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Substituent effects on strained rings. part A ; The kinetics of hydrolysis of A quinuclidone using FTIR. part B

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ABSTRACT

Title of Thesis: PART A. SUBSTITUENT EFFECTS ON STRAINED RINGS.
PART B. THE KINETICS of HYDROLYSIS of A
QUINUCLIDONE USING FTIR.

Yeu-Yi Chiu, Master of Science, 1989

Thesis directed by: Dr. Arthur Greenberg
Professor of Chemistry
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and Chemistry.

PART A: The energies of a series of monosubstitued propane, cyclopropane and cyclopropene compounds were calculated using ab initio molecular orbital calculations optimized at the 3-21G level using Gaussian 82 and Gaussian 86 programs. The effects of substituents on stabilization energies and geometries are rationalized with respect to the parent molecules. The result is presented which indicated that for substituted cyclopropyl and cyclopropenyl compounds, most of the substituents induce stabilization except the $-NC$ substituent group is destabilizing in cyclopropyl and cyclopropenyl systems. Indications of relative electrostatic and resonance effects are also analyzed. A linear free energy relationship has been examined by comparing the stabilization energies and appropriate Taft Dual Substituent Parameter equation substituent constants:σ_I (induction effect) and σ_R (resonance effect).

PART B: The synthesis of 6,6,7,7-Tetramethyl-1-azabicyclo[2.2.2] octan-2-one (6,6,7,7-tetramethyl-2-quinuclidone) was done by Dr. Wu Guanli. Some kinetic data are obtained using conditions from a paper by Pracejus and co-workers. FTIR was employed to monitor the rate of decomposition which was then compared with others, less sterically-hindered, guinuclidone derivatives.

PART A. SUBSTITUENT EFFECTS ON STRAINED RINGS

PART B. THE KINETICS of HYDROLYSIS of A QUINUCLIDONE USING FTIR.

by

Yeu-Yi Chiu

Thesis submitted to the faculty of the Graduate School of
the New Jersey Institute of Technology in partial fulfillment of
the requirements for the degree of
Master of Science
1989

APPROVAL SHEET

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PART B: THE KINETICS of HYDROLYSIS of A QUINUCLIDONE USING FTIR.

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

PART A

SUBSTITUENT EFFECTS ON STRAINED RINGS

Chapter 1

INTRODUCTION AND METHODOLOGY

1.1 INTRODUCTION

There are many theoretical [1][2][3][4] and experimental [5][6][7][8] papers describing the effects of substituents on the structure of cyclopropanes and related isopropyl and related derivatives. However, only a few papers consider cyclopropene derivatives, thus we are interested in a series of cyclopropenyl-x study. The influences of substituents on bond lengths and bond angles in these componds have received considerable attention in these papers.

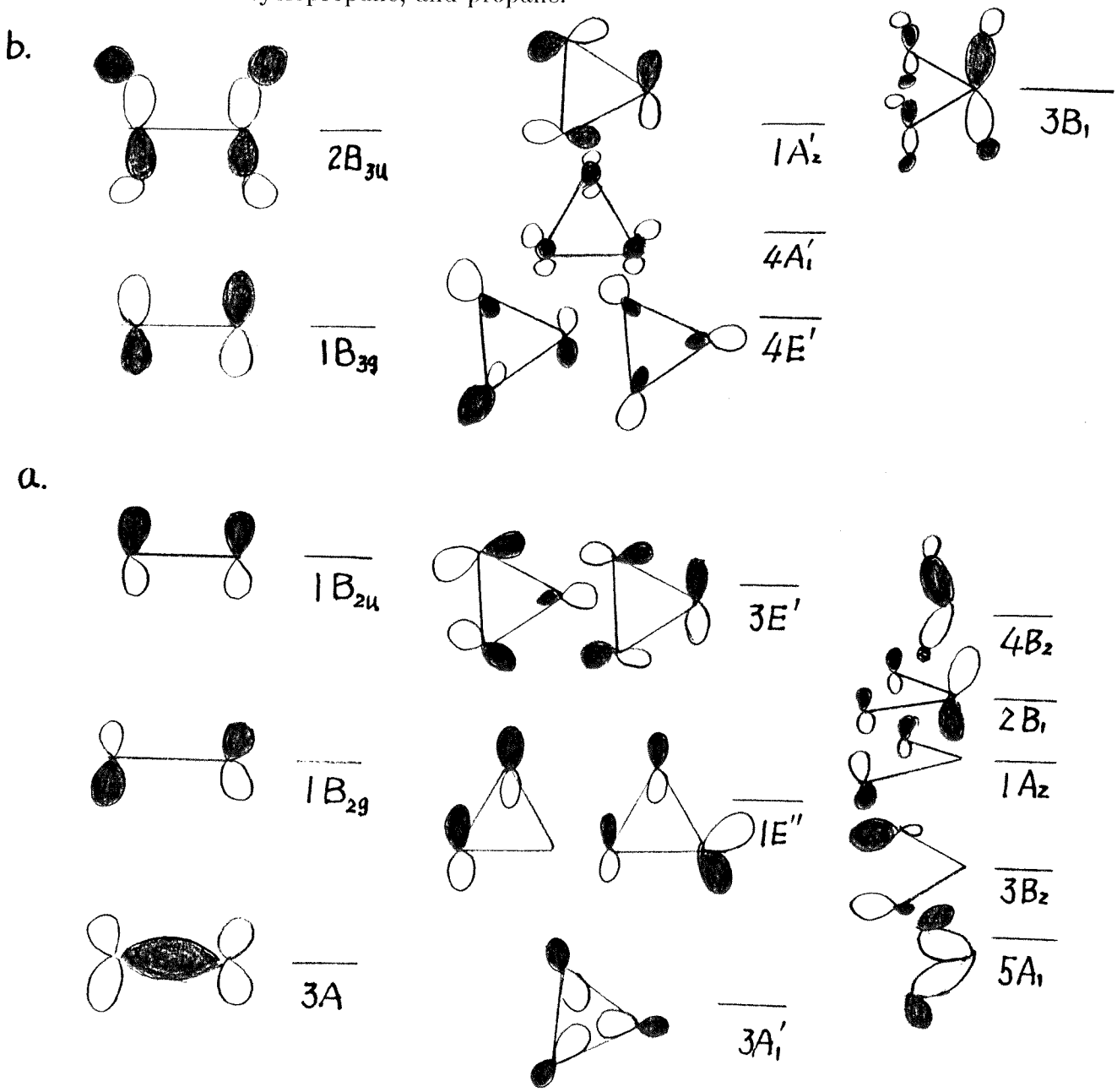
Hoffmann first developed a general theory of substituent effects on cyclopropanes [9][10]. Later other groups of researches [12][13][14][15][16][17] published work relating to substituent effects on strained rings. They employed Walsh orbitals to explain their results.

Figure 1-1 depicts the molecular orbitals of ethylene, propane and cyclopropane with emphasis on the relationship with the Walsh orbitals. [11][12] Isopropyl and cyclopropenyl show some similarities to cyclopropane.

Figure 1-1.(a) High-Lying Occupied and

(b) Low-Lying Unoccupied Molecular Orbitals of ethylene,

cyclopropane, and propane.



Investigations into the role of pi-accepting substituents on ring geometry [12] received their main impetus from the predictions of Hoffmann and coworkers. Assuming the dominant interaction to be between the cyclopropane 3E′ Walsh type orbital and the vacant p or π^* orbital on a substituent, they predicted lengthening of the vicinal bond and shortening of the distal bonds. This is because transfer of electron density from the 3E′ orbital decreases the antibonding electron density in the distal bond and decreases the bonding electron density in the vicinal bonds.

There (Figure 1-2) has been comparatively little work on substituted cyclopropenes. [12] These compounds are of particular interest since one might imagine that a limiting sigma-withdrawing substituent might produce stabilization mimicking the aromatic cyclopropenium cation. Conversely, limiting sigma-donation by a substituent could mimic the destabilization of an antiaromatic cyclopropenide anion. Thus, calculations have been performed on 3-substituted cyclopropenes in order to investigate these potential effects.

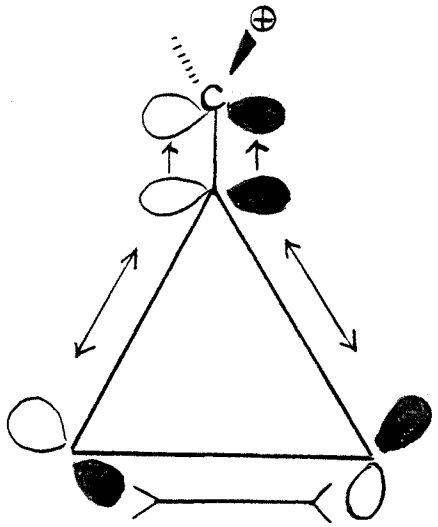


Figure 1-2. Interaction of Cyclopropane *HOMO* with vacant p orbital.

Figure 1-3 [9] gives a schematic representation of the Walsh type *MO*'s of cyclopropane.

When the substituent is a good pi-acceptor, mixing the acceptor orbital into the antisymmetric compound [12] of the occupied degenerated Walsh orbital pair in cyclopropane is an important stabilizing interaction. The interaction is depicted in Figure 1-3 and in scheme 1.

The lower-lying the unoccupied pi-molecular orbital of the substituent the stronger the interaction between it and the Walsh orbital in cyclopropane.

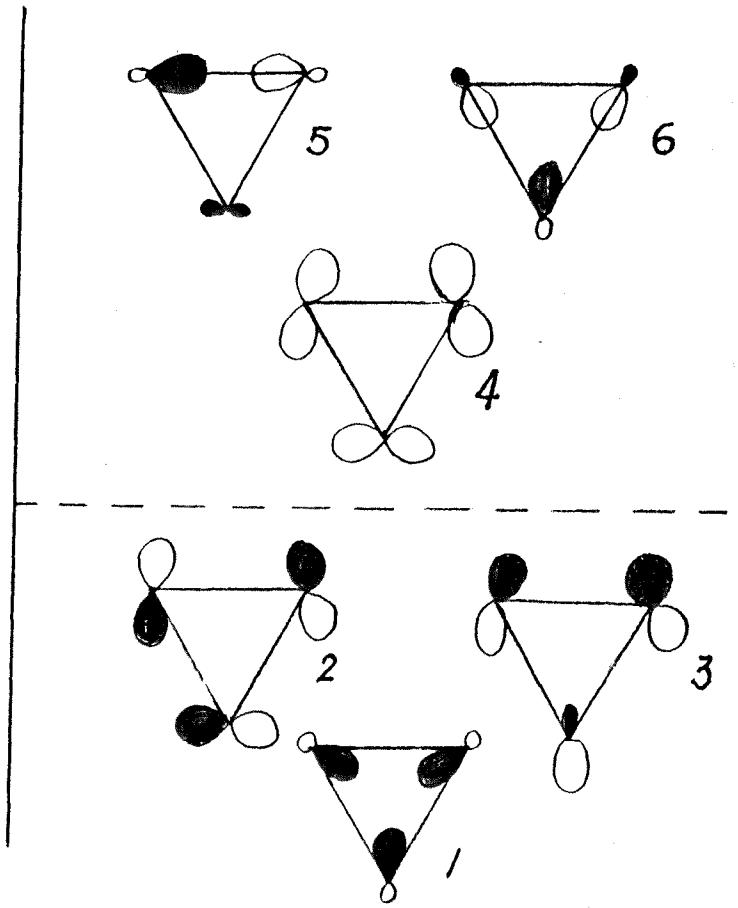
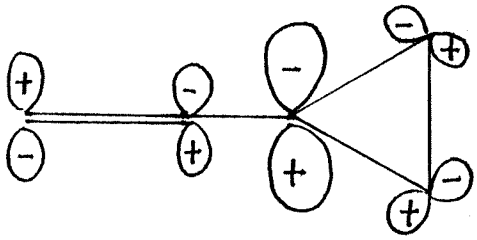


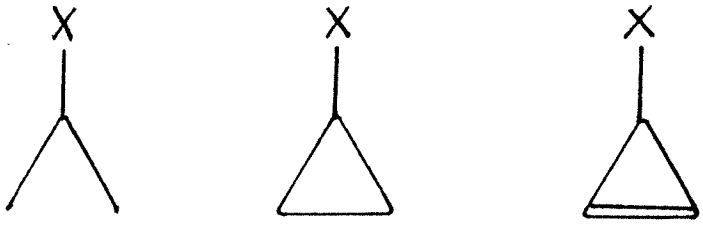
Figure 1-3.The Walsh *MO*'s of cyclopropane, a and b indicate, if occupation of the MO would add to the corresponding bond, antibonding or boding contributions, respectivelly.

Scheme 1.



Caculations of substituted cyclopropanes have been used to show that pi-acceptors result in a shortening of the distal bond and a lengthening of the vicinal bonds. Cyclopropanes substituted by pi-donor substituents have adopted structures not readily explicable in terms of Hoffmann's theory. Specifically, Hoffmann and co-workers considered the main interaction to be one involving the $A'2$ Walsh-type antibonding orbital in cyclopropane. This interaction is dominant only for substituents such as O^-, which has an occupied orbital of very high energy and is capable of lengthening both vicinal and distal bonds, but not for other substituents. We also see that the O^- substituent in cyclopropene has the same result of lengthening both vicinal and distal bonds and lengthening vicinal bond in isopropyl-x.

We have examined a series of 3-substituted cyclopropenes to compare the results with corresponding cyclopropyl and isopropyl molecules. (Figure 1-4) :



isopropyl-X cyclopropyl-X 3-cyclopropenyl-X

Figure 1-4 $X = H, F, CH_3, NH_2, OH, O^-, CN, NC, NH_3^+$

Now, we start a series of calculations of monosubstituted propane, cyclopropane, and cyclopropene molecules to compare their substituent effects, stablization energies, geometry structures, and free energy relationships will yield theoretical insights.

The calculational results must be compared to the theoretical predictions of Hoffmann's theory using Walsh-type orbitals, hybridization, conjugation, resonance effects and inductive /electronegativity effects. One should note that a cyclopropyl group is a strong pi-donor. [12] This is due to the importance of overlap of the $3E'$ orbital with the vacant p or π^* orbital of a conjugated substituent. Furthermore, while cyclopropane is a strong pi-donor it is a weak pi-acceptor.

1.2 METHODOLOGY

Chemical calculations that can predict structures, energies and other properties of known molecules and unstable molecules and intermediates have often been heralded as important new tools in chemical research. Calculation can easily be performed for compounds that have never been made, or cannot even exist under real conditions. Calculation results are often in remarkably good agreement with experiment. [29]

Many simple MO treatments, such as Huckel and extended Huckel theories, are based on one-electron treatments in which the electron is considered not to interact with other electrons in the molecule. This is not realistic. The methods discussed in the thesis, however, take electron-electron repulsion into account by considering the interaction between an electron in a given orbital and the mean field of the other electrons in the molecule. This approach is known as the self-consistent field (SCF) method. The SCF method is also known as Hartree-Fock or single-determinant theory. [13]

One of the major problems in using the SCF-MO method is how to treat both

open- and closed-shell molecules consistently (i.e., to calculate molecules with and without unpaired electrons at the same level of approximation). Closed-shell systems are almost always calculated using restricted Hartree-Fock (RHF) theory also known as spin restricted Hartree-Fock theory. Open-shell restricted Hartree-Fock calculations are possible with ab initio programs such as GAUSSIAN 82, but not with the usual semi-empirical [30] programs.

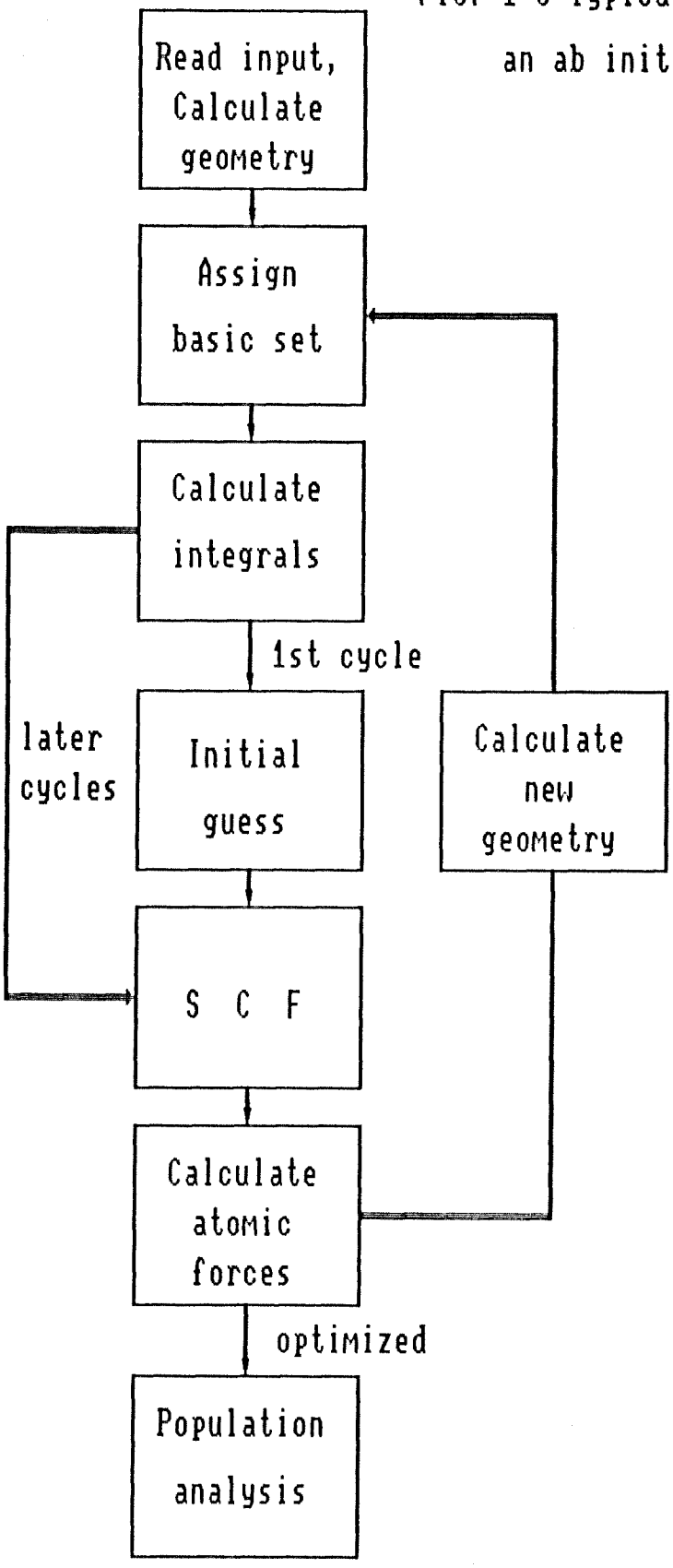
Ab initio molecular orbital calculations employ the Gaussian 82 and Gaussian 86 programs on a VAX 785, VAX 8800 computer. Usually, the program must be bought, either from the Quantum Chemistry Program Exchange (QCPE) or via a software agreement. [31] QCPE, which is based in Indiana University, is a nonprofit organization for the distribution of a wide range of programs for chemistry. GAUSSIAN 82 and 86 are available as the VAX and CRAY1 source (FORTRAN) version directly from professor J. A. Pople. There are a number of simplifying assumptions in ab initio theory, but the calculations are more complete, and therefore more expensive, than those of the semiempirical methods. Ab initio theory makes use of the Born-Oppenheimer approximation that the nuclei remain fixed on the time scale of electron movement, that is, that the electronic wave function is unaffected by nuclear motion. Almost all modern ab initio calculations employ GAUSSIAN Type Orbital (GTO) basis sets.

The simplest of the optional basis sets in GAUSSIAN 82 are the STO-nG bases, of which STO-3G is the only one to have found wide use. STO-nG is an abbreviation for Slater-Type-Orbitals simulated by n Gaussian functions added together. 3-21G has now replaced STO-3G for all but the largest molecules, and is the standard basis set for initial geometry optimizations. [29]

Geometry optimizations used in the present study gradient optimization proce-

dures at the 3-21G level (these calculations are denoted as 3-21G//3-21G) and for substituents that are negatively charged calculation at these geometries were performed at the 6-31G$\star$ level (denoted 6-31G$\star$//3-21G) because diffuse functions in the program must be added for minus charge substituted molecules. [30] (Figure 1-5)

FIG. 1-5 Typical Flow Chart for an ab initio optimization.



Chapter 2

SUBSTITUENT EFFECT ON STRAINED RINGS

We have calculated a series of monosubstituted propane, cyclopropane and cyclopropene molecules. The substituted elements are different which get the influence of changing stabilized energy, bond length and bond angle.

Ab initio molecular orbital calculations are carried out for 2-propyl-x, cyclopropyl-x and 3-cyclopropenyl-x, where X are the following substituents:
$H, F, CH_3, NH_2, OH, CN, NC, O^-$ and NH_3^+. Geometries are optimized at the 3-21G level.

The calculations will be analyzed in terms of current models. These models of how a strained ring is affected through substituent electronic effects have been outlined by Dill, Greenberg and Liebman. Two major effects [15] were recognized: 1). Inductive effect : it operates through the localized exocyclic ring-substituent bond, i.e., the 1e″ molecular orbital of cyclopropane. 2). Resonance effect : it operates through the delocalized molecular orbitals of a ring, i.e., the 3a′, 3e′, and 1a′ orbitals of cyclopropane. (see Fig. 2-1)

The first component of the substituent electronic effect is described by Taft's inductive substituent constant [17] and Topsom electronegativity and/or field effect

parameters. [18] We should note that a substituent's stabilizing effect on a strained ring is measured relative to its effect on an acyclic species. (e.g., isopropyl). The substituent inductive effect on strained ring systems is compared to unstrained acyclic systems as proposed by Dill et al. [15] These workers point out that if a substituent is σ electron donating, it will form a bonding pair with the ring that is largely localized on the ring, i.e., the 1e'' *MO* of cyclopropane. [16] The same will occur for bonding with the acyclic species, but since the exocyclic ring orbital is lower in energy than the counterpart of the unstrained molecule, net stabilization of the ring molecule occurs relative to the unstrained molecule. [16] (Fig. 2-2)

If the substituent is a σ electron withdrawing substituent the oppositive condition occurs. The bonding electron pair is largely localized on the substituent. The energy of the exocyclic ring orbital is lower than the corresponding orbital of the unstrained molecule, the energy gain is greater for the acylic molecule, and hence destabilization occurs in the strained ring. [16] (Fig. 2-3)

According to the views of Topsom and co-workers [18][19][20][21] there are actually two "non-resonance" substituent effects of importance when considering a reaction site of close proximity to the substituent. These are the inductive or electronegativity (through-bond), and dipole (field) effect. Doubtless, the above mentioned description for a substituent's "inductive" effect (the more corr- ect term is "electrostatic", covering all non-resonance effects), is an oversimplification. We hope the correlation analyses will explain more exactly the substistueent electrostatic effect on a strained ring.

Figure 2-1 The delocalized molecular orbittals of cyclooropane.

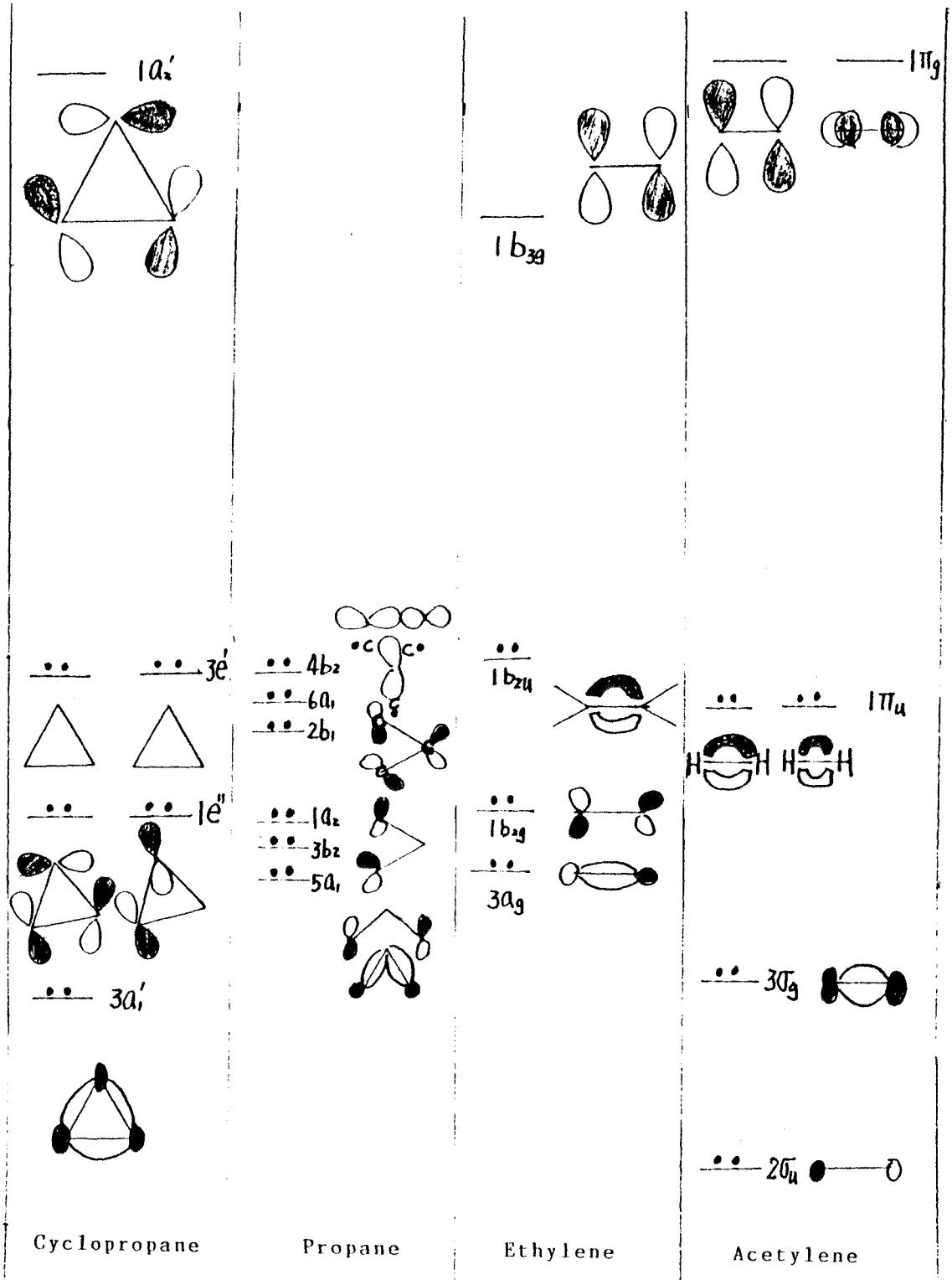


Figure 2-2 The stablization of the cyclic molecule relative to the unstrained molecule.

x = electropositive, ipr is isopropyl.

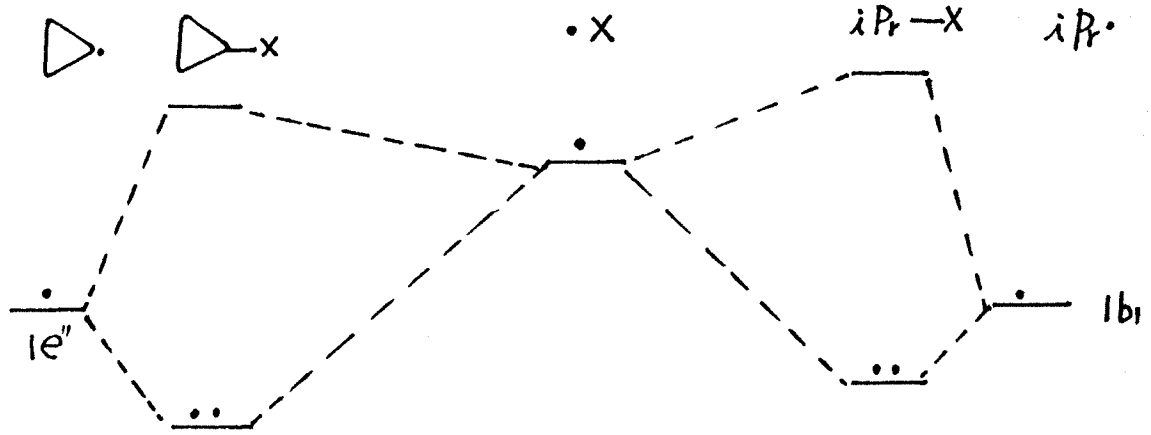
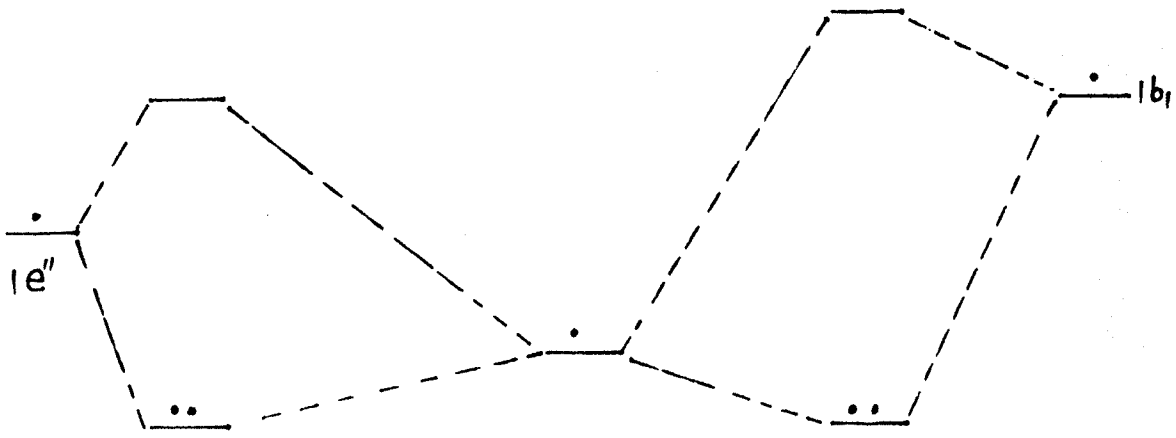


Figure 2-3 Destablization in the strained ring.

x = electronegative, ipr is isopropyl.

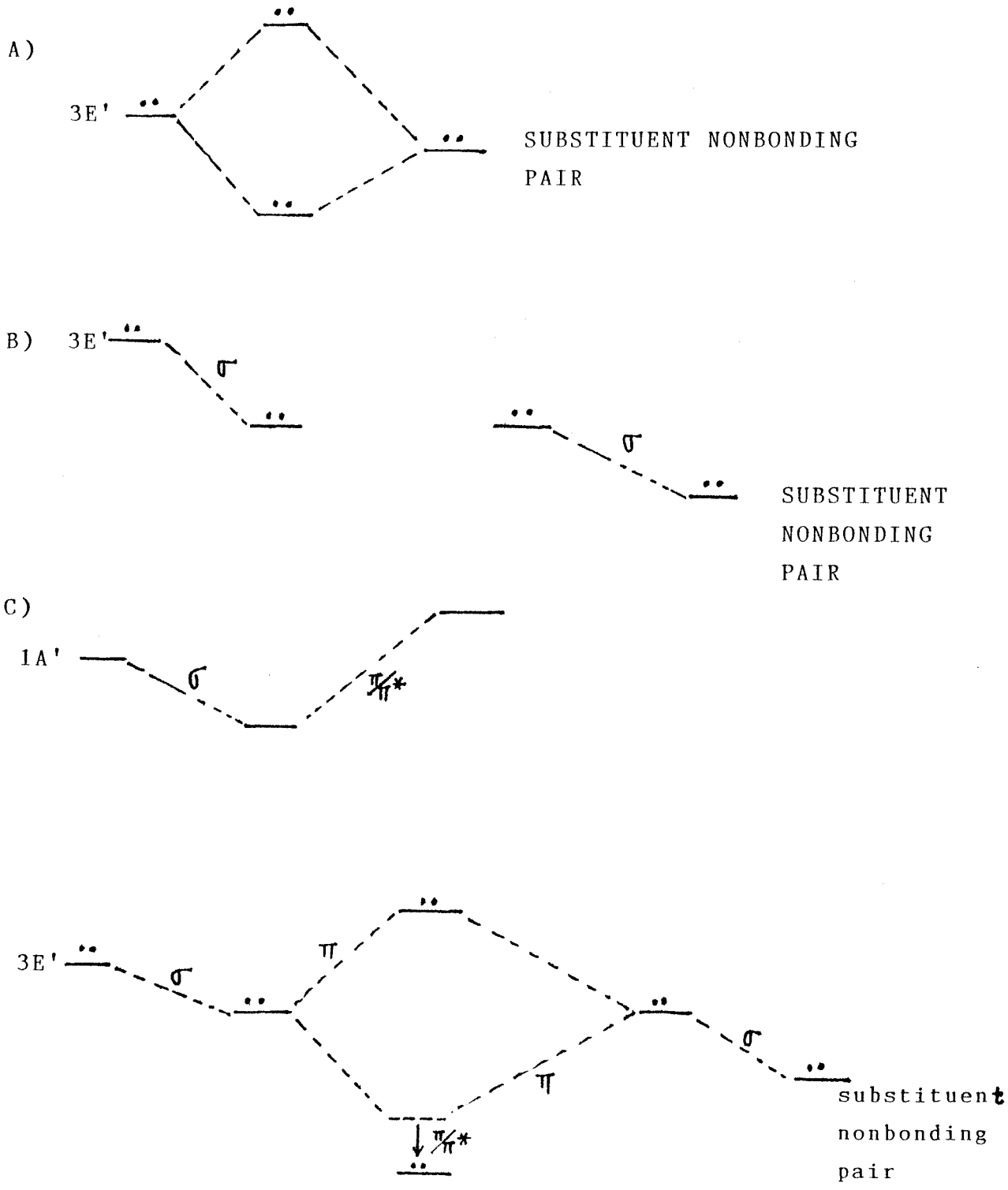


The second component of the substituent electronic effect is the resonance effect. It operates through delocalized ring orbitals. For cyclopropane the MO's involved in the resonance effect are the character orbitals of overall symmetry, 3e′ and 1a′. [16][22][23] (Fig. 2-1)

Dill, et al. have discussed the effects of a pi-electron donating substituent on a pi-system. The pi-donor (e.g., F, OH, NH_2) normally has lone pairs of electrons in proper orientations to interact with the pi-systems. For example [16], the interaction between cyclopropane and a halogen is depicted in figure 2-4a. The halogen nonbonding pair and cyclopropane's pi-type pair interact to form a bonding and an antibonding orbital. For this example, the bonding pair is largely localized on the substituent, therefore stabilizing these electrons, while the antibonding pair is largely made up of the ring pi-type electrons, thereby destabilizing this orbital. This would have the effect of increasing ring strain. [12][24] Superimposed on this would be the substituent's electronegativity effect which, if electron withdrawing, would work against the resonance effect (Fig. 2-4b). [24] It depends on the individual substituent if the resonance effect is outweighed by the electronegativity effect. Furthermore, there is the most important interaction, that of the substituent pi-electrons and the framework $LUMO$, or low-lying π^* type molecular orbital. Figure 2-4c [24] provides an example of the final ordering of orbitals for the case of a typical pi-donating substituent. The main consideration of stabilization in this system is the lowering in energy of the substituent nonbonding pair, which could not occur in bonding to an acyclic species. It is the interaction that builds up exocyclic bonding. Notice that in this case the ring and orbitals are slightly lowered in energy due to the substituent's electronegativity, but the resonance interaction causes an overall destabilization of the pi orbital. We should know that: a substituent's stabilizing or destabilizing ef-

fects cannot be determined from the overall MO diagram of Figure 2-4c, because one must compare this to the substituent effect on an acyclic model, and also because the field effect is not included. The overall MO ordering in a substituted ring is due to electronegativity and resonance effects. In conclusion, pi electron donation has a stabilizing effect due to the favorable interaction between the electrons of the substituent and the $LUMO$ of the strained ring. Cyclopropyl and cyclopropenyl systems should have the same interactions for the Walsh orbitals.

Figure 2-4 The interaction between cyclopropane and halogen.

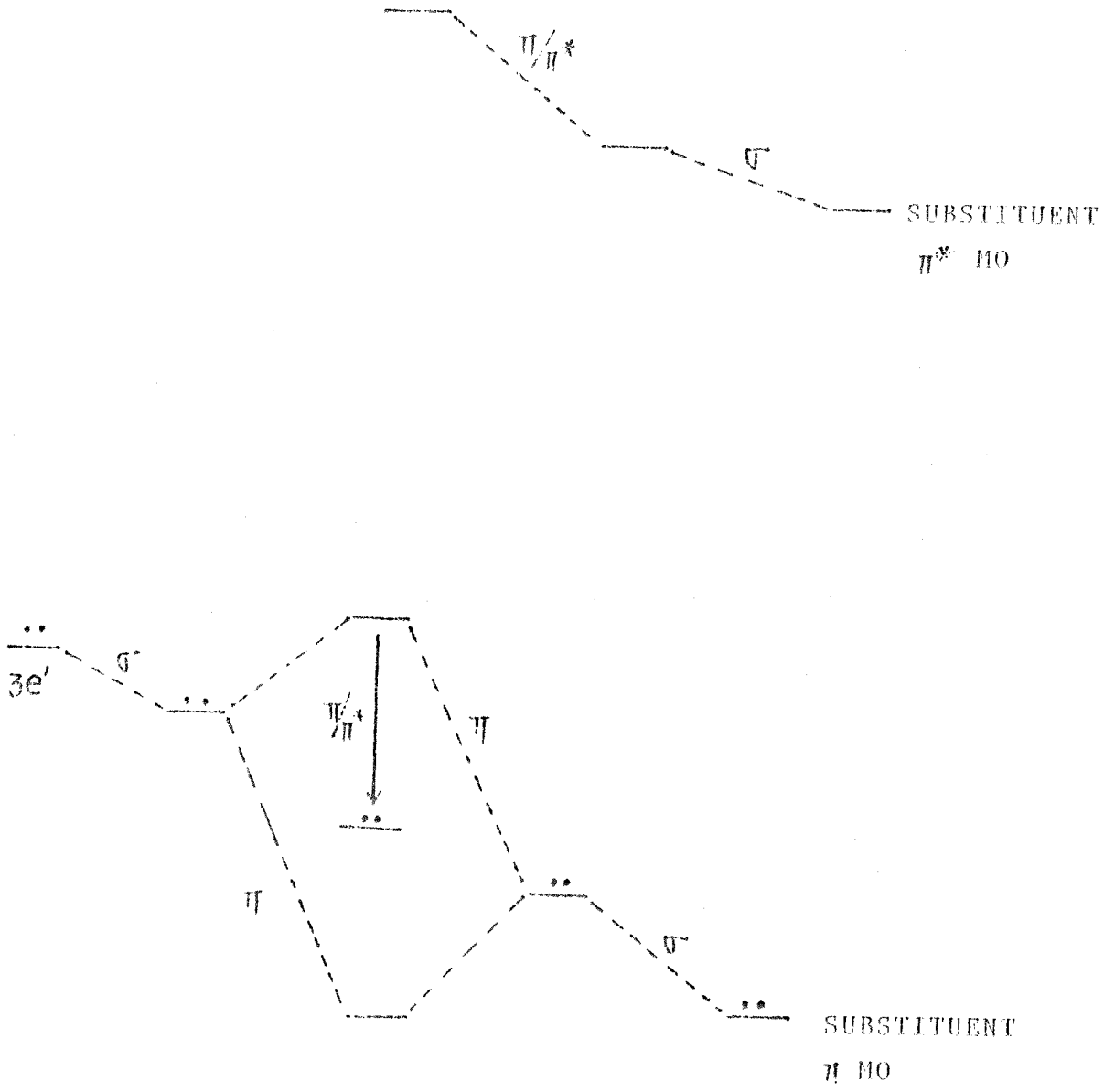


Pi electron accepting substituents also have a stabilizing mechanism (Fig 2-5). Like pi-acceptors, pi-donors have similar electronegativity effects, and similar resonance effects between the two filled pi-type MO's. Also like pi-donors, the most important stabilizing interaction here is between the ring $HOMO$ and substituent $LUMO$, Figure 2-5 [16] shows an example of a complete MO diagram for cyclopropane and a pi-accepting substituent. The stabilization for this example comes from the lowering of the substituent's and the substrate's pi-electrons. However, the MO diagram will depend on the individual substituent. For this case, the ring strain will generally be reduced, unless the interaction between the two filled MO's is strong enough to destabilize the ring pi type electron. [24]

In conclusion, the strained ring substituted system is stabilized relative to the unstrained acyclic-substituted system if the substituent is a donor or acceptor, ignoring the overall electrostatic effect.

It is one of the purposes of this thesis to find whether crrelation analysis provides insights into the nature of the substituent interaction in 3-substituted cyclopropenes.

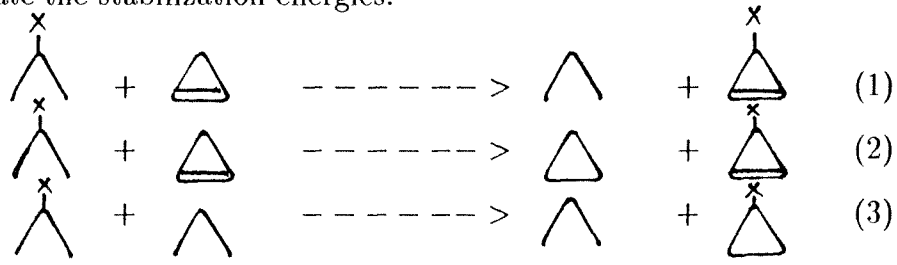
Figure 2-5 An example of a complete *MO* diagram for cyclopropane and a pi-accepting substituent.



Chapter 3

STABILIZATION ENERGY

The relative effect of substituents on the stabilities of the cyclopropyl-x, 3-cyclopropenyl-x and isopropyl-x can be asse- ssed by using the homodesmotic equations 1, 2, and 3 to calculate the stabilization energies.



$X = F, CH_3, CN, OH, NH_2, NH_3^+, NC, O^-$

EQ.(1) - EQ.(3) = EQ.(2)

The calculation of stabilization energies relates to the calculation of strain energies. Thus, we should talk about the concept of ring strain.

Rings smaller than cyclohexane have inherent angle strain, and are therefore less stable thermodynamically than cyclohexane, although still quite stable. It is recognized that the reason for this strain is the fact that the $C - C - C$ bond angles are forced to be less than the idealized tetrahedral angles of 109.47 degree for $sp3$ -hybridized carbon. In cyclopropane, the smallest ring, the intra-ring bond angles are 60 degrees, thereby introducing considerable strain.

The concept of strain can be examined through examination of the types of molecular orbitals occupied relative to those occupied by unstrained species. (see Fig.2-1) Observing the compu- tergenerated molecular orbital pictures of cyclopropane, there are two occupied degenerate "pi-type" molecular orbitals, as compared to the more strongly bonding type orbitals of propane. The small angles, are the reason for the ring strain because they cause the high-energy pi-type MO's to form.

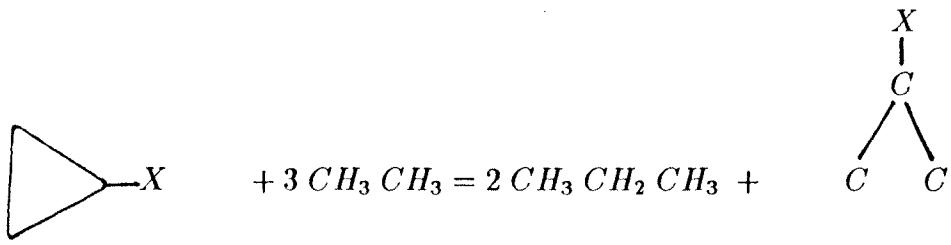
A method of calculating strain energies was described by Dill et al and this was modeled on the work of George et al using the homodesmotic reaction, or what Dill et al., call a " group separation reaction ". This type of reaction is a special case of the isodesmic reaction, defined by Hehre, et al. Hehre et al, proposed the overall hydrogenation should be considered as a two- step reaction: step (a) consisting of bond separation, and step (b) full hydrogenation of the reaction products. The bond separation was attributed to the matching of the bonds in reactant and product species according to their formal type (single, double, or triple), resulting in a more complete cancellation of effects aris- ing from electron correlation and use of a limited size basis set. Such reactions were termed "isodesmic". To distinguish this special subclass of reactions, George introduced the term "homodesmotic", is the sole criterion for an isodesmic reaction. An isodesmic reaction is one in which there is a retention of a number of bonds of a given formal type while changing their relation to one another. Hehre calls the resulting energy the " bond separation energy", such as : The isodesmic equation for the bond separation of cyclopropane.

$$+ 3\ CH_4 = 3\ CH_3\ CH_3 \tag{3.1}$$

The homodesmotic equation for the strain energy of cyclopropane.

$$+ 3\ CH_3\ CH_3 = 3\ CH_3\ CH_2\ CH_3 \tag{3.2}$$

For example, the strain energy of a substituted cyclopropane is shown below :

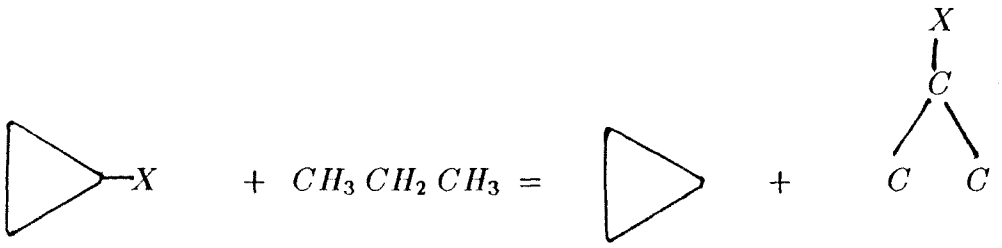


(3.3)

$$\Delta E = \Delta E \text{ (strain)}$$

If a substituent is introduced to the strained ring, it can be characterized by two unsubstituted and one substituted secondary carbon (cyclopropane).

The overall stabilization energy is substracted from reaction 3-d, such as :



(3.4)

The above equation indicates that in switching the substituent from a cyclic to an acyclic species, the endothermicity of this equation gives the stabilization energy of the substituted ring relative to the substituted isopropyl case.

Ab initio molecular orbital calculations were performed by using the Gaussian 82 and Gaussian 86 programs, at the 3-21G optrimized basis set. [29]

RESULTS:

The data in Table 3-1, Table 3-2, and Table 3-3 indicate the total energies (hartrees) of substituted 3-cyclopropenyl-x, cyclopropyl-x, and isopropyl-x.

Table 3-1.

Total Energies Calculated ΔE (Hartress) for Substituted 3-Cyclopropenyl-x

X substituent	STO-3G energies	3-21g//3-21g energies
H	-114.4011573	-115.1620050
F	-211.8610967	-213.4873291
CH_3	-152.9848602	-153.9842299
CN	-204.9535784	-206.3838416
OH	-188.2390840	-189.6013335
NH_2	-168.7181839	-169.8777115
NH_3^+		-170.2651815
NC		-206.3430579
O^-		-188.9505481

Table 3-2.

Total Energies (Hartress) for Substituted Cyclopropenyl-x

X substituent	3-21g//3-21g energies
H	-116.4012062
F	-214.7157280
CH_3	-155.2231844
CN	-207.6223412
OH	-190.8295848
NH_2	-171.1167074
NH_3^+	-171.4916463
NC	-207.5891537
O^-	-190.1748024

Table 3-3.

Total Energies (Hartress) for Substituted isopropyl-x

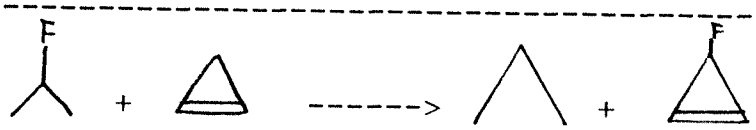
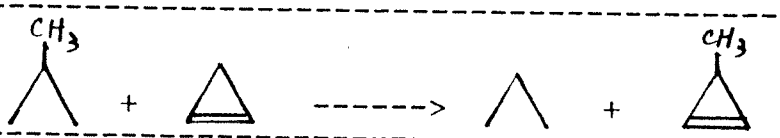
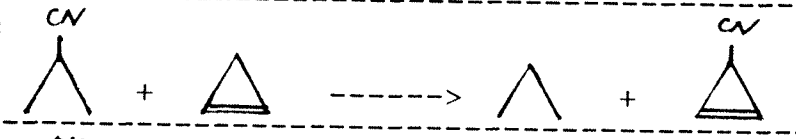
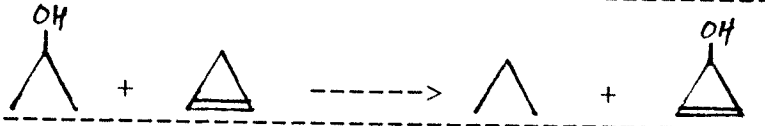
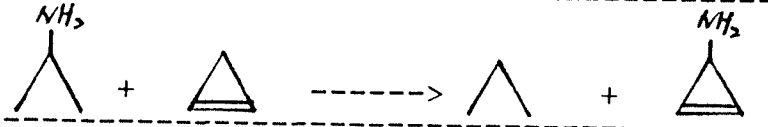
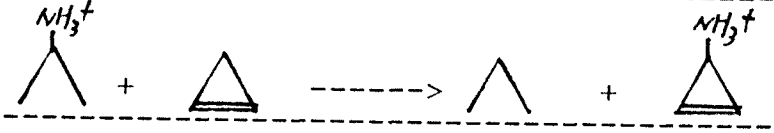
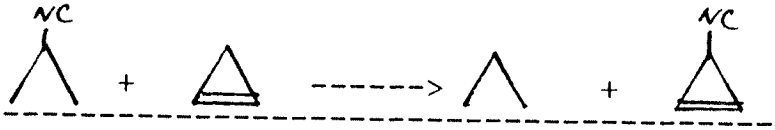
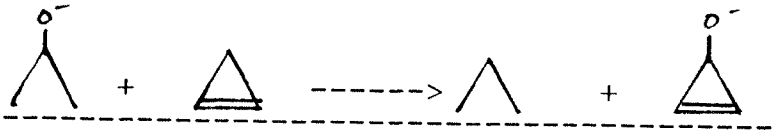
X substituent	3-21g//3-21g energies
H	-117.6133009
F	-215.9361379
CH_3	-156.4344710
CN	-208.8299883
OH	-192.0472748
NH_2	-172.3209555
NH_3^+	-172.7113443
NC	-208.8042020
O^-	-191.3845748

Table 3-4 lists homodesmotic stabilization energies calculated at the 3-21G//3-21G level for 3-substituted cyclopropenes. A negative energy value means that the substituted cyclopropene is favored versus the isopropyl case.

Table 3-5, ΔE refers to the stabilization energy calculated at the 3-21G//3-21G level for 3-cyclopropenyl-x versus cyclopropyl-x. A negative value means that 3-cyclopropenyl is more stabilized.

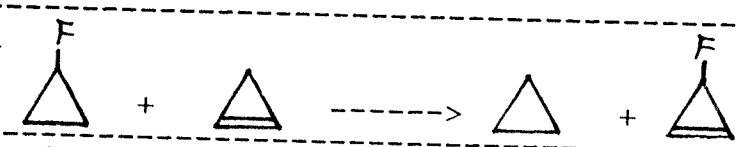
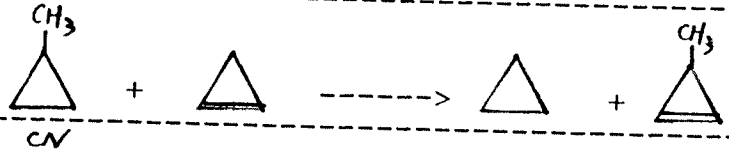
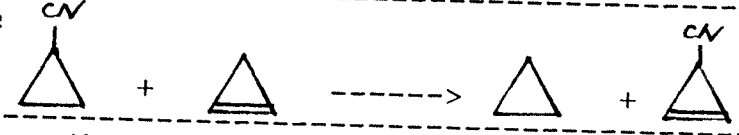
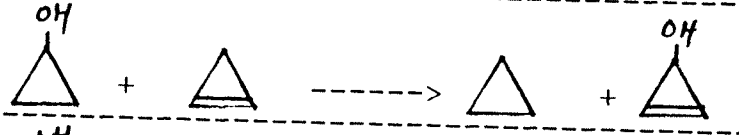
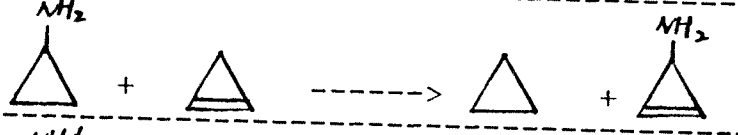
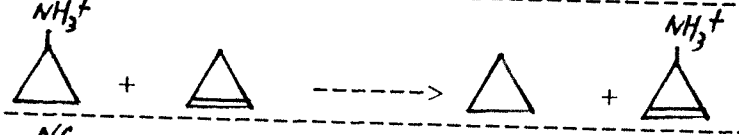
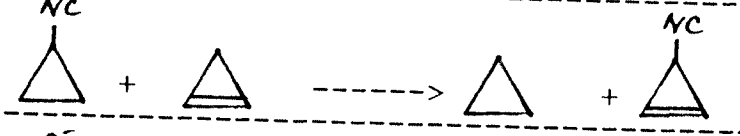
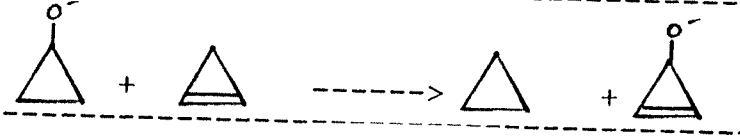
Table 3-6, E refers to the stabilization energy calculated at the 3-21G//3-21G level. A negative value means that cyclopropyl-x is more stable than isopropyl-x.

TABLE 3-4.Use of Isodesmic Reactions, the ability of 3-21G basis set data to calculate the stabilization energy: $\Delta E = \Delta E_{stab}$

Reaction	ΔE (Kcal/mol) a
	3-21G
1-a 	-1.6
1-b 	-0.7
1-c 	-3.2
1-d 	-3.4
1-e 	-5.1
1-f 	-3.2
1-g 	6.2
1-h 	-10.8

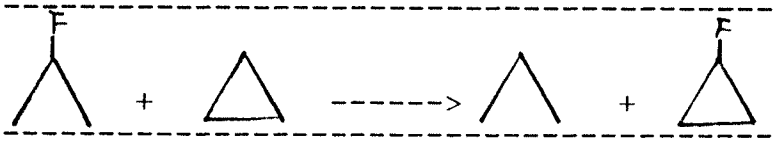
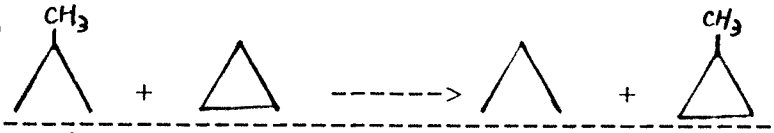
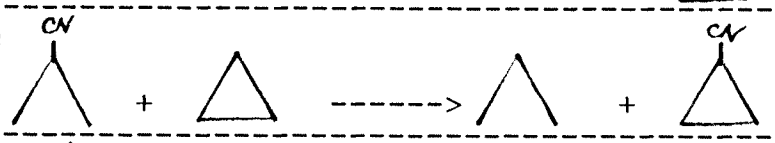
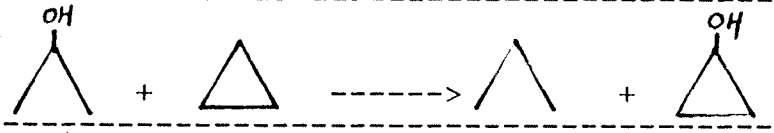
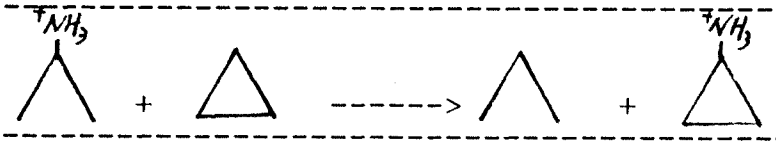
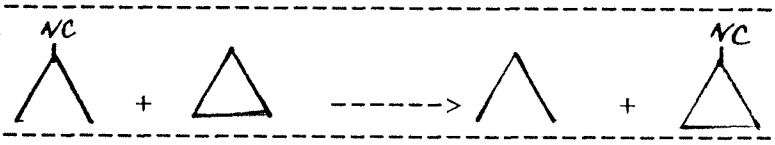
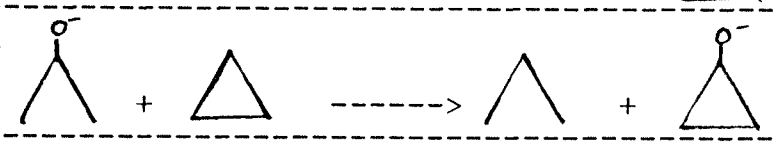
a. ΔE calculated energy (hartree) can be changed to Kcal/mol by multiplying by 627.73 kcal/mol.hartree.

TABLE 3-5. Use of Isodesmic Reactions, the ability of 3-21G basis set data to calculate the stabilization energy: $\Delta E = \Delta E_{stab}$

Reaction	E (Kcal/mol) a
	3-21G
2-a 	-6.8
2-b 	-0.2
2-c 	-0.4
2-d 	-6.9
2-e 	-0.1
2-f 	-8.0
2-g 	4.3
2-h 	-9.4

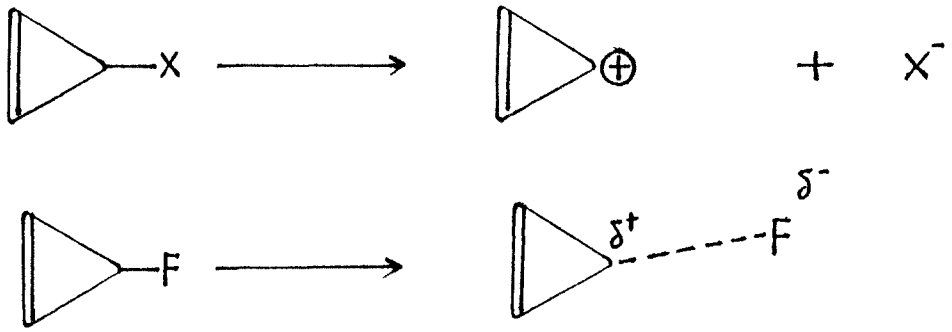
a. ΔE calculated energy (hartree) can be changed to Kcal/mol by multiplying by 627.73 kcal/mol.hartree.

TABLE 3-6. Use of Isodesmic Reactions, the ability of 3-21G basis set data to calculate the stabilization energy: $\Delta E = \Delta E_{stab}$

	Reaction	E (Kcal/mol)[a] 3-21G
3-a		5.2
3-b		-0.5
3-c		-2.8
3-d		3.5
3-e		-4.9
3-f		4.8
3-g		1.9
3-h		-1.5

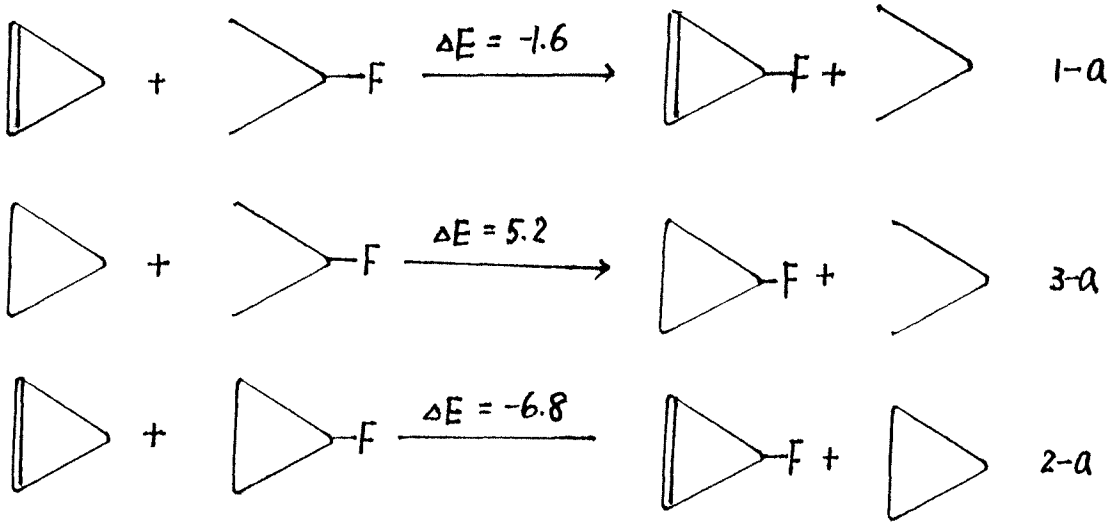
a. ΔE calculated energy (hartree) can be changed to Kcal/mol by multiplying by 627.73 kcal/mol.hartree.

In table 3-5. the relative effect of substituents on the stabilities of the cyclopropyl-x and 3-cyclopropenyl-x can be ass- essed by using EQ. 2 (see table). The greatest stabilizations of 3-cyclopropenyl-x occur for $X = O^-, NH_3^+, OH$ and F. There are especially electronegative substituents, with O^- showing some back donation.



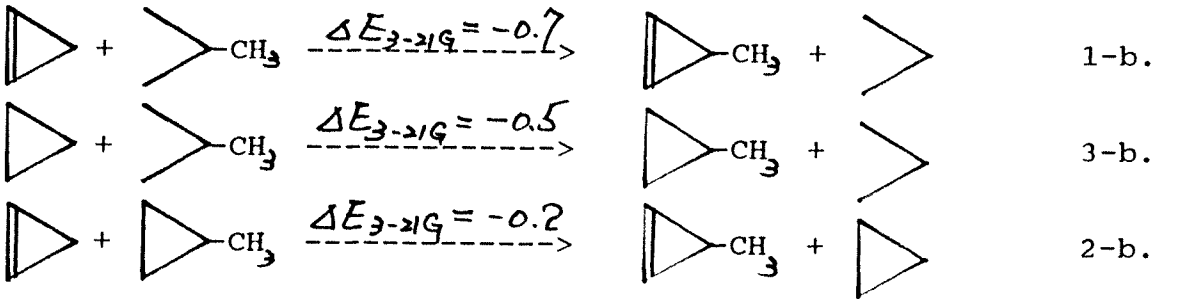
In the limiting extreme case 1 sigma-withdrawal may mimic an ionic bond. The resulting carbocation center should have some aromatic character, possibly stabilizing these molecules. In contrast, the NC substituent is destabilized in the cyclopropene system compared to cyclopropyl.

The reaction series 1-a, 2-a and 3-a is instructive.

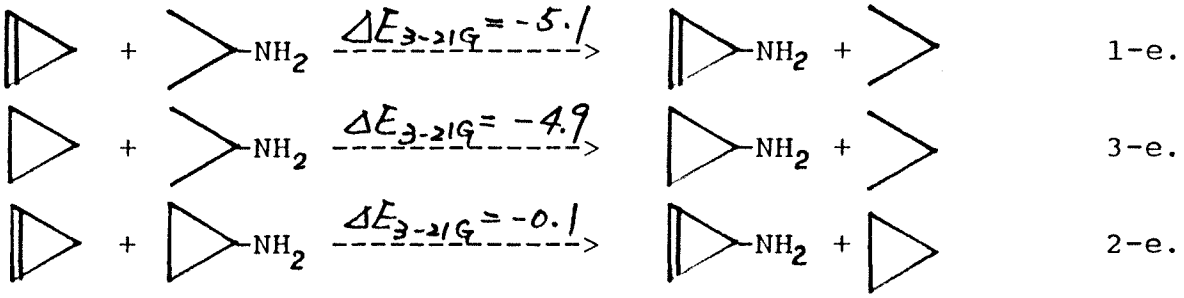


Here it is seen that stabilization occurs in 3-flurocyclo- propene, but destablization occurs in fluorocyclopropane. Fluoro is strongly electronegative and a weak pi-electron donor. Similar conditions apply to the hydroxy($-OH$) and $-NH_3^+$ substituents.

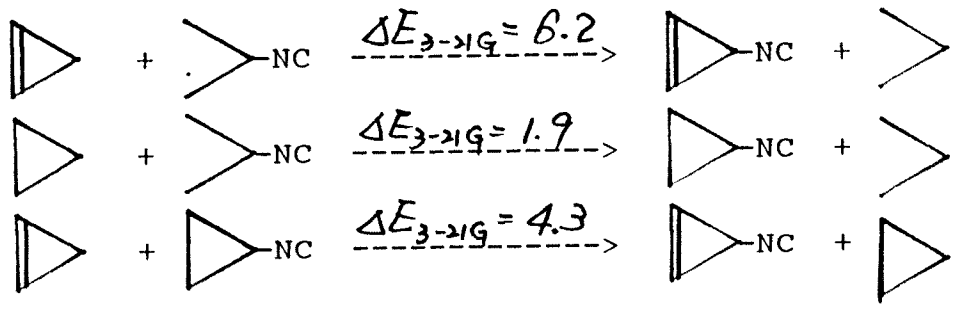
A fluorine substituent in a cyclopropyl moiety does not act as pi- donor but predominantly as sigma-acceptor. The destabilization of fluorocyclopropane can be explained on this basis. [34]



For the methyl series it is seen that stabilization occurs in 3-methylcyclopropene and methylcyclopropane. The methyl group is an electron donor and has a slight stabilizing ability.



For the amino series it is seen that a slightly greater stabilization occurs in eq 1e and 3e. This is probably an indication that 3-aminocyclopropene and aminocyclopropane have greater stabilization energies than aminoisopropane.

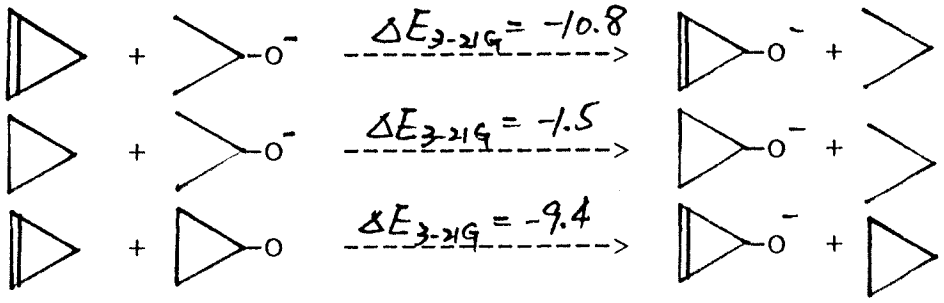


1-g.

3-g.

2-g.

The oxide anion which has very high-energy occupied orbitals, is a good electron donor group, which is stabilizing in cyclopropane and cyclopropene. Similar conditions apply to the cyano ($-CN$) substituent, which is an electron acceptor and the stabilizing ability is less than oxide anion substituent.



1-h.

3-h.

2-h.

The $-NC$ substituent is the only one which destabilizes all the reactions in eq 1-g, 2-g and 3-g. $-NC$ is an electron acceptor and the total energies of substituted compounds are also similar to cyano substituted compounds.

From Table 3-4 and 3-5, the substituted cyclopropenes are favored versus the isopropyl and cyclopropyl cases. The oxide anion substituent has the strongest ability for stabilization.

In all the series, the order of stabilization in Table 3-4 is $O^- > NH_3^+ > OH > NH_2(CN) > F > CH_3 >> NC$. The order in Table 3-5 is $O^- > NH_3^+ > OH > F > CN > CH_3 > NH_2 >> NC$. Here it is seen that 3-cyclopropenyl-x stabilizations occur in eq 1 and 2 for all substituents, except $-NC$ substituent which destabilized all the reactions. From the above equations the following order is seen: O^-, OH, F and CN are strong substituents inducing strong stabilization energies and $-CH_3$ is a weak substituent inducing a slight stabilization energy. Clearly, cyclopropenes have almost no ability to stabilize attached carbon centers. All substituents, except $-NC$, will stabilize the ring.

From Table 3-6, cyclopropyl is a poor pi-acceptor and thus shows little conjugation with pi-donor substituents. For example, the lowest energy conformer of cyclopropylamine does not have suitable geometry for conjugation between the ring and the amino substituent. [35] It is consistent with the observation that cyclopropanes have almost no ability to stabilize attached carbon centers. [36][37] F has no significant conjugation with ring and that only strong pi-donors such as O^- and NH_2 may stabilize the ring very well, but sigma-acceptor groups destabilize the ring.

Chapter 4

SUBSTITUENT EFFECT IN GEOMETRY

In a study of molecular structure, Allen [38][39] concluded on the basis of C-substituent bond lengths that cyclopropyl is about 70% as effective a conjugating group as vinyl with pi-acceptor substituents. Durmaz and Kollmar concluded, also on the basis of molecular structure trends, that cyclopropyl has negligible resonance interactions with pi-donor substituents. It is interesting to see these predictions compared with those of 3-cyclopropenyl-x, isopropyl-x and cyclopropyl-x groups [34].

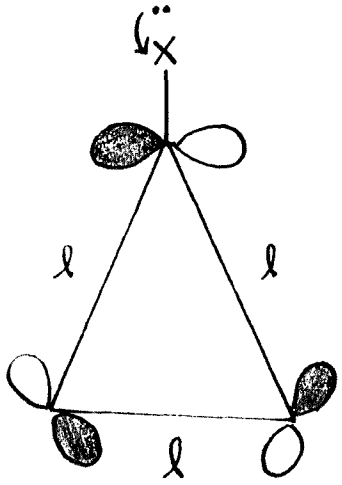
Comparison of the structure of cyclopropene with those of the 3-cyclopropenyl-x shows that substituents which are electron donors such as $-F, -NH_2, -OH, -CH_3$ and $-O^-$ decrease the vicinal $C-C$ bond length and increase the distal $C-C$ bond length, but the O^- which increases both the vicinal and distal bond length. The order of the difference between the electron donor and cyclopropene in vicinal bond length is $F > OH > NH_2 > CH_3$, but in distal bond length the order is $O^- > F > CH_3 > NH_2$. The result of cyclopropyl-x [34] is similar to that of 3-cyclopropenyl-x.

Now, we compare the substituents which are electron acceptors such as NH_3^+ , NC, CN with each other. The NH_3^+ substituent decreases the distal bond length but

increases the vicinal bond length. The substituent, $-CN, -NC$ increases the vicinal bond length but decreases the distal bond length (see Table 4-1).

Ideally during inversion at a carbon center in cyclopropane, the bond angle increases from tetrahedral ($109°28'$) to trigonal. ($120°$) However, in the inversion of the cyclopropyl-x the decreased angle is around ($0.02° \sim 5.69°$), except $-CH_3 and - NH$ substituents which increase the bond angle comparing to the cyclopropane ($114.85°$). The smallest internal bond angle is in the hydroxy group ($109.16°$), which is similar to a carbon center which is tetrahedral ($109.25°$). The increase in CCC angle is accompanied by a slightly increasing the distal bond length.

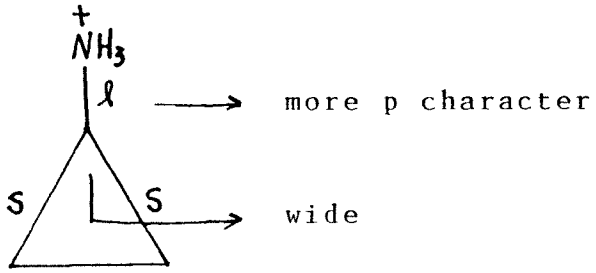
The exception of the oxide anion substituent is shown : The oxide anion is an electron donor but cyclopropane is a strong pi-donor and a weak pi-acceptor, so it induced both the vicinal and distal bond lengthening.(see scheme 1)



From Bent's rule :

$$-C - - - - X$$

If X has very strong electronegativity, the $C - X$ bond has high p-character and increases the $C-X$ bond length. For example, the substituent, NH_3^+ , will enlarge the CCC angle and lengthening the distal bond length.(see scheme 2) From calculations the cyclopropene system is fit but cyclopropane is not. (see Table 4-1, 4-2)



From pi effect in cyclopropyl-x, if the substituent cyano is electron-acceptor, it will decrease the bonding orbital and make the vicinal bond longer, but will decrease the antibonding orbital then make the distal bond length shorter.(see scheme 3)

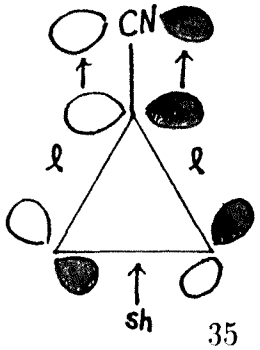
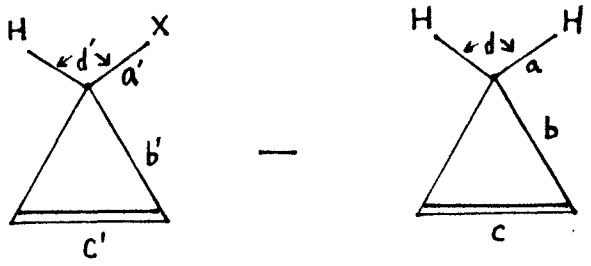
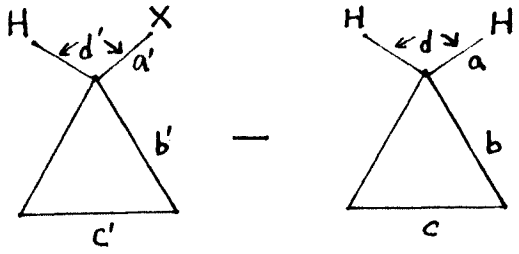


Table 4-1 3-Cyclopropenyl-x, Bond lengths and Angles Comparison of the difference bond length, bond angle with their parent molecules, is shown below: (see scheme 4)



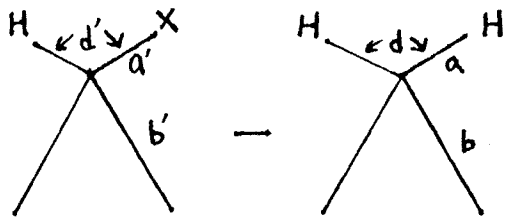
X substituent	(a) c-x	(b) vicinal	(c) distal	(d) angle
F	0.2954	-0.0429	0.0112	-5.15
NH_3^+	0.4606	-0.0380	0.0076	-6.25
CH_3	0.4203	-0.0018	0.0023	0.06
NC	0.3140	0.0017	-0.0133	-0.77
CN	0.3380	0.0032	-0.0041	0.15
NH_2	0.3469	-0.0096	0.0001	2.51
OH	0.3195	-0.0252	0.0139	-6.74
O^-	0.1904	0.0857	0.02591	4.73

Table 4-2 Cyclopropyl-x, Bond lengths and Angles Comparison of the difference bond length, bond angle with their parent molecules, is shown below: (see scheme 5)



X substituent	(a) c-x	(b) vicinal	(c) distal	(d) angle
F	0.309	-0.0213	0.0100	-1.29
NH_3^+	0.445	-0.0090	-0.0009	-4.05
CH_3	0.4421	-0.0001	0.0045	0.12
NC	0.3319	-0.0031	0.0006	-1.4
CN	0.3574	0.0093	-0.0096	-0.02
NH_2	0.371	-0.0051	0.0012	4.05
OH	0.3428	-0.012	0.0161	-5.69
O^-	0.2644	0.0376	0.0328	-1.15

Table 4-3 Isopropyl-x, Bond lengths and Angles Comparison of the difference bond length, bond angle with their parent molecules, is shown below: (see scheme 6)

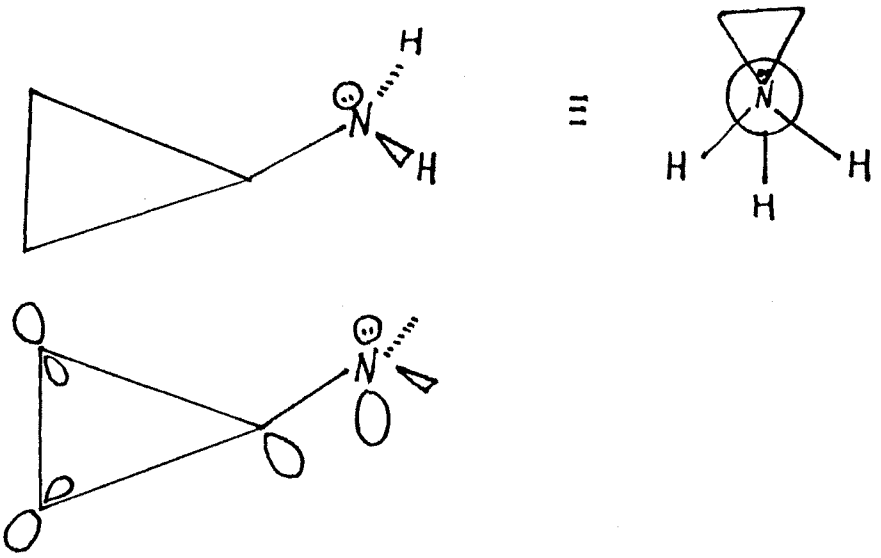


X substituent	(a) c-x	(b) vicinal	(d) angle
F	0.3305	-0.0182	0.1
NH_3^+	0.4597	-0.0045	0.58
CH_3	0.4550	-0.0001	1.38
NC	0.3524	-0.0009	1.24
CN	0.4324	-0.0226	1.41
NH_2	0.3966	-0.0053	5.67
OH	0.3580	-0.0158	4.14
O^-	0.2601	0.0383	9.63

Aminocyclopropane is an interesting molecule that may well merit structural reinvestigation. Its conformation is one in which the amino group is pyramidal and the HNH angle is bisected by the molecules' plane of symmetry. Although the stable conformation of aminocyclopropane can be described as a perpendicular conformation having a pyramidal amino group, the possibility for pi conjugation still remains. The mechanism for conjugation in overlap (see scheme 7) between the substituent lone pair orbital and the vacant 4E′ of cyclopropane is said to be the most effective pi-accepting *MO*. Dominant pi donation into this orbital would increase vicinal and decrease distal bond lengths. This is not consistent with calculational results.

Possible conjugation' mechanism in aminocyclopropane.

Scheme 7



The explanations of the effects on ring geometries produced by pi-donor substituents that are all acceptors have been subtle and not altogether convincing. We should consider lots of resons. One way to explain the asymmetry in bond lengths in these pi-donor-substituented cyclopropanes is to invoke hybridization effects. Although Durmaz and Kollmar seem to attempt to separate the acceptor capability

properties of a substituent from effects on hybridization of the attached carbon, it seems impossible to do this in light of Bent's rules.

The cyclopropene ring is primed to interact with substituents. Its very high strain energy (54.5Kcal/mol) can be significantly reduced through interaction with Walsh-type as well as pi orbitals. The $HOMO$ of cyclopropene has particularly large coefficients at C_3, which are well suited for coupling substituents at this position to the pi orbitals.

Some substituents at the 3-position can interact strongly enough with cyclopropenes in the double bond to produce what we may regard as a new entity rather than a perturbed cyclopropene. Cyclopropene has geminal pi-acceptors at C_3 and maintains a shortened distal bond and lengthened vicinal bonds just as in the related cyclopropanes.

All the electron donor substituents decrease the vicinal bond lengths and increase the distal bond length, except that the oxide anion substituent increases both vicinal and distal bond lengths. The order of the difference between electron donor substituents and cyclopropene in the vicinal bond is : $F > OH > NH_2 > CH_3$. A similar comparison is observed in cyclopropane.

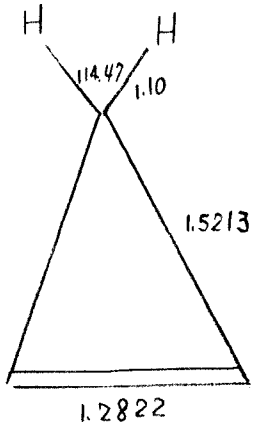
The extreme electronegativity of the NH_3^+ group results in the vicinal bonds being much shorter in vicinal bond length than in the cyclopropene. The order in the distal bond is $O^- > OH > F > CH_3 > NH_2$,which is different from cyclopropyl-x. From the internal angle difference, some decrease but some increase ($-6.7^o \sim 4.7^o$). The smallest decreased angle is in the hydroxy substituent (107.69°) which is accompanied by increasing in the distal bond and decreasing in the vicinal bond. Similar results are shown in cyclopropyl-x (see Table 4-2).

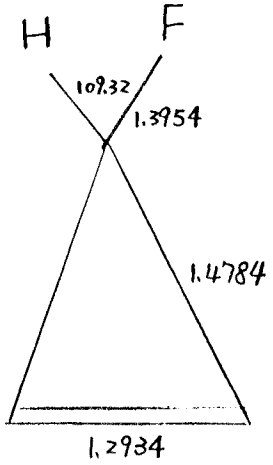
The structure of the cyclopropyl-x (see Fig. 4-2) decreases the vicinal bond length

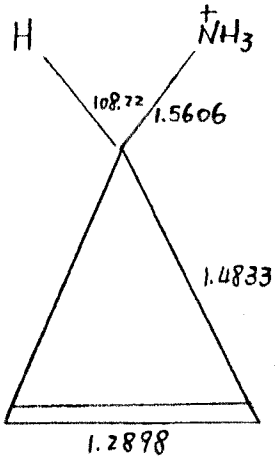
by all substituents, which tend to increase the internal bond angles, except the oxide anion substituent.

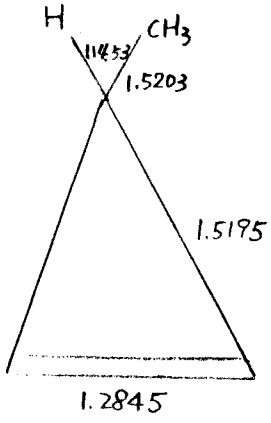
The order of difference of isopropyl in vicinal bond is : $CN > F > OH > NH_2 > NH_3^+ > NC$.

Fig4-1 The structure of Cyclopropenyl-x in (3-21G) level









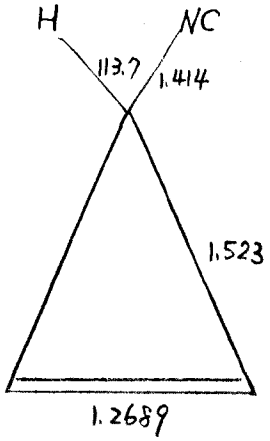
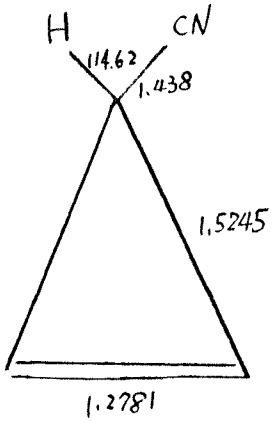
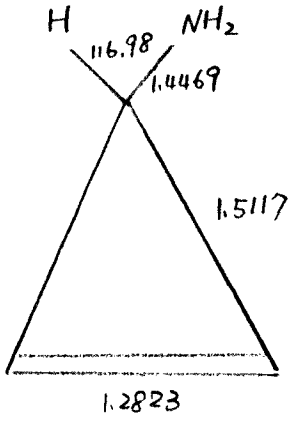
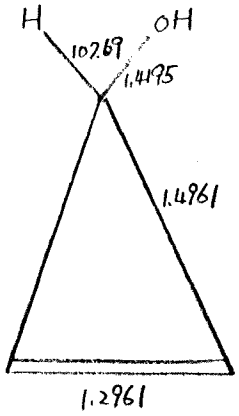
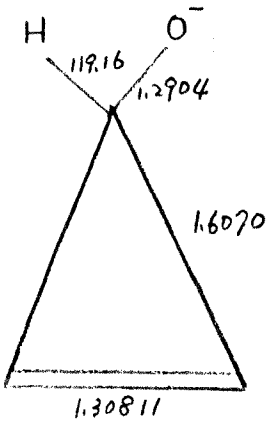


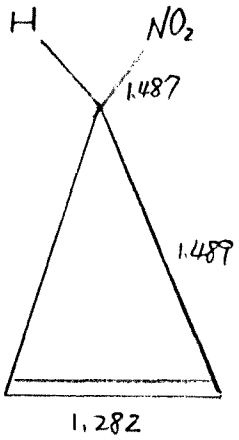
Fig4-1 (continue) The structure of Cyclopropenyl-x in (3-21G) level











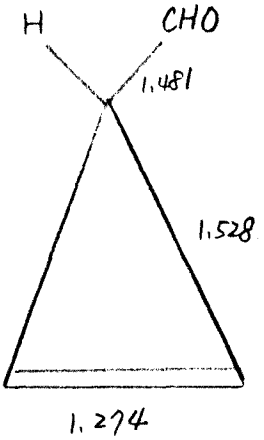
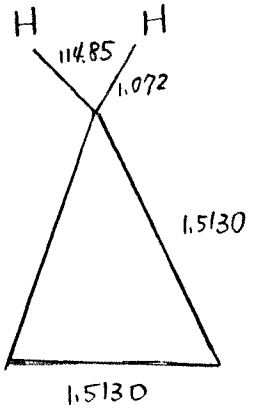
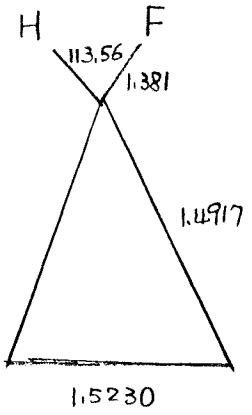
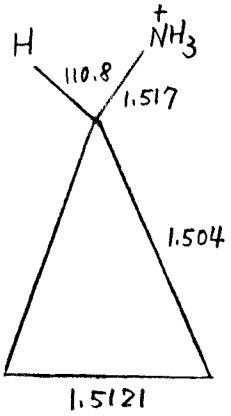
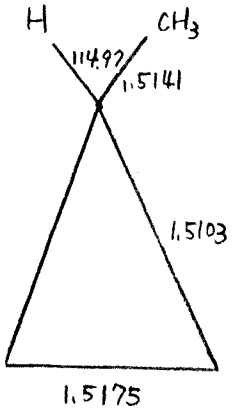


Fig4-2 The structure of Cyclopropyl-x in (3-21G) level









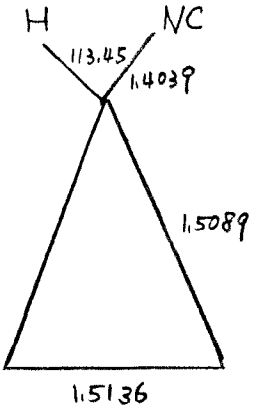
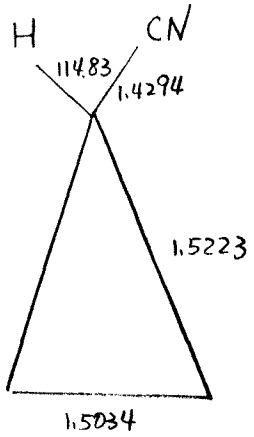
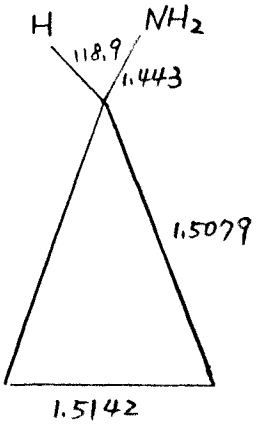
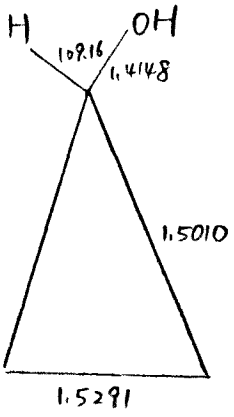
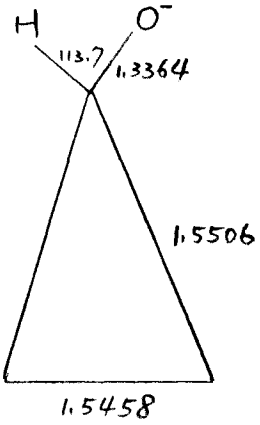


Fig4-2 (continue) The structure of Cyclopropyl-x in (3-21G) level









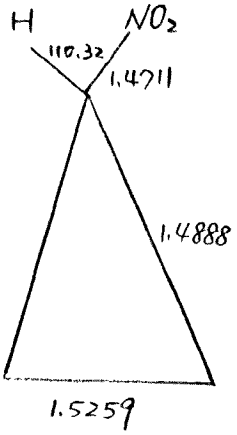
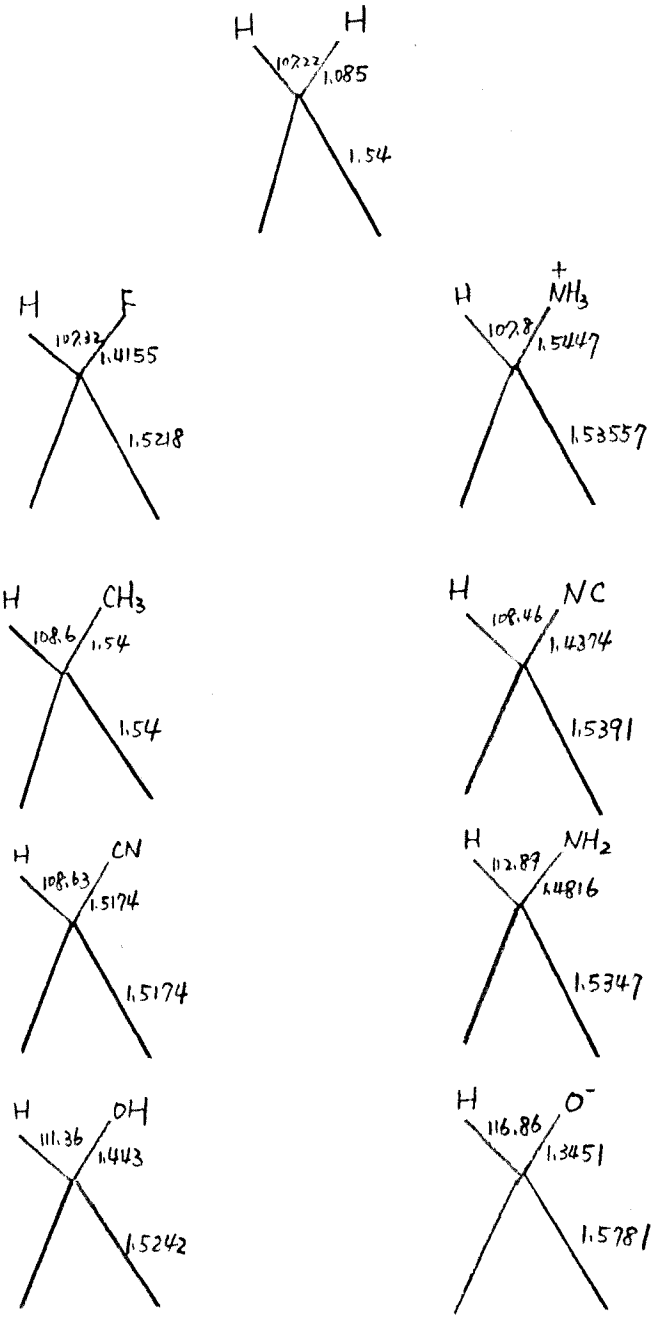


Fig4-3 The structure of Isopropyl-x in (3-21G) level



Chapter 5

FREE ENERGY RELATIONSHIPS AND CONCLUSIONS

5.1 FREE ENERGY RELATIONSHIPS

The Hammett equation is an example of a linear free energy relationship. Equilibrium constants and rate coefficients are related to the Gibbs energy differences by the equations :

$$\log K = -\Delta G^{\theta}/2.3RT \tag{5.1}$$

$$\log k = \log(KbT/h) - \Delta G^{\ddagger}/2.3RT \tag{5.2}$$

$$k = (KbT/h)\exp(-\Delta G^{\ddagger}/RT) \tag{5.3}$$

$$= (KbT/h)\exp(\Delta S^{\ddagger}/R)\exp(-\Delta H^{\ddagger}/RT)$$

Therefore, the Hammett equation can be written :

$$\log(K_X/K_O) = \log K_X - \log k_O = \Delta\Delta G_X/2.3RT = \rho\sigma_X \tag{5.4}$$

σ_X : substituent constant

K : the equilibrium constant

Kb : Boltzman constant

h : Planck's constant

k : the unsubstituted system

σ_X , substituent constants involved in the thesis are Taf's σ_I and σ_R. The substituent constants are also described by Topsom and Charton's σ_X, σ_F and σ_R. A substituent's electronic effect is made up of field, F(through space or dipole), electronegativity, X(through bond polarization or inductive), and resonance effects. The term "inductive effect" is often used to cover both the field and through bond effects, as it is by Charton and Shorter.

In attempting to employ isodesmic stabilization energies or enthalpies to obtain correlations with substituent constants, it is assumed that isodesmic entropies of reaction are negligible and this is true with some readily understandable exceptions. Another point that must be addressed is that both pi-donors and pi-acceptors can cause stabilization. Thus, one must treat them separately or in terms of an analogue of the DSP equation in which there are separate terms for pi-donating and pi-accepting substituents.

The Hammett equation is normally used to correlate free energy changes and not entropy changes. It is assumed that the entropy change for the isodesmic equations employed in the calculation of stabilization energies is negligible. There is very little difference in the resulting entropy from substrate to substituent in the isodesmic equation. Therefore the assumption is : $\Delta H = \Delta G$. By the way, we just consider the gases condition in the isodesmic equation, so $\Delta E = \Delta H = \Delta G$. We used an initio molecular orbital program to calculate the total energy of the molecule.

Taft has used the equation

$$\log K/K_O = \rho_I \sigma_I + \rho_R \sigma_R + \delta \tag{5.5}$$

Where ρ_I and ρ_R are the sensitivity parameters for the inductive and resonance

effects. We substituted the $\log K/K_O$ value by ΔE (assumed $\Delta E = \Delta H = \Delta G$), so σ_I and σ_R are correlated versus ΔE,

$$\Delta E = \Delta H = \Delta G = -2.303RT(\log K/K_O)$$

This type of relationship is known as a linear free energy relationship and has been formalized by Hammett as follows :

$$\Delta E \sim= \log(K/K_O) = \log(K'/K'_O) \tag{5.6}$$

$$= \log(K'/K'_O)$$

$$\log(K/K_O) = \sigma\rho$$

ρ is referred to as the reaction constant. In general, the pi-donating substituents interact through donation of lone pair electrons (F, OH, NH_2). These substituents would have no molecular orbital of π^* type. However, among the pi-accepting substituents, there are many with pi systems that would have such an orbital (CHO, CN, NC). It might be suggested then that a possible reason for the failure of correlations with pi-accepting substituents is because such substituents would have another interaction with the ring, that is, the π^* MO of the substituent with the pi orbital of the strained system.

Table 5-1 lists correlations of cyclopropyl, cyclopropenyl and isopropyl stabilization energies, respectively, using the Taft DSP approach.

Figure 5-1,2,3,4,5,6 shows the plot of the relationship between : ΔE (stabilized energy) of the substituents molecules vs. (σ_I and σ_R).

A number of points are apparent: (a) correlations of pi donors appear to be considerably better than correlations of pi-acceptors; (b) cyclopropane's behavior is much more sensitive to σ_I than to σ_R (see Table 5-2, 5-5); (c) [41] From the tables, the resonance stabilization is fairly independent of the model chosen (cyclopropyl, cyclopropenyl, isopropyl). However, the inductive effect (destabilizing for the majority

of substituents examined which are sigma-withdrawers) is highly dependent on the model compound. Thus, sigma-withdrawal is most destabilizing when isopropyl is the model; (d) for pi-acceptor substituents, conjugation plays a significant and perhaps dominant role (in cyclopropyl-x system).

5.2 CONCLUSION

In conclusion, the substituent effect induces stabilization energies, so 3-cyclopropenyl-X is more stable than cyclopropyl-X and isopropyl-X compounds. The $-F, -NH_3^+$ and $-O^-$ substituents have the largest stabilization energies in the cyclopropene ring. They induce a carbocation center which should have some aromatic character thus stabilizing the ring.

From the free energy relationship results, some substituents have good correlation between the stabilization energy and substituent parameter, such as the Table 5-2 and 5-7 have a good linear relationship, thus when the substituent is introduced, the perturbation of the relative energy could be obtained from the plot.

For some reactions the plot of $\log(K/K_O)$ failed to give a good relationship. This implies a breakdown in one or other of Hammett's fundamental postulates ; either is being influenced by the substituent or by the reaction. We did most of the free energy relationships of stabilization energies, TDS parameters, however did not have the good correlation.

Table 5-1 The relationship between ΔE_{stab} and substitutent constants. (σ_I and σ_R). Values from M. Chaston, Prog. Phys. Org. Chem. R. W. Taft(ed), Vol. 13, Wiley, 1981, pp.119-251.

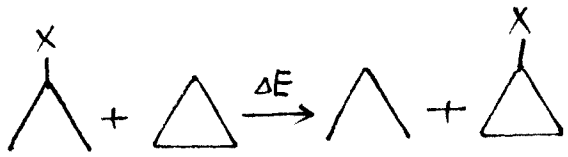
a: O. Exner in Correlation Analysis in Chemistry: Recent Advances, N. B. Chapmon and J. Shorter(eds) Plenun, New York, 1978, pp. 439-540.

X substituent	σ_I	σ_R			
H	0	0	0	0	0
F	0.54	-0.48	5.2	-1.6	-6.8
CH_3	-0.01	-0.16	-0.5	-0.7	-0.2
CN	0.57	0.08	-2.8	-3.2	-0.4
OH	0.24	-0.62	3.5	-3.4	-6.9
NH_2	0.17	-0.8	-4.9	-5.1	-0.1
NH_3^+	1.07	-0.11	4.8	-3.2	-8.0
NC	0.63	0.02^{a}	1.9	6.2	4.3
O^-	-0.16^{a}	-0.6^{a}	-1.5	-10.8	-9.4

Table 5-2 Table of Stabilization Energy and Substituent Constant values in Cyclopropyl-x system.

Point	X (σ_I)	Y (ΔE)
1	-0.16	-1.5
2	-0.01	-0.5
3	0	0
4	0.17	-4.9
5	0.24	3.5
6	0.54	5.2
7	0.57	-2.8
8	0.63	1.9
9	1.07	4.8

Slope = 4.742006 ± 2.820264
Intercept = -0.9736798 ± 3.136572
Correlation = 0.5363633
Calculated on points 1 to 9



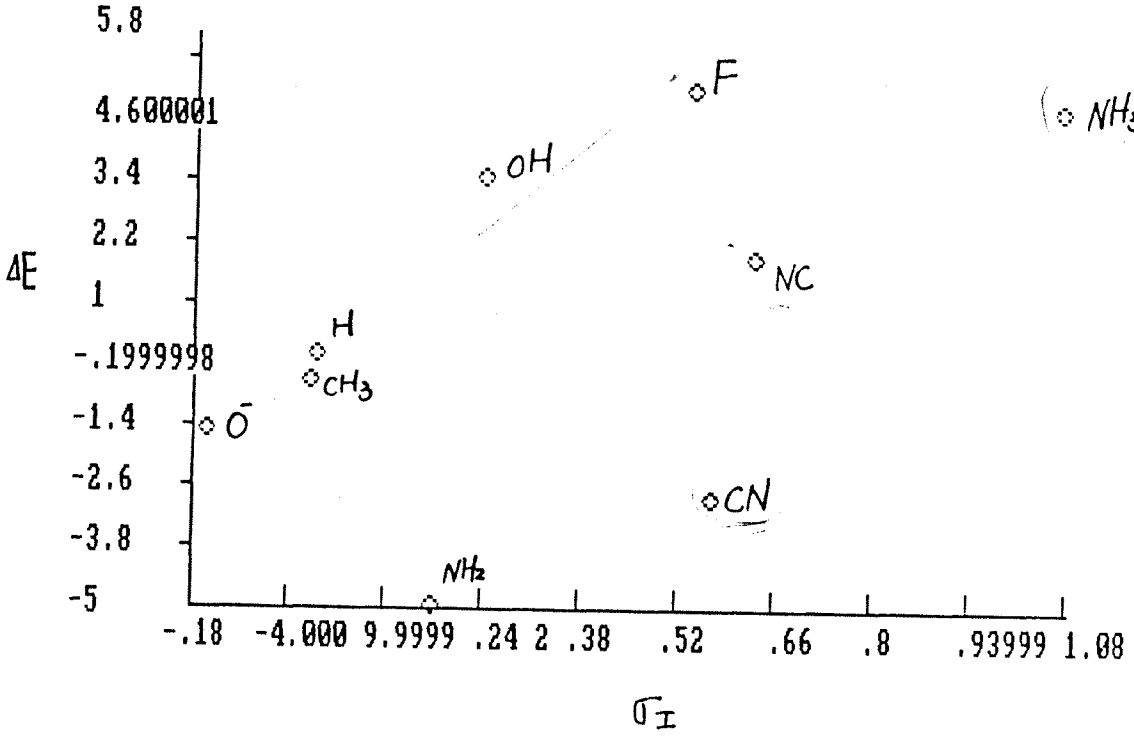
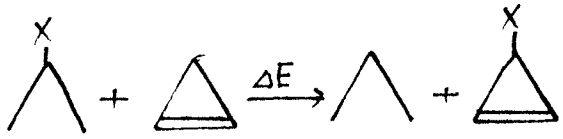


Fig 5-1 The plot between stabilization energy and substituent constant

Table 5-3 List of Stabilization Energy and Substituent Constant values

Point	X (σ_I)	Y (ΔE)
1	-0.16	-10.8
2	-0.01	-0.7
3	0	0
4	0.17	-5.1
5	0.24	-3.4
6	0.54	-1.6
7	0.57	-3.2
8	0.63	6.2
9	1.07	-3.2

Slope = 4.231406 ± 4.03876
Intercept = -3.856199 ± 4.491728
Correlation = 0.3681768
Calculated on points 1 to 9



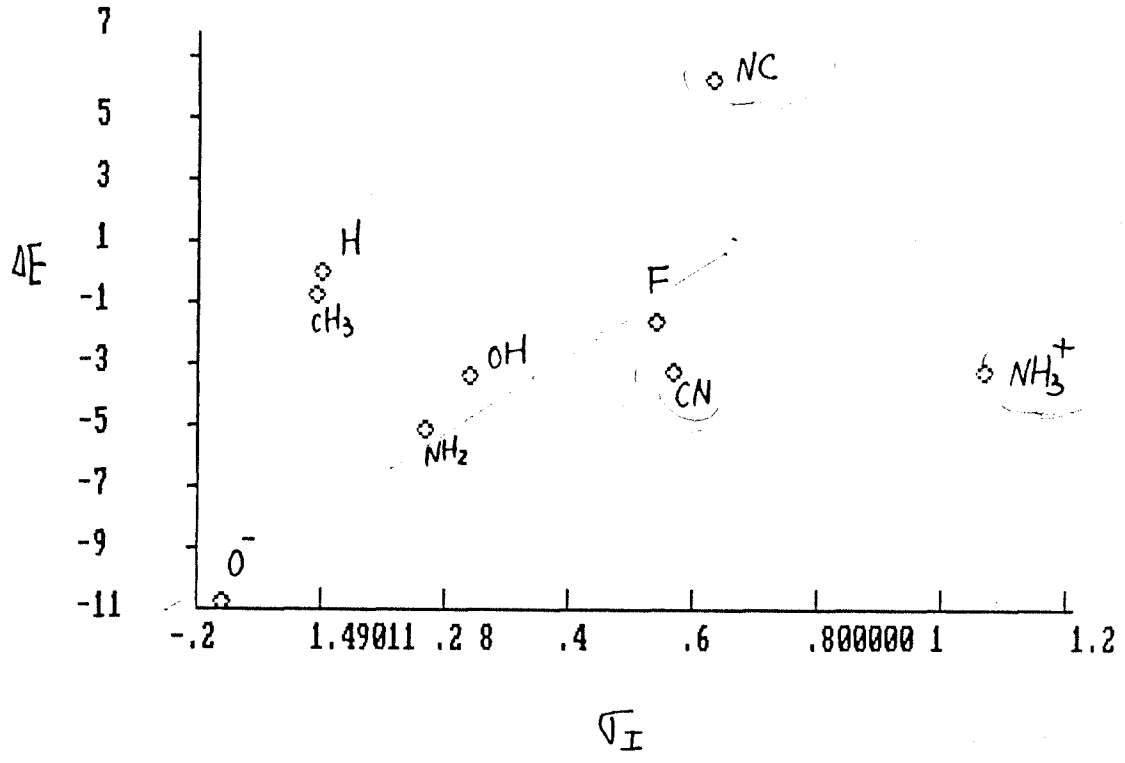
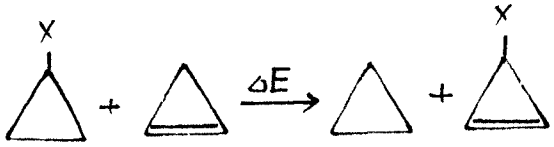


Fig 5-2 The plot between stabilization energy and substituent constant

Table 5-4 List of Stabilization Energy and Substituent Constant values

Point	X (σ_I)	Y (ΔE)
1	-0.16	-9.399999
2	-0.01	-0.2
3	0	0
4	0.17	-0.1
5	0.24	-6.9
6	0.54	-6.8
7	0.57	-0.4
8	0.63	4.3
9	1.07	-8

Slope = -0.4839202 ± 4.567048
Intercept = -2.891561 ± 5.079265
Correlation = 0.0400167
Calculated on points 1 to 9



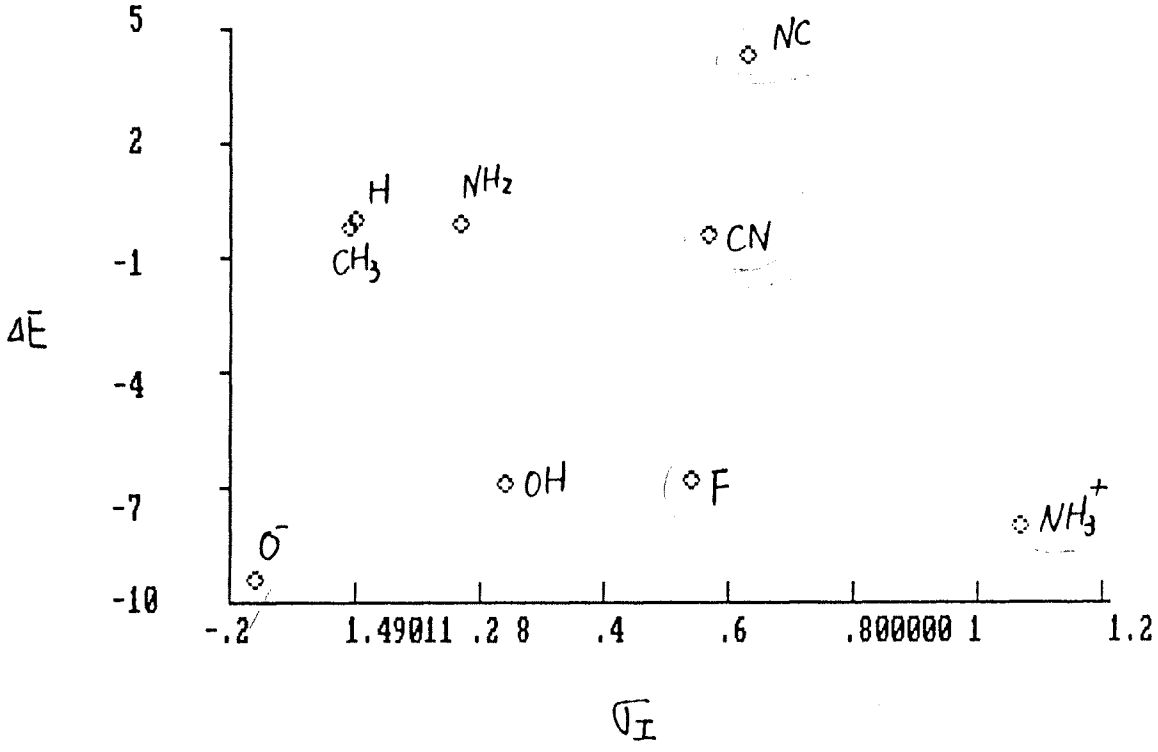
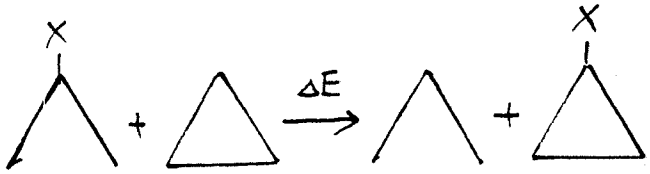


Fig 5-3 The plot between stabilization energy and substituent constant

Table 5-5 List of Stabilization Energy and Substituent Constant values

Point	X (σ_I)	Y (ΔE)
1	-0.8	-4.9
2	-0.62	3.5
3	-0.6	-1.5
4	-0.48	5.2
5	-0.16	-0.5
6	-0.11	4.8
7	0	0
8	0.02	1.9
9	0.08	-2.8

Slope = 1.396449 ± 3.955741
Intercept = 1.047613 ± 3.683727
Correlation = 0.1322563
Calculated on points 1 to 9



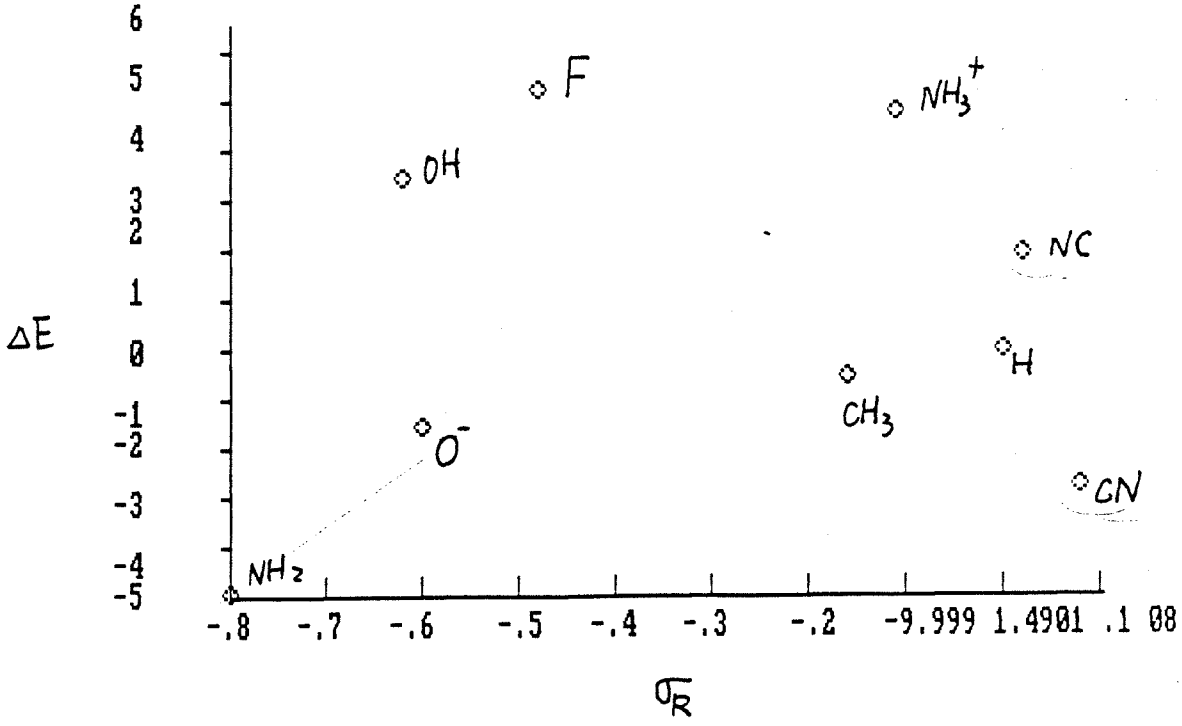
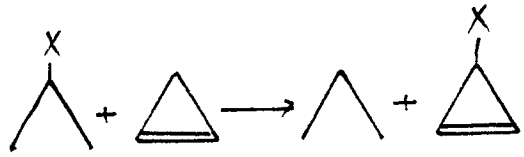


Fig 5-4 The plot between stabilization energy and substituent constant

Table 5-6 List of Stabilization Energy and Substituent Constant values

Point	X (σ_I)	Y (ΔE)
1	-0.8	-5.1
2	-0.62	-3.4
3	-0.6	-10.8
4	-0.48	-1.6
5	-0.16	-0.7
6	-0.11	-3.2
7	0	0
8	0.02	6.2
9	0.08	-3.2

Slope = 8.418666 ± 4.097394
Intercept = 7.531505E-02 ± 3.815639
Correlation = 0.6133513
Calculated on points 1 to 9



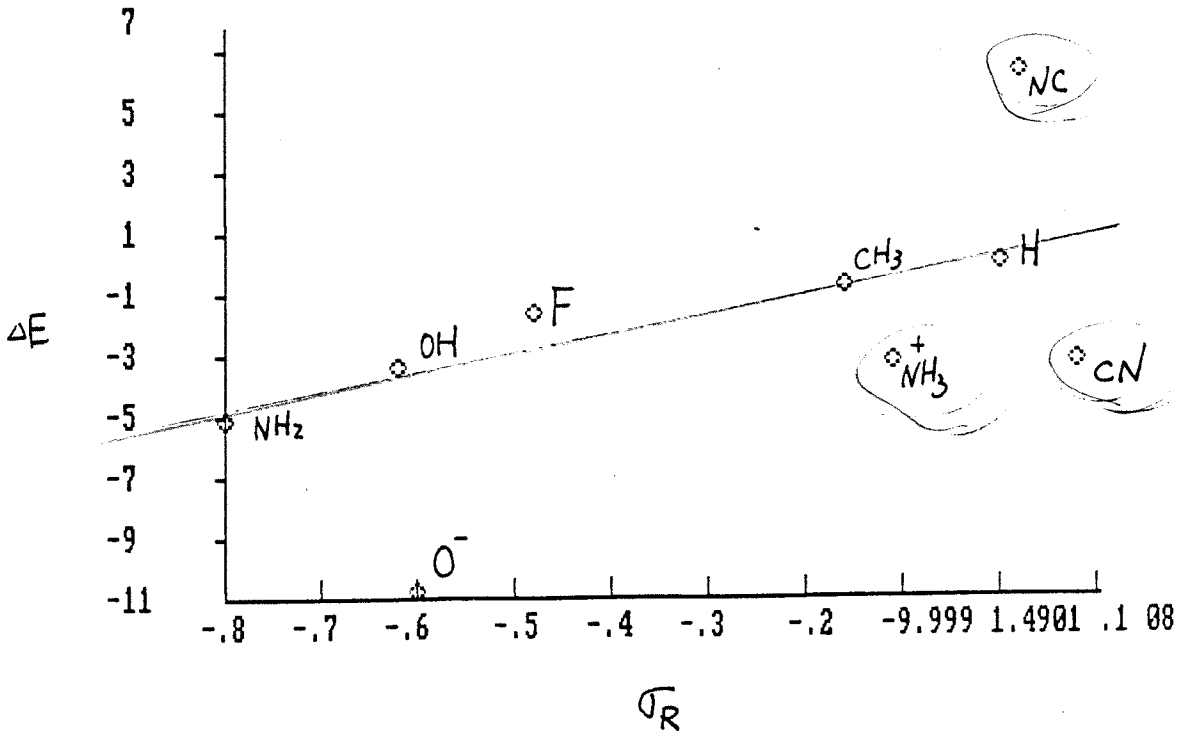
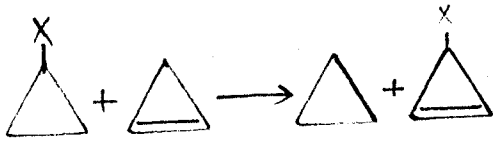


Fig 5-5 The plot between stabilization energy and substituent constant

Table 5-7 List of Stabilization Energy and Substituent Constant values

Point	X (σ_I)	Y (ΔE)
1	-0.8	-0.1
2	-0.62	-6.9
3	-0.6	-9.4
4	-0.48	-6.8
5	-0.16	-0.2
6	-0.11	-8
7	0	0
8	0.02	4.3
9	0.08	-0.4

Slope = 6.999154 ± 4.774842
Intercept = -0.97914 ± 4.446502
Correlation = 0.4846266
Calculated on points 1 to 9



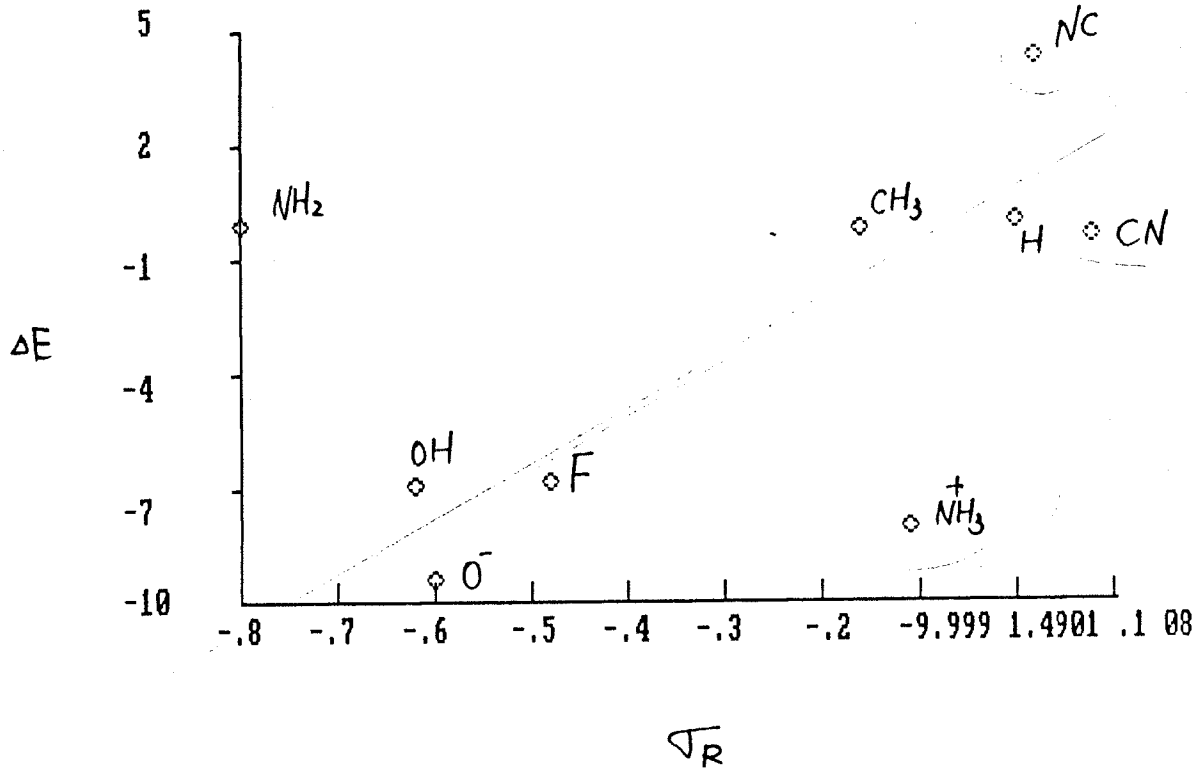


Fig 5-6 The plot between stabilization energy and substituent constant

REFERENCE :

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PART B

THE KINETICS OF HYDROLYSIS OF A QUINUCLIDONE USING FTIR

Chapter 6

INTRODUCTION

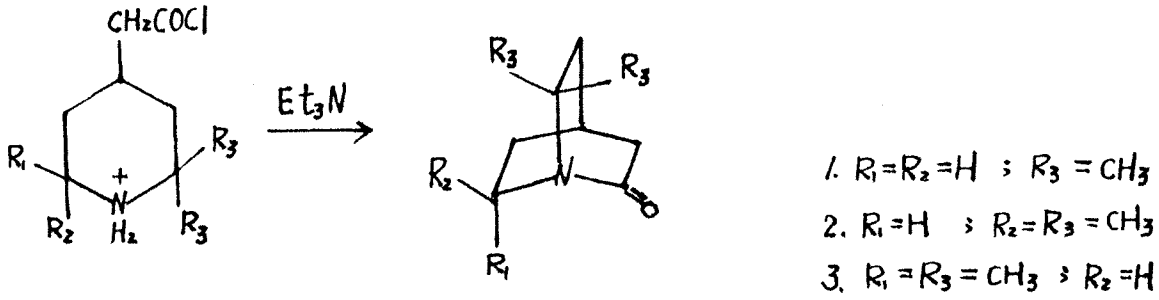
Recently, interest in bridgehead bicyclic lactams has accelerated due to their potential for helping the understanding of the structure and function of peptides, proteins, and enzymes. Furthermore, twisted bridgehead bicyclic lactam research relates to research in pharmaceuticals, biochemistry, polymers, physical organic and theoretical areas. [1]

The interest in bicyclic bridgehead lactams is due, in part, to their apparent violation of Bredt's Rule. In 1938, Lukes noted that lack of resonance stabilization of the $N-C=O$ moiety in the same manner as Bredt's Rule, [1] forbids bridgehead lactams. Bredt's Rule expressed the idea that carbon-carbon double bonds at the bridgeheads of certain bicyclic systems should be incapable of existence. The reason for this prohibition is that in such olefins p orbitals are held perpendicular to each other. An anti-Bredt bicyclic lactam, if it could be synthesized, would possess an additional driving force for reaction in general and polymerization in particular compared to monocyclic and nonbridgehead bicyclic lactams because the $N-C=O$ resonance energy would be recovered in the polymer.

Pracejus used ethyl chloroformate and triethylamine to react with amino acylchlorides to synthesize three derivatives of 2-quinuclidone. [2][3](see Scheme 1) Although

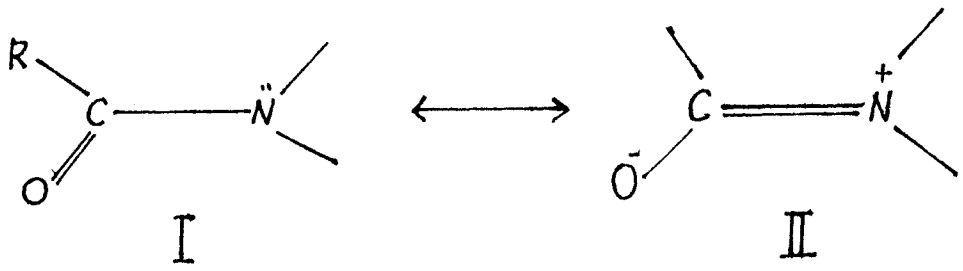
some of these lactams are very sensitive to moisture and easily polymerized, these factors do not limit the study and synthesis of these compounds. [1]

Scheme 1.



An amide or a medium-ring lactam should have a planar functional group due to resonance stabilization involving structure I and II (Scheme 2).

Scheme 2.



The 20 kcal/mol resonance usually assumed reflects the rotational barrier of simple amides. A small bridgehead lactam such as 2-quinuclidone and its derivatives will lack part or all of the resonance stabilization. The amide or lactam group need not be confined to small bridgehead bicyclic systems in order to be twisted. Small mono-

cyclic lactams are exclusively cis while the larger rings revert to the trans structure characteristic of simple amides. Medium-ring lactams can adopt the trans structure but this is accompanied by twisting of the lactam linkage.

Bicyclic amides with an angular nitrogen atom of the 2- quinuclidone type are characterized by a rigidly fixed structure in which it is sterically impossible for the free p electrons of nitrogen and the pi-electron cloud of the carbonyl group to be parallel. The absence of conjugation of the $>N-C=O$ type, observed in the usual amides, [4] provided a basis for Lukes and Fawcett to express doubt about the possibility of the real existence of such compounds. However, in 1956 Levkoeva and Robtsov and in 1959-1965 Pracejus and co-workers [3] reported the preparation of 2-quinuclidones by cyclization of acid chlorides of the corresponding 4-piperidylacetic acids in the presence of hydrogen chloride acceptors.

The initial entries into the small bridgehead bicyclic lactam class (2-quinuclidones) [5] were synthesized by Pracejus and co-workers. Later, less strained molecules were reported. Synthesis of the parent lactram, 1-Azabicyclo[3,3,1]nonan-2-one was reported in 1979. There also have been some related molecules synthesized such as 6,6,7,7-tetramethyl-2-quinuclidone. [4] Praocejus reported the kinetics of base-induced decomposition of three 2- quinuclidone derivatives but they did not have 6,6,7,7-tetramethyl-2-quinuclidone, the most sterically-hindered of the set. Recently, modification of the published synthesis of 6,6,7,7-tetramethyl-2-quinuclidone was done by Professor Guanli Wu and student Jung-Chou Tsai in our laboratory. The goal of the work described in this thesis is to obtain kinetic data for this compound and to compare them with dimethyl and trimethyl 2-quinuclidone derivatives(scheme 1) which are less sterically-hindered.

FTIR was employed to monitor the rate of decomposition of 6,6,7,7-tetramethyl-

2-quinuclidone and measure the transmittance change as a function of time for the 1748 cm^{-1} Carbonyl band.

The development of FTIR spectrometers began with the invention of the two-beam interferometer by Michelson almost a century ago. After this period, both Michelson and Lord Rayleigh recognized that it was theoretically possible to obtain spectra from the interference pattern generated by the interferometer through the computation of its Fourier transform, but it was not used for the measurement of IR spectra for another 50 years. The only reason then for measuring FTIR spectra was the capability to resolve the fine structure of atomic lines.

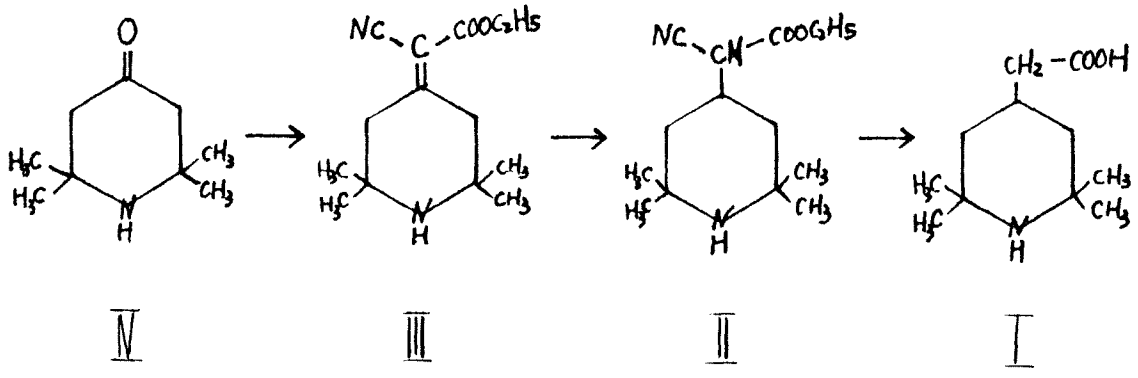
Two key discoveries were made around 1950. The first was the recognition by Fellgett that information from all spectral elements is measured simultaneously with an interferometer. The second was the discovery of the fast Fourier transform (FFT) algorithm by Cooley and Tukey in 1964. By 1975, FTIR spectrometry had become an accepted technique for measuring high-quality IR spectra, but the cost of this instrument is high.

In this research a Perkin-Elmer Company, 1600 series FTIR ,belonging to Professor S. Sofer Biotechnoly Laboratory at NJIT has been employed for the kinetic study.

Chapter 7

MODIFICATION of THE SYNTHETIC METHOD FOR 6,6,7,7-TETRAMETHYL-2-QUINUCLIDONE

E. S. Nikitskaya and co-workers published a paper which is devoted to a description of the optimum conditions for obtaining (I) according to the following scheme. [6]



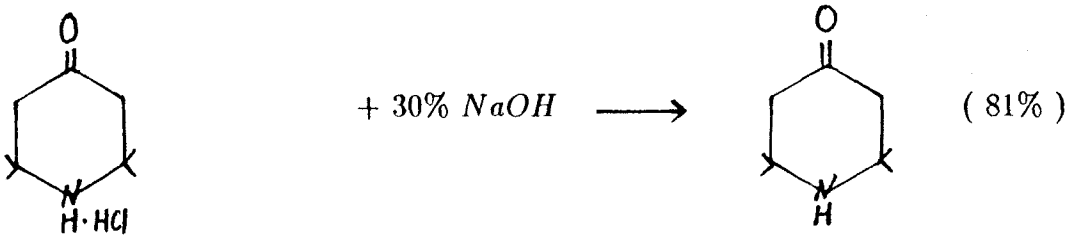
IV III II I

E. I. Levkoeva and co-workers had done the synthesis and transformations of 6,6,7,7-tetramethyl-2-quinuclidone but the yield was low (27%). [4] We followed the

procedure of this paper and repeated it several times but failed to obtained the quinuclidone. Dr. Guanli Wu and graduate student Jung-Chou Tsai successfully modified the cyclization part of Levkoeva's method. The modified synthetic method which combined the procedures of Nikitskaya, Levkoeva's and Dr. Guanli Wu is shown in Scheme 1-5 we also have done the infrared spectra for each reaction, and for the kinetic study of 6,6,7,7- tetramethyl-2-quinuclidone (Scheme 6).

Scheme 1.

The neutralization of 2,2,6,6-tetramethyl-4-piperidone Hydrochloride.

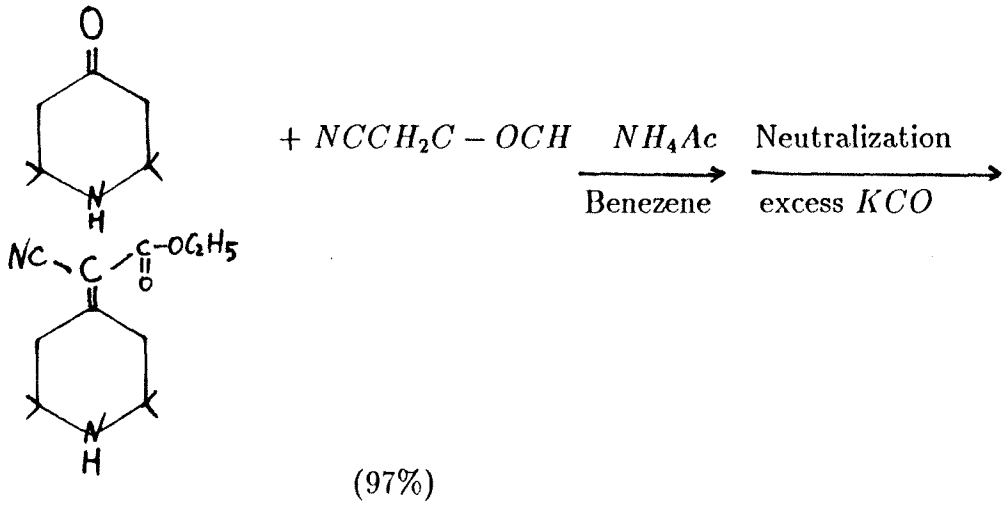


1

IR : 1702.2 cm^{-1} for $-\overset{\overset{O}{\|}}{C}-$

Scheme 2.

The preparation of 2,2,6,6-tetramethyl-4-(carboethoxycyano-methylene)piperidine.



(97%)

3

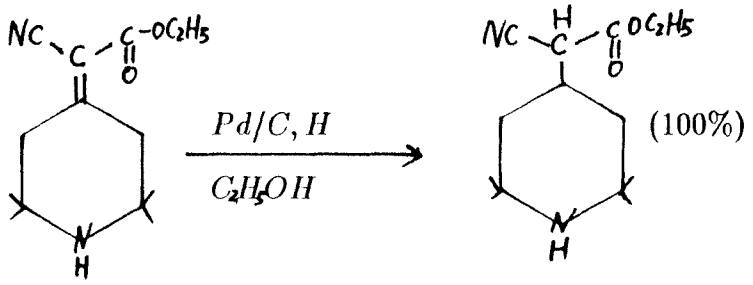
IR : 1737.0 cm^{-1} for $-\overset{\overset{O}{\|}}{C}-OC_2H_5$

1629.3 cm^{-1} for $\overset{\backsim}{C}=C\overset{\diagup}{\diagdown}$

1702.2 cm^{-1} for $-\overset{\overset{O}{\|}}{C}-$ peak was disappeared

Scheme 3.

The preparation of 2,2,6,6-tetramethyl-4-(carboxycyano-methyl)piperidine.

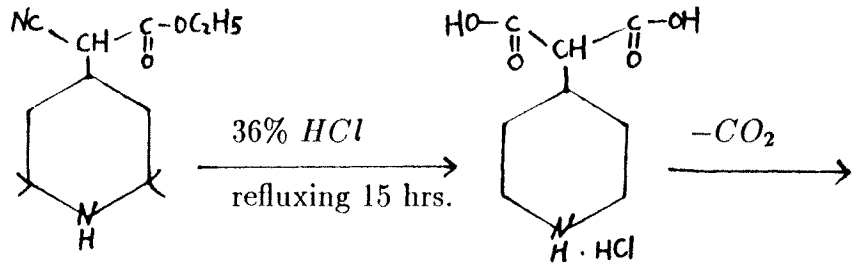


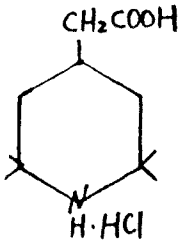
4 (see Fig. 7-3)

IR : 1629.3 cm^{-1} for $\overset{\backslash}{C} = \overset{/}{C}$ was disappeared.

Scheme 4.

The preparation of 2,2,6,6-tetramethylpiperidyl-4-aceticacid Hydrochloride.





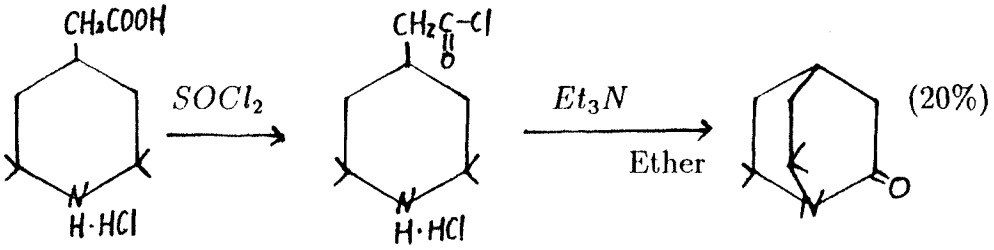
(93%)

5 (see Fig. 7-4)

IR : *KBr* 1719.2 cm^{-1} for $-\overset{\overset{O}{\|}}{C}-OH$

Scheme 5.

The preparation of 6,6,7,7-tetramethyl-2-quinuclidon.



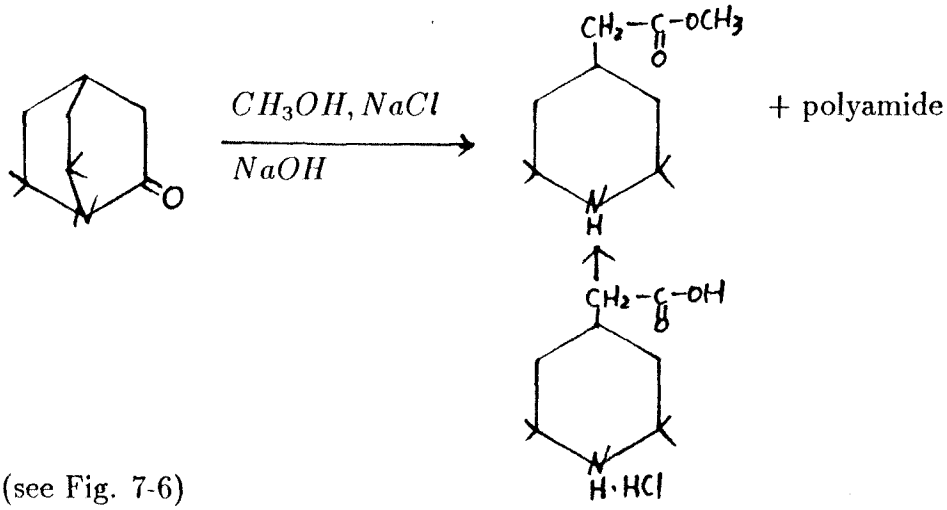
6 (see Fig. 7-5, 7-8, 7-9)

IR : 1748.6 cm^{-1} for $-N-\overset{\overset{O}{\|}}{C}-(CHCl_3)$

1757.9 cm^{-1} for $-N-\overset{\overset{O}{\|}}{C}-(CH_3OH)$

Scheme 6.

The kinetic study of 2-quinuclidone.

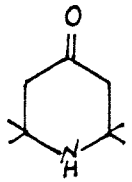


+ polyamide

(see Fig. 7-6)

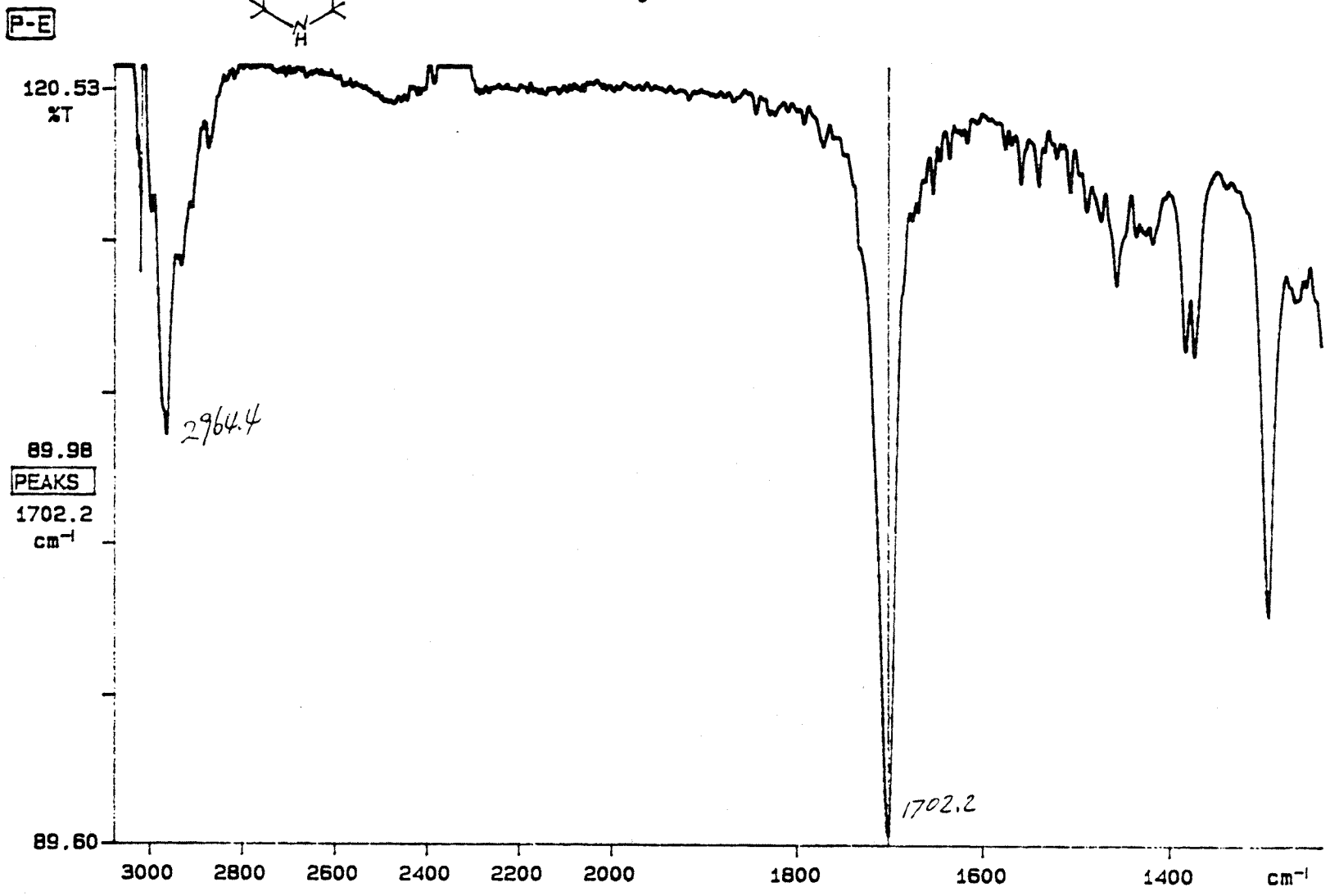
IR : 1737.5 cm^{-1} for $-\overset{\overset{O}{\|}}{C}-OCH_3$ (see Fig.7-7)

Figure 7-1.



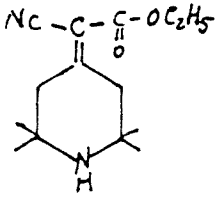
($CHCl_3$)

1702.2 cm^{-1} for -C-
O



89/04/12 12:11
X: 1 scan, 4.0cm-1

Figure 7-2.



(KBr) After recrystallization

2222.8 cm^{-1} for -CN

1737.0 cm^{-1} for $-\overset{\overset{O}{\|}}{C}-OC_2H_5$

1629.3 cm^{-1} for >C=C<

1702.2 cm^{-1} for $-\overset{\overset{O}{\|}}{C}-$ was disappeared

P-E

37.02
%T

1.80
PEAKS
1629.3
cm^{-1}

-0.26

2972.0

2222.8

1737.0

1629.3

4000 3500 3000 2500 2000 1500 1000 cm^{-1} 500

89/01/13 15:43
X: 4 scans, 4.0cm-1

Figure 7-3.

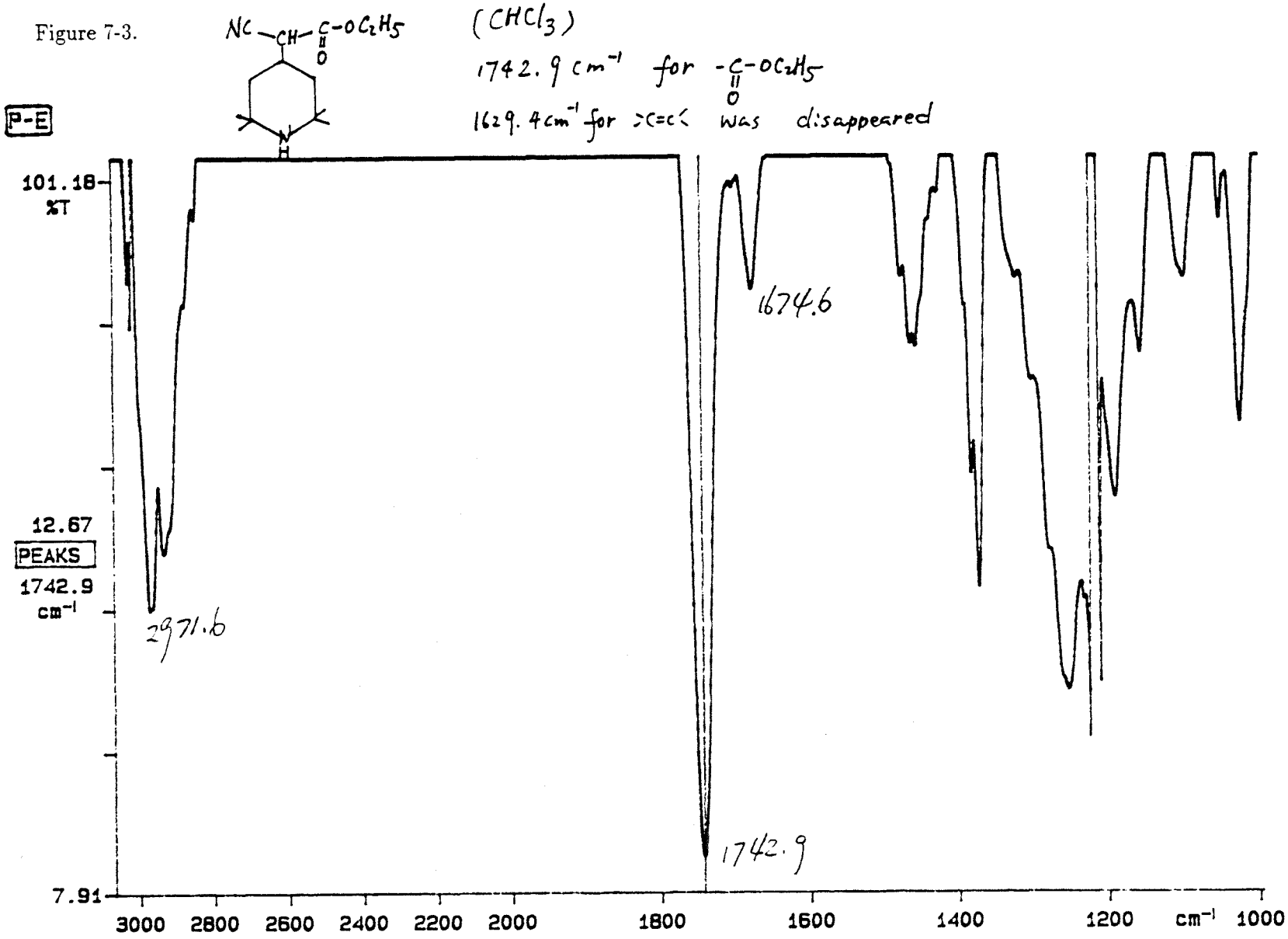

(CHCl3)
1742.9 cm-1 for -C(=O)-OC2H5
1629.4cm-1 for >C=C< was disappeared
P-E
101.18
%T
12.67
PEAKS
1742.9
cm-1
2971.6
1674.6
1742.9
7.91
3000 2800 2600 2400 2200 2000 1800 1600 1400 1200 cm-1 1000
89/04/12 11:20
X: 1 scan, 4.0cm-1

Figure 7-4.

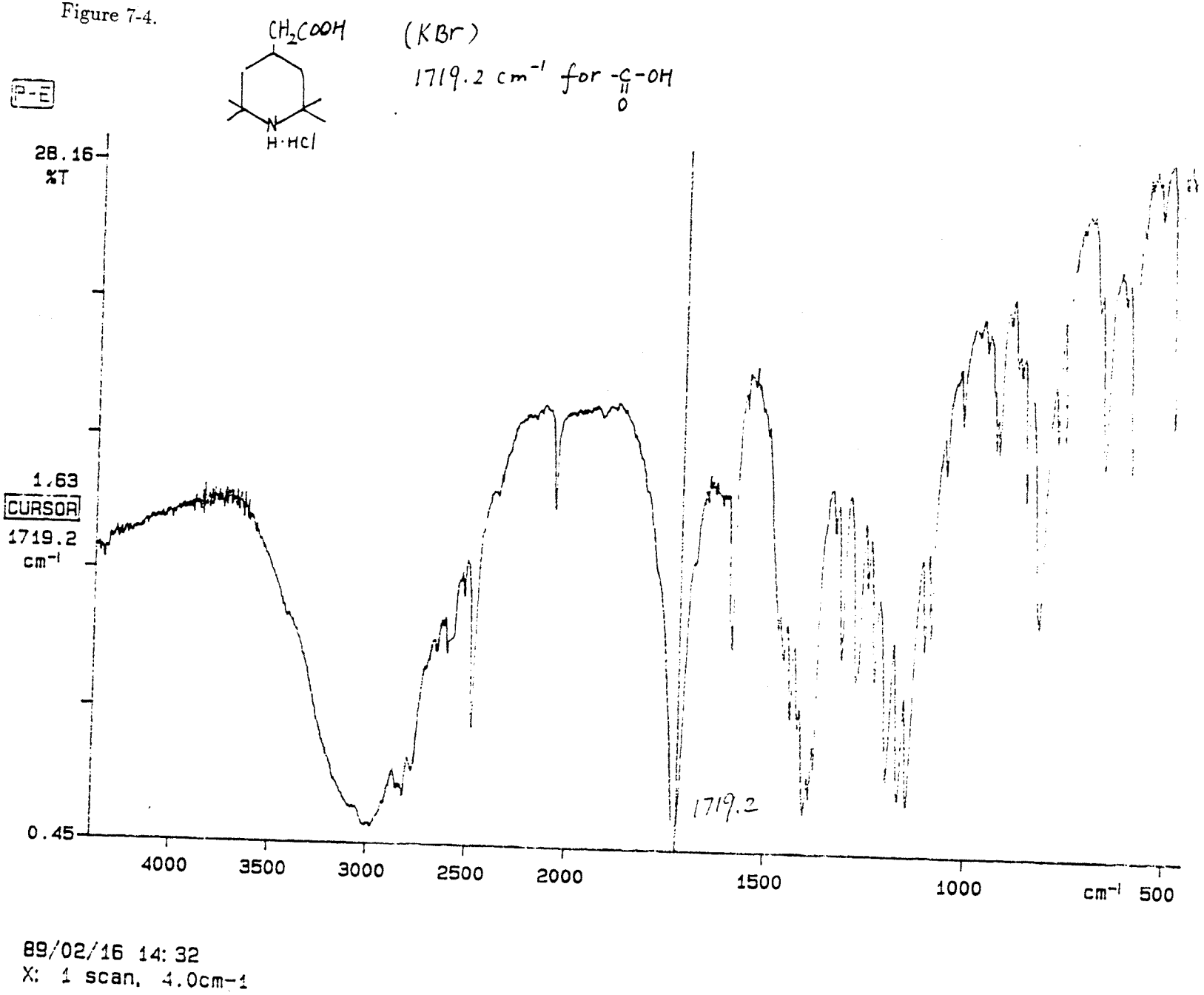

CH2COOH
N
H·HCl
(KBr)
1719.2 cm-1 for -C-OH
O
P-E
28.16
%T
1.63
CURSOR
1719.2
cm-1
0.45
1719.2
4000
3500
3000
2500
2000
1500
1000
cm-1
500
89/02/16 14:32
X: 1 scan, 4.0cm-1

Figure 7-5.

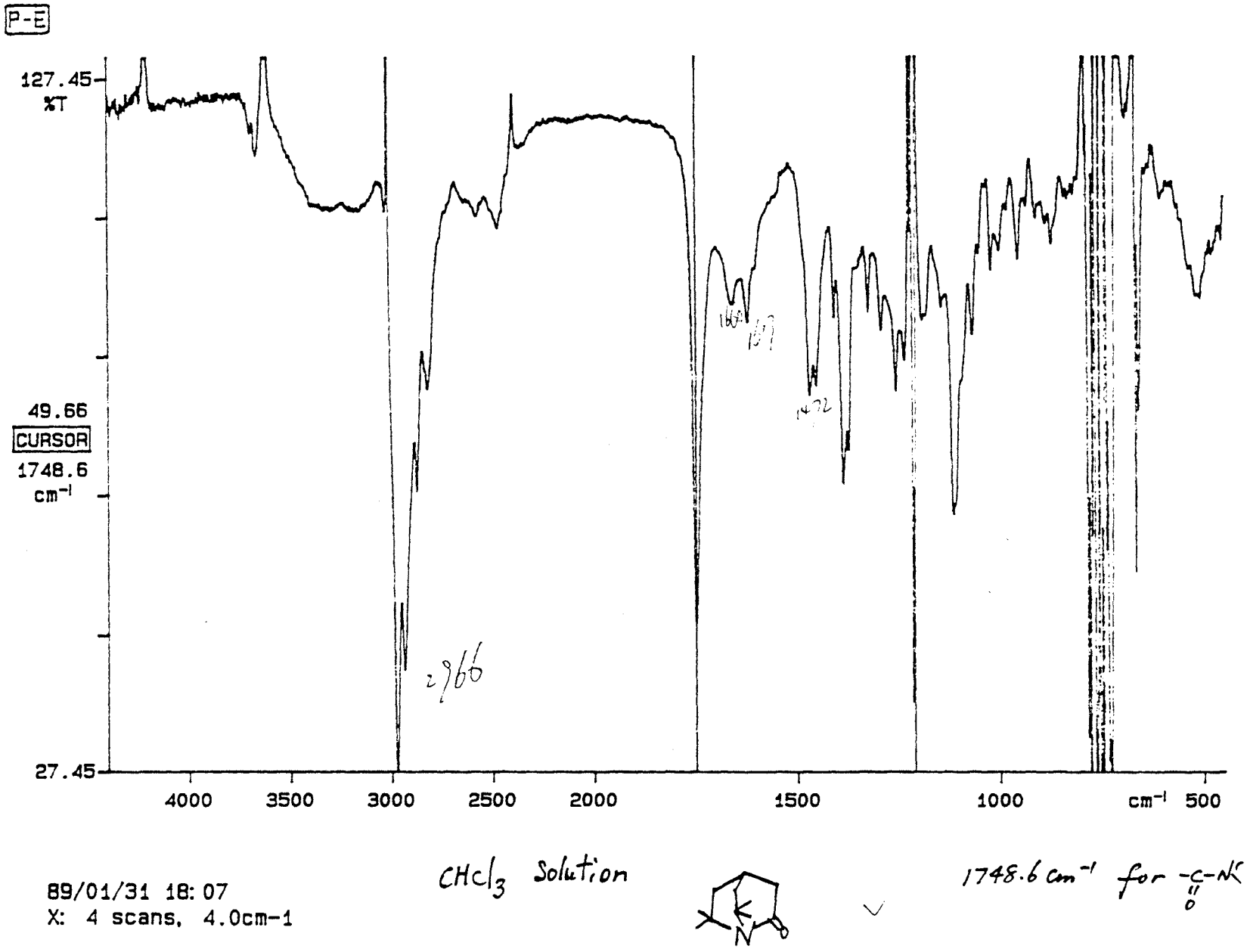

P-E
127.45
%T
49.66
CURSOR
1748.6
cm-1
27.45
4000
3500
3000
2500
2000
1500
1000
cm-1
500
2966
1660
1597
1432
89/01/31 18:07
X: 4 scans, 4.0cm-1
CHCl3 Solution
1748.6 cm-1 for -C-NC
O

Figure 7-6.

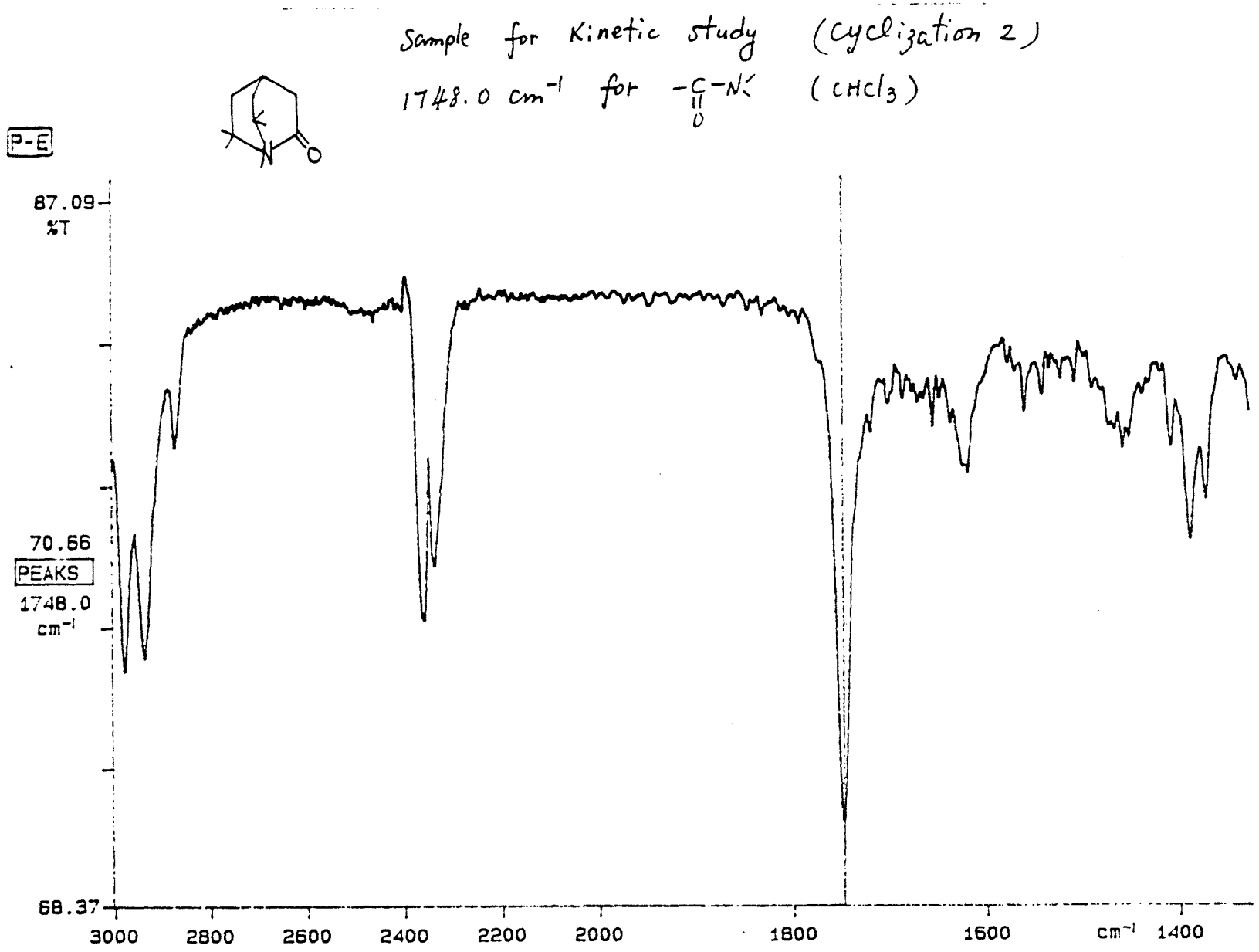
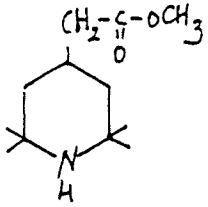

Sample for Kinetic study (cyclization 2)
1748.0 cm⁻¹ for -C(=O)-N< (CHCl3)
P-E
87.09
%T
70.66
PEAKS
1748.0
cm⁻¹
68.37
3000
2800
2600
2400
2200
2000
1800
1600
cm⁻¹
1400

Figure 7-7.



1737.5 cm^{-1} for $-\overset{\overset{O}{\|}}{C}-OCH_3$ ($CHCl_3$)

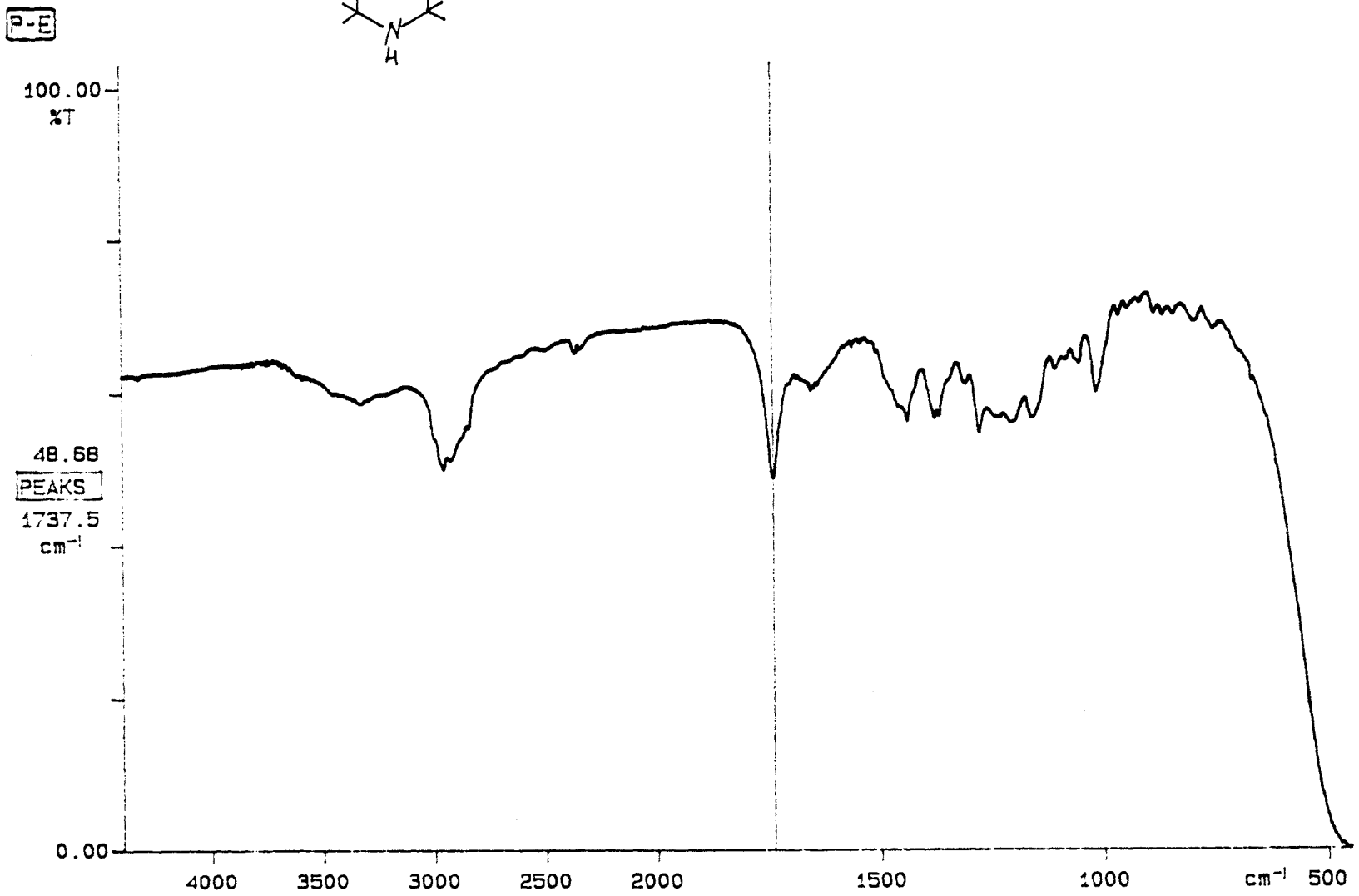
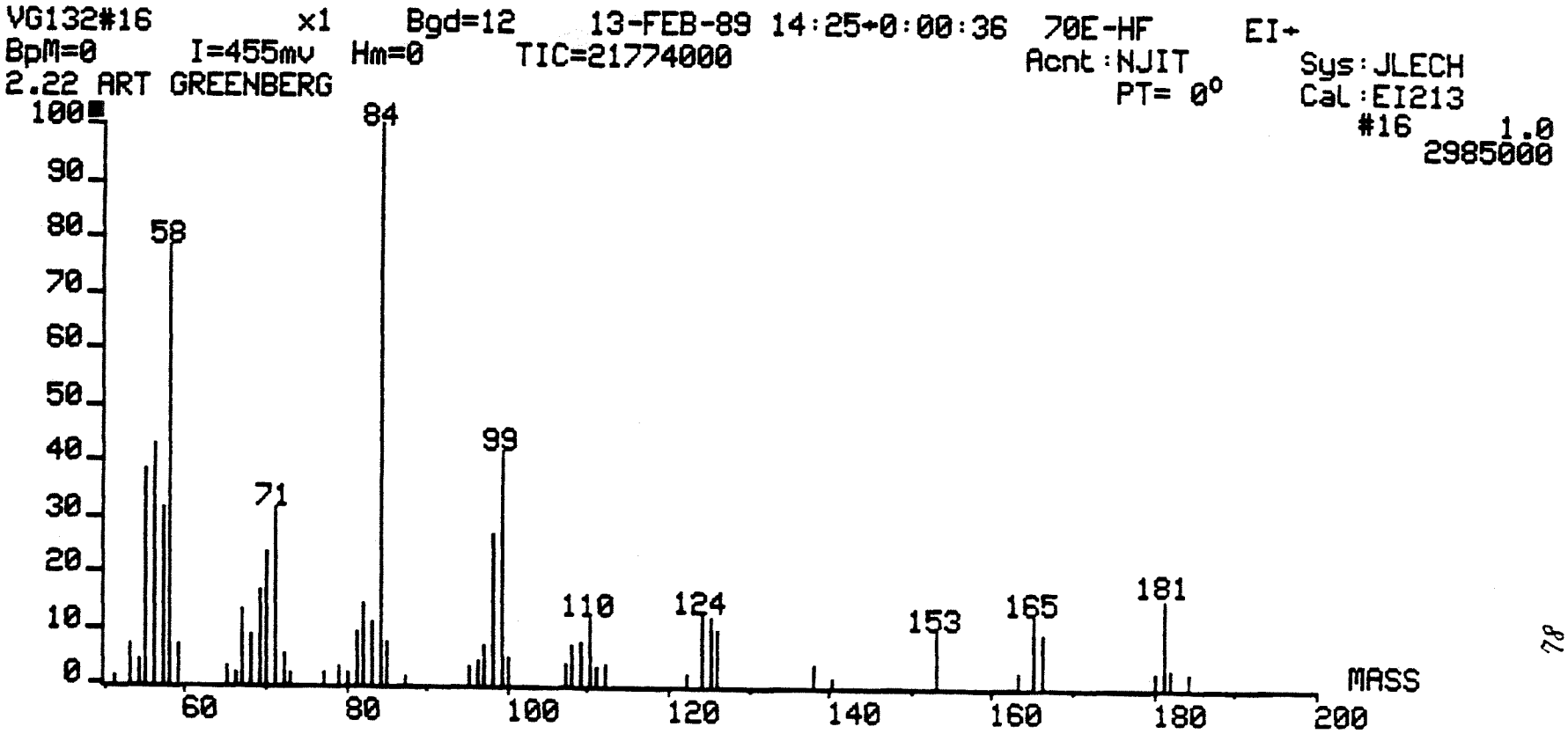
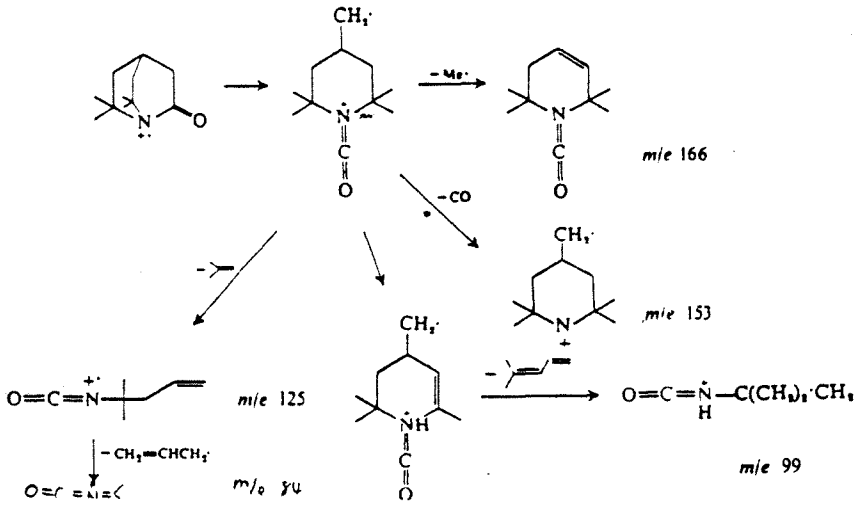


Figure 7-8.





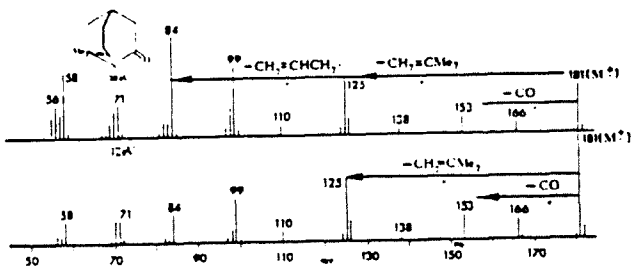
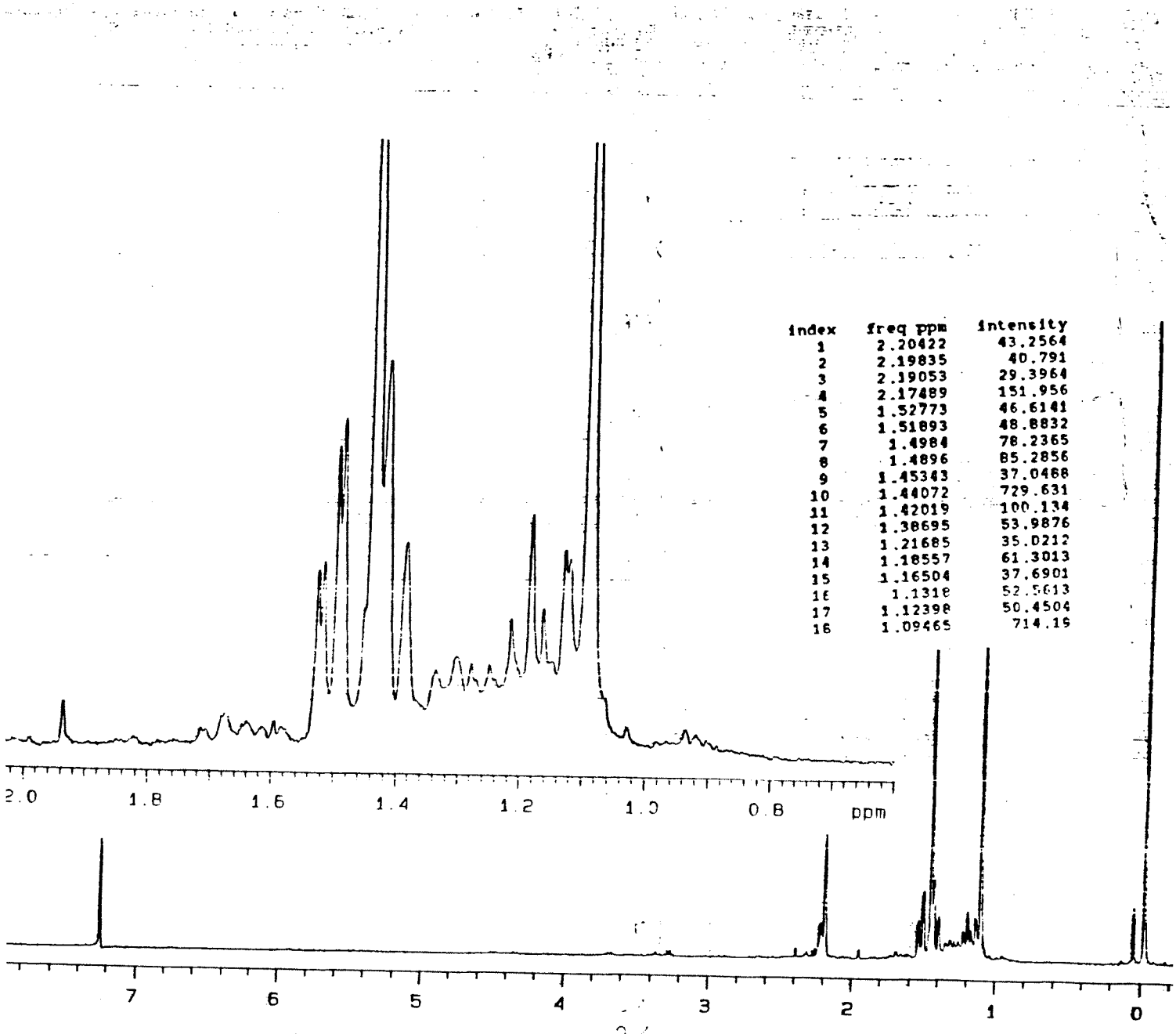
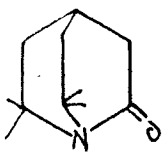


FIG. 6

Figure 7-9.

NMR Spectra of 6,6,7,7-tetramethyl-2-quinuclidone





8

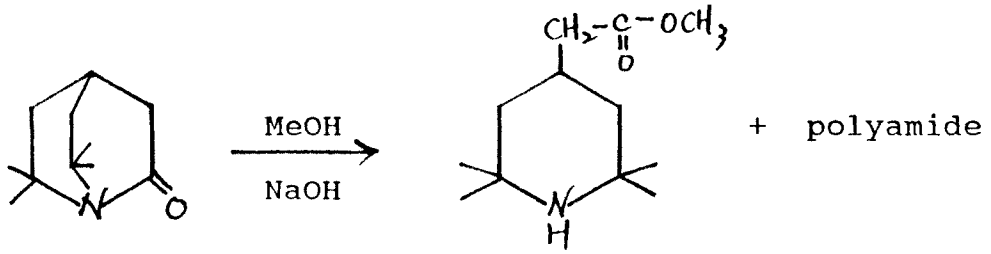
Chapter 8

EXPERIMENTAL KINETICS STUDY

6,6,7,7-Tetramethyl-2-quinuclidone was employed to do the kinetic reaction which was then compared with dimethyl- and trimethyl 2-quinuclidones, less sterically-hindered quinuclidone derivatives, using FTIR. This compound which is more stericall-hindered has four methyl group ; we expect it is more stable than other, 2-quinuclidone derivatives.

The simple theory of decomposition of 6,6,7,7-tetramethyl-2-quinuclidone by base solution is as follows (see Scheme 1)

Scheme 1.



IR : 1758.0 cm^{-1} for $-N-\overset{\overset{O}{\|}}{C}-$; 1737.3 cm^{-1} for $-\overset{\overset{O}{\|}}{C}-OCH_3$

(CH_3OH) (CH_3OH)

6,6,7,7-tetramethyl-2-quinuclidone in the base decomposition experiment has a peak, 1758 cm^{-1} , and the peak's transmittance will become bigger with decomposition. It is more sterically hindered than other quinuclidone derivatives (see Scheme 1), so we expect that the transmittance change is slower than for the others; i.e., tetramethyl is more stable because it is more sterically hindered.

APPARATUS:

FTIR	Perkin Elmer, 1600 series FT-IR
CaF Cell	Pathlength 0.111 mm
Furnace	Thermolyne 1400 Furnace
pH meter	
Pipette	1 ml

PREPARATION SOLUTIONS:

Following Pracejus' method (1959), prepare the basic solution as follows:

A) Weigh sodium chloride 20g, putting in Furnace ($250°C$) for drying 3-4 hours, then cool down to room temperature in dessicator.

B) Weigh sodium hydroxide 0.04g, putting in Furnace ($150°C$) for drying 3 hours, then cool down to room temperature in dessicator.

C) Put some molecular sieves (4A) in Furnace for drying 2 hours, then cool down to room temperature in dessicator.

D) Put 100 ml anhydrous methanol in 500 ml bottle.

We add C, B and A to make a methanolic solution (0.01M), then check the pH value (above 9) using a pH meter.

Prepare 0.1 M reaction solution: 6,6,7,7-tetramethyl-2-quinuclidone: 7 mg was dissolved in 0.39 ml basic solution (transfered by 1 ml pipette) at room temperature, and the mixture immediately transfered to the FTIR spectrometer.

KINETIC MEASUREMENTS:

All reactions were carried out in calcium fluoride cuvettes (path length = 0.111 mm) at room temperature. First, measure the IR spectra of sample solution, to make sure there is a 1748.6 cm^{-1} peak in $CHCl_3$ solution and 1758.0 cm^{-1} peak in CH_3OH solution. Secondly, put the base solution in IR cuvettes as reference (background) solution and store the IR spectra in computer. The reaction was initiated by adding a freshly-prepared solution of 6,6,7,7-tetra-methyl-2-quinuclidone to the basic solution. The transmittance of the 1758 cm^{-1} peak was measured every five minutes in the cuvettes. Reactions were monitored continuously at 1758 cm^{-1} peak until there was no further change in transmittance. The kinetic runs were repeated three times and plot was made of transmittance versus time. (see Fig 8-2,8-3,8-4)

CALCULATION (A):

Calculation of the extinction coefficient of the 1758.0 cm^{-1} peak as follows: (Table 8-1, Fig. 8-1)

$E = 1/(C \times L)\log(T_O/T_S)$

T_S: the transmittance of the solvent

T_O: the transmittance of the sample

$E = 1/(C \times L)\log(100/T)$

$= 900.9\log(100/T)$

$T = (T_S/T_O) \times 100\%$ reading from FTIR screen

C: concentration of sample solution

$C = (7mg/181)/0.39ml$

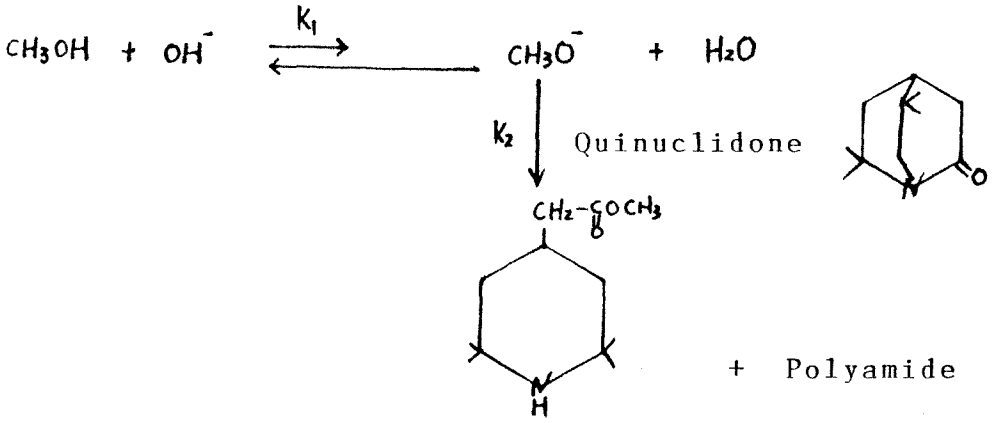
$= 0.1M$

L : cell pathlength $CaF_2(0.0111cm)$

CACULATION (B):

Calculation of rate constants and Gibbs energy change in this kinetic experiment is shown below.

In this kinetics experiment, 6,6,7,7-tetramethyl-2-quinuclidone was decomposed by base solution, and the reaction equation was shown bellow:



$Rate = K_2\,[Quinuclidone]\,K_1\,\frac{[OH^-]}{[H_2O]}$

suppose, pH = constant , so $\frac{[OH^-]}{[H_2O]}$ is constant.

$K' = K_2\,K_1\,\frac{[OH^-]}{[H_2O]}$

Consequently, the observed behaviour is that of a first order reaction (pseudo-first kinetics):

$Rate = K'\,[Quinuclidone]$

First order equations in which the reactant is monitored integrate as follows:

$Rate = -d[A]/dt = K_A[A]$

therefore,

$\ln[A] - \ln[A_O] = -K_A\,t$

where $[A]$ is the initial concentration of A at time $t = 0$, thus a plot of $\ln[A]$ verus time is linear with slope $-K_A$ and intercept $\ln[A_O]$.

$$\ln[A] = -K_A\ t + \ln[A_O]$$

$\Delta G = -RT\ \ln K$ $\quad$ ΔG = Gibbs energy change

$R = 1.987 cal/(^oK$ mole)

T = room temp.(298^oK)

From figure 8-5 , we can approximately get the rate constant and Gibbs energy of each curve, individually. The result is shown below:

Curve I : $K_A = 0.11$ $\quad$ $\Delta G^{\ddagger} = 1.3$ Kcal/mole

Curve II :$K_A = 0.00044$ $\quad$ $\Delta G^{\ddagger} = 4.6$ Kcal/mole

Curve III:$K_A = 0.0061$ $\quad$ $\Delta G^{\ddagger} = 3.0$ Kcal/mole

Curve IV $K_A = 0.00037$ $\quad$ $\Delta G^{\ddagger} = 4.7$ Kcal/mole

The ratio of rate constant is shown:

suppose curve IV $K_A = 1$, then

Curve IV = 1

Curve II = 1.2

Curve III = 16.5

Curve I = 297

We can compare the stability of Quinuclidone derivatives using above values. 6,6,7,7-tetramethyl-2-quinuclidone is the most stable compound.

DISCUSSION AND CONCLUSIONS:

At first, we did the experiment using KBr cells which were corroded by strong basic solution, thus yielding poor results. After changing from a KBr cell to a calcium floride (CaF_2) cell, we obtained good results and thus the choice of the type of cell is very important. In this kinetic experiment, CaF_2 IR cuvettes were used, since their

very low solubility in base makes them durable and precise cells for the region of interest. CaF_2 is insoluble in water; resists most acids and alkalides, but cannot be used with solutions of ammonium salts.

Pracejus has performed a similar kinetic experiment with three derivatives of 2-quinuclidone (see scheme 1), and we examined 6,6,7,7-tetramethyl-2-quinuclidone because it was not available to Pracejus. We have related our kinetic curve to Pracejus' curves for comparison, and get the curves in Figure 8-5. From Table 8-2 and Figure 8-1, it is clear that little reaction occurs over 110 minutes and the tetramethyl derivative is more stable than the other three quinuclidone derivatives examined by Pracejus.

After several additional experiments, it was found that 8,8,9,9-tetramethyl-1-Azabicyclo[3,3,1]noan-2-one (see Appendix A), and raw 6,6,7,7-tetramethyl-2-quinuclidone (see Appendix B) also have the similar stabilization ability compared with 6,6,7,7-tetramethyl-2-quinuclidone in kinetic experiments. We known that 8,8,9,9-tetramethyl-1-Azabicyclo[3,3,1]noan-2-one has tetra-methyl, but it is not so twist as 6,6,7,7-tetramethyl-2-quinuclidone, so it is more stable than 6,6,7,7-tetramethyl-2- quinuclidone.

During the experiment, we found several interesting phenomena. The IR spectra of a sample in different solvents effected the shift of the peak of a lactam. Generally speaking, a little shift of frequency can be accepted, but only quinuclidon derivatives have a large change, from chlorform solvent to methanol solvent. We did not have enough experience to explain the phenomena, but it is worth studying in the future. (see Appendix C)

Table 8-1 (The kinetic Data)

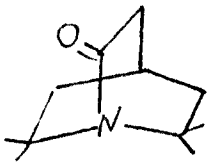
$$E = \frac{1}{C \bullet l} \log\left(\frac{100}{T}\right)$$
$$= 900.9 \log\left(\frac{100}{T}\right)$$

Point	X (time)	Y (Extinction) $E = Y \times 10^3$
1	0	0.14877
2	4	0.14683
3	6	0.14637
4	10	0.14558
5	15	0.14446
6	18	0.13688
7	20	0.13643
8	24	0.13190
9	30	0.12940
10	35	0.13125
11	40	0.13065
12	45	0.13284
13	50	0.13356
14	55	0.13351
15	60	0.13334
16	65	0.13483
17	70	0.13384
18	75	0.13566
19	80	0.13511
20	85	0.13516
21	90	0.13411

Fig 8-1

6,6,7,7-tetramethyl-2-quinuclidone

Kinetic Reactional curve



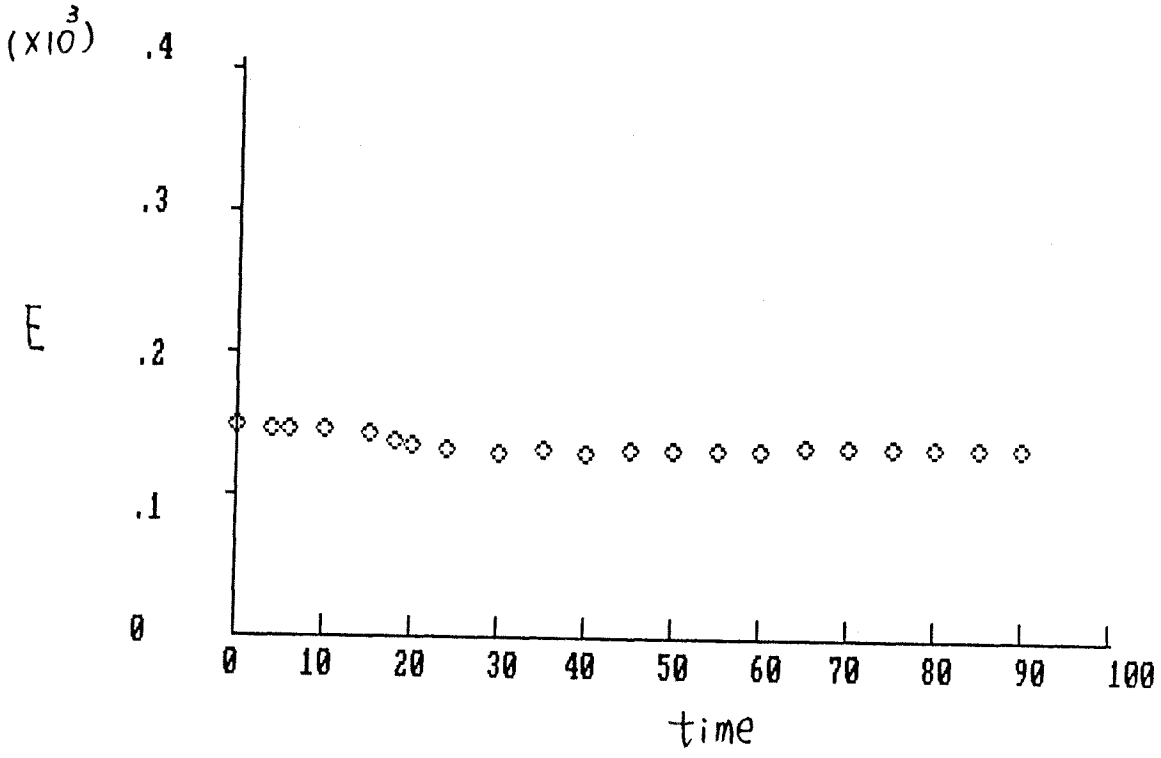
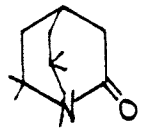
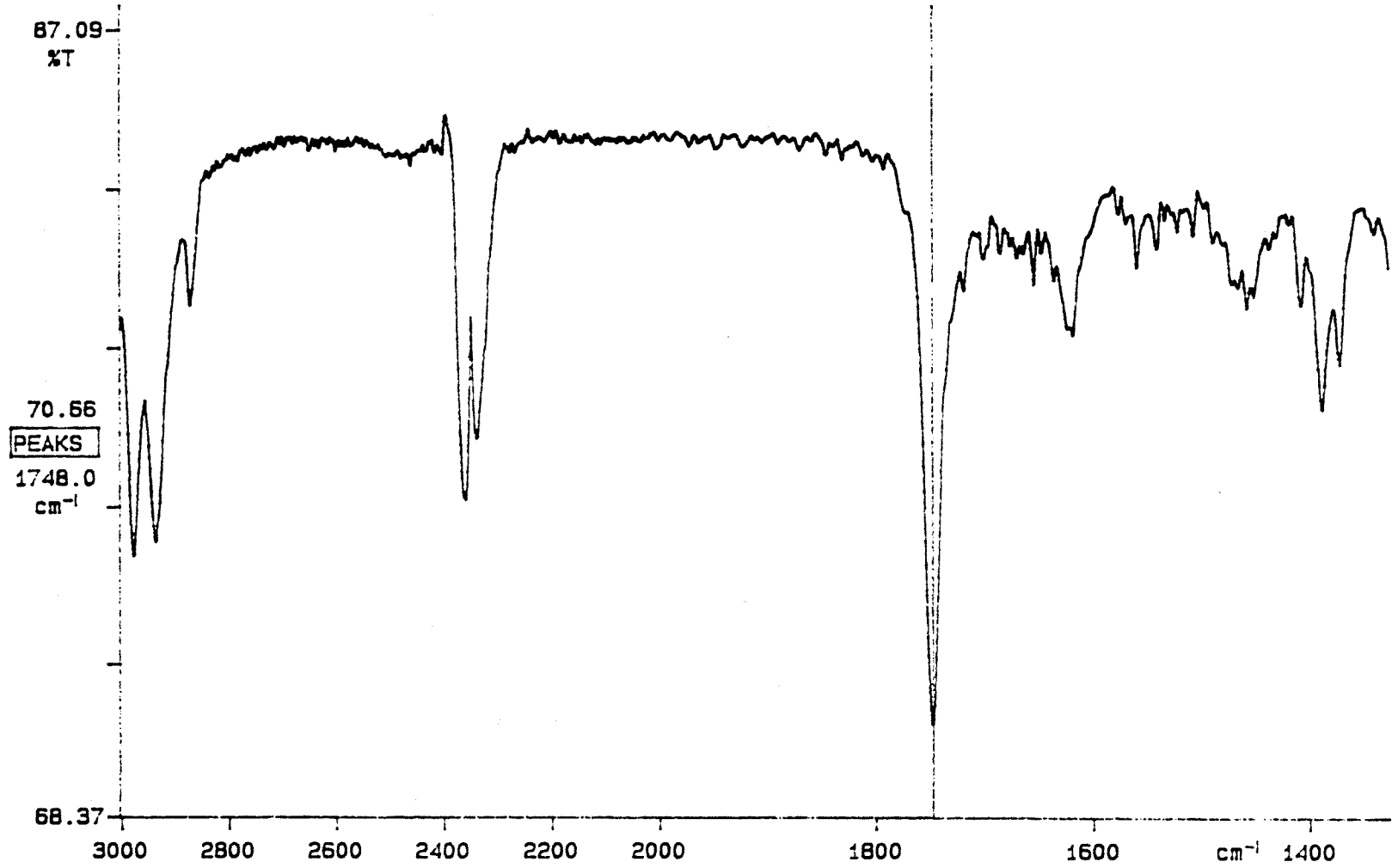


Fig 8-2

Sample for Kinetic study (cyclization 2)

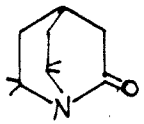
1748.0 cm^{-1} for $-\overset{\overset{O}{\|}}{C}-N<$ ($CHCl_3$)





89/04/13 14: 42
X: 1 scan, 4.0cm-1

Fig 8-3



1758.4 cm^{-1} for $-\overset{\overset{O}{\|}}{C}-N<$ (MeOH + NaOH)

" Kinetic study " first.

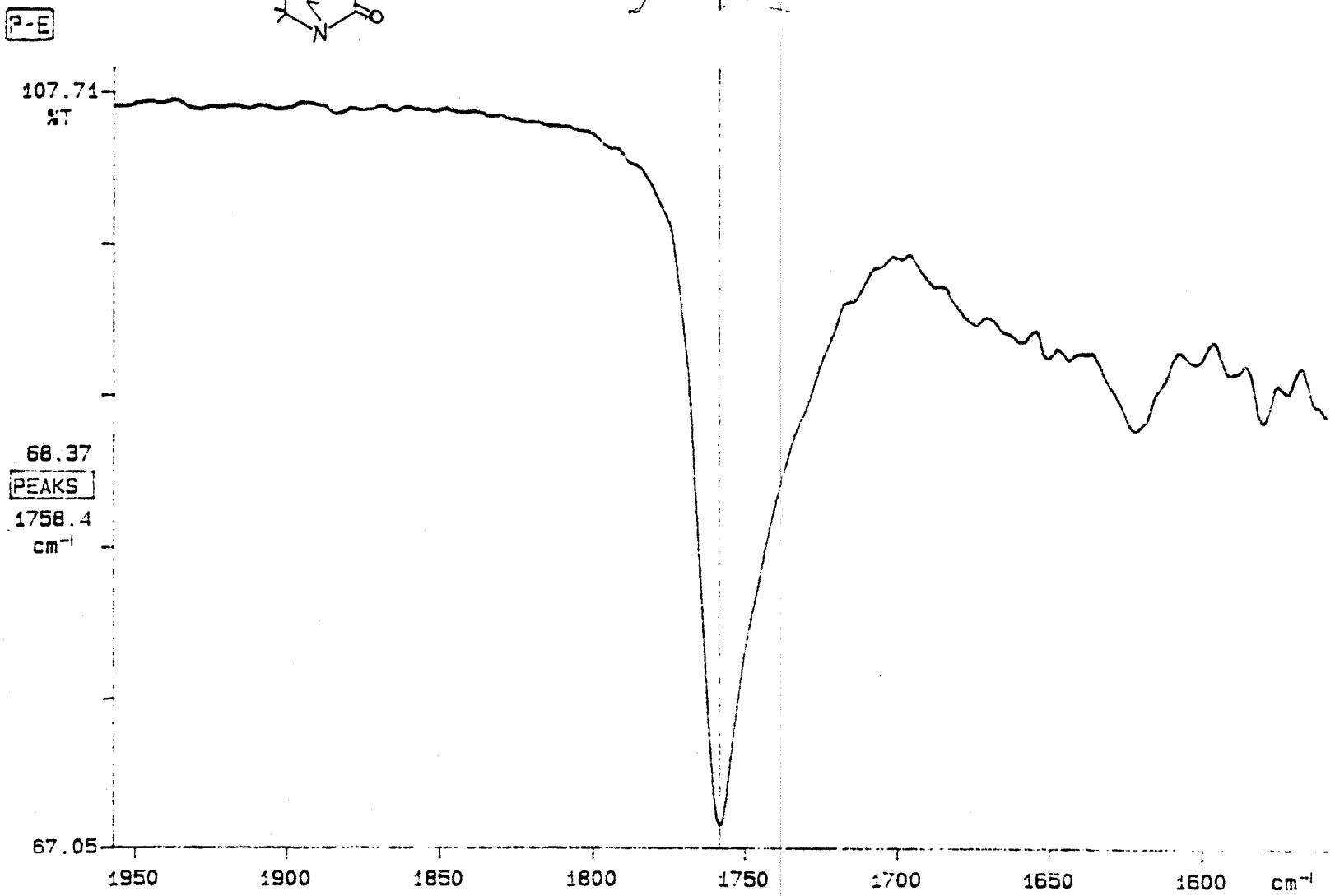
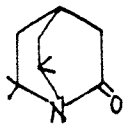
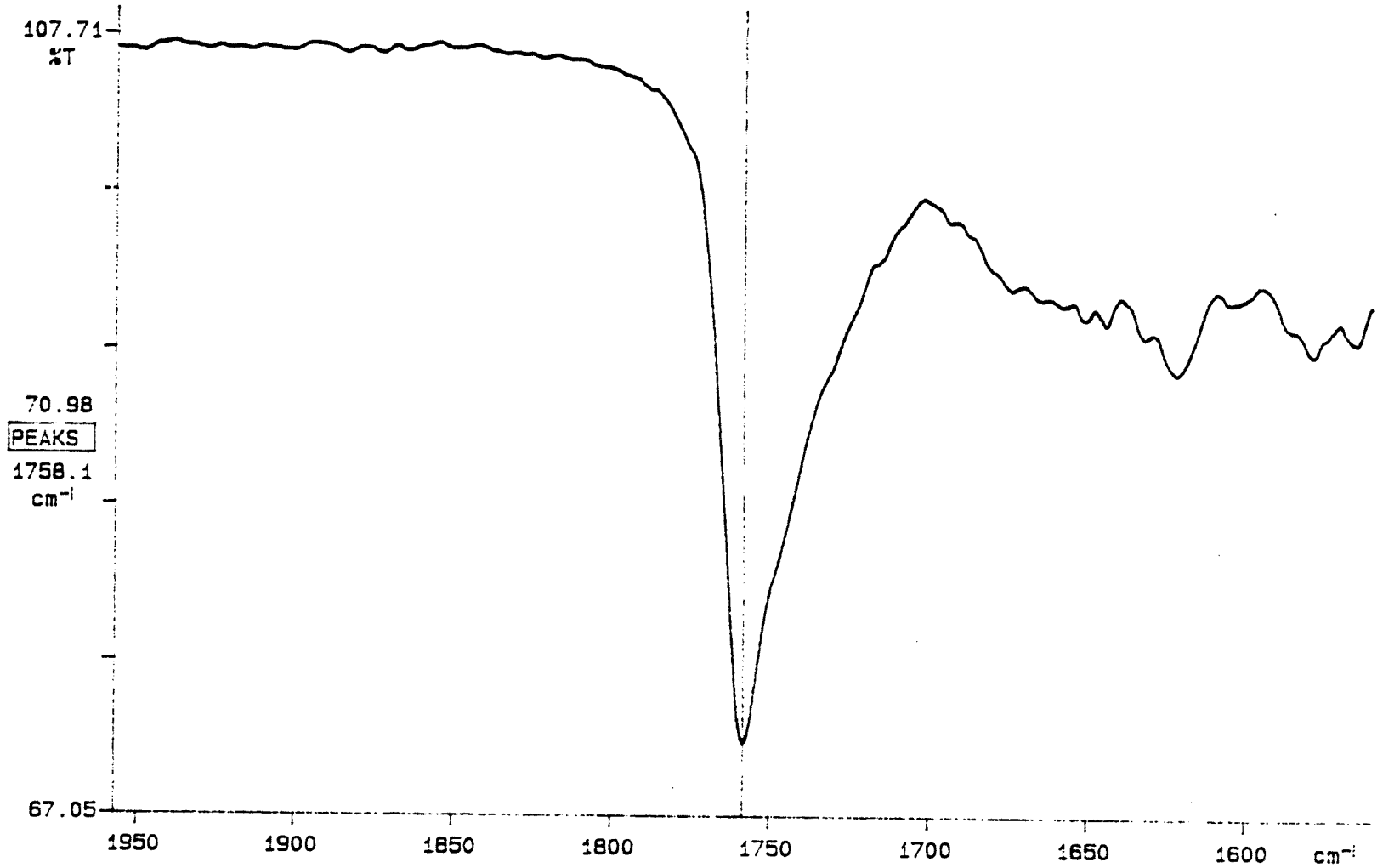


Fig 8-4



1758.1 cm^{-1} for $-\overset{\overset{O}{\|}}{C}-N\langle$ (MeOH + NaOH) After 110 minutes
"Kinetic Study" last



89/04/13 17:00
X: 1 scan, 4.0cm-1

Fig 8-5 The curve of kinetic experiment

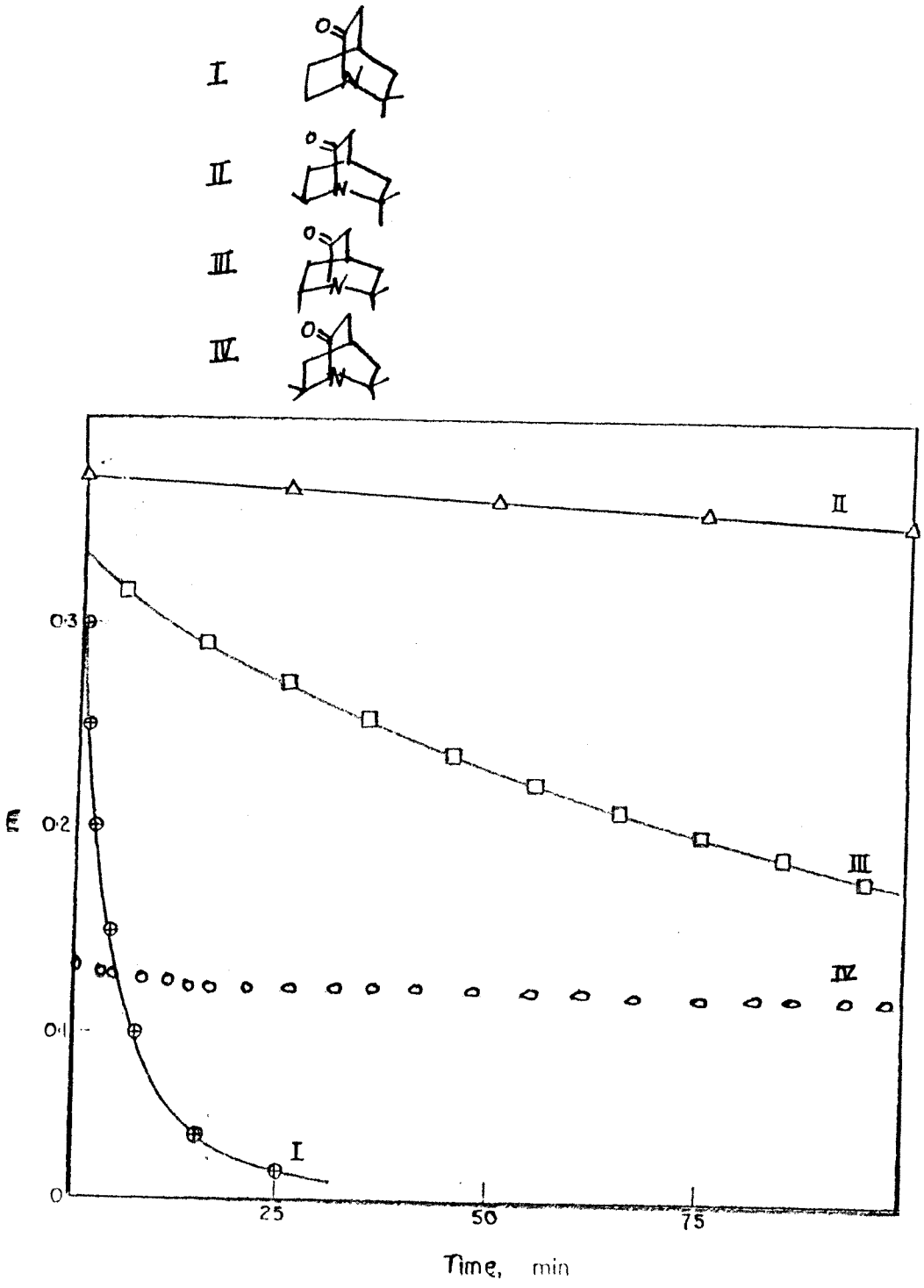


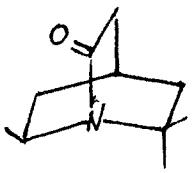
Table 8-2 List of kinetics experimental data

I

Point	X (time)	Y (ln[A])
1	0.3	-1.204
2	1.5	-1.386
3	2.5	-1.609
4	4.9	-1.897
5	7.9	-2.302
6	15	-3.270
7	25	-3.963

Slope = -0.113857 ± 7.616235E-03
Intercept = -1.304253 ± 0.1667307
Correlation = 0.9889975
Calculated on points 1 to 7

II

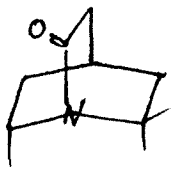


Point	X (time)	Y (ln[A])
1	0	-0.996
2	25	-1.0023
3	50.8	-1.0161
4	75	-1.027
5	100	-1.038

Slope = -4.347886E-04 ± 2.407762E-05
Intercept = -0.994071 ± 1.903581E-03
Correlation = 0.9954316
Calculated on points 1 to 5

Table 8-2 (continues) List of kinetics experimental data

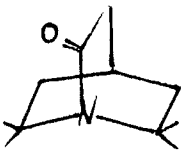
III



Point	X (time)	Y (ln[A])
1	6.25	-1.152
2	15	-1.237
3	25	-1.294
4	35.8	-1.386
5	55	-1.487
6	65.4	-1.541
7	75	-1.608
8	85	-1.6607
9	95	-1.698

Slope = -6.096197E-03 ± 1.827082E-04
Intercept = -1.141703 ± 1.646728E-02
Correlation = 0.9964262
Calculated on points 1 to 10

IV



Point	X (time)	Y (ln[A])
1	0	-1.9053
2	24	-2.0257
3	30	-2.0448
4	35	-2.03065
5	40	-2.0352
6	45	-2.0186
7	50	-2.013
8	55	-2.01356
9	60	-2.0118
10	70	-2.0111
11	80	-2.0016
12	85	-2.00129
13	90	-2.009

Slope = -3.671119E-04 ± 3.749264E-04
Intercept = -1.990603 ± 3.387003E-02
Correlation = 0.2831428
Calculated on points 1 to 13

REFERENCE :

[1] A. Greenberg, Twisted Bridgehead Bicyclic Lactams, Vol. 7, Ch 4, pp 141

[2] H. Pradejus, M. Kehlen, H. Kelen and H. Matschiner, Tetrahedron, 1965. Vol. 21, pp 2257-2270.

[3] H. Pradejus, Chem. Ber. 1959, Vol. 21, pp. 998; 1965, Vol. 98, pp 2989.

[4] E. I. Levkoev, E. S. Nikitskaya, and L. N. Yakhontov, Pharmaceutical Chemstry, Moscow, 1971. No. 3, pp. 378-384.

[5] A. Greenberg, Synthesis of 8,8,9,9-Tetramethyl-1-Azabicyclo[3,3,1] Nonan-2-one, Unpublished paper.

[6] E. S. Nikitskaya, I. M. Sharapov and E. I. Levkoeva, New Drug Preparations , Vol. 4, 1970 No. 10, pp. 58-61.

[7] G. Michael, J.Skalfe and I. Trevor, J. Ame. S. 1980, 2nd, pp. 3650-3668.

APPENDIX A

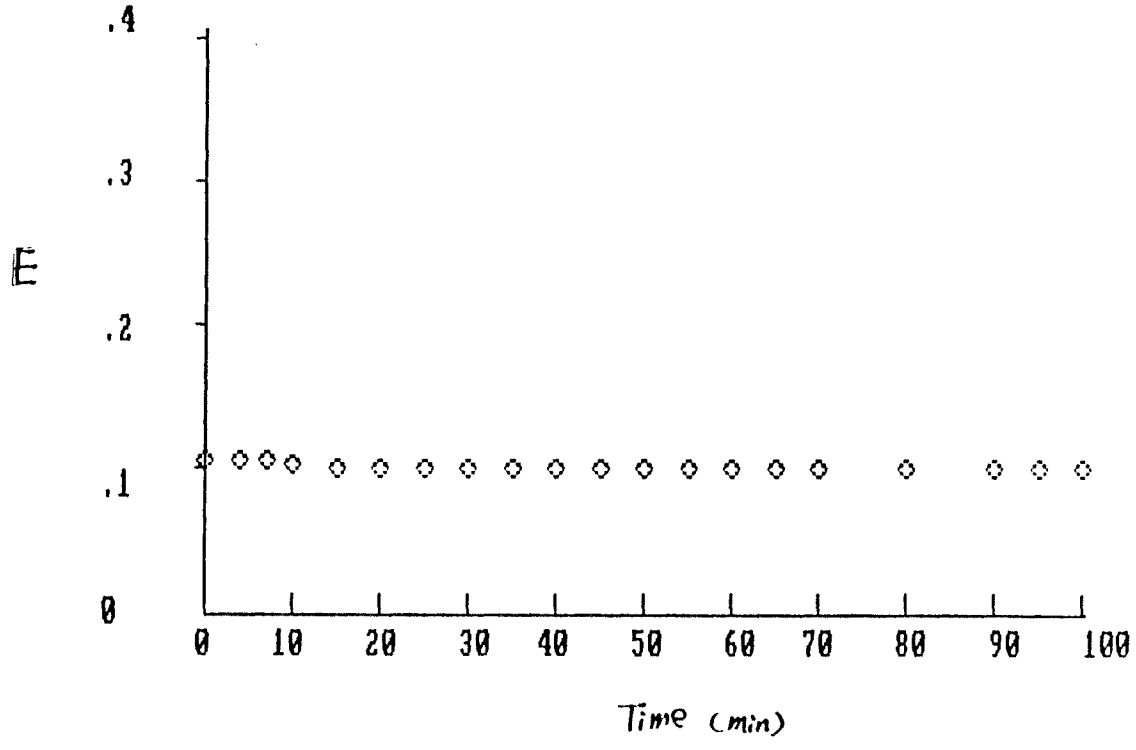
The kinetics experiment of 8,8,9,9-Tetramethyl-1-Azabicyclo[3,3,1]noan-2-one

Appendix A-1

Kinetics Reaction Data

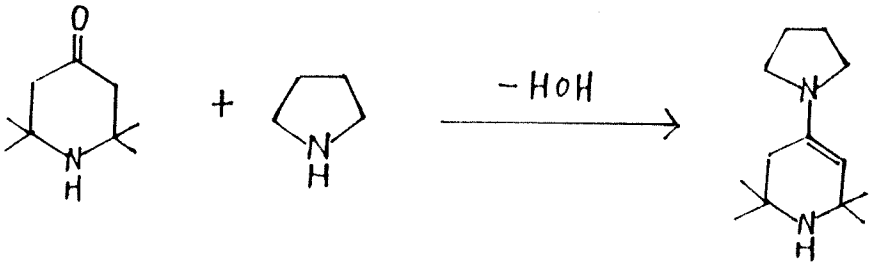
POINT	X (Time)	Y (Extinction)
1	0	.10547
2	4	.104196
3	7	.104196
4	10	.10246
5	15	.10099
6	20	.10124
7	25	.09988
8	30	.10059
9	35	.10038
10	40	.10084
11	45	.10069
12	50	.10008
13	55	.09927
14	60	.10044
15	65	.09882
16	70	.09877
17	80	.09968
18	90	.09943
19	95	9.952999E-02
20	100	.10003

Slope = -4.515252E-05 +/- 8.920692E-06
Intercept = .1028719 +/- 1.223118E-03
Correlation = .7663773
Calculated on points 1 TO 20



Scheme 1

preparation of 2,2,6,6-tetramethyl-4-(N,N-tetramethylene-imino) piperidine-3-ene



(81%)

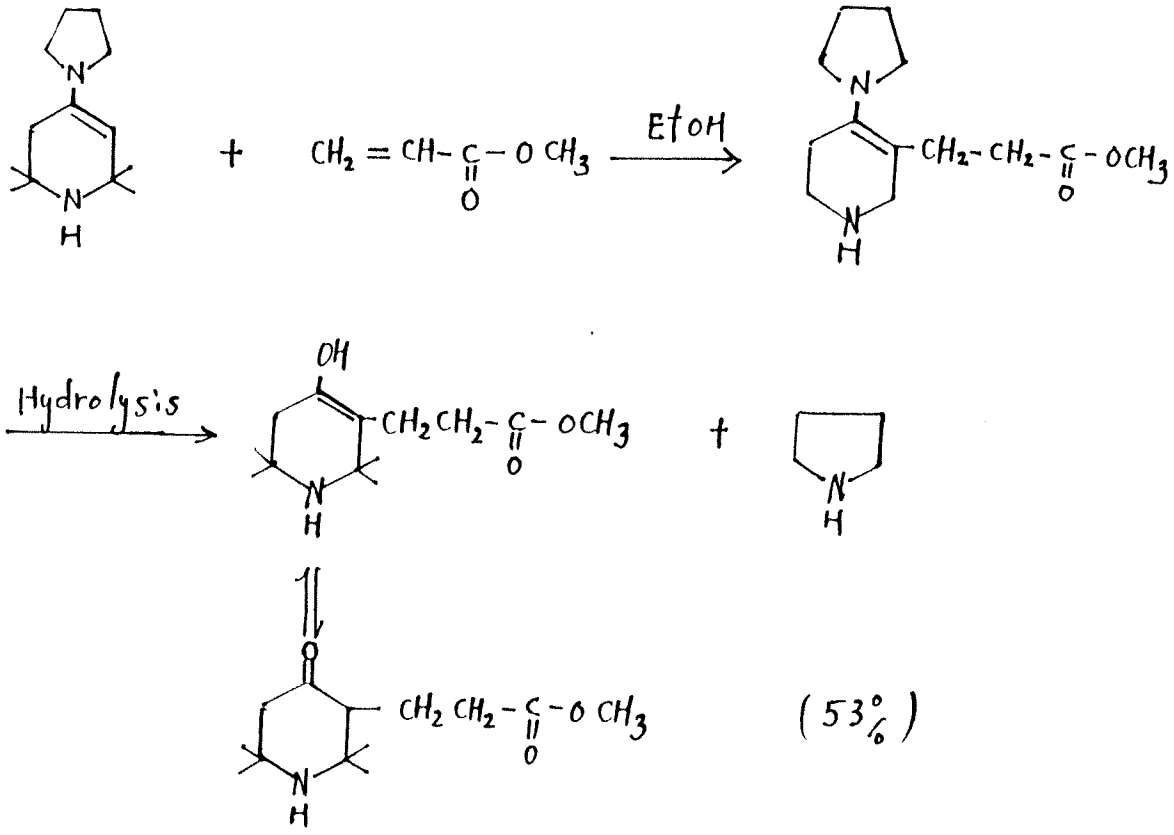
b.p. 110-112°c/2mmHg

IR: 1640 cm^{-1} for >C=C< Was observed

1700 cm^{-1} for -C(=O)- Was disappeared

Scheme 2

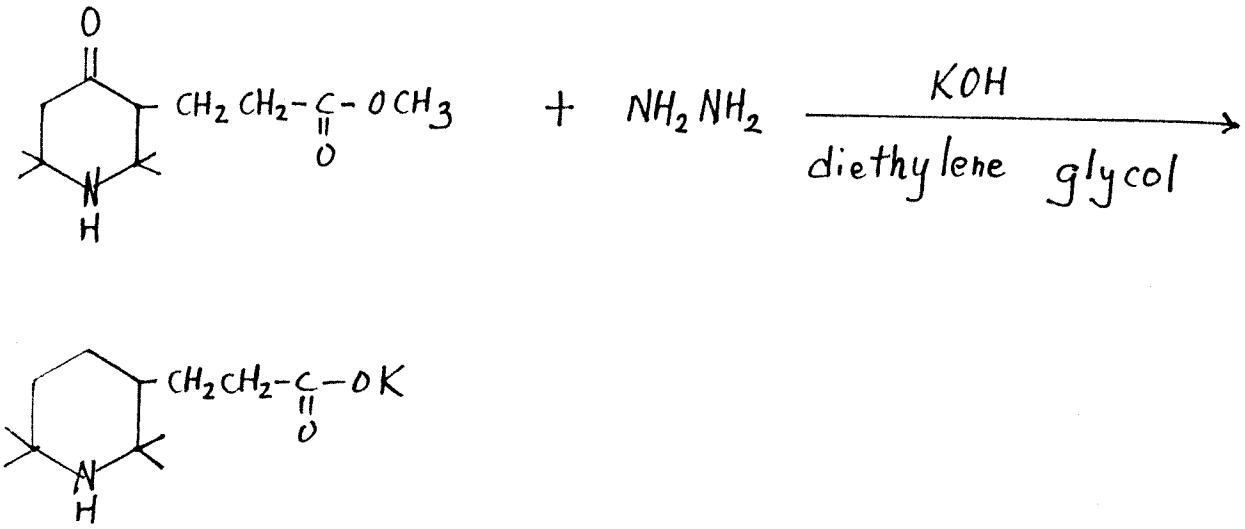
preparation of 2,2,6,6-tetramethyl-3-(2'-methoxycarbonyl-ethylene)-piperidine-4-one



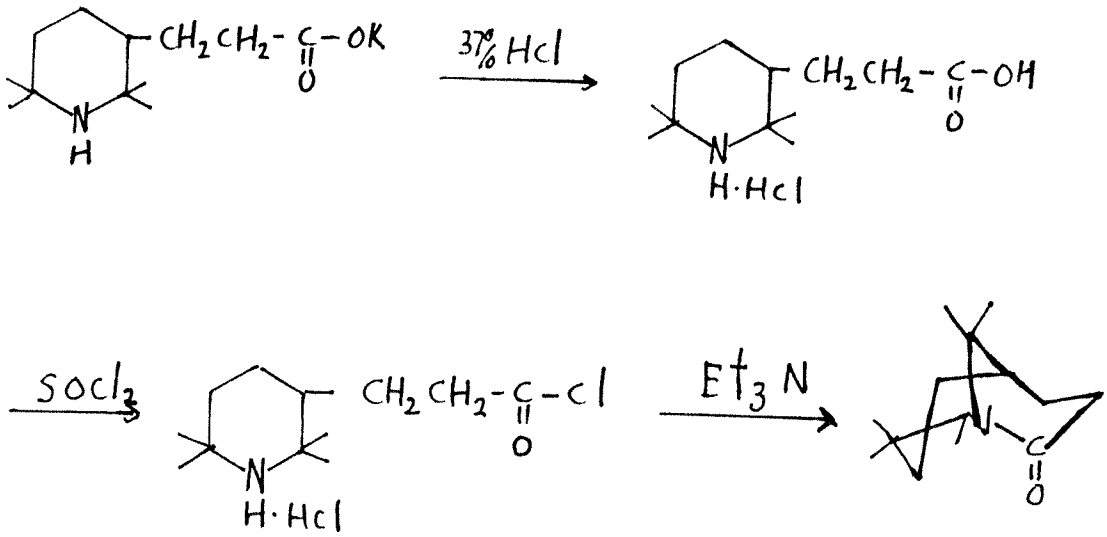
IR: 1700, 1715 cm^{-1} for $-\overset{O}{\overset{\|}{C}}-$, $-\overset{O}{\overset{\|}{C}}-OCH_3$ was observed

1640 cm^{-1} for $>C=C<$ was disappeared

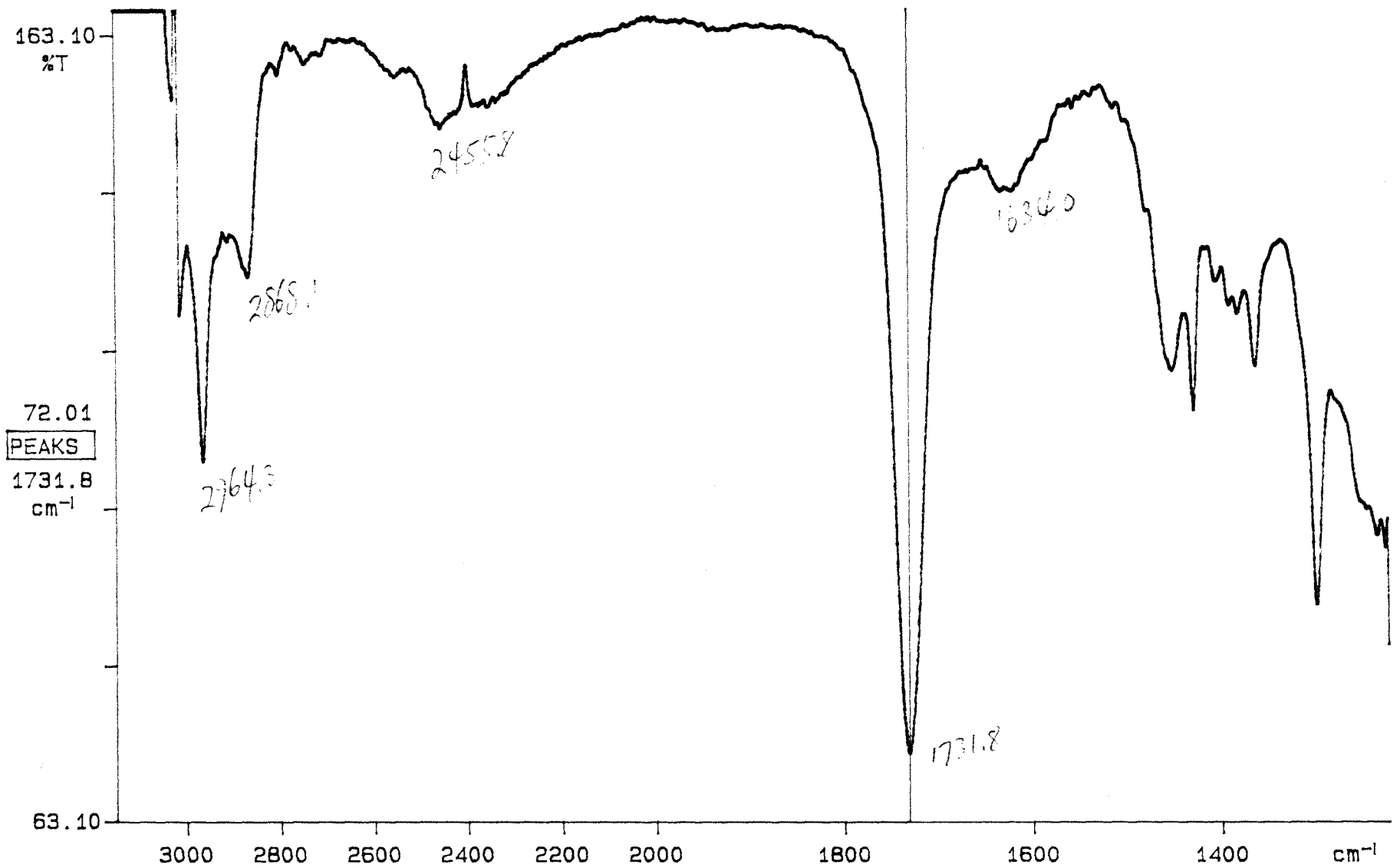
Scheme 3



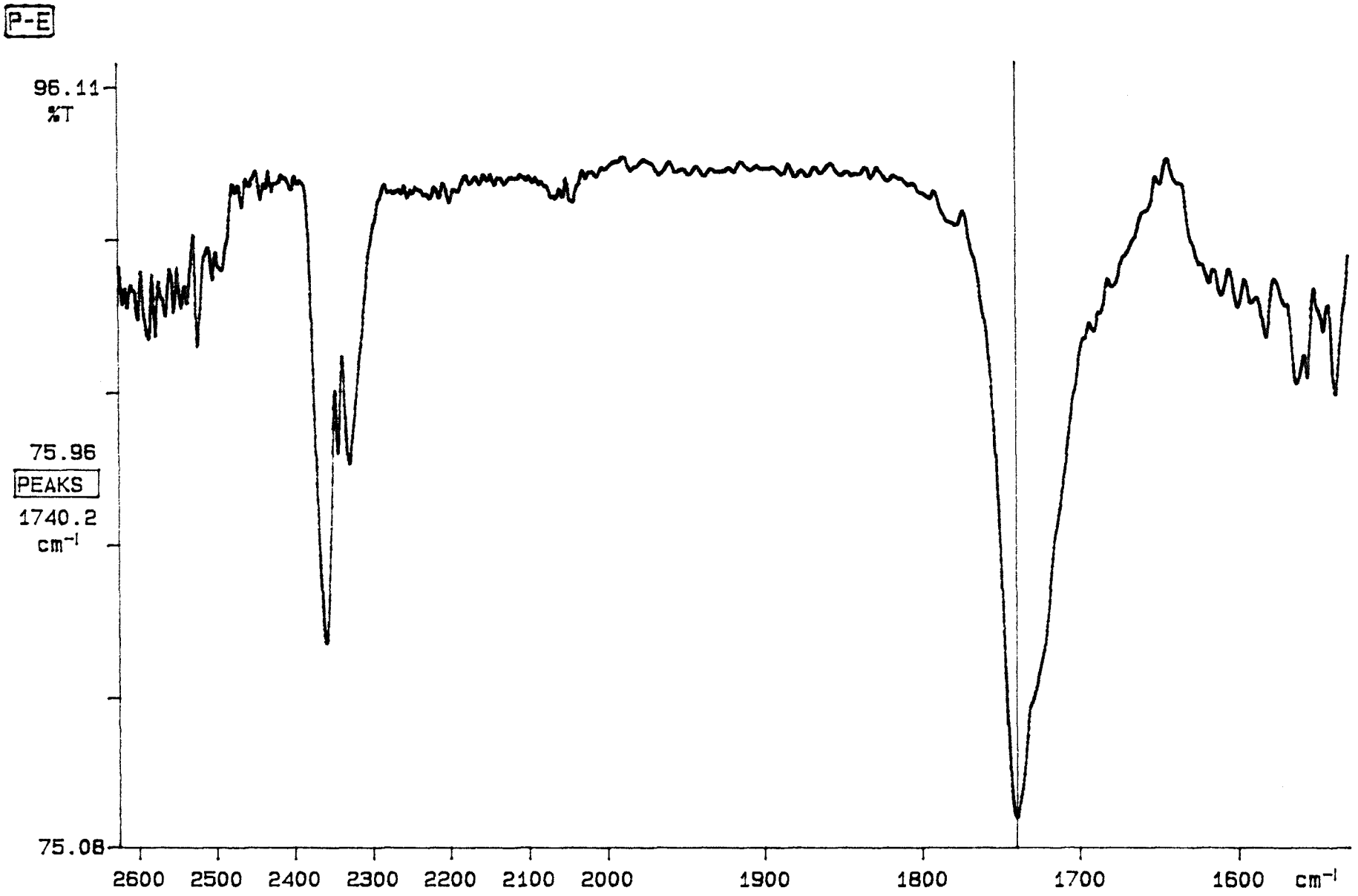
Scheme 4



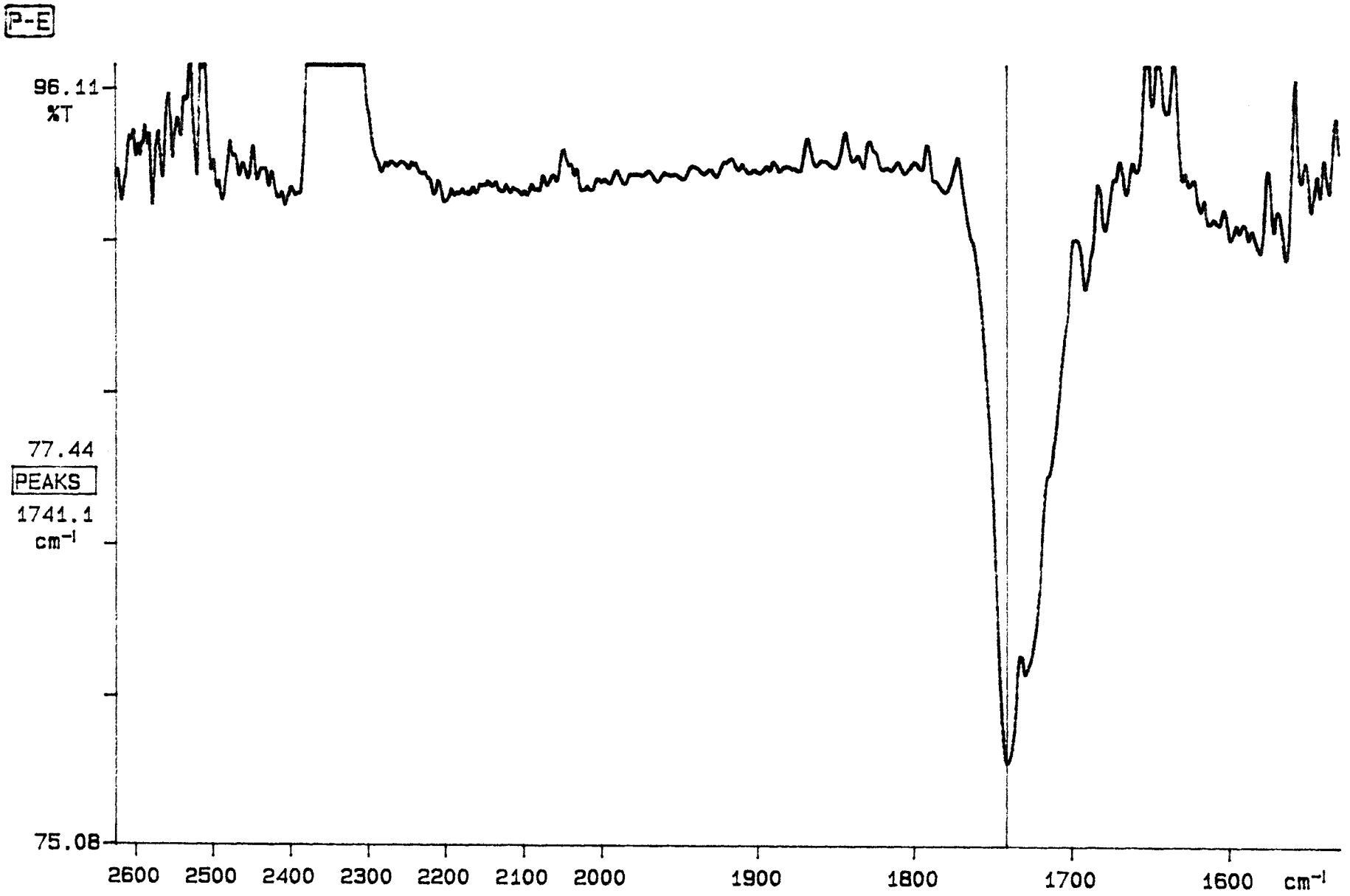
P-E



89/04/14 14:10
X: 1 scan, 4.0cm-1



89/04/14 15:23
X: 1 scan, 4.0cm-1

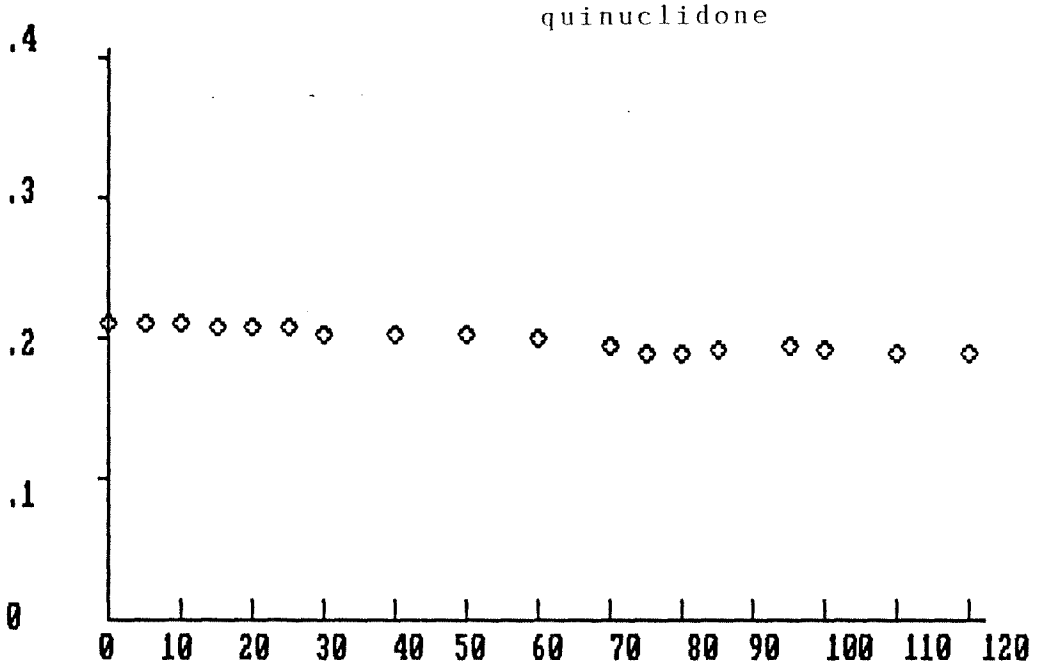


89/04/14 17:03
X: 1 scan, 4.0cm-1

APPENDIX B

The kinetics experiment of raw 6,6,7,7-Tetramethyl-2-Quinuclidone

Appendix B-1 Raw material 6,6,7,7-tetramethyl-2-quinuclidone



$$E = \frac{1}{C \times l} \log_{10}\left(\frac{100}{T}\right) = 529.94 \log_{10}\left(\frac{100}{T}\right)$$

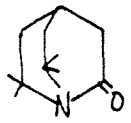
POINT	X	Y
1	0	.2121
2	5	.2116
3	10	.2107
4	15	.2073
5	20	.2077
6	25	.2075
7	30	.2036
8	40	.2024
9	50	.2019
10	60	.1993
11	70	.1944
12	75	.1896
13	80	.1896
14	85	.1918
15	95	.1942
16	100	.1925
17	110	.1889
18	120	.1889

Slope = -2.123818E-04 +/- 1.571348E-05
ntercept = .2113477 +/- 2.494438E-03
orrelation = .9588898
Calculated on points 1 TO 18

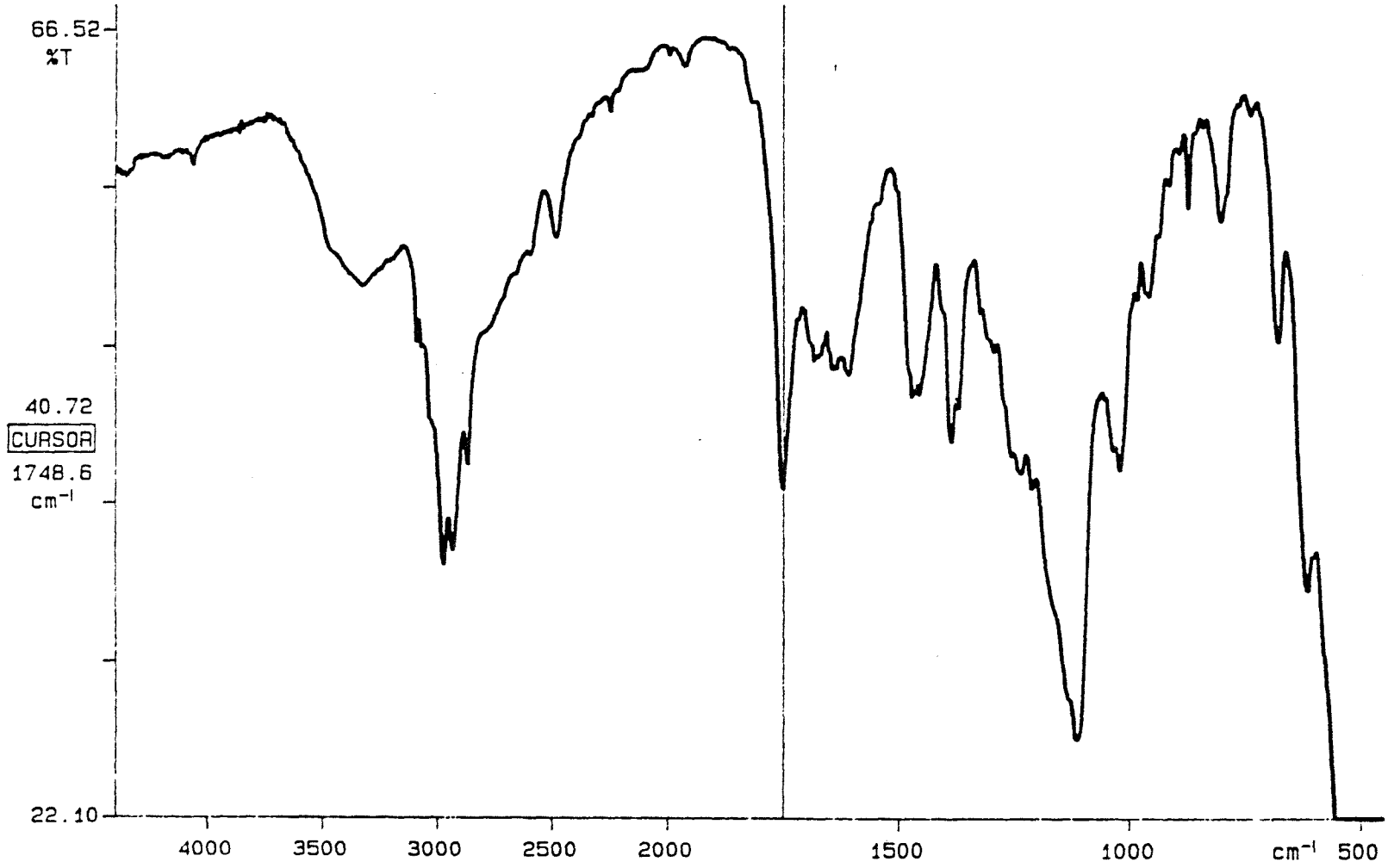
Appendix B-2

Cyclization (5) Sample for Kinetic Study (100 mg)

1748.6 cm^{-1} for $-\overset{O}{\overset{\|}{C}}-N$ ($CHCl_3$)

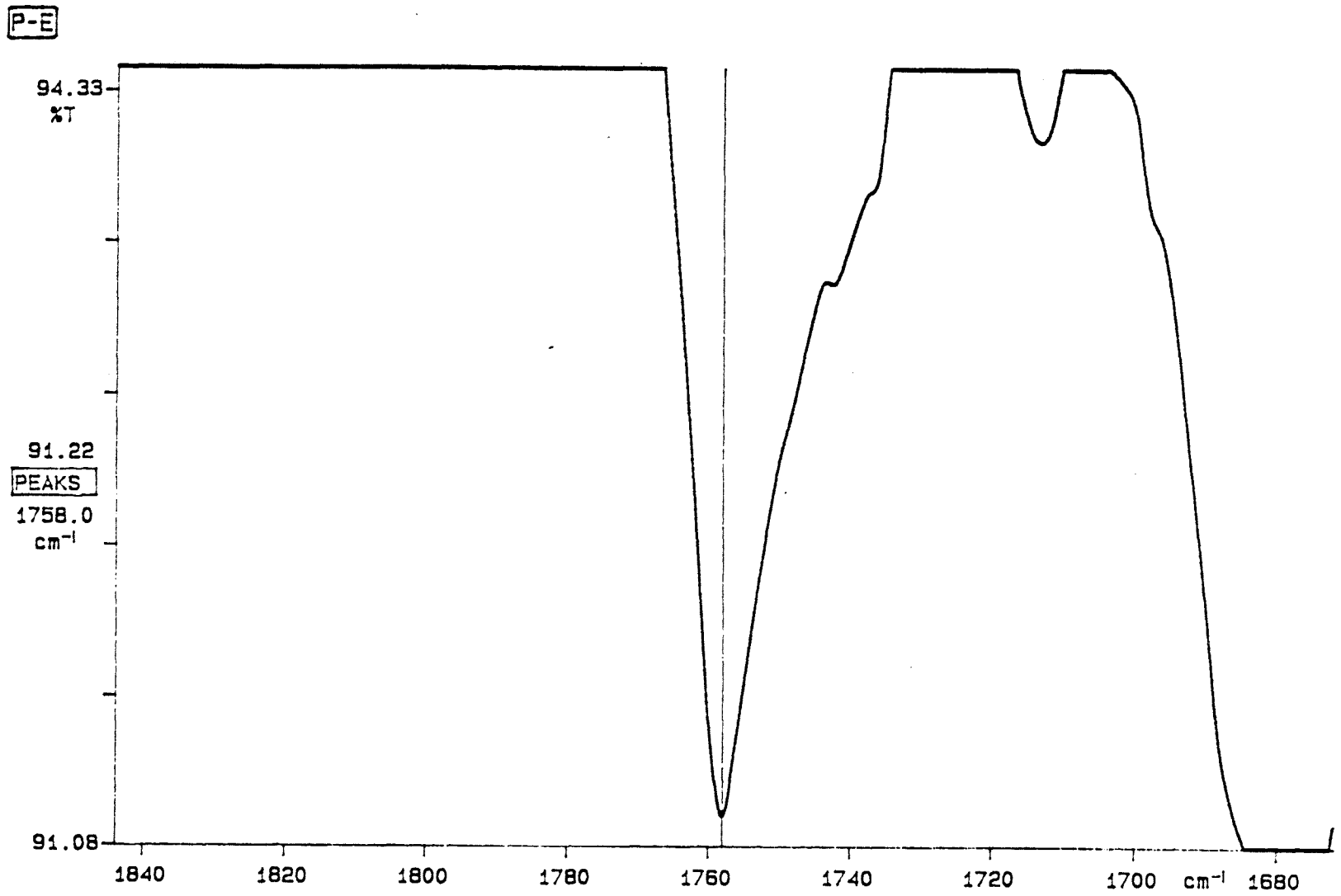


P-E

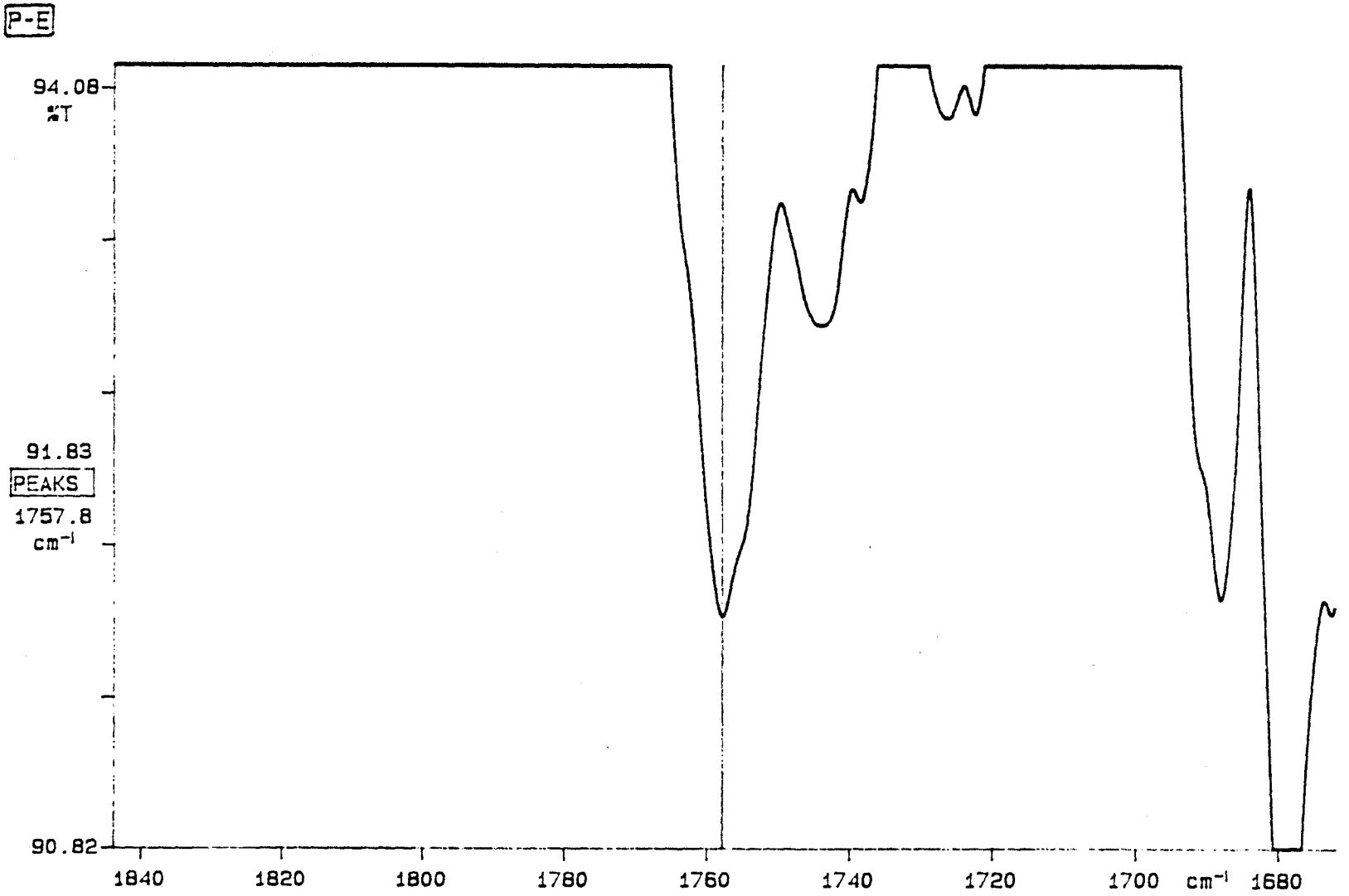


89/03/09 17:43
X: 4 scans, 4.0cm-1

Kinetic reaction (t=0)



Kinetic reaction ($t = i$ 120 minutes)



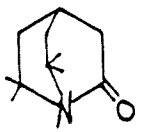
APPENDIX C

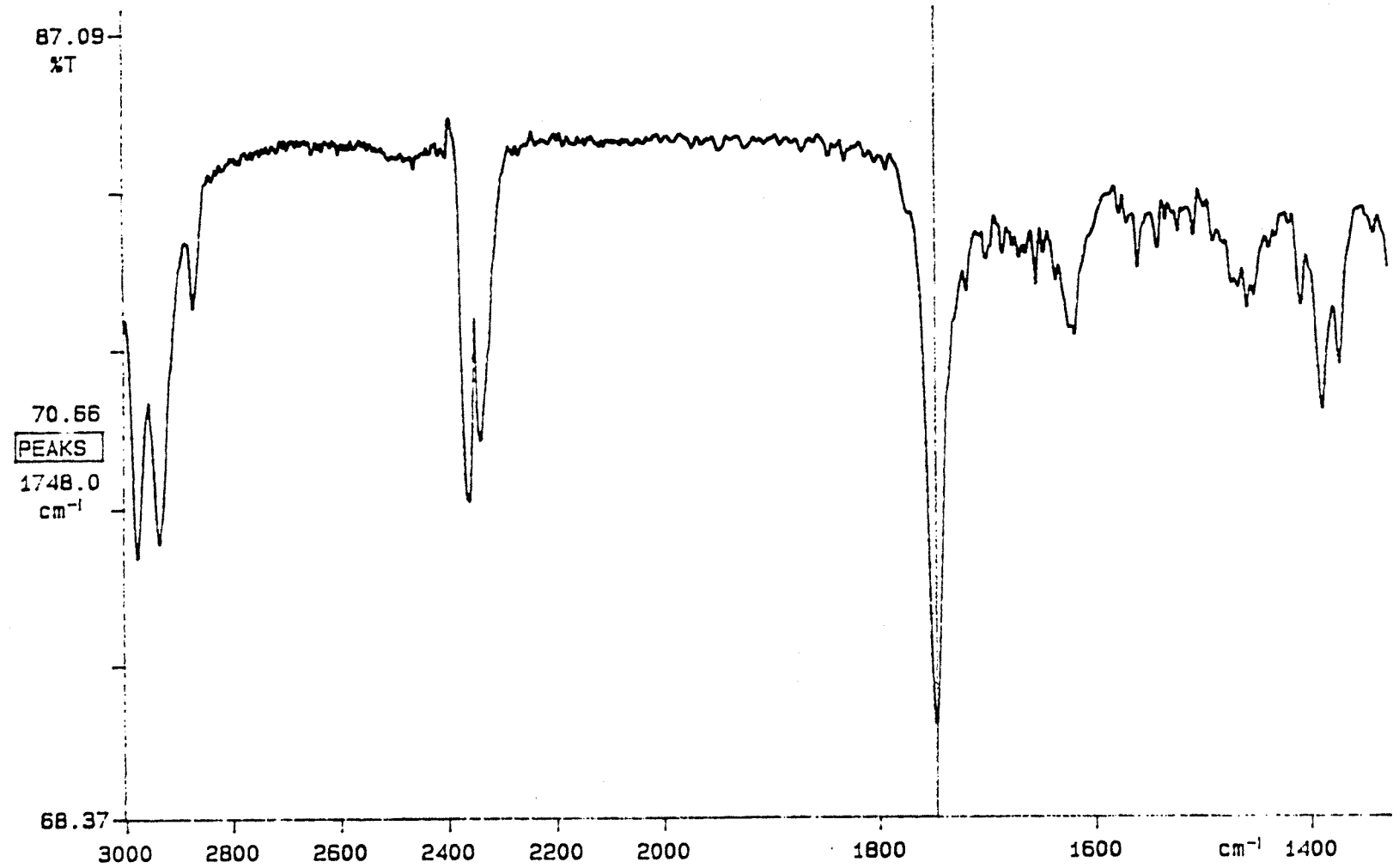
The study of peak shift of IR spectra

Appendix C-1

Sample for Kinetic study (cyclization 2)

1748.0 cm^{-1} for $-\overset{\overset{O}{\|}}{C}-N<$ ($CHCl_3$)

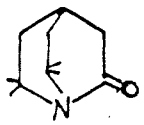




C-2

1758.4 cm^{-1} for $-\overset{O}{\overset{\|}{C}}-N<$ (MeOH + NaOH)

"kinetic study" first [illegible]



P-E

107.71
%T

68.37

PEAKS

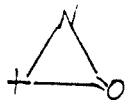
1758.4
cm^{-1}

67.05

1950 1900 1850 1800 1750 1700 1650 1600 cm^{-1}

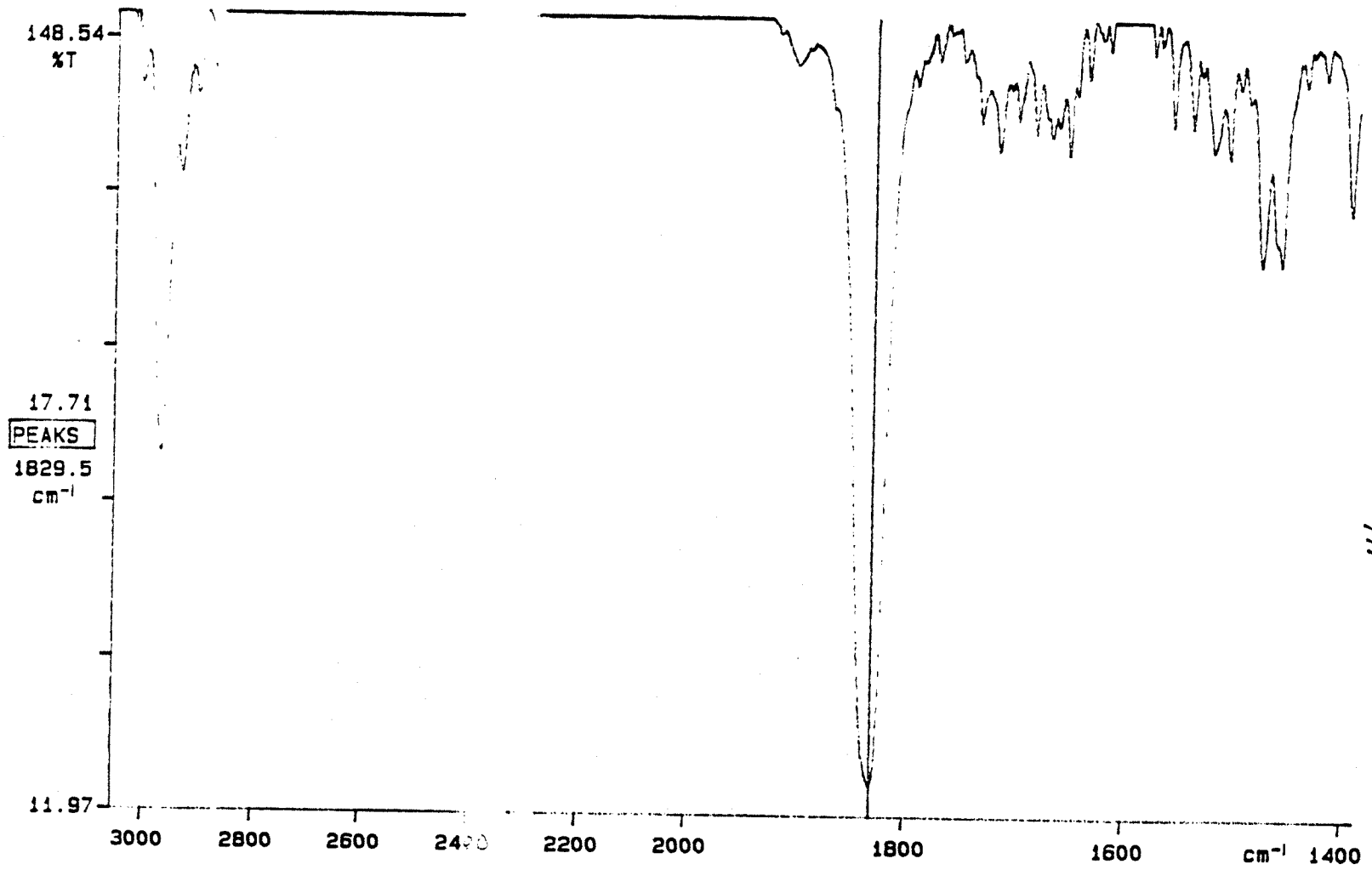
110

C-3



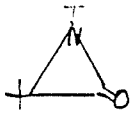
1829.5 cm^{-1}

($CHCl_3$)

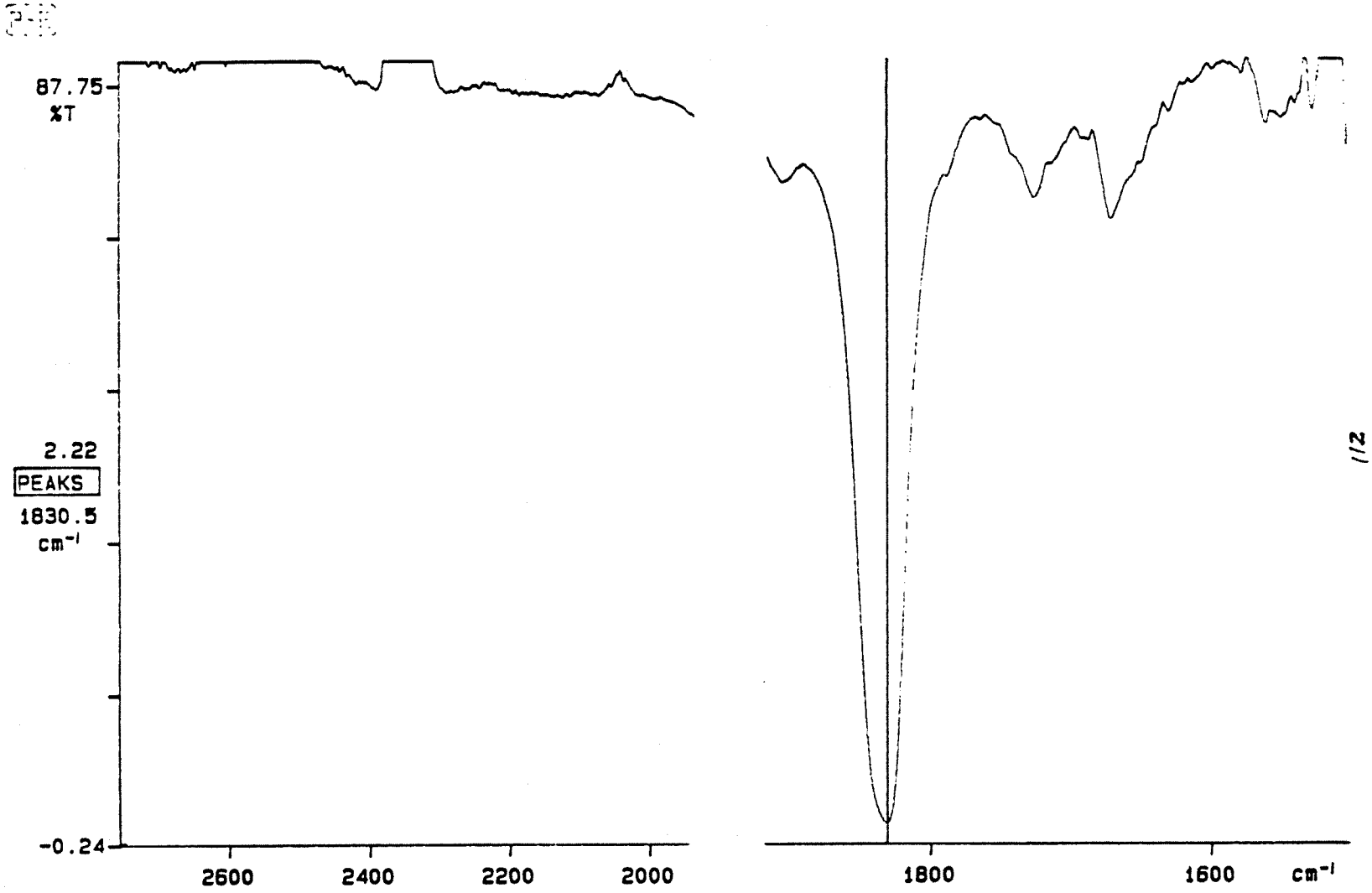


89/04/26 14:21
X: 1 scan, 4.0cm-1

C-4

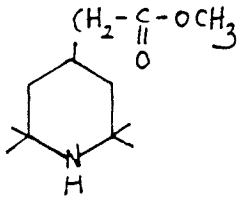


1830.5 cm^{-1}
(CH_3OH)



89/04/26 14:46
X: 1 scan, 4.0cm-1

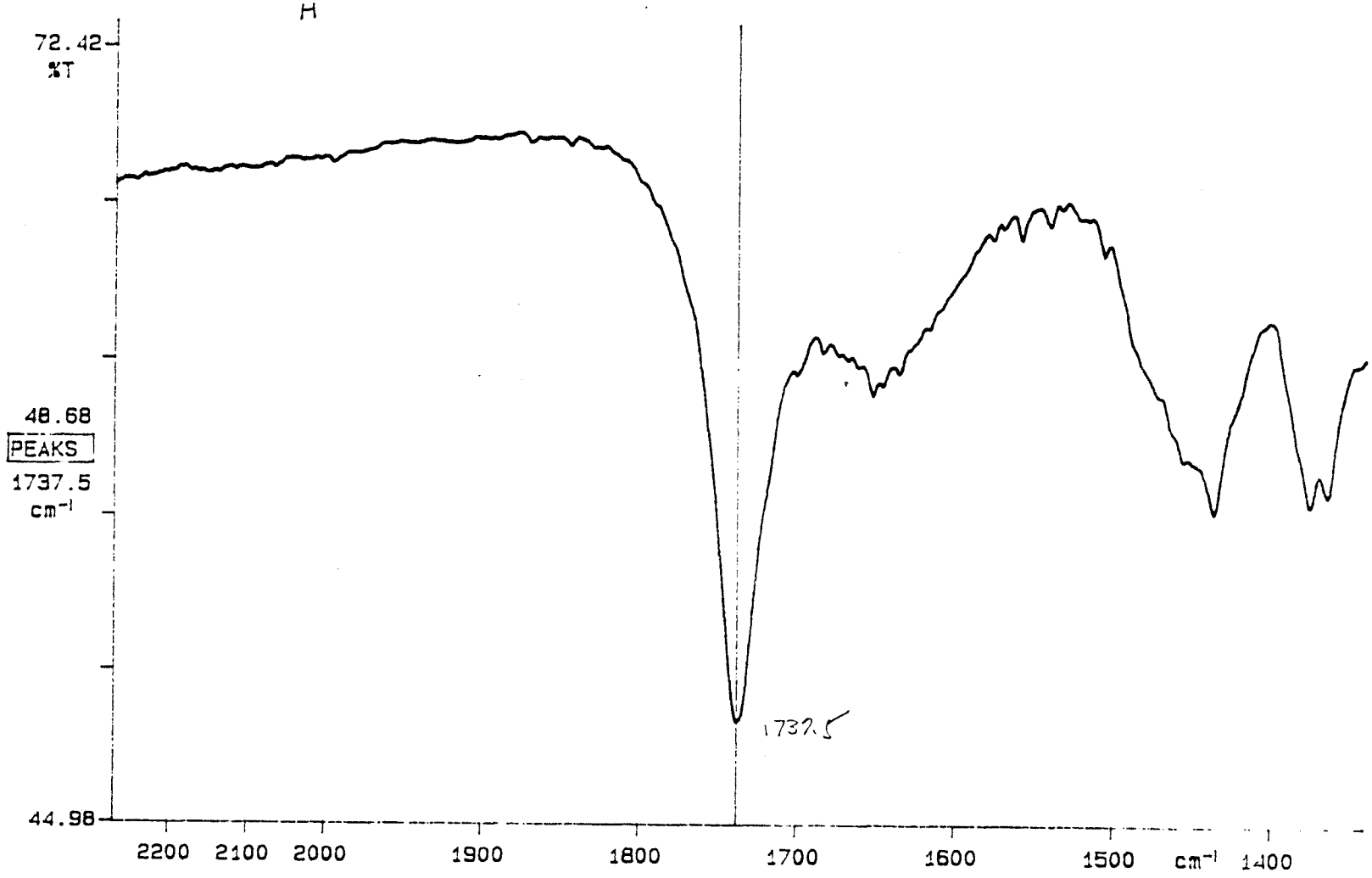
C-5



NaCl

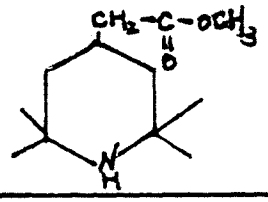
1737.5 cm^{-1} for $-\overset{\overset{O}{\|}}{C}-OCH_3$

P-E



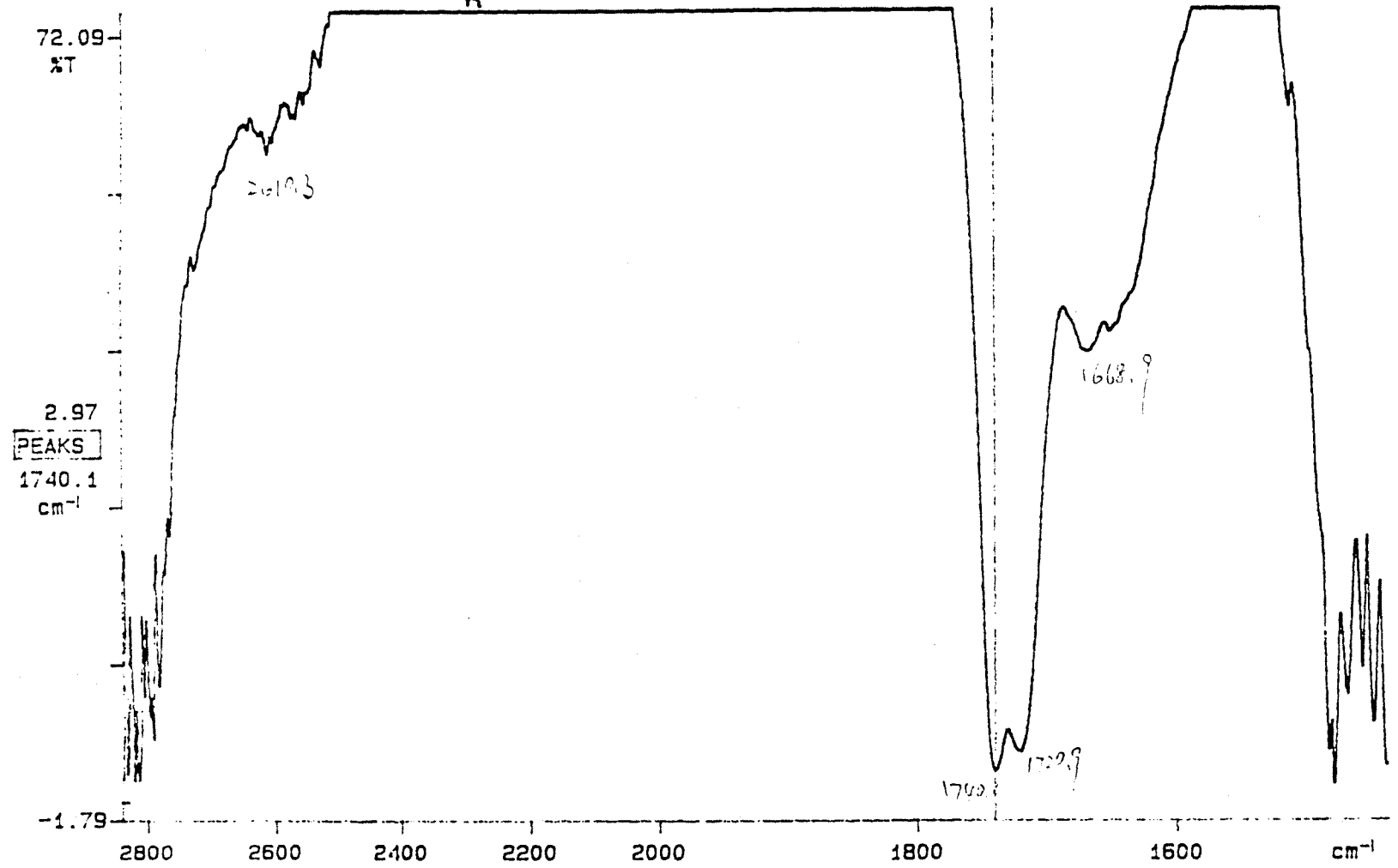
89/04/10 10:55

C-6



1740.1 cm^{-1}
(CH_3OH)

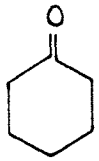
P-E



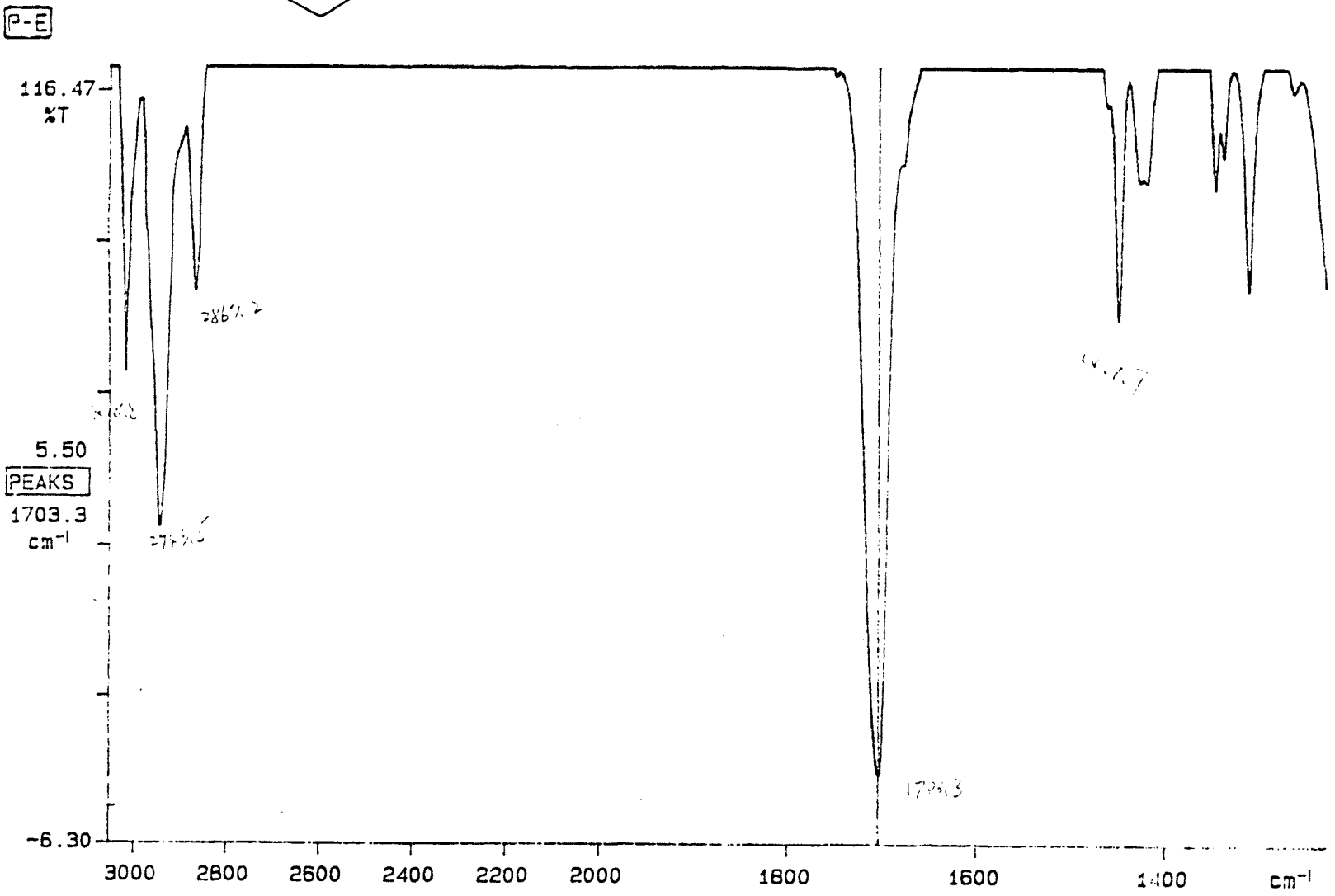
89/04/13 17:20
X: 1 scan, 4.0cm-1

in MeOH

C-7

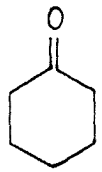


1703.3 cm^{-1} for $-\overset{\overset{O}{\|}}{C}-$ ($CHCl_3$)



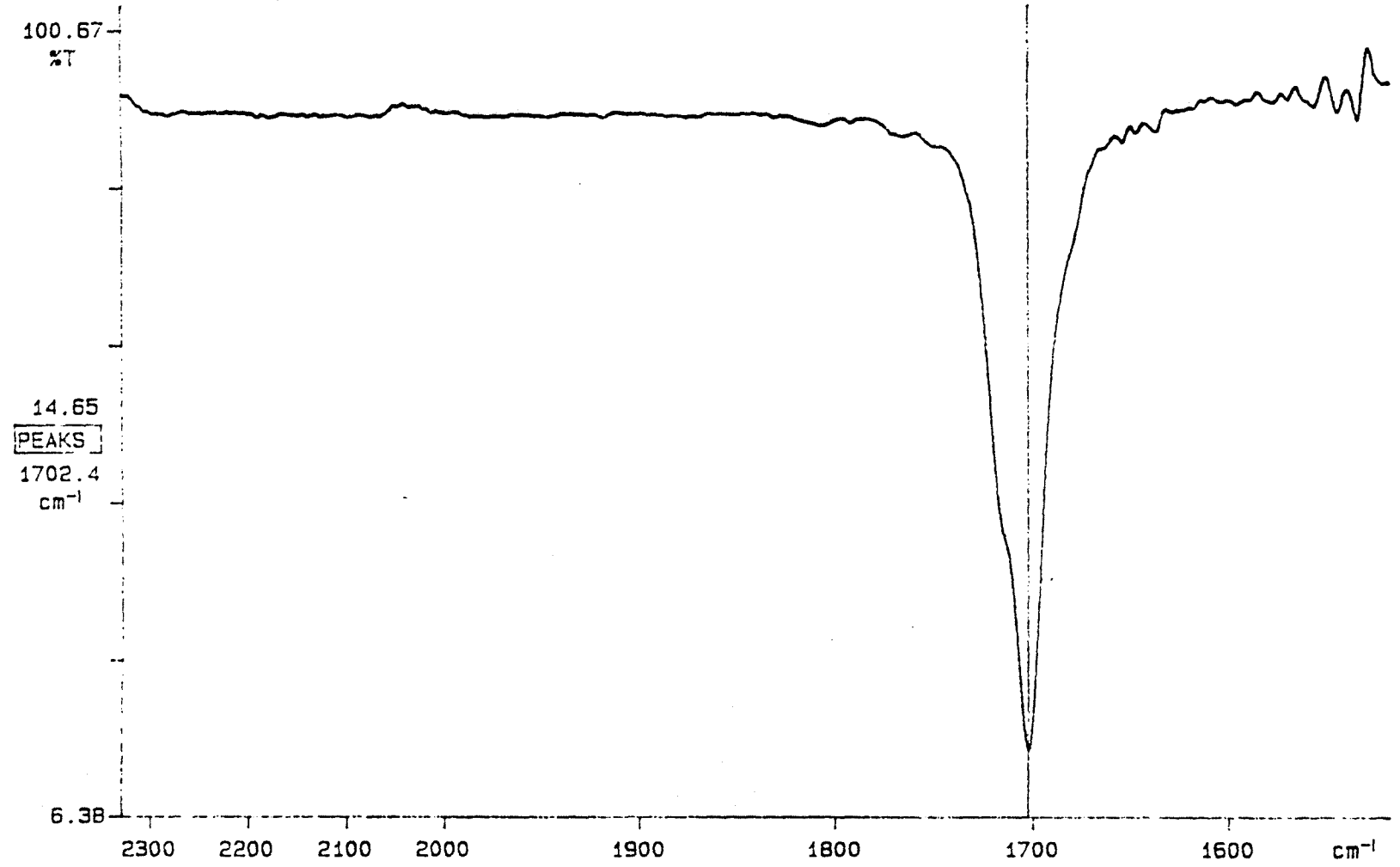
89/04/12 12:25

C-8

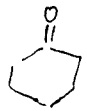


1702.4 cm^{-1} for -C(=O)- (CH_3OH)

P-E



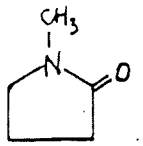
89/04/12 12:37
X: 1 scan, 4.0cm-1



(CH_3OH)

1702.4cm^{-1} for -C(=O)-

C-9



1672.5 cm^{-1} for $-\overset{\overset{O}{\|}}{C}-N<$ (CH_3OH)

P-E

68.90
%T

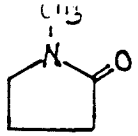
10.25
PEAKS
1672.5
cm^{-1}

7.63

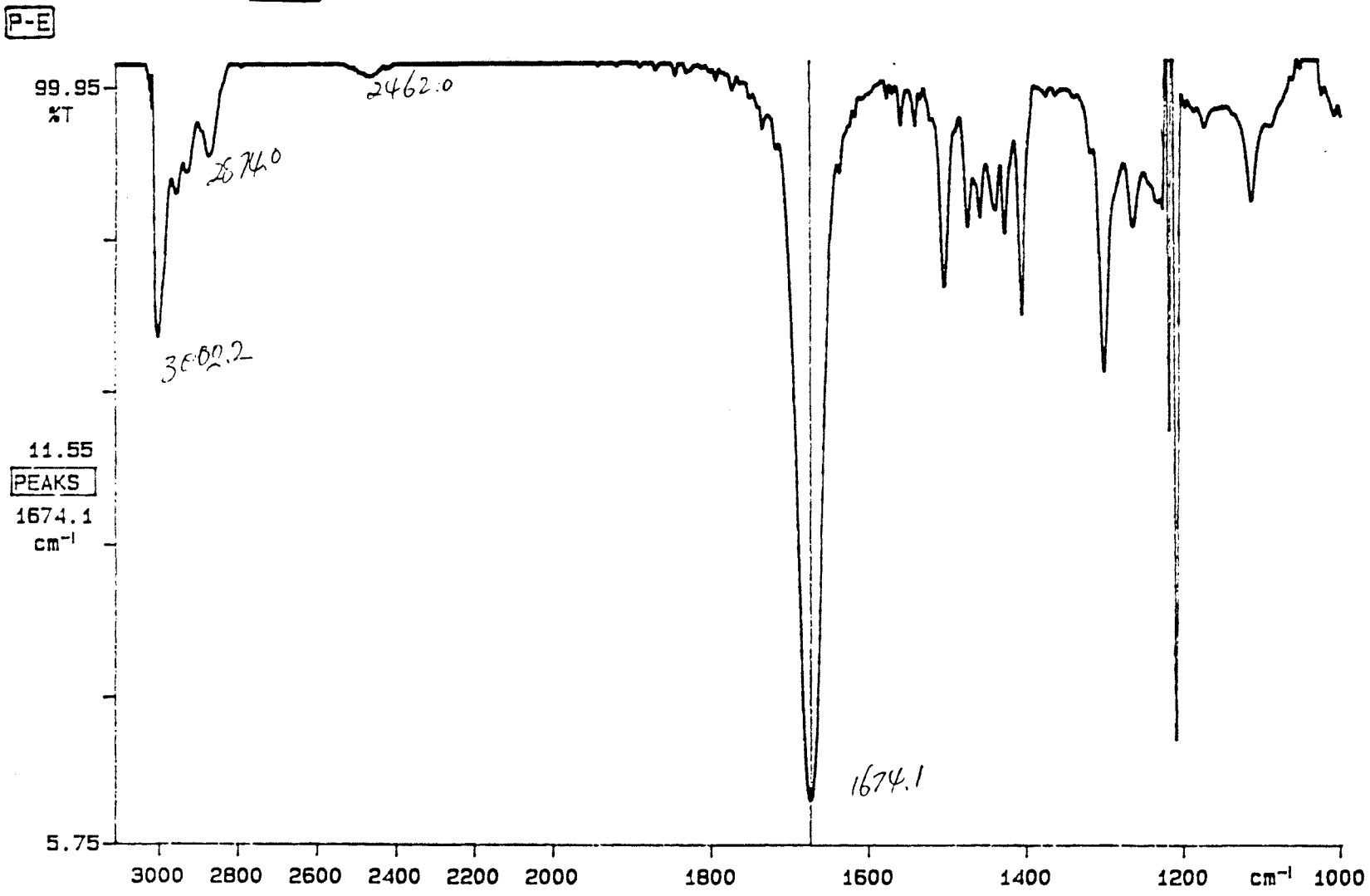
2000 1900 1800 1700 1600 cm^{-1}

89/04/12 13:01

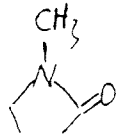
C-10



1674.1 cm^{-1} for $-\overset{\overset{O}{\|}}{C}-N<$ ($CHCl_3$)



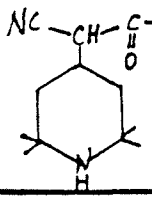
89/04/12 11:48
X: 4 scans, 4.0cm-1



($CHCl_3$)

1674.1 cm^{-1} for $-\overset{\overset{O}{\|}}{C}-N<$

C-11



(CHCl$_3$)

1742.9 cm^{-1} for $-\overset{\overset{O}{\|}}{C}-OC_2H_5$

1629.4 cm^{-1} for $>C=C<$ was disappeared

P-E

101.18
%T

12.67
PEAKS
1742.9
cm^{-1}

7.91

2971.6

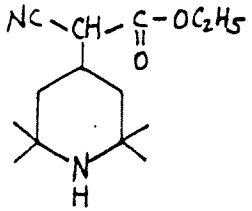
1674.6

1742.9

3000 2800 2600 2400 2200 2000 1800 1600 1400 1200 cm^{-1} 1000

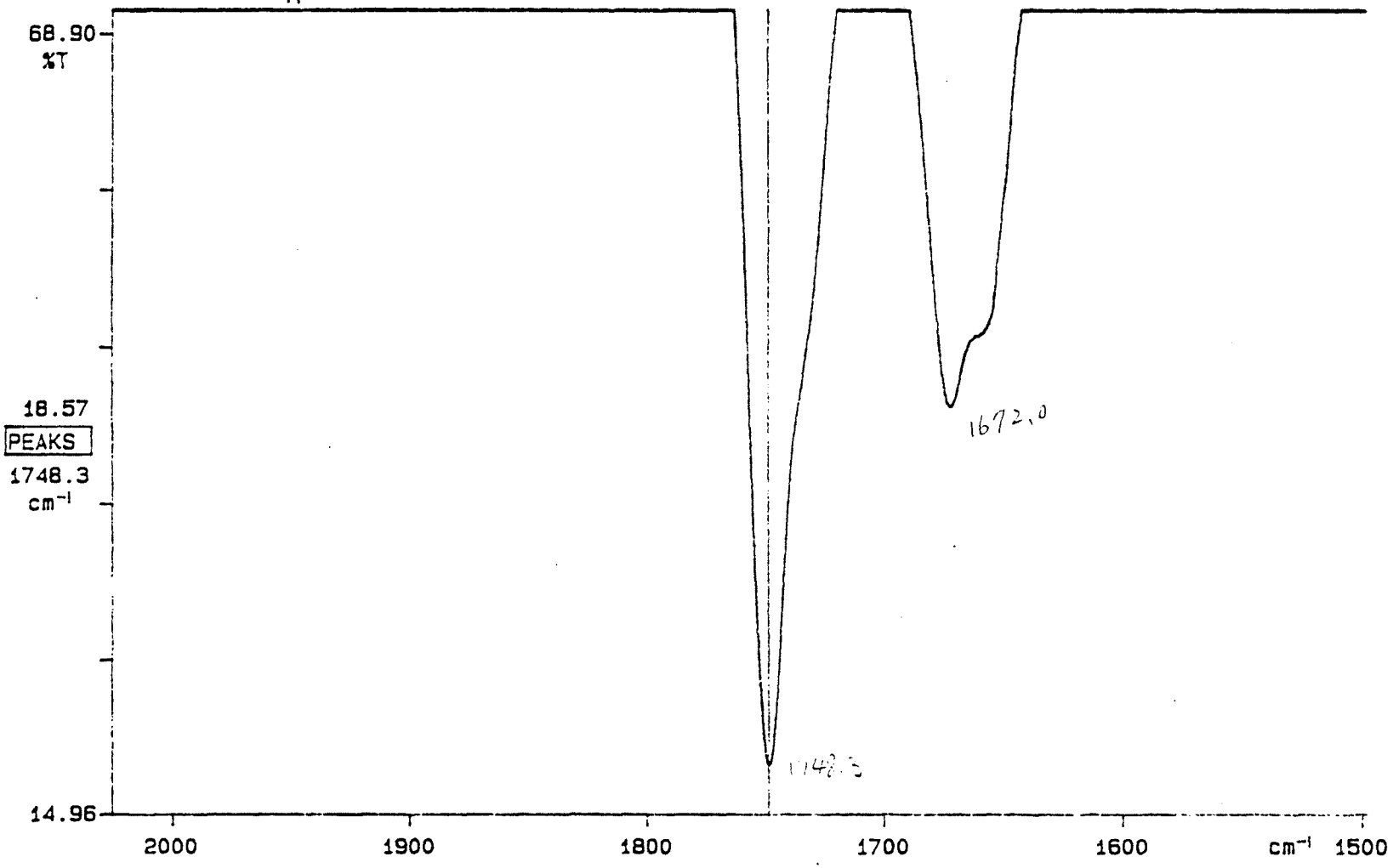
89/04/12 11:20

C-12



1748.3 cm^{-1} for $-\overset{\overset{O}{\|}}{C}-OC_2H_5$ (CH_3OH)

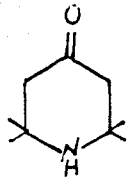
P-E



89/04/12 13: 10

Y: 1 scan 4.0cm-1

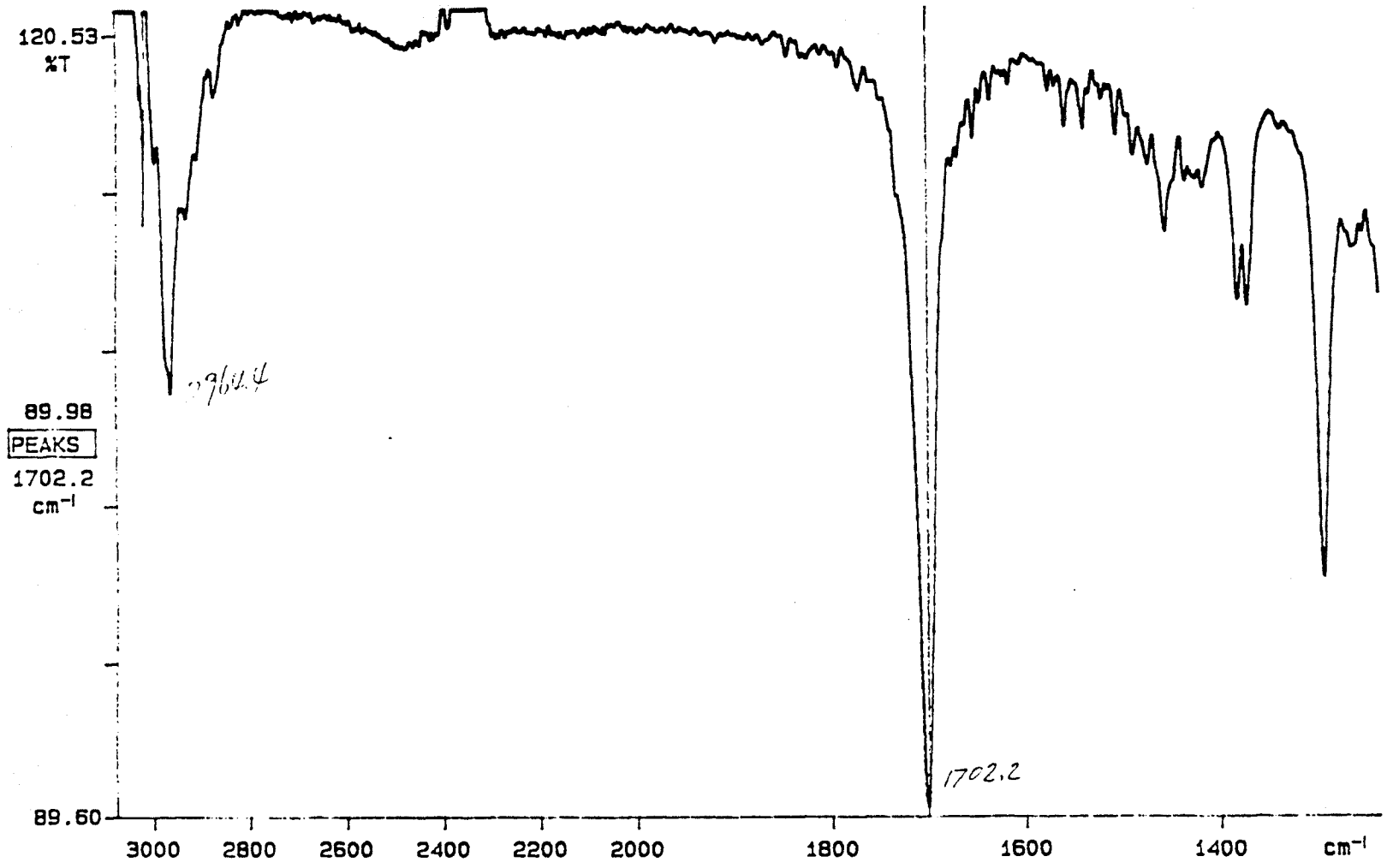
C-13



($CHCl_3$)

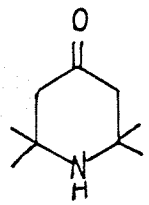
1702.2 cm^{-1} for $-\overset{\overset{O}{\|}}{C}-$

P-E



89/04/12 12:11
X: 1 scan, 4.0cm-1

C-14



1701.2 cm^{-1} for $-\overset{\overset{O}{\|}}{C}-$ (CH_3OH)