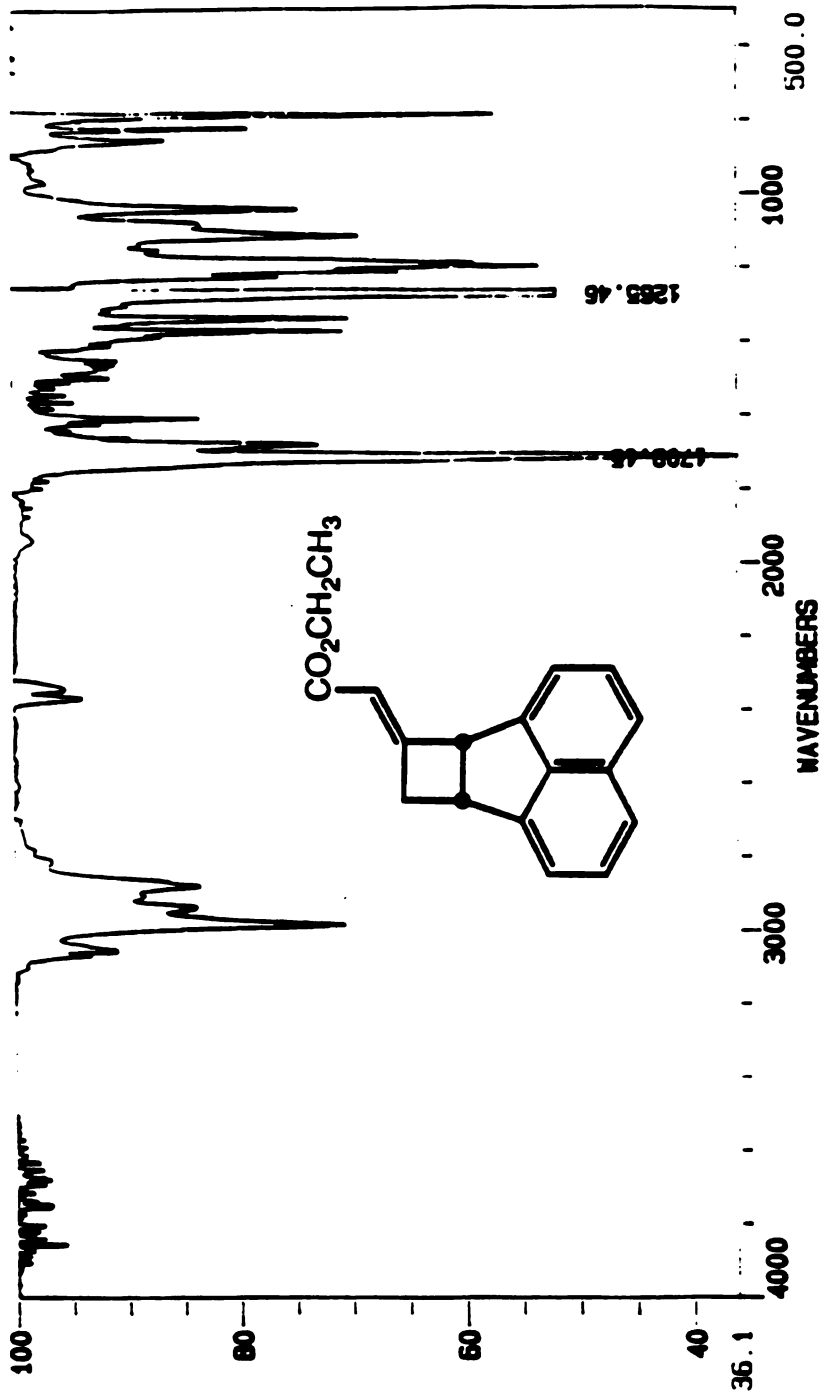

Figure 54. Infrared Spectrum of 8a.

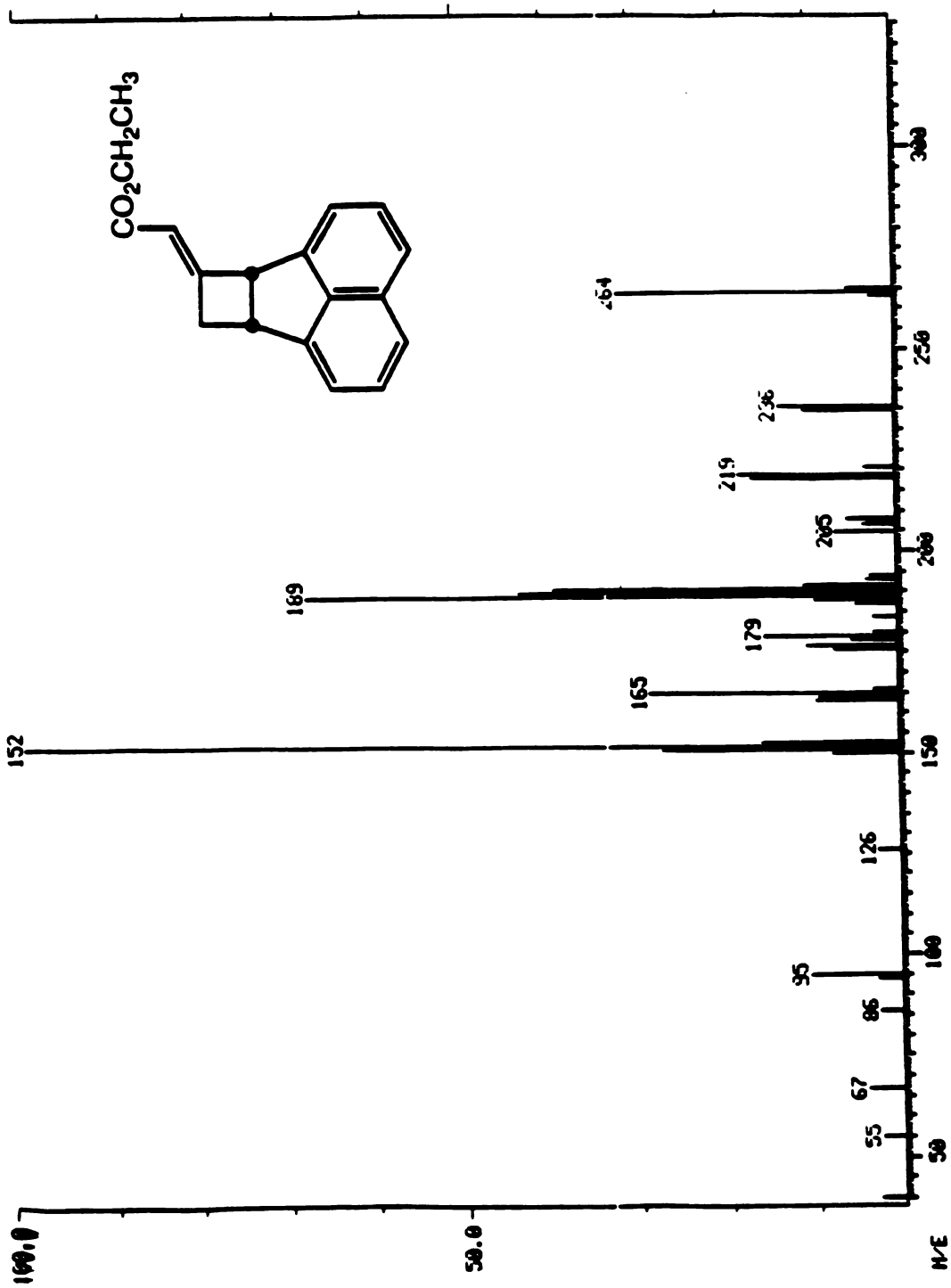

Figure 55. Mass Spectrum of 8a.

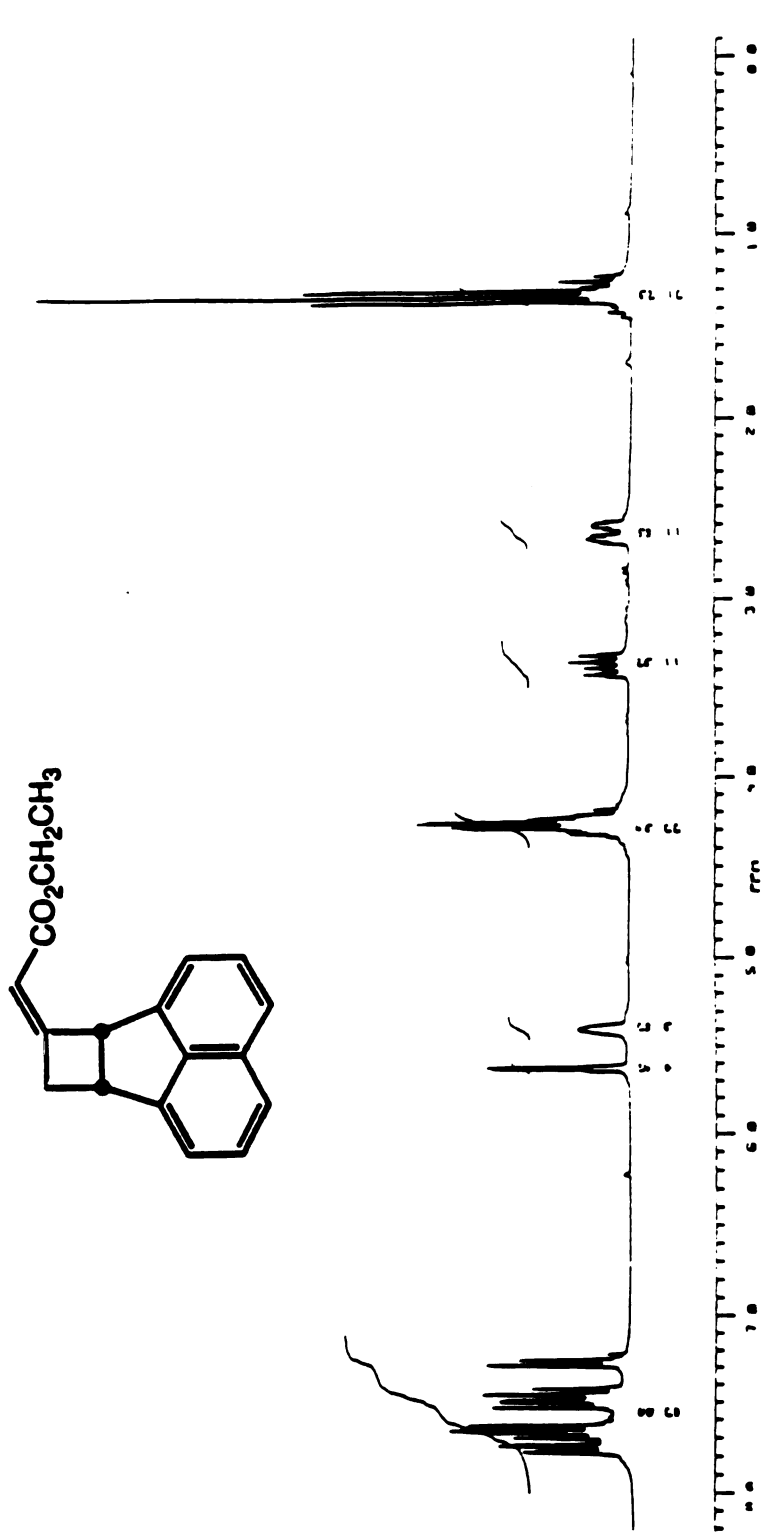

Figure 56. ^{1}H NMR Spectrum of 8b.

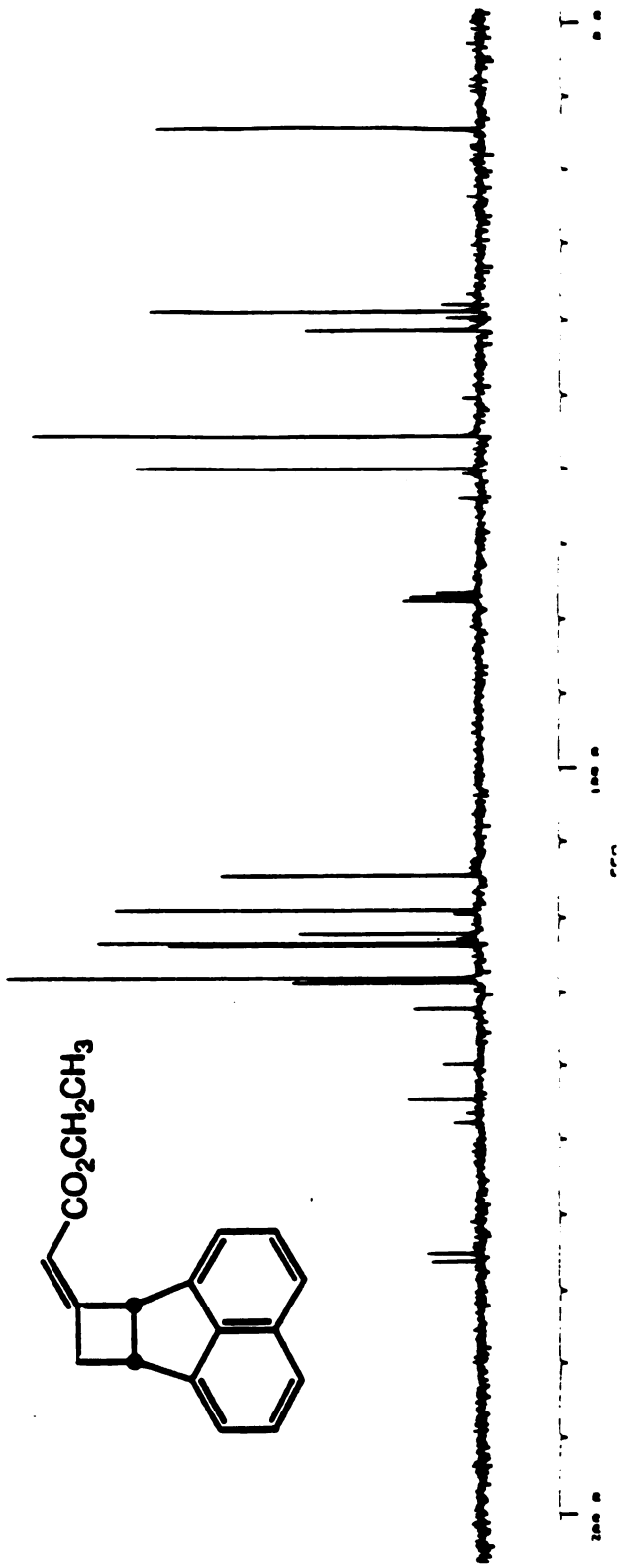

Figure 57. ^{13}C NMR Spectrum of **8b**.

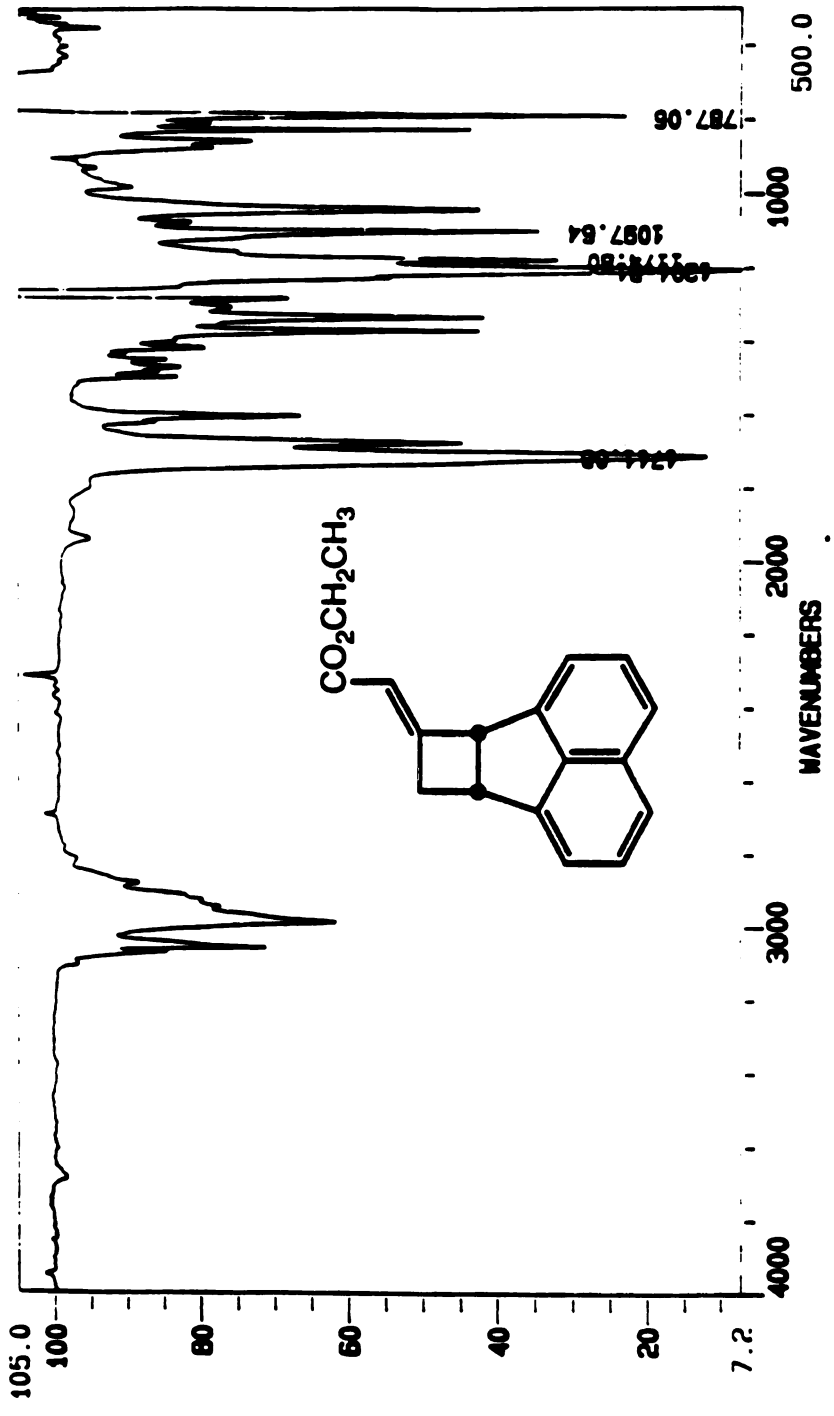

Figure 58. Infrared Spectrum of **8b**.

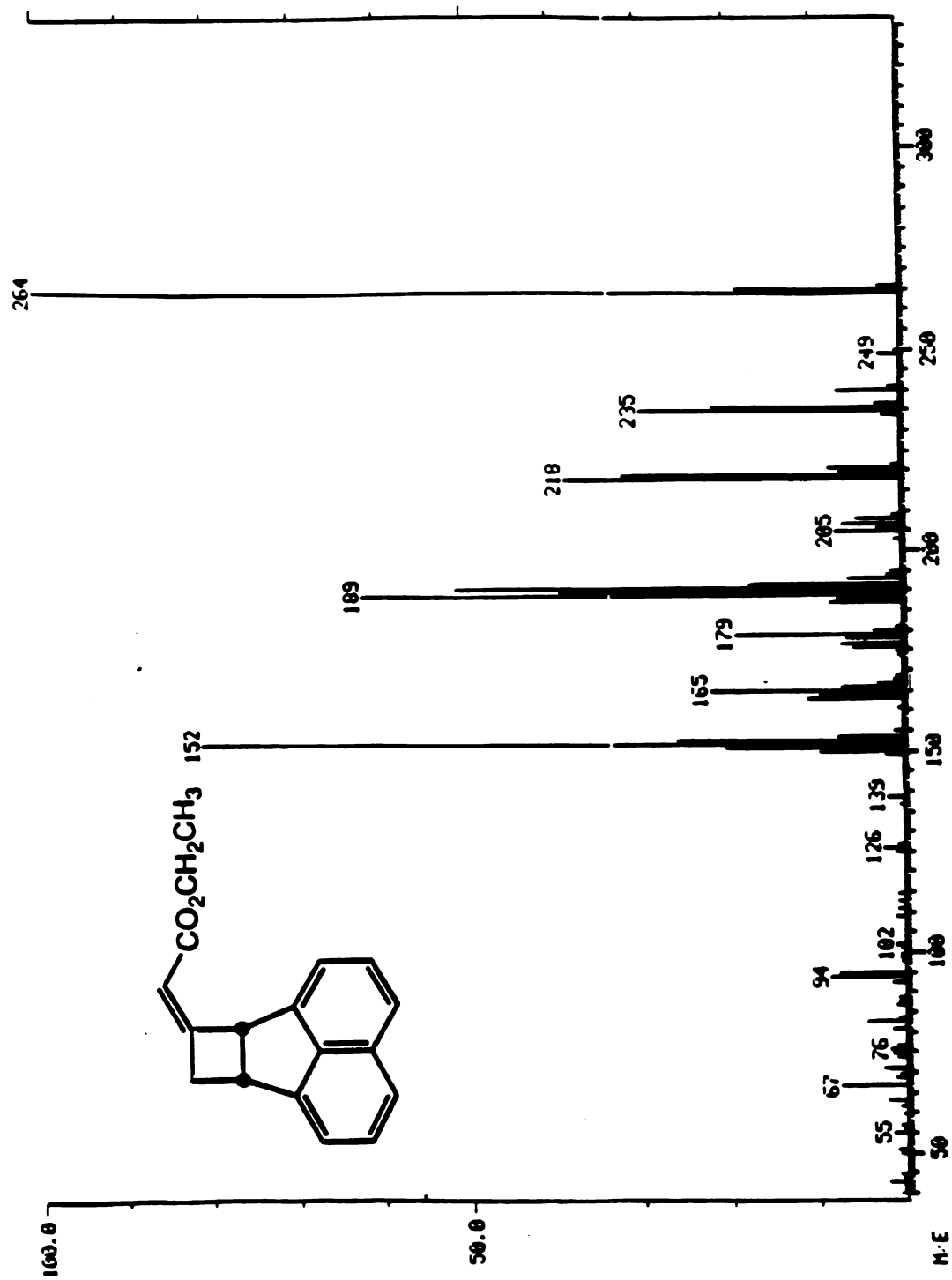

Figure 59. Mass Spectrum of 8b.

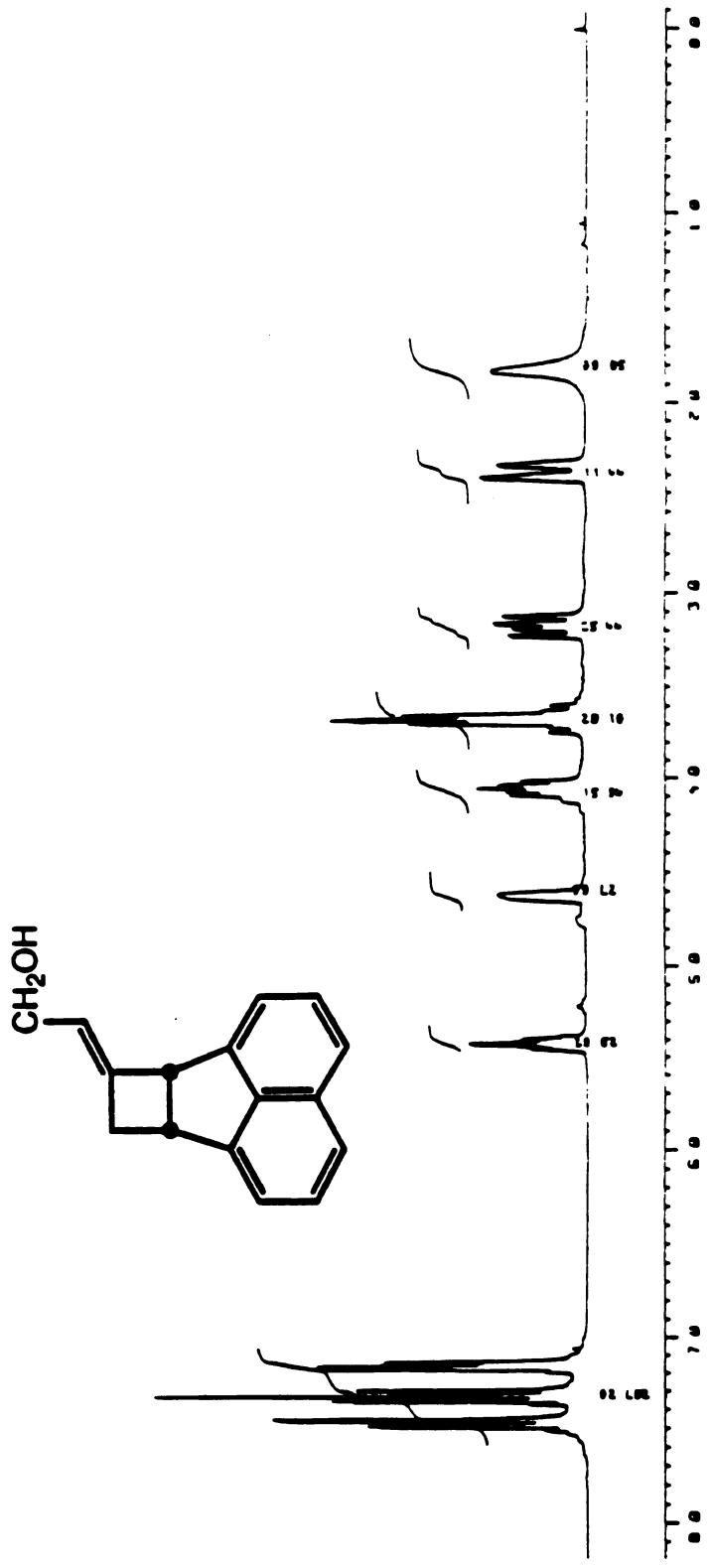

Figure 60. ^{1}H NMR Spectrum of **9**.

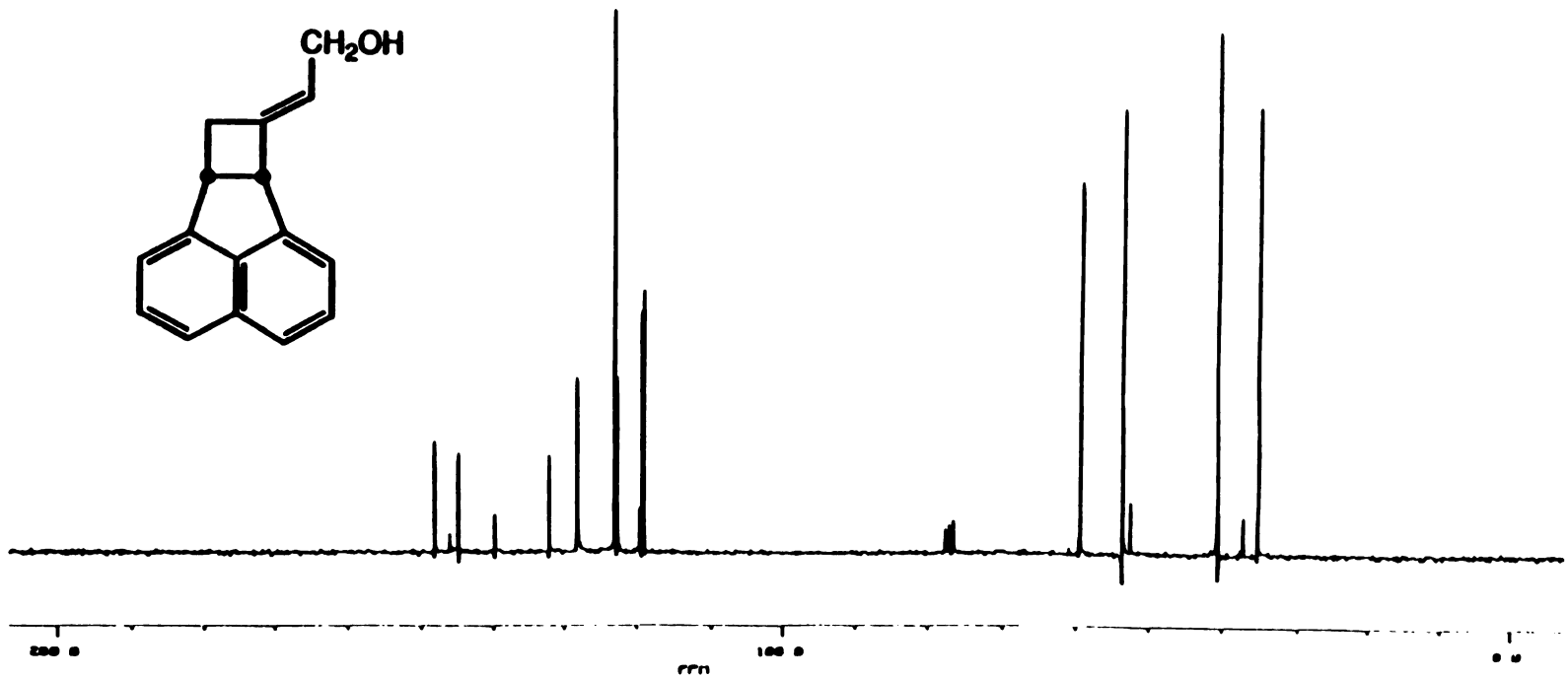

Figure 61. ^{13}C NMR Spectrum of 9.

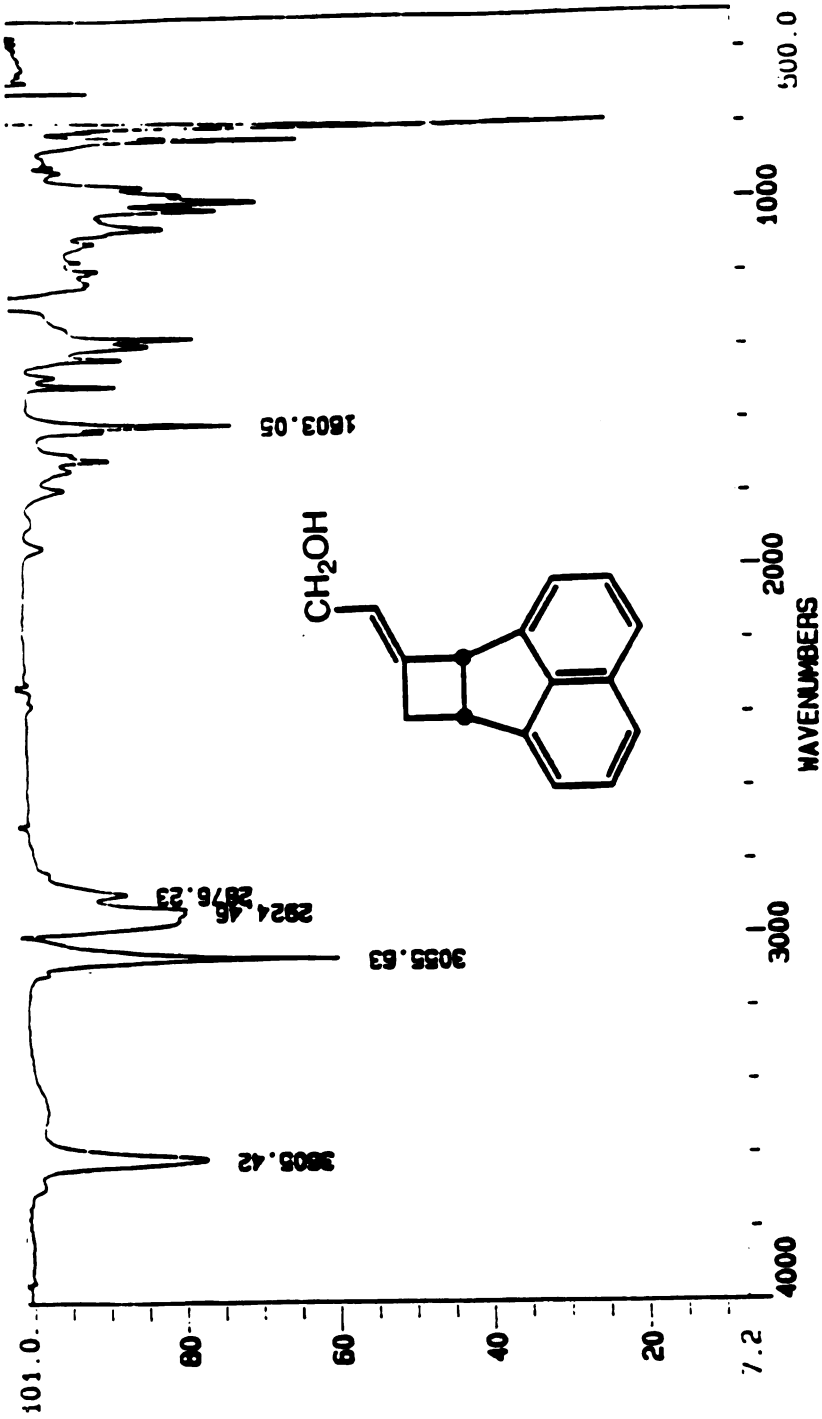

Figure 62. Infrared Spectrum of **9**.

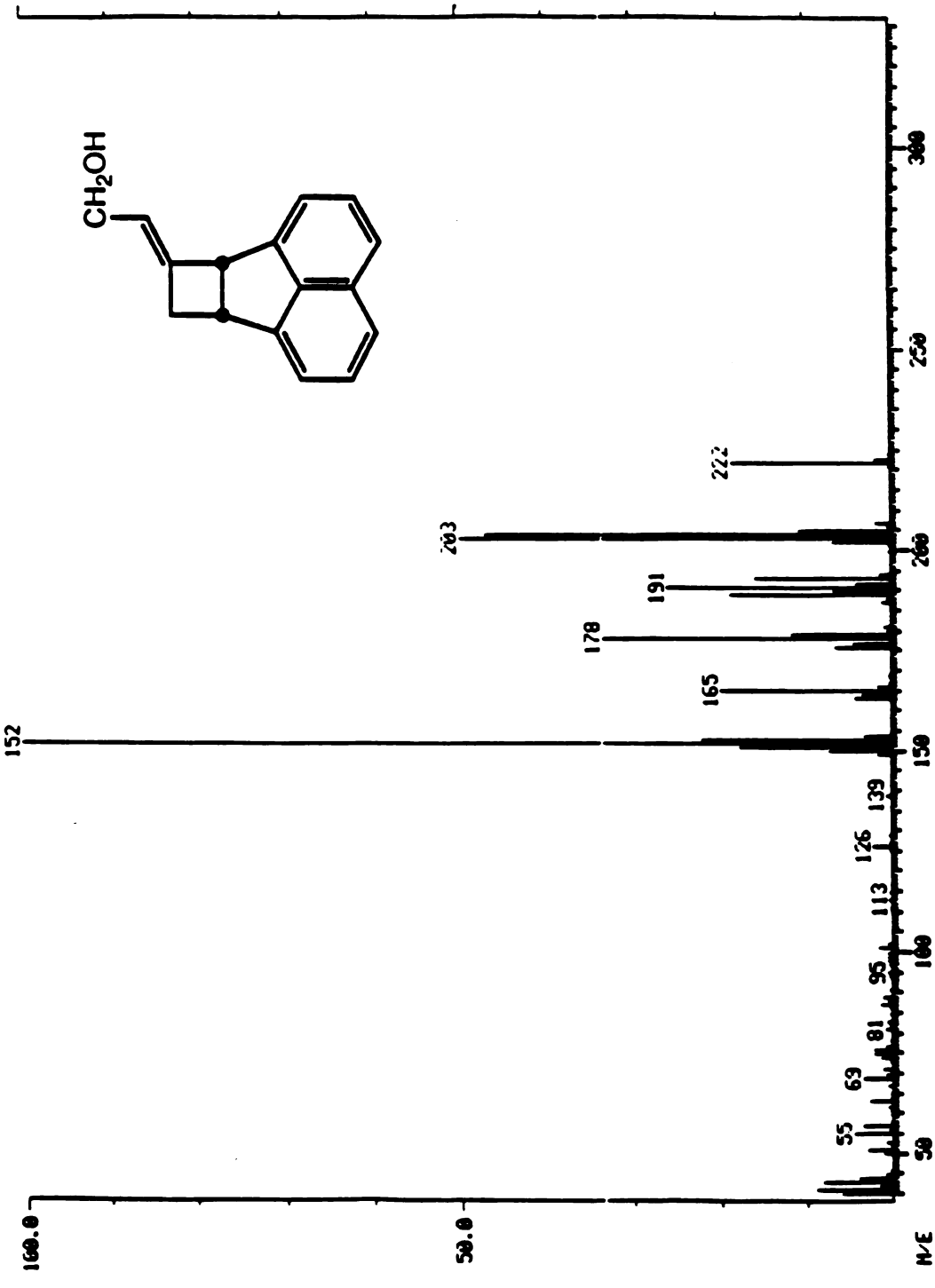

Figure 63. Mass Spectrum of 9.

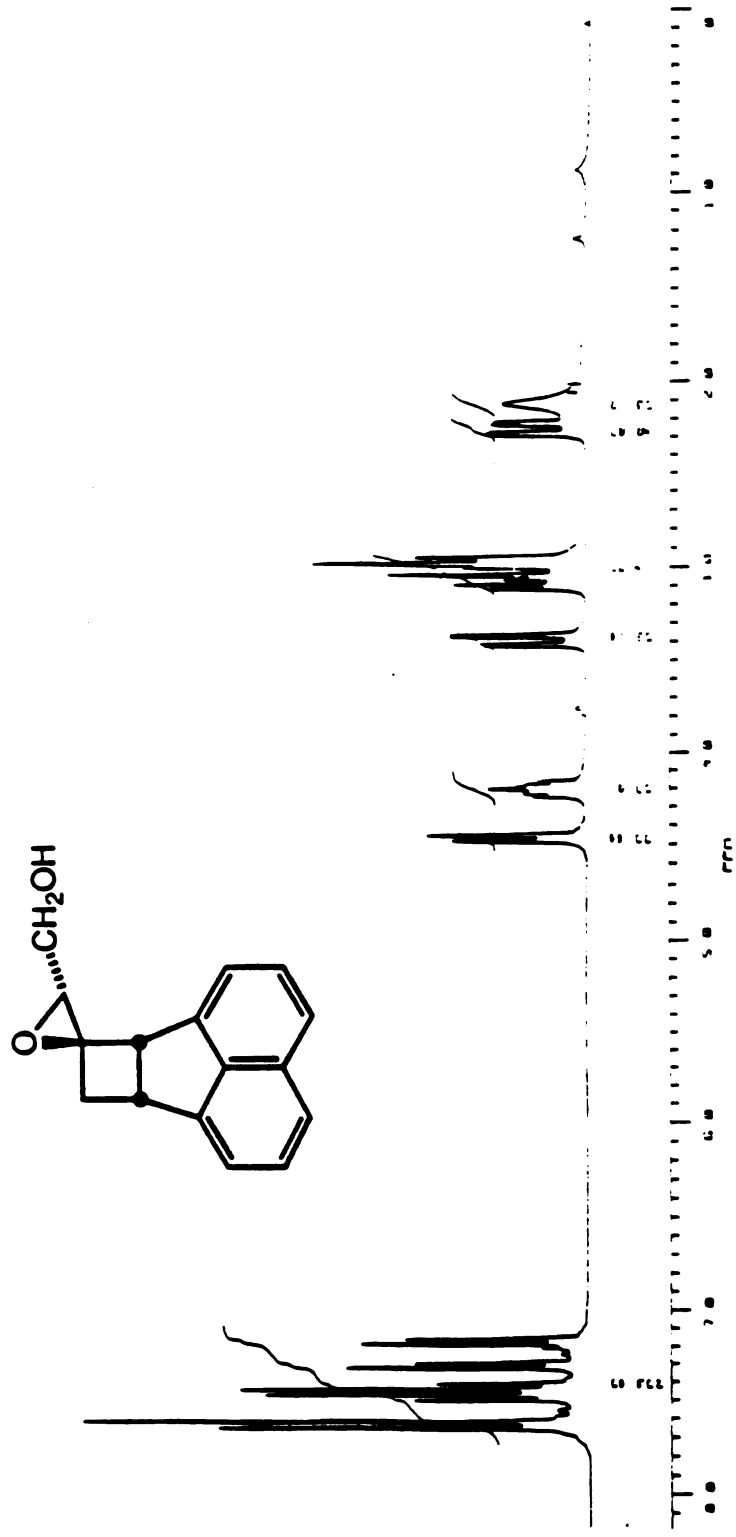

Figure 64. ^{1}H NMR Spectrum of 10a.

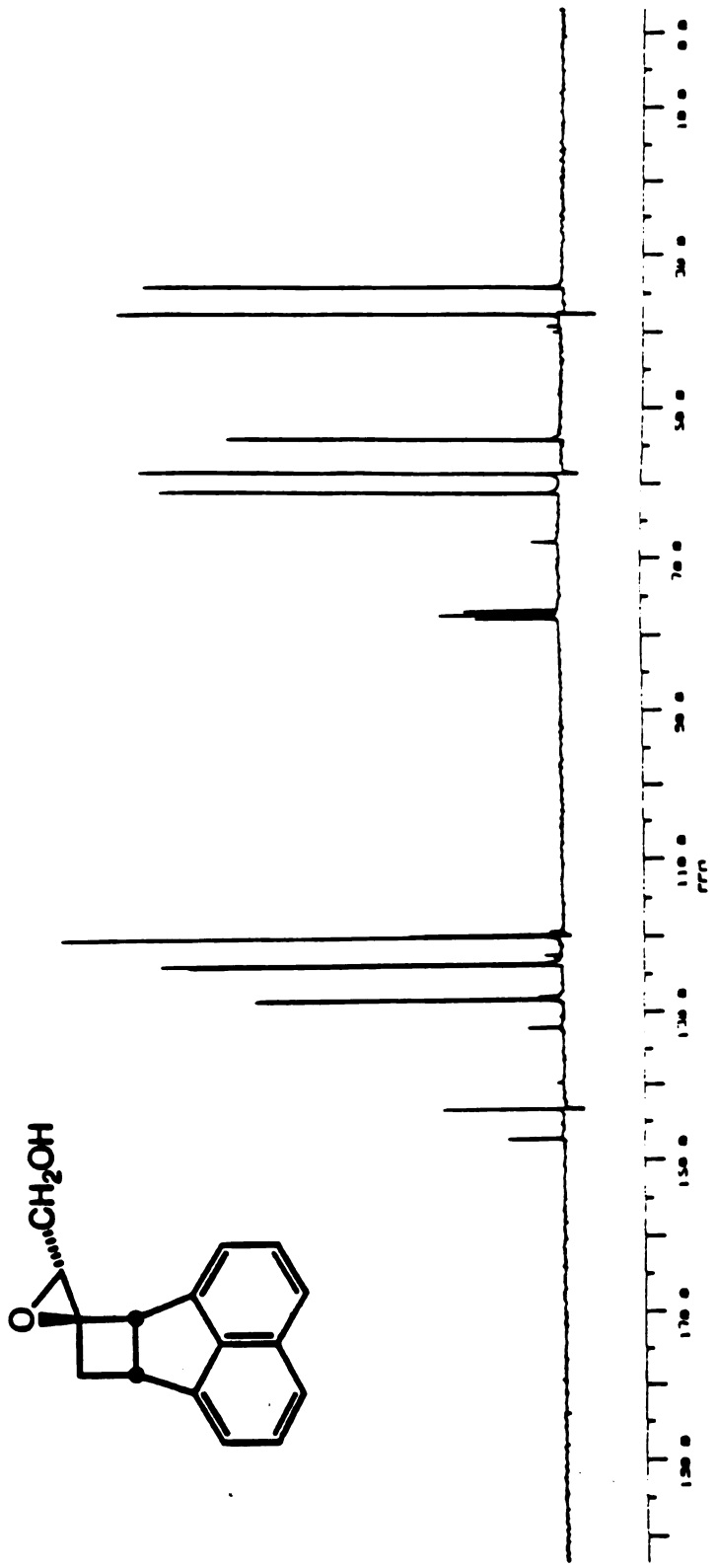

Figure 65. ^{13}C NMR Spectrum of **10a**.

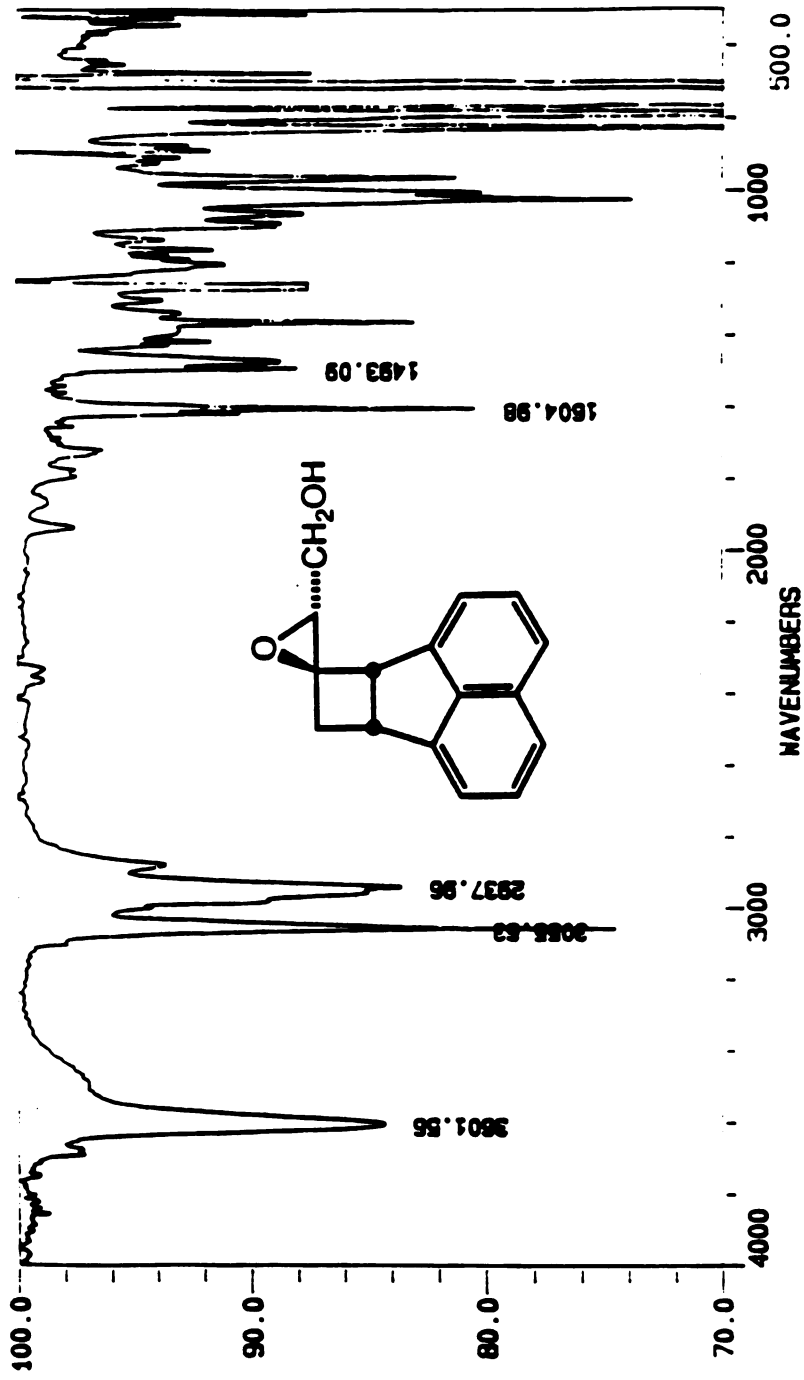

Figure 66. Infrared Spectrum of **10a**.

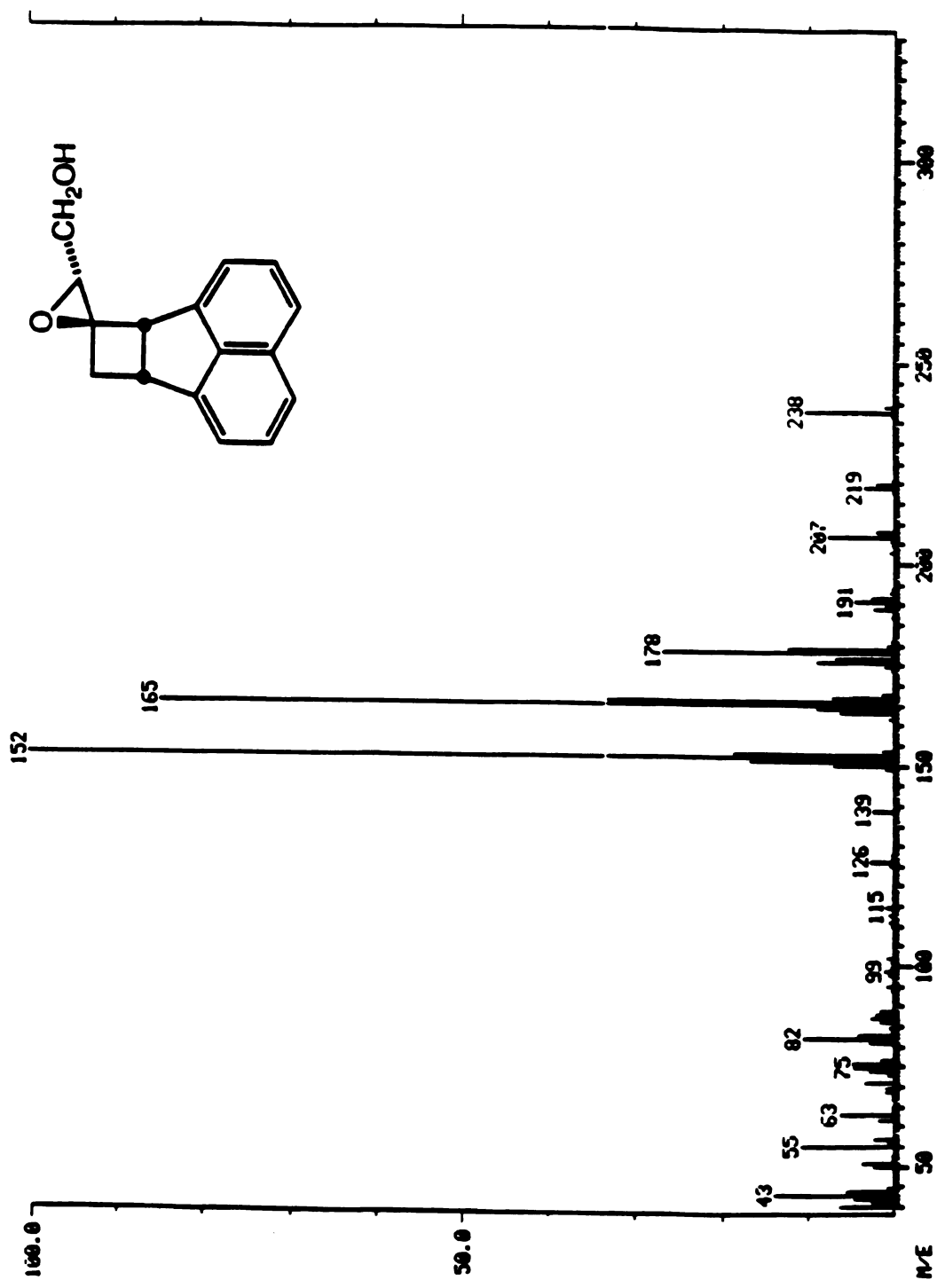

Figure 67. Mass Spectrum of 10a.

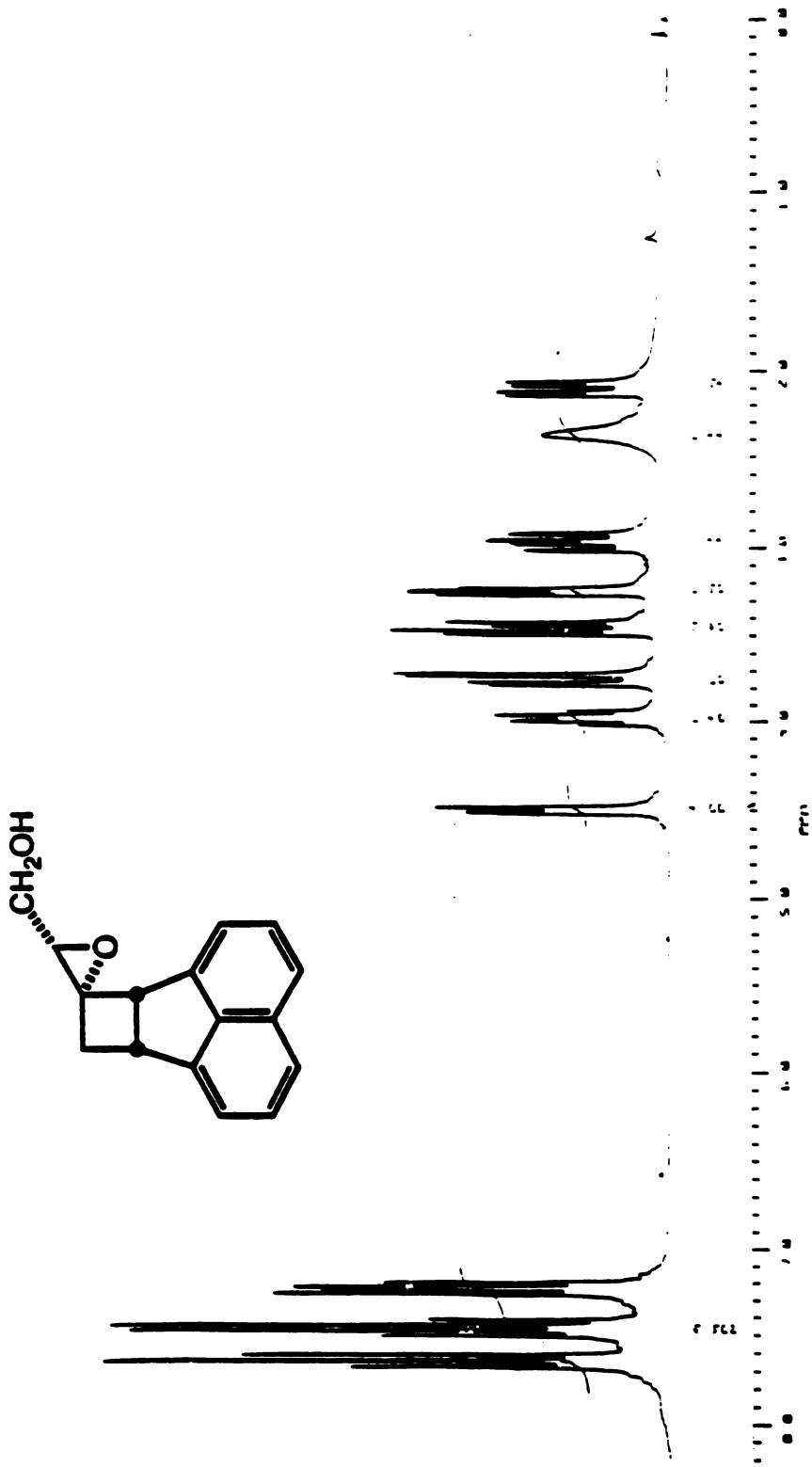

Figure 68. ^{1}H NMR Spectrum of 10b.

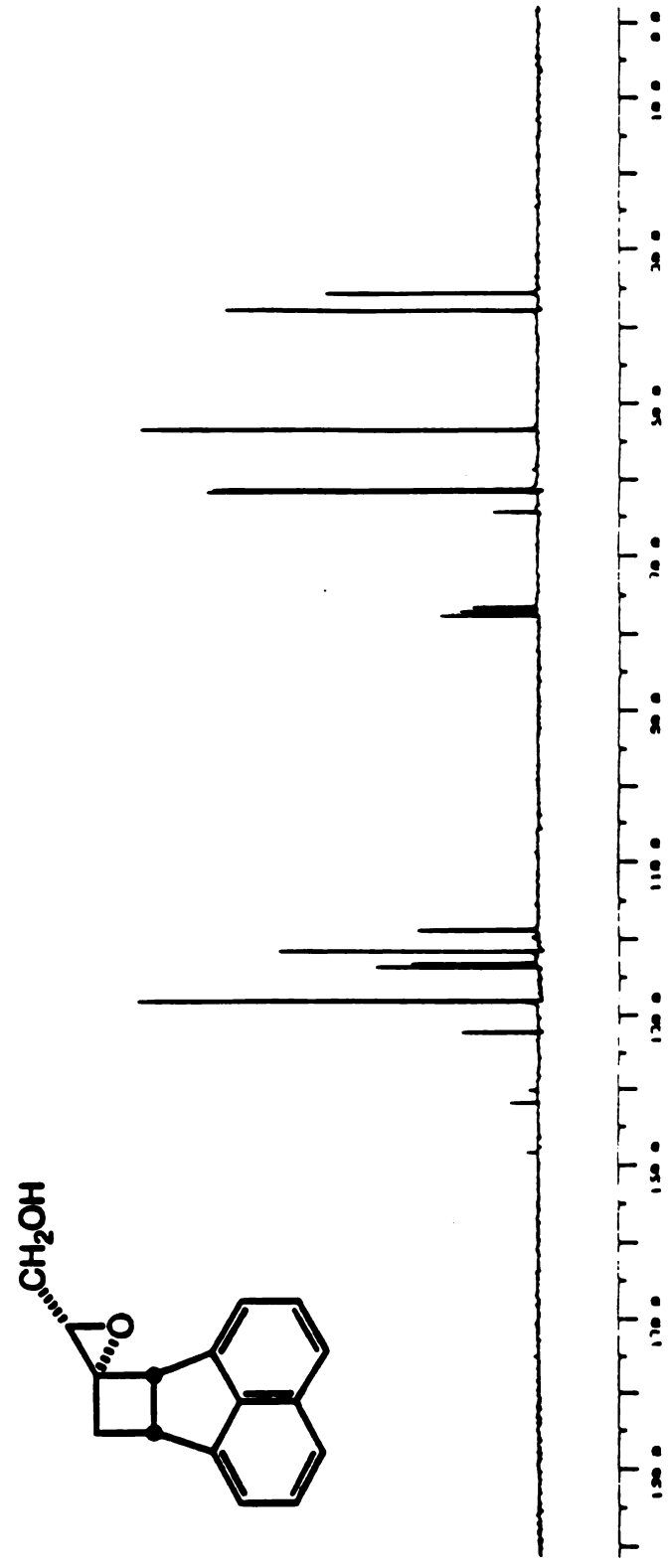

Figure 69. ^{13}C NMR Spectrum of **10b**.

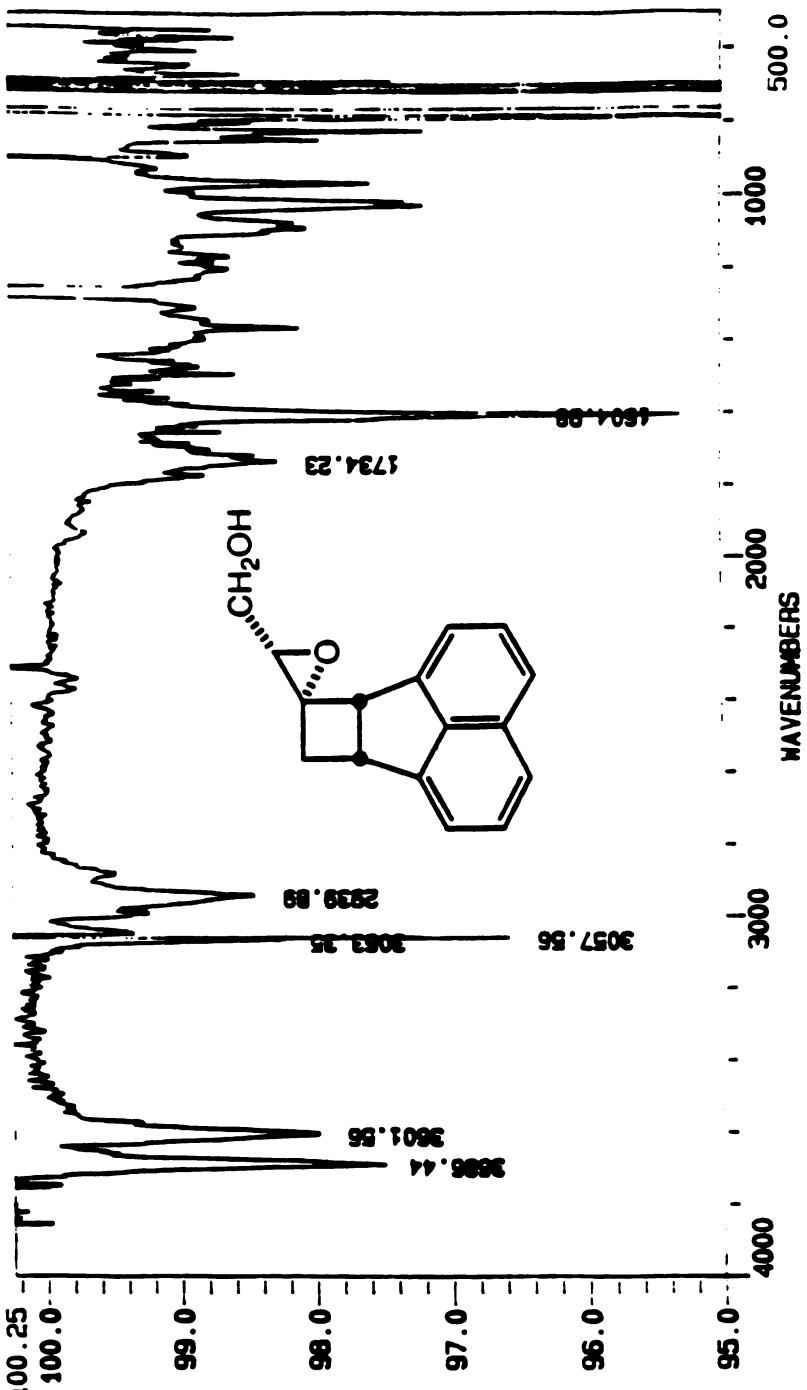

Figure 70. Infrared Spectrum of **10b**.

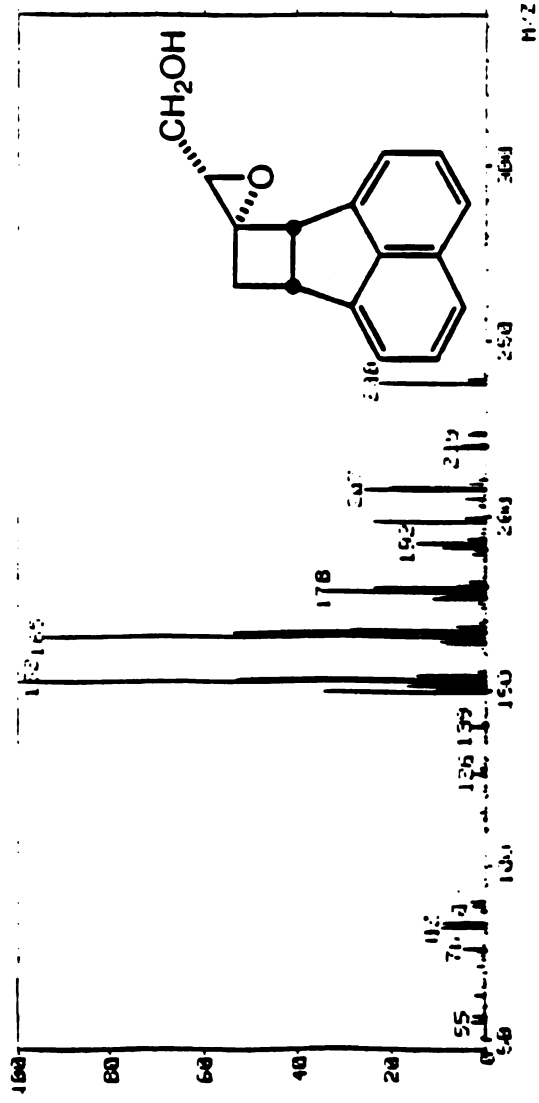

Figure 71. Mass Spectrum of **10b**.

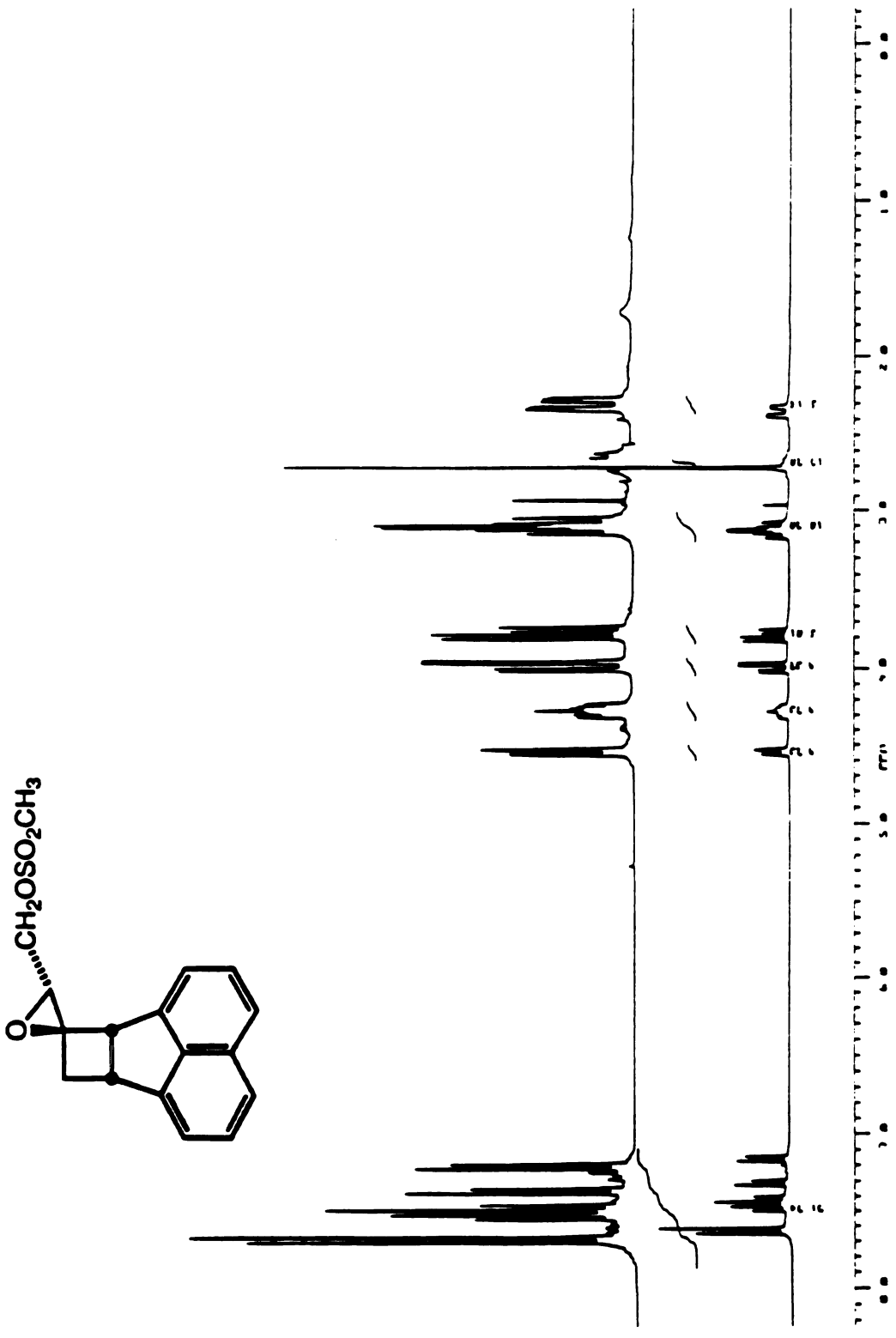

Figure 72. ^{1}H NMR Spectrum of 12a.

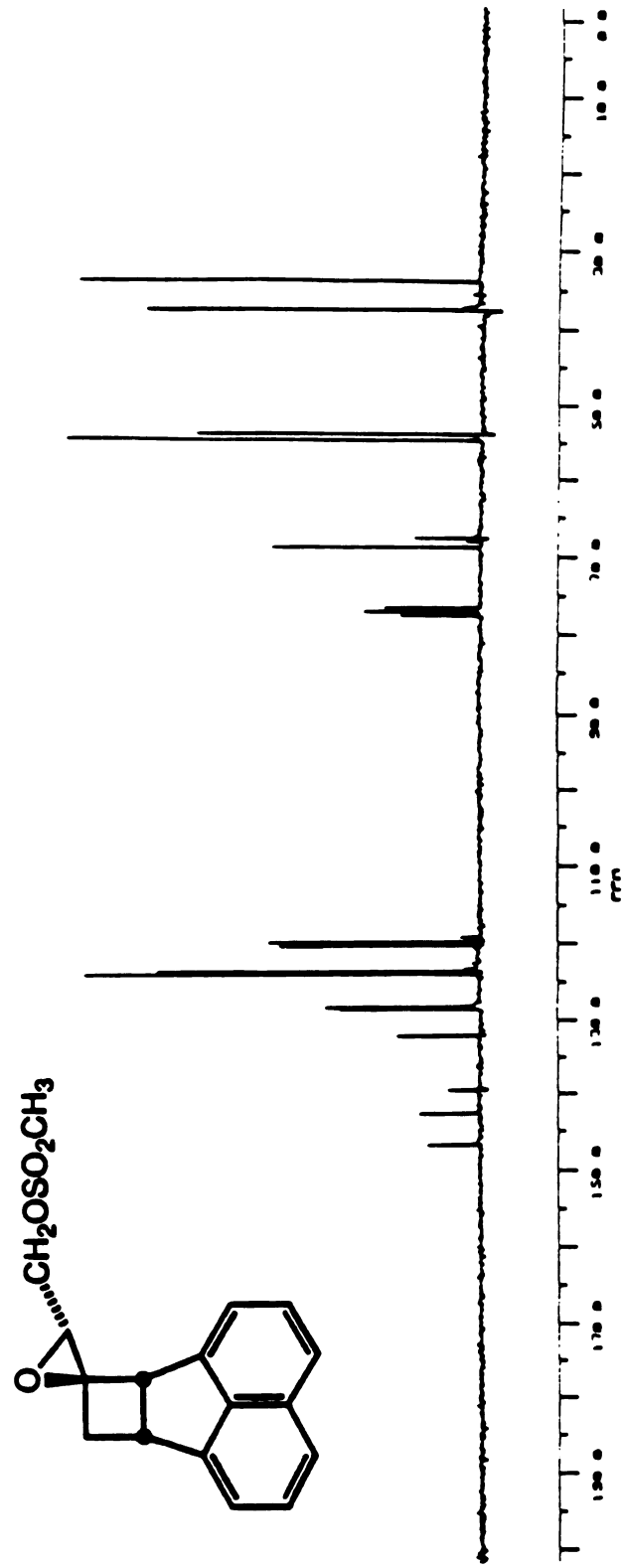

Figure 73. ^{13}C NMR Spectrum of 12a.

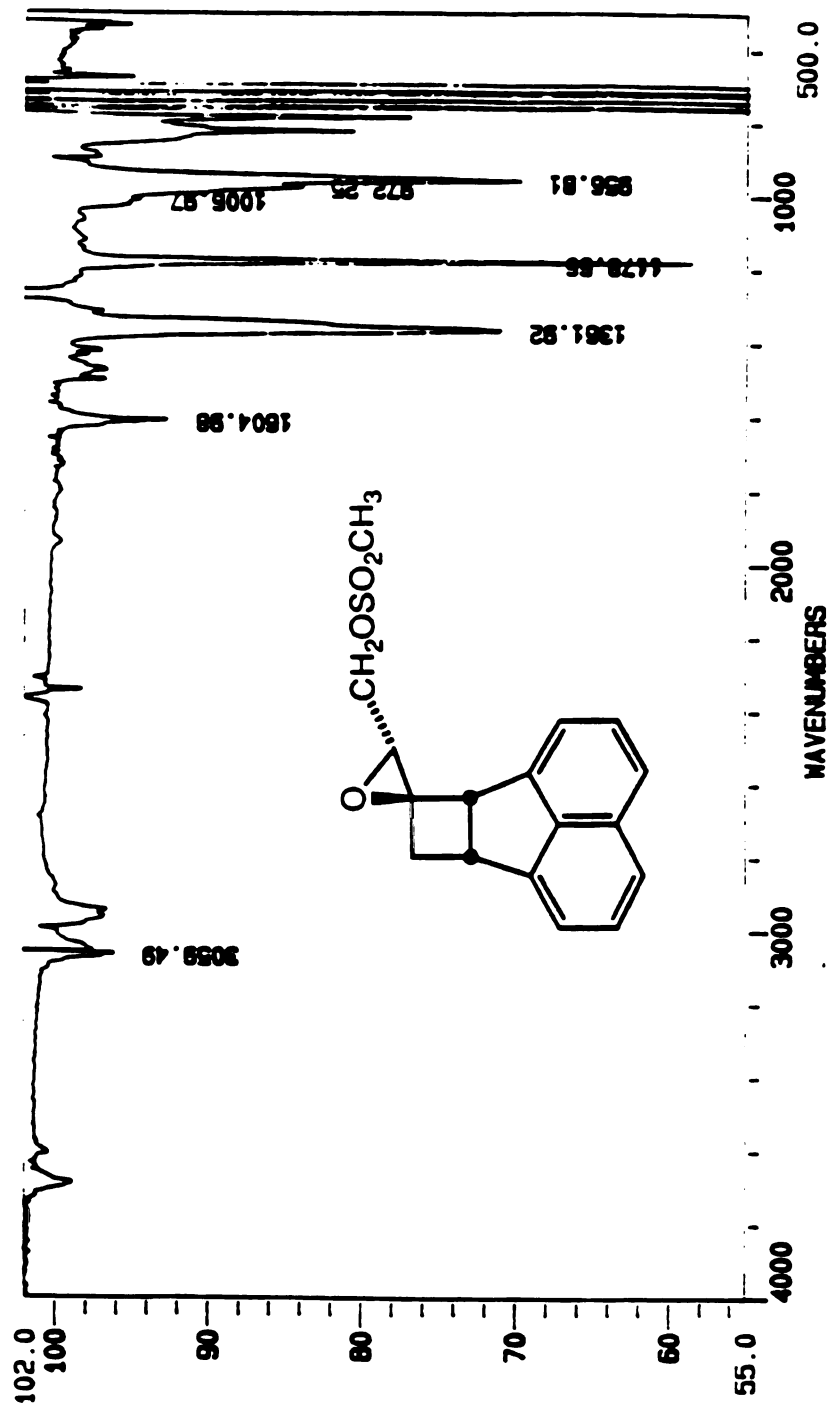

Figure 74. Infrared Spectrum of 12a.

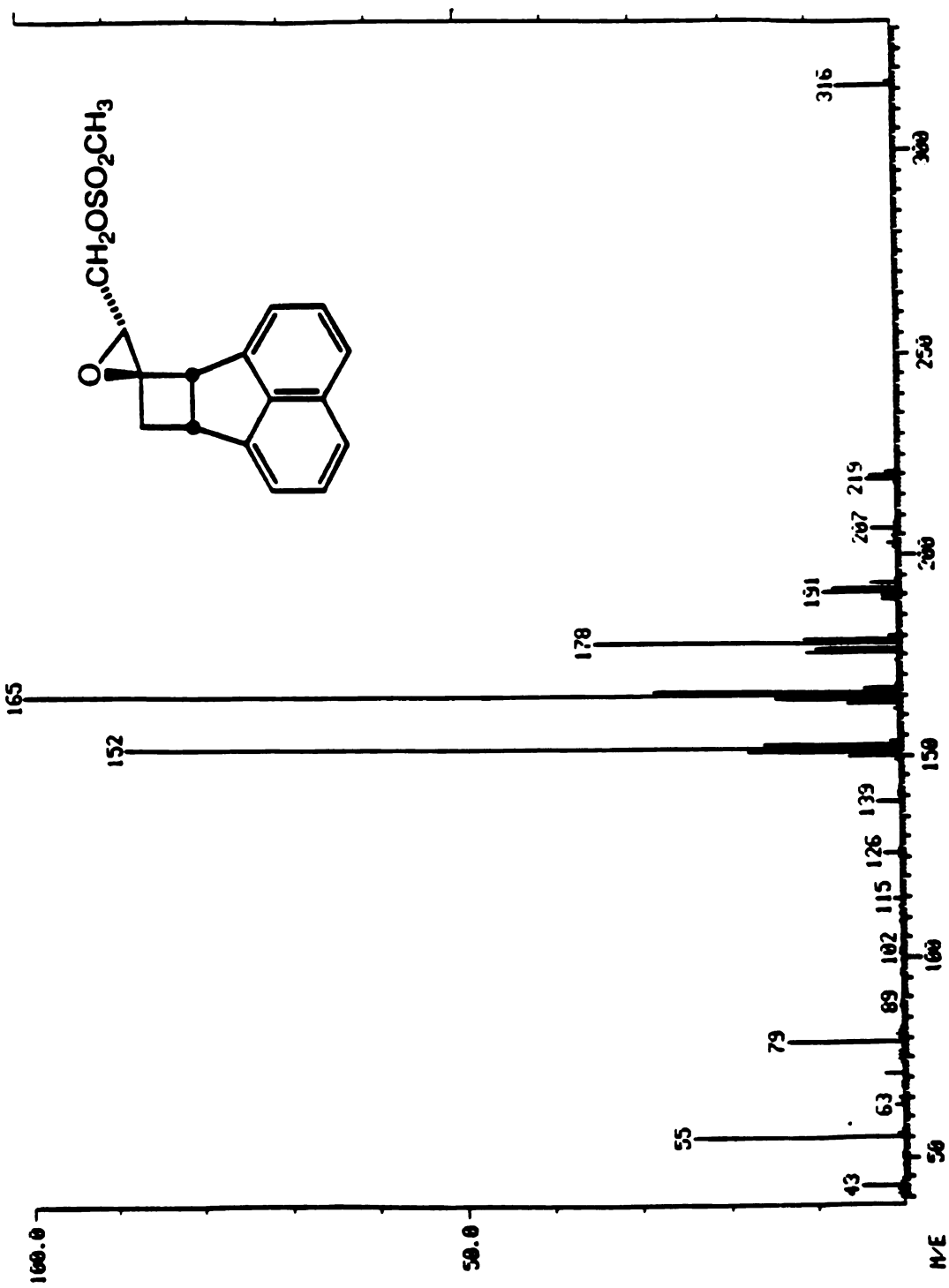

Figure 75. Mass Spectrum of 12a.

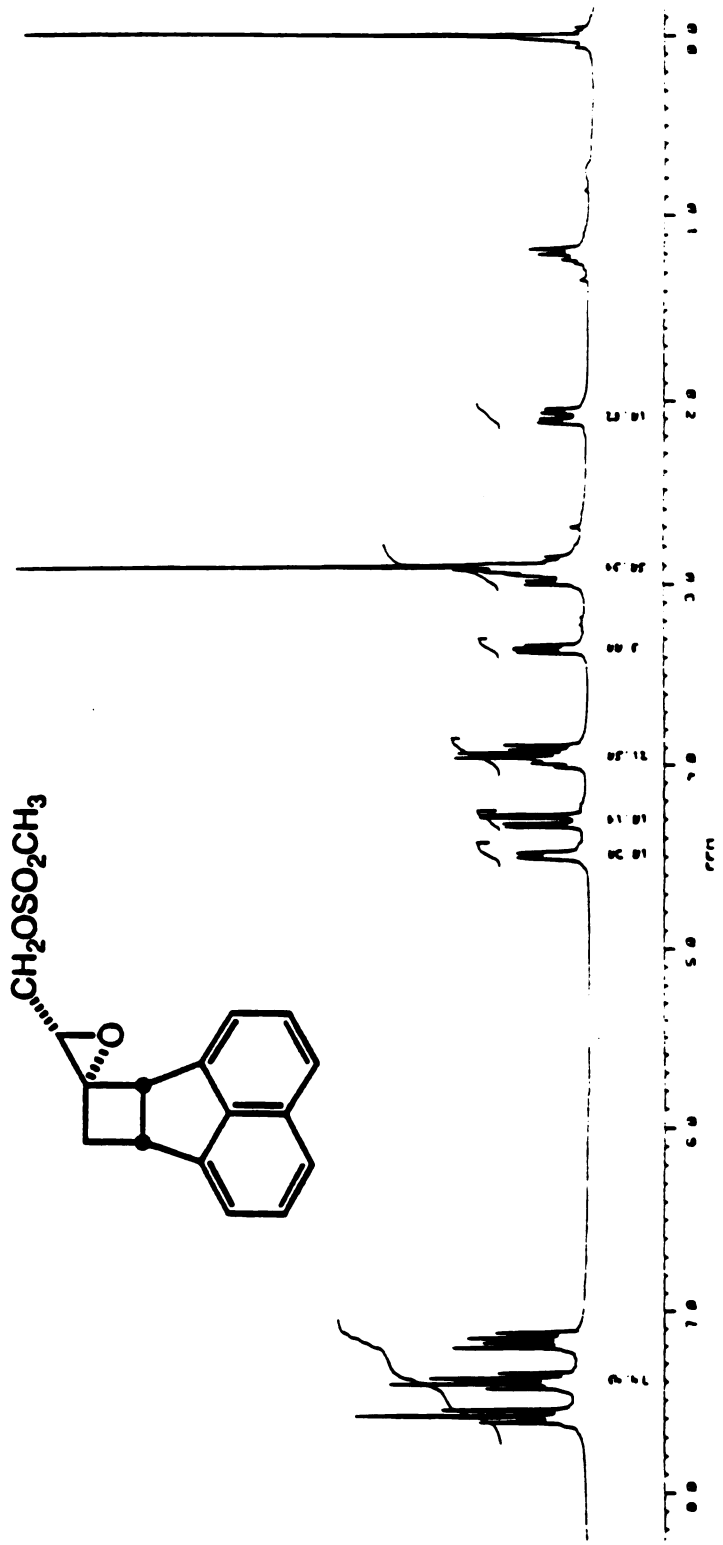

Figure 76. ^{1}H NMR Spectrum of 12b.

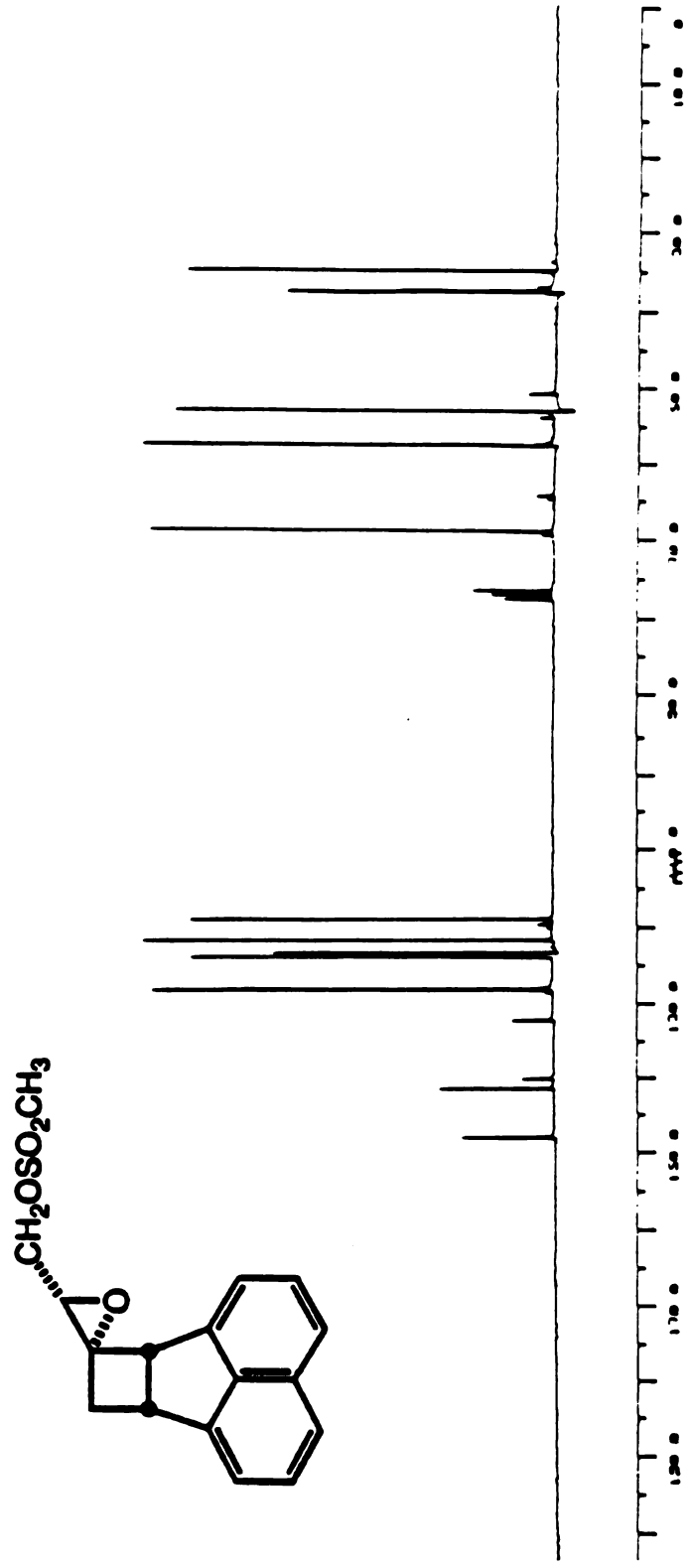

Figure 77. ^{13}C NMR Spectrum of 12b.

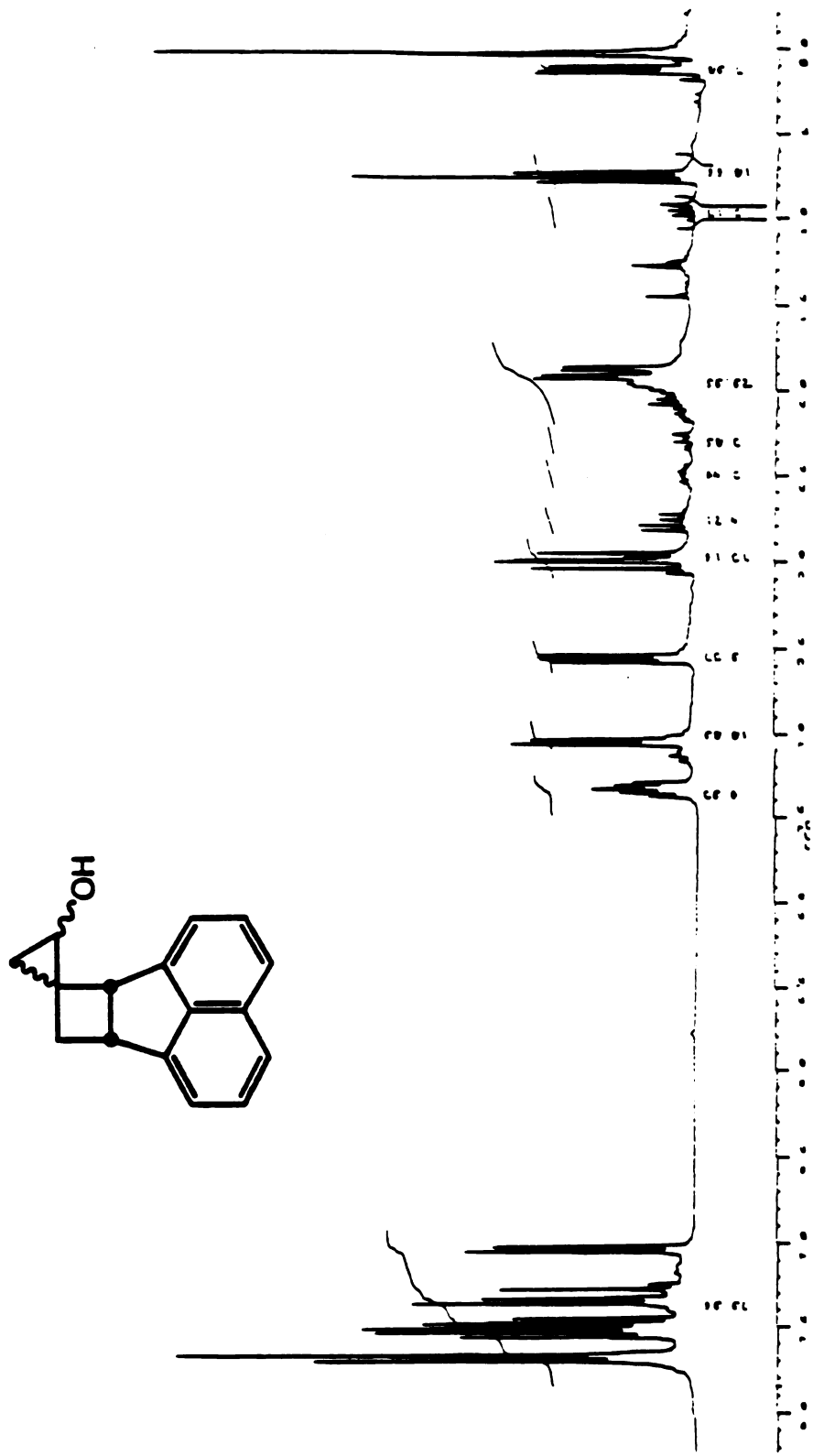

Figure 78. ^{1}H NMR Spectrum of 13.

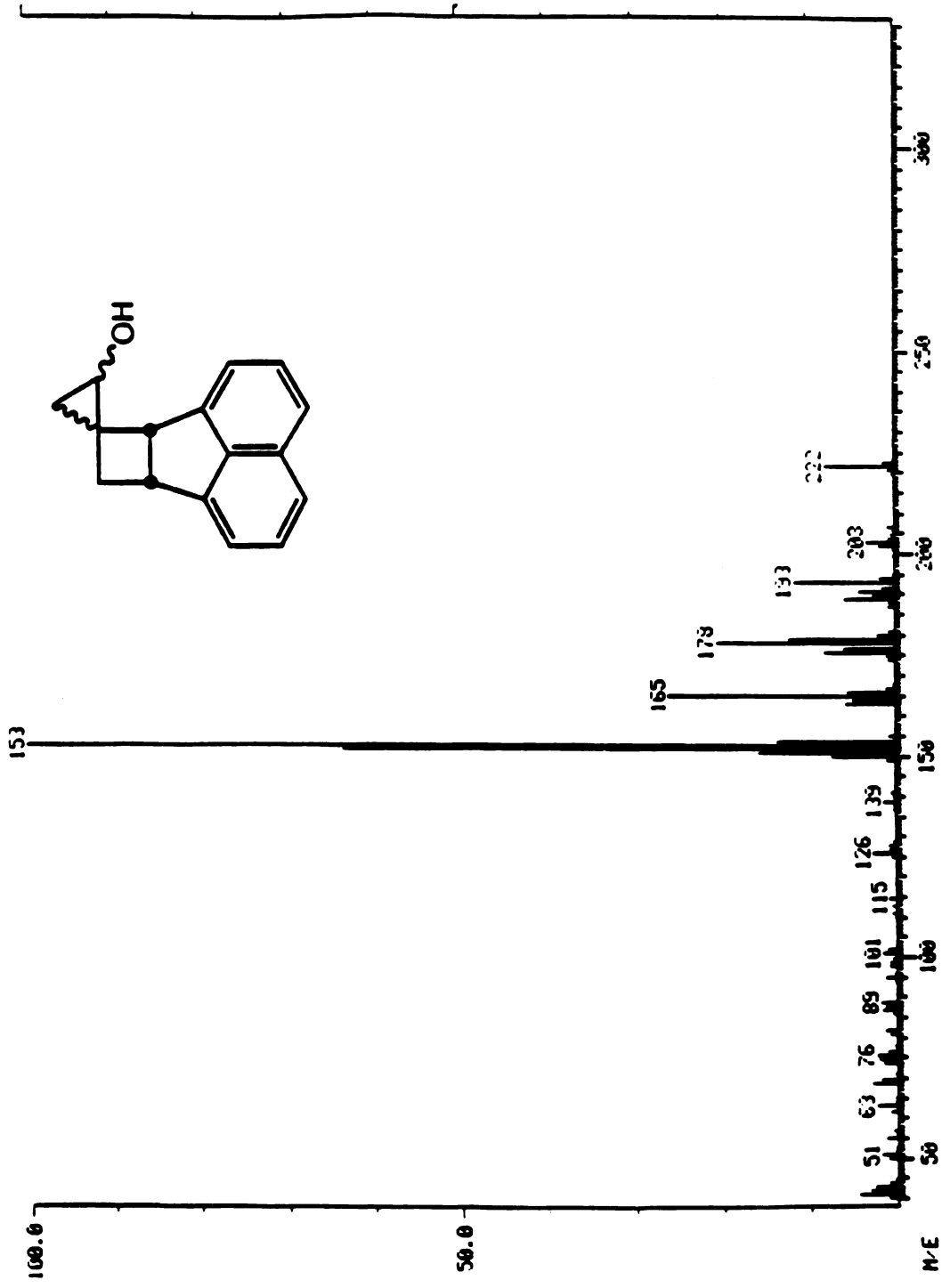

Figure 79. Mass Spectrum of 13.

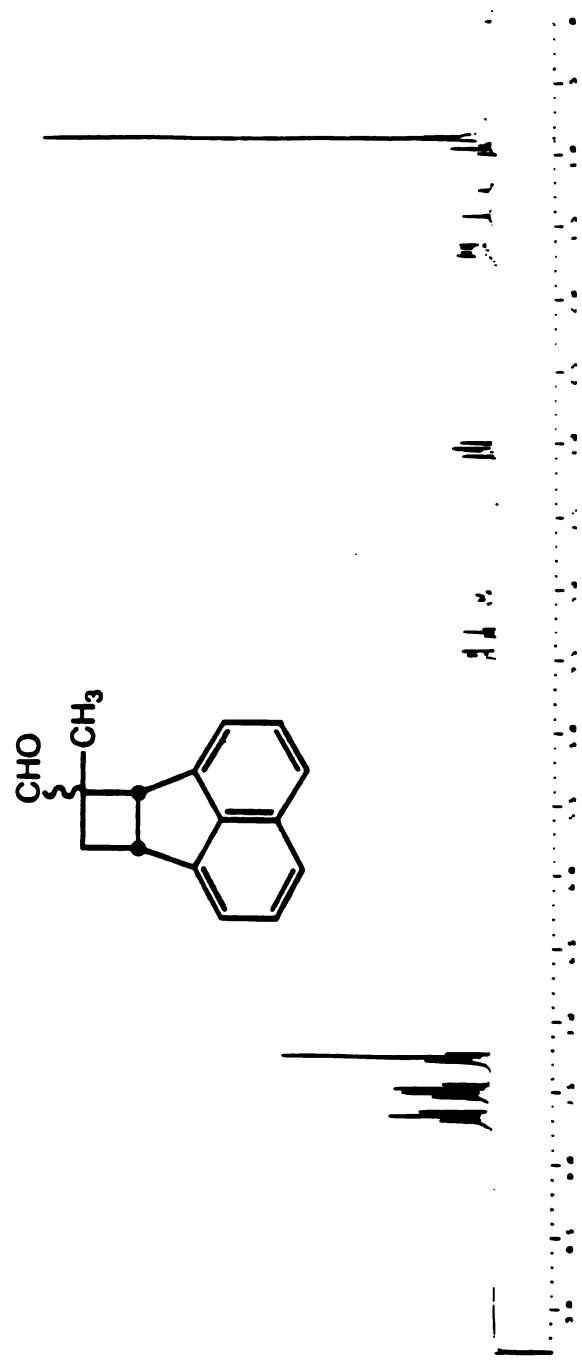

Figure 80. ^{1}H NMR Spectrum of 14.

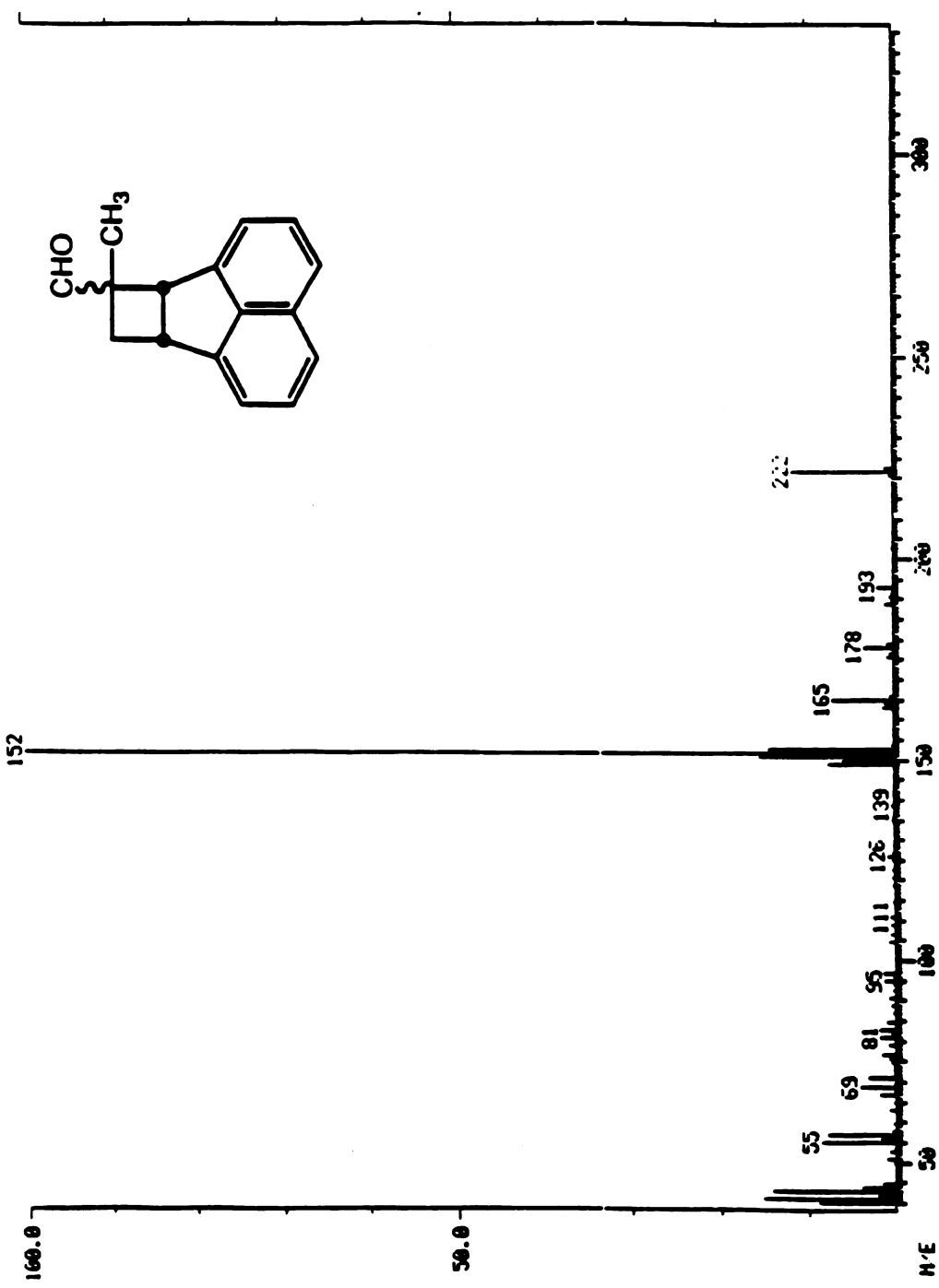

Figure 81. Mass Spectrum of 14.

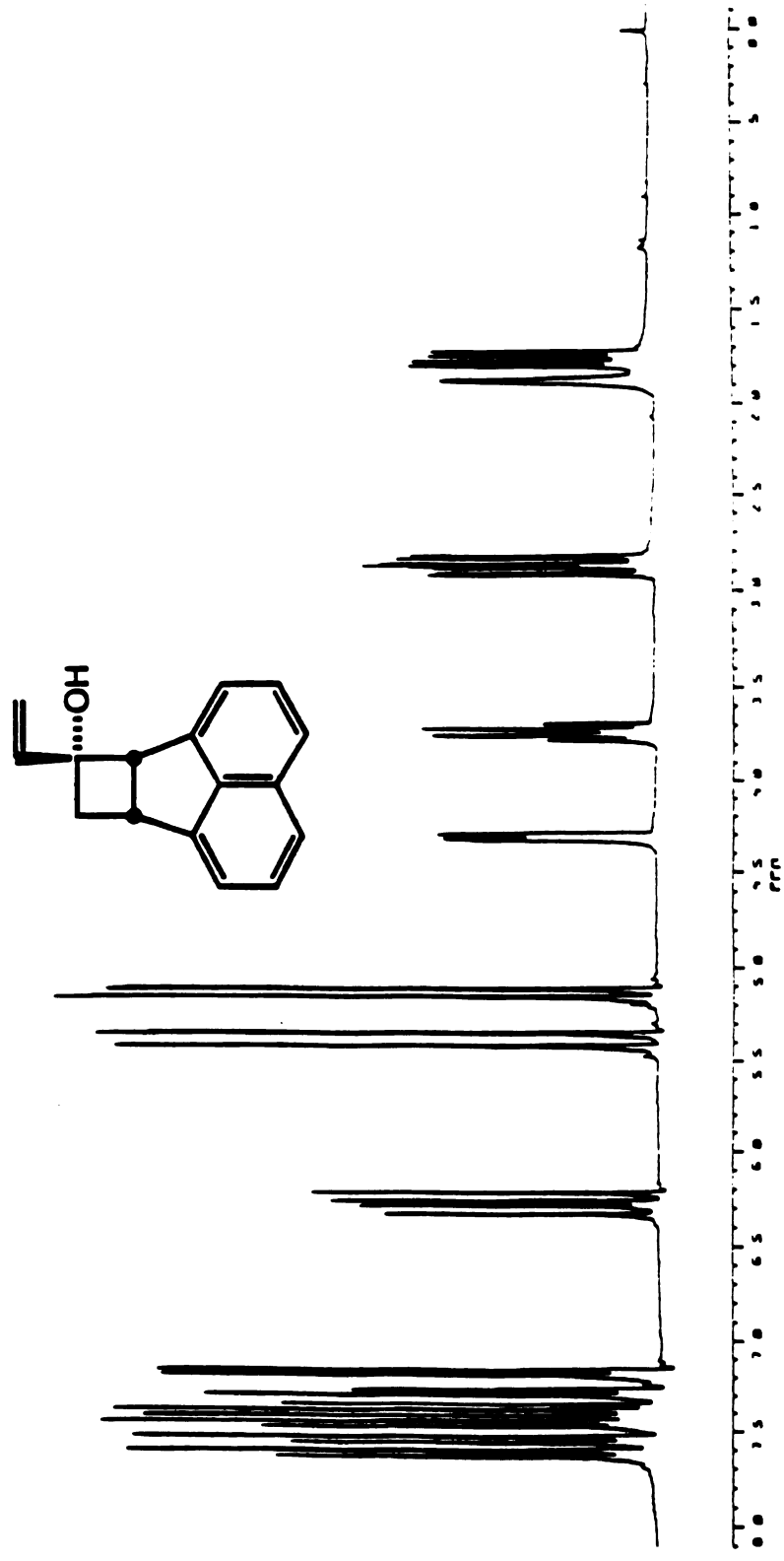

Figure 82. ^{1}H NMR Spectrum of **19**.

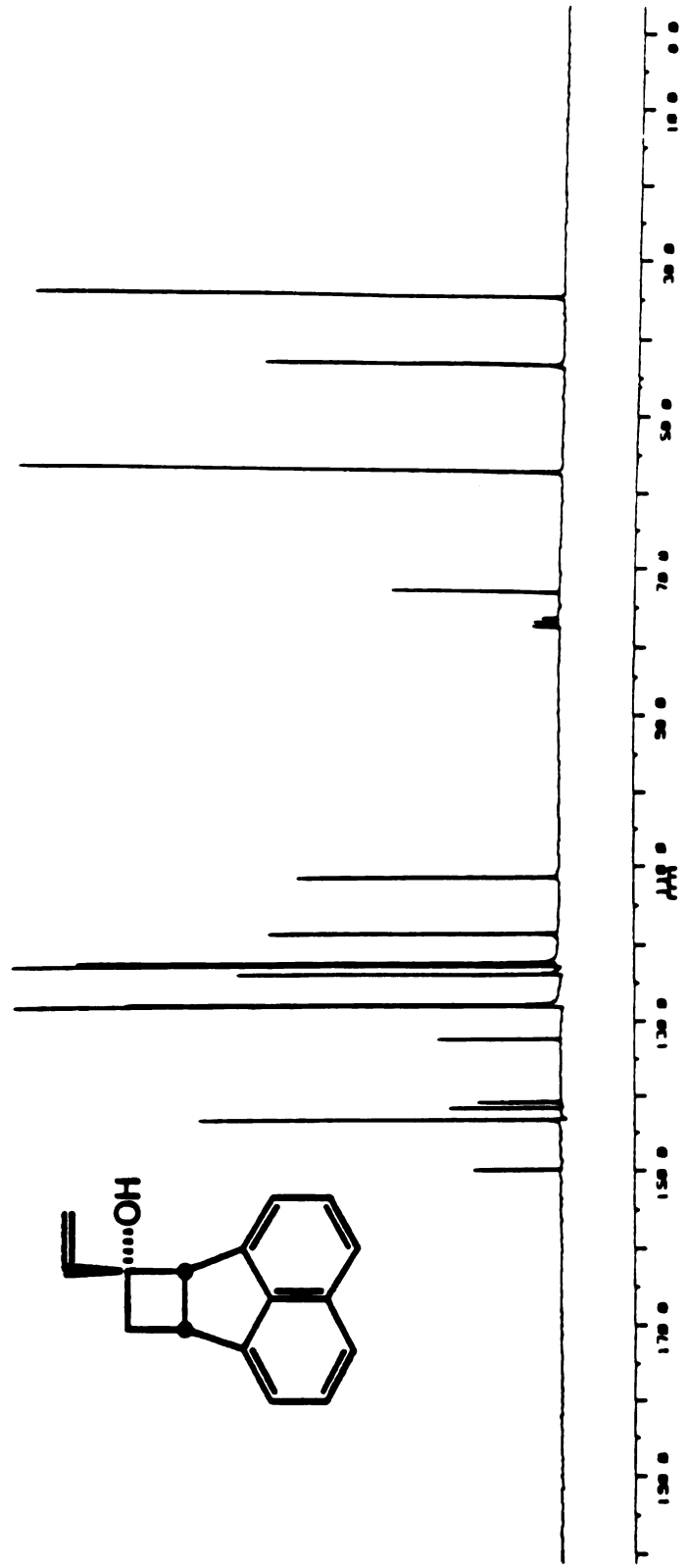

Figure 83. ^{13}C NMR Spectrum of **19**.

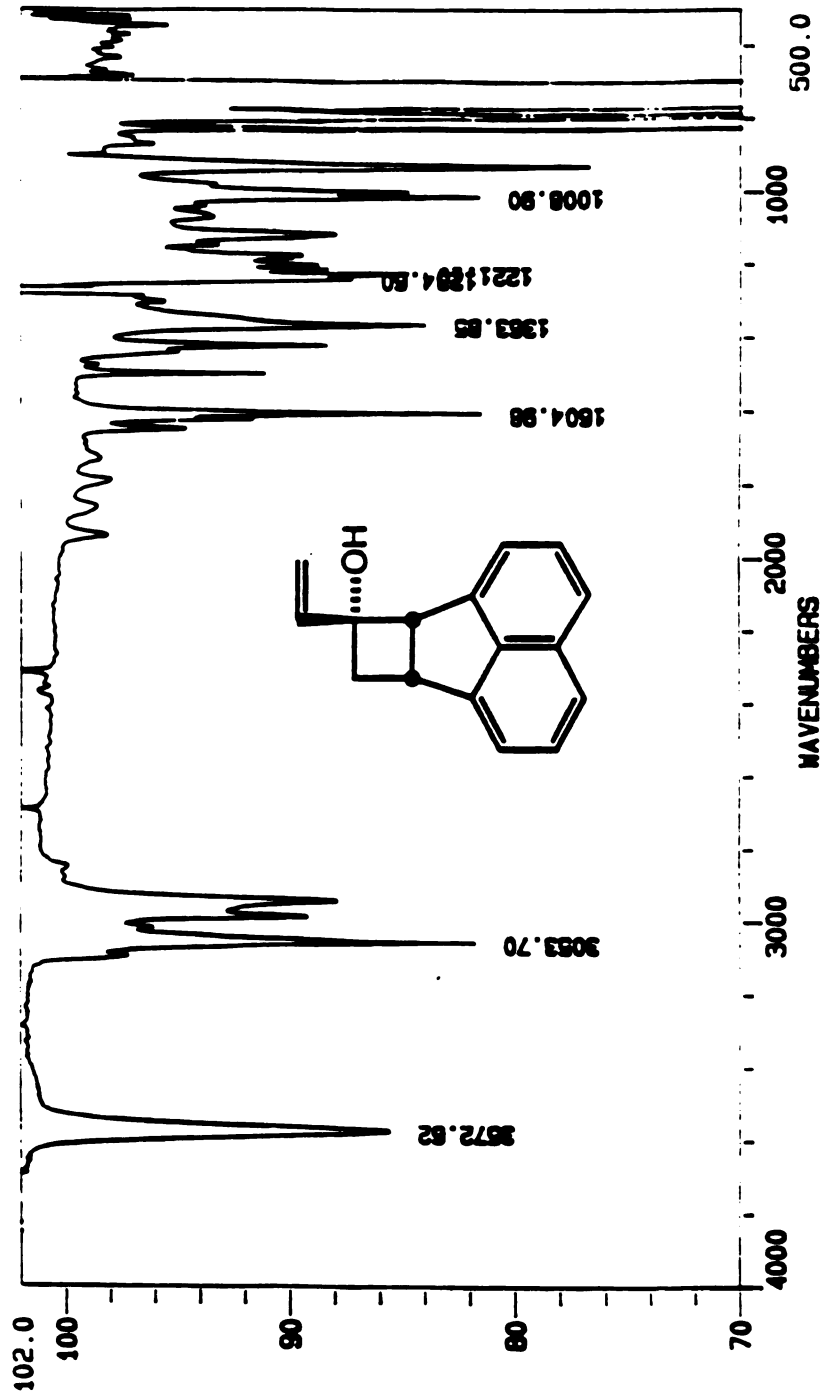

Figure 84. Infrared Spectrum of **19**.

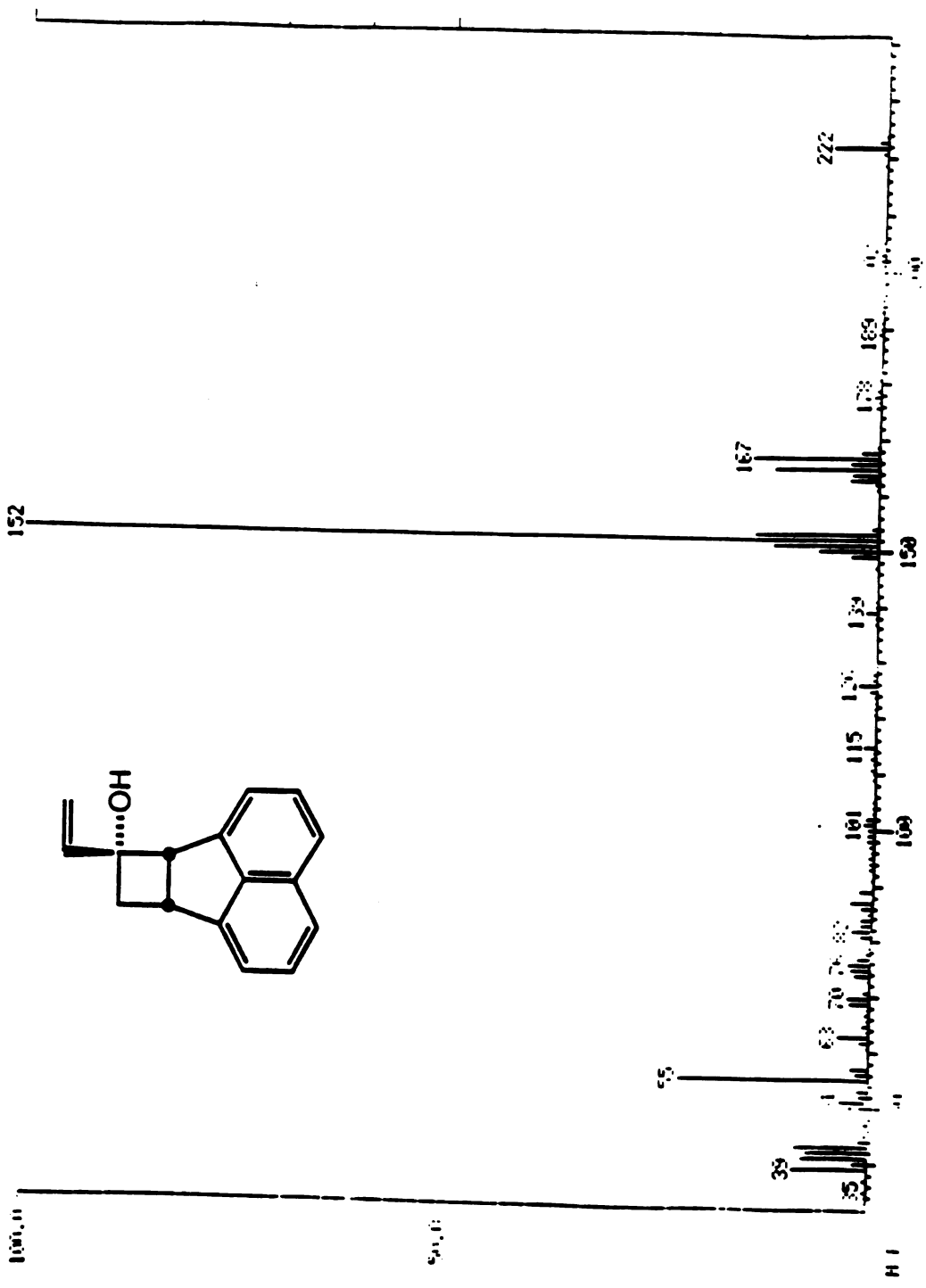

Figure 85. Mass Spectrum of 19.

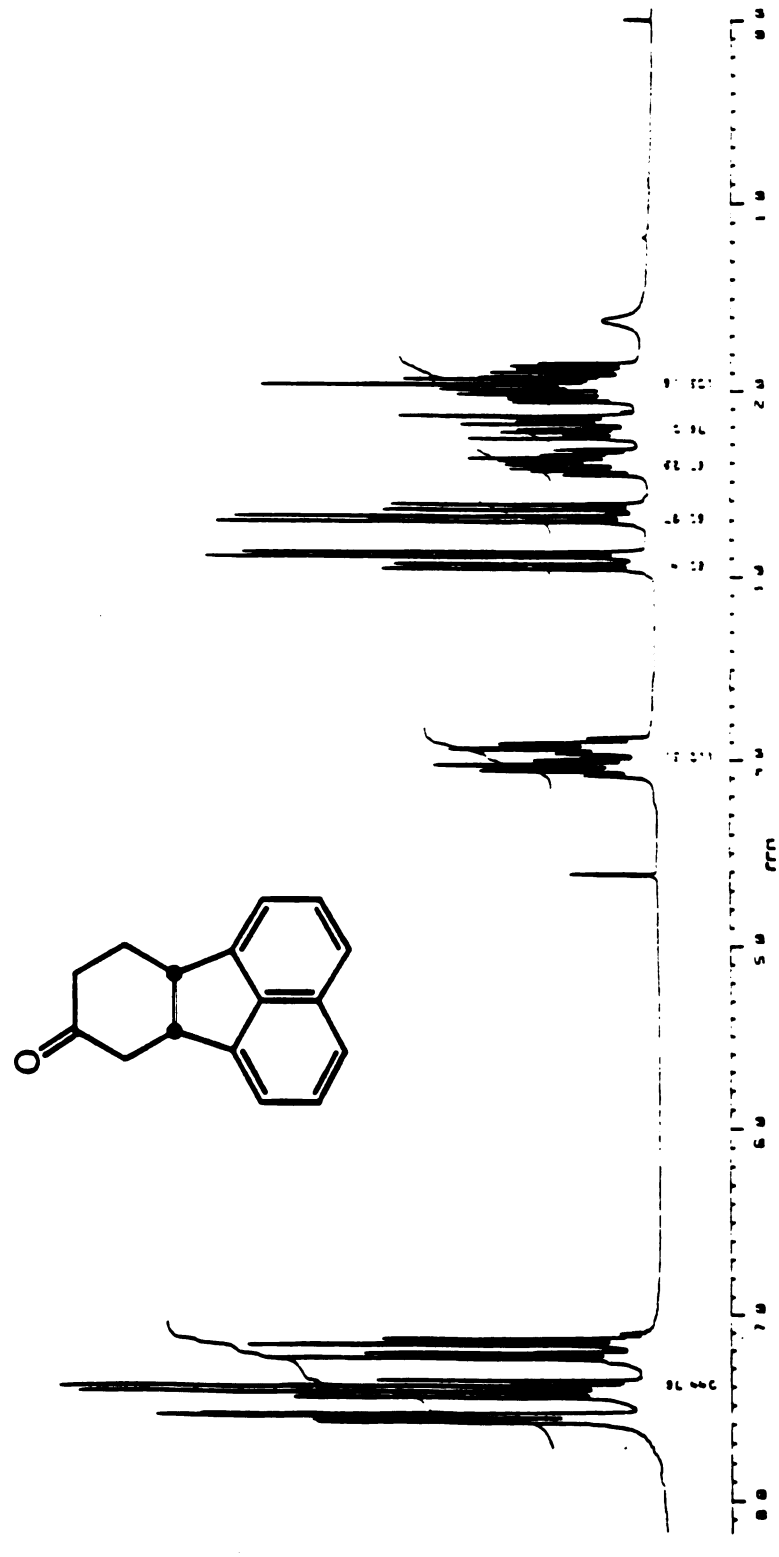

Figure 86. ^{1}H NMR Spectrum of 21.

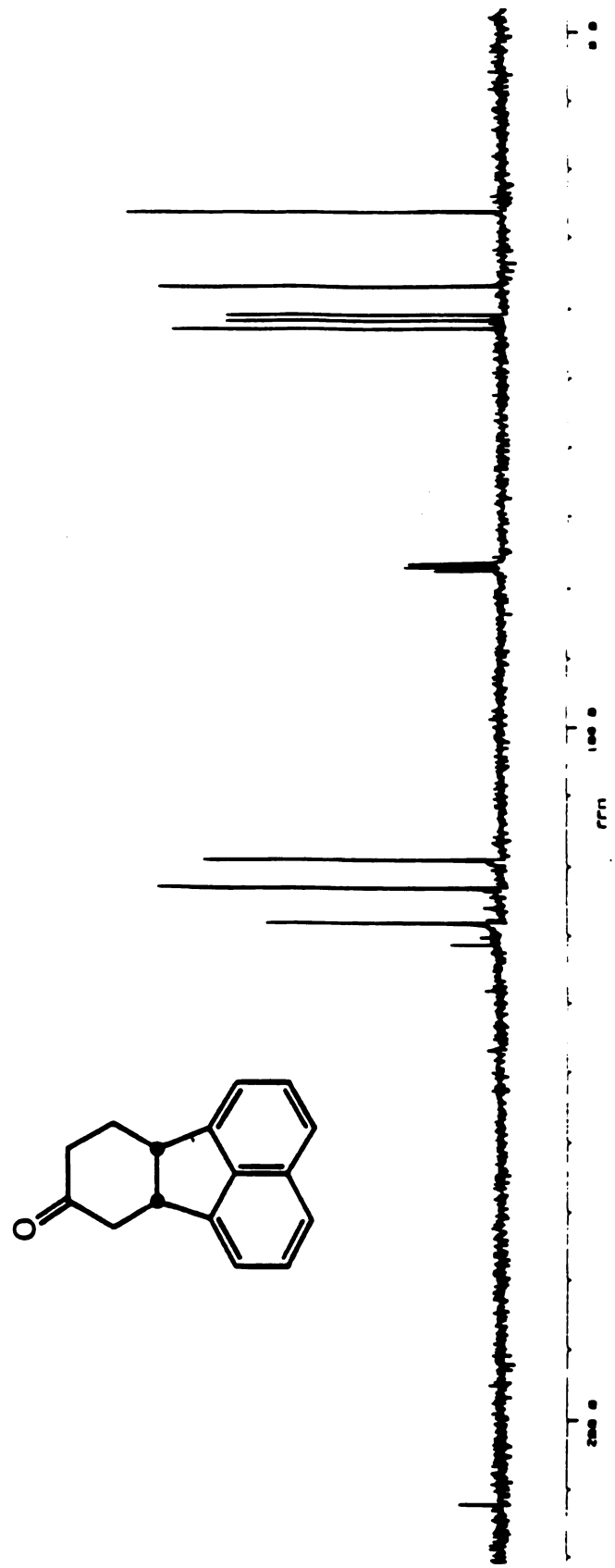

Figure 87. ^{13}C NMR Spectrum of 21.

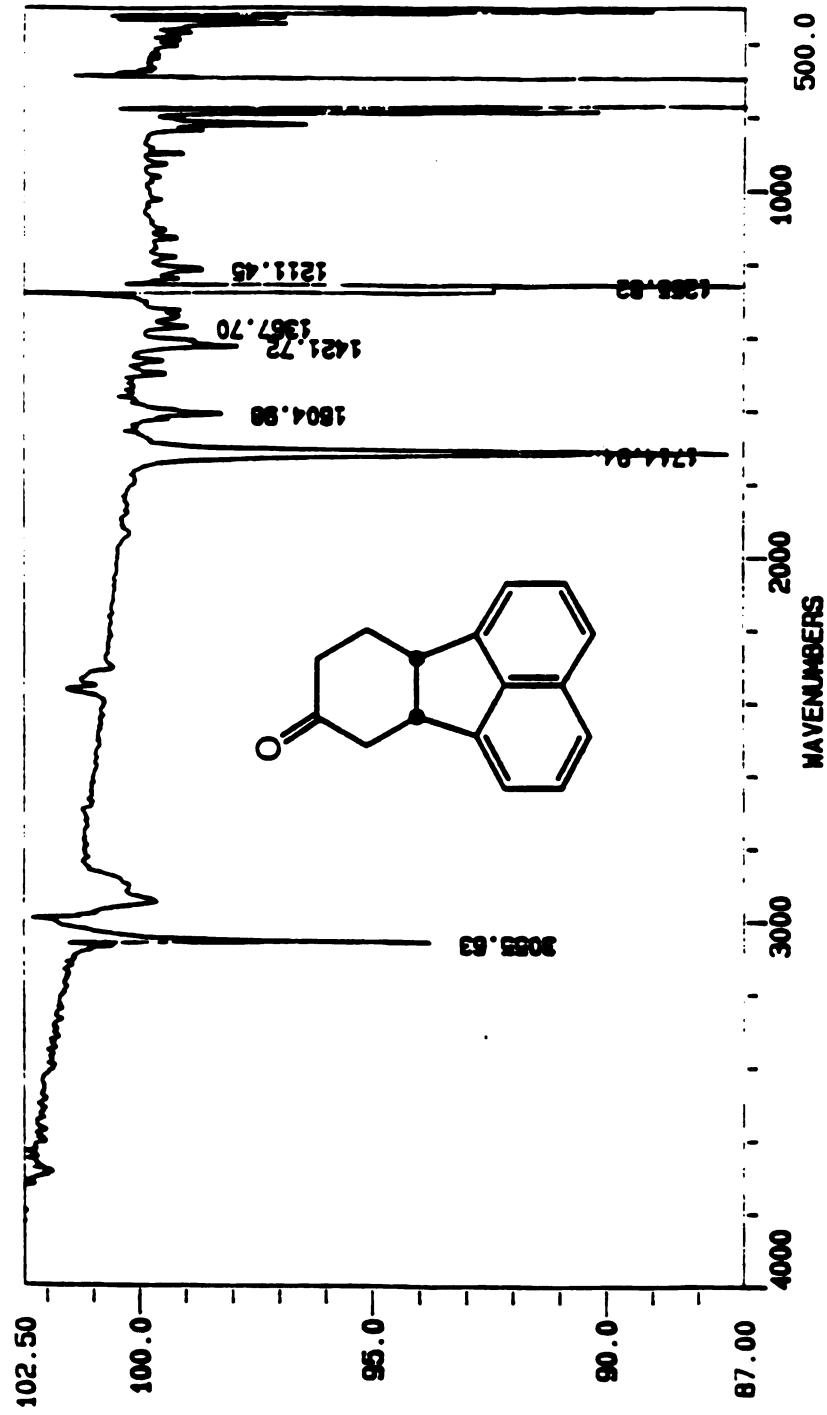

Figure 88. Infrared Spectrum of 21.

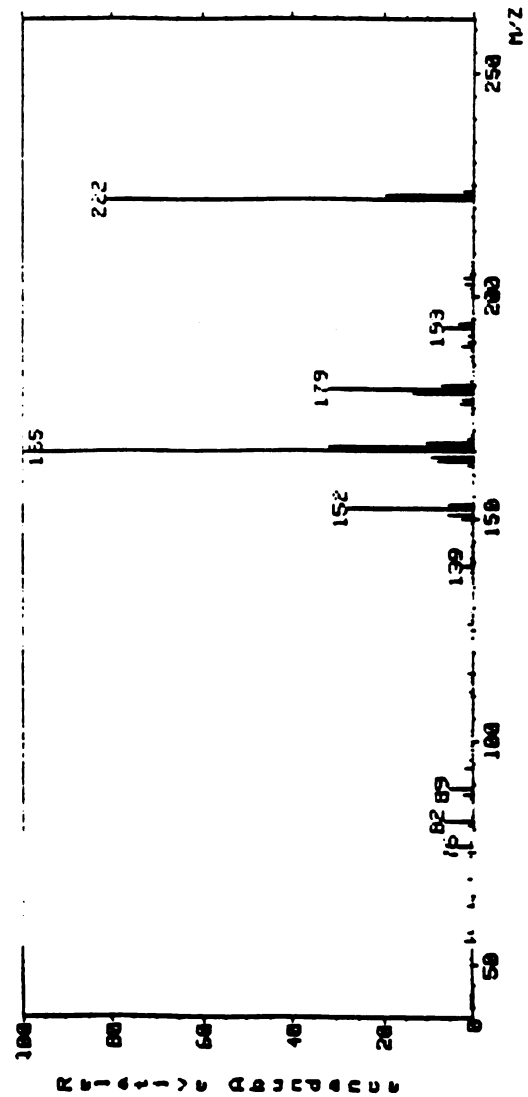

Figure 89. Mass Spectrum of 21.

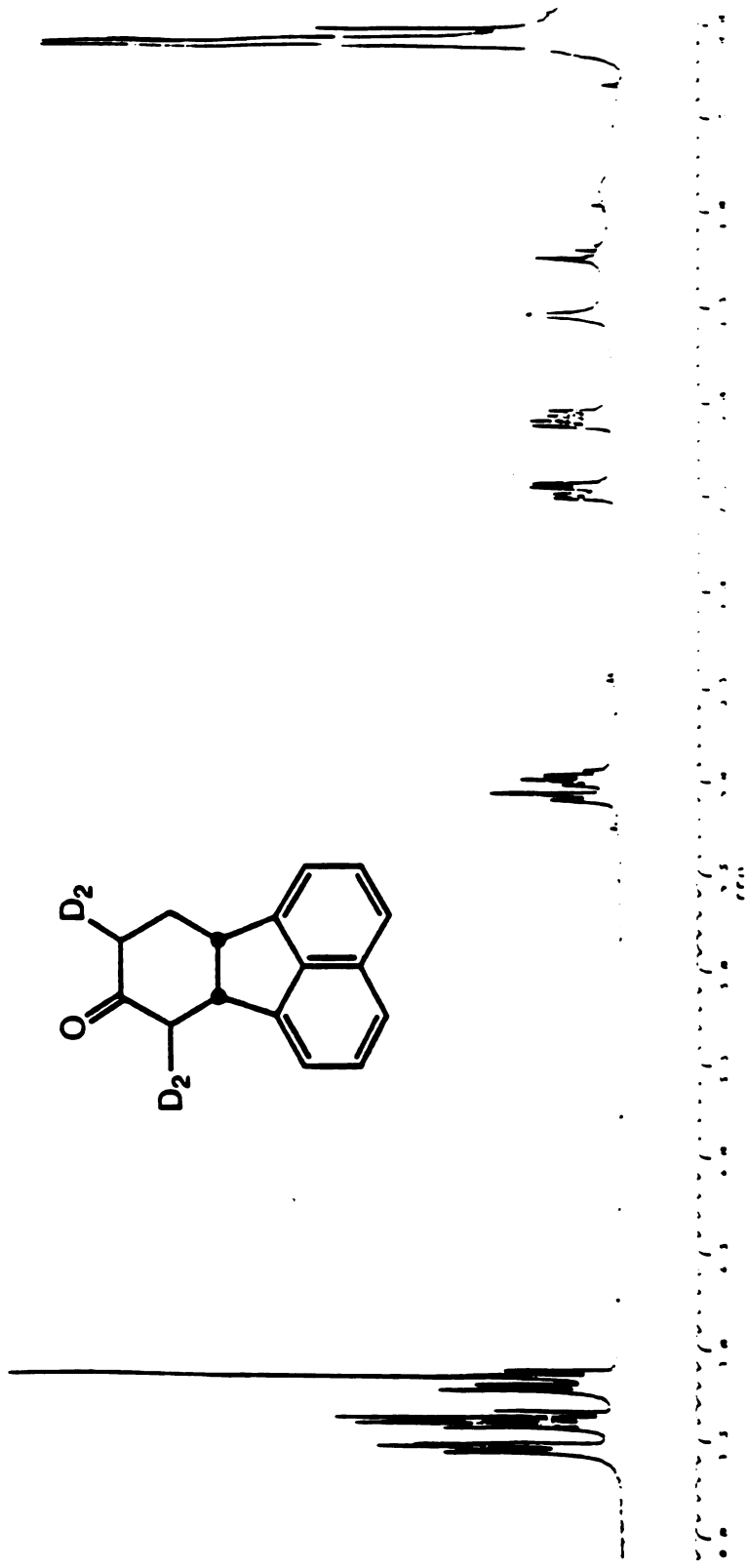

Figure 90. ^{1}H NMR Spectrum of 23a.

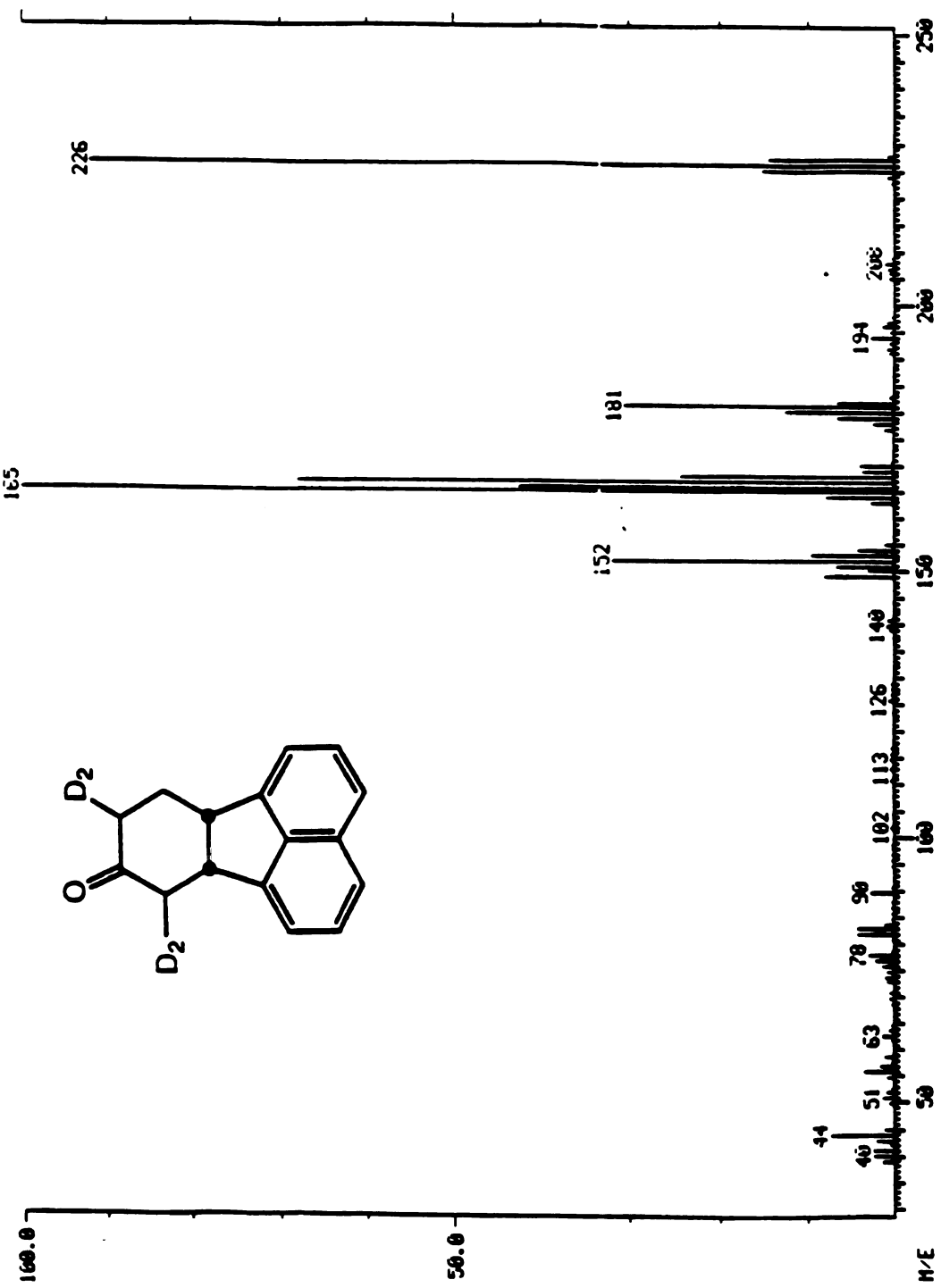

Figure 91. Mass Spectrum of 23a.

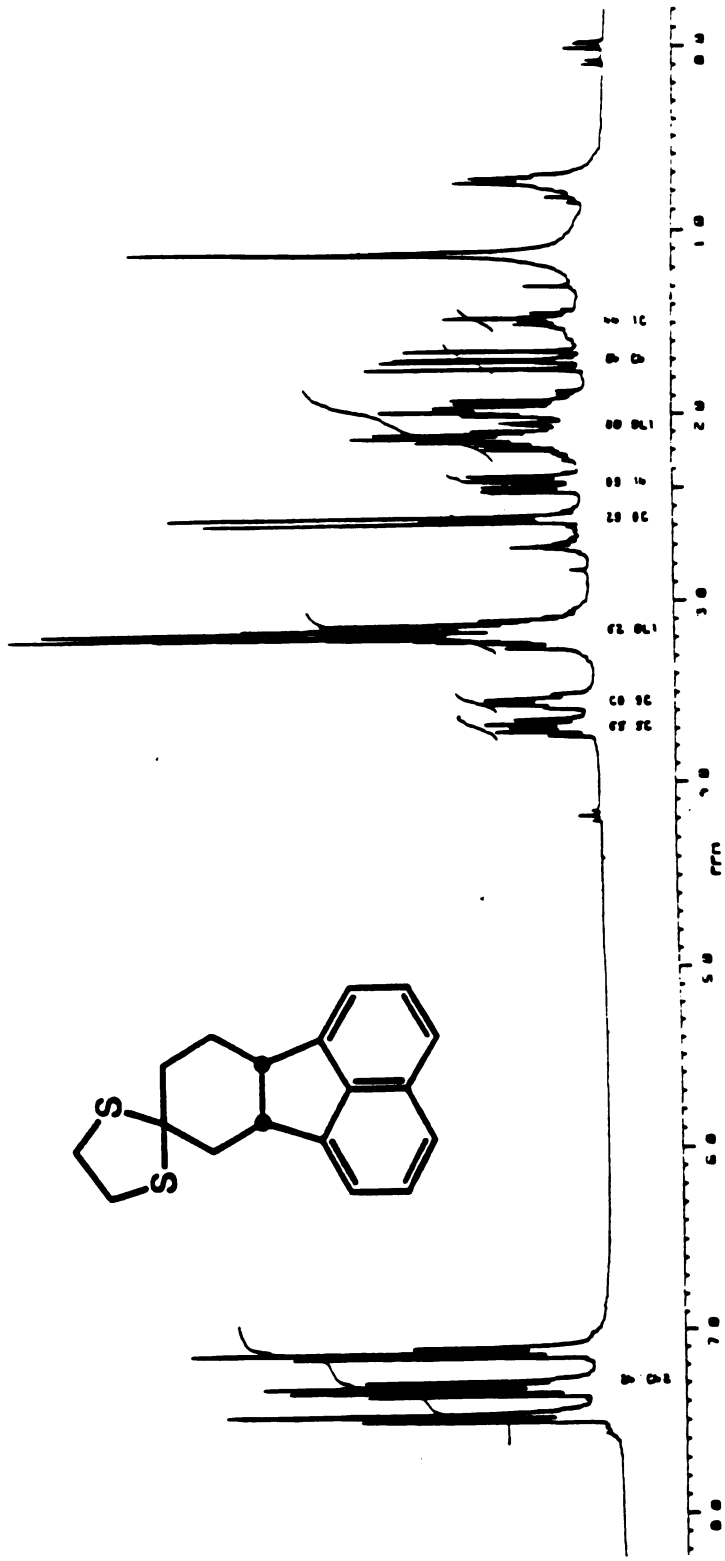

Figure 92. ^{1}H NMR Spectrum of 24.

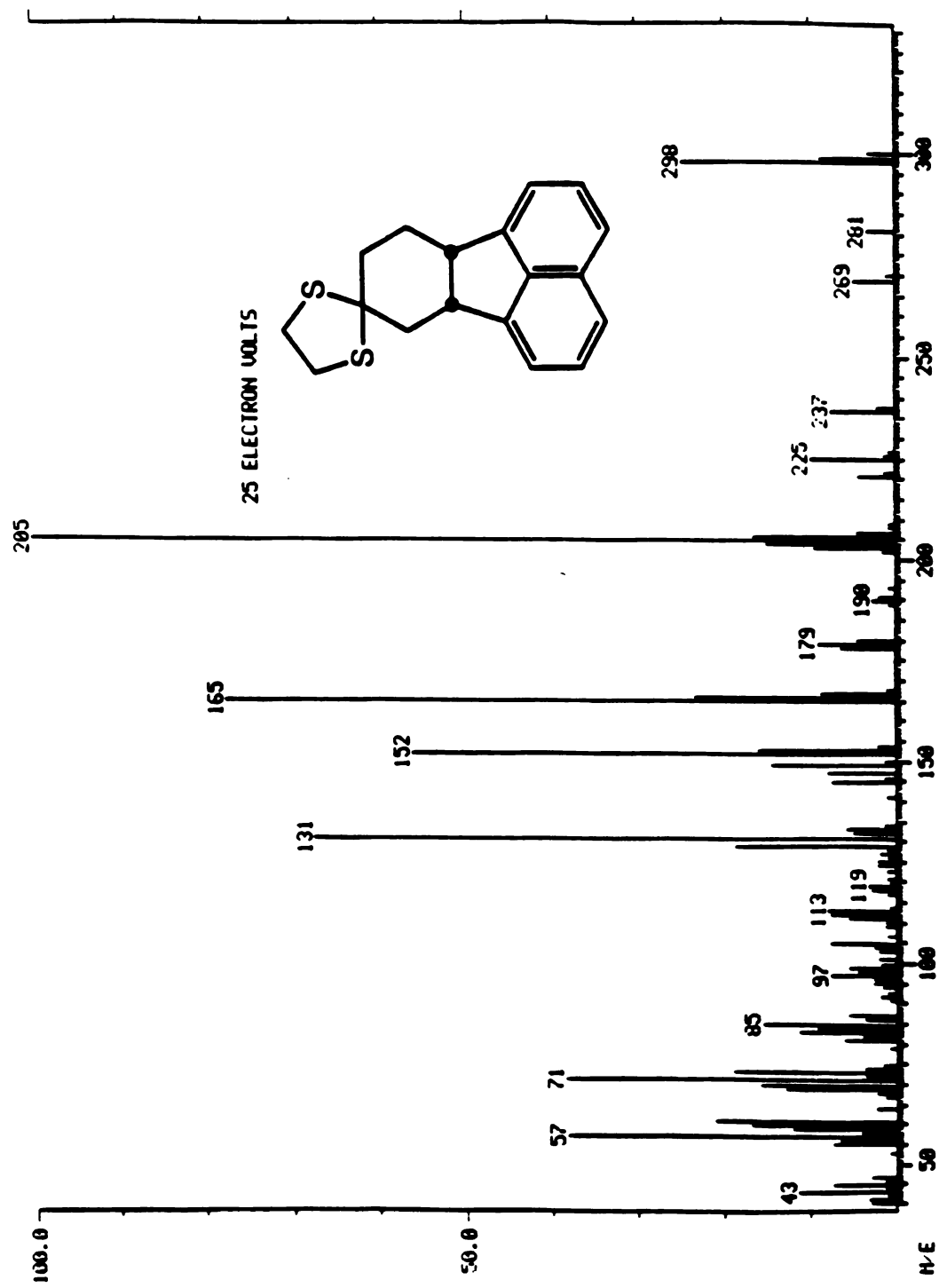

Figure 93. Mass Spectrum of 24.

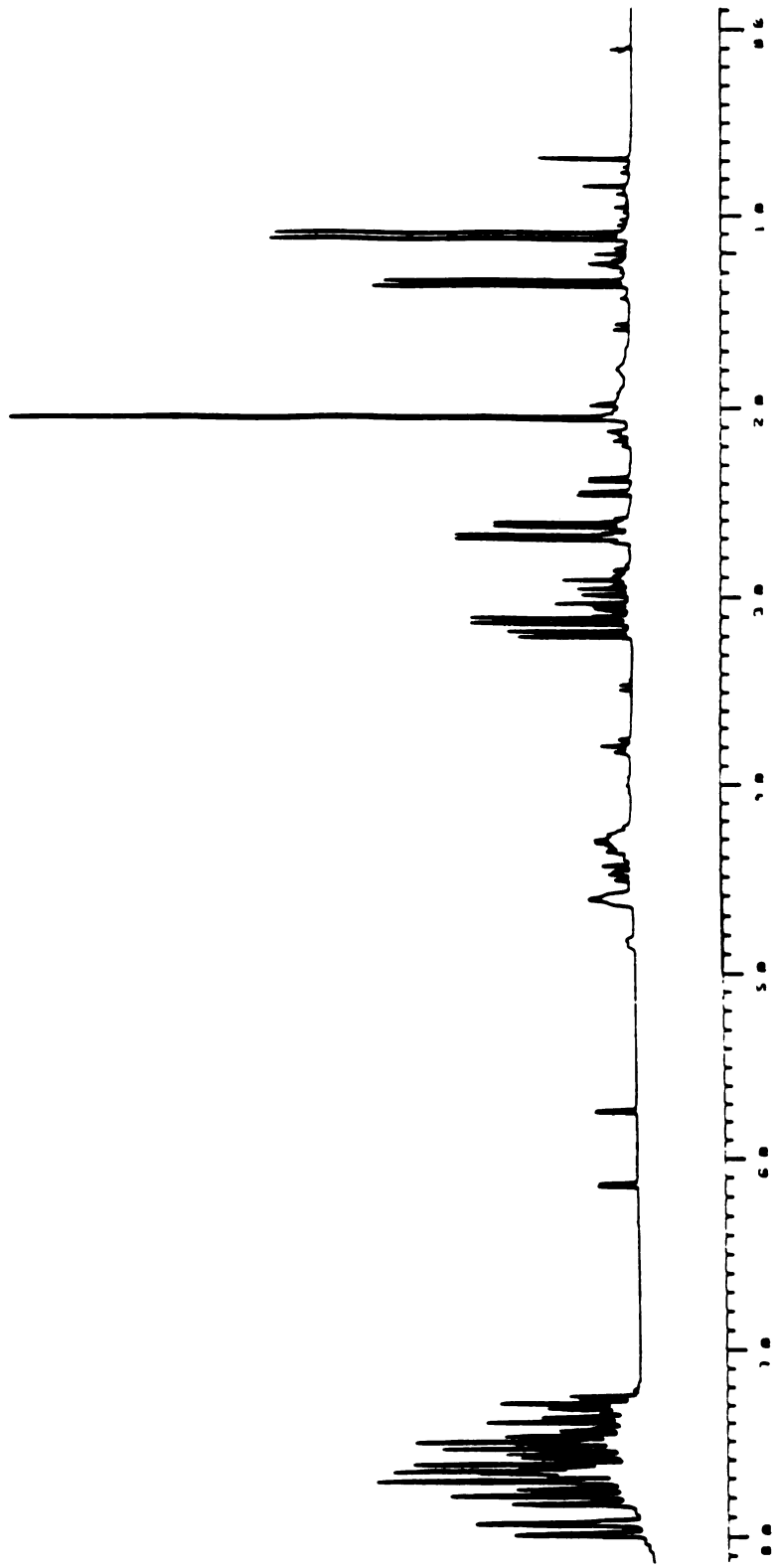

Figure 94. ^1H NMR Spectrum of Mixture of 25/26/27/28.

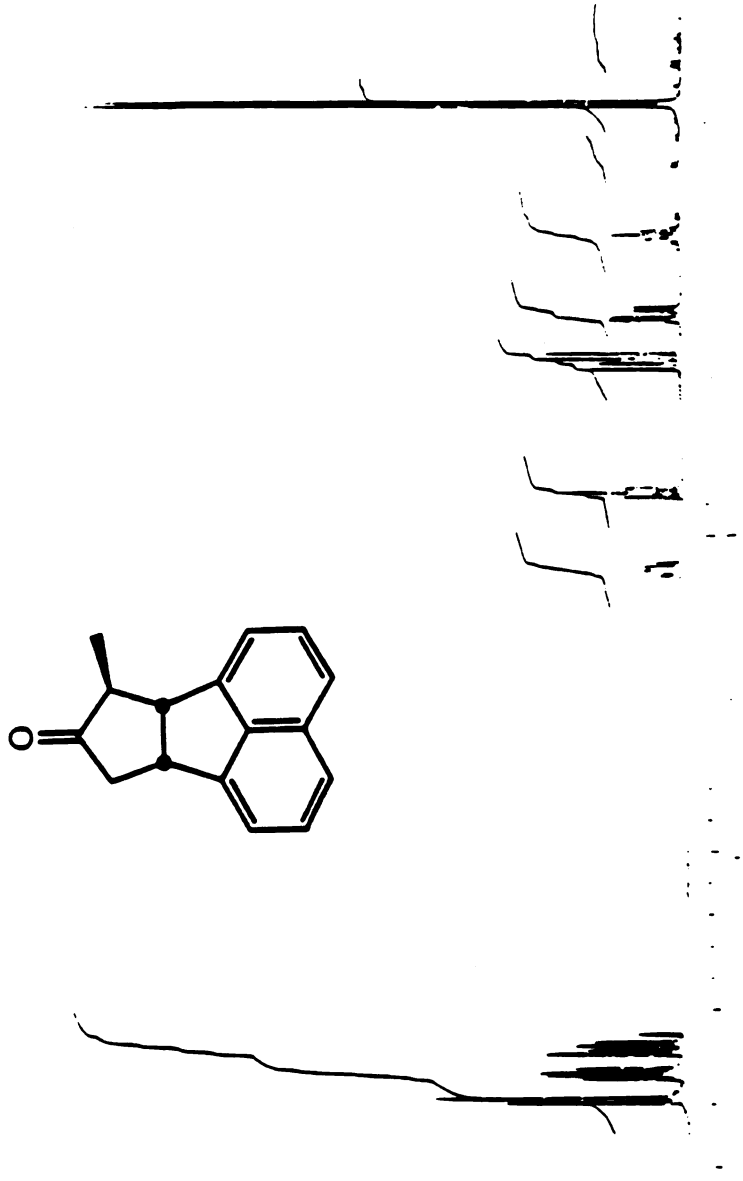

Figure 95. ^{1}H NMR Spectrum of 27.

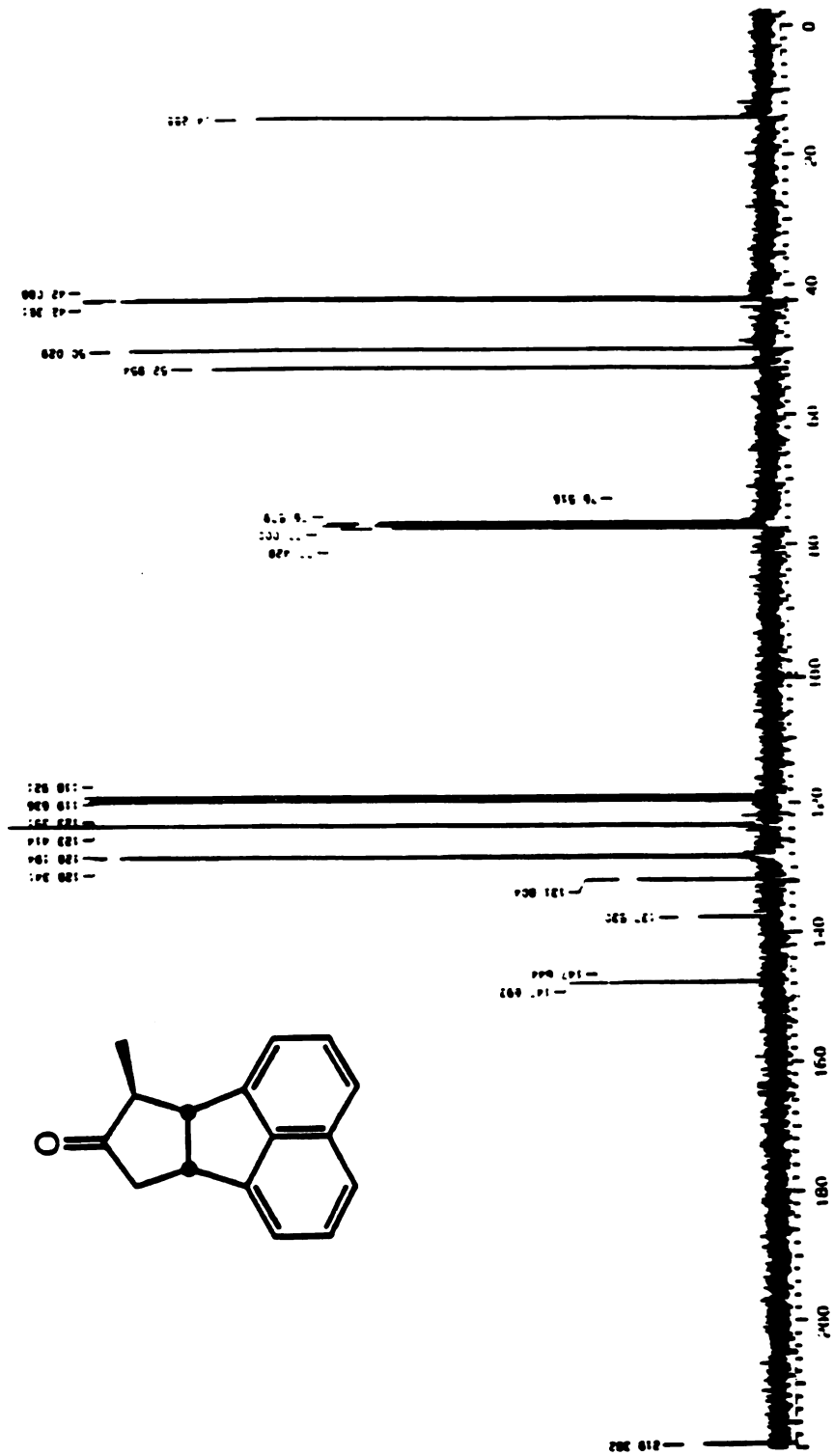

Figure 96. ^{13}C NMR Spectrum of 27.

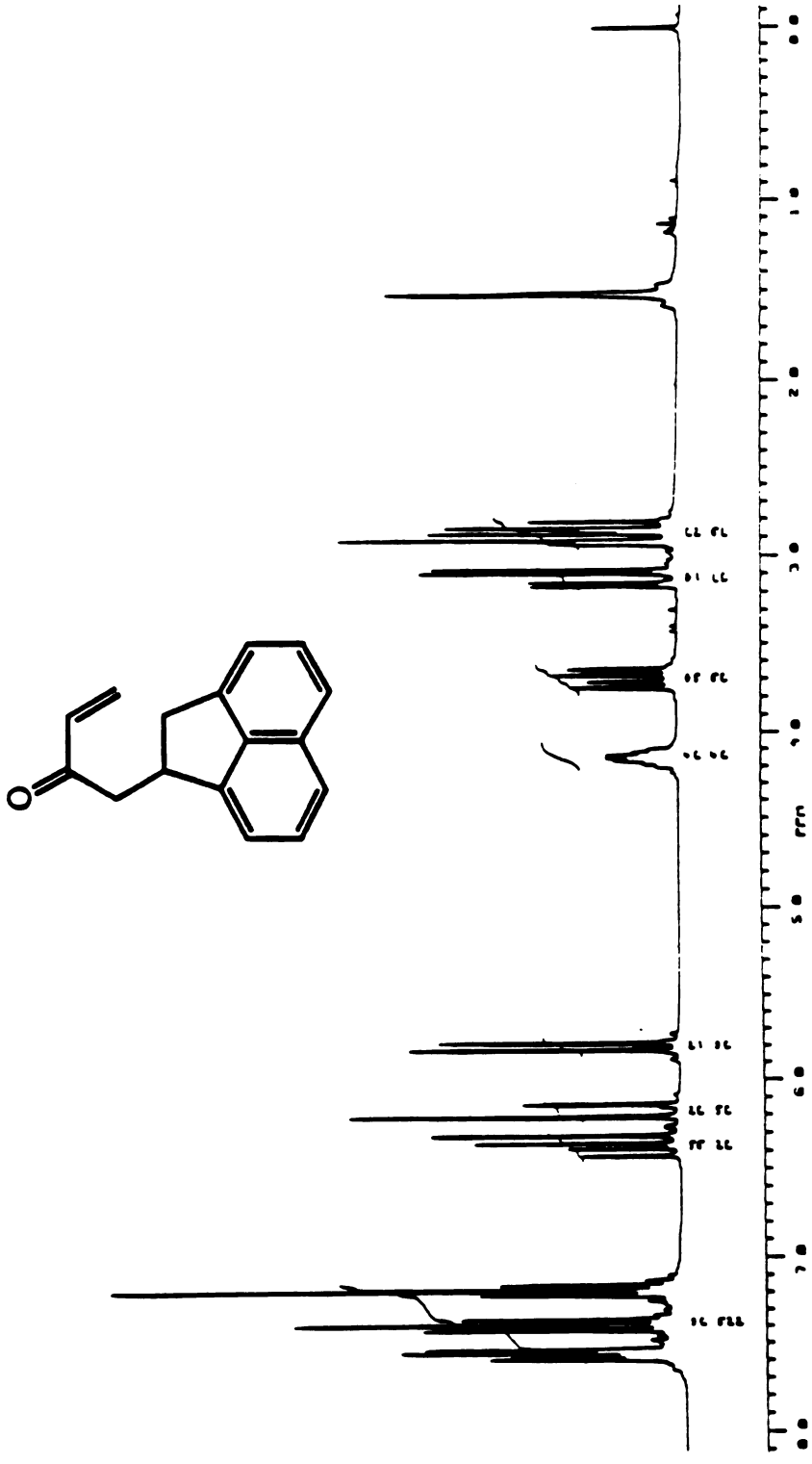

Figure 97. ^{1}H NMR Spectrum of 29.

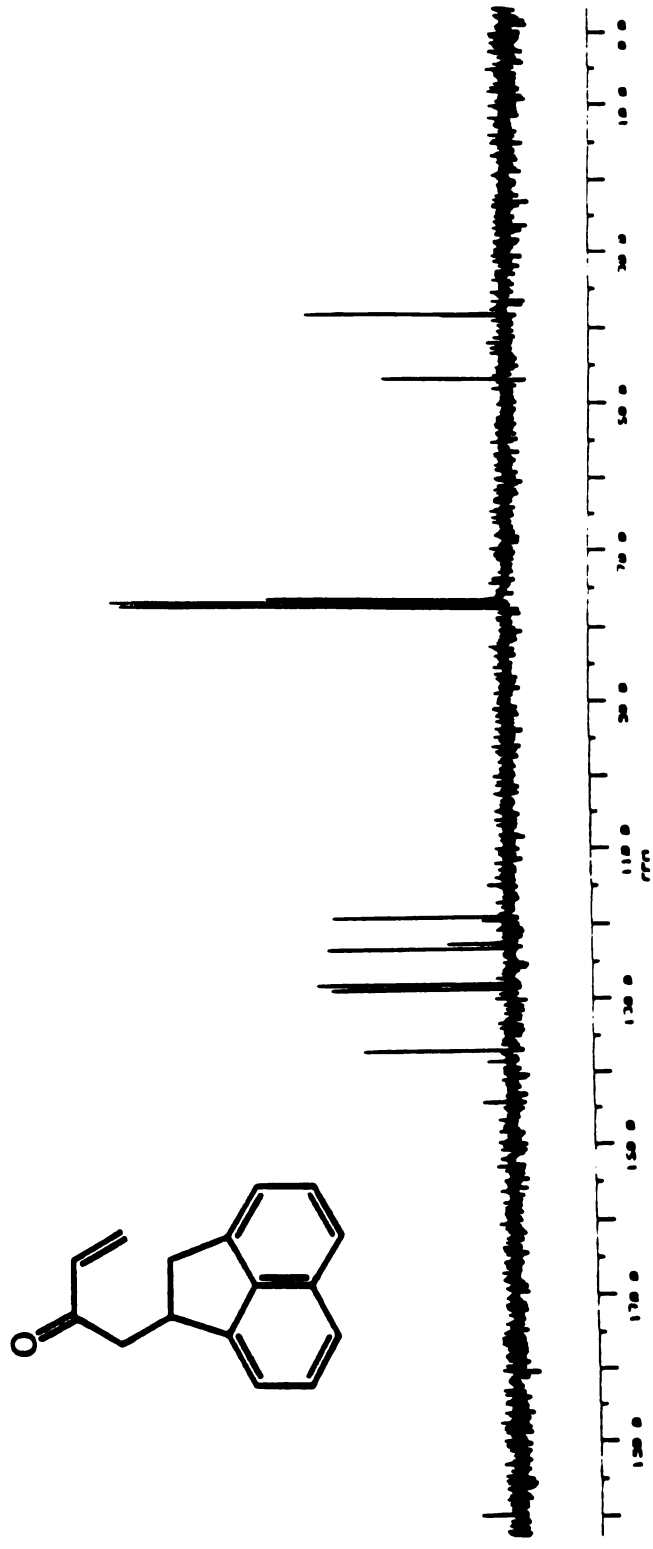

Figure 98. ^{13}C NMR Spectrum of 29.

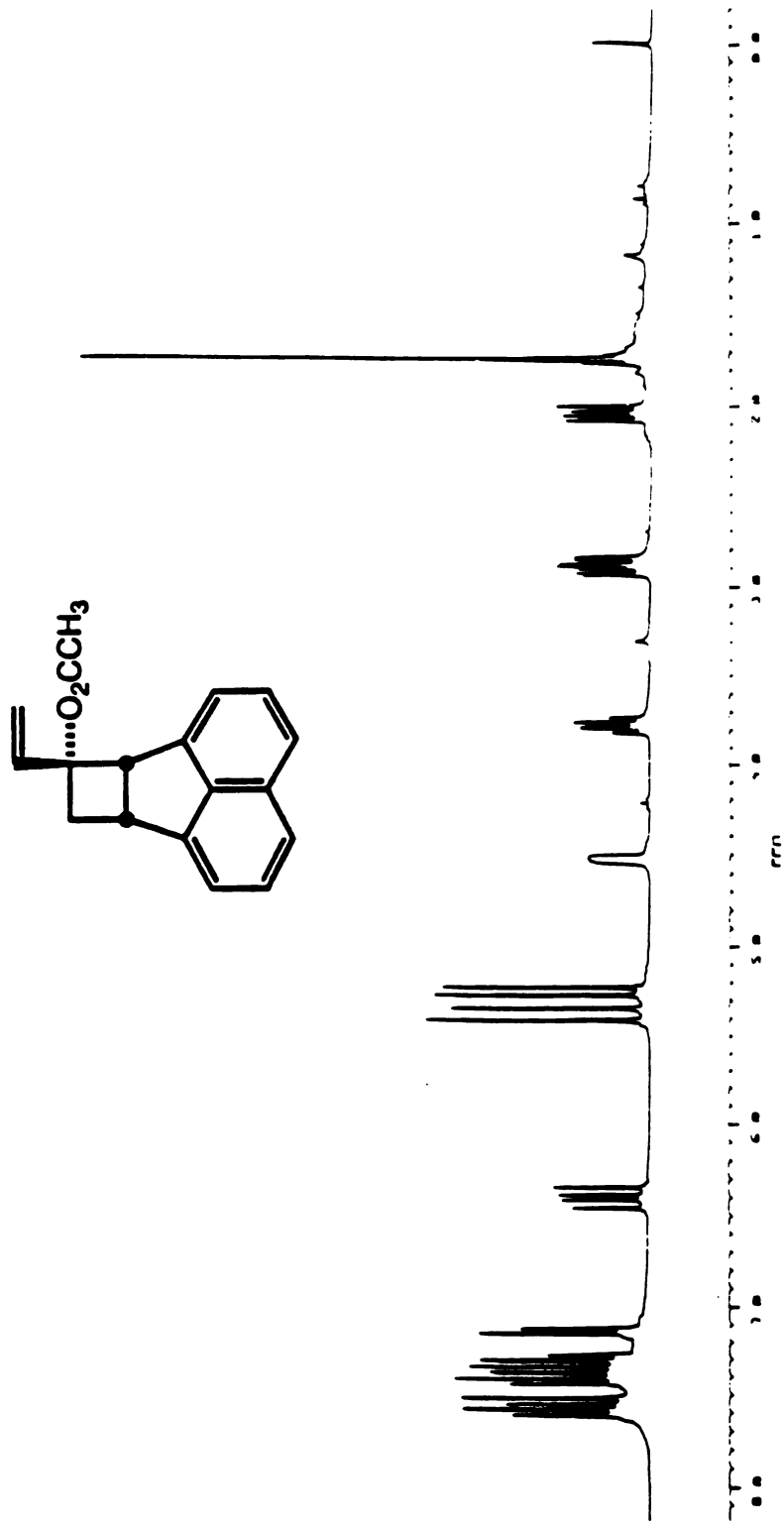

Figure 99. ^1H NMR Spectrum of 30.

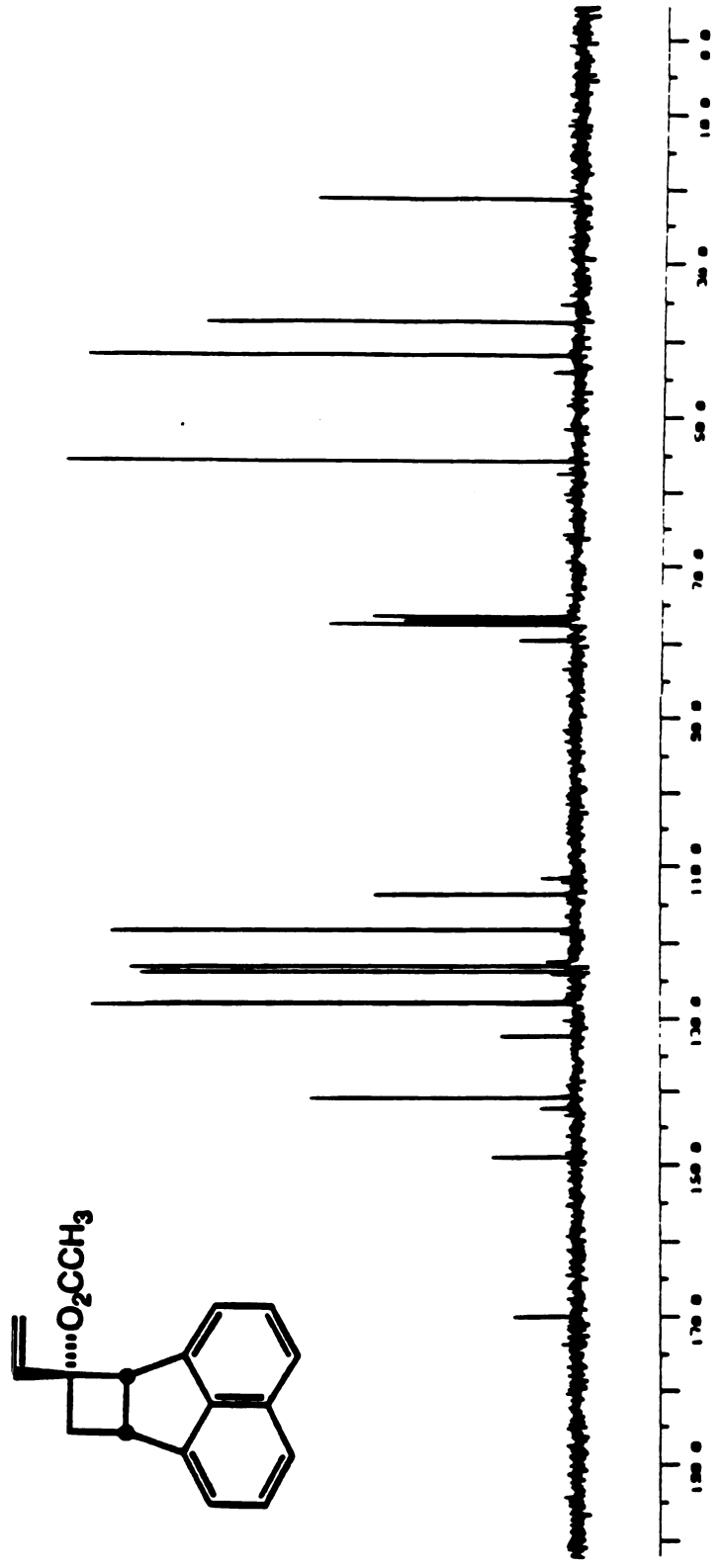

Figure 100. ^{13}C NMR Spectrum of **30**.

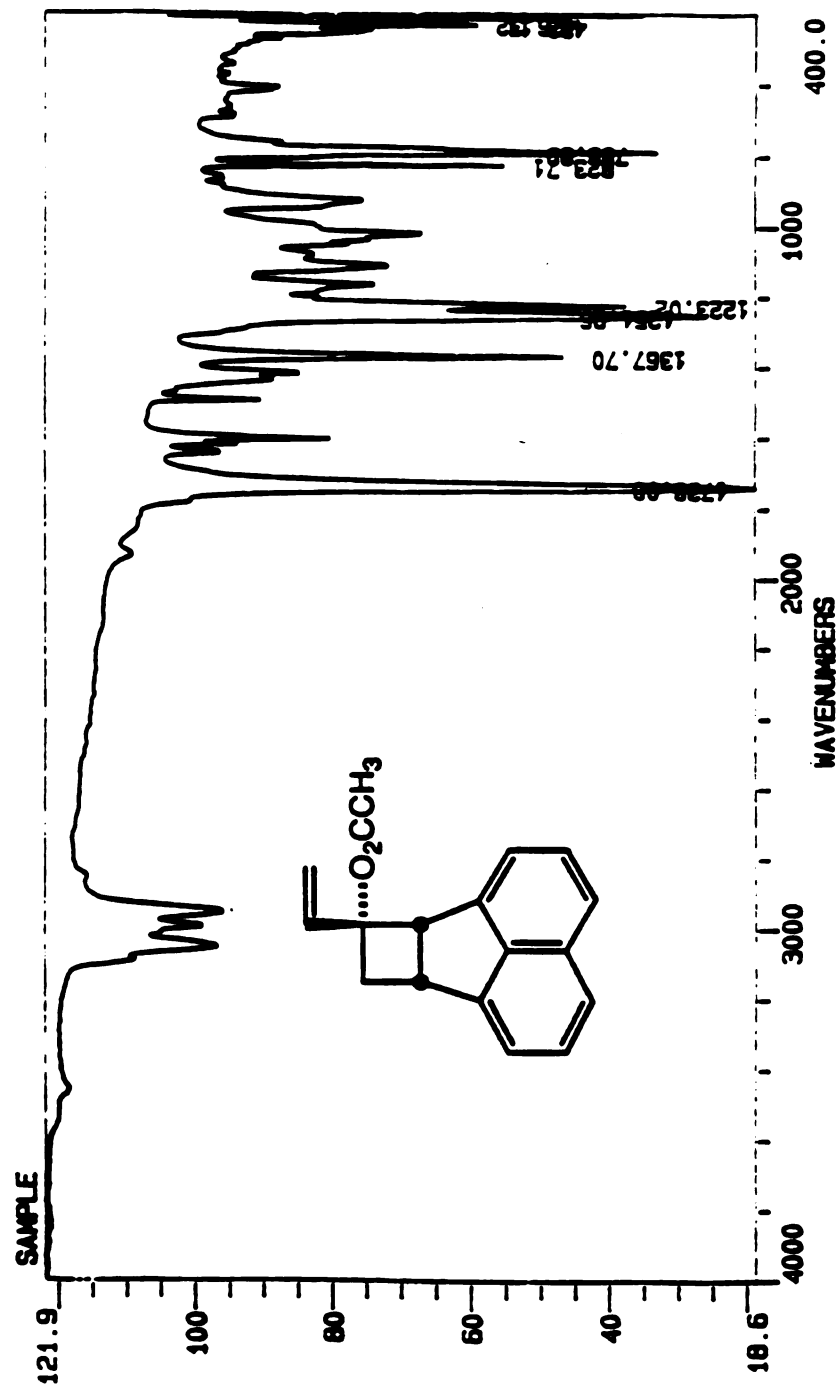

Figure 101. Infrared Spectrum of 30.

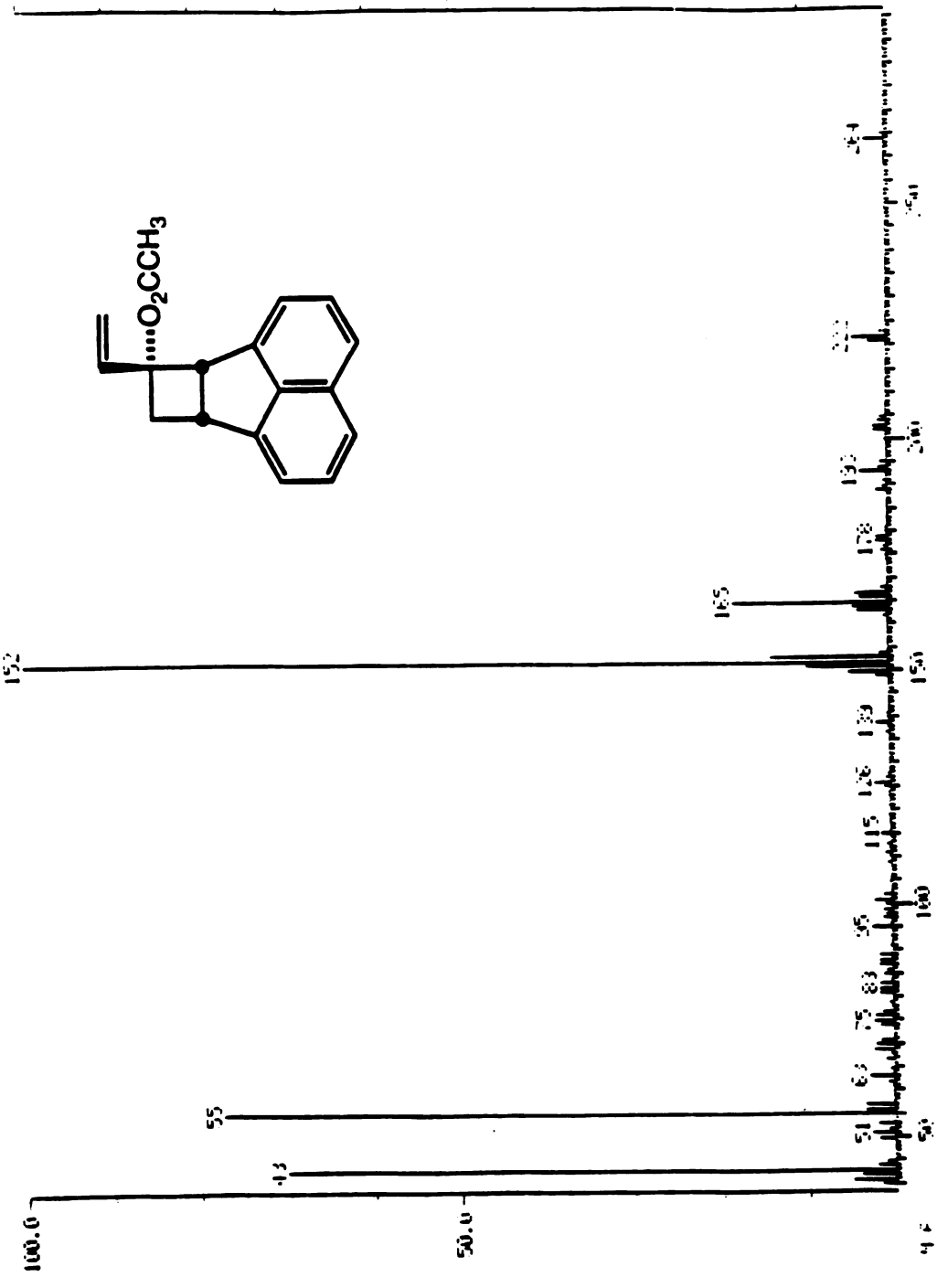

Figure 102. Mass Spectrum of 30.

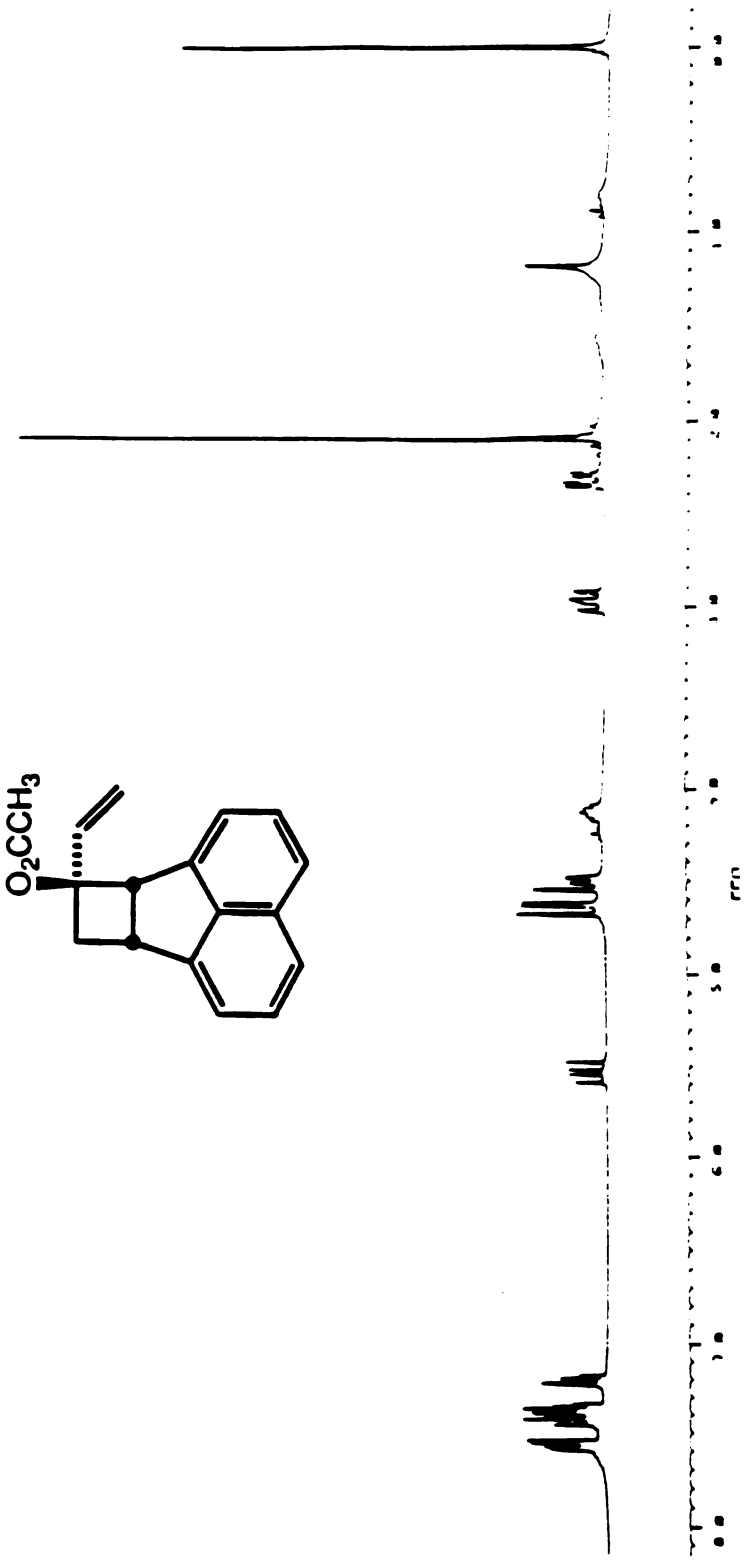

Figure 103. ^{1}H NMR Spectrum of 31.

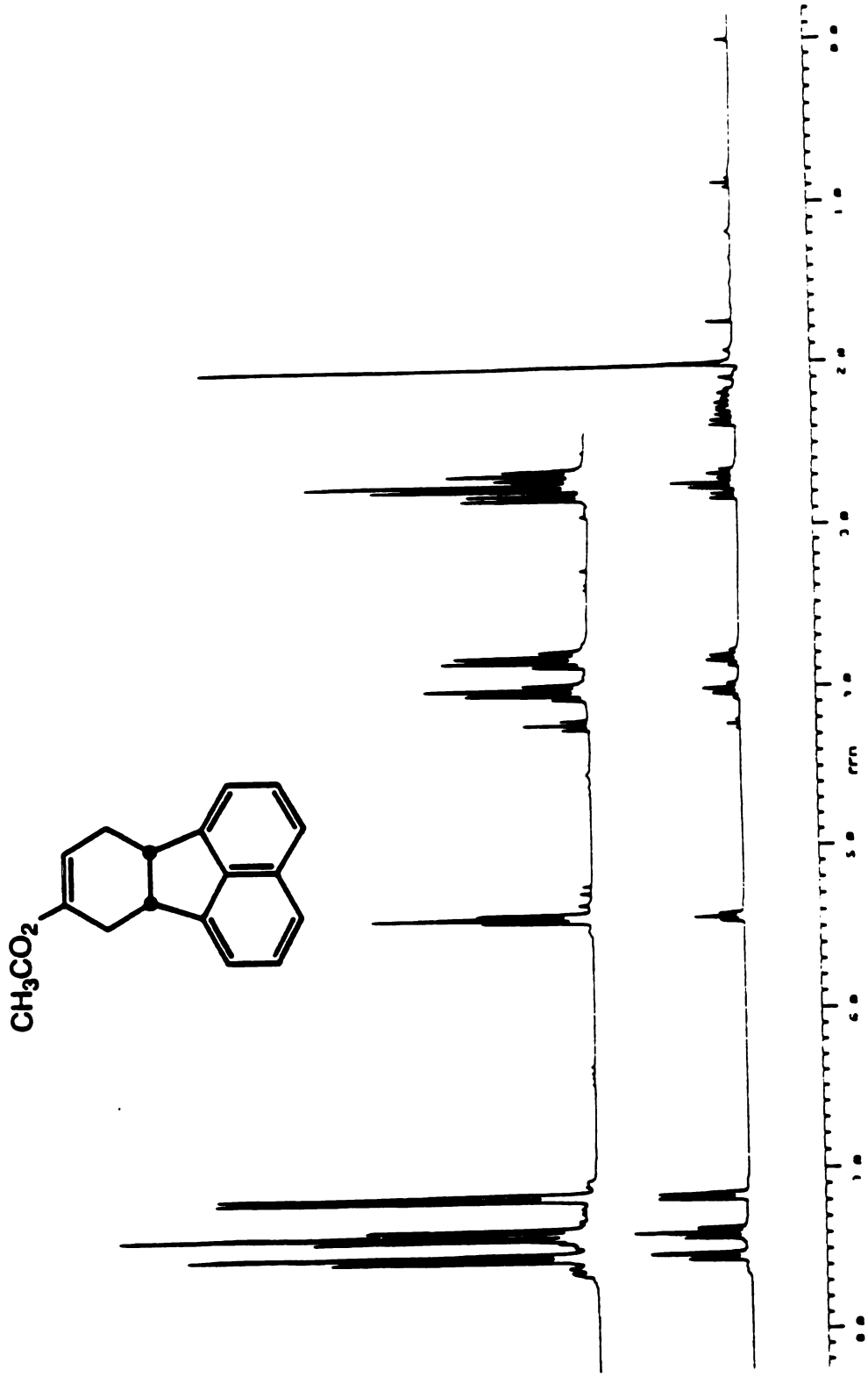

Figure 104. ^{1}H NMR Spectrum of 32.

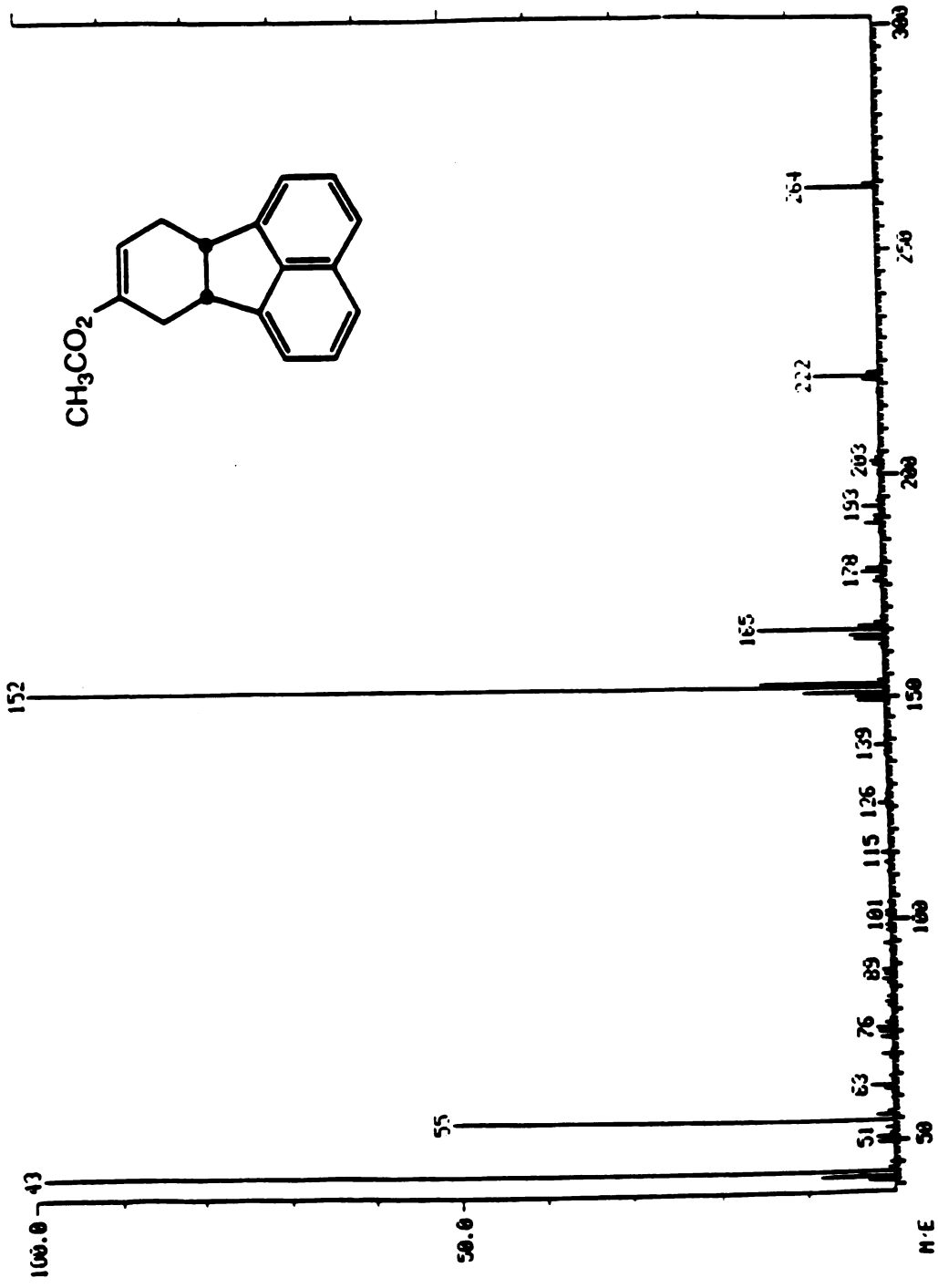

Figure 105. Mass Spectrum of 32.

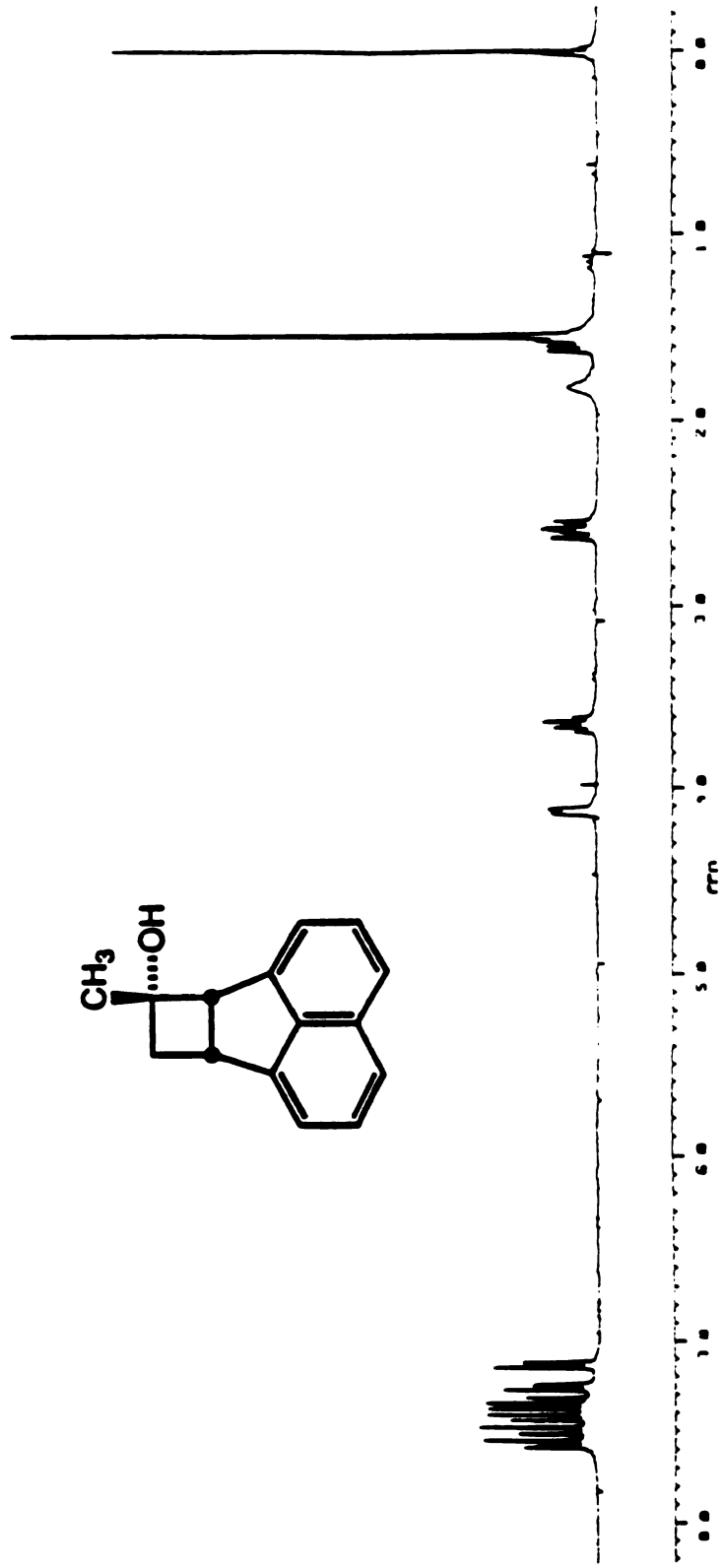

Figure 106. ^{1}H NMR Spectrum of 33.

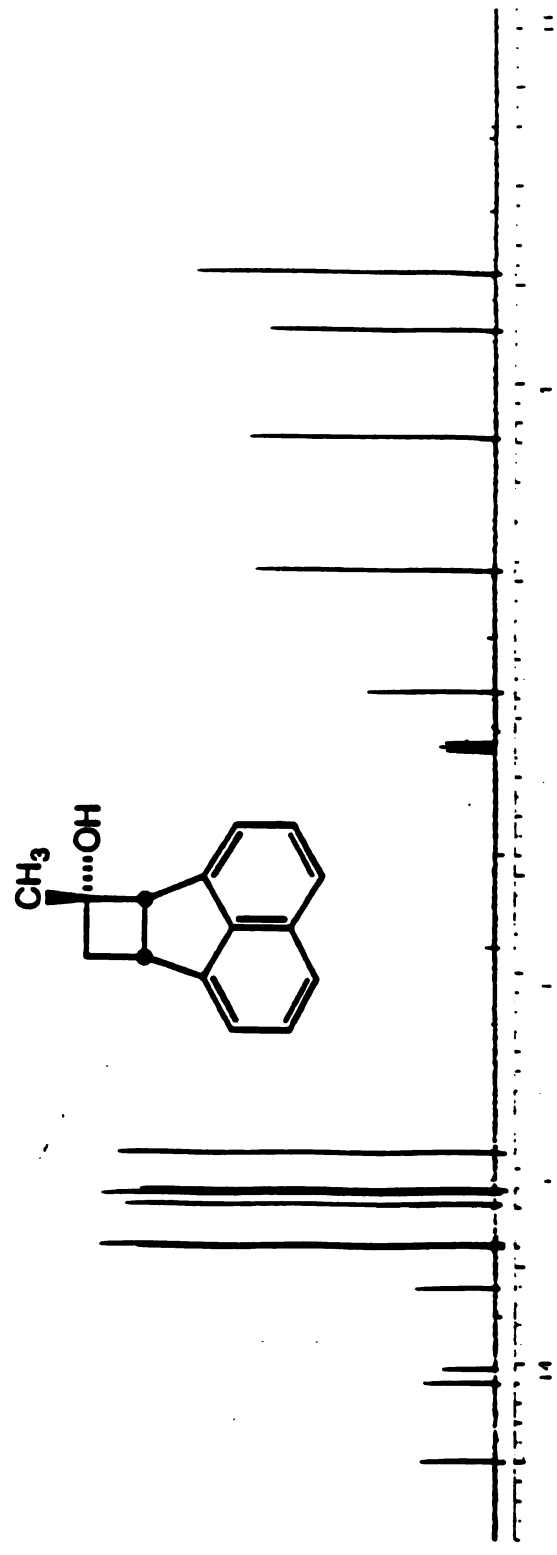

Figure 107. ^{13}C NMR Spectrum of 33.

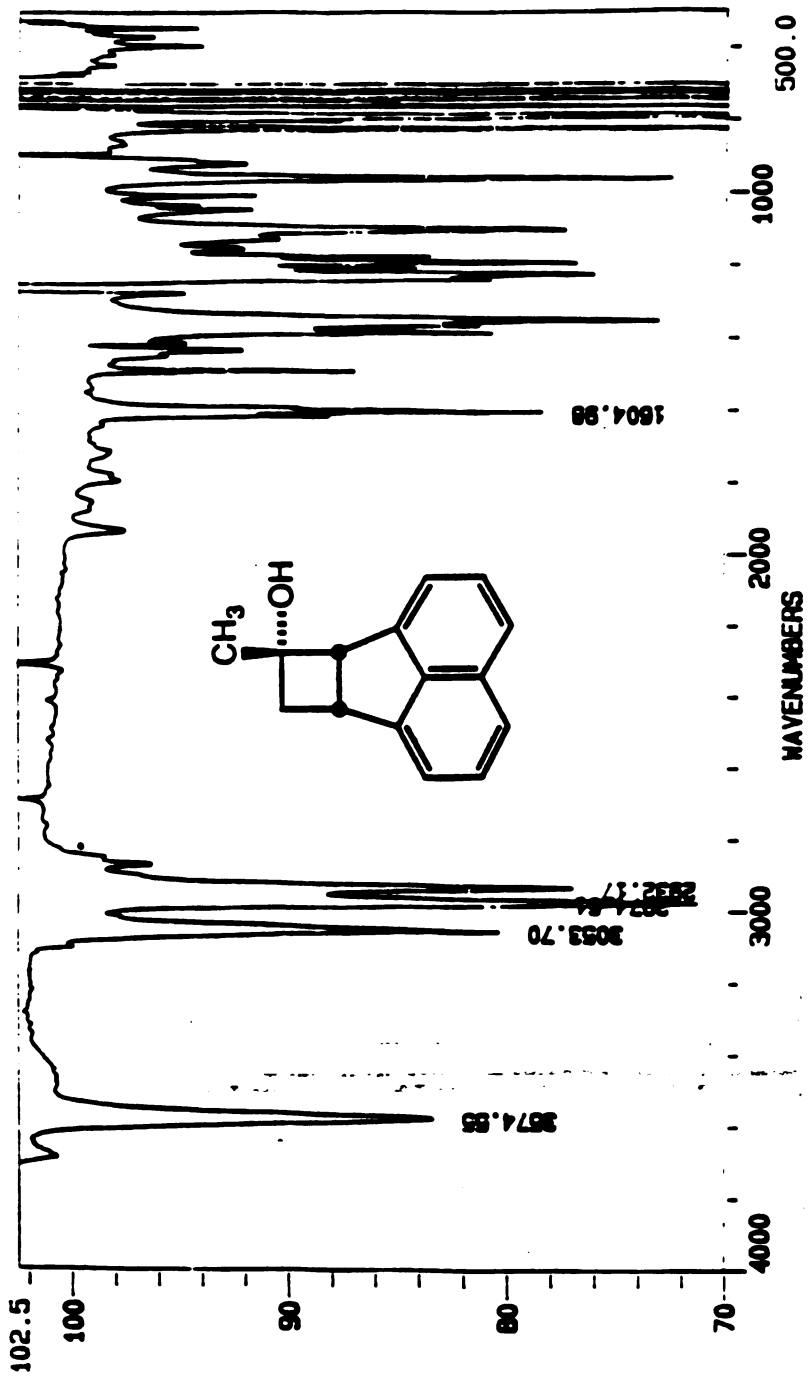

Figure 108. Infrared Spectrum of 33.

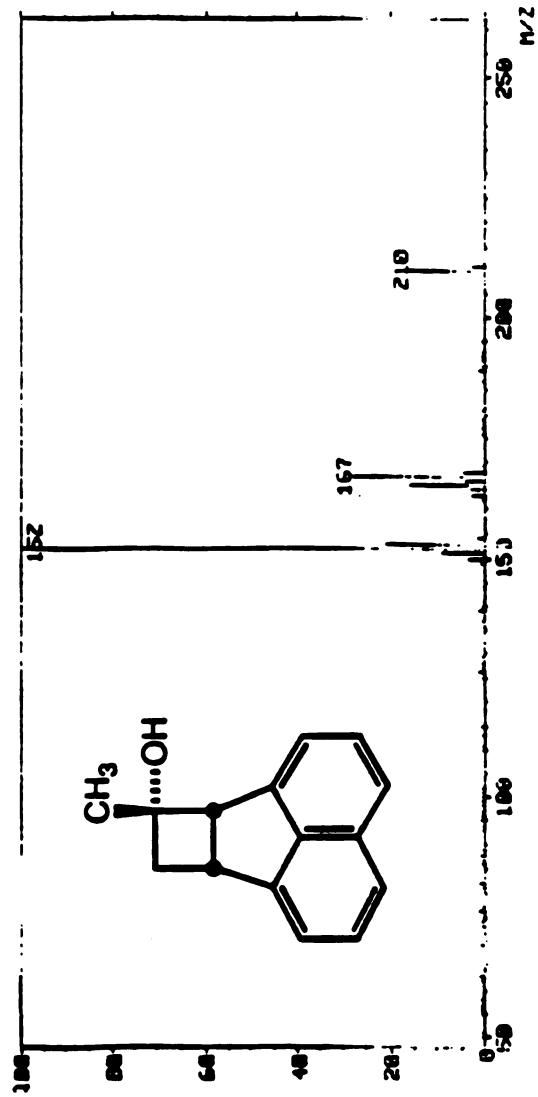

Figure 109. Mass Spectrum of 33.

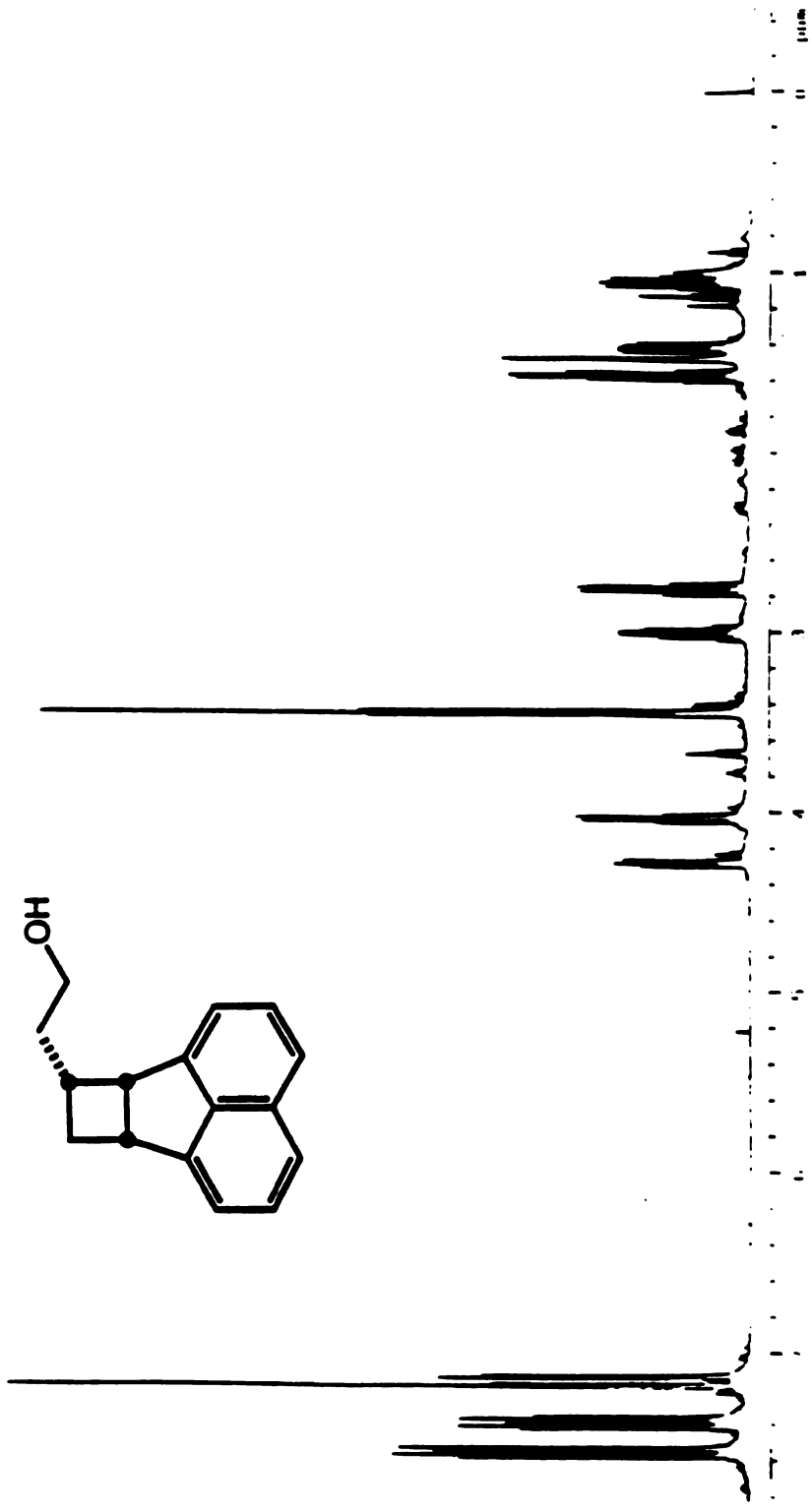

Figure 110. ^{1}H NMR Spectrum of 36.

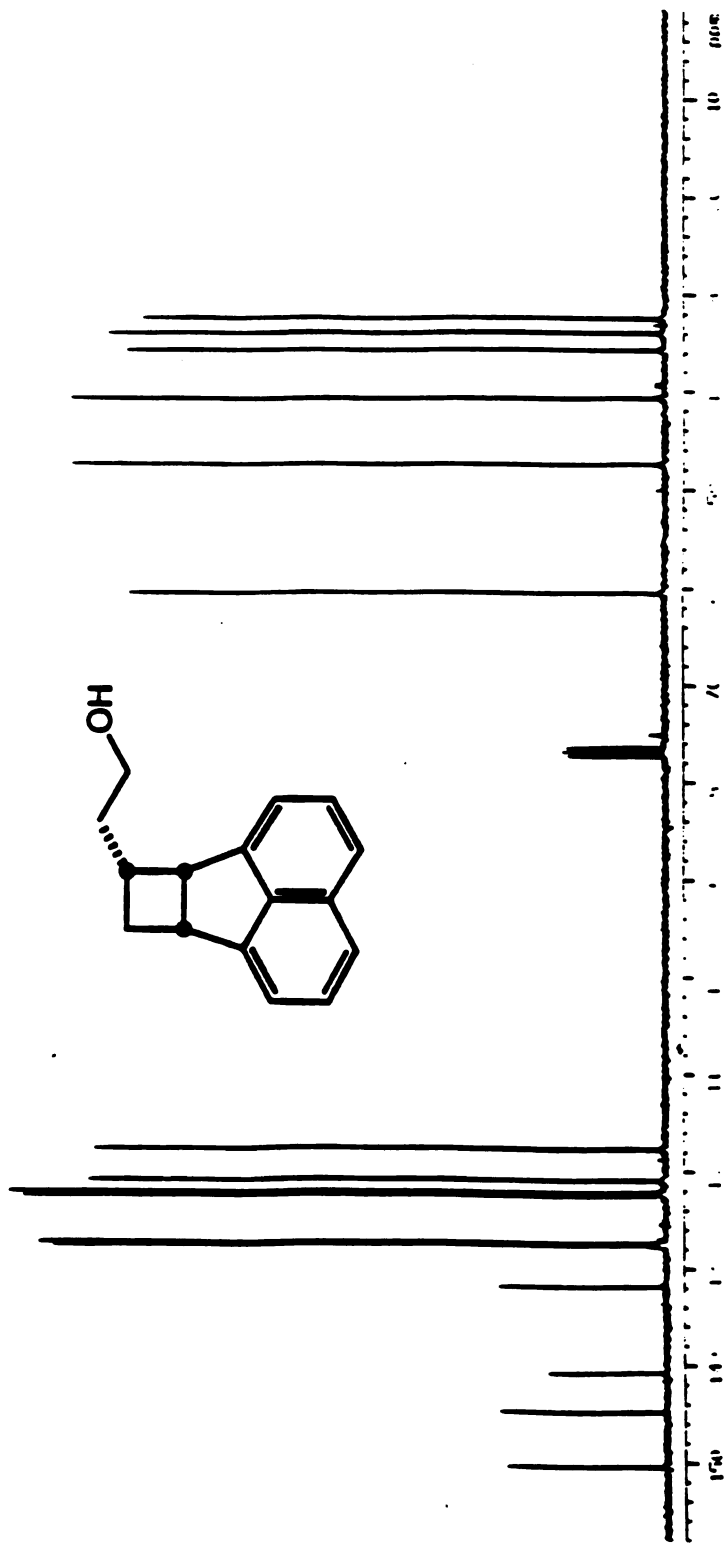

Figure 111. ^{13}C NMR Spectrum of 36.

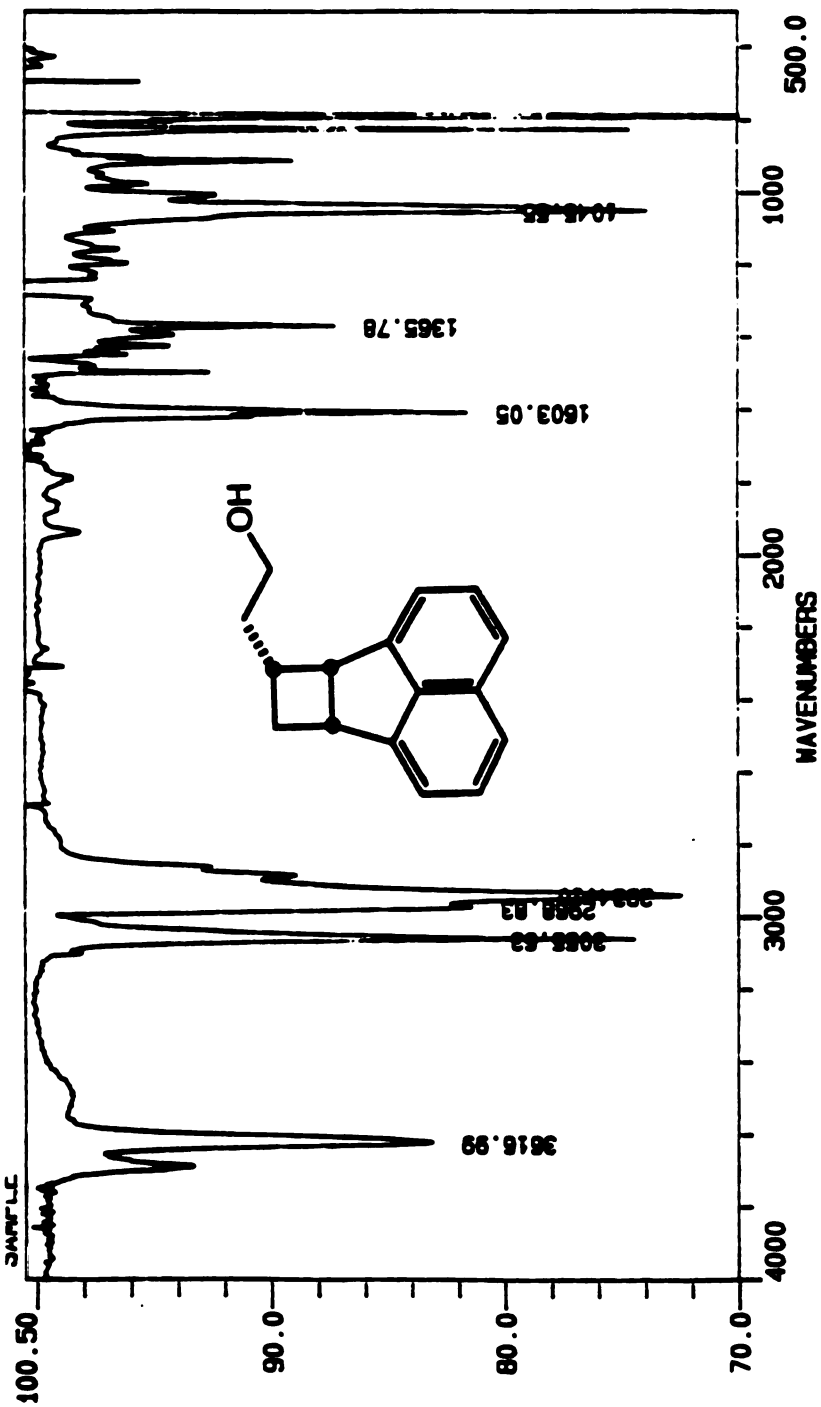

Figure 112. Infrared Spectrum of 36.

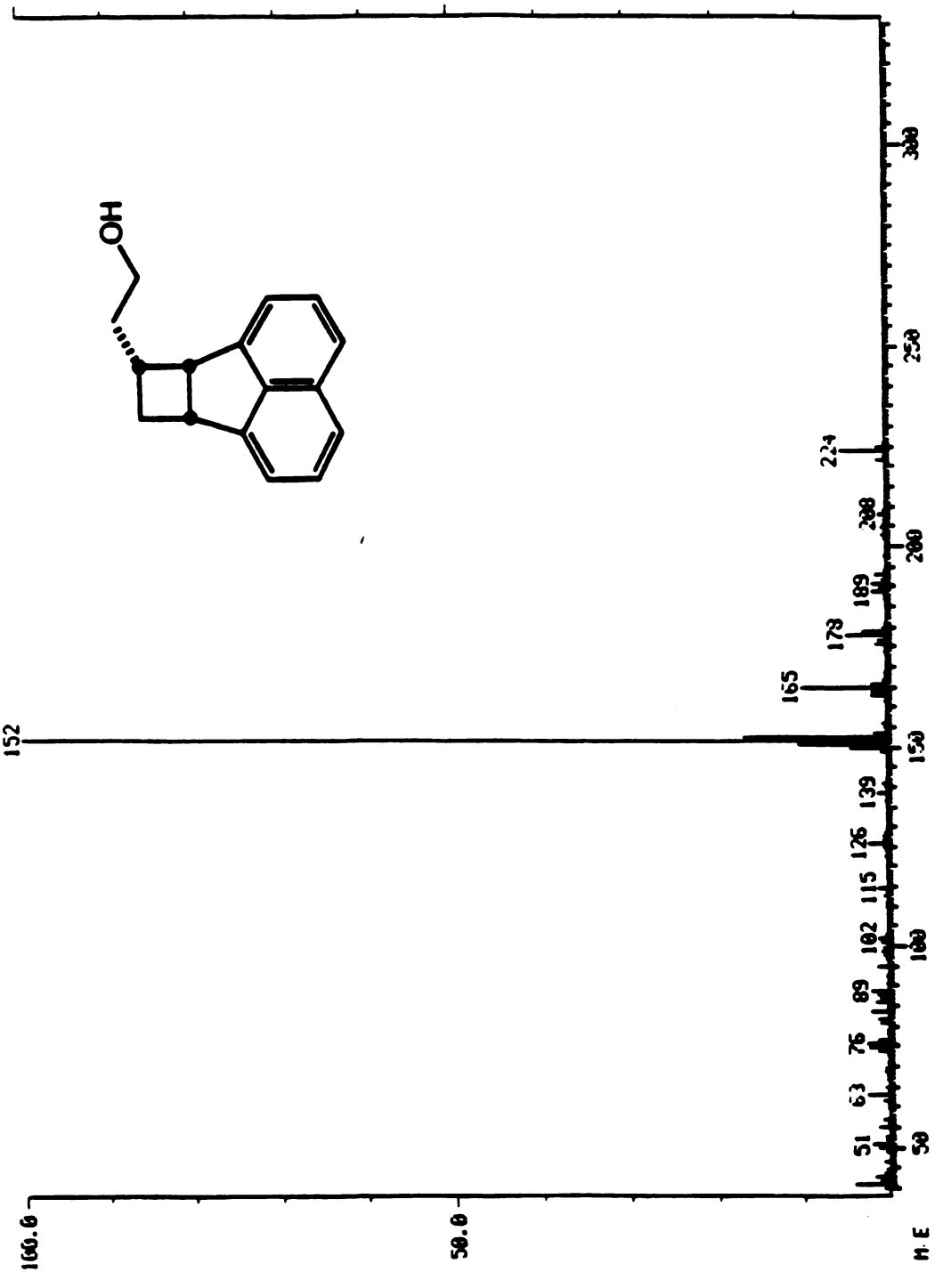

Figure 113. Mass Spectrum of 36.

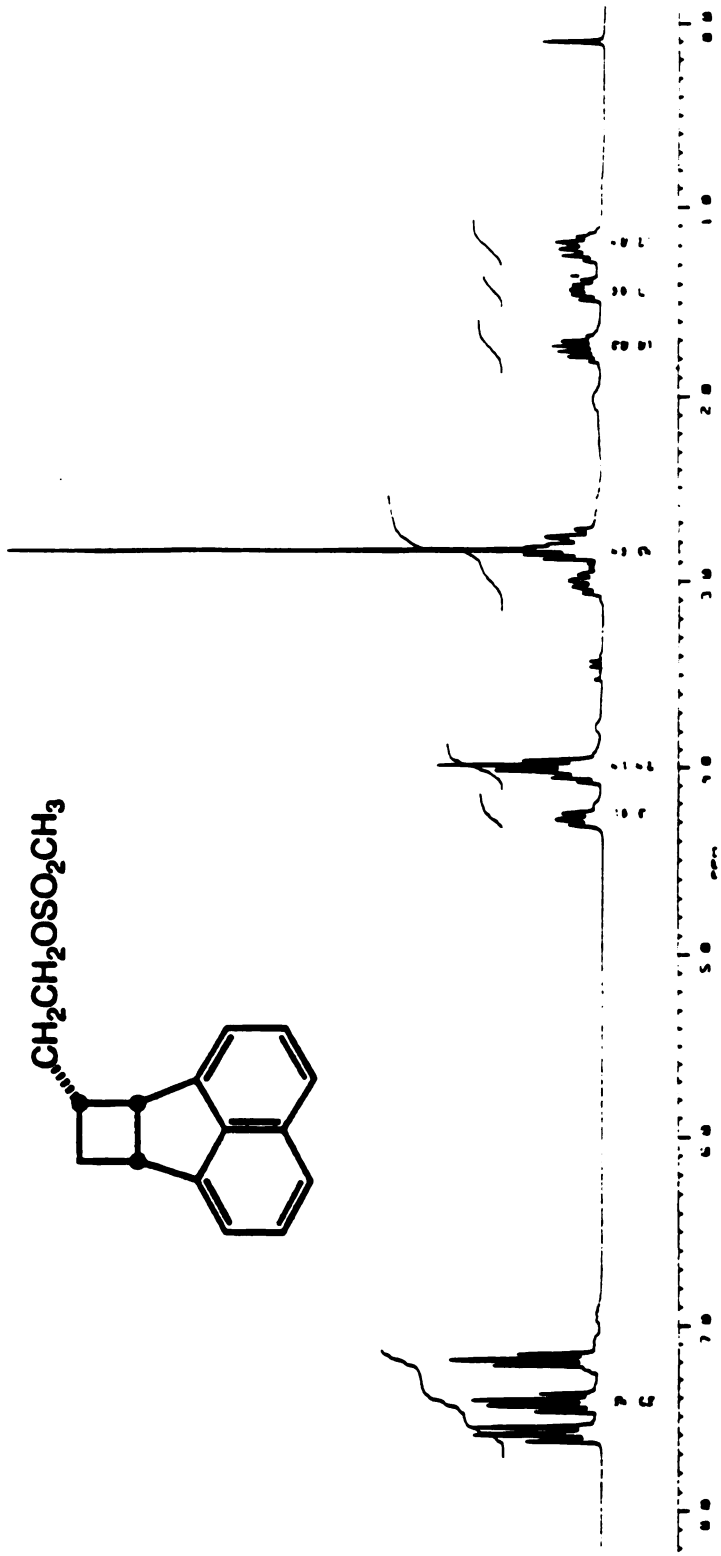

Figure 114. ^{1}H NMR Spectrum of 38.

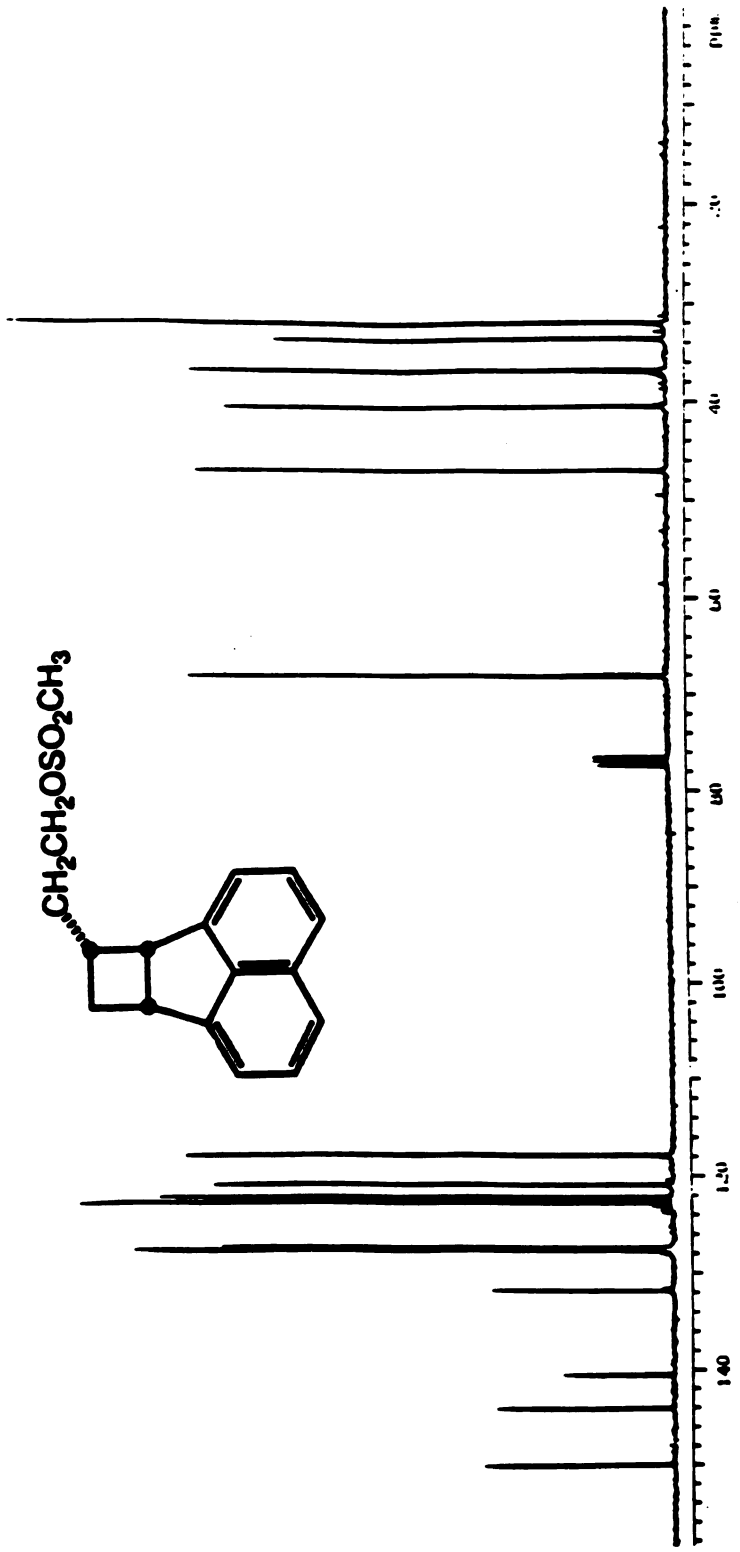

Figure 115. ^{13}C NMR Spectrum of 38.

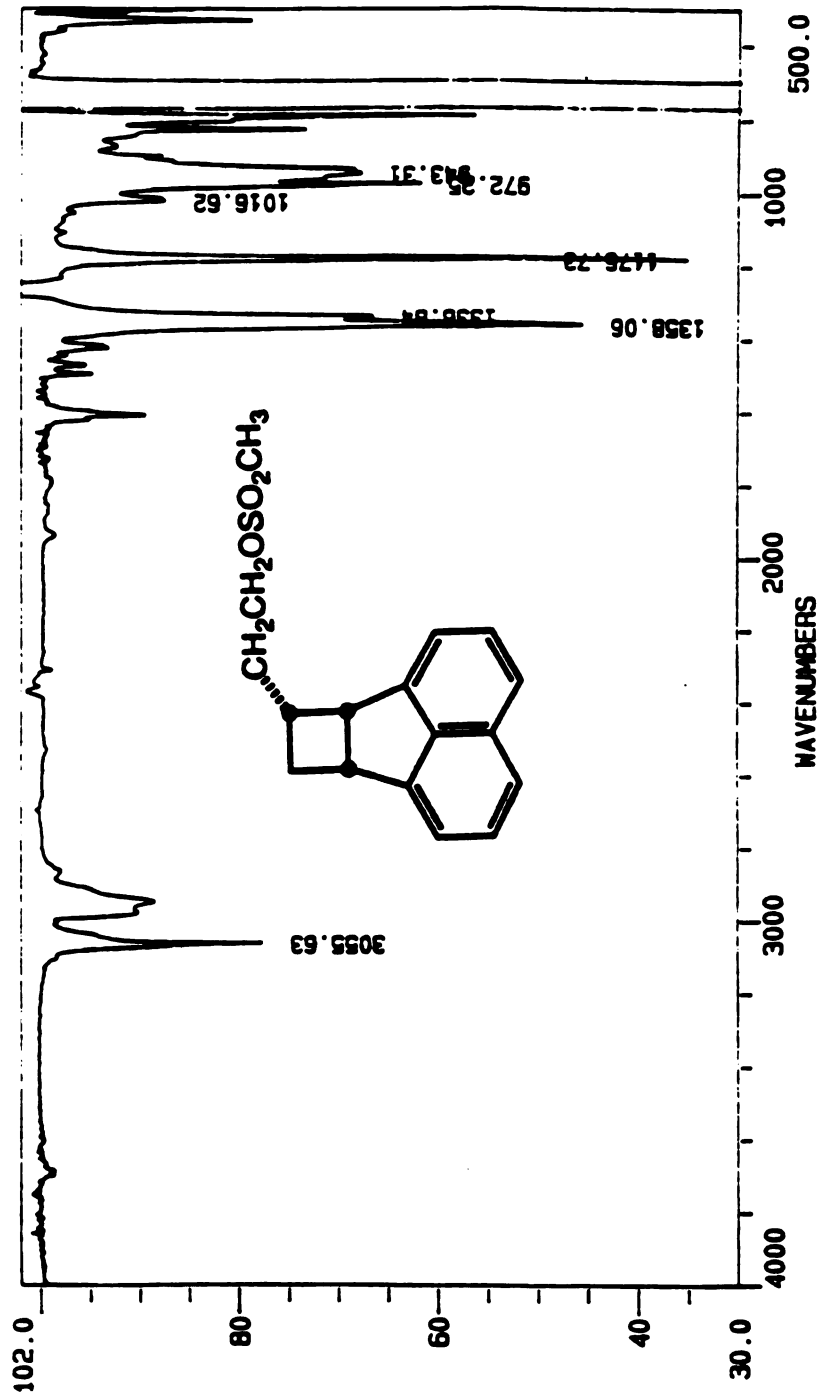

Figure 116. Infrared Spectrum of 38.

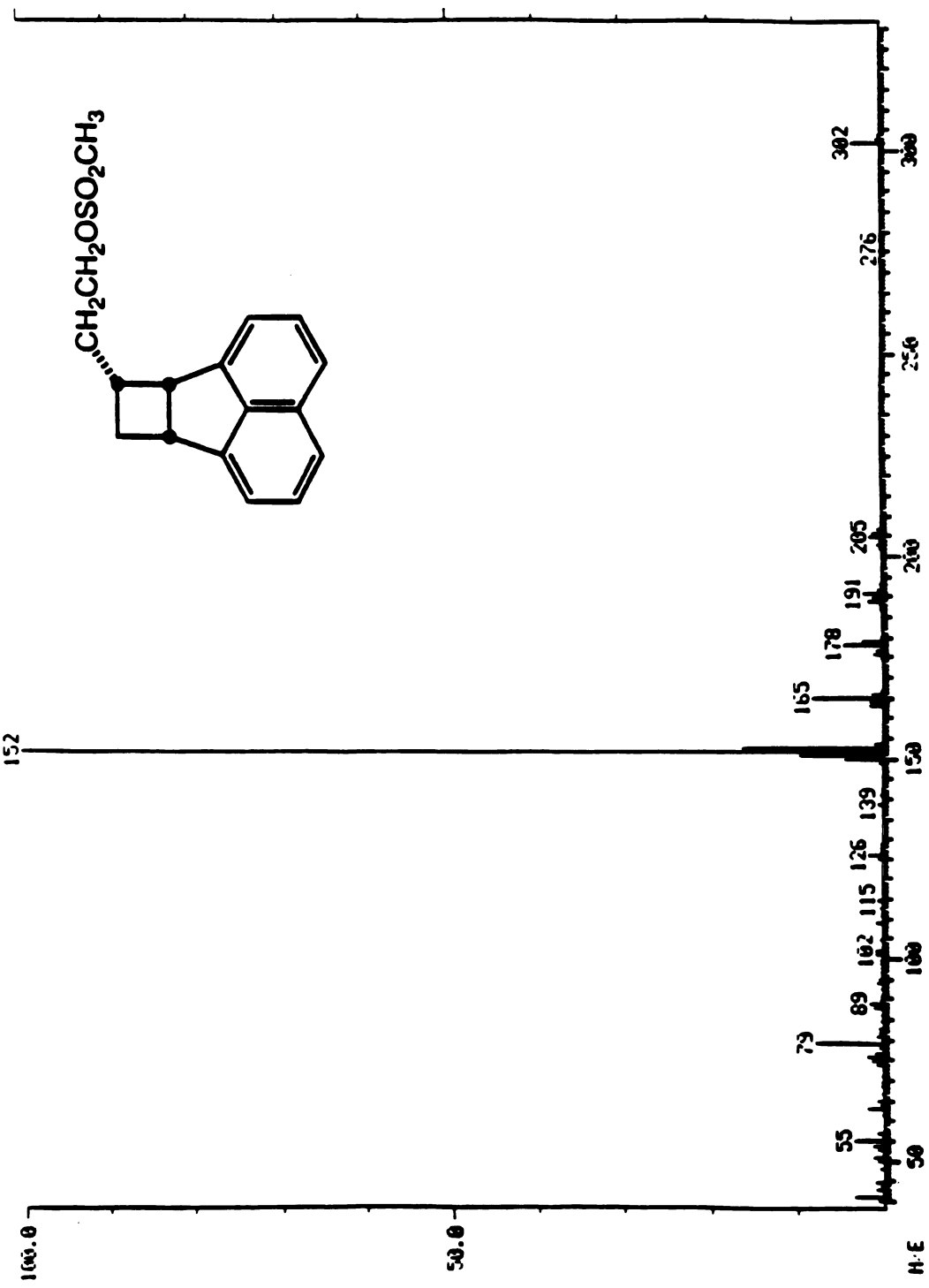

Figure 117. Mass Spectrum of 38.

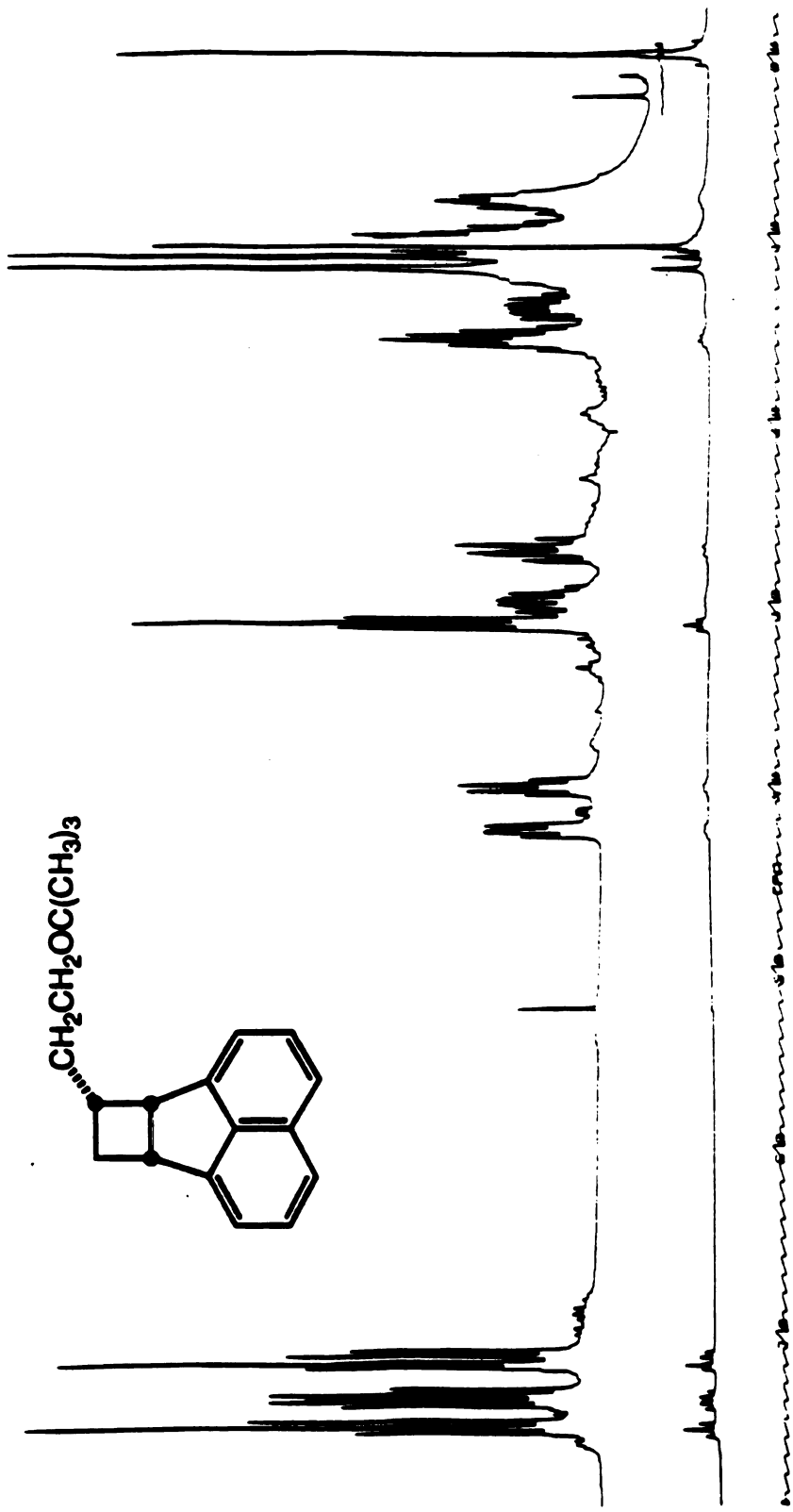

Figure 118. ^{1}H NMR Spectrum of 39.

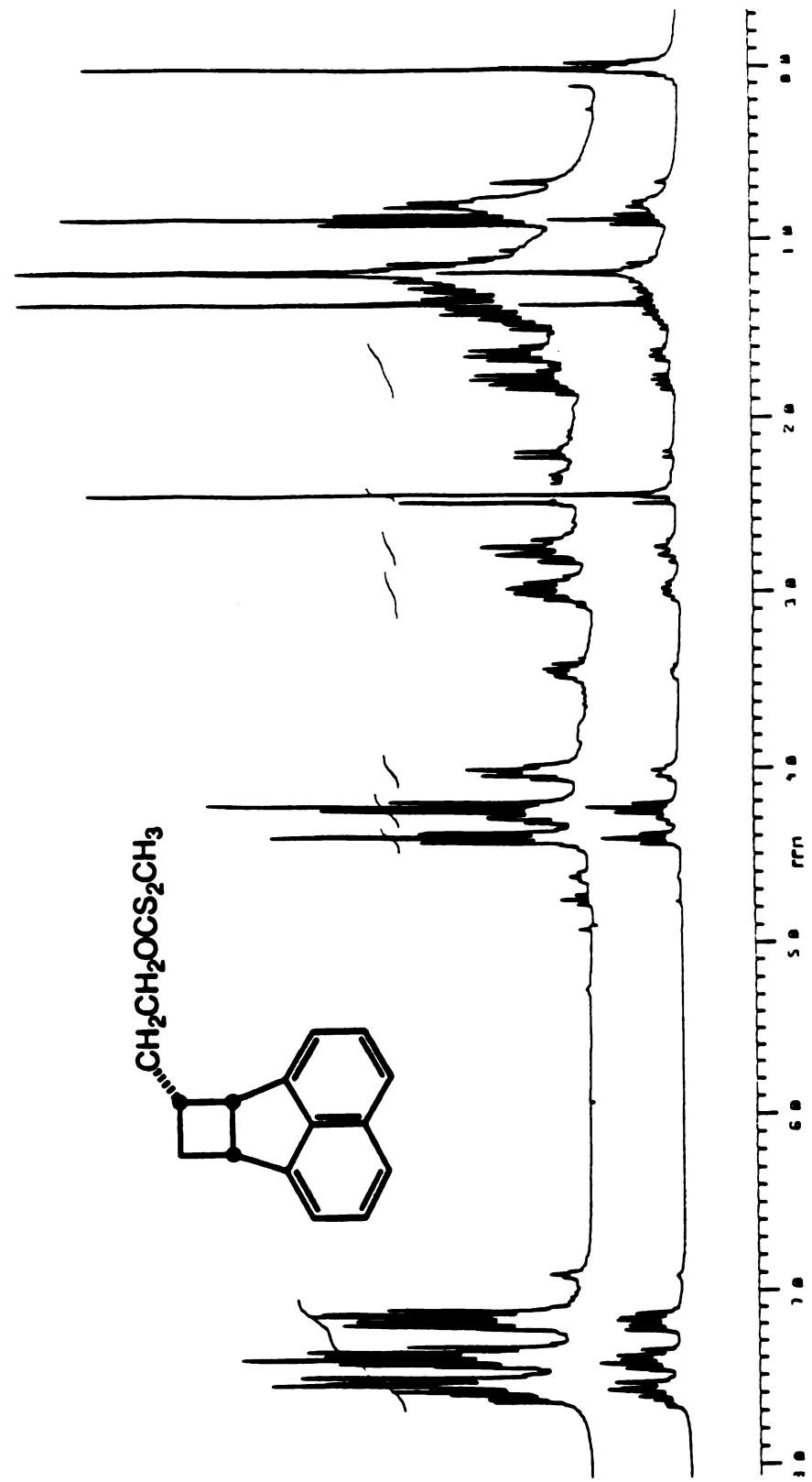

Figure 119. ^{1}H NMR Spectrum of **40**.

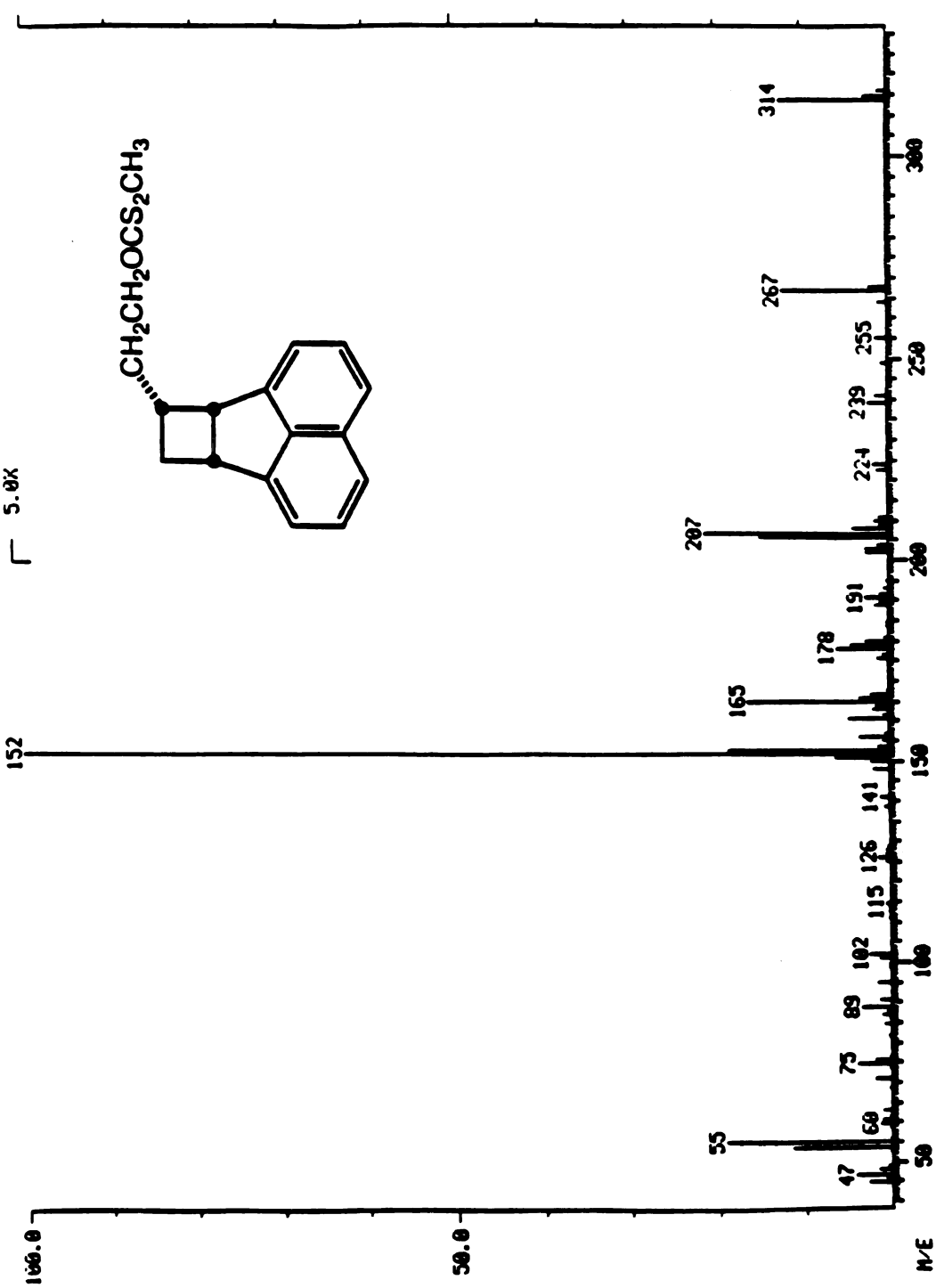

Figure 120. Mass Spectrum of **40**.

Figure 121. ^{1}H NMR Spectrum of **41**.

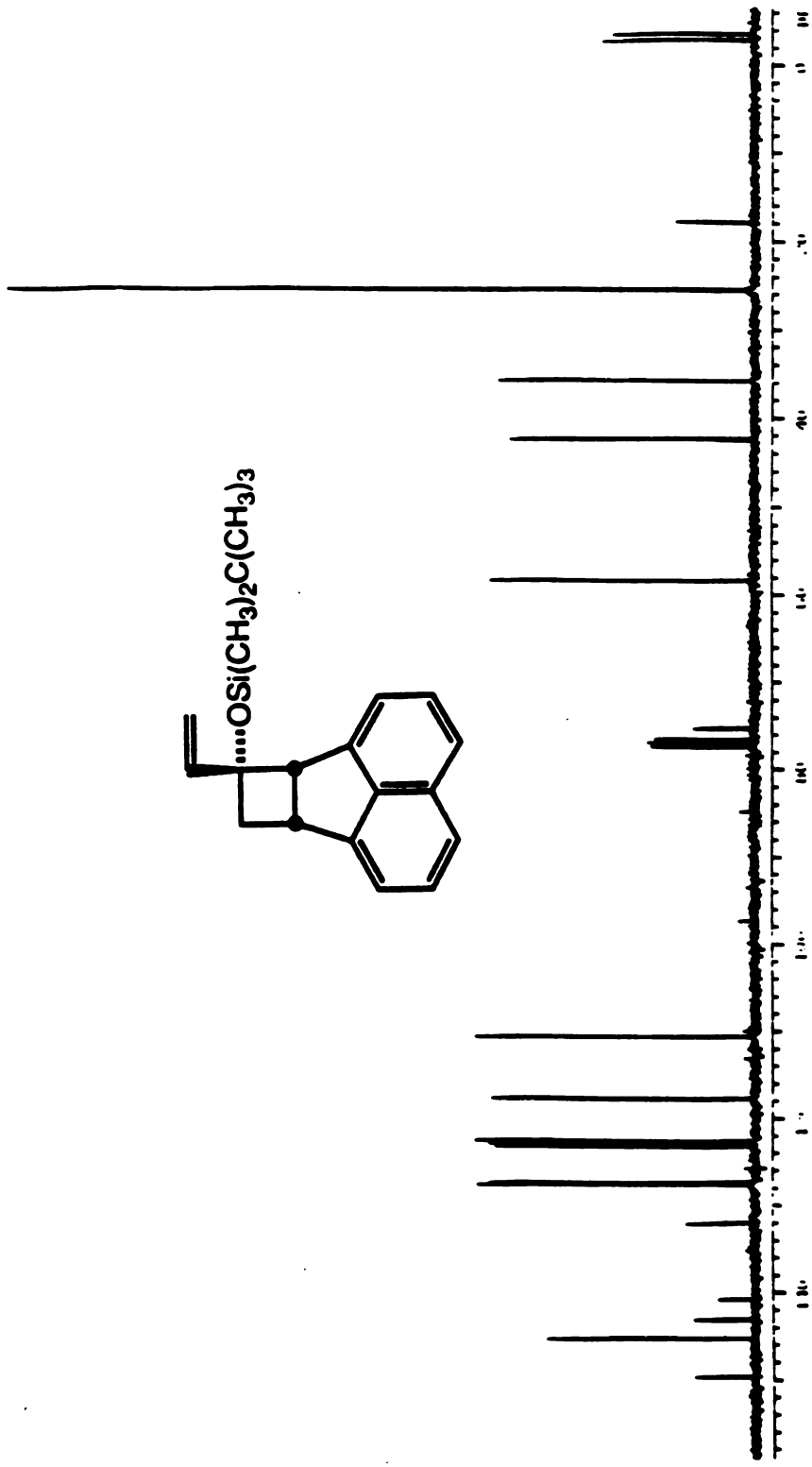

Figure 122. ^{13}C NMR Spectrum of **41**.

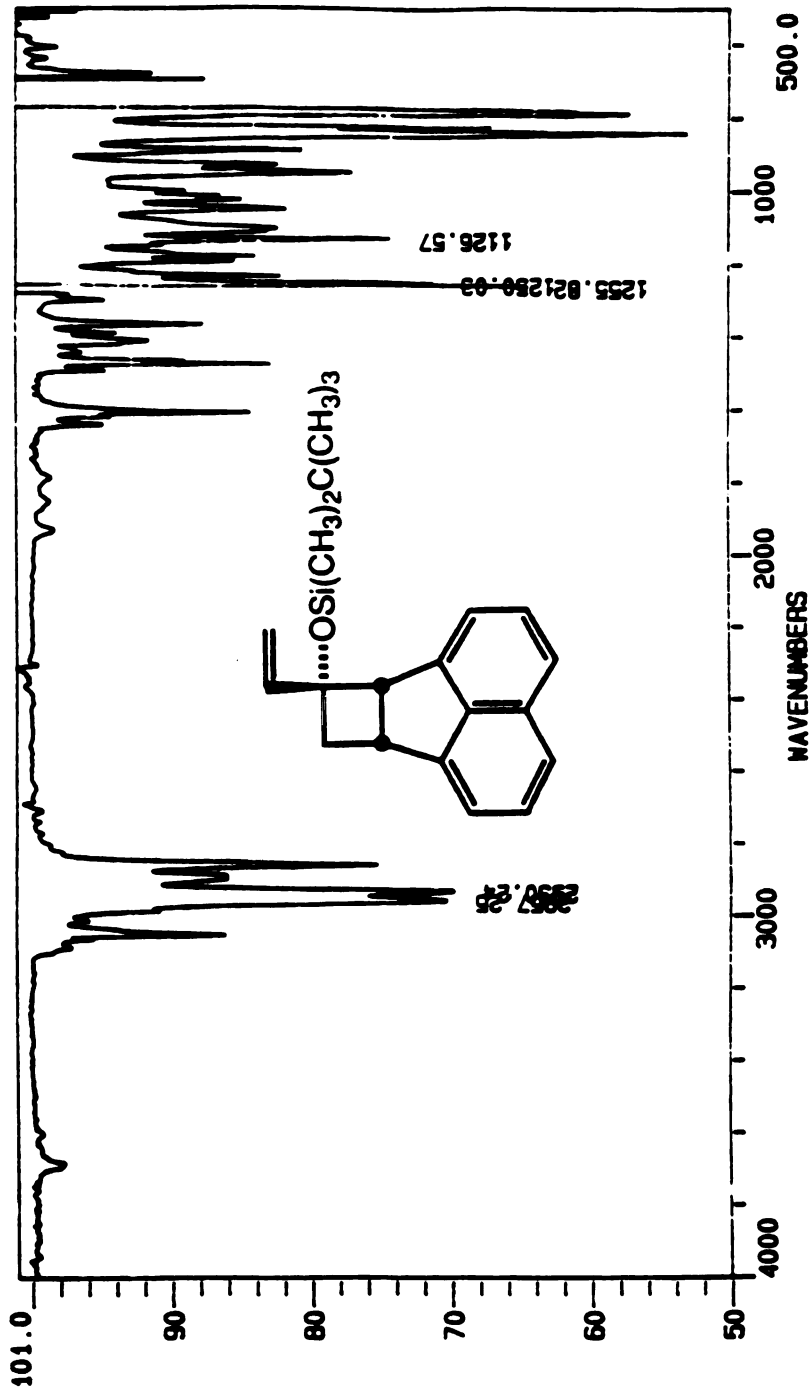

Figure 123. Infrared Spectrum of 41.

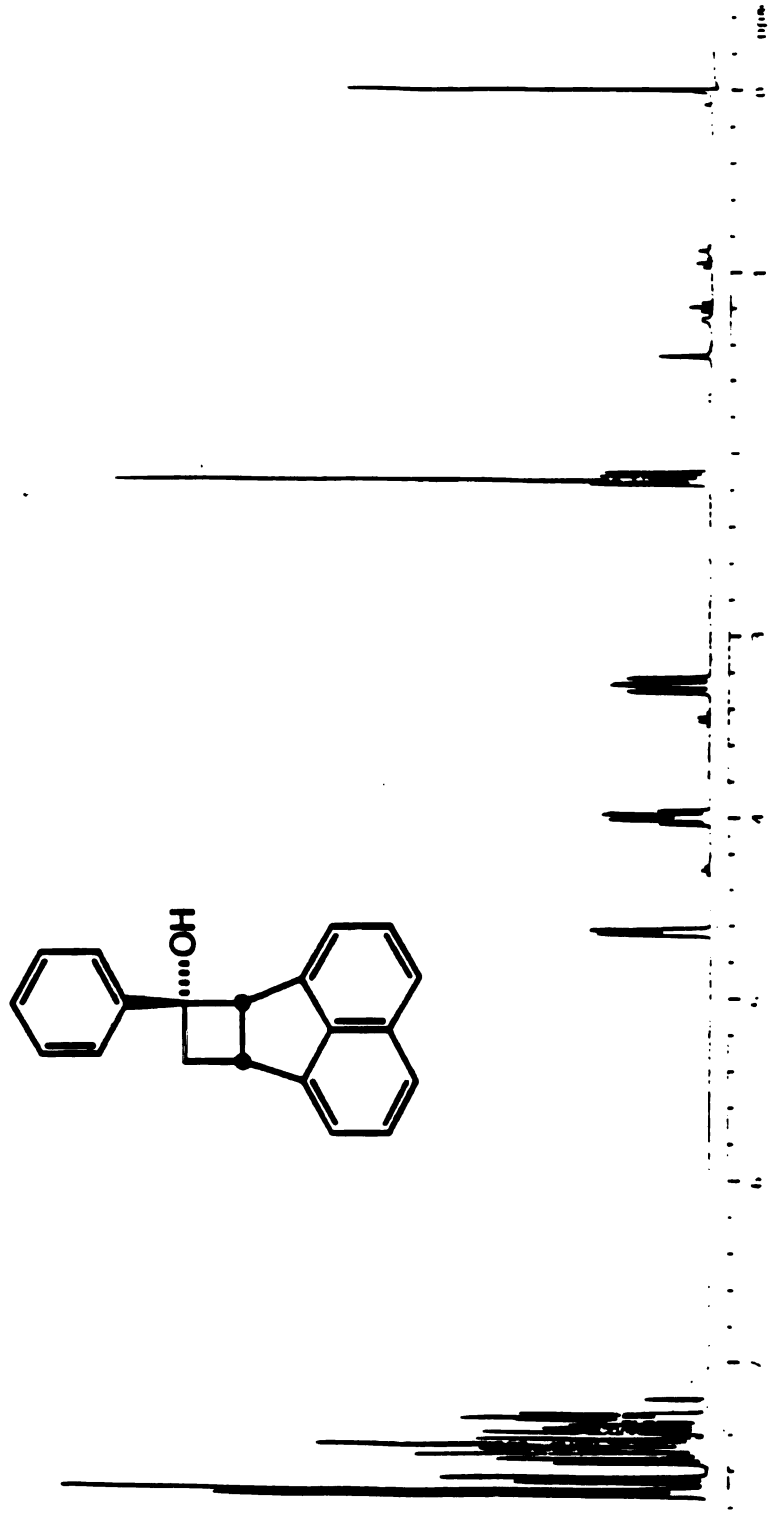

Figure 124. ^{1}H NMR Spectrum of 42.

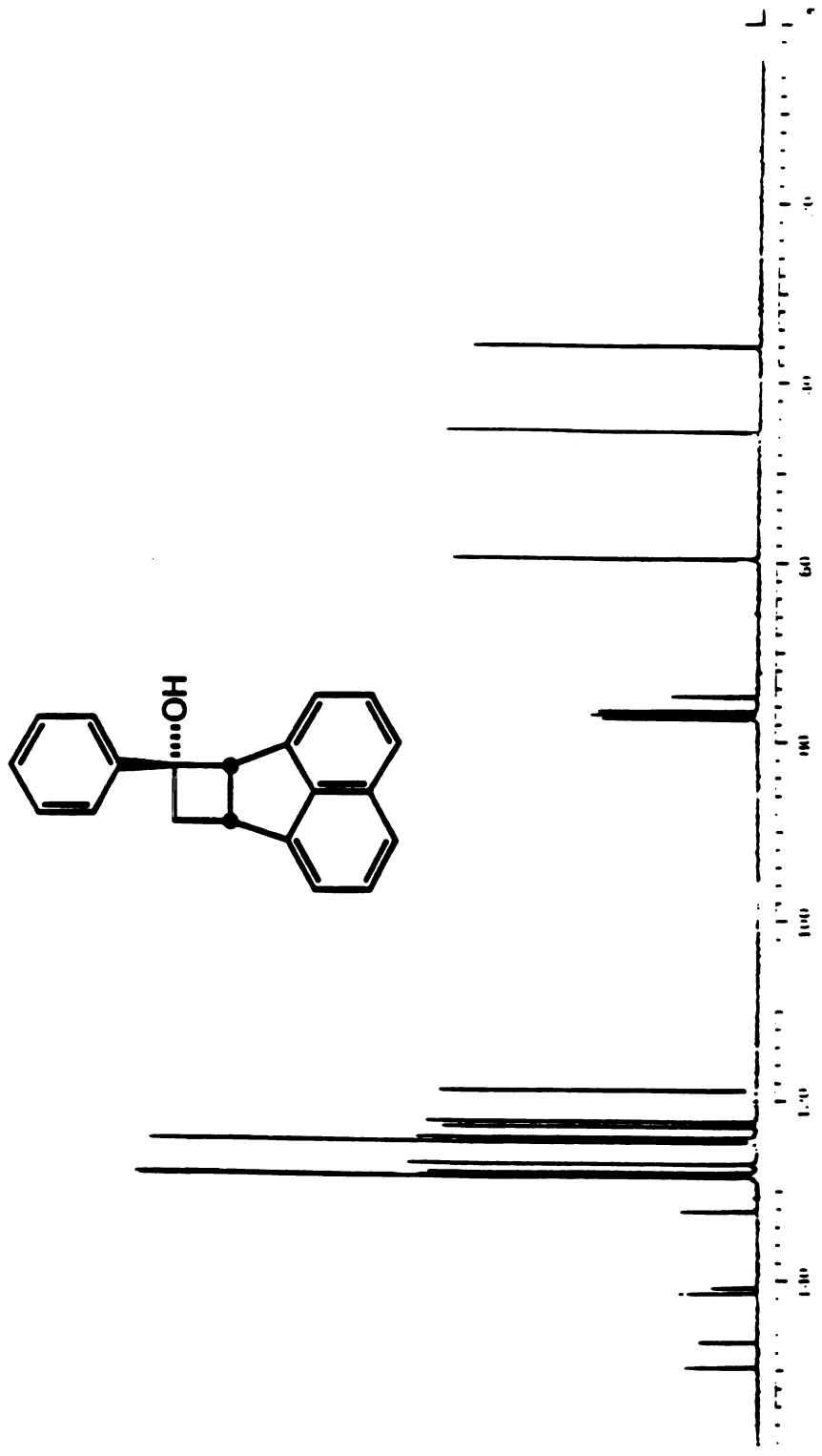

Figure 125. ^{13}C NMR Spectrum of 42.

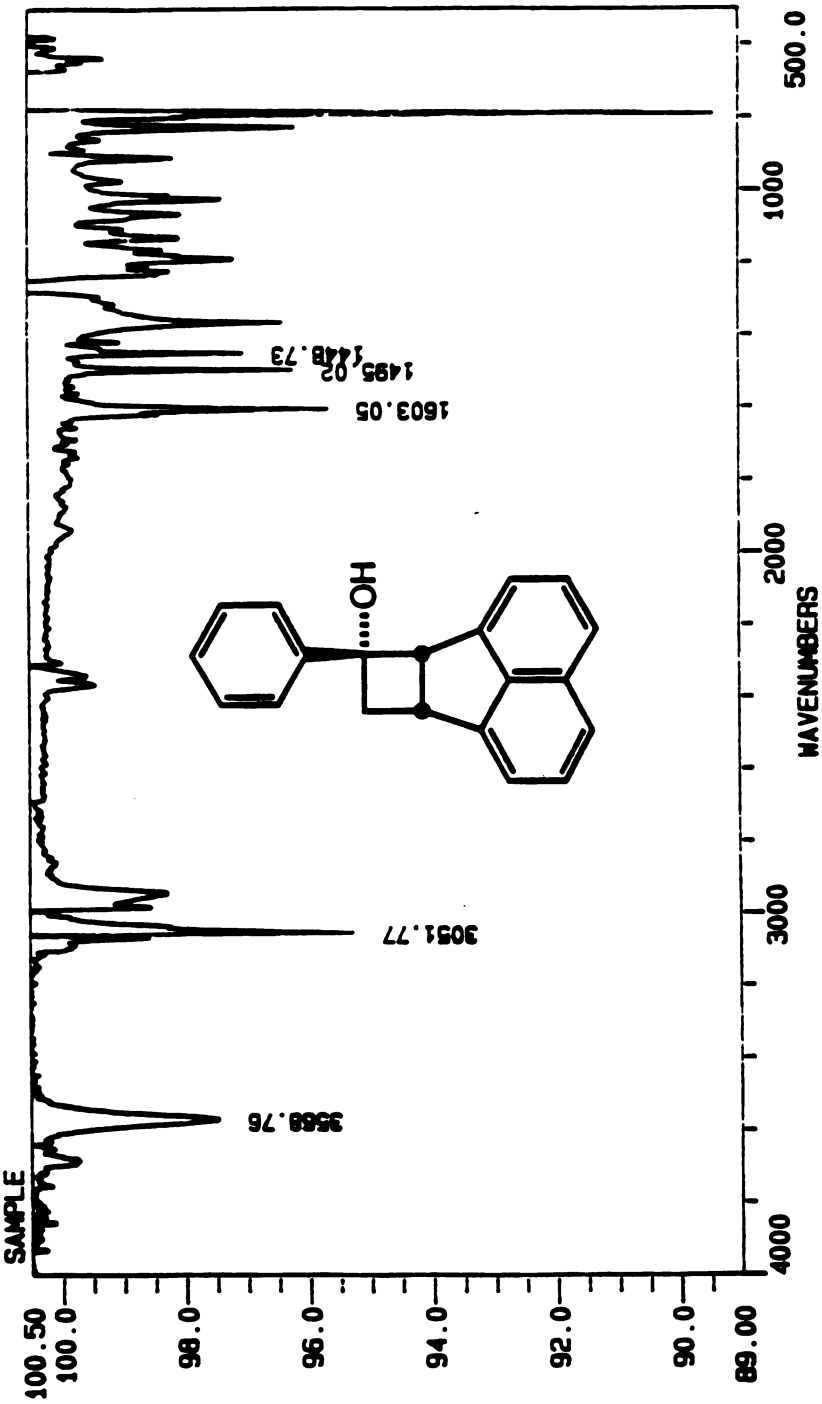

Figure 126. Infrared Spectrum of 42.

Figure 127. ^{1}H NMR Spectrum of 45.

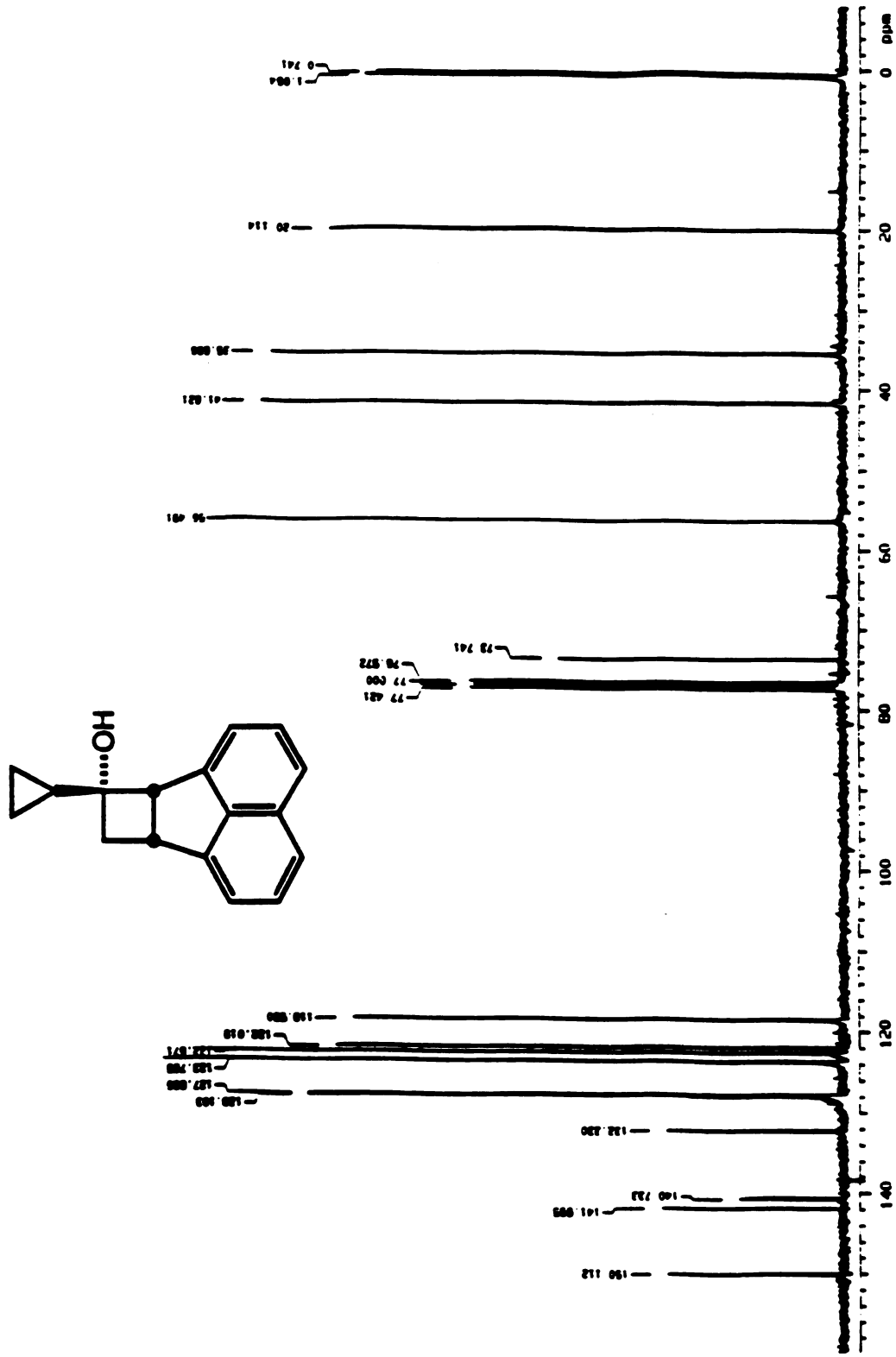

Figure 128. ^{13}C NMR Spectrum of **45**.

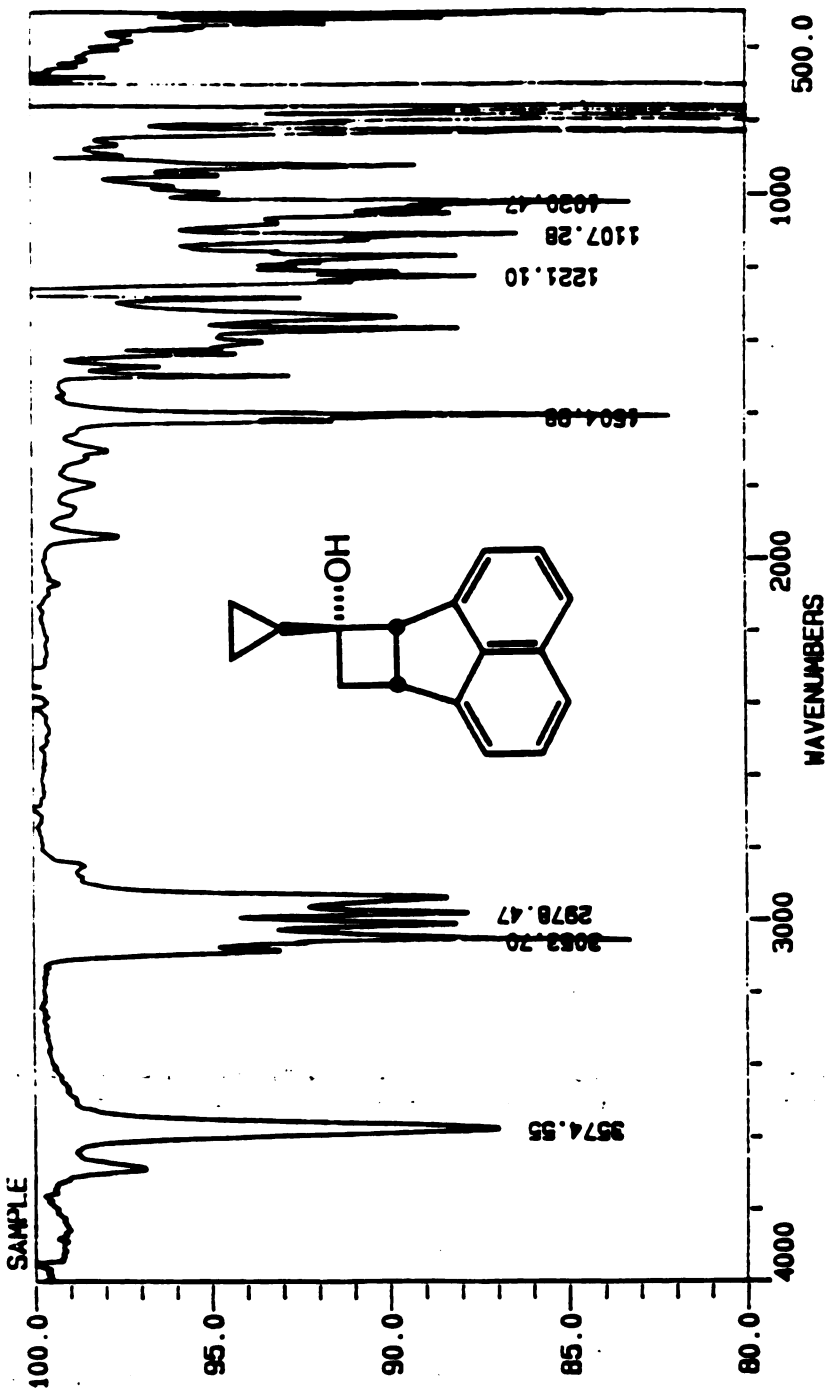

Figure 129. Infrared Spectrum of 45.

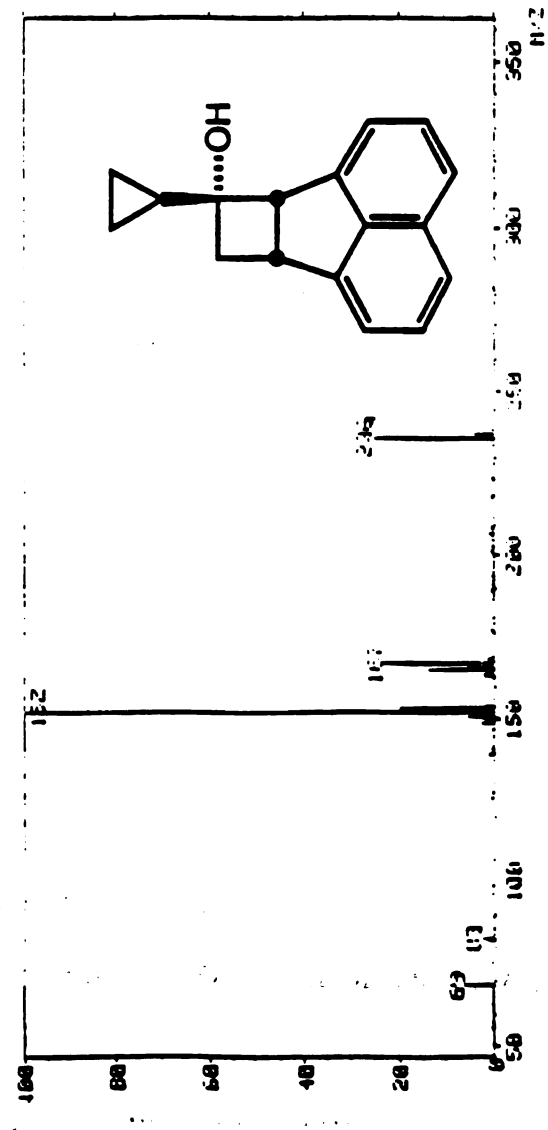

Figure 130. Mass Spectrum of 45.

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