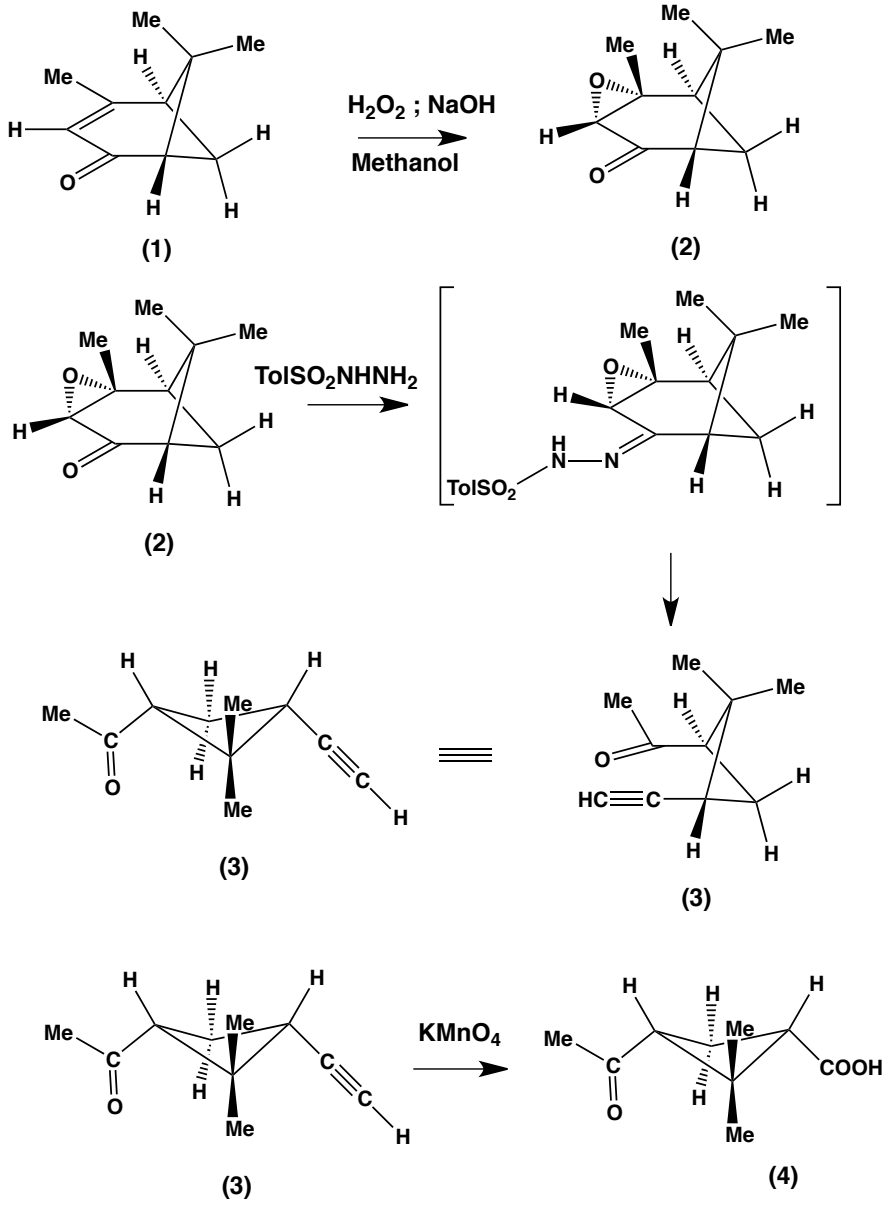
EXPERIMENT A

EPOXIDATION OF AN α,β-UNSATURATED KETONE;

TOSYLHYDRAZONE CLEAVAGE OF AN α,β-EPOXY KETONE;

OXIDATIVE $KMnO_4$ CLEAVAGE OF AN ALKYNE

The goal of this experiment is the correct assignment of the 1D- and 2D- NMR spectra of a series of organic compounds. The chemistry related to the syntheses of the target compounds is described in the attached photocopied material, along with authentic spectra of the products for comparison with your isolated products. In summary, an optically active natural product (-)-verbenone **(1)** is reacted with basic H_2O_2 to add O to the C=C double bond forming an epoxide or oxirane **(2)**. Epoxide **(2)** is reacted with a hydrazine, followed by cleavage of the resulting hydrazone leading to an alkyne **(3)**. Finally alkyne **(3)** is oxidized with permanganate to give the ketocarboxylic acid **(4).**



ALL MANIPULATIONS MUST BE CARRIED OUT IN A FUMEHOOD.
PROTECTIVE EYEGLASSES AND GLOVES MUST BE WORN.

Session 1

1. EPOXIDATION OF AN α,β-UNSATURATED KETONE

Clamp a 500 mL 3 necked flask to the rack with an empty cooling bath and magnetic stirrer beneath. Slide in (do not drop) a magnetic stir bar and stir while you add in order, **60 mL methanol, 15 mL (171 mmol) of 35% H_2O_2** (care: avoid skin contact) and **9.25 mL (by syringe) verbenone (d = 0.974 g/mL).** Affix a thermometer into one neck of the flask ensuring its bulb is in the liquid but away from the stir bar. Add just enough ice to the bath to immerse only the bottom of the flask. When the internal temperature reaches ca.15 ˚C raise the flask so it is just out of the ice/water and with stirring, begin a very slow dropwise addition of **5.0 mL 6N NaOH** solution using a pipet. Add this NaOH over 20 mins, keeping the internal temperature at 15-20 ˚C by briefly raising the ice/water bath as needed. Note from the mechanism that hydroxide is regenerated so your addition progressively increases the OH^- concentration, thus adjusting the rate for loss of enone and H_2O_2. When addition is complete, stir the mixture another 15 min, keeping the temperature at 20-25 ˚C.

Add 75 mL of ice-cold water to the mixture and extract it with 3 portions of diethyl ether. Wash the combined extracts 2x with water to remove MeOH, then once with 20 mL of a 3% KI solution to reduce any remaining H_2O_2, and finally with another 20 mL of water. Dry the extracts with $MgSO_4$ and transfer the filtered extracts to a flask suitable for the rotary evaporator. Remove the solvents on the evaporator taking care not o overheat the sample, nor use too high a vacuum. Transfer the residue via pipette to a small flask for distillation. Pre-weigh a small collection flask, then distill the product under high vacuum using the Schlenk line and the short path distillation apparatus into the pre-weighed flask. Heat the flask using a heat gun (NO flames). Weigh your product, determine the % yield and save 50 mg for IR, GC/MS and ^1H and ^{13}C NMR spectroscopy. Stopper your product flask and store in the refridgerator until the next session.

Session 2

2. TOSYLHYDRAZONE CLEAVAGE OF AN α,β-EPOXY KETONE

Weigh out accurately the largest whole-gram amount of epoxy ketone **(1)** into a three-necked 500-mL round bottom flask, add a stirring bar and affix a thermometer into one neck of the flask ensuring its bulb is in the liquid but away from the stir bar. Clamp the flask to the rack above a magnetic stirrer. With stirring add the following in order: **40 mL absolute ethanol (per gram of epoxy ketone) and 1.12 g of *p*-Toluenesulfonylhydrazide (per gram of epoxy ketone).** Place a balloon over the neck of the flask and stir the sealed flask at room temperature for 40 mins. After the 40 mins stirring period, heat the flask with a 50 ˚C water bath until gas evolution has essentially stopped. Finally raise the bath temperature slowly to 65 ˚C and then remove your flask for workup. Pour the mixture into a 1.0 L separatory funnel, add 400 mL of ice-cold water and extract it with 3 portions of diethyl ether. Wash the combined extracts 2x with small amounts of cold, dilute $NaHCO_3$, 2x with cold water and once with saturated NaCl solution. Dry the solution, filter and evaporate the solvents on the rotary evaporator. Transfer the residue to a small flask and distill into a pre-weighed collection flask using the short path distillation apparatus on the Schlenk line. The boiling point of the product is low (ca. 65 ˚C) so make

sure there is a good flow of cold water in the condenser. On the other hand the melting point of the pure keto-alkyne is low (43 ˚C) so watch that it doesn't freeze in the condenser and block it. Weigh your product, determine the % yield and save 50 mg for IR, GC/MS and ^{1}H and ^{13}C NMR spectroscopy. Stopper your product flask and store in the refridgerator until the next session.

Q1. In this step the mixture is first stirred @ 25 ˚C for 40 min. Why? Specify what would happen if heating was started immediately instead of waiting 40 min?

Q2. What would happen if two equivalnts of toluenesulfonylhydrazide were used?

Q3. Why does the distillation procedure produce such a black tarry residue at the end? HINT: toluenesulfonyl is used because it is a good leaving group; what does this imply about its conjugate acid and why might that create problems?

Q4. A distillate impurity occasionally appears which is a stereoisomer of the expected product. What is it and how does it arise? How could it be dealt with in the next step?

Session 3

3. OXIDATIVE $KMnO_4$ CLEAVAGE OF AN ALKYNE

Weigh out accurately the largest whole-gram amount of keto alkyne **(2)** into a small vial. Set up a 250 mL Erlenmeyer flask containing a stirring bar and clamp it to the rack in an ice+water bath above a magnetic stirrer. Add **15 mL water (per gram of keto alkyne) and 1.58 g of $KMnO_4$ (per gram of keto alkyne).** After this has stirred for 5 minutes, use a bulb pipet and add your keto alkyne along with **2.5 mL of acetic acid (per gram of keto alkyne)** using half to dissolve it and half to rinse the container and the pipet for complete transfer. Stir the mixture for 2 hrs, allowing the temperature to rise as the ice melts.After 2 hrs, add **1.0 mL of isopropanol (per gram of keto alkyne)** to consume the excess oxidant and stir 5 min. more. Now add **2.0 mL of conc. HCl (per gram of keto alkyne).** Test to be sure the pH is 3 or lower and suction filter the mixture to remove the brown MnO_2 sludge. Rinse the flask several times with small portions of water and CH_2Cl_2 to capture all of your product. Discard the MnO_2 (but not the stir bar) into the trash, transfer the filtrate into a separatory funnel and thoroughly mix and separate the layers. Extract the aqueous layer 2x wih Et_2O, combine all organic extracts and wash 2x with water before drying and evaporating the solvents on the rotary evaporator. Add a few mL (2-3) of diethylether to the residue and transfer to a vial. Layer hexane onto the ether solution and place the sealed vial in the refrigerator to crystallize until the next session.

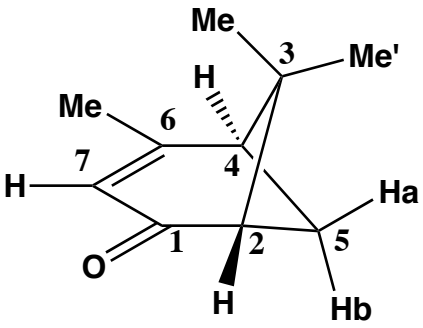
The next part must be done during the first period of the subsequent experiment.

Remove the vial form the refrigerator and inspect for formation of crystals. Decant the mother liquors with a pipet (do not discard this solvent, in case it contains substantial product) and dry the cystls on the vacuum line for a few minutes. Weigh your product, determine the % yield and obtain IR, GC/MS and ^{1}H and ^{13}C NMR spectra of the product.

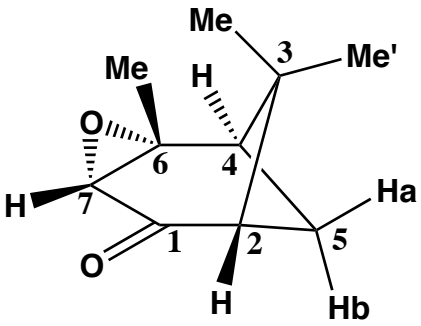
QUANTITIES TO BE USED FOR SPECTRAL MEASUREMENTS FOR ALL SAMPLES:

IR ca. 1 mg; GCMS ca. 1 mg; ^{1}H NMR alone ca. 5 mg; ^{1}H and ^{13}C NMR together at least 25 mg.

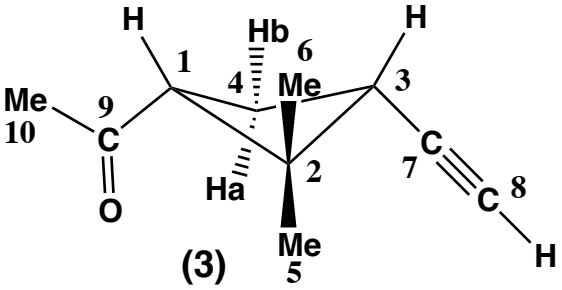
ASSIGN YOUR NMR SPECTRA USING THE FOLLOWING LABELLING



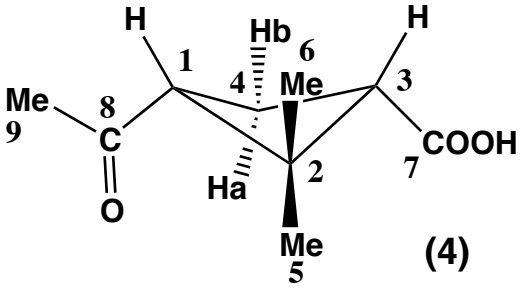
(1)



(2)



(3)

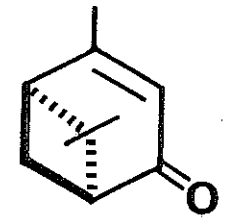


(4)

Authentic NMR spectra, including 2D COSY and NOESY spectra are attached to these instructions. Use these to help assign your spectra.

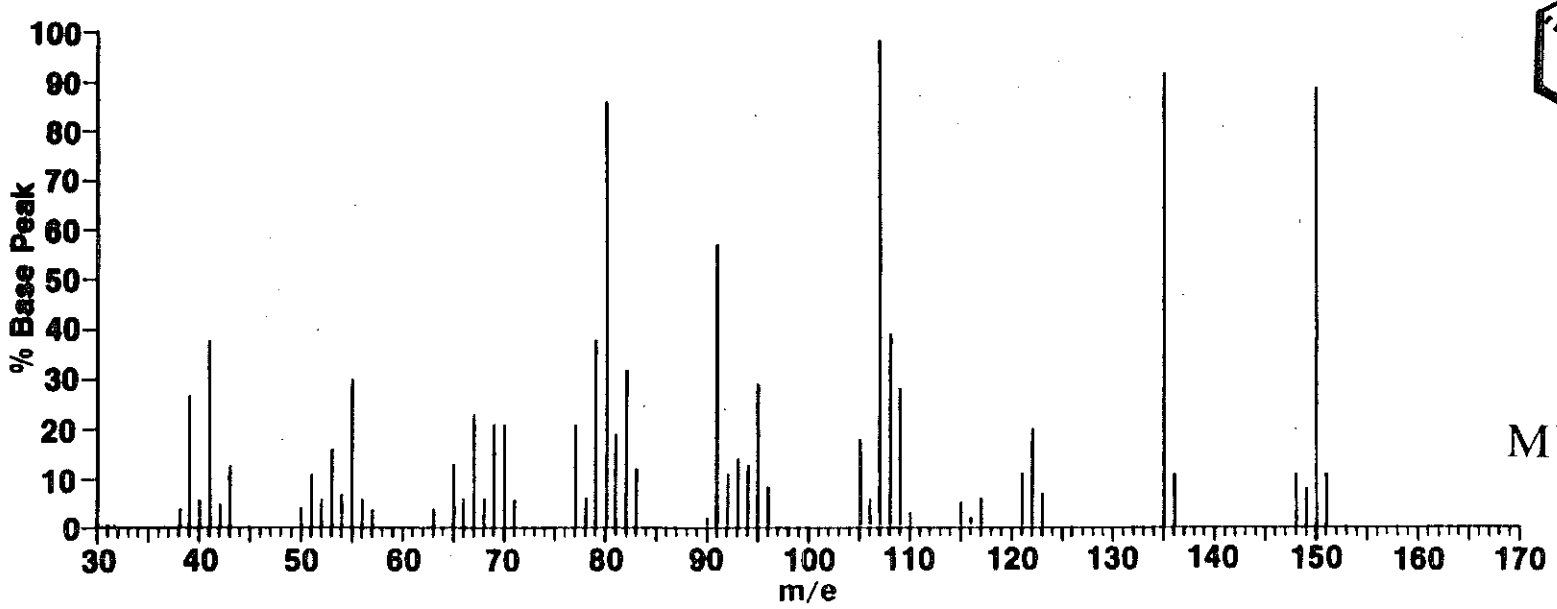
JBS 01/09/2013 BASED ON HWT LAB EXPERIMENTAL 12/18/08.

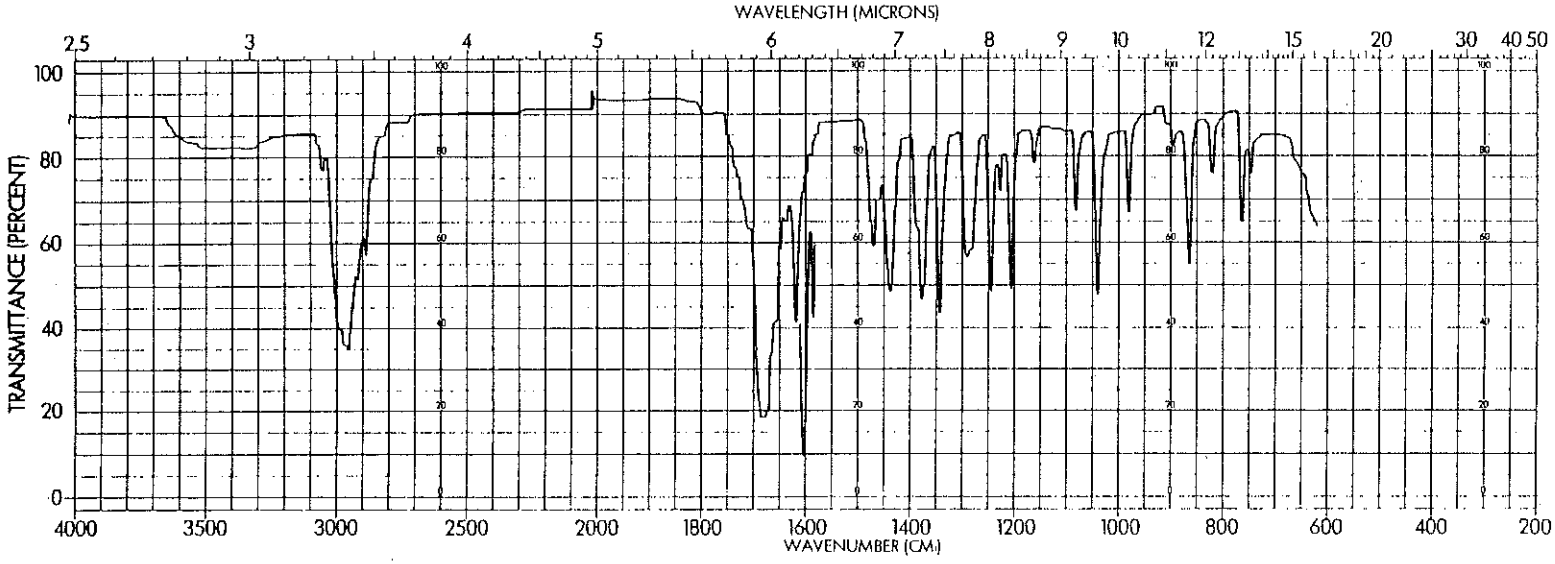
Verbenone



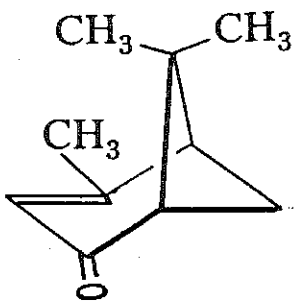
$C_{10}H_{14}O$

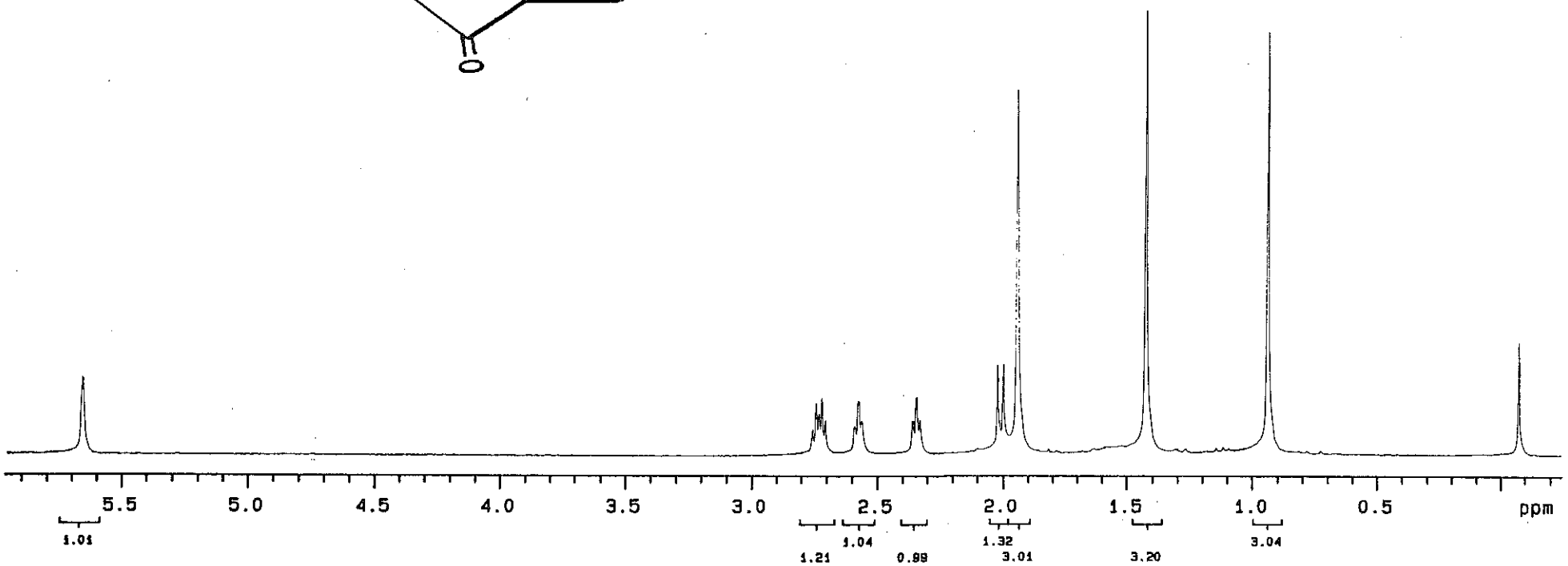
MW 150.22





Verbenone


CH3
CH3
CH3
O


5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
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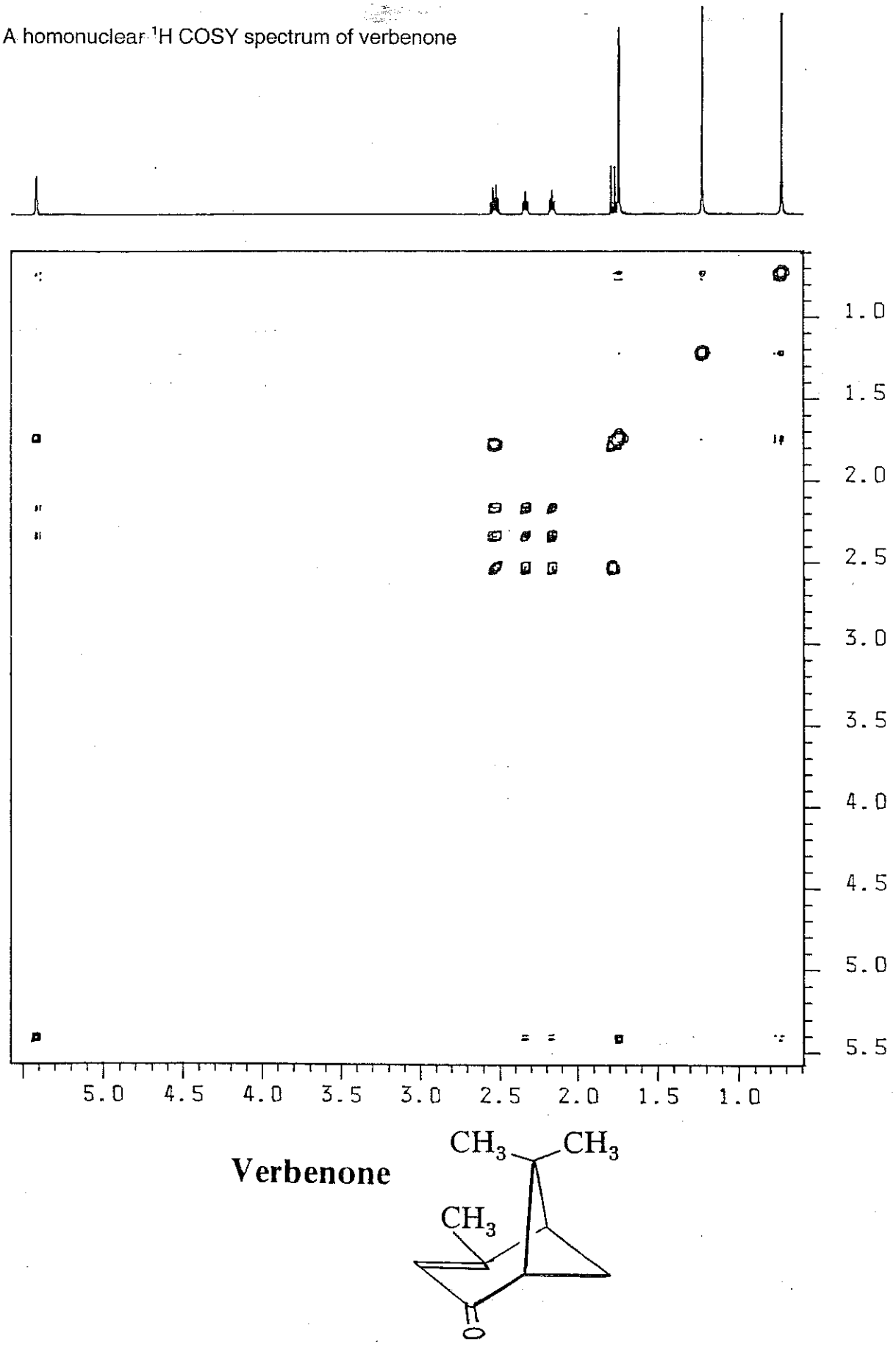
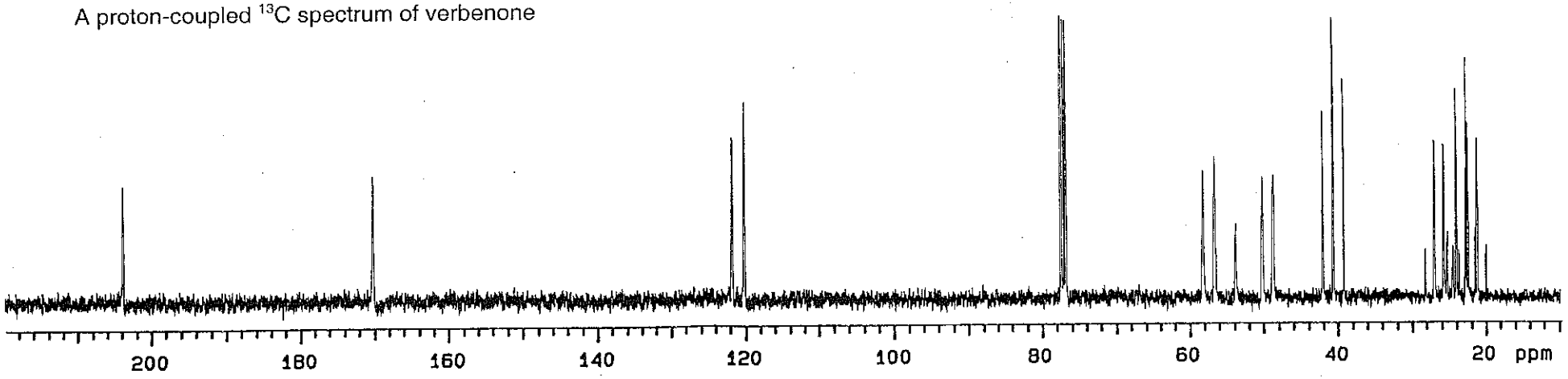
ppm
1.01
1.21
1.04
0.99
1.32
3.01
3.20
3.04

A homonuclear ^1H COSY spectrum of verbenone

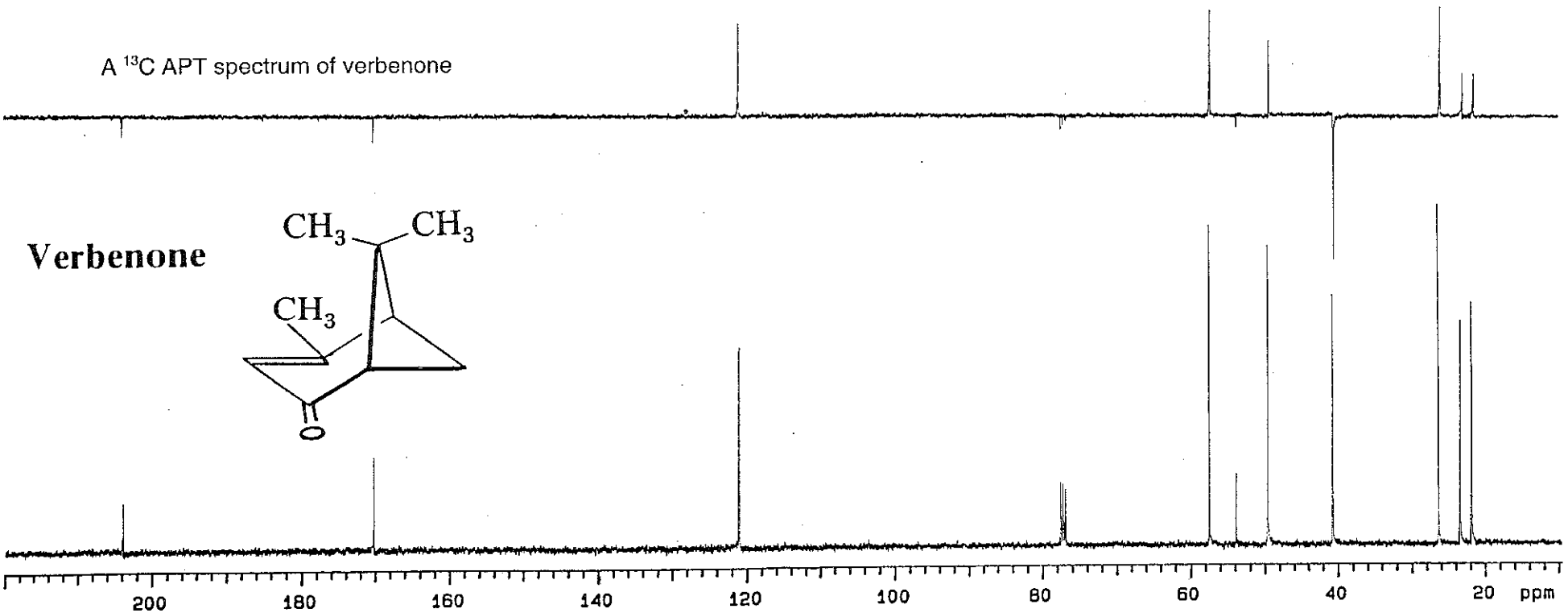


Verbenone

A proton-coupled ^{13}C spectrum of verbenone

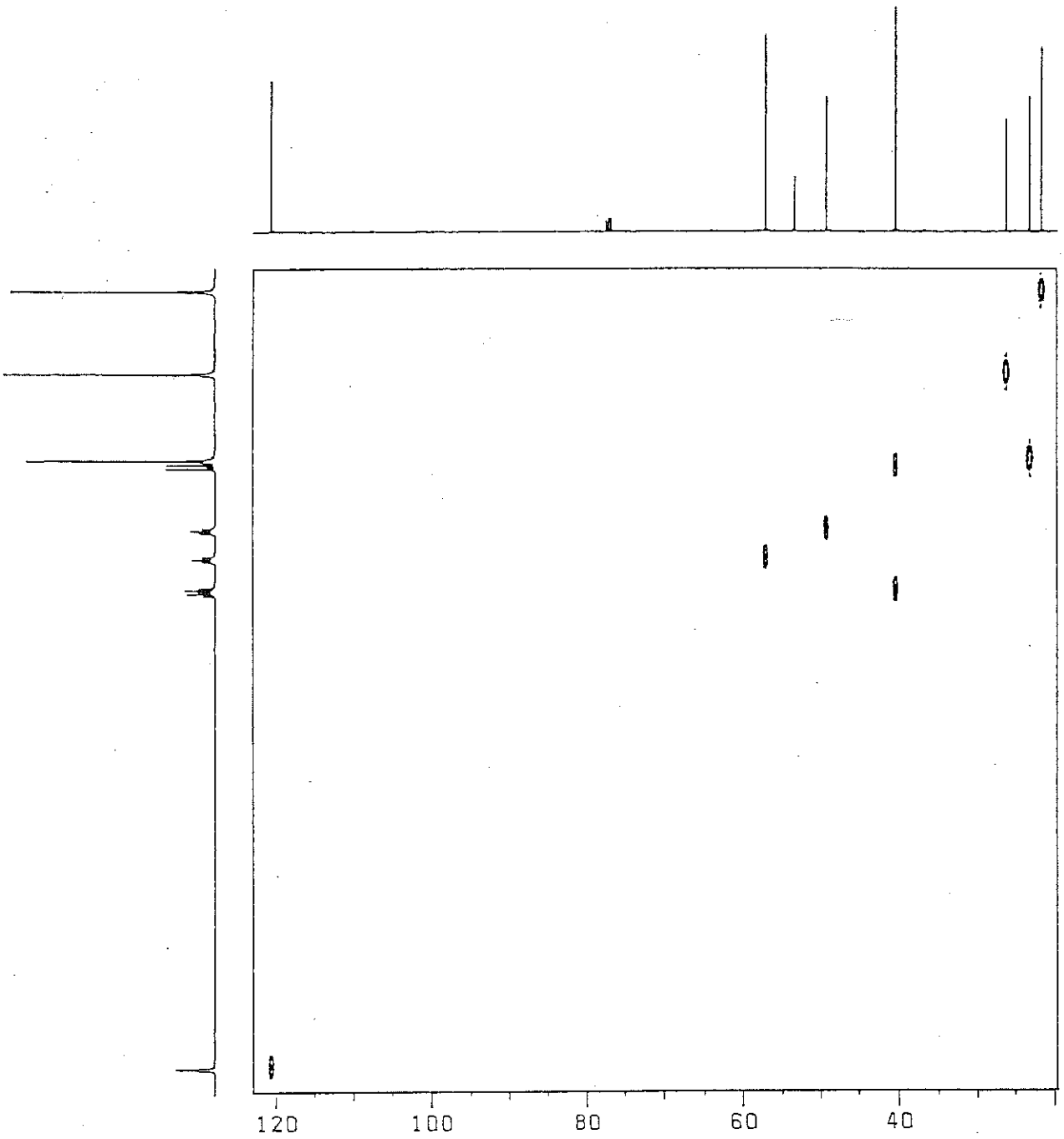


A ^{13}C APT spectrum of verbenone

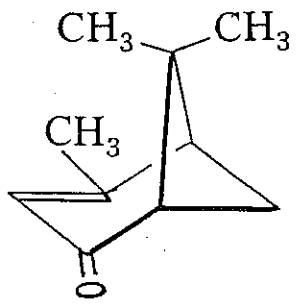


Verbenone

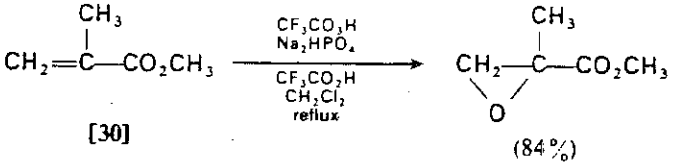
A heteronuclear ^{1}H-^{13}C COSY (HETCOR) spectrum of verbenone



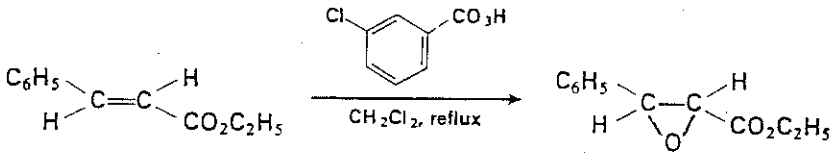
Verbenone



reactive than CH_3CO_3H) or of electron-donating groups in the olefin.[1,15] Thus, olefins with three or four alkyl substituents are rapidly epoxidized by peracids whereas terminal, monosubstituted olefins react very slowly[1] unless a highly reactive peracid such as peroxytrifluoroacetic acid is used.[22,31c] This effect is well illustrated by the previously described selective epoxidation of only the more highly substituted double bond in the diene **[16]**. Conjugation of the olefin with aromatic rings or with other multiple bonds also reduces the rate of epoxidation, since the delocalization of pi electrons possible in the conjugated systems reduces the electron density at the double bond undergoing electrophilic attack.[15] Although the rate of reaction of α,β-unsaturated esters with peracids is relatively slow, it is possible to epoxidize the double bond in these compounds either with peroxytrifluoroacetic acid (e.g., **[30]**), with peracetic acid, or with *m*-chloroperbenzoic acid (e.g., **[31]**). On the other hand, the reaction of α,β-unsaturated ketones with peracids usually does not lead to epoxidation of the double bond; as illustrated in the accompanying equations, reaction with the double bond is retarded sufficiently that the subsequently discussed reaction of the peracid with the ketone usually becomes the predominant process.[33,34]



[30] (84%) (Ref. 20b)



[31] (47%) (Ref. 21a, 33b)

However, α,β-unsaturated ketones (e.g., **[32]**) can be epoxidized, using nucleophilic reagents such as the sodium salt of hydrogen peroxide (NaOOH)[35a] or the sodium salt of *t*-butyl hydroperoxide[35b] rather than a peracid. The reaction is believed to proceed by nucleophilic addition of the hydroperoxide anion at the

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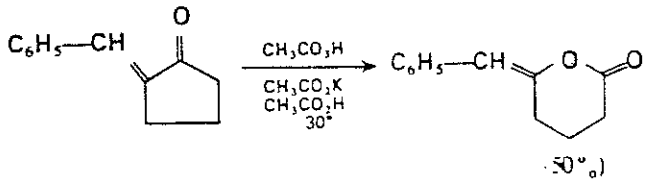
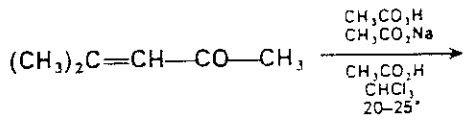
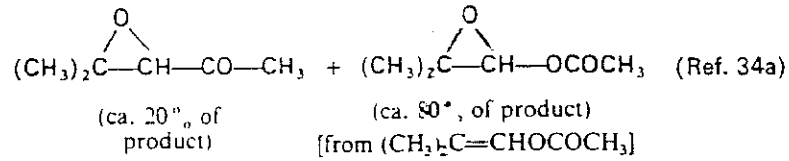
33. (a) H. M. Walton, *J. Org. Chem.*, **22**, 1161 (1957). (b) V. R. Valente and J. L. Wolfhagen, *ibid.*, **31**, 2509 (1966).
34. (a) G. B. Payne and P. H. Williams, *J. Org. Chem.*, **24**, 284 (1959). (b) M. Gorodetsky, N. Danieli, and Y. Mazur, *ibid.*, **32**, 760 (1967). (c) C. R. Zanesco, *Helv. Chim. Acta*, **49**, 1002 (1966). (d) For an exception to this generality, see Ref. 40i.
35. (a) Since such salts of hydrogen peroxide are thermally unstable, it is necessary to control the temperature of reactions in which they are used. For a study of the stability of alkaline solutions of hydrogen peroxide, see W. D. Nicoll and A. F. Smith, *Ind. Eng. Chem.*, **47**, 2548 (1955). (b) N. C. Yang and R. A. Finnegan, *J. Am. Chem. Soc.*, **80**, 5845 (1958).

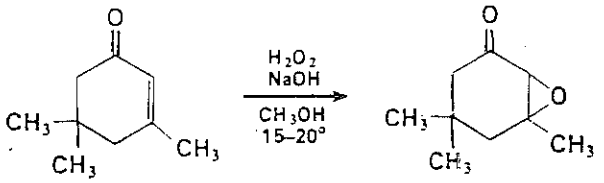


(Ref. 33a)



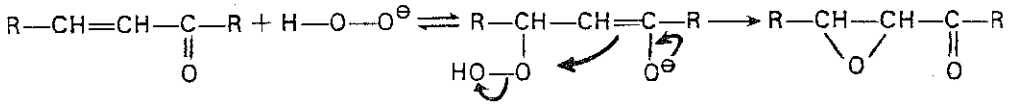


(Ref. 34a)



[32] (70–72%) (Ref. 36)

beta carbon of the unsaturated ketone followed by intramolecular displacement of hydroxide ion, as illustrated.[37]



Similar reaction conditions have been used for the epoxidation of alkylidenemalonic esters[38] and α,β-unsaturated aldehydes (e.g., **[33]**) as well as α,β-unsaturated nitro compounds, α,β-unsaturated sulfones, and vinyl phosphonates.[39]

Epoxidation with alkaline hydrogen peroxide differs from peracid epoxidation in that the former is not stereospecific (i.e. the stereochemistry of the reactant and

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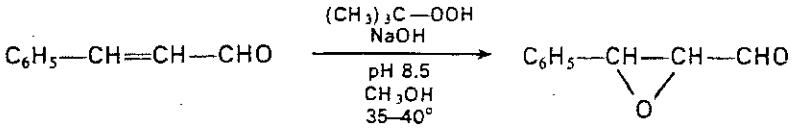
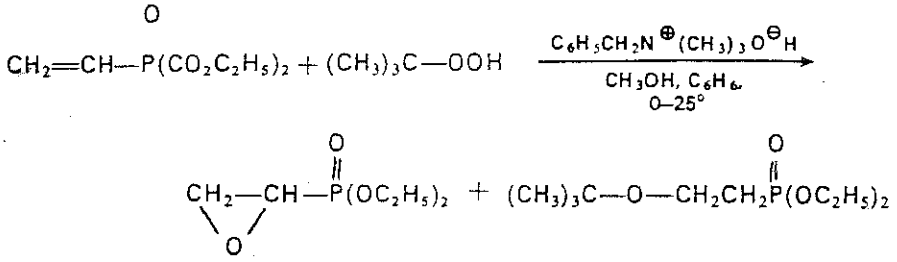
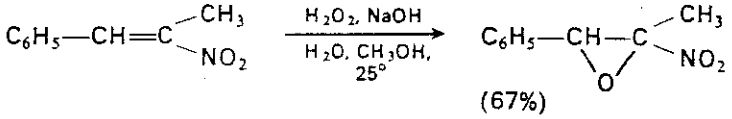
36. R. L. Wasson and H. O. House, *Org. Syn.*, **Coll. Vol. 4**, 552 (1963).
37. C. A. Bunton and G. J. Minkoff, *J. Chem. Soc.*, 665 (1949).
38. G. B. Payne, *J. Org. Chem.*, **24**, 2048 (1959).
39. (a) G. B. Payne, *J. Org. Chem.*, **25**, 275 (1960). (b) G. B. Payne, *J. Am. Chem. Soc.*, **81**, 4901 (1959). (c) C. E. Griffin and S. K. Kundu, *J. Org. Chem.*, **34**, 1532 (1969). (d) H. Newman and R. B. Angier, *Tetrahedron*, **26**, 825 (1970). (e) B. Zwanenburg and J. ter Wiel, *Tetrahedron Letters*, **No. 12**, 935 (1970). (f) T. Durst and K. C. Tin, *ibid.*, **No. 27**, 2369 (1970); also see D. F. Tavares, R. E. Estep, and M. Blezard, *ibid.*, **No. 27**, 2373 (1970).



[33] (73%) (Ref. 39a, b)

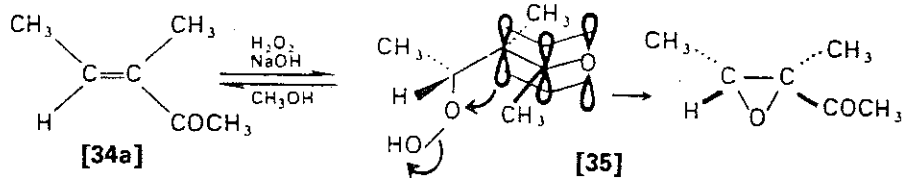


(61%) (23%) (Ref. 39c)

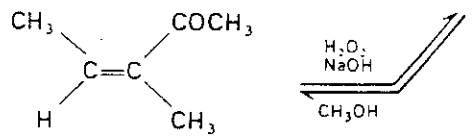


(67%) (Ref. 39d)

the product do not bear a definite relationship to one another) but is stereoselective (i.e., a single stereoisomer of the product is formed, which bears no definite relationship to the stereochemistry of the reactant).[40a,b,l] Thus, epoxidation of either isomer of the unsaturated ketone [34] yields a single epoxyketone in which



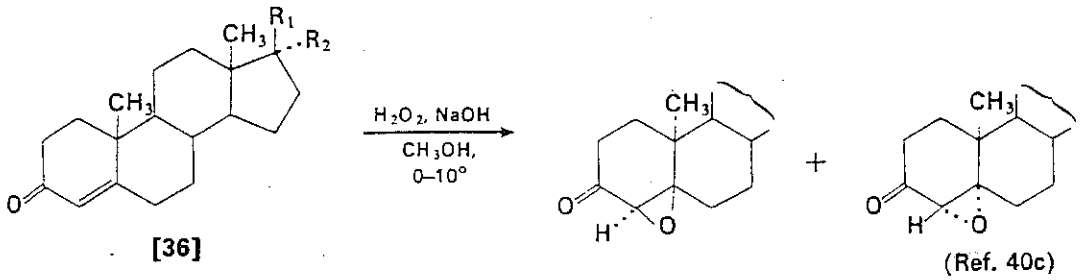
[34a] [35]



[34b] (Ref. 40a)

40. (a) H. O. House and R. S. Ro, *J. Am. Chem. Soc.*, **80**, 2428 (1958). (b) H. E. Zimmerman, L. Singer, and B. S. Thyagarajan, *ibid.*, **81**, 108 (1959). (c) H. B. Henbest and W. R. Jackson, *J. Chem. Soc.*, C, 2459 (1967). (d) H. B. Henbest, W. R. Jackson, and I. Malunowicz, *ibid.*, C, 2469 (1967). (e) H. O. House and R. L. Wasson, *J. Org. Chem.*, **22**, 1157

the ketone function and the larger group on the beta carbon atom are *trans* to one another. This stereoselectivity has been justified on the basis that the intermediate enolate anion **[35]** will be more stable if it is not eclipsed with a large *beta* substituent in the transition state, leading to formation of the three-membered ring.[40b] It should also be noted that, at least for the example cited, the *cis* starting material **[34b]** is isomerized to the more stable *trans* isomer **[34a]** in the reaction mixture at approximately the same rate as it is epoxidized; consequently, stereospecific epoxidation would not be expected in any case. Just as was observed in the previously described epoxidations of olefins with peracids, the stereochemistry of epoxidation of enones (e.g., **[36]**) with sodium hydroperoxide is influenced by the presence of remote polar substituents. This effect is presumably attributable to an electrostatic interaction between the polar substituent and the intermediate enolate anion (e.g., **[35]**). Since the formation of these stereoisomeric intermediate enolate anions from **[36]** is reversible, such an electrostatic interaction could influence the relative rates at which the intermediates either give epoxy ketone products or return to starting materials.



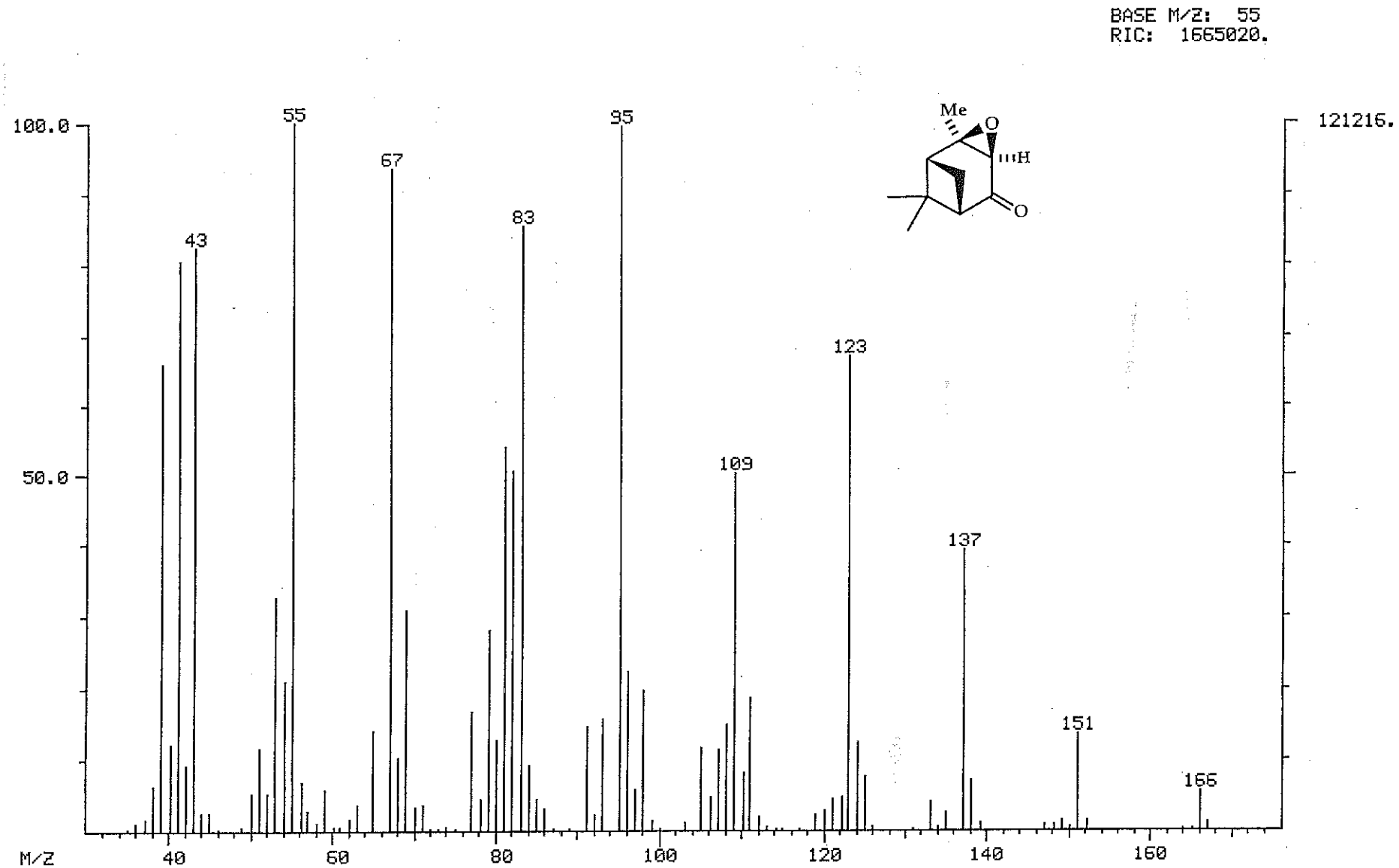
[36]

(Ref. 40c)

R_1	R_2	Product composition	
H	H	100%	0%
OH	H	69%	31%
H	OH	73%	27%

In cases where the carbon-carbon double bond of the enone is highly substituted and the carbonyl group is relatively reactive, or where reaction with sodium hydroperoxide is continued for relatively long periods of time, the usual epoxide formation may be accompanied by or superseded by oxidative cleavage. This cleavage, illustrated by the following examples, appears to involve the subsequently discussed attack of the hydroperoxide anion at the carbonyl function.[44c–h] The epoxy ketone products from a normal epoxidation may also be cleaved by further reaction with alkaline hydrogen peroxide.[40k]

(1957); D. L. Coffen and D. G. Korzan, *ibid.*, **36**, 390 (1971). (f) S. M. Marmor and M. M. Thomas, *ibid.*, **32**, 252 (1967). (g) W. S. Johnson, B. Bannister, R. Pappo, and J. E. Pike, *J. Am. Chem. Soc.*, **78**, 6354 (1956). (h) S. D. Levine, *J. Org. Chem.*, **31**, 3189 (1966). (i) D. D. Keane, W. I. O'Sullivan, E. M. Philbin, R. M. Simons, and P. C. Teague, *Tetrahedron*, **26**, 2533 (1970). (j) For oxidative degradations of enones with a mixture of hydrogen peroxide and selenium dioxide, see E. Caspi and Y. Shimizu, *J. Org. Chem.*, **30**, 223 (1965). (k) R. D. Temple, *ibid.*, **35**, 1275 (1970).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M/Z
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83
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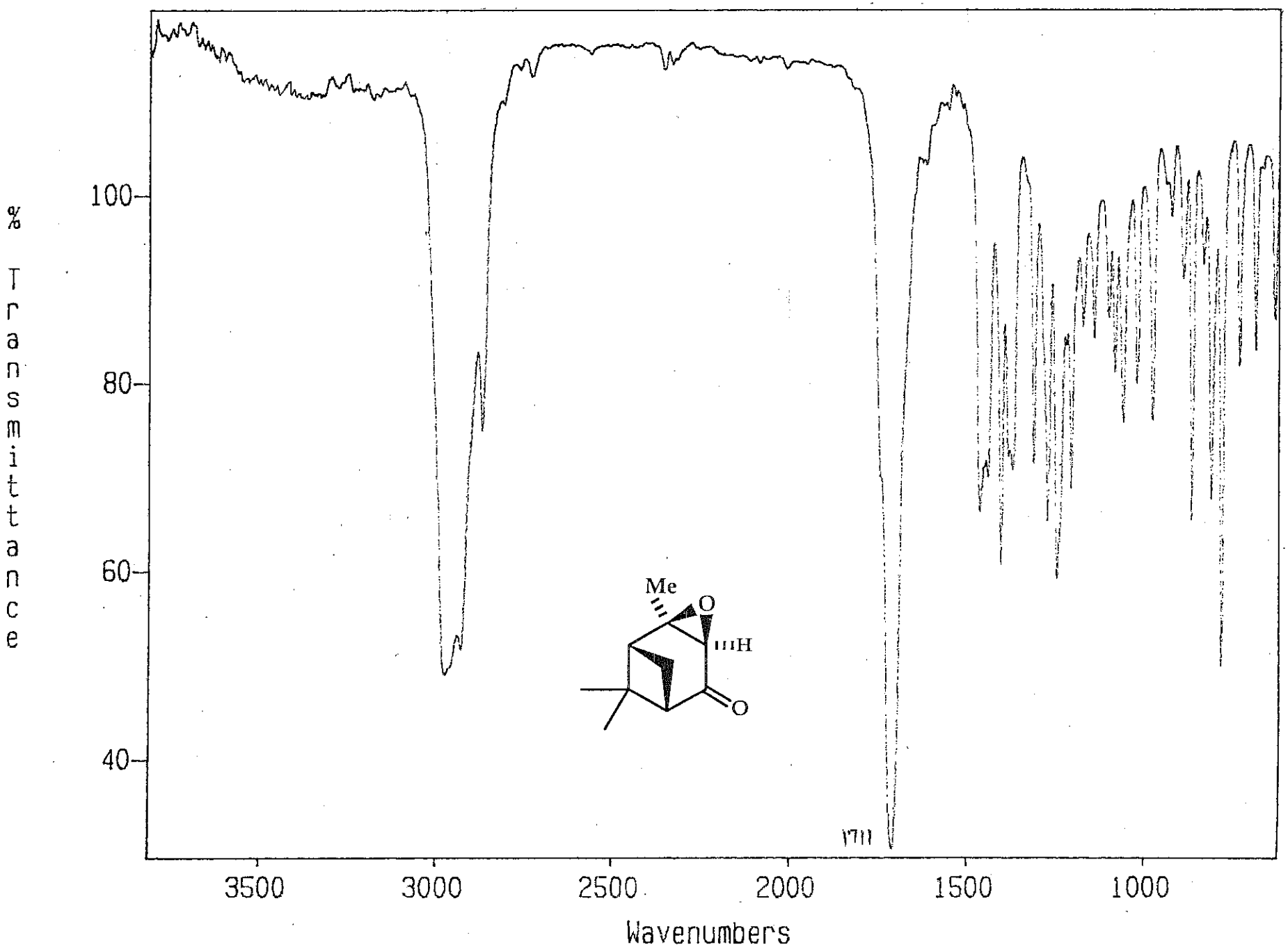
O
H
O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3500
3000
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1500
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Wavenumbers
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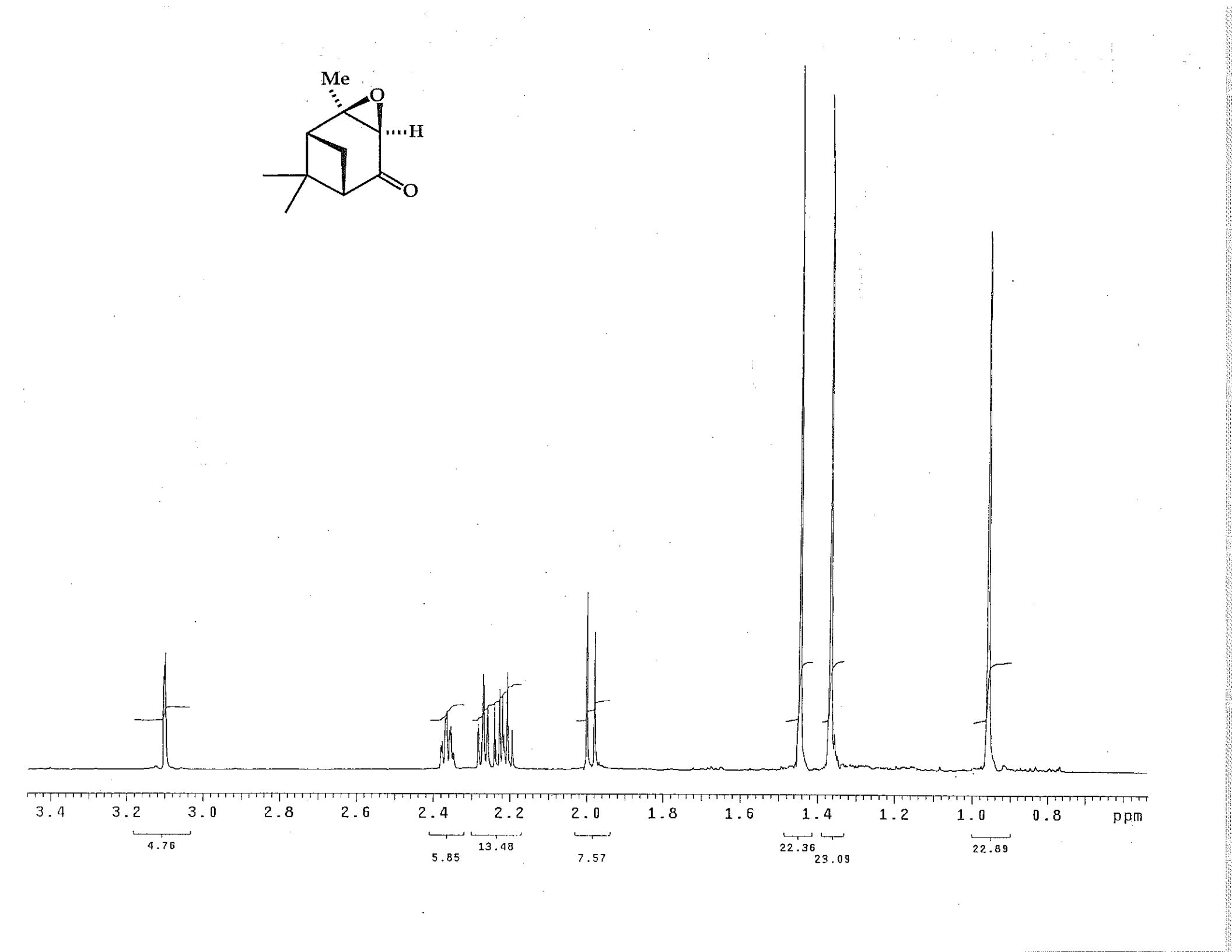
Me
O
H
O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O
H
O
3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0
0.8
ppm
4.76
5.85
13.48
7.57
22.36
23.09
22.89

STANDARD PROTON PARAMETERS

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Temp. 25.0 C / 298.1 K
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Width 2006.5 Hz
2D Width 2006.5 Hz
Arrayed repetitions
2 x 128 increments
OBSERVE H1, 499.9029485 MHz
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center at 0.050 sec
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Gauss window 0.018 sec
center at 0.020 sec
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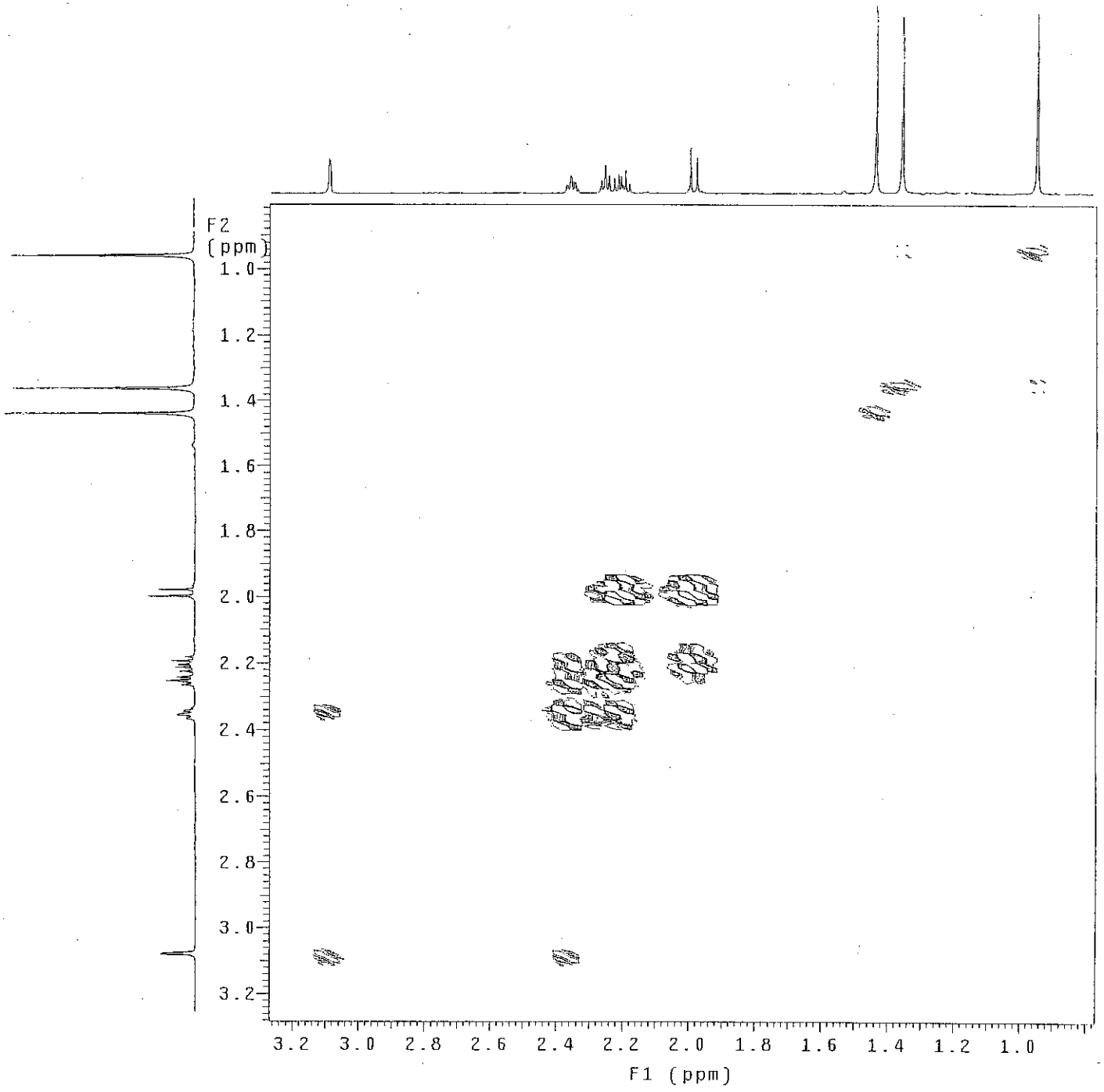
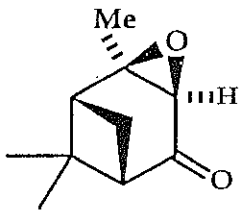
Total time 2.4 hours



Homonuclear ^{1}H COSY spectrum of 3,4-epoxyverbanone courtesy of Dr. L. T. Kakalis



STANDARD PROTON PARAMETERS

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Relax. delay 2.000 sec
Mixing 0.400 sec
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Width 4400.0 Hz
2D Width 4400.0 Hz
16 repetitions
2 x 512 increments
OBSERVE H1, 499.8931476 MHz
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F1 DATA PROCESSING
Gauss apodization 0.050 sec
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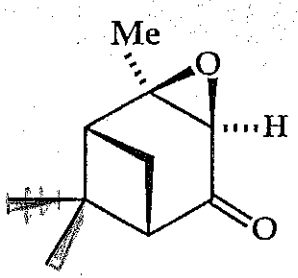
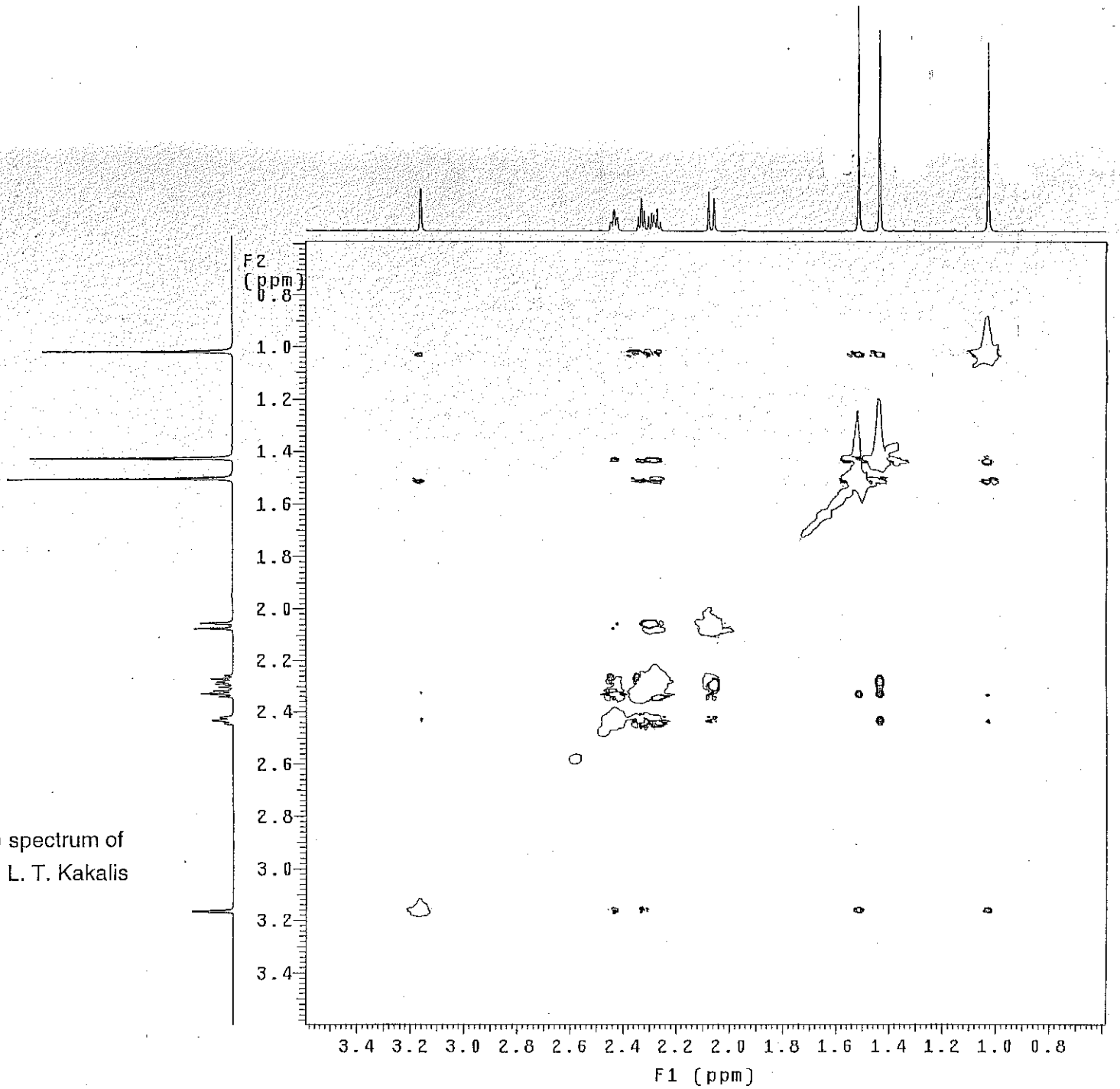
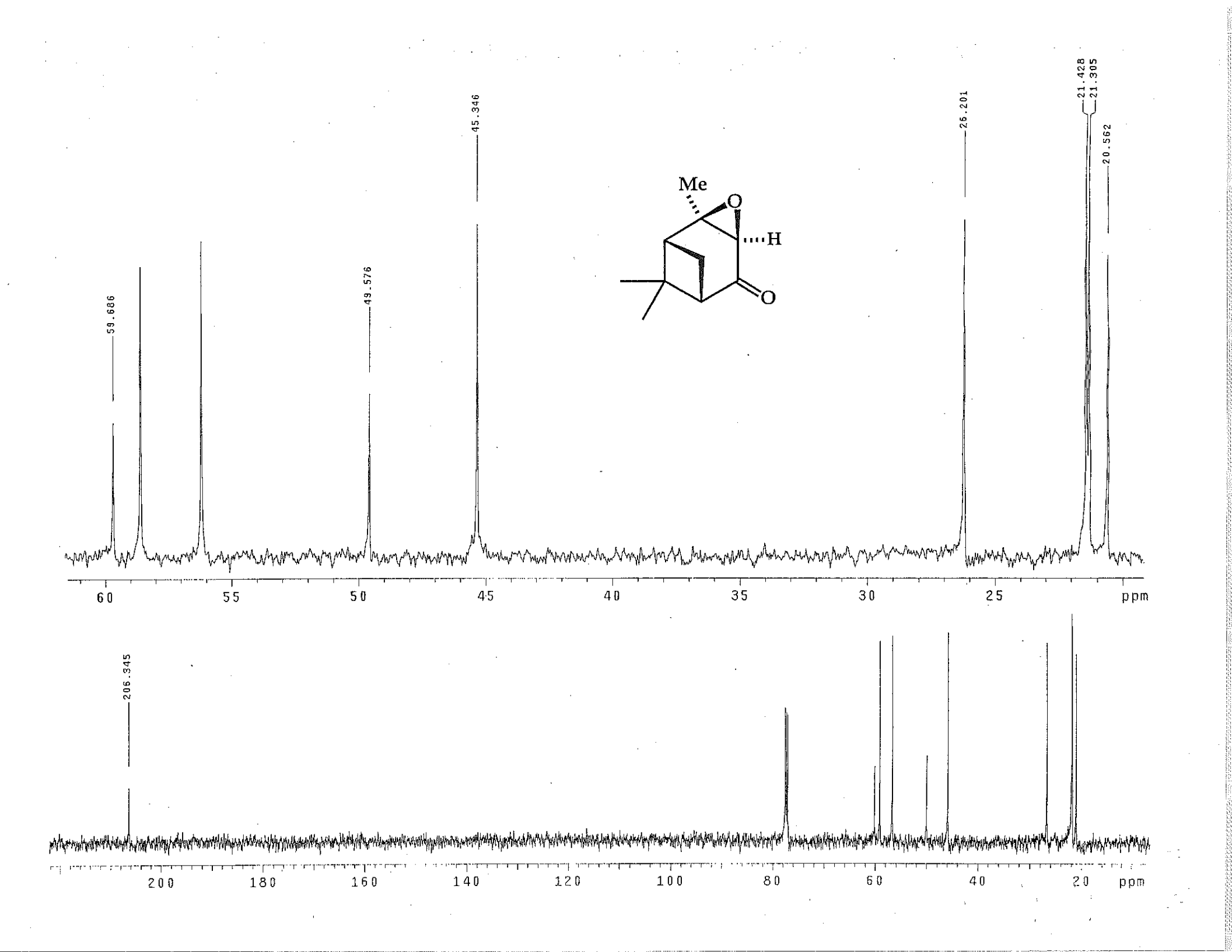




^{1}H-^{1}H nuclear Overhauser (NOESY) spectrum of 3,4-epoxyverbanone courtesy of Dr. L. T. Kakalis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20.562
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H
O
60
55
50
45
40
35
30
25
ppm
206.345
200
180
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40
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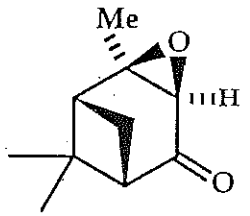
ppm

^{13}C DEPT spectra of
3,4-epoxyverbanone
courtesy of Dr. L. T. Kakalis



STANDARD PROTON PARAMETERS
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INOVA-500 "newark5"

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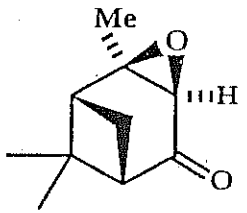
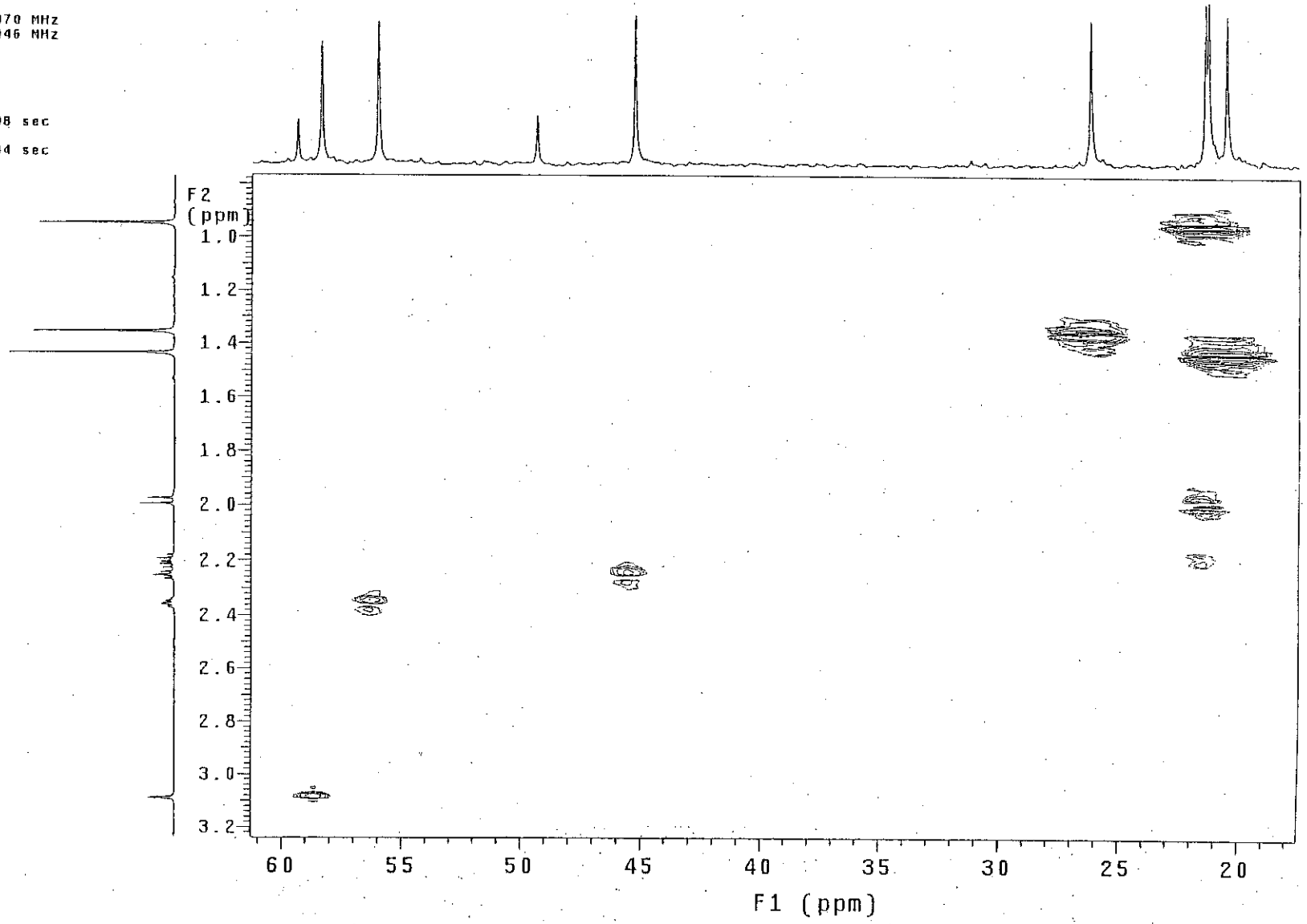
2D Width 12500.0 Hz
Arrayed repetitions
2 x 128 increments
OBSERVE H1, 499.9029470 MHz
DECOUPLE C13, 125.7061446 MHz
Power 46 dB
on during acquisition
off during delay
GARP-1 modulated
DATA PROCESSING
Gauss apodization 0.108 sec
F1 DATA PROCESSING
Gauss apodization 0.004 sec
FT size 1024 x 512
Total time 2.6 hours

Heteronuclear ^{1}H-^{13}C COSY (HETCOR) spectrum of 3,4-epoxyverbanone courtesy of Dr. L. T. Kakalis





Tetrahedron Letters No.40, pp. 3943-3946, 1967. Pergamon Press Ltd. Printed in Great Britain.

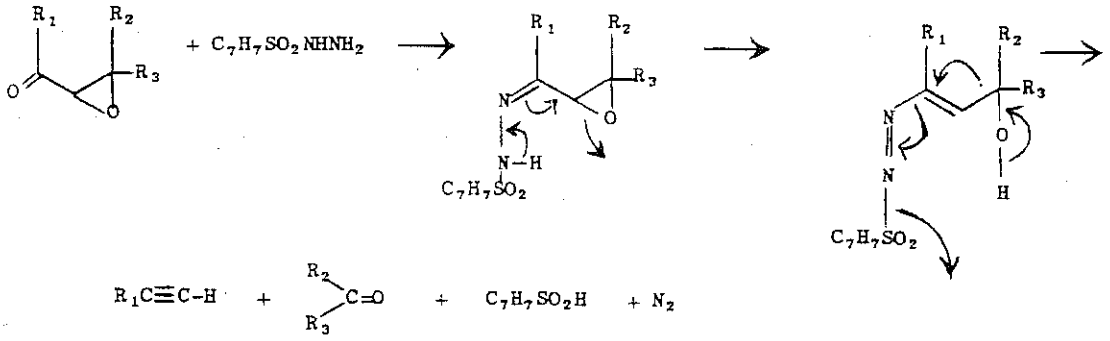
A NOVEL FRAGMENTATION REACTION OF α,β-EPOXYKETONES THE SYNTHESIS OF ACETYLENIC KETONES[1]

Masato Tanabe, David F. Crowe, and Robert L. Dehn
Stanford Research Institute
Menlo Park, California

(Received in USA 17 May 1967)

We wish to report that p-toluenesulfonylhydrazones of certain α,β-epoxyketones undergo a novel fragmentation reaction to yield an acetylene and a ketone as shown in Scheme 1.

Scheme 1



The application of this fragmentation method for the formation of medium-sized rings is exemplified by the reaction of 9,10-epoxy-1-decalone[2] (I) with 1 equivalent of p-toluenesulfonylhydrazine in ethanol at 50°. After 2 hours nitrogen evolution ceased and none of the intermediate p-toluenesulfonylhydrazine was detected by thin-layer chromatography on silica G plates. From the reaction a 50% yield of distilled cyclodecyn-6-one (II), 75-80°/2 mm; $\lambda_{max.}^{film}$ 5.85 μ; was isolated. The structure of II was confirmed by the catalytic absorption of 2 mole equivalents of hydrogen to yield cyclodecanone. This reaction thus affords a convenient method for the formation of medium sized rings[3a-h] and internal acetylenes via α,β-unsaturated ketones.

The utility of the reaction for the preparation of terminal acetylenic ketones from α,β-unsaturated ketones is exemplied by the conversion of 10-methyl-$\Delta^{1,9}$-octalone-2 (VI)

to the cyclohexanone derivative IV. The preparation of the epoxydecalone III from VI was accomplished with alkaline hydrogen peroxide. Reaction of III with 1.17 equivalents of p-toluenesulfonylhydrazine in ethanol at 25° proceeded with the evolution of nitrogen. After 1/2 hour the fragmenced terminal acetylenic ketone IV was isolated by distillation in 35% yield, 76-80°/1.0 mm; n_D^{23} 1.4829; $\lambda_{max.}^{film}$ 3.0 μ (C≡C-H); 4.5 μ (C≡C); 5.85 μ (C=O)

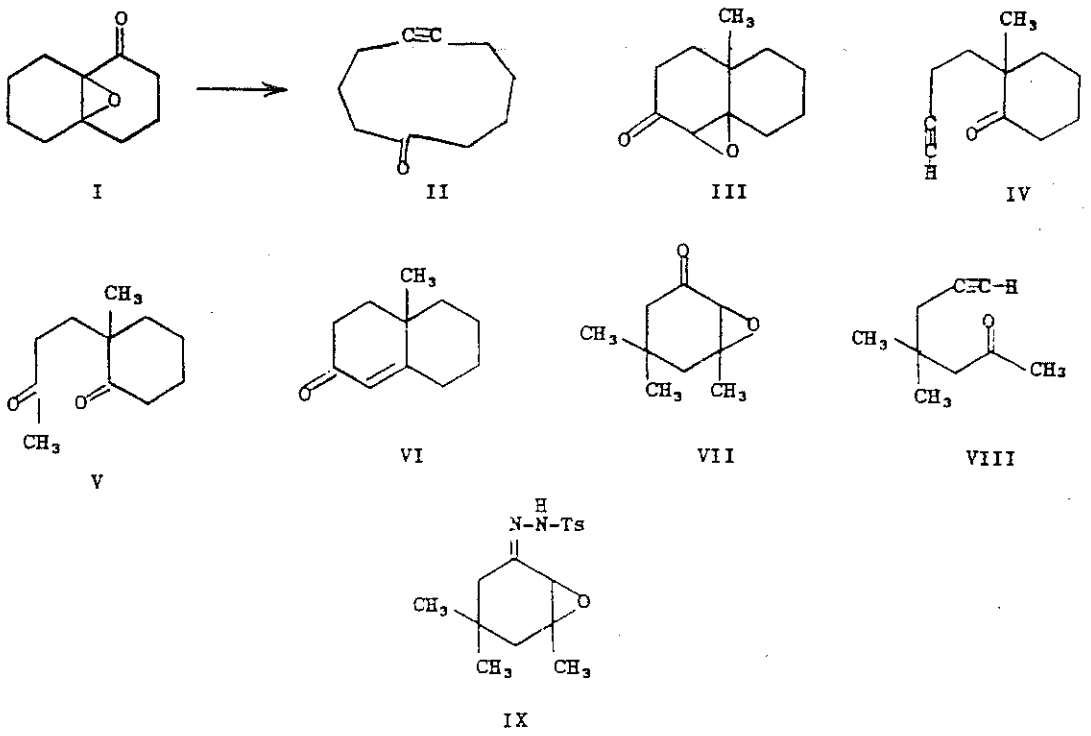
Confirmation of structure IV was achieved by hydration of the triple bond in IV, catalyzed by mercuric oxide in the presence of sulfuric acid. The intermediate methyl ketone V was converted under these conditions back to the octalone derivative VI.

A further illustration of this reaction is the conversion of isophorone oxide VII to 4,4-dimethylheptyn-6-one VIII. A solution of 15.4 g (0.1 M) VII in 1100 ml of ethanol and 18.6 g (0.1 M) of p-toluenesulfonylhydrazine was heated at 55° for 2 hours. Isolation of the product by extraction into chloroform, followed by distillation yielded 5.5 g of VIII, 40%, 75-80°/14 mm; $\lambda_{max.}^{film}$ 3.0 μ and 4.72 μ (C≡C-H); 5.85 (C=O); $\tau_{TMS}^{CCl_4}$ 7.85 ($-\overset{O}{\overset{\|}{C}}-CH_3$), 7.93 (quartet, ≡C-H).

In an alternate procedure the reaction of isophorone oxide with 1.1 equivalents of p-toluenesulfonylhydrazine in ethanol at 20° for 20 minutes yielded the unstable p-toluenesulfonylhydrazone derivative IX; $\lambda_{max.}^{Nujol}$ 3.15 (NH); 6.23, 7.5 and 8.6 μ ($C_7H_7SO_2$-); $\lambda_{max.}^{MeOH}$ 227 mμ (ε = 21,000). Decomposition of IX occurred readily at 50° in ethanol with brisk nitrogen evolution to afford the acetylenic ketone VIII in 80-85% yield.

We have observed that 2,3-epoxycyclohexanone does not yield the expected fragmentation product 1-hexyn-6-al. This result appears to indicate that the presence of a β-hydrogen alters the course of the reaction.

Our initial studies of this new reaction have been limited to cyclic α,β-epoxyketones. These cyclic p-toluenesulfonylhydrazones meet the necessary geometric requirements for facile concerted fragmentation since the ketonic carbon-nitrogen bond and the C_α-C_β bond maintain a trans co-planar alignment[4] in the N-p-toluenesulfonylazo intermediate (Scheme 1). This reaction is formally related to the reaction of an



I II III IV V VI VII VIII IX

α,β-epoxyketone with hydrazine described by Wharton,[5] where the intermediate hydrazone decomposes to the allylic alcohol and nitrogen.

Padwa[6] reports that an acyclic α,β-epoxyketone, trans-chalcone oxide, reacts with p-toluenesulfonylhydrazine in acidic ethanol to yield a cyclic product, 1-p-toluenesulfonyl-3,5-diphenyl-4-hydroxypyrazoline. Thus it appears that an alternate mode of reaction other than the fragmentation process is available to acyclic α,β-epoxyketones.[7]

Further studies on the application of this reaction with other α,β-unsaturated ketones will be reported.[8]

References

1. Since the completion of this work A. Eschenmoser, D. Felix, and G. Ohloff, Helv. Chim. Acta 50, 708 (1967) have described the fragmentation of bicyclo [10.3.0]-1,12-epoxy-13-pentadecanone with p-toluenesulfonylhydrazine to the large ring ketone 4-cyclopentadecyn-1-one.

2. All new compounds reported herein gave satisfactory analytical data. The epoxydecalone I was prepared from $\Delta^{9,10}$ -1-octalone $\xrightarrow{a.}$ 1-hydroxy-$\Delta^{9,10}$ octalin $\xrightarrow{b.}$ 1-hydroxy-9,10-epoxy-octalin $\xrightarrow{c.}$ I; a = LAH, b = M-chloroperbenzoic acid, c = CrO_3 + pyridine, with isolation of the intermediates in an over-all yield of 25%.

3. For other fragmentation methods for the preparation of medium sized rings see (a) P. S. Wharton, J. Org. Chem. 26, 4781 (1961); (b) P. S. Wharton and G. A. Hiegel, ibid, 30, 3254 (1965); (c) E. J. Corey, R. B. Mitra, and H. Uda, J. Am. Chem. Soc. 86, 485 (1964); (d) P. S. Wharton, Y. Sumi, and R. A. Kretchmer, J. Org. Chem. 30, 234 (1965); (e) E. J. Corey and E. Hamanaka, J. Am. Chem. Soc. 86, 1641 (1964); (f) E. J. Corey and A. G. Hortmann, ibid. 87, 5736 (1965); (g) M. Tanabe and D. F. Crowe, J. Org. Chem. 30, 2776 (1965); (h) J. A. Marshall and C. J. V. Scanio, ibid. 30, 3019 (1965). For a more recent new fragmentation process see, J. A. Marshall and G. L. Bundy, J. Am. Chem. Soc. 88, 4291 (1966).

4. C. A. Grob, IUPAC Kekule Symposium, London, Sept. 1958, Butterworth and Co., Ltd. London, p. 114ff. C. A. Grob and P. W. Schess, Angew. Chemie, International Ed. 6, 1 (1967).

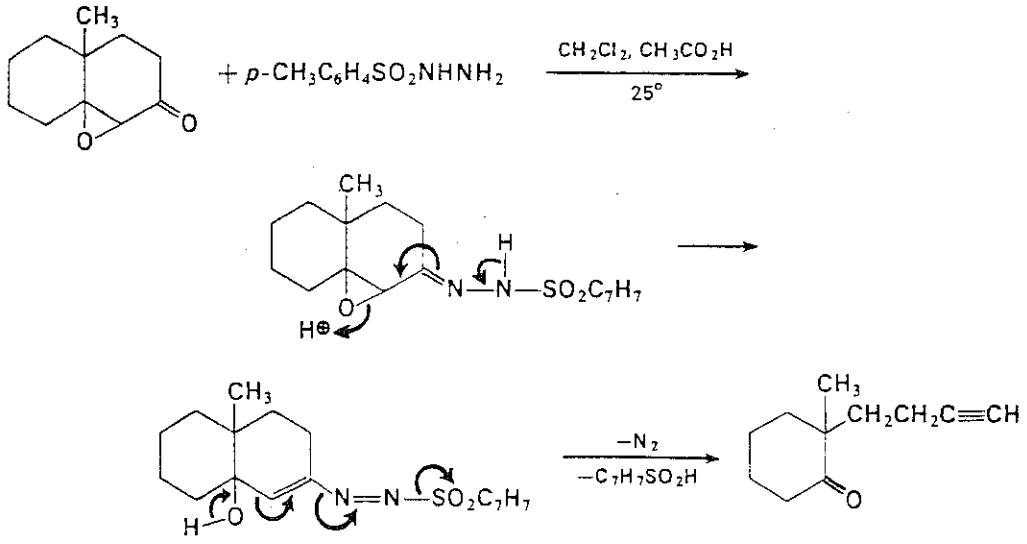
5. P. S. Wharton and P. H. Bohlen, J. Org. Chem. 26, 3615 (1961).

6. A. Padwa, J. Org. Chem. 30, 1274 (1965).

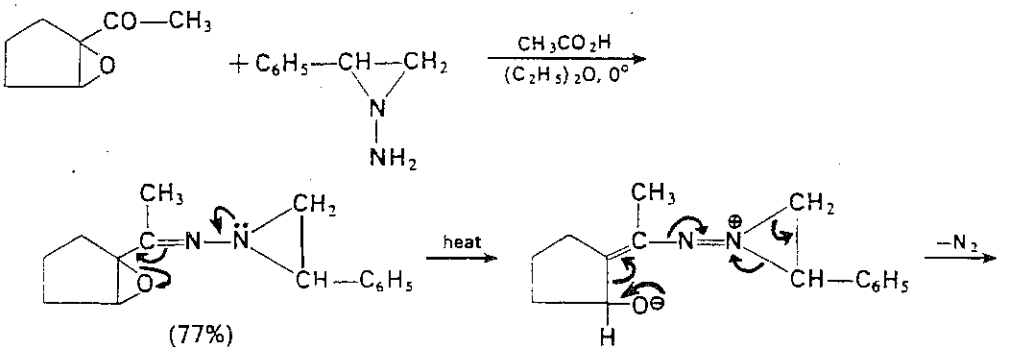
7. We have observed the formation of pyrazolines from other cyclic α,β-epoxyketones.

8. M. Tanabe, D. Crowe, R. Dehn, and G. Detre, Tetrahedron Letters, in press.

Carbonyl compounds with heteroatom substituents at the *alpha* carbon form tosylhydrazones which may undergo elimination of the α-substituent during base-catalyzed decomposition.[28a–c] One of the most interesting applications of this reaction has been to α,β-epoxy ketones.[28d–f] In these cases the intermediate azo olefin undergoes further fragmentation to form an acetylene and a carbonyl compound as illustrated in the following examples. This reaction may also be effected by reaction of the epoxy ketone with other nitrogen-containing reactants[28f] such as 1-amino-2-phenylaziridine.



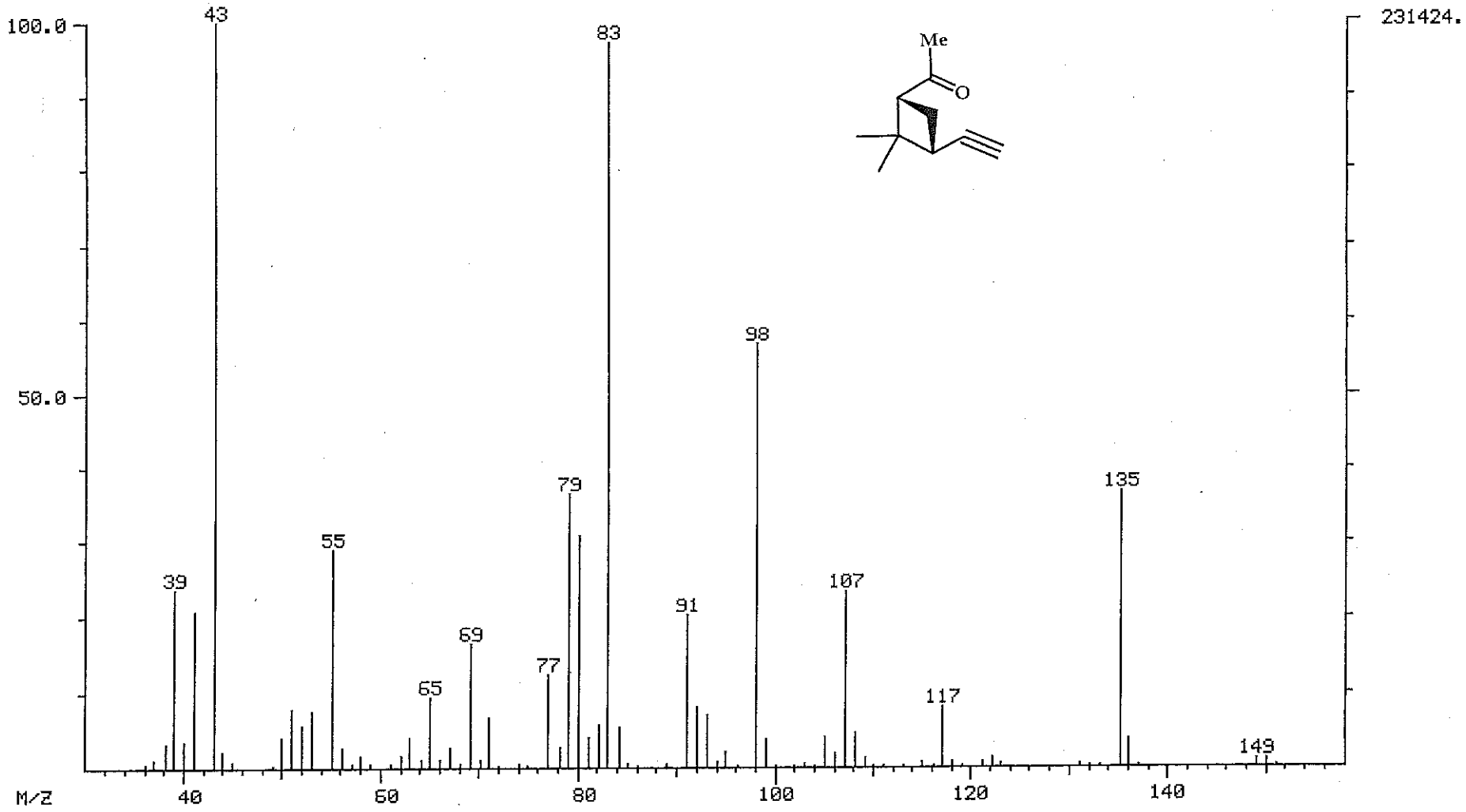
(67%) (Ref. 28e)



$CH_3C{\equiv}C(CH_2)_3CHO + C_6H_5CH{=}CH_3$

(94%) (Ref. 28f)

28. (a) R. K. Bartlett and T. S. Stevens, *J. Chem. Soc.*, C, 1964 (1967). (b) L. Caglioti, P. Grasselli, F. Morlacchi, and G. Rosini, *Chem. Ind.* (London), 25 (1968). (c) T. Iwadare, I. Adachi, M. Hayashi, A. Matsunaga, and T. Kitai, *Tetrahedron Letters,* **No. 51**, 4447 (1969). (d) M. Tanabe, D. F. Crowe, R. L. Dehn, and G. Detre, *ibid.,* **No. 38**, 3739 (1967); M. Tanabe, D. F. Crowe, and R. L. Dehn, *ibid.,* **No. 40**, 3943 (1967). (e) A. Eschenmoser, D. Felix, and G. Ohloff, *Helv. Chim. Acta,* **50**, 708 (1967); J. Schrieber and co-workers, *ibid.,* **50**, 2101 (1967). (f) For other modifications of this acetylene synthesis, see P. Wieland, H. Kaufmann, and A. Eschenmoser, *ibid.,* **50**, 2108 (1967); D. Felix, J. Schreiber, K. Piers, U. Horn, and A. Eschenmoser, *ibid.,* **51**, 1461 (1968); P. Weiland, *ibid.,* **53**, 171 (1970). R. K. Müller, D. Felix, J. Schreiber, and A. Eschenmoser, *ibid.,* **53**, 1479 (1970).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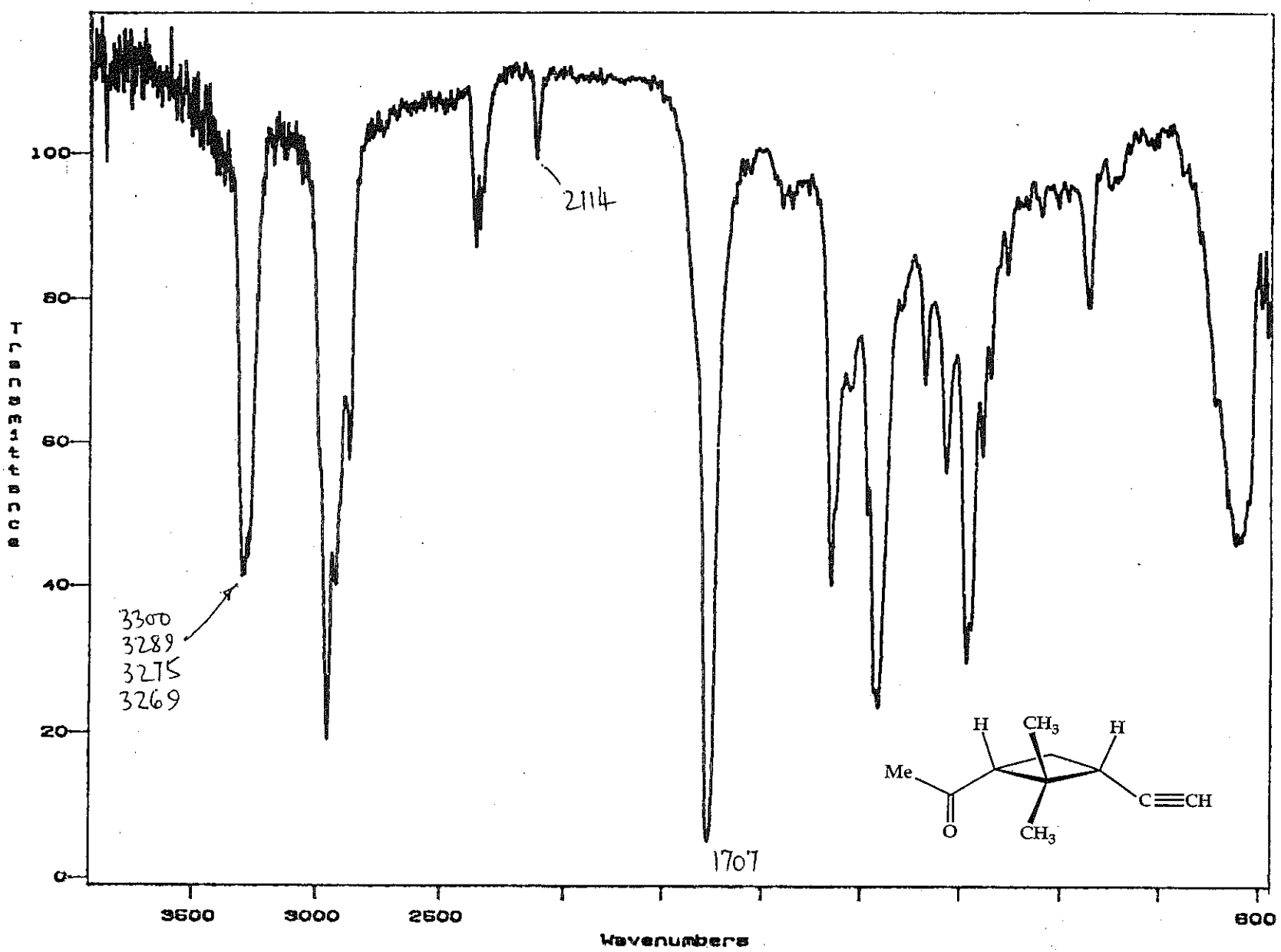
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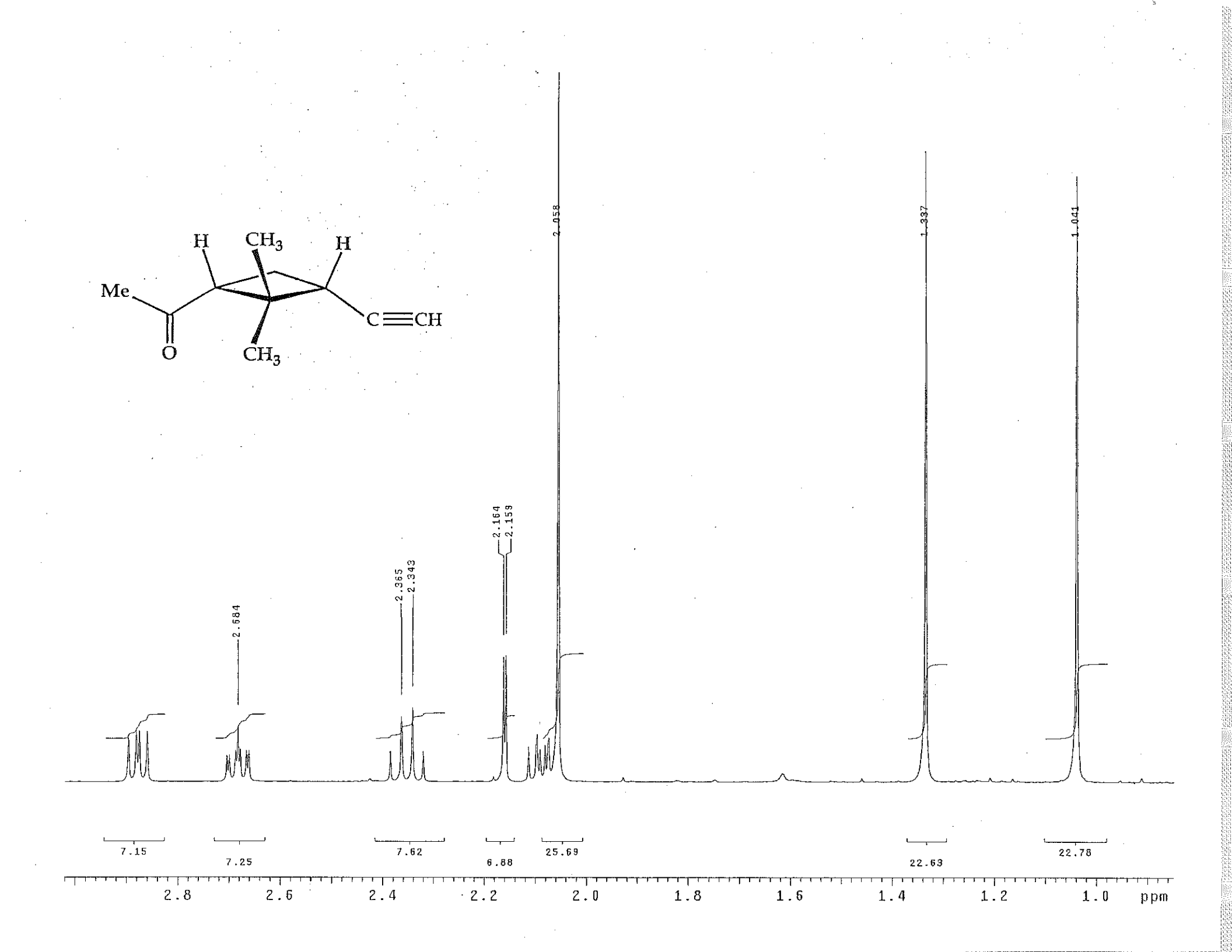
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ppm

STANDARD PROTON PARAMETERS
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2D Width 2080.2 Hz
Arrayed repetitions
2 x 128 increments
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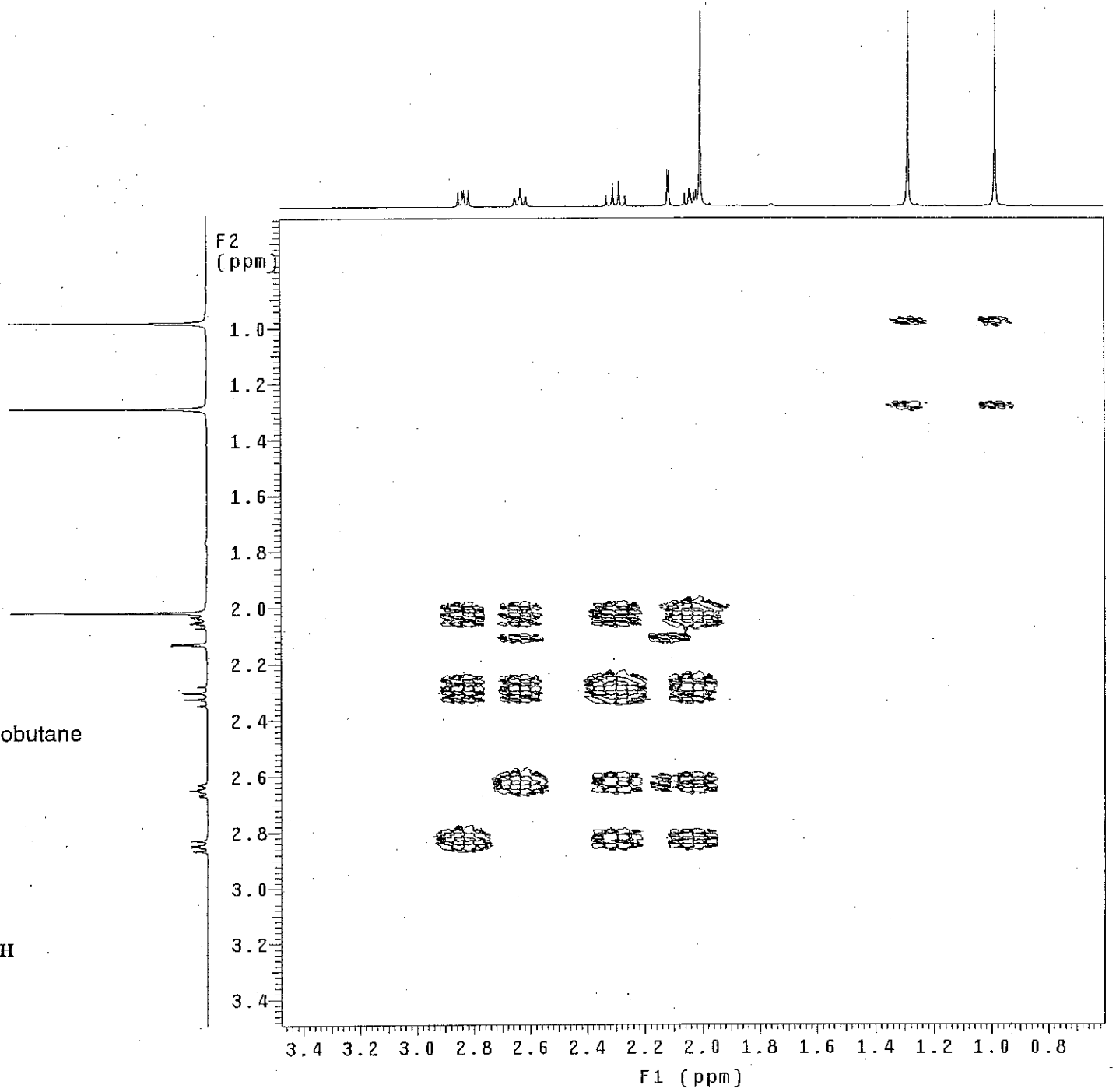
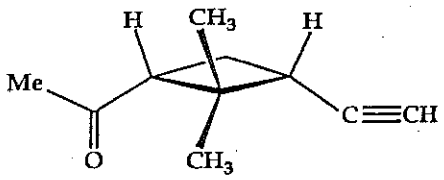


Homonuclear ^{1}H COSY spectrum of
cis-1-acetyl-3-ethinyl-2,2-dimethylcyclobutane
courtesy of Dr. L. T. Kakalis



STANDARD PROTON PARAMETERS

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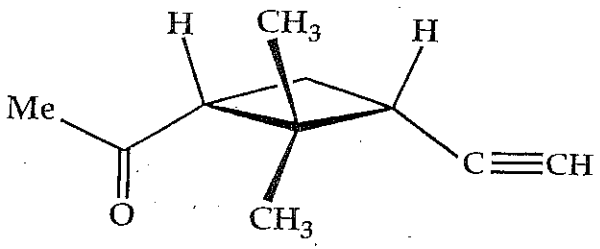
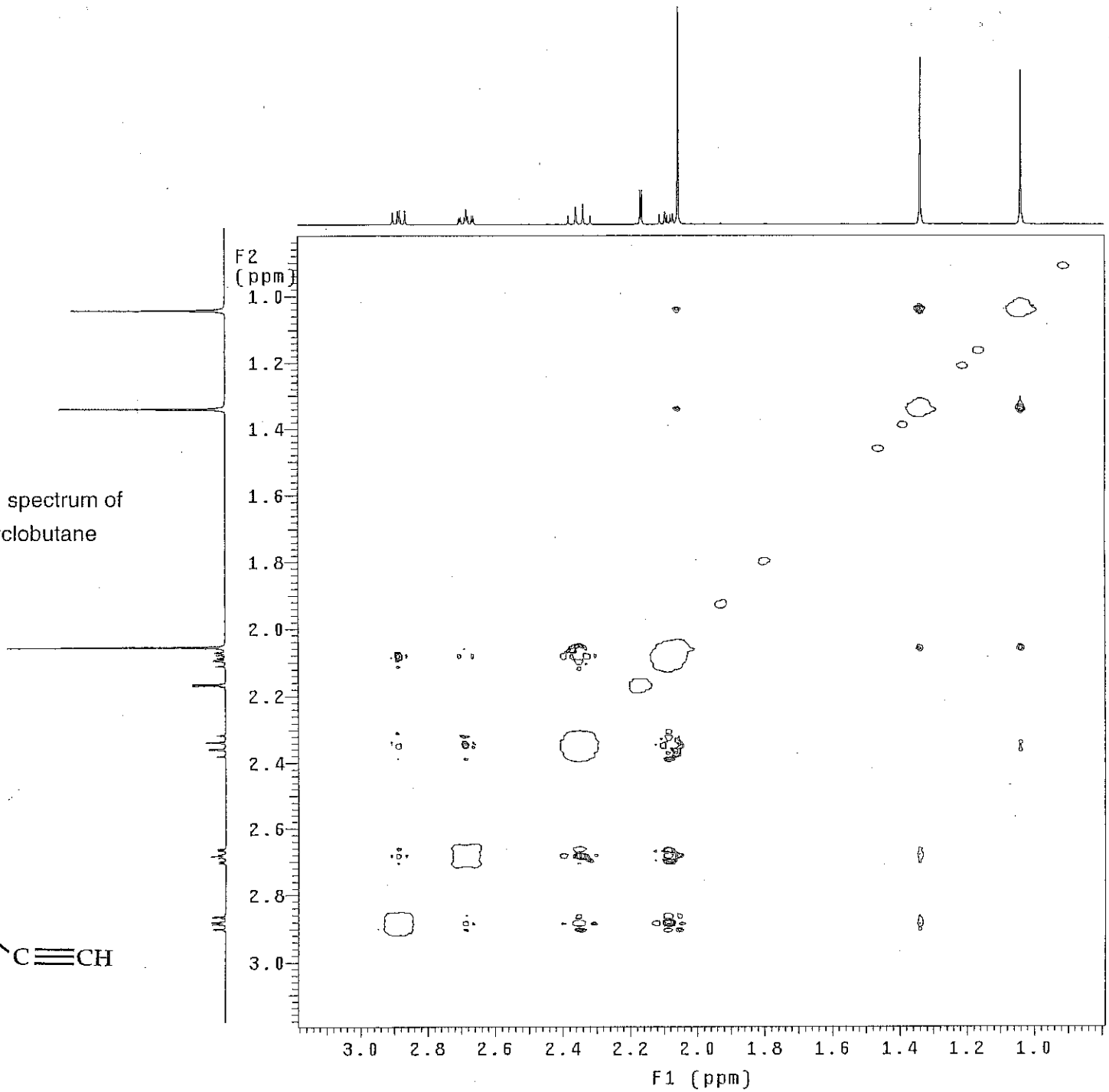
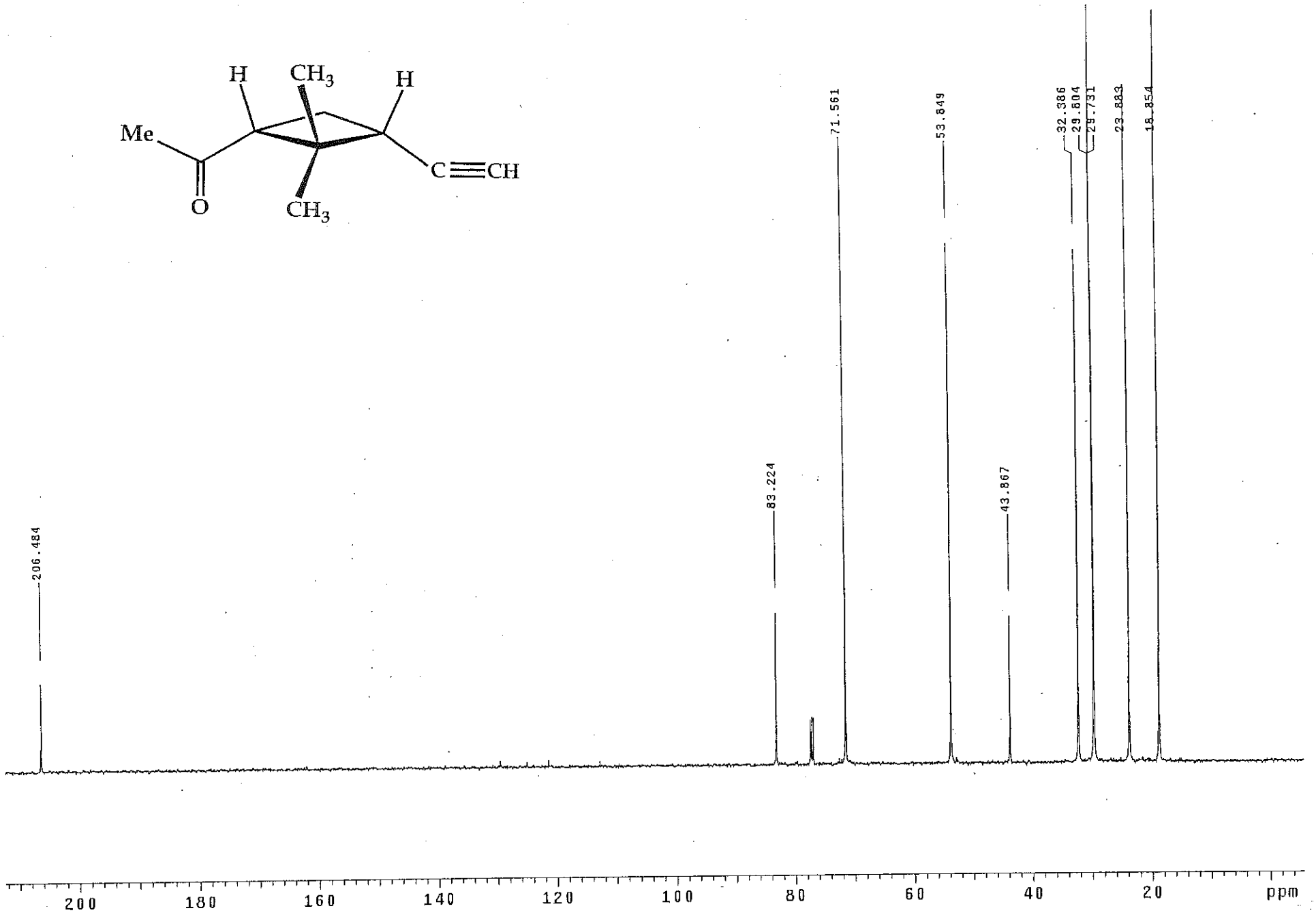
2D Width 4400.0 Hz
16 repetitions
2 x 512 increments
OBSERVE H1, 499.8931668 MHz
DATA PROCESSING
Gauss apodization 0.097 sec
F1 DATA PROCESSING
Gauss apodization 0.047 sec
FT size 2048 x 2048
Total time 12 hr, 19 min, 55 sec

^{1}H-^{1}H nuclear Overhauser (NOESY) spectrum of *cis*-1-acetyl-3-ethinyl-2,2-dimethylcyclobutane courtesy of Dr. L. T. Kakalis



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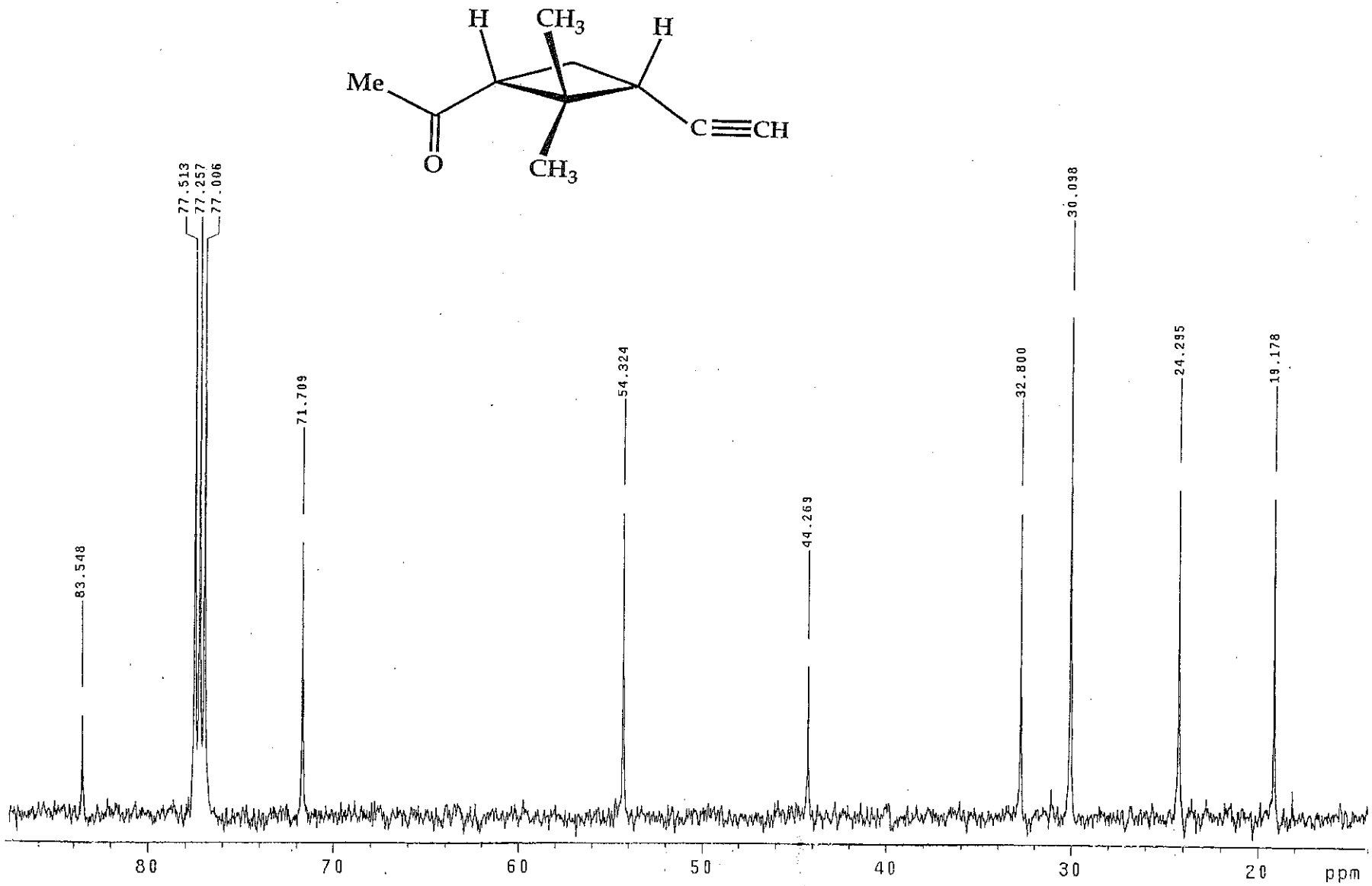
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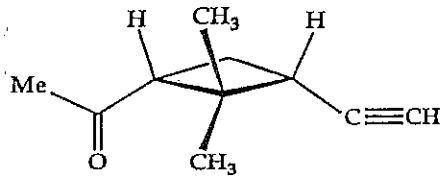
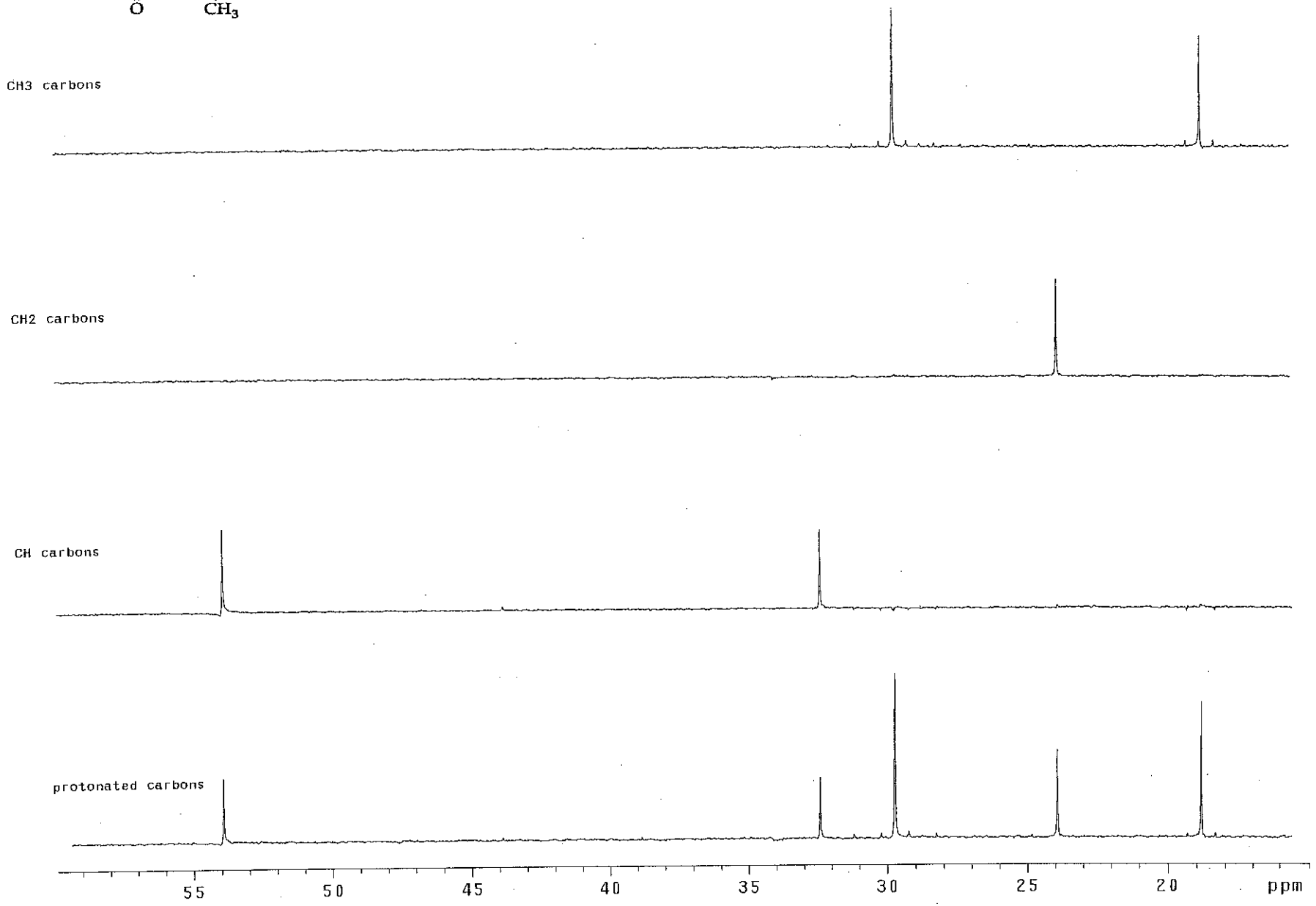


^{13}C DEPT spectra of
cis-1-acetyl-3-ethinyl-2,2-dimethylcyclobutane
courtesy of Dr. L. T. Kakalis



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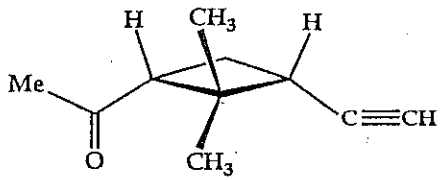
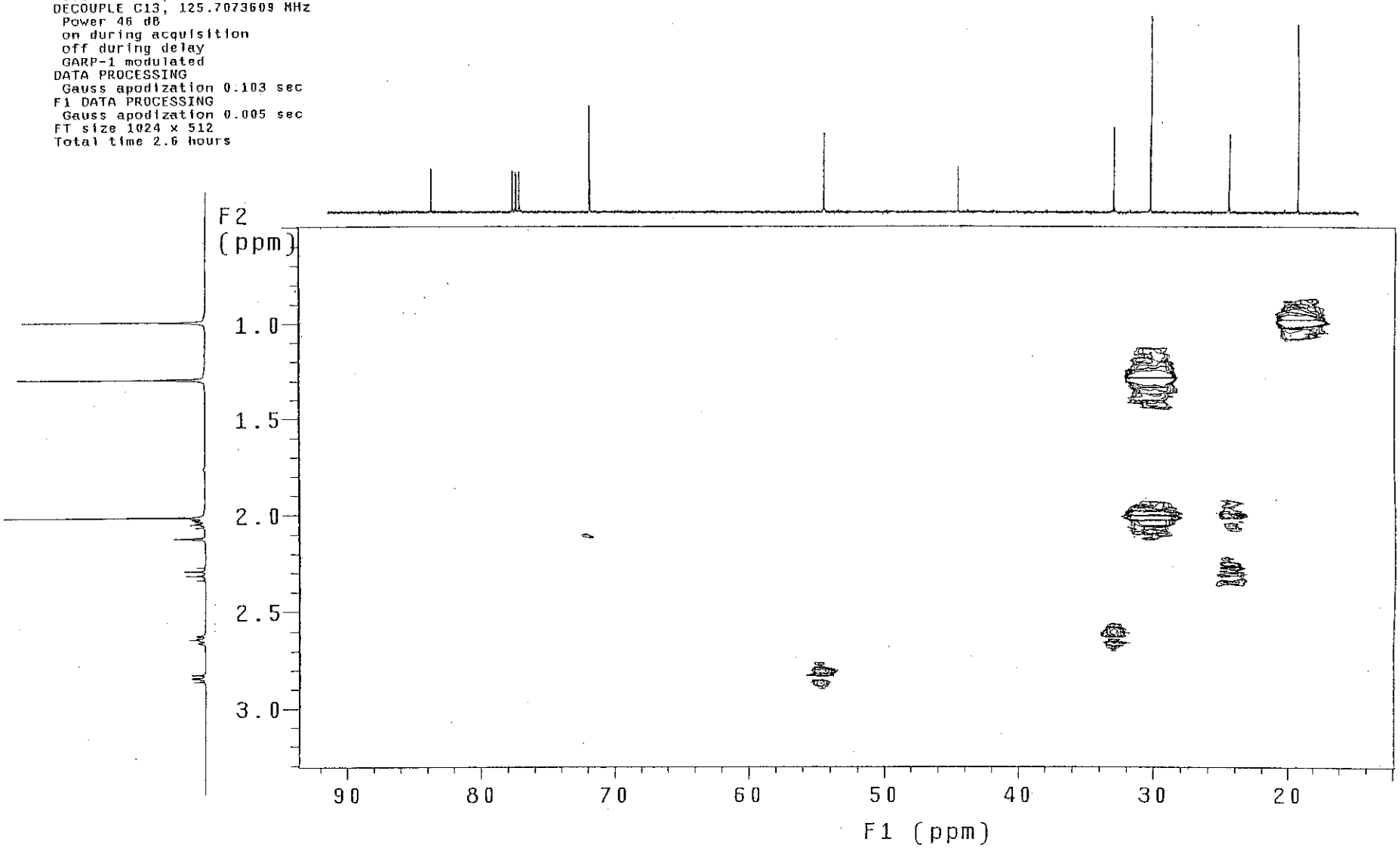
Heteronuclear ^{1}H-^{13}C COSY (HETCOR) spectrum of *cis*-1-acetyl-3-ethinyl-2,2-dimethylcyclobutane courtesy of Dr. L. T. Kakalis





X-ray crystal structure of *cis*-1-acetyl-3-ethinyl-2,2-dimethylcyclobutane
courtesy of R. A. Lalancette

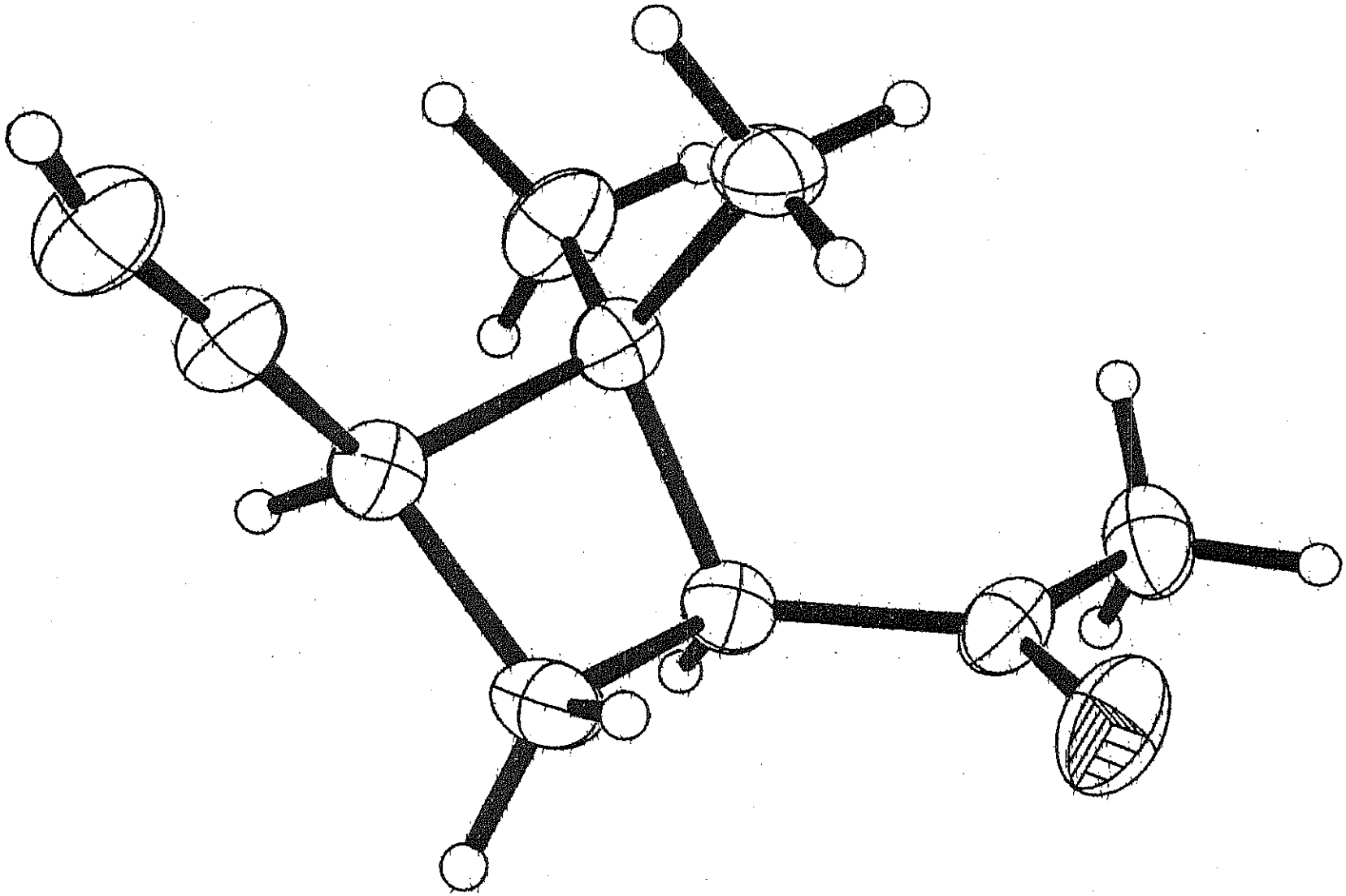


Table IV. Permanganate Oxidations of α-Olefins

Registry no.	α-Olefin[a]	Product	Isolated yield, %[b]
111-66-0	1-Octene	Heptanoic acid	80
872-05-9	1-Decene	Nonanoic acid	85
821-95-4	1-Undecene	Decanoic acid	86
112-41-4	1-Dodecene	Undecanoic acid	90
1120-36-1	1-Tetradecene	Tridecanoic acid	83
629-73-2	1-Hexadecene	Pentadecanoic acid	84
112-88-9	1-Octadecene	Heptadecanoic acid	80
3452-07-1	1-Eicosene	Nonadecanoic acid	90

[a] See Experimental Section for a typical procedure. [b] Purity of at least 97% in all cases. Less than 3% contamination with the overoxidation product. Products were distilled or crystallized.

present and could exert some surface catalytic effect).

The initial intermediates which are formed during oxidations of alkenes by permanganate[7] are the cyclic manganese(V) or manganese(VI) species. These intermediates could then lead to aldehydes,[7] diols (in cold, dilute alkaline permanganate solutions), or ketols (low hydroxide concentration). Diols would be cleaved to the expected acids but they could also undergo oxidations to ketols, keto aldehydes, or keto acids (sources of overoxidized acids). The aldehydes could be rapidly oxidized to carboxylic acids. Another pathway for the aldehydes is oxidative cleavage via an enol or enolate to yield the carboxylic acid of one less carbon.

In order to probe into the possibility of overoxidation of the aldehyde intermediate, nonanal and valeraldehyde were oxidized under conditions similar to the α-olefins. Treatment of nonanal (0.03 mol) with permanganate (0.03 mol) in a benzene (150 mL)–water (150 mL) medium with Aliquat 336 (0.1 g) led to nonanoic acid which contained less than 3% octanoic acid. If the same reaction is performed with the aqueous phase initially 0.1 M in KOH, a comparable result was seen. Similarly the two-phase oxidation of valeraldehyde under basic conditions led to valeric acid with about 2% butyric acid.

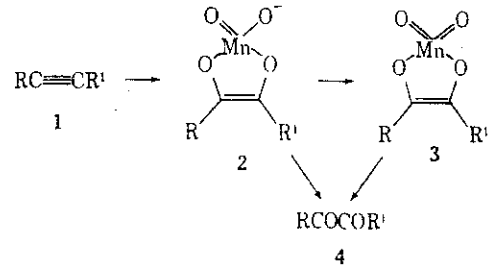
The amount of overoxidation seen in the permanganate oxidations of the α-olefins does not appear to be solely explicable on the premise that the aldehyde initially formed in the cleavage is further oxidatively cleaved.

The function of the acetic acid (soluble in water, benzene, and pentane) in suppressing overoxidation in the reactions conducted under heterogeneous two-phase conditions in the presence of a phase-transfer agent may merely reflect its solubility in the organic phase and rapid destruction of OH^- formed during the disproportionation of manganese(VI) intermediates.[7] Since the acetic acid itself is oxidized at a moderate rate, it might additionally function to destroy any excess permanganate and prevent further oxidation of the initially formed carboxylic acid. In those cases where both the acetic acid and phase-transfer agent are present, it does appear that phase-transfer-type catalysis is occurring.[4]

Since the goal of this research was to produce high-purity carboxylic acids, a series of α-olefins was oxidized using aqueous permanganate and adding solutions of the α-olefins in benzene, acetic acid, and a quaternary ammonium salt. The results of these reactions are tabulated in Table IV. Good yields of reasonably pure carboxylic acids can be obtained in this manner.

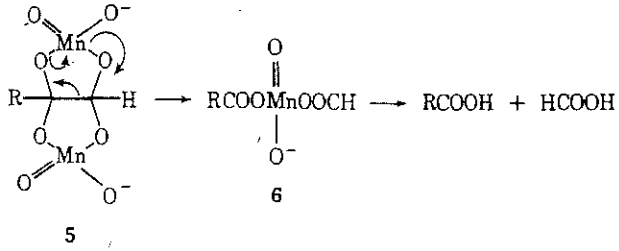
Our attention was next turned to the permanganate oxidations of terminal acetylenes. In Raphael's book[11] several examples of permanganate oxidations of internal alkynes are referenced,[12] and it is stated "As becomes an unsaturated centre the triple bond is very readily attacked by potassium permanganate, the end products being two carboxylic acid molecules". Under controlled conditions α-diketones can be isolated. For example, stearolic acid has been converted into 9,10-diketo stearic acid (92–96%) by performing the oxidation in the pH range 7.0–7.5 (MnO_4^-:acid = 2).[13] The diketo acid is oxidatively cleaved at high (>12) or low (<1) pH.

Scheme I



In mechanistic studies dealing with permanganate oxidations of acetylenes, a cyclic manganese(V) intermediate has been proposed as the first step in the cleavage process.[14] The formation of diones from internal acetylenes 1 (R = R^1 = alkyl) could arise via the pathway depicted in Scheme I.

The α-keto aldehyde 4 (R^1 = H, R = alkyl) which would arise from a terminal acetylene by this route would be expected to undergo further oxidation to the α-keto acid 4 (R^1 = OH, R = alkyl) and then this acid would be oxidized to RCOOH and CO_2.



It is also possible that a bicyclic intermediate such as 5 might be involved in the cleavages of triple bonds [only the manganese(V) state is shown and the manganese(VI) state could also play a role].[14] Breakdown of 5 would lead to 6 which on further reaction would yield the acid fragments.

The stoichiometry for the cleavage of a terminal acetylene (if MnO_2 and CO_2 are the products) under acid and basic conditions is represented in the following equations:

$$3RC{\equiv}CH + 8MnO_4^- + 8H^+ \rightarrow 3RCO_2H + 3CO_2 + 8MnO_2 + 4H_2O$$

$$3RC{\equiv}CH + 8MnO_4^- + OH^- \rightarrow 3RCO_2^- + 3CO_3^{2-} + 8MnO_2 + 2H_2O$$

In studies similar to the olefin oxidations previously discussed, several alkynes were treated with permanganate under a variety of conditions. The results of experiments on 1-hexyne are summarized in Table V.

It can be seen from the data in Table V that 1-hexyne can be oxidized in good yields without too much problem of overoxidation under a variety of reaction conditions.

Permanganate oxidations of 1-octyne are listed in Table VI.

In the oxidations of 1-octyne the amount of overoxidation increases as the basicity of the aqueous phase increases. The reaction can be performed using aqueous permanganate alone. The oxidation proceeds in the two-phase pentane–water system, and phase-transfer catalysis appears to be occurring to some extent (entries 6 and 7).

A few oxidations were performed using 1-decyne, and the results are tabulated in Table VII.

Table V. Permanganate Oxidations of 1-Hexyne

Additive	Reaction time, h	Valeric acid	Butyric acid
None[a]	7	98	2
0.13 M KOH[b]	7	94	6
150 mL of benzene,[c] 0.1 g of bzl-PTC	4	99	1
300 mL of pentane,[d] 60 mL of acetic acid 0.2 g of Aliquat 336	2	99	1

[a] $KMnO_4$ (0.06 mol) in 75 mL of water to which 1-hexyne (0.015 mol) was added. The mixture was stirred magnetically and a 60–70% yield of the crude acid could be isolated. Any 1-hexyne which did not react would have been lost in the concentration process on workup. [b] 0.6 g of KOH (0.01 mol) was added to the aqueous $KMnO_4$ and the reaction was performed as in *a*. [c] $KMnO_4$ (0.10 mol) in 150 mL of water to which 1-hexyne (0.06 mol) and listed PTC were added. A 54% crude yield of acid was obtained. [d] $KMnO_4$ (0.19 mol) in 300 mL of water to which 1-hexyne (0.06 mol) was added containing the listed additives. Isolated crude product in a 60% yield.

Table VI. Permanganate Oxidations of 1-Octyne

Additives[a]	Reaction time, h	1-Octyne	Hexanoic acid	Heptanoic acid
None	5	28	5	66
0.1 M KOH[b]	5	1	14	85
0.5 M KOH[c]	3	2	50	48
150 mL of pentane	5	50	2	48
150 mL of pentane, 30 mL of acetic acid	7.5	21	2	77
150 mL of pentane, 0.2 g of Aliquat 336	5	35	2	64
150 mL of pentane, 0.8 g of Aliquat 336	5	13	3	84
30 mL of acetic acid[d]	2	1	4	95
150 mL of pentane, 30 mL of acetic acid, 0.2 g of Aliquat 336	5	10	2	88

[a] $KMnO_4$ (0.12 mol) was placed in 200 mL of water in a 1-L flask equipped with a mechanical stirrer and blade. The mixture was immersed in an ice bath and 1-octyne (0.03 mol) was added in one portion with any listed additive. Product recovery in all cases was greater than 80%. [b] 1.5 g of KOH was added to the $KMnO_4$ solution. [c] 5.5 g of KOH was added to the $KMnO_4$ solution. [d] Added to the aqueous layer before octyne addition.

Preparative oxidations of 1-hexyne, 1-octyne, and 1-decyne (pentane, aqueous permanganate, acetic acid, and Aliquat 336) yielded the carboxylic acids in 70–80% yields of greater than 97% overall purity. This is an extremely convenient method to effect oxidations of terminal acetylenes.

Comparative oxidations performed in aqueous permanganate showed that 1-octyne oxidized somewhat more rapidly than 1-octene and less overoxidation occurred in the case of 1-octyne. However, 1-decene and 1-decyne oxidize at comparable rates with more overoxidation in the 1-decene case. Both of these substrates proceed much slower than the oxidations of 1-octene and 1-octyne.

The mechanistic pathway leading to the overoxidation which is seen in the case of 1-octyne as the basicity of the aqueous phase increases is unclear. The question of the importance (in some of the oxidations performed with quaternary ammonium salts) of phase-transfer catalysis also is difficult to assess.

Experimental Section

Materials. All α-olefins (99% purity) were obtained from the Humphrey Chemical Co., North Haven, Conn. 06473, and were used as received. 1-Octene (99.9%) and all the acetylenes were obtained from the Chemical Samples Co., Columbus, Ohio. Aliquat 336 (tricaprylylammonium chloride was kindly provided by General Mills Chemical Co., Minneapolis, Minn. 55435) and benzylhexadecyldimethylammonium chloride (J. T. Baker, practical grade) were used as phase-transfer agents. Potassium permanganate (Fisher Certified) was used as received.

Table VII. Permanganate Oxidations of 1-Decyne

Additives	Reaction time, h	1-Decyne	Octanoic acid	Nonanoic acid
None[a]	15	77	2	21
15 mL of acetic acid[a]	3.5	2	6	92
100 mL of pentane,[b] 50 mL of acetic acid 0.2 g of Aliquat 336	8	21	3	76

[a] $KMnO_4$ (0.06 mol) in 75 mL of water and 1-decyne (0.015 mol) were added. [b] $KMnO_4$ (0.15 mol) in 200 mL of water and 1-decyne (0.045 mol) and listed additives were added.

All acids which were prepared had ^1H NMR spectra in agreement with their structures and these data are not listed here. All boiling and melting points of the acids closely corresponded to the literature values.

(A) General Procedure for All Oxidations. The aqueous $KMnO_4$ (0.12 mol) in about 150–200 mL of water was cooled with stirring in an ice bath. The substrate (0.03 mol), and any solvent (100–150 mL), acetic acid (30 mL), or PTC (0.2 g), was added in one portion. The reaction was allowed to proceed for the specified time and recooled. In those runs without solvent, pentane or benzene was added at this point. Sodium sulfite (20 g) was slowly added and then either aqueous HCl (25 mL of concentrated HCl in 50 mL of water) *or* aqueous H_2SO_4 (25 g of concentrated H_2SO_4 in 100 mL of water) was slowly added. Two clear layers form; the organic layer is washed once with cold water and dried over Na_2SO_4. Distillation or concentration on a Buchi rotary evaporator leaves the crude product. The crude product was treated with ethereal CH_2N_2 and the methyl esters were analyzed by GLC (DC-200 column).

(B) α-Olefin Oxidations. Preparative Runs. (1) Typical Procedure. Tridecanoic Acid. A 1-L rb flask is charged with $KMnO_4$ (32 g, 0.20 mol) and 300 mL of water. The flask is immersed in an ice bath and stirred vigorously via an egg-shaped magnet (1 in.). A solution of 1-tetradecene (11.8 g, 0.06 mol), 300 mL of benzene, 60 mL of glacial acetic acid, and benzylhexadecyldimethylammonium chloride (0.2 g, 0.5 mmol) is added in one portion. Stirring is continued without any further addition of ice to the bath for about 4 hr. A total of 35 g of Na_2SO_3 is added to the cooled reaction mixture followed by the slow addition of a solution of 35 mL of concentrated HCl in 35 mL of water. Two clear layers result. The layers are separated and the benzene layer is washed once with a 100-mL portion of cold water. The benzene layer is dried over anhydrous sodium sulfate, the drying agent is removed by filtration, and the bulk of the benzene is removed by distillation. The residual benzene is removed on a rotary evaporator to yield 12.7 g (99%) of crude solid. The crude acid is dissolved in pentane (60 mL), filtered to remove traces of insoluble material, and placed in the freezer overnight. Filtration yields 10.6 g (83%) of tridecanoic acid of mp 43–44 °C (lit. mp 44–45 °C).[16] Treatment of a sample of the crude or crystallized acid with CH_2N_2 followed by GLC analysis showed about 2% contamination by dodecanoic acid and a trace amount of a short retention time impurity.

(2) Pentadecanoic acid was prepared as in the typical procedure, except 1-hexadecene (13.4 g, 0.06 mol) and 1 g of Aliquat 336 were used. The reaction was allowed to proceed overnight (10 h). The crude solid weighed 14.4 g (99%). Crystallization from ligroin (35–60 °C) gave 12.2 g (84%) of mp 52–53 °C (lit. mp 53–54 °C).[16] GLC of the methyl esters showed 2% contamination by tetradecanoic acid.

(3) Heptadecanoic acid was prepared as in the typical procedure, except 1-octadecene (15.4 g, 0.06 mol) and 0.1 g of bzl-PTC were used and the reaction was allowed to proceed for 6 h. Workup yielded 13.0 g (80%) of acid after crystallization from ligroin. GLC analysis of the methyl esters showed about 3% contamination by hexadecanoic acid and 0.5% of an unidentified peak of short retention time.

(4) Nonadecanoic acid was prepared as in the typical procedure, except 1-eicosene (16.8 g, 0.06 mol) and 1 g of Aliquat 336 were used and the reaction was allowed to proceed for 3 h. The crude white solid was placed in cold ethanol and filtered to yield 15.5 g (86%) of acid of mp 65–67 °C (lit. mp 69 °C).[16] Crystallization from CH_3CN raised

the melting point to 67–68 °C. GLC of the methyl esters showed 3% contamination by stearic acid.

(5) Decanoic acid was prepared as in the typical procedure, except 1-undecene (9.2 g, 0.06 mol) was used. The reaction was allowed to proceed overnight and on workup the crude acid (10.2 g, 99%) was obtained. Distillation, 105–107 °C/0.5 mm, yielded 8.6 g (84%) of decanoic acid which solidified. GLC of the methyl esters showed about 3% contamination by nonanoic acid.

(6) Undecanoic acid was prepared as in the typical procedure, except 1-dodecene (0.06 mol) and a reaction time of 4 h was used. The crude acid, 11.1 g (99%), was distilled at 110–115 °C/0.1 mm to yield 9.9 g (90%) of undecanoic acid. GLC of the methyl esters showed about 3% contamination by decanoic acid and less than 0.5% of a short retention time impurity.

(7) Nonanoic acid was prepared as above, except 1-decene (0.06 mol) and 0.1 g of bzl-PTC were used and the reaction was allowed to proceed for 4 h. The crude acid was distilled, bp 89–90 °C/0.1 mm, to yield 8.0 g (85%) of 97% pure nonanoic acid (GLC of esters).

(8) Heptanoic acid was prepared as above, except 1-octene (6.7 g, 0.06 mol) was used and the reaction was allowed to proceed for 3 h. Distillation at 83–84 °C/1.5 mm gave 6.2 g (80%) of acid of 98% purity (GLC of methyl esters).

(C) Acetylene Oxidations. Preparative Runs. (1) Typical Procedure: 1-Octyne → Heptanoic Acid. In a 1-L rb flask fitted with a 1-in. egg-shaped spinbar is placed $KMnO_4$ (28 g, 0.18 mol) and 200 mL of tap water. The mixture is stirred and immersed in an ice bath. A solution of 1-octyne (5.0 g, 0.045 mol), 120 mL of pentane, 60 mL of acetic acid, and 0.2 g of Aliquat 336 is added in one portion. The mess is stirred for 5 h without replenishing the ice. The black-brown mixture is cooled in an ice bath and Na_2SO_3 (30 g) is added in several portions. A solution of 60 mL of concentrated HCl in 60 mL of water is then cautiously added. The top pentane layer is separated and the acidic layer is extracted once with 50 mL of pentane. The combined pentane extracts are washed with 50 mL of cold water, dried over Na_2SO_4, decanted from the drying agent, and concentrated on a Buchi rotary evaporator to yield 5.4 g of crude product (90% recovery). Vacuum distillation yields 4.1 g (70%) of heptanoic acid (98% pure by GLC of the methyl esters, trace amounts of short retention time impurities were also present).

(2) Nonanoic acid was prepared as above, except 1-decyne (0.045 mol) was used and the reaction was run for 8 h. On distillation, 4.6 g (70%) of acid was obtained of 98% purity (GLC of methyl esters).

(3) Pentanoic acid was prepared as above, except $KMnO_4$ (0.24 mol), 300 mL of water, 1-hexyne (0.06 mol), 250 mL of pentane, and 0.3 g of Aliquat 336 were used, and the reaction was run for 3 h to yield 4.0 g (66%) of acid of 98% purity (GLC of methyl esters).

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Registry No.—$KMnO_4$, 7722-64-7; decanoic acid, 334-48-5; undecanoic acid, 112-37-8; nonanoic acid, 112-05-0; heptanoic acid, 11-14-8; allylbenzene, 300-57-2; 1-hexyne, 693-02-7; 1-octyne, 629-05-0; 1-decyne, 764-93-2.

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(2) Fellow of the Humphrey Chemical Co., Fall 1974.
(3) National Science Foundation Undergraduate Research Participant.
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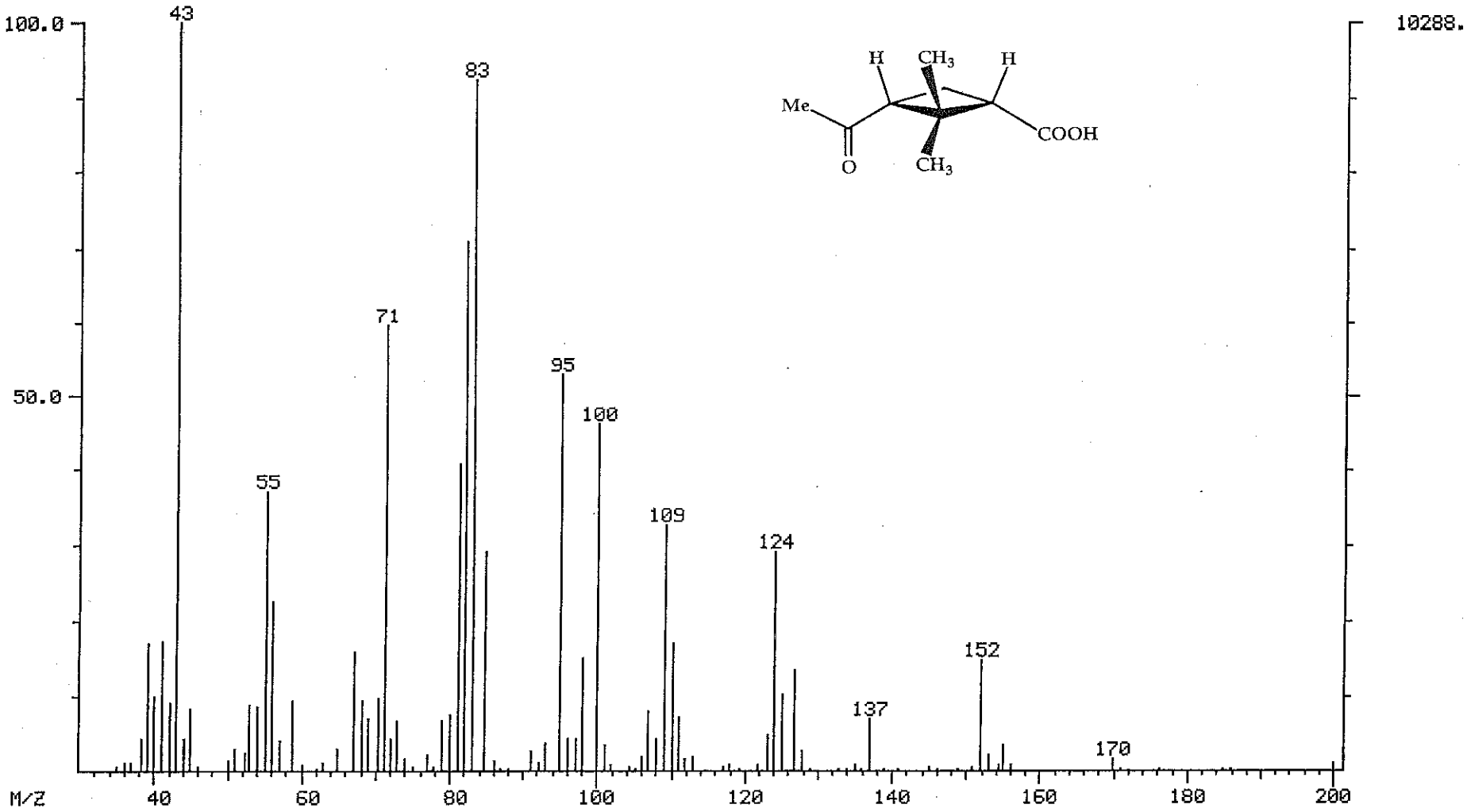

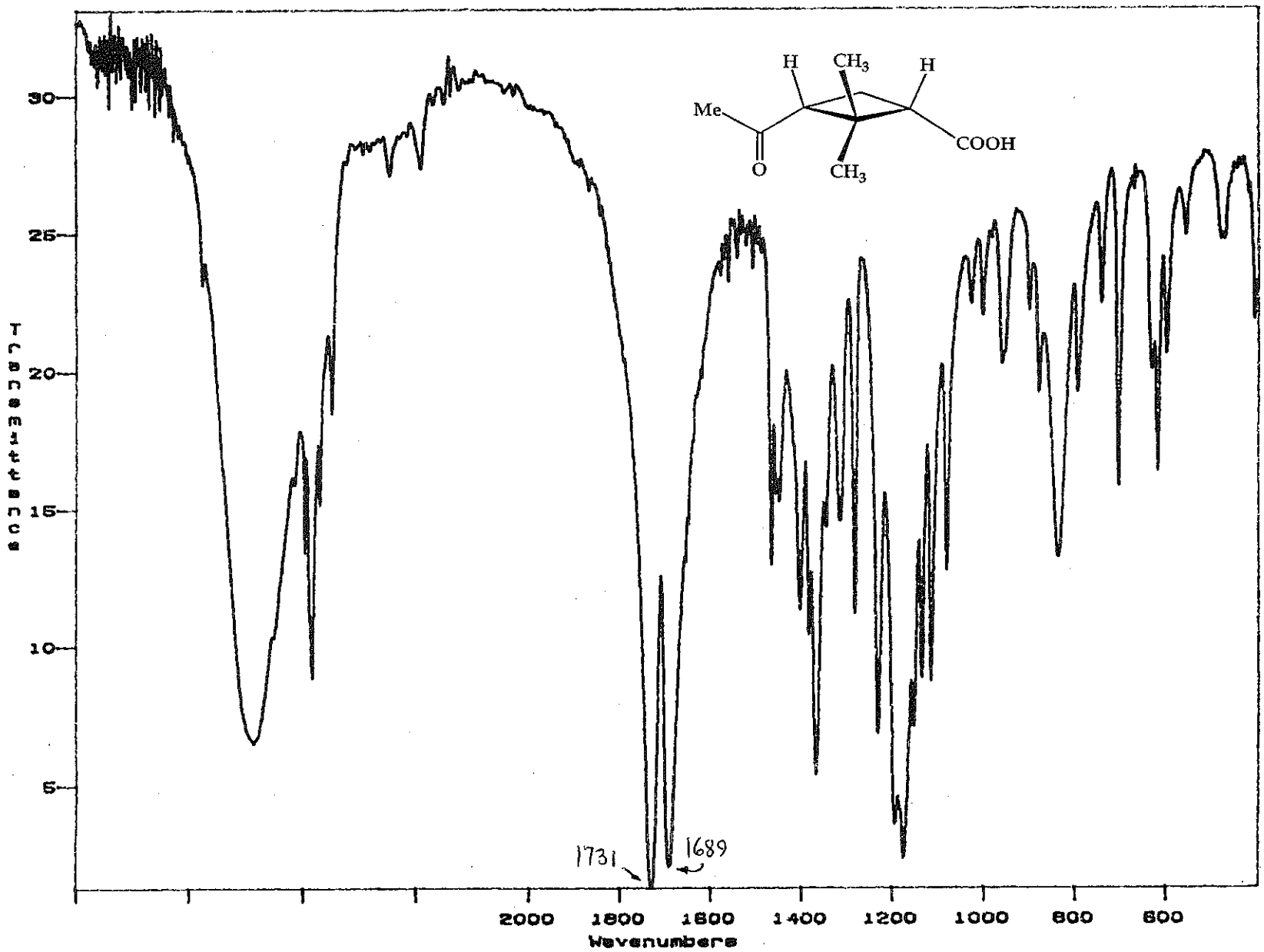
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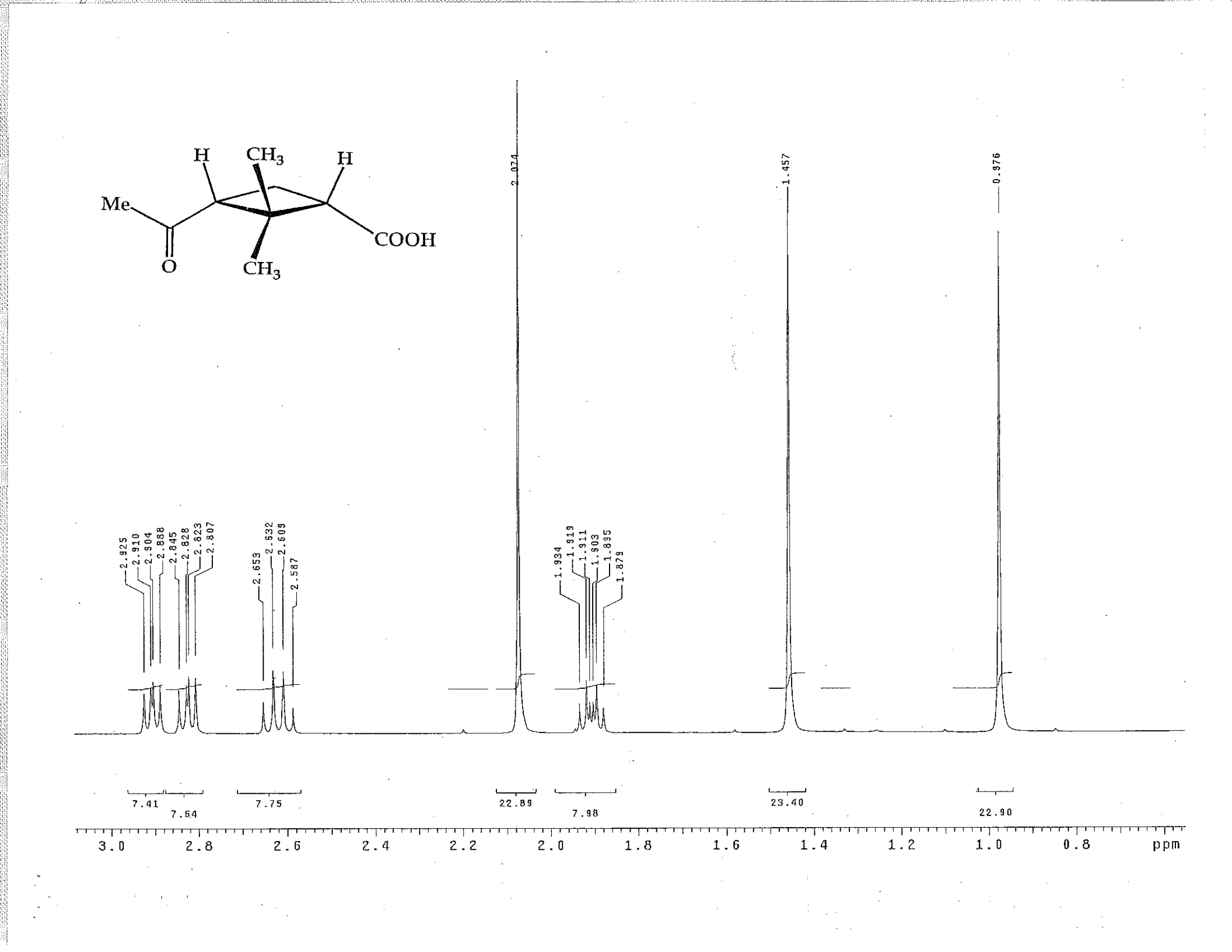
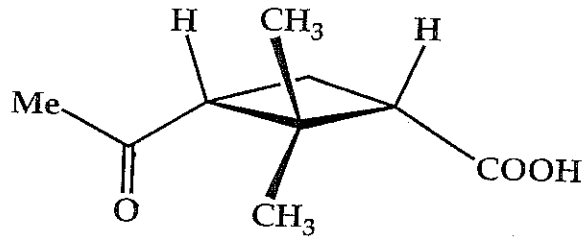
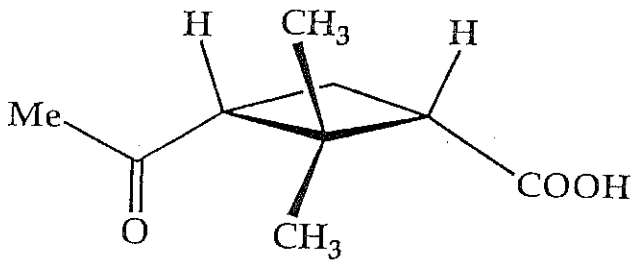
600
Wavenumbers

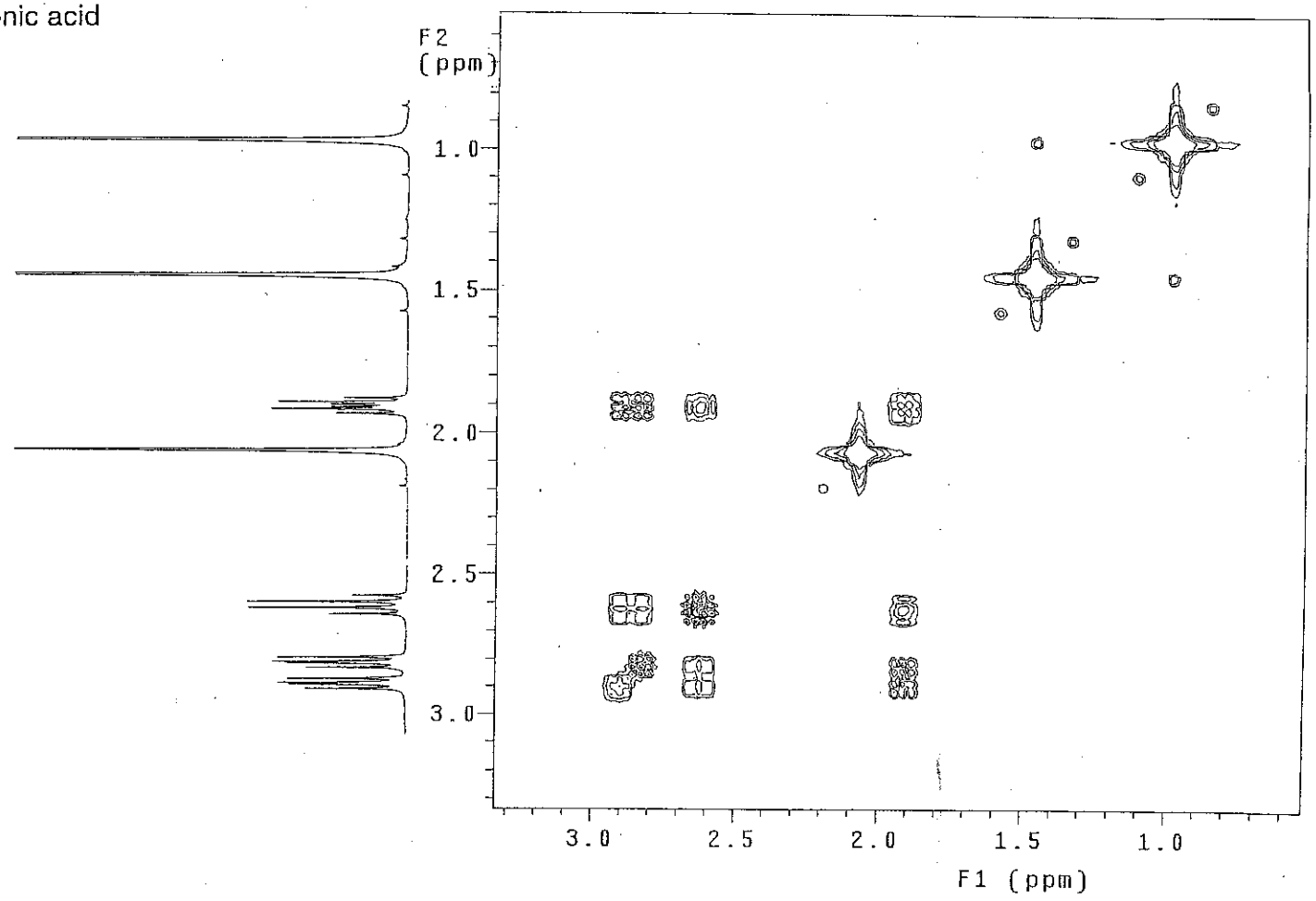

H
CH3
H
Me
COOH
O
CH3
2.074
1.457
0.976
2.925
2.910
2.904
2.888
2.845
2.828
2.823
2.807
2.653
2.632
2.609
2.587
1.934
1.919
1.911
1.903
1.835
1.879
7.41
7.64
7.75
22.89
7.98
23.40
22.90
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0
0.8
ppm


H
CH3
H
Me
COOH
O
CH3

12
10
8
6
4
2
0



A homonuclear ^{1}H COSY spectrum of (-)-*cis*-pinononic acid



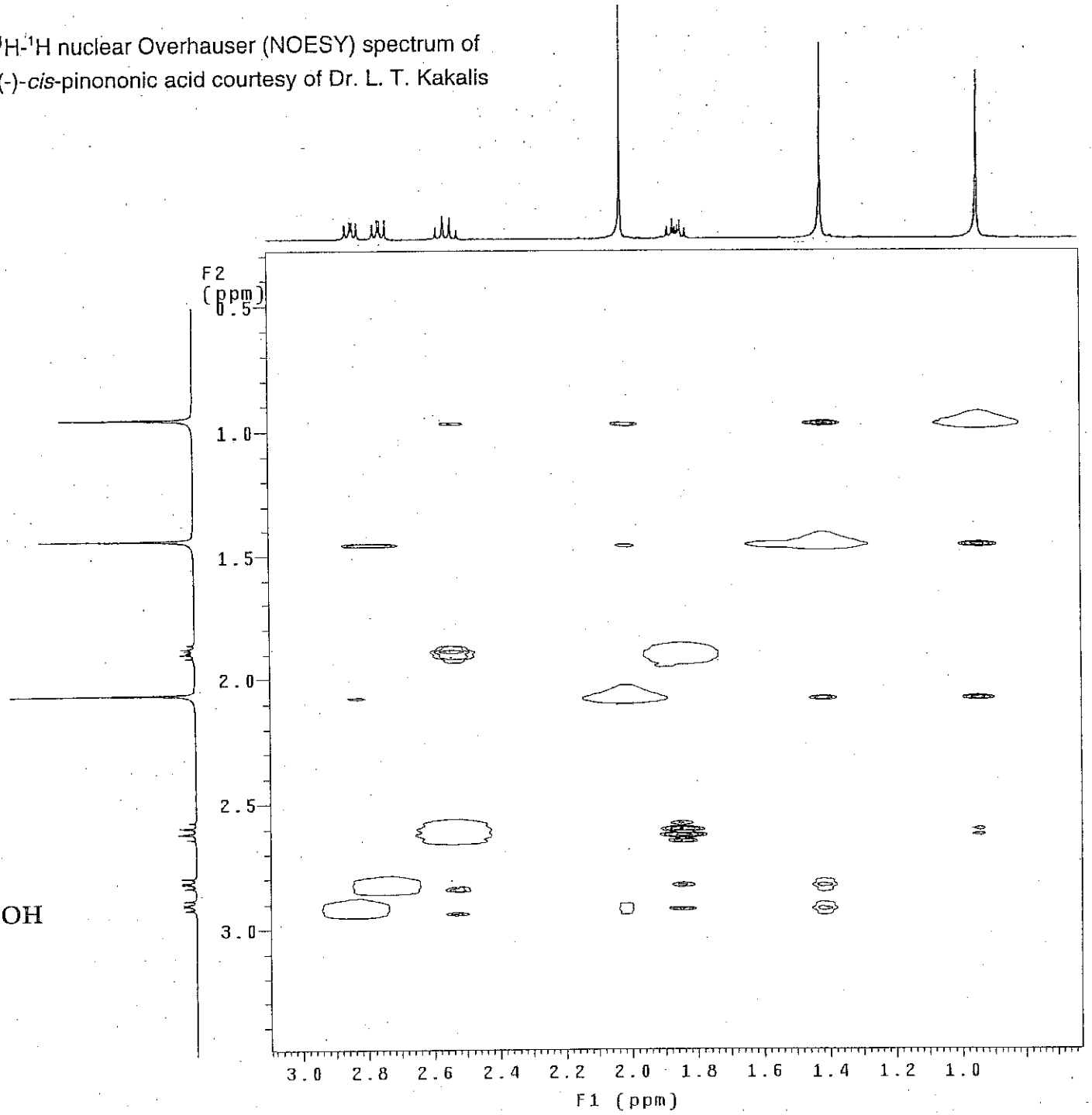
STANDARD PROTON PARAMETERS

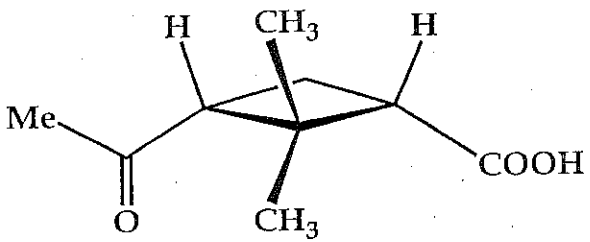
Pulse Sequence: NOESY

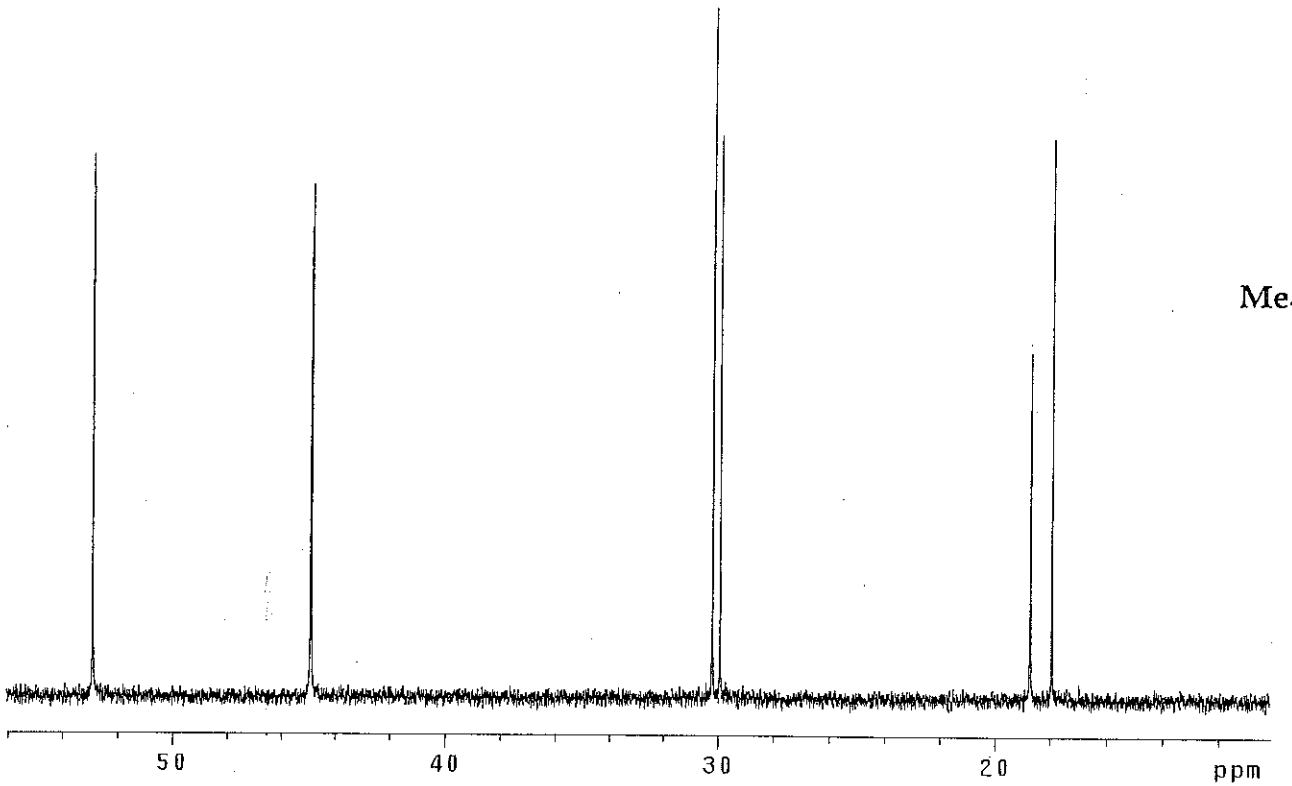
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
File: hwt_pinononic_noesy400_090403
INOVA-500 "newnmr5.rutgers.edu"

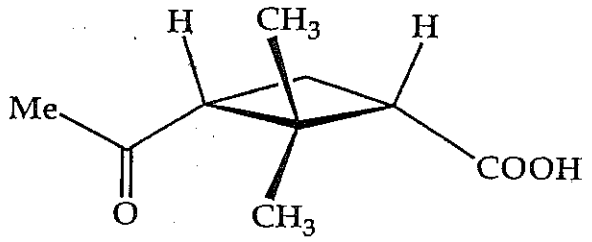
Relax. delay 2.000 sec
Mixing 0.400 sec
Acq. time 0.255 sec
Width 2004.4 Hz
2D Width 2004.4 Hz
8 repetitions
2 x 64 increments
OBSERVE H1, 499.8931624 MHz
DATA PROCESSING
Gauss apodization 0.084 sec
F1 DATA PROCESSING
Gauss apodization 0.012 sec
FT size 2048 x 256
Total time 46 min, 10 sec

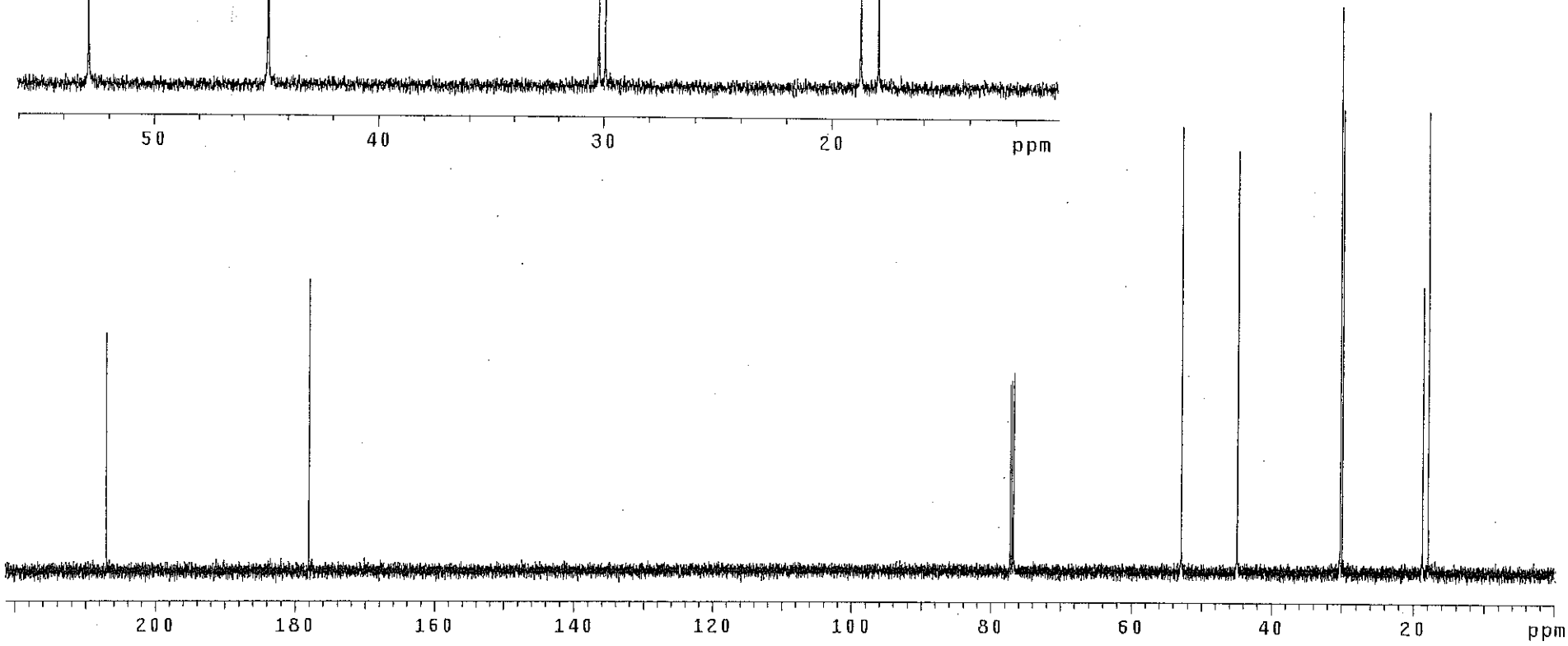
^{1}H-^{1}H nuclear Overhauser (NOESY) spectrum of
(-)-*cis*-pinononic acid courtesy of Dr. L. T. Kakalis

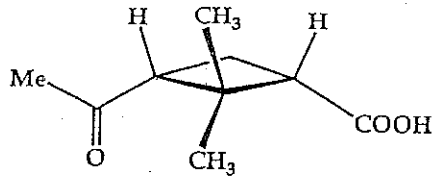




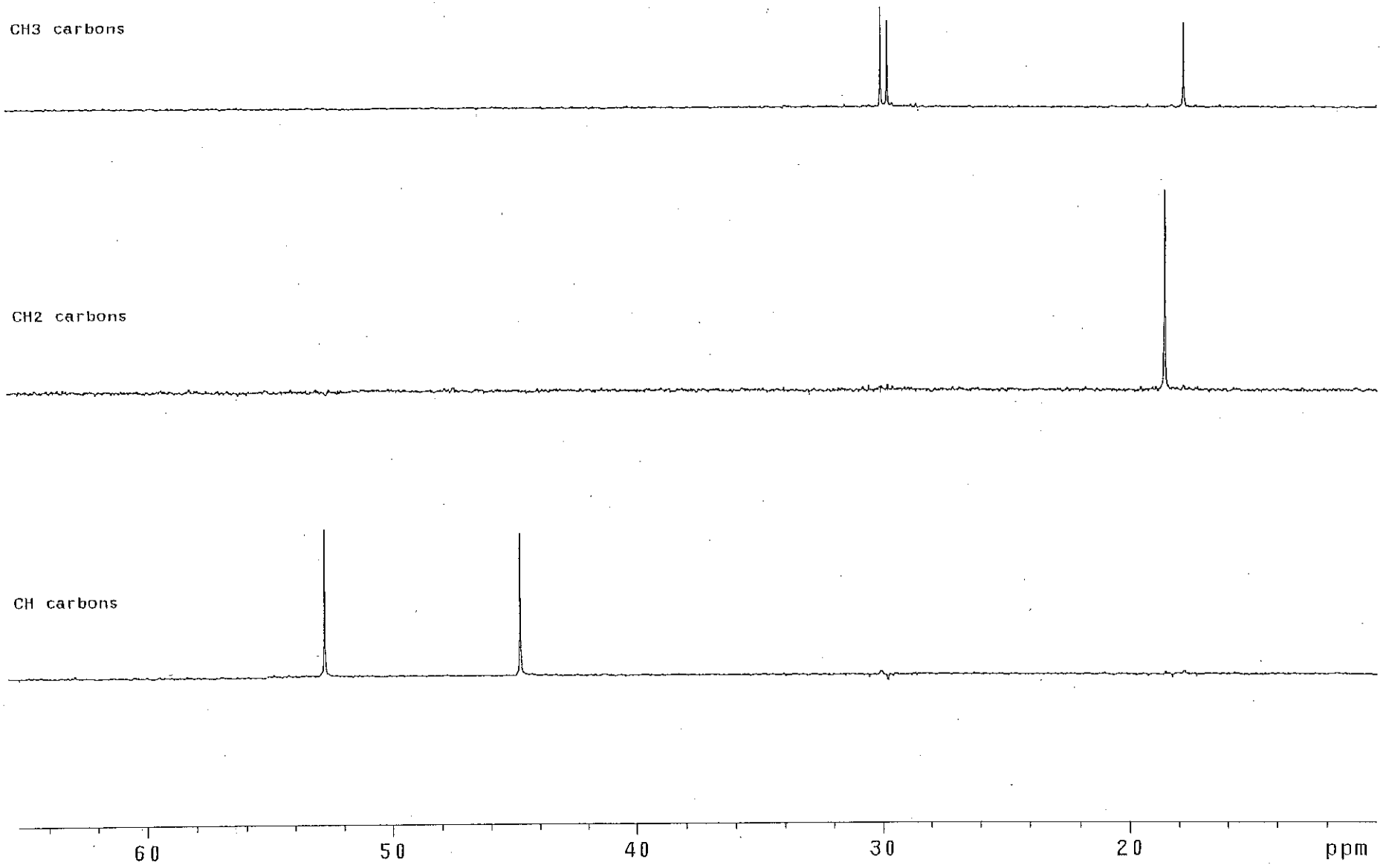

50
40
30
20
ppm


H
CH3
H
Me
COOH
O
CH3


200
180
160
140
120
100
80
60
40
20
ppm

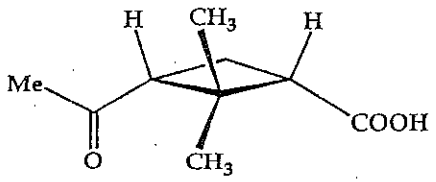


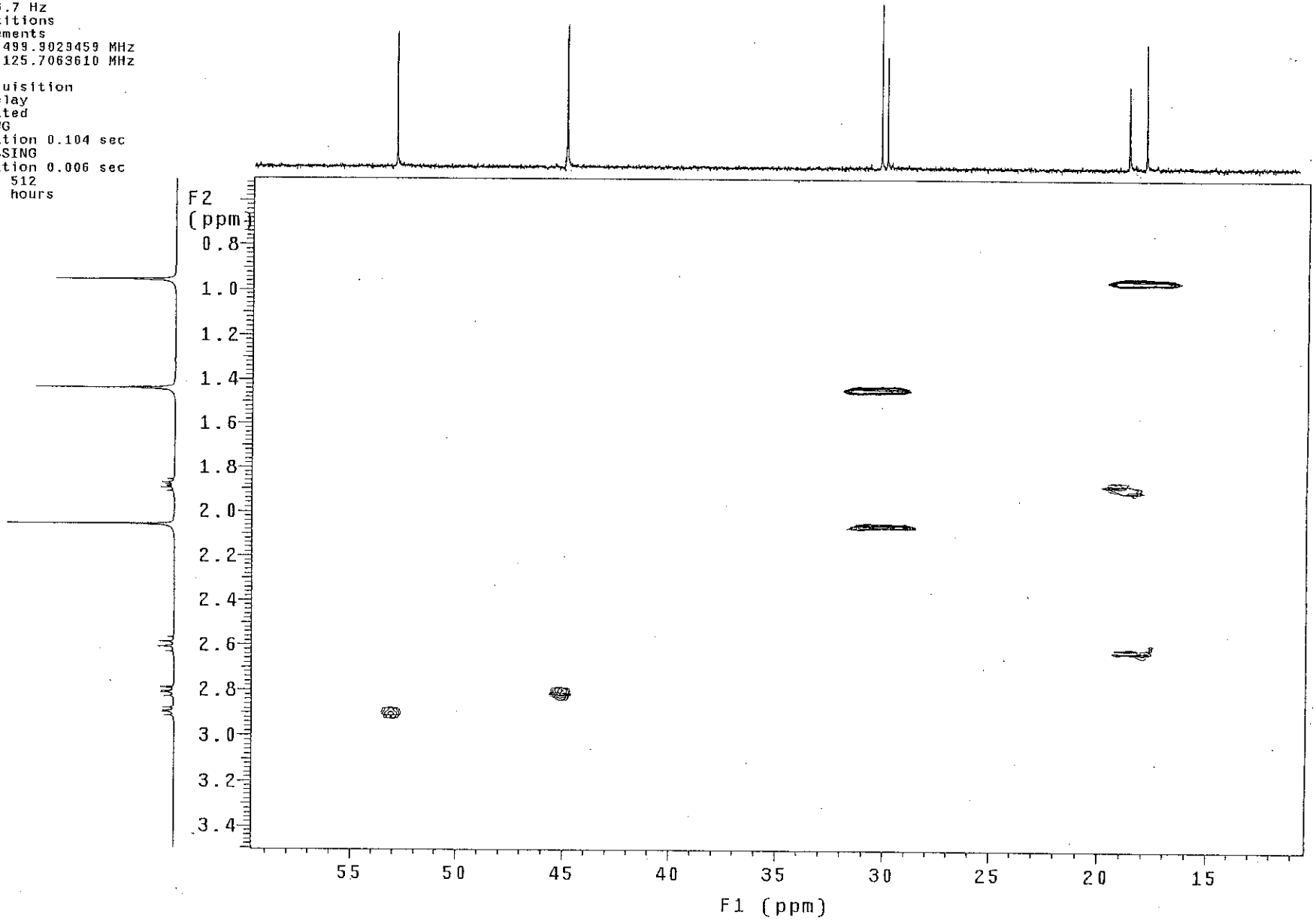
^{13}C DEPT spectra of (-)-*cis*-pinononic acid
courtesy of Dr. L. T. Kakalis



STANDARD PROTON PARAMETERS
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
User: 1-14-87
INOVA-500 "newark5"
PULSE SEQUENCE: hmqc
Relax. delay arrayed
Acq. time 0.244 sec
Width 2100.2 Hz
2D Width 8776.7 Hz
Arrayed repetitions
2 x 128 increments
OBSERVE H1, 499.9029459 MHz
DECOUPLE C13, 125.7063610 MHz
Power 46 dB
on during acquisition
off during delay
GARP-1 modulated
DATA PROCESSING
Gauss apodization 0.104 sec
F1 DATA PROCESSING
Gauss apodization 0.006 sec
FT size 1024 x 512
Total time 5.1 hours

Heteronuclear ^{1}H-^{13}C COSY (HETCOR) spectrum of
(-)-*cis*-pinononic acid courtesy of Dr. L. T. Kakalis





X-ray crystal structure of (-)-*cis*-pinononic acid
courtesy of M. L. Coté & R. A. Lalancette